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Datasheet for the decision of 9 March 2023

Case Number: T 2034/21 - 3.3.04

Application Number: 10821297.8

Publication Number: 2482849

IPC: A61K39/395, A61P35/00, C07K16/28

Language of the proceedings: EN

Title of invention:
Combination immunotherapy for the treatment of cancer

Patent Proprietor:
Memorial Sloan-Kettering Cancer Center
Board of Regents, The University of Texas System

Opponents:
GlaxoSmithKline Intellectual Property Development Limited
Kymab Limited

Headword:
Combination immunotherapy/SLOAN-KETTERING

Relevant legal provisions:
EPC Art. 100(c), 123(2)
RPBA 2020 Art. 13(2)

Keyword:

Main request: Amendments - added subject-matter (yes)
Auxiliary request 1: Amendment to case - reasons for submitting amendment in appeal proceedings (no)
Auxiliary requests 2 to 10: Amendments - added subject-matter (yes)

Decisions cited:

T 0881/01, T 0752/16, T 1187/16, T 1791/16, T 2610/16, T 0042/17, T 0995/18, T 1996/17

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Case Number: T 2034/21 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 9 March 2023

Appellant I: (Opponent 1)	GlaxoSmithKline Intellectual Property Development Limited 980 Great West Road Brentford Middlesex TW8 9GS (GB)
Representative:	Kim, Young In Timothy GlaxoSmithKline Global Patents GSK House (CN9.25.1) 980 Great West Road Brentford, Middlesex TW8 9GS (GB)
Appellant II: (Opponent 2)	Kymab Limited The Bennet Building (B930) Babraham Research Campus Cambridge Cambridgeshire CB22 3AT (GB)
Representative:	Leonard, Thomas Charles Kilburn & Strode LLP Lacon London 84 Theobalds Road London WC1X 8NL (GB)
Respondent: (Patent Proprietor 1)	Memorial Sloan-Kettering Cancer Center 1275 York Avenue New York, NY 10021 (US)
Respondent: (Patent Proprietor 2)	Board of Regents, The University of Texas System 210 West 7th Street Austin, TX 78701 (US)
Representative:	J A Kemp LLP 80 Turnmill Street London EC1M 5QU (GB)

Decision under appeal: **Interlocutory decision of the Opposition Division of the European Patent Office posted on 21 September 2021 concerning maintenance of the European Patent No. 2482849 in amended form.**

Composition of the Board:

Chairwoman M. Pregetter
Members: B. Rutz
R. Romandini

Summary of Facts and Submissions

I. The appeals by opponent 1 (appellant I) and opponent 2 (appellant II) lie from the opposition division's decision to maintain European patent No. 2 482 849 on the basis of the claims as granted and an amended description.

II. Claims 1 and 2 as granted read as follows:

"1. A composition comprising an agonist anti-ICOS antibody for use in treating cancer in a patient, wherein said agonist anti-ICOS antibody is for use in combination with a blocking agent to a T cell inhibitory receptor selected from the group consisting of an anti-CTLA-4 antibody and an anti-PD-L1 antibody that blocks binding of PD-1 to PD-L1 and inhibits PD-1 signalling.

2. A composition comprising a blocking agent to a T cell inhibitory receptor selected from the group consisting of an anti-CTLA-4 antibody and an anti-PD-L1 antibody that blocks binding of PD-1 to PD-L1 and inhibits PD-1 signalling, for use in treating cancer in a patient, wherein said blocking agent to a T cell inhibitory receptor is for use in combination with an agonist anti-ICOS antibody."

III. The patent had been opposed on the grounds of Article 100(a) EPC, in relation to novelty (Article 54 EPC) and inventive step (Article 56 EPC), and Article 100(b) and (c) EPC.

IV. With its statement of grounds of appeal, appellant II filed documents D94 to D99.

V. With their reply to the appeals, the respondents (patent proprietors) re-filed auxiliary requests 1 to 7, which were identical to auxiliary requests 1 to 7 before the opposition division. In addition, they filed new auxiliary requests 8 and 9 and document D100.

VI. Claims 1 and 2 of auxiliary request 1 are identical to the respective claims of the main request.

Claims 1 and 2 of auxiliary request 2 differ from the respective claims of the main request in that the anti-ICOS antibody has "an IgG1, IgG3 or IgG4 isotype".

