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**Datasheet for the decision of 6 July 2021**

**Case Number:** T 2923/18 - 3.3.07

**Application Number:** 11763292.7

**Publication Number:** 2552415

**IPC:** A61K9/14, A61K31/337, A61K31/555, A61P35/00, A61K45/06, A61N5/10, A61K33/24

**Language of the proceedings:** EN

**Title of invention:**
METHODS OF TREATING CANCER

**Patent Proprietor:**
Abraxis BioScience, LLC

**Opponents:**
Teva Pharmaceutical Industries Ltd
Generics (UK) Ltd

**Headword:**
Methods of treating cancer / ABRAXIS BIOSCIENCE

**Relevant legal provisions:**
EPC Art. 56

**Keyword:**
Inventive step - (no)

**Decisions cited:**
T 0715/03, T 1915/10

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**Case Number: T 2923/18 - 3.3.07**

# D E C I S I O N
# of Technical Board of Appeal 3.3.07
# of 6 July 2021

| | |
|---|---|
| **Appellant:** (Patent Proprietor) | Abraxis BioScience, LLC<br>86 Morris Avenue<br>Summit, NJ 07901 (US) |
| **Representative:** | Jones Day<br>Rechtsanwälte, Attorneys-at-Law, Patentanwälte<br>Prinzregentenstrasse 11<br>80538 München (DE) |
| **Respondent:** (Opponent 1) | Teva Pharmaceutical Industries Ltd<br>5 Basel Street<br>P.O. Box 3190<br>49131 Petah Tiqva (IL) |
| **Representative:** | D Young & Co LLP<br>120 Holborn<br>London EC1N 2DY (GB) |
| **Respondent:** (Opponent 2) | Generics (UK) Ltd<br>Station Close<br>Potters Bar<br>Hertfordshire EN6 1TL (GB) |
| **Representative:** | Elkington and Fife LLP<br>Prospect House<br>8 Pembroke Road<br>Sevenoaks, Kent TN13 1XR (GB) |
| **Decision under appeal:** | **Decision of the Opposition Division of the European Patent Office posted on 4 October 2018 revoking European patent No. 2552415 pursuant to Article 101(3)(b) EPC.** |

**Composition of the Board:**

| | |
|---|---|
| **Chairman** | A. Usuelli |
| **Members:** | E. Duval |
| | A. Jimenez |

## Summary of Facts and Submissions

I. European patent 2 552 415 ("the patent") was granted on the basis of 15 claims. Claim 1 of the patent related to a composition comprising nanoparticles comprising paclitaxel and an albumin for use in a method of treating non-small-cell lung cancer (NSCLC) in an individual, wherein the NSCLC is squamous cellular carcinoma (SCC), wherein the method further comprises administering a platinum-based agent to the individual.

II. Two oppositions were filed against the patent on the grounds that its subject-matter lacked novelty and inventive step, it was not sufficiently disclosed and it extended beyond the content of the application as filed.

III. The appeal was filed by the patent proprietor (appellant) against the decision of the opposition division to revoke the patent.

The decision was based on a main request filed (as auxiliary request 2) on 24 November 2017.

Claim 1 of this main request read as follows:

"A composition comprising nanoparticles comprising paclitaxel and an albumin for use in a method of treating NSCLC in a human, wherein the human is at least 70 years old, wherein the NSCLC is squamous cellular carcinoma, and wherein the method further comprises administering a platinum-based agent to the human."

