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[Continued on next page]

(54) Title: METHOD OF TREATING CANCER USING COMBINATION OF BRAF INHIBITOR, MEK INHIBITOR, AND ANTI-CTLA-4 ANTIBODY

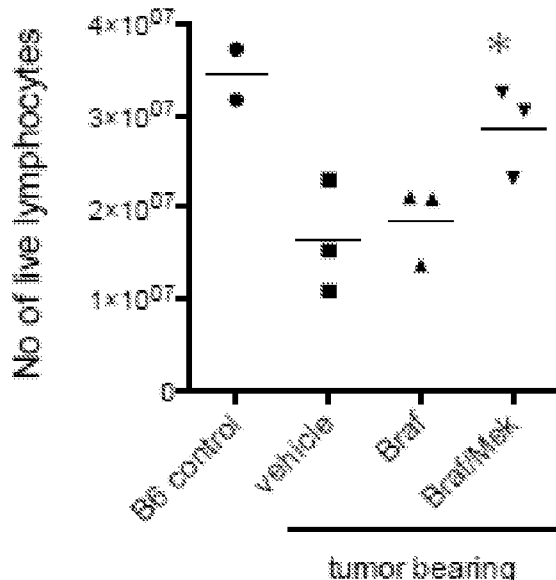


Fig. 1

(57) Abstract: A combination of anti-neoplastic agents that provides increased activity over monotherapy. In particular, the drug combination that includes an anti-CTLA-4 antibody, in combination with the B-Raf inhibitor N-{3-[5-(2-Amino-4-pyrimidinyl)-2-(1,1-dimethylethyl)-1,3-thiazol-4-yl]-2-fluorophenyl}-2,6-difluorobenzenesulfonamide, or a pharmaceutically acceptable salt thereof, and MEK inhibitor N-(3-{3-cyclopropyl-5-[(2-fluoro-4-iodophenyl)amino]-6,8-dimethyl-2,4,7-trioxo-3,4,6,7-tetrahydropyrido[4,3-d]pyrimidin-1(2H)-yl}phenyl)acetamide, or a pharmaceutically acceptable salt or solvate thereof is described.





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- *with international search report (Art. 21(3))*
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 12/48552

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61K 45/00; A61K 39/395; A61K 31/54 (2012.01)
USPC - 424/85.1
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)
IPC(8) - A61K 45/00; A61K 39/395; A61K 31/54 (2012.01)
USPC - 424/85.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
IPC(8) - B65H 59/12; A61K 31/54 (2012.01)
USPC - 424/155.1, 514/227.8

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PubWEST, Dialog
MEK inhibitor, BRAF (B-raf) inhibitor, anti-CTLA-4 antibody (MDX-010, Ipilimumab), methanesulfonate, Dabrafenib mesylate

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2011/0003859 A1 (AHRENDT) 6 January 2011 (06.01.2011) para[0009], para[0011], para [0184], para[0186], para[0211]	1-3 and 5-6
Y	US 2009/0298815 A1 (ADAMS et al.) 3 December 2009 (03.12.2009) para[0060], para[0088], para[0285], para[0434]	1-3 and 5-6
Y	WO 2005/121142 A1 (SAKAI et al.) 22 December 2005 (22.12.2005) Abstract, pgae 6, ln 15-20, page 174 Example 4-1 This document can be viewed by entering the doc number at the following url: http://worldwide.espacenet.com/numberSearch?locale=en_EP	3 and 5-6
Y	Natarajan et al. Novel Immunotherapeutic Agents and Small Molecule Antagonists of Signalling Kinases for the Treatment of Metastatic Melanoma. Drugs: 9 July 2011 - Volume 71 - Issue 10 - pp 1233-1250; page 1235, col 2, page 1238, col 2, pg 1239, col 1-2	3 and 5-6
A	US 2007/0020232 A1 (ROSSIGNOL et al.) 25 January 2007 (25.01.2007) Abstract, para[0022], para[0073]	1-3 and 5-6
A	US 2009/0098135 A1 (BELVIN et al.) 16 April 2009 (16.04.2009) para[0102], para[0105], para [0180]	1-3 and 5-6
A	Eggermont et al. New drugs in melanoma: It's a whole new world. European Journal of Cancer (2011) pages unknown	1-3 and 5-6

Further documents are listed in the continuation of Box C.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent but published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search 25 September 2012 (25.09.2012)	Date of mailing of the international search report 04 FEB 2013
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Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774
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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 12/48552

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. Claims Nos.: 4 and 7-10
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

- Remark on Protest**
- The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
 - The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
 - No protest accompanied the payment of additional search fees.