UNITED STATE DISTRICT COURT
EASTERN DISTRICT OF TENNESSEE
AT KNOXVILLE

IRENE JENKINS, Plaintiff, V. NOVARTIS PHARMECEUTICALS CORP., Defendant.	)))))))	No. 3:11-CV-342 (CAMPBELL/SHIRLEY)

SANDRA THORN, Plaintiff, V. NOVARTIS PHARMECEUTICALS CORP., Defendant.	)))))))	No. 3:11-CV-373 (CAMPBELL/SHIRLEY)

MEMORANDUM AND ORDER

These cases are before the undersigned pursuant to 28 U.S.C. § 636, the Rules of this Court, and the orders of the District Judge. Now before the Court is Novartis Pharmaceuticals Corporation's Daubert Motion to Exclude Testimony of Plaintiffs' Experts Dr. Robert Fletcher, Dr. Keith Skubitz, Dr. James Vogel, Professor Wayne Ray, Dr. Suzanne Parisian, and Dr. Robert Marx. This Daubert motion has been filed in both of the cases captioned above.

On June 14, 2012, the parties appeared before the Court to address this motion. The parties and the Court agreed that the Court would decide the Daubert challenge to the testimony of Wayne Ray, Ph.D., on the papers. The parties have submitted their materials on this issue to the Court, and the Court has completed its review. For the reasons stated below, the Daubert challenge to Wayne Ray, Ph.D., will be **GRANTED IN PART** and **DENIED IN PART**.

I. BACKGROUND

Both Plaintiff Jenkins and Plaintiff Thorn ("the Plaintiffs") underwent treatment for cancer in the late 1990s and early 2000s. Plaintiffs were prescribed Aredia by their physicians.[1] It is undisputed that Novartis was in the business of manufacturing, marketing, distributing, promoting, testing, labeling, and selling Aredia. The Plaintiffs allege that they suffered from osteonecrosis of the jaw caused by Aredia, and they argue that Novartis should be held liable for their personal injuries under theories of strict liability and negligence. Novartis disputes both general causation and specific causation.

The parties agree that Aredia is a bisphosphonate and the principal pharmacological action of Aredia is inhibition of bone resorption. Bisphosphonates are approved by the Food and Drug Administration ("FDA") for prevention and treatment of osteoporosis. Aredia and Zometa are "FDA-approved intravenous bisphosphonate drugs typically prescribed by oncologists to prevent bone pain, fracture and other skeletal complications in patients with cancer that has metastasized to bone." [MDL No. 3:06-MD-1760, Doc. 4695 at 2].

II. STANDARD

Federal Rule of Evidence 702 governs the admission of expert testimony. It provides:

> If scientific, technical, or other specialized knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue, a witness qualified as an expert by knowledge, skill, experience, training, or education, may testify thereto in the form of an opinion or otherwise, if (1) the testimony is based upon sufficient facts or data, (2) the testimony is the product of reliable principles and methods, and (3) the witness has applied the principles and methods reliably to the facts of the case.

[1] Plaintiff Jenkins currently has a pending motion to amend her Complaint. The motion requests leave to add an allegation that she was also prescribed and took Zometa. The Court finds that the disposition of the motion to amend will not affect the Court's rulings on the Daubert challenges to Dr. Marx and Dr. Parisian.

Fed. R. Evid. 702.

In Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579 (1993), the Supreme Court of the United States stated that a district court, when evaluating evidence proffered under Rule 702, must act as a gatekeeper, ensuring "that any and all scientific testimony or evidence admitted is not only relevant, but reliable." Id. at 589.

The Daubert standard "attempts to strike a balance between a liberal admissibility standard for relevant evidence on the one hand and the need to exclude misleading 'junk science' on the other." Best v. Lowe's Home Ctrs., Inc., 563 F.3d 171, 176–77 (6th Cir. 2009). There is no definitive checklist for applying the Daubert standard. However, there are four relevant inquiries: (1) whether the theory or technique can be or has been tested; (2) whether it "has been subjected to peer review and publication"; (3) whether there is a "known or potential rate of error"; and (4) whether the theory or technique enjoys general acceptance in the relevant scientific community. 509 U.S. at 593–94. These factors are neither "definitive, nor exhaustive, and may or may not be pertinent to the assessment in any particular case." Nelson v. Tenn. Gas Pipeline Co., 243 F.3d 244, 251 (6th Cir. 2001). "The inquiry envisioned by Rule 702 is . . . a flexible one." Daubert, 509 U.S. at 594.

