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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte ROBERT J. LUTZ and JOSE PONTE

Appeal 2018-004572
Application 14/509,809
Technology Center 1600

Before DONALD E. ADAMS, DEBORAH KATZ, and JOHN G. NEW, *Administrative Patent Judges*.

ADAMS, *Administrative Patent Judge*.

DECISION ON APPEAL

Pursuant to 35 U.S.C. § 134(a), Appellant[1] appeals from the Examiner's decision to reject claims 1 and 225–354. 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. Appellant identifies the real party in interest as ImmunoGen, Inc. (Appellant's October 10, 2017 Appeal Brief (Appeal Br.) 3).

STATEMENT OF THE CASE

Appellant's disclosure "relates to methods of administering anti-FOLR1 immunoconjugates for the treatment of diseases, such as cancer. The methods provide dosing regimens that minimize unwanted side-effects." (Spec. ¶ 3).[2] Appellant's claim 1 is representative and reproduced below:

> 1. A method for treating a human patient having an FOLR1-expressing ovarian cancer or cancer of the peritoneum comprising administering to the patient an immunoconjugate which binds to FOLRl polypeptide,
>
> wherein the immunoconjugate comprises an antibody or antigen-binding fragment thereof that comprises the variable light chain (VL) complementarity determining region (CDR)-1, VL CDR-2, VL CDR-3, variable heavy chain (VH) CDR-1, VH CDR-2, and VH CDR-3 of SEQ ID NOs: 6-9, 11, and 12, respectively, and a maytansinoid, and
>
> wherein the immunoconjugate is administered at a dose of 6 milligrams (mg) per kilogram (kg) of adjusted ideal body weight (AIBW) of the patient.

(Appeal Br. 36.)

Grounds of rejection before this Panel for review:[3]

Claims 1, 225, 226, 228, 229, 231–243, 245, 247–254, 258, 259, 261–267, 269, 271–277, 279, 281–288, 292, 293, 295–301, and 306–354 stand rejected under 35 U.S.C. § 102(a)(1) and (a)(2) as anticipated by Lutz '282,[4] as evidenced by Ab '181.[5]

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[2] Appellant's October 8, 2014 Specification.
[3] Application 14/245,797 abandoned November 13, 2017. Application 15/388,873 abandoned December 7, 2018. Thus, the provisional obviousness-type double patenting rejections, based on the claims of these Applications, are moot and will not be further discussed.
[4] Lutz et al., US 2012/0282282 A1, published Nov. 8, 2012.
[5] Ab et al., US 2012/0009181 A1, published Jan. 12, 2012.

Claims 1, 225, 226, 228–243, 245–254, 258–267, 269–277, 279–288, 292–301, and 305–354 stand rejected under 35 U.S.C. § 102(a)(1) as anticipated by Ab '528.[6]

Claims 1, 225, 226, 228–243, 245–254, 258–267, 269–277, 279–288, 292–301, and 305–354 stand rejected under 35 U.S.C. § 102(a)(1) as anticipated by Carrigan '675,[7] as evidenced by Ab '181.

Claims 1 and 225–354 stand rejected under 35 U.S.C. § 103(a) as unpatentable over the combination of Lutz '282, Ab '181, and Armstrong.[8]

Claims 1 and 225–354 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Ab '528 or Carrigan '675 in combination with Armstrong.

Claims 1 and 225–354 stand rejected under 35 U.S.C. § 103(a) as unpatentable over the combination of Lutz '282, Ab '181, Armstrong, Green,[9] Geraghty,[10] Fuchs,[11] and Narain.[12]

Claims 1 and 225–354 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Ab '528 or Carrigan '675 in combination with Armstrong, Green, Geraghty, Fuchs, and Narain.

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[6] Ab et al., WO 2011/106528 A1, published Sept. 1, 2011.
[7] Carrigan et al., WO 2012/135675 A2, published Oct. 4, 2012.
[8] D.K. Armstrong et al., *Efficacy and safety of farletuzumab, a humanized monoclonal antibody to folate receptor alpha, in platinum-sensitive relapsed ovarian cancer subjects: preliminary data from a phase-2 study*, 7 European Journal of Cancer Supplements 450, Abstr. 8000 (2009).
[9] Bruce Green & Stephen B. Duffull, *What is the best size descriptor to use for pharmacokinetic studies in the obese?*, 58 Brit. J. Clinical Pharmacology 119–33 (2004).
[10] Geraghty et al., US 2009/0162374 A1, published June 25, 2009.
[11] Fuchs et al., US 2012/0148577 A1, published June 14, 2012.
[12] Narain et al., US 2014/0302014 A1, published Oct. 9, 2014.

Claims 1, 225, 226, 228–243, 245–254, 258–267, 269–277, 279–288, 292–301, and 305–354 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of Ab '275[13] in view of Green, Geraghty, Fuchs, and Narain.

Claims 1, 225, 226, 228–243, 245–254, 258–267, 269–277, 279–288, 292–301, and 305–354 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of Ab '966[14] in view of Green, Geraghty, Fuchs, and Narain.

Claims 1, 225, 226, 228–243, 245–254, 258–267, 269–277, 279–288, 292–301, and 305–354 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of Carrigan '432[15] in view of Ab '181, Green, Geraghty, Fuchs, and Narain.

Claims 1, 225, 226, 228–243, 245–254, 258–267, 269–277, 279–288, 292–301, and 305–354 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of Ab '280[16] in view of Green, Geraghty, Fuchs, and Narain.

Claims 1, 225, 226, 228–243, 245–254, 258–267, 269–277, 279–288, 292–301, and 305–354 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of Ab '490[17] in view of Green, Geraghty, Fuchs, and Narain.

[13] Ab et al., US 9,133,275 B2, issued Sept. 15, 2015.
[14] Ab et al., US 8,557,966 B2, issued Oct. 15, 2013.
[15] Carrigan et al., US 8,709,432 B2, issued Apr. 29, 2014.
[16] Ab et al., US 9,670,280 B2, issued June 6, 2017.
[17] Ab et al., US 9,598,490 B2, issued Mar. 21, 2017.

