IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

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| IN RE: ZOSTAVAX (ZOSTER VACCINE LIVE) PRODUCTS LIABILITY LITIGATION | : | MDL NO. 2848<br><br>CIVIL ACTION NO. 18-md-2848 |
| THIS DOCUMENT RELATES TO:<br><br>KAY KOBYLINSKI & THOMAS EUGENE KOBYLINSKI v. MERCK & CO., INC., et al.<br>Civil Action No. 19-4772 | : | |

MEMORANDUM IN SUPPORT OF PRETRIAL ORDER NO. 507

Bartle, J. October 4, 2023

Plaintiffs Kay Kobylinski and her husband Thomas Eugene Kobylinski have sued defendants Merck & Co., Inc. and Merck Sharp & Dohme Corp. ("Merck") in this product liability action. Ms. Kobylinski alleges that she suffers from persistent daily headache ("PDH") as a result of being inoculated with Zostavax, a vaccine developed by defendants to prevent shingles.[1] This action, which is part of Multidistrict Litigation No. 2848, has been selected as a bellwether case for trial. Before the

1. Ms. Kobylinski presently asserts claims for negligence and strict liability design defect. She has stipulated to dismiss claims for negligent manufacturing, strict liability manufacturing defect, breaches of express and implied warranty, negligent misrepresentation, unjust enrichment, negligent failure to warn, and strict liability failure to warn. Mr. Kobylinski maintains a claim for loss of consortium.

court is the motion of defendants to exclude the general and specific causation opinions of plaintiffs' expert Joseph Jeret, M.D., on the ground that he has not met the standards required under Rule 702 of the Federal Rules of Evidence[2] and Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579 (1993).

I

Rule 702 of the Federal Rules of Evidence provides that:

> A witness who is qualified as an expert by knowledge, skill, experience, training, or education may testify in the form of an opinion or otherwise if:
> (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.

Our Court of Appeals has described Rule 702 as requiring expert testimony to meet three criteria: (1) qualification, (2) reliability, and (3) fit. See, e.g.,

2. Defendant also cites Rules 401 and 403 of the Rules of Evidence to support their motion. Rule 401 provides the test for relevance and Rule 403 allows the court to exclude relevant evidence for prejudice, confusion, waste of time, or other reasons.

Schneider ex rel. Estate of Schneider v. Fried, 320 F.3d 396, 404 (3d Cir. 2003).

The court operates in a "gatekeeping role" that ensures that the testimony "both rests on a reliable foundation and is relevant to the task at hand." Daubert, 509 U.S. at 597. This gatekeeping prevents opinion testimony that does not meet these requirements from reaching the jury. Schneider, 320 F.3d at 404. The party presenting the expert need not show that the opinions of the expert are correct but rather by a preponderance of the evidence that the opinions of the expert are reliable. In re Paoli R.R. Yard PCB Litig., 35 F.3d 717, 744 (3d Cir. 1994). This inquiry under Rule 702 is a "flexible one" that is focused "solely on principles and methodology, not on the conclusions that they generate." Daubert, 509 U.S. at 594-95. Instead "[t]he analysis of the conclusions themselves is for the trier of fact." Kannankeril v. Terminix Int'l, Inc., 128 F.3d 802, 807 (3d Cir. 1997).

II

Ms. Kobylinski was inoculated with Zostavax on January 25, 2017. She was 68 years old at the time. She describes her symptoms as beginning in early March 2017, when she rode in a car back to Illinois from a vacation in Florida. At that time, she developed lightheadedness, blurry vision, dizziness, and

concentration problems.[3] These symptoms lasted roughly thirty seconds. She distinctly remembers this episode as the first time she experienced these symptoms.

She testified at her deposition that she endured similar symptoms while visiting with friends during Memorial Day weekend that year. This time she also felt added pressure in her head. Her symptoms lasted all day until she went to bed. The record is silent as to any further specific headache symptoms until March 29, 2018. On that date, she visited a nurse practitioner at Southern Illinois Healthcare, who recorded Ms. Kobylinski's description of her "headache" in her medical history:

> This is a recurrent problem. The current episode started 1 to 4 weeks ago. The problem occurs daily. The problem has been unchanged. The pain is located in the right unilateral region. The pain does not radiate. The quality of the pain described as band-like and dull. The pain is mild.

