In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 14-442V

Filed: March 9, 2020

ANGELA ALLARD,	*	TO BE PUBLISHED
Petitioner,	*	
v.	*	Dismissal; Ruling on the Record; Human Papillomavirus ("HPV") Vaccine; Idiopathic Thrombocytopenic Purpura ("ITP")
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	

Mark Sadaka, Esq., Mark T. Sadaka, LLC, Englewood, NJ, for petitioner.
Debra Begley, Esq., U.S. Department of Justice, Washington, DC, for respondent.

DECISION[1]

Roth, Special Master:

On May 23, 2014, Angela Allard ("Ms. Allard" or "petitioner") filed a petition for compensation pursuant to the National Vaccine Injury Compensation Program.[2] Petitioner alleges that she received a human papillomavirus ("HPV") vaccination on June 2, 2011, and thereafter suffered from idiopathic thrombocytopenic purpura ("ITP"), which was either caused or significantly aggravated by the HPV vaccine. *See* Petition ("Pet."), ECF No. 1. On November 15, 2018, petitioner filed a Motion for Ruling on the Record. ECF No. 88. After careful review of the record, I find that petitioner has failed to carry her burden of showing that the HPV vaccination caused or significantly aggravated her ITP. The petition is accordingly dismissed.

[1] This Decision has been designated "to be published," which means I am directing it to be posted on the Court of Federal Claims's website, in accordance with the E-Government Act of 2002, Pub. L. No. 107-347, 116 Stat. 2899, 2913 (codified as amended at 44 U.S.C. § 3501 note (2006)). **This means the Decision will available to anyone with access to the internet.** However, the parties may object to the Decision's inclusion of certain kinds of confidential information. Specifically, under Vaccine Rule 18(b), each party has fourteen days within which to request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Otherwise, the whole Ruling will be available to the public. *Id.*

[2] National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755. Hereinafter, for ease of citation, all "§" references to the Vaccine Act will be to the pertinent subparagraph of 42 U.S.C. § 300aa (2012).

I. Procedural History

The petition was filed May 23, 2014. Petition, ECF No. 1. Petitioner filed medical records on May 30, 2014 and July 2, 2014. Petitioner's Exhibits ("Pet. Ex.") 1-8, ECF Nos. 5, 7. On August 19, 2014, respondent filed his Rule 4(c) Report, stating that this matter was not appropriate for compensation. Resp. Report, ECF No. 8. Petitioner continued to file additional medical records through August of 2015. Pet. Ex. 9-19, ECF Nos. 9, 11, 22-23, 27, 30-31.

On December 4, 2015, petitioner filed an expert report from Dr. Eric Gershwin. Pet. Ex. 20-21, ECF No. 34. Petitioner later filed supporting medical literature. Pet. Ex. 22-101, ECF No. 36. A status conference was held on January 7, 2016. The special master previously assigned to this matter discussed Dr. Gershwin's expert report with the parties and identified several issues for Dr. Gershwin to address in a supplemental expert report. Scheduling Order at 1-2, ECF No. 35.[3]

Petitioner filed a supplemental expert report from Dr. Gershwin on February 25, 2016. Pet. Ex. 103, ECF No. 40. Petitioner filed additional medical records on March 17, 2016. Pet. Ex. 104.1-104.3, ECF No. 41.

Respondent filed expert reports from Dr. Thomas Forsthuber and Dr. Steven McKenzie on June 27, 2016. Resp. Ex. A-B, ECF No. 45.

A status conference was held on August 3, 2016. Petitioner was ordered to file a supplemental report from Dr. Gershwin specifically addressing issues associated with petitioner's medical history, including petitioner's Gardnerella infection, petitioner's use of phentermine at the time of her vaccination, petitioner's prior instances of ITP, and an assault that petitioner endured that led to an emergency room visit on June 5, 2011. Scheduling Order at 1, ECF No. 47. Additionally, respondent stated that his expert hematologist had noted references to platelet counts dating from December of 2009 that had not been filed into the record. *Id*. Petitioner was ordered to file a status report regarding attempts to locate her platelet counts between December of 2009 and June 2, 2011, the date of vaccination. *Id*. at 1-2.

Petitioner filed medical records in October and December of 2016. Pet. Ex. 130-131, ECF Nos. 52, 54-55. These records did not include information regarding petitioner's platelet counts in 2009 through the date of vaccination, June 2, 2011. Petitioner filed a third report from Dr. Gershwin on December 19, 2016. Pet. Ex. 132, ECF No. 56.

During a status conference held on February 7, 2017, I noted that Dr. Gershwin's third report did not address any of the issues that he was asked to address during the previous status conference. Scheduling Order at 1, ECF No. 57. Petitioner was ordered to file an additional report from Dr. Gershwin addressing those issues. *Id*. Medical records documenting petitioner's platelet counts from December 2009 through 2011 had not been filed; petitioner advised that he had filed all records received but they did not include any platelet counts between December 2009 and June of 2011. *Id*. Respondent noted that Petitioner's Exhibit 102 contained records from "Catholic Healthcare West" and suggested that there may be additional records from that facility that had

[3] This case was reassigned to me on January 13, 2016. ECF No. 37.

not yet been filed. *Id*. Petitioner was given 90 days to secure and file the missing medical records. *Id*. at 1-2. Petitioner's counsel was directed to consult with his client to determine if the relevant records were available through another facility. *Id.* at 2.

Petitioner filed additional medical records on April 28, 2017. Pet. Ex. 133, ECF No. 61. These records did not include information regarding petitioner's platelet counts from 2009 through June 2, 2011. *See id.*

Petitioner filed a status report on May 8, 2017, advising that, despite requests to various healthcare providers, she had been unable to locate lab results documenting petitioner's platelet counts between 2009 and 2011. Pet. S.R. at 1, ECF No. 62. Petitioner filed a fourth report from Dr. Gershwin and medical literature on June 12, 2017. Pet. Ex. 134-39, ECF No. 64.

A status conference was held on August 22, 2017, during which I emphasized that petitioner's bloodwork from 2009 to 2011 was important to the ultimate outcome of this matter. Scheduling Order at 1, ECF No. 65. I encouraged petitioner's counsel to continue his efforts to locate these lab results. *Id*. Petitioner filed additional medical records in September and October of 2017. Pet. Ex. 140-41, ECF No. 66-67. These records showed that petitioner had an abnormally low platelet count on October 20, 2009, when she was not pregnant. Pet. Ex. 140 at 67. These medical records contained no reference to petitioner's platelet counts in 2010 or 2011.

Respondent filed supplemental expert reports from Dr. McKenzie and Dr. Forsthuber on April 18, 2018. Resp. Ex. C-D, ECF No. 77.

A status conference was held on May 15, 2018. I noted respondent's experts' opinions that petitioner's low platelet count in October 2009 indicated that she had ITP unrelated to pregnancy. Scheduling Order at 1, ECF No. 79. I further noted that Dr. Gershwin opined that the HPV vaccine caused petitioner's ITP but had not provided a mechanism by which the HPV vaccine could trigger ITP. *Id.* at 2. I advised petitioner that Dr. Gershwin needed to provide a plausible biological mechanism causally connecting the HPV vaccine to the development or aggravation of ITP and address the issues raised by respondent's experts, including the fact that petitioner had low platelet counts in October of 2009 when she was not pregnant, which suggested that she had ITP prior to her HPV vaccination. *Id*. Petitioner was ordered to file either a supplemental expert report or a status report by July 16, 2018. *Id*.

On June 11, 2018, petitioner filed a status report stating that she had received consistent medical treatment from January 2009 through September 2010, and although petitioner's records document a low platelet count in October 2009, she was found to have normal platelet counts on follow-up labs performed on December 22, 2009. Pet. S.R. at 1-2, ECF No. 80. However, no lab records to substantiate this representation from December 2009 through June 2011 were ever filed.

An entitlement hearing was scheduled to begin on November 13, 2019. *See* Prehearing Order, ECF No. 83. On September 14, 2019, petitioner filed a status report indicating that she intended to file a Motion for a Ruling on the Record instead of proceeding to an entitlement hearing. *See* Pet. S.R., ECF No. 84. Accordingly, the entitlement hearing was cancelled. ECF No. 85.

Petitioner filed a Motion for a Ruling on the Record on November 15, 2018. ECF No. 88. Respondent filed updated medical literature and a response to petitioner's motion on April 23, 2019. Resp. Ex. C1-3, ECF No. 92; Response, ECF No. 93. Petitioner filed a reply on April 30, 2019. Reply, ECF No. 94.

