In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. 17-215V
Filed: February 14, 2020
PUBLISHED

JULIA BALASCO, Petitioner, v. SECRETARY OF HEALTH AND HUMAN SERVICES, Respondent.	Special Master Horner Dismissal; Ruling on the Written Record; HPV Vaccine; Gardasil; Postural Orthostatic Tachycardia Syndrome (POTS); Orthostatic Intolerance (OI); Fibromyalgia; Autonomic Disorder or Dysfunction

Andrew Downing, Van Cott & Talamante, PLLC, Phoenix, AZ, for petitioner
Alexis Babcock, U.S. Department of Justice, Washington, DC, for respondent.

DECISION[1]

On February 14, 2017, petitioner Julia Balasco filed a petition under the National Childhood Vaccine Injury Act, 42 U.S.C. § 300aa-10-34 (2012),[2] alleging that an adverse reaction to Gardasil Human papillomavirus (HPV) vaccines administered August 4, 2014, and October 16, 2014, caused injuries including autonomic dysfunction, postural orthostatic tachycardia syndrome (POTS), fibromyalgia, and orthostatic intolerance (OI).[3] (ECF No. 1.) For all the reasons discussed below, I find that petitioner is not entitled to compensation under the terms of the Vaccine Act and therefore dismiss the petition.

Rather than suffering either postural orthostatic tachycardia or orthostatic intolerance, the evidence presented preponderates in favor of a finding that petitioner

[1] Because this decision contains a reasoned explanation for the special master's action in this case, it will be posted on the United States Court of Federal Claims' website in accordance with the E-Government Act of 2002. *See* 44 U.S.C. § 3501 note (2012) (Federal Management and Promotion of Electronic Government Services). **This means the decision will be available to anyone with access to the Internet.** In accordance with Vaccine Rule 18(b), petitioner has 14 days to identify and move to redact medical or other information the disclosure of which would constitute an unwarranted invasion of privacy. If the special master, upon review, agrees that the identified material fits within this definition, it will be redacted from public access.

[2] Within this decision, all citations to § 300aa will be the relevant sections of the Vaccine Act at 42 U.S.C. § 300aa-10-34.

[3] Initially the petition was brought on behalf of petitioner by her parents as she was a minor at that time.

experienced fibromyalgia, for which she has a diagnosis by a treating rheumatologist, potentially accompanied by a migraine disorder, diagnosed by her treating otoneurologist. However, contrary to petitioner's assertion, there is not preponderant evidence that fibromyalgia is an autonomic disorder. Moreover, I did not find preponderant evidence of any HPV-vaccine syndrome that could explain petitioner's alleged post-vaccination symptoms.

I. Applicable Statutory Scheme

Under the National Vaccine Injury Compensation Program, compensation awards are made to individuals who have suffered injuries after receiving vaccines. In general, to gain an award, a petitioner must make a number of factual demonstrations, including showing that an individual received a vaccination covered by the statute; received it in the United States; suffered a serious, long-standing injury; and has received no previous award or settlement on account of the injury. Finally – and the key question in most cases under the Program – the petitioner must also establish a *causal link* between the vaccination and the injury. In some cases, the petitioner may simply demonstrate the occurrence of what has been called a "Table Injury." That is, it may be shown that the vaccine recipient suffered an injury of the type enumerated in the "Vaccine Injury Table," corresponding to the vaccination in question, within an applicable time period following the vaccination also specified in the Table. If so, the Table Injury is presumed to have been caused by the vaccination, and the petitioner is automatically entitled to compensation, unless it is affirmatively shown that the injury was caused by some factor other than the vaccination. § 300aa-13(a)(1)(A); § 300 aa-11(c)(1)(C)(i); § 300aa-14(a); § 300aa-13(a)(1)(B).

In many cases, however, the vaccine recipient may have suffered an injury *not* of the type covered in the Vaccine Injury Table. In such instances, an alternative means exists to demonstrate entitlement to a Program award. That is, the petitioner may gain an award by showing that the recipient's injury was "caused-in-fact" by the vaccination in question. § 300aa-13(a)(1)(B); § 300aa-11(c)(1)(C)(ii). In such a situation, of course, the presumptions available under the Vaccine Injury Table are inoperative. The burden is on the petitioner to introduce evidence demonstrating that the vaccination actually caused the injury in question. *Althen v. Sec'y of Health & Human Servs.*, 418 F.3d 1274, 1278 (Fed. Cir. 2005); *Hines v. Sec'y of Health & Human Servs.*, 940 F.2d 1518, 1525 (Fed. Cir. 1991).

The showing of "causation-in-fact" must satisfy the "preponderance of the evidence" standard, the same standard ordinarily used in tort litigation. § 300aa-13(a)(1)(A); *see also Althen*, 418 F.3d at 1279; *Hines*, 940 F.2d at 1525. Under that standard, the petitioner must show that it is "more probable than not" that the

vaccination was the cause of the injury. *Althen*, 418 F.3d at 1279. The petitioner need not show that the vaccination was the sole cause of the injury or condition, but must demonstrate that the vaccination was at least a "substantial factor" in causing the condition, and was a "but for" cause. *Shyface v. Sec'y of Health & Human Servs.*, 165 F.3d 1344, 1352 (Fed. Cir. 1999). Thus, the petitioner must supply "proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury;" the logical sequence must be supported by "reputable medical or scientific explanation, *i.e*., evidence in the form of scientific studies or expert medical testimony." *Althen*, 418 F.3d at 1278; *Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). A petitioner may not receive a Vaccine Program award based solely on his or her assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. § 300aa-13(a)(1).

In what has become the predominant framing of this burden of proof, the *Althen* court described the "causation-in-fact" standard, as follows:

> Concisely stated, [petitioner's] burden is to show by preponderant evidence that the vaccination brought about her injury by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of proximate temporal relationship between vaccination and injury. If [petitioner] satisfies this burden, she is "entitled to recover unless the [government] shows, also by a preponderance of the evidence, that the injury was in fact caused by factors unrelated to the vaccine."

Althen, 418 F.3d at 1278 (citations omitted). The *Althen* court noted that a petitioner need not necessarily supply evidence from medical literature supporting petitioner's causation contention, so long as the petitioner supplies the medical opinion of an expert. *Id*. at 1279-80. The court also indicated that, in finding causation, a Program fact-finder may rely upon "circumstantial evidence," which the court found to be consistent with the "system created by Congress, in which close calls regarding causation are resolved in favor of injured claimants." *Id*. at 1280.

In this case, petitioner has alleged that the HPV vaccine, Gardasil, caused her to suffer injuries of autonomic nervous system deregulation, including POTS, orthostatic intolerance, and fibromyalgia. Since these conditions are not listed on the Vaccine Injury Table, petitioner must satisfy the above-described *Althen* test for establishing causation-in-fact.

II. Procedural History

Petitioner filed medical records between February 21, 2017, and June 23, 2017. (ECF Nos. 7-9, 11-13.) On July 5, 2017, a status conference was held before Special Master Millman, and petitioner was ordered to file an expert report. (ECF No. 16.) In support of her claim, petitioner filed expert reports from Dr. Yehuda Shoenfeld on October 23, 2017, and from Dr. Mitchell Miglis on November 29, 2017. (ECF Nos. 22-23.)

On May 18, 2018, respondent filed a Rule 4(c) report in accordance with Vaccine Rule 4(c) recommending that petitioner's entitlement to compensation under the Vaccine Act be denied. (ECF No. 35.) On that same day, respondent filed expert reports from Dr. Lindsay Whitton and Dr. William Talman in support of his position. (ECF No. 36.)

In response to respondent's expert reports, petitioner filed a supplemental expert report from Dr. Miglis on June 25, 2018, along with the medical literature referenced in the report on July 3, 2018. (ECF Nos. 37-39.) On July 5, 2018, petitioner also filed a rebuttal expert report from Dr. Shoenfeld. (ECF No. 40.) On July 17, 2018, respondent filed a status report indicating that he wished to file a supplemental expert report, which he filed on August 17, 2018. (ECF Nos. 41-42.)

On September 13, 2018, petitioner indicated in a status report that she wished to proceed by moving for judgment on the record before Special Master Millman. (ECF No. 43.) On November 5, 2018, petitioner filed a motion for decision on the record. (ECF No. 50.) Subsequently, respondent filed a response on December 20, 2018, again requesting that petitioner's claim be denied. (ECF No. 54.) However, Special Master Millman retired prior to ruling on petitioner's motion and this case was assigned to me on July 18, 2019, with a pending motion for a ruling on the record. (ECF No. 61.)

On August 5, 2019, the parties appeared before me for a status conference. During the conference, I gave petitioner the opportunity to confirm whether petitioner still wished to resolve the case based on the written record in light of Special Master Millman's retirement. Petitioner's counsel indicated that the issues in the case had been adequately explained in the parties' motion fillings, and that petitioner still wished to proceed with a ruling based on the record. (ECF No. 63.) However, subsequent to filing her motion, petitioner had filed multiple articles to support petitioner's theory of causation (Exs. 89-91) and respondent requested 30 days to file a supplemental expert report to discuss the late-filed articles. (ECF No. 63.) I allowed respondent the opportunity to file a supplemental expert report and also ordered petitioner to file certain outstanding medical records. (*Id.*)

Thereafter, petitioner filed the requested medical records. (ECF Nos. 64-66.) On August 28, 2019, respondent filed a supplemental expert report from Dr. Lindsay Whitton. (ECF No. 67.) However, on September 6, 2019, respondent filed a Notice of Additional Authority, attaching a position statement from the American Autonomic Society to support his position. (ECF No. 69.) In response, on September 23, 2019, petitioner filed additional medical literature and a status report indicating her concerns with respondent's article from the American Autonomic Society. (ECF Nos. 70-71.)

Subsequently, on September 23, 2019, I ordered the parties to again confirm that this case is ripe for a ruling on the written record. They did so on October 7, 2019. (ECF No. 72.) In total, petitioner filed 95 numbered exhibits, including 57 separate studies and medical articles.[4] Although I have not cited all of these exhibits in the discussion below, I have reviewed the entire record of this case. Accordingly, the case is now ripe for a decision.

III. Factual History

a. As Reflected in the Medical Records

Petitioner was born on October 14, 2000. At the time of the first administration of the HPV vaccine that forms the basis of this petition, she was 13 years old. (Ex. 2, p. 2.) She was fourteen at the time of the second administration of the vaccine. (*Id.*)

Petitioner filed pre-vaccination records dating back to 2010 beginning with treatment from her primary care physician, Dr. Budio Thomas. (Ex. 3.) These earlier records are mostly unremarkable, including visits for strep throat, pharyngitis, and a dislocated finger. On August 22, 2011, petitioner was found to be physically fit to participate in Pop Warner Cheer. (*Id.* at 21.) Petitioner visited Dr. Thomas on November 14, 2011 "complaining of frontal headaches worse with head down three days." (*Id*. at 7.)

On August 20, 2012, petitioner saw Dr. Thomas for her next physical to participate in Pop Warner Cheer. (Ex. 3, p. 18.) At this visit, she received her Tdap vaccine. (*Id.* at 3.) Petitioner again saw Dr. Thomas with complaints of a sore throat and a positive rapid strep test on November 15, 2012. (Ex. 15, p. 1.) On March 5, 2013, petitioner complained of sore throat and congestion with a negative rapid strep test. (*Id*.) Petitioner saw Dr. Thomas complaining of left hip pain on October 15, 2013 after she had been fallen on by another cheerleader. (*Id*.) On January 9, 2014, petitioner was given the Menactra vaccine. (*Id*.)

[4] Exhibits 28, 42, 45-47, 53, and 65, were duplicate filings of previously marked exhibits.

On August 4, 2014, petitioner received her first dose of the Gardasil vaccine. (Ex. 2, p. 2.) She received her second dose on October 16, 2014. (Ex. 15, p. 2.) On November 24, 2014, Petitioner saw Dr. Thomas complaining that her ear was blocked and that she had been experiencing "hearing loss times one year." (*Id*.) Dr. Thomas noted mild lower frequency loss and possible eustachian tube dysfunction.[5] (*Id*.)

On December 16, 2014, petitioner presented to otolaryngologist, Mark Andreozzi, D.O. for an evaluation of her hearing, where he noted a history of speech delay. (Ex. 8, p. 32.) He further noted that she was experiencing fluctuating hearing loss, which began approximately a year and a half prior, associated with dizziness, ringing, and blockage in her ear. (*Id*.) His impression was a diagnosis of Meniere's disease,[6] and he wrote a note for petitioner's school indicating that it would be helpful for petitioner if she could be seated in front of the classroom due to her fluctuating hearing loss. (*Id.* at 31-32.)

The next month, on January 30, 2015, petitioner was referred to otoneurologist, Melissa Ramocki, M.D. for an otoneurologic consultation regarding dizziness and possible bilateral Meniere's disease. (Ex. 4 p. 24; Ex. 83, p. 26.) Dr. Ramocki noted a history of delayed speech and a question of congenital versus early onset hearing loss. (*Id*.) According to Dr. Ramocki's notes, petitioner began complaining about the deterioration of hearing approximately three years prior, and began complaining of dizziness in August or September 2014. (*Id*.) The dizziness was described as lightheadedness with postural change, and a development of throbbing headaches with rapid body movements. (*Id*.) During the dizzy spells, it was reported that petitioner also could become nauseated and experience photophobia, phonophobia, and vertigo which lasted seconds at a time. (*Id*.) She experienced these symptoms approximately twenty days each month, which caused her to miss school on occasion. *(Id*.)

At that visit, Dr. Ramocki ruled out Meniere's disease, reporting that "[s]he does not meet diagnostic criteria for Meniere's disease, and this diagnosis is exceptionally rare in her age group." (Ex. 4, p. 25.) Instead, Dr. Ramocki was concerned for possible enlarged vestibular aqueduct syndrome[7] (EVA) or some other form of early onset

---

[5] The eustachian tube is also known as the auditory tube. (*Dorland's Illustrated Medical Dictionary*, p. 1976 (32nd ed. 2012).) Eustachian tube dysfunction occurs when there is a disturbance, impairment, or abnormality with the organ. (*Id*. at 577.)

[6] Meniere disease is characterized by "hearing loss, tinnitus, and vertigo resulting from nonsuperative disease of the labyrinth with edema." (*Dorland's*, p. 539.)

[7] The vestibular aqueduct is a "bony canal running from the vestibule and opening on the posterior surface of the petrous portion of the temporal bone, giving passage to the endolymphatic duct and a small vein." Enlarged vestibular aqueduct syndrome is "a form of inner ear dysplasia associated with a delayed

hearing loss. (*Id*.) Dr. Ramocki hypothesized that petitioner's vestibular symptoms could have been related to EVA, a manifestation of vestibular migraine, or that it was possible that the migraines were exacerbating co-existing inner ear disease. (*Id*.) Dr. Ramocki also noted that petitioner's postural dizziness could have been related to low sodium intake, and suggested dietary changes. (*Id*.) Dr. Ramocki subsequently reviewed petitioner's audiogram and added an addendum to the medical record on February 20, 2015, noting some mild sensorineural hearing loss[8] on the left at 500HZ although 250-1000HZ is relatively worse compared with the higher frequencies." (*Id*. at 26.)

On February 13, 2015, petitioner returned to Dr. Ramocki regarding her migraines, vertigo, postural dizziness, and mild SNHL. (Ex. 4, p 23; Ex. 83, p. 25.) Petitioner reported that her symptoms had improved with the initiation of the migraine elimination diet, but worsened with her menstrual period. (*Id*.) Dr. Ramocki believed that a vestibular migraine disorder explained her symptoms well. (*Id*.) On that same day, petitioner underwent a visual vestibular interaction test which came back normal. (Ex. 4, p. 4.)

Petitioner returned to Dr. Thomas with her mother on February 19, 2015 to discuss any possible side effects of the HPV vaccine. Her mother decided to decline the third dose of Gardasil. (Ex. 15, p. 2.)

On May 15, 2015, petitioner visited Dr. Ramocki to follow up on her vestibular migraines. (Ex. 4, p 21; Ex. 83, p. 23.) She reported that her headaches had decreased in frequency, but the vertigo spells continued to persist. (*Id*.) Dr. Ramocki noted that Dr. Andreozzi gave petitioner a prescription for Triptan,[9] which petitioner had not yet taken, and that petitioner was taking Meclizine,[10] which helped with her vertigo spells. (*Id*.) At this visit, Dr. Ramocki prescribed 10mg of Amitriptyline[11] for treatment of petitioner's migraines, to increase to 50mg in one month if well tolerated. (*Id*.)

On June 9, 2015, Dr. Thomas noted that petitioner had been complaining of headaches for approximately eight or nine months and had started on Amitriptyline.

---

onset of sensory neural hearing loss, which may be fluctuating and progressive. An enlarged vestibular aqueduct can be demonstrated on high-resolution CT scan. (*Stedman's Medical Dictionary*, 58410.)

[8] Noted in the medical record by the abbreviation SNHL.

[9] Triptans are a group of serotonin receptor agonists used in treatment of migraines. (*Dorland's*, p. 1969.)

[10] An antihistamine used in the management of nausea, vomiting, and dizziness associated with motion sickness and of vertigo associated with disease affecting the vestibular system. (*Dorland's*, p. 1117.)

[11] A tricyclic antidepressant of the dibenzocycloheptadiene group, also having sedative effects; it is also used in the treatment of enuresis, chronic pain, peptic ulcer, and bulimia nervosa. (*Dorland's*, p. 63.)

(Ex. 15, p. 2.) On June 11, 2015, petitioner underwent a standard digital electroencephalogram (EEG),[12] conducted by Uzma Sharif, MD at Rhode Island Hospital. Dr. Sharif noted a history of concussion, hearing loss, vestibular migraine, and vertigo. (Ex. 84, p. 32-33.) The EEG returned normal with no events concerning for seizure activity. (*Id*.)

The next month, on July 13, 2015, petitioner returned to Dr. Ramocki's office for a routine checkup. (Ex. 4, p. 19; Ex. 83, p. 21.) Petitioner's amitriptyline was discontinued, as her symptoms were worsening, and she reported having spells where she "space[d] out." (*Id*.) Her headaches seemed to have resolved with the Topiramate, but the motion induced dizziness persisted, and Dr. Ramocki ordered magnetic resonance imaging (MRI),[13] with attention to the internal auditory canals. (Ex. 4, pp. 1, 19.) The MRI was unremarkable, with everything appearing normal. (*Id*.) At this visit, Dr. Ramocki increased petitioner's Topiramate to 50mg and discussed the use of Triptan for headache and Meclizine for nausea. (*Id*. at 19.)

Petitioner returned to Dr. Ramocki's office on September 25, 2015 regarding her vestibular migraines. (Ex. 4, p. 17; Ex. 83, p. 19.) She reported an improvement in the "spaciness" and dizziness, but she continued to experience the illusion that the ground was moving with running. (*Id*.) Dr. Ramocki increased petitioner's Topiramate dosage and wrote a note for accommodation at school. (*Id*.) Three days later, on September 28, 2015, petitioner returned for a follow up visit with Dr. Andreozzi. Although Dr. Andreozzi agreed with Dr. Ramocki's assessment of vestibular migraines, he also maintained his earlier diagnosis of Meniere's disease, and wrote a note limiting Ms. Balasco's participation in physical activity at school. (Ex. 8, pp. 22, 26.)