Anticipation:

ISSUE

Does the preponderance of evidence on this record support Examiner's finding that Appellant's claimed invention is anticipated?

FACTUAL FINDINGS (FF)

FF 1. Appellant defines

> [t]he term "ideal body weight" (IBW) . . . [as] a size descriptor that is unrelated to total body weight. IBW is an estimate of weight corrected for sex and height, and optionally frame size. IBW can be calculated, for example, using the formulas IBW = 0.9H-88 (for males) and IBW = 0.9H-92 (for females), wherein H=height in cm.

(Spec. ¶ 69.)

FF 2. Appellant defines "[t]he term 'adjusted ideal body weight' (AIBW) or 'adjusted body weight' (ADJ) . . . [as] a size descriptor that accounts for sex, total body weight, and height. . . . AIBW (ADJ) can be calculated, for example, using the formula ADJ = IBW + 0.4(weight in kg – IBW)" (Spec. ¶ 71).

FF 3. Ab '181 discloses that "Folate Receptor 1 (FOLR1), also known as Folate Receptor-alpha, or Folate Binding Protein, is an N-glycosylated protein expressed on plasma membrane of cells" (Ab '181 ¶ 4; *see also* Ab '528 ¶ 4; Carrigan '675 ¶ 4; Spec. ¶ 4).

FF 4. Ab '181 discloses that "FOLR1 is overexpressed in [a] vast majority of ovarian cancers" (*see* Ab '181 ¶ 5; *see also* Ab '528 ¶ 5; Carrigan '675 ¶ 5; Spec. ¶ 5).

FF 5. Ab '181 "relates to antibodies and immunoconjugates that bind to human folate receptor 1, as well as to methods of using the antibodies and immunoconjugates for the treatment of diseases, such as cancer" (Ab '181

¶ 2; *see also id.* ¶ 249 (Ab '181 discloses a "methods of treating[, *inter alia*, ovarian] cancer comprising administering a therapeutically effective amount of a FOLR1-finding agent to a subject"); *id.* ¶ 263 (Ab '181 discloses that "[t]he administering physician can easily determine optimum dosages, dosing methodologies and repetition rates")).

FF 6. Lutz '282 "relates to the identification that inclusion of at least one charged group on a cross linker decreases ocular toxicity associated with administration of an antibody drug conjugate [(ADC)]" (Lutz '282 ¶ 2; *see id.* ¶ 8 (Lutz '282 "provides a method of reducing ADC-induced side effects or toxicity arising from the use of an ADC"); *see also id.* ¶¶ 9–11; *see* Ans. 4 (citing Lutz '282 ¶ 373) (Examiner finds that Lutz '282 discloses "intravenous administration of the conjugate")).

FF 7. Lutz '282:

> [P]rovides a method of inhibiting tumor growth in a subject comprising administering an ADC of the following formula CB-L-DM4 or DM4-L-CB to said subject, wherein CB is a cell binding agent, L is a linker containing at least one charged group, and DM4 is N(2')deacetyl-N2'-(4-mercapto-4-methyl-1-oxopentyl)-maytansine, said method comprising administering said ADC at a dose or frequency equivalent to a dose or frequency of an ADC, which has the same CB and DM4, but the linker does not contain at least one charged group, that induces ocular toxicity when administered to a subject of the same mammalian species.

(Lutz '282 ¶ 7.)

FF 8. Lutz '282 discloses that ovarian tumor is tumor within the scope of Lutz '282's disclosure (Lutz '282 ¶ 268; *see* Ans. 4–5).

FF 9. Lutz '282 discloses administering an ADC at a dose of "between about 4 mg/kg and about 16 mg/kg" (Lutz '282 ¶ 8; *see* Ans. 4).

FF 10. Lutz '282 discloses "anti-FOLR1 antibodies (e.g., huMov19 (M9346A))" as an example of a cell-binding agent (CB) (Lutz '282 ¶ 119; *see* Ans. 4 (Examiner finds that Lutz '282 "discloses a conjugate of huMov19-sulfo-SPDB-DM4," wherein the huMov19 antibody comprises sequences as set forth in Appellant's SEQ ID Nos: 6–9, 11, and 12)).

FF 11. Examiner finds that Lutz '282 discloses "conjugates of 6–7.6 maytansinoids per antibody" (Ans. 5 (citing Lutz '282 ¶¶ 83 and 368)).

FF 12. Ab '528:

> [P]rovides a method of inhibiting tumor growth in a subject comprising administering a therapeutically effective amount of an immunoconjugate having the formula (A) - (L) - (C), wherein: (A) is an antibody or antigen binding fragment thereof that specifically binds a human folate receptor 1; (L) is a linker; and (C) is a cytotoxin selected from the group consisting of a maytansinoid and a maytansinoid analog.

(Ab '528 ¶ 34; *see also id.* ¶ 2 (Ab '528 "relates to antibodies and immunoconjugates that bind to human folate receptor 1, as well as to methods of using the antibodies and immunoconjugates for the treatment of diseases, such as cancer"); *id.* ¶ 11; *see* Ans. 6 (Examiner finds that Ab '528 discloses the use of huMov19-sulfo-SPDB-DM4 for use "in vivo to treat tumors in mice," wherein the conjugate "can be administered parenterally in addition to intravenously for the treatment of tumors").)

FF 13. Ab '528 defines the term cancer as including ovarian cancer (Ab '528 ¶ 86; *see* Ans. 6).

FF 14. Ab '528 discloses the use of "FOLR-1 binding agents [that] are humanized versions of the murine Mov19 antibody," i.e. huMov19 (Ab '528 ¶¶ 108 and 113; *see* Ans. 5–6 (Examiner finds that Ab '528 discloses

"huMov19-sulfo-SPDB-DM4," wherein the huMov19 antibody comprises sequences as set forth in Appellant's SEQ ID Nos: 6–9, 11, and 12)).

