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(54) **Title**: A METHOD FOR TREATING TUMOR BY USING RECOMBINANT INTERFERON WITH CHANGED SPATIAL CONFIGURATION

(57) **Abstract**: The present invention provides methods for treating tumors m subjects by using a recombinant interferon (rSIFN-coand optionally, methods for treating solid tumors, such as lung cancer among others with or without prior surgery and as a first line or second line monotherapy or in combination with one or more other anti-tumor therapies. The present invention further provides non-surgical methods for eliminating tumors or reducing tumor sizes in subjects, and/or preventing postoperative tumor recurrence and/or metastases in subjects by using the recombinant interferon (rSIFN-co) which comprises a unique spatial configuration, alone or in conjunction with radiotherapy, chemotherapy, and/or one or more anti-tumor drugs such as biological agents, targeted drugs, small molecules, Traditional Chinese Medicine (TCM) and the like.

A METHOD FOR TREATING TUMOR BY USING RECOMBINANT INTERFERON WITH CHANGED SPATIAL CONFIGURATION

FIELD OF THE INVENTION

[0001] The present invention relates to methods for treating tumors in subjects by using recombinant interferon, and to methods for treating solid tumors, including lung cancers in subjects. The present invention further relates to non-surgical methods for eliminating tumors or reducing the sizes of tumors in subjects, or preventing postoperative tumor recurrence and/or metastases and/or prolonging tumor free survival in subjects by using a recombinant interferon (rSIFN-co) with changed spatial configuration, either alone, or in conjunction with radiotherapy, chemotherapy, and/or anti-tumor drugs such as biological agents, targeted drugs and the like.

BACKGROUND OF THE INVENTION

[0002] Cancer is one of the major causes of death in people around the world. The total number of cases worldwide continues to increase. According to the statistics of the world health organization (WHO), it is estimated that the global cancer deaths will be increased by 45% (from 7,900,000 to 11,500,000) from 2007 to 2030, and the new cases of cancer will zoom from 11,300,000 in 2007 to 15,500,000 in 2030 in the same period, wherein the incidence rate and the death rate of the lung cancer ranks first in the global malignant tumors. According to the statistical data, the amount of the worldwide new cases of lung cancer every year is more than 3,000,000 and increases continuously (see Gray, J. et al. Chest, 2007, 132, 56S-68S). The number of deaths caused by lung cancer is more than 1,300,000 around the world every year, which is more than the sum of the number of cancer-related deaths caused by other three common cancers (breast cancer, prostate cancer and colorectal cancer).

[0003] The classic methods for treating cancer include surgical therapy, radiotherapy and chemotherapy. However, the surgical therapy is not suitable for all

types of solid tumors. The surgical therapy may not eliminate cancer cells thoroughly due to metastatic lesions and the like, so as not to achieve the purpose of cure. Radiotherapy is only suitable for the tumors situated at positions that are sensitive to rays, take muscles as tumor beds and have better blood circulation, and the radiotherapy may accidentally injure normal cells to cause various side effects, so as to affect the quality of life of the patients. The effect of the chemotherapy as the systemic treatment means is determined by the types and the states of cancers. Chemotherapy can suppress the growth and the spread of the cancers more especially, and same with the radiotherapy, the chemotherapy can also accidentally injure normal cells to affect the quality of life of the patients.

[0004] Surgical therapy can be performed to eliminate tumors, improve the quality of life and provide time for follow-up treatment for some early or medium-term solid tumor patients; but for some advanced patients with metastasized solid tumors, the treatment methods in the prior art are only chemotherapy, radiotherapy or combining the chemotherapy, radiotherapy and other treatment methods when the quality of life is obviously affected and life is even threatened, these treatment methods are not ideal in effects and cannot achieve the purpose of eliminating the tumors and completely alleviating the condition of the patients.

[0005] According to the mass data, the existing methods for treating cancer, in particular, chemotherapy, cannot obtain the satisfied treatment effect for advanced lung cancer patients, and the number of complete remission (CR) cases is few and is even zero. For example, in the clinical trial of 78 cases which employed cis-platinum for combining Navelbine, Gemzar and Taxotere, respectively, to treat advanced non-small cell lung cancers, no complete remission appeared in any case (see Song, Y. et al, Journal of Modern Oncology, 2005, 13(4), 494-496); however, in the clinical observation of 1155 cases which employed four chemotherapy protocols (Cisplatin + Paclitaxel, Cisplatin + Gemcitabine, Cisplatin + Docetaxel, and Carboplatin + Paclitaxel) for treating the advanced non-small cell lung cancers, complete response was observed, but the complete response (CR) rate was less than 1% (see Schiller, J.H. et al. N Engl J Med, 2002, 346(2), 92-98); and in a random, double-blind, control and

multicenter III-stage clinical research which employed recombinant human endostatin for combining NP to treat the advanced non-small cell lung cancers, the 486 evaluable cases in the test group and the control group yielded no cases of complete remission (see Wang, J. W. et al, Chinese Journal of Lung Cancer, 2005, 8(4), 283-290).

[0006] In the recent 20 years, due to the in depth research on the cell biology, molecular biology, tumor immunology and the like and the development of the bio-engineering technology, the biotherapy has become the important treatment means for cancer treatment after surgical therapy, radiotherapy and chemotherapy has been performed.

[0007] Since Isaacs and Lindenmann discovered interferon (IFN), interferon has been widely researched. Interferon (IFN) is a kind of soluble protein produced by a variety of cells which has many important biological functions, including anti-viral, anti-tumor, and immunoregulatory functions. Interferons can be divided into type I, type II, and type III interferons according to the differences in the types of producing cells, receptors and biological activities, etc. Type I IFNs, which are mostly induced by viruses and synthetic double-stranded RNA, are also known as anti-viral interferons. There are three forms of type I interferons: interferon-alpha or alpha-interferon (IFNα), interferon-beta (INFβ) and interferon omega (IFNω).

[0008] In recent years, many companies in the world have engaged in the research of interferon. For example, U.S. Patent Nos. 4,695,623 and 4,897,471 disclosed new types of human interferon polypeptides which possessed amino acid sequences containing the common or predominant amino acids found in naturally occurring α-interferon polypeptides. One new type of interferon was named IFN-con (consensus interferon α). Compared with leukocyte interferon or other type I interferons, studies have shown that recombinant IFN-con has higher anti-viral, anti-proliferative and natural killer cell activities *in vitro*. By the end of 1997, the FDA had approved the use of human IFN-con, which was produced by US Amgen and sold under the brand name INFERGEN® (interferon alfacon-1), for clinical treatment of hepatitis C.

[0009] It is generally known that the amino acid sequence of a protein can

determine the three-dimensional structure of the protein and further determine the functionality thereof. However, in recent years, evidence shows that synonymous mutation(s) of the nucleotide sequence encoding the protein (that is, codon mutation(s) with no change in the amino acid sequence of the encoded protein) can affect the spatial structure and the function of the encoded protein, namely, the nucleotide sequence with synonymous mutation(s) can express and generate proteins with different final spatial structure and different function compared with the wild type protein (see Sarfaty, C. K. et al. Science, 2007, 315:525-528).

[0010] A recombinant interferon (rSIFN-co) which has enhanced therapeutic effects, smaller side effects and can be used in a larger doses was disclosed in US 7,364,724, US 7,585,647, US 8,114,395, CN 1740197 A, CN 101001644 A, US 2009/0123417, US 2011/0158941 and WO 2011072487A1. This recombinant interferon, rSIFN-co, has the same amino acid sequence as that of INFERGEN®, but the encoding nucleotide sequences of this recombinant interferon, rSIFN-co, and that of INFERGEN® are different (i.e. synonymous mutations exists in the nucleotide sequence encoding the recombinant interferon, rSIFN-co), resulting in changes in spatial configuration of the recombinant interferon, rSIFN-co, and qualitative changes in its biological efficacy.

SUMMARY OF THE INVENTION

[0011] One of the objects of the present invention is to provide new methods for treating tumors in subjects by using the recombinant interferon, rSIFN-co encoded by the nucleotide sequence of SEQ ID NO: 2. Another one of the objects of the present invention is to provide new methods for treating lung cancers in subjects by using the recombinant interferon encoded by the nucleotide sequence of SEQ ID NO: 2 (hereafter also be referred to as recombinant super-compound interferon or rSIFN-co).

[0012] The present invention is illustrated by the various embodiments described below. However, the present invention is not limited by these illustrative

embodiments and should be interpreted to include those embodiments taught by the description herein and as understood by persons skilled in the art. Illustrative examples of the various embodiments of the present invention include:

[0013] In one aspect, the present invention provides:

[0014] (1) A method for treating a tumor in a subject, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2.

[0015] (2) The method of (1), wherein the tumor in the subject comprises a metastasized tumor.

[0016] (3) The method of (1) or (2), wherein the subject is an early, medium-term, or advanced cancer patient, optionally, the subject is a medium-term, or advanced cancer patient, further optionally, the subject is an advanced cancer patient.

[0017] (4) The method of (1) or (2), wherein the subject is a stage 0, I, II, III, or IV cancer patient, optionally, the subject is a stage III or stage IV cancer patient.

[0018] (5) The method of any one of (1)-(4), wherein the tumor is a cancer or a solid tumor that is indicated or appropriate for surgery.

[0019] (6) The method of any one of (1)-(4), wherein the tumor is a cancer or a solid tumor that is not indicated nor appropriate for surgery.

[0020] (7) The method of any one of (1)-(5), wherein the tumor is a tumor that is capable of being resected.

[0021] (8) The method of any one of (1)-(4) and (6), wherein the tumor is a tumor that is not capable of being resected.

[0022] (9) The method of (7) or (8), wherein the tumor is resected by a surgical resection.

[0023] (10) The method of any one of (1)-(9), wherein the tumor is a solid tumor.

[0024] (11) The method of (10), wherein the solid tumor comprises one or more of: lung cancer, liver cancer, hepatocellular carcinoma (HCC), esophageal cancer, cholangiocarcinoma, gallbladder carcinoma, stomach cancer, abdominal cancer, gastrointestinal cancer, gastric cancer, pancreatic cancer, renal cell carcinoma, renal cancer, bone cancer, breast cancer, ovarian cancer, uterine cancer, cervical

cancer, endometrial cancer, colorectal cancer, colon cancer, rectal cancer, bladder cancer, superficial bladder cancer, prostate cancer, adrenal tumors, squamous cell carcinoma, neuroma, malignant neuroma, myoepithelial carcinoma, synovial sarcoma, rhabdomyosarcoma, gastrointestinal interstitial cell tumor, skin cancer, basal cell carcinoma, malignant melanoma, thyroid cancer, nasopharyngeal carcinoma, hemangioma, epidermoid carcinoma, head and neck cancer, glioma, or Kaposi's sarcoma.

[0025] (12) The method of (11), wherein the solid tumor comprises lung cancer, optionally, the lung cancer comprises small cell lung cancer (SCLC), non small cell lung cancer (NSCLC), or both.

[0026] (13) The method of any one of (1)-(4), wherein the tumor is a non-solid tumor.

[0027] (14) The method of (13), wherein the non-solid tumor comprises one or more of: leukemia, acute leukemia, chronic leukemia, chronic myelocytic leukemia, acute myelogenous leukemia, chronic myelogenous leukemia, chronic lymphocytic leukemia, acute lymphoblastic leukemia, T-cell leukemia, hairy cell leukemia, polycythemia, myelodysplastic syndrome, multiple myeloma, lymphadenoma, Hodgkin's lymphoma, and Non-Hodgkin's lymphoma.

[0028] (15) The method of any one of (1)-(14), wherein the recombinant interferon is administered to the subject by at least one of: systemic administration, local administration, and topical administration.

[0029] (16) The method of any one of (1)-(15), wherein the recombinant interferon is administered to the subject by an administration route, the administration route comprises one or more of: oral, rectal, sublingual, intravenous, intra-arterial, intramuscular, subcutaneous, intra-bone, intracutaneous, intra-articular, intraperitoneal, intrathecal, intracerebral, vaginal, percutaneous, transdermal, epidermal, transmucosal, transocular, pulmonary, nasal, abdominal, intrapleural, intraventricular, pericardial, inhalation, intratumoral, uterine, infiltration, and intravesical administration.

[0030] (17) The method of any one of (1)-(16), wherein an effective amount of recombinant interferon encoded by the nucleotide sequence of SEQ ID NO: 2 is

administered to the subject, optionally, the effective amount is a therapeutically effective amount.

[0031] (18) The method of any one of (1)-(17), wherein the recombinant interferon is administered to the subject in a single dose in a range of about 2μg to about 2000μg, optionally, the recombinant interferon is administered to the subject in a single dose in a range of about 4μg to about 1500μg, further optionally, the recombinant interferon is administered to the subject in a single dose in a range of about 9μg to about 1000μg.

[0032] (19) The method of any one of (1)-(18), wherein the recombinant interferon is administered in one or more treatment cycles, optionally, the more treatment cycles comprises 2, 3, 4, 5, 6, 7, 8, 9, 10 treatment cycles, further optionally, the number of treatment cycles comprises more than 10 treatment cycles.

[0033] (20) The method of (19), wherein the duration of the treatment cycle is at least about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or optionally, the recombinant interferon can be administered for a long time, including over the life time of the subject; or the duration of recombinant interferon treatment can also be about 1 day to about 6 years, about 1 week to about 4 years, about 2 weeks to about 3 years, about 1 month to about 1 year, or about 2 months to about 9 months and the like.

[0034] (21) The method of (19) or (20), wherein the time interval between any two adjacent treatment cycles of the more treatment cycles is at least about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4

years, about 5 years, or about 6 years and the like; or optionally the time interval can be about 2 days to about 6 years, about 4 days to about 3 years, about 1 week to about 1 year, about 2 months to about 9 months, or about 3 months to about 6 months and the like.

[0035] (22) The method of any one of (1)-(21), wherein the recombinant interferon is administered to the subject as monotherapy.

[0036] (23) The method of any one of (1)-(21), further comprising at least one other anti-cancer therapy administered to the subject, optionally, the at least one other anti-cancer therapy is administered to the subject before, simultaneously, and/or after administration of the recombinant interferon.

[0037] (24) The method of (23), wherein the at least one other anti-cancer therapy comprises at least one of: chemotherapy, radiotherapy, surgical therapy, interventional therapy, biotherapy, gene therapy, ablation therapy, immunotherapy, targeted therapy, and traditional Chinese medicine therapy.

[0038] (25) The method of (24), wherein the at least one other anti-cancer therapy comprises at least one of: chemotherapy, radiotherapy, surgical therapy, targeted therapy, and biotherapy.

[0039] (26) The method of (25), wherein the at least one other anti-cancer therapy comprises at least one of: chemotherapy and radiotherapy.

[0040] (27) The method of any one of (24)-(26), wherein the chemotherapy is administered as first-line chemotherapy, optionally, one or more chemotherapeutic drugs used in the first-line chemotherapy comprise platinum compounds, such as Cisplatin.

[0041] (28) The method of any one of (24)-(27), wherein the targeted therapy comprises at least one of: Gefitinib, Erlotinib, and recombinant human endostatin.

[0042] (29) The method of any one of (1)-(28), wherein the therapies eliminate the tumor or reduce the size of the tumor as compared to the tumor before treatment.

[0043] (30) The method of (29), wherein the reduced size of the tumor converts the tumor to a resectable tumor.

[0044] (31) The method of (30), wherein the tumor is indicated for a surgical resection.

[0045] (32) The method of any one of (1)-(28), wherein the tumor, such as cancer or solid tumor, that is not earlier indicated nor appropriate for surgery becomes one that is indicated or appropriate for surgery.

[0046] (33) The method of (32), further comprising surgery to resect the tumor.

[0047] (34) The method of any one of (30)-(31) and (33), further comprising administering to the subject the recombinant interferon after resecting the tumor, to prevent tumor recurrence and/or metastasis, or to prolong or maintain a tumor-free status, optionally, a prophylactically effective amount of the recombinant interferon is administered to the subject to prevent tumor recurrence and/or metastasis, and/or to prolong or maintain a tumor-free status.

[0048] (35) A method for treating tumor in a subject, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2, and at least one other anti-cancer therapy, wherein the at least one other anti-cancer therapy is administered to the subject before, simultaneously, and/or after administration of the recombinant interferon, and wherein the tumor is a cancer or solid tumor that is not indicated nor appropriate for surgery, or the tumor is a solid tumor that cannot be resected, and the combination of the recombinant interferon and the at least one other anti-cancer therapy eliminate the tumor or reduce the size of the tumor compared to the tumor before treatment.

[0049] (36) The method of embodiment 35, wherein the subject is a medium-term, advanced cancer patient, or stage III or stage IV cancer patient, optionally, the subject is an advanced, or stage III or stage IV cancer patient.

[0050] (37) The method of any one of (1)-(29) and (35)-(36), wherein the therapies are the non-surgical therapies.

[0051] In another aspect, another embodiment of the present invention provides:

[0052] (1) A method for preventing tumor recurrence and/or metastasis or

prolonging or maintaining a tumor-free status in a subject with a tumor after at least one anti-cancer therapy, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2.

[0053] (2) The method of (1), wherein the tumor in the subject comprises a metastasized tumor.

[0054] (3) The method of (1) or (2), wherein the subject is an early, medium-term, or advanced cancer patient.

[0055] (4) The method of (1) or (2), wherein the subject is a stage 0, I, II, III, or IV cancer patient.

[0056] (5) The method of any one of (1)-(4), wherein the tumor is a cancer or solid tumor that is indicated or appropriate for surgery.

[0057] (6) The method of any one of (1)-(4), wherein the tumor is a cancer or solid tumor that is not indicated nor appropriate for surgery.

[0058] (7) The method of any one of (1)-(4), wherein the tumor is a tumor that is capable of being resected.

[0059] (8) The method of any one of (1)-(4), wherein the tumor is a tumor that is not capable of being resected.

[0060] (9) The method of (7) or (8), wherein the tumor is resected by a surgical resection.

[0061] (10) The method of any one of (1)-(9), wherein the tumor is a solid tumor.

[0062] (11) The method of (10), wherein the solid tumor comprises one or more of: lung cancer, liver cancer, hepatocellular carcinoma (HCC), esophageal cancer, cholangiocarcinoma, gallbladder carcinoma, stomach cancer, abdominal cancer, gastrointestinal cancer, gastric cancer, pancreatic cancer, renal cell carcinoma, renal cancer, bone cancer, breast cancer, ovarian cancer, uterine cancer, cervical cancer, endometrial cancer, colorectal cancer, colon cancer, rectal cancer, bladder cancer, superficial bladder cancer, prostate cancer, adrenal tumors, squamous cell carcinoma, neuroma, malignant neuroma, myoepithelial carcinoma, synovial sarcoma, rhabdomyosarcoma, gastrointestinal interstitial cell tumor, skin cancer, basal cell

carcinoma, malignant melanoma, thyroid cancer, nasopharyngeal carcinoma, hemangioma, epidermoid carcinoma, head and neck cancer, glioma, or Kaposi's sarcoma.

[0063] (12) The method of (11), wherein the solid tumor comprises lung cancer, optionally, the lung cancer comprises small cell lung cancer (SCLC), non small cell lung cancer (NSCLC), or both.

[0064] (13) The method of any one of (1)-(4), wherein the tumor comprises a non-solid tumor.

[0065] (14) The method of (13), wherein the non-solid tumor comprises one or more of: leukemia, acute leukemia, chronic leukemia, chronic myelocytic leukemia, acute myelogenous leukemia, chronic myelogenous leukemia, chronic lymphocytic leukemia, acute lymphoblastic leukemia, T-cell leukemia, hairy cell leukemia, polycythemia, myelodysplastic syndrome, multiple myeloma, lymphadenoma, Hodgkin's lymphoma, and Non-Hodgkin's lymphoma.

[0066] (15) The method of any one of (1)-(14), wherein the recombinant interferon is administered to the subject by at least one of: systemic administration, local administration, and topical administration.

[0067] (16) The method of any one of (1)-(15), wherein the recombinant interferon is administered to the subject by an administration route, the administration route comprises one or more of: oral, rectal, sublingual, intravenous, intra-arterial, intramuscular, subcutaneous, intra-bone, intracutaneous, intra-articular, intraperitoneal, intrathecal, intracerebral, vaginal, percutaneous, transdermal, epidermal, transmucosal, transocular, pulmonary, nasal, abdominal, intrapleural, intraventricular, pericardial, inhalation, intratumoral, uterine, infiltration, and intravesical administration.

[0068] (17) The method of any one of (1)-(16), wherein an effective amount of recombinant interferon encoded by the nucleotide sequence of SEQ ID NO: 2 is administered to the subject, optionally, the effective amount is a prophylactically effective amount.

[0069] (18) The method of any one of (1)-(17), wherein the recombinant interferon is administered to the subject in a single dose in the range of about 2μg to

about 2000μg, optionally, the recombinant interferon is administered to the subject in a single dose in the range of about 4μg to about 1500μg, more optionally, the recombinant interferon is administered to the subject in a single dose in the range of about 9μg to about 1000μg.

[0070] (19) The method of any one of (1)-(18), wherein the recombinant interferon is administered in one or more prevention cycles, optionally, the more prevention cycles comprises 2, 3, 4, 5, 6, 7, 8, 9, or 10 prevention cycles, or optionally, more than 10 prevention cycles.

[0071] (20) The method of (19), wherein the duration of each prevention cycle is at least about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject; or the duration can also be about 1 day to about 6 years, about 1 week to about 4 years, about 2 weeks to about 3 years, about 1 month to about 1 year, or about 2 months to about 9 months and the like.

[0072] (21) The method of (19) or (20), wherein the time interval between any two adjacent prevention cycles of the more prevention cycles is at least about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like; or the time interval can also be about 2 days to about 6 years, about 4 days to about 3 years, about 1 week to about 1 year, about 2 months to about 9 months, or about 3 months to about 6 months and the like.

[0073] (22) The method of any one of (1)-(21), wherein the at least one

anti-cancer therapy comprises at least one of: chemotherapy, radiotherapy, surgical therapy, interventional therapy, biotherapy, gene therapy, ablation therapy, immunotherapy, targeted therapy, and traditional Chinese medicine therapy, optionally, the at least one anti-cancer therapy comprises at least one of: chemotherapy, radiotherapy, surgical therapy, and biotherapy.

[0074] (23) The method of (22), wherein the at least one anti-cancer therapy comprises surgical therapy.

[0075] (24) The method of (23), wherein the recombinant interferon is administered to the operative site of the surgical therapy.

[0076] (25) The method of (24), wherein the recombinant interferon is administered to the operative site by topical or local administration.

[0077] (26) The method of (24) or (25), wherein the recombinant interferon is administered to the operative site by an administration route, the administration route comprises one or more of: infiltration administration, intrapleural administration, abdominal administration, pericardial administration, uterine administration, intravesical administration, intratumoral administration, pulmonary administration, nasal administration, percutaneous administration, transdermal administration, epidermal administration, and transmucosal administration.

[0078] (27) The method of (26), wherein the intrapleural administration, abdominal administration, pericardial administration, uterine administration, or intravesical administration comprises intrapleural perfusion administration, abdominal perfusion administration, pericardial perfusion administration, uterine perfusion administration, or intravesical perfusion administration, respectively.

[0079] (28) The method of (26), wherein the intratumoral administration comprises intratumoral injection.

[0080] (29) The method of (26), wherein the pulmonary administration or nasal administration comprises pulmonary inhalation administration or nasal inhalation administration, respectively.

[0081] (30) The method of (26), wherein the percutaneous administration, transdermal administration, epidermal administration, or transmucosal administration

comprises percutaneous spray administration, transdermal spray administration, epidermal spray administration, or transmucosal spray administration, respectively.

[0082] (31) The method of any one of (25)-(30), wherein the recombinant interferon is further administered to the subject by systemic administration before, simultaneously, and/or after the topical or local administration of the recombinant interferon.

[0083] (32) The method of (31), wherein the systemic administration comprises at least one of: subcutaneous and intramuscular administration, optionally, the protocols in (24)-(32) also apply to the above-specified method for treatment of tumor in a subject.

[0084] (33) The method of any one of (1)-(32), wherein the recombinant interferon is administered to the subject as monotherapy.

[0085] In another aspect, another embodiment of the present invention provides:

[0086] (1) A non-surgical method for eliminating a tumor in a subject or reducing the size of a tumor in a subject, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2.

[0087] (2) The method of (1), wherein the tumor is a cancer or a solid tumor that is indicated or appropriate for surgery.

[0088] (3) The method of (1), wherein the tumor is a cancer or a solid tumor that is not indicated nor appropriate for surgery.

[0089] (4) The method of (1), wherein the tumor is a tumor that is capable of being resected.

[0090] (5) The method of (1), wherein the tumor is a tumor that is not capable of being resected.

[0091] (6) The method of (4) or (5), wherein the tumor is resected by a surgical resection.

[0092] (7) The method of any one of (1)-(6), wherein the subject is an early, medium-term, or advanced cancer patient, optionally, the subject is a medium-term, or advanced cancer patient, or further optionally, the subject is an advanced cancer

patient.

[0093] (8) The method of any one of (1)-(6), wherein the subject is a stage 0, I, II, III, or IV cancer patient, optionally, the subject is a stage III or IV cancer patient.

[0094] (9) The method of any one of (1)-(8), wherein the subject is a medium-term, or advanced cancer patient, or a stage III or stage IV cancer patient, optionally, the subject is an advanced, or stage III or stage IV cancer patient.

[0095] (10) The method of any one of (1)-(9), wherein the tumor is a solid tumor.

[0096] (11) The method of (10), wherein the solid tumor comprises one or more of: lung cancer, liver cancer, hepatocellular carcinoma (HCC), esophageal cancer, cholangiocarcinoma, gallbladder carcinoma, stomach cancer, abdominal cancer, gastrointestinal cancer, gastric cancer, pancreatic cancer, renal cell carcinoma, renal cancer, bone cancer, breast cancer, ovarian cancer, uterine cancer, cervical cancer, endometrial cancer, colorectal cancer, colon cancer, rectal cancer, bladder cancer, superficial bladder cancer, prostate cancer, adrenal tumors, squamous cell carcinoma, neuroma, malignant neuroma, myoepithelial carcinoma, synovial sarcoma, rhabdomyosarcoma, gastrointestinal interstitial cell tumor, skin cancer, basal cell carcinoma, malignant melanoma, thyroid cancer, nasopharyngeal carcinoma, hemangioma, epidermoid carcinoma, head and neck cancer, glioma, or Kaposi's sarcoma.

[0097] (12) The method of (11), wherein the solid tumor comprises lung cancer, optionally, the lung cancer comprises small cell lung cancer (SCLC), non small cell lung cancer (NSCLC), or both.

[0098] (13) The method of any one of (1)-(12), wherein the recombinant interferon is administered to the subject by at least one of: systemic administration, local administration, and topical administration, optionally, the recombinant interferon is administered to the subject by topical or local administration, further optionally, the recombinant interferon is administered to the subject by local administration.

[0099] (14) The method of any one of (1)-(13), wherein the recombinant interferon is administered to the subject by an administration route, the administration

route comprises one or more of: infiltration administration, intrapleural administration, abdominal administration, pericardial administration, uterine administration, intravesical administration, intratumoral administration, pulmonary administration, nasal administration, percutaneous administration, transdermal administration, epidermal administration, and transmucosal administration.

[00100] (15) The method of (14), wherein the intratumoral administration comprises intratumoral injection.

[00101] (16) The method of (15), wherein the recombinant interferon is administered in an amount in a range of: about 60μg to about 600μg, optionally about 60μg to about 500μg, further optionally, about 80μg to about 400μg, still optionally about 100μg to about 250μg, by one intratumoral injection.

[00102] (17) The method of (15) or (16), wherein the recombinant interferon is administered by intratumoral injection once every about 1 day to about 10 days, optionally, every about 1 day to about 7 days, such as every about 1, 2, 3, 4, 5, 6, or 7 days.

[00103] (18) The method of any one of (14)-(17), wherein the protocol of intratumoral administration is as follows: the recombinant interferon is administered by intratumoral injection once every about 1 day for about 4 to about 8 times, and then the recombinant interferon is administered by intratumoral injection once every about 3 days to about 5 days for about 4 to about 8 times, and then the recombinant interferon is administered by intratumoral injection once every about 7 days, the intratumoral administration is stopped when the tumor disappears or becomes too small to conduct the intratumoral injection.

[00104] (19) The method of (14), wherein the intrapleural administration, abdominal administration, pericardial administration, uterine administration, or intravesical administration comprises intrapleural perfusion administration, abdominal perfusion administration, pericardial perfusion administration, uterine perfusion administration, or intravesical perfusion administration, respectively.

[00105] (20) The method of (14), wherein the pulmonary administration, or nasal administration comprises pulmonary inhalation administration, or nasal

inhalation administration, respectively.

[00106] (21) The method of (14), wherein the percutaneous administration, transdermal administration, epidermal administration, or transmucosal administration comprises percutaneous spray administration, transdermal spray administration, epidermal spray administration, or transmucosal spray administration, respectively.

[00107] (22) The method of any one of (13)-(21), wherein the recombinant interferon is further administered to the subject by systemic administration, and/or at least one other therapeutic drug is administered to the subject by topical, local and/or systemic administration before, simultaneously, and/or after the topical or local administration of the recombinant interferon.

[00108] (23) The method of (22), wherein the recombinant interferon is further administered to the subject by systemic administration, and/or at least one other therapeutic drug is administered to the subject by topical, local and/or systemic administration simultaneously and/or after the topical or local administration of the recombinant interferon.

[00109] (24) The method of (22) or (23), wherein the at least one other therapeutic drug comprises at least one antitumor drug.

[00110] (25) The method of (24), wherein the at least one antitumor drug comprises one or more chemotherapeutic drugs, targeted drugs, and/or biological drugs.

[00111] (26) The method of (25), wherein the one or more chemotherapeutic drugs comprise platinum compounds, such as Cisplatin.

[00112] (27) The method of (25), wherein one or more targeted drugs comprise Gefitinib, Erlotinib, and/or recombinant human endostatin.

[00113] In another aspect, another embodiment of the present invention provides:

[00114] (1) A method for eliminating or reducing the pleural effusion, ascites, and/or pericardial effusion in a subject with tumor, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2.

[00115] (2) The method of (1), wherein the tumor is a cancer or a solid tumor

that is indicated or is appropriate for surgery.

[00116] (3) The method of (1), wherein the tumor is a cancer or a solid tumor that is not indicated nor appropriate for surgery.

[00117] (4) The method of (1), wherein the tumor is a tumor that is capable of being resected.

[00118] (5) The method of (1), wherein the tumor is a tumor that is not capable of being resected.

[00119] (6) The method of (4) or (5), wherein the tumor is resected by a surgical resection.

[00120] (7) The method of any one of (1)-(6), wherein the subject is an early, medium-term, or advanced cancer patient, optionally, the subject is a medium-term, or advanced cancer patient, or further optionally, the subject is an advanced cancer patient.

[00121] (8) The method of any one of (1)-(6), wherein the subject is a stage 0, I, II, III, or IV cancer patient, optionally, the subject is a stage III or stage IV cancer patient.

[00122] (9) The method of any one of (1)-(8), wherein the subject is a medium-term, or advanced cancer patient, or stage III or stage IV cancer patient, optionally, the subject is an advanced, or stage III or stage IV cancer patient.

[00123] (10) The method of any one of (1)-(9), wherein the tumor is a solid tumor.

[00124] (11) The method of (10), wherein the solid tumor comprises one or more of: lung cancer, liver cancer, hepatocellular carcinoma (HCC), esophageal cancer, cholangiocarcinoma, gallbladder carcinoma, stomach cancer, abdominal cancer, gastrointestinal cancer, gastric cancer, pancreatic cancer, renal cell carcinoma, renal cancer, bone cancer, breast cancer, ovarian cancer, uterine cancer, cervical cancer, endometrial cancer, colorectal cancer, colon cancer, rectal cancer, bladder cancer, superficial bladder cancer, prostate cancer, adrenal tumors, squamous cell carcinoma, neuroma, malignant neuroma, myoepithelial carcinoma, synovial sarcoma, rhabdomyosarcoma, gastrointestinal interstitial cell tumor, skin cancer, basal cell

carcinoma, malignant melanoma, thyroid cancer, nasopharyngeal carcinoma, hemangioma, epidermoid carcinoma, head and neck cancer, glioma, or Kaposi's sarcoma.

[00125] (12) The method of (11), wherein the solid tumor comprises lung cancer, optionally, the lung cancer comprises small cell lung cancer (SCLC), non small cell lung cancer (NSCLC), or both.

[00126] (13) The method of any one of (1)-(12), wherein the pleural effusion is a malignant pleural effusion, the ascites is a malignant ascites, and/or the pericardial effusion is a malignant pericardial effusion.

[00127] (14) The method of any one of (1)-(13), wherein the recombinant interferon is administered to the subject by at least one of: systemic administration, local administration, and topical administration, optionally, by topical and local administration, further optionally, by local administration.

[00128] (15) The method of any one of (1)-(14), wherein the recombinant interferon is administered to the subject by an administration route, the administration route comprises one or more of: infiltration administration, intrapleural administration, abdominal administration, and pericardial administration.

[00129] (16) The method of any one of (1)-(15), wherein the administration is conducted by perfusion.

[00130] (17) The method of any one of (14)-(16), wherein the recombinant interferon is administered in an amount in a range of about 30μg to about 2000μg, optionally, about 100μg to about 1500μg, further optionally, about 150μg to about 1000μg, still further optionally, about 200μg to about 800μg, still optionally, about 200μg to about 400μg by one topical or local administration.

[00131] (18) The method of any one of (14)-(17), wherein the recombinant interferon is administered by topical or local administration once every about 1 to about 10 days, optionally every about 1 to about 7 days, such as every about 1, 2, 3, 4, 5, 6, or 7 days.

[00132] (19) The method of any one of (14)-(18), wherein the recombinant interferon is further administered to the subject by systemic administration, and at

least one other therapeutic drug is administered to the subject by topical, local and/or systemic administration before, simultaneously, and/or after the topical or local administration of the recombinant interferon.

[00133] (20) The method of (19), wherein the recombinant interferon is further administered to the subject by systemic administration, and at least one other therapeutic drug is administered to the subject by topical, local and/or systemic administration simultaneously and/or after the topical or local administration of the recombinant interferon.

[00134] (21) The method of (19) or (20), wherein the at least one other therapeutic drug comprises an antitumor drug.

[00135] (22) The method of (21), wherein the antitumor drug comprises at least one of: chemotherapeutic drug, targeted drug, and biological drug.

[00136] (23) The method of (22), wherein the at least one chemotherapeutic drug comprises at least one platinum compounds, such as Cisplatin.

[00137] (24) The method of (22), wherein at least one targeted drug comprises at least one of: Gefitinib, Erlotinib, and recombinant human endostatin.

[00138] (25) The method of any one of (1)-(24), wherein the therapies eliminate the tumor or reduce the size of the tumor compared to the tumor before treatment.

[00139] (26) The method of any one of (1)-(25), wherein the therapies are the non-surgical therapies.

[00140] In another aspect, another embodiment of the present invention provides:

[00141] (1) A method for treating tumor in a subject, comprising topically or locally administering to the tumor lesions of the subject a recombinant interferon encoded by SEQ ID NO: 2.

[00142] (2) The method of (1), wherein the tumor lesions comprise metastatic tumor lesions.

[00143] (3) A method for eliminating or reducing metastatic tumor lesions in a subject, comprising topically or locally administering to the metastatic tumor lesions

of the subject a recombinant interferon encoded by SEQ ID NO: 2.

[00144] (4) The method of any one of (1)-(3), wherein the tumor lesions comprise at least one of: bone lesions, muscular lesions, subcutaneous tissue lesions, prostatic lesions and lymph node lesions, and the tumor metastatic lesions comprise at least one of: bone metastatic lesions, muscular metastatic lesions, subcutaneous tissue metastatic lesions, prostatic metastatic lesions, and lymph node metastatic lesions, optionally, the tumor metastatic lesions comprise bone metastatic lesions.

[00145] (5) The method of any one of (1)-(4), wherein the subject is a medium-term, advanced, or stage III or stage IV cancer patient, optionally, the subject is an advanced, or stage III or stage IV cancer patient.

[00146] (6) The method of any one of (1)-(4), wherein the tumor or the metastatic tumor lesions comprise a cancer or a solid tumor that is not indicated nor appropriate for surgery.

[00147] (7) The method of any one of (1)-(6), wherein the topical or local administration comprises at least one of: infiltration administration, percutaneous administration, transdermal administration, epidermal administration and transmucosal administration, optionally, the topical and local administration comprises transdermal administration, or infiltration administration.

[00148] (8) The method of (7), wherein the infiltration administration comprises one or more of: percutaneous infiltration administration, epidermal infiltration administration, transdermal infiltration administration, and transmucosal infiltration administration.

[00149] (9) The method of (7), wherein the percutaneous administration, transdermal administration, epidermal administration, or transmucosal administration comprises percutaneous spray administration, transdermal spray administration, epidermal spray administration, or transmucosal spray administration, respectively.

[00150] (10) The method of any one of (1)-(9), wherein the recombinant interferon is administered in an amount in a range of about 2μg to about 2000μg, optionally about 4μg to about 1500μg, further optionally about 9μg to about 1000μg by one topical or local administration.

[00151] (11) The method of any one of (1)-(10), wherein the recombinant interferon is administered to the subject by topical or local administration about 1, 2, 3, 4, 5, 6, 7, 8, or more times per day, or the recombinant interferon is administered to the subject by topical or local administration once at the time interval of every about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or 21 days, every month, every 2 months, or a longer time.

[00152] (12) The method of any one of (7)-(11), wherein the recombinant interferon is administered in an amount in a range of about 6μg to about 100μg, optionally about 10μg to about 40μg, further optionally about 20μg to about 40μg by one spray administration when the topical or local administration is conducted by spray administration.

[00153] (13) The method of (12), wherein the recombinant interferon is administered by spray administration about 1 to about 6 times, such as about 1, 2, 3, 4, 5, or 6 times, per day.

[00154] (14) The method of any one of (1)-(13), wherein the recombinant interferon and/or one or more other therapeutic drugs are administered to the subject by systemic administration before, simultaneously, and/or after the topical or local administration of the recombinant interferon.

[00155] (15) The method of (14), wherein the systemic administration comprises subcutaneous and/or intramuscular administration.

[00156] (16) The method of (15), wherein the subcutaneous administration comprises subcutaneous injection.

[00157] (17) The method of (15), wherein the intramuscular administration comprises intramuscular injection.

[00158] (18) The method of any one of (15)-(17), wherein the recombinant interferon is administered one or more times by subcutaneous administration and/or intramuscular administration at an induction dose in the range of about 2μg to about 10μg each time, optionally, about 4μg to about 10μg each time, more optionally about 4.5μg to about 9μg each time, such as about 4.5μg each time or about 9μg each time, and then the recombinant interferon is administered more times by subcutaneous

administration and/or intramuscular administration at a therapeutic dose of about 10μg to about 70μg each time, optionally about 12μg to about 50μg each time, more optionally about 12μg to about 30μg each time.

[00159] (19) The method of (18), wherein the time interval between administration of induction dose and administration of therapeutic dose is about 1 day to about 1 month, optionally about 1 day to about 1 week, further optionally about 1 day to about 3 days, comprising such as about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, or about 1 month.

[00160] (20) The method of (18) or (19), wherein the recombinant interferon is administered once every about 1 day to about 10 days, optionally every about 1 day to about 7 days, further optionally every about 1 to about 2 days, comprising such as every about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 days when the recombinant interferon is administered more times at an induction dose.

[00161] (21) The method of any one of (18)-(20), wherein the recombinant interferon is administered at a therapeutic dose once every about 1 day to about 10 days, optionally every about 1 day to about 7 days, further optionally every about 1 to about 2 days, comprising such as every about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 days.

[00162] (22) The method of any one of (18)-(21), wherein the duration of administration of induction dose and therapeutic dose is at least: about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject.

[00163] (23) The method of any one of (1)-(22), wherein the recombinant interferon is administered to the subject as monotherapy.

[00164] (24) The method of any one of (1)-(22), further comprising at least one other anti-cancer therapy administered to the subject, optionally, the at least one other

anti-cancer therapy is administered to the subject before, simultaneously, and/or after administration of the recombinant interferon.

[00165] (25) The method of (24), wherein the at least one other anti-cancer therapy comprises one or more of: chemotherapy, radiotherapy, surgical therapy, interventional therapy, biotherapy, gene therapy, ablation therapy, immunotherapy, targeted therapy, and traditional Chinese medicine therapy.

[00166] (26) The method of any one of (1)-(25), wherein the recombinant interferon therapy and/or at least one other anti-cancer therapy eliminate the tumor or tumor metastatic lesions or reduce the size of the tumor or tumor metastatic lesions compared to the tumor or tumor metastatic lesions before treatment.

[00167] (27) A method for eliminating or reducing the bone metastatic lesions of tumor in a subject, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2 by topical or local administration, wherein the topical or local administration comprises transdermal administration and/or infiltration administration, optionally, the recombinant interferon is administered to the bone metastatic lesions of tumor of the subject.

[00168] (28) A method for eliminating or reducing the bone lesions of tumor such as bone metastatic lesions of tumor, muscular lesions of tumor such as muscular metastatic lesions of tumor, subcutaneous tissue lesions of tumor such as subcutaneous tissue metastatic lesions of tumor, prostatic lesions of tumor such as prostatic metastatic lesions of tumor, and/or lymph node lesions of tumor such as lymph node metastatic lesions of tumor in a subject, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2 by any administration route through the skin, so that eliminating or reducing the bone lesions of tumor such as bone metastatic lesions of tumor, muscular lesions of tumor such as muscular metastatic lesions of tumor, subcutaneous tissue lesions of tumor such as subcutaneous tissue metastatic lesions of tumor, prostatic lesions of tumor such as prostatic metastatic lesions of tumor, and/or lymph node lesions of tumor such as lymph node metastatic lesions of tumor, optionally, the recombinant interferon is administered to the metastatic lesions of tumor of the subject.

[00169] (29) The method of any one of (1)-(28), wherein the therapies are non-surgical therapies.

[00170] In another aspect, another embodiment of the present invention provides:

[00171] (1) A method for treating lung cancer in a subject, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2.

[00172] (2) The method of (1), wherein the lung cancer comprises small cell lung cancer (SCLC), non small cell lung cancer (NSCLC), or both.

[00173] (3) The method of (1) or (2), wherein the lung cancer in the subject comprises a metastasized tumor.

[00174] (4) The method of any one of (1)-(3), wherein the subject is an early, medium-term, or advanced cancer patient, optionally, the subject is a medium-term, or advanced cancer patient, further optionally, the subject is an advanced cancer patient.

[00175] (5) The method of any one of (1)-(3), wherein the subject is a stage 0, I, II, III, or IV cancer patient, optionally, the subject is an stage III or stage IV cancer patient.

[00176] (6) The method of any one of (1)-(5), wherein the lung cancer comprises a lung cancer that is indicated or appropriate for surgery.

[00177] (7) The method of any one of (1)-(5), wherein the lung cancer comprises a lung cancer that is not indicated nor appropriate for surgery.

[00178] (8) The method of any one of (1)-(5), wherein the lung cancer comprises a lung cancer that is capable of being resected.

[00179] (9) The method of any one of (1)-(5), wherein the lung cancer comprises a lung cancer that is not capable of being resected.

[00180] (10) The method of (8) or (9), wherein the lung cancer is resected by a surgical resection.

[00181] (11) The method of any one of (1)-(10), wherein an effective amount of recombinant interferon encoded by the nucleotide sequence of SEQ ID NO: 2 is administered to the subject, optionally, the effective amount is a therapeutically effective amount.

[00182] (12) The method of any one of (1)-(11), wherein the recombinant interferon is administered to the subject by at least one of: systemic administration, topical administration, and local administration.

[00183] (13) The method of any one of (1)-(12), wherein the recombinant interferon is administered to the subject by an administration route, the administration route comprises one or more of: oral, rectal, sublingual, intravenous, intra-arterial, intramuscular, subcutaneous, intra-bone, intracutaneous, intra-articular, intraperitoneal, intrathecal, intracerebral, vaginal, percutaneous, transdermal, epidermal, transmucosal, transocular, pulmonary, nasal, abdominal, intrapleural, intraventricular, pericardial, inhalation, intratumoral, uterine, infiltration, and intravesical administration.

[00184] (14) The method of any one of (1)-(13), wherein the recombinant interferon is administered to the subject by subcutaneous administration and/or intramuscular administration.

[00185] (15) The method of (14), wherein the subcutaneous administration comprises subcutaneous injection.

[00186] (16) The method of (14), wherein the intramuscular administration comprises intramuscular injection.

[00187] (17) The method of any one of (14)-(16), wherein the recombinant interferon is administered in an amount in a range of about 2μg to about 70μg by one subcutaneous and/or intramuscular administration.

[00188] (18) The method of (17), wherein the recombinant interferon is administered in an amount in a range of about 4μg to about 50μg by one subcutaneous and/or intramuscular administration.

[00189] (19) The method of (18), wherein the recombinant interferon is administered in an amount in a range of about 4μg to about 30μg by one subcutaneous and/or intramuscular administration.

[00190] (20) The method of any one of (14)-(19), wherein the recombinant interferon is administered by subcutaneous and/or intramuscular administration once every about 1 to about 7 days.

[00191] (21) The method of (20), wherein the recombinant interferon is

administered by subcutaneous and/or intramuscular administration once every about 1 to about 2 days.

[00192] (22) The method of any one of (1)-(21), wherein the recombinant interferon is administered to the subject by inhalation administration.

[00193] (23) The method of (22), wherein the recombinant interferon is administered by pulmonary and/or nasal inhalation.

[00194] (24) The method of (22) or (23), wherein the inhalation administration comprises dry powder inhalation and/or aerosol inhalation.

[00195] (25) The method of any one of (22)-(24), wherein the recombinant interferon is administered in an amount in a range of about 100μg to about 2000μg, optionally about 100μg to about 1500μg by one inhalation administration.

[00196] (26) The method of (25), wherein the recombinant interferon is administered in an amount in a range of about 150μg to about 800μg by one inhalation administration.

[00197] (27) The method of (26), wherein the recombinant interferon is administered in an amount in a range of about 200μg to about 600μg by one inhalation administration.

[00198] (28) The method of any one of (22)-(27), wherein the recombinant interferon is administered by inhalation administration once every about 1 to about 3 days.

[00199] (29) The method of (28), wherein the recombinant interferon is administered by inhalation administration once every about 1 day.

[00200] (30) The method of any one of (1)-(29), wherein the subject has the pleural effusion, ascites, and/or pericardial effusion.

[00201] (31) The method of (30), wherein the pleural effusion comprises a malignant pleural effusion, the ascites comprises a malignant ascites, and/or the pericardial effusion comprises a malignant pericardial effusion.

[00202] (32) The method of (30) or (31), wherein the recombinant interferon is administered to the subject by intrapleural administration, abdominal administration, and/or pericardial administration.

[00203] (33) The method of (32), wherein the intrapleural administration comprises intrapleural perfusion.

[00204] (34) The method of (32), wherein the abdominal administration comprises abdominal perfusion.

[00205] (35) The method of (32), wherein the pericardial administration comprises pericardial perfusion.

[00206] (36) The method of any one of (32)-(35), wherein the recombinant interferon is administered in an amount in a range of about 30μg to about 2000μg, optionally about 100μg to about 1500μg, further optionally about 150μg to about 1000μg, still optionally about 200μg to about 800μg by one intrapleural, abdominal, and/or pericardial administration.

[00207] (37) The method of (36), wherein the recombinant interferon is administered in an amount in a range of about 200μg to about 400μg by one intrapleural, abdominal, and/or pericardial administration.

[00208] (38) The method of any one of (32)-(37), wherein the recombinant interferon is administered by intrapleural, abdominal, and/or pericardial administration once every about 1 to about 10 days, optionally every about 1 to about 7 days, such as every about 1, 2, 3, 4, 5, 6, or 7 days.

[00209] (39) The method of any one of (1)-(13), wherein the recombinant interferon is administered to the subject by intratumoral administration.

[00210] (40) The method of (39), wherein the intratumoral administration comprises intratumoral injection.

[00211] (41) The method of (39) or (40), wherein the recombinant interferon is administered in an amount in a range of about 60μg to about 600μg, optionally about 60μg to about 500μg by one intratumoral administration.

[00212] (42) The method of (41), wherein the recombinant interferon is administered in an amount in a range of about 80μg to about 400μg by one intratumoral administration.

[00213] (43) The method of (42), wherein the recombinant interferon is administered in an amount in a range of about 100μg to about 250μg by one

intratumoral administration.

[00214] (44) The method of any one of (39)-(43), wherein the recombinant interferon is administered by intratumoral administration once every about 1 day to about 10 days, optionally every about 1 day to about 7 days such as every about 1, 2, 3, 4, 5, 6, or 7 days.

[00215] (45) The method of any one of (39)-(44), wherein the protocol of intratumoral administration is as follow: the recombinant interferon is administered by intratumoral injection once every about 1 day for about 4 to about 8 times, and then the recombinant interferon is administered by intratumoral injection once every about 3 days to about 5 days for about 4 to about 8 times, and then the recombinant interferon is administered by intratumoral injection once every about 7 days, the intratumoral administration is stopped when the tumor disappears or becomes too small to conduct the intratumoral injection.

[00216] (46) The method of any one of (1)-(45), wherein the lung cancer in the subject comprises tumor metastasis in at least one of: skin, mucosa, superficial lymph nodes, and subcutaneous tissue.

[00217] (47) The method of (46), wherein the recombinant interferon is administered to the subject by spray administration.

[00218] (48) The method of (47), wherein the spray administration comprises at least one of: percutaneous spray administration, transdermal spray administration, epidermal spray administration, and transmucosal spray administration.

[00219] (49) The method of (47) or (48), wherein the recombinant interferon is administered in an amount in a range of about 6μg to about 100μg by one spray administration.

[00220] (50) The method of (49), wherein the recombinant interferon is administered in an amount in a range of about 10μg to about 40μg, optionally about 20μg to about 40μg by one spray administration.

[00221] (51) The method of any one of (47)-(50), wherein the recombinant interferon is administered by spray administration about 1 to about 6 times such as about 1, 2, 3, 4, 5, or 6 times per day.

[00222] (52) The method of any one of (1)-(51), wherein the recombinant interferon is administered to the subject by an administration route, the administration route comprises at least one of: subcutaneous administration, intramuscular administration, inhalation administration, infiltration administration, intrapleural administration, abdominal administration, pericardial administration, intratumoral administration, and spray administration.

[00223] (53) The method of any one of (1)-(52), wherein the recombinant interferon is administered to the subject as monotherapy.

[00224] (54) The method of any one of (1)-(52), further comprising at least one other anti-cancer therapy administered to the subject, optionally, the at least one other anti-cancer therapy is administered to the subject before, simultaneously, and/or after administration of the recombinant interferon.

[00225] (55) The method of (54), wherein the at least one other anti-cancer therapy comprises at least one of: chemotherapy, radiotherapy, surgical therapy, interventional therapy, biotherapy, gene therapy, ablation therapy, immunotherapy, targeted therapy, and traditional Chinese medicine therapy.

[00226] (56) The method of (55), wherein the at least one other anti-cancer therapy comprises chemotherapy.

[00227] (57) The method of (56), wherein the chemotherapy is the first-line chemotherapy.

[00228] (58) The method of (57), wherein at least one chemotherapeutic drugs used for the first-line chemotherapy comprise platinum compounds, such as Cisplatin.

[00229] (59) The method of (55), wherein the at least one other anti-cancer therapy comprises radiotherapy.

[00230] (60) The method of (59), wherein the radiotherapy comprises head gamma knife therapy when the lung cancer metastasizes to brain.

[00231] (61) The method of (55), wherein the at least one other anti-cancer therapy comprises surgical therapy.

[00232] (62) The method of (55), wherein the at least one other anti-cancer therapy comprises targeted therapy.

[00233] (63) The method of (62), wherein the targeted therapy comprises administering Gefitinib, Erlotinib, and/or recombinant human endostatin.

[00234] (64) The method of (55), wherein the at least one other anti-cancer therapy comprises biotherapy.

[00235] (65) The method of any one of (1)-(64), wherein the recombinant interferon is administered in at least one treatment cycle, optionally, the at least one treatment cycle comprises 2, 3, 4, 5, 6, 7, 8, 9, or 10 treatment cycles, or optionally, more than 10 treatment cycles.

[00236] (66) The method of (65), wherein the duration of the treatment cycle is at least about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject; or the duration can also be about 1 day to about 6 years, about 1 week to about 4 years, about 2 weeks to about 3 years, about 1 month to about 1 year, or about 2 months to about 9 months and the like.

[00237] (67) The method of (65) or (66), wherein the time interval between any two adjacent treatment cycles of the more treatment cycles is at least about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like; or the time interval can also be about 2 days to about 6 years, about 4 days to about 3 years, about 1 week to about 1 year, about 2 months to about 9 months, or about 3 months to about 6 months and the like.

[00238] (68) The method of any one of (1)-(67), wherein the therapies

eliminate the tumor of the lung or reduce the size of the tumor of the lung compared to the tumor size before treatment.

[00239] (69) A method for treating lung cancer in a subject, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2 and one or more chemotherapeutic drugs in two or more treatment cycles, and then administering to the subject a recombinant interferon encoded by SEQ ID NO: 2 and one or more targeted drugs in one or more treatment cycles.

[00240] (70) The method of (69), wherein the therapies eliminate the tumor of the lung or reduce the size of the tumor of the lung compared to the tumor size before treatment.

[00241] (71) The method of (69) or (70), wherein the one or more chemotherapeutic drugs comprise platinum compounds, such as Cisplatin.

[00242] (72) The method of any one of (69)-(71), wherein the one or more targeted drugs comprise Gefitinib, Erlotinib, and/or recombinant human endostatin.

[00243] (73) The method of any one of (69)-(72), wherein an effective amount of recombinant interferon, encoded by the nucleotide sequence of SEQ ID NO: 2, is administered to the subject, optionally, the effective amount is a therapeutically effective amount.

[00244] (74) The method of any one of (1)-(73), wherein the therapies are the non-surgical therapies.

[00245] In another aspect, another embodiment of the present invention provides:

[00246] (1) A method for treating lung cancer in a subject, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2 by subcutaneous administration and/or intramuscular administration, wherein the recombinant interferon is administered in an amount in a range of about 2 μ g to about 70μg, optionally about 4μg to about 50μg, further optionally about 4μg to about 30μg by one subcutaneous administration and/or intramuscular administration, the recombinant interferon is administered by subcutaneous administration and/or

intramuscular administration once every about 1 to about 7 days, optionally every about 1 to about 2 days, lasting at least about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject; or the duration can also be about 1 day to about 6 years, about 1 week to about 4 years, about 2 weeks to about 3 years, about 1 month to about 1 year, or about 2 months to about 9 months and the like.

[00247] (2) The method of (1), wherein the lung cancer comprises small cell lung cancer (SCLC), non small cell lung cancer (NSCLC), or both.

[00248] (3) The method of (1) or (2), wherein the lung cancer in the subject comprises a metastasized tumor.

[00249] (4) The method of any one of (1)-(3), wherein the subject is an early, medium-term, or advanced cancer patient, optionally, the subject is a medium-term, or advanced cancer patient, further optionally, the subject is an advanced cancer patient.

[00250] (5) The method of any one of (1)-(3), wherein the subject is a stage 0, I, II, III, or IV cancer patient, optionally, the subject is a stage III or IV cancer patient.

[00251] (6) The method of any one of (1)-(5), wherein the lung cancer is a lung cancer that is indicated or appropriate for surgery.

[00252] (7) The method of any one of (1)-(5), wherein the lung cancer is a lung cancer that is not indicated nor appropriate for surgery.

[00253] (8) The method of any one of (1)-(5), wherein the lung cancer is a lung cancer that is capable of being resected.

[00254] (9) The method of any one of (1)-(5), wherein the lung cancer is a lung cancer that is not capable of being resected.

[00255] (10) The method of (8) or (9), wherein the lung cancer is resected by a surgical resection.

[00256] (11) The method of any one of (1)-(10), wherein the subcutaneous administration comprises subcutaneous injection.

[00257] (12) The method of any one of (1)-(10), wherein the intramuscular administration comprises intramuscular injection.

[00258] (13) The method of any one of (1)-(12), further comprising administering to the subject the recombinant interferon by inhalation administration.

[00259] (14) The method of (13), wherein the inhalation administration is conducted before, simultaneously, and/or after the subcutaneous administration and/or intramuscular administration.

[00260] (15) The method of (13) or (14), wherein the inhalation administration comprises pulmonary and/or nasal inhalation administration.

[00261] (16) The method of any one of (13)-(15), wherein the inhalation administration comprises aerosol inhalation.

[00262] (17) The method of any one of (13)-(16), wherein the recombinant interferon is administered in an amount in a range of about 100μg to about 2000μg, optionally about 100μg to about 1500μg, further optionally about 150μg to about 800μg, still optionally about 200μg to about 600μg by one inhalation administration, the recombinant interferon is administered by inhalation administration once every about 1 day to about 3 days, optionally every about 1 day, lasting at least about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject; or the duration can also be about 1 day to about 6 years, about 1 week to about 4 years, about 2 weeks to about 3 years, about 1 month to about 1 year, or about 2 months to about 9 months and the like.

[00263] (18) The method of any one of (1)-(17), further comprising

administering to the subject the recombinant interferon by intratumoral administration.

[00264] (19) The method of (18), wherein the intratumoral administration is conducted before, simultaneously, and/or after the subcutaneous administration and/or intramuscular administration.

[00265] (20) The method of (18), wherein the intratumoral administration is conducted before, simultaneously, and/or after the inhalation administration.

[00266] (21) The method of any one of (18)-(20), wherein the intratumoral administration comprises intratumoral injection.

[00267] (22) The method of any one of (18)-(21), wherein the recombinant interferon is administered in an amount in a range of about 60μg to about 600μg, optionally about 60μg to about 500μg, further optionally about 80μg to about 400μg, still further optionally about 100μg to about 250μg by one intratumoral administration, and the recombinant interferon is administered by intratumoral administration once every about 1 day to about 10 days, optionally every about 1 day to about 7 days such as every about 1, 2, 3, 4, 5, 6, or 7 days, the duration of the intratumoral administration is at least about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject; or the duration can also be about 1 day to about 6 years, about 1 week to about 4 years, about 2 weeks to about 3 years, about 1 month to about 1 year, or about 2 months to about 9 months and the like.

[00268] (23) The method of any one of (18)-(22), wherein the protocol of intratumoral administration is as follows: the recombinant interferon is administered by intratumoral injection once every about 1 day for about 4 to about 8 times, and then the recombinant interferon is administered by intratumoral injection once every

about 3 days to about 5 days for about 4 to about 8 times, and then the recombinant interferon is administered by intratumoral injection once every about 7 days, the intratumoral administration is stopped when the tumor disappears or becomes too small to conduct the intratumoral injection.

[00269] (24) The method of any one of (1)-(23), wherein the subject has the pleural effusion, ascites, and/or pericardial effusion.

[00270] (25) The method of (24), wherein the pleural effusion is a malignant pleural effusion, the ascites is a malignant ascites, and/or the pericardial effusion is a malignant pericardial effusion.

[00271] (26) The method of (24) or (25), wherein the recombinant interferon is administered to the subject by an administration route, the administration route comprises at least one of: intrapleural administration, abdominal administration, and pericardial administration.

[00272] (27) The method of (26), wherein the intrapleural administration comprises intrapleural perfusion.

[00273] (28) The method of (26), wherein the abdominal administration comprises abdominal perfusion.

[00274] (29) The method of (26), wherein the pericardial administration comprises pericardial perfusion.

[00275] (30) The method of any one of (26)-(29), wherein the recombinant interferon is administered in an amount in a range of about 30μg to about 2000μg, optionally about 100μg to about 1500μg, further optionally about 150μg to about 1000μg, still optionally about 200μg to about 800μg by one intrapleural, abdominal, and/or pericardial administration.

[00276] (31) The method of (30), wherein the recombinant interferon is administered in an amount in a range of about 200μg to about 400μg by one intrapleural, abdominal, and/or pericardial administration.

[00277] (32) The method of any one of (26)-(31), wherein the recombinant interferon is administered by intrapleural, abdominal, and/or pericardial administration once every about 1 day to about 10 days, optionally every about 1 day

to about 7 days, such as every about 1, 2, 3, 4, 5, 6, or 7 days.

[00278] (33) The method of any one of (1)-(32), wherein the lung cancer in the subject comprises tumor metastasis in at least one of: skin, mucosa, superficial lymph nodes, and subcutaneous tissue.

[00279] (34) The method of (33), wherein the recombinant interferon is administered to the subject by spray administration.

[00280] (35) The method of (34), wherein the spray administration comprises at least one of: percutaneous spray administration, transdermal spray administration, epidermal spray administration, and transmucosal spray administration.

[00281] (36) The method of (34) or (35), wherein the recombinant interferon is administered in an amount in a range of about 6μg to about 100μg by one spray administration.

[00282] (37) The method of (36), wherein the recombinant interferon is administered in an amount of about 10μg to about 40μg, optionally about 20μg to about 40μg by one spray administration.

[00283] (38) The method of any one of (34)-(37), wherein the recombinant interferon is administered by spray administration about 1 to about 6 times per day, such as about 1, 2, 3, 4, 5, or 6 times per day.

[00284] (39) The method of any one of (1)-(38), wherein the recombinant interferon is administered to the subject as monotherapy.

[00285] (40) The method of any one of (1)-(38), further comprising at least one other anti-cancer therapy administered to the subject, optionally, the at least one other anti-cancer therapy is administered to the subject before, simultaneously, and/or after administration of the recombinant interferon.

[00286] (41) The method of (40), wherein the at least one other anti-cancer therapy comprises one or more of: chemotherapy, radiotherapy, surgical therapy, interventional therapy, biotherapy, gene therapy, ablation therapy, immunotherapy, targeted therapy, and traditional Chinese medicine therapy.

[00287] (42) The method of (41), wherein the at least one other anti-cancer therapy comprises chemotherapy.

[00288] (43) The method of (42), wherein the chemotherapy is the first-line chemotherapy.

[00289] (44) The method of (43), wherein one or more chemotherapeutic drugs used for the first-line chemotherapy comprise platinum compounds, such as Cisplatin.

[00290] (45) The method of (41), wherein the at least one other anti-cancer therapy comprises radiotherapy.

[00291] (46) The method of (45), wherein the radiotherapy comprises head gamma knife therapy when the lung cancer metastasizes to brain.

[00292] (47) The method of (41), wherein the at least one other anti-cancer therapy comprises surgical therapy.

[00293] (48) The method of (41), wherein the at least one other anti-cancer therapy comprises targeted therapy.

[00294] (49) The method of (48), wherein the targeted therapy comprises administering Gefitinib, Erlotinib, and/or recombinant human endostatin.

[00295] (50) The method of (41), wherein the at least one other anti-cancer therapy comprises biotherapy.

[00296] (51) The method of any one of (1)-(50), wherein the therapies eliminate the tumor or reduce the size of the tumor or the number of tumor metastasis compared to the tumor before treatment.

[00297] (52) The method of any one of (1)-(51), wherein the therapies are the non-surgical therapies.

[00298] In another aspect, another embodiment of the present invention provides:

[00299] (1) A method for treating lung cancer in a subject, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2 by subcutaneous administration and/or intramuscular administration, wherein the recombinant interferon is administered one or more times by subcutaneous administration and/or intramuscular administration at an induction dose in a range of about 2μg to about 10μg each time, optionally about 4μg to about 10μg each time, further optionally about 4.5μg to about 9μg each time, such as about 4.5μg each time

or about 9μg each time, and then the recombinant interferon is administered more times by subcutaneous administration and/or intramuscular administration at a therapeutic dose in a range of about 10μg to about 70μg each time, optionally about 12μg to about 50μg each time, further optionally about 12μg to about 30μg each time.

[00300] (2) The method of (1), wherein the lung cancer comprises small cell lung cancer (SCLC), non small cell lung cancer (NSCLC), or both.

[00301] (3) The method of (1) or (2), wherein the tumor in the subject comprises a metastasized tumor.

[00302] (4) The method of any one of (1)-(3), wherein the subject is an early, medium-term, or advanced cancer patient, optionally, the subject is a medium-term, or advanced cancer patient, further optionally, the subject is an advanced cancer patient.

[00303] (5) The method of any one of (1)-(3), wherein the subject is a stage 0, I, II, III, or IV cancer patient, optionally, the subject is a stage III or IV cancer patient.

[00304] (6) The method of any one of (1)-(5), wherein the lung cancer is a lung cancer that is indicated or appropriate for surgery.

[00305] (7) The method of any one of (1)-(5), wherein the lung cancer is a lung cancer that is not indicated nor appropriate for surgery.

[00306] (8) The method of any one of (1)-(5), wherein the lung cancer is a lung cancer that is capable of being resected.

[00307] (9) The method of any one of (1)-(5), wherein the lung cancer is a lung cancer that is not capable of being resected.

[00308] (10) The method of (8) or (9), wherein the lung cancer is resected by a surgical resection.

[00309] (11) The method of any one of (1)-(10), wherein the subcutaneous administration comprises subcutaneous injection.

[00310] (12) The method of any one of (1)-(10), wherein the intramuscular administration comprises intramuscular injection.

[00311] (13) The method of any one of (1)-(12), wherein the time interval between administration of induction dose and administration of therapeutic dose is about 1 day to about 1 month, optionally about 1 day to about 1 week, further

optionally about 1 day to about 3 days, comprising such as about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, or about 1 month.

[00312] (14) The method of any one of (1)-(13), the recombinant interferon is administered once every about 1 day to about 10 days, optionally every about 1 day to about 7 days, further optionally every about 1 to about 2 days, comprising such as every about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 days when the recombinant interferon is administered more times at an induction dose.

[00313] (15) The method of any one of (1)-(14), wherein the recombinant interferon is administered at a therapeutic dose once every about 1 day to about 10 days, optionally every about 1 day to about 7 days, further optionally every about 1 to about 2 days, comprising such as every about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 days.

[00314] (16) The method of any one of (1)-(15), wherein the duration of administration of induction dose and therapeutic dose is at least about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject.

[00315] (17) The method of any one of (1)-(16), further comprising administering to the subject the recombinant interferon by inhalation administration.

[00316] (18) The method of (17), wherein the inhalation administration is conducted before, simultaneously, and/or after the subcutaneous administration and/or intramuscular administration.

[00317] (19) The method of (17) or (18), wherein the inhalation administration comprises pulmonary and/or nasal inhalation administration.

[00318] (20) The method of any one of (17)-(19), wherein the inhalation administration comprises aerosol inhalation.

[00319] (21) The method of any one of (17)-(20), wherein the recombinant interferon is administered in an amount in a range of about 100μg to about 2000μg, optionally about 100μg to about 1500μg, further optionally about 150μg to about 800μg, still further optionally about 200μg to about 600μg by one inhalation administration, the recombinant interferon is administered by inhalation administration once every about 1 day to about 3 days, optionally every about 1 day, lasting at least about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject; or the duration can also be about 1 day to about 6 years, about 1 week to about 4 years, about 2 weeks to about 3 years, about 1 month to about 1 year, or about 2 months to about 9 months and the like.

[00320] (22) The method of any one of (1)-(21), further comprising administering to the subject the recombinant interferon by intratumoral administration.

[00321] (23) The method of (22), wherein the intratumoral administration is conducted before, simultaneously, and/or after the subcutaneous administration and/or intramuscular administration.

[00322] (24) The method of (22), wherein the intratumoral administration is conducted before, simultaneously, and/or after the inhalation administration.

[00323] (25) The method of any one of (22)-(24), wherein the intratumoral administration comprises intratumoral injection.

[00324] (26) The method of any one of (22)-(25), wherein the recombinant interferon is administered in an amount in a range of about 60μg to about 600μg, optionally about 60μg to about 500μg, further optionally about 80μg to about 400μg, still further optionally about 100μg to about 250μg by one intratumoral administration,

and the recombinant interferon is administered by intratumoral administration once every about 1 day to about 10 days, optionally every about 1 day to about 7 days such as every about 1, 2, 3, 4, 5, 6, or 7 days, the duration of the intratumoral administration is at least about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject; or the duration can also be about 1 day to about 6 years, about 1 week to about 4 years, about 2 weeks to about 3 years, about 1 month to about 1 year, or about 2 months to about 9 months and the like.

[00325] (27) The method of any one of (22)-(26), wherein the protocol of intratumoral administration is as follows: the recombinant interferon is administered by intratumoral injection once every about 1 day for about 4 to about 8 times, and then the recombinant interferon is administered by intratumoral injection once every about 3 days to about 5 days for about 4 to about 8 times, and then the recombinant interferon is administered by intratumoral injection once every about 7 days, the intratumoral administration is stopped when the tumor disappears or becomes too small to conduct the intratumoral injection.

[00326] (28) The method of any one of (1)-(27), wherein the subject has the pleural effusion, ascites, and/or pericardial effusion.

[00327] (29) The method of (28), wherein the pleural effusion is a malignant pleural effusion, the ascites is a malignant ascites, and/or the pericardial effusion is a malignant pericardial effusion.

[00328] (30) The method of (28) or (29), wherein the recombinant interferon is administered to the subject by an administration route, the administration route comprises at least one of: intrapleural administration, abdominal administration, and pericardial administration.

[00329] (31) The method of (30), wherein the intrapleural administration comprises intrapleural perfusion.

[00330] (32) The method of (30), wherein the abdominal administration comprises abdominal perfusion.

[00331] (33) The method of (30), wherein the pericardial administration comprises pericardial perfusion.

[00332] (34) The method of any one of (30)-(33), wherein the recombinant interferon is administered in an amount in a range of about 30μg to about 2000μg, optionally about 100μg to about 1500μg, further optionally about 150μg to about 1000μg, still optionally about 200μg to about 800μg by one intrapleural administration, abdominal administration, and/or pericardial administration.

[00333] (35) The method of (34), wherein the recombinant interferon is administered in an amount in a range of about 200μg to about 400μg by one intrapleural administration, abdominal administration, and/or pericardial administration.

[00334] (36) The method of any one of (30)-(35), wherein the recombinant interferon is administered by intrapleural administration, abdominal administration, and/or pericardial administration once every about 1 day to about 10 days, optionally every about 1 day to about 7 days, such as every about 1, 2, 3, 4, 5, 6, or 7 days.

[00335] (37) The method of any one of (1)-(36), wherein the lung cancer in the subject comprises tumor metastasis in at least one of: skin, mucosa, superficial lymph nodes, and subcutaneous tissue.

[00336] (38) The method of (37), wherein the recombinant interferon is administered to the subject by spray administration.

[00337] (39) The method of (38), wherein the spray administration comprises at least one of: percutaneous spray administration, transdermal spray administration, epidermal spray administration, and transmucosal spray administration.

[00338] (40) The method of (38) or (39), wherein the recombinant interferon is administered in an amount in a range of about 6μg to about 100μg by one spray administration.

[00339] (41) The method of (40), wherein the recombinant interferon is administered in an amount in a range of about 10μg to about 40μg, optionally about 20μg to about 40μg by one spray administration.

[00340] (42) The method of any one of (38)-(41), wherein the recombinant interferon is administered by spray administration about 1 to about 6 times per day, such as about 1, 2, 3, 4, 5, or 6 times per day.

[00341] (43) The method of any one of (1)-(42), wherein the recombinant interferon is administered to the subject as monotherapy.

[00342] (44) The method of any one of (1)-(42), further comprising at least one other anti-cancer therapy administered to the subject, optionally, the at least one other anti-cancer therapy is administered to the subject before, simultaneously, and/or after administration of the recombinant interferon.

[00343] (45) The method of (44), wherein the at least one other anti-cancer therapy comprises one or more of: chemotherapy, radiotherapy, surgical therapy, interventional therapy, biotherapy, gene therapy, ablation therapy, immunotherapy, targeted therapy, and traditional Chinese medicine therapy.

[00344] (46) The method of (45), wherein the at least one other anti-cancer therapy comprises chemotherapy.

[00345] (47) The method of (46), wherein the chemotherapy is the first-line chemotherapy.

[00346] (48) The method of (47), wherein one or more chemotherapeutic drugs are used for the first-line chemotherapy and comprise platinum compounds, such as Cisplatin.

[00347] (49) The method of (45), wherein the at least one other anti-cancer therapy comprises radiotherapy.

[00348] (50) The method of (49), wherein the radiotherapy comprises head gamma knife therapy when the lung cancer metastasizes to brain.

[00349] (51) The method of (45), wherein the at least one other anti-cancer therapy comprises surgical therapy.

[00350] (52) The method of (45), wherein the at least one other anti-cancer

therapy comprises targeted therapy.

[00351] (53) The method of (52), wherein the targeted therapy comprises administering Gefitinib, Erlotinib, and/or recombinant human endostatin.

[00352] (54) The method of (45), wherein the at least one other anti-cancer therapy comprises biotherapy.

[00353] (55) The method of any one of (1)-(54), wherein the therapies eliminate the tumor of the lung or reduce the size of the tumor of the lung compared to the tumor size before treatment.

[00354] (56) The method of any one of (1)-(55), wherein the therapies are the non-surgical therapies.

[00355] In another aspect, another embodiment of the present invention provides:

[00356] (1) A method for treating cancer in a subject, wherein the cancer originates from lung cancer in the subject and metastasizes to brain, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2, wherein the recombinant interferon is administered one or more times by subcutaneous administration and/or intramuscular administration at an induction dose in a range of about 2μg to about 10μg each time, optionally about 4μg to about 10μg each time, further optionally about 4.5μg to about 9μg each time, such as about 4.5μg each time or about 9μg each time, and then the recombinant interferon is administered more times by subcutaneous administration and/or intramuscular administration at a therapeutic dose in a range of about 10μg to about 70μg each time, optionally about 12μg to about 50μg each time, further optionally about 12μg to about 30μg each time, and the recombinant interferon is administered to the subject by inhalation administration before, simultaneously, and/or after the subcutaneous administration and/or intramuscular administration, the recombinant interferon is administered in an amount in a range of about 100μg to about 2000μg, optionally about 100μg to about 1500μg, further optionally about 150μg to about 800μg, still further optionally about 200μg to about 600μg by one inhalation administration, and the recombinant interferon is administered by inhalation administration once every about 1 day to

about 3 days, optionally every about 1 day.

[00357] (2) The method of (1), wherein the subject is a medium-term, advanced, or stage III or stage IV cancer patient, optionally, the subject is an advanced, or stage III or stage IV cancer patient.

[00358] (3) The method of (1) or (2), wherein the cancer is a cancer that is not indicated nor appropriate for surgery.

[00359] (4) The method of (1) or (2), wherein the tumor is a tumor that is not capable of being resected.

[00360] (5) The method of (4), wherein the tumor is resected by a surgical resection.

[00361] (6) The method of any one of (1)-(5), wherein the subcutaneous administration comprises subcutaneous injection.

[00362] (7) The method of any one of (1)-(5), wherein the intramuscular administration comprises intramuscular injection.

[00363] (8) The method of any one of (1)-(7), wherein the inhalation administration comprises pulmonary and/or nasal inhalation administration.

[00364] (9) The method of any one of (1)-(8), wherein the inhalation administration comprises aerosol inhalation.

[00365] (10) The method of any one of (1)-(9), wherein the time interval between administration of induction dose and administration of therapeutic dose is about 1 day to about 1 month, optionally about 1 day to about 1 week, further optionally about 1 day to about 3 days, comprising such as about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, or about 1 month.

[00366] (11) The method of any one of (1)-(10), wherein the recombinant interferon is administered once every about 1 day to about 10 days, optionally every about 1 day to about 7 days, further optionally every about 1 to about 2 days, comprising such as every about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 days when the recombinant interferon is administered more times at an induction dose.

[00367] (12) The method of any one of (1)-(11), wherein the recombinant interferon is administered at a therapeutic dose once every about 1 day to about 10 days, optionally every about 1 day to about 7 days, further optionally every about 1 to about 2 days, comprising such as every about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 days.

[00368] (13) The method of any one of (1)-(12), wherein the duration of administration of induction dose and therapeutic dose is at least about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject.

[00369] (14) The method of any one of (1)-(13), wherein the duration of the inhalation administration is at least about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject; or the duration can also be about 1 day to about 6 years, about 1 week to about 4 years, about 2 weeks to about 3 years, about 1 month to about 1 year, or about 2 months to about 9 months and the like.

[00370] (15) The method of any one of (1)-(14), wherein the recombinant interferon is administered to the subject as monotherapy.

[00371] (16) The method of any one of (1)-(15), further comprising at least one other anti-cancer therapy administered to the subject, optionally, the at least one other anti-cancer therapy is administered to the subject before, simultaneously, and/or after administration of the recombinant interferon.

[00372] (17) The method of (16), wherein the at least one other anti-cancer

therapy comprises one or more of: chemotherapy, radiotherapy, surgical therapy, interventional therapy, biotherapy, gene therapy, ablation therapy, immunotherapy, targeted therapy, and traditional Chinese medicine therapy.

[00373] (18) The method of (17), wherein the chemotherapy is the first-line chemotherapy, optionally, one or more chemotherapeutic drugs are used for the first-line chemotherapy and comprise platinum compounds, such as Cisplatin.

[00374] (19) The method of (17), wherein the targeted therapy comprises administering Gefitinib, Erlotinib, and/or recombinant human endostatin.

[00375] (20) The method of (17), wherein the at least one other anti-cancer therapy comprises radiotherapy.

[00376] (21) The method of (20), wherein the radiotherapy comprises gamma knife therapy.

[00377] (22) The method of (21), wherein the gamma knife therapy comprises head gamma knife therapy.

[00378] (23) The method of any one of (1)-(22), wherein the therapies eliminate the tumor or reduce the size of the tumor compared to the tumor before treatment.

[00379] (24) The method of any one of (1)-(23), wherein the therapies are the non-surgical therapies.

[00380] In another aspect, another embodiment of the present invention provides:

[00381] (1) A method for treating cancer in a subject, wherein the cancer originates from lung cancer in the subject and metastasizes to bone or liver, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2, wherein the recombinant interferon is administered one or more times by subcutaneous administration and/or intramuscular administration at an induction dose in a range of about 2μg to about 10μg each time, optionally about 4μg to about 10μg each time, further optionally about 4.5μg to about 9μg each time, such as about 4.5μg each time or about 9μg each time, and then the recombinant interferon is administered more times by subcutaneous administration and/or intramuscular administration at a

therapeutic dose of about 10μg -about 70μg each time, optionally about 12μg to about 50μg each time, further optionally about 12μg to about 30μg each time.

[00382] (2) The method of (1), wherein the subject is a medium-term, advanced, or stage III or stage IV cancer patient, optionally, the subject is an advanced, or stage III or stage IV cancer patient.

[00383] (3) The method of (1) or (2), wherein the cancer is a cancer that is not indicated nor appropriate for surgery.

[00384] (4) The method of (1) or (2), wherein the tumor is a tumor that is not capable of being resected.

[00385] (5) The method of (4), wherein the tumor is resected by a surgical resection.

[00386] (6) The method of any one of (1)-(5), wherein the subcutaneous administration comprises subcutaneous injection.

[00387] (7) The method of any one of (1)-(5), wherein the intramuscular administration comprises intramuscular injection.

[00388] (8) The method of any one of (1)-(7), wherein the time interval between administration of induction dose and administration of therapeutic dose is about 1 day to about 1 month, optionally about 1 day to about 1 week, further optionally about 1 day to about 3 days, comprising such as about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, or about 1 month.

[00389] (9) The method of any one of (1)-(8), wherein the recombinant interferon is administered once every about 1 day to about 10 days, optionally every about 1 day to about 7 days, further optionally every about 1 to about 2 days, comprising such as every about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 days when the recombinant interferon is administered more times at an induction dose.

[00390] (10) The method of any one of (1)-(9), wherein the recombinant interferon is administered at a therapeutic dose once every about 1 day to about 10 days, optionally every about 1 day to about 7 days, further optionally every about 1 to

about 2 days, comprising such as every about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 days.

[00391] (11) The method of any one of (1)-(10), wherein the duration of administration of induction dose and therapeutic dose is at least about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject.

[00392] (12) The method of any one of (1)-(11), further comprising administering to the subject the recombinant interferon by inhalation administration.

[00393] (13) The method of (12), wherein the inhalation administration is conducted before, simultaneously, and/or after the subcutaneous administration and/or intramuscular administration.

[00394] (14) The method of (12) or (13), wherein the inhalation administration comprises pulmonary and/or nasal inhalation administration.

[00395] (15) The method of any one of (12)-(14), wherein the inhalation administration comprises aerosol inhalation.

[00396] (16) The method of any one of (12)-(15), wherein the recombinant interferon is administered in an amount in a range of about 100μg to about 2000μg, optionally about 100μg to about 1500μg, further optionally about 150μg to about 800μg, still further optionally about 200μg to about 600μg by one inhalation administration, the recombinant interferon is administered by inhalation administration once every about 1 day to about 3 days, optionally every about 1 day, and the duration of the inhalation administration is at least about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or

about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject; or the duration can also be about 1 day to about 6 years, about 1 week to about 4 years, about 2 weeks to about 3 years, about 1 month to about 1 year, or about 2 months to about 9 months and the like.

[00397] (17) The method of any one of (1)-(16), wherein the recombinant interferon is administered to the subject as monotherapy.

[00398] (18) The method of any one of (1)-(16), further comprising at least one other anti-cancer therapy administered to the subject, optionally, the at least one other anti-cancer therapy is administered to the subject before, simultaneously, and/or after administration of the recombinant interferon.

[00399] (19) The method of (18), wherein the at least one other anti-cancer therapy comprises one or more of: chemotherapy, radiotherapy, surgical therapy, interventional therapy, biotherapy, gene therapy, ablation therapy, immunotherapy, targeted therapy, and traditional Chinese medicine therapy.

[00400] (20) The method of (19), wherein the at least one other anti-cancer therapy comprises chemotherapy.

[00401] (21) The method of (20), wherein the chemotherapy is first-line chemotherapy.

[00402] (22) The method of (21), wherein one or more chemotherapeutic drugs are used for the first-line chemotherapy and comprise platinum compounds, such as Cisplatin.

[00403] (23) The method of (19), wherein the at least one other anti-cancer therapy comprises targeted therapy.

[00404] (24) The method of (23), wherein the targeted therapy comprises administering Gefitinib, Erlotinib, and/or recombinant human endostatin.

[00405] (25) The method of (19), wherein the at least one other anti-cancer therapy comprises biotherapy.

[00406] (26) The method of any one of (1)-(25), wherein the therapies eliminate the tumor or reduce the size of the tumor compared to the tumor before treatment.

[00407] (27) The method of any one of (1)-(26), wherein the therapies are the non-surgical therapies.

[00408] In another aspect, another embodiment of the present invention provides:

[00409] (1) A method for treating cancer in a subject, wherein the cancer originates from lung cancer in the subject and metastasizes to lymph nodes, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2, wherein the recombinant interferon is administered one or more times by subcutaneous administration and/or intramuscular administration at an induction dose in a range of about 2μg to about 10μg each time, optionally about 4μg to about 10μg each time, further optionally about 4.5μg to about 9μg each time, such as about 4.5μg each time or about 9μg each time, and then the recombinant interferon is administered more times by subcutaneous administration and/or intramuscular administration at a therapeutic dose of about 10μg to about 70μg each time, optionally about 12μg to about 50μg each time, further optionally about 12μg to about 30μg each time, and the recombinant interferon is administered to the tumor and/or the lymph nodes metastases by topical or local administration before, simultaneously, and/or after the subcutaneous administration and/or intramuscular administration.

[00410] (2) The method of (1), wherein the subject is a medium-term, advanced, or stage III or stage IV cancer patient, optionally, the subject is an advanced, or stage III or stage IV cancer patient.

[00411] (3) The method of (1) or (2), wherein the cancer is a cancer that is not indicated nor appropriate for surgery.

[00412] (4) The method of (1) or (2), wherein the tumor is a tumor that is not capable of being resected.

[00413] (5) The method of (4), wherein the tumor is resected by a surgical resection.

[00414] (6) The method of any one of (1)-(5), wherein the subcutaneous administration comprises subcutaneous injection.

[00415] (7) The method of any one of (1)-(5), wherein the intramuscular

administration comprises intramuscular injection.

[00416] (8) The method of any one of (1)-(7), wherein the time interval between administration of induction dose and administration of therapeutic dose is about 1 day to about 1 month, optionally about 1 day to about 1 week, further optionally about 1 day to about 3 days, comprising such as about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, or about 1 month.

[00417] (9) The method of any one of (1)-(8), wherein the recombinant interferon is administered once every about 1 day to about 10 days, optionally every about 1 day to about 7 days, further optionally every about 1 to about 2 days, comprising such as every about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 days when the recombinant interferon is administered more times at an induction dose.

[00418] (10) The method of any one of (1)-(9), wherein the recombinant interferon is administered at a therapeutic dose once every about 1 day to about 10 days, optionally every about 1 day to about 7 days, further optionally every about 1 to about 2 days, comprising such as every about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 days.

[00419] (11) The method of any one of (1)-(10), wherein the duration of administration of induction dose and therapeutic dose is at least about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject.

[00420] (12) The method of any one of (1)-(11), wherein the local administration comprises intratumoral administration when the lymph nodes are the deep lymph nodes.

[00421] (13) The method of (12), wherein the intratumoral administration comprises intratumoral injection.

[00422] (14) The method of (12) or (13), wherein the recombinant interferon is administered in an amount in a range of about 60μg to about 600μg, optionally about 60μg to about 500μg, further optionally about 80μg to about 400μg, still further optionally about 100μg to about 250μg by one intratumoral administration, and the recombinant interferon is administered by intratumoral administration once every about 1 day to about 10 days, optionally every about 1 day to about 7 days such as every about 1, 2, 3, 4, 5, 6, or 7 days, the duration of the intratumoral administration is at least about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject; or the duration can also be about 1 day to about 6 years, about 1 week to about 4 years, about 2 weeks to about 3 years, about 1 month to about 1 year, or about 2 months to about 9 months and the like.

[00423] (15) The method of any one of (12)-(14), wherein the protocol of intratumoral administration is as follow: the recombinant interferon is administered by intratumoral injection once every about 1 day for about 4 to about 8 times, and then the recombinant interferon is administered by intratumoral injection once every about 3 days to about 5 days for about 4 to about 8 times, and then the recombinant interferon is administered by intratumoral injection once every about 7 days, the intratumoral administration is stopped when the tumor and/or metastasized lymph nodes are disappeared or become too small to conduct the intratumoral injection.

[00424] (16) The method of any one of (1)-(11), wherein the topical or local administration comprises at least one of: infiltration administration, percutaneous administration, transdermal administration, epidermal administration, and transmucosal administration when the lymph nodes are superficial lymph nodes.

[00425] (17) The method of (16), wherein the local administration comprises

infiltration administration.

[00426] (18) The method of (17), wherein the infiltration administration is conducted by perfusion.

[00427] (19) The method of (16), wherein the percutaneous administration, transdermal administration, epidermal administration, or transmucosal administration comprises percutaneous spray administration, transdermal spray administration, epidermal spray administration, or transmucosal spray administration, respectively.

[00428] (20) The method of (19), wherein the recombinant interferon is administered in an amount in a range of about 6μg to about 100μg by one spray administration.

[00429] (21) The method of (20), wherein the recombinant interferon is administered in an amount of about 10μg to about 40μg, optionally about 20μg to about 40μg by one spray administration.

[00430] (22) The method of any one of (19)-(21), wherein the recombinant interferon is administered by spray administration about 1 to about 6 times such as about 1, 2, 3, 4, 5, or 6 times per day.

[00431] (23) The method of any one of (1)-(22), wherein the recombinant interferon is administered to the subject as monotherapy.

[00432] (24) The method of any one of (1)-(22), further comprising at least one other anti-cancer therapy administered to the subject, optionally, the at least one other anti-cancer therapy is administered to the subject before, simultaneously, and/or after administration of the recombinant interferon.

[00433] (25) The method of (24), wherein the at least one other anti-cancer therapy comprises one or more of: chemotherapy, radiotherapy, surgical therapy, interventional therapy, biotherapy, gene therapy, ablation therapy, immunotherapy, targeted therapy, and traditional Chinese medicine therapy.

[00434] (26) The method of (25), wherein the at least one other anti-cancer therapy comprises chemotherapy.

[00435] (27) The method of (26), wherein the chemotherapy is first-line chemotherapy.

[00436] (28) The method of (27), wherein one or more chemotherapeutic drugs are used for the first-line chemotherapy and comprise platinum compounds, such as Cisplatin.

[00437] (29) The method of (25), wherein the at least one other anti-cancer therapy comprises targeted therapy.

[00438] (30) The method of (29), wherein the targeted therapy comprises administering Gefitinib, Erlotinib, and/or recombinant human endostatin.

[00439] (31) The method of (25), wherein the at least one other anti-cancer therapy comprises biotherapy.

[00440] (32) The method of any one of (1)-(31), wherein the therapies eliminate the tumor or reduce the size of the tumor compared to the tumor before treatment.

[00441] (33) The method of any one of (1)-(32), wherein the therapies are the non-surgical therapies.

[00442] In another aspect, another embodiment of the present invention provides:

[00443] (1) A method for treating lung cancer in a subject, wherein the subject has pleural effusion, ascites and/or pericardial effusion, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2 by topical or local administration.

[00444] (2) The method of (1), wherein the subject is a medium-term, advanced, or stage III or stage IV cancer patient, optionally, the subject is an advanced, or stage III or stage IV cancer patient.

[00445] (3) The method of (1) or (2), wherein the lung cancer is a lung cancer that is not indicated nor appropriate for surgery.

[00446] (4) The method of (1) or (2), wherein the lung cancer is a lung cancer that is not capable of being resected.

[00447] (5) The method of (4), wherein the tumor is resected by a surgical resection.

[00448] (6) The method of any one of (1)-(5), wherein the pleural effusion is a

malignant pleural effusion, the ascites is a malignant ascites, and/or the pericardial effusion is a malignant pericardial effusion.

[00449] (7) The method of any one of (1)-(6), wherein the local administration comprises at least one of:infiltration administration, intrapleural administration, abdominal administration, and pericardial administration.

[00450] (8) The method of (7), wherein the local administration is conducted by perfusion.

[00451] (9) The method of (8), wherein the recombinant interferon is administered in an amount in a range of about 30μg to about 2000μg, optionally about 100μg to about 1500μg, further optionally about 150μg to about 1000μg, still optionally about 200μg to about 800μg, still further optionally about 200μg to about 400μg by one perfusion administration.

[00452] (10) The method of (8) or (9), wherein the recombinant interferon is administered by perfusion administration once every about 1 to about 10 days, optionally every about 1 to about 7 days, such as every about 1, 2, 3, 4, 5, 6, or 7 days.

[00453] (11) The method of (10), wherein the recombinant interferon is administered by perfusion administration once every about 1 day, lasting about 4 to about 6 times.

[00454] (12) The method of any one of (1)-(11), wherein the recombinant interferon is administered to the subject by systemic administration before, simultaneously, and/or after the topical or local administration.

[00455] (13) The method of (12), wherein the systemic administration comprises subcutaneous and/or intramuscular administration.

[00456] (14) The method of (13), wherein the subcutaneous administration comprises subcutaneous injection.

[00457] (15) The method of (13), wherein the intramuscular administration comprises intramuscular injection.

[00458] (16) The method of any one of (13)-(15), wherein the recombinant interferon is administered one or more times by subcutaneous administration and/or intramuscular administration at an induction dose in a range of about 2μg to about

10μg each time, optionally about 4μg to about 10μg each time, further optionally about 4.5μg to about 9μg each time, such as about 4.5μg each time or about 9μg each time, and then the recombinant interferon is administered more times by subcutaneous administration and/or intramuscular administration at a therapeutic dose of about 10μg to about 70μg each time, optionally about 12μg to about 50μg each time, further optionally about 12μg to about 30μg each time.

[00459] (17) The method of (16), wherein the time interval between administration of induction dose and administration of therapeutic dose is about 1 day to about 1 month, optionally about 1 day to about 1 week, further optionally about 1 day to about 3 days, comprising such as about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, or about 1 month.

[00460] (18) The method of (16) or (17), wherein the recombinant interferon is administered once every about 1 day to about 10 days, optionally every about 1 day to about 7 days, further optionally every about 1 to about 2 days, comprising such as every about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 days when the recombinant interferon is administered more times at an induction dose.

[00461] (19) The method of any one of (16)-(18), wherein the recombinant interferon is administered at a therapeutic dose once every about 1 day to about 10 days, optionally every about 1 day to about 7 days, further optionally every about 1 to about 2 days, comprising such as every about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 days.

[00462] (20) The method of any one of (16)-(19), wherein the duration of administration of induction dose and therapeutic dose is at least about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject.

[00463] (21) The method of any one of (1)-(20), wherein other therapeutic

drugs are further administered by topical, local and/or systemic administration

[00464] (22) The method of (21), wherein the other therapeutic drugs comprise antitumor drugs.

[00465] (23) The method of (22), wherein the antitumor drugs comprise one or more chemotherapeutic drugs, targeted drugs, or biological drugs.

[00466] (24) The method of (23), wherein one or more chemotherapeutic drugs comprise platinum compounds, such as Cisplatin.

[00467] (25) The method of (23), wherein one or more targeted drugs comprise Gefitinib, Erlotinib, and/or recombinant human endostatin

[00468] (26) The method of any one of (1)-(25), wherein the therapies eliminate the tumor or reduce the size of the tumor compared to the tumor size before treatment.

[00469] (27) The method of any one of (1)-(26), wherein the therapies are the non-surgical therapies.

[00470] More specifically, in one embodiment, in any one of the methods of the present invention mentioned above, the tumor is a solid tumor; optionally, the solid tumor comprises one or more of: lung cancer, liver cancer, hepatocellular carcinoma (HCC), esophageal cancer, cholangiocarcinoma, gallbladder carcinoma, stomach cancer, abdominal cancer, gastrointestinal cancer, gastric cancer, pancreatic cancer, renal cell carcinoma, renal cancer, bone cancer, breast cancer, ovarian cancer, uterine cancer, cervical cancer, endometrial cancer, colorectal cancer, colon cancer, rectal cancer, bladder cancer, superficial bladder cancer, prostate cancer, adrenal tumors, squamous cell carcinoma, neuroma, malignant neuroma, myoepithelial carcinoma, synovial sarcoma, rhabdomyosarcoma, gastrointestinal interstitial cell tumor, skin cancer, basal cell carcinoma, malignant melanoma, thyroid cancer, nasopharyngeal carcinoma, hemangioma, epidermoid carcinoma, head and neck cancer, glioma, or Kaposi's sarcoma.

[00471] In any one of methods of the present invention mentioned above, the tumor is a tumor such as cancer or solid tumor without indications for surgery or not indicated or appropriate for surgery; and/or the subject is a medium-term, advanced

cancer patient, or III or IV stage cancer patient, optionally, the subject is an advanced, or III or IV stage cancer patient.

[00472] In any one of methods of the present invention mentioned above, the recombinant interferon is administered to the subject as monotherapy; or, further comprising one or more other anti-cancer therapies administered to the subject, optionally, other anti-cancer therapies are administered to the subject before, simultaneously, and/or after administration of the recombinant interferon. Optionally, the other anti-cancer therapies comprise one or more of: chemotherapy, radiotherapy, surgical therapy, interventional therapy, biotherapy, gene therapy, ablation therapy, immunotherapy, targeted therapy, and traditional Chinese medicine therapy.

[00473] And, in another aspect, another embodiment of the present invention also provides:

[00474] (1) A method of treating a tumor in a subject comprising administering to the subject a recombinant interferon that comprises an anti-tumor effect as a first line monotherapy.

[00475] (2) The method of (1), wherein the tumor comprises one of: lung cancer, uterine cancer, cervical cancer, and pancreatic cancer.

[00476] (3) The method of (2), wherein the lung cancer comprises non-small cell lung cancer.

[00477] (4) The method of (1), wherein the tumor is not a kidney cancer.

[00478] (5) A method of treating a tumor in a subject comprising administering to the subject a recombinant interferon that comprises an antitumor effect as a second line monotherapy.

[00479] (6) The method of (5), wherein the tumor comprises one of: lung cancer, colorectal cancer, malignant melanoma, ovarian cancer, cervical cancer, liver cancer, breast cancer, gastrointestinal cancer, prostate cancer, neuroma, and squamous cell carcinoma.

[00480] (7) The method of (6), wherein the colorectal cancer comprises colon cancer.

[00481] (8) The method of (6), wherein the colorectal cancer comprises rectal

cancer.

[00482] (9) The method of (6), wherein the lung cancer comprises non-small cell lung cancer.

[00483] (10) The method of (6), wherein the liver cancer comprises HCC.

[00484] (11) The method of (6), wherein the gastrointestinal cancer comprises gastric cancer.

[00485] (12) A method of treating a tumor in a subject comprising administering to the subject a recombinant interferon that comprises an anti-tumor effect as a first line therapy in combination with one or more other anti-cancer therapy.

[00486] (13) The method of (12), wherein the tumor comprises one of: lung cancer, prostate cancer, and lymphoma.

[00487] (14) The method of (13), wherein the lung cancer comprises at least one of non-small cell lung cancer and small cell lung cancer.

[00488] (15) The method of (12), wherein the tumor is not an ovarian cancer.

[00489] (16) A method of treating a tumor in a subject comprising administering to the subject a recombinant interferon that comprises an anti-tumor effect as a second line therapy in combination with one or more other anti-cancer therapies.

[00490] (17) The method of (16), wherein the tumor comprises one of: lung cancer, lymphoma, cervical cancer, and cholangioadenocarcinoma.

[00491] (18) The method of (17), wherein the lung cancer comprises at least one of non-small cell lung cancer and small cell lung cancer.

[00492] (19) The method of (17), wherein the lymphoma is non-Hodgkins lymphoma.

[00493] (20) The method of any of (12), (13), (14), (15), (16), (17), (18), or (19), wherein the one or more other anti-cancer therapies comprise at least one of: radiotherapy, small molecule therapy, chemotherapy, biologics therapy, TCM, and surgery.

[00494] (21) The method of (20), wherein the small molecule in the small

molecule therapy comprises Getifinib.

[00495] (22) The method of (20), wherein the biologics therapy comprises treatment with at least one of: a recombinant protein and isolated cells.

[00496] (23) The method of (22), wherein the recombinant protein comprises Endostar.

[00497] (24) The method of (22), wherein the isolated cells comprises at least one of: stem cells and NK cells.

[00498] (25) The method of (20), wherein the recombinant interferon is administered after surgical treatment of cancer.

[00499] (26) The method of any of (20)-(24), wherein the recombinant interferon is administered prior to surgical treatment of cancer.

[00500] (27) The method of any of (1)-(26), wherein the recombinant interferon is administered by at least one of the following routes: systemically and locally.

[00501] (28) The method of any of (1)-(26), wherein the recombinant interferon is administered by at least one of the following routes: intramuscularly, intraperitoneally, intravenously, intra-arterially, intratumorally, by injection into lymph nodes, topically, locally on the tumor, intranasally, subcutaneously, by spraying, by inhalation, by perfusion, and by infusion.

[00502] (29) The method of any of (1)-(28), wherein the recombinant interferon comprises rSIFN-co.

[00503] (30) The method of (29), wherein the recombinant interferon is administered at a dose in a range of about 2μg to about 2500μg per treatment.

[00504] (31) The method of (29), wherein recombinant interferon is administered at a dose in a range of about 9μg to about 2100μg per treatment.

[00505] (32) The method of (29), wherein recombinant interferon is administered at a dose of one or more of the following doses: 2μg, 4μg, 9 μg, 13.5μg, 15μg, 18μg, 21μg, 24μg, 25.5μg, 30μg, 36μg, 45μg, 70μg, 84μg, 90μg, 100μg, 105μg, 120μg, 126μg, 139μg, 150μg, 168μg, 180μg, 189μg, 198μg, 200μg, 207μg, 210μg, 240μg, 252μg, 273μg, 300μg, 315μg, 400μg, 500μg, 600μg, 1000μg, 2000μg,

2100μg.

[00506] (33) The method of any of (1)-(32), wherein the recombinant interferon comprises a specified activity.

[00507] (34) The method of (33), wherein the recombinant interferon comprises an activity in the range of about 4.4 x 10^8 IU/mg to about 1.0 x 10^9 IU/mg, and optionally greater than 5.5 x 10^8 IU/mg.

[00508] (35) A method of preventing tumor recurrence in a subject comprising administering an amount of a recombinant interferon that comprises an amino acid sequence that is encoded by a nucleic acid sequence comprising the sequence of SEQ ID NO: 2 after surgery, chemotherapy, radiotherapy, cryoablation, radiofrequency ablation, biologics therapy, intervention therapy, and/or rSIFN-co therapy, whereby the recombinant interferon is administered after tumor bulk in the subject has been reduced.

[00509] (36) A method of prolonging tumor-free survival in a subject comprising administering an amount of a recombinant interferon that comprises an amino acid sequence that is encoded by a nucleic acid sequence comprising the sequence of SEQ ID NO: 2 after surgery, chemotherapy, radiotherapy, cryoablation, radiofrequency ablation, biologics therapy, intervention therapy, and/or rSIFN-co therapy, whereby the recombinant interferon is administered after tumor bulk in the subject has been reduced.

BRIEF DESCRIPTION OF THE DRAWINGS

[00510] FIG. 1 shows the comparative difference in the structures of the present recombinant interferon (rSIFN-co) and IFN-α2b, wherein in a side view and a top view in the FIG. 1, the red shows rSIFN-co, the green shows IFN-α2b, the red is black in a black and white print drawing, and the green is grey in the black and white print drawing.

[00511] FIG. 2 shows the comparative difference of the three-dimensional structure of the recombinant interferon rSIFN-co of the present invention and the

computation model structure of INFERGEN® (being indicated as am-Infergen or Infergen) of the US Amgen, wherein in a circle in the right drawing, a thin line in yellow is rSIFN-co, and a thick spiral in blue is am-Infergen. Meanwhile, in the right drawing, the red shows rSIFN-co, and the green shows am-Infergen, wherein the red is black in the black and white print drawing, and the green is grey in the black and white print drawing.

[00512] FIG. 3 shows the treatment situation of patient 1, wherein an arrow in FIG. 3a shows state of the original lesion observed in a CT image on 8th Nov., Year 2, after 12 months of medication; and an arrow in FIG. 3b shows state of the original lesion observed in a CT image on 1st Feb., Year 3, after 15 months of medication, the year of the start of treatment being Year 1.

[00513] FIG. 4 shows the treatment situation of patient 2, wherein FIG. 4a shows a PET/CT imaging diagnosis before rSIFN-co medication, and an arrow indicates the lesion; and FIG. 4b shows a PET/CT imaging diagnosis after rSIFN-co medication, and an arrow indicates the state of the original lesion after treatment.

[00514] FIGS. 5 and 6 show the treatment situation of patient 3, wherein FIG. 5a shows a lung CT image before rSIFN-co medication, and an arrow indicates the lesion; FIG. 5b shows head and chest CT imaging diagnoses after rSIFN-co medication, and an arrow indicates the state of the original lesion after treatment; FIG. 6a shows a brain CT image before rSIFN-co medication, and an arrow indicates the lesion; and figure 6b shows head and chest imaging diagnoses after rSIFN-co medication, and an arrow indicates the state of the original lesion after treatment.

[00515] FIG. 7 and FIG. 8 show the treatment situation of patient 4, wherein FIGS. 7a and 8a show imaging diagnoses before rSIFN-co medication: as shown in PET/CT after chemotherapy, arrows in the FIGS. 7a and 8a indicate the lesions; and FIGS. 7b and 8b show imaging diagnoses after rSIFN-co medication: as shown in PET/CT, an arrow indicates the state of the original lesion after treatment.

[00516] FIGS. 9-11 show the treatment situation of patient 5, wherein FIGS. 9a, 10a and 11a show imaging diagnoses before rSIFN-co medication: as shown in PET/CT, and arrows in the FIGS. 9a, 10a and 11a show the lesions; and FIGS. 9b, 10b and 11b show imaging diagnoses after rSIFN-co medication: as shown in PET/CT, and arrows in the FIGS. 9b, 10b and 11b show the states of the original lesions after treatment.

[00517] FIG. 12 shows the treatment situation of patient 6, wherein FIG. 12a shows a chest CT imaging diagnosis before rSIFN-co medication, and an arrow shows the original lesion; and FIG. 12b shows a CT imaging diagnosis after rSIFN-co medication, and an arrow shows the state of the original lesion after treatment.

[00518] FIGS. 13 and 14 show the treatment situation of patient 7, wherein FIGS. 13a and 14a show CT imaging diagnoses before rSIFN-co medication, and arrows show the original lesions; and FIGS. 13b and 14b show CT imaging diagnoses after rSIFN-co medication, and arrows show the states of the original lesions after treatment.

[00519] FIGS. 15 and 16 show the treatment situation of patient 8, wherein FIGS. 15a and 16a show CT imaging diagnoses before rSIFN-co medication, and arrows show the original lesions; and FIGS. 15b and 16b show CT imaging diagnoses after rSIFN-co medication, and arrows show the states of the original lesions after treatment.

[00520] FIG. 17 shows the treatment situation of patient 9, wherein FIGS. 17a shows a CT imaging diagnosis before rSIFN-co medication, and an arrow shows the original lesion; and FIGS. 17b shows a CT imaging diagnosis after rSIFN-co medication, and an arrow shows the state of the original lesion after treatment.

[00521] FIGS. 18 and 19 show the treatment situation of patient 10, wherein the FIG. 18 shows pleural effusion change before and after the treatment; FIG. 19a shows a chest CT imaging diagnosis before rSIFN-co medication, and an arrow shows the original lesion; and FIG. 19b shows a chest CT imaging

diagnosis after rSIFN-co medication, and an arrow shows the state of the original lesion after treatment.

[00522] FIGS. 20-23 show the treatment situation of patient 11, wherein FIG. 20 shows the biopsy of patient before treatment, FIGS. 21a, 22a and 23a show PET/CT imaging diagnoses before rSIFN-co medication, and arrows show the original lesions; and FIGS. 21b, 22b and 23b show PET/CT imaging diagnoses after rSIFN-co medication, and arrows show the states of the original lesions after treatment.

[00523] FIG. 24 shows the treatment situation of patient 12, wherein FIG. 24a shows a CT image at the beginning of the medicine administration, and an arrow shows the original lesion; and FIG. 24b shows an imaging diagnosis after rSIFN-co medication, and an arrow shows the state of the original lesion after treatment.

[00524] FIG. 25 shows the treatment situation of patient 13, wherein FIG. 25a shows a CT image at the early stage of the treatment, and an arrow shows suspicious lesions of inferior lobe of right lung; and FIG. 25b shows a chest CT image at the later stage of the treatment, and an arrow shows the state of original suspicious lesions of inferior lobe of right lung after treatment.

[00525] FIG. 26 shows the treatment situation of patient 14, wherein FIG. 26a shows a CT image at the beginning of the medicine administration (after surgery), and an arrow shows the original lesion; and FIG. 26b shows a CT image at the later stage of the treatment, and an arrow shows the state of the original lesion after treatment.

[00526] FIG. 27 shows the treatment situation of patient 15, wherein FIG. 27a shows a pelvic cavity MRI imaging diagnosis before rSIFN-co medication, and an arrow shows the original lesion; and FIG. 27b shows a pelvic cavity MRI imaging diagnosis after rSIFN-co medication, and an arrow shows the state of the original lesion after treatment.

[00527] FIG. 28 shows a pathological diagnosis of patient 16, and an arrow shows adenocarcinoma cells.

[00528] FIG. 29 shows the treatment situation of the patient 16, wherein FIG. 29a shows a PEC/CT imaging diagnosis before rSIFN-co medication, and an arrow shows the original lesion; and FIG. 29b shows a PEC/CT imaging diagnosis after rSIFN-co medication, and an arrow show the state of the original lesion after treatment.

DETAILED DESCRIPTION OF THE INVENTION

[00529] The inventor found that rSIFN-co can be advantageously used to control cancer, either alone or in combination with other anti-cancer therapies, as a first line or second line monotherapy or in combination with other treatment modalities. The advantages are: Firstly, the recombinant interferon (rSIFN-co) has broad-spectrum anti-tumor effects, which is effective to treat both solid tumors and non-solid tumors. At the same time, rSIFN-co has good synergetic effect with existing treatment means such as surgical therapy, chemotherapy, radiotherapy, other biotherapies and other anti-tumor drugs. Secondly, rSIFN-co has low toxicity, which means that little or no harm to normal cells has been observed when rSIFN-co is used in large doses. Thirdly, rSIFN-co is convenient to use and can be directly applied to tumors located in any part of the body. Thus, rSIFN-co can be used by subcutaneous or intramuscular injection to control systemic progression of tumor, by intrapleural or abdominal perfusion to eliminate effusion and intrapleural or abdominal tumors, by topical or local injection to eliminate primary or metastatic tumors, and by infiltration (transdermal) administration to treat tumor lesions in bone, skin, muscle, prostate and the like. Also, rSIFN-co can be administered by aerosol inhalation or by nasal spray.

[00530] According to the above advantages of rSIFN-co, its effective rate on tumors, as a monotherapy and as one element of a combination therapy, is not lower than 90%. With regard to early or medium-term cancer cases, rSIFN-co can be used after surgery in place of chemotherapy and effectively prevent recurrence and tumor metastasis or prolong the period of disease-free survival; with regard to advanced cancer cases or cancer cases that are not indicated for surgery, rSIFN-co can be used

to eliminate or reduce the size of tumors without surgery; with regard to tumors that are not indicated for surgery, rSIFN-co can be used to transform the tumors into ones for which surgery is possible, that is, turning a non-resectable tumor into a resectable tumor, thereby creating conditions appropriate for surgery. Therefore, rSIFN-co, alone or in combination with other one or more anti-tumor therapy, is capable of controlling cancer in a large number of instances.

1. The recombinant interferon (rSIFN-co) and preparation method thereof

[00531] In one aspect, the amino acid sequence of the present recombinant interferon, as well as the nucleotide sequence encoding the same (together with a termination codon), are shown below as SEQ ID NO:1 and SEQ ID NO:2, respectively. These sequences are also referenced in U.S. Patent Nos. 7,585,647; 7,364,724; 8,114,395 and 8,287,852:

M C D L P Q T H S L G N R R A L I L L A

1 ATGTGCGACC TGCCGCAGAC CCACTCCCTG GGTAACCGTC GTGCTCTGAT CCTGCTGGCT

TACACGCTGG ACGGCGTCTG GGTGAGGGAC CCATTGGCAG CACGAGACTA GGACGACCGA

Q M R R I S P F S C L K D R H D F G F P

61 CAGATGCGTC GTATCTCCCC GTTCTCCTGC CTGAAAGACC GTCACGACTT CGGTTTCCCG

GTCTACGCAG CATAGAGGGG CAAGAGGACG GACTTTCTGG CAGTGCTGAA GCCAAAGGGC

Q E E F D G N Q F Q K A Q A I S V L H E

121 CAGGAAGAAT TCGACGGTAA CCAGTTCCAG AAAGCTCAGG CTATCTCCGT TCTGCACGAA

GTCCTTCTTA AGCTGCCATT GGTCAAGGTC TTTCGAGTCC GATAGAGGCA AGACGTGCTT

M I Q Q T F N L F S T K D S S A A W D E

181 ATGATCCAGC AGACCTTCAA CCTGTTCTCC ACCAAAGACT CCTCCGCTGC TTGGGACGAA

TACTAGGTCG TCTGGAAGTT GGACAAGAGG TGGTTTCTGA GGAGGCGACG AACCCTGCTT

S L L E K F Y T E L Y Q Q L N D L E A C

241 TCCCTGCTGG AAAAATTCTA CACCGAACTG TACCAGCAGC TGAACGACCT GGAAGCTTGC

AGGGACGACC TTTTTAAGAT GTGGCTTGAC ATGGTCGTCG ACTTGCTGGA CCTTCGAACG

V I Q E V G V E E T P L M N V D S I L A

301 GTTATCCAGG AAGTTGGTGT TGAAGAAACC CCGCTGATGA ACGTTGACTC CATCCTGGCT

CAATAGGTCC TTCAACCACA ACTTCTTTGG GGCGACTACT TGCAACTGAG GTAGGACCGA

V K K Y F Q R I T L Y L T E K K Y S P C

361 GTTAAAAAAT ACTTCCAGCG TATCACCCTG TACCTGACCG AAAAAAAATA CTCCCCGTGC

CAATTTTTTA TGAAGGTCGC ATAGTGGGAC ATGGACTGGC TTTTTTTTAT GAGGGGCACG

A W E V V R A E I M R S F S L S T N L Q

421 GCTTGGGAAG TTGTTCGTGC TGAAATCATG CGTTCCTTCT CCCTGTCCAC CAACCTGCAG

CGAACCCTTC AACAAGCACG ACTTTAGTAC GCAAGGAAGA GGGACAGGTG GTTGGACGTC

E R L R R K E (SEQ ID NO:1)

481 GAACGTCTGC GTCGTAAAGA ATAA (SEQ ID NO:2)

CTTGCAGACG CAGCATTTCT TATT (SEQ ID NO:3)

[00532] Compared with the IFN-α2b as published and the interferon such as interferon alfacon-1 (INFERGEN®), which has the amino acid sequence of SEQ ID NO: 1, but is not encoded by the nucleotide sequence of SEQ ID NO: 2, the three-dimensional structure of the present recombinant interferon (rSIFN-co) is different from the three-dimensional structure of IFN-α2b (see FIG. 1, wherein in the side view and the top view in the figure 1, the red represents rSIFN-co, the green represents IFN-α2b, the red is black in the black-and-white print drawing, and the

green is grey in the black-and-white print drawing) and the computation model structure of the interferon alfacon-1 (see KORN, AP, Journal of Interferon Research 1994, 14:1-9). According to the comparison result between the present recombinant interferon and the interferon alfacon-1, there are obvious differences between the AB loops of the two, and their BC loops also cannot overlap completely (see FIG 2).

[00533] In addition, after intramuscular injection of the present recombinant interferon into subjects whose BMI ranged from about 18 to about 23, the time of blood sample collection was plotted against the concentration of 2-5A oligonucleotidase (also referred to as 2', 5'-OAS) in the serum of the subjects. The chart generally shows a two-peak pattern, and the resulting area under the curve of this chart is significantly greater than that of interferon alfacon-1 (INFERGEN®) after injection under the same conditions. Furthermore, the half-life period of this recombinant interferon is longer than that of interferon alfacon-1 (INFERGEN®) after injection into the body (see CN 1740197A; Zeng, J. P. et al. Modern Preventive Medicine, 2008, 35(5), 982-984).

[00534] The experimental results have also confirmed that the present recombinant interferon is more effective than any interferon used clinically at present (including interferon alfacon-1 (INFERGEN®)). For example, for HBV, the present recombinant interferon is capable of not only inhibiting DNA replication of HBV, but also inhibiting secretion of both hepatitis B surface antigen (HBsAg) and hepatitis B e antigen (HBeAg). The efficiency of inhibiting DNA replication of hepatitis B core antigen (HBcAg) by this interferon is about twice that of interferon alfacon-1 (INFERGEN®). The *in vitro* pharmacodynamics of the present recombinant interferon shows that it is capable of not only inhibiting the DNA replication of HBV, but also inhibiting secretion of both hepatitis B surface antigen and hepatitis B e antigen. The cytotoxicity of the present recombinant interferon is only 1/8 that of the current clinically used interferons, but its antiviral activity is as much as 5-20 times greater; meanwhile, the biological responses

of the present recombinant interferon is more effective, more broad-spectrum and longer lasting in the human body (see CN 1740197A).

[00535] Furthermore, with respect to prevention of viral diseases or treatment of tumor, the present recombinant interferon shows higher antiviral activity and less side effects compared with any other interferons (including interferon alfacon-1 (INFERGEN®)). For example, this recombinant interferon possesses not only an antiviral activity 20 times as great as that of the interferons currently in clinical use, but also a more effective inhibiting tumor cell growth or promoting apoptosis function compared with recombinant human interferon α.

[00536] Thus, the present recombinant interferon has a different spatial configuration, enhanced biologic activities and/or different pharmacokinetics characteristics as compared with the interferon such as interferon alfacon-1 (INFERGEN®), which has the amino acid sequence of SEQ ID NO: 1, but is not encoded by the nucleotide sequence of SEQ ID NO: 2.

[00537] Therefore, in some embodiments, the present recombinant interferon has the amino acid sequence of SEQ ID NO: 1, such as consisting of the amino acid sequence of SEQ ID NO: 1. In some embodiments, the present recombinant interferon is encoded by the nucleotide sequence of SEQ ID NO: 2. In some embodiments, the present recombinant interferon has the amino acid sequence of SEQ ID NO: 1, and is encoded by the nucleotide sequence of SEQ ID NO: 2. Further, the recombinant interferon comprises the amino acid sequence of SEQ ID NO: 1, and is encoded by the nucleotide sequence of SEQ ID NO: 2. Still further, the recombinant interferon is consisted of the amino acid sequence of SEQ ID NO: 1, and is encoded by the nucleotide sequence of SEQ ID NO: 2.

[00538] In some embodiments, in comparison with interferon such as interferon alfacon-1 (INFERGEN®), which has the amino acid sequence of SEQ ID NO: 1, but is not encoded by the nucleotide sequence of SEQ ID NO: 2, the present recombinant interferon has a changed spatial configuration

and/or enhanced biologic activities and/or different pharmacokinetics characteristics. For example, the present recombinant interferon has a changed spatial configuration and enhanced biologic activities, changed spatial configuration and different pharmacokinetics characteristics, or changed spatial configuration, enhanced biologic activities and different pharmacokinetics characteristics. The enhanced biological activities include: enhanced antiviral activity, enhanced tumor cell growth inhibition or proapoptotic effect, less side effects and/or could be used in large dose (e.g. each dose > 10 million IU). For example, the enhanced biological activities can be enhanced antiviral activity and/or enhanced tumor cell (such as breast cancer cell or cervical cancer cell) growth inhibition or proapoptotic effect (see Zheng, J. et al. J Sichuan Univ (Med Sci Edi), 2010, 41(1), 29-34; Chen, Y, et al. J Sichuan Univ (Med Sci Edi), 2008, 39(5), 715-718). The different pharmacokinetics characteristics include: after intramuscular injection of the recombinant interferon in subjects whose BMI ranged from about 18 to about 23, the time of blood sample collection was plotted against the concentration of 2-5A oligonucleotidase in the serum of the subjects, and the resulting area under the curve of this chart is significantly greater and/or the half-life of this recombinant interferon in the body is longer than those of the interferon such as interferon alfacon-1 (INFERGEN®), which has the amino acid sequence of SEQ ID NO: 1, but is not encoded by the nucleotide sequence of SEQ ID NO: 2 after injection under the same conditions.

[00539] In some embodiments, the present recombinant interferon has the amino acid sequence of SEQ ID NO: 1, and is encoded by the nucleotide sequence of SEQ ID NO: 2, wherein the recombinant interferon has increased inhibitory activities on the expression of hepatitis B surface antigen (HBsAg) and hepatitis B e antigen (HBeAg) of Hepatitis B Virus as compared to an interferon interferon such as interferon alfacon-1 (INFERGEN®), which has the amino acid sequence of SEQ ID NO: 1, but is not encoded by the nucleotide sequence of SEQ ID NO: 2.

[00540] In another aspect, the recombinant interferon (rSIFN-co) used in the present invention can be produced by the methods disclosed in, for example, US 7,364,724, US 7,585,647, US 8,114,395, CN 1740197 A, CN 101001644 A, US 2009/0123417, US 2011/0158941 and WO 2011072487A1. In a specific embodiment, the present recombinant interferon can be produced by the method comprising the following steps: introducing a nucleotide sequence comprising SEQ ID NO: 2 that encodes the recombinant interferon into an isolated host cell; culturing the host cell under appropriate condition for expression of the recombinant interferon; and harvesting the recombinant interferon, wherein the recombinant interferon has an amino acid sequence of SEQ ID NO: 1, and the recombinant interferon inhibits secretion of hepatitis B surface antigen (HBsAg) and hepatitis B e antigen (HBeAg) of Hepatitis B Virus. Further, the host cell is *Escherichia coli*, such as *Escherichia coli* LGM 194. Further, the nucleotide sequence comprising SEQ ID NO: 2 is under the control of the promoter P_{BAD}. Further, the harvesting step comprises extraction of the interferon from the fermentation broth, collection of the inclusion bodies, denaturation and renaturation of the harvested interferon. Still further, the harvesting step also comprises separation and purification of the recombinant interferon.

[00541] The person skilled in the art can prepare intramuscular injection dosage form, spray dosage form, or inhalation dosage form and the like of the present recombinant interferon with reference to the contents of the following part D with title of Pharmaceutical composition and administration route.

[00542] The specific activity of the present recombinant interferon is in a range of about 4.4×10^8 IU/mg to about 1.0×10^9 IU/mg, and optionally greater than 5.5×10^8 IU/mg. Such specific activity is the ratio of the biological activity and the content of protein. The biological activity is measured by a method well-known by the person skilled in the art such as the biological activity measurement method for the interferon (i.e. the cell lesion inhibition method) published in the Appendix X C in Chinese Pharmacopoeia (the third book), Edition 2010; and the content of the protein is measured by a method well-known by the person skilled in the art such as the second

method (i.e. the Lowry method) of protein measurement method published in the Appendix VI B in Chinese Pharmacopoeia (the third book), Edition 2010.

2. Therapeutic uses

[00543] The inventor has found that the present recombinant interferon (rSIFN-co) can be effectively used for treating tumors, in particular, solid tumors such as lung cancers and the like. Monotherapy using the present recombinant interferon, rSIFN-co, can suppress the growth of the tumors in patients, reduce the size of tumors in the patients effectively, even non-surgically directly eliminate tumors in the patients, reduce and even eliminate malignant pleural effusion, malignant ascites and/or malignant pericardial effusion, reduce tumor markers, effectively prolong the survival and/or tumor-free survival of the tumor patients and prevent postoperative cancer recurrence and/or metastasis of the tumor in the patients, and effectively treat advanced cancer patients and the cancer patients that are not indicated or appropriate for surgery. Combining other anti-cancer therapies such as one or more of chemotherapy, radiotherapy, surgical therapy, or targeted therapy, the present recombinant interferon can effectively eliminate the tumors of the patients so as to achieve the effect of cure in some embodiments. In addition, compared with existing interferons such as INFERGEN®, the present recombinant interferon has less side effects, so that it can be used in larger doses.

A. Diseases and Conditions

[00544] The diseases and conditions suitable for the treatment and/or prevention method of the invention include tumors. As used herein, the term "tumor" refers to all uncontrolled and malignant neoplastic cell growth and proliferation as well as all cancerous cells and tissues, and abnormally or aberrantly proliferative cells. In some embodiments, the tumors include malignant tumors. As used herein, the term "cancer" refers to physiological conditions of mammal generally characterized by unregulated cell growth and/or proliferation. In the context, the terms "cancer" and "malignant tumor" can be used interchangeably.

[00545] In some embodiments, the tumors include solid tumors and non-solid tumors, optionally, the solid tumors. As used herein, the term "solid tumor" refers to the abnormal growth or caking of tissues, and generally does not include cyst or liquid areas. As used herein, the term "non-solid tumor" refers to neoplasia of the hemopoietic system, such as lymphoma, myeloma and leukemia, or neoplasia without solid formation generally and with spread substantially.

[00546] In some embodiment, the solid tumors include but not limited to lung cancer, liver cancer, hepatocellular carcinoma (HCC), esophageal cancer, cholangiocarcinoma, gallbladder carcinoma, stomach cancer, abdominal cancer, gastrointestinal cancer, gastric cancer, pancreatic cancer, renal cell carcinoma, renal cancer, bone cancer, breast cancer, ovarian cancer, uterine cancer, cervical cancer, endometrial cancer, colorectal cancer, colon cancer, rectal cancer, bladder cancer, superficial bladder cancer, prostate cancer, adrenal tumors, squamous cell carcinoma, neuroma, malignant neuroma, myoepithelial carcinoma, synovial sarcoma, rhabdomyosarcoma, gastrointestinal interstitial cell tumor, skin cancer, basal cell carcinoma, malignant melanoma, thyroid cancer, nasopharyngeal carcinoma, hemangioma, epidermoid carcinoma, head and neck cancer, glioma, or Kaposi's sarcoma.

[00547] In some embodiments, the non-solid tumors include but not limited to leukemia, acute leukemia, chronic leukemia, chronic myelocytic leukemia, acute myelogenous leukemia, chronic myelogenous leukemia, chronic lymphocytic leukemia, acute lymphoblastic leukemia, T-cell leukemia, hairy cell leukemia, polycythemia, myelodysplastic syndrome, multiple myeloma, lymphadenoma, Hodgkin's lymphoma, and Non-Hodgkin's lymphoma.