IV. In the decision of the opposition division, reference was made to the following documents among others :

D1: Socinski *et al.*, *Retrospective analysis of a phase II study of nab-paclitaxel ...*, Journal of Thoracic Oncology, 2009, 4 (9S), p. S449
D2: Business Wire, *Results from a Phase 2 Study of ABRAXANE® in combination with carboplatin ...* , Aug. 03, 2009
D22: Kosmidis *et al.*, *Paclitaxel (175 mg/m$^2$) plus carboplatin (6 AUC) versus paclitaxel (225 mg/m$^2$) plus carboplatin (6 AUC) ...*, Annals of Oncology, 2000, 11, pp. 799-805
D29: Phase III NSCLC clinical trial CA 031
D30: Socinski *et al.*, *Safety and efficacy of weekly nab®-paclitaxel in combination with carboplatin ...*, Annals of Oncology, 2013, 24, pp. 314-321
D31: Ito *et al.*, *Low podoplanin expression of tumor cells predicts poor prognosis ...*, Lung Cancer, 2009, 63, pp. 418-424
D33: Expert Declaration of Dr. Rafia Bhore and CV
D34: https://clinicaltrials.gov/ct2/show/record/NCT00540514 (Tabular View)
D34a: https://clinicaltrials.gov/ct2/show/record/NCT00540514 (Study Details)
D36: Supplementary Expert Declaration of Dr. Rafia Bhore

V. In particular, the opposition division decided that:

(a) The main request met the requirements of Article 123(2) EPC and of sufficiency of disclosure.

(b) The subject-matter of the main request was novel over D1 and D2 because neither D1 nor D2 disclosed the treatment of patients at least 70 years old.

(c) D1 or D2 represented suitable closest prior art. The problem to be solved was the provision of a further group of patients responsive to the same therapy disclosed in D1 or D2. With regards to the post-published evidence D33 and D36, an improvement linked to the selected elderly patient group could not be taken into account because such an effect was not derivable from the application as filed. The claimed solution was obvious because it was seen as an arbitrary and obvious selection of a patient group.

VI. The patent proprietor (appellant) lodged an appeal against the decision of the opposition division. In its statement setting out the grounds of appeal, the appellant defended its case on the basis of the main request underlying the appealed decision (see III. above).

VII. Both opponent 1 (respondent 1) and opponent 2 (respondent 2) replied to the appeal. In the course of the appeal proceedings, respondent 1 filed the following documents:

D37: SEER Cancer Statistics Review 2001
D38: The approved prescribing information for Abraxane

VIII. The Board issued a communication under Article 15(1) RPBA setting out its preliminary opinion.

IX. Oral proceedings were held before the Board.

X. The appellant's arguments regarding inventive step for the main request can be summarised as follows:

D1 or D2 were suitable starting points for the problem-solution approach. Both documents taught *nab*-paclitaxel in combination with carboplatin for treating advanced NSCLC, wherein some of the patients had SCC.

Neither D1 nor D2 disclosed the claimed group of "at least 70 years old" patients.

The objective technical problem could be formulated as the provision of a subgroup of patients responsive to the combination therapy with *nab*-paclitaxel and a platinum-based agent.

The solution was a selection from the patients disclosed in D1 and D2 which was not rendered obvious by the prior art.

D1 and D2 reported on a retrospective analysis of a Phase II clinical study of *nab*-paclitaxel plus carboplatin in advanced NSCLC. D1 and D2 were not concerned with the analysis of clinical response in different age groups, and did not point to age as a potential differentiation criterion. Similarly, D22 did not provide a pointer towards the claimed specific group of patients of at least 70 years, because it related to a different study, and because in the study of D22, the patients were not stratified by age, and the age of patients ranged from 31.5 to 79.5 years (see Table 1 on page 801).

Furthermore, established EPO jurisprudence required that an "arbitrary and obvious selection" be a choice from a larger number of equally suitable alternative solutions to the technical problem which was not associated with any unexpected effect. Here, the skilled person would not have considered the claimed

elderly patient group as "equally suitable" compared to younger patients. On the contrary, D31 showed that patient age (>70 years) was a marker of poor outcome after complete resection of the affected lung site (see the Abstract and section 3.1 on page 420). D37 also reported a lower survival rate for elderly patients (see table XV.9). This indicated that the skilled person would not expect that older adults would be as responsive to the claimed treatment as any other group.

