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Datasheet for the decision of 26 February 2016

Case Number: T 2239/14 - 3.3.04

Application Number: 00931938.5

Publication Number: 1180040

IPC: A61K38/18, A61K39/395

Language of the proceedings: EN

Title of invention:
Methods for treating congestive heart failure

Applicants:
Cambridge Neuroscience, Inc.
The Brigham and Women's Hospital, Inc.
Beth Israel Deaconess Medical Center

Headword:
Treatment of congestive heart failure/CAMBRIDGE NEUROSCIENCE

Relevant legal provisions:
EPC Art. 123(2)
EPC R. 103(1)(a)
RPBA Art. 13(1)

Keyword:
Late filed main request and auxiliary request 1 - admitted (no)
Auxiliary requests 2 to 5 - added matter (yes)
Reimbursement of appeal fee (no)

Decisions cited:

Catchword:
-

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Case Number: T 2239/14 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 26 February 2016

Appellants: (Applicants)

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Decision under appeal:

Decision of the Examining Division of the European Patent Office posted on 23 July 2014 refusing European patent application No. 00931938.5 pursuant to Article 97(2) EPC.

Composition of the Board:

Chairwoman G. Alt
Members: B. Claes
M.-B. Tardo-Dino

Summary of Facts and Submissions

I. The appeal lies from the decision of the examining division to refuse European patent application No. 00931938.5, published as international patent application WO 00/64400 (hereinafter "the application"). The application has the title "*Methods for treating congestive heart failure*".

II. Claims 1 and 5 to 9 of the application read:

"1. A method for treating or preventing congestive heart failure in a mammal, said method comprising administering a polypeptide comprising an epidermal growth factor-like (EGF-like) domain to said mammal, wherein said EGF-like domain is encoded by a neuregulin gene, wherein said administering is in an amount effective to treat or prevent heart failure in said mammal.

5. The method of claim 1, wherein said neuregulin gene is the NRG-2 gene.

6. The method of claim 5, wherein said polypeptide is encoded by the NRG-2 gene.

7. The method of claim 1, wherein said neuregulin gene is the NRG-3 gene.

8. The method of claim 7, wherein said polypeptide is encoded by the NRG-3 gene.

9. The method of claim 1, wherein said mammal is a human."

III. In its decision the examining division held that the subject-matter of claim 1 of the main request and of auxiliary requests 1 and 2 (all submitted with a letter dated 21 May 2014) did not meet the requirements of Article 123(2) EPC. The examining division decided furthermore not to admit auxiliary request 3, filed with the same letter, into the proceedings pursuant to Rule 116 EPC.

IV. Claim 1 of the requests filed with the statement of grounds of appeal, all of them being subject to the decision under appeal, read:

Main request

"1. A polypeptide comprising an epidermal growth factor-like (EGF-like) domain for use in treating or preventing congestive heart failure in a human associated with reduced expression of ErbB2 and ErbB4, wherein said polypeptide is encoded by the NRG-2 gene or the NRG-3 gene."

Auxiliary request 1

"1. A polypeptide comprising an epidermal growth factor-like (EGF-like) domain for use in early treating congestive heart failure or preventing the transition to early congestive heart failure in a human, wherein the congestive heart failure or the transition to early congestive heart failure is characterised by a decrease in cardiomyocyte ErbB2 and ErbB4 levels, and wherein said polypeptide is encoded by the NRG-2 gene or the NRG-3 gene."

Auxiliary request 2

"1. A polypeptide comprising an epidermal growth factor-like (EGF-like) domain for use in treating or preventing a decrease in cardiomyocyte ErbB2 and ErbB4 levels in a human, which decrease occurs during the transition from early compensatory hypertrophy to early congestive heart failure or during early congestive heart failure, wherein said polypeptide is encoded by the NRG-2 gene of the NRG-3 gene."

Auxiliary request 3

"1. A polypeptide comprising an epidermal growth factor-like (EGF-like) domain for use in treating or preventing a decrease in cardiomyocyte ErbB2 and ErbB4 levels during the transition from early compensatory hypertrophy to early congestive heart failure in a human, wherein said polypeptide is encoded by the NRG-2 gene of the NRG-3 gene."

Claim 9 of all four requests read:

"9. A medicament for treating or preventing congestive heart failure in a human associated with reduced expression of ErbB2 and ErbB4, the medicament comprising the polypeptide according to any of the preceding claims."

V. With the statement of grounds of appeal the applicants (appellants) requested that the decision under appeal be set aside and the patent be maintained on the basis of a main request or, alternatively, that it be maintained on the basis of one of three auxiliary requests, these requests being the same as dealt with in the decision under appeal. The appellants further

requested that the appeal fee be reimbursed because the way of handling the case by the examining division represented a substantial procedural violation.

