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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.*

FINAL WRITTEN DECISION

35 U.S.C. § 318(a) and 37 C.F.R. § 42.73

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.

On November 6, 2017, we instituted an *inter partes* review of all challenged claims and consolidated Petitioner's two grounds into one ground.[1] Paper 6 ("Dec. Inst."). On February 26, 2018, Patent Owner filed a Patent Owner Response to the Petition. Paper 24 ("PO Resp."). On May 24, 2018, Petitioner filed a Reply to the Patent Owner Response. Paper 29 ("Reply").

Petitioner and Patent Owner each filed a Motion to Exclude Evidence. Papers 38 and 42. Each party filed an Opposition to the other party's motion. Papers 45 and 47. Each party also filed a Reply to the other party's Opposition. Papers 48 and 49. Patent Owner filed a Motion for Observation on Cross-Examination Testimony. Paper 41. Petitioner filed a Response to Patent Owner's Motion for Observation. Paper 46.

On July 24, 2018, the parties presented arguments at an oral hearing. The hearing transcript has been entered in the record. Paper 57 ("Tr.").

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[1] The Board has determined that this consolidation of grounds satisfies the requirements of *SAS Inst., Inc. v. Iancu*, 138 S. Ct. 1348 (2018), and Office Guidance on the Impact of *SAS* on AIA Trial Proceedings (https://www.uspto.gov/patents-application-process/patent-trial-and-appeal-board/trials/guidance-impact-sas-aia-trial), as the consolidation reflects all claims and all grounds presented in the Petition.

We issue this Final Written Decision pursuant to 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73. Having considered the record before us, we determine that Petitioner has shown by a preponderance of the evidence that claims 1–5 are unpatentable. *See* 35 U.S.C. § 316(e). Additionally, the Motions to Exclude Evidence by Petitioner and Patent Owner have been decided, as discussed below in Section III.

A. Related Proceedings

Petitioner and Patent Owner have not identified any other pending proceedings involving the '873 patent. Pet. 7; Paper 5, 2. Petitioner filed petitions for *inter parties* review of claims in related U.S. Patent Nos. 8,329,172 B2 (IPR2017-01166) and 8,557,244 B1 (IPR2017-01167). Both of those petitions were denied. *See* IPR2017-01166, Papers 9 (denying institution); IPR2017-01167, Papers 8 (denying institution) and 12 (denying rehearing).

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 a chimeric anti-CD20 antibody, i.e., "RITUXAN® rituximab," and CHOP (cyclophosphamide, hydroxydaunorubicin/doxo-rubicin, vincristine, and prednisone/prednisolone) chemotherapy, wherein the antibody is administered in combination with stem cell transplantation. *Id*. at 3:49–50; 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.
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> 4. The method of claim 1, wherein the lymphoma is accompanied by bone marrow involvement.

D. The Instituted Ground of Unpatentability

Petitioner challenges the patentability of claims 1–5 of the '873 patent

under 35 U.S.C. § 103(a) as obvious over Moreau,[2] Link,[3] McNeil,[4] Maloney,[5] and Coiffier.[6]

Petitioner also relies upon the Declarations of Howard Ozer, M.D., Ph.D. (Ex. 1002), Scott Bennett, Ph.D. (Ex. 1016), and Dr. Robert J. Soiffer, M.D. (Ex. 1035). Patent Owner relies upon the declaration of Dr. Brad S. Kahl, M.D. (Ex. 2011).

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) (affirming the Board's application of the broadest reasonable construction standard in *inter partes* review proceedings). Under that standard, and

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[2] 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).
[3] 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).
[4] McNeil, *Non-Hodgkin's Lymphoma Trials In Elderly Look Beyond CHOP*, 90 J. NAT. CANCER INST. 266–67 (1998) (Ex. 1003).
[5] 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).
[6] 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).

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); *Trivascular, Inc. v. Samuels*, 812 F.3d 1056, 1062 (Fed. Cir. 2016) ("Under a broadest reasonable interpretation, words of the claim must be given their plain meaning, unless such meaning is inconsistent with the specification and prosecution history.").

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 assert that the broadest reasonable interpretation of the terms of the '873 patent is their plain and ordinary meaning. Pet. 30. In particular, Petitioner asserts that the claim term "in combination with" recited in claims 1 and 5 includes "the administration of the anti-CD20 antibody (e.g., rituximab) at the 'induction' of CHOP chemotherapy but before the actual collecting or transplanting of stem cells." *Id.* As support, Petitioner refers to the Specification description that "rituximab can be administered at induction, in vivo purging, mobilization, conditioning, post-transplant reinfusion and at any other time during bone marrow or stem cell transplant for the purpose of improving the survival rate of transplant recipients." *Id.* at 30–31 (quoting Ex. 1001, 6:13–17). Additionally, Petitioner refers to the discussion in the Specification explaining that "induction" refers to "the initial therapies aimed at achieving induction of remission," wherein the induction typically involves "the administration of some type of chemotherapy, i.e., CHOP." *Id.* at 31 (quoting Ex. 1001, 6:17–20).

Referring to the same Specification descriptions, Patent Owner asserts that a person of ordinary skill in the art would have understood that "the anti-CD20 antibody is administered at any time during bone marrow or stem cell transplantation, including at the listed times—or any other time—during a stem cell transplantation regimen." PO Resp. 17–18 (citing Ex. 1001, 6:13–17 and Ex. 2011 ¶ 57). According to Patent Owner, the claim recitation of "in combination with" is not met by administering rituximab "before stem cell transplantation" because the Specification describes "rituximab treatment at the various stages of transplantation," which a person of ordinary skill in the art would understand to mean "rituximab treatment during the transplantation regimen." *Id.* at 18–19 (citing Ex. 1001, 6:54–58).

In the Reply, Petitioner asserts that there is no real dispute as to the construction of the claim phrase "in combination with." Reply 7–8. Petitioner explains that it "does not argue that claim 1 includes administration of rituximab before all phases of the entire stem cell transplantation regimen." *Id.* at 8. Instead, Petitioner explains that its position is that "in combination with stem cell transplantation" includes administering rituximab in the "induction phase" of the stem cell transplantation regimen, "which indisputably is part of the stem cell transplantation regimen [and] precedes the actual stem cell transplantation, which is conducted in the harvest phase of the regimen." *Id.* In other words, Petitioner asserts that induction is a phase or stage of the stem cell transplantation regimen.

