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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte JUTTA AMERSDORFFER, STEFAN STEIDL, MARK WINDERLICH, SUSANNE KROHN, and LISA ROJKJAER

Appeal 2019-000249
Application 14/126,928
Technology Center 1600

Before ULRIKE W. JENKS, TIMOTHY G. MAJORS, and MICHAEL A. VALEK *Administrative Patent Judges*.

JENKS, *Administrative Patent Judge.*

DECISION ON APPEAL

Pursuant to 35 U.S.C. § 134(a), Appellant[1] appeals from Examiner's decision to reject the claims as obvious and provisionally on the ground of nonstatutory obviousness-type double patenting. We have jurisdiction under 35 U.S.C. § 6(b).

We AFFIRM.

[1] We use the word Appellant to refer to "applicant" as defined in 37 C.F.R. § 1.42(a). Appellant identifies the real party in interest as MorphoSys AG. Appeal Br. 4.

STATEMENT OF THE CASE

Claims 1, 4–6, and 9–12 are on appeal, and can be found in the Claims Appendix of the Appeal Brief. Claim 1, reproduced below, is the sole independent claim and is illustrative of the claimed subject matter:

> 1. A synergistic combination of an
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> antibody specific for CD19 comprising an HCDRl region of sequence SYVMH (SEQ ID NO: 1), an HCDR2 region of sequence NPYNDG (SEQ ID NO: 2), an HCDR3 region of sequence GTYYYGTRVFDY (SEQ ID NO: 3), an LCDRl region of sequence RSSKSLONVNGNTYL Y (SEQ ID NO: 4), an LCDR2 region of sequence RMSNLNS (SEQ ID NO: 5), and an LCDR3 region of sequence MQHLEYPIT (SEQ ID NO: 6) and wherein a constant region comprises amino acids 2390 and 332E, wherein the Fc numbering is according to the EU index as in Kabat and
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> bendamustine for use in the treatment of non-Hodgkin's lymphoma, chronic lymphocytic leukemia and/or acute lymphoblastic leukemia
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> wherein said synergistic combination exhibits a synergistic level of cell killing in a chronic B-cell leukemia cell line in comparison to antibody or bendamustine alone and a combination index (CI) of less than 0.75 in cell killing of MEC-1 leukemia cells, wherein the CI is calculated according to the CI-isobol method of Chou-Talalay.

Appeal Br. 24 (Claims Appendix) (formatting added).

REFERENCES

The prior art relied upon by Examiner is:

Name	Reference	Date
Bernett et al. ("Bernett")	US 8,524,867 B2	Sept. 3, 2013
Herting et al. ("Herting")	US 2011/0165151 A1	July 7, 2011
Weidmann et al., *Bendamustine is effective in relapsed or refractory aggressive non-Hodgkin's lymphoma*, 13 Annals of Oncology 1285-89 (2002) ("Weidmann")		
Horton et al., *Potent In vitro and In vivo Activity of an Fc-Engineered Anti-CD19 Monoclonal Antibody against lymphoma and leukemia*, 68 Cancer Research 8049-56 (2008) ("Horton")		
Woyach et al., *A phase 1 trial of the Fc-engineered CD19 antibody XmAb5574 (MOR00208) demonstrates safety and preliminary efficacy in relapsed CLL*, 124 Blood 3553–60 (2014) ("Woyach")		

REJECTIONS

The following grounds of rejection are before us for review:

I. Claims 1, 4–6, and 9–12 under 35 U.S.C. § 103(a) as unpatentable over Horton, Bernett, Weidmann, Herting, as evidenced by Woyach.

II. Claims 1, 4–6, and 9–12 provisionally on the ground of nonstatutory obviousness-type double patenting over U.S. Application Serial No. 14/127,217 in view of Weidman and Herting.

I. Obviousness

The issue is whether the preponderance of evidence of record supports Examiner's conclusion that one of ordinary skill in the art based on the teaching of the references would have arrived at a combination therapy composition containing an anti-CD19 antibody and bendamustine.

