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D E C I S I O N
of 6 October 2004

Case Number: T 0918/01 - 3.3.04

Application Number: 93904830.2

Publication Number: 0625912

IPC: A61K 39/395

Language of the proceedings: EN

Title of invention:

Treatment for inflammatory bowel disease

Patentee:

BIOGEN, INC.

Opponent:

Neumann Lydia Ellen
Celltech Therapeutics Ltd.

Headword:

Inflammatory Bowel Disease/BIOGEN

Relevant legal provisions:

EPC Art. 54, 56, 84, 114(2), 123(2)(3)

Keyword:

"Main and first auxiliary request - inventive step (no)"
"Second auxiliary request - not admissible"

Decisions cited:

-

Catchword:

-



Case Number: T 0918/01 - 3.3.04

D E C I S I O N
of the Technical Board of Appeal 3.3.04
of 6 October 2004

Appellant: Celltech Therapeutics Ltd.
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Decision under appeal: Interlocutory decision of the Opposition
Division of the European Patent Office posted
6 June 2001 concerning maintenance of European
patent No. 0625912 in amended form.

Composition of the Board:

Chair: U. M. Kinkeldey
Members: G. L. Alt
S. C. Perryman

Summary of Facts and Submissions

I. European patent No. 0 625 912 with the title "Treatment for inflammatory bowel disease" was granted with 22 claims on the basis of European patent application 93904830.2. Claims 1, 8, 9 and 10 as granted read:

"1. Use of an anti-VLA-4 antibody for manufacture of a medicament for the treatment of inflammatory bowel disease which treatment comprises administering to a mammal suffering from inflammatory bowel disease a composition comprising an anti-VLA-4 antibody."

"8. Use according to Claim 1, wherein the mammal is a human."

"9. Use according to Claim 8, wherein the mammal suffers from ulcerative colitis."

"10. Use according to Claim 8, wherein the mammal suffers from Crohn's disease."

II. The patent was opposed by three opponents. The grounds invoked were that the invention was not new and did not involve an inventive step (Article 100(a) EPC in combination with Articles 54 and 56 EPC) and it was not sufficiently disclosed (Article 100(b) EPC). The opposition division maintained the patent on the basis of a main request comprising amended claims 1 to 20 and an adapted description. Claim 1 of this request read:

"1. Use of an anti-VLA-4 antibody capable of binding to the B1 or B2 epitope of the α_4 subunit of VLA-4 for manufacture of a medicament for the treatment of

inflammatory bowel disease which treatment comprises administering to a mammal suffering from inflammatory bowel disease a composition comprising said antibody."

III. In its decision the opposition division considered that:

- Amendments introduced into claim 1 had a basis on page 7, lines 4-6 of the application as originally filed.
- The opposed patent though confining itself to giving general instructions on how to produce monoclonal antibodies to VLA-4 (very late antigen 4) was enabling in view of the prior art information already available on such antibodies, such as in documents D1 and D47, the latter being referred to in the patent.
- Claim 1 was novel over document D1 which did not disclose the claimed antibody for the preparation of a medicament against inflammatory bowel diseases, but only referred generically to "diseases involving an autoimmune response". This did not amount to an implicit disclosure of inflammatory bowel diseases.
- Claim 1 was novel over document D3 as this was limited to a hypothetical statement of the role of the anti-VLA-4 monoclonal antibodies in the disease.
- For considering inventive step document D2 was taken as the closest prior art, since it was concerned with the treatment of inflammatory bowel

diseases, and the problem to be solved was formulated as finding an alternative approach to that suggested in document D2, namely using an anti-VCAM-1 (vascular cell adhesion molecule 1) antibody. While document D3 referred to a newly defined receptor pair VCAM-1/VLA-4 "is likely to play a role in inflammatory disorders with an immune component [...] such as inflammatory bowel disease", it was considered that in the absence of in vivo evidence in documents D2 or D3 or the other cited documents, the skilled person might at most have been led to speculate as to alternatives, but would have lacked guidance to arrive at what was claimed in an obvious way.

