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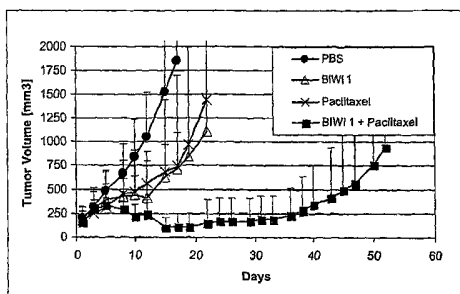
Anke [DE/AT]; Groisbach 13, A-2534 Alland (AT). **HEI-
DER, Karl-Heinz** [DE/AT]; Johann-Strauss-Promenade
4/11, A-2000 Stockerau (AT).

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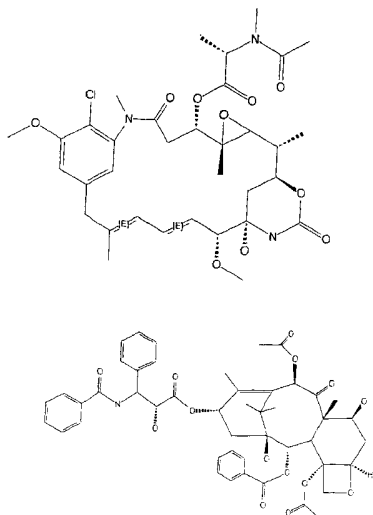
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[Continued on next page]

(54) Title: COMPOSITIONS AND METHODS FOR TREATING CANCER USING MAYTANSINOID CD44 ANTIBODY IM-
MONOCONJUGATES AND CHEMOTHERAPEUTIC AGENTS



(57) Abstract: The invention relates to the combined use of con-
jugates of CD44 specific antibodies with cytotoxic compounds and
chemotherapeutic agents in cancer therapy, pharmaceutical compo-
sitions comprising such compounds and/or chemotherapeutic agents,
and methods of cancer treatment. Preferred conjugates contain may-
tansinoids as cytotoxic compounds, and preferred chemotherapeutic
agents are taxanes.





Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

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INTERNATIONAL SEARCH REPORT

International Application No
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B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K C07K

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 practical, search terms used)

EP0-Internal, BIOSIS, CHEM ABS Data, MEDLINE, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in 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 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

"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

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INTERNATIONAL SEARCH REPORT

International Application No

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International Application No

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International Application No

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International Application No

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International Application No

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International Application No

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/09166

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	LIU C ET AL: "Cure of human colon cancer xenografts by a C242-maytansinoid conjugate" PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL MEETING, vol. 36, 1995, page 407 ABSTRACT NO 2428, XP001156090 & EIGHTY-SIXTH ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH; TORONTO, ONTARIO, CANADA; MARCH 18-22, 1995 ISSN: 0197-016X the whole document -----	1-49
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INTERNATIONAL SEARCH REPORT

International application No.
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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:

Although claims 40-43 are directed to a method of treatment of the human/animal body, a search has been carried out, based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 1-49 in part
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

As a result of the prior review under R. 40.2(e) PCT,
part additional fees are to be refunded.

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.:

1-49 in part, insofar as relating to inventions 1 and 2
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.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 40-43 are directed to a method of treatment of the human/animal body, a search has been carried out, based on the alleged effects of the compound/composition.

Continuation of Box I.2

Claims Nos.: 1-49 in part

Present claims 1-49 relate to an extremely large number of possible compounds, to methods for their preparation, to compositions containing them, and to their uses. 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 compounds 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 compounds prepared in the examples, and to the general idea of combining an anticancer agent as specifically claimed with a conjugate of a CD44v6-antibody and a maytansinoid, insofar as relating to the inventions, for which a search fee has been paid.