1. Findings of Fact

We agree with and adopt Examiner's findings of fact and reasoning regarding the scope and content of the prior art. For emphasis only we highlight the following:

FF1. Horton teaches that "CD19 is a 95-kDa transmembrane glycoprotein of the immunoglobulin superfamily containing two extracellular immunoglobulin-like domains and an extensive cytoplasmic tail." Horton 8049. Horton teaches that "CD19 is an attractive alternative target for the immunotherapy of lymphoproliferative disorders, due to its expression on a wide range of lymphomas and leukemias, including some early B-cell malignancies that do not express CD20." *Id.* 8055.

FF2. Horton teaches "[a] humanized anti-CD19 antibody with an engineered Fc domain (XmAb5574)." Horton Abstract.

FF3. Woyach teaches that CD19 antibody XmAb5574 (a.k.a. MOR00208) is a humanized CD19 monoclonal antibody with an engineered Fc region to enhance Fcγ receptor binding affinity. Woyach Abstract.

FF4. Specification describes "MOR208" and "XmAb5574" as synonymous and encompassed by the claims. Spec. 9. Additionally, the Specification explains that "MOR208 is [fully] described in US patent application No. 12/377,251" now issued as US 8,524,867 B2 (Bernett). *Id.*

FF5. Bernett teaches methods of treating diseases of B-cell origin such as, for example, "non-Hodgkin's lymphoma (NHL), acute lymphoblastic leukemia (ALL), and autoimmune related diseases" using modified anti-CD19 antibodies. *See e.g.*, Bernett 12:27–36.

FF6. Bernett teaches using the modified anti-CD19 antibodies in conjunction with chemotherapeutic agents including "alkylating agents such as thiotepa and cyclosphosphamide (CYTOXAN™)". Bernett 66:57–59.

FF7. Weidmann teaches that "[b]endamustine, an alkylating agent with a nitrogen mustard group and a purine-like benzimidazol group, has been shown to be effective in several solid tumors and indolent non-Hodgkin's lymphomas." Weidmann Abstract. Weidmann teaches "bendamustine as a single agent in aggressive non-Hodgkin's lymphoma." Weidmann 1285.

FF8. Herting teaches that "[b]endamustine is a nitrogen mustard used in the treatment of chronic lymphocytic leukemia (CLL) . . . non-Hodgkin's lymphoma (NHL)." Herting ¶ 34. Bendamustine "belongs to the family of drugs called alkylating agents." *Id.*

FF9. Herting teaches co-administration of bendamustine with anti-CD20 antibody and that the "co-administration can be simultaneous or sequential in either order, wherein preferably there is a time period while both (or all) active agents simultaneously exert their biological activities." *Id.* ¶ 77. "[T]he dosage of bendamustine will be in the range from 0.01 mg/kg to about 30 mg/kg." *Id.* at 82.

2. Analysis

We have reviewed Appellant's contentions that Examiner erred in rejecting claims 1, 4–6, and 9–12 as obvious over the cited art. Appeal Br. 8–20; Reply Br. 2–4. We disagree with Appellant's contentions and find that Examiner presented sufficient evidence in Examiner's Answer and Non-

Final Office Action dated December 27, 2017 to a support a conclusion of obviousness.

A. Claim interpretation

We begin with claim interpretation so we can properly compare the scope of the claims to the prior art. "During examination, 'claims . . . are to be given their broadest reasonable interpretation consistent with the specification, and . . . claim language should be read in light of the specification as it would be interpreted by one of ordinary skill in the art."' *In re Am. Acad. of Sci. Tech. Ctr.*, 367 F.3d 1359, 1364 (Fed. Cir. 2004) (quoting *In re Bond*, 910 F. 2d. 831, 833 (Fed. Cir. 1990)).

