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**Datasheet for the decision
of 8 October 2024**

Case Number: T 1569/22 - 3.3.04

Application Number: 15198284.0

Publication Number: 3023788

IPC: A61K39/00, A61P35/00, G01N33/68

Language of the proceedings: EN

Title of invention:
Compositions of tumor specific neoantigens for use in treating tumours

Patent Proprietors:
The General Hospital Corporation
Dana-Farber Cancer Institute, Inc.

Opponent:
James Poole Limited

Headword:
Neoantigens/DANA-FARBER

Relevant legal provisions:
EPC Art. 111(1)

Keyword:
Remittal - deficiency in first-instance proceedings (yes)



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Case Number: T 1569/22 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 8 October 2024

Appellants:

(Patent Proprietors)

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Decision under appeal:

**Decision of the Opposition Division of the
European Patent Office posted on 14 April 2022
revoking European patent No. 3023788 pursuant to
Article 101(3) (b) EPC.**

Composition of the Board:

Chairwoman M. Pregetter
Members: O. Lechner
 L. Bühler

Summary of Facts and Submissions

- I. The patentees (appellants) filed an appeal against the opposition division's decision to revoke European patent No. 3 023 788.

- II. In its decision the opposition division held that claims 1 and 8 of the main request (claims as granted) were novel but lacked an inventive step pursuant to Articles 100(a) and 56 EPC. Claims 1 and 8 of auxiliary request 1 (submitted as auxiliary request 6 by letter of 6 April 2021 and renumbered during oral proceedings before the opposition division) were found to lack an inventive step under Article 56 EPC. Auxiliary requests 2 to 11 (submitted as auxiliary requests 1 to 5 by letter of 6 April 2021 and auxiliary requests 7 to 11 by letter of 28 January 2022) were not admitted into the proceedings. Documents D34 to D36 and D39 were admitted into the proceedings, whilst D37 and D38 were not.

- III. With their statement of grounds of appeal the appellants provided arguments on why the subject-matter of the claims as granted (main request) involved an inventive step. They also submitted sets of claims according to auxiliary requests 1 to 11 (underlying the decision under appeal), and according to a new auxiliary request 12.

- IV. The opponent (respondent) replied to the statement of grounds of appeal.

- V. Both parties submitted further letters. The appellants also filed a declaration by Dr Patrick Ott (document D40).
- VI. The board issued a communication pursuant to Article 15(1) RPBA.
- VII. Oral proceedings took place as scheduled. At the end of the proceedings the Chairwoman announced the board's decision.
- VIII. Claim 1 of the main request (patent as granted) reads as follows.

"1. A tumor-specific immunogenic composition comprising two or more mutant peptides or polypeptides, wherein each mutant peptide or polypeptide comprises a tumor-specific neoepitope comprising a tumor-specific mutation selected from a point, splice-site, frameshift, read-through or gene-fusion mutation, for use in a method of vaccinating or treating a subject for cancer, the method comprising:

A. selecting the two or more mutant peptides or polypeptides by a method comprising:

a. identifying a plurality of tumor mutations in expressed genes of the subject by whole genome or whole exome nucleic acid sequencing of tumor and normal tissue samples from the subject, wherein the mutations are present in the genome of the cancer cells of the subject but not in normal tissue from the subject; wherein when said mutation identified is a:

- i. point mutation further identifying a mutant peptide having the point mutation; and/or
- ii. splice-site, frameshift, read-through or gene-fusion mutation further identifying a mutant polypeptide encoded by the mutation;

b. applying a validated peptide-MHC binding prediction algorithm to select two or more mutant peptides or polypeptides identified in step (a), each mutant peptide or polypeptide comprising a tumor-specific neoepitope comprising a tumor-specific mutation selected from a point, splice-site, frameshift, read-through or gene-fusion mutation, wherein the tumor-specific neoepitope binds to a class I HLA protein in the subject with a predicted IC50 of less than 150nM; and

B. administering the tumor-specific immunogenic composition to the subject."

IX. Reference is made to the following document.

D22: Willard H. and Ginsburg G. (eds); Genomic and Personalized Medicine Volumes I & II (2009); CHAPTER 50; Rammensee H. et al.; pages 573-589

X. The appellants' arguments, where relevant to the decision, can be summarised as follows.

(a) Admittance of documents D34 to D36 and D39

None of documents D34 to D36 and D39 could be deemed *prima facie* relevant since they did not pertain to the prediction of cancer neoantigen binding.

