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Datasheet for the decision of 9 February 2018

Case Number: T 1317/13 - 3.3.04

Application Number: 08760116.7

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New indications for anti-IL-I-beta therapy

Applicant:
Novartis AG

Headword:
anti-IL-1β therapy/NOVARTIS

Relevant legal provisions:
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T 0021/81

Catchword:

-

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Case Number: T 1317/13 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 9 February 2018

Appellant: (Applicant)	Novartis AG Lichtstrasse 35 4056 Basel (CH)
Representative:	Carpmaels & Ransford LLP One Southampton Row London WC1B 5HA (GB)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 3 January 2013 refusing European patent application No. 08760116.7 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairwoman	G. Alt
Members:	B. Claes
	L. Bühler

Summary of Facts and Submissions

I. The appeal lies from the decision of the examining division to refuse European patent application No. 08 760 116.7, which was published as international patent application WO2008/145664, having the title "*New indications for Anti-IL-1-beta therapy*".

II. The examining division held in the decision under appeal that the subject-matter of claim 1 of the sole (main) request, filed during the oral proceedings on 10 October 2012, did not involve an inventive step (Article 56 EPC).

Claim 1 of the main request read:

"1. A medicament for use in the treatment of an auto-inflammatory syndrome in a patient in need thereof, the medicament comprising a human IL-1 beta binding antibody, the antibody comprising:

a first domain having an amino acid sequence as shown in SEQ ID NO:1 and a second domain having an amino acid sequence as shown in SEQ ID NO:2, wherein said auto-inflammatory syndrome is gout, gouty arthritis or pseudogout."

III. With the statement of grounds of appeal the patent proprietor (hereinafter "appellant") re-submitted the main request, submitted an auxiliary request and requested that the decision under appeal be set aside.

IV. 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 claim 1 of the main and of the auxiliary request lacked an inventive step (Article 56 EPC).

V. In response to the communication of the board, the appellant with a letter dated 9 January 2018 submitted three auxiliary requests and withdrew the auxiliary request filed with the statement of grounds of appeal. It also submitted observations in reply to the board's observations in its communication.

Claim 1 of the 1st auxiliary request read:

"1. A medicament for use in the treatment of an auto-inflammatory syndrome in a patient in need thereof, the medicament comprising a human IL-1 beta binding antibody as the sole active ingredient, the antibody comprising:

a first domain having an amino acid sequence as shown in SEQ ID NO:1 and a second domain having an amino acid sequence as shown in SEQ ID NO:2, wherein said auto-inflammatory syndrome is gout, gouty arthritis or pseudogout." (emphasis added by the board)

Claim 1 of the 2nd auxiliary request read:

"1. A medicament for use in the treatment of an auto-inflammatory syndrome in a patient in need thereof, the medicament comprising a human IL-1 beta binding antibody, the antibody comprising:

a first domain having an amino acid sequence as shown in SEQ ID NO:1 and a second domain having an amino acid sequence as shown in SEQ ID NO:2, wherein said auto-inflammatory syndrome is gout, gouty arthritis or pseudogout, and wherein said antibody is administered

once every week or less frequently." (emphasis added by the board)

Claim 1 of the 3rd auxiliary request read:

"1. A medicament for use in the treatment of an auto-inflammatory syndrome in a patient in need thereof, the medicament comprising a human IL-1 beta binding antibody, the antibody comprising:

a first domain having an amino acid sequence as shown in SEQ ID NO:1 and a second domain having an amino acid sequence as shown in SEQ ID NO:2, wherein said auto-inflammatory syndrome is gout, gouty arthritis or pseudogout, and wherein said antibody is administered once every month or less frequently." (emphasis added by the board)

VI. Oral proceedings took place on 9 February 2018, and at the end of these the chair announced the board's decision.

VII. The following documents are mentioned in the present decision:

D1: WO2007/050607

D2: So *et al.* (2007), Arthritis Research & Therapy, 9:R28, pages 1-6.

D5: Martinon *et al.* (2006), Nature, Vol. 440, No. 9, pages 237-241.

