In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: August 30, 2019

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JAMILEH BERENJI and BAHMAN YOUSEFI on behalf of S.Y.,	
Petitioners,	PUBLISHED
v.	No. 14-699V
SECRETARY OF HEALTH AND HUMAN SERVICES,	Special Master Gowen
Respondent.	Motion for Reconsideration in Light of Additional Evidence; Vaccine Rule 10(e)(1); RCFC 59(a)(1).
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Mark T. Sadaka, Mark T. Sadaka, LLC, Englewood, NJ, for petitioners.
Sarah C. Duncan, United States Department of Justice, Washington, DC, for respondent.

ORDER DENYING PETITIONERS' MOTION FOR RECONSIDERATION[1]

On August 4, 2014, Jamileh Berenji and Bahman Yousefi ("petitioners"), on behalf of their minor child S.Y., filed a petition for compensation in the National Vaccine Injury Compensation Program.[2] S.Y. received influenza ("flu"), measles-mumps-rubella ("MMR"), varicella, and pneumococcal conjugate ("Prevnar") vaccines on October 17, 2011. Petitioners alleged that those vaccines significantly aggravated S.Y.'s pre-existing asymptomatic Evans syndrome and that significant aggravation included a multitude of phenomena including but not limited to autoimmune hepatitis and pulmonary veno-occlusive disease (PVOD). Petition (ECF No. 1). Respondent recommended against awarding compensation to petitioners. Respondent's Report filed March 23, 2015 (ECF No. 17).

[1] Pursuant to the E-Government Act of 2002, *see* 44 U.S.C. § 3501 note (2012), because this opinion contains a reasoned explanation for the action in this case, I am required to post it on the website of the United States Court of Federal Claims. The court's website is at http://www.uscfc.uscourts.gov/aggregator/sources/7. **This means the opinion will be available to anyone with access to the Internet.** Before the opinion is posted on the court's website, each party has 14 days to file a motion requesting 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). An objecting party must provide the court with a proposed redacted version of the opinion. *Id.* **If neither party files a motion for redaction within 14 days, the opinion will be posted on the court's website without any changes.** *Id.*

[2] The National Vaccine Injury Compensation Program is set forth in Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755, codified as amended, 42 U.S.C. §§ 300aa-1 to 34 (2012) ("Vaccine Act" or "the Act"). Hereinafter, individual section references will be to 42 U.S.C. § 300aa of the Act.

On May 29, 2019, I issued a decision denying compensation to petitioners. *Berenji v. Sec'y of Health & Human Servs.*, No. 14-699V (May 29, 2019) (ECF No. 99) (hereinafter the "Original Decision"). The original decision summarized the procedural history to that date, including respondent's recommendation against compensation, petitioner's submission of expert reports and testimony from Dr. M. Eric Gershwin, and respondent's submission of expert reports and testimony from Dr. Mehrdad Matloubian and Dr. Joan Cox Gill. *Id.* at 2-4. I made conclusions with regards to *Loving* prong one (that S.Y. had pre-existing asymptomatic Evans syndrome prior to the vaccines); *Loving* prong two (S.Y.'s diagnosis, symptoms, and complications of Evans syndrome after receiving the vaccines); and *Loving* prong three (that S.Y. experienced a significant worsening of Evans syndrome after receiving the vaccines). *Id.* at 6-14.

I also concluded that petitioners failed to provide preponderant evidence that the vaccines S.Y. received on October 17, 2011, caused that significant worsening. Under *Loving* prong four (*Althen* prong one), I did not reject petitioners' expert Dr. Gershwin's theory that a person can be predisposed to autoimmunity and go through a crucial early stage in which the addition of vaccines can induce or more relevant to this case, significantly aggravate autoimmune disease, through the process of bystander activation.

Under *Loving* prongs five and six (*Althen* prongs two and three), I concluded: "[T]here can be little question that S.Y.'s condition became markedly worse after receiving the vaccines on October 17, 2011. His treating doctors generally thought that the process including fever, seizure and full body rash were likely attributable to the vaccines. However, that short-term injury, if attributed to the vaccines, did not last for more than six months. It is significantly more difficult to find a logical and temporal association between S.Y.'s vaccines and his long-term course which is at least somewhat similar to other patients with Evans syndrome. The available literature on this very rare disease suggests that Evans syndrome is chronic and refractory to treatment. S.Y.'s development of antinuclear antibodies, antiphospholipid antibodies, hepatitis, and PVOD seems particularly rare. However, those conditions are unlikely to be caused by B cells stimulated by the vaccines, which were eliminated and replaced in the intervening time period. Thus, there is not a logical sequence of cause and effect or an acceptable temporal association between the vaccines and S.Y.'s long-term course." Original Decision at 24-25. Thus, I found that petitioners were not entitled to compensation.

