In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 15-146V

(to be published)

* *	Chief Special Master Corcoran
C. VANESSA RANDOLPH *as executor of* the estate of DOROTHY T. GRAY, *	
*	Filed: November 12, 2021
Petitioner, *	
v. *	
*	
SECRETARY OF HEALTH AND HUMAN SERVICES, *	
*	
Respondent. *	
*	
* *	

Andrew Donald Downing, Van Cott & Talamante, PLLC, Phoenix, AZ, for Petitioner.

Kelly Heidrich, U.S. Dep't of Justice, Washington, DC, for Respondent.

ENTITLEMENT DECISION[1]

On February 18, 2015, Dorothy Gray filed a petition for compensation pursuant to the National Vaccine Injury Compensation Program, 42 U.S.C. §§ 300aa-10 to -34 (2012) (the "Vaccine Program").[2] (ECF No. 1) ("Pet."). She alleged that as a result of receiving a seasonal influenza ("flu") vaccine on October 11, 2011, she suffered neurological symptoms later diagnosed as Bickerstaff Brainstem Encephalitis ("BBE"). Pet. at ¶ 2. Mrs. Gray passed away

[1] This Decision shall be posted on the Court of Federal Claims' website in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 (2012)). **This means that the Decision will be available to anyone with access to the internet.** As provided by 42 U.S.C. § 300aa-12(d)(4)(B), 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 Decision will be available to the public. *Id*.

[2] The Vaccine Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3758, codified as amended at 42 U.S.C. §§ 300aa-10 through -34 (2012) [hereinafter "Vaccine Act" or "the Act"]. Individual section references hereafter will be to Section 300aa of the Act (but will omit the statutory prefix).

due to other causes[3] on December 17, 2016, and her daughter, C. Vanessa Randolph, subsequently appeared as the Petitioner. Status Report at 1, filed on July 13, 2017 (ECF No. 57).

The parties have agreed that the matter could be fairly resolved on the papers. After reviewing the record, all expert reports and associated literature, and the parties' respective briefs, I hereby deny entitlement. Although Petitioner did successfully establish the flu vaccine can likely cause BBE in the timeframe at issue, she did not preponderantly demonstrate it likely did so *to Mrs. Gray* under the facts of this case.

I. Factual Background

Prior Medical History and Vaccination

Mrs. Gray was born on May 4, 1932. Pet. at 1. She received the flu vaccine on October 11, 2011, when she was 79 years old. *Id.* At the time of vaccination, Mrs. Gray suffered from asthma and Chronic Obstructive Pulmonary Disease ("COPD"). Ex. 17 at 12. Previously Mrs. Gray also had pulmonary nodules, allergic rhinitis, and depression. Ex. 2 at 8. Of particular significance to this case, Mrs. Gray was predisposed to frequent urinary tract infections ("UTI"). *Id.* The record contains no evidence of any post-vaccine reaction during the entire remainder of the month of October 2011.

Post-Vaccination Medical Issues

On November 11, 2011—a full month after the relevant vaccination—Mrs. Gray was seen by Dr. Vicki Brewer for recurrent UTI symptoms. Ex. 17 at 25. Although Mrs. Gray had taken medication in self-treatment, her issues continued. *Id.* She was also experiencing coughing, pulmonary issues, urinary frequency and urgency, was feverish, and felt unsteady. *Id.* She was prescribed Levaquin and a Medrol dose pack. *Id.* She was also told to obtain a complete blood count ("CBC") test and follow up with her primary care doctor. *Id.*

Mrs. Gray was next seen by Dr. Ingrid Antonsen, her Primary Care Physician, three days later, on November 14, 2011, for generalized weakness and fatigue. Ex. 17 at 22. At this time, she reported that she had not been feeling well, spending lots of time in bed, and was not eating or drinking as she normally had. *Id.* A chest x-ray was conducted and revealed nothing concerning, her CBC test results were deemed "unremarkable." *Id.* However, serologic testing did reveal elevated biomarkers for inflammation/kidney dysfunction, with her BUN[4] and creatine

[3] It thus is not claimed herein that Mrs. Gray's death was attributable to the flu vaccine.

[4] "BUN" stands for blood urea nitrogen levels, urea being "a compound . . . formed in the liver via the urea cycle from ammonia produced by the deamination of amino acids and later excreted by the kidney." DORLAND'S ILLUSTRATED MEDICAL DICTIONARY 1975 (33rd ed. 2020) ("DORLAND'S"). A BUN test is a blood test used to measure the amount

levels notably high (BUN at 33 mg/dl (normal 7–18), and creatine at 1.2 mg/dl (normal .6–1.0)). *Id.* at 27.

At this time, Mrs. Gray had no urinary frequency or urgency as previously noted, and denied difficulties speaking or swallowing. Ex. 17 at 22. Ms. Randolph informed Dr. Antonsen that Mrs. Gray had been consuming liquids and felt better. *Id.* It was concluded that her symptoms were responding to antibiotic treatment, and that her current complaint could be associated with a viral infection. *Id.* at 23. An MRI of Mrs. Gray's brain, and an MRI angiogram of the head and neck, were ordered by Dr. Antonsen, and both produced normal readings. Ex. 4 at 28. Additional MRIs were performed on November 22, 2011, one with and one without gadolinium contrast.[5] Ex. 17 at 6. From the MRIs, it was concluded that "[p]eriventricular and deep white matter changes" were present, with also evidence of "[i]ncreased signal in mastoids bilaterally," but no diagnosis was reached in reaction to the findings. *Id.*

Three days later, Mrs. Gray was taken to the emergency room on November 25, 2011, after experiencing choking, vertigo, headaches at the top of her head, and imbalance. Ex. 17 at 12. Petitioner (who accompanied her mother to the ER) explained to the ER doctors that on Thanksgiving Eve (which that year would have been November 23, 2011), Mrs. Gray had complained that it felt like something was stuck in her throat. *Id.* Ms. Randolph had given her a nebulizer on Thanksgiving, and Mrs. Gray had a productive cough. *Id.* A CT scan was conducted that was negative for acute intracranial abnormality and mild generalized volume loss and microvascular disease. *Id.* at 18.

Mrs. Gray was thereafter admitted to Provena Covenant Medical Center in Urbana, Illinois ("Provena"). *See generally* Ex. 17. On November 26, 2011, two procedures were conducted: an upper endoscopy and an esophageal dilation. *Id.* at 16. After this the postoperative findings included hoarseness of voice, questionable dysphagia, regurgitation, probable cricopharyngeal dysphagia, normal trachea opening, normal esophagus, mild gastritis, and no ulcers or cancer. *Id.*

A second CT scan was completed, and it was found that there "is no evidence of radiopaque foreign body noted in the oropharyngeal, nasopharyngeal pharynx, hypopharynx and cervical esophagus or upper airway." Ex. 17 at 8. Additionally, no abnormalities were found in

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of urea nitrogen in the blood. See Blood Urea Nitrogen (BUN) Test, Mayo Clinic, https://www.mayoclinic.org/tests-procedures/blood-ureanitrogen/about/pac-20384821 (last accessed on November 9, 2021). Urea nitrogen is a chemical waste product that is typically removed from the body through the kidneys. DORLAND'S at 1975. A higher than normal BUN test can suggest that the kidneys or liver may not be working properly. *Id.* It can also be evidence of inflammation or infection, especially when compared to creatine levels.

[5] Gadolinium is the "complex of gadolinium with diethylenetriamine pentetic acid bismethylamide, and is used as a paramagnetic contrast medium in magnetic resonance imaging." DORLAND'S at 745; *L.Z. v. Sec'y of Health & Hum. Servs.*, No. 14-920V, 2018 WL 5784525, at *3 n.7 (Fed. Cl. Spec. Mstr. Aug. 24, 2018).

Mrs. Gray's parotid glands, submandibular glands, tonsils, and adenoids. *Id.* There was further no evidence of lymphadenopathy or soft tissues mass noted in the neck, and Mrs. Gray's thyroid gland was of normal size. *Id.* There were arthritic changes noted in some of the cervical spine, along with degenerative disk disease. *Id.* At this time, Mrs. Gray also presented with some nasal congestion and post-nasal drainage. *Id.* at 12.

On November 28, 2011, a chest x-ray was performed that determined Mrs. Gray's lungs were normal, except for scarring in the left base. Ex. 17 at 10. Likely scarring within the lingula of the left lower lobe was noted as well. *Id.* The following day, Mrs. Gray's presentation and history was reviewed by Dr. Kaushik J. Patel, who found that she had an increased cough with no clear etiology. *Id.* at 14. Along with this, Dr. Patel observed in her history that she had experienced aspiration. *Id.* Dr. Patel chose to have Mrs. Gray continue with nebulizer treatments twice daily, and along with use of combined albuterol and ipratropium nebulizer treatments four times a day. *Id.* She was also given a Medrol Dosepack and instructed to use a nasal spray. *Id.*

On December 1, 2011, Mrs. Gray was seen again at Provena, where a videostrobe[6] was performed. Ex. 4 at 162. Based on the findings, treaters proposed a diagnosis of a paralyzed left vocal cord that was neurological in origin, and they advised that a neurologic specialist should be consulted as soon as possible. *Id.* Dr. John Helfrich, neurologist, then saw Mrs. Gray the same day and performed many tests, noting left side weakness, nystagmus,[7] and cerebellar ataxia. *Id.* A barium test was conducted, and Mrs. Gray was found to have penetration. *Id.* at 147. Based upon the penetration Dr. Cary Siegel found that there was "[m]ild pharyngeal deficit with trace aspiration." *Id.*

The next day (December 2, 2011), Mrs. Gray was admitted to Barnes Jewish Hospital. *See generally* Ex. 4. Notes from the neurologic exam she received recorded that her symptoms had begun three weeks prior, when she first experienced acute vertigo (although the record reveals a later onset). *Id.* at 28. On December 4, 2011, Mrs. Gray received a steroid injection of the left true vocal cord. *Id.* at 24. A lumbar puncture was performed on December 5, 2011. *Id.* at 158. It revealed normal protein and glucose levels, along with negative tests for oligoclonal bands, Lyme disease antibody, culture tests for Staphylococcus aureus, Pseudomonas aeruginosa, beta-hemolytic streptococci, fungus, Cryptococcus neoformans antigen, Cytomegalovirus PCR, Varicella Zoster Virus PCR, and Herpes Simplex Virus PCR. *Id.* at 158–67. She also tested negative for paraneoplastic antibodies, and CTs of Mrs. Gray's neck and chest were also

[6] A videostrobe involves insertion of a camera through the mouth or nose, giving a view of the vocal cords as they move in slow motion. *Voice Disorders Diagnosis & Treatment*, MAYO CLINIC (Oct. 2, 2020), https://www.mayoclinic.org/diseases-conditions/voice-disorders/diagnosis-treatment/drc-20353024.

[7] Nystagmus is the "involuntary, rapid, rhythmic movement of the eyeball, which may be horizontal, vertical, rotatory, or mixed." DORLAND'S at 1289.

inconclusive. *Id.* at 145, 149, 173–74.