FF 15. Ab '528 discloses that "[t]he administering physician can easily determine optimum dosages, dosing methodologies and repetition rates[, wherein] [i]n certain embodiments, dosage is from 0.01 μg to 100 mg per kg of body weight, and can be given once or more daily, weekly, monthly or yearly" (Ab '528 ¶ 237; *see* Ans. 6).

FF 16. Carrigan '675 "relates to increasing the efficacy of the treatment of cancers characterized by the overexpression of human folate receptor 1 (FOLR1) . . . with a FOLR1 antagonist, e.g., a FOLR1 immunoconjugate" (Carrigan '675 ¶ 2; *see* Ans. 7 (citing Carrigan '675) (Examiner finds that the immunoconjugate "can be administered parenterally in addition to intravenously for the treatment of tumors")).

FF 17. Carrigan '675 defined

> [t]he term "immunoconjugate" . . . as . . . a compound or a derivative thereof that is linked to a cell binding agent (i.e., an anti-FOLR1 antibody or fragment thereof) and is defined by a generic formula: C-L-A, wherein C = cytotoxin, L = linker, and A = cell binding agent or anti-FOLR1 antibody or antibody fragment.

(Carrigan '675 ¶ 70.)

FF 18. Carrigan '675 discloses that "the anti-FOLR1 antibody is huMOV19" (Carrigan '675 ¶ 16; *see* Ans. 7 (Examiner finds that Carrigan '675 discloses "huMov19-sulfo-SPDB-DM4 IMGN853," wherein the huMov19 antibody comprises sequences as set forth in Appellant's SEQ ID Nos: 6–9, 11, and 12)).

FF 19. Carrigan '675 defines the term cancer as including ovarian cancer (Carrigan '675 ¶ 72; *see* Ans. 7).

FF 20. Carrigan '675 discloses that the cytotoxin may be maytansinoid (Carrigan '675 ¶ 16).

FF 21. Carrigan '675 discloses that "[t]he administering physician can easily determine optimum dosages, dosing methodologies and repetition rates. In certain embodiments, dosage is from 0.01 μg to 100 mg per kg of body weight, and can be given once or more daily, weekly, monthly or yearly" (Carrigan '675 ¶ 155; *see* Ans. 7 (Examiner finds that Carrigan '675 discloses dosages in the range "of 0.1-20 mg/kg" that "can be administered monthly . . . and once every three weeks," wherein "the administering physician can determine the optimum dosages")).

ANALYSIS

Examiner finds that each of Lutz '282 and Carrigan '675, as evidenced by Ab '181, and Carrigan '675 anticipate Appellant's claimed invention (Ans. 4–8). We are not persuaded.

As Appellant explains, "the cited references disclose dosing based on . . . [Total Body Weight (TBW)]" and, therefore, cannot anticipate Appellant's claimed invention, which requires "administration based on adjusted ideal body weight (AIBW)" (Appeal Br. 8; *cf.* FF 1–2 (defining the terms ideal body weight (IBW) and adjusted ideal body weight (AIBW), respectively); *see* Birrer Decl.[18] ¶ 8 ("all of the[] dose ranges in Lutz ['282], Ab ['181], and Carrigan ['675] refer to doses based on total body weight"); First Ponte Decl.[19] ¶ 10 ("Neither Lutz nor Ab ['181] provides any reasons to administer an anti-FOLR1 immunoconjugate to a human patient based on AIBW. The only doses even mentioned in these documents are based on

[18] Declaration of Michael J. Birrer, M.D., Ph.D., signed April 10, 2017.
[19] Declaration of Dr. Jose Ponte, signed November 30, 2015.

milligrams per kilograms of total body weight"); Rashkova Decl.[20] ¶ 7 ("AIBW is a different method than either TBW or [body surface areas (BSA)] . . . for calculating the dose of medicine to be administered to a patient"); *see generally* Reply Br. 3–9).

In response, Examiner asserts that "Examiner is well aware that TBW dosing is different from AIBW dosing" and directs attention to Green, Geraghty, Fuchs, and Narain "all of which[, Examiner asserts,] have been used in the 103 rejections" (Ans. 37). Nonetheless, Examiner finds that Lutz '282 is "anticipatory to the extent that there is a species within the dose range in the reference that reads on [A]ppellant's dose" (Ans. 38). Stated differently, Lutz '282 inherently teaches Appellant's claimed invention because Lutz '282 may teach a TBW dosage that might fall within the scope of Appellant's AIBW dosage. We are not persuaded. *See In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999) ("Inherency . . . may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.") (citations and internal quotation marks omitted).

For the foregoing reasons, we find that Examiner failed to establish an evidentiary basis on this record to support a finding of anticipation.

CONCLUSION

The preponderance of evidence on this record fails to support Examiner's finding that Appellant's claimed invention is anticipated.

The rejection of claims 1, 225, 226, 228, 229, 231-243, 245, 247–254, 258, 259, 261–267, 269, 271–277, 279, 281–288, 292, 293, 295–301, and

[20] Declaration of Rashkova, Ph.D., Pharm.D., BCPS, signed April 10, 2017.

306–354 under 35 U.S.C. § 102(a)(1) and (a)(2) as anticipated by Lutz '282, as evidenced by Ab '181 is reversed.

The rejection of claims 1, 225, 226, 228–243, 245–254, 258–267, 269–277, 279–288, 292–301, and 305–354 under 35 U.S.C. § 102(a)(1) as anticipated by Ab '528 is reversed.

The rejection of claims 1, 225, 226, 228–243, 245–254, 258–267, 269–277, 279–288, 292–301, and 305–354 under 35 U.S.C. § 102(a)(1) as anticipated by Carrigan '675, as evidenced by Ab '181 is reversed.

