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Datasheet for the decision of 30 November 2023

Case Number: T 1210/20 - 3.3.02

Application Number: 08729939.2

Publication Number: 2124547

IPC: A01N33/16, A61K31/655

Language of the proceedings: EN

Title of invention:
CANCER TREATMENT METHOD

Patent Proprietor:
Novartis AG

Opponent:
HGF Limited

Headword:

Relevant legal provisions:
EPC Art. 123(2), 83

Keyword:
Amendments
Sufficiency of disclosure

Decisions cited:
G 0002/21, T 0667/08

Catchword:

Europäisches Patentamt
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Beschwerdekammern

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Case Number: T 1210/20 - 3.3.02

D E C I S I O N
of Technical Board of Appeal 3.3.02
of 30 November 2023

Appellant: (Opponent)	HGF Limited 1 City Walk Leeds Yorkshire LS11 9DX (GB)
Representative:	Elkington and Fife LLP Prospect House 8 Pembroke Road Sevenoaks, Kent TN13 1XR (GB)
Respondent: (Patent Proprietor)	Novartis AG Lichtstrasse 35 4056 Basel (CH)
Representative:	Carpmaels & Ransford LLP One Southampton Row London WC1B 5HA (GB)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 23 March 2020 rejecting the opposition filed against European patent No. 2124547 pursuant to Article 101(2) EPC.**

Composition of the Board:

Chairman	M. O. Müller
Members:	P. O'Sullivan
	B. Burm-Herregodts

Summary of Facts and Submissions

I. The appeal of the opponent (hereinafter appellant) lies from the decision of the opposition division according to which the opposition against European patent 2 124 547 was rejected.

II. The following documents *inter alia* were cited during opposition proceedings and referred to in appeal proceedings:

D9: O'Shaughnessy *et al.*, Clinical Cancer Research, February 2002, Vol. 8, pages 314-346

D10: Berman *et al.*, Cancer Detection and Prevention, 30(2006), pages 387-394.

III. In a communication pursuant to Article 15(1) RPBA sent in preparation for oral proceedings, the board *inter alia* expressed the preliminary view that the treatment of a precancerous syndrome with eltrombopag specifically to prevent cancer was credible on the basis of the anti-proliferative test data comprised within the examples of the application as filed.

IV. Oral proceedings by videoconference took place as scheduled on 30 November 2023 in the presence of both parties.

V. Requests relevant to the present decision

The appellant requested that the contested decision be set aside, and that the patent be revoked in its entirety.

The respondent (patent proprietor) requested as main request remittal of the case to the opposition division with the order to maintain the patent on the basis of the set of claims of auxiliary request 1a, or alternatively on the basis of one of the sets of claims of the auxiliary requests 1b-d, 2, 2a-d, 3, 3a-d, 4, 4a-d, 5, 5a-d, 6, 6a-d, 7, 7a-d, 8, 8a-d, 9, 9a-d, 10 and 10a-d, all submitted with the reply to the statement of grounds of appeal.

VI. For the relevant party submissions, reference is made to the reasons for the decision, below.

Reasons for the Decision

Main request (auxiliary request 1a submitted with the statement of grounds of appeal)

1. In appeal proceedings the appellant raised objections against the set of claims of auxiliary request 1a (main request) only in relation to added subject-matter and sufficiency of disclosure, and only against independent claims 15 and 18 and claims dependent thereon.

2. Article 123(2) EPC

3. Independent claims 15 and 18 read as follows:

"15. *Use of 3'-{N'-[1-(3,4-Dimethylphenyl)-3-methyl-5-oxo-1,5-dihydropyrazol-4-ylidene]hydrazino}-2'-hydroxybiphenyl-3-carboxylic acid and/or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for use in the treatment of a precancerous syndrome in a human in need thereof,* ***wherein the treatment is prevention of cancer.***

"18. *A pharmaceutical composition for use in the treatment of a precancerous syndrome in humans comprising 3'-{N'-[1-(3,4-Dimethylphenyl)-3-methyl-5-oxo-1,5-dihydropyrazol-4-ylidene]hydrazino}-2'-hydroxybiphenyl-3-carboxylic acid and/or a pharmaceutically acceptable salt thereof,* ***wherein the treatment is prevention of cancer.***" (bold denoting added text compared to claims 15 and 18 of the **patent as granted**).