This matter is now ripe for decision.

II. Overview of ITP

Idiopathic thrombocytopenic purpura is a common autoimmune disorder of unknown etiology characterized by immune-mediated platelet destruction and impaired platelet formation. Resp. Ex. A at 3 (citing Resp. Ex. A2[4] at 306; Resp. Ex. A3[5] at 344; Resp. Ex. A4[6] at 6512-13). The British Society of Hematology defines ITP as "an autoimmune disorder characterized by persistent thrombocytopenia due to autoantibody binding to platelet antigen(s) causing their premature destruction by the reticuloendothelial system,[7] and in particular the spleen." Pet. Ex. 20 at 3 (citing Pet. Ex. 37[8] at 4). ITP has been described as a syndrome as there is no one single cause. Resp. Ex. B at 4 (citing Resp. Ex. B3[9] at 396). It typically presents as either primary ITP, unrelated to other diseases or external factors, or secondary ITP associated with other conditions including autoimmune diseases and infections such as measles, mumps, rubella, varicella, H. pylori, and hepatitis C, drugs, or other risk factors including pregnancy.[10] Resp. Ex. A at 3 (citing Resp. Ex. A4 at 6513-15); Resp. Ex B at 4 (citing Resp. Ex. B3 at 396).

The average person generally has platelet levels of 150 k/ul (thousand per microliter) or higher. Resp. Ex. B at 1-2. When a person's platelet count drops below that, a diagnosis of thrombocytopenia is appropriate. *Id.* A platelet count between 50 and 150 k/ul is indicative of mild

[4] Jill Johnson, *Pathogenesis in Immune Thrombocytopenia: New Insights*, AM. SOC'Y OF HEMATOLOGY 306-12 (2012), filed as Resp. Ex. A2.

[5] Sean Deane et al., *The Geoepidemiology of Immune Thrombocytopenic Purpura*, 9 AUTOIMMUNITY REVS. 342 (2010), filed as Resp. Ex. A3.

[6] Douglas B. Cines et al., *The ITP Syndrome: Pathogenic and Clinical Diversity*, 113 BLOOD 6511 (2009), filed as Resp. Ex. A4.

[7] The reticuloendothelial system is "a group of cells having the ability to take up and sequester inert particles and vital dyes; it includes macrophages and macrophage precursors; specialized endothelial cells lining the sinusoids of the liver, spleen, and bone marrow." *Reticuloendothelial system*, DORLAND'S at 1862.

[8] James N. George et al., *Idiopathic Thrombocytopenic Purpura: A Practice Guideline Developed by Explicit Methods for The American Society of Hematology*, 88 BLOOD 3 (1996), filed as Pet. Ex. 37.

[9] Adam Cuker et al., *Can Immune Thrombocytopenia Be Cured with Medical Therapy*, 41 SEMINARS IN THROMBOSIS & HEMOSTASIS 395 (2015), filed as Resp. Ex. B3.

[10] Pregnancy-induced ITP typically presents in the first trimester and platelet counts in patients with pregnancy-induced ITP can drop lower than 70 k/ul, both of which are atypical in patients with gestational thrombocytopenia. *See* Pet. Ex. 2 at 125-29; Resp. Ex. A at 3 (citing Resp. Ex. A5 at 397-98). Keith R. McCrae, *Thrombocytopenia in Pregnancy*, AM. SOC'Y OF HEMATOLOGY 397 (2010), filed as Resp. Ex. A5.

thrombocytopenia, a count between 20 and 50 k/ul is considered moderate, and severe thrombocytopenia occurs when a blood count drops below 20 k/ul. *Id.* at 2.

Gestational thrombocytopenia ("GT") is relatively common during pregnancy and is characterized by "incidental and clinically asymptomatic thrombocytopenia in the absence of previous thrombocytopenia, which resolves spontaneously after delivery." Resp. Ex. A at 3 (citing Resp. Ex. A5 at 397-98). "Platelet counts in GT rarely fall below [70 k/ul] and gestational thrombocytopenia usually becomes apparent during the second and third trimester," as opposed to pregnancy-induced ITP which presents in the first trimester with platelet counts that drop below 70 k/ul. *Id.* (citing Resp. Ex. A6[11] at 47-48); *see* Pet. Ex. 2 at 125-29. However, it can be difficult to clinically distinguish between gestational thrombocytopenia and ITP and is usually accomplished with ongoing follow-up after delivery. *Id.* (citing Resp. Ex. A6 at 48).

III. Petitioner's Medical History

A. Petitioner's Medical History Prior to the Allegedly Causal Vaccination

Petitioner initially suffered from an abnormally low platelet count when she was pregnant with her first child in 2007. Pet. Ex. 9 at 1. Between July and August 2007, petitioner's platelet count fluctuated between 41 k/ul and 55 k/ul. *See id.* at 67, 73. Shortly before giving birth, petitioner was given oral steroids on September 14, 2007, which caused her platelet count to rise to 82 k/ul. *Id.* at 75. After giving birth on September 19, 2007, petitioner's platelet count was 102 k/ul and rose to 168 k/ul by September 21, 2007. *Id.* at 67.

No records were filed thereafter until 2009 when petitioner was pregnant with her second child. Her platelet counts were monitored throughout her pregnancy and she had normal platelets counts in January of 2009 and again in March of 2009, when she delivered her second child. Pet. Ex. 141 at 30, 120. No records were filed thereafter until October 20, 2009, when petitioner had a platelet count of 100 k/ul, which is below the average platelet count of 150 k/ul. Pet. Ex. 140 at 67. Petitioner was not pregnant on this date. *See id.*

Despite multiple requests from the court and respondent's counsel,[12] petitioner failed to file any lab work from 2010 or 2011 prior to her receipt of the allegedly causal vaccine, so it is unknown if her platelet count continued to be low after October 20, 2009. *See* Resp. Response at 2, ECF No. 93.

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[11] Junko Kasai et al., *Clinical Features of Gestational Thrombocytopenia Difficult to Differentiate from Immune Thrombocytopenia Diagnosed During Pregnancy*, 41 J. OBSTETRICS & GYNECOLOGY RESEARCH 44 (Jan. 2015), filed as Resp. Ex. A6.

[12] During status conferences held on August 3, 2016, February 7, 2017, and August 22, 2017, I specifically requested that petitioner file any records containing petitioner's platelet counts during 2010 and 2011 as they are necessary for her to prove her claim. *See* Scheduling Orders, ECF Nos. 47, 57, 65.

B. Petitioner's Medical History at the Time of and Following the Allegedly Causal Vaccination

On May 24, 2011, petitioner presented to Sutter Amador Women's Services for an annual women's health exam. Pet. Ex. 1 at 17. At this visit she tested positive for Gardnerella[13] and a physical exam revealed "HPV genital warts." *Id.* at 17, 64. She also reported abnormal bleeding while she had been on Mirena.[14] *Id.* at 64. She was prescribed Aldera cream[15] to be used three times per week. *Id.* at 64. She was noted to be due for Gardasil and Tdap immunizations. Pet. Ex. 1 at 63-64. She also reported being under significant stress due to a change in jobs and her two special needs children. *Id.* There is some discrepancy as to when petitioner received the allegedly causal HPV vaccine. One record indicates she received the HPV vaccine at her visit on May 24, 2011 and another record suggests she received the HPV vaccine on June 2, 2011. *See* Pet. Ex. 1 at 49, 56; *but see* Pet. Ex. 1 at 46.

On June 5, 2011, petitioner presented to Lodi Memorial Hospital where she reported that she had been assaulted by her ex-boyfriend the previous night. Pet. Ex. 16 at 9-10. She stated that she felt "sore all over" with neck, back, and elbow pain, headache, and abrasions. *Id.* She had been taking 1 tab of phentermine[16] daily. *Id.* at 8. She left the hospital against medical advice. *Id.* at 19.

On June 14, 2011, petitioner presented to Women's Health Services for an ultrasound following a positive at-home pregnancy test. Pet. Ex. 1 at 62, 81. The ultrasound confirmed that she was approximately four weeks pregnant. *Id.* at 62.

On July 5, 2011, petitioner's lab work revealed a platelet count of 64 k/ul. Pet. Ex. 1 at 12.

