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Datasheet for the decision of 22 September 2020

Case Number: T 0777/17 - 3.3.04

Application Number: 09711390.6

Publication Number: 2249859

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Language of the proceedings: EN

Title of invention:
Treatment of metastatic stage prostate cancer with degarelix

Patent Proprietor:
Ferring B.V.

Opponent:
Generics (UK) Ltd (trading as Mylan)

Headword:
Degarelix in metastatic stage prostate cancer/FERRING

Relevant legal provisions:
EPC Art. 56
RPBA Art. 13
RPBA 2020 Art. 25, 13

Keyword:
Main request, auxiliary requests 2 and 3 - Inventive step (no)
Auxiliary requests 1 and 4 to 7 - admitted into the proceedings (no)
Late-filed argument - admitted into the proceedings (no)

Decisions cited:
T 0967/97, T 1742/12

Catchword:

Europäisches Patentamt
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Beschwerdekammern

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Case Number: T 0777/17 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 22 September 2020

Appellant: (Opponent)	Generics (UK) Ltd (trading as Mylan) Albany Gate Darkes Lane Potters Bar EN6 1AG Hertfordshire (GB)
Representative:	Elkington and Fife LLP Prospect House 8 Pembroke Road Sevenoaks, Kent TN13 1XR (GB)
Respondent: (Patent Proprietor)	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 Opposition Division of the European Patent Office posted on 13 February 2017 rejecting the opposition filed against European patent No. 2249859 pursuant to Article 101(2) EPC.**

Composition of the Board:

Chairman	B. Claes
Members:	D. Luis Alves
	P. de Heij

Summary of Facts and Submissions

I. European patent No. 2 249 859, entitled "*Treatment of metastatic stage prostate cancer with degarelix*", was granted on the basis of European patent application No. 09 711 390.6, filed as an international application published as WO 2009/101533.

II. The opponent (appellant) filed an appeal against the opposition division's decision to reject the opposition. The opponent had invoked Article 100(a) EPC in combination with Articles 54 and 56 EPC and Article 100(b) EPC as grounds of opposition.

III. With their reply to the appeal, the patent proprietor (respondent) requested that the appeal be dismissed (main request) or, alternatively, that the decision under appeal be set aside and the patent be maintained on the basis of the claims according to re-submitted auxiliary request 1 or 2, dealt with in the decision under appeal. In support of their case they filed four further documents.

IV. Prior to the board issuing summons to oral proceedings, both the appellant and the respondent made further submissions, the former including three further documents and the latter including one further document.

V. In response, by letter dated 23 December 2019, the respondent submitted further arguments and filed sets of claims in auxiliary requests 3 to 6.

VI. Thereafter the appellant addressed, *inter alia*, inventive step (Article 56 EPC) and added subject-matter (Article 123(2) EPC) concerning the claims of auxiliary requests 3 to 6.

VII. In a communication pursuant to Article 15(1) RPBA 2020, the board informed the parties of its preliminary opinion on some of the substantive and legal matters concerning the appeal. In particular, the board considered that the patent did not provide sufficiently clear and complete information for the claimed invention to be carried out by the skilled person, and that the claimed subject-matter was novel over the disclosure of document D14 but did not involve an inventive step over that disclosure. The same conclusions seemed to apply to auxiliary requests 1 and 2. Whilst the board was minded not to admit auxiliary requests 3 to 6 into the appeal proceedings, it also noted that its negative assessment on inventive step seemed to apply to these requests as well.

VIII. By letter dated 20 August 2020, the respondent requested that the oral proceedings be postponed.

IX. The following day, the respondent requested, on an auxiliary basis, to attend the oral proceedings with more than two persons and replied to the preliminary opinion expressed in the board's communication. They filed two further documents. By letter dated 25 August 2020 the appellant requested that the oral proceedings not be postponed.

X. The board informed the parties in a communication that the respondent's request for the oral proceedings to be postponed was not allowed, but that the request for attending with more than two persons was allowed.

XI. Subsequently, the respondent requested that the oral proceedings be held by video conference. The appellant agreed.

XII. Oral proceedings were accordingly held by video conference on the date as scheduled previously. At the oral proceedings the respondent filed a set of claims in a new auxiliary request 1 and renumbered the previous auxiliary requests 1 to 6 as auxiliary requests 2 to 7, respectively.

At the end of the oral proceedings, the respondent requested that it be recorded in the minutes of the oral proceedings and in the decision that they had requested that the oral proceedings be postponed, which had however been rejected, and that this rejection had been detrimental to their case.

