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Datasheet for the decision of 23 June 2022

Case Number: T 2900/18 - 3.3.04

Application Number: 12174216.7

Publication Number: 2527371

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Language of the proceedings: EN

Title of invention:
Method for the treatment of glomerulonephritis

Patent Proprietor:
R-Pharm International, LLC

Opponent:
Ablynx N.V.

Headword:
Treatment of glomerulonephritis/R-PHARM

Relevant legal provisions:
EPC Art. 54

Keyword:
Novelty - (no)

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Case Number: T 2900/18 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 23 June 2022

Appellant: (Opponent)	Ablynx N.V. Technologiepark 21 9052 Ghent-Zwijnaarde (BE)
Representative:	Friedrich, Rainer Df-mp Dörries Frank-Molnia & Pohlman Patentanwälte Rechtsanwälte PartG mbB Fünf Höfe / Theatinerstraße 16 80333 München (DE)
Respondent: (Patent Proprietor)	R-Pharm International, LLC 19 bldg.1, floor 1 Premises V, office 9 Berzarina Street 123154 Moscow (RU)
Representative:	Zellentin & Partner mbB Patentanwälte Rubensstraße 30 67061 Ludwigshafen (DE)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 10 October 2018 rejecting the opposition filed against European patent No. 2527371 pursuant to Article 101(2) EPC.**

Composition of the Board:

Chair	M. Pregetter
Members:	A. Chakravarty
	F. Bostedt

Summary of Facts and Submissions

I. European patent No. 2 527 371, entitled "*Method for the treatment of glomerulonephritis*" was opposed under Article 100(a) in combination with Articles 54 and 56 EPC and Article 100(b) and (c) EPC.

II. The patent was granted with claim 1 as follows:

"1. An inhibitor of IL-6 activity which is an antibody or functionally-active fragment, which antibody or functionally-active fragment selectively interacts with an IL-6 polypeptide or an IL-6R polypeptide for use in the treatment and/or prophylaxis of glomerulonephritis associated with a vasculitic disorder".

III. In the decision under appeal, the opposition division considered grounds of opposition raised under Article l00(a) EPC in combination with Articles 54 and 56 EPC and Article l00(b) and (c) EPC.

IV. The opposition division decided to reject the opposition. An appeal was filed by the opponent (appellant) against this decision. The patent proprietor is respondent to this appeal.

V. With the statement of grounds of appeal, the appellant submitted documents D26 to D28.

VI. The respondent replied to the statement of grounds of appeal, requesting as its main and sole request that the appeal be dismissed and that the patent be maintained as granted.

VII. Following documents are mentioned in this decision.

D1: Liang B., Gardner D.B., Griswold D.E., Bugelski P.J., Song X.Y.R., 2006, "*Anti-interleukin-6 monoclonal antibody inhibits autoimmune responses in a murine model of systemic lupus erythematosus*", Immunology, 119, 296-305.

D7: Kitching A.R., Holdsworth S.R., Hickey M.J., 2008, "*Targeting Leukocytes in Immune Glomerular Diseases*". Curr. Med. Chem., 15, 448-458.

D8: Guillevin, L., Dörner, T., 2007, "*Vasculitis: mechanisms involved and clinical manifestations*". Arthritis Res Ther, 9(Suppl 2), S9.

D14: EP 1 004 315 A1

VIII. Oral proceedings before the board were held as scheduled. At the end of these proceedings, the Chair announced the decision of the board.

IX. The submissions of the appellant are summarised as follows.

Main request(maintenance of the patent as granted) - claim 1

Claim construction

The claim was for a second medical use. The medical purpose mentioned in the claim was the treatment and/or prophylaxis of glomerulonephritis associated with a vasculitic disorder. The skilled person would understand that "associated with" glomerulonephritis did not mean that the glomerulonephritis was

necessarily caused by the vasculitic disorder (or *vice-versa*). Instead, it was sufficient that e.g., the glomerulonephritis and the vasculitic disorder appeared at the same time in the same organism. In any case, "glomerulonephritis associated with a vasculitic disorder" included glomerulonephritis associated with a disease or disorder that itself was associated a vasculitic disorder.

The novelty of the claimed subject-matter hinged on the interpretation of the expression "glomerulonephritis associated with a vasculitic disorder" found in the independent claims. In the decision under appeal, the opposition division took the view that 'associated with' simply meant 'connected with', which, led it to conclude that the claimed treatment with the anti-IL-6 antibody must involve both diseases.

