

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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HOSPIRA, INC.,  
Petitioner,

v.

GENENTECH, INC.,  
Patent Owner.

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Case IPR2017-00731  
Patent 7,846,441 B1

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Before ZHENYU YANG, CHRISTOPHER G. PAULRAJ, and  
ROBERT A. POLLOCK, *Administrative Patent Judges*.

YANG, Administrative Patent Judge.

DECISION  
Granting Request for Rehearing  
Institution of *Inter Partes* Review  
*37 C.F.R. §§ 42.71(d), 42.108*

## INTRODUCTION

Hospira, Inc. (“Petitioner”) filed a Petition requesting an *inter partes* review of claims 1–14 of U.S. Patent No. 7,846,441 B1 (Ex. 1001, “the ’441 patent”). Paper 1 (“Pet.”). Genentech, Inc. (“Patent Owner”) filed a Preliminary Response to the Petition. Paper 8 (“Prelim. Resp.”). We initially denied the Petition. Paper 19 (“Dec.”). Petitioner filed a Request for Rehearing of the Decision. Paper 21 (“Reh’g Req.”).

When rehearing a decision on institution, the Board reviews the decision for an abuse of discretion. 37 C.F.R. § 42.71(c). An abuse of discretion occurs when a “decision was based on an erroneous conclusion of law or clearly erroneous factual findings, or . . . a clear error of judgment.” *PPG Indus. Inc. v. Celanese Polymer Specialties Co.*, 840 F.2d 1565, 1567 (Fed. Cir. 1988) (citations omitted). The request must identify, specifically, all matters the party believes the Board misapprehended or overlooked. 37 C.F.R. § 42.71(d).

For the following reasons, we grant Petitioner’s Request for Rehearing, and institute an *inter partes* review of claims 1–14 of the ’441 patent. *See* 35 U.S.C. § 314(a).

### *Related Proceedings*

The ’441 patent is the subject of a petition for an *inter partes* review filed by Celltrion, Inc. IPR2017-01121, Paper 1. We instituted trial in that case. *Celltrion, Inc. v. Genentech, Inc.*, IPR2017-01121 (PTAB October 4, 2017) (Paper 9).

Petitioner has also filed IPR2017-00737 and IPR2017-00739, challenging certain claims of U.S. Patent No. 7,892,549 (“the ’549 patent”), a patent in the same family as the ’441 patent. Pet. 3–4; Paper 8, 2–3. We

denied institution in one case (*Hospira, Inc. v. Genentech, Inc.*, IPR2017-00739 (PTAB July 27, 2017) (Paper 16)), but instituted trial in another (*Hospira, Inc. v. Genentech, Inc.*, IPR2017-00737 (PTAB July 27, 2017) (Paper 19)). Additionally, Celltrion filed IPR2017-01122, challenging claims of the '549 patent. IPR2017-01122, Paper 1. We instituted trial in that case. *Celltrion, Inc. v. Genentech, Inc.*, IPR2017-01122 (PTAB October 4, 2017) (Paper 9).

### *The '441 Patent*

The '441 patent relates to the treatment of disorders characterized by the overexpression of ErbB2. Ex. 1001, Abstract, 1:11–12.

According to the Specification, “human ErbB2 gene (erbB2, also known as her2, or c-erbB-2), which encodes a 185-kd transmembrane glycoprotein receptor (p185<sup>HER2</sup>) related to the epidermal growth factor receptor (EGFR), is overexpressed in about 25% to 30% of human breast cancer.” *Id.* at 1:23–27. Before the '441 patent, a recombinant humanized anti-ErbB2 monoclonal antibody (a humanized version of the murine anti-ErbB2 antibody 4D5, also referred to as rhuMAb HER2, trastuzumab, or HERCEPTIN®) had been approved to treat patients with ErbB2-overexpressing metastatic breast cancers. *Id.* at 3:34–39.

According to the '441 patent, ErbB2 overexpression was known to be linked to resistance to chemotherapeutic regimens, including anthracyclines. *Id.* at 3:41–49. On the other hand, “the odds of HER2-positive patients responding clinically to treatment with taxanes were greater than three times those of HER2-negative patients.” *Id.* at 3:51–54.

