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**Datasheet for the decision
of 26 February 2015**

Case Number: T 2141/10 - 3.3.02
Application Number: 01978921.3
Publication Number: 1334731
IPC: A61K45/00, A61K39/395,
C07K16/24, C07K16/28
Language of the proceedings: EN

Title of invention:

PREVENTIVES OR REMEDIES FOR PSORIASIS CONTAINING AS THE ACTIVE
INGREDIENT IL-6 ANTAGONIST

Patent Proprietor:

CHUGAI SEIYAKU KABUSHIKI KAISHA

Opponent:

Ablynx N.V.

Headword:

IL-6-receptor antibodies for treatment of psoriasis/CHUGAI

Relevant legal provisions:

EPC Art. 56

Keyword:

Inventive step - (no)

Decisions cited:

Catchword:



**Beschwerdekammern
Boards of Appeal
Chambres de recours**

European Patent Office
D-80298 MUNICH
GERMANY
Tel. +49 (0) 89 2399-0
Fax +49 (0) 89 2399-4465

Case Number: T 2141/10 - 3.3.02

D E C I S I O N
of Technical Board of Appeal 3.3.02
of 26 February 2015

Appellant: CHUGAI SEIYAKU KABUSHIKI KAISHA
(Patent Proprietor) 5-1, Ukima 5-chome,
Kita-ku
Tokyo, 115-8543 (JP)

Representative: Vossius & Partner
P.O. Box 86 07 67
81634 München (DE)

Respondent: Ablynx N.V.
(Opponent) Technologiepark 21
9052 Ghent-Zwijnaarde (BE)

Representative: Vlassak, Katrien
Ablynx NV
Technologiepark 21
9052 Zwijnaarde (BE)

Decision under appeal: **Decision of the Opposition Division of the
European Patent Office posted on 30 July 2010
revoking European patent No. 1334731 pursuant to
Article 101(3) (b) EPC.**

Composition of the Board:

Chairman U. Oswald
Members: T. Sommerfeld
D. Prietzel-Funk

Summary of Facts and Submissions

- I. European patent No. 1334731, based on application No. 01978921.3, entitled "Preventives or remedies for psoriasis containing as the active ingredient IL-6 antagonist" and published as international application WO 02/034292, was granted with 9 claims.

Independent claim 1 as granted read as follows:

"1. Use of an anti-interleukin-6 (IL-6) receptor antibody that can block the binding of IL-6 to IL-6 receptor for the manufacture of a medicament for treating psoriasis."

Dependent claims 2 to 9 further defined the antibody.

- II. An opposition was filed against the granted patent, the opponent requesting revocation of the patent in its entirety on the grounds of lack of novelty and lack of inventive step (Articles 54(2) and 56 EPC and Article 100(a) EPC), lack of sufficiency of disclosure (Article 100(b) EPC) and added subject-matter (Article 100(c) EPC).
- III. During the proceedings before the opposition division, the patent proprietor requested that the opposition be rejected and that the patent be maintained as granted.
- IV. The documents cited during the proceedings before the opposition division and the board of appeal include the following:

D2 Hirano et al. (1990), Immunology Today 11(12),
443-449

D3 Ogata et al. (1999), Rinsho Byouri 47(4), 321-326

and its English translation D3A

- D6 EP 0409607
- D25 Ohta et al. (1991), Archives of Dermatological Research 283, 351-356
- D38 Turksen et al. (1992), Proc. Natl. Acad. Sci. USA 89, 5068-5072
- D42 Shinkura et al. (1998), Anticancer Research 18, 1217-1222
- D46 Schoen M.P. (1999), The Journal of Investigative Dermatology 112, 405-410
- D48 Takematsu et al. (1994), The Tohoku Journal of Experimental Medicine 172, 243-252
- D52 Gillitzer et al. (1991), J. Invest. Dermatol. 97, 73-79
- D53 Lemster et al. (1995), Clin. Exp. Immunol. 99, 148-154
- D58 Yoshizaki et al. (1998), Springer Seminars in Immunopathology 20, 247-259

V. By its decision pronounced at oral proceedings on 6 July 2010 and posted on 30 July 2010, the opposition division revoked the patent under Article 101(2), (3) (b) EPC.

