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Datasheet for the decision of 27 January 2022

Case Number: T 1416/18 - 3.3.04

Application Number: 06076149.1

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IPC: C07K14/71, A61K38/17, A61K39/395, A61K48/00, C07K16/32

Language of the proceedings: EN

Title of invention:
Compositions and methods of treating tumors

Patent Proprietor:
The Trustees of The University of Pennsylvania

Opponents:
F. Hoffmann-La Roche AG / Genentech, Inc.
Eli Lilly and Company
European Oppositions Limited

Headword:
Treatment of tumors/UNIVERSITY OF PENNSYLVANIA

Relevant legal provisions:
EPC Art. 76(1), 123(2)

Keyword:
Divisional application - subject-matter extends beyond content of earlier application (yes)
Amendments - extension beyond the content of the application as filed (yes)

Decisions cited:
G 0002/10

Europäisches Patentamt
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Beschwerdekammern

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Case Number: T 1416/18 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 27 January 2022

Appellant: (Patent Proprietor)	The Trustees of The University of Pennsylvania 3160 Chestnut Street, Suite 200 Philadelphia, PA 19104 (US)
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Decision under appeal: **Decision of the Opposition Division of the European Patent Office posted on 27 March 2018 revoking European patent No. 1745799 pursuant to Article 101(3)(b) EPC**

Composition of the Board:

Chair B. Claes
Members: A. Schmitt
M. Blasi

Summary of Facts and Submissions

I. The appeal of the patent proprietor (appellant) lies from the decision of the opposition division to revoke European patent No. 1 745 799 (patent).

II. The patent, entitled "*Compositions and methods of treating tumors*", was granted on European patent application No. 06 076 149.1 (application), which had been filed as a divisional application in respect of the earlier European patent application No. 99 908 641.6. This earlier application had been filed as an international application under the PCT and was published as WO 99/44645 (earlier application). The description of the application consists of the description of the earlier application and the claims of the latter as disclosed embodiments.

III. Three oppositions had been filed against the patent in its entirety. The opposition proceedings were based on the grounds of lack of novelty (Article 54 EPC) and lack of inventive step (Article 56 EPC) in Article 100(a) EPC and on the grounds in Article 100(b) and (c) EPC.

IV. In the decision under appeal, the opposition division considered, *inter alia*, that the claims of a main request (submitted on 23 January 2017) related to subject-matter that did not extend beyond the disclosure of the (earlier) application as filed (Article 123(2) and Article 76(1) EPC). However, the invention as defined in claim 1 of the main request, claim 1 of auxiliary request 1 (submitted on 23 January 2017) and claim 1 of auxiliary request 2 (submitted on 5 January 2018) was found not to be

disclosed in the patent in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art (Article 83 EPC).

Claim 1 of the main request reads as follows:

" 1. An antibody for use in the treatment of an individual with an erbB mediated tumour, to be administered to said individual in combination with anti-cancer radiation, wherein the tumour is characterised by
a) erbB homodimers that are mutant EGFR homodimers or p185 homodimers and/or
b) erbB heterodimers that are p185/EGFR heterodimers, p185/mutant EGFR heterodimers, p185/erbB3 heterodimers, p185/erb4 heterodimers or EGFR/mutant EGFR heterodimers,
wherein said antibody is a humanized anti-p185 antibody or fragment thereof or a humanized anti-EGFR antibody, or fragment thereof, wherein the antibody or fragment thereof disrupts the kinase activity associated with the dimers, resulting in a cytostatic effect on the tumour cells, and renders the previously radiation resistant tumour cells radiation sensitive, wherein the radiation therapy is commenced once the antibody has disrupted the kinase activity associated with the dimers."

Claim 1 of auxiliary request 1 is identical to claim 1 of the main request except that the feature "*and renders the previously radiation resistant tumour cells radiation sensitive*" is replaced with the feature "*and renders the tumour cells, previously resistant to radiation-induced cell death, radiation sensitive*".