Subsequently, the chair announced the board's decision.

XIII. Claim 1 of the **main request** (identical to claim 1 of the patent as granted, see section III.) reads:

"1. A composition comprising degarelix for use in the treatment of metastatic stage prostate cancer in a subject identified as having a baseline serum alkaline phosphatase (S-ALP) level of 200 IU/L or greater (prior to treatment)."

Claim 1 of **auxiliary request 1** (see section XII.; differences from the main request emphasised by the board) reads:

"1. A composition comprising degarelix for use in the treatment of metastatic stage prostate cancer <u>to treat</u>

skeletal or bone metastasis in a subject identified as having a baseline serum alkaline phosphatase (S-ALP) level of 200 IU/L or greater (prior to treatment)."

Claim 1 of **auxiliary request 2** (see section III.) differs from claim 1 of the main request in that it comprises the additional feature:

"wherein the subject has a hemoglobin (Hb) level of 130g/L or less".

Claim 1 of **auxiliary request 3** (see section III.; differences from the main request emphasised by the board) reads:

"1. A composition comprising degarelix for use in the treatment of metastatic stage prostate cancer in a subject identified as having a baseline serum alkaline phosphatase (S-ALP) level of 300 IU/L or greater (prior to treatment), wherein the subject has a hemoglobin (Hb) level of 130g/L or less."

Claim 1 of **auxiliary request 4** (see section V.) differs from claim 1 of the main request in that it comprises the additional features:

"wherein the treated subject's S-ALP is reduced by at least 50 IU/L below the baseline level for a period extending beyond 364 days".

Claim 1 of **auxiliary request 5** (see section V.) differs from claim 1 of the main request in that it comprises the additional features:

"wherein the treated subject's S-ALP is reduced by at least 50 IU/L below the baseline level for a period

extending beyond 364 days until at least day 448 of treatment".

Claim 1 of **auxiliary requests 6 and 7** (see section V.) differs from claim 1 of auxiliary requests 4 and 5, respectively, in that it comprises the additional features:

"and wherein the composition is for administration at an initial dose of degarelix of about 240 mg; and at a maintenance dose of about 80 mg degarelix once every approximately 28 days of treatment."

XIV. The following documents are referred to in this decision:

D10: Debruyne F.M.J., Reviews in Urology, 6, suppl. 7, 2004, pages S25-S32.

D14: Klotz L. *et al.*, BJU International, 102 (11), December 2008, pages 1531-1538.

D19: Chernecky C.C., Berger B.J.: "Laboratory Tests and Diagnostic Procedures", fifth edition, Saunders, 2008, pages 119-120.

D22: Magnusson P. *et al.*, Clinical Chemistry, 44(8) part 1, August 1998, pages 1621-1628.

D23: Medline Plus Medical Encyclopedia: ALP (22 February 2007).

D26: Huggins Charles *et al.*, Cancer Research, 1, 1941, pages 293-297.

D26a: Huggins Charles *et al.*, The Journal of Urology, vol. 168, 2002, pages 9-12.

D27: Van Poppel Hendrik *et al.*, Urology, vol. 71, 2008, pages 1001-1006.

XV. The appellant's arguments, insofar as relevant to the decision, may be summarised as follows:

Main request - claim 1
Inventive step (Article 56 EPC)

Document D14 disclosed the treatment of prostate cancer patients with degarelix. About 20% of the treated patients suffered from metastatic stage disease (Table 2). Nearly 100% of the patients responded to the treatment (page 1533, right-hand column, last paragraph), and thus also metastatic stage patients.

The technical effect to be taken into account for the formulation of the objective technical problem should be achieved by the feature differentiating the claimed invention from the disclosure representing the closest prior art. In this case, this feature was that the patient to be treated was "identified as having a baseline serum alkaline phosphatase (S-ALP) level of 200 IU/L or greater (prior to treatment)."

However, no such technical effect could be ascertained from Figures 1 and 3 of the patent because they did not relate to the treatment effect in patients characterised by s-ALP levels of 200 IU/L or greater. The objective technical problem was therefore the provision of an alternative patient group to be treated with degarelix. The patient group from claim 1 was an

arbitrary selection, specified by an arbitrary marker. The claimed subject-matter was therefore obvious.

The claimed degarelix composition for use in the treatment of metastatic stage prostate cancer patients was not restricted to those patients with bone metastasis. While the claim recited a particular minimum level of s-ALP in the treated patient group, only the bone isoform of s-ALP correlated with bone metastasis (see documents D19, D22 and D23).

