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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte GENA DALZIEL, BRIAN JAMES DEAN,
MARK JASON DRESSER, ADAM FRYMOYER,
SCOTT NAYLOR HOLDEN, JIN YAN JIN,
JOSEPH ALAN WARE, and LESLIE Z. BENET

Appeal 2016-000202
Application 13/650,274¹
Technology Center 1600

Before ULRIKE W. JENKS, ELIZABETH A. LAVIER, and
TAWEN CHANG, *Administrative Patent Judges*.

LAVIER, *Administrative Patent Judge*.

DECISION ON APPEAL

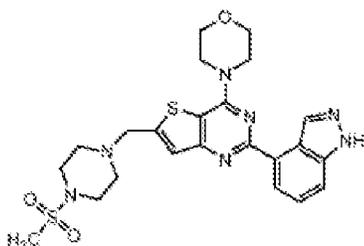
Pursuant to 35 U.S.C. § 134(a), Appellants seek reversal of the Examiner's rejection of claims 1, 3, 4, 6, 9, and 10. We have jurisdiction under 35 U.S.C. § 6(b). For the reasons set forth below, we AFFIRM.

¹ Appellants state the real parties in interest are Genentech, Inc. and the Regents of the University of California. Br. 2.

BACKGROUND

The Specification describes “methods of treating pharmacological-induced hypochlorhydria in cancer patients with a re-acidification compound.” Spec. 7:13–14. Claims 1 and 10, the independent claims, are illustrative:

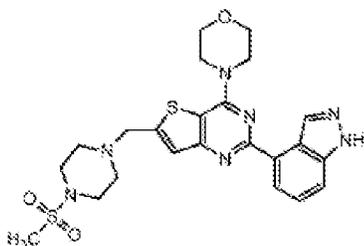
1. A method of treating a patient with a hyperproliferative disorder comprising administering to the patient a re-acidification compound selected from betaine hydrochloride and glutamic acid hydrochloride, and GDC-0941 having the formula:



GDC-0941;

wherein the patient has received a gastric acid-reducing therapeutic selected from a proton-pump inhibitor, an H₂-receptor antagonist, and an antacid.

10. A method of increasing the bioavailability of GDC-0941, having the formula:



GDC-0941;

comprising coadministering to a patient receiving a gastric acid-reducing therapeutic agent, an effective amount of a re-acidification compound effective to enhance the bioavailability of GDC-0941.

Br. 8–9 (Claims Appendix).

REJECTION MAINTAINED ON APPEAL

Claims 1, 3, 4, 6, 9, and 10 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Chuckowree,² Ogawa,³ Naunton,⁴ and Knapp.⁵ Ans. 3.

DISCUSSION

The Examiner’s findings regarding the § 103(a) rejection are set forth on pages 3–8 of the Final Action. As these findings pertain to understanding the Examiner’s rejection of illustrative claims 1 and 10,⁶ the Examiner cites Chuckowree as teaching treatment of disorders arising from abnormal cell growth, function, or behavior, including gastric cancer, with a compound having the same structure as GDC-0941. *See* Final Action 4 (citing Chuckowree claims 1, 22, 24, ¶ 29). Further, Naunton, which discloses that a significant number of patients diagnosed with gastric cancer undergo long-term anti-ulcer treatment, with an H₂-antagonist or proton-pump inhibitor,

² Chuckowree et al., US 2008/0076768 A1, published Mar. 27, 2008.

³ Oji et al., *Expression of the Wilms’ Tumor Gene WT1 in Solid Tumors and its Involvement in Tumor Cell Growth*, 90 JPN. J. CANCER RES. 194 (1999) (English Abstract only). Appellants and the Examiner both refer to this reference as “Ogawa,” the name of the second author. For consistency, we do the same. From the record, it appears that the Examiner relies on the Abstract of Ogawa, which is in English, rather than the whole article. *See* Final Action 4.

