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(57) **Abrégé/Abstract:**
Methods for treating cancer patients with human platelet derived growth factor receptor alpha inhibiting compounds, in which the patient is identified as having a cancer that is human platelet derived growth factor receptor beta negative.

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Abstract:

Methods for treating cancer patients with human platelet derived growth factor receptor alpha inhibiting compounds, in which the patient is identified as having a cancer that is human platelet derived growth factor receptor beta negative.

Methods of Treating Cancer with PDGFR Alpha Inhibitors

The present invention relates to the field of cancer. More specifically, the present invention relates to the treatment of cancer patients with platelet derived growth factor receptor alpha ("PDGFRα") inhibiting compounds. Even more particularly, the present invention relates to the treatment of cancer patients with PDGFRα inhibiting compounds, wherein the cancer patients are identified as being PDGFR beta ("PDGFRβ") negative.

Cancer is a disease with extensive histoclinical heterogeneity including wide variations in tumor morphology and physiology. Although some conventional histologic and clinical features have been correlated to prognosis, the vast heterogeneity across the forms of cancer, spanning from the cellular to the tissue level, impacts response to therapy and subsequent benefit to the patient. Therefore, selectively treating cancer patients who will benefit from a particular treatment continues to pose a challenge.

PDGFRα inhibiting compounds have shown promise as a therapeutic for cancer in preclinical and clinical studies. Despite this promise, PDGFRα inhibiting compounds have failed to meet therapeutic endpoints in some oncology clinical trials. For example, in clinical trials for treating soft tissue sarcoma, LARTRUVO®, an antibody that specifically binds human PDGFRα, failed to meet certain therapeutic endpoints. Thus, a need exists for improved methods for treating patients with PDGFRα inhibiting compounds. In particular, such methods should provide prognostic, diagnostic or predictive value for cancer patients treated with PDGFRα inhibiting compounds. The present disclosure addresses this need by providing methods of treating cancer patients with PDGFRα inhibiting compounds.

Although in some instances, methods for treating particular types of cancer, or treating patients with specific therapeutics, have shown promise, with regard to treating cancer patients using PDGFRα inhibiting compounds, no reliable methods currently exist. The present disclosure, surprisingly provides methods of treating cancer patients with PDGFRα inhibiting compounds which provide prognostic, diagnostic or predictive value for cancer patients treated with PDGFRα inhibiting compounds. More particularly, embodiments of the present disclosure provide methods for treating cancer patients having a cancer that is human PDGFRβ negative by administering a PDGFRα inhibiting compound.

Embodiments of the present disclosure further provide a method of treating cancer in a patient in need thereof, comprising administering to the patient an effective amount of a PDGFRα inhibiting compound. Specifically, embodiments of the present disclosure provide methods of treating cancer in a patient in need thereof, comprising administering to the patient an effective amount of a PDGFRα inhibiting compound, wherein the patient is identified as having a cancer that is human PDGFRβ negative. In yet another embodiment, the present disclosure provides a method of treating a patient having a human PDGFRβ negative cancer, comprising administering to the patient an effective amount of a PDGFRα inhibiting compound.

Accordingly, embodiments of the present disclosure provide methods of treating cancer in a patient comprising identifying a patient as having a cancer that is human PDGFRβ negative. In an embodiment the present disclosure provides a method of treating cancer in a patient in need thereof, comprising identifying the patient as having a cancer that is human PDGFRβ negative, and administering an effective amount of a PDGFRα inhibiting compound to the patient. In a further embodiment the present disclosure provides a method of treating cancer in a patient in need thereof, by administering to the patient an effective amount of a PDGFRα inhibiting compound, wherein the patient is identified as having a cancer that is human PDGFRβ negative and human PDGFRα positive.

In some embodiments of the present disclosure methods of identifying a patient as having a cancer that is human PDGFRβ negative comprise, contacting a biological sample from the patient with an antibody that specifically binds human PDGFRβ, and detecting binding of the antibody to human PDGFRβ in the biological sample.

According to embodiments of the present disclosure, a method of detecting PDGFRβ in a biological sample is provided. Such methods comprise performing an assay on a biological sample from the patient. Embodiments of the present disclosure further provide a method comprising contacting the biological sample with an antibody that specifically binds human PDGFRβ and detecting binding of the antibody to human PDGFRβ in the biological sample.

According to embodiments of the present disclosure, a method of diagnosing a patient with cancer as in need of treatment with a PDGFRα inhibiting compound is provided. Such methods comprise identifying the patient as having a cancer that is

human PDGFRβ negative. Such methods further comprise performing an assay on a biological sample from the patient. Embodiments of the present disclosure further provide a method comprising contacting the biological sample with an antibody that specifically binds human PDGFRβ and detecting binding of the antibody to human PDGFRβ in the biological sample.

According to embodiments of the present disclosure, a method of quantifying human PDGFRβ in a biological sample is provided. Such methods comprise contacting a biological sample from a patient with an antibody that specifically binds human PDGFRβ and detecting binding of the antibody to human PDGFRβ in the biological sample.

In an embodiment of the present disclosure, the biological sample is determined to be PDGFRβ negative when PDGFRβ in the biological sample is determined to be present in less than about 10% of tumor cells of the biological sample. In yet other embodiments the biological sample is determined to be PDGFRβ positive when PDGFRβ in the biological sample is determined to be present in greater than or equal to about 10% of tumor cells of the biological sample. In a further embodiment of the present disclosure the patient is administered a PDGFRα inhibiting compound if the biological sample from the patient is determined to be PDGFRβ negative.

In particular embodiments the present disclosure provides a method of diagnosing a cancer patient as in need of treatment with a PDGFRα inhibiting compound, comprising the steps of: obtaining a biological sample from the patient; contacting the biological sample with an antibody or antigen-binding fragment thereof that specifically binds human PDGFRβ, wherein a complex of the antibody or antigen-binding fragment thereof and human PDGFRβ is formed; contacting with a second antibody or antigen binding fragment thereof, the complex of the human PDGFRβ antibody or antigen-binding fragment thereof and human PDGFRβ, wherein the second antibody comprises a detectable label; detecting a signal provided by said detectable label; and wherein, if the biological sample from the cancer patient is determined as PDGFRβ negative the cancer patient is diagnosed as in need of treatment with a PDGFRα inhibiting compound. In a further embodiment the present disclosure comprises the step of administering to the cancer patient an effective amount of a PDGFRα inhibiting compound, if the biological sample is determined to be PDGFRβ negative.

