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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PFIZER, INC.,
Petitioner,

v.

BIOGEN, INC.,
Patent Owner.

Case IPR2017-01168
Patent 8,821,873 B2

Before ERICA A. FRANKLIN, SHERIDAN K. SNEDDEN, and JACQUELINE T. HARLOW, *Administrative Patent Judges*.

FRANKLIN, *Administrative Patent Judge*.

DECISION
Institution of *Inter Partes* Review
37 C.F.R. § 42.108

I. INTRODUCTION

Pfizer, Inc. ("Petitioner") filed a Petition requesting an *inter partes* review of claims 1–5 of U.S. Patent No. 8,821,873 B2 (Ex. 1001, "the '873 patent"). Paper 2 ("Pet."). Biogen, Inc. ("Patent Owner") did not file a Preliminary Response to the Petition.

We have authority under 35 U.S.C. § 314 to determine whether to institute an *inter partes* review. 35 U.S.C. § 314(b); *see also* 37 C.F.R. § 42.4 (a). Upon considering the Petition, we determine that Petitioner has shown a reasonable likelihood that it would prevail in showing the unpatentability of claims 1–5. Accordingly, we institute an *inter partes* review with respect to those claims.

A. Related Proceedings

Petitioner and Patent Owner have not identified any other pending proceedings involving the '873 patent. Pet. 7; Paper 5, 2. Both parties have explained that Petitioner has filed petitions for *inter parties* review involving related U.S. Patent Nos. 8,329,172 B2 (IPR2017-01166) and 8,557,244 B1 (IPR2017-01167).

B. The '873 Patent

The '873 patent relates to methods for treating a patient who is greater than 60 years old and has diffuse large cell lymphoma ("DLCL"), and in one embodiment, wherein the lymphoma is accompanied by bone marrow involvement. Ex. 1001, 1:17–21. DLCL refers to an aggressive form of non-Hodgkin's lymphoma ("NHL"). *Id*. at 3:1–9. The treatment comprises administering rituximab, a chimeric anti-CD20 antibody, and CHOP (cyclophosphamide, hydroxydaunorubicin/doxorubicin, vincristine, and prednisone/prednisolone) chemotherapy, wherein the antibody is

administered in combination with a stem cell transplantation regimen. *Id*. at 6:8–17. Transplant regimens include autologous bone marrow transplant, allogeneic bone marrow transplant, or peripheral blood stem cell transplant (PBSCT). *Id*. at 2:34–39. According to the Specification, when there is bone marrow involvement accompanying the lymphoma, patients may benefit from prior treatment with the anti-CD20 antibody before bone marrow harvesting because doing so may decrease the quantity of tumor cells in the bone marrow or stem cell preparation. *Id*. at 6:8–13.

C. Illustrative Claims

Claims 1 and 4 are illustrative and are reproduced below:

> 1. A method of treating a patient with diffuse large cell lymphoma comprising administering anti-CD20 antibody and chemotherapy to the patient, wherein the patient is >60 years old, wherein the chemotherapy comprises CHOP (cyclophosphamide, hydroxydaunorubicin/doxorubicin, vincristine, and prednisone/prednisolone), and wherein the anti-CD20 antibody is administered to the patient in combination with stem cell transplantation regimen.
>
> 4. The method of claim 1, wherein the lymphoma is accompanied by bone marrow involvement.

D. The Asserted Grounds of Unpatentability

Petitioner challenges the patentability of claims 1–5 of the '873 patent on the following grounds:

Claims	Basis	References
1–5	§ 103	Moreau, [1] Link,[2] McNeil,[3] and Maloney[4]
1–5	§ 103	Moreau, Link, McNeil, Maloney, and Coiffier[5]

Petitioner also relies upon the Declarations of Howard Ozer, M.D., Ph.D. (Ex. 1002) and Scott Bennett, Ph.D. (Ex. 1016).