- IV. An appeal was lodged by opponent 03 against the interlocutory decision of the opposition division.
- V. In reply to the statement of the grounds of appeal, the respondent (patentee) filed observations.
- VI. The summons to oral proceedings originally to be held on 23 and 24 June 2004, were accompanied by a communication pursuant to Article 11(1) RPBA, setting out certain concerns of the Board on some of the issues of the appeal.
- VII. Subsequently, as requested by the respondent, the Board postponed and set a new date for the oral proceedings.
- VIII. The Board issued a further communication pursuant to Article 11(1) RPBA in order to clarify certain procedural issues that had been raised by both the

appellant and respondent in response to the summons to oral proceedings.

IX. Oral proceedings took place on 6 October 2004.

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

D1: WO91/03252

D2: WO92/00751

D3: Cell, vol. 62, 1990, pages 3-6

D5: Salmi & Jalkanen, Gastroenterol. Clin. North Am., 1991, vol. 20(3), pages 495-509.

D7: Podolsky *et al.*, J. Clin. Invest., 1993, vol. 92, pages 372-380.

D28: Walsh *et al.*, J. Immun., 1991, vol. 146(10), pages 3419-3423.

D31: Weller *et al.*, Proc. Natl. Acad. Sci. USA, 1991, vol. 88, pages 7430-7433.

D40: Elices *et al.*, Cell, 1990, vol. 60, pages 577-584.

D47: Pulido *et al.*, J. Biol. Chemistry 266, 10241-10245 (1991)

XI. Claim 1 of the **main request** corresponds to claim 1 as maintained by the opposition division.

Claim 1 of the **first auxiliary request**, filed during oral proceedings before the Board, reads:

"1. Use of an anti-VLA-4 antibody capable of binding to the B1 or B2 epitope of the α_4 subunit of VLA-4 for manufacture of a medicament for the treatment of inflammatory bowel disease which treatment comprises administering to a mammal suffering from inflammatory bowel disease a composition comprising said antibody, *wherein said treatment does not include the use of said anti-VLA 4 antibody in combination with anti-ELAM-1, anti-VCAM-1, anti-ICAM-1, anti-CDX, anti-CD18, and/or anti-LFA-1 antibodies.*" (emphasis added by the Board).

Claim 1 of the **second auxiliary request**, filed during oral proceedings before the Board reads:

"1. Use of an anti-VLA-4 antibody capable of binding to the B1 or B2 epitope of the α_4 subunit of VLA-4 for manufacture of a medicament for the treatment of *Crohn's* disease which treatment comprises administering to a mammal suffering from inflammatory bowel disease a composition comprising said antibody, *wherein said treatment does not include the use of said anti-VLA 4 antibody in combination with anti-ELAM-1, anti-VCAM-1, anti-ICAM-1, anti-CDX, anti-CD18, and/or anti-LFA-1 antibodies.*" (emphasis added by the Board).

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

Main Request

Novelty

- Document D1 suggested the use of an antibody as now claimed for inhibiting the adherence of lymphocytes to endothelial cells comprising exposing the lymphocytes to an effective amount of an antibody, or a fragment or derivative thereof, that binds $\alpha 4\beta 1$ receptor, for the treatment of diseases involving autoimmune responses. Since a skilled person knew that inflammatory bowel diseases fell in this category, document D1 implicitly disclosed the antibody for the treatment now claimed, and destroyed the novelty of claim 1.

- Document D3 disclosed the ligand-receptor pair VCAM-1/VLA-4 as important for the recruitment of leukocytes to sites of inflammation, and suggested new therapies could be based on blocking specific adhesion pathways, including for diseases such as inflammatory bowel diseases. This destroyed the novelty of claim 1.

Inventive step

- Treating document D2 as the closest prior art since it specifically mentioned inflammatory bowel disease as one disease to be treated by either a soluble form of VCAM-1 or an anti-VCAM-1 antibody, the problem to be solved could be stated as providing an alternative treatment of inflammatory bowel disease. Document D2 stated at page 2 that

"A prerequisite for the accumulation of eosinophils at sites of inflammation is the binding of eosinophils to adhesion molecules, i.e. VCAM, present on endothelial cells. In view of this, it would be of considerable interest for the prophylaxis or treatment of chronic inflammatory conditions to prevent eosinophil binding to VCAMs." As before the date of the patent, it was known, for example from documents D28 and D31, that eosinophil binding to endothelial cells occurred via the VLA-4/VCAM-1 binding pair, it would be apparent to the skilled person that binding of the members of this pair would be blocked by either an anti-VCAM-1 antibody as in document D2 or an anti-VLA-4 antibody as now claimed, with the same beneficial effect on inflammatory bowel disease. Accordingly, claim 1 lacked an inventive step in view of document D2 considered alone or in combination with either of documents D28 or D31.

