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Datasheet for the decision of 27 June 2013

Case Number: T 1046/09 - 3.3.04

Application Number: 97927282.0

Publication Number: 942741

IPC: A61K 38/16, A23L 1/305

Language of the proceedings: EN

Title of invention:
Lectin compositions and uses thereof

Patent Proprietor:
Alizyme Therapeutics Limited

Opponent:
Phylogix, Inc.

Headword:
Lectin compositions/ALIZYME

Relevant legal provisions:
EPC Art. 56

Keyword:
"Main request - inventive step (yes)"

Decisions cited:
G 0002/08, T 0600/05

Catchword:
-

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 1046/09 - 3.3.04

D E C I S I O N
of the Technical Board of Appeal 3.3.04
of 27 June 2013

Appellant: (Patent Proprietor)
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Decision under appeal:
Decision of the Opposition Division of the European Patent Office posted 17 March 2009 revoking European patent No. 942741 pursuant to Article 101(3)(b) EPC.

Composition of the Board:

Chairman: C. Rennie-Smith
Members: R. Morawetz
M. Montrone

Summary of Facts and Submissions

I. This is an appeal by the proprietor (hereinafter "appellant") against the decision of the opposition division of 17 March 2009 whereby European patent No. 0 942 741 was revoked.

II. The patent at issue has the title "Lectin compositions and uses thereof". It was granted on European patent application No. 97927282.0 which originated from International patent application PCT/GB97/01668 published as WO 97/049420.

III. The patent was opposed under Article 100(a) EPC 1973 on the grounds of lack of patentable subject-matter (Articles 52(2) and 52(4) EPC 1973), lack of novelty (Article 54 EPC 1973), lack of inventive step (Article 56 EPC 1973) and lack of susceptibility of industrial application (Article 57 EPC 1973), and under Article 100(b) EPC 1973.

IV. The opposition division revoked the patent on the grounds that the main and auxiliary requests then on file did not fulfil the requirements of Articles 54 and 83 EPC 1973 (hereinafter "first decision" of the opposition division).

V. An appeal was lodged by the proprietor against this first decision of the opposition division. The board, in a composition different from the present one, decided in the first appeal proceedings (cf. decision T 0600/05 of 23 May 2006) that the main request before it (which is identical to the present main request) fulfilled the requirements of Articles 83 and 54 EPC

1973. Since no examination of the remaining grounds of opposition had yet taken place, the case was remitted to the department of first instance for further prosecution on the basis of claims 1 to 13 of the main request submitted with letter of 23 March 2006.

VI. In its second decision regarding the patent in suit (hereinafter the "decision under appeal") the opposition division decided that the main request submitted with letter of 23 March 2006 (which is identical to the main request before the board) lacked an inventive step (Article 56 EPC) and revoked the patent anew.

VII. Independent claims 1 and 9 of the main request read as follows:

"1. Use of a lectin in the manufacture of a medicament for the reduction and/or treatment of damage to mucosal cells and/or tissues, wherein the damage is caused by radiotherapy, a chemotherapeutic agent or a combination thereof, wherein the lectin causes proliferation of said mucosal cells and/or tissues.

9. A pharmaceutical composition comprising a lectin and a cytoprotectant selected from a radiosensitiser, a chemoprotectant, a growth factor or combinations thereof wherein the lectin causes proliferation of mucosal cells and/or tissues."

Claims 2 to 8 and 10 to 13 relate to specific embodiments of the use according to claim 1 and the pharmaceutical composition according to claim 9, respectively.

VIII. The proprietor (appellant) has lodged an appeal against this second decision of the opposition division to revoke the patent.

IX. By a communication of 29 November 2012 the parties were summoned to oral proceedings to be held on 27 June 2013.

X. In letters of 25 March 2013 and 24 May 2013 respectively, the respondent (opponent) and the appellant informed the board that they would not participate in the oral proceedings.

XI. In a communication of 11 June 2013 the board informed the parties of its preliminary view on inventive step and the other remaining grounds of opposition.