Claim 1 of auxiliary request 2 is identical to claim 1 of the main request except that the feature "*and renders the previously radiation resistant tumour cells radiation sensitive*" is replaced with the feature "*and renders the tumour cells, previously resistant to radiation-induced cell death, sensitive to radiation-induced apoptosis*".

V. With the statement of grounds of appeal, the appellant submitted three documents and arguments that the patent sufficiently disclosed the invention as defined in the claims of the main request and auxiliary requests 1 and 2.

VI. Joint opponents 1 and opponent 2 (respondents I and II) replied to the appeal and submitted, *inter alia*, arguments that claim 1 of each of the main request and auxiliary requests 1 and 2 related to subject-matter that extended beyond the disclosure of the (earlier) application as filed. Opponent 3 (respondent III) did not make any substantive submissions in the appeal proceedings.

VII. The board summoned the parties to oral proceedings, in accordance with their requests, and issued a communication pursuant to Article 15(1) RPBA, in which it expressed, *inter alia*, the preliminary opinion that claim 1 of the main request and each of auxiliary requests 1 and 2 related to subject-matter which extended beyond the disclosure of the (earlier) application as filed.

VIII. The appellant and respondents I and II replied to the board's communication.

IX. Respondent III did not attend the oral proceedings as announced in writing. During the oral proceedings, the respondents referred to, *inter alia*, passages on pages 8 and 65 of the (earlier) application, which, however, are not relevant for the board's decision. At the end of the oral proceedings, the Chair announced the board's decision.

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

D14 US 5,470,571

D29 US 5,677,171

D30 US 5,705,157

XI. The appellant's arguments, where relevant to the decision, are summarised as follows.

Main request - claim 1

Added subject-matter (Articles 123(2) and 76(1) EPC)

In the (earlier) application, passages on antibodies as active agents for use in the treatment recited in the claim were found on page 11, lines 23 to 24 and 31; page 13, lines 12 to 14; and page 35, lines 15 to 16 and 17 to 22. The first three passages disclosed (humanised) antibodies for use in the treatment recited in the claim; the last passage disclosed anti-p185 and anti-EGFR antibodies.

All features of the claimed subject-matter except for the anti-p185 and anti-EGFR antibodies were disclosed on page 34, line 12 to page 35, line 2 and page 35,

lines 9 to 16 of the (earlier) application, i.e. in the paragraphs immediately preceding the disclosure of the anti-p185 and anti-EGFR antibodies.

The general framework of the claimed subject-matter was disclosed on page 34, lines 12 to 18, which was mirrored on page 34, line 26 to page 35, line 2. These passages disclosed the disruption of the erbB protein dimers, which rendered the tumour radiation sensitive, and the sequential administration of cancer radiation.

Directly following these passages, antibodies were disclosed as active agents (page 35, lines 9 to 16), which could be monoclonal or humanised antibodies (page 35, lines 17 to 19) and, in the next sentence, with reference to three US patents (documents D14, D29 and D30 in the proceedings), anti-p185 and anti-EGFR antibodies were disclosed (page 35, lines 19 to 22). Subsequent passages of the (earlier) application (page 35, line 25 to page 37, line 16) further confirmed that these antibodies were embodiments for use in the combination therapy described in the preceding passages by disclosing further embodiments of the described combination therapy relating to other active agents such as peptides (page 35, lines 25 to 32) and nucleic acid molecules (page 36, line 1 ff.).

The (earlier) application also disclosed that tumour cells were rendered radiation-sensitive by disrupting the kinase activity of erbB dimers (see page 33, lines 19 to 23 and page 34, line 19 to page 35, line 2) and that antibody agents prevented dimer formation by interacting with the erbB dimers' monomeric components (see page 35, lines 9 to 17, and page 11, lines 20 to 24 and 29 to 31). Since the monomers were p185 and

EGFR proteins, this mechanism of action of the active agents also supported that anti-p185 and anti-EGFR antibodies were embodiments of the claimed subject-matter.