- The literature made out a substantial case why the use of antibodies to block the binding pair should work, and it was obvious to try what was claimed with a reasonable expectation of success, even in the absence of any in vivo verification.

- Reasonable expectation of success did not mean certainty of success, which would only come from tests on humans. Even from the animal experiments reported in the patent in suit, the skilled person could not be certain that the treatment would work in humans.

XIII. The respondent's arguments in writing and during oral proceedings in so far as they are relevant to the present decision, may be summarised as follows:

Main Request

Novelty

- For the reasons stated in the decision under appeal, the disclosure of neither of documents D1 or D3 was prejudicial to the novelty of the subject-matter of claim 1.

Inventive step

- Document D2 represented the closest prior art and mentioned inflammatory bowel disease amongst other diseases and using anti-VCAM antibody as one possible treatment of such diseases. The objective technical problem to be solved starting from the teaching of document D2 was therefore to provide an alternative treatment of inflammatory bowel disease with a non-chemical substance.
- Document D2 did not contain any specific disclosure of a treatment for inflammatory bowel disease, but based its suggested treatment on speculations based on in vitro effects concerning the binding of eosinophils to VCAM on endothelial cells. The skilled person would have no firm evidence that even the suggestions of document D2 would work, let alone that any modification of these might work given the unpredictability that

existed for such effects in the art at the time as accepted by the decision under appeal.

- Furthermore, in contrast to VCAM-1, VLA-4 was present on circulating eosinophils and bound to two different partners, i.e. fibronectin and VCAM-1 (as disclosed e.g. in document D1). Antibodies to VCAM-1 and to VLA-4 were therefore not equivalent. Accordingly, these two types of antibodies would not be recognized as alternatives which would both prevent the binding of eosinophils to VCAM-1, so the skilled person would not derive the suggestion to use anti-VLA-4 antibodies from document D2 taken on its own.

- Nor would a skilled person arrive at the invention by relying on other documents in combination with document D2. If anything, rather than relying on any of documents D3, D28 or D31 to find alternatives to the suggestion of document D2, the skilled person would refer document D5, a review article concerned with inflammatory bowel disease published shortly before the relevant date of the patent in suit, referring at page 506, last two lines to page 507, last line, to ICAM-1 and ELAM-1 as playing a central role in the pathology of inflammatory bowel disease, and not to VLA-4. This would lead the skilled person in quite a different direction than the claimed subject-matter when looking for an alternative to the suggestion of document D2.

- As to the combination of document D2 with document D28, the latter was totally silent on the

treatment of inflammatory bowel disease, but rather related to asthma or parasitic infections. Furthermore, any references to anti-VLA-4 antibody-mediated complete blockage of eosinophil binding were qualified in document D28 with caution and with the need for further investigation.

- Document D31 was silent on inflammatory bowel disease and rather related to in vitro studies in the context of asthma. It would not lead the skilled person in the direction of what was presently claimed.

- Document D3, at page 5, right hand column, lines 29 to 44, reflected the uncertainty of the skilled person in respect of interpreting murine and in vivo results in humans relating to the recruitment and binding of lymphocytes to endothelial cells. Furthermore, at page 5, right-hand column, lines 45-50, document D3 reported ICAM-1 and/or ICAM-2 to be responsible for the basal binding of lymphocytes to unstimulated endothelial cells. Thus, document D3 would not cause the skilled person to arrive at the present invention.

- Post-published document D7 (by authors including the inventor named in the patent in suit) evidenced the unpredictability of in vivo effects based on in vitro results with antibodies blocking the receptor. It qualified the results as obtained in the patent on the other hand as "surprising".

Auxiliary request 1

Inventive step

- In view of the prior art teachings of documents D3 and D5 that ICAM-1 and ELAM-1 were key players in inflammatory bowel disease pathology, the skilled person would not expect the subject-matter of claim 1, which excluded the simultaneous use of antibodies such as e.g. against ICAM-1 and ELAM-1, to be a possible treatment.