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

(O7): Pusztai A., European Journal of Clinical Nutrition, vol. 47, pages 691-699 (1993)

(O8): Pusztai A., Archivos Latinoamericanos de Nutricion, vol. 44, no. 4 (Suppl.), pages 10S-15S (1994)

(O25): Wimer B.M., Mol. Biother., vol. 2, pages 74-90, (1990)

(O26): Kutian G. et al., Tumori, vol. 79, pages 74-76, (1993)

(O27): Ganguli C. et al., Ind. J. Med. & Ped. Oncol., vol. 16, pages 148-155 (1995)

(O35): Richter M. et al., The Lancet, vol. 2, page 894 (1967)

(O36): Morelli D. et al., Cancer Research, vol. 56, pages 2082-2085 (May 1996)

(O37): Skubitz K.M. et al., J. Lab. Clin. Med. vol. 127, pages 223-228 (February 1996)

XIII. The appellant requests that the decision under appeal be set aside and the patent be maintained on the basis of the main request filed on 23 March 2006.

XIV. The respondent did not submit any arguments or requests during these appeal proceedings.

Reasons for the Decision

Main request

1. The patent as granted has *inter alia* been opposed under Article 100(a) EPC 1973 on the grounds of lack of patentable subject-matter (Articles 52(2) and 52(4) EPC 1973) and lack of susceptibility of industrial application (Article 57 EPC 1973). The department of first instance has not rendered a decision on these grounds of opposition. It appears to the board from the opponent's reply of 3 September 2007 to the communication of the opposition division of 23 April 2007 that, following the earlier appeal, the only objection it maintained was lack of inventive step. That view is reinforced by the absence of any written submissions by the respondent during these appeal proceedings. The board is therefore not convinced that it has to render a decision on these issues but will do so nevertheless for the sake of legal certainty.

2. The respondent submits that discoveries are not patentable inventions in the light of Article 52(2) EPC and argues (see page 55 of the notice of opposition) that: "*Even if the patentee has "discovered" that damage caused in certain ways or affecting certain parts of the gastrointestinal tract can be treated with lectins, this is simply an unpatentable discovery and does not amount to a patentable invention. Here it should be recalled that the use of lectins to treat/repair damage to mucosal cells was already known*[22] [reference to sections 4 and 5 of the notice of the opposition] *and merely indicating that particular agents could cause the damage or that particular parts of the gastrointestinal tract could be damaged, does not amount to a new medical use.*"

3. It appears to the board that the objection under Article 52(2) EPC is in fact another objection as to lack of novelty which has been rendered moot by decision T 600/05 (*supra*, see point 19 of the reasons) which held that the present main request relates to a novel medical use.

4. The objection under Articles 52(4) and 57 EPC 1973 has been raised against claim 9 as granted which is drawn up in the so-called Swiss-format and relates to a dosage regime. Claim 6 of the main request corresponds to claim 9 as granted. The argument brought forward by the respondent (see page 55 of the notice of opposition) is that claims relying "*upon features that relate to unpatentable method of treatment steps, rather than to true medical use features*" fall foul of Article 52(4) EPC 1973 and Article 57 EPC 1973.

5. The board notes that the Enlarged Board has decided (see decision G 02/08, OJ EPO 2010, 456) that dosage regimes are patentable. In particular the Enlarged Board held (see point 5.10.9 of the reasons) that "*Thus, decision T 1020/03 (OJ EPO 2007, 204, point 36 of the Reasons) was correct in stating that "... there is a seamless fit, either a method of using a composition is not a treatment by therapy and therefore falls outside the provision of Article 52(4) EPC [1973] first sentence, and so is patentable subject to compliance with the other provisions of the EPC, or else a method is a treatment by therapy and therefore inside the provision of Article 52(4) EPC [1973] first sentence, and so not itself patentable, but use of a composition for making a medicament for use in such treatment by therapy is patentable for unspecified therapy as a first medical indication or for a specified therapy as a further medical indication, again subject to compliance with the other provisions of the EPC, in particular novelty and inventive step.*"

6. The board concludes that the objections under Article 52(4) and Article 57 EPC 1973 fall in the light of decision G 02/08, *supra*, of the Enlarged Board of Appeal.