Having considered the evidence and arguments, we determine that, in light of the Specification, the broadest reasonable construction of the claim

phrase directed to administering rituximab "in combination with stem cell transplantation,"[7] means that the rituximab may be administered "at induction, in vivo purging, mobilization, conditioning, post-transplant reinfusion and at any other time during bone marrow or stem cell transplant for the purpose of improving the survival rate of transplant recipients," as set forth in the Specification. Ex. 1001, 6:13–17. The Specification describes each of those "various stages of transplantation." *Id.* at 6:17–63. In particular, the Specification explains that "'[i]nduction' is meant to refer to the initial therapies aimed at achieving induction of remission. Typically, induction involves the administration of some type of chemotherapy, i.e., CHOP." Ex. 1001, 6:17–20. Thus, we agree with Petitioner that "the administration of the anti-CD20 antibody (e.g., rituximab) at the induction of CHOP chemotherapy but before the actual collecting or transplanting of stem cells" is encompassed in the claim phrase directed to administering rituximab "in combination with stem cell transplantation." Indeed, Patent Owner acknowledges that "[e]ven administration of an anti-CD20 antibody at an induction stage of a stem cell transplantation regimen can fall within the scope of the claims." PO Resp. 19.

We determine that construction of additional claim terms is not necessary for purpose of this Decision. *See Vivid Techs., Inc. v. Am. Sci. &*

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[7] Independent claim 1 recites "in combination with stem cell transplantation regimen," and independent claim 5 recites "in combination with stem cell transplantation." The parties' proposed constructions treat those phrases the same. We do too, as the Specification uses "stem cell transplantation" and "stem cell transplantation regimen" interchangeably, wherein both phrases refer to the "various stages of transplantation." *See, e.g.*, Ex. 1001, 6:13–63.

Eng'g, Inc., 200 F.3d 795, 803 (Fed. Cir. 1999) (only terms which are in controversy need to be construed).

B. Level of Ordinary Skill in the Art

The level of skill in the art is a factual determination that provides a primary guarantee of objectivity in an obviousness analysis. *Al-Site Corp. v. VSI Int'l Inc.*, 174 F.3d 1308, 1324 (Fed. Cir. 1999) (citing *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966); *Ryko Mfg. Co. v. Nu-Star, Inc.*, 950 F.2d 714, 718 (Fed. Cir. 1991)).

According to Petitioner, a person of ordinary skill in the art at the time of the invention would have "include[d] a practicing oncologist with at least an M.D. degree and several years of experience treating patients with NHL and/or researching treatments for NHL, including with chemotherapeutic drugs." Pet. 9 (citing Ex. 1002 ¶ 15).

Patent Owner disagrees with Petitioner's description of the level of ordinary skill in the art, asserting that oncologists having ordinary skill in the field of treating intermediate- and high-grade NHL "would have had experience treating patients, but would not have had experience researching new treatments for patients." PO Resp. 16 (citing Ex. 2011 ¶ 25). According to Patent Owner and its declarant, Dr. Kahl, only a person whose skill in the art was "extraordinary" would have had "'experience researching treatments for NHL, and those oncologists were innovators,' not people having only ordinary skill in the art." *Id.* at 15–16 (citing Ex. 2011 ¶ 24). Therefore, Patent Owner asserts that a person of ordinary skill in the art "would have on average been a practicing oncologist with at least an M.D. degree and about one to three years of experience treating patients with NHL." *Id.* at 15.

In the Reply, Petitioner explains that because the Specification describes clinical trial testing, a person of ordinary skill in the art would have had clinical research expertise. Reply 4–5. Petitioner asserts also that Dr. Ozer is qualified under either Petitioner's or Patent Owner's description of the level of ordinary skill in the art. Further, Petitioner asserts that Dr. Kahl does not satisfy either description, as he is a hematologist and not an oncologist. *Id.* at 5 (citing Ex. 1034, 27:3–5).

Based upon our consideration of the arguments and evidence, we determine that the record, as a whole, supports finding that a person having ordinary skill in the art of treating NHL, including DLCL, in elderly patients, would have at least an M.D. degree, with more than one year of experience treating patients with NHL as a practicing oncologist or hematologist, and would have had familiarity with published research and clinical trials directed toward treating NHL patients. In particular, Petitioner's declarant, Dr. Ozer, confirmed that "one to three years" of experience satisfies Petitioner's and his description of "several years of experience." Ex. 2008, 15:11–15. Regarding the relevant medical field, Patent Owner asserts that the person of ordinary skill in the art is a "practicing oncologist," but offers a hematologist as its declarant. PO Resp. 15–16 (citing Ex. 2011 ¶¶ 23–24). Despite that apparent contradiction, we determine that the record as a whole supports finding that a hematologist with the requisite experience treating NHL, including DLCL, also exemplifies a person having ordinary skill in the art. Indeed, Petitioner's description of the person having ordinary skill in the art is not limited to a practicing oncologist, as Petitioner states the person "include[s] a practicing oncologist." Pet. 9. Further, Petitioner's declarant, Dr. Ozer, confirmed

that a practicing hematologist with an M.D. degree and the required experience meets his definition of a person having ordinary skill in the art. Tr. 26:3–7. Additionally, we note that the applied prior art reflects the appropriate level of skill at the time of the claimed invention. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001).

Based upon our review of the credentials of Drs. Ozer, Soiffer, and Kahl, we consider each of them to be qualified to provide an opinion on the knowledge of a person of ordinary skill in the art at the time of the invention.[8] The relative weight that we assign such testimony, however, is subject to additional factors. *See, e.g.*, Office Patent Trial Practice Guide, 77 Fed. Reg. 48,756, 48,763 (Aug. 14, 2012) ("Opinions expressed without disclosing the underlying facts or data may be given little or no weight.").

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

Petitioner asserts that claims 1–5 of the '873 patent are unpatentable as obvious over a combination of Moreau, Link, McNeil, Maloney, and Coiffier. Pet. 42–54. Patent Owner disagrees. PO Resp. 21–61.

"The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 416 (2007). "If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability." *Id*. at 417.

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[8] Petitioner does not rely on Dr. Bennett's testimony (Ex. 1016) to support its contentions regarding the level of ordinary skill in the art. *See, e.g.*, Pet. 31 (referring to Ex. 1016 as support for the public accessibility of cited references).