On July 8, 2011 petitioner presented to Sutter Amador emergency department for vaginal bleeding which started one day earlier and unusual bruising that had started one week prior. Pet. Ex. 3 at 2, 6. Petitioner reported that she had experienced similar symptoms and low platelet counts during a previous pregnancy. *Id.* Her platelet count at this visit was 66 k/ul. *Id.* at 4.

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[13] Gardnerella is defined as "a genus of small, pleomorphic, gram-negative rod-shaped bacteria found in the normal female genital tract and also as a major case of bacterial vaginitis." *Gardnerella,* DORLAND'S ILLUSTRATED MEDICAL DICTIONARY 761 (32d ed. 2012) [hereinafter DORLAND'S]. Vaginitis is defined as "inflammation of the vagina; it is marked by pain and by a purulent discharge." *Vaginitis,* DORLAND'S at 2019.

[14] Mirena is defined as "trademark for a preparation of levonorgestrel." *Mirena,* DORLAND'S at 1168. Levonorgestrel is defined as "the levorotatory form of norgestrel, administered as a subdermal contraceptive implant or in combination with an estrogen component in an oral contraceptive." *Levonorgestrel,* DORLAND'S at 1032.

[15] The active ingredient of Aldera cream is Imiquimod, which is defined as "a biologic response modifier used topically in the treatment of condyloma acuminatum of the external genitalia and perianal region." Resp. Ex. D at 2; *Imiquimod,* DORLAND'S at 916. Condyloma acuminatum is defined as "a type of papilloma usually found on the mucous membrane or skin of the external genitals or in the perianal region. Lesions are usually few in number but may aggregate to form large cauliflowerlike masses." *Condyloma acuminatum,* DORLAND'S at 402.

[16] Phentermine is a weight-loss medication associated with many side effects including gastrointestinal issues, constipation and diarrhea. Resp. Ex. D at 2.

On July 11, 2011, petitioner tested positive for platelet specific antibodies. Pet. Ex. 1 at 10. She also had a low platelet count at 73 k/ul and a low lymphocyte count. *Id.* at 11.

On August 4, 2011, petitioner's platelet count dropped to 20 k/ul but increased to 133 k/ul after taking 100 mg of prednisone.[17] Pet. Ex. 1 at 51, 61.

On August 10, 2011, petitioner presented to Dr. Kiwan, a hematologist, for treatment of her low platelet counts. Pet. Ex. 2 at 125. Petitioner reported her current symptoms included easy bruising, gingival bleeding, and vaginal spotting. *Id.* Petitioner's platelet count at this visit was 20 k/ul. *Id.* Dr. Kiwan noted that petitioner was twelve weeks pregnant and indicated that because petitioner had such low platelet levels during her first trimester, she qualified for a diagnosis of ITP rather than a diagnosis of gestational thrombocytopenia. Pet. Ex. 2 at 125-28. Dr. Kiwan explained that platelet counts in patients with gestational thrombocytopenia typically do not fall below 70 k/ul, and when platelet levels drop lower, an ITP diagnosis is more appropriate. *Id.* at 126.

Petitioner's platelet count was monitored regularly during the final months of her pregnancy. Her platelet counts fluctuated between 12 k/ul and 184 k/ul and she experienced several bouts of major vaginal bleeding. *See* Pet. Ex. 1 at 8; Pet. Ex. 2 at 45, 76-79, 83-90, 128, 133, 139; Pet. Ex. 141 at 171. She was treated with oral steroids and intravenous immune globulin ("IVIG") treatments. *See* Pet. Ex. 2 at 76-77, 131-33, 139.

On December 19, 2011, petitioner presented to the Sutter Health emergency department for premature rupture of the membranes and uterine contractions. Pet. Ex. 5 at 118-20. She was treated with antibiotics to prevent infection and attempt to prolong her pregnancy. *Id.* at 120.

Petitioner delivered her third child via Caesarean section on December 22, 2011. *Id.* at 281-84.

On December 23, 2011, petitioner's platelet count had improved to 105 k/ul. Pet. Ex. 5 at 302. By December 28, 2011, her platelets were at 270 k/ul. Pet. Ex. 2 at 94. Her baby was diagnosed with transient thrombocytopenia and treated with IVIG immediately after delivery. *Id.*

Petitioner discontinued oral steroids on her own on February 1, 2012. *Id.* at 94. By February 6, 2012, her platelet count was down to 9 k/ul. *Id.* She was noted to have recurrent ITP and was restarted on 80 mg of prednisone daily and a course of IVIG. *Id.*

Petitioner presented to Dr. Kiwan on February 14, 2012. *Id.* at 96. Petitioner's platelet count was up to 322 k/ul and accordingly, she was started on a gradual steroid taper. *Id.*

[17] Prednisone is defined as "a synthetic glucocorticoid derived from cortisone, administered orally as an anti-inflammatory and immunosuppressant in a wide variety of disorders." *Prednisone*, DORLAND'S at 1509. Glucocorticoid is defined as "any of the corticosteroids (steroids produced by the adrenal cortex) that regulate carbohydrate, lipid, and protein metabolism and inhibit the release of corticotropin." *Glucocorticoid*, DORLAND'S at 789.

Petitioner returned to Dr. Kiwan on March 13, 2012 requesting that she be taken off prednisone and advising that she had begun tapering it faster than recommended. *Id.* at 100. Her platelets were at 111 k/ul. *Id.* Due to continued side-effects from steroids and her request, she was switched to rituximab. *Id.* at 100-01.

Petitioner returned to Dr. Kiwan on March 21, 2012 and April 20, 2012 with progressive fatigue and platelet counts of 51 k/ul and 56 k/ul. *Id.* at 105-07, 110-12. She was continued on rituximab. *Id.* at 105.

On June 6, 2012, petitioner presented to Dr. Kiwan with a platelet count of 52 k/ul and reports of easy bruising and fatigue. *Id.* at 115. Dr. Kiwan noted that testing from June 4, 2012 revealed that petitioner's platelet count had fallen to 25 k/ul while she was suffering from a urinary tract infection. *Id.* at 119. Dr. Kiwan decided to hold any further treatment until and unless petitioner's platelets fell below 50 k/ul again. *Id.*

Petitioner presented to the Sutter Memorial Hospital emergency department on August 1, 2012 with complaints of a constant skin rash on her trunk and lower extremities that had persisted for five weeks. Pet. Ex. 5 at 69. She was noted to have a history of ITP. *Id.* At this visit, petitioner's platelet count was 47 k/ul. *Id.* at 70.

On November 15, 2012, petitioner returned to Dr. Kiwan. She had recently been diagnosed with pleurisy.[18] Pet. Ex. 8 at 27. Her platelet count was 77 k/ul. *Id.* at 30. Dr. Kiwan noted that petitioner was taking ibuprofen for her pleurisy and had developed mild hemoptysis.[19] *Id.* at 27-29, 36.

On February 1, 2013, petitioner had a follow up visit with Dr. Kiwan, who noted that petitioner received an HPV vaccine "two weeks" before her symptoms began, though he did not explain where this information came from. *Id.* at 35. Her platelet count was 115 k/ul. *Id.*

On August 20, 2013, petitioner presented to Dr. D'Acquisto, an oncologist, complaining of skin rashes, headaches, left facial numbness, lower abdominal pain, pleurisy, constant chest discomfort, and severe fatigue. Pet. Ex. 7 at 3-5. Her platelet count was 89 k/ul. *Id.* at 6. Dr. D'Acquisto agreed with the diagnosis of ITP. *Id.* He explained to petitioner that because she was refusing to take oral steroids, and because her condition did not resolve with IVIG or rituximab, the only other treatment available was a splenectomy, which was not imperative because she was stable. *Id.*

[18] Pleurisy is defined as "inflammation of the pleura, with exudation into its cavity and upon its surface . . . Symptoms include localized chest pain and dry cough." *Pleurisy*, DORLAND'S at 1461.

[19] Hemoptysis is defined as "the expectoration of blood or of blood-stained sputum." *Hemoptysis*, DORLAND'S at 842.

Petitioner returned to Dr. D'Acquisto on September 5, 2013. *Id.* at 10. Her platelet count was 89 k/ul. *Id.* An abdominal CT ruled out splenomegaly[20] and secondary hypersplenism.[21] *Id.* at 11. He noted that petitioner's "multiple somatic complaints are not explained by the ITP." *Id.*

During a follow-up visit with Dr. D'Acquisto on December 15, 2013, petitioner had a platelet count of 75 k/ul. *Id.* at 9. She was diagnosed with stable chronic ITP. *Id.*

On January 20, 2014, petitioner had a platelet count of 183 k/ul. Pet. Ex. 7 at 15. No further medical records were filed.