3.1 The compound mentioned in these claims will be referred to in the following as "eltrombopag", the term used by the parties in appeal proceedings.

3.2 The appellant submitted that the above amendment compared to granted claims 15 and 18 lacked basis in the application as filed.

3.3 Hence the objection under Article 123(2) EPC for claims 15 and 18 of the main request concerns only the question of whether the application as filed provides basis for the limitation of the claimed treatment to the prevention of cancer. Basis for claim 15 or 18

absent this limitation (i.e. for claims 15 and 18 as granted) was not subject to an objection under Article 123(2) EPC.

3.4 The respondent submitted that basis for specifying that the treatment is "prevention of cancer" was provided in the application as filed, *inter alia* in the passage on page 14, lines 17-24, which read as follows:

"By the phrases "to a therapeutic extent", "treating" and "therapeutically effective amount" and derivatives thereof as used herein, unless otherwise defined, *is meant that amount of non-peptide TPO receptor agonist that will elicit the biological or medical response of a tissue, system, animal or human that is being sought, for instance, by a researcher or clinician. Furthermore, the term "therapeutically effective amount" means any amount which, as compared to a corresponding subject who has not received such amount, results in improved treatment, healing,* ***prevention****, lessening in severity or amelioration* ***of cancer****"* (emphasis added by the board)

3.5 The appellant argued that this passage merely defined the term "therapeutically effective amount", and did not describe the manner in which a precancerous syndrome is treated as specified in claims 15 and 18. In said claims, the context of the wording in the above passage had been changed to create a combination between the prevention of cancer and the treatment of precancerous syndromes which was absent from the application as filed, in contravention of Article 123(2) EPC.

3.6 The board acknowledges that the above passage does not provide literal basis for the amended portion of claims

15 and 18 of the main request. However, for the requirements of Article 123(2) EPC to be met, literal support in terms of an explicit disclosure is not required by Article 123(2) EPC (see for example T 667/08, reasons 4.1.4). What is required is that the amendment is directly and unambiguously derivable, in view of the common general knowledge, from the application as filed.

3.7 The cited passage belongs to the section of the application as filed entitled "detailed description of the invention", starting on page 5. Hence, it is clear that the various definitions provided therein for terms used throughout the application, including the definition of "therapeutically effective amount", apply to each and every embodiment disclosed later in the application as filed, such as the treatment of a precancerous syndrome (e.g. page 35, line 7 - page 36, line 11; claims 32-35).

3.8 The board also acknowledges that in the cited passage, the prevention of cancer is disclosed only in relation to the definition of therapeutic amounts, while there is at least no explicit restriction to therapeutic amounts in claims 15 and 18 of the main request. However, as argued by the respondent, while not explicitly stated in claims 15 and 18, the use of a "therapeutically effective amount" of eltrombopag is implicit by virtue of the fact that the prevention of cancer in a precancerous syndrome is required by said claims, since otherwise no therapeutic effect would occur.

3.9 In addition, the examples of the patent are all concerned with the anti-proliferative effect of eltrombopag, indicating that the intended treatment of

a precancerous syndrome disclosed in the application as filed at least includes the treatment to prevent cancer.

3.10 Therefore, the limitation in claims 15 and 18 to the treatment of a precancerous syndrome by prevention of cancer is directly and unambiguously disclosed in the application as filed.

3.11 The further arguments of the appellant failed to convince the board.

3.11.1 Firstly, it was argued that a selection from two separate lists was required to arrive at the subject-matter of claims 15 or 18. Specifically, a selection of "prevention" was required from among "*improved treatment, healing, prevention, lessening in severity or amelioration*" in the above passage (final two lines), and a selection of a precancerous syndrome was required from among the two possible treatments disclosed in the application as filed, namely cancer or a precancerous syndrome.

3.11.2 The board disagrees. First, such a formalistic approach ignores what the skilled person would understand, taking into account the teaching of the application as filed as a whole. Secondly, there is no true double selection in the view of the board, at least because in the latter alleged selection, one of the two possibilities is contradictory: one cannot "prevent" cancer in a cancer, because cancer is already present. Hence, the choice of prevention of cancer in the first alleged selection already implies the choice of a treatment of a precancerous syndrome, rather than the treatment of cancer, in the second alleged selection. Hence, insofar as a selection is required, a choice

must be made from a single list only. A choice of one member from a single list however does not contravene Article 123(2) EPC.