Claims 1 and 2 of auxiliary requests 3 and 4 differ from the respective claims of the main request in that the antibody is "for use in treating **a** cancer" (highlighting added by the board) and that the CTLA-4 antibody is characterised as "blocking".

Claims 1 and 2 of auxiliary request 5 combine the features of the respective claims of auxiliary requests 2 and 3.

Claims 1 and 2 of auxiliary request 6 differ from the respective claims of the main request in that the antibody is "for use in treating **a** cancer" (highlighting added by the board) and in that the "blocking agent to a T cell inhibitory receptor is a blocking anti-CTLA-4 antibody".

Claims 1 and 2 of auxiliary request 7 differ from the respective claims of the main request in that the antibody is "for use in treating **a** cancer" (highlighting added by the board) and in that the "blocking agent to a T cell inhibitory receptor is

a blocking anti-PD-L1 antibody that blocks binding of PD-1 to PD-L1 and inhibits PD-1 signalling".

Claims 1 and 2 of auxiliary request 8 differ from the respective claims of the main request in that the antibody is "for use in treating **a** cancer" (highlighting added by the board), in that the anti-ICOS antibody has "an IgG1, IgG3 or IgG4 isotype" and in that the "blocking agent to a T cell inhibitory receptor is a blocking anti-CTLA-4 antibody".

Claims 1 and 2 of auxiliary request 9 differ from the respective claims of the main request in that the antibody is "for use in treating **a** cancer" (highlighting added by the board), in that the anti-ICOS antibody has "an IgG1, IgG3 or IgG4 isotype" and in that the "blocking agent to a T cell inhibitory receptor is a blocking anti-PD-L1 antibody that blocks binding of PD-1 to PD-L1 and inhibits PD-1 signalling".

VII. The board summoned the parties to oral proceedings and informed them of its preliminary opinion in a communication pursuant to Article 15(1) RPBA.

VIII. With a letter dated 15 December 2022, appellant II filed document D101.

IX. With a letter dated 20 January 2023, appellant I informed the board that it would not be attending oral proceedings.

X. Oral proceedings before the board took place on 9 March 2023 (in the absence of appellant I) in the form of a videoconference as requested by both attending parties. During the oral proceedings, the

respondents filed a new auxiliary request 1 and renumbered the remaining auxiliary requests as 2 to 10.

Claims 1 and 2 of the new auxiliary request 1 read as follows:

"1. A composition comprising an agonist anti-ICOS antibody for use in treating a cancer in a patient in combination with a blocking agent to a T cell inhibitory receptor selected from the group consisting of an anti-CTLA-4 antibody and an anti-PD-L1 antibody that blocks binding of PD-1 to PD-L1 and inhibits PD-1 signalling.

2. A composition comprising a blocking agent to a T cell inhibitory receptor selected from the group consisting of an anti-CTLA-4 antibody and an anti-PD-L1 antibody that blocks binding of PD-1 to PD-L1 and inhibits PD-1 signalling, for use in treating cancer in a patient in combination with an agonist anti-ICOS antibody."

At the end of the oral proceedings, the Chairwoman announced the board's decision.

XI. The appellants' arguments as far as relevant to the decision may be summarised as follows.

Main request
Amendments (Article 123(2) EPC)

The wording of claims 1 and 2 was ambiguous and highly unusual for a second medical use claim based on a combination of agents. It was settled in the case law of the boards of appeal of the EPO that a "mind willing to understand" did not require broad terms to be

interpreted narrowly. Instead, a broad term "*should be interpreted with regard to all technically logical interpretations thereof*" (see Case Law of the Boards of Appeal, 10th edition 2022, II.E.1.3.9(e)).

In the case of claim 1, the amended claim specified that only the agonist anti-ICOS antibody was comprised in the composition for use in treating cancer. The blocking agent to a T cell inhibitory receptor was no longer comprised in the composition for use in treating cancer. The same applied to claim 2, in which only the blocking agent, i.e. anti-CTLA-4 antibody or anti-PD-L1 antibody, was comprised in the composition for use in treating cancer.

