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Declarations under Rule 4.17:

— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))

— as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))

Published:

— with international search report (Art. 21(3))

— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

— with sequence listing part of description (Rule 5.2(a))

(88) Date of publication of the international search report:

07 December 2017 (07.12.2017)

(54) Title: METHODS FOR MONITORING AND TREATING CANCER

(57) Abstract: The present invention provides therapeutic and diagnostic methods and compositions for cancer, for example, kidney cancer. The invention provides, inter alia, methods of treating cancer and methods of monitoring the response of a patient having a cancer to treatment with an anti-cancer therapy comprising a VEGF antagonist (e.g., an anti-VEGF antibody) and a PD-L1 axis binding antagonist (e.g., an anti-PD-L1 antibody).



INTERNATIONAL SEARCH REPORT

International application No

PCT/US2017/027768

A. CLASSIFICATION OF SUBJECT MATTER

INV. G01N33/574 A61K39/00
ADD.

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)

G01N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Wayne Kuznar: "Adding Anti-PD-L1 Antibody to Bevacizumab Induces Responses in mRCC", 2 March 2015 (2015-03-02), XP055396450, Retrieved from the Internet: URL: http://www.onclive.com/conference-coverage/gu-2015/adding-anti-pd-l1-antibody-to-bevacizumab-induces-responses-in-mrcc [retrieved on 2017-08-07]	118, 119, 123
Y	abstract ----- -/-	1, 2, 5-7, 14-18, 25, 37, 39, 40, 43-45, 52-55, 69-105, 112-123



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"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)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"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

"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

"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

"&" document member of the same patent family

Date of the actual completion of the international search

9 August 2017

Date of mailing of the international search report

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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2017/027768

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	ROY S. HERBST ET AL: "Predictive correlates of response to the anti-PD-L1 antibody MPDL3280A in cancer patients", NATURE, vol. 515, no. 7528, 26 November 2014 (2014-11-26), pages 563-567, XP055262130, ISSN: 0028-0836, DOI: 10.1038/nature14011 figure 7	1,2,5-7, 14-18, 25,37, 39,40, 43-45, 52-55, 69-105, 112-123
T	----- JEFFREY J. WALLIN ET AL: "Atezolizumab in combination with bevacizumab enhances antigen-specific T-cell migration in metastatic renal cell carcinoma", NATURE COMMUNICATIONS, vol. 7, 30 August 2016 (2016-08-30), page 12624, XP055396190, DOI: 10.1038/ncomms12624 -----	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2017/027768

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.:
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:

see additional sheet

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 an 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.:

1, 2, 5-7, 14-18, 25, 37, 39, 40, 43-45, 52-55, 69-105
112-123(all partially)

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1, 2, 5-7, 14-18, 25, 37, 39, 40, 43-45, 52-55, 69-105, 112-123(all partially)

Methods, entities and uses encompassing a combination treatment of a VEGF antagonist and a PD-L1 axis binding antagonist in kidney cancer patients wherein levels of biomarkers are determined, and wherein the biomarker is CD8A.

- 2-7. claims: 1, 2, 5-7, 14-18, 25, 37, 39, 40, 43-45, 52-55, 69-105, 112-123(all partially)

Methods, entities and uses encompassing a combination treatment of a VEGF antagonist and a PD-L1 axis binding antagonist in kidney cancer patients wherein levels of biomarkers are determined, and wherein the biomarker is CD8B (invention 2) ... up to ... PRF1 (invention 7).

- 8-11. claims: 1, 3, 8-10, 14, 15, 19-21, 25, 37, 39, 41, 46-48, 52, 56-58, 69-105, 112-116(all partially)

Methods, entities and uses encompassing a combination treatment of a VEGF antagonist and a PD-L1 axis binding antagonist in kidney cancer patients wherein levels of biomarkers are determined, and wherein the biomarker is CXCL9 (invention 8) ... up to ... CXCL13 (invention 11).

- 12-14. claims: 1, 4, 11-15, 22-25, 37, 39, 42, 49-52, 59-61, 69-105, 112-116(all partially)

Methods, entities and uses encompassing a combination treatment of a VEGF antagonist and a PD-L1 axis binding antagonist in kidney cancer patients wherein levels of biomarkers are determined, and wherein the biomarker is GZMB (invention 12) ... up to ... SLAMF7 (invention 14).

15. claims: 26-30, 38, 62-64, 106-108(completely); 37, 69-102, 112-116(partially)

Methods, entities and uses encompassing a combination treatment of a VEGF antagonist and a PD-L1 axis binding antagonist in kidney cancer patients wherein levels of biomarkers are determined, and wherein the biomarker is MHC-I.

- 16-22. claims: 31-37, 65-102, 109-116(all partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Methods, entities and uses encompassing a combination treatment of a VEGF antagonist and a PD-L1 axis binding antagonist in kidney cancer patients wherein levels of biomarkers are determined, and wherein the biomarker is CX3CR1 (invention 16) ... up to ... CXCL10 (invention 22).