Article 56 EPC

7. For the assessment of inventive step the Boards of Appeal apply the "problem and solution approach" which, as a first step, requires the definition of the "closest prior art". The Boards have repeatedly pointed out that the closest prior art for assessing inventive step is normally a prior art document disclosing

subject-matter conceived for the same purpose or aiming at the same objective as the claimed invention and having the most relevant technical features in common, i.e. requiring the minimum of structural modifications (Case Law of the Boards of Appeal of the European Patent Office, 6th edition 2010, I.D.3.1). In the present case, the invention aims at the reduction and/or treatment of damage to mucosal cells and/or tissues caused by radiotherapy and/or chemotherapy.

8. The opposition division considered that either document (O25) or document (O7) could be considered to represent the closest prior art. However, the board notes that neither document (O25) nor document (O7) disclose subject-matter conceived for the same purpose or aiming at the same objective as the claimed invention.

9. Document (O25) is a review article on therapeutic activities of PHA-L4. In a section entitled "*Phytohemagglutinin as a direct hematopoietic protectant against radiation and chemotherapy*", see right hand column on page 83, document (O25) reports that PHA protects lymphocytes against the lethal effects of irradiation. In the same section document (O25) reports that it has also been shown in rabbits that PHA is capable of neutralizing the debilitating effects of mercaptopurine. Animals protected with concomitant injections of PHA lost no weight and experienced no leukopenia, whereas all unprotected rabbits lost 20% to 30% weight and experienced a drop in leukocytes (see reference 139, which corresponds to document (O35) in the present proceedings). However, document (O25) is silent on any protective effect of PHA - or any other lectin - on cells other than

hematopoietic cells. In decision T 0600/05, *supra*, point 17 of the reasons, the then competent board had moreover held that the skilled person could not directly and unambiguously derive from document (O25) or document (O35) that the reduction of weight loss upon concomitant administration of PHA was due to the healing of mucositis.

10. Document (O7) is a review article on the *in vivo* effects of dietary lectins on the body and reports that dietary lectins are metabolic signals for the gut and modulate immune and hormone functions. According to page 692, right hand column, first full paragraph: "(…)*it is possible that low concentrations of non-toxic lectins (tomato lectin, wheat germ agglutinin, etc.) may, in future, be used safely as growth stimulants in small intestinal hypoplasia induced by total parenteral feeding, resection or other gut lesions.*" As already pointed out in decision T 600/05 (*supra*, see point 18 of the reasons) there is no disclosure in document (O7) of treating damage to mucosal cells and/or tissues caused by radiotherapy and/or chemotherapy, which is a pathological situation different from e.g. a bacteria-induced gut lesion.

11. In the board's judgement document (O36) can be considered to represent the closest prior art. This document discloses that oral administration of anti-doxorubicin monoclonal antibody prevents chemotherapy-induced gastrointestinal mucositis in mice. As regards the objective technical problem to be solved, the board takes the view that it can be defined as the provision of further means for the reduction and/or treatment of damage to mucosal cells and/or tissues caused by

radiotherapy and/or chemotherapy. The claim under consideration is drawn up in the so-called Swiss-format and the statement of purpose thus limits the claim to lectins which can be used for the purpose of preparing a medicament for the reduction and/or treatment of damage to mucosal cells and/or tissues. In view of the finding in decision T 600/05 (*supra*, see points 4 to 9 of the reasons) with respect to sufficiency of disclosure, the board concludes that the whole subject-matter as claimed is to be regarded as a solution to this problem.

12. It remains to be answered whether the skilled person, when facing the objective technical problem defined above, would have modified the teaching in the closest prior art document (O36)- possibly in the light of other teachings in the prior art - so as to arrive at the claimed invention in an obvious manner.

13. Document (O36) mentions that approaches to prevent and treat mucositis are under way, but is silent on the effects of lectins on mucosal cells or tissues. Notably, document (O36) discloses (see page 2085, left hand column, third paragraph) that partial protection, confined to oral mucosa, against 5-fluorouracil-induced stomatitis was obtained by topical administration of transforming growth factor beta3, a potent inhibitor of epithelial as well as hematopoietic stem cell growth. The board concludes that document (O36) on its own provides no hint that mitogenic lectins could be used to solve the technical problem formulated above.