Petitioner visited Meredith Leone, PA-C, at ENT and Allergy, Inc., on February 24, 2016, presenting with a history/chief complaint of vestibular migraines and likelihood of Meniere's with ancillary symptoms of joint pain, sleep disturbance, and fatigue. (Ex. 8, p. 20.) Petitioner reported that her sleep disturbances were not always due to headaches, and sometimes were due to a "restless sensation and fuzziness in her head." (*Id*.) At the visit, petitioner took a self-guided dizziness test in which she reported lightheadedness, a swimming sensation in the head, tendency to fall to the right, sensation of spinning, loss of balance, nausea, pressure, and constant dizziness which first occurred over a year prior. (*Id*. at 18.) Ms. Leone discussed seeking a

[12] The recording of the potentials on the skull generated by currents emanating spontaneously from nerve cells in the brain. (*Dorland's*, p. 600.)

[13] A method of visualizing the soft tissues of the body by applying an external magnetic field that makes it possible to distinguish between hydrogen atoms in different environments. (*Dorland's* p. 916.)

second opinion from a neurologist, undergoing a sleep study, and a visit with a rheumatologist. (*Id*. at 20.)

Petitioner saw her primary physician, Dr. Thomas, on March 3, 2016 and received a diagnosis of costochondritis.[14] (Ex. 15, p. 2.) Subsequently, on March 21, 2016, petitioner had a follow up appointment with Dr. Ramocki regarding her migraine disorder, and was referred to pediatric rheumatology. (Ex. 4, p. 15; Ex. 83, p. 17.) Petitioner's mother reported that petitioner was experiencing daily headaches and increasing fatigue and muscle and joint pain. (*Id*.) On April 8, 2016, petitioner underwent a full polysomnography[15] to diagnose her sleep disturbances. No apneas or hypopneas were noted. (Ex. 7, p. 6.)

Petitioner established care at Partners in Obstetrics & Gynecology on May 5, 2016 to discuss her "painful, heavy, and slightly irregular menses," along with a painful breast lump. (Ex. 5, pp. 2-3.) She saw Megan McMahon, M.D., who noted that petitioner had only two of the three HPV vaccines because she believed she had an adverse reaction. (*Id*. at 2.) Four days later, on May 9, 2016, petitioner had a pelvic ultrasound for her history of menorrhagia and irregular menses. There were no significant findings, and her uterus appeared normal. (*Id*. at 7.)

On May 17, 2016, petitioner saw Ali Yalcindag, MD in the clinic of pediatric rheumatology at Rhode Island Hospital after being referred for joint pain, fatigue, and chest pain. (Ex. 11, pp. 1-4; Ex. 84 pp. 35-38.) Dr. Yalcindag noted a history of headaches and vertigo, and diagnoses of Meniere's disease and migraines. While she did not provide a potential cause for the symptoms, she did note "mom thinks her problems started with her first HPV vaccine and got worse after the second." (Ex. 84, p. 35.) Dr. Yalcindag found that petitioner "qualifies for a diagnosis of fibromyalgia,"[16] and recommended aerobic activity. (*Id*. at 37.) On May 23, 2016, petitioner made a visit to the emergency room for her chest pain with numbness and tingling radiating down her left arm. (*Id*. at 3.) The attending physician, Dr. Dietrich noted: "?menigers [sic] disease. Has been worked up for migraines, seizures and fibromyalgia." (*Id*. at 4.) She was discharged the same day to follow up with her neurologist, Dr. Ramocki. (*Id*. at 8.)

Over the next month, petitioner continued to follow up with Dr. Ramocki regarding her migraines. On June 1, 2016, Dr. Ramocki referred her to therapy, noting

---

[14] Costochondritis is the "inflammation of the cartilaginous junction between a rib or ribs and the sternum." (*Dorland's*, p. 423.)

[15] A polysomnography is the polygraphic recording during sleep of multiple physiologic variables, both directly and indirectly related to the state and stages of sleep, to assess possible biological causes of sleep disorders. (*Dorland's*, p. 1494.)

[16] Pain and stiffness in the muscles and joints that either is diffuse or has multiple trigger points (*Dorland's*, p. 703.)

the diagnosis of fibromyalgia, her minimal endurance for activity, and the need for coping skills related to her chronic health concerns. (Ex. 4, p. 13; Ex. 83, p. 15.) Dr. Ramocki noted that petitioner had been missing a lot of school due to headaches and fatigue, and on the days she did go to school, she spent a lot of days sleeping in the nurse's office. (Ex. 4, p. 13.)

Petitioner continued to experience sleep disturbances and on June 13, 2016, she had her initial evaluation at the Pediatric Sleep Disorders Clinic with physician Richard Millman, M.D. (Ex. 7, p. 1.) Dr. Millman detailed a lengthy history including "sleep problems, characterized by significant fatigue and daytime sleepiness, difficulty with sleep onset, restlessness, anxiety, depression." (*Id*.) He continued, noting that petitioner's onset of sleep problems occurred the year prior, "Pt had HPV vaccine and got flu like symptoms. Started that day with migraine, dizziness, ear problems. After second dose in November, fatigue kicked in, muscle aches, joint aches, and menstrual problems… [m]ost recent diagnosis is vestibular migraines and fibromyalgia." (*Id*.) Dr. Millman opined that petitioner's symptoms were likely the result of a culmination of multiple factors including her fibromyalgia, vestibular migraines, potential underlying medical causes, and poor sleep hygiene. (*Id*. at 3.)

On August 30, 2016, petitioner saw Dr. Yalcindag in the pediatric rheumatology clinic for follow up. (Ex. 11, pp. 5-8; Ex. 84, pp. 43-46.) Petitioner reported that she had not been exercising because she would experience dizziness with exercise. (Ex. 84, p. 43.) She also reported continuing fatigue and body pain. (*Id*.) Dr. Yalcindag noted that a cardiac evaluation, including a tilt table test would be appropriate to assess petitioner's exercise tolerance, and petitioner's mother was to pursue counseling for petitioner's anxiety and depression symptoms. (*Id*. at 45.)

Dr. Thomas referred petitioner to a cardiologist, Dr. Ibrahim Elgabry, MD. Petitioner saw him on September 14, 2016. (Ex. 6, p. 5.) At this visit, petitioner reported that she experienced dizziness upon arising from a sitting position, "however once she is still standing and engaging in activities, she still continues to be dizzy." (*Id*.) She also noted that while she had not had an actual syncopal event, she had experienced symptoms of presyncope, and that she experienced chest discomfort while walking up stairs. (*Id*.) Dr. Elgabry noted that the symptoms began after 2014 at her "first HBV [sic] injection." (*Id*.) The cardiologist scheduled petitioner for a tilt table test, after noting that petitioner had been experiencing daily dizziness. (*Id*. at 8.) She also returned to Dr. Ramocki on September 21, 2016. (Ex. 83, p. 8.)

Before the tilt table test, on September 29, 2016, petitioner returned for a follow up with Dr. McMahon for an ultrasound of the left breast. The impression was a 2.5cm oval mass "most likely a fibroadenoma" suspicious for malignancy, and a surgical consult was recommended. (Ex. 5, p. 5.)

On October 5, 2016, the tilt table test was performed, as ordered by Dr. Elgabry. (Ex. 10, pp. 2-3.) The tilt table test produced a vasovagal response of nausea, vomiting, and dizziness after twenty-three minutes. (*Id*. at 8.) Two days after the tilt table test, petitioner had a follow up appointment with Dr. Elgabry to discuss the results of the test. He noted that the test indicated vasovagal syncope,[17] and recommended that she continue with adequate hydration, thigh high stockings, and increased salt intake. (Ex. 6, pp. 1-4.)

Petitioner continued to experience chest discomfort, fibromyalgia pain, headaches, and nausea. (Ex. 7, p. 3; Ex. 4 p. 8.) On November 2, 2016, petitioner tested positive "for the Anti a-1-adrenergic Antibody; the Anti B-2 adrenergic Antibodies, and the anti-Muscarinic Cholinergic Receptor 4-Antibodies. The test found that petitioner is 'at risk' for the anti-Muscarinic Cholinergic Recepter 3-Antibodies."[18] (Ex. 12, p. 1.) The next day, Dr. Andreozzi wrote a note to petitioner's school to allow petitioner to enroll in online classes, noting that petitioner has "chronic conditions that cause her to have symptoms that include lightheadedness, fatigue, and headaches… because of the nature of this problem and the unpredictability of the symptoms, there are days where she cannot get up early or has a difficult time functioning throughout the day." (Ex. 8, pp. 1-2.) His impression was "Eustachian tube dysfunction w/ TMJ,[19] postural orthostatic tachycardic syndrome (POTS),[20] vestibular migraine, allergic rhinitis, fibromyalgia." *(Id*. at 3.) Petitioner continued to seek treatment for her fibromyalgia and "possible POTS syndrome" throughout the end of 2016 and the beginning of 2017. (Ex. 13, p. 1.)

On November 21, 2016, petitioner reported to Dr. Ramocki that she had a normal echocardiogram, but an abnormal tilt table test and conservative measures for orthostatic intolerance were recommended. (Ex. 83, p. 6.) Dr. Ramocki indicated she would follow up with Dr. Elegabry. (*Id*.) She felt the antibody panel did not have clinical

---

[17] Vasovagal syncope is a "transient vascular and neurogenic reaction marked by pallor, nausea, sweating, bradycardia, and rapid fall in arterial blood pressure which, when below a critical level, results in loss of consciousness and characteristic electroencephalographic [electric currents developed in the brain] changes." (*Dorland's*, pp. 1818, 600.)

[18] These results were generated by a commercial lab and the tests were not ordered by petitioner's physicians. Respondent has challenged the clinical significance of the results. This is addressed in Section IV(b), below.

[19] Temporomandibular joint dysfunction

[20] Dr. Shoenfeld defined POTS as "a disease with heterogenous presentation affecting the autonomic nervous system. POTS is defined as the presence of chronic symptoms of orthostatic intolerance (at least 6 months) accompanied by an increased HR ≥ 30bpm within 10 minutes of assuming an upright posture and in the absence of orthostatic hypotension." (Ex. 18, p.11.) Dr. Talman indicated that "the cardinal features of POTS are symptoms produced by change in posture, resolution of symptoms upon assuming a recumbent position." (Ex. C, p. 4.)

relevance. (*Id*.) On November 29, 2016, petitioner returned to see Dr. Yalcindag for a follow up appointment. (Ex. 84, p. 47.) Dr. Yalcindag remarked that petitioner had her tilt table testing done, and that petitioner's mother reported evidence for POTS. (*Id*.)

On February 7, 2017, petitioner returned to her gynecologist for a follow up on the fibroadenoma in her left breast. (Ex. 14, p. 5.) Petitioner reported increasing discomfort in the area and expressed her desire to have the mass removed. After discussing the risks and benefits of excision, Dr. Bansil began scheduling the procedure. Dr. Bansil noted that petitioner was being seen by a cardiologist for her vasovagal syncope, and that the cardiology notes would be sent to the office. (*Id*.) On February 23, 2017, petitioner underwent surgery to have her left breast mass removed. (*Id*. at 1.) Just five days later, on February 28, 2019, petitioner saw Dr. Yalcindag for another follow up. She reported having body aches and fatigue along with intermittent diarrhea and hives. (Ex. 84, p. 51; Ex. 86, pp. 1-5.) At this visit, Dr. Yalcindag reported that petitioner carried diagnoses of POTS and fibromyalgia. (*Id*.) Petitioner returned for a follow up for her fibroadenoma excision on March 3, 2017. (Ex. 14, p. 7.) Dr. Bansil assured petitioner and her mother that the mass was completely benign and would require no follow up. (*Id*.)

Petitioner had another follow up appointment with Dr. Yalcindag on May 30, 2017, where she reported continued body pain and dizziness with exercise. (Ex. 84, p. 56; Ex. 86, pp. 6-8.) Dr. Yalcindag asked her to begin graded aerobic exercise and noted that petitioner would see "cardiology for tips related to her POTS." (Ex. 84, p. 58.)

On June 12, 2017, petitioner reported to Dr. Ramocki that she was experiencing headaches three times a week with nausea, but that orthostatic symptoms have been infrequent. (Ex. 83, p. 3.) Dr. Ramocki noted that petitioner did not think topiramate had helped. Tapering off topiramate was discussed, but Dr. Ramocki did not want to switch to any other medication that may lower blood pressure. (*Id.*)

Petitioner returned to Dr. Yalcindag on September 22, 2017, for a follow up appointment with a complaint of few episodes of chest pain. (Ex. 86, pp. 9-12.) And on September 26, 2017, petitioner saw both Dr. Ramocki and a new cardiologist, Dr. Kristin Lombardi. (Ex. 83, p. 1.) She saw Dr. Ramocki regarding migraine disorder and orthostatic hypotension. (*Id.*) Dr. Ramocki noted that petitioner continued to have daily headaches, but that the migraine attacks had been infrequent. (*Id*.) Dr. Ramocki also noted that petitioner was completing an online curriculum at school and that the decreased stress allowed her to be more active, although she stopped participating in cheer and other activities. (*Id*.) Dr. Ramocki received petitioner's antibody panel, but rejected the validity of the results, noting that "the relevance of these results and treatments are the source of ongoing research." (Ex. 83, p. 6.)

Petitioner's visit with Dr. Lombardi on that same day was for an initial evaluation of chest pain and a follow up regarding her alleged POTS. (Ex. 93, p. 1.) Petitioner reported that while she previously experienced constant dizziness, she had begun experiencing dizziness with change in position going up many stairs, or standing for extended periods of time. (*Id*.) She reported experiencing chest pain once a day which sometimes would radiate up to her left shoulder area which lasted for various times, from a few minutes up to an hour. (*Id*.) Dr. Lombardi noted that petitioner was not orthostatic on the day of the appointment, which she found to be encouraging. (*Id*.) Dr. Lombardi further explained the diagnosis of "typical vagally-meditated presyncope/postural orthostasis, which are usually characterized by a typical warning such as lightheadedness, visual changes, or nausea, and often occur in the context of dehydration, rapid position change, prolonged standing, hunger, or pain or emotional stress." (*Id*. at 3.) Dr. Lombardi suggested behavior modifications to treat these symptoms including increased hydration, salt, caffeine avoidance, rest, and the avoidance of prolonged standing or rapid position change. (*Id*.)

On September 27, 2017, petitioner began her physical therapy at Healy Physical Therapy & Sports Medicine Inc. (Ex. 88, p. 20.) She reported that she began with "headaches, dizziness, nausea, ear pressure, leg pain, hips pain, knee pain, ankle pain, shoulder pain, chest and rib pain, neck, mid back and lower back pain" which started in 2014 and became progressively worse since then. (*Id*. at 50.) Dr. Ramocki had referred petitioner to physical therapy with the diagnoses of obesity, joint pain, orthostatic dizziness and chronic headaches, and at the appointment, petitioner's mother reported that petitioner's head and body aches, joint pain, and dizziness occurred shortly after the administration of her HPV vaccine. (*Id*.) The physical therapist, Michael Healy, recommended a physical therapy program for "manual therapy to address her soft tissue and structural biomechanical issues that [were] limiting her physical and functional abilities while slowly adding the Fit Kid program in with core and scapular exercises." (*Id*.) Mr. Healy also suggested a nutritional program to supplement the therapy. (*Id*.)

On October 2, 2017, petitioner sought treatment for lower abdominal pain and diarrhea at Rhode Island Hospital and was seen by Carolina Cerezo, MD. (Ex. 67, pp. 1-2.) Petitioner reported that she had been experiencing "intermittent periumbilical and lower abdominal pain associated with urgency to go to the BR" for nine months, with more frequent symptoms for the previous three months. (*Id*. at 6.) Petitioner also reported feeling tired and having frequent muscle and joint pains. Dr. Cerezo noted that the symptoms may have been triggered by stress. (*Id*.) She further noted that petitioner was at risk for GERD and chronic constipation because of her obesity (BMI 33) and had a family history of IBD." (*Id*. at 8.) The next day, petitioner had an ultrasound of her right breast to examine a palpable right breast mass. (Ex. 66, p. 7.)

The impression was a "mass in the right breast at 7 o'clock, most likely representing a fibroadenoma." (*Id*.) On November 3, 2017, she had another ultrasound done on the right breast which found two solid masses, which were listed as "probably benign." (*Id*. at 9.) Petitioner planned a surgical excision for the two masses in her right breast. (*Id*.)

On December 6, 2017, Dr. Bansil wrote a letter stating that petitioner would be unable to return to physical therapy until December 18, 2017 due to her diagnosis and treatment regimen. (Ex. 88, p. 33.) Petitioner attended Healy Physical Therapy for a total of nineteen sessions, the last of which was on December 20, 2017. (Ex. 88, p. 29.) She was scheduled for four later appointments but did not attend, and was discharged secondary to non-compliance on January 22, 2018. (*Id*.)

b. As Reflected in the Affidavit

At the time of filing, Ms. Balasco's mother was the petitioner, as petitioner had not yet reached majority age. Thus, the representations made in the affidavit are those from petitioner's mother.

Petitioner's mother asserted that prior to receiving her Gardasil vaccine, petitioner was a happy and healthy child who enjoyed cheerleading. (Ex. 1, p. 1.) She acknowledged some typical childhood illnesses, including colds and strep throat, along with a question about petitioner's hearing because of her delay in speech, but she maintained that testing was performed, and no issue was identified prior to vaccination. (*Id*.) The affidavit indicated that petitioner received her first Gardasil vaccine on August 4, 2014 during a cheerleading physical and immediately after, petitioner experienced "flu-like symptoms including achiness, headache, nausea, and low-grade fever," which lasted between 24 and 48 hours. (*Id*.) Petitioner's mother reported speaking to a nurse regarding petitioner's reaction, who noted that she had not heard of any major reactions to Gardasil "with the exception of some kids fainting when they received the vaccine." (*Id*.)

As petitioner's symptoms progressed over a few months, she began to complain of ear pressure, tinnitus, and headaches, which petitioner's mother attributed to possible allergies. (*Id*. at 2.) The affidavit indicates that these symptoms were not typical for petitioner, and the ear pain and tinnitus continued to be a problem for her by late October and early November of 2014. (*Id*.) On October 16, 2014, petitioner received a second dose of Gardasil and again experienced flu-like symptoms for approximately 24-48 hours. (*Id*.) According to the affidavit, petitioner could not tolerate Prednisone,[21] and was referred to an ENT. Petitioner continued to experience an increase of symptoms including daily headaches, and regular complaints regarding ear issues, body aches, muscle weakness, fatigue, and dizziness. (*Id*.) Petitioner's mother noted that on

[21] A synthetic glucorticoid derived from cortisone, administered orally as an anti-inflammatory and immunosuppressant in a wide variety of disorders. (*Dorland's*, p. 1509.)

December 16, 2014, petitioner was diagnosed with Meniere's Disease by Dr. Andreozzi and began "spiraling downward," missing many days of school. (*Id*.)

Petitioner's mother reported that in January of 2015 she called Dr. Andreozzi because petitioner continued to have bad dizzy spells which were accompanied by ear pressure and tinnitus. (*Id*.) She hoped to gain more helpful information to decrease petitioner's dizzy spells when she was referred to Dr. Ramocki, a vestibular and balance neurologist. (Ex. 1, p. 3.) Dr. Ramocki assured petitioner that she did not have Meniere's disease, and instead diagnosed petitioner with vestibular migraines, and suggested diet changes and for petitioner to track triggers. (*Id*.) Subsequently, on February 13, 2015, vestibular function tests were performed. (*Id*.) The affidavit reflected that petitioner's diet was changed to no avail. (*Id*.)