IV. The Experts

A. Petitioner's Expert, Dr. M. Eric Gershwin

Petitioner filed four expert reports from her expert, Dr. M. Eric Gershwin. *See* Pet. Ex. 20, 103, 132, 134. Dr. Gershwin obtained his medical degree from Stanford University and completed his residency at Tufts-New England Medical Center. Pet. Ex. 21 at 1-2. He is board certified in rheumatology, allergy, and clinical immunology. *Id.* at 2. He has been a Professor of Medicine in Rheumatology, Allergy, and Clinical Immunology at the University of California School of Medicine at Davis since 1981. *Id.*

B. Respondent's Expert, Dr. Thomas Forsthuber

Respondent filed two expert reports from Dr. Thomas Forsthuber. *See* Resp. Ex. A, D. Dr. Forsthuber received his medical degree from the University of Tubingen in Germany and completed his residency at University Hospitals of Cleveland. Resp. Ex. A1 at 3. He is board certified in anatomical and clinical pathology. He has been a Professor of Immunology at the University of Texas at San Antonio since 2005. *Id.* He also holds adjunct appointments in pathology, microbiology, and immunology at the University of Texas Health Sciences Center. *Id.* at 3-4.

C. Respondent's Expert, Dr. Steven McKenzie

Respondent filed two expert reports from Dr. Steven McKenzie. *See* Resp. Ex. B, C. Dr. McKenzie has a medical degree and a doctoral degree in bioengineering from the University of Pennsylvania. Resp. Ex. B, Tab 1, at 2. He completed both a residency in pediatrics and a fellowship in pediatric hematology-oncology at Children's Hospital of Philadelphia. *Id.* He is board certified in pediatrics and pediatric hematology/oncology. He has been a Professor of Medicine and Pediatrics at Thomas Jefferson University since 2000. *Id.* at 3.

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[20] Splenomegaly is defined as "enlargement of the spleen." *Splenomegaly*, DORLAND'S at 1752.

[21] Hypersplenism is defined as "a condition characterized by exaggeration of the suggested inhibitory or destructive functions of the spleen, resulting in deficiency of the peripheral blood elements, singly or in combination, hypercellularity of the bone marrow, and usually, but not always, splenomegaly." *Hypersplenism*, DORLAND'S at 896.

V. Discussion

A. Legal Standard

The Vaccine Act provides two avenues for petitioners to receive compensation. First, a petitioner may demonstrate a "Table" injury—i.e., an injury listed on the Vaccine Injury Table that occurred within the provided time period. § 11(c)(1)(C)(i). "In such a case, causation is presumed." *Capizzano v. Sec'y of Health & Human Servs.*, 440 F.3d 1317, 1320 (Fed. Cir. 2006); *see* § 13(a)(1)(B). Second, where the alleged injury is not listed on the Vaccine Injury Table, a petitioner may demonstrate an "off-Table" injury, which requires that the petitioner "prove by a preponderance of the evidence that the vaccine at issue caused the injury." *Capizzano*, 440 F.3d at 1320; *see* § 11(c)(1)(C)(ii).

To prove causation for an "off-Table" injury, petitioner must satisfy the three-pronged test established in *Althen v. Sec'y of Health & Human Servs.*, 418 F.3d 1274 (Fed. Cir. 2005). *Althen* requires that petitioner show by preponderant evidence that the vaccination caused his 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 a proximate temporal relationship between vaccination and injury." *Id.* at 1278. A petitioner need not show that the vaccination was the sole cause, or even the predominant cause, of the alleged injury; showing that the vaccination was a "substantial factor" and a "but for" cause of the injury is sufficient for recovery. *Pafford v. Sec'y of Health & Human Servs.*, 451 F.3d 1352, 1355 (Fed. Cir. 2006); *Shyface v. Sec'y of Health & Human Servs.*, 165 F.3d 1344, 1352 (Fed. Cir. 1999).[22] Causation is determined on a case-by-case basis, with "no hard and fast *per se* scientific or medical rules." *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). Petitioner is not required to identify "specific biological mechanisms" to establish causation, nor are they required to present "epidemiologic studies, rechallenge, the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities." *Capizzano*, 440 F.3d at 1325 (quoting *Althen*, 418 F.3d at 1280). "[C]lose calls regarding causation are resolved in favor of injured claimants." *Althen*, 418 F.3d at 1280. Once a petitioner has proven causation by preponderant evidence, "the burden then shifts to the respondent to show by a preponderance of the evidence that the injury is due to factors unrelated to the administration of the vaccine." *Deribeaux ex rel. Deribeaux v. Sec'y of Health & Human Servs.*, 717 F.3d 1363, 1367 (Fed. Cir. 2013) (citing § 13(a)(1)(B)).

The process for making factual determinations in Vaccine Program cases begins with analyzing the medical records, which are required to be filed with the petition. § 11(c)(2). Medical records created contemporaneously with the events they describe are presumed to be accurate and "complete" such that they present all relevant information on a patient's health problems. *Cucuras v. Sec'y of Health & Human Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993). In making contemporaneous reports, "accuracy has an extra premium" given that the "proper treatment hang[s] in the balance." *Id.* Contemporaneous medical records that are clear, consistent, and complete warrant substantial weight "as trustworthy evidence." *Id*. Indeed, "where later testimony

[22] The Vaccine Act also requires petitioners to show by preponderant evidence that the "residual effects or complications" of the alleged vaccine-related injury lasted for more than six months. § 11(c)(1)(D)(i). It is undisputed that this six-month requirement is satisfied in this case.

conflicts with earlier contemporaneous documents, courts generally give the contemporaneous documentation more weight." *Campbell ex rel. Campbell v. Sec'y of Health & Human Servs.*, 69 Fed. Cl. 775, 779 (2006); *see United States v. U.S. Gypsum Co.*, 333 U.S. 364, 396 (1948). But petitioners can support their claim with oral testimony if it is credible and consistent with the medical records. *See, e.g.*, *Stevenson ex rel. Stevenson v. Sec'y of Health & Human Servs.*, No. 90-2127V, 1994 WL 808592, at *7 (Fed. Cl. Spec. Mstr. June 27, 1994) (crediting the testimony of a fact witness whose "memory was sound" and "recollections were consistent with the other factual evidence"). In short, "the record as a whole" must be considered. § 13(a).

Furthermore, establishing a sound and reliable medical theory connecting the vaccine to the injury often requires a petitioner to present expert testimony in support of his or her claim. *Boatmon v. Sec'y of Health & Human Servs.*, 941 F.3d 1351, 1359-60 (Fed. Cir. 2019); *Lampe v. Sec'y of Health & Human Servs.*, 219 F.3d 1357, 1361 (Fed. Cir. 2000). The Supreme Court's opinion in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993), requires that courts determine the reliability of an expert opinion before it may be considered as evidence. "In short, the requirement that an expert's testimony pertain to 'scientific knowledge' establishes a standard of evidentiary reliability." *Id*. at 590 (citation omitted). Thus, for Vaccine Act claims, a "special master is entitled to require some indicia of reliability to support the assertion of the expert witness." *Moberly ex rel. Moberly v. Sec'y of Health & Human Servs.*, 592 F.3d 1315, 1324 (Fed. Cir. 2010). The *Daubert* factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health & Human Servs.*, 94 Fed. Cl. 53, 66-67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"). Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Human Servs.*, 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe*, 219 F.3d at 1362). And nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder ex rel. Snyder v. Sec'y of Health & Human Servs.*, 88 Fed. Cl. 706, 743 (2009) (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)).

Finally, although this decision discusses some but not all of the literature in detail, I have reviewed and considered all of the medical records and literature submitted in this matter. *See Moriarty ex rel. Moriarty v. Sec'y of Health & Human Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("We generally presume that a special master considered the relevant record evidence even though [s]he does not explicitly reference such evidence in h[er] decision."); *Simanski v. Sec'y of Health & Human Servs.*, 115 Fed. Cl. 407, 436 (2014) ("[A] Special Master is 'not required to discuss every piece of evidence or testimony in her decision.'" (citation omitted)), *aff'd*, 601 F. App'x 982 (Fed. Cir. 2015).

B. Analysis of *Althen* Factors

Because petitioner does not allege an injury listed on the Vaccine Injury Table, her claim is classified as "off-Table." As noted above, for petitioner to prevail on an "off-Table" claim, she must show by preponderant evidence that her injury resulted from the vaccination at issue.