There was no evidence in the proceedings that s-ALP levels as required by the claim were an indicator of very high levels of metastasis or of patients that were particularly difficult to treat.

Even assuming that s-ALP levels reflected bone metastasis, the claimed subject-matter lacked an inventive step. The skilled person expected metastatic stage prostate cancer patients to benefit from treatment with degarelix, irrespective of whether they suffered from metastasis to the bone or elsewhere. Indeed, most metastasis in prostate cancer was to the bone (documents D27, page 1002, left-hand column, last paragraph and D10, abstract).

It was entirely predictable for the skilled person that degarelix would suppress testosterone and delay progression of the disease to hormone-refractory stage. Documents D26 and D27 disclosed the mechanism of action of degarelix to provide testosterone suppression and not to act directly on bone.

As concerns a comparison with leuprolide, antagonists were known to be preferable to agonists. They were always beneficial and in particular for patients with

bone metastasis (D27, figure 2; abstract; page 1001, first paragraph and page 1002, right-hand column, second and last paragraphs).

The study described in document D14 was designed as a "non-inferiority study" over a period of one year, as was common for comparison with state-of-the-art approved medicines. This did not mean, however, that the authors did not conclude the treatment with degarelix to be superior to that with leuprolide, and in fact they did so. The fact that five patients discontinued treatment did not provide teaching leading away from the treatment with degarelix because, in fact, five patients in a total of 400 would not be seen as a bad result.

The disclosure of document D10 would not have discouraged the skilled person from using degarelix, which was known to be more effective than abarelix in suppressing testosterone (see document D27, Table 1 and page 1004, right-hand column, third paragraph to page 1005, left-hand column, second paragraph).

Admittance of a line of argument into the appeal proceedings

The respondent's line of argument that degarelix had an effect not only on testosterone suppression but also directly on the cancer cells should not be admitted into the proceedings.

It was presented at the oral proceedings for the first time and was not supported by any evidence.

Auxiliary request 1
Admittance into the appeal proceedings

The request should not be admitted into the appeal proceedings.

It was filed at the latest possible stage in the appeal proceedings and should have been filed earlier in the opposition proceedings.

The request was not a response to new developments. In fact, the argument that the s-ALP levels defined in claim 1 did not limit the claimed composition to use in the treatment of patients suffering from bone metastasis had already been raised in the opposition proceedings and again in the appeal proceedings. The board had also already expressed the opinion that the subject-matter of claim 1 lacked an inventive step in its communication pursuant to Article 15(1) RPBA 2020.

The claim request was not clearly allowable (no specific details were submitted in this context).

Auxiliary request 2
Admittance into the appeal proceedings

This claim request should not be admitted into the appeal proceedings (Article 12(4) RPBA 2007).

Admittance of a line of argument into the appeal proceedings

The respondent had argued that the treatment of the patients as defined by the haemoglobin and s-ALP levels in claim 1 related to patients who were close to

hormone-refractory stage. The results in Figure 2 of the patent showed a technical effect associated with both the haemoglobin and s-ALP levels. The respondent had alleged that the claimed subject-matter solved the objective technical problem of providing a treatment of metastatic stage prostate cancer in patients with a haemoglobin level of 130 g/l or less which prevented or delayed the disease from entering the hormone-refractory state and that the skilled person had no expectation that degarelix would solve the problem because those patients no longer responded to testosterone reduction.

Both the line of argument and the reference to Figure 2 in this respect were submitted for the first time at the oral proceedings in the appeal proceedings. Previously, the respondent's arguments concerning inventive step had amounted merely to a reference to the reasons they had provided in the context of the main request.

The new line of argument should not be admitted into the proceedings as it could not reasonably be expected to be dealt with without adjournment of the oral proceedings (Article 13(3) RPBA 2007).

The respondent had referred to the grounds of appeal, point 62, as having introduced a discussion on haemoglobin levels; however, aside from the fact that these were filed by the appellant and thus did not present the respondent's reasoning, the passage in question did not discuss haemoglobin levels.

Inventive step (Article 56 EPC) - Claim 1

The respondent's allegation that the patients with the haemoglobin and s-ALP levels in the claim were close to hormone-refractory stage was not supported by evidence.

Auxiliary request 3
Inventive step (Article 56 EPC)

No arguments were submitted that were specific to this request.

Auxiliary requests 4 to 7
Admittance into the appeal proceedings

The admittance of these requests was governed by Article 13(3) RPBA 2007. Because they were filed after the reply to the statement of grounds of appeal, they should also be assessed under Article 13(1) RPBA 2020.

