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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

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

(57) Abstract: The present invention relates to methods for treatment or prevention of neoplasia disorders using protein tyrosine kinase inhibitors in combination with cyclooxygenase inhibitors, in particular cyclooxygenase-2 selective inhibitors.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/25797

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 31/50, 31/44, 31/47, 31/445, 31/42, 31/415, 31/40, 31/38, 31/35, 31/34
 US CL : 514/247, 300, 311, 323, 334, 374, 378, 406, 414, 432, 454, 456, 473

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)

U.S. : 514/247, 300, 311, 323, 334, 374, 378, 406, 414, 432, 454, 456, 473

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)
 Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,972,986 A (SEIBERT et al) 26 October 1999 (26.10.1999), columns 1-5 and the claims.	1, 2, 9-18, 22-50
Y	US 6,077,850 A (CARTER et al) 20 June 2000 (20.06.2000), columns 1-5 and the claims.	1-8 and 19-46
Y, E	US 2002/0156292 A1 (TANG et al) 24 October 2002, pages 1-4 and the claims.	1-50

☐

Further documents are listed in the continuation of Box C.

☐

See patent family annex.

* Special categories of cited documents:		"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
"A"	document defining the general state of the art which is not considered to be of particular relevance	"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
"E"	earlier application or patent published on or after the international filing date	"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
"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)	"&"	document member of the same patent family
"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		

Date of the actual completion of the international search

07 February 2003 (07.02.2003)

Date of mailing of the international search report

14 MAR 2003

Name and mailing address of the ISA/US

Commissioner of Patents and Trademarks
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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/25797

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

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

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claim 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. ☐ Claim 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:
Please See Continuation 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.:

Remark on Protest

☐
☐

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

No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

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BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claims 1-8 and 19-46, drawn to a method for the treatment or prevention of cancers comprising administering a protein kinase inhibitor of Formula I in combination with a cyclooxygenase-2 (COX-2) inhibitor of Formula II.

Group II, claims 1, 2, 9-18, and 22-50, drawn to a method for the treatment or prevention of cancers comprising administering a protein kinase inhibitor of Formula I in combination with a cyclooxygenase-2 (COX-2) inhibitor of Formula III.

The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Although the two groups have in common the technical feature of being COX-2 inhibitors, this is not a special technical feature since the COX-2 inhibitors of both Formula II and III were well-known at the time of applicant's invention as made evident by the prior art references cited herein. Furthermore, the claimed COX-2 inhibitors were also known to be effective at treating conditions other than cancer, such as inflammatory disorders. Accordingly, this finding of lack of unity of invention is proper.

Continuation of B. FIELDS SEARCHED Item 3:

STN (REGISTRY (structure searches of each Markush group of compounds), CAPLUS, USPATFUL)

search terms: cancer, tumor, tumour, neoplasm, protein kinase inhibitor, cyclooxygenase-2 inhibitor, COX-2 inhibitor