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(54) Title: COMBINATION DRUG THERAPY FOR THE TREATMENT OF CANCER

(57) Abstract: A combination of drugs was used to kill or inhibit the growth of cancer cells. The combination drug therapy includes administering to a human or animal patient diagnosed with cancer at least one drug that inhibits the activity of an intracellular protein that repairs alkylated DNA and a drug that inhibits the interaction between Hdm2 and p53. The combination drug therapy is useful in the treatment of tumors including some tumors that have become drug resistant. In some instances the combination drug therapy allows the drugs to be administered to a patient at therapeutically effective submyeloablative levels. Still another aspect provides a combination drug therapy that includes administering to a cancer patient a therapeutically effective dose of at least one compound that alkylates DNA, at least one compound that inhibits at least one DNA repair protein and at least one compound that prolongs the half-life of p53 by inhibiting the interaction of p53 with HDM2.



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INTERNATIONAL SEARCH REPORT

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PCT/US 08/32924

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 31/00 (2009.01)

USPC - 514/1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
USPC- 514/1Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC- 514/11 514/269 514/365 514/492 514/34; 514/221 514/283 514/49; 424/133.1; 424/85.2;Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
<http://uspto.gov/go/classification/>, PubWest, Google, Google Scholar: benzyguanine, methylguanine dna methyltransferase, lomustine, foremustine, dacarbazine, procarbazine, up-regulates, 'p53 induced', p53, apoptosis, nutlin3, alkylates, DNA, carmustine, myeloablative, methylates, TMZ, expression, 'DNA repair', 6BG, MGMT

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Ueno, et al. Modulation of Chemotherapy Resistance in Regional Therapy: A Novel Therapeutic Approach to Advanced Extremity Melanoma. Molecular Cancer Therapeutics 2006, 5(3):731-38; pg 734, col 2, last para; pg 737, col 1, para 2	1-22
Y	US 2006/0211757 A1 (Wang et al.) 21 Sep 2006 (21.09.2006) para [0011], [0034], [0108]	1-22
Y	Cairncross, et al. Myelocablative Chemotherapy for Recurrent Aggressive Oligodendroglioma. Neuro-Oncology Apr 2000, 2:114-119; Abstract, pg 115, col 1, para 1, 2	6, 13, 14
Y	McKeown, et al. DNA Repair: Therapeutic Implications. Brit. J. Radiol. 2006, 79:91-93; pg 92, col 1, para 2	7, 20
A	Chang, et al. Differential Mechanisms in the Regulation of Endogenous Levels of Thrombopoietin and Interleukin-11 During Thrombocytopenia: Insight Into the Regulation of Platelet Production. Blood 1996, 88:3354-3362; pg 3355	1-22
A	Cai, et al. Mitochondrial Targeting of Human O6-Methylguanine DNA Methyltransferase Protects Against Cell Killing by Chemotherapeutic Alkylating Agent. Cancer Research 2005, 65(8):3319-3327	1-22
A	GenBank Accession Number 1T39_A. Chain A, Human O6-Alkylguanine-Dna Alkyltransferase Covalently Crosslinked To DNA. (01-OCT-2007). [Retrieved from the Internet 02 Jun 2009: < http://www.ncbi.nlm.nih.gov/sviewer/viewer.fcgi?51247521:PROT:5241323 >]	2, 16

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