The '441 patent states that

[T]he invention concerns a method for the treatment of a human patient susceptible to or diagnosed with a disorder characterized by overexpression of ErbB2 receptor comprising administering a therapeutically effective amount of a combination of an anti-ErbB2 antibody and a chemotherapeutic agent other than an anthracycline derivative, e.g. doxorubicin or epirubicin, in the absence of an anthracycline derivative, to the human patient.

*Id.* at 4:4–11.

*Illustrative Claim*

Among the challenged claims, claims 1, 11, 13, and 14 are independent. Claim 1 is representative and is reproduced below:

1. A method for the treatment of a human patient with a malignant progressing tumor or cancer characterized by overexpression of ErbB2 receptor, comprising administering a combination of an intact antibody which binds to epitope 4D5 within the ErbB2 extracellular domain sequence and a taxoid, in the absence of an anthracycline derivative, to the human patient in an amount effective to extend the time to disease progression in said human patient, without increase in overall severe adverse events.

*Asserted Grounds of Unpatentability*

Petitioner asserts the following grounds, each of which challenges the patentability of claims 1–14:

Basis	References
§ 103	Baselga '97 <sup>1</sup> and Baselga '94 <sup>2</sup>

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<sup>1</sup> Baselga et al., HER2 Overexpression and Paclitaxel Sensitivity in Breast Cancer: Therapeutic Implications, 11(3) (Suppl. 2) ONCOLOGY 43–48 (1997) (Ex. 1006).

<sup>2</sup> Baselga et al., Anti-HER2 Humanized Monoclonal Antibody (MAb) Alone and in Combination with Chemotherapy Against Human Breast Carcinoma Xenografts, 13 Proc. AM. SOC. CLIN. ONCOL. 63 (Abstract 53) (1994) (Ex. 1005).

Basis	References
§ 103	Baselga '96 <sup>3</sup> and Baselga '94

In support of its patentability challenges, Petitioner relies on the Declaration of Dr. Allan Lipton (Ex. 1007).

As explained in the Decision, because “the applicant successfully antedated Baselga '97 [during prosecution], we exercise our discretion under 35 U.S.C. § 325(d) and decline to institute *inter partes* review” based on the combination of Baselga '97 and Baselga '94. Dec. 7–8. We, thus, focus our analysis on whether Petitioner has established a reasonable likelihood of prevailing in showing the obviousness of at least one challenged claim over the combination of Baselga '96 and Baselga '94.

## ANALYSIS

### *Claim Construction*

In an *inter partes* review, the Board interprets a claim term in an unexpired patent according to its broadest reasonable construction in light of the specification of the patent in which it appears. 37 C.F.R. § 42.100(b); *Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2144–46 (2016). Under that standard, and absent any special definitions, we assign 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 the context of the entire patent disclosure. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007). Any special definitions for claim terms must be set forth with

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<sup>3</sup> Baselga et al., Phase II Study of Weekly Intravenous Recombinant Humanized Anti-p185<sup>HER2</sup> Monoclonal Antibody in Patients with HER2/*neu*-Overexpressing Metastatic Breast Cancer, 14 J. CLIN. ONCOL. 737–44 (1996) (Ex. 1004).

reasonable clarity, deliberateness, and precision. *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

“Administering a Combination”

Patent Owner proposes that we construe the term “administering a combination” as requiring “a single treatment regimen in which the patient receives all drugs that are part of the claimed combination.” Prelim. Resp. 32–33. According to Patent Owner, this definition is supported by the Specification and claim language. *Id.* at 33. For example, Patent Owner argues that “the absence of an anthracycline derivative” language in each challenge “would make no sense if ‘administering a combination’ included drugs received as part of a different treatment regimen” because in the working example of the ’441 patent, “patients were administered the combination of the anti-ErbB2 antibody and a taxoid in the absence of an anthracycline derivative only if they had ‘received any anthracycline therapy in the adjuvant setting’ (i.e., as part of a different treatment regimen).” *Id.* (citing Ex. 1001, 28:15–21). We find Patent Owner’s argument reasonable. Thus, for purpose of this Decision, and based on the present record, we adopt Patent Owner’s proposed definition of “administering a combination.” *See also Hospira, Inc. v. Genentech, Inc.*, IPR2017-00737 (PTAB July 27, 2017), Paper 19, 10 (construing the term the same way).