Diagnostic Efforts

Up to this point, treaters could not pinpoint the nature of Mrs. Gray's illness. Her diagnostic differential included the Miller-Fisher variant of Guillain-Barré syndrome ("GBS"), brainstem encephalitis, remote effects of cancer, BBE, and others. Ex. 2 at 140. However, by December 6, 2011, Mrs. Gray was first noted as having a seventh nerve palsy—also known as Bell's palsy, meaning a "unilateral facial paralysis of sudden onset"—and thus additional evidence of neurologic injury was discovered. Ex. 4 at 45.[8] She was now started on a prednisone 60 mg per day. *Id.* She also at this time was experiencing a drastic mental decline. Dr. Antonsen's affidavit stated that Mrs. Gray "lacked the mental capacity to make decision on her own. Her daughter had to handle all decision making for her," and was "completely reliant on her daughter." Ex. 5. Dr. Edwin McCammack also saw Mrs. Gray several times between December 2011 and March 2012, noting that during this time period she was "extremely impaired" and was "certainly not capable of making any decision on her own." Ex. 10.

The following day, December 7, 2011, Mrs. Gray was discharged and diagnosed with BBE from Barnes-Jewish Hospital. Ex. 4 at 112. Upon reviewing all of the tests and information Dr. Helfrich proposed the view that she likely had "brainstem encephalitis, possibly paraneoplastic, possibly Bickerstaff brainstem encephalitis, possibly some immunological issue for encephalitis." Ex. 2 at 140. The differential at this point relied on Mrs. Gray's symptoms of laryngeal nerve palsy, facial nerve palsy, nystagmus, and prior autonomic dysfunction now resolved. *Id.* at 55. No mention was made of the flu vaccine as possibly causal, however, or having contributed to Mrs. Gray's illness in any way.

Treatment in 2012 and Beyond

A videostroboscopy was completed on January 23, 2012, at which time Mrs. Gray was having difficulty with her voice and swallowing. Ex. 2 at 93. Decline in her vocal quality continued into the early spring of 2012. *Id.* at 62. A follow-up visit with Mrs. Gray was conducted on May 21, 2012, however, at which time she showed some improvement. *Id.* at 40. Several other follow-up visits reported similar positive progressions for Mrs. Gray. *See, e.g.*, *id.* at 24.

In the subsequent three years, Mrs. Gray continued to have therapy to help with her condition. In a check-up on December 10, 2012, Dr. Antonsen saw her again and stated she had been recovering well, even being released from neurology care the prior week, and was becoming more active and able to live independently. Ex. 2 at 12. Mrs. Gray had some remaining issues of acute right otitis externa secondary to an atomycosis, bilateral hearing aids, anemia, COPD,

[8] DORLAND'S at 1345.

asthma, and obstructive sleep apnea. *Id.*

A year later, on December 2, 2013, Mrs. Gray had a visit with Dr. Henry W. Lipps, who noted that she had successfully weathered a thyroplasty[9] with good results. Ex. 2 at 244. Another videostroboscopy was conducted the month before, determining that while she was still having trouble swallowing, prior treatments were still likely to be beneficial once they fully resolved. *Id.* at 254. And by December 19, 2014, treaters observed that Mrs. Gray had made good recovery overall, even though her voice remained slightly thin and raspy. *Id.* at 217. Mrs. Gray passed away on December 17, 2016 from right perihilar pneumonia and COPD. ECF No. 37.

II. Expert Reports

A. *Petitioner's Expert: Lawrence Steinman, M.D.*

Dr. Steinman submitted two expert reports on behalf of Petitioner. Report, dated as February 11, 2017, filed as Ex. 21 (ECF No. 45-1) ("First Steinman Rep."); Supplemental Expert Report, dated as July 23, 2017, filed as Ex. 48 (ECF No. 60-1) ("Second Steinman Rep."). Dr. Steinman opines that Mrs. Gray developed BBE as a result of the flu vaccine she received on October 11, 2011. First Steinman Rep. at 1. He also proposes that the onset of Mrs. Gray's symptoms likely occurred five weeks after receiving the vaccine, or on November 17, 2011, and that this timeframe is consistent with what would be expected for similar inflammatory neuropathy conditions. *Id.* at 24.

As shown in his CV, Dr. Steinman received his B.A. from Dartmouth College and his M.D. from Harvard Medical School. Ex. 22 at 1 (ECF No. 45-2) (Dr. Steinman's Curriculum Vitae ("Steinman CV")). He then completed residencies in neurology and pediatrics at Stanford University. *Id.* He has worked as a professor of neurology and pediatrics at Stanford for the past forty-one years. *Id.* Dr. Steinman has also published over five hundred peer-reviewed publications on neurology and autoimmune disease. *Id*. at 5–45. He has special expertise in the study of encephalitis and demyelination, having several articles published on the issues. *Id.* at 2–45. Dr. Steinman is part of the American Association of Immunologists and the Clinical Immunology Society, with patents in the field and many papers on the topic. *See generally id*.

First Report

Dr. Steinman's first report began with an overview of some of Mrs. Gray's relevant

[9] Thyroplasty is a treatment where "[a] small opening is created in the cartilage from the outside of [the] voice box. The doctor inserts an implant through the opening and pushes it against the paralyzed vocal cord, moving it closer to [the] other vocal cord." *Voice Disorders Diagnosis & Treatment*, MAYO CLINIC (Oct. 2, 2020), https://www.mayoclinic.org/diseases-conditions/voice-disorders/diagnosis-treatment/drc-20353024.

medical history. First Steinman Rep. at 3–7. He concurred with the BBE diagnosis, adding that treaters had not embraced antecedent infection as an explanation (although he did not elaborate how the record supported that contention). *Id.* at 7.

Dr. Steinman then proposed a theory for how the flu vaccine could cause BBE. He noted at the outset that the 2011–12 formulation of the flu vaccine (which he assumed to be equivalent to the version Petitioner received in October 2011) could elicit the production of anti-ganglioside antibodies that would (in an autoimmune process) cause the nerve damage specific to a neuropathic injury like BBE. First Steinman Rep. at 8. To support this contention, he offered medical literature discussing animal studies evaluating the impact different versions of the flu vaccine had in the context of the comparable peripheral neuropathy of GBS. *Id.*; I. Nachamkin et al., *Anti-Ganglioside Antibody Induction by Swine (A/NJ/1976/H1N1) and Other Influenza Vaccines: Insights into Vaccine-Associated Guillain-Barré Syndrome*, 198 J. of Infectious Diseases 226 (2008), filed as Ex. 34 on Feb. 13, 2017 (ECF No. 46-4) ("Nachamkin") (finding that all inoculated mice developed IgM and IgG anti-ganglioside antibodies). Indeed, Dr. Steinman went a step further, maintaining that the vaccine likely *already contained* gangliosides that are associated with neuroinflammatory conditions such as BBE, or other wild virus components that could contribute to an autoimmune process. First Steinman Rep. at 11.[10]

These same kinds of anti-ganglioside antibodies were identified in individuals suffering from BBE. First Steinman Rep. at 8–9; N. Yuki, *Guillain-Barré Syndrome and Anti-Ganglioside Antibodies: A Clinician-Scientist's Journey*, 88 Proc. Japan Acad., Series B 299 (2012), filed as Ex. 35 on Feb. 13, 2017 (ECF No. 46-5) ("Yuki"), explaining that it shows GT1a, GQ1b and

[10] Dr. Steinman did not bulwark this contention with much in the way of direct proof. Rather, he relied on an argument that the flu vaccine formulation that Mrs. Gray received also happened to contain neuraminidase—an enzyme enabling the wild influenza virus's infectious processes—and that one purpose of the vaccine was to promote an antibody response to this enzyme (and thus make it less likely, in the immune response to a future wild virus infection, that the virus could successfully infect). First Steinman Rep. at 8–10; I. Sultana et al., *Stability of Neuraminidase in Inactivated Influenza Vaccines*, 32 Vaccine 2225 (2014), filed as Ex. 37 on Feb. 13, 2017 (ECF No. 46-7) ("Sultana"); *see also* M. Laguio-Vila et al., *Comparison of Serum Hemagglutinin and Neuraminidase Inhibition Antibodies After 2010-2011 Trivalent Inactivated Influenza Vaccination in Healthcare Personnel*, 2 Open Forum Infectious Diseases 1 (2014), filed as Ex. 36 on Feb. 13, 2017 (ECF No. 46-6) (establishing that the relevant version of the flu vaccine caused the production of neuraminidase-specific antibodies).

In effect, Dr. Steinman seems to contend that the flu vaccine could not only result in the production of ganglioside-specific autoantibodies, but also autoantibodies specific to the neuraminidase enzyme so important to the process by which a wild infectious process would propagate—thus suggesting the vaccine's pathologic capabilities were quite large. I note, however, that articles like Sultana speak far more about the *intended* function of vaccination than they do about its potential aberrant capacity. *See, e.g.*, Sultana at 2229–30 (discussing the immunogenicity and stability of the flu vaccine as the true goal of the study). Thus, the fact that neuraminidase might play a role in encouraging the wild virus's infectious process—such that antibodies against it could help arrest that that process—*does not mean* the presence of this enzyme, due to the vaccine's inherent inclusion of wild virus components, implies another avenue for unintended pathology. Nevertheless, Dr. Steinman's overall opinion was not particularly weakened by this somewhat misleading detour (and my *Althen* prong one finding in Petitioner's favor obviates the need to follow up this point with detailed analysis).

GD1b antibodies are found in Bickerstaff's brainstem encephalitis. *See id.*. This paper was a general review of Yuki's clinician studies, including a focus on two patients with GBS and demonstrations of molecular mimicry in a patient with GBS. *See generally id*. Thus, Dr. Steinman was able to discern an association between the vaccine's capacity to elicit the antibodies and the injury at issue (although the strength of this association is not self-evident from these items of literature). The anti-ganglioside antibodies elicited could recognize the "chemical building blocks" BBE targets, attacking them and thus causing injury. First Steinman Rep. at 11.[11]

Other antigenic components of the relevant version of the flu vaccine could also, in Dr. Steinman's view, have played a role in Petitioner's injury. For example, the vaccine likely contained "molecular mimics" to MOG and myelin basic protein ("MBP"), two nerve protein components relevant to inflammatory encephalitis (a condition somewhat comparable to Mrs. Gray's BBE). First Steinman Rep. at 13; A. Pohl-Koppe et al., *Myelin Basic Protein Reactive Th2 T Cells are Found in Acute Disseminated Encephalomyelitis*, 91 J. of Neuroimmunology 19 (1998) filed as Ex. 41 on Feb. 13, 2017 (ECF No. 47-1); A. Gautam et al., *A Viral Peptide with Limited Homology to a Self Peptide Can Induce Clinical Sings of Experimental Autoimmune Encephalomyelitis*, 161 J. of Immunology 60 (1998), filed as Ex. 42 on Feb. 13, 2017 (ECF No. 47-2). Relying on the scientific concept of molecular mimicry, Dr. Steinman maintained that certain vaccine antigens were sufficiently similar (in terms of sequential amino acid components) to self structures to result in an autoimmune cross-attack, as antibodies generated in response to the antigens also attacked the homologous self structures.

To demonstrate the scientific basis for this contention, Dr. Steinman conducted several BLAST searches,[12] comparing five amino acid-sequences from the vaccine antigens to the relevant nerve proteins, to identify matches. First Steinman Rep. at 13, 17–23. He deemed a chain of that length sufficient to produce a cross-reaction. *Id.* at 14. And his "in silica" research[13] revealed sufficient homology for him to conclude that the relevant form of the flu vaccine could trigger BBE. *Id.* at 23.

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[11] Dr. Steinman acknowledged that a Chinese study suggested that a slightly different formulation of the flu vaccine from the same time period had not been found to elicit the same anti-ganglioside antibodies. First Steinman Rep. at 12–13; T. Lei et al., *Anti-ganglioside Antibodies were not Detected in Human Subjects Infected with or Vaccinated Against 2009 Pandemic Influenza A (H1N1) Virus*, 30 Vaccine 2605, 2606 (2012), filed as Ex. 38 on Feb. 13, 2017 (ECF No. 46-8). But Dr. Steinman deemed the study distinguishable, since it not only considered a monovalent version of the vaccine, but also involved only eight relevant subject patients, making it difficult to reliably extrapolate its findings to this case. First Steinman Rep. at 13.