Petitioner's third dose of Gardasil was scheduled around the same time, and petitioner's mother reported that this appointment reminder caused her to believe that petitioner's symptoms were caused by the vaccine. (*Id*.) She created a timeline (discussed below) of all the symptoms petitioner had experienced, including uptick in symptoms that arose with the administration of the second vaccine. (Id.) Petitioner's mother declined the third dose, due to her hypothesis that the vaccine was causing petitioner's recent symptoms. (*Id*.) The doctor noted that while the timeline was "suspicious," he would not be able to say for certain whether the vaccine was the cause of petitioner's symptoms. (*Id*.) However, petitioner's mother reports that the doctor presented a vaccine pamphlet which listed many of petitioner's symptoms. (*Id*.) The affidavit describes how petitioner's mother would consistently mention the "vaccine connection" she made at petitioner's follow-up appointments, and the doctors told her that "she could be that one-in-a-million but that there was no proof." (*Id*.)

According to the affidavit, petitioner was on Amitriptyline for a short time before she began to have moments where she "would have a blank look and then just as quickly shake her head and say, 'wait what?' quite often." (*Id*.) Petitioner's mother called the doctor out of concern that petitioner's moments constituted seizure activity, but an EEG was done with normal results. (*Id.)* Due to these concerns, petitioner was taken off amitriptyline and began taking Topiramate. Her mother reports that she began her freshman year of high school in fall of 2015 and was on the cheer squad for school but missed many events and school days. While petitioner tried to keep up with the cheer team and managed to compete in Nationals, petitioner's mother reports that she was exhausted "far beyond what is normal for a teenager." (*Id*.) According to the affidavit, petitioner spent a day at Nationals asleep in the hotel room, and her symptoms seemed to be worsening. (*Id*.) At this time, petitioner's Topiramate dosage was decreased because her cognitive skills seemed to be impaired. (*Id*.)

In the spring of 2016, petitioner was enrolled in two online courses to alleviate some stress. (Ex. 1, p. 4.) She received a referral for a sleep study and made an appointment with a gynecologist due to issues with her menstrual cycle. (*Id*.) Petitioner returned to the neurologist as she was missing more school and averaging two days in class each week. (*Id*.) The neurologist referred petitioner to a rheumatologist, who diagnosed her with fibromyalgia. (*Id*.) Petitioner's mother recounts having petitioner take walks and do low resistance workouts in a blow-up pool during the summer of 2016. (*Id*.) However, petitioner's symptoms continued to worsen, and she spent much of the summer too ill to spend time with her friends. (*Id*.) Petitioner's mother concluded that petitioner's life has been altered in a dramatic way, leaving her unable to do many "normal teenage activities." (*Id*.)

c. Petitioner's Mother's Handwritten Timeline

On May 5, 2016, petitioner's mother created a handwritten timeline. (ECF No. 64; Ex. 92.) The timeline begins with July 2014, and described petitioner as being fine, with a normal health history. (Ex. 92, p. 1.) The next entry on the timeline was for August 4, 2014, when Ms. Balasco received her first HPV vaccine. (*Id*.) Petitioner's mother reported that after the vaccine administration, petitioner experienced flu-like symptoms, characterized as "achey [sic], feverish, headache." (*Id*.) While these symptoms lasted approximately 48 hours, the timeline reported that within a few weeks, petitioner's complaints of headaches, ear pain, and ear pressure became more frequent. (*Id*.) By mid-October, the timeline explained, all the symptoms appeared more frequently, and petitioner also began to experience dizziness. Petitioner's mother attributed all of these symptoms to seasonal allergies. (*Id*.)

The timeline asserted that in early November of that same year, petitioner began to experience ringing in her ears and continuous headaches, and was referred to an ENT. (*Id*.) After her December 14, 2014 appointment at which she received her second dose of the Gardasil vaccine, the timeline reports that petitioner again experienced immediate flu like symptoms, and in the following weeks experienced an uptick of additional symptoms including ear issues, hearing issues, dizzy spells, daily headaches, and increased tiredness. (Ex. 92, p. 2.) The timeline further explained that after petitioner was diagnosed with Meniere's disease in December 2014, she was put on a low to no salt diet, but after a month, her symptoms continued to worsen. (*Id*. at 3.) Petitioner's dizzy spells appeared more frequently, along with constant headaches ranging from dull pain to migraines. (*Id*.) She further experienced increased tinnitus, exhaustion, and joint and muscle pain. (*Id*.)

The next entry on the timeline was for January of 2015. (Ex. 92, p. 4.) Petitioner was referred to the vestibular neurologist who she saw the next month. (*Id*.) The neurologist ruled out Meniere's and asked petitioner to watch for triggers; however,

petitioner's mother asserted that everything was a trigger. (*Id*.) In April of 2015, petitioner's neurologist prescribed her amitriptyline for her migraines, and shortly thereafter, petitioner began complaining that her eyes could not focus, " they lock and can't move," and petitioner's family began to notice that for brief seconds she would be in a fog and would say "wait, what" mid conversation.[22] (*Id*.) Thus, petitioner was taken off amitriptyline and placed on Topiramate, though the headaches remained the same. (*Id*. at 5.)

Between May and July 2015, the timeline reported that petitioner continued to experience the same symptoms, with an increase in exhaustion and seemingly no relief. (Ex. 92, p. 5.) The timeline reports that petitioner missed many days of school over the prior year and that "[petitioner] and the [school] nurse are on a first name basis." (*Id*.) In July of 2015, the timeline explained, petitioner's ENT prescribed her another migraine medication and insisted that she had Meniere's disease. (*Id*.) During this time, petitioner's mother reported that petitioner began experiencing heavier periods and severe cramping. (*Id*.)

According to the handwritten timeline, petitioner had "failed considerably" since August of 2014. (Ex. 92, p. 6.) None of the symptoms had changed, and in fact, there was an increase of symptoms with no explanation. The neurologist recommended that petitioner see a rheumatologist, and the ENT recommended a sleep study. (*Id*.)

Petitioner's mother expressed that she was happy that she did not allow the third dose of Gardasil, and reported that the different physicians "said the timeline is very suspicious," that the cause of petitioner's symptoms was "possibly vaccine" related, and that petitioner "could be [the] one in a million." (Ex. 92, pp. 6-7.) In total, the handwritten timeline reported the following symptoms: "headaches, dizzy spells, ear pressure, tinnitus, visual focus issues (absent seizures) … muscle aches/weakness, joint pain, very slow gait at times, heavy periods, severe cramps, spotting between periods, [petitioner] leans slightly to the right as if off balance, dry skin, acne, rash on face, [and] pale, ashen skin." (Ex. 92, p. 8.)

IV. Expert Opinions and Qualifications

a. Petitioner's Experts

In support of her claim, petitioner relies on two experts: Mitchell Miglis, MD, and Yehuda Shoenfeld, MD. Dr. Miglis is a neurologist and his opinion focused on the autonomic nervous system and its relation to petitioner's alleged injuries. Dr.

[22] Based on my review of this hand-written notation, it appears that the timeline actually says that petitioner's "ears" cannot focus properly. (Ex. 92, p. 4.) However, in the context of the specific quotation that "they lock and can't move," it appears that this intended to say that her eyes cannot focus.

Shoenfeld's opinion focused on the relationship between vaccines and autoimmunie diseases.

i. Mitchell Gordon Miglis, M.D.

Dr. Miglis is a faculty member in the department of Neurology at Stanford University specializing in autonomic nervous system disorders. He is board certified in Sleep Medicine by the American Academy of Sleep Medicine, and in Neurology by the American Board of Psychiatry and Neurology. Dr. Miglis has lectured on POTS and other disorders of Orthostatic Intolerance at local and national conferences and has published peer reviewed articles on POTS in medical literature. (Ex. 21, p. 2.) Additionally, Dr. Miglis has directly managed patients with various autonomic disorders, and supervises autonomic testing, interpreting the data to aid in the diagnosis of autonomic disorders. (Ex. 20, p. 1.)

Dr. Miglis reviewed the medical records from petitioner along with medical literature and opined that while petitioner does not meet the consensus heart rate criteria for POTS based on the tilt table test, "her autonomic diagnosis is consistent with Orthostatic Intolerance (OI)." (Ex. 20, pp. 11-12.) He further opined that "based on the fact that her symptoms persisted for at least 6 months after her vaccination, and she was not experiencing these symptoms prior to her vaccination … more likely than not this vaccination led to her development of OI and symptoms of autonomic impairment." (*Id*. at 12.)

In support of his opinion, Dr. Miglis noted a variety of symptoms in petitioner's medical records that were "consistent with orthostatic intolerance." (Ex. 20, p. 6.) First, he highlighted petitioner's description of "lightheadedness with postural change" and her migraines, which are "common in patients with POTS and OI." (*Id.)* Then, he noted that petitioner's exercise intolerance is also "common in patients with POTS and OI." (*Id*. at 7.) He also referenced petitioner's initial visit to the cardiologist where she describes other symptoms consistent with a POTS or OI diagnosis such as chest pain, palpitations, shortness of breath, and symptoms of presyncope. (*Id*.) All of these symptoms, combined with petitioner's positive testing for anti-alpha-1-adrenergic antibodies, anti-beta-2 adrenergic antibodies, and the anti-muscarinic cholinergic receptor 4 antibodies, which have been associated with POTS, helped guide Dr. Miglis to his opinion.

On June 25, 2018, petitioner filed Dr. Miglis's supplemental report. (Ex. 68.) Dr. Miglis maintained his diagnosis of orthostatic intolerance and further explained his opinion that petitioner's symptoms could not be wholly explained by positional vertigo or vestibular migraines. Rather he opined that her migraines support the existence of an autonomic disorder. (Ex. 68, p. 3.) He rejected the assertion by respondent's expert that "orthostatic intolerance would never produce symptoms that would worsen or not

clear when the subject assumed a recumbent position" and noted that many patients with POTS and OI report symptoms of autonomic hyperactivity that occur while recumbent and can interfere with sleep. (*Id*. at 4.) Dr. Miglis stressed that "there are several publications to support the involvement of [adrenergic and muscarinic cholinergic] antibodies in patients with POTS" and that the presence of specific antibodies in patients with "cardiovascular disorders is not a recent discovery and have been described in association with other disorders of autonomic dysfunction including inappropriate sinus tachycardia and orthostatic hypotension." (*Id*. at 6.)

ii. Yehuda Shoenfeld, M.D., FRCP

Dr. Shoenfeld is the founder and director of The Center for Autoimmune Diseases at the Sheba Medical Center, the largest hospital in Israel. His work focuses on autoimmune and rheumatic diseases, and he has published over 1800 peer review papers. (Ex. 18, p. 1; Ex. 19.) He is on the editorial board of 32 journals and has published many articles on the issues of vaccination and autoimmunity. Additionally, Dr. Shoenfeld is the incumbent of the Laura Schwarz-Kipp Chair for Research of Autoimmune diseases ay Tel-Aviv University. (Ex. 19.)

Dr. Shoenfeld opined that petitioner's illness was triggered by "an exaggerated pathological vaccine-related autoimmune response." (Ex. 18, p. 22.) He noted that vaccines induce an immune response similarly to infections, and that petitioner's experience of post-vaccination flu-like symptoms represent a hyperinflammatory response, which could result in "an exacerbation of normal responses resulting in full blown autoimmune disease such as POTS or other autoimmune diseases." (*Id*.)

Dr. Shoenfeld opined based on two potential diagnoses for petitioner's condition. He first noted that petitioner had a positive tilt table test and tested positive for anti-alpha-1-adrenergic antibodies, anti-beta-2 adrenergic antibodies, and the anti-muscarinic cholinergic receptor 4 antibodies, which "raises the likelihood of autonomic dysautonomia." (Ex. 18, p. 21.) Accordingly, Dr. Shoenfeld opined that the autonomic dysautonomia could be the result of POTS syndrome, as petitioner has experienced many of the symptoms associated with the syndrome. However, he also opined that petitioner's fibromyalgia "could be of the subtype that presents with autonomic dysautonomia" which would also explain her symptoms. (*Id*.)

Based in significant part on studies examining autoantibodies against adrenergic and cholinergic receptors, Dr. Shoenfeld opined that POTS is an autoimmune disorder. (*Id*. at 11-13.) He further opined that substantial overlap among various conditions, including POTS, OI, chronic fatigue syndrome, and fibromyalgia, points to a shared autoimmune etiology for all of these conditions. (*Id*.) Dr. Shoenfeld proposed that cross-reactivity between human proteins and HPV 16 demonstrates molecular mimicry which, combined with a hyperimmune response triggered by aluminum adjuvant, may

break self-tolerance and lead to an autoimmune disorder. (*Id*. at 18-21.) Dr. Shoenfeld also provided a supplemental report reiterating several points and responding to respondent's experts. (Ex. 82.)[23]

b. Respondent's Experts

Respondent also relies on two experts to support his position. Dr. William Talman is an expert in neurology and in the physiology and pathophysiology of the autonomic nervous system, and opines on the neurological and autonomic aspects of the case. Dr. Lindsay Whitton is an expert in immunology, and his opinion is focused on the autoimmune component of petitioner's claim.

i. William Talman, M.D.

Dr. Talman is a Professor Emeritus of Neurology and Neuroscience at the University of Iowa. He directed the Laboratory of Neurobiology "which performed basic research in the physiological basis of the regulation of autonomic function and cerebral blood flow," and has been recognized among Best Doctors in America. (Ex. C, p. 1.) Though he is retired now, Dr. Talman continues to work part-time as a clinical neurologist and a teacher at the University of Iowa. (*Id*.)

Dr. Talman opined that petitioner did not experience orthostatic intolerance, and that instead, a better diagnosis based on petitioner's symptoms is positional vertigo or continuing inner ear problems. (Ex. C, p. 7.) Dr. Talman noted that petitioner saw improvement to her symptoms with the administration of Meclizine, a treatment for vertigo. (*Id*. at 2-3.) Dr. Talman further commented that petitioner's general dizziness could have been explained by a low sodium diet or petitioner's potential predilection to migraines occurring with menstrual period. (*Id*. at 3.) Throughout his report, Dr. Talman provided various alternative explanations of petitioner's symptoms. (*Id*. at 4.)

Dr. Talman further opined that petitioner does not have POTS, as she reported that lying down provided no relief to her symptoms. (Ex. C, p. 5.) He explained that "the cardinal features of POTS are symptoms produced by change in posture, resolution of symptoms upon assuming a recumbent position." (*Id*.) According to Dr. Talman,

[23] In his report at Ex. 18, while discussing alum particles and their causative role in macrophagic myofasciitis lesion in patients with myalgic encephalomyelitis and chronic fatigue syndrome, Dr. Shoenfeld references an article titled "Special Online Consulting for Patients with Eating Disorders and Their Relatives: Analysis of User Characteristics and E-Mail Content." In his responsive report, Dr. Whitton notes that the relevance of this paper to the case at hand is unclear. (Ex. A, p. 8.) I agree, and Dr. Shoenfeld did not provide any response explaining the relevance of the reference to this paper, so I did not consider it in my analysis. Additionally, throughout his report Dr. Shoenfeld cited reference "36" when referring to the U.S. VAERS database. However, reference number 36 is an article titled "The variation in quality and content of patient-focused health information on the Internet for otitis media."

neither petitioner's tilt table test nor her antibody test results diagnose her with autonomic dysfunction or POTS. (*Id*.) He noted that the tilt table test is an inexact diagnostic tool. (*Id*. at 6.) Moreover, he explained that petitioner's syncope experienced during the test was very common, and that the lack of significant change in her blood pressure is "compelling evidence against autonomic dysfunction." (*Id*.) Lastly, Dr. Talman asserted that there is no sound literature to support the diagnostic significance of petitioner's positive antibody findings or involvement of such antibodies in the pathogenesis of autonomic dysfunction or POTS. (*Id*. at 7.)

In his supplemental report, Dr. Talman maintained his position that symptoms of POTS and OI should clear upon assuming a recumbent posture, despite Dr. Miglis' contrary opinion. (Ex. E, p. 2.) He acknowledged that "some question can be raised about antibodies as pathogenetic in POTS" but maintained that petitioner does not have POTS and that her symptoms were not caused by the HPV vaccine. (*Id*. at 3.)

ii. Lindsay Whitton, M.D., Ph.D.

Dr. Lindsay Whitton is a professor in the Department of Immunology and Microbiology at Scripps research Institute in La Jolla, California. (Ex. B, p. 1.) He received his Ph.D. studying herpesvirus transcription at the University of Glasgow, Scotland. (*Id*.) Dr. Whitton has never sought licensure in the United States. (Ex. A, p. 1.)

Dr. Whitton opined that although petitioner's alleged flu-like symptoms that occurred 24-48 hours after vaccination may have been caused by the HPV vaccine, there is no evidence to support causation of any of petitioner's subsequent symptoms. (Ex. A. p. 12.) Dr. Whitton noted that petitioner's treating physicians neither diagnosed petitioner with an autonomic dysfunction nor mentioned the terms "autonomic dysfunction" throughout the medical records. (*Id*. at 4.) He further noted that medical literature has not identified a statistically significant association between the HPV and POTS. (*Id*. at 11.)

Dr. Whitton opined that the assertion that POTS is autoimmune is an "unsupportable conclusion" based on an assemblage of "weak evidence." (*Id*. at 5.) He characterized Dr. Shoenfeld's opinion that adjuvanted vaccines cause a stronger immune response a "risible" and stressed that a temporal association is not enough to infer causation between a vaccine and injury. (*Id*. at 7.) Dr. Whitton also disputed Dr. Shoenfeld's assertion that he had demonstrated cross-reactivity between HPV and human proteins. (*Id*. at 8-9.) Instead, he indicated that the Kanduc article[24] showed

[24] Darja Kanduc, *Quantifying the Possible Cross-Reactivity Risk of an HPV16 Vaccine*, 8 J OF EXPERIMENTAL THERAPEUTICS & ONCOLOGY 65 (2009) (Ex. 59).

only expected homologies that "cannot be used to sensibly infer any biological effect." (Ex. A, p. 8.)

Dr. Whitton also filed a supplemental report specifically responding to two articles filed by petitioner. (Ex. F.)

V. Petitioner's Alleged Injury – The Evidence Preponderates in Favor of Diagnoses of Fibromyalgia and Migraine Disorder in Preference to Either POTS or OI

In this case, petitioner has a fairly complicated medical history and her correct diagnosis is disputed. In cases such as this, when there are multiple alleged diagnoses, the Federal Circuit has found it appropriate for special masters to determine which diagnosis is best supported by the evidence in the record before applying the *Althen* test "so that the special master could subsequently determine causation relative to the injury." *Broekelschen v. Sec'y of Health & Human Servs.*, 618 F.3d 1339, 1346 (Fed. Cir. 2010). The Court explained that because each prong of the *Althen* test is decided relative to the injury, identifying the injury is a prerequisite to the analysis. *Id*. And, in any event, a petitioner must prove by a preponderance of the evidence the factual circumstances surrounding her claim. § 300aa–13(a)(1)(A). Accordingly, a threshold question is whether petitioner actually suffered the injury she alleged.

