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Datasheet for the decision of 1 February 2018

Case Number: T 1044/14 - 3.3.04

Application Number: 09709538.4

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Language of the proceedings: EN

Title of invention:
Method of treating prostate cancer with the GNRH antagonist degarelix

Applicant:
Ferring B.V.

Headword:
Method of treating prostate cancer/FERRING

Relevant legal provisions:
EPC Art. 54, 123(2)

Keyword:
Main request - novelty - (no)
Auxiliary request - amendments - allowable (no)

Decisions cited:
T 1399/04

Catchword:

Europäisches Patentamt
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Case Number: T 1044/14 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 1 February 2018

Appellant: (Applicant)	Ferring B.V. Polaris Avenue 144 2132 JX Hoofddorp (NL)
Representative:	Bates, Philip Ian Reddie & Grose LLP The White Chapel Building 10 Whitechapel High Street London E1 8QS (GB)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 5 December 2013 refusing European patent application No. 09709538.4 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairwoman	G. Alt
Members:	M. Montrone
	L. Bühler

Summary of Facts and Submissions

I. An appeal was lodged by the applicant (hereinafter "appellant") against the decision of the examining division to refuse European patent application No. 09 709 538.4. The application was filed as an international application and published as WO 2009/101530 (hereinafter "the application as filed") with the title "*Method of treating prostate cancer with the GNRH antagonist degarelix*".

II. The examining division held in the decision under appeal that claim 1 of the main request and auxiliary request 1 related to subject-matter extending beyond the content of the application as filed and that the subject-matter of claims 6 and 7 of auxiliary request 1 lacked novelty over the disclosure of several documents, including D6 (van Poppel *et al.*, Europ. Urol. Supp., vol. 5, 2006, page 251).

III. With the statement of grounds of appeal, the appellant submitted a main request and an auxiliary request which were both different from the requests dealt with in the decision under appeal.

IV. The appellant was informed of the board's preliminary view in a communication pursuant to Article 15(1) RPBA. The board indicated that claim 1 of the main request related to subject-matter extending beyond the content of the application as filed and that the subject-matter of claim 1 of auxiliary request 1 lacked novelty in view of the disclosure of document D6.

V. Oral proceedings before the board were held on 1 February 2018, during which the appellant inverted the order of its requests.

Thus, claim 1 of the main request reads:

"1. A composition comprising degarelix for use in the treatment of locally advanced prostate cancer in a subject, the treatment having a reduced incidence and/or likelihood of arthralgia in the treated subject."

Claim 1 of auxiliary request 1 reads:

"1. A composition comprising degarelix for use in reducing the incidence and/or likelihood of arthralgia in a subject with locally advanced prostate cancer."

VI. The appellant's arguments, as far as they are relevant to the present decision, may be summarised as follows:

Main request

Novelty (Article 54 EPC) - claim 1

Claim 1 related to a composition comprising degarelix for use in the treatment of locally advanced prostate cancer in a subject, the treatment having a reduced incidence and/or likelihood of arthralgia in the treated subject.

Document D6 disclosed a clinical trial wherein subjects with prostate cancer were treated with degarelix. The document mentioned that the patients were at four different stages of the disease, one being locally advanced prostate cancer. However, it was not derivable from document D6 that patients with locally advanced prostate cancer were singled out or selected with the expectation of a reduced arthralgia in the course of the treatment with degarelix compared with other patients in the study.

The feature "*in the treatment of locally advanced prostate cancer in a subject, the treatment having a reduced incidence and/or likelihood of arthralgia in the treated subject*" referred to in claim 1 was a technical effect that led to a new medical application, namely (i) the treatment of a specific group of patients, i.e. those with locally advanced prostate cancer, benefiting from (ii) a reduced arthralgia as one of the side effects caused by the treatment.

The group was not arbitrarily selected, as there was a functional relationship between the particular physiological or pathological status of this group (locally advanced breast cancer) and the pharmacological effect achieved (arthralgia).

The selected group overlapped with the whole group disclosed in document D6 only to a small extent, by 32%.

Thus, the subject-matter of claim 1 met all the criteria required for acknowledging a new patient sub-group developed by the case law in, for example, decision T 1399/04.