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.[9] Eight of the original fourteen 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 fourteen patients were administered three courses of CHOP therapy. *Id*. The eleven 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 eleven 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 fourteen patients. *Id*. Although seven of the initial fourteen 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*.

[9] We reference exhibit page numbers added by the filing party, rather than the original page numbering therein, except for the '873 patent (Ex. 1001).

2. Link

Link describes a phase II pilot study of the safety and efficacy of administering Rituxan in combination with CHOP chemotherapy to thirty-one patients with previously untreated intermediate- or high-grade NHL. Ex. 1005, 5 (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 nineteen patients having a complete response, ten 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, 1. McNeil explains that the trial, organized by the Eastern Cooperative Oncology Group ("ECOG"), "will recruit 630 patients age 60 and over" to receive either CHOP alone or CHOP with Rituxan. *Id*. McNeil explains that researchers are focusing more on NHL in older patients because the incidence of NHL in those patients is rising and CHOP, the standard chemotherapy for intermediate-grade NHL, cures only about half as many elderly patients as younger patients. *Id.* McNeil describes "[o]ne more approach to NHL in the elderly involves peripheral stem cell transplants[,] an approach that is combined with low-dose chemotherapy regimens." *Id.* at 2.

4. Maloney

Maloney describes a phase I multiple-dose trial using "the chimeric anti-CD20 monoclonal antibody (mAb) IDEC-C2B8," i.e., 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 one IWF-G patient, received a dose of 250 mg/m^2, and ten patients (median age 59.5 years), including one 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 given 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

Independent claims 1 and 5 are directed to a method of treating a patient who has DLCL and is >60 years old by administering rituximab and CHOP, wherein rituximab is administered to the patient in combination with stem cell transplantation.[10] Petitioner asserts that Moreau taught all of the

[10] As discussed in the claim construction analysis above in section II. A., consistent with the parties' proposed constructions, we treat the phrases "in combination with stem cell transplantation" and "in combination with stem cell transplantation regimen" the same, based upon their usage in the Specification as both referring to the "various stages of transplantation." Ex. 1001, 6:13–63.

elements of claims 1 and 5, 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). According to Petitioner, 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).

Patent Owner does not dispute that Moreau taught all of the elements of claims 1 and 5, except for the addition of rituximab. *See, e.g.*, PO Resp. 26 (acknowledging Petitioner's assertion that Moreau taught all elements of claim 1, except administering rituximab); *see also* Ex. 1034, 71:19–73:10 (deposition testimony of Dr. Kahl, comparing claim 1 with Moreau). Rather, the points of contention involving Petitioner's challenge to those claims are whether Petitioner has established by a preponderance of the evidence that a person of ordinary skill in the art would have been motivated to combine rituximab with the CHOP in Moreau's treatment method, and whether the person of ordinary skill in the art would have had a reasonable expectation of success in treating Moreau's patient, i.e., a DLCL patient greater than 60 years old, by doing so. Thus, we next consider the arguments and evidence relating to those issues.

According to Petitioner, a person of ordinary skill in the art would have been motivated to find and combine with Moreau's method a treatment that could have "increased efficacy, reduced toxicity, or d[one] both" because only half of Moreau's DLCL patients achieved complete responses

with regimen combining CHOP and PBSCT. Pet. 44. Specifically, Petitioner asserts that Link and McNeil would have provided a skilled artisan a reason to combine rituximab with Moreau's method. *Id*. at 44–47; Ex. 1002 ¶¶ 88–90. Petitioner explains that Link teaches that a regimen combining CHOP and rituximab to treat intermediate- and high-grade NHL, including 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). Based upon those teachings, Petitioner asserts that an ordinarily skilled artisan would have been motivated to combine rituximab with a reduced CHOP regimen because doing so could achieve the same efficacy as CHOP monotherapy, with less toxicity, or more 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 plus rituximab, with a reasonable expectation of success. Pet. 46. Petitioner asserts that McNeil (a) explains that elderly patients have poorer outcomes with CHOP due to it being more toxic in that age group, *id.* (citing Ex. 1003, 1; Ex. 1002 ¶¶ 90–93), and (b) suggests that an alternative to standard CHOP therapy may be CHOP plus rituximab, *id*. at 46–47 (citing Ex. 1003, 1). According to Petitioner, an ordinarily skilled artisan would have reasonably expected from the combined teachings of Link and McNeil, that modifying Moreau's CHOP regimen to include rituximab could successfully provide Moreau's elderly patients with a more effective therapy without increasing toxicity. *Id*. at 47.

Additionally, Petitioner asserts that Maloney provides a person of ordinary 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 twenty 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 [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, an ordinarily 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.

Patent Owner asserts that Petitioner failed to identify any prior art disclosure of administering rituximab to a patient during a stem cell transplantation regimen. PO Resp. 23–24. However, such an express disclosure is not required to demonstrate obviousness. Rather, "a patent claiming the combination of elements of prior art" may be shown to be obvious if "the improvement is [no] more than the predictable use of prior art elements according to their established functions." *KSR*, 550 U.S. at 417; *see also In re Rosselet*, 347 F.2d 847, 851 (CCPA 1965) ("test of obviousness is not express suggestion of the claimed invention in any or all the references but rather what the references taken collectively would suggest to those of ordinary skill in the art"). Petitioner has shown persuasively how the combined teachings of the prior art would have

motivated a person of ordinary skill in the art to administer rituximab with CHOP in Moreau's stem cell transplantation patients for the reasons just discussed. Petitioner has particularly shown how the teachings of Link and McNeil would have provided a person of ordinary skill in the art a reason to add rituximab to CHOP in Moreau's method, Pet. 44–47, and has further explained how Moreau would have suggested to the artisan that rituximab would be suitable for use in a stem cell transplantation, Pet. 47 (citing Ex. 1008, 10).