Capizzano, 440 F.3d at 1320. Doing so shifts the burden to respondent to show that the injury was caused by factors unrelated to the vaccination. *Deribeaux*, 717 F.3d at 1367.

As an initial matter, the parties do not dispute that petitioner has ITP. Response at 8. Therefore, in order to prevail, petitioner must establish by preponderant evidence a medical theory that causally connects her ITP and receipt of the HPV vaccination.

1. Petitioner Failed to Advance a Sound and Reliable Medical Theory

The first *Althen* prong requires petitioner to provide a "reputable medical theory" demonstrating that the vaccines received *can* cause the type of injury alleged. *Pafford*, 451 F.3d at 1355-56 (citation omitted). To satisfy this prong, petitioner's "theory of causation must be supported by a 'reputable medical or scientific explanation.'" *Andreu ex rel. Andreu v. Sec'y of Health & Human Servs.*, 569 F.3d 1367, 1379 (Fed. Cir. 2009) (quoting *Althen*, 418 F.3d at 1278). This theory need only be "legally probable, not medically or scientifically certain." *Id.* at 1380 (emphasis omitted) (quoting *Knudsen*, 35 F.3d at 548). This standard was recently clarified by the Federal Circuit. *See Boatmon*, 941 F.3d at 1359-60 (stating that the correct standard for *Althen* prong one is "reputable," and "sound and reliable" not a "lower reasonable standard" (internal quotations omitted)). Nevertheless, "petitioners [must] proffer trustworthy testimony from experts who can find support for their theories in medical literature." *LaLonde v. Sec'y of Health & Human Servs.*, 746 F.3d 1334, 1341 (Fed. Cir. 2014). In this case, petitioner has not offered a reputable medical theory of causation that the HPV vaccine caused or significantly aggravated petitioner's ITP.

Dr. Gershwin opined that an HPV vaccine can cause ITP via molecular mimicry, stating, "Molecular mimicry is considered to be the primary molecular mechanism by which ITP develops . . .". Pet. Ex. 20 at 11. He quoted literature discussing molecular mimicry as a mechanism by which autoimmune disorders can be caused, but never specifically discussed how the HPV vaccination can cause ITP via this mechanism. *See* Pet. Ex. 103 at 1 (citing Pet. Ex. 106[23] at 159). Dr. Gershwin also attempted to compare the measles-mumps-rubella ("MMR") to the HPV vaccines, citing several articles discussing molecular mimicry as the mechanism by which the MMR vaccine can cause ITP but neglected to explain the similarities between the two vaccinations to warrant such a comparison. Pet. Ex. 20 at 10 (citing Pet. Ex. 89[24] at 228-29; Pet. Ex. 90[25] at 613;

[23] Michael B.A. Oldstone, *Molecular Mimicry: Its Evolution from Concept to Mechanism as a Cuase of Autoimmune Diseases*, 33 MONOCLONAL ANTIBODIES IN IMMUNODIAGNOSIS & IMMUNOTHERAPY 158 (2014), filed as Pet. Ex. 106.

[24] E. Miller et al., *Idiopathic Thrombocytopenic Purpura and MMR Vaccine*, 84 ARCH DIS CHILD 227 (2015), filed as Pet. Ex. 89.

[25] Jan Neiderud, *Thrombocytopenic Purpura After a Combined Vaccine Against Morbilli, Parotitis and Rubella*, 72 ACTA PADIATR SCAND 613 (1983), filed as Pet. Ex. 90.

Pet. Ex. 91[26] at 1265-67; Pet. Ex. 92[27] at 268-70; Pet. Ex. 93[28] at 354-56; Pet. Ex. 94[29] at 1604-05; Pet. Ex. 95[30] at 568-69).

Dr. Gershwin submitted that ITP is commonly associated with community-acquired viral infections, rubella infection, and the administration of *live* viral vaccinations. *Id.* at 8 (citing Pet. Ex. 38[31] at 582). Dr. Gershwin wrote, to that end, a causal relationship between the MMR vaccination and ITP was accepted in the 1994 Institute of Medicine Report on the grounds of biological plausibility. *Id.* at 9 (citing Pet. Ex. 94 at 1605). Dr. Gershwin further described the pathophysiology of ITP in terms of the promiscuous response against platelet antigens and noted that this was like other autoimmune diseases, which tend to reflect a genetic predisposition and environmental factors. *Id.* (citing Pet. Ex. 43[32] at 6516-19; Pet. Ex. 96[33] at 156-57). However, Dr. Gershwin did not clarify what environmental factors he was referring to. *See id.*

Dr. Gershwin conceded that while there have been attempts to study whether the HPV vaccine is associated with the change in the risk of autoimmunity in young women, the authors of these studies did not detect an increase in the prevalence of ITP in the study participants. *Id.*[34] He also cited a 2013 study from Denmark and Sweden in which almost one million girls who received the HPV vaccine were studied to find evidence supporting an association between the vaccine and autoimmunity, but no such evidence was found. *Id.* (citing Pet. Ex. 101[35] at 4-5).

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[26] Margareta Bottiger, *Swedish Experience of Two Dose Vaccination Programme Aiming at Eliminating Measles, Mumps, and Rubella*, 295 BRITISH MED. J. 1264 (1987), filed as Pet. Ex. 91.

[27] U. Nieminen et al., *Acute Thrombocytopenic Purpura Following Measles, Mumps and Rubella Vaccination. A Report on 23 Patients*, 82 ACTA PAEDIATR 267 (1993), filed as Pet. Ex. 92.

[28] Frank A. Oski & J. Lawrence Naiman, *Effect of Live Measles on the Platelet Count*, 275 NEW ENGL. J. MED. 352 (1966), filed as Pet. Ex. 93.

[29] Kathleen R. Stratton et al., *Adverse Events Associated with Childhood Vaccines Other than Pertussis and Rubella*, 271 JAMA 1602 (1994), filed as Pet. Ex. 94.

[30] Paddy Farrington et al., *A New Method for Active Surveillance of Adverse Events from Diphtheria/Tetanus/Pertussis and Measles/Mumps/Rubella Vaccines*, 345 THE LANCET 567 (1995), filed as Pet. Ex. 95.

[31] *Guidelines for the Investigation and Management of Idiopathic Thrombocytopenic Purpura in Adults, Children and in Pregnancy*, 120 BRITISH J. HAEMATOLOGY 574 (2003), filed as Pet. Ex. 38.

[32] Douglas B. Cines et al., *The ITP Syndrome: Pathogenic and Clinical Diversity*, 113 BLOOD 6511 (2009), filed as Pet. Ex. 42.

[33] Dimitrios P. Bogdanos et al., *Twin Studies in Autoimmune Disease: Genetics, Gender and Environment*, 38 J. AUTOIMMUNITY 156 (2012), filed as Pet. Ex. 96.

[34] Dr. Gershwin did not actually cite any studies in support of these assertions.

[35] Lisen Arnheim-Dahlstrom et al., *Autoimmune, Neurological, and Venous Thromboembolic Adverse Events After Immunisation of Adolescent Girls with Quadrivalent Human Papillomavirus in Denmark and Sweden: Cohort Study*, 347 BRITISH MED. J. 1 (2013), filed as Pet. Ex. 101.

Dr. Forsthuber criticized Dr. Gershwin's comparison of ITP induced by the MMR vaccine and ITP induced by the HPV vaccine, highlighting the differences between the two vaccines. Resp. Ex. A at 7. First, the MMR vaccine is an attenuated live virus containing three different viruses while the HPV vaccine is made up of only recombinant (dead) HPV L1 viral proteins that are incapable of replicating, unlike the MMR viruses. *Id.* (citing Resp. Ex. A23[36] at 950). Second, the MMR and HPV viruses are not related and therefore comparison between the viruses is inappropriate as there is no evidence that the two vaccines can induce similar immune responses. *See id. d.*at 7-8 (citing Resp. Ex. A22[37] at 31-32; Resp. Ex. A24[38] at 691-91) ("MMR vaccination showed a low, but significant risk of ITP, whereas large vaccination studies have failed to show any association of the HPV vaccine with autoimmune diseases, specifically ITP"). Dr. Forsthuber further submitted that "molecular mimicry may be necessary, but not sufficient to induce human autoimmune pathology and that other factors may be critical to induce pathology, such as bystander activation or dual TCRs on T cells, or failure of immune regulation." Resp. Ex. A at 4-5 (citing Resp. Ex. A7[39] at 103; Resp. Ex. A8[40] at 105; Resp. Ex. A9[41] at 1098). However, Dr. Forsthuber concluded that, "there is no doubt that even if significant molecular mimicry is observed between a particular pathogen and human self-antigens it cannot be assumed *de facto* as being causative for a human autoimmune disease condition . . .". *Id.* Dr. Forsthuber also opined that Dr. Gershwin's argument of molecular mimicry as the appropriate mechanism present in this case is highly speculative and not plausible. *Id.* Dr. Forsthuber ultimately concluded that the HPV vaccine petitioner received on June 2, 2011 was not causally related to her ITP and that no specific cause can be assigned to it. *Id.* at 10.

