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Datasheet for the decision of 15 January 2024

Case Number: T 0025/23 - 3.3.04

Application Number: 13708435.6

Publication Number: 2825558

IPC: C07K16/22, A61K31/337

Language of the proceedings: EN

Title of invention:
Combination therapy for the treatment of ovarian cancer

Patent Proprietor:
F. Hoffmann-La Roche AG

Opponents:
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Amgen Inc.

Headword:
Bevacizumab for the treatment of ovarian cancer/HOFFMANN LA ROCHE

Relevant legal provisions:
EPC Art. 83, 111(1), 113(1), 123(2)
EPC R. 103(1)(a)
RPBA 2020 Art. 11, 12(6)

Keyword:

Decisions cited:

Catchword:

Europäisches Patentamt
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Office européen des brevets

Beschwerdekammern

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Case Number: T 0025/23 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 15 January 2024

Appellant: (Patent Proprietor)	F. Hoffmann-La Roche AG Grenzacherstrasse 124 4070 Basel (CH)
Representative:	Mewburn Ellis LLP Aurora Building Counterslip Bristol BS1 6BX (GB)
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Respondent II: (Opponent 2)	Mabxience Research, S.L. Manuel Pombo Angulo, 28, 3ª planta 28050 Madrid (ES)
Respondent IV: (Opponent 4)	STADA Arzneimittel AG Stadastrasse 2-18 61118 Bad Vilbel (DE)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 25 October 2022 revoking European patent No. 2825558 pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chairwoman	M. Pregetter
Members:	A. Chakravarty
	L. Bühler

Summary of Facts and Submissions

I. The patent proprietor (appellant) filed an appeal against the opposition division's decision to revoke European patent No. 2 825 558, with the title "*Combination therapy for the treatment of ovarian cancer*". The patent was filed as an international application under the PCT and published as WO 2013/135602 (the "application as filed" or "the application").

II. The patent was opposed by nine opponents (opponents 1 to 9). Opponents 3 and 5 to 9 subsequently withdrew their oppositions. Opponents 1, 2 and 4 are respondents I, II and IV to the patent proprietor's appeal.

III. In the decision under appeal, the opposition division considered objections under Article 100(b) EPC and Article 100(c) EPC. It held that the main request did not meet the requirements of Article 123(2) EPC with respect to the subject matter of claim 8. Auxiliary request 1 was not allowable because claims 8 and 9 did not meet the requirements for clarity under Article 84 EPC. Auxiliary request 2 was not allowable because claim 1 did not meet the requirements of Article 83 EPC. Auxiliary request 3 was not allowable because claim 1 contravened the requirements in Article 123(2) EPC. Finally, auxiliary requests 4 to 20 were not allowable because they did not meet the requirements of Article 83 EPC for the same reasons as auxiliary request 2.

IV. The patent proprietor filed a statement of grounds of appeal in which it maintained auxiliary request 2

considered in the decision under appeal as its main request. Alternatively, it maintained previous auxiliary requests 10, 15 and 20 as auxiliary requests 1 to 3.

V. Each of the respondents submitted a reply to the patent proprietor's statement of grounds of appeal. With its reply, respondent II submitted documents D113 and D114 (renumbered by the board as D118 and D119, see section VIII.). With its reply to the patent proprietor's statement of grounds of appeal, respondent IV submitted documents D113 to D117 and with its letter dated 4 December 2023 it submitted document D120.

VI. Claim 1 of the main request reads:

"1. Bevacizumab for use in a method of treating a patient diagnosed with a platinum-resistant epithelial ovarian cancer (EOC), a platinum-resistant fallopian tube carcinoma (FTC), or a platinum-resistant primary peritoneal carcinoma (PPC), wherein the method comprises administering to said patient an effective amount of bevacizumab and paclitaxel, wherein said patient received two or fewer prior anticancer regimens, wherein said treatment prolongs said patient's median progression-free survival time [PFS] as compared to a platinum-resistant epithelial ovarian cancer (EOC), a platinum-resistant fallopian tube carcinoma (FTC), or a platinum-resistant primary peritoneal carcinoma (PPC) patient receiving paclitaxel alone".

VII. Claims 1, 2, 7 and 13 of the application as filed read:

"1. A method of treating a patient diagnosed with a platinum-resistant ovarian cancer comprising

administering to said patient an effective amount of an anti-VEGF antibody and a chemotherapeutic, wherein said patient received two or fewer prior anti-cancer regimens, wherein said treatment prolongs said patient's median progression-free survival time as comp ared to a platinum-resistant ovarian cancer patient receiving said chemotherapeutic alone.

2. The method of claim 1, wherein said platinum-resistant ovarian cancer is an epithelial ovarian cancer (EOC), a fallopian tube carcinoma (FTC), or a primary peritoneal carcinoma (PPC).