Therefore, the opposition division's decision to admit these documents was based on incorrect principles.

(b) Admittance of document D40

Although filed after the statement of grounds of appeal, document D40 – a declaration by the technical expert Dr Patrick Ott – directly addressed the respondent's allegations raised in points 19 and 20 of its reply to the statement of grounds of appeal regarding the appellants' position on the relevance of documents D34 to D36 and D39 as being artificial and incorrect. Document D40 aligned with and expanded upon the appellants' initial arguments.

(c) Admittance of the new data filed with the statement of grounds of appeal

The new data filed in point 4.57 and Figure 1 of the statement of grounds of appeal had been filed in response to the opposition division's allegation in the decision under appeal that the half-maximal inhibitory concentration (IC50) threshold value of 150 nM was arbitrary. The data also demonstrated that a predicted IC50 of 150 nM was an inflection point in the number of expected immunogenic epitopes that would be present in the vaccine. An IC50 below 150 nM as an upper limit would have resulted in fewer immunogenic epitopes, while setting an upper limit above 150 nM would not have yielded any additional immunogenic epitopes.

(d) Admittance of novelty objections against the main request

The respondent's general novelty objections in the reply to the statement of grounds of appeal were

unsubstantiated, with no reasons given to justify reversing the opposition division's decision on this matter.

(e) Inventive step - Articles 100(a) and 56 EPC

Document D22 represented the closest prior art.

The opposition division had erred by not considering the therapeutic effect of the claimed immunogenic composition to be a distinguishing feature over document D22. The only clinical trial reported in document D22 on page 578, left-hand column, used tumour-associated antigens (TAA), but did not relate to a vaccine comprising tumour-specific neoantigens, especially not to a vaccine prepared using a whole genome/exome sequencing approach.

Document D22 was not enabling for any vaccine prepared according to the three approaches in Figure 50.1, as it did not provide therapeutic results for those vaccines. No such vaccine had been produced or tested for efficacy. In addition, page 576, right-hand column, paragraph 4 of document D22 mentioned that the ideal tumour vaccine could never be achieved, indicating that only future developments might yield better approximations than current possibilities. Therefore, a skilled person would not have known whether it was feasible to prepare a vaccine according to Figure 50.1.

To the contrary, Examples 1 to 4 and 7 of the patent in suit provided credible evidence of a therapeutic effect. According to decision G 2/21, this initial evidence could be supported by post-filing evidence in documents D21 and D32. The vaccines described in these

two documents had been prepared based on the approach described in the patent in suit, which employed whole genome/exome sequencing to identify tumour-specific mutations and selected peptides with a predicted IC50 of less than 150 nM.

Therefore, the subject-matter of claim 1 differed from the method of developing antigenic compositions for the ideal tumour vaccine according to Figure 50.1 of document D22 on account of the mere fact that it achieved a therapeutic effect.

(f) Remittal - Article 111(1) EPC

The appellants did not comment on the board's intention to remit the case to the opposition division.

XI. The respondent's arguments, where relevant to the decision, can be summarised as follows.

(a) Admittance of documents D34 to D36 and D39

The opposition division had correctly exercised its discretion in admitting documents D34 to D36 and D39. The appellants had not demonstrated any errors in applying this discretion and had failed to demonstrate that the opposition division had acted based on incorrect principles, ignored relevant criteria, or acted arbitrarily or unreasonably, as outlined in decision G 7/93, point 2.6 of the Reasons.

(b) Admittance of document D40

Document D40 was only filed in response to the respondent's reply to the statement of grounds of appeal and did not address the legal aspect of the

proper exercise of discretion by the opposition division, but only discussed the technical content of documents D34 to D36 and D39. This should have been included in the statement of grounds of appeal.

(c) Admittance of the new data filed with the statement of grounds of appeal

The new data in point 4.57 and Figure 1 of the statement of grounds of appeal were not to be admitted. They had been introduced by incorrectly asserting that the feature "IC50 less than 150 nM" supported patentability. These data were not part of the decision under appeal, making them inadmissible amendments to the appellants' case under Article 12(4) and (6) RPBA. The appellants had failed to adequately identify these data as an amendment or to provide convincing reasons for their late submission.

(d) Admittance of novelty objections against the main request

The respondent did not address the board's preliminary opinion, outlined in point 18 of the communication under Article 15(1) RPBA, which stated that the respondent's objections regarding novelty were insufficiently substantiated in its reply to the statement of grounds of appeal.

