Internal distribution code:

(A) [-] Publication in OJ
(B) [-] To Chairmen and Members
(C) [-] To Chairmen
(D) [X] No distribution

Datasheet for the decision of 26 May 2023

Case Number: T 1675/20 - 3.3.04

Application Number: 15720069.2

Publication Number: 3137104

IPC: A61K39/00, A61K39/395, C07K16/28, A61K35/15

Language of the proceedings: EN

Title of invention:
Vaccine

Applicant:
Medizinische Hochschule Hannover

Headword:
Prime-boost compositions with antigen/MHH

Relevant legal provisions:
EPC Art. 83

Keyword:
Sufficiency of disclosure - (no)

Decisions cited:
T 0609/02, T 0895/13

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

Boards of Appeal

Chambres de recours

Boards of Appeal of the
European Patent Office
Richard-Reitzner-Allee 8
85540 Haar
GERMANY
Tel. +49 (0)89 2399-0
Fax +49 (0)89 2399-4465

Case Number: T 1675/20 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 26 May 2023

Appellant: (Applicant)	Medizinische Hochschule Hannover Carl Neuberg Straße 1 30625 Hannover (DE)
Representative:	Taruttis, Stefan Georg TARUTTIS Patentanwaltskanzlei Aegidientorplatz 2b 30159 Hannover (DE)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 3 January 2020 refusing European patent application No. 15720069.2 pursuant to Article 97(2) EPC**

Composition of the Board:

Chairman	B. Rutz
Members:	D. Luis Alves
	M. Blasi

Summary of Facts and Submissions

I. The applicant (appellant) filed an appeal against the decision of the examining division refusing European patent application No. 15 720 069.2 entitled "Vaccine".

II. In the decision under appeal the examining division dealt with a main request and two auxiliary requests. As regards the claims of the main request, the examining division held that claims 1, 3, 14 and 15 were not clear (Article 84 EPC), that the invention defined in claim 1 was not sufficiently disclosed in the application (Article 83 EPC), and that claim 13 related to subject-matter extending beyond the content of the application as filed (Article 123(2) EPC). These objections applied also to auxiliary requests 1 and 2.

III. With the notice of appeal the appellant resubmitted sets of claims of a main request and auxiliary requests 1 and 2, all being identical to those considered in the decision under appeal, each accompanied by description pages.

IV. With the statement setting out the grounds of appeal the appellant filed sets of claims of auxiliary requests 3 to 5 as well as documents D12 to D19 (see numbering below).

V. The board appointed oral proceedings, as requested by the appellant. In a communication pursuant to Article 15(1) RPBA the board gave its preliminary opinion, *inter alia*, concerning sufficiency of disclosure. In particular, it indicated that the application did not demonstrate the suitability for use

in medical treatment of compositions having as the co-stimulatory antibody an anti-ICOS (anti-CD278) antibody.

VI. With its letter dated 3 April 2023 the appellant filed a new claim set and an adapted description as its main request, and withdrew all requests previously on file.

VII. Oral proceedings were held as scheduled in the appellant's absence. The board contacted the appellant's representative by phone before opening the oral proceedings and was informed that the appellant did not intend to attend the oral proceedings. In accordance with Rule 115(2) EPC and Article 15(3) RPBA the proceedings were continued in the absence of the appellant, and the appellant was treated as relying on its written case. By not attending the oral proceedings the appellant did not make use of the opportunity to present any further comments. At the end of the oral proceedings the Chair announced the board's decision.

VIII. Claim 1 of the main (sole) request reads:

"1. Pharmaceutical combination of compositions for use in medical treatment, the combination comprising a first composition comprising dendritic cells which are immunologically compatible with a recipient and which are associated with a target antigen, wherein the dendritic cells are associated with the target antigen by being contacted with the target antigen, and a second composition comprising the target antigen in soluble form and a co-stimulatory antibody effective for activating T-cells and/or the dendritic cells, which co-stimulatory antibody is selected from an anti-CD137 antibody, an anti-CD40 antibody, an anti-OX40 antibody, an anti-ICOS antibody, an anti-CD27

antibody, an anti-CD28 antibody, an anti-GITR antibody, an anti-TIM1 antibody, and wherein the second composition is for administration at a time at least 1 day subsequent to administration of the first composition."