Initially, petitioner alleged that she suffered "autonomic nervous system[25] dysregulation" that was caused by her vaccinations. (ECF No. 1, p. 9.) As petitioner explained, "the autonomic system controls essential functions of the body such as heart rate, blood pressure, digestion, dilation and constriction of pupils, and body temperature." (ECF No. 55, p. 2.) More specifically, in her motion for a ruling on the record, petitioner asserts that she may meet the criteria for a diagnosis of POTS and, even if she does not, argues that there is no question that she suffers from OI and fibromyalgia. (*Id*. at 20.) Therefore, she characterizes her injury as "autonomic dysfunction, fibromyalgia, and/or OI." (ECF No. 50, pp. 19-20.) In her reply brief, petitioner stressed that "[b]oth OI and POTS fall under the umbrella term 'autonomic dysfunction,' so whether the Special Master decides to call her illness OI or POTS, Julia's illness still falls under this umbrella." (ECF No. 55, p. 2.) Additionally, petitioner also posited that dysautonomia may be a factor underlying the development of fibromyalgia. (ECF No. 50, p. 20 (citing Manuel Martínez-Lavín, *Hypothesis: Human Papillomavirus Vaccination Syndrome – Small Fiber Neuropathy and Dysautonomia Could be its Underlying Pathogenesis*, 34 CLIN RHEUMATOLOGY 392 (2014) (Ex. 70).) Therefore, petitioner effectively further claimed that her fibromyalgia also constitutes

[25] The autonomic nervous system is "the portion of the nervous system concerned with regulation of the activity of cardiac muscle, smooth muscle, and glandular epithelium." (*Dorland's*, p. 1859.)

evidence of autonomic dysfunction. Thus, petitioner asserts that she has one or more of three conditions, each of which she characterizes as constituting autonomic dysfunction.

In addition to arguing that she demonstrates the clinical presentations of these conditions, petitioner asserts that her alleged autonomic dysfunction is also evidenced by positive tests for anti α-1-adrenergic Antibodies, anti β-2-adrenergic Antibodies, and anti-Muscarinic Cholinergic Receptor 4 Antibodies. (ECF No. 50, p. 29 (citing Ex. 12; Ex. 18, p. 21).) Petitioner argues that these antibodies have been associated with POTS and OI. (ECF No. 55, p. 6.)

Respondent does not dispute that POTS is a condition of autonomic dysfunction but does dispute that petitioner experienced either POTS or OI. (ECF No. 54, pp. 16-19.) Conversely, respondent accepts petitioner's fibromyalgia diagnosis, but does dispute that fibromyalgia has any shared pathology with either POTS or OI, stressing that fibromyalgia is a rheumatological condition. (*Id*. at pp. 17, n. 12, 19, n. 15.) Respondent also disputes the validity of petitioner's positive antibody tests and that the antibodies at issue are involved in the pathogenesis of autonomic dysfunction or POTS. (*Id*. at 25.) In all events, respondent disputes that petitioner had autonomic dysfunction of any kind. (*Id*. at 17.)

For the reasons discussed below, the evidence presented preponderates in favor of a finding that petitioner experienced fibromyalgia, for which she has a diagnosis by a treating rheumatologist, potentially accompanied by a migraine disorder, diagnosed by her treating otoneurologist. However, I do not find preponderant evidence that fibromyalgia is an autonomic disorder. Accordingly, I do not find preponderant evidence that petitioner suffered autonomic dysfunction as alleged.

a. There is not Preponderant Evidence that Petitioner had Postural Tachycardia Syndrome (POTS) or Orthostatic Intolerance (OI)

The first question to be addressed is whether petitioner's medical history supports a finding that petitioner suffered either POTS or OI based on her clinical presentation. For the reasons described below, there is not preponderant evidence that petitioner suffered either POTS or OI.

i. Postural Orthostatic Tachycardia Syndrome (POTS) and Orthostatic Intolerance (OI) Explained

When a person is in a supine position, *i.e*. lying down, about one-quarter of their blood volume resides in the chest area. (Amy C. Arnold, Jessica Ng & Satish R. Raj, *Postural Tachycardia Syndrome – Diagnosis, Physiology, and Prognosis*, 215 AUTONOMIC NEUROSCIENCE 3 (2018) (Ex. C, Tab 1, p. 1).) When that person moves into an upright posture, a significant amount of that blood shifts to the lower extremities.

(*Id*.) This temporarily causes impaired return of blood flow to the heart which in turn reduces blood pressure. Normally, the autonomic nervous system adjusts the heartrate to counteract this effect and the hemodynamic changes are negligible. (*Id*. at 1-2.)

However, orthostatic[26] hypotension occurs when there is a sustained reduction of systolic blood pressure of at least 20 mmHg[27] or diastolic blood pressure of 10 mmHg within three minutes of standing. (Roy Freeman et al., *Consensus Statement on the Definition of Orthostatic Hypotension, Neutrally Mediated Syncope and the Postural Tachycardia Syndrome*, 21 CLIN AUTON RESP 69 (2011) (Ex. 22).) Clinically, orthostatic hypotension is characterized by lightheadedness, dizziness, and syncope[28] or pre-syncope. (*Id*. at 2.) Orthostatic hypotension may be symptomatic or asymptomatic. (*Id*. at 1.) The symptoms associated with orthostatic hypotension may also be called orthostatic intolerance. (Ex. 20, p. 4; Mohammed Ruzieh et al., *The Role of Autoantibodies in the Syndromes of Orthostatic Intolerance: A Systematic Review*, 51 SCANDINAVIAN CARDIOVASCULAR J. 243 (2017) (Ex. 17).)

Significantly, a person can experience temporary symptoms resulting from these types of hemodynamic shifts in an acute setting without evidencing any autonomic disorder. (Arnold, Ng & Raj, *supra*, at Ex. C, Tab 1, p. 2.) For example, Dr. Talman explained that "[o]n a hot summer day, after I have stooped in my garden while planting, and after heavy sweating during my labor, I immediately experience a sense of faintness, near fainting, and darkening of vision upon rapidly standing." (Ex. E, p. 2.) Dr. Talman noted that, even if this scenario happened repeatedly, it would not constitute a disorder of autonomic function. (*Id*.)

Postural orthostatic tachycardia syndrome, or "POTS," is a clinical syndrome wherein the body's autonomic nervous system fails to compensate for upright posture. (Howraa Abed, Patrick A. Ball & Le-Xin Wang, *Diagnosis and Management of Postural Orthostatic Tachycardia Syndrome: A Brief Review*, 9(1) J. GERIATRIC CARDIOLOGY 61 (2012) (Ex. 33).) It is characterized by sustained and excessive sinus tachycardia[29] upon standing in the absence of orthostatic hypotension and with chronic symptoms of orthostatic intolerance. (Arnold, Ng & Raj, *supra*, at Ex. C, Tab 1, p. 1.) In adults POTS is defined as a sustained increase in heartrate of at least 30 beats per minute within the first 10 minutes of standing or tilt table testing. (Ex. 20, pp. 3-4; Freeman et al., *supra*,

---

[26] Orthostatic means "pertaining to or caused by standing erect." (*Dorland's*, p. 1339.)

[27] mmHG refers to "millimeter" "mercury." (*Dorland's*, pp. 1167, 858.)

[28] Syncope is the medical term for "fainting" defined as "a temporary suspension of consciousness due to generalized cerebral ischemia." (*Dorland's*, p. 1818.)

[29] Tachycardia is "excessive rapidity in the action of the heart; the term is usually applied to a heart rate above 100bpm in an adult." (*Dorland's*, p. 1867.)

at Ex. 22, p. 3.) For those aged 12-19 years, the required increment is 40 beats per minute. (*Id*.) A diagnosis of POTS also requires symptoms of orthostatic intolerance for greater than six months and the absence of any overt cause for sinus tachycardia. (Arnold, Ng & Raj, *supra*, at Ex. C, Tab 1, p. 2.)

A diagnosis of POTS cannot be made "in the absence of typical symptoms that are worse in the upright posture and better with recumbence." (*Id*.) Orthostatic symptoms of POTS include palpitation, chest pain, lightheadedness, blurred vision, shortness of breath, headache, nausea, fatigue, and tremulousness. (Arnold, Ng & Raj, *supra*, at Ex. C, Tab 1, p. 2; Freeman et al., *supra*, at Ex. 22, p. 4.) POTS patients may also experience dependent acrocyanosis,[30] cognitive dysfunction, sleep disturbances, and exercise intolerance. Symptoms can be exacerbated by other factors such as dehydration, heat, alcohol consumption, menstruation, and acute exercise. (Arnold, Ng & Raj, *supra*, at Ex. C, Tab 1, p. 2.)

Petitioner's neurology expert, Dr. Miglis suggests that when a patient fails to meet the specific criteria for a diagnosis of POTS, they may still be given a label of "orthostatic intolerance," not merely as a symptom, but as a diagnosis. (Ex. 20, p. 4.) Dr. Miglis effectively asserts that, in the absence of tachycardia, orthostatic intolerance represents a clinical manifestation of autonomic dysfunction similar to POTS but representing a milder degree of dysautonomia. (Ex. 20, p. 4 (citing Ajay K. Parsiak et al., *Orthostatic Intolerance Without Postural Tachycardia: How much Dysautonomia?*, 23 CLIN. AUTON. RESP. 181 (2013) (Ex. 23).) Dr. Miglis acknowledged, however, that while some consider orthostatic intolerance to be a variant of POTS, as a diagnostic entity it is "a poorly defined syndrome." (*Id*.) Moreover, some consider it to be a functional or psychosomatic disorder. (*Id*.)

Dr. Talman did not directly address Dr. Miglis's suggestion that orthostatic intolerance could constitute a diagnosis in itself, but did caution that symptoms of orthostatic intolerance do not necessarily indicate any derangement of autonomic function. (Ex. E, p. 2.) He explained that "[a]utonomic dysfunction of a primary or iatrogenic[31] nature may be associated with ancillary symptoms, but those ancillary symptoms (posit fatigue as an example) never occur without the concomitant presence of primary symptoms of autonomic dysfunction. Among the symptoms that could be produced by autonomic dysfunction are postural syncope or presyncope, anhidrosis

[30] Acrycyanosis refers to "symmetrical cyanosis of the extremities, with persistent, uneven blue or red discoloration of the skin of the digits, wrists, and ankles accompanied by profuse sweating and coldness of the digits." (*Dorland's*, p. 19.)

[31] Iatrogenic means "resulting from the activity of physicians." (*Dorland's*, p. 910.)

(absence of sweat) or patchy alterations in sweating, incontinence (loss of bladder control), and, in men, erectile dysfunction." (Ex. C, p. 7.)

ii. Petitioner's Tilt Table Results do not Support her Allegation of Autonomic Dysfunction

As noted above, the signature characteristic that separates POTS from other forms of autonomic dysfunction is the presence of sustained and extended tachycardia upon standing. (Ex. 20, p. 4.) One of the ways this can be tested is by using a head-up tilt table test. Tilt table testing has been in use since the 1980's for evaluation of hemodynamic changes in cases of both vasovagal syncope and conditions related to orthostatic intolerance. (Wouter Wieling et al., *Cardiac Output and Vasodilation in the Vasovagal Response: An Analysis of the Classic Papers*, 13 HEART RHYTHM 798 (2016) (Ex. C, Tab 6).) In contrast to Dr. Miglis's assertion that tilt table testing is the "gold standard" for diagnosing disorders of orthostatic intolerance (Ex. 20, pp. 1-2, 7), Dr. Talman was critical of this type of testing (Ex. C, p. 6).

Petitioner underwent a tilt table test on October 5, 2016. (Ex. 10.) At the beginning of the test, she had a heartrate of 77 bpm and blood pressure of 128/59. (Ex. 10, p. 8.) By the ten-minute mark, her heartrate had increased to 109 bpm and her blood pressure was at 119/61. (*Id*.) After about twenty minutes, petitioner reportedly began experiencing dizziness. After twenty-five minutes, she began feeling nausea, and before thirty minutes the test was stopped when she began vomiting. (*Id*.) At that time her heartrate was no longer elevated (74 bpm at twenty minutes and 61 bpm when the procedure was stopped) and her systolic blood pressure had dropped to 98 while her diastolic remained at 68. (*Id*.) Her mean blood pressure remained relatively stable throughout the test. (*Id*.) Although petitioner's test results report only presyncope, her discharge diagnosis was vasovagal syncope. (Ex. 10, pp. 4, 8.) There is no specific reference to petitioner having lost consciousness.

According to respondent's expert, Dr. Talman, petitioner's test results show that she never manifested postural tachycardia. (Ex. C, p. 6.) Moreover, focusing on her mean blood pressure, Dr. Talman opined that "the complete absence of any significant change in [petitioner's] BP is compelling evidence against autonomic dysfunction." (*Id*.) This latter point goes to Dr. Miglis's alternative suggestion that petitioner had orthostatic intolerance in the absence of POTS. POTS is defined as tachycardia "in the absence of orthostatic hypotension." (Ex. 68, pp. 5-6; Freeman et al., *supra*, at Ex. 22, p. 3.) However, orthostatic intolerance represents symptoms consistent with orthostatic hypotension which, in itself, does represent a drop in blood pressure. (Freeman et al., *supra*, at Ex. 22, pp. 1-2.)

Dr. Miglis disputed Dr. Talman's suggestion that petitioner's blood pressure constituted evidence against POTS or OI (Ex. 68, pp. 5-6), but did agree that

petitioner's heartrate measurements were inadequate to support a POTS diagnosis (Ex. 20, pp. 7-8; Breann N. Butts, Phillip R. Fischer & Kenneth J. Mack, *Human Papillomavirus Vaccine and Postural Orthostatic Tachycardia Syndrome: A Review of Current Literature*, 32(11) J. OF CHILD NEUROLOGY 956 (2017) (Ex. 65).) Specifically, Dr. Miglis indicated that petitioner's tilt table test "demonstrated a postural tachycardia that approached, but did not meet criteria for an exaggerated postural tachycardia in an adolescent, with a heart rate increase of 32 bpm within 10 minutes of upright tilt (77 bpm supine to 109 bpm by minute 10), without a significant decrement in blood pressure." (Ex. 20, pp. 7-8.) Accordingly, he agreed that petitioner's heartrate response to upright tilt did not meet the definition of an exaggerated postural tachycardia in an adolescent. (Butts, Fischer & Mack, *supra*, at Ex. 65, p. 5.) He also opined that her tilt table test did not support a POTS diagnosis. (Ex. 20, p. 11.)[32]

Dr. Miglis did not readily ascribe any significance to petitioner's vasovagal syncope during the tilt test. He noted that vasovagal syncope is common in patients with POTS, but indicated that the prevalence is "less clear" among those with orthostatic intolerance. (Ex. 20, p. 8.) Nonetheless, he also noted that vasovagal syncope, which he acknowledged to be "common fainting," is "very common" and can be brought on by the stress of a tilt table test. (*Id*.) Given her steady blood pressure, Dr. Talman similarly opined that petitioner's presyncope demonstrated during the test likely stemmed from hyperventilation brought on by the stress of the test. (Ex. C, p. 6.)

However, Dr. Talman further opined that a vasovagal response to tilt testing in a patient with no history of fainting is itself considered "indicative of a false positive test." (*Id.*) Noting that petitioner had no prior history of syncope (*see also* Ex. 10, p. 2), he opined that petitioner's syncope "is of no clinical relevance or significance." (Ex. C, p. 6.) Dr. Talman cited a study comparing tilt table tests from a group of individuals with neurocardiogenic syncope with those of a control group. (Fabio Leonelli et al., *supra*, at Ex. C, Tab 7.) The study observed false positives among the control group and noted

[32] With regard to heartrate, petitioner also underwent a 24-hour Holter monitor in September 2016 that did not detect any tachycardia. (Ex. 6, pp. 9-21.) Overall, that study showed normal sinus rhythm with "occasional" premature arterial contraction. Dr. Talman noted that this study did not allow for documentation of potential symptomatic events during the testing period, but stressed that, not only was no tachycardia was observed, petitioner demonstrated bradycardia during the Holter monitoring, which is the opposite of tachycardia. (Ex. C, p. 5.) Dr. Miglis interpreted the results the same way, but he noted that Holter monitors are "typically not illustrative in patients with POTS and OI." (Ex. 20, p. 7; Ex. 68, p 5.) Electrocardiograms and extended Holter monitors are typically used to rule out other cardiac abnormalities, not necessarily to detect episodes of postural tachycardia. (Arnold, Ng & Raj, *supra*, at Ex. C, Tab 1, p. 3.) Accordingly, while the 24-hour Holter does not support petitioner's claim, it also does not appear to constitute evidence against her claim.

that "fainting may be considered one of the expected responses to this test" even among "normal individuals."[33] (*Id*.)

In opining that petitioner did nonetheless have orthostatic intolerance, Dr. Miglis relied on petitioner's clinical presentation of symptoms consistent with OI. (Ex. 68, p. 5; Ex. 20, p. 11). Apart from noting the "less clear" association between syncope and OI, he did not specifically opine that petitioner's tilt table testing was supportive of his opinion that petitioner had OI even in the absence of POTS.[34] In fact, to the contrary, he indicated that "the magnitude of postural tachycardia on objective testing does not necessarily correlate with the severity of a patient's symptoms." (Ex. 68, p. 4.) Nor, as discussed in greater detail below, did any of petitioner's treating physicians indicate that petitioner's tilt table test was suggestive of either POTS or OI.

In light of the foregoing, it does not appear that petitioner's tilt table test results add any support to a diagnosis of either POTS or OI. Moreover, notwithstanding her syncopal (or presyncopal) event, the failure of the test to detect any significant tachycardia or orthostatic hypotension weighs *against* petitioner's claim that she has either POTS or OI.

iii. Petitioner's Medical Records do not Provide Preponderant Evidence of a POTS Diagnosis

As noted above, based in large part on petitioner's tilt table test, petitioner's autonomic expert in this case conceded that petitioner did not meet the diagnostic criteria for POTS. Nonetheless, some of petitioner's medical records did reference a possible POTS diagnosis. Petitioner stressed, in particular, a record by Dr. Lombardi (her second cardiologist) that included POTS in the assessment section. (ECF No. 50, p 20 (citing Ex. 86, p. 8; Ex. 85, p. 7).) Significantly, though, the basis for that diagnosis is not well established.

Petitioner was first referred for a cardiology work-up, including the above-described Holter monitoring and tilt table testing, as part of her follow up for

[33] Of note, Dr. Talman's use of the phrase "false positive test" may be a bit confusing. The study he cited was specifically exploring syncopal events. So, a syncopal event in a control subject was literally a false positive within the context of the study. Here, however, to the extent the tilt table test was exploring POTS, it was not necessarily seeking to detect syncope. Dr. Talman is persuasive in opining that petitioner's syncope (or presyncope) was a "false positive" in the sense of having no clinical significance due to being an expected outcome even among asymptomatic controls, but he has not established on this point that petitioner's syncopal event at the end of the test created a "false positive test" in the sense of invalidating any of the blood pressure or heart rate findings during the test. He has, however, separately explained why he believes tilt table testing may be less significant than standing tests. (Ex. C, p. 6.)