D7: Chen *et al.* (2006), J. Clin. Invest., Vol. 116, No. 8, pages 2262-2271.

D8: Data slides on ACZ885

D9: Schlesinger *at al.* (2011), Arthritis Research & Therapy, 13:R53, pages 1-13.

D12: Cronstein & Terkeltaub (2006), Arthritis Research & Therapy, 8(suppl 1):DS3, pages 1-7.

D13: Terkeltaub (2003), The New England J. Medicine, Vol. 349, pages 1647-1655.

D15: Hoffman *et al* (2004), Lancet, Vol. 364(9447), pages 1779-1785.

D16: Hawkins *et al*. (N. Engl. J. Med., Vol. 348, pages 2583-2584.

D17: Clinical trials register for NCT00663169, version 21st April 2008.

D18: Roseff *et al.* (1987), J. Rheumatol., Vol. 14, No. 5, pages 974-977 (abstract PubMed PMID:2448456).

D19: So *et al*. (2010), Arthrit. Rheum., Vol. 62, pages 3064-76.

D20: Dumont (2006), Expert Opinion on Therapeutic Patents Vol. 16, No. 7, pages 879-912.

VIII. The appellant's arguments in relation to inventive step (Article 56 EPC) of the subject-matter of claim 1 of the respective requests can be summarised as follows:

Main request - claim 1

Document D5 represented the closest prior art. The claimed invention differed from the disclosure therein by the use of the human anti-interleukin (IL)-1β monoclonal antibody ACZ885 (also known as "canakinumab", disclosed in document D1) as the medicament instead of colchicine for the treatment of gout, gouty arthritis and pseudogout. (In the following the three disorders will be generally referred to as "gout".)

Colchicine was known to be toxic to patients and was therefore administered initially in hourly doses of 0.6 mg until nausea, diarrhoea or vomiting occurred, followed by daily dosing (see e.g. document D12, Table 1 and page 6, left-hand column, lines 40 to 46; and right-hand column, lines 4 to 8).

From the application the skilled person could derive explicitly or implicitly three improvements of the therapy with the antibody ACZ885 over that with colchicine.

ACZ885 had a long duration of action. Example 3 disclosed that administration of ACZ885 to humans suffering from Muckle Wells syndrome (MWS; characterised by mutations in the NALP3 protein) at a dose of 10mg/kg led to the alleviation of clinical symptoms (e.g. skin rash, muscle pain, fever and fatigue) and the lowering of the levels of two acute phase proteins, serum amyloid protein (SAA) and c-

reactive protein (CRP). Elevated levels of body temperature and of SAA and CRP were considered as biomarkers for gout (see document D18). Symptom remission lasted for at least 134 days in the treated patients. From the application it was thus explicitly apparent that ACZ885 could be administered less often than colchicine, i.e. every few weeks rather than every hour (see document D12, table 1).

ACZ885 was safe and thus not toxic. Example 3 assessed *inter alia* the safety of ACZ885 in humans suffering from MWS and did not mention any negative effect or toxic side-effects in the human patients for at least 134 days. ACZ885 was later confirmed as a well-tolerated medicine in human gout patients (e.g. see document D9).

ACZ885 provided pain relief. Rapid pain relief was a priority in gout therapy (see document D9, page 9, left-hand column, lines 41 to 43; and document D13, page 1649, left-hand column, lines 2 to 4). The application disclosed that IL-1β was involved in pain perception and amplified neurogenic signals, and thus suggested the usefulness of ACZ885 in various pain conditions (see page 2, lines 7 to 12). Therefore, whereas colchicine and ACZ885 both relieved pain by inhibiting its cause (i.e. the inflammatory aspects of gout due to uric acid crystals), it could be derived from the application that ACZ885 additionally provided indirect pain relief by interfering with pain perception pathways.