[00548] In some embodiments, the tumors are lung tumors, and include but not limited to abnormally proliferative or aberrantly proliferative lung cells and/or malignant lung tumor. As used herein, the term "lung tumor" refers to any lung tumors, therefore, such tumors can be primary lung tumors and/or metastatic lung tumors, for example, the tumors are formed in a way that tumors at other positions are metastasized to the lung through various metastasis modes. The lung tumors can be

benign (non-carcinous), preinvasive lesion (precancerous lesion), or malignant (carcinous) lung tumors, such as lung cancers.

[00549] In a specific embodiment, the lung tumors are the lung cancers, and include but not limited to small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). As used herein, the term "lung cancer" refers to all types of lung cancers, and include but not limited to small cell lung cancer (SCLC) and the non-small cell lung cancer (NSCLC, including but not limited to adenocarcinoma, squamous cell carcinoma, large cell carcinoma, adenosquamous carcinoma and sarcomatoid carcinoma). Further, the SCLC includes but not limited to complex small cell lung cancer; and the NSCLC includes but not limited to adenocarcinoma, squamous cell carcinoma, large cell carcinoma, adenosquamous carcinoma, sarcomatoid carcinoma, carcinoid and salivary gland cancer. As used herein, the term "complex small cell lung cancer" refers to one lung cancer, wherein the ingredients of the non-small cell lung cancer, such as large cell carcinoma, are mixed in the small cell lung cancer.

[00550] In an embodiment, the lung tumors are preinvasive lesion (precancerous lesion), and include but not limited to squamous epithelial dysplasia of the lung, lung carcinoma in situ, atypical adenomatous hyperplasia of the lung, and diffuse and idiopathic neuroendocrine cell proliferation of the lung. In one embodiment, the metastatic lung tumors are the tumors formed in a way that breast cancer, colorectal cancer, stomach cancer, pancreatic cancer, renal cancer, malignant melanoma, prostate cancer, liver cancer, thyroid cancer and adrenal tumors and the like are metastasized to the lung.

[00551] In some embodiments, the tumors are metastasized, and such metastasis can be in situ and in the distance. As used herein and related to cancers or malignant tumors, the term "metastasis" refers to the spread of cancers or malignant tumors from the in-situ position to other in-vivo positions. Cancer cells can separate from in-situ tumors, penetrate into lymphatic vessels and blood vessels, and then grow in distant lesions in normal tissues at other in-vivo positions through blood circulation. The metastasis can be in situ or at the distance. The lung tumors such as lung cancers

can metastasize to lymph nodes, brain, central nervous system, bone, liver, adrenal, skin, intestine, thyroid, ovary, prostate and the like. Therefore, the present recombinant interferon can be used for treating these metastasized tumors such as metastasized lung cancers; particularly, the present recombinant interferon can relieve the symptoms caused by partial stress and invasion of the lung cancers to adjacent tissues, and treat the distant metastasis of the lung cancers. The symptoms caused by the partial stress and invasion of the lung cancers include but not limited to dyscatabrosis caused by the metastasis and hyperplasia of lymph node around esophagus as well as dyspnea caused by the spread of tumors through the lung parenchyma lymphatic vessels. The distant metastases of the lung cancers include but not limited to brain metastases of the lung cancers, central nervous system metastases of the lung cancers, bone metastases of the lung cancers, liver metastases of the lung cancers, adrenal metastases of the lung cancers, and other metastases such as skin metastases, thyroid metastases, ovary metastases, prostate metastases and the like of the lung cancers.

[00552] In some embodiments, the tumors can be multiple primary cancers, for example, in the condition that the tumors are the lung cancers, such lung cancers can be multiple primary lung cancers such as the multiple primary lung cancers at different pulmonary segments or pulmonary lobes. As used herein, the term "multiple primary cancers" refers to more than two kinds of multiple primary malignant tumors that are formed at the same time or successively on a same body. Such multiple primary malignant tumors must be confirmed to be malignant and non-external metastasis tumors by histology. As used herein, the term "multiple primary lung cancers" refers to more than two multiple primary malignant tumors which are identical in histology and independent in existence, do not have metastasis between each other, and are generated at different pulmonary segments or pulmonary lobes.

[00553] The disease suitable for the treatment and/or prevention method of the invention also includes cancer emergencies, for example advanced cancer emergencies such as pleural effusion, ascites and/or pericardial effusion. In some embodiments, the pleural effusion, ascites and/or pericardial effusion are malignant

pleural effusion, malignant ascites and/or malignant pericardial effusion. In some embodiments, the malignant pleural effusion can be caused by pleural primary tumors or pleural metastasized tumors, and is the common emergencies in the advanced lung cancers. The pleural primary tumors include malignant and diffuse mesothelioma, and the pleural metastasized tumors are originated from lung cancer, breast cancer, lymphoma, ovarian cancer, endometrial cancer, cervical cancer, stomach cancer, colorectal cancer, pancreatic cancer, bladder cancer, liver cancer and the like. In some embodiments, the malignant pericardial effusion can be caused by lung cancer, breast cancer and the like. For example, the malignant pericardial effusion can be caused in a way that the lung cancer can be metastasized or can directly invade pericardium, which is also the common expression of the advanced lung cancers. In some embodiments, the malignant ascites can be caused by malignant tumors, wherein excessive liquid is accumulated in enterocoelia, and the malignant ascites is one of the advanced emergencies of cancers, and the malignant ascites are generally caused by ovarian cancer, cervical cancer, endometrial cancer, digestive tract tumor, lymphoma, breast cancer, peritoneal mesothelioma and the like.

B. Subjects

[00554] The subject suitable for the treatment and/or prevention method of the invention includes mammal, which comprises but not limited to human and non-human mammal, optionally, the subject is human. In the context, the terms "subject" and "patient" can be used interchangeably. In some embodiments, the subject with tumors is the subject previously diagnosed with tumors such as malignant tumors.

[00555] In some embodiments, the subjects include but not limited to a subject with tumors such as malignant tumors that are not capable of being resected, a subject with tumors such as malignant tumors that are capable of being resected, a subject with cancers, a subject with metastasized tumors such as metastasized malignant tumors, and/or a subject with pleural effusion, ascites and/or pericardial effusion such as malignant pleural effusion, malignant ascites and/or malignant pericardial effusion.

In some embodiments, the tumor is optionally resected by a surgical resection. In some embodiments, the subjects suffered from solid tumors. In some embodiments, the solid tumors are capable of being resected or are not capable of being resected, such as solid tumors that are capable of being resected or are not capable of being resected surgically. In some embodiments, the solid tumors that are capable of being resected or are not capable of being resected, such as solid tumors that are capable of being resected or are not capable of being resected surgically, are advanced, or stage III or stage IV solid tumors. In some embodiments, the subjects are the subjects with or without indications for cancers or tumors surgery such as lung cancers surgery. In some embodiments, the solid tumors are solid tumors with or without indications for surgery such as indications for tumor surgery. In some embodiments, the solid tumors with or without indications for surgery such as indications for tumor surgery, are advanced, or stage III or stage IV solid tumors. In some embodiments, the solid tumors are lung cancers.

[00556] As used herein, the term "indication for surgery" or "indicated for surgery" or "appropriate for surgery" refers to a surgical method which is employed when a disease is in accordance with the standard specified by treatment routine and cannot be cured by a non-surgical method and the surgical method can be employed for being helpful for the treatment of the disease. In some embodiments, the cancers without indications or not indicated for surgery include: (1) non-solid tumors or systematic tumors, such as leukemia, malignant lymphoma, bone tumor and the like; (2) cancers with extensive systematic metastases for which surgical treatment is of no value; (3) cancers at a position which is difficult for surgical resection, such as nasopharyngeal carcinoma, upper esophageal carcinoma, radix linguae carcinoma and the like; (4) cancers which easily metastasize at a very early stage, such as undifferentiated small cell lung cancer, so that surgical resection is generally not suggested; and (5) cancers with carcinoma cells which infiltrate into surrounding tissues while growing, have unclear boundary and cannot be completely resected by surgery, such as tonsil carcinoma, pancreas carcinoma and the like. In some embodiments, the solid tumors without indications or not indicated for surgery

include: (1) systematic solid tumors such as bone tumor and the like; (2) solid tumors with extensive systematic metastases for which surgical treatment is of no value; (3) solid tumors at a position which is difficult for surgical resection, such as nasopharyngeal carcinoma, upper esophageal carcinoma, radix linguae carcinoma and the like; (4) solid tumors which easily metastasize at a very early stage, such as undifferentiated small cell lung cancer; and (5) solid tumors with carcinoma cells which infiltrate into surrounding tissues while growing, have unclear boundary and cannot be completely resected by surgery, such as tonsil carcinoma, pancreas carcinoma and the like.

[00557] As used herein, the term "tumors that are capable of being resected" are tumors which are limited to primary organs and are suitable for surgical therapy, such as malignant tumors. A subject with tumors such as malignant tumors that are not capable of being resected also includes a subject with tumors such as malignant tumors that are not capable of being resected surgically. Such surgery can include surgical procedures, minimally invasive operation and the like. In a specific embodiment, the subject with tumors such as malignant tumors that are capable of being resected includes a subject with tumors such as malignant tumors which can be resected surgically.

[00558] In some embodiments, the subjects include but not limited to early cancer patients, medium-term and advanced cancer patients, optionally medium-term or advanced cancer patients. As used herein, the term "early cancer" includes cancer in situ and stage I cancer, the term "medium-term cancer" includes stage II and stage III cancers, and the term "advanced cancer" refers to metastatic cancers with extensive infiltration in situ or with metastises at remote organs, such as stage IV cancer. In some embodiments, the subjects include but not limited to stage 0, I, II, III or IV cancer patients, optionally stage III or stage IV cancer patients; and the subjects with metastasized tumors such as metastasized malignant tumors includes but not limited to subjects with tumors such as malignant tumors which are metastasized in situ or in the distance. It should be understood that when the tumor or cancer is referred to as stage 0, I, II, III, or IV tumor or cancer, the stages of the tumor or cancer

is defined by the TNM staging method well known in the art (see AJCC Cancer Staging Manual (Sixth Edition), Greene, F. L. et al. editor. LIAONING SCIENCE AND TECHNOLOGY PUBLISHING HOUSE, August 2005). For example, in the TNM staging method, the Stage 0 means $T_0N_0M_0$; the Stage Ia means $T_1N_0M_0$; the Stage Ib means $T_2N_0M_0$; the Stage IIa means $T_1N_1M_0$; the Stage IIb means $T_2N_1M_0$ and $T_3N_0M_0$; the Stage IIIa stage means $T_3N_1M_0$ and $T_{1-3}N_2M_0$; the Stage IIIb means any T, N_3 and M_0, T4, and any N and M_0; and Stage IV means any T, and any N and M_1. In some embodiments, the subjects are medium-term, advanced, or Stage III or Stage IV cancer patients. In some embodiments, the subjects are advanced, or Stage III or Stage IV cancer patients.

[00559] In some embodiments, the subjects with malignant pleural effusion, malignant ascites and/or malignant pericardial effusion include the subjects with malignant pleural effusion, malignant ascites and/or malignant pericardial effusion caused by cancers such as advanced, or Stage III or Stage IV cancers. In one embodiment, the cancers are lung cancers.

[00560] In some embodiments, the subjects suffered from tumors which can be lung tumors, such as lung cancers. In one embodiment, the subjects can be lung cancer patients, such as patients of lung cancer that is not capable of being resected surgically, the medium-term and advanced lung cancer patients, the Stage 0, I or II lung cancer patients, or Stage III or IV lung cancer patients, and the metastasized lung cancer patients or the lung cancer patients with malignant pleural effusion, malignant ascites and/or malignant pericardial effusion. In one embodiment, the lung cancer patients include but not limited to small cell lung cancer patients and non-small cell lung cancer patients.

C. Combination therapy

[00561] In some embodiments of the method of the invention, other therapies or drugs can be administered to the subject before, simultaneously, and/or after administration of the present recombinant interferon. In some embodiments, the therapies are optionally anti-cancer therapies, and the drugs are optionally anti-tumor

drugs. As used herein, the term "administration" refers to giving a substance to achieve the therapeutic purposes. As used herein, the term "combination therapy" refers to employing two or more treatment means for the subjects in the process of the treatment period, such as employing the present recombinant interferon and extra treatment means. The extra treatment means can be employed for the subjects before, simultaneously, and/or after administration of the present recombinant interferon. As used herein, the term "anti-cancer therapy" refers to a useful therapy in the cancer treatment.

[00562] In some embodiments, the other anti-cancer therapies include but not limited to chemotherapy, radiotherapy, surgical therapy, interventional therapy, biotherapy, gene therapy, ablation therapy, immune therapy, targeted therapy, traditional Chinese medicine therapy and any combination thereof. The other anti-cancer therapies can be easily determined by the person skilled in the art. In some embodiments, the other anti-cancer therapies are optionally chemotherapy, radiotherapy, surgical therapy, targeted therapy and/or biotherapy. In some embodiments, the other anti-cancer therapies are optionally chemotherapy and/or radiotherapy.

[00563] As used herein, the term "chemotherapy" refers to a drug therapy affecting cell growth and cell division, namely, the drug therapy is taken as a cell proliferation inhibitor or is used for inducing cell death (cell apoptosis). Compared with normal cells, cancer cells grow and divide uncontrollably so that the chemotherapy should be more effective to the cancer cells. In a specific embodiment, chemotherapy includes arterial infusion chemotherapy and embolism-form chemotherapy. In a specific embodiment, for different cancers, the chemotherapy can be the common first-line chemotherapy for the cancers. For example, chemotherapeutic drugs used in the first-line chemotherapy for treating lung cancer include but not limited to platinum compounds such as Cisplatin.

[00564] The chemotherapeutic drugs used in the chemotherapy for the cancers in the invention include but not limited to alkylating agents such as nitrogen mustards including but not limited to chlormethine hydrochloride, chlorambucil, phenylalanine

mustard, chlornaphazine, estramustine, cyclophosphamide, ifosfamide, Mechlorethamine, mustron, Melphalan, novembichin, phenesterin, Prednimustine, Trofosfamide and Uramustine; ethyleneimines and methyl melamines including but not limited triethylenemelamine, Thiotepa, MST-16, altretamine, triethylene melamine, triethylene phosphamide, triethylene Thiophosphoramide and trimethylol melamine; sulfoacid alkyl esters including but not limited to busulfan, improsulfan and piposulfan; and nitrosoureas including but not limited to carmustine, Semustine, Streptozotocin, chlorozotocin, Fotemustine, Lomustine, Nimustine and Ranimustine; antimetabolites such as anti-folate antimetabolite including but not limited to methopterin (MTX), trimethyl-oxy quinazoline, dimethyl folate, pteropterin, trimetrexate, leucovorin and Pemetrexed (Alimta); pyrimidine antimetabolites including 5-fluorouracil (5-FU), floxuridine, ftorafur (Tegafur), Capecitabine (Xeloda), Ancitabine, Carmofur, di-deoxyuridine, Doxifluridine and enocitabine; cytidines antimetabolites including but not limited to cytarabine, Azacytidine, ancitabine and Gemcitabine (Gemzar); purines antimetabolites including but not limited to 6-mercaptopurine, 6-thioguanine, deoxycoformycin, Fludarabine and thiamiprine; plant-origin anti-tumor drugs such as Vinca Alkaloids including but not limited to vinblastine, vindesine, vincristine, vindesine, Vinorelbine, vinblastine sulfate, vincristine sulfate, Vinorelbine Tartrate and Vinflunine; Harringtonine and Homoharringtonine; Indirubin and analogue thereof including but not limited to N-methyllisoinidog-tin; etoposide drugs including but not limited to Teniposide (VM-26) and Etoposide (VP-16); Camptotheca and Camptothecin compounds including but not limited to Camptothecin, Topotecan (TPT) and Irinotecan (CPT-11); Paclitaxel compound including but not limited to Paclitaxel (Paclitaxel Liposome For Injection), Docetaxel (Docetaxel Injection, Taxotere) and paclitaxel liposome; antitumor antibiotics such as anthracyclines including but not limited to daunorubicin, adriamycin, aclacinomycin A, Epirubicin, mitoxantrone and marcellomycin; Glycopeptides including but not limited to bleomycin, tallysomycine, Leroymycin, pepreomycin and Pingyangmycin; actinomycins including but not limited to actinomycin C, actinomycin D, aurantin and dactinomycin; glucosides including but

not limited to mithramycin, chromomycin A3 and Olivomycin; mitomycins including but not limited to mitomycin C; and Streptozotocin; the platinum compounds include but not limited to Spiroplatin, Cisplatin, Carboplatin, Nedaplatin, oxaliplatin, Lobaplatin, JM-216, Ring Platinum, SKI2053R, L-NDDP and TRK-710; retinoid compounds include but not limited to all-trans retinoic acid and 13-cis-retinoic acid; hormones include androgens including but not limited to Testosterone Propionate, Methyltestosterone, Fluoxymesterone, durabolin, calusterone, propionic-acid methyl androstane pregnanolone, epithioandrostanol, mepitiostane and testolactone; antiandrogens including but not limited to flutamide, Nilutamide, Bicalutamide (Casodex), Goserelin, Leuprorelin and Androcur; estrogens including but not limited to diethylstilbestrol, estradiol and ethinyloestradiol; estrogen receptor blocker and composite drug formed by transplanting estrogen, including but not limited to Tamoxifen, Toremifene, Anastrozole and Exemestane; progesterones including but not limited to Methylhydroxyprogesterone and Megestrol Acetate; Gonadotropin releasing hormone analogues including but not limited to Leuprorelin, Gonadorelin and Dingsi-relin and naphthoxy-propyl-relin; adrenocortical hormone including but not limited to metacortandracin (prednisone) and dexamethasone (DXM); adrenal-cortex selective damaging agent including but not limited to Mitotane; thyroid hormones including but not limited to thyroxine; and others including but not limited to Bacillus Calmette Guerin (BCG), Asparaginase, hydroxycarbamide, Ibenzmethyzin and Dacarbazine (DTIC); and pharmaceutically acceptable salts, acids or derivatives of any above substance.

[00565] In some embodiments, chemotherapy protocols used for treating cancers such as lung cancers in the invention include but not limited to a CMC protocol (cyclohexyl nitrosourea, cyclophosphamide and Methotrexate), an EP protocol (etoposide and Cisplatin), an IVP protocol (ifosfamide, vindesine and Cisplatin), an ICE protocol (ifosfamide, Cisplatin and etoposide), a NIP protocol (Navelbine, ifosfamide and Cisplatin), a Paclitaxel + DDP/CBP protocol (Paclitaxel and Cisplatin/carboplatin), a docetaxel + DDP/CBP protocol (docetaxel and Cisplatin/carboplatin), a topotecan+DDP protocol (topotecan and Cisplatin), an IP

protocol (Irinotecan and carboplatin), a MVP protocol (mitomycin, vindesine and Cisplatin), a NP protocol (Navelbine and Cisplatin), a docetaxel protocol, a GEM+DDP (GP) protocol or GEM+CBP protocol (Gemzar and Cisplatin/carboplatin) and the like (see Lung Oncology Phymatology, First Edition, September 2008, Liao, M. L. editor, Shanghai Scientific and Technical Publisher, pages 323-326).

[00566] In addition, other chemotherapy protocols used for treating tumors such as cancers in the invention include but not limited to an FOLFOX protocol (see *Newest Chemotherapy Development of Malignant Tumors,* July, 2009, chief editor: Zheng Cuiping, Beijing: People's Military Medical Press, 1031), a DP protocol (see *Newest Chemotherapy Development of Malignant Tumors*, July, 2009, chief editor: Zheng Cuiping, Beijing: People's Military Medical Press, 232), a CHOPE protocol, a MTX protocol, a GCE protocol, an ESAP protocol, a CMOP protocol, a CHOP protocol (see *Practical Anti-tumor Pharmacotherapeutics*, 2002, chief editor: Liu Xinchun etc., Beijing: People's Medical Publishing House, 1031), a bleomycin+CHOP+ Methotrexate protocol, a GP+Endostar protocol, a GP-T2 protocol, a TP protocol (see *Practical Anti-tumor Pharmacotherapeutics*, 2002, chief editor: Liu Xinchun etc., Beijing: People's Medical Publishing House, 668 and 744), a Cisplatin+ mitomycin protocol and the like.

[00567] As used herein, the term "radiotherapy" refers to employing high-energy radiation for treating tumors such as cancers. The radiotherapy includes external radiation such as external radiotherapy from a linear accelerator, and brachytherapy for which radioactive sources are placed near the surface of the human body or in the body cavity. In the radiotherapy of the invention, the radioactive sources include but not limited to α, β and γ rays generated by radioactive nuclides, and electron beams, proton beams. Neutron beams, -π meson beams and other heavy particle beams generated by various accelerators. The radioactive nuclides include but not limited to ^{137}Cs, ^{60}Co, ^{131}I, ^{125}I, ^{32}P, ^{198}Au, ^{192}Ir, ^{90}Y, ^{186}Re and ^{109}Pd. Such radioactive sources can perform radiation in vitro and/or in vivo.

[00568] It should be understood that many methods known in the art can be used for determining the accumulation and duration of the radiotherapy. The typical

radiotherapy is employed as one-time administration, and the usual dose is in the range of about 1 to about 200 grays/day, such as about 2 to about 150 grays/day, about 5 to about 100 grays/day, about 10 to about 70 grays/day, about 10 to about 50 grays/day and the like. In one embodiment, the radiotherapy used in the invention includes but not limited to two-dimensional conventional radiotherapy, three-dimensional conformal radiotherapy (3D-CRT), proton radiotherapy, brachytherapy, intensity modulated radiotherapy (IMRT), stereotactic radiotherapy (SRT), respiratory gating four-dimensional radiotherapy (4DRT) and gamma knife therapy, such as systematic gamma knife therapy and head gamma knife therapy.

[00569] As used herein, the term "targeted therapy" refers to a therapy aiming at identifying specific target molecules which can be, for example, play a role in tumorigenesis or tumor proliferation or cell repairing. Such identification may be, for example, lead to the combination between the targeted therapy and the target molecules, and can enhance or reduce the activity of the target molecules. Drugs used for the targeted therapy includes antibodies, in particular to monoclonal antibodies and small molecule drugs. Potential targets include EGFR receptors, which playing a role in vasculogenesis, VEGFA ligands, which being important in vasculogenesis, or PARP1, which being important in cell repairing, because the tumors with cancer gene defect can be more sensitive to the chemical therapy due to the suppression to the PARP1.

[00570] In the targeted therapy of the present invention, the targeted drug includes but not limited to an anti-angiogenesis drug, Kinase inhibitor, pan Kinase inhibitor or growth factor inhibitor. The anti-angiogenesis drug includes but not limited to EGF inhibitor, EGFR inhibitor, VEGF inhibitor, VEGFR inhibitor, TIE2 inhibitor, IGF1R inhibitor, COX-II (cyclo-oxygenase-II) inhibitor, MMP-2 (matrix metalloproteinase-2) inhibitor and MMP-9 (matrix metalloproteinase-9) inhibitor. A targeted drug that can be used herein includes but not limited to at least one of: Gefitinib (Iressa), Erlotinib (TARCEVA®), Lapatinib (GSK572016), Vatalanib (PTK787), Imatinib (GLEEEVEC®), Dasatinib (Sprycel), Sunitinib (SUTENT®), Nilotinib (Tasigna), Semaxanib (SU5416), Pazopanib (GW-786034), Erbitux

(IMC-C225), Panitumumab (Vectibix), Trastuzumab (Herceptin), Recombinant Human Endostatin (Endostar), Sorafenib (NEXAVAR®), Bevacizumab (Avastin), Alemtuzumab (Campath), Gemtuzumab (Mylotarg), ibritumomab tiuxetan (Zevalin), tositumomab (Bexxar), Affinitak (LY90003/ISI3521), Farnesyltransferase inhibitors, Tipifanib, Lonafanib, BMS214-662, R115777 (Zarnestra), SCH-66336 (Sarasar), L-778,123, ZD6474 (ZACTIMA®), AZD2171, OSI-7904, ZD6126 (ANG453), ZD1839, AMG706, AG013736, MLN-518, CEP-701, PKC-412, VELCADE®, XL880 and CHIR-265. In some embodiments, the targeted drug in the targeted therapy used for treating cancers such as lung cancers in the invention includes but not limited to Gefitinib (Iressa), Erlotinib (TARCEVA®), and Recombinant Human Endostatin (Endostar).

[00571] The dose and duration of the drugs and/or the radioactive sources used in the chemical therapy, radiotherapy and/or targeted therapy can be easily determined by skilled physicians according to the experience and the practical situations of patients such as age, weight, general health state, gender, diet, administration time, drug interaction and illness severity.

[00572] As used herein, the term "surgical therapy" refers to an invasive cancer therapy aiming at physically eliminating cancer cells. The surgical therapy includes, for example, tumor resection and lymph node dissection.

[00573] As used herein, the term "gene therapy" refers to a therapy by delivering recombinant genetic materials by virus or non-virus carriers ex vivo or in vivo so as to treat or prevent diseases or medical conditions, such as cancers.

[00574] As used herein, the term "ablation therapy" refers to a well known tissue damage method, such as high-temperature ablation such as radio frequency, microwave and laser ablation, low-temperature ablation such as cryocare knife cryotherapy, chemical ablation, radioactive ablation and the like.

[00575] As used herein, the term "immunotherapy" refers to a treatment strategy which is employed for regulating the immune system so as to prevent and/or treat specific diseases such as cancers. For example, vaccination is one immunotherapy. The vaccine used in the present immunotherapy includes but limited

to ALLOVECTIN® vaccine, LEUVECTIN® vaccine, VAXID® vaccine and the like.

[00576] As used herein, the term "interventional therapy" refers to a treatment method with smallest trauma for performing local treatment to the lesion under the condition that the lesion is not operated through tiny channels made on the skin or original channels of the human body under the guidance of imaging equipment (such as a Digital Subtraction Angiography, a perspective machine, CT, MR and B ultrasonic). When being used for treating the tumors, the interventional therapy includes but not limited to transcatheter arterial chemoembolization, arterial infusion chemotherapy, high-temperature ablation such as radio frequency, microwave and laser ablation, low-temperature ablation such as cryocare knife cryotherapy, chemical ablation, radioactive ablation, gene drug arterial infusion, stent implantation and the like.

[00577] As used herein, the term "biotherapy" refers to all treatment methods employing modern biotechnologies and the products (small molecule compounds, polypeptide, polysaccharide, protein, cells, tissues, genes, RNAs and the like) thereof. When being used for treating the tumors, the biotherapy can directly or indirectly mediate anti-tumor and tumor-killing effects. The biotherapy used for treating the tumors includes but not limited to the application of non-specific immunologic stimulant, Biological Response Modifier (BRM), a tumor cell factor treatment and immunological effect cell treatments such as NK cell anti-tumor therapy, biology supporting therapy, tissue and cell transplanting therapy and the like.

[00578] As used herein, the term "traditional Chinese medicine therapy" refers to all methods employing the traditional Chinese medicine and drugs guided by Chinese medicine theories for treating diseases such as cancers.

[00579] In addition, other anti-tumor drugs which can be administered together with the present recombinant interferon include but not limited to biological agents used in the biotherapy such as tumor necrosis factors including TNF-α or TNF-β and the like; interferon such as interferon α including interferon α-1a, interferon α-1b, interferon α-2a, interferon α-2b and the like, interferon β including interferon β-1a, interferon β-1b and the like, interferon γ including interferon γ-1b and the like,

consensus interferon such as interferonα-con1, long-acting interferon such as PEGylation interferon, fusion protein of interferon and albumin, and fusion protein of interferon and IgG Fc fragment; colony stimulating factors (CSF) such as macrophage-colony stimulating factor (M-CSF), granulocyte-macrophage (GM-CSF) and granulocyte-colony stimulating factor (G-CSF); interleukin (IL) such as IL-1, IL-1α, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, and Thymosin; antisense oligonucleotide, especially those for inhibition of the expression of genes (such as PKC-α, Raf and H-Ras) in signaling pathway involved in the proliferation of adherent cells; siRNA and the like.

D. Pharmaceutical composition and administration route

[00580] The present recombinant interferon can be incorporated into pharmaceutical compositions, so as to be administered to subjects. Generally, the pharmaceutical composition comprises the present recombinant interferon and pharmaceutically acceptable carriers. The "pharmaceutically acceptable carrier" herein includes any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like that are physiologically compatible. Examples of pharmaceutically acceptable carriers include one or more of water, saline, phosphate buffered saline, dextrose, glycerol, ethanol and the like, as well as combinations thereof. In many cases, it will be preferable to include isotonic agents, for example, sugars, polyalcohols such as mannitol, sorbitol, or sodium chloride in the composition. Pharmaceutically acceptable carriers may further comprise minor amounts of auxiliary substances such as wetting or emulsifying agents, preservatives or buffers, which enhance the shelf life or effectiveness of the present recombinant interferon.

[00581] The pharmaceutical compositions of the invention may be in a variety of forms. These include, for example, liquid, semi-solid and solid dosage forms, such as liquid solutions (*e.g.*, injectable and infusible solutions), dispersions or suspensions, aqueous solutions, tablets, capsules, oral solutions, patchs, sprays, suppositorys, powders and lyophilized powders. The form appropriate for use depends on the

intended mode of administration and therapeutic application. Typical pharmaceutical compositions are in the form of injectables or infusible solutions, lyophilized powders, sprays, and aqueous solutions.

[00582] The pharmaceutical composition can be prepared by any well known method in the pharmaceutical field with reference to: Gilman, etc., (editor) 1990, The Pharmacological Bases of Therapeutics, the 8th version, Pergamon Press; A. Gennaro (editor), Remington's Pharmaceutical Sciences, the 18th version, 1990, Mack Publishing Co., Easton, Pennsylvania.; Avis, etc., (editor) 1993, Pharmaceutical Dosage Forms: Parenteral Medications Dekke, New York; Lieberman, etc., (editor) 1990, Pharmaceutical Dosage Forms: Tablets Dekker, New York; and Lieberman, etc., (editor) 1990, Pharmaceutical Dosage Forms: Disperse Systems Dekker, New York.

[00583] The present recombinant interferon can be administered to the subjects through at least one of: systemic administration, topical administration, and local administration. As used herein, the term "systemic administration" refers to a mode for administering compositions or drugs to a subject, in a manner that leads to systemic circulation of the drugs or compositions in the subject, such as the spreading or distribution of the administered compositions or drugs to all parts of the body. Examples of systemic administration include, but are not limited to: intravenous injection, intra-arterial injection, intramuscular injection, subcutaneous injection, intra-lymphatic injection, oral administration, and the like.

[00584] As used herein, the term "local administration" refers to administering a composition or drug into a limited or partial anatomy space. Examples of local administration include but are not limited to: intratumoral, intra-lymph node, intra-pleural space, intraperitoneal cavity and the like.

[00585] As used herein, the term "topical administration" refers to administering a drug or composition on the surface of skin or mucous membrane. For example, topical administration includes but is not limited to spraying the drug or composition onto the skin of a subject.

[00586] In some embodiments, the present recombinant interferon can be administered to the subject by at least one administration route, the administration

route comprises but not limited to: oral, rectal, sublingual, intravenous, intra-arterial, intramuscular, subcutaneous, intra-bone, intracutaneous, intra-articular, intraperitoneal, intrathecal, intracerebral, vaginal, percutaneous, transdermal, epidermal, transmucosal, transocular, pulmonary, nasal, abdominal, intrapleural, intraventricular, pericardial, inhalation, intratumoral, uterine, infiltration, and intravesical administration. In some embodiments, the present recombinant interferon can be administered to the subject by injection route, such as subcutaneous, intramuscular, intravenous, intra-arterial, intracerebral, intraperitoneal and/or intratumoral injection. In some embodiments, the present recombinant interferon can be administered to the subject by inhalation, such as pulmonary inhalation and nasal inhalation. In some embodiments, the inhalation can be dry powder inhalation and/or aerosol inhalation. In some embodiments, the present recombinant interferon can be administered to the subject by perfusion, such as intrapleural perfusion, abdominal perfusion, pericardial perfusion, uterine perfusion and/or intravesical perfusion. In some embodiments, the present recombinant interferon can be administered to lesion (such as the surfaces of skin and mucosa, superficial lymph nodes and/or subcutaneous tissue) by spray, such as percutaneous, epidermal, transdermal and/or transmucosal spray administration. In some embodiments, the infiltration administration includes pulmonary infiltration administration, percutaneous infiltration administration, epidermal infiltration administration, transmucosal infiltration administration, intrapleural infiltration administration, abdominal infiltration administration, uterine infiltration administration, vaginal infiltration administration, intravesical infiltration administration, pericardial infiltration administration and the like.

Injection/perfusion administration

[00587] The pharmaceutical compositions suitable for injection/perfusion include sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersion. In all cases, the composition must be sterile and should be fluid so as to be administered using a syringe. Such compositions should be stable during

manufacture and storage and must be preserved against contamination from microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (such as glycerol, propylene glycol, and liquid polyethylene glycol), and suitable mixtures. Various antibacterial and antifungal agents; for example, parabens, chlorobutanol, phenol, ascorbic acid, and thimerosal; isotonic agents; for example, sugars, polyalcohols such as manitol, sorbitol, and sodium chloride can be included in the composition. Compositions that can delay absorption include agents such as aluminum monostearate and gelatin.

[00588] Sterile injection/perfusion solutions can be prepared by incorporating the present recombinant interferon in the required amount in an appropriate solvent with one or a combination of ingredients as required, followed by sterilization. Generally, dispersions are prepared by incorporating the present recombinant interferon into a sterile vehicle that contains a basic dispersion medium, and the other required ingredients. Sterile powders for the preparation of sterile injection/perfusion solutions, methods of preparation include vacuum drying and freeze-drying that yield a powder containing the active ingredient and any desired ingredient from a sterile solutions.

Inhalation administration

[00589] The present recombinant interferon can be delivered by any of a variety of inhalation devices know in the art for administration of a therapeutic agent by inhalation. These devices include metered dose inhalers, nebulizers, dry powder generators, sprayers, and the like. Other devices suitable for inhalation administration of the present recombinant interferon are also known in the art.

[00590] Metered dose inhalers like the Ventolin® metered dose inhaler, typically use a propellent gas and require actuation during inspiration (See, e.g., WO 94/16970, WO 98/35888). Dry powder inhalers like Turbuhaler™ (Astra), Rotahaler® (Glaxo), Diskus® (Glaxo), Spiros™ inhaler (Dura), devices marketed by Inhale Therapeutics, and the Spinhaler® powder inhaler (Fisons), use breath-actuation of a

mixed powder (US 4668218 Astra, EP 237507 Astra, WO 97/25086 Glaxo, WO 94/08552 Dura, US 5458135 Inhale, WO 94/06498 Fisons). Nebulizers like AERx™ Aradigm, the Ultravent® nebulizer (Mallinckrodt), the Acorn II® nebulizer (Marquest Medical Products) (US 5404871 Aradigm, WO 97/22376), and the AP-100200 type spray inhaler (Taiwan Albert incorporated company). Producing aerosols from solutions, while metered dose inhalers, dry powder inhalers, etc. generate small particle aerosols.

[00591] Optionally, the present recombinant interferon is delivered by a nebulizer. The inhalation devices for administering the present recombinant interferon have several desirable features. For example, delivery by the inhalation device is advantageously reliable, reproducible, and accurate. The inhalation device can optionally deliver small dry particles or aerosol, e.g., less than about 10 μm, for example about 0.5 μm to about 5 μm, for good respirability.

Spray administration

[00592] A spray including the present recombinant interferon can be produced by forcing a suspension or solution of the recombinant interferon through a nozzle under pressure. The nozzle size and configuration, the applied pressure, and the liquid feed rate can be chosen to achieve the desired output and particle size. An electrospray can be produced, for example, by an electric field in connection with a capillary or nozzle feed. Advantageously, particles delivered by a sprayer have a particle size less than about 10 μm, optionally, in the range of about 0.5 μm to about 5 μm.

[00593] Formulations of the present recombinant interferon suitable for use with a sprayer typically include ones at a concentration in a range of about 0.01 mg to about 5 mg, such as about 0.03mg to about 2mg, about 0.05mg to about 1mg, and about 0.1mg to about 0.5mg of the recombinant interferon per ml of solution. The formulation can include an excipient or agent for stabilization of the present recombinant interferon, such as a buffer, a reducing agent, a bulk protein, or a carbohydrate. Bulk proteins useful in formulating the recombinant interferon include

albumin, protamine, or the like. Typical carbohydrates useful in formulating the recombinant interferon include sucrose, mannitol, lactose, trehalose, glucose, or the like. The present recombinant interferon formulation can also include a surfactant, which can reduce or prevent surface-induced aggregation of the recombinant interferon caused by atomization of the solution in forming an aerosol.

E. Administration dosage and administration protocol

[00594] Effective amount of the present recombinant interferon can be administered to the subjects such as cancer subjects, and such effective amount can be a therapeutically effective amount or a prophylactically effective amount according to the method of the invention. As used herein, the term "effective amount" refers to an amount effective, at dosages and for periods of time necessary, to achieve the desired therapeutic or prophylactic result. A therapeutically effective amount of the present recombinant interferon may vary according to factors such as the disease state, age, sex, and weight of the individual, and the ability of the recombinant interferon to elicit a desired response in the individual. A therapeutically effective amount is also one in which any toxic or detrimental effects of the recombinant interferon are outweighed by the therapeutically beneficial effects. A "prophylactically effective amount" refers to an amount effective, at dosages and for periods of time necessary, to achieve the desired prophylactic result. Typically but no surely, since a prophylactic dose is used in subjects prior to or at an earlier stage of disease, the prophylactically effective amount will be less than the therapeutically effective amount.

[00595] The present recombinant interferon can be administered to the subjects such as the cancer subjects in different amounts of single doses. For example, the single doses of the present recombinant interferon can be in the range of about 2μg to about 2000μg, optionally about 4μg to about 1500μg, and further optionally about 9μg to about 1000μg. As used herein, the term "single dose" refers to an amount of drug which can be at administered one time, that can be therapeutically or prophylactically effective by itself or cumulatively with other single doses. Such administration includes systemic administration, local administration and/or topical administration.

[00596] When the present recombinant interferon is systemically administered via injection administration (such as subcutaneous injection, intramuscular injection, intravenous injection, intra-arterial injection, intracerebral injection and/or intraperitoneal injection), the single dose of the recombinant interferon can be in the range of about 4μg to about 70μg, optionally, about 4μg to about 50μg, and further optionally, about 4μg to about 30μg, wherein the single dose can be about 4μg, about 4.5μg, about 5μg, about 6μg, about 7μg, about 8μg, about 9μg, about 10μg, about 11μg, about 12μg, about 13μg, about 13.5μg, about 14μg, about 15μg, about 16μg, about 17μg, about 18μg, about 19μg, about 20μg, about 21μg, about 22μg, about 23μg, about 24μg, about 25μg, about 25.5μg, about 26μg, about 27μg, about 28μg, about 29μg, about 30μg, about 31μg, about 32μg, about 33μg, about 34μg, about 35μg, about 36μg, about 37μg, about 38μg, about 39μg, about 40μg, about 41μg, about 42μg, about 43μg, about 44μg, about 45μg, about 46μg, about 47μg, about 48μg, about 49μg, about 50μg, about 51μg, about 52μg, about 53μg, about 54μg, about 55μg, about 56μg, about 57μg, about 58μg, about 59μg, about 60μg, about 61μg, about 62μg, about 63μg, about 64μg, about 65μg, about 66μg, about 67μg, about 68μg, about 69μg, and about 70μg.

[00597] When the present recombinant interferon is locally administered via injection administration (such as the intratumoral injection), the single dose of the recombinant interferon can be in a range of about 60μg to about 600μg, optionally, about 60μg to about 500μg, further optionally, about 80μg to about 400μg, and still further optionally, about 100μg to about 250μg, wherein the single dose can be about 60μg, about 70μg, about 80μg, about 90μg, about 100μg, about 110μg, about 120μg, about 130μg, about 140μg, about 150μg, about 160μg, about 170μg, about 180μg, about 190μg, about 200μg, about 210μg, about 220μg, about 230μg, about 240μg, about 250μg, about 260μg, about 270μg, about 280μg, about 290μg, about 300μg, about 310μg, about 320μg, about 330μg, about 340μg, about 350μg, about 360μg, about 370μg, about 380μg, about 390μg, about 400μg, about 410μg, about 420μg, about 430μg, about 440μg, about 450μg, about 460μg, about 470μg, about 480μg, about 490μg, about 500μg, about 510μg, about 520μg, about 530μg, about 540μg,

about 550μg, about 560μg, about 570μg, about 580μg, about 590μg, and about 600μg.

[00598] When the present recombinant interferon is administered through inhalation administration (such as pulmonary inhalation and nasal inhalation, including dry powder inhalation and aerosol inhalation), the single dose of the recombinant interferon can be in a range of about 100μg to about 2000μg, optionally, about 100μg to about 1500μg, further optionally, about 150μg to about 800μg, and still further optionally, about 200μg to about 600μg, wherein the single dose can be about 100μg, about 110μg, about 120μg, about 130μg, about 140μg, about 150μg, about 160μg, about 170μg, about 180μg, about 190μg, about 200μg, about 210μg, about 220μg, about 230μg, about 240μg, about 250μg, about 260μg, about 270μg, about 280μg, about 290μg, about 300μg, about 310μg, about 320μg, about 330μg, about 340μg, about 350μg, about 360μg, about 370μg, about 380μg, about 390μg, about 400μg, about 410μg, about 420μg, about 430μg, about 440μg, about 450μg, about 460μg, about 470μg, about 480μg, about 490μg, about 500μg, about 510μg, about 520μg, about 530μg, about 540μg, about 550μg, about 560μg, about 570μg, about 580μg, about 590μg, about 600μg, about 610μg, about 620μg, about 630μg, about 640μg, about 650μg, about 660μg, about 670μg, about 680μg, about 690μg, about 700μg, about 710μg, about 720μg, about 730μg, about 740μg, about 750μg, about 760μg, about 770μg, about 780μg, about 790μg, about 800μg, about 810μg, about 820μg, about 830μg, about 840μg, about 850μg, about 860μg, about 870μg, about 880μg, about 890μg, about 900μg, about 910μg, about 920μg, about 930μg, about 940μg, about 950μg, about 960μg, about 970μg, about 980μg, about 990μg, about 1000μg, about 1100μg, about 1200μg, about 1300μg, about 1400μg, about 1500μg, about 1600μg, about 1700μg, about 1800μg, about 1900μg, and about 2000μg.

[00599] When the present recombinant interferon is administered through perfusion or infiltration administration (such as intrapleural perfusion, abdominal perfusion, pericardial perfusion, uterine perfusion and intravesical perfusion), the single dose of the recombinant interferon can be in a range of about 30μg to about 2000μg, optionally, about 100μg to about 1500μg, further optionally, about 150μg to

about 1000μg, still optionally, about 200μg to about 800μg, and still further optionally, about 200μg to about 400μg, wherein the single dose can be about 30μg, about 40μg, about 50μg, about 60μg, about 70μg, about 80μg, about 90μg, about 100μg, about 110μg, about 120μg, about 130μg, about 140μg, about 150μg, about 160μg, about 170μg, about 180μg, about 190μg, about 200μg, about 210μg, about 220μg, about 230μg, about 240μg, about 250μg, about 260μg, about 270μg, about 280μg, about 290μg, about 300μg, about 310μg, about 320μg, about 330μg, about 340μg, about 350μg, about 360μg, about 370μg, about 380μg, about 390μg, about 400μg, about 410μg, about 420μg, about 430μg, about 440μg, about 450μg, about 460μg, about 470μg, about 480μg, about 490μg, about 500μg, about 510μg, about 520μg, about 530μg, about 540μg, about 550μg, about 560μg, about 570μg, about 580μg, about 590μg, about 600μg, about 610μg, about 620μg, about 630μg, about 640μg, about 650μg, about 660μg, about 670μg, about 680μg, about 690μg, about 700μg, about 710μg, about 720μg, about 730μg, about 740μg, about 750μg, about 760μg, about 770μg, about 780μg, about 790μg, about 800μg, about 810μg, about 820μg, about 830μg, about 840μg, about 850μg, about 860μg, about 870μg, about 880μg, about 890μg, about 900μg, about 910μg, about 920μg, about 930μg, about 940μg, about 950μg, about 960μg, about 970μg, about 980μg, about 990μg, about 1000μg, about 1100μg, about 1200μg, about 1300μg, about 1400, about 1500μg, about 1600μg, about 1700μg, about 1800μg, about 1900μg, and about 2000μg.

[00600] When the present recombinant interferon is administered to the lesions (such as surfaces of the skin and the mucosa, superficial lymph nodes and/or subcutaneous tissue) by spray administration such as percutaneous spray, epidermal spray, transdermal spray, transmucosal spray, the single dose of the recombinant interferon can be in a range of about 6μg to about 100μg, optionally, about 10μg to about 40μg, and further optionally, about 20μg to about 40μg, wherein the single dose can be about 6μg, about 7μg, about 8μg, about 9μg, about 10μg, about 11μg, about 12μg, about 13μg, about 14μg, about 15μg, about 16μg, about 17μg, about 18μg, about 19μg, about 20μg, about 21μg, about 22μg, about 23μg, about 24μg, about 25μg, about 26μg, about 27μg, about 28μg, about 29μg, about 30μg, about 31μg, about 32μg,

about 33μg, about 34μg, about 35μg, about 36μg, about 37μg, about 38μg, about 39μg, about 40μg, about 41μg, about 42μg, about 43μg, about 44μg, about 45μg, about 46μg, about 47μg, about 48μg, about 49μg, about 50μg, about 51μg, about 52μg, about 53μg, about 54μg, about 55μg, about 56μg, about 57μg, about 58μg, about 59μg, about 60μg, about 61μg, about 62μg, about 63μg, about 64μg, about 65μg, about 66μg, about 67μg, about 68μg, about 69μg, about 70μg, about 71μg, about 72μg, about 73μg, about 74μg, about 75μg, about 76μg, about 77μg, about 78μg, about 79μg, about 80μg, about 81μg, about 82μg, about 83μg, about 84μg, about 85μg, about 86μg, about 87μg, about 88μg, about 89μg, about 90μg, about 91μg, about 92μg, about 93μg, about 94μg, about 95μg, about 96μg, about 97μg, about 98μg, about 99μg, and about 100μg.

[00601] The present recombinant interferon can be administered to the subjects through different administration protocols. For example, for the purpose of treatment, the present recombinant interferon can be administered to the subject about 1, 2, 3, 4, 5, 6, 7, 8, or more times per day, or the present recombinant interferon can be administered to the subject once at the time interval of every about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or 21 days, every month, every 2 months, or longer time. For the purpose of prevention, the present recombinant interferon can be administered to the subject once at the time interval of every about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, every 2 weeks, every 3 weeks, every month, every 2 months, every 3 months, every half year, every 1 year, or a longer time.

[00602] The present recombinant interferon can be administered to the subjects in one or more treatment cycles. As used herein, the term "treatment cycle" refers to a biological or medical response time length reached by the present recombinant interferon or the pharmaceutical composition comprising the recombinant interferon, and explored for researchers, veterinarians, medical practitioners or other clinicians observed in tissues, systems, animals, individuals or human beings. The duration of such one treatment cycle is at least about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months,

about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or the duration can also be about 1 day to about 6 years, about 1 week to about 4 years, about 2 weeks to about 3 years, about 1 month to about 1 year, or about 2 months to about 9 months and the like. The present recombinant interferon can be administered for a long time, namely, namely, the lasting prolonged time in one treatment cycle includes over the life time of the subject so as to improve or control or limit the symptom of the subjects. In one treatment cycle, the present recombinant interferon can be administered to the subjects one or more times.

[00603] Alternatively, the present recombinant interferon can be administered to the subjects in more treatment cycles. For example, such treatment cycles can be 2, 3, 4, 5, 6, 7, 8, 9, 10, or more treatment cycles; and the duration of the treatment cycles can include over the life time of the subject. The time intervals (i.e. withdrawal period) of any two adjacent treatment cycles in all the treatment cycles can be the same or different, for example, the time interval can be at least about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, about 6 years and the like; and such time interval can also be about 2 days to about 6 years, about 4 days to about 3 years, about 1 week to about 1 year, about 2 months to about 9 months, or about 3 months to about 6 months and the like.

[00604] When the present recombinant interferon is administered for more times in one treatment cycle, the dose in every administration can be the same or different, for example, the present recombinant interferon is administered for one or more times in a lower dose, and then the present recombinant interferon is administered for one or more times in an increased or gradually-increased dose; or, the present recombinant interferon is administered for one or more times in a smaller dose, then the present recombinant interferon is administered for one or more times in an increased or gradually-increased dose, and the present recombinant interferon is

administered for one or more times in a decreased or gradually-decreased dose; or, the present recombinant interferon is administered for one or more times in a larger dose, and then the present recombinant interferon is administered for one or more times in a decreased or gradually-decreased dose; or, the present recombinant interferon is administered for one or more times in a larger dose, then the present recombinant interferon is administered for one or more times in a decreased or gradually-decreased dose, and the present recombinant interferon is administered for one or more times in an increased or gradually-increased dose. In some embodiments, the smaller dose can be the induction dose.

[00605] Compared with the previously administered dose, the later increasingly administered dose can be about 110% to about 500%, including, for example about 110%, about 120%, about 130%, about 140%, about 150%, about 160%, about 170%, about 180%, about 190%, about 200%, about 220%, about 240%, about 260%, about 280%, about 300%, about 350%, about 400%, about 450% and about 500%, of the previously administered dose. Compared with the previously administered dose, the later gradually-increased administered dose can be about 110% to about 500% including, for example about 110%, about 120%, about 130%, about 140%, about 150%, about 160%, about 170%, about 180%, about 190%, about 200%, about 220%, about 240%, about 260%, about 280%, about 300%, about 350%, about 400%, about 450% and about 500%, of the previously administered dose sequentially. The gradually-increased dose can be increased by 1 time, 2 times, 3 times, 4 times, 5 times, 6 times, 7 times, 8 times, 9 times, 10 times, or more times, and then the last dose can be kept till the end of the treatment cycle.

[00606] Compared with the previously administered dose, the later decreasingly administered dose can be about 5% to about 99% including, for example, about 5%, about 6%, about 7%, about 8%, about 9%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95% and about 99%, of the previously administered dose. Compared with the previously administered dose, the later gradually-decreased administered dose can

be about 5% to about 99% including, for example, about 5%, about 6%, about 7%, about 8%, about 9%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95% and 99%, of the previously administered dose sequentially. The gradually-decreased dose can be decreased by 1 time, 2 times, 3 times, 4 times, 5 times, 6 times, 7 times, 8 times, 9 times, 10 times, or more times, and then the last dose can be kept till the end of the treatment cycle.

[00607] In addition, when the present recombinant interferon is administered for one or more times in the same single dose in each of the treatment cycles, the single doses of the present recombinant interferon in two different treatment cycles can be the same or different. For example, the single dose can be gradually increased or decreased. Compared with the previously administered dose, the increasing or decreasing degree is as mentioned above.

[00608] In some embodiments, the gradually increasing or the gradually decreasing can be linear increasing or decreasing, for example, the first administered drug is 9μg, then the later increased dose is 18μg, 36μg, 72μg and the like sequentially, namely, the sequential increasing rate is 100%; or, the gradually increasing or the gradually decreasing can be non-linear increasing or decreasing, for example, the first administered drug is 9μg, then the later increased dose can be 15μg, 18μg, 21μg and the like, namely, compared with the previous administered drug, the drug increasing degree at every time can be different.

[00609] It should be noted that the administration dosage and the administration protocol can be changed reasonably by the person skilled in the art based on the teaching of the invention, with the type and severity of the disorder to be released, the subject, the administration methods and the like.

F. Specific treatment methods and pharmaceutical applications.

[00610] Specific treatment methods and pharmaceutical applications with use of the present recombinant interferon are provided herein.

[00611] In one aspect, the present invention provides a method for treating a tumor in a subject, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2.

[00612] In one embodiment, the present invention provides a method for treating tumor in a subject, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2, and at least one other anti-cancer therapy, wherein the at least one other anti-cancer therapy is administered to the subject before, simultaneously, and/or after administration of the recombinant interferon, and wherein the tumor is a cancer or solid tumor that is not indicated nor appropriate for surgery, or the tumor is a solid tumor that cannot be resected, and the combination of the recombinant interferon and the at least one other anti-cancer therapy eliminate the tumor or reduce the size of the tumor compared to the tumor before treatment.

[00613] In one embodiment, the present invention provides a method for preventing tumor recurrence and/or metastasis or prolonging or maintaining a tumor-free status in a subject with a tumor after at least one anti-cancer therapy, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2.

[00614] In one embodiment, the present invention provides a non-surgical method for eliminating a tumor in a subject or reducing the size of a tumor in a subject, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2.

[00615] In one embodiment, the present invention provides a method for eliminating or reducing the pleural effusion, ascites, and/or pericardial effusion in a subject with tumor, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2.

[00616] In one embodiment, the present invention provides a method for treating tumor in a subject, comprising topically or locally administering to the tumor lesions of the subject a recombinant interferon encoded by SEQ ID NO: 2.

[00617] In one embodiment, the present invention provides a method for eliminating or reducing metastatic tumor lesions in a subject, comprising topically or

locally administering to the metastatic tumor lesions of the subject a recombinant interferon encoded by SEQ ID NO: 2.

[00618] In one embodiment, the present invention provides a method for eliminating or reducing the bone metastatic lesions of tumor in a subject, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2 by topical or local administration, wherein the topical or local administration comprises transdermal administration and/or infiltration administration, optionally, the recombinant interferon is administered to the bone metastatic lesions of tumor of the subject.

[00619] In one embodiment, the present invention provides a method for eliminating or reducing the bone lesions of tumor such as bone metastatic lesions of tumor, muscular lesions of tumor such as muscular metastatic lesions of tumor, subcutaneous tissue lesions of tumor such as subcutaneous tissue metastatic lesions of tumor, prostatic lesions of tumor such as prostatic metastatic lesions of tumor, and/or lymph node lesions of tumor such as lymph node metastatic lesions of tumor in a subject, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2 by any administration route through the skin, so that eliminating or reducing the bone lesions of tumor such as bone metastatic lesions of tumor, muscular lesions of tumor such as muscular metastatic lesions of tumor, subcutaneous tissue lesions of tumor such as subcutaneous tissue metastatic lesions of tumor, prostatic lesions of tumor such as prostatic metastatic lesions of tumor, and/or lymph node lesions of tumor such as lymph node metastatic lesions of tumor, optionally, the recombinant interferon is administered to the metastatic lesions of tumor of the subject.

[00620] In another aspect, the present invention provides a method for treating lung cancer in a subject, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2.

[00621] In one embodiment, the present invention provides a method for treating lung cancer in a subject, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2 and one or more chemotherapeutic

drugs in two or more treatment cycles, and then administering to the subject a recombinant interferon encoded by SEQ ID NO: 2 and one or more targeted drugs in one or more treatment cycles.

[00622] In one embodiment, the present invention provides a method for treating lung cancer in a subject, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2 by subcutaneous administration and/or intramuscular administration, wherein the recombinant interferon is administered in an amount in a range of about 2μg to about 70μg, optionally about 4μg to about 50μg, further optionally about 4μg to about 30μg by one subcutaneous administration and/or intramuscular administration, the recombinant interferon is administered by subcutaneous administration and/or intramuscular administration once every about 1 to about 7 days, optionally every about 1 to about 2 days, lasting at least about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject; or the duration can also be about 1 day to about 6 years, about 1 week to about 4 years, about 2 weeks to about 3 years, about 1 month to about 1 year, or about 2 months to about 9 months and the like.

[00623] In one embodiment, the present invention provides a method for treating lung cancer in a subject, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2 by subcutaneous administration and/or intramuscular administration, wherein the recombinant interferon is administered one or more times by subcutaneous administration and/or intramuscular administration at an induction dose in a range of about 2μg to about 10μg each time, optionally about 4μg to about 10μg each time, further optionally about 4.5μg to about 9μg each time, such as about 4.5μg each time or about 9μg each time, and then the

recombinant interferon is administered more times by subcutaneous administration and/or intramuscular administration at a therapeutic dose in a range of about 10μg to about 70μg each time, optionally about 12μg to about 50μg each time, further optionally about 12μg to about 30μg each time.

[00624] In one embodiment, the present invention provides a method for treating cancer in a subject, wherein the cancer originates from lung cancer in the subject and metastasizes to brain, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2, wherein the recombinant interferon is administered one or more times by subcutaneous administration and/or intramuscular administration at an induction dose in a range of about 2μg to about 10μg each time, optionally about 4μg to about 10μg each time, further optionally about 4.5μg to about 9μg each time, such as about 4.5μg each time or about 9μg each time, and then the recombinant interferon is administered more times by subcutaneous administration and/or intramuscular administration at a therapeutic dose in a range of about 10μg to about 70μg each time, optionally about 12μg to about 50μg each time, further optionally about 12μg to about 30μg each time, and the recombinant interferon is administered to the subject by inhalation administration before, simultaneously, and/or after the subcutaneous administration and/or intramuscular administration, the recombinant interferon is administered in an amount in a range of about 100μg to about 2000μg, optionally about 100μg to about 1500μg, further optionally about 150μg to about 800μg, still further optionally about 200μg to about 600μg by one inhalation administration, and the recombinant interferon is administered by inhalation administration once every about 1 day to about 3 days, optionally every about 1 day.

[00625] In one embodiment, the present invention provides a method for treating cancer in a subject, wherein the cancer originates from lung cancer in the subject and metastasizes to bone or liver, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2, wherein the recombinant interferon is administered one or more times by subcutaneous administration and/or intramuscular administration at an induction dose in a range of about 2μg to about

10μg each time, optionally about 4μg to about 10μg each time, further optionally about 4.5μg to about 9μg each time, such as about 4.5μg each time or about 9μg each time, and then the recombinant interferon is administered more times by subcutaneous administration and/or intramuscular administration at a therapeutic dose of about 10μg -about 70μg each time, optionally about 12μg to about 50μg each time, further optionally about 12μg to about 30μg each time.

[00626] In one embodiment, the present invention provides a method for treating cancer in a subject, wherein the cancer originates from lung cancer in the subject and metastasizes to lymph nodes, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2, wherein the recombinant interferon is administered one or more times by subcutaneous administration and/or intramuscular administration at an induction dose in a range of about 2μg to about 10μg each time, optionally about 4μg to about 10μg each time, further optionally about 4.5μg to about 9μg each time, such as about 4.5μg each time or about 9μg each time, and then the recombinant interferon is administered more times by subcutaneous administration and/or intramuscular administration at a therapeutic dose of about 10μg to about 70μg each time, optionally about 12μg to about 50μg each time, further optionally about 12μg to about 30μg each time, and the recombinant interferon is administered to the tumor and/or the lymph nodes metastases by topical or local administration before, simultaneously, and/or after the subcutaneous administration and/or intramuscular administration.

[00627] In one embodiment, the present invention provides a method for treating lung cancer in a subject, wherein the subject has pleural effusion, ascites and/or pericardial effusion, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2 by topical or local administration.

[00628] In another aspect, the present invention provides uses of a recombinant interferon encoded by SEQ ID NO: 2 in preparation of drugs for treating tumors in a subject.

[00629] In one embodiment, the present invention provides uses of a recombinant interferon encoded by SEQ ID NO: 2 and other anti-tumor drugs in

preparation of drugs for treating tumors in a subject.

[00630] In one embodiment, the present invention provides uses of a recombinant interferon encoded by SEQ ID NO: 2 in preparation of drugs for preventing tumor recurrence and/or metastasis after anti-tumor therapies in a subject.

[00631] In one embodiment, the present invention provides uses of a recombinant interferon encoded by SEQ ID NO: 2 in preparation of drugs for eliminating a tumor or reducing the size of a tumor in a subject by non-surgical method.

[00632] In one embodiment, the present invention provides uses of a recombinant interferon encoded by SEQ ID NO: 2 in preparation of drugs for eliminating or reducing pleural effusion, ascites, and/or pericardial effusion in a subject with tumor.

[00633] In one embodiment, the present invention provides a uses of a recombinant interferon encoded by SEQ ID NO: 2 in preparation of drugs for treating lung cancer in a subject.

[00634] In one embodiment, the present invention provides uses of a recombinant interferon encoded by SEQ ID NO: 2 in preparation of drugs for treating lung cancer in a subject in combination with chemotherapeutic drugs, targeted drugs.

[00635] In some embodiments, the subject is an early, medium-term, or advanced cancer patient, optionally, the subject is a medium-term, or advanced cancer patient, further optionally, the subject is an advanced cancer patient, such as an advanced lung cancer patient.

[00636] In some embodiments, the subject can be a stage 0, I, II, III, or IV cancer patient, optionally, the subject is an stage III or stage IV cancer patient, such as an stage III or stage IV lung cancer patient. Such cancer patient can be a patient with metastasized tumors, such as the tumors which are metastasized in situ or in the distance.

[00637] In some embodiments, the subject is a medium-term, advanced cancer patient, or stage III or stage IV cancer patient, optionally, the subject is an advanced, or stage III or stage IV cancer patient.

[00638] In some embodiments, the tumor is a cancer or a solid tumor with or without indications for surgery.

[00639] In some embodiments, the tumor in a subject is a tumor that is capable of being resected. In some embodiments, the tumor in a subject is a tumor that is not capable of being resected. In some embodiments, the surgeries include but not limited to surgical procedures.

[00640] In some embodiments, the subject is a subject with solid tumors.

[00641] In some embodiments, the solid tumor is a solid tumor that is capable of or is not capable of being resected.

[00642] In some embodiments, the solid tumor that is capable of or is not capable of being resected is an advanced solid tumor.

[00643] In some embodiments, the solid tumor is a solid tumor with or without indications for surgery, such as indications for tumor surgery.

[00644] In some embodiments, the solid tumor with or without indications for surgery such as indications for tumor surgery is an advanced, or stage III or stage IV solid tumor.

[00645] In some embodiments, the tumor is a solid tumor. The solid tumor comprises one or more of: lung cancer, liver cancer, hepatocellular carcinoma (HCC), esophageal cancer, cholangiocarcinoma, gallbladder carcinoma, stomach cancer, abdominal cancer, gastrointestinal cancer, gastric cancer, pancreatic cancer, renal cell carcinoma, renal cancer, bone cancer, breast cancer, ovarian cancer, uterine cancer, cervical cancer, endometrial cancer, colorectal cancer, colon cancer, rectal cancer, bladder cancer, superficial bladder cancer, prostate cancer, adrenal tumors, squamous cell carcinoma, neuroma, malignant neuroma, myoepithelial carcinoma, synovial sarcoma, rhabdomyosarcoma, gastrointestinal interstitial cell tumor, skin cancer, basal cell carcinoma, malignant melanoma, thyroid cancer, nasopharyngeal carcinoma, hemangioma, epidermoid carcinoma, head and neck cancer, glioma, or Kaposi's sarcoma; optionally, lung cancer; further optionally, the lung cancer comprises small cell lung cancer (SCLC), non small cell lung cancer (NSCLC), or both.

[00646] In some embodiments, the tumor is a non-solid tumor. The non-solid

tumor comprises one or more of leukemia, acute leukemia, chronic leukemia, chronic myelocytic leukemia, acute myelogenous leukemia, chronic myelogenous leukemia, chronic lymphocytic leukemia, acute lymphoblastic leukemia, T-cell leukemia, hairy cell leukemia, polycythemia, myelodysplastic syndrome, multiple myeloma, lymphadenoma, Hodgkin's lymphoma, or Non-Hodgkin's lymphoma.

[00647] In some embodiments, the effective amount is a therapeutically effective amount or a prophylactically effective amount. In some embodiments, the present recombinant interferon can be administered to the subject in single dose of about 2μg to about 2000μg, optionally, about 4μg to about 1500μg, further optionally, about 9μg to about 1000μg, and still further optionally, about 9μg to about 600μg. In certain embodiments, when the present recombinant interferon is administered by systemic administration, the therapeutically effective amount is about 2μg to about 70μg, optionally about 4μg to about 50μg, further optionally about 4μg to about 30μg, and still further optionally, about 9μg to about 30μg. In specific embodiments, when the present recombinant interferon is administered by systemic administration, the prophylactically effective amount is about 2μg to about 70μg, optionally about 4μg to about 50μg, further optionally about 4μg to about 30μg, and still further optionally, about 9μg to about 30μg.

[00648] In some embodiments, the present recombinant interferon and/or chemotherapeutic drugs, targeted drugs, biological drugs and the like combined with the present recombinant interferon can be administered to the subject by at least one of: systemic administration, topical administration, and local administration. In some embodiments, the present recombinant interferon and/or chemotherapeutic drugs, targeted drugs, biological drugs and the like combined with the present recombinant interferon can be administered to the subject by an administration route, the administration route comprises one or more of oral, rectal, sublingual, intravenous, intra-arterial, intramuscular, subcutaneous, intra-bone, intracutaneous, intra-articular, intraperitoneal, intrathecal, intracerebral, vaginal, percutaneous, transdermal, epidermal, transmucosal, transocular, pulmonary, nasal, abdominal, intrapleural, intraventricular, pericardial, inhalation, intratumoral, uterine, infiltration, or

intravesical administration. In some specific embodiments, the present recombinant interferon and/or chemotherapeutic drugs, targeted drugs, biological drugs and the like combined with the present recombinant interferon can be administered to the subject by subcutaneous, intramuscular, inhalation, infiltration, intrapleural, abdominal, pericardial, intratumoral, spary administration or any combination thereof. In some embodiments, the present recombinant interferon and/or chemotherapeutic drugs, targeted drugs, biological drugs and the like combined with the present recombinant interferon can be administered to the subject by intramuscular and/or subcutaneous administration. In some embodiments, when the present recombinant interferon and/or chemotherapeutic drugs, targeted drugs, biological drugs and the like combined with the present recombinant are administered to the operative site, which can be administered to the subject by topical or local administration, such as infiltration, intrapleural, abdominal, pericardial, uterine, intravesical, intratumoral, pulmonary, nasal, percutaneous, transdermal, epidermal, and/or transmucosal administration.

[00649] In some embodiments, the present recombinant interferon and/or chemotherapeutic drugs, targeted drugs, biological drugs and the like combined with the present recombinant interferon can be administered to the subject by injection, such as subcutaneous, intramuscular, intravenous, intra-arterial, intracerebral, intraperitoneal, intratumoral, intra-articular, intrathecal and intra-bone injection and the like. In some embodiments, when administering by inhalation, the inhalation can be pulmonary and/or nasal inhalation. In some specific embodiments, the inhalation administration can be dry powder inhalation or aerosol inhalation. In some embodiments, when administering by intrapleural, abdominal, uterine, intravesical, pericardial administration, the present recombinant interferon and/or chemotherapeutic drugs, targeted drugs, biological drugs and the like combined with the present recombinant interferon can be further administered to the subject by perfusion, such as intrapleural, abdominal, uterine, intravesical, and/or pericardial perfusion. In some embodiments, when administering by percutaneous, transdermal, epidermal or transmucosal administration, the present recombinant interferon and/or

chemotherapeutic drugs, targeted drugs, biological drugs and the like combined with the present recombinant interferon can be further administered to the subject by spray, such as percutaneous, epidermal, transdermal and/or transmucosal spray.

[00650] When the present recombinant interferon is systemically administered via injection administration (such as subcutaneous injection, intramuscular injection), the single dose can be about 2μg to about 70μg, optionally about 4μg to about 50μg, and further optionally about 4μg to about 30μg, including but not limited to about 2μg, about 3μg, about 4μg, about 4.5μg, about 9μg, about 13.5μg, about 15μg, about 18 μg, about 21μg, about 25.5μg, about 30μg, about 40μg, about 50μg, about 60μg, and about 70μg. In some embodiments, the present recombinant interferon is administered by subcutaneous and/or intramuscular administration once every about 1 day to about 7 days, optionally once every about 1 day to about 2 days. In some embodiments, the injection lasts at least about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject; or the duration can also be about 1 day to about 6 years, about 1 week to about 4 years, about 2 weeks to about 3 years, about 1 month to about 1 year, or about 2 months to about 9 months and the like.

[00651] When the present recombinant interferon is locally administered via injection administration (such as the intratumoral injection), the single dose of the recombinant interferon can be in the range of about 60μg to about 600μg, optionally about 60μg to about 500μg, further optionally about 80μg to about 400μg, and still further optionally about 100μg to about 250μg. In some embodiments, the present recombinant interferon is administered via intratumoral administration once every about 1 day to about 10 days, optionally once every about 1 day to about 7 days such as every about 1, 2, 3, 4, 5, 6 or 7 days. In some embodiments, the intratumoral

administration such as intratumoral injection lasts at least about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject; or the duration can also be about 1 day to about 6 years, about 1 week to about 4 years, about 2 weeks to about 3 years, about 1 month to about 1 year, or about 2 months to about 9 months and the like. In specific embodiments, when the present recombinant interferon is administered via intratumoral administration, the protocol of intratumoral administration is as follow: the recombinant interferon is administered by intratumoral injection once every about 1 day for about 4 to about 8 times, and then the recombinant interferon is administered by intratumoral injection once every about 3 days to about 5 days for about 4 to about 8 times, and then the recombinant interferon is administered by intratumoral injection once every about 7 days, the intratumoral administration is stopped when the tumor disappears or becomes too small to conduct the intratumoral injection, wherein the recombinant interferon is administered in an amount of about 60μg to about 600μg, optionally about 60μg to about 500μg, further optionally about 80μg to about 400μg, still further optionally about 100μg to about 250μg by once intratumoral injection.

[00652] When the present recombinant interferon is administered via inhalation (such as pulmonary and nasal inhalation, including dry powder inhalation and aerosol inhalation), the single dose of the recombinant interferon can be about 100μg to about 2000μg, optionally about 100μg to about 1500μg, further optionally about 150μg to about 800μg, and still further optionally about 200μg to about 600μg, including but not limited to about 100μg, about 200μg, about 300μg, about 400μg, about 500μg, about 600μg, about 700μg, about 800μg, about 900μg and about 1000μg. In some embodiments, the present recombinant interferon is administered via inhalation once

every about 1 day to about 3 days, optionally every about 1 day. In some embodiments, the inhalation lasts at least about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject; or the duration can also be about 1 day to about 6 years, about 1 week to about 4 years, about 2 weeks to about 3 years, about 1 month to about 1 year, or about 2 months to about 9 months and the like.

[00653] When the present recombinant interferon is administered via perfusion (such as intrapleural, abdominal, uterine, intravesical, pericardial perfusion), the single dose of the recombinant interferon can be about 30μg to about 2000μg, optionally about 100μg to about 1500μg, further optionally about 150 to about 1000μg, still optionally about 200 to about 800μg, and still further optionally about 200 to about 400μg. In some embodiments, the present recombinant interferon is administered via intrapleural, abdominal and/or pericardial administration once every about 1 day to about 10 days, optionally once every about 1 day to about 7 days such as every about 1, 2, 3, 4, 5, 6, or 7 days. In some embodiments, the perfusion lasts at least about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject; or the duration can also be about 1 day to about 6 years, about 1 week to about 4 years, about 2 weeks to about 3 years, about 1 month to about 1 year, or about 2 months to about 9 months and the like.

[00654] When the present recombinant interferon is administered to the lesions (such as the surfaces of skin and mucosa) by spray, such as percutaneous, epidermal, transdermal, transmucosal spray, the single dose of the recombinant interferon can be about 6μg to about 100μg, optionally about 10μg to about 40μg, and further optionally about 20μg to about 40μg. In some embodiments, the present recombinant interferon is administered by spray administration about 1 to about 6 times such as about 1, 2, 3, 4, 5, or 6 times per day. In some embodiments, the spray lasts at least about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject; or the duration can also be about 1 day to about 6 years, about 1 week to about 4 years, about 2 weeks to about 3 years, about 1 month to about 1 year, or about 2 months to about 9 months and the like.

[00655] In some embodiments, for the purpose of treatment, the present recombinant interferon can be administered to the subject about 1, 2, 3, 4, 5, 6, 7, 8, or more times per day, or the present recombinant interferon can be administered to the subject once at the time interval of every about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or 21 days, every month, every 2 months, or a longer time. In some embodiments, for the purpose of prevention, the present recombinant interferon can be administered to the subject once at the time interval of every about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, every 2 weeks, every 3 weeks, every month, every 2 months, every 3 months, every half year, every 1 year, or a longer time.

[00656] In some embodiments, the present recombinant interferon is administered in one or more treatment cycles. Optionally, the more cycles can be 2, 3, 4, 5, 6, 7, 8, 9, 10, or more treatment cycles. In specific embodiments, duration of the one treatment cycle is at least about 1 day, about 2 days, about 3 days, about 4 days,

about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, about 6 years and the like, or the duration can also be about 1 day to about 6 years, about 1 week to about 4 years, about 2 weeks to about 3 years, about 1 month to about 1 year, or about 2 months to about 9 months and the like. In specific embodiments, the present recombinant interferon can be administered for a long time, including over the life time of the subject, so as to improve or control or limit the symptom of the subjects.

[00657] In some embodiments, the present recombinant interferon could be administered in more treatment cycles. In certain embodiments, the treatment cycles are 2 or more treatment cycles. In specific embodiments, the duration of the multiple treatment cycles may include over the life time of the subject. In some embodiments, the time intervals of any two adjacent treatment cycles in all the treatment cycles can be the same or different. In specific embodiments, the time intervals can be at least about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, about 6 years and the like; or the time intervals can be about 2 days to about 6 years, about 4 days to about 3 years, about 1 weeks to about 1 years, about 2 months to about months, about 3 months to about 6 months and the like.

[00658] In some embodiments, when the present recombinant interferon is administered more times in one treatment cycle, the present recombinant interferon can be administered for one or more times in a smaller dose, then the present recombinant interferon is administered for one or more times in an increased or gradually-increased dose. In specific embodiments, when the present recombinant interferon is systemically administered via subcutaneous, intramuscular

administration (such as subcutaneous, intramuscular injection), the present recombinant interferon can be administered once at a smaller dose such as about 4.5μg or 9μg, then the recombinant interferon can be administered for more times in an increased (such as to be about 15μg, about 18μg, about 21μg) or gradually-increased dose. In embodiments, the present recombinant interferon is administered once every about 1 day to abut 2 days. In embodiments, the duration for administration of the present recombinant interferon is about 1 week to about 2 years, optionally about 2 weeks to about 1 year, or further optionally about 1 month to about 9 months, including about 2 months to about 6 months, or over the life time of the subject. In embodiments, the gradually-increased administered dose can be about 110% to about 500% of the previously administered dose sequentially. In embodiments, a smaller dose of the present recombinant interferon (such as about 4.5μg or about 9μg) can be administered, followed by about 12μg to about 18μg (such as about 13.5μg, about 15μg, about 18μg), and then about 15μg to about 30μg (such as about 18μg, about 21μg, about 25.5μg, about 30μg), once every about 2 days, and for about 2 months to about 3 years, or over the life time of the subject.

[00659] In some embodiments, the recombinant interferon can be administered one or more times at an induction dose, and then one or more times at a therapeutic dose. In some embodiments, the induction dose is about 2μg to about 10μg each time, optionally about 4μg to about 10μg each time, further optionally about 4.5μg to 9μg each time, for example, about 4.5μg each time or about 9μg each time. In some embodiments, the therapeutic dose is about 10μg to about 70μg each time, optionally about 12μg to about 50μg each time, further optionally about 12μg to about 30μg each time. In some embodiments, the induction dose is about 4μg to about 10μg each time, and the therapeutic dose is about 12μg to about 50μg each time. In some embodiments, the induction dose is usually lower than the therapeutic dose. In some embodiments, the time interval between administration of the induction dose and the therapeutic dose is about 1 day to about 1 month, optionally about 1 day to 1 week, further optionally about 1 day to about 3 days, including, for example, about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8

days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks and about 1 month. In some embodiments, when the induction dose is administered more times, it is administered once every about 1 day to about 10 days, optionally every about 1 day to about 7 days, further optionally every about 1 day to about 2 days, including, for example every about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 days. In some embodiments, when the therapeutic dose is administered more times, it is administered once every about 1 day to about 10 days, optionally every about 1 day to about 7 days, further optionally every about 1 day to about 2 days, including, for example, every about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 days. In some embodiments, the total administration time of the induction and therapeutic dose should last at least about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, about 6 years and the like, o or the recombinant interferon can be administered for a long time, including over the life time of the subject.

[00660] In some embodiments, the treatment has reduced the tumor size of the subject, for example, by about 10%, about 20%, about 30%, about 40%, about 50%, about 60%, about 70%, about 80%, about 90%, about 95%, or about 100% or more, or even completely eliminate the tumor, according to the tumor size at the beginning of treatment. In some embodiments, the treatment has reduced the number of cancer cells in tumor, malignant pleural effusion, malignant ascites and/or malignant pericardial effusion of the subjects, for example, by about 10%, about 20%, about 30%, about 40%, about 50%, about 60%, about 70%, about 80%, about 90%, about 95%, about 100% or more, or even the number of cancer cells is zero, according to the number of cancer cells at the beginning of treatment. In some embodiments, the treatment has inhibited (including reduced to some degree and/or terminated) the infiltration of tumor cells into peripheral organs; inhibited or prevented tumor metastasis, such as the in-situ or distant metastasis of tumors, or micrometastasis of tumors; reduced the size of the lesions; brought about downstaging of tumor; and also

inhibited or killed micrometastasis in the blood and lymphatic channels; thereby allowing complete resection of initially unresectable tumors or helping to resect tumor which is capable of being resected, such resection is for example a surgical resection. As for the method, it can be a "neoadjuvant method" or an "introducing method". As used herein, term "neoadjuvant method" or "introducing method" refers to a therapy given prior to surgery, the goal of the therapy is to reduce the size of the lesions, bring about downstaging of tumor, inhibit or kill micrometastases in the blood and lymphatic channels, reduce the tumor size thereby allowing more conveniently resect tumors or completely resect of initially unresectable tumors. In addition, the present recombinant interferon can be further administered to the subject to prevent recurrence and/or metastasis of the tumors after resection of the tumors.

[00661] In some embodiments, the method has reduced or eliminated malignant pleural effusion, malignant ascites and/or malignant pericardial effusion, for example, by about 10%, about 20%, about 30%, about 40%, about 50%, about 60%, about 70%, about 80%, about 90%, about 95%, about 100% or more, or even completely eliminated malignant pleural effusion, malignant ascites and/or malignant pericardial effusion, according to the volume of malignant pleural effusion, malignant ascites and/or malignant pericardial effusion at the beginning of treatment.

[00662] In some embodiments, the method for preventing recurrence of tumor has reduced the possibility of tumor recurrence after the subject with tumors received treatment. In some embodiments, the subject with tumors has been identified and treated prior to administration of the present recombinant interferon (rSIFN-co); such treatments may be the method with the present recombinant interferon, or one or more other different anti-cancer therapies such as chemotherapy, radiotherapy, surgical therapy, interventional therapy, biotherapy, gene therapy, ablation therapy, immunotherapy, targeted therapy, traditional Chinese medicine therapy or any combination thereof. The treatment results can be clinical or basic healing. In some embodiments, such preventive therapies can inhibit or eliminate possible micrometastasis in the blood channel and lymphatic channel, so as to prevent recurrence and/or metastasis of the tumor, such

micrometastasis can or cannot be clinically detected.

[00663] In some embodiments, the present recombinant interferon could delay the growth of tumor in the subject, for example, by about 10%, about 20%, about 30%, about 40%, about 50%, about 60%, about 70%, about 80%, about 90%, about 95% or more, according to the tumor growth speed at the beginning of the treatment.

[00664] In some embodiments, the present recombinant interferon is administered to the subject as monotherapy. In some embodiments, further comprising one or more other anti-cancer therapies administered to the subject, optionally, other anti-cancer therapies are administered to the subject before, simultaneously, and/or after administration of the recombinant interferon. In some embodiments, the other anti-cancer therapies comprise one or more of: chemotherapy, radiotherapy, surgical therapy, interventional therapy, biotherapy, gene therapy, ablation therapy, immunotherapy, targeted therapy, and traditional Chinese medicine therapy. In certain embodiments, the other anti-cancer therapies comprise one or more of chemotherapy, radiotherapy, surgical therapy, targeted therapy, and biotherapy. In some embodiments, the other anti-cancer therapies comprise chemotherapy, radiotherapy, or both. In some embodiments, the other anti-cancer therapies comprise chemotherapy such as first-line chemotherapy, for example, chemotherapeutic drugs and/or chemotherapeutic protocols comprising platinum compounds, such as Cisplatin.

[00665] In some embodiments, when in the treatment for lung cancer, chemotherapeutic drugs used in the chemotherapy combined with the present recombinant interferon include but not limited to platinum compounds such as Cisplatin, Carboplatin, Eloxatin and the like; Paclitaxel compounds such as Docetaxel (Docetaxel Injection, Taxotere) and the like; cytidine antimetabolite such as Gemcitabine (Gemzar) and the like; antifolic antimetabolite such as Pemetrexed (Alimta) and the like; pyrimidine antimetabolite such as Capecitabine (Xeloda) and the like; as well as any combination of the chemotherapeutic agents. Or otherwise the following chemotherapy protocols are used, including but not limited to chemotherapy protocols containing platinum compounds, such as GP, TP, EP, GP-T2 protocols and the like. In specific embodiments, when in the treatment for the lung

cancer, the chemotherapy protocol applied in conjunction with the present recombinant interferon includes Cisplatin nebulized inhalation, Cisplatin pericardial perfusion and the like.

[00666] In some embodiments, when in the treatment for lung cancer, the targeted drugs used in the targeted therapy combined with the present recombinant interferon include but not limited to Gefitinib, Erlotinib and/or recombinant human endostatin and the like.

[00667] In some embodiments, when in the treatment for the lung cancer, other anti-cancer therapies applied in combination with the present recombinant interferon include any combination of the chemotherapeutic drugs/chemotherapy protocols and targeted drugs.

[00668] In specific embodiments, when in the treatment for the lung cancer, other anti-cancer therapies applied in combination with the present recombinant interferon include GP protocol combined with recombinant human endostatin, EP protocol combined with Cisplatin nebulized inhalation and the like.

[00669] In some embodiments, the method of the present invention is a non-surgical therapy.

G. Evaluation standard of curative effect and adverse effect

[00670] The curative effect evaluation on the present recombinant interferon in the aspect of clinical treatment for tumors such as solid tumors adopts the Response Evaluation Criteria in Solid Tumors standard (RECIST standard) published in 1999 (see James, K. et al. J Natl Cancer Inst, 1999, 91, 523-528).

[00671] The tumor lesions are divided into measurable lesions and un-measurable lesions, wherein the measurable lesions are defined as target lesions; the longest diameter represents the size of each lesion; at most 5 lesions can be selected in each involved organ, the sum of the measured lesions of all the involved organ is not more than 10, and the sum of the longest diameters of all

the lesions is the overall diameter of the target lesion. The un-measurable lesions are defined as non-target lesions, only the existence of the lesions are recorded and tracked, but the sizes of the lesions are not measured.

[00672] The curative effect evaluation standard of the target lesion is divided into 4 grades, the curative effect evaluation standard of the non-target lesion is divided into 3 grades, and the overall curative effect evaluation is obtained by combining the curative effects of the two kinds of lesions. It is specifically described as follows:

[00673] The curative effect evaluation standard of the target lesions: (1) CR (complete remission): all the target lesions disappear; (2) PR (partial remission): the overall diameter of the target lesions is decreased by more than 30%; (3) NC or SD (no change or stable disease): the target lesions are neither decreased to "PR" nor increased to "PD"; and (4) PD (progression disease): the overall diameter of the target lesions is increased by more than 20%, or one or more new lesions appear.

[00674] The curative effect evaluation standard of the non-target lesion: (1) CR: all the non-target lesions disappear, and the tumor marker level is normal; (2) IR (incomplete response)/SD: one or more non-target lesions is/are not changed, and/or the tumor markers exceed the normal limit; and (3) PD: one or more new lesions appear, and/or the non-target lesions are obviously developed.

[00675] The overall curative effect evaluation standard of solid tumors.

Table 1 The overall curative effect evaluation standard of solid tumors

Target lesion	Non-target lesion	New lesion	Overall curative effect
CR	CR	No	CR
CR	IR/SD	No	PR
PR	Non-PD	No	PR

NC/SD	Non-PD	No	NC/SD
PD	Any	Yes or No	PD
Any	PD	Yes or No	PD
Any	Any	Yes	PD

[00676] The adverse effect evaluation on the present recombinant interferon for clinical treatment for the tumors such as the solid tumors takes the reference to the "WHO" Toxicity Grading Standard.

[00677] Compared with the prior art, the recombinant interferon has the beneficial effects as follows:

[00678] The recombinant interferon rSIFN-co used in the present invention has obvious different structural features and physiological activities compared with the existing interferons such as INFERGEN® (interferon alfacon-1) of the US Amgen. On one hand, the recombinant interferon can be singly used and/or can be combined with radiotherapy, chemotherapy, biological agents, and/or targeted drugs and the like, so as to non-surgically eliminate or reduce the tumors of the solid tumor subjects, particularly advanced tumors; specifically, the recombinant interferon can eliminate or reduce the solid tumors without indications for surgery, particularly the advanced solid tumors without indications for surgery. On the other hand, the recombinant interferon can be singly administered through topical or local administration such as intratumoral injection/epidermal spray administration and the like, or through the combination of the topical or local administration together with the systemic administration (using the present recombinant interferon or radiotherapy/other anti-tumor drugs and the like), so as to non-surgically (namely, without surgery) eliminate or reduce the solid tumors. Further, the recombinant interferon has obvious effect in replacing the chemotherapy drugs for preventing post-surgery recurrence or metastasis of the tumors, particularly various metastatic lesions such as bone metastasis which cannot be eliminated by existing treatment means; however,

drugs can be directly administered to the lesions by the present invention, especially by the topical or local administration, to obviously reduce or eliminate the tumors. In addition, the recombinant interferon can be singly administered through intrapleural or abdominal perfusion so as to for effectively eliminate or decrease malignant pleural effusion and/or malignant ascites.

[00679] Furthermore, cancer can be controlled by the rSIFN-co combination therapy. Firstly, the present recombinant interferon (rSIFN-co) has broad-spectrum anti-tumor effects, which is effective on both solid tumors and non-solid tumors while, at the same time, rSIFN-co has a good synergetic effect with existing treatment means such as surgical therapy, chemotherapy, radiotherapy, biotherapy and other anti-tumor drugs. Secondly, rSIFN-co has low toxicity which means no harm to normal cells has been observed when rSIFN-co is used in large doses. Thirdly, rSIFN-co is convenient to use and can be directly applied to tumors in any position. The rSIFN-co can be used by subcutaneous/intramuscular injection to control systemic progress of tumor, by intrapleural/abdominal perfusion to eliminate effusion and intrapleural/abdominal tumors, by topical or local injection to eliminate primary or metastatic tumors, and by infiltration (transdermal) administration to treat tumor lesions in bone, skin, muscle, prostate and the like; and rSIFN-co can also be administered by aerosol inhalation. According to above three advantages of rSIFN-co, effective rate of the combination therapy is no lower than 90%. With regard to early or medium-term cancer cases, rSIFN-co can be used after surgery to replace chemotherapy and effectively prevent recurrence and metastasis; with regard to advanced cancer cases or cancer cases without indications for therapy, rSIFN-co can be used to eliminate tumors without surgery; with regard to cases without indications for surgery, rSIFN-co can be used to transformed the cases into ones with indications for surgery, thereby creating surgical conditions. Therefore, we believe the rSIFN-co combination therapy is capable of curing cancer.

Embodiments

[00680] The present invention will be specifically described in the following

examples that are only used to elaborate the purpose but not to limit the scope of the present invention. The present invention can be modified without deviating from its scope. All publications, patents and patent applications that are referenced, the contents of which are hereby incorporated by reference into this application as every independent publication, patent and patent application are separately incorporated by reference into this application.

[00681] Informed Consent Forms have been signed by all patients involved in the following embodiments, and Confidentiality Agreements have been signed by and between the applicants and hospitals. At the same time, the test processes are conducted in accordance with the requirements set forth by Ethics Committee for Clinical Drug Trials.

Example 1: Preparation of the composition of the recombinant interferon

[00682]

Ingredients of recombinant interferon freeze-dried injection (freeze-dried powder)

rSIFN-co stock solution solution of present invention	34.5μg/ml
pH 7.0 phosphate buffer (PB)	10mmol/L
Glycine	0.4mol/L

[00683] Preparation procedures: raw materials were weighed by the ingredients and dissolved by sterile and pyrogen-free water for injected; then filtered by a membrane of 0.22μm pore diameter for sterilization, and preserved at 6-10℃; the materials were sampled for sterile and pyrogen inspections and then separately loaded in vials after qualified inspections, each with a single dose of 0.3-0.5. And then, the materials were put into freeze dryer for freezing and drying.

[00684]

Ingredients of recombinant interferon water solution injection

rSIFN-co stock solution of present invention	34.5μg/ml
pH 7.0 phosphate buffer (PB)	25mmol/L
sodium chloride	0.4mol/L

[00685] Preparation procedures: raw materials were weighed by the ingredients and dissolved by sterile and pyrogen-free water for injection; then filtered by a membrane of 0.22μm pore diameter for sterilization, and preserved at 6-10℃; the materials were sampled for sterile and pyrogen inspections and then separately loaded in sealed containers after qualified inspections, each with a single dose of 0.3-0.5. And then, the finished product were preserved at 2-10℃ in dark places.

[00686] Ingredients of Recombinant Interferon Spray

[00687] The ingredient content percentages in the table below are based on weight percentages.

EDTA	0.01%
Tween 80	0.05%
Trisodium citrate	10mmol/L
Glycerol	1.26%
Sodium chloride	0.03%
Benzyl alcohol	0.5%
Human albumin	0.1%
Recombinant super-compound interferon	10μg/ml

[00688] The preparation method refers to conventional preparation method of spray.

[00689] Preparation of recombinant interferon inhalant

[00690] Conventional preparation methods of interferon inhalant were adopted. The recombinant interferon inhalant of the present invention was prepared

according to conventional preparation methods of interferon inhalant.

Example 2: clinical data of patients treated by the present recombinant interferon (58 cases)

[00691] Following is a summary clinical treatment table (table 2) of 58 patients of various cancer types who have been treated by the present recombinant interferon until July 1, 2012.

Table 2: Summary of Clinical Treatment of Multiple Types of Cancers in 58 Patients

[0692]

Patient No.	Sex	Age	Diagnosed Condition(s)	Stage	Treatment prior to drug administration	Dosage regimens for Interferon	Regimens for Combined therapy	Treatment results	Total therapeutic effectiveness
1	Male	53	Non small cell lung cancer in right lung	IIIb	DP Regimen® was provided from October 14, Year 1 to November 25, Year 1: 75 mg of Taxotere and 75 mg of Cisplatin on Day 1. Two cycles of chemotherapy were performed in total, each lasting for 21 days.	The rSIFN-co therapy started in November, Year 1. Intramuscular injection of rSIFN-co was done once every other day: 9μg for the 1st time, 15μg for the 2nd time and 18μg for the 3rd time and thereafter. Therapy continued till February, Year 3, during which rSIFN-co treatment had been stopped for 1 month in April, Year 2, leading to a total treatment duration of 15 months.	Radiotherapy® (DT40Gy) on right lung and mediastinal lymph nodes started on December 2, Year 1 followed by X-knife therapy (DT20Gy)	Primary lesions on right pulmonary hilum disappeared and cured.	CR
2	Male	40	Non small cell lung adenocarcinoma	IV	Systematic chemotherapy began at January, Year 1: Taxotere and Carboplatin. One cycle of 21 days was provided.	The rSIFN-co therapy began on April 14, Year 1. Intramuscular injection of rSIFN-co was done once every other day: 9μg for the 1st time, 15μg for the 2nd time, 18μg for the 3rd time and 21μg for the 4th time and thereafter. Meanwhile, aerosol inhalation of rSIFN-co was done once every day:	From April 20, Year 1 to September 3, Year 1, Endostar® was administrated every day: 7.5 mg/m^2 per dose, 1.2×10^{5}U/m^2. Four cycles were performed totally with each lasting for 14 days. Meanwhile, GP regimen was	The size of the primary lesions on upper lobe of right lung reduced from about 10.2×8.2×7.7cm to 1.2×1.4cm. Metastatic lesions in the right liver and multiple	PR

						300μg for the 1st time, 500μg for the 2nd time, 600μg for the 3rd time and thereafter. Administration of rSIFN-co ended in April Year 2.	combined: 1600mg of Gemcitabine on days 1 and 8 and 40mg of Cisplatin on days 1~3. Four cycles were performed, each being 15 days. One intrapericardial infusion with Cisplatin (30mg) was performed on July 19, Year 1. Aerosol inhalation of Cisplatin was added from December 23, Year 1 to January 14, Year 2: 10mg/dose, 2 doses per day. The second course of Endostar treatment was provided from January 18, Year 2 to January 30, Year 2 with same dosage. Chemotherapy using Pemetrexed ® proceeded from December 25, Year 1 to January 19, Year 2: iv. 500mg/m^2, every 3 to 4 weeks.	lymph nodes disappeared. The metastatic lesions on the two lungs decreased in size and the radioactive concentration/accumulation decreased.	

3	Female	51	Non small cell lung cancer	IV		Treatment with rSIFN-co started on May 29, Year 1. Intramuscular injection of rSIFN-co was done once every other day: 9μg for the 1st time, 18μg for the 2nd time and 21μg for the 3rd time and thereafter. Aerosol inhalation of rSIFN-co was simultaneously performed: 200μg/every other day. From July 14, Year 1, 18μg of rSIFN-co was used in intramuscular	During this period, Gamma knife radiotherapy for the brain lesions was conducted.	The primary lesion of about 5.1×3.2cm on the upper lobe of right lung disappeared. The enlarged lymph nodes in the mediastinum and the metastatic lesions in the brain of about 3.7×2.6cm basically disappeared.	CR
						As none of the treatments had any obvious effect, the chemotherapy during February 15, Year 2 to April 25, Year 2 was replaced with DP regimen® (75mg/m^2 of Taxotere and 75mg/ m^2 of Cisplatin on day 1) in combination with administration with Tarceva (150mg/day) for 4 cycles with 21 days per cycle. A Gamma knife therapy was performed on head on June 29, Year 2.			

						injection. Aerosol inhalation of 400μg of rSIFN-co was simultaneously performed every other day. The administration continued for more than 3 months till September 16, Year 1.			
4	Male	49	Small cell lung cancer in right lung	IV	The first cycle of EP® chemotherapy was conducted from March 25, Year 1 to Apr 9, Year 1: 100mg of Etoposide and 30mg of Cisplatin.	The treatment of rSIFN-co began on April 12, Year 1. Intramuscular injection was done once every other day: 9μg for the 1st time, 15μg for the 2nd time and 18μg for the 3rd time and thereafter. Aerosol inhalation of rSIFN-co was performed once every other day: 0.5~2ml/dose (200μg/ml). From July 16, Year 1, 21μg of rSIFN-co was used in intramuscular injection. Aerosol inhalation of rSIFN-co continued but the amount per dose was changed to 200μg . The first cycle finished by the end of March Year 2 (lasting for almost 1 year). The administration of rSIFN-co was stopped for 1 month because Aerosol inhalation of Cisplatin (one dose per day and 10mg per dose) was	Five cycles of EP chemotherapy were conducted from March 25, Year 1 to September 10, Year 1 and the same regimen as mentioned above was used. An interventional cryoablation was conducted on the supraclavicular lesions on September 3, Year 2. From October Year 1, a 15-day regimen of aerosol inhalation of Cisplatin was added: 10mg per dose, 1 dose per day. Two cycles were done, each lasting for 15 days.	A primary lesion of about 0.6×0.4cm, on the apex of right lung disappeared. A lesion with a nodule of about 2.6×2.2cm on the of right clavicle disappeared. Mutilple nodules appearing in neighboring areas of the mediastinal brachiocephalic trunk, right brachiocephalic veins, superior vena cava, and trachea, part of which fused and lesions of about 5.5cm×4.9cm in size disappeared.	CR

						performed throughout September Year 1. The 2nd cycle of treatment proceeded from October 9, Year 2 to January 26, Year 3 during which 18μg of rSIFN-co was intramuscularly injected every other day.			
5	Female	42	Metastatic moderately differentiated lung adenocarcinoma (in right humerus)	IV	A surgical repair of right humerus was performed on February 23, Year 1. After that surgery, patient was given 4 courses of DP® chemotherapy: 75mg of Taxotere and 75mg of Cisplatin on day 1.	Treatment with rSIFN-co began on April 15, Year 1. Intramuscular injection was performed once every other day: 9μg for the 1st time and 21μg for the 2nd time and thereafter. The treatment was provided for a total of 3 months till September 15, Year 1, during which rSIFN-co administration was suspended for 1 month due to chemotherapy (the chemotherapy regimen shown below related to aerosol inhalation of Cisplatin) and for 1 month because of the patient's physical condition. Aerosol inhalation of rSIFN-co was added on September 16, Year 1: 1ml (200μg/ml) per day. Till February , Year 2, the co-administration regimen	Aerosol inhalation of Cisplatin began on September 16, Year 1: 10mg per dose and 2 doses per day. Eight cycles were conducted with each cycle being 15 days.	Radioactive concentrations at the primary lesion of right lung tumor, right humerus and the T6 vertebra evidently decreased. Metastatic lesions on pelvis and lumbar vertebrae as well as enlarged paratracheal lymph nodes disappeared.	CR

						was provided for 5 months. From September 15, Year 2, intramuscular injection of 15μg was provided every other day.			
6	Male	39	Moderately-poorly differentiated adenocarcinoma in left lung	IV	The first cycle of GP Regimen ® began in September Year 1 with each cycle lasting for 21 days: 1000mg/m^2 of Gemcitabine on day 1 and 8 and 75mg/ m^2 of Cisplatin on day 1.	Treatment with rSIFN-co began on October 12, Year 1 with aerosol inhalation of 600μg every day. Intramuscular injection of rSIFN-co started on December 12, Year 1, once every other day: 9μg for 1st time, 15μg for 2nd time and 18μg for 3rd time and thereafter. Local spraying on bone metastases began on March 12, Year 2: 70μg~139μg/does/site, 4~5 doses/day.	The second cycle of GP Regimen ® started on October 14, Year 1 (the regimen was exactly the same as mentioned above). Gefinitib was taken from November 24, Year 1: 1 pill/dose (250mg/pill), 1 dose/day.	Primary lesion of about 9×3.5cm in size at the left lung almost disappeared. Enlarged lymph nodes of about 1.0cm×0.7cm at left segment of neck, nodules of about 1.2cm×0.8cm at left supraclavicular fossa and nodules of about 1.4cm×1.1cm at right and root segment of neck disappeared. Metastatic lesions on sternum disappeared; and metastatic lesions at right sternoclavicular joints, ribs and pelvis shrank and relieved to some extent.	CR
7	Female	53	Metastatic lung adenocarcinoma (lymph nodes at left	IV		Treatment with rSIFN-co began on July 31, Year 1. Intramuscular injection was done once every other	Meanwhile, Iressa (Gefinitib) ® produced in India was administered in combination	Primary lesions in right lung and metastatic lesions in both lungs and several bones	PR

			clavicle)			day: 9μg for 1st time, 18μg for 2nd time and 21μg for 3rd time and thereafter. Seventy-five times of intramuscular injection were done till January 2, Year 2 (totally 5 months).	for 1 year: 1 pill/dose (250mg/pill), 1 dose/day.	shrank with radioactive concentration decreased; metastasis in liver disappeared.	
8	Female	68	Lung cancer in right lung	IV		Treatment with rSIFN-co began on July 21, Year 1 Intramuscular injection was done once every other day: 9μg for 1st time, 15μg for 2nd time and 18μg for 3rd time and thereafter. Meanwhile, aerosol inhalation of rSIFN-co of 600μg was performed once a day. Administration of rSIFN-co continued for 3 months till October 31, Year 1.	Administration of Gefinitib (Iressa)® was added in July Year 1: 250mg/pill, 1 pill/dose, 1 dose/day.	Lesions of about 3.0×3.9cm at the lower lobe of right lung, and metastatic lesions in left ilium disappeared basically.	CR
9	Male	55	Squamous cell carcinoma	IIb		Treatment with rSIFN-co began on March 18, Year 1. Aerosol inhalation of rSIFN-co of 600μg was performed once a day. A course completed till July 20, Year 1 (for 4 months) with 100 doses of acrosol inhalation done.	Four cycles of chemotherapy (GP regimen®) were performed with the first one beginning at April 12, Year 1 and each cycle lasting for 21 days: 1600mg of Gemcitabine on days 1 and 8 and 40mg of Cisplatin on days 1 and 3.	Primary lesions of about 3.3×2.4×2.0cm in right lung basically disappeared and enlarged lymph nodes in right hilum of about 2.0×2.2cm disappeared.	CR

10	Female	48	Non small cell lung cancer in left lung	IIIb		Treatment with rSIFN-co began on March 9, Year 1. Intramuscular injection of rSIFN-co was performed once every other day: 18μg for 1st	Meanwhile, 3 cycles of Endostar® administration were performed with 14 days as one cycle: 7.5mg/m^2 (1.2×10^5U/m^2) per dose, 1 dose/day. Second cycle of chemotherapy began on May 10, Year 1 with the same regimen. Third cycle of chemotherapy began on June 7, Year 1 with the same regimen. Fourth cycle of chemotherapy began on July 7, Year 1 with the same regimen. Four cycles of chemotherapies were totally performed.	Primary lesions of about 2.0×2.0cm in left lung basically disappeared and malignant pleural effusion	CR

						time, 21μg for 2nd time and thereafter. Such administration continued for almost 1 year till March, Year 2. Intrapleural perfusion of rSIFN-co was done once every 8 days from April 29, Year 1: 9μg×4 vials for 1st and 2nd time and 9μg×5 vials for 3rd time. Three perfusions were provided totally. Four CT-guided interventional operations were performed in July and August Year 2. The rSIFN-co was injected into relatively large lesions in lungs and 21μg×10 vials were used each time.		disappeared.	
11	Male	40	Non-hodgkin lymphoma on mesenteric lymph nodes	IV	Chemotherapy was performed for 7 times (five times of CHOPE regimen and two times of MTX regimen) began on August, Year 1. Autologous stem cell transplantation was done in March Year 2. Chemotherapy were provided for	Treatment with rSIFN-co began on June 9, Year 3. An aerosol preparation of rSIFN-co (72μg/ml) was sprayed onto the nasopharynx and Oral Cavity 2~3 times every day. Administration continued till August 27, Year 3 with 5 days of suspension because of chemotherapy (see chemotherapy describebd below). Local injections on lymph nodes in	Four cycles of CHOP[11] chemotharepy were provided from July Year 3 to November 28, Year 3 with each cycle lasting for 21days. Radiotherapy began on June 11, Year 3 (scheduled for 25 times) and stopped on July 5, Year 3 as the patient was weak due to	Soft tissure around nasopharynx and oropharynx with the thickest part of 3.0cm entirely disappeared, and the largest fused lymph node among those at submaxillary region, neck and clavicular region shrank from 7.4cm × 2.4cm × 14.6cm to 1.1cm × 1.5cm.	PR

					4 times (1 time of GCE regimen and 3 times of ESAP regimen) began on August, Year 2. The forth one ended on November 26, Year 2. Chemotherapy was administered 6 times (3 times of large-dosed CHOPE regimen, 2 times of CMOP regimen and 1 time of a regimen of "bleomycin + CHOP[00] + Methotrexate ") began on January, Year 3, in combination with stem cell therapy.	neck started on June 11, Year 3. Injection was performed every other day by injection at multiple sites in a quincunx: 15μg × 10 vials per treatment. Two times later, local subcutaneous injection was performed every other day: 30μg per treatment. Till August 27, Year 3 (more than 2 months), for a total of 10 times.	myelosuppression.		
12	Male	67	Non small cell lung adenocarcinoma in right lung	IIb	From August 16, Year 1, two cycles of GP regimen® were provided: 1000mg/m^2 of Gemcitabine on day 1 and 8 and 75mg / m^2 of Cisplatin on day 1. Intrathoracic injection of Cisplatin was also performed for 5 times. 1 dose every 7 days, 30-40mg per dose.	Treatment with rSIFN-co began on November 10, Year 1. Intramuscular injection of rSIFN-co was provided once every two days: 9μg for 1st time, 18μg for 2nd time and 21μg for 3rd time and thereafter. Administration lasted for almost 1 year till October 27, Year 2.		The mass reduced from about 3.1 × 4.2cm to 2.2 × 1.5cm after 2 months' treatment, and the lesion further reduced in size after administration for 3 months.	PR
13	Male	63	Poorly differentiated adenocarcinoma (upper lobe of right lung)	IIIb	On October 15, Year 1, resection of upper lobe of right lung and lymph node dissection were done as well as wedge resection of nodules on lower lobe of right	Treatment with rSIFN-co began on December 10, Year 1. Intramuscular injection of rSIFN-co was provided once every other days: 9μg for 1st time, 21μg for 2nd time and		After surgery on primary lesions, no tumor recurrence or metastasis occurred.	CR

					lung.	thereafter). The first course was finished on April 9, Year 2. The second course was performed from December Year 2 to July Year 3 during which intramuscular injection was done every other day with 21μg per dose. The third course was performed from February 21, Year 4 to May 21, Year 4 during which intramuscular injection was done every other day with 18μg per dose.			
14	Male	44	Non small cell lung cancer (poorly differentiated adenocarcinoma)	IIIb	Upper lobe of right lung was resected on October 20, Year 1.	Treatment of rSIFN-co began on November 6, Year 1. Intramuscular injection of rSIFN-co was administered once every other day: 18μg for 1st time, 21μg for 2nd time and thereafter. A first course of 6 months ended on May 10, Year 2. The second course started on March 18, Year 3 and continued for the next following 3 months. Intramuscular injection of rSIFN-co was provided every other day with 15μg per dose.		After surgery, no tumor recurrence or metastasis was found at primary lesions.	CR

					Intramuscular injection of rSIFN-co and Aerosol inhalation were administered for 3 months from November Year 4. Intramuscular injection was done once every other day with 15μg per dose. Aerosol inhalation was performed every day and a total of 300μg was used for one day.		
15	Male	68	Lung cancer with systemic metastases	IV	Treatment with Gamma Knife was done under local anesthesia on April 27, Year 3. Sr-89 therapy was done by Nuclear Medicine Department on April 30, Year 3. Oral administration of Gefitinib (Iressa) was provided from December Year 1 to June Year 3: 1 dose/day, 1 pill/dose, 250mg/pill.	Treatment of rSIFN-co began on June 25, Year 3. The rSIFN-co was injected into lymph nodes of groin Intramuscularly every day: 15μg×6 vials for 1st time, 15μg×8 vials for 2nd time and 15μg×10 vials for 3rd time and thereafter. Eleven injections were done till July 20, Year 3 (Severe diarrhea occurred after 3 injections and administration was stopped for 2 weeks; after that injection was performed every day and 8 injections in total were continuasly provided). Discontinuous local injection in lymph nodes were performed for 6 times from August 18, Year 3 toSeptember 16, Year 3: 15μg × 10 vials for each time.	Mass of about 11.3×4.9cm in pelvic cavity reduced in size to 7.52×7.67×6.72cm	PR

						Local injection in lymph nodes were performed every 3 days from October 8, Year 3 to October 12, Year 3: 15μg × 10 vials for each time.			
16	Female	63	Well to moderately differentiated adenocarcinoma was found in rectum and mucinous adenocarcinoma was found in part of rectum. Cancer invaded into deep muscularis of intestinal wall and formed cancerous nodules in mesorectum.	IIIb	Laparoscopic-assisted abdominal perineal radical resection of rectal cancer was done on May 16, Year 1.	Treatment of rSIFN-co began on May 23, Year 1. Intramuscular injection of rSIFN-co was provided once every other day: 21μg for each time. The first course of 8 months ended on February Year 2. The second course was provided from January Year 3 to April Year 3. Intramuscular injection of rSIFN-co was provided once every other day with 9μg each time and continued for 3 months. The third course was administered from December Year 3 to March Year 4. Intramuscular injection was performed every other day with 15μg each time.		After surgery, no tumor recurrence or metastasis occurred at primary lesions.	CR
17	Female	25	cervical cancer	Ib1		Treatment of rSIFN-co began on May 14, Year 1. Intramuscular injection of rSIFN-co was provided once every other day: 9μg for 1st time, 15μg for		Malignant cervical lesion disappeared, and test of high-risk HPV became negative. Also, no tumor	CR

					2nd time and 18μg for 3rd time and thereafter. Meanwhile, uterine perfusion was done once a day: at 1000μg per dose, for 2 hours. Uterine perfusion ended on June 28, Year 1 (lasted for more than 1 month) and intramuscular injection was stopped on September 12, Year 1 (lasted for 4 months).		cells were found in cervical smear.	
18	Male	64	Prostatic cancer	IV	Treatment of rSIFN-co began on November 15, Year 1. Intramuscular injection of rSIFN-co was provided once every other day: 9μg for 1st time, 15μg for 2nd time, 18μg for 3rd time and 24μg for 4th time and thereafter. Meanwhile, the drug was locally applied by spraying to the skin surface where prostate biopsy was done: 4~5 doses per day and at 70μg~139μg per dose. The amount of rSIFN-co to be intramuscularly injected changed to 21μg from December 15, Year 1 to July 1, Year 2.	Radiotherapy on prostate (EBRT)® was performed for 38 times from December 5, Year 1 to February 26, Year 2.	Prostate of 4.7×3.5×5.6cm reduced normal size; two lymph nodes in right ischiorectal fossa were eliminated; the posterior wall of fundus of urinary bladder, bilateral seminal vesicles and anterior rectal wall infected by lesions recovered; and the level of specific antigen of Prostatic cancer (PSA) become normal.	CR
19	Female	43	Melanoma of nose (after a surgery) combined with bone	IV	Two cycles were provided on October 30, Year 1 and November 30, Year 1: 15mg of Endostar on December 21, Year 1. Intramuscular injection of rSIFN-co was provided		Multiple enlarged lymph nodes at bilateral shoulder joints and axillae	CR

			metastases at bilateral hip joints, bilateral femurs, bilateral humeri, ribs and bilateral shoulder joints.		day 1~10 and 200mg of temozolomide on day 1~5, oral administration. Targeted radiotherapy (50Gy/25f) was done on November 2, Year 1 and the targets were right maxillary sinus + 1/4 of the left maxillary sinus, bilateral ethmoid sinus, frontal sinus and the adjacent tissues of the right eyeball. Radiotherapy ended on December 7, Year 1.	once every other day: 9μg for 1st time, 15μg for 2nd time, 18μg for 3rd time and thereafter. Meanwhile, the drug was locally applied by spraying onto the skin surface of the right shouder: 70μg - 139μg/dose/site, 4-5 doses/day. Spraying was provided to skin surface of the left shoulder and other sites with bone metastasis began on February 27, Year 2: 70μg - 139μg/dose/site, 4-5 doses/day.		disappeared; recurrence and metastatic lesions at residual right sinus and nasal cavity after surgery as well as multiple abnormal signals at bilateral hip joints and upper parts of femora disappeared.	
20	Male	40	Lung cancer	IV		Treatment by administering Recombinant super- compound interferon ("rSIFN-co") began on October 12, Year 1; Intramuscular injection once every other day: 9μg for the 1st time, 15μg for the 2nd time and 21μg for the 3rd time and thereafter; Aerosol inhalation of 1ml (200μg/ml) daily began from December 28, Year 1; Aerosol inhalation of 1ml (300μg/ml)	Chemotherapy was conducted 3 times: GP-T2 regimen (cisplatin day 1-4, gemcitabine day 1) from October 25, Year 1 to November 7, Year 1; (no "gemcitabine" was administered at day 8 due to the low white blood cell level of the patient). DDP40mg on day 1 and day 2 plus MMC 10mg chemotherapy 1 time,	Primary lesions of the right lower lung was reduced; swollen lymph nodes within the mediastinum were eliminated; pleural effusion was subsided.	PR

						daily began from January 13, Year 2.	beginning from November 26, Year 1. Administered DP regimen (Cisplatin 40mg on day 1-2 and 30mg on day 3, Docetaxel 120mg day 1) from December 6, Year 1 to December 18, Year 1.		
21	Female	75	Lung cancer with bone metastases	IIIb	Self-medication with traditional Chinese medicine ("TCM"), ganoderma lucidum extract, spore powder and Gefitinib.	Treatment by administering rSIFN-co began on March 10, Year 1; Intramuscular injection once every other day: 9μg for the 1st time, 15μg for the 2nd time, and 18μg for the 3rd time and thereafter. From September 18, Year 1 to November 17, Year 1, discontinuous spray inhalation 1 ml each time (200μg/ml).	Gefitinib.	Primary lesions of the right upper lung and swollen lymph nodes within the mediastinum were eliminated	CR
22	Male	50	Lung cancer with hepatic metastases	IIIa	4 courses of "Paclitaxel + Carboplatin" chemotherapy began from October 3, Year 1. Argon-helium cryoablation surgery of the lower left lung cancer was performed on January	Intramuscular injection of 18μg once every other day for two months from January 19, Year 2 followed by 21μg every other day thereafter.	The 3rd radiofrequency ablation targeting liver metastases was performed on March 17, Year 2. Hepatic local perfusion of "Paclitaxel + Carboplatin"	Primary lesions of the left lung was eliminated, while no apparent change in liver metastases was observed.	PR

					6, Year 2. Radiofrequency ablation of the liver metastases was performed on January 13, Year 2.		was performed on April 21, Year 2.		
23	Male	57	Lung adenocarcinoma in the left lung with metastases to the left pleura, mediastinal lymph nodes and bone	IV	One course of "PTX + DDP" chemotherapy began on September 9, Year 1; drip infusion of 4 mg of zoledronic acid to treat metastases to bone was administered on September 9, Year 1. The 2nd course of TP chemotherapy began on October 6, Year 1; The 3rd course of chemotherapy of TP chemotherapy began on October 29, Year 1.	Treatment by administering rSIFN-co began on December 6, Year 1; Intramuscular injection once every other day: 9μg for the 1st time and 2nd time, and 21μg for the 3rd time and thereafter till February 15, Year 2.		Primary lesions in the left lung and systemic multiple metastatic lesions were eliminated.	CR
24	Male	73	Lung cancer	IIIb		Treatment by administering rSIFN-co began on March 19, Year 1; Beginning from March 21, Year 1, intramuscular injection once every other day: 9μg for the 1st time, 13.5μg for the 2nd time and 21μg for the 3rd time and thereafter;		Pleural effusion was reduced.	PR

25	Male	48	Lung cancer	IIIa	Intrapleural perfusion of 21μg × 6 vials began from March 19, Year 1; Intrapleural perfusion of 21μg × 8 vials was performed on March 25, Year 1; Intrapleural perfusion of 21μg × 10 vials was performed on April 21, Year 1; Intrapleural perfusion of 21μg × 10 vials was performed on April 30, Year 1; Intrapleural injection of 21μg × 10 vials was performed on May 8, Year 1; Intrapleural perfusion of 21μg × 12 vials was performed on May 15, Year 1.	Treatment by administering rSIFN-co began on November 19, Year 1; Intramuscular injection once every other day: 9μg from November 19, Year 1 to November 25, Year 1, and	Radiotherapy (time and regimen unknown).	PD

						21μg from November 27, Year 1 to April 17, Year 2.			
26	Female	51	lung cancer with brain metastases	IV	"Self-medication with Gefitinib"	Treatment by administering rSIFN-co began on December 18, Year 1; Discontinuous treatment by intramuscular injection once every other day: 21μg, beginning December 18, Year 1 From May 7, Year 3 to January Year 4: intramuscular injection of 18ug, every other day. From May 17, Year 3 to September 18, Year 3: spray inhalation 100ug/day. From September 19, Year 3 to December 28, Year 3: spray inhalation 400ug/day. From December 29, Year 3 to January, Year 4: spray inhalation 300ug/day.	Erlotnib hydrochloride.	Brain metastases lesions were reduced, while no apparent change in primary lesions in the lungs was observed.	PR
27	Male	46	Metastases to both lungs after surgery of the cancer in left lung	IIb	Radical surgery of the cancer in left lung in May Year 1, followed by chemotherapy and	Treatment by administering rSIFN-co began on August 22, Year 2;			NC/SD

					radiotherapy (details unknown).	Intramuscular injection once every other day: 9μg for the 1st time, and 21μg for the 2nd time and thereafter.			
28	Male	53	Cancer in the right upper lung with intrapulmonary metastasis and metastases to the right thoracic cavity.	IIb	Wedge resection of the right upper lung via video assisted thoracoscopic surgery (VATS), pleural biopsy and pleural nodules burning were performed on January 20, Year 1. After 3 days, intrapleural perfusion of "Vivatuxin" to the right thoracic cavity was performed.	Treatment by administering rSIFN-co began on March 13, Year 1; Intramuscular injection once every other day: 9μg for the 1st time, and 21μg for the 2nd time and thereafter; nasal spray of aerosol, 3 times/day; Aerosol inhalation of 0.2ml (1mg/ml) once a day began July 27, Year 1. September 2, Year 1: intramuscular injection of 21ug, every other day, spray inhalation 200μg/day. October 15, Year 1: stopped using rSIFN-co.			NC/SD
29	Male	76	Lung cancer	IIIa	The right upper lung was resected on August 17, Year 1.	Treatment by administering rSIFN-co began on September 2 Year 1; Intramuscular injection once every other day: 9μg for the 1st time, 18μg for the 2nd time and thereafter till September 20, Year 1,	Radiofrequency ablation targeting lung was performed on March 11, Year 3.		NC/SD

						21μg from November 22, Year 1 to April 27, Year 2; In combination with nasal spray of 40μg/ml aerosol, 3 times/day from April 29, Year 2.			
30	Male	47	Lung adenocarcinoma with brain metastases	IV	Whole brain radiotherapy 30GY/10FX (10 times) was performed in December Year 1. 4 courses of GP-T1 chemotherapy regimen (gemcitabine day 1 and day 8; DDP140mg day 1) began on January 3, Year 2. Gefitinib was taken in March Year 2.	Treatment by administering rSIFN-co began on July 18, Year 2; Intramuscular injection of 21μg once every other day in combination with aerosol inhalation of 1ml (200μg/ml) every day lasted for 8 months.		Pulmonary nodules reduced (5 months later), brain lesions basically subsided (6 months later).	PR
31	Male	71	Right lung cancer with bone metastases	IV		Treatment by administering rSIFN-co began on June 29, Year 1; Intramuscular injection once every other day: 9μg for the 1st time, 13.5μg for the 2nd time, and 18μg for the 3rd time and thereafter; Aerosol spray of 20μg/ml rSIFN-co to lymph nodes at nasal cavity and neck began on August 20, Year 1;			PD

						Injection of 21μg rSIFN-co every other day began on September 16, Year 1.			
32	Female	69	Lung cancer	IIb	Three chemotherapy treatments were performed in March, April and May of Year 1; Began taking Gefitinib on June 10, Year 1.	Treatment by administering rSIFN-co began on July 9, Year 2; Intramuscular injection once every other day: 9μg for the 1st time, 13.5μg for the 2nd time, and 18μg for the 3rd time and thereafter; Aerosol inhalation of 300μg per day.	Gefitinib.	Lung tumor shrunk, and swollen lymph nodes disappeared.	PR
33	Female	75	Lung cancer	IIIb	"Left lower lung lobectomy, lymph node dissection, resection of part of thoracic aortic adventitia via VATS" under general anesthesia were performed on December 24, Year 1.	Treatment by administering rSIFN-co began on September 22, Year 2; Intramuscular injection once every other day: 4.5μg for the 1st time, 9μg for the 2nd time, 13.5μg for the 3rd time, and 18μg for the 4th time and thereafter; Injection of 9μg every other day from September 29, Year 2. Later changed to 2 times of injection per week. Perfusion of rSIFN-co at 21μg × 5 vials once every 6-8 days began on September 22, Year 2, depending on			PD

						the subject's pleural effusion level and tolerance.. Perfusion of rSIFN-co at 21μg × 6 to 8 or 10 vials once every 4 days began on October 21, Year 2, depending on the subject's pleural effusion level and tolerance.			
34	Male	79	Lung cancer with multiple metastases	IV		Treatment by administering rSIFN-co began on October 12, Year 1; Intramuscular injection of 18μg once every other day in combination with aerosol inhalation of 1ml (200μg/ml) per day. Stopped using rSIFN in December, Year 1.	Local brain radiotherapy was received 2 times in November Year 1; Treatment with anti-cancer TCM began on mid-December Year 1.		NC/SD
35	Female	29	Lung adenocarcinoma with bone metastases	IV	Beginning on June 28, Year 1, 1 course of chemotherapy (Gemcitabine 1.6g on day 1 and day 8 + Cisplatin 60mg on day 1 and day 2).	Treatment by administering rSIFN-co began on July 1, Year 1; Intramuscular injection once every other day: 15μg for the first time, 18μg for the second time and thereafter, and in combination with aerosol inhalation at the same time, 1 time a day, 600μg each time.	From July 18, Year 1 to October 9, Year 1: 3 courses of chemotherapy. GP chemotherapy regimen: Gemcitabine + Cisplatin. Radiofrequency ablation targeting lung was performed on December 18, Year 1.	Shrinkage of the primary lesion on the dorsal segment of the lower lobe of the left lung was evident.	PR

							Beginning in December, Year 1, began discontinuous use of Gefitinib.		
36	Female	73	Ovarian cancer	IIIb	"Hysterectomy, bilateral Salpingo oophorectomy, omentectomy, superior end rectum resection, anastomosis, urinary bladder rupture repair and cytoreductive surgery" were performed on May 19, Year 1.	Treatment by administering rSIFN-co began on February 13, Year 2; Intramuscular injection once every other day: 9μg for the first time, 15μg for the second time, 18μg for the third time and thereafter; Intramuscular injection of 21μg every other day beginning from March 13, Year 2 until May 21, Year 2.		The pleural effusion in left thoracic cavity was disappeared; the pleural effusion right thoracic cavity was reduced.	PR
37	Female	46	cervical cancer, after radiotherapy and chemotherapy	IV	Radiotherapy was performed in Year 1: DT 5040Gy each time for 56 times; Treatment with PF regimen and radiotherapy were performed in August Year 2; Chemotherapy by arterial infusion for cervical cancer was performed on August 13, Year 2, primary drugs administered: Paclitaxel liposome + Carboplatin.	Treatment by administering rSIFN-co began on November 30, Year 2; Intramuscular injection of 21μg every other day.		Size of cervical lesions were reduced from 64 × 58mm to 52 × 40mm; Swollen left inguinal lymph nodes were disappeared.	PR

38	Female	31	Uterine papillary serous carcinoma (UPSC) mixed with clear cell carcinoma	IV		Treatment by administering rSIFN-co began on August 1, Year 1; Intramuscular injection of 18μg every other day in combination with uterine drip once a day for a week and once every 5 days thereafter at 1ml (200μg/ml) each time.			NC/SD
39	Female	41	Poorly differentiated cervical squamous cell carcinoma	Ib2	Laparoscopic extensive total hysterectomy + pelvic abdominal aortic lymphadenectomy + bilateral ovarian suspension were performed on June 3, Year 1. Following surgery, 1 course of PT chemotherapy regimen was administered.	Treatment by administering rSIFN-co began on November 26, Year 1; Intramuscular injection once every other day: 9μg for the first time, 15μg for the second time and thereafter. Use of rSIFN for 6 months altogether.	NK cell therapy	High-risk human papillomavirus (HPV) changed from positive to negative.	CR
40	Female	70	Cancer of hepatic flexure of colon, with lung metastases after surgery	IV	Radical resection was performed on May 4, Year 1. Six chemotherapy treatments had been performed from May Year 1 to September Year 1, with the regimen of XELOX, capecitabine tablets 3000mg, oral, d1-d14; oxaliplatin 200mg, intravenous drip, d1.	Treatment by administering rSIFN-co began on March 17, Year 4; Intramuscular injection once every other day: 9μg for the first time, 21μg for the second time and thereafter.	Radiofrequency ablation targeting right lung metastases was performed on March 28, Year 4; Argon-helium cryosurgery targeting the right upper lung metastases was performed on April 9, Year 4; the right arm plexus was found damaged after the surgery;		PD

					1 course of chemotherapy treatment was performed from October 26, Year 2. Oxaliplatin 150mg, intravenous drip, QD, d1; cetuximab 600mg, intravenous drip, QD, d1; irinotecan 240mg, intravenous drip, QD, d2; fluorouracil 2500mg, continuous intravenous drip for 48 hours; TCM treatment had been performed from November Year 2 to August Year 3.		Radiofrequency ablations targeting left lung metastases were performed 2 times on May 5, Year 4and June 13, Year 4, respectively; The right lower lung metastases were treated by ion implantation on May 27, Year 4. 2 courses of chemotherapy in December Year 4: capecitabine tablets 3000mg, oral, d1-d14. Systemic chemotherapy on March 9, Year 5, cetuximab + alimta. Avastin and NK cells were added for treatment on March 23, Year 5. Radiotherapy of hepatic metastases from April 21, Year 5 to May 19, Year 5.		
41	Male	57	Colon cancer with	IV	Hepatic interventions were	Treatment by administering rSIFN-co			NC/SD

			hepatic metastases		performed 2 times in August Year 1 and on September 12, Year 1, respectively.	began on September 30, Year 1; Intramuscular injection once every other day: 9μg for the 1st time; 21μg from October 2, Year 1 to December 10, Year 1; 21-25.5μg from December 12, Year 1 to January 9, Year 2; 21μg from January 11, Year 2 to July 17, Year 2; Injection into liver tumor: 21μg × 5 vials on January 15, Year 2; 21μg × 8 vials on January 22, Year 2 21μg × 10 vials on February 1, Year 2.			
42	Female	47	cholangiocarcinoma with hepatic metastases after surgery	IV	Diagnosed with intraheptic biliary cystadenocarcinoma on May 31, Year 1 and radical surgery of intraheptic biliary cystadenocarcinoma was performed; Resection of right hepatic posterior lobe and caudate lobe mass + clearance of abdominal lymph node + I^{125} ion	Treatment by administering rSIFN-co began on November 21, Year 2; Intramuscular injection once every other day: 9μg for the 1st time; 18μg for the 2nd time; 21μg from February 27, Year 3 to July 5, Year 4; Administration was stopped for 3	Ovarian cancer surgery was performed on June 18, Year 3.	The volume of multiple space-occupying lesions of the right and left lobes of liver is significantly reduced and the number of the lesions is also reduced.	PR

					implantation + abdominal drainage were performed on November 23, Year 2.	months from May Year 3 to August Year 3. Started using recombinant super-compound interferon treatment again from June 5, Year 5.			
43	Female	50	Intrahepatic cholangiocarcinoma with intrahepatic metastases	IV	Right half liver resection + cholecystectomy + abdominal lymphadenectomy were performed on November 8, Year 1. Transcatheter arterial chemoembolization (TACE) was performed on December 22, Year 1. The 2nd TACE on liver was performed on June 4, Year 2. Chemotherapy by continuous hepatic arterial infusion (cisplatin + epirubicin +5 FM) was performed on July 2, Year 2. The 3rd TACE was performed on August 2, Year 2.	Treatment by administering rSIFN-co began on November 15, Year 2; Intramuscular injection of 9μg once every other day; intramuscular injection of 21μg every other day from November 21, Year 2 to May 20, Year 3.			PD

					Argon-helium cryoablation targeting multiple intrahepatic lesions was performed in September Year 2. The 2nd argon-helium cryoablation was performed on November 7, Year 2.				
44	Male	58	Liver cancer with lung metastases	IV	Liver transplantation in Year 1. Wedge resection of left lung superior lobe masses was performed on July 6, Year 4.	Treatment by administering rSIFN-co began on September 5, Year 4; Intramuscular injection of 9μg every other day from September 5, Year 4 to September 9, Year 4. Intramuscular injection of 18μg every other day from September 11, Year 4 to October 23, Year 4. Intramuscular injection of 21μg every other day from October 25, Year 4 to February 25, Year 5.			PD
45	Male	40	Liver cancer with intrahepatic metastases	IV	Hepatic arterial embolization was performed on August 9, Year 1.	Treatment by administering rSIFN-co began on August 21, Year 1, 1 time every other day; Intramuscular injection of 9μg at the 1st time; Intramuscular injection of 18μg from the 2nd time and thereafter; Intramuscular injection of 21μg every		The original massive primary space-occupying lesions of the left liver clearly shrunk; the swollen retroperitoneal or abdominal para-aortic lymph nodes were disappeared.	PR

						other day from September 17, Year 1 to February 1, Year 2.			
46	Female	37	breast cancer with lymph node metastases after surgery	IIIc	Breast-conserving cancer surgery was performed on June 3, Year 1, with 1/11 axillary lymph nodes; 6 times of chemotherapy were performed after surgery (main drug: perarubicin); 33 times of radiotherapy were performed 1 month after the end of the chemotherapy. 4 times of "docetaxel + xeloda" chemotherapy were performed after another metastatic lymph node resection in January Year 2.	Treatment by administering rSIFN-co began on May 18, Year 2. Intramuscular injection of 18μg every other day till September 16, Year 2.			PD
47	Female	58	breast cancer, recurrence after surgery	IV	Left mastectomy and lymphadenectomy were performed on December 26, Year 1after 6 courses of chemotherapy beginning in July Year 1 (details unknow); Multiple courses of chemotherapy (details undknown) were performed after the mastectomy;	Treatment by administering rSIFN-co began on February 5, Year 3: Intrapleural injection of 21μg × (5 or 7 or 8 or 10 or 13 vials) each time from February 5, Year 3 to May 23, Year 3; Local injection to points of the left anterior chest wall 5 times from May 30, Year 3 to July 11, Year 3, 1	Oral administration of tamoxifen, exemestane (Italy), anastrozole tablets. Carboplatin combined with thoracic perfusion of rSIFN-co.		PD

					Left pleural effusion appeared in July Year 2and was improved after 2 courses of chemotherapy with "paclitaxel."	time/week, 21μg × 8 vials each time; Intramuscular injection of 21μg every other day from July 14, Year 3 to September 30, Year 3.			
48	Female	45	Left breast cancer, after surgery	IIa	Left breast-conserving surgery with clearance of tumor cells plus right breast lobectomy were performed on August 22, Year 1.	Treatment by administering rSIFN-co began on March 5, Year 2, 1 time every other day: intramuscular injection of 9μg at the 1st time, intramuscular injection of 15μg at the 2nd time, intramuscular injection of 18μg at the 3rd time, and intramuscular injection of 21μg from the 4th time and thereafter; Intramuscular injection of 18μg every other day from April 23, Year 3. Administration was stopped from June 26, Year 2 to April 20, Year 3.		2 years after left breast-conserving surgery, subcutaneous layers of both breasts were clear without any abnormalities; no defined mass was detected in both breasts.	CR
49	Female	39	Breast cancer, recurrence after surgery	IV	Radical surgery of right breast with clearance of cancer cells was performed in November Year 1, followed by chemotherapy (details unknown).	Treatment by administering rSIFN-co began on November 29, Year 2: Local injection, 4 times, 15μg / × 6 vials each time, from November 29, Year 2 to December 20, Year 2;			NC/SD

						Intramuscular injection of 9ug, every other day, from December 11, Year 2 to December 20, Year 2. Intramuscular injection of 21μg every other day from January 31, Year 3 to April 22, Year 3.			
50	Male	64	Gastric cancer, after radical surgery	IV	"Radical surgery of gastric cancer " was performed on March 15, Year 1.	Treatment by administering rSIFN-co began on April 14, Year 1, 1 time every other day: Intramuscular injection of 9μg at the 1st time, Intramuscular injection of 18μg from the 2nd time and thereafter. Intramuscular injection of 15μg every other day from September 1, Year 1 to January 22, Year 2. Intramuscular injection of 21μg every other day from January 24, Year 2 to August 29, Year 2. Administration was stopped for 2 months from September Year 2 to November Year 2. Intraperitoneal injection of 21μg x (8			PD

						-10 vials) each time to lesions in abdominal cavity under type-B ultrasound guidance from November 28, Year 2 to December 24, Year 2. Intramuscular injection of 21ug, every other day, from November 13, Year 2 to March 16, Year 3.			
51	Male	59	Gastric cancer , with abdominal cavity metastases	IV	From October, Year 1 to May, Year 3, Chemotherapy was administered for 9 times (regimen unknown).	Treatment by administering rSIFN-co began on November 2, Year 3. Intraperitoneal perfusion, 1 time every other day: 15μg × 8 vials at the 1st time, 15μg × 12 vials at the 2nd time, 15μg × 14 vials at the 3rd time, and 15μg × 16 vials at the 4th time, total 4 times until November 10, Year 3.		Ascites were significantly reduced; cancer cells in the ascites disappeared.	PR
52	Fema le	73	Pancreatic cancer	III		Treatment by administering rSIFN-co began on December 27, Year 1. Intramuscular injection of 9μg every other day. Intramuscular injection of 21μg every other day from January 2, Year 2 to September 15, Year 2.		Lesions in the portacaval space shrank.	PR
53	Male	73	prostate cancer with	IV	Oral Casodex, zoladex and	Treatment by administering rSIFN-co	Casodex.	Some of pelvic metastastic	NC/SD

			pelvic metastases		flutamide. Androgen depreviation was performed on January 16, Year 1. Radiofrequency ablation targeting a large pelvic lymph node was performed on June 26, Year 1. I-125 particle implantation was performed on July 18, Year 1.	began on November 30, Year 1, once every other day: Intramuscular injection of 9μg at the 1st time; Intramuscular injection of 21μg from the 2nd time and thereafter; Intraperitoneal perfusion, 7 times, 21μg × 8 vials each time.	Three-dimensional conformal radiotherapy was performed 24 times, beginning December 12, Year 1 (60Gy 2.5x24 times)..	lesions were eliminated or shrank.	
54	Female	46	Gastrointestinal stromal tumors	Ib	Duodenal tumorectomy was performed on July 13, Year 1. Radiotherapy was performed on November 16, Year 1after duodenal surgery.	Treatment by administering rSIFN-co began on December Year 1. 1 time every other day: Intramuscular injection for 6 months 9μg at the 1st time; 21μg from the 2nd time and thereafter;. The 2nd treatment was received for 3months from Year 3 to August Year 4. The 3rd treatment of rSIFN-co was received on September 26, Year 4.		No signs of apparent tumor recurrence and metastasis were observed by imaging examination.	CR
55	Male	16	Embryonal rhabdomyosarcoma,	IV	Beginning on July 29, Year 1: 4 courses of chemotherapy was	Treatment by administering rSIFN-co began on February 2, Year 2, once			PD

			with metastases after the surgery		administered (main drugs: epirubicin and oxaliplatin). On September 1, Year 1: Radiotherapy of the left upper chest was administered.	every other day: Intramuscular injection of 9μg at the first time; intramuscular injection of 15μg at the 2nd time and thereafter; Intramuscular injection of 18μg every other day from April 21, Year 2 to May 19, Year 2. Intramuscular injection of 21μg every other day from May 21, Year 2 to July 11, Year 2. Intramuscular injection of 9μg every other day from July 13, Year 2 to November 5, Year 2. Intramuscular injection of 18μg every other day from November 7, Year 2 to December 2, Year 2. Intramuscular injection of 21μg every other day from December 4, Year 2 to March 25, Year 3. Lymph node and intratumoral injections, 4 times, 21μg × 8 vials			

						each time, from November 12, Year 2 to November 28, Year 2.			
56	Female	17	Lymphoma	III		Treatment by administering rSIFN-co began on December 29, Year 1. Intramuscular injection of 21μg every other day from February 24, Year 2 to April 22, Year 2; Intramuscular injection of 18μg every other day from April 24, Year 2 to June 5, Year 2; Intratumoral injection in the neck, 1 time every other day, 21μg × (8-10-12-12-12-13-15 vials) each time, from December 29, Year 1 to February 18, Year 2; 21μg × 10 vials each time from March 24, Year 2; 9μg × 20-23 vials each time from April 25, Year 2 to May 5, Year 2; 1 ml each time, 500μg/ml from May 7, Year 2 to May 25, Year 2.	Chemotherapy was received twice after the Spring Festival of Year 2. Treatment was in combination with TCM with detoxifying function.	Lymphoma apparently shrank; breathing and eating functions returned to normal; the hearing of the right ear recovered from no hearing weak hearing.	PR
57	Female	19	malignant neuroma of the right hip, recurrence after surgery	IIIc	Surgeries were performed in January Year 1and in September Year 1; postoperative radiotherapy and chemotherapy were received (details unknown).	Treatment by administering rSIFN-co began on February 9, Year 4. Intramuscular injection of 21μg every other day.	TCM		NC/SD

58	Female	61	Metastatic poorly differentiated squamous cell carcinoma in the right chest, after surgery for	IIIa	Tumor resection in the right anterior chest wall was performed on June 11, Year 1.	Radiotherapy and chemotherapy were received again in January Year 2 (details unknown). Recurrence in January Year 3. Radiotherapy and chemotherapy were received again (details unknown). Recurrence in January Year 4; ultrasonic scalpel and TCM treatments were received.	Treatment by administering rSIFN-co began on July 7, Year 1, intramuscular injection once time every other day: 9μg at the 1st time, 21μg from the 2nd time and thereafter, until January 6, Year 2 Hip intratumoral injection every 2-3 days, 21μg x 4 vials each time.	Postoperative radiotherapy after surgery of metastatic cancer in the upper right chest wall was performed from July 7, Year 1 to August 8, Year 1.	NC/SD

Example 3: Clinical data on typical patients treated with the recombinant interferon of the invention (19 patients)

[0693] Clinical data collected until July 1, 2012 of 19 patients treated with the recombinant interferon of the invention are provided below (Patients numbered by 1-19 correspond to Patients 1-19, respectively, in the "Summary of Clinical Treatment of Multiple Types of Cancers in 58 Patients" in aforementioned Table 2 of Example 2).