The criteria to be applied were thus whether the requests resolved the existing issues and did not give rise to new ones.

The feature defining the period of time did not resolve the outstanding issues. Additionally, the combinations of features in auxiliary requests 5 to 7 gave rise to new issues. Therefore, none of the requests should be admitted into the appeal proceedings.

XVI. The respondent's arguments, insofar as relevant to the decision, may be summarised as follows:

Postponement of the oral proceedings

Due to the COVID-19 pandemic, the in-house counsel for the respondent was unable to attend the oral proceedings in person.

Without their presence it was not possible to present a complete case. This constituted serious reasons relating to the representative. The in-house counsel had attended and made contributions in all other oral proceedings relating to degarelix, as was apparent from the list provided with the request for postponement.

Main request - claim 1
Inventive step (Article 56 EPC)

The disclosure in document D10 represented the closest prior art. It was directed to the same purpose or effect as the invention because it provided an overview of the treatment of prostate cancer with a GnRH antagonist in patients at an advanced, metastatic stage of the disease. In contrast, document D14 did not focus on metastatic stage patients, but instead disclosed treatment of patients at all stages of the disease. Moreover, it did not contain any information on the progression of metastasis.

The claimed composition for treatment of metastatic stage prostate cancer patients was distinguished from that disclosed in document D14 in that the patient to be treated was "identified as having a baseline serum alkaline phosphatase (S-ALP) level of 200 IU/L or greater (prior to treatment)". The technical effect achieved was a reduction in bone metastatic activity as measured by a reduction in s-ALP levels.

The objective technical problem was thus the provision of a treatment of prostate cancer which identified patients with highly active skeletal metastatic stage disease and which delayed the progression of that disease.

This problem was solved by the claimed invention, as demonstrated in the patent in Figures 1 and 3, interpreted in combination with Table 2, showing a reduction in s-ALP levels, this being indicative of a reduction in bone metastasis.

Whilst the treatment as disclosed in document D14 relied on the suppression of testosterone levels (see page 1536, middle column), the invention relied on the reduction of s-ALP levels. The latter levels correlated with bone metastasis (see document D22, which disclosed that 60% of prostate cancer patients developed bone metastasis; document D26a, which disclosed that elevated levels of s-ALP usually correlated with bone lesions and document D23, which stated that s-ALP levels correlated with osteoblastic bone cancer).

Testosterone and s-ALP levels were independent parameters, as demonstrated by the results in the patent: while testosterone suppression was similar for degarelix and leuprolide (Figure 7), this was not the case for reduction of s-ALP (Figures 1 and 3).

The invention was based on the finding that patients with high degree of bone metastatic activity, as evidenced by increased s-ALP levels, could be treated with degarelix. Degarelix did not just suppress testosterone levels, but also acted directly on the cancer cells.

The prostate cancer patients as defined in the claim suffered from a high degree of bone metastasis and were close to the hormone-refractory stage. It was surprising to the skilled person that such patients could be treated with degarelix. Furthermore, the patent showed that degarelix was superior to leuprolide in its effect on s-ALP levels.

The disclosure in document D14 did not motivate the skilled person to use degarelix to treat prostate cancer patients with metastasis to the bone. In fact, it merely disclosed, for a restricted study period of one year, that degarelix was not inferior to leuprolide for the treatment of prostate cancer (see document D14, page 1536, middle column; abstract, "Conclusions"). Furthermore, the skilled person would conclude that the treatment resulted from suppression of testosterone levels. Since the document did not mention s-ALP levels of the treated patients, it was not possible for the skilled person to find out that the treatment was not being effective for bone metastasis. Moreover, five patients discontinued the treatment due to progression of prostate cancer, one of which due to worsening of bone metastasis (see page 1536, left-hand column, second full paragraph).

Treatment of stage D2 prostate cancer patients with abarelix, which, like degarelix, is a GnRH receptor antagonist, resulted in disease progression within one year (see document D10, page S31, paragraph bridging the middle and right-hand columns). The skilled person would therefore not expect that patients with metastasis to the bone could be effectively treated with degarelix.

Admittance of a line of argument into the appeal proceedings

The line of argument that degarelix did not just suppress testosterone levels, but also acted directly on the cancer cells, was submitted in response to allegations by the appellant. Evidence supporting the argument was provided by Figures 1, 3 and 7 of the patent.