Auxiliary request 1

Amendments (Article 123(2) EPC) - claim 1

The subject-matter of claim 1 had a basis in claims 1, 11 and 12 as filed in conjunction with the disclosure in paragraphs [009], [011], [023] and [024] of the application as filed. In particular, paragraphs [009] and [011] disclosed that the treatment resulted in a reduced risk of side effects, including arthralgia.

VII. The appellant requested that the decision under appeal be set aside and that the case be remitted to the examining division with the order to grant a patent on the basis of the set of claims of the main request filed as auxiliary request 1 with its statement of grounds of appeal, or, alternatively, on the basis of the set of claims of auxiliary request 1, filed as the main request with its statement of grounds of appeal.

Reasons for the Decision

Main request

Novelty (Article 54 EPC)

1. Claim 1 is directed to a composition comprising degarelix for use in the treatment of locally advanced prostate cancer, the treatment having a reduced incidence and/or likelihood of arthralgia.

2. It is established case law of the boards of appeal that the use of a compound that is known in the treatment of a disease of a particular group of subjects can represent a novel application in the treatment of the same disease with the same compound, provided that it is carried out on a new group of subjects which is distinguished from the former by its physiological or pathological status (see Case Law of the Boards of Appeal of the EPO, 8th edition 2016 ("CLBA"), I.C.6.2.3 a)).

3. Document D6 discloses a multi-centre randomised one-year clinical study of degarelix in the treatment of patients suffering from prostate cancer (see title).

With regard to the patients, the document reports in the paragraph headed "*MATERIAL & METHODS*" that "*187 patients (age 52-93, median 72 years) with histologically confirmed CaP and PSA ≥2 ng/mL received degarelix subcutaneously every 28 days. Median baseline T was 4.4 ng/mL and PSA was 28 ng/mL. 19% of patents had metastatic, 32% had locally advanced and 22% had localised CaP, 27% were M0/MX and not T-staged. Tumour grade was well differentiated (Gleason 2-4) in 19%, moderately differentiated (5-6) in 41%, and poorly differentiated (7-10) in 39% of the patients*" ("*CaP*", "*PSA*" and "*T*" are the abbreviations of prostate cancer, prostate specific antigen and testosterone respectively; see paragraph headed "*INTRODUCTION & OBJECTIVES*" in document D6; remark and emphasis added by the board).

4. Thus, document D6 discloses that the 187 patients enrolled in the study comprise four groups of prostate cancer patients characterised by different tumour stages, including one group diagnosed with locally advanced prostate cancer ("*32%*"). Furthermore, it is derivable from the statement "*187 patients* [...] *with histologically confirmed CaP*" in document D6 that the determination of the pathological status of the individual patients and their separation into four groups took place before the actual treatment with degarelix started.

5. Document D6 further discloses that the therapeutic effect was assessed by measuring testosterone and PSA levels. It reports, in relation to the patients who finished the study, that "*Degarelix treatment for one year resulted in a fast, profound and sustained suppression of testosterone (<0.5 ng/ml) and fast, profound and sustained reduction of PSA levels.*

Degarelix was well tolerated without evidence of testosterone surge or systemic allergic reactions."

6. Consequently, document D6 discloses that patients with locally advanced prostate cancer had been treated with degarelix as a sub-group of the 187 patients, but it does not disclose that any of the treated patients, in particular those diagnosed with locally advanced prostate cancer, had a "*reduced incidence and/or likelihood of arthralgia*".

7. The appellant argued that the patients referred to in claim 1 represented a sub-group of the locally advanced prostate cancer patients reported in document D6, since the patients were singled out in the expectation of having a reduced incidence rate and/or likelihood for developing arthralgia, which, moreover, related to a new technical effect. Therefore, the patient group referred to in claim 1 was not arbitrarily selected and overlapped with the patient group in document D6 by 32% only. The pathological and physiological status of this patient group was consequently different from the status of the patient group disclosed in document D6, and met all of the criteria developed by the case law for acknowledging a new patient sub-group (see e.g. decision T 1399/04, point 35 of the reasons).