Patent Owner urges us to view Maloney narrowly as suggesting administration of rituximab only after stem cell transplantation or recent chemotherapy. PO Resp. 42 (citing Ex. 2011 ¶¶ 99, 144). We instead credit Drs. Ozer's and Soiffer's testimony that a person of ordinary skill in the art "would have understood Maloney to be suggesting the combination of rituximab with CHOP and stem cell transplantation." Ex. 1002 ¶ 71; Ex. 1035 ¶ 28. The obviousness analysis "can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *KSR*, 550 U.S. at 418. "A person of ordinary skill is also a person of ordinary creativity, not an automaton." *Id.* at 421. In particular, Dr. Soiffer explained that in Maloney, "the key teaching is that rituximab 'does not appear to impair marrow reserves,' further suggesting that rituximab would have been an obvious agent to test with a stem cell transplantation regimen." Ex. 1035 ¶ 28 (citing Ex. 1008, 10). As Dr. Soiffer explained, a person of ordinary skill in the art would have realized that "Maloney's suggestion of using rituximab following high-dose therapy was but one example of a possible application." *Id.*

Patent Owner also takes issue with Maloney because there were only two DLCL patients in the study and they did not respond to the administered rituximab dose. PO Resp. 40–42. However, Dr. Soiffer explains persuasively that a person of ordinary skill in the art would have understood that "Maloney's teaching applies to *all* grades of NHL." Ex. 1035 ¶ 28. Specifically, Dr. Soiffer states that "[a]lthough there were only two DLCL patients in that study who happened not to improve, a POSA would not have understood [Maloney's] teaching about rituximab's impact on marrow reserves to have been limited by this fact." *Id.* Further, Dr. Soiffer explains that "DLCL patients have a significant mortality rate even with treatment, and poor results in a few patients would not have deterred a POSA from using or studying a drug in a broader patient population." *Id.*

Patent Owner asserts also that a person of ordinary skill in the art would not have been motivated to add rituximab to CHOP and a stem cell transplantation regimen because "no two of those therapies had been shown to be better than the individual therapies alone—even in lymphoma patients generally, let alone the claimed DLCL patients >60 years old." PO Resp. 27. Patent Owner, however, has not provided any authority for applying such a standard for establishing a motivation to combine known elements according to their established functions, nor do we recognize such a standard. There need only be "some articulated reasoning with rational underpinnings to support the legal conclusion of obviousness." *KSR*, 550 U.S. at 418 (quoting *In re Kahn*, 441 F.3d 977, 989 (Fed. Cir. 2006).

Here, Petitioner has articulated persuasively that, as part of the combination of references, Link would have provided a reason for a person of ordinary skill in the art to administer rituximab with CHOP when treating

DLCL in patients over 60 years of age. Pet. 44–49. Specifically, Link discloses treating thirty-one patients with previously untreated intermediate- or high-grade NHL, including twenty-one patients with IWF-G pathology, i.e., DLCL, with a combination of rituximab and CHOP. Ex. 1005, 5. Link reports that there were no deaths in the study, and that the thirty patients evaluable for response include nineteen demonstrating a complete response, ten with a partial response, and one progression. *Id.* According to Link, its combination of rituximab and CHOP "represents 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.*

Patent Owner takes issue with Link because it did not study patients over 60. PO Resp. 32. According to Patent Owner, "a POSA would have known that age was a critical prognostic factor for NHL." *Id.* In support of that contention, Patent Owner quotes McNeil's teaching that "age—being over age 60—was the most important factor independently associated with poorer survival in patients with intermediate- and high-grade lymphoma." *Id.* (quoting Ex. 1003, 1).

Although treating elderly DLCL patients was not a focus of Link, as it only discloses that the median age of the patients enrolled in the study was forty-nine, Petitioner and Dr. Ozer explain credibly that a person of ordinary skill in the art would have been motivated to use Link's combination in elderly patients because those patients were known to have a greater risk of toxicity and Link taught that the combination of rituximab and CHOP may offer higher response rates than CHOP alone with no greater frequency of serious adverse effects than encountered with CHOP alone. Pet. 45–46;

Ex. 1002 ¶¶ 88–90. Indeed, Petitioner and Dr. Ozer rely on the teaching of McNeil cited by Patent Owner describing the criticality of age to survival in intermediate- and high-grade lymphoma. As noted by Petitioner and Dr. Ozer, McNeil also explains that "[o]ne alternative could be CHOP plus the monoclonal antibody [rituximab]," and describes a clinical trial of the combination therapy in patients age 60 and over. Ex. 1003, 1. According to Dr. Ozer, those teachings and suggestions in McNeil "would have motivated a POSA to do what McNeil suggested—namely, combine CHOP and rituximab in patients over 60 years old with intermediate grades of lymphoma." Ex. 1002 ¶ 91. We agree.

Further, Dr. Soiffer explains that "although Link did not specifically study rituximab and CHOP in patients over 60, Coiffier would have disclosed to a POSA that rituximab was safe for use with DLCL patients over 60." Ex. 1035 ¶ 26. Of the fifty-two patients in Coiffier's study, thirty had DLCL. Ex. 1006, 3, Table 3. Coiffier describes a dominant feature of the population of patients was "relatively old age." *Id*. at 5. Coiffier concludes generally 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. Dr. Soiffer explains that "[a]lthough Coiffier did not break down the study's results by age, a POSA would have concluded that its general findings applied to patients over 60." Ex. 1035 ¶ 26. Indeed, Patent Owner's declarant, Dr. Kahl, similarly concluded that "you can look at [Coiffier] and look at the toxicity profile and determine that this [rituximab] is a tolerable treatment for older patients, that's . . . just fairly clear from the paper." Ex. 1034, 114:21–24.

Still further, Petitioner supports its contentions relating to a motivation to combine rituximab with CHOP in Moreau's method by referring to the teachings of Maloney, Pet. 47–48, for the reasons discussed above, i.e., Maloney explains that rituximab "does not appear to impair marrow reserves," Ex. 1008, 10. According to Drs. Ozer and Soiffer, "a POSA reading Maloney would have understood that rituximab could be added to CHOP in combination with PBSCT as disclosed in Moreau for treating elderly patients with DLCL." Ex. 1002 ¶ 92; Ex. 1035 ¶ 28.

Based upon our review of the record as a whole, the foregoing provides sound reasoning, supported by a preponderance of the evidence, for combining rituximab with CHOP in Moreau's method of treating DLCL in elderly patients. Indeed, based upon the combined teachings of Moreau, Link, McNeil and Maloney, as discussed above, Petitioner has demonstrated persuasively that the modification of Moreau amounts to no more than "the predictable use of prior art elements according to their established functions." *KSR*, 550 U.S. at 417.