Auxiliary request 1
Admittance into the appeal proceedings

The request was a direct response to the board's findings at the oral proceedings and should be admitted into the appeal proceedings.

The amendments consisted of the simple combination of independent claim 1 and claim 7, which was dependent thereon, as granted. The appellant should therefore have been prepared to be heard on the request.

Auxiliary request 2
Admittance of a line of argument into the appeal proceedings

The patient's haemoglobin levels were addressed in the statement of grounds of appeal.

Inventive step (Article 56 EPC) - Claim 1

The patients as defined in the claim were anaemic and "*very much bordering on hormone-refractory stage*". For these patients the treatment was not reflected by testosterone suppression. The patent showed in

Figures 2 and 7 that these patients responded differently to leuprolide and degarelix.

The objective technical problem addressed was the provision of a treatment of metastatic stage prostate cancer in patients with a haemoglobin level of 130g/l or lower which delayed or prevented entry into the hormone-refractory stage.

The skilled person had no reasonable expectation of success since the patients no longer responded to therapy aimed at testosterone suppression.

Auxiliary request 3
Inventive step

No arguments were submitted that were specific to this request.

Auxiliary requests 4 to 7
Admittance into the appeal proceedings

These requests were filed in response to the appellant's argument that the length of treatment achieved with degarelix would be an inherent property and not an effect resulting from the features in the claim.

XVII. The appellant requested that the decision under appeal be set aside and the patent be revoked in its entirety, and that auxiliary request 1, filed during the oral proceedings, auxiliary requests 2 and 3, filed as former auxiliary requests 1 and 2 with the reply to the statement of grounds of appeal, and auxiliary requests 4 to 7, filed as former auxiliary requests 3

to 6 by letter dated 23 December 2019, not be admitted into the proceedings.

The respondent requested that the appeal be dismissed (main request) or, alternatively, that the patent be maintained on the basis of one of the sets of claims in auxiliary request 1, filed during the oral proceedings, auxiliary requests 2 and 3, filed as former auxiliary requests 1 and 2 with the reply to the statement of grounds of appeal, and auxiliary requests 4 to 7, filed as former auxiliary requests 3 to 6 by letter dated 23 December 2019.

Reasons for the Decision

1. The appeal complies with Articles 106 to 108 and Rule 99 EPC and is therefore admissible.

Request to postpone the oral proceedings

2. The respondent requested that the date of the oral proceedings be postponed, whereas the appellant requested that the oral proceedings take place as scheduled (see sections VIII. and IX.).

3. The reason provided by the respondent for requesting the postponement related to the impossibility of in-house counsel attending these oral proceedings; however, this reason is specifically listed in Article 15(2)(c)(iv) RPBA 2020 as one of the reasons which, as a rule, do not justify a change to the date of the oral proceedings. The argument that the representative is relying on the support of the in-house counsel is not convincing as the

representative must be presumed to be able to properly present the case without such support.

4. Accordingly the board decided not to allow the respondent's request.

Main request - claim 1
Inventive step (Article 56 EPC)

Closest prior art

5. Document D14, which has not been contested as being comprised in the state of the art according to Article 54(2) EPC, discloses degarelix in the treatment of patients with metastatic stage prostate cancer. It provides results and conclusions of a 12-month randomized phase III clinical trial on degarelix in the treatment of patients with prostate cancer. The study aimed to evaluate the efficacy and safety of degarelix *versus* leuprolide for achieving and maintaining testosterone suppression (see title and page 1531, "Objective") and involved patients at all disease stages, with metastatic stage patients representing 20% of the total patients (see page 1531, "Patients and methods" and Table 2). Specifically, for those patients treated with degarelix, 20% or 18%, respectively, suffered from metastatic stage disease (those on dosing regimen 240/160 mg or 240/80 mg, respectively). A response to treatment was observed in 98.3% or 97.2% of the total degarelix-treated patients for the former and latter dosing regimen, respectively (see page 1531, "Results").

6. The disclosure in document D14 constitutes an appropriate starting point for assessing whether the claimed subject-matter involves an inventive step,

since it concerns treatment of the patients with the same indication, i.e. metastatic stage prostate cancer, and with the same substance, i.e. degarelix, as in the claim at issue.

7. The respondent argued that, instead, the disclosure in document D10, which provided an overview of the treatment of prostate cancer with a GnRH antagonist in patients at an advanced, metastatic stage of the disease and thus addressed the same problem as the invention, represented the most suitable starting point, and thus the closest prior art, for the assessment of inventive step.