However, the correct interpretation of "associated with" did not necessarily imply that the glomerulonephritis had to be caused or somehow characterised by the vasculitic disorder (or that the vasculitic disorder is caused or characterised by the glomerulonephritis, for that matter). Instead, a loose "association" between the glomerulonephritis and a vasculitic disorder was encompassed by the expression used in the claims.

Novelty (Article 54 EPC)
Document D1

Document D1 disclosed an anti-IL-6 antibody for use in treating glomerulonephritis in murine systemic lupus erythematosus (SLE) cases (see page 300; Figures 4e and 4f and Table 1). The authors of document D1 observed periarterial inflammatory infiltrate that was reduced

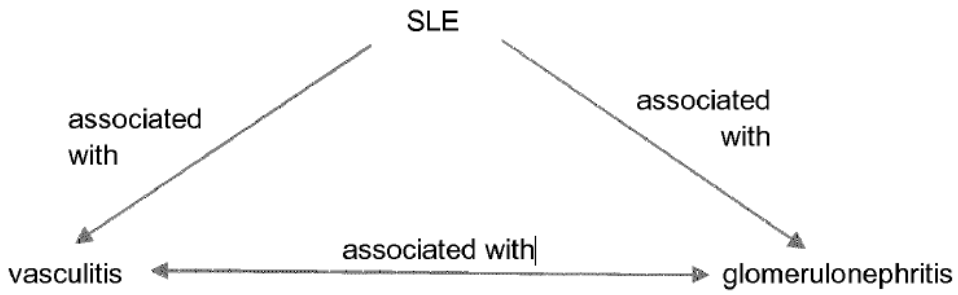
by treatment with an anti-IL-6 antibody. Accordingly, the mice used in document D1 had glomerulonephritis associated with vasculitis. Thus, the anti-IL-6 antibody reduced glomerulonephritis associated with (arterial) vasculitis. The claimed subject-matter therefore lacked novelty.

Document D14

Document D14 disclosed an anti-IL-6 receptor (IL-6R) antibody for use as a preventive and/or therapeutic agent for nephritis in murine SLE. This antibody inhibited the binding of IL-6 to IL-6R thereby neutralising the biological activity of IL-6.

The experiments disclosed in document D14 demonstrated that administration of anti-IL-6R antibody markedly delayed the appearance of urinary protein and markedly suppressed the incidence of the disease (see paragraph [0152]). The IL-6R antibody also prolonged the survival of NZB/W F1 mice (see paragraph [0153]).

Document D14 disclosed the treatment of "glomerulonephritis associated with a vasculitic disorder" because glomerulonephritis was a pathological hallmark feature of SLE (see document D1, pages 297 and 300, left column, or document D7, Table 3) and SLE was associated with vasculitis (see, e.g. document D8, page 2, left column). Accordingly, the mice treated in document D14 had a "glomerulonephritis associated with a vasculitic disorder" as illustrated below (illustration taken from page 13 of the statement of grounds of appeal).



X. The submissions of the respondent are summarised as follows.

Main request (maintenance of the patent as granted) - claim 1

Claim construction

The skilled person would have considered that the therapeutic aim of the claimed product was treatment of "glomerulonephritis associated with a vasculitic disorder". This referred only to glomerulonephritis **caused** by the disease it was associated with (emphasis added by the board). The patent clearly defined that diseases such Goodpasture's syndrome, vasculitis and IgA nephropathy presented glomerulonephritis as a consequence of the disease and not as a possible concomitant occurrence of two separate diseases.

The expression "glomerulonephritis associated with a vasculitic disorder" did not include cases where the glomerulonephritis and the vasculitic disorder were symptoms of the same disease/disorder if they did not occur in the same patient and/or at the same time in a patient.

Novelty (Article 54 EPC)
Document D1

The teaching of document D1 was largely similar to that in document D14 (see below). It openly acknowledged that NZB/W F1 mice were an accepted model of lupus nephritis (page 297 left hand column, last paragraph). The skilled person would not even have considered that document D1 disclosed an anti-IL6 antibody for treating for lupus nephritis, let alone glomerulonephritis associated with a vasculitic disorder. Table 1, in document D1 in fact disclosed that there was no statistically significant difference in the median between control antibody and anti-IL-6 monoclonal antibody. This was further repeated at page 300, right hand column, mid paragraph: "*Histopathological analysis showed that treatment with anti-IL6 mAb significantly reduced the disease severity to that of WHO class II to III disease*". Thus, according to the table at page 296 of D1, the disease severity was still high but not as severe as a classification in group IV-VI.

