Datasheet for the decision of 17 September 2015

Case Number: T 2197/10 - 3.3.04
Application Number: 00968780.7
Publication Number: 1223964
IPC: A61K38/17

Language of the proceedings: EN

Title of invention:
APRIL Receptor (BCMA) and uses thereof

Patent Proprietor:
Biogen Idec MA Inc.
Apotech R&D S.A.

Opponent:
Amgen Inc.

Headword:
APRIL Receptor/BIOGEN

Relevant legal provisions:
EPC Art. 56
RPBA Art. 13(1)

Keyword:
All requests: Inventive step (no)

Decisions cited:
T 0816/90, T 0609/02, R 0016/09
Catchword:
Case Number: T 2197/10 - 3.3.04

DECISION
of Technical Board of Appeal 3.3.04
of 17 September 2015

Appellant: Biogen Idec MA Inc.
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Decision under appeal: Interlocutory decision of the Opposition
Division of the European Patent Office posted on
26 August 2010 concerning maintenance of the

Composition of the Board:
Chairwoman G. Alt
Members: A. Chakravarty
L. Bühler
Summary of Facts and Submissions

I. Appeals were filed by the two patent proprietors (hereinafter "appellant I") and the opponent (hereinafter "appellant II") against the interlocutory decision of the opposition division maintaining in amended form European patent No. 1 223 964, entitled "April Receptor (BCMA) And Uses Thereof".

II. The patent had been opposed by appellant II under Article 100(a) EPC, on the grounds of lack of novelty (Article 54 EPC) and lack of inventive step (Article 56 EPC) and under Articles 100(b) and 100(c) EPC.

III. The opposition division decided that the subject-matter of claim 1 of the patent as granted and of the first auxiliary request did not involve an inventive step. Claim 1 of auxiliary request 2 was found not to comply with the requirements of Article 123(3) EPC. Auxiliary request 3 however was found to meet the requirements of the EPC.

IV. In statement of grounds of appeal, appellant I requested as a main request that the patent be maintained as granted. Three auxiliary requests were also filed, corresponding to auxiliary requests 1, 3 and 4 as pending before the opposition division.

V. In a communication dated 27 February 2015, the board informed the parties of its preliminary and non-binding opinion on some of the substantive and legal issues concerning the appeal. In this communication, the question was raised whether a document other than WO 99/12965 (document D3), such as one of the documents mentioned in the description of the patent at
paragraphs [0005] to [0008] disclosing methods for treating cancer using receptors binding TNF family ligands, might represent a suitable starting point for the consideration of inventive step in the context of the problem and solution approach.

VI. Both appellants I and II replied to the communication of the board with letters dated 17 July 2015. Appellant I's letter was accompanied by auxiliary claim requests 4 to 7.

VII. Oral proceedings before the board were held on 17 September 2015. During the proceedings, appellant I requested the admission of auxiliary claim requests 8 to 11 into the appeal proceedings. These requests included the definition of the tumour to be treated as a B-cell tumour. At the end of the oral proceedings the Chairwoman announced the decision of the board.

VIII. The following documents are cited in this decision.

D3: WO 99/12965

D5: Madry C. et al., 1998, International Immunology, 10(11), 1693-1702


D7: Gras M-P. et al., 1995, International Immunology, 7(7), 1093-1106

D11: Rennert P. et al., 4 December 2000, J. Exp. Med., 192(11), 1677-1683

R2: Beutler B., 1999, J. Rheumatol., 26, 57, 16-21


R4: Mackay F. et al., 1998, Gastroenterology, 115(6), 1464-1475


IX. Claim 1 of the main request and of auxiliary requests 1 to 7, is reproduced below, with the auxiliary requests having been edited by the board as appropriate:

Main request

"1. Use of
 a) a polypeptide comprising an amino acid sequence that is
 (i) at least 80% identical to the sequence set forth from amino acid 1 to amino acid 184 of SEQ ID NO:8 and
 (ii) capable of binding to APRIL;
 b) a polypeptide comprising an amino acid sequence that is
 (i) at least 80% identical to the sequence set forth from amino acid 1 to amino acid 52 of SEQ ID NO:8 and
 (ii) capable of binding to APRIL;
 c) a polypeptide comprising the amino acid sequence set forth from amino acid 8 to amino acid 41 of SEQ ID NO: 8; or
 d) an antibody directed against SEQ ID NO:8
for the preparation of a pharmaceutical composition for treating a tumour cell that expresses A Proliferation Inducing Ligand (APRIL)."