[12] A BLAST search involves review of an online database to "compare[] nucleotide and protein sequences, to search for a homology between the [] vaccine and [the body's myelin basic protein]." *Montgomery v. Sec'y of Health & Hum. Servs.*, No. 15-1037V, 2019 WL 2511352, at *5 (Fed. Cl. Spec. Mstr. May 21, 2019).

[13] Dr. Steinman has previously employed the term "in silica" to describe a desktop computer review of information held in online databases (in contrast to *in vitro* or *in vivo* experiments). *Pek v. Sec'y of Health & Hum. Servs.*, No. 16-0736V, 2020 WL 1062959, at *16 (Fed. Cl. Spec. Mstr. Jan. 31, 2020).

Dr. Steinman briefly reviewed the timeframe in which Mrs. Gray's BBE manifested. He identified her onset as November 17, 2011, based on a full history included in a neuro-ophthalmology write-up from December 12, 2011 (although the record establishes that the earlier November date was for treatment of a then-existing UTI, rather than for the neurologic symptoms that subsequently manifested more clearly the day before Thanksgiving 2011). First Steinman Rep. at 24; Ex. 7 at 7. Nevertheless, Dr. Steinman deemed a five-week interval (October 11–November 17) as consistent with the timeframe for onset of comparable inflammatory neuropathies (GBS in particular). First Steinman Rep. at 24; L. Schonberger et al., *Guillain-Barré Syndrome Following Vaccination in the National Influenza Immunization Program, United State, 1976–1977*, 110 American J. of Epidemiology 105 (1976), filed as Ex. 45 on Feb. 13, 2017 (ECF No. 47-5) ("Schonberger").

Dr. Steinman rejected out of hand the possibility that Mrs. Gray's BBE might have been attributable to the infection (UTI or upper respiratory tract infection ("URI")) she appears to have been experiencing prior to onset of her neurologic symptoms. He observed from the medical records an absence of evidence that she had suffered an "antecedent campylobacter" infection. First Steinman Rep. at 5. He also noted that treaters looked for alternatives causes, such as other possible infection, such as "antecedent infection and paraneoplastic syndrome", but that they were excluded. *Id.* at 7. Dr. Steinman otherwise failed to address to any degree of specificity, however, why Mrs. Gray's documented, and treated, infection prior to vaccination could not be connected to her BBE.

Second Steinman Report

Dr. Steinman's Second Report focused on addressing issues raised by the special master formerly presiding over this action, in the wake of Respondent's expert's report.

First, Dr. Steinman attempted to expand upon his earlier contentions regarding the molecular mimics he had identified, and how they fit into the pathophysiology of the disease process leading to BBE. Steinman Second Rep. at 1. In so doing, however, he merely reiterated his prior argument (bulwarked by Yuki) that the flu vaccine could elicit anti-ganglioside antibodies, given the homology between antigens in the vaccines and components of the gangliosides themselves. *Id.* at 1–2. Although he deemed this by itself a sufficient causal explanation for how the vaccine could have caused BBE, he also noted that he had proposed other vaccine contents (like neuraminidase, present due to its existence as part of the inactivated wild flu virus itself) could also spark a cross-reaction similarly attributable to mimicry. *Id.* at 2.

Second, Dr. Steinman argued that science pertaining to a distinguishable central nervous system demyelinating condition, acute disseminated encephalomyelitis ("ADEM"), shed light on BBE's physiology. Second Steinman Rep. at 3. He deemed BBE "a form of ADEM,"

distinguishable primarily because it was limited to the brainstem, and also again referenced Yuki to support the idea that ganglioside antibodies are targets for autoimmune attack in BBE. *Id;* Yuki at 301. BBE could be mimicked by other vaccine components in a similar manner, resulting in cross-attack—and thus BBE and ADEM provided fair comparable circumstances. Second Steinman Rep. at 3.

Dr. Steinman next reacted specifically to some of Respondent's expert's assertions. In response to the claim that the "self-protective" immune cells/autoantibodies purportedly caused by vaccination herein (and allegedly responsible for BBE) are present naturally (and thus cannot be assumed to be pathogenic per se simply because a person possesses them concurrently with disease), Dr. Steinman maintained that these cells were more frequent, and prone to prompt immune dysregulation, in individuals experiencing neuroinflammation. Second Steinman Rep. at 3; *see* K. Ota et al., *T-cell Recognition of an Immuno-dominant Myelin Basic Protein Epitope in Multiple Sclerosis*, 346 Nature 183 (1990), filed as Ex. 49 on July 25, 2017 (ECF No 60-2) (finding that in multiple sclerosis patients that T cells recognizing the autoantigen were more common). But this assertion did not illuminate how a vaccine would fit into the neuroinflammatory milieu his arguments assumed—and in any event Mrs. Gray was never tested for the autoantibodies alleged to be causal of BBE.

Another paper Dr. Steinman cited showed that myelin-reactive cells were more highly activated in those experiencing neuroinflammation than in healthy individuals. J. Zhang et al., *Increased Frequency of Interleukin 2-responsive T Cells Specific for Myelin Basic Protein and Proteolipid Protein in Peripheral Blood and Cerebrospinal Fluid of Patients with Multiple Sclerosis*, 179 J. Experimental Med. 973 (1994), filed as Ex. 50 on July 25, 2017 (ECF No. 60-3). As a result, evidence of the potential for mimicry between a vaccine's antigens and the targets of such cells was in Dr. Steinman's view a reasonable "first step" in assessing how immune dysregulation would occur (although he added that the kind of studies necessary to provide more definitive proof could not be performed simply by considering the individual cases of Program claimants). Second Steinman Rep. at 3.

Dr. Steinman also sought to refute the argument that merely demonstrating homology was insufficient, given the thousands of combinations of amino acids that can occur, and be sequentially similar to self structures, but not lead to disease. Second Steinman Rep. at 3. He proposed in response that (a) reliable scientific evidence supported the conclusion that chains of five similar amino acids in a given protein was enough in at least an experimental context to trigger an autoimmune cross-reaction, and (b) it was already understood by medical science that "[m]imics exist" between the flu vaccine at issue and nerve gangliosides understood to be BBE targets. *Id.* at 3–4; Yuki at 316–17.

The remainder of Dr. Steinman's second report considered issues relating to the onset of

Mrs. Gray's BBE. He vouched for November 17, 2011, as the proper onset, arguing that the record he obtained the date from (even if associated with treatment occurring in the following month) was "highly reliable." Second Steinman Rep. at 4. But even if onset had been as late as November 24th (more than seven weeks post-vaccination), it would still be medically acceptable to associate it with vaccination—although to support this aspect of his opinion, Dr. Steinman relied on Schonberger, an article solely specific to GBS. Schonberger at 106. He admitted, however, that Mrs. Gray's earlier symptoms were consistent with a viral illness—but added that there was no confirmation of a specific infection such that a "formal diagnosis" of such an illness was possible. Second Steinman Rep. at 4. By contrast, it was known that Mrs. Gray *had* received the flu vaccine several weeks prior, and Dr. Steinman gave the certainty of that fact more weight in his opinion. *Id.* at 4–5.

Dr. Steinman took issue with the concept that an autoimmune response to vaccination would likely occur far *sooner* than even the November 17th date he posited as Mrs. Gray's onset. Second Steinman Rep. at 5. He cited literature aimed specifically at measuring the "effectiveness and duration" of the version of the flu vaccine administered in the relevant time period, noting it remained 54 to 67 percent effective up to 180 days post-vaccination. *Id.;* J. Radin et al., *Influenza Vaccine Effectiveness: Maintained Protection Throughout the Duration of Influenza Seasons 2010-2011 through 2013-2014*, 34 Vaccine 3907 (2016), filed as Ex. 52 on July 25, 2017 (ECF No. 60-5) ("Radin"). As a result, a five- to six-week post-vaccine onset for an autoimmune process was reasonable. Dr. Steinman's conclusion, however, appears to conflate the timeframe for overall vaccine *effectiveness* in response to challenge by a wild virus with the timeframe in which an adaptive/secondary immune response provoked by *initial* vaccination would reasonably occur. Radin at 3909–11. And he otherwise disputed the assertion that BBE's nadir would be expected to be swift after onset, deeming the course of the illness to be "highly variable," although he did not substantiate this particular contention. Second Steinman Rep. at 5.

B. *Respondent's Expert: Timothy Vartanian, M.D., Ph.D.*

Dr. Vartanian submitted two expert reports on behalf of Respondent. Report, filed as Ex. B on April 18, 2017 (ECF No. 54-1) ("First Vartanian Rep."); Report, filed as Ex. S on September 29, 2017 (ECF No. 63-1) ("Second Vartanian Rep."). Dr. Vartanian opines that Mrs. Gray's BBE was much more likely caused by an infection instead of the flu vaccine, and in fact that the date for onset of her symptoms "all but excludes vaccination as a possibility." First Vartanian Rep. at 13.

Dr. Vartanian received his B.A. from Oakland University, along with his M.D. and Ph.D. from the University of Chicago. Ex. C at 1, filed on April 18, 2017 (ECF No. 54-2) (Dr. Vartanian's Curriculum Vitae ("Vartanian CV")). He completed a residency at Massachusetts General Hospital in Neurology. *Id.* at 2. He then completed two fellowships, the first at Beth

Israel Hospital and the second at Harvard Medical School. *Id.* Dr. Vartanian held positions as an assistant professor at Harvard Medical School until 2009, when he was appointed as a professor at Weill Cornell Medicine. *Id.* He has also held neurologist positions at Massachusetts General Hospital and Beth Israel Deaconess, currently an attending neurologist at New York Presbyterian Hospital since 2009. *Id.* Dr. Vartanian belongs to the American Society of Neuroscientists. *Id.* at 3. He is conducting research centered around pattern recognition receptors, specifically in the developing and diseased central nervous system. *Id.* at 8–9. He has published a substantial number of articles, with many focused upon myelin protein, autoimmune diseases, and generally the central nervous system. *Id.* at 12–20.

First Report

Dr. Vartanian began with a discussion of the similarities and differences between GBS and BBE. First Vartanian Rep. at 4. Although he asserted there existed no specific diagnostic guidelines for BBE, most experts agree that it is characterized by "the presence acute bilateral ophthalmoplegia, ataxia, and altered cognition." *Id.* It is also reasonable to evaluate BBE in light of what is already known about GBS. Although the two are not wholly congruent, the "overlap in clinical presentation, symptoms, signs, and laboratory findings between [GBS] and [BBE] are well described." *Id.* Dr. Vartanian also agreed that specific pathogenic antibodies, consistent with what Dr. Steinman had proposed would be central to a cross-reactive autoimmune attack, were understood to mediate BBE. *Id.* at 5; M. Odaka et al., *Bickerstaff's Brainstem Encephalitis: Clinical Features of 62 Cases and a Subgroup Associated with Guillain-Barré Syndrome*, 126 Brain 2279, 2284 (2003), filed as Ex. G on April 18, 2017 (ECF No. 54-6) ("Odaka").