The applicant's attention is drawn to the fact that 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. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-12, 20-29, 37-49 in part, 13-19 and 30-36

Use, method, composition and kit as claimed, based on the combination of a conjugate of an anti-CD44v6 antibody to a maytansinoid toxin, with a chemotherapeutic agent, wherein the chemotherapeutic agent is a tubulin binding agent

1.1. claims: 1-49 in part

Use, method, composition and kit as claimed, based on the combination of a conjugate of an anti-CD44v6 antibody to a maytansinoid toxin, with a chemotherapeutic agent, wherein the chemotherapeutic agent is a taxane

1.2. claims: 1-49 in part

Use, method, composition and kit as claimed, based on the combination of a conjugate of an anti-CD44v6 antibody to a maytansinoid toxin, with a chemotherapeutic agent, wherein the chemotherapeutic agent is an epothilone

2. claims: 1-12, 20-29, 37-49 in part

Use, method, composition and kit as claimed, based on the combination of a conjugate of an anti-CD44v6 antibody to a maytansinoid toxin, with a chemotherapeutic agent, wherein the chemotherapeutic agent is a platinum compound.

3. claims: 1-12, 20-29 and 37-49 in part

Use, method, composition and kit as claimed, based on the combination of a conjugate of an anti-CD44v6 antibody to a maytansinoid toxin, with a chemotherapeutic agent, wherein the chemotherapeutic agent is a camptothecin

4. claims: 1-12, 20-29 and 37-49 in part

Use, method, composition and kit as claimed, based on the combination of a conjugate of an anti-CD44v6 antibody to a maytansinoid toxin, with a chemotherapeutic agent, wherein the chemotherapeutic agent is a cryptophycin

5. claims: 1-12, 20-29 and 37-49 in part

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Use, method, composition and kit as claimed, based on the combination of a conjugate of an anti-CD44v6 antibody to a maytansinoid toxin, with a chemotherapeutic agent, wherein the chemotherapeutic agent is a dolastatin

6. claims: 1-12, 20-29 and 37-49 in part

Use, method, composition and kit as claimed, based on the combination of a conjugate of an anti-CD44v6 antibody to a maytansinoid toxin, with a chemotherapeutic agent, wherein the chemotherapeutic agent is a 5,6-dihydroindolo[2,1-a]isoquinoline derivative

7. claims: 1-12, 20-29 and 37-49 in part

Use, method, composition and kit as claimed, based on the combination of a conjugate of an anti-CD44v6 antibody to a maytansinoid toxin, with a chemotherapeutic agent, wherein the chemotherapeutic agent is a spongistatin

8. claims: 1-12, 20-29 and 37-49 in part

Use, method, composition and kit as claimed, based on the combination of a conjugate of an anti-CD44v6 antibody to a maytansinoid toxin, with a chemotherapeutic agent, wherein the chemotherapeutic agent is an epipodophyllotoxin

9. claims: 1-12, 16, 20-29, 33 and 37-49 in part

Use, method, composition and kit as claimed, based on the combination of a conjugate of an anti-CD44v6 antibody to a maytansinoid toxin, with a chemotherapeutic agent, wherein the chemotherapeutic agent is an alkylating agent.

10. claims: 1-12, 20-29 and 37-49 in part

Use, method, composition and kit as claimed, based on the combination of a conjugate of an anti-CD44v6 antibody to a maytansinoid toxin, with a chemotherapeutic agent, wherein the chemotherapeutic agent is a purine antagonist

11. claims: 1-12, 20-29 and 37-49 in part

Use, method, composition and kit as claimed, based on the combination of a conjugate of an anti-CD44v6 antibody to a maytansinoid toxin, with a chemotherapeutic agent, wherein the chemotherapeutic agent is a pyrimidine antagonist

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

12. claims: 1-12, 20-29 and 37-49 in part

Use, method, composition and kit as claimed, based on the combination of a conjugate of an anti-CD44v6 antibody to a maytansinoid toxin, with a chemotherapeutic agent, wherein the chemotherapeutic agent is a DNA intercalator

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 03/09166

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0124763	A	12-04-2001	AU 7988500 A	10-05-2001
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