On June 21, 2019, petitioners filed a motion for reconsideration of the original decision "based on new evidence on how bystander activation played a role in the development of the pulmonary and liver conditions [S.Y.] developed." Petitioners' Motion for Reconsideration ("Pet. Mot.") (ECF No. 101) at 1. The motion was accompanied by two pieces of medical literature published in 2019 and a supplemental report from Dr. Gershwin about their relevance to this case. Petitioner's Exhibit ("Pet. Ex.") 137 and Tabs 1-2.[3] Petitioners request that the

[3] Hadjadj J. et al., *Pediatric Evans syndrome is Associated with a High Frequency of Potentially Damaging Variants in Immune Genes*, Blood (April 2, 2019), pii: blood-2018-11-887141, doi: 10.1182/blood-2018-11-887141 [Pet. Ex. 137-1]; Lee H. et al., *Pathogenic Function of Bystander-Activated Memory-Like CD4 T Cells in Autoimmune Encephalomyelitis*, Nature Communications, Volume 10, Article Number 709 (2019) [Pet. Ex. 137-2].

Court vacate the original decision and allow them to present this new evidence and explain how it supports their theory. Pet. Mot. at 3.

Petitioners' motion was granted to the extent that the original decision was withdrawn for further review. A decision determining whether petitioners were entitled to any additional relief (a substantive change in outcome) was deferred to allow respondent to file a response. Order on Motion filed June 28, 2019 (ECF No. 105). On July 12, 2019, respondent timely filed a response ("Resp. Response") (ECF No. 107) and a supplemental report from Dr. Matloubian (Resp. Ex. F) (ECF No. 106). On July 19, 2019, petitioners filed an unsolicited reply ("Pet. Reply") (ECF No. 109) and another supplemental report from Dr. Gershwin (Pet. Ex. 138). The parties' additional arguments have been considered. For the reasons discussed below, petitioners' motion for reconsideration is **DENIED.**

I. Relevant Standards

1. Applicable Rule and Resulting Deadline

Petitioners' motion for reconsideration was filed 23 days after the decision denying entitlement.[4] Petitioners cite the Rules of the Court of Federal Claims, Rule 59(a)(1), which provides that a motion for reconsideration may be granted: "(A) for any reason for which a new trials has heretofore been granted in an action at law in federal court; (B) for any reason for which a rehearing has heretofore been granted in a suit in equity in federal court; or (C) upon the showing of satisfactory evidence, cumulative or otherwise, that any fraud, wrong, or injustice has been done in the United States." RCFC 59(a)(1). The time frame for filing a motion for reconsideration pursuant to this rule is "no later than 28 days after the entry of judgment." RCFC 59(b)(1). This would suggest that petitioners' motion is timely.

However, the Rules for the Court of Federal Claims, including the rule cited above, "apply only to the extent they are consistent with the Vaccine Rules," which are more specific to proceedings in the Vaccine Program. Vaccine Rule 1(c). There is a separate, specific rule for motions for reconsideration for petitioners filed in this Program, which provides a shorter filing period. That rule provides: "Either party may file a motion for reconsideration of the special master's decision *within 21 days after the issuance of the decision*, if a judgment has not been entered and no motion for review under Vaccine Rule 23 has been filed." Vaccine Rule 10(e)(1) (emphasis added). Petitioners do not cite this rule in their motion. However, it is controlling and renders petitioners' motion for reconsideration untimely, by two days. I have considered the impact of my decision denying compensation on this family and the limited delay to file the motion for reconsideration. In my discretion, I will *sua sponte* grant petitioners the necessary extension of time and treat the motion for reconsideration as timely filed. *See* Vaccine Rule 3(b)(2) (providing that the special master is responsible for "affording each party a full and fair opportunity to present its case"); Vaccine Rule 10(e)(3) (providing that the special master "has the discretion to grant or deny the motion, in the interest of justice").

[4] The decision denying entitlement was issued on Wednesday, May 29, 2019. The motion for reconsideration was filed on Friday, June 21, 2019.