[0694] **Patient 1. Non-small-cell lung cancer; the primary lesions in the right pulmonary hilum and the mediastinal lymph node metastasis disappeared after treatment by intramuscular injection of recombinant super-compound interferon (rSIFN-co) in combination with radiotherapy.**

[0695]

Patient 1	Gender: Male	Age: 53
Pathological diagnosis :	Squamous cell carcinoma	
Clinical and pathological staging①:	$T_3N_2M_0$. IIIb	
Regimens before administration of rSIFN-co:	DP Regimen® was provided from October 14, Year 1 to November 25, Year 1: 75 mg of Taxotere and 75 mg of Cisplatin on Day 1. Two cycles of chemotherapy were performed in total, each lasting for 21 days.	
Regimens: administration of rSIFN-co combined with radiotherapy	The rSIFN-co therapy started in November, Year 1. Intramuscular injection of rSIFN-co was done once every other day: 9μg for the 1st time, 15μg for the 2nd time and 18μg for the 3rd time and thereafter. Therapy continued till February, Year 3, during which rSIFN-co treatment had been stopped for 1 month in April, Year 2, leading to a total treatment duration of 15 months.	

	Radiotherapy® (DT40Gy) on right lung and mediastinal lymph nodes started on December 2, Year 1 followed by X-knife therapy (DT20Gy)
Response to rSIFN-co treatment:	CR② (primary lesions on right pulmonary hilum disappeared and cured)
Survival time:	After about 80 months (from October Year 1 ~ July Year 8), the patient remained alive and lived a normal life. No recurrence or metastasis was observed upon imaging examinations.
Diagnostic imaging before administration of rSIFN-co:	CT scan on November 25, Year 1 after chemotherapy: The right main bronchus was obstructed by the invasive masses originated from right hilum, resulting in atelectasis of upper lobe of the right lung; multiple nodules occurred at the lower lobe of right lung. These signs indicated progression of tumor. The patient had breathing difficulty and breath sound disappeared.
Diagnostic imaging after administration of rSIFN-co:	CT scans on January 4, Year 2: The masses at right hilum were reduced in size, relieving atelectasis at the upper lobe of the right lung. Part of mediastinal lymph nodes also decreased in size. CT scans on June 12, Year 2: The mediastinal lymph nodes continued to shrink and infiltration of right lung was

	absorbed. CT-scan on November 08, Year 2 (12 months after administration): Please refer to the location indicated by arrow in FIG. 3a where the lesions originally occurred. CT-scan on February 1, Year 3 (15 months after administration): Please refer to the location indicated by arrow in FIG. 3a where the lesions originally occurred. CT scan on October 19, Year 3: The blood vessels or lymph nodes on the right hilum were a little larger than normal and more infiltration on lower lobe of right lung was absorbed; other changes were not obvious.
Description of FIG. 3:	After 12 months of treatment, the lesions on the right lung were obviously reduced in size. After 15 months of rSIFN-co administration, progression or metastasis of lesions was not observed.

[0696] **Patient 2. Non-small-cell lung adenocarcinoma with systemic metastases on body parts including bilateral lungs, liver and lymph nodes/Intramuscular injection and aerosol inhalation of rSIFN-co combined with chemotherapy (GP regimen) and administration of recombinant human endostatin (Endostar). After treatment, the primary lesions in the lungs evidently became reduced in size and the metastatic lesions disappeared in the liver and in**

many of the lymph nodes.

[0697]

Patient 2	Gender: Male	Age: 40
Pathological diagnosis :	Lung Adenocarcinoma	
Clinical and pathological staging①:	$T_3N_3M_1$. IV	
Regimens before administration of rSIFN-co:	Systematic chemotherapy began at January, Year 1: Taxotere and Carboplatin. One cycle of 21 days was provided.	
Regimens: administration of rSIFN-co combined with chemotherapy and other biotherapies	The rSIFN-co therapy began on April 14, Year 1. Intramuscular injection of rSIFN-co was done once every other day: 9μg for the 1st time, 15μg for the 2nd time, 18μg for the 3rd time and 21μg for the 4th time and thereafter. Meanwhile, aerosol inhalation of rSIFN-co was done once every day: 300μg for the 1st time, 500μg for the 2nd time, 600μg for the 3rd time and thereafter. Administration of rSIFN-co ended in April Year 2. From April 20, Year 1 to September 3, Year 1, Endostar® was administrated every day: 7.5 mg/m^2 per dose, 1.2×10^5U/m^2. Four cycles were performed totally with each lasting for 14 days. Meanwhile, GP regimen was combined: 1600mg of Gemcitabine on days 1 and 8 and 40mg of Cisplatin on days 1~3. Four cycles were performed, each being 15 days. One intrapericardial infusion with Cisplatin (30mg) was performed on July 19, Year 1.	

	Aerosol inhalation of Cisplatin was added from December 23, Year 1 to January 14, Year 2: 10mg/dose, 2 doses per day. The second course of Endostar treatment was provided from January 18, Year 2 to January 30, Year 2 with same dosage. Chemotherapy using Pemetrexed® proceeded from December 25, Year 1 to January 19, Year 2: iv. 500mg/m^2, every 3 to 4 weeks. As none of the treatments had any obvious effect, the chemotherapy during February 15, Year 2 to April 25, Year 2 was replaced with DP regimen® （75mg/m^2 of Taxotere and 75mg/ m^2 of Cisplatin on day 1） in combination with administration with Tarceva (150mg/day) for 4 cycles with 21 days per cycle. A Gamma knife therapy was performed on head on June 29, Year 2.
Response to rSIFN-co treatment:	PR® (the size of the primary lesions on upper lobe of right lung reduced from about 10.2×8.2×7.7cm to 1.2×1.4cm; metastatic lesions in the right liver and multiple lymph nodes disappeared; the metastatic lesions on the two lungs decreased in size and the radioactive concentration/accumulation decreased.)
Survival:	About 18 months from start of this treatment: (January 20, Year 1 to August 3, Year 2)

Diagnostic imaging before administration of rSIFN-co:	Diagnostic imaging after administration of rSIFN-co:
PET/CT on April 19, Year 1 (see the lesions indicated by the arrow in FIG. 4a) : 1. A mass shadow of was found in the upper lobe of right lung whose size was about 10.2×8.2×7.7cm and CT value was about 38.8Hu, indicating the existence of a central lung cancer; 2. Multiple lymph node metastases were found at the right side of trachea, root of neck (right-side) and the nearby regions at the right-side of pancreas head,; size of the maximum lesions was about 1.4×1.1cm. 3. A large quantity of miliary nodule shadows were diffusely distributed on both lungs with radioactive uptake increased. Diffuse metastases happened in both lungs. 4. The maximum size of the metastatic lesions on the right lobe of liver is about 1.2×0.9cm.	PET/CT on June 18, Year 1 (see the lesions indicated by arrow in FIG. 4b): 1. The size of primary mass in the upper lobe of right lung was 1.2×1.4cm. Lesions shrank and radioactive concentration reduced significantly. The maximum SUV value was 2.9, and the average value was 2.1; 2. Multiple metastatic lesions of lymph nodes at the right side of trachea, root of neck (right-side) and the nearby regions beside the pancreas head had all disappeared; 3. Patches, flocculent shadows and reticular shadows were extensively distributed at other parts of the lungs with slightly increased radioactive uptake. Space-occupying lesions and consolidation were not found. The size of lesions shrank evidently and the radioactive uptake reduced significantly. 4. Two metastatic lesions on the right lobe of the liver disappeared.
Description of FIG. 4:	After 2 months' treatment, lesions on the upper lobes of both lungs evidently shrank or disappeared.

[0698] **Patient 3. Non-small-cell lung cancer with brain metastases/Intramuscular injection and aerosol inhalation of rSIFN-co combined with Gamma knife treatment. After the treatment, primary lesions on right lung and brain metastatic lesions were cleared up.**

[0699]

Patient 3	Gender: Female	Age: 51
Pathological diagnosis :	None	
Clinical and pathological staging①:	$T_2N_2M_1$. IV	
Regimens before administration of rSIFN-co:	None	
Regimens: administration of rSIFN-co combined with Gamma knife treatment	Treatment with rSIFN-co started on May 29, Year 1. Intramuscular injection of rSIFN-co was done once every other day: 9μg for the 1st time, 18μg for the 2nd time and 21μg for the 3rd time and thereafter. Aerosol inhalation of rSIFN-co was simultaneously performed: 200μg/every other day. From July 14, Year 1, 18μg of rSIFN-co was used in intramuscular injection. Aerosol inhalation of 400μg of rSIFN-co was simultaneously performed every other day. The administration continued for more than 3 months till September 16, Year 1. During this period, Gamma knife radiotherapy for the brain lesions was conducted.	
Response to rSIFN-co treatment:	CR②(the primary lesion of about 5.1×3.2cm on the upper lobe of right lung disappeared; the enlarged lymph nodes in the mediastinum and the metastatic lesions in the brain of about	

	3.7×2.6cm basically disappeared.)
Survival:	About 13 months from start of the treatment (from May Year 1 to June Year 2)
Diagnostic imaging before administration of rSIFN-co:	Diagnostic imaging after administration of rSIFN-co:
Lung CT scans on May 14, Year 1 (see the lesions indicated by arrow in FIG. 5a): An irregular soft-tissue density shadow of about 5.1×3.2cm was found at the apex of right lung, which had an obscure boundary and connected to anterior pleural membrane. Enlarged lymph nodes were found in neighboring mediastinum. Diagnostic imaging showed that it was a space-occupying lesion in the apex of right lung. Brain CT scans on May 14, Year 1 (see the lesion indicated by arrow in FIG. 6a): Multiple hybrid-density shadows were found at frontal lobe, temporal lobe and parietal lobe of both sides, which were surrounded by low density shadows especially on the right side. The lateral ventricle was pressed to be narrower and the	CT scans on September 16, Year 1 for brain (FIG. 6b) and chest (FIG. 5b): 1. Irregular increased density shadows were found at upper lobe of right lung near mediastinum, suggesting the possible occurrence of inflammation in the right lung. The thorax was symmetrical, and the perivascular space in mediastinum was clear with no enlarged lymph node found. (See the original location of the lesions indicated by arrow in FIG. 5b) 2. Irregular low-density shadows could be seen in the right frontal lobe and left temporal lobe. The anterior horn of right lateral ventricle was narrowed. Cerebral fissures and sulcus were not widened and the midline structure was centered. (See the original location of the lesions indicated by arrow in FIG. 6b)

midline structure was shifted leftwards. The pathline of the lesions at the right frontal lobe was about 3.7×2.6cm.	
Description of FIG. 5:	After 3-month of treatment, the mass at the apex of right lung completely disappeared.
Description of FIG. 6:	After treatment, the metastatic brain lesions disappeared.

[0700] **Patient 4. Small-cell lung cancer with metastases in the mediastinal lymph nodes and clavicles/Intramuscular injection and aerosol inhalation of rSIFN-co combined with chemotherapy (aerosol inhalation of Cisplatin and EP regimen) and interventional therapy for supraclavicular lesions. After the treatment, primary lesions in the right lung and metastases in mediastinal lymph nodes and clavicles cleared up.**

[0701]

Patient 4	Gender: Male	Age: 49
Pathological diagnosis :	Small-cell lung cancer	
Clinical and pathological staging①:	$T_4N_3M_1$. IV	
Regimes before administration of rSIFN-co:	The first cycle of EP② chemotherapy was conducted from March 25, Year 1 to Apr 9, Year 1: 100mg of Etoposide and 30mg of Cisplatin.	
Regimes : administration of rSIFN-co combined with chemotherapy and interventional therapy	The treatment of rSIFN-co began on April 12, Year 1. Intramuscular injection was done once every other day: 9μg for the 1st time, 15μg for the 2nd time and 18μg for the 3rd time and thereafter. Aerosol inhalation of rSIFN-co was performed once every other	

	day: 0.5~2ml/dose (200μg/ml). From July 16, Year 1, 21μg of rSIFN-co was used in intramuscular injection. Aerosol inhalation of rSIFN-co continued but the amount per dose was changed to 200μg . The first cycle finished by the end of March Year 2 (lasting for almost 1 year). The administration of rSIFN-co was stopped for 1 month because Aerosol inhalation of Cisplatin (one dose per day and 10mg per dose) was performed throughout September Year 1. The 2nd cycle of treatment proceeded from October 9, Year 2 to January 26, Year 3 during which 18μg of rSIFN-co was intramuscularly injected every other day. Five cycles of EP chemotherapy were conducted from March 25, Year 1 to September 10, Year 1 and the same regimen as mentioned above was used. An interventional cryoablation was conducted on the supraclavicular lesions on September 3, Year 2. From October Year 1, a 15-day regimen of aerosol inhalation of Cisplatin was added: 10mg per dose, 1 dose per day. Two cycles were done, each lasting for 15 days.
Response to rSIFN-co treatment:	CR® (a primary lesion of about 0.6×0.4cm, on the apex of right lung disappeared.; a

	lesion with a nodule of about 2.6×2.2cm on the of right clavicle disappeared; Mutilple nodules appearing in neighboring areas of the mediastinal brachiocephalic trunk, right brachiocephalic veins, superior vena cava, and trachea, part of which fused and lesions of about 5.5cm×4.9cm in size disappeared.)
Survival:	After about 39 months (from March 23, Year 1 to July Year 4), the patient remained alive and had a normal life. No recurrence or metastasis was observed upon imaging.
Diagnostic imaging before administration of rSIFN-co:	Diagnostic imaging after administration of rSIFN-co:
PET/CT scans on April 8, Year 1 (see the lesions indicated by arrows in FIG 7a-8a) after the chemotherapy: 1. One nodule with coarse edge and slight lobulated appearance was found at the apex of right lung (diameter: 0.6×0.4cm). PET showed abnormal radioactive concentration and the SUV value was 4.1. 2. Nodules of about 2.6×2.2cm were observed at right clavicle, the boundaries of which were obscure. PET showed abnormal radioactive concentration and the SUV value was 9.1. 3. Multiple nodules of about 5.5cm×4.9cm appeared around the	PET/CT scans on December 24, Year 1 (see the original lesion locations indicated by arrows in FIG 7a-8a) : 1. The nodule at the apex of right lung were not obviously shown; 2. The nodules on right clavicle were significantly downsized. PET showed abnormal radioactive concentration with a SUV value of 4.7; 3. The nodules around the mediastinal brachiocephalic trunk, right brachiocephalic veins, and trachea were not clearly observed. superior vena cava; 4. Multiple nodules were found around the superior vena cava. PET did not show an obvious radioactive concentration, indicating

mediastinal brachiocephalic trunk, right brachiocephalic veins, superior vena cava, and trachea. The boundaries of these nodules were not distinct and some were partially fused together. PET showed abnormal radioactive concentration and the SUV value was 11.5). Metastasis of lymph nodes should be taken into account. 4. The superior vena cava could not be excluded.	the suppression on the lesions' metabolism. PET/CT scans on July 26,Year 3: 1. Streaky shadows were found in the upper lobe of right lung while patchy shadows were found in dorsal segment of lower lobe. PET scan did not show obvious radioactive concentration; 2. After cryotherapy was conducted for the right supraclavicular metastasis, no obvious nodules or masses were found in the right clavicle and PET image did not show obvious radioactive concentration. PET scans on other parts showed similar metabolic images as before. PET/CT on February 7, Year 4 (after treatment of "small-cell cancer of right lung" and compared to PET/CT scans taken on July 26, Year 3): 1. The posterior wall of left nasopharynx was thickened slightly and PET imaging showed radioactive concentration, suggesting the possible occurrence of an inflammatory lesion; 2. Multiple nodules were at deep cervical and submentum and PET imaging did not show abnormal radioactive concentration, suggesting the possible occurrence of inflammatory hyperplasia of lymph nodes; 3. The wall of greater gastric curvature was

	slightly thickened and PET imaging did not show radioactive concentration. Inflammatory lesion could be taken into consideration; 4. PET/CT scans on other parts did not show significant changes.
Description of FIG. 7:	After 8 months of treatment, the lesions on the apex of the right lung disappeared.
Description of FIG. 8:	After 8 months of treatment, the metastatic lesions in mediastinum disappeared.

[0702] **Patient 5. Non-small-cell lung cancer with metastases to the right humerus, after surgeries/Intramuscular injection and aerosol inhalation of rSIFN-co combined with chemotherapy (aerosol inhalation of Cisplatin). After treatment, the metastatic lesions in right lung hilum, paratracheal lymph nodes and several sites of spinal metastases disappeared.**

[0703]

Patient 5	Gender: Female	Age: 42
Pathological diagnosis①:	Metastatic adenocarcinoma (in right humerus) (moderately differentiated adenocarcinoma)	
Clinical and pathological staging①:	$T_2N_2M_1$. IV	
Regimes before administration of rSIFN-co:	A surgical repair of right humerus was performed on February 23, Year 1. After that surgery, patient was given 4 courses of DP® chemotherapy: 75mg of Taxotere and 75mg of Cisplatin on day 1.	
Regimes: administration of rSIFN-co combined with chemotherapy	Treatment with rSIFN-co began on April 15, Year 1. Intramuscular injection was performed once every other day: 9μg for the	

	1st time and 21μg for the 2nd time and thereafter. The treatment was provided for a total of 3 months till September 15, Year 1, during which rSIFN-co administration was suspended for 1 month due to chemotherapy (the chemotherapy regimen shown below related to aerosol inhalation of Cisplatin) and for 1 month because of the patient's physical condition. Aerosol inhalation of rSIFN-co was added on September 16, Year 1: 1ml (200μg/ml) per day. Till February, Year 2, the co-administration regimen was provided for 5 months. From September 15, Year 2, intramuscular injection of 15μg was provided every other day. Aerosol inhalation of Cisplatin began on September 16, Year 1: 10mg per dose and 2 doses per day. Eight cycles were conducted with each cycle being 15 days.
Response to rSIFN-co treatment:	CR②(radioactive concentrations at the primary lesion of right lung tumor, right humerus and the T6 vertebra evidently decreased. Metastatic lesions on pelvis and lumbar vertebrae as well as enlarged paratracheal lymph nodes disappeared.)
Survival:	After about 40 months (February Year 1 to

	July Year 4), the patient remained alive with a normal life. No recurrence or metastasis was observed upon imaging.
Diagnostic imaging before administration of rSIFN-co:	Diagnostic imaging after administration of rSIFN-co:
PET/CT scans on February 26, Year 1 after surgery (See lesions indicated by arrows in FIG. 9a-11a) : 1. A circular nodule shadow of about 24mm×19mm×18mm was found at the front end of right lung' upper lobe. 2. Metastases happened to the right upper lung hilum and lymph nodes on anterior tracheal space. Metastatic lesions were also observed at right humerus. 3. Accumulated lesions on the right upper humerus were found which was considered as changes during the recovery phase after the surgery. 4. Increased radionuclide metabolism was observed at chest, lumbar and bilateral ilia. Multiple bone metastases probably happened. 5. Tiny nodular shadows of 2mm were found on the posterior portion of the upper lobe of right lung, which was recommended to be continually observed.	PET/CT scans on March 2, Year 2 (see original locations of lesions indicated by arrows in FIG. 9b-11b): 1. The mass on the soft tissue of anterior segment of upper lobe of right lung did not change in shape, size and density. The extent of radionuclide metabolism decreased (SUVmax reduced from 9.5 to 1.7); 2. The glucose metabolism of lymph nodes on anterior tracheal space became normal and calcified lymph nodes at right upper lung hilum showed a mild radioactive concentration. 3. The radioactive concentration at upper segment of right humerus and T6 vertebra reduced (SUVmax decreased from 6.3 and 3.8 to 2.9 and 1.7, respectively); 4. No abnormal distribution of radionuclide was obviously found in lumbar, sacrum and pelvis. 5. Tiny modules were almost the same as seen before in lateral segment of middle lobe of right lung and the lateral basal segment of lower lobe of left lung. No radionuclide was

CT scans on April 13, Year 1 after chemotherapy: Cancer on upper portion of right lung, tiny nodules on right lung, circumscribed pleural thickening and enlarged mediastinal lymph nodes were found. The results suggested that the chemotherapy was not effective and the lesions had progressed.	abnormally distributed.
Description of FIG. 9:	After treatment, the radionuclide metabolism reduced significantly in the primary lesions of right lung.
Description of FIG. 10:	The radioactive concentration of the lesions at upper segment of right humerus decreased.
Description of FIG. 11:	Metastatic lesions on pelvis disappeared.

[0704] **Patient 6. Non-small-cell lung cancer with multiple lymph node metastases in mediastinum, left segment of neck, right and root segment of neck, left supraclavicular fossa; left-sided pleural effusion; multiple bone metastases in vertebral column, bilateral ribs, right clavicle joint, sternum and left sacrum, and obvious generalized pain/Intramuscular injection, aerosol inhalation and local spraying of rSIFN-co combined with chemotherapy (GP regimen) and Gefinitib (Iressa) therapy. After the treatment, primary lesions on left lung disappeared and metastatic lesions around the body shrank. Further, generalized pain was relieved.**

[0705]

Patient 6	Gender: Male	Age: 39
Pathological diagnosis :	Moderately-poorly differentiated adenocarcinoma	

Clinical and pathological staging①:	$T_4N_3M_{1b}$. IV
Regimens before administration of rSIFN-co:	The first cycle of GP Regimen ⑨ began in September Year 1 with each cycle lasting for 21 days: 1000mg/m^2 of Gemcitabine on day 1 and 8 and 75mg/ m^2 of Cisplatin on day 1.
Regimens : administration of rSIFN-co combined with chemotherapy and other biological therapies	Treatment with rSIFN-co began on October 12, Year 1 with aerosol inhalation of 600μg every day. Intramuscular injection of rSIFN-co started on December 12, Year 1, once every other day: 9μg for 1st time, 15μg for 2nd time and 18μg for 3rd time and thereafter. Local spraying on bone metastases began on March 12, Year 2: 70μg~139μg/does/site, 4~5 doses/day. The second cycle of GP Regimen ⑨ started on October 14, Year 1 (the regimen was exactly the same as mentioned above). Gefinitib was taken from November 24, Year 1: 1 pill/dose (250mg/pill), 1 dose/day.
Response to rSIFN-co treatment:	CR②(primary lesion of about 9×3.5cm in size at the left lung almost disappeared; enlarged lymph nodes of about 1.0cm×0.7cm at left segment of neck, nodules of about 1.2cm×0.8cm at left supraclavicular fossa and nodules of about 1.4cm×1.1cm at right and root segment of neck disappeared; metastatic lesions on sternum disappeared; and metastatic lesions at right sternoclavicular

	joints, ribs and pelvis shrank and relieved to some extent.)
Survival:	After 10 months (from September 27, Year 1 to July Year 2), the patient remained alive and had a normal life. Further, his condition was stable.
Diagnostic imaging before administration of rSIFN-co:	Diagnostic imaging after administration of rSIFN-co:
Chest CT scans on September 21, Year 1 (see primary lesions indicated by arrows in FIG 12a): A blocky shadow (9×3.5cm) of high density was found around left mediastinum and CT value was 39Hu. The boundaries between this shadow and part of great vessels in mediastinum superius, left hilum and left posterior pleura were obscure. Patchy shadow of inflammatory exudation with high density could be seen in lung. Enlarged lymph nodes were found in mediastinum. A few patchy shadows with high density were seen inhomogeneous in upper segment of right lung, boundaries of which were clear. Arched effusions were found on left posterior side. Diagnosis conclusion: lung cancer in left mediastinum combined with	CT scans on November 15, Year 1: Shadows of soft tissues of about 3.6×4.2cm were found; sheet-like density shadows were scattered and had obscure boundaries; no enlarged lymph nodes were seen in the mediastinum (the original ones disappeared). CT scans on December 12, Year 1 (see original locations of lesions indicated by arrows in FIG 12b): Sheet-like and single-sheet-like shadows with increased density were scattered in both lungs. The boundaries were obscure and two hila were not larger. The tracheas were clear and no enlarged lymph nodes were seen in the mediastinum. Pneumonia of both lungs might happen. Bone scans on December 6, Year 1: Multiple spot-like, mass-like and sheet-like shadows with abnormal radioactive concentration could be seen in right sternoclavicular joints, ribs, spinal column and

pleural effusion and obstructive pneumonia; multiple patchy shadows were present in hilum, suggesting the possible occurrence of metastases. Color Doppler ultrasound on September 30, Year 1: Multiple hypoechoic nodules were at left segment of neck, which had clear boundaries and had no hilum of lymph nodes. The big hypoechoic nodule was 1.0cm×0.7cm in size. One hypoechoic nodule of about 1.2cm×0.8cm was at left supraclavicular fossa. It had clear boundary but had no hilum of lymph node. One hypoechoic nodule of about 1.4cm×1.1cm was at root segment of neck on the right side. It had clear boundary but had no hilum of lymph node. Diagnosis conclusion: hypoechoic nodules were found at left segment of neck, left supraclavicular fossa and root segment of neck on the right side. Bone scans on September 29, Year 1: Multiple lesions with radioactive concentrations were found in spinal column, bilateral ribs, right-sided	pelvis. Radioactive distributions in other parts were basically uniform and symmetrical. Diagnosis conclusion: systemic bone metastases shrank in size and were relieved to some extent than before. PET/CT scans on December 29, Year 1 : A nodule with diameter of about 8mm was observed at the apex of left lung and radioactive distribution was slightly increased. Patchy shadows with slightly higher (than normal) density and fabric lesions were found in surrounding area of lung and the radioactive distribution was slight increased. Scattered, patchy shadows with slightly higher density were found in both lungs and the radioactive distribution was not obviously abnormal. Conclusion: 1. After treatment, no obvious increase of FDG metabolism was found on at lesions of the apex of left lung, suggesting the inactivation of most tumor cells; 2. Asymmetric hyperosteogeny was found in whole body and FDG metabolism in some lesions was inhomogeneous with a few increased.

sternoclavicular joints, sternum, left-sided sacroiliac joints and left-sided ilium. Conclusion: Systemic bone lesions with radioactive concentration were found, suggesting the possible occurrence of systematic bone metastases.	
Description of FIG. 12:	After treatment of 2 months, lesions in the left lung disappeared.

[0706] **Patient 7. Non-small-cell lung cancer with metastases in both lungs, both livers and bones of whole body/Intramuscular injection and aerosol inhalation of rSIFN-co combined with administration of Gefinitib (Iressa). After treatment, metastases disappeared or shrank in lungs and several bones, and metastatic lesions of lymph nodes disappeared in liver and mediastinum.**

[0707]

Patient 7	Gender: Female	Age: 53
Pathological diagnosis:	metastatic adenocarcinoma (lymph nodes at left clavicle)	
Clinical and pathological staging①:	$T_4N_3M_1$. IV	
Regimens before administration of rSIFN-co:	None	
Regimens: administration of rSIFN-co combined with administration of other biological agents	Treatment with rSIFN-co began on July 31, Year 1. Intramuscular injection was done once every other day: 9μg for 1st time, 18μg for 2nd time and 21μg for 3rd time and thereafter. Seventy-five times of intramuscular injection were done till January 2, Year 2 (totally 5	

	months). Meanwhile, Iressa (Gefinitib) ® produced in India was administered in combination for 1 year: 1 pill/dose (250mg/pill), 1 dose/day.
Response to rSIFN-co treatment:	PR®(primary lesions in right lung and metastatic lesions in both lungs and several bones shrank with radioactive concentration decreased; metastasis in liver disappeared.)
Survival:	About 28 months (From June 9, Year 1 to October 15, Year 3)
Diagnostic imaging before administration of rSIFN-co:	Diagnostic imaging after administration of rSIFN-co:
CT scans on June 26, Year 1: 1. Sheet-like lesions with radioactive concentration could be found in the upper lobe of right lung and multiple lesions at nodules were found in both lungs; shadows with radioactive concentration could be found in liver and lumbar, suggesting the happening of metastases. 2. Bone scans all over the body showed metastatic lesions were widely spread (parietal bone, left shoulder joint, both shoulder blades and bilateral ribs) (See lesions indicated by arrows in FIG. 13a). CT imaging on July 2, Year 1: see lesions indicated by arrows in	CT scans on October 22, Year 1 (See original locations for lesions indicated by arrows in FIG. 13b) : 1. Lung cancer with metastases in two lungs and liver (recovered compared with previous CT scan); 2. Bone scans showed that metastatic lesions were widely spread in bones all over the body (slightly recovered compared with previous CT scan). CT scans on January 2, Year 2 (see original locations of lesions indicated by arrows in FIG. 14b): 1. The disease was diagnosed as lung cancer in July. Specifically, patchy nodular lesions in the lower lobe of right lung and circumjacent spot-like shadows with high density were

FIG. 14a.	seen. Condition was improved as compared with previous CT scans. 2. The size and shape of liver were normal. Density of liver is even and no focal density abnormality was found. CT scans on March 3, Year 2: Compared with the imaging on October 22, Year 1, no new lesion was found and partial sclerotin radiation was reduced. Multiple bone metastases existed with lung cancer, but improved after treatment.
Description of FIG. 13:	After treatment, systemic metastatic lesions at bones partially disappeared or shrank.
Description of FIG. 14:	After treatment, metastatic lesions in both lungs disappeared and lesions in right lung evidently shrank.

[0708] **Patient 8. Non-small-cell lung cancer with bone metastases/Intramuscular injection and aerosol inhalation of rSIFN-co combined with administration of Gefinitib (Iressa). After treatment, the metastatic lesions in the lungs disappeared and the primary lesions in right lung shrank evidently.**

[0709]

Patient 8	Gender: Female	Age: 68
Clinical and pathological staging①:	$T_4N_2M_1$. IV	
Regimens before administration of rSIFN-co:	None	
Regimens: administration of rSIFN-co combined with other	Treatment with rSIFN-co began on July 21, Year 1 Intramuscular injection was done once	

biological therapies	every other day: 9μg for 1st time, 15μg for 2nd time and 18μg for 3rd time and thereafter. Meanwhile, aerosol inhalation of rSIFN-co of 600μg was performed once a day. Administration of rSIFN-co continued for 3 months till October 31, Year 1. Administration of Gefinitib (Iressa) ® was added in July Year 1: 250mg/pill, 1 pill/dose, 1 dose/day.
Response to rSIFN-co treatment:	CR②(lesions of about 3.0×3.9cm at the lower lobe of right lung, and metastatic lesions in left ilium disappeared basically.)
Survival:	After about 12 months (from June 15, Year 1 to July Year 2), the patient remained alive and had stable conditions.
Diagnostic imaging before administration of rSIFN-co:	Diagnostic imaging after administration of rSIFN-co:
CT scans on July 17, Year 1 (see lesions indicated by arrows in FIG. 15a): The thorax was symmetrical. The lung markings increased and disorganized and transmittance of lung field was low. Spot-like and reticular density shadows were diffusely distributed in bilateral lungs. A density shadow of soft tissue mass (3.0×3.9cm) was found in lower lobe of right lung. The	CT scans on August 20, Year 1 (see original locations of lesions in FIG. 15b-16b): The lesions in the lower lobe of right lung and metastatic lesions in left Ilium were evidently absorbed and shrank after one-month therapy. CT scans on October 10, Year 1: Thorax was symmetrical and barrel shaped. The lung markings increased and disordered and transmittance of lung field was elevated. Lesions on the lower lobe of right lung were obviously absorbed and shrank, and spot-like calcified shadows were in the lesions; the

shadow had obscure and irregular boundary and had burrs and spinous protuberance at the border. CT imaging on July 17, Year 1: See lesions shown in FIG. 16a.	diffusely distributed spot-like density shadows in both lungs were further absorbed and patchy calcified shadows were found in right hilum. Mediastinal lymph nodes were seen and calcified shadows of lymph nodes were found below carina.
Description of FIG. 15:	After treatment, lesions in the lower lobe of right lung was evidently absorbed and shrunk.
Description of FIG. 16:	After treatment, metastatic lesions in left ilium was evidently absorbed and shrunk.

[0710] **Patient 9. Non-small-cell lung squamous cell carcinoma/Aerosol inhalation of rSIFN-co combined with chemotherapy (GP regimen) and administration of recombinant human endostatin (Endostar). After treatment, masses of soft tissue at hilum of lower lobe of right lung evidently shrank and enlarged lymph nodes at right lung hilum disappeared.**

[0711]

Patient 9	Gender: Male	Age: 55
Pathological diagnosis :	Squamous cell carcinoma	
Clinical and pathological staging①:	$T_2N_1M_0$, IIb	
Regimens before administration of rSIFN-co:	None	
Regimens: rSIFN-co combined with chemotherapy.	Treatment with rSIFN-co began on March 18, Year 1. Aerosol inhalation of rSIFN-co of 600μg was performed once a day. A course completed till July 20, Year 1 (for 4 months) with 100 doses of aerosol inhalation done. Four cycles of chemotherapy (GP regimen⑨) were performed with the first one beginning at	

	April 12, Year 1 and each cycle lasting for 21 days: 1600mg of Gemcitabine on days 1 and 8 and 40mg of Cisplatin on days 1 and 3. Meanwhile, 3 cycles of Endostar® administration were performed with 14 days as one cycle: 7.5mg/m^2(1.2×10^{5}U/m^2) per dose, 1 dose/day. Second cycle of chemotherapy began on May 10, Year 1 with the same regimen. Third cycle of chemotherapy began on June 7, Year 1 with the same regimen. Fourth cycle of chemotherapy began on July 7, Year 1 with the same regimen. Four cycles of chemotherapies were totally performed.
Response to rSIFN-co treatment:	CR®(primary lesions of about 3.3×2.4×2.0cm in right lung basically disappeared and enlarged lymph nodes in right hilum of about 2.0×2.2cm disappeared.)
Survival:	After 16 months (from March 1, Year 1 to July Year 2), the patient remained alive and had normal life. His condition was stable.
Diagnostic imaging before administration of rSIFN-co:	Diagnostic imaging after administration of rSIFN-co:
CT scans on February 28, Year 1: see the size of lesions indicated by arrows in FIG. 17a. Chest PET/CT scans on March 18, Year 1:	CT scans on May 23, Year 1: 1. Irregular tissue shadows were seen in right hilum and masses shrank. Spot-like calcified lesions were at right hilum. 2. The enlarged lymph nodes at right

1. Soft tissue nodules of about 3.3×2.4×2.0cm with obscure boundary from neighboring hilum and extremely high radioactive uptake (SUVmax=10.2) was observed at opening segment of bronchus on lower lobe of right lung. 2. Enlarged lymph nodes of about 2.0×2.2cm was observed at right hilum with increased radioactive uptake (SUVmax= 6.6.)	hilum shrank. CT scans on July 18, Year 1 (see size of tumors indicated by arrows in FIG. 17b): Several density shadows of soft tissue could be found at the right lower hilum. Enhancement could be observed after enhancement scan. Spot-like calcified lesions could be found at right hilum; mediastinum was centered with no obvious shadows of enlarged lymph nodes
Description of FIG. 17:	After treatment of 4 months, soft tissue masses at hilum of lower lobe of right lung evidently shrank.

[0712] **Patient 10. Non-small-cell lung cancer with metastases in lung and pleura; pleural effusion/Intramuscular injection of rSIFN-co alone or intrapleural perfusion of rSIFN-co alone. After treatment, primary lesions on the apical segment of upper lobe of left lung were cleared up and metastatic lesions on lingual segment of left lung shrank.**

[0713]

Patient 10	Gender: Female	Age: 48
Clinical and pathological staging①:	$T_4N_0M_0$. IIIb	
Regimens before administration of rSIFN-co:	None	
Regimens: administration of rSIFN-co alone	Treatment with rSIFN-co began on March 9, Year 1. Intramuscular injection of rSIFN-co was performed once every other day: 18μg for 1st time, 21μg for 2nd time and thereafter.	

	Such administration continued for almost 1 year till March, Year 2. Intrapleural perfusion of rSIFN-co was done once every 8 days from April 29, Year 1: 9μg×4 vials for 1st and 2nd time and 9μg×5 vials for 3rd time. Three perfusions were provided totally. Four CT-guided interventional operations were performed in July and August Year 2. The rSIFN-co was injected into relatively large lesions in lungs and 21μg×10 vials were used each time.
Response to rSIFN-co treatment:	CR②(primary lesions of about 2.0×2.0cm in left lung basically disappeared and malignant pleural effusion disappeared.)
Survival:	Patient died after about 19 months later due to renal and hepatic failure caused by traditional Chinese medicine (from February 22, Year 1 to October Year 2).
Cytological diagnosis before administration of rSIFN-co:	Cytological diagnosis after administration of rSIFN-co:
Pleural fluid smear (March 2, Year 1): poorly differentiated cancer cells were found.	Pleural fluid smear and cell mass (September 18, Year 1): Lymphocytes, neutrophils and necrotic materials were found, no tumor cells was found.
Diagnostic imaging before administration of rSIFN-co :	Diagnostic imaging after administration of rSIFN-co:
Chest CT scans on February 23, Year	CT scans on August 1, Year 1 (see original

1: 1. A mass of 2.0×2.0cm was found at apical segment of the upper lobe of the left lung, suggesting the possible occurrence of lung cancer. 2. Multiple nodular lesions were seen in the upper lobe of left lung, indicating the possibility of metastases happening. 3. Pleural effusion was observed in left thoracic cavity. CT imaging on March 6, Year 1: See lesions indicated by arrows in FIG. 19a.	locations of lesions indicated by arrows in FIG. 19b): 1. After treatment on left lung, small nodular shadows in the posterior segment of upper lobe of left lung were completely absorbed and dissipated. 2. Nodular lesions in the lingual segment of left lung were absorbed and shrunken. 3. Left-sided pleural effusion was evidently reduced and streaky nodular lesions on the left pleura were evidently absorbed and relieved.
Description of FIG. 18:	After treatment, pleural effusion was reduced evidently.
Description of FIG. 19:	After treatment, lesions in left lung shrank obviously and pleural effusion was evidently reduced.

[0714] **Patient 11. Non-hodgkin lymphoma/Aerosol inhalation (though nasopharynx and Oral Cavity) of rSIFN-co and local injection into enlarged lymph nodes at neck combined with radiotherapy. After local administration, lesions in the nasal cavity, oropharynx, neck and submaxillary region disappeared or shrank.**

[0715]

Patient 11	Gender: Male	Age: 40
Pathological diagnosis:	Non-hodgkin lymphoma on mesenteric lymph nodes	

Clinical and pathological staging①:	IV
Immunohistochemical examination:	Non-Hodgkin malignant lymphoma (B-cell-originated) (see tumor cells shown by arrows in FIG.20)
Regimens before administration of rSIFN-co:	Chemotherapy was performed for 7 times (five times of CHOPE regimen and two times of MTX regimen) began on August, Year 1. Autologous stem cell transplantation was done in March Year 2. Chemotherapy were provided for 4 times (1 time of GCE regimen and 3 times of ESAP regimen) began on August, Year 2. The forth one ended on November 26, Year 2. Chemotherapy was administered 6 times (3 times of large-dosed CHOPE regimen, 2 times of CMOP regimen and 1 time of a regimen of "bleomycin + CHOP[qd] + Methotrexate ") began on January, Year 3, in combination with stem cell therapy.
Regimens: rSIFN-co combined with chemotherapy and radiotherapy	Treatment with rSIFN-co began on June 9, Year 3. An aerosol preparation of rSIFN-co (72μg/ml) was sprayed onto the nasopharynx and Oral Cavity 2~3 times every day. Administration continued till August 27, Year 3 with 5 days of suspension because of chemotherapy (see chemotherapy describebd below). Local injections on lymph nodes in neck started on June 11, Year 3. Injection was

	performed every other day by injection at multiple sites in a quincunx: 15μg × 10 vials per treatment. Two times later, local subcutaneous injection was performed every other day: 30μg per treatment. Till August 27, Year 3 (more than 2 months), for a total of 10 times. Four cycles of CHOP[11] chemotharepy were provided from July Year 3 to November 28, Year 3 with each cycle lasting for 21days. Radiotherapy began on June 11, Year 3 (scheduled for 25 times) and stopped on July 5, Year 3 as the patient was weak due to myelosuppression.
Response to rSIFN-co treatment:	PR② (soft tissure around nasopharynx and oropharynx with the thickest part of 3.0cm entirely disappeared, and the largest fused lymph node among those at submaxillary region, neck and clavicular region shrank from 7.4cm × 2.4cm × 14.6cm to 1.1cm × 1.5cm.)
Survival:	about 32 months (August 2, Year 1 to April 17, Year 4)
Diagnostic imaging before administration of rSIFN-co:	Diagnostic imaging after administration of rSIFN-co:
PET / CT scans on July 8, Year 3 (see the lesions indicated by arrows in FIG.21a-23a): 1. Nasopharyngeal cavity and oropharyngeal cavity become	PET / CT scans on August 27, Year 3 (see original locations of lesions indicated by arrows in FIG.21b-23b): 1. The thickening of soft tissue at nasopharyngeal cavity and oropharyngeal

significantly narrower; surrounding soft tissues were thickened with the thickest part of 3.0cm; and choanae was blocked. 2. A large number of lymph nodes were enlarged and fused at bilateral submaxillay, neck and supraclavicular and infraclavicular regions with the biggest of about 7.4cm × 2.4cm × 14.6cm.	cavity disappeared, and radioactive uptake was significantly reduced. 2. The number, volume and radioactive uptake of enlarged fused lymph nodes at bilateral mandible, neck and supraclavicular and infraclavicular region reduced as compared to the previous examination. Only two slightly bigger lymph nodes of about 1.1cm × 1.5cm with elevated radioactive uptake were seen in the left submaxillay.
Description of FIG.21:	After treatment, a large number of primary enlarged lymph nodes at neck disappeared.
Description of FIG.22:	After treatment, primary lesions at bilateral mandible disappeared.
Description of FIG.23:	After treatment, primary lesions at pharyngeal disappeared.

[0716] **<u>Patient 12.</u> Non-small-cell lung cancer with metastasis in pleura/Intramuscular injection of rSIFN-co. After treatment, lesions on lower lobe of right lung evidently shrank.**

[0717]

Patient 12	Gender: Male	Age: 67
Cytologic diagnosis:	Lung adenocarcinoma	
Clinical and pathological staging①:	$T_3N_0M_0$. IIb	
Regimens before administration of rSIFN-co:	From August 16, Year 1, two cycles of GP regimen② were provided: 1000mg/m^2 of Gemcitabine on day 1 and 8 and 75mg / m^2 of Cisplatin on day 1. Intrathoracic injection of Cisplatin was also performed for 5 times. 1	

	dose every 7 days, 30- 40mg per dose.
Regimens: administration of rSIFN-co alone	Treatment with rSIFN-co began on November 10, Year 1. Intramuscular injection of rSIFN-co was provided once every two days: 9μg for 1st time, 18μg for 2nd time and 21μg for 3rd time and thereafter. Administration lasted for almost 1 year till October 27, Year 2.
Response to rSIFN-co treatment:	PR②(the mass reduced from about 3.1 × 4.2cm to 2.2 × 1.5cm after 2 months' treatment, and the lesion further reduced in size after administration for 3 months.)
Survival:	about 28 months (from Augugst 11, Year 1 to Year 4)
Diagnostic imaging before administration of rSIFN-co:	Diagnostic imaging after administration of rSIFN-co:
Chest CT scans on October 10, Year 1 after chemotherapy: A shadow of tumor mass of about 3.1×4.2cm was found at opening segment of bronchus on lower lobe of right lung, probably to be central type lung cancer. Right-sided pneumothorax occurred. Lung tissue was compressed by about 10% in size and not much pleural effusion were seen in right-sided thoracic cavity. CT imaging on November 15, Year 1	CT scans on January 10, Year 2: The mass was about 2.2×1.5cm on lower segment of right hilum which was significantly smaller than before. CT scans on February 12, Year 2 (see original locations of lesions indicated by arrows in FIG.24b): After 3 months' treatment, the mass on lower segment of right hilum evedently shrank. CT scans on October 23, Year 2: Masses were seen at dorsal segment of lower lobe of right lung. Not much effusion was in right thoracic cavity and right pleura was

when administration was newly conducted: see lesions nidicated by arrows in FIG.24a).	thicker. There was not much changes compared with the previous CT.
Description of FIG.24:	After treatment of nearly 3 months', masses on lower segment of right hilum had significantly shrunk.

[0718] Patient 13. Non-small-cell lung cancer, after surgeries/Intramuscular injection of rSIFN-co alone. After the treatment, no tumor recurrence or metastasis was found in right lung and the whole body.

[0719]

Patient 13	Gender: Male	Age: 63
Pathological diagnosis:	poorly differentiated adenocarcinoma (upper lobe of right lung)	
Clinical and pathological staging①:	$T_4N_2M_0$. IIIb	
Regimens before administration of rSIFN-co:	On October 15, Year 1, resection of upper lobe of right lung and lymph node dissection were done as well as wedge resection of nodules on lower lobe of right lung.	
Postoperative pathology report:	Poorly differentiated adenocarcinoma occured on upper lobe of right lung; the tumor was 4.5 × 4.5 × 4cm in size and grew to regions below visceral pleura. Poorly differentiated adenocarcinoma was found in two suture zones on nodules of dorsal and lower segment of lungs with diameters of 0.8cm and 1.2cm. (lymph nodes): metastasis was found in: "Group 2" (1/8), group 4 (2/4), and Group 10	

	(1/2).
Regimens: treatment with rSIFN-co alone	Treatment with rSIFN-co began on December 10, Year 1. Intramuscular injection of rSIFN-co was provided once every other days: 9μg for 1st time, 21μg for 2nd time and thereafter). The first course was finished on April 9, Year 2. The second course was performed from December Year 2 to July Year 3 during which intramuscular injection was done every other day with 21μg per dose. The third course was performed from February 21, Year 4 to May 21, Year 4 during which intramuscular injection was done every other day with 18μg per dose.
Response to rSIFN-co:	CR② (After surgery on primary lesions, no tumor recurrence or metastasis occurred.)
Survival:	After 45 months (from September 13, Year 1 to July Year 5), the patient remained alive and had normal life. No recurrence or metastases was observed on imaging test.
Diagnostic imaging before administration of rSIFN-co:	Diagnostic imaging after administration of rSIFN-co:
	CT scans on May 25, Year 3: see the suspicious lesion at lower lobe of right lung indicated by arrows in FIG 25a. Chest CT scans on February 11, Year 4: 1. After surgery on the lung cance in upper

	lobe of right lung, no recurrence signs were found in bronchial stump. 2. Compared with previous CT, no significant change was found in the irregular nodular shadow of 1.6cm on lateral basal segment of lower lobe of right lung. Chest CT scans on January 2, Year 5 (see original location of the suspicious lesion at lower lobe of right lung indicated by arrow in FIG.25b): 1. After surgery on lung cancer of upper lobe of right lung: no recurrence signs were found in bronchial stump compared to CT scans on February 11, Year 4; nodules in lateral basal segment of the lower lobe of right lung was not found. 2. Inflammatory lesions were scattered in residue of right lung; the right-sided pleura was slightly thickened.
Description of FIG.25:	After treatment, the space occupying at lower lobe of right lung disappeared and no tumor recurrence or metastasis was found.

[0720] **Patient 14. Non-small-cell lung adenocarcinoma, after surgery/Intramuscular injection of rSIFN-co alone. After the treatment, no tumor recurrence and metastasis was found.**

[0721]

Patient 14	Gender: Male	Age: 44
Pathological diagnosis:	Poorly differentiated adenocarcinoma	

Clinical and pathological staging①:	$T_4N_3M_0$, IIIb
Regimens before administration of rSIFN-co:	Upper lobe of right lung was resected on October 20, Year 1.
Postoperative pathology report:	Examination on October 27, Year 1: (masses at upper lobe of the right lung) part of lung tissue was resected. Alveolar epithelium hyperplasia and chronic inflammatory cell infiltration were observed under microscope. Fibroplasia happened at the side of pleura with collagenization. Focal hemorrhage and necrosis were also observed while poorly differentiated adenocarcinoma was found. Immunohistochemistry of the cancer tissue showed CK7(+), P63(-)and TTF1(-).
Regimens: administration of rSIFN-co alone	Treatment of rSIFN-co began on November 6, Year 1. Intramuscular injection of rSIFN-co was administered once every other day: 18μg for 1st time, 21μg for 2nd time and thereafter. A first course of 6 months ended on May 10, Year 2. The second course started on March 18, Year 3 and continued for the next following 3 months. Intramuscular injection of rSIFN-co was provided every other day with 15μg per dose. Intramuscular injection of rSIFN-co and Aerosol inhalation were administered for 3 months from November Year 4. Intramuscular injection was done once every other day with

	15μg per dose. Aerosol inhalation was performed every day and a total of 300μg was used for one day.
Response to rSIFN-co treatment:	CR② (after surgery, no tumor recurrence or metastasis was found at primary lesions.)
Survival:	After about 44 months (from October 14, Year 1 to July Year 5), the patient remained alive and had a normal life. No initial recurrence or metastases was observed upon imaging.
Diagnostic imaging before administration of rSIFN-co:	Diagnostic imaging after administration of rSIFN-co:
Chest CT scans on October 13, Year 1: Peripheral lung cancer was found in posterior segment of right upper lobe; the tumor of about 4.0 × 2.9cm in size grew into posterosuperior segment of right-sided pleura and implantation metastasis happened at right-sided pleura; not much pleural effusion occurred in thoracic cavity. CT scans on November 13, Year 1, when drug use was just started (after surgery): See the surgical site of primary lesion indicated by arrows in FIG. 26a	CT scans on February 22, Year 3 (see the original surgical site indicated by arrow in FIG.26b): High-density stripe-like shadows were found in residual part of upper lobe of right lung and local bronchiectasia happened, which were mainly postoperative changes. No significant change was found in lesions as compared with previous CT.
Description of FIG. 26:	After treatment, no tumor recurrence and metastasis was found in residual end of right

	lung and the neighering regions.

[0722] **Patient 15. Non-small-cell lung cancer with systemic metastases, local injection of rSIFN-co into enlarged lymph nodes in groin. After local injections, metastatic lesions in the lymph nodes in pelvic cavity and inguinal area were cleared up or shrank.**

[0723]

Patient 15	Gender: Male	Age: 68
Pathological diagnosis:	none	
Clinical and pathological staging①:	$T_4N_3M_1$. Ⅳ	
Regimens before administration of rSIFN-co:	Treatment with Gamma Knife was done under local anesthesia on April 27, Year 3. Sr-89 therapy was done by Nuclear Medicine Department on April 30, Year 3. Oral administration of Gefitinib (Iressa) was provided from December Year 1 to June Year 3: 1 dose/day, 1 pill/dose, 250mg/pill.	
Regimens: administration of rSIFN-co alone	Treatment of rSIFN-co began on June 25, Year 3. The rSIFN-co was injected into lymph nodes of groin Intramuscularly every day: 15μg×6 vials for 1st time, 15μg×8 vials for 2nd time and 15μg×10 vials for 3rd time and thereafter. Eleven injections were done till July 20, Year 3 (Severe diarrhea occurred after 3 injections and administration was stopped for 2 weeks; after that injection was performed every day and 8 injections in total were continuasly provided).	

	Discontinuous local injection in lymph nodes were performed for 6 times from August 18, Year 3 toSeptember 16, Year 3: 15μg × 10 vials for each time. Local injection in lymph nodes were performed every 3 days from October 8, Year 3 to October 12, Year 3: 15μg × 10 vials for each time.
Response to rSIFN-co treatment:	PR® (mass of about 11.3×4.9cm in pelvic cavity reduced in size to 7.52×7.67×6.72cm).
Survival:	about 24 months (from December Year 1 to December 13, Year 3)
Diagnostic imaging before administration of rSIFN-co:	Diagnostic imaging after administration of rSIFN-co:
MRI of pelvic cavity on June 6, Year 3 (see lesions indicated by arrows in FIG.27a): Bone distruction was found at left ilium, sacroiliac joint, left-sided corpora ossis pubis, superior ramus of pubis and femoral head with slightly longer T1 and slightly longer T2 signal. The left gluteus minimus, obturator internus and obturator externus, musculus adductor magnus and longus, and rectus femoris were involved and the fascia was obviously swollen. Irregular mass of about 11.3cm×4.9cm with slightly	MRI of pelvic cavity on July 28, Year 3 (see original locations of lesions indicated by arrows in FIG.27b): Bone destruction at left pubis was replaced by shadow of soft tissue with long T2 signal and fused into block with the swollen soft tissue of pelvic wall within a range of 7.52 cm x 7.67 cm x 6.72 cm. Left acetabulum, ala of ilium, obturator internus and obturator externus, vastus medialis and soft tissue in groin were involved.

longer T2 signal were seen at acetabular plane in left pelvis which was slightly enhanced after reinforcement.	
Description of FIG 27:	After 1 month's treatment, the enlarged lymph nodes in pelvis and groin disappeared or shrank.

[0724] **Patient 16. Rectal cancer, after a surgery/Intramuscular injection of rSIFN-co alone. After the treatment, no tumor recurrence or metastasis was found.**

[0725]

Patient 16	Gender: Female	Age: 63
Pathological diagnosis:	Well to moderately differentiated adenocarcinoma was found in rectum and mucinous adenocarcinoma was found in part of rectum. Cancer invaded into deep muscularis of intestinal wall and formed cancerous nodules in mesorectum (see the cancer cells indicated by arrows in FIG28)	
Clinical and pathological staging①:	$T_4N_1M_X$. IIIb	
Regimens before administration of rSIFN-co:	Laparoscopic-assisted abdominal perineal radical resection of rectal cancer was done on May 16, Year 1.	
Regimens: administration of rSIFN-co alone	Treatment of rSIFN-co began on May 23, Year 1. Intramuscular injection of rSIFN-co was provided once every other day: 21μg for each time. The first course of 8 months ended on	

	February Year 2. The second course was provided from January Year 3 to April Year 3. Intramuscular injection of rSIFN-co was provided once every other day with 9μg each time and continued for 3 months. The third course was administered from December Year 3 to March Year 4. Intramuscular injection was performed every other day with 15μg each time.
Response to rSIFN-co treatment:	CR② (after surgery, no tumor recurrence or metastasis occurred at primary lesions.)
Survival:	After about 49 months (from May Year 1 to July Year 5), the patient remained alive. No recurrence or metastases was observed upon imaging.
Diagnostic imaging before administration of rSIFN-co:	Diagnostic imaging after administration of rSIFN-co:
PET/CT scans on April 30, Year 1 (see primary lesions indicated by arrows in FIG29a): 1. Mass with high metabolic rate was seen in rectum combined with intestinal wall thickened, suggesting the posibility of malignant tumor happening (rectal cancer or lymphoma). 2. A nodular lesion of high metabolic rate was found beside the left-sided	PET/CT scans on June 17, Year 3 (see the original location of lesions indicated by arrows in FIG29b): No signs were found on recurrence of primary lesions or systemic metastases. PET/CT scans on March 3, Year 4: 1. After surgery on rectal cancer, no signs of malignant tumor were found in colorectum and the artificial fistula in lower segment of left-sided abdomen. 2. Two slightly enlarged lymph nodes beside

external iliac vessels in pelvic cavity, suggesting the possible occurrence of lymphatic metastasis. No signs of malignant tumor were found in pelvic cavity, other parts and retroperitoneum.	the left-sided external iliac vessels and great vessel in pelvic cavity and metabolism was not increased. It might be caused by inflammation of lymph nodes in view of sevel inmaging examination (It can be seen that the enlarged lymph nodes were not metastatic lesions.).
Description of FIG.29:	During 25 months after surgery, no recurrence or systemic metastasis occurred in the cured primary lesions.

[0726] **Patient 17. In situ cervical cancer in situ/Intramuscular injection of rSIFN-co alone or uterine perfusion of rSIFN-co alone. After treatment, cervical tumor was basically inhibited and test of high-risk HPV became negative. Also, no tumor cells were found in cervical smear.**

[0727]

Patient 17	Gender: Female	Age: 25
Cytologic diagnosis:	Cervical smear on May 11, Year 1 showed high-grade intraepithelial lesion.	
Clinical and pathological staging①:	Ib1	
Regimens before administration of rSIFN-co:	none	
Regimens: administration of rSIFN-co alone	Treatment of rSIFN-co began on May 14, Year 1. Intramuscular injection of rSIFN-co was provided once every other day: 9μg for 1st time, 15μg for 2nd time and 18μg for 3rd time and thereafter. Meanwhile, uterine perfusion was done once a day: at 1000μg per dose, for 2 hours.	

	Uterine perfusion ended on June 28, Year 1 (lasted for more than 1 month) and intramuscular injection was stopped on September 12, Year 1 (lasted for 4 months).
Response to rSIFN-co treatmenr:	CR② (malignant cervical lesion disappeared, and test of high-risk HPV became negative. Also, no tumor cells were found in cervical smear.)
Survival:	After about 26 months (from May 5, Year 1 to July Year 3), the patient remained alive and had normal life. No recurrence or metastases was observed upon imaging.
Pathological diagnosis before administration of rSIFN-co:	Pathological diagnosis after administration of rSIFN-co:
On May 5, Year 1, cervical intraepithelial lesion of grade II~III was seen with glands involved.	Chronic endocervicitis was found on June 24, Year 1.
Viral diagnosis (HC2HPV DNA) before administration of rSIFN-co:	Viral diagnosis (HC2HPV DNA) after administration of rSIFN-co
April 14, Year 1, High-risk subtypes (15 kinds): positive- HPV16	June 25, Year 1: RLU/CO 0.23 (negative)
Diagnostic imaging before administration of rSIFN-co:	Diagnostic imaging after administration of rSIFN-co:
PET/CT scans on May 14, Year 1: 1. Cervical hypertrophy was found and FDG metabolism was slightly increased, suggesting the possible occurrence of low-grade malignant lesion.	PET/CT scans on November 8, Year 1: The FDG metabolism in the cervix significantly reduced, indicating that the tumor activity was locally inhibited; FDG metabolism was inhomogeneous and obscure, indicating that inflammatory change might

2. No metastatic lesion was found in pelvic cavity and pelvic wall.	happen.

[0728] **Patient 18. Prostatic cancer/Intramuscular injection of rSIFN-co and local spraying (to skin surface where prostate biopsy was done) of rSIFN-co combined with local radiotherapy. After treatment, the prostate tumor and two lymph nodes in right-sided ischiorectal fossa were eliminated; the posterior wall of fundus of urinary bladder, bilateral seminal vesicles and anterior rectal wall infected by lesions recovered; and the level of tumor marker (PSA) become normal.**

[0729]

Patient 18	Gender: Male	Age: 64
Pathological diagnosis:	Adenocarcinoma was found in the 1st -10th prostate biopsy.	
Clinical and pathological staging①:	$T_4N_1M_0$, IV	
Regimens before administration of rSIFN-co:	none	
Regimens: administration of rSIFN-co combined with radiotherapy	Treatment of rSIFN-co began on November 15, Year 1. Intramuscular injection of rSIFN-co was provided once every other day: 9μg for 1st time, 15μg for 2nd time, 18μg for 3rd time and 24μg for 4th time and thereafter. Meanwhile, the drug was locally applied by spraying to the skin surface where prostate biopsy was done: 4~5 doses per day and at 70μg~139μg per dose. The amount of rSIFN-co to be intramuscularly injected changed to 21μg from December 15, Year 1 to July 1, Year 2.	

	Radiotherapy on prostate (EBRT)[12] was performed for 38 times from December 5, Year 1 to February 26, Year 2.
Response to rSIFN-co treatment:	CR[2] (prostate of 4.7×3.5×5.6cm reduced normal size; two lymph nodes in right ischiorectal fossa were eliminated; the posterior wall of fundus of urinary bladder, bilateral seminal vesicles and anterior rectal wall infected by lesions recovered; and the level of specific antigen of Prostatic cancer (PSA) become normal.)
Survival:	After about 8 months (from November 11, Year 1 to July Year 2), the patient remained alive.
Level of specific antigen of Prostatic cancer (PSA) before administration of rSIFN-co:	Level of specific antigen of Prostatic cancer (PSA) after administration of rSIFN-co:
Examination on November 2, Year 1: Total specific antigen of Prostatic cancer (T-PSA): 23.090ng/ml (reference value<3 ng/ml) Free PSA (F-PSA): 1.850 ng/ml (reference value<0.75 ng/ml) Ratio of antigen of Prostatic cancer (F-PSA/PSA): 8.01%(reference value 25~100)	Examination on March 7, Year 2: Total specific antigen of Prostatic cancer (T-PSA):: 0.006ng/ml (reference value<3) Free PSA (F-PSA): <0.010 ng/ml (reference value<0.75 ng/ml)
Diagnostic imaging before administration of rSIFN-co:	Diagnostic imaging after administration of rSIFN-co:

MRI scans on November 4, Year 1: 1. Prostate was significantly enlarged and irregular mass shadows of about 4.7×4.3×5.6cm in size were formed with obsecure border and inhomogeneous signals. Inhomogeneous reinforcement happened in enhanced scan. All these suggested the occurrence of prostatic cancer. 2. Two lymph nodes in right-sided ischiorectal fossa were found with diameter of about 1cm, suggesting the occurrence of metastasis. 3. The posterior wall of fundus of urinary bladder, bilateral seminal vesicles and anterior rectal wall might be invaded.	MRI (March 31, Year 2): 1. The prostate was smaller in size and left posterior part protruded slightly. No obvious abnormality was found in each imaging sequence signal. 2. Bladder wall was inhomogeneously thickened: inflammation? 3. No effusion and enlarged lymph nodes were found in pelvic cavity.

[0730] **Patient 19. Melanoma of nose (after a surgery) combined with bone metastases at bilateral hip joints, bilateral femurs, bilateral humeri, ribs and bilateral shoulder joints/Intramuscular injection of rSIFN-co and local spraying of rSIFN-co on lesions. After treatment, multiple enlarged lymph nodes at bilateral shoulder joints and subaxillary were cleared up as well as recurrence and metastases at bilateral hip joints, upper femur, residual right paranasal sinuses and nasal cavity after surgery.**

[0731]

Patient 19	Gender: Female	Age: 43
Pathological diagnosis:	Tumors were found in the neoplasma inside	

	the right maxillary sinus. Malignant melanoma was proved by immunohistochemistry: (HMB45 (part+), MART1 (-), S100 (-), CD63 (+), NSE (-), PCK (-), EMA (+), CD56 (-) and KI671 25%).
Clinical and pathological staging ①:	pT_3NxM_1. Ⅳ
Regimens before administration of rSIFN-co:	Two cycles were provided on October 30, Year 1 and November 30, Year 1: 15mg of Endostar on day 1~10 and 200mg of temozolomide on day 1~5, oral administration. Targeted radiotherapy (50Gy/25f) was done on November 2, Year 1 and the targets were right maxillary sinus + 1/4 of the left maxillary sinus, bilateral ethmoid sinus, frontal sinus and the adjacent tissues of the right eyeball. Radiotherapy ended on December 7, Year 1.
Regimens: administration of rSIFN-co alone	Treatment of rSIFN-co began on December 21, Year 1. Intramuscular injection of rSIFN-co was provided once every other day: 9μg for 1st time, 15μg for 2nd time, 18μg for 3rd time and thereafter. Meanwhile, the drug was locally applied by spraying onto the skin surface of the right shouder: 70μg - 139μg/dose/site, 4-5 doses/day. Spraying was provided to skin surface of the left shoulder and other sites with bone

	metastasis began on February 27, Year 2: 70μg - 139μg/dose/site, 4-5 doses/day.
Response to rSIFN-co treatment:	CR② (Multiple enlarged lymph nodes at bilateral shoulder joints and axillae disappeared; recurrence and metastatic lesions at residual right sinus and nasal cavity after surgery as well as multiple abnormal signals at bilateral hip joints and upper parts of femora disappeared.)
Survival:	After about 11 months (from August Year 1 to July Year 2), the patient remained alive.
Diagnostic imaging before administration of rSIFN-co:	Diagnostic imaging after administration of rSIFN-co:
MRI of paranasal sinus on December 8, Year 1: 1. Compared with the previous imaging (taken on October 26, Year 1, after surgery in right sinus and nasal cavity), soft tissues surrounding residual cavity were thickened and intensification was apparent, suggesting recurrence. 2. Several lymph nodes at the neck were enlarged. 3. Hypertrophy was found at left-sided inferior nasal concha and inflammation was seen at left maxillary sinus, sphenoid sinus and ethmoid sinus.	MRI of shoulder joint on May 2, Year 2: No obvious bone destruction was found at left shoulder. Spot-like shadows with long T2 and long T1 signals were seen in humeral head, mostly small cystic lesions. Pelvis MRI on May 2, Year 2: Long T1 and long T2 signals changed at upper branch of the left pubis and signals were intensified significantly as shown in the intensified image. No obvious abnormality was seen in remaining part of the pelvis. Brain MRI on May 2, Year 2: 1. No intracranial abnormality; 2. Bilateral otitis media and mastoiditis; 3. Nasal conchae of middle and lower segments at right side were missing and inner wall of

4. Otitis media and mastoiditis was observed at right side.. MRI scans of hip joint on December 8, Year 1: Lesions with long T1 and long T2 signal were seen at left acetabulum. And lesions extended to left ischium, High signals with significant enhancement in fat suppression sequences were found. Lesions with significantly intensified long T1 and long T2 signals were seen at lower portions of bilateral ilia and right anterior acetabulum,. Conclusion: multiple lesions were found in the bone mass of bilateral hip joints and bone metastasis probably happened. MRI of shoulder joint on December 8, Year 1: Sheet-like shadows with long T1 and long T2 signals, inhomogeneous enhancement and obscure boundaries were found at bilateral acromial ends of clavicles, right glenoid cavity of scapula, bone surrounding bilateral scapula, upper parts of bilateral humeri and ribs. Multiple lymph nodes were found at bilateral axillae with part enlarged. Conclusion:	maxillary sinus at right side was missing, leading to an empty cavity formed by connecting sinus cavity and nasal cavity; 4. Left maxillary sinusitis; 5. Sphenoid sinusitis and frontal sinusitis. MRI of lumbar, head and shoulder joint on June 26, Year 2: 1. Fat deposition was found on lumbar 2 from the back with the remaining corpus vertebrae and intervertebral disc being normal; 2. Intracranial brain tissue was normal; 3. The lack of nasal conchae at right nasal cavity and inner wall of the right maxillary sinus was as shown above; 4 Bilateral ethmoiditis and sphenoid sinusitis, and bilateral mastoiditis were found; 5. No further enlargement was found at the lymph nodes on either side of the neck; 6. Femoral heads of bilateral shoulder joints were normal.

multiple metastases of bilateral shoulder joints and axillae happened.	

[0732] ① Standard for cancer staging, refer to *AJCC Cancer Staging Manual (6th Edition)*/ Edited by F.L. Greene, D.L. Page and I.D. Fleming etc. Shenyang: Liaoning Science and Technology Press, 2005.8;

[0733] ② Standard for effect evaluation of antitumor drugs, refer to *Practical Therapeutics of Antitumor Drugs* /Edited by Liu Xinchun etc. (Beijing: People's Medication Publishing House, 2002) p1100-1101;

[0734] ③ Radiotherapy of lung cancer, refer to *Modern Lung Cancer Pathology and Clinical Practice*/ Edited by Xiong Min and Wu Yilong, (Beijing: Science Press, 2003.6), p324-365;

[0735] ④ TC regimen, refer to *Modern Lung Cancer Pathology and Clinical Practice*/ Edited by Xiong Min and Wu Yilong, (Beijing: Science Press, 2003.6), p386;

[0736] ⑤ "Endostar", refer to *Chemotherapy and Targeted Therapy of Lung Cancer*/Edited by Liao Meilin, (Beijing: People's Medication Publishing House, 2009.8), p261;

[0737] ⑥ "Pemetrexed", refer to *Chemotherapy and Targeted Therapy of Lung Cancer*/Edited by Liao Meilin, (Beijing: People's Medication Publishing House,2009.8), p94;

[0738] ⑦ EP regimen, refer to *Modern Lung Cancer Pathology and Clinical Practice*/ Edited by Xiong Min and Wu Yilong, (Beijing: Science Press,2003.6), p386;

[0739] ⑧ DP regimen, refer to *Modern Lung Cancer Pathology and Clinical Practice*/ Edited by Xiong Min and Wu Yilong, (Beijing: Science Press,2003.6), p386;

[0740] ⑨ GP chemotherapy, refer to *Chemotherapy and Targeted Therapy of Lung Cancer*/Edited by Liao Meilin, (Beijing: People's Medication Publishing House,2009.8), p222-230;

[0741] ⑩ "Gefitinib", refer to *Chemotherapy and Targeted Therapy of Lung Cancer*/Edited by Liao Meilin, (Beijing: People's Medication Publishing

House,2009.8), p222-230;

[0742] (11) CHOP chemotherapy, refer to *Practical Therapeutics of Antitumor Drugs* /Edited by Liu Xinchun etc. (Beijing: People's Medication Publishing House, 2002), p931;

[0743] (12) Radiotherapy of prostatic cancer, refer to *Advance in Clinical Oncology* /Edited by Sun Yan and Zhao Ping, (Beijing: Peking Union Medical College Press, 2005.9ISBN7-81072-711-7), p1009-1010.

Example 4: Data of clinical effectiveness of rSIFN-co of the present invention

[0744] In the following tables, the number listed before the brackets represents the number of patients conforming to the condition described in that row and column; the number between each pair of parenthesis represents the number as a percentage of all the patients listed in either that column or that row; finally, II / III / IV between parentheses represent cancer staging. The cancer staging was made in accordance with *AJCC Cancer Staging Manual (6th Edition)*/ Edited by F.L. Greene, D.L. Page and I.D. Fleming etc. Shenyang: Liaoning Science and Technology Press, 2005.8.

Table 3 Efficacy of rSIFN-co administration on lung cancer at different stages

[0745]

Tumor staging	CR	PR	NC/SD	PD	Total
II	1(20.00%)	2(40.00%)	2(40.00%)	0(0.00)	5
III	5(50.00%)	2(20.00%)	1(10.00%)	2(20.00%)	10
IV	6(40.00%)	7(46.67%)	1(6.67%)	1(6.67%)	15
Total	12(40.00%)	11(36.67%)	4(13.33%)	3(10.00%)	30

Note: for detailed regimens, refer to those described in example 2.

Table 4 Efficacy of rSIFN-co administration on lung cancer after or without surgery*

[0746]

Group	CR	PR	NC/SD	PD	Total
After surgery	2(33.33%)(III/IV)	0(0.00%)	3(50.00%)(II/III/IV)	1(16.67%)(III)	6
Without surgery	10(41.67%)(II/III/IV)	11(45.83%)(II/III/IV)	1(4.17%)(IV)	2(8.33%)(III/IV)	24
Total	12(40.00%)	11(36.67%)	4(13.33%)	3(10.00%)	30

Note: for detailed regimens, refer to those described in example 2.

*In this table, surgery does not include cryoablation or radiofrequency ablation.

Table 5 Efficacy of administration provided in different ways on lung cancer

[0747]

Way to administer	CR	PR	NC/SD	PD	Total
Systemic administration	4(44.44%)(II/IV)	3(33.33%)(II/III)	1(11.11%)(II)	1(11.11%)(III)	9
Systemic + local	6(33.33%)(II/IV)	7(38.89%)(II/III/IV)	3(16.67%)(II/III/IV)	2(11.11%)(III/IV)	18
Local	2(66.67%)(II/III/IV)	1(33.33%)(IV)	0(00.00%)	0(00.00%)	3
Total	12(40.00%)	11(36.67%)	4(13.33%)	3(10.00%)	30

Note: systemic administration refers to intramuscular or subcutaneous administration; local administration refers to aerosol inhalation and spraying on skin surface; refer to those described in example 2 for detailed regimens.

Table 6 Efficacy of rSIFN-co administration on lung cancer with different

durations

[0748]

Medication duration (month(s))	CR	PR	NC/SD	PD	Total
<3	1(50.00%)(IV)	0(00.00%)	1(50.00%)(IV)	0(00.00%)	2
3~6	3(50.00%)(IV)	3(50.00%)(III/IV)	0(00.00%)	0(00.00%)	6
7~12	2(20.00%)(III)	4(40.00%)(II/IV)	2(20.00%)(II)	2(20.00%)(III/IV)	10
>12	6(50.00%)(II/III/IV)	4(33.33%)(III/IV)	1(8.33%)(III)	1(8.33%)(III)	12
Total	12(40.00%)	11(36.67%)	4(13.33%)	3(10.00%)	30

Note: for detailed regimens, refer to those described in example 2.

Table 7 Efficacy of drug combination on lung cancer

[0749]

drug combination	CR	PR	NC/SD	PD	Total
Yes	8(42.11%)(II/III/IV)	7(36.84%)(III/IV)	3(15.79%)(II/III/IV)	1(5.26%)(III)	19
No	4(36.36%)(III/IV)	4(36.36%)(II/III/IV)	1(9.09%)(II)	2(18.18%)(III/IV)	11
Total	12(40.00%)	11(36.67%)	4(13.33%)	3(10.00%)	30

Note: drug combination or combined therapy includes: chemotherapy, radiotherapy, radiofrequency ablation, biological medicine and traditional Chinese medicine, but excludes surgery; for detailed regimens, refer to those described in example 2.

Table 8 Efficacy of administration on lung cancer with/without metastasis

[0750]

Metastasis	CR	PR	NC/PD	PD	Total
Yes	11(44.00%)(II/III/IV)	9(36.00%)(II/IIII/IV)	4(16.00%)(II/IIII/IV)	1(4.00%)(IV)	25
No	1(20.00%)(III)	2(40.00%)(II/III)	0(0.00%)	2(40.00%)(III)	5
Total	12(40.00%)	11(36.67%)	4(13.33%)	3(10.00%)	30

Note: for detailed regimens, refer to those described in example 2.

Table 9 Efficacy of rSIFN-co administration on tumor of different stages

[0751]

Tumor staging	CR	PR	NC/SD	PD	Total
I	3(100.00%)	0(0.00%)	0(0.00%)	0(0.00%)	3
II	2(33.33%)	2(33.33%)	2(33.33%)	0(0.00)	6
III	6(35.29%)	5(29.41%)	3(17.64%)	3(17.64%)	17
IV	8(25.00%)	12(37.50%)	5(15.62%)	7(21.88%)	32
Total	19(32.76%)	19(32.76%)	10(17.24%)	10(17.24%)	58

Note: for detailed regimens, refer to those described in example 2, wherein:

Tumor of stage I includes: cervical cancer, gastrointestinal stromal tumor;

Tumor of stage II includes: lung cancer, breast cancer;

Tumor of stage III includes: lung cancer, ovarian cancer, cervical cancer, rectal cancer, breast cancer, pancreatic cancer, lymphoma, malignant neuroma and metastatic poorly differentiated squamous carcinoma;

Tumor of stage IV includes: lung cancer, cervical cancer, endometrial or uterine papillary serous carcinoma with hybrid clear-cell carcinoma, colon cancer, cholangiocarcinoma, including cholangioadenocarcinoma, liver cancer including hepatocellular carcinoma, breast cancer, gastric cancer, prostate cancer, embryonal rhabdomyosarcoma, malignant melanoma and lymphoma, including Non-Hodgkin's

lymphoma.

Table 10 Efficacy of rSIFN-co administration on tumor after or without surgery

[0752]

Group	CR	PR	NC/SD	PD	Total
After surgery	8(32.00%)	2(8.00%)	7(28.00%)	8(32.00%)	25
Without surgery	11(33.33%)	17(51.52%)	3(9.09%)	2(6.06%)	33
Total	19(32.76%)	19(32.76%)	10(17.24%)	10(17.24%)	58

Note: for detailed regimens, refer to those described in example 2.

Table 11 Efficacy of administration provided in different ways

[0753]

Way to administrate	CR	PR	NC/SD	PD	Total
Systemic	8(34.78%)	8(34.78%)	2(8.70%)	5(21.74%)	23
Systemic + local	10(32.26%)	8(25.81%)	8(25.81%)	5(16.13%)	31
Local	1(25.00%)	3(75.00%)	0(00.00%)	0(00.00%)	4
Total	19(32.76%)	19(32.76%)	10(17.24%)	10(17.24%)	58

Note: for detailed regimens, refer to those described in example 2.

Table 12 Efficacy of rSIFN-co administration with different durations

[0754]

Medication duration(month(s))	CR	PR	NC/PD	PD	Total

<3	2(40.00%)	1(20.00%)	2(40.00%)	0(00.00%)	5
3~6	4(25.00%)	6(37.50%)	3(18.75%)	3(18.75%)	16
7~12	3(18.75%)	6(37.50%)	3(18.75%)	4(25.00%)	16
>12	10(47.62%)	6(28.57%)	2(9.52%)	3(14.29%)	21
Total	19(32.76%)	19(32.76%)	10(17.24%)	10(17.24%)	58

Note: for detailed regimens, refer to those described in example 2.

Table 13 Efficacy of drug combination

[0755]

drug combination	CR	PR	NC/PD	PD	Total
Yes	10(34.48%)	10(34.48%)	6(20.69%)	3(10.34%)	29
No	9(31.03%)	9(31.03%)	4(13.79%)	7(24.14%)	29
Total	19(32.76%)	19(32.76%)	10(17.24%)	10(17.24%)	58

Note: combined medication includes: chemotherapy, radiotherapy, radiofrequency ablation, biological medicine and traditional Chinese medicine; for detailed regimens, refer to those described in example 2.

Table 14 Efficacy of administration on tumor with/without metastasis

[0756]

Metastasis	CR	PR	NC/SD	PD	Total
Yes	14(29.79%)	16(34.04%)	9(19.15%)	8(17.02%)	47
No	5(45.45%)	3(27.27%)	1(9.09%)	2(18.18%)	11
Total	19(32.76%)	19(32.76%)	10(17.24%)	10(17.24%)	58

Note: for detailed regimens, refer to those described in example 2.

Table 15. Patients in Complete Remission (CR) up until the date of last count.

[0757]

Patient No.	Cancer	Cell type	Stage	Staging	Therapies	Response	rSIFN-co Tx Duration (months)	rSIFN-co admin	Amount of rSIFN-co per dose
1	NSCLC	sqamous cell carcinoma	IIIb	$T_3N_2M_0$	prior CTx, rSIFN-co + RTx	CR	15	im, *qod*	9ug, 15ug, 18ug
3	NSCLC	lung adenocarcinoma	IV	$T_2N_2M_1$	rSIFN-co+RTx	CR	3+	im, *qod* + inhalation *qod*	9ug, 18ug, 21ug, 200ug, 400ug
4	SCLC		IV	$T_4N_3M_1$	prior CTx, rSIFN-co+CTx+cryoablation	CR	16+	im, *qod* + inhalation *qod*	9ug, 15ug, 18ug, 200ug, 21ug, 100ug-400ug
5	NSCLC	moderately differentiated adenocarcinoma	IV	$T_2N_2M_1$	prior CTx, rSIFN-co+CTx	CR	8+	im, *qod* + inhalation *qd*	9ug, 21ug, 200ug, 15 ug
6	NSCLC	moderately to poorly differentiated adenocarcinoma	IV	$T_4N_3M_{1b}$	prior CTx, rSIFN-co+CTx+Gefinitib (Iressa)	CR	5+	im, *qod* + inhalation *qd* + spraying *qd 4-5x/day*	600ug, 9ug, 15ug, 18ug, 70ug-139ug

8	NSCLC		IV	$T_4N_2M_1$	rSIFN-co+Iressa	CR	3	im, *qod* + inhalation *qd*	9ug, 15ug, 18ug, 600ug
9	NSCLC	squamous cell carcinoma	IIb	$T_2N_1M_0$	rSIFN-co+CTx+Endostar	CR	4	inhalation, *qd*	600ug
10	NSCLC		IIIb	$T_4N_0M_0$	rSIFN-co	CR	15	im, *qod* + thoracic perfusion every 7 days + intralesion	18ug, 21ug, 36ug, 45ug, 2100ug
13	NSCLC	poorly differentiated adenocarcinoma	IIIb	$T_4N_2M_0$	prior surgery, rSIFN-co	CR	15	im, *qod*	9ug, 21ug, 18ug
14	NSCLC	poorly differentiated adenocarcinoma	IIIb	$T_4N_3M_0$	prior surgery, rSIFN-co	CR	12	im, *qod* + inhalation *qd*	18ug, 21ug, 15ug, 300ug
16	rectum	moderately differentiated adenocarcinoma	IIIb	T_4N_1Mx	prior surgery, rSIFN-co	CR	15	im, *qod*	21ug, 9ug, 15ug
17	uterine cervical	squamous intraepithelial lesion	1b1	no metastasis	rSIFN-co	CR	4	im, *qod* + uterine perfusion, *qd*	9ug, 15ug, 18g,1000ug

18	prostate	adenocarcinoma	IV	$T_4N_1M_0$	rSIFN-co+RTx	CR		im, *qod*+spray topically, *qd*, 4-5x/day	9ug, 15ug, 18ug, 24ug, 70ug-139ug, 21ug
19	malignant melanoma	melanoma	IV	$pT_3N_xM_1$	Prior Endostar+ CTx+RTx, rSIFN-co	CR		im, qod+spray topically, *qd*, 4-5x/day	9ug, 15ug, 18ug, 70ug-139ug
21	lung		IIIb	metastasis to bone	Prior TCM+Iressa, rSIFN-co + Iressa	CR		im, *qod*	9ug, 15ug, 18g
23	lung	adenocarcinoma	IV	metastasis to pleural cavity, mediastinal lymph nodes & bone	prior CTx + rSIFN-co	CR	2	im, *qod*	9ug, 21ug
39	cervical	poorly differentiated squamous cell carcinoma	Ib2		prior surgery+CTx, rSIFN-co+NK cell Tx	CR	6	im, *qod*	9ug, 15ug
48	breast		IIa		prior surgery, rSIFN-co	CR	4+	im, *qod*	9ug, 15ug, 18ug, 21ug
54	GI		Ib		prior surgery +RTx, rSIFN-co	CR	9+	im, *qod*	9ug, 21ug

Table 16. Patients in Partial Remission (PR) up until the date of last count.

[0758]

Patient No.	Cancer	Cell type	Stage	Staging	Therapies	Response	rSIFN-co Tx Duration (months)	rSIFN-co admin	Amount of rSIFN-co per dose
2	NSCLC	lung adenocarcinoma	IV	$T_3N_3M_1$	prior CTx, rSIFN-co+Endostar+CTx	PR	12	im, qod + inhalation, qd	9ug, 15ug, 18ug, 21ug, 300ug, 500ug, 600ug
7	NSCLC	lung adenocarcinoma	IV	$T_4N_3M_1$	rSIFN-co+Iressa	PR	5	im, qod	9ug, 18ug, 21ug
11	Non-Hodgkin lymphoma		IV		prior CTx, prior stem cell Tx, rSIFN-co+CTx+RTx	PR	4.5	inhalation, qd, 2-3x/day + intralesion, qod + s.c., qod	72ug/ml,150ug, 30ug
12	NSCLC	lung adenocarcinoma	IIb	$T_3N_0M_0$	prior CTx, rSIFN-co	PR	12	im, qod	9ug, 18ug, 21ug
15	NSCLC		IV	$T_4N_3M_1$	prior RTx+Iressa, rSIFN-co	PR	1.5+	inj into part of inguinal LN, qd	90ug, 120ug, 150ug

20	lung		IV		rSIFN-co +CTx	PR	3+	im, qod + inhalation, qd	9ug, 15ug, 21ug, 200ug, 300ug
22	lung		IIIa	liver mets	prior CTx+RFA , rSIFN-co	PR	2+	im, qod	18ug, 21ug
24	lung		IIIb		rrSIFN-co-co	PR	2	im, qod + intrapleural injection	9ug, 13.5ug, 21ug,126ug, 168ug,210ug, 252ug
26	lung		IV	brain mets	prior Iressa, rSIFN-co + Iressa	PR	24+	im, qod + inhalation qd	21ug, 18ug, 100ug, 300ug, 400ug
30	lung	adenocarcinoma	IV	brain mets	prior RTx+CTx, rSIFN-co	PR		im, qod + inhalation, qd	21ug, 200ug
32	lung		IIb		prior CTx+Gefitinib, rSIFN-co + Gefitinib	PR		im, qod + inhalation, qd	9ug, 13.5ug, 18ug, 300ug
35	lung	adenocarcinoma	IV		prior CTx, rSIFN-co + CTx + RFA	PR		im, qod + inhalation, qd	15ug, 18ug, 600ug
36	ovarian		IIIb		prior surgery, rSIFN-co	PR	3+	im,, qod	9ug, 15ug, 18ug, 21ug
37	cervical		IV		prior RTx+CTx, rSIFN-co	PR		im,, qod	21ug
42	cholangioadenocarcinoma		IV	liver mets	prior surgery+RTx, rSIFN-co+surgery	PR	18+	im,, qod	9ug, 18ug, 21ug
45	HCC		IV	intrahepatic mets	prior surgery, rSIFN-co	PR	5.5 +	im,, qod	9ug, 18ug, 21ug

51	gastric		IV	abdominal mets	prior CTx, rSIFN-co	PR	8 days	intraperitoneal perfusion, qod	120ug, 180ug, 210ug, 240ug
52	pancreatic		III		rSIFN-co	PR	9	im, qod	9ug, 21ug
56	lymphoma		III		rSIFN-co+ CTx+TCM	PR	6	im, qod + intratumoral injection	21ug, 18 ug, 168ug, 210ug, 252ug, 273ug, 315ug, 180ug, 189ug, 198ug, 207ug, 500ug

Table 17. Patients with No Change (NC) or Stable Disease (SD) up until the date of last count.

[0759]

Patient No.	Cancer	Cell type	Stage	Metastases	Therapies	Response	rSIFN-co Tx Duration (months)	rSIFN-co admiin	Amount of rSIFN-co per dose
27	lung		IIb	lung mets	prior surgery+CTx+RTx, rSIFN-co	NC/SD		im, qod	9ug, 21ug
28	lung		IIb	lung +intrapleural cavity mets	prior surgery+Vivatuxin, rSIFN-co	NC/SD	7	im, qod + nasal spray, tid + inhalation, qd	9ug, 21ug, 200ug
29	lung		IIIa		prior	NC/SD	5.5+	im, qod +	9ug,18ug,

					surgery+radioimmunotherapy, rSIFN-co+radiofrequency ablation (RFA)			nasal spray, tid	21ug
34	lung		IV	multiple mets	rSIFN-co+RTx+TCM	NC/SD	2	im, qod + inhalation, qd	18ug, 200ug
38	uterine papillary serous adenocarcinoma	mixed with clear cell carcinoma	IV		rSIFN-co	NC/SD		im, qod + uterine drip, qd, then once every 5 days	18ug, 200ug
41	colonic carcinoma		IV	liver mets	prior surgery, rSIFN-co	NC/SD	4+	im, qod, intratumor injection	9ug, 21ug, 21 - 25.5ug, 105ug, 168ug, 210ug
49	breast	recurrence after breast surgery	IV		prior surgery+ CTx, rSIFN-co	NC/SD	5	local injection + im, qod	90ug, 21ug., 9ug
53	prostate		IV		prior antiandrogen + hormone + RFA + radioactive seeds, rSIFN-co+RTx	NC/SD		im, qod, intraperitoneal injection	9ug, 21ug, 168ug
57	neuroma	recurrence after surgery	IIIc		Prior surgery + CTx + TCM, rSIFN-co	NC/SD		im, qod + intratumoral	21ug, 84ug
58	poorly differentiated squamous cell carcinoma in right chest		IIIa		prior surgery, rSIFN-co	NC/SD	6	im, qod	9ug, 21ug

Table 18. Patients with Progressive Disease (PD) up until the date of last count.

[0760]

Patient No.	Cancer	Stage	Metastases	Therapies	Response	rSIFN-co Tx Duration (in months)	rSIFN-co admin	Amount of rSIFN-co per dose
25	lung	IIIa		rSIFN-co + RTx	PD	5	im, *qod*	9ug, 21ug
31	lung	IV	bone metastasis	rSIFN-co	PD	3+	im, *qod;* spray	9ug, 13.5ug, 18ug, 20ug/ml, 21ug
33	lung	IIIb		prior sugery, rSIFN-co	PD	1+	im, *qod*; im, twice a week; pleural perfusion	4.5ug, 9ug, 13.5ug, 18ug, 105ug, 126ug, 147ug, 168ug, 189ug, 210ug
40	colon	IV	lung metastasis	prior surgery+CTx+TCM, rSIFN-co+RFA+CTx+RTx	PD		im, *qod*	9ug, 21ug
43	intrahepatic cholangiocarcinoma	IV	liver metastasis	prior sugery+CTx, rSIFN-co+surgery	PD	6	im, *qod*	9ug, 21ug

44	hepatocellular carcinoma	IV	lung metastasis	prior surgery, rSIFN-co	PD	5.5+	im, *qod*	9ug, 18ug, 21ug
46	breast	IIIc	LN metastasis	prior surgery+CTx+RTx, rSIFN-co	PD	4	im, *qod*	18ug
47	breast	IV		prior surgery+CTx, rSIFN-co	PD	7.5+	intrapleural injection; local injection, once a week; im, *qod*	105ug, 147ug, 168ug, 210ug, 273ug, 21ug
50	gastric	IV		prior surgery, rSIFN-co	PD	20.5	im, *qod*; intraperitoneal injection	9ug, 18ug, 15ug, 21ug, 168ug, 189ug, 210ug
55	embryonal rhabdomyosarcoma	IV	metastasis	prior surgery+CTx+RTx, rSIFN-co	PD	13	im, *qod*; lymph node injection, intratumor injection	9ug, 15ug, 18ug, 21ug,168ug

What is claimed is:

1. A method for treating a tumor in a subject, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2.

2. The method of claim 1, wherein the tumor in the subject comprises a metastasized tumor.

3. The method of claim 1 or 2, wherein the subject is an early, medium-term, or advanced cancer patient, optionally, the subject is a medium-term, or advanced cancer patient, further optionally, the subject is an advanced cancer patient.

4. The method of claim 1 or 2, wherein the subject is a stage 0, I, II, III, or IV cancer patient, optionally, the subject is a stage III or stage IV cancer patient.

5. The method of any one of claims 1-4, wherein the tumor is a cancer or a solid tumor that is indicated or appropriate for surgery.

6. The method of any one of claims 1-4, wherein the tumor is a cancer or a solid tumor that is not indicated nor appropriate for surgery.

7. The method of any one of claims 1-5, wherein the tumor is a tumor that is capable of being resected.

8. The method of any one of claims 1-4 and 6, wherein the tumor is a tumor that is not capable of being resected.

9. The method of claim 7 or 8, wherein the tumor is resected by a surgical resection.

10. The method of any one of claims 1-9, wherein the tumor is a solid tumor.

11. The method of claim 10, wherein the solid tumor comprises one or more of: lung cancer, liver cancer, hepatocellular carcinoma (HCC), esophageal cancer, cholangiocarcinoma, gallbladder carcinoma, stomach cancer, abdominal cancer, gastrointestinal cancer, gastric cancer, pancreatic cancer, renal cell carcinoma, renal cancer, bone cancer, breast cancer, ovarian cancer, uterine cancer, cervical cancer, endometrial cancer, colorectal cancer, colon cancer, rectal cancer, bladder cancer, superficial bladder cancer, prostate cancer, adrenal tumors, squamous cell carcinoma, neuroma, malignant neuroma, myoepithelial carcinoma, synovial sarcoma, rhabdomyosarcoma, gastrointestinal interstitial cell tumor, skin cancer, basal cell

carcinoma, malignant melanoma, thyroid cancer, nasopharyngeal carcinoma, hemangioma, epidermoid carcinoma, head and neck cancer, glioma, or Kaposi's sarcoma.

12. The method of claim 11, wherein the solid tumor comprises lung cancer, optionally, the lung cancer comprises small cell lung cancer (SCLC), non small cell lung cancer (NSCLC), or both.

13. The method of any one of claims 1-4, wherein the tumor is a non-solid tumor.

14. The method of claim 13, wherein the non-solid tumor comprises one or more of: leukemia, acute leukemia, chronic leukemia, chronic myelocytic leukemia, acute myelogenous leukemia, chronic myelogenous leukemia, chronic lymphocytic leukemia, acute lymphoblastic leukemia, T-cell leukemia, hairy cell leukemia, polycythemia, myelodysplastic syndrome, multiple myeloma, lymphadenoma, Hodgkin's lymphoma, and Non-Hodgkin's lymphoma.

15. The method of any one of claims 1-14, wherein the recombinant interferon is administered to the subject by at least one of: systemic administration, local administration, and topical administration.

16. The method of any one of claims 1-15, wherein the recombinant interferon is administered to the subject by an administration route, the administration route comprises one or more of: oral, rectal, sublingual, intravenous, intra-arterial, intramuscular, subcutaneous, intra-bone, intracutaneous, intra-articular, intraperitoneal, intrathecal, intracerebral, vaginal, percutaneous, transdermal, epidermal, transmucosal, transocular, pulmonary, nasal, abdominal, intrapleural, intraventricular, pericardial, inhalation, intratumoral, uterine, infiltration, and intravesical administration.

17. The method of any one of claims 1-16, wherein an effective amount of recombinant interferon encoded by the nucleotide sequence of SEQ ID NO: 2 is administered to the subject, optionally, the effective amount is a therapeutically effective amount.

18. The method of any one of claims 1-17, wherein the recombinant interferon is administered to the subject in a single dose in a range of about 2μg to about 2000μg, optionally, the recombinant interferon is administered to the subject in a single dose in

a range of about 4μg to about 1500μg, further optionally, the recombinant interferon is administered to the subject in a single dose in a range of about 9μg to about 1000μg.

19. The method of any one of claims 1-18, wherein the recombinant interferon is administered in one or more treatment cycles, optionally, the more treatment cycles comprises 2, 3, 4, 5, 6, 7, 8, 9, 10 treatment cycles, further optionally, the number of treatment cycles comprises more than 10 treatment cycles.

20. The method of claim 19, wherein the duration of the treatment cycle is at least about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or optionally, the recombinant interferon can be administered for a long time, including over the life time of the subject; or the duration of recombinant interferon treatment can also be about 1 day to about 6 years, about 1 week to about 4 years, about 2 weeks to about 3 years, about 1 month to about 1 year, or about 2 months to about 9 months and the like.

21. The method of claim 19 or 20, wherein the time interval between any two adjacent treatment cycles of the more treatment cycles is at least about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like; or optionally the time interval can be about 2 days to about 6 years, about 4 days to about 3 years, about 1 week to about 1 year, about 2 months to about 9 months, or about 3 months to about 6 months and the like.

22. The method of any one of claims 1-21, wherein the recombinant interferon is administered to the subject as monotherapy.

23. The method of any one of claims 1-21, further comprising at least one other

anti-cancer therapy administered to the subject, optionally, the at least one other anti-cancer therapy is administered to the subject before, simultaneously, and/or after administration of the recombinant interferon.

24. The method of claim 23, wherein the at least one other anti-cancer therapy comprises at least one of: chemotherapy, radiotherapy, surgical therapy, interventional therapy, biotherapy, gene therapy, ablation therapy, immunotherapy, targeted therapy, and traditional Chinese medicine therapy.

25. The method of claims 24, wherein the at least one other anti-cancer therapy comprises at least one of: chemotherapy, radiotherapy, surgical therapy, targeted therapy, and biotherapy.

26. The method of claim 25, wherein the at least one other anti-cancer therapy comprises at least one of: chemotherapy and radiotherapy.

27. The method of any one of claims 24-26, wherein the chemotherapy is administered as first-line chemotherapy, optionally, one or more chemotherapeutic drugs used in the first-line chemotherapy comprise platinum compounds, such as Cisplatin.

28. The method of any one of claims 24-27, wherein the targeted therapy comprises at least one of: Gefitinib, Erlotinib, and recombinant human endostatin.

29. The method of any one of claims 1-28, wherein the therapies eliminate the tumor or reduce the size of the tumor as compared to the tumor before treatment.

30. The method of claim 29, wherein the reduced size of the tumor converts the tumor to a resectable tumor.

31. The method of claim 30, wherein the tumor is indicated for a surgical resection.

32. The method of any one of claims 1-28, wherein the tumor, such as cancer or solid tumor, that is not earlier indicated nor appropriate for surgery becomes one that is indicated or appropriate for surgery.

33. The method of claim 32, further comprising surgery to resect the tumor.

34. The method of any one of claims 30-31 and 33, further comprising administering to the subject the recombinant interferon after resecting the tumor, to

prevent tumor recurrence and/or metastasis, or to prolong or maintain a tumor-free status, optionally, a prophylactically effective amount of the recombinant interferon is administered to the subject to prevent tumor recurrence and/or metastasis, and/or to prolong or maintain a tumor-free status.

35. A method for treating tumor in a subject, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2, and at least one other anti-cancer therapy, wherein the at least one other anti-cancer therapy is administered to the subject before, simultaneously, and/or after administration of the recombinant interferon, and wherein the tumor is a cancer or solid tumor that is not indicated nor appropriate for surgery, or the tumor is a solid tumor that cannot be resected, and the combination of the recombinant interferon and the at least one other anti-cancer therapy eliminate the tumor or reduce the size of the tumor compared to the tumor before treatment.

36. The method of claims 35, wherein the subject is a medium-term, advanced cancer patient, or stage III or stage IV cancer patient, optionally, the subject is an advanced, or stage III or stage IV cancer patient.

37. The method of any one of claims 1-29 and 35-36, wherein the therapies are the non-surgical therapies.

38. A method for preventing tumor recurrence and/or metastasis or prolonging or maintaining a tumor-free status in a subject with a tumor after at least one anti-cancer therapy, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2.

39. The method of claim 38, wherein the tumor in the subject comprises a metastasized tumor.

40. The method of claim 38 or 39, wherein the subject is an early, medium-term, or advanced cancer patient.

41. The method of claim 38 or 39, wherein the subject is a stage 0, I, II, III, or IV cancer patient.

42. The method of any one of claims 38-41, wherein the tumor is a cancer or solid tumor that is indicated or appropriate for surgery.

43. The method of any one of claims 38-41, wherein the tumor is a cancer or solid tumor that is not indicated nor appropriate for surgery.

44. The method of any one of claims 38-41, wherein the tumor is a tumor that is capable of being resected.

45. The method of any one of claims 38-41, wherein the tumor is a tumor that is not capable of being resected.

46. The method of claim 44 or 45, wherein the tumor is resected by a surgical resection.

47. The method of any one of claims 38-46, wherein the tumor is a solid tumor.

48. The method of claims 47, wherein the solid tumor comprises one or more of: lung cancer, liver cancer, hepatocellular carcinoma (HCC), esophageal cancer, cholangiocarcinoma, gallbladder carcinoma, stomach cancer, abdominal cancer, gastrointestinal cancer, gastric cancer, pancreatic cancer, renal cell carcinoma, renal cancer, bone cancer, breast cancer, ovarian cancer, uterine cancer, cervical cancer, endometrial cancer, colorectal cancer, colon cancer, rectal cancer, bladder cancer, superficial bladder cancer, prostate cancer, adrenal tumors, squamous cell carcinoma, neuroma, malignant neuroma, myoepithelial carcinoma, synovial sarcoma, rhabdomyosarcoma, gastrointestinal interstitial cell tumor, skin cancer, basal cell carcinoma, malignant melanoma, thyroid cancer, nasopharyngeal carcinoma, hemangioma, epidermoid carcinoma, head and neck cancer, glioma, or Kaposi's sarcoma.

49. The method of claim 48, wherein the solid tumor comprises lung cancer, optionally, the lung cancer comprises small cell lung cancer (SCLC), non small cell lung cancer (NSCLC), or both.

50. The method of any one of claims 38-41, wherein the tumor comprises a non-solid tumor.

51. The method of claim 50, wherein the non-solid tumor comprises one or more of: leukemia, acute leukemia, chronic leukemia, chronic myelocytic leukemia, acute myelogenous leukemia, chronic myelogenous leukemia, chronic lymphocytic leukemia, acute lymphoblastic leukemia, T-cell leukemia, hairy cell leukemia,

polycythemia, myelodysplastic syndrome, multiple myeloma, lymphadenoma, Hodgkin's lymphoma, and Non-Hodgkin's lymphoma.

52. The method of any one of claims 38-51, wherein the recombinant interferon is administered to the subject by at least one of: systemic administration, local administration, and topical administration.

53. The method of any one of claims 38-52, wherein the recombinant interferon is administered to the subject by an administration route, the administration route comprises one or more of: oral, rectal, sublingual, intravenous, intra-arterial, intramuscular, subcutaneous, intra-bone, intracutaneous, intra-articular, intraperitoneal, intrathecal, intracerebral, vaginal, percutaneous, transdermal, epidermal, transmucosal, transocular, pulmonary, nasal, abdominal, intrapleural, intraventricular, pericardial, inhalation, intratumoral, uterine, infiltration, and intravesical administration.

54. The method of any one of claims 38-53, wherein an effective amount of recombinant interferon encoded by the nucleotide sequence of SEQ ID NO: 2 is administered to the subject, optionally, the effective amount is a prophylactically effective amount.

55. The method of any one of claims 38-54, wherein the recombinant interferon is administered to the subject in a single dose in the range of about 2μg to about 2000μg, optionally, the recombinant interferon is administered to the subject in a single dose in the range of about 4μg to about 1500μg, more optionally, the recombinant interferon is administered to the subject in a single dose in the range of about 9μg to about 1000μg.

56. The method of any one of claims 38-55, wherein the recombinant interferon is administered in one or more prevention cycles, optionally, the more prevention cycles comprises 2, 3, 4, 5, 6, 7, 8, 9, or 10 prevention cycles, or optionally, more than 10 prevention cycles.

57. The method of claim 56, wherein the duration of each prevention cycle is at least about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months,

about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject; or the duration can also be about 1 day to about 6 years, about 1 week to about 4 years, about 2 weeks to about 3 years, about 1 month to about 1 year, or about 2 months to about 9 months and the like.

58. The method of claim 56 or 57, wherein the time interval between any two adjacent prevention cycles of the more prevention cycles is at least about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like; or the time interval can also be about 2 days to about 6 years, about 4 days to about 3 years, about 1 week to about 1 year, about 2 months to about 9 months, or about 3 months to about 6 months and the like.

59. The method of any one of claims 38-58, wherein the at least one anti-cancer therapy comprises at least one of: chemotherapy, radiotherapy, surgical therapy, interventional therapy, biotherapy, gene therapy, ablation therapy, immunotherapy, targeted therapy, and traditional Chinese medicine therapy, optionally, the at least one anti-cancer therapy comprises at least one of: chemotherapy, radiotherapy, surgical therapy, and biotherapy.

60. The method of claim 59, wherein the at least one anti-cancer therapy comprises surgical therapy.

61. The method of claim 60, wherein the recombinant interferon is administered to the operative site of the surgical therapy.

62. The method of claim 61, wherein the recombinant interferon is administered to the operative site by topical or local administration.

63. The method of claim 61 or 62, wherein the recombinant interferon is

administered to the operative site by an administration route, the administration route comprises one or more of: infiltration administration, intrapleural administration, abdominal administration, pericardial administration, uterine administration, intravesical administration, intratumoral administration, pulmonary administration, nasal administration, percutaneous administration, transdermal administration, epidermal administration, and transmucosal administration.

64. The method of claim 63, wherein the intrapleural administration, abdominal administration, pericardial administration, uterine administration, or intravesical administration comprises intrapleural perfusion administration, abdominal perfusion administration, pericardial perfusion administration, uterine perfusion administration, or intravesical perfusion administration, respectively.

65. The method of claim 63, wherein the intratumoral administration comprises intratumoral injection.

66. The method of claim 63, wherein the pulmonary administration or nasal administration comprises pulmonary inhalation administration or nasal inhalation administration, respectively.

67. The method of claim 63, wherein the percutaneous administration, transdermal administration, epidermal administration, or transmucosal administration comprises percutaneous spray administration, transdermal spray administration, epidermal spray administration, or transmucosal spray administration, respectively.

68. The method of any one of claims 62-67, wherein the recombinant interferon is further administered to the subject by systemic administration before, simultaneously, and/or after the topical or local administration of the recombinant interferon.

69. The method of claim 68, wherein the systemic administration comprises at least one of: subcutaneous and intramuscular administration.

70. The method of any one of claims 38-69, wherein the recombinant interferon is administered to the subject as monotherapy.

71. A non-surgical method for eliminating a tumor in a subject or reducing the size of a tumor in a subject, comprising administering to the subject a recombinant

interferon encoded by SEQ ID NO: 2.

72. The method of claim 71, wherein the tumor is a cancer or a solid tumor that is indicated or appropriate for surgery.

73. The method of claim 71, wherein the tumor is a cancer or a solid tumor that is not indicated nor appropriate for surgery.

74. The method of claim 71, wherein the tumor is a tumor that is capable of being resected.

75. The method of claim 71, wherein the tumor is a tumor that is not capable of being resected.

76. The method of claim 74 or 75, wherein the tumor is resected by a surgical resection.

77. The method of any one of claims 71-76, wherein the subject is an early, medium-term, or advanced cancer patient, optionally, the subject is a medium-term, or advanced cancer patient, or further optionally, the subject is an advanced cancer patient.

78. The method of any one of claims 71-76, wherein the subject is a stage 0, I, II, III, or IV cancer patient, optionally, the subject is a stage III or IV cancer patient.

79. The method of any one of claims 71-78, wherein the subject is a medium-term, or advanced cancer patient, or a stage III or stage IV cancer patient, optionally, the subject is an advanced, or stage III or stage IV cancer patient.

80. The method of any one of claims 71-79, wherein the tumor is a solid tumor.

81. The method of claim 80, wherein the solid tumor comprises one or more of: lung cancer, liver cancer, hepatocellular carcinoma (HCC), esophageal cancer, cholangiocarcinoma, gallbladder carcinoma, stomach cancer, abdominal cancer, gastrointestinal cancer, gastric cancer, pancreatic cancer, renal cell carcinoma, renal cancer, bone cancer, breast cancer, ovarian cancer, uterine cancer, cervical cancer, endometrial cancer, colorectal cancer, colon cancer, rectal cancer, bladder cancer, superficial bladder cancer, prostate cancer, adrenal tumors, squamous cell carcinoma, neuroma, malignant neuroma, myoepithelial carcinoma, synovial sarcoma, rhabdomyosarcoma, gastrointestinal interstitial cell tumor, skin cancer, basal cell

carcinoma, malignant melanoma, thyroid cancer, nasopharyngeal carcinoma, hemangioma, epidermoid carcinoma, head and neck cancer, glioma, or Kaposi's sarcoma.

82. The method of claim 81, wherein the solid tumor comprises lung cancer, optionally, the lung cancer comprises small cell lung cancer (SCLC), non small cell lung cancer (NSCLC), or both.

83. The method of any one of claims 71-82, wherein the recombinant interferon is administered to the subject by at least one of: systemic administration, local administration, and topical administration, optionally, the recombinant interferon is administered to the subject by topical or local administration, further optionally, the recombinant interferon is administered to the subject by local administration.

84. The method of any one of claims 71-83, wherein the recombinant interferon is administered to the subject by an administration route, the administration route comprises one or more of: infiltration administration, intrapleural administration, abdominal administration, pericardial administration, uterine administration, intravesical administration, intratumoral administration, pulmonary administration, nasal administration, percutaneous administration, transdermal administration, epidermal administration, and transmucosal administration.

85. The method of claim 84, wherein the intratumoral administration comprises intratumoral injection.

86. The method of claim 85, wherein the recombinant interferon is administered in an amount in a range of: about 60μg to about 600μg, optionally about 60μg to about 500μg, further optionally, about 80μg to about 400μg, still optionally about 100μg to about 250μg, by one intratumoral injection.

87. The method of claim 85 or 86, wherein the recombinant interferon is administered by intratumoral injection once every about 1 day to about 10 days, optionally, every about 1 day to about 7 days, such as every about 1, 2, 3, 4, 5, 6, or 7 days.

88. The method of any one of claims 84-87, wherein the protocol of intratumoral administration is as follows: the recombinant interferon is administered by

intratumoral injection once every about 1 day for about 4 to about 8 times, and then the recombinant interferon is administered by intratumoral injection once every about 3 days to about 5 days for about 4 to about 8 times, and then the recombinant interferon is administered by intratumoral injection once every about 7 days, the intratumoral administration is stopped when the tumor disappears or becomes too small to conduct the intratumoral injection.

89. The method of claim 84, wherein the intrapleural administration, abdominal administration, pericardial administration, uterine administration, or intravesical administration comprises intrapleural perfusion administration, abdominal perfusion administration, pericardial perfusion administration, uterine perfusion administration, or intravesical perfusion administration, respectively.

90. The method of claim 84, wherein the pulmonary administration, or nasal administration comprises pulmonary inhalation administration, or nasal inhalation administration, respectively.

91. The method of claim 84, wherein the percutaneous administration, transdermal administration, epidermal administration, or transmucosal administration comprises percutaneous spray administration, transdermal spray administration, epidermal spray administration, or transmucosal spray administration, respectively.

92. The method of any one of claims 83-91, wherein the recombinant interferon is further administered to the subject by systemic administration, and/or at least one other therapeutic drug is administered to the subject by topical, local and/or systemic administration before, simultaneously, and/or after the topical or local administration of the recombinant interferon.

93. The method of claims 92, wherein the recombinant interferon is further administered to the subject by systemic administration, and/or at least one other therapeutic drug is administered to the subject by topical, local and/or systemic administration simultaneously and/or after the topical or local administration of the recombinant interferon.

94. The method of claim 92 or 93, wherein the at least one other therapeutic drug comprises at least one antitumor drug.

95. The method of claim 94, wherein the at least one antitumor drug comprises one or more chemotherapeutic drugs, targeted drugs, and/or biological drugs.

96. The method of claim 95, wherein the one or more chemotherapeutic drugs comprise platinum compounds, such as Cisplatin.

97. The method of claim 95, wherein one or more targeted drugs comprise Gefitinib, Erlotinib, and/or recombinant human endostatin.

98. A method for eliminating or reducing the pleural effusion, ascites, and/or pericardial effusion in a subject with tumor, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2.

99. The method of claim 98, wherein the tumor is a cancer or a solid tumor that is indicated or is appropriate for surgery.

100. The method of claim 98, wherein the tumor is a cancer or a solid tumor that is not indicated nor appropriate for surgery.

101. The method of claim 98, wherein the tumor is a tumor that is capable of being resected.

102. The method of claim 98, wherein the tumor is a tumor that is not capable of being resected.

103. The method of claim 101 or 102, wherein the tumor is resected by a surgical resection.

104. The method of any one of claims 98-103, wherein the subject is an early, medium-term, or advanced cancer patient, optionally, the subject is a medium-term, or advanced cancer patient, or further optionally, the subject is an advanced cancer patient.

105. The method of any one of claims 98-103, wherein the subject is a stage 0, I, II, III, or IV cancer patient, optionally, the subject is a stage III or stage IV cancer patient.

106. The method of any one of claims 98-105, wherein the subject is a medium-term, or advanced cancer patient, or stage III or stage IV cancer patient, optionally, the subject is an advanced, or stage III or stage IV cancer patient.

107. The method of any one of claims 98-106, wherein the tumor is a solid

tumor.

108. The method of claim 107, wherein the solid tumor comprises one or more of: lung cancer, liver cancer, hepatocellular carcinoma (HCC), esophageal cancer, cholangiocarcinoma, gallbladder carcinoma, stomach cancer, abdominal cancer, gastrointestinal cancer, gastric cancer, pancreatic cancer, renal cell carcinoma, renal cancer, bone cancer, breast cancer, ovarian cancer, uterine cancer, cervical cancer, endometrial cancer, colorectal cancer, colon cancer, rectal cancer, bladder cancer, superficial bladder cancer, prostate cancer, adrenal tumors, squamous cell carcinoma, neuroma, malignant neuroma, myoepithelial carcinoma, synovial sarcoma, rhabdomyosarcoma, gastrointestinal interstitial cell tumor, skin cancer, basal cell carcinoma, malignant melanoma, thyroid cancer, nasopharyngeal carcinoma, hemangioma, epidermoid carcinoma, head and neck cancer, glioma, or Kaposi's sarcoma.