Patent Owner asserts also that a person of ordinary skill in the art would not have been motivated to add rituximab to CHOP in Moreau's method because doing so "would have confounded the analysis of patient chemosensitivity." PO Resp. 29. For this contention, Patent Owner asserts that "a person having ordinary skill in the art would have known that stem cell transplantation was not indicated for patients who did not have chemosensitive disease." *Id.* (citing Ex. 1010, 12). Patent Owner refers also to Dr. Ozer's deposition testimony that "it was known that a patient whose disease is refractory to chemotherapy is not a good candidate to begin a stem cell transplantation regimen." *Id.* (quoting Ex. 2008, 39:7–11). Patent

Owner and Dr. Kahl assert that physicians would administer chemotherapy to a patient shortly before starting the patient on a stem cell transplantation regimen, as Moreau did, to determine whether such chemosensitivity exists, i.e., to determine if a patient's disease is responsive or resistant to chemotherapy. *Id.* at 30 (citing Ex. 2011 ¶¶ 48, 73, 123–124; Ex. 1007, 1). According to Patent Owner, "[a] POSA would have known that adding rituximab to those three doses of CHOP would have confounded that assessment," as a response seen in a patient may be a result of rituximab and not CHOP. *Id.* (citing Ex. 2011 ¶ 124).

Based on the record as a whole, we find that Petitioner's declarant, Dr. Soiffer, more precisely describes the determination of a patient's disease sensitivity during the induction stage of stem cell transplantation as concerning "treatment sensitivity" rather than specifically "chemosensitivity." Reply 21 (citing Ex. 1035 ¶¶ 32–35). Dr. Soiffer explains persuasively that at the time of the invention there was no evidence "that a lymphoma had to previously respond to chemotherapy per se to improve the likelihood of a successful outcome with transplantation." Ex. 1035 ¶ 35. Rather, Dr. Soiffer clarifies that "*[a]ny* modality that substantially decreased tumor burden could render a patient an appropriate transplant candidate." *Id.* In particular, Dr. Soiffer explains that adding "rituximab to a regimen like CHOP had and still has the potential to kill more lymphoma cells, allowing patients to enter transplant with a lower burden of disease." *Id.* According to Dr. Soiffer, "[t]he reduction in the burden of disease, not the specific modality to achieve that reduction, determines a patient's prognosis with respect to transplant outcome." *Id.* As Dr. Soiffer has provided a more comprehensive discussion regarding the

determination of disease sensitivity during the induction stage of a stem cell transplant regimen, we find his testimony relating to treatment sensitivity more credible and reliable than the limited discussion provided by Dr. Kahl. *See, e.g.*, Ex. 2011 ¶¶ 45–48, 121–123.

Patent Owner raises additional arguments asserting that "Petitioner fails to establish that any of Link, McNeil, or Maloney would have motivated a POSA to add rituximab to the three doses of CHOP in Moreau." PO Resp. 31. Patent Owner supports those contentions by identifying how each of those references, separately, differs from Moreau. *See id.* at 31–44. For example, Patent Owner asserts that Link would not have motivated a person having ordinary skill in the art to add rituximab to the CHOP in Moreau because Link does not disclose (a) treating patients older than 60 years of age, (b) the same number of CHOP cycles as Moreau, or (c) stem cell transplantation. *Id*. at 31–32. Patent Owner asserts that McNeil would not have motivated a person having ordinary skill in the art to add rituximab to CHOP in Moreau because McNeil does not suggest administering rituximab in combination with stem cell transplantation and does not report any results from the phase III trial of rituximab and CHOP that is discusses. *Id.* at 37. Patent Owner asserts that Maloney would not have motivated a person having ordinary skill in the art to add rituximab to CHOP in Moreau because Maloney is a study of rituximab monotherapy that does not disclose responses in DLCL patients, and "describes administration of rituximab only *after* the stem cell transplantation or recent chemotherapy pretreatment." *Id*. at 41–42. As for Coiffier, Patent Owner asserts that the reference studied rituximab monotherapy using eight doses of rituximab on a weekly basis, did not report any responders as older than 60 years of age, and did not

suggest any combination of rituximab with CHOP or stem cell transplantation. *Id.* at 44–45. Each of those arguments, however, is misdirected as they consider only Moreau and each cited reference, separately, rather than considering the combined teachings of each of the cited references together. In an obviousness analysis, the references "must be read, not in isolation, but for what [they] fairly teach[] in combination with the prior art as a whole." *In re Merck & Co, Inc.*, 800 F.2d 1091, 1097 (Fed. Cir. 1986); *see also Intellectual Ventures I LLC v. Motorola Mobility LLC*, 870 F.3d 1320, 1335 (Fed. Cir. 2017) ("Obviousness is determined based on the teachings in the prior art, and whether it would have been obvious to select and combine these teachings."). Moreover, we have addressed above how Petitioner has shown by a preponderance of the evidence that those combined teachings would have motivated a person of ordinary skill in the art to add rituximab to Moreau's method of treating DLCL patients over 60.

Patent Owner asserts also that Link, Maloney, and Coiffier each teaches administering rituximab on a different dosing schedule than would likely be used for the CHOP in Moreau. *See* PO Resp. 34, 42, and 45. In particular, Patent Owner asserts that Link administers six doses of rituximab, whereas Moreau administers three doses of CHOP, *id.* at 34; Maloney administers four doses of rituximab weekly, and although Moreau does not disclose the cycle days for CHOP, CHOP is usually administered every 21 days, *id.* at 42; and Coiffier administers eight doses of rituximab on a weekly basis, *id.* at 45. Insofar as Patent Owner asserts that there would have been no motivation to add rituximab to Moreau's CHOP therapy based upon the dosing used for rituximab in Link, Maloney or Coiffier, *see* PO Resp. 34, 42,

and 45, we disagree. To begin, adding rituximab to Moreau's CHOP therapy does not require administering the medications simultaneously, for the same number of doses, and/or at the same interval. Indeed, the challenged claims do not recite any requirement to do so. Rather, regarding the administration of rituximab, the claims are directed to administering rituximab "in combination with stem cell transplantation" or "in combination with stem cell transplantation regimen." As discussed, Petitioner has shown persuasively that the preponderance of the evidence supports finding motivation to administer rituximab at the *same stage* of the stem cell transplantation as CHOP, without requiring the dosing schedule within that stage to be precisely the same as that of CHOP. It is the time frame, i.e., stage, during which rituximab is administered, not the dosing schedule therein, that is relevant and sufficient to meet the claim recitation of administering rituximab "in combination with" stem cell transplantation.

