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UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF CALIFORNIA

PLEXXIKON INC.,

Plaintiff,

v.

NOVARTIS PHARMACEUTICALS
CORPORATION,

Defendant.

Case No. [17-cv-04405-HSG](#)

**ORDER GRANTING IN PART AND
DENYING IN PART MOTION TO
EXCLUDE THE EXPERT TESTIMONY
OF SUSANA ORTIZ-URDA**

Re: Dkt. No. 204

Pending before the Court is Defendant Novartis Pharmaceuticals Corporation's motion to exclude the testimony of Plaintiff Plexxikon Inc.'s expert Susana Ortiz-Urda. Dkt. No. 204. The Court heard argument on this motion on November 1, 2019. See Dkt. No. 341. As detailed below, the Court **GRANTS IN PART** and **DENIES IN PART** the motion.

I. BACKGROUND

Defendant challenges the testimony of Plaintiff's clinical expert, Dr. Susana Ortiz-Urda, as speculative and not based on any reliable methodology. Dkt. No. 204. In her expert report, Dr. Ortiz-Urda offers opinions about the treatment of melanoma, its evolution, and how physicians would respond in the hypothetical scenario in which Defendant's drug Tafenlar was not available as a combination therapy with Mekinist. See Dkt. No. 227-2 ("Ortiz-Urda Report").

Dr. Ortiz-Urda explains that both immunotherapies and targeted therapies are widely prescribed for the treatment of metastatic melanoma. See *id.* at ¶ 57. However, she explains that there are some circumstances in which targeted therapies are more appropriate for certain BRAF^{V600E} metastatic melanoma patients. See *id.* at ¶¶ 57–62. There are only a few such targeted therapies currently available. See *id.* at ¶ 62. The combination of Tafenlar and Mekinist became the first combination therapy to be approved for the treatment of metastatic melanoma in

United States District Court
Northern District of California

1 January 2014. See *id.* at ¶ 43. In November 2015, Plaintiff’s Zelboraf drug was approved by the
2 Food and Drug Administration (“FDA”) in combination with Cotellic. See *id.* at ¶ 48. The FDA
3 then approved a third combination therapy, Braftvoi and Mektovi, in June 2018. *Id.* at ¶ 50. Dr.
4 Ortiz-Urda states that these combination therapies, as opposed to monotherapies, have become the
5 standard of care for patients with metastatic melanoma. *Id.* at ¶ 51. She clarifies that in her
6 experience, physicians often prescribe the Tafinlar-Mekinist combination therapy because they are
7 more familiar with it as the first to market, but not because it “is superior from a therapeutic
8 perspective” to the other combination therapies. *Id.* at ¶ 63. In a single paragraph, Dr. Ortiz-Urda
9 also notes that the Tafinlar–Mekinist combination therapy is approved for the treatment of certain
10 other cancers for which the Zelboraf–Cotellic combination is not approved. See *id.* at ¶ 72.

11 Dr. Ortiz-Urda then offers two primary opinions regarding a hypothetical world in which
12 the Tafinlar-Mekinist combination was not an option for treating physicians: (1) BRAF^{V600E}
13 metastatic melanoma patients who were prescribed the combination therapy of Tafinlar and
14 Mekinist would be prescribed another targeted therapy, including Plaintiff’s Zelboraf drug in
15 combination with Cotellic; and (2) also that “some percentage of prescribing physicians would
16 prescribe the Zelboraf–Cotellic combination off label to patients for indications for which
17 Tafinlar–Mekinist is approved but the Zelboraf–Cotellic combination is not.” *Id.* at ¶ 6(a)–(b); see
18 also *id.* at ¶¶ 66–68, 72. In particular, in addition to metastatic melanoma, Dr. Ortiz-Urda notes
19 that the Tafinlar–Mekinist combination is approved by the FDA for the treatment of non-small cell
20 lung cancer and metastatic anaplastic thyroid cancer. *Id.* at ¶ 72. Although the Zelboraf–Cotellic
21 combination is not approved for the treatment of these cancers, Dr. Ortiz-Urda opines that
22 “physicians would reasonably conclude” that it would be effective against them and prescribe
23 them anyway as they have a similar “mechanism of action” to the Tafinlar–Mekinist combination.
24 See *id.* Dr. Ortiz-Urda repeated similar opinions in her reply report. See Dkt. No. 227-4, Ex. 3
25 (“Ortiz-Urda Reply Report”).