109. The method of claim 108, wherein the solid tumor comprises lung cancer, optionally, the lung cancer comprises small cell lung cancer (SCLC), non small cell lung cancer (NSCLC), or both.

110. The method of any one of claims 98-109, wherein the pleural effusion is a malignant pleural effusion, the ascites is a malignant ascites, and/or the pericardial effusion is a malignant pericardial effusion.

111. The method of any one of claims 98-110, wherein the recombinant interferon is administered to the subject by at least one of: systemic administration, local administration, and topical administration, optionally, by topical and local administration, further optionally, by local administration.

112. The method of any one of claims 98-111, wherein the recombinant interferon is administered to the subject by an administration route, the administration route comprises one or more of: infiltration administration, intrapleural administration, abdominal administration, and pericardial administration.

113. The method of any one of claims 98-112, wherein the administration is conducted by perfusion.

114. The method of any one of claims 111-113, wherein the recombinant

interferon is administered in an amount in a range of about 30μg to about 2000μg, optionally, about 100μg to about 1500μg, further optionally, about 150μg to about 1000μg, still further optionally, about 200μg to about 800μg, still optionally, about 200μg to about 400μg by one topical or local administration.

115. The method of any one of claims 111-114, wherein the recombinant interferon is administered by topical or local administration once every about 1 to about 10 days, optionally every about 1 to about 7 days, such as every about 1, 2, 3, 4, 5, 6, or 7 days.

116. The method of any one of claims 111-115, wherein the recombinant interferon is further administered to the subject by systemic administration, and at least one other therapeutic drug is administered to the subject by topical, local and/or systemic administration before, simultaneously, and/or after the topical or local administration of the recombinant interferon.

117. The method of claim 116, wherein the recombinant interferon is further administered to the subject by systemic administration, and at least one other therapeutic drug is administered to the subject by topical, local and/or systemic administration simultaneously and/or after the topical or local administration of the recombinant interferon.

118. The method of claim 116 or 117, wherein the at least one other therapeutic drug comprises an antitumor drug.

119. The method of claim 118, wherein the antitumor drug comprises at least one of: chemotherapeutic drug, targeted drug, and biological drug.

120. The method of claim 119, wherein the at least one chemotherapeutic drug comprises at least one platinum compounds, such as Cisplatin.

121. The method of claim 119, wherein at least one targeted drug comprises at least one of: Gefitinib, Erlotinib, and recombinant human endostatin.

122. The method of any one of claims 98-121, wherein the therapies eliminate the tumor or reduce the size of the tumor compared to the tumor before treatment.

123. The method of any one of claims 98-122, wherein the therapies are the non-surgical therapies.

124. A method for treating tumor in a subject, comprising topically or locally administering to the tumor lesions of the subject a recombinant interferon encoded by SEQ ID NO: 2.

125. The method of claim 124, wherein the tumor lesions comprise metastatic tumor lesions.

126. A method for eliminating or reducing metastatic tumor lesions in a subject, comprising topically or locally administering to the metastatic tumor lesions of the subject a recombinant interferon encoded by SEQ ID NO: 2.

127. The method of any one of claims 124-126, wherein the tumor lesions comprise at least one of: bone lesions, muscular lesions, subcutaneous tissue lesions, prostatic lesions and lymph node lesions, and the tumor metastatic lesions comprise at least one of: bone metastatic lesions, muscular metastatic lesions, subcutaneous tissue metastatic lesions, prostatic metastatic lesions, and lymph node metastatic lesions, optionally, the tumor metastatic lesions comprise bone metastatic lesions.

128. The method of any one of claims 124-127, wherein the subject is a medium-term, advanced, or stage III or stage IV cancer patient, optionally, the subject is an advanced, or stage III or stage IV cancer patient.

129. The method of any one of claims 124-127, wherein the tumor or the metastatic tumor lesions comprise a cancer or a solid tumor that is not indicated nor appropriate for surgery.

130. The method of any one of claims 124-129, wherein the topical or local administration comprises at least one of: infiltration administration, percutaneous administration, transdermal administration, epidermal administration and transmucosal administration, optionally, the topical and local administration comprises transdermal administration, or infiltration administration.

131. The method of claim 130, wherein the infiltration administration comprises one or more of: percutaneous infiltration administration, epidermal infiltration administration, transdermal infiltration administration, and transmucosal infiltration administration.

132. The method of claim 130, wherein the percutaneous administration,

transdermal administration, epidermal administration, or transmucosal administration comprises percutaneous spray administration, transdermal spray administration, epidermal spray administration, or transmucosal spray administration, respectively.

133. The method of any one of claims 124-132, wherein the recombinant interferon is administered in an amount in a range of about 2μg to about 2000μg, optionally about 4μg to about 1500μg, further optionally about 9μg to about 1000μg by one topical or local administration.

134. The method of any one of claims 124-133, wherein the recombinant interferon is administered to the subject by topical or local administration about 1, 2, 3, 4, 5, 6, 7, 8, or more times per day, or the recombinant interferon is administered to the subject by topical or local administration once at the time interval of every about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or 21 days, every month, every 2 months, or a longer time.

135. The method of any one of claims 130-134, wherein the recombinant interferon is administered in an amount in a range of about 6μg to about 100μg, optionally about 10μg to about 40μg, further optionally about 20μg to about 40μg by one spray administration when the topical or local administration is conducted by spray administration.

136. The method of claim 135, wherein the recombinant interferon is administered by spray administration about 1 to about 6 times, such as about 1, 2, 3, 4, 5, or 6 times, per day.

137. The method of any one of claims 124-136, wherein the recombinant interferon and/or one or more other therapeutic drugs are administered to the subject by systemic administration before, simultaneously, and/or after the topical or local administration of the recombinant interferon.

138. The method of claim 137, wherein the systemic administration comprises subcutaneous and/or intramuscular administration.

139. The method of claim 138, wherein the subcutaneous administration comprises subcutaneous injection.

140. The method of claim 138, wherein the intramuscular administration

comprises intramuscular injection.

141. The method of any one of claims 138-140, wherein the recombinant interferon is administered one or more times by subcutaneous administration and/or intramuscular administration at an induction dose in the range of about 2μg to about 10μg each time, optionally, about 4μg to about 10μg each time, more optionally about 4.5μg to about 9μg each time, such as about 4.5μg each time or about 9μg each time, and then the recombinant interferon is administered more times by subcutaneous administration and/or intramuscular administration at a therapeutic dose of about 10μg to about 70μg each time, optionally about 12μg to about 50μg each time, more optionally about 12μg to about 30μg each time.

142. The method of claim 141, wherein the time interval between administration of induction dose and administration of therapeutic dose is about 1 day to about 1 month, optionally about 1 day to about 1 week, further optionally about 1 day to about 3 days, comprising such as about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, or about 1 month.

143. The method of claim 141 or 142, wherein the recombinant interferon is administered once every about 1 day to about 10 days, optionally every about 1 day to about 7 days, further optionally every about 1 to about 2 days, comprising such as every about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 days when the recombinant interferon is administered more times at an induction dose.

144. The method of any one of claims 141-143, wherein the recombinant interferon is administered at a therapeutic dose once every about 1 day to about 10 days, optionally every about 1 day to about 7 days, further optionally every about 1 to about 2 days, comprising such as every about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 days.

145. The method of any one of claims 141-144, wherein the duration of administration of induction dose and therapeutic dose is at least: about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years,

about 4 years, about 5 years, or about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject.

146. The method of any one of claims 124-145, wherein the recombinant interferon is administered to the subject as monotherapy.

147. The method of any one of claims 124-145, further comprising at least one other anti-cancer therapy administered to the subject, optionally, the at least one other anti-cancer therapy is administered to the subject before, simultaneously, and/or after administration of the recombinant interferon.

148. The method of claim 147, wherein the at least one other anti-cancer therapy comprises one or more of: chemotherapy, radiotherapy, surgical therapy, interventional therapy, biotherapy, gene therapy, ablation therapy, immunotherapy, targeted therapy, and traditional Chinese medicine therapy.

149. The method of any one of claims 124-148, wherein the recombinant interferon therapy and/or at least one other anti-cancer therapy eliminate the tumor or tumor metastatic lesions or reduce the size of the tumor or tumor metastatic lesions compared to the tumor or tumor metastatic lesions before treatment.

150. A method for eliminating or reducing the bone metastatic lesions of tumor in a subject, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2 by topical or local administration, wherein the topical or local administration comprises transdermal administration and/or infiltration administration, optionally, the recombinant interferon is administered to the bone metastatic lesions of tumor of the subject.

151. A method for eliminating or reducing the bone lesions of tumor such as bone metastatic lesions of tumor, muscular lesions of tumor such as muscular metastatic lesions of tumor, subcutaneous tissue lesions of tumor such as subcutaneous tissue metastatic lesions of tumor, prostatic lesions of tumor such as prostatic metastatic lesions of tumor, and/or lymph node lesions of tumor such as lymph node metastatic lesions of tumor in a subject, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2 by any administration

route through the skin, so that eliminating or reducing the bone lesions of tumor such as bone metastatic lesions of tumor, muscular lesions of tumor such as muscular metastatic lesions of tumor, subcutaneous tissue lesions of tumor such as subcutaneous tissue metastatic lesions of tumor, prostatic lesions of tumor such as prostatic metastatic lesions of tumor, and/or lymph node lesions of tumor such as lymph node metastatic lesions of tumor, optionally, the recombinant interferon is administered to the metastatic lesions of tumor of the subject.

152. The method of any one of claims 124-151, wherein the therapies are non-surgical therapies.

153. A method for treating lung cancer in a subject, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2.

154. The method of claim 153, wherein the lung cancer comprises small cell lung cancer (SCLC), non small cell lung cancer (NSCLC), or both.

155. The method of claim 153 or 154, wherein the lung cancer in the subject comprises a metastasized tumor.

156. The method of any one of claims 153-155, wherein the subject is an early, medium-term, or advanced cancer patient, optionally, the subject is a medium-term, or advanced cancer patient, further optionally, the subject is an advanced cancer patient.

157. The method of any one of claims 153-155, wherein the subject is a stage 0, I, II, III, or IV cancer patient, optionally, the subject is an stage III or stage IV cancer patient.

158. The method of any one of claims 153-157, wherein the lung cancer comprises a lung cancer that is indicated or appropriate for surgery.

159. The method of any one of claims 153-157, wherein the lung cancer comprises a lung cancer that is not indicated nor appropriate for surgery.

160. The method of any one of claims 153-157, wherein the lung cancer comprises a lung cancer that is capable of being resected.

161. The method of any one of claims 153-157, wherein the lung cancer comprises a lung cancer that is not capable of being resected.

162. The method of claim 160 or 161, wherein the lung cancer is resected by a

surgical resection.

163. The method of any one of claims 153-162, wherein an effective amount of recombinant interferon encoded by the nucleotide sequence of SEQ ID NO: 2 is administered to the subject, optionally, the effective amount is a therapeutically effective amount.

164. The method of any one of claims 153-163, wherein the recombinant interferon is administered to the subject by at least one of: systemic administration, topical administration, and local administration.

165. The method of any one of claims 153-164, wherein the recombinant interferon is administered to the subject by an administration route, the administration route comprises one or more of: oral, rectal, sublingual, intravenous, intra-arterial, intramuscular, subcutaneous, intra-bone, intracutaneous, intra-articular, intraperitoneal, intrathecal, intracerebral, vaginal, percutaneous, transdermal, epidermal, transmucosal, transocular, pulmonary, nasal, abdominal, intrapleural, intraventricular, pericardial, inhalation, intratumoral, uterine, infiltration, and intravesical administration.

166. The method of any one of claims 153-165, wherein the recombinant interferon is administered to the subject by subcutaneous administration and/or intramuscular administration.

167. The method of claim 166, wherein the subcutaneous administration comprises subcutaneous injection.

168. The method of claim 166, wherein the intramuscular administration comprises intramuscular injection.

169. The method of any one of claims 166-168, wherein the recombinant interferon is administered in an amount in a range of about 2μg to about 70μg by one subcutaneous and/or intramuscular administration.

170. The method of claim 169, wherein the recombinant interferon is administered in an amount in a range of about 4μg to about 50μg by one subcutaneous and/or intramuscular administration.

171. The method of claim 170, wherein the recombinant interferon is administered in an amount in a range of about 4μg to about 30μg by one subcutaneous

and/or intramuscular administration.

172. The method of any one of claims 166-171, wherein the recombinant interferon is administered by subcutaneous and/or intramuscular administration once every about 1 to about 7 days.

173. The method of claim 172, wherein the recombinant interferon is administered by subcutaneous and/or intramuscular administration once every about 1 to about 2 days.

174. The method of any one of claims 153-173, wherein the recombinant interferon is administered to the subject by inhalation administration.

175. The method of claim 174, wherein the recombinant interferon is administered by pulmonary and/or nasal inhalation.

176. The method of claim 174 or 175, wherein the inhalation administration comprises dry powder inhalation and/or aerosol inhalation.

177. The method of any one of claims 174-176, wherein the recombinant interferon is administered in an amount in a range of about 100μg to about 2000μg, optionally about 100μg to about 1500μg by one inhalation administration.

178. The method of claim 177, wherein the recombinant interferon is administered in an amount in a range of about 150μg to about 800μg by one inhalation administration.

179. The method of claim 178, wherein the recombinant interferon is administered in an amount in a range of about 200μg to about 600μg by one inhalation administration.

180. The method of any one of claims 174-179, wherein the recombinant interferon is administered by inhalation administration once every about 1 to about 3 days.

181. The method of claim 180, wherein the recombinant interferon is administered by inhalation administration once every about 1 day.

182. The method of any one of claims 153-181, wherein the subject has the pleural effusion, ascites, and/or pericardial effusion.

183. The method of claim 182, wherein the pleural effusion comprises a

malignant pleural effusion, the ascites comprises a malignant ascites, and/or the pericardial effusion comprises a malignant pericardial effusion.

184. The method of claim 182 or 183, wherein the recombinant interferon is administered to the subject by intrapleural administration, abdominal administration, and/or pericardial administration.

185. The method of claim 184, wherein the intrapleural administration comprises intrapleural perfusion.

186. The method of claim 184, wherein the abdominal administration comprises abdominal perfusion.

187. The method of claim 184, wherein the pericardial administration comprises pericardial perfusion.

188. The method of any one of claims 184-187, wherein the recombinant interferon is administered in an amount in a range of about 30μg to about 2000μg, optionally about 100μg to about 1500μg, further optionally about 150μg to about 1000μg, still optionally about 200μg to about 800μg by one intrapleural, abdominal, and/or pericardial administration.

189. The method of claim 188, wherein the recombinant interferon is administered in an amount in a range of about 200μg to about 400μg by one intrapleural, abdominal, and/or pericardial administration.

190. The method of any one of claims 184-189, wherein the recombinant interferon is administered by intrapleural, abdominal, and/or pericardial administration once every about 1 to about 10 days, optionally every about 1 to about 7 days, such as every about 1, 2, 3, 4, 5, 6, or 7 days.

191. The method of any one of claims 153-165, wherein the recombinant interferon is administered to the subject by intratumoral administration.

192. The method of claim 191, wherein the intratumoral administration comprises intratumoral injection.

193. The method of claim 191 or 192, wherein the recombinant interferon is administered in an amount in a range of about 60μg to about 600μg, optionally about 60μg to about 500μg by one intratumoral administration.

194. The method of claim 193, wherein the recombinant interferon is administered in an amount in a range of about 80μg to about 400μg by one intratumoral administration.

195. The method of claim 194, wherein the recombinant interferon is administered in an amount in a range of about 100μg to about 250μg by one intratumoral administration.

196. The method of any one of claims 191-195, wherein the recombinant interferon is administered by intratumoral administration once every about 1 day to about 10 days, optionally every about 1 day to about 7 days such as every about 1, 2, 3, 4, 5, 6, or 7 days.

197. The method of any one of claims 191-196, wherein the protocol of intratumoral administration is as follow: the recombinant interferon is administered by intratumoral injection once every about 1 day for about 4 to about 8 times, and then the recombinant interferon is administered by intratumoral injection once every about 3 days to about 5 days for about 4 to about 8 times, and then the recombinant interferon is administered by intratumoral injection once every about 7 days, the intratumoral administration is stopped when the tumor disappears or becomes too small to conduct the intratumoral injection.

198. The method of any one of claims 153-197, wherein the lung cancer in the subject comprises tumor metastasis in at least one of: skin, mucosa, superficial lymph nodes, and subcutaneous tissue.

199. The method of claim 198, wherein the recombinant interferon is administered to the subject by spray administration.

200. The method of claim 199, wherein the spray administration comprises at least one of: percutaneous spray administration, transdermal spray administration, epidermal spray administration, and transmucosal spray administration.

201. The method of claim 199 or 200, wherein the recombinant interferon is administered in an amount in a range of about 6μg to about 100μg by one spray administration.

202. The method of claim 201, wherein the recombinant interferon is

administered in an amount in a range of about 10μg to about 40μg, optionally about 20μg to about 40μg by one spray administration.

203. The method of any one of claims 199-202, wherein the recombinant interferon is administered by spray administration about 1 to about 6 times such as about 1, 2, 3, 4, 5, or 6 times per day.

204. The method of any one of claims 153-203, wherein the recombinant interferon is administered to the subject by an administration route, the administration route comprises at least one of: subcutaneous administration, intramuscular administration, inhalation administration, infiltration administration, intrapleural administration, abdominal administration, pericardial administration, intratumoral administration, and spray administration.

205. The method of any one of claims 153-204, wherein the recombinant interferon is administered to the subject as monotherapy.

206. The method of any one of claims 153-204, further comprising at least one other anti-cancer therapy administered to the subject, optionally, the at least one other anti-cancer therapy is administered to the subject before, simultaneously, and/or after administration of the recombinant interferon.

207. The method of claim 206, wherein the at least one other anti-cancer therapy comprises at least one of: chemotherapy, radiotherapy, surgical therapy, interventional therapy, biotherapy, gene therapy, ablation therapy, immunotherapy, targeted therapy, and traditional Chinese medicine therapy.

208. The method of claim 207, wherein the at least one other anti-cancer therapy comprises chemotherapy.

209. The method of claim 208, wherein the chemotherapy is the first-line chemotherapy.

210. The method of claim 209, wherein at least one chemotherapeutic drugs used for the first-line chemotherapy comprise platinum compounds, such as Cisplatin.

211. The method of claim 207, wherein the at least one other anti-cancer therapy comprises radiotherapy.

212. The method of claim 211, wherein the radiotherapy comprises head gamma

knife therapy when the lung cancer metastasizes to brain.

213. The method of claim 207, wherein the at least one other anti-cancer therapy comprises surgical therapy.

214. The method of claim 207, wherein the at least one other anti-cancer therapy comprises targeted therapy.

215. The method of claim 214, wherein the targeted therapy comprises administering Gefitinib, Erlotinib, and/or recombinant human endostatin.

216. The method of claim 207, wherein the at least one other anti-cancer therapy comprises biotherapy.

217. The method of any one of claims 153-216, wherein the recombinant interferon is administered in at least one treatment cycle, optionally, the at least one treatment cycle comprises 2, 3, 4, 5, 6, 7, 8, 9, or 10 treatment cycles, or optionally, more than 10 treatment cycles.

218. The method of claim 217, wherein the duration of the treatment cycle is at least about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject; or the duration can also be about 1 day to about 6 years, about 1 week to about 4 years, about 2 weeks to about 3 years, about 1 month to about 1 year, or about 2 months to about 9 months and the like.

219. The method of claim 217 or 218, wherein the time interval between any two adjacent treatment cycles of the more treatment cycles is at least about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years,

about 5 years, or about 6 years and the like; or the time interval can also be about 2 days to about 6 years, about 4 days to about 3 years, about 1 week to about 1 year, about 2 months to about 9 months, or about 3 months to about 6 months and the like.

220. The method of any one of claims 153-219, wherein the therapies eliminate the tumor of the lung or reduce the size of the tumor of the lung compared to the tumor size before treatment.

221. A method for treating lung cancer in a subject, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2 and one or more chemotherapeutic drugs in two or more treatment cycles, and then administering to the subject a recombinant interferon encoded by SEQ ID NO: 2 and one or more targeted drugs in one or more treatment cycles.

222. The method of claim 221, wherein the therapies eliminate the tumor of the lung or reduce the size of the tumor of the lung compared to the tumor size before treatment.

223. The method of claim 221 or 222, wherein the one or more chemotherapeutic drugs comprise platinum compounds, such as Cisplatin.

224. The method of any one of claims 221-223, wherein the one or more targeted drugs comprise Gefitinib, Erlotinib, and/or recombinant human endostatin.

225. The method of any one of claims 221-224, wherein an effective amount of recombinant interferon, encoded by the nucleotide sequence of SEQ ID NO: 2, is administered to the subject, optionally, the effective amount is a therapeutically effective amount.

226. The method of any one of claims 153-225, wherein the therapies are the non-surgical therapies.

227. A method for treating lung cancer in a subject, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2 by subcutaneous administration and/or intramuscular administration, wherein the recombinant interferon is administered in an amount in a range of about 2μg to about 70μg, optionally about 4μg to about 50μg, further optionally about 4μg to about 30μg by one subcutaneous administration and/or intramuscular administration, the

recombinant interferon is administered by subcutaneous administration and/or intramuscular administration once every about 1 to about 7 days, optionally every about 1 to about 2 days, lasting at least about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject; or the duration can also be about 1 day to about 6 years, about 1 week to about 4 years, about 2 weeks to about 3 years, about 1 month to about 1 year, or about 2 months to about 9 months and the like.

228. The method of claim 227, wherein the lung cancer comprises small cell lung cancer (SCLC), non small cell lung cancer (NSCLC), or both.

229. The method of claim 227 or 228, wherein the lung cancer in the subject comprises a metastasized tumor.

230. The method of any one of claims 227-229, wherein the subject is an early, medium-term, or advanced cancer patient, optionally, the subject is a medium-term, or advanced cancer patient, further optionally, the subject is an advanced cancer patient.

231. The method of any one of claims 227-229, wherein the subject is a stage 0, I, II, III, or IV cancer patient, optionally, the subject is a stage III or IV cancer patient.

232. The method of any one of claims 227-231, wherein the lung cancer is a lung cancer that is indicated or appropriate for surgery.

233. The method of any one of claims 227-231, wherein the lung cancer is a lung cancer that is not indicated nor appropriate for surgery.

234. The method of any one of claims 227-231, wherein the lung cancer is a lung cancer that is capable of being resected.

235. The method of any one of claims 227-231, wherein the lung cancer is a lung cancer that is not capable of being resected.

236. The method of claim 234 or 235, wherein the lung cancer is resected by a

surgical resection.

237. The method of any one of claims 227-236, wherein the subcutaneous administration comprises subcutaneous injection.

238. The method of any one of claims 227-236, wherein the intramuscular administration comprises intramuscular injection.

239. The method of any one of claims 227-238, further comprising administering to the subject the recombinant interferon by inhalation administration.

240. The method of claim 239, wherein the inhalation administration is conducted before, simultaneously, and/or after the subcutaneous administration and/or intramuscular administration.

241. The method of claim 239 or 240, wherein the inhalation administration comprises pulmonary and/or nasal inhalation administration.

242. The method of any one of claims 239-241, wherein the inhalation administration comprises aerosol inhalation.

243. The method of any one of claims 239-242, wherein the recombinant interferon is administered in an amount in a range of about 100μg to about 2000μg, optionally about 100μg to about 1500μg, further optionally about 150μg to about 800μg, still optionally about 200μg to about 600μg by one inhalation administration, the recombinant interferon is administered by inhalation administration once every about 1 day to about 3 days, optionally every about 1 day, lasting at least about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject; or the duration can also be about 1 day to about 6 years, about 1 week to about 4 years, about 2 weeks to about 3 years, about 1 month to about 1 year, or about 2 months to about 9 months and the like.

244. The method of any one of claims 227-243, further comprising administering to the subject the recombinant interferon by intratumoral administration.

245. The method of claim 244, wherein the intratumoral administration is conducted before, simultaneously, and/or after the subcutaneous administration and/or intramuscular administration.

246. The method of claim 244, wherein the intratumoral administration is conducted before, simultaneously, and/or after the inhalation administration.

247. The method of any one of claims 244-246, wherein the intratumoral administration comprises intratumoral injection.

248. The method of any one of claims 244-247, wherein the recombinant interferon is administered in an amount in a range of about 60μg to about 600μg, optionally about 60μg to about 500μg, further optionally about 80μg to about 400μg, still further optionally about 100μg to about 250μg by one intratumoral administration, and the recombinant interferon is administered by intratumoral administration once every about 1 day to about 10 days, optionally every about 1 day to about 7 days such as every about 1, 2, 3, 4, 5, 6, or 7 days, the duration of the intratumoral administration is at least about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject; or the duration can also be about 1 day to about 6 years, about 1 week to about 4 years, about 2 weeks to about 3 years, about 1 month to about 1 year, or about 2 months to about 9 months and the like.

249. The method of any one of claims 244-248, wherein the protocol of intratumoral administration is as follows: the recombinant interferon is administered by intratumoral injection once every about 1 day for about 4 to about 8 times, and then the recombinant interferon is administered by intratumoral injection once every

about 3 days to about 5 days for about 4 to about 8 times, and then the recombinant interferon is administered by intratumoral injection once every about 7 days, the intratumoral administration is stopped when the tumor disappears or becomes too small to conduct the intratumoral injection.

250. The method of any one of claims 227-249, wherein the subject has the pleural effusion, ascites, and/or pericardial effusion.

251. The method of claim 250, wherein the pleural effusion is a malignant pleural effusion, the ascites is a malignant ascites, and/or the pericardial effusion is a malignant pericardial effusion.

252. The method of claim 250 or 251, wherein the recombinant interferon is administered to the subject by an administration route, the administration route comprises at least one of: intrapleural administration, abdominal administration, and pericardial administration.

253. The method of claim 252, wherein the intrapleural administration comprises intrapleural perfusion.

254. The method of claim 252, wherein the abdominal administration comprises abdominal perfusion.

255. The method of claim 252, wherein the pericardial administration comprises pericardial perfusion.

256. The method of any one of claims 252-255, wherein the recombinant interferon is administered in an amount in a range of about 30μg to about 2000μg, optionally about 100μg to about 1500μg, further optionally about 150μg to about 1000μg, still optionally about 200μg to about 800μg by one intrapleural, abdominal, and/or pericardial administration.

257. The method of claim 256, wherein the recombinant interferon is administered in an amount in a range of about 200μg to about 400μg by one intrapleural, abdominal, and/or pericardial administration.

258. The method of any one of claims 252-257, wherein the recombinant interferon is administered by intrapleural, abdominal, and/or pericardial administration once every about 1 day to about 10 days, optionally every about 1 day

to about 7 days, such as every about 1, 2, 3, 4, 5, 6, or 7 days.

259. The method of any one of claims 227-258, wherein the lung cancer in the subject comprises tumor metastasis in at least one of: skin, mucosa, superficial lymph nodes, and subcutaneous tissue.

260. The method of claim 259, wherein the recombinant interferon is administered to the subject by spray administration.

261. The method of claim 260, wherein the spray administration comprises at least one of: percutaneous spray administration, transdermal spray administration, epidermal spray administration, and transmucosal spray administration.

262. The method of claim 260 or 261, wherein the recombinant interferon is administered in an amount in a range of about 6μg to about 100μg by one spray administration.

263. The method of claim 262, wherein the recombinant interferon is administered in an amount of about 10μg to about 40μg, optionally about 20μg to about 40μg by one spray administration.

264. The method of any one of claims 260-263, wherein the recombinant interferon is administered by spray administration about 1 to about 6 times per day, such as about 1, 2, 3, 4, 5, or 6 times per day.

265. The method of any one of claims 227-264, wherein the recombinant interferon is administered to the subject as monotherapy.

266. The method of any one of claims 227-264, further comprising at least one other anti-cancer therapy administered to the subject, optionally, the at least one other anti-cancer therapy is administered to the subject before, simultaneously, and/or after administration of the recombinant interferon.

267. The method of claim 266, wherein the at least one other anti-cancer therapy comprises one or more of: chemotherapy, radiotherapy, surgical therapy, interventional therapy, biotherapy, gene therapy, ablation therapy, immunotherapy, targeted therapy, and traditional Chinese medicine therapy.

268. The method of claim 267, wherein the at least one other anti-cancer therapy comprises chemotherapy.

269. The method of claim 268, wherein the chemotherapy is the first-line chemotherapy.

270. The method of claim 269, wherein one or more chemotherapeutic drugs used for the first-line chemotherapy comprise platinum compounds, such as Cisplatin.

271. The method of claim 267, wherein the at least one other anti-cancer therapy comprises radiotherapy.

272. The method of claim 271, wherein the radiotherapy comprises head gamma knife therapy when the lung cancer metastasizes to brain.

273. The method of claim 267, wherein the at least one other anti-cancer therapy comprises surgical therapy.

274. The method of claim 267, wherein the at least one other anti-cancer therapy comprises targeted therapy.

275. The method of claim 274, wherein the targeted therapy comprises administering Gefitinib, Erlotinib, and/or recombinant human endostatin.

276. The method of claim 267, wherein the at least one other anti-cancer therapy comprises biotherapy.

277. The method of any one of claims 227-276, wherein the therapies eliminate the tumor or reduce the size of the tumor or the number of tumor metastasis compared to the tumor before treatment.

278. The method of any one of claims 227-277, wherein the therapies are the non-surgical therapies.

279. A method for treating lung cancer in a subject, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2 by subcutaneous administration and/or intramuscular administration, wherein the recombinant interferon is administered one or more times by subcutaneous administration and/or intramuscular administration at an induction dose in a range of about 2μg to about 10μg each time, optionally about 4μg to about 10μg each time, further optionally about 4.5μg to about 9μg each time, such as about 4.5μg each time or about 9μg each time, and then the recombinant interferon is administered more times by subcutaneous administration and/or intramuscular administration at a therapeutic dose in a range of

about 10μg to about 70μg each time, optionally about 12μg to about 50μg each time, further optionally about 12μg to about 30μg each time.

280. The method of claim 279, wherein the lung cancer comprises small cell lung cancer (SCLC), non small cell lung cancer (NSCLC), or both.

281. The method of claim 279 or 280, wherein the tumor in the subject comprises a metastasized tumor.

282. The method of any one of claims 279-281, wherein the subject is an early, medium-term, or advanced cancer patient, optionally, the subject is a medium-term, or advanced cancer patient, further optionally, the subject is an advanced cancer patient.

283. The method of any one of claims 279-281, wherein the subject is a stage 0, I, II, III, or IV cancer patient, optionally, the subject is a stage III or IV cancer patient.

284. The method of any one of claims 279-283, wherein the lung cancer is a lung cancer that is indicated or appropriate for surgery.

285. The method of any one of claims 279-283, wherein the lung cancer is a lung cancer that is not indicated nor appropriate for surgery.

286. The method of any one of claims 279-283, wherein the lung cancer is a lung cancer that is capable of being resected.

287. The method of any one of claims 279-283, wherein the lung cancer is a lung cancer that is not capable of being resected.

288. The method of claim 286 or 287, wherein the lung cancer is resected by a surgical resection.

289. The method of any one of claims 279-288, wherein the subcutaneous administration comprises subcutaneous injection.

290. The method of any one of claims 279-288, wherein the intramuscular administration comprises intramuscular injection.

291. The method of any one of claims 279-290, wherein the time interval between administration of induction dose and administration of therapeutic dose is about 1 day to about 1 month, optionally about 1 day to about 1 week, further optionally about 1 day to about 3 days, comprising such as about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days,

about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, or about 1 month.

292. The method of any one of claims 279-291, the recombinant interferon is administered once every about 1 day to about 10 days, optionally every about 1 day to about 7 days, further optionally every about 1 to about 2 days, comprising such as every about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 days when the recombinant interferon is administered more times at an induction dose.

293. The method of any one of claims 279-292, wherein the recombinant interferon is administered at a therapeutic dose once every about 1 day to about 10 days, optionally every about 1 day to about 7 days, further optionally every about 1 to about 2 days, comprising such as every about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 days.

294. The method of any one of claims 279-293, wherein the duration of administration of induction dose and therapeutic dose is at least about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject.

295. The method of any one of claims 279-294, further comprising administering to the subject the recombinant interferon by inhalation administration.

296. The method of claim 295, wherein the inhalation administration is conducted before, simultaneously, and/or after the subcutaneous administration and/or intramuscular administration.

297 The method of claim 295 or 296, wherein the inhalation administration comprises pulmonary and/or nasal inhalation administration.

298. The method of any one of claims 295-297, wherein the inhalation administration comprises aerosol inhalation.

299. The method of any one of claims 295-298, wherein the recombinant interferon is administered in an amount in a range of about 100μg to about 2000μg,

optionally about 100μg to about 1500μg, further optionally about 150μg to about 800μg, still further optionally about 200μg to about 600μg by one inhalation administration, the recombinant interferon is administered by inhalation administration once every about 1 day to about 3 days, optionally every about 1 day, lasting at least about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject; or the duration can also be about 1 day to about 6 years, about 1 week to about 4 years, about 2 weeks to about 3 years, about 1 month to about 1 year, or about 2 months to about 9 months and the like.

300. The method of any one of claims 279-299, further comprising administering to the subject the recombinant interferon by intratumoral administration.

301. The method of claim 300, wherein the intratumoral administration is conducted before, simultaneously, and/or after the subcutaneous administration and/or intramuscular administration.

302. The method of claim 300, wherein the intratumoral administration is conducted before, simultaneously, and/or after the inhalation administration.

303. The method of any one of claims 300-302, wherein the intratumoral administration comprises intratumoral injection.

304. The method of any one of claims 300-303, wherein the recombinant interferon is administered in an amount in a range of about 60μg to about 600μg, optionally about 60μg to about 500μg, further optionally about 80μg to about 400μg, still further optionally about 100μg to about 250μg by one intratumoral administration, and the recombinant interferon is administered by intratumoral administration once every about 1 day to about 10 days, optionally every about 1 day to about 7 days such as every about 1, 2, 3, 4, 5, 6, or 7 days, the duration of the intratumoral

administration is at least about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject; or the duration can also be about 1 day to about 6 years, about 1 week to about 4 years, about 2 weeks to about 3 years, about 1 month to about 1 year, or about 2 months to about 9 months and the like.

305. The method of any one of claims 300-304, wherein the protocol of intratumoral administration is as follows: the recombinant interferon is administered by intratumoral injection once every about 1 day for about 4 to about 8 times, and then the recombinant interferon is administered by intratumoral injection once every about 3 days to about 5 days for about 4 to about 8 times, and then the recombinant interferon is administered by intratumoral injection once every about 7 days, the intratumoral administration is stopped when the tumor disappears or becomes too small to conduct the intratumoral injection.

306. The method of any one of claims 279-305, wherein the subject has the pleural effusion, ascites, and/or pericardial effusion.

307. The method of claim 306, wherein the pleural effusion is a malignant pleural effusion, the ascites is a malignant ascites, and/or the pericardial effusion is a malignant pericardial effusion.

308. The method of claim 306 or 307, wherein the recombinant interferon is administered to the subject by an administration route, the administration route comprises at least one of: intrapleural administration, abdominal administration, and pericardial administration.

309. The method of claim 308, wherein the intrapleural administration comprises intrapleural perfusion.

310. The method of claim 308, wherein the abdominal administration comprises

abdominal perfusion.

311. The method of claim 308, wherein the pericardial administration comprises pericardial perfusion.

312. The method of any one of claims 308-311, wherein the recombinant interferon is administered in an amount in a range of about 30μg to about 2000μg, optionally about 100μg to about 1500μg, further optionally about 150μg to about 1000μg, still optionally about 200μg to about 800μg by one intrapleural administration, abdominal administration, and/or pericardial administration.

313. The method of claim 312, wherein the recombinant interferon is administered in an amount in a range of about 200μg to about 400μg by one intrapleural administration, abdominal administration, and/or pericardial administration.

314. The method of any one of claims 308-313, wherein the recombinant interferon is administered by intrapleural administration, abdominal administration, and/or pericardial administration once every about 1 day to about 10 days, optionally every about 1 day to about 7 days, such as every about 1, 2, 3, 4, 5, 6, or 7 days.

315. The method of any one of claims 279-314, wherein the lung cancer in the subject comprises tumor metastasis in at least one of: skin, mucosa, superficial lymph nodes, and subcutaneous tissue.

316. The method of claim 315, wherein the recombinant interferon is administered to the subject by spray administration.

317. The method of claim 316, wherein the spray administration comprises at least one of: percutaneous spray administration, transdermal spray administration, epidermal spray administration, and transmucosal spray administration.

318. The method of claim 316 or 317, wherein the recombinant interferon is administered in an amount in a range of about 6μg to about 100μg by one spray administration.

319. The method of claim 318, wherein the recombinant interferon is administered in an amount in a range of about 10μg to about 40μg, optionally about 20μg to about 40μg by one spray administration.

320. The method of any one of claims 316-319, wherein the recombinant interferon is administered by spray administration about 1 to about 6 times per day, such as about 1, 2, 3, 4, 5, or 6 times per day.

321. The method of any one of claims 279-320, wherein the recombinant interferon is administered to the subject as monotherapy.

322. The method of any one of claims 279-320, further comprising at least one other anti-cancer therapy administered to the subject, optionally, the at least one other anti-cancer therapy is administered to the subject before, simultaneously, and/or after administration of the recombinant interferon.

323. The method of claim 322, wherein the at least one other anti-cancer therapy comprises one or more of: chemotherapy, radiotherapy, surgical therapy, interventional therapy, biotherapy, gene therapy, ablation therapy, immunotherapy, targeted therapy, and traditional Chinese medicine therapy.

324. The method of claim 323, wherein the at least one other anti-cancer therapy comprises chemotherapy.

325. The method of claim 324, wherein the chemotherapy is the first-line chemotherapy.

326. The method of claim 325, wherein one or more chemotherapeutic drugs are used for the first-line chemotherapy and comprise platinum compounds, such as Cisplatin.

327. The method of claim 323, wherein the at least one other anti-cancer therapy comprises radiotherapy.

328. The method of claim 327, wherein the radiotherapy comprises head gamma knife therapy when the lung cancer metastasizes to brain.

329. The method of claim 323, wherein the at least one other anti-cancer therapy comprises surgical therapy.

330. The method of claim 323, wherein the at least one other anti-cancer therapy comprises targeted therapy.

331. The method of claim 330, wherein the targeted therapy comprises administering Gefitinib, Erlotinib, and/or recombinant human endostatin.

332. The method of claim 323, wherein the at least one other anti-cancer therapy comprises biotherapy.

333. The method of any one of claims 279-332, wherein the therapies eliminate the tumor of the lung or reduce the size of the tumor of the lung compared to the tumor size before treatment.

334. The method of any one of claims 279-333, wherein the therapies are the non-surgical therapies.

335. A method for treating cancer in a subject, wherein the cancer originates from lung cancer in the subject and metastasizes to brain, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2, wherein the recombinant interferon is administered one or more times by subcutaneous administration and/or intramuscular administration at an induction dose in a range of about 2μg to about 10μg each time, optionally about 4μg to about 10μg each time, further optionally about 4.5μg to about 9μg each time, such as about 4.5μg each time or about 9μg each time, and then the recombinant interferon is administered more times by subcutaneous administration and/or intramuscular administration at a therapeutic dose in a range of about 10μg to about 70μg each time, optionally about 12μg to about 50μg each time, further optionally about 12μg to about 30μg each time, and the recombinant interferon is administered to the subject by inhalation administration before, simultaneously, and/or after the subcutaneous administration and/or intramuscular administration, the recombinant interferon is administered in an amount in a range of about 100μg to about 2000μg, optionally about 100μg to about 1500μg, further optionally about 150μg to about 800μg, still further optionally about 200μg to about 600μg by one inhalation administration, and the recombinant interferon is administered by inhalation administration once every about 1 day to about 3 days, optionally every about 1 day.

336. The method of claim 335, wherein the subject is a medium-term, advanced, or stage III or stage IV cancer patient, optionally, the subject is an advanced, or stage III or stage IV cancer patient.

337. The method of claim 335 or 336, wherein the cancer is a cancer that is not

indicated nor appropriate for surgery.

338. The method of claim 335 or 336, wherein the tumor is a tumor that is not capable of being resected.

339. The method of claim 338, wherein the tumor is resected by a surgical resection.

340. The method of any one of claims 335-339, wherein the subcutaneous administration comprises subcutaneous injection.

341. The method of any one of claims 335-339, wherein the intramuscular administration comprises intramuscular injection.

342. The method of any one of claims 335-341, wherein the inhalation administration comprises pulmonary and/or nasal inhalation administration.

343. The method of any one of claims 335-342, wherein the inhalation administration comprises aerosol inhalation.

344. The method of any one of claims 335-343, wherein the time interval between administration of induction dose and administration of therapeutic dose is about 1 day to about 1 month, optionally about 1 day to about 1 week, further optionally about 1 day to about 3 days, comprising such as about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, or about 1 month.

345. The method of any one of claims 335-344, wherein the recombinant interferon is administered once every about 1 day to about 10 days, optionally every about 1 day to about 7 days, further optionally every about 1 to about 2 days, comprising such as every about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 days when the recombinant interferon is administered more times at an induction dose.

346. The method of any one of claims 335-345, wherein the recombinant interferon is administered at a therapeutic dose once every about 1 day to about 10 days, optionally every about 1 day to about 7 days, further optionally every about 1 to about 2 days, comprising such as every about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 days.

347. The method of any one of claims 335-346, wherein the duration of

administration of induction dose and therapeutic dose is at least about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject.

348. The method of any one of claims 335-347, wherein the duration of the inhalation administration is at least about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject; or the duration can also be about 1 day to about 6 years, about 1 week to about 4 years, about 2 weeks to about 3 years, about 1 month to about 1 year, or about 2 months to about 9 months and the like.

349. The method of any one of claims 335-348, wherein the recombinant interferon is administered to the subject as monotherapy.

350. The method of any one of claims 335-349, further comprising at least one other anti-cancer therapy administered to the subject, optionally, the at least one other anti-cancer therapy is administered to the subject before, simultaneously, and/or after administration of the recombinant interferon.

351. The method of claim 350, wherein the at least one other anti-cancer therapy comprises one or more of: chemotherapy, radiotherapy, surgical therapy, interventional therapy, biotherapy, gene therapy, ablation therapy, immunotherapy, targeted therapy, and traditional Chinese medicine therapy.

352. The method of claim 351, wherein the chemotherapy is the first-line chemotherapy, optionally, one or more chemotherapeutic drugs are used for the

first-line chemotherapy and comprise platinum compounds, such as Cisplatin.

353. The method of claim 351, wherein the targeted therapy comprises administering Gefitinib, Erlotinib, and/or recombinant human endostatin.

354. The method of claim 351, wherein the at least one other anti-cancer therapy comprises radiotherapy.

355. The method of claim 354, wherein the radiotherapy comprises gamma knife therapy.

356. The method of claim 355, wherein the gamma knife therapy comprises head gamma knife therapy.

357. The method of any one of claims 335-356, wherein the therapies eliminate the tumor or reduce the size of the tumor compared to the tumor before treatment.

358. The method of any one of claims 335-357, wherein the therapies are the non-surgical therapies.

359. A method for treating cancer in a subject, wherein the cancer originates from lung cancer in the subject and metastasizes to bone or liver, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2, wherein the recombinant interferon is administered one or more times by subcutaneous administration and/or intramuscular administration at an induction dose in a range of about 2μg to about 10μg each time, optionally about 4μg to about 10μg each time, further optionally about 4.5μg to about 9μg each time, such as about 4.5μg each time or about 9μg each time, and then the recombinant interferon is administered more times by subcutaneous administration and/or intramuscular administration at a therapeutic dose of about 10μg -about 70μg each time, optionally about 12μg to about 50μg each time, further optionally about 12μg to about 30μg each time.

360. The method of claim 359, wherein the subject is a medium-term, advanced, or stage III or stage IV cancer patient, optionally, the subject is an advanced, or stage III or stage IV cancer patient.

361. The method of claim 359 or 360, wherein the cancer is a cancer that is not indicated nor appropriate for surgery.

362. The method of claim 359 or 360, wherein the tumor is a tumor that is not

capable of being resected.

363. The method of claim 362, wherein the tumor is resected by a surgical resection.

364. The method of any one of claims 359-363, wherein the subcutaneous administration comprises subcutaneous injection.

365. The method of any one of claims 359-363, wherein the intramuscular administration comprises intramuscular injection.

366. The method of any one of claims 359-365, wherein the time interval between administration of induction dose and administration of therapeutic dose is about 1 day to about 1 month, optionally about 1 day to about 1 week, further optionally about 1 day to about 3 days, comprising such as about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, or about 1 month.

367. The method of any one of claims 359-366, wherein the recombinant interferon is administered once every about 1 day to about 10 days, optionally every about 1 day to about 7 days, further optionally every about 1 to about 2 days, comprising such as every about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 days when the recombinant interferon is administered more times at an induction dose.

368. The method of any one of claims 359-367, wherein the recombinant interferon is administered at a therapeutic dose once every about 1 day to about 10 days, optionally every about 1 day to about 7 days, further optionally every about 1 to about 2 days, comprising such as every about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 days.

369. The method of any one of claims 359-368, wherein the duration of administration of induction dose and therapeutic dose is at least about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the

subject.

370. The method of any one of claims 359-369, further comprising administering to the subject the recombinant interferon by inhalation administration.

371. The method of claim 370, wherein the inhalation administration is conducted before, simultaneously, and/or after the subcutaneous administration and/or intramuscular administration.

372. The method of claim 370 or 371, wherein the inhalation administration comprises pulmonary and/or nasal inhalation administration.

373. The method of any one of claims 370-372, wherein the inhalation administration comprises aerosol inhalation.

374. The method of any one of claims 370-373, wherein the recombinant interferon is administered in an amount in a range of about 100μg to about 2000μg, optionally about 100μg to about 1500μg, further optionally about 150μg to about 800μg, still further optionally about 200μg to about 600μg by one inhalation administration, the recombinant interferon is administered by inhalation administration once every about 1 day to about 3 days, optionally every about 1 day, and the duration of the inhalation administration is at least about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject; or the duration can also be about 1 day to about 6 years, about 1 week to about 4 years, about 2 weeks to about 3 years, about 1 month to about 1 year, or about 2 months to about 9 months and the like.

375. The method of any one of claims 359-374, wherein the recombinant interferon is administered to the subject as monotherapy.

376. The method of any one of claims 359-374, further comprising at least one other anti-cancer therapy administered to the subject, optionally, the at least one other

anti-cancer therapy is administered to the subject before, simultaneously, and/or after administration of the recombinant interferon.

377. The method of claim 376, wherein the at least one other anti-cancer therapy comprises one or more of: chemotherapy, radiotherapy, surgical therapy, interventional therapy, biotherapy, gene therapy, ablation therapy, immunotherapy, targeted therapy, and traditional Chinese medicine therapy.

378. The method of claim 377, wherein the at least one other anti-cancer therapy comprises chemotherapy.

379. The method of claim 378, wherein the chemotherapy is first-line chemotherapy.

380. The method of claim 379, wherein one or more chemotherapeutic drugs are used for the first-line chemotherapy and comprise platinum compounds, such as Cisplatin.

381. The method of claim 377, wherein the at least one other anti-cancer therapy comprises targeted therapy.

382. The method of claim 381, wherein the targeted therapy comprises administering Gefitinib, Erlotinib, and/or recombinant human endostatin.

383. The method of claim 377, wherein the at least one other anti-cancer therapy comprises biotherapy.

384. The method of any one of claims 359-383, wherein the therapies eliminate the tumor or reduce the size of the tumor compared to the tumor before treatment.

385. The method of any one of claims 359-384, wherein the therapies are the non-surgical therapies.

386. A method for treating cancer in a subject, wherein the cancer originates from lung cancer in the subject and metastasizes to lymph nodes, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2, wherein the recombinant interferon is administered one or more times by subcutaneous administration and/or intramuscular administration at an induction dose in a range of about 2μg to about 10μg each time, optionally about 4μg to about 10μg each time, further optionally about 4.5μg to about 9μg each time, such as about 4.5μg

each time or about 9μg each time, and then the recombinant interferon is administered more times by subcutaneous administration and/or intramuscular administration at a therapeutic dose of about 10μg to about 70μg each time, optionally about 12μg to about 50μg each time, further optionally about 12μg to about 30μg each time, and the recombinant interferon is administered to the tumor and/or the lymph nodes metastases by topical or local administration before, simultaneously, and/or after the subcutaneous administration and/or intramuscular administration.

387. The method of claim 386, wherein the subject is a medium-term, advanced, or stage III or stage IV cancer patient, optionally, the subject is an advanced, or stage III or stage IV cancer patient.

388. The method of claim 386 or 387, wherein the cancer is a cancer that is not indicated nor appropriate for surgery.

389. The method of claim 386 or 387, wherein the tumor is a tumor that is not capable of being resected.

390. The method of claim 389, wherein the tumor is resected by a surgical resection.

391. The method of any one of claims 386-390, wherein the subcutaneous administration comprises subcutaneous injection.

392. The method of any one of claims 386-390, wherein the intramuscular administration comprises intramuscular injection.

393. The method of any one of claims 386-392, wherein the time interval between administration of induction dose and administration of therapeutic dose is about 1 day to about 1 month, optionally about 1 day to about 1 week, further optionally about 1 day to about 3 days, comprising such as about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, or about 1 month.

394. The method of any one of claims 386-393, wherein the recombinant interferon is administered once every about 1 day to about 10 days, optionally every about 1 day to about 7 days, further optionally every about 1 to about 2 days,

comprising such as every about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 days when the recombinant interferon is administered more times at an induction dose.

395. The method of any one of claims 386-394, wherein the recombinant interferon is administered at a therapeutic dose once every about 1 day to about 10 days, optionally every about 1 day to about 7 days, further optionally every about 1 to about 2 days, comprising such as every about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 days.

396. The method of any one of claims 386-395, wherein the duration of administration of induction dose and therapeutic dose is at least about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject.

397. The method of any one of claims 386-396, wherein the local administration comprises intratumoral administration when the lymph nodes are the deep lymph nodes.

398. The method of claim 397, wherein the intratumoral administration comprises intratumoral injection.

399. The method of claim 397 or 398, wherein the recombinant interferon is administered in an amount in a range of about 60μg to about 600μg, optionally about 60μg to about 500μg, further optionally about 80μg to about 400μg, still further optionally about 100μg to about 250μg by one intratumoral administration, and the recombinant interferon is administered by intratumoral administration once every about 1 day to about 10 days, optionally every about 1 day to about 7 days such as every about 1, 2, 3, 4, 5, 6, or 7 days, the duration of the intratumoral administration is at least about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9

months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject; or the duration can also be about 1 day to about 6 years, about 1 week to about 4 years, about 2 weeks to about 3 years, about 1 month to about 1 year, or about 2 months to about 9 months and the like.

400. The method of any one of claims 397-399, wherein the protocol of intratumoral administration is as follow: the recombinant interferon is administered by intratumoral injection once every about 1 day for about 4 to about 8 times, and then the recombinant interferon is administered by intratumoral injection once every about 3 days to about 5 days for about 4 to about 8 times, and then the recombinant interferon is administered by intratumoral injection once every about 7 days, the intratumoral administration is stopped when the tumor and/or metastasized lymph nodes are disappeared or become too small to conduct the intratumoral injection.

401. The method of any one of claims 386-396, wherein the topical or local administration comprises at least one of: infiltration administration, percutaneous administration, transdermal administration, epidermal administration, and transmucosal administration when the lymph nodes are superficial lymph nodes.

402. The method of claim 401, wherein the local administration comprises infiltration administration.

403. The method of claim 402, wherein the infiltration administration is conducted by perfusion.

404. The method of claim 401, wherein the percutaneous administration, transdermal administration, epidermal administration, or transmucosal administration comprises percutaneous spray administration, transdermal spray administration, epidermal spray administration, or transmucosal spray administration, respectively.

405. The method of claim 404, wherein the recombinant interferon is administered in an amount in a range of about 6μg to about 100μg by one spray administration.

406. The method of claim 405, wherein the recombinant interferon is

administered in an amount of about 10μg to about 40μg, optionally about 20μg to about 40μg by one spray administration.

407. The method of any one of claims 404-406, wherein the recombinant interferon is administered by spray administration about 1 to about 6 times such as about 1, 2, 3, 4, 5, or 6 times per day.

408. The method of any one of claims 386-407, wherein the recombinant interferon is administered to the subject as monotherapy.

409. The method of any one of claims 386-407, further comprising at least one other anti-cancer therapy administered to the subject, optionally, the at least one other anti-cancer therapy is administered to the subject before, simultaneously, and/or after administration of the recombinant interferon.

410. The method of claim 409, wherein the at least one other anti-cancer therapy comprises one or more of: chemotherapy, radiotherapy, surgical therapy, interventional therapy, biotherapy, gene therapy, ablation therapy, immunotherapy, targeted therapy, and traditional Chinese medicine therapy.

411. The method of claim 410, wherein the at least one other anti-cancer therapy comprises chemotherapy.

412. The method of claim 411, wherein the chemotherapy is first-line chemotherapy.

413. The method of claim 412, wherein one or more chemotherapeutic drugs are used for the first-line chemotherapy and comprise platinum compounds, such as Cisplatin.

414. The method of claim 410, wherein the at least one other anti-cancer therapy comprises targeted therapy.

415. The method of claim 414, wherein the targeted therapy comprises administering Gefitinib, Erlotinib, and/or recombinant human endostatin.

416. The method of claim 410, wherein the at least one other anti-cancer therapy comprises biotherapy.

417. The method of any one of claims 386-416, wherein the therapies eliminate the tumor or reduce the size of the tumor compared to the tumor before treatment.

418. The method of any one of claims 386-417, wherein the therapies are the non-surgical therapies.

419. A method for treating lung cancer in a subject, wherein the subject has pleural effusion, ascites and/or pericardial effusion, comprising administering to the subject a recombinant interferon encoded by SEQ ID NO: 2 by topical or local administration.

420. The method of claim 419, wherein the subject is a medium-term, advanced, or stage III or stage IV cancer patient, optionally, the subject is an advanced, or stage III or stage IV cancer patient.

421. The method of claim 419 or 420, wherein the lung cancer is a lung cancer that is not indicated nor appropriate for surgery.

422. The method of claim 419 or 420, wherein the lung cancer is a lung cancer that is not capable of being resected.

423. The method of claim 422, wherein the tumor is resected by a surgical resection.

424. The method of any one of claims 419-423, wherein the pleural effusion is a malignant pleural effusion, the ascites is a malignant ascites, and/or the pericardial effusion is a malignant pericardial effusion.

425. The method of any one of claims 419-424, wherein the local administration comprises at least one of: infiltration administration, intrapleural administration, abdominal administration, and pericardial administration.

426. The method of claim 425, wherein the local administration is conducted by perfusion.

427. The method of claim 426, wherein the recombinant interferon is administered in an amount in a range of about 30μg to about 2000μg, optionally about 100μg to about 1500μg, further optionally about 150μg to about 1000μg, still optionally about 200μg to about 800μg, still further optionally about 200μg to about 400μg by one perfusion administration.

428. The method of claim 426 or 427, wherein the recombinant interferon is administered by perfusion administration once every about 1 to about 10 days,

optionally every about 1 to about 7 days, such as every about 1, 2, 3, 4, 5, 6, or 7 days.

429. The method of claim 428, wherein the recombinant interferon is administered by perfusion administration once every about 1 day, lasting about 4 to about 6 times.

430. The method of any one of claims 419-429, wherein the recombinant interferon is administered to the subject by systemic administration before, simultaneously, and/or after the topical or local administration.

431. The method of claim 430, wherein the systemic administration comprises subcutaneous and/or intramuscular administration.

432. The method of claim 431, wherein the subcutaneous administration comprises subcutaneous injection.

433. The method of claim 431, wherein the intramuscular administration comprises intramuscular injection.

434. The method of any one of claims 431-433, wherein the recombinant interferon is administered one or more times by subcutaneous administration and/or intramuscular administration at an induction dose in a range of about 2μg to about 10μg each time, optionally about 4μg to about 10μg each time, further optionally about 4.5μg to about 9μg each time, such as about 4.5μg each time or about 9μg each time, and then the recombinant interferon is administered more times by subcutaneous administration and/or intramuscular administration at a therapeutic dose of about 10μg to about 70μg each time, optionally about 12μg to about 50μg each time, further optionally about 12μg to about 30μg each time.

435. The method of claim 434, wherein the time interval between administration of induction dose and administration of therapeutic dose is about 1 day to about 1 month, optionally about 1 day to about 1 week, further optionally about 1 day to about 3 days, comprising such as about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 1 week, about 2 weeks, about 3 weeks, or about 1 month.

436. The method of claim 434 or 435, wherein the recombinant interferon is administered once every about 1 day to about 10 days, optionally every about 1 day to

about 7 days, further optionally every about 1 to about 2 days, comprising such as every about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 days when the recombinant interferon is administered more times at an induction dose.

437. The method of any one of claims 434-436, wherein the recombinant interferon is administered at a therapeutic dose once every about 1 day to about 10 days, optionally every about 1 day to about 7 days, further optionally every about 1 to about 2 days, comprising such as every about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 days.

438. The method of any one of claims 434-437, wherein the duration of administration of induction dose and therapeutic dose is at least about 1 week, about 2 weeks, about 3 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, or about 6 years and the like, or the recombinant interferon can be administered for a long time, including over the life time of the subject.

439. The method of any one of claims 419-438, wherein other therapeutic drugs are further administered by topical, local and/or systemic administration.

440. The method of claim 439, wherein the other therapeutic drugs comprise antitumor drugs.

441. The method of claim 440, wherein the antitumor drugs comprise one or more chemotherapeutic drugs, targeted drugs, or biological drugs.

442. The method of claim 441, wherein one or more chemotherapeutic drugs comprise platinum compounds, such as Cisplatin.

443. The method of claim 441, wherein one or more targeted drugs comprise Gefitinib, Erlotinib, and/or recombinant human endostatin.

444. The method of any one of claims 419-443, wherein the therapies eliminate the tumor or reduce the size of the tumor compared to the tumor size before treatment.

445. The method of any one of claims 419-444, wherein the therapies are the non-surgical therapies.

446. A method of treating a tumor in a subject comprising administering to the

subject a recombinant interferon that comprises an anti-tumor effect as a first line monotherapy.

447. The method of claim 446, wherein the tumor comprises one of: lung cancer, uterine cancer, cervical cancer, and pancreatic cancer.

448. The method of claim 447, wherein the lung cancer comprises non-small cell lung cancer.

449. The method of claim 446, wherein the tumor is not a kidney cancer.

450. A method of treating a tumor in a subject comprising administering to the subject a recombinant interferon that comprises an antitumor effect as a second line monotherapy.

451. The method of claim 450, wherein the tumor comprises one of: lung cancer, colorectal cancer, malignant melanoma, ovarian cancer, cervical cancer, liver cancer, breast cancer, gastrointestinal cancer, prostate cancer, neuroma, and squamous cell carcinoma.

452. The method of claim 451, wherein the colorectal cancer comprises colon cancer.

453. The method of claim 451, wherein the colorectal cancer comprises rectal cancer.

454. The method of claim 451, wherein the lung cancer comprises non-small cell lung cancer.

455. The method of claim 451, wherein the liver cancer comprises HCC.

456. The method of claim 451, wherein the gastrointestinal cancer comprises gastric cancer.

457. A method of treating a tumor in a subject comprising administering to the subject a recombinant interferon that comprises an anti-tumor effect as a first line therapy in combination with one or more other anti-cancer therapy.

458. The method of claim 457, wherein the tumor comprises one of: lung cancer, prostate cancer, and lymphoma.

459. The method of claim 458, wherein the lung cancer comprises at least one of non-small cell lung cancer and small cell lung cancer.

460. The method of claim 457, wherein the tumor is not an ovarian cancer.

461. A method of treating a tumor in a subject comprising administering to the subject a recombinant interferon that comprises an anti-tumor effect as a second line therapy in combination with one or more other anti-cancer therapies.

462. The method of claim 461, wherein the tumor comprises one of: lung cancer, lymphoma, cervical cancer, and cholangioadenocarcinoma.

463. The method of claim 462, wherein the lung cancer comprises at least one of non-small cell lung cancer and small cell lung cancer.

464. The method of claim 462, wherein the lymphoma is non-Hodgkins lymphoma.

465. The method of any of claims 457, 458, 459, 460, 461, 462, 463, or 464, wherein the one or more other anti-cancer therapies comprise at least one of: radiotherapy, small molecule therapy, chemotherapy, biologics therapy, TCM, and surgery.

466. The method of claim 465, wherein the small molecule in the small molecule therapy comprises Getifinib.

467. The method of claim 465, wherein the biologics therapy comprises treatment with at least one of: a recombinant protein and isolated cells.

468. The method of claim 467, wherein the recombinant protein comprises Endostar.

469. The method of claim 467, wherein the isolated cells comprises at least one of: stem cells and NK cells.

470. The method of claim 465, wherein the recombinant interferon is administered after surgical treatment of cancer.

471. The method of any of claims 465-469, wherein the recombinant interferon is administered prior to surgical treatment of cancer.

472. The method of any of claims 446-471, wherein the recombinant interferon is administered by at least one of the following routes: systemically and locally.

473. The method of any of claims 446-471, wherein the recombinant interferon is administered by at least one of the following routes: intramuscularly,

intraperitoneally, intravenously, intra-arterially, intratumorally, by injection into lymph nodes, topically, locally on the tumor, intranasally, subcutaneously, by spraying, by inhalation, by perfusion, and by infusion.

474. The method of any of claims 446-473, wherein the recombinant interferon comprises rSIFN-co.

475. The method of claim 474, wherein the recombinant interferon is administered at a dose in a range of about 2μg to about 2500μg per treatment.

476. The method of claim 474, wherein recombinant interferon is administered at a dose in a range of about 9μg to about 2100μg per treatment.

477. The method of claim 474, wherein recombinant interferon is administered at a dose of one or more of the following doses: 2μg, 4μg, 9 μg, 13.5μg, 15μg, 18μg, 21μg, 24μg, 25.5μg, 30μg, 36μg, 45μg, 70μg, 84μg, 90μg, 100μg, 105μg, 120μg, 126μg, 139μg, 150μg, 168μg, 180μg, 189μg, 198μg, 200μg, 207μg, 210μg, 240μg, 252μg, 273μg, 300μg, 315μg, 400μg, 500μg, 600μg, 1000μg, 2000μg, 2100μg.

478. The method of any of claims 446-477, wherein the recombinant interferon comprises a specified activity.

479. The method of claim 478, wherein the recombinant interferon comprises an activity in the range of about 4.4 x 10^8 IU/mg to about 1.0 x 10^9 IU/mg, and optionally greater than 5.5 x 10^8 IU/mg.

480. A method of preventing tumor recurrence in a subject comprising administering an amount of a recombinant interferon that comprises an amino acid sequence that is encoded by a nucleic acid sequence comprising the sequence of SEQ ID NO: 2 after surgery, chemotherapy, radiotherapy, cryoablation, radiofrequency ablation, biologics therapy, intervention therapy, and/or rSIFN-co therapy, whereby the recombinant interferon is administered after tumor bulk in the subject has been reduced.

481. A method of prolonging tumor-free survival in a subject comprising administering an amount of a recombinant interferon that comprises an amino acid sequence that is encoded by a nucleic acid sequence comprising the sequence of SEQ ID NO: 2 after surgery, chemotherapy, radiotherapy, cryoablation, radiofrequency

ablation, biologics therapy, intervention therapy, and/or rSIFN-co therapy, whereby the recombinant interferon is administered after tumor bulk in the subject has been reduced.

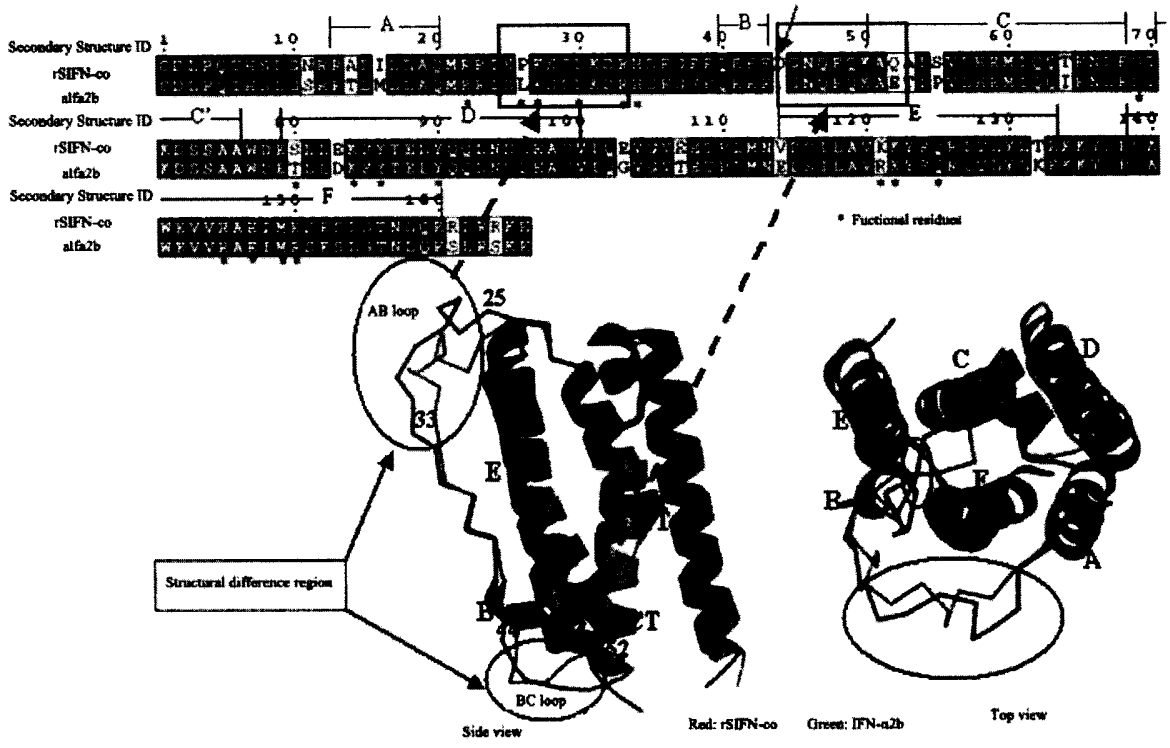


Figure 1

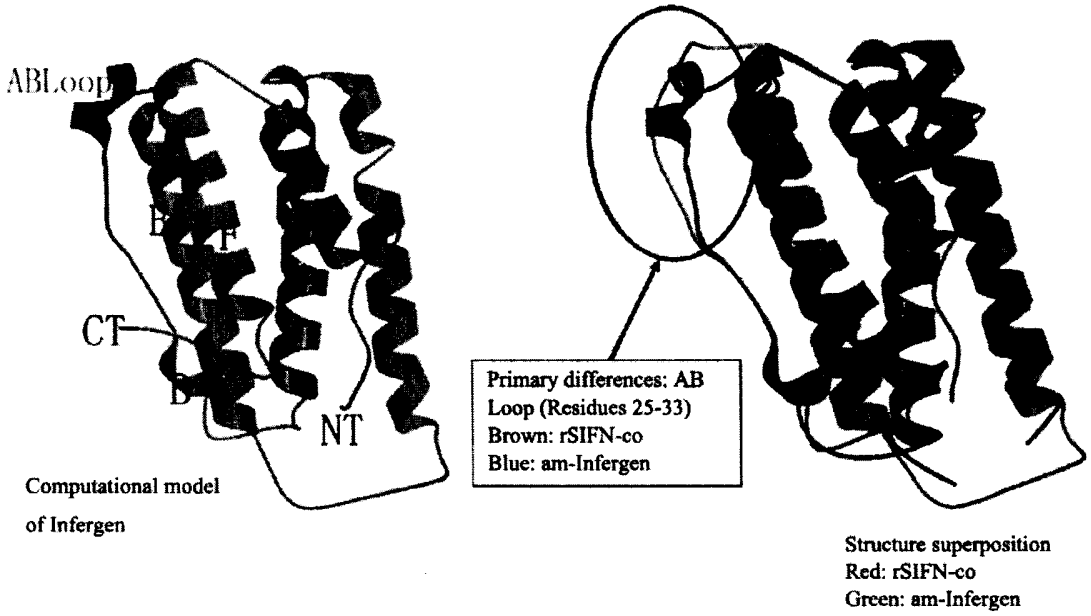
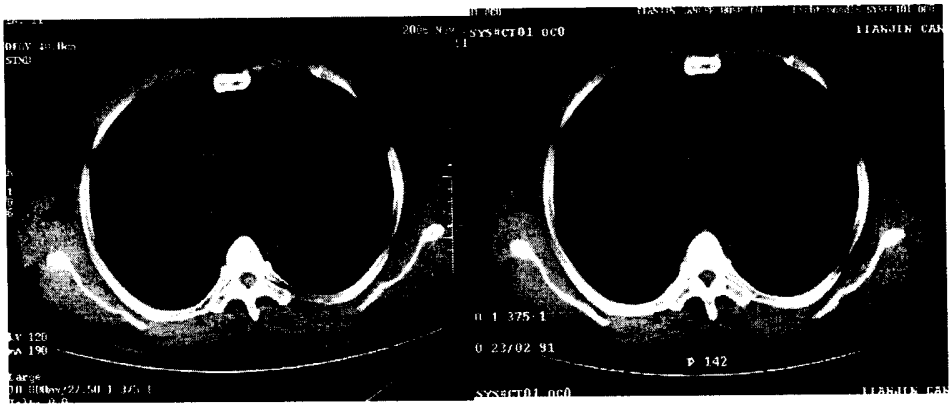
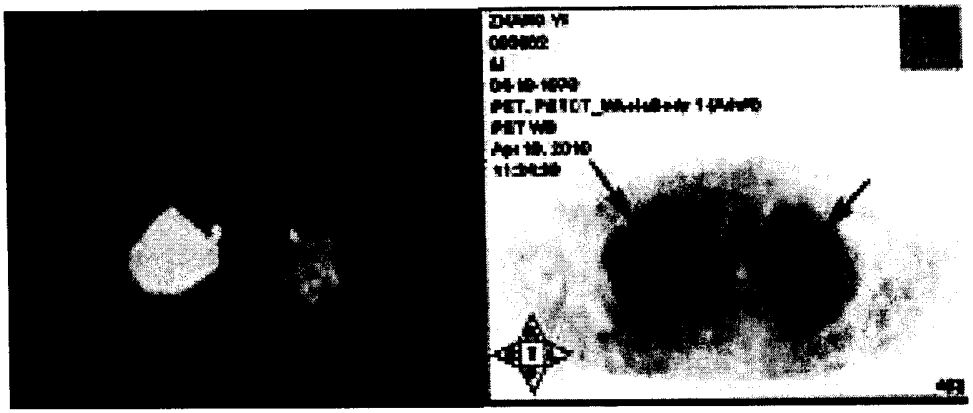


Figure 2

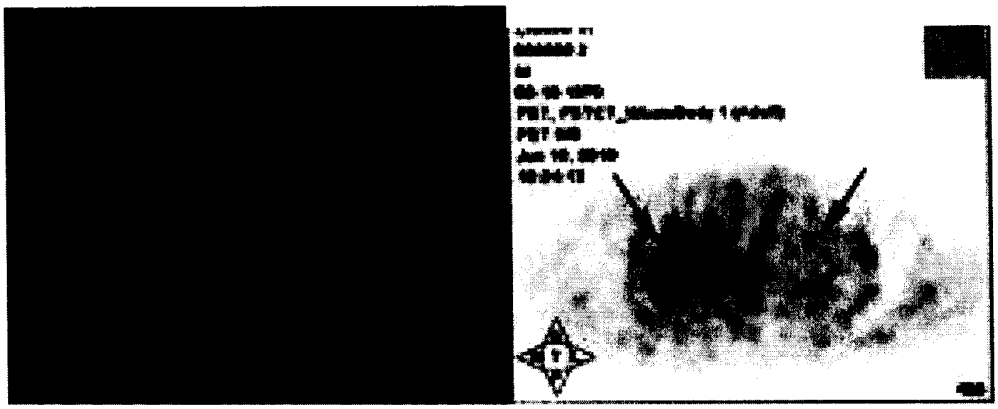


a b

Figure 3

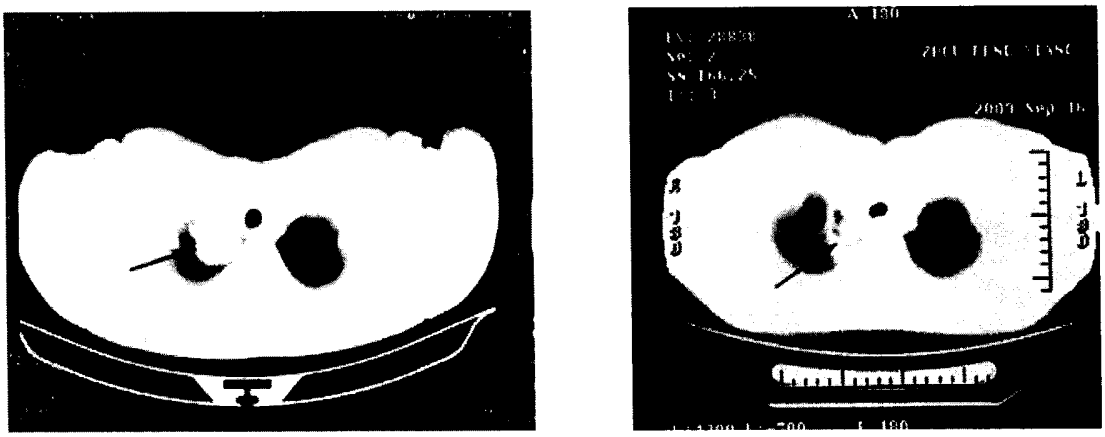


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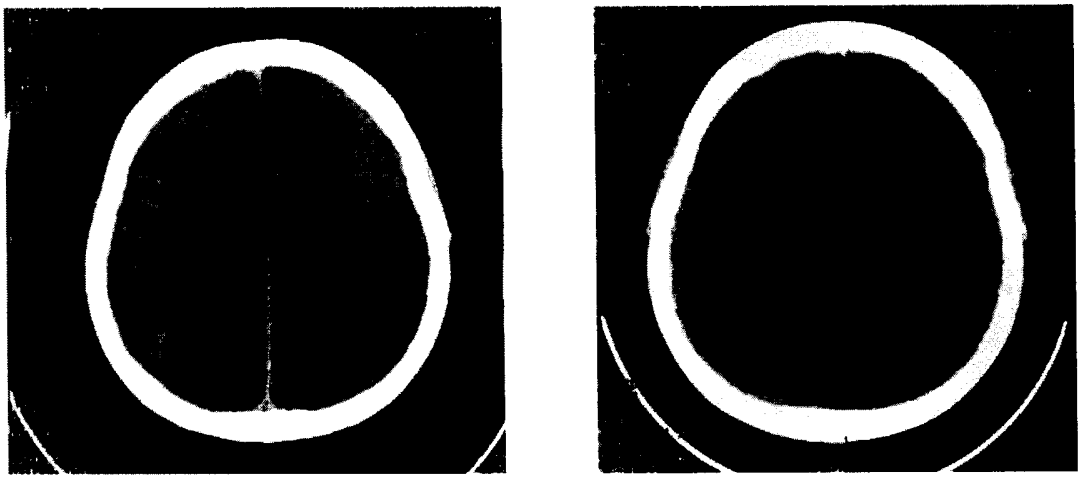
b

Figure 4



a b

Figure 5



a b

Figure 6

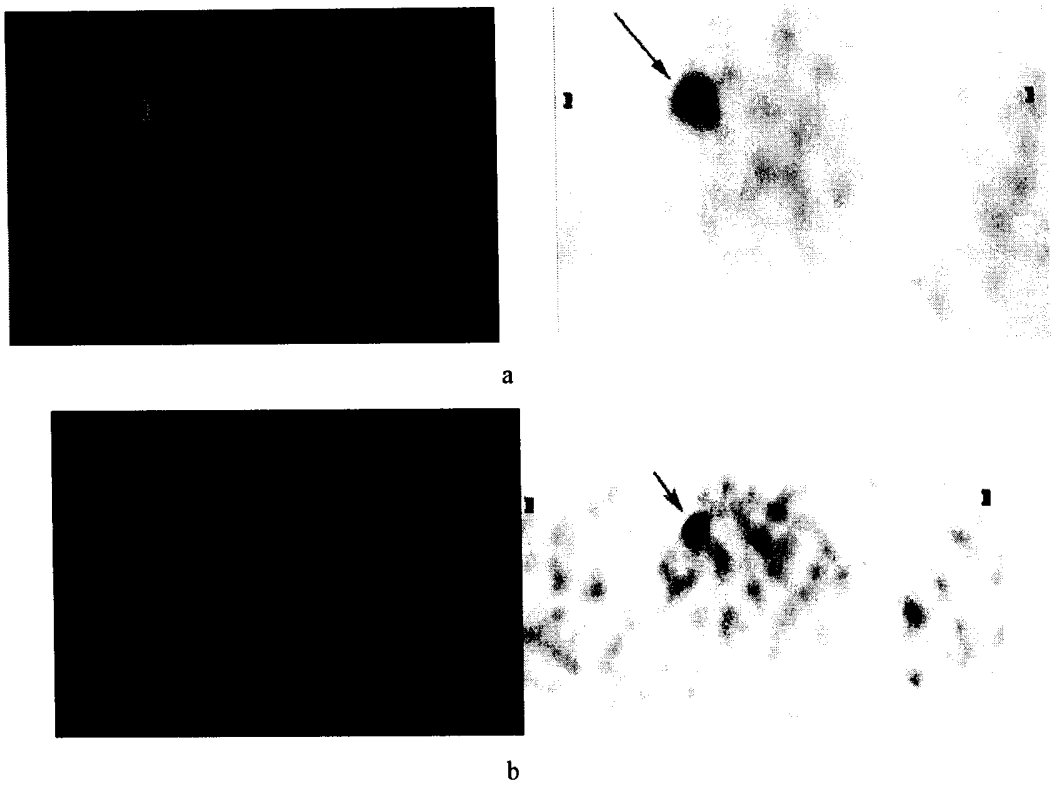


Figure 7

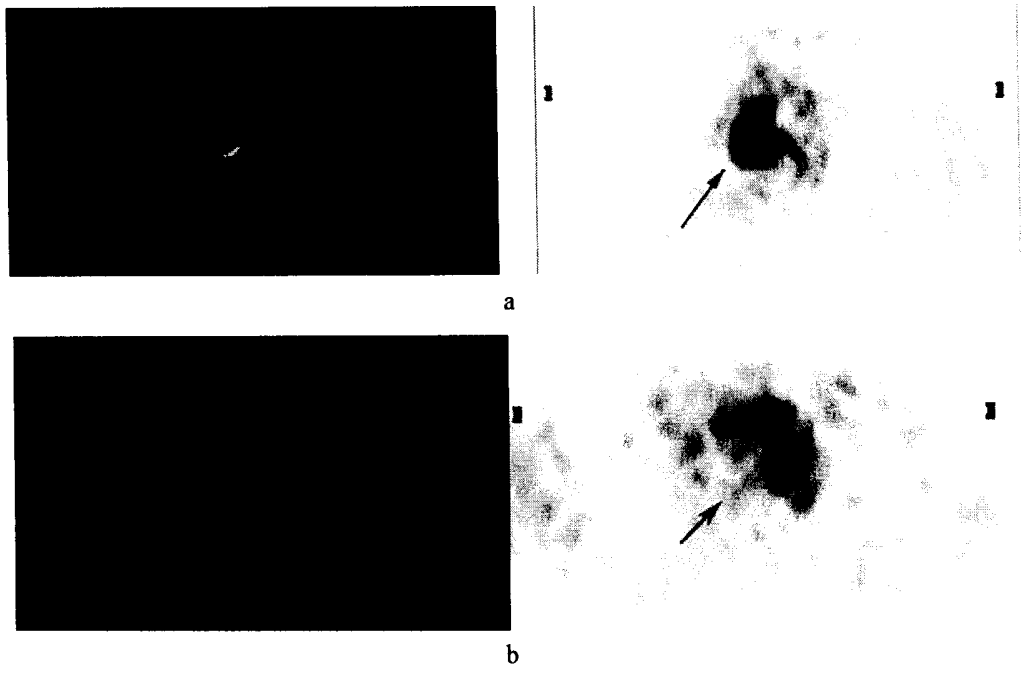
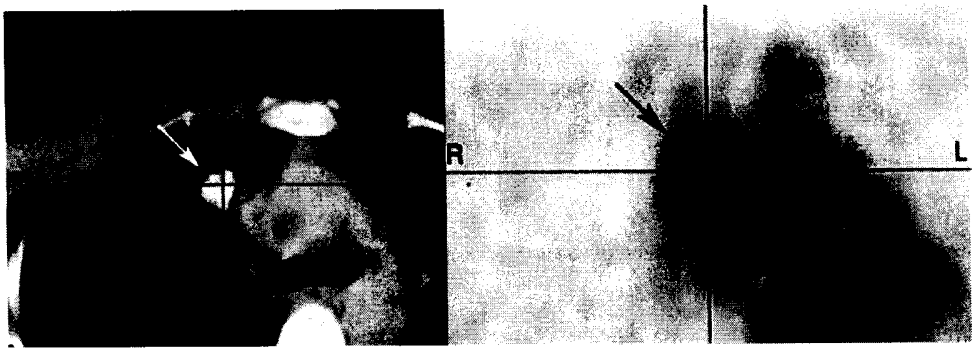
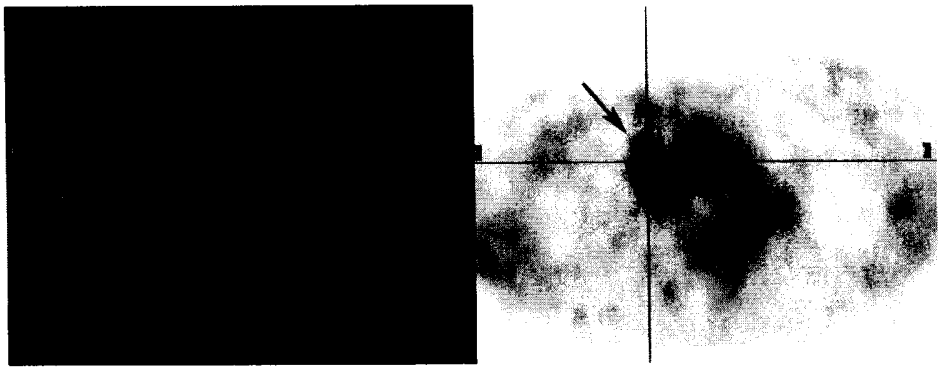


Figure 8



a



b

Figure 9

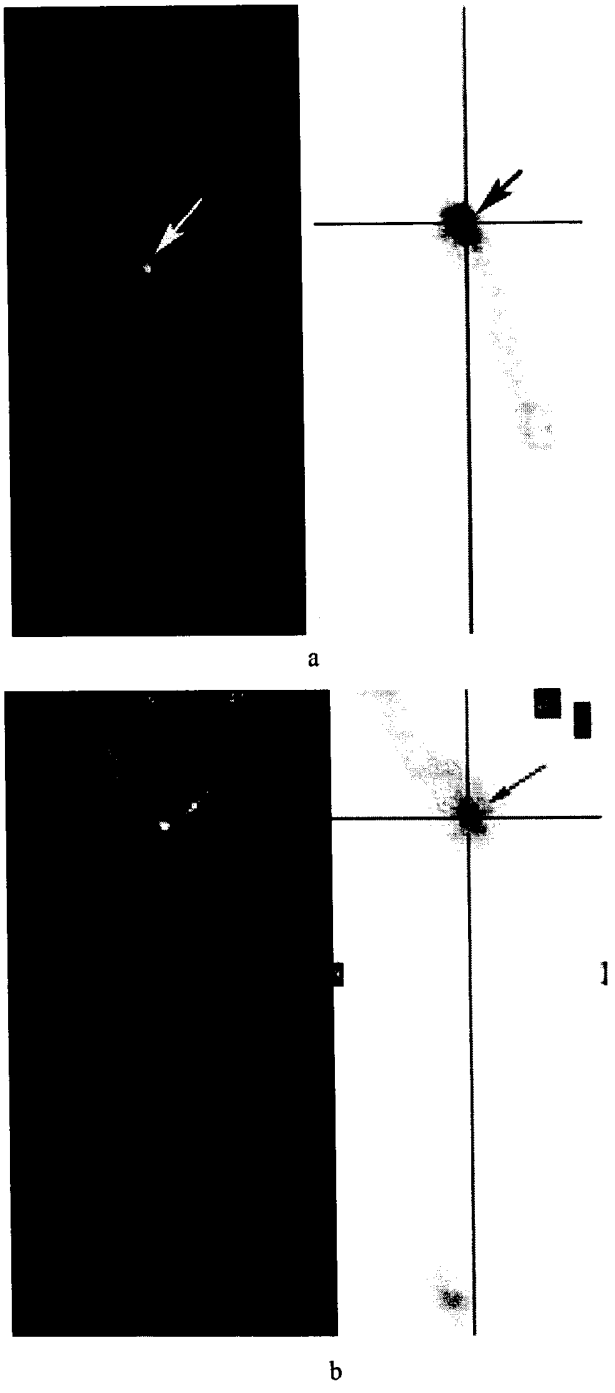


Figure 10

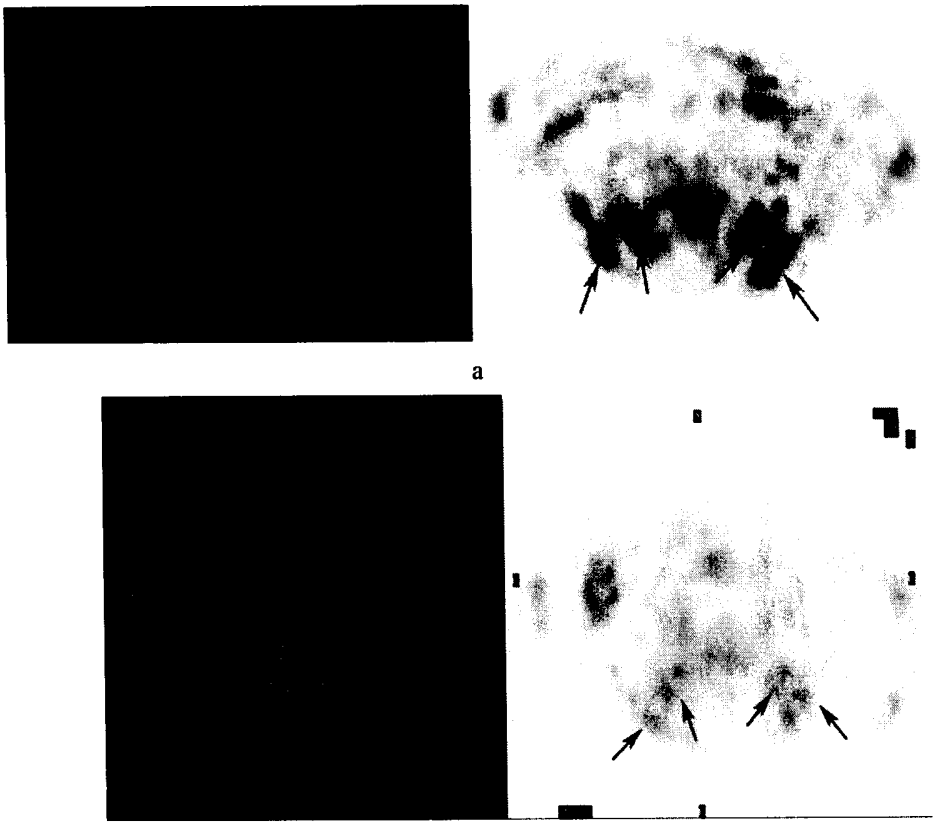
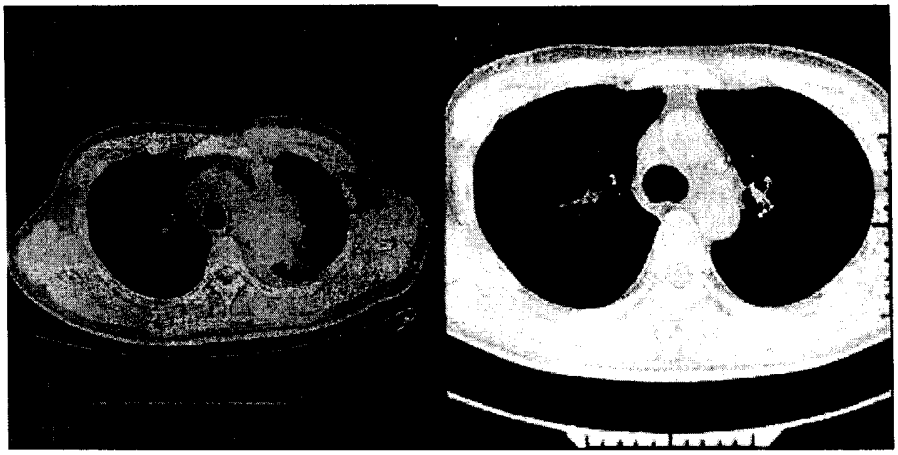
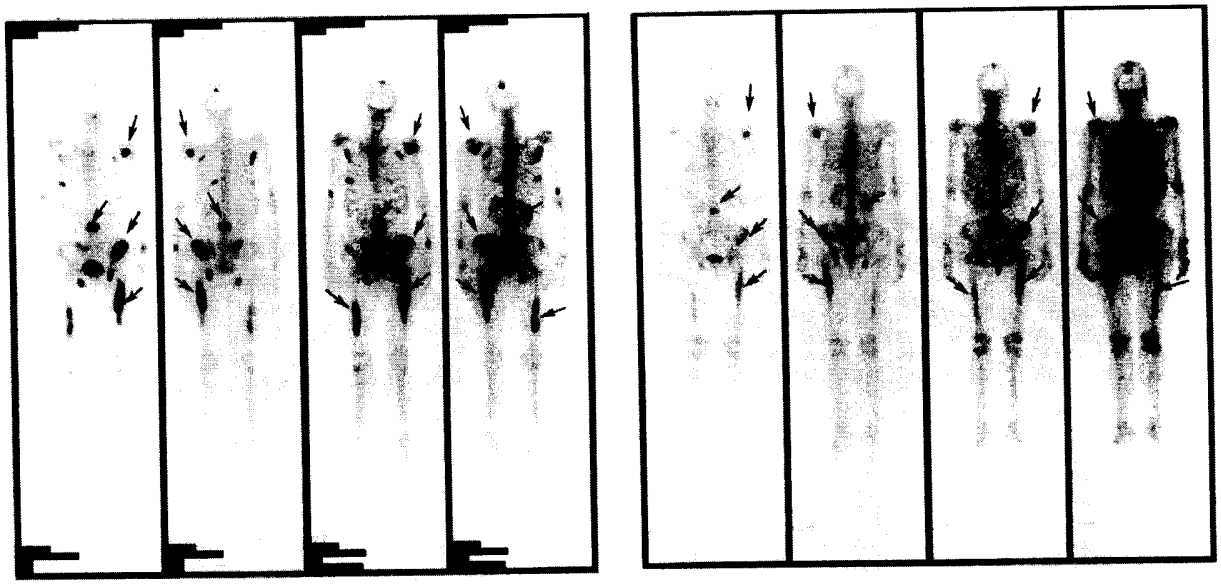


Figure 11



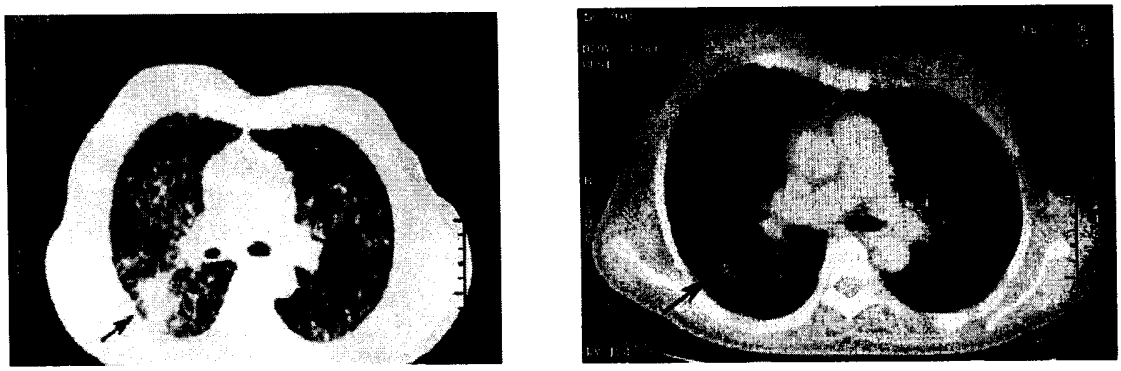
a b

Figure 12



a b

Figure 13

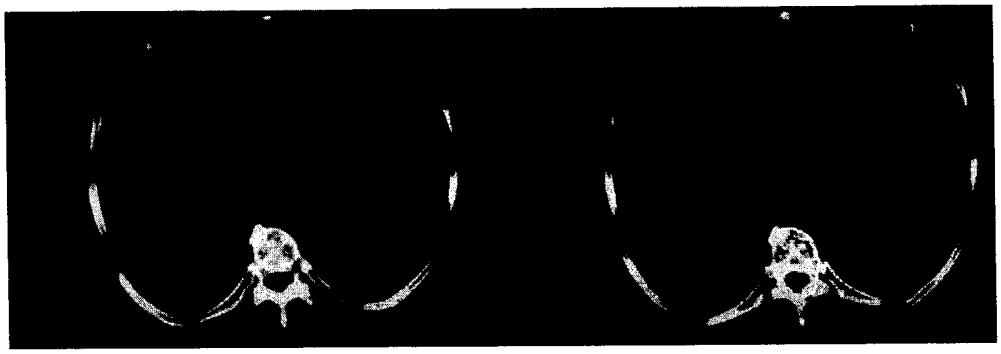


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Figure 14

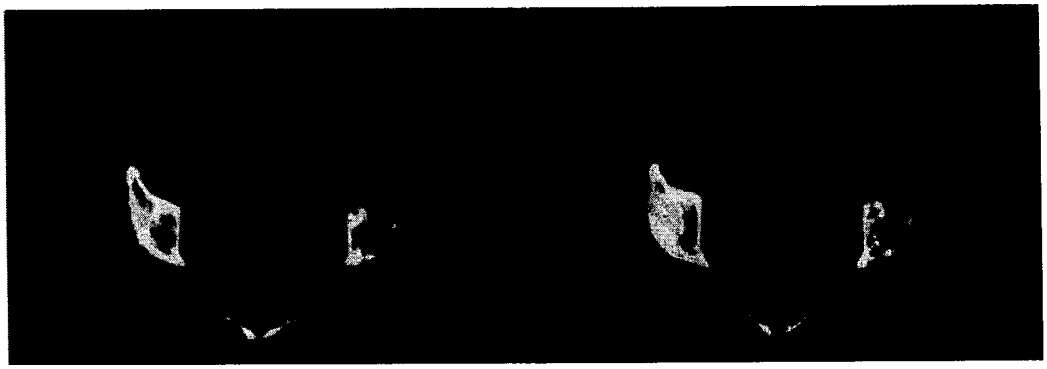


a



b

Figure 15

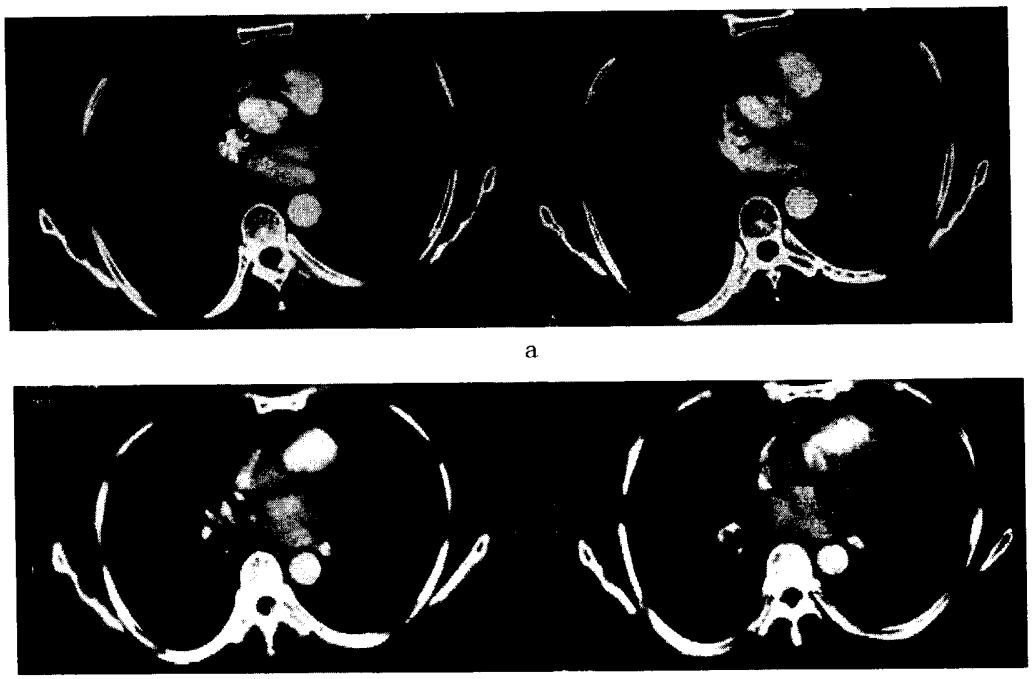


a



b

Figure 16



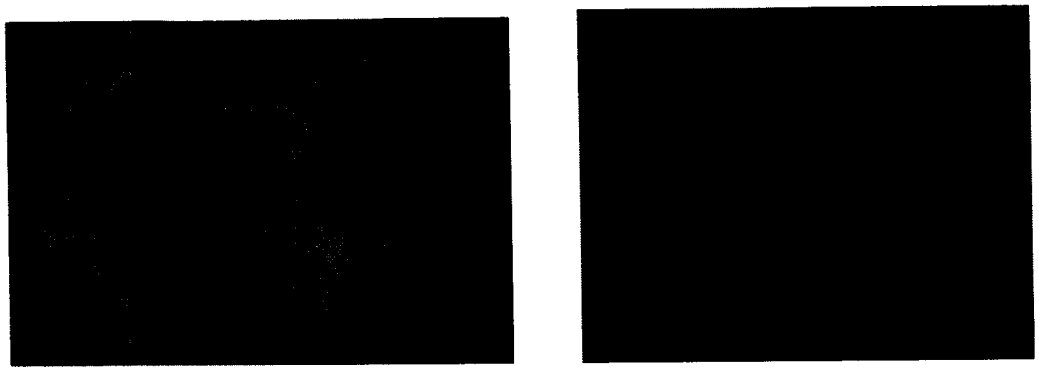
a

b

Figure 17

	Date	Amount of drawn pleural effusion (ml)	Interval (day)
Before the treatment	2006-2-22	800	
	2006-2-24	800	2
	2006-3-2	400	6
	2006-3-6	400	2
	2006-3-10	500	4
Start administration	2006-3-9		
After the treatment	2006-3-28	520	22
	2006-4-11	430	14
	2006-4-29	400	18
	2006-6-5	350	36

Figure 18



a b

Figure 19

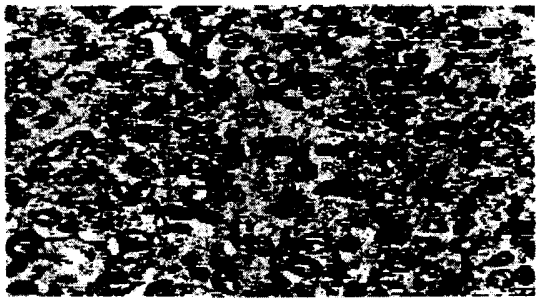
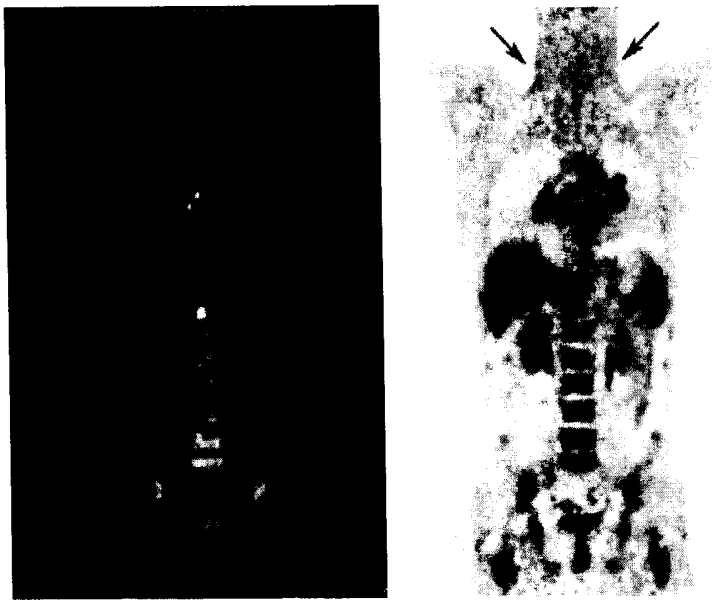


Figure 20



a



b

Figure 21

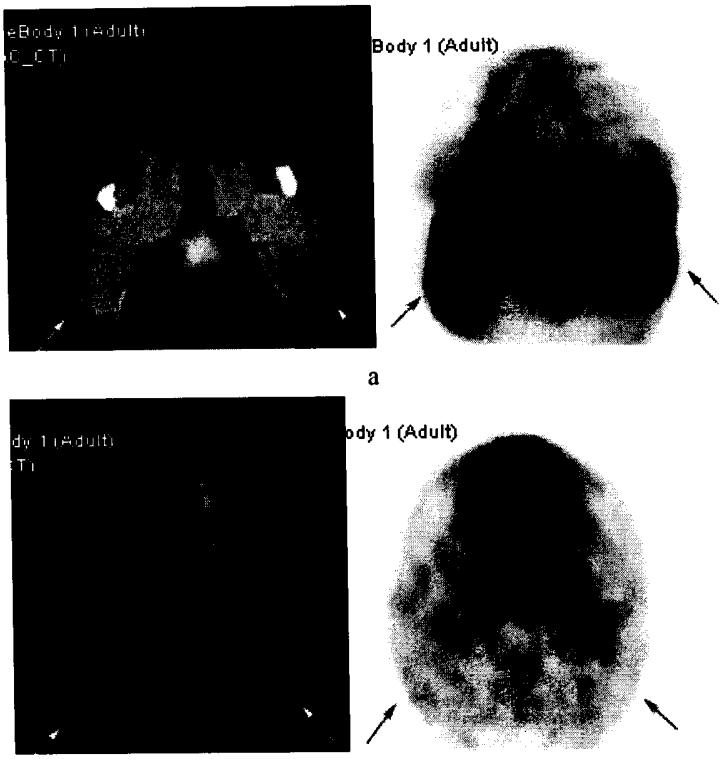


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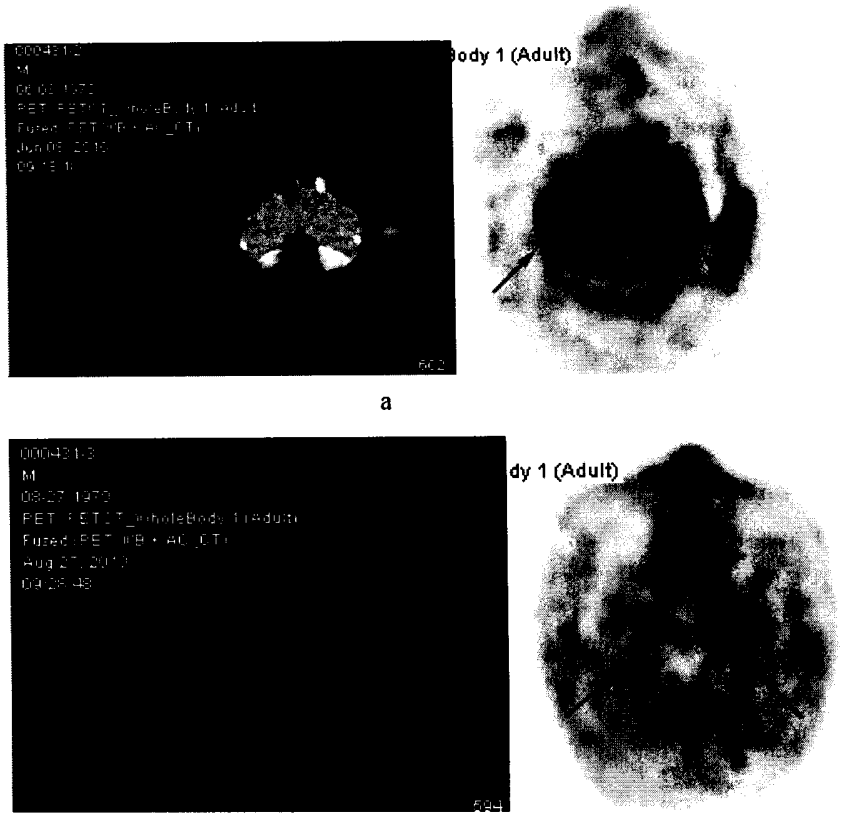
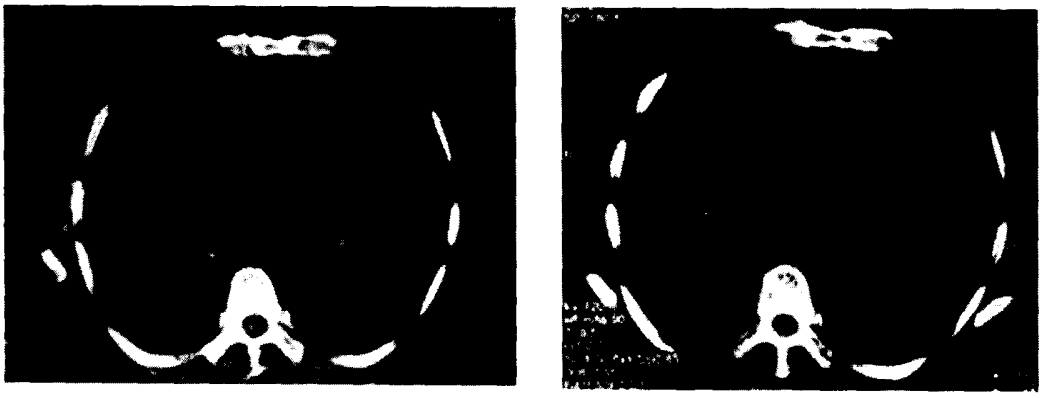
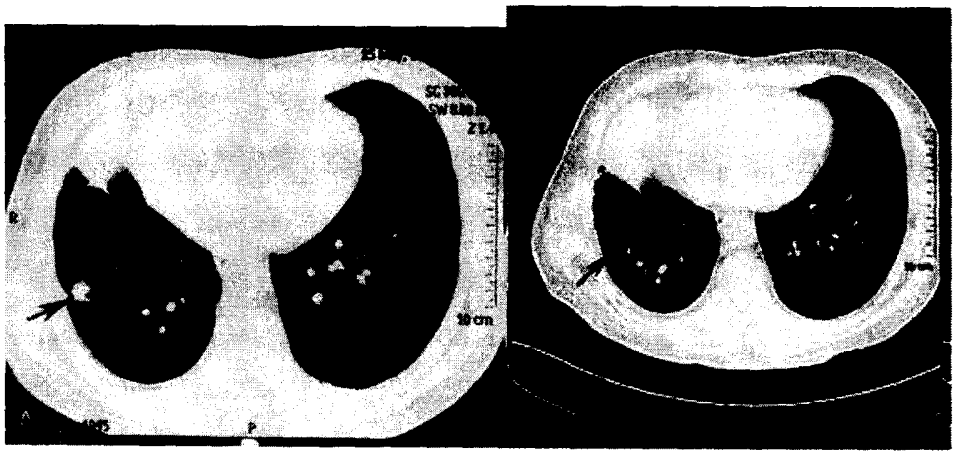


Figure 23



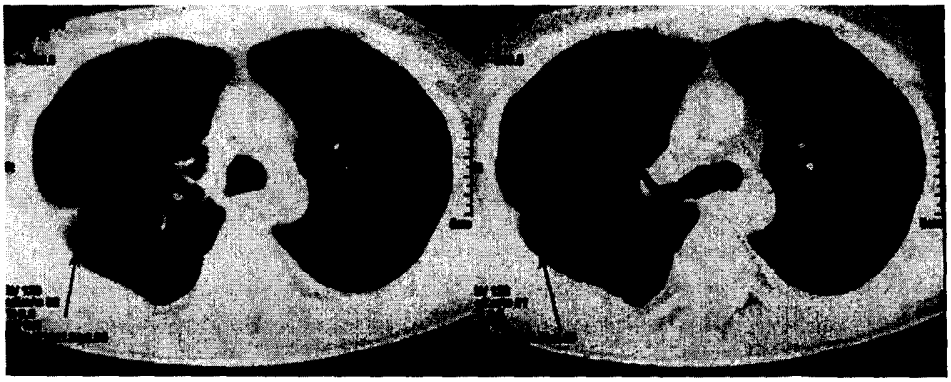
a b

Figure 24

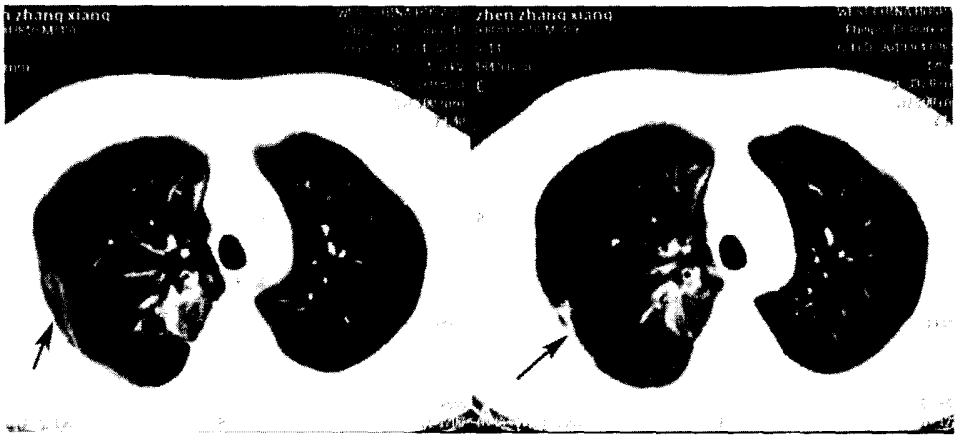


a b

Figure 25

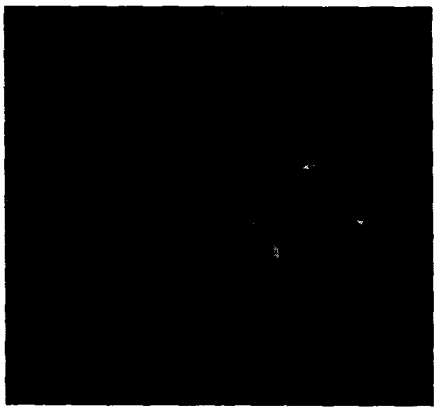


a

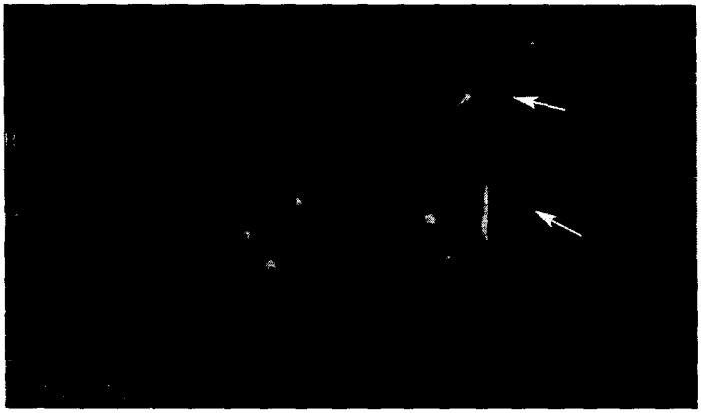


b

Figure 26



a



b

Figure 27

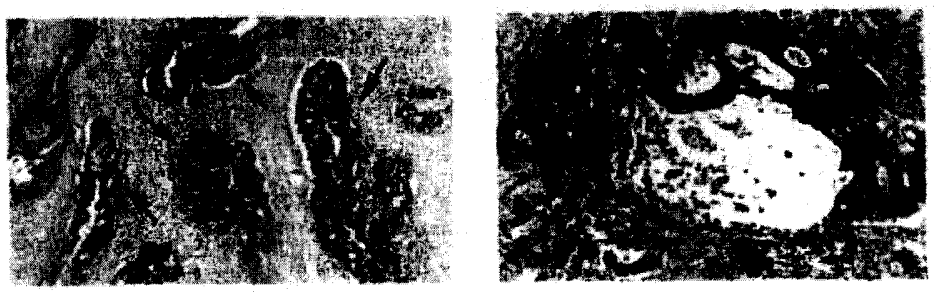
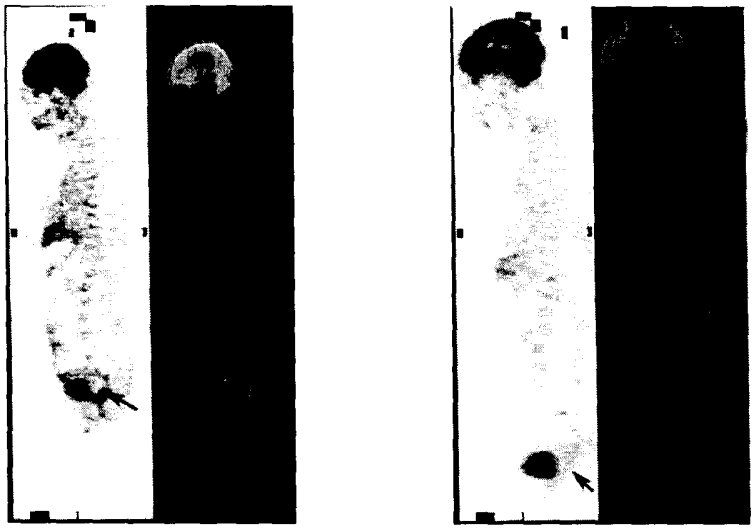


Figure 28



a b

Figure 29

(19)中华人民共和国国家知识产权局

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代理人 张国梁
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权利要求书29页 说明书123页
序列表2页 附图16页

(54)发明名称

用空间构象改变的重组干扰素治疗肿瘤的方法

(57)摘要

本发明提供了用重组干扰素(rSIFN-co)治疗受试者中肿瘤的方法,以及任选地,用于治疗实体瘤例如肺癌的方法,尤其是用药前进行了手术或没有进行手术,以及作为一线或二线单一疗法或与一种或更多种其它抗肿瘤疗法联用治疗实体瘤例如肺癌的方法。本发明进一步提供了包含独特空间构象的重组干扰素(rSIFN-co)单用或联用放疗、化疗和/或一种或更多种抗肿瘤药物例如生物制剂、靶向药物、小分子、中药(TCM)等非手术消除受试者中肿瘤或减小受试者中肿瘤大小,和/或防止术后肿瘤复发和/或转移的方法。

CN 104994866 A

1. 一种治疗受试者中的肿瘤的方法，包括向所述受试者施用由 SEQ ID NO :2 编码的重组干扰素。

2. 根据权利要求 1 的方法，其中所述受试者中的肿瘤包含转移的肿瘤。

3. 根据权利要求 1 或 2 的方法，其中所述受试者是早期、中期或晚期癌症患者，任选地，所述受试者是中期或晚期癌症患者，更任选地，所述受试者是晚期癌症患者。

4. 根据权利要求 1 或 2 的方法，其中所述受试者是 0、I、II、III 或 IV 期癌症患者，任选地，所述受试者是 III 或 IV 期癌症患者。

5. 根据权利要求 1-4 任一的方法，其中所述肿瘤为具备手术指征或适于手术的癌症或实体瘤。

6. 根据权利要求 1-4 任一的方法，其中所述肿瘤为不具备手术指征也不适于手术的癌症或实体瘤。

7. 根据权利要求 1-5 任一的方法，其中所述肿瘤是可切除的肿瘤。

8. 根据权利要求 1-4 和 6 任一的方法，其中所述肿瘤是不可切除的肿瘤。

9. 根据权利要求 7 或 8 的方法，其中所述肿瘤通过手术切除被切除。

10. 根据权利要求 1-9 任一的方法，其中所述肿瘤是实体瘤。

11. 根据权利要求 10 的方法，其中所述实体瘤包括如下的一种或更多种 :肺癌、肝癌、肝细胞癌 (HCC)、食道癌、胆管癌、胆囊癌、胃癌 (stomach cancer)、腹部癌 (abdominal cancer)、胃肠道癌、胃癌 (gastric cancer)、胰腺癌、肾细胞癌、肾癌、骨癌、乳腺癌、卵巢癌、子宫癌、宫颈癌、子宫内膜癌、结直肠癌、结肠癌、直肠癌、膀胱癌、浅表性膀胱癌、前列腺癌、前列腺癌、肾上腺瘤、鳞状细胞癌、神经瘤、恶性神经瘤、肌上皮癌、滑膜肉瘤、横纹肌肉瘤、胃肠道间质细胞瘤、皮肤癌、基底细胞癌、恶性黑色素瘤、甲状腺癌、鼻咽癌、血管瘤、表皮样癌、头颈癌、神经胶质瘤、或卡波济氏肉瘤。

12. 根据权利要求 11 的方法，其中所述实体瘤包括肺癌，任选地，所述肺癌包括小细胞肺癌 (SCLC)、非小细胞肺癌 (NSCLC) 或两者。

13. 根据权利要求 1-4 任一的方法，其中所述肿瘤是非实体瘤。

14. 根据权利要求 13 的方法，其中所述非实体瘤包括如下的一种或更多种 :白血病、急性白血病、慢性白血病、慢性粒细胞性白血病、急性髓性白血病、慢性髓性白血病、慢性淋巴细胞白血病、急性淋巴细胞白血病、T 细胞白血病、毛细胞白血病、红细胞增多症、骨髓增生异常综合征、多发性骨髓瘤、淋巴腺瘤、霍奇金氏淋巴瘤和非霍奇金氏淋巴瘤。

15. 根据权利要求 1-14 任一的方法，其中通过如下至少一种 :全身给药、局部给药 (local administration) 和表面给药 (topical administration)，向受试者施用所述重组干扰素。

16. 根据权利要求 1-15 任一的方法，其中通过给药途径向受试者施用所述重组干扰素，所述给药途径包括如下的一种或更多种 :经口、直肠、舌下、静脉内、动脉内、肌肉、皮下、骨内、皮内、关节内、腹膜内、鞘内、脑内、阴道、经皮、透皮、表皮、粘膜、经眼、经肺、经鼻、腹腔、胸腔、心室内、心包、吸入、瘤内、子宫、浸润和膀胱内给药。

17. 根据权利要求 1-16 任一的方法，其中向所述受试者施用有效量的由 SEQID NO :2 的核苷酸序列编码的重组干扰素，任选地，所述有效量为治疗有效量。

18. 根据权利要求 1-17 任一的方法，其中向所述受试者施用约 2 μg- 约 2000 μg 单次

剂量的所述重组干扰素，任选地，向所述受试者施用约 4 μg- 约 1500 μg 单次剂量的所述重组干扰素，更任选地，向所述受试者施用约 9 μg- 约 1000 μg 单次剂量的所述重组干扰素。

19. 根据权利要求 1-18 任一的方法，其中在一个或更多个治疗周期中施用所述重组干扰素，任选地，所述更多个治疗周期包含 2、3、4、5、6、7、8、9、10 个治疗周期，更任选地，所述治疗周期的数目包含多于 10 个治疗周期。

20. 根据权利要求 19 的方法，其中所述一个治疗周期的持续时间为至少约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、或约 6 年等，或任选地，可长期施用所述重组干扰素，包括受试者生命的整个期间；或者所述重组干扰素治疗的持续时间还可以是约 1 天 - 约 6 年，约 1 周 - 约 4 年，约 2 周 - 约 3 年，约 1 个月 - 约 1 年、或约 2 个月 - 约 9 个月等。

21. 根据权利要求 19 或 20 的方法，其中所述更多个治疗周期中的任意相邻两个治疗周期之间的间隔时间为至少约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、或约 6 年等；或任选地，所述间隔时间可为约 2 天 - 约 6 年，约 4 天 - 约 3 年、约 1 周 - 约 1 年、约 2 个月 - 约 9 个月、或约 3 个月 - 约 6 个月等。

22. 根据权利要求 1-21 任一的方法，其中所述重组干扰素作为单一疗法向受试者施用。

23. 根据权利要求 1-21 任一的方法，进一步包含向所述受试者施用至少一种其它抗癌疗法，任选地，在施用所述重组干扰素之前、同时和 / 或之后给予所述受试者至少一种其它抗癌疗法。

24. 根据权利要求 23 的方法，其中所述至少一种其它抗癌疗法包括如下的至少一种：化学治疗、放射治疗、手术治疗、介入治疗、生物治疗、基因治疗、消融治疗、免疫治疗、靶向治疗和中药治疗。

25. 根据权利要求 24 的方法，其中所述至少一种其它抗癌疗法包括如下的至少一种：化学治疗、放射治疗、手术治疗、靶向治疗和生物治疗。

26. 根据权利要求 25 的方法，其中所述至少一种其它抗癌疗法包括如下的至少一种：化学治疗和放射治疗。

27. 根据权利要求 24-26 任一的方法，其中所述化学治疗作为一线化学治疗被给予，任选地，所述一线化学治疗使用的一种或更多种化学治疗剂包括铂类化合物，例如顺铂。

28. 根据权利要求 24-27 任一的方法，其中所述靶向治疗包括如下的至少一种：吉非替尼、厄洛替尼和重组人血管内皮抑制素。

29. 根据权利要求 1-28 任一的方法，其中与治疗前的肿瘤相比，所述治疗消除了所述肿瘤或减小了所述肿瘤的大小。

30. 根据权利要求 29 的方法，其中所述肿瘤的大小的减小将所述肿瘤转变为可切除的肿瘤。

31. 根据权利要求 30 的方法，其中所述肿瘤具有手术切除指征。

32. 根据权利要求 1-28 任一的方法，其中所述肿瘤例如癌症或实体瘤由较早的不具备手术指征也不适于手术转变为具备手术指征或适于手术。

33. 根据权利要求 32 的方法，进一步包括进行手术以切除所述肿瘤。

34. 根据权利要求 30-31 和 33 任一的方法，进一步包括在切除所述肿瘤后给予受试者所述重组干扰素以防止肿瘤复发和 / 或转移，或者延长或维持无瘤状态，任选地，给予受试者预防有效量的所述重组干扰素以防止肿瘤复发和 / 或转移，和 / 或延长或维持无瘤状态。

35. 一种治疗受试者中肿瘤的方法，包括向所述受试者施用由 SEQ ID NO :2 编码的重组干扰素以及至少一种其它抗癌疗法，其中在施用所述重组干扰素之前、同时和 / 或之后给予所述受试者至少一种其它抗癌疗法，以及其中所述肿瘤为不具备手术指征也不适于手术的癌症或实体瘤，或所述肿瘤为不可切除的实体瘤，并且与治疗前的肿瘤相比，所述重组干扰素和至少一种其它抗癌疗法的联用消除了所述肿瘤或减小了所述肿瘤的大小。

36. 根据权利要求 35 的方法，其中所述受试者是中、晚期癌症患者，或 III 或 IV 期癌症患者，任选地，所述受试者是晚期或 III 或 IV 期癌症患者。

37. 根据权利要求 1-29 和 35-36 任一的方法，其中所述治疗方法为非手术治疗方法。

38. 一种在具有肿瘤的受试者经至少一种抗癌疗法后防止肿瘤复发和 / 或转移，或者延长或维持无瘤状态的方法，包括向所述受试者施用由 SEQ ID NO :2 编码的重组干扰素。