Obviousness:

ISSUE

Does the preponderance of evidence relied upon by Examiner support a conclusion of obviousness?

FACTUAL FINDINGS (FF)

FF 22. Examiner relies on Lutz '282, Ab '181, Ab '528, and Carrigan '675 as discussed above (*see* FF 3–21; *see generally* Ans. 9 and 13).

FF 23. Examiner finds that Ab '181 "discloses antibodies to FOLR1 and immunoconjugates thereof wherein the antibody" comprises sequences as set forth in Appellant's SEQ ID Nos: 6–9, 11, 12, 13, and 15 "and the use of these compounds for the treatment of cancer" (Ans. 9).

FF 24. Examiner finds that Ab '181 discloses "huMov19-sulfo-SPDB-DM4 and its use[] in vivo to treat tumors in mice," including "ovarian cancer and cancer of the peritoneum" (Ans. 9).

FF 25. Examiner finds that Ab '181 discloses "dosages . . . [in the] range from 0.01µg-100mg/kg and can be administered monthly . . . and once every

three weeks and the administering physician can determine the optimum dosages" (Ans. 9; *see also* Ab '181 ¶ 263).

FF 26. Examiner finds that Ab '181 discloses that the immunoconjugate "can be administered parenterally in addition to intravenously for the treatment of tumors" (Ans. 9–10; *see* Ab '181 ¶ 261).

FF 27. Examiner finds that the combination of Lutz '282 and Ab '181 fails to disclose "parenteral administration" or an "ovarian cancer . . . [that is] platinum resistant, relapsed or refractory" (Ans. 9).

FF 28. Examiner finds that Ab '528 and Carrigan '675 fail to disclose an "ovarian cancer . . . [that is] platinum resistant, relapsed or refractory" (Ans. 13).

FF 29. Examiner finds that Armstrong discloses the "use of anti-folate antibodies for the treatment of platinum sensitive relapsed and platinum resistant ovarian cancers (Ans. 10 (citing Armstrong, Abstract); *see also id.* at 12, 13, and 15).

FF 30. Examiner finds that the combination of Lutz '282, Ab '181 and Armstrong fails to "determin[e] the [immunoconjugate] dose using AIBW" (Ans. 11).

FF 31. Examiner finds that either of Ab '528 or Carrigan '675 in combination with Armstrong fails to "determin[e] the [immunoconjugate] dose using AIBW" (Ans. 14).

FF 32. Green discloses:

> For drugs that are dosed chronically, and therefore . . . [clearance] is of primary concern, dosing for obese patients should not be based on their total weight. If a weight-based dose individualization is required then we would suggest that chronic drug dosing in the obese subject should be

> based on lean body weight, at least until a more robust size descriptor becomes available.

(Green, Abstract; Ans. 12 (Examiner finds that Green "discloses the use of ABW . . . for dosing in obese patients"); *see also* Ans. 15.)

FF 33. Geraghty discloses "methods and compositions for the treatment of autoimmune and alloimmune diseases" (Geraghty ¶ 3).

FF 34. Examiner finds that Geraghty "discloses the use of dosing according to adjusted ideal body weight or actual body weight (whichever is lower) when administering thiotepa" (Ans. 12 (citing Geraghty ¶ 84); *see id.* at 15).

FF 35. Fuchs discloses "[a] lymphocytotoxic, but hematopoietic stem cell-sparing, high-dose amount of an oxazaphosphorine drug such as, for example, cyclophosphamide, administered post-transplantation can be used to reduce transplant rejection, including graft-versus-hose-disease (GVHD)" (Fuchs, Abstract).

FF 36. Examiner finds that Fuchs "discloses the use of dosing according to adjusted ideal body weight or actual body weight (whichever is lower) when administering cyclophosphamide" (Ans. 12 (citing Fuchs ¶ 120); *see id.* at 15).

FF 37. Narain "relates to methods for the treatment of oncological disorders comprising administration of coenzyme Q10 (CoQ10) and a chemotherapeutic agent" (Narain ¶ 2).

FF 38. Examiner finds that Narain "discloses the use of dosing according to adjusted ideal body weight or actual body weight (whichever is lower) when administering Busulfan (chemotherapeutic)" (Ans. 12 (citing Narain, Table 3, page 46); *see id.* at 15).

ANALYSIS

The rejections over: (a) Lutz '282 and Ab '181, (b) Ab '528, or (c) Carrigan '675, in combination with Armstrong:

Each of Lutz '282, Ab '181, Ab '528, and Carrigan '675 are discussed above, with respect to the anticipation rejection (*see* FF 22).

Examiner finds that the combination of Lutz '282 and Ab '181 fails to disclose "parenteral administration" or an "ovarian cancer . . . [that is] platinum resistant, relapsed or refractory" (FF 27) and that Ab '528 and Carrigan '675 fail to disclose an "ovarian cancer . . . [that is] platinum resistant, relapsed or refractory" (FF 28). Examiner, therefore, relies on Armstrong to make up for these deficiencies (FF 29; *see* Ans. 10 and 13, respectively).

Based on the combination of Lutz '282, Ab '181, and Armstrong, Examiner concludes that, at the time Appellant's invention was made, it would have been prima facie obvious to one of ordinary skill in the art before the effective filing date of the claimed invention to administer the conjugates either parenterally or intravenously with the expected benefit of treating the tumors (Ans. 10). With respect to the rejection based on Ab '528 or Carrigan '675 in combination with Armstrong, Examiner concludes that, at the time Appellant's invention was made, it would have been prima facie obvious to one of ordinary skill in the art before the effective filing date of the claimed invention to use the anti-folate antibody "conjugate of either of the primary references for the treatment of" "platinum sensitive relapsed and platinum resistant ovarian cancers" (Ans. 13–14). We are not persuaded.