26 **II. LEGAL STANDARD**

27 Federal Rule of Evidence 702 allows a qualified expert to testify “in the form of an opinion
28 or otherwise” where:

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(a) the expert’s scientific, technical, or other specialized knowledge will help the trier of fact to understand the evidence or to determine a fact in issue; (b) the testimony is based on sufficient facts or data; (c) the testimony is the product of reliable principles and methods; and (d) the expert has reliably applied the principles and methods to the facts of the case.

Fed. R. Evid. 702. Expert testimony is admissible under Rule 702 if it is both relevant and reliable. See *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 597 (1993). “[R]elevance means that the evidence will assist the trier of fact to understand or determine a fact in issue.” *Cooper v. Brown*, 510 F.3d 870, 942 (9th Cir. 2007); see also *Primiano v. Cook*, 598 F.3d 558, 564 (9th Cir. 2010) (“The requirement that the opinion testimony assist the trier of fact goes primarily to relevance.”) (quotation omitted).¹ Under the reliability requirement, the expert testimony must “ha[ve] a reliable basis in the knowledge and experience of the relevant discipline.” *Primiano*, 598 F.3d at 565. To ensure reliability, the Court “assess[es] the [expert’s] reasoning or methodology, using as appropriate such criteria as testability, publication in peer reviewed literature, and general acceptance.” *Id.* at 564.

III. DISCUSSION

Defendant contends that as a dermatologist and melanoma specialist at the University of California at San Francisco (“UCSF”) Melanoma Center, Dr. Ortiz-Urda is unaware of the behavior of prescribing physicians outside of her own practice group at UCSF. See Dkt. No. 204 at 7–9. Defendant thus seeks to preclude her testimony about how physicians outside UCSF would respond in the hypothetical world in which Tafenlar and Mekinist were not available. *Id.* The Court addresses Defendant’s argument as it pertains to each of Dr. Ortiz-Urda’s opinions about prescription practices for: (1) metastatic melanoma; and (2) other cancers.

A. Prescription Practices for Metastatic Melanoma

First, Dr. Ortiz-Urda opines that if Tafenlar and Mekinist were not available, metastatic melanoma patients who were prescribed this combination therapy would be prescribed another

¹ Whether to admit expert testimony is evaluated “under the law of the regional circuit,” so in this case, under the law of the Ninth Circuit. See *Micro Chem., Inc. v. Lextron, Inc.*, 317 F.3d 1387, 1391 (Fed. Cir. 2003).

1 targeted therapy. See Ortiz-Urda Report at ¶¶ 57–62.

2 Defendant does not argue that Dr. Ortiz-Urda is unqualified to offer opinions about the
3 treatment of melanoma. Rather, Defendant contends that her opinions about what physicians
4 would do without Tafenlar and Mekinist are wholly speculative because during her deposition, Dr
5 Ortiz-Urda acknowledged that she is “less familiar” with the prescribing practices of physicians
6 outside of UCSF. See *id.* at 7 (citing Dkt. No. 204-4, Ex. 3 (“Ortiz-Urda Depo.”) at 51:3–52:5;
7 150:17–151:12). She also explained that prescribing practices may differ based on physicians’
8 perception of side effects and their own clinical experiences. See *id.* (citing Ortiz-Urda Depo. at
9 31:19–25; 42:24–43:12; 90:13–19). Defendant also points out that Dr. Ortiz-Urda did not engage
10 in any systematic analysis outside her own firsthand experience to obtain information about other
11 physicians’ practices. See *id.* at 5, 7–8.

12 The Court is not persuaded that these statements from Dr. Ortiz-Urda’s deposition taken
13 together render her opinions speculative and unreliable. Neither Daubert nor Rule 702 requires
14 experts to conduct 50-state surveys before they may offer opinions about the standard of care.
15 Rather, the Supreme Court has cautioned that the Daubert inquiry is intended to be flexible, and
16 when evaluating specialized or technical expert opinion testimony, “the relevant reliability
17 concerns may focus upon personal knowledge or experience.” See *Kumho Tire Co. v.*
18 *Carmichael*, 526 U.S. 137, 150 (1999). The Ninth Circuit has recognized that this is particularly
19 true in the medical context:

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21 Despite the importance of evidence-based medicine, much of medical
22 decision-making relies on judgment—a process that is difficult to
23 quantify or even to assess qualitatively. Especially when a relevant
24 experience base is unavailable, physicians must use their knowledge
25 and experience as a basis for weighing known factors along with the
26 inevitable uncertainties to mak[e] a sound judgment.