This is the first mention of such symptoms in her medical records.

At some point, Ms. Kobylinski mentioned her symptoms[4] to her cardiologist, Dr. Jain. He referred her to Matthew

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3. Ms. Kobylinski has at times expressed uncertainty about whether her symptoms began in late February or early March. For present purposes, the court will assume her symptoms began in early March.

4. The record does not disclose what Ms. Kobylinski said to Dr. Jain about her symptoms.

Loftspring, M.D., a neurologist. In April 2018, Ms. Kobylinski saw Dr. Loftspring, who ordered an MRI to rule out a brain tumor or other neurological defect as the cause for her headaches. He also authored a note in her medical history: "In February in [F]lorida and had double vision in her right eye that lasted 5 minutes. In March, it [occ]urred more frequently. At the end of March, she developed difficulty focusing (pressure and diplopia). The double vision (unsure if horizontal or vertical) ended at that time." While he does not specify in the note whether he was referring to "February" and "March" 2017 or 2018, Dr. Loftspring stated during his deposition that based on the way he typically documents plaintiff histories, he "was referring to the present year," that is 2018. He further clarified that if Ms. Kobylinski had stated that her symptoms had started in March 2017, he would have noted the year in the medical record. Dr. Loftspring ultimately prescribed amitriptyline to Ms. Kobylinski in the summer of 2018.

According to Ms. Kobylinski, her symptoms typically last for fifteen to thirty seconds before dissipating. She sometimes experiences nausea. She describes her headaches as "mild" and responsive to medication such as Ibuprofen. She takes prescription medication which diminishes her symptoms by "95%." Multiple treating physicians have stated that Ms. Kobylinski likely suffers from migraine headaches. Her medical

records show that she reported migrainous symptoms in October 2016 before these post-vaccination headaches began.

III

Dr. Jeret, plaintiffs' expert, is a board-certified neurologist who actively practices neurology at the Icahn School of Medicine at Mount Sinai Medical Center in New York. He offers both general and specific causation opinions in this matter, that is, he opines that Zostavax can cause PDH and that Ms. Kobylinski developed PDH as a result of her inoculation with Zostavax.

Defendants do not challenge Dr. Jeret's qualification to testify as an expert or the fit of his opinion. Rather, they contend that Dr. Jeret's general and specific causation opinions are not the product of reliable methods.

Dr. Jeret's opinions were offered without meeting, examining, or speaking to Ms. Kobylinski and are based on a limited review of forty-four pages of Ms. Kobylinski's medical history and her, Dr. James Kim's, and Dr. David Lardizabal's depositions.[5] Dr. Jeret has still not reviewed a full record and

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5. Dr. Kim is an ophthalmologist that Ms. Kobylinski saw in July 2020 and Dr. Lardizabal is a neurologist with whom Ms. Kobylinski had a tele-health visit in September 2020. According to his report, Dr. Jeret did not review the deposition of Dr. Loftspring.

has not reviewed the depositions of defendants' experts.[6] Prior to Ms. Kobylinski, Dr. Jeret had never diagnosed any individual with PDH.

IV

The International Classification of Headache Disorders, 3rd Edition ("ICHD-3") describes PDH as "[p]ersistent headache, daily from its onset, which is clearly remembered. The pain lacks characteristic features, and may be migraine-like or tension-type-like, or have elements of both." Headache Classification Comm. of the Int'l Headache Soc'y, The International Classification of Headache Disorders, 3rd Edition, 38 Cephalagia 1, 55 (2018). According to the ICHD-3, PDH is diagnosed based on the following criteria:

> A. Persistent headache fulfilling criteria B and C
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> B. Distinct and clearly remembered onset, with pain becoming continuous and unremitting within 24 hours
>
> C. Present for >3 months

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6. The court notes the following problematic issues with regard to Dr. Jeret's status as an expert. First, his expert report was accompanied by a list of "Additional Materials Considered," only a small percentage of which he had in fact considered in advance of finalizing his expert report. Next, after Dr. Jeret submitted his expert report and in the week leading up to his deposition, plaintiffs' counsel provided him with more of Ms. Kobylinski's medical records. Shortly after, Dr. Jeret performed an additional literature search for relevant articles, some of which he produced in advance of his deposition.

