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**Datasheet for the decision
of 10 April 2014**

Case Number: T 1771/10 - 3.3.02

Application Number: 05745265.8

Publication Number: 1743038

IPC: G01N33/574, C12Q1/68, G01N33/53

Language of the proceedings: EN

Title of invention:
MN/CA IX/ CA9 AND RENAL CANCER PROGNOSIS

Applicant:
Bayer Healthcare

Headword:
MN/CA9 and renal cancer/BAYER

Relevant legal provisions:
RPBA Art. 15(3)
EPC Art. 123(2)

Keyword:
Amendments - intermediate generalisation

Decisions cited:
G 0004/92

Catchword:



**Beschwerdekammern
Boards of Appeal
Chambres de recours**

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Case Number: T 1771/10 - 3.3.02

D E C I S I O N
of Technical Board of Appeal 3.3.02
of 10 April 2014

Appellant: Bayer Healthcare
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Decision under appeal: **Decision of the Examining Division of the European Patent Office posted on 9 April 2010 refusing European patent application No. 05745265.8 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman: U. Oswald
Members: T. Sommerfeld
L. Bühler

Summary of Facts and Submissions

I. The appeal lies from the decision of the examining division posted on 9 April 2010, in which European patent application 05745265.8, based on an international application published as WO 2005/108623 (hereinafter, application as filed), was refused under Article 97(2) EPC.

II. The application as filed comprised 21 claims, of which claim 1 read as follows:

"1. A method which is prognostic for renal cell carcinoma afflicting a vertebrate, said method comprising:

(a) detecting the presence or absence of MN/CA9 gene expression product in a sample comprising neoplastic cells taken from said vertebrate,

(b) if MN/CA9 gene expression product is present in said sample, quantitating the level and/or extent of said MN/CA9 gene expression product relative to the number of cells in said sample, and

(c) determining that said vertebrate has a poorer prognosis if the level and/or extent of MN/CA9 gene expression product of steps (a) and (b) indicates that 50% or fewer of cells in said sample express MN/CA9 gene expression product;

wherein said MN/CA9 gene expression product is encoded by a nucleotide sequence selected from the group consisting of:

(2[sic]) SEQ ID NO: 1's coding region;

(2) nucleotide sequences that hybridize under stringent hybridization conditions of 50% formamide at 42 degree C. to complement of SEQ ID NO: 1's coding region; and

(3) nucleotide sequences that differ from SEQ ID NO: 1's coding region or from the nucleotide sequences of (2) in codon sequence due to the degeneracy of the genetic code."

III. The documents cited in the examination and appeal proceedings include the following:

D8 Guinan et al. 1997, Cancer 80(5), pp.992-993
D10 Elmore et al. 2003, Cancer 98(11), pp.2329-2334

IV. The decision of the examining division was based on the set of claims of the sole request which was filed with letter dated 4 December 2009.

This set of claims comprised 16 claims; claim 1 differed from originally filed claim 1 by the following amendments (additions underlined, deletions struck through):

"1. A method which is prognostic for nonmetastatic renal clear cell carcinoma afflicting a vertebrate, wherein the carcinoma T-stage is 2 or lower, said characterized in that the method ~~comprising~~ comprises:

(a) detecting the presence or absence of MN/CA9 gene expression product in a sample comprising neoplastic cells taken from the said vertebrate,

(b) if MN/CA9 gene expression product is present in the said sample, quantitating the level and/or extent of the said MN/CA9 gene expression product relative to the number of cells in the said sample, and

(c) determining that the said vertebrate has a ~~poorer~~ prognosis of shorter cumulative survival if the level and/or extent of MN/CA9 gene expression product of ~~steps~~ (a) and (b) indicates that 50% or fewer of cells in the said sample express MN/CA9 gene expression

product, than if more than 50% of cells in the said sample express MN/CA9 gene expression product;

wherein the said MN/CA9 gene expression product is encoded by a nucleotide sequence selected from ~~the group consisting of:~~

(~~2~~1) SEQ ID NO: 1's coding region;

(2) nucleotide sequences that hybridize under stringent hybridization conditions of 50% formamide at 42 ~~degree~~ °C. to complement of SEQ ID NO: 1's coding region;

and

(3) nucleotide sequences that differ from SEQ ID NO: 1's coding region or from the nucleotide sequences of (2) in codon sequence due to the degeneracy of the genetic code."