As Examiner recognizes: (a) Lutz '282 and Ab '181, (b) Ab '528, or (c) Carrigan '675, in combination with Armstrong fail to "determin[e] the

[immunoconjugate] dose using AIBW" (FF 30–31). Thus, these rejection suffer the same deficiency discussed above with respect to the anticipation rejections and are reversed (*see generally* Appeal Br. 17–25; Reply Br. 10–13).

The rejection over: (a) Lutz '282 and Ab '181, (b) Ab '528, or (c) Carrigan '675, in combination with Armstrong, Green, Geraghty, Fuchs, and Narain.

Appellant does not separately argue its claims. Thus, Appellant's claim 1, reproduced above, is representative.

Based on the combination of Lutz '282, Ab '181, Armstrong, Green, Geraghty, Fuchs, and Narain, Examiner concludes that, at the time Appellant's invention was made, it would have been prima facie

> obvious to one of ordinary skill in the art before the effective filing date of the claimed invention to administer the conjugates either parenterally or intravenously with the expected benefit of treating the tumors. [Because] Armstrong . . . disclose[s] the treatment of platinum resistant (refractory) or platinum sensitive relapsed ovarian cancers using antifolate antibodies and the primary reference uses anti-folate antibodies in their conjugate, the use of the conjugate of the primary reference to treat the aforementioned cancers would also be obvious. Additionally, . . . [Ab '181] discloses that "the administering physician can determine the optimum dosages" and . . . [Green, Geraghtry, Fuchs, and Narain] all disclose the use of AIBW to determine dosages and [because] dosing according to AIBW is known in the art, it would have obvious in view of the statement in . . . [Ab '181] to dose according to AIBW.

(Ans. 12–13.) With respect to the rejection based on Ab '528 or Carrigan '675 in combination with Armstrong, Green, Geraghty, Fuchs, and Narain, Examiner concludes that, at the time Appellant's invention was made, it would have been prima facie

> obvious to one of ordinary skill in the art before the effective filing date of the claimed invention to the use of the conjugate of either of . . . [Ab '528 or Carrigan '675] for the treatment of the aforementioned cancers. Additionally, both . . . [Ab '528 or Carrigan '675] disclose that "the administering physician can determine the optimum dosages" and . . . [Green, Geraghty, Fuchs, and Narain] all disclose the use of AIBW to determine dosages and [because] dosing according to AIBW is known in the art, it would have obvious in view of the statement in either Ab et al or Carrigan et al to dose according to AIBW.

(Ans. 15–16.)

Appellant contends, however, that each of Lutz '282, Ab '181, Ab '528, and Carrigan '675 "refer to TBW-based dosing [and,] [t]hus, one would have no reason to move away from these explicit teachings of TBW-based dosing of FOLR1 immunoconjugates, especially given that other immunoconjugates in clinical trials were also being administered using TBW-based dosing" (Appeal Br. 26; *see generally* Reply Br. 14–15). Appellant further contends that given the disclosure of TBW-based dosing in each of Lutz '282, Ab '181, Ab '528, and Carrigan '675

> one would have no reason to turn to the limited teachings of Green, Geraghtry, Fuchs, or Narain regarding AIBW dosing. [Because] [n]one of these references relate to immunoconjugates, antibody-based drugs, or ocular toxicity. . . . Instead these references discuss AIBW dosing in the limited context of obese patients and/or small molecule chemotherapeutic agents.

(Appeal Br. 26 (citations omitted); *see id.* (Appellant contends that "none of . . . [Green, Geraghty, Fuchs, or Narain] contain any information that would lead one to believe that AIBW dosing would be useful for administering an immunoconjugate"); *id.* at 27 (Appellant contends that "none of the references cited by the Examiner contains even the slightest

indication that AIBW-based dosing would be useful for administering immunoconjugates"); *see generally* Reply Br. 15–19.) We are not persuaded.

There can be no doubt in this art that there is both a design need and market pressure to identify effective cancer treatments. In addition, those of ordinary skill in this art recognized that, prior to Appellant's filing date, the anti-FOLR1 immunoconjugate disclosed in the art, and within the scope of Appellant's claimed invention, exhibited ocular toxicity (*see* Hearing Transcript[21] 8:1–11). During the October 2, 2019 Oral Hearing Appellant's counsel explained, however, that the ocular toxicity problem associated with an anti-FOLR1 immunoconjugate, within the scope of Appellant's claimed invention, was solved by Lutz '282 prior to the filing date of Appellant's claimed invention (*see id.* 8:13–9:1). *See Riverwood-Int'l Corp. v. R.A. Jones & Co.*, 324 F.3d 1346, 1354 (Fed. Cir. 2003) (citation omitted) ("Valid prior art may be created by the admissions of the parties"). Although Appellant's counsel associated the solution to the ocular toxicity problem with the use of a charged linker, we find that Appellant's claim 1 does not exclude the use of an immunoconjugate that comprises a charged linker to avoid ocular toxicity issues (*see* Hearing Transcript 8:13–9:1; *see also* FF 6–7).

Thus, the issue before this Panel distills down to the selection of a dosing regimen, i.e. AIBW-based dosing, from among the various dosing regimens known to those of ordinary skill in this art.

[21] Transcript of Appellant's October 2, 2019 Oral Hearing.

As Examiner explains, "[c]hemotherapeutics and immunoconjugates are both used for the treatment of cancers" and, thus, those of ordinary skill in this art would look to art relating to dosing to determine an appropriate dosing regimen (*see* Ans. 46–47; *see generally* FF 5, 15, and 21). Among the finite number of dosing regimens known in the art, AIBW is disclosed by Green, Geraghty, Fuchs, and Narain (*see* FF 32–38; *see generally* Ans. 47).

> When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that is was obvious under § 103.

KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398, 421 (2007). Thus, we find no error in Examiner's conclusion that an administering physician looking to determine an optimum dosage for a therapeutic agent, as disclosed in each of Ab '181, Ab '528, and Carrigan '675, would have found it prima facie obvious to look to the AIBW dosing regimen disclosed by Green, Geraghty, Fuchs, and Narain (*see* Ans. 47; *see also id.* at 48).