8. The board is not convinced by these arguments, for the following reasons.

8.1 Firstly, as set out in point 4 above, document D6 discloses the treatment of four sub-groups of prostate cancer patients by the administration of degarelix, including a group of patients diagnosed with a locally advanced prostate cancer stage. Thus, the sub-groups disclosed in document D6 are distinguished from each

other by their pathological status. Furthermore, there is no evidence on file that the expectation of a lower incidence rate for developing degarelix-associated arthralgia has an impact on the pathology or physiology of locally advanced prostate cancer patients. This has also not been argued by the appellant.

8.2 Secondly, arthralgia, i.e. joint pain, is a serious adverse effect experienced by a low percentage of prostate cancer patients treated with androgen deprivation therapies (see e.g. paragraph [052] of the application as filed). In this context, the application as filed discloses that "*9% of leuprolide patients experienced arthralgia (joint pain) during the course of treatment while only 4% of all degarelix-treated patients experienced arthralgia*" (see paragraph [0195]). This effect is "*statistically significant*" in patients suffering from locally advanced prostate cancer treated with degarelix compared to "*LUPRON DEPOT^{TM}*" (see paragraph [0231] and Table 12).

8.3 In the board's view, it is derivable from the passages cited in point 8.2 above that arthralgia is a side effect experienced by all androgen deprivation therapies, including degarelix. Thus, the development of arthralgia is necessarily linked to the administration of degarelix. Moreover, since the group of locally advanced prostate cancer patients disclosed in Table 12 of the application as filed is characterised by this pathological status only, a statistically significant incidence rate of "*2%*" arthralgia indicates that all patients belonging to this group are likewise affected by this low incidence rate. In other words, it is derivable from the application as filed that the low risk of developing arthralgia is inherently associated with all patients

affected by locally advanced prostate cancer when treated with degarelix.

8.4 Document D6 discloses that one of the patient groups is likewise diagnosed with locally advanced prostate cancer and treated by degarelix (see point 3 above). Thus, in view of point 8.3.above, the patients in this group experience inherently the same low incidence rate for developing arthralgia as all other patients in this group. Therefore, neither the singling out of patients in the expectation of a reduced incidence rate nor the reduced incidence rate as a technical effect are physiological or pathological characteristics distinguishing the patients referred to in claim 1 from the locally advanced prostate cancer patients disclosed in document D6.

9. The present situation therefore differs from the case dealt with in decision T 1399/04, where members of the patient group were described as being "*infected by a specific genotype of HCV, genotype 1, which is a pathological characteristic allowing to differentiate members of this group from all other HCV patients, and it is further defined by a viral load of greater than 2 million copies per ml of serum, which is a physiologically characterising feature*" (see point 35 of the reasons, emphasis added). Since in the hepatitis C virus (HCV) patients disclosed in the prior art neither the specific genotype of the HCV nor the actual virus load were determined, a distinction could be made between members of the two groups based on their individual "*physiological and pathological status*" (see point 35 of the reasons).

10. In view of the reasons set out in point 8.4 above, the appellant's considerations that the patient group referred to in claim 1 was not an arbitrary selection or that it only overlapped with another group to a small extent are not relevant and need not be dealt with by the board for the purposes of this decision.

11. The board therefore concludes that the subject-matter of claim 1 is not novel in view of the disclosure of document D6, and hence that the main request does not meet the requirements of Article 54 EPC.

Auxiliary request 1

Amendments (Article 123(2) EPC)

12. In contrast to claim 1 of the main request, which uses degarelix for "the treatment of locally advanced prostate cancer", claim 1 of auxiliary request 1 uses degarelix for "reducing the incidence and/or likelihood of arthralgia in a subject with locally advanced prostate cancer".

13. In the board's view, the skilled person would construe the claim such as to encompass treatments of arthralgia not caused by the administration of degarelix, for example, the treatment of a pre-existing arthralgia in locally advanced prostate cancer patients.

14. The issue to be assessed with regard to Article 123(2) EPC is whether or not the skilled person would derive such a treatment directly and unambiguously, using common general knowledge, and seen objectively and relative to the date of filing, from the disclosure of the application as a whole (see CLBA, II.E.1).

15. In the following, the references are to paragraphs and claims in the application as filed.

16. The appellant argued that the subject-matter of claim 1 had a basis in claims 1, 11 and 12 in conjunction with the disclosure in paragraphs [009], [011], [023] and [024] of the application.