2. Legal Standard for Reconsideration

A party seeking reconsideration "must support the motion by a showing of extraordinary circumstances which justify relief." *Fru-Con Constr. Corp. v. United States*, 44 Fed. Cl. 298, 300 (1999). The motion for reconsideration "must be based 'upon manifest error of law, or mistake of fact, and is not intended to give an unhappy litigant an additional chance to sway the court.'" *Prati v. United States*, 82 Fed. Cl. 373, 376 (2008) (quoting *Fru-Con Constr. Corp.*, 44 Fed. Cl. at 300).

"A court may grant such a motion when the movant shows '(1) that an intervening change in the controlling law has occurred; (2) that previously unavailable evidence is now available; or (3) that the motion is necessary to prevent manifest injustice.'" *System Fuels, Inc. v. United States*, 79 Fed. Cl. 182, 184 (2007), quoting *Amber Resources Co. v. United States*, 78 Fed. Cl. 508, 514 (2007). Granting such relief requires "a showing of extraordinary circumstances." *Caldwell v. United States*, 391 F.3d 1226, 1235 (Fed. Cir. 2004) (citation omitted), *cert. denied*, 546 U.S. 826 (2005). Within the Vaccine Program, special masters have the discretion to grant a motion for reconsideration if to do so would be in the "interest of justice." Vaccine Rule 10(e)(3); *see also Hall v. Sec'y of Health & Human Servs.*, 93 Fed. Cl. 239, 251 (2010), *aff'd* 640 F.3d 1351 (Fed. Cir. 2011).

As noted by other special masters, there is little case law interpreting Vaccine Rule 10(e)(3) beyond the conclusion that it is within the special master's discretion to decide what the "interest of justice" is in a given case. *See Krakow v. Sec'y of Health & Human Servs.*, No. 03-632V, 2010 WL 5572074, at *3 (Fed. Cl. Spec. Mstr. Jan. 10, 2011) (granting reconsideration of motion to dismiss case for failure to prosecute).

In this case, petitioners seek reconsideration "based on new evidence," specifically, two articles that were published after the case was litigated but shortly before the decision denying entitlement was issued. Pet. Mot. at 1. Petitioners aver that this new evidence must be considered "to prevent manifest injustice." *Id.* at 2. They argue: "This case was dismissed largely based on petitioner's failure to prove a logical sequence of cause and effect. The new evidence filed as Exhibit 137 supports petitioner's causation theory and should be considered by the Court before dismissing petitioners' claim." *Id.* at 3.

Respondent contends that these articles should not be considered because their filing was untimely. The article by Lee et al. (Pet. Ex. 137-2) was made publicly available on February 12, 2019 and the article by Hadjadj et al. (Pet. Ex. 137-1) was made publicly available on April 2, 2019. Accordingly, both were available prior to the original decision's issuance on May 29, 2019. Respondent contends that petitioners could have sought leave to file the two articles before the original decision was issued. Resp. Response at 2. Petitioners reply that there is no rule or law that defines the timeliness of the submission of new evidence. Petitioners contend that it is unrealistic for experts and counsel to "continuously monito[r] the publications for new literature after post-hearing briefs" and "bring it to the Court's attention immediately when it is not clear that additional evidence was needed in the first place." Pet. Reply at 1. Petitioners further contend that it is difficult to understand what issues governed the outcome in this case and that they did not learn until the issuance of the original decision "that Dr. Matloubian's

attack on bystander activation was persuasive." *Id.* at 1-2.

This case involves a very serious condition affecting this child and by extension, his family. There is not a clear standard for when new evidence is "timely." I am inclined to agree that it is somewhat unrealistic for counsel and/ or experts to monitor the literature and file additional articles in a case after post-hearing briefing is completed and it is unclear what issues need further supporting evidence. Indeed, in certain cases, I have critiqued both parties for filing medical literature that is redundant and/or focused on inconsequential issues. Here, petitioners' expert and their counsel promptly reviewed the original opinion and filed two articles that had only been publicly available for a few months. These are not so untimely that they should not even be considered.

Additionally, petitioners are correct that the literature on Evans syndrome is sparse, due to the condition's rarity. The article by Hadjadj et al. (Pet. Ex. 137-1) is a significant new study on this very rare condition which I find worthy of consideration.

For the reasons set forth below, even if petitioners had presented these two articles at a time when they could have been considered as part of my original decision, they would not have changed the outcome.

II. Analysis

1. *Loving* Prongs One, Two, and Three

i. Original Decision

As detailed in the original decision, under *Loving* prong one, I concluded that S.Y. had asymptomatic undiagnosed Evans syndrome before receiving the vaccines at issue in this case. *See* Original Decision at 6-7.

