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Datasheet for the decision of 11 July 2007

Case Number: T 1117/05 - 3.3.04

Application Number: 01905031.9

Publication Number: 1251866

IPC: A61K 38/21

Language of the proceedings: EN

Title of invention:
Combination of temozolomide and pegylated interferon-alpha for treating cancer

Applicant:
SCHERING CORPORATION

Opponent:
-

Headword:
Combination therapy/SCHERING

Relevant legal provisions:
EPC Art. 56

Keyword:
"All requests - inventive step (no)"

Decisions cited:
-

Catchword:
-

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 1117/05 **-** 3.3.04

D E C I S I O N
of the Technical Board of Appeal 3.3.04
of 11 July 2007

Appellant: (Applicant)
SCHERING CORPORATION
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Decision under appeal:
Decision of the Examining Division of the European Patent Office posted 17 March 2005 refusing European Patent application No. 01905031.9 pursuant to Article 97(1) EPC.

Composition of the Board:

Chairman: M. Wieser
Members: B. Claes
G. Weiss

Summary of Facts and Submissions

I. The European patent application No. 01 905 031.9 published as WO 01/52882 with the title "Combination of temozolomide and pegylated interferon-alpha for treating cancer" was refused by the examining division pursuant to Article 97(1) EPC.

II. In its decision dated 17 March 2005, the examining division refused the main request based on the finding that the subject-matter of claims 1 to 12 of the set of claims of a new main request submitted with letter dated 29 December 2003 did not involve an inventive step (Article 56 EPC) as required by Article 52(1) EPC for a claimed invention to be patentable.

Claim 1 of this main request read:

"1. Use of therapeutically effective amounts of temozolomide and pegylated interferon alpha for manufacturing a medicament for treating a human patient afflicted with cancer."

III. The board sent a communication pursuant to Article 12 of the Rules of Procedure of the Boards of Appeal setting out its preliminary non-binding opinion.

IV. In answer to the board's communication and with letter dated 29 June 2007, the appellant submitted further arguments and a main request and seven auxiliary requests.

V. During the oral proceedings which took place on 11 July 2007, the appellant filed a new main request as well as new auxiliary requests 1 to 7.

Claim 1 of the new main request read:

" 1. Use of therapeutically effective amount of temozolomide for manufacturing a medicament for treating a human patient afflicted with cancer wherein the treatment comprises a combination therapy with a therapeutically effective amount of temozolomide and a therapeutically effective amount of pegylated interferon alpha."

Claim 1 of the new auxiliary request 1 was identical to claim 1 of the main request but specified at the end of the claim wording: "wherein the pegylated interferon alpha is administered once a week."

Claim 1 of the new auxiliary request 2 was identical to claim 1 of the main request but specified at the end of the claim wording: "wherein the temozolomide is to be administered daily for six weeks at a dose of 50 to 150 $mg/m^2/day$."

Claim 1 of the new auxiliary request 3 was identical to claim 1 of the main request but specified at the end of the claim wording: "wherein the temozolomide is to be administered daily for six weeks at a dose of 50 to 150 $mg/m^2/day$ and wherein the pegylated interferon alpha is administered once a week."

Claim 1 of the new auxiliary request 4 was identical to claim 1 of the request on which the examining division has based its decision (see section II above).

Claim 1 of the new auxiliary request 5 was identical to claim 1 of auxiliary request 4 but specified at the end of the claim wording: "wherein the pegylated interferon alpha is administered once a week."

Claim 1 of the new auxiliary request 6 was identical to claim 1 of auxiliary request 4 but specified at the end of the claim wording: " wherein the temozolomide is to be administered daily for six weeks at a dose of 50 to 150 $mg/m^2/day$."

Claim 1 of the new auxiliary request 7 was identical to claim 1 of auxiliary request 4 but specified at the end of the claim wording: "wherein the temozolomide is to be administered daily for six weeks at a dose of 50 to 150 $mg/m^2/day$ and wherein the pegylated interferon alpha is administered once a week."

VI. The following documents are referred to in this decision:

(1): WO 97/12630

(4): EP-A-0 809 996

(6): Poster from the American Society of Clinical Oncology Conference held in New Orleans in 2004 (document submitted by the appellant during the examination proceedings with letter dated 23 June 2004)

VII. The appellant's arguments in writing and during oral proceedings which are relevant for the present decision may be summarised as follows:

– Starting from closest prior art document (1), which disclosed a medicament for treating a human patient afflicted with cancer wherein the treatment comprises a combination therapy with temozolomide and interferon alpha, the problem to be solved was to treat cancer patients to obtain a higher response rate and/or reduced side-effects. This problem was recited in the application at page 1, lines 22 and 23.

– The application provided a detailed description of clinical trials which could be performed and dosage regimens which could be tested.