The opposition division decided that the claims as granted met the requirements of Article 123(2) EPC, Article 54 EPC and Article 83 EPC, but not those of Article 56 EPC.

VI. The patent proprietor (appellant) lodged an appeal against that decision. With the statement of the grounds of appeal, the appellant requested that the decision of the opposition division be set aside and that the patent be maintained as granted. New documents numbered D49 to D53 were submitted.

VII. With its letter of reply to the grounds of appeal, the opponent (respondent) requested to dismiss the appeal and submitted new documents numbered D54 to D60.

VIII. In reaction to the respondent's letter, the appellant filed further submissions and requested that documents D56, D57 and D59 be not admitted into the proceedings.

IX. A summons for oral proceedings was issued by the board without accompanying communication.

X. With a letter sent "in response to the Summons to attend oral proceedings", the appellant submitted further arguments and new documents: D61 (in Japanese) and its translation into English D61a, and D62. With a further letter, the appellant submitted a corrected page 6 of the translation of the description as filed.

XI. Oral proceedings before the board took place on 26 February 2015 as scheduled.

XII. The appellant's submissions may be summarised as follows:

Document D3 did not provide any evidence of a role of IL-6 in psoriasis, and actually only stated that IL-6 was thought to contribute to the disease. The skilled person would thus not consider that IL-6 was causative of psoriasis, and even if the skilled person did assume this, it would not be prompted to use antibodies against IL-6 receptor as therapy for psoriasis because he would be aware of the fact that IL-6 receptor is not expressed in psoriatic skin (D25, page 353, right column). The in vivo experiments with IL-6 transgenic mice also showed that overexpression of IL-6 did not cause psoriasis (D38, page 5070, right column, and page

5071, discussion, right column, penultimate paragraph). D48, D52 and D53 taught that other cytokines had a more important role than IL-6 in psoriasis. D3 on the other hand made it clear that the cytokine network was important, and thus that other cytokines would compensate for a lack of IL-6 (page 3, first paragraph, of D3A). D3 did not specifically teach targeting IL-6 receptor in psoriasis but instead in other diseases, namely Castleman's disease, rheumatoid arthritis and myeloma; these diseases were known to express IL-6 receptor (e.g. D58, page 248, second sentence from bottom, and page 250, second paragraph from bottom), which was not the case for psoriasis, and they did not belong to the same group of diseases as psoriasis (D2, box 1). In addition, there were a number of alternative approaches, including the use of anti-IL-6 antibodies rather than anti-IL-6-receptor antibodies. D42 did not mention psoriasis at all, but only those diseases for which the presence of IL-6 receptor at the target site had been demonstrated. Clearly if the target antigen was not present, then the skilled person could not expect to achieve an effect with antibodies directed thereto.

XIII. The respondent's arguments may be summarised as follows:

Document D3 was the closest prior art and concerned IL-6 related disorders, among which psoriasis. In its last paragraph, it provided a clear incentive to use anti-IL-6 receptor antibodies for treatment of IL-6 related disorders. It was thus obvious to try with a reasonable expectation of success. D6 on the other hand provided antagonistic antibodies directed against the IL-6 receptor; these were also disclosed in D42 and in paragraph [0020] of the patent. D3 clearly stated that

IL-6 played an important role in psoriasis, e.g. in section VI. Like D3, D42 suggested that antibodies against IL-6 receptor were effective for IL-6 related diseases (e.g. page 1220, last paragraph of discussion), and D2 also listed psoriasis among the IL-6 related diseases (box 1 on page 444). As regards D25, it did not conclude that there was no involvement of IL-6 in psoriasis; to the contrary, it showed that there was IL-6 expression in the transition zone, i.e. in the zone where the lesions are formed (page 353, right column; abstract, second last sentence; page 355, left column, second paragraph). Even if a membrane-bound IL-6 receptor could not be identified in the diseased skin, it was known in the art that IL-6 can also signal through a soluble receptor, as acknowledged in D3 (page 2, section II, line 14, of D3A). In any case, the teachings of D25 would have been taken into consideration by the authors of D3, which was published 8 years later.

XIV. The appellant requested that the decision under appeal be set aside and that the patent be maintained as granted, with corrected page 6 of the description as submitted with letter of 24 February 2015. Moreover the appellant requested that documents D56, D57 and D59 be not admitted into the proceedings.