(i) Preamble: A synergistic combination of an

"If the preamble adds no limitations to those in the body of the claim, the preamble is not itself a claim limitation and is irrelevant to proper construction of the claim." *IMS Technology, Inc. v. Haas Automation, Inc.*, 206 F.3d 1422, 1434 (Fed. Cir. 2000). The preamble in context with the relevant portion of the body of claim 1 reads as follows:

> 1. A synergistic combination of an
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> . . .
>
> wherein said synergistic combination exhibits a synergistic level of cell killing in a chronic B-cell leukemia cell line in comparison to antibody or bendamustine alone and a combination index (CI) of less than 0.75 in cell killing of MEC-1 leukemia cells, wherein the CI is calculated according to the CI-isobol method of Chou-Talalay.

Appeal Br. 24 (Claims Appendix). Here, the preamble informs us that we are considering a product. The question is does the preamble recitation of "synergistic" by itself limit the claim structurally? *See Catalina Mktg. Int'l, Inc. v. Coolsavings.com, Inc.*, 289 F.3d 801, 809 (Fed. Cir. 2002). ("[T]he patentability of apparatus or composition claims depends on the claimed

structure, not on the use or purpose of that structure."). On this point, we do not find evidence (*see below* I.2.A.iv) that the "synergistic" recitation in the preamble provides structural information with respect to the product. In other words, the recitation of "synergistic" in the preamble does not limit claim 1 beyond those structural requirements recited in the body of the claim.

> *(ii) Claim body: antibody specific for CD19 comprising an HCDRl region of sequence SYVMH (SEQ ID NO:1), an HCDR2 region of sequence NPYNDG (SEQ ID NO: 2), an HCDR3 region of sequence GTYYYGTRVFDY (SEQ ID NO: 3), an LCDRl region of sequence RSSKSLONVNGNTYLY (SEQ ID NO: 4), an LCDR2 region of sequence RMSNLNS (SEQ ID NO: 5), and an LCDR3 region of sequence MQHLEYPIT (SEQ ID NO: 6) and wherein the heavy chain constant region comprises amino acids 239D and 332E, wherein the Fc numbering is according to the EU index as in Kabat . . . .*

This element recites an antibody that recognizes a particular protein structure and also contains structural limitations pertaining to the antibody itself.

> *(iii) bendamustine for use in the treatment of non Hodgkin's lymphoma, chronic lymphocytic leukemia and/or acute lymphoblastic leukemia . . . .*

The element recites a chemotherapeutic agent.

Therefore, claim 1 is directed to a combination product containing two active ingredients: (1) anti-CD19 antibody and (2) bendamustine.

> *(iv) wherein said synergistic combination exhibits a synergistic level of cell killing in a chronic B-cell leukemia cell line in comparison to antibody or bendamustine alone and a combination index (CI) of less than 0.75 in cell killing of MEC-1 leukemia cells, wherein the CI is calculated according to the CI-isobol method of Chou-Talalay.*

The wherein clause of the claim describes that the combination exhibits a particular level of activity – a synergistic level – in a particular assay system using a particular cell killing assay while applying a particular statistical analysis. The Specification provides that "synergistic" means "more than the expected additive effect of a combination." Spec. 7. The claim, however, does not recite a particular concentration level for each component. In other words, the wherein clause describes a result achieved by the combination product namely a particular level of activity for "treatment of non-Hodgkin's lymphoma, chronic lymphocytic leukemia and/or acute lymphoblastic leukemia" but does not recite the amount of each component that achieves this result.

Thus, the dispute resolves on whether the "synergistic level" limitation recited in the claim imparts a structural limitation on the combination product itself or whether this limitation simply recites a property that is necessarily present anytime the recited components are combined and thereby inherent.