[34] However, one study filed by petitioner indicated that for purposes of the study OI was defined as an increase in heartrate of less than 30 beats per minute upon head-up tilt. (Parsaik et al., *supra*, at Ex. 23, p. 2.)

fibromyalgia. (Ex. 11, p. 7.) Dr. Yalcindag had recommended graded aerobic exercise (*Id*. at 3), but in an August 2016 follow up, petitioner noted dizziness when exercising (*Id*. at 5). Therefore, Dr. Yalcindag wanted to "assess exercise tolerance." (*Id*. at 7.) When petitioner returned to Dr. Elgabry (the cardiologist who performed the tilt table test) for a post-test follow up, he indicated only that the test demonstrated vasovagal syncope. (Ex. 6, p. 1.) There is no assessment (or mention) of either POTS or OI. (*Id*.) Dr. Elgabry acknowledged petitioner's symptoms of dizziness, but petitioner's cardiac exam was normal. (*Id*. at 1-3.)

Petitioner's otolaryngologist, Dr. Andreozzi was the first to add POTS to his diagnostic impressions in November of 2016, about a month after petitioner's follow up with Dr. Elgabry. (Ex. 8, p. 2.) Dr. Andreozzi did not record any assessment or exam relating to POTS, but only indicated in the history of present illness that "[s]ince I have seen Julia, she has been diagnosed with fibromyalgia in addition to postural orthostatic tachycardic syndrome with a positive tilt test via her cardiologist . . ." (*Id*.)

Later that month, petitioner returned to her otoneurologist, Dr. Ramocki, and it was noted that, although her ECG had been normal, "she believes that tilt table testing was abnormal." (Ex. 83, p. 6.) The specific result was not indicated. Petitioner reported, however, that "[c]onservative treatment measures for orthostatic intolerance were recommended." (*Id*.) Significantly though, as noted above, Dr. Elgabry's records contain no indication that he suspected orthostatic intolerance or that he counseled treatment for that disorder. (Ex. 6.) Dr. Ramocki did not make any assessment as to POTS, noting only that she did not yet have Dr. Elgabry's report and recommending that petitioner continue to follow up with him, but thereafter she did begin referring to petitioner as having orthostatic hypotension. (*Id*.) Dr. Ramocki would later refer petitioner to physical therapy for "obesity, joint pain, orthostatic dizziness, [and] chronic headaches." (Ex. 88, p. 18.)

A little over a week after seeing Dr. Ramocki, petitioner returned to Dr. Yalcindag. (Ex. 84, p. 47.) At that time, Dr. Yalcindag recorded of petitioner that "[s]ince her last visit she had tilt table testing done outside. By mom's report she had evidence for postural tachycardia syndrome." (*Id*.) Dr. Yalcindag did not note any findings related to POTS or make any recommendations but described petitioner as a "16 y/o with POTS." (*Id*. at 49.)

Later, in September of 2017, petitioner presented to a different cardiologist, Dr. Lombardi, for an initial evaluation with a chief complaint of "[history of] POTS, now with chest pain." (Ex. 93, p. 1.) Dr. Lombardi noted petitioner's diagnosis of POTS to have been "made elsewhere." (*Id*.) Petitioner's pulse was elevated, but her exam showed

regular rate and rhythm. (*Id*. at 2.) An EKG was interpreted as normal.[35] (*Id*.) Her cardiac evaluation was described as "reassuring," with no sign of being orthostatic.[36] Dr. Lombardi felt that petitioner's chest pain was non-cardiac in etiology and felt that no further cardiac testing was warranted. (*Id*. at 3.)

Upon my review, I do not find persuasive evidence that any of petitioner's treating physicians affirmatively diagnosed POTS. Rather, they appear to have accepted that the diagnosis was previously made based on the histories petitioner provided. However, given Dr. Elgabry's records as well as the expert opinions provided in this case, that appears to have been incorrect.[37] If any of these physicians was made aware of the specific results of petitioner's tilt table test (*i.e*. steady mean blood pressure and an elevated heartrate that did not meet the consensus criteria for POTS), that was not recorded in the medical records.

According to the Heart Rhythm Society, diagnosis of POTS requires a complete medical history inclusive of "details on the nature of tachycardia including chronicity, triggers, modifying factors, presyncopal or syncopal episodes, symptoms and impact on daily activities" as well as " a physical examination including "detailed cardiovascular, neurologic, autonomic, and other systems assessment," plus orthostatic vitals, including blood pressure and heart rate as well as electrocardiogram. (Arnold, NG & Raj, *supra*, at Ex. C, Tab 1, p. 3 (Table 2).) Although Dr. Lombardi included POTS in her assessment upon initial presentation, she recorded no significant findings on her physical exam supportive of a POTS diagnosis. And, again, she stressed that the diagnosis had been made elsewhere.

Even assuming *arguendo* that Dr. Lombardi, or any of petitioner's other treating physicians, had made a diagnosis of POTS, the opinions or diagnoses of treating physicians are not "sacrosanct" and the Vaccine Act itself provides that special masters are not bound any specific "diagnosis, conclusion, judgment, test result, report, or summary" contained in petitioner's medical record. *Snyder v. Sec'y of Health & Human Servs.,* 88 Fed. Cl. at 746 n.67; § 300aa-13(b)(1). Rather, the views of treating physicians should be weighed against other, contrary evidence also present in the record. *Hibbard v. Sec'y of Health & Human Servs.*, 100 Fed.Cl. 742, 749 (2011) (not

---

[35] Specifically, it was recorded as "Sinus tachycardia; normal axis and intervals, normal EKG." (Ex. 93, p. 2.)

[36] Specifically, Dr. Lombardi noted that petitioner "is not orthostatic by vital signs today." (Ex. 93, p. 3.) I interpret this to mean petitioner was not showing signs of orthostatic intolerance or hypotension.

[37] Notably, petitioner was indicating to her physicians that only conservative treatment had been recommended for orthostatic intolerance. (Ex. 83, p. 6.) Accordingly, the possible consequences of accepting a misdiagnosis from another physician were likely very minor where, as here, the physicians simply added the other diagnosis to their assessment and did not accept it in preference to treatment for the conditions they had themselves diagnosed.

arbitrary or capricious for special master to weigh competing treating physicians' conclusions against each other), *aff'd*, 698 F.3d 1355 (Fed. Cir. 2012); *Caves v. Sec'y of Health & Human Servs.*, 100 Fed. Cl. 119, 136 (2011), *aff'd*, 463 Fed. Appx. 932 (Fed. Cir. 2012); *Veryzer v. Sec'y of Health & Human Servs.*, No. 06–522V, 2011 WL 1935813, at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), *mot. for review den'd*, 100 Fed. Cl. 344, 356 (2011), *aff'd without opinion*, 475 Fed. Appx. 765 (Fed. Cir. 2012).

In this case, I give some weight to the fact that multiple of petitioner's treating physicians appear to have accepted the POTS label in light of what they knew about the history of petitioner's reported symptoms. However, the only physician to have completed any well-documented assessment (Dr. Lombardi) consistent with the above-cited diagnostic standard, did not record any findings indicative of orthostatic intolerance or POTS. Moreover, contrary to what was reported to her physicians, petitioner's tilt table test was not supportive of a POTS diagnosis. Thus, given the specific history above, the references to POTS in petitioner's medical records are far outweighed by the much more detailed consideration given to this question by the experts opining in this case, including, most significantly, petitioner's own autonomic expert who opined that petitioner did not meet the criteria for a POTS diagnosis.

iv. There is not Preponderant Evidence that Petitioner's Symptoms Constitute Orthostatic Hypotension or Orthostatic Intolerance

Setting aside the specific diagnosis of POTS, Dr. Miglis also opined that petitioner may qualify for a diagnosis of orthostatic intolerance even in the absence of POTS. As noted above, the primary symptoms of orthostatic intolerance (or orthostatic hypotension) are lightheadedness, dizziness, and syncope or presyncope. (Freeman et al., *supra*, at Ex. 22, p. 1.) Although petitioner never reported syncope (apart from during the tilt table test[38]), it is undisputed that she repeatedly described episodes of dizziness and lightheadedness. However, petitioner's medical records do not offer a clear or consistent diagnosis to explain petitioner's dizziness and lightheadedness. Accordingly, the exact nature and etiology of those episodes has been extensively debated.

Petitioner first reported dizziness to her physicians in December of 2014 when she described dizziness associated with a year and a half history of fluctuating hearing loss to her otolaryngologist, Dr. Andreozzi. (Ex. 8, p. 32.) Meniere's disease was suspected. (*Id*.) In further follow up, she described to Dr. Ramocki "complaints of

[38] As addressed above, Dr. Talman was persuasive in explaining that petitioner's syncopal event during the tilt table was a "false positive" caused by the test itself and not clinically relevant. (*See* n. 33, *supra*.) Petitioner did describe presyncope to Dr. Ramocki and Dr. Andreozzi on numerous occasions. (*See* Ex. 4, p. 24; Ex. 8, p.1.)

dizziness in August or September of 2014. She describes this as lightheadedness with postural change." (Ex. 4, p. 24.) She also described headaches with rapid head movement and vertigo lasting seconds. (*Id*.) Positional dizziness was described as "rarely." (*Id*.) Dr. Ramocki disagreed with the suspicion of Meniere's disease and felt a vestibular migraine disorder may explain her symptoms along with low sodium intake resulting in postural dizziness. (*Id*. at 25.)

Thereafter, petitioner continued to treat with both Dr. Ramocki and Dr. Andreozzi over a period of years. Dr. Andreozzi maintained that petitioner had Meniere's disease, but also later agreed that she had a vestibular migraine disorder. (Ex. 8, p. 26.) Eventually, however, Dr. Ramocki appears to have accepted that petitioner was experiencing symptoms of orthostatic hypotension, though she never abandoned the additional diagnosis of a migraine disorder. (Ex. 83, pp. 1-6.) Dr. Lombardi also counseled petitioner regarding vagally-mediated presyncope and postural orthostasis, though she never observed petitioner to be orthostatic by vital signs. (Ex. 93, pp. 1-3.)

However, respondent's expert, Dr. Talman, endorsed Dr. Ramocki's initial diagnosis of a vestibular migraine disorder. (Ex. C, p. 3.) Additionally, he raises several significant points that suggest that petitioner's dizziness and lightheadedness may not be related to orthostatic intolerance or hypotension.

First, Dr. Talman suggests that petitioner's reported symptoms are potentially consistent with positional vertigo. (Ex. C, p. 2.) Notwithstanding that Dr. Ramocki referenced "lightheadedness with postural change," Dr. Talman focused on her reference to symptoms with rapid head movement, which he explained is consistent with vertigo.[39] (Ex. C, pp. 2-3.) Moreover, he further stressed that Dr. Ramocki also explicitly recorded vertigo as a symptom and that petitioner initially responded to treatment with meclizine (Bonine), which is a treatment for vertigo, but not orthostatic intolerance.[40] (*Id*.) Conversely, for much of the relevant period, petitioner was taking

[39] When petitioner later appeared for a physical therapy evaluation for, *inter alia*, orthostatic dizziness, the physical therapist also noted her symptoms of orthostatic dizziness to be associated with quick positional changes. (Ex. 88, p. 52.)

[40] Petitioner argues in her motion that, contrary to Dr. Talman's interpretation, her records should be interpreted as reporting dizziness, not vertigo. (ECF No. 50, pp. 33-34.) This argument is based on a questionnaire that petitioner filled out for Dr. Andreozzi's office on September 28, 2015, and February 24, 2016. (*Id*. (citing Ex. 8, pp. 20, 23).) However, even if she reported dizziness and not vertigo to Dr. Andreozzi, Dr. Ramocki explicitly recorded vertigo at multiple visits. (Ex. 4, pp. 21, 23, 24.) That petitioner reported her symptoms differently between visits with different doctors is not necessarily evidence that Dr. Ramocki incorrectly recorded symptoms. Notably, Dr. Ramocki recorded both dizziness and vertigo, making it unlikely that she failed to make any distinction.

topiramate for her migraines, a known side effect of which is dizziness.[41] (Ex. C, pp. 3-4.)

Dr. Miglis disputed Dr. Talman's analysis of Dr. Ramocki's record, noting, in particular, that she described lightheadedness with postural change, which is consistent with orthostatic intolerance, and that petitioner had a normal Dix-Hallpike test, which is commonly abnormal in vertigo patients. (Ex. 68, p. 2.) Nonetheless, Dr. Miglis acknowledged that "some of [petitioner]'s symptoms are consistent with a form of disequilibrium as seen in [benign paroxysmal positional vertigo ("BPPV")] and vestibular migraines." (*Id*. at 1-2.) He argued, however, that petitioner's symptoms overall "cannot be completely explained" by either positional vertigo, BPPV, or vestibular migraines. (*Id*. at 3.) Since migraines with vestibular dysfunction occur in POTS and OI patients, he argued that this comorbidity supports the OI phenotype.[42] (*Id*.)

However, Dr. Talman also strongly urged that "postural, or orthostatic, intolerance with or without putative POTS, by definition, would never produce symptoms that would worsen or not clear when the subject assumed a recumbent position." (Ex. C, p. 4 (emphasis original).) In that regard, Dr. Talman stressed Mrs. Balasco's description of petitioner's condition as having "no relief lying down."[43] (Ex. C, p. 4 (citing Ex. 1, p. 2).) He also noted that petitioner reported that her condition interfered with her recumbent sleep, resulting in a referral for a sleep study to confirm whether any sleep disorder was contributing to her fatigue and other symptoms.[44] (Ex. C, pp. 4-5; Ex. 8, p. 20.) In contrast, he noted that petitioner's positional dizziness was recorded by Dr.

---

[41] Petitioner argues that Dr. Talman's suggestion that topiramate could explain petitioner's dizziness is "unfounded." (ECF No. 55, p. 7.) Petitioner stresses that she was not using topiramate when her symptoms began and that her treaters did not discontinue topiramate to see if it was causing her symptoms. (*Id*.) Notably, however, one record from Dr. Ramocki on September 25, 2015, noted that petitioner's headaches had recurred when she reduced her dose from 50mg daily of topiramate to 25 mg daily, but in that same history, it was reported that petitioner's dizziness had been better controlled. (Ex. 4, p. 17.) Dr. Ramocki recommended increasing topiramate more slowly. (*Id*.) Topiramate need not have been the precipitating cause of petitioner's dizziness to have had an impact on the overall course of her symptoms.

[42] Dr. Miglis interpreted Dr. Talman's reference to vertigo as referring to benign paroxysmal positional vertigo or "BPPV" and disputed that petitioner had BPPV for a number of reasons. (Ex. 68, p. 1.) In a responsive report, Dr. Talman indicated that he was not referring to BPPV and agrees that petitioner did not have BPPV for the reasons Dr. Miglis explained. (Ex. E, p. 1.) Instead, he stressed that he was referencing the report of positional vertigo. (*Id*.) However, as noted here, Dr. Miglis did also assert that positional vertigo cannot completely explain petitioner's symptoms. (Ex. 68, p. 3.)

[43] Mrs. Balasco's statement was filed February 21, 2017. (Ex. 1.) In a later physical therapy record dated September 27, 2017, petitioner did report to her physical therapist that she felt her symptoms improved upon lying down. (Ex. 88, p. 50.)

[44] Petitioner complained that headaches and "'fuzziness' in her head" contributed to her sleep problems. (Ex. 8, p. 20.)

Ramocki as occurring "rarely."[45] (Ex. C, p. 3 (citing Ex. 4, p. 24).) Moreover, petitioner's later tilt table test showed no drop in mean blood pressure, which is inconsistent with orthostatic hypotension. (Ex. C, p. 6.)

Overall, although petitioner sometimes specifically reported that her dizziness or lightheadedness was postural (*see, e.g.*, Ex. 4, p. 23, 24; Ex. 8, p. 23; Ex. 88, p. 50; Ex. 93, p. 1), she also often reported dizziness without relating it to posture or standing and sometimes related her dizziness to her headaches or exertion instead (*see, e.g.*, Ex. 8, p. 32 (fluctuating with hearing loss); Ex. 4, p. 17 ("only with running"), p. 10 ("especially with exertion"), p. 8 (with headaches and with exertion); Ex. 86, p. 6 ("with exercise").) Notably, Mrs. Balasco's handwritten timeline of symptoms never associated onset of petitioner's dizziness with standing or posture. (Ex. 92.) And, as discussed above, Mrs. Balasco's sworn statement supporting this case specifically disclaimed any relief from symptoms when lying. (Ex. 1, p. 2.)

Significantly, it was not until much later that petitioner began reporting that her symptoms were alleviated by lying down. (Ex. 88, pp. 50, 61.) It is well documented in petitioner's medical records and in her allegations that throughout the course of her treatment history she became increasingly sedentary and often spent significant amounts of time sleeping or lying down.[46] (*See* Ex. 8, pp. 1, 26, Ex. 2, p. 3, Ex. 4, p. 13,

[45] Dr. Miglis disagreed with Dr. Talman's assertion that orthostatic symptoms would fail to resolve in recumbency. (Ex. 68, p. 4.) He argued that while symptoms may improve with recumbency, they rarely completely resolve. (*Id.*) This is not persuasive as presented. In support of his position, Dr. Miglis cited two papers of his own (in co-authorship with others) that examined sleep disorders among POTS patients. (Mitchell G. Miglis & Fiona Barwick, *Sleep Disorders in Patients with Postural Tachycardia Syndrome: A Review of the Literature and Guide for Clinicians*, J. AUTONOMIC NEUROSCIENCE (2017) (Ex. 71); Mitchell G. Miglis et al., *Sleep Disorders in Patients with Postural Tachycardia Syndrome*, 26 CLIN. AUTON. RESP. 67 (2016) (Ex. 73).) In the first, the authors observed that many POTS patients report fatigue and subjective sleep complaints and sought to hypothesize the cause for that correlation. (Miglis & Barwick, *supra*, at Ex. 71, pp. 24-25.) The authors noted, however, that polysomnography has failed to demonstrate any consistent abnormalities. (*Id.* at 24.) In the second, the authors again concluded that their findings "indicate that while POTS patients report greater fatigue and sleep-related complaints, they have no more sleep issues than other patients who are referred for sleep evaluation, and there is no sleep disorder yet identified that is unique to POTS." (Miglis et al., *supra*, at Ex. 73, p. 6.) Dr. Miglis did not effectively refute Dr. Talman's broader assertion that petitioner's overall medical history is inconsistent in demonstrating symptoms that are postural in nature. Nor has he persuasively countered Dr. Talman's assertion that symptoms that respond to recumbency are definitional to POTS and orthostatic intolerance. (*See also* Arnold, Ng & Raj, *supra*, at Ex. C, Tab 1, p. 2 (explaining that "POTS is a clinical syndrome and not just a physiological finding. The diagnosis cannot be made in the absence of typical symptoms that are worse in the upright posture and better with recumbence.").) Indeed, in his initial report he himself characterized the symptoms of POTS as "worse with standing and relived with sitting or lying flat." (Ex. 20, p. 4.)

[46] For example, in one particularly detailed note, Dr. Ramocki recorded of petitioner that "[s]he is spending a lot of days sleeping in the nurse's office at school. She misses a lot of school due to headaches and fatigue. She has minimal endurance for activities: e.g. she had to sleep for hours after floating in a blow-up back yard pool in the afternoon." (Ex. 4, p. 13.)

