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. These Daubert motions have been filed in both of the cases captioned above.

On October 4, 2012, the parties appeared before the Court to address these motions. Attorney Robert Germany was present representing Plaintiff Jenkins. Attorney Sidney Gilreath was present representing Plaintiff Thorn. Attorneys William Cople and Dwight Tarwater were present representing the Defendant.

The hearing on October 4, 2012, was set to address the Defendant's Daubert challenges to the testimony of Robert Marx, D.D.S., and Suzanne Parisian, M.D. Both Dr. Marx and Dr.

Parisian testified at the hearing. The instant Memorandum and Order will rule only on the challenges relating to Dr. Marx and Dr. Parisian. The remaining Daubert challenges will be addressed in later orders of the Court. For the reasons stated below, the Daubert motions 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 if manufacturing, marketing, distributed, 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].

[1] Plaintiff Jenkins currently has a motion to amend her Complaint pending. 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.

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.

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 challenge. 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

A. Daubert Rulings in the Multi-District Litigation

These cases were originally part of a multi-district case presided over by the Honorable Todd Campbell, United States District Judge for the Middle District of Tennessee. The Defendant pursued Daubert challenges to both Robert Marx, D.D.S., and Suzanne Parisian, M.D., in the multi-district litigation. Judge Campbell found that "testimony of Plaintiffs' expert Dr. Robert Marx was admissible, for purposes of summary judgment, on the issues of causal connection and treatment and preventative measures for ONJ." [MDL No. 3:06-MD-1760, Doc. 4695 (citing Doc. 2814)]. Judge Campbell declined to address a Daubert challenge to Dr. Parisian. [MDL No. 3:06-MD-1760, Doc. 2816].

In its own analysis, the Court has considered Judge Campbell's ruling that, for purposes of summary judgment, Dr. Marx's testimony is admissible as to causal causal connection and treatment and preventative measures for ONJ. However, in reaching its decision in these cases, the Court has also considered Dr. Marx's testimony presented before the undersigned and considered the ability of this testimony to withstand a Daubert challenge as this matter proceeds toward trial by jury.

B. Robert Marx, D.D.S.

Robert Marx, D.D.S., is a dentist and maxillofacial surgeon, who has been licensed to practice dental surgery in Illinois, since 1971, and Florida, since 1984. Currently, Dr. Marx is a Professor of Surgery and Chief of the Division of Oral and Maxillofacial Surgery at the University of Miami, Miller School of Medicine. Dr. Marx estimates that in this position he devotes one day per week to treatment and consultation with established and new patients and devotes the other four days to surgeries. Dr. Marx has published monographs, textbooks, and peer-reviewed articles addressing diagnosis and surgical treatment of maxillofacial diseases and disorders. His publications include Oral and Maxillofacial Pathology: A Rationale for Diagnosis and Treatment, (Quintessence Pub. Co. 2002), authored with Diane Stern, D.D.S., which received the American Medical Writers Best Book of the Year Award in 2002, and over fifty-five articles in refereed scientific journals.

At the hearing, Dr. Marx explained the bone resorption, *i.e.* bone turn-over, process that is allegedly inhibited to bisphosphonates such as Aredia. Specifically, he explained the destruction of osteoclasts, the effect of this destruction on the jawbone, and how ONJ can result. He testified that he has prescribed Aredia and Zometa on a handful of occasions and testified that his practice has developed what is now the standard of care for dental pretreatment to prevent bisphosphonate-related ONJ. Dr. Marx testified that he has experience in oncological surgery – specifically, he performs head and neck surgery – but he acknowledged that he is not a medical oncologist. Dr. Marx testified that as of the week of the hearing, he had seen over three hundred patients with ONJ.

As an initial matter, the Court finds that Dr. Marx is qualified, generally, to testify to the matters before the Court. The Court finds that Dr. Marx is well-versed in the resorption by the

jawbone that is at the heart of this matter. He is experienced in oncologic surgery and is well-qualified to testify to dental and medical issues relating to the jaw. Moreover, the Court finds that Dr. Marx possesses an ability to explain complicated biological matters in practical and easily-digestible terms.

The Court turns now to the specific challenges posed to Dr. Marx's testimony under Daubert. The issues presented to the Court at the hearing conducted on October 4, 2012, were greatly narrowed from the Defendant's initial filing. Thus, to the extent any previous Daubert challenge or aspect of a challenge to Dr. Marx's testimony was not addressed at the hearing, the Defendant has both implicitly and explicitly represented that such challenges are moot, and they are **DENIED AS MOOT**.

Further, at the hearing, counsel for the Plaintiffs represented that Dr. Marx would not offer certain testimony identified in the Defendant's motion, including: (1) Dr. Marx's 'new' opinion that he can look at pathology and distinguish between osteomyelitis and osteonecrosis of the jaw ("ONJ"); (2) Dr. Marx's testimony regarding bad faith on the part of Novartis; (3) Dr. Marx's testimony criticizing clinical trials relating to Aredia; and (4) his opinion that specific patients in clinical trials of Aredia and/or Zometa had ONJ, which Novartis erroneously failed to detect.