D. Not better accounted for by another ICHD-3 diagnosis.

Id. Dr. Jeret, in making his diagnosis and providing his opinion, relies on the ICHD-3 definition of PDH.

A case of PDH may also be present with other symptoms including "sleep disturbances, light-headedness, blurred vision, neck stiffness, concentration problems, sensory disturbances such as numbness or tingling, vertigo, [and] lethargy." Nooshin Yamani & Jes Olesen, New Daily Persistent Headache: A Systematic Review on an Enigmatic Disorder, J. Headache & Pain, 2019, at 3 ("Yamani article"). Oftentimes, the cause of PDH is not known. The Yamani article, on which Dr. Jeret relies, stated that in 2016 a study found that 53% of PDH cases do not have a known precipitating factor. Of cases with a known precipitating factor, the most common was infection or flu-like illness, which was noted in 22% of PDH cases. Id.

V

Dr. Jeret's general causation opinion consists of the following reasoning: First, it is undisputed that Zostavax is a live-attenuated virus vaccine, which can cause infections and headaches. The Zostavax warning label confirms that headaches can result. Second, the most commonly known trigger of PDH is "infection and flu-like illness." Id. Dr. Jeret notes that 22% of the cases of PDH are a result of infection. Third, the odds

of contracting PDH from an infection increases in individuals with immunosenescence, that is, individuals whose immune systems have weakened with age, and in individuals with prior trauma. Fourth, Dr. Jeret concludes Zostavax can cause PDH in older people.

Dr. Jeret's conclusion is not reliable. It does not follow that simply because Zostavax can cause an infection and headaches in older people or people that have experienced head trauma, that it can cause PDH. See, e.g., In re Diet Drugs Prods. Liab. Litig., MDL No. 1203, 2000 WL 962545, at *7, *11 (E.D. Pa. June 28, 2000). Dr. Jeret fails to provide a specific link between Zostavax and PDH.

Epidemiological studies are often critical to support an expert's opinion as to whether a vaccine or drug is capable of causing a disease or medical condition. Such studies compare the risk or rate of a disease or condition in a group exposed to a certain vaccine or drug to the risk or rate in a group not exposed. There must be a properly selected control group for the comparison to be scientifically valid. Id. at *6. Here, such a study would involve the comparison of incidences of PDH in a group vaccinated with Zostavax and a properly selected group not vaccinated with Zostavax. No epidemiological study is cited that ties Zostavax to PDH. The lack of such a study, however, is not surprising here as PDH is a rare condition. As

stated in Daubert, "[s]ome propositions, moreover, are too particular, too new, or of too limited interest to be published." 509 U.S. at 593.

Dr. Jeret simply references literature demonstrating that viruses such as Covid-19 or Epstein-Barr can trigger PDH. This literature, however, makes no mention of Zostavax. Infections have various causes, and claiming that any infection from Zostavax could result in PDH is merely a theory based on biological plausibility. Such plausibility is insufficient to establish general causation. See id. at 595-96. Dr. Jeret's opinion, based on this literature, that Zostavax can result in PDH is no more reliable than an opinion that moonlight can cause skin cancer merely because there is a study that sunlight can cause skin cancer. Nor does Dr. Jeret have any relevant clinical experience with which to support his conclusion about how patients contract PDH. As noted above, he has never diagnosed anyone with PDH before Ms. Kobylinski.

Dr. Jeret attempts to connect Zostavax with PDH by highlighting the Zostavax warning label, which states that "headache" and injection site reactions are "the most frequent adverse reactions" of the vaccination. He then leaps to the conclusion that Zostavax can cause PDH. While clinical trials show that headaches are the most reported adverse event after Zostavax, with 1.4% of Zostavax recipients reporting headache

after Zostavax, in comparison to 0.8% of placebo recipients, there is no evidence that clinical trials have ever shown that PDH can result because of Zostavax.

It is undisputed that PDH is a condition distinct from common headaches: a diagnosis of PDH requires continuous and unrelenting pain over the course of months. The headaches experienced by participants in the clinical trial were typically mild, transient headaches, and none was diagnosed with PDH. Merely demonstrating that headaches are a common side effect of Zostavax at best establishes biological plausibility that Zostavax causes PDH. This does not suffice. Daubert, 509 U.S. at 595-96.