Auxiliary request 2

Article 123(2) EPC

- Claim 1 of this request was based on claim 10 as originally filed.

Inventive step

- The submitted press release demonstrated particular functionality of the anti-VLA-4 antibody in the treatment of Crohn's disease, which was a form of inflammatory bowel disease, more difficult to treat than ulcerative colitis. Both the press release and the auxiliary request 2 to which it was particularly relevant, should thus be admitted into the proceedings.

XIV. The appellant (opponent 03) had requested in writing that the decision under appeal be set aside and that the patent be revoked.

The respondent (patentee) requested during the oral proceedings that the appeal be dismissed or

as auxiliary request that the decision under appeal be set aside and that the patent be maintained on the basis of the claims of the first auxiliary request submitted at the oral proceedings on 6 October 2004, or

as second auxiliary request that the press release submitted at oral proceedings be admitted into the proceedings and that the case be remitted to the first instance on the basis of the claims of the second auxiliary request filed at the oral proceedings on 6 October 2004.

Reasons for the Decision

1. The appeal is admissible.

Main request - claim 1

Novelty

2. Whereas document D1 suggests the use of an antibody as now claimed for inhibiting the adherence of lymphocytes to endothelial cells comprising exposing the lymphocytes to an effective amount of an antibody, or a fragment or derivative thereof, that binds $\alpha 4\beta 1$ receptor, for the treatment of diseases involving autoimmune responses, it does not specify inflammatory bowel disease(s) as specific instances of such diseases involving autoimmune responses. In accordance with established jurisprudence such a generic disclosure

cannot be taken as destroying the novelty of a claim. If, as put forward by the appellant, a skilled person knew that inflammatory bowel diseases fell in this category, this may be relevant for inventive step, but is not sufficient to destroy novelty.

3. Document D3 discloses that:

"MAbs to VCAM1 and to VLA4 can be expected to help determine physiological and pathological functions of this newly defined receptor-ligand pair. It is likely to play a role in inflammatory disorders with an immune component, such as rheumatoid arthritis, asthma, inflammatory bowel diseases, sepsis and dermatoses. [...] Currently available anti-inflammatory drugs have limited efficacy in interrupting the self-perpetuating cycle of tissue damage seen in chronic diseases of this type. Furthermore, many of these drugs have severe side effects. Therefore it would be useful to have other forms of therapy that could replace or alternate with currently used drugs. Although the MAbs that are now being used experimentally to block leukocyte migration have theoretical drawbacks as drugs to treat chronic diseases, the expected side effects, such as vascular damage due to immune complex deposition on the endothelium, may not inevitably occur in practice (see e.g. Wegner et al., 1990). Alternatively it may be possible to develop small peptides or other molecules that will specifically block adhesive interactions of ligand-receptor pair. Thus, study of leukocyte adhesion and migration through the endothelium may make

accessible a new point of intervention in both acute and chronic inflammatory disorders."

The Board considers that, while document D3 suggests various lines of research for which monoclonal antibodies to VLA-4 might be useful, there is no clear and unambiguous disclosure to use such an antibody for the treatment of inflammatory bowel diseases, so that document D3 does not destroy the novelty of claim 1.

4. No documents other than documents D1 and D3 were relied on as destroying novelty of claim 1, so novelty can be acknowledged.

Inventive step

5. In accordance with established case law of the Boards of Appeal related to the problem-solution approach, the document representing the closest prior art must disclose subject-matter conceived for the same purpose or aiming at the same objective as the claimed invention and having the most relevant technical features in common, i.e. requiring the minimum of structural modifications to arrive at the claimed invention.

- 5.1 According to the first paragraph, the patent in suit relates, in general, to a treatment for inflammatory bowel disease using antibodies. The two most common forms of inflammatory bowel disease are ulcerative colitis and Crohn's disease. Examples III and IV of the patent in suit disclose in particular that in cotton top tamarins which exhibit symptoms of spontaneous