“Extend the Time to Disease Progression in Said Human Patient, Without Increase in Overall Severe Adverse Events”

Petitioner does not propose an express construction for any claim term. Pet. 22. We, however, note that each challenged claim, either explicitly or through dependency, recites “extend the time to disease progression in said human patient, without increase in overall severe adverse

events.” This is a relative term, but we do not discern that the claims, standing alone, identify the intended comparator.

The facial ambiguity of this phrase was expressly addressed during prosecution where the examiner rejected then-pending claims as indefinite under 35 U.S.C. § 112. Ex. 1011, Vol. 2, 324–25 (OA dated 7/17/2001).

The examiner stated:

The phrase “extend the time to disease progression” . . . is a relative term which renders the claim[s] indefinite. The term “extend time to disease progression” is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Specifically, it is never set forth what the extension of time to disease progress is relative to, for example, is the extension of time to disease progress relative to untreated patients? Patients who received antibody or taxoid alone? Patients who received antibody and an anthracycline?

*Id.* The applicant responded that

the expression[] “extend the time to disease progression”. . . [is] clear from the specification . . . and would be readily understood by the skilled oncologist. Clearly, the combination of anti-ErbB2 antibody and taxoid is administered in an amount effective to extend the time to disease progression relative to an untreated patient.

*Id.* at 356 (Response dated 1/17/2002). In the next office action, the examiner withdrew the rejection. *See* Ex. 1011, Vol. 3, 230 (OA dated 3/27/2002) (stating “[a]ll claims were allowable” but suspending prosecution due to potential interference); *see also id.* at 240–45 (OA dated 8/12/2003) (new grounds of rejection not relating to the phrase “extend the time to disease progression”).

Under the broadest-reasonable-interpretation standard, we must “consult the patent’s prosecution history in proceedings in which the patent has been brought back to the agency for a second review.” *Microsoft Corp. v. Proxyconn, Inc.*, 789 F.3d 1292, 1298 (Fed. Cir. 2015) (overruled on other grounds). “Any explanation, elaboration, or qualification presented by the inventor during patent examination is relevant, for the role of claim construction is to ‘capture the scope of the actual invention’ that is disclosed, described, and patented.” *Trivascular, Inc. v. Samuels*, 812 F.3d 1056, 1063 (Fed. Cir. 2016) (citation omitted). Here, given the applicant’s unequivocal statement to overcome the indefiniteness rejection during prosecution, we determine that the proper analysis of the term “extend the time to disease progression in said human patient, without increase in overall severe adverse events” is to compare the claimed combination treatment to no treatment. *See also Hospira, Inc. v. Genentech, Inc.*, IPR2017-00737 (PTAB July 27, 2017), Paper 19, 12 (construing the term the same way); *Celltrion, Inc. v. Genentech, Inc.*, IPR2017-01121 (PTAB October 4, 2017), Paper 9, 6 (construing the term the same way); *Celltrion, Inc. v. Genentech, Inc.*, IPR2017-01122 (PTAB October 4, 2017), Paper 9, 12–13 (construing the term the same way).

Claim terms need only be construed to the extent necessary to resolve the controversy. *Wellman, Inc. v. Eastman Chem. Co.*, 642 F.3d 1355, 1361 (Fed. Cir. 2011). On this record and for purposes of this Decision, we see no need to expressly construe any other claim terms.



*Disclosures of Prior Art*

Baselga '94

Baselga '94 teaches that HER2 overexpressing tumors were grown in nude mice followed by treatment with the 4D5-antibody in combination with paclitaxel. Ex. 1005, 4. Although the antibody or paclitaxel alone produced 35% growth inhibition, the combination of the two resulted in 93% growth inhibition without increasing toxicity. *Id.*

Baselga '96

Baselga '96 reports the results of a phase II clinical trial in patients with ErbB2-overexpressing metastatic breast cancer who had received extensive prior therapy. Ex. 1004, 9. According to Baselga '96, "patients were selected to have many sites of metastatic involvement, one of the most dire prognostic characteristics regarding response to therapy." *Id.* at 13. Each patient received a loading dose of 250 mg of intravenous rhuMAb HER2, followed by 10 weekly doses of 100 mg. *Id.* at 10. According to Baselga '96, "[a]dequate pharmacokinetic levels of rhuMAb HER2 were obtained in 90% of the patients. Toxicity was minimal and no antibodies against rhuMAb HER2 were detected in any patients." *Id.* at 9. Objective responses were seen with an 11.6% remission rate. *Id.* at 13. In addition, "37% of patients achieved minimal responses or stable disease." *Id.* "The median time to progression for the patients with either minor or stable disease was 5.1 months." *Id.* at 12.