IX. In the present decision reference is made to the following documents:

D12: Naik, S.H. *et al.*, The Journal of Immunology 174, 2005, pages 6592-6597

D13: Nimanong, S. *et al.*, Cancer Research 77(8), 2017, pages 1918-1926

D14: Supplemental Figure S3 of D13

D15: Hamilton, S.E. and Hardy, J.T., The Journal of Immunology 169, 2002, pages 4936-4944

D16: Hamilton, S.E. *et al.*, Nature Immunology 5(2), 2004, pages 159-168

D17: Pamer, E.G., Nature Reviews Immunology 4, 2004, pages 812-823

D18: Chen, L. and Flies, B., Nature Reviews Immunology 13, 2013, pages 227-242

D19: McInturff, J.E. *et al*, The Journal of Investigative Dermatology 125, 2005, pages 1-8

D20: Experimental results "STV 38" (3 pages) filed on 17 September 2019

D21: Experimental results "STV40" (3 pages) filed on 17 September 2019

X. The appellant's arguments relevant to the present decision may be summarised as follows.

The co-stimulatory antibodies in the claimed compositions for use in medical treatment were limited to those for which experimental results were available.

The application showed experimental results obtained with compositions including a co-stimulatory antibody against CD137, CD40, OX40 (CD137) or ICOS (CD278).

The most relevant experimental results for assessing the effect of the claimed compositions upon antigen-specific CD8+ T-cells were those in figure 15. The latter represented the number of antigen-specific CD8+ T-cells as a proportion of the total number of activated CD8+ T-cells. This figure showed that the numbers of these T-cells were increased relative to the control, and this applied for all compositions tested, including those in which the co-stimulatory antibody was directed to ICOS.

In addition, documents D13 and D14 showed experimental results obtained with compositions including an antibody against CD137, CD40 or OX40 as the co-stimulatory antibody. Moreover, the experimental results filed on 17 September 2019 (D20 and D21), during the examination proceedings, showed that boost compositions containing anti-ICOS antibody, anti-CD28 antibody, anti-CD27 antibody, anti-GITR antibody, anti-TIM1 antibody or anti-CD40 antibody as the co-stimulatory antibody were effective in generating an immune response to the antigen.

Moreover, the application showed a therapeutic effect in a murine model of cancer (see Example 3).

XI. The appellant requested in writing that the decision of the examining division be set aside and a patent be granted on the basis of the set of claims and description pages according to the main request filed with the letter dated 3 April 2023.

Reasons for the Decision

Main (sole) request

Admittance into the appeal proceedings (Article 13(2) RPBA)

1. This request was filed after notification of the summons to oral proceedings. Thus, Article 13(2) RPBA applies.

2. The board considers the filing of this request to constitute a response to objections raised for the first time in the communication under Article 15(1) RPBA (see points 13 to 15 of that communication) and therefore decides to take the request into account.

Disclosure of the invention (Article 83 EPC)

3. Claim 1 is drafted in the form of a purpose-limited product claim, pursuant to Article 54(4) EPC, and is directed to a combination for use in medical treatment comprising (i) a first (prime) composition comprising

dendritic cells which are associated with a target antigen and are immunologically compatible with the recipient of the treatment and (ii) a second (boost) composition comprising (a) the target antigen in soluble form and (b) a co-stimulatory antibody effective for activating T-cells and/or dendritic cells, the antibody being directed to CD137, CD40, OX40, ICOS, CD27, CD28, GITR or TIM1 (the exact claim wording is reproduced in point VIII.).

4. Where a therapeutic application is claimed in the form according to Article 54(4) or (5) EPC, attaining the claimed therapeutic effect constitutes a functional technical feature of the claim. As a consequence, in order to fulfil the requirements of Article 83 EPC, the suitability of the product for the claimed therapeutic application must be disclosed in the application, unless this is already known to the skilled person at the priority date (see decisions T 609/02, Reasons 9, and T 895/13, Reasons 3 to 5).

5. Claim 1 encompasses compositions wherein the co-stimulatory antibody may be directed to any of the eight targets CD137, CD40, OX40, ICOS, CD27, CD28, GITR or TIM1. In contrast, in the application only one specific combination is tested for its therapeutic effect in a murine model of cancer, namely the combination "DC-COAT Ndufs", which includes a Ndufs1 peptide (a tumour-derived antigen), an anti-CD40 antibody and the TLR3 agonist Poly I:C (see Example 3).

6. In the case at hand, therefore, the question is whether the application nevertheless contains information regarding the suitability of all claimed combinations for the therapeutic application. It has not been argued that this information was common general knowledge.