The data from human clinical trials in documents D8, D9 (both being available to the skilled person after the relevant date of the present application) and document D1 confirmed that the antibody ACZ885 provided a better

gout therapy than colchicine, offering reduced toxicity and prolonged efficacy as well as an effect on pain perception. Also the disclosures in documents D17 to D19 (also both being available to the skilled person after the relevant date of the present application) confirmed the efficacy of the antibody ACZ885 in treating gout.

Based on these advantages over the therapy of gout with colchicine, the problem to be solved by the claimed invention was the provision of an improved medicament for the therapy of gout in a patient.

Document D5, in particular the passage on page 240, left-hand column, lines 10 to 24, contained the following passage in lines 19 to 24 relied on by the board in its communication: "*Importantly, inflammation in hereditary periodic fevers patients with mutations in NALP3 can be markedly improved by treatments designated to block IL-1ß*[20,21]*. Owing to the similarity between NALP3-mediated hereditary periodic fevers and gout and pseudogout, we can anticipate that similar treatments could benefit gout and pseudogout patient*" (emphasis added). It did not suggest to the skilled person to treat gout in patients by blocking specifically IL-1β because (i) there was no technical basis for interpreting document D5 so as to focus on IL-1β in particular, and (ii) administering the antibody ACZ885, i.e. an antibody blocking IL-1β, was not a treatment "*similar*" to the treatments alluded to in the passage.

Firstly, as to point (i) above, the prior art implicated both isoforms of IL-1, i.e. IL-1α and IL-1β, which both bind to the IL-1 receptor, in the blocking of the IL-1 receptor to effectively inhibiting gouty

inflammation. Indeed, although document D5 referred in the passage cited above to "*treatments designated to block IL-1β*[20,21]", neither of the cited references 20 or 21 (documents D15 and D16 in these proceedings, respectively) disclosed in fact specifically blocking the β-subunit of IL-1, as they both concerned the use of "*IL-1Ra*", also referred to as "Kineret", i.e. a recombinant form of the natural IL-1 receptor antagonist which blocked the IL-1 receptor's ability to bind both IL-1α and IL-1β, thereby thus inhibiting both ligands. Document D5 did not therefore suggest to the skilled person to block IL-1β. Rather an objective reading would suggest using an antagonist of the IL-1 receptor.

Moreover, the skilled person was taught in document D7 that, although a mixture of anti-IL-1α and anti-IL-1β antibodies caused a significant reduction in the mono-sodium urate (MSU) crystal inflammatory response in a mouse gout model, this reduction in acute inflammation was not as great as that observed in IL-1 receptor-deficient mice. This was explained by the fact that, presumably the mixed antibody treatment did not neutralise IL-1 completely (see page 2265, left-hand column, lines 7 to 14). Accordingly, the skilled person would learn from document D7 that blocking IL-1β alone would not prevent receptor activation. Thus, also in the light of document D7 the skilled person would prefer blocking the IL-1 receptor.

Secondly, as to point (ii) above, ACZ885 was an antibody specific for soluble IL-1β, whereas Kineret was a recombinant cytokine which targeted the IL-1 (transmembrane) receptor and thus blocked the activity of both IL-1α and IL-1β. Example 3 of the application taught that a single infusion of ACZ885 relieved

symptoms for at least 134 days, whereas Kineret had a short *in vivo* duration of action and required daily injection {see e.g. abstract of document D2 and document D16). Therefore the use of ACZ885 was not a treatment "*similar*" to the ones suggested by document D5 in the passage on page 240 - as the function, structure and duration of action of ACZ885 were very different from Kineret.

Hence, on an objective reading, document D5 actually suggested to the skilled person to use an antagonist of the IL-1 receptor (such as Kineret, i.e. "*similar treatments*") rather than an antagonist of IL-1β such as an anti-IL-1β antibody (such as the antibody ACZ885).

Furthermore, nothing prompted the skilled person to look to ACZ885 in the expectation of providing an improvement in the treatment of pain associated with gout. None of the cited prior art, in particular documents D1 and D5, reported the effect of an anti-IL-1β antibody on pain perception. The effect of robust pain reduction by ACZ885 was demonstrated after the relevant date in document D9 (see e.g. page 9, left-hand column, lines 41 to 47) and was reported to be in contrast to reductions reported for another inhibitor of IL-1β signalling which failed to demonstrate significant improvements in pain in patients with gouty arthritis (see page 9, right-hand column, lines 34 to 39).