According to the Specification, all combinations of anti-CD19 antibody with bendamustine produce a synergistic level of response. For example, the Specification recites the use of the combination product in an *in vitro* a cell-killing assay using MEC-1 leukemia cells and applying the recited statistical analysis. *See* Spec. 15–18 (Example 1). The Specification provides two additional *in vivo* assays using the recited combination product

in a treatment application in mice. The first *in vivo* assay system uses a "subcutaneously (SC)-implanted human Ramos Burkitt's B-cell lymphoma tumor growth model." *Id.* at 19–20 (Example 2). The second *in vivo* model injects Ramos human Burkitt's lymphoma cells into the tail vain of a mouse and measures survival. *Id.* at 20–25 (Example 3). The Specification, therefore, establishes that a synergistic level of activity is achieved in three different experimental settings, applying different concentrations of the products, and applying different statistical analysis.

Based on these disclosures in the Specification, we find that the "synergistic level" limitation is not structural. This is because the Specification does not provide evidence that shows that the "synergistic level" response is achieved with some combinations but not with others when the components are used within their known therapeutic range. A showing that some combination of components produces a synergistic level response, while other combinations do not, *might* support a conclusion that recited effect is due to the particular manner in which the components are combined together and, therefore, that claim is limited to that particular structure. Because we find the recited "synergistic level" of activity in the wherein clause of the claim does not impart any additional structural requirement, we determine on this record that the recited "synergistic level" is a property that is necessarily present anytime the two components are used together.

B. Combining two components each known to treat lymphoma such as non-Hodgkin's lymphoma

We agree with and adopt Examiner's rationale that it would have been obvious to arrive at the combination product based on the disclosed references because both compounds are known to be therapeutically

effective in treating lymphomas such as non-Hodgkin's lymphoma. *See* Ans. 7 (citing *In re Kerkhoven*, 626 F.2d 846, 850 (CCPA 1980), MPEP 2144.06); FF1–FF3, FF5–FF9.

Appellant contends that the cited combination of art is in no "way predictive to the skilled artisan of the synergistic combination of an antibody specific for CD19 and bendamustine achieving a synergistic level." Appeal Br. 10.

We are not persuaded by Appellant's contention. Bernett teaches the use of the anti-CD19 antibody, the same antibody as recited in the instant claims (*see* FF4–FF6), and instructs that the antibody be administered in conjunction with chemotherapeutic agents that include but are not limited to "alkylating agents such as thiotepa and cyclosphosphamide (CYTOXAN™)" (FF6). Thus, Bernett teaches alkylating agents as a suitable class of chemotherapeutic agents to use in combination with the recited anti-CD19 antibody.

Weidmann teaches the use of bendamustine, an alkylating agent within the same class of chemotherapeutic agents taught in Bernett, to treat aggressive non-Hodgkin's lymphoma. FF7. Weidmann even suggests using bendamustine in combination therapy. Weidmann 1288 ("Due to the efficacy and tolerability of bendamustine, the question arises of whether the drug should be included in combination chemotherapy regimens for treatment of aggressive non-Hodgkin's lymphoma prior to the palliative situation.").

Here, both Bernett and Weidmann suggest using the individual components in combination therapy. Accordingly, we find no error with Examiner's conclusion that the combination of references supports the position that it would be obvious to combine two components each known to

be effective individually to treat non-Hodgkin's lymphoma in order to arrive at the combination product as presently claimed. *See* Ans. 7; FF1–3, FF5–FF9.

C. Inherency

Appellant contends that obviousness cannot be predicated on what is not known at the time of the invention. Appeal Br. 15 (citing *In re Rijckaert*, 9 F.3d 1531, 1534 (Fed. Cir. 1993); MPEP 2141.02); Reply Br. 3. It is Appellant's position that unless the prior art has done the experiments there is no way to predict that the composition has the recited effect on cell killing based on the CI-Isobel analysis. We are not persuaded by Appellant's contention. The anti-CD19 antibody and bendamustine composition "cannot become nonobvious simply by . . . claiming the [synergistic level property] . . . . To hold otherwise would allow any formulation—no matter how obvious—to become patentable merely by testing and claiming an inherent property." *Santarus, Inc. v. Par Pharm., Inc.*, 694 F.3d 1344, 1354 (Fed. Cir. 2012).