Ex. 92, p. 5.) In that regard, Dr. Talman stressed the concept of deconditioning, which represents a change in cardiovascular function after prolonged periods of weightlessness likely related to the shifting of blood from lower limbs to the thorax. (Ex. C, p. 5; *Dorland's*, p. 475.) He submitted a study in which researchers induced delayed orthostatic intolerance in eight out of eleven healthy subjects after 24-hours of bedrest.[47] (W. Hildebrandt et al., *Enhanced Slow Caudad Fluid Shifts in Orthostatic Intolerance After 24-h Bed-Rest*, 69 EUR. J. APPLIED PHYSIOLOGY 61 (1994) (Ex. C, Tab 2).) Additionally, deconditioning has been identified as a confounding factor when studying or assessing POTS and orthostatic intolerance. (Parsaik et al., *supra*, at Ex. 23, p. 2; Freeman et al., *supra*, at Ex. 22, p. 2.) It has also been suggested that POTS itself mimics the phenotype of deconditioning from prolonged bed rest, though it remains controversial whether bed rest can be considered a cause of POTS. (Arnold, Ng & Raj, *supra*, at Ex. C, Tab 1, p. 7.) Dr. Miglis did not directly contest that deconditioning was present in this case, noting only that deconditioning is often seen among patients with POTS or OI and would not explain all of petitioner's symptoms.[48] (Ex. 68, p. 4.) Moreover, he acknowledged that a diagnosis of POTS must account for the presence of prolonged bed rest to be considered accurate. (Ex. 20, p. 4.)

Although petitioner's dizziness remains somewhat enigmatic, I do not find preponderant evidence that petitioner's symptoms are explained by orthostatic hypotension or orthostatic intolerance. Dr. Talman has raised significant doubts that petitioner's symptoms are consistent with such a condition. Moreover, given that she did not consistently characterize her dizziness as related to position and did not initially report improvement with recumbency (which would be expected if it were orthostatic hypotension or intolerance), it is noteworthy that both parties' experts opined that her symptoms could at least imperfectly be explained by disequilibrium related to either vertigo or vestibular migraines, both of which were recognized by Dr. Ramocki throughout the course of petitioner's treatment. Accordingly, petitioner's diagnosed vestibular migraine disorder represents a more likely explanation for her lightheadedness and dizziness.

---

[47] Delayed orthostatic hypotension has no known clinical significance. (Freeman et al., *supra*, at Ex. 22, p. 2.) This calls to mind Dr. Talman's analogy to becoming lightheaded after stooping in the garden, which he explained is not indicative of autonomic dysfunction, even if it happens repeatedly. (Ex. E, p. 2.)

[48] In particular, Dr. Miglis cited a study in which researchers found that 95% of POTS subjects and 91% of orthostatic intolerance subjects showed evidence of deconditioning. (Ajay K. Parsaik et al., *Deconditioning in Patients with Orthostatic Intolerance*, 79 NEUROLOGY 1435 (2012) (Ex. 72.) This study does not, however, provide any evidence against Dr. Talman's suggestion that deconditioning can cause delayed orthostatic intolerance in the complete absence of autonomic dysfunction. In fact, the study authors noted that they were unable to predict deconditioning based on autonomic parameters. (*Id*. at 4.)

b. Petitioner's Fibromyalgia and Vestibular Migraine Diagnoses Better Explain her Condition

Dr. Miglis's assertion that petitioner suffered orthostatic intolerance (as a diagnosis, not merely a symptom) is not limited to recognizing the symptom of dizziness. However, petitioner also has an undisputed diagnosis of fibromyalgia (Ex. 11; ECF No. 54, p. 17, n. 12.) and petitioner has herself argued that "POTS, OI, and fibromyalgia seem to have a similar symptomology . . ." (ECF No. 50, p. 20). This raises the question of whether any (or all) of petitioner's symptoms can be better explained by her diagnosed fibromyalgia in preference to Dr. Miglis's suggestion that orthostatic intolerance itself constitutes a diagnosis.

Petitioner first sought treatment from a rheumatologist (Dr. Yalcindag) in May of 2016. (Ex. 11.) By that time, she had been exploring the nature of her condition for nearly two years with Drs. Andreozzi and Ramocki. Petitioner presented with a chief complaint of joint pain, fatigue, and chest pain. (Ex. 11, p. 1.) She explained that her initial symptoms were headaches and vertigo with later development of diffuse body aches, fatigue, and "bad sleep." (*Id*.) Based on this presentation, as well as finding multiple trigger point hypersensitivity, petitioner was diagnosed with fibromyalgia. (Ex. 11, p. 3.) Dr. Yalcindag maintained the fibromyalgia diagnosis even after petitioner reported having been diagnosed with POTS. (Ex. 86.)

In the most basic terms, fibromyalgia is defined as "pain and stiffness in the muscles and joints that either is diffuse or has multiple trigger points." (*Dorland's*, p. 703.) It represents a "centralized" pain state and can be considered a discrete diagnosis. (Daniel J. Clauw, *Fibromyalgia: A Clinical Review*, 311(15) JAMA 1547 (2014) (Ex. 31).) After osteoarthritis, it is the second most common rheumatic disorder, effecting between 2-8% of the population. (*Id*. at 2.) Fibromyalgia is diagnosed clinically based on subjective symptoms with no known biomarker. (Ann Vincent et al., *Patients with Fibromyalgia have Significant Autonomic Symptoms but Modest Autonomic Dysfunction*, 8(5) PMR 425 (2016) (Ex. 41).)

The first diagnostic criteria for fibromyalgia were released by the American College of Rheumatology in 1990. (Clauw, *supra*, at Ex. 31, p. 3.) These criteria focused on assessing widespread pain by assessing 18 possible tender points. (*Id*.) In 2011, alternative diagnostic criteria were released for epidemiological study. (*Id*.) In addition to assessing tender points, the updated criteria screened for additional symptoms of fatigue, sleep disturbances, memory difficulties, headaches, irritable bowel, and mood problems. (*Id*.) Petitioner has also filed literature suggesting that fibromyalgia patients routinely report additional symptoms across "all domains" that could be characterized as autonomic symptoms, including lightheadedness, palpitations, and sensitivity to light and sound, as well as dizziness and positional

syncope. (Vincent et al., *supra*, at Ex. 41, p. 2; Roland Staud, *Autonomic Dysfunction in Fibromyalgia Syndrome: Postural Orthostatic Tachycardia*, 10 CURRENT RHEUMATOLOGY REPORTS 463 (2008) (Ex. 40).) The same literature further suggests that fibromyalgia patients may be prone to these symptoms due to sedentary behavior and deconditioning. (Vincent et al., *supra*, at Ex. 41, p. 2.)

Notably, these symptoms potentially account for the same symptoms Dr. Miglis identified as diagnostic of orthostatic intolerance. Specifically, in addition to the symptom of orthostatic intolerance itself, Dr. Miglis identified the presence of the following specific symptoms as supporting his opinion that petitioner suffered orthostatic intolerance: chest pain, shortness of breath, exercise intolerance, fatigue, sleep complaints and gastrointestinal symptoms. (Ex. 20, p. 11.) He also, more generally, opined that migraines are common among patients with either POTS or OI. (*Id*. at 6.)

Significantly, Dr. Miglis did stress that in general "the presence of one diagnosis does not invalidate the other." (Ex. 68, p. 2.) Dr. Talman persuasively countered, however, that POTS is "a syndrome and not a unitary diagnosis. It reflects a patient's symptom complex – but that symptom complex can occur with many conditions. Thus, it is a label that can give a physician a false sense of understanding when the underlying condition may be poorly understood, if at all." (Ex. E, p. 2.) This is all the more significant regarding the lesser orthostatic intolerance "diagnosis," which Dr. Miglis himself noted to be "a poorly defined syndrome" believed by many physicians to be functional or psychosomatic. (Ex. 20, p. 4.)

In advancing his opinion, Dr. Miglis cites a study by Parsaik et al., that examined one-hundred patients with orthostatic intolerance and compared them to eighty-four patients meeting the diagnostic criteria for POTS. (Parsaik et al., *supra*, at Ex. 23.) The study found similar, but "minimal," autonomic deficits among the two groups.[49] (*Id*. at 6.) The study authors stressed, however, that compared to POTS, orthostatic intolerance "has remained a nondescript entity." (*Id*.) The authors also noted a "wide spectrum of clinical complaints" that were "disproportionate to the degree of abnormality found on testing." (*Id*.) For this reason, they suggested that the clinical symptoms of the study group (both POTS and orthostatic intolerance groups) could not be explained by autonomic abnormalities alone and may share a common psychologic element. (*Id*.) They noted the etiology of orthostatic intolerance to be "incompletely understood and likely heterogeneous." (*Id*.) This casts doubt on Dr. Miglis's reliance on orthostatic intolerance as an accepted diagnosis in itself. Other literature cited by petitioner obliquely references syndromes of orthostatic intolerance more broadly when discussing POTS, but none of the articles filed in this case sheds any further light on the

[49] The authors stressed that the autonomic dysfunction was "undeniably present, albeit mild." (Parsaik et al., *supra*, at Ex. 23, p. 6.)

specific idea of orthostatic intolerance constituting its own diagnosis nor described any diagnostic criteria or considerations for such a proposed condition. One paper filed by petitioner suggested that orthostatic tachycardia syndrome may actually be explained as chronic fatigue syndrome. (Julian M. Stewart et al., *Patterns of Orthostatic Intolerance: The Tachycardia Syndrome and Adolescent Chronic Fatigue*, 135 J. OF PEDIATRICS 218 (1999) (Ex. 36).)

In contrast, fibromyalgia is a recognized rheumatic diagnosis with published diagnostic criteria.[50] (*See, e.g.*, Clauw, *supra*, at Ex. 31, p. 3.) Additionally, fibromyalgia is better supported by petitioner's medical history. In particular, fatigue, sleep complaints, chest pain, and exercise intolerance were all addressed to Dr. Yalcindag in the context of assessing petitioner and concluding that she has fibromyalgia. (Exs. 11, 86.) In contrast, for the reasons discussed in Section V (a)(iii)-(iv), above, petitioner's medical records do not present any reliable diagnosis of POTS and orthostatic intolerance (as a diagnosis) was never separately assessed. The only time petitioner was ever specifically screened by a cardiologist for POTS (by Dr. Lombardi),[51] there was no evidence of being orthostatic. (Ex. 93, p. 3.) Moreover, despite reporting lightheadedness and dizziness, petitioner has consistently denied experiencing syncope. (Ex. 93, p. 1; Ex. 10, p. 2.) Dr. Talman opined that it is unlikely petitioner would have experienced ancillary symptoms of orthostatic intolerance without also evidencing primary symptoms of autonomic dysfunction, such as syncope. (Ex. C, p. 7.) To the extent petitioner reported dizziness, lightheadedness, or presyncope, it was not consistently characterized in a manner consistent with orthostatic intolerance and is more likely attributable to her diagnosed vestibular migraine disorder.

Accordingly, notwithstanding that petitioner's medical history includes reports of lightheadedness and dizziness of uncertain origin, fibromyalgia, which may potentially have been accompanied by a migraine disorder, is a more likely explanation for petitioner's condition.

---

[50] However, it should also be noted that fibromyalgia is also a clinical syndrome and laboratory testing is generally not considered informative. (Clauw, *supra*, at Ex. 31, p. 3.) One paper filed by petitioner criticizes fibromyalgia as being "ill-defined" and contends that some cases of fibromyalgia are misdiagnosed and better explained as small fiber polyneuropathy. (Anne L. Oaklander et al., *Objective Evidence that Small-Fiber Polyneuropathy Underlies Some Illnesses Currently Labeled as Fibromyalgia*, 154 PAIN 11 (2001) (Ex. 69).)

[51] The first time petitioner went to a cardiologist, it was for an assessment of exercise tolerance relative to her fibromyalgia. Dr. Elgabry administered the tilt table test, but, based on his records, did not otherwise record any assessment of petitioner for POTS.

c. There is not preponderant evidence that fibromyalgia is a disorder of autonomic function

Having concluded that fibromyalgia is a more likely explanation of petitioner's condition, the next question is whether fibromyalgia itself represents an autonomic disorder. In particular, petitioner argues that "small fiber neuropathy has been recently recognized in [complex regional pain syndrome], POTS, and fibromyalgia" and that "small fiber neuropathy could be the common underlying pathogenesis to the group of rare, but severe reactions that follow HPV vaccination. ((ECF No. 50, p. 20) (citing Ex. 70, p. 1).)

Reported symptoms of fibromyalgia have significant overlap with symptoms associated with POTS, orthostatic intolerance, and chronic fatigue syndrome, and have been characterized as appearing to be autonomic in nature. (Vincent et al., *supra*, at Ex. 41, p. 2; Staud, *supra*, at Ex. 40, p. 1; Manuel Martínez-Lavín, *Fibromyalgia-like Illness in 2 Girls After Human Papillomavirus Vaccination*, 20 J. OF CLINICAL RHEUMATOLOGY 392 (2014) (Ex. 51).) On that basis, a 2008 paper appearing in Current Rheumatology Reports speculated on a possible relationship between fibromyalgia and POTS. (Staud, *supra*, at Ex. 40.) The paper acknowledged that POTS is generally considered a primary disorder, even when associated with another disorder such as fibromyalgia, but urged that "[g]iven the similarities between symptoms of [fibromyalgia] and those complaining of orthostatic intolerance, it is reasonable to assume common mechanisms between these conditions." (*Id*. at 2.) The paper noted, in particular, a prior study that demonstrated 60% of fibromyalgia patients experienced either a drop in blood pressure or tachycardia during head-up tilt table testing.[52] (*Id*. at 3.)

Critically, however, more recent literature filed by petitioner examined autonomic function among fibromyalgia patients and found no clinically significant autonomic abnormalities upon objective testing.[53] (Vincent et al., *supra*, at Ex. 41, p. 9.) The study authors observed that prior studies addressing symptoms of autonomic dysfunction

[52] That prior study referenced by Staud is not a part of the record of this case. However, petitioner also filed two additional papers, both by Manuel Martínez-Lavín, that assert without significant explanation that fibromyalgia represents an autonomic disorder. (Martínez-Lavín, *supra*, at Ex. 70; Svetlana Blitshteyn et al., *Autonomic Dysfunction and HPV Immunization: An Overview*, 66 IMMUNOLOGIC RESEARCH 744 (2018) (Ex. 89).) In fact, the first of these two papers forms the basis of petitioner's suggestion that small fiber neuropathy may explain fibromyalgia symptoms. (*See* Martínez-Lavín, *supra*, at Ex. 70, p. 3.) As presented in the record of this case, the assertion appears conclusory, based primarily, if not entirely, on the existence of overlapping symptoms.

[53] This study used a method known as CASS – Composite Autonomic Scoring Scale – to assess autonomic function based on objective data generated by Autonomic Reflex Screening (ARS), which measures quantitative sudmotor axon reflex, heart rate response to deep breathing, heart rate and blood pressure responses to the Valsalva maneuver, and assessment of heart rate and blood pressure response to postural tilt. (Vincent et al., *supra*, at Ex. 41, p. 5.)

among fibromyalgia patients had relied on subjective assessments based on questionnaire. (*Id*.) However, this was the first study to compare these subjective assessments against objective testing data and it found that "[a]lthough patients with fibromyalgia report a high degree of symptoms across all domains, objective measures of autonomic function only showed a modest difference in adrenergic indices in our sample." (*Id*. at 11.) The authors determined that "our data suggest that a majority of fibromyalgia patients have no or only mild autonomic abnormalities" and that "clinically significant levels of autonomic dysfunction may not be present in patients with fibromyalgia with moderate symptom severity." (*Id*. at 9.)

Nonetheless, petitioner also suggests that fibromyalgia may have an autonomic component insofar as it may be related to small fiber neuropathy. (ECF No. 50, p. 20.) Petitioner's supporting materials, however, do not establish that fibromyalgia and small fiber neuropathy have a shared pathophysiology, but only that some fibromyalgia patients may instead have unrecognized small fiber neuropathy. (Oaklander, *supra*, at Ex. 69.) Although the two conditions have symptoms in common, small fiber neuropathy has an established pathophysiology wherein symptoms are caused by degeneration of peripheral axons. (*Id*. at 2.) In contrast, fibromyalgia is believed to represent a "centralized" pain state wherein the central nervous system is responsible for generating or amplifying the pain experienced by the patient. (Oaklander, *supra*, at Ex. 69, p. 2; Clauw, *supra*, at Ex. 31, p. 2.) Thus, the two conditions are considered "distinct." (Oaklander, *supra*, at Ex. 69, pp. 1, 8.)

Unlike fibromyalgia, small fiber neuropathy can be diagnosed with objective testing, including skin biopsy and autonomic testing. (Oaklander, *supra*, at Ex. 69, p. 2.) There is no medical or expert opinion in this case suggesting that petitioner has small fiber neuropathy in preference to fibromyalgia.

d. Positive Test Results for Anti α-1-adrenergic Antibodies, Anti β-2-Adrenergic Antibodies, and Anti-Muscarinic Cholinergic Receptor 4 Antibodies have no Diagnostic Value

Additionally, both as evidence of her diagnosis and as a stand-alone proposition, petitioner asserts that her positive test results for anti α-1-adrenergic Antibodies, anti β-2-adrenergic Antibodies, and anti-Muscarinic Cholinergic Receptor 4 Antibodies, also constitute evidence of an autonomic dysfunction. However, any reliance by petitioner on her adrenergic cholinergic antibody assays as evidence that she suffered POTS, OI, or any other manifestation of autonomic dysregulation, is misplaced. On this record,

there is not sufficient evidence supporting the reliability or diagnostic significance of the results.[54]

As noted in the above medical summary, petitioner underwent testing for certain serum antibodies in late October of 2016. (Ex. 12; Ex. 83, p. 6.) These tests were not recommended by any of petitioner's treating physicians, but were direct to consumer tests by CellTrend GmbH explored at the suggestion of a family friend. (Ex. 83, p. 6.) Based on the reference ranges provided by the testing laboratory, petitioner tested "positive" for anti α-1-adrenergic Antibodies, anti β-2-adrenergic Antibodies, and anti-Muscarinic Cholinergic Receptor 4 Antibodies. (Ex. 12, p. 1.) She tested "at risk" for anti-Muscarinic Cholinergic Receptor 3 Antibodies. (*Id*.)

Notably, however, the test results caution that "each laboratory should determine its own normal and abnormal values."[55] (*Id*.) In that regard, when petitioner presented these test results to Dr. Ramocki (her treating otoneurologist), Dr. Ramocki declined to assign any clinical significance to the findings, explaining that "to the best that I can determine, the antibody panel is not yet something with clinical relevance." (Ex. 83, p. 6.) To the extent any of petitioner's other treating physicians later contemplated a POTS diagnosis, none cited these tests. (Ex. 6, p. 1; Ex. 8, p. 2; Ex. 84, p. 47; Ex. 93, p. 1.)

Moreover, although petitioner's immunology expert, Dr. Shoenfeld, opined that these assay results raise "the likelihood of autonomic dysautonomia," this was discussed in the context of opining that petitioner's condition may be autoimmune. (Ex. 18, p. 21.) Dr. Shoenfeld did not discuss or substantiate the diagnostic value of these tests. In contrast, petitioner's proffered expert for autonomic disorders, Dr. Miglis, opined that "it is important to note that this assay has not been standardized, and the accuracy of these results cannot be validated." (Ex. 20, p. 11.) Respondent's autonomic expert, Dr. Talman, also opined that these test results are not diagnostic.[56] (Ex. C, pp. 5-6.)

---

[54] Petitioner has presented a number of studies purporting to link these antibodies to POTS as a means of demonstrating that some subset of POTS may be autoimmune. (*See* Section VII, below.) However, this is a different question from petitioner's own diagnosis.