Appellant directs attention to Lutz, who declares that each of Green Geraghty, Fuchs, and Narain "discuss using non-total-body-weight-based dosing regimens solely in the context of obese patients and/or for dosing of small molecule chemotherapeutic agents" (*see* Appeal Br. 27–28; *see generally* Reply Br. 17; *see also* Lutz Decl. ¶ 32). We note, however, that Appellant's claim 1 does not exclude the treatment of obese patients. Thus, we find no error in Examiner's conclusion that a person of ordinary skill in this art would have found it prima facie obvious to optimize a known dosing

regimen, i.e. AIBW, for the administration of an immunoconjugate, such as an anti-FOLR1 immunoconjugate (*see* Ans. 46–47).

For the foregoing reasons, we are not persuaded by Appellant's contention that "it could not have been predictable that AIBW dosing would be useful at all in administering an entirely different type of therapeutic, such as anti-FOLR1 immunoconjugate," as opposed to a small molecule chemotherapeutic (Appeal Br. 28).

We recognize Lutz's statement that

> by 2012, the American Society of Clinical Oncology issued guidelines that "if a dose reduction is employed in response to toxicity, consideration should be given to the resumption of full weight-based doses" and that there is "no evidence to support the need for greater dose reductions for obese patients compared with non-obese patients."

(Lutz Decl. ¶ 32 (citing Griggs,[22] Abstract).) Griggs, however, identifies limitations associated with its disclosure and indicates that "[w]ell-designed prospective studies with planned analysis of body composition and adverse events would be valuable" (Griggs 1558–59). Given the limitations of Griggs' disclosure and Griggs' appreciation of the need for "[w]ell-designed prospective studies with planned analysis of body composition and adverse events," we are not persuaded by Appellant's reliance on Griggs to support a "recommended TBW-based dosing even for administering chemotherapeutic drugs to obese patients" (Appeal Br. 29; *see generally* Reply Br. 17–19).

We recognize Appellant's contentions regarding "unpredictability in the field of dosing immunoconjugates" (Appeal Br. 30–31). We find,

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[22] Jennifer J. Griggs et al., *Appropriate Chemotherapy Dosing for Obese Adult Patients With Cancer: American Society of Clinical Oncology Clinical Practice Guideline*, 30 J. Clinical Oncology 1553–1561 (2012).

however, that the evidence, on this record, supports Examiner's conclusion of obviousness, where the prior art teaches the use of an anti-FOLR1 immunoconjugate, within the scope of Appellant's claimed invention, to treat FOLR1-expressing ovarian cancer, using the art recognized AIBW-based dosing regimen that is optimized by an administering physician (*see* FF 22–38; *see also* Ans. 47–48).

For the foregoing reasons, we are not persuaded by Appellant's intimation that the lack of clinical trials "using AIBW for administration of an immunoconjugate," supports a conclusion of non-obviousness (Appeal Br. 30–31 (citing Lutz Decl. ¶¶ 16, 17, 21–27, 29–31)). In this regard, we note that Appellant's claim 1 "recites a combination of elements that were all known in the prior art, and all that was required to obtain that combination was to substitute one well-known . . . [dosing method] for another." *Wm. Wrigley Jr. Co. v. Cadbury Adams USA LLC*, 683 F.3d 1356, 1364 (Fed. Cir. 2012).

As discussed above, the prior art solved the ocular toxicity problem associated with an anti-FOLR1 immunoconjugate, prior to the filing date of Appellant's claimed invention, through the use of a charged linker (*see* Hearing Transcript 8:13–9:1; *see also* FF 6–7). Appellant's claim 1 does not exclude the use of an anti-FOLR1 immunoconjugate comprising a charged linker as was known in the art at the time of Appellant's claimed invention to avoid ocular toxicity. Thus, we are not persuaded by Appellant's contention that "it was both unpredictable and surprising that changing from TBW to AIBW dosing would eliminate Grade III ocular toxicities" (Appeal Br. 31). To the contrary, for the reasons set forth above, we agree with Examiner's conclusion that Appellant's claimed method would have been

prima facie obvious in view of the combination of (a) Lutz ’282 and Ab ’181, (b) Ab ’528, or (c) Carrigan ’675, in combination with Armstrong, Green, Geraghty, Fuchs, and Narain.

To the extent that Appellant contends that the combination of prior art relied upon by Examiner does not make obvious a method for treating a human patient having an FOLR1-expressing ovarian cancer comprising administering an immunoconjugate within the scope of Appellant’s claimed invention at a dosage of 6 milligrams per kilogram of adjusted ideal body weight (AIBW) of the patient we note that “where[, as here,] the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.” *In re Aller*, 220 F.2d 454, 456 (CCPA 1955) (citation omitted); *see also* FF 5, 15, and 21 (explaining that an “administering physician can easily determine optimum dosages, dosing methodologies and repetition rates”).

CONCLUSION

The preponderance of evidence relied upon by Examiner fails to support a conclusion of obviousness with respect to the rejections over: (a) Lutz ’282 and Ab ’181, (b) Ab ’528, or (c) Carrigan ’675, in combination with Armstrong.

The rejection of claims 1 and 225–354 under 35 U.S.C. § 103(a) as unpatentable over the combination of Lutz ’282, Ab ’181, and Armstrong is reversed.

The rejection of claims 1 and 225–354 under 35 U.S.C. § 103(a) as unpatentable over Ab ’528 or Carrigan ’675 in combination with Armstrong is reversed.

The preponderance of evidence relied upon by Examiner supports a conclusion of obviousness, with respect to the rejection over: (a) Lutz '282 and Ab '181, (b) Ab '528, or (c) Carrigan '675, in combination with Armstrong, Green, Geraghty, Fuchs, and Narain.