– Document (6), a post-published document filed during the examination proceedings, documented in table 4 that in 34% of patients afflicted with advanced melanoma and treated by the therapy of the invention a partial or complete tumour response could be observed. The document further concluded that "*[t]he combination of temozolomide, given on an extended daily dosing schedule for 6 weeks, together with pegylated interferon alpha-2b, given by weekly subcutaneous injection for 8 weeks, is generally safe and well tolerated in patients with advanced malignant melanoma without brain metastases.*" (see one before last paragraph of the document).

VIII. The appellant requested that the decision of the examining division be set aside and that a patent be granted on the basis of the new main request filed during the oral proceedings or alternatively on the basis of one of the auxiliary requests 1 to 7 equally submitted during the oral proceedings.

Reasons for the Decision

1. The present decision is solely concerned with the question whether the subject-matter of claim 1 of the main request and claim 1 of each of auxiliary requests 1 to 7 involves an inventive step (Article 56 EPC).

2. For assessing inventive step, the boards of appeal consistently apply the "problem and solution" approach, which requires as a first step the identification of the closest prior art. In accordance with established case law of the boards of appeal the closest prior art is generally a teaching in a document conceived for the same purpose or aiming at the same objective as the claimed invention and having the most relevant technical features in common.

3. The closest prior art is document (1) which discloses the use of a therapeutically effective amount of temozolomide for manufacturing a medicament for treating a human patient afflicted with cancer wherein the treatment comprises a combination therapy with a therapeutically effective amount of temozolomide and a therapeutically effective amount of interferon alpha.

4. The appellant has argued that starting from closest prior art document (1), and conform with the specification of the application at page 1, lines 22 and 23, the problem to be solved was to treat cancer patients to obtain a higher response rate and/or reduced side-effects. The board notes however that the patent fails to identify any reference points for these features. Furthermore, neither the patent application itself nor the disclosure in document (6) contain any data which could be considered as to constitute a comparison with the teaching in closest prior art document (1) supporting alleged advantages as referred to by the appellant in the formulated problem. In particular, document (6) merely discloses in its table 4 that with the disclosed therapy a partial or complete tumour response could be observed in 34% of patients afflicted with advanced melanoma. Similarly, the one before last paragraph of the document merely refers to the fact that the therapy of the application is "*generally safe and well tolerated in patients with advanced malignant melanoma without brain metastases.*". The problem to be solved by the claimed invention as formulated by the appellant is therefore not correct.

5. The application states on page 5, lines 4 to 7, that the objective was to improve the delivery of the interferon alpha protein by significantly prolonging its plasma half-life, and thereby provide protracted activity of interferon alpha. Therefore, starting from the closest prior art the problem to be solved is defined as the provision of a combination therapy for treating cancer in patients based on temozolomide and interferon alpha whereby the delivery of the interferon alpha protein is improved. The solution provided in the

application and claimed is the use of a pegylated form of interferon alpha in the combination therapy with temozolomide.

6. The relevant question to be answered is therefore whether the person skilled in the art would have specified, in the cancer combination therapy of the prior art based on temozolomide and interferon alpha as disclosed in document (1), interferon alpha for pegylated interferon alpha with a view to provide an improved interferon alpha delivery.

7. There are a number of documents cited in the search report which disclose pegylated interferon alpha and uses thereof. The board considers of all these documents document (4) to be the most pertinent one.

8. Document (4) discloses that the bioavailability of protein therapeutics is often limited due to their short plasma half-life, thus preventing them from attaining their maximum clinical potency. Conjugates of such biomolecules and polyethylene glycol (PEG) polymers on the other hand possess useful clinical properties, which include longer *in vivo* circulating half-life, decreased clearance and enhancing potency. The document reports in particular that, compared to its unmodified form, the pegylated interferon alpha has an enhanced antiproliferative activity in human tumor cells, increased circulating half-life and plasma residence time as well as a reduced immunogenicity (see page 2, lines 7 to 26, 31 to 33 and page 2 line 55 to page 3 line 1). Therefore, document (4) teaches the skilled person that pegylation of interferon alpha improves *inter alia* the delivery of the biomolecule.

9. In view of the above the board considers the specification of the interferon alpha used in such combination therapy to be a pegylated form thereof with a view to provide an improved interferon alpha delivery obvious to the skilled person.

10. For the above reasons the subject-matter of claim 1 of the main request and of auxiliary request 4 lacks inventive step.

11. Closest prior art document (1) discloses both the features that are added to claims 1 of auxiliary requests 1 to 3 and 5 to 7, i.e. the combination therapy involving temozolomide interferon alpha whereby i) the interferon alpha is administered once a week (page 5 line 1, claim 2) and ii) temozolomide is administered daily for six weeks at a dose of 50 to 150 mg/m^2/day (page 4 lines 5 to 8). The board comes to the conclusion that based on the same reasoning as for claims 1 of the main and auxiliary request 4, the subject-matter of claims 1 of auxiliary requests 1 to 3 and 5 to 7 is likewise obvious to the skilled person.

12. For the above reasons the board judges the subject-matter of claims 1 of auxiliary requests 1 to 3 and 5 to 7 to lack inventive step (Article 56 EPC).

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar The Chairman

P. Cremona M. Wieser