Dr. McKenzie added that Dr. Gershwin misstated the epidemiological studies referenced in his report. Resp. Ex. B at 5. Specifically, there has been no documented association between the HPV quadrivalent recombinant peptide antigen vaccination and ITP in the several studies that have been performed. *Id.* (citing Resp. Ex. B4[42] at 404; Resp. Ex. B5[43] at 4-5). Dr. McKenzie further

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[36] Irja Davidkin et al., *Persistence of Measles, Mumps, and Rubella Antibodies in an MMR-Vaccincated Cohort: A 20-Year Follow-up*, 197 J. INFECTIOUS DISEASES 950 (2008), filed as Resp. Ex. A23.

[37] Laura J. Sauve & David Scheifele, *Do Childhood Vaccines Cause Thrombocytopenia*, 14 PAEDIATRIC CHILD HEALTH 31 (2009), filed as Resp. Ex. A22.

[38] Eric K. France et al., *Risk of Immune Thrombocytopenic Purpura After Measles-Mumps-Rubella Immunization in Children*, 121 PEDIATRICS 687 (2008), filed as Resp. Ex. A24.

[39] Matthew F. Cusick et al., *Molecular Mimicry as a Mechanism of Autoimmune Disease*, 42 CLINIC REV. ALLERG. IMMUNOL. 102 (2012), filed as Resp. Ex. A7.

[40] Robert Root-Bernstein & DeLisa Fairweather, *Unresolved Issues in Theories of Autoimmune Disease Using Myocarditis as a Framework*, 375 J. THEORETICAL BIOLOGY 101 (2015), filed as Resp. Ex. A8.

[41] Jean-Marie Fourneau et al., *Th Elusive Case for a Role of Mimicry in Autoimmune Diseases*, 40 MOLECULAR IMMUNOLOGY 1095 (2004), filed as Resp. Ex. A9.

[42] Lamiae Grimaldi-Bensouda et al., *Autoimmune Disorders and Quadrivalent Human Papillomavirus Vaccination of Young Female Subjects*, 275 J. INTNT'L MED. 398 (2014), filed as Resp. Ex. B4.

[43] Lisen Arnheim-Dahlstrom et al., *Autoimmune, Neurological, and Venous Thromboembolic Adverse Events After Immunisation of Adolescent Girls with Quadrivalent Human Papillomavirus in Denmark and Sweden: Cohort Study*,

opined that there are no biological studies that support Dr. Gershwin's theory that the HPV vaccine can cause ITP. *Id.* He also noted that the HPV vaccine is indicated for immunodeficient patients in the 2015 Advisory Committee on Immunization Practices on behalf of the American Academy of Pediatrics, the American Academy of Family Physicians, and the American College of Obstetricians and Gynecologists. *Id.* Finally, Dr. McKenzie noted that, "Natural infections with HPV have not been associated with ITP." *Id.*

Dr. McKenzie submitted four significant studies in which it was determined that "those that were given HPV vaccine were not at an increased risk of developing ITP following HPV vaccinations." *See generally*, Resp. Ex. B4, Resp. Ex. B5, Resp. Ex. C2,[44] Resp. Ex. C3.[45] He provided two studies performed by Grimaldi-Bensouda which analyzed safety data related to HPV administration from December 2007 through December 2014 in France. Resp. Ex. B4 at 402, 404; Resp. Ex. C2 at 85. Both studies found no association between the HPV vaccination and ITP. *See id.* Dr. McKenzie also submitted a study performed in Denmark and Sweden in which 296,826 women were studied from October 2006 through December 2010 looking for an increased occurrence of autoimmune disorders, including ITP, following the HPV vaccine. Resp. Ex. B5 at 2. No increased rate of ITP was found. *Id.* He confirmed that "[n]o new biological studies to establish a connection between the peptides in the HPV vaccine and ITP have been reported to date." *Id.* Dr. McKenzie further submitted a French study in which 2.2 million women were studied post-HPV vaccination and no increased rate of ITP was found. Resp. Ex. C3 at 4763-65. This was "the largest study evaluating the risk of [autoimmune disease] after HPV vaccination, thus allowing the assessment of rare diseases not investigated previously." *Id.* at 4766. Based on these studies, respondent concluded, "Simply put, in terms of whether the HPV causes ITP, the scientific community is not a field 'bereft of science.' Rather, a potential association between HPV and ITP has been heavily researched, and no association has been found." Resp. Response at 12.

Ultimately, Dr. Gershwin's cursory assertions that the HPV vaccine can cause ITP via molecular mimicry does not hold weight against Drs. Forsthuber and McKenzie's explanations as to why molecular mimicry is not a sufficient mechanism. Petitioner has failed to provide sound, reliable evidence supporting a connection between ITP and the HPV vaccine; Dr. Gershwin has only submitted generic articles discussing autoimmune disorders caused via molecular mimicry. As noted by Dr. Forsthuber, "[Dr. Gershwin] has not adequately considered that the attenuated viruses contained in the MMR vaccine are structurally and biologically unrelated to the HPV L1 particles contained in the Gardasil vaccine. Moreover, he has not provided any evidence for sequence or structural homology between the MMR viruses and the Gardasil HPV L1 particles." Resp. Ex. A at 7. While Dr. Gershwin did provide evidence supporting a connection between the MMR vaccine and ITP, he neglected to explain why the MMR and HPV vaccines are comparable vaccinations in light of differences between the two highlighted by respondent's experts. Moreover, Dr. Gershwin relied on literature concluding that no evidence exists to support a connection between the HPV vaccine and ITP, which was contrary to Dr. Gershwin's assertions

347 BRITISH MED. J. 1 (2013), filed as Resp. Ex. B5. This study was also filed at Pet. Ex. 101.

[44] Lamiae Grimaldi-Bensouda, *Risk of Autoimmune Diseases and Human Papilloma Virus (HPV) Vaccines: Six Years of Case-Reference Surveillance*, 79 J. AUTOIMMUNITY 84 (2017), filed as Resp. Ex. C2.

[45] Sara Miranda et al., *Human Paillomavirus Vaccination and Risk Autoimmune Diseases: A Large Cohort Study of Over 2 Million Young Girls in France*, 35 VACCINE 4761 (2017), filed as Resp. Ex. C3.

that the HPV vaccine can cause ITP via molecular mimicry. Therefore, without any evidence supporting a biologically sound and reliable mechanism, petitioner has failed to support her burden under *Althen* prong I.

2. Lack of Logical Connection

The second *Althen* prong requires proof of a "logical sequence of cause and effect." *Capizzano*, 440 F.3d at 1326 (quoting *Althen*, 418 F.3d at 1278). In other words, even if the vaccinations can cause the injury, petitioner must show "that it did so in [this] particular case." *Hodges v. Sec'y of Health & Human Servs.*, 9 F.3d 958, 962 n.4 (Fed. Cir. 1993) (citation omitted). "A reputable medical or scientific explanation must support this logical sequence of cause and effect," *id.* at 961 (citation omitted), and "treating physicians are likely to be in the best position to determine whether a logical sequence of cause and effect show[s] that the vaccination was the reason for the injury," *Paluck v. Sec'y of Health & Human Servs.*, 786 F.3d 1373, 1385 (Fed. Cir. 2015) (quoting *Andreu*, 569 F.3d at 1375). Petitioner is not, however, required "to eliminate alternative causes as part of establishing [their] prima facie case." *Doe v. Sec'y of Health & Human Servs.*, 601 F.3d 1349, 1357-58 (Fed. Cir. 2010); *see Walther v. Sec'y of Health & Human Servs.*, 485 F.3d 1146, 1152 (Fed. Cir. 2007) (holding that a "petitioner does not bear the burden of eliminating alternative independent potential causes").

a. Petitioner likely had pre-existing ITP prior to her receipt of the allegedly causal HPV vaccine.