The rejection of claim 1 under 35 U.S.C. § 103(a) as unpatentable over the combination of Lutz '282, Ab '181, Armstrong, Green, Geraghty, Fuchs, and Narain is affirmed. Claims 225–354 are not separately argued and fall with claim 1.

The rejection of claim 1 under 35 U.S.C. § 103(a) as unpatentable over Ab '528 or Carrigan '675 in combination with Armstrong, Green, Geraghty, Fuchs, and Narain is affirmed. Claims 225–354 are not separately argued and fall with claim 1.

Obviousness-type Double Patenting:

ISSUE

Does the preponderance of evidence relied upon by Examiner support a conclusion of obviousness-type double patenting?

FACTUAL FINDINGS (FF)

FF 39. Examiner finds that Ab '275 claims methods for treating ovarian cancers comprising the administration of immunoconjugates, within the scope of Appellant's claimed invention (Ans. 17; *see* Ab '275: cols. 181–182 (claims 12–14, 16, 17, 22–27, and 29–35)).

FF 40. Ab '275 discloses that "[t]he administering physician can easily determine optimum dosages, dosing methodologies and repetition rates" (Ab '275 58:19–21; *see id.* at ll. 26–31 ("[T]he dosage of the antibody or other FOLR1-binding agent is from about 0.1 mg to about 20 mg per kg of body

weight. The treating physician can estimate repetition rates for dosing based on measured residence times and concentrations of the drug in bodily fluids or tissues."); *see also* Ans. 17–18).

FF 41. Examiner finds that Ab '966 claims an immunoconjugate, within the scope of Appellant's claimed invention (Ans. 20; *see* Ab '966: cols. 201–203 (claims 2–11 and 18)).

FF 42. Ab '966 discloses that its immunoconjugate may be used in a method of treating cancer, including ovarian cancer (Ab '966, Abstract; *see id.* at 15:24–34; Ans. 20).

FF 43. Ab '966 discloses that "[t]he administering physician can easily determine optimum dosages, dosing methodologies and repetition rates" (Ab '966 58:3–5; *see* Ans. 21).

FF 44. Examiner finds that Carrigan '432 claims methods for treating ovarian cancers comprising the administration of immunoconjugates, within the scope of Appellant's claimed invention (Ans. 23; *see* Carrigan '432: cols. 50–54 (claims 1–45)).

FF 45. Carrigan '432 discloses that "[t]he administering physician can easily determine optimum dosages, dosing methodologies and repetition rates" (Carrigan '432 29:39–41; *see* Ans. 24).

FF 46. Examiner relies on Ab '181 as discussed above (*see* FF 23–26; *see generally* Ans. 24).

FF 47. Examiner finds that Ab '280 claims methods for treating ovarian cancers comprising the administration of immunoconjugates, within the scope of Appellant's claimed invention (Ans. 29–30; *see* Ab '280: cols. 200–204 (claims 18–27, 30, 33–54, 59–64, 67, 69, 70, and 73)).

FF 48. Ab '280 discloses that "[t]he administering physician can easily determine optimum dosages, dosing methodologies and repetition rates" (Ab '280 60:18–20; *see* Ans. 31).

FF 49. Examiner finds that Ab '490 claims methods for treating ovarian cancers comprising the administration of immunoconjugates, within the scope of Appellant's claimed invention (Ans. 34; *see* Ab '280: cols. 207–211 (claims 1–40)).

FF 50. Examiner finds that "[t]he only difference between [the claims of Ab '275, Ab '966, Carrigan '432 in view of Ab '181, Ab '280, and Ab '490], if any, is determining the dose using AIBW" and relies on Green, Geraghty, Fuchs, and Narain, as discussed above, to make up for this deficiency (Ans. 17–18, 20–21, 23–24, 30–31, and 35; *see also* FF 32–38) (emphasis omitted).

ANALYSIS

The rejection over the claims of (a) Ab '275, (b) Ab '966, (c) Carrigan '432 in view of Ab '181, (d) Ab '280, and (e) Ab '490 in view of Green, Geraghty, Fuchs, and Narain:

Based on the claims of (a) Ab '275, (b) Ab '966, (c) Carrigan '432 in view of Ab '181, (d) Ab '280, and (e) Ab '490 in view of Green, Geraghty, Fuchs, and Narain, Examiner concludes that because

> the patent claims the treatment of cancers (ovarian and cancer of the peritoneum) using the same immunoconjugate as appellant and since the patent discloses that "the administering physician can determine the optimum dosages", it would have been obvious to one of ordinary skill in the art before the effective filing date of the claimed invention for a physician to use a known dosing determination for the determination of the dose.

(Ans. 18; *see also id.* at 21, 24, 31, and 35.)

Appellant contends that

> even assuming, arguendo, one were to combine the claims of the cited patents . . . with Green, Geraghtry, Fuchs and Narain, one would still not arrive at the presently claimed specific dose of *6 mg/kg* AIBW as none of these references provide that specific amount or any reasons to arrive at it.

(Appeal Br. 33). We are not persuaded.

The claims of the cited patents are drawn to methods of treating cancer, such as ovarian cancer with an immunoconjugate within the scope of Appellant's claimed invention or immunoconjugates, within the scope of Appellant's claimed invention, useful in the treatment of cancer, such as ovarian cancer (*see* FF 39–49). In this regard, we note that a patent disclosure may be used as a dictionary to learn the meaning of a term in the patent's claim. *See e.g.*, *Toro Co. v. White Consol. Indus., Inc.*, 199 F.3d 1295, 1299 (Fed. Cir. 1999). Although, as Examiner recognizes, the patents do not expressly claim AIBW-based dosing, Green, Geraghty, Fuchs, and Narain suggest the use of AIBW-based dosing regimens.