XV. The respondent requested to dismiss the appeal. It further requested that the admissibility of the appellant's latest submissions be discussed, and that the appellant's request to correct the description of the granted patent be dismissed.

Reasons for the Decision

1. The appeal is admissible.
2. Admissibility of late-filed documents
 - 2.1 The appellant requested that documents D56, D57 and D59 be not admitted into the proceedings. Similarly, the respondent requested that the admissibility of the appellant's latest submissions, which included new documents D61/D61a and D62, be discussed. In view of the fact that the present decision does not rely on any of these late-filed documents, a decision was not taken concerning their admissibility.
 - 2.2 The respondent also requested that the appellant's request for correction of page 6 of the description's translation be dismissed. In view of the outcome of the present appeal, there was however no need to address this issue.
3. Added subject-matter, novelty, sufficiency of disclosure
 - 3.1 During appeal, the respondent maintained all the objections which had already been raised in the notice of opposition.
 - 3.2 However, in view of the conclusions reached under Article 56 EPC, the board does not find it necessary to decide upon the further outstanding issues.
4. Inventive step
 - 4.1 It is established practice in proceedings before the EPO that inventive step is assessed according to the

problem-solution-approach, which involves the determination of the closest prior art document, the formulation of the problem to be solved in view of the closest prior art document and its solution. According to established case law the closest prior art document is a disclosure providing the most promising springboard towards the claimed invention; this is normally a document disclosing subject-matter conceived for the same purpose or aiming at the same objective as the claimed invention.

- 4.2 Granted claim 1 is in the form of a Swiss-type medical use claim, the therapeutical agent being "an anti-interleukin-6 (IL-6) receptor antibody that can block the binding of IL-6 to IL-6 receptor" and the therapeutical indication being psoriasis. The purpose of the invention as claimed is thus the treatment of psoriasis. The closest prior art should accordingly also be a disclosure directed to the treatment of psoriasis.
- 4.3 Document D3, which was considered by both the appellant and the respondent to represent the closest prior art, is a review on IL-6 and its clinical applications. On section VI of D3A - the English translation of D3 (Japanese) -, plaque psoriasis is listed among other diseases for which IL-6 is considered to play a role (see also Table 3 of D3), and D3A concludes by stating in its last sentence that "anti-IL-6-receptor antibody therapy can be expected to offer very efficacious treatment for disorders in which the role of IL-6 is important". D3/D3A clearly refers to treatment of IL-6 related disorders, and thus it is a promising springboard towards the invention.

- 4.4 The difference to the claimed subject-matter is thus that treatment of psoriasis is not specifically mentioned, nor is the use of anti-IL-6 receptor antibodies that block the binding of IL-6 to IL-6 receptor disclosed. The technical problem can thus be formulated as the provision of an IL-6 based treatment for psoriasis, which is consistent with the technical problem as formulated in the patent (see e.g. paragraphs [0010] and [0011]).
- 4.5 According to claim 1, the solution is the use of anti-IL-6 receptor antibodies that block the binding of IL-6 to IL-6 receptor. Since the Working Example of the patent in suit shows that administration of a blocking anti-IL-6- receptor antibody to mice results in a reduction of psoriasis-like lesions (Table 1), the board is satisfied that the problem has been plausibly solved by the claimed subject-matter. It thus has to be determined whether or not the skilled person would arrive at the claimed solution in an obvious way.
- 4.6 The board considers that from D3 alone the skilled person would be motivated to test anti-IL-6 receptor antibodies not only in those diseases which are specifically mentioned in section VIII of D3 (multiple myeloma, Castleman's disease and rheumatoid arthritis), but also in other IL-6 related disorders, including psoriasis. D3 teaches (section VI) that, out of three main patterns of contribution of IL-6 to disease, two are present in psoriasis: in the first type, IL-6 acts locally as a cell growth factor, and in the second type, IL-6 acts as a mediator of inflammation. The first mechanism is seen also in myeloma and in Castleman's disease, while the second mechanism is also present in rheumatoid arthritis and Castleman's disease. In view of the teaching of D3 (section VIII),

reporting positive results for the therapeutic use of anti-IL-6-receptor antibodies in multiple myeloma, Castleman's disease and rheumatoid arthritis, the skilled person would have a reasonable expectation of success when considering the same therapy for psoriasis, which was known to share IL-6 mediated pathogenic mechanisms with these diseases (supra).