3.11.3 Secondly, the appellant argued that the "prevention of cancer" mentioned in the above passage was broader than the claimed prevention of cancer, which was limited to the prevention of cancer in a precancerous syndrome.

3.11.4 The board also disagrees. As set out above, the passage cited as basis by the respondent applies to each and every embodiment disclosed later in the application as filed, including the treatment of a precancerous syndrome. Hence, the treatment by prevention of cancer mentioned in said passage can be understood to apply directly and unambiguously *inter alia* to the treatment of a precancerous syndrome, and hence to the treatment referred to in claims 15 and 18 of the main request.

3.12 It follows from the foregoing that the subject-matter of claims 15 and 18 meets the requirements of Article 123(2) EPC.

4. Sufficiency of disclosure (Article 83 EPC)

4.1 Independent claim 15 set out above is a "Swiss-type" second medical use claim directed to the use of eltrombopag in the manufacture of a medicament for the treatment of precancerous syndrome wherein the treatment is prevention of cancer (hereinafter referred to simply as the "prevention of cancer in a precancerous syndrome"). Independent claim 18 is a second medical use claim pursuant to Article 54(5) EPC directed to a pharmaceutical composition comprising eltrombopag for use in the prevention of cancer in a precancerous syndrome.

4.2 Precancerous syndromes according to claims 15 and 18 include the diseases listed in dependent claim 16, such as aplastic anemia, hepatitis and cirrhosis. According to paragraph [0021] of the patent, precancerous syndromes are conditions which "can progress to cancer".

4.3 It is established case law that in a second medical use claim, the therapeutic effect, in the present case the prevention of cancer in a precancerous syndrome, is a technical feature of the claim. It was undisputed that the issue of whether this effect is achieved is a question of sufficiency of disclosure under Article 83 EPC.

4.4 The application as filed comprises examples with data demonstrating that eltrombopag elicits an anti-proliferative effect on several cancer cell lines ("Cancer Proliferation Assay", page 31 and associated table on page 32). This data is hereinafter referred to as the data in the application as filed. The credibility of this data was not called into question by the appellant insofar as the treatment of cancer was concerned.

4.5 The appellant argued however that the data in the application as filed did not constitute proof that eltrombopag was effective specifically in preventing a precancerous syndrome from progressing to cancer as required by claims 15 and 18. Such proof was required according to Enlarged Board of Appeal decision G 2/21, in particular in view of point 77 of the reasons for the decision. Since the application as filed was absent any proof of the claimed effect, the invention defined in claims 15 and 18 was not sufficiently disclosed.

4.6 Point 77 of G 2/21, cited by the appellant in support of the argument that proof is required reads as follows:

"*The reasoned findings of the boards of appeal in the decisions referred to above make clear that the scope of reliance on post published evidence is much narrower under sufficiency of disclosure (Article 83 EPC) compared to the situation under inventive step (Article 56 EPC). In order to meet the requirement that the disclosure of the invention be sufficiently clear and complete for it to be carried out by the person skilled in the art,* ***the proof of a claimed therapeutic effect has to be provided in the application as filed, in particular if, in the absence of experimental data in the application as filed, it would not be credible to the skilled person that the therapeutic effect is achieved****. A lack in this respect cannot be remedied by post-published evidence.*" (emphasis added by the present board)

4.7 The board acknowledges that as stated by the appellant, the data in the application as filed, which concerns the treatment of cancer, does not represent direct proof that eltrombopag is effective in preventing cancer in a precancerous syndrome.

4.8 However, the appellant's contention that according to the above paragraph of G 2/21, proof of a technical effect is unconditionally required in the application as filed, is not correct. Rather, this paragraph refers to the requirement for proof in the application as filed in particular if it would not be credible to the skilled person that the claimed therapeutic effect is achieved on the basis of the application as filed. The

corollary of this statement is that if a therapeutic effect is rendered credible by the application as filed, then such proof - in terms of concrete experimental data - may not be necessary.