[55] To the extent reference ranges were provided, they were based on the "ELISA" method discussed in an article by Loebel et al. (Ex. 12 (citing Madlen Loebel et al., *Antibodies to β Adrenergic and Muscarinic Cholinergic Receptors in Patients with Chronic Fatigue Syndrome*, 52 BRAIN, BEHAVIOR, AND IMMUNITY 32 (2016) (Ex. 30); Ex. 20, p. 11.) That study explored chronic fatigue syndrome, not POTS or OI.

[56] One point initially raised by Dr. Whitton and also endorsed by Dr. Talman was that the single test for these autoantibodies could not demonstrate that the autoantibodies were not also present prior to the vaccinations at issue because petitioner never had any test for these antibodies prior to vaccination. (Ex. A, p. 4; Ex. C, p. 7.) In her motion, petitioner stressed that she "wants to ensure that she is not held to the extremely high burden of needing to present a 'normal' autoantibody test prior to vaccination, as no

Accordingly, for purposes of determining the nature of petitioner's condition and/or her correct diagnosis, I assign no weight to petitioner's positive assay results for anti α-1-adrenergic Antibodies, anti β-2-adrenergic Antibodies, and anti-Muscarinic Cholinergic Receptor 4 Antibodies. There is insufficient evidence supporting the validity or diagnostic significance of these results.

VI. There is not Preponderant Evidence of any "HPV Syndrome"

For all the reasons discussed in Section V, above, there is not preponderant evidence that petitioner suffered POTS, OI, or any other form of autonomic dysfunction as she alleged. But regardless of petitioner's specific diagnosis, it is also necessary to examine petitioner's symptoms through an alternative framework. "The function of a special master is not to 'diagnose' vaccine-related injuries, but instead to determine 'based on the record as a whole and the totality of the case, whether it has been shown by a preponderance of the evidence that a vaccine caused the [petitioner]'s injury.'" *Andreu v. Sec'y of Health & Human Servs*., 569 F.3d 1367, 1382 (Fed. Cir. 2009) (quoting *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 549 (Fed. Cir. 1994)). In that regard, in a status report filed early in the pendency of this case, petitioner also asserted that she meets eight of ten major criteria for an adverse reaction to the HPV vaccine as set forth in certain medical literature seeking to discover an association between the HPV vaccine and such potential adverse reactions.[57] (ECF No. 19 (citing Kazuki Ozawa et al., *Suspected Adverse Effects After Human Papillomavirus Vaccination: A Temporal Relationship Between Vaccine Administration and the Appearance of Symptoms in Japan*, 40 DRUG SAFETY 1219 (2017) (Ex. 16), Ruzieh et

---

medical file would ever have that type of information." (ECF No. 50, p. 29.) I agree with petitioner on this point and note that I am not relying on this aspect of Dr. Talman's opinion; however, Dr. Talman's opinion that the autoantibody tests are not diagnostic was broader than this specific point.

[57] In her status report, petitioner specifically asserted that the relevant "major symptoms" are: (1) prolonged general fatigue; (2) chronic headache, especially after standing up; (3) widespread pain (migratory joint pain, limb pain, or myalgia); (4) limb shaking (tremor or myoclonus); (5) dysautonomic symptoms (orthostatic fainting, postural orthostatic tachycardia, or delayed or rapid gastrointestinal motility); (6) Motor dysfunction (frequent sudden falls, limb weakness or paralysis, gait disturbance); (7) abnormal sensation (coldness in limbs, limb paresthesia, photophobia); (8) Sleep disturbance (hypersomnia, insomnia); (9) Learning impairment (memory impairment, difficulties in concentration, verbal dyspraxia); (10) menstrual abnormality (amenorrhea, hypermenorrhea, irregular menstruation). (ECF No. 19.) These are based on the parameters used in the Ozawa study (filed as Exhibit 16), which is discussed below. Petitioner asserts that she had all of these symptoms except limb shaking and learning impairment. (ECF No. 19, pp. 2-3.) Upon my review of the records, there is not preponderant evidence supporting that assertion. In particular, for all the reasons described above, there is not preponderant evidence that petitioner had dysautonomia symptoms. Moreover, I do not see preponderant evidence of motor dysfunction or any significant menstrual abnormality. Additionally, petitioner's records raise questions as to some of the other symptoms. For example, petitioner was advised that her difficulty sleeping may be due to poor sleep hygiene. (Ex. 7, p.1.)

al., *supra*, at Ex. 17).) This type of adverse reaction has likewise been characterized as a form of dysautonomia. (Martínez-Lavín, *supra*, at Ex. 70.)

Still, petitioner must "specify [her] vaccine-related injury and shoulder the burden of proof on causation." *Broekelschen*, 618 F.3d at 1346. "Although the Vaccine Act does not require absolute precision, it does require the petitioner to establish an injury – the Act specifically creates a claim for compensation for 'vaccine-related injury or death.'" *Stillwell v. Sec'y of Health & Human Servs*., 118 Fed. Cl. 47, 56 (2014) (quoting 42.U.S.C. § 300aa-11(c)). Although petitioner later filed literature positing the existence of something referred to as "HPV syndrome" (Manuel Martínez-Lavín, Laura-Aline Martínez-Martínez & Paola Reyes-Loyola, *HPV Vaccination Syndrome. A Questionnaire-Based Study*, 34 CLINICAL RHEUMATOLOGY 1981 (2015) (Ex. 50); Martínez-Lavín, *supra*, at Ex. 70), on review of the complete record, I am not persuaded that there is preponderant evidence establishing "HPV syndrome" as a cognizable injury.

In advancing the concept of HPV Syndrome, the literature submitted by petitioner, particularly by Blitshteyn, stresses that prior cases have shown "symptom clusters [that] are remarkably similar and include disabling fatigue, headache, widespread pain, fainting, gastrointestinal dysmotility, limb weakness, memory impairment episodes of altered awareness, and abnormal movements." (Svetlana Blitshteyn et al., *Autonomic Dysfunction and HPV Immunization: An Overview*, 66 IMMUNOLOGICAL RESEARCH 744 (2018) (Ex. 89).) However, these symptom "clusters" are not well established. That is, it is not clear that all studied individuals report all, or even most, of the symptoms discussed. Moreover, many of those symptoms that are shared are non-specific. Thus, it appears as though reports of adverse events are being grouped together in a conclusory manner.

For example, in the above-discussed article by Blitshteyn et al., the authors cite thirteen prior papers[58] reporting on a variety of different conditions as evidence of previously reported adverse effects of the HPV vaccine. (Blitshteyn et al., *supra*, at Ex. 89, pp. 2, 9, refs. 6-18.) Among these thirteen citations are both a single case report by Blitshteyn of a diagnosis of POTS and a case report by Martínez-Lavín of two girls presenting with fibromyalgia. (Blitshteyn et al., *supra*, at Ex. 89, p. 9; *see also* Svetlana Blitshteyn, *Postural Tachycardia Syndrome After Vaccination with Gardasil*, 17 EUROPEAN J. OF NEUROLOGY (2010) (Ex. 38), Martínez-Lavín, *supra*, at Ex. 51.) In the former case, the primary symptoms were related to orthostatic intolerance confirmed by tilt table test (Blitsheyn, *supra*, at Ex. 38) while in the latter two cases the primary symptoms were related to widespread pain and paresthesia typical of fibromyalgia (Martínez-Lavín, *supra*, at Ex. 51). Apart from the non-specific symptom of fatigue, the

[58] Some, but not all, of these papers have been filed into the record of this case.

cases share no evident commonality. A different case report by Blitshteyn identified two out of six subjects as having paresthesia and only one as reporting limb pain. (Blitsheyn et al., *supra*, at Ex. 89, p. 9, ref 11; Svetlana Blitshteyn, *Postural Tachycardia Syndrome After Vaccination with Gardasil*, 21 EUROPEAN J. OF NEUROLOGY 136 (2014) (Ex. 24).)

Another of the cited studies, Kinoshita et al., followed forty Japanese adolescent girls. (Blitsheyn et al., *supra*, at Ex. 89, p. 9 (citing Tomomi Kinoshita et al., *Peripheral Sympathetic Nerve Dysfunction in Adolescent Japanese Girls Following Immunization with the Human Papillomavirus Vaccine*, 54 INTERNAL MEDICINE 1955 (2015) (Ex. 25)).) However, of all the examined symptoms, only headaches (70%), general fatigue (53%), and coldness of the legs (53%), were reported by a majority of the subjects. (Kinoshita et al., *supra*, at Ex. 25, p. 2.) Limb pain was reported by exactly half of the subjects. The remaining symptoms of limb weakness, difficulty getting up, orthostatic fainting, decreased ability to learn, arthralgia, limb tremors, gait disturbances, disturbed menstruation, and dizziness, were reported by only a minority of the subjects. (*Id*.) A larger study (Ozawa et al.) was later completed with a population of 120 subjects. (Ozawa et al., *supra*, at Ex. 16.) That study found a greater degree of commonality of symptoms among subjects deemed "diagnosed," "definite," or "probable," but also had a population of forty-eight cases that remained "undiagnosed" with fewer commonality of symptoms. (Ozawa et al., *supra*, at Ex. 16, p. 5, Table 2.) Moreover, that study had developed a new set of diagnostic criteria specifically for purposes of screening subjects for the study. Accordingly, they cautioned of their diagnostic criteria that "their validity and reliability have not been established." (*Id*. at 3.) One Danish cohort study had much higher prevalence of relevant symptoms. (Louise S. Brinth et al., *Suspected Adverse Effects of Vaccination Against Human Papilloma Virus*, 62 DANISH MEDICAL J. 4 (2015) (Ex. 48).) However, that study has been criticized for choosing its subjects to fit the pre-specified hypothesis of an HPV vaccine-induced illness and lacking any control group. (Alexandru Barboi et al., *Human Papillomavirus (HPV) Vaccine and Autonomic Disorders: A Position Statement from the American Autonomic Society*, CLINICAL AUTONOMIC RESEARCH (Sep. 2, 2019) (Ex. G).) Accordingly, the authors acknowledged that the study does not confirm any link to the HPV vaccine. (Brinth et al., *supra*, at Ex. 48, p. 4.)

An additional significant issue is that many of these studies rely at least in part on subjective self-reporting questionnaires to record the purported autonomic symptoms. (*See, e.g.*, Ozawa, *supra*, at Ex. 16; Louise S. Brinth et al., *Orthostatic intolerance and postural tachycardia syndrome as suspected adverse effects of vaccination against human papilloma virus*, 33 VACCINE 2602 (2015) (Ex. 26); Brinth et al., *supra*, at Ex. 48;

Martínez-Lavín, *supra*, at Ex. 50.)[59] Several papers filed in this case, however, demonstrate that autonomic symptoms are prone to exaggerated self-reporting that cannot be correlated to objective findings. (*See, e.g.*, Vincent et al., *supra*, at Ex. 41 (explaining that "[p]atients with fibromyalgia report more severe symptoms across all domains including physical activity and autonomic symptoms when compared to controls, but the objective assessments only showed modest differences."); Parsaik et al., *supra*, at Ex. 23 (explaining of POTS and OI that "[a]s the wide spectrum of clinical complaints is generally disproportionate to the degree of abnormality found on testing, it cannot be completely explained by the autonomic abnormalities, suggesting that the two disorders may share a psychologic substrate or overlay."); Oaklander et al., *supra*, at Ex. 69 (describing small fiber neuropathy as presenting complaints of chronic widespread pain that are "subjective and nonspecific" and noting that quantitative sensory testing is not recommended for diagnosis of the condition because it relies on subjective report).) And, indeed, one of these studies – Martínez-Lavín et al., noted that "[t]he clear limitation of our study is the lack of direct medical examination of affected individuals." (Martínez-Lavín et al., *supra*, at Ex. 50, p. 3.)

Further, "[t]his constellation of symptoms and signs has been labeled with different diagnoses such as complex regional pain syndrome (CRPS), postural orthostatic tachycardia syndrome (POTS), small fiber neuropathy (SFN), myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), or fibromyalgia." (Blitsheyn et al., *supra*, at Ex. 89, p. 1.) However, casting further doubt on the association of these various symptoms is the fact that, notwithstanding the assumption that all of the implicated conditions involve autonomic activity, there is little or no substantiation of any shared pathophysiology. For example, as noted above, fibromyalgia is likely a centralized pain state originating with the central nervous system while small fiber neuropathy impacts peripheral nerves. (Oaklander et al., *supra*, at Ex. 69, p. 2; Clauw, *supra*, at Ex. 31, p. 2.) The pathophysiology of POTS is unknown and may be heterogeneous. (Freeman et al., *supra*, at Ex. 22, p. 4.) Accordingly, I do not see a basis in the supporting literature for discarding these other established diagnoses in favor of a novel syndrome of vaccine reaction.[60] Of note, a more recent study following on from the Kinoshito study failed to detect any statistically meaningful association between clinical symptoms and positive serum autoantibody tests among girls complaining of post-HPV vaccine adverse effects, including orthostatic dysregulation

[59] The Danish study (Brinth et al. *supra*, at Ex. 48) indicated that subjects were interviewed and that the interviews were supplemented with the International Physical Activity Questionnaire (IPAQ-SF).

[60] Notably, the diagnoses of POTS and fibromyalgia, in particular, are not beyond debate. Nonetheless, each is separately studied in the context of a specific medical discipline and are subject to established, regularized diagnostic criteria. (Satish R. Raj, *Postural Tachycardia Syndrome (POTS)*, 127 CIRCULATION 2336 (2013) (Ex. 32); Clauw, *supra*, at Ex. 31, p. 2.)

and complex regional pain syndrome. (Shu-Ichi Ikeda et al., *Autoantibodies Against Autonomic Nerve Receptors in Adolescent Japanese Girls after Immunization with Human Papillomavirus Vaccine*, 2 ARTHRITIS AND CLINICAL RHEUMATOLOGY 1014 (2019) (Ex. 95).)

And, finally, to the extent these studies and case reports largely focus on a temporal relationship between vaccination and onset of these symptoms, it has been acknowledged that onset can be difficult to establish, and the association appears weak. In the largest of these studies, which is itself only 120 subjects,[61] the observed period of onset from the first dose of the HPV vaccine "showed a wide range (average 319.7 [plus or minus] 349.3 days)."[62] (Ozawa et al., *supra*, at Ex. 16, p. 2.) Also significant, many of these overlapping conditions have a higher prevalence among adolescent women (who tend to be the focus of these study populations) than the general population and these conditions are far from unique to HPV recipients. Vaccination has been identified as a potential trigger in only 4% of POTS cases. (Blitsheyn et al., *supra*, at Ex. 89, p. 3.) However, POTS is a condition affecting 500,000 individuals in the U.S. alone and is most common in young women, with a female to male ration of 5:1. (Hongliang Li et al., *Autoimmune Basis for Postural Tachycardia Syndrome*, 3 J. OF THE AMERICAN HEART ASSOCIATION (2014) (Ex. 42); Brinth et al., *supra*, at Ex. 26, p. 2.) Fibromyalgia is the second most common rheumatological injury, effecting between 2-8% of the population. (Clauw, *supra,* at Ex. 31, p. 2.) It often begins in adolescence and affects women three to four times more than men. (Clauw, *supra*, at Ex. 31, p. 2; Oaklander et al., *supra*, at Ex. 69, p. 2.) Chronic Fatigue Syndrome has a lower, but still frequent, prevalence of 0.2-0.3% of the population. (Madlen Loebel et al., *Antibodies to β adrenergic and muscarinic cholinergic receptors in patients with Chronic Fatigue Syndrome*, 52 BRAIN, BEHAVIOR, AND IMMUNITY 32 (2016) (Ex. C, Tab. 12, p. 1).)[63] Indeed, citing to a number of much larger population studies, the American Autonomic Society has concluded that "the data do not support a causal relationship between HPV vaccination and CRPS, POTS, or other forms of dysautonomia."[64] (Barboi et al., *supra*, at Ex. G, p. 3.)

---

[61] In fact, 163 subjects were screened for the study, but 43 were excluded, leaving 120 subjects. (Ozawa et al., *supra*, at Ex. 16, p. 1.)

[62] The study excluded 15 subjects due to having onset prior to vaccination. (Ozawa et al., *supra*, at Ex. 16, p. 3.)

[63] Petitioner also filed the same article as Exhibit 30.

[64] Petitioner challenges the credibility of this document as a "consensus statement" for a number of reasons, but did not suggest that the underlying studies themselves were mischaracterized. (ECF No. 71.) Respondent's expert, Dr. Whitton, also addressed the fact that large-scale studies have failed to detect a causal relationship between HPV vaccine and either autoimmune diseases or POTS. (Ex. A, pp. 9-11.)

Upon my review of the complete record,[65] I do not find preponderant evidence of any HPV Syndrome or that the above-discussed literature, considered individually or as a whole, provides a basis for petitioner to assert a claim for an adverse reaction to her HPV vaccine. The Federal Circuit has stated:

> Although *Althen* and *Capizzano* make clear that a claimant need not produce medical literature or epidemiological evidence to establish causation under the Vaccine Act, where such evidence is submitted, the special master can consider it in reaching an informed judgment as to whether a particular vaccination likely caused a particular injury. . .. Medical literature and epidemiological evidence must be viewed, however, not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard.

Andreu, 569 F.3d at 1380 (referencing *Althen*, 418 F.3d 1274; *Capizzano v. Sec'y of Health & Human Servs.,* 440 F.3d 1317 (Fed. Cir. 2006)). As one of the papers filed by petitioner concludes: "[o]ur findings do not confirm or dismiss a causal link to the HPV-vaccine – but suggest that further research is urgently warranted in order to clarify the pathophysiology of the symptoms experienced, [and] elucidate the probability and nature of a causal link to the vaccine . . ." (Brinth et al., *supra*, at Ex. 26, p. 4.)

VII. *Althen* Prong 1 - Petitioner's Theory of Causation

Under *Althen* prong one, petitioner must provide a "reputable medical theory," demonstrating that the vaccine received can cause the type of injury alleged. *Pafford v. Sec'y of Health & Human Servs.*, 451 F.3d 1352, 1355–56 (Fed. Cir. 2006) (citations omitted). Such a theory must only be "legally probable, not medically or scientifically certain." *Id.* at 549. Petitioner may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu*, 569 F.3d at 1367 (citing *Capizzano,* 440 F.3d at 1325–26). However, "[a] petitioner must provide a 'reputable medical or scientific explanation' for [her] theory. While it does not require medical or scientific certainty, it must still be 'sound and reliable.'" *Boatmon v. Sec'y of Health & Human Servs.,* 941 F.3d 572 (Fed. Cir. 2019) (quoting *Knudsen*, 35 F.3d at 548-49).

---

[65] Notably, in addition to the above-discussed literature, Dr. Shoenfeld also cited a number of reports from the VAERS database. (Ex. 18, p. 22, 26-39.) Dr. Whitton observed, however, that the existence of a VAERS report does not indicate causation and that no denominator is available (*i.e.* the number of vaccines administered to generate this number of reports). (Ex. A, p. 6.) Accordingly, these VAERS reports constitute only isolated case reports. "[C]ase reports 'do not purport to establish causation definitively, and this deficiency does indeed reduce their evidentiary value'…. [but] 'the fact that case reports can by their nature only present indicia of causation does not deprive them of all evidentiary weight.'" *See Paluck v. Sec'y of Health & Human Servs.,* 104 Fed. Cl. 457, 475 (2012) (quoting *Campbell v. Sec'y of Health & Human Servs.*, 97 Fed. Cl. 650, 668 (2011)).