**Auxiliary request 1**

1. Use of
   [...]  
   c) an antibody directed against the amino acid sequence set forth from amino acid 1 to amino acid 52 or amino acid 8 to amino acid 41 of SEQ ID NO:8 for the preparation of a pharmaceutical composition for treating a tumour cell that expresses A Proliferation Inducing Ligand (APRIL)."

**Auxiliary request 2**

"1. Use of
   [...]  
   (b) an antibody directed against the amino acid sequence set forth from amino acid 8 to amino acid 41 of SEQ ID NO: 8 for the preparation of a pharmaceutical composition for treating a tumour cell that expresses A Proliferation Inducing Ligand (APRIL)."

**Auxiliary request 3**

"1. Use of an antibody directed against the amino acid sequence set forth from amino acid 8 to amino acid 41 of SEQ ID NO:8 for the preparation of a pharmaceutical composition for treating a tumour cell that expresses A Proliferation Inducing Ligand (APRIL)."
Auxiliary request 4

"1. Use of
a) a polypeptide comprising an amino acid sequence that is
  (i) at least 80% identical to the sequence set forth from amino acid 1 to amino acid 184 of SEQ ID NO:8
  [...] for the preparation of a pharmaceutical composition for treating a tumour cell that expresses A Proliferation Inducing Ligand (APRIL)."

Auxiliary request 5

"1. Use of
[...]
(c) an antagonistic antibody directed against the amino acid sequence set forth from amino acid 1 to amino acid 52 or amino acid 8 to amino acid 41 of SEQ ID NO:8 for the preparation of a pharmaceutical composition for treating a tumour cell that expresses A Proliferation Inducing Ligand (APRIL)."

Auxiliary request 6

"1. Use of
[...]
(b) an antagonistic antibody directed against the amino acid sequence set forth amino acid 8 to amino acid 41 of SEQ ID NO:8 for the preparation of a pharmaceutical composition for treating a tumour cell that expresses A Proliferation Inducing Ligand (APRIL)."
Auxiliary request 7

"1. Use of an antagonistic antibody directed against the amino acid sequence set forth from amino acid 8 to amino acid 41 of SEQ ID NO:8 for the preparation of a pharmaceutical composition for treating a tumour cell that expresses A Proliferation Inducing Ligand (APRIL)."

X. Appellant I's arguments relevant to the decision can be summarised as follows:

Main request

Inventive step (Article 56 EPC)

Claim 1

The claim related to the medical use of B-cell maturation antigen (BCMA), represented by SEQ ID NO: 8, as well as specific fragments thereof and antibodies recognising it, in the treatment of tumours expressing A Proliferation Inducing Ligand (APRIL).

The contribution to the art made by the invention lay in the identification of BCMA as the receptor for this ligand. While BCMA had been known in the art, its involvement with APRIL had not been known nor had there been any indication of BCMA's utility in the treatment of tumours expressing APRIL. In fact, until the invention represented by the patent, APRIL had been known (from document D3) as an orphan ligand of the TNFα family.

Document D3, which disclosed APRIL and its use in treating tumours, was the most suitable starting point
for assessing inventive step of the claimed subject-matter. The documents R1 to R5, cited in the description of the patent, provided only general background information relating to members of the TNF superfamily and their receptors. In particular they related to the cytokine TNFα (tumour necrosis factor) and its receptor and to the cytokine lymphotoxin α/β and its receptor. These documents did not mention APRIL or relate to the APRIL signalling pathway and could therefore not be considered as the closest prior art for assessing inventive step of the claimed invention. Starting from document D3 (or document D6, which had the same technical content), the objective technical problem was the provision of alternative pharmaceutical compositions to treat tumours expressing APRIL. In essence, this problem was the identification of a receptor for APRIL to be used for treating APRIL expressing tumours.