(e) Inventive step - Articles 100(a) and 56 EPC

Document D22 represented the closest prior art.

Contrary to the appellants' assertion, the features of achieving a therapeutic effect did not distinguish the subject-matter from document D22, since document D22

enabled the therapeutic effect at the same level as the patent in suit.

During oral proceedings, the appellants had argued for the first time that document D22 did not enable a skilled person to prepare the vaccine without undue burden or to achieve a therapeutic effect; however, document D22 disclosed a therapeutic effect similar to that in the patent in suit. The legend for Figure 50.1 indicated that vaccine preparation involved comparative gene expression and HLA ligand analysis of tumour and normal tissue. No critical elements were missing that would have prevented a skilled person from achieving the therapeutic effect (T 919/90). The appellants had not presented serious doubts substantiated by verifiable facts regarding this issue.

Therefore, the therapeutic effect was not a distinguishing technical feature between the subject-matter of claim 1 and the method for preparing vaccine compositions disclosed in document D22.

(f) Remittal - Article 111(1) EPC

The respondent did not comment on the board's intention to remit the case to the opposition division.

XII. The parties' relevant requests for the decision were as follows:

- (a) The appellants request that
- the decision under appeal be set aside and that the patent be maintained as granted (main request), or, alternatively that the patent be maintained on the basis of the set of claims of one of auxiliary requests 1 to 12;

- the case be remitted to the opposition division for consideration of Article 100(b) and (c) EPC if the subject matter of the main request was considered to involve an inventive step under Articles 100(a) and 56 EPC;
- the opposition division's decision to not admit auxiliary requests 2 to 11 be overturned;
- documents D34 to D36 and D39 not be admitted; and
- document D40 be admitted.

(b) The respondent requests that

- the appeal be dismissed;
- the appellants' data filed with the statement of grounds of appeal as "Figure 1" in point 4.57 not be admitted;
- documents D37 and D38 be admitted in case the other relevant documents on file were considered insufficient to show that the claimed subject-matter lacks an inventive step;
- the appellants' request for reversing the opposition division's decision to admit documents D34 to D36 and D39 be rejected;
- the appellants' request for reversing the opposition division's decision to not admit auxiliary requests 2 to 11 be rejected;
- auxiliary request 12 not be admitted;
- document D40 not be admitted; and
- the case not be remitted to the opposition division to decide on outstanding issues.

Reasons for the Decision

Admittance of documents D34 to D36 and D39

1. It has to be assessed whether the opposition division had exercised its discretion according to the right principles and in a reasonable manner when admitting documents D34 to D36 and D39.
2. The opposition division decided to admit documents D34, D35 and D39 since, in its view, they were *prima facie* relevant and filed in direct response to the opposition division's negative preliminary opinion on the respondent's inventive step objection.

The opposition division considered that document D36, i.e. decision T 1396/06, supported a legal argument which could be introduced at any stage of the proceedings. In the decision under appeal, document D36 was not used as a combination document for discussing technical aspects of inventive step.

Therefore, the opposition division had exercised its discretion according to the right principles.

3. Consequently, the board decided that documents D34 to D36 and D39 form part of the appeal proceedings (Article 12(2) RPBA).

Admittance of document D40

4. The appellants argued that document D40 had been filed in response to the respondent's arguments in points 19 and 20 of its reply to the statement of grounds of appeal. Document D40 discusses that a skilled person would not consider document D34, D35 or D39 to be *prima*

facie relevant for selecting epitopes for a personal cancer vaccine given that they do not relate to the identification and selection of tumour-specific neoantigens.

5. However, documents D34, D35 and D39 had already been submitted by the respondent by letter dated 28 January 2022 in response to the opposition division's preliminary opinion within the time limit under Rule 116(1) EPC. Therefore, document D40 could have been submitted even earlier.
6. Consequently, document D40, the declaration by Dr Patrick Ott as filed with the appellants' letter dated 22 August 2023, is not admitted in accordance with Article 13(1) RPBA.

*Admittance of novelty objections under
Articles 100(a) and 54 EPC*

7. In its notice of opposition, the opponent raised objections relating to novelty, inventive step, sufficiency of disclosure and added matter under Article 100(a), (b) and (c) EPC against the claims as granted.

In its preliminary opinion the opposition division held that none of the grounds of opposition under Article 100(a), (b) and (c) EPC prejudiced the maintenance of the patent as granted.