Considering the technical field of the invention, namely the field of cancer treatment, particularly treatment of elderly patients with SCC, it could not be reasonably expected that the claimed combination therapy would successfully treat the claimed elderly patients of at least 70 years old.

Hence the subject-matter of the main request involved an inventive step.

XI. The respondent's arguments regarding inventive step for the main request can be summarised as follows:

The closest prior art D1 and D2 disclosed the use of *nab*-paclitaxel (Abraxane®) in combination with carboplatin for the treatment of SCC. The distinguishing feature was the claimed patient group, namely humans who were at least 70 years old. The technical problem was the provision of a subgroup of patients responsive to the defined combination therapy.

The main request merely defined patients of an arbitrary age. In the absence of a technical effect, these patients were just an obvious embodiment of the prior art. The skilled person would have expected patients of all ages with SCC to be treated with the

known combination. As shown in D37, it was well known that NSCLC was far more prevalent in the age group of 70 years or older compared to the age group of 69 years or younger.

Hence the subject-matter of the main request did not involve an inventive step.

XII. The appellant requests that the decision under appeal be set aside, that the patent be maintained on the basis of the main request filed (as auxiliary request 2) on 24 November 2017 and that document D38 be not admitted into the proceedings

XIII. Both respondent 1 and respondent 2 request that the appeal be dismissed.

## Reasons for the Decision

1. Inventive step, main and sole request

1.1 The parties agree on the choice of D1 or D2 as closest prior art. The Board concurs.

Both D1 and D2 disclose the effective treatment, in a phase 2 study, of patients with SCC using nab-paclitaxel or Abraxane (i.e. a composition comprising nanoparticles comprising paclitaxel and albumin) in combination with carboplatin (a platinum-based agent).

1.2 The age of the patients is reported neither in D1 nor in D2. There is no direct and unambiguous disclosure in any of D1 and D2 that the patients were aged 70 years or older. Thus the subject-matter of claim 1 of the

main request differs in that the human to be treated is at least 70 years old.

1.3 As part of the problem-solution approach, the next step is to assess the technical effect(s) achieved by the claimed invention when compared with the closest state of the art, before defining the objective technical problem.

1.3.1 The differentiating feature, namely that the patient is at least 70 years old, is not stated, in the patent or in the application as filed, to result in any technical effect. This group of elderly patients is merely mentioned in paragraph [0109] of the application as filed, without any emphasis, among many other patient ages and characteristics. The data in the examples (see the studies of examples 1 and 2, pages 64-84) give no information about the age of the tested subjects, or about any effect associated therewith.

1.3.2 During the appeal proceedings, the appellant, relying on post-published evidence (D29, D30, D33 and D36), initially asserted that the claimed treatment achieved an *improved* effect in the claimed elderly patient group, as compared with other age groups. The respondents contested that this effect, and the evidence supporting it, could be taken into account for the formulation of the technical problem. However, during the oral proceedings before the Board, the appellant stated it did not want to rely on a improved effect associated with the treatment of patients older than 70 years for the assessment of inventive step. Consequently, this question of an improvement can be left unanswered.

1.3.3 Thus, all parties agree on the definition of the objective technical problem as the provision of a group of patients responsive to the combination therapy defined in claim 1, namely the combination of paclitaxel and albumin nanoparticles with a platinum-based agent.

1.4 The respondents do not dispute that the claimed combination therapy can treat SCC in humans aged 70 or older.

The Board sees no reason to differ and considers that the above problem is solved by the claimed subject-matter. The general efficacy of the claimed combination treatment against SCC is credibly shown in the patent (see the studies of examples 1 and 2). Although no information is given in examples 1 and 2 as to the age of the tested subjects, there is no cause to suspect that the claimed treatment would be ineffective in humans aged 70 years or older.

1.5 For the following reasons, the Board comes to the conclusion that the claimed solution does not involve an inventive step.