This problem was solved by the APRIL receptor (BCMA) and antibodies thereto. BCMA could serve as decoy receptor for APRIL and antibodies to APRIL could block the APRIL/APRIL-R (BCMA) interaction. This solution was not foreseeable from the prior art for a number of reasons.

Firstly, APRIL had been an orphan ligand which in principle had no obvious medical use. Secondly, it would not have been obvious for the skilled person to provide BCMA (and antibodies thereto) as a solution to the technical problem. Starting from document D3, the skilled person would not have had a reasonable expectation of success that BCMA (or antibodies thereto) could or would be a receptor for APRIL. This was because, at the effective date of the patent, the skilled person would not have known that there were in
fact three different molecules, BCMA, "transmembrane activator and calcium-modulator and cyclophilin ligand interactor" (TACI) and proteoglycans, which could have been identified as an APRIL receptor.

Moreover, although the identification of a receptor for APRIL might have seemed theoretically straightforward, the skilled person, would have been confronted with unexpected difficulties when following this straightforward path and would have needed to exercise inventive skill to overcome them (cf. decision T 816/90).

In the case of APRIL, the existence of TACI and/or proteoglycans as well as BCMA as receptors for APRIL meant that the skilled person trying to identify such a receptor might have not have arrived at the claimed solution when following the guidance of Example 3 of document D3. Arriving at either TACI or proteoglycans, the skilled person would have had no reason to continue screening for additional receptors.

A further difficulty for the skilled person trying to carry out the scheme proposed in Example 3 of document D3, was that BCMA was not present in all of the cell lines mentioned in document D3. In fact it had later been established that some of these cell lines expressed both TACI and BCMA, some just TACI, some just BCMA and some neither (document D11, Fig. 3). All these uncertainties contributed to the lack of expectation of success.
Auxiliary requests 1 to 7

Inventive step (Article 56 EPC)

Claim 1

The subject-matter of auxiliary requests 1 and 2 related to the medical use of a specific portion of BCMA, namely the extracellular domain (ECD) and antibodies directed to it. Auxiliary request 3 related to the medical use of antibodies binding to the BCMA ECD. There was no pointer in document D3 to the particular extracellular domain fragments or to antibodies thereto, now mentioned in the claim. Auxiliary requests 4 to 7 corresponded to the main and auxiliary requests 1 to 3 but additionally explicitly defined the antibody as an "antagonistic" antibody. This was done in response to the objection of sufficiency of disclosure and as a precaution in the light of decision T 848/10.

As the subject-matter of the auxiliary requests was progressively further removed from the disclosure of document D3, it required more and more additional and not obvious steps to be carried out by the skilled person to arrive at the claimed subject-matter.

Admissibility of auxiliary requests 8 to 11

These requests had been occasioned by the opinions expressed by the board during the oral proceedings. The amendments were limited and easy to understand, consisting of the further definition of the tumour to be treated as a B-cell tumour. There was no suggestion in document D3 that such a tumour could be treated as
claimed. Thus the requests should be admitted into the appeal proceedings.

XI. Appellant II's arguments relevant to the decision can be summarised as follows:

Main request

Inventive step (Article 56 EPC)

Document D3 was the closest prior art for the purpose of assessing inventive step of the subject-matter of claim 1 as it disclosed APRIL and antagonists thereto for anti-cancer applications. It also disclosed the fact that a receptor for APRIL existed but that it had not been identified. From this the skilled person would have understood that the yet to be identified APRIL receptor and antibodies to it were likely to be therapeutically useful for the treatment of tumour cells expressing APRIL (see page 11, lines 11 to 23 of document D3).