In addition to the specified medical use, there was a second "for use" statement in claim 1 which, in the broadest reasonable (and technically meaningful) interpretation, specified that the agonist anti-ICOS antibody was suitable for use in combination with a blocking agent to a T cell inhibitory receptor. The suitability for use meant that the agents were capable of combined use (i.e. not incompatible with one another when the first agent was used to treat cancer). This was not, as alleged by the respondents, "*an unreasonable and unrealistic interpretation*". It was both a technically sensible interpretation (agents can be unsuitable for use in treating patients who are already receiving other specific agents) and it was an interpretation that was in line with general principles of claim interpretation and the EPO Guidelines relating to medical use claims.

The description and the drawings did not contain anything which rendered this claim interpretation technically nonsensical or incompatible with the

claimed invention. In the examples of the patent, the blocking agent and the agonist anti-ICOS antibody were not always administered together.

In the interests of legal certainty, all technically reasonable interpretations of an ambiguous claim had to be considered. If one of those interpretations contained matter that extended beyond the content of the application as originally filed, it had to be concluded that there was added subject-matter. The application as filed did not disclose treating cancer with either an agonist anti-ICOS antibody or a blocking agent selected from an anti-CTLA-4 antibody or an anti-PD-L1 antibody; it only disclosed combination treatments. The subject-matter of claims 1 and 2 thus extended beyond the content of the application as filed.

Auxiliary request 1
Admittance (Article 13(2) RPBA)

This new claim request had not been filed until the oral proceedings on appeal, so the provisions of Article 13(2) RPBA applied. The issue of the interpretation of the unusually worded medical use claims 1 and 2 had been a fundamental issue from the start of the opposition proceedings. The respondents could and should have filed a corresponding claim request during the opposition proceedings, or at the latest with their reply to the statement of grounds of appeal submitted by opponent 2, which re-emphasised the issue. The board changing its opinion from its preliminary opinion was an ordinary development in appeal proceedings and could not be considered exceptional circumstances. The nature of the amendment was irrelevant under Article 13(2) RPBA, but the timing

of the submission was crucial. A reference to Rule 80 EPC as a reason for not being able to file amended claims earlier was inappropriate because claim interpretation was relevant for the grounds of opposition set out in Article 100(a) and 100(c) EPC. The claim request should therefore not be admitted into the proceedings.

Auxiliary requests 2 to 10

The same added-matter objections as for the main request applied.

XII. The respondents' arguments as far as relevant to the decision may be summarised as follows.

Main request
Amendments (Article 123(2) EPC)

The claims referred specifically to each agent being "for use in combination". The claims thus clearly required the two agents to be for use in combination to treat cancer.

Appellant II's interpretation was unreasonable because it meant that claims 1 and 2 each recited two separate uses, i.e. a first use which was a medical use and a second use which was separate and not a medical use and which merely required the first antibody to be "suitable" for use with the second antibody. This interpretation was unreasonable and nonsensical because a single claim cannot define an antibody by two separate uses.

EPO practice and the case law of the boards of appeal was clear on second medical use claims in that the

medical use specified in any such claim was a technical requirement of the claim. Claims 1 and 2 thus required two antibodies to be used in combination in the treatment of cancer.

Claims 1 and 2 each defined a single therapy, and they required the anti-ICOS antibody and the anti-CTLA-4 or anti-PD-L1 antibody to be "for use in treating cancer". Therefore, the claims also required both antibodies in the combination to exert a therapeutic effect. The medical use defined in the claims required both antibodies to be combined, so both antibodies were part of the medical use and both had to exert a therapeutic effect.

This was also supported by the text of the patent (e.g. in paragraphs [0001] and [0007]), which showed that no purpose other than using the two antibodies together in the treatment of cancer was envisaged. The patent showed that both antibodies had a therapeutic effect and were not used merely as adjuvants or carriers.

Using only one antibody without the other would amount to a different therapeutic effect not falling under the claims.