⁴ Naunton et al., *Overuse of Proton Pump Inhibitors*, 25 J. CLINICAL PHARM. & THERAPEUTICS 333 (2000).

⁵ Knapp et al., *Modification of Gastric pH with Oral Glutamic Acid Hydrochloride*, 10 CLINICAL PHARMACY 866 (1991).

⁶ The Examiner cites Ogawa as evidence that gastric cancer is a solid tumor, as is relevant to claim 6. *See* Final Action 4 (citing Ogawa Abstract).

prior to their cancer diagnosis. *See id.* at 4–5 (citing Naunton 334). Due to reduced stomach acidity, Naunton reports that patients taking proton-pump inhibitors are susceptible to bacterial enteritis. *See id.* at 5 (citing Naunton 334). Knapp teaches that hypochlorhydria (physiological or pharmacologically-induced decrease in gastric acid secretion) “may alter the dissolution and absorption of certain drugs and dosage forms that have pH-dependent release characteristics.” *Id.* at 5 (citing Knapp 866). Knapp further teaches dosages and regimens of oral glutamic acid hydrochloride that can be used to lower gastric pH and enhance drug absorption, and suggests “plasma gastrin levels should be monitored in patients receiving long-term treatment.” *Id.* (citing Knapp 867).

The Examiner finds that it would have been obvious to one of ordinary skill in the art at the time of the invention “to modify the generic gastric cancer patient population taught by Chuckowree et al to include patients receiving proton-pump inhibitors such as the ones taught by Naunton et al.” Final Action 5–6. Naunton’s teaching that many patients with gastric cancer had long-term anti-ulcer treatment with an H₂-antagonist or proton-pump inhibitor prior to diagnosis would have provided a reasonable expectation of success. *Id.* at 6. Further, in view of Knapp, the ordinarily skilled artisan would have reasonably expected success in administering glutamic acid hydrochloride to re-acidify the stomach to physiological pH. *Id.* Although the Examiner recognizes that the prior art does not teach increased bioavailability of GDC-0941 in the presence of a

re-acidification compound, as recited in claim 10, *see* Final Action 6,⁷ the Examiner notes that this is the result of an administration step, and “[s]ince the claimed administration steps are taught by the prior art, these results would necessarily be achieved,” *id.*

Appellants first argue that the Examiner’s application of the references “seems misdirected.” Br. 5. This assertion is supported only by equally general allegations that the cited references do not teach or suggest the limitations of claims 1 and 10. *See id.* These conclusory arguments are unresponsive and unpersuasive, as they fail to point out with particularity or explain why the claims are patentable. *See Ex parte Belinne*, No. 2009-004693, slip op. at 7–8 (BPAI Aug. 10, 2009) (informative) (discussing the insufficiency of argument that “restates elements of the claim language” and fails to explain why Examiner’s findings are erroneous); *cf. In re Lovin*, 652 F.3d 1349, 1357 (Fed. Cir. 2011) (explaining that the Board has “reasonably interpreted Rule 41.37 to require more substantive arguments in an appeal brief than a mere recitation of the claim elements and a naked assertion that the corresponding elements were not found in the prior art”).

⁷ The Examiner makes this finding specifically in regard to claims 7 and 8, which are cancelled. *See* Final Action 6; Ans. 6. However, the analysis is the same for claim 10, insofar as claim 10 recites increased bioavailability of GDC-0941.

Next, Appellants point to two post-filing articles, Ware⁸ and Yago,⁹ as evidence of unexpected results. *See* Br. 5–7. Ware reports on the effects of coadministration with rabeprazole (a proton-pump inhibitor) on GDC-0941 pharmacokinetics, for both fasting and fed patients. Br. 6 (citing Ware 4047). Providing an introductory summation of its results, Ware states:

The results of the current investigations emphasize the complex nature of physicochemical interactions and the importance of gastric acid for the dissolution and solubilization processes of GDC-0941. Given these findings, dosing of GDC-0941 in clinical trials was not constrained relative to fasted/fed states, but the concomitant use of ARAs (*acid-reducing agents*) was restricted. Mitigation strategies to limit the influence of pH on exposure of molecularly targeted agents such as GDC-0941 with pH-dependent solubility are discussed.