The prior art cited by Examiner provides a reasonable expectation of success that the co-administration of anti-CD19 antibody and alkylating agent, such as bendamustine, results in the reduction of diseases of B-cell origin non-Hodgkin's lymphoma (NHL), acute lymphoblastic leukemia (ALL), and autoimmune related diseases. FF1–FF3, FF5–FF9; *see O'Farrell*, 853 F.3d 894, 903–04 (Fed. Cir. 1988) ("Obviousness does not require absolute predictability of success . . . all that is required is a reasonable expectation of success."). Our reviewing court has held that when the prior art does not expressly disclose a claim limitation, inherency may supply the missing element. *See Persion Pharm. LLC v. Alvogen Malta Operations Ltd.*, Case No. 18-2361 (Fed. Cir. Dec. 27, 2019) and *Hospira,*

Inc. v. Fresenius Kabi USA, LLC., Case No. 19-1329, 19-1367 (Fed. Cir. Jan. 9, 2020). "Inherency is established in the context of obviousness when 'the limitation at issue necessarily must be present, or the natural result of the combination of elements explicitly disclosed by the prior art.'" *Hospira*, slip op. at 10 (Fed. Cir. Jan. 9, 2020) (citing *Par Pharm. v. TWI Pharm., Inc.*, 773 F.3d 1186, 1195–96 (Fed. Cir. 2014)). Here, we agree with Examiner's finding that the functions recited in the wherein clause flow naturally from the teachings of the prior art. Ans. 16 (citing *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985 ("The fact that appellant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious."), and *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347 (Fed. Cir. 1999) ("[T]he discovery of . . . a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer.")).

As discussed above, the Specification and other evidence of record does not provide any indication from which to conclude that the "synergistic level" limitation as recited in the wherein clause of claim 1 imparts a structural limitation onto the claimed combination. We, therefore, agree with Examiner that based on at least the teaching of Bernett that it would have been reasonable to conclude that the combination anti-CD19 antibody with an alkylating agent would be effective for the purpose of treating diseases of B-cell origin such as non-Hodgkin's lymphoma (NHL), acute lymphoblastic leukemia (ALL), and autoimmune related diseases. FF6; *see* Ans. 3–8. This teaching in conjunction with the teaching that the alkylating agent bendamustine is effective at treating non-Hodgkin's lymphoma provides a reasonable expectation that the combination of bendamustine

with anti-CD19 would also be effective at treating non-Hodgkin's lymphoma. *See* FF6–FF9. An obvious formulation cannot become nonobvious simply by measuring and claiming an activity of the formulation in a particular context, "because '[t]o hold otherwise would allow any formulation—no matter how obvious—to become patentable merely by testing and claiming an inherent property.'" *Persion Pharm.*, slip op. at 13 (Fed. Cir. Dec. 27, 2019) (citing *Santarus, Inc. v. Par Pharm., Inc.*, 694 F.3d 1344, 1354 (Fed. Cir. 2012)); *see also Gen. Elec. Co. v. Jewel Incandescent Lamp Co.*, 326 U.S. 242, 249 (1945) ("It is not invention to perceive that the product which others had discovered had qualities they failed to detect.").

D. Unexpected results

Although, as discussed above, we interpret that the wherein clause does not provide any structural limitation on the combination product, the limitation is still part of the claim and can reasonably be interpreted to encompass an allegedly unexpected property of the claimed combination. We have reviewed Appellant's unexpected result arguments (*see* Appeal Br. 19), but do not find them persuasive. As Examiner explains, secondary considerations, when present, must be taken into account but do not control the obviousness conclusion. *See* Ans. 16. "[W]e attribute no magic status to synergism per se since it may be expected or unexpected." *In re Huellmantel*, 324 F.2d 998, 1003 (CCPA 1963).