Auxiliary request 1
Admittance (Article 13(2) RPBA)

The respondents had always interpreted the claims as being directed to a combination treatment. This interpretation had been adopted by the opposition division and accepted by the board in its preliminary opinion. Against this background, the wording of the amendment did not change the case but merely clarified the subject-matter which had always been intended. No

new features had been incorporated from the description into the claims, and the board and the opponents had already based their analysis of patentability on the assumption of a combination treatment. There were exceptional circumstances in that the claims had no new features and the substance of the appeal had not changed. In addition, in terms of procedural economy, there was therefore no burden on the opponent or the board because they had already dealt with the claimed combination treatment. The claim request should therefore be admitted into the proceedings.

Auxiliary requests 2 to 10

The same arguments as for the main request applied.

XIII. Appellants I and II request that the decision under appeal be set aside and the patent be revoked.
Appellant II further requests:
- not to admit auxiliary requests 4, 7 and 8 to 10 (submitted as auxiliary requests 3, 6 and 7 to 9) and documents D89 and D90 into the appeal proceedings
- to admit documents D95 to D99 and D101 into the appeal proceedings

The respondents request:
- to dismiss the appeals, i.e. to maintain the patent based on the main request
- alternatively, to maintain the patent based on the sets of claims of auxiliary request 1 filed as auxiliary request 10 at the oral proceedings or auxiliary requests 2 to 10 filed with the statement of grounds of appeal as auxiliary requests 1 to 9
- to admit documents D89 and D90 into the appeal proceedings

- not to admit documents D70, D71, D71a, D80, D95 to D99 and D101 into the appeal proceedings

Reasons for the Decision

Main request
Claim interpretation - claims 1 and 2

1. Claims 1 and 2 read as follows:
"1. A composition comprising an agonist anti-ICOS antibody for use in treating cancer in a patient, wherein said agonist anti-ICOS antibody is for use in combination with a blocking agent to a T cell inhibitory receptor selected from the group consisting of an anti-CTLA-4 antibody and an anti-PD-L1 antibody that blocks binding of PD-1 to PD-L1 and inhibits PD-1 signalling.

2. A composition comprising a blocking agent to a T cell inhibitory receptor selected from the group consisting of an anti-CTLA-4 antibody and an anti-PD-L1 antibody that blocks binding of PD-1 to PD-L1 and inhibits PD-1 signalling, for use in treating cancer in a patient, wherein said blocking agent to a T cell inhibitory receptor is for use in combination with an agonist anti-ICOS antibody."

2. Both claims adopt the format of a further medical use as per Article 54(5) EPC by specifying that the composition comprising an antibody is "for use in treating cancer in a patient". This was undisputed in the appeal proceedings. The question is, however, what the further feature "wherein said [antibody] is for use in combination with" means in this context.

3. The appellants interpret this wording as a functional definition of the antibody mentioned first in each of claims 1 and 2. According to established rules of interpretation, when a product such as an antibody is defined as "for use", this should be read as "suitable for use" (see Case Law of the Boards of Appeal, 10th edition 2022, I.C.8.1.5). The antibody which was part of the composition thus only had to be suitable for the use in combination with a second antibody. This meant that the presence of the second antibody was not required in the treatment.

4. The respondents, in contrast, interpret the wording "for use in combination with" as further defining the medical use as a combination treatment which required the presence of the second antibody in the treatment.

5. Claims 1 and 2 are clear in that they define a further medical use ("for use in treating cancer in a patient") of a composition comprising an antibody. It can be left undecided whether the term "wherein" in claims 1 and 2 refers to the composition or to its therapeutic use because the characterisation "is for use" clearly relates to "said agonist" or "said blocking agent", i.e. the antibody comprised in the composition. Therefore, it applies only to the antibody, not to the therapeutic use, and only requires the antibody to be "for use in combination with" a second antibody. Since this "for use" is not semantically linked to the therapeutic use of the composition, it cannot be inferred from the wording of the claim that the combined use of two antibodies is a requirement of the treatment. Rather, the wording "is for use in combination" further defines the antibody in that it has to be suitable to be combined with a second antibody.

6. The respondents argue that the skilled person with a mind willing to understand would rule out that interpretation.

7. The board disagrees because compounds can be defined by functional features other than the medical use of the claim. This can include the compatibility or incompatibility with other compounds but does not necessarily require the claim to relate to a combination treatment. Functional features of compounds used in a composition for medical use can also be tested independently of the treatment, e.g. by *in vitro* tests prior to the actual treatment. The respondents have not provided reasons why the skilled person would rule out a medical use in which a therapeutically active antibody is further defined as being suitable for use in combination with another antibody. On the contrary, the board holds that a claim interpretation cannot lead to a situation where additional limiting features are read into the claim (see Case Law of the Boards of Appeal, 10th edition 2022, II.A.6.3.4).