8. In the board's judgement, however, in a case such as this it is immaterial whether the disclosure in document D14 or that in document D10, or even in other documents, constitutes a *more* promising starting point for arriving at the claimed invention, since patentable subject-matter ought to be inventive when starting from any suitable teaching in the relevant technical field (see also e.g. decision T 967/97, point 3.2 of the Reasons and decision T 1742/12, point 10.3 of the Reasons and further decisions cited in the Case Law of the Boards of Appeal of the European Patent Office, 9th edition 2019, section I.D.3.1). In fact, in the case at hand, starting from the disclosure in document D14, the board indeed comes to the conclusion that the claimed invention is obvious to the skilled person (see point 26.).

Objective technical problem

9. For the sake of the present assessment, as was submitted by the respondent but contested by the appellant, the board considers that the claimed

invention, unlike the disclosure in document D14, concerns a patient group to be treated "identified as having a baseline serum alkaline phosphatase (S-ALP) level of 200 IU/L or greater (prior to treatment)" and that the effect of the treatment was a reduction in bone metastatic activity in that group of patients.

10. The board notes that during the oral proceedings the respondent confirmed that they were no longer relying on the effect of a long-term delay of the progression of the disease, as they had put forward in their written submissions. The board also notes that it has seen no evidence for the respondent's allegation, which was also contested by the appellant, that the particular (high) s-ALP level defining these patients restricts the group of patients to those patients who are suffering from *highly active* bone metastasis and are close to the hormone-refractory stage of the disease. The board therefore does not consider it appropriate to take these alleged facts into account for formulating the technical problem.

11. Accordingly, rather than the more ambitious problem formulated by the respondent, the board considers the objective technical problem to be that of providing a treatment of metastatic stage prostate cancer patients having metastasis to the bone.

Obviousness

12. It remains to be decided whether or not it was obvious to the skilled person that treatment with degarelix could provide a therapeutic benefit to metastatic stage prostate cancer patients suffering from metastasis to the bone.

13. The clinical study disclosed in document D14 involves prostate cancer patients at all stages of cancer progression and therefore does not show that the study designers expected low efficacy of the treatment and/or an increased risk of adverse side effects in particular patients, such as metastatic stage patients. Furthermore, the fact that 97 to 98% of the total patients, of which 18 to 20% were in the metastatic stage of the disease, responded to treatment with degarelix (depending on the dosing) cannot be considered to teach the skilled person that this treatment was not beneficial for patients with a particular kind of metastasis, in particular such as that to the bone, knowing that most prostate cancer patients in fact develop such metastases to the bone (see document D22, page 1621, right-hand column, second sentence). Instead, the board considers that, based on the results disclosed in document D14, the skilled person in fact expected a large percentage of the metastatic stage patients involved, who nevertheless responded to treatment, to suffer from metastasis to the bone.

14. The board accordingly concludes that the design of the study and the reported results disclosed in document D14 itself provided the skilled person with a reasonable expectation that degarelix provided a medical benefit for patients with - at least some degree of - bone metastasis.

15. In a first line of argument, the respondent submitted that, in contrast to the study disclosed in document D14, which relied on testosterone levels, the invention relied on s-ALP levels, which correlated with bone metastasis, to monitor the efficacy of the treatment and relied on the finding in the patent that

administering degarelix resulted in a reduction in s-ALP levels in metastatic stage prostate cancer patients.

16. The board concluded, however, that the skilled person had a reasonable expectation that degarelix treatment provided a medical benefit for patients with skeletal metastasis, based on observed responses to treatment in more than 97% of the degarelix-treated patients, who suffered from metastasis in 18 to 20% of cases. This conclusion was reached independently of the particular parameter to measure treatment success (see point 14. above). It is therefore inconsequential that, in the experiments disclosed in the patent, the effect of degarelix administration is monitored in terms of s-ALP levels. This line of argument must therefore fail.

17. The board also notes in this context that in view of the above finding, the arguments submitted by the parties regarding the specific details of the mechanism of action of degarelix in treating prostate cancer, in particular concerning the alleged direct effect on cancer cells, are not decisive for the board to reach a conclusion on the first line of argument.

18. A second line of argument by the respondent was based on the submission that document D14 did not go beyond a conclusion on the non-inferiority of degarelix *versus* leuprolide and concerned a study over a period up to one year only in which five patients had withdrawn, one of them for reasons of worsening bone metastasis. The respondent argued that the disclosure therefore failed to motivate the skilled person to administer degarelix for the treatment of prostate cancer patients with bone metastasis.