Patent Owner asserts that "Petitioner never contended that adding rituximab to the three doses of CHOP in Moreau would have resulted in administering rituximab *during* a stem cell transplantation regimen." PO Resp. 46 (emphasis added). However, as discussed above in Section II. A., we have determined that the broadest reasonable construction of the claim phrase directed to administering rituximab "in combination with stem cell transplantation," means that the rituximab may be administered "at induction, in vivo purging, mobilization, conditioning, post-transplant reinfusion and at any other time during bone marrow or stem cell transplant for the purpose of improving the survival rate of transplant recipients," as described in the Specification. Ex. 1001, 6:13–17. Further, we explained that the Specification describes "induction" as referring to the initial

therapies aimed at achieving induction of remission, typically involving the administration of chemotherapy, i.e., CHOP. *Id.* at 6:17–20. Thus, as Petitioner asserts, "the administration of the anti-CD20 antibody (e.g., rituximab) at the 'induction' of CHOP chemotherapy but before the actual collecting or transplanting of stem cells" is encompassed in the claim phrase directed to administering rituximab "'in combination with' stem cell transplantation." *See* Pet. 30. That is the precise stage at which Moreau discloses administering CHOP. *See* Ex. 1003, 1. Thus, combining rituximab with Moreau's administration of CHOP at that stage meets the claim limitation requiring administration of rituximab in combination with stem cell transplantation.

Patent Owner asserts that "Petitioner fails to show that a POSA would have had a reasonable expectation of success in combining Moreau, Link, McNeil, Maloney, and Coiffier to arrive at the claimed invention." PO Resp. 47. In particular, Patent Owner asserts that "Petitioner could not reasonably contend that so long as the toxicities of the multiple therapies did not overlap, a multiple therapy regimen with no efficacy would have been considered by a POSA to be successful." *Id.* at 49. Further, Patent Owner asserts that Petitioner fails to adduce evidence that a POSA would have had "a reasonable expectation of any [] improved prognosis" for patients over 60 years of age. *Id.* at 50. According to Patent Owner, none of the asserted prior art "reports successful treatment of DLCL patients > 60 years old with rituximab alone, much less rituximab plus CHOP." *Id.* at 50.

The proper inquiry regarding a reasonable expectation of success involves considering whether a person of ordinary skill in the art would have had a reasonable expectation of successfully making the *claimed invention*

in light of the prior art. *See Amgen, Inc. v. F. Hoffman–La Roche Ltd.*, 580 F.3d 1340, 1362 (Fed. Cir. 2009) ("An obviousness determination requires that a skilled artisan would have perceived a reasonable expectation of success in making the invention in light of the prior art."); *see also Intelligent Bio-Sys, Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1367 (Fed. Cir. 2016) (referring to the "likelihood of success in combining references to meet the limitations of the claimed invention"). "[O]bviousness cannot be avoided simply by a showing of some degree of unpredictability in the art so long as there was a reasonable probability of success." *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1364 (Fed. Cir. 2007). Under the proper standard, "the expectation of success need only be reasonable, not absolute." *Id.*

Based upon our review of the record as a whole, we find that Petitioner has established by a preponderance of the evidence that a person having ordinary skill in the art would have had a reasonable expectation of success in treating a DLCL patient over the age of 60 with a modified version of Moreau's method that includes administering rituximab with CHOP. As previously discussed, Petitioner has established by a preponderance of the evidence that Moreau taught a method of treating patients over the age of 60 with DLCL by administering CHOP at the induction stage of the stem cell transplant, and again after stem cell collection. Ex. 1007, 1–2. Based on its pilot study, Moreau concluded that its stem cell transplantation "can probably be performed in patients between 61 and 65 years of age," as no severe cardiac, renal, hepatic, or pulmonary toxicity was documented, and that seven of the eleven patients who underwent the transplantation stage were found to be free from disease. *Id.*

at 3. In other words, Moreau disclosed a successful method of treating DLCL patients over 60 years of age that was tolerable with "no toxic deaths," and effective because it led to complete responses in half of the DLCL patients over 60. Ex. 1007, 3 and Table 3; *see* Ex. 1035 ¶ 25 (explaining that Moreau's study was successful).

Petitioner demonstrated also that a person having ordinary skill in the art would have understood from the combined teachings of Link, McNeil, Maloney, and Coiffier that an alternative to CHOP in elderly patients may be CHOP plus rituximab (McNeil), that the CHOP plus rituximab combination may provide an increased response in DLCL patients (Link), that rituximab therapy has significant anti-lymphoma activity in DLCL (Coiffier), and that rituximab does not impair bone marrow reserves (Maloney). Those combined teachings serve not only as motivation for combining rituximab with Moreau's method, as discussed above, but also serve to demonstrate why a person of ordinary skill would have had a reasonable expectation of successfully treating a 60 year old DLCL patient by doing so. Rituximab was shown to be a well-tolerated drug alone and in combination with CHOP, making it attractive for use in the elderly "who were known to have larger risk of toxicity." Ex. 1002 ¶ 89. Further, Dr. Ozer explained that a person having ordinary skill in the art would have understood from the combined prior art, particularly Maloney, that rituximab may be used with stem cell transplantation because it was shown not to impair bone marrow reserves. *Id.* at ¶¶ 70–71. Thus, we agree with Petitioner that a person of skill in the art would have reasonably expected Moreau's well-tolerated and effective method would remain so upon adding rituximab. In other words, the preponderance of the evidence suggests encouraging results from such a

combination that would provide a person of ordinary skill in the art a reasonable expectation of success in treating elderly DLCL patients.[11]

Accordingly, based on the foregoing, we find that Petitioner has established by a preponderance of the evidence that a person having ordinary skill in the art (a) would have been motivated to add rituximab to the CHOP administered in Moreau's method of treating DLCL patients over 60 years of age with CHOP and PBSCT, in a manner that yields the inventions of claims 1 and 5, and (b) would have had a reasonable expectation of successfully treating those patients with that modified method. Patent Owner does not submit or rely upon any objective evidence of nonobviousness for us to consider regarding claims 1 and 5. *See Graham*, 383 U.S. at 1. Therefore, we conclude that Petitioner has established by a preponderance of the evidence that claims 1 and 5 are unpatentable over the combined teachings of Moreau, Link, McNeil, Maloney, and Coiffier.