Dr Jeret's opinion is merely an ipse dixit analysis, that is his bare say-so. As stated in General Electric Co. v. Joiner, "nothing in either Daubert or the Federal Rules of Evidence requires a district court to admit opinion evidence that is connected to existing data only by the ipse dixit of the expert." 522 U.S. 136, 146 (1997). Dr. Jeret has not offered an opinion employing reliable methods to establish that Zostavax can cause PDH, and for this reason, his general causation opinion fails.

VI

Even if Dr. Jeret had provided a reliable opinion on general causation, his opinion on specific causation misses the

mark. First, he does not reliably opine that Ms. Kobylinski ever suffered from PDH.

Dr. Jeret testified at his deposition that "headache is not a diagnosis that's made on imaging; it's not a diagnosis that's made on blood tests; it's made entirely on history." Proper methodology requires doctors to consider a patient's self-reporting of headache symptoms and diagnose them by reviewing diagnostic criteria set forth in the ICHD-3. A diagnosis of PDH requires a persistent headache with a "[d]istinct and clearly remembered onset", that is continuous and unremitting within 24 hours, and lasts for three or more months. ICHD-3, at 55.

Ms. Kobylinski said that the "onset" event was the episode she experienced on her drive home from Florida in early March 2017. However, there is nothing in the testimony of Ms. Kobylinski or in her medical records that her headaches and other symptoms precipitated a continuous and unremitting headache that lasted for at least three months, as the ICHD-3 diagnostic criteria require. Ms. Kobylinski herself described her symptoms in March 2017 as "headaches, lack of focus and concentration." Her pain, as she reported it, was mild and can be treated with medication. Furthermore, she did not have another flare up of her symptoms until at least two months later, on Memorial Day 2017. She never noted any similar

symptoms thereafter until the few weeks before her visit with Dr. Loftspring in April 2018 when she reported a "current episode" which "started 1 to 4 weeks ago." There is an unexplained gap after Memorial Day 2017 of close to a year. Plaintiffs' attempt at oral argument to fill the void by relying on the Plaintiff Fact Sheet and Ms. Kobylinski's answers to defendants' interrogatories is to no avail. These sources simply note the onset of headache, with little detail as to duration or severity.[7] In any event, the record does not demonstrate that Dr. Jeret ever saw the Plaintiff Fact Sheet or interrogatory answers.

In sum, there is no support in her medical records or her deposition testimony that she has ever experienced a continuous and unrelenting headache of three months or more. At most, the longest headache of which she complained lasted between one and four weeks, leading up to her visit with Dr. Loftspring in April 2018.

7. The Plaintiff Fact Sheet, filed well before her deposition, simply states that Ms. Kobylinski began suffering from "headaches, lost ability to focus" starting in approximately March 2017, and that this was diagnosed on June 11, 2018. Plaintiff's answers to defendants' interrogatories are similarly sparse, and simply state that "plaintiff is permanently damaged" and has been on medication since the summer of 2018. There is no information regarding the duration or persistence of these headaches in either of these sources.

The ICHD-3 definition of PDH also includes as one of the criteria: "not better accounted for by another ICHD-3 diagnosis." In reaching his opinion that Ms. Kobylinski has PDH, Dr. Jeret never accounted for or even referenced her history of migraine headaches. Her medical records establish she had headaches as of October 2016, only three months before she received the Zostavax vaccine. Her records from Washington University in St. Louis stated that in June 2018, Dr. Loftspring "suspect[ed] she has migraine-like headaches," and in a follow-up in September 2019, she was assessed as having "[m]igraine without aura." In June 2020, the Marion Eye Center diagnosed her with migraines as well. Dr. Jeret's silence on whether her symptoms are better accounted for as PDH rather than as migraines further undermines the reliability of his opinion that Ms. Kobylinski has suffered from PDH.

Rule 702(b) of the Federal Rules of Evidence requires that the expert's testimony be "based on sufficient facts or data." Dr. Jeret's opinion does not satisfy this requirement. Whatever it is that has afflicted Ms. Kobylinski since March 2017, Dr. Jeret does not have good grounds for diagnosing Ms. Kobylinski with PDH. See Paoli, 35 F.3d at 756.

Even assuming, however, that Dr. Jeret has reliably diagnosed Ms. Kobylinski with PDH, his opinion is still not admissible. He does not reliably connect her PDH to Zostavax.