17. Claims 1, 11 and 12 read as follows:

"*1. A composition comprising degarelix for the treatment of prostate cancer in a subject, the treatment having a reduced incidence and/or likelihood of a side effect other than an injection site related side effect*".

"*11. A composition according to any preceding claim for treatment with reduced incidence and/or likelihood of one or more of a musculoskeletal disorder and/or a connective tissue disorder in the treated subject*".

"*12. A composition according to claim 11 for treatment with reduced incidence or likelihood of arthralgia and/or musculoskeletal stiffness*".

18. Thus, the subject-matter of claim 12 in combination with claims 1 and 11 is directed to compositions comprising degarelix for use in the treatment of prostate cancer, wherein the treatment has a reduced likelihood or incidence rate of certain diseases, including arthralgia. Therefore, claim 12 is directed to the treatment of prostate cancer and not to the treatment of arthralgia.

19. Furthermore, paragraph [023] in the application reads as follows: "*In still further embodiments, the treated subject has a decreased likelihood of developing or experiencing an increase in arthralgia and/or musculoskeletal stiffness during treatment compared to treatment with the gonadotrophin releasing hormone (GnRH) agonist leuprolide. In particularly useful embodiments thereof, the treated subject has locally advanced prostate cancer*" (emphasis added). A similar disclosure is derivable from paragraph [024] in the application.

20. In the board's view, the skilled person would construe the term "*treated subject*" in the passage of the application in point 19 above as referring to subjects having received degarelix in the treatment of disorders mentioned either in paragraphs [023] and [024] of the application or in the preceding ones. The treatment of arthralgia as a separate, non-degarelix associated disorder is not mentioned in any of these paragraphs in the application.

21. Paragraph [009] in the application reads as follows: "*Applicants have found that a relatively low dose of degarelix GnRH antagonist, delivered about once every 28 days (e.g., monthly), can safely and rapidly suppress testosterone levels to therapeutic levels in prostate cancer patients, without causing a testosterone spike and with an appreciably diminished risk of causing an undesirable side effect (other than an administration site e.g. injection site related side effect) associated with androgen deprivation therapy such as a cardiac disorder, arthralgia, and/or a urinary tract infection. Advantages of the use of degarelix for the treatment of prostate cancer may include a diminished likelihood of occurrence and/or*

diminished severity of symptoms of adverse reactions, adverse events or side effects to organs or tissues" (emphasis added).

21.1 Furthermore, paragraph [011] in the application reads as follows: "*The treatment may be with, or associated with, a reduced incidence or likelihood of one or more of cardiovascular and/or vascular side effects (for example with reduced incidence and/or likelihood of one or more of myocardial infarction, chest pain, chest pain development, cardiac murmur, cardiac murmur development, myocardial ischemia, atrioventricular blockage, deep vein thrombosis (DVT), cardiac arrhythmia, coronary artery disorder, and/or cardiac disorder), musculoskeletal disorder (for example arthralgia [...])*" (emphasis added).

21.2 In the board's view, the skilled person would derive from paragraph [009] in point 21 above that the administration of degarelix treats prostate cancer by suppressing testosterone which is accompanied by a reduced risk of developing treatment-associated side effects including arthralgia. Thus, in the light of the disclosure in paragraph [009], the statement in paragraph [011] of the application (see point 21.1 above) reading that the "*treatment may be with, or associated with, a reduced incidence or likelihood of one or more [...] musculoskeletal disorder (for example arthralgia [...])*" can only be understood as referring to the treatment of disorder(s) mentioned in the preceding paragraphs [009] and [010], which is "*prostate cancer*" (see point 21 above).

22. Therefore, none of the passages in the application as filed and relied on by the appellant disclose directly and unambiguously a treatment of arthralgia *per se* by

the administration of degarelix in a subject with locally advanced prostate cancer as encompassed by the subject-matter of claim 1. Consequently, claim 1 comprises subject-matter which extends beyond the content of the application as filed, and auxiliary request 1 does not therefore meet the requirements of Article 123(2) EPC.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairwoman:

P. Cremona G. Alt

Decision electronically authenticated