II. ANALYSIS

A. Claim Construction

In an *inter partes* review, the Board interprets claim terms in an unexpired patent according to the broadest reasonable construction in light of the specification of the patent in which they appear. 37 C.F.R. § 42.100(b); *Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2142 (2016)

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[1] Moreau et al., *Peripheral blood stem cell transplantation as front-line therapy in patients aged 61 to 65 years: a pilot study*, 21 BONE MARROW TRANSPLANTATION 1193–96 (1998) (Ex. 1007).
[2] Link et al., *Phase II Pilot Study of the Safety and Efficacy of Rituximab in Combination with CHOP Chemotherapy in Patients with Previously Untreated Intermediate- or High-Grade NHL, Program/Proceedings*, 17 AM. SOC. CLIN. ONCOL. 3a (Abstract 7) (1998) (Ex. 1005).
[3] McNeil, *Non-Hodgkin's Lymphoma Trials In Elderly Look Beyond CHOP*, 90 J. NAT. CANCER INST. 266–67 (1998) (Ex. 1003).
[4] Maloney et al., *IDEC-C2B8: Results of a Phase I Multiple-Dose Trial in Patients with Relapsed Non-Hodgkin's Lymphoma*, 15 J. Clin. Oncology 3266–3274 (1997) (Ex. 1008).
[5] Coiffier et al., *Rituximab (Anti-CD20 Monoclonal Antibody) for the Treatment of Patients with Relapsing or Refractory Aggressive Lymphoma: A Multicenter Phase II Study*, 92 BLOOD 1927–32 (1998) (Ex. 1006).

(affirming applicability of broadest reasonable construction standard to *inter partes* review proceedings). Under that standard, and absent any special definitions, we give claim terms their ordinary and customary meaning, as would be understood by one of ordinary skill in the art at the time of the invention. *In re Translogic Tech., Inc*., 504 F.3d 1249, 1257 (Fed. Cir. 2007). Any special definitions for claim terms must be set forth with reasonable clarity, deliberateness, and precision. *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

Petitioner proposes a construction for the claim term "in combination with." Pet. 30–31. In view of our analysis, we determine that construction of claim terms is not necessary for purpose of this Decision. *See Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999) (Only terms which are in controversy need to be construed, and only to the extent necessary to resolve the controversy).

B. Obviousness over Moreau, Link, McNeil, Maloney, and Coiffier

Both of Petitioner's obviousness grounds challenge claims 1–5 of the '873 patent and include a combination of Moreau, Link, McNeil, and Maloney. Pet. 8–9. In the second ground, Petitioner additionally relies upon Coiffier in the combination. *Id*. at 9. We exercise our discretion to consolidate those two grounds into one challenge of claims 1–5 over the combination of Moreau, Link, McNeil, Maloney, and Coiffier.

1. Moreau

Moreau describes a drug trial designed to investigate the feasibility of high-dose therapy followed by autologous peripheral blood stem cell transplantation (PBSCT) as a component of front-line therapy for patients with disseminated intermediate- and high-grade NHL, aged 61–65 years.

Ex. 1007, 1. Eight of the original 14 patients in the study had B cell lymphoma, Working Formulation (IWF) subtype "G." *Id*. at 2, Table 1. Patients with mantle-cell, lymphoblastic or diffuse small non-cleaved cell lymphomas were excluded from the analysis. *Id*. at 1. Initially, all 14 patients were administered three courses of CHOP therapy. *Id*. The 11 patients who achieved a partial or complete response to CHOP, including seven IWF-G patients, were eligible for PBSCT after granulocyte colony-stimulating factor (G-CSF) priming. *Id*. After stem cell collection, and before intensive therapy, a fourth course of CHOP was administered. *Id*. at 2. Moreau reports that seven of the 11 transplanted patients "are alive and free from disease." *Id*. at 3. "No severe cardiac, renal, hepatic or pulmonary toxicity was documented" for any of the 14 patients. *Id*. Although seven of the initial 14 patients died either before or after stem cell transplant, those deaths were due to progressive disease and not toxicity. *Id*. Moreau explains that its "pilot study demonstrates that PBSCT can probably be performed in patients between 61 and 65 years of age." *Id*.

2. Link

Link describes a phase II pilot study of the safety and efficacy of administering Rituxan in combination with CHOP chemotherapy to 31 patients with previously untreated intermediate- or high-grade NHL. Ex. 1005, 3a (Abstract 7). Patients had a median age of 49 and included those with a pathology of IWF G (DLCL). *Id*. Link describes Rituxan as "rituximab, IDEC-C2B8," a chimeric monoclonal antibody that targets the CD20 antigen expressed on normal and malignant B-cells. *Id*. Link reports that the study resulted in 19 patients having a complete response, 10 patients having a partial response, and one patient with progression. *Id*. According

to Link, the study regimen "represents a tolerable therapy . . . and may offer higher response rates" than seen with conventional CHOP therapy alone. *Id*.