He first relies on the short temporal proximity, less than two months, between the date Ms. Kobylinski received a dose of Zostavax and the time when she asserts her symptoms first began.[8] Dr. Jeret agrees that if her symptoms began in the spring of 2018, as some of the evidence suggests, he can see no causal link between her inoculation with Zostavax in March 2017 and her PDH. Second, he factors in that she was 68 years old at the time she was inoculated and thus was experiencing immunosenescence. Third, he opines her 1994 head injury from horseback riding predisposed her to developing PDH, although he concludes that it was Zostavax, and not this injury, that ultimately caused her to develop PDH.

Temporal proximity alone is insufficient to establish causation. An expert's opinion cannot be considered reliable simply based on a post hoc ergo propter hoc analysis. In re Zostavax (Zoster Vaccine Live) Prods. Liab. Litig., 579 F. Supp. 3d 675, 683 (E.D. Pa. 2021) (citing McClain v. Metabolife Int'l, Inc., 401 F.3d 1233, 1243 (11th Cir. 2005); Ohio v. U.S. Dep't of Interior, 880 F.2d 432, 473 (D.C. Cir. 1989)). As explained in Heller v. Shaw Industries, Inc., while temporal proximity can be relied upon in an expert opinion, it cannot be the only

8. The court will assume for present purposes that, despite compelling contrary evidence, Ms. Kobylinski first developed headaches in 2017, not long after she received the Zostavax vaccine, and not in 2018.

factor to support causation. 167 F.3d 146, 154-55 (3d Cir. 1999).

For a medical opinion to be admitted, an expert must perform a differential analysis. A differential diagnosis is the hallmark of internal medicine and is used to reach a diagnosis by ruling in conditions and ruling out alternative explanations for symptoms. Paoli, 35 F.3d at 756. As explained by our Court of Appeals in Kannankeril,

> We have recognized "differential diagnosis" as a technique that involves assessing causation with respect to a particular individual. Differential diagnosis is defined for physicians as "the determination of which of two or more diseases with similar symptoms is the one from which the patient is suffering, by a systematic comparison and contrasting of the clinical findings."

128 F.3d at 807 (citations omitted).

To perform a sufficiently reliable differential diagnosis, an expert must rule out, not all other possible causes, but only obvious alternative causes. Heller, 167 F.3d at 156. In excluding an alternative cause, the expert must provide "good grounds" for doing so. Paoli, 35 F.3d at 743. The type of evidence a physician must consider in conducting a differential diagnosis varies from case to case and frequently includes medical records, peer-reviewed literature and

scientific studies, as well as clinical experience. See, e.g., Kannankeril, 128 F.3d at 807-09; Heller, 167 F.3d at 155-56.

Dr. Jeret does rule out her 1994 injury from horseback riding. Nevertheless, he does not rule out idiopathic, that is, unknown and unexplained causes. When unexplained causes are common, a differential diagnosis is lacking unless those unexplained causes are eliminated. Pritchard v. Dow Argo Scis., 705 F. Supp. 2d 471, 492 (W.D. Pa. 2010), aff'd, 430 F. App'x 102 (3d Cir. 2011); Perry v. Novartis Pharms. Corp., 564 F. Supp. 2d 452, 469-70 (E.D. Pa. 2008). The Yamani article, on which Dr. Jeret relies, states that 53% of PDH cases do not have a known precipitating factor. In the present circumstances, Dr. Jeret's opinion that Zostavax is the known cause of Ms. Kobylinski's PDH is unreliable as he does not exclude idiopathic causes of her PDH. This leaves Dr. Jeret with a conclusion based solely on post hoc ergo propter hoc reasoning.

The insufficient factual support for Ms. Kobylinski's PDH diagnosis, the lack of a reliable differential diagnosis, and the remaining reliance on temporal proximity to establish the causal connection between Zostavax and PDH all render Dr. Jeret's specific causation opinion too unreliable to be admitted into evidence.

VII

Dr. Jeret does not employ reliable methods in reaching his general causation opinion, that is that Zostavax can cause PDH, or his specific causation opinion, that is that Zostavax caused Ms. Kobylinski to develop PDH. Accordingly, the court will grant the motion of Merck to exclude the causation opinions of Joseph Jeret, M.D.