An embodiment of the present disclosure, provides an in vitro method of diagnosing a cancer patient as in need of treatment with an antibody or antigen binding fragments thereof, that specifically binds human PDGFRα, comprising: obtaining a biological sample from the patient; contacting the biological sample with an antibody or antigen-binding fragment thereof that specifically binds human PDGFRβ, wherein a complex of the PDGFRβ antibody or antigen-binding fragment thereof and human PDGFRβ is formed; removing any non-specifically bound PDGFRβ antibody or antigen-binding fragment thereof; detecting and quantifying the human PDGFRβ in the biological sample; and wherein, if the biological sample from the cancer patient is determined to be PDGFRβ negative the cancer patient is diagnosed as in need of treatment with an antibody or antigen binding fragment thereof, that specifically binds human PDGFRα. In yet further embodiments the step of detecting human PDGFRβ in the biological sample comprises detecting with a second antibody or antigen binding fragment thereof, the complex of the PDGFRβ antibody or antigen-binding fragment thereof and human PDGFRβ in the biological sample. In yet even further embodiments of the present disclosure, at least one of the PDGFRβ antibody or antigen binding fragment thereof, or the second antibody or antigen binding fragment thereof, comprises a detectable label. In yet a further embodiment said step of detecting human PDGFRβ in the biological sample comprises detecting a signal provided by the detectable label upon formation of the complex comprising, the PDGFRβ antibody and human PDGFRβ or the second antibody and human PDGFRβ. In yet a further embodiment said step of detecting human PDGFRβ in the biological sample comprises detecting a signal provided by the detectable label upon formation of the complex comprising, the antibody, human PDGFRβ, and the second antibody.

Further embodiments of the present disclosure comprise the step of administering to the cancer patient an effective amount of an antibody specifically binding PDGFRα, if the biological sample is determined to be PDGFRβ negative.

In embodiments of the present disclosure the PDGFRα inhibiting compound is an antibody or an antigen binding fragment thereof. In other embodiments of the present disclosure the PDGFRα inhibiting compound is a small molecule inhibitor. In particular embodiments, the PDGFRα inhibiting compound is an antibody that specifically binds PDGFRα. In even more particular embodiments, the antibody specifically binding

PDGFRα is olaratumab. In some embodiments the PDGFRα inhibiting compound is an antibody drug conjugate. In some embodiments the PDGFRα inhibiting compound is an antibody where the antibody is labeled with a radiopharmaceutical targeting agent.

According to some embodiments, antibodies are provided that specifically bind PDGFRα. In more specific embodiments, the antibody that specifically binds PDGFRα comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises heavy chain complementarity determining regions (HCDR) HCDR1, HCDR2, and HCDR3, and the VL comprises light chain complementarity determining regions (LCDR) LCDR1, LCDR2, and LCDR3, wherein: the HCDR1 comprises SEQ ID NO: 5, the HCDR2 comprises SEQ ID NO: 6, the HCDR3 comprises SEQ ID NO: 7, the LCDR1 comprises SEQ ID NO: 8, the LCDR2 comprises SEQ ID NO: 9, and the LCDR3 comprises SEQ ID NO: 10. In a further embodiment, the VH of the antibody that specifically binds PDGFRα comprises SEQ ID NO: 3 and the VL comprises SEQ ID NO: 4. In yet even a further embodiment, the antibody which specifically binds PDGFRα comprises a heavy chain (HC) and a light chain (LC), wherein the HC comprises SEQ ID NO: 1 and the LC comprises SEQ ID NO: 2. In yet a particular embodiment, the antibody which specifically binds PDGFRα is olaratumab.

In yet further embodiments of the present disclosure, an effective amount of antibody or antigen binding fragment thereof, that specifically binds PDGFRα is administered to a patient identified as having a cancer that is human PDGFRβ negative. In such embodiments an effective amount of antibody or antigen binding fragment thereof is administered to the patient identified as having a cancer that is human PDGFRβ negative at a loading dose of about 15 mg/kg, or about 20 mg/kg, or about 25 mg/kg on each of day 1 and day 8 of a first 21-day cycle or on each of day 1 and day 8 of a first 28-day cycle, followed by administering a standard dose of the antibody or antigen binding fragment thereof to the patient, at about 15 mg/kg, about 20 mg/kg, or about 25 mg/kg on each of day 1 and day 8 of a subsequent 21-day cycle or on each of day 1 and day 8 of a subsequent 28-day cycle. In yet a further embodiment the antibody or antigen binding fragment thereof is administered in simultaneous, separate, or sequential combination with one or more chemotherapeutic agents. In an embodiment the chemotherapeutic agent comprises at least one of nab-paclitaxel, doxorubicin, gemcitabine, or docetaxel.

In yet further embodiments of the present disclosure, an effective amount of olaratumab is administered to a patient identified as having a cancer that is human PDGFRβ negative. In such embodiments an effective amount of olaratumab is administered to the patient identified as having a cancer that is human PDGFRβ negative, at a loading dose of about 15 mg/kg, or about 20 mg/kg, or about 25 mg/kg, on each of day 1 and day 8 of a first 21-day cycle or on each of day 1 and day 8 of a first 28-day cycle, followed by administering a standard dose of olaratumab to the patient at about 15 mg/kg, about 20 mg/kg, or about 25 mg/kg, on each of day 1 and day 8 of a subsequent 21-day cycle or on each of day 1 and day 8 of a subsequent 28-day cycle. In yet a further embodiment olaratumab is administered in simultaneous, separate, or sequential combination with one or more chemotherapeutic agents. In an embodiment the chemotherapeutic agent comprises at least one of nab-paclitaxel, doxorubicin, gemcitabine, or docetaxel.

In some embodiments of the present disclosure, the cancer determined as PDGFRβ negative is soft tissue sarcoma, pancreatic cancer, endometrial cancer, ovarian cancer, osteosarcoma, chondrosarcoma, rhabdomyosarcoma, breast cancer, bone cancer, or prostate cancer. In some embodiments the cancer is leiomyosarcoma. In some embodiments the cancer is liposarcoma. In an embodiment of the present disclosure the cancer is a primary tumor. In an embodiment the cancer is a metastatic cancer. In yet other embodiments the cancer has metastasized. In particular embodiments of the present disclosure the patient is female, and the female is determined to have a PDGFRβ negative cancer.

Platelet derived growth factor receptor alpha (PDGFRα) and platelet derived growth factor receptor beta (PDGFRβ) belong to the type III tyrosine kinase receptor (RTK) family and are implicated in various cancer types. PDGFRα has been considered as a relevant factor in tumor proliferation, angiogenesis, and metastatic dissemination in various cancer types.