V. The examining division decided that the sole claim request on file, and in particular its claim 1, did not comply with the requirements of Article 123(2) EPC because *"the claimed combination of the features "nonmetastatic" and "T-stage 2 or lower" was neither individualised in the application as filed in general, nor in the specific embodiment of CCC [clear cell carcinoma]"*. In order to arrive at the claimed combination of features, the skilled person would have to choose individual items from more than two lists; moreover the importance of the presence or absence of metastases was not highlighted anywhere in the description. The examining division thus concluded that claim 1 contained new information which was not directly and unambiguously derivable from the application as filed.

VI. The applicant (hereinafter, the appellant) lodged an appeal against the decision of the examining division, requesting that the decision be set aside and that a

patent be granted according to the claim request decided upon by the examining division.

- VII. As an annex to the summons to oral proceedings, the board issued a communication pursuant to Article 15(1) RPBA.

In said communication, the board summarised the situation and expressed a detailed negative opinion on the claims of the sole request on file as regards Article 123(2) EPC.

- VIII. The appellant did not file any substantive reply to the board's communication but instead informed the board, by fax received on 11 March 2014, that it would not attend oral proceedings and requested the board "to decide in accordance with the records".

- IX. Oral proceedings took place on 10 April 2014 as scheduled and in the absence of the appellant.

- X. The appellant's arguments, in so far as relevant to the present decision, may be summarised as follows:

From the pathologic stage information on page 36 of the application, it was clear that all of the T-stage 1 and 2 clear cell carcinoma (CCC) patients of the application were non-metastatic; therefore the survival study results of Table 4 on page 39 of the application concerning "Low T-stg-Low CA IX" CCC patients related to low T-stage (T-stage 1 or T-stage 2) CCC patients that were non-metastatic. Hence it was apparent from Table 4 that lower CA IX expression for those T-stage 1 or T-stage 2 non-metastatic CCC patients was a statistically significant marker of poor survival (Table 4, bottom section under "T stage (Stg) and CA

IX"). As shown in D8, the TNM staging of renal cell carcinoma defined pathologic stage I as always implying a T-stage 1 while pathologic stage II always implied a T-stage 2. When reading the passage at page 36, lines 12 to 19, and Table 2 on page 37 in the light of these definitions, it became apparent that all 22 T-stage 1 patients of the study had to be in pathologic Stage I, and all 22 T-stage 1 patients of the study had to be non-metastatic (as they were by definition pathologic Stage I); likewise, also all 31 T-stage 2 patients in the study had to be in pathologic Stage II, and were thus non-metastatic.

In conclusion, from the information given in the last paragraph of page 36 (lines 12-19), in view of Table 2 (page 37) it was apparent that all 22 T-stage 1 and all 31 T-stage 2 CCC patients of the study were non-metastatic CCC patients.

- XI. The appellant requested in writing that the decision under appeal be set aside and that a patent be granted on the basis of claims 1 to 16 filed with letter dated 4 December 2009.

Reasons for the Decision

1. The appeal is admissible.
2. The oral proceedings before the board took place in the absence of the appellant, who had been duly summoned but decided not to attend.
The present decision is based on facts and evidence put forward during the written proceedings and on which the appellant has had an opportunity to comment.
Therefore the conditions set forth in Enlarged Board of Appeal opinion G 4/92, OJ EPO 1994, 149, are met.

Moreover, as stipulated by Article 15(3) RPBA the board is not obliged to delay any step in the proceedings, including its decision, by reason only of the absence at the oral proceedings of any party duly summoned who may then be treated as relying only on its written case.

3. Added subject-matter

3.1 In the present claim set, claim 1 has been restricted to a prognostic method for non-metastatic renal clear cell carcinomas, wherein the carcinoma T-stage is 2 or lower; a prognosis of shorter cumulative survival is determined if 50% or fewer of the cells in the sample express MN/CA9 gene expression product.