VI. In a communication pursuant to Article 15(1) RPBA accompanying the summons to oral proceedings, the board expressed its preliminary opinion that the subject-matter of none of the requests filed with the statement of grounds of appeal complied with the requirements of Article 123(2) EPC. The board furthermore noted that, in relation to auxiliary request 3, the decision of the examining division not to admit the request into the proceedings needed to be examined and that the request for the reimbursement of the appeal fee only would become relevant if and when the appeal were successful.

VII. With a letter dated 26 January 2016, in response to the board's communication, the appellants filed a new main request and new auxiliary request 1 along with arguments why the claims of these requests complied with the requirements of Article 123(2) EPC. The four requests submitted with the statement of grounds of appeal (see section IV) were renumbered as auxiliary requests 2 to 5, respectively.

Claim 1 of the new main request read:

"1. A polypeptide for use in treating or preventing congestive heart failure in a human, wherein the polypeptide comprises an epidermal growth factor-like (EGF-like) domain to said human, wherein said EGF-like domain is encoded by a neuregulin gene, wherein said the polypeptide is for administering in an amount effective to treat or prevent heart failure in said human, wherein said neuregulin gene is either:

(a) the NRG- 2 gene and said polypeptide is encoded by the NRG-2 gene, or
(b) the NRG- 3 gene and said polypeptide is encoded by the NRG-3 gene."

Claim 1 of the new auxiliary request 1 read:

"1. A polypeptide encoded by an NRG-2 or NRG-3 gene that binds and activates ErbB2, ErbB3 and ErbB4 receptors, or combinations thereof, for use in preventing, minimizing or reversing congestive heart disease, wherein the polypeptide are involved in stimulating compensatory hypertrophic growth in response to increased physiologic stress, as well as inhibiting apoptosis of myocardial cells subjected to such stress."

VIII. On 8 February 2016 the representative of the appellants was informed that the board, on a preliminary basis, had concerns under Article 13(1) RPBA in relation to the newly filed main request and auxiliary request 1 and that in the board's opinion the oral proceedings were required as requested in order for the board to come to a final decision.

IX. With a letter dated 22 February 2016 the representative of the appellants informed the board that they would not be represented at the oral proceedings.

X. Oral proceedings were held on 26 February 2016 without the appellants being represented. The appellants had requested in writing that the decision under appeal be set aside and that a patent be granted on the basis of the main request or of auxiliary request 1, both filed with the letter dated 26 January 2016, or of auxiliary requests 2 to 5, corresponding to the main request and

auxiliary requests 1 to 3 as filed with the statement of grounds of appeal. The appellants had further requested that the appeal fee be reimbursed because of a substantial procedural violation.

At the end of the oral proceedings the chairwoman announced the decision of the board.

XI. The appellants' arguments can be summarised as follows:

Main request and auxiliary request 1 submitted with the letter dated 26 January 2016

The claims of these requests complied with the requirements of Article 123(2) EPC.

Auxiliary request 2 - claim 1 - added subject-matter

The examining division was wrong to find that this claim was directed to added subject-matter. The skilled person, reading the application as a whole, in particular having read the introductory passages at pages 1 to 4 which set out the field and background of the invention, before moving on to the details of the invention, would have had no difficulty in directly and unambiguously deriving the claimed subject-matter from the application.

The application disclosed a patient group that suffered from "congestive heart failure associated with reduced expression of ErbB2 and ErbB4". Although literal textual support for this wording might not exist, the skilled person understood from the disclosure of the application that it was directed to the treatment of congestive heart failure in mammals. Moreover, it

referred to ErbB2 and ErbB4 at multiple points throughout.

Claim 1 found support *inter alia* on page 5, lines 1 to 9; page 13, lines 23 to 25 and pages 47 and 48 (Example VI) of the application. Furthermore, on page 12, lines 21 to 23 of the application it was stated that "*ErbB2 and ErbB4 levels ... decrease during ... heart failure*". The paragraph bridging pages 12 and 13 of the application stated that "*These observations indicate that neuregulin treatment will be useful for preventing, minimizing, or reversing congestive heart disease".* Example III provided data showing that ErbB2 and ErbB4 expression levels decrease in early heart failure.

Auxiliary request 3 - claim 1 - added subject-matter

The examining division also erred in its evaluation of this claim. Support for the variation from the wording of claim 1 of auxiliary request 2 principally derived from page 12 at lines 22 and 23, taken with the opening paragraphs of the application on page 1 and the entire passage bridging pages 12 and 13 of the application.