7. The method of claim 1, wherein said chemotherapeutic is selected from the group consisting of paclitaxel, topotecan or a pegylated liposomal doxorubicin (PLD)

13. The method of claim 1, wherein said anti-VEGF antibody is bevacizumab."

Document numbering

VIII. The following documents are mentioned in this decision.

D7a: ClinicalTrials.gov archive entry #19 on AURELIA study of March 15, 2011; URL: https://clinicaltrials.gov/ct2/history/NCT00976911?V_19=View#Study Page Top; accessed on February 4, 2020;

D20: Teoh D. and Alvarez Secord A., Int. J. Gynecol. Cancer, 2012, 22(3),348-359;

D62: Sato S. and Itamochi H., Curr. Opin. Obstet. Gynecol., 2012, 24(1), 8-13;

D112: Declaration of Dr Maurie Markman, dated 2 March 2023;

D113: WHO Classification of Tumours of Female Reproductive Organs, editors: Kurman R.J. *et al.*, International Agency for Research on Cancer, 2014;

D114: Peres L.C. *et al.*, JNCI J. Natl. Cancer Inst., 2019, 111(1), 60-68;

D115: Takano M. et al., J. Exp. Clin. Cancer Res., 2012, 31(53), 1-7;

D116: Neuhausen S.L. et al., Anticancer Res., 2017, 37(6),3069-3072;

D117: Greco F.A. et al., Cancer J Sci Am., 5(3), 1999, 179-191;

D118: Summary of Product Characteristics for Avastin, pages 1 to 5 (filed as D113 by opponent 2);

D119: EMA market authorization for bevacizumab biosimilar "Alymsys – bevacizumab" (filed as D114 by opponent 2);

D120: WHO Classification of Tumours; Pathology and Genetics of Tumours of the Breast and Female Genital Organs, Eds. Tavassoli F. and Devilee P, International Agency for Research on Cancer, 2003.

IX. Oral proceedings before the board were held, as requested by the parties. At the end of the these proceedings, the Chairwoman announced the board's decision.

X. The appellant's arguments relevant to the decision are summarised as follows:

Admission of the documents submitted by respondent IV and the associated lines of argument - Article 12(4) and (6) RPBA

Respondent IV submitted documents D113 to D117 with its reply to the statement of grounds of appeal and document D120 with its letter dated 04 December 2023. These documents and the lines of argument associated with them should be held inadmissible under Article 12(4) RPBA. No justification for their late filing had been given. According to respondent IV, documents D113 to D116 and D120 were filed to support its arguments relating to the definitions of EOC, FTC and PPC, their histological types, and treatment. This subject had been under discussion since the beginning of opposition proceedings and so these documents were not filed in response to a new turn of events or new arguments brought forward in the proceedings.

Moreover, respondent IV's argument concerning clear cell carcinoma, which relied on document D115, was a new argument that was not raised before the opposition division. This line of argument should also be held inadmissible.

It was also noted that *inter alia* document D113 was published after the effective filing date of the patent and therefore did not form part of the state of the art at the priority date of the patent and was therefore not relevant to the proceedings.

Respondent IV had filed document D116 to support its assertion that PPC could be present in both males and

females. The argument and the document had been completely new at the oral proceedings before opposition division. After the chairman of the opposition division had indicated the opposition division was inclined not to admit it, the respondent had withdrawn its request for the admission of the document. The request for admission of document D116 and the associated line of argument had therefore not been maintained. The document and the line of argument should be held inadmissible under Article 12(6) RPBA.

Main request (claim 1)

Disclosure of the invention (Article 83 EPC)

Single group of diseases

The opposition division had correctly found that EOC, FTC and PPC were one group of diseases from a treatment point of view. They were very similar to each other, as was well-known in the technical field. In fact, it was often difficult for medical professionals to distinguish between them as it was challenging to determine the exact origin of an ovarian cancer. For example, it was difficult to tell the difference between fallopian tube carcinoma and epithelial ovarian cancer that has spread to the fallopian tube (see, for example, document D112 on page 1, final sentence). The similarity of EOC, FTC and PPC was due in part to the fact that the relevant tissues (e.g. the lining of the abdomen and surface of the ovary) originate from the same tissue during development.

Mismatch of the study population and the population defined in the claim

The opposition division's decision that the claimed invention was insufficiently disclosed was based entirely on the erroneous conclusion that there was a "mismatch" between the patient group studied in the example and the patient group of the claims. The erroneous conclusion stemmed from an incorrect interpretation of the histological types in paragraph paragraph [00149] of the application as filed, especially the term "*endometrioid carcinoma*". The opposition division mistakenly considered that this referred to carcinomas that originated in the endometrium or uterus – meaning that the example related to treatment of cancers other than EOC, FTC, and PPC – when in fact, the term "*endometrioid*" meant that the tissue resemb led that of the endometrium. There was no inconsistency between this histological type and ovarian cancer. The opposition division did not substantiate any other reason why there was a mismatch between the inclusion criteria of the example and the claimed treatment of patients with EOC, FTC, or PPC.

The above point was further illustrated as follows: The title of the example read: "*A multi-center, open-label, randomised, two-arm Phase III trial of bevacizumab plus chemotherapy versus chemotherapy alone in patients with platinum-resistant, epithelial ovarian, fallopian tube, or primary peritoneal cancer (AURELIA)*". From this the skilled person understood that the patients treated in the example had platinum-resistant EOC, FTC, or PPC, which matched the patient group specified in the claims. Secondly, it was apparent that the example reported the results of the AURELIA trial, which specifically included patients with the three claimed subtypes of ovarian cancer.