Baselga '96 further teaches that in preclinical studies, "rhuMAb HER2 markedly potentiated the antitumor effects of several chemotherapeutic agents, including cisplatin, doxorubicin, and paclitaxel, without increasing their toxicity." *Id.* at 15. As a result, Baselga '96 reports

that “[l]aboratory studies of the mechanism of this effect and clinical trials of such combination therapy [were] . . . in progress.” *Id.*

*Asserted Obviousness Ground Based on Baselga ’96 and Baselga ’94*

Petitioner contends that claims 1–14 would have been obvious over the teachings of Baselga ’94 and Baselga ’96. Pet. 42–58. Upon reconsidering the current record, we determine Petitioner has established a reasonable likelihood that it would prevail on this assertion at least in relation to claim 1.

Petitioner refers to Baselga ’96 for teaching using rhuMAb HER2 to treat “adult women whose metastatic breast carcinomas overexpressed HER2.” Pet. 42 (citing Ex. 1004, 9, 10). According to Petitioner, rhuMAb HER2 is an intact antibody that binds to epitope 4D5 of the ErbB2 receptor, as recited in claim 1.

For the recited combination of an antibody and “a taxoid,” Petitioner argues that because certain patients were previously treated with taxoids, Baselga ’96 teaches this limitation. *Id.* at 44 (citing Ex. 1004, 13, Table 5). Petitioner also relies on the preclinical studies combining anti-HER2 MAbs with paclitaxel, as taught in Baselga ’96 and Baselga ’94. Pet. 44–45 (citing Ex. 1004, 15; Ex. 1005, 4).

For the limitation of “an effective amount to extend the time to disease progression in said human patient,” Petitioner refers to the dosing regimen of rhuMAb HER2 in Baselga ’96. *Id.* at 46–47 (citing Ex. 1004, 9–11). Under that dosing regimen, more than 90% of the patients achieved adequate pharmacokinetic levels of rhuMAb HER2, that is, “rhuMAb HER2 trough serum concentrations greater than 10 µg/mL, a level associated with optimal inhibition of cell growth in the preclinical model.” *Id.* at 46–47

(citing Ex. 1004, 9–11). Petitioner points out that in Baselga '96, some patients experienced a partial or complete remission, while others achieved minor responses or stable disease state, which “lasted for a median of 5.1 months.” *Id.* at 47 (citing Ex. 1004, 9, 13). According to Petitioner, because Baselga '96 and Baselga '94 teach that rhuMAb HER2 “markedly potentiated the antitumor effect” of paclitaxel in preclinical models, they suggest that the combination of rhuMAb HER2 of paclitaxel would improve time to disease progression, as claim 1 recites. *Id.* at 47–48.

Petitioner also argues the combination of Baselga '96 and Baselga '94 teaches the limitation “without increase in overall severe adverse events” because rhuMAb HER2 “was remarkably well tolerated” in clinical trial and there was no increase in the toxicity of paclitaxel when administered in combination with rhuMAb HER2 in preclinical models. *Id.* at 48 (citing Ex. 1004, 11, 13, 15; Ex. 1005, 4).

Patent Owner counters that an ordinary artisan would not have combined an anti-ErbB2 antibody and a taxoid based on Baselga '96 and Baselga '94. Prelim. Resp. 48–52. According to Patent Owner, Petitioner also has not established a reasonable expectation of success in achieving either the claimed clinical efficacy or the claimed clinical safety. 39–48, 54–55. Based on the current record, we find Petitioner’s arguments more persuasive.<sup>4</sup>

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<sup>4</sup> Patent Owner further contends that Petitioner has not shown an ordinary artisan would have avoided anthracyclines when pursuing the combination therapy of anti-ErbB2 antibody with a taxoid. Prelim. Resp. 52–54. We address this issue separately in the section discussing Petitioner’s Request for Rehearing. *See infra* pp. 16–18.