39. 根据权利要求 38 的方法，其中所述受试者中的肿瘤包含转移的肿瘤。

40. 根据权利要求 38 或 39 的方法，其中所述受试者是早期、中期或晚期癌症患者。

41. 根据权利要求 38 或 39 的方法，其中所述受试者是 0、I、II、III 或 IV 期癌症患者。

42. 根据权利要求 38-41 任一的方法，其中所述肿瘤为具备手术指征或适于手术的癌症或实体瘤。

43. 根据权利要求 38-41 任一的方法，其中所述肿瘤为不具备手术指征也不适于手术的癌症或实体瘤。

44. 根据权利要求 38-41 任一的方法，其中所述肿瘤是可切除的肿瘤。

45. 根据权利要求 38-41 任一的方法，其中所述肿瘤是不可切除的肿瘤。

46. 根据权利要求 44 或 45 的方法，其中所述肿瘤通过手术切除被切除。

47. 根据权利要求 38-46 任一的方法，其中所述肿瘤是实体瘤。

48. 根据权利要求 47 的方法，其中所述实体瘤包括如下的一种或更多种 :肺癌、肝癌、肝细胞癌 (HCC)、食道癌、胆管癌、胆囊癌、胃癌 (stomach cancer)、腹部癌 (abdominal cancer)、胃肠道癌、胃癌 (gastric cancer)、胰腺癌、肾细胞癌、肾癌、骨癌、乳腺癌、卵巢癌、子宫癌、宫颈癌、子宫内膜癌、结直肠癌、结肠癌、直肠癌、膀胱癌、浅表性膀胱癌、前列腺癌、前列腺癌、肾上腺瘤、鳞状细胞癌、神经瘤、恶性神经瘤、肌上皮癌、滑膜肉瘤、横纹肌肉瘤、胃肠道间质细胞瘤、皮肤癌、基底细胞癌、恶性黑色素瘤、甲状腺癌、鼻咽癌、血管瘤、表皮样癌、头颈癌、神经胶质瘤、或卡波济氏肉瘤。

49. 根据权利要求 48 的方法，其中所述实体瘤包括肺癌，任选地，所述肺癌包括小细胞肺癌 (SCLC)、非小细胞肺癌 (NSCLC) 或两者。

50. 根据权利要求 38-41 任一的方法，其中所述肿瘤包括非实体瘤。

51. 根据权利要求 50 的方法，其中所述非实体瘤包括如下的一种或更多种 :白血病、急性白血病、慢性白血病、慢性粒细胞性白血病、急性髓性白血病、慢性髓性白血病、慢性淋巴

细胞白血病、急性淋巴细胞白血病、T 细胞白血病、毛细胞白血病、红细胞增多症、骨髓增生异常综合征、多发性骨髓瘤、淋巴腺瘤、霍奇金氏淋巴瘤和非霍奇金氏淋巴瘤。

52. 根据权利要求 38-51 任一的方法，其中通过如下至少一种：全身给药、局部给药 (local administration) 和表面给药 (topical administration)，向受试者施用所述重组干扰素。

53. 根据权利要求 38-52 任一的方法，其中通过给药途径向受试者施用所述重组干扰素，所述给药途径包括如下的一种或更多种：经口、直肠、舌下、静脉内、动脉内、肌肉、皮下、骨内、皮内、关节内、腹膜内、鞘内、脑内、阴道、经皮、透皮、表皮、粘膜、经眼、经肺、经鼻、腹腔、胸腔、心室内、心包、吸入、瘤内、子宫、浸润和膀胱内给药。

54. 根据权利要求 38-53 任一的方法，其中向所述受试者施用有效量的由 SEQ ID NO：2 的核苷酸序列编码的重组干扰素，任选地，所述有效量为预防有效量。

55. 根据权利要求 38-54 任一的方法，其中向所述受试者施用约 2 μg- 约 2000 μg 单次剂量的所述重组干扰素，任选地，向所述受试者施用约 4 μg- 约 1500 μg 单次剂量的所述重组干扰素，更任选地，向所述受试者施用约 9 μg- 约 1000 μg 单次剂量的所述重组干扰素。

56. 根据权利要求 38-55 任一的方法，其中在一个或更多个预防周期中施用所述重组干扰素，任选地，所述更多个预防周期包含 2、3、4、5、6、7、8、9 或 10 个预防周期，或任选地，多于 10 个预防周期。

57. 根据权利要求 56 的方法，其中每个预防周期的持续时间为至少约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、或约 6 年等，或长期施用所述重组干扰素，包括受试者生命的整个期间；或者所述持续时间还可以是约 1 天 - 约 6 年，约 1 周 - 约 4 年，约 2 周 - 约 3 年，约 1 个月 - 约 1 年、或约 2 个月 - 约 9 个月等。

58. 根据权利要求 56 或 57 的方法，其中所述更多个预防周期中的任意相邻两个预防周期之间的间隔时间为至少约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、或约 6 年等；或者所述间隔时间还可以为约 2 天 - 约 6 年，约 4 天 - 约 3 年、约 1 周 - 约 1 年、约 2 个月 - 约 9 个月、或约 3 个月 - 约 6 个月等。

59. 根据权利要求 38-58 任一的方法，其中所述至少一种抗癌疗法包括如下的至少一种：化学治疗、放射治疗、手术治疗、介入治疗、生物治疗、基因治疗、消融治疗、免疫治疗、靶向治疗和中药治疗，任选地，所述至少一种抗癌疗法包括如下的至少一种：化学治疗、放射治疗、手术治疗和生物治疗。

60. 根据权利要求 59 的方法，其中所述至少一种抗癌疗法包括手术治疗。

61. 根据权利要求 60 的方法，其中向所述手术治疗的手术部位施用所述重组干扰素。

62. 根据权利要求 61 的方法，其中经表面 (topical) 或局部 (local) 给药向手术部位施用所述重组干扰素。

63. 根据权利要求 61 或 62 的方法，其中通过给药途径向手术部位施用所述重组干扰素，所述给药途径包括如下的一种或更多种：浸润给药、胸腔给药、腹腔给药、心包给药、子

宫给药、膀胱内给药、瘤内给药、经肺给药、经鼻给药、经皮给药、透皮给药、表皮给药和粘膜给药。

64. 根据权利要求 63 的方法，其中所述胸腔给药、腹腔给药、心包给药、子宫给药或膀胱内给药分别包括胸腔灌注给药、腹腔灌注给药、心包灌注给药、子宫灌注给药或膀胱内灌注给药。

65. 根据权利要求 63 的方法，其中所述瘤内给药包括瘤内注射。

66. 根据权利要求 63 的方法，其中所述经肺给药或经鼻给药分别包括经肺吸入给药或经鼻吸入给药。

67. 根据权利要求 63 的方法，其中所述经皮给药、透皮给药、表皮给药或粘膜给药分别包括经皮喷雾给药、透皮喷雾给药、表皮喷雾给药或粘膜喷雾给药。

68. 根据权利要求 62-67 任一的方法，其中在表面 (topical) 或局部 (local) 给药所述重组干扰素的之前、同时和 / 或之后，经全身给药向所述受试者进一步施用所述重组干扰素。

69. 根据权利要求 68 的方法，其中所述全身给药包括如下的至少一种 ：皮下和肌肉给药。

70. 根据权利要求 38-69 任一的方法，其中所述重组干扰素作为单一疗法向受试者施用。

71. 一种非手术消除受试者中肿瘤或减小受试者中肿瘤的大小的方法，包括向所述受试者施用由 SEQ ID NO ：2 编码的重组干扰素。

72. 根据权利要求 71 的方法，其中所述肿瘤为具备手术指征或适于手术的癌症或实体瘤。

73. 根据权利要求 71 的方法，其中所述肿瘤为不具备手术指征也不适于手术的癌症或实体瘤。

74. 根据权利要求 71 的方法，其中所述肿瘤是可切除的肿瘤。

75. 根据权利要求 71 的方法，其中所述肿瘤是不可切除的肿瘤。

76. 根据权利要求 74 或 75 的方法，其中所述肿瘤通过手术切除被切除。

77. 根据权利要求 71-76 任一的方法，其中所述受试者是早期、中期或晚期癌症患者，任选地，所述受试者是中期或晚期癌症患者，或更任选地，所述受试者是晚期癌症患者。

78. 根据权利要求 71-76 任一的方法，其中所述受试者是 0、I、II、III 或 IV 期癌症患者，任选地，所述受试者是 III 或 IV 期癌症患者。

79. 根据权利要求 71-78 任一的方法，其中所述受试者是中期或晚期癌症患者，或 III 或 IV 期癌症患者，任选地，所述受试者是晚期或 III 或 IV 期癌症患者。

80. 根据权利要求 71-79 任一的方法，其中所述肿瘤为实体瘤。

81. 根据权利要求 80 的方法，其中所述实体瘤包括如下的一种或更多种 ：肺癌、肝癌、肝细胞癌 (HCC)、食道癌、胆管癌、胆囊癌、胃癌 (stomach cancer)、腹部癌 (abdominal cancer)、胃肠道癌、胃癌 (gastric cancer)、胰腺癌、肾细胞癌、肾癌、骨癌、乳腺癌、卵巢癌、子宫癌、宫颈癌、子宫内膜癌、结直肠癌、结肠癌、直肠癌、膀胱癌、浅表性膀胱癌、前列腺癌、前列腺癌、肾上腺瘤、鳞状细胞癌、神经瘤、恶性神经瘤、肌上皮癌、滑膜肉瘤、横纹肌肉瘤、胃肠道间质细胞瘤、皮肤癌、基底细胞癌、恶性黑色素瘤、甲状腺癌、鼻咽癌、血管瘤、表

皮样癌、头颈癌、神经胶质瘤、或卡波济氏肉瘤。

82. 根据权利要求 81 的方法，其中所述实体瘤包括肺癌，任选地，所述肺癌包括小细胞肺癌 (SCLC)、非小细胞肺癌 (NSCLC) 或两者。

83. 根据权利要求 71-82 任一的方法，其中通过如下至少一种 ：全身给药、局部给药 (local administration) 和表面给药 (topical administration)，向受试者施用所述重组干扰素，任选地，通过表面或局部给药向受试者施用所述重组干扰素，更任选地，通过局部给药向受试者施用所述重组干扰素。

84. 根据权利要求 71-83 任一的方法，其中通过给药途径向所述受试者施用所述重组干扰素，所述给药途径包括如下的一种或更多种 ：浸润给药、胸腔给药、腹腔给药、心包给药、子宫给药、膀胱内给药、瘤内给药、经肺给药、经鼻给药、经皮给药、透皮给药、表皮给药和粘膜给药。

85. 根据权利要求 84 的方法，其中所述瘤内给药包括瘤内注射。

86. 根据权利要求 85 的方法，其中所述重组干扰素以如下范围的量施用 ：一次瘤内注射约 60 μ g- 约 600 μ g，任选地，约 60 μ g- 约 500 μ g，更任选地，约 80 μ g- 约 400 μ g，还更任选地，约 100 μ g- 约 250 μ g。

87. 根据权利要求 85 或 86 的方法，其中每约 1 天 - 约 10 天，任选地，每约 1 天 - 约 7 天，例如每约 1、2、3、4、5、6 或 7 天瘤内注射一次所述重组干扰素。

88. 根据权利要求 84-87 任一的方法，其中瘤内给药的给药方案如下 ：每约 1 天瘤内注射一次所述重组干扰素，持续约 4 次 - 约 8 次，接着每约 3 天 - 约 5 天瘤内注射一次所述重组干扰素，持续约 4 次 - 约 8 次，然后每约 7 天瘤内注射一次所述重组干扰素，当瘤体消失或瘤体小至无法进行瘤内注射时，停止瘤内给药。

89. 根据权利要求 84 的方法，其中所述胸腔给药、腹腔给药、心包给药、子宫给药或膀胱内给药分别包括胸腔灌注给药、腹腔灌注给药、心包灌注给药、子宫灌注给药或膀胱内灌注给药。

90. 根据权利要求 84 的方法，其中所述经肺给药或经鼻给药分别包括经肺吸入给药或经鼻吸入给药。

91. 根据权利要求 84 的方法，其中所述经皮给药、透皮给药、表皮给药或粘膜给药分别包括经皮喷雾给药、透皮喷雾给药、表皮喷雾给药或粘膜喷雾给药。

92. 根据权利要求 83-91 任一的方法，其中在表面或局部给药所述重组干扰素的之前、同时和 / 或之后，经全身给药向所述受试者进一步施用所述重组干扰素，和 / 或经表面给药、局部给药和 / 或全身给药向所述受试者施用至少一种其它治疗药物。

93. 根据权利要求 92 的方法，其中在表面或局部给药所述重组干扰素的同时和 / 或之后，经全身给药向所述受试者进一步施用所述重组干扰素，和 / 或经表面给药、局部给药和 / 或全身给药向所述受试者施用至少一种其它治疗药物。

94. 根据权利要求 92 或 93 的方法，其中所述至少一种其它治疗药物包括至少一种抗肿瘤药物。

95. 根据权利要求 94 的方法，其中所述至少一种抗肿瘤药物包括一种或更多种化学治疗剂、靶向药物和 / 或生物制剂。

96. 根据权利要求 95 的方法，其中所述一种或更多种化学治疗剂包括铂类化合物，例

如顺铂。

97. 根据权利要求 95 的方法，其中所述一种或更多种靶向药物包括吉非替尼、厄洛替尼和 / 或重组人血管内皮抑制素。

98. 一种消除或减少具有肿瘤的受试者中的胸腔积液、腹腔积液和 / 或心包积液的方法，包括向所述受试者给予由 SEQ ID NO :2 编码的重组干扰素。

99. 根据权利要求 98 的方法，其中所述肿瘤为具备手术指征或适于手术的癌症或实体瘤。

100. 根据权利要求 98 的方法，其中所述肿瘤为不具备手术指征也不适于手术的癌症或实体瘤。

101. 根据权利要求 98 的方法，其中所述肿瘤是可切除的肿瘤。

102. 根据权利要求 98 的方法，其中所述肿瘤是不可切除的肿瘤。

103. 根据权利要求 101 或 102 的方法，其中所述肿瘤通过手术切除被切除。

104. 根据权利要求 98-103 任一的方法，其中所述受试者是早期、中期或晚期癌症患者，任选地，所述受试者是中期或晚期癌症患者，或更任选地，所述受试者是晚期癌症患者。

105. 根据权利要求 98-103 任一的方法，其中所述受试者是 0、I、II、III 或 IV 期癌症患者，任选地，所述受试者是 III 或 IV 期癌症患者。

106. 根据权利要求 98-105 任一的方法，其中所述受试者是中期或晚期癌症患者，或 III 或 IV 期癌症患者，任选地，所述受试者是晚期或 III 或 IV 期癌症患者。

107. 根据权利要求 98-106 任一的方法，其中所述肿瘤为实体瘤。

108. 根据权利要求 107 的方法，其中所述实体瘤包括如下的一种或更多种 :肺癌、肝癌、肝细胞癌 (HCC)、食道癌、胆管癌、胆囊癌、胃癌 (stomach cancer)、腹部癌 (abdominal cancer)、胃肠道癌、胃癌 (gastric cancer)、胰腺癌、肾细胞癌、肾癌、骨癌、乳腺癌、卵巢癌、子宫癌、宫颈癌、子宫内膜癌、结直肠癌、结肠癌、直肠癌、膀胱癌、浅表性膀胱癌、前列腺癌、前列腺癌、肾上腺瘤、鳞状细胞癌、神经瘤、恶性神经瘤、肌上皮癌、滑膜肉瘤、横纹肌肉瘤、胃肠道间质细胞瘤、皮肤癌、基底细胞癌、恶性黑色素瘤、甲状腺癌、鼻咽癌、血管瘤、表皮样癌、头颈癌、神经胶质瘤、或卡波济氏肉瘤。

109. 根据权利要求 108 的方法，其中所述实体瘤包括肺癌，任选地，所述肺癌包括小细胞肺癌 (SCLC)、非小细胞肺癌 (NSCLC) 或两者。

110. 根据权利要求 98-109 任一的方法，其中所述胸腔积液为恶性胸腔积液，所述腹腔积液为恶性腹腔积液，和 / 或所述心包积液为恶性心包积液。

111. 根据权利要求 98-110 任一的方法，其中通过如下至少一种 :全身给药、局部给药 (local administration) 和表面给药 (topical administration)，向受试者施用所述重组干扰素，任选地，通过表面给药和局部给药向受试者施用所述重组干扰素，更任选地，通过局部给药向受试者施用所述重组干扰素

112. 根据权利要求 98-111 任一的方法，其中通过给药途径向所述受试者施用所述重组干扰素，所述给药途径包括如下的一种或更多种 :浸润给药、胸腔给药、腹腔给药和心包给药。

113. 根据权利要求 98-112 任一的方法，其中通过灌注进行所述给药。

114. 根据权利要求 111-113 任一的方法，其中所述重组干扰素以如下范围的量施用 :

一次表面或局部给药约 30 μg- 约 2000 μg，任选地，约 100 μg- 约 1500 μg，更任选地，约 150 μg- 约 1000 μg，还任选地，约 200 μg- 约 800 μg，还更任选地，约 200 μg- 约 400 μg。

115. 根据权利要求 111-114 任一的方法，其中每约 1- 约 10 天，任选地，每约 1- 约 7 天，例如每约 1、2、3、4、5、6 或 7 天表面或局部给药一次所述重组干扰素。

116. 根据权利要求 111-115 任一的方法，其中在表面或局部给药所述重组干扰素的之前、同时和 / 或之后，经全身给药向所述受试者进一步施用所述重组干扰素，和经表面给药、局部给药和 / 或全身给药向所述受试者施用至少一种其它治疗药物。

117. 根据权利要求 116 的方法，其中在表面或局部给药所述重组干扰素的同时和 / 或之后，经全身给药向所述受试者进一步施用所述重组干扰素，和经表面给药、局部给药和 / 或全身给药向所述受试者施用至少一种其它治疗药物。

118. 根据权利要求 116 或 117 的方法，其中所述至少一种其它治疗药物包括抗肿瘤药物。

119. 根据权利要求 118 的方法，其中所述抗肿瘤药物包括如下的至少一种 ：化学治疗剂、靶向药物和生物制剂。

120. 根据权利要求 119 的方法，其中所述至少一种化学治疗剂包括至少一种铂类化合物，例如顺铂。

121. 根据权利要求 119 的方法，其中所述至少一种靶向药物包括如下的至少一种 ：吉非替尼、厄洛替尼和重组人血管内皮抑制素。

122. 根据权利要求 98-121 任一的方法，其中与治疗前的肿瘤相比，所述治疗消除了所述肿瘤或减小了所述肿瘤的大小。

123. 根据权利要求 98-122 任一的方法，其中所述治疗为非手术治疗。

124. 一种治疗受试者中的肿瘤的方法，包括通过表面或局部给药向受试者的肿瘤病灶施用由 SEQ ID NO ：2 编码的重组干扰素。

125. 根据权利要求 124 的方法，其中所述肿瘤病灶包括肿瘤转移病灶。

126. 一种消除或减小受试者中的肿瘤转移病灶的方法，包括通过表面或局部给药向受试者的肿瘤转移病灶施用由 SEQ ID NO ：2 编码的重组干扰素。

127. 根据权利要求 124-126 任一的方法，其中所述肿瘤病灶包括如下的至少一种 ：骨病灶、肌肉病灶、皮下组织病灶、前列腺病灶和淋巴结病灶，以及所述肿瘤转移病灶包括如下的至少一种 ：骨转移病灶、肌肉转移病灶、皮下组织转移病灶、前列腺转移病灶和淋巴结转移病灶，任选地，所述肿瘤转移病灶包括骨转移病灶。

128. 根据权利要求 124-127 任一的方法，其中所述受试者是中期、晚期或 III 或 IV 期癌症患者，任选地，所述受试者是晚期或 III 或 IV 期癌症患者。

129. 根据权利要求 124-127 任一的方法，其中所述肿瘤或肿瘤转移病灶包括不具备手术指征也不适于手术的癌症或实体瘤。

130. 根据权利要求 124-129 任一的方法，其中所述表面或局部给药包括如下的至少一种 ：浸润给药、经皮给药、透皮给药、表皮给药和粘膜给药，任选地，所述表面和局部给药包括透皮给药或浸润给药。

131. 根据权利要求 130 的方法，其中所述浸润给药包括如下的至少一种 ：经皮浸润给药、表皮浸润给药、透皮浸润给药和粘膜浸润给药。

132. 根据权利要求 130 的方法，其中所述经皮给药、透皮给药、表皮给药或粘膜给药分别包括经皮喷雾给药、透皮喷雾给药、表皮喷雾给药或粘膜喷雾给药。

133. 根据权利要求 124-132 任一的方法，其中所述重组干扰素以如下范围的量施用：一次表面或局部给药约 2μg- 约 2000μg，任选地，约 4μg- 约 1500μg，更任选地，约 9μg- 约 1000μg。

134. 根据权利要求 124-133 任一的方法，其中每天向受试者表面或局部给药约 1、2、3、4、5、6、7、8 或更多次重组干扰素，或者每约 2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20 或 21 天、每个月、每 2 月或更久的时间间隔向受试者表面或局部给药 1 次重组干扰素。

135. 根据权利要求 130-134 任一的方法，其中当通过喷雾给药进行表面或局部给药时，所述重组干扰素以如下范围的量施用：一次喷雾给药约 6μg- 约 100μg，任选地，约 10μg- 约 40μg，更任选地，约 20μg- 约 40μg。

136. 根据权利要求 135 的方法，其中每天喷雾给药约 1- 约 6 次，例如约 1、2、3、4、5 或 6 次重组干扰素。

137. 根据权利要求 124-136 任一的方法，其中在表面或局部给药所述重组干扰素的之前、同时和 / 或之后，经全身给药向所述受试者施用所述重组干扰素和 / 或一种或更多种其它治疗药物。

138. 根据权利要求 137 的方法，其中所述全身给药包括皮下和 / 或肌肉给药。

139. 根据权利要求 138 的方法，其中所述皮下给药包括皮下注射。

140. 根据权利要求 138 的方法，其中所述肌肉给药包括肌肉注射。

141. 根据权利要求 138-140 任一的方法，其中以约 2μg/ 次 - 约 10μg/ 次，任选地，约 4μg/ 次 - 约 10μg/ 次，更任选地，约 4.5μg/ 次 - 约 9μg/ 次，例如约 4.5μg/ 次或约 9μg/ 次的诱导剂量通过皮下给药和 / 或肌肉给药施用一次或更多次所述重组干扰素，之后以约 10μg/ 次 - 约 70μg/ 次，任选地，约 12μg/ 次 - 约 50μg/ 次，更任选地，约 12μg/ 次 - 约 30μg/ 次的治疗剂量通过皮下给药和 / 或肌肉给药施用多次所述重组干扰素。

142. 根据权利要求 141 的方法，其中施用诱导剂量与施用治疗剂量之间的间隔为约 1 天 - 约 1 个月，任选地，约 1 天 - 约 1 周，更任选地，约 1 天 - 约 3 天，包括，例如约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、或约 1 个月。

143. 根据权利要求 141 或 142 的方法，其中当多次施用诱导剂量的重组干扰素时，每约 1 天 - 约 10 天施用一次所述重组干扰素，任选地，每约 1 天 - 约 7 天施用一次所述重组干扰素，更任选地，每约 1- 约 2 天施用一次所述重组干扰素，包括，例如每约 1、2、3、4、5、6、7、8、9 或 10 天施用一次所述重组干扰素。

144. 根据权利要求 141-143 任一的方法，其中每约 1 天 - 约 10 天施用一次治疗剂量的重组干扰素，任选地，每约 1 天 - 约 7 天施用一次治疗剂量的重组干扰素，更任选每约 1- 约 2 天施用一次治疗剂量的重组干扰素，包括，例如每约 1、2、3、4、5、6、7、8、9 或 10 天施用一次治疗剂量的重组干扰素。

145. 根据权利要求 141-144 任一的方法，其中诱导剂量和治疗剂量的施用的持续时间为至少约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个

月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年或约 6 年等，或者可长期施用所述重组干扰素，包括患者生命的整个期间。

146. 根据权利要求 124-145 任一的方法，其中所述重组干扰素作为单一疗法向受试者施用。

147. 根据权利要求 124-145 任一的方法，进一步包括向所述受试者施用至少一种其它抗癌疗法，任选地，在施用所述重组干扰素之前、同时和 / 或之后给予所述受试者至少一种其它抗癌疗法。

148. 根据权利要求 147 的方法，其中所述至少一种其它抗癌疗法包括如下的一种或更多种 ：化学治疗、放射治疗、手术治疗、介入治疗、生物治疗、基因治疗、消融治疗、免疫治疗、靶向治疗和中药治疗。

149. 根据权利要求 124-148 任一的方法，其中与治疗前的肿瘤或肿瘤转移病灶相比，所述重组干扰素治疗和 / 或至少一种其它抗癌疗法消除了所述肿瘤或肿瘤转移病灶，或减小了所述肿瘤或肿瘤转移病灶的大小。

150. 一种消除或减小受试者中的肿瘤骨转移病灶的方法，包括通过表面或局部给药向受试者施用由 SEQ ID NO :2 编码的重组干扰素，其中所述表面或局部给药包括透皮给药和 / 或浸润给药，任选地，向所述受试者的肿瘤骨转移病灶施用所述重组干扰素。

151. 一种消除或减小受试者中的肿瘤骨病灶如肿瘤骨转移病灶、肌肉病灶如肌肉转移病灶、皮下组织病灶如皮下组织转移病灶、前列腺病灶如前列腺转移病灶和 / 或淋巴结病灶如淋巴结转移病灶的方法，包括通过任何透过皮肤的给药途径向所述受试者施用由 SEQ ID NO :2 编码的重组干扰素，以消除或减小所述肿瘤骨病灶如肿瘤骨转移病灶、肌肉病灶如肌肉转移病灶、皮下组织病灶如皮下组织转移病灶、前列腺病灶如前列腺转移病灶和 / 或淋巴结病灶如淋巴结转移病灶，任选地，向所述受试者的肿瘤转移病灶施用所述重组干扰素。

152. 根据权利要求 124-151 任一的方法，其中所述治疗方法为非手术治疗方法。

153. 一种治疗受试者中的肺癌的方法，包括向所述受试者施用由 SEQ ID NO :2 编码的重组干扰素。

154. 根据权利要求 153 的方法，其中肺癌包括小细胞肺癌 (SCLC)、非小细胞肺癌 (NSCLC) 或两者。

155. 根据权利要求 153 或 154 的方法，其中所述受试者中的肺癌包含转移的肿瘤。

156. 根据权利要求 153-155 任一的方法，其中所述受试者是是早期、中期或晚期癌症患者，任选地，所述受试者是中期或晚期癌症患者，更任选地，所述受试者是晚期癌症患者。

157. 根据权利要求 153-155 任一的方法，其中所述受试者是 0、I、II、III 或 IV 期癌症患者，任选地，所述受试者是 III 或 IV 期癌症患者。

158. 根据权利要求 153-157 任一的方法，其中所述肺癌包含具备手术指征或适于手术的肺癌。

159. 根据权利要求 153-157 任一的方法，其中所述肺癌包含不具备手术指征也不适于手术的肺癌。

160. 根据权利要求 153-157 任一的方法，其中所述肺癌包括可切除的肺癌。

161. 根据权利要求 153-157 任一的方法，其中所述肺癌包括不可切除的肺癌。

162. 根据权利要求 160 或 161 的方法，其中所述肺癌通过手术切除被切除。

163. 根据权利要求 153-162 任一的方法，其中向所述受试者施用有效量的由 SEQ ID NO :2 的核苷酸序列编码的重组干扰素，任选地，所述有效量为治疗有效量。

164. 根据权利要求 153-163 任一的方法，其中通过如下至少一种 :全身给药、表面给药和局部给药向受试者施用所述重组干扰素。

165. 根据权利要求 153-164 任一的方法，其中通过给药途径向受试者施用所述重组干扰素，所述给药途径包括如下的一种或更多种 :经口、直肠、舌下、静脉内、动脉内、肌肉、皮下、骨内、皮内、关节内、腹膜内、鞘内、脑内、阴道、经皮、透皮、表皮、粘膜、经眼、经肺、经鼻、腹腔、胸腔、心室内、心包、吸入、瘤内、子宫、浸润和膀胱内给药。

166. 根据权利要求 153-165 任一的方法，其中通过皮下给药和 / 或肌肉给药向受试者施用所述重组干扰素。

167. 根据权利要求 166 的方法，其中所述皮下给药包括皮下注射。

168. 根据权利要求 166 的方法，其中所述肌肉给药包括肌肉注射。

169. 根据权利要求 166-168 任一的方法，其中所述重组干扰素以如下范围的量施用 :一次皮下和 / 或肌肉给药约 2 μ g- 约 70 μ g。

170. 根据权利要求 169 的方法，其中所述重组干扰素以如下范围的量施用 :一次皮下和 / 或肌肉给药约 4 μ g- 约 50 μ g。

171. 根据权利要求 170 的方法，其中所述重组干扰素以如下范围的量施用 :一次皮下和 / 或肌肉给药约 4 μ g- 约 30 μ g。

172. 根据权利要求 166-171 任一的方法，其中每约 1 天 - 约 7 天皮下和 / 或肌肉给药一次所述重组干扰素。

173. 根据权利要求 172 的方法，其中每约 1 天 - 约 2 天皮下和 / 或肌肉给药一次所述重组干扰素。

174. 根据权利要求 153-173 任一的方法，其中通过吸入给药向受试者施用所述重组干扰素。

175. 根据权利要求 174 的方法，其中通过经肺和 / 或经鼻吸入所述重组干扰素。

176. 根据权利要求 174 或 175 的方法，其中所述吸入给药包括干粉吸入和 / 或雾化吸入。

177. 根据权利要求 174-176 任一的方法，其中所述重组干扰素以如下范围的量施用 :一次吸入给药约 100 μ g- 约 2000 μ g，任选地，约 100 μ g- 约 1500 μ g。

178. 根据权利要求 177 的方法，其中所述重组干扰素以如下范围的量施用 :一次吸入给药约 150 μ g- 约 800 μ g。

179. 根据权利要求 178 的方法，其中所述重组干扰素以如下范围的量施用 :一次吸入给药约 200 μ g- 约 600 μ g。

180. 根据权利要求 174-179 任一的方法，其中每约 1 天 - 约 3 天吸入给药一次所述重组干扰素。

181. 根据权利要求 180 的方法，其中每约 1 天吸入给药一次所述重组干扰素。

182. 根据权利要求 153-181 任一的方法，其中所述受试者带有胸腔积液、腹腔积液和 / 或心包积液。

183. 根据权利要求 182 的方法，其中所述胸腔积液包含恶性胸腔积液，所述腹腔积液包含恶性腹腔积液，和 / 或所述心包积液包含恶性心包积液。

184. 根据权利要求 182 或 183 的方法，其中通过胸腔给药、腹腔给药和 / 或心包给药向受试者施用所述重组干扰素。

185. 根据权利要求 184 的方法，其中所述胸腔给药包括胸腔灌注。

186. 根据权利要求 184 的方法，其中所述腹腔给药包括腹腔灌注。

187. 根据权利要求 184 的方法，其中所述心包给药包括心包灌注。

188. 根据权利要求 184-187 任一的方法，其中所述重组干扰素以如下范围的量施用：一次胸腔、腹腔和 / 或心包给药约 30 μg- 约 2000 μg，任选地，约 100 μg- 约 1500 μg，更任选地，约 150 μg- 约 1000 μg，还任选地，约 200 μg- 约 800 μg。

189. 根据权利要求 188 的方法，其中所述重组干扰素以如下范围的量施用：一次胸腔、腹腔和 / 或心包给药约 200 μg- 约 400 μg。

190. 根据权利要求 184-189 任一的方法，其中每约 1 天 - 约 10 天，任选地，每约 1 天 - 约 7 天，例如每约 1、2、3、4、5、6 或 7 天胸腔、腹腔和 / 或心包给药一次所述重组干扰素。

191. 根据权利要求 153-165 任一的方法，其中通过瘤内给药向受试者施用所述重组干扰素。

192. 根据权利要求 191 的方法，其中所述瘤内给药包括瘤内注射。

193. 根据权利要求 191 或 192 的方法，其中所述重组干扰素以如下范围的量施用：一次瘤内给药约 60 μg- 约 600 μg，任选地，约 60 μg- 约 500 μg。

194. 根据权利要求 193 的方法，其中所述重组干扰素以如下范围的量施用：一次瘤内给药约 80 μg- 约 400 μg。

195. 根据权利要求 194 的方法，其中所述重组干扰素以如下范围的量施用：一次瘤内给药约 100 μg- 约 250 μg。

196. 根据权利要求 191-195 任一的方法，其中每约 1 天 - 约 10 天，任选地，每约 1 天 - 约 7 天，例如每约 1、2、3、4、5、6 或 7 天瘤内给药一次所述重组干扰素。

197. 根据权利要求 191-196 任一的方法，其中瘤内给药的给药方案如下：每约 1 天瘤内注射一次所述重组干扰素，持续约 4 次 - 约 8 次，接着每约 3 天 - 约 5 天瘤内注射一次所述重组干扰素，持续约 4 次 - 约 8 次，然后每约 7 天瘤内注射一次所述重组干扰素，当瘤体消失或瘤体小至无法进行瘤内注射时，停止瘤内给药。

198. 根据权利要求 153-197 任一的方法，其中所述受试者中的肺癌包含在如下至少一处中的肿瘤转移：皮肤、粘膜、浅表淋巴结和皮下组织。

199. 根据权利要求 198 的方法，其中通过喷雾给药向受试者施用所述重组干扰素。

200. 根据权利要求 199 的方法，其中所述喷雾给药包括如下的至少一种：经皮喷雾给药、透皮喷雾给药、表皮喷雾给药和粘膜喷雾给药。

201. 根据权利要求 199 或 200 的方法，其中所述重组干扰素以如下范围的量施用：一次喷雾给药约 6 μg- 约 100 μg。

202. 根据权利要求 201 的方法，其中所述重组干扰素以如下范围的量施用：一次喷雾给药约 10 μg- 约 40 μg，任选地，约 20 μg- 约 40 μg。.

203. 根据权利要求 199-202 任一的方法，其中每天喷雾给药约 1- 约 6 次，例如约 1、2、

3、4、5 或 6 次所述重组干扰素。

204. 根据权利要求 153-203 任一的方法，其中通过给药途径向受试者施用所述重组干扰素，所述给药途径包括如下的至少一种：皮下给药、肌肉给药、吸入给药、浸润给药、胸腔给药、腹腔给药、心包给药、瘤内给药和喷雾给药。

205. 根据权利要求 153-204 任一的方法，其中所述重组干扰素作为单一疗法向受试者施用。

206. 根据权利要求 153-204 任一的方法，进一步包括向所述受试者施用至少一种其它抗癌疗法，任选地，在施用所述重组干扰素之前、同时和 / 或之后给予所述受试者所述至少一种其它抗癌疗法。

207. 根据权利要求 206 的方法，其中所述至少一种其它抗癌疗法包括如下的至少一种：化学治疗、放射治疗、手术治疗、介入治疗、生物治疗、基因治疗、消融治疗、免疫治疗、靶向治疗和中药治疗。

208. 根据权利要求 207 的方法，其中所述至少一种其它抗癌疗法包括化学治疗。

209. 根据权利要求 208 的方法，其中所述化学治疗为一线化学治疗。

210. 根据权利要求 209 的方法，其中所述一线化学治疗使用的至少一种化学治疗剂包括铂类化合物，例如顺铂。

211. 根据权利要求 207 的方法，其中所述至少一种其它抗癌疗法包括放射治疗。

212. 根据权利要求 211 的方法，其中当肺癌转移至脑时，所述放射治疗包括头部伽玛刀治疗。

213. 根据权利要求 207 的方法，其中所述至少一种其它抗癌疗法包括手术治疗。

214. 根据权利要求 207 的方法，其中所述至少一种其它抗癌疗法包括靶向治疗。

215. 根据权利要求 214 的方法，其中所述靶向治疗包括施用吉非替尼、厄洛替尼和 / 或重组人血管内皮抑制素。

216. 根据权利要求 207 的方法，其中所述至少一种其它抗癌疗法包括生物治疗。

217. 根据权利要求 153-216 任一的方法，其中在至少一个治疗周期中施用所述重组干扰素，任选地，所述至少一个治疗周期包括 2、3、4、5、6、7、8、9 或 10 个治疗周期，或任选地，多于 10 个治疗周期。

218. 根据权利要求 217 的方法，其中所述一个治疗周期的持续时间为至少约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、或约 6 年等，或可长期施用所述重组干扰素，包括受试者生命的整个期间；或者所述重组干扰素治疗的持续时间还可以是约 1 天 - 约 6 年，约 1 周 - 约 4 年，约 2 周 - 约 3 年，约 1 个月 - 约 1 年、或约 2 个月 - 约 9 个月等。

219. 根据权利要求 217 或 218 的方法，其中所述多个治疗周期中的任意相邻两个治疗周期之间的间隔时间为至少约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、或约 6 年等；或者所述间隔时间还可以为约 2 天 - 约 6 年，约 4 天 - 约 3 年、约 1 周 - 约 1 年、约 2 个月 - 约

9 个月、或约 3 个月 - 约 6 个月等。

220. 根据权利要求 153-219 任一的方法，其中与治疗前的肿瘤大小相比，所述治疗消除了所述肺部肿瘤或减小了所述肺部肿瘤的大小。

221. 一种治疗受试者中肺癌的方法，包括在两个或更多个治疗周期中向所述受试者施用由 SEQ ID NO :2 编码的重组干扰素以及一种或更多种化学治疗剂，然后在一个或更多个治疗周期中向所述受试者施用由 SEQ ID NO :2 编码的重组干扰素以及一种或更多种靶向药物。

222. 根据权利要求 221 的方法，其中与治疗前的肿瘤大小相比，所述治疗消除所述肺部肿瘤或减小所述肺部肿瘤的大小。

223. 根据权利要求 221 或 222 的方法，其中所述一种或更多种化学治疗剂包括铂类化合物，例如顺铂。

224. 根据权利要求 221-223 任一的方法，其中所述一种或更多种靶向药物包括吉非替尼、厄洛替尼和 / 或重组人血管内皮抑制素。

225. 根据权利要求 221-224 任一的方法，其中向所述受试者施用有效量的由 SEQ ID NO :2 的核苷酸序列编码的重组干扰素，任选地，所述有效量为治疗有效量。

226. 根据权利要求 153-225 任一的方法，其中所述治疗方法为非手术治疗方法。

227. 一种治疗受试者中的肺癌的方法，包括通过皮下给药和 / 或肌肉给药向所述受试者施用由 SEQ ID NO :2 编码的重组干扰素，其中所述重组干扰素以如下范围的量施用 ：一次皮下给药和 / 或肌肉给药约 2 μ g- 约 70 μ g，任选地，约 4 μ g- 约 50 μ g，更任选地，约 4 μ g- 约 30 μ g，每约 1- 约 7 天，任选地，每约 1- 约 2 天皮下给药和 / 或肌肉给药一次所述重组干扰素，持续至少约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、或约 6 年等，或可长期施用所述重组干扰素，包括受试者生命的整个期间 ；或者所述持续时间还可以是约 1 天 - 约 6 年，约 1 周 - 约 4 年，约 2 周 - 约 3 年，约 1 个月 - 约 1 年、或约 2 个月 - 约 9 个月等。

228. 根据权利要求 227 的方法，其中所述肺癌包括小细胞肺癌 (SCLC)、非小细胞肺癌 (NSCLC) 或两者。

229. 根据权利要求 227 或 228 的方法，其中所述受试者中的肺癌包含转移的肿瘤。

230. 根据权利要求 227-229 任一的方法，其中所述受试者是早期、中期或晚期癌症患者，任选地，所述受试者是中期或晚期癌症患者，更任选地，所述受试者是晚期癌症患者。

231. 根据权利要求 227-229 任一的方法，其中所述受试者是 0、I、II、III 或 IV 期癌症患者，任选地，所述受试者是 III 或 IV 期癌症患者。

232. 根据权利要求 227-231 任一的方法，其中所述肺癌为具备手术指征或适于手术的肺癌。

233. 根据权利要求 227-231 任一的方法，其中所述肺癌为不具备手术指征也不适于手术的肺癌。

234. 根据权利要求 227-231 任一的方法，其中所述肺癌是可切除的肺癌。

235. 根据权利要求 227-231 任一的方法，其中所述肺癌是不可切除的肺癌。

236. 根据权利要求 234 或 235 的方法，其中所述肺癌通过手术切除被切除。

237. 根据权利要求 227-236 任一的方法，其中所述皮下给药包括皮下注射。

238. 根据权利要求 227-236 任一的方法，其中所述肌肉给药包括肌肉注射。

239. 根据权利要求 227-238 任一的方法，进一步包括通过吸入给药向受试者施用所述重组干扰素。

240. 根据权利要求 239 的方法，其中在皮下给药和 / 或肌肉给药的之前、同时和 / 或之后进行所述吸入给药。

241. 根据权利要求 239 或 240 的方法，其中所述吸入给药包括经肺和 / 或经鼻吸入给药。

242. 根据权利要求 239-241 任一的方法，其中所述吸入给药包括雾化吸入。

243. 根据权利要求 239-242 任一的方法，其中所述重组干扰素以如下范围的量施用 ：一次吸入给药约 100 μ g- 约 2000 μ g，任选地，约 100 μ g- 约 1500 μ g，更任选地，约 150 μ g- 约 800 μ g，还更任选地，约 200 μ g- 约 600 μ g，每约 1 天 - 约 3 天，任选地，每约 1 天吸入一次所述重组干扰素，持续至少约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、或约 6 年等，或可长期施用所述重组干扰素，包括受试者生命的整个期间 ；或者所述持续时间还可以是约 1 天 - 约 6 年，约 1 周 - 约 4 年，约 2 周 - 约 3 年，约 1 个月 - 约 1 年、或约 2 个月 - 约 9 个月等。

244. 根据权利要求 227-243 任一的方法，进一步包括通过瘤内给药向受试者施用所述重组干扰素。

245. 根据权利要求 244 的方法，其中在皮下给药和 / 或肌肉给药的之前、同时和 / 或之后进行所述瘤内给药。

246. 根据权利要求 244 的方法，其中在吸入给药的之前、同时和 / 或之后进行所述瘤内给药。

247. 根据权利要求 244-246 任一的方法，其中所述瘤内给药包括瘤内注射。

248. 根据权利要求 244-247 任一的方法，其中所述重组干扰素以如下范围的量施用 ：一次瘤内给药约 60 μ g- 约 600 μ g，任选地，约 60 μ g- 约 500 μ g，更任选地，约 80 μ g- 约 400 μ g，还更任选地，约 100 μ g- 约 250 μ g，每约 1 天 - 约 10 天，任选地，每约 1 天 - 约 7 天，例如每约 1、2、3、4、5、6 或 7 天瘤内给药一次所述重组干扰素，持续至少约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、或约 6 年等，或可长期施用所述重组干扰素，包括受试者生命的整个期间 ；或者所述持续时间还可以是约 1 天 - 约 6 年，约 1 周 - 约 4 年，约 2 周 - 约 3 年，约 1 个月 - 约 1 年、或约 2 个月 - 约 9 个月等。

249. 根据权利要求 244-248 任一的方法，其中瘤内给药的给药方案如下 ：每约 1 天瘤内注射一次所述重组干扰素，持续约 4 次 - 约 8 次，接着每约 3 天 - 约 5 天瘤内注射一次所述重组干扰素，持续约 4 次 - 约 8 次，然后每约 7 天瘤内注射一次所述重组干扰素，当瘤体消失或瘤体小至无法进行瘤内注射时，停止瘤内给药。

250. 根据权利要求 227-249 任一的方法，其中所述受试者带有胸腔积液、腹腔积液和 / 或心包积液。

251. 根据权利要求 250 的方法，其中所述胸腔积液为恶性胸腔积液，所述腹腔积液为恶性腹腔积液，和 / 或所述心包积液为恶性心包积液。

252. 根据权利要求 250 或 251 的方法，其中通过给药途径向受试者施用所述重组干扰素，所述给药途径包括如下的至少一种 ：胸腔给药、腹腔给药和心包给药。

253. 根据权利要求 252 的方法，其中所述胸腔给药包括胸腔灌注。

254. 根据权利要求 252 的方法，其中所述腹腔给药包括腹腔灌注。

255. 根据权利要求 252 的方法，其中所述心包给药包括心包灌注。

256. 根据权利要求 252-255 任一的方法，其中所述重组干扰素以如下范围的量施用 ：一次胸腔、腹腔和 / 或心包给药约 30 μ g- 约 2000 μ g，任选地，约 100 μ g- 约 1500 μ g，更任选地，约 150 μ g- 约 1000 μ g，还任选地，约 200 μ g- 约 800 μ g。

257. 根据权利要求 256 的方法，其中所述重组干扰素以如下范围的量施用 ：一次胸腔、腹腔和 / 或心包给药约 200 μ g- 约 400 μ g。

258. 根据权利要求 252-257 任一的方法，其中每约 1 天 - 约 10 天，任选地，每约 1 天 - 约 7 天，例如每约 1、2、3、4、5、6 或 7 天胸腔、腹腔和 / 或心包给药一次所述重组干扰素。

259. 根据权利要求 227-258 任一的方法，其中所述受试者中的肺癌包含在如下至少一处中的肿瘤转移 ：皮肤、粘膜、浅表淋巴结和皮下组织。

260. 根据权利要求 259 的方法，其中通过喷雾给药向受试者施用所述重组干扰素。

261. 根据权利要求 260 的方法，其中所述喷雾给药包括如下的至少一种 ：经皮喷雾给药、透皮喷雾给药、表皮喷雾给药和粘膜喷雾给药。

262. 根据权利要求 260 或 261 的方法，其中所述重组干扰素以如下范围的量施用 ：一次喷雾给药约 6 μ g- 约 100 μ g。

263. 根据权利要求 262 的方法，其中所述重组干扰素以如下范围的量施用 ：一次喷雾给药约 10 μ g- 约 40 μ g，任选地，约 20 μ g- 约 40 μ g。

264. 根据权利要求 260-263 任一的方法，其中每天喷雾给药约 1- 约 6 次，例如约 1、2、3、4、5 或 6 次所述重组干扰素。.

265. 根据权利要求 227-264 任一的方法，其中所述重组干扰素作为单一疗法向受试者施用。

266. 根据权利要求 227-264 任一的方法，进一步包括向所述受试者施用至少一种其它抗癌疗法，任选地，在施用所述重组干扰素之前、同时和 / 或之后给予所述受试者至少一种其它抗癌疗法。

267. 根据权利要求 266 的方法，其中所述至少一种其它抗癌疗法包括如下的一种或更多种 ：化学治疗、放射治疗、手术治疗、介入治疗、生物治疗、基因治疗、消融治疗、免疫治疗、靶向治疗和中药治疗。

268. 根据权利要求 267 的方法，其中所述至少一种其它抗癌疗法包括化学治疗。

269. 根据权利要求 268 的方法，其中所述化学治疗为一线化学治疗。

270. 根据权利要求 269 的方法，其中所述一线化学治疗使用的一种或更多种化学治疗剂包括铂类化合物，例如顺铂。

271. 根据权利要求 267 的方法，其中所述至少一种其它抗癌疗法包括放射治疗。

272. 根据权利要求 271 的方法，其中当肺癌转移至脑时，所述放射治疗包括头部伽玛刀治疗。

273. 根据权利要求 267 的方法，其中所述至少一种其它抗癌疗法包括手术治疗。

274. 根据权利要求 267 的方法，其中所述至少一种其它抗癌疗法包括靶向治疗。

275. 根据权利要求 274 的方法，其中所述靶向治疗包括施用吉非替尼、厄洛替尼和 / 或重组人血管内皮抑制素。

276. 根据权利要求 267 的方法，其中所述至少一种其它抗癌疗法包括生物治疗。

277. 根据权利要求 227-276 任一的方法，其中与治疗前的肿瘤相比，所述治疗消除了所述肿瘤或减小了所述肿瘤的大小或所述肿瘤转移的数量。

278. 根据权利要求 227-277 任一的方法，其中所述治疗方法为非手术治疗方法。

279. 一种治疗受试者中的肺癌的方法，包括通过皮下给药和 / 或肌肉给药向受试者施用由 SEQ ID NO :2 编码的重组干扰素，其中以约 2 μ g/ 次 - 约 10 μ g/ 次，任选地，约 4 μ g/ 次 - 约 10 μ g/ 次，更任选地，约 4.5 μ g/ 次 - 约 9 μ g/ 次，例如约 4.5 μ g/ 次或约 9 μ g/ 次的诱导剂量经皮下给药和 / 或肌肉给药施用一次或更多次所述重组干扰素，之后以约 10 μ g/ 次 - 约 70 μ g/ 次，任选地，约 12 μ g/ 次 - 约 50 μ g/ 次，更任选地，约 12 μ g/ 次 - 约 30 μ g/ 次的治疗剂量经皮下给药和 / 或肌肉给药施用多次所述重组干扰素。

280. 根据权利要求 279 的方法，其中所述肺癌包括小细胞肺癌 (SCLC)、非小细胞肺癌 (NSCLC) 或两者。

281. 根据权利要求 279 或 280 的方法，其中所述受试者中的肿瘤包含转移的肿瘤。

282. 根据权利要求 279-281 任一的方法，其中所述受试者是早期、中期或晚期癌症患者，任选地，所述受试者是中期或晚期癌症患者，更任选地，所述受试者是晚期癌症患者。

283. 根据权利要求 279-281 任一的方法，其中所述受试者是 0、I、II、III 或 IV 期癌症患者，任选地，所述受试者是 III 或 IV 期癌症患者。

284. 根据权利要求 279-283 任一的方法，其中所述肺癌为具备手术指征或适于手术的肺癌。

285. 根据权利要求 279-283 任一的方法，其中所述肺癌为不具备手术指征也不适于手术的肺癌。

286. 根据权利要求 279-283 任一的方法，其中所述肺癌是可切除的肺癌。

287. 根据权利要求 279-283 任一的方法，其中所述肺癌是不可切除的肺癌。

288. 根据权利要求 286 或 287 的方法，其中所述肺癌通过手术切除被切除。

289. 根据权利要求 279-288 任一的方法，其中所述皮下给药包括皮下注射。

290. 根据权利要求 279-288 任一的方法，其中所述肌肉给药包括肌肉注射。

291. 根据权利要求 279-290 任一的方法，其中施用诱导剂量与施用治疗剂量之间的间隔为约 1 天 - 约 1 个月，任选地，约 1 天 - 约 1 周，更任选地，约 1 天 - 约 3 天，包括，例如约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、或约 1 个月。

292. 根据权利要求 279-291 任一的方法，其中多次施用诱导剂量时，每约 1 天 - 约 10 天施用一次所述重组干扰素，任选地，每约 1 天 - 约 7 天施用一次所述重组干扰素，更任选

地，每约 1 天 - 约 2 天施用一次所述重组干扰素，包括，例如每约 1、2、3、4、5、6、7、8、9 或 10 天施用一次所述重组干扰素。

293. 根据权利要求 279-292 任一的方法，其中每约 1 天 - 约 10 天施用一次治疗剂量的所述重组干扰素，任选地，每约 1 天 - 约 7 天施用一次治疗剂量的所述重组干扰素，更任选地，每约 1 天 - 约 2 天施用一次治疗剂量的所述重组干扰素，包括，例如每约 1、2、3、4、5、6、7、8、9 或 10 天施用一次治疗剂量的所述重组干扰素。

294. 根据权利要求 279-293 任一的方法，其中诱导剂量和治疗剂量的施用的持续时间为至少约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、或约 6 年等，或可长期施用所述重组干扰素，包括受试者生命的整个期间。

295. 根据权利要求 279-294 任一的方法，进一步包括通过吸入给药向受试者施用所述重组干扰素。

296. 根据权利要求 295 的方法，其中在皮下给药和 / 或肌肉给药的之前、同时和 / 或之后进行所述吸入给药。

297. 根据权利要求 295 或 296 的方法，其中所述吸入给药包括经肺和 / 或经鼻吸入给药。

298. 根据权利要求 295-297 任一的方法，其中所述吸入给药包括雾化吸入。

299. 根据权利要求 295-298 任一的方法，其中所述重组干扰素以如下范围的量施用：一次吸入给药约 100 μg- 约 2000 μg，任选地，约 100 μg- 约 1500 μg，更任选地，约 150 μg- 约 800 μg，还更任选地，约 200 μg- 约 600 μg，每约 1 天 - 约 3 天，任选地，每约 1 天吸入一次所述重组干扰素，持续至少约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、或约 6 年等，或可长期施用所述重组干扰素，包括受试者生命的整个期间；或者所述持续时间还可以是约 1 天 - 约 6 年，约 1 周 - 约 4 年，约 2 周 - 约 3 年，约 1 个月 - 约 1 年、或约 2 个月 - 约 9 个月等。

300. 根据权利要求 279-299 任一的方法，进一步包括通过瘤内给药向受试者施用所述重组干扰素。

301. 根据权利要求 300 的方法，其中在皮下给药和 / 或肌肉给药的之前、同时和 / 或之后进行所述瘤内给药。

302. 根据权利要求 300 的方法，其中在吸入给药的之前、同时和 / 或之后进行所述瘤内给药。.

303. 根据权利要求 300-302 任一的方法，其中所述瘤内给药包括瘤内注射。

304. 根据权利要求 300-303 任一的方法，其中所述重组干扰素以如下范围的量施用：一次瘤内给药约 60 μg- 约 600 μg，任选地，约 60 μg- 约 500 μg，更任选地，约 80 μg- 约 400 μg，还更任选地，约 100 μg- 约 250 μg，每约 1 天 - 约 10 天，任选每约 1 天 - 约 7 天，例如每约 1、2、3、4、5、6 或 7 天瘤内给药一次所述重组干扰素，持续至少约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约

10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、或约 6 年等，或可长期施用所述重组干扰素，包括受试者生命的整个期间；或者所述持续时间还可以是约 1 天 - 约 6 年，约 1 周 - 约 4 年，约 2 周 - 约 3 年，约 1 个月 - 约 1 年、或约 2 个月 - 约 9 个月等。

305. 根据权利要求 300-304 任一的方法，其中瘤内给药的给药方案如下：每约 1 天瘤内注射一次所述重组干扰素，持续约 4- 约 8 次，接着每约 3- 约 5 天瘤内注射一次所述重组干扰素，持续约 4- 约 8 次，然后每约 7 天瘤内注射一次所述重组干扰素，当瘤体消失或瘤体小至无法进行瘤内注射时，停止瘤内给药。

306. 根据权利要求 279-305 任一的方法，其中所述受试者带有胸腔积液、腹腔积液和 / 或心包积液。

307. 根据权利要求 306 的方法，其中所述胸腔积液为恶性胸腔积液，所述腹腔积液为恶性腹腔积液，和 / 或所述心包积液为恶性心包积液。

308. 根据权利要求 306 或 307 的方法，其中通过给药途径向受试者施用所述重组干扰素，所述给药途径包括如下的至少一种：胸腔给药、腹腔给药和心包给药。

309. 根据权利要求 308 的方法，其中所述胸腔给药包括胸腔灌注。

310. 根据权利要求 308 的方法，其中所述腹腔给药包括腹腔灌注。

311. 根据权利要求 308 的方法，其中所述心包给药包括心包灌注。

312. 根据权利要求 308-311 任一的方法，其中所述重组干扰素以如下范围的量施用：一次胸腔给药、腹腔给药和 / 或心包给药约 30 μg- 约 2000 μg，任选地，约 100 μg- 约 1500 μg，更任选地，约 150 μg- 约 1000 μg，还任选地，约 200 μg- 约 800 μg。

313. 根据权利要求 312 的方法，其中所述重组干扰素以如下范围的量施用：一次胸腔给药、腹腔给药和 / 或心包给药约 200 μg- 约 400 μg。

314. 根据权利要求 308-313 任一的方法，其中每约 1 天 - 约 10 天，任选地，每约 1 天 - 约 7 天，例如每约 1、2、3、4、5、6 或 7 天胸腔给药、腹腔给药和 / 或心包给药一次所述重组干扰素。

315. 根据权利要求 279-314 任一的方法，其中所述受试者中的肺癌包含在如下至少一处中的肿瘤转移：皮肤、粘膜、浅表淋巴结和皮下组织。

316. 根据权利要求 315 的方法，其中通过喷雾给药向受试者施用所述重组干扰素。

317. 根据权利要求 316 的方法，其中所述喷雾给药包括如下的至少一种：经皮喷雾给药、透皮喷雾给药、表皮喷雾给药和粘膜喷雾给药。

318. 根据权利要求 316 或 317 的方法，其中所述重组干扰素以如下范围的量施用：一次喷雾给药约 6 μg- 约 100 μg。

319. 根据权利要求 318 的方法，其中所述重组干扰素以如下范围的量施用：一次喷雾给药约 10 μg- 约 40 μg，任选地，约 20 μg- 约 40 μg。

320. 根据权利要求 316-319 任一的方法，其中每天喷雾给药约 1- 约 6 次，例如约 1、2、3、4、5 或 6 次所述重组干扰素。

321. 根据权利要求 279-320 任一的方法，其中所述重组干扰素作为单一疗法向受试者施用。

322. 根据权利要求 279-320 任一的方法，进一步包括向所述受试者施用至少一种其它抗癌疗法，任选地，在施用所述重组干扰素之前、同时和 / 或之后给予所述受试者至少一种

其它抗癌疗法。

323. 根据权利要求 322 的方法，其中所述至少一种其它抗癌疗法包括如下的一种或更多种：化学治疗、放射治疗、手术治疗、介入治疗、生物治疗、基因治疗、消融治疗、免疫治疗、靶向治疗和中药治疗。

324. 根据权利要求 323 的方法，其中所述至少一种其它抗癌疗法包括化学治疗。

325. 根据权利要求 324 的方法，其中所述化学治疗为一线化学治疗。

326. 根据权利要求 325 的方法，其中所述一线化学治疗使用的一种或更多种化学治疗剂包括铂类化合物，例如顺铂。

327. 根据权利要求 323 的方法，其中所述至少一种其它抗癌疗法包括放射治疗。

328. 根据权利要求 327 的方法，其中当肺癌转移至脑时，所述放射治疗包括头部伽玛刀治疗。

329. 根据权利要求 323 的方法，其中所述至少一种其它抗癌疗法包括手术治疗。

330. 根据权利要求 323 的方法，其中所述至少一种其它抗癌疗法包括靶向治疗。

331. 根据权利要求 330 的方法，其中所述靶向治疗包括施用吉非替尼、厄洛替尼和 / 或重组人血管内皮抑制素。

332. 根据权利要求 323 的方法，其中所述至少一种其它抗癌疗法包括生物治疗。

333. 根据权利要求 279-332 任一的方法，其中与治疗前的肿瘤大小相比，所述治疗消除了所述肺部肿瘤或减小了所述肺部肿瘤的大小。

334. 根据权利要求 279-333 任一的方法，其中所述治疗方法为非手术治疗方法。

335. 一种治疗受试者中的癌症的方法，其中所述癌症源于受试者中的肺癌并转移至脑，包括向受试者施用由 SEQ ID NO :2 编码的重组干扰素，其中以约 2 μg/ 次 - 约 10 μg/ 次，任选地，约 4 μg/ 次 - 约 10 μg/ 次，更任选地，约 4.5 μg/ 次 - 约 9 μg/ 次，例如约 4.5 μg/ 次或约 9 μg/ 次的诱导剂量通过皮下给药和 / 或肌肉给药施用一次或更多次所述重组干扰素，之后以约 10 μg/ 次 - 约 70 μg/ 次，任选地，约 12 μg/ 次 - 约 50 μg/ 次，更任选地，约 12 μg/ 次 - 约 30 μg/ 次的治疗剂量通过皮下给药和 / 或肌肉给药施用多次所述重组干扰素，在所述皮下给药和 / 或肌肉给药的之前、同时和 / 或之后通过吸入给药向受试者施用所述重组干扰素，所述重组干扰素以如下范围的量施用：一次吸入给药约 100 μg- 约 2000 μg，任选地，约 100 μg- 约 1500 μg，更任选地，约 150 μg- 约 800 μg，还更任选地，约 200 μg- 约 600 μg，以及每约 1 天 - 约 3 天，任选地每约 1 天吸入给药一次所述重组干扰素。

336. 根据权利要求 335 的方法，其中所述受试者是中期、晚期或 III 或 IV 期癌症患者，任选地，所述受试者是晚期或 III 或 IV 期癌症患者。

337. 根据权利要求 335 或 336 的方法，其中所述癌症为不具备手术指征也不适于手术的癌症。

338. 根据权利要求 335 或 336 的方法，其中所述肿瘤是不可切除的肿瘤。

339. 根据权利要求 338 的方法，其中所述肿瘤通过手术切除被切除。

340. 根据权利要求 335-339 任一的方法，其中所述皮下给药包括皮下注射。

341. 根据权利要求 335-339 任一的方法，其中所述肌肉给药包括肌肉注射。

342. 根据权利要求 335-341 任一的方法，其中所述吸入给药包括经肺和 / 或经鼻吸入给药。

343. 根据权利要求 335-342 任一的方法，其中所述吸入给药包括雾化吸入。

344. 根据权利要求 335-343 任一的方法，其中施用诱导剂量与施用治疗剂量之间的时间间隔为约 1 天 - 约 1 个月，任选地，约 1 天 - 约 1 周，更任选地，约 1 天 - 约 3 天，包括，例如约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、或约 1 个月。

345. 根据权利要求 335-344 任一的方法，其中多次施用诱导剂量的重组干扰素时，每约 1 天 - 约 10 天施用一次所述重组干扰素，任选地，每约 1 天 - 约 7 天施用一次所述重组干扰素，更任选地，每约 1 天 - 约 2 天施用一次所述重组干扰素，包括，例如每约 1、2、3、4、5、6、7、8、9 或 10 天施用一次所述重组干扰素。

346. 根据权利要求 335-345 任一的方法，其中每约 1 天 - 约 10 天施用一次治疗剂量的所述重组干扰素，任选地，每约 1 天 - 约 7 天施用一次治疗剂量的所述重组干扰素，更任选地，每约 1- 约 2 天施用一次治疗剂量的所述重组干扰素，包括，例如每约 1、2、3、4、5、6、7、8、9 或 10 天施用一次治疗剂量的所述重组干扰素。

347. 根据权利要求 335-346 任一的方法，其中诱导剂量和治疗剂量的施用的持续时间为至少约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年或约 6 年等，或者可长期施用所述重组干扰素，包括受试者生命的整个期间。

348. 根据权利要求 335-347 任一的方法，其中所述吸入给药的持续时间为至少约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年或约 6 年等，或者可长期施用所述重组干扰素，包括受试者生命的整个期间；或者所述持续时间还可以是约 1 天 - 约 6 年，约 1 周 - 约 4 年，约 2 周 - 约 3 年，约 1 个月 - 约 1 年或约 2 个月 - 约 9 个月等。

349. 根据权利要求 335-348 任一的方法，其中所述重组干扰素作为单一疗法向受试者施用。

350. 根据权利要求 335-349 任一的方法，进一步包括向所述受试者施用至少一种其它抗癌疗法，任选地，在施用所述重组干扰素之前、同时和 / 或之后给予所述受试者至少一种其它抗癌疗法。

351. 根据权利要求 350 的方法，其中所述至少一种其它抗癌疗法包括如下的一种或更多种：化学治疗、放射治疗、手术治疗、介入治疗、生物治疗、基因治疗、消融治疗、免疫治疗、靶向治疗和中药治疗。

352. 根据权利要求 351 的方法，其中所述化学治疗为一线化学治疗，任选地，所述一线化学治疗使用的一种或更多种化学治疗剂包括铂类化合物，例如顺铂。

353. 根据权利要求 351 的方法，其中所述靶向治疗包括施用吉非替尼、厄洛替尼和 / 或重组人血管内皮抑制素。

354. 根据权利要求 351 的方法，其中所述至少一种其它抗癌疗法包括放射治疗。

355. 根据权利要求 354 的方法，其中所述放射治疗包括伽玛刀治疗。

356. 根据权利要求 355 的方法，其中所述伽玛刀治疗包括头部伽玛刀治疗。

357. 根据权利要求 335-356 任一的方法，其中与治疗前的肿瘤相比，所述治疗消除了所述肿瘤或减小了所述肿瘤的大小。

358. 根据权利要求 335-357 任一的方法，其中所述治疗方法为非手术治疗方法。

359. 一种治疗受试者中的癌症的方法，其中所述癌症源于受试者中的肺癌并转移至骨或肝脏，包括向受试者施用由 SEQ ID NO :2 编码的重组干扰素，其中以约 2 μg/ 次 - 约 10 μg/ 次，任选地，约 4 μg/ 次 - 约 10 μg/ 次，更任选地，约 4.5 μg/ 次 - 约 9 μg/ 次，例如约 4.5 μg/ 次或约 9 μg/ 次的诱导剂量通过皮下给药和 / 或肌肉给药施用一次或更多次所述重组干扰素，之后以约 10 μg/ 次 - 约 70 μg/ 次，任选地，约 12 μg/ 次 - 约 50 μg/ 次，更任选地，约 12 μg/ 次 - 约 30 μg/ 次的治疗剂量通过皮下给药和 / 或肌肉给药施用多次所述重组干扰素。

360. 根据权利要求 359 的方法，其中所述受试者是中期、晚期或 III 或 IV 期癌症患者，任选地，所述受试者是晚期或 III 或 IV 期癌症患者。

361. 根据权利要求 359 或 360 的方法，其中所述癌症为不具备手术指征也不适于手术的癌症。

362. 根据权利要求 359 或 360 的方法，其中所述肿瘤是不可切除的肿瘤。

363. 根据权利要求 362 的方法，其中所述肿瘤通过手术切除被切除。

364. 根据权利要求 359-363 任一的方法，其中所述皮下给药包括皮下注射。

365. 根据权利要求 359-363 任一的方法，其中所述肌肉给药包括肌肉注射。

366. 根据权利要求 359-365 任一的方法，其中施用诱导剂量与施用治疗剂量之间的时间间隔为约 1 天 - 约 1 个月，任选地，约 1 天 - 约 1 周，更任选地，约 1 天 - 约 3 天，包括，例如约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周或约 1 个月。

367. 根据权利要求 359-366 任一的方法，其中多次施用诱导剂量的重组干扰素时，每约 1 天 - 约 10 天施用一次所述重组干扰素，任选地，每约 1 天 - 约 7 天施用一次所述重组干扰素，更任选地，每约 1 天 - 约 2 天施用一次所述重组干扰素，包括，例如每约 1、2、3、4、5、6、7、8、9 或 10 天施用一次所述重组干扰素。

368. 根据权利要求 359-367 任一的方法，其中每约 1 天 - 约 10 天施用一次治疗剂量的所述重组干扰素，任选地，每约 1 天 - 约 7 天施用一次治疗剂量的所述重组干扰素，更任选地，每约 1- 约 2 天施用一次治疗剂量的所述重组干扰素，包括，例如每约 1、2、3、4、5、6、7、8、9 或 10 天施用一次治疗剂量的所述重组干扰素。

369. 根据权利要求 359-368 任一的方法，其中诱导剂量和治疗剂量的施用的持续时间为至少约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年或约 6 年等，或者可长期施用所述重组干扰素，包括受试者生命的整个期间。

370. 根据权利要求 359-369 任一的方法，进一步包括通过吸入给药向受试者施用所述重组干扰素。

371. 根据权利要求 370 的方法，其中在皮下给药和 / 或肌肉给药的之前、同时和 / 或之后进行所述吸入给药。

372. 根据权利要求 370 或 371 的方法，其中所述吸入给药包括经肺和 / 或经鼻吸入给

药。

373. 根据权利要求 370-372 任一的方法，其中所述吸入给药包括雾化吸入。

374. 根据权利要求 370-373 任一的方法，其中所述重组干扰素以如下范围的量施用：一次吸入给药约 100 μg- 约 2000 μg，任选地，约 100 μg- 约 1500 μg，更任选地，约 150 μg- 约 800 μg，还更任选地，约 200 μg- 约 600 μg，每约 1 天 - 约 3 天，任选地，每约 1 天吸入一次所述重组干扰素，所述吸入给药的持续时间为至少约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年或约 6 年等，或者可长期施用所述重组干扰素，包括受试者生命的整个期间；或者所述持续时间还可以是约 1 天 - 约 6 年，约 1 周 - 约 4 年，约 2 周 - 约 3 年，约 1 个月 - 约 1 年或约 2 个月 - 约 9 个月等。

375. 根据权利要求 359-374 任一的方法，其中所述重组干扰素作为单一疗法向受试者施用。

376. 根据权利要求 359-374 任一的方法，进一步包括向所述受试者施用至少一种其它抗癌疗法，任选地，在施用所述重组干扰素之前、同时和 / 或之后给予所述受试者至少一种其它抗癌疗法。

377. 根据权利要求 376 的方法，其中所述至少一种其它抗癌疗法包括如下的一种或更多种：化学治疗、放射治疗、手术治疗、介入治疗、生物治疗、基因治疗、消融治疗、免疫治疗、靶向治疗和中药治疗。

378. 根据权利要求 377 的方法，其中所述至少一种其它抗癌疗法包括化学治疗。

379. 根据权利要求 378 的方法，其中所述化学治疗为一线化学治疗。

380. 根据权利要求 379 的方法，其中所述一线化学治疗使用的一种或更多种化学治疗剂包括铂类化合物，例如顺铂。

381. 根据权利要求 377 的方法，其中所述至少一种其它抗癌疗法包括靶向治疗。

382. 根据权利要求 381 的方法，其中所述靶向治疗包括施用吉非替尼、厄洛替尼和 / 或重组人血管内皮抑制素。

383. 根据权利要求 377 的方法，其中所述至少一种其它抗癌疗法包括生物治疗。

384. 根据权利要求 359-383 任一的方法，其中与治疗前的肿瘤相比，所述治疗消除了所述肿瘤或减小了所述肿瘤的大小。

385. 根据权利要求 359-384 任一的方法，其中所述治疗方法为非手术治疗方法。

386. 一种治疗受试者中的癌症的方法，其中所述癌症源于受试者中的肺癌并转移至淋巴结，包括向受试者施用由 SEQ ID NO:2 编码的重组干扰素，其中以约 2 μg/ 次 - 约 10 μg/ 次，任选地，约 4 μg/ 次 - 约 10 μg/ 次，更任选地，约 4.5 μg/ 次 - 约 9 μg/ 次，例如约 4.5 μg/ 次或约 9 μg/ 次的诱导剂量通过皮下给药和 / 或肌肉给药施用一次或更多次所述重组干扰素，之后以约 10 μg/ 次 - 约 70 μg/ 次，任选地，约 12 μg/ 次 - 约 50 μg/ 次，更任选地，约 12 μg/ 次 - 约 30 μg/ 次的治疗剂量通过皮下给药和 / 或肌肉给药施用多次所述重组干扰素，在所述皮下给药和 / 或肌肉给药的之前、同时和 / 或之后通过表面或局部给药向所述肿瘤和 / 或所述淋巴结转移灶施用所述重组干扰素。

387. 根据权利要求 386 的方法，其中所述受试者是中期、晚期或 III 或 IV 期癌症患者，

任选地，所述受试者是晚期或 III 或 IV 期癌症患者。

388. 根据权利要求 386 或 387 的方法，其中所述癌症为不具备手术指征也不适于手术的癌症。

389. 根据权利要求 386 或 387 的方法，其中所述肿瘤是不可切除的肿瘤。

390. 根据权利要求 389 的方法，其中所述肿瘤通过手术切除被切除。

391. 根据权利要求 386-390 任一的方法，其中所述皮下给药包括皮下注射。

392. 根据权利要求 386-390 任一的方法，其中所述肌肉给药包括肌肉注射。

393. 根据权利要求 386-392 任一的方法，其中施用诱导剂量与施用治疗剂量之间的时间间隔为约 1 天 - 约 1 个月，任选地，约 1 天 - 约 1 周，更任选地，约 1 天 - 约 3 天，包括，例如约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周或约 1 个月。

394. 根据权利要求 386-393 任一的方法，其中多次施用诱导剂量的重组干扰素时，每约 1 天 - 约 10 天施用一次所述重组干扰素，任选地，每约 1 天 - 约 7 天施用一次所述重组干扰素，更任选地，每约 1 天 - 约 2 天施用一次所述重组干扰素，包括，例如每约 1、2、3、4、5、6、7、8、9 或 10 天施用一次所述重组干扰素。

395. 根据权利要求 386-394 任一的方法，其中每约 1 天 - 约 10 天施用一次治疗剂量的所述重组干扰素，任选地，每约 1 天 - 约 7 天施用一次治疗剂量的所述重组干扰素，更任选地，每约 1 天 - 约 2 天施用一次治疗剂量的所述重组干扰素，包括，例如每约 1、2、3、4、5、6、7、8、9 或 10 天施用一次治疗剂量的所述重组干扰素。

396. 根据权利要求 386-395 任一的方法，其中诱导剂量和治疗剂量的施用的持续时间为至少约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年或约 6 年等，或者可长期施用所述重组干扰素，包括受试者生命的整个期间。

397. 根据权利要求 386-396 任一的方法，其中当所述淋巴结为深部淋巴结时，所述局部给药包括瘤内给药。

398. 根据权利要求 397 的方法，其中所述瘤内给药包括瘤内注射。

399. 根据权利要求 397 或 398 的方法，其中所述重组干扰素以如下范围的量施用：一次瘤内给药约 60 μg- 约 600 μg，任选地，约 60 μg- 约 500 μg，更任选地，约 80 μg- 约 400 μg，还更任选地，约 100 μg- 约 250 μg，每约 1 天 - 约 10 天，任选地，每约 1 天 - 约 7 天，例如每约 1、2、3、4、5、6 或 7 天瘤内给药一次所述重组干扰素，所述瘤内给药的持续时间为至少约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年或约 6 年等，或者可长期施用所述重组干扰素，包括受试者生命的整个期间；或者所述持续时间还可以是约 1 天 - 约 6 年，约 1 周 - 约 4 年，约 2 周 - 约 3 年，约 1 个月 - 约 1 年或约 2 个月 - 约 9 个月等。

400. 根据权利要求 397-399 任一的方法，其中瘤内给药的给药方案如下：每约 1 天瘤内注射一次所述重组干扰素，持续约 4 次 - 约 8 次，接着每约 3 天 - 约 5 天瘤内注射一次所述重组干扰素，持续约 4- 约 8 次，然后每约 7 天瘤内注射一次所述重组干扰素，当瘤体和 /

或被转移的淋巴结消失或小至无法进行瘤内注射时，停止瘤内给药。

401. 根据权利要求 386-396 任一的方法，其中当淋巴结为浅表淋巴结时，所述表面或局部给药包括如下的至少一种：浸润给药、经皮给药、透皮给药、表皮给药和粘膜给药。

402. 根据权利要求 401 的方法，其中所述局部给药包括浸润给药。

403. 根据权利要求 402 的方法，其中通过灌注进行所述浸润给药。

404. 根据权利要求 401 的方法，其中所述经皮给药、透皮给药、表皮给药或粘膜给药分别包括经皮喷雾给药、透皮喷雾给药、表皮喷雾给药或粘膜喷雾给药。

405. 根据权利要求 404 的方法，其中所述重组干扰素以如下范围的量施用：一次喷雾给药约 6 μg- 约 100 μg。

406. 根据权利要求 405 的方法，其中所述重组干扰素以如下范围的量施用：一次喷雾给药约 10 μg- 约 40 μg，任选地，约 20 μg- 约 40 μg。

407. 根据权利要求 404-406 任一的方法，其中每天喷雾给药约 1- 约 6 次，例如约 1、2、3、4、5 或 6 次所述重组干扰素。

408. 根据权利要求 386-407 任一的方法，其中所述重组干扰素作为单一疗法向受试者施用。

409. 根据权利要求 386-407 任一的方法，进一步包括向所述受试者施用至少一种其它抗癌疗法，任选地，在施用所述重组干扰素之前、同时和 / 或之后给予所述受试者至少一种其它抗癌疗法。

410. 根据权利要求 409 的方法，其中所述至少一种其它抗癌疗法包括如下的一种或更多种：化学治疗、放射治疗、手术治疗、介入治疗、生物治疗、基因治疗、消融治疗、免疫治疗、靶向治疗和中药治疗。

411. 根据权利要求 410 的方法，其中所述至少一种其它抗癌疗法包括化学治疗。

412. 根据权利要求 411 的方法，其中所述化学治疗为一线化学治疗。

413. 根据权利要求 412 的方法，其中所述一线化学治疗使用的一种或更多种化学治疗剂包括铂类化合物，例如顺铂。

414. 根据权利要求 410 的方法，其中所述至少一种其它抗癌疗法包括靶向治疗。

415. 根据权利要求 414 的方法，其中所述靶向治疗包括施用吉非替尼、厄洛替尼和 / 或重组人血管内皮抑制素。

416. 根据权利要求 410 的方法，其中所述至少一种其它抗癌疗法包括生物治疗。

417. 根据权利要求 386-416 任一的方法，其中与治疗前的肿瘤相比，所述治疗消除了所述肿瘤或减小了所述肿瘤的大小。

418. 根据权利要求 386-417 任一的方法，其中所述治疗方法为非手术治疗方法。

419. 一种治疗受试者中的肺癌的方法，其中所述受试者具有胸腔积液、腹腔积液和 / 或心包积液，包括经表面或局部给药向所述受试者给予由 SEQ ID NO：2 编码的重组干扰素。

420. 根据权利要求 419 的方法，其中所述受试者是中期、晚期或 III 或 IV 期癌症患者，任选地，所述受试者是晚期或 III 或 IV 期癌症患者。

421. 根据权利要求 419 或 420 的方法，其中所述肺癌为不具备手术指征也不适于手术的肺癌。

422. 根据权利要求 419 或 420 的方法，其中所述肺癌是不可切除的肺癌。

423. 根据权利要求 422 的方法，其中所述肿瘤通过手术切除被切除。

424. 根据权利要求 419-423 任一的方法，其中所述胸腔积液为恶性胸腔积液，所述腹腔积液为恶性腹腔积液，和 / 或所述心包积液为恶性心包积液。

425. 根据权利要求 419-424 任一的方法，其中所述局部给药包括如下的至少一种 ：浸润给药、胸腔给药、腹腔给药和心包给药。

426. 根据权利要求 425 的方法，其中通过灌注进行所述局部给药。

427. 根据权利要求 426 的方法，其中所述重组干扰素以如下范围的量施用 ：一次灌注给药约 30 μg- 约 2000 μg，任选地，约 100 μg- 约 1500 μg，更任选地，约 150 μg- 约 1000 μg，还任选地，约 200 μg- 约 800 μg，还更任选地，约 200 μg- 约 400 μg。

428. 根据权利要求 426 或 427 的方法，其中每约 1 天 - 约 10 天，任选地，每约 1 天 - 约 7 天，例如每约 1、2、3、4、5、6 或 7 天灌注给药 1 次所述重组干扰素。

429. 根据权利要求 428 的方法，其中每约 1 天灌注给药 1 次所述重组干扰素，持续约 4 次 - 约 6 次。

430. 根据权利要求 419-429 任一的方法，其中在所述表面或局部给药的之前、同时和 / 或之后，经全身给药向所述受试者施用所述重组干扰素。

431. 根据权利要求 430 的方法，其中所述全身给药包括皮下和 / 或肌肉给药。

432. 根据权利要求 431 的方法，其中所述皮下给药包括皮下注射。

433. 根据权利要求 431 的方法，其中所述肌肉给药包括肌肉注射。

434. 根据权利要求 431-433 任一的方法，其中以约 2 μg/ 次 - 约 10 μg/ 次，任选地，约 4 μg/ 次 - 约 10 μg/ 次，更任选地，约 4.5 μg/ 次 - 约 9 μg/ 次，例如约 4.5 μg/ 次或约 9 μg/ 次的诱导剂量通过皮下给药和 / 或肌肉给药施用一次或更多次所述重组干扰素，之后以约 10 μg/ 次 - 约 70 μg/ 次，任选地，约 12 μg/ 次 - 约 50 μg/ 次，更任选地，约 12 μg/ 次 - 约 30 μg/ 次的治疗剂量通过皮下给药和 / 或肌肉给药施用多次所述重组干扰素。

435. 根据权利要求 434 的方法，其中施用诱导剂量与施用治疗剂量之间的时间间隔为约 1 天 - 约 1 个月，任选地，约 1 天 - 约 1 周，更任选地，约 1 天 - 约 3 天，包括，例如约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周或约 1 个月。

436. 根据权利要求 434 或 435 的方法，其中多次施用诱导剂量的重组干扰素时，每约 1 天 - 约 10 天施用一次所述重组干扰素，任选地，每约 1 天 - 约 7 天施用一次所述重组干扰素，更任选地，每约 1 天 - 约 2 天施用一次所述重组干扰素，包括，例如每约 1、2、3、4、5、6、7、8、9 或 10 天施用一次所述重组干扰素。

437. 根据权利要求 434-436 任一的方法，其中每约 1 天 - 约 10 天施用一次治疗剂量的所述重组干扰素，任选地，每约 1 天 - 约 7 天施用一次治疗剂量的所述重组干扰素，更任选地，每约 1 天 - 约 2 天施用一次治疗剂量的所述重组干扰素，包括，例如每约 1、2、3、4、5、6、7、8、9 或 10 天施用一次治疗剂量的所述重组干扰素。

438. 根据权利要求 434-437 任一的方法，其中诱导剂量和治疗剂量的施用的持续时间为至少约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年或约 6 年等，或者可长期施用所述重组干扰素，包括患者生命的整个期间。

439. 根据权利要求 419-438 任一的方法，其中经表面给药、局部给药和 / 或全身给药进一步给予其它治疗药物。

440. 根据权利要求 439 的方法，其中所述其它治疗药物包括抗肿瘤药物。

441. 根据权利要求 440 的方法，其中所述抗肿瘤药物包括一种或更多种化学治疗剂、靶向药物或生物制剂。

442. 根据权利要求 441 的方法，其中所述一种或更多种化学治疗剂包括铂类化合物，例如顺铂。

443. 根据权利要求 441 的方法，其中一种或更多种靶向药物包括吉非替尼、厄洛替尼和 / 或重组人血管内皮抑制素。

444. 根据权利要求 419-443 任一的方法，其中与治疗前的肿瘤大小相比，所述治疗消除了所述肿瘤或减小了所述肿瘤的大小。

445. 根据权利要求 419-444 任一的方法，其中所述治疗方法为非手术治疗方法。

446. 一种治疗受试者中肿瘤的方法，包括向所述受试者施用包含抗肿瘤作用的重组干扰素，作为一线单一疗法。

447. 根据权利要求 446 的方法，其中所述肿瘤包括如下一种 :肺癌、子宫癌、宫颈癌和胰腺癌。

448. 根据权利要求 447 的方法，其中所述肺癌包括非小细胞肺癌。

449. 根据权利要求 446 的方法，其中所述肿瘤不是肾癌。

450. 一种治疗受试者中肿瘤的方法，包括向所述受试者施用包含抗肿瘤作用的重组干扰素，作为二线单一疗法。

451. 根据权利要求 450 的方法，其中所述肿瘤包含如下的一种 :肺癌、结直肠癌、恶性黑素瘤、卵巢癌、宫颈癌、肝癌、乳腺癌、胃肠道癌、前列腺癌、神经瘤和鳞状细胞癌。

452. 根据权利要求 451 的方法，其中所述结直肠癌包括结肠癌。

453. 根据权利要求 451 的方法，其中所述结直肠癌包括直肠癌。

454. 根据权利要求 451 的方法，其中所述肺癌包括非小细胞肺癌。

455. 根据权利要求 451 的方法，其中所述肝癌包括 HCC。

456. 根据权利要求 451 的方法，其中所述胃肠道癌包括胃癌。

457. 一种治疗受试者中肿瘤的方法，包括向所述受试者施用包含抗肿瘤作用的重组干扰素，作为一线疗法，并联合一种或更多种其它抗癌疗法。

458. 根据权利要求 457 的方法，其中所述肿瘤包括如下的一种 :肺癌、前列腺癌和淋巴瘤。

459. 根据权利要求 458 的方法，其中所述肺癌包括非小细胞肺癌和小细胞肺癌中的至少一种。

460. 根据权利要求 457 的方法，其中所述肿瘤不是卵巢癌。

461. 一种治疗受试者中肿瘤的方法，包括向所述受试者施用包含抗肿瘤作用的重组干扰素，作为二线单一疗法，并联合一种或更多种其它抗癌疗法。

462. 根据权利要求 461 的方法，其中所述肿瘤包括如下的一种 :肺癌、淋巴瘤、宫颈癌和胆管腺癌。

463. 根据权利要求 462 的方法，其中所述肺癌包括非小细胞肺癌和小细胞肺癌中的至

少一种。

464. 根据权利要求 462 的方法，其中所述淋巴瘤是非霍奇金氏淋巴瘤。

465. 根据权利要求 457、458、459、460、461、462、463 或 464 任一的方法，其中所述一种或更多种其它抗癌疗法包括如下的至少一种：放射疗法、小分子疗法、化学疗法、生物治疗、TCM 和手术治疗。

466. 根据权利要求 465 的方法，其中在所述小分子疗法中的小分子包括吉非替尼。

467. 根据权利要求 465 的方法，其中所述生物治疗包括用如下的至少一种来治疗：重组蛋白和分离的细胞。

468. 根据权利要求 467 的方法，其中所述重组蛋白包括重组人血管内皮抑制素。

469. 根据权利要求 467 的方法，其中所述分离的细胞包括如下的至少一种：干细胞和 NK 细胞。

470. 根据权利要求 465 的方法，其中在癌症手术治疗后施用所述重组干扰素。

471. 根据权利要求 465-469 任一的方法，其中在癌症的手术治疗前施用所述重组干扰素。

472. 根据权利要求 446-471 任一的方法，其中所述重组干扰素通过如下至少一种途径施用：全身和局部。

473. 根据权利要求 446-471 任一的方法，其中所述重组干扰素通过如下至少一种途径施用：肌内、腹膜内、静脉内、动脉内、瘤内、注射入淋巴结中、表面 (topically) 于肿瘤上、局部 (locally) 于肿瘤上、鼻内、皮下、喷雾、吸入、灌注以及输注。

474. 根据权利要求 446-473 任一的方法，其中所述重组干扰素包括 rSIFN-co。

475. 根据权利要求 474 的方法，其中所述重组干扰素以每次治疗约 2 μg 至约 2500 μg 的剂量施用。

476. 根据权利要求 474 的方法，其中所述重组干扰素以每次治疗约 9 μg 至约 2100 μg 的剂量施用。

477. 根据权利要求 474 的方法，其中所述重组干扰素以如下的一种或更多种剂量施用：2 μg、4 μg、9 μg、13.5 μg、15 μg、18 μg、21 μg、24 μg、25.5 μg、30 μg、36 μg、45 μg、70 μg、84 μg、90 μg、100 μg、105 μg、120 μg、126 μg、139 μg、150 μg、168 μg、180 μg、189 μg、198 μg、200 μg、207 μg、210 μg、240 μg、252 μg、273 μg、300 μg、315 μg、400 μg、500 μg、600 μg、1000 μg、2000 μg、2100 μg。

478. 根据权利要求 446-477 任一的方法，其中所述重组干扰素包含特定的活性。

479. 根据权利要求 478 的方法，其中所述重组干扰素包含约 $4.4x10^8$ IU/mg 至约 $1.0x10^9$ IU/mg，以及任选地大于 $5.5x10^8$ IU/mg 的活性。

480. 一种在受试者中预防肿瘤复发的方法，包括在手术治疗、化学疗法、放射疗法、冷冻消融、射频消融、生物治疗、介入治疗和 / 或 rSIFN-co 治疗后，使用包含为包含 SEQ ID NO：2 的序列的核酸序列编码的氨基酸序列的量的重组干扰素，在受试者中瘤块已减小后由此施用所述重组干扰素。

481. 一种延长受试者无瘤生存的方法，包括在手术治疗、化学疗法、放射疗法、冷冻消融、射频消融、生物治疗、介入治疗和 / 或 rSIFN-co 治疗后，使用包含为包含 SEQ ID NO：2 的序列的核酸序列编码的氨基酸序列的量的重组干扰素，在受试者中瘤块已减小后由此施

用所述重组干扰素。

用空间构象改变的重组干扰素治疗肿瘤的方法

发明领域

[0001] 本发明涉及用重组干扰素治疗受试者中肿瘤的方法，以及用于治疗受试者中实体瘤包括肺癌的方法。本发明进一步涉及空间构象改变的重组干扰素（rSIFN-co）单用或联合放射治疗、化学治疗和/或抗肿瘤药物如生物制剂、靶向药物等非手术消除受试者中肿瘤或缩小肿瘤瘤体，或防止受试者肿瘤术后复发和/或转移和/或延长无瘤生存的方法。

[0002] 发明背景

[0003] 癌症是世界范围内人的主要死因之一。全世界病例总数不断增加。据世界卫生组织（WHO）统计，从2007年至2030年全球癌症死亡人数预计增加45%（从790万人增加至1150万人），同一时期内癌症新病例估计从2007年的1130万人跃升至2030年的1550万人。其中，肺癌的发病率和死亡率在全球恶性肿瘤中居首位。有资料统计，每年全世界肺癌新病例大于300万且不断在增加（参见Gray，J.et al.Chest，2007，132，56S-68S）。在世界范围内肺癌每年导致超过130万人死亡，超过了其他三种最常见癌症（乳腺癌、前列腺癌和结直肠癌）所导致的癌症相关死亡人数的总和。

[0004] 经典的癌症治疗方法包括：手术治疗、放射治疗和化学治疗。然而，并非所有类型的实体瘤都适合于手术治疗。由于病灶的转移等原因，手术治疗可能无法彻底清除癌细胞，因而无法达到根治的目的。而放射治疗仅适用于对射线敏感、且瘤床为肌肉而血液循环又较好的部位的肿瘤，而且放射治疗会误伤正常细胞，引发多种副作用，从而影响患者生存质量。作为全身治疗手段的化学治疗，其效果取决于癌症的类型和病况，更多的是抑制癌症生长和扩散，与放射治疗相同，化学治疗也会误伤正常细胞，影响患者生存质量。

[0005] 对于一些早、中期的实体瘤患者行手术治疗可消除瘤体、改善生活质量、以及为后续治疗提供时间；但对于晚期已转移的实体瘤患者，已明显影响生活质量、甚至危及生命时，现有技术的治疗方法也仅限于化疗、放疗或放化疗联合其他治疗方法，这些治疗方法效果均不理想，不能达到消除瘤体、完全缓解患者病症的目的。

[0006] 大量数据表明，对于晚期肺癌患者，现有的癌症治疗方法尤其是化学治疗无法取得令人满意的治疗效果，完全缓解（CR）的病例数量很少甚至没有。例如，在应用顺铂分别联合诺维本、健择、泰索帝治疗晚期非小细胞肺癌的78例临床研究中，均无完全缓解（CR）病例出现（参见宋扬等，现代肿瘤医学，2005，13(4)，494-496）；而在使用四种化疗方案（顺铂+紫杉醇、顺铂+吉西他滨、顺铂+多西紫杉醇、以及卡铂+紫杉醇）治疗晚期非小细胞肺癌的总计1155例的临床观察中，完全应答率（CR）小于1%（参见Schiller，J.H.et al.N Engl J Med，2002，346(2)，92-98）；以及在使用重组人血管内皮抑制素联合NP方案治疗晚期非小细胞肺癌的随机、双盲、对照、多中心III期临床研究中，试验组和对照组的486例可评价患者中均无完全缓解的病例（参见王金万等，中国肺癌杂志，2005，8(4)，283-290）。

[0007] 近二十多年来，随着细胞生物学、分子生物学、肿瘤免疫学等研究的深入与生物工程技术的发展，生物治疗已成为继手术治疗、放射治疗和化学治疗之后的治疗癌症的又一重要的治疗手段。

[0008] 自Isaacs和Lindenmann发现干扰素（IFNs）以来，已对其进行了广泛研究。干扰

素是一种由多种细胞产生的可溶性蛋白质，其具有多种重要的生物功能，包括抗病毒、抗肿瘤和免疫调节功能。根据产生细胞类型、受体、生物活性等的不同，干扰素可分为Ⅰ型、II型和III型干扰素。Ⅰ型干扰素主要由病毒及合成的双链RNA所诱导，因此也称为抗病毒干扰素。现有三种类型的Ⅰ型干扰素：IFNα、IFNβ 和 IFNω。

[0009] 近年来，世界上许多公司都在参与干扰素的研究。举例来说，US4,695,623 和 US 4,897,471 公开了新型人干扰素多肽，其氨基酸序列包含存在于天然 α－干扰素多肽中的共同或占优势的氨基酸。一种新型干扰素多肽被命名为IFN-con（共有干扰素 α）。研究表明与白细胞干扰素或其他Ⅰ型干扰素相比，该重组IFN-con具有更高的体外抗病毒、抗增殖及天然杀伤细胞活性。1997 年底，美国食品与药品管理局 (FDA) 批准了美国安进 (Amgen) 公司生产的人共有干扰素作为丙型肝炎临床治疗用药，商品名为干复津（INFERGEN®，干扰素 alfacon-1）。

[0010] 一直以来，都认为蛋白质的氨基酸序列决定了其三维结构，进而决定了其功能。然而，近年来有证据表明，编码蛋白质的核苷酸序列的同义突变（即不改变所编码蛋白质的氨基酸序列的密码子突变）能影响所编码蛋白质的空间结构和功能，即这样的带同义突变的核苷酸序列能表达生成与野生型蛋白相比具有不同的最终结构和功能的蛋白（参见 Sarfaty, C. K. et al. Science, 2007, 315, 525-528）。

[0011] 在 US 7,364,724、US 7,585,647、US 8,114,395、CN 1740197 A、CN101001644 A、US 2009/0123417、US 2011/0158941 和 WO 2011072487A1 中公开了一种功效增强、副作用更小且能够大剂量使用的重组干扰素 (rSIFN-co)。所述重组干扰素 rSIFN-co 具有与干复津（INFERGEN®）相同的氨基酸序列，但彼此的编码核苷酸序列不同（即编码该重组干扰素 rSIFN-co 的核苷酸序列存在同义突变），由此导致其空间构象发生了变化、生物效力得到了质的改变。

[0012] 发明概述

[0013] 本发明的一个目的在于提供使用由 SEQ ID NO:2 的核苷酸序列编码的重组干扰素 rSIFN-co 治疗受试者中的肿瘤的新方法。本发明的另一个目的还在于提供使用由 SEQ ID NO:2 的核苷酸序列编码的重组干扰素（以下也可称为“重组高效复合干扰素”或“rSIFN-co”）治疗受试者中的肺癌的新方法。

[0014] 本发明通过下述多个实施方案予以举例说明。然而，本发明并不限于这些例证性的实施方案，并且应当被解释以包括根据本文描述所教导的以及如本领域技术人员所理解的那些实施方案。本发明多个实施方案的示例包括：

[0015] 在一个方面，本发明提供了：

[0016] (1) 一种治疗受试者中的肿瘤的方法，包括向所述受试者施用由 SEQ ID NO:2 编码的重组干扰素。

[0017] (2) 根据 (1) 的方法，其中所述受试者中的肿瘤包含转移的肿瘤。

[0018] (3) 根据 (1) 或 (2) 的方法，其中所述受试者是早期、中期或晚期癌症患者，任选地，所述受试者是中期或晚期癌症患者，更任选地，所述受试者是晚期癌症患者。

[0019] (4) 根据 (1) 或 (2) 的方法，其中所述受试者是 0、I、II、III 或 IV 期癌症患者，任选地，所述受试者是 III 或 IV 期癌症患者。

[0020] (5) 根据 (1)-(4) 任一的方法，其中所述肿瘤为具备手术指征或适于手术的癌症

或实体瘤。

[0021] (6) 根据 (1)-(4) 任一的方法，其中所述肿瘤为不具备手术指征也不适于手术的癌症或实体瘤。

[0022] (7) 根据 (1)-(5) 任一的方法，其中所述肿瘤是可切除的肿瘤。

[0023] (8) 根据 (1)-(4) 和 (6) 任一的方法，其中所述肿瘤是不可切除的肿瘤。

[0024] (9) 根据 (7) 或 (8) 的方法，其中所述肿瘤通过手术切除被切除。

[0025] (10) 根据 (1)-(9) 任一的方法，其中所述肿瘤是实体瘤。

[0026] (11) 根据 (10) 的方法，其中所述实体瘤包括如下的一种或更多种：肺癌、肝癌、肝细胞癌 (HCC)、食道癌、胆管癌、胆囊癌、胃癌 (stomach cancer)、腹部癌 (abdominal cancer)、胃肠道癌、胃癌 (gastric cancer)、胰腺癌、肾细胞癌、肾癌、骨癌、乳腺癌、卵巢癌、子宫癌、宫颈癌、子宫内膜癌、结直肠癌、结肠癌、直肠癌、膀胱癌、浅表性膀胱癌、前列腺癌、前列腺癌、肾上腺瘤、鳞状细胞癌、神经瘤、恶性神经瘤、肌上皮癌、滑膜肉瘤、横纹肌肉瘤、胃肠道间质细胞瘤、皮肤癌、基底细胞癌、恶性黑色素瘤、甲状腺癌、鼻咽癌、血管瘤、表皮样癌、头颈癌、神经胶质瘤、或卡波济氏肉瘤。

[0027] (12) 根据 (11) 的方法，其中所述实体瘤包括肺癌，任选地，所述肺癌包括小细胞肺癌 (SCLC)、非小细胞肺癌 (NSCLC) 或两者。

[0028] (13) 根据 (1)-(4) 任一的方法，其中所述肿瘤是非实体瘤。

[0029] (14) 根据 (13) 的方法，其中所述非实体瘤包括如下的一种或更多种：白血病、急性白血病、慢性白血病、慢性粒细胞性白血病、急性髓性白血病、慢性髓性白血病、慢性淋巴细胞白血病、急性淋巴细胞白血病、T 细胞白血病、毛细胞白血病、红细胞增多症、骨髓增生异常综合征、多发性骨髓瘤、淋巴腺瘤、霍奇金氏淋巴瘤和非霍奇金氏淋巴瘤。

[0030] (15) 根据 (1)-(14) 任一的方法，其中通过如下至少一种：全身给药、局部给药 (local administration) 和表面给药 (topical administration)，向受试者施用所述重组干扰素。

[0031] (16) 根据 (1)-(15) 任一的方法，其中通过给药途径向受试者施用所述重组干扰素，所述给药途径包括如下的一种或更多种：经口、直肠、舌下、静脉内、动脉内、肌肉、皮下、骨内、皮内、关节内、腹膜内、鞘内、脑内、阴道、经皮、透皮、表皮、粘膜、经眼、经肺、经鼻、腹腔、胸腔、心室内、心包、吸入、瘤内、子宫、浸润和膀胱内给药。

[0032] (17) 根据 (1)-(16) 任一的方法，其中向所述受试者施用有效量的由 SEQ ID NO：2 的核苷酸序列编码的重组干扰素，任选地，所述有效量为治疗有效量。

[0033] (18) 根据 (1)-(17) 任一的方法，其中向所述受试者施用约 2μg- 约 2000μg 单次剂量的所述重组干扰素，任选地，向所述受试者施用约 4μg- 约 1500μg 单次剂量的所述重组干扰素，更任选地，向所述受试者施用约 9μg- 约 1000μg 单次剂量的所述重组干扰素。

[0034] (19) 根据 (1)-(18) 任一的方法，其中在一个或更多个治疗周期中施用所述重组干扰素，任选地，所述更多个治疗周期包含 2、3、4、5、6、7、8、9、10 个治疗周期，更任选地，所述治疗周期的数目包含多于 10 个治疗周期。

[0035] (20) 根据 (19) 的方法，其中所述一个治疗周期的持续时间为至少约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个

月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、或约 6 年等，或任选地，可长期施用所述重组干扰素，包括受试者生命的整个期间；或者所述重组干扰素治疗的持续时间还可以是约 1 天 - 约 6 年，约 1 周 - 约 4 年，约 2 周 - 约 3 年，约 1 个月 - 约 1 年、或约 2 个月 - 约 9 个月等。

[0036] (21) 根据 (19) 或 (20) 的方法，其中所述更多个治疗周期中的任意相邻两个治疗周期之间的间隔时间为至少约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、或约 6 年等；或任选地，所述间隔时间可为约 2 天 - 约 6 年，约 4 天 - 约 3 年、约 1 周 - 约 1 年、约 2 个月 - 约 9 个月、或约 3 个月 - 约 6 个月等。

[0037] (22) 根据 (1)-(21) 任一的方法，其中所述重组干扰素作为单一疗法向受试者施用。

[0038] (23) 根据 (1)-(21) 任一的方法，进一步包含向所述受试者施用至少一种其他抗癌疗法，任选地，在施用所述重组干扰素之前、同时和 / 或之后给予所述受试者至少一种其他抗癌疗法。

[0039] (24) 根据 (23) 的方法，其中所述至少一种其他抗癌疗法包括如下的至少一种：化学治疗、放射治疗、手术治疗、介入治疗、生物治疗、基因治疗、消融治疗、免疫治疗、靶向治疗和中药治疗。

[0040] (25) 根据 (24) 的方法，其中所述至少一种其他抗癌疗法包括如下的至少一种：化学治疗、放射治疗、手术治疗、靶向治疗和生物治疗。

[0041] (26) 根据 (25) 的方法，其中所述至少一种其他抗癌疗法包括如下的至少一种：化学治疗和放射治疗。

[0042] (27) 根据 (24)-(26) 任一的方法，其中所述化学治疗作为一线化学治疗被给予，任选地，所述一线化学治疗使用的一种或更多种化学治疗剂包括铂类化合物，例如顺铂。

[0043] (28) 根据 (24)-(27) 任一的方法，其中所述靶向治疗包括如下的至少一种：吉非替尼、厄洛替尼和重组人血管内皮抑制素。

[0044] (29) 根据 (1)-(28) 任一的方法，其中与治疗前的肿瘤相比，所述治疗消除了所述肿瘤或减小了所述肿瘤的大小。

[0045] (30) 根据 (29) 的方法，其中所述肿瘤的大小的减小将所述肿瘤转变为可切除的肿瘤。

[0046] (31) 根据 (30) 的方法，其中所述肿瘤具有手术切除指征。

[0047] (32) 根据 (1)-(28) 任一的方法，其中所述肿瘤例如癌症或实体瘤由较早的不具备手术指征也不适于手术转变为具备手术指征或适于手术。

[0048] (33) 根据 (32) 的方法，进一步包括进行手术以切除所述肿瘤。

[0049] (34) 根据 (30)-(31) 和 (33) 任一的方法，进一步包括在切除所述肿瘤后给予受试者所述重组干扰素以防止肿瘤复发和 / 或转移，或者延长或维持无瘤状态，任选地，给予受试者预防有效量的所述重组干扰素以防止肿瘤复发和 / 或转移，和 / 或延长或维持无瘤状态。

[0050] (35) 一种治疗受试者中肿瘤的方法，包括向所述受试者施用由 SEQ ID NO：2 编码

的重组干扰素以及至少一种其他抗癌疗法，其中在施用所述重组干扰素之前、同时和/或之后给予所述受试者至少一种其他抗癌疗法，以及其中所述肿瘤为不具备手术指征也不适于手术的癌症或实体瘤，或所述肿瘤为不可切除的实体瘤，并且与治疗前的肿瘤相比，所述重组干扰素和至少一种其他抗癌疗法的联用消除了所述肿瘤或减小了所述肿瘤的大小。

[0051] (36) 根据实施方案 35 的方法，其中所述受试者是中、晚期癌症患者，或 III 或 IV 期癌症患者，任选地，所述受试者是晚期或 III 或 IV 期癌症患者。

[0052] (37) 根据 (1)-(29) 和 (35)-(36) 任一的方法，其中所述治疗方法为非手术治疗方法。

[0053] 在另一个方面，本发明的其他实施方案提供了：

[0054] (1) 一种在具有肿瘤的受试者经至少一种抗癌疗法后防止肿瘤复发和/或转移，或者延长或维持无瘤状态的方法，包括向所述受试者施用由 SEQ ID NO:2 编码的重组干扰素。

[0055] (2) 根据 (1) 的方法，其中所述受试者中的肿瘤包含转移的肿瘤。

[0056] (3) 根据 (1) 或 (2) 的方法，其中所述受试者是早期、中期或晚期癌症患者。

[0057] (4) 根据 (1) 或 (2) 的方法，其中所述受试者是 0、I、II、III 或 IV 期癌症患者。

[0058] (5) 根据 (1)-(4) 任一的方法，其中所述肿瘤为具备手术指征或适于手术的癌症或实体瘤。

[0059] (6) 根据 (1)-(4) 任一的方法，其中所述肿瘤为不具备手术指征也不适于手术的癌症或实体瘤。

[0060] (7) 根据 (1)-(4) 任一的方法，其中所述肿瘤是可切除的肿瘤。

[0061] (8) 根据 (1)-(4) 任一的方法，其中所述肿瘤是不可切除的肿瘤。

[0062] (9) 根据 (7) 或 (8) 的方法，其中所述肿瘤通过手术切除被切除。

[0063] (10) 根据 (1)-(9) 任一的方法，其中所述肿瘤是实体瘤。

[0064] (11) 根据 (10) 的方法，其中所述实体瘤包括如下的一种或更多种：肺癌、肝癌、肝细胞癌 (HCC)、食道癌、胆管癌、胆囊癌、胃癌 (stomach cancer)、腹部癌 (abdominal cancer)、胃肠道癌、胃癌 (gastric cancer)、胰腺癌、肾细胞癌、肾癌、骨癌、乳腺癌、卵巢癌、子宫癌、宫颈癌、子宫内膜癌、结直肠癌、结肠癌、直肠癌、膀胱癌、浅表性膀胱癌、前列腺癌、前列腺癌、肾上腺瘤、鳞状细胞癌、神经瘤、恶性神经瘤、肌上皮癌、滑膜肉瘤、横纹肌肉瘤、胃肠道间质细胞瘤、皮肤癌、基底细胞癌、恶性黑色素瘤、甲状腺癌、鼻咽癌、血管瘤、表皮样癌、头颈癌、神经胶质瘤、或卡波济氏肉瘤。

[0065] (12) 根据 (11) 的方法，其中所述实体瘤包括肺癌，任选地，所述肺癌包括小细胞肺癌 (SCLC)、非小细胞肺癌 (NSCLC) 或两者。

[0066] (13) 根据 (1)-(4) 任一的方法，其中所述肿瘤包括非实体瘤。

[0067] (14) 根据 (13) 的方法，其中所述非实体瘤包括如下的一种或更多种：白血病、急性白血病、慢性白血病、慢性粒细胞性白血病、急性髓性白血病、慢性髓性白血病、慢性淋巴细胞白血病、急性淋巴细胞白血病、T 细胞白血病、毛细胞白血病、红细胞增多症、骨髓增生异常综合征、多发性骨髓瘤、淋巴腺瘤、霍奇金氏淋巴瘤和非霍奇金氏淋巴瘤。

[0068] (15) 根据 (1)-(14) 任一的方法，其中通过如下至少一种：全身给药、局部给药 (local administration) 和表面给药 (topical administration)，向受试者施用所述重组

干扰素。

[0069] (16) 根据 (1)-(15) 任一的方法，其中通过给药途径向受试者施用所述重组干扰素，所述给药途径包括如下的一种或更多种：经口、直肠、舌下、静脉内、动脉内、肌肉、皮下、骨内、皮内、关节内、腹膜内、鞘内、脑内、阴道、经皮、透皮、表皮、粘膜、经眼、经肺、经鼻、腹腔、胸腔、心室内、心包、吸入、瘤内、子宫、浸润和膀胱内给药。

[0070] (17) 根据 (1)-(16) 任一的方法，其中向所述受试者施用有效量的由 SEQ ID NO：2 的核苷酸序列编码的重组干扰素，任选地，所述有效量为预防有效量。

[0071] (18) 根据 (1)-(17) 任一的方法，其中向所述受试者施用约 2μg-约 2000μg 单次剂量的所述重组干扰素，任选地，向所述受试者施用约 4μg-约 1500μg 单次剂量的所述重组干扰素，更任选地，向所述受试者施用约 9μg-约 1000μg 单次剂量的所述重组干扰素。

[0072] (19) 根据 (1)-(18) 任一的方法，其中在一个或更多个预防周期中施用所述重组干扰素，任选地，所述更多个预防周期包含 2、3、4、5、6、7、8、9 或 10 个预防周期，或任选地，多于 10 个预防周期。

[0073] (20) 根据 (19) 的方法，其中每个预防周期的持续时间为至少约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、或约 6 年等，或长期施用所述重组干扰素，包括受试者生命的整个期间；或者所述持续时间还可以是约 1 天 - 约 6 年，约 1 周 - 约 4 年，约 2 周 - 约 3 年，约 1 个月 - 约 1 年、或约 2 个月 - 约 9 个月等。

[0074] (21) 根据 (19) 或 (20) 的方法，其中所述更多个预防周期中的任意相邻两个预防周期之间的间隔时间为至少约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、或约 6 年等；或者所述间隔时间还可以为约 2 天 - 约 6 年，约 4 天 - 约 3 年、约 1 周 - 约 1 年、约 2 个月 - 约 9 个月、或约 3 个月 - 约 6 个月等。

[0075] (22) 根据 (1)-(21) 任一的方法，其中所述至少一种抗癌疗法包括如下的至少一种：化学治疗、放射治疗、手术治疗、介入治疗、生物治疗、基因治疗、消融治疗、免疫治疗、靶向治疗和中药治疗，任选地，所述至少一种抗癌疗法包括如下的至少一种：化学治疗、放射治疗、手术治疗和生物治疗。

[0076] (23) 根据 (22) 的方法，其中所述至少一种抗癌疗法包括手术治疗。

[0077] (24) 根据 (23) 的方法，其中向所述手术治疗的手术部位施用所述重组干扰素。

[0078] (25) 根据 (24) 的方法，其中经表面 (topical) 或局部 (local) 给药向手术部位施用所述重组干扰素。

[0079] (26) 根据 (24) 或 (25) 的方法，其中通过给药途径向手术部位施用所述重组干扰素，所述给药途径包括如下的一种或更多种：浸润给药、胸腔给药、腹腔给药、心包给药、子宫给药、膀胱内给药、瘤内给药、经肺给药、经鼻给药、经皮给药、透皮给药、表皮给药和粘膜给药。

[0080] (27) 根据 (26) 的方法，其中所述胸腔给药、腹腔给药、心包给药、子宫给药或膀胱内给药分别包括胸腔灌注给药、腹腔灌注给药、心包灌注给药、子宫灌注给药或膀胱内灌注

给药。

[0081] (28) 根据 (26) 的方法，其中所述瘤内给药包括瘤内注射。

[0082] (29) 根据 (26) 的方法，其中所述经肺给药或经鼻给药分别包括经肺吸入给药或经鼻吸入给药。

[0083] (30) 根据 (26) 的方法，其中所述经皮给药、透皮给药、表皮给药或粘膜给药分别包括经皮喷雾给药、透皮喷雾给药、表皮喷雾给药或粘膜喷雾给药。

[0084] (31) 根据 (25)-(30) 任一的方法，其中在表面 (topical) 或局部 (local) 给药所述重组干扰素的之前、同时和 / 或之后，经全身给药向所述受试者进一步施用所述重组干扰素。

[0085] (32) 根据 (31) 的方法，其中所述全身给药包括如下的至少一种 ：皮下和肌肉给药，任选地，上述 (24)-(32) 中的方案同样适用于前文提及的治疗受试者中的肿瘤的方法。

[0086] (33) 根据 (1)-(32) 任一的方法，其中所述重组干扰素作为单一疗法向受试者施用。

[0087] 在另一个方面，本发明的其他实施方案提供了 ：

[0088] (1) 一种非手术消除受试者中肿瘤或减小受试者中肿瘤的大小的方法，包括向所述受试者施用由 SEQ ID NO ：2 编码的重组干扰素。

[0089] (2) 根据 (1) 的方法，其中所述肿瘤为具备手术指征或适于手术的癌症或实体瘤。

[0090] (3) 根据 (1) 的方法，其中所述肿瘤为不具备手术指征也不适于手术的癌症或实体瘤。

[0091] (4) 根据 (1) 的方法，其中所述肿瘤是可切除的肿瘤。

[0092] (5) 根据 (1) 的方法，其中所述肿瘤是不可切除的肿瘤。

[0093] (6) 根据 (4) 或 (5) 的方法，其中所述肿瘤通过手术切除被切除。

[0094] (7) 根据 (1)-(6) 任一的方法，其中所述受试者是早期、中期或晚期癌症患者，任选地，所述受试者是中期或晚期癌症患者，或更任选地，所述受试者是晚期癌症患者。

[0095] (8) 根据 (1)-(6) 任一的方法，其中所述受试者是 0、I、II、III 或 IV 期癌症患者，任选地，所述受试者是 III 或 IV 期癌症患者。

[0096] (9) 根据 (1)-(8) 任一的方法，其中所述受试者是中期或晚期癌症患者，或 III 或 IV 期癌症患者，任选地，所述受试者是晚期或 III 或 IV 期癌症患者。

[0097] (10) 根据 (1)-(9) 任一的方法，其中所述肿瘤为实体瘤。

[0098] (11) 根据 (10) 的方法，其中所述实体瘤包括如下的一种或更多种 ：肺癌、肝癌、肝细胞癌 (HCC)、食道癌、胆管癌、胆囊癌、胃癌 (stomach cancer)、腹部癌 (abdominal cancer)、胃肠道癌、胃癌 (gastric cancer)、胰腺癌、肾细胞癌、肾癌、骨癌、乳腺癌、卵巢癌、子宫癌、宫颈癌、子宫内膜癌、结直肠癌、结肠癌、直肠癌、膀胱癌、浅表性膀胱癌、前列腺癌、前列腺癌、肾上腺瘤、鳞状细胞癌、神经瘤、恶性神经瘤、肌上皮癌、滑膜肉瘤、横纹肌肉瘤、胃肠道间质细胞瘤、皮肤癌、基底细胞癌、恶性黑色素瘤、甲状腺癌、鼻咽癌、血管瘤、表皮样癌、头颈癌、神经胶质瘤、或卡波济氏肉瘤。

[0099] (12) 根据 (11) 的方法，其中所述实体瘤包括肺癌，任选地，所述肺癌包括小细胞肺癌 (SCLC)、非小细胞肺癌 (NSCLC) 或两者。

[0100] (13) 根据 (1)-(12) 任一的方法，其中通过如下至少一种 ：全身给药、局部给药

(local administration)和表面给药(topical administration),向受试者施用所述重组干扰素,任选地,通过表面或局部给药向受试者施用所述重组干扰素,更任选地,通过局部给药向受试者施用所述重组干扰素。

[0101] (14)根据(1)-(13)任一的方法,其中通过给药途径向所述受试者施用所述重组干扰素,所述给药途径包括如下的一种或更多种:浸润给药、胸腔给药、腹腔给药、心包给药、子宫给药、膀胱内给药、瘤内给药、经肺给药、经鼻给药、经皮给药、透皮给药、表皮给药和粘膜给药。

[0102] (15)根据(14)的方法,其中所述瘤内给药包括瘤内注射。

[0103] (16)根据(15)的方法,其中所述重组干扰素以如下范围的量施用:一次瘤内注射约60μg-约600μg,任选地,约60μg-约500μg,更任选地,约80μg-约400μg,还更任选地,约100μg-约250μg。

[0104] (17)根据(15)或(16)的方法,其中每约1天-约10天,任选地,每约1天-约7天,例如每约1、2、3、4、5、6或7天瘤内注射一次所述重组干扰素。

[0105] (18)根据(14)-(17)任一的方法,其中瘤内给药的给药方案如下:每约1天瘤内注射一次所述重组干扰素,持续约4次-约8次,接着每约3天-约5天瘤内注射一次所述重组干扰素,持续约4次-约8次,然后每约7天瘤内注射一次所述重组干扰素,当瘤体消失或瘤体小至无法进行瘤内注射时,停止瘤内给药。

[0106] (19)根据(14)的方法,其中所述胸腔给药、腹腔给药、心包给药、子宫给药或膀胱内给药分别包括胸腔灌注给药、腹腔灌注给药、心包灌注给药、子宫灌注给药或膀胱内灌注给药。

[0107] (20)根据(14)的方法,其中所述经肺给药或经鼻给药分别包括经肺吸入给药或经鼻吸入给药。

[0108] (21)根据(14)的方法,其中所述经皮给药、透皮给药、表皮给药或粘膜给药分别包括经皮喷雾给药、透皮喷雾给药、表皮喷雾给药或粘膜喷雾给药。

[0109] (22)根据(13)-(21)任一的方法,其中在表面或局部给药所述重组干扰素的之前、同时和/或之后,经全身给药向所述受试者进一步施用所述重组干扰素,和/或经表面给药、局部给药和/或全身给药向所述受试者施用至少一种其他治疗药物。

[0110] (23)根据(22)的方法,其中在表面或局部给药所述重组干扰素的同时和/或之后,经全身给药向所述受试者进一步施用所述重组干扰素,和/或经表面给药、局部给药和/或全身给药向所述受试者施用至少一种其他治疗药物。

[0111] (24)根据(22)或(23)的方法,其中所述至少一种其他治疗药物包括至少一种抗肿瘤药物。

[0112] (25)根据(24)的方法,其中所述至少一种抗肿瘤药物包括一种或更多种化学治疗剂、靶向药物和/或生物制剂。

[0113] (26)根据(25)的方法,其中所述一种或更多种化学治疗剂包括铂类化合物,例如顺铂。

[0114] (27)根据(25)的方法,其中所述一种或更多种靶向药物包括吉非替尼、厄洛替尼和/或重组人血管内皮抑制素。

[0115] 在另一个方面,本发明的其他实施方案提供了:

[0116] (1) 一种消除或减少具有肿瘤的受试者中的胸腔积液、腹腔积液和 / 或心包积液的方法，包括向所述受试者给予由 SEQ ID NO :2 编码的重组干扰素。

[0117] (2) 根据 (1) 的方法，其中所述肿瘤为具备手术指征或适于手术的癌症或实体瘤。

[0118] (3) 根据 (1) 的方法，其中所述肿瘤为不具备手术指征也不适于手术的癌症或实体瘤。

[0119] (4) 根据 (1) 的方法，其中所述肿瘤是可切除的肿瘤。

[0120] (5) 根据 (1) 的方法，其中所述肿瘤是不可切除的肿瘤。

[0121] (6) 根据 (4) 或 (5) 的方法，其中所述肿瘤通过手术切除被切除。

[0122] (7) 根据 (1)-(6) 任一的方法，其中所述受试者是早期、中期或晚期癌症患者，任选地，所述受试者是中期或晚期癌症患者，或更任选地，所述受试者是晚期癌症患者。

[0123] (8) 根据 (1)-(6) 任一的方法，其中所述受试者是 0、I、II、III 或 IV 期癌症患者，任选地，所述受试者是 III 或 IV 期癌症患者。

[0124] (9) 根据 (1)-(8) 任一的方法，其中所述受试者是中期或晚期癌症患者，或 III 或 IV 期癌症患者，任选地，所述受试者是晚期或 III 或 IV 期癌症患者。

[0125] (10) 根据 (1)-(9) 任一的方法，其中所述肿瘤为实体瘤。

[0126] (11) 根据 (10) 的方法，其中所述实体瘤包括如下的一种或更多种 :肺癌、肝癌、肝细胞癌 (HCC)、食道癌、胆管癌、胆囊癌、胃癌 (stomach cancer)、腹部癌 (abdominal cancer)、胃肠道癌、胃癌 (gastric cancer)、胰腺癌、肾细胞癌、肾癌、骨癌、乳腺癌、卵巢癌、子宫癌、宫颈癌、子宫内膜癌、结直肠癌、结肠癌、直肠癌、膀胱癌、浅表性膀胱癌、前列腺癌、前列腺癌、肾上腺瘤、鳞状细胞癌、神经瘤、恶性神经瘤、肌上皮癌、滑膜肉瘤、横纹肌肉瘤、胃肠道间质细胞瘤、皮肤癌、基底细胞癌、恶性黑色素瘤、甲状腺癌、鼻咽癌、血管瘤、表皮样癌、头颈癌、神经胶质瘤、或卡波济氏肉瘤。

[0127] (12) 根据 (11) 的方法，其中所述实体瘤包括肺癌，任选地，所述肺癌包括小细胞肺癌 (SCLC)、非小细胞肺癌 (NSCLC) 或两者。

[0128] (13) 根据 (1)-(12) 任一的方法，其中所述胸腔积液为恶性胸腔积液，所述腹腔积液为恶性腹腔积液，和 / 或所述心包积液为恶性心包积液。

[0129] (14) 根据 (1)-(13) 任一的方法，其中通过如下至少一种 :全身给药、局部给药 (local administration) 和表面给药 (topical administration)，向受试者施用所述重组干扰素，任选地，通过表面给药和局部给药向受试者施用所述重组干扰素，更任选地，通过局部给药向受试者施用所述重组干扰素。

[0130] (15) 根据 (1)-(14) 任一的方法，其中通过给药途径向所述受试者施用所述重组干扰素，所述给药途径包括如下的一种或更多种 :浸润给药、胸腔给药、腹腔给药和心包给药。

[0131] (16) 根据 (1)-(15) 任一的方法，其中通过灌注进行所述给药。

[0132] (17) 根据 (14)-(16) 任一的方法，其中所述重组干扰素以如下范围的量施用 :一次表面或局部给药约 30 μg- 约 2000 μg，任选地，约 100 μg- 约 1500 μg，更任选地，约 150 μg- 约 1000 μg，还任选地，约 200 μg- 约 800 μg，还更任选地，约 200 μg- 约 400 μg。

[0133] (18) 根据 (14)-(17) 任一的方法，其中每约 1- 约 10 天，任选地，每约 1- 约 7 天，例如每约 1、2、3、4、5、6 或 7 天表面或局部给药一次所述重组干扰素。

[0134] (19) 根据 (14)-(18) 任一的方法，其中在表面或局部给药所述重组干扰素的之前、同时和 / 或之后，经全身给药向所述受试者进一步施用所述重组干扰素，和经表面给药、局部给药和 / 或全身给药向所述受试者施用至少一种其他治疗药物。

[0135] (20) 根据 (19) 的方法，其中在表面或局部给药所述重组干扰素的同时和 / 或之后，经全身给药向所述受试者进一步施用所述重组干扰素，和经表面给药、局部给药和 / 或全身给药向所述受试者施用至少一种其他治疗药物。

[0136] (21) 根据 (19) 或 (20) 任一的方法，其中所述至少一种其他治疗药物包括抗肿瘤药物。

[0137] (22) 根据 (21) 的方法，其中所述抗肿瘤药物包括如下的至少一种 ：化学治疗剂、靶向药物和生物制剂。

[0138] (23) 根据 (22) 的方法，其中所述至少一种化学治疗剂包括至少一种铂类化合物，例如顺铂。

[0139] (24) 根据 (22) 的方法，其中所述至少一种靶向药物包括如下的至少一种 ：吉非替尼、厄洛替尼和重组人血管内皮抑制素。

[0140] (25) 根据 (1)-(24) 任一的方法，其中与治疗前的肿瘤相比，所述治疗消除了所述肿瘤或减小了所述肿瘤的大小。

[0141] (26) 根据 (1)-(25) 任一的方法，其中所述治疗为非手术治疗。

[0142] 在另一个方面，本发明的其他实施方案提供了 ：

[0143] (1) 一种治疗受试者中的肿瘤的方法，包括通过表面或局部给药向受试者的肿瘤病灶施用由 SEQ ID NO ：2 编码的重组干扰素。

[0144] (2) 根据 (1) 的方法，其中所述肿瘤病灶包括肿瘤转移病灶。

[0145] (3) 一种消除或减小受试者中的肿瘤转移病灶的方法，包括通过表面或局部给药向受试者的肿瘤转移病灶施用由 SEQ ID NO ：2 编码的重组干扰素。

[0146] (4) 根据 (1)-(3) 任一的方法，其中所述肿瘤病灶包括如下的至少一种 ：骨病灶、肌肉病灶、皮下组织病灶、前列腺病灶和淋巴结病灶，以及所述肿瘤转移病灶包括如下的至少一种 ：骨转移病灶、肌肉转移病灶、皮下组织转移病灶、前列腺转移病灶和淋巴结转移病灶，任选地，所述肿瘤转移病灶包括骨转移病灶。

[0147] (5) 根据 (1)-(4) 任一的方法，其中所述受试者是中期、晚期或 III 或 IV 期癌症患者，任选地，所述受试者是晚期或 III 或 IV 期癌症患者。

[0148] (6) 根据 (1)-(4) 任一的方法，其中所述肿瘤或肿瘤转移病灶包括不具备手术指征也不适于手术的癌症或实体瘤。

[0149] (7) 根据 (1)-(6) 任一的方法，其中所述表面或局部给药包括如下的至少一种 ：浸润给药、经皮给药、透皮给药、表皮给药和粘膜给药，任选地，所述表面和局部给药包括透皮给药或浸润给药。