If the skilled person had had any doubts as to whether the patent itself showed that the example was conducted in patients with EOC, FTC, or PPC, these could have been resolved by recourse to common general knowledge at the priority date of the patent, which confirmed that the AURELIA trial was indeed carried out in such patients. For example, the skilled person had access to document D7a, the trial record on ClinicalTrials.gov. Document D7a was a prior art version of the AURELIA protocol, available to the skilled person at the priority date. The "*Inclusion Criteria*" on page 7 clearly stated that the AURELIA clinical trial was being carried out on patients with EOC, FTC or PPC, as did the "*Official title*" on page 4 and the "Brief Summary" on page 5.

Further confirmation that it was common general knowledge at the priority date that the AURELIA trial was conducted in patients with EOC, FTC or PPC came from review articles D20 and D62 (see Table 3 of document D20 and page 11, left column, paragraph 1 of document D62).

In relation to the question of whether the application made the treatment of EOC/FTC/PPC patients plausible, reference was made to the disclosure in the example. Here it was clearly demonstrated that the combination of bevacizumab and paclitaxel prolonged the progression free survival (PFS) for the patient group defined in the claim. Even if the skilled person had disregarded the title of the example and the fact that it had been common general knowledge that the trial had been conducted in this patient group, the remainder of the example still made the effective treatment of this "single group of diseases" at least plausible.

In response to the argument that the exclusion criteria listed "malignant mixed Müllerian tumours" and "borderline tumours", which could in theory be classified as epithelial tumours, the appellant observed that this did not mean that there was a mismatch between the data in the example and the group of patients defined in the claim. It was entirely conventional and legitimate that such patients were excluded from trials for EOC, FTC and PPC and this exclusion did not cast doubt on the suitability of the claimed treatment for platinum-resistant EOC, FTC and PPC.

Similarly, the fact that certain, rare histological types of epithelial ovarian cancer (e.g. clear cell carcinoma) may in theory be treated differently, did not cast doubt on whether EOC, FTC and PPC were in fact managed in the same way or mean that the patent did not credibly demonstrate that the claimed combination was effective. The skilled person would have understood that the invention allowed the skilled person to provide bevacizumab and paclitaxel to improve PFS compared with treatment with paclitaxel alone in the claimed group of cancers.

Another point was that the respondents had not provided any evidence that the claimed treatment was ineffective in any of EOC, FTC or PPC, regardless of the inclusion criteria, meaning that they had failed to satisfy the standard of proof for an objection of insufficiency.

Remittal (Article 111(1) EPC)

The decision under appeal did not deal with the novelty or the inventive step of any claim request. Remittal to the opposition division for further prosecution was

therefore appropriate under Article 11 RPBA to preserve the possibility for the parties to be heard on those grounds of opposition by two instances.

Reimbursement of the appeal fee (Rule 103 EPC)

The appeal fee should be reimbursed because the opposition division's decision on then pending auxiliary request 2 (now the main request) was based on an objection to which there was no opportunity to respond, contrary to Article 113(1) EPC.

Specifically, the meaning of the term "endometrioid" was not discussed in the context of auxiliary request 2 during the oral proceedings. None of the opponents had put forward an argument relating to this term in writing and so the first time this objection was raised was in the decision.

In fact, the meaning of "endometrioid" was discussed in the oral proceedings, but only in the context of auxiliary request 3, once the opposition division had already announced its opinion that auxiliary request 2 did not comply with Article 83 EPC. Furthermore, the discussion of "endometrioid" (with respect to auxiliary request 3) during the oral proceedings was raised in a discussion of Article 123(2) EPC, not Article 83 EPC.

XI. The respondents' arguments relevant to the decision are summarised as follows.

Admission of the documents submitted by respondent IV and the associated lines of argument - Article 12(4) and (6) RPBA

Documents D113 to D117 were filed in response to statements made in the new declaration of Dr Markman (D112), filed with the statement of grounds of appeal. They were filed to show that the allegation in document D112, made during the oral proceedings before the opposition division, that "*these cancers [EOC, FTC and PPC] have always been treated in the same manner and their management has not taken into consideration which subtype a patient has, either for chemotherapy or other aspects of management. He [Dr Markman] knows of no conversation in the literature that would disagree with this characterisation*" was incorrect.

In relation to document D113, its publication in 2014 was not relevant because it was not used to attack novelty or inventive step of the claimed subject matter but to illustrate the terms of the opposed patent and the consequences on sufficiency of disclosure and the credibility of the declaration of Dr Markman (D112). For this purpose D113 should be considered as a publication of common general knowledge from 2014. Nevertheless, the points based document D113 were also supported by document D120, which was an earlier version of document D113, published in 2003.