As an initial matter, we disagree with Petitioner that because, in Baselga '96, patients were treated at different times with an anti-ErbB2 antibody and a taxoid, an ordinary artisan would have had a reason to administer a combination of an anti-ErbB2 antibody and a taxoid. *See* Pet. 44 (citing Ex. 1004, 13, Table 5). As explained above, we construe the term “administering a combination” as requiring “a single treatment regimen in which the patient receives all drugs that are part of the claimed combination.” *Supra* p. 6. As a result, prior systemic therapy using a taxoid, followed by monotherapy with rhuMAb HER2, does not amount to a combination of the two.

Petitioner, however, points to other evidence to show that prior art teaches an ordinary artisan to combine an anti-ErbB2 antibody with a taxoid. Specifically, Petitioner refers to Baselga '94 for teaching that, in mouse xenografts, “individual treatment with either anti-HER2 4D5 or paclitaxel alone resulted in 35% growth inhibition whereas the combination ‘resulted in a major antitumor activity with 93% inhibition of growth’ without increasing toxicity.” *Id.* at 45 (citing Ex. 1005 at 4). Similarly, Baselga '96, citing Baselga '94, teaches that “[i]n preclinical studies, both in vitro and in xenografts, rhuMAb HER2 markedly potentiated the antitumor effects of several chemotherapeutic agents, including ... paclitaxel without increasing their toxicity.” *Id.* at 44 (quoting Ex. 1004, 15). Based on these teachings, we are persuaded that an ordinary artisan would have had a reason to treat HER2-positive breast cancer patients with a combination of rhuMAb HER2 and a taxoid.

Patent Owner points out that Baselga '94 also teaches combining anthracycline with anti-HER2 MAb. Prelim. Resp. 50 (citing Ex. 1005, 4).

According to Patent Owner,

Petitioner cannot have it both ways. If the disclosures in Baselga '94 would not have motivated a skilled artisan to treat patients with the combination of rhuMAb HER2 and anthracyclines (an established breast cancer chemotherapy), then they would not have caused a skilled artisan to pursue rhuMAb HER2 combined with a taxoid either.

*Id.* We are not persuaded.

First, Patent Owner inaccurately characterizes Petitioner's argument. Petitioner does not argue that an ordinary artisan would not combine anti-HER2 MAb with anthracyclines. Instead, Petitioner contends that an ordinary artisan would not "add doxorubicin [an anthracycline derivative] to the combination therapy with rhuMAb HER2 and paclitaxel." Pet. 46; *see also id.* at 29, 31–32.

Second, we disagree with the premise of Patent Owner's argument that Baselga '94, by itself, would not have motivated the skilled artisan to combine anti-HER2 MAb with anthracyclines. After all, Baselga '94 shows that the combination of the two resulted in 70% tumor growth inhibition as compared to 35% and 27% inhibition when administered separately.

Ex. 1005, 4.

Third, that the prior art teaches "a multitude of effective combinations does not render any particular formulation less obvious. This is especially true because the claimed composition is used for the identical purpose taught by the prior art." *Merck & Co. v. Biocraft Labs., Inc.*, 874 F.2d 804, 807 (Fed. Cir. 1989). Here, whether an ordinary artisan would have had a reason to combine anti-HER2 MAb with a taxoid is separate and independent from whether an ordinary artisan would have had a reason to combine anti-HER2 MAb with anthracyclines.

Moreover, as Petitioner points out, Baselga '94 shows that the combination of anti-HER2 MAb with paclitaxel was superior to the combination anti-HER2 MAb with doxorubicin. Pet. 46 (citing Ex. 1005, 4). Thus, based on current record, we are not persuaded by Patent Owner's argument that Baselga '94 does not teach combining anti-HER2 MAb with a taxoid.