- colitis, acute inflammation decreases after administration of HP1/2, an antibody against VLA-4.
- 5.2 Document D2 relates to the treatment of inflammatory diseases and conditions, including inflammatory bowel disease (page 3, lines 13 to 17 and e.g. claim 7).
- 5.2.1 Document D2 discloses on page 3, lines 12-34 that eosinophils, which in normal immune response processes are triggered to degranulate, participate actively in inflammatory diseases, including ulcerative colitis. The intracellular secretory granules of eosinophils contain cytotoxic substances which are assumed to be responsible for the tissue damage associated with these diseases. Since VCAM-1, a protein expressed on the surface of vascular endothelial cells, is capable of binding eosinophils, and this binding is a prerequisite for the accumulation of eosinophils at the site of inflammation, it is suggested to treat inter alia inflammatory bowel disease (see claim 7) by administration of antibodies to VCAM-1 in order to prevent the adherence of eosinophils to vascular endothelial cells.
- 5.3 Thus, document D2 relates at least in part to treating the same disease as the patent in suit, and both aim to prevent the attachment of leukocytes to inflamed sections of the gut. Therefore, and in agreement with the parties and the opposition division, the Board considers that this document represents the closest prior art for the purpose of assessing inventive step.

6. In the light of document D2 and in the absence of any evidence that use of an anti-VLA-4 antibody gives any advantages over the suggestions in document D2, the technical problem to be solved by the invention in claim 1 can be stated as the provision of alternative compounds for the manufacture of a medicament for the treatment of inflammatory bowel disease.
 - 6.1 The invention of claim 1 solves the above formulated problem by the use of anti-VLA-4 antibodies capable of binding to the B1 or B2 epitope of the α_4 subunit of VLA-4. The Board is satisfied that this presents a plausible solution for the technical problem in view of the results presented in Examples III and IV of the patent in suit.
7. The question to be answered for the assessment of inventive step is whether the prior art rendered the use of anti-VLA-4 antibodies capable of binding to the B1 or B2 epitope of the α_4 subunit of VLA-4 for the manufacture of a medicament for the treatment of inflammatory bowel disease obvious to the skilled person.
8. As has been noted above, document D2 envisages the treatment of diseases or conditions such as inflammatory bowel disease, involving the binding of eosinophils to vascular endothelial cells expressing VCAM by inhibiting the binding of VCAM-1 to its ligand on the surface of eosinophils, by the administration of anti-VCAM-1 antibodies. This leads to blocking VCAM-1 on the endothelial cells and hence prevents binding of the eosinophils.

- 8.1 However, as can also be taken inter alia from e.g. the top and lines 30-35 of page 3, document D2 also suggests an alternative to the above treatment, namely the inhibition of adhesion of VCAM-1 to its ligand on the surface of eosinophils by the administration of (soluble) VCAM-1. This leads to blocking the ligand on the eosinophils and hence prevents them from binding to VCAM-1 on the endothelial cells.
- 8.2 Furthermore, document D2, on page 14, lines 33-36, states that the specific ligand for VCAM-1 on the surface of eosinophils is VLA-4. This is in accordance with what is stated in documents D3, D28 and D31, and this can be considered part of the common general knowledge of the skilled person in this field at the date of the patent.
- 8.3 Given that document D2 teaches the skilled reader that inflammatory bowel disease can be treated by blocking the adherence of eosinophils to VCAM-1 on vascular endothelial cells, and that the skilled person knows that the specific ligand for VCAM-1 on the surface of eosinophils is VLA-4, the use of anti-VLA-4 monoclonal antibodies as a way of blocking eosinophils to VCAM-1 would suggest itself to the skilled person as an alternative to the specific suggestions of doing so in document D2, namely using anti-VCAM-1 antibodies, as a skilled person would know that the interaction of a ligand-receptor pair would be blocked either by blocking the receptor, here VCAM-1 on the endothelial cells, or by blocking its counterpart ligand, here VLA-4 on the eosinophils.

- 8.4 Any doubts the skilled person might have had on the basis of document D2 alone about the feasibility of using such anti-VLA-4 antibodies, would be removed by considering document D1 which, as mentioned in point 2 above, suggests exactly this type of antibody for diseases involving autoimmune responses.
9. The respondent argued that the cited prior art merely reported on **in vitro** experimentation relating to the inhibition of VCAM-1/VLA-4-mediated binding of eosinophils to vascular endothelial cells. It could be taken from post-published document D7 that such in vitro experimentation was not suitable for predicting successful in vivo effects of this inhibition in the treatment of inflammatory bowel disease. Document D7 disclosed namely that anti-ELAM-1 antibodies - ELAM-1 being known as an inducible leukocyte adhesion molecule expressed on endothelial surfaces and present at sites of active inflammation in patients with inflammatory bowel disease (see e.g. document D5) - had no in vivo therapeutic effect on inflammatory bowel disease. In the absence of any evidence in the prior art for in vivo success for an anti-VLA-4 antibody the skilled person could derive no suggestion from document D2 with the reasonable expectation of success required to deprive the claimed subject-matter of inventive step.
- 9.1 However, firstly, the jurisprudence of the Boards of Appeal makes a clear distinction between reasonable expectation of success and certainty of success. Certainty of success is not required. If certainty were the criterion, then for claims covering the use of a particular compound to treat a particular disease in humans it would be necessary to provide evidence of