Main request (claim 1)

Disclosure of the invention (Article 83 EPC)

Single group of diseases

The opposition division was right to find that the claimed invention was insufficiently disclosed. However, it was wrong to hold that there was no genuine distinction between EOC, FTC and PPC and that they needed to be considered as one single group of

diseases. There were three distinct types of patients mentioned in the claim, namely those with EOC, FTC or PPC. Thus, the patent (application) needed to demonstrate that a prolonged median PFS after treatment with the combination of bevacizumab and paclitaxel as compared to a monotherapy with paclitaxel patients was achieved for each of the specifically named diseases. It was not clear from which of these diseases the reference patient receiving the monotherapy suffered.

Moreover, the fact that EOC, FTC and PPC had been treated similarly in the past was no predictor of how these different patients would respond in the future. There was no evidence in the application or elsewhere on file which would imply that this would be the case.

Mismatch of the study population and the population defined in the claim

The opposition division was right to hold that there was a mismatch between the patients in the study population of the example in the patent and those defined in the claim. This mismatch meant that the disclosure in the application did not allow a conclusion to be drawn that Bevacizumab was suitable for the therapeutic purpose defined in the claim.

In document D112 Dr Markman had stated that EOC, FTC and PPC were treated in the same manner and that sub-type was not taken into consideration. This was incorrect. While epithelial ovarian cancer indeed had sub-types, fallopian tube carcinoma and primary peritoneal carcinoma were both sub-types of specific cancers of fallopian tube cancer and peritoneal cancer, respectively. Therefore, it was scientifically incorrect to talk about the subtype of "fallopian tube

carcinoma" and "primary peritoneal carcinoma". This could be proven from the WHO classification of female genital tumors in document D120, which made it clear that there was no sub-type of fallopian tube carcinoma.

The appellant submitted that all of the histology classes recited in the inclusion criteria were epithelial ovarian cancer, and therefore, the results pertain to epithelial ovarian cancer. However, the exclusion criteria explicitly mentioned certain epithelial cancers such as borderline tumors and malignant mixed Müllerian tumours. Therefore, there was serious doubt about whether the claimed therapy would be effective in all epithelial ovarian cancers since certain epithelial cancers were specifically excluded from the trial.

The results on PFS in Table 2 on page 21 of the patent mentioned "platinum-resistant ovarian cancer" only, but not EOC, FTC or PPC. It was therefore not apparent why the skilled person should conclude that the data in Table 2 pertained to those groups. The title of Example 1, mentioned them but it was not clear why the skilled person would have ignored the content of Example 1 (specifically when talking about the results in terms of PFS), which was about platinum-resistant ovarian cancer and not about the three specific diseases recited in claim 1. This explained the opposition division's concern that there was no teaching that the patient population of the example is specific to epithelial ovarian cancer (i.e. the diseases listed in the claim).

The term "platinum-resistant ovarian cancer" mentioned when disclosing the results in paragraph [00139] of the patent encompassed all types of ovarian cancers and not

only epithelial ovarian cancers. This could be seen from pages 114 and 203 of the WHO classification of female genital tumors (D120).

The appellant had argued that all of the histology classes recited in the inclusion criteria related to epithelial ovarian cancer, and therefore, the results in Table 2 pertained to epithelial ovarian cancer. However, this assertion was difficult to follow when the exclusion criteria explicitly excluded certain epithelial cancers such as borderline tumors and malignant mixed Müllerian tumors.

In summary, the opposition division was correct that there was a mismatch between the patients of the trial and what is claimed, leading to a lack of sufficient disclosure of the claimed invention in the sense that the patent (application) did not demonstrate the suitability of Bevacizumab for the therapeutic purpose defined in the claim.

Amendments (Article 123(2) EPC)

There was no basis for individual diseases together with the combination therapy and the PFS prolongation as set out in claim 1. The opposition division's decision was incorrect that original claims could be used as a basis for the features of claim 1 because the embodiments were not disclosed in the original claims in combination, so their combination was not directly and unambiguously disclosed. Moreover, the application as filed did not disclose an individualised embodiment in which a combination of paclitaxel and bevacizumab improved the PFS in comparison with paclitaxel alone for each of the three diseases individually.

The example failed to disclose whether the paclitaxel plus bevacizumab cohort included subjects with all three diseases and whether the PFS improved in the paclitaxel plus bevacizumab cohort for each of the three diseases. Furthermore, there was no direct and unambiguous disclosure that one patient of each of the three diseases in the paclitaxel plus bevacizumab cohort had a prolonged PFS compared to each of the three diseases in the paclitaxel-only group.

The appellant's requests

XII. The appellant requested that the decision under appeal be set aside and that the case be remitted to for further prosecution based on the set of claims of the main request, or of auxiliary requests 1 to 3. Alternatively, the appellant requested that the patent be maintained based on the set of claims of the main request or of auxiliary requests 1 to 3. The appellant further requested the appeal fee be refunded in view of a substantial procedural violation. Moreover, it requested that

- document D112 be admitted into the proceedings;
- documents D113 to D117 and D120 not be admitted into the proceedings;
- respondent IV's lines of argument regarding a) clear cell carcinoma, b) malignant mixed Müllerian tumors, and c) borderline tumors not be admitted into the appeal proceedings.