Further evidence for this teaching could be found on page 35, last paragraph and in Example 8, where peptidomimetics of anti-p185 antibodies were disclosed as active agents that mimicked the functions of anti-p185 antibodies and thus had the same capability of disrupting the dimers as these antibodies.

In view of this evidence, the disclosure of the anti-p185 and anti-EGFR antibodies on page 35, lines 19 to 22 could only be read by the skilled person as a disclosure of antibodies for use in the therapeutic treatment as recited in the claim.

Auxiliary requests 1 and 2 - claim 1

Added subject-matter (Articles 123(2) and 76(1) EPC)

The appellant did not submit specific arguments in this context.

XII. The respondents' arguments, where relevant to the decision, are summarised as follows.

Main request - claim 1

Added subject-matter (Articles 123(2) and 76(1) EPC)

The (earlier) application as filed failed to directly and unambiguously disclose anti-p185 and anti-EGFR antibodies having the functional features recited in

the claim for use in the medical treatment recited in the claim.

The appellant referred to passages on pages 11 and 13 as a basis for the claimed subject-matter. However, these passages comprised only generic references to antibodies without identifying their targets. Furthermore, the sentence on page 35, lines 19 to 22, also cited by the appellant, was not linked to the combination therapy delineated in the preceding paragraphs and merely disclosed that antibodies against p185 and EGFR were described in patents. It therefore could not serve as a basis for the claimed subject-matter either. The same was true for the disclosure in Example 8 where a specific p185 antibody was used in a proliferation assay but not as a therapeutic agent.

Auxiliary requests 1 and 2 - claim 1

Added subject-matter (Articles 123(2) and 76(1) EPC)

The same feature combination was present in claim 1 of each of auxiliary requests 1 and 2 which therefore did not have a basis in the (earlier) application as filed for the same reasons as claim 1 of the main request.

XIII. The appellant requested that the decision under appeal be set aside and the patent be maintained in amended form based on the set of claims of the main request filed on 23 January 2017 or, alternatively, one of the sets of claims of auxiliary requests 1 and 2, filed on 23 January 2017 and 5 January 2018, respectively.

The respondents requested that the appeal be dismissed.

Reasons for the Decision

1. The appeal complies with Articles 106 to 108 and Rule 99 EPC and is admissible.

Main request - claim 1

Added subject-matter (Articles 123(2) and 76(1) EPC)

2. The requirements of Article 123(2) EPC are assessed according to the "gold standard" as set out in decision G 2/10 of the Enlarged Board of Appeal (OJ EPO 2012, 376, point 4.3 of the Reasons). Accordingly, in the case at hand, the skilled person must be able to derive directly and unambiguously, using common general knowledge, and seen objectively and relative to the date of filing, from the whole of the (earlier) application as filed (see section II.), a humanised anti-p185 antibody or fragment thereof or a humanised anti-EGFR antibody or fragment thereof for use in the therapeutic treatment recited in the claim. If not, the claim contains subject-matter which extends beyond the content of the (earlier) application as filed (Article 123(2) EPC and Article 76(1) EPC).

3. Antibodies as active agents for use in the treatment of a subject having an erbB-mediated tumour in combination with a (gamma) radiation therapy are disclosed on page 11, lines 20 to 24 and 31; page 13, lines 12 to 14; and page 35, lines 15 to 16 of the (earlier) application as filed. However, in these passages, antibodies are only listed as possible active agents without identifying their targets or specificities.

4. Indeed, page 11, lines 20 to 24 discloses that "[*i*]*n some embodiments, the compound that interacts with an*

erbB protein ... is an antibody. In some embodiments, the antibody is a monoclonal antibody". Line 31, page 11 also only refers to "*an antibody*". The same is true for page 13 (lines 12 to 14), where it is disclosed that in some embodiments, "*the composition that disrupts the kinase activity associated with the multimeric receptor ensemble comprises an active agent selected from the group consisting of antibodies, peptides, and non-proteinaceous kinase inhibitors*", and page 35 (lines 15 to 16), where it is disclosed that "*[e]xamples of active agents which physically alter the monomer include antibodies, proteins, peptides and non-proteinaceous molecules*".