In the end, the party proffering expert testimony must show by a preponderance of the proof that the expert whose testimony is being offered is qualified and will offer testimony, based on scientific knowledge, which "will assist the trier of fact in understanding and disposing of the case." Pride v. BIC Corp., 218 F.3d 566, 578 (6th Cir. 2000).

III. ANALYSIS

The Court will address the issue of whether Prof. Ray is qualified, generally, to offer testimony in this matter. The Court will then turn to the Defendant's challenges to specific portions of Prof. Ray's testimony.

A. Prof. Ray's Background and Qualifications

Prof. Ray received his Bachelor of Science degree in mathematics from the University of Washington. He obtained a master's degree in biostatistics from Vanderbilt University. Prof. Ray also holds a doctorate degree in computer science from Vanderbilt, which he employees in analyzing medical metadata for public health studies. He currently serves as a Professor of Preventative Medicine at Vanderbilt University School of Medicine. At Vanderbilt he the Director of the Division of Pharmacoepidemiology, and until recently, he served as the Director of the Master of Public Health Program. As director of this program, Prof. Ray taught advanced epidemiology courses and supervised Masters and Ph.D. candidates' thesis work. Prof. Ray is not a medical doctor.

Prof. Ray has carried out pharmacoepidemiologic research for more than thirty years, and he is actively involved in the design, execution, and analysis of numerous pharmacoepidemiologic studies. Prof. Ray is the Principal Investigator for the Vanderbilt Center for Education and Research on Therapeutics; he is also the Principal Investigator for a Contract with the FDA. Prof. Ray has published 191 manuscripts in scientific journals and publications and he reviews articles for numerous medical journals including the *New England Journal of Medical*, the *Journal of the American Medical Association*, and the *Lancet*.

Dr. Ray has been offered as an expert witness in many other cases alleging personal injuries through ONJ induced by Zometa or Aredia usage. These Courts have found that Prof. Ray is generally qualified to testify with regard to Pharmacoepidemiology.

The Court in Winter v. Novartis Pharmaceuticals Corp., 2012 WL 827305 (W.D. Mo. 2012), another case involving allegations of bisphosphonate-induced ONJ, explained Prof. Ray's qualifications well:

> It is clear the methods followed and analyses performed by Dr. Ray in reaching his opinions set forth in his expert report are consistent with the methodologies used by others in Dr. Ray's field of expertise. Dr. Ray has decades of experience in the field of pharmacoepidimiologic research where he has designed, executed, analyzed and evaluated studies on the adverse effects of medication, as is the issue in this case. Large numbers of companies and organizations, including governmental organizations such as the FDA, have utilized Dr. Ray and his studies, thus, affirming their value. Clearly, Dr. Ray has the expertise to perform the study in this case, including the meta-analysis, and to give his opinions. NPC's motion to preclude Dr. Ray's testimony on these bases is denied.

[Id. at *10]. The Court in Deutsch v. Novartis Pharmaceuticals Corp., 768 F. Supp. 2d 420 (E.D.N.Y. 2011) echoed these findings by stating, "Prof. Ray has considerable experience spanning more than 30 years in designing, executing, and analyzing research studies on the adverse effects of medications, and his expertise in evaluating the methodology in others studies renders his crafting of this study and interpretation of the cohort studies particularly reliable."

Based upon the foregoing, the Court finds, as an initial matter, that Prof. Ray is well-qualified to testify as to pharmacoepidemiologic studies. Stated differently, he is qualified to testify regarding the effect of drugs and other pharmacology in populations.

B. Challenges to Prof. Ray's Testimony

The Defendant challenges six portions of Prof. Ray's testimony: (1) Table Six containing meta-analysis purporting to establish that Zometa poses a higher risk of causing ONJ than does Aredia; (2) testimony regarding the adequacy of FDA-approved labeling for Aredia and Zometa; (3) testimony regarding the outcome of the AZURE clinical trials; (4) testimony that approximately 5% of patients receiving intravenous bisphosphonate develop ONJ; (5) testimony that ONJ is not "rare"; and (6) testimony that NPC 'could have' concluded in 2003 that intravenous bisphosphonates cause ONJ. [Doc. 71 at 19].[2]

The Court will address each of the challenges in turn.

