Title: USE OF AN INTEGRIN ANTAGONIST AND RADIATION IN THE TREATMENT OF NEOPLASIA

Abstract: The present invention provides methods to treat neoplasia disorders in a mammal using a combination of radiation and an integrin antagonist.
**INTERNATIONAL SEARCH REPORT**

**A. CLASSIFICATION OF SUBJECT MATTER**

| IPC   | A61K41/00 | A61P35/00 |

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   | A61K | A61P |

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

Electronic database consulted during the international search (name of database and, where practical, search terms used).

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

<table>
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<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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<tr>
<td>X</td>
<td>WO 98 31359 A (DUGGAN MARK E ; MERCK &amp; CO INC (US)) 23 July 1998 (1998-07-23) cited in the application claims 21-25 page 20, line 14-21</td>
<td>1,2, 16-20</td>
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<td>WO 98 14192 A (COUSINS RUSSELL DONOVAN ; SMITHKLINE BEECHAM CORP (US); KWON CHET () 9 April 1998 (1998-04-09) cited in the application page 6, line 12-24,33-35</td>
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<td>Y</td>
<td>WO 97 41844 A (ALCON LAB INC ; DOSHI RUPA (US); CLARK ABBOT F (US)) 13 November 1997 (1997-11-13) page 5-6; table 5</td>
<td>1-3, 16-20</td>
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Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

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*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 document 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

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Date of the actual completion of the international search

28 April 2000

Date of mailing of the international search report

19.07.00

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk
Tel. (+31-70) 340-3040, Tx. 31 651 epo nl, Fax. (+31-70) 340-3016

Authorized officer

Herrera, S

Form PCT/ISA/01 (second sheet) (July 1992)
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<td>P,X</td>
<td>WO 99 31099 A (HUTCHINSON JOHN H; MEISSNER ROBERT S (US); ASKEW BEN C (US); DUGGA)</td>
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INTERNATIONAL SEARCH REPORT

Box I  Observations where certain claims were found unsearchable (Continuation of item 1 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:
   see FURTHER INFORMATION sheet PCT/ISA/210

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 II  Observations where unity of invention is lacking (Continuation of item 2 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 fee, this Authority did not invite payment of any additional fee.

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, 16 - 20 (all partly), 3.1-3.10

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (1)) (July 1998)
Continuation of Box I.2

The present claims relate to an extremely large number of possible methods and combinations. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the methods and combinations claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the methods and combinations referring to the general concept of the application, i.e. the combined use of integrin antagonists as defined in the dependent claims and radiation for the treatment or prevention of neoplasia.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.
1. Claims: 1-2,16-20 (all partly), 3.1-3.10
   Use of radiation therapy together with the structurally
   related integrin antagonists as defined in claims 3.1-3.10
   in the treatment of neoplasia

   Use of radiation therapy together with the structurally
   related integrin antagonists as defined in claims 3.11-3.12
   in the treatment of neoplasia

   Use of radiation therapy together with the integrin
   antagonist as defined in claim 3.13 in the treatment of
   neoplasia

   Use of radiation therapy together with the integrin
   antagonist as defined in claim 3.14 in the treatment of
   neoplasia

5. Claims: 1-2,16-20 (all partly), 3.15
   Use of radiation therapy together with the integrin
   antagonist as defined in claim 3.15 in the treatment of
   neoplasia

6. Claims: 1-2,16-20 (all partly), 3.16,5
   Use of radiation therapy together with the integrin
   antagonist as defined in claims 3.16, 5 in the treatment of
   neoplasia

7. Claims: 1-2,16-20 (all partly), 3.17-3.18,3.35,4.1-4.3,
   4.14,6,7,14s
   Use of radiation therapy together with the structurally
   related integrin antagonists as defined in claims
   3.17-3.18,3.35,4.1-4.3, 4.14, 6,7,14 in the treatment of
   neoplasia

8. Claims: 1-2,16-20 (all partly), 3.19,8
   Use of radiation therapy together with the integrin
antagonist as defined in claims 3.19, 8 in the treatment of neoplasia

9. Claims: 1-2,16-20 (all partly), 3.20-3.22, 4.5-4-7
   Use of radiation therapy together with the structurally related integrin antagonists as defined in claims 3.20-3.22, 4.5-4.7 in the treatment of neoplasia

10. Claims: 1-2,16-20 (all partly), 3.23, 4.8, 9
    Use of radiation therapy together with the integrin antagonist as defined in claims 3.23, 4.8, 9 in the treatment of neoplasia

11. Claims: 1-2,16-20 (all partly), 3.24, 4.8, 10
    Use of radiation therapy together with the integrin antagonist as defined in claims 3.24, 4.8, 10 (vitaxin antibody (Ixsys)) in the treatment of neoplasia

12. Claims: 1-2,16-20 (all partly), 3.25, 4.9, 11
    Use of radiation therapy together with the integrin antagonist as defined in claims 3.25, 4.9, 11 (MErck KGcaA EMD-121974) in the treatment of neoplasia

13. Claims: 1-2,16-20 (all partly), 3.26, 4.11,
    Use of radiation therapy together with the integrin antagonist as defined in claims 3.26, 4.11 in the treatment of neoplasia

14. Claims: 1-2,16-20 (all partly), 3.27, 4.12, 12
    Use of radiation therapy together with the integrin antagonist as defined in claims 3.27, 4.12, 12 in the treatment of neoplasia

15. Claims: 1-2,16-20 (all partly), 3.28
    Use of radiation therapy together with the integrin antagonist as defined in claim 3.28 in the treatment of neoplasia

16. Claims: 1-2,16-20 (all partly), 3.29
Use of radiation therapy together with the integrin antagonist as defined in claim 3.29 in the treatment of neoplasia

17. Claims: 1-2,16-20 (all partly), 3.30

Use of radiation therapy together with the integrin antagonist as defined in claim 3.30 in the treatment of neoplasia

18. Claims: 1-2,16-20 (all partly), 3.31, 4.4

Use of radiation therapy together with the integrin antagonist as defined in claims 3.31 and 4.4 in the treatment of neoplasia

19. Claims: 1-2,16-20 (all partly), 3.32

Use of radiation therapy together with the integrin antagonist as defined in claim 3.32 for the treatment of neoplasia

20. Claims: 1-2,16-20 (all partly), 3.33

Use of radiation therapy together with the integrin antagonist as defined in claim 3.33 for the treatment of neoplasia


Use of radiation therapy together with the integrin antagonist as defined in claims 3.34, 4.13, 13 for the treatment of neoplasia


Use of radiation therapy together with the structurally related integrin antagonists as defined in claims 3.37-3.41, 16 for the treatment of neoplasia

23. Claims: 1-2,16-20 (all partly), 3.42

Use of radiation therapy together with the integrin antagonist as defined in claim 3.42 for the treatment of neoplasia

24. Claims: 1-2,16-20 (all partly), 3.43
Use of radiation therapy together with the integrin antagonist as defined in claim 3.43 for the treatment of neoplasia.

25. Claims: 1-2, 16-20 (all partly), 3.36, 4.15, 15

Use of radiation therapy together with the integrin antagonist as defined in claims 3.36, 4.15, 15 for the treatment of neoplasia.
<table>
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