The terms "PDGFR alpha inhibiting compound" or "PDGFR alpha inhibitor" as used interchangeably herein, is a compound that decreases, blocks, inhibits, abrogates, or interferes with signal transduction resulting from the interaction of PDGFRα with either one or more of its ligands or binding partners. PDGFRα inhibiting compounds can be extracellular inhibitors or intracellular inhibitors and more than one inhibitor may be

employed. Extracellular inhibitors include, but are not limited to, compounds that bind to PDGFRα or one or more of its ligands (for example, PDGF-AA, -AB, -BB, -CC). Intracellular inhibitors include, but are not limited to, small molecule receptor tyrosine kinase inhibitors. Non-limiting examples of PDGFRα inhibiting compounds include antibodies, antigen binding fragments thereof, small molecule inhibitors, antibody drug conjugates, fusion proteins, immunoadhesin molecules, and oligopeptides.

The terms "antibody," and 'antigen binding fragments thereof' as used herein, refers to an immunoglobulin molecule that specifically binds an antigen. In an embodiment the antibody or antigen binding fragment thereof specifically binds PDGFRα. An exemplary antibody of the present disclosure is an immunoglobulin G type 1 (IgG1) antibody or antigen binding fragment thereof. According to particular embodiments, such antibody or antigen binding fragment thereof, comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises CDRs HCDR1, HCDR2 and HCDR3 and the VL comprises complementarity determining regions (CDRs) LCDR1, LCDR2, and LCDR3 wherein HCDR1 has the amino acid sequence of SEQ ID NO: 3, HCDR2 has the amino acid sequence of SEQ ID NO: 4, and HCDR3 has the amino acid sequence of SEQ ID NO: 5, LCDR1 has the amino acid sequence of SEQ ID NO: 6, LCDR2 has the amino acid sequence of SEQ ID NO: 7, and LCDR3 has the amino acid sequence of SEQ ID NO: 8. According to some embodiments the antibody or antigen binding fragment thereof provided by the present disclosure, the VH has the amino acid sequence of SEQ ID NO: 3 and the VL has the amino acid sequence of SEQ ID NO: 4. According to some embodiments the antibody or antigen binding fragment thereof provided by the present disclosure, comprises a light chain (LC) and a heavy chain (HC) wherein the HC has the amino acid sequence of SEQ ID NO: 1 and the LC has the amino acid sequence of SEQ ID NO: 2. In an embodiment of the present disclosure the antibody is olaratumab.

According to some embodiments, antibodies of the present disclosure may be humanized. In some embodiments, antibodies of the present disclosure comprise an IgG1 heavy chain. In some embodiments, antibodies of the present disclosure comprise a kappa light chain. According to even further embodiments, the present disclosure provides pharmaceutical compositions comprising an antibody of the present disclosure and one or more pharmaceutically acceptable carriers, diluents or excipients.

Embodiments of an antibody include a monoclonal antibody, polyclonal antibody, human antibody, humanized antibody, chimeric antibody, bispecific or multispecific antibody, or conjugated antibody. The antibodies can be of any class (e.g., IgG, IgE, IgM, IgD, IgA), and any subclass (e.g., IgG1, IgG2, IgG3, IgG4).

Assignment of amino acid residues to the CDRs may be done according to the well-known schemes, including those described in Kabat (Kabat et al., "Sequences of Proteins of Immunological Interest," National Institutes of Health, Bethesda, Md. (1991)), Chothia (Chothia et al., "Canonical structures for the hypervariable regions of immunoglobulins", Journal of Molecular Biology, 196, 901-917 (1987); Al-Lazikani et al., "Standard conformations for the canonical structures of immunoglobulins", Journal of Molecular Biology, 273, 927-948 (1997)), North (North et al., "A New Clustering of Antibody CDR Loop Conformations", Journal of Molecular Biology, 406, 228-256 (2011)), or IMGT (the international ImMunoGeneTics database available on at www.imgt.org; see Lefranc et al., Nucleic Acids Res. 1999; 27:209-212).

The term "specifically binds PDGFRα" or "binds PDGFRα" as used herein, refers to an interaction of an antibody with an epitope region of human PDGFRα as provided in e.g., NCBI reference sequence P16234.1 (SEQ ID NO: 11). As used herein, the term "specifically binds PDGFRβ" or "binds PDGFRβ" refers to an interaction of an antibody with an epitope region of human PDGFRβ as provided in e.g., NCBI reference sequence P09619.1 (SEQ ID NO: 12).

The terms "PDGFRβ negative" or "PDGFRβ positive" as used herein, refer to whether the form of cancer of a patient is a PDGFRβ negative or PDGFRβ positive form of cancer. As detailed herein, whether the form of cancer of a patient is a PDGFRβ negative or PDGFRβ positive form of cancer may be determined based on a qualitative or quantitative determination. According to embodiments here, whether the form of cancer of a patient is a PDGFRβ negative or PDGFRβ positive form of cancer may be determined based on an assessment of approximate levels of PDGFRβ present in a biological sample from a cancer patient when compared to a reference value. According to a more particular embodiment, a patient is determined to have a PDGFRβ negative form of cancer when the approximate level of PDGFRβ present in the biological sample is less than about 10% of tumor cells in a biological sample from the patient, as determined by an IHC assay. In another embodiment, a patient is determined to have a

PDGFRβ negative form of cancer based on levels of PDGFRβ as determined by a grading system using reference value(s).

Levels of PDGFRβ, as provided by assays of the present disclosure or assays known in the art, may be absolute values (e.g., level within a biological sample) or relative values (e.g., level compared to a reference). Levels of PDGFRβ in tumor cells can be evaluated via assays including, but not limited to, immunohistochemistry (IHC), polymerase chain reaction (PCR), quantitative, qualitative or semi-quantitative reverse transcription PCR (RT-PCR), applications of automated or semi-automated image analysis of IHC or other quantitative/semi-quantitative/qualitative assessments of protein expression or mRNA expression, artificial intelligence analysis of scanned slides or other laboratory acquired data for protein expression, brightfield in situ hybridization (BRISH), fluorescent in situ hybridization (RNA FISH), protein immunofluorescence, quantitative/semi-quantitative/qualitative proteomics methods, cytological assays, and RNA sequencing.