Id. (quoting Ware 4047). Appellants assert that Ware thus shows “surprising and unexpected effects of the proton-pump inhibitor rabeprazole on the pharmacokinetics of GDC-0941.” *Id.* As to Yago, Appellants point to findings that “re-acidification compounds betaine HCl (BHCl) and citric acid greatly improve the in vitro dissolution of GDC-0941, and BHCl enhances the absorption of GDC-0941 in the famotidine-induced hypochlorhydric dog (Figures 2A and 2B).” *Id.* Appellants characterize Yago as evidence of “surprising and unexpected effects of re-acidification compounds on GDC-0941.” *Id.*

⁸ Ware et al., *Impact of Food and the Proton Pump Inhibitor Rabeprazole on the Pharmacokinetics of GDC-0941 in Healthy Volunteers: Bench to Bedside Investigation of pH-Dependent Solubility*, 10 MOL. PHARMACEUTICS 4074 (2013).

⁹ Yago et al., *Gastric Reacidification with Betaine HCl in Healthy Volunteers with Rabeprazole-Induced Hypochlorhydria*, 10 MOL. PHARMACEUTICS 4032 (2013).

Like the Examiner, we are unpersuaded that Ware or Yago report unexpected effects, so much as expected ones. *See* Final Action 7–8. As the Examiner finds regarding Yago:

Even if Applicants presented unexpected data that glutamic acid hydrochloride enhances absorption of GDC-0941, such data would not be unexpected because Knapp et al teach patient with hypochlorhydria may experience inadequate dissolution and absorption of drugs and dosage forms that have pH-dependent release characteristics; elevation of gastric pH have been associated with a decrease in bioavailability, (See page 868, second col). Moreover, Knapp et al teach glutamic hydrochloride has been used to lower gastric pH and enhance drug absorption.”

Final Action 8. Further, we agree with the Examiner that Ware focuses not only on the effect of rabeprazole on the pharmacokinetics of GDC-0941, but also on the impact of food, while the claims are silent regarding administration of food. *See id.* at 7. Accordingly, the alleged unexpected results of Ware are not commensurate in scope with the claims. Likewise, we agree with the Examiner that Yago is not responsive to the rejection because Yago’s data use betaine hydrochloride as the re-acidification compound, whereas the rejection is based on glutamic acid hydrochloride as the re-acidification compound. *See id.*

Finally, Appellants return to arguing that the cited references fail to teach or suggest the claimed invention:

In particular, there was no teaching or suggestion that the re-acidification compounds betaine hydrochloride and glutamic acid hydrochloride improve the bioavailability and pharmacokinetics of GDC-0941. There is no teaching or suggestion in the cited references that GDC-0941 has a pharmacological deficiency related to dissolution or absorption. Furthermore, there is no teaching or suggestion in the cited

references that any such deficiency would be influenced by the administration of a re-acidification compound.

Br. 7. These arguments are unpersuasive to the extent that they address the references individually, not the Examiner's findings regarding the combination of the references. *See In re Keller*, 642 F.2d 413, 426 (CCPA 1981) ("But one cannot show non-obviousness by attacking references individually where, as here, the rejections are based on combinations of references."). Further, these arguments relate to the properties of GDC-0941 in the presence of a re-acidification compound, and the "[m]ere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention." *In re Baxter-Travenol Labs.*, 952 F.2d 388, 392 (Fed. Cir. 1991); *see also In re Woodruff*, 919 F.2d 1575, 1577–78 (Fed. Cir. 1990) (obviousness rejection affirmed where using claimed elements in the manner suggested by the prior art necessarily resulted in claim-recited effect).

CONCLUSION

The rejection of claims 1, 3, 4, 6, 9, and 10 is affirmed for the reasons of record and as explained herein. No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv).

AFFIRMED