Document D14

Document D14 was silent about treating glomerulonephritis associated with a vasculitic disorder nor was this information directly and unambiguously derivable from the prior art. The skilled person would have known that document D14 included data coming from the NZB/W mouse model of nephritis associated with SLE, which was not suitable for studying other diseases such as "glomerulonephritis associated with a vasculitic disorder". Accordingly, the skilled person would not have considered that document D14 clearly and unambiguously provided

evidence that glomerulonephritis associated with a vasculitic disorder could be treated.

XI. The appellant requested that the decision under appeal be set aside and that the European patent No. 25 27 371 be revoked. Furthermore, documents D26 to D28, filed with the statement setting out the grounds of appeal, should be admitted into the appeal proceedings.

XII. The respondent requested that the appeal be dismissed. Moreover, documents D26 to D28, as well as documents D6, D9, D10 and D13, should be held inadmissible.

Reasons for the Decision

Admittance of documents

1. The board reached its decision without needing to take documents D26 to D28 or D6, D9, D10 and D13 into account. It is therefore not necessary to decide on their admittance.

Main request - Claim 1

Claim construction

2. The claim is for a purpose-limited product under Article 54(5) EPC, i.e. a so-called second or further medical use. The product is "an inhibitor of IL-6 activity which is an antibody or functionally-active fragment". The board will in this decision use "antibody" to refer to both the antibody and its functionally active fragment. The claimed antibody is further defined by its function, that function being the ability to selectively interact with an IL-6 polypeptide or an IL-6R polypeptide. The therapeutic

purpose is "the treatment and/or prophylaxis of glomerulonephritis associated with a vasculitic disorder". The board will refer to the claim as having feature (a): "an inhibitor of IL-6 activity which is an antibody or functionally-active fragment, which antibody or functionally-active fragment selectively interacts with an IL-6 polypeptide or an IL-6R polypeptide" and feature (b): "for use in the treatment and/or prophylaxis of glomerulonephritis associated with a vasculitic disorder", where "glomerulonephritis associated with a vasculitic disorder" is a sub-category of glomerulonephritis in general.

3. There was disagreement between the parties about how the skilled person would interpret feature (b). The respondent was of the view that the skilled person would consider that it referred only to glomerulonephritis caused by a disease it was associated with. The appellant on the other hand argued that "glomerulonephritis associated with a vasculitic disorder" included glomerulonephritis associated with a disease or disorder that itself was associated a vasculitic disorder (see Sections IX. and X.).

4. The board construes the claim in accordance with the principles developed in the case law of the boards of appeal. Thus, terms in claims are given their normal meaning in the relevant art (see Case Law of the Boards of Appeal of the European Patent Office, 9th edition 2019, II.A. 6.3.3). In the present case, it is necessary to construe the expression "glomerulonephritis associated with a vasculitic disorder". It is noted that no case has been made by either party that the expression had a special meaning to the skilled person. Moreover, the description of the patent contains no definition of what "associated" is

intended to mean or of what is to be understood by "vasculitic disorder". Instead, paragraph [0008] defines vasculitis as including "*systemic and small vessel vasculitis such as that associated with diseases with anti-neutrophil circulating antibodies, for example, Wegener's disease (also called Wegener's granulomatosus). Wegener's disease involves inflammation of the arteries of the lungs, nasal passages and kidneys*".

5. The board understands that "vasculitis" being a subclass of "vasculitic disorder". From the use of "*such as*" in paragraph [0008] it is understood that Wegener's disease is given merely as an example of a disease associated with vasculitis. In other words, Wegener's disease cannot be the only disease in which glomerulonephritis is associated with a vasculitic disorder. This conclusion is supported throughout the description where "a vasculitic disorder" and "Wegener's disease" are listed separately, see e.g. paragraph [0001] of the patent, implying that they are not equivalent.

6. In the absence of any definition of "associated", the board considers that the skilled person would interpret the term to mean in some way "linked to". Thus, "glomerulonephritis associated with a vasculitic disorder" would be understood to be a glomerulonephritis linked to a vasculitic disorder. A link could exist, for instance if the glomerulonephritis were part of the same disease complex as a vasculitic disorder.

Novelty (Article 54 EPC)

Document D1

7. Document D1 discloses an anti-IL-6 antibody for use in treating SLE. It is entitled "*Anti-interleukin-6 monoclonal antibody inhibits autoimmune responses in a murine model of systemic lupus erythematosus*" (see title). It describes a study on "*NZB/W F1 mice that spontaneously develop an autoantibody response against DNA and chromatin antigens as well as polyclonal hypergammaglobulinaemia and ultimately severe immune complex-mediated glomerulonephritis*". These mice "*have been widely used as a model to study lupus nephritis*" (see page 297, left column). It concludes that "*Upon administration of anti-IL-6 mAb in our studies, the disease severity of glomerulonephritis was significantly reduced in NZB/W F1 mice" (see page 304, left column)*".