In view of this, the technical problem to be solved by the skilled person starting from document D3 was to identify and develop additional methods for treating cancer growth by identifying a receptor for APRIL and generating antibodies thereto. Although document D3 did not provide or characterise an APRIL receptor, it contained repeated suggestions that it would be useful to find and characterise such a protein. In Example 3 it even provided a scheme setting out how the skilled person should go about identifying the receptor and generating antibodies to it. Indeed, document D3 also taught the skilled person which cells a receptor for APRIL was likely to be found in, being those that proliferated in response to APRIL treatment.
Admissibility of the auxiliary requests

Auxiliary requests 1 to 7

There were no objections to the admissibility of auxiliary request 1 to 7.

Auxiliary requests 8 to 11

These requests were filed at the oral proceedings before the board. No convincing reason had been provided for their late submission although the objection of lack of inventive step with respect to document D3, which they were supposed to overcome, had already been raised in the statement of grounds of appeal. The proprietor had therefore had ample time to file the amendments earlier. The late filing meant that there had not been sufficient time to prepare a proper response to them which would now have required an adjournment of the oral proceedings.

Auxiliary request 1 to 7

Inventive step (Article 56 EPC)

Claim 1

Once it was established that the provision of the APRIL receptor itself was obvious, all other subject-matter, such as the use of extra-cellular domain of BCMA or antagonistic antibodies thereto in the treatment of cancer, was suggested directly by document D3.

XII. Appellant I requested that the decision under appeal be set aside and that the patent be maintained as granted (main request) or alternatively, on the basis of one of
auxiliary requests 1 to 3, filed with the statement of 
grounds of appeal or alternatively, on the basis of one 
of auxiliary requests 4 to 7, filed with letter dated 
17 July 2015, or alternatively, on the basis of one of 
auxiliary requests 8 to 11 filed during the oral 
proceedings of 17 September 2015.

XIII. Appellant II requested that the decision under appeal 
be set aside and that the patent be revoked.

Reasons for the Decision

Admissibility of the auxiliary requests

Auxiliary requests 1 to 7

1. The admissibility of auxiliary requests 1 to 7 was not 
contested and the board sees no reason, in view of 
Article 114(2) EPC in combination with Articles 12(4) 
and 13(1) RPBA, to either exclude them from (auxiliary 
requests 1 to 3) or not admit them into (auxiliary 
requests 4 to 7) the proceedings.

Auxiliary requests 8 to 11

2. These requests were submitted during the oral 
proceedings before the board.

3. Appellant I argued that the filing of auxiliary 
requests 8 to 11 during oral proceedings was occasioned 
by an unexpected procedural development, being the 
board's opinion on inventive step of the subject-matter 
of the main request with respect to the disclosure of 
document D3. The amendments made were limited and easy 
to understand, consisting only of the addition of the 
further definition of the tumour to be treated as a
B-cell tumour. There was no suggestion in document D3 that a B-cell tumour could be treated as claimed.

4. Appellant II argued that there was no convincing reason provided for the late filing of the requests. The objection of lack of inventive step with respect to document D3 which they were supposed to overcome had already been raised in the statement of grounds of appeal. Moreover, the admission of the auxiliary requests into the appeal proceedings would require a postponement of the oral proceedings to allow sufficient time for them to be properly studied.

5. The admissibility of requests filed after a party has filed its statement setting out the grounds of appeal or the reply thereto and after a board has arranged oral proceedings is subject to Article 13(1) and (3) RPBA. By virtue of Article 13(1) RPBA, a board's discretion in admitting any amendment to a party's case "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". Thus, the board has discretion to decide which of those criteria take precedence according to the circumstances of the case such that the importance of one of them may outweigh the others (see R 16/09, points 2.2.11 and 2.2.12 of the reasons). Pursuant to Article 13(3) RPBA, amendments shall not be admitted "if they raise issues which the Board or the other party or parties cannot reasonably be expected to deal with without adjournment of the oral proceedings".