[0150] (8) 根据 (7) 的方法，其中所述浸润给药包括如下的至少一种 ：经皮浸润给药、表皮浸润给药、透皮浸润给药和粘膜浸润给药。

[0151] (9) 根据 (7) 的方法，其中所述经皮给药、透皮给药、表皮给药或粘膜给药分别包括经皮喷雾给药、透皮喷雾给药、表皮喷雾给药或粘膜喷雾给药。

[0152] (10) 根据 (1)-(9) 任一的方法，其中所述重组干扰素以如下范围的量施用 ：一次

表面或局部给药约 2 μg- 约 2000 μg，任选地，约 4 μg- 约 1500 μg，更任选地，约 9 μg- 约 1000 μg。

[0153] (11) 根据 (1)-(10) 任一的方法，其中每天向受试者表面或局部给药约 1、2、3、4、5、6、7、8 或更多次重组干扰素，或者每约 2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20 或 21 天、每个月、每 2 月或更久的时间间隔向受试者表面或局部给药 1 次重组干扰素。

[0154] (12) 根据 (7)-(11) 任一的方法，其中当通过喷雾给药进行表面或局部给药时，所述重组干扰素以如下范围的量施用：一次喷雾给药约 6 μg- 约 100 μg，任选地，约 10 μg- 约 40 μg，更任选地，约 20 μg- 约 40 μg。

[0155] (13) 根据 (12) 的方法，其中每天喷雾给药约 1- 约 6 次，例如约 1、2、3、4、5 或 6 次重组干扰素。

[0156] (14) 根据 (1)-(13) 任一的方法，其中在表面或局部给药所述重组干扰素的之前、同时和 / 或之后，经全身给药向所述受试者施用所述重组干扰素和 / 或一种或更多种其他治疗药物。

[0157] (15) 根据 (14) 的方法，其中所述全身给药包括皮下和 / 或肌肉给药。

[0158] (16) 根据 (15) 的方法，其中所述皮下给药包括皮下注射。

[0159] (17) 根据 (15) 的方法，其中所述肌肉给药包括肌肉注射。

[0160] (18) 根据 (15)-(17) 任一的方法，其中以约 2 μg/ 次 - 约 10 μg/ 次，任选地，约 4 μg/ 次 - 约 10 μg/ 次，更任选地，约 4.5 μg/ 次 - 约 9 μg/ 次，例如约 4.5 μg/ 次或约 9 μg/ 次的诱导剂量通过皮下给药和 / 或肌肉给药施用一次或更多次所述重组干扰素，之后以约 10 μg/ 次 - 约 70 μg/ 次，任选地，约 12 μg/ 次 - 约 50 μg/ 次，更任选地，约 12 μg/ 次 - 约 30 μg/ 次的治疗剂量通过皮下给药和 / 或肌肉给药施用多次所述重组干扰素。

[0161] (19) 根据 (18) 的方法，其中施用诱导剂量与施用治疗剂量之间的间隔为约 1 天 - 约 1 个月，任选地，约 1 天 - 约 1 周，更任选地，约 1 天 - 约 3 天，包括，例如约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、或约 1 个月。

[0162] (20) 根据 (18) 或 (19) 的方法，其中当多次施用诱导剂量的重组干扰素时，每约 1 天 - 约 10 天施用一次所述重组干扰素，任选地，每约 1 天 - 约 7 天施用一次所述重组干扰素，更任选地，每约 1- 约 2 天施用一次所述重组干扰素，包括，例如每约 1、2、3、4、5、6、7、8、9 或 10 天施用一次所述重组干扰素。

[0163] (21) 根据 (18)-(20) 任一的方法，其中每约 1 天 - 约 10 天施用一次治疗剂量的重组干扰素，任选地，每约 1 天 - 约 7 天施用一次治疗剂量的重组干扰素，更任选每约 1- 约 2 天施用一次治疗剂量的重组干扰素，包括，例如每约 1、2、3、4、5、6、7、8、9 或 10 天施用一次治疗剂量的重组干扰素。

[0164] (22) 根据 (18)-(21) 任一的方法，其中诱导剂量和治疗剂量的施用的持续时间为至少约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年或约 6 年等，或者可长期施用所述重组干扰素，包括患者生命的整个期间。

[0165] (23) 根据 (1)-(22) 任一的方法，其中所述重组干扰素作为单一疗法向受试者施

用。

[0166] (24) 根据 (1)-(22) 任一的方法，进一步包括向所述受试者施用至少一种其他抗癌疗法，任选地，在施用所述重组干扰素之前、同时和 / 或之后给予所述受试者至少一种其他抗癌疗法。

[0167] (25) 根据 (24) 的方法，其中所述至少一种其他抗癌疗法包括如下的一种或更多种 :化学治疗、放射治疗、手术治疗、介入治疗、生物治疗、基因治疗、消融治疗、免疫治疗、靶向治疗和中药治疗。

[0168] (26) 根据 (1)-(25) 任一的方法，其中与治疗前的肿瘤或肿瘤转移病灶相比，所述重组干扰素治疗和 / 或至少一种其他抗癌疗法消除了所述肿瘤或肿瘤转移病灶，或减小了所述肿瘤或肿瘤转移病灶的大小。

[0169] (27) 一种消除或减小受试者中的肿瘤骨转移病灶的方法，包括通过表面或局部给药向受试者施用由 SEQ ID NO :2 编码的重组干扰素，其中所述表面或局部给药包括透皮给药和 / 或浸润给药，任选地，向所述受试者的肿瘤骨转移病灶施用所述重组干扰素。

[0170] (28) 一种消除或减小受试者中的肿瘤骨病灶如肿瘤骨转移病灶、肌肉病灶如肌肉转移病灶、皮下组织病灶如皮下组织转移病灶、前列腺病灶如前列腺转移病灶和 / 或淋巴结病灶如淋巴结转移病灶的方法，包括通过任何透过皮肤的给药途径向所述受试者施用由 SEQ ID NO :2 编码的重组干扰素，以消除或减小所述肿瘤骨病灶如肿瘤骨转移病灶、肌肉病灶如肌肉转移病灶、皮下组织病灶如皮下组织转移病灶、前列腺病灶如前列腺转移病灶和 / 或淋巴结病灶如淋巴结转移病灶，任选地，向所述受试者的肿瘤转移病灶施用所述重组干扰素。

[0171] (29) 根据 (1)-(28) 任一的方法，其中所述治疗方法为非手术治疗方法。

[0172] 在另一个方面，本发明的其他实施方案提供了 :

[0173] (1) 一种治疗受试者中的肺癌的方法，包括向所述受试者施用由 SEQ ID NO :2 编码的重组干扰素。

[0174] (2) 根据 (1) 的方法，其中肺癌包括小细胞肺癌 (SCLC)、非小细胞肺癌 (NSCLC) 或两者。

[0175] (3) 根据 (1) 或 (2) 的方法，其中所述受试者中的肺癌包含转移的肿瘤。

[0176] (4) 根据 (1)-(3) 任一的方法，其中所述受试者是是早期、中期或晚期癌症患者，任选地，所述受试者是中期或晚期癌症患者，更任选地，所述受试者是晚期癌症患者。

[0177] (5) 根据 (1)-(3) 任一的方法，其中所述受试者是 0、I、II、III 或 IV 期癌症患者，任选地，所述受试者是 III 或 IV 期癌症患者。

[0178] (6) 根据 (1)-(5) 任一的方法，其中所述肺癌包含具备手术指征或适于手术的肺癌。

[0179] (7) 根据 (1)-(5) 任一的方法，其中所述肺癌包含不具备手术指征也不适于手术的肺癌。

[0180] (8) 根据 (1)-(5) 任一的方法，其中所述肺癌包括可切除的肺癌。

[0181] (9) 根据 (1)-(5) 任一的方法，其中所述肺癌包括不可切除的肺癌。

[0182] (10) 根据 (8) 或 (9) 的方法，其中所述肺癌通过手术切除被切除。

[0183] (11) 根据 (1)-(10) 任一的方法，其中向所述受试者施用有效量的由 SEQ ID NO :

2 的核苷酸序列编码的重组干扰素，任选地，所述有效量为治疗有效量。

[0184] (12) 根据 (1)-(11) 任一的方法，其中通过如下至少一种 :全身给药、表面给药和局部给药向受试者施用所述重组干扰素。

[0185] (13) 根据 (1)-(12) 任一的方法，其中通过给药途径向受试者施用所述重组干扰素，所述给药途径包括如下的一种或更多种 :经口、直肠、舌下、静脉内、动脉内、肌肉、皮下、骨内、皮内、关节内、腹膜内、鞘内、脑内、阴道、经皮、透皮、表皮、粘膜、经眼、经肺、经鼻、腹腔、胸腔、心室内、心包、吸入、瘤内、子宫、浸润和膀胱内给药。

[0186] (14) 根据 (1)-(13) 任一的方法，其中通过皮下给药和 / 或肌肉给药向受试者施用所述重组干扰素。

[0187] (15) 根据 (14) 的方法，其中所述皮下给药包括皮下注射。

[0188] (16) 根据 (14) 的方法，其中所述肌肉给药包括肌肉注射。

[0189] (17) 根据 (14)-(16) 任一的方法，其中所述重组干扰素以如下范围的量施用 :一次皮下和 / 或肌肉给药约 2 μ g- 约 70 μ g。

[0190] (18) 根据 (17) 的方法，其中所述重组干扰素以如下范围的量施用 :一次皮下和 / 或肌肉给药约 4 μ g- 约 50 μ g。

[0191] (19) 根据 (18) 的方法，其中所述重组干扰素以如下范围的量施用 :一次皮下和 / 或肌肉给药约 4 μ g- 约 30 μ g。

[0192] (20) 根据 (14)-(19) 任一的方法，其中每约 1 天 - 约 7 天皮下和 / 或肌肉给药一次所述重组干扰素。

[0193] (21) 根据 (20) 的方法，其中每约 1 天 - 约 2 天皮下和 / 或肌肉给药一次所述重组干扰素。

[0194] (22) 根据 (1)-(21) 任一的方法，其中通过吸入给药向受试者施用所述重组干扰素。

[0195] (23) 根据 (22) 的方法，其中通过经肺和 / 或经鼻吸入所述重组干扰素。

[0196] (24) 根据 (22) 或 (23) 的方法，其中所述吸入给药包括干粉吸入和 / 或雾化吸入。

[0197] (25) 根据 (22)-(24) 任一的方法，其中所述重组干扰素以如下范围的量施用 :一次吸入给药约 100 μ g- 约 2000 μ g，任选地，约 100 μ g- 约 1500 μ g。

[0198] (26) 根据 (25) 的方法，其中所述重组干扰素以如下范围的量施用 :一次吸入给药约 150 μ g- 约 800 μ g。

[0199] (27) 根据 (26) 的方法，其中所述重组干扰素以如下范围的量施用 :一次吸入给药约 200 μ g- 约 600 μ g。

[0200] (28) 根据 (22)-(27) 任一的方法，其中每约 1 天 - 约 3 天吸入给药一次所述重组干扰素。

[0201] (29) 根据 (28) 的方法，其中每约 1 天吸入给药一次所述重组干扰素。

[0202] (30) 根据 (1)-(29) 任一的方法，其中所述受试者带有胸腔积液、腹腔积液和 / 或心包积液。

[0203] (31) 根据 (30) 的方法，其中所述胸腔积液包含恶性胸腔积液，所述腹腔积液包含恶性腹腔积液，和 / 或所述心包积液包含恶性心包积液。

[0204] (32) 根据 (30) 或 (31) 的方法，其中通过胸腔给药、腹腔给药和 / 或心包给药向受

试者施用所述重组干扰素。

[0205] (33) 根据 (32) 的方法，其中所述胸腔给药包括胸腔灌注。

[0206] (34) 根据 (32) 的方法，其中所述腹腔给药包括腹腔灌注。

[0207] (35) 根据 (32) 的方法，其中所述心包给药包括心包灌注。

[0208] (36) 根据 (32)-(35) 任一的方法，其中所述重组干扰素以如下范围的量施用：一次胸腔、腹腔和 / 或心包给药约 30 μg- 约 2000 μg，任选地，约 100 μg- 约 1500 μg，更任选地，约 150 μg- 约 1000 μg，还任选地，约 200 μg- 约 800 μg。

[0209] (37) 根据 (36) 的方法，其中所述重组干扰素以如下范围的量施用：一次胸腔、腹腔和 / 或心包给药约 200 μg- 约 400 μg。

[0210] (38) 根据 (32)-(37) 任一的方法，其中每约 1 天 - 约 10 天，任选地，每约 1 天 - 约 7 天，例如每约 1、2、3、4、5、6 或 7 天胸腔、腹腔和 / 或心包给药一次所述重组干扰素。

[0211] (39) 根据 (1)-(13) 任一的方法，其中通过瘤内给药向受试者施用所述重组干扰素。

[0212] (40) 根据 (39) 的方法，其中所述瘤内给药包括瘤内注射。

[0213] (41) 根据 (39) 或 (40) 的方法，其中所述重组干扰素以如下范围的量施用：一次瘤内给药约 60 μg- 约 600 μg，任选地，约 60 μg- 约 500 μg。

[0214] (42) 根据 (41) 的方法，其中所述重组干扰素以如下范围的量施用：一次瘤内给药约 80 μg- 约 400 μg。

[0215] (43) 根据 (42) 的方法，其中所述重组干扰素以如下范围的量施用：一次瘤内给药约 100 μg- 约 250 μg。

[0216] (44) 根据 (39)-(43) 任一的方法，其中每约 1 天 - 约 10 天，任选地，每约 1 天 - 约 7 天，例如每约 1、2、3、4、5、6 或 7 天瘤内给药一次所述重组干扰素。

[0217] (45) 根据 (39)-(44) 任一的方法，其中瘤内给药的给药方案如下：每约 1 天瘤内注射一次所述重组干扰素，持续约 4 次 - 约 8 次，接着每约 3 天 - 约 5 天瘤内注射一次所述重组干扰素，持续约 4 次 - 约 8 次，然后每约 7 天瘤内注射一次所述重组干扰素，当瘤体消失或瘤体小至无法进行瘤内注射时，停止瘤内给药。

[0218] (46) 根据 (1)-(45) 任一的方法，其中所述受试者中的肺癌包含在如下至少一处中的肿瘤转移：皮肤、粘膜、浅表淋巴结和皮下组织。

[0219] (47) 根据 (46) 的方法，其中通过喷雾给药向受试者施用所述重组干扰素。

[0220] (48) 根据 (47) 的方法，其中所述喷雾给药包括如下的至少一种：经皮喷雾给药、透皮喷雾给药、表皮喷雾给药和粘膜喷雾给药。

[0221] (49) 根据 (47) 或 (48) 的方法，其中所述重组干扰素以如下范围的量施用：一次喷雾给药约 6 μg- 约 100 μg。

[0222] (50) 根据 (49) 的方法，其中所述重组干扰素以如下范围的量施用：一次喷雾给药约 10 μg- 约 40 μg，任选地，约 20 μg- 约 40 μg。

[0223] (51) 根据 (47)-(50) 任一的方法，其中每天喷雾给药约 1- 约 6 次，例如约 1、2、3、4、5 或 6 次所述重组干扰素。

[0224] (52) 根据 (1)-(51) 任一的方法，其中通过给药途径向受试者施用所述重组干扰素，所述给药途径包括如下的至少一种：皮下给药、肌肉给药、吸入给药、浸润给药、胸腔给

药、腹腔给药、心包给药、瘤内给药和喷雾给药。

[0225] (53) 根据 (1)-(52) 任一的方法，其中所述重组干扰素作为单一疗法向受试者施用。

[0226] (54) 根据 (1)-(52) 任一的方法，进一步包括向所述受试者施用至少一种其他抗癌疗法，任选地，在施用所述重组干扰素之前、同时和 / 或之后给予所述受试者所述至少一种其他抗癌疗法。

[0227] (55) 根据 (54) 的方法，其中所述至少一种其他抗癌疗法包括如下的至少一种 :化学治疗、放射治疗、手术治疗、介入治疗、生物治疗、基因治疗、消融治疗、免疫治疗、靶向治疗和中药治疗。

[0228] (56) 根据 (55) 的方法，其中所述至少一种其他抗癌疗法包括化学治疗。

[0229] (57) 根据 (56) 的方法，其中所述化学治疗为一线化学治疗。

[0230] (58) 根据 (57) 的方法，其中所述一线化学治疗使用的至少一种化学治疗剂包括铂类化合物，例如顺铂。

[0231] (59) 根据 (55) 的方法，其中所述至少一种其他抗癌疗法包括放射治疗。

[0232] (60) 根据 (59) 的方法，其中当肺癌转移至脑时，所述放射治疗包括头部伽玛刀治疗。

[0233] (61) 根据 (55) 的方法，其中所述至少一种其他抗癌疗法包括手术治疗。

[0234] (62) 根据 (55) 的方法，其中所述至少一种其他抗癌疗法包括靶向治疗。

[0235] (63) 根据 (62) 的方法，其中所述靶向治疗包括施用吉非替尼、厄洛替尼和 / 或重组人血管内皮抑制素。

[0236] (64) 根据 (55) 的方法，其中所述至少一种其他抗癌疗法包括生物治疗。

[0237] (65) 根据 (1)-(64) 任一的方法，其中在至少一个治疗周期中施用所述重组干扰素，任选地，所述至少一个治疗周期包括 2、3、4、5、6、7、8、9 或 10 个治疗周期，或任选地，多于 10 个治疗周期。

[0238] (66) 根据 (65) 的方法，其中所述一个治疗周期的持续时间为至少约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、或约 6 年等，或可长期施用所述重组干扰素，包括受试者生命的整个期间 ;或者所述重组干扰素治疗的持续时间还可以是约 1 天 - 约 6 年，约 1 周 - 约 4 年，约 2 周 - 约 3 年，约 1 个月 - 约 1 年、或约 2 个月 - 约 9 个月等。

[0239] (67) 根据 (65) 或 (66) 的方法，其中所述多个治疗周期中的任意相邻两个治疗周期之间的间隔时间为至少约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、或约 6 年等 ;或者所述间隔时间还可以为约 2 天 - 约 6 年，约 4 天 - 约 3 年、约 1 周 - 约 1 年、约 2 个月 - 约 9 个月、或约 3 个月 - 约 6 个月等。

[0240] (68) 根据 (1)-(67) 任一的方法，其中与治疗前的肿瘤大小相比，所述治疗消除了所述肺部肿瘤或减小了所述肺部肿瘤的大小。

[0241] (69) 一种治疗受试者中肺癌的方法，包括在两个或更多个治疗周期中向所述受试者施用由 SEQ ID NO :2 编码的重组干扰素以及一种或更多种化学治疗剂，然后在一个或更多个治疗周期中向所述受试者施用由SEQ ID NO :2编码的重组干扰素以及一种或更多种靶向药物。

[0242] (70) 根据 (69) 的方法，其中与治疗前的肿瘤大小相比，所述治疗消除所述肺部肿瘤或减小所述肺部肿瘤的大小。

[0243] (71) 根据 (69) 或 (70) 的方法，其中所述一种或更多种化学治疗剂包括铂类化合物，例如顺铂。

[0244] (72) 根据 (69)-(71) 任一的方法，其中所述一种或更多种靶向药物包括吉非替尼、厄洛替尼和 / 或重组人血管内皮抑制素。

[0245] (73) 根据 (69)-(72) 任一的方法，其中向所述受试者施用有效量的由 SEQ ID NO : 2 的核苷酸序列编码的重组干扰素，任选地，所述有效量为治疗有效量。

[0246] (74) 根据 (1)-(73) 任一的方法，其中所述治疗方法为非手术治疗方法。

[0247] 在另一个方面，本发明的其他实施方案提供了 :

[0248] (1) 一种治疗受试者中的肺癌的方法，包括通过皮下给药和 / 或肌肉给药向所述受试者施用由SEQ ID NO :2编码的重组干扰素，其中所述重组干扰素以如下范围的量施用 : 一次皮下给药和 / 或肌肉给药约 2 μg- 约 70 μg，任选地，约 4 μg- 约 50 μg，更任选地，约 4 μg- 约 30 μg，每约 1- 约 7 天，任选地，每约 1- 约 2 天皮下给药和 / 或肌肉给药一次所述重组干扰素，持续至少约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、或约 6 年等，或可长期施用所述重组干扰素，包括受试者生命的整个期间 ；或者所述持续时间还可以是约 1 天 - 约 6 年，约 1 周 - 约 4 年，约 2 周 - 约 3 年，约 1 个月 - 约 1 年、或约 2 个月 - 约 9 个月等。

[0249] (2) 根据 (1) 的方法，其中所述肺癌包括小细胞肺癌 (SCLC)、非小细胞肺癌 (NSCLC) 或两者。

[0250] (3) 根据 (1) 或 (2) 的方法，其中所述受试者中的肺癌包含转移的肿瘤。

[0251] (4) 根据 (1)-(3) 任一的方法，其中所述受试者是早期、中期或晚期癌症患者，任选地，所述受试者是中期或晚期癌症患者，更任选地，所述受试者是晚期癌症患者。

[0252] (5) 根据 (1)-(3) 任一的方法，其中所述受试者是 0、I、II、III 或 IV 期癌症患者，任选地，所述受试者是 III 或 IV 期癌症患者。

[0253] (6) 根据 (1)-(5) 任一的方法，其中所述肺癌为具备手术指征或适于手术的肺癌。

[0254] (7) 根据 (1)-(5) 任一的方法，其中所述肺癌为不具备手术指征也不适于手术的肺癌。

[0255] (8) 根据 (1)-(5) 任一的方法，其中所述肺癌是可切除的肺癌。

[0256] (9) 根据 (1)-(5) 任一的方法，其中所述肺癌是不可切除的肺癌。

[0257] (10) 根据 (8) 或 (9) 的方法，其中所述肺癌通过手术切除被切除。

[0258] (11) 根据 (1)-(10) 任一的方法，其中所述皮下给药包括皮下注射。

[0259] (12) 根据 (1)-(10) 任一的方法，其中所述肌肉给药包括肌肉注射。

[0260] (13) 根据 (1)-(12) 任一的方法，进一步包括通过吸入给药向受试者施用所述重组干扰素。

[0261] (14) 根据 (13) 的方法，其中在皮下给药和 / 或肌肉给药的之前、同时和 / 或之后进行所述吸入给药。

[0262] (15) 根据 (13) 或 (14) 的方法，其中所述吸入给药包括经肺和 / 或经鼻吸入给药。

[0263] (16) 根据 (13)-(15) 任一的方法，其中所述吸入给药包括雾化吸入。

[0264] (17) 根据 (13)-(16) 任一的方法，其中所述重组干扰素以如下范围的量施用 ：一次吸入给药约 100 μg- 约 2000 μg，任选地，约 100 μg- 约 1500 μg，更任选地，约 150 μg- 约 800 μg，还更任选地，约 200 μg- 约 600 μg，每约 1 天 - 约 3 天，任选地，每约 1 天吸入一次所述重组干扰素，持续至少约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、或约 6 年等，或可长期施用所述重组干扰素，包括受试者生命的整个期间 ；或者所述持续时间还可以是约 1 天 - 约 6 年，约 1 周 - 约 4 年，约 2 周 - 约 3 年，约 1 个月 - 约 1 年、或约 2 个月 - 约 9 个月等。

[0265] (18) 根据 (1)-(17) 任一的方法，进一步包括通过瘤内给药向受试者施用所述重组干扰素。

[0266] (19) 根据 (18) 的方法，其中在皮下给药和 / 或肌肉给药的之前、同时和 / 或之后进行所述瘤内给药。

[0267] (20) 根据 (18) 的方法，其中在吸入给药的之前、同时和 / 或之后进行所述瘤内给药。

[0268] (21) 根据 (18)-(20) 任一的方法，其中所述瘤内给药包括瘤内注射。

[0269] (22) 根据 (18)-(21) 任一的方法，其中所述重组干扰素以如下范围的量施用 ：一次瘤内给药约 60 μg- 约 600 μg，任选地，约 60 μg- 约 500 μg，更任选地，约 80 μg- 约 400 μg，还更任选地，约 100 μg- 约 250 μg，每约 1 天 - 约 10 天，任选地，每约 1 天 - 约 7 天，例如每约 1、2、3、4、5、6 或 7 天瘤内给药一次所述重组干扰素，持续至少约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、或约 6 年等，或可长期施用所述重组干扰素，包括受试者生命的整个期间 ；或者所述持续时间还可以是约 1 天 - 约 6 年，约 1 周 - 约 4 年，约 2 周 - 约 3 年，约 1 个月 - 约 1 年、或约 2 个月 - 约 9 个月等。

[0270] (23) 根据 (18)-(22) 任一的方法，其中瘤内给药的给药方案如下 ：每约 1 天瘤内注射一次所述重组干扰素，持续约 4 次 - 约 8 次，接着每约 3 天 - 约 5 天瘤内注射一次所述重组干扰素，持续约 4 次 - 约 8 次，然后每约 7 天瘤内注射一次所述重组干扰素，当瘤体消失或瘤体小至无法进行瘤内注射时，停止瘤内给药。

[0271] (24) 根据 (1)-(23) 任一的方法，其中所述受试者带有胸腔积液、腹腔积液和 / 或心包积液。

[0272] (25) 根据 (24) 的方法，其中所述胸腔积液为恶性胸腔积液，所述腹腔积液为恶性腹腔积液，和 / 或所述心包积液为恶性心包积液。

[0273] (26) 根据 (24) 或 (25) 的方法，其中通过给药途径向受试者施用所述重组干扰素，所述给药途径包括如下的至少一种：胸腔给药、腹腔给药和心包给药。

[0274] (27) 根据 (26) 的方法，其中所述胸腔给药包括胸腔灌注。

[0275] (28) 根据 (26) 的方法，其中所述腹腔给药包括腹腔灌注。

[0276] (29) 根据 (26) 的方法，其中所述心包给药包括心包灌注。

[0277] (30) 根据 (26)-(29) 任一的方法，其中所述重组干扰素以如下范围的量施用：一次胸腔、腹腔和 / 或心包给药约 30 μg- 约 2000 μg，任选地，约 100 μg- 约 1500 μg，更任选地，约 150 μg- 约 1000 μg，还任选地，约 200 μg- 约 800 μg。

[0278] (31) 根据 (30) 的方法，其中所述重组干扰素以如下范围的量施用：一次胸腔、腹腔和 / 或心包给药约 200 μg- 约 400 μg。

[0279] (32) 根据 (26)-(31) 任一的方法，其中每约 1 天 - 约 10 天，任选地，每约 1 天 - 约 7 天，例如每约 1、2、3、4、5、6 或 7 天胸腔、腹腔和 / 或心包给药一次所述重组干扰素。

[0280] (33) 根据 (1)-(32) 任一的方法，其中所述受试者中的肺癌包含在如下至少一处中的肿瘤转移：皮肤、粘膜、浅表淋巴结和皮下组织。

[0281] (34) 根据 (33) 的方法，其中通过喷雾给药向受试者施用所述重组干扰素。

[0282] (35) 根据 (34) 的方法，其中所述喷雾给药包括如下的至少一种：经皮喷雾给药、透皮喷雾给药、表皮喷雾给药和粘膜喷雾给药。

[0283] (36) 根据 (34) 或 (35) 的方法，其中所述重组干扰素以如下范围的量施用：一次喷雾给药约 6 μg- 约 100 μg。

[0284] (37) 根据 (36) 的方法，其中所述重组干扰素以如下范围的量施用：一次喷雾给药约 10 μg- 约 40 μg，任选地，约 20 μg- 约 40 μg。

[0285] (38) 根据 (34)-(37) 任一的方法，其中每天喷雾给药约 1- 约 6 次，例如约 1、2、3、4、5 或 6 次所述重组干扰素。

[0286] (39) 根据 (1)-(38) 任一的方法，其中所述重组干扰素作为单一疗法向受试者施用。

[0287] (40) 根据 (1)-(38) 任一的方法，进一步包括向所述受试者施用至少一种其他抗癌疗法，任选地，在施用所述重组干扰素之前、同时和 / 或之后给予所述受试者至少一种其他抗癌疗法。

[0288] (41) 根据 (40) 的方法，其中所述至少一种其他抗癌疗法包括如下的一种或更多种：化学治疗、放射治疗、手术治疗、介入治疗、生物治疗、基因治疗、消融治疗、免疫治疗、靶向治疗和中药治疗。

[0289] (42) 根据 (41) 的方法，其中所述至少一种其他抗癌疗法包括化学治疗。

[0290] (43) 根据 (42) 的方法，其中所述化学治疗为一线化学治疗。

[0291] (44) 根据 (43) 的方法，其中所述一线化学治疗使用的一种或更多种化学治疗剂包括铂类化合物，例如顺铂。

[0292] (45) 根据 (41) 的方法，其中所述至少一种其他抗癌疗法包括放射治疗。

[0293] (46) 根据 (45) 的方法，其中当肺癌转移至脑时，所述放射治疗包括头部伽玛刀治疗。

[0294] (47) 根据 (41) 的方法，其中所述至少一种其他抗癌疗法包括手术治疗。

[0295] (48) 根据 (41) 的方法，其中所述至少一种其他抗癌疗法包括靶向治疗。

[0296] (49) 根据 (48) 的方法，其中所述靶向治疗包括施用吉非替尼、厄洛替尼和 / 或重组人血管内皮抑制素。

[0297] (50) 根据 (41) 的方法，其中所述至少一种其他抗癌疗法包括生物治疗。

[0298] (51) 根据 (1)-(50) 任一的方法，其中与治疗前的肿瘤相比，所述治疗消除了所述肿瘤或减小了所述肿瘤的大小或所述肿瘤转移的数量。

[0299] (52) 根据 (1)-(51) 任一的方法，其中所述治疗方法为非手术治疗方法。

[0300] 在另一个方面，本发明的其他实施方案提供了 ：

[0301] (1) 一种治疗受试者中的肺癌的方法，包括通过皮下给药和 / 或肌肉给药向受试者施用由 SEQ ID NO :2 编码的重组干扰素，其中以约 2 μg/ 次 - 约 10 μg/ 次，任选地，约 4 μg/ 次 - 约 10 μg/ 次，更任选地，约 4.5 μg/ 次 - 约 9 μg/ 次，例如约 4.5 μg/ 次或约 9 μg/ 次的诱导剂量经皮下给药和 / 或肌肉给药施用一次或更多次所述重组干扰素，之后以约 10 μg/ 次 - 约 70 μg/ 次，任选地，约 12 μg/ 次 - 约 50 μg/ 次，更任选地，约 12 μg/ 次 - 约 30 μg/ 次的治疗剂量经皮下给药和 / 或肌肉给药施用多次所述重组干扰素。

[0302] (2) 根据 (1) 的方法，其中所述肺癌包括小细胞肺癌 (SCLC)、非小细胞肺癌 (NSCLC) 或两者。

[0303] (3) 根据 (1) 或 (2) 的方法，其中所述受试者中的肿瘤包含转移的肿瘤。

[0304] (4) 根据 (1)-(3) 任一的方法，其中所述受试者是早期、中期或晚期癌症患者，任选地，所述受试者是中期或晚期癌症患者，更任选地，所述受试者是晚期癌症患者。

[0305] (5) 根据 (1)-(3) 任一的方法，其中所述受试者是 0、I、II、III 或 IV 期癌症患者，任选地，所述受试者是 III 或 IV 期癌症患者。

[0306] (6) 根据 (1)-(5) 任一的方法，其中所述肺癌为具备手术指征或适于手术的肺癌。

[0307] (7) 根据 (1)-(5) 任一的方法，其中所述肺癌为不具备手术指征也不适于手术的肺癌。

[0308] (8) 根据 (1)-(5) 任一的方法，其中所述肺癌是可切除的肺癌。

[0309] (9) 根据 (1)-(5) 任一的方法，其中所述肺癌是不可切除的肺癌。

[0310] (10) 根据 (8) 或 (9) 的方法，其中所述肺癌通过手术切除被切除。

[0311] (11) 根据 (1)-(10) 任一的方法，其中所述皮下给药包括皮下注射。

[0312] (12) 根据 (1)-(10) 任一的方法，其中所述肌肉给药包括肌肉注射。

[0313] (13) 根据 (1)-(12) 任一的方法，其中施用诱导剂量与施用治疗剂量之间的间隔为约 1 天 - 约 1 个月，任选地，约 1 天 - 约 1 周，更任选地，约 1 天 - 约 3 天，包括，例如约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、或约 1 个月。

[0314] (14) 根据 (1)-(13) 任一的方法，其中多次施用诱导剂量时，每约 1 天 - 约 10 天施用一次所述重组干扰素，任选地，每约 1 天 - 约 7 天施用一次所述重组干扰素，更任选地，每约 1 天 - 约 2 天施用一次所述重组干扰素，包括，例如每约 1、2、3、4、5、6、7、8、9 或 10 天施用一次所述重组干扰素。

[0315] (15) 根据 (1)-(14) 任一的方法，其中每约 1 天 - 约 10 天施用一次治疗剂量的所述重组干扰素，任选地，每约 1 天 - 约 7 天施用一次治疗剂量的所述重组干扰素，更任选地，

每约 1 天 - 约 2 天施用一次治疗剂量的所述重组干扰素，包括，例如每约 1、2、3、4、5、6、7、8、9 或 10 天施用一次治疗剂量的所述重组干扰素。

[0316] (16) 根据 (1)-(15) 任一的方法，其中诱导剂量和治疗剂量的施用的持续时间为至少约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、或约 6 年等，或可长期施用所述重组干扰素，包括受试者生命的整个期间。

[0317] (17) 根据 (1)-(16) 任一的方法，进一步包括通过吸入给药向受试者施用所述重组干扰素。

[0318] (18) 根据 (17) 的方法，其中在皮下给药和 / 或肌肉给药的之前、同时和 / 或之后进行所述吸入给药。

[0319] (19) 根据 (17) 或 (18) 的方法，其中所述吸入给药包括经肺和 / 或经鼻吸入给药。

[0320] (20) 根据 (17)-(19) 任一的方法，其中所述吸入给药包括雾化吸入。

[0321] (21) 根据 (17)-(20) 任一的方法，其中所述重组干扰素以如下范围的量施用 ：一次吸入给药约 100 μg- 约 2000 μg，任选地，约 100 μg- 约 1500 μg，更任选地，约 150 μg- 约 800 μg，还更任选地，约 200 μg- 约 600 μg，每约 1 天 - 约 3 天，任选地，每约 1 天吸入一次所述重组干扰素，持续至少约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、或约 6 年等，或可长期施用所述重组干扰素，包括受试者生命的整个期间 ；或者所述持续时间还可以是约 1 天 - 约 6 年，约 1 周 - 约 4 年，约 2 周 - 约 3 年，约 1 个月 - 约 1 年、或约 2 个月 - 约 9 个月等。

[0322] (22) 根据 (1)-(21) 任一的方法，进一步包括通过瘤内给药向受试者施用所述重组干扰素。

[0323] (23) 根据 (22) 的方法，其中在皮下给药和 / 或肌肉给药的之前、同时和 / 或之后进行所述瘤内给药。

[0324] (24) 根据 (22) 的方法，其中在吸入给药的之前、同时和 / 或之后进行所述瘤内给药。

[0325] (25) 根据 (22)-(24) 任一的方法，其中所述瘤内给药包括瘤内注射。

[0326] (26) 根据 (22)-(25) 任一的方法，其中所述重组干扰素以如下范围的量施用 ：一次瘤内给药约 60 μg- 约 600 μg，任选地，约 60 μg- 约 500 μg，更任选地，约 80 μg- 约 400 μg，还更任选地，约 100 μg- 约 250 μg，每约 1 天 - 约 10 天，任选每约 1 天 - 约 7 天，例如每约 1、2、3、4、5、6 或 7 天瘤内给药一次所述重组干扰素，持续至少约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、或约 6 年等，或可长期施用所述重组干扰素，包括受试者生命的整个期间 ；或者所述持续时间还可以是约 1 天 - 约 6 年，约 1 周 - 约 4 年，约 2 周 - 约 3 年，约 1 个月 - 约 1 年、或约 2 个月 - 约 9 个月等。

[0327] (27) 根据 (22)-(26) 任一的方法，其中瘤内给药的给药方案如下 ：每约 1 天瘤内注射一次所述重组干扰素，持续约 4- 约 8 次，接着每约 3- 约 5 天瘤内注射一次所述重组干

扰素，持续约 4- 约 8 次，然后每约 7 天瘤内注射一次所述重组干扰素，当瘤体消失或瘤体小至无法进行瘤内注射时，停止瘤内给药。

[0328] (28) 根据 (1)-(27) 任一的方法，其中所述受试者带有胸腔积液、腹腔积液和 / 或心包积液。

[0329] (29) 根据 (28) 的方法，其中所述胸腔积液为恶性胸腔积液，所述腹腔积液为恶性腹腔积液，和 / 或所述心包积液为恶性心包积液。

[0330] (30) 根据 (28) 或 (29) 的方法，其中通过给药途径向受试者施用所述重组干扰素，所述给药途径包括如下的至少一种 ：胸腔给药、腹腔给药和心包给药。

[0331] (31) 根据 (30) 的方法，其中所述胸腔给药包括胸腔灌注。

[0332] (32) 根据 (30) 的方法，其中所述腹腔给药包括腹腔灌注。

[0333] (33) 根据 (30) 的方法，其中所述心包给药包括心包灌注。

[0334] (34) 根据 (30)-(33) 任一的方法，其中所述重组干扰素以如下范围的量施用 ：一次胸腔给药、腹腔给药和 / 或心包给药约 30 μ g- 约 2000 μ g，任选地，约 100 μ g- 约 1500 μ g，更任选地，约 150 μ g- 约 1000 μ g，还任选地，约 200 μ g- 约 800 μ g。

[0335] (35) 根据 (34) 的方法，其中所述重组干扰素以如下范围的量施用 ：一次胸腔给药、腹腔给药和 / 或心包给药约 200 μ g- 约 400 μ g。

[0336] (36) 根据 (30)-(35) 任一的方法，其中每约 1 天 - 约 10 天，任选地，每约 1 天 - 约 7 天，例如每约 1、2、3、4、5、6 或 7 天胸腔给药、腹腔给药和 / 或心包给药一次所述重组干扰素。

[0337] (37) 根据 (1)-(36) 任一的方法，其中所述受试者中的肺癌包含在如下至少一处中的肿瘤转移 ：皮肤、粘膜、浅表淋巴结和皮下组织。

[0338] (38) 根据 (37) 的方法，其中通过喷雾给药向受试者施用所述重组干扰素。

[0339] (39) 根据 (38) 的方法，其中所述喷雾给药包括如下的至少一种 ：经皮喷雾给药、透皮喷雾给药、表皮喷雾给药和粘膜喷雾给药。

[0340] (40) 根据 (38) 或 (39) 的方法，其中所述重组干扰素以如下范围的量施用 ：一次喷雾给药约 6 μ g- 约 100 μ g。

[0341] (41) 根据 (40) 的方法，其中所述重组干扰素以如下范围的量施用 ：一次喷雾给药约 10 μ g- 约 40 μ g，任选地，约 20 μ g- 约 40 μ g。

[0342] (42) 根据 (38)-(41) 任一的方法，其中每天喷雾给药约 1- 约 6 次，例如约 1、2、3、4、5 或 6 次所述重组干扰素。

[0343] (43) 根据 (1)-(42) 任一的方法，其中所述重组干扰素作为单一疗法向受试者施用。

[0344] (44) 根据 (1)-(42) 任一的方法，进一步包括向所述受试者施用至少一种其他抗癌疗法，任选地，在施用所述重组干扰素之前、同时和 / 或之后给予所述受试者至少一种其他抗癌疗法。

[0345] (45) 根据 (44) 的方法，其中所述至少一种其他抗癌疗法包括如下的一种或更多种 ：化学治疗、放射治疗、手术治疗、介入治疗、生物治疗、基因治疗、消融治疗、免疫治疗、靶向治疗和中药治疗。

[0346] (46) 根据 (45) 的方法，其中所述至少一种其他抗癌疗法包括化学治疗。

[0347] (47) 根据 (46) 的方法，其中所述化学治疗为一线化学治疗。

[0348] (48) 根据 (47) 的方法，其中所述一线化学治疗使用的一种或更多种化学治疗剂包括铂类化合物，例如顺铂。

[0349] (49) 根据 (45) 的方法，其中所述至少一种其他抗癌疗法包括放射治疗。

[0350] (50) 根据 (49) 的方法，其中当肺癌转移至脑时，所述放射治疗包括头部伽玛刀治疗。

[0351] (51) 根据 (45) 的方法，其中所述至少一种其他抗癌疗法包括手术治疗。

[0352] (52) 根据 (45) 的方法，其中所述至少一种其他抗癌疗法包括靶向治疗。

[0353] (53) 根据 (52) 的方法，其中所述靶向治疗包括施用吉非替尼、厄洛替尼和 / 或重组人血管内皮抑制素。

[0354] (54) 根据 (45) 的方法，其中所述至少一种其他抗癌疗法包括生物治疗。

[0355] (55) 根据 (1)-(54) 任一的方法，其中与治疗前的肿瘤大小相比，所述治疗消除了所述肺部肿瘤或减小了所述肺部肿瘤的大小。

[0356] (56) 根据 (1)-(55) 任一的方法，其中所述治疗方法为非手术治疗方法。

[0357] 在另一个方面，本发明的其他实施方案提供了 ：

[0358] (1) 一种治疗受试者中的癌症的方法，其中所述癌症源于受试者中的肺癌并转移至脑，包括向受试者施用由 SEQ ID NO :2 编码的重组干扰素，其中以约 2 μg/ 次 - 约 10 μg/ 次，任选地，约 4 μg/ 次 - 约 10 μg/ 次，更任选地，约 4.5 μg/ 次 - 约 9 μg/ 次，例如约 4.5 μg/ 次或约 9 μg/ 次的诱导剂量通过皮下给药和 / 或肌肉给药施用一次或更多次所述重组干扰素，之后以约 10 μg/ 次 - 约 70 μg/ 次，任选地，约 12 μg/ 次 - 约 50 μg/ 次，更任选地，约 12 μg/ 次 - 约 30 μg/ 次的治疗剂量通过皮下给药和 / 或肌肉给药施用多次所述重组干扰素，在所述皮下给药和 / 或肌肉给药的之前、同时和 / 或之后通过吸入给药向受试者施用所述重组干扰素，所述重组干扰素以如下范围的量施用 ：一次吸入给药约 100 μg- 约 2000 μg，任选地，约 100 μg- 约 1500 μg，更任选地，约 150 μg- 约 800 μg，还更任选地，约 200 μg- 约 600 μg，以及每约 1 天 - 约 3 天，任选地每约 1 天吸入给药一次所述重组干扰素。

[0359] (2) 根据 (1) 的方法，其中所述受试者是中期、晚期或 III 或 IV 期癌症患者，任选地，所述受试者是晚期或 III 或 IV 期癌症患者。

[0360] (3) 根据 (1) 或 (2) 的方法，其中所述癌症为不具备手术指征也不适于手术的癌症。

[0361] (4) 根据 (1) 或 (2) 的方法，其中所述肿瘤是不可切除的肿瘤。

[0362] (5) 根据 (4) 的方法，其中所述肿瘤通过手术切除被切除。

[0363] (6) 根据 (1)-(5) 任一的方法，其中所述皮下给药包括皮下注射。

[0364] (7) 根据 (1)-(5) 任一的方法，其中所述肌肉给药包括肌肉注射。

[0365] (8) 根据 (1)-(7) 任一的方法，其中所述吸入给药包括经肺和 / 或经鼻吸入给药。

[0366] (9) 根据 (1)-(8) 任一的方法，其中所述吸入给药包括雾化吸入。

[0367] (10) 根据 (1)-(9) 任一的方法，其中施用诱导剂量与施用治疗剂量之间的时间间隔为约 1 天 - 约 1 个月，任选地，约 1 天 - 约 1 周，更任选地，约 1 天 - 约 3 天，包括，例如约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、或约 1 个月。

[0368] (11) 根据 (1)-(10) 任一的方法，其中多次施用诱导剂量的重组干扰素时，每约 1 天 - 约 10 天施用一次所述重组干扰素，任选地，每约 1 天 - 约 7 天施用一次所述重组干扰素，更任选地，每约 1 天 - 约 2 天施用一次所述重组干扰素，包括，例如每约 1、2、3、4、5、6、7、8、9 或 10 天施用一次所述重组干扰素。

[0369] (12) 根据 (1)-(11) 任一的方法，其中每约 1 天 - 约 10 天施用一次治疗剂量的所述重组干扰素，任选地，每约 1 天 - 约 7 天施用一次治疗剂量的所述重组干扰素，更任选地，每约 1- 约 2 天施用一次治疗剂量的所述重组干扰素，包括，例如每约 1、2、3、4、5、6、7、8、9 或 10 天施用一次治疗剂量的所述重组干扰素。

[0370] (13) 根据 (1)-(12) 任一的方法，其中诱导剂量和治疗剂量的施用的持续时间为至少约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年或约 6 年等，或者可长期施用所述重组干扰素，包括受试者生命的整个期间。

[0371] (14) 根据 (1)-(13) 任一的方法，其中所述吸入给药的持续时间为至少约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年或约 6 年等，或者可长期施用所述重组干扰素，包括受试者生命的整个期间；或者所述持续时间还可以是约 1 天 - 约 6 年，约 1 周 - 约 4 年，约 2 周 - 约 3 年，约 1 个月 - 约 1 年或约 2 个月 - 约 9 个月等。

[0372] (15) 根据 (1)-(14) 任一的方法，其中所述重组干扰素作为单一疗法向受试者施用。

[0373] (16) 根据 (1)-(15) 任一的方法，进一步包括向所述受试者施用至少一种其他抗癌疗法，任选地，在施用所述重组干扰素之前、同时和 / 或之后给予所述受试者至少一种其他抗癌疗法。

[0374] (17) 根据 (16) 的方法，其中所述至少一种其他抗癌疗法包括如下的一种或更多种：化学治疗、放射治疗、手术治疗、介入治疗、生物治疗、基因治疗、消融治疗、免疫治疗、靶向治疗和中药治疗。

[0375] (18) 根据 (17) 的方法，其中所述化学治疗为一线化学治疗，任选地，所述一线化学治疗使用的一种或更多种化学治疗剂包括铂类化合物，例如顺铂。

[0376] (19) 根据 (17) 的方法，其中所述靶向治疗包括施用吉非替尼、厄洛替尼和 / 或重组人血管内皮抑制素。

[0377] (20) 根据 (17) 的方法，其中所述至少一种其他抗癌疗法包括放射治疗。

[0378] (21) 根据 (20) 的方法，其中所述放射治疗包括伽玛刀治疗。

[0379] (22) 根据 (21) 的方法，其中所述伽玛刀治疗包括头部伽玛刀治疗。

[0380] (23) 根据 (1)-(22) 任一的方法，其中与治疗前的肿瘤相比，所述治疗消除了所述肿瘤或减小了所述肿瘤的大小。

[0381] (24) 根据 (1)-(23) 任一的方法，其中所述治疗方法为非手术治疗方法。

[0382] 在另一个方面，本发明的其他实施方案提供了：

[0383] (1) 一种治疗受试者中的癌症的方法，其中所述癌症源于受试者中的肺癌并转移

至骨或肝脏，包括向受试者施用由 SEQ ID NO :2 编码的重组干扰素，其中以约 2 μg/ 次 - 约 10 μg/ 次，任选地，约 4 μg/ 次 - 约 10 μg/ 次，更任选地，约 4.5 μg/ 次 - 约 9 μg/ 次，例如约 4.5 μg/ 次或约 9 μg/ 次的诱导剂量通过皮下给药和 / 或肌肉给药施用一次或更多次所述重组干扰素，之后以约 10 μg/ 次 - 约 70 μg/ 次，任选地，约 12 μg/ 次 - 约 50 μg/ 次，更任选地，约 12 μg/ 次 - 约 30 μg/ 次的治疗剂量通过皮下给药和 / 或肌肉给药施用多次所述重组干扰素。

[0384] (2) 根据 (1) 的方法，其中所述受试者是中期、晚期或 III 或 IV 期癌症患者，任选地，所述受试者是晚期或 III 或 IV 期癌症患者。

[0385] (3) 根据 (1) 或 (2) 的方法，其中所述癌症为不具备手术指征也不适于手术的癌症。

[0386] (4) 根据 (1) 或 (2) 的方法，其中所述肿瘤是不可切除的肿瘤。

[0387] (5) 根据 (4) 的方法，其中所述肿瘤通过手术切除被切除。

[0388] (6) 根据 (1)-(5) 任一的方法，其中所述皮下给药包括皮下注射。

[0389] (7) 根据 (1)-(5) 任一的方法，其中所述肌肉给药包括肌肉注射。

[0390] (8) 根据 (1)-(7) 任一的方法，其中施用诱导剂量与施用治疗剂量之间的时间间隔为约 1 天 - 约 1 个月，任选地，约 1 天 - 约 1 周，更任选地，约 1 天 - 约 3 天，包括，例如约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周或约 1 个月。

[0391] (9) 根据 (1)-(8) 任一的方法，其中多次施用诱导剂量的重组干扰素时，每约 1 天 - 约 10 天施用一次所述重组干扰素，任选地，每约 1 天 - 约 7 天施用一次所述重组干扰素，更任选地，每约 1 天 - 约 2 天施用一次所述重组干扰素，包括，例如每约 1、2、3、4、5、6、7、8、9 或 10 天施用一次所述重组干扰素。

[0392] (10) 根据 (1)-(9) 任一的方法，其中每约 1 天 - 约 10 天施用一次治疗剂量的所述重组干扰素，任选地，每约 1 天 - 约 7 天施用一次治疗剂量的所述重组干扰素，更任选地，每约 1- 约 2 天施用一次治疗剂量的所述重组干扰素，包括，例如每约 1、2、3、4、5、6、7、8、9 或 10 天施用一次治疗剂量的所述重组干扰素。

[0393] (11) 根据 (1)-(10) 任一的方法，其中诱导剂量和治疗剂量的施用的持续时间为至少约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年或约 6 年等，或者可长期施用所述重组干扰素，包括受试者生命的整个期间。

[0394] (12) 根据 (1)-(11) 任一的方法，进一步包括通过吸入给药向受试者施用所述重组干扰素。

[0395] (13) 根据 (12) 的方法，其中在皮下给药和 / 或肌肉给药的之前、同时和 / 或之后进行所述吸入给药。

[0396] (14) 根据 (12) 或 (13) 的方法，其中所述吸入给药包括经肺和 / 或经鼻吸入给药。

[0397] (15) 根据 (12)-(14) 任一的方法，其中所述吸入给药包括雾化吸入。

[0398] (16) 根据 (12)-(15) 任一的方法，其中所述重组干扰素以如下范围的量施用 :一次吸入给药约 100 μg- 约 2000 μg，任选地，约 100 μg- 约 1500 μg，更任选地，约 150 μg- 约 800 μg，还更任选地，约 200 μg- 约 600 μg，每约 1 天 - 约 3 天，任选地，每约 1 天吸入一次

所述重组干扰素，所述吸入给药的持续时间为至少约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年或约 6 年等，或者可长期施用所述重组干扰素，包括受试者生命的整个期间；或者所述持续时间还可以是约 1 天 - 约 6 年，约 1 周 - 约 4 年，约 2 周 - 约 3 年，约 1 个月 - 约 1 年或约 2 个月 - 约 9 个月等。

[0399] (17) 根据 (1)-(16) 任一的方法，其中所述重组干扰素作为单一疗法向受试者施用。

[0400] (18) 根据 (1)-(16) 任一的方法，进一步包括向所述受试者施用至少一种其他抗癌疗法，任选地，在施用所述重组干扰素之前、同时和 / 或之后给予所述受试者至少一种其他抗癌疗法。

[0401] (19) 根据 (18) 的方法，其中所述至少一种其他抗癌疗法包括如下的一种或更多种：化学治疗、放射治疗、手术治疗、介入治疗、生物治疗、基因治疗、消融治疗、免疫治疗、靶向治疗和中药治疗。

[0402] (20) 根据 (19) 的方法，其中所述至少一种其他抗癌疗法包括化学治疗。

[0403] (21) 根据 (20) 的方法，其中所述化学治疗为一线化学治疗。

[0404] (22) 根据 (21) 的方法，其中所述一线化学治疗使用的一种或更多种化学治疗剂包括铂类化合物，例如顺铂。

[0405] (23) 根据 (19) 的方法，其中所述至少一种其他抗癌疗法包括靶向治疗。

[0406] (24) 根据 (23) 的方法，其中所述靶向治疗包括施用吉非替尼、厄洛替尼和 / 或重组人血管内皮抑制素。

[0407] (25) 根据 (19) 的方法，其中所述至少一种其他抗癌疗法包括生物治疗。

[0408] (26) 根据 (1)-(25) 任一的方法，其中与治疗前的肿瘤相比，所述治疗消除了所述肿瘤或减小了所述肿瘤的大小。

[0409] (27) 根据 (1)-(26) 任一的方法，其中所述治疗方法为非手术治疗方法。

[0410] 在另一个方面，本发明的其他实施方案提供了：

[0411] (1) 一种治疗受试者中的癌症的方法，其中所述癌症源于受试者中的肺癌并转移至淋巴结，包括向受试者施用由 SEQ ID NO:2 编码的重组干扰素，其中以约 2μg/ 次 - 约 10μg/ 次，任选地，约 4μg/ 次 - 约 10μg/ 次，更任选地，约 4.5μg/ 次 - 约 9μg/ 次，例如约 4.5μg/ 次或约 9μg/ 次的诱导剂量通过皮下给药和 / 或肌肉给药施用一次或更多次所述重组干扰素，之后以约 10μg/ 次 - 约 70μg/ 次，任选地，约 12μg/ 次 - 约 50μg/ 次，更任选地，约 12μg/ 次 - 约 30μg/ 次的治疗剂量通过皮下给药和 / 或肌肉给药施用多次所述重组干扰素，在所述皮下给药和 / 或肌肉给药的之前、同时和 / 或之后通过表面或局部给药向所述肿瘤和 / 或所述淋巴结转移灶施用所述重组干扰素。

[0412] (2) 根据 (1) 的方法，其中所述受试者是中期、晚期或 III 或 IV 期癌症患者，任选地，所述受试者是晚期或 III 或 IV 期癌症患者。

[0413] (3) 根据 (1) 或 (2) 的方法，其中所述癌症为不具备手术指征也不适于手术的癌症。

[0414] (4) 根据 (1) 或 (2) 的方法，其中所述肿瘤是不可切除的肿瘤。

[0415] (5) 根据 (4) 的方法，其中所述肿瘤通过手术切除被切除。

[0416] (6) 根据 (1)-(5) 任一的方法，其中所述皮下给药包括皮下注射。

[0417] (7) 根据 (1)-(5) 任一的方法，其中所述肌肉给药包括肌肉注射。

[0418] (8) 根据 (1)-(7) 任一的方法，其中施用诱导剂量与施用治疗剂量之间的时间间隔为约 1 天 - 约 1 个月，任选地，约 1 天 - 约 1 周，更任选地，约 1 天 - 约 3 天，包括，例如约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周或约 1 个月。

[0419] (9) 根据 (1)-(8) 任一的方法，其中多次施用诱导剂量的重组干扰素时，每约 1 天 - 约 10 天施用一次所述重组干扰素，任选地，每约 1 天 - 约 7 天施用一次所述重组干扰素，更任选地，每约 1 天 - 约 2 天施用一次所述重组干扰素，包括，例如每约 1、2、3、4、5、6、7、8、9 或 10 天施用一次所述重组干扰素。

[0420] (10) 根据 (1)-(9) 任一的方法，其中每约 1 天 - 约 10 天施用一次治疗剂量的所述重组干扰素，任选地，每约 1 天 - 约 7 天施用一次治疗剂量的所述重组干扰素，更任选地，每约 1 天 - 约 2 天施用一次治疗剂量的所述重组干扰素，包括，例如每约 1、2、3、4、5、6、7、8、9 或 10 天施用一次治疗剂量的所述重组干扰素。

[0421] (11) 根据 (1)-(10) 任一的方法，其中诱导剂量和治疗剂量的施用的持续时间为至少约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年或约 6 年等，或者可长期施用所述重组干扰素，包括受试者生命的整个期间。

[0422] (12) 根据 (1)-(11) 任一的方法，其中当所述淋巴结为深部淋巴结时，所述局部给药包括瘤内给药。

[0423] (13) 根据 (12) 的方法，其中所述瘤内给药包括瘤内注射。

[0424] (14) 根据 (12) 或 (13) 的方法，其中所述重组干扰素以如下范围的量施用 ：一次瘤内给药约 60 μg- 约 600 μg，任选地，约 60 μg- 约 500 μg，更任选地，约 80 μg- 约 400 μg，还更任选地，约 100 μg- 约 250 μg，每约 1 天 - 约 10 天，任选地，每约 1 天 - 约 7 天，例如每约 1、2、3、4、5、6 或 7 天瘤内给药一次所述重组干扰素，所述瘤内给药的持续时间为至少约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年或约 6 年等，或者可长期施用所述重组干扰素，包括受试者生命的整个期间 ；或者所述持续时间还可以是约 1 天 - 约 6 年，约 1 周 - 约 4 年，约 2 周 - 约 3 年，约 1 个月 - 约 1 年或约 2 个月 - 约 9 个月等。

[0425] (15) 根据 (12)-(14) 任一的方法，其中瘤内给药的给药方案如下 ：每约 1 天瘤内注射一次所述重组干扰素，持续约 4 次 - 约 8 次，接着每约 3 天 - 约 5 天瘤内注射一次所述重组干扰素，持续约 4- 约 8 次，然后每约 7 天瘤内注射一次所述重组干扰素，当瘤体和 / 或被转移的淋巴结消失或小至无法进行瘤内注射时，停止瘤内给药。

[0426] (16) 根据 (1)-(11) 任一的方法，其中当淋巴结为浅表淋巴结时，所述表面或局部给药包括如下的至少一种 ：浸润给药、经皮给药、透皮给药、表皮给药和粘膜给药。

[0427] (17) 根据 (16) 的方法，其中所述局部给药包括浸润给药。

[0428] (18) 根据 (17) 的方法，其中通过灌注进行所述浸润给药。

[0429] (19) 根据 (16) 的方法，其中所述经皮给药、透皮给药、表皮给药或粘膜给药分别包括经皮喷雾给药、透皮喷雾给药、表皮喷雾给药或粘膜喷雾给药。

[0430] (20) 根据 (19) 的方法，其中所述重组干扰素以如下范围的量施用：一次喷雾给药约 6μg- 约 100μg。

[0431] (21) 根据 (20) 的方法，其中所述重组干扰素以如下范围的量施用：一次喷雾给药约 10μg- 约 40μg，任选地，约 20μg- 约 40μg。

[0432] (22) 根据 (19)-(21) 任一的方法，其中每天喷雾给药约 1- 约 6 次，例如约 1、2、3、4、5 或 6 次所述重组干扰素。

[0433] (23) 根据 (1)-(22) 任一的方法，其中所述重组干扰素作为单一疗法向受试者施用。

[0434] (24) 根据 (1)-(22) 任一的方法，进一步包括向所述受试者施用至少一种其他抗癌疗法，任选地，在施用所述重组干扰素之前、同时和 / 或之后给予所述受试者至少一种其他抗癌疗法。

[0435] (25) 根据 (24) 的方法，其中所述至少一种其他抗癌疗法包括如下的一种或更多种：化学治疗、放射治疗、手术治疗、介入治疗、生物治疗、基因治疗、消融治疗、免疫治疗、靶向治疗和中药治疗。

[0436] (26) 根据 (25) 的方法，其中所述至少一种其他抗癌疗法包括化学治疗。

[0437] (27) 根据 (26) 的方法，其中所述化学治疗为一线化学治疗。

[0438] (28) 根据 (27) 的方法，其中所述一线化学治疗使用的一种或更多种化学治疗剂包括铂类化合物，例如顺铂。

[0439] (29) 根据 (25) 的方法，其中所述至少一种其他抗癌疗法包括靶向治疗。

[0440] (30) 根据 (29) 的方法，其中所述靶向治疗包括施用吉非替尼、厄洛替尼和 / 或重组人血管内皮抑制素。

[0441] (31) 根据 (25) 的方法，其中所述至少一种其他抗癌疗法包括生物治疗。

[0442] (32) 根据 (1)-(31) 任一的方法，其中与治疗前的肿瘤相比，所述治疗消除了所述肿瘤或减小了所述肿瘤的大小。

[0443] (33) 根据 (1)-(32) 任一的方法，其中所述治疗方法为非手术治疗方法。

[0444] 在另一个方面，本发明的其他实施方案提供了：

[0445] (1) 一种治疗受试者中的肺癌的方法，其中所述受试者具有胸腔积液、腹腔积液和 / 或心包积液，包括经表面或局部给药向所述受试者给予由 SEQ ID NO:2 编码的重组干扰素。

[0446] (2) 根据 (1) 的方法，其中所述受试者是中期、晚期或 III 或 IV 期癌症患者，任选地，所述受试者是晚期或 III 或 IV 期癌症患者。

[0447] (3) 根据 (1) 或 (2) 的方法，其中所述肺癌为不具备手术指征也不适于手术的肺癌。

[0448] (4) 根据 (1) 或 (2) 的方法，其中所述肺癌是不可切除的肺癌。

[0449] (5) 根据 (4) 的方法，其中所述肿瘤通过手术切除被切除。

[0450] (6) 根据 (1)-(5) 任一的方法，其中所述胸腔积液为恶性胸腔积液，所述腹腔积液

为恶性腹腔积液，和 / 或所述心包积液为恶性心包积液。

[0451] (7) 根据 (1)-(6) 任一的方法，其中所述局部给药包括如下的至少一种 :浸润给药、胸腔给药、腹腔给药和心包给药。

[0452] (8) 根据 (7) 的方法，其中通过灌注进行所述局部给药。

[0453] (9) 根据 (8) 的方法，其中所述重组干扰素以如下范围的量施用 :一次灌注给药约 30 μg- 约 2000 μg，任选地，约 100 μg- 约 1500 μg，更任选地，约 150 μg- 约 1000 μg，还任选地，约 200 μg- 约 800 μg，还更任选地，约 200 μg- 约 400 μg。

[0454] (10) 根据 (8) 或 (9) 的方法，其中每约 1 天 - 约 10 天，任选地，每约 1 天 - 约 7 天，例如每约 1、2、3、4、5、6 或 7 天灌注给药 1 次所述重组干扰素。

[0455] (11) 根据 (10) 的方法，其中每约 1 天灌注给药 1 次所述重组干扰素，持续约 4 次 - 约 6 次。

[0456] (12) 根据 (1)-(11) 任一的方法，其中在所述表面或局部给药的之前、同时和 / 或之后，经全身给药向所述受试者施用所述重组干扰素。

[0457] (13) 根据 (12) 的方法，其中所述全身给药包括皮下和 / 或肌肉给药。

[0458] (14) 根据 (13) 的方法，其中所述皮下给药包括皮下注射。

[0459] (15) 根据 (13) 的方法，其中所述肌肉给药包括肌肉注射。

[0460] (16) 根据 (13)-(15) 任一的方法，其中以约 2 μg/ 次 - 约 10 μg/ 次，任选地，约 4 μg/ 次 - 约 10 μg/ 次，更任选地，约 4.5 μg/ 次 - 约 9 μg/ 次，例如约 4.5 μg/ 次或约 9 μg/ 次的诱导剂量通过皮下给药和 / 或肌肉给药施用一次或更多次所述重组干扰素，之后以约 10 μg/ 次 - 约 70 μg/ 次，任选地，约 12 μg/ 次 - 约 50 μg/ 次，更任选地，约 12 μg/ 次 - 约 30 μg/ 次的治疗剂量通过皮下给药和 / 或肌肉给药施用多次所述重组干扰素。

[0461] (17) 根据 (16) 的方法，其中施用诱导剂量与施用治疗剂量之间的时间间隔为约 1 天 - 约 1 个月，任选地，约 1 天 - 约 1 周，更任选地，约 1 天 - 约 3 天，包括，例如约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周或约 1 个月。

[0462] (18) 根据 (16) 或 (17) 的方法，其中多次施用诱导剂量的重组干扰素时，每约 1 天 - 约 10 天施用一次所述重组干扰素，任选地，每约 1 天 - 约 7 天施用一次所述重组干扰素，更任选地，每约 1 天 - 约 2 天施用一次所述重组干扰素，包括，例如每约 1、2、3、4、5、6、7、8、9 或 10 天施用一次所述重组干扰素。

[0463] (19) 根据 (16)-(18) 任一的方法，其中每约 1 天 - 约 10 天施用一次治疗剂量的所述重组干扰素，任选地，每约 1 天 - 约 7 天施用一次治疗剂量的所述重组干扰素，更任选地，每约 1 天 - 约 2 天施用一次治疗剂量的所述重组干扰素，包括，例如每约 1、2、3、4、5、6、7、8、9 或 10 天施用一次治疗剂量的所述重组干扰素。

[0464] (20) 根据 (16)-(19) 任一的方法，其中诱导剂量和治疗剂量的施用的持续时间为至少约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年或约 6 年等，或者可长期施用所述重组干扰素，包括患者生命的整个期间。

[0465] (21) 根据 (1)-(20) 任一的方法，其中经表面给药、局部给药和 / 或全身给药进一步给予其他治疗药物。

[0466] (22) 根据 (21) 的方法，其中所述其他治疗药物包括抗肿瘤药物。

[0467] (23) 根据 (22) 的方法，其中所述抗肿瘤药物包括一种或更多种化学治疗剂、靶向药物或生物制剂。

[0468] (24) 根据 (23) 的方法，其中所述一种或更多种化学治疗剂包括铂类化合物，例如顺铂。

[0469] (25) 根据 (23) 的方法，其中一种或更多种靶向药物包括吉非替尼、厄洛替尼和 / 或重组人血管内皮抑制素。

[0470] (26) 根据 (1)-(25) 任一的方法，其中与治疗前的肿瘤大小相比，所述治疗消除了所述肿瘤或减小了所述肿瘤的大小。

[0471] (27) 根据 (1)-(26) 任一的方法，其中所述治疗方法为非手术治疗方法。

[0472] 更具体地，在一个实施方案中，在以上提及的本发明的任一种方法中，所述肿瘤是实体瘤；任选地，所述实体瘤包括如下的一种或更多种：肺癌、肝癌、肝细胞癌 (HCC)、食道癌、胆管癌、胆囊癌、胃癌 (stomach cancer)、腹部癌 (abdominal cancer)、胃肠道癌、胃癌 (gastric cancer)、胰腺癌、肾细胞癌、肾癌、骨癌、乳腺癌、卵巢癌、子宫癌、宫颈癌、子宫内膜癌、结直肠癌、结肠癌、直肠癌、膀胱癌、浅表性膀胱癌、前列腺癌、前列腺癌、肾上腺瘤、鳞状细胞癌、神经瘤、恶性神经瘤、肌上皮癌、滑膜肉瘤、横纹肌肉瘤、胃肠道间质细胞瘤、皮肤癌、基底细胞癌、恶性黑色素瘤、甲状腺癌、鼻咽癌、血管瘤、表皮样癌、头颈癌、神经胶质瘤、或卡波济氏肉瘤。

[0473] 在以上提及的本发明的任一种方法中，所述肿瘤为不具备手术指征或既不具备手术指征也不适于手术的肿瘤如癌症或实体瘤；和 / 或所述受试者是中期、晚期癌症患者，或 III 或 IV 期癌症患者，任选地，所述受试者是晚期或 III 或 IV 期癌症患者。

[0474] 在以上提及的本发明的任一种方法中，所述重组干扰素作为单一疗法向受试者施用；或者，进一步包括给予所述受试者一种或更多种其他抗癌疗法，任选地，在施用所述重组干扰素之前、同时和 / 或之后给予所述受试者其他抗癌疗法。任选地，所述其他抗癌疗法包括如下的一种或更多种：化学治疗、放射治疗、手术治疗、介入治疗、生物治疗、基因治疗、消融治疗、免疫治疗、靶向治疗和中药治疗。

[0475] 以及，在另一个方面，本发明的其他实施方案还提供了：

[0476] (1) 一种治疗受试者中肿瘤的方法，包括向所述受试者施用包含抗肿瘤作用的重组干扰素，作为一线单一疗法。

[0477] (2) 根据 (1) 的方法，其中所述肿瘤包括如下一种：肺癌、子宫癌、宫颈癌和胰腺癌。

[0478] (3) 根据 (2) 的方法，其中所述肺癌包括非小细胞肺癌。

[0479] (4) 根据 (1) 的方法，其中所述肿瘤不是肾癌。

[0480] (5) 一种治疗受试者中肿瘤的方法，包括向所述受试者施用包含抗肿瘤作用的重组干扰素，作为二线单一疗法。

[0481] (6) 根据 (5) 的方法，其中所述肿瘤包含如下的一种：肺癌、结直肠癌、恶性黑素瘤、卵巢癌、宫颈癌、肝癌、乳腺癌、胃肠道癌、前列腺癌、神经瘤和鳞状细胞癌。

[0482] (7) 根据 (6) 的方法，其中所述结直肠癌包括结肠癌。

[0483] (8) 根据 (6) 的方法，其中所述结直肠癌包括直肠癌。

[0484] (9) 根据 (6) 的方法，其中所述肺癌包括非小细胞肺癌。

[0485] (10) 根据 (6) 的方法，其中所述肝癌包括 HCC。

[0486] (11) 根据 (6) 的方法，其中所述胃肠道癌包括胃癌。

[0487] (12) 一种治疗受试者中肿瘤的方法，包括向所述受试者施用包含抗肿瘤作用的重组干扰素，作为一线疗法，并联合一种或更多种其他抗癌疗法。

[0488] (13) 根据 (12) 的方法，其中所述肿瘤包括如下的一种 ：肺癌、前列腺癌和淋巴瘤。

[0489] (14) 根据 (13) 的方法，其中所述肺癌包括非小细胞肺癌和小细胞肺癌中的至少一种。

[0490] (15) 根据 (12) 的方法，其中所述肿瘤不是卵巢癌。

[0491] (16) 一种治疗受试者中肿瘤的方法，包括向所述受试者施用包含抗肿瘤作用的重组干扰素，作为二线单一疗法，并联合一种或更多种其他抗癌疗法。

[0492] (17) 根据 (16) 的方法，其中所述肿瘤包括如下的一种 ：肺癌、淋巴瘤、宫颈癌和胆管腺癌。

[0493] (18) 根据 (17) 的方法，其中所述肺癌包括非小细胞肺癌和小细胞肺癌中的至少一种。

[0494] (19) 根据 (17) 的方法，其中所述淋巴瘤是非霍奇金氏淋巴瘤。

[0495] (20) 根据 (12)、(13)、(14)、(15)、(16)、(17)、(18) 或 (19) 任一的方法，其中所述一种或更多种其他抗癌疗法包括如下的至少一种 ：放射疗法、小分子疗法、化学疗法、生物治疗、TCM 和手术治疗。

[0496] (21) 根据 (20) 的方法，其中在所述小分子疗法中的小分子包括吉非替尼。

[0497] (22) 根据 (20) 的方法，其中所述生物治疗包括用如下的至少一种来治疗 ：重组蛋白和分离的细胞。

[0498] (23) 根据 (22) 的方法，其中所述重组蛋白包括重组人血管内皮抑制素。

[0499] (24) 根据 (22) 的方法，其中所述分离的细胞包括如下的至少一种 ：干细胞和 NK 细胞。

[0500] (25) 根据 (20) 的方法，其中在癌症手术治疗后施用所述重组干扰素。

[0501] (26) 根据 (20)-(24) 任一的方法，其中在癌症的手术治疗前施用所述重组干扰素。

[0502] (27) 根据 (1)-(26) 任一的方法，其中所述重组干扰素通过如下至少一种途径施用 ：全身和局部。

[0503] (28) 根据 (1)-(26) 任一的方法，其中所述重组干扰素通过如下至少一种途径施用 ：肌内、腹膜内、静脉内、动脉内、瘤内、注射入淋巴结中、表面 (topically) 于肿瘤上、局部 (locally) 于肿瘤上、鼻内、皮下、喷雾、吸入、灌注以及输注。

[0504] (29) 根据 (1)-(28) 任一的方法，其中所述重组干扰素包括 rSIFN-co。

[0505] (30) 根据 (29) 的方法，其中所述重组干扰素以每次治疗约 2μg 至约 2500μg 的剂量施用。

[0506] (31) 根据 (29) 的方法，其中所述重组干扰素以每次治疗约 9μg 至约 2100μg 的剂量施用。

[0507] (32) 根据 (29) 的方法，其中所述重组干扰素以如下的一种或更多种剂量施用 ：

2μg、4μg、9μg、13.5μg、15μg、18μg、21μg、24μg、25.5μg、30μg、36μg、45μg、70μg、84μg、90μg、100μg、105μg、120μg、126μg、139μg、150μg、168μg、180μg、189μg、198μg、200μg、207μg、210μg、240μg、252μg、273μg、300μg、315μg、400μg、500μg、600μg、1000μg、2000μg、2100μg。

[0508] (33) 根据 (1)-(32) 任一的方法，其中所述重组干扰素包含特定的活性。

[0509] (34) 根据 (33) 的方法，其中所述重组干扰素包含约 4.4x 10^8IU/mg 至约 1.0x 10^9IU/mg，以及任选地大于 5.5x 10^8IU/mg 的活性。

[0510] (35) 一种在受试者中预防肿瘤复发的方法，包括在手术治疗、化学疗法、放射疗法、冷冻消融、射频消融、生物治疗、介入治疗和 / 或 rSIFN-co 治疗后，使用包含为包含 SEQ ID NO :2 的序列的核酸序列编码的氨基酸序列的量的重组干扰素，在受试者中瘤块已减小后由此施用所述重组干扰素。

[0511] (36) 一种延长受试者无瘤生存的方法，包括在手术治疗、化学疗法、放射疗法、冷冻消融、射频消融、生物治疗、介入治疗和 / 或 rSIFN-co 治疗后，使用包含为包含 SEQ ID NO :2 的序列的核酸序列编码的氨基酸序列的量的重组干扰素，在受试者中瘤块已减小后由此施用所述重组干扰素。

[0512] 附图简述

[0513] 图 1 显示了本发明重组干扰素 (rSIFN-co) 与 IFN-α 2b 的结构的比较差异，其中图 1 的侧视图和俯视图中的红色表示 rSIFN-co，绿色表示 IFN-α 2b，其中红色在黑白打印图中显示为黑色，绿色在黑白打印图中显示为灰色。

[0514] 图 2 显示了本发明重组干扰素 rSIFN-co 三维结构与美国安进公司的干复津 (INFERGEN®) (以 am-Infergen 或 Infergen 表示) 的计算模型结构的比较差异，其中右图圆圈中的黄色细线为 rSIFN-co，蓝色粗螺旋为 am-Infergen。同时，右图中红色表示 rSIFN-co，绿色表示 am-Infergn，其中红色在黑白打印图中显示为黑色，绿色在黑白打印图中显示为灰色。

[0515] 图 3 显示了患者 1 的治疗情况，其中图 3a 箭头所示患者用药 12 月后第 2 年 11 月 8 日 CT 成像显示原病灶状态 ；以及图 3b 箭头所示患者用药 15 月后第 3 年 2 月 1 日 CT 成像显示原病灶处状态，治疗的起始年为第 1 年。

[0516] 图 4 显示患者 2 的治疗情况，其中图 4a 显示使用 rSIFN-co 前 PET/CT 影像学诊断，箭头指示病灶 ；以及图 4b 显示使用 rSIFN-co 后 PET/CT 影像学诊断，箭头指示原病灶治疗后状态。

[0517] 图 5 和图 6 显示患者 3 的治疗情况，其中图 5a 显示使用 rSIFN-co 前肺 CT 影像学，箭头所示病灶处 ；图 5b 显示使用 rSIFN-co 后头部及胸部 CT 影像学诊断，箭头所示原病灶处治疗后状态 ；图 6a 显示使用 rSIFN-co 前脑部 CT 影像学，箭头所示病灶处 ；以及图 6b 显示使用 rSIFN-co 后头部及胸部影像学诊断，箭头所示原病灶处治疗后状态。

[0518] 图 7 和图 8 显示患者 4 的治疗情况，其中图 7a 和图 8a 显示使用 rSIFN-co 前影像学诊断，如化疗后的 PET/CT 所示，图 7a-8a 箭头所示病灶 ；图 7b 和图 8b 显示使用 rSIFN-co 后影像学诊断，如 PET/CT 所示，箭头所示原病灶处治疗后状态。

[0519] 图 9- 图 11 显示患者 5 的治疗情况，其中图 9a、图 10a 和图 11a 显示使用 rSIFN-co 前影像学诊断，如 PET/CT 所示，图 9a、图 10a 和图 11a 中箭头所示病灶 ；图 9b、图 10b 和图

11b 显示使用 rSIFN-co 后影像学诊断，如 PET/CT 所示，图 9b、图 10b 和图 11b 中箭头所示原病灶处治疗后状态。

[0520] 图 12 显示患者 6 的治疗情况，其中图 12a 显示使用 rSIFN-co 前胸部 CT 影像学诊断，箭头所示原发病灶处；以及图 12b 显示使用 rSIFN-co 药物后 CT 影像学诊断，箭头所示原病灶处治疗后状态。

[0521] 图 13 和 14 显示患者 7 的治疗情况，其中图 13a 和图 14a 显示使用 rSIFN-co 前 CT 影像学诊断，箭头所示原发病灶处；以及图 13b 和图 14b 显示使用 rSIFN-co 后 CT 影像学诊断，箭头所示原病灶处治疗后状态。

[0522] 图 15 和 16 显示患者 8 的治疗情况，其中图 15a 和 16a 显示使用 rSIFN-co 前 CT 影像学诊断，箭头所示原发病灶处；以及图 15b 和 16b 显示使用 rSIFN-co 后 CT 影像学诊断，箭头所示原病灶处治疗后状态。

[0523] 图 17 显示患者 9 的治疗情况，其中图 17a 显示使用 rSIFN-co 前 CT 影像学诊断，箭头所示原发病灶处；以及图 17b 显示使用 rSIFN-co 后 CT 影像学诊断，箭头所示原病灶处治疗后状态。

[0524] 图 18 和 19 显示患者 10 的治疗情况，其中图 18 显示治疗前后胸水变化；图 19a 显示使用 rSIFN-co 前胸部 CT 影像学诊断，箭头所示原发病灶处；以及图 19b 显示使用 rSIFN-co 后胸部 CT 影像学诊断，箭头所示原病灶处治疗后状态。

[0525] 图 20-23 显示患者 11 的治疗情况，其中图 20 显示患者治疗前的病理切片；图 21a、22a 和 23a 显示使用 rSIFN-co 前 PET/CT 影像学诊断，箭头所示原发病灶处；以及图 21b、22b 和 23b 显示使用 rSIFN-co 后 PET/CT 影像学诊断，箭头所示原病灶处治疗后状态。

[0526] 图 24 显示患者 12 的治疗情况，其中图 24a 显示刚用药时 CT 成像，箭头所示病灶处；以及图 24b 显示使用 rSIFN-co 后影像学诊断，箭头所示原病灶处治疗后状态。

[0527] 图 25 显示患者 13 的治疗情况，其中图 25a 显示治疗前期 CT 成像，箭头所示右肺下叶可疑病灶；以及图 25b 显示治疗后期胸部 CT 成像，箭头所示原右肺下叶可疑病灶处治疗后状态。

[0528] 图 26 显示患者 14 的治疗情况，其中图 26a 显示刚用药时（手术后）CT 成像，箭头所示原病灶手术处；以及图 26b 显示治疗后期 CT，箭头所示原病灶手术处治疗后状态。

[0529] 图 27 显示患者 15 的治疗情况，其中图 27a 显示使用 rSIFN-co 前盆腔 MRI 影像学诊断，箭头所示病灶处；以及图 27b 显示使用 rSIFN-co 后盆腔 MRI 影像学诊断，箭头所示原病灶处治疗后状态。

[0530] 图 28 显示患者 16 的病理诊断，箭头所示腺癌细胞。

[0531] 图 29 显示患者 16 的治疗情况，其中图 29a 显示使用 rSIFN-co 前 PET/CT 影像学诊断，箭头所示原发病灶处；以及图 29b 显示使用 rSIFN-co 后 PET/CT 影像学诊断，箭头所示原病灶处治疗后状态。

[0532] 发明详述

[0533] 发明人发现 rSIFN-co 单独使用或联合其他抗癌疗法，作为一线或二线单一疗法或与其他治疗方法联用，可有利地用于攻克癌症。其优点在于：首先，重组干扰素 (rSIFN-co) 具有广谱的抗肿瘤作用，其对于实体瘤和非实体瘤都有治疗作用。同时，rSIFN-co 与现有的治疗手段，如手术、化疗、放疗、其他生物治疗及其它抗肿瘤药物都具有

很好的协同作用。其次，rSIFN-co 是低毒的，即当 rSIFN-co 大剂量使用时观察到对正常细胞很少的伤害或没有伤害。再次，rSIFN-co 使用方便，对身体任何部位的肿瘤都可直接使用。因此，rSIFN-co 可皮下或肌肉注射控制肿瘤的全身进展、可胸腔或腹腔灌注来消除积液及胸腹腔肿瘤、可表面或局部注射来消除原发或转移的肿瘤、以及可浸润（透皮）给药来治疗骨、皮肤、肌肉、前列腺等中的肿瘤病灶。同样，rSIFN-co 可雾化吸入或经鼻喷雾给药。

[0534] 基于 rSIFN-co 的前述优点，无论是单用还是联用，其对肿瘤的有效率不低于 90％。对于早中期癌症病例，rSIFN-co 可在手术后使用以代替化疗，并有效预防复发和肿瘤转移，或延长无病生存期；对于晚期癌症病例或不具备手术指征的癌症病例，rSIFN-co 可用于非手术消除瘤体或减小瘤体的大小；对于不具备手术指征的肿瘤，rSIFN-co 可用于将所述肿瘤转变为可手术的肿瘤，即将不可切除的肿瘤转变为可切除的肿瘤，从而创造适合手术的条件。因此，无论是单用还是与其他一种或更多种抗肿瘤疗法联用，rSIFN-co 能在大量的病例中攻克肿瘤。

[0535] 1. 重组干扰素（rSIFN-co）及其制备方法

[0536] 在一方面，本发明的重组干扰素的氨基酸序列及其编码核苷酸序列（连同终止密码子）如下 SEQ ID NO：1 和 SEQ ID NO：2 分别所示。这些序列也参见美国专利第 7,585,647 号；第 7,364,724 号；第 8,114,395 号和第 8,287,852 号：

[0537]

M C D L P Q T H S L G N R R A L I L L A

1 ATGTGCGACC TGCCGCAGAC CCACTCCCTG GGTAACCGTC GTGCTCTGAT CCTGCTGGCT

TACACGCTGG ACGGCGTCTG GGTGAGGGAC CCATTGGCAG CACGAGACTA GGACGACCGA

Q M R R I S P F S C L K D R H D F G F P

61 CAGATGCGTC GTATCTCCCC GTTCTCCTGC CTGAAAGACC GTCACGACTT CGGTTTCCCG

GTCTACGCAG CATAGAGGGG CAAGAGGACG GACTTTCTGG CAGTGCTGAA GCCAAAGGGC

Q E E F D G N Q F Q K A Q A I S V L H E

121 CAGGAAGAAT TCGACGGTAA CCAGTTCCAG AAAGCTCAGG CTATCTCCGT TCTGCACGAA

GTCCTTCTTA AGCTGCCATT GGTCAAGGTC TTTCGAGTCC GATAGAGGCA AGACGTGCTT

M I Q Q T F N L F S T K D S S A A W D E

181 ATGATCCAGC AGACCTTCAA CCTGTTCTCC ACCAAAGACT CCTCCGCTGC TTGGGACGAA

[0538]

TACTAGGTCG TCTGGAAGTT GGACAAGAGG TGGTTTCTGA GGAGGCGACG AACCCTGCTT

S L L E K F Y T E L Y Q Q L N D L E A C

241 TCCCTGCTGG AAAAATTCTA CACCGAACTG TACCAGCAGC TGAACGACCT GGAAGCTTGC

AGGGACGACC TTTTTAAGAT GTGGCTTGAC ATGGTCGTCG ACTTGCTGGA CCTTCGAACG

V I Q E V G V E E T P L M N V D S I L A

301 GTTATCCAGG AAGTTGGTGT TGAAGAAACC CCGCTGATGA ACGTTGACTC CATCCTGGCT

CAATAGGTCC TTCAACCACA ACTTCTTTGG GGCGACTACT TGCAACTGAG GTAGGACCGA

V K K Y F Q R I T L Y L T E K K Y S P C

361 GTTAAAAAAT ACTTCCAGCG TATCACCCTG TACCTGACCG AAAAAAAATA CTCCCCGTGC

CAATTTTTTA TGAAGGTCGC ATAGTGGGAC ATGGACTGGC TTTTTTTTAT GAGGGGCACG

A W E V V R A E I M R S F S L S T N L Q

421 GCTTGGGAAG TTGTTCGTGC TGAAATCATG CGTTCCTTCT CCCTGTCCAC CAACCTGCAG

CGAACCCTTC AACAAGCACG ACTTTAGTAC GCAAGGAAGA GGGACAGGTG GTTGGACGTC

E R L R R K E （SEQ ID NO:1）

481 GAACGTCTGC GTCGTAAAGA ATAA （SEQ ID NO:2）

CTTGCAGACG CAGCATTTCT TATT （SEQ ID NO:3）

[0539] 与已公布的 IFN-α 2b 以及具有 SEQ ID NO :1 的氨基酸序列但不为 SEQ ID NO :2 的核苷酸序列编码的干扰素例如干扰素 alfacon-1（干复津，INFERGEN®）相比，本发明的重组干扰素 (rSIFN-co) 的三维结构既不同于 IFN-α 2b 的三维结构（参见图 1，其中图 1 的侧视图和俯视图中的红色表示 rSIFN-co，绿色表示 IFN-α 2b，其中的红色在黑白打印图中显示为黑色，绿色在黑白打印图中显示为灰色），也不同于干扰素 alfacon-1 的计算模型结构（参见 KORN，AP，Journal of Interferon Research 1994，14 :1-9）。由本发明重组干扰素与干扰素 alfacon-1 的比较结果可见二者的 AB 环有着明显的区别，它们的 BC 环也无法完全重合（参见图 2）。

[0540] 另外，本发明的重组干扰素在肌肉注射给体重指数 (BMI) 为约 18- 约 23 范围内的人体后，以采血时间对受试人体血清中的 2-5A 寡聚核苷酸酶（也称为 2’，5’ -OAS) 浓度作图，所得曲线一般表现为双峰，其曲线下面积显著大于在同一条件下注射干扰素 alfacon-1（干复津，INFERGEN®）所获得的曲线下面积。此外，本发明的重组干扰素在

注射给人体后其在人体内的半衰期比干扰素 alfacon-1（干复津，INFERGEN®）在人体内的半衰期更长（参见 CN 1740197A；曾洁萍等，现代预防医学，2008，35(5)，982-984）。

[0541] 已进行的实验的结果还证实，本发明的重组干扰素具有比目前投入临床使用的其他任何干扰素（包括干扰素 alfacon-1（干复津，INFERGEN®））更强的效力。例如，对于乙型肝炎病毒而言，本发明的重组干扰素不仅能抑制乙型肝炎病毒的 DNA 复制而且还能抑制乙肝病毒表面抗原 (HBsAg) 和乙肝病毒 e 抗原 (HBeAg) 的分泌，抑制乙肝病毒核心抗原 (HBcAg)DNA 复制的效力与干扰素 alfacon-1（干复津，INFERGEN®）相比提高约一倍。本发明的重组干扰素的体外药效学显示它不仅能抑制乙型肝炎病毒的 DNA 复制，而且能抑制乙型肝炎病毒表面抗原和乙型肝炎病毒 e 抗原的分泌，其细胞学毒性仅为临床现用干扰素的 1/8，但抗病毒活性却是临床现用干扰素的 5-20 倍，同时在人体内具有更高更广谱更长时间的生物学应答反应（参见 CN 1740197A）。

[0542] 此外，无论是就病毒性疾病的预防还是就肿瘤的治疗而言，本发明的重组干扰素都具有与其他干扰素（包括干扰素 alfacon-1（干复津，INFERGEN®））相比，更高的抗病毒活性和更低的副作用。例如，本发明的重组干扰素不但具有强于临床现用干扰素 20 倍的抗病毒活性，以及明显强于重组人 α 型干扰素的抑制肿瘤细胞生长或促凋亡作用。

[0543] 因此，与具有 SEQ ID NO：1 的氨基酸序列但不为 SEQ ID NO：2 的核苷酸序列编码的干扰素，例如干扰素 alfacon-1（干复津，INFERGEN®）相比，本发明的重组干扰素具有不同的空间构象、增强的生物学活性和 / 或不同的药代动力学特性。

[0544] 因此，在一些实施方案中，本发明的重组干扰素具有 SEQ ID NO：1 的氨基酸序列，例如由 SEQ ID NO：1 的氨基酸序列组成。在一些实施方案中，本发明的重组干扰素由 SEQ ID NO：2 的核苷酸序列编码。在一些实施方案中，本发明的重组干扰素具有 SEQ ID NO：1 的氨基酸序列且由 SEQ ID NO：2 的核苷酸序列编码，进一步地，所述重组干扰素包含 SEQ ID NO：1 的氨基酸序列且由 SEQ ID NO：2 的核苷酸序列编码。更进一步地，所述重组干扰素由 SEQ ID NO：1 的氨基酸序列组成且由 SEQ ID NO：2 的核苷酸序列编码。

[0545] 在一些实施方案中，与具有 SEQ ID NO：1 的氨基酸序列但不为 SEQ ID NO：2 的核苷酸序列编码的干扰素，例如干扰素 alfacon-1（干复津，INFERGEN®）相比，本发明的重组干扰素具有改变的空间构象和 / 或增强的生物学活性和 / 或不同的药代动力学特性。举例来说，本发明的重组干扰素具有改变的空间构象和增强的生物学活性，具有改变的空间构象和不同的药代动力学特性，或具有改变的空间构象、增强的生物学活性以及不同的药代动力学特性。所述增强的生物学活性包括：增强的抗病毒活性、增强的抑制肿瘤细胞生长或促凋亡作用、更低的副作用和 / 或能大剂量使用（例如每剂用量可＞ 1000 万 IU）。举例来说，所述增强的生物学活性可以是增强的抗病毒活性和 / 或增强的抑制肿瘤细胞（如乳腺癌细胞或宫颈癌细胞）生长或促凋亡作用（参见：郑洁等，四川大学学报（医学版），2010，41(1)，29-34；陈研等，四川大学学报（医学版），2008，39(5)，715-718）；所述不同的药代动力学特性包括：在肌肉注射给体重指数 (BMI) 为约 18- 约 23 范围内的受试者后，以采血时间对受试者血清中的 2-5A 寡聚核苷酸酶浓度作图，所得曲线的曲线下面积显著大于在同一条件下注射具有 SEQ ID NO：1 的氨基酸序列但不为 SEQ ID NO：2 的核苷酸序列编码的干扰素例如干扰素 alfacon-1（干复津，INFERGEN®）所获得的曲线下面积和 / 或与

之相比更长的半衰期。

[0546] 在一些实施方案中，本发明的重组干扰素具有SEQ ID NO:1的氨基酸序列且由SEQ ID NO:2的核苷酸序列编码，其中与具有SEQ ID NO:1的氨基酸序列但不为SEQ ID NO:2的核苷酸序列编码的干扰素例如干扰素alfacon-1（干复津，INFERGEN®）相比，所述重组干扰素具有增强的针对乙肝病毒表面抗原(HBsAg)和乙肝病毒e抗原(HBeAg)表达的抑制活性。

[0547] 在另一方面，本发明中所使用的重组干扰素(rSIFN-co)可根据上述例如在US 7,364,724、US 7,585,647、US 8,114,395、CN 1740197 A、CN101001644 A、US 2009/0123417、US 2011/0158941和WO 2011072487A1中所披露的方法来制备。在特定的实施方案中，本发明中使用的重组干扰素可由如下方法所产生，所述方法包括如下步骤：将编码重组干扰素的包含SEQ ID NO:2的核苷酸序列导入分离的宿主细胞中，在适合于表达所述重组干扰素的条件下培养所述宿主细胞，和收获所述重组干扰素，其中所述重组干扰素具有SEQ ID NO:1的氨基酸序列，并且所述重组干扰素抑制乙肝病毒表面抗原(HBsAg)和乙肝病毒e抗原(HBeAg)的分泌。进一步地，所述宿主是大肠杆菌(Escherichia coli)，例如大肠杆菌LGM 194。进一步地，包含SEQ ID NO:2的核苷酸序列处于启动子P_{BAD}的控制下。进一步地，收获步骤包括从培养发酵液中提取干扰素，收集包涵体，所收获重组干扰素的变性和复性。更进一步地，所述收获步骤还包括分离纯化所述重组干扰素。

[0548] 本领域技术人员可以参考以下部分D“药物组合物和给药途径”的内容将本发明的重组干扰素制备成肌注剂型、喷雾剂型或吸入剂型等。

[0549] 本发明的重组干扰素的比活性相当于约4.4×10^{8}IU/mg-约1.0×10^{9}IU/mg，任选地大于$5.5x\ 10^{8}$IU/mg。这样的比活性是生物学活性与蛋白质含量之比。该生物学活性是通过本领域技术人员公知的方法如中华人民共和国药典2010版三部附录X C干扰素生物学活性测定法（即细胞病变抑制法）测定的；蛋白质含量是通过本领域技术人员公知的方法如中华人民共和国药典2010版三部附录VI B蛋白质测定法第二法（即Lowry法）测定的。

[0550] 2.治疗应用

[0551] 本发明人发现本发明的重组干扰素(rSIFN-co)可有效地用于肿瘤尤其是实体瘤例如肺癌等的治疗。使用本发明的重组干扰素rSIFN-co的单一疗法能抑制患者中肿瘤的生长，有效地缩小患者肿瘤大小乃至于能非手术直接消除患者肿瘤，减少乃至消除恶性胸腔积液、恶性腹腔积液和/或恶性心包积液，降低肿瘤标志物，有效地延长肿瘤患者生存期和/或无瘤生存期，以及防止术后癌症复发和/或患者肿瘤转移，并可有效治疗晚期癌症患者和不具有手术指征也不适于手术的癌症患者。本发明的重组干扰素与其他抗癌疗法例如一种或更多种化学治疗、放射疗法、手术疗法或靶向疗法联用，在一些病例中可以有效消除患者的肿瘤，达到治愈的效果。此外，与现有干扰素如干复津（INFERGEN®）相比，本发明的重组干扰素副作用小，因此可大剂量使用。

[0552] A.疾病和病症

[0553] 适合于本发明的治疗和/或预防方法的疾病和病症包括肿瘤。当在本文中使用时，术语“肿瘤”指所有不受控制及恶性赘生性细胞生长和增殖，以及所有癌性细胞和组织，以及异常或失控的增殖细胞。在一些实施方案中，所述肿瘤包括恶性肿瘤。当在本文中使

用时，术语“癌症”指通常以不受调节的细胞生长 / 增殖为特征的哺乳动物中的生理情况。在本文中，术语“癌症”和“恶性肿瘤”可交换地使用。

[0554] 在一些实施方案中，所述肿瘤包括实体瘤和非实体瘤，任选地，实体瘤。当在本文中使用时，术语“实体瘤”指组织的异常生长或结块，通常不包括囊肿或液体区域。当在本文中使用时，术语“非实体瘤”指造血系统的瘤形成，例如淋巴瘤、骨髓瘤和白血病，或由于通常不形成实体而实质上扩散的瘤形成。

[0555] 在一些实施方案中，所述实体瘤包括但不限于肺癌、肝癌、肝细胞癌 (HCC)、食道癌、胆管癌、胆囊癌、胃癌 (stomach cancer)、腹部癌 (abdominal cancer)、胃肠道癌、胃癌 (gastric cancer)、胰腺癌、肾细胞癌、肾癌、骨癌、乳腺癌、卵巢癌、子宫癌、宫颈癌、子宫内膜癌、结直肠癌、结肠癌、直肠癌、膀胱癌、浅表性膀胱癌、前列腺癌、前列腺癌、肾上腺瘤、鳞状细胞癌、神经瘤、恶性神经瘤、肌上皮癌、滑膜肉瘤、横纹肌肉瘤、胃肠道间质细胞瘤、皮肤癌、基底细胞癌、恶性黑色素瘤、甲状腺癌、鼻咽癌、血管瘤、表皮样癌、头颈癌、神经胶质瘤、或卡波济氏肉瘤。

[0556] 在一些实施方案中，所述非实体瘤包括但不限于白血病、急性白血病、慢性白血病、慢性粒细胞性白血病、急性髓性白血病、慢性髓性白血病、慢性淋巴细胞白血病、急性淋巴细胞白血病、T 细胞白血病、毛细胞白血病、红细胞增多症、骨髓增生异常综合征、多发性骨髓瘤、淋巴腺瘤、霍奇金氏淋巴瘤和非霍奇金氏淋巴瘤。

[0557] 在一些实施方案中，所述肿瘤是肺部肿瘤，包括但不限于异常增殖的或失控增殖的肺细胞和 / 或恶性肺肿瘤。在本文中使用时，术语“肺部肿瘤”指肺部的任何肿瘤，因此，这样的肿瘤可以是肺部原发的肿瘤和 / 或肺的转移性肿瘤，例如其他部位的肿瘤以各种转移方式转移至肺部的肿瘤。肺部肿瘤可以是良性的（非癌性的）、侵袭前病变（癌前病变）或恶性的（癌性的）肺部肿瘤，例如肺癌。

[0558] 在特定的实施方案中，所述肺部肿瘤是肺癌，包括但不限于小细胞肺癌 (SCLC) 和非小细胞肺癌 (NSCLC)。当在本文中使用时，术语“肺癌”指所有类型的肺癌，包括但不限于小细胞肺癌 (SCLC) 以及非小细胞肺癌 (NSCLC，包括但不限于腺癌、鳞状癌、大细胞癌、腺鳞癌以及肉瘤样癌）。进一步地，所述小细胞肺癌 (SCLC) 包括但不限于复合性小细胞肺癌；以及非小细胞肺癌 (NSCLC) 包括但不限于腺癌、鳞状细胞癌、大细胞癌、腺鳞癌、肉瘤样癌、类癌和唾液腺型癌。当在本文中使用时，术语“复合性小细胞肺癌”指小细胞肺癌中混合有非小细胞肺癌成分如大细胞肺癌的一种肺癌。

[0559] 在一个实施方案中，所述肺部肿瘤是侵袭前病变（癌前病变），包括但不限于肺鳞状上皮异型增生、肺原位癌、肺不典型腺瘤样增生和肺弥漫性特发性神经内分泌细胞增生。在一个实施方案中，肺的转移性肿瘤来自乳腺癌、结直肠癌、胃癌、胰腺癌、肾癌、恶性黑素瘤、前列腺癌、肝癌、甲状腺癌、肾上腺癌等转移至肺部的肿瘤。

[0560] 在一些实施方案中，上述肿瘤已转移，这样的转移可以是原处或远处的。当在本文中使用时，在涉及癌或恶性肿瘤时，术语“转移”指癌或恶性肿瘤从其原发部位向体内其他地方的扩散。癌细胞可从原发肿瘤脱离，渗入淋巴管和血管，通过血液循环并在体内别处的正常组织中的远处病灶中生长。转移可以是原处或远处的。对于肺部肿瘤如肺癌而言，可转移到淋巴、脑、中枢神经系统、骨、肝、肾上腺、皮肤、肠、甲状腺、卵巢、前列腺等。因此，本发明的重组干扰素可用于治疗这些已转移的肿瘤，例如已转移的肺癌，尤其是本发明的重组

干扰素可缓解肺癌局部压迫侵犯邻近组织引起的症状并治疗其远道转移。所述肺癌局部压迫侵犯邻近组织引起的症状包括但不限于因食管周围淋巴结转移增生而导致的咽下困难，因肿瘤经肺实质淋巴管扩散引起的呼吸困难。所述肺癌的远道转移包括但不限于肺癌的脑转移，肺癌的中枢神经系统转移，肺癌的骨转移，肺癌的肝转移、肺癌的肾上腺转移以及肺癌的其他转移如皮肤转移、肠转移、甲状腺转移、卵巢转移、前列腺转移等。

[0561] 在一些实施方案中，上述肿瘤可以是多原发癌，例如在所述肿瘤是肺癌的情况下，这样的肺癌可以是多原发肺癌，例如在不同的肺段或肺叶处发生的多原发肺癌。当在本文中使用时，术语“多原发癌”指在同一个体上，同时或先后发生两种以上的原发恶性肿瘤。这样的原发恶性肿瘤必须由组织学确认为恶性且不为外转移瘤。当在本文中使用时，术语“多原发肺癌”指组织学相同的、独立存在的、无互相转移可能性的、在不同的肺段或肺叶处的同时或先后发生的两个以上的原发恶性肿瘤。

[0562] 适合于本发明的治疗和/或预防方法的疾病还包括癌症的急症，例如晚期癌症的急症，如胸腔积液、腹腔积液和/或心包积液。在一些实施方案中，所述胸腔积液、腹腔积液和/或心包积液为恶性胸腔积液、恶性腹腔积液和/或恶性心包积液。在一些实施方案中，所述恶性胸腔积液可由胸膜的原发性肿瘤或转移性肿瘤所致，是晚期肺癌的一个常见急症。所述胸膜的原发性肿瘤包括恶性弥漫性间皮瘤，以及所述胸膜的转移性肿瘤来自肺癌、乳腺癌、淋巴瘤、卵巢癌、子宫内膜癌、宫颈癌、胃癌、结肠癌、胰腺癌、膀胱癌和肝癌等。在一些实施方案中，所述恶性心包积液可由肺癌、乳房癌等所致，例如所述恶性心包积液可由肺癌转移或直接侵犯心包膜所致，亦是晚期肺癌的一个常见表现。在一些实施方案中，所述恶性腹腔积液可由恶性肿瘤引起的腹腔过量液体积聚，是癌症的晚期急症之一，其常继发于卵巢癌、宫颈癌、子宫内膜癌、消化道肿瘤、淋巴瘤、乳腺癌、腹膜间皮瘤等。

[0563] B. 治疗对象

[0564] 适合于本发明的治疗和/或预防方法的受试者包括哺乳动物，包括但不限于人和非人哺乳动物，任选地，所述受试者是人。在本文中术语“受试者 (subject)”和“患者 (patient)”可交换地使用。在一些实施方案中，具有肿瘤的受试者是之前已被诊断患有肿瘤如恶性肿瘤的受试者。

[0565] 在一些实施方案中，所述受试者包括但不限于具有不可切除的肿瘤如恶性肿瘤的受试者、具有可切除的肿瘤如恶性肿瘤的受试者、患有癌症的受试者、带有转移的肿瘤如转移的恶性肿瘤的受试者、和/或带有胸腔积液、腹腔积液和/或心包积液例如恶性胸腔积液、恶性腹腔积液和/或恶性心包积液的受试者。在一些实施方案中，所述肿瘤任选地通过手术切除被切除。在一些实施方案中，所述受试者具有实体瘤。在一些实施方案中，所述实体瘤为可切除或不可切除例如可手术切除或不可手术切除的实体瘤。在一些实施方案中，所述可切除或不可切除如可手术切除或不可手术切除的实体瘤为晚期或 III 或 IV 期实体瘤。在一些实施方案中，所述受试者具备或不具备癌症或肿瘤手术指征如肺癌手术指征。在一些实施方案中，所述实体瘤为具备或不具备手术指征如肿瘤手术指征的实体瘤。在一些实施方案中，所述具备或不具备手术指征如肿瘤手术指征的实体瘤为晚期或 III 或 IV 期实体瘤。在一些实施方案中，所述实体瘤为肺癌。

[0566] 当在本文中使用时，术语“手术适应症”或“手术指征”或“适于手术”是指当某种疾病符合诊疗常规所规定的标准，采用非手术治疗方式无法治愈疾病，采用手术方式将有

助于疾病的治疗时，所应采用的手术方式。在一些实施方案中，所述不具备手术适应症或手术指征的癌症包括：(1) 非实体瘤或全身性肿瘤，如白血病、恶性淋巴瘤、骨肿瘤等，(2) 发生全身广泛转移的癌症，手术治疗已失去价值，(3) 发生部位手术切除困难的癌症，如鼻咽癌、食管上段癌、舌根癌等，(4) 很早就容易发生转移的癌症，如肺部未分化小细胞癌等，多不主张手术治疗，以及 (5) 癌细胞向四周浸润性生长、边界不清、手术无法切除干净的癌症，如扁桃体癌、胰腺癌等。在一些实施方案中，所述不具备手术适应症或手术指征的实体瘤包括：(1) 全身性实体瘤，如骨肿瘤等，(2) 发生全身广泛转移的实体瘤，手术治疗已失去价值，(3) 发生部位手术切除困难的实体瘤，如鼻咽癌、食管上段癌、舌根癌等，(4) 很早就容易发生转移的实体瘤，如肺部未分化小细胞癌等，以及 (5) 癌细胞向四周浸润性生长、边界不清、手术无法切除干净的实体瘤，如扁桃体癌、胰腺癌等。

[0567] 当在本文中使用时，术语“可切除的肿瘤”是被局限于原发器官并适于手术治疗的肿瘤如恶性肿瘤。所述具有不可切除的肿瘤如恶性肿瘤的受试者还包括具有手术无法切除的肿瘤如恶性肿瘤的受试者，这样的手术可包括外科手术、微创手术等。在特定的实施方案中，所述具有可切除的肿瘤如恶性肿瘤的受试者包括具有可进行手术切除的肿瘤如恶性肿瘤的受试者。

[0568] 在一些实施方案中，所述受试者包括但不限于早期癌症患者、中期癌症患者和晚期癌症患者，任选地，中期或晚期癌症患者。当在本文中使用时，术语“早期癌”包括原位癌和 I 期癌，术语“中期癌”包括 II 期和 III 期癌，以及术语“晚期癌”指在原发部位有广泛浸润，或有远地器官的转移性癌，如 IV 期癌。在一些实施方案中，所述受试者包括但不限于 0、I、II、III 或 IV 期癌症患者，任选地，III 或 IV 期癌症患者；以及所述肿瘤如恶性肿瘤已转移的受试者包括但不限于肿瘤如恶性肿瘤已原处或远处转移的受试者。当提及肿瘤或癌为 0、I、II、III 或 IV 期时，应当理解是指用本领域公知的 TNM 分期法（参见 AJCC 癌症分期手册（第六版），F.L. 格林尼等主编，辽宁科学技术出版社，2005 年 8 月）进行的肿瘤或癌的分期。举例来说，在 TNM 分期中，0 期：$T_0N_0M_0$；Ia 期：$T_1N_0M_0$；Ib 期：$T_2N_0M_0$；IIa 期：$T_1N_1M_0$；IIb 期：$T_2N_1M_0$ 和 $T_3N_0M_0$；IIIa 期：$T_3N_1M_0$ 和 $T_{1-3}N_2M_0$；IIIb 期：任何 T、N_3 和 M_0，T_4、任何 N 和 M_0；IV 期：任何 T、任何 N 和 M_1。在一些实施方案中，所述受试者是中期、晚期或 III 或 IV 期癌症患者。在一些实施方案中，所述受试者是晚期或 III 或 IV 期癌症患者。

[0569] 在某些实施方案中，所述带有恶性胸腔积液、恶性腹腔积液和 / 或恶性心包积液的受试者包括因癌症如晚期或 III 或 IV 期癌症引起的恶性胸腔积液、恶性腹腔积液和 / 或恶性心包积液的受试者。在一个实施方案中，上述癌症为肺癌。

[0570] 在一些实施方案中，所述受试者具有的肿瘤可以是肺部肿瘤，例如肺癌。在一个实施方案中，所述受试者可以是肺癌患者，例如具有手术无法切除的肺癌的患者，中期和晚期肺癌患者，0、I 或 II 期肺癌患者，或 III 或 IV 期肺癌患者，已转移的肺癌患者或带有恶性胸腔积液、恶性腹腔积液和 / 或恶性心包积液的肺癌患者。在一个实施方案中，所述肺癌患者包括但不限于小细胞肺癌患者和非小细胞肺癌患者。

[0571] C. 联合疗法

[0572] 在本发明方法的一些实施方案中，可在施用本发明的重组干扰素之前、同时和 / 或之后向受试者施用其他治疗方法或治疗药物。在一些实施方案中，所述治疗方法任选地为抗癌疗法，以及所述治疗药物任选地为抗肿瘤药物。当在本文中使用时，术语“施用”或

“给予”或“给药”指给予物质以达到治疗目的。当在本文中使用时，术语“联合疗法”指在治疗期的过程中给予受试者两种或更多种治疗手段，例如给予本发明的重组干扰素和额外的治疗手段。该额外的治疗手段可在给予本发明的重组干扰素的之前、同时和 / 或之后给予受试者。当在本文中使用时，术语“抗癌疗法”指在癌症治疗中有用的疗法。

[0573] 在一些实施方案中，所述其他抗癌疗法包括但不限于化学治疗、放射治疗、手术治疗、介入治疗、生物治疗、基因治疗、消融治疗、免疫治疗、靶向治疗、中药治疗和它们的任意组合。所述其他抗癌疗法对于本领域的普通技术人员而言是可以容易确定的。在一些实施方案中，所述其他抗癌疗法任选地为化学治疗、放射治疗、手术治疗、靶向治疗和 / 或生物治疗。在一些实施方案中，所述其他抗癌疗法任选地为化学治疗和 / 或放射治疗。

[0574] 当在本文中使用时，术语“化学治疗”指一种影响细胞生长和细胞分裂的药物疗法，即其充当一种细胞增殖抑制药，或其诱导细胞死亡（细胞凋亡）。由于癌细胞不可控的生长和分裂，因此与正常细胞相比，化学治疗对它们应当更有效。在特定的实施方案中，化学治疗包括动脉灌注化疗以及以栓塞的形式进行化疗。在特定的实施方案中，对于不同的癌症，化学治疗可为针对所述癌症常用的一线化学治疗。例如，对于治疗肺癌，这样的一线化学治疗所使用的化学治疗剂包括但不限于铂类化合物，例如顺铂。

[0575] 可用于本发明癌症化学治疗中的化学治疗剂包括但不限于烷化剂类，例如氮芥类，包括但不限于盐酸氮芥、苯丁酸氮芥、苯丙氨酸氮芥、萘氮芥、雌氮芥、环磷酰胺、异环磷酰胺、氮芥、盐酸氧氮芥、美法仑、新氮芥、苯芥胆甾醇、泼尼莫司汀、曲磷胺和乌拉莫司汀；乙撑亚胺类和甲基蜜胺类，包括但不限于曲他胺、噻替呱、MST-16、六甲蜜胺、三乙撑蜜胺、三乙撑磷酰胺、三乙撑硫代磷酰胺和三羟甲蜜胺；磺酸烷基酯类，包括但不限于白消安、英丙舒凡和呱泊舒凡；亚硝脲类，包括但不限于卡莫司汀、司莫司汀、链脲霉素、氯脲菌素、福莫司汀、洛莫司汀、尼莫司汀和雷莫司汀；抗代谢物类，例如抗叶酸抗代谢物，包括但不限于甲氨喋呤 (MTX)、三甲氧喹唑啉、二甲叶酸、蝶罗呤、三甲曲沙、甲酰四氢叶酸和培美曲塞（力比泰）；嘧啶类抗代谢物，包括 5- 氟尿嘧啶 (5-FU)、氟尿苷、呋喃氟尿嘧啶（替加氟）、卡培他滨（希罗达）、安西他滨、卡莫氟、双脱氧尿苷、脱氧氟尿苷和依诺他滨；胞苷类抗代谢物，包括但不限于阿糖胞苷、氮胞苷、安西他滨和吉西他滨（健择）；嘌呤类抗代谢物，包括但不限于 6- 巯嘌呤、6- 硫鸟嘌呤、脱氧考福霉素、氟达拉滨和硫咪嘌呤；植物来源的抗肿瘤药物，例如长春花生物碱类，包括但不限于长春碱、长春地辛、长春新碱、长春酰胺、长春瑞滨、硫酸长春碱、硫酸长春新碱、酒石酸长春瑞滨和长春氟宁；三尖杉酯碱及高三尖杉酯碱；靛玉红及其类似物，包括但不限于异靛甲 (N-methyllisoinidog-tin)；表鬼臼毒类药物，包括但不限于替尼泊苷 (VM-26) 和依托泊苷 (VP-16)；喜树及喜树碱类化合物，包括但不限于喜树碱、托泊替康 (TPT) 和伊立替康 (CPT-11)；紫杉醇类化合物，包括但不限于紫杉醇（注射用紫杉醇脂质体）、多西苷（多西他赛注射液、泰索帝、紫杉特尔）和脂质体紫杉醇；抗肿瘤抗生素类，例如蒽环类，包括但不限于柔红霉素、阿霉素、阿克拉霉素 A、表柔比星、米托蒽醌和麻西罗霉素；糖肽类，包括但不限于博来霉素、泰来霉素、利来霉素 (Leroymycin)、培来霉素和平阳霉素；放线菌素类，包括但不限于放线菌素 C、放线菌素 D、橙色菌素和更生霉素；糖苷类，包括但不限于光辉霉素、色霉素 A3 和橄榄霉素；丝裂霉素类，包括但不限于丝裂霉素 C；以及链脲霉素；铂类化合物，包括但不限于螺铂、顺铂、卡铂、奈达铂、奥利沙铂、洛铂、JM-216、环铂、SKI2053R、L-NDDP 和 TRK-710；维甲类化合物，包括

但不限于全反式维甲酸和 13- 顺式维甲酸；激素类，例如雄激素类，包括但不限于丙酸睾酮、甲睾酮、氟甲睾酮、苯丙酸诺龙、卡鲁睾酮、丙酸甲雄烷醇酮、环硫雄醇、美雄烷和睾内酯；抗雄激素类，包括但不限于氟他胺、尼鲁米特、比卡鲁胺（康士得）、戈舍瑞林、亮丙瑞林和色普龙；雌激素类，包括但不限于己烯雌酚、雌二醇和炔雌醇；雌激素受体阻断剂以及抑制雌激素合成的药物，包括但不限于他莫昔芬、托瑞米芬、阿那曲唑和依西美坦；孕酮类，包括但不限于甲孕酮和醋酸甲地孕酮；促性腺激素释放素同类物，包括但不限于利普安、戈那瑞林、丁丝瑞林和萘丙瑞林；肾上腺皮质激素，包括但不限于强的松（泼尼松）和地塞米松 (DXM)；肾上腺皮质选择性损伤剂，包括但不限于米托坦；甲状腺激素类，包括但不限于甲状腺素；以及杂类，包括但不限于卡介苗 (BCG)、门冬酰胺酶、羟基脲、甲基苄肼和达卡巴嗪 (DTIC)；以及任何上述物质的药学上可接受的盐、酸或衍生物。

[0576] 在一些实施方案中，在本发明中可用于治疗癌症如肺癌的化学治疗方案包括但不限于：CMC 方案（环己亚硝脲、环磷酰胺和甲氨喋呤）、EP 方案（依托泊苷和顺铂）、IVP 方案（异环磷酰胺、长春地辛和顺铂）、ICE 方案（异环磷酰胺、顺铂和依托泊苷）、NIP 方案（诺维本、异环磷酰胺和顺铂）、紫杉醇 +DDP/CBP 方案（紫杉醇和顺铂 / 卡铂）、多西他赛 +DDP/CBP 方案（多西他赛和顺铂 / 卡铂）、托泊替康 +DDP 方案（托泊替康和顺铂）、IP 方案（伊立替康和卡铂）、MVP 方案（丝裂霉素、长春地辛和顺铂）、NP 方案（诺维本和顺铂）、多西紫杉醇方案、GEM+DDP（即 GP 方案）方案或 GEM+CBP 方案（健择和顺铂 / 卡铂）等（参见，肺部肿瘤学，2008 年 9 月第 1 版，廖美琳编，上海科学技术出版社，第 323-326 页）。

[0577] 此外，其他在本发明中可用于治疗肿瘤如癌症的化学治疗方案包括但不限于：FOLFOX 方案（参见，恶性肿瘤最新化疗进展，2009 年 7 月出版，郑翠苹主编，北京：人民军医出版社，第 1031 页）、DP 方案（参见，恶性肿瘤最新化疗进展，2009 年 7 月出版，郑翠苹主编，北京：人民军医出版社，第 232 页）、CHOPE 方案、MTX 方案、GCE 方案、ESAP 方案、CMOP 方案、CHOP 方案（参见，实用抗肿瘤药物治疗学，2002 年出版，刘新春等主编，北京：人民卫生出版社，第 1031 页）、博来霉素 +CHOP+ 甲氨喋呤方案、GP+ 恩度方案、GP-T2 方案、TP 方案（参见，实用抗肿瘤药物治疗学，2002 年出版，刘新春等主编，北京：人民卫生出版社，第 668、744 页）、顺铂 + 丝裂霉素方案等。

[0578] 当在本文中使用时，术语“放射治疗”指使用高能辐射来治疗肿瘤例如癌症。放射治疗包括外部给予的辐射，例如来自线性加速器的外放射治疗，以及近距放射治疗，其中放射源被放置以接近身体表面或放置在体腔内。在本发明的放射治疗中，放射源包括但不限于放射性核素产生的 α、β、γ 射线，各类加速器产生的电子束、质子束、中子束、负 π 介子束以及其他重粒子束等。所述放射性核素包括但不限于铯 -137（^{137}Cs）、钴 -60（^{60}Co）、碘 -131（^{131}I）、碘 -125（^{125}I）、磷 -32（^{32}P）、金 -198（^{198}Au）、铱 -192（^{192}Ir）、钇 -90（^{90}Y）、铼 -186（^{186}Re）和钯 -109（^{109}Pd）。这些放射源可在体外和 / 或体内进行照射。

[0579] 应当理解有许多本领域已知的方法可用来确定放射治疗的积累和持续时间。典型的放射治疗是作为一次施用提供的且通常的剂量为约 1 戈瑞 / 天 - 约 200 戈瑞 / 天，例如约 2 戈瑞 / 天 - 约 150 戈瑞 / 天、约 5 戈瑞 / 天 - 约 100 戈瑞 / 天、约 10 戈瑞 / 天 - 约 70 戈瑞 / 天、约 10 戈瑞 / 天 - 约 50 戈瑞 / 天等。在一个实施方案中，用于本发明的放射治疗包括但不限于二维的常规放射治疗、三维适形放射治疗 (3D-CRT)、质子治疗、近距离放射治疗、调强放射治疗 (IMRT)、立体定向放射治疗 (SRT)、呼吸门控四维放射治疗 (4DRT)、以及

伽玛刀治疗，例如全身伽玛刀和头部伽玛刀治疗。

[0580] 当在本文中使用时，术语“靶向治疗”指一种目的在于识别特定靶标分子的疗法，所述靶标分子可例如在肿瘤发生或肿瘤增殖或细胞修复中起作用。这样的识别可例如导致靶向治疗与所述靶标分子的结合，可增强或降低该靶标分子的活性。用于这样的靶向治疗的药物包括抗体，特别是单克隆抗体，以及小分子药物。潜在的靶标包括例如EGFR受体，其在血管发生中起重要作用；VEGFA配体，同样其对于血管发生是重要的；或PARP1，其对于细胞修复起重要作用，因为对其的抑制可使得癌基因缺陷的肿瘤对化学治疗更加敏感。

[0581] 在本发明的靶向治疗中，靶向药物包括但不限于：抗血管发生药、激酶抑制剂、pan激酶抑制剂或生长因子抑制剂。抗血管发生药包括但不限于：EGF抑制剂、EGFR抑制剂、VEGF抑制剂、VEGFR抑制剂、TIE2抑制剂、IGF1R抑制剂、COX-II（环加氧酶II）抑制剂、MMP-2（基质金属蛋白酶2）抑制剂和MMP-9（基质金属蛋白酶9）抑制剂。可用于此的靶向药物包括但不限于如下的至少一种：吉非替尼（易瑞沙）、厄洛替尼（特罗凯，TARCEVA®）、拉帕替尼（GSK572016）、瓦他拉尼（PTK787）、伊马替尼（格列卫，GLEEVEC®）、达沙替尼（Sprycel）、舒尼替尼（索坦，SUTENT®）、尼洛替尼（Tasigna）、司马沙尼（SU5416）、帕唑帕尼（GW-786034）、西妥昔单抗（爱必妥，IMC-C225）、帕木单抗（Vectibix）、曲妥单抗（赫赛汀）、重组人血管内皮抑制素（恩度）、索拉非尼（NEXAVAR®）、贝伐单抗（阿瓦斯丁）、阿仑珠单抗（Campath）、吉妥珠单抗（Mylotarg）、替伊莫单抗（Zevalin）、托西莫单抗（Bexxar）、Affinitak（LY90003/ISI3521）、法尼基转移酶抑制剂、Tipifanib、Lonafanib、BMS214-662、R115777（Zarnestra）、SCH-66336（Sarasar）、L-778，123、ZD6474（ZACTIMA®）、AZD2171、OSI-7904、ZD6126（ANG453）、ZD1839、AMG706、AG013736、MLN-518、CEP-701、PKC-412、万珂（VELCADE®）、XL880和CHIR-265。在某些实施方案中，用于本发明的癌症例如肺癌的靶向治疗的靶向药物包括但不限于吉非替尼（易瑞沙）、厄洛替尼（特罗凯，TARCEVA®）和/或重组人血管内皮抑制素（恩度）。

[0582] 对于上述化学治疗、放射治疗和/或靶向治疗中所使用的药物和/或放射源的剂量和持续时间，可由熟练医师根据经验以及患者的实际情况例如年龄、体重、一般健康状况、性别、饮食、施用时间、药物相互作用和病状的严重性来容易地确定。

[0583] 当在本文中使用时，术语“手术治疗”是一种侵入性的癌症疗法，目的在于物理除去癌细胞。手术治疗包括例如肿瘤切除术和淋巴结清扫术。

[0584] 当在本文中使用时，术语“基因治疗”指通过病毒或非病毒载体经离体或体内递送包含重组遗传物质的组合物以治疗或预防疾病或医学病症，例如癌症。

[0585] 当在本文中使用时，术语“消融治疗”指通常所知的组织破坏方法，例如高温消融如射频、微波和激光消融，低温消融如氩氦刀冷冻治疗，化学消融，放射性消融等。

[0586] 当在本文中使用时，术语“免疫治疗”指一种治疗策略，其用于调节免疫系统以达到针对特定疾病如癌症的预防和/或治疗目标。例如接种疫苗是一种免疫治疗的方式。可用于本发明免疫治疗中的疫苗包括但不限于：ALLOVECTIN®疫苗、LEUVECTIN®疫苗和VAXID®疫苗等。

[0587] 当在本文中使用时，术语“介入治疗”指在不开刀暴露病灶的情况下，在皮肤上作微小通道，或经人体原有的管道，在影像设备（例如数字血管造影机、透视机、CT、MR、B 超）的引导下对病灶局部进行治疗的创伤最小的治疗方法。当用于治疗肿瘤时，所述介入治疗包括但不限于经导管动脉栓塞化疗，动脉灌注化疗，高温消融如射频、微波和激光消融，低温消融如氩氦刀冷冻治疗，化学消融，放射性消融，基因药物动脉灌注和支架植入术等。

[0588] 当在本文中使用时，术语“生物治疗”指一切应用现代生物技术及其产品（小分子化合物、多肽、多糖、蛋白质、细胞、组织、基因、RNA 等）进行治疗的方法。当用于治疗肿瘤时，所述生物治疗能直接或间接地介导抑瘤和杀瘤效应。用于治疗肿瘤的生物治疗包括但不限于非特异免疫刺激剂以及生物反应调节剂 (BRM) 的应用、肿瘤细胞因子与免疫效应细胞治疗如 NK 细胞抗肿瘤治疗、生物支持治疗、组织与细胞移植治疗等。

[0589] 当在本文中使用时，术语“中药治疗”指一切利用中国传统医学以及在中医理论指导下的药物所进行的疾病例如癌症的治疗方法。

[0590] 此外，还可与本发明的重组干扰素一起施用的其他抗肿瘤药物包括但不限于：在生物治疗中所使用的生物制剂，例如：肿瘤坏死因子包括 TNF-α 或 TNF-β 等；干扰素例如干扰素 α 包括干扰素 α-1a、干扰素 α-1b、干扰素 α-2a、干扰素 α-2b 等，干扰素 β 包括干扰素 β-1a、干扰素 β-1b 等，干扰素 γ 包括干扰素 γ-1b 等，共有干扰素如干扰素 α-con1，长效干扰素如 PEG 化干扰素、干扰素与白蛋白的融合蛋白、干扰素与 IgGFc 片段的融合蛋白；集落刺激因子 (CSF) 例如巨噬细胞 - 集落刺激因子 (M-CSF)、粒细胞 - 巨噬细胞 - 集落刺激因子 (GM-CSF) 和粒细胞集落刺激因子 (G-CSF)；白细胞介素 (IL) 例如 IL-1、IL-1α、IL-2、IL-3、IL-4、IL-5、IL-6、IL-7、IL-8、IL-9、IL-10、IL-11、IL-12 和胸腺肽；反义寡核苷酸，尤其是抑制在粘附细胞增殖中涉及的信号通路中的基因（例如，诸如 PKC-α、Raf 和 H-Ras) 的表达的那些反义寡核苷酸；以及 siRNA 等。