Auxiliary request 4 - claim 1 - added subject-matter

The examining division had held that for arriving at the subject-matter of this claim the skilled person *inter alia* had to combine the passages on page 12, lines 20 to 23; page 12 line 24 to page 13, line 5; and page 43, lines 7 to 13 but that there existed no clear indication in the description for such a combination.

However, the first two cited paragraphs were consecutive and were both part of the opening

paragraphs of the specific description. There was no reason why the skilled person would consider the two passages separately or otherwise unrelated or disconnected in any way. Equally, there was no reason why the skilled person would consider Example III on page 43 separately from the introductory passages of the detailed description of the invention at pages 12 and 13. On the contrary, the skilled person would understand that the examples are linked with the general discussion which precedes the examples, in this case the passages on page 12 and 13.

Auxiliary request 5 - claim 1 - added subject-matter

In contrast to the examining division's view, page 12 provided support for the wording of this claim.

Request for the reimbursement of the appeal fee

The examining division had committed a number of substantial procedural violations at the stage of the summons to oral proceedings and on the level of the decision. Therefore the examining division's way of handling of the case justified reimbursement of the appeal fee.

Reasons for the Decision

1. The appeal is admissible.

2. The duly summoned appellants did not attend the oral proceedings as previously announced. In accordance with Rule 115(2) EPC and Article 15(3) RPBA, the board decided to continue the proceedings in their absence.

Admittance into the proceedings of the main request and auxiliary request 1

3. Both the main request and auxiliary request 1 (see section VII) were filed by the appellants after the term for filing the statement of grounds of appeal. In view of Article 13(1) RPBA these requests thus are an amendment of the parties' case and their admission into the proceedings is subject to the discretion of the board. In accordance with Article 13(1) RPBA this discretion shall be exercised in view of *inter alia* the complexity of the new subject-matter submitted, the current state of the proceedings and the need for procedural economy.

4. The appellants filed the two requests after having learnt from the board's communication that it considered that none of the four requests filed with the statement of grounds of appeal complied with the requirements of Article 123(2) EPC. The board notes however that the examining division, in the decision under appeal, had already expressed the same view with regard to the very same requests.

5. The board therefore considers that the new main and auxiliary request could and should have more appropriately been filed at an earlier stage into the appeal proceedings in order to constitute a timely reaction. Hence, the state of the proceedings at the time these requests were filed and the need for procedural economy prevents the board from admitting them into the proceedings (Article 13 RPBA).

Auxiliary request 2 - claim 1 and claim 9 - added matter

6. As compared to claim 1 combined with claims 5 to 9 (see section II), which referred to "*treating or preventing congestive heart failure in a human*", claim 1 now refers to "*treating or preventing congestive heart failure in a human associated with reduced expression of ErbB2 and ErbB4*", thereby thus defining a different patient group.

7. It has not been contested by the appellant that the application does not provide literal support for this feature. The appellant rather referred to a number of passages in the application which enabled the skilled person, when reading the application as a whole and in particular having read the introductory passages at pages 1 to 4 setting out the field and background of the invention, without difficulty to directly and unambiguously derive the claimed subject-matter from the application.

8. The appellant has *inter alia* referred to the introductory part of the application on pages 1 to 4; to page 5, lines 1 to 9; to page 13, lines 23 to 25 and to Example VI on pages 47 and 48 of the application. The board notes however that these passages rather refer to patients suffering from congestive heart failure *in general* than to such patients in which this failure is associated with reduced expression of ErbB2 and ErbB4. Accordingly, as such they cannot provide support for the claim.

9. Reference was also made by the appellants to the passage on page 12, lines 21 to 23 of the application and to the first sentence of the paragraph bridging pages 12 and 13 of the application. These passages in

their context constitute the three first paragraphs starting the "Detailed description of the Invention" section (page 12 lines 17 to page 13, line 5) and read:

"*We have found that neuregulins promote survival and hypertrophic growth of cultured cardiac myocytes through activation of ErbB2 and ErbB4 receptors.*

In addition, we have observed, in animals with experimentally induced intracardiac pressure overload, that cardiomyocyte ErbB2 and ErbB4 levels are normal during early compensatory hypertrophy and decrease during the transition to early heart failure.

Together, our in vitro and in vivo findings show that neuregulins are involved in stimulating compensatory hypertrophic growth in response to increased physiologic stress, as well as inhibiting apoptosis of myocardial cells subjected to such stress. These observations indicate that neuregulin treatment will be useful for preventing, minimizing, or reversing congestive heart disease. While not wishing to be bound by theory, it is likely that neuregulin treatment will strengthen the pumping ability of the heart by stimulating cardiomyocyte hypertrophy, and will partially or completely inhibit further deterioration of the heart by suppressing cardiomyocyte apoptosis."