6. Claim 1 of each of auxiliary requests 8 to 11 contains the phrase "wherein the tumor cell is a B-cell" in the definition of the medical indication to be treated. This subject-matter has been taken from the description
and has presumably not been searched. Thus, admitting these requests into the procedure would have obliged the board to remit the case to the opposition division. Such a course would not be in keeping with considerations of procedural economy.

7. Accordingly, the board has decided that auxiliary requests 8 to 11 are not admitted into the appeal proceedings.

Main request

The claimed invention

8. Claim 1 is, **inter alia**, for the medical use of a polypeptide comprising the amino acid sequence, SEQ ID NO: 8 (human BCMA), for treating a tumour cell that expresses "A Proliferation Inducing Ligand" (APRIL), where APRIL is a member of the tumour necrosis factor ligand superfamily (see paragraph [0010] of the description).

9. The invention is said to be based on the fact that the inventors "found that BCMA [B-cell mediated protein, also known as B-cell maturation antigen] is a receptor for the tumour necrosis factor, APRIL" (patent in suit, paragraph [0014]).

10. In the patent, BCMA is also referred to as APRIL-receptor (APRIL-R). The amino acid sequence of human full length (184 amino acid) BCMA is given as SEQ ID NO: 8 (paragraph [0018] and Fig. 3B). BCMA (APRIL-R) is said to have an extracellular domain (APRIL-R ECD) which is "a form of APRIL-R which is essentially free of transmembrane and cytoplasmic domains of APRIL-R". The ECD may comprise amino acid
residues 1 to 51, 1 to 52, 1 to 53, 4 to 51 or 8 to 41 of SEQ ID NO: 8 (paragraph [0024]). The "transmembrane domain identified for the APRIL-R polypeptide of the present invention is identified pursuant to criteria routinely employed in the art for identifying that type of hydrophobic domain [and] the exact boundaries of a transmembrane domain may vary but most likely by no more than about 5 amino acids at either end of the domain specifically mentioned" (see paragraph [0024] of the patent).

**Inventive step (Article 56 EPC)**

**Closest prior art**

11. To assess whether or not a claimed invention meets the requirements of Article 56 EPC, the boards of appeal apply the "problem and solution" approach, which requires as a first step, the identification of the closest prior art. In accordance with the established case law of the boards of appeal, the closest prior art is a teaching in a document conceived for the same purpose or aiming at the same objective as the claimed invention (Case Law of the Boards of Appeal of the European Patent Office, 7th edition 2013, I.D.3.1).

12. The purpose of the present invention is the achievement of the therapeutic effect defined in the claim, i.e. treating a tumour cell that expresses APRIL.

13. Both parties and the opposition division selected document D3 as representing the closest prior art to the claimed subject-matter.

14. Document D3 discloses pharmaceutical compositions comprising the cytokine APRIL for the treatment of
cancer (claim 19). It also discloses that "the methods [of the invention] for the treatment of cancers involve the administration to a patient [...] of an effective amount of a claimed composition comprising a blocking agent capable of interfering with the association between APRIL and its receptor. Such blocking agents include, but are not limited to soluble APRIL, anti-APRIL antibodies, anti-APRIL receptor antibodies, or biologically active fragments thereof" (page 26, lines 1 to 10) and that "Pharmaceutical compositions of the invention may comprise a therapeutically effective amount of APRIL, or its receptor [...]" (Id., lines 21 to 23).

15. That the tumour cells to be treated express APRIL is disclosed in document D3 at page 11, lines 20 to 23: "APRIL appears to be unique among the members of the TNF family as it is both abundantly expressed in tumor cells [...]".

16. In summary, document D3 discloses the use of APRIL in the treatment of tumours expressing it and puts forward the hypothesis that the yet unidentified receptor for APRIL and antibodies to it would be able to serve the same purpose.

17. Thus, the purpose of the agents disclosed in document D3 is the same purpose as addressed by the subject-matter of present claim 1.

Technical problem and solution

18. The difference between the closest prior art represented by document D3 and the subject-matter as claimed is that the receptor for APRIL, referred to in a hypothetical way in document D3, is in fact provided
and characterised. The technical effect of this difference is the concrete provision of a receptor for APRIL and its use in the treatment of tumours expressing APRIL.