As explained above, the combination of references teaches all of the elements of claim 1 and provides an express motivation to combine those teachings as articulated in Examiner's rejection for the treatment of diseases such as non-Hodgkin's lymphoma. *See* Ans. 7 ("One of ordinary skill in the art would have been motivated to do so, and have a reasonable expectation of success, because both compounds [(the anti-CD19 antibody with S239D

and I332E amino acid substitutions in the Fc region and bendamustine)] are known to be therapeutic[ally] effective in treating lymphomas such as non-Hodgkin's lymphoma"); FF1–FF3, FF5–FF9. Weighing that evidence together with Appellant's evidence of a purportedly unexpected result as now incorporated into the claim, which on balance is weak, we determine that the preponderance of the evidence supports Examiner's obviousness rejection. *See, e.g.*, *Bayer Pharma AG v. Watson Labs., Inc.*, 874 F.3d 1316, 1329 (Fed. Cir. 2017) (weighing evidence of unexpected results and copying together with other evidence, including "strong evidence of a motivation to make the claimed combination" in the cited prior art, to conclude that combination was obvious); *Bayer Healthcare*, 713 F.3d at 1377 (finding that secondary indicia evidence did not "overcome[] the plain disclosures and express motivation to combine those disclosures in the prior art").

E. Summary

For the reasons discussed, we are not persuaded that Examiner failed to make out a prima facie case of obviousness. We are also not persuaded that the evidence advanced by Appellant to show an unexpected result outweighs the evidence supporting a conclusion of obviousness. Accordingly, we affirm the rejection of claim 1.

F. Substitution of antibodies

Lastly, Examiner presents an alternative theory that "the substitution of the known afucosylated anti-CD20 antibody for the Fc modified anti-CD19 antibody XmAb5574 would have yielded predictable result of synergistic effect in killing lymphoma cells" because they share a common mechanism of action. Ans. 8.

Appellant contends that Examiner's reliance on the "common mechanism of action based upon enhanced ADCC function alone" is

misplaced because it does not take into account "the multiple differences between these antibodies and the multiple differences between their targets." Reply Br. 3–4; *see* Appeal Br. 12; *see* Steidl Dec.[2] ¶¶ 4–5. "[T]he number of target molecules on the cell surface has an influence on the cytotoxicity of ADCC inducing antibodies." Steidl Dec. ¶ 5; *see* Appeal Br. 12.

Examiner responds that the claimed Fc engineered anti-CD19 antibody "also exhibit[s] enhanced immune cell-mediated effector functions including ADCC and increased apoptosis." Ans. 7, 13; FF1–FF3, FF5, FF6. We agree with Examiner that there is clear teaching in Bernett to combine the anti-CD19 and an alkylating agent for the purpose of treating non-Hodgkin's lymphoma and that a skilled artisan would have had a reasonable expectation of success in doing so.

We do not, however, agree with Examiner's position that just because CD19 and CD20 are both cell surface molecules expressed on B-cells is sufficient commonality to say they are functional equivalents. *See* Ans. 17 (obvious "to replace the prior art afucosylated anti-CD20 antibody in the combination with bendamustine with the anti-CD19 antibody modified in the Fc region for enhanced ADCC function"); *see* Steidl Dec. ¶¶ 4–6; *see* Appeal Br. 11. "CD19 is a 95-kDa transmembrane glycoprotein of the immunoglobulin superfamily containing two immunoglobulin-like domains and an extensive cytoplasmic tail." FF1. "It is B-lineage-specific and functions as a positive regulator of B-cell receptor signaling." Horton, 8049. Horton teaches that "CD19 cell surface expression is lower relative to CD20, but [notes that expression] begins earlier and persists longer through B-cell

[2] Declaration under 37 C.F.R. § 1.132 by Stefan Steidl signed June 17, 2017 ("Steidl Dec.").

maturation." *Id.* Additionally, Horton notes that some B-cell tumors lack or lose CD20 expression over time. *Id.* Here, the record supports Appellant's position that CD19 and CD20 are different molecules with different, yet overlapping, cellular expression patterns. Because of these different structural and cellular expression patterns, we do not agree with Examiner's alternative theory, which is based on a simple substitution of anti-CD20 antibody taught in Herting for the anti-CD19 taught in Horton or Bernett to arrive at the claimed combination product.