27 Primiano, 598 F.3d at 565 (quotations omitted).

28 Here, Dr. Ortiz-Urda’s opinions about what metastatic melanoma patients would be
prescribed without Tafenlar and Mekinist is based on her “more than ten years of clinical
experience treating patients for melanoma,” including with the use of targeted therapies such as

1 Zelboraf, Cotellic, Tafenlar, and Mekinist, and other immunooncology drugs.² See Ortiz-Urda
2 Report at ¶ 1. She also helped create a multidisciplinary melanoma program at UCSF, in which
3 she incorporated her research and clinical experience. See id. at ¶ 3. Dr. Ortiz-Urda’s expert
4 report acknowledges that no head-to-head studies have been done comparing Zelboraf to Tafenlar
5 as monotherapies, or comparing the Tafenlar–Mekinist combination with the Zelboraf–Cotellic
6 combination. See id. at ¶ 63. Nevertheless, she cites documents and studies about the relative
7 efficacy and side effects of the available treatments. See id. at ¶¶ 43, 47–51, 63–68. She explains
8 that in her experience physicians prescribe Tafenlar–Mekinist with more frequency than the other
9 combination therapies because it was the first to market, rather than because of a distinction in its
10 therapeutic benefits. See id. at ¶ 63. Dr. Ortiz-Urda also explains why, from a clinical
11 perspective, some patients require targeted therapies as opposed to immunotherapies. Id. at ¶¶ 57–
12 62. And during her deposition, Dr. Ortiz-Urda explained that her understanding of how patients
13 would be treated if the Tafenlar–Mekinist combination were unavailable was premised not only on
14 her years of experience and published data, but also on conversations she has had with other
15 physicians outside UCSF. See Ortiz-Urda Depo. at 51:17–52:5.

16 As the Ninth Circuit has acknowledged, “[l]ack of certainty is not, for a qualified expert,
17 the same thing as guesswork.” Primiano, 598 F.3d at 565. Rather, expert opinion testimony “is
18 reliable if the knowledge underlying it has a reliable basis in the knowledge and experience of the
19 relevant discipline.” Id. For purposes of this Daubert motion, the Court finds that Dr. Ortiz-Urda
20 is qualified and has sufficient expertise in the treatment of metastatic melanoma for her testimony
21 about the treatment of metastatic melanoma to be useful to the jury. She has provided sufficient
22 support for her opinions about what she believes to be the standard of care as well as what
23 treatment options and other considerations a prescriber such as herself would have in the
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25 ² To the extent Defendant suggests that the Court cannot consider the content of Dr. Ortiz-Urda’s
26 expert report in evaluating Defendant’s Daubert motion, see Dkt. No. 243 at 1, that argument is
27 frivolous. The only case Defendant cites, *Hunt v. City of Portland*, 599 F. App’x 620, 621 (9th
28 Cir. 2013), is inapposite. There, the Ninth Circuit concluded that it was error for the district court
to admit an expert report at trial because it constituted hearsay to which no hearsay exception
applies. Defendant does not cite, and the Court is not aware, of any case that limits the Court’s
Daubert analysis to deposition excerpts.

1 counterfactual world where the Tafenlar–Mekinist combination was unavailable.

2 To the extent Defendant disagrees with Dr. Ortiz-Urda’s opinions, Defendant may present
3 its own evidence at trial. See Daubert, 509 U.S. at 596 (“Vigorous cross-examination,
4 presentation of contrary evidence, and careful instruction on the burden of proof are the traditional
5 and appropriate means of attacking shaky but admissible evidence.”). As Defendant’s own
6 authority notes, “Daubert makes the district court a gatekeeper, not a fact finder.” See United
7 States v. Sandoval-Mendoza, 472 F.3d 645, 654 (9th Cir. 2006). The jury will ultimately have to
8 decide how persuasive Dr. Ortiz-Urda’s counterfactual testimony is. At this stage, the Court finds
9 that Dr. Ortiz-Urda may testify about the standard of care for metastatic melanoma and, based on
10 this, how she thinks that standard of care would change and adapt were the Tafenlar–Mekinist
11 combination no longer available on the market for treating metastatic melanoma.