A "reference value" as used herein refers to a known, or approximate level of a reference value that can be an absolute or relative level, a range, a minimum level, a mean level, a threshold level, and/or a median level. Additionally, a reference value can also serve as a baseline or threshold value. According to a particular embodiment as used herein, a "reference value" of PDGFRβ indicates whether a form of cancer of a patient is a PDGFRβ negative or positive form of cancer.

The terms "biological sample" or "patient sample" used interchangeably herein, refers to a human sample. Non-limiting sources of a biological sample for use in the present invention include cancer, tumors, tumor biopsy. biopsy aspirates, solid tissues, tumor cells, and metastatic, migrating, circulating tumor cells. Additionally, biological sample may also refer to blood, plasma, serum, lymph fluid, ascites, fluidic extracts, the external sections of the skin, respiratory, nasal, intestinal, and genitourinary tracts, tears, saliva, milk, organs, cell cultures and / or cell culture constituents.

The term "about" as used herein, means within 5%.

The term "cancer" as used herein, is a disease pathologically characterized by the physiological condition in a mammal that is typically characterized by unregulated cell proliferation, immortality, metastatic potential, rapid growth and proliferation rate, and/or certain characteristic morphological features. Often, cancer cells are in the form of a

tumor, but such cells may exist alone or may circulate in the blood stream as independent cells, such as leukemic cells, or metastatic, migrating, or circulating, tumor cells. The cancer may be a solid tumor or a leukemia. Tumors may be benign, malignant, or dormant and may also be characterized as primary tumors or metastatic tumors. In some embodiments, non-limiting examples of cancer include soft tissue sarcoma, pancreatic cancer, endometrial cancer, osteosarcoma, chondrosarcoma, rhabdomyosarcoma, breast cancer, bone cancer, prostate cancer, gastrointestinal cancer, colon cancer, squamous cell carcinoma, head and neck cancer, small-cell lung cancer, non-small cell lung cancer, glioblastoma, cervical cancer, ovarian cancer, bladder cancer, hepatoma, colorectal cancer, salivary gland carcinoma, kidney cancer, vulval cancer, thyroid cancer, hepatic cancer, and/or laryngeal cancer.

The terms "soft tissue sarcoma" or "STS" as used herein, is a type of cancer that begins in the tissues that connect, support and surround other body structures. This includes fat, muscle, fibrous tissues, blood vessels, nerves, tendons, linings of joints, or deep skin tissues, and/or the lining of joints. They can be found in any part of the body. More than 50 subtypes of soft tissue sarcoma exist. Types of STS include, but are not limited to, angiosarcoma, dermatofibrosarcoma protuberans, epithelioid sarcoma, gastrointestinal stromal tumor (GIST), Kaposi's sarcoma, liposarcoma, malignant peripheral nerve sheath tumors, myxofibrosarcoma, rhabdomyosarcoma, solitary fibrous tumor, synovial sarcoma, or undifferentiated pleomorphic sarcoma.

Chemotherapeutic agents are chemical agents or drugs that are selectively destructive to cancer cells and tissues. Chemotherapeutics may include but are not limited to compounds such as, taxane compounds, compounds that act via taxane mechanisms, platinum compounds, anthracycline compounds, antimetabolites, epipodophyllotoxin compounds, camptothecin compounds, or any combination thereof. Chemotherapy drugs can be administered alone or in combination with other therapeutic agents. In some embodiments a chemotherapeutic agent comprises nab-paclitaxel, doxorubicin, docetaxel, or gemcitabine.

The term "diagnosis" as used herein, is used to refer to the identification or classification of a molecular or pathological state, disease or condition (e.g., cancer). For example, "diagnosis" may refer to identification of a particular type of cancer. "Diagnosis" may also refer to the classification of a particular subtype of cancer, e.g., by

histopathological criteria, or by molecular features (e.g., a subtype characterized by expression of one or a combination of biomarkers (e.g., particular genes or proteins encoded by said genes, or expression levels of particular genes or proteins encoded by said genes)).

Embodiments of the present disclosure also pertain to methods of clinical diagnosis, or prognosis, of a subject performed by a medical professional using the methods disclosed herein. The methods, as described herein, can, for example, be performed by an individual, a health professional, or a third party, for example a service provider who interprets information from the subject. As explained herein, a medical professional may initiate or modify treatment after receiving information regarding a diagnostic method of the present disclosure. For example, a medical professional may recommend a therapy, a change in therapy or an additional diagnostic assessment.

The terms "treat" or "treating" or "treatment" as used herein, refer to processes involving a slowing, interrupting, arresting, controlling, stopping, reducing, regressing, and/or reversing the progression or severity of an existing disease such as cancer, but does not necessarily involve a total elimination of the disease, or disease state.

The term an "effective amount" as used herein, refers to an amount of a protein or nucleic acid or vector or composition or inhibiting compound that will elicit the biological or medical response of a subject, for example, reduction or inhibition of an enzyme or a protein activity, or ameliorate symptoms, alleviate conditions, slow or delay disease progression, or prevent a disease, etc. In a non-limiting embodiment, the term "effective amount" refers to an amount necessary (at dosages and for periods of time and for the means of administration) of a protein or nucleic acid or vector or composition or inhibiting compound that, when administered to a subject, is effective to at least partially alleviate, inhibit, prevent and/or ameliorate a condition, or a disorder or a disease to achieve the desired therapeutic result. An effective amount of the protein or nucleic acid or vector or composition or inhibiting compound may vary according to factors such as the disease type and state, age, sex, and weight of the individual, and the ability of the protein or nucleic acid or vector or composition, or therapeutic, such as an antibody, to elicit a desired response in the individual. An effective amount is also one in which any toxic or detrimental effects of the protein or nucleic acid or vector or composition or

inhibiting compound of the present invention are outweighed by the therapeutically beneficial effects.

The terms "patient," "subject," and "individual," as used interchangeably herein, refers to a human. In certain embodiments, the patient is further characterized with a disease, disorder, or condition (e.g., cancer). In another embodiment, the patient is further characterized as being at risk of developing a disorder, disease, or condition (metastasis, growth, spread of the cancer or tumor) and would benefit from a reduction in the risk of metastasis, growth, spread of the cancer or tumor.

An antibody of the present invention can be incorporated into a pharmaceutical composition which can be prepared by methods well known in the art and comprise an antibody of the present invention and one or more pharmaceutically acceptable carrier(s) and/or diluent(s) (e.g., Remington, The Science and Practice of Pharmacy, 22nd Edition, Loyd V., Ed., Pharmaceutical Press, 2012, which provides a compendium of formulation techniques as are generally known to practitioners). Suitable carriers for pharmaceutical compositions include any material which, when combined with an antibody of the present invention, retains the molecule's activity and is non-reactive with the patient's immune system. A pharmaceutical composition comprising an antibody of the present invention can be administered to a patient at risk for, or exhibiting, diseases or disorders as described herein by parental routes (e.g., intravenous, subcutaneous, intraperitoneal, intramuscular, or transdermal).