successful clinical trials. This has never been required, and it would be unreasonable to require it as applicants cannot be expected to have completed clinical trials before applying for a patent. What constitutes reasonable expectation of success must be considered on a case by case basis. In the present case several different documents make success plausible, what remained to be done is checking, in a known manner by first animal trials and then clinical trials, whether use of anti-VLA-4 was indeed safe and effective. The patentee has gone further down the road of these routine checks, in confirming in experiments with monkeys that the treatment appears effective, but this cannot be taken as evidence that there was not already a reasonable expectation of success derivable from the prior art.

- 9.2 Secondly: Document D7 was published after the relevant date for the patent in suit. Therefore, in any case, for the purpose of considering what would have influenced the skilled person at the priority date, its post-published experimental results cannot be used.

10. The respondent furthermore argued that a number of documents in the prior art, including documents D28 and D5, a review article published shortly before the priority date of the patent in suit, taught the skilled person that two compounds different from VCAM-1, namely ICAM-1 and ELAM-1 and their eosinophilic ligands, played a central role in the binding of eosinophils to endothelial cells at sites of inflammation. It was therefore not obvious to a skilled person that the blocking of (solely) the VCAM-1/VLA-4 binding would result in a therapeutically relevant effect.

- 10.1 To support this argument the respondent referred to document D7 cited in this context as an expert opinion reflecting the experimental mood of the skilled person confronted with the search for a solution to the formulated technical problem. The document described at page 379, left-hand column, lines 31 to 37 the results of the patent in suit as being surprising because the blocking of the VCAM-1/VLA-4 binding gave a more profound effect than disrupting the ELAM-1-mediated pathway despite ELAM-1 being the more characteristic inflammatory cell hallmark of acute inflammation in inflammatory bowel disease.
- 10.2 However, this line of argument seems to be inconsistent with the suggestions of document D2 which concentrates on the blocking of the VCAM-1/VLA-4 binding. It may be that a treatment of inflammatory bowel disease can be improved or that there are other useful treatments, but this does not affect the conclusion that what is claimed can be derived in an obvious manner from the prior art. Even document D5 in the section "Molecules involved in lymphocyte binding to endothelial cells" starting at page 498, deals with the VCAM-1/VLA-4 on an equal basis as with other molecules such as ELAM-1, ICAM-1 and further molecules.
- 10.3 Furthermore, document D31 at page 7432, right hand column, lines 3-6 of the part "Discussion", states that although eosinophils can bind to ICAM-1 and ELAM-1, these adhesion molecules also bind to neutrophils and would hence not provide a means for the preferential recruitment of eosinophils to sites of inflammation, as occurs e.g. in the case of inflammatory bowel disease.

10.4 The Board considers therefore that the skilled person, despite being aware of other pathways that play an important role in in vivo mechanisms leading to inflammatory bowel disease, and starting from document D2 would straightforwardly apply anti-VLA-4 antibodies for attaining the same therapeutically relevant effect.

11. In a further line of argumentation the respondent also contended that at the priority date of the patent in suit, it was known to the skilled person that antibodies to VCAM-1 and VLA-4 were not equivalent in that VCAM-1 had only one binding partner whereas VLA-4, besides VCAM-1, had another binding partner, i.e. fibronectin. In solving the above formulated technical problem the skilled person would therefore not consider choosing anti-VLA-4 antibodies.