Thus, for the foregoing reasons, the evidence on this record, as relied upon by Examiner, sets forth the general conditions of Appellant's claimed invention. Where, as here, the evidence, as relied upon by Examiner sets froth the general conditions of Appellant's claim, "it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456 (CCPA 1955). Therefore, we find no error in Examiner's rationale that a person of ordinary skill in this art would have found it prima facie obvious to use AIBW-based dosing regimens to administer an immunoconjugate within the scope of Appellant's claimed invention to a human patient to treat cancer, including ovarian cancer. In

doing so, a person of ordinary skill in this art would have determined the appropriate dosage through routine experimentation.

For the reasons discussed above, with respect to the obviousness rejections, we are not persuaded by Appellant's contentions that "Green, Geraghty, Fuchs and/or Narain . . . [do not] relate to immunoconjugates, antibody-based drugs, or ocular toxicity," based on Griggs, "it is unclear whether one of ordinary skill would have even considered adjusting the dosing method for small molecule chemotherapeutics . . . to obese patients . . . at the time the application was filed," or that "it was completely unpredictable that changing from TBW to AIBW dosing would have eliminated Grade III ocular toxicities" (Appeal Br. 33–34; *see generally* Reply Br. 19–20).

CONCLUSION

The preponderance of evidence relied upon by Examiner supports a conclusion of obviousness-type double patenting.

The rejection of claim 1 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of Ab '275 in view of Green, Geraghty, Fuchs, and Narain is affirmed. Claims 225, 226, 228–243, 245–254, 258–267, 269–277, 279–288, 292–301, and 305–354 are not separately argued and, therefore, fall with Appellant's claim 1.

The rejection of claim 1 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of Ab '966 in view of Green, Geraghty, Fuchs, and Narain is affirmed. Claims 225, 226, 228–243, 245–254, 258–267, 269–277, 279–288, 292–301, and

305–354 are not separately argued and, therefore, fall with Appellant's claim 1.

The rejection of claim 1 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of Carrigan '432 in view of Ab '181, Green, Geraghty, Fuchs, and Narain is affirmed. Claims 225, 226, 228–243, 245–254, 258–267, 269–277, 279–288, 292–301, and 305–354 are not separately argued and, therefore, fall with Appellant's claim 1.

The rejection of claim 1 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of Ab '280 in view of Green, Geraghty, Fuchs, and Narain is affirmed. Claims 225, 226, 228–243, 245–254, 258–267, 269–277, 279–288, 292–301, and 305–354 are not separately argued and, therefore, fall with Appellant's claim 1.

The rejection of claim 1 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of Ab '490 in view of Green, Geraghty, Fuchs, and Narain is affirmed. Claims 225, 226, 228–243, 245–254, 258–267, 269–277, 279–288, 292–301, and 305–354 are not separately argued and, therefore, fall with Appellant's claim 1.

DECISION SUMMARY

In summary:

Claims Rejected	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
1, 225, 226, 228, 229, 231–243,	102(a)(1) and (a)(2)	Lutz '282, Ab '181		1, 225, 226, 228, 229, 231–

Claims Rejected	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
245, 247–254, 258, 259, 261–267, 269, 271–277, 279, 281–288, 292, 293, 295–301, 306–354				243, 245, 247–254, 258, 259, 261–267, 269, 271–277, 279, 281–288, 292, 293, 295–301, 306–354
1, 225, 226, 228–243, 245–254, 258–267, 269–277, 279–288, 292–301, 305–354	102(a)(1)	Ab ’528		1, 225, 226, 228–243, 245–254, 258–267, 269–277, 279–288, 292–301, 305–354
1, 225, 226, 228–243, 245–254, 258–267, 269–277, 279–288, 292–301, 305–354	102(a)(1)	Carrigan ’675, Ab ’181		1, 225, 226, 228–243, 245–254, 258–267, 269–277, 279–288, 292–301, 305–354
1, 225–354	103	Lutz ’282, Ab ’181, Armstrong		1, 225–354
1, 225–354	103	Ab ’528 or Carrigan ’675, Armstrong		1, 225–354
1, 225–354	103	Lutz ’282, Ab ’181, Armstrong, Green, Geraghty, Fuchs, Narain	1, 225–354	

Claims Rejected	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
1, 225–354	103	Ab ’528 or Carrigan ’675, Armstrong, Green, Geraghty, Fuchs, Narain	1, 225–354	
1, 225, 226, 228–243, 245–254, 258–267, 269–277, 279–288, 292–301, 305–354	Obviousness-type double patenting	Ab ’275 in view of Green, Geraghty, Fuchs, Narain	1, 225, 226, 228–243, 245–254, 258–267, 269–277, 279–288, 292–301, 305–354	
1, 225, 226, 228–243, 245–254, 258–267, 269–277, 279–288, 292–301, 305–354	Obviousness-type double patenting	Ab ’966, Green, Geraghty, Fuchs, Narain	1, 225, 226, 228–243, 245–254, 258–267, 269–277, 279–288, 292–301, 305–354	
1, 225, 226, 228–243, 245–254, 258–267, 269–277, 279–288, 292–301, 305–354	Obviousness-type double patenting	Carrigan ’432, Ab ’181, Green, Geraghty, Fuchs, Narain	1, 225, 226, 228–243, 245–254, 258–267, 269–277, 279–288, 292–301, 305–354	
1, 225, 226, 228–243, 245–254, 258–267, 269–277, 279–288,	Obviousness-type double patenting	Ab ’280, Green, Geraghty, Fuchs, Narain	1, 225, 226, 228–243, 245–254, 258–267, 269–277, 279–	

Claims Rejected	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
292–301, 305–354			288, 292–301, 305–354	
1, 225, 226, 228–243, 245–254, 258–267, 269–277, 279–288, 292–301, 305–354	Obviousness-type double patenting	Ab '490, Green, Geraghty, Fuchs, Narain	1, 225, 226, 228–243, 245–254, 258–267, 269–277, 279–288, 292–301, 305–354	
Overall Outcome			1, 225–354	

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).

AFFIRMED