The respondents' requests

XIII. The respondents all requested that the appellant's appeal be dismissed.

Respondents II and IV further requested that the case not be remitted to the opposition division for further prosecution. Respondent IV also requested that lines of argument regarding a) clear cell carcinoma, b) malignant mixed Müllerian tumors, and c) borderline tumors be admitted into the appeal proceedings.

Reasons for the Decision

Admission of documents D113 to D117 and D120 and the associated lines of argument (Article 12(6) RPBA)

1. Documents D113 to D117 were filed by respondent IV with its reply to the statement of grounds of appeal with the aim of supporting lines of argument to the effect that the skilled person at the relevant date of the patent would not have regarded the conditions EOC, FTC and PPC as defined in the claim, as a single group for purposes of treatment. Respondent IV submitted that the documents were filed in response to the filing by the appellant of document D112, a declaration of Dr. Markmann corresponding to his statement read out during the oral proceedings before the opposition division.

2. In more detail, document D113, is the WHO classification of female genital tumors published in 2014. It was submitted as evidence about what the skilled person would have understood as epithelial ovarian tumours. in particular, borderline tumors were epithelial ovarian cancers. Document D114 was submitted to support the argument that epithelial ovarian cancer, fallopian tube carcinoma and primary peritoneal carcinoma were not always treated in the same way in the art. It concerned malignant mixed Müllerian tumors. Document D115 was submitted as evidence that clear cell carcinoma, a type of ovarian epithelial cancer, was

managed differently from other epithelial cancers. Document D116 was submitted to support the arguments that that PPC can also occur in men. Document D117 was submitted in relation to auxiliary requests 1 and 3, to show that 1 hour infusion of paclitaxel was known in the art and to provide evidence that this was common general knowledge.

3. The question of whether EOC, FTC and PPC, as defined in the claim, form a single group for purposes of treatment, had already been raised in the proceedings before the opposition division and was dealt with in the decision under appeal (see point 25.1). The evidence and the associated lines of argument regarding a) clear cell carcinoma, b) malignant mixed Müllerian tumors, and c) borderline tumors had not been presented or made, although they address this same issue. The respondents did not argue that there was any reasoning in the decision under appeal which was new to them and which would have justified the submission of the new lines of argument and the associated documents, nor can the board identify such circumstances. The citation from document D112 referred to in respondent IV's reply to the statement of grounds of appeal does not go beyond what was already alleged in the written proceedings before the opposition division (see e.g. the patent proprietor's reply to the notice of opposition, page 11, second full paragraph) and hence does not justify the submission of new evidence, allegations of fact and associated lines of argument in this regard.

4. In relation to the line of argument based on D116, i.e. that PPC can also occur in males, it was made during the oral proceedings before the opposition division (see point 14 of the minutes of the oral proceedings

before the opposition division) but it is not recorded if admission of the document was requested. It is also not apparent from the minutes if the line of argument was admitted or not and the point is not dealt with in the decision under appeal. In any case, the board accepts that the skilled person knew that PPC can sometimes occur in males as part of their common general knowledge.

5. In view of these considerations, neither the documents D113 to D116 nor the associated lines of argument were admitted pursuant to Article 12(4) RPBA, because the decision under appeal was not based on them and also pursuant to Article 12(6) RPBA because they could and should have been submitted in the proceedings before the opposition division. There is no need to give reasons for the non-admittance of document D117 because it was submitted in relation to auxiliary requests, whereas the board found that the main request was allowable under Articles 83 and Article 123(2) EPC (see points 28. and 30. below).

6. Document D120 was submitted by respondent IV with its letter dated 17 July 2023. The document was admitted by the board. The appellant had requested that it not be admitted, however no reason need be given for its admittance because, although taken into account in the decision under appeal, its consideration has no detrimental effect for the appellant.

Main request (auxiliary request 2 considered in the decision under appeal)

Disclosure of the invention (Article 83 EPC)

Single group of diseases

7. In the decision under appeal, the opposition division held that the claimed invention did not meet the requirements of Article 83 EPC. It held that there was "*no genuine distinction between EOC, FTC and PPC*" and therefore "*considered [them] as one single group of diseases*". Nevertheless, the opposition division considered that there was "*a fundamental lack of information in the patent resulting in a lack of disclosure*". This was because there was "*a mismatch between the studied patient group in the example and the patient group of the claims*". In particular the opposition division noted an inconsistency between the patient group as identified e.g. in the title of the example and as described in the inclusion criteria for the study reported in Example 1 (the AURELIA trail). Furthermore, the opposition division considered that the evidence in the patent (application*) did not sufficiently demonstrate that the progression free survival (PFS) in the treated population was in fact better than in the control, see decision (see decision under appeal, paragraph bridging pages 13 and 14).

* The example in the application as filed is identical to the example in the patent. In this decision, reference to the example therefore means the example in the patent or the example in the application.