[0591] D. 药物组合物和给药途径

[0592] 本发明的重组干扰素可掺入药物组合物中给予所述受试者。通常，药物组合物包含本发明的重组干扰素和药学上可接受的载体。所述的“药学上可接受的载体”在此包括生理学上可相容的任何一种和全部的溶剂、分散介质、包衣、抗细菌和抗真菌剂，等渗剂和吸收延迟剂等。药学上可接受的载体的实例包括一种或多种水、盐水、磷酸盐缓冲盐水、葡萄糖、甘油、乙醇等，以及它们的组合。在多数情况下，在组合物中优选包括等渗剂，例如糖类，多元醇如甘露糖醇、山梨糖醇或氯化钠。药学上可接受的载体可进一步包括少量的增加本发明的重组干扰素的贮存期限或有效性的辅助性物质，例如润湿剂或乳化剂、防腐剂或缓冲剂。

[0593] 本发明的药物组合物可以多种剂型存在。这些包括例如液体、半固体和固体剂型，例如液体溶液（如可注射的和可输注的溶液）、分散液或混悬剂、水溶液、片剂、胶囊、口服液、贴剂、喷雾剂、栓剂、粉剂和冻干粉剂。适合使用的剂型取决于预期的给药方式以及治疗应用。典型地，药物组合物以可注射的或可灌注的溶液、冻干粉剂、喷雾剂和水溶液的形式存在。

[0594] 所述药物组合物可以通过药学领域中任何公知的方法制备；例如参见 Gilman 等，（编）(1990)，The Pharmacological Bases of Therapeutics，第 8 版，Pergamon Press；A.Gennaro（编），Remington’s Pharmaceutical Sciences，第 18 版，(1990)，

Mack Publishing Co., Easton, Pennsylvania. ;Avis 等, (编) (1993) Pharmaceutical Dosage Forms :Parenteral Medications Dekke, New York ;Lieberman 等, (编) (1990) Pharmaceutical Dosage Forms :Tablets Dekker, New York ; 和 Lieberman 等, (编) (1990), Pharmaceutical Dosage Forms :Disperse Systems Dekker, New York。

[0595] 本发明的重组干扰素可通过如下至少一种途径施用于受试者 :全身给药、表面 (topical) 给药和局部 (local) 给药。当在本文中使用时, 术语“全身给药”指以这样的一种方式给予组合物或药物, 该方式使得所述组合物或药物导入受试者循环系统中, 例如使给予的组合物或药物扩散或分布到身体各处。全身给药的实例包括但不限于 :静脉注射、动脉注射、肌肉注射、皮下注射、淋巴管注射、经口给药等。

[0596] 当在本文中使用时, 术语“局部给药 (local administration)”指给予组合物或药物以进入有限的、或局限的解剖学空间中。局部给药的实例包括但不限于 :瘤内、淋巴结内、胸腔内、腹腔内等。

[0597] 当在本文中使用时, 术语“表面给药 (topical administration)”指在皮肤表面或粘膜表面施用药物或组合物。例如, 表面给药包括但不限于将药物或组合物喷在受试者的皮肤上。

[0598] 在一些实施方案中, 可通过如下至少一种给药途径向受试者施用本发明的重组干扰素, 所述给药途径包括但不限于经口、直肠、舌下、静脉内、动脉内、肌肉、皮下、骨内、皮内、关节内、腹膜内、鞘内、脑内、阴道、经皮、透皮、表皮、粘膜、经眼、经肺、经鼻、腹腔、胸腔、心室内、心包、吸入、瘤内、子宫、浸润和膀胱内给药。在一些实施方案中, 通过注射施用本发明的重组干扰素, 例如皮下注射、肌肉注射、静脉注射、动脉注射、脑内注射、腹膜内注射和 / 或瘤内注射。在一些实施方案中, 可通过吸入如经肺吸入和经鼻吸入施用本发明的重组干扰素。在一些实施方案中, 所述吸入可以是干粉吸入和 / 或雾化吸入。在一些实施方案中, 通过灌注施用本发明的重组干扰素, 例如胸腔灌注、腹腔灌注、心包灌注、子宫灌注和 / 或膀胱内灌注。在一些实施方案中, 通过喷雾向患处 (如皮肤和粘膜的表面、浅表淋巴结和 / 或皮下组织) 施用本发明的重组干扰素, 例如经皮、表皮、透皮和 / 或粘膜喷雾给药。在一些实施方案中, 所述浸润给药包括经肺浸润给药、经皮浸润给药、表皮浸润给药、透皮浸润给药、粘膜浸润给药、胸腔浸润给药、腹腔浸润给药、子宫浸润给药、阴道浸润给药、膀胱浸润给药、心包浸润给药等。

[0599] 注射 / 灌注给药

[0600] 适合于注射 / 灌注的药物组合物包括无菌水溶液 (在可溶于水的情况下) 或分散剂以及用于临时制备无菌可注射溶液或分散剂的无菌粉剂。在所有的情况下, 所述组合物必须是无菌的, 且应当是流动的以致利用注射器给药。这样的组合物在制造和贮藏期间应当是稳定的, 并且必须保存以免受诸如的细菌和真菌的微生物污染。载体可以是包含例如水、乙醇、多元醇 (如甘油、丙二醇和液体聚乙二醇) 及合适的混合物的溶剂或分散介质。各种抗细菌剂和抗真菌剂 ;例如对羟基苯甲酸酯类、氯代丁醇、苯酚、抗坏血酸和硫柳汞。等渗剂 ;例如糖类、多元醇如甘露糖醇、山梨糖醇以及氯化钠可包括在组合物中。能延迟吸收的组合物包括诸如单硬脂酸铝和明胶的试剂。

[0601] 可通过将以需要的量溶解在合适的溶剂中的本发明的重组干扰素与根据需要的一种成分或成分组合相混合, 继之以灭菌制备无菌可注射 / 灌注溶液。一般而言, 通过将本

发明的重组干扰素掺入含有基础分散介质以及其他必需成分的无菌赋形物中制备分散剂。用于制备无菌可注射 / 灌注溶液的无菌粉末的制备方法包括由无菌溶液生产含有活性成分以及任何期望成分的粉末的真空干燥和冷冻干燥。

[0602] 吸入给药

[0603] 可通过任何多种本领域中已知的用于通过吸入给药治疗药物的吸入装置递送本发明的重组干扰素。这些装置包括计量吸入器、雾化器、干粉发生器、喷雾器等。其他适合于本发明的重组干扰素吸入给药的装置也为本领域所已知。

[0604] 计量吸入器如Ventolin®计量吸入器在吸入期间通常使用了抛射剂并需要启动(参见如WO 94/16970，WO 98/35888)。干粉吸入器如Turbuhaler™(Astra)、Rotahaler®(Glaxo)、Diskus® (Glaxo)、Spiros™吸入器(Dura)、Inhale Therapeutics销售的装置和Spinhaler®干粉吸入器(Fisons)，使用了呼吸驱动的混合粉末(US 4668218 Astra，EP 237507 Astra，WO 97/25086 Glaxo，WO 94/08552Dura，US 5458135 Inhale，WO 94/06498 Fisons)。雾化器如AERx™雾化器(Aradigm)、Ultravent®雾化器(Mallinckrodt)、Acorn II®雾化器(Marquest Medical Products)(US 5404871 Aradigm，WO 97/22376)和AP-100200型喷雾吸入器(台湾雅博股份有限公司)。由溶液产生了气雾剂，而计量吸入器、干粉吸入器等则产生了微粒气雾剂。

[0605] 任选地，通过雾化器递送本发明的重组干扰素。对于施用本发明的重组干扰素，吸入装置有着几种所需要的特性。例如，通过吸入装置的递送优势在于可靠、可重复以及精确。吸入装置能任选地递送小颗粒或气雾剂，例如小于约10μm，例如约0.5μm-约5μm，非常适合呼吸。

[0606] 喷雾给药

[0607] 可通过加压本发明的重组干扰素的混悬液或溶液通过喷嘴产生包含所述重组干扰素的喷雾剂。可选择喷嘴大小和外形、所施加的压力以及液体进料速度以获得期望的输出量和粒度。可例如通过与毛细管或喷嘴进料管结合的电场产生电喷雾剂。有利地，通过喷雾器递送的颗粒具有小于约10μm的粒度，任选地，在约0.5μm-约5μm范围内。

[0608] 适用于喷雾器的本发明的重组干扰素的配方通常包括在约0.01mg-约5mg、例如约0.03mg-约2mg、约0.05mg-约1mg、约0.1mg-约0.5mg的所述重组干扰素 / 毫升溶液。该配方可包括赋形剂或用于稳定本发明的重组干扰素的试剂，例如缓冲剂、还原剂、填充蛋白或碳水化合物。用于配制所述重组干扰素的填充蛋白包括白蛋白、鱼精蛋白等。用于配制所述重组干扰素的代表性的碳水化合物包括蔗糖、甘露糖醇、乳糖、海藻糖、葡萄糖等。本发明的重组干扰素的配方还可包括表面活性剂，其能减少或阻止由于在气雾剂形成中溶液雾化所引起的表面诱导的所述重组干扰素聚集。

[0609] E. 给药剂量及给药方案

[0610] 可向受试者如癌症患者施用有效量的本发明的重组干扰素，根据本发明的方法，这样的有效量可以是治疗有效量或预防有效量。当在本文中使用时，术语“有效量”指一种在剂量上以及必要的一段时间内有效实现期望治疗或预防结果的量。本发明的重组干扰素的治疗有效量可随诸如疾病状态、年龄、性别和个体重量以及所述重组干扰素引发个体中

期望应答的能力的因素而改变。治疗有效量还是一种其中所述重组干扰素的任何毒效应或有害效果为治疗有益效果所超过的量。“预防有效量”指一种在剂量上以及必要的一段时间内有效实现期望预防结果的量。通常但非必定地，由于在疾病早期之前或在疾病早期在受试者中使用预防剂量，因此预防有效量应小于治疗有效量。

[0611] 本发明的重组干扰素可以不同的单次剂量施用于受试者如癌症患者。举例来说，本发明的重组干扰素的单次剂量可为约 2 μg- 约 2000 μg，任选地，约 4 μg- 约 1500 μg，更任选地，约 9 μg- 约 1000 μg。当在本文中使用时，术语“单次剂量”指当施用一次时，自身或与其他单次剂量累积产生治疗或预防效果的药物的量。这样的施用包括了全身给药、局部给药和 / 或表面给药。

[0612] 当通过注射给药（如皮下注射、肌肉注射、静脉注射、动脉注射、脑内注射和 / 或腹膜内注射）全身施用本发明的重组干扰素时，所述重组干扰素的单次剂量可为约 4 μg- 约 70 μg，任选地，约 4 μg- 约 50 μg，更任选地，约 4 μg- 约 30 μg，其中这样的单次剂量可为约 4 μg、约 4.5 μg、约 5 μg、约 6 μg、约 7 μg、约 8 μg、约 9 μg、约 10 μg、约 11 μg、约 12 μg、约 13 μg、约 13.5 μg、约 14 μg、约 15 μg、约 16 μg、约 17 μg、约 18 μg、约 19 μg、约 20 μg、约 21 μg、约 22 μg、约 23 μg、约 24 μg、约 25 μg、约 25.5 μg、约 26 μg、约 27 μg、约 28 μg、约 29 μg、约 30 μg、约 31 μg、约 32 μg、约 33 μg、约 34 μg、约 35 μg、约 36 μg、约 37 μg、约 38 μg、约 39 μg、约 40 μg、约 41 μg、约 42 μg、约 43 μg、约 44 μg、约 45 μg、约 46 μg、约 47 μg、约 48 μg、约 49 μg、约 50 μg、约 51 μg、约 52 μg、约 53 μg、约 54 μg、约 55 μg、约 56 μg、约 57 μg、约 58 μg、约 59 μg、约 60 μg、约 61 μg、约 62 μg、约 63 μg、约 64 μg、约 65 μg、约 66 μg、约 67 μg、约 68 μg、约 69 μg、以及约 70 μg。

[0613] 当通过注射给药（如瘤内注射）局部施用本发明的重组干扰素时，所述重组干扰素的单次剂量可为约 60 μg- 约 600 μg，任选地，约 60 μg- 约 500 μg，更任选地，约 80 μg- 约 400 μg，还更任选地，约 100 μg- 约 250 μg，其中这样的单次剂量可为约 60 μg、约 70 μg、约 80 μg、约 90 μg、约 100 μg、约 110 μg、约 120 μg、约 130 μg、约 140 μg、约 150 μg、约 160 μg、约 170 μg、约 180 μg、约 190 μg、约 200 μg、约 210 μg、约 220 μg、约 230 μg、约 240 μg、约 250 μg、约 260 μg、约 270 μg、约 280 μg、约 290 μg、约 300 μg、约 310 μg、约 320 μg、约 330 μg、约 340 μg、约 350 μg、约 360 μg、约 370 μg、约 380 μg、约 390 μg、约 400 μg、约 410 μg、约 420 μg、约 430 μg、约 440 μg、约 450 μg、约 460 μg、约 470 μg、约 480 μg、约 490 μg、约 500 μg、约 510 μg、约 520 μg、约 530 μg、约 540 μg、约 550 μg、约 560 μg、约 570 μg、约 580 μg、约 590 μg、以及约 600 μg。

[0614] 当通过吸入给药（如经肺吸入和经鼻吸入，包括干粉吸入和雾化吸入）施用本发明的重组干扰素时，所述重组干扰素的单次剂量可为约 100 μg- 约 2000 μg，任选地，约 100 μg- 约 1500 μg，更任选地，约 150 μg- 约 800 μg，还更任选地，约 200 μg- 约 600 μg，其中这样的单次剂量可为约 100 μg、约 110 μg、约 120 μg、约 130 μg、约 140 μg、约 150 μg、约 160 μg、约 170 μg、约 180 μg、约 190 μg、约 200 μg、约 210 μg、约 220 μg、约 230 μg、约 240 μg、约 250 μg、约 260 μg、约 270 μg、约 280 μg、约 290 μg、约 300 μg、约 310 μg、约 320 μg、约 330 μg、约 340 μg、约 350 μg、约 360 μg、约 370 μg、约 380 μg、约 390 μg、约 400 μg、约 410 μg、约 420 μg、约 430 μg、约 440 μg、约 450 μg、约 460 μg、约 470 μg、约 480 μg、约 490 μg、约 500 μg、约 510 μg、约 520 μg、约 530 μg、约 540 μg、约 550 μg、

约 560 μg、约 570 μg、约 580 μg、约 590 μg、约 600 μg、约 610 μg、约 620 μg、约 630 μg、约 640 μg、约 650 μg、约 660 μg、约 670 μg、约 680 μg、约 690 μg、约 700 μg、约 710 μg、约 720 μg、约 730 μg、约 740 μg、约 750 μg、约 760 μg、约 770 μg、约 780 μg、约 790 μg、约 800 μg、约 810 μg、约 820 μg、约 830 μg、约 840 μg、约 850 μg、约 860 μg、约 870 μg、约 880 μg、约 890 μg、约 900 μg、约 910 μg、约 920 μg、约 930 μg、约 940 μg、约 950 μg、约 960 μg、约 970 μg、约 980 μg、约 990 μg、约 1000 μg、约 1100 μg、约 1200 μg、约 1300 μg、约 1400 μg、约 1500 μg、约 1600 μg、约 1700 μg、约 1800 μg、约 1900 μg、约 2000 μg。

[0615] 当通过灌注或浸润给药（如胸腔灌注、腹腔灌注、心包灌注、子宫灌注、膀胱内灌注）施用本发明的重组干扰素时，所述重组干扰素的单次剂量可为约 30 μg- 约 2000 μg，任选地，约 100 μg- 约 1500 μg，更任选地，约 150 μg- 约 1000 μg，还任选地，约 200 μg- 约 800 μg，还更任选地，约 200 μg- 约 400 μg，其中这样的单次剂量可为约 30 μg、约 40 μg、约 50 μg、约 60 μg、约 70 μg、约 80 μg、约 90 μg、约 100 μg、约 110 μg、约 120 μg、约 130 μg、约 140 μg、约 150 μg、约 160 μg、约 170 μg、约 180 μg、约 190 μg、约 200 μg、约 210 μg、约 220 μg、约 230 μg、约 240 μg、约 250 μg、约 260 μg、约 270 μg、约 280 μg、约 290 μg、约 300 μg、约 310 μg、约 320 μg、约 330 μg、约 340 μg、约 350 μg、约 360 μg、约 370 μg、约 380 μg、约 390 μg、约 400 μg、约 410 μg、约 420 μg、约 430 μg、约 440 μg、约 450 μg、约 460 μg、约 470 μg、约 480 μg、约 490 μg、约 500 μg、约 510 μg、约 520 μg、约 530 μg、约 540 μg、约 550 μg、约 560 μg、约 570 μg、约 580 μg、约 590 μg、约 600 μg、约 610 μg、约 620 μg、约 630 μg、约 640 μg、约 650 μg、约 660 μg、约 670 μg、约 680 μg、约 690 μg、约 700 μg、约 710 μg、约 720 μg、约 730 μg、约 740 μg、约 750 μg、约 760 μg、约 770 μg、约 780 μg、约 790 μg、约 800 μg、约 810 μg、约 820 μg、约 830 μg、约 840 μg、约 850 μg、约 860 μg、约 870 μg、约 880 μg、约 890 μg、约 900 μg、约 910 μg、约 920 μg、约 930 μg、约 940 μg、约 950 μg、约 960 μg、约 970 μg、约 980 μg、约 990 μg、约 1000 μg、约 1100 μg、约 1200 μg、约 1300 μg、约 1400 μg、约 1500 μg、约 1600 μg、约 1700 μg、约 1800 μg、约 1900 μg、以及约 2000 μg。

[0616] 当通过喷雾给药向患处（如皮肤和粘膜的表面、浅表淋巴结和 / 或皮下组织）（如经皮喷雾、表皮喷雾、透皮喷雾、粘膜喷雾）施用本发明的重组干扰素时，所述重组干扰素的单次剂量可为约 6 μg- 约 100 μg，任选地，约 10 μg- 约 40 μg，更任选地，约 20 μg- 约 40 μg，其中这样的单次剂量可为约 6 μg、约 7 μg、约 8 μg、约 9 μg、约 10 μg、约 11 μg、约 12 μg、约 13 μg、约 14 μg、约 15 μg、约 16 μg、约 17 μg、约 18 μg、约 19 μg、约 20 μg、约 21 μg、约 22 μg、约 23 μg、约 24 μg、约 25 μg、约 26 μg、约 27 μg、约 28 μg、约 29 μg、约 30 μg、约 31 μg、约 32 μg、约 33 μg、约 34 μg、约 35 μg、约 36 μg、约 37 μg、约 38 μg、约 39 μg、约 40 μg、约 41 μg、约 42 μg、约 43 μg、约 44 μg、约 45 μg、约 46 μg、约 47 μg、约 48 μg、约 49 μg、约 50 μg、约 51 μg、约 52 μg、约 53 μg、约 54 μg、约 55 μg、约 56 μg、约 57 μg、约 58 μg、约 59 μg、约 60 μg、约 61 μg、约 62 μg、约 63 μg、约 64 μg、约 65 μg、约 66 μg、约 67 μg、约 68 μg、约 69 μg、约 70 μg、约 71 μg、约 72 μg、约 73 μg、约 74 μg、约 75 μg、约 76 μg、约 77 μg、约 78 μg、约 79 μg、约 80 μg、约 81 μg、约 82 μg、约 83 μg、约 84 μg、约 85 μg、约 86 μg、约 87 μg、约 88 μg、约 89 μg、约 90 μg、约 91 μg、约 92 μg、约 93 μg、约 94 μg、约 95 μg、约 96 μg、约 97 μg、约 98 μg、约 99 μg、以及约 100 μg。

[0617] 本发明的重组干扰素可以不同的给药方案向受试者施用。例如，为了治疗目的，可每天向受试者施用约 1、2、3、4、5、6、7、8 或更多次本发明的重组干扰素，或者每约 2、3、4、5、6、7、8、9、10、11、12、13、14、15、16、17、18、19、20、21 天、每个月、每 2 月或更久的时间间隔向受试者施用 1 次本发明的重组干扰素。为了预防目的，可每约 1、2、3、4、6、7、8、9、10 天、每两周、每三周、每个月、每 2 月、每 3 月、每半年、每 1 年或更久的时间间隔向受试者施用 1 次本发明的重组干扰素。

[0618] 可在一个或更多个治疗周期中向受试者施用本发明的重组干扰素。当在本文中使用时，术语“治疗周期”指本发明的重组干扰素或包含所述重组干扰素的药物组合物达到为研究人员、兽医、执业医生或其他临床医师在组织、系统、动物、个体或人中所探寻的生物学或医学应答的时间长度。这样的一个治疗周期的持续时间可以是至少约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、或约 6 年等，所述持续时间还可以是约 1 天 - 约 6 年，约 1 周 - 约 4 年，约 2 周 - 约 3 年，约 1 个月 - 约 1 年、或约 2 个月 - 约 9 个月等。可长期施用本发明的重组干扰素，也就是说，一个治疗周期持续延长的时间，包括患者生命的整个期间，以改善或控制或限制患者的病症的症状。在一个治疗周期内可向受试者施用一次或更多次的本发明的重组干扰素。

[0619] 可选择地，可在多个治疗周期中向受试者施用本发明的重组干扰素。例如这样的治疗周期可以是 2、3、4、5、6、7、8、9、10 个或更多个治疗周期，所述多个治疗周期所持续的时间可包括患者生命的整个期间。所述多个治疗周期中的任意相邻两个治疗周期之间的间隔时间（即休药期）可以是相同的，也可以是不同的，例如这样的间隔时间可为至少约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、约 6 年等；以及这样的间隔时间还可以为约 2 天 - 约 6 年，约 4 天 - 约 3 年、约 1 周 - 约 1 年、约 2 个月 - 约 9 个月、或约 3 个月 - 约 6 个月等。

[0620] 当在一个治疗周期中多次施用本发明的重组干扰素时，每次施用的剂量可以相同、也可以不同，例如，可以较小的剂量施用 1 次或更多次本发明的重组干扰素，之后以增加或以逐渐递增的剂量施用 1 次或更多次本发明的重组干扰素；或者，可以较小的剂量施用 1 或更多次本发明的重组干扰素，之后以增加或以逐渐递增的剂量施用 1 次或更多次本发明的重组干扰素，再接着以减少或以逐渐递减的剂量施用 1 次或更多次本发明的重组干扰素；或者，可以较大的剂量施用 1 次或更多次本发明的重组干扰素，之后以减少或以逐渐递减的剂量施用 1 次或更多次本发明的重组干扰素；或者，可以较大的剂量施用 1 次或更多次本发明的重组干扰素，之后以减少或以逐渐递减的剂量施用 1 次或更多次本发明的重组干扰素，再接着以增加或以逐渐递增的剂量施用 1 次或更多次本发明的重组干扰素。在一些实施方案中，所述较小的剂量可以是诱导剂量。

[0621] 与之前一次施用的剂量相比，所述之后施用的增加的剂量可以是所述剂量的约 110％ - 约 500％，包括，例如约 110％、约 120％、约 130％、约 140％、约 150％、约 160％、约 170％、约 180％、约 190％、约 200％、约 220％、约 240％、约 260％、约 280％、约 300％、约 350％、约 400％、约 450％、约 500％。与之前一次施用的剂量相比，所述之后施用的以逐渐

递增的剂量可以依次是前次施用剂量的约 110％－约 500％，包括，例如约 110％、约 120％、约 130％、约 140％、约 150％、约 160％、约 170％、约 180％、约 190％、约 200％、约 220％、约 240％、约 260％、约 280％、约 300％、约 350％、约 400％、约 450％、约 500％。这样的以逐渐递增的剂量可以增加 1 次、2 次、3 次、4 次、5 次、6 次、7 次、8 次、9 次、10 次或更多次，之后保持最后一次的剂量直至治疗周期结束。

[0622] 与之前一次施用的剂量相比，所述之后施用的减少的剂量可以是上述剂量的约 5％－约 99％，包括，例如约 5％、约 6％、约 7％、约 8％、约 9％、约 10％、约 15％、约 20％、约 25％、约 30％、约 35％、约 40％、约 45％、约 50％、约 55％、约 60％、约 65％、约 70％、约 75％、约 80％、约 85％、约 90％、约 95％、约 99％。与之前一次施用的剂量相比，所述之后施用的以逐渐递减的剂量可以依次是前次施用剂量的约 5％－约 99％，包括，例如约 5％、约 6％、约 7％、约 8％、约 9％、约 10％、约 15％、约 20％、约 25％、约 30％、约 35％、约 40％、约 45％、约 50％、约 55％、约 60％、约 65％、约 70％、约 75％、约 80％、约 85％、约 90％、约 95％、约 99％。这样的以逐渐递减的剂量可以减少 1 次、2 次、3 次、4 次、5 次、6 次、7 次、8 次、9 次、10 次或更多次，之后保持最后一次的剂量直至治疗周期结束。

[0623] 此外，当多个治疗周期的每个治疗周期中 1 次或更多次施用相同单次剂量的本发明的重组干扰素时，不同的两个治疗周期中的本发明的重组干扰素的单次剂量可以是相同或不同的。例如，这样的单次剂量可以逐渐递增或递减。与之前一次施用的剂量相比，递增或递减的程度如上所述。

[0624] 在一些实施方案中，上述逐渐递增或逐渐递减可以是以线性的方式递增或递减，例如第 1 次给药 9 μg，则之后递增的剂量依次为 18 μg、36 μg、72 μg 等，即依次递增 100％；或者可以是以非线性的方式递增或递减，例如第 1 次给药 9 μg，则之后递增的剂量可依次为 15 μg、18 μg、21 μg 等，即与前次给药相比，每次增加的剂量的幅度并不相同。

[0625] 应当注意上述给药剂量和给药方案可由本领域的普通技术人员基于本发明的教导，随要被缓解的病症的类型和严重程度、给药对象、给药方式等而合理地改变。

[0626] F. 特定治疗方法及制药应用

[0627] 以下提供了使用本发明的重组干扰素的特定治疗方法及制药应用。

[0628] 在一个方面，本发明提供了一种治疗受试者中的肿瘤的方法，包括向所述受试者施用由 SEQ ID NO :2 编码的重组干扰素。

[0629] 在一个实施方案中，本发明提供了一种治疗受试者中肿瘤的方法，包括向所述受试者施用由 SEQ ID NO :2 编码的重组干扰素以及至少一种其他抗癌疗法，其中在施用所述重组干扰素之前、同时和 / 或之后给予所述受试者至少一种其他抗癌疗法，以及其中所述肿瘤为不具备手术指征也不适于手术的癌症或实体瘤，或所述肿瘤为不可切除的实体瘤，并且与治疗前的肿瘤相比，所述重组干扰素和至少一种其他抗癌疗法的联用消除了所述肿瘤或减小了所述肿瘤的大小。

[0630] 在一个实施方案中，本发明提供了一种在具有肿瘤的受试者经至少一种抗癌疗法后防止肿瘤复发和 / 或转移，或者延长或维持无瘤状态的方法，包括向所述受试者施用由 SEQ ID NO :2 编码的重组干扰素。

[0631] 在一个实施方案中，本发明提供了一种非手术消除受试者中肿瘤或减小受试者中肿瘤的大小的方法，包括向所述受试者施用由 SEQ ID NO :2 编码的重组干扰素。

[0632] 在一个实施方案中，本发明提供了一种消除或减少具有肿瘤的受试者中的胸腔积液、腹腔积液和/或心包积液的方法，包括向所述受试者给予由SEQ ID NO:2编码的重组干扰素。

[0633] 在一个实施方案中，本发明提供了一种治疗受试者中的肿瘤的方法，包括通过表面或局部给药向受试者的肿瘤病灶施用由SEQ ID NO:2编码的重组干扰素。

[0634] 在一个实施方案中，本发明提供了一种消除或减小受试者中的肿瘤转移病灶的方法，包括通过表面或局部给药向受试者的肿瘤转移病灶施用由SEQ ID NO:2编码的重组干扰素。

[0635] 在一个实施方案中，本发明提供了一种消除或减小受试者中的肿瘤骨转移病灶的方法，包括通过表面或局部给药向受试者施用由SEQ ID NO:2编码的重组干扰素，其中所述表面或局部给药包括透皮给药和/或浸润给药，任选地，向所述受试者的肿瘤骨转移病灶施用所述重组干扰素。

[0636] 在一个实施方案中，本发明提供了一种消除或减小受试者中的肿瘤骨病灶如肿瘤骨转移病灶、肌肉病灶如肌肉转移病灶、皮下组织病灶如皮下组织转移病灶、前列腺病灶如前列腺转移病灶和/或淋巴结病灶如淋巴结转移病灶的方法，包括通过任何透过皮肤的给药途径向所述受试者施用由SEQ ID NO:2编码的重组干扰素，以消除或减小所述肿瘤骨病灶如肿瘤骨转移病灶、肌肉病灶如肌肉转移病灶、皮下组织病灶如皮下组织转移病灶、前列腺病灶如前列腺转移病灶和/或淋巴结病灶如淋巴结转移病灶，任选地，向所述受试者的肿瘤转移病灶施用所述重组干扰素。

[0637] 在另一方面，本发明提供了一种治疗受试者中的肺癌的方法，包括向所述受试者施用由SEQ ID NO:2编码的重组干扰素。

[0638] 在一个实施方案中，本发明提供了一种治疗受试者中肺癌的方法，包括在两个或更多个治疗周期中向所述受试者施用由SEQ ID NO:2编码的重组干扰素以及一种或更多种化学治疗剂，然后在一个或更多个治疗周期中向所述受试者施用由SEQ ID NO:2编码的重组干扰素以及一种或更多种靶向药物。

[0639] 在一个实施方案中，本发明提供了一种治疗受试者中的肺癌的方法，包括通过皮下给药和/或肌肉给药向所述受试者施用由SEQ ID NO:2编码的重组干扰素，其中所述重组干扰素以如下范围的量施用：一次皮下给药和/或肌肉给药约2μg-约70μg，任选地，约4μg-约50μg，更任选地，约4μg-约30μg，每约1-约7天，任选地，每约1-约2天皮下给药和/或肌肉给药一次所述重组干扰素，持续至少约1天、约2天、约3天、约4天、约5天、约6天、约7天、约8天、约9天、约10天、约1周、约2周、约3周、约1个月、约2个月、约3个月、约4个月、约5个月、约6个月、约7个月、约8个月、约9个月、约10个月、约11个月、约1年、约2年、约3年、约4年、约5年、或约6年等，或可长期施用所述重组干扰素，包括受试者生命的整个期间；或者所述持续时间还可以是约1天-约6年，约1周-约4年，约2周-约3年，约1个月-约1年、或约2个月-约9个月等。

[0640] 在一个实施方案中，本发明提供了一种治疗受试者中的肺癌的方法，包括通过皮下给药和/或肌肉给药向受试者施用由SEQ ID NO:2编码的重组干扰素，其中以约2μg/次-约10μg/次，任选地，约4μg/次-约10μg/次，更任选地，约4.5μg/次-约9μg/次，例如约4.5μg/次或约9μg/次的诱导剂量经皮下给药和/或肌肉给药施用一次或更

多次所述重组干扰素，之后以约 10 μg/ 次 - 约 70 μg/ 次，任选地，约 12 μg/ 次 - 约 50 μg/ 次，更任选地，约 12 μg/ 次 - 约 30 μg/ 次的治疗剂量经皮下给药和 / 或肌肉给药施用多次所述重组干扰素。

[0641] 在一个实施方案中，本发明提供了一种治疗受试者中的癌症的方法，其中所述癌症源于受试者中的肺癌并转移至脑，包括向受试者施用由 SEQ ID NO :2 编码的重组干扰素，其中以约 2 μg/ 次 - 约 10 μg/ 次，任选地，约 4 μg/ 次 - 约 10 μg/ 次，更任选地，约 4.5 μg/ 次 - 约 9 μg/ 次，例如约 4.5 μg/ 次或约 9 μg/ 次的诱导剂量通过皮下给药和 / 或肌肉给药施用一次或更多次所述重组干扰素，之后以约 10 μg/ 次 - 约 70 μg/ 次，任选地，约 12 μg/ 次 - 约 50 μg/ 次，更任选地，约 12 μg/ 次 - 约 30 μg/ 次的治疗剂量通过皮下给药和 / 或肌肉给药施用多次所述重组干扰素，在所述皮下给药和 / 或肌肉给药的之前、同时和 / 或之后通过吸入给药向受试者施用所述重组干扰素，所述重组干扰素以如下范围的量施用 :一次吸入给药约 100 μg- 约 2000 μg，任选地，约 100 μg- 约 1500 μg，更任选地，约 150 μg- 约 800 μg，还更任选地，约 200 μg- 约 600 μg，以及每约 1 天 - 约 3 天，任选地每约 1 天吸入给药一次所述重组干扰素。

[0642] 在一个实施方案中，本发明提供了一种治疗受试者中的癌症的方法，其中所述癌症源于受试者中的肺癌并转移至骨或肝脏，包括向受试者施用由 SEQ ID NO :2 编码的重组干扰素，其中以约 2 μg/ 次 - 约 10 μg/ 次，任选地，约 4 μg/ 次 - 约 10 μg/ 次，更任选地，约 4.5 μg/ 次 - 约 9 μg/ 次，例如约 4.5 μg/ 次或约 9 μg/ 次的诱导剂量通过皮下给药和 / 或肌肉给药施用一次或更多次所述重组干扰素，之后以约 10 μg/ 次 - 约 70 μg/ 次，任选地，约 12 μg/ 次 - 约 50 μg/ 次，更任选地，约 12 μg/ 次 - 约 30 μg/ 次的治疗剂量通过皮下给药和 / 或肌肉给药施用多次所述重组干扰素。

[0643] 在一个实施方案中，本发明提供了一种治疗受试者中的癌症的方法，其中所述癌症源于受试者中的肺癌并转移至淋巴结，包括向受试者施用由 SEQ ID NO :2 编码的重组干扰素，其中以约 2 μg/ 次 - 约 10 μg/ 次，任选地，约 4 μg/ 次 - 约 10 μg/ 次，更任选地，约 4.5 μg/ 次 - 约 9 μg/ 次，例如约 4.5 μg/ 次或约 9 μg/ 次的诱导剂量通过皮下给药和 / 或肌肉给药施用一次或更多次所述重组干扰素，之后以约 10 μg/ 次 - 约 70 μg/ 次，任选地，约 12 μg/ 次 - 约 50 μg/ 次，更任选地，约 12 μg/ 次 - 约 30 μg/ 次的治疗剂量通过皮下给药和 / 或肌肉给药施用多次所述重组干扰素，在所述皮下给药和 / 或肌肉给药的之前、同时和 / 或之后通过表面或局部给药向所述肿瘤和 / 或所述淋巴结转移灶施用所述重组干扰素。

[0644] 在一个实施方案中，本发明提供了一种治疗受试者中的肺癌的方法，其中所述受试者具有胸腔积液、腹腔积液和 / 或心包积液，包括经表面或局部给药向所述受试者给予由 SEQ ID NO :2 编码的重组干扰素。

[0645] 在另一方面，本发明提供了由 SEQ ID NO :2 编码的重组干扰素在制备用于治疗受试者中的肿瘤的药物中的应用。

[0646] 在一个实施方案中，本发明提供了由 SEQ ID NO :2 编码的重组干扰素和其他抗肿瘤药物在制备用于治疗受试者中的肿瘤的药物中的应用。

[0647] 在一个实施方案中，本发明提供了由 SEQ ID NO :2 编码的重组干扰素在制备用于预防受试者在抗肿瘤疗法后肿瘤复发和 / 或转移的药物中的应用。

[0648] 在一个实施方案中，本发明提供了由 SEQ ID NO :2 编码的重组干扰素在制备通过非手术方法用于消除受试者中肿瘤或减小受试者中肿瘤的大小的药物中的应用。

[0649] 在一个实施方案中，本发明提供了由 SEQ ID NO :2 编码的重组干扰素在制备用于消除或减少具有肿瘤的受试者中胸腔积液、腹腔积液和 / 或心包积液的药物中的应用。

[0650] 在一个实施方案中，本发明提供了由 SEQ ID NO :2 编码的重组干扰素在制备用于治疗受试者中的肺癌的药物中的应用。

[0651] 在一个实施方案中，本发明提供了由 SEQ ID NO :2 编码的重组干扰素联合化学治疗剂、靶向药物在制备用于治疗受试者中肺癌的药物中的应用。

[0652] 在一些实施方案中，所述受试者是早期、中期或晚期癌症患者，任选地，所述受试者是中期或晚期癌症患者，更任选地，所述受试者是晚期癌症患者，例如晚期肺癌患者。

[0653] 在一些实施方案中，所述受试者可以是 0、I、II、III 或 IV 期癌症患者，任选地，III 或 IV 期癌症患者，例如 III 或 IV 期肺癌患者，这样的癌症患者还可以是具有转移的肿瘤的患者，例如所述肿瘤已原处或远处转移的患者。

[0654] 在一些实施方案中，所述受试者为中期、晚期或 III 或 IV 期癌症患者，任选地，所述受试者为晚期或 III 或 IV 期癌症患者。

[0655] 在一些实施方案中，所述肿瘤为具备或不具备手术指征的癌症或实体瘤。

[0656] 在一些实施方案中，所述受试者中的肿瘤是可手术切除的。在一些实施方案中，所述受试者中的肿瘤是不可手术切除的。在一些实施方案中，所述手术包括但不限于外科手术。

[0657] 在一些实施方案中，所述受试者具有实体瘤。

[0658] 在一些实施方案中，所述实体瘤为可切除或不可切除的实体瘤。

[0659] 在一些实施方案中，所述可切除或不可切除的实体瘤为晚期实体瘤。

[0660] 在一些实施方案中，所述实体瘤为具备或不具备手术指征如肿瘤手术指征的实体瘤。

[0661] 在一些实施方案中，所述具备或不具备手术指征如肿瘤手术指征的实体瘤为晚期或 III 或 IV 期实体瘤。

[0662] 在一些实施方案中，所述肿瘤是实体瘤。所述实体瘤包括如下的一种或更多种 :肺癌、肝癌、肝细胞癌 (HCC)、食道癌、胆管癌、胆囊癌、胃癌 (stomach cancer)、腹部癌 (abdominal cancer)、胃肠道癌、胃癌 (gastric cancer)、胰腺癌、肾细胞癌、肾癌、骨癌、乳腺癌、卵巢癌、子宫癌、宫颈癌、子宫内膜癌、结直肠癌、结肠癌、直肠癌、膀胱癌、浅表性膀胱癌、前列腺癌、前列腺癌、肾上腺瘤、鳞状细胞癌、神经瘤、恶性神经瘤、肌上皮癌、滑膜肉瘤、横纹肌肉瘤、胃肠道间质细胞瘤、皮肤癌、基底细胞癌、恶性黑色素瘤、甲状腺癌、鼻咽癌、血管瘤、表皮样癌、头颈癌、神经胶质瘤、或卡波济氏肉瘤 ;任选地，肺癌 ;更任选地，所述肺癌包括小细胞肺癌 (SCLC)、非小细胞肺癌 (NSCLC) 或两者。

[0663] 在一些实施方案中，所述肿瘤是非实体瘤。所述非实体瘤包括如下的一种或更多种 :白血病、急性白血病、慢性白血病、慢性粒细胞性白血病、急性髓性白血病、慢性髓性白血病、慢性淋巴细胞白血病、急性淋巴细胞白血病、T 细胞白血病、毛细胞白血病、红细胞增多症、骨髓增生异常综合征、多发性骨髓瘤、淋巴腺瘤、霍奇金氏淋巴瘤或非霍奇金氏淋巴瘤。

[0664] 在一些实施方案中，所述有效量是治疗有效量或预防有效量。在一些实施方案中，可向所述受试者施用例如约 2 μg- 约 2000 μg，任选地，约 4 μg- 约 1500 μg，更任选地，约 9 μg- 约 1000 μg，还更任选约 9 μg- 约 600 μg 的单次剂量的本发明的重组干扰素。在某些实施方案中，当通过全身给药施用本发明的重组干扰素时，所述治疗有效量为约 2 μg- 约 70 μg，任选地，约 4 μg- 约 50 μg，更任选地，约 4 μg- 约 30 μg，还更任选地，约 9 μg- 约 30 μg。在特定的实施方案中，当通过全身给药施用本发明的重组干扰素时，所述预防有效量为约 2 μg- 约 70 μg，任选地，约 4 μg- 约 50 μg，更任选地，约 4 μg- 约 30 μg，还更任选地，约 9 μg- 约 30 μg。

[0665] 在一些实施方案中，可通过如下的至少一种 :全身给药、表面给药和局部给药将本发明的重组干扰素和 / 或与本发明的重组干扰素联用的化学治疗剂、靶向药物、生物制剂等施用于受试者。在一些实施方案中，可通过包括如下的一种或更多种的给药途径 :经口、直肠、舌下、静脉内、动脉内、肌肉、皮下、骨内、皮内、关节内、腹膜内、鞘内、脑内、阴道、经皮、透皮、表皮、粘膜、经眼、经肺、经鼻、腹腔、胸腔、心室内、心包、吸入、瘤内、子宫、浸润或膀胱内给药向受试者施用本发明的重组干扰素和 / 或与本发明的重组干扰素联用的化学治疗剂、靶向药物、生物制剂等。在某些特定的实施方案中，可通过皮下、肌肉、吸入、浸润、胸腔、腹腔、心包、瘤内、喷雾给药和它们的任意组合向受试者施用本发明的重组干扰素和 / 或与本发明的重组干扰素联用的化学治疗剂、靶向药物、生物制剂等。在某些实施方案中，可通过肌肉和 / 或皮下给药向受试者施用本发明的重组干扰素和 / 或与本发明的重组干扰素联用的化学治疗剂、靶向药物、生物制剂等。在一些实施方案中，当向手术部位施用本发明的重组干扰素和 / 或与本发明的重组干扰素联用的化学治疗剂、靶向药物、生物制剂等时，其可通过表面或局部给药，例如浸润、胸腔、腹腔、心包、子宫、膀胱、瘤内、经肺、经鼻、经皮、透皮、表皮和 / 或粘膜给药施用。

[0666] 在一些实施方案中，可通过注射给药将本发明的重组干扰素和 / 或与本发明的重组干扰素联用的化学治疗剂、靶向药物、生物制剂等施用于受试者，例如皮下注射、肌肉注射、静脉注射、动脉注射、脑内注射、腹膜内注射、瘤内注射、关节内注射、鞘内注射和骨内注射等。在一些实施方案中，当通过吸入给药时，可经肺吸入和 / 或经鼻吸入。在某些特定的实施方案中，所述吸入给药可以是干粉吸入或雾化吸入。在一些实施方案中，当通过胸腔、腹腔、子宫、膀胱、心包给药时，可进一步通过灌注给药将本发明的重组干扰素和 / 或与本发明的重组干扰素联用的化学治疗剂、靶向药物、生物制剂等施用于受试者，例如胸腔灌注、腹腔灌注、子宫灌注、膀胱内灌注和 / 或心包灌注。在一些实施方案中，当通过经皮、透皮、表皮或粘膜给药时，可进一步通过喷雾给药将本发明的重组干扰素和 / 或与本发明的重组干扰素联用的化学治疗剂、靶向药物、生物制剂等施用于受试者，例如经皮喷雾、表皮喷雾、透皮喷雾和 / 或粘膜喷雾。

[0667] 当通过注射给药（如皮下注射、肌肉注射）全身施用本发明的重组干扰素时，上述单次剂量可为约 2 μg- 约 70 μg，任选地，约 4 μg- 约 50 μg，更任选地，约 4 μg- 约 30 μg，包括但不限于约 2 μg、约 3 μg、约 4 μg、约 4.5 μg、约 9 μg、约 13.5 μg、约 15 μg、约 18 μg、约 21 μg、约 25.5 μg、约 30 μg、约 40 μg、约 50 μg、约 60 μg 和约 70 μg。在一些实施方案中，每约 1 天 - 约 7 天，任选地，每约 1 天 - 约 2 天皮下和 / 或肌肉给药一次本发明的重组干扰素。在一些实施方案中，所述注射持续至少约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约

6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、约 6 年等，或者可长期施用所述重组干扰素，包括受试者生命的整个期间；或者所述持续时间还可以是约 1 天 - 约 6 年，约 1 周 - 约 4 年，约 2 周 - 约 3 年，约 1 个月 - 约 1 年、或约 2 个月 - 约 9 个月等。

[0668] 当通过注射给药（如瘤内注射）局部施用本发明的重组干扰素时，所述重组干扰素的单次剂量可为约 60 μg- 约 600 μg，任选地，约 60 μg- 约 500 μg，更任选地，约 80 μg- 约 400 μg，还更任选地，约 100 μg- 约 250 μg。在一些实施方案中，每约 1 天 - 约 10 天，任选地，每约 1 天 - 约 7 天，例如每约 1、2、3、4、5、6 或 7 天瘤内给药一次本发明的重组干扰素。在一些实施方案中，所述瘤内给药如瘤内注射持续至少约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、约 6 年等，或者可长期施用所述重组干扰素，包括受试者生命的整个期间；或者所述持续时间还可以是约 1 天 - 约 6 年，约 1 周 - 约 4 年，约 2 周 - 约 3 年，约 1 个月 - 约 1 年、或约 2 个月 - 约 9 个月等。在特定的实施方案中，当通过瘤内给药本发明的重组干扰素时，所述瘤内给药的给药方案如下：每约 1 天瘤内注射一次所述重组干扰素，持续约 4 次 - 约 8 次，接着每约 3 天 - 约 5 天瘤内注射一次所述重组干扰素，持续约 4 次 - 约 8 次，然后每约 7 天瘤内注射一次所述重组干扰素，当瘤体消失或瘤体小至无法进行瘤内注射时，停止瘤内给药，其中每次瘤内注射约 60 μg- 约 600 μg，任选地，约 60 μg- 约 500 μg，更任选地，约 80 μg- 约 400 μg，还更任选地，约 100 μg- 约 250 μg 的所述重组干扰素。

[0669] 当通过吸入（如经肺和经鼻吸入，包括干粉吸入和雾化吸入）施用本发明的重组干扰素时，所述重组干扰素的单次剂量可为约 100 μg- 约 2000 μg，任选地，约 100 μg- 约 1500 μg，更任选地，约 150 μg- 约 800 μg，还更任选地，约 200 μg- 约 600 μg，包括但不限于约 100 μg、约 200 μg、约 300 μg、约 400 μg、约 500 μg、约 600 μg、约 700 μg、约 800 μg、约 900 μg、和约 1000 μg。在一些实施方案中，每约 1 天 - 约 3 天，任选地，每约 1 天吸入给药一次本发明的重组干扰素。在一些实施方案中，所述吸入给药持续至少约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、约 6 年等，或者可长期施用所述重组干扰素，包括受试者生命的整个期间；或者所述持续时间还可以是约 1 天 - 约 6 年，约 1 周 - 约 4 年，约 2 周 - 约 3 年，约 1 个月 - 约 1 年、或约 2 个月 - 约 9 个月等。

[0670] 当通过灌注（如胸腔灌注、腹腔灌注、子宫灌注、膀胱内灌注、心包灌注）施用本发明的重组干扰素时，所述重组干扰素的单次剂量可为约 30 μg- 约 2000 μg，任选地，约 100 μg- 约 1500 μg，更任选地，约 150 μg- 约 1000 μg，还任选地，约 200 μg- 约 800 μg，还更任选地，约 200 μg- 约 400 μg。在一些实施方案中，每约 1 天 - 约 10 天，任选地，每约 1 天 - 约 7 天，例如每约 1、2、3、4、5、6 或 7 天胸腔、腹腔和 / 或心包给药一次本发明的重组干扰素。在一些实施方案中，所述灌注持续至少约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个

月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、约 6 年等，或者可长期施用所述重组干扰素，包括受试者生命的整个期间；或者所述持续时间还可以是约 1 天 - 约 6 年，约 1 周 - 约 4 年，约 2 周 - 约 3 年，约 1 个月 - 约 1 年、或约 2 个月 - 约 9 个月等。

[0671] 当通过喷雾如经皮喷雾、表皮喷雾、透皮喷雾、粘膜喷雾向病灶（如皮肤表面和粘膜）施用本发明的重组干扰素时，所述重组干扰素的单次剂量可为约 6 μg- 约 100 μg，任选地，约 10 μg- 约 40 μg，更任选地，约 20 μg- 约 40 μg。在一些实施方案中，每天喷雾给药约 1 次 - 约 6 次例如约 1、2、3、4、5 或 6 次本发明的重组干扰素。在一些实施方案中，所述喷雾持续至少约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、约 6 年等，或者可长期施用所述重组干扰素，包括受试者生命的整个期间；或者所述持续时间还可以是约 1 天 - 约 6 年，约 1 周 - 约 4 年，约 2 周 - 约 3 年，约 1 个月 - 约 1 年、或约 2 个月 - 约 9 个月等。

[0672] 在一些实施方案中，为了治疗目的，可每天向受试者施用约 1、2、3、4、5、6、7、8 或更多次本发明的重组干扰素，或者每约 2 天、3 天、4 天、5 天、6 天、7 天、8 天、9 天、10 天、11 天、12 天、13 天、14 天、15 天、16 天、17 天、18 天、19 天、20 天、21 天、每个月、每 2 月或更久的时间间隔向受试者施用 1 次本发明的重组干扰素。在一些实施方案中，为了预防目的，可每约 1 天、2 天、3 天、4 天、5 天、6 天、7 天、8 天、9 天、10 天、每两周、每三周、每个月、每 2 月、每 3 月、每半年、每 1 年或更久的时间间隔向受试者施用 1 次本发明的重组干扰素。

[0673] 在一些实施方案中，在一个或更多个治疗周期中施用本发明的重组干扰素。任选地，所述多个治疗周期可以是 2、3、4、5、6、7、8、9、10 个或更多个治疗周期。在特定的实施方案中，所述一个治疗周期的持续时间为至少约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、约 6 年等；或者所述持续时间还可以是约 1 天 - 约 6 年，约 1 周 - 约 4 年，约 2 周 - 约 3 年，约 1 个月 - 约 1 年、或约 2 个月 - 约 9 个月等。在特定的实施方案中，可长期施用本发明的重组干扰素，包括患者生命的整个期间，以改善或控制或限制受试者的症状。

[0674] 在一些实施方案中，可在多个治疗周期中向受试者施用本发明的重组干扰素。在某些实施方案中，所述多个治疗周期为 2 个或更多个治疗周期。在特定的实施方案中，所述多个治疗周期的持续时间可包括患者生命的整个期间。在一些实施方案中，所述多个治疗周期中的任意相邻两个治疗周期之间的间隔时间可以是相同的，也可以是不同的。在特定的实施方案中，所述间隔时间可为至少约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、约 6 年等；或者所述间隔时间还可以为约 2 天 - 约 6 年，约 4 天 - 约 3 年、约 1 周 - 约 1 年、约 2 个月 - 约 9 个月、约 3 个月 - 约 6 个月等。

[0675] 在一些实施方案中，当在一个治疗周期中多次施用本发明的重组干扰素时，可以

较小的剂量施用 1 次或更多次本发明的重组干扰素，之后以增加或以逐渐递增的剂量施用 1 次或更多次本发明的重组干扰素。在特定的实施方案中，当通过皮下、肌肉给药（如皮下注射、肌肉注射）全身施用本发明的重组干扰素时，可以较小的剂量如约 4.5 μg 或约 9 μg 施用 1 次本发明的重组干扰素，之后以增加（如增加至约 15 μg、约 18 μg、约 21 μg）或以逐渐递增的剂量施用多次本发明的重组干扰素。在实施方案中，每约 1 天 - 约 2 天给药一次本发明的重组干扰素。在实施方案中，施用本发明的重组干扰素的持续时间为约 1 周 - 约 2 年，任选地，约 2 周 - 约 1 年，更任选地，约 1 个月 - 约 9 个月，包括约 2 个月 - 约 6 个月，或可包括患者生命的整个期间。在实施方案中，所述逐渐递增的剂量可以依次是前次施用剂量的约 110％ - 约 500％。在实施方案中，可以较小的剂量如约 4.5 μg 或约 9 μg 施用本发明的重组干扰素，之后以约 12 μg- 约 18 μg（例如约 13.5 μg、约 15 μg、约 18 μg）施用本发明的重组干扰素，接着以约 15 μg- 约 30 μg（例如约 18 μg、约 21 μg、约 25.5 μg、约 30 μg）施用本发明的重组干扰素，每约 2 天给药一次，持续约 2 个月 - 约 3 年，或包括患者生命的整个期间。

[0676] 在一些实施方案中，可以诱导剂量施用一次或更多次所述重组干扰素，之后以治疗剂量施用一次或更多次所述重组干扰素。在一些实施方案中，所述诱导剂量为约 2 μg/ 次 - 约 10 μg/ 次，任选地，约 4 μg/ 次 - 约 10 μg/ 次，更任选地，约 4.5 μg/ 次 - 约 9 μg/ 次，例如约 4.5 μg/ 次或约 9 μg/ 次。在一些实施方案中，所述治疗剂量为约 10 μg/ 次 - 约 70 μg/ 次，任选地，约 12 μg/ 次 - 约 50 μg/ 次，更任选约 12 μg/ 次 - 约 30 μg/ 次。在一些实施方案中，所述诱导剂量为约 4 μg/ 次 - 约 10 μg/ 次，以及所述治疗剂量为约 12 μg/ 次 - 约 50 μg/ 次。在一些实施方案中，所述诱导剂量一般小于治疗剂量。在一些实施方案中，施用诱导剂量与施用治疗剂量之间的时间间隔为约 1 天 - 约 1 个月，任选地，约 1 天 - 约 1 周，更任选地，约 1 天 - 约 3 天，包括，例如约 1 天、约 2 天、约 3 天、约 4 天、约 5 天、约 6 天、约 7 天、约 8 天、约 9 天、约 10 天、约 1 周、约 2 周、约 3 周、和约 1 个月。在一些实施方案中，当多次施用诱导剂量时，每约 1 天 - 约 10 天施用一次，任选地，每约 1 天 - 约 7 天施用一次，更任选地，每约 1 天 - 约 2 天施用一次，包括，例如每约 1 天、2 天、3 天、4 天、5 天、6 天、7 天、8 天、9 天或 10 天施用一次。在一些实施方案中，当多次施用治疗剂量时，每约 1 天 - 约 10 天施用一次，任选地，每约 1 天 - 约 7 天施用一次，更任选地，每约 1 天 - 约 2 天施用一次，包括，例如每约 1 天、2 天、3 天、4 天、5 天、6 天、7 天、8 天、9 天或 10 天施用一次。在一些实施方案中，所述诱导剂量和治疗剂量的总施用时间应持续至少约 1 周、约 2 周、约 3 周、约 1 个月、约 2 个月、约 3 个月、约 4 个月、约 5 个月、约 6 个月、约 7 个月、约 8 个月、约 9 个月、约 10 个月、约 11 个月、约 1 年、约 2 年、约 3 年、约 4 年、约 5 年、约 6 年等，或者可长期施用本发明的重组干扰素，包括患者生命的整个期间。

[0677] 在一些实施方案中，所述治疗减少了受试者中的肿瘤大小，例如，按开始治疗时的肿瘤体积计，减小约 10％、约 20％、约 30％、约 40％、约 50％、约 60％、约 70％、约 80％、约 90％、约 95％、约 100％或更多的肿瘤体积，乃至于完全消除肿瘤。在一些实施方案中，所述治疗减少了肿瘤、恶性胸腔积液、恶性腹腔积液和 / 或恶性心包积液中的癌细胞数目，例如按开始治疗时的癌细胞数目计，减少约 10％、约 20％、约 30％、约 40％、约 50％、约 60％、约 70％、约 80％、约 90％、约 95％、约 100％或更多的癌细胞，乃至于不存在癌细胞。在一些实施方案中，所述治疗抑制（包括降低至某种程度和 / 或终止）了肿瘤细胞浸润入外周器官

中；抑制或阻止了肿瘤转移，例如肿瘤的原位或远处转移、或者肿瘤的微转移；缩小病变；使得肿瘤降期；以及还抑制、杀死存在于血道、淋巴道内的微转移灶；由此容许完全切除最初无法切除的肿瘤或利于可切除的肿瘤被切除，这样的切除例如是手术切除。对于这样的方法而言，其可以是一种“新辅助疗法”或“诱导治疗”。当在本文中使用时，术语“新辅助疗法”或“诱导治疗”指在手术前提供的疗法，该疗法的目的在于缩小病变，争取肿瘤降期，抑制、杀死存在于血道、淋巴道内的微转移灶，减小肿瘤大小由此容许更加方便地切除肿瘤或者完全切除最初无法切除的肿瘤。此外，在切除所述肿瘤后可进一步向所述受试者施用本发明的重组干扰素以预防所述肿瘤的复发和/或转移。

[0678] 在一些实施方案中，所述方法减少或消除了恶性胸腔积液、腹腔积液和/或心包积液，例如按开始治疗时的恶性胸腔积液、腹腔积液和/或心包积液体积计，减小约10％、约20％、约30％、约40％、约50％、约60％、约70％、约80％、约90％、约95％、约100％或更多的体积，乃至于完全消除恶性胸腔积液、腹腔积液和/或心包积液。

[0679] 在一些实施方案中，所述预防肿瘤复发的方法减小了具有肿瘤的受试者治疗后肿瘤复发的可能性。在一些实施方案中，所述具有肿瘤的受试者在给予本发明的重组干扰素(rSIFN-co)之前已被识别并得到了治疗，这样的治疗可以是上述使用本发明的重组干扰素的治疗，或使用了一种或更多种不同于本发明的重组干扰素的其他抗癌疗法如化学治疗、放射治疗、手术治疗、介入治疗、生物治疗、基因治疗、消融治疗、免疫治疗、靶向治疗、中药治疗和它们的任意组合，这样的治疗的结果可以是临床上治愈或基本上治愈。在一些实施方案中，这样的预防方法可抑制、杀死存在于血道、淋巴道内的可能的微转移灶，从而阻止所述肿瘤的复发和/或转移，这样的微转移灶可以是或可以不是临床上可检测到的。

[0680] 在一些实施方案中，施用本发明的重组干扰素可以延缓具有肿瘤的受试者中肿瘤的生长，例如按开始治疗时的肿瘤生长速度计，减小约10％、约20％、约30％、约40％、约50％、约60％、约70％、约80％、约90％、约95％或更多的肿瘤生长速度。

[0681] 在一些实施方案中，本发明的重组干扰素作为单一疗法向受试者施用。在一些实施方案中，进一步包括向所述受试者施用一种或更多种其他抗癌疗法，任选地，在施用本发明的重组干扰素之前、同时和/或之后给予所述受试者其他抗癌疗法。在一些实施方案中，所述其他抗癌疗法包括如下的一种或更多种：化学治疗、放射治疗、手术治疗、介入治疗、生物治疗、基因治疗、消融治疗、免疫治疗、靶向治疗和中药治疗。在某些实施方案中，所述其他抗癌疗法包括一种或更多种化学治疗、放射治疗、手术治疗、靶向治疗和生物治疗。在一些实施方案中，所述其他抗癌疗法包括化学治疗、放射治疗或两者。在一些实施方案中，所述其他抗癌疗法包括化学治疗，例如一线化学治疗，如包含铂类化合物例如顺铂的化学治疗剂和/或化学治疗方案。

[0682] 在一些实施方案中，当治疗肺癌时，与本发明的重组干扰素联用的化学治疗中所使用的化学治疗剂包括但不限于：铂类化合物例如顺铂、卡铂、奥利沙铂等，紫杉醇类化合物例如多西他赛（多西他赛注射液、泰索帝、紫杉特尔）等，胞苷类抗代谢物例如吉西他滨（健择）等，抗叶酸抗代谢物例如培美曲塞（力比泰）等，嘧啶类抗代谢物例如卡培他滨（希罗达）等，以及上述化学治疗剂的任意组合。或者使用如下化学治疗方案，例如包括但不限于包含铂类化合物的化学治疗方案，如GP、TP、EP、GP-T2方案等。在特定的实施方案中，当治疗肺癌时，与本发明的重组干扰素联用的化学治疗方案包括顺铂雾化吸入、顺铂心

包灌注等。

[0683] 在一些实施方案中，当治疗肺癌时，与本发明的重组干扰素联用的靶向治疗中所使用的靶向药物包括但不限于：吉非替尼、厄洛替尼和/或重组人血管内皮抑制素等。

[0684] 在一些实施方案中，当治疗肺癌时，与本发明的重组干扰素联用的其他抗癌疗法包括上述化学治疗剂/化学治疗方案与靶向药物的任意组合。

[0685] 在特定的实施方案中，当治疗肺癌时，与本发明的重组干扰素联用的其他抗癌疗法包括GP方案联合重组人血管内皮抑制素、EP方案联合顺铂雾化吸入等。

[0686] 在一些实施方案中，本发明的治疗方法为非手术治疗方法。

[0687] G. 疗效和不良反应评价标准

[0688] 本发明的重组干扰素临床治疗肿瘤如实体瘤的疗效评价采用1999年公布的实体瘤疗效评价标准(RECIST标准)(参见James，K. 等.J Natl Cancer Inst,1999,91,523-528)。

[0689] 肿瘤病灶分为可测量病灶和不可测量病灶，其中可测量病灶被判定为靶病变，以最长直径表示病灶大小，每个受累器官最多选定5个病灶，所有受累器官的被测病灶总数不得超过10个，各个病灶最长直径之和为靶病变的总直径。不可测量病灶被判定为非靶病变，只记录病变的存在与否及追踪，不测量大小。

[0690] 靶病变的疗效评价标准定为四级，非靶病变的疗效评价标准定为三级，再综合两类病变的疗效得到总疗效评价。具体如下：

[0691] 靶病变的疗效评价标准：(1)CR(完全缓解)：所有靶病变消失；(2)PR(部分缓解)：靶病变总直径减少30%以上；(3)NC或SD(没有改变或稳定的疾病)：靶病变既未减少至“PR”，亦未增大至“PD”；(4)PD(发展疾病)：靶病变总直径增大20%以上，或出现一个至多个新病灶。

[0692] 非靶病变的疗效评价标准：(1)CR：所有非靶病变消失及肿瘤标记物水平正常；(2)IR(不完全应答)/SD：一个至多个非靶病变无变化和或肿瘤标记物超出正常界限；(3)PD：出现一个或更多个新病灶和/或非靶病变明显发展。

[0693] 实体瘤总疗效评价标准。

[0694] 表1 实体瘤总疗效评价标准

[0695]

靶病变	非靶病变	新病变	总疗效
CR	CR	无	CR
CR	IR/SD	无	PR
PR	非PD	无	PR
NC/SD	非PD	无	NC/SD
PD	任何	有或无	PD
任何	PD	有或无	PD
任何	任何	有	PD

[0696] 本发明的重组干扰素临床治疗肿瘤如实体瘤的不良反应评价参考“WHO”毒性分级

标准。

[0697] 与现有技术相比，本发明的重组干扰素具有如下的有益效果：

[0698] 本发明所用的重组干扰素rSIFN-co与美国安进(Amgen)公司的干复津(INFERGEN®，干扰素alfacon-1)等的现有干扰素具有明显不同的结构特征和生理活性。一方面，该重组干扰素单用和/或联合放疗、化疗、生物制剂和/或靶向药物等，可非手术消除或缩小实体瘤患者的瘤体特别是晚期瘤体；特别地，该重组干扰素可消除或缩小不具备手术指征的实体瘤，尤其是不具备手术指征的晚期实体瘤。另一方面，该重组干扰素单独表面或局部施用如瘤内注射/表皮喷雾给药等，或者表面或局部使用联合全身给药(可联合本发明的重组干扰素或者联合放疗/其他抗肿瘤药物等)，也可非手术(即不通过手术的方式)消除或缩小实体瘤。进一步地，该重组干扰素可替代化疗药物，用于预防肿瘤术后复发或转移，效果显著；特别对于各种转移病灶如骨转移等，现有治疗手段均无法消除，而通过本发明方法尤其是通过表面或局部给药使药物直达病灶，可取得明显的减小或消除瘤体的效果。此外，该重组干扰素单独胸腔或腹腔灌注，可有效的消除或减少恶性胸腔和/或腹腔积液。

[0699] 更进一步地，rSIFN-co联合治疗可攻克癌症：首先，本发明所用的重组干扰素(rSIFN-co)具有广谱的抗肿瘤作用，其对于实体瘤和非实体瘤都有作用，与现有的治疗手段，如手术、化疗、放疗、生物治疗及其它抗肿瘤药物都具有很好的协同作用；其次，rSIFN-co是低毒的，即其可以大剂量使用且对正常细胞没有任何伤害；再次，rSIFN-co使用方便，对任何部位的瘤体都可直接使用。其可皮下/肌肉注射控制肿瘤全身发展、可胸/腹腔灌注消除积液及胸/腹腔瘤体、可表面或局部注射消除原发或转移的肿瘤、可浸润(透皮)给药治疗骨、皮肤、肌肉、前列腺等的肿瘤病灶；还可雾化吸入给药。基于rSIFN-co的前述三个优点，其联用后的有效率在90％以上。对于早中期癌症病例，可手术后使用以代替化疗，并有效预防复发和转移；对于晚期、无治疗指征癌症病例也可做到非手术消除瘤体；对于不具备手术指征的病例，还可通过rSIFN-co的治疗使之转变为具备手术指征，从而创造手术条件。因此，我们认为rSIFN-co联合治疗可以攻克癌症。

具体实施方式

[0700] 本发明将通过下列实施例得以详细描述，所述实施例仅作为解释说明目的，并不意在限制本发明的范围。可对本发明进行修改而不背离的本发明的范围。所有出版物、专利和专利申请在此以其整体并入作为参考，如同每篇独立出版物、专利或专利申请被明确且单独地指出以其整体并入作为参考一样。

[0701] 在下述实施例中所涉及的患者均签署了知情同意书，并且申请人与所在医院签署了保密协议书，同时实验过程符合当地关于药物临床试验伦理道德委员会的要求。

[0702] 实施例1：重组干扰素组合物的制备

[0703] 重组干扰素冻干注射剂(冻干粉)的配方

[0704] 本发明rSIFN-co原液 34.5μg/ml

[0705] pH 7.0磷酸盐缓冲液(PB) 10mmol/L

[0706] 甘氨酸 0.4mol/L

[0707] 制备工艺：按配方称料，无菌无热原注射水溶解，0.22μm孔径滤膜过滤除菌，于

6-10℃保存，取样作无菌和热原检查合格后分装西林瓶中，每瓶 0.3-0.5 的单次剂量，分装后放置至冻干机中冷冻干燥。

[0708] 重组干扰素水溶液注射剂的配方

[0709] 本发明 rSIFN-co 原液 34.5μg/ml

[0710] pH 7.0 磷酸盐缓冲液 (PB) 25mmol/L

[0711] 氯化钠 0.4mol/L

[0712] 制备工艺：按配方称料，无菌无热原注射水溶解，0.22μm 孔径滤膜过滤除菌，于 6-10℃保存，取样作无菌和热原检查合格后分装于密闭容器中，每瓶 0.3-0.5 的单次剂量，分装后成品置 2-10℃暗处保存。

[0713] 重组干扰素喷雾剂的配方

[0714] 下表中各成分含量百分比为重量百分比

[0715]

EDTA	0.01%
吐温 80	0.05%
柠檬酸三钠	10mmol/L
丙三醇	1.26%
氯化钠	0.03%
苯甲醇	0.5%
人血白蛋白	0.1%
重组高效复合干扰素	10μg/ml

[0716] 制备方法是常规的喷雾制剂的制备方法。

[0717] 重组干扰素吸入剂的制备

[0718] 采用常规的干扰素吸入剂配制方法。按照常规的干扰素吸入剂配制方法配制本发明的重组干扰素吸入剂。

[0719] 实施例 2：本发明重组干扰素治疗患者的临床资料 (58 例)

[0720] 以下是截止至 2012 年 7 月 1 日的本发明重组干扰素治疗 58 例多种癌症患者的临床治疗汇总表 (表 2)。

[0721]

[0722]

表 2：58 例多种癌症临床治疗汇总表

患者编号	性别	年龄	诊断的病种	分期	用药前治疗	干扰素给药方案	联合治疗方案	治疗后效果	总疗效
1	男	53	右肺非小细胞肺癌	IIIb	第 1 年 10 月 14 日至第 1 年 11 月 25 日行 DP 方案®：紫杉特尔 75mg 第 1 天，顺铂 75mg 第 1 天，共计化疗 2 周期，每个周期 21 天。	第 1 年 11 月开始使用 rSIFN-co 治疗。隔日肌注 1 次 rSIFN-co：第 1 次肌注 9μg，第 2 次肌注 15μg，从第 3 次开始肌注 18μg。治疗持续至第 3 年 2 月，期间 rSIFN-co 治疗停药 1 个月（在第 2 年 4 月），共计用药时间 15 个月。	第 1 年 12 月 2 日开始行右肺+纵隔淋巴结放疗®，DT40Gy，继行 X-刀治疗，DT20Gy。	右肺门原发病灶消失治愈。	CR
2	男	40	非小细胞肺腺癌	IV	第 1 年 1 月行 1 周期（每周期 21 天）全身化疗（紫杉特尔+卡铂）。	第 1 年 4 月 14 日开始使用 rSIFN-co 治疗。隔日肌注 1 次 rSIFN-co：第 1 次肌注 9μg，第 2 次肌注 15μg，第 3 次肌注 18μg，从第 4 次开始肌注 21μg。配合 rSIFN-co 雾化吸入，每日 1 次，第 1 次吸入 300μg，第 2 次吸入 500μg 从第 3 次开始吸入 600μg。rSIFN-co 用药至第 2 年 4 月。	第 1 年 4 月 20 日至第 1 年 9 月 3 日联合恩度®：每日给药，每次 7.5mg/m^2（1.2×10^5U/m^2），连续给药 14 天为 1 周期，共进行了 4 个周期的治疗，以及同时联合 GP 方案：吉西他滨 1600mg 第 1、8 天，顺铂 40mg 第 1-3 天，一个疗程为 15 天，共连续进行了 4 个周期的治疗。第 1 年 7 月 19 日行 1 次	原右肺上叶病灶由原来的大小约 10.2 cm×8.2 cm×7.7cm 减小到 1.2 cm×1.4 cm。右肝转移病灶及多处淋巴结转移病灶消失，双肺转移病灶缩小，放射性浓聚减低。	PR

							顺铂（30mg）心包内灌注。第 1 年 12 月 23 日至第 2 年 1 月 14 日联合顺铂雾化吸入：10mg/次，2 次/日。第 2 年 1 月 18 日至第 2 年 1 月 30 日行第 2 周期恩度治疗，用量同前。第 1 年 12 月 25 日至第 2 年 1 月 19 日行培美曲赛®化疗：iv.500mg/m^2，每 3-4 周一次。因以上化疗无任何明显效果，于第 2 年 2 月 15 日至第 2 年 4 月 25 日改化疗方案为 DP 方案®：紫杉特尔 75mg/ m^2 第 1 天，顺铂 75mg/ m^2 第 1 天，联合特罗凯（150mg/日）治疗，共计 4 个周期，每周期 21 天。 于第 2 年 6 月 29 日行头颅伽马刀治疗。	右肺上叶原发病灶大小约 5.1 cm×3.2 cm 消失，纵隔肉肿大淋巴结及脑部转移病灶大小约 3.7 cm×2.6 cm 也基本消失。	CR
3	女	51	非小细胞肺癌	IV		第 1 年 5 月 29 日开始使用 rSIFN-co 治疗。隔日肌注 1 次 rSIFN-co：第 1 次肌注 9μg，第 2 次肌注 18μg，从第 3 次开始肌注 21μg，同时配合 rSIFN-co 雾化吸入：200μg/隔日。第 1 年 7 月 14 日开始隔日肌注 18μg 配合隔口雾化吸入 400μg	在此期间进行了 1 次头部病灶伽马刀治疗。		

[0723]

						rSIFN-co. 至第 1 年 9 月 16 日，用药持续 3 个多月。		
4	男	49	右肺小细胞肺癌	IV	第 1 年 3 月 25 日至 4 月 9 日给予第 1 周期 EP 方案[①]化疗：依托泊苷 100mg，顺铂 30mg。	于第 1 年 4 月 12 日开始使用 rSIFN-co 治疗。隔日肌注 1 次，第 1 次肌注 9μg，第 2 次肌注 15μg，从第 3 次开始肌注 18μg，配合喷雾吸入 rSIFN-co，隔日 1 次，0.5-2ml/次（200μg/ml）。从第 1 年 7 月 16 日开始肌注 21μg，配合喷雾吸入 rSIFN-co，但每次吸入的量变为 200μg。至第 2 年 3 月底结束第 1 周期（持续近 1 年）的治疗。在第 1 年 9 月因进行顺铂雾化吸入（1 次/山，10mg/次），暂停使用 rSIFN-co 1 个月。从第 2 年 10 月 9 日至第 3 年 1 月 26 日进行第 2 周期的治疗，用药方案为隔日肌注 18μg 的 rSIFN-co。	从第 1 年 3 月 25 日至第 1 年 9 月 10 日进行了 5 个周期的 EP 方案化疗，方案同前。 第 2 年 9 月 3 日行锁骨上病灶点介入冷冻消融术。 第 1 年 10 月起，配合 15 天的顺铂雾化吸入方案：每天雾化吸入 1 次，10mg/次，每 1 周期 15 天，共使用 2 个周期。	右肺尖原发病灶大小约 0.6cm×0.4cm 消失；右锁骨上结节大小约 2.6cm×2.2cm 病灶消失；纵隔内头臂干旁，右头臂静脉周围、上腔静脉周围、气管旁多发结节，部分融合大约 5.5cm×4.9cm 病灶消失。	CR
5	女	42	（右肱骨）转移性中分化肺腺癌	IV	第 1 年 2 月 23 日行右肱骨修复术。术后行 4 个疗程 DP 化疗方案[②]：紫杉特尔 75mg 第 1 天，顺铂 75mg 第 1 天。	第 1 年 4 月 15 日开始使用 rSIFN-co 治疗。隔日肌注 1 次，第 1 次肌注 9μg，从第 2 次开始肌注 21μg，至第 1 年 9 月 15 日，期间因化疗停药 1 月（化疗方案见下，顺铂雾化吸入），因身体原因停药 1 月，用药时间共计 3 个月。从第 1 年 9 月 16 日开始同时配合雾化吸入 rSIFN-co 每日 1ml(200μg/ml)，至第 2 年 2 月，联合用药时间共计 5 个月。第 2 年 9 月 15 日	从第 1 年 9 月 16 日开始联合顺铂雾化吸入 10mg/次（2 次/日），每个周期 15 天，共使用了 8 个周期。	右肺原发病灶、右肱骨及 T6 椎体放射性浓聚明显降低，盆骨、腰椎转移病灶及原气管间隙的肿大淋巴结基本消失。	CR

[0724]

6	男	39	左肺中/低分化腺癌	IV	第 1 年 9 月行第 1 周期（每周期 21 天）GP 化疗方案[9]：吉西他滨 1000mg/m^2 第 1、8 天+顺铂 75mg/ m^2 第 1 天。	开始 15μg 隔日肌注。第 1 年 10 月 12 日开始使用 rSIFN-co 治疗，每日 600μg 雾化吸入。第 1 年 12 月 12 日开始肌注 rSIFN-co，隔日 1 次，第 1 次肌注 9μg，第 2 次肌注 15μg，从第 3 次开始肌注 18μg。从第 2 年 3 月 12 日开始给予骨转移部位局部喷雾治疗，每日 4-5 次，每个部位每次剂量 70μg-139μg。	第 1 年 10 月 14 日起行第 2 周期 GP 化疗方案[9]治疗（方案同前）；第 1 年 11 月 24 日开始服用吉非替尼，每日 1 次，一次 1 片（250mg/片）。	原左肺原发病灶大小约 9 cm×3.5 cm 基本消失；左侧颈部肿大淋巴结大者约 1.0 cm×0.7 cm 消失；左侧锁骨上窝结节大约 1.2 cm×0.8 cm 消失；右侧颈根部结节大小约 1.4 cm×1.1 cm 消失；胸骨转移病灶消失，右侧胸锁关节、肋骨、脊柱骨盆骨转移病灶范围缩小，程度减轻。	CR
7	女	53	（左锁骨上淋巴结）转移性肺腺癌	IV		于第 1 年 7 月 31 日开始使用 rSIFN-co 治疗。隔日肌注 1 次，第 1 次肌注 9μg，第 2 次肌注 18μg，从第 3 次开始肌注 21μg。至第 2 年 1 月 2 日（总共 5 个月），患者使用 rSIFN-co 肌注共计 75 次。	在此期间，联合印度产[9]治易瑞沙（吉非替尼）治疗 1 年；每日 1 次，一次 1 片（250mg/片）。	右肺原发病灶及肉肺、全身多处骨转移病灶均有所缩小，放射性浓聚较前减低；肝脏转移病灶消失。	PR
8	女	68	右肺癌	IV		于第 1 年 7 月 21 日开始使用 rSIFN-co 治疗。隔日肌注 1 次，第 1 次肌注 9μg，第 2 次肌注 15μg，从第 3 次开始肌注 18μg，配合雾化吸入 rSIFN-co 每日 1 次 600μg。至第 1 年 10 月 31 日，持续用药 rSIFN-co 3 个月。	从第 1 年 7 月开始联合吉非替尼（易瑞沙）[9]治疗，每日 1 次，一次 1 片（250mg/片）。	原右肺下叶病灶大小约 3.0 cm×3.9 cm 及左髂骨内转移病灶基本消失。	CR
9	男	55	鳞状细胞癌	IIb		于第 1 年 3 月 18 日开始使用 rSIFN-co 治疗。雾化吸入 rSIFN-co 每日 1 次，每次吸入 600μg。至第 1 年 7 月 20 日使	从第 1 年 4 月 12 日开始第 1 周期化疗（GP 方案[9]：吉西他滨，1600mg/日，第 1、8 天；顺铂，	右肺原发病灶大小约 3.3 cm×2.4 cm×2.0 cm 基本消失，右肺门肿大淋巴结大小约 2.0	CR

[0725]

					用 rSIFN-co 治疗 1 个疗程（4 个月），雾化吸入共计 100 次。	40mg/日，第 1、3 天），每周期 21 天，共使用 4 个周期。联合恩度®每日给药 1 次，每次 7.5mg/m^2(1.2×10^{5}U/m^2)，连续给药 14 天为 1 周期，共使用 3 个周期。于第 1 年 5 月 10 日行第 2 周期化疗，方案同前。于第 1 年 6 月 7 日行第 3 周期化疗，方案同前。第 1 年 7 月 7 日行第 4 周期化疗，方案同前。共计 4 周期化疗治疗。	cm×2.2 cm 消失。	
10	女	48	左肺非小细胞肺癌	IIIb	第 1 年 3 月 9 日开始使用 rSIFN-co 治疗。隔日肌注 1 次，第 1 次肌注 18μg，从第 2 次开始肌注 21μg，至第 2 年 3 月，持续用药近 1 年。从第 1 年 4 月 29 日开始胸腔灌注 rSIFN-co，每隔 7 天灌 1 次，第 1、2 次 9μg×4 支，第 3 次 9μg×5 支，共计 3 次胸腔灌注治疗。第 2 年 7-8 月，在 CT 引导下，进行了 4 次介入手术对肺内较大病灶点注射 rSIFN-co，每次使用剂量为 21μg×10 支。		左肺原发病灶大小约 2.0 cm×2.0 cm 基本消失，恶性胸水消失。	CR
11	男	40	肠系膜淋巴结非霍奇金淋巴瘤	IV	第 1 年 8 月起行 7 次化疗，分别采用 5 次 CHOPE 方案和 2 次 MTX 方案，并于第 2 年 3 月行自体干细胞移	于第 3 年 6 月 9 日开始使用 rSIFN-co 治疗。使用 rSIFN-co 喷雾剂规格为 72μg/ml，每日对准鼻咽部及口腔喷 2-3 次 / 日。	于第 3 年 7 月至第 3 年 11 月 28 日开始给予 CHOP^{lite}化疗，共计 4 个周期，每个周期 21 天。	鼻咽及口咽周围软组织最厚处 3.0 cm 已完全消失，颌下、颈部及锁骨区大量的融合淋巴结最	PR

[0726]

					植。第 2 年 8 月起行 4 次化疗，分别采用 1 次 GCE 方案和 3 次 ESAP 方案，第 4 次化疗于第 2 年 11 月 26 日结束。第 3 年 1 月起行 6 次化疗，分别采用 3 次大剂量 CHOPE 方案、2 次 CMOP 方案和 1 次“博莱霉素+CHOP^{m}+甲氨蝶呤”方案，同时联合干细胞治疗。	至第 3 年 8 月 27 日，除因化疗（化疗方案见下面描述）停药 5 天外每天坚持使用。 于第 3 年 6 月 11 日开始行局部（颈部）淋巴结注射，15μg×10 支/隔日，以梅花点方式对准淋巴结局部注射，注射 2 次后改为颈淋巴系统处局部皮下注射，隔日 30μg/次，至第 3 年 8 月 27 日（2 月余）共计 10 次。	第 3 年 6 月 11 日开始行放疗，拟行 25 次，但因患者骨髓抑制明显，身体虚弱，于第 3 年 7 月 5 日停止放疗。	大的 7.4 cm × 2.4 cm × 14.6 cm 减小到 1.1 cm × 1.5 cm，明显缩小。	
12	男	67	右肺非小细胞肺腺癌	IIb	第 1 年 8 月 16 日开始给予 GP 方案®（吉西他滨 1000mg/m^{2}第 1、8 天+顺铂 75mg/ m^{2}第 1 天）化疗 2 个周期及顺铂胸腔内注射（每 7 天灌 1 次，每次用量 30-40mg，连行 5 次）。	第 1 年 11 月 10 日开始使用 rSIFN-co 治疗。隔日肌注 1 次，第 1 次肌注 9μg，第 2 次肌注 18μg，从第 3 次开始肌注 21μg。至第 2 年 10 月 27 日，持续用药近 1 年。		在治疗 2 个月后肿块由原来的大小约 3.1 cm×4.2 cm 减小到 2.2 cm×1.5 cm，在用药后约 3 个月是病灶再次缩小。	PR
13	男	63	（右肺上叶）低分化腺癌	IIIb	第 1 年 10 月 15 日行右上肺叶切除+淋巴结清扫+右肺下叶结节楔形切除术。	第 1 年 12 月 10 日开始接受 rSIFN-co 治疗。隔日肌注 1 次，第 1 次肌注 9μg，从第 2 次开始肌注 21μg。至第 2 年 4 月 9 日完成第一周期治疗。第 2 年 12 月至第 3 年 7 月完成第二阶段治疗，方案为隔日肌注 21μg/次。第 4 年 2 月 21 日至第 4 年 5 月 21 日完成第三阶段治疗，方案为隔日肌注 18μg/次。		原发病灶手术后肿瘤未出现复发或转移。	CR
14	男	44	非小细胞肺癌（低分化腺癌）	IIIb	第 1 年 10 月 20 日行右肺上叶切除术。	第 1 年 11 月 6 日开始使用 rSIFN-co 治疗。隔日肌注 1 次，第 1 次肌注 18μg，从第 2 次开始肌注 21μg。用药后 6 月，手		原病灶手术后肿瘤未见复发或转移。	CR

[0727]

					第2年5月10日完成第1阶段治疗。第3年3月18日开始第2阶段 rSIFN-co 治疗，隔日肌注 15μg/次，连续用药3月。第4年11月使用 rSIFN-co 肌注，15μg/次隔日，联合雾化吸入 300μg/日，连续3个月。				
15	男	68	肺癌伴全身多处转移	IV	第3年4月27日在局麻下行伽马刀治疗。第3年4月30日由核医学科行锶-89 治疗。从第1年12月至第3年6月口服吉非替尼（易瑞沙）治疗，每日1次，一次1片（250mg/片）。	第3年6月25日开始使用 rSIFN-co 治疗。每日局部腹股沟淋巴结注射 rSIFN-co：第1次 15μg×6 支，第2次 15μg×8 支，从第3次开始每次 15μg×10 支，至第3年7月20日，共计11次（在用药3次后出现严重腹泻，因此停药2周，后连续每日用药8次）。第3年8月18日至第3年9月16日非连续局部淋巴结注射6次，剂量为 15μg×10 支/次。第3年10月8日至第3年10月12日每隔两日局部淋巴结注射，剂量是 15μg×10 支/次。		盆腔肿块由原来的大小约 11.3 cm×4.9 cm 缩小到 7.52 cm×7.67 cm×6.72 cm。	PR
16	女	63	（直肠）高至中分化腺癌，局部为粘液腺癌，侵及肠壁深肌层并在系膜内形成癌性结节。	IIIb	第1年5月16日行腹腔镜辅助腹会阴联合直肠癌根治术。	第1年5月23日开始使用 rSIFN-co 治疗。隔日肌注 21μg/次。经干扰素治疗8个月，第2年2月停药，完成第1阶段的治疗。第3年1月至第3年4月进入第2阶段的治疗，隔日肌注 9μg/次，连续注射3个月。从第3年12月至第4年3月完成第3阶段的治疗，方案为隔		原发肿瘤病灶手术后未出现肿瘤复发或转移。	CR

[0728]

					以肌注 15μg/次。				
17	女	25	宫颈癌	Ib1		第 1 年 5 月 14 日开始使用 rSIFN-co 治疗。隔日肌注 1 次，第 1 次肌注 9μg，第 2 次肌注 15μg，从第 3 次开始肌注 18μg，配合子宫灌注每日 1 次，每次 1000μg，于病灶处保持 2 小时。子宫灌注治疗止于第 1 年 6 月 28 日（持续 1 个余月），肌注治疗止于第 1 年 9 月 12 日（持续 4 个月）。		宫颈恶性病变消失，高危型 HPV 转为阴性，宫颈涂片未见肿瘤细胞。	CR
18	男	64	前列腺癌	IV		从第 1 年 11 月 15 日开始使用 rSIFN-co 治疗。隔日肌注 1 次，第 1 次肌注 9μg，第 2 次肌注 15μg，第 3 次肌注 18μg，从第 4 次开始肌注 24μg。同时给予前列腺穿刺部位皮肤表面局部喷雾治疗，每日 4-5 次，每次剂量 70μg-139μg。第 1 年 12 月 15 日起肌注改为隔日 21μg 至第 2 年 7 月 1 日。	第 1 年 12 月 5 日至第 2 年 2 月 26 日行前列腺局部外放射治疗（EBRT）®38 次。	前列腺大小由原来的 4.7 cm×3.5 cm×5.6 cm 恢复正常；右侧坐骨直肠窝内两个淋巴结消失；膀胱底后壁、双侧精囊腺及直肠前壁受侵处恢复正常；前列腺癌特异抗原 PSA 恢复到正常范围。	CR
19	女	43	鼻部黑色素瘤术后伴双侧髋关节、双侧股骨、双侧肱骨、肋骨及双侧肩关节骨转移。	IV	于第 1 年 10 月 30 日及 11 月 30 日行两周期恩度 15mg d1-10 + 替莫唑胺 200mg d1-5，口服。 第 1 年 11 月 2 日行靶区放疗，放疗靶区位右侧上颌窦 + 左侧 1/4 上颌窦，双侧筛窦，额窦，右侧眼球旁组织，放疗剂量为 50Gy/25f，并于第 1 年 12 月 7 日完成	从第 1 年 12 月 21 日开始使用 rSIFN-co 治疗。隔日肌注 1 次，第 1 次肌注 9μg，第 2 次肌注 15μg，从第 3 次开始肌注 18μg。同时给予右肩部皮肤表面局部喷雾治疗，每日 4-5 次，每个部位每次剂量 70μg-139μg。 从第 2 年 2 月 27 日开始给予左肩及其他骨转移部皮肤表面局部喷雾治疗，每日 4-5 次，每		双侧肩关节，膝窝多发肿大淋巴结，右侧鼻窦及鼻腔肿瘤术后残腔内复发转移病灶，双侧髋关节，股骨上段骨折多发异常信号消失。	CR

[0729]

20	男	40	肺癌	IV		第 1 年 10 月 12 日开始使用重组高效复合干扰素（rSIFN-co）治疗。隔日肌注 1 次，第 1 次肌注 9μg，第 2 次肌注 15μg，从第 3 次开始肌注 21μg。第 1 年 12 月 28 日开始每天雾化吸入 1ml（200μg/ml），第 2 年 1 月 13 日开始每天雾化吸入 1ml(300μg/ml)。	3 次化疗：第 1 年 10 月 25 日至第 1 年 11 月 7 日行 GP-T2 方案(顺铂 d1-4 天，吉西他滨 d1)，因患者白细胞较低，第 8 天“吉西他滨”没有进行。第 1 年 11 月 26 日起行 DDP 40mg d1，2+MMC 10mg 化疗 1 次。第 1 年 12 月 6 日至第 1 年 12 月 18 日行 DP 方案(顺铂 40mg d1-2 30mg d3，多西他赛 120mg d1)。	减小了右下肺原发病灶，消除了纵膈内肿大淋巴结，胸水消退。	PR
21	女	75	肺癌伴骨转移	IIIb	白服中药，灵芝膏、孢子粉和吉非替尼。	第 1 年 3 月 10 日开始使用 rSIFN-co 治疗。隔日肌注 1 次，第 1 次肌注 9μg，第 2 次肌注 15μg，从第 3 次开始肌注 18μg。第 1 年 9 月 18 日至第 1 年 11 月 17 日间断雾化吸入 1ml/次(200μg/ml)。	吉非替尼。	消除了右上肺部原发病灶及纵膈内肿大淋巴结。	CR
22	男	50	肺癌伴肝转移	IIIa	第 1 年 10 月 3 日开始“紫杉醇+卡铂”化疗 4 周期。第 2 年 1 月 6 日行左下肺癌血氯冷冻消融术。第 2 年 1 月 13 口行肝转移瘤射频消融术。	第 2 年 1 月 19 日起隔日肌注 18μg/次，持续 2 个月，后隔日肌注 21μg/次。	第 2 年 3 月 17 日行第 3 次肝转移瘤射频消融术。于第 2 年 4 月 21 日行“紫杉醇+卡铂”肝局部灌注。	消除了左肺原发病灶，肝脏转移病灶无明显变化。	PR
23	男	57	左肺腺癌伴左侧胸膜、纵隔淋巴结及骨转移。	IV	第 1 年 9 月 9 日起行 PTX+DDP 化疗 1 周期；第 1 年 9 月 9 日行唑来膦酸 4mg 静滴治疗骨转移；	第 1 年 12 月 6 日开始使用 rSIFN-co 治疗。隔日肌注 1 次。第 1 次肌注 9μg，从第 3 次开始至第 2 年 2		消除了左肺原发病灶及全身多处转移病灶。	CR

[0730]

				年10月6日起行TP第2周期化疗。第1年10月29日起行TP第3周期化疗。	月15日肌注21μg。			
24	男	73	肺癌	IIIb	第1年3月19日开始使用rSIFN-co治疗。从第1年3月21日开始肌注，隔日1次，第1次肌注9μg，第2次肌注13.5μg，从第3次开始肌注21μg。第1年3月19日开始胸腔灌注21μg×6支，第1年3月25日胸腔灌注21μg×8支，第1年4月21日胸腔灌注21μg×10支，第1年4月30日胸腔灌注21μg×10支，第1年5月8日胸腔灌注21μg×10支，第1年5月15日胸腔灌注21μg×12支。		胸水减少。	PR
25	男	48	肺癌	IIIa	第1年11月19日开始使用rSIFN-co治疗。第1年11月19日至第1年11月25日隔日肌注9μg，第1年11月27日至第2年4月17日隔日肌注21μg。	放疗（时间方案不详）。		PD
26	女	51	肺癌脑转移	IV	自服“吉非替尼”。	第1年12月18日开始使用rSIFN-co治疗。第1年12月18日开始间断用药隔日肌注21μg。第3年5月7日至第4年1月，隔日肌注18μg。第3年5月17日至第3年9月18日雾化吸入100μg/天。第3年9月19日至第3年12月28日，雾化吸入400μg/天。第3年12月29日至第4年1月雾化吸入	盐酸厄洛替尼。	缩小了脑部转移病灶，肺部原发病灶无明显变化。	PR

[0731]

						300μg/天。			
27	男	46	左肺癌术后伴双肺转移。	IIb	第 1 年 5 月行左肺癌根治术，术后化疗，放疗（具体不详）。	第 2 年 8 月 22 日开始接受 rSIFN-co 治疗。隔日肌注 1 次，第 1 次肌注 9μg，从第 2 次开始肌注 21μg。			NC/SD
28	男	53	右上肺癌伴肺内及右侧胸腔转移。	IIb	第 1 年 1 月 20 日行 VATS 右上肺占位楔形切除，胸膜活检，胸膜结节烧灼。并于术后 3 天给予"唯美生"右胸腔灌注。	第 1 年 3 月 13 日开始接受 rSIFN-co 治疗。隔日肌注 1 次，第 1 次肌注 9μg，从第 2 次开始肌注 21μg。喷雾剂，鼻部喷，3 次/日。 第 1 年 7 月 27 日开始使用喷雾吸入，每日 1 次，每次 0.2ml(1mg/ml)。第 1 年 9 月 2 日行 21μg 肌注，隔日，喷雾吸入 200μg/日。第 1 年 10 月 15 日停用 rSIFN-co 治疗。			NC/SD
29	男	76	肺癌	IIIa	第 1 年 8 月 17 日右上肺癌切除术。	第 1 年 9 月 2 日开始使用 rSIFN-co 治疗。隔日肌注 1 次，第 1 次肌注 9μg，从第 2 次开始至第 1 年 9 月 20 日隔日肌注 18μg，第 1 年 11 月 22 日至第 2 年 4 月 27 日隔日肌注 21μg。第 2 年 4 月 29 日同时配合喷雾剂 40μg/ml 使用，喷鼻部，1 日 3 次。	第 3 年 3 月 11 日行肺部射频消融术。		NC/SD
30	男	47	肺腺癌脑转移	IV	第 1 年 12 月予以全颅放疗 30GY/10FX（10 次）。第 2 年 1 月 3 日开始行化疗 GP-T1 方案（健择 d1，8；DDP140mg d1）4 个周期。第 2 年 3 月服用吉非替尼。	第 2 年 7 月 18 日开始接受 rSIFN-co 治疗。隔日肌注 21μg/次，联合每日雾化吸入 1ml（200μg/ml）。持续用药 8 个月。		肺部结节减少（5 个月后），脑部病灶基本消退（6 个月后）。	PR

[0732]

31	男	71	右肺癌伴骨转移	IV		第 1 年 6 月 29 日开始使用 rSIFN-co 治疗。隔日肌注 1 次，第 1 次肌注 9μg，第 2 次肌注 13.5μg，从第 3 次开始肌注 18μg。第 1 年 8 月 20 日开始使用 rSIFN-co 喷雾剂(20μg/ml)，进行鼻腔和颈部淋巴结喷射治疗。第 1 年 9 月 16 日开始隔日注射 21μg 的 rSIFN-co。		PD
32	女	69	肺癌	IIb	第 1 年 3、4、5 月化疗 3 次，第 1 年 6 月 10 日开始服用吉非替尼。	第 2 年 7 月 9 日开始使用 rSIFN-co 治疗。隔日肌注 1 次，第 1 次肌注 9μg，第 2 次肌注 13.5μg，从第 3 次开始每次注射 18μg。每日雾化吸入 300μg。	吉非替尼。	肺部肿瘤缩小，肿大淋巴结消失。	PR
33	女	75	肺癌	IIIb	第 1 年 12 月 24 日于全麻下行“VATS 左肺下叶切除、淋巴结清扫术、部分胸主动脉外膜切除术”。	第 2 年 9 月 22 日开始使用 rSIFN-co 治疗。隔日肌注 1 次，第 1 次注射 4.5μg，第 2 次注射 9μg，第 3 次注射 13.5μg，第 4 次开始注射 18μg。第 2 年 9 月 29 日开始隔日注射 9μg。后改为每周注射 2 次。第 2 年 9 月 22 日开始根据胸水和病人耐受情况，隔 5 至 7 日灌注重组高效复合干扰素 1 次。每次 21μg×5 支。第 2 年 10 月 21 日嘱根据胸水和病人耐受情况，隔 3 日灌注 rSIFN-co 21μg×（6-8-10 支）。		PD
34	男	79	肺癌多发转移	IV		第 1 年 10 月 12 日开始接受 rSIFN-co 治疗。隔日肌注 18μg/次。联合每日雾化吸入 1ml	第 1 年 11 月接受脑部局部放疗 2 次，第 1 年 12 月中旬开始使用抗肿瘤	NC/SD

[0733]

						（200μg/ml）。第 1 年 12 月开始停用 rSIFN-co。	中药治疗。		
35	女	29	肺腺癌伴骨转移	IV	第 1 年 6 月 28 日起行 GP 化疗（健择 1.6g D1，8+顺铂 60mg D1，2）1 次。	第 1 年 7 月 1 日开始使用 rSIFN-co 治疗。隔日肌注 1 次，第 1 次肌注 15μg，从第 2 次开始肌注 18μg，并同时配合雾化吸入，每日 1 次，每次 600μg。	第 1 年 7 月 18 日至第 1 年 10 月 9 日行 3 周期化疗，GP 化疗方案；健择+顺铂。 第 1 年 12 月 18 日行肺部射频消融。于第 1 年 12 月开始间断服用吉非替尼。	原左肺下叶背段病灶明显缩小。	PR
36	女	73	卵巢癌	IIIb	第 1 年 5 月 19 日行“子宫全切术+双附件切除术+大网膜切除术+直肠高位切除+吻合术+膀胱破裂修补术+肿瘤细胞减灭术”。	第 2 年 2 月 13 日开始使用 rSIFN-co 治疗。隔日肌注 1 次，第 1 次肌注 9μg，第 2 次肌注 15μg，从第 3 次开始肌注 18μg。第 2 年 3 月 13 日开始隔日肌注 21μg，至第 2 年 5 月 21 日。		左侧胸腔积液消失，右侧胸腔积液减少。	PR
37	女	46	宫颈癌放化疗后	IV	第 1 年行放射治疗：DT 5040Gy/56 次，第 2 年 8 月行 PF 方案治疗及放疗，第 2 年 8 月 13 日行宫颈癌动脉灌注化疗术，主要药物：力朴素+卡铂。	第 2 年 11 月 30 日开始使用 rSIFN-co 治疗。隔日肌注 21μg。		子宫颈病变较前缩小（64 mm× 58 mm 至 52 mm× 40 mm）；左侧腹股沟肿大淋巴结消失。	PR
38	女	31	子宫内膜浆液性乳头状癌及透明细胞癌混合型	IV		第 1 年 8 月 1 日开始使用 rSIFN-co 治疗。隔日肌注 18μg。联合子宫滴注，每天 1 次，1 周后改为 5 天 1 次，每次使用 1ml（200μg/ml）。			NC/SD
39	女	41	宫颈低分化鳞状细胞癌	IIb2	第 1 年 6 月 3 日行腹腔镜下广泛全子宫+盆腔腹主动脉淋巴结清扫+双侧卵巢悬吊术。术后行 PT 化疗方案 1	第 1 年 11 月 26 日开始使用 rSIFN-co 治疗。隔日肌注 1 次，第 1 次肌注 9μg，从第 2 次开始肌注 15μg。共计用药 6 个月。	NK 细胞治疗。	高危型人乳头瘤病毒由阳性转为阴性。	CR

[0734]

				个周期。					PD
40	女	70	结肠肝曲癌术后伴双肺转移	IV	第1年5月4日行根治术切除术。第1年5月至第1年9月6次化疗，方案为XELOX，卡培他滨片3000mg，口服，第1-14天；草酸铂200mg，静滴，第1天。第2年10月26山行1周期化疗：草酸铂150mg，静滴QD第1天；西妥昔单抗600mg，静滴QD第1天；伊立替康240mg，静滴QD第2天；氟尿嘧啶2500mg，持续静滴48小时，于第2年11月至第3年8月中医治疗。	第4年3月17日开始使用rSIFN-co治疗。隔日肌注1次，第1次肌注9μg，从第2次开始肌注21μg。	第4年3月28日行右肺转移瘤射频消融术；第4年4月9日行右卜肺转移瘤氩氦冷冻消融术，术后出现右臂丛神经损伤。第4年5月5日及第4年6月13山分别2次行左肺转移瘤射频消融术，第4年5月27日行右下肺转移瘤离子置入术。第48年12月行2周期化疗，卡培他滨片3000mg，口服，d1-14。第5年3月9山行全身化疗，西妥昔单抗+力比泰。第5年3月23日开始加用阿瓦斯丁和NK细胞治疗。第5年4月21日至第5年5月19日行肝转移灶放疗。		NC/SD
41	男	57	结肠癌转移至肝	IV	分别于第1年8月和第1年9月12日行2次肝介入术。	第1年9月30日开始使用rSIFN-co治疗。隔日肌注1次，第1次肌注9μg，第1年10月2日至第1年12月10日隔日肌注21μg，第1年12月12日至第2年1月9日隔日肌注21-25.5μg，第2年1月11日至第2年7月17日隔日肌注21μg。肝癌体内注射，第2年1月15日21μg×5支，第2年1			

[0735]

42	女	47	胆管癌术后伴肝转移	IV	第 1 年 5 月 31 日诊断为肝胆管腺癌，并行肝胆管癌根治术。第 2 年 11 月 23 日行右肝后叶、尾叶包块切除术+腹腔淋巴结清扫术+I^{125} 离子植入术+腹腔引流术。	月 22 日 21μg×8 支，第 2 年 2 月 1 日 21μg×10 支。	第 3 年 6 月 18 日行卵巢癌手术。	肝脏左右叶多发占位病变范围明显缩小，数目也有减少。	PR
43	女	50	肝内胆管细胞癌伴肝内转移	IV	第 1 年 11 月 8 日行右半肝切除+胆囊切除+腹腔淋巴结清扫术。第 1 年 12 月 22 日行 TACE 术。第 2 年 6 月 4 日行第 2 次肝脏 TACE 术。第 2 年 7 月 2 日行连续性肝动脉化疗灌注（顺铂+表阿霉素+5Fu）。第 2 年 8 月 2 日行第 3 次 TACE 术。第 2 年 9 月行肝内多发灶氩氦冷冻消融术。第 2 年 11 月 7 日行第 2 次氩氦冷冻消融术。	第 2 年 11 月 15 日开始使用 rSIFN-co 治疗。隔日肌注 9μg，第 2 年 11 月 21 日至第 3 年 5 月 20 日隔日肌注 21μg。			PD
44	男	58	肝癌伴肺转移	IV	第 1 年做肝移植术。第 4 年 7 月 6 日行左肺上叶包块楔形切除术。	第 4 年 9 月 5 日开始使用 rSIFN-co 治疗。第 4 年 9 月 5 日至第 4 年 9 月 9 日隔日肌注 9μg 。第 4 年 9 月 11 日至第 4 年 10 月 23 日隔日肌注 18μg。第 4 年 10 月 25 日至第 5 年 2 月 25 日隔日肌注 21μg。			PD
45	男	40	肝癌伴肝内转移	IV	第 1 年 8 月 9 日行肝动脉栓	第 1 年 8 月 21 日开始使用		原左肝巨大占位明显缩	PR

[0736]

				塞术。	rSIFN-co 治疗。隔日肌注 1 次，第 1 次肌注 9μg，从第 2 次开始肌注 18μg。第 1 年 9 月 17 日至第 2 年 2 月 1 日隔日肌注 21μg。		小，腹膜后即腹主动脉旁肿大淋巴结消失。	
46	女	37	乳腺癌术后淋巴结转移	IIIc	第 1 年 6 月 3 日行保乳手术，腋下有 1/11 淋巴结。术后做 6 次化疗（主要药物为：吡柔吡星），化疗完 1 个月后又做 33 次放疗。 第 2 年 1 月再次行转移淋巴结切除术后行“多帕菲+希罗达”化疗 4 次。	第 2 年 5 月 18 日开始使用 rSIFN-co 治疗。至第 2 年 9 月 16 日隔日肌注 18μg。			PD
47	女	58	乳腺癌术后复发	IV	第 1 年 7 月开始化疗 6 周期（具体不详）后于第 1 年 12 月 26 日行左乳全切术并淋巴结清扫术。术后经多次化疗（具体不详），于第 2 年 7 月出现左胸积液，用“紫杉醇”化疗 2 个周期好转。	第 3 年 2 月 5 日开始使用 rSIFN-co 治疗。第 3 年 2 月 5 日至第 3 年 5 月 23 日胸腔灌注 21μg ×（5-7-8-10-13 支）/次，第 3 年 5 月 30 日至第 3 年 7 月 11 日左前胸壁点局部注射 5 次，1 周 1 次，21μg × 8 支 / 次。第 3 年 7 月 14 日至第 3 年 9 月 30 日隔日肌注 21μg。	口服：他莫昔芬，依西美坦（意大利），阿那曲挫片。卡铂联合 rSIFN-co 胸腔灌注。		PD
48	女	45	左乳癌术后	IIa	第 1 年 8 月 22 日行左乳保乳术及乳癌根除术+右乳腺叶切除术。	第 2 年 3 月 5 日开始使用 rSIFN-co 治疗。隔日 1 次，第 1 次肌注 9μg，第 2 次肌注 15μg，第 3 次肌注 18μg，从第 4 次开始肌注 21μg。第 3 年 4 月 23 口开始隔口肌注 18μg。第 2 年 6 月 26 日停药至第 3 年 4 月 20 日。		左侧乳腺保乳术后 2 年，双侧乳腺皮下层清晰，未见异常；双乳未见确切团块。	CR
49	女	39	乳腺癌术后复发	IV	第 1 年 11 日行右侧乳腺癌根治术后并化疗（具体不	第 2 年 11 月 29 日开始使用 rSIFN-co 治疗。第 2 年 11 月 29			NC/SD

[0737]

					详)。	日至第 2 年 12 月 20 日局部注射 4 次，15μg× 6 支/次。 第 2 年 12 月 11 日至第 2 年 12 月 20 日肌注 9μg/隔日。 第 3 年 1 月 31 日至第 3 年 4 月 22 日隔日肌注 21μg。			
50	男	64	胃癌根治术后	IV	第 1 年 3 月 15 日行“胃癌根治手术”。	第 1 年 4 月 14 日开始使用 rSIFN-co 治疗。隔日 1 次，第 1 次肌注 9μg，从第 2 次开始肌注 18μg。第 1 年 9 月 1 日至第 2 年 1 月 22 日隔日肌注 15μg。第 2 年 1 月 24 日至第 2 年 8 月 29 日隔日肌注 21μg。第 2 年 9 月至 11 月停药 2 月。第 2 年 11 月 28 日至第 2 年 12 月 24 日，B 超引导下腹腔病灶部注射 4 次，21μg x (8-10 支)/次。第 2 年 11 月 13 日至第 3 年 3 月 16 日隔日肌注 21μg。			PD
51	男	59	胃癌腹腔转移	IV	第 1 年 10 月至第 3 年 5 月行了 9 次化疗（方案不详）。	第 3 年 11 月 2 日开始使用 rSIFN-co 治疗。腹腔灌注，隔日 1 次，第 1 次 15μg×8 支，第 2 次 15μg×12 支，第 3 次 15μg×14 支，第 4 次 15μg×16 支，至第 3 年 11 月 10 日，共计用药 4 次。		腹水明显减少，腹水中癌细胞消失。	PR
52	女	73	胰腺癌	III		第 1 年 12 月 27 日开始使用 rSIFN-co 治疗。隔日肌注 9μg。第 2 年 1 月 2 日至第 2 年 9 月 15 日隔日肌注 21μg。		门腔间隙病灶缩小。	PR
53	男	73	前列腺癌盆腔转	IV	口服康士得，诺雷得，氟他	第 1 年 11 月 30 日开始使用	康士得。	消除或缩小盆腔部分转	NC/S

[0738]

			移			rSIFN-co 治疗。隔日 1 次，第 1 次肌注 9μg，从第 2 次开始肌注 21μg。腹腔灌注 7 次，21μg×8 支/次。	第 1 年 12 月 12 日起行 3 维适形放疗 24 次（60Gy 2.5 X 24 次）。	移病灶。	D
					胺。第 1 年 1 月 16 日行去势手术。第 1 年 6 月 26 日行对盆腔一个较大淋巴结射频消融。第 1 年 7 月 18 日行碘 125 粒子植入手术。				
54	女	46	胃肠道间质细胞瘤	Ib	第 1 年 7 月 13 日进行十二指肠肿瘤切除手术。第 1 年 11 月 16 日行十二指肠术后放疗。	第 1 年 12 月开始接受 rSIFN-co 治疗。隔日 1 次，第 1 次肌注 9μg，从第 2 次开始肌注 21μg。用药 6 个月。从第 3 年至第 4 年 8 月为第 2 次用药（接受用药 3 个月）。第 4 年 9 月 26 日接受 rSIFN-co 第 3 次治疗。		影像学检查未见明显肿瘤复发及转移征象。	CR
55	男	16	胚胎性横纹肌肉瘤术后转移	IV	于第 1 年 7 月 29 日起行 4 周期化疗（主要药物为：表阿霉素、奥沙利铂）。第 1 年 9 月 1 日行左上胸部横纹肌肉瘤放疗。	第 2 年 2 月 2 日开始使用 rSIFN-co 治疗。隔日 1 次，第 1 次肌注 9μg，第 2 次肌注 15μg。第 2 年 4 月 21 日至第 2 年 5 月 19 日隔日肌注 18μg。第 2 年 5 月 21 日至第 2 年 7 月 11 日隔日肌注 21μg。第 2 年 7 月 13 日至第 2 年 11 月 5 日隔日肌注 9μg。第 2 年 11 月 7 日至第 2 年 12 月 2 日隔日肌注 18μg。第 2 年 12 月 4 日至第 3 年 3 月 25 日隔日肌注 21μg。淋巴结及瘤体内注射 4 次，第 2 年 11 月 12 日至第 2 年 11 月 28 日 21μg×8 支/次。			PD
56	女	17	淋巴瘤	III		第 1 年 12 月 29 日开始使用 rSIFN-co 治疗。第 2 年 2 月 24 日至第 2 年 4 月 22 日隔日肌注 21μg。第 2 年 4 月 24 日至第 2	第 2 年春节后接受 2 次化疗。配合排毒性质中	淋巴瘤明显减小。呼吸，进食功能已恢复正常，右耳从无听力恢复至微弱听力。	PR

[0739]

					年6月5日隔日肌注18μg。第1年12月29日至第2年2月18日，颈部瘤体内注射，隔日1次，21μg×（8-10-12-12-12-13-15支）第2年3月24日21μg×10支/次 第2年4月25日至第2年5月5日，9μg×20-23支/次，第2年5月7日至第2年5月25日，1ml/次，500μg/ml。	药治疗。		NC/SD
					第1年1月手术，第1年9月再次手术，术后接受放化疗（具体不详）。第2年1月出次接受放化疗（具体不详）。第3年1月再次复发，又接受放化疗(具体不详)。第4年1月复发，接受超声刀和中药治疗。	第4年2月9日开始使用rSIFN-co治疗。隔日肌注21μg。臀部瘤体内每2-3天注射21μg×4支/次。	中药		NC/SD
57	女	19	右臀部恶性神经癌术后复发	IIIc					
58	女	61	右胸部转移性低分化鳞癌术后	IIIa	第1年6月11日行右前胸壁肿瘤切除术。	第1年7月7日开始使用rSIFN-co治疗。隔日1次，第1次肌注9μg，从第2次开始肌注21μg，用约至第2年1月6日。	于第1年7月7日至第1年8月8日行右上胸壁转移癌术后放疗。		NC/SD

[0740] 实施例3：本发明重组干扰素治疗典型患者的临床资料（19例）

[0741] 以下是截止至2012年7月1日的本发明重组干扰素治疗19例患者的临床资料

（患者编号 1-19 分别与上述实施例 2 的 58 例多种癌症患者临床治疗汇总表中的患者 1-19 一一对应）。

[0742] 患者 1非小细胞肺癌 ;rSIFN-co 肌注联合放疗治疗，经过治疗消除了右肺门处病灶及纵隔内淋巴结转移病灶。

[0743]

患者 1	性别：男	年龄：53 岁
病理诊断：	鳞状细胞癌	
临床、病理分期①：	IIIb 期 $T_3N_2M_0$	
使用 rSIFN-co 前的治疗方案：	第 1 年 10 月 14 日至第 1 年 11 月 25 日行 DP 方案⑧：紫杉特尔 75mg 第 1 天，顺铂 75mg 第 1 天，共计化疗 2 周期，每个周期 21 天。	
治疗方案：rSIFN-co 联合放疗治疗	第 1 年 11 月开始使用重组高效复合干扰素治疗。隔日肌注 1 次，第 1 次肌注 9μg，第 2 次肌注 15μg，从第 3 次开始肌注 18μg。治疗持续至第 3 年 2 月，期间 rSIFN-co 治疗停药 1 个月（在第 2 年 4 月），共计用药时间 15 个月。 第 1 年 12 月 2 日开始行右肺+纵隔淋巴结放疗⑨，DT40Gy，继行 X-刀治疗，DT20Gy。	
rSIFN-co 疗效评价：	CR⑩（右肺门原发病灶消失治愈。）	
生存期:	第 1 年 10 月～第 8 年 7 月截止统计日期约 80 个月，患者仍然健在，正常生活工作，且影像学检查未见复发及转移病灶。	
使用 rSIFN-co 前影像学诊断：	化疗后第 1 年 11 月 25 日 CT 示： 右肺门肿物向腔内生长，突入右主支气管，使其闭塞，右肺上叶不张；右肺下叶多发浅淡小结。提示肿瘤进展。	

[0744]

	患者呼吸音消失，呼吸困难。
使用 rSIFN-co 后影像学诊断：	第 2 年 1 月 4 日 CT 示： 右肺门肿物较前缩小 ，右上肺不张较前缓解，纵隔内部分淋巴结有所缩小。 第 2 年 6 月 12 日 CT 提示： 纵隔内淋巴结较前缩小，右肺浸润有所吸收。 用药 12 月后第 2 年 11 月 8 日 CT 成像参见图 3a 箭头所示原病灶处。 用药 15 月后第 3 年 2 月 1 日 CT 成像参见图 3b 箭头所示原病灶处。 第 3 年 10 月 19 日 CT 提示： 右肺门稍饱满，右肺下叶片状浸润较前部分吸收，余部分不明显。
附图 3 说明：	经过 12 月的治疗，右肺病灶明显吸收缩小，在用药 15 个月时，病灶未见增大和转移。

[0745] 患者 2非小细胞肺腺癌伴双肺、肝及淋巴结等全身多处转移；rSIFN-co 肌注、雾化吸入联合化疗（GP 方案）及重组人血管内皮抑制素（恩度）治疗，经过治疗后肺部原发病灶明显缩小，消除了肝区及多处淋巴结转移病灶。

[0746]

患者 2	性别：男	年龄：40 岁
病理诊断：	肺腺癌	
临床、病理分期[①]：	$T_3N_3M_1$ IV 期	
使用 rSIFN-co 前的治疗方案：	第 1 年 1 月行 1 周期（每周期 21 天）全身化疗（紫杉特尔+卡铂）。	
治疗方案：rSIFN-co 联合化疗及其	第 1 年 4 月 14 日开始使用重组高效复合干	

[0747]

他生物治疗	扰素治疗。隔日肌注 1 次，第 1 次肌注 9μg，第 2 次肌注 15μg，第 3 次肌注 18μg，从第 4 次开始肌注 21μg。配合 rSIFN-co 雾化吸入，每日 1 次，第 1 次吸入 300μg，第 2 次吸入 500μg，从第 3 次开始吸入 600μg。rSIFN-co 用药至第 2 年 4 月。 第 1 年 4 月 20 日至第 1 年 9 月 3 日联合恩度®：每日给药，每次 7.5mg/m^2(1.2×10^5U/m^2)，连续给药 14 天为 1 周期，共进行了 4 个周期的治疗，以及同时联合 GP 方案⑨：吉西他滨 1600mg 第 1、8 天，顺铂 40mg 第 1-3 天，一个疗程为 15 天，共连续进行了 4 个周期的治疗。第 1 年 7 月 19 日行了 1 次顺铂心包内灌注（用量 30mg）。第 1 年 12 月 23 日至第 2 年 1 月 14 日联合顺铂雾化吸入：10mg/次（2 次/日）治疗。于第 2 年 1 月 18 日至第 2 年 1 月 30 日行第 2 周期恩度治疗，（用量同前）。于第 1 年 12 月 25 日至第 2 年 1 月 19 日行培美曲赛®化疗(iv.500mg/m^2,每 3-4 周一次)治疗。因以上化疗无明显效果，于第 2 年 2 月 15 日至第 2 年 4 月 25 日改化疗方案为 DP 方案®（紫杉特尔 75mg/ m^2 第 1 天，顺铂 75mg/ m^2 第 1 天），联合特罗凯（150mg/日）治疗，共计 4 个周期（每周期 21 天）。 于第 2 年 6 月 29 日行头颅伽马刀治疗。
rSIFN-co 疗效评价：	PR②（原右肺上叶病灶由原来的大小约 10.2 cm×8.2 cm×7.7 cm 减小到 1.2 cm×1.4 cm；右肝及多处转移淋巴结消失，双肺转移病灶缩小，放射性浓聚减低。）

[0748]

生存期:	第 1 年 1 月 20 日～2 第 2 年 8 月 3 日（约 18 个月）
使用 rSIFN-co 前影像学诊断：	使用 rSIFN-co 后影像学诊断：
第 1 年 4 月 19 日 PET/CT 示（参见图 4a 箭头所示病灶处）： 1.右肺上叶见团块影，范围约 10.2×8.2×7.7cm，CT 值约 38.8Hu；符合中央型肺癌； 2.气管右侧、右颈根部、胰头右旁多发淋巴结转移；最大约 1.4×1.1cm。 3.双肺弥漫性分布大量粟粒样小结节影伴放射性摄取增高，双肺弥漫转移； 4.肝右叶转移灶最大约 1.2×0.9 cm。	第 1 年 6 月 18 日 PET/CT 示（参见图 4b 箭头所示原病灶处）： 1.原右肺上叶肿块 1.2×1.4cm，病灶范围较前显著缩小，放射浓聚较前显著降低，SUV 最大值 2.9，平均值 2.1； 2.原气管右侧、右颈根部、胰头旁多发淋巴结转移灶已消失； 3.余双肺广泛散在分布斑片、云絮及网状影伴放射性摄取轻度增高，未见占位及实变影，较前病灶范围明显缩小放射性摄取较前显著减低； 4.原肝右叶转移灶（2 个）消失。
附图 4 说明：	经过 2 个月治疗，双肺上叶病灶明显缩小或消失。

[0749] 患者 3非小细胞肺癌伴脑转移；rSIFN-co 肌注、雾化吸入联合伽马刀治疗，经治疗后消除了右肺原发病灶及脑部转移病灶。

[0750]

患者 3	性别：女	年龄：51 岁
病理诊断：	无	
临床、病理分期①：	$T_2N_2M_1$. IV 期	
使用 rSIFN-co 前的治疗方案：	无	
治疗方案：rSIFN-co 联合伽马刀治疗	第 1 年 5 月 29 日开始使用重组高效复合干扰素治疗。隔日肌注 1 次。第 1 次肌注 9μg，第 2 次肌注 18μg，从第 3 次开始肌注 21μg，同	

[0751]

	时配合 rSIFN-co 喷雾吸入（200μg/隔日）使用。第 1 年 7 月 14 日开始隔日肌注 18μg，配合喷雾 400μg rSIFN-co 吸入隔日使用。至第 1 年 9 月 16 日，持续用药 3 个多月。 在此期间进行了 1 次头部病灶伽马刀治疗。
rSIFN-co 疗效评价：	CR©（右肺上叶原发病灶大小约 5.1 cm×3.2 cm 消失，纵隔内肿大淋巴结及脑部转移病灶大小约 3.7 cm×2.6 cm 也基本消失。）
生存期:	第 1 年 5 月～第 2 年 6 月（约 13 个月）
使用 rSIFN-co 前影像学诊断：	使用 rSIFN-co 后影像学诊断：
第 1 年 5 月 14 日肺 CT 示（参见图 5a 箭头所示病灶处）： 右肺尖见不规则软组织密度影，大小约 5.1 cm×3.2 cm，边界欠清，与前胸膜宽基地相连，附近纵隔内见肿大的淋巴结。影像诊断：右肺尖占位性病变。 第 1 年 5 月 14 日脑部 CT 示（参见图 6a 箭头所示病灶处））： 双侧额，颞，顶叶见多发混杂密度影，周围见低密度影环绕，以右侧为着，右侧侧脑室受压变窄，中线结构向左侧移位元。右额叶病灶径线约为 3.7 cm×2.6 cm。影像诊断：脑内多发占位性病变。	第 1 年 9 月 16 日头部（图 6b）及胸部（图 5b）CT 示： 1.右肺上叶纵隔旁可见不规则密度增高影，考虑右肺炎症；胸廓对称，纵隔内血管间隙清晰，未见肿大淋巴结。（参见图 5b 箭头所示原病灶处） 2.右额叶、左颞叶可见不规则低密度区。右侧侧脑室前角变窄。脑裂及脑沟未见增宽。脑中线结构居中。（参见图 6b 箭头所示原病灶处）
附图 5 说明：	经过 3 个月治疗，原右肺尖占位完全消失。
附图 6 说明：	经过治疗，颅内转移灶消失。

[0752] 患者 4小细胞肺癌伴纵隔淋巴结及锁骨上转移；rSIFN-co 肌注、雾化吸入联合化疗（顺铂雾化、EP 方案）、锁骨上病灶点介入术治疗，经过治疗后消除了右肺原发病灶、纵隔内淋巴结及锁骨上转移病灶。

[0753]

患者 4	性别：男	年龄：49 岁
病理诊断：	小细胞肺癌	
临床、病理分期①：	$T_4N_3M_1$ IV 期	
使用 rSIFN-co 前的治疗方案：	第 1 年 3 月 25 日至第 1 年 4 月 9 日给予第 1 周期 EP⑦方案化疗：依托泊苷 100mg，顺铂 30mg。	
治疗方案：rSIFN-co 联合化疗、介入治疗	于第 1 年 4 月 12 日开始使用重组高效复合干扰素治疗。隔日肌注 1 次，第 1 次肌注 9μg，第 2 次肌注 15μg，从第 3 次开始肌注 18μg，配合喷雾吸入 rSIFN-co，隔日 1 次，0.5-2ml/次（200μg/ml）。从第 1 年 7 月 16 日开始肌注 21μg，配合喷雾吸入 rSIFN-co，但每次吸入的量变为 200μg。至第 2 年 3 月底结束第 1 周期（持续近 1 年）的重组高效复合干扰素的治疗。在第 1 年 9 月因进行顺铂雾化吸入（10mg/次，1 次/日），暂停使用 rSIFN-co 1 个月。从第 2 年 10 月 9 日至第 3 年 1 月 26 日进行第 2 周期的治疗，用药方案为隔日肌注 18μg 的 rSIFN-co。 从第 1 年 3 月 25 日至第 1 年 9 月 10 日进行了 5 个周期的 EP 方案化疗，方案同前。第 2 年 9 月 3 日行锁骨上病灶点介入冷冻消融术。 第 1 年 10 月起，配合 15 天的顺铂雾化吸入方案，每天雾化吸入 1 次，10mg/次，每 1 周期 15 天，共使用 2 个周期。	