Patent Owner argues that Exhibit 2029, which states that "breast cancers that overexpress p185 [i.e., HER2] will not respond well to Taxol," teaches away from the claimed combination therapy. Prelim. Resp. 51 (citing Ex. 2029,<sup>5</sup> 1362). We are not persuaded on this record. In an obviousness inquiry, we must analyze the prior art as a whole, and not individually. *See In re Fulton*, 391 F.3d 1195, 1200 (Fed. Cir. 2004) (explaining that the question is "whether there is something in the prior art as a whole to suggest the *desirability*, and thus the obviousness, of making the combination"). Other evidence of record shows paclitaxel had been approved for treating breast cancer (*see, e.g.*, Ex. 1025, 10), demonstrates synergy of paclitaxel and an anti-ErbB2 antibody in human breast cancer xenografts (*see, e.g.*, Ex. 1005, 4; Ex. 1004, 15), and suggests clinical trials of the combination therapy (*see, e.g.*, Ex. 1005, 4; Ex. 1004, 15). Weighing all evidence of record, we are not persuaded that prior art as a whole teaches away from combining paclitaxel and an anti-ErbB2 antibody in treating HER2-positive cancers.

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<sup>5</sup> Yu et al., *Overexpression of c-erbB-2/neu in Breast Cancer Cells Confers Increased Resistance to Taxol Via mdr-1-independent Mechanisms*, 13 ONCOGENE 1359–65 (1996).

Patent Owner further asserts that “preclinical results at that time were not a reliable predictor of clinical efficacy and safety.” Prelim. Resp. 51. According to Patent Owner, because “numerous other therapies . . . initially showed promise in mouse models, but ultimately failed in humans,” an ordinary artisan would not have combined paclitaxel and an anti-ErbB2 antibody. *Id.* at 51–52. We are not persuaded on this record. Each of Baselga ’94 and Baselga ’96 specifically teaches the claimed combination and suggests clinical trials to test the effectiveness. Nothing more is required to satisfy the combination limitation.

To the extent this argument relates to the expectation of success, we are not persuaded by this argument either. Obviousness does not require absolute predictability of success. *In re O’Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988). Instead, all that is required is a reasonable expectation of success. *Id.* at 904. *See also Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1364 (Fed. Cir. 2007) (“the expectation of success need only be reasonable, not absolute”); *Hoffmann-La Roche Inc. v. Apotex Inc.*, 748 F.3d 1326, 1331 (Fed. Cir. 2014) (“Conclusive proof of efficacy is not necessary to show obviousness. All that is required is a reasonable expectation of success.”). Thus, the ultimate failure of certain combination therapy in humans does not negate the reasonable expectation of success of the combination of paclitaxel and an anti-ErbB2 antibody.

This is especially true in view of the claim language. On the claimed efficacy and safety, we reiterate that the proper analysis of “extend the time to disease progression in said human patient, without increase in overall severe adverse events” is to compare the claimed combination treatment to no treatment. *Supra* pp. 7–8. On the claimed efficacy, Baselga ’96 reports

that, when treated with rhuMAb HER2, 11.6% of patients with metastatic breast cancer experienced a complete or partial remission, and 37% achieved minimal responses or stable disease. Ex. 1004, 13. In Baselga '96, “[t]ime to tumor progression was calculated from the beginning of therapy to progression,” which is the same calculation used in the '441 patent for “time to disease progression.” *Compare id.* at 10 with Ex. 1001, 29:1–2.

According to Baselga '96, the median time to progression for the patients with either minor or stable disease was “unusually long durations” of 5.1 months. Ex. 1020, 12, 13. On the present record, we determine that, compared with no treatment, anti-ErbB2 antibodies alone would extend the time to disease progression in patients with breast cancer. Neither Patent Owner, nor our present reading of the prior art, suggests that combining a taxoid with rhuMAb HER2 would abrogate the effect of the antibody.

On the claimed safety, we observe that an adverse event is “[a]n unexpected medical problem that happens during treatment with a drug or other therapy. Adverse events do not have to be caused by the drug or therapy, and they may be mild, moderate, or severe.” Ex. 3001.<sup>6</sup> As Patent Owner points out, before the priority date of the challenged claims, “a diagnosis of HER2-positive breast cancer was effectively a death sentence; even with prior art treatments, the disease frequently recurred and rapidly spread. In 1996, HER2-positive breast cancer patients had an average life expectancy of only 18 months.” Prelim. Resp. 1; *see also* Ex. 1004, 12 (teaching HER2-positive cancers are associated with poor prognoses).

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<sup>6</sup> NCI [National Cancer Institute] Dictionary of Cancer Terms, entry for “adverse event.”