The present situation did not match the "bonus effect" case law. If there had been prior art directly suggesting that ACZ885 was useful for treating gout, the effect on pain perception might be seen as a "bonus". However there was no such prior art. As already observed, document D5 suggested that treatments

"*similar*" to those with Kineret might be useful for gout therapy, but ACZ885 was not "*similar*" to Kineret. Arguments about a "bonus effect" were often used when there was effectively a "one-way-street" situation in which the skilled person was inevitably guided towards a particular destination, such that any surprising effects would be a "bonus" which would have been achieved anyway. Here, there was no such one-way-street situation, since document D20 described various different approaches for inhibiting the IL-1 system (see section 4) which were summarised in Table 3. A skilled person following the suggestion in document D5 to test "*similar treatments*" to Kineret might choose other molecules in the same class in Table 3 (i.e. synthetic receptor antagonists or anti-IL-1 receptor antibodies).

The claimed subject-matter accordingly involved an inventive step.

Auxiliary requests

Prior art gout treatments were typically combination therapies. For example, document D21 disclosed that a combination of colchicine with non-steroidal, anti-inflammatory drugs (NSAID) was in fact the third most common combination. In contrast, ACZ885 was used as a monotherapy for treating gout. The ability of ACZ885 to provide gout therapy, even when given on its own, was a further contribution which underpinned the inventive step of the subject-matter of the claims of the first auxiliary request.

The second and third auxiliary request specified that ACZ885 was administered "once every week or less frequently" or "once every month or less frequently".

Based on the disclosure in Example 3 which noted remission of symptoms after ACZ885 administration for "*at least 134 days*", the problem to be solved *vis-à-vis* document D5, which disclosed daily dosing, was therefore also related to the additional improvement of providing less, or even much less, frequent dosing. The use of ACZ885 to solve this problem in gout therapy was not obvious.

IX. The appellant requested that the decision under appeal be set aside and that the case be remitted to the examining division with the order to grant a patent on the basis of the set of claims of the main request filed with the statement of grounds of appeal, or alternatively on the basis of the set of claims of one of the 1st to 3rd auxiliary requests filed with the letter dated 9 January 2018.

Reasons for the Decision

1. The appeal is admissible.

2. The sole issue decided by the board in this appeal is whether or not the subject-matter of claim 1 of the main request and of the auxiliary requests involves an inventive step (Article 56 EPC).

Main request - claim 1

3. The claimed subject-matter (see section II) is a medicament for use in the treatment of auto-inflammatory syndromes, namely gout, gouty arthritis or pseudogout (for the ease of reading the three disorders will in the following be referred to as "gout"). The medicament is defined as comprising a human interleukin (IL)-1β binding antibody characterised by comprising a

first and second domain defined by particular amino acid sequences. The anti-human IL-1β monoclonal antibody ACZ885, an example of an antibody falling under this definition, was used in the examples of the application. The antibody ACZ885 was known to the skilled person from the disclosure in document D1.

Closest prior art

4. A frequently applied line of therapy for treating patients suffering from auto-inflammatory diseases such as gout at the priority date of the application was the oral administration of colchicine. This treatment is in particular able to resolve the initial inflammatory phase of gout but was also known to be poorly tolerated because of predictable gastrointestinal side-effects (see e.g. document D5, page 238, right-hand column, lines 15 to 17; page 239, right-hand column, lines 10 to 12, and document D12, e.g. abstract, last sentence, and Table 1, final part).

5. The appellant agreed with the board and the examining division that document D5, disclosing *inter alia* the colchicine standard therapy of gout (see point 4), represented the closest prior art for the assessment of inventive step for the claimed subject-matter.

The problem to be solved

6. Instead of administering colchicine for treating patients suffering from gout, the claimed invention provides for the administration of antibodies which bind to IL-1β, such as the specific antibody "ACZ885".