19. Taking into account the closest prior art, the difference between it and the claimed subject-matter and the technical effect of this difference, the objective technical problem can be seen as the provision of a pharmaceutical composition for the treatment of a tumour cell that expresses APRIL (cf. Case Law of the Boards of Appeal of the European Patent Office, 7th edition, II.D. 4.3.1).

20. As to whether the claimed subject-matter provides a solution to the problem, the board observes that the statement of purpose recited in the claim limits its subject-matter to that which provides a solution to the problem (cf. decision T 609/02, point 9 of the reasons).

Obviousness

21. The skilled person starting from the closest prior art document D3 and seeking to solve the problem formulated in point 19. would, in the board's view, have been motivated to try to identify the receptor for APRIL. This is because document D3 explicitly suggests that APRIL-R and antibodies to it would be useful in treating cancers expressing APRIL, by blocking the association between a yet to be identified APRIL receptor and this (orphan) ligand.

22. A general protocol for isolation of a receptor binding to APRIL is provided in Example 3 of document D3. The protocol involves the fusion of the 5' end of the
extracellular domain of APRIL (i.e. the receptor binding sequence of APRIL) to a marker or tagging sequence and the addition of a leader sequence to force secretion of APRIL in an expression system. According to the Example, "cells expressing the receptor can be identified by exposing them to the tagged ligand. Cells with bound ligand are identified in a FACS experiment by labeling the myc tag with an anti-myc peptide antibody (9E10) followed by phycoerythrin (or a similar label) labeled anti-mouse immunoglobulin. FACS positive cells can be readily identified and would serve as a source of RNA encoding for the receptor. An expression library would then be prepared from this RNA via standard techniques and separated into pools. Pools of clones would be transfected into a suitable host cell and binding of the tagged ligand to receptor positive transfected cells determined via microscopic examination, following labeling of bound myc peptide tag with an enzyme labeled anti-mouse Ig reagent, i.e. galactosidase, alkaline phosphatase or luciferase labeled antibody. Once a positive pool has been identified, the pool size would be reduced until the receptor encoding cDNA is identified. This procedure could be carried out with either the mouse or human APRIL, as one may more readily lead to a receptor".

23. Appellant I argued that the skilled person starting from document D3 would not have had a reasonable expectation of success of at arriving at the claimed solution to the objective technical problem due to the existence of multiple binding partners for APRIL (see Section (X.), paragraphs 6 and 7).

24. The board however, considers that since the knowledge of multiple binding partners for APRIL came to light only after the effective date of the patent (see for
instance, document D11) this fact could not have caused the skilled person to be uncertain about the ability of the method disclosed in document D3 (Example 3 - "Isolation of a receptor binding to APRIL") to actually identify BCMA as a receptor for APRIL.

25. It remains to be assessed if the skilled person would when following the above mentioned protocol have arrived at the claimed invention or not.

26. Appellant I argued that the situation was analogous to that dealt with in decision T 816/90 of 7 September 1993, in which the competent board, in point 5.2.7, found that "even when it is possible to theoretically conceive a straightforward approach to solve a specific technical problem, the skilled person might be confronted with unexpected difficulties when trying to put the conceived strategy into practice." Appellant I's argument was that the existence of multiple receptors for APRIL would have caused the skilled person such unexpected difficulties, because depending on the cell type chosen to "expose to the tagged ligand" (see document D3, page 32, lines 26 and 27) when implementing the protocol of Example 3, any of BCMA, TACI or proteoglycans might have been isolated. Should the skilled person have first obtained TACI, he would not have realised that there was a further receptor and would not have identified BCMA as an APRIL receptor and therefore would not have arrived at the subject-matter of claim 1 without inventive effort.