EXAMPLES

Example 1: Assessment of Overall Survival in PDGFRβ negative advanced or metastatic Soft Tissue Sarcoma patients

Study Design: Patients with advanced or metastatic soft tissue sarcoma are treated with olaratumab (20 mg/kg loading dose on Days 1 and 8 of a 21-day cycle in Cycle 1, followed by 15 mg/kg on Days 1 and 8 in subsequent 21-day cycle) in combination with doxorubicin (75 mg/m^2 on Day 1) ("investigational cohort") and compared to patients treated with placebo (on Days 1 and 8) plus doxorubicin (75 mg/m^2 on Day 1) ("control cohort"). Patients are treated for 8 cycles, followed by olaratumab monotherapy or placebo until evidence of progressive disease, unacceptable toxicity or death. PDGFRβ tumor expression status of patients is determined substantially as described herein.

Patients are assessed for median overall survival (OS).

Methods of determining PDGFRβ expression: PDGFRβ expression in tumor cells can be evaluated via methods including, but not limited to, immunohistochemistry, quantitative, qualitative or semi-quantitative reverse transcription PCR (RT-PCR), applications of automated or semi-automated image analysis of IHC or other quantitative/semi-quantitative/qualitative assessments of protein expression, artificial intelligence analysis of scanned slides or other laboratory acquired data for protein expression, brightfield in situ hybridization (BRISH), fluorescent in situ hybridization (RNA FISH), protein immunofluorescence, quantitative/semi-quantitative/qualitative proteomics methods and RNA sequencing.

Immunohistochemistry Assay to determine PDGFRβ expression: For immunohistochemistry analysis, tumor tissue from patients is collected, formalin-fixed in 10% neutral buffered formalin, and paraffin-embedded (FFPE). PDGFRβ protein expression on tumor cells is assessed by immunohistochemistry. Briefly, from FFPE tissue blocks containing the patient tumor tissue, a 4-6 micrometer section is obtained and placed on a positively charged glass slide. Anti-PDGFRβ mouse monoclonal antibody 2B3 is used to detect expression of PDGFRβ (clone 2B3, Cell Signaling Technology® catalog number 3175S), diluted in Dako Primary Antibody Diluent with Background Reducing Components (Dako/Agilent catalog number S3022) at 0.25 μg/mL. Immunohistochemistry is performed on a Dako Autostainer Link 48/PT Link Incubator. Deparaffinization with the Link 48/PT Link Incubator is accomplished at 97 °C for 20 minutes. Target retrieval is next accomplished with immersion of the unstained slides into EnVision™ FLEX Target Retrieval Solution High pH (Dako) on the Dako Link48/PT Link Incubator. Following a rinse in RT EnVision™ FLEX Wash Buffer (1x), specific immunohistochemical staining with the 2B3 antibody is accomplished by FLEX Peroxidase Block for 5 minutes, application of the 0.25 ug/mL concentration of anti-human PDGFRβ antibody 2B3 with incubation for 60 minutes, followed by FLEX/HRP application and incubation for 20 minutes, then application of FLEX DAB+ Substrate Chromogen for 10 minutes, and finally FLEX hematoxylin for 5 minutes. Ready-to-use FLEX Mouse Negative Control (Dako/Agilent catalog number IR750) is performed alongside PDGFRβ staining and used as a quality control (negative control) for the assay. Stained slides are then evaluated by trained personnel using a brightfield

microscope. PDGFRβ tumor expression status is provided dichotomously as "positive" or "negative", where a "positive" result is defined as samples where at least 10% of the tumor cells present (rounded to the nearest decile) demonstrate at least weak but specific membranous staining (1+ on a 0, 1+, 2+, 3+ scale of staining intensity, with 1+ being weakest but still specific membrane staining and 3+ being strong and diffuse membrane staining). "Negative" corresponded to staining that did not meet these criteria.

Results:

***STS Patients*:** As demonstrated in Table 1, STS patients identified as having PDGFRβ negative tumor status had a significant improvement in median OS of 28.32 months in the investigational cohort when compared to 20.57 months for patients in the control cohort (HR=0.85 [95% CI: 0.54-1.33] p=0.4861). Furthermore, patients in the investigational cohort identified as having both PDGFRβ negative tumors status and PDGFRα positive tumor status also showed a significant improvement in median OS of 28.5 months (N=66) vs. 20.6 months (N=75) in the control cohort. However, no significant differences in median OS between the investigational and control cohort were observed in patients whose tumor status was identified as, PDGFRβ positive (18.8 months vs 19.9 months respectively for the investigational and control cohort), PDGFRα positive (17.2 months vs 19.1 months respectively for the investigational and control cohort), and PDGFRα negative (23.6 months vs 21.9 months respectively for the investigational and control cohort).

Table 1: Median OS in STS Patients

Category of Patients	Olaratumab + Doxorubicin		Placebo + Doxorubicin		
	N	Median OS months (95% CI)	N	Median OS months (95% CI)	HR (95% CI) p-value
PDGFRβ negative	66	28.32 (14.42 - NA)	75	20.57 (16.49 - NA)	0.85 (0.54 - 1.33) p=0.4861
PDGFRβ positive	163	18.79 (15.24 - 21.19)	160	19.88 (15.57 - 23.75)	1.10 (0.84 - 1.44) p=0.4759

N = patients treated in investigation cohort or control cohort; OS = Overall Survival; HR = Hazard Ratio; CI = confidence interval, p-value = Stratified Log-rank p-value.

***LMS Patients*:** As demonstrated in Table 2, LMS patients in the investigational cohort identified as having PFGDRβ negative tumor status had a significant improvement in median OS of 29.11 months (N=29) compared to 21.88 months (N=37) in the control cohort (HR=0.65 [95% CI: 0.33-1.25; p=0.1970). However, no differences in median OS in LMS patients identified as having PDGFRβ positive tumor status was observed between the investigational cohort (20.14 months; N=77) and the control cohort (21.39 months; N=73) (HR=1.05 [95% CI: 0.71-1.55; p=0.7951).