10. The skilled person is taught by these passages that in animals suffering from experimentally-induced intracardiac pressure overload the ErbB2 and ErbB4 levels were normal during the early compensatory hypertrophy phase and decreased during the transition to early heart failure. Based on this observation the skilled person was then suggested that neuregulin treatment would be useful for preventing, minimizing or

reversing congestive heart disease in patients in general. The board cannot, however, infer from these passages a clear and unambiguous disclosure of a particular human patient group which suffers from congestive heart failure "associated with reduced expression of ErbB2 and ErbB4".

11. Further reference was made by the appellants to Example III of the application on page 39 to page 42 and entitled "*Example III: ErbB2 and ErbB4 expression levels decrease in aortic stenosis rats in transition from chronic hypertrophy to early heart failure".* The example concerns the experimental detail of the observation summarised in the middle paragraph of the passage referred to in point 9 above. The board notes that the example concerns an animal model and that it concludes that "*a decrease in both LV message and protein levels of ErbB2 and ErbB4 is present at the stage of early failure in this model of pressure overload*" (see page 43, lines 12 and 13). As with the previous passages referred to by the appellants, however, example III is silent on a particular human patient group which suffers from congestive heart failure "associated with reduced expression of ErbB2 and ErbB4".

12. In view of the above considerations, the board judges that claim 1 of auxiliary request 2 fails to comply with the requirements of Article 123(2) EPC.

13. Independent claim 9 (see section IV) recites the same patient group as claim 1 for which the board has come to the conclusion that the requirements of Article 123(2) EPC were not met (see point 12). Accordingly, the considerations in points 8 to 11 above apply *mutatis mutandis* and the board judges, as also

the examining division held in the decision under appeal, that therefore claim 9 fails to comply with the requirements of Article 123(2) EPC.

Auxiliary requests 3 to 5

14. Auxiliary requests 3 to 5 all comprise an independent claim 9 which is identical to claim 9 of auxiliary request 2 (see section IV). The conclusions of point 13 therefore also apply to claim 9 of auxiliary request 3 to 5.

15. In its communication accompanying the summons to oral proceedings the board had expressed its preliminary opinion that the feature of i) treating or preventing heart failure in a human which heart failure is characterised by a decrease in cardiomyocyte ErbB2 and ErbB4 levels in claim 1 of then auxiliary request 1, now auxiliary request 3, and of ii) treating or preventing a decrease in cardiomyocyte ErbB2 and ErbB4 levels in a human of then auxiliary requests 2 and 3, now auxiliary requests 4 and 5, was not directly and unambiguously derivable from the application as filed. The board adheres to this view, but considers that, since auxiliary requests 3 and 4 comprise a claim which does not comply with the requirements of Article 123(2) EPC, a reasoned justification for the preliminary opinion of the board on claim 1 of these auxiliary requests is not necessary.

Auxiliary request 5 - Decision of the examining division to not admit an identical request (then auxiliary request 3) into the proceedings

16. With the statement of grounds of appeal, the appellants have re-submitted former auxiliary request 3. The

examination division had not admitted this request into the proceedings pursuant to Rule 116 EPC for the reason that the applicants themselves considered the request "*slightly unclear and not completely consistent with the disclosure*" and that consequently the request was not clearly allowable.

17. In paragraph 10 of the board's communication accompanying the summons to oral proceedings (see section VI), the appellants were informed that at the oral proceedings they would be heard on the issue whether or not the examining division had correctly exercised its discretionary power not to admit this auxiliary request into the proceedings.

18. In view of the board's judgement in relation to auxiliary request 5 and added subject-matter in points 14 and 15 above, this issue is no longer decisive for the outcome of the present appeal and accordingly the board does not have to take a decision on this issue.

Request for the reimbursement of the appeal fee

19. Pursuant to Rule 103(1)(a) EPC "the appeal fee shall be reimbursed in full when the Board of Appeal deems an appeal to be allowable, if such reimbursement is equitable by reason of a substantial procedural violation".

20. Since in the present case the appeal is not allowable, the first requirement of this provision for the reimbursement of the appeal fee is not complied with. Accordingly, the request of the appellant is rejected.

Order

For these reasons it is decided that:

1. The appeal is dismissed.

2. The request for reimbursement of the appeal fee is rejected.

The Registrar: The Chairwoman:

D. Hampe G. Alt

Decision electronically authenticated