3. McNeil

McNeil describes a randomized trial for elderly patients with intermediate-grade NHL involving a combination treatment of CHOP and Rituxan (IDEC-C2B8). Ex. 1003, 266. McNeil explains that the trial, organized by the Eastern Cooperative Oncology Group ("ECOG"), "will recruit 630 patients age 60 and over" to receive the combination therapy. *Id*.

4. Maloney

Maloney describes a phase I multiple-dose trial using IDEC-C2B8, the chimeric anti-CD20 monoclonal antibody (rituximab) to treat 20 patients with relapsed low-grade or intermediate/high-grade NHL. Ex. 1008, 3, 4. Two patients had intermediate-grade NHL, with a histologic grade "G," i.e., IWF-G. *Id*. at 5, Table 1. All twenty patients were scheduled to receive four weekly IV infusions of rituximab, three patients (median age 48 years) received a dose of 125 mg/m^2, seven patients (median age 59 years), including 1 IWF-G patient, received a dose of 250 mg/m^2, and ten patients (median age 59.5 years), including 1 IWF-G patient, received 375 mg/m^2. *Id*. at 5. All patients required therapy due to disease progression after failing to respond to prior chemotherapy. *Id.* Marrow involvement was present in 50% of patients. *Id*. Tumor responses occurred in peripheral blood, bone marrow, spleen, bulky lymph nodes, and extranodal sites. *Id*. at 3. Eighteen patients were assessable for efficacy. *Id*. at 7. The overall clinical response rate was 33%. *Id*. Two of the four patients with intermediate-grade lymphoma bulky disease died two and four months following treatment due to progressive lymphoma. *Id*. at 8.

Maloney concludes that rituximab is a "practical outpatient treatment giver over a brief, 3-week course." *Id*. at 8. Maloney reasons that "[s]ince this antibody does not appear to impair marrow reserves, it could possibly be used in patients who are myelosuppressed due to recent chemotherapy or following high-dose chemotherapy with ABMT [autologous bone marrow transplantation] or peripheral stem-cell rescue." *Id*. at 10.

5. Coiffier

Coiffier describes a phase II study to evaluate the efficacy and

tolerability of rituximab in patients with more aggressive types of lymphoma. Ex. 1006, 1. Of the 52 patients in the study, 30 had DLCL. *Id*. at 2 and 3, Table 3. Patients received eight weekly infusions of either a standard or higher dose of rituximab. *Id*. at 1, 6. Coiffier describes a dominant feature of the population of patients was "relatively old age." *Id*. at 5. Specifically, 50% of the patients receiving the standard dose and 62% of patients receiving the higher dose were older than 60 years of age. *Id*. at 6. Coiffier explains that there were no responses observed in patients whose largest tumor was greater than 10 cm in diameter. *Id*. at 4. As for the results in the remaining patients, Coiffier concludes that the results of the study "indicate that rituximab therapy has significant anti-lymphoma activity in DLCL and [mantle cell lymphoma] patients without the toxicity commonly observed with combination chemotherapy regimens." *Id*. at 6.

6. Analysis

Petitioner asserts that Moreau taught all of the elements of claims 1, except for the addition of rituximab. Pet. 44. In particular, Petitioner asserts that Moreau disclosed treating patients over the age of 60 having DLCL with a reduced CHOP regimen in combination with PBSCT. *Id*. at 43. Petitioner asserts that seven of the eight patients over 60 with DLCL responded to the initial CHOP therapy, and that four of those eight had a complete response following PBSCT. *Id*. (citing Ex. 1007, 2–3, Tables 1 and 3). Petitioner assert that, based on the study results, Moreau concluded that CHOP and PBSCT "can probably be performed in patients between 61 and 65 years of age." *Id*. (quoting Ex. 1007, 3). Petitioner asserts also that McNeil reported that the approach involving PBSCT combined with low-dose chemotherapy regimens have provided "impressive responses." *Id*. (citing Ex. 1003, 2).