8. On appeal, the appellant argued that while the opposition division had been right to hold that the

person skilled in the art would have regarded platinum-resistant EOC, a platinum-resistant FTC and platinum-resistant PPC as forming a single group of diseases, which were treated in the same way, it had been mistaken in then holding that there was a mismatch between the patient group studied in the trial disclosed in the example of the patent and the patient group defined in the claim. It was this alleged mismatch that led the opposition division to mistakenly conclude that the patent claimed invention was not sufficiently disclosed.

9. The respondents disagreed with the appellant's view. They relied on the wording of the claim as relating to specific separate conditions and on the wording in the example of the patent, which was in their view not consistent with the inclusion and exclusion criteria given in the example. The wording of the claim meant that the application had to provide data showing that bevicizumab was suitable for the claimed therapeutic indication for each of three diseases listed in the claim individually. The application did not provide this information.

10. The criteria established in the case law of the boards of appeal for deciding on whether or not the claimed second medical use is sufficiently disclosed are that the application must credibly show that the claimed therapeutic use is achieved (see Case Law of the Boards of Appeal of the European Patent Office, 10th edition, II.C.7.2.1).

11. The application as filed in Example 1, discloses the results of "*A multi-centre, open-label, randomised, two-arm Phase III trial of bevacizumab plus chemotherapy versus chemotherapy alone in patients with*

platinum-resistant, epithelial ovarian, fallopian tube or primary peritoneal cancer (AURELIA)" (see title).

12. The "*trial evaluated the efficacy and safety of bevacizumab in combination with chemotherapy for platinum-resistant ovarian cancer. [It] was designed as a prospective, open-label, randomised, two-arm Phase III evaluation of bevacizumab plus chemotherapy versus chemotherapy alone. To be eligible, patients must have ovarian cancer that progressed within 6 months of previous platinum-based therapy. Paclitaxel, topotecan or pegylated liposomal doxorubicin (PLD) was selected as chemotherapeutic combination partners [...]. By adding bevacizumab to chemotherapy, the AURELIA trial aimed to improve PFS for this group of patients who have limited therapeutic options and face a particularly poor prognosis. The primary objective was to compare progression-free survival (PFS) of patients randomised to selected chemotherapy only or to selected chemotherapy plus bevacizumab*" (see the application, paragraph [00140]).

13. The example also discloses the inclusion and exclusion criteria of the study population (see paragraphs [00148] and [00149] and paragraphs [00152] and [00153], respectively).

14. The results of the study are given in Tables 1 and 2 and are summarised *inter alia* in paragraph [00164] as follows: "*Analysis by chemotherapy cohort is summarized in Table 2 below. In platinum-resistant ovarian cancer, the improvement in PFS and ORR gained by adding bevacizumab to single-agent chemotherapy was observed across all chemotherapy cohorts*". As noted in the decision under appeal, neither Table 1 or 2 stratifies the results by cancer type or gives any information on

the improvement in PFS for patients having the individual cancer types EOC, FTC, or PPC.

15. The board is satisfied that at the relevant date of the patent, the person skilled in the art would have regarded FTC and PPC, which are not formally ovarian cancers when classified in respect of their originating organ, as being generally managed in the same way as epithelial ovarian cancer (EOC). This view is supported by the set-up of the clinical trial reported in the example, which recruited patients with all of these cancer types. This is also confirmed in document D7a. Document D7a is a version of the AURELIA trial protocol (i.e. the same trial for which the results are reported in the patent), which is part of the state of the art for the patent. The "*Inclusion Criteria*" on page 7 of document D7a state that the AURELIA clinical trial was to be carried out on patients with EOC, FTC or PPC. There is no indication in document D7a that there was any intention to differentiate between these patients but instead implies that they were to be treated as a group, and that the results would apply to the group as a whole.

16. Furthermore, EOC, FTC or PPC patients had been treated as a group in other clinical trials, such as those mentioned in document D20. Document D20 aims to provide an "*overview of angiogenesis, including the rationale for targeting angiogenesis as a treatment strategy for epithelial ovarian cancer (EOC) and to discuss available clinical trial data with antiangiogenic agents in EOC, with a focus on combinations with chemotherapy*" (see abstract). It provides details of a number clinical trials combining antiangiogenic agents with chemotherapy (*ibid*). Table 3 has the title "*Recruiting phases 2 and 3 clinical trials of*

antiangiogenic agents in combination with chemotherapy in ovarian cancer". The last column with the heading "*Setting*" gives information about which type of cancers were included. It can be seen that EOC, PPC and FTC were all used to refer to ovarian cancer.

17. Similarly, document D62 (entitled "*Bevacizumab and ovarian cancer*") is a further review on the same topic as document D20, which makes a specific reference to the AURELIA trial. Throughout the document repeated reference is made to the aim of investigating the effect of Bevacizumab on "*ovarian cancer*". Patients with EOC, PPC and FTC are referred to in the context of clinical trials investigating "*ovarian cancer*" and "*EOC*" (see e.g. page 10, both columns and page 11 left column). Indeed, both "*ovarian cancer*" and "*EOC*" are used in a manner that implies that the skilled person would recognise that these terms included PPC and FTC and that all these conditions were treated as a group in terms of treatment and outcome.