7. The appellant argued that the application explicitly or implicitly taught that the technical effect of the

different treatment consisted in three improvements over the therapy with colchicine. Firstly, it was derivable from example 3 that ACZ885 had a long duration of action and could therefore be administered once every few weeks, rather than every hour as was the case with the therapy with colchicine. Secondly, example 3, which assessed *inter* alia the safety of ACZ885 in humans, was silent on negative effects of the administration for a time span of at least 134 days. Finally and thirdly, based on the knowledge that IL-1β was involved in pain perception and amplified neurogenic signals, the application disclosed the usefulness of ACZ885 in various pain conditions. Therefore, whereas colchicine and ACZ885 both relieved pain by inhibiting its cause (i.e. the inflammatory aspects of gout due to uric acid crystals), ACZ885 additionally provided indirect pain relief by interfering with pain perception pathways.

8. The appellant accordingly held that the technical problem to be solved by the claimed invention was the provision of an *improved* medicament, as compared to colchicine, for the treatment of gout, gouty arthritis and pseudogout in a patient.

9. The board can concur with the formulation of this problem and is satisfied that in view of the disclosure in example 3 this problem is solved by the claimed invention. Therefore, it is to be determined whether the skilled person, starting from the known colchicine-based treatment and addressing the problem to be solved, would have arrived at implementing the claimed invention in an obvious manner.

Obviousness

10. Document D5, i.e. the document representing the closest prior art, provides insight into the molecular mechanisms underlying the chronic inflammatory responses induced by the deposition of monosodium urate (MSU) and calcium pyrophosphate dihydrate (CPPD) crystals in joints and periarticular tissues, typical of gout. Both crystals were found to engage the caspase-1-activating NALP3 inflammasome, resulting in the processing and production of active IL-1β. These findings in the context of gout were considered to support the known pivotal role of the inflammasome also in several auto-inflammatory diseases (see abstract, last sentence) and to confirm that "*Increased production of IL-1β was the cause of several auto-inflammatory diseases, providing clear evidence for a pivotal role of this cytokine in triggering auto-inflammation*" (see page 237, left-hand column, lines 7 to 10). Document D5 refers in this context in particular to familial auto-inflammatory diseases such as Muckle-Wells syndrome, familial cold auto-inflammatory syndrome, chronic infantile neurologic cutaneous and articular syndrome and hereditary periodic fevers in which particular mutations in the NALP3 inflammasome protein itself lead to a constitutive processing and resultant production of active IL-1β (see page 240, left-hand column, lines 10 to 21).

11. The board considers document D5 to be of particular further interest for a skilled person searching to identify and validate targets for treatments of gout with a view to solving the objective problem. In particular document D5 contains a report on the disclosure in the prior art of the observation that

pre-treatment of experimental animal models of gout with intravenous colchicine (the therapeutic compound known in the prior art for treatment of gout, see point 4 above) before intra-articular MSU crystal injections greatly reduced crystal-induced inflammation, and the observation of the authors of document D5 that pre-treatment with colchicine completely blocked *in vitro* the processing and production of IL-1β (see passage on page 238, right-hand column, line 15 to page 239, left-hand column, line 2 and page 239, right hand column, lines 9 to 11). Of similar further interest is the reference in document D5 to knowledge of the person skilled in the art that "[i]*mportantly, inflammation in hereditary periodic fevers patients with mutations in NALP3 can be markedly improved by treatments designated to block IL-1β[20,21]. Owing to the similarity between NALP3-mediated hereditary periodic fevers and gout and pseudogout, we can anticipate that similar treatments could benefit gout and pseudogout patients.*" (see page 240, left-hand column, lines 19 to 24; emphasis added).

12. In summary, the board is satisfied that document D5 teaches the skilled person that: (i) increased production of IL-1β is the trigger for the auto-inflammation in gout as in other auto-inflammatory diseases; (ii) administration of colchicine completely blocks the crystal-induced production of IL-1β and leads to greatly reduced inflammation and, (iii) gout patients were anticipated to benefit from treatments designated to block IL-1β.