8. The respondents further argue that the appellant's interpretation was "unreasonable and nonsensical" because a single claim cannot define an antibody by two separate uses.

9. The board disagrees. In medical use claims it might be opportune or necessary to define compounds by characteristics other than the intended use, and this definition might include functional features which need not be part of the medical use (see point 7. above).

10. Lastly, the respondents argue that the whole patent was related to combination treatments, referring to

paragraphs [0001] and [0007] and the examples of the patent.

11. However, even if the claim wording is considered ambiguous, all technically reasonable claim interpretations must be considered (see T 1791/16, point 11 of the Reasons). A discrepancy between the claims and the description is not a valid reason to ignore the clear literal content of a claim (T 1996/17, point 7 of the Reasons) or to give a different meaning to a claim feature which in itself gives the skilled reader clear, credible technical teaching (see also T 881/01, point 2.1 of the Reasons).

Amendments (Article 123(2) EPC)

12. According to the claim interpretation above, claims 1 and 2 are directed to compositions comprising a single antibody for the treatment of cancer, the antibody being an agonist anti-ICOS antibody in the case of claim 1 and an anti-CTLA-4 antibody or an anti-PD-L1 antibody in the case of claim 2. The application as filed does not disclose a medical use of such compositions, nor have the respondents pointed to any passage which could provide the basis for such disclosure.

13. The subject-matter of claims 1 and 2 extends beyond the content of the application as filed (Article 123(2) EPC).

Auxiliary request 1
Admittance (Article 13(2) RPBA)

14. The set of claims of auxiliary request 1 represents an amendment to the appeal case after the summons to oral

proceedings and thus has to fulfil the requirements set out in Article 13(2) RPBA.

15. The respondents argued that the board's view with regard to claim interpretation expressed during oral proceedings changed from that in the preliminary opinion. This represented exceptional circumstances under Article 13(2) RPBA.

16. Unless a board raises a "new objection", i.e. one not covered by those previously raised by the board or a party, this cannot be regarded as exceptional circumstances (see also Case Law of the Boards of Appeal, 10th edition 2022, V.A.4.5.6(h) and (i), and cited decisions T 2610/16 and T 42/17). Where an objection had already been raised by the opposition division or a party, the board's raising of that objection (e.g. T 1187/16; even where this involved a change in the board's opinion, e.g. T 752/16, T 995/18) represents an ordinary development in the appeal proceedings which cannot justify the filing of new requests.

17. The respondents further argued that the amendment made in claims 1 and 2 was only "clarifying" the subject-matter, did not change the subject-matter intended by them throughout the proceedings and had also been adopted by the opposition division. The amendment did not jeopardise procedural economy either as the appellants in their submissions had already dealt with the claims according to the interpretation that was now being clarified in the claims.

18. The board could not agree with these arguments either. With regard to Article 13(2) RPBA it is immaterial whether the "amendment to a party's appeal case"

relates to subject-matter that has already been explicitly or implicitly addressed by the parties. What matters is whether there have been exceptional circumstances justified by cogent reasons which would allow the amendment to be admitted. The board has not been presented with any such circumstances and therefore does not admit the claim request.

Auxiliary requests 4, 7 and 8 to 10
Admittance (Article 12(4) and (6) RPBA)

19. The board admitted the claim requests into the proceedings. In view of its finding that auxiliary requests 2 to 10 are not allowable (see below) the board does not deem it necessary to provide reasons for admitting these requests.

Auxiliary requests 2 to 10
Amendments (Article 123(2) EPC)

20. Claims 1 and 2 of these requests suffer from the same deficiency as the main request with regard to Article 123(2) EPC because they contain the same wording with regard to the antibody in the composition, i.e. "is for use in combination". The same considerations as for the main request therefore apply.

21. The requests are not allowable under Article 123(2) EPC.

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:

I. Aperribay M. Pregetter

Decision electronically authenticated