***LMS Female Patients*:** Analysis of PDGFRβ status in LMS female patients, showed a significant improvement in OS HR in the subpopulation of LMS female patients identified as having PDGFRβ negative tumor status (0.55; N = 53; p = 0.14) when compared to OS HR for LMS female patients identified as having PDGFRβ positive tumor status (1.34; N = 115; p = 0.20). Further adjusting for ECOG PS, the OS HR for PDGFRβ positive women with LMS was 1.34 (N = 115; p = 0.20), while the OS HR for PDGFRβ negative women with LMS was 0.55 (N = 53; p= 0.14) . This difference in OS HR between PDGFRβ positive and negative women with LMS resulted in a statistically significant "treatment by PDGFRβ " interaction (N = 168; p = 0.040).

LMS Patients, where LMS Female Patients having PDGFRβ positive tumor status are excluded: As demonstrated in Table 2, LMS patients, where the LMS Female Patients identified as having PDGFRβ positive tumor status are excluded from the LMS Median OS analysis, a significant overall survival benefit in the investigational cohort of 28.5 months (N=58) is observed when compared to 20.9 months (N=61) in the control cohort (HR = 0.60; N=119; p = 0.035). This interaction of PDGFRβ expression status is not observed for men with LMS.

Table 2. Median OS in LMS Patients

Category of Patients	Olaratumab + Doxorubicin	Placebo + Doxorubicin	

	N	Median OS months (95% CI)	N	Median OS months (95% CI)	Hazard Ratio (95% CI) p-value
LMS PDGFRβ negative	29	29.11 (20.73, NA)	37	21.88 (16.72, 35.55)	0.65 (0.33, 1.25) p=0.1970
LMS PDGFRβ positive	77	20.14 (13.08, 22.11)	73	21.39 (15.57, 24.57)	1.05 ((0.71, 1.55) p=0.7951
LMS Patients excluding PDGFRβ positive Females	58	28.5	61	20.9	0.60; p = 0.035

N = patients treated in investigation cohort or control cohort; OS = Overall Survival; HR = Hazard Ratio; CI = confidence interval; p-value = stratified Log-rank p-value.

Example 2: Assessment of Overall Survival in PDGFRβ negative non-resectable metastatic Pancreatic Cancer patients

***Study Design*:** Median overall survival of patients with PDGFRβ negative non-resectable metastatic Pancreatic cancer are treated with olaratumab in a dose escalation schedule (15 mg/kg, 20 mg/kg, or 25 mg/kg administered on days 1, 8, and 15 of a 28-day cycle) in combination with nab-paclitaxel and gemcitabine (administered on days 1, 8, and 15 for a 28-day cycle per USPI insert). Patients with non-resectable metastatic Pancreatic cancer are treated with olaratumab on days 1, 8, and 15 of a 28-day cycle followed by administration of nab-paclitaxel (125 mg/m2), and gemcitabine (1000 mg/m2) on days 1, 8, and 15 of each 28-day cycle. Patients are assessed for overall survival.

Example 3: Assessment of Overall Survival in PDGFRβ negative advanced Soft Tissue Sarcoma patients

***Study Design*:** Median overall survival of patients with PDGFRβ negative advanced or metastatic soft tissue sarcoma are treated with olaratumab in a dose escalation study at 15 mg/kg of olaratumab (administered on days 1 and 8) or 20 mg/kg of olaratumab (administered on days 1 and 8), in combination with gemcitabine administered at 900

mg/m2 on days 1 and 8 and docetaxel administered at 75 mg/m2 on day 8 of a 21-day cycle. Patients are assessed for overall survival.

SEQUENCES

SEQ ID NO: 1 (HC of human PDGFR alpha antibody)

MGWSCIILFLVATATGVHSQLQLQESGPGLVKPSETLSLTCTVSGGSINSSSYYWG
WLRQSPGKGLEWIGSFFYTGSTYYNPSLRSRLTISVDTSKNQFSLMLSSVTAADT
AVYYCARQSTYYYGSGNYYGWFDRWDQGTLVTVSSASTKGPSVFPLAPSSKSTS
GGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSS
SLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKP
KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSR
EEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKL
TVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

SEQ ID NO: 2 (LC of human PDGFR alpha antibody)

MGWSCIILFLVATATGVHSEIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQ
QKPGQAPRLLIYDASNRATGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQRSN
WPPAFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQW
KVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLS
SPVTKSFNRGEC

SEQ ID NO: 3 (VH of human PDGFR alpha antibody)

QLQLQESGPGLVKPSETLSLTCTVSGGSINSSSYYWGWLRQSPGKGLEWIGSFFY
TGSTYYNPSLRSRLTISVDTSKNQFSLMLSSVTAADTAVYYCARQSTYYYGSGNY
YGWFDRWDQGTLVTVSS

SEQ ID NO: 4 (VL of human PDGFR alpha antibody)

EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRAT
GIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQRSNWPPAFGQGTKVEIK

SEQ ID NO: 5 (HCDR1 of human PDGFR alpha antibody)

SSSYY

SEQ ID NO: 6 (HCDR2 of human PDGFR alpha antibody)