3. Conclusion

We conclude, considering the totality of the cited evidence and arguments, that the preponderance of the evidence supports Examiner's conclusion of obviousness with respect to claim 1 (*see above* I.2.B–I.2.E), and Appellant has not provided sufficient rebuttal evidence or evidence of secondary considerations that outweighs the evidence supporting Examiner's conclusion. As Appellant does not argue the claims separately, claims 4–6 and 9–12 fall with claim 1. 37 C.F.R. § 41.37 (c)(1)(iv).

II. Provisional Nonstatutory Obviousness-Type Double Patenting

The issue is whether the preponderance of evidence of record supports Examiner's conclusion that claims of the copending U.S. Application No. 14/127,217 are not patentably distinct.

1. Findings of Fact

FF10. Claim 1 of co-pending U.S. Application No. 14/127,217 reads as follows:

> 1. A synergistic combination of an
> (a) antibody specific for CD19 comprising an HCDR1 region of sequence SYVMH (SEQ ID NO:1), an HCDR2 region of sequence NPYNDG (SEQ ID NO: 2), an HCDR3

> region of sequence GTYYYGTRVFDY (SEQ ID NO: 3), an LCDR1 region of sequence RSSKSLONVNGNTYLY (SEQ ID NO: 4), an LCDR2 region of sequence RMSNLNS (SEQ ID NO: 5), and an LCDR3 region of sequence MQHLEYPIT (SEQ ID NO: 6) and wherein the heavy chain constant region comprises amino acids 239D and 332E, wherein the Fc numbering is according to the EU index as in Kabat and
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> (b) fludarabine for use in the treatment of non-Hodgkin's lymphoma, chronic lymphocytic leukemia and/or acute lymphoblastic leukemia,
>
> wherein said synergistic combination exhibits a synergistic level with a combination index (CI) of less than or equal to 0.3 in cell killing of MEC-1 leukemia cells, wherein the CI is calculated according to the CI-isobol method of Chou-Talalay.
>
> U.S. Application No. 14/127,217 (Amendment of July 20, 2017.)

2. Analysis

According to Examiner, "the conflicting claims are not identical, they are not patentably distinct from each other because like the fludarabine as recited in the copending claims, bendamustine was also known to be one of the most used drugs for lymphoma therapy." Ans. 8.

Appellant contends that the CD19 antibody "is used in combination with a completely different therapeutic agent than claimed, specifically bendamustine versus fludarabine." Appeal Br. 21. Furthermore, Appellant contends that "fludarabine and bendamustine are different chemotherapeutic agents with different chemical structures." Reply Br. 4. Fludarabine is a purine analog (*see* Bernett 66:25–26) while bendamustine is an alkylating agent (*see* FF7–FF9). Although Examiner identified that these two compounds are used for treating lymphomas, they do not share a common mechanism of action, nor has Examiner demonstrated that one of skill in the art would consider them to be within the same class of chemotherapeutic

agents. Therefore, we agree with Appellant that Examiner has not provided a sufficient rationale to establish that fludarabine and bendamustine are functional equivalents, such that it would have been obvious to replace one for the other, to support the conclusion that the present claims and those in copending U.S. Application No. 14/127,217 are not patentably distinct.

3. Conclusion

We conclude that the evidence cited by Examiner does not support a conclusion that the copending claims render the present claims obvious. Accordingly, we reverse the provisional nonstatutory obviousness-type double patenting rejection.

DECISION SUMMARY

In summary:

Claims Rejected	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
1, 4–6, 9–12	103	Horton, Bernett, Weidmann, Herting, Woyach	1, 4−6, 9−12	
1, 4–6, 9–12		Nonstatutory obviousness-type double patenting		1, 4−6, 9−12
Overall Outcome			1, 4–6, 9−12	

TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a). *See* 37 C.F.R. § 1.136(a)(1)(iv).

AFFIRMED