Petitioner showed signs of ITP throughout the duration of her first pregnancy in 2007. She had low platelet counts during all three trimesters and her platelet counts dropped as low as 44 k/ul. Pet. Ex. 9 at 1, 67, 73-75. Her first pregnancy ITP symptoms were inconsistent with traditional gestational thrombocytopenia patients but instead appeared to be symptoms of ITP. *See* Pet. Ex. 2 at 168-28; Resp. Ex. A at 3 (citing Resp. Ex. A6 at 47). While petitioner did not have ITP symptoms during her second pregnancy in 2009, she presented with a low platelet count, 100 k/ul on October 20, 2009, when she was not pregnant, which is consistent with mild ITP. Resp. Ex. B at 4 (citing Pet. Ex. 102, 105). Since no records were filed from 2010 and 2011 leading up to her HPV vaccine, there is no proof that her platelet count was normal after 2009 or remained consistent with mild ITP. Accordingly, both Drs. McKenzie and Forsthuber opined that it is likely petitioner had preexisting ITP prior to her receipt of the HPV vaccine. *Id.*; Resp. Ex. D at 2.

Dr. Gershwin has not expressly refuted that petitioner had preexisting ITP, but opined that petitioner's history of ITP "would reflect her own genetic predisposition . . . [which] would make her more susceptible to subsequent developments of thrombocytopenia." *Id.* He further stated that "the pathophysiology of ITP is essentially a promiscuous response against platelet antigens and, as such, [she] would be expected to have memory cells against platelet antigens based on her previous episode of ITP." Resp. Ex. 20 at 10. Again, Dr. Gershwin neglected to provide evidence in support of this assertion. *See id.* He referenced his original report in which he "emphasized the role of molecular mimicry and cited the examples of the MMR vaccine." *Id.* He also stated that if any other clinically significant risk factors were identified, then he would have considered them in his analysis (ignoring several risk factors identified below). *Id.*

In response to the foregoing, Dr. Forsthuber submitted that Dr. Gershwin clearly accepted that petitioner had developed ITP prior to her allegedly causal HPV vaccine. Resp. Ex. D at 2 (citing Pet. Ex. 134 at 3). Dr. Forsthuber acknowledged that petitioner's thrombocytopenia symptoms during her first pregnancy were thought to be signs of GT, although ITP was never definitively ruled out. *Id.* Additionally, Dr. Forsthuber explained that it is difficult to differentiate between GT and pregnancy-induced ITP as there is no reliable laboratory testing to confirm the diagnosis. *Id.* However, during petitioner's first pregnancy, her platelet levels dropped as low as 41 k/ul, lower than what is expected from a patient with GT, whose platelet counts typically only drop to 70 to 80 k/ul. *Id.* (citing Pet. Ex. 1 at 111). He also pointed out that petitioner's platelet count dropped abnormally low in October 2009, when she was not pregnant. *Id.* (citing Pet. Ex. 102 at 105, 132).

Petitioner clearly had low platelet counts when she was not pregnant before and after receipt of the HPV vaccine, and during the first trimester of her pregnancies which is atypical for gestational thrombocytopenia. Additionally, while some of petitioner's treaters diagnosed her with gestational thrombocytopenia, Dr. Forsthuber differentiated the symptoms of GT and petitioner's ITP, namely that petitioner's platelet count dropped significantly lower than typical patients with GT, and that her counts dropped earlier in her pregnancy than is typical of GT. Upon evaluation of these facts, I find that petitioner more likely than not suffered from ITP prior to her receipt of the HPV vaccine. This Court previously stated, "[P]etitioners must offer preponderant evidence that an allegedly vaccine-caused illness began after receipt of the vaccination to demonstrate entitlement to damages." *Johnson v. Sec'y of Health & Human Servs.*, No. 14-113V, 2017 WL 772534, at *18 (Fed. Cl. Spec. Mstr. Jan. 6, 2017). Accordingly, petitioner is not entitled to compensation.

It is of note that a significant aggravation analysis may have been appropriate here if petitioner had provided a sound and reliable mechanism for causation. *See W.C. v. Sec'y of Health & Human Servs.*, 704 F.3d 1352, 1357 (Fed. Cir. 2013) ("[A] petitioner in an off-table case must show the vaccine actually caused the significant aggravation—not just that, accepting petitioner's medical theory as sound, the person's condition worsened within a medically-acceptable timeframe"). However, because petitioner failed to provide a sound and reliable mechanism for causation and failed to provide any expert opinion of aggravation, that analysis is unnecessary.

b. Petitioner was experiencing several risk factors at the time of onset of her ITP symptoms that are known causes of ITP.

Even if Dr. Gershwin had offered a sound and reliable mechanism of causation by which petitioner's ITP could have been caused by the HPV vaccine, several risk factors known to cause ITP were present at the time of vaccination that Dr. Gershwin failed to acknowledge as potential causes of petitioner's ITP.[46] Dr. Gershwin contended that petitioner was not affected by any extrinsic unrelated factors that could have caused her ITP. Pet. Ex. 20 at 11. Dr. Gershwin was alerted of the shortcomings in his reports by three orders of the Court giving him several opportunities to remedy these issues. *See* Scheduling Orders, ECF Nos. 47, 57, 79. However, Dr.

[46] Respondent asserted that he was not pleading alternative causes but pointed out that Dr. Gershwin flatly disregarding petitioner's medical history. *See* Resp. Response at 16, ECF No. 93.

Gershwin failed to take these opportunities to address the specific factors that petitioner was experiencing before and during her pregnancy, including extreme stress, Gardnerella vaginalis, HPV herpes warts, and the medication for those warts and ultimately concluded that there was no evidence linking these factors and ITP. *See* Pet. Ex. 103 at 1-3; Pet. Ex. 134 at 1-2. Dr. Forsthuber responded to these statements by identifying the following possible contributory factors. Resp. Ex. A at 5.

i. Petitioner's HPV and Aldera cream use at the time of vaccination

Petitioner had HPV genital warts on May 24, 2011 for which she was treated with Aldera cream, approximately two weeks prior to her receipt of the HPV vaccine. Resp. Ex. D at 2 (citing Pet. Ex. 1 at 64). Dr. Gershwin did not address petitioner's actual HPV infection at the time of vaccination, despite his assertions that HPV antigens in the vaccine can induce molecular mimicry and cause ITP or differentiate between the HPV antigens petitioner had at the time of vaccination because of her genital warts and those present in the HPV vaccination. Moreover, Dr. Gershwin did not discuss the Aldera cream petitioner was prescribed to treat her genital warts, even though, as Dr. Forsthuber asserted, the active ingredient of Aldera cream is Imiquimod. Imiquimod is a Toll-like receptor ("TLR") 7 agonist 4 that has been shown to "promote proinflammatory cytokine production by macrophages from ITP patients, and to decrease platelet counts, i.e. promote thrombocytopenia in an experimental mouse model of ITP." *Id.* (citing Resp. Ex. D4[47] at 239). He also indicated that at least one medical report has linked Imiquimod treatment as a cause ITP. *Id.* (citing Resp. Ex. D5[48] at 79-80). Dr. Gershwin did not address petitioner's Aldera cream usage despite Dr. Forsthuber's assertions. *See generally* Pet. Ex. 103, 134.

ii. Petitioner's history of bacterial vaginosis with Gardnerella

In response to the Court's inquiry as to the role of petitioner's Gardnerella vaginalis as the cause of her ITP, Dr. Gershwin cursorily stated, "Essentially, there is no evidence that Gardnerella produces thrombocytopenia." Pet. Ex.134 at 1. In response, Dr. Forsthuber opined, "[I]n many patients, vaginal Gardnerella infection induces *systemic* immunoglobulin production; therefore, it can generate a *systemic* immune response which could potentially induce autoantibodies and autoreactive T cells via molecular mimicry." Resp. Ex D at 1. Additionally, *candida* species, a typical coinfection with vaginosis, have been associated with chronic ITP. *Id.* (citing Resp. Ex. D3[49] at 202-03). Therefore, Dr. Forsthuber opined that petitioner's Gardnerella and bacterial vaginosis could have been contributing factors to petitioner's ITP. *Id.*

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[47] Qing Yang et al., *TLR7 Promotes Th1 Polarization in Immune Thrombocytopenia*, 128 THROMBOSIS RESEARCH 237 (2011), filed as Resp. Ex. D4.