The parties agreed that argument and/or testimony on these points was unnecessary because this testimony would not be presented. The Court finds that the Plaintiffs have agreed that Dr. Marx will not offer testimony on the four points identified above. This agreement essentially grants the Defendants' request and, therefore, moots the need for the Court to rule on the issue. The Court, thus, finds that the Defendant's request that Dr. Marx be prohibited from

testifying on this issue is **DENIED AS MOOT** but based on Plaintiffs' representation and agreements as to Dr. Marx's testimony.

The three Daubert challenges that remain in contention are: (1) Dr. Marx's opinion that pretreatment dental screenings and "drug holidays" are useful in preventing ONJ; (2) Dr. Marx's opinion that adverse event reports support his general causation opinion; and (3) Dr. Marx's opinion regarding the mechanism by which bisphosphonates allegedly cause ONJ. With regard to these opinions the Court finds as follows.

1. Pretreatment Dental Screenings and Drug Holidays

The Court finds that Dr. Marx is qualified to testify regarding pretreatment dental screenings based upon his experience as a dentist and oral and maxillofacial surgeon. Moreover, Dr. Marx testified that his work with patients at the University of Miami helped develop the current industry standard for pretreatment, by which patients are now referred to a dental provider prior to beginning their bisphosphonate therapy. [See Marx Report at ¶ 52]. The Court finds that Dr. Marx is qualified to testify with regard to pretreatment dental screenings as a preventative measure to prevent ONJ induced by biphosphates.

The perplexing part of the Daubert challenge regarding the pretreatment testimony is that Dr. Marx and the Defendant appear to hold the same opinion regarding pretreatment, *yet* the Defendant argues that Dr. Marx's opinion is not reliable. Dr. Marx's opinion, as stated at the hearing, is that: undertaking dental care prior to beginning a bisphosphonate regimen will prevent ONJ from developing in a significant number of cases, because the provocative factor for ONJ is trauma to the jaw. Stated differently, pretreatment can prevent intrusive procedures – such as tooth extractions – that provoke ONJ.

A flyer for Zometa was admitted into evidence as Exhibit 4 to the hearing. It was described by Plaintiff's counsel as coming from Novartis's website; the Defendant did not dispute its origin. The flyer, which contains Novartis's company emblem, endorses the same opinion regarding pretreatment's role in preventing ONJ. It states that ONJ may be prevented by: (a) obtaining a dental exam prior to starting the bisphosphonate regimen and (b) avoiding invasive dental procedures and soft-tissue injuries to the maxillofacial area. See Ex. 4 to Hrg. The Court cannot reconcile this statement, contained in materials endorsed by Novartis, with Novartis's position that Dr. Marx's opinion is unreliable.

Regardless, the Court finds that Dr. Marx's opinion regarding pretreatment has shown a sufficient degree of reliability to withstand the Daubert challenge. In reaching this conclusion, the Court has considered Dr. Marx's general qualifications in this area, the fact that he developed his opinion through his treatment of patients at the University of Miami, and his numerous scholastic writings on the issue. The Court would specifically note that the white paper/letter to the editor, admitted as Exhibit 3 to the hearing, demonstrates the opinion's reliability. The letter, composed by Dr. Marx, relies upon thirty-six cases at the University of Miami in concluding that "[p]revention, surgically by avoiding tooth removals if possible, control of periodontal disease by nonsurgical means, avoiding dental implants, and using soft liners on dentures also seems prudent." Ex. 3 to Hrg. At 1117.

The Court finds that Dr. Marx's opinion as to pretreatment as a preventative measure against ONJ is relevant, reliable, and offered by a qualified source. Accordingly, the Court finds that the Daubert challenge to this testimony is not well-taken. It is **DENIED**.

As to drug holidays, the Court finds that drug holidays are not at issue in these cases. Drug holidays have been considered as a possible preventative or remedial measure for ONJ

caused by oral bisphosphonates. Neither party has argued that the Plaintiffs in this matter used oral bisphosphonates, and Dr. Marx did not offer any relevant testimony regarding drug holidays at the hearing. The Court finds that such testimony is not relevant to these cases, and any challenge to this testimony under Daubert is **GRANTED** based upon this lack of relevance.

2. Adverse Event Reports

Dr. Marx did not testify at any length that adverse event reports support his general causation opinion. Plaintiffs directed the Court to paragraph sixty-one of Dr. Marx's report for discussion of "adverse event reports." The Court has reviewed paragraph sixty-one and finds it discusses only generally the causal connection between various medical conditions and the conditions or exposures that are widely believed to cause such conditions. The Defendant maintained that there was no "adverse event reports" opinion in Dr. Marx's report, and the Plaintiff conversely argued that a challenge to any "adverse event reports" opinion was not properly before the Court. The parties essentially conceded this issue was not ripe. Having considered the posture of this issue and the contents of Dr. Marx's report, the Court finds that it does not have sufficient evidence to rule on a challenge to this testimony, and the Court declines to so rule at this time.