According to Petitioner, a person of skill in the art would have found it obvious to modify Moreau's treatment method to further improve the efficacy of that method because only half of the DLCL patients achieved complete responses. *Id*. at 44. In particular, Petitioner asserts that Link and McNeil would have provided a skilled artisan a reason to combine rituximab with Moreau' method. *Id*. at 44–47; Ex. 1002 ¶¶ 88–90. Petitioner explains that Link teaches that a regimen combining CHOP and rituximab to treat patients, including those with DLCL, provides a "tolerable therapy with serious adverse events occurring with a frequency similar to that seen with conventional CHOP therapy alone and may offer higher response rates." *Id*. at 45 (quoting Ex. 1005, 5). According to Petitioner, a skilled artisan would have understood from Link that combining rituximab with Moreau's reduced CHOP regimen to improve the regiment efficacy without adding toxicity. *Id*. at 45–46.

Petitioner asserts that McNeil bolsters the motivation to combine the teachings of Moreau and Link to provide a therapy comprising CHOP and rituximab, with a reasonable expectation of success. Petitioner asserts that McNeil (a) explains that elderly patients have poorer outcomes with CHOP due to it being more toxic in that age group, Pet. 46 (citing Ex. 1003, 1; Ex. 1002 ¶¶ 90–93), and (b) suggests that an alternative to standard CHOP therapy may be CHOP plus the monoclonal antibody rituximab, *id*. at 46–47 (citing Ex. 1003, 1). According to Petitioner, a skilled artisan would have understood from McNeil, that modifying Moreau's CHOP regimen to include rituximab could provide Moreau's patients with a more effective therapy without increasing toxicity. *Id*. at 47.

Additionally, Petitioner asserts that Maloney independently provides a person of skill in the art with a reason to combine the teachings of Moreau and Link. Pet. 47. According to Petitioner, Maloney studied the use of rituximab in 20 patients with all grades of NHL who had relapsed after previous treatments. *Id*. at 22 (citing Ex. 1008, 3). Petitioner asserts that Maloney reasoned that "[s]ince this antibody [rituximab] does not appear to impair marrow reserves, it could possibly be used in patients who are myelosuppressed due to recent chemotherapy or following high-dose chemotherapy with AMBT [autologous bone marrow transplantation] or peripheral stem-cell rescue." *Id*. at 47 (quoting Ex. 1008, 10). According to Petitioner, a skilled artisan would have been motivated to add rituximab to Moreau's method, which included patients receiving transplantation, because Maloney taught that rituximab does not negatively affect the cells needed for transplantation. *Id*. at 47–48.

On the current record, we discern no deficiency in Petitioner's characterization of the cited references, as set forth above, or in Petitioner's assertions as to the reasonable inferences an ordinary artisan would make from those references. Thus, based on the information presented at this stage of the proceeding, Petitioner has shown sufficiently that there is a reasonable likelihood that it would prevail in showing the unpatentability of independent claims 1 and 5 over the combination of Moreau, Link, McNeil, and Maloney.

We have also reviewed Petitioner's showing with respect to the dependent claims, including claim 4 (further combining the teachings of Coiffier to support Petitioner's position that a person of skill in the art would have found it obvious that Moreau's modified therapy could successfully

treat patients whose lymphoma is accompanied by bone marrow involvement). Pet. 50–53. At this stage of the proceeding, we determine that Petitioner has shown sufficiently that there is also a reasonable likelihood that it would prevail in showing the unpatentability of those dependent claims over the combination of Moreau, Link, McNeil, Maloney and Coiffier.

III. CONCLUSION

For the foregoing reasons, we conclude that the information presented in the Petition establishes a reasonable likelihood that Petitioner would prevail in showing that claims 1–5 of the ’873 patent are unpatentable.

At this stage of the proceeding, the Board has not made a final determination as to the patentability of any challenged claim or the construction of any claim term.

ORDER

Accordingly, it is hereby:

ORDERED that pursuant to 35 U.S.C. § 314, an *inter partes* review is instituted as to claims 1–5 of the ’873 patent on the following ground of unpatentability:

> Claims 1–5 under 35 U.S.C. § 103(a) as obvious over Moreau, Link, McNeil, Maloney, and Coiffier;

FURTHER ORDERED that no other proposed grounds of unpatentability are authorized; and

FURTHER ORDERED that pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4, notice is hereby given of the institution of a trial commencing on the entry date of this Decision.

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