18. In view of the above considerations and in agreement with the opposition division in the decision under appeal, it is concluded that the skilled person at the relevant date of the patent would have regarded EOC, PPC and FTC, as defined in the claim, as a single group to be treated in the same way and with reported results applicable to the group as a whole.

19. The respondents have argued that the fact that EOC, PPC and FTC were treated in the same way in the past, was no predictor that they would respond in the same way to new treatments. The board is not persuaded by this line of argument because, as set out above, all three named diseases were regarded by the skilled person as part of a group which was generally treated the same way. This

also explains why EOC, PPC and FTC are mentioned separately in the claim.

20. Respondent IV also submitted that PPC could also occur in males which made it apparent that PPC was different from epithelial ovarian cancer but which was nevertheless encompassed by the claim. However, this argument fails because, as has been explained in points 11. to 18. above, the PPC referred to is part of a single group of diseases occurring in female patients, as further evident from the fact that the group of diseases is also referred to as platinum-resistant "ovarian cancer", e.g. in paragraph [0120] of the patent in the context of the AURELIA trail.

21. A further objection raised by the respondents was that it is not clear from the wording of the claim which of EOC, PPC and FTC the reference patient suffered from. This however is an objection of lack of clarity under Article 84 EPC, which is not available in the present case because the disputed wording was present in the granted claim and Article 84 EPC is not a ground for opposition.

Mismatch between the patient group in the example and the patient group of the claims

22. In the decision under appeal, the opposition division held that due to "*a mismatch between the studied patient group in the example and the patient group of the claims*", the disclosure in the application did not allow the skilled person to conclude that bevacizumab was suitable for attaining the therapeutic effect defined in the claim. This mismatch arose from the inclusion and exclusion criteria disclosed in paragraphs [0148] to [0154] of the application. The

opposition division was unsure if patients with endometrial adenocarcinoma were included ("*For example, it is questionable whether or not an endometrial adenocarcinoma is included*", see decision under appeal, paragraph bridging pages 13 and 14). Moreover, the lack of stratification of the results into patients with EOC, PPC and FTC, meant that the patent did not demonstrate that an improvement of PFS for the single group of diseases was shown in the patent (*ibid*).

23. The board is of the view that there is a mistake in the opposition division's chain of reasoning. It cannot be understood why, having concluded that at the relevant date of the patent, no distinction was made between EOC, PPC and FTC and these were treated together as a group, it should then be necessary for the patent to provide results where these conditions are stratified separately. Moreover, the board cannot agree that the skilled reader would consider that there was a mismatch between the inclusion and exclusion criteria in the example and the disease conditions specified in the claim. As already mentioned, the only example of a mismatch given in the decision is that "*it is questionable whether or not an endometrial adenocarcinoma is included*" (*ibid*). However, as pointed out by the appellant, the opposition division mistakenly considered the reference to endometrioid adenocarcinoma to refer to endometrial carcinoma, i.e. tumours that originate in the endometrium or uterus instead of an ovarian cancer with tissue that resembles that of the endometrium. Endometrioid adenocarcinoma however cannot serve as an example of the alleged mismatch.

24. It is also apparent from document D120 (see pages 113 to 115), which formed part of the skilled person common

general knowledge, that there is no other mismatch between the conditions mentioned in the inclusion criteria in paragraphs [0149] to [0151] of the application and the conditions which the skilled person knew to be tumours of the ovary, since all included histological types are to be found in the corresponding WHO classification.

25. The opposition division gave no example of a mismatch between the exclusion criteria and the conditions mentioned in the claim and the board has not been able to identify any. The cancer related exclusion criteria in the example are "*Patients whose disease was refractory to their previous platinum treatment. Refractory disease is defined as those patients who progressed during the preceding platinum treatment; non-epithelial, including malignant mixed Müllerian tumours; ovarian tumours with low malignant potential (i.e. borderline tumours); history of other clinically active malignancy within 5 years of enrolment, except for tumours with a negligible risk for metastasis or death, such as adequately controlled basal-cell carcinoma or squamous-cell carcinoma of the skin or carcinoma in situ of the cervix or breast*".

26. The respondents gave malignant mixed Müllerian tumours and borderline tumours as examples of a mismatch between the exclusion criteria and the conditions mentioned in the claim, because they could in theory be classified as epithelial tumours, but were excluded.

27. There is nothing in these criteria that would lead the skilled person to doubt that the results reported in the application are not applicable to patients diagnosed with a platinum-resistant EOC, FTC or PPC.

There are also legitimate explanations of why malignant mixed Müllerian tumors and borderline tumours were excluded. Malignant mixed Müllerian tumors are very rare and have malignant epithelial and mesenchymal elements (see document D120, page 133). Similarly, borderline epithelial tumours occupy a state between benign and malignant tumours and require a different management as shown in document D94, page 31.

28. In view of the above considerations, the board is persuaded that the invention as claimed meets the requirements of Article 83 EPC.