27. The board considers that in the present case, following the protocol provided in Example 3 of document D3 can be considered to be routine experimental work that could be expected of a skilled person. Furthermore, in the board's judgment, the skilled person, seeking to
fill any gaps in the instructions given in Example 3 of document D3 about which cell type to use would, as a matter of normal practice, have turned first to the disclosure of document D3 itself for further instruction. Here he would have found in Example 2 the disclosure of experiments on the induction of proliferation in various tumor cell lines by exposure to purified recombinant FLAG-tagged soluble APRIL. An increase in proliferation being seen in Jurkat T lymphoma cells (page 30, line 31), human Raji B-cell lymphomas, mouse A20 cells (page 31, line 15) and in cell lines of epithelial origin such as COS and HeLa, as well as melanomas (page 31, line 16). The results of the experiment of Example 2 being illustrated in Fig. 3.

28. Thus, document D3 discloses to the skilled person that Jurkat T lymphoma cells, human Raji cell, mouse A20 cells and on cell lines of epithelial origin such as COS and HeLa, as well as melanomas, express a receptor for APRIL and would therefore be good candidate cell lines to use in the protocol Example 3.

29. Post-published document D11 provides evidence that confirms that Raji cells express message for both TACI and BCMA and also are positive for both BAFF and APRIL staining.

30. The board therefore considers that the skilled person, when following the routine methods described in document D3, would have used all of the above mentioned cells lines in the protocol of Example 3 of document D3 and consequently would have isolated both BCMA and TACI, at least from Raji cells.
31. That the (yet to be identified) receptor for APRIL could be useful in treating tumor cells expressing APRIL was explicitly disclosed in document D3 (see page 11, line 24 and page 26, lines 21 and 22).

32. In view of the above considerations, the subject-matter of claim 1 is considered to be obvious in the light of the teaching of document D3. That BCMA is one of several receptors for APRIL does not affect this assessment because it represents one of several equally obvious alternatives.

33. The main request therefore fails to meet the requirements of Article 56 EPC and is not allowable.

**Auxiliary request 4**

34. This finding also applies to the subject-matter of claim 1 of auxiliary request 4, since it also relates to the medical use of full length BCMA (SEQ ID NO: 8).

**Auxiliary requests 1, 2, 3, 5, 6 and 7**

**Inventive step**

35. The medical use for treating a tumour cell that expresses a Proliferation Inducing Ligand (APRIL) of an antagonistic antibody directed to the extracellular domain (ECD) of human BCMA (i.e. "an antibody directed against the amino acid sequence set forth from amino acid 8 to amino acid 41 of SEQ ID NO: 8" that is able to "inhibit receptor ligand interactions"; cf. paragraph [0089] of the patent) is common subject-matter of claim 1 of each of auxiliary requests 1 to 3 and 5 to 7.

36. The blocking of the interaction of BCMA with the ligand APRIL using (antagonistic) antibodies to it and the use
of such antibodies to treat APRIL expressing tumour cells was explicitly suggested in document D3: "APRIL appears to be unique among the members of the TNF [ligand] family as it is both abundantly expressed in tumor cells and stimulates growth of many different tumor cell lines. Given the apparent role of APRIL is tumorigenesis, the **antagonistic antibodies** to APRIL, or the **APRIL receptor**, will provide novel approaches to cancer treatment" (page 11, lines 20 to 25; emphasis added by the board). Since the production of antibodies was routine for the skilled person at the effective date of the patent, the board considers that it would have been a matter of routine for the skilled person to generate antibodies to BCMA. That these antibodies would be able to block (antagonise) its interaction with APRIL was disclosed by document D3. That the antagonistic antibodies should recognise the ECD of BCMA is a consequence of the fact, reflected in its name, that the ECD is exposed on the cell surface and is therefore the part of the molecule involved in ligand interaction and available for antibody binding. Indeed, document D5 disclosed the structural characterisation of BCMA including the identification of the ECD (see page 1696, right column).

37. In view of the above considerations, the board concludes that the subject-matter of claim 1 of auxiliary requests 1 to 3 and 5 to 7 is obvious and therefore lacks an inventive step.
Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chairwoman:

P. Cremona G. Alt

Decision electronically authenticated