1. Table Six

Table Six compares the relative risk of developing ONJ from use of Zometa to the relative risk of developing ONJ from use of Aredia. Table Six tabulates ten cohort studies that Prof. Ray found had "both use of differential individual IV bisphosphonates and had information sufficient to calculate the proportion of patients on each [drug] who developed [ONJ]." [Doc. 71-28 at 27]. The studies tabulated in the table were published in peer-reviewed journals [see Doc. 71-28 at 52-56], and Prof. Ray has explained the tabulation performed and the meta-analysis underlying his relative risk finding, [id. at 71-28 at 27-28].

The parties have agreed that Professor Ray will not offer testimony that the meta-analysis contained in Table Six purports to establish that Zometa carries a higher risk of ONJ than Aredia. [Doc. 99 at 2 in No. 3:11-CV-342; Doc. 103 at 2 in No. 3:11-CV-373]. This risk comparison is the only meta-analysis that Table Six purports to undertake. The Court, thus, finds that the parties have agreed that Professor Ray will not testify regarding Table Six. Pursuant to the

[2] Unless otherwise noted, document references are to the filings made in Jenkins v. Novartis, Case No. 3:11-CV-342.

parties agreement, testimony relating to Table Six is excluded pursuant to Daubert, and Novartis's motion is **GRANTED** as to this testimony.

2. Adequacy of Labeling

Prof. Ray does not discuss drug labeling in his expert reports, nor does he, in the Court's opinion, hold himself out to be an expert in labeling. Novartis has not directed the Court to any portion of Prof. Ray's report that focuses upon labeling, and the Court's own review has not revealed any discussion of labeling. Moreover, the parties have agreed that Prof. Ray will not testify regarding the adequacy of FDA-approved labeling for Aredia and Zometa. [Doc. 99 at 2].

Novartis's request that this testimony be excluded pursuant to Daubert and Rule 702 of the Federal Rules of Civil Procedure is **GRANTED**.

3. AZURE Clinical Trial

Novartis next challenges any testimony "[r]egarding the outcome of the AZURE clinical trials." Prof. Ray has previously testified that he relied on the preliminary abstract from the AZURE clinical trial as a component of his analysis. Novartis argues that the AZURE clinical trials were based upon faulty methodology.

In previous trial testimony, Prof. Ray explained that the AZURE clinical trial was funded by Novartis and was a randomized clinic trial, where women presented with breast cancer and were randomly assigned to one of two groups: either a group receiving IV bisphosphonates or a group not receiving IV bisphosphonates. Mahaney Tr. Vol. 3, pp. 28-29. A pool of 3,360 women was divided evenly into these respective groups. Id. at 29. Prof. Ray testified that the preliminary results were that the women in the group receiving IV bisphosphonates were diagnosed with eleven cases of ONJ, while the group not receiving IV bisphosphonates had no diagnoses of ONJ. Id.

On cross-examination, Prof. Ray confirmed that in 2008 he viewed an abstract of the study. Id. at 50. He acknowledged that in 2011 the AZURE clinical trial was published. Id. Further, when Novartis's counsel asked if the AZURE findings published in 2011 "found a 1.1 percent incidence rate," Prof. Ray confirmed that a 1.1 percent rate sounded correct. Id. at 73.

Prof. Ray's testimony about the AZURE clinical trials is limited in scope and falls within his pharmacoepidemiologic expertise. Other courts evaluating requests to exclude the AZURE testimony have declined to exclude the testimony. See, e.g., Winter, 2012 WL 827305 at *12-13 (denying request to exclude this testimony). Prof. Ray acknowledges that he reviewed a preliminary abstract in formulating his opinion, and counsel for the Plaintiffs has agreed that Prof. Ray will testify only as to the interim AZURE data. [Doc. 99 at 3].

The Court finds that Prof. Ray is qualified to testify generally about the interim portion of the AZURE clinical trial that he has reviewed. The Court finds that this testimony is based on Prof. Ray's scientific knowledge and will aid the trier of fact. The Court finds that the methodology defects alleged by Novartis go to the weight of Prof. Ray's testimony, and Novartis may employ cross-examination to expose the alleged defects.