14. Document (O8) discusses the interaction of lectins with the intestinal mucosa and discloses (sentence bridging

columns on page 11-S) that mitogenic lectins can be used to stimulate growth in intestinal hypoplasia caused by parenteral feeding, gut resection and other gut lesions. Document (O8) is however silent on any beneficial effect of mitogenic lectins on damage to mucosal cells and/or tissues caused by radiotherapy and/or chemotherapy.

15. Document (O26) discloses that an aqueous extract of European mistletoe partially reversed the side effects of radiation and chemotherapy. According to document (O26) the underlying cause is most probably due to stimulation of the immune system by enhancement of proliferation and maturation of leukocytes (see page 76, left hand column, first full paragraph). Document (O26) is silent on any effect of the extract on mucosal cells or tissues and consequently provides no hint that lectins could be used to solve the technical problem identified above.

16. Document (O27) studies the efficacy of sequential treatment with anticancer drugs and plant lectins and reports that plant lectins enhance the cytotoxic effect of antitumor agents (page 150, left hand column, first full paragraph) but is silent on any effect of lectins on mucosal cells or tissues.

17. Document (O35) discloses that whilst rabbits treated with 6-mercaptopurine (6-M.P.) alone experienced a loss of weight and decreased white-blood-cell counts, concomitant administration of PHA prevented the loss of weight and the leukopenia. In the decision under appeal the opposition division held "(…)*that it is likely that 6-MP causes some damage to the mucosa, like many other*

chemotherapeutic agents, (see O37). It seems also established or at least very likely, that the extent of mucositis correlates with the weight loss experienced during chemotherapy, (cf. O36 and T 0600/05 point 15. of reasons). It therefore appears obvious that the reduction in weight loss observed in O35 could be at least partly due to beneficial effects on the intestinal mucosa".

18. The board disagrees. Document (O35) does not report any data or observation regarding the effect of PHA on mucosal cells, nor any disclosure that any of the animals in the study were suffering from mucositis, nor any discussion that mucositis may be treated using PHA. Nor has it been established by the opposition division that the skilled person would understand that the loss of weight observed in document (O35) was entirely due to mucositis or that the effect of the lectin was to only treat mucositis. As already pointed out in decision T 600/05 (*supra*, point 15 of the reasons), the skilled person could have reasonably concluded that the total weight loss of 20 to 30 % reported in document (O35) could be ascribed to different factors such as leukopenia, lack of food intake, dehydration, myelosuppression or cachexia. The board concludes that there is no teaching whatsoever in document (O35) that PHA was having any effect on the mucosa and accordingly (O35) provides no hint to use PHA - or any other mitogenic lectin - to solve the above-formulated problem.

19. Document (O37) discloses that oral glutamine supplementation can significantly decrease the severity of chemotherapy-induced oropharyngeal stomatitis

(abstract; page 227, left hand column, first full paragraph). From the mere fact that administration of glutamine, an amino acid, has a beneficial effect on mucositis the skilled person cannot possibly derive any hint that a structurally and functionally unrelated compound such as a mitogenic lectin would have the same beneficial effect.

20. In summary, the board concludes that none of the documents relied on by the opposition division in the decision under appeal provides any hint that would have motivated the skilled person to modify the teaching in the closest prior art document (O36) so as to arrive at the claimed invention in an obvious manner.

21. The above considerations in respect of claim 1 of the main request apply *mutatis mutandis* to the subject-matter of claims 2 to 8 which are all dependent on claim 1. In the decision under appeal no objections under Article 56 EPC against claim 9 of the main request were raised. The board sees also no reason to object to this or its dependent claims under Article 56 EPC. Therefore, the main request complies with the requirements of Article 56 EPC.

22. In view of the decision on the main request, there is no need to consider the auxiliary requests.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the department of first instance with the order to maintain the patent on the basis of the main request filed with appellant's letter of 23 March 2006 and a description and figures to be adapted thereto.

The Registrar: The Chairman:

P. Cremona C. Rennie-Smith