Claim 2 recites "[t]he method of claim 1, wherein the antibody comprises a chimeric anti-CD20 antibody," and claim 3 recites "[t]he method of claim 2, wherein the antibody comprises rituximab." Petitioner asserts that those claims would have been obvious over the combined teachings of the cited art for the same reasons as discussed regarding claim 1, particularly because the antibody that Maloney suggests adding to the combination therapy is described as "rituximab," a "chimeric anti-CD20 monoclonal antibody." Pet. 50. We agree. Patent Owner does not

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[11] We note that the claims are directed to a method of "treating" DLCL patients over the age of 60, without requiring such treatment to achieve a particular result or to provide any improved result over a treatment with CHOP and/or PBSCT either alone or combined.

separately argue claims 2 and 3. Nor does Patent Owner submit or rely upon any objective evidence of nonobviousness for us to consider regarding claims 2 and 3. Thus, for the same reasons discussed regarding claim 1, we conclude that Petitioner has established by a preponderance of the evidence that claims 2 and 3 are unpatentable over the combined teachings of Moreau, Link, McNeil, Maloney, and Coiffier.

Claim 4 recites "[t]he method of claim 1, wherein the lymphoma is accompanied by bone marrow involvement." Petitioner asserts that claim 4 is obvious over the same combination of references as claim 1, particularly because Maloney disclosed that marrow involvement was present in 50% of the patients in its study, and reported tumor responses in bone marrow. Pet. 50 (citing Ex. 1008, 3, 5). According to Petitioner, a person of ordinary skill in the art would have understood from Maloney that "adding rituximab to CHOP therapy could successfully treat patients with cancerous cells in the bone marrow." *Id.* at 51. Additionally, Petitioner relies on Dr. Ozer's testimony that "[t]here is nothing atypical about lymphoma accompanied by bone marrow involvement, and certainly nothing that requires unique treatment." *Id.* (quoting Ex. 1002 ¶ 97). Further, Petitioner asserts that "Coiffier disclosed that rituximab successfully treated 43% – nearly half – of intermediate-grade patients with bone marrow involvement." *Id.* at 53 (citing Ex. 1006, 3, Table 3; Ex. 1002 ¶¶ 100–101).

Patent Owner asserts that claim 4 "would not have been obvious over the Maloney reference" because "Maloney did not even report success in any DLCL patients without bone marrow involvement, let alone DLCL patients >60 years old with bone marrow involvement, as claimed." PO Resp. 59. However, that argument misses the point as we have determined

that the preponderance of the evidence supports Petitioner's contention that a person having ordinary skill in the art would have considered Maloney's teaching that rituximab does not impact marrow reserves, in combination with the teachings and suggestions of Moreau, Link, McNeil and Coiffier as providing motivation to add rituximab to Moreau's method with a reasonable expectation of successfully treating Moreau's DLCL patients over 60 years of age, as discussed regarding claim 1, including those having bone marrow involvement. Indeed, as Drs. Ozer, Soiffer, and Kahl acknowledge, a person of ordinary skill in the art would have not treated lymphoma patients with bone marrow involvement any differently than those without such involvement. Ex. 1002 ¶¶ 97–98; Ex. 1034, 85:9–16; Ex. 1035 ¶ 29.

Patent Owner does not submit or rely upon any objective evidence of nonobviousness for us to consider regarding claim 4. Therefore, for the foregoing reasons, we conclude that Petitioner has established by a preponderance of the evidence that claim 4 is also unpatentable over the combined teachings of Moreau, Link, McNeil, Maloney, and Coiffier.

III. MOTIONS TO EXCLUDE

Petitioner and Patent Owner each filed a motion to exclude evidence. Papers 38 and 42.

A. Petitioner's Motion

Petitioner moves to exclude Patent Owner's Exhibits 2013–2015 and 2017–2019. Paper 38, 1. Patent Owner opposes the motion. Paper 47. As the moving party, Petitioner has the burden of proof to establish that it is entitled to the requested relief.

Petitioner asserts that Patent Owner introduced Exhibits 2013–2015 and 2017–2019 for the first time during the deposition of Petitioner's Reply declarant, Dr. Soiffer. Paper 38, 3. According to Petitioner, those exhibits were untimely submitted during Dr. Soiffer's deposition as they were not within the scope of his direct testimony. *Id.*; Paper 48, 4. Patent Owner urges that Petitioner failed to adequately object to the introduction of those exhibits during Dr. Soiffer's deposition, and that it was not improper to introduce those new exhibits at that time. Paper 47, 1. We have not relied upon those exhibits in this Final Written Decision, nor has Patent Owner referred to them or the portion of Dr. Soiffer's deposition testimony relating to them in any subsequent filings other than its opposition to Petitioner's motion to exclude them. Accordingly, we dismiss Petitioner's Motion to Exclude those exhibits as moot.

B. Patent Owner's Motion

Patent Owner moves to exclude Petitioner's Exhibits 1004, 1023, 1033, 1036, 1037, 1039, and parts of Exhibit 2020. Paper 42. Petitioner opposes the motion. Paper 45. As the moving party, Patent Owner has the burden of proof to establish that it is entitled to the requested relief.

Exhibit 1004 is described by Petitioner as the "Rituxan™ (rituximab) labeling (Nov. 1997), i.e., the Rituxan label. Pet. vi. Patent Owner asserts that the exhibit should be excluded because it allegedly lacks authentication under Federal Rules of Evidence "FRE" 901 and represents hearsay under FRE 802. Paper 42, 8. Patent Owner asserts that Petitioner's declarant for this matter, Dr. Bennett, at most provides testimony that Exhibit 1004 is currently available from the FDA's website. *Id.* at 9. According to Patent Owner, Petitioner has not established that the exhibit existed and was

available in 1997. *Id.* That issue, however, relates to the status of the exhibit as prior art and should have been raised in the briefing and not a motion to exclude. *See generally Groupon Inc. v. Blue Calypso, LLC*, Case CBM2013-00033, slip op. at 25 (PTAB May 12, 2013) (Paper 29) (distinguishing admissibility of evidence from sufficiency of evidence).