13. The board therefore concludes that document D5 itself suggests to the skilled person the treatment of gout by blocking IL-1β.

14. Document D1 is an international patent application published shortly before the priority date of the present application. The applications have two inventors in common. The disclosure content of document D1 is largely identical to that of the latter, and in particular, all three examples are identical. The complete experimental disclosure of the application as filed was thus already known to the skilled person.

15. Document D1 discloses compounds suitable for blocking IL-1ß in patients suffering in general from auto-inflammatory syndromes, in particular also the ACZ885 antibody as an embodiment of the antibodies defined in claim 1. Like example 3 of the application, example 3 of document D1 discloses that administration of the ACZ885 antibody to patients suffering from Muckle Wells syndrome, i.e. an auto-inflammatory syndrome characterised by particular NALP3 mutations (see point 10), leads to the alleviation in these patients of particular clinical symptoms, such as elevated body temperature and the levels of two acute phase proteins, serum amyloid protein (SAA) and c-reactive protein (CRP). These clinical symptoms were argued by the appellant to constitute accepted biomarkers for gout (see also document D18). Accordingly, document D1 provides the skilled person straightforwardly with the monoclonal antibody for blocking IL-1ß.

16. The board is thus satisfied, in view of the prior knowledge of the skilled person from the disclosure of document D5, the tools disclosed in document D1 and the experimental results in example 3 of the same document, that the skilled person at the priority date of the application would have administered the anti-IL-1β antibody ACZ885 for the treatment of gout.

17. The board considers furthermore that the skilled person would also have administered the medicament, here the antibody ACZ885, as disclosed in document D1 for solving the above-formulated more ambitious problem of providing an improved medicament, as formulated by the appellant (see point 8 above), at least in view of the two first envisaged improvements over the treatment of gout with colchicine as put forward by the appellant, which are both derivable from the application, i.e. the substantially longer duration of activity and the absence of toxic side-effects, over the treatment of gout by colchicine. Indeed, these advantages are obviously also derivable from the identical example 3 in document D1.

18. The appellant has argued that on an objective reading of document D5 - in particular in the light of the disclosures in documents D7, D15 and D16 (the latter being references 20 and 21 in document D5) - the skilled person would aim at blocking the IL-1 receptor, rather than IL-lß. It was submitted that document D5 did not focus on IL-lβ in particular. The reference to "*similar treatment*" in the passage on page 240, left-hand column, lines 10 to 24, contains in particular the passage in lines 19 to 24: *"Importantly, inflammation in hereditary periodic fevers patients with mutations in NALP3 can be markedly improved by treatments designated to block IL-lß[20,21]. Owing to the similarity between NALP3-mediated hereditary periodic fevers and gout and pseudogout, we can anticipate that similar treatments could benefit gout and pseudogout patients".* Whereas document D5 referred in the passage cited above to "*treatments designated to block IL-lβ[20,21]*", these did not relate to the blocking of IL-lβ by an antibody since the cited reference documents D15 and D16 (numbering in the present proceedings) in fact

concerned the blocking of "IL-1Ra", i.e. a recombinant form of the natural IL-1 receptor antagonist known as "Kineret", thus blocking the IL-1 receptor's ability to bind both IL-1α and IL-1β, which had also been demonstrated in document D7 as being required to obtain a significant reduction in the monosodium urate (MSU) crystal inflammatory response in an IL-1 receptor-deficient mice model.

19. The board however refers in this context to point 12 above and in particular to the disclosure in document D5 that administration of colchicine completely blocks the crystal-induced production of IL-1β in the experimental system used and leads to greatly reduced inflammation. The board is satisfied that this correlation anticipated by the authors of document D5 is not related to the activity of the receptor of IL-1β, but rather related to the biological availability of IL-1β itself. Indeed the board considers that the reference to the disclosures in documents D15 and D16 constitutes proof of concept rather than a "teaching away" from the general suggestion in document D5 of treating gout with "*similar treatments*" that constitute blocking IL-1β. The board judges therefore that, even when taking the considerations referred to by the appellant into account, the skilled person is taught straightforwardly by document D5 that blocking the biological availability (activity) of IL-1β as such would lead to a greatly reduced inflammation, which can be considered to represent a relief of symptoms in gout, i.e. a treatment for gout.