19. In the board's view, the results presented in document D14 are not invalidated by conclusions merely referring to the non-inferiority of degarelix *versus* leuprolide. In fact, "non-inferiority" studies are a standard option in the medical field for comparison with a conventional standard therapy, in this case leuprolide treatment. In addition, a response to degarelix was observed in at least 97% of treated patients (see point 5.), and this therefore also includes the patients referred to in the claim. In the context of the fact that the study in document D14 concerns a one-year period, the board notes that Figure 3 demonstrates a constant depressed testosterone level for the whole period of the study. The skilled person therefore had no reason to conclude that the results would deteriorate over time. In addition, the fact that five out of 400 patients being treated with degarelix discontinued treatment cannot be considered a result that would lead the skilled person to disregard treatment with degarelix because, in percentage terms, this number represents 1.25% of the patients and a medical benefit for all the patients would not have been expected.

20. In conclusion, in the board's view the issues raised by the respondent in this line of argument concerning the disclosure in document D14 would not affect the skilled person's expectation that treatment with degarelix would also benefit prostate cancer patients with metastasis to the bone.

21. The respondent further submitted that the skilled person, based on the disclosure in document D14, would have expected degarelix to merely provide the same results as leuprolide, and thus would not have had motivation to provide degarelix for the treatment of

prostate cancer patients with bone metastasis; however, the results disclosed in the patent showed superior results with degarelix as compared with leuprolide.

22. The board notes, however, that in view of the objective technical problem that the skilled person was seeking to solve (see point 11.), it merely needs to be established whether the skilled person had a reasonable expectation that a composition with degarelix provided a medical benefit to prostate cancer patients with metastasis to the bone, and not whether degarelix provided improved treatment of those patients. This argument must therefore also fail.

23. The respondent also referred to document D10, which disclosed that treatment of metastatic stage prostate cancer patients with abarelix resulted in disease progression within one year. They argued that since degarelix was, like aberalix, a GnRH receptor antagonist, the skilled person would not expect treatment with yet another GnRH antagonist to be beneficial to prostate cancer patients with metastasis to the bone.

24. However, in the board's view, the skilled person equally had knowledge of publications relating to GnRH receptor agonists and antagonists in the treatment of prostate cancer patients, i.e. in the same technical field, such as document D27. This document sets out the outcome of a number of studies on the treatment of prostate cancer with degarelix, abarelix and leuprolide, as measured by testosterone suppression (see Table 1). Degarelix was superior to abarelix in the therapy and was associated with a more favourable side-effect profile ("[...] *the use of abarelix was restricted to patients for whom no alternative therapy*

was available, because abarelix was associated with an increased risk of serious, potentially life-threatening, allergic reactions"; (page 1004, right-hand column, last full paragraph)). The authors conclude that "[t]*hese data suggest that the efficacy of degarelix to achieve rapid and sustained suppression of serum testosterone levels compares favourably with that reported for abarelix. In addition, degarelix was well tolerated, and no systemic allergic reactions were observed*" (page 1005, left-hand column, first full paragraph). Therefore, on the basis of the teaching in document D27, the board can see no merit in the respondent's argument based on the antagonistic nature of degarelix.

25. In view of the above considerations the board concludes that, with due regard to the state of the art, the skilled person had a reasonable expectation that degarelix would treat metastatic stage prostate cancer patients with bone metastasis.

26. Accordingly, the subject-matter of claim 1 does not involve an inventive step (Article 56 EPC).

Auxiliary request 1
Admittance into the appeal proceedings

27. In this appeal, the parties were notified of the summons to oral proceedings before 1 January 2020. Therefore, Article 13(2) RPBA 2020 does not apply, but instead, Article 13 RPBA 2007 applies (Article 25(3) RPBA 2020).

28. The request, filed during the oral proceedings, represents an amendment to the respondent's case as governed by Article 13(1) RPBA 2007 and its admittance

into the appeal proceedings is thus subject to the board's discretion to be exercised in view of the complexity of the new subject-matter submitted, the current state of the proceedings, and the need for procedural economy, *inter alia*.

29. The respondent justified the timing of the filing as a response to the board's prior finding at the oral proceedings in relation to the main request.