A common etiologic explanation for BBE is an antecedent infectious illness, like a URI, with one study (specific to Japanese BBE patients) revealing that over 75 percent of BBE patients experienced some kind of infectious symptoms before onset. First Vartanian Rep. at 5; M. Koga et al., *Nationwide Survey of Patients in Japan with Bickerstaff Brainstem Encephalitis: Epidemiological and Clinical Characteristics*, 83 J. Neurology, Neurosurgery & Psychiatry 1210, 1212 & 1214 (2012), filed as Ex. F on April 18, 2017 (ECF No. 54-5) ("Koga"); *see also* Odaka at 2284 (*C. jejuni* or mycoplasma pneumoniae bacterial infections were reported in cases of individuals experiencing BBE or BBE overlapping with GBS). The "nadir of disability in BBE," in Dr. Vartanian's view, typically occurred within a week of onset. First Vartanian Rep. at 5; Koga at 1213.

Based on an overview of the medical history (First Vartanian Rep. at 2–4), Dr. Vartanian deemed Mrs. Gray's "constellation of vocal cord paralysis, ataxia, nystagmus, dysarthria, and altered cognition" to be consistent with BBE, adding that her "altered sensorium clearly distinguishes her from [GBS] where cognition is unaltered." *Id.* at 4. Mrs. Gray's normal MRI results, Dr. Vartanian opined, did not rule out the BBE diagnosis, adding that abnormal MRI

results in suspected cases of BBE simply aided treatment by providing prognostic assistance. *Id.* at 5.

Dr. Vartanian then turned to Dr. Steinman's causation theories, identifying the aspects he disagreed with. Regarding the flu vaccine itself, Dr. Vartanian allowed that it might possibly "contain" gangliosides, as Dr. Steinman maintained, although he noted this depended ultimately on the manufacturing process, and the degree to which it might "leave in" as remnants these aspects of the underlying viral antigen. First Vartanian Rep. at 5–6. He also agreed that versions of the flu vaccine could cause the production of anti-ganglioside antibodies, although he contested that *all* such antibodies were necessarily pathogenic. *Id.* at 6. Thus, even if it were the case that BBE patients often tested positive for these antibodies, they were "normal components of a healthy immune system," and thus Dr. Vartanian did not simply concede their presence implied a likely pathogenic process. *Id.*

Dr. Vartanian directly questioned Dr. Steinman's assertions regarding the proposed applicability of molecular mimicry to explain vaccine-caused BBE. He deemed "low stringency Blast comparisons" to easily be able to demonstrate homologous amino acid chains between a vaccine's antigenic proteins and the proteins making up self structures in the body. First Vartanian Rep. at 6. Indeed, this kind of sequential homology was common. *Id.* at 7; E. Ellwardt et al., *Understanding the Role of T Cells in CNS Homeostasis*, 37 Trends in Immunology 154 (2016), filed as Ex. I on April 18, 2017 (ECF No. 54-8); David M. Richards et al., *Re-examining the Nature and Function of Self-Reactive T Cells*, 37 Trends in Immunology 114 (2016), filed as Ex. J on April 18, 2017 (ECF No. 54-9) ("Richards").

Richards in particular had observed that "self-antigen specific" T and B cells were common in individuals with autoimmune diseases—but scientific advancements in serologic testing for these kinds of cells had revealed they also could readily be identified in healthy individuals, thus casting doubt on the conclusion that their presence explained pathogenicity. Richards at 117; First Vartanian Rep. at 8.[14] In fact, one of the articles filed by Dr. Steinman specifically observed that certain autoreactive antibodies observed in patients with GBS and/or BBE were "probably produced as *a result of the myelin damage rather than cause the demyelination.*" First Vartanian Rep. at 9.[15] Dr. Vartanian thus rejected the proposition that it could be inferred from the presence of these autoantibodies that they were necessarily causal of

[14] Some such potentially cross-reactive immune cells might actually exist to serve a protective function. First Vartanian Rep. at 8; T. Rothstein, *Natural Antibodies as Rheostats for Susceptibility to Chronic Diseases in the Aged*, 7 Frontiers in Immunology 1 (2016), filed as Ex. K on April 18, 2017 (ECF No. 54-10); S. Söllvander et al., *Increased Number of Plasma B Cells Producing Autoantibodies Against Aβ42 Protofibrils in Alzheimer's Disease*, 48 J. of Alzheimer's Disease 63 (2015), filed as Ex. L on April 18, 2017 (ECF No. 55-1) (self-reactive antibodies against beta-amyloid, the proposed pathogenic molecule in Alzheimer's Disease, serve to clear away the molecule rather than instigate the disease process).

[15] Dr. Vartanian cited (and quoted) an article for this proposition, but it was not filed.

autoimmune disease. First Vartanian Rep. at 9.

Ultimately, for molecular mimicry to have reliable applicability in these circumstances, Dr. Vartanian maintained, several criteria needed to be satisfied. Specifically, there needed to be shown (a) some association between the underling infectious agent that the vaccine was directed against and the relevant disease, (b) identification of what kinds of immune cells were deemed mechanistically responsible for the autoimmune cross-reaction, (c) identification of a self-mimic that would serve as the attack's target, and (d) evidence in at least an animal model that such a cross-attack could occur. First Vartanian Rep. at 7; *see also* Yuki at 306. But here, all Dr. Steinman offered was potential mimicry.

The specific facts gleaned from Mrs. Gray's medical history, Dr. Vartanian contended, made it impossible to conclude the vaccine was more likely causal of her BBE than an antecedent infection. First Vartanian Rep. at 9. Mrs. Gray was never tested for the specific antibodies deemed pathologic in BBE. *Id.* at 5. More importantly to Dr. Vartanian, Mrs. Gray's "infectious work up was minimal and primarily consisted of [cerebrospinal fluid] PCR studies intended to look for evidence of an active CNS viral (by either varicella zoster virus, herpes simplex virus) or bacterial infection." *Id.* at 7. But the record showed that treaters had *not* looked for evidence reflecting an ongoing/acute or resolved infection that *would* be associated with BBE/GBS, such as *C. jejuni*—even though it was also evident from the same medical record that Mrs. Gray had prior to her acute onset been suffering from *both* a UTI as well as some kind of URI. *Id.* at 7, 13.

It was therefore "illogical" to conclude the vaccine had to be causal merely because it preceded onset. First Vartanian Rep. at 9. And Dr. Vartanian cited several items of literature underscoring how many different kinds of infections were associated with BBE. *See, e.g.*, M. Sharma et al., *The Presence of Mycoplasma Pneumoniae Infection and GM1 Ganglioside Antibodies in Guillain-Barré Syndrome*, 5 J. Infection in Developing Counties 459, 459 (2011), filed as Ex. N on April 18, 2017 (ECF No. 55-3) (stating that "[a]bout two thirds of the patients report preceding illnesses (usually respiratory or gastro-intestinal infections) within 12 weeks before the onset of the neurologic illness"); C. Caudie, *Preceding Infections and Anti-Ganglioside Antibody Profiles Assessed by a Dot Immunoassay in 306 French Guillain-Barré Syndrome Patients*, 258 J. Neurology 1958, 1958–59 (2011), filed as Ex. O on April 18, 2017 (ECF No. 55-4) (observing that multiple different infectious agents are associated with GBS); S. Sinha et al., *Preceding Infections and Anti-Ganglioside Antibodies in Patients with Guillain-Barré Syndrome: A Single Centre Prospective Case-Control Study*, 13 Clinical Microbiology and Infection 334, 334 (2007), filed as Ex. P on April 18, 2017 (ECF No. 55-5) (noting "[p]revious infections were more frequent among GBS patients than among controls").

Dr. Vartanian's first report also addressed the medical acceptability of Mrs. Gray's symptoms onset. Although Mrs. Gray received the BBE diagnosis on December 7, 2011 (after

evidence of seventh nerve palsy), the first symptom she displayed that Dr. Vartanian deemed suggestive of BBE manifested approximately two weeks before (Wednesday, November 23, 2011), around the time of her pre-Thanksgiving episode of feeling a sensation of choking/food caught in her throat. First Vartanian Rep. at 9. This sensation, he proposed, could be attributed to a "loss of coordinated movement of the swallowing" that in turn was associated with cranial nerve dysfunction. *Id.* He rejected Dr. Steinman's contention that onset was instead the week before, on November 17, 2011, observing that the medical records established the symptoms at this time were associated primarily with an infectious process (URI or UTI). *Id.*

Based on a November 23rd onset (which would have been 43 days post-vaccination), Dr. Vartanian opined that the start of Mrs. Gray's BBE manifested too long after vaccination to deem the flu vaccine causal. In support, he referenced Nachamkin, an article also cited by Dr. Steinman. Nachamkin's authors determined that a prior version of the flu vaccine likely induced production of certain anti-ganglioside antibodies thought to be involved in causing GBS (although the study itself disclaimed whether the antibodies so induced in fact were pathogenic). Nachamkin at 231–32. In the course of performing the study (as reflected in the figures reproduced in Dr. Vartanian's report), however, Nachamkin observed a "rapid and robust" vaccine-induced response as soon as a week after vaccination (First Vartanian Rep. at 10–12), although the same figures also show a robust response within 35 days as well. Based on this, Dr. Vartanian opined (and despite the longer period of response the figures he offers demonstrate) that the timeframe between Mrs. Gray's receipt of the flu vaccine and neurologic symptoms onset was too much a "stretch" to be deemed medically acceptable. First Vartanian Rep. at 12.

Second Report

Dr. Vartanian's second expert report addressed some of Dr. Steinman's specific claims. The majority of the second report was aimed at questioning Dr. Steinman's contention that the Yuki article essentially established that BBE was mediated by specific anti-ganglioside antibodies either contained in the flu vaccine or likely to be produced in response to it. Second Vartanian Rep. at 1–4. In so doing, Dr. Vartanian provided a detailed evaluation of Yuki's findings, comparing it to what Nachamkin revealed.

Yuki's abstract summarizes its principal conclusion: that certain anti-ganglioside antibodies "were common" to both a common GBS variant and BBE, "suggesting that they are part of the same disease spectrum." Yuki at 299. Dr. Vartanian walked through Yuki's discourse specifically, observing that its author had identified the relevant anti-ganglioside antibodies in one of his first patients—along with the fact that a triggering bacterial infection (*C. jejuni*) was suspected to be causally associated with the antibody's elicitation, as well as that these antibodies could cross-react to cause disease. Second Vartanian Rep. at 1–2. Indeed, Yuki went on to identify a fairly direct association between the two—while a mix of animal and human

experiments (some of which the author had conducted) had not similarly determined that the flu vaccine *also* elicited this antibody. *Id.* at 3; Yuki at 306–07.