[48] E.A. Whatling et al., *Immune Thrombocytopenic Purpura: A Rare Side Effect in a Patient Treated with Imiquimod for Lentigo Maligna*, 13 JPRAS OPEN INTNT'L J. OPEN ACCESS J. OF SURGICAL RECONSTRUCTION 77 (2017), filed as Resp. Ex. D5.

[49] Mahmoud H. Ayesh et al., *Candida Albicans-Induced Chronic Thrombocytopenic Purpura*, 126 ACTA. HAEMATOL. 202 (2011), filed as Resp. Ex. D3.

iii. Petitioner's pregnancy

ITP triggered by pregnancy typically appears in the first trimester as opposed to gestational thrombocytopenia which occurs during the second and/or third trimester. Resp. Ex. A at 3 (citing Resp. Ex. A5 at 397-98). As noted by petitioner's hematologist, petitioner suffered from pregnancy related ITP rather than gestational thrombocytopenia as her platelet counts dropped lower than 70 k/ul and onset of her symptoms occurred in the first trimester as opposed to later in her pregnancy. See Pet. Ex. 2 at 125-28. Additionally, literature cited by Dr. Gershwin stated that "many hematologic problems develop in pregnancy or can be triggered by the pregnant state," and that "pregnancy can exacerbate underlying hematologic disorders." *Id.* at 9. Dr. Gershwin, however opined that "[t]here is no known relationship between gestational ITP and [petitioner's] subsequent development of ITP." Dr. Gershwin further opined that petitioner's heavy bleeding during her pregnancy would be consistent with thrombocytopenia but that, "It is not possible for [him] to provide a percentage of contribution of the thrombocytopenia versus local placental factors and the heavy bleeding that occurred during pregnancy." *Id.* Dr. Gershwin disregarded blood work that showed a low platelet count when she was not pregnant, which suggests that she had ITP prior to this pregnancy.

Dr. Forsthuber explained that pregnancy alone can impact a woman's immune system and "represents a significant disturbance to the immune homeostasis and challenge to immune tolerance mechanisms." Resp. Ex. A at 6. He noted the first trimester is considered a proinflammatory phase which could have increased petitioner's risk of developing ITP during her pregnancy. *Id.* (citing 14-15).

iv. Petitioner's ongoing stress

When petitioner received the allegedly causal HPV vaccine, she admittedly was suffering from a substantial amount of stress. She had just started a new job and had two other children with serious medical issues. Pet. Ex. 16 at 63. She also presented to the emergency room within a week of receiving the HPV after having been physically assaulted by an ex-boyfriend. *Id.* at 7-19, 59. During this visit, several injuries were noted, and petitioner was reported to be especially anxious. *Id.* at 9-10. She subsequently found out she was pregnant within two weeks of this emergency department visit. Pet. Ex. 1 at 62, 81.

Dr. Gershwin denied that there is acceptable data that stress can trigger ITP or exacerbate a person's ITP symptoms. Pet. Ex. 134 at 2. Dr. Gershwin submitted that there has been no data found associating individuals in combat zones with higher instances of ITP or other autoimmune diseases. *Id.*

Dr. Forsthuber, however, argued that "[t]here is a vast amount of peer reviewed medical literature implicating psychological stress in the development and modulation of a variety of autoimmune conditions." Resp. Ex. D at 3 (citing Resp. Ex. D6[50] at 365, 369-72). Specifically, Dr. Forsthuber identified a study in which Iraq and Afghanistan veterans with post-traumatic stress disorder have shown an elevated risk for autoimmune disorders, and thus petitioner's stress related

[50] Aoife O'Donovan et al., *Elevated Risk for Autoimmune Disorders in Iraq and Afghanistan Veterans with Posttraumatic Stress Disorder*, 77 BIOLOGICAL PSYCHIATRY 365 (2015), filed as Resp. Ex. D6.

to her domestic abuse, pregnancy, and children with health issues could have been a factor in her development of ITP. *Id.* (citing 6).

v. Petitioner's phentermine usage during pregnancy

Dr. Gershwin admitted that phentermine use during pregnancy is contraindicated but there is little information available and thrombocytopenia is not listed as a side effect of the drug. Pet. Ex. 132 at 1-2. He claimed to have researched phentermine side effects on the FDA website and peer reviewed publications and found no such relationship between ITP and the drug. *Id.* Yet, he cited to eHealthMe, a website, that stated "of 11,467 people reported to have side effects from phentermine, 17, or .15%, had thrombocytopenia." *Id.* at 1-2.

As phentermine is associated with several gastrointestinal side effects including constipation and diarrhea, Dr. Forsthuber noted that petitioner's prolonged use of this drug could have affected her intestinal homeostasis and "thereby alter[ed] intestinal microbiota composition, which, in turn, has moved to the forefront of interest in autoimmune research." Resp. Ex. D at 2. Dr. Forsthuber further stated that significant evidence in the autoimmunity research field has suggested intestinal microbiota may trigger autoimmune disease pathology. *Id.* Therefore, he concluded that petitioner's phentermine usage could have "played a surreptitious role in [petitioner's] disease condition. *Id.*

Dr. McKenzie pointed out that Dr. Gershwin criticized respondent's experts for identifying risk factors without evidence that they could cause ITP, stating it was ironic that petitioner's expert did not apply the same logic to the HPV vaccine. *Id.* Dr. McKenzie concluded that out of the all external factors both he and Dr. Forsthuber referenced as present in petitioner at the outset of her ITP symptoms in 2011, including the HPV vaccine, the only event for which no epidemiologic or scientific evidence exists is the vaccine. *Id.*

Petitioner presented with and suffered from a host of risk factors that could have contributed to her preexisting ITP at the time of her HPV vaccine. Dr. Gershwin failed to address any of these items; he also failed to provide any persuasive evidence that the HPV vaccine can cause or aggravate ITP. While petitioner is not required to eliminate alternative causes to satisfy prong II, her expert failed to address how the vaccine could have been the cause of or aggravated her ITP in the first place while respondent provided evidence for each of the other illnesses and or medication and their associations to ITP. *See* Pet. Ex. 20 at 11 ("During this time [approximately one month prior to vaccination], there were no other risk factors identified . . .").

Given petitioner's likely pre-existing ITP and the several risk factors present before and at the time of receipt of the allegedly causal vaccination, petitioner has failed to satisfy her burden under *Althen* prong II.

3. Proximate Temporal Relationship

To satisfy the third *Althen* prong, petitioner must establish a "proximate temporal relationship" between the vaccination and the alleged injury. *Althen*, 418 F.3d at 1281. This "requires preponderant proof that the onset of symptoms occurred within a timeframe for which,

given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation-in-fact." *de Bazan*, 539 F.3d at 1352. Typically, "a petitioner's failure to satisfy the proximate temporal relationship prong is due to the fact that onset was too late after the administration of a vaccine for the vaccine to be the cause." *Id.* However, "cases in which onset is too soon" also fail this prong; "in either case, the temporal relationship is not such that it is medically acceptable to conclude that the vaccination and the injury are causally linked." *Id.*; *see also Locane v. Sec'y of Health & Human Servs.*, 685 F.3d 1375, 1381 (Fed. Cir. 2012) ("[If] the illness was present before the vaccine was administered, logically, the vaccine could not have caused the illness.").

As discussed above, there is considerable evidence that petitioner suffered from ITP prior to vaccination. However, even if petitioner had proven that she did not have pre-existing ITP, petitioner has provided no evidence of a medically acceptable timeframe for onset of ITP following the HPV vaccine. Dr. Gershwin submitted evidence regarding a medically acceptable timeframe for onset of ITP following an MMR vaccine, but provided no evidence as to whether the same timeframe would be medically acceptable for the HPV vaccine. Accordingly, petitioner has also failed to satisfy his burden under *Althen* prong III.

VI. Conclusion

Upon careful evaluation of all of the evidence submitted in this matter—including the medical records, expert reports, and medical literature—I conclude that petitioner has not shown by preponderant evidence that she is entitled to compensation under the Vaccine Act. Petitioner has failed to offer sufficient evidence showing that the HPV vaccination caused her ITP. **The petition is therefore DISMISSED. The Clerk shall enter judgment accordingly.**[51]

IT IS SO ORDERED.

s/ Mindy Michaels Roth
Mindy Michaels Roth
Special Master

[51] Pursuant to Vaccine Rule 11(a), entry of judgment can be expedited by each party filing a notice renouncing the right to seek review.