20. The appellant further argued that anti-IL-1β antibodies had an additional effect on pain perception which was not reported in any of the cited prior art, in

particular not in documents D1 and D5, which was however an effect which was indeed achieved by the antibody ACZ885 as demonstrated by the results in the post-published document D9. This extra effect was thus unexpected, and the claimed subject-matter should be held to be non-obvious for that reason.

21. It has been held by the boards of appeal in relation to unexpected effects in the context of the assessment of inventive step that if, "*having regard to the state of the art, it would already have been obvious for the skilled person to arrive at something falling within the terms of a claim, because an advantageous effect could be expected to result from the combination of teachings of the prior art documents, such claim lacks inventive step, irrespective of the circumstance that an extra effect (possibly unforeseen) was obtained*" (see decision T 21/81, OJ EPO 1983, page 15 *ff.*, Reasons 6; confirmed later, see Case Law of the Boards of Appeal, 2016, I.D.10.8 and the decisions cited therein).

22. The board considers that the present situation matches the one described in this case law. In fact, it has come to the conclusion that, having regard to the available prior art, the skilled person would implement the administration of ACZ885 for the treatment of gout in an obvious manner (see point 12 above). In this context therefore, the effect on pain perception, even if it may be an extra effect and may be unforeseen when implementing the treatment, is not an effect which contributes to the non-obviousness of the claimed treatment. Thus, the appellant's argument does not convince the board.

23. In the context of extra effects, the appellant has further submitted that "*arguments about a 'bonus effect' were often used when there was effectively a 'one-way-street' situation*", which according to the appellant was a situation "*in which the skilled person was inevitably guided towards a particular destination, such that any surprising effects would be a 'bonus' which would have been achieved anyway*." However, the present situation was not a one-way-street situation since document D20 described various different approaches to inhibiting the IL-1 system.

24. This argument does not convince the board to change its conclusion in point 22 above either. In fact, decision T 21/81, *supra*, considers a situation in which it was already obvious that the skilled person would arrive at something falling within the terms of a claim, because an advantageous effect was expected to result from the combination of teachings of the prior art documents, resulting in a situation in which an extra effect cannot establish inventive step. Accordingly, a "one-way-street" situation in the sense defined by the appellant cannot be inferred as a mandatory prerequisite for the principle established in this decision.

25. Thus, the effect of ACZ885 on pain perception cannot be considered an unexpected effect and thus cannot support the presence of an inventive step.

26. In view of all the considerations above, the board concludes that the skilled person would have arrived at the subject-matter of claim 1 of the main request in an obvious way. Therefore, this subject-matter lacks an inventive step.

1st to 3rd auxiliary requests - claim 1

27. In relation to the 1st auxiliary request the appellant has argued that the ability of ACZ885 to be used in a monotherapy for gout was a further contribution which underpinned an inventive step.

28. The board notes however that it has concluded that precisely the monotherapy of gout based on the antibody ACZ885 was obvious to the skilled person.

29. The appellant has further argued that administration "once every week or less frequently" (2nd auxiliary request) and "once every month or less frequently" (3rd auxiliary request) was based on example 3 and constituted additional improvements. The use of ACZ885 to solve the problem with these additional improvements in gout therapy was not obvious.

30. However, as observed above in point 15, the experiments and results thereof reported on in example 3 of the application as filed were already known to the skilled person from the disclosure in document D1.

31. Accordingly, for the same reasons that the subject-matter of claim 1 of the main request lacked inventive step, claim 1 of the 1st, 2nd and 3rd auxiliary requests fail to involve an inventive step.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chair:

S. Lichtenvort G. Alt

Decision electronically authenticated