8. In view of its effect on *NZB/W F1 mice*, it is concluded that document D1 discloses feature (a) of claim 1, i.e. an anti-IL-6 antibody which acts as an inhibitor of IL-6 activity. Regarding feature (b), document D1 discloses use of an anti-IL-6 antibody for inhibiting autoimmune responses, which *inter alia* lead to glomerulonephritis. Thus, document D1 discloses an anti-IL-6 antibody for use in treating glomerulonephritis associated with systemic lupus erythematosus (SLE).

9. The respondent's argument that document D1 does not disclose the use of an anti-IL-6 antibody for the treatment of lupus nephritis is not persuasive. As pointed out by the respondent itself, page 300, right-hand column, discloses that "*Histopathological analysis*

showed that treatment with anti-IL6 mAb significantly reduced the disease severity to that of WHO class II to III disease". Contrary to the respondent's view, a treatment of a disease is disclosed in a document even if the treatment only reduces the severity of the disease.

10. Furthermore, it was not disputed by the respondent that, as disclosed in document D8 (see page 2, left-hand column, paragraph 1), vasculitis may occur as a symptom of SLE. Document D8 is an article entitled "*Vasculitis: mechanisms involved and clinical manifestations*". It discloses that "*...there is evidence to suggest that vasculitis accelerating atherosclerosis is a complicating feature of most, possibly all, autoimmune diseases. This includes connective tissue diseases (CTDs) such as rheumatoid arthritis (RA), scleroderma, sarcoidosis and systemic lupus erythematosus (SLE)*" (see page 1, paragraph 1; emphasis added by the board). Furthermore, on page 2 (left column, Figure 1 and paragraph 1) it is explained that "*The vasculitides that occur in autoimmune diseases usually affect small-sized vessels, as is the case in SLE, systemic sclerosis and Sjogren's syndrome*".

11. The respondent's argument in favour of novelty of the claimed subject-matter over that disclosed in document D1 relies on the construction of the phrase "glomerulonephritis associated with a vasculitic disorder" as not including glomerulonephritis occurring in SLE.

12. However, as set out in the section on claim construction above (see points 2. to 6.), the board has decided that the glomerulonephritis to be treated by

the claimed product includes any that is associated or linked to vasculitis. Since it has been convincingly established that both glomerulonephritis and vasculitis occur in SLE, the board considers that document D1 discloses anti-IL-6 antibodies for use in treating "glomerulonephritis associated with a vasculitic disorder", i.e. a disease as claimed.

13. In view of the claim construction, the fact that document D1 does not disclose treating an SLE patient simultaneously having both glomerulonephritis and vasculitis, is not relevant as this is not a feature of the claim.

Document D14

14. The board also considers that the disclosure in document D14 anticipates the claimed subject-matter. The considerations are similar to those given above in relation to document D1, since they also turn on whether or not treating glomerulonephritis associated with SLE falls within the meaning of "glomerulonephritis associated with a vasculitic disorder".

15. Document D14 discloses anti-IL-6 receptor (IL-6R) antibodies for treating SLE, for instance paragraph [0018] reads "*The present invention provides a preventive and/or therapeutic agent for systemic lupus erythematosus comprising an anti-IL-6 receptor antibody as an active ingredient*". Indeed document D14 uses the same mouse model of SLE as used in document D1, NZB/W F1 mice. It discloses that IL-6R antibodies inhibit the binding of IL-6 to IL-6R, neutralizing the activity of IL-6 (see paragraph [0032]). The experiments reported in document D14 demonstrate that the timing of

appearance of urinary protein was markedly delayed, and the incidence of the disease was also markedly suppressed ([0152]). The IL-6R antibody prolonged the days of survival ([0153]). It was not in dispute that the presence of urinary protein was a symptom of glomerulonephritis.

16. Given the claim construction applied by the board (see point 6., above), SLE is a disease in which patients suffer from both glomerulonephritis and vasculitic disorders (vasculitis). Thus, the treatment of glomerulonephritis associated with SLE is also treatment of glomerulonephritis associated with a vasculitic disorder. Therefore, the disclosure in document D14 anticipates the subject-matter of claim 1.

17. Since the subject matter of claim 1 of the patent as granted lacks novelty and no other claim requests are on file, the patent must be revoked.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chair:

I. Aperribay M. Pregetter

Decision electronically authenticated