Nachamkin, by contrast, corroborated the view that the flu vaccine's capacity to cause production of anti-ganglioside antibodies existed—but also suggested reasons for doubting that the expression of these antibodies would invariably be pathologic. Thus, in addition to considering the antibody inducement of the flu vaccine, Nachamkin also looked to see if mice vaccinated with the 1976 version of the flu vaccine (which had been reliably shown to have been associated with GBS) would display the kind of mimic antibodies known to be generated in response to *C. jejuni*.[16] Nachamkin at 227. But the tested mice did not. In fact, the serum from the tested/vaccinated mice did not even cross-react with *C. jejuni,* regardless of the concentration level—further undermining the proposition that at least this version of the vaccine could instigate production of the relevant autoantibodies. *Id.* at 228–31. Mice receiving *C. jejuni* directly, however, did develop the relevant anti-ganglioside antibodies. *Id.* at 230.[17]

In addition to the aforementioned discourse, Dr. Vartanian reiterated his prior point that the existence of specific autoantibodies in a human did not always lead to an autoimmune disease, or that autoreactive immune cells could be assumed in cases involving demyelination to be part of a disease process. Second Vartanian Rep. at 4–5. He rejected Dr. Steinman's lumping of BBE with ADEM, noting that although both were "monophasic immune mediated inflammatory diseases of the CNS," it was not unquestionably established that both reflected either an autoimmune attack on MBP or were otherwise mechanistically the same. *Id.* at 4–5. He questioned whether homology in the form of a five-amino acid sequence was invariably sufficient for an autoimmune cross-reaction to occur, since if this were the case "in the real world of human vaccination," there would exist persuasive epidemiologic/statistical evidence of a vaccine-autoimmune disease connection. *Id.* at 5. And he again stressed his belief that the evidence that Mrs. Gray was experiencing some kind of infection prior to her neurologic symptoms provided a far more likely causal explanation for her BBE than the flu vaccine, which he noted had not been demonstrated to be associated with BBE. *Id.*

III. Procedural History

As noted, the case was initiated in February 2015, with medical records filed on March

[16] This was performed based on the hypothesis that the reason the 1976 flu vaccine formulation caused GBS was that eggs used to produce it may have been unknowingly contaminated with *C. jejuni*. Nachamkin at 230–31.

[17] To back-stop his supposition, Dr. Vartanian also apparently sent an email to Nachamkin's eponymous primary author, Dr. Irving Nachamkin, to ask him about the study's disease-specific findings. *See* email, dated September 19, 2017, filed as Ex. T (ECF No. 63-2). Dr. Nachamkin responded that none of the tested mice developed clinical signs of GBS, although no brain tissue was tested to confirm or reject the presence of pathology. Ex. T at 2.

23, 2015. Respondent immediately filed a motion to dismiss the Petition on March 24, 2015, arguing that the claim was time-barred (since onset of symptoms occurred no later than November 2011—meaning the three-year limitations period had run by November 2014). ECF No. 11. But the motion was denied on February 4, 2016, based on the determination by the prior special master in the case that Petitioner was entitled to the opportunity to prove (as alleged) that she was mentally disabled for several months due to her BBE, thereby entitling her to toll the statute for a period of time. Order, dated February 4, 2016 (ECF No. 15). A second motion to dismiss was later also resolved in Petitioner's favor, after a fact-finding that Petitioner had successfully demonstrated sufficient mental incapacity to justify tolling (and thereby render the February 2015 filing timely). ECF No. 28.

A year later, after Mrs. Gray's death, Ms. Randolph was substituted as Petitioner. The parties subsequently exchanged the expert reports identified above, and it was determined that the case should be resolved on the papers. Scheduling Order, dated November 12, 2020 (ECF No. 92). Petitioner filed her motion in favor of entitlement on January 11, 2021 (ECF No. 93) ("Mot."), Respondent opposed on February 24, 2021 (ECF No. 97) ("Opp."), and Petitioner offered a reply on March 11, 2021 (ECF No. 98) ("Reply"). In the ensuing time period, the matter was reassigned to me. It is now ripe for resolution.

IV. Parties' Arguments

A. *Petitioner*

Petitioner argues that the flu vaccine has the capacity to elicit the production of anti-ganglioside antibodies central to BBE's pathogenesis, relying both on aspects of Dr. Steinman's report about the vaccine in particular as well as the overlap between GBS and BBE (which Dr. Vartanian accepted)—and in particular the mechanisms they likely share for how each related disease is mediated. Mot. at 24; Ex. 48 at 1. Dr. Steinman also referenced other items of literature establishing that gangliosides could be the target antigens for neuroinflammatory conditions like BBE. *Id*. (citing Ex. 34, 36, 37). And Petitioner maintains that proteins in the vaccine could trigger an autoimmune inflammatory disorder such as BBE. Mot. at 28. Petitioner even notes a previous BBE case that was compensated. *See Beeson v. Sec'y of Health & Hum. Servs.*, No. 17-1781V, 2019 WL 6118175 (Fed. Cl. Spec. Mstr. Sept. 5, 2019). Petitioner does acknowledge, however, that *Beeson* was not technically decided but resolved via settlement. Reply at 4. Petitioner also highlights Mrs. Gray's vaccination, noting that before it she had "[g]enerally . . . been in good health." Ex. 2 at 192–93.

Regarding onset, Petitioner maintains that (based on Dr. Steinman's interpretation of the record) Mrs. Gray's symptoms began November 17, 2011. This date—approximately 37 days after

the vaccine's administration—clearly falls within the 3–42-day timeframe for a flu-GBS claim under the Vaccine Injury Table (which does apply to variants of GBS). 42 C.F.R. §100.3(a); Motion at 30. Indeed, onset would be almost in this timeframe if it were found to be November 23rd, as argued by Respondent, and seven weeks has previously been found to be acceptable in a non-Table context in any event. Mot. at 30; *Chinea v. Sec'y of Health & Hum. Servs.*, No.15-095V, 144 Fed. Cl. 378, 384 (2019) (timeframe for GBS onset has been considered to go as far out as "six to eight weeks").

Petitioner also attempts in her briefs to rebut Respondent's theory that an antecedent infection explained Mrs. Gray's illness, arguing that the record did not support such an alternative cause. *See* Ex. B at 7. Thus, no treating physicians clearly opined that her BBE had a specific infectious cause (although the hospital discharge summary states her injury was "most likely brain stem encephalitis *secondary to a viral* versus an inflammatory etiology"). Ex. 4 at 112. Even extensive bloodwork did not identify a specific infectious cause for the BBE. Reply at 1. And Respondent did not establish that Mrs. Gray's otherwise-demonstrated UTI, and likely URI were causal. Mot. at 32. Even though the record clearly demonstrates that she experienced repeated UTIs (*see, e.g.*, Ex. 2 at 194), the fact that she did not previously experience BBE undermined the contention that the two were related. Reply at 6.

B. *Respondent*

Respondent maintains Petitioner has not met her burden of proof to establish the vaccine caused her BBE. Report at 4. First, Respondent attacks the sufficiency of Petitioner's "can cause" showing. Opp. at 7. As Dr. Vartanian explained, the causal chain put forth by Petitioner is strained by inferences and assumptions. First Vartanian Rep. at 6–9. Dr. Steinman's theory proposed that the flu vaccine could elicit an anti-ganglioside response that would trigger an inflammatory disorder brainstem encephalitis. *Id.* at 4. But the contention that anti-ganglioside antibodies are pathogenic was overstated, demonstrated only in animals. Opp. at 6. Indeed, anti-ganglioside antibodies occur in healthy immune systems, and are thus not inevitably pathogenic. *Id.* Otherwise, Petitioner's theory is unsupported by medical literature and is ultimately hypothetical. Opp. at 6; First Vartanian Rep. at 6, 9, 13. And the fact that cases alleging BBE as an injury have been settled has no bearing on this matter, since the determination by Respondent to settle does not amount to a concession on the causation theory. Opp. at 8.

Second, Respondent highlights the evidence of a pre-onset infection as a more likely causal explanation for Mrs. Gray's BBE. Opp. at 5. Antecedent infection is a "common feature of [BBE], occurring in over 75% of patients . . . ." First Vartanian Rep. at 5. Dr. Steinman flatly rejected the possibility of an antecedent infection trigger based upon the negative viral workup (Ex. 21 at 5), but Respondent maintains that the medical record reveals the infectious workup Mrs. Gray received was minimal, focusing upon identifying specific, active *CNS* viral and bacterial infections

(which relied on cerebrospinal fluid testing). First Vartanian Rep. at 7. None of the known organisms that are associated with BBE were tested serologically, even though Mrs. Gray was unquestionably suffering from respiratory and urinary tract infections prior to the onset of the symptoms. *Id.*

A causal link thus cannot be found when there is evidence of a clear illness that could have caused BBE. *Munn v. Sec'y of Health & Hum. Servs.*, 970 F.2d 863, 865 (Fed. Cir. 1991) (child's death not attributable to vaccine received four days prior; child was diagnosed with "acute febrile illness of unknown etiology" a few days after receipt of vaccination, and that rather than vaccine was found to be causal). And the medical records clearly show Mrs. Gray was suffering from one or more infectious illnesses before developing BBE, making it difficult to attribute "'but-for' causation to the vaccine." *Pafford v. Sec'y of Health & Hum. Servs*., 451 F.3d 1352, 1355, 1358 (Fed. Cir. 2006). This intervening infection was more likely explanatory of her BBE than a vaccine. First Vartanian Rep. at 6–7.

Finally, Respondent attacks the medical acceptability of a 43-day post-vaccination onset. This was especially a lengthy period when compared to the more reasonable approximately 12-day period between Mrs. Gray's UTI/URI symptoms on November 11th and her first manifestation of neurologic symptoms on November 23rd (which Respondent maintains is the better-supported onset date). First Vartanian Rep. at 5, 9; Ex. 1 at 3. Indeed, the timeframe was in Respondent's estimation even inconsistent with Petitioner's theory, since there is authority suggesting the most likely timeframe for a GBS-like neurologic injury post-vaccination is, at the longest, six weeks. *Tullio v. Sec'y of Health & Hum. Servs.*, No. 15-51V, 2019 WL 7580149, at *28 (Fed. Cl. Spec. Mstr. Dec 19, 2019), *mot. for review den'd,* 149 Fed. Cl. 448 (June 18, 2020). And some literature cited by Dr. Steinman actually suggested rapid onset (within a week of vaccination) was most likely, although that unquestionably did not occur in this case.

V. Applicable Law

A. *Standards for Vaccine Claims*

To receive compensation in the Vaccine Program, petitioners must prove that: (1) they suffered an injury falling within the Vaccine Injury Table (i.e., a "Table Injury"); or (2) they suffered an injury actually caused by a vaccine (i.e., a "Non-Table Injury). *See* Sections 13(a)(1)(A), 11(c)(1), and 14(a), as amended by 42 C.F.R. § 100.3; § 11(c)(1)(C)(ii)(I); *see also Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1320 (Fed. Cir. 2006). In this case, Petitioner does not assert a Table claim.

For both Table and Non–Table claims, Vaccine Program petitioners bear a "preponderance of the evidence" burden of proof. Section 13(1)(a). That is, a petitioner must offer evidence that leads the "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the judge of the fact's existence." *Moberly*, 592 F.3d at 1322 n.2; *see also Snowbank Enter., Inc. v. United States*, 6 Cl. Ct. 476, 486 (1984) (explaining that mere conjecture or speculation is insufficient under a preponderance standard). On one hand, proof of medical certainty is not required. *Bunting v. Sec'y of Health & Hum. Servs.*, 931 F.2d 867, 873 (Fed. Cir. 1991). But on the other hand, a petitioner must demonstrate that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly*, 592 F.3d at 1321 (quoting *Shyface v. Sec'y of Health & Hum. Servs.*, 165 F.3d 1344, 1352–53 (Fed. Cir. 1999)); *Pafford*, 451 F.3d at 1355. A petitioner may not receive a Vaccine Program award based solely on his assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. Section 13(a)(1).

In attempting to establish entitlement to a Vaccine Program award of compensation for a Non–Table claim, a petitioner must satisfy all three of the elements established by the Federal Circuit in *Althen v. Sec'y of Health and Hum. Servs.,* 418 F.3d 1274, 1278 (Fed. Cir. 2005): "(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." Each *Althen* prong requires a different showing and is discussed in turn along with the parties' arguments and my findings.

Under *Althen* prong one, petitioners must provide a "reputable medical theory," demonstrating that the vaccine received *can cause* the type of injury alleged. *Pafford*, 451 F.3d at 1355–56 (citations omitted). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Hum. Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). Such a theory must only be "legally probable, not medically or scientifically certain." *Id.* at 549.