During oral proceedings before the opposition division, the novelty and inventive step of the main request were discussed. The opposition division found the subject-matter of claims 1 and 8 as granted to be novel over document D12 (point 17.4.3 of the contested decision).

7.1 In its reply to the statement of grounds of appeal, the respondent simply stated that it maintained all objections as set forth under Article 100(a) EPC in its submissions at the first-instance proceedings, which were annexed to its reply. No detailed reasoning was given for why it considered the opposition division's decision to be wrong.

8. The respondent's objection of lack of novelty is insufficiently substantiated in the reply to the statement of grounds of appeal and is therefore not admitted under Article 12(3) and (5) RPBA.

Admittance of the new data filed with the statement of grounds of appeal

9. In point 4.57 and Figure 1 (see page 12) of their statement of grounds of appeal, the appellants presented new data to demonstrate that, for the vaccines described in documents D21 and D32, an IC50 of 150 nM was not an arbitrary cut-off value.

10. Document D21 was filed with the notice of opposition and document D32 was filed by the patent proprietor in reply to this. The relevance of a predicted IC50 of less than 150 nM had been under discussion since the beginning of the opposition proceedings (see e.g. page 5, point 1 of the notice of opposition). From the appellants' line of argument in the statement of grounds of appeal it is not apparent why the new data provided in point 4.57 and Figure 1 were only provided with the statement of grounds of appeal and not already during the opposition proceedings. During the oral proceedings before the board the appellants

did not give any reasons for submitting these data only on appeal.

11. Therefore, the new data presented in point 4.57 and Figure 1 of the statement of grounds of appeal could and should have been submitted during the opposition proceedings.
12. The board decided, in exercising its discretion, not to admit the new data filed in point 4.57 and Figure 1 of the statement of grounds of appeal into the proceedings (Article 12(4) and (6) RPBA).

Remittal - Article 111(1) EPC

13. The parties agreed that claim 1 is drafted in the form of a further medical use claim pursuant to Article 54(5) EPC. The claimed therapeutic indication is for the vaccination against or treatment of cancer.
14. According to the established case law of the boards of appeal, attaining the claimed therapeutic effect is a functional technical feature of claims relating to a further medical use. To satisfy the requirement of sufficiency of disclosure, the proof of a claimed therapeutic effect has to be provided in the application as filed (G 2/21, OJ EPO 2023, A85, point 77 of the Reasons). The issue of whether the therapeutic effect is attained, i.e., in the present case, whether vaccination or treatment of cancer was effective, is to be established when assessing sufficiency of disclosure (G 1/03, OJ EPO 2004, 413, point 2.5.2 of the Reasons).

15. During the parties' presentations on inventive step at the oral proceedings, it became evident that a crucial part of their arguments centred on enabling the therapeutic use both as defined in claim 1 and as described in the closest prior art, document D22.

Based on differing assessments, both parties disagreed on the number of technical features that the closest prior art and the subject-matter of claim 1 had in common. The appellants argued *inter alia* that, contrary to the patent in suit, document D22 did not enable a therapeutic effect, while the respondent argued that document D22 enabled the therapeutic effect at the same level as the patent in suit.

16. The problem-solution approach can only be correctly applied once it has been established whether the therapeutic effect under consideration, i.e. the (effective) vaccination against or treatment for cancer, is attained. Therefore, for taking a final decision on inventive step, it is fundamental that it has been assessed whether this claimed functional technical feature has been sufficiently disclosed.
17. The decision under appeal, however, does not contain an assessment of whether the ground for opposition under Article 100(b) EPC prejudices the maintenance of the patent. Without this assessment the case is not considered ready to be decided. Consequently, the decision on Article 100(a) EPC with regard to inventive step cannot be upheld.
18. Since the opposition division did not decide on this point, which is relevant for the assessment of inventive step, the board considers that there are special reasons to exercise its discretion to remit the

case to the opposition division under Article 11(1) RPBA for further prosecution in accordance with Article 111(1) EPC.

19. The respondent's initial request not to remit the case to the opposition division referred to an earlier situation and has become moot. The respondent did not reiterate this request following the developments in the discussion on inventive step during the oral proceedings.
20. Therefore, the board decided to set aside the decision under appeal and to remit the case to the opposition division for further prosecution (Article 111(1) EPC).

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The case is remitted to the opposition division for further prosecution.

The Registrar:

The Chairwoman:



I. Aperribay

M. Pregetter

Decision electronically authenticated