SFFYTGSTYYNPSLRS

SEQ ID NO: 7 (HCDR3 of human PDGFR alpha antibody)
QSTYYYGSGNYYGWFDR

SEQ ID NO: 8 (LCDR1 of human PDGFR alpha antibody)
RASQSVSSYLA

SEQ ID NO: 9 (LCDR2 of anti-human PDGFR alpha antibody)
DASNRAT

SEQ ID NO: 10 (LCDR3 of human PDGFR alpha antibody)
QQRSNWPPA

SEQ ID NO: 11 (human PDGFR alpha)
MGTSHPAFLVLGCLLTGLSLILCQLSLPSILPNENEKVVQLNSSFSLRCFGESEVSW
QYPMSEEESSDVEIRNEENNSGLFVTVLEVSSASAAHTGLYTCYYNHTQTEENEL
EGRHIYIYVPDPDVAFVPLGMTDYLVIVEDDDSAIIPCRTTDPETPVTLHNSEGVV
PASYDSRQGFNGTFTVGPYICEATVKGKKFQTIPFNVYALKATSELDLEMEALKT
VYKSGETIVVTCAVFNNEVVDLQWTYPGEVKGKGITMLEEIKVPSIKLVYTLTVP
EATVKDSGDYECAARQATREVKEMKKVTISVHEKGFIEIKPTFSQLEAVNLHEVK
HFVVEVRAYPPPRISWLKNNLTLIENLTEITTDVEKIQEIRYRSKLKLIRAKEEDSG
HYTIVAQNEDAVKSYTFELLTQVPSSILDLVDDHHGSTGGQTVRCTAEGTPLPDIE
WMICKDIKKCNNETSWTILANNVSNIITEIHSRDRSTVEGRVTFAKVEETIAVRCL
AKNLLGAENRELKLVAPTLRSELTVAAAVLVLLVIVIISLIVLVVIWKQKPRYEIR
WRVIESISPDGHEYIYVDPMQLPYDSRWEFPRDGLVLGRVLGSGAFGKVVEGTA
YGLSRSQPVMKVAVKMLKPTARSSEKQALMSELKIMTHLGPHLNIVNLLGACTK
SGPIYIITEYCFYGDLVNYLHKNRDSFLSHHPEKPKKELDIFGLNPADESTRSYVIL
SFENNGDYMDMKQADTTQYVPMLERKEVSKYSDIQRSLYDRPASYKKKSMLDS
EVKNLLSDDNSEGLTLLDLLSFTYQVARGMEFLASKNCVHRDLAARNVLLAQG
KIVKICDFGLARDIMHDSNYVSKGSTFLPVKWMAPESIFDNLYTTLSDVWSYGIL
LWEIFSLGGTPYPGMMVDSTFYNKIKSGYRMAKPDHATSEVYEIMVKCWNSEPE

KRPSFYHLSEIVENLLPGQYKKSYEKIHLDFLKSDHPAVARMRVDSDNAYIGVTY
KNEEDKLKDWEGGLDEQRLSADSGYIIPLPDIDPVPEEEDLGKRNRHSSQTSEESA
IETGSSSSTFIKREDETIEDIDMMDDIGIDSSDLVEDSFL

SEQ ID NO: 12 (human PDGFR beta)

MRLPGAMPALALKGELLLLSLLLLLEPQISQGLVVTPPGPELVLNVSSTFVLTCSG
SAPVVWERMSQEPPQEMAKAQDGTFSSVLTLTNLTGLDTGEYFCTHNDSRGLET
DERKRLYIFVPDPTVGFLPNDAEELFIFLTEITEITIPCRVTDPQLVVTLHEKKGDV
ALPVPYDHQRGFSGIFEDRSYICKTTIGDREVDSDAYYVYRLQVSSINVSVNAVQ
TVVRQGENITLMCIVIGNEVVNFEWTYPRKESGRLVEPVTDFLLDMPYHIRSILHI
PSAELEDSGTYTCNVTESVNDHQDEKAINITVVESGYVRLLGEVGTLQFAELHRS
RTLQVVFEAYPPPTVLWFKDNRTLGDSSAGEIALSTRNVSETRYVSELTLVRVKV
AEAGHYTMRAFHEDAEVQLSFQLQINVPVRVLELSESHPDSGEQTVRCRGRGMP
QPNIIWSACRDLKRCPRELPPTLLGNSSEEESQLETNVTYWEEEQEFEVVSTLRLQ
HVDRPLSVRCTLRNAVGQDTQEVIVVPHSLPFKVVVISAILALVVLTIISLIILIML
WQKKPRYEIRWKVIESVSSDGHEYIYVDPMQLPYDSTWELPRDQLVLGRTLGSG
AFGQVVEATAHGLSHSQATMKVAVKMLKSTARSSEKQALMSELKIMSHLGPHL
NVVNLLGACTKGGPIYIITEYCRYGDLVDYLHRNKHTFLQHHSDKRRPPSAELYS
NALPVGLPLPSHVSLTGESDGGYMDMSKDESVDYVPMLDMKGDVKYADIESSN
YMAPYDNYVPSAPERTCRATLINESPVLSYMDLVGFSYQVANGMEFLASKNCVH
RDLAARNVLICEGKLVKICDFGLARDIMRDSNYISKGSTFLPLKWMAPESIFNSLY
TTLSDVWSFGILLWEIFTLGGTPYPELPMNEQFYNAIKRGYRMAQPAHASDEIYEI
MQKCWEEKFEIRPPFSQLVLLLERLLGEGYKKKYQQVDEEFLRSDHPAILRSQAR
LPGFHGLRSPLDTSSVLYTAVQPNEGDNDYIIPLPDPKPEVADEGPLEGSPSLASST
LNEVNTSSTISCDSPLEPQDEPEPEPQLELQVEPEPELEQLPDSGCPAPRAEAEDSF
L

WE CLAIM:

1. A method of treating cancer in a patient in need thereof, comprising administering to the patient an effective amount of a PDGFRα inhibiting compound, wherein the patient is identified as having a cancer that is human PDGFRβ negative.
2. A method of treating a patient having a human PDGFRβ negative cancer, comprising administering to the patient an effective amount of a PDGFRα inhibiting compound.
3. A method of treating cancer in a patient in need thereof, comprising:

identifying the patient as having a cancer that is human PDGFRβ negative; and

administering an effective amount of a PDGFRα inhibiting compound to the patient.
4. A method of diagnosing a patient with cancer as in need of treatment with a PDGFRα inhibiting compound, comprising identifying the patient as having a cancer that is human PDGFRβ negative.
5. The method of Claim 4, wherein the patient is administered an effective amount of a PDGFRα inhibiting compound if the patient is identified as having a cancer that is human PDGFRβ negative.
6. The method of any one of Claims 1, 3 and 4, wherein identifying the patient as having a cancer that is human PDGFRβ negative comprises performing an assay on a biological sample from the patient.
7. The method of Claim 6, wherein the biological sample comprises tissue or bodily fluid.
8. The method of Claim 7, wherein the tissue comprises tumor tissue.
9. The method of Claim 7, wherein the bodily fluid comprises blood, plasma, or serum.
10. The method of any one of Claims 6 to 9, wherein the assay comprises performing an in vitro assay on the biological sample.
11. The method of Claim 10, wherein the in vitro assay comprises a histological assay, or cytological assay.
12. The method of Claim 10, wherein the in vitro assay comprises an immunoassay or polymerase chain reaction assay.

13. The method of any one of Claims 6 to 11, wherein the assay comprises, contacting the biological sample with an antibody, wherein the antibody specifically binds human PDGFRβ, and detecting binding of the antibody to human PDGFRβ in the biological sample.

14. The method of Claim 13, wherein the assay further comprises, quantifying human PDGFRβ in the biological sample and determining whether the biological sample is PDGFRβ negative.

15. The method of Claim 14, wherein the biological sample is determined to be PDGFRβ negative when PDGFRβ in the biological sample is determined to be present in less than about 10% of tumor cells of the biological sample.