Accordingly, the undersigned declines to rule on any challenge to potential testimony that adverse event reports support Dr. Marx's general causation opinion. This challenge, to the extent it has even been presented, is **DENIED WITHOUT PREJUDICE**. If this testimony is, in fact, offered at the trial of this matter, the District Judge will have heard the relevant trial testimony and be better equipped to rule on this issue at that time.

3. The Mechanism by Which Bisphosphonates Allegedly Cause ONJ

The Court finds that Dr. Marx is well-qualified to testify as to the mechanism by which bisphosphonates allegedly cause ONJ. As more fully described above, the Court finds that Dr. Marx is well-versed in the resorption by the jawbone that is at the heart of this matter. The Court further finds that his testimony regarding the resorption mechanism is relevant to this case and goes to the heart of this matter. His discussion and demonstration of the role of osteoclast destruction will aid the jury in understanding the condition for which Plaintiffs seek to hold Defendant liable. The Court further finds that Dr. Marx's testimony is reliable, because it is based on a combination of relevant academic findings and his experience with patients with ONJ. See Marx Rpt. at ¶¶ 17, 53-54.

Moreover, as stated initially, the Court finds that the MDL rulings as to his causation testimony are the law of this case.

Thus, the Court finds that Dr. Marx's testimony regarding the mechanism by which bisphosphonates allegedly cause ONJ is relevant, reliable, and offered by a qualified source. Accordingly, the Court finds that the Daubert challenge to this testimony is not well-taken. It is **DENIED**.

B. Suzanne Parisian, M.D.

Suzanne Parisian, M.D., received her medical doctorate degree from the University of South Florida in 1978 and her board certification in anatomic and clinical pathology in 1989. She testified that she was a general practitioner in Lenoir, North Carolina early in her career. From 1991 to 1995, she served as an officer in the United States Public Health Service and was assigned to the Office of the Medical Examiner for the Armed Forces, Washington, D.C. From

1991 to 1993, Dr. Parisian was a FDA Medical Officer, providing regulatory support to the FDA's Office of Compliance and Office of Device Evaluation. Dr. Parisian submits that she has presided over 162 health risk assessments for the FDA. Dr. Parisian testified that she is familiar with the Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S.C. §§ 301, *et seq.*, and its application.

As with Dr. Marx, the Daubert challenges posed to Dr. Parisian have been reduced through the agreement of the parties. The parties have agreed that Dr. Parisian cannot testify to: (1) general or specific causation between Aredia or Zometa and ONJ; (2) the intent and/or motives of Novartis; and (3) the means by which Novartis should have conducted clinical trials or critique the clinical trials conducted. In addition, the challenges not argued before the Court were represented to the Court as no longer being pursued in this matter. Therefore, the Daubert challenges to the testimony listed above and the testimony not addressed before the Court are **DENIED AS MOOT**.

The Court finds that Dr. Parisian is qualified to offer testimony as to the FDA requirements applicable to Aredia and Zometa and the FDA labeling requirements and the labeling process. She is also qualified to testify as to what materials Novartis submitted to the FDA and when. She may not, however, decide what Novartis knew and did not know at various times during the relevant period. Novartis's knowledge is an issue for the jury. Dr. Parisian has no specialized knowledge or scientific/medical expertise that provides her with a superior ability to judge Novartis's knowledge, and there is no basis for finding that the jury needs her assistance in evaluating Novartis's knowledge. Dr. Parisian's testimony will be guided by and related to the FDCA.

Moreover, the Court finds that Dr. Parisian's FDA/FDCA-related testimony is relevant and reliable so as to satisfy the Daubert standard. To the extent the Defendant challenges this

FDA/FDCA-related testimony, pursuant to Daubert, the Court finds that the challenge is not well-taken. It is **DENIED**.

The Court finds that Dr. Parisian is not qualified to testify as to the mechanism by which Zometa and Aredia, or bisphosphonates generally, cause ONJ. While Dr. Parisian holds a doctor of medicine, she testified that the vast majority of her career has been spent in the field of medical regulation rather than the practice of even general medicine. Moreover, the Plaintiff has not presented any evidence indicating that Dr. Parisian has any special experience treating bisphosphonate-related disorders, jaw conditions, or bone conditions. Further, there is no evidence in the record to indicate that Dr. Parisian has either treated ONJ or studied ONJ in an academic setting. Finally, Dr. Parisian did not offer causation testimony at the hearing before the undersigned, and she, at least implicitly, acknowledged that ONJ causation was not her area of expertise. Thus, the Court finds that the Defendant's Daubert challenge with respect to such testimony is well-taken, and it is **GRANTED**.

IV. CONCLUSION

In sum, 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 **[Doc. 42 in No. 3:11-CV-342; Doc. 26 in No. 3:11-CV-373]**, as it relates to the testimony of Robert Marx, D.D.S., and Suzanne Parisian, M.D., is **DENIED IN PART** and **GRANTED IN PART** to the extent stated above. The challenges to the other experts referenced in the motion will be addressed in orders of the Court to follow this Memorandum and Order.

IT IS SO ORDERED.

ENTER:

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