In this case, petitioner's theory of causation is based on a number of interrelated concepts and ideas, endorsed by both her experts, but largely discussed by Dr. Shoenfeld. And, indeed, petitioner conceptualizes her claim in two distinct ways. First, she contends, as she explained in her motion for a ruling on the record, that she suffers a diagnosed autonomic dysfunction (either POTS, OI, or fibromyalgia) that she can demonstrate to be vaccine-caused. (*See, e.g.*, ECF No. 50, pp. 19-20.) Second, as she previously explained in a status report earlier in the case, she contends that, regardless of diagnosis, there is evidence of adverse reactions to HPV constituting something of an HPV-vaccine syndrome likely implicating the autonomic nervous system. (ECF No. 19.)

There is little question, however, that petitioner's theory is predicated on the notion that petitioner has some form of autonomic dysfunction and that autonomic dysfunction can be demonstrated to be autoimmune. (*See, e.g*. ECF No. 50, p. 34 (explaining in conclusion that petitioner "satisfied the first prong of *Althen*, as she has set forth a biologically plausible theory establishing that POTS can have an autoimmune basis, and that through either molecular mimicry, epitope spreading, or bystander activation, the HPV vaccine can induce an autoimmune response resulting in OI, fibromyalgia, and autonomic dysfunction.").) The theory can be broken down as follows:

- First, petitioner contends that there is sufficient evidence establishing that POTS is autoimmune. This is based on both studies examining autoantibodies against adrenergic and cholinergic receptors among POTS patients as well as a purported predisposition among those with POTS toward autoimmune conditions. (Ex. 18, p. 13; Ex. 20, pp. 10-11.)
- Second, there is substantial overlap of several conditions believed to be related to autonomic dysfunction, including POTS, orthostatic intolerance, and chronic fatigue syndrome, suggesting that evidence of autoimmunity in POTS is significant to all of these conditions. (Ex. 18, p. 11-12; Ex. 20, pp. 10-11.)
- Third, and relatedly, fibromyalgia patients demonstrate many symptoms that are consistent with autonomic dysfunction and it is reasonable to conclude that fibromyalgia shares an underlying etiology with POTS and other autonomic disorders. (Ex. 18, p. 12.)
- Fourth, studies exploring adverse effects of the HPV vaccine have detected post-vaccination symptoms among HPV vaccines that are consistent with the symptoms of autonomic dysfunction, including POTS, orthostatic intolerance, and fibromyalgia. (Ex. 18, pp.13-18.)
- Fifth, a "proof of concept" paper has demonstrated cross-reactivity between human proteins and HPV 16, providing a potential basis for molecular mimicry. (Ex. 18, pp. 20-21.)
- And, finally, the presence of alum adjuvant may lead to a hyperimmune response that, in connection with molecular mimicry, may break self-tolerance and cause an autoimmune disorder. (Ex. 18, pp. 18-21.)

For the reasons described in Section V, above, however, I have concluded that there is not preponderant evidence that petitioner experienced any autonomic dysfunction. Instead, I concluded that the evidence preponderates in favor of finding that petitioner suffered fibromyalgia and vestibular migraines as diagnosed by her treating physicians. In Section V(c), I further found that there is not preponderant evidence that fibromyalgia is an autonomic condition (or that it is related to small fiber neuropathy). Additionally, in Section VI, I determined that there is not preponderant evidence of any HPV-vaccine syndrome that could explain petitioner's alleged post-vaccination symptoms. Accordingly, petitioner's stated theory of causation is largely inapplicable to her own condition. Petitioner has not articulated any causal theory that directly links the HPV vaccine to fibromyalgia and/or vestibular migraines without relying on either the alleged commonality between fibromyalgia and autonomic disorders such as POTS or the existence of a novel HPV-vaccine syndrome.

Moreover, to the extent much of petitioner's theory is predicated, regardless of the specific diagnosis, on extrapolation from the autoimmune nature of POTS in particular, the literature cited by petitioner makes clear that only preliminary evidence exists regarding this hypothesis. The search for an autoimmune basis for POTS has examined several possible autoantibodies. (S. Dahan, L. Tomljenovic & Y. Shoenfeld, *Postural Orthostatic Tachycardia Syndrome (POTS) – A Novel Member of the Autoimmune Family*, 25 LUPUS 339 (2016) (Ex. 43); Svetlana Blitshteyn & Jill Brook, *Autoimmune Markers and Autoimmune Disorders in Patients with Postural Tachycardia Syndrome (POTS)*, 24 LUPUS 1364 (2015) (Ex. 44); Svetlana Blitshteyn & Jill Brook, *Postural Tachycardia Syndrome (POTS) with Anti-NMDA Receptor Antibodies After Human Papillomavirus Vaccination*, 65 IMMUNOLOGIC RESEARCH 282 (2016) (Ex. 49); Steven Vernino et al., *Prevalence of Ganglionic AChR Antibodies in Postural Tachycardia Syndrome (POTS)*, 84 NEUROLOGY 276 (2015) (Ex. 81); William T. Gunning et al*., Postural Orthostatic Tachycardia Syndrome is Associated with Elevated G-Protein Coupled Receptor Autoantibodies*, 8 J. OF THE AMERICAN HEART ASSOCIATION (2019) (Ex. 94).) However, the most widely suspected antibodies appear to be adrenergic and cholinergic antibodies. Petitioner's experts cite a number of studies from 2006 to 2016 that have shown the presence of adrenergic and cholinergic antibodies in higher proportions among POTS and OI subjects than among controls.[66]

[66] Petitioner also filed two additional, more recent, studies pertaining separately to chronic fatigue syndrome and adrenergic receptor antibodies (Scheibenbogen et al.) and chronic fatigue syndrome and aluminum adjuvant (Gherardi et al.). (*See* ECF No. 59; Romain K. Gherardi, Guillemette Crépeaux & François-Jérome Authier, *Myalgia and Chronic Fatigue Syndrome Following Immunization: Macrophagic Myofasciitis and Animal Studies Support Linkage to Aluminum Adjuvant Persistency and Diffusion in the Immune System*, 18 AUTOIMMUNITY REVIEWS 691 (2019) (Ex. 90); Carmen Scheibenbogen et al., *Immunoadsorption to Remove ß2 Adrenergic Receptor Antibodies in Chronic Fatigue Syndrome CFS/ME*, 13 PLOS ONE e0193672 (2018) (Ex. 91).) Petitioner noted the latter study to contain a further reference to adrenergic and muscarinic receptors playing a role in clinical manifestation of POTS and chronic fatigue syndrome. (ECF No. 59, p. 2 (quoting Gherardi, Crépeaux & Authier, *supra*, at Ex. 90).) In a supplemental report devoted entirely to petitioner's Notice of Additional Authority, Dr. Whitton questioned the relevance of Gherardi et al., and persuasively addressed the shortcoming of the Schiebenbogen

(Li et al., *supra*, at Ex. 42); Artur Fedorowski et al., *Antiadrenergic Autoimmunity in Postural Tachycardia Syndrome*, 19 EP EUROPACE 121 (2016) (Ex. 77); Pablo A. Chiale et al., *Inappropriate sinus tachycardia may be related to an immunologic disorder involving cardiac β andrenergic receptors*, 3 Heart Rhythm 1182 (2006) (Ex. 78); Xichun Yu et al., *Autoantibody Activation of Beta-Adrenergic and Muscarinic Receptors Contributes to an "Autoimmune" Orthostatic Hypotension*, 6 J. OF THE AMERICAN SOCIETY OF HYPERTENSION 40 (2012) (Ex. 79).)

A review study cited by Dr. Miglis summarizes the state of this research. Consistent with my review of the studies filed in this case (which have study populations ranging from six to twenty-five subjects), that review notes that smaller studies have consistently shown a correlation between adrenergic and cholinergic receptor antibodies and orthostatic intolerance. (Ruzieh et al., *supra*, at Ex. 17, p. 5.) However, further large-scale studies are lacking and are warranted. (*Id.*) The authors note that to date, the available literature supports only the hypothesis that adrenergic and cholinergic autoantibodies may play a role in the pathogenesis of orthostatic intolerance syndromes. As of yet, "[t]hese autoantibodies do not explain the complex pathophysiology of orthostatic intolerance syndromes." (*Id.*) Indeed, one study of fifty-five Japanese adolescents sought to examine the presence of these antibodies among girls who had complained of adverse effects following HPV vaccination. (Ikeda et al., *supra*, at Ex. 95.) Although the researchers found the autoantibodies to be significantly elevated compared to controls, they observed that "there was no statistically meaningful association between clinical symptoms and elevated serum levels of these antibodies." (*Id*. at 1.)

Another recent article later filed by petitioner (without remark from her experts) further explains that "[t]here remains a paucity of knowledge of the autoimmune basis of POTS, due in part to a lack of commercially available laboratory testing and due in part to a lack of comprehensive knowledge about the putative autoantigen targets." (Blitsheyn et al., *supra*, at Ex. 89, p. 4.) As Dr. Miglis noted regarding petitioner's own autoantibody assay, this paper similarly stresses the lack of any certified test for α or β adrenergic receptor antibodies in the United States. (*Id.*) Significantly, one study separately filed by both parties indicated that while studying antibodies to β adrenergic and muscarinic cholinergic receptors in patients with chronic fatigue syndrome, they also found these antibodies to be elevated in the controls as well. (Loebel et al., *supra*, at Ex. 30, p. 4, and Ex. C, Tab 12, p. 4.) Respondent urged that this must cast doubt on the validity of testing for these antibodies, though petitioner disputes that this is significant. (ECF No. 54, p. 22 (citing Dr. Talman's opinion at Ex. C, p. 7); ECF No. 55, p. 5.)

Notably, there have been a number of prior decisions from other special masters addressing and rejecting causal theories linking the HPV vaccine to POTS and/or

---

study, including small study population, lack of any control group, and mixed findings among the subjects. (Ex. F.)

autonomic nervous system dysfunction. *See, e.g., Johnson v. Sec'y of Health & Human Servs.*, No. 14-254V, 2018 WL 2051760 (Fed. Cl. Spec. Mstr. Mar. 23, 2018); *Combs v. Sec'y of Health & Human Servs.*, No.14-878V, 2018 WL 1581672 (Fed. Cl. Spec. Mstr. Feb. 15, 2018); *L.A.M. v. Sec'y of Health & Human Servs.*, No. 11-852V, 2017 WL 527576 (Fed. Cl. Spec. Mstr. Jan. 31, 2017); *Turkopolis v. Sec'y of Health & Human Servs.*, No. 10-351V, 2014 WL 2872215 (Fed. Cl. Spec. Mstr. May 30, 2014). Petitioner acknowledges this, noting in particular the previously-assigned special master's decision in *Turkopolis*, but nonetheless argues that "since 2014, there has been an explosion of medical literature regarding the autoimmune basis for POTS, and autonomic dysfunction following the HPV vaccination. (ECF No. 50, p. 17.) Distinguishing the previously-assigned special master's *Turkopolis* decision, petitioner stresses in particular the presence in this record of articles by Ozawa, Ruzieh, Li, Kinoshita, Brinth, Blitshteyn, Fedoroswki, and Dahan. (*Id*. at 18.) I have reviewed these articles, but do not find them persuasive for all the reasons discussed herein.

In sum, I do not find preponderant evidence of a reliable medical theory causally connecting petitioner's HPV vaccinations to either POTS generally or her own fibromyalgia and/or vestibular migraines in particular. Accordingly, petitioner has not met her burden under *Althen* prong one.[67]

VIII. *Althen* Prong 2 – Logical Sequence of Cause and Effect

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375–77; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). Here, for all the reasons described in Section V, above, there is not preponderant evidence that petitioner suffered POTS, orthostatic intolerance, or any other autonomic dysfunction. Moreover, none of petitioner's treating physicians attributed her fibromyalgia, vestibular migraines, or any other aspect of petitioner's condition to her vaccination.[68] Even assuming *arguendo* that many of petitioner's symptoms developed close in time to her vaccination, a temporal association alone would be insufficient to meet her burden of proof. Additionally, for the reasons described in Section VI, above, the mere allegation that petitioner demonstrated a collection of symptoms consistent with those studied in Ozawa et al., is insufficient to establish the presence of an adverse reaction to the HPV vaccine. For all these reasons, I find that petitioner has not met her burden under *Althen* prong two.

[67] Because the foregoing includes threshold issues for petitioner's theory, I need not reach Dr. Shoenfeld's further assertions regarding molecular mimicry and aluminum adjuvants.

[68] To be sure, some physicians recorded petitioner's reports that she believed her condition to have been caused by her HPV vaccines (*see, e.g.,* Ex. 8, p. 28; Ex. 11, p.1); however, none opined that this was so.

IX. *Althen* Prong 3 – Medically Appropriate Timeframe

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must also coincide with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id.* at 1352; *Shapiro v. Sec'y of Health & Human Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. den'd after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 503 Fed. Appx. 952 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Human Servs.*, No. 11–355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for review den'd* (Fed. Cl. 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

As a threshold matter, petitioner's mother asserted in her sworn statement that petitioner experienced flu-like symptoms within hours to a day of receipt of each of her two doses of HPV vaccine. (Ex. 1, pp. 1-2.) In her earlier handwritten timeline, petitioner's mother recorded flu-like symptoms after the first dose. (Ex. 92, p. 1.) However, this assertion is not substantiated by petitioner's contemporaneous medical records nor has it been persuasively linked to her fibromyalgia or vestibular migraines. With regard to her overall condition, petitioner stresses that the type of injury she suffered is notable for insidious onset. (ECF No. 55, p. 8.) She also notes that her early treatment history was focused on visits with inner-ear specialists due to her history of hearing loss, which is unrelated to her condition. (*Id.*) This does make it more difficult to determine the precise onset of the symptoms that ultimately constitute her fibromyalgia.

By the time petitioner first saw a rheumatologist in May of 2016, her History of Present Illness makes clear that she had already attributed her condition to her vaccinations. (Ex. 11, p. 1.) Thus, the history she provided suggests that her condition, inclusive of initial symptoms of headaches and vertigo, began after her first HPV vaccine. (*Id.*) Earlier records, however, are inconsistent. The first time petitioner reported dizziness to Dr. Andreozzi, she reported it in the context of a one-and-a half year history of fluctuating hearing loss (i.e. beginning mid-2013). (Ex. 8, p. 32.) This places onset well before she received her first HPV vaccine. However, shortly thereafter, the first time she saw Dr. Ramocki, she reported onset in August or September of 2014, which is shortly after her first HPV vaccination. (Ex. 4, p. 24.) Joint pain was not reported until February of 2016, at which point the onset is not clearly described. (Ex. 8, p. 20.) Petitioner's mother's handwritten timeline and sworn statement place onset of fatigue and joint/muscle pain in December of 2014. (Ex. 1, p. 2; Ex. 92, pp. 2-3.)

Viewing the record as a whole, it appears more likely than not that onset of petitioner's fibromyalgia was no earlier than December of 2014, which falls approximately four months after her first HPV vaccination and one and a half to two months after her second dose of HPV vaccine. Onset of her vestibular migraines was earlier and occurred in August of 2014 at the latest, but likely before given the history provided to Dr. Andreozzi.

Critically, however, petitioner's experts were entirely unpersuasive in identifying any medically relevant period of onset. Dr. Miglis's opinion as to the timing of petitioner's condition was never more specific than noting that she was asymptomatic prior to vaccination, which is a questionable assumption given Dr. Andreozzi's above-referenced record. (Ex. 20, pp. 11-12; Ex. 68, p. 7.) Dr. Shoenfeld opined that post-vaccination adverse immune phenomena can have a variably latency of up to ten months. (Ex. 18, p. 16.) However, he addressed this only in the context of demyelinating conditions which are not relevant to this case. (*Id*. (citing Charles M. Poser & Peter O. Behan, *Late Onset of Guillan-Barre Syndrome*, 3 J. OF NEUROIMMUNOLOGY 27 (1982) (Ex. 52)).) Isolated case reports cited by Dr. Shoenfeld identified fibromyalgia developing within four weeks of the HPV vaccine, which is a shorter latency than what would be present in this case. (Ex. 18, p. 15 (citing Martínez-Lavín, *supra*, at Ex. 51, p. 1).) Otherwise, Dr. Shoenfeld did not separately address the appropriate latency period for an alleged post-vaccination fibromyalgia.

With regard to post-HPV vaccine reactions, Dr. Shoenfeld noted that Ozawa et al., observed onset ranging from one to 1,532 days. (Ex. 18, p. 17 (citing Kazuki Ozawa et al., *Susptected Adverse Effects After Human Papillomavirus Vaccination: A Temporal Relationship Between Vaccine Administration and the Appearance of Symptoms in Japan*, 40 DRUG SAFETY 1219 (2017) (Ex. 53).[69]) He also observed that the Ozawa authors noted a prior study to have reported an onset period of one day to 43 months. (*Id*.) Based on this, he noted the average interval from first vaccination to be 319.5 days. (Ex. 18, pp. 17-18.) However, especially in light of the issues identified in Section VI, above, neither Dr. Shoenfeld nor the cited studies offer adequate explanation for why symptoms developing over three years after a vaccination could be causally linked to that vaccination and, accordingly, why the average interval of 319.5 days is valid.[70]

[69] This is the same article filed as Exhibit 16.

[70] In contrast, a different study cited by petitioner sought questionnaire responses from 45 subjects who suspected that they had experienced a post-HPV vaccine reaction similar to what was examined by Ozawa et al. (Martínez-Lavín, Martínez- Martínez & Reyes-Loyola, *supra*, at Ex. 50.) In that study, respondents reported a mean onset of 2.3 weeks, plus or minus 3.1 weeks. (*Id*.) Twenty-nine percent of respondents reported onset within 24 hours. (*Id*.) Dr. Shoenfeld included a table in his report identifying prior case reports of post-HPV vaccine POTS. (Ex. 18, p. 24.) With the exception of four cases examined by Kinoshita et al., all of the cited cases had onset occurring within two months of vaccination. (*Id*.) A two-month period of onset could arguably support a temporal relationship in this case relative to the onset of petitioner's fibromyalgia following her second HPV vaccine; however, these are small studies

For all these reasons, I am not persuaded that petitioner has established by preponderant evidence that her alleged injury occurred within what would be a medically appropriate timeframe to infer causation. Accordingly, petitioner has not met her burden under *Althen* prong three.

X. Conclusion

Undoubtedly, petitioner has endured a prolonged medical setback that greatly interfered with what had been an active and seemingly happy adolescence. Moreover, the search for a clear diagnosis was very difficult. For these reasons she has my sympathy. However, for all the reasons discussed above, after weighing the evidence of record within the context of this program, I cannot find by preponderant evidence that petitioner suffered a vaccine-caused injury related to either her August 4, 2014 or October 16, 2014 Gardasil vaccinations. Therefore, this case is dismissed.[71]

IT IS SO ORDERED.

s/Daniel T. Horner
Daniel T. Horner
Special Master

and isolated case reports. On the whole, it does not appear that a period of onset for the type of adverse vaccine reaction hypothesized by Ozawa et al. (and others) has been fully elucidated.

[71] In the absence of a timely-filed motion for review of this Decision, the Clerk of the Court shall enter judgment accordingly.