5. The paragraph that follows lines 15 to 16 on page 35 (lines 17 to 22) reads: "*As used herein, the term "antibody" is meant to refer to antibodies, as well as antibody fragments such as FAb and F(Ab)$_2$ fragments. Antibodies may, in some preferred embodiments, be monoclonal antibodies or humanized antibodies. Antibodies against p185 are described in U.S. Patent No. 5,677,171 issued October 14, 1997 which is incorporated herein by reference, and U.S. Patent No. 5,705,157 issued January 6, 1998, which is incorporated herein by reference, and which also describes antibodies against EGFR.*"

6. This paragraph hence defines the meaning of the term "antibody" in a general manner and informs that anti-p185 and anti-EGFR antibodies are described in particular patents.

7. The appellant's first line of argument was that the skilled person derived from the context of the disclosure on page 35, lines 17 to 22 that anti-p185 and anti-EGFR antibodies were embodiments of the cancer

treatment recited in the claim. In a second line of argument, the appellant considered that the mechanism by which the active agents disrupted the kinase activity and rendered the tumour cells radiation-sensitive (see page 11, lines 20 to 24 and 29 to 31; page 33, lines 19 to 23; page 34, line 19 to page 35, line 2; and page 35, lines 9 to 17) and the disclosure of p185 antibody peptidomimetics as active agents on page 35, last paragraph and in Example 8 corroborated that the skilled person could only read the sentence on page 35, lines 19 to 22 of the (earlier) application as disclosing specific antibodies for use in the treatment recited in the claim.

8. However, the sentence on page 35, lines 19 to 22 merely teaches that anti-p185 and anti-EGFR antibodies are disclosed in particular patents; it is silent on any use of these antibodies (see points 5. and 6. above). In addition, it follows a sentence that provides a general definition of the term "antibody" as used in the (earlier) application which is not connected to a particular use of antibodies either. The board therefore cannot identify a clear, unambiguous link of this section to the combination therapies described in the previous paragraphs. Such a link can also not be established when taking the subsequent passages into account since they disclose embodiments of the described combination therapy relating to other active agents. The appellant's first line of argument therefore fails to convince the board.

9. Furthermore, it might be possible that the teaching of the active agents' mechanism of disrupting kinase activity disclosed in the (earlier) application led the skilled person to consider that anti-p185 and anti-EGFR antibodies could also have this effect when binding to

their target (the monomeric components). However, the (earlier) application does not disclose that this was indeed the case. The board therefore considers the appellant's second line of argument to be about an aspect of obviousness rather than identifying a direct and unambiguous disclosure of the claimed subject-matter.

10. Moreover, Example 8 of the (earlier) application only discloses the use of a particular anti-p185 antibody (4D5) in a proliferation assay (Figure 5) but not its therapeutic use. Therefore, it cannot corroborate the use of anti-p185 antibodies in a combination therapy as recited in the claim.

11. In view of the above considerations, the (earlier) application as filed does not directly and unambiguously disclose a humanised anti-p185 antibody or fragment thereof or humanised anti-EGFR antibody or fragment thereof for use in the treatment of an individual with an erbB mediated tumour as recited in claim 1.

12. Claim 1 of the main request therefore relates to subject-matter that extends beyond the disclosure of the (earlier) application as filed within the meaning of Article 123(2) EPC and Article 76(1) EPC.

Auxiliary requests 1 and 2 - claim 1

Added subject-matter (Articles 123(2) and 76(1) EPC)

13. The same considerations for claim 1 of the main request apply to claim 1 of auxiliary requests 1 and 2, which also relate to an anti-p185 or anti-EGFR antibody for use in the treatment of an individual with an erbB-

mediated tumour (see section IV.) and for which the appellant has not submitted separate arguments.

14. Consequently, auxiliary requests 1 and 2 relate to subject-matter which extends beyond the disclosure of the (earlier) application as filed (Article 123(2) EPC and Article 76(1) EPC).

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chair:

I. Aperribay B. Claes

Decision electronically authenticated