However, the Federal Circuit has *repeatedly* stated that the first prong requires a preponderant evidentiary showing. *See Boatmon v. Sec'y of Health & Hum. Servs.*, 941 F.3d 1351, 1360 (Fed. Cir. 2019) ("[w]e have consistently rejected theories that the vaccine only "likely caused" the injury and reiterated that a "plausible" or "possible" causal theory does not satisfy the standard"); *see also Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Broekelschen v. Sec'y of Health & Hum. Servs*., 618 F.3d 1339, 1350 (Fed. Cir. 2010). This is consistent with the petitioner's ultimate burden to establish his overall entitlement to damages by preponderant evidence. *W.C. v. Sec'y of Health & Hum. Servs.*, 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted). If a claimant must *overall* meet the preponderance standard, it is logical that they be required also to meet each individual prong with the same degree of evidentiary

showing (even if the *type* of evidence offered for each is different).

Petitioners may offer a variety of individual items of evidence in support of the first *Althen* prong, and are not obligated to resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health & Hum. Servs.*, 569 F.3d 1367, 1378–79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325–26). No one "type" of evidence is required. Special masters, despite their expertise, are not empowered by statute to conclusively resolve what are essentially thorny scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed "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. Nevertheless, even though "scientific certainty" is not required to prevail, the individual items of proof offered for the "can cause" prong must *each* reflect or arise from "reputable" or "sound and reliable" medical science. *Boatmon,* 941 F.3d at 1359-60.

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 & Hum. Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). In establishing that a vaccine "did cause" injury, the opinions and views of the injured party's treating physicians are entitled to some weight. *Andreu*, 569 F.3d at 1367; *Capizzano*, 440 F.3d at 1326 ("medical records and medical opinion testimony are favored in vaccine cases, as 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'") (quoting *Althen*, 418 F.3d at 1280). Medical records are generally viewed as particularly trustworthy evidence, since they are created contemporaneously with the treatment of the patient. *Cucuras v. Sec'y of Health & Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993).

However, medical records and/or statements of a treating physician's views do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. Section 13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"); *Snyder v. Sec'y of Health & Hum. Servs*., 88 Fed. Cl. 706, 746 n.67 (2009) ("there is nothing . . . that mandates that the testimony of a treating physician is sacrosanct—that it must be accepted in its entirety and cannot be rebutted"). As with expert testimony offered to establish a theory of causation, the opinions or diagnoses of treating physicians are only as trustworthy as the reasonableness of their suppositions or bases. The views of treating physicians should also be weighed against other, contrary evidence also present in the record—including conflicting opinions among such individuals. *Hibbard v. Sec'y of Health & Hum. Servs.*, 100 Fed. Cl. 742, 749 (2011) (stating it is not arbitrary or capricious for special master to weigh competing treating physicians' conclusions against each other), *aff'd*, 698 F.3d 1355 (Fed. Cir. 2012); *Veryzer v. Sec'y*

of Health & Hum. 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, 356–57 (2011), *aff'd without opinion*, 475 F. App'x. 765 (Fed. Cir. 2012).

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." *de Bazan v. Sec'y of Health & Hum. 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 & Hum. Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. den'd after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 2013 WL 1896173 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Hum. Servs.*, No. 11–355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for review den'd* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

B. *Law Governing Analysis of Fact Evidence*

The process for making determinations in Vaccine Program cases regarding factual issues begins with consideration of the medical records. Section 11(c)(2). The special master is required to consider "all [ ] relevant medical and scientific evidence contained in the record," including "any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death," as well as the "results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions." Section 13(b)(1)(A). The special master is then required to weigh the evidence presented, including contemporaneous medical records and testimony. *See Burns v. Sec'y of Health & Hum. Servs*., 3 F.3d 415, 417 (Fed. Cir. 1993) (determining that it is within the special master's discretion to determine whether to afford greater weight to contemporaneous medical records than to other evidence, such as oral testimony surrounding the events in question that was given at a later date, provided that such determination is evidenced by a rational determination).

As noted by the Federal Circuit, "[m]edical records, in general, warrant consideration as trustworthy evidence." *Cucuras*, 993 F.2d at 1528; *Doe/70 v. Sec'y of Health & Hum. Servs.*, 95 Fed. Cl. 598, 608 (2010) ("[g]iven the inconsistencies between petitioner's testimony and his contemporaneous medical records, the special master's decision to rely on petitioner's medical records was rational and consistent with applicable law"), *aff'd*, *Rickett v. Sec'y of Health & Hum. Servs*., 468 F. App'x 952 (Fed. Cir. 2011) (non-precedential opinion). A series of linked propositions explains why such records deserve some weight: (i) sick people visit medical

professionals; (ii) sick people are likely to honestly report their health problems to those professionals; and (iii) medical professionals record what they are told or observe when examining their patients in as accurate a manner as possible, so that they are aware of enough relevant facts to make appropriate treatment decisions. *Sanchez v. Sec'y of Health & Hum. Servs.*, No. 11–685V, 2013 WL 1880825, at *2 (Fed. Cl. Spec. Mstr. Apr. 10, 2013); *Cucuras v. Sec'y of Health & Hum. Servs.*, 26 Cl. Ct. 537, 543 (1992), *aff'd*, 993 F.2d at 1525 (Fed. Cir. 1993) ("[i]t strains reason to conclude that petitioners would fail to accurately report the onset of their daughter's symptoms").

Accordingly, if the medical records are clear, consistent, and complete, then they should be afforded substantial weight. *Lowrie v. Sec'y of Health & Hum. Servs*., No. 03–1585V, 2005 WL 6117475, at *20 (Fed. Cl. Spec. Mstr. Dec. 12, 2005). Indeed, contemporaneous medical records are often found to be deserving of greater evidentiary weight than oral testimony—especially where such testimony conflicts with the record evidence. *Cucuras*, 993 F.2d at 1528; *see also Murphy v. Sec'y of Health & Hum. Servs*., 23 Cl. Ct. 726, 733 (1991), *aff'd per curiam*, 968 F.2d 1226 (Fed. Cir. 1992), *cert. den'd*, *Murphy v. Sullivan*, 506 U.S. 974 (1992) (citing *United States v. United States Gypsum Co.*, 333 U.S. 364, 396 (1947) ("[i]t has generally been held that oral testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight.")).

However, the Federal Circuit has also noted that there is no formal "presumption" that records are accurate or superior on their face to other forms of evidence. *Kirby v. Sec'y of Health & Hum. Servs.,* 997 F.3d 1378, 1383 (Fed. Cir. 2021). There are certainly situations in which compelling oral or written testimony may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. *Campbell v. Sec'y of Health & Hum. Servs*., 69 Fed. Cl. 775, 779 (2006) ("like any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking"); *Lowrie*, 2005 WL 6117475, at *19 ("[w]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent") (quoting *Murphy*, 23 Cl. Ct. at 733)). Ultimately, a determination regarding a witness's credibility is needed when determining the weight that such testimony should be afforded. *Andreu*, 569 F.3d at 1379; *Bradley v. Sec'y of Health & Hum. Servs*., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

When witness testimony is offered to overcome contemporaneous medical records, such testimony must be "consistent, clear, cogent, and compelling." *Sanchez*, 2013 WL 1880825, at *3 (citing *Blutstein v. Sec'y of Health & Hum. Servs*., No. 90–2808V, 1998 WL 408611, at *5 (Fed. Cl. Spec. Mstr. June 30, 1998)). In determining the accuracy and completeness of medical records, the Court of Federal Claims has listed four possible explanations for inconsistencies between contemporaneously created medical records and later testimony: (1) a person's failure to recount to the medical professional everything that happened during the relevant time period; (2) the medical professional's failure to document everything reported to her or him; (3) a person's faulty

recollection of the events when presenting testimony; or (4) a person's purposeful recounting of symptoms that did not exist. *La Londe v. Sec'y of Health & Hum. Servs*., 110 Fed. Cl. 184, 203–04 (2013), *aff'd*, 746 F.3d 1334 (Fed. Cir. 2014). In making a determination regarding whether to afford greater weight to contemporaneous medical records or other evidence, such as testimony at hearing, there must be evidence that this decision was the result of a rational determination. *Burns*, 3 F.3d at 417.

C. *Evaluation of Expert Opinions*

Establishing a sound and reliable medical theory often requires a petitioner to present expert testimony in support of his claim. *Lampe v. Sec'y of Health & Hum. Servs*., 219 F.3d 1357, 1361 (Fed. Cir. 2000). Vaccine Program expert testimony is usually evaluated according to the factors for analyzing scientific reliability set forth in *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 594–96 (1993). *See Cedillo v. Sec'y of Health & Hum. Servs.*, 617 F.3d 1328, 1339 (Fed. Cir. 2010) (citing *Terran v. Sec'y of Health & Hum. Servs.*, 195 F.3d 1302, 1316 (Fed. Cir. 1999). Under *Daubert*, the factors for analyzing the reliability of testimony are:

> (1) whether a theory or technique can be (and has been) tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and (4) whether the theory or technique enjoys general acceptance within a relevant scientific community.

Terran, 195 F.3d at 1316 n.2 (citing *Daubert*, 509 U.S. at 592–95).

In the Vaccine Program the *Daubert* factors play a slightly different role than they do when applied in other federal judicial settings, like the district courts. Typically, *Daubert* factors are employed by judges (in the performance of their evidentiary gatekeeper roles) to exclude evidence that is unreliable or could confuse a jury. By contrast, in Vaccine Program cases these factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health & Hum. 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"). The flexible use of the *Daubert* factors to evaluate the persuasiveness and reliability of expert testimony has routinely been upheld. *See, e.g.*, *Snyder*, 88 Fed. Cl. at 742–45. In this matter (as in numerous other Vaccine Program cases), *Daubert* has not been employed at the threshold, to determine what evidence should be admitted, but instead to determine whether expert testimony offered is reliable and/or persuasive.

Respondent frequently offers one or more experts in order to rebut a petitioner's case. 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 & Hum. Servs*., 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing

Lampe, 219 F.3d at 1362). However, 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*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 146 (1997)); *see also Isaac v. Sec'y of Health & Hum. Servs*., No. 08–601V, 2012 WL 3609993, at *17 (Fed. Cl. Spec. Mstr. July 30, 2012), *mot. for review den'd*, 108 Fed. Cl. 743 (2013), *aff'd*, 540 F. App'x. 999 (Fed. Cir. 2013) (citing *Cedillo*, 617 F.3d at 1339). Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Moberly*, 592 F.3d at 1325–26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); *see also Porter v. Sec'y of Health & Hum. Servs*., 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("this court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act").

D. *Disposition of Case Without Hearing*

I am resolving this claim on the papers, rather than by holding a hearing, in accordance with the parties' expressed preference. ECF No. 91. The Vaccine Act and Rules not only contemplate but encourage special masters to decide petitions on the papers where (in the exercise of their discretion) they conclude that doing so will properly and fairly resolve the case. Section 12(d)(2)(D); Vaccine Rule 8(d). The decision to rule on the record in lieu of hearing has been affirmed on appeal. *Kreizenbeck v. Sec'y of Health & Hum. Servs.*, 945 F.3d 1362, 1366 (Fed. Cir. 2020); *see also Hooker v. Sec'y of Health & Hum. Servs.,* No. 02-472V, 2016 WL 3456435, at *21 n.19 (Fed. Cl. Spec. Mstr. May 19, 2016) (citing numerous cases where special masters decided case on the papers in lieu of hearing and that decision was upheld).