Petitioner has shown that rhuMAb HER2 was effective in treating breast cancer with minimal toxicity (Ex. 1004, 9), and paclitaxel had been approved to treat breast cancer (Ex. 1025, 10). Thus, based on the current record, we are persuaded that compared with no treatment, the claimed combination treatment does not increase the overall severe adverse events.

Request for Rehearing

Each challenged claim, either explicitly or through dependency, recites “in the absence of an anthracycline derivative.” In the Petition and the Preliminary Response, neither party proposed a construction for that term. Patent Owner, however, argues that “[e]ven if a person of ordinary skill would have chosen to combine an anti-ErbB2 antibody and a taxoid, there is no reason an ordinarily skilled artisan would have *avoided* anthracyclines as part of that treatment.” Prelim. Resp. 52 (emphasis added). In our Decision denying institution, we agreed with Patent Owner, stating that evidence of the record is “insufficient to suggest that an ordinary artisan would have *avoided* anthracyclines while pursuing the combination therapy with anti-ErbB2 antibody and a taxoid in a treatment regimen for humans.” Dec. 10 (emphasis added).

In its Request for Rehearing, Petitioner contends that we erred in interpreting the limitation “in the absence of an anthracycline derivative” as requiring “avoidance” of an anthracycline derivative. Reh’g Req. 6. According to Petitioner, this term “is a negative limitation that is satisfied by anti-ErbB2 antibody–paclitaxel combinations that do not include an [anthracycline] derivative.” *Id.* at 5. After reconsidering the current record, we find Petitioner’s argument persuasive. In particular, because Baselga ’94 suggests a therapeutic composition consisting of an anti-ErbB2 antibody and

paclitaxel, and does not suggest that doxorubicin must necessarily be included as part of the same treatment regimen, we are persuaded that the reference satisfies the limitation “in the absence of an anthracycline derivative.” *Cf. Upsher-Smith Labs., Inc. v. Pamlab, L.L.C.*, 412 F.3d 1319, 1322 (Fed. Cir. 2005) (concluding the prior art anticipates a claim requiring a composition “essentially free of antioxidants,” because the prior art teaches “optional inclusion” of antioxidants, “despite no express teaching to exclude the antioxidants”).

In sum, Petitioner has presented sufficient evidence, for purposes of instituting trial, to show that in considering prior therapy received, an ordinary artisan would have been motivated to treat patients with ErbB2-overexpressing breast cancer by administering a combination of an anti-ErbB2 antibody and a taxoid, and “in the absence of an anthracycline derivative.”

We acknowledge the evidence of secondary considerations and Patent Owner’s argument that such evidence establishes the non-obviousness of the challenged claims. Prelim. Resp. 56–62. Indeed, evidence of secondary considerations, when present, must always be considered in determining obviousness. *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 1538–39 (Fed. Cir. 1983). Here, most of the secondary-considerations evidence Patent Owner relies on is first presented together with the Preliminary Response (*see* Prelim. Resp. 56–62 (citing Exs. 2004, 2012, 2018, 2033, 2034, 2035), and Petitioner has not yet had an opportunity to respond to those evidence and arguments. Thus, in this case, a better course of action is to permit the parties to fully develop the record during trial before further weighing the alleged evidence of secondary considerations.

## CONCLUSION

For the foregoing reasons, we find that Petitioner has offered sufficient evidence to institute an *inter partes* review. The information presented in the Petition and accompanying evidence establishes a reasonable likelihood that Petitioner would prevail in showing the unpatentability of at least claim 1 of the '441 patent.

At this stage of the proceeding, the Board has not made a final determination as to the construction of any claim term or the patentability of any challenged claim. Thus, our view with regard to any conclusion reached in the foregoing could change upon consideration of Patent Owner's merits response and upon completion of the current record.

## ORDER

Accordingly, it is

ORDERED that pursuant to 35 U.S.C. § 314, an *inter partes* review is hereby instituted to determine whether claims 1–14 of the '441 patent would have been obvious over the combination of Baselga '94 and Baselga '96;

FURTHER ORDERED that no other ground of unpatentability is authorized in this *inter partes* review; and

FURTHER ORDERED that pursuant to 35 U.S.C. § 314(a), *inter partes* review of the '196 patent is hereby instituted commencing on the entry date of this Order, and 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.

IPR2017-00731  
Patent 7,846,441 B1

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