3.2 In the application as filed, page 9, lines 28 to 33, discloses that "if the tumor T-stage is 2 or lower (...) in said vertebrate, if 50% or less of cells in said sample express MN/CA9 gene expression product, said vertebrate has a worse prognosis (...)". Page 6, lines 1 to 2, teaches that "[a] poorer prognosis can be measured, for example, in terms of shortened cumulative survival (...)". Page 4, lines 22 to 26, makes it clear that the claimed prognostic methods are valid for renal cell carcinoma (RCC) in general, and in particular for clear cell carcinoma (CCC); also, the results presented in Tables 2 to 5 were obtained from samples of CCC. However none of these passages disclose the feature "non-metastatic", and this feature is not to be found in the application as filed in combination with the other features of the claim. In fact, the only passages in the application as filed which refer to absence of metastasis are on page 37, line 10, stating that "63 patients had no distant metastasis", Table 3 on page

38, and page 40, line 19, stating that "only 42.9% of cases with no metastasis stained in the same pattern [low CA IX expression]".

3.3 The appellant's arguments are mainly based on the assumption that, according to the TNM classification of tumors, carcinoma T-stages 1 and 2 always imply TNM pathological stages I and II, which correspond to tumors with carcinoma T-stage 1 or 2, respectively, and absence of any metastasis: in the TNM classification, this would mean T1 or T2, N0, M0, wherein T refers to the carcinoma T-stage, N to lymph involvement and M to distant metastases (D8, left column of second page, table entitled "Stage grouping"). Such a subset of renal cell carcinoma would be implicitly disclosed in the application as filed, in particular in Tables 1 to 3, read in the light of the last paragraph of pages 36 and 37.

3.4 However there is no reference at all to the TNM staging system in the application; in particular it is not stated that the pathological stages disclosed are classified according to this system. Nor does the application further define how pathological stages I and II are characterised. Even assuming that the tumors are indeed classified according to TNM, it would still not be clear how each stage is to be defined, since it is known that TNM staging for a given tumor may change with time: that this is indeed true in the case of RCC is clearly apparent from document D8, which discloses a revision of the TNM staging system for RCC, and further evidenced by document D10, which states on page 2330, left column, first paragraph, that the size cut-off between T1 and T2 organ-confined RCC was changed from 2.5 cm to 7 cm in the 5th edition of the TNM (published in 1997), and suggests that said uppersize cut-off

should be still further changed to a cutoff of 4 to 5 cm (page 2330, last sentence of abstract). Thus, in the absence of a clear reference to a specific document or to a given edition of the TNM classification of malignant tumors, it is not apparent how the pathological stages/carcinoma T-stages are to be defined. Different definitions may apply, and as such it cannot be concluded that a given subject-matter is implicitly disclosed, merely relying on an interpretation according to one prior-art document which is not cited in the application.

3.5 Finally, it is noted that present claim 1 is not restricted to a subset of RCC which is (TNM) pathological stage I or II and at the same time carcinoma T-stage 1 or 2, but instead to a subset of RCC which is "non-metastatic renal clear cell carcinoma (CCC) ... wherein the carcinoma T-stage is 2 or lower". In the present application, the term "non-metastatic" is defined as solely concerning distant metastases: see e.g. Table 3, where lymph involvement ("nodes") and presence of metastases ("metastasis") are evaluated separately. Thus present claim 1, directed to "non-metastatic RCC wherein carcinoma T-stage is 2 or lower" does not necessarily refer to the group which is disclosed above, i.e. a group corresponding to pathological stages I and II (T1 or T2, N0, M0), but also encompasses other groups, namely: pathological stages III (T1 N1 M0 or T2 N1 M0) and IV (T1 N2 M0 or T2 N2 M0); see table entitled "Stage grouping", left column of second page of D8. For this intermediate generalisation between the general disclosure of RCC and the specific subset (allegedly disclosed in Tables 1 to 3 and page 36 of the application) there is no basis in the application as filed.

3.6 The board thus concludes that the sole claim request on file does not fulfil the requirements of Article 123(2) EPC.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chairman:



N. Maslin

U. Oswald

Decision electronically authenticated