4.7 The board cannot follow the appellant's arguments that the skilled person would not derive from the prior art that the IL-6 receptor was a promising therapeutic target in psoriasis. These arguments were mostly based on the observations that the IL-6 receptor was not found in psoriatic skin (D25), that IL-6 transgenic mice did not develop psoriasis (D38), and that other cytokines were shown to have a more important role in psoriasis than IL-6 (D48, D52, D53). The board notes that all the above cited documents were published years earlier than D3 and still their teachings did not prevent the authors of D3 from considering that psoriasis was an IL-6 related disorder and thus a priori susceptible of treatment by blocking of IL-6 signalling. Contrary to Appellant's arguments, these documents actually provide further evidence for the involvement of IL-6 signalling in psoriasis: even if they do not identify it as the causative agent, they certainly confirm that it plays a role (and an important one) in psoriasis. This would be sufficient to justify a legitimate expectation that blocking of IL-6 signalling would have a therapeutical effect for psoriasis, even if not a curative one.

4.8 D3 suggests anti-IL-6-receptor antibodies as agents that can be therapeutically used in IL-6-related disorders. While D3 does not specify that the antibodies to be used are those that "can block the

binding of IL-6 to IL-6 receptor", it is however obvious for the skilled person that, in order to achieve a therapeutic effect in disorders wherein IL-6 has a role, the signalling of IL-6 should be inhibited: for anti-IL-6-receptor antibodies this usually means that they should block the binding of IL-6 to its receptor. Indeed such antibodies and their use in therapy had already been disclosed (e.g. D6, D42).

- 4.9 The appellant further argued that the skilled person would have a number of other alternative therapeutic targets from which to choose and would not consider using anti-IL-6 receptor antibodies because the IL-6 receptor was not present in the psoriatic skin (D25). The board notes that, while other therapeutic targets might have been possible, targeting of IL-6 signalling was nevertheless one of the strong candidate strategies in view of the whole body of prior art on IL-6 involvement in psoriasis and of the existing evidence that such therapy was successful in other IL-6 related diseases (see above). D25 itself identifies IL-6 and IL-1 as two of the cytokines which were known to be implicated in the pathological processes of the epidermis which lead to psoriasis, and concludes that "IL-6 and IL-6R expression correlate well with the lesion-forming process in psoriasis in which IL-1 may initiate expression of the mRNA." (D25, last paragraph). The fact that the IL-6 receptor was only weakly detectable by immunochemistry in the psoriatic lesions is not interpreted in D25 as a sign of non-involvement of the IL-6 receptor in psoriasis; to the contrary, D25 hypothesises that "[e]xternal stimuli applied to the skin can stimulate IL-6 production and IL-6R receives IL-6 to initiate psoriatic epidermal proliferation" (page 355, left column, third paragraph). Blocking of IL-6 binding to its receptor -

e.g. by means of anti-IL-6-receptor antibodies - thus presents itself as a plausible therapeutic strategy with a reasonable expectation of success.

- 4.10 This expectation would not be reduced by the presumption that other cytokines of the network might exert a compensatory effect, since the same therapeutical strategy had already been used with success for other IL-6 related disorders, wherein these compensation mechanisms would presumably take place as well. D3 itself discusses this cytokine functional redundancy (section III) and nevertheless suggests therapy directed at blocking IL-6 signalling.
- 4.11 In summary, the board concludes that the skilled person would be prompted by D3 to test anti-IL-6 receptor antibodies for the therapy of IL-6-related disorders, which include psoriasis, and would consider this suggestion of D3 to be solidly backed up by the findings of the prior art wherein a role of IL-6 in psoriasis had been established. Moreover the skilled person would have all the tools to proceed, since animal models for psoriasis were available (e.g. D46) as were antagonistic antibodies, which had also already been successfully tested as therapeutics for other diseases (e.g. D6, D42).
- 4.12 The board thus comes to the conclusion that the claimed subject-matter does not fulfil the requirements of Article 56 EPC.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chairman:



N. Maslin

U. Oswald

Decision electronically authenticated