ANALYSIS

I. Overview of Alleged Injury

This claim asserts BBE as a vaccine injury. As noted by Dr. Vartanian, there are no specific clinical guidelines for diagnosing BBE. However, its symptoms are understood to include oropharyngeal palsy, ataxia, external ophthalmoplegia, impaired consciousness, and sensory disturbance at the distal extremities. Koga at 1210. BBE features an acute, progressive symptoms progression, with a monophasic course and good recovery. *Id.* BBE is considered a "minor clinical" GBS variant. *Id.* at 1215. And it is unquestionably established by filed medical literature in this case that a number of infections, viral or bacterial, are associated with it. *Id.* at 1212, 1214; Odaka at 2286 (bacterial infectious processes like *C. jejuni* known as causal of GBS also observed to predate cases of BBE).

I have identified no reasoned prior Program decisions in which BBE was the claimed injury, eliminating any on-point decisions that can be referred to for guidance. And I concur with Respondent's assertions that *settled* cases involving BBE provide little utility in understanding the claim herein (even if Petitioner reasonably points to them to suggest that in settling, Respondent has indirectly acknowledged such a claim's legitimacy). However, because BBE overlaps with GBS, it is not unreasonable under the circumstances to note that GBS has *repeatedly* been deemed to be reliably associated with the flu vaccine. *See, e.g.*, S*payde v. Sec'y of Health & Hum. Servs.*, No. 16-1499V, 2021 WL 686682, at *8 (Fed. Cl. Spec. Mstr. Jan. 27, 2021). Indeed, a case of BBE with onset occurring in the 3–42-day timeframe for a flu-GBS Table claim would *itself* likely qualify as an acceptable Table claim, since the BBE diagnosis is not an exclusionary criterion. 42 C.F.R. § 100.3 (2017). In the non-Table context, most special masters have proposed an onset up to six weeks (or 42 days) post-vaccination to be medically acceptable for GBS variant symptoms manifestation. *Osorio v. Sec'y of Health & Hum. Servs.*, No. 18-1835V, 2021 WL 3370218, at *5 (Fed. Cl. Spec. Mstr. July 9, 2021) (dismissing a claim for an onset of 65 days, well outside the 3–42-day window).

II. Petitioner's Onset Was Most Likely November 23, 2011

Although the parties seem to agree that Mrs. Gray was properly diagnosed with BBE, they dispute the onset of her illness. Respondent, however, showed how the record establishes November 23rd as the first time she manifested any neurologic symptoms, over Dr. Steinman's far less-persuasive contentions that Mrs. Gray's obviously infection-related symptoms began November 14th to 17th. Dr. Steinman's preferred onset date was largely derived from a history contained in a medical report prepared a month after the onset, making it somewhat less reliable than immediately-contemporary records. First Steinman Rep. at 24; Ex. 7 at 7. Of particular note, there is no medical record support of Mrs. Gray even having an appointment on November 17th, only on the 14th. Around this time, Mrs. Gray was unquestionably being treated for then-existing UTI symptoms, as well as a possible URI. First Steinman Rep. at 24. These kind of symptoms are nonspecific for BBE ,or any comparable neurologic injury for that matter. *Chinea*, 144 Fed. Cl. at 387 (evidence of infectious-like malaise or fatigue does not constitute onset of neurologic symptoms classically associated with GBS). Indeed, Dr. Steinman admitted that Mrs. Gray's symptoms on November 14, 2011 were *consistent* with a viral illness. Second Steinman Rep. at 4.

Petitioner's witness testimony does not overcome what the record suggests about her most likely onset. Petitioner states in her affidavit that "[o]n November 18, 2011, my mother developed unprecedented neurological symptoms." Ex. 1 at 1. But the medical record does not corroborate the statement. And Petitioner also has admitted that at this time, Mrs. Gray had been diagnosed with a UTI (which the record establishes was first treated on November 11th). *Id.*; Ex. 17 at 25.

The overall medical record preponderates against the earlier onset date proposed by Petitioner.

III. Petitioner Has Not Carried Her Burden of Proof

This matter presents the uncommon case in which most of the *Althen* prongs have been satisfied, except (in my determination) the most fundamental—whether the vaccine Mrs. Gray received more likely than not *did cause* her injury. Because Petitioner has not preponderantly established this *Althen* prong, her claim cannot succeed.

A. *Althen* Prongs One and Three Have Been Preponderantly Met

Petitioner has preponderantly established the flu vaccine "can cause" BBE. The injury at issue (which the parties do not dispute is the proper diagnosis for Mrs. Gray's injury) is a variant of GBS itself—and ample authority, bulwarked by reasonable and reliable medical science, supports the conclusion that GBS can be caused by the flu vaccine. *Spayde*, 2021 WL 686682, at *8; *Stitt v. Sec'y of Health & Hum. Servs.*, No. 09-653V, 2013 WL 3356791, at *10 (Fed. Cl. Spec. Mstr. May 31, 2013). Although Mrs. Gray did not suffer from the most typical form of GBS, I conclude that BBE could be triggered by the flu vaccine in the same way, and largely in the manner proposed by Dr. Steinman (although I was unpersuaded entirely by his argument that neuraminidase is an additional avenue for autoantibody development and cross-reaction). Indeed, as noted above a case of BBE that occurred *sooner* than the one at issue herein could arguably constitute a viable Table claim (in which case causation would be presumed).

Of course, not *all* peripheral neuropathies characterized by demyelination and/or an autoimmune pathologic process are the same—even some that do overlap with GBS.[18] But here, the commonalities and similarities between BBE and GBS far outweigh the distinctions—and hence justify reliance on the science more specific to GBS. Both are acute conditions; Dr. Vartanian actually seemed to be of the opinion that BBE *must* be acute, since its nadir is reached so rapidly. First Vartanian Rep. at 10–12. And both seem to have a common pathogenesis involving attacks on anti-ganglioside antibodies. Dr. Steinman's opinion vouching for the association is also entitled to some weight, given his demonstrated expertise in both neurologic and immunologic issues.[19]

[18] Thus, I have repeatedly rejected the contention that chronic inflammatory demyelinating polyneuropathy ("CIDP") is nothing more than "persistent GBS," and have noted as well that the science that reliably associates the flu vaccine with GBS cannot simply be plugged into a CIDP case. *See Patel v. Sec'y of Health & Hum. Servs*., No. 16-848V, 2020 WL 2954950 (Fed. Cl. Spec. Mstr. May 1, 2020).

[19] I give some credit to Dr. Vartanian's arguments that the assumption the flu vaccine can cause BBE is scientifically flawed in several respects (regardless of the treatment the Program would give to this kind of claim). The flu wild virus, for example, is not known to be associated with BBE (even though it has been reliably associated with GBS itself). Molecular mimicry does not explain all autoimmune illnesses, and the mere possession of autoantibodies

In addition, the November 23rd day of onset for Mrs. Gray's BBE occurred in a medically acceptable timeframe, measuring from the date of her vaccination the month before. Again, the GBS "template" is useful in evaluating Petitioner's success in meeting this *Althen* prong. Special masters have often found onsets of up to six weeks post-vaccination to be medically acceptable in such circumstances. *Osorio*, 2021 WL 3370218, at *5. I have determined that Mrs. Gray's BBE symptoms manifested in 43 days—one day over six weeks. Because this is not a Table claim, rigid application of a particular timeframe is not called for, so the inability to meet that Table requirement herein does not preclude a favorable finding. And although Dr. Vartanian convincingly maintained that *in most* cases BBE would more likely begin close in time to the instigating trigger, his arguments that the immune reaction to the flu vaccine would be inherently more robust (relying on the Nachamkin figures) were less persuasive, given that those same figures revealed that the vaccine's immunogenicity continued *30 or more days* post-vaccination (thus allowing for the conclusion that the autoantibodies alleged to be causal herein could continue to be produced by a prior vaccination). Nachamkin at 230.

Admittedly, the timing of onset was fairly lengthy when measured from the date of vaccination. I take this attenuated course into account (along with other record evidence discussed below) in evaluating Petitioner's success in establishing the second *Althen* prong. But looking *solely* at whether (all things being equal) a 43-day timeframe is medically acceptable; I find that preponderant evidence supports Petitioner's position.

B. Petitioner did not Preponderantly Establish that the Flu Vaccine More Likely than Not Caused Mrs. Gray's BBE

Despite the above, the record does *not* preponderantly support the conclusion that the flu vaccine was likely responsible for Mrs. Gray's BBE. The determination I reach on this "did cause" prong of the *Althen* test involves a consideration of the actual record, measured against both the other two prongs as well as Federal Circuit law governing Program determinations generally.

For the most part, the record in this case reveals mainly a temporal association between vaccination and injury. Indeed, the record is completely silent as to *any* adverse reaction in the twenty days in October after vaccination. Since the mechanism proposed by Dr. Steinman is

known to be associated with one autoimmune disease does not mean *either* that the autoantibodies are causal, or (more significantly) that the vaccine instigated their creation. Nor does showing sequential homology (Dr. Steinman's "go-to" approach in case after case) between amino acid sequences in a vaccine's antigens and self-structures prove much in the way of anything, absent additional factors suggesting the same vaccine components are likely associated with the relevant disease. Dr. Vartanian's detailed discussion of Nachamkin and Yuki also revealed the extent to which it may be a mistake for medical science to continue to accept at face value the contention that the flu vaccine inerrantly causes the production of anti-ganglioside antibodies that other infectious processes *known* to be associated with GBS or BBE (like *C. jejuni*) have been demonstrated to do. It is entirely possible that such criticisms might one day result in reliable scientific research that alters the Program's "take" on these matters—but that day has not yet come.

autoimmune process driven by an aberrant secondary immune response to the flu vaccine, resulting in an antibody-driven cross-reaction attack against nerve gangliosides, there should be record "evidence pointing to the initiation of an autoimmune process or the onset of a massive inflammatory response." *Dillon v. Sec'y of Health & Hum. Servs.,* No. 10-850V, 2013 WL 3745900, at *16 (Fed. Cl. Spec. Mstr. June 25, 2013) (claim that flu vaccine caused transverse myelitis not preponderantly established under *Althen* prong two).

But there is no such evidence in the record for a considerable period post-vaccination. And even before onset of neurologic symptoms on November 23, 2011, there is competing evidence of a UTI and/or URI, far *closer* in time to onset of her neurologic symptoms (no more than twelve days, if measured from the November 11, 2011 doctor's visit). Ex. 17 at 22–25. The records from this period reveal Mrs. Gray had a slight fever, and she tested positive for inflammatory biomarkers as well. *Id.* at 22–23, 25. And unlike cases where vaccination is deemed to have *first* triggered fever or some intervening problem that in turn resulted in harm, Petitioner does not herein allege (nor could she establish) that her November infection was vaccine-caused, or that the two interacted. *See Sharpe v. Sec'y of Health & Hum. Servs.*, No. 14-65V, 2021 WL 1291720 (Fed. Cl. Spec. Mstr. Feb. 19, 2021) (vaccine established to have caused fever in infant, leading directly to series of seizures thereafter). Nor did any contemporaneous treaters ever identify the flu vaccine as likely causal of Mrs. Grey's BBE. Dr. Vartanian also persuasively established that a variety of infectious processes were as likely to cause BBE as a vaccine (if not more so). *See, e.g.*, Koga at 1212.