7. In addition to the murine model of cancer in Example 3, the application describes experiments carried out in mice in order to measure the immune response in terms of antigen-specific CD8+ T-cells. Mice were administered different boost compositions comprising soluble antigen, Poly I:C and a co-stimulatory antibody selected from anti-CD137, anti-CD40, anti-CD134 (anti-OX40) or anti-CD278 (anti-ICOS). Figures 14 and 15 represent the values for antigen-specific CD8+ T-cells measured 7 days after administration of the compositions to mice, these values being expressed as a percentage of the total white blood cells (figure 14) or as a percentage of the total activated CD8+ T-cells (figure 15). Specifically, the proportion of antigen-specific CD8+ T-cells in the total white blood cells is above 10% for compositions comprising one of the anti-CD137 antibodies, and is less than half of that value for the other anti-CD137 antibody. The proportion is nearly 30% for the anti-CD40 antibody and is indistinguishable from the negative control for the anti-ICOS antibody (see figure 14 - CD278 is ICOS). When one considers the immune response in terms of the proportion of antigen-specific CD8+ T-cells in the total activated CD8+ T-cells, large differences between the compositions remain. Indeed, the value is greater than 0.50 for the anti-CD40 antibody whereas it is less than 0.10 for the anti-ICOS antibody (see figure 15 - CD278 is ICOS), i.e. being similar to the negative control of an unspecific IgG2 preparation ("RatIgG2").

8. The results in the murine model of cancer in Example 3 were obtained with boost compositions comprising anti-CD40 antibody as the co-stimulatory antibody. As summarised above, figures 14 and 15 show that the immune response was the largest precisely for this

antibody. In light of these experimental results, the board considers that the therapeutic effect observed in Example 3 for this antibody cannot be extrapolated to every co-stimulatory antibody tested, regardless of the magnitude of the immune response observed. In view of the difference in magnitude between the T-cell responses observed for the anti-ICOS antibody and the anti-CD40 antibody, the board considers that the therapeutic effect of an anti-ICOS antibody is not made credible in the application.

9. Moreover, the board is not convinced that the application shows an increase in the immune response, in terms of antigen-specific CD8+ T-cells, for every composition having an anti-ICOS antibody as the co-stimulatory antibody. The reasons for the board's position in this regard are set out below.

9.1 All experiments reported in the application were carried out with second (boosting) compositions comprising the TLR3 agonist Poly I:C.

9.2 The application describes experiments carried out with two different amounts of anti-CD40 antibody as the co-stimulatory antibody, as well as two different amounts of Poly I:C. The results are represented in figure 11. This figure shows antigen-specific CD8+ T-cells as a percentage of total CD8+ T-cells, for each boosting composition. The bar furthest to the left represents the response to the negative control and is followed by two bars representing a first amount of antibody and increasing amounts of Poly I:C. Finally, the two bars furthest to the right represent a higher amount of antibody and the previous two amounts of Poly I:C. A comparison between the second and third bars shows the effect of increasing the amount of Poly I:C. The same

is true for a comparison of the two bars furthest to the right. Thus, the results in figure 11 demonstrate that both Poly I:C and the antibody contribute to the effect on antigen-specific CD8+ T-cells.

9.3 In light of the results in figure 11, and contrary to the appellant's argument, it is not possible to reliably conclude from figure 15 whether or not any increase for the anti-ICOS antibody relative to the negative control would be achieved in the absence of Poly I:C. In other words, it is not possible to distinguish between the presence of Poly I:C and the presence of anti-ICOS antibody as being the cause of the observed increase.

10. Since claim 1 does not require the presence of Poly I:C, it encompasses embodiments for which no therapeutic effect has been demonstrated.

11. The appellant referred to the "Experimental results filed on 17 September 2019" in this regard. However, all experiments for which results are shown in this document were carried out in the presence of Poly I:C. Moreover, in these experiments the stimulation achieved by the anti-ICOS antibody in the presence of Poly I:C is similar to the stimulation for the control and much weaker than in case of the anti-CD40 antibody (see D21, page 1 - compare "unstimulated" with "Adpgkmut" for Group 1 "ICOSab", and page 3 - compare "unstimulated" with "Adpgkmut" for Group 5 "CD40ab"). Consequently, no further support for a credible effect in relation to the embodiment of claim 1 directed to anti-ICOS co-stimulatory antibody can be derived from this document.

12. The appellant referred to post-published documents D13 and D14, in the context of compositions comprising anti-CD40, anti-CD137 and anti-OX40 antibodies. Consequently, these documents are not relevant in relation to the compositions of claim 1 comprising anti-ICOS co-stimulatory antibodies and do not need to be considered further. Document D12 and documents D15 to D19 were filed with the statement of grounds of appeal in relation to issues other than those on which the board is basing its decision.

13. In conclusion, the requirements of Article 83 EPC are not met because the embodiment of claim 1 relating to compositions comprising an anti-ICOS antibody for use in medical treatment is not disclosed in the application in a manner sufficiently clear and complete for it to be carried out by a skilled person.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

I. Aperribay B. Rutz

Decision electronically authenticated