12 **B. Off Label Prescription Practices for Other Cancers**

13 Second, Dr. Ortiz-Urda opines that if Tafenlar and Mekinist were not available, “physicians
14 would reasonably conclude that the Zelboraf–Cotellic combination would be effective against”
15 cancers for which the Tafenlar–Mekinist combination is approved, but for which the Zelboraf–
16 Cotellic combination is not approved. See Ortiz-Urda Report at ¶¶ 69–72. Defendant again
17 contends that Dr. Ortiz-Urda’s opinions are speculative and not based on a reliable methodology
18 as she lacks knowledge of how prescribing physicians would behave in this counterfactual world.
19 See Dkt. No. 204. In reply, Defendant clarifies that this speculation is particularly acute for Dr.
20 Ortiz-Urda’s opinions about off-label use of Zelboraf and Cotellic because Dr. Ortiz-Urda is not
21 an oncologist and does not treat patients for non-small cell lung cancer or anaplastic thyroid
22 cancer. See Dkt. No. 243 at 3, 7.

23 Plaintiff offers little explanation why Dr. Ortiz-Urda should be permitted to testify about
24 physicians’ likely behavior when treating cancers other than metastatic melanoma. See Dkt. No.
25 227; see also Dkt. No. 341 at 89:15–94:6. Plaintiff instead responds that Dr. Ortiz-Urda’s opinion
26 remains reliable because it is premised on the fact that Tafenlar–Mekinist and Zelboraf-Cotellic
27 have “the same mechanism of action.” See Ortiz-Urda Report at ¶ 72. During her deposition, Dr.
28 Ortiz-Urda further explained that off-label use is more prevalent in the treatment of terminal

1 diseases where “the patient doesn’t have a lot of choices[] and they are running out of time.” See
2 Ortiz-Urda Depo. at 149:16–150:5. Plaintiff also notes that Defendant’s own expert does not
3 challenge Dr. Ortiz-Urda’s opinion that off-label use of drugs exists, only its likely frequency in
4 the case of Zelboraf and Cotellic. See Dkt. No. 227 at 3.

5 However, Dr. Ortiz-Urda does not proffer any data on the prevalence or efficacy of the off-
6 label use of Zelboraf or Cotellic, as monotherapies or in combination. To the contrary, she
7 acknowledges that “the prevalence of off-label use focusing on targeted therapies has not been
8 investigated in detail.” See Ortiz-Urda Report at ¶ 71. Moreover, she acknowledged in her
9 deposition that “[i]t’s not true as a general matter that all drugs with the same mechanism of action
10 are clinically equivalent to each other” and “sometimes drugs that have the same mechanism of
11 action may be effective for different indications.” See Ortiz-Urda Depo. at 149:3-15. In short, Dr.
12 Ortiz-Urda has not provided any facts or data that would raise her opinion about the likelihood of
13 off-label use of Zelboraf and Cotellic beyond a speculative level. And unlike her opinions about
14 the treatment of metastatic melanoma discussed in Section III.A above, her experience cannot fill
15 the gaps here, as she appears to lack any experience in the treatment (off label or otherwise) of
16 non-small cell lung cancer or anaplastic thyroid cancer. As Dr. Ortiz-Urda explains, “[t]he goal of
17 off-label prescribing is to offer a patient an alternative treatment in the absence of a suitable
18 licensed therapy or a lack of clinical trial access.” See Ortiz-Urda Report at ¶ 71. However, she
19 offers no information about the availability of suitable alternative therapies for other cancers such
20 as non-small cell lung cancer or anaplastic thyroid cancer were Tafenlar and Mekinist unavailable.

21 Thus, Dr. Ortiz-Urda may not testify about whether and to what extent prescribing
22 physicians would prescribe the Zelboraf–Cotellic combination off label to patients for indications
23 for which Tafenlar–Mekinist is approved but the Zelboraf–Cotellic combination is not.

24 **IV. CONCLUSION**

25 Accordingly, the Court **GRANTS IN PART** and **DENIES IN PART** the motion. Dr.
26 Ortiz-Urda may testify from her own experience about the standard of care for the treatment of
27 metastatic melanoma patients and how she would anticipate patients’ treatment changing were
28 Tafenlar and Mekinist not available for metastatic melanoma treatment. However, Dr. Ortiz-Urda

1 is precluded from offering testimony about whether and to what extent she would anticipate
2 physicians would prescribe the Zelboraf–Cotellic combination for the treatment of any other
3 indications outside metastatic melanoma, including off-label use for the treatment of non-small
4 cell lung cancer and metastatic anaplastic thyroid cancer.

5 **IT IS SO ORDERED.**

6 Dated: 5/26/2020

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8 HAYWOOD S. GILLIAM, JR.
9 United States District Judge
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