Amendments (Article 123(2) EPC)

29. The respondents submitted that subject-matter of claim 1 was not directly and unambiguously disclosed in the application in the sense that it did not disclose bevacizumab used in combination with paclitaxel for the treatment of the individual diseases (EOC, FTC and PPC) together with the PFS prolongation. Moreover, an individualised embodiment in which a combination of paclitaxel and bevacizumab improved the PFS in comparison with paclitaxel alone in each of the three diseases (individually) was absent in the application as filed.

30. The board is however in agreement with the opposition division in the decision under appeal that the claimed subject-matter is directly and unambiguously disclosed in the application.

31. Claim 1 of the application as filed differs from claim 1 in that it does not specify bevacizumab as the anti-VEGF antibody, paclitaxel as the chemotherapeutic or epithelial ovarian cancer (EOC), fallopian tube

carcinoma (FTC) and primary peritoneal carcinoma (PPC) as the ovarian cancer.

32. These features are disclosed in dependent claims 13, 7 and 2 of the application, respectively. The opposition division held that the skilled person would have understood from the application as a whole that, despite the dependency of each of these dependent claims on claim 1 only, the respective subject-matter of these dependent claims could be combined. The board agrees because in this case, the disclosure in the claims is also present without the dependency in paragraphs [0005], [0006] and [0009] of the application. Paragraph [0005] discloses that "*In one embodiment, the platinum-resistant ovarian cancer is an epithelial ovarian cancer (EOC), a fallopian tube carcinoma (FTC), or a primary peritoneal carcinoma (PPC)*". Paragraph [0009] discloses bevacizumab as the antibody and paragraph [0006] discloses the same three chemotherapeutic agents as disclosed in claim 7. There remains only the selection of paclitaxel from the list of these three chemotherapeutic agents. Furthermore, this disclosure is reflected in the example.

33. Respondent IV also objected that the application as filed did not disclose an individualised embodiment in which the combination of paclitaxel and bevacizumab improved the PFS in comparison to paclitaxel alone for each of the three named diseases.

34. In view of the board's decision that EOC, FTC and PPC were treated as a single disease (see point 18. above), a disclosure of such an individualised embodiment is not required. In any case, the objection appears to be one of lack of sufficient disclosure under

Article 83 EPC rather than one of added-matter under Article 123(2) EPC.

Remittal to the opposition division (Article 111(1) EPC and Article 11 RPBA)

35. The board decided to remit the case to the opposition division for further prosecution under Article 111(1) EPC.

36. In exercising its discretion on whether or not to remit the case to the opposition division for further prosecution a board must take the circumstances of the individual case into account. These circumstances include *inter alia* whether the opposition division's decision dealt with all grounds for opposition raised by the opponents, procedural economy and the burden associated with dealing with issues not dealt with in the decision under appeal.

37. In the present case, the opposition division has not given a decision on the novelty or the inventive step of the subject-matter of the main request. Such a situation may represent "special circumstances" for remittal under Article 11 RPBA (see Case Law of the Boards of Appeal of the European Patent Office, 10th edition 2020, V.A.9.3,2). Moreover, remittal is in line with Article 12(2) RPBA which recounts the primary object of the appeal proceedings as review of the decision in a judicial manner, i.e. to give the losing party an opportunity to challenge the decision of the opposition division on its merits.

Right to be heard (Article 113(1) EPC)
Reimbursement of the appeal fee (Rule 103 EPC)

38. The question to be answered in deciding on reimbursement of the appeal fee under Rule 103(1)(a) EPC is whether or not the reimbursement is equitable by reason of a substantial procedural violation.

39. The appellant submitted that its right to be heard had been violated because it had not been given the opportunity to discuss the opposition division's objections under Article 83 EPC in relation to (former) auxiliary request 2 at the oral proceedings before the opposition division. In particular, it alleged that the meaning of the term "*endometrioid*" was not discussed in the context of auxiliary request 2 during the oral proceedings and that the first time this objection was raised was in the decision under appeal.

40. The board is of the view that the appellant's complaint is justified. An objection relating to a mismatch between the patients studied in Example 1 and those defined in claim 1, illustrated by the example of those suffering from "*endometrial adenocarcinoma*" was the central element of the opposition division's reasoning for holding that the invention defined in claim 1 of then pending auxiliary request 2 (now the main request) did not meet the requirements of Article 83 EPC. However, this objection was not mentioned in either the communication sent with the summons to oral proceedings or in the minutes of the oral proceedings before the opposition division in respect of the set of claims corresponding to the current main request. There is therefore no record of the appellant having had an opportunity to present its arguments on this matter.

41. In view of this factual situation, the board concludes that the appellant's right to be heard under Article 113(1) EPC was not respected and that a substantial procedural violation was committed by the opposition division in this respect. Moreover, since there is a causal link between substantial procedural violation and need to file an appeal, the refund of the appeal fee is equitable. The appeal fee is reimbursed in full.

Order

For these reasons it is decided that:

The decision under appeal is set aside.

The case is remitted to the opposition division for further prosecution.

The appeal fee is reimbursed.

The Registrar: The Chairwoman:

C. Moser M. Pregetter

Decision electronically authenticated