16. The method of any one of Claims 1 to 15, wherein the PDGFRα inhibiting compound is an antibody, an antigen binding fragment thereof, or a small molecule inhibitor.

17. The method of Claim 16, wherein the PDGFRα inhibiting compound is an antibody, wherein the antibody specifically binds PDGFRα.

18. The method of Claim 17, wherein the antibody which specifically binds PDGFRα comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises heavy chain complementarity determining regions (HCDR) HCDR1, HCDR2, and HCDR3, and the VL comprises light chain complementarity determining regions (LCDR) LCDR1, LCDR2, and LCDR3, wherein:

the HCDR1 comprises SEQ ID NO: 5,
the HCDR2 comprises SEQ ID NO: 6,
the HCDR3 comprises SEQ ID NO: 7,
the LCDR1 comprises SEQ ID NO: 8,
the LCDR2 comprises SEQ ID NO: 9, and
the LCDR3 comprises SEQ ID NO: 10.

19. The method of Claim 18, wherein the VH comprises SEQ ID NO: 3 and the VL comprises SEQ ID NO: 4.

20. The method of Claim 17, wherein the antibody which specifically binds PDGFRα comprises a heavy chain (HC) and a light chain (LC), wherein the HC comprises SEQ ID NO: 1 and the LC comprises SEQ ID NO: 2.

21. The method of any one of Claims 17 to 20, wherein the antibody which specifically binds PDGFRα is olaratumab.

22. The method of Claim 21, wherein an effective amount of olaratumab is administered to the patient, at a loading dose of about 15 mg/kg, or about 20 mg/kg, or about 25 mg/kg, on each of day 1 and day 8 of a first 21-day cycle or on each of day 1 and day 8 of a first 28-day cycle, followed by administering a standard dose of olaratumab at about 15 mg/kg, about 20 mg/kg, or about 25 mg/kg, on each of day 1 and day 8 of a subsequent 21-day cycle or on each of day 1 and day 8 of a subsequent 28-day cycle.

23. The method of Claim 22, wherein olaratumab is administered in simultaneous, separate, or sequential combination with one or more chemotherapeutic agents.

24. The method of Claim 23, wherein the chemotherapeutic agent comprises of at least one of nab-paclitaxel, doxorubicin, gemcitabine, or docetaxel.

25. The method of any one of Claims 1 to 24, wherein the cancer is soft tissue sarcoma, pancreatic cancer, endometrial cancer, ovarian cancer, bone cancer, osteosarcoma, chondrosarcoma, rhabdomyosarcoma, or prostate cancer.

26. The method of Claim 25, wherein the soft tissue sarcoma is leiomyosarcoma.

27. The method of Claim 25, wherein the soft tissue sarcoma is liposarcoma.

28. The method of any one of Claims 1 to 27, wherein the cancer is metastatic cancer.

29. The method of any one of Claims 1 to 28, wherein the patient is female and wherein the female is determined to have a PDGFRβ negative cancer.

30. A method of identifying a cancer patient having a PDGFRβ in a biological sample from a cancer patient, comprising the steps of:

contacting the sample with an antibody that specifically binds human PDGFRβ; and

detecting binding of the antibody to the human PDGFRβ in the sample.

31. A method of diagnosing a cancer patient as in need of treatment with a PDGFRα inhibiting compound, comprising the steps of:

obtaining a biological sample from the patient;

contacting the biological sample with a first antibody or antigen binding fragment thereof that specifically binds human PDGFRβ, wherein a complex of

the first antibody or antigen binding fragment thereof and human PDGFRβ is formed;

contacting with a second antibody or antigen binding fragment thereof, the complex of the human PDGFRβ antibody or antigen binding fragment thereof and human PDGFRβ, wherein the second antibody comprising a detectable label;

detecting a signal provided by said detectable label; and

wherein, if the biological sample from the cancer patient is determined as PDGFRβ negative the cancer patient is diagnosed as in need of treatment with a PDGFRα inhibiting compound.

32. An in vitro method of diagnosing a cancer patient as in need of treatment with an antibody or antigen binding fragments thereof, that specifically binds human PDGFRα, comprising:

a. obtaining a biological sample from the patient;

b. contacting the biological sample with an antibody or antigen-binding fragment thereof that specifically binds human PDGFRβ, wherein a complex of the PDGFRβ antibody or antigen-binding fragment thereof and human PDGFRβ is formed;

c. removing any non-specifically bound first antibody or antigen-binding fragment thereof;

d. detecting and quantifying the human PDGFRβ in the biological sample; and

wherein, if the biological sample from the cancer patient is determined to be PDGFRβ negative the cancer patient is diagnosed as in need of treatment with an antibody or antigen binding fragments thereof, that specifically binds human PDGFRα.

33. The method of Claim 32, wherein the step of detecting comprises detecting with a second antibody the complex of the PDGFRβ antibody or antigen binding fragment thereof and human PDGFRβ in the biological sample.

34. The method of any one of Claims 32 or 33, wherein at least one of the antibody or the second antibody comprises a detectable label and wherein said step of detecting comprises detecting a signal provided by the detectable label upon

formation of the complex comprising, the antibody and human PDGFRβ or the second antibody and human PDGFRβ.

35. The method of any one of Claims 32 or 33, wherein the second antibody comprises a detectable label and wherein said step of detecting comprises detecting a signal provided by the detectable label upon formation of the complex comprising, the antibody, human PDGFRβ, and the second antibody.

36. The method of any one of claims 30 to 35, further comprising the step of administering to the cancer patient an effective amount of an antibody specifically binding PDGFRα, if the biological sample is determined to be PDGFRβ negative.

37. The method of Claim 36, wherein the antibody is olaratumab.

38. The method of Claim 37, wherein an effective amount of olaratumab is administered to a patient in need thereof at a loading dose of about 15 mg/kg, or about 20 mg/kg, or about 25 mg/kg, on each of day 1 and day 8 of a first 21-day cycle or on each of day 1 and day 8 of a first 28-day cycle, followed by administering a standard dose of olaratumab at about 15 mg/kg, or about 20 mg/kg, or about 25 mg/kg, on each of day 1 and day 8 of a subsequent 21-day cycle or on each of day 1 and day 8 of a subsequent 28-day cycle.

39. The method of Claim 38, wherein olaratumab is administered in simultaneous, separate, or sequential combination with one or more chemotherapeutic agents.

40. The method of claim 39, wherein the chemotherapeutic agent comprises at least one of nab-paclitaxel, doxorubicin, gemcitabine, or docetaxel.