Novartis's request that this testimony be excluded pursuant to Daubert and Rule 702 of the Federal Rules of Civil Procedure is **GRANTED IN PART** and **DENIED IN PART**. Prof. Ray will be limited to testifying only as to the interim AZURE data.

4. ONJ in 5% of Cases

In his rebuttal report, Prof. Ray explained that his "report identified 26 cohort studies of patients treated with IV bisphosphonates." [Doc. 71-28 at 10 (internal citation omitted)]. He explained that the cumulative incidence of ONJ in these studies varied from 0.7% to 27.5%, with a median of approximately 5%. [Id.]. Referencing these numbers, Prof. Ray concluded "the

totality of the available data suggest[s] that approximately 1 in 20 of treated patients will experience this potentially serious adverse effect." [Id.]. Novartis argues that Prof. Ray did not rely on random controlled studies that reflect a lower incidence rate and, therefore, the testimony is unreliable.

The undersigned finds that this testimony regarding the rarity of the condition at issue in this case is both relevant and scientifically reliable. It will assist the trier of fact in understanding the evidence, determining facts in issue, and evaluating his opinions.

The Court finds that Novartis's challenges go to the weight to be afforded to this testimony, not its admissibility under Rule 702. Novartis will be afforded an opportunity to cross-examine Prof. Ray regarding this opinion, and rigorous cross-examination will highlight any bases for discounting this opinion. See Maheny (Kyle) v. Novartis Pharm. Corp., 1:06-CV-035, Memorandum Opinion and Order Doc. 151 at 24 (W.D. Ky. Sept. 12, 2011) (Russell, C.J.) (finding that Novartis's objections to the 5% finding "should be addressed on cross examination"); see also Rutz v. Novartis Pharm. Corp, 12-CV-0026-MJR, Memorandum and Order, Doc. 134-1 at 25 (S.D. Ill. Dec. 21, 2012) (Reagan, D.J.). To the extent he did not include the complete universe of studies or academic work on the topic in his findings, Novartis may present this critique through its cross-examination of Prof. Ray.

Novartis's request that this testimony be excluded pursuant to Daubert and Rule 702 of the Federal Rules of Civil Procedure is **DENIED**.

5. Whether ONJ is "Rare"

In a related challenge, Novartis argues that Prof. Ray should be precluded from testifying about whether ONJ is "rare" in cancer patients who are treated with IV bisphosphonate drugs. The parties have agreed that Prof. Ray will not be permitted to testify at trial regarding his

opinion that ONJ is not "rare." [Doc. 99 at 2]. Accordingly, Novartis's request that this testimony be excluded pursuant to Daubert and Rule 702 of the Federal Rules of Civil Procedure is **GRANTED**.

6. Novartis's Ability to Conclude Intravenous Bisphosphonates Cause ONJ in 2003

The parties have agreed that Prof. Ray will not testify that Novartis "could have" concluded in 2003 that intravenous bisphosphonates cause ONJ. [Doc. 99 at 2]. Accordingly, Novartis's request that this testimony be excluded pursuant to Daubert and Rule 702 of the Federal Rules of Civil Procedure is **GRANTED**.

IV. CONCLUSION

In sum, the Court finds that Professor Wayne Ray, Ph.D., is well-qualified to testify in this case to matters within his knowledge and experience. The Court finds, however, that the Defendant's requests to preclude Professor Ray from testifying with regard to the matters identified above are well-taken in part. Accordingly, and for the reasons more fully stated above, the Motion to Exclude Testimony of Plaintiffs' Experts Dr. Robert Fletcher, Dr. Keith Skubitz, Dr. James Vogel, Professor Wayne Ray, Dr. Suzanne Parisian, and Dr. Robert Marx **[Doc. 42 in Case No. 3:11-CV-342, Doc. 26 in Case No. 3:11-CV-373]** is **GRANTED IN PART** and **DENIED IN PART**, as stated above, with regard to the testimony of Professor Wayne Ray, Ph.D.

IT IS SO ORDERED.

ENTER:

s/ C. Clifford Shirley, Jr.
United States Magistrate Judge