[0754]

rSIFN-co 疗效评价：	CR②（右肺尖原发病灶大小约 0.6 cm×0.4 cm 消失；右锁骨上结节大小约 2.6 cm×2.2 cm 病灶消失；纵隔内头臂干旁，右头臂静脉周围、上腔静脉周围、气管旁多发结节，部分融合大约 5.5 cm×4.9 cm 病灶消失。）
生存期：	第 1 年 3 月 23 日～第 4 年 7 月截止统计日期约 39 个月，患者仍然健在，正常生活工作，且影像学检查未见复发及转移病灶。
使用 rSIFN-co 前影像学诊断：	使用 rSIFN-co 后影像学诊断：
化疗后第 1 年 4 月 8 日 PET/CT 示（参见图 7a-8a 箭头所示病灶）： 1.右肺尖可见一小结节，边缘毛糙伴浅分叶，直径 0.6×0.4 cm，PET 显示异常放射性浓聚，SUV 值 4.1。 2.右锁骨上可见结节，边界欠清，大小约 2.6×2.2 cm，相应 PET 显示异常放射性浓聚，SUV 值 9.1。 3.纵隔内头臂干旁，右头臂静脉周围、上腔静脉周围、气管旁多发结节，部分融合，边界欠清相应 PET 显示异常放射性浓聚，SUV 值 11.5，大约 5.5 cm×4.9 cm，考虑为淋巴结转移。 4.邻近上腔静脉不除外受累。	第 1 年 12 月 24 日 PET/CT 示（参见图 7b-8b 箭头所示原病灶处）： 1.原右肺尖小结节此次未见明确显示。 2.右锁骨上结节较前明显减小，相应 PET 显示异常放射性浓聚，SUV 值 4.7。 3.原纵隔内头臂干旁，右头臂静脉周围，气管旁结节，此次未见明确显示。 4.纵隔内上腔静脉周围多发小结节，相应 PET 显像未见明显放射性浓聚，提示病灶代谢减低活性被抑制。 第 3 年 7 月 26 日 PET/CT 示： 1.右肺上叶条索，下叶背段斑片，此次 PET 显像仍未见明显放射性浓聚。 2.右锁骨上结节冷冻治疗后，此次右锁骨上仍未见明显结节及肿块，PET 显像未见明显异常放射性浓聚，余全身 PET 代谢显像较前未见明显变化。 第 4 年 2 月 7 日 PET/CT 示： “右肺小细胞肺癌”治疗后，与第 3 年 7 月 26 日 PET/CT 片比较：

[0755]

	1、左侧鼻咽后壁略增厚，PET 显像可见放射性浓聚，考虑为炎性病变； 2、双侧劲深及颏下多发小结节，PET 显像未见异常放射性浓聚，考虑为淋巴结炎性反应性增生； 3、胃大弯侧胃壁略增厚，PET 显像可见放射性浓聚，考虑为炎性病变； 4、余全身 PET 代谢显像及 CT 显像较前未见明显变化。
附图 7 说明：	经过近 8 个月的治疗，原右肺尖病灶消失。
附图 8 说明：	经过近 8 个月的治疗，原纵隔内转移病灶消失。

[0756] 患者 5非小细胞肺癌伴右肱骨转移术后 ;rSIFN-co 肌注、雾化吸入联合化疗（顺铂雾化吸入）治疗，经治疗后消除了右肺门、气管间隙淋巴结及脊柱多处转移病灶。

[0757]

患者 5	性别：女	年龄：42 岁
病理诊断：	（右肱骨）转移性腺癌（中分化腺癌）	
临床、病理分期①：	$T_2N_2M_1$ IV 期	
使用 rSIFN-co 前的治疗方案：	第 1 年 2 月 23 日行右肱骨修复术。术后行 4 个疗程 DP 化疗方案②：紫杉特尔 75mg 第 1 天，顺铂 75mg 第 1 天。	
治疗方案：rSIFN-co 联合化疗治疗	第 1 年 4 月 15 日开始使用重组高效复合干扰素治疗。隔日肌注 1 次，第 1 次肌注 9μg，从第 2 次开始肌注 21μg，至第 1 年 9 月 15 日，期间因化疗停药 1 月（化疗方案见下，顺铂雾化吸入），因身体原因停药 1 月，用药时间共计 3 个月。从第 1 年 9 月 16 日开	

[0758]

	始同时配合雾化吸入 rSIFN-co 每日 1ml(200μg/ml)，至第 2 年 2 月，联合用药时间共计 5 个月。第 2 年 9 月 15 日开始 15μg 隔日肌注。 从第 1 年 9 月 16 日开始联合顺铂雾化吸入 10mg/次（2 次/日），每个周期 15 天，共使用了 8 个周期。
rSIFN-co 疗效评价：	CR②（右肺原发病灶、右肱骨及 T6 椎体放射性浓聚明显降低，盆骨、腰椎转移病灶及原气管间隙的肿大淋巴结基本消失。）
生存期:	第 1 年 2 月～第 4 年 7 月截止统计日期约 40 个月，患者仍然健在，正常生活工作，且影像学检查未见复发及转移病灶。
使用 rSIFN-co 前影像学诊断：	使用 rSIFN-co 后影像学诊断：
术后第 1 年 2 月 26 日 PET/CT 示（参见图 9a-11a 箭头所示病灶）： 1.右肺上叶前端可见一类圆形结节影，大小约 24 mm×19 mm×18 mm。 2.右上肺门、气管前间隙淋巴结转移，右肱骨上段骨转移。 3.右肱骨上段浓集灶，多为术后修复期改变。 4.胸、腰段椎体及双侧髂骨核素代谢增高，多发骨转移高度可疑。 5.右肺上叶后微小结节影（大小 2mm），建议观察。 化疗后第 1 年 4 月 13 日 CT 示： 右上肺癌、右肺微结节影、局限性胸膜增厚、纵隔淋巴结肿大。提示化疗	第 2 年 3 月 2 日 PET/CT 示（参见图 9b-11b 箭头所示原病灶处）： 1.右肺上叶前段软组织块影形态、大小、密度较前无明显变化，放射性核素摄取程度明显减低（SUVmax 由 9.5 减至 1.7）； 2.气管前间隙淋巴结葡萄糖代谢恢复正常，右上肺门钙化淋巴结放射性核素轻度浓聚； 3.右肱骨上段、T6 椎体放射性核素浓聚减低（SUVmax 分别由 6.3 和 3.8 分别减低至 2.9 和 1.7）； 4.腰椎、骶骨、骨盆未见明显放射性核素异常分布； 5.右肺中叶外侧段、左肺下叶外基地段微结节大者同前多次扫描所见，无放射性核

[0759]

无效，疾病进展。	素异常分布。
附图 9 说明：	经过治疗，右肺原发病灶放射性核素摄取代谢明显降低。
附图 10 说明：	右肱骨上段病灶放射性核素浓聚减低。
附图 11 说明：	经过治疗，盆骨转移病灶消失。

[0760] 患者 6非小细胞肺癌伴纵隔内、左侧颈部，右侧颈根部、左侧锁骨上窝多发淋巴结转移；左侧胸腔积液；脊柱、双侧肋骨、右侧锁骨关节、胸骨、左侧骶骨等多发骨转移，且全身疼痛明显，rSIFN-co 肌注、雾化吸入、病灶部位局部喷雾联合化疗（GP 方案）及吉非替尼（易瑞沙）治疗，消除了左肺原发病灶，缩小了全身骨转移病灶，全身疼痛缓解。

[0761]

患者 6	性别：男	年龄：39 岁
病理诊断：	中-低分化腺癌	
临床、病理分期①：	$T_4N_3M_{1b}$ IV 期	
使用 rSIFN-co 前的治疗方案：	第 1 年 9 月行第 1 周期（每周期 21 天）GP 化疗方案②：吉西他滨 1000mg/m^2，第 1、8 天+顺铂 75mg/ m^2，第 1 天。	
治疗方案：使用 rSIFN-co 联合化疗及其他生物治疗	第 1 年 10 月 12 日开始使用重组高效复合干扰素治疗，每日 600μg 雾化吸入。第 1 年 12 月 12 日开始肌注重组高效复合干扰素，隔日 1 次，第 1 次肌注 9μg，第 2 次肌注 15μg，从第 3 次开始肌注 18μg。从第 2 年 3 月 12 日 开始给予骨转移部位局部喷雾治疗，每日 4-5 次，每个部位每次剂量 70μg-139μg。第 1 年 10 月 14 日行第 2 周期 GP 化疗方案②治疗（方案同前）； 第 1 年 11 月 24 日开始服用吉非替尼，每日	

[0762]

	1 次，一次 1 片（250mg/片）。
rSIFN-co 疗效评价：	CR[②]（原左肺原发病灶大小约 9 cm×3.5 cm 基本消失；左侧颈部肿大淋巴结大者约 1.0 cm×0.7cm 消失；左侧锁骨上窝结节大小约 1.2 cm×0.8 cm 消失；右侧颈根部结节大小约 1.4 cm×1.1 cm 消失；胸骨转移病灶消失，右侧胸锁关节、肋骨、脊柱骨盆骨转移病灶范围缩小，程度减轻。）
生存期:	第 1 年 9 月 27 日～第 2 年 7 月截止统计日期约 10 个月，患者仍然健在，正常生活及工作，且病情稳定。
使用 rSIFN-co 前影像学诊断：	使用 rSIFN-co 后影像学诊断：
第 1 年 9 月 21 日胸部 CT 示（参见图 12a 箭头所示原发病灶处）： 左侧纵隔旁可见块状高密度影，左右及前后径分别为 9 cm×3.5 cm，CT 值 39Hu，与上纵隔部分大血管、左肺门结构及左后胸膜分界欠清晰，肺组织可见斑片状高密度炎性渗出影，纵隔内可见增大淋巴结。右上肺门区可见少量斑片状高密度影，边界尚清晰，密度不均。左后可见弧形积液影。 诊意断见：左侧纵隔型肺癌伴左侧胸腔积液及周围阻塞性肺炎；肺门多发斑片影，不除外转移性病变。 第 1 年 9 月 30 日彩超示： 左侧颈部见多发低回声结节，大	第 1 年 11 月 15 日 CT 示： 左上肺见大小约为 3.6 cm×4.2 cm 的软组织影；两肺见散在片状密度影，边界模糊；纵隔未见肿大淋巴结（原纵隔内肿大淋巴结消失）。 第 1 年 12 月 12 日 CT 示（参见图 12b 箭头所示原病灶处）： 两肺见散在片状、单片状密度增高影，边缘模糊，两肺门无增大，气管通畅，纵隔内未见肿大淋巴结。考虑两肺肺炎。 第 1 年 12 月 6 日骨扫描示： 右侧胸锁关节、肋骨、脊柱骨、盆骨可见多处点状、团状、片状异常放射性浓聚影，其余各部位骨骼放射性分布基本均匀，对称。 诊断：全身多发肿瘤骨转移较旧片部分病灶范围缩小，程度减轻。

[0763]

者 1.0 cm×0.7 cm，边界清楚，未见淋巴门结构。左侧锁骨上窝见一低回声结节，大小约 1.2 cm×0.8 cm，边界清楚，未见淋巴门结构。右侧颈根部见一低回声结节，大小约 1.4 cm×1.1 cm，边界清楚，未见淋巴门结构。 超声诊断：左颈部、左锁骨上窝及右侧颈根部低回声结节，异常淋巴结。 第 1 年 9 月 29 日全身骨扫描示： 脊柱、双侧肋骨、右侧胸锁关节、胸骨、左侧骶髂关节、左侧髂骨可见多发放射性浓聚灶。 检查结论：全身多发骨浓聚灶，考虑多发骨转移。	第 1 年 12 月 29 日 PET/CT 示： 左肺尖可见一直径约 8 mm 小结节，放射性分布轻度升高，邻近肺组织可见小片状略高密度影及纤维灶，放射性分布稍升高，两肺可见散在斑片状略高密度影，放射性分布未见明显异常。 结论：1.左上肺癌治疗后，左肺尖病灶 FDG 代谢未见明显增高，考虑为治疗后大部分肿瘤细胞灭活；2.全身多处骨不均匀性骨质增生，部分病灶 FDG 代谢不均匀，少部分病灶 FDG 代谢增高。
附图 12 说明：	经过两个月的治疗，患者左肺病灶已完全消失。

[0764] 患者 7非小细胞肺癌伴双肺、双肝及全身骨转移 :rSIFN-co 肌注、雾化吸入联合吉非替尼（易瑞沙）治疗，经治疗后消除或缩小了双肺及全身多处骨转移病灶，消除了肝脏及纵膈淋巴结转移灶。

[0765]

患者 7	性别：女	年龄：53 岁
病理诊断：	（左锁骨上淋巴结）转移性腺癌	
临床、病理分期©：	$T_4N_3M_1$ IV 期	
使用 rSIFN-co 前的治疗方案：	无	
治疗方案：rSIFN-co 联合其他生物剂治疗	于第 1 年 7 月 31 日开始使用重组高效复合干扰素治疗。隔日肌注 1 次，第 1 次肌注 9μg，	

[0766]

	第 2 次肌注 18μg，从第 3 次开始肌注 21μg。至第 2 年 1 月 2 日（共计 5 个月），患者使用 rSIFN-co 肌注共计 75 次。 在此期间，联合印度产易瑞沙（吉非替尼）®治疗 1 年，每日 1 次，一次 1 片（250mg/片）。
rSIFN-co 疗效评价：	PR②（右肺原发病灶及两肺、全身多处骨转移病灶均有所缩小，放射性浓聚较前减低；肝脏转移病灶消失。）
生存期:	第 1 年 6 月 9 日～第 3 年 10 月 15 日（约 28 个月）
使用 rSIFN-co 前影像学诊断：	使用 rSIFN-co 后影像学诊断：
第 1 年 6 月 26 日 CT 示： 1.右肺上叶可见片状浓聚灶，两肺内多发小结节灶；肝脏，腰椎内可见放射性浓聚影，考虑转移； 2.全身骨扫描显示全身骨骼多部位(项骨、左侧肩关节、两侧肩胛骨、双侧肋骨)，广泛转移灶存在。（参见图 13a 箭头所示病灶） 第 1 年 7 月 2 日 CT 成像见图 14a 箭头所示病灶。	第 1 年 10 月 22 日 CT 提示（参见图 13b 箭头所示原病灶处）： 1.肺癌伴两肺内，肝脏转移。（对照前片有所好转）； 2.全身骨扫描示全身骨骼多部位、广泛转移灶存在（对照前片有所好转）。 第 2 年 1 月 2 日 CT 示（参见图 14b 箭头所示原病灶处： 1.确诊肺癌 7 月复查，右肺下叶斑片结节灶，周边小斑点密度增高影与前片对比有好转； 2.肝脏大小，形态正常，肝内密度均匀，未见局灶性密度异常。 第 2 年 3 月 3 日 CT 示： 与第 1 年 10 月 22 日图像相比未见新病灶，且部分骨质放射性较前减低。肺癌并发多发骨转移，治疗后改变。

[0767]

附图 13 说明：	经过治疗，全身多发骨转移病灶部分消失或减小。
附图 14 说明：	经过治疗，双肺转移病灶消失，右肺病灶明显减小。

[0768] 患者 8非小细胞肺癌伴骨转移；rSIFN-co 肌注、雾化吸入联合吉非替尼（易瑞沙）治疗，经治疗后消除了双肺转移病灶，明显缩小了右肺原发病灶。

[0769]

患者 8	性别：女	年龄：68 岁
临床、病理分期①：	$T_4N_2M_1$ IV 期	
使用 rSIFN-co 前的治疗方案：	无	
治疗方案：rSIFN-co 联合其他生物治疗	于第 1 年 7 月 21 日开始使用重组高效复合干扰素 rSIFN-co 治疗。隔日肌注 1 次，第 1 次肌注 1 支 9μg，第 2 次肌注 1 支 15μg，从第 3 次开始肌注 18μg，配合喷雾吸入 rSIFN-co 每日 1 次 600μg。至第 1 年 10 月 31 日，持续用药 rSIFN-co 3 个月。 从第 1 年 7 月开始此联合吉非替尼（易瑞沙）⑩治疗，每日 1 次，一次 1 片（250mg/片）。	
rSIFN-co 疗效评价：	CR⑫（原右肺下叶病灶大小约 3.0 cm×3.9 cm 及左髂骨内转移病灶基本消失。）	
生存期:	第 1 年 6 月 15 日～第 2 年 7 月截止统计日期约 12 个月，患者仍然健在且病情稳定。	
使用 rSIFN-co 前影像学诊断：	使用 rSIFN-co 后影像学诊断：	
第 1 年 7 月 17 日 CT 示（参见图 15a 箭头所示病灶）： 胸廓左、右对称，双肺纹理增多、紊乱，肺野透光度低，双肺弥漫分	第 1 年 8 月 20 日复查 CT 提示（参见图 15b-16b 所示原病灶处）： 经过近 1 个月的治疗，患者原右肺下叶病灶及左髂骨内转移病灶明显吸收、缩小。	

[0770]

布点状及网织状密度影。右肺下叶见约 3.0 cm×3.9 cm 团块状软组织密度影，边界不清，边缘不规则，边界有毛刺和棘状突起。 第 1 年 7 月 17 日 CT 成像参见图 16a 所示病灶。	第 1 年 10 月 10 日 CT 示： 胸廓呈桶状，左、右对称，双肺纹理增多、紊乱，肺野透光度增加；原右肺下叶病灶较前明显吸收、缩小，灶内见小点状钙化影；原双肺弥漫斑点状较高密度影较前吸收，右肺门见斑点状钙化影；纵隔淋巴结显示，隆突下见淋巴结钙化影。
附图 15 说明：	经过治疗，原右肺下叶病灶明显吸收，缩小。
附图 16 说明：	经过治疗，左髂骨内转移病灶明显吸收，缩小。

[0771] 患者 9非小细胞肺鳞癌 ;rSIFN-co 雾化吸入联合化疗（GP 方案）、重组人血管内皮抑制素（恩度）治疗，经过治疗后明显缩小了右肺下叶肺门处软组织肿块，并且消除了原右肺门肿大淋巴结。

[0772]

患者 9	性别：男	年龄：55 岁
病理诊断：	鳞状细胞癌	
临床、病理分期⑪：	$T_2N_1M_0$. IIb 期	
使用 rSIFN-co 前的治疗方案：	无	
治疗方案：rSIFN-co 联合化疗治疗	患者于第 1 年 3 月 18 日开始使用重组高效复合干扰素治疗。雾化吸入 rSIFN-co 每日 1 次， 每次吸入 600μg。至第 1 年 7 月 20 日患者使用重组高效复合干扰素治疗 1 个疗程（4 个月），雾化吸入共计 100 次。从第 1 年 4 月 12 日开始第 1 周期化疗（GP 方案⑨：吉西他滨 1600mg/日，第 1、8 天；顺铂 40mg/日，第 1、3 天 ），每周期 21 天，共使用 4 个周期。联合恩度⑤每日给药 1 次，每次 7.5mg/m^2(1.2×10^5U/m^2)，连续给药 14	

[0773]

	天为 1 周期，共使用 3 个周期。于第 1 年 5 月 10 日行第 2 周期化疗，方案同前。于第 1 年 6 月 7 日行第 3 周期化疗，方案同前。第 1 年 7 月 7 日行第 4 周期化疗，方案同前。共计 4 周期化疗治疗。
rSIFN-co 疗效评价：	CR②（右肺原发病灶大小约 3.3 cm×2.4 cm×2.0cm 基本消失，右肺门肿大淋巴结大小约 2.0 cm×2.2 cm 消失。）
生存期:	第 1 年 3 月 1 日～第 2 年 7 月截止统计日期约 16 个月，患者仍然健在，正常生活及工作，且病情稳定。
使用 rSIFN-co 前影像学诊断：	使用 rSIFN-co 后影像学诊断：
第 1 年 2 月 28 日 CT 成像参见图 17a 箭头所示病灶大小。 第 1 年 3 月 18 日胸部 PET/CT 示： 1.右肺下叶支气管开口区见软组织结节，与邻近肺门结构分界不清，射性摄取异常增高，范围：3.3 cm×2.4 cm×2.0 cm，SUV 最大值为 10.2。 2.右肺门淋巴结肿大，约 2.0 cm×2.2cm，射性摄取增高，SUV 最大值为 6.6。	第 1 年 5 月 23 日胸部 CT 示： 1.右肺门处可见不规则组织影，肿块较前缩小，右肺门区可见点状钙化灶； 2.右肺门增大淋巴结较前缩小。 第 1 年 7 月 18 日 胸部 CT 示（参见图 17b 箭头所示肿瘤大小）： 右下肺门处可见少许软组织密度影，增强后可见强化，右肺门区可见点状钙化灶；纵隔居中，其内未见明显肿大淋巴结影。
附图 17 说明：	经过近 4 个月的治疗后右肺下叶肺门处软组织肿块明显缩小。

[0774] 患者 10非小细胞肺癌伴肺内及胸膜转移、胸腔积液；单用 rSIFN-co 肌注、胸腔灌注治疗，经治疗后消除了左肺上叶尖段原发病灶，缩小了左肺舌段转移病灶。

[0775]

患者 10	性别：女	年龄：48 岁
临床、病理分期①：	$T_4N_0M_0$, IIIb 期	
使用 rSIFN-co 前的治疗方案：	无	
治疗方案：单独使用 rSIFN-co 治疗	第 1 年 3 月 9 日开始使用重组高效复合干扰素治疗。隔日肌注 1 次，第 1 次肌注 18μg，从第 2 次开始肌注 21μg，至第 2 年 3 月，持续用药近 1 年。从第 1 年 4 月 29 日开始胸腔灌注 rSIFN-co，每隔 7 天灌 1 次，第 1、2 次 9μg×4 支，第 3 次 9μg×5 支，共计 3 次胸腔灌注治疗。第 2 年 7-8 月，在 CT 引导下，进行了 4 次介入手术对肺内较大病灶点注射 rSIFN-co，每次使用剂量为 21μg×10 支。	
rSIFN-co 疗效评价：	CR②（左肺原发病灶大小约 2.0 cm×2.0 cm 基本消失，恶性胸水消失。）	
生存期:	第 1 年 2 月 22 日～第 2 年 10 月因中药致肝肾功能衰竭死亡（约 19 个月）	
使用 rSIFN-co 前细胞学诊断：	使用 rSIFN-co 后细胞学诊断：	
第 1 年 3 月 2 日胸水涂片查见低分化癌细胞。	第 1 年 9 月 18 日胸水涂片及细胞块查见较多淋巴细胞及中性粒细胞及坏死物，未见肿瘤细胞。	
使用 rSIFN-co 前影像学诊断：	使用 rSIFN-co 后影像学诊断：	
第 1 年 2 月 23 日胸部 CT 示： 1.左肺上叶尖段 2.0 cm×2.0 cm 肿块，考虑肺癌； 2.左肺上叶内多个小结节灶，考虑转移可能； 3.左侧胸腔中量积液。	第 1 年 8 月 1 日 CT 示（参见图 19b 箭头所示病灶处）： 1.左肺癌治疗后见，左肺上叶后段小结影已完全吸收消散； 2.左肺舌段小结节性病化灶吸收缩小； 3.左侧胸腔积液较前明显减少；左侧胸	

[0776]

第 1 年 3 月 6 日 CT 成像参见图 19a 箭头所示病灶。	膜条索状结节灶吸收减轻。
附图 18 说明：	经过治疗，胸水明显减少。
附图 19 说明：	经过治疗，左肺病灶明显减小，胸水量较前明显减少。

[0777] 患者 11非霍奇金淋巴瘤 ;rSIFN-co 喷雾剂鼻咽及口腔雾化吸入、颈部肿大淋巴结局部注射联合放疗治疗，经过局部用药治疗后消失或缩小了鼻腔、口咽、颈部，颌下等病灶。

[0778]

患者 11	性别：男	年龄：40 岁
病理诊断：	肠系膜淋巴结非霍奇金淋巴瘤	
临床、病理分期①：	IV 期	
免疫组化检查：	非霍奇金恶性淋巴瘤（B 细胞源性）（参见图 20 箭头所示肿瘤细胞）	
使用 rSIFN-co 前的治疗方案：	第 1 年 8 月起行 7 次化疗，分别采用 5 次 CHOPE 和 2 次 MTX 方案，并于第 2 年 3 月行自体干细胞移植。第 2 年 8 月起行 4 次化疗，分别采用 1 次 GCE 和 3 次 ESAP 方案，第 4 次化疗于第 2 年 11 月 26 日结束。第 3 年 1 月起行 6 次化疗，分别采用 3 次大剂量 CHOPE、2 次 CMOP 和 1 次“博莱霉素 +CHOP[00]+甲氨蝶呤”方案，同时联合干细胞治疗。	
治疗方案：rSIFN-co 联合放化疗治疗	于第 3 年 6 月 9 日开始使用重组高效复合干扰素 rSIFN-co 治疗。使用 rSIFN-co 喷雾剂规格为 72μg/ml，每日对准鼻咽部及口腔喷 2-3 次 / 日。至第 3 年 8 月 27 日，除因化疗（化疗方案见下面描述）停药 5 天外每天坚持使	

[0779]

	用。 于第 3 年 6 月 11 日开始行局部（颈部）淋巴结注射，15μg×10 支/隔日，以梅花点方式对准淋巴结局部注射，注射 2 次后改为颈淋巴系统处局部皮下注射，隔日 30μg/次，至第 3 年 8 月 27 日（2 月余）共计 10 次。 于第 3 年 7 月至第 3 年 11 月 28 日开始给予 CHOP[①]化疗，共计 4 个周期，每个周期 21 天。 第 3 年 6 月 11 日开始行放疗，拟行 25 次，但因患者骨髓抑制明显，身体虚弱，于第 3 年 7 月 5 日停止放疗。
rSIFN-co 疗效评价：	PR[②]（鼻咽及口咽周围软组织最厚处 3.0 cm 已完全消失，颌下、颈部及锁骨区大量的融合淋巴结最大的 7.4 cm×2.4 cm×14.6 cm 减小到 1.1 cm×1.5 cm，明显缩小。）
生存期:	第 1 年 8 月 2 日～第 4 年 4 月 17 日（约 32 个月）
使用 rSIFN-co 前影像学诊断：	使用 rSIFN-co 后影像学诊断：
第 3 年 6 月 8 日 PET/CT 示（参见图 21a-23a 箭头所示病灶处）： 1.鼻咽及口咽腔明显变窄，周围软组织增厚，最厚处约 3.0 cm，鼻后孔闭塞； 2.双侧颌下、颈部、锁骨上下区可见大量淋巴结增大、融合，最大范围约 7.4 cm×2.4 cm×14.6 cm。	第 3 年 8 月 27 日 PET/CT 示（参见图 21b-23b 箭头所示原病灶处）： 1.原鼻咽及口咽腔软组织增厚已消失，放射性摄取较前明显减低； 2.原双侧颌下、颈部、锁骨上下区大量淋巴结增大融合，对比前次检查，数量明显较前减少，体积明显较前缩小，放射性摄取明显较前减低，仅左侧颌下见两个稍大淋巴结影伴放射性摄取增高，最大约 1.1 cm×1.5 cm。
附图 21 说明：	经过治疗，原颈部大量肿大淋巴结消失。

[0780]

附图 22 说明：	经治疗，原双侧颌下病灶已消失。
附图 23 说明：	经治疗，原咽部病灶已消失。

[0781] 患者 12非小细胞肺癌伴胸膜转移；单用 rSIFN-co 肌注治疗，经过治疗后明显缩小了右肺下叶病灶。

[0782]

患者 12	性别：男	年龄：67 岁
细胞学诊断：	肺腺癌	
临床、病理分期①：	$T_3N_0M_0$. IIb 期	
使用 rSIFN-co 前的治疗方案：	第 1 年 8 月 16 日开始给予 GP 方案⑤（吉西他滨 1000mg/m^2 第 1、8 天+顺铂 75mg/ m^2 第 1 天)化疗 2 个周期及顺铂胸腔内注射(每 7 天灌 1 次，每次用量 30-40mg，进行 5 次)。	
治疗方案：单独使用 rSIFN-co 治疗	第 1 年 11 月 10 日开始使用重组高效复合干扰素治疗。隔日肌注 1 次，第 1 次肌注 9μg，第 2 次肌注 18μg，从第 3 次开始肌注 21μg。至第 2 年 10 月 27 日，持续用药近 1 年。	
rSIFN-co 疗效评价：	PR②（在治疗 2 个月后肿块由原来的大小约 3.1 cm×4.2 cm 减小到 2.2 cm×1.5 cm，在用药后约 3 个月是病灶再次缩小。）	
生存期:	第 1 年 8 月 11 日～第 4 年（约 28 个月）	
使用 rSIFN-co 前影像学诊断：	使用 rSIFN-co 后影像学诊断：	
化疗后第 1 年 10 月 10 日胸部 CT 示： 右肺下叶支气管开口处肿瘤块影，大小约 3.1 cm×4.2 cm，考虑中心型肺癌。右侧气胸。肺组织压缩约 10%右侧胸腔少量积液。 刚用药时第 1 年 11 月 15 日 CT	第 2 年 1 月 10 日 CT 示： 右下肺门部肿块约 2.2 cm×1.5 cm，和旧片对比肿块明显缩小。 第 2 年 2 月 12 日复查 CT 示（参见图 24b 箭头所示原病灶处)： 经过 3 个月的治疗，患者右下肺门部肿块明显缩小。	

[0783]

成像见图 24a 箭头所示病灶处。	第 2 年 10 月 23 日 CT 示： 右肺下叶背段肿块，右胸少量积液，右侧胸膜厚。和旧片对比无明显变化。
附图 24 说明：	经过近 3 月的治疗，右下肺门部肿块明显缩小。

[0784] 患者 13非小细胞肺癌术后；单用 rSIFN-co 肌注治疗，经过治疗右肺及全身未见肿瘤复发及转移。

[0785]

患者 13	性别：男	年龄：63 岁
病理诊断：	（右肺上叶）低分化腺癌	
临床、病理分期①：	$T_4N_2M_0$. IIIb 期	
使用 rSIFN-co 前的治疗方案：	第 1 年 10 月 15 日行右上肺叶切除+淋巴结清扫+右肺下叶结节楔形切除术。	
术后病理报告：	（右肺上叶）低分化腺癌，肿瘤体积 4.5 cm×4.5 cm×4 cm，侵达脏层胸膜下方。（下肺背段结节）2 处栓线区查见低分化腺癌累及，直径分别为 0.8 cm 及 1.2 cm。（淋巴结）：“第 2 组”（1/8）枚，第 4 组（2/4）枚及“第 10 组”（1/2）枚均查见癌转移。	
治疗方案：单独使用 rSIFN-co 治疗	第 1 年 12 月 10 日开始接受重组高效复合干扰素治疗。隔日肌注 1 次，第 1 次肌注 9μg，从第 2 次开始肌注 21μg。至第 2 年 4 月 9 日完成第一周期治疗。第 2 年 12 月至第 3 年 7 月完成第二阶段治疗，方案为隔日肌注 21μg/次。第 4 年 2 月 21 日至第 4 年 5 月 21 日完成第三阶段治疗，方案为隔日肌注 18μg/次。	
rSIFN-co 疗效评价：	CR②（原发病灶手术后肿瘤未出现复发或转	

[0786]

	移。）
生存期:	第 1 年 9 月 13 日～第 5 年 7 月截止统计日期约 45 个月，患者仍然健在，正常生活及工作，且影像学检查未见复发及转移病灶
使用 rSIFN-co 前影像学诊断：	使用 rSIFN-co 后影像学诊断：
	第 3 年 5 月 25 日 CT 成像参见图 25a 箭头所示右肺下叶可疑病灶。 第 4 年 2 月 11 日胸部 CT 示： 1.右肺上叶肺癌术后，支气管残留端未见确切复发征象。 2.右肺下叶外基底段不规则小结节影（1.6cm），与旧片相比，未见明显变化。 第 5 年 1 月 2 日胸部 CT 示（参见图 25b 箭头所示原右肺下叶可疑病灶处）： 1.“右肺上叶肺 Ca 术后”：与第 4 年 2 月 11 日 CT 图像对比，支气管残端未见确切肿瘤复发征象；原右肺下叶外基底段结节未见显示。 2.右残肺内散在炎性病灶；右侧胸膜略增厚。
附图 25 说明：	经过治疗，右肺下叶可疑占位消失，且未见肿瘤复发和转移。

[0787] 患者 14非小细胞肺腺癌术后；单用 rSIFN-co 肌注治疗，经过治疗肿瘤未复发和转移。

[0788]

患者 14	性别：男	年龄：44 岁
病理诊断：	低分化腺癌	
临床、病理分期①：	$T_4N_3M_0$, IIIb 期	

[0789]

使用 rSIFN-co 前的治疗方案：	第 1 年 10 月 20 日行右肺上叶切除术。
术后病理报告：	第 1 年 10 月 27 日病检：（右上肺叶包块）部分切除肺组织，镜检肺泡上皮增生，慢性炎性细胞侵润，胸膜侧纤维组织增生伴胶原化，灶性出血，坏死，其内查见低分化腺癌累及。免疫组化示癌组织 CK7（＋），P63（－），TTF1（－）。
治疗方案：单独使用 rSIFN-co 治疗。	第 1 年 11 月 6 日开始使用重组高效复合干扰素治疗。隔日肌注 1 次，第 1 次肌注 18μg ，从第 2 次开始肌注 21μg。用药后 6 月，于第 2 年 5 月 10 日完成第 1 阶段治疗。第 3 年 3 月 18 日开始重组高效复合干扰素第 2 阶段治疗，隔日 15μg/次肌注，连续用药 3 月。第 4 年 11 月使用重组高效复合干扰素肌注，15μg/次隔日，联合雾化吸入 300μg/日，连续 3 个月。
rSIFN-co 疗效评价：	CR©（原病灶手术后肿瘤未见复发和转移）
生存期:	第 1 年 10 月 14 日～第 5 年 7 月截止统计日期约 44 个月，患者仍然健在，正常生活及工作，且影像学检查未见复发及转移病灶。
使用 rSIFN-co 前影像学诊断：	使用 rSIFN-co 后影像学诊断：
第 1 年 10 月 13 日胸部 CT 示： 右上叶后段周围性肺癌，肿瘤（大小约 4.0 cm×2.9 cm）直径侵犯右后上胸膜及右侧胸膜种植转移，胸腔少量积液。 刚用药时（手术后） 第 1 年 11 月 13 日 CT 成像参见图 26a 箭头所示原病灶手术处。	第 3 年 2 月 22 日 CT 示（参见图 26b 箭头所示原病灶手术处）： 右肺上叶残部见较高密度条索影，局部支气管稍扩张，多系术后改变，与旧片对比病灶无明显变化。

[0790]

附图说明 26 说明：	经过治疗，右肺手术残端及周围未见肿瘤复发及转移病灶。

[0791] 患者 15非小细胞肺癌伴全身多处转移；rSIFN-co 腹股沟肿大淋巴结局部注射治疗，经过局部注射治疗后消除或缩小了盆腔、腹股沟淋巴结转移灶。

[0792]

患者 15	性别：男	年龄：68 岁
病理诊断：	无	
临床、病理分期①：	$T_4N_3M_1$ Ⅳ期	
使用 rSIFN-co 前的治疗方案：	第 3 年 4 月 27 日在局麻下行伽马刀治疗。第 3 年 4 月 30 日由核医学科行锶-89 治疗。从第 1 年 12 月至第 3 年 6 月口服吉非替尼（易瑞沙）治疗，每日 1 次，一次 1 片（250mg/片）。	
治疗方案：单独使用 rSIFN-co 治疗。	第 3 年 6 月 25 日开始使用重组高效复合干扰素治疗。每日局部腹股沟淋巴结注射 rSIFN-co：第 1 次 15μg×6 支，第 2 次 15μg×8 支，从第 3 次开始每次 15μg×10 支，至第 3 年 7 月 20 日，共计 11 次（在用药 3 次后出现严重腹泻，因此停药 2 周，后连续每日用药 8 次）。第 3 年 8 月 18 日至第 3 年 9 月 16 日非连续局部淋巴结注射 6 次，剂量为 15μg×10 支/次。第 3 年 10 月 8 日至第 3 年 10 月 12 日每隔两日局部淋巴结注射，剂量是 15μg×10 支/次。	
rSIFN-co 疗效评价：	PR②（盆腔肿块由原来的大小约 11.3 cm×4.9 cm 缩小到 7.52 cm×7.67 cm×6.72 cm。）	
生存期:	第 1 年 12 月～第 3 年 12 月 13 日（约 24 个	

[0793]

	月)。
使用 rSIFN-co 前影像学诊断：	使用 rSIFN-co 后影像学诊断：
第 3 年 6 月 25 日盆腔 MRI 示（参见图 27a 箭头所示病灶处)： 左侧髂骨、骶髂关节、左侧耻骨体、耻骨上支、股骨头骨质破坏，呈稍长 T1 稍长 T2 信号，左侧臀小肌、闭孔内外肌，股大、长、收肌，股直肌受累并筋膜肿胀明显，髋臼平面左侧骨盆内见不规则稍长 T2 肿块影，约 11.3 cm×4.9 cm，增强后稍有强化。	第 3 年 7 月 28 日盆腔 MRI 示（参见图 27b 箭头所示原病灶处）： 左侧耻骨骨质破坏，被长 T2 信号软组织影代替，于盆腔壁肿胀软组织融合成块，范围约 7.52 cm×7.67 cm×6.72 cm，累及左侧髋臼、髂骨翼、闭孔内外肌、股内侧肌群及腹股沟区软组织。
附图 27 说明：	经过 1 个月治疗，盆腔、腹股沟肿大淋巴结消失或缩小。

[0794] 患者 16直肠癌术后 ;单用 rSIFN-co 肌注治疗,经过治疗肿瘤未复发和转移。

[0795]

患者 16	性别：女	年龄：63 岁
病理诊断：	（直肠)高至中分化腺癌,局部为粘液腺癌,侵及肠壁深肌层并在系膜内形成癌性结节。（参见图 28 箭头所示腺癌细胞）	
临床、病理分期①：	$T_4N_1M_x$, IIIb 期	
使用 rSIFN-co 前的治疗方案：	第 1 年 5 月 16 日行腹腔镜辅助腹会阴联合直肠癌根治术。	
治疗方案：单独使用 rSIFN-co 治疗	第 1 年 5 月 23 日开始使用重组高效复合干扰素治疗。隔日肌注 21μg/次。经干扰素治疗 8 个月，第 2 年 2 月停药，完成第 1 阶段的治疗。第 3 年 1 月至第 3 年 4 月进入第 2	

[0796]

	阶段的治疗，隔日肌注 9μg/次，连续注射 3 个月。从第 3 年 12 月至第 4 年 3 月完成第 3 阶段的治疗，方案为隔日肌注 15μg/次。
rSIFN-co 疗效评价：	CR②（原发肿瘤病灶手术后未出现肿瘤复发和转移。）
生存期:	第 1 年 5 月～第 5 年 7 月截止统计日期约 49 个月，患者仍然健在且影像学检查未见复发及转移病灶。
使用 rSIFN-co 前影像学诊断：	使用 rSIFN-co 后影像学诊断：
第 1 年 4 月 30 日 PET/CT 示（参见图 29a 箭头所示原发病灶处）： 1.直肠内见块状高代谢病灶伴肠壁增厚，考虑恶性肿瘤病灶（直肠癌或者淋巴瘤）。 2.盆腔内左侧髂外血管旁见 1 个结节状高代谢病灶，考虑为淋巴结转移，盆腔及其他部位及腹膜后未见恶性肿瘤征象。	第 3 年 6 月 17 日 PET/CT 示（参见图 29b 箭头所示原病灶处）： 患者直肠原发病灶部位无复发及全身转移征象。 第 4 年 3 月 3 日 PET/CT 示： 1.直肠癌术后，结直肠未见恶性肿瘤征象；左下腹人工造瘘口处未见恶性肿瘤征象。 2. 盆腔内左侧髂外血管旁及左侧髂总血管旁见 2 个淋巴结稍增大，代谢未见增高，结合既往多次显像结果，多考虑为淋巴结炎症所致。（可见肿大淋巴结不是转移病灶）
附图 29 说明：	术后 25 个月，经治疗结直肠原发病灶部位无复发及全身转移征象。

[0797] 患者 17原位宫颈癌；单用 rSIFN-co 肌注、子宫灌注治疗，经过治疗后宫颈肿瘤基本受抑，高位型 HPV 转为阴性，宫颈涂片未见肿瘤细胞。

[0798]

患者 17	性别：女	年龄：25 岁

[0799]

细胞学诊断：	第 1 年 5 月 11 日（宫颈）涂片见：鳞状上皮内高度病变。
临床、病理分期①：	Ib1 期
使用 rSIFN-co 前的治疗方案：	无
治疗方案：单独使用 rSIFN-co 治疗。	第 1 年 5 月 14 日开始使用重组高效复合干扰素治疗。隔日肌注 1 次，第 1 次肌注 9μg，第 2 次肌注 15μg，从第 3 次开始肌注 18μg，配合子宫灌注每日 1 次，每次 1000μg，于病灶处保持 2 小时。子宫灌注治疗止于第 1 年 6 月 28 日（持续 1 个余月），肌注治疗止于第 1 年 9 月 12 日（持续 4 个月）。
rSIFN-co 疗效评价：	CR②（宫颈恶性病变消失，高位型 HPV 转为阴性，宫颈涂片未见肿瘤细胞。）
生存期:	第 1 年 5 月 5 日～第 3 年 7 月截止统计日期约 26 个月，患者仍然健在，正常生活及工作，且影像学检查未见复发及转移病灶。
使用 rSIFN-co 前病理诊断：	使用 rSIFN-co 后病理诊断：
第 1 年 5 月 5 日宫颈上皮内瘤变Ⅱ~Ⅲ级并累及腺体。	第 1 年 6 月 24 日慢性宫颈内膜炎。
使用 rSIFN-co 前病毒（HC2HPV DNA）诊断：	使用 rSIFN-co 后病毒（HC2HPV DNA）诊断：
第 1 年 4 月 14 日高危亚型(15 种)：阳性-HPV16 型	第 1 年 6 月 25 日 RLU/CO 0.23（阴性）。
使用 rSIFN-co 前影像学诊断：	使用 rSIFN-co 后影像学诊断：
第 1 年 5 月 14 日 PET/CT 示： 1.宫颈肥大伴 FDG 代谢轻度增高，考虑为低度恶性病变。 2.盆腔及盆壁未见转移性病变。	第 1 年 11 月 8 日 PET/CT 示： 宫颈 FDG 代谢明显减低，提示局部肿瘤活性基本受抑；FDG 代谢不均匀模糊，考虑炎性变。

[0800] 患者 18前列腺癌 ;rSIFN-co 肌注、局部喷雾（行前列腺穿刺的皮肤表面）、联合局部放疗治疗，经过治疗消除了前列腺肿块及右侧坐骨直肠窝内两个淋巴结，膀胱底后壁、双

侧精囊腺及直肠前壁受侵处恢复正常，肿瘤标志物（PSA）恢复正常。

[0801]

患者 18	性别：男	年龄：64 岁
病理诊断：	前列腺第 1 针-第 10 穿针刺均查见腺癌。	
临床、病理分期①：	$T_4N_1M_0$ IV 期	
使用 rSIFN-co 前的治疗方案：	无	
治疗方案：rSIFN-co 联合放疗治疗。	从第 1 年 11 月 15 日开始使用重组高效复合干扰素。隔日肌注 1 次，第 1 次肌注 9μg，第 2 次肌注 15μg，第 3 次肌注 18μg，从第 4 次开始肌注 24μg。同时给予前列腺穿刺部位皮肤表面局部喷雾治疗，每日 4-5 次，每次剂量 70μg -139μg。第 1 年 12 月 15 日肌注改为隔日 21μg 至第 2 年 7 月 1 日。 第 1 年 12 月 5 日至第 2 年 2 月 26 日行前列腺外放射治疗（EBRT）②38 次。	
rSIFN-co 疗效评价：	CR②（前列腺大小由原来的 4.7 cm×3.5 cm×5.6 cm 恢复正常；右侧坐骨直肠窝内两个淋巴结消失；膀胱底后壁、双侧精囊腺及直肠前壁受侵处恢复正常；前列腺癌特异抗原 PSA 恢复到正常范围。）	
生存期:	第 1 年 11 月 11 日～第 2 年 7 月截止统计日期约 8 个月，患者仍健在。	
使用 rSIFN-co 前前列腺癌特异抗原（PSA）值：	使用 rSIFN-co 后前列腺癌特异抗原（PSA）值：	
第 1 年 11 月 2 日 检查： 前列腺总特异抗原（T-PSA）：	第 2 年 3 月 7 日检查： 前列腺总特异抗原（T-PSA）：	

[0802]

23.090 ng/ml(参考值＜3 ng/ml)，游离 PSA（F-PSA）：1.850 ng/ml(参考值＜0.75 ng/ml)，前列腺抗原百分比（F-PSA/PSA）：8.01％（参考值 25-100）	0.006 ng/ml (参考值＜3 ng/ml) 游离 PSA（F-PSA）：＜0.010 ng/ml (参考值＜0.75 ng/ml)
使用 rSIFN-co 前影像学诊断：	使用 rSIFN-co 后影像学诊断：
第 1 年 11 月 4 日 MRI 示： 1、前列腺明显增大并形成不规则肿块影，大小约 4.7 cm×4.3 cm×5.6 cm，边界不清，信号不均匀，增强扫描呈明显不均匀强化，考虑前列腺癌。 2、右侧坐骨直肠窝内两个淋巴结显示，直径约 1 cm，考虑转移。 3、膀胱底后壁、双侧精囊腺受侵，直肠前壁可疑受侵。	第 2 年 3 月 31 日 MRI 示： 1、前列腺体积较小，左后份稍显外突，各成像序列信号未见明显异常。 2、膀胱壁不均匀性稍增后，炎症？ 3、盆腔未见积液及肿大淋巴结。

[0803] 患者 19鼻部黑色素瘤术后伴双侧髋关节、双侧股骨、双侧肱骨、肋骨及双侧肩关节骨转移；rSIFN-co 肌注、病灶部位局部喷雾。经过治疗，消除了双侧肩关节，腋窝多发肿大淋巴结，双侧髋关节、股骨上段骨，右侧鼻窦及鼻腔肿瘤术后残腔内复发转移病灶。

[0804]

患者 19	性别：女	年龄：43 岁
病理诊断：	右上颌窦内新生物均查见肿瘤，免疫组化 HMB45（部分+），MART1（-），S100（-），CD63（+），NSE(-)，PCK（-），EMA(+)，CD56(-)，KI671 25％，诊断为恶性黑色素瘤。	
临床、病理分期①：	pT_3NxM_1. Ⅳ期	
使用 rSIFN-co 前的治疗方案：	于第 1 年 10 月 30 日及第 1 年 11 月 30	

[0805]

	日行两周期恩度 15mg d1-10＋替莫唑胺 200mg d1-5，口服。 第 1 年 11 月 2 日行靶区放疗，放疗靶区位右侧上颌窦＋左侧 1/4 上颌窦，双侧筛窦，额窦，右侧眼球球旁组织，放疗剂量为 50Gy/25f，并于第 1 年 12 月 7 日完成放疗。
治疗方案：单独使用 rSIFN-co 治疗。	从第 1 年 12 月 21 日开始使用重组高效复合干扰素。隔日肌注 1 次，第 1 次肌注 9μg，第 2 次肌注 15μg，从第 3 次开始肌注 18μg。同时给予右肩部皮肤表面局部喷雾治疗，每日 4-5 次，每个部位每次剂量 70μg-139μg。 从第 2 年 2 月 27 日开始给予左肩及其他骨转移部皮肤表面局部喷雾治疗，每日 4-5 次，每个部位每次剂量 70μg-139μg。
rSIFN-co 疗效评价：	CR®（双侧肩关节，腋窝多发肿大淋巴结，右侧鼻窦及鼻腔肿瘤术后残腔内复发转移病灶，双侧髋关节、股骨上段骨折多发异常信号消失。）
生存期:	第 1 年 8 月～第 2 年 7 月截止统计日期约 11 个月，患者仍健在。
使用 rSIFN-co 前影像学诊断：	使用 rSIFN-co 后影像学诊断：
第 1 年 12 月 8 日鼻副窦 MRI 示： 1.右侧鼻窦及鼻腔肿瘤术后表现，与第 1 年 10 月 26 日旧片比较，残腔周围软组织增厚，强化明显，不排除复发可能。 2.扫及颈部多枚淋巴结显示，部分增	第 2 年 5 月 2 日肩关节 MRI 示：左肩诸骨目前未见明显骨质破坏。肱骨头内见点状长 T2 长 T1 信号影，多系小囊性灶。 第 2 年 5 月 2 日骨盆 MRI 示：左侧耻骨上支见长 T1 长 T2 信号改变，增强

[0806]

大。 3.左侧下鼻甲肥大，左侧上颌窦、蝶窦及筛窦炎。 4.右侧中耳乳突炎。 第 1 年 12 月 8 日 髋关节 MRI 示：左侧髋臼见状长 T1 长 T2 异常信号影，病灶向左侧坐骨延伸，脂肪抑制序列呈高信号，增强后明显强化；双侧髂骨下份及右髋臼前柱均见结节样长 T1 长 T2 异常信号，明显强化。总结意见：双侧髋关节骨质内多发异常信号影，累及范围如述，多考虑为骨转移。 第 1 年 12 月 8 日肩关节 MRI 示：双侧锁骨肩峰端、右肩胛盂下骨质、双侧肩胛骨周边骨质、双侧肱骨上段、扫及双侧多根肋骨见等长 T1 长 T2 片状影，明显不均匀强化，边界不清。双侧腋窝见多个淋巴结显示，部分增大。总结意见：上述改变结合病史考虑双侧肩关节及腋窝多发转移瘤。	像上明显强化。骨盆其余诸骨信号未见明显异常。 第 2 年 5 月 2 日头部 MRI 是：1.颅内未见异常；2.双侧中耳乳突炎；3.右侧中、下鼻甲缺失，右上颌窦内壁缺失，窦腔与鼻腔连成一空腔；4.左上颌窦炎；5.蝶窦炎、额窦炎。 第 2 年 6 月 26 日腰椎、头部、肩关节 MRI 示： 1.腰椎 2 后上脂肪沉积，其余椎体骨质及椎间盘未见异常； 2.颅内脑组织未见异常； 3.右侧鼻腔鼻甲及右侧上颌窦内侧壁术后缺如表现； 4.双侧筛窦、蝶窦炎症，双侧乳突炎； 5.双侧颈部淋巴结未见肿大强化； 6.双侧肩关节股骨头未见异常。

[0807] ①癌症分期标准参见 :AJCC 癌症分期手册（第六版）/F. L. 格林尼，D. L 佩基，I. D. 弗莱明等主编 . - 沈阳 :辽宁科学技术出版社，2005. 8 ；

[0808] ②抗肿瘤药物疗效评定标准参见 :实用抗肿瘤药物治疗学 / 刘新春等主编 . - 北京 :人民卫生出版社 2002 第 1100-1101 页 ；

[0809] ③肺癌放疗参见 :现代肺癌病理与临床 / 熊敏，吴一龙 主编 . - 北京 :科学出版社，2003. 6 第 324-365 页 ；

[0810] ④ TC 方案参见 :现代肺癌病理与临床 / 熊敏，吴一龙 主编 . - 北京 :科学出版社，2003. 6 第 386 页 ；

[0811] ⑤“恩度”参见 :肺癌化疗和靶向治疗 / 廖美琳主编 . - 北京 :人民卫生出版社，2009. 8 第 261 页 ；

[0812] ⑥“培美曲塞”参见 :肺癌化疗和靶向治疗 / 廖美琳主编 . - 北京 :人民卫生出版社，2009. 8 第 94 页 ；

[0813] ⑦ EP 方案参见 :现代肺癌病理与临床 / 熊敏，吴一龙 主编 . - 北京 :科学出版社，

2003.6 第 386 页 ;

[0814] ⑧ DP 方案参见 :现代肺癌病理与临床 / 熊敏,吴一龙 主编 . - 北京 :科学出版社,2003.6 第 386 页 ;

[0815] ⑨ GP 化疗方案参见 :肺癌化疗和靶向治疗 / 廖美琳主编 . - 北京 :人民卫生出版社,2009.8 第 222-230 页 ;

[0816] ⑩“吉非替尼”参见 :肺癌化疗和靶向治疗 / 廖美琳主编 . - 北京 :人民卫生出版社,2009.8 第 222-230 页 ;

[0817] (11)CHOP 化疗方案参见 :实用抗肿瘤药物治疗学 / 刘新春等主编 . - 北京 :人民卫生出版社 2002 第 931 页 ;

[0818] (12) 前列腺癌放疗治疗参见 :临床肿瘤学进展 / 孙燕,赵平主编 . - 北京 :中国协和医科大学出版社,2005.9ISBN7-81072-711-7 第 1009-1010 页。

[0819] 实施例 4 :本发明 rSIFN-co 临床有效性数据

[0820] 在下表中,每一行中括号前的数字表示该类情形的患者个数,括号内的数字表示该类患者占第一列情形患者中的百分比,最后,括号内的 II/III/IV 等表示癌症分期,其中癌症分期参考文献 :AJCC 癌症分期手册 (第六版)/F.L. 格林尼,D.L. 佩基,I.D. 弗莱明等主编 . - 沈阳 :辽宁科学技术出版社,2005.8。

[0821] 表 3 肺癌不同进展期使用 rSIFN-co 疗效比较

[0822]

肿瘤分期	CR	PR	NC/SD	PD	合计
II	1(20.00%)	2(40.00%)	2(40.00%)	0(0.00)	5
III	5(50.00%)	2(20.00%)	1(10.00%)	2(20.00%)	10
IV	6(40.00%)	7(46.67%)	1(6.67%)	1(6.67%)	15
合计	12(40.00%)	11(36.67%)	4(13.33%)	3(10.00%)	30

[0823] 注 :治疗方案参照实施例 2 中患者的治疗方案。

[0824] 表 4 肺癌手术后、未手术使用 rSIFN-co 疗效比较 *

[0825]

组别	CR	PR	NC/SD	PD	合计
手术后	2(33.33%)(III/IV)	0(0.00%)	3(50.00%)(II/III/IV)	1(16.67%)(III)	6
未手术	10(41.67%)(II/III/IV)	11(45.83%)(II/III/IV)	1(4.17%)(IV)	2(8.33%)(III/IV)	24
合计	12(40.00%)	11(36.67%)	4(13.33%)	3(10.00%)	30

[0826] 注 :其具体治疗方案参照实施例 2 中患者的治疗方案。

[0827] * 在该表中,手术部不包括冷冻消融或射频消融。

[0828] 表 5 肺癌不同给药方式疗效比较

[0829]

给药方式	CR	PR	NC/SD	PD	合计
全身给药	4(44.44%)(II/IV)	3(33.33%)(II/III)	1(11.11%)(II)	1(11.11%)(III)	9
全身+局部	6(33.33%)(II/IV)	7(38.89%)(II/III/IV)	3(16.67%)(II/III/IV)	2(11.11%)(III/IV)	18
局部给药	2(66.67%)(II/III/IV)	1(33.33%)(IV)	0(00.00%)	0(00.00%)	3
合计	12(40.00%)	11(36.67%)	4(13.33%)	3(10.00%)	30

[0830] 注：全身给药指肌注或皮下给药；局部给药指雾化吸入及皮肤表面喷雾给药；其具体治疗方案参照实施例 2 中患者的治疗方案。

[0831] 表 6 肺癌使用 rSIFN-co 时间长短疗效比较

[0832]

用药时间（月）	CR	PR	NC/SD	PD	合计
＜3	1(50.00%)(IV)	0(00.00%)	1(50.00%)(IV)	0(00.00%)	2
3～6	3(50.00%)(IV)	3(50.00%)(III/IV)	0(00.00%)	0(00.00%)	6
7～12	2(20.00%)(III)	4(40.00%)(II/IV)	2(20.00%)(II)	2(20.00%)(III/IV)	10
＞12	6(50.00%)(II/III/IV)	4(33.33%)(III/IV)	1(8.33%)(III)	1(8.33%)(III)	12
合计	12(40.00%)	11(36.67%)	4(13.33%)	3(10.00%)	30

[0833] 注：其具体治疗方案参照实施例 2 中患者的治疗方案。

[0834] 表 7 肺癌是否联合用药疗效比较

[0835]

联合用药	CR	PR	NC/SD	PD	合计
有	8(42.11%)(II/III/IV)	7(36.84%)(III/IV)	3(15.79%)(II/III/IV)	1(5.26%)(III)	19
无	4(36.36%)(III/IV)	4(36.36%)(II/III/IV)	1(9.09%)(II)	2(18.18%)(III/IV)	11
合计	12(40.00%)	11(36.67%)	4(13.33%)	3(10.00%)	30

[0836] 注：联合用药或联合治疗包括：化疗、放疗、射频消融、生物药和中药，但排除手

术，其具体治疗方案参照实施例 2 中患者的治疗方案。

[0837] 表 8 肺癌用药前肿瘤是否已转移疗效比较

[0838]

转移情况	CR	PR	NC/PD	PD	合计
有	11(44.00%)(II/III/IV)	9(36.00%)(II/IIII/IV)	4(16.00%)(II/IIII/IV)	1(4.00%)(IV)	25
无	1(20.00%)(III)	2(40.00%)(II/III)	0(0.00%)	2(40.00%)(III)	5

[0839]

合计	12(40.00%)	11(36.67%)	4(13.33%)	3(10.00%)	30

[0840] 注：其具体治疗方案参照实施例 2 中患者的治疗方案。

[0841] 表 9 不同肿瘤进展期使用 rSIFN-co 疗效比较

[0842]

肿瘤分期	CR	PR	NC/SD	PD	合计
I	3(100.00%)	0(0.00%)	0(0.00%)	0(0.00%)	3
II	2(33.33%)	2(33.33%)	2(33.33%)	0(0.00)	6
III	6(35.29%)	5(29.41%)	3(17.64%)	3(17.64%)	17
IV	8(25.00%)	12(37.50%)	5(15.62%)	7(21.88%)	32
合计	19(32.76%)	19(32.76%)	10(17.24%)	10(17.24%)	58

[0843] 注：其具体治疗方案参照实施例 2 中患者的治疗方案，其中：

[0844] I 期肿瘤包括宫颈癌、胃肠道间质细胞瘤；

[0845] II 期肿瘤包括肺癌、乳腺癌；

[0846] III 期肿瘤包括肺癌、卵巢癌、宫颈癌、直肠癌、乳腺癌、胰腺癌、淋巴瘤、恶性神经瘤、转移性低分化鳞癌；

[0847] IV 期肿瘤包括肺癌、宫颈癌、子宫内膜或子宫浆液性乳头状癌及透明细胞癌混合型、结肠癌、胆管癌，包括胆管腺癌、肝癌，包括肝细胞癌、乳腺癌、胃癌、前列腺癌、胚胎性横纹肌肉瘤、恶性黑素瘤、和淋巴瘤，包括非霍奇金淋巴瘤。

[0848] 表 10 手术后、未手术使用 rSIFN-co 疗效比较

[0849]

组别	CR	PR	NC/SD	PD	合计
手术后	8(32.00%)	2(8.00%)	7(28.00%)	8(32.00%)	25
未手术	11(33.33%)	17(51.52%)	3(9.09%)	2(6.06%)	33
合计	19(32.76%)	19(32.76%)	10(17.24%)	10(17.24%)	58

[0850] 注：其具体治疗方案参照实施例 2 中患者的治疗方案。

[0851] 表 11 不同给药方式疗效比较

[0852]

给药方式	CR	PR	NC/SD	PD	合计
全身给药	8(34.78%)	8(34.78%)	2(8.70%)	5(21.74%)	23
全身+局部	10(32.26%)	8(25.81%)	8(25.81%)	5(16.13%)	31
局部给药	1(25.00%)	3(75.00%)	0(00.00%)	0(00.00%)	4
合计	19(32.76%)	19(32.76%)	10(17.24%)	10(17.24%)	58

[0853] 注：其具体治疗方案参照实施例 2 中患者的治疗方案。

[0854] 表 12 使用 rSIFN-co 时间长短疗效比较

[0855]

用药时间（月）	CR	PR	NC/PD	PD	合计
<3	2(40.00%)	1(20.00%)	2(40.00%)	0(00.00%)	5
3～6	4(25.00%)	6(37.50%)	3(18.75%)	3(18.75%)	16
7～12	3(18.75%)	6(37.50%)	3(18.75%)	4(25.00%)	16
>12	10(47.62%)	6(28.57%)	2(9.52%)	3(14.29%)	21
合计	19(32.76%)	19(32.76%)	10(17.24%)	10(17.24%)	58

[0856] 注：其具体治疗方案参照实施例 2 中患者的治疗方案。

[0857] 表 13 是否联合用药疗效比较

[0858]

联合用药	CR	PR	NC/PD	PD	合计
有	10(34.48%)	10(34.48%)	6(20.69%)	3(10.34%)	29
无	9(31.03%)	9(31.03%)	4(13.79%)	7(24.14%)	29
合计	19(32.76%)	19(32.76%)	10(17.24%)	10(17.24%)	58

[0859] 注：联合用药包括：化疗、放疗、射频消融、生物药、中药，其具体治疗方案参照实施例 2 中患者的治疗方案。

[0860] 表 14 用药前肿瘤是否已转移疗效比较

[0861]

转移情况	CR	PR	NC/SD	PD	合计
有	14(29.79%)	16(34.04%)	9(19.15%)	8(17.02%)	47
无	5(45.45%)	3(27.27%)	1(9.09%)	2(18.18%)	11
合计	19(32.76%)	19(32.76%)	10(17.24%)	10(17.24%)	58

[0862] 注 :其具体治疗方案参照实施例 2 中患者的治疗方案。

[0863]

表 15 直至最后统计日完全缓解（CR）的患者

患者编号	癌种	细胞类型	病期	分期	治疗方法	应答	rSIFN-co 治疗持续时间(月)	rSIFN-co 给药方式	rSIFN-co 每次用药量
1	NSCLC	鳞状细胞癌	IIIb	$T_3N_2M_0$	用药前 CTx, rSIFN-co + RTx	CR	15	im, *qod*	9μg, 15μg, 18μg
3	NSCLC	肺腺癌	IV	$T_2N_2M_1$	rSIFN-co+RTx	CR	3+	im, *qod* + 吸入 *qod*	9μg, 18μg, 21μg, 200μg, 400μg
4	SCLC		IV	$T_4N_3M_1$	用药前 CTx, rSIFN-co+CTx+冷冻消融	CR	16+	im, *qod* + 吸入 *qod*	9μg, 15μg, 18μg, 200μg, 21μg, 100μg-400μg
5	NSCLC	中分化腺癌	IV	$T_2N_2M_1$	用药前 CTx, rSIFN-co+CTx	CR	8+	im, *qod* + 吸入 *qd*	9μg, 21μg, 200μg, 15 μg
6	NSCLC	中-低分化腺癌	IV	$T_4N_3M_{1b}$	用药前 CTx, rSIFN-co+CTx+吉非替尼（易瑞沙）	CR	5+	im, *qod* + 吸入 *qd* + 喷雾 *qd* *4-5x/天*	600μg, 9μg, 15μg, 18μg, 70μg-139μg
8	NSCLC		IV	$T_4N_2M_1$	rSIFN-co+易瑞沙	CR	3	im, *qod* + 吸入 *qd*	9μg, 15μg, 18μg, 600μg
9	NSCLC	鳞状细胞癌	IIb	$T_2N_1M_0$	rSIFN-co+CTx+恩度	CR	4	吸入, *qd*	600μg

[0864]

10	NSCLC		IIIb	$T_4N_0M_0$	rSIFN-co	CR	15	im, *qod* + 胸腔灌注 每隔 7 天 + 病灶内	18μg, 21μg, 36μg, 45μg, 2100μg
13	NSCLC	低分化腺癌	IIIb	$T_4N_2M_0$	用药前手术, rSIFN-co	CR	15	im, *qod*	9μg, 21μg, 18μg
14	NSCLC	低分化腺癌	IIIb	$T_4N_3M_0$	用药前手术, rSIFN-co	CR	12	im, *qod* + 吸入 *qd*	18μg, 21μg, 15μg, 300μg
16	直肠癌	中分化腺癌	IIIb	T_4N_1Mx	用药前手术, rSIFN-co	CR	15	im, *qod*	21μg, 9μg, 15μg
17	宫颈癌	鳞状上皮病变	1b1	无转移	rSIFN-co	CR	4	im, *qod* + 子宫灌注, *qd*	9μg, 15μg, 18g,1000μg
18	前列腺癌	腺癌	IV	$T_4N_1M_0$	rSIFN-co+RTx	CR		im, *qod*+局部喷雾, *qd*, 4-5x/天	9μg, 15μg, 18μg, 24μg, 70μg-139μg, 21μg
19	恶性黑素瘤	黑素瘤	IV	$pT_3N_xM_1$	用药前恩度+ CTx+RTx, rSIFN-co	CR		im, qod+局部喷雾, *qd*, 4-5x/天	9μg, 15μg, 18μg, 70μg-139μg
21	肺癌		IIIb	转移至骨	用药前 TCM+易瑞沙, rSIFN-co + 易瑞沙	CR		im, *qod*	9μg, 15μg, 18g
23	肺癌	腺癌	IV	转移至胸膜腔、纵隔淋巴结以及骨	用药前 CTx + rSIFN-co	CR	2	im, *qod*	9μg, 21μg

[0865]

[0866]

39	宫颈癌	低分化鳞状细胞癌	Ib2		用药前手术+CTx, rSIFN-co+NK 细胞 Tx	CR	6	im, *qod*	9μg, 15μg
48	乳腺癌		IIa		用药前手术, rSIFN-co	CR	4+	im, *qod*	9μg, 15μg, 18μg, 21μg
54	胃肠道间质细胞瘤		Ib		用药前手术+RTx, rSIFN-co	CR	9+	im, *qod*	9μg, 21μg

表 16 直至最后统计日部分缓解（PR）的患者

患者编号	癌种	细胞类型	病期	分期	治疗方法	应答	**rSIFN-co** 治疗持续时间 (月)	**rSIFN-co** 给药方式	**rSIFN-co** 每次用药量
2	NSCLC	肺腺癌	IV	$T_3N_3M_1$	用药前 CTx, rSIFN-co+恩度+CTx	PR	12	im, qod + 吸入, qd	9μg, 15μg, 18μg, 21μg, 300μg, 500μg, 600μg
7	NSCLC	肺腺癌	IV	$T_4N_3M_1$	rSIFN-co+易瑞沙	PR	5	im, qod	9μg, 18μg, 21μg
11	非霍奇金淋巴瘤		IV		用药前 CTx, 用药前干细胞 Tx, rSIFN-co+CTx+RTx	PR	4.5	吸入, qd, 2-3x/天 + 病灶内, qod + s.c., qod	72μg/ml,150μg, 30μg

12	NSCLC	肺腺癌	IIb	$T_3N_0M_0$	用药前 CTx, rSIFN-co	PR	12	im, qod	9μg, 18μg, 21μg
15	NSCLC		IV	$T_4N_3M_1$	用药前 RTx+易瑞沙, rSIFN-co	PR	1.5+	局部腹股沟淋巴结注射, qd	90μg, 120μg, 150μg
20	肺癌		IV		rSIFN-co +CTx	PR	3+	im, qod + 吸入, qd	9μg, 15μg, 21μg, 200μg, 300μg
22	肺癌		IIIa	肝转移	用药前 CTx+RFA , rSIFN-co	PR	2+	im, qod	18μg, 21μg
24	肺癌		IIIb		rSIFN-co	PR	2	im, qod + 胸腔灌注	9μg, 13.5μg, 21μg,126μg, 168μg,210μg, 252μg
26	肺癌		IV	脑转移	用药前易瑞沙, rSIFN-co + 易瑞沙	PR	24+	im, qod + 吸入 qd	21μg, 18μg, 100μg, 300μg, 400μg
30	肺癌	腺癌	IV	脑转移	用药前 RTx+CTx, rSIFN-co	PR		im, qod + 吸入, qd	21μg, 200μg
32	肺癌		IIb		用药前 CTx+吉非替尼, rSIFN-co +吉非替尼	PR		im, qod + 吸入, qd	9μg, 13.5μg, 18μg, 300μg
35	肺癌	腺癌	IV		用药前 CTx, rSIFN-co + CTx + RFA	PR		im, qod + 吸入, qd	15μg, 18μg, 600μg
36	卵巢癌		IIIb		用药前手术, rSIFN-co	PR	3+	im,, qod	9μg, 15μg, 18μg, 21μg
37	宫颈癌		IV		用药前 RTx+CTx,	PR		im,, qod	21μg

[0867]

					rSIFN-co				
42	胆管腺癌		IV	肝转移	用药前手术+RTx, rSIFN-co+手术	PR	18+	im,, qod	9μg, 18μg, 21μg
45	肝细胞癌		IV	肝内转移	用药前手术, rSIFN-co	PR	5.5 +	im,, qod	9μg, 18μg, 21μg
51	胃癌		IV	腹腔转移	用药前 CTx, rSIFN-co	PR	8 天	腹腔灌注, qod	120μg, 180μg, 210μg, 240μg
52	胰腺癌		III		rSIFN-co	PR	9	im, qod	9μg, 21μg
56	淋巴瘤		III		rSIFN-co+ CTx+TCM	PR	6	im, qod + 瘤内注射	21μg, 18 μg, 168μg, 210μg, 252μg, 273μg, 315μg, 180μg, 189μg, 198μg, 207μg, 500μg

表 17 直至最后统计日没有改变（NC）或稳定的疾病（SD）的患者

患者编号	癌种	细胞类型	病期	转移情况	治疗方法	应答	rSIFN-co 治疗持续时间（月）	rSIFN-co 给药方式	rSIFN-co 每次用药量
27	肺癌		IIb	肺转移	用药前手术+CTx+RTx, rSIFN-co	NC/SD		im, qod	9μg, 21μg

[0868]

28	肺癌		IIb	肺 +胸腔内转移	用药前手术+唯美生, rSIFN-co	NC/SD	7	im, qod + 鼻喷雾, tid + 吸入, qd	9μg, 21μg, 200μg
29	肺癌		IIIa		用药前手术+放射免疫疗法, rSIFN-co+射频消融术(RFA)	NC/SD	5.5+	im, qod + 鼻喷雾, tid	9μg,18μg, 21μg
34	肺癌		IV	多发转移	rSIFN-co+RTx+TCM	NC/SD	2	im, qod + 吸入, qd	18μg, 200μg
38	子宫内膜浆液性乳头状癌	混合透明细胞癌	IV		rSIFN-co	NC/SD		im, qod + 子宫滴注, qd, 然后每 5 天 1 次	18μg, 200μg
41	结肠癌		IV	肝转移	用药前手术, rSIFN-co	NC/SD	4+	im, qod, 瘤内注射	9μg, 21μg, 21 - 25.5μg, 105μg, 168μg, 210μg
49	乳腺癌	术后复发	IV		用药前手术+ CTx, rSIFN-co	NC/SD	5	局部注射 + im, qod	90μg, 21μg,, 9μg
53	前列腺癌		IV		用药前抗雄激素+激素+ RFA + 放射性粒子, rSIFN-co+RTx	NC/SD		im, qod, 腹腔灌注	9μg, 21μg, 168μg
57	神经瘤	术后复发	IIIc		用药前手术 + CTx + TCM, rSIFN-co	NC/SD		im, qod + 瘤内	21μg, 84μg
58	右胸低分化鳞状细胞癌		IIIa		用约前手术, rSIFN-co	NC/SD	6	im, qod	9μg, 21μg

表 **18** 直至最后统计日发展疾病（**PD**）的患者

[0869]

患者编号	癌种	病期	转移情况	治疗方法	应答	rSIFN-co 治疗持续时间(月)	rSIFN-co 给药方式	rSIFN-co 每次用药量
25	肺癌	IIIa		rSIFN-co + RTx	PD	5	im, *qod*	9μg, 21μg
31	肺癌	IV	骨转移	rSIFN-co	PD	3+	im, *qod*,喷雾	9μg, 13.5μg, 18μg, 20μg/ml, 21μg
33	肺癌	IIIb		用药前手术, rSIFN-co	PD	1+	im, *qod*; im, 一周 2 次; 胸腔灌注	4.5μg, 9μg, 13.5μg, 18μg, 105μg, 126μg, 147μg, 168μg, 189μg, 210μg
40	结肠癌	IV	肺转移	用药前手术 +CTx+TCM, rSIFN-co+RFA+ CTx+RTx	PD		im, *qod*	9μg, 21μg
43	肝内胆管癌	IV	肝转移	用药前手术 +CTx, rSIFN-co+ 手术	PD	6	im, *qod*	9μg, 21μg
44	肝细胞癌	IV	肺转移	用药前手术, rSIFN-co	PD	5.5+	im, *qod*	9μg, 18μg, 21μg
46	乳腺癌	IIIc	淋巴结转移	用药前手术 +CTx+RTx, rSIFN-co	PD	4	im, *qod*	18μg

[0870]

47	乳腺癌	IV		用药前手术 +CTx, rSIFN-co	PD	7.5+	胸腔灌注,局部注射，一周 1 次; im, *qod*	105μg, 147μg, 168μg, 210μg, 273μg, 21μg
50	胃癌	IV		用药前手术, rSIFN-co	PD	20.5	im, *qod*; 腹腔注射	9μg, 18μg, 15μg, 21μg, 168μg, 189μg, 210μg
55	胚胎性横纹肌肉瘤	IV	转移	用药前手术 +CTx+RTx, rSIFN-co	PD	13	im, *qod*; 淋巴结注射，瘤内注射	9μg, 15μg, 18μg, 21μg,168μg

[0001]

序列表

<110> 远东超级实验室有限公司

<120> 用空间构象改变的重组干扰素治疗肿瘤的方法

<130> 1202-PCT-CN

<160> 3

<170> PatentIn version 3.5

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<213> 人工序列
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<223> 重组干扰素的氨基酸序列

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35 40 45

Phe Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln
50 55 60

Thr Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu
65 70 75 80

Ser Leu Leu Glu Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp
85 90 95

Leu Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu
100 105 110

Met Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile
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Thr Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val
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tactaggtcg tctggaagtt ggacaagagg tggtttctga ggaggcgacg aaccctgctt 240

agggacgacc tttttaagat gtggcttgac atggtcgtcg acttgctgga ccttcgaacg 300

caataggtcc ttcaaccaca acttctttgg ggcgactact tgcaactgag gtaggaccga 360

caatttttta tgaaggtcgc atagtgggac atggactggc tttttttttat gaggggcacg 420

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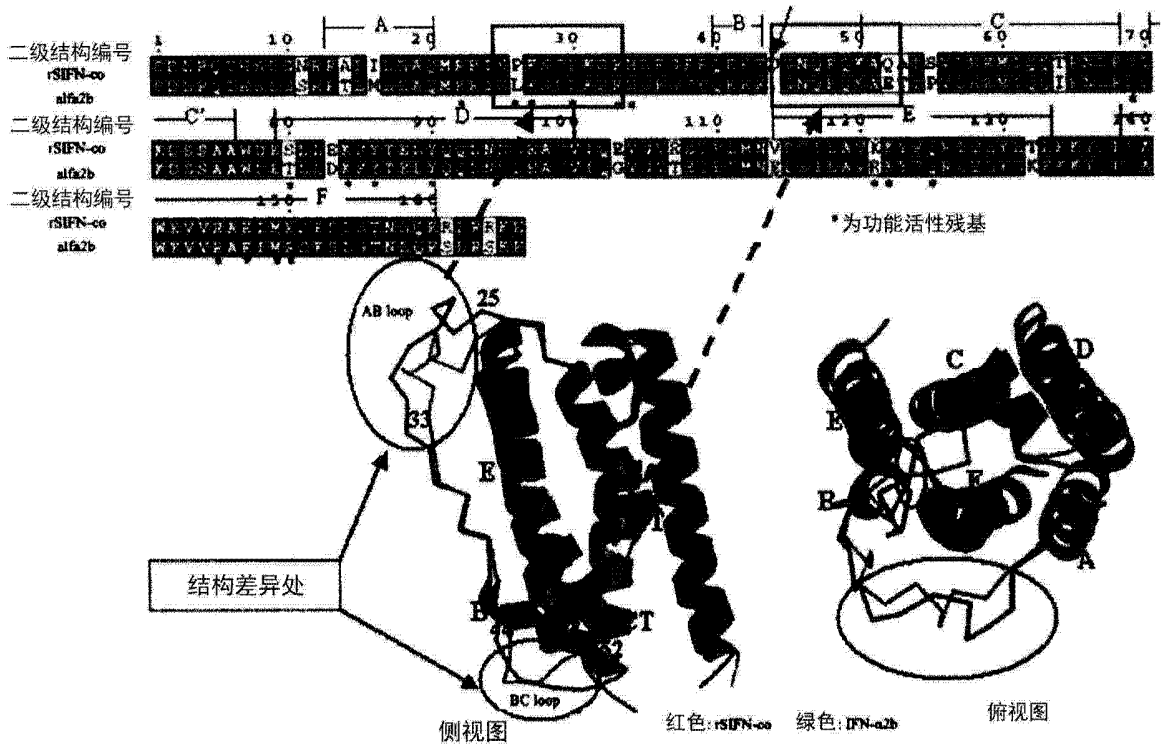

二级结构编号
rSIFN-co
alfa2b
*为功能活性残基
AB loop
结构差异处
BC loop
侧视图
红色:rSIFN-co
绿色:IFN-a2b
俯视图

图 1

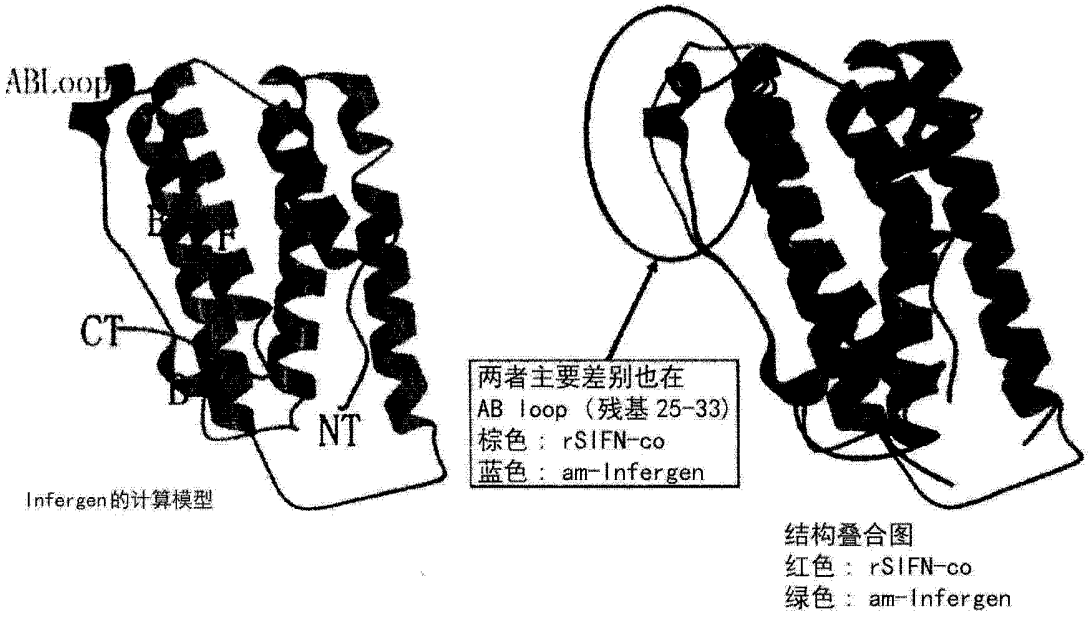
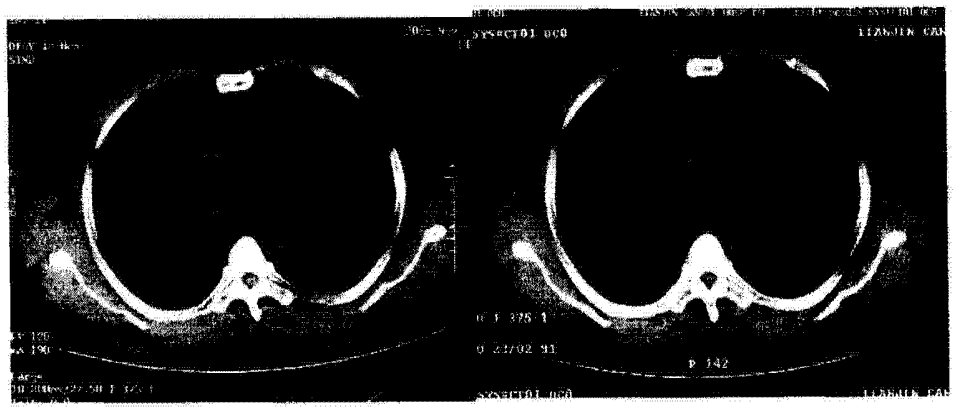
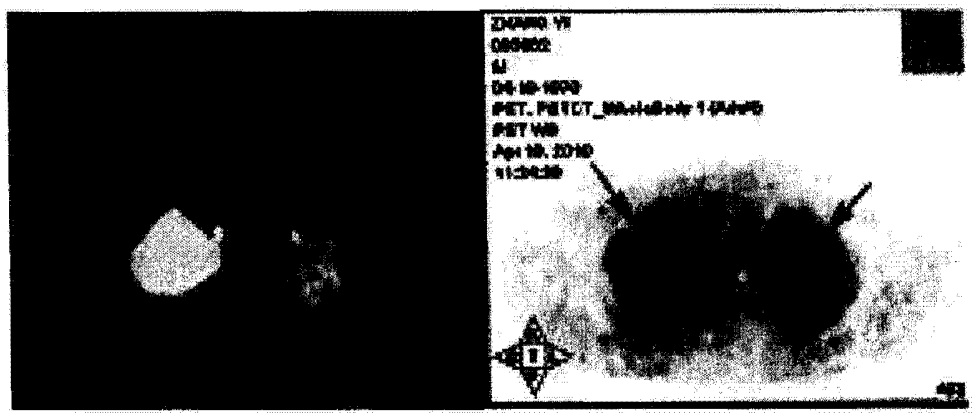

ABLoop
CT
NT
Infergen的计算模型
两者主要差别也在
AB loop (残基 25-33)
棕色： rSIFN-co
蓝色： am-Infergen
结构叠合图
红色： rSIFN-co
绿色： am-Infergen

图 2

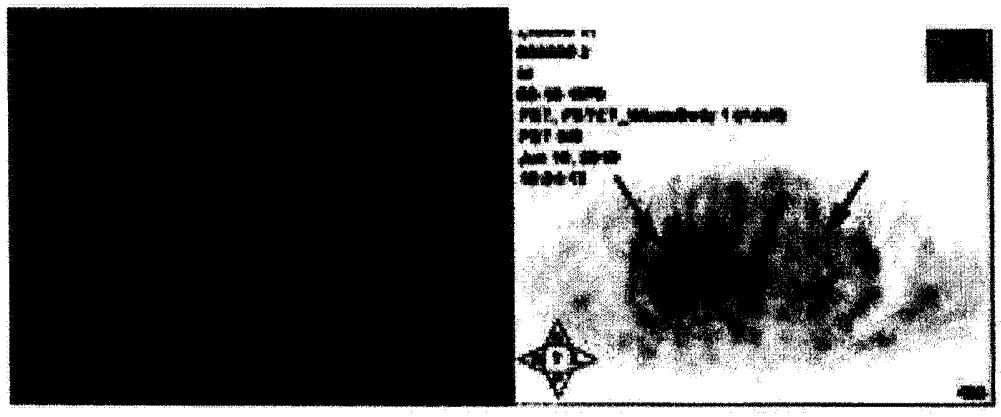


a b

图 3

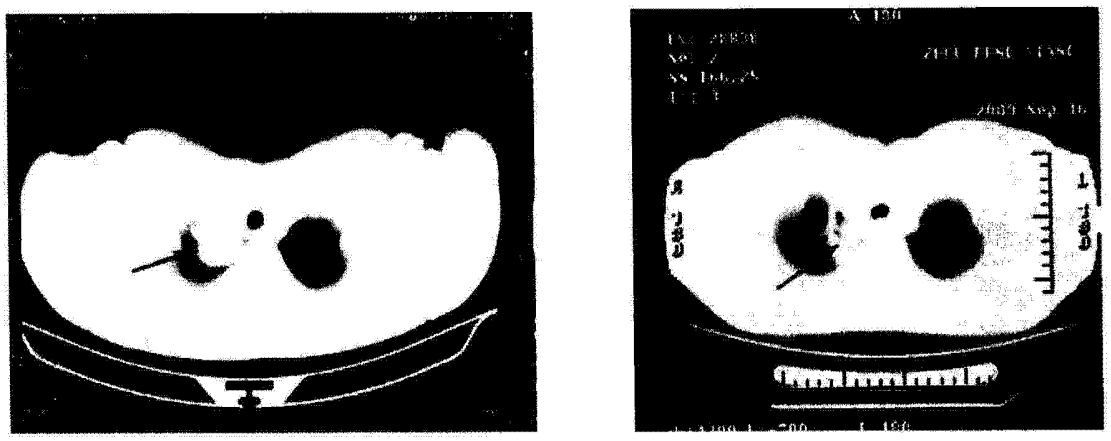


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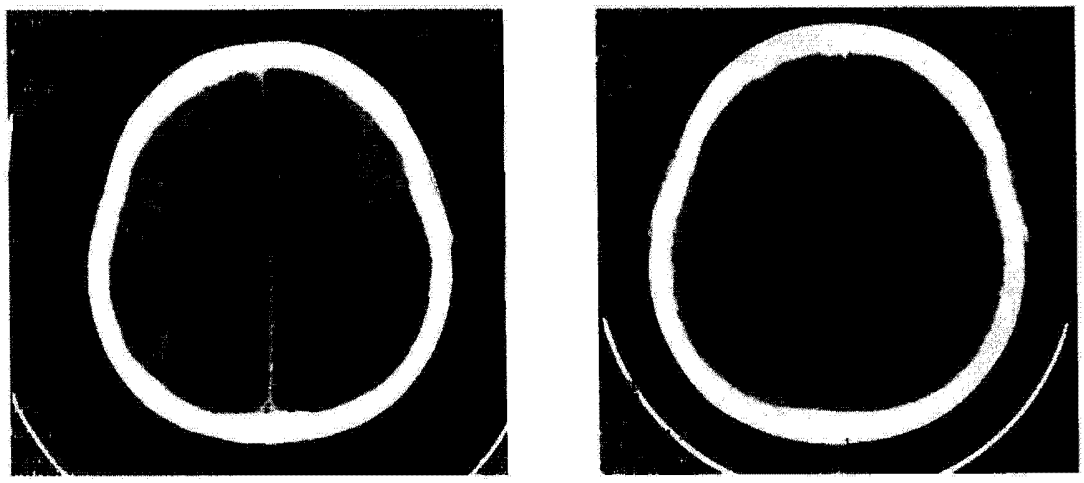
b

图 4



a b

图 5



a b

图 6

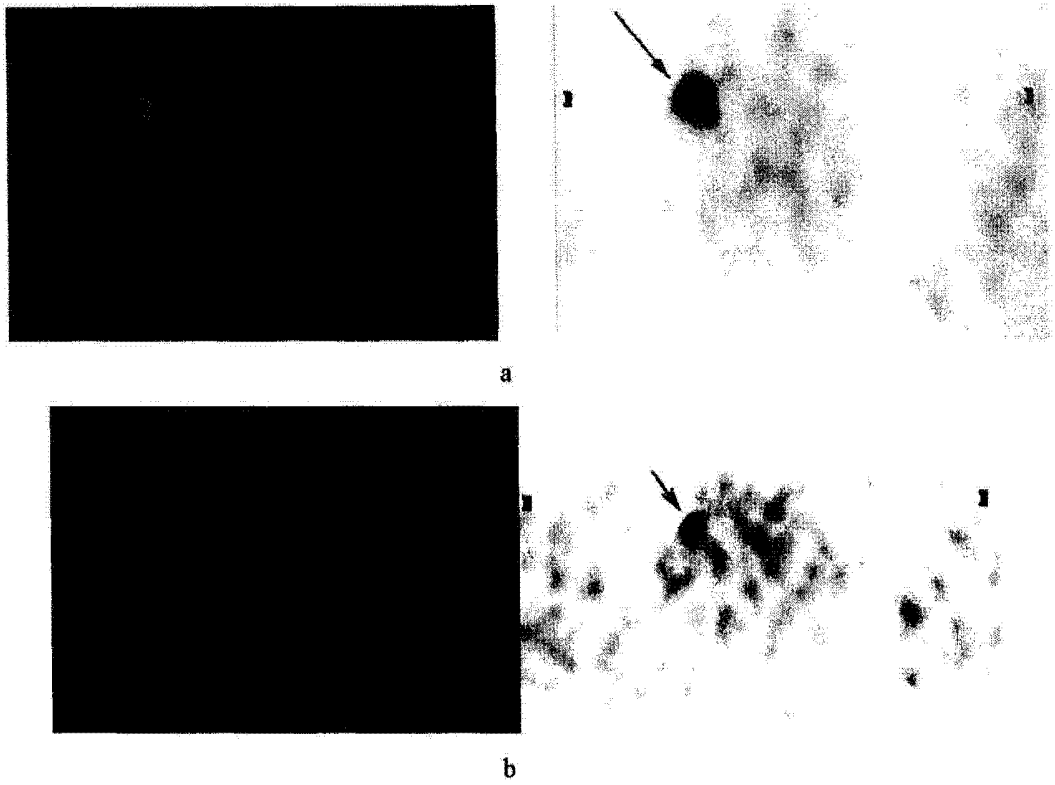


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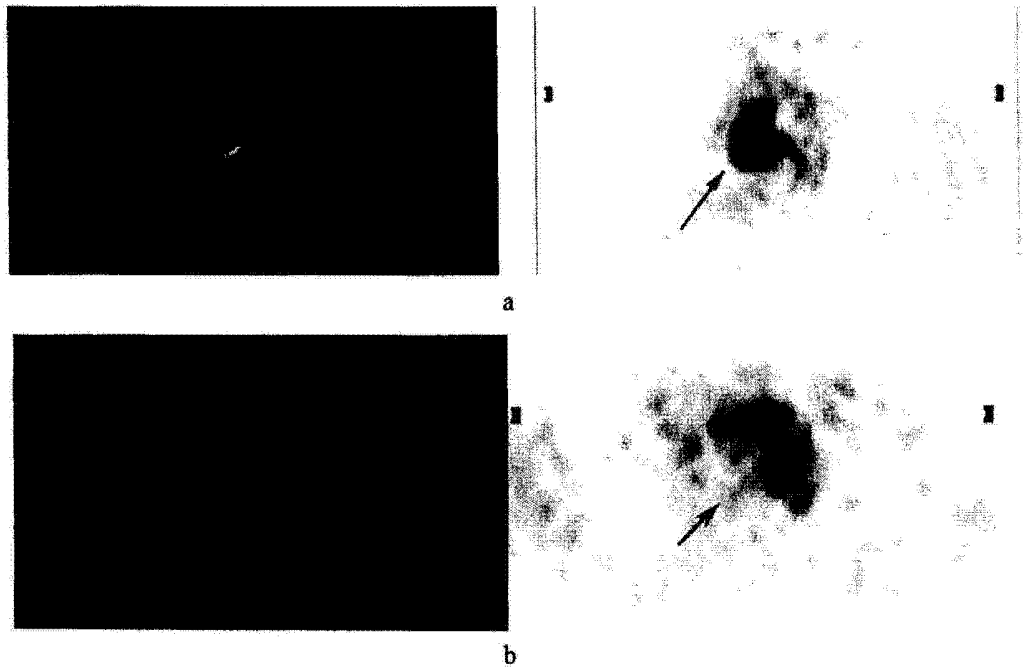


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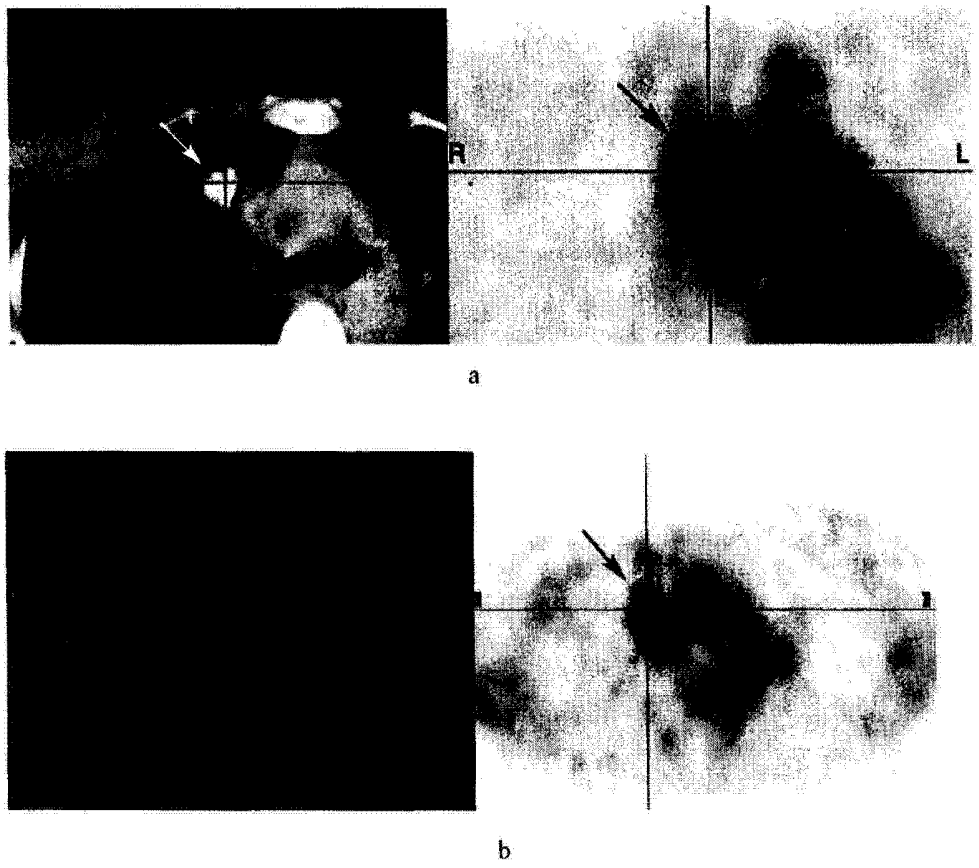


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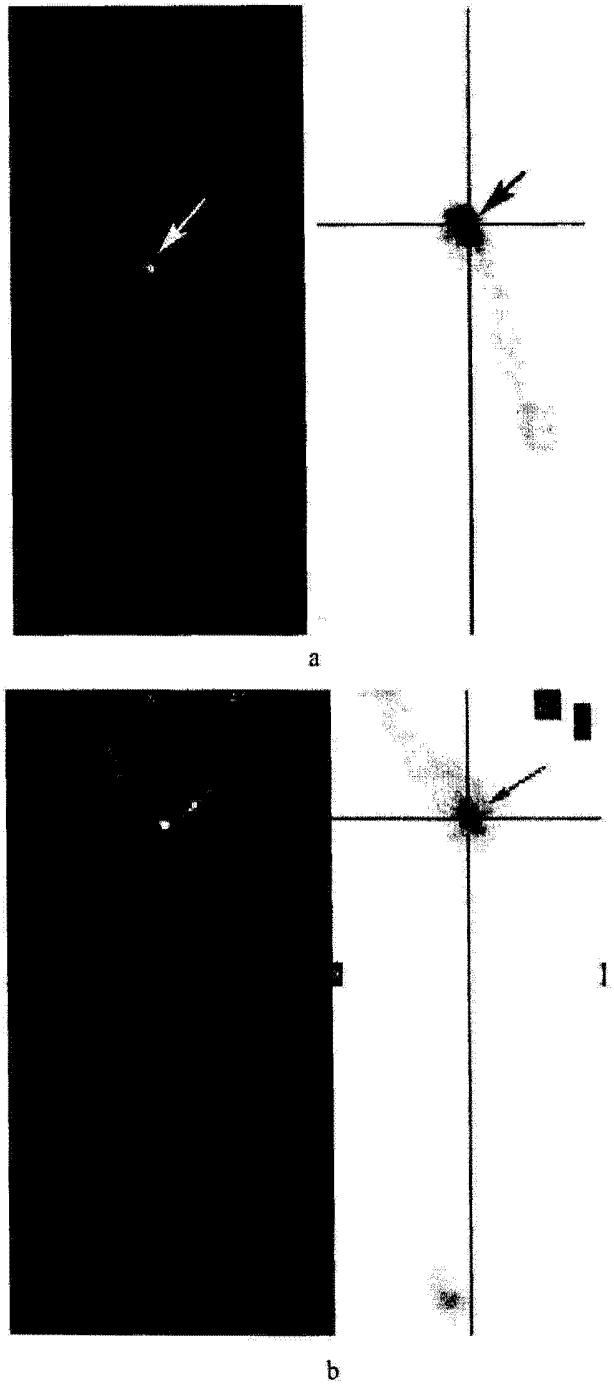


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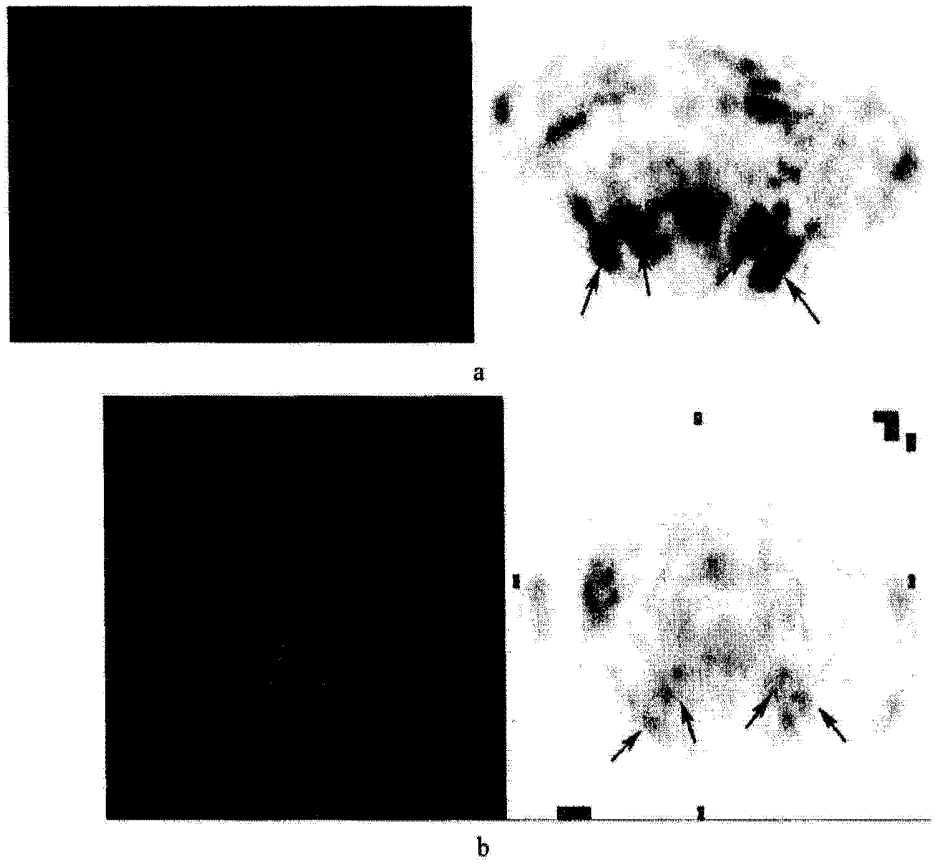


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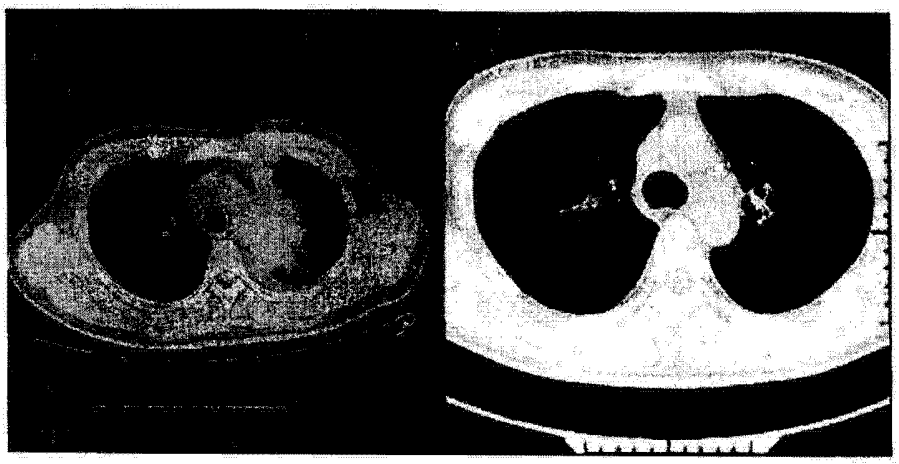
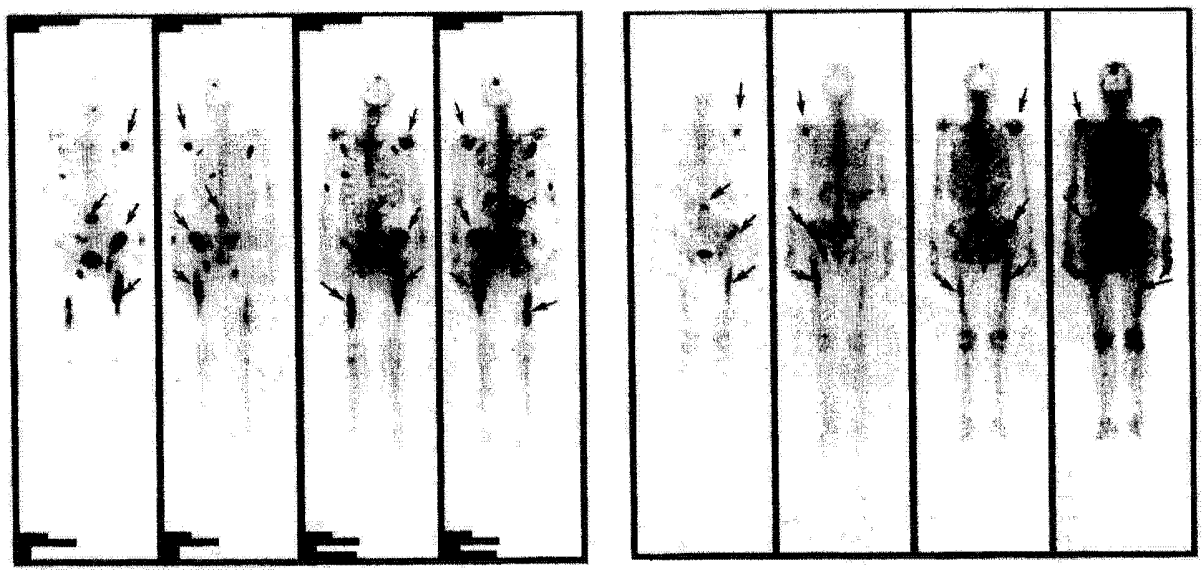
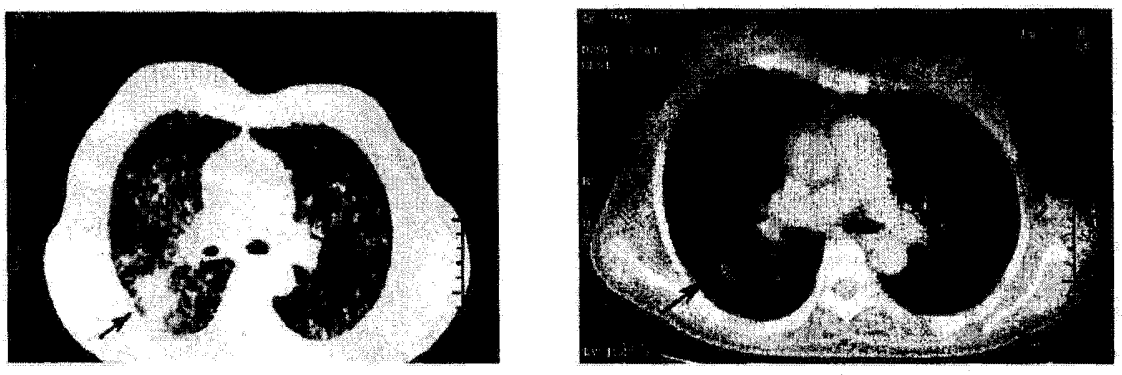


图 12



a b

图 13



a b

图 14

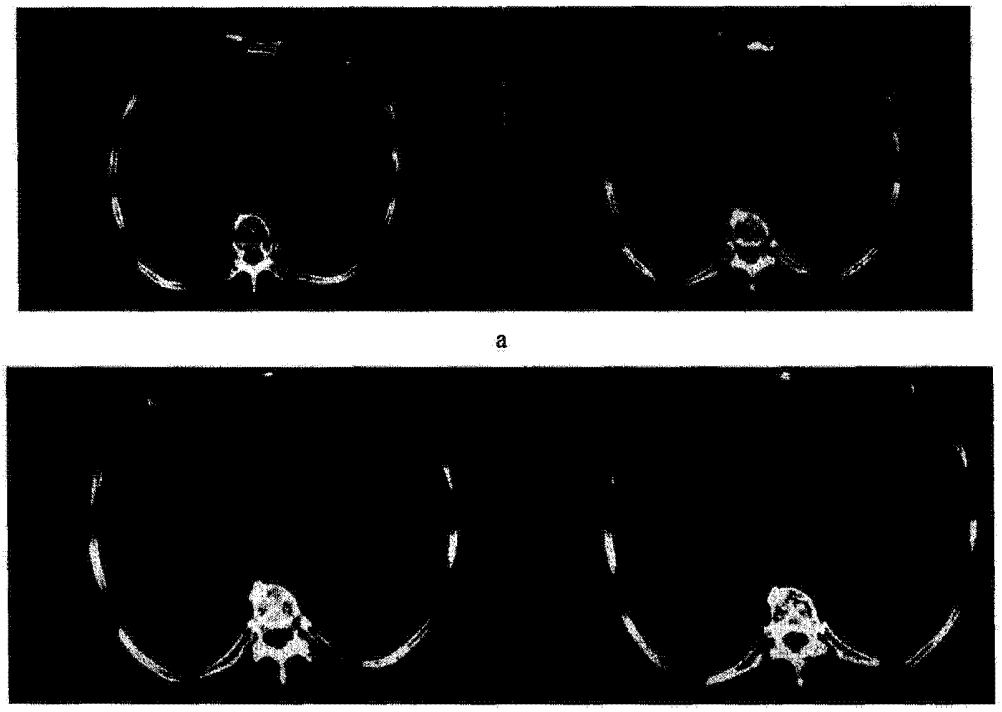


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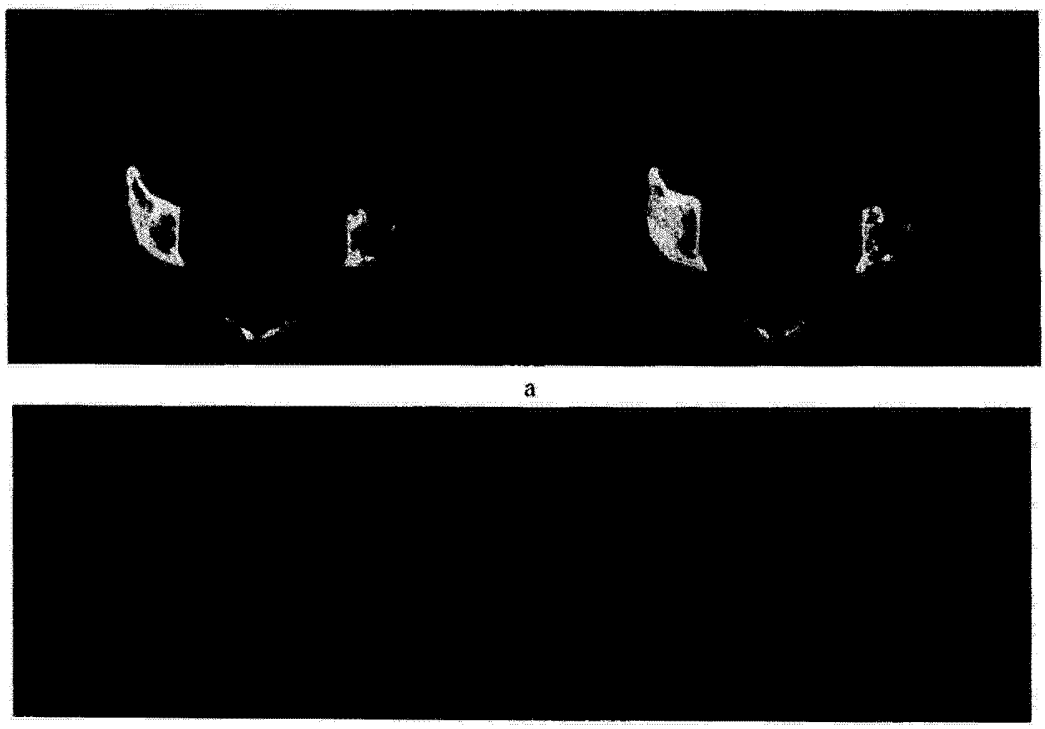
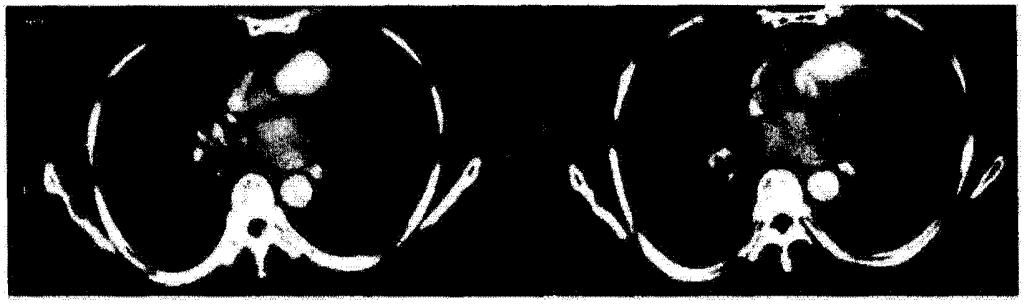


图 16



a



b

图 17

	日期	抽胸水量 (ml)	间隔天数（天）
治疗前	2006-2-22	800	
	2006-2-24	800	2
	2006-3-2	400	6
	2006-3-6	400	2
	2006-3-10	500	4
开始用药	2006-3-9		
治疗后	2006-3-28	520	22
	2006-4-11	430	14
	2006-4-29	400	18
	2006-6-5	350	36

图 18

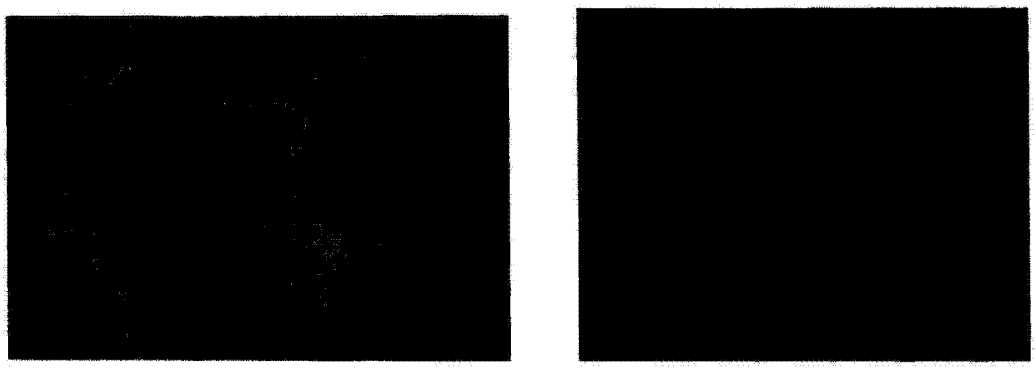


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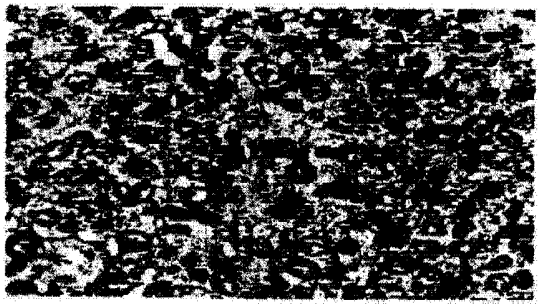


图 20



图 21

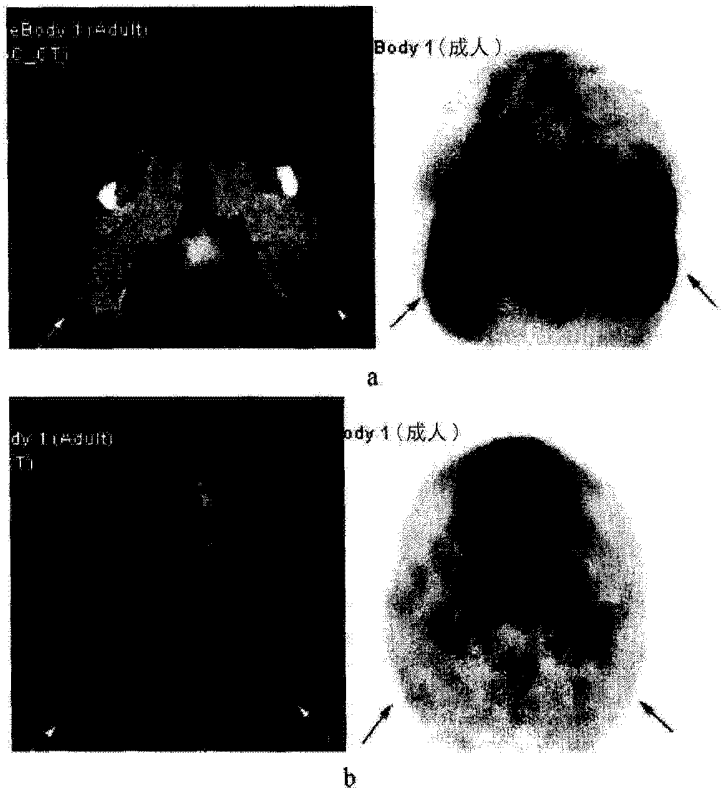


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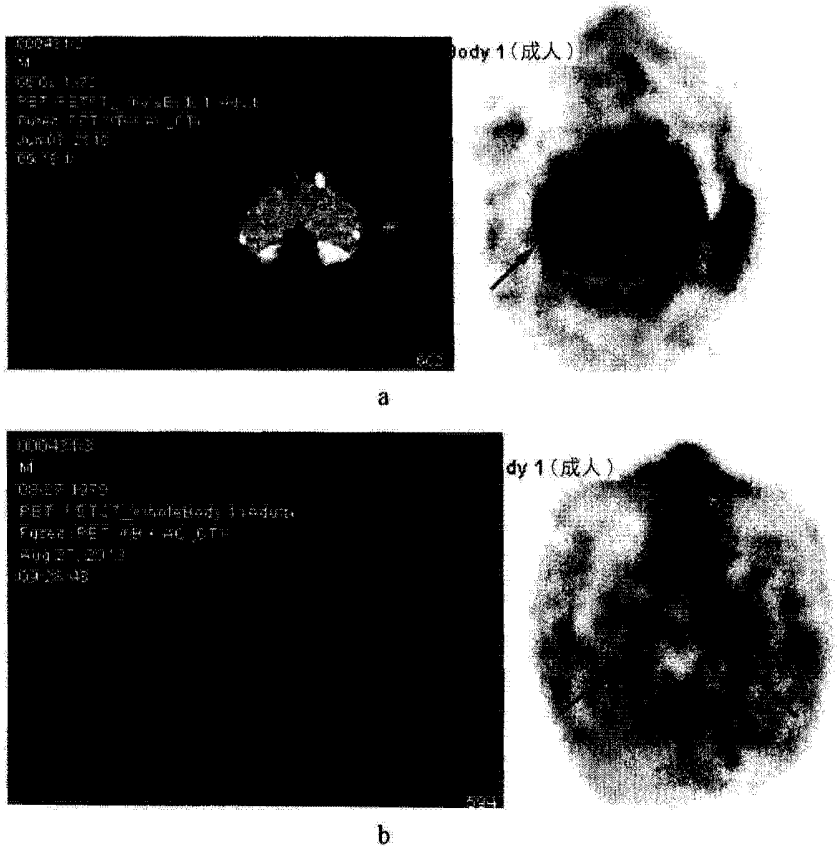


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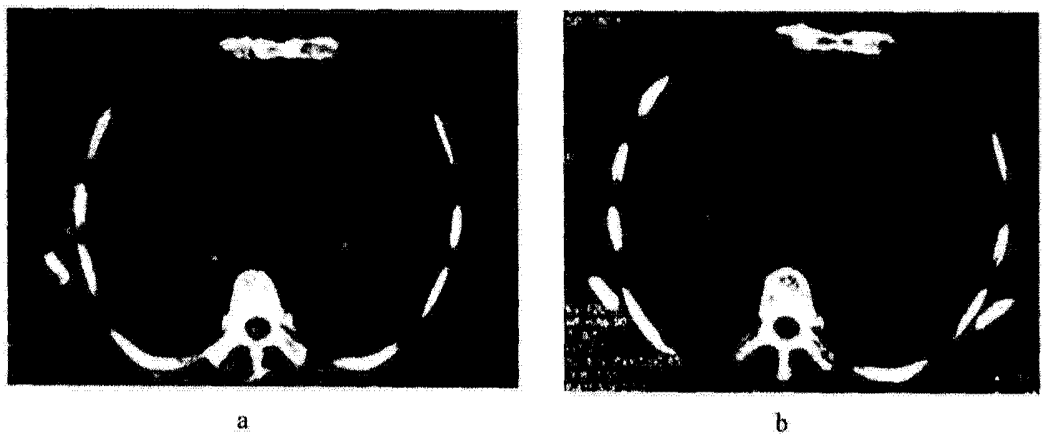
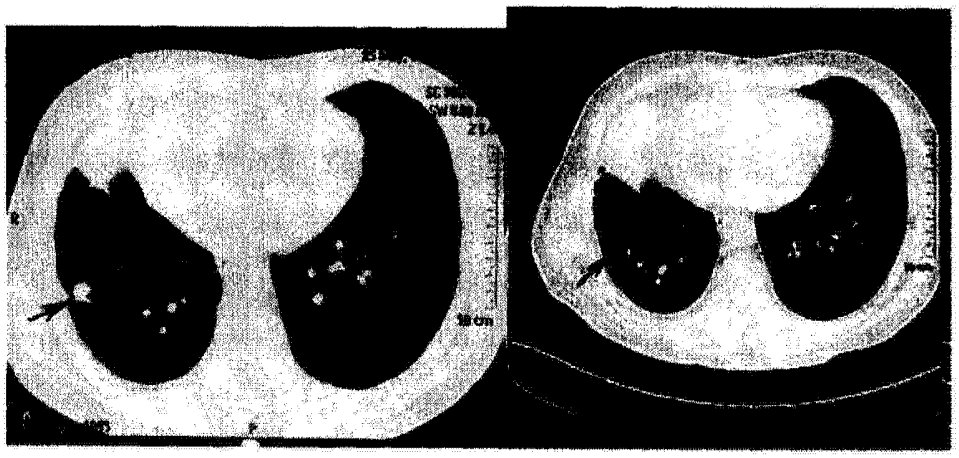
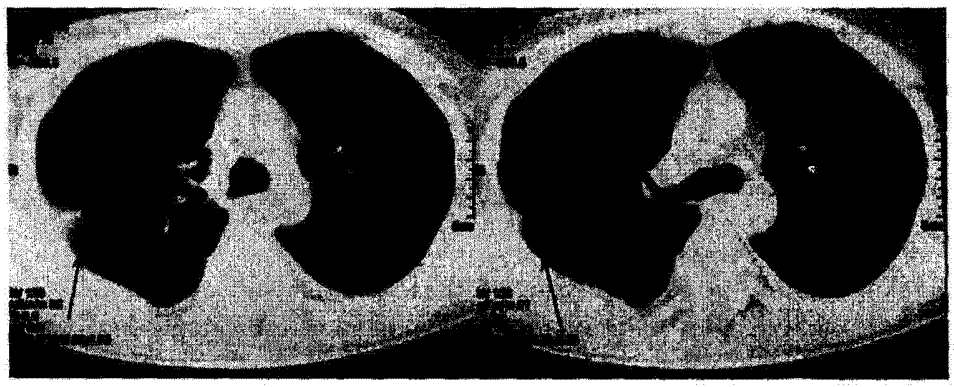


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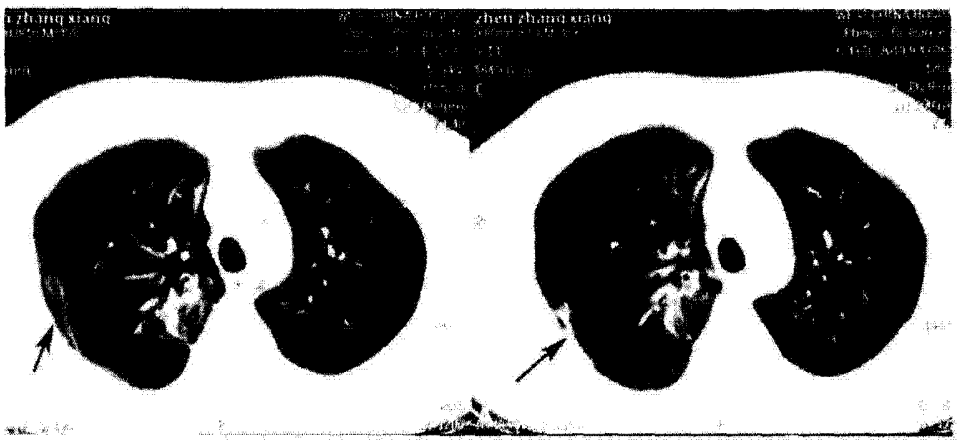


a b

图 25

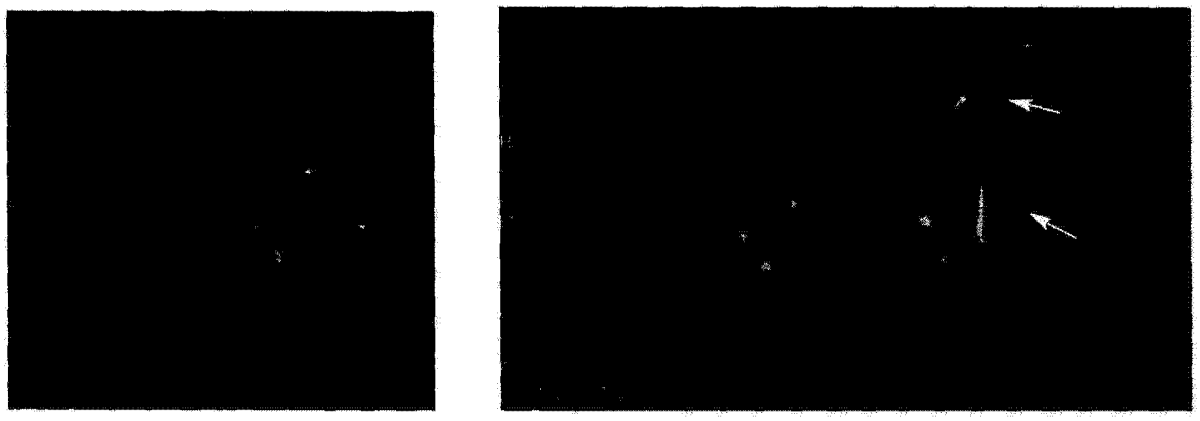


a



b

图 26



a b

图 27

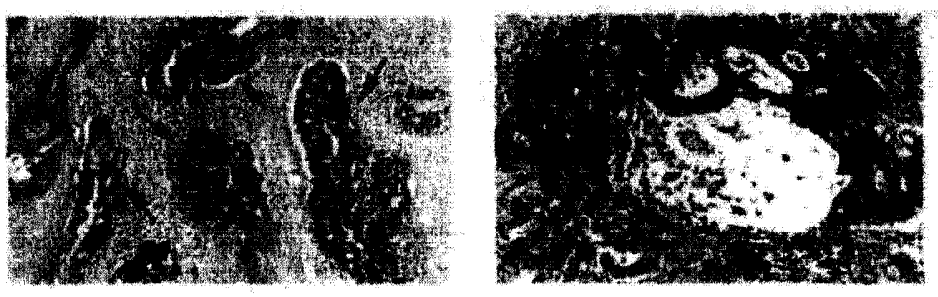
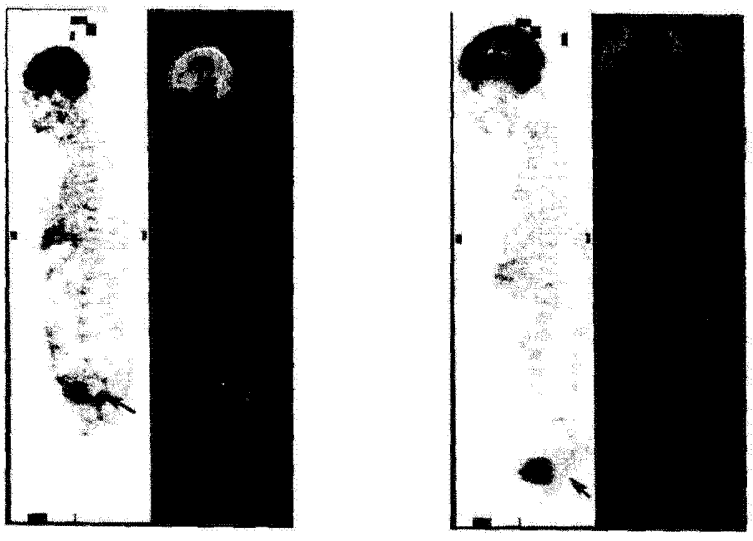


图 28



a b

图 29