30. However, already in its communication pursuant to Article 15(2) RPBA 2020 (see points 20 and 21), the board had informed the parties of its preliminary opinion that the claimed subject-matter of the main request did not involve an inventive step. In particular, the board stated that "[...] *in absence of reasons not to do so, the skilled person would pursue degarelix as a solution to the problem. The board has not been presented with any such reasons.*". In formulating the objective technical problem the board took into account the s-ALP levels recited in claim 1 of the main request. Claim 1 of the present request introduces a reference to the treatment of skeletal or bone metastasis; however, whether the s-ALP levels as required in the claim reflected the presence of bone metastasis had already been the subject of submissions by the parties. Therefore, in its preliminary opinion the board had in essence pointed to the very same reasons underlying the present negative decision on the inventive step of the main request.

31. The board therefore cannot concur with the respondent's argument that the board's findings at the oral proceedings constituted an unexpected development. The request should therefore have been filed earlier in the proceedings.

32. The board accordingly decided not to admit the new auxiliary request into the proceedings.

Auxiliary request 2
Admittance into the appeal proceedings

33. The board admitted this request into the appeal proceedings in spite of the appellant's request not to; however, in view of the decision reached by the board with regard to inventive step (see point 38. below) it is not necessary for the board to give reasons on this point.

Admittance of a new line of argument into the proceedings which was presented for the first time at the oral proceedings

34. In the context of the assessment of inventive step, during the oral proceedings, for the first time in the proceedings, the respondent relied on a line of argument linking the haemoglobin levels of the patients and their stage of the disease, which was defined as "very much bordering on hormone-refractory stage".

35. Since this line of argument was presented for the first time at the oral proceedings, it constitutes an amendment of the party's case and its admittance is at the discretion of the board (Article 13 RPBA 2007).

36. The board held it not to be reasonable to expect the appellant and the board to deal with this entirely new issue without adjournment of the oral proceedings for further preparation (Article 13(3) RPBA 2007). The board accordingly decided not to admit the line of argument into the proceedings.

Inventive step (Article 56 EPC) - Claim 1

37. With the board's communication under Article 15(1) RPBA 2020, setting out its preliminary opinion on the appeal, the parties were informed that the negative conclusions as regards inventive step of the main request applied equally to the claims of this request (formerly auxiliary request 1). The board also noted the absence of any arguments by the respondent relating to the features specific to this request.

38. In view of the fact that the board did not admit the new line of argument brought up for the first time by the respondent at the oral proceedings (see points 34. to 36. above), the board notes that it has seen no arguments from the respondent that would allow it to conclude that the claimed subject-matter involves an inventive step.

Auxiliary request 3
Admittance into the appeal proceedings

39. This request was filed with the reply to the statement of grounds of appeal.

40. The board admits this request into the appeal proceedings as well. The reasons for admittance can be omitted in view of the decision reached by the board with regard to inventive step (see point 41. below).

Inventive step (Article 56 EPC) - Claim 1

41. Since the respondent did not submit arguments in relation to this request, the reasons given with respect to auxiliary request 2 in the context of inventive step (see point 38.) apply, *mutatis mutandis*,

to the claimed invention of this request. Accordingly, the claimed subject-matter does not involve an inventive step (Article 56 EPC).

Auxiliary requests 4 to 7
Admittance into the appeal proceedings

42. The amendments presented with each of these requests address the aspect of the long-term effect of the claimed therapy.

43. The respondent submitted that the requests were filed in response to the appellant's submission dated 8 January 2019, in point 44 thereof (see letter of 23 December 2019, point 2) [Note by the board: the respondent must be referring to appellant's letter of 8 January 2018, which has a point 44 dealing with the aspect of long-term effect; there is no submission in the proceedings with the date 8 January 2019].

44. However, as can be ascertained from the file, the present requests were not filed in reply to the appellant's above-mentioned letter. Instead, the respondent did not file any claim requests with its submissions dated 20 May 2019. In fact, the requests were filed with a subsequent letter, dated 23 December 2019.

45. The board also notes that the long-term effect of the therapy was an aspect that had already been addressed by the respondent as early as with their reply to the statement of grounds of appeal (point 6.2.1.2 of the reply).

46. Contrary to the respondent's contention, this was not a new aspect introduced by the appellant at a later stage

in the appeal proceedings, but rather a line of argument used by the respondent to support the involvement of an inventive step. Incidentally, as noted in point 10., the respondent abandoned this line of argument at the oral proceedings.

47. In conclusion, the present situation is not one of a response to a new development in the proceedings but, quite to the contrary, a response that should have been introduced at an earlier stage of the proceedings.

48. The board thus decides not to admit auxiliary requests 4 to 7 into the appeal proceedings (Article 13 RPBA 2007, see point 27).

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chairman:

I. Aperribay B. Claes

Decision electronically authenticated