11.1 Document D3 discloses on page 6, left-hand column, lines 2-10 that VCAM-1 binding to leukocytic VLA-4 occurs via a different site on VLA-4 than that which binds fibronectin. Document D5, at page 499, lines 11-15 reports that VLA-4 interactions with VCAM-1 and fibronectin can be independently inhibited by monoclonal antibodies. Similarly, document D28 reports that VCAM-1 and fibronectin recognise different epitopes of VLA-4 and discloses, on the one hand, monoclonal antibody HP1/3 binding only to the VCAM-1-binding site and, on the other hand, monoclonal antibody HP1/2 recognising as well the VCAM-1 binding site as the fibronectin binding site (page 3422, right-hand column, lines 37-45). Thus, in the prior art antibodies linking to either the VCAM-1 or the fibronectin binding site on VLA-4 or to both were known.

11.2 The Board can concur with the respondent that from the above knowledge of the dual binding of VLA-4, the skilled person would be cautious in selecting antibodies appropriate for attaining the desired therapeutic effect and possibly not impairing the VLA-4/fibronectin interaction. However, notwithstanding this attitude, the skilled person would, in the Board's judgement, none the less choose the antibodies referred to in claim 1 since his cautiousness would be outbalanced by the prior art teaching leading him, as set out in points 5 to 10 above, directly to this choice.

12. For these reasons, claim 1 is found to lack an inventive step and thus the main request as a whole is not allowable under Article 52(1) EPC in conjunction with Article 56 EPC.

Auxiliary request 1 - claim 1

Articles 123(2) and (3) EPC, Article 84 EPC

13. Claim 1 is limited, by means of a disclaimer, to a more exclusive use of an anti-VLA-4 antibody capable of binding to the B1 or B2 epitope of the α_4 subunit of VLA-4 for the manufacture of a medicament for the treatment of inflammatory bowel disease. The amendment amounts to a limitation of the protection conferred as compared to that of granted claim 1. Furthermore, basis for this amendment is present on page 11 to page 12, line 6 of the original application documents, as well as in the examples where only one single antibody is used. Finally, the amended claim is clear, precise and

supported by the description. Consequently, claim 1 meets the requirements of Articles 123(2), 123(3) and 84 EPC. The appellant has not raised any objection in this respect.

Inventive step

14. The reasoning of the Board in relation to the lack of inventive step of claim 1 of the main request applies equally to claim 1 of this first auxiliary request, since it did not depend on the presence or absence of other antibodies. Accordingly, the first auxiliary request must also be refused since its claim 1 lacks inventive step.

Admissibility of auxiliary request 2 and the press release into the proceedings

15. At the very end of the oral proceedings the respondent sought to introduce into the proceedings a second auxiliary request in which the claims had been restricted to the treatment of Crohn's disease, as well as a press release dated 29 September 2004, which allegedly demonstrated that the treatment with anti-VLA-4-antibodies worked for Crohn's disease, the latter being a particular form of inflammatory bowel disease which is allegedly particularly difficult to treat.
16. Evidence of success in treating Crohn's disease does not introduce anything new for the assessment of inventive step as such success merely confirms what the patent suggested. The Board is thus not persuaded that the press release is of sufficient relevance to be introduced into the proceedings and is therefore not

prepared to exercise its discretion in favour of allowing the press release into them.

17. It is common general knowledge in this field, as also stated in the patent in suit, that there are two forms of inflammatory bowel disease, namely ulcerative colitis and Crohn's disease. The patent, while containing a separate claim to the treatment of Crohn's disease, provides no information that does not apply to treating both forms of inflammatory bowel disease. The restriction to Crohn's disease does not avoid the line of reasoning on which the Board found the claim 1 of each of the main request and first auxiliary request obvious, as this reasoning is based on prior art which, like the patent in suit, makes no distinction between these two varieties of inflammatory bowel disease. The Board thus considers that the patent provides no basis for treating inventive step of a claim limited to the treatment of Crohn's differently from the claims 1 of the main request or first auxiliary request directed to the treatment of unspecified inflammatory bowel disease.

18. In view of the absence of the appellant from the oral proceedings, the respondent asked that the case be remitted to the opposition division for further examination on the basis of the second auxiliary request. However, given that the second auxiliary request would prima facie not avoid the ground of lack of inventive step on which the earlier requests failed, the Board is not prepared to exercise its discretion in favour of allowing the second auxiliary request into the proceedings at such a late stage.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The patent is revoked.

Registrar:

Chair:

P. Cremona

U. Kinkeldey