Regarding authentication, Patent Owner asserts that Dr. Bennett testified that "Attachment 6a is a true and accurate copy of the original 1997 drug label for Rituxan available from Drugs@FDA: FDA Approved Drug Products," but does not state the same for Exhibit 1004. *Id.* at 8 quoting Ex. 1016, 27–28. A side-by-side comparison of Attachment 6a and Exhibit 1004 reveals that the documents are identical copies. *Compare* Ex. 1016, Attachment 6a *with* Exhibit 1004. Thus, Patent Owner has not demonstrated that Dr. Bennett has not sufficiently authenticated Exhibit 1004. Nor are we persuaded that Exhibit 1004 constitutes hearsay as Patent Owner has not demonstrated that Petitioner offers the exhibit to prove the truth of the matter asserted in any "statement" contained therein. *See* FRE 801 and 802. Accordingly, we deny Patent Owner's motion to exclude with respect to Exhibit 1004.

Patent Owner also moves to exclude Exhibits 1023 (an excerpt from the Physician's Desk Reference, 53rd ed. 1999), 1033 (a journal article discussing "A Novel Preparing Regiment for Autologous Transplant in Non-Hodgkin's Lymphomas: Long-Term Experience with Etoposide and Thiotepa"), 1036 (a journal article discussing "CHOP Chemotherapy Plus Rituximab Compared with CHOP Alone in Elderly Patients with Diffuse Large B Cell Lymphoma"), and 1037 (a journal article discussing a "Phase II Study of Rituximab in Combination with CHOP Chemotherapy in Patients

with Previously Untreated, Aggressive Non-Hodgkin's Lymphoma") as hearsay. Paper 42, 11–12. We are unpersuaded that any of those exhibits consists of inadmissible hearsay as Patent Owner has not explained its contention adequately by merely asserting that their contents are "being offered for the purpose of attempting to prove the truth of the matter asserted in the statements." *See id.* Accordingly, we deny Patent Owner's motion to exclude with respect to Exhibits 1023, 1033, 1036, and 1037.

Patent Owner asserts that its request to exclude Exhibit 1039 is contingent on the Board granting Petitioner's motion to exclude Patent Owner's Exhibits 2013–2015 and 2017–2019, as all of those exhibits were similarly introduced as a new exhibits during the deposition of a reply declarant. Paper 42, 7. We have dismissed Petitioner's motion regarding Exhibits 2013–2015 and 2017–2019, and, therefore, we dismiss Patent Owner's contingent motion to exclude with respect to Exhibit 1039 also.

Exhibit 2020 is the transcript of the deposition of Petitioner's Reply declarant, Dr. Soiffer. Patent Owner requests that we exclude the entirety of the redirect testimony contained therein. Paper 42, 1 (citing Ex. 2020, 171:7–189:11). To begin, Patent Owner asserts that the testimony is unreliable because Petitioner's counsel allegedly coached Dr. Soiffer during the break prior to the redirect examination. *Id.* However, Patent Owner supports that contention only with testimony from Dr. Soiffer that he discussed the redirect with Petitioner's counsel during the break. *Id.* at 2 (citing Ex. 2020, 192:6–10). According to Patent Owner, "[i]t appears, therefore, that during the break, Petitioner's counsel identified for Dr. Soiffer what testimony he gave during cross-examination that counsel wanted to change, and then discussed how to change that testimony through

redirect questions." *Id.* We are unpersuaded, as that argument is based merely upon speculation.

Next, Patent Owner asserts that the redirect testimony should be excluded because the majority of the questions asked by Petitioner's counsel were leading. *Id.* at 1. For example, Patent Owner asserts that Petitioner's counsel directed Dr. Soiffer to read the relevant portion of his declaration or an article before asking leading questions about the contents therein. *Id.* at 3 (citing Ex. 2020, 174:21–175:12). Patent Owner, however, has not demonstrated that Petitioner's questions were leading. Without a better explanation from Patent Owner, our review of the cited testimony appears to involve Dr. Soiffer attempting to answer a question relating to whether an exhibit was cited in his declaration after Petitioner provided him with a copy of the declaration for his reference. *See* Ex. 2020, 174:21–175:12.

Finally, Patent Owner asserts that the redirect testimony should be excluded because the majority of the redirect testimony was outside the scope of the cross-examination. Paper 42, 1. We disagree. Patent Owner acknowledges that during cross-examination, Patent Owner asked Dr. Soiffer, "were there any other documents you reviewed that are not cited in your declaration?" *Id.* at 5 (citing Ex. 2020, 17:11–14). Dr. Soiffer's answer referenced a "Freedman manuscript from 1997." *Id.* (citing Ex. 2020, 17:19–21). Patent Owner asserts that Dr. Soiffer's redirect testimony exceeded the scope of the cross-examination because Petitioner provided Dr. Soiffer with copies of two Freedman articles, Exs. 1038 and 1039, and asked if he had cited or intended to cite those references in his declaration. Paper 42, 5–7 (citing Ex. 2020, 175:9–178:7, 185:22–188:22). Based upon our review, however, we find that Patent Owner characterizes

the scope of the cross-examination too narrowly. We agree with Petitioner that Patent Owner "opened the door" to testimony concerning Exhibits 1038, 1039 by asking about documents that Dr. Soiffer had reviewed in preparation of his declaration. *See* Paper 45, 6.

Accordingly, based on the foregoing, we deny Patent Owner's Motion to Exclude the redirect testimony contained in Exhibit 2020.

IV. CONCLUSION

For the foregoing reasons, we conclude that Petitioner has shown by a preponderance of the evidence that claims 1–5 of the '873 patent are unpatentable.

ORDER

Accordingly, it is hereby:

ORDERED that claims 1–5 of the '873 patent are unpatentable under 35 U.S.C. § 103(a) as obvious over Moreau, Link, McNeil, Maloney, and Coiffier;

FURTHER ORDERED that Petitioner's Motion to Exclude is *dismissed* as moot;

FURTHER ORDERED that Patent Owner's Motion to Exclude is *denied* as to Exhibits 1004, 1023, 1033, 1036, 1037, and parts of Exhibit 2020, and *dismissed* as moot as to Exhibit 1039; and

FURTHER ORDERED that because this is a Final Written Decision, parties to the proceeding seeking judicial review of the decision must comply with the notice and service requirements of 37 C.F.R. § 90.2.

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