1.5.1 Just as the patent or the application as filed, D1 and D2 report the efficacy of the claimed combination treatment against SCC, without precision as to the age of the tested subjects. In this sense, the technical information given in the patent regarding responsiveness of elderly patients to the claimed combination therapy does not go beyond that of D1/D2.

1.5.2 The appellant asserted that the closest prior art did not give any reasonable expectation that patients aged 70 years or older would be effectively treated. The

Board firstly notes that this argument contradicts the appellant's position, and the opposition division's finding regarding sufficiency of disclosure, that the patent, which contains the same information, plausibly supports that the claimed combination therapy is effective in treating the claimed patient group (see the grounds of appeal, paragraph 1.3).

1.5.3 In any case, the Board comes to the conclusion that D1 and D2 give a reasonable expectation that the combination treatment would be effective also for patients aged 70 years or older, for the reasons given below. There is accordingly no need to rely on the post-published evidence D34 and D34a to conclude that the claimed combination therapy effectively treats patients aged 70 years or older, since this is already made credible both by the patent and by D1 and D2.

Although neither D1 nor D2 mention the age of the patients, a skilled person reading these documents would have no reason to suspect that patients aged 70 years or older were excluded from the study, or that the conclusion drawn therein as to the effectiveness of the treatment would not apply to elderly patients. D22 does not support the appellant's argument that older patient were under-represented in studies on SCC and thus constituted an unmet medical need, since the study in D22 covers patients aged from 31.5 to 79.5 years (see Table 1 on page 801), thus including humans aged 70 years or older.

On the contrary, since NSCLC is known to be prevalent in the elderly patient group (see D37, table XV-5), the silence in D1 and D2 can only be understood as an indication that no lack of responsiveness to the combination of paclitaxel-albumin nanoparticles with a

platinum-based agent was observed for older patients. Neither D31 (see the abstract and section 3.1 on page 420) nor D37 (see table XV-9) would lead the skilled reader to a different conclusion, since these documents do not concern the same treatment. The poor prognosis for older patients mentioned in D31 and D37 is not surprising considering their age and at any rate does not point to a lack of effectiveness of the combination therapy of D1/D2.

1.5.4 The technical problem is formulated as the provision of an alternative, namely the provision of a group of patients responsive to the claimed combination therapy. In light of D1 and D2, the skilled person would expect elderly patients to respond, to some level, to the claimed combination therapy. The extent of the response, in comparison with younger patients or otherwise, is in this respect not relevant. Consequently, the Board agrees with the respondents that the selection of humans aged 70 years or older does not, in the absence of associated technical effect, involve an inventive step.

In this respect, the present case can be distinguished from cases T 715/03 and T 1915/10 cited by the appellant. In T 715/03, starting from document (1) as closest prior art, the competent Board defined the problem to be solved as the provision of an alternative treatment for Tourette's syndrome. The claimed solution, namely the use of ziprasidone, was found to involve an inventive step because none of the cited documents gave any hint to the skilled person when looking for compounds suitable for the treatment of TS with respect to ziprasidone (see point 2.4.3 of the reasons). In T 1915/10, starting from the combination of detoxified Ply and PspA of the closest prior art

(D1), the competent Board defined the problem to be solved as the provision of an alternative composition useful for protection against a *S. pneumoniae* infection. The claimed solution was the combination of detoxified Ply and PhtD. The Board concluded that the skilled person would not be motivated to replace PspA by PhtD because the skilled person would not have considered PhtD to be a virulence factor (see point 22 of the reasons). The criteria of inventive step were accordingly fulfilled.

In contrast, in the present case, the skilled person would expect, in light of the prior art, that the selected group of patients be responsive to the claimed combination therapy.

1.6 Accordingly, the main request does not meet the requirements of Article 56 EPC.

**Order**

**For these reasons it is decided that:**

The appeal is dismissed.

The Registrar: The Chairman:

B. Atienza Vivancos A. Usuelli

Decision electronically authenticated