Thus, this case clearly features clinical evidence of a potential infectious cause for Mrs. Gray's BBE, closer in time to onset than a vaccine received *30* days before even the intervening UTI/URI symptoms. And that 30-day period reveals no evidence of any aberrant immune response. The connection between infection and BBE is better established on this record than the more remote-in-time vaccination—and prevents Petitioner from successfully establishing preponderantly that the flu vaccine "did cause" Mrs. Gray's injury.[20]

Dr. Steinman's reports ineffectively rebutted this conclusion. Clinical evidence of an infection of some sort exists in this record—and indeed was conceded by Dr. Steinman. *See* Second Steinman Rep. at 4 (admitting that Mrs. Gray's November 14, 2011 symptoms were "consistent with a viral illness and/or an encephalitis"). Dr. Steinman's primary response was to protest that no specific infection was ever serologically confirmed, and hence, absent a "formal diagnosis" of a specific virus, the vaccine's causality remained more likely. *Id.* But by so arguing, he is in effect giving great weight to the (somewhat attenuated) temporal association between vaccine and injury—something controlling precedent indicates is not a sufficient basis for entitlement. *Grant*,

[20] Petitioner proposes that the UTI's causal role is undermined by the fact that Mrs. Gray experienced UTIs in the past without developing BBE, and this contention has some merit. But it does not *preclude* the determination that an intervening infection was more likely causal—any more than the fact that a petitioner received a vaccine before without injury undermines the determination that in the *relevant* time the vaccine was injurious.

956 F.2d at 1148. He is also demanding a degree of certainty from Respondent that Program petitioners *themselves* are not required to satisfy. *Knudsen,* 35 F.3d at 549 ("the standards that apply to a petitioner's proof of actual causation in fact in off-table cases should be the same as those that apply to the government's proof of alternative actual causation in fact"). Causation claims do not succeed merely because Respondent cannot prove with certainty what *was* causal—any more than petitioners prevail by isolating the causal role of a vaccine simply by eliminating other possible causes. *Thomas v. Sec'y of Health & Human Servs*., No. 01-645V, 2007 WL 470410, at *25 (Fed. Cl. Spec. Mstr. Jan. 23, 2007) ("merely showing an absence of an alternative cause of injury does not meet a petitioner's burden of proof" (*citing Grant,* 956 F.2d at 1149)).

At bottom, I am allowed to give weight to the unrebutted evidence of Mrs. Gray's pre-BBE onset infectious illness, even if its precise etiology cannot be determined—and determine that it undermines Petitioner's "did cause" showing, regardless of whether it in fact explains the cause of Mrs. Gray's BBE. *Knudsen*, 35 F.3d at 547–48. Controlling precedent recognizes that my weighing of such evidence in the context of evaluating a petitioner's success in carrying her burden of proof on the second prong (instead of "saving" it for an alternative cause analysis) is not error. As the Federal Circuit has observed, "like any defendant, [Respondent] is permitted to offer evidence to demonstrate the inadequacy of the petitioner's evidence on a requisite element of the petitioner's case-in-chief." *de Bazan*, 539 F.3d at 1353; *see also Stone v. Sec'y of Health & Hum. Servs.*, 676 F.3d 1373, 1379 (Fed. Cir. 2012) (deeming it a "commonsense proposition that evidence of other possible sources of injury can be relevant not only to the "factors unrelated" defense, but *also to whether a prima facie showing has been made that the vaccine was a substantial factor in causing the injury in question*") (emphasis added).[21]

The fact that this claim's success turns solely on my *Althen* prong two determination is also not improper. Putting aside the fact that claimants must satisfy *all three* causation prongs in any entitlement action, the Circuit has recognized that the second prong is not an afterthought, easily satisfied once the other prongs are met, but *itself* requires the same preponderant showing, and can be dispositive if not satisfied:

> [t]here may well be a circumstance where it is found that a vaccine can cause the injury at issue and where the injury was temporally proximate to the vaccination, but it is illogical to conclude that the injury was actually caused by the vaccine. A claimant could satisfy the first and third prongs without satisfying the second prong

[21] I thus do not find that the burden of proof shifted to Respondent, because Petitioner did not make a prima facie case on this particular prong. Under different facts, however, the alternative cause burden-shifting analysis would be appropriate. For example, if Petitioner could have shown that her BBE began far closer in time to vaccination under a more constricted timeframe, the potential interplay between vaccine and any subsequent infection would impel me to find (especially given my *Althen* prong one and three determinations) that a prima facie case was made—and hence to require Respondent to preponderantly demonstrate the intervening infections were causal before denying entitlement.

> when medical records and medical opinions do not suggest that the vaccine caused the injury, or where the probability of coincidence *or another cause* prevents the claimant from proving that the vaccine caused the injury by preponderant evidence.

Capizzano, 440 F.3d at 1327 (emphasis added).

Petitioner's arguments about uncertainty regarding an alternative cause, when compared to certainty of vaccination (*see* Second Steinman Rep. at 5 ("I *do* know what kind of vaccine she had on Oct. 11, 2011") (emphasis added)), are thus unavailing. This only prevents me from determining the actual cause of her BBE on this record—not from finding that the cause was *not,* more likely than not, a vaccine received a month *prior* to the infection. Otherwise, Dr. Steinman has not proposed in his reports that Mrs. Gray's post-vaccination infections interacted with the prior vaccination, such that *either* co-exist as "but for" explanations,[22] and he disclaims entirely the possibility that the intervening infections were causal in any respect.

My favorable *Althen* prong three finding is also not inconsistent with this determination. As noted above, evidence in this case does establish preponderantly that it is medically acceptable for 43 days to pass between receipt of the flu vaccine and onset of a GBS variant like BBE. But this does *not* mean that what actually happens in a particular case in that 43-day timeframe is irrelevant. The facts of the specific case at issue matter. Here, the interplay between the date of Mrs. Gray's onset, its remoteness in time from vaccination, and a documented intercurrent infectious process that could explain her injury all weigh against the conclusion that the flu vaccine "more likely than not" was responsible in any part. Indeed, she received the vaccine on October 11th, with no sign at all for the remaining 20 days of that month of any reaction or immune process that might have led to the production of the purportedly cross-reactive anti-ganglioside antibodies. By November 11th (now a month post-vaccination—still with no sign of an aberrant immune response) Mrs. Gray began to seek treatment for her UTI/URI, and then less than two weeks later

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[22] I also do not find in this case that *both* vaccine and infection could have played an equal role in producing Mrs. Gray's BBE. In many cases in which there are competing "explanations" for a post-vaccination injury, special masters invoke the *Shyface* decision to justify the determination that the vaccine was a "but for" cause. *Shyface*, 165 F.3d at 1347–48. Experts cannot always tease out the interplay between a vaccine's role in causing harm and other concurrent or intervening events, and where the vaccine likely played a demonstrable part in the sequence resulting in injury, it is reasonable to find the "did cause" prong met, even if the vaccine was not *solely* or *predominantly* causal. The facts of *Shyface* itself illustrate how this can work in practice. *Id.* at 1353.

But this kind of showing cannot be made in every case where a vaccine otherwise is known to have the capacity to cause a particular injury. The Federal Circuit's ruling in *Pafford* is illustrative. *Pafford*, 451 F.3d at 1358–60. *Pafford* mostly turned on the lack of a demonstrated medically acceptable temporal association (and hence is ultimately distinguishable from the present case, since I *do* find that association exists). But the Federal Circuit therein also observed from the facts of that case (as outlined by the special master who originally decided it) a number of "other contemporaneous events unrelated" to vaccination, but which stood as counter-explanations for injury, including positive evidence of a bacterial and viral infection. *Id.* at 1356. Here, similar evidence undermines the conclusion that the vaccine was causal.

displayed her first true neurologic symptoms.

This secondary timeframe (November 11th to November 23rd) was *also* a medically acceptable period for how long it would take a wild infectious process to result in an adaptive immune response capable of producing the anti-ganglioside antibodies that Dr. Steinman identified as causal of the demyelination characteristic of BBE. Indeed, the somewhat lengthy timeframe that Dr. Steinman proposes is acceptable for generation of the relevant BBE-causing antibodies also covers the shorter period in this case between infection and BBE onset. *See, e.g.*, *Chinea*, 144 Fed. Cl. at 384; Schonberger at 109–12 (finding the drop-off of cases after vaccination does not occur until several weeks later). It certainly is a *more* direct association than between Mrs. Gray's BBE and the vaccine she received 43-plus days before.[23]

From a purely factual standpoint, this record largely establishes only that a specific vaccine that can be associated with BBE preceded Mrs. Gray's onset by slightly over six weeks. But it is axiomatic in the Program that *not all post-vaccination injuries are due to vaccination. P.M. v. Sec'y of Health & Hum. Servs.*, No. 16-949V, 2019 WL 5608859, at *27 (Fed. Cl. Spec. Mstr. Oct. 31, 2019). When the medical record lacks the kind of inferential "hints" that suggest the vaccination was causing an immunologic response later manifesting as disease, while also containing evidence suggestive of an intervening, closer-in-time explanation, it is reasonable to find that the second *Althen* prong has not been met.

III. This Case Was Appropriately Decided on the Papers

In ruling on the record, I am choosing not to hold a hearing. Determining how best to resolve a case is a matter that lies generally within my discretion, and although the parties have not objected to this method of adjudication, I shall explain why a hearing was not required.

Prior decisions have recognized that a special master's discretion in deciding whether to conduct an evidentiary hearing "is tempered by Vaccine Rule 3(b)," or the duty to "afford[] each party a full and fair opportunity to present its case." *Hovey*, 38 Fed. Cl. at 400–01 (citing Rule 3(b)). But that rule also includes the obligation of creation of a record "sufficient to allow review of the special master's decision." *Id*. Thus, the fact that a claim is legitimately disputed, such that the special master must exercise his intellectual faculties in order to decide a matter, is not itself

[23] In other cases involving autoimmune demyelinating diseases like GBS, I have noted that the patient's age might bear on how long the adaptive immune process takes to begin creating autoantibodies, since aged immune systems respond less robustly to antigenic environmental stimulation. *See Rowan v. Sec'y of Health & Hum. Servs.*, No. 17-760V, 2020 WL 2954954, at *18 (Fed. Cl. Spec. Mstr. April 28, 2020). But here, Petitioner has not established that a ten to fourteen-day period from wild virus or bacterial exposure to onset of BBE would be too short for an elderly individual—and I note that in *Rowan.* the problem with onset was that it occurred in less than *two days*. *Id.* at 17. Other literature filed in this case supports this timeframe as being medically acceptable.

grounds for a trial (for if it were, trials would be required in every disputed case). Special masters are expressly empowered to resolve fact disputes without a hearing—although they should only so act if a party has been given the proper "full and fair" chance to prove their claim.

The present claim could be, and was, resolved fairly without the need for live testimony from the experts. The parties agreed Mrs. Gray suffered from BBE, a variant of GBS. While the onset date was disputed, my determination of that issue did not ultimately impact the outcome (and indeed, I ultimately found in Petitioner's favor on *Althen* prong three). This left only whether in this case the vaccine was more likely than not the cause of Mrs. Gray's BBE. I was able to fairly resolve that question without a hearing, based on the filed reports and briefs.

CONCLUSION

Petitioner has not met her burden of proof and is therefore not entitled to an award of damages. In the absence of a motion for review filed pursuant to RCFC Appendix B, the Clerk of the Court **SHALL ENTER JUDGMENT** in accordance with the terms of this Decision.[24]

IT IS SO ORDERED.

/s/ Brian H. Corcoran
Brian H. Corcoran
Chief Special Master

[24] Pursuant to Vaccine Rule 11(a), the parties may expedite entry of judgment if (jointly or separately) they file notices renouncing their right to seek review.