4.9 This understanding is also supported by point 74 of the reasons (final paragraph) of G 2/21, in which the Enlarged Board stated that at the date of filing it must be rendered credible that the therapeutic agent in question is suitable for the claimed therapeutic application. Hence this paragraph is consistent with point 77 of the decision in that it does not state that proof in the application as filed is a requirement for sufficiency of disclosure to be acknowledged.

4.10 Hence, in order to fulfill the requirements of sufficiency of disclosure, it is enough that the application as filed renders the claimed therapeutic application credible.

4.11 Since the application as filed is read by the skilled reader, the reader's common general knowledge at the filing date can be taken into account when deciding whether the purported technical effect is rendered credible by the application as filed.

4.12 The respondent argued that it had been understood since long before the filing date of the application that cells at the precancerous stage were in the progression from normal healthy cells to cancerous cells, and were recognised to share many of the same characteristics of cancer cells. The respondent referred in this respect to D9 and D10, and argued that on the basis of the information therein, the application as filed credibly demonstrated that eltrombopag was effective in preventing cancer in a precancerous syndrome.

4.13 D9 is a journal article published in 2002 providing the recommendations of the American Association for Cancer Research Task Force on the treatment and prevention of intraepithelial neoplasia, a synonym for precancer according to the abstract (first line). D9 therefore represents the common general knowledge of the skilled person at the filing date of the application.

4.14 It is explained in the abstract of D9 that precancer has *inter alia* some phenotypic characteristics of invasive cancer that predict a substantial likelihood of developing invasive cancer. Figure 1 on page 315 graphically illustrates how the progression of a collection of normal cells (left hand side of the figure) can gradually progress to cancer via the stages of precancer (right hand side of the figure). Specifically, the central three images depict stages characterised by mild, moderate and severe dysplasia (i.e. the abnormal development of cells). The second and third of these central stages is also characterised as IEN, or precancer (see text below the said three graphics).

4.15 As argued by the respondent and not disputed by the appellant, figure 1 of D9 progressively depicts the increasing proliferation of cell numbers from normal cells to precancerous cells and finally to cancer cells. Hence, precancerous conditions are at least partly characterised by abnormally proliferating cells.

4.16 The respondent also referred to D10 in support of its arguments.

D10 is a review article published in 2006 entitled "Precancer: A conceptual working definition - Results of a Consensus Conference". Similarly to D9, it represents the common general knowledge of the skilled person at the filing date of the patent. The authors of D9 discuss the difficulties of distinguishing between a "precancer" and a "cancer". It is stated that the properties most often used to distinguish precancers from cancers on a practical level are stromal invasion and the ability to spread (D10, page 390, right hand column, point 3.3.4). Furthermore in point (3) of this paragraph it is indicated that the difference between a population of precancer cells and a population of cancer cells tends to be superficial and unrelated to the cancer phenotype, and in point (4) that the features of the cancer phenotype are found in precancers.

Hence, as argued by the respondent, on the basis of the information in D10, since abnormal proliferation is indisputably an important characteristic of cancer, the same must apply to precancers which are said to possess the same phenotypic characteristics. This is consistent with the disclosure in D9 of the progression of normal cells to cancer cells illustrated in figure 1, and the statement in the abstract thereof that precancer has some of the phenotypic characteristics of invasive cancer.

4.17 As established above, the data in the application as filed credibly demonstrates the anti-proliferative effect of eltrombopag. Since as set out above it was known at the filing date of the patent that precancerous conditions are also at least in part characterised by abnormally proliferating cells, it is credible on the basis of this data that eltrombopag is also effective in the treatment of precancerous syndromes by prevention of cell proliferation, and hence the prevention of cancer. No evidence to the contrary was submitted by the appellant.

Consequently, the invention defined in claims 15 and 18 of auxiliary request 1a is disclosed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.

5. Conclusion

Since there were no further objections from the appellant in relation to the claims of auxiliary request 1a, this request is allowable.

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 with the order to maintain the patent on the basis of the claims according to auxiliary request 1a and a description to be adapted thereto, where applicable.

The Registrar: The Chairman:

M. Schalow M. O. Müller

Decision electronically authenticated