Under *Loving* prong two, I discussed that on October 17, 2011, at S.Y.'s twelve-month primary care appointment, he received the vaccines at issue. At the same appointment, at his mother's request, S.Y. underwent bloodwork which unexpectedly revealed significantly low platelets and hemoglobin counts. In the next few days, S.Y. underwent repeat bloodwork which showed even lower platelet and red blood cell counts. A Coombs test was positive, which showed that gammaglobulins were binding to his red blood cells, thereby confirming that his condition was autoimmune. S.Y. was diagnosed with Evans syndrome. Whole-exome sequencing did not find any genetic explanation for that condition. In late October 2011, S.Y. was hospitalized for a persistent fever and rash; during this hospitalization, he had one episode of febrile seizure. Over the next several years, S.Y.'s condition deteriorated further and he was hospitalized multiple times. His Evans syndrome was resistant to numerous treatments, including Rituximab beginning in February – March 2012. S.Y. had various complications, including pulmonary veno-occlusive disease (PVOD) and hepatitis in 2013. Finally, in 2015, he received a course of Velcade (bortezomib), which reduced or eliminated the blood plasma cells which produced antibodies. This treatment appears to have been effective. S.Y. was going to school and he stopped taking Rituximab and was able to wean off supplemental oxygen during

the day. S.Y. continued to use supplemental oxygen at night and undergo IVIg every other month. Original Decision at 7-13.

Under *Loving* prong three, I repeated that S.Y. had Evans syndrome before receiving the vaccines on October 17, 2011. Bloodwork taken approximately one hour later showed significantly low platelets and hemoglobin counts. "The experts agreed that these vaccinations could not have impacted this bloodwork within such a short period of time." Thus, there was no dispute that S.Y. had Evans syndrome before the vaccines. Original Decision at 14.

I then concluded that after receiving the vaccines, S.Y. "experienced a very significant change in his condition." However, that did not constitute a finding that the "change, worsening, or 'significant aggravation' of S.Y.'s condition implie[d] vaccine causation." That was addressed under Loving prongs five and six (*Althen* prongs two and three). Original Decision at 14.

ii. Additional Evidence

The parties do not argue that I should reconsider my conclusions on *Loving* prongs one, two, or three. Neither do I find it necessary following a review of the new briefs, expert reports, and medical literature.

2. *Loving* Prong Four (*Althen* Prong One)

i. Original Decision

Under *Loving* prong four (*Althen* prong one), I evaluated Dr. Gershwin's opinion that a person can have an underlying bias towards a Th-1 immune response and autoimmunity. For such a person, there is a crucial early stage in which the immune cells are rapidly dividing and becoming more promiscuous. This could involve the onset of an autoimmune condition. If a treating physician is aware that a person is in this stage, vaccines should not be given. Dr. Gershwin opined that vaccines elicit an immune response including pro-inflammatory cytokines, which likely activate dormant cells which are not directed against the vaccine antigens, but against the self. This process is called bystander activation. Dr. Gershwin opined that bystander can cause or more relevant in this case, significantly aggravate an autoimmune condition. Original Decision at 15-16.

I noted that respondent's experts did not particularly respond to Dr. Gershwin's opinion about the predisposition towards a Th-1 immune response and autoimmunity. *Id.* at 16. I noted that Dr. Matloubian opined that the "bystander pathway has fallen out of favor," but I *rejected* that opinion. The Wucherpfennig article cited by Dr. Matloubian actually supported Dr. Gershwin's theory that "an active autoimmune process could be amplified by cytokine production," which is related to bystander activation. I did not find that the *general* concept of bystander activation was out-of-date or unreliable. *Id.* at 16-18. Rather, under *Loving* prong four (*Althen* prong one), I concluded:

> [I]t is not well understood whether a trigger or other stimulus is necessary for the onset of Evans syndrome. I do not see any reference to whether any immune stimulus can be enough to trigger the failure of the regulatory immune system. Moreover, I do not see any reference to whether a particular stimulus from live virus(es) or vaccine(s) can heighten the dysregulated response resulting in a more debilitating course of this very rare condition.
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> Dr. Gershwin's theory of a predisposition toward autoimmunity characterized by a Th-1 pro-inflammatory response, further stimulation by vaccinations, and bystander activation may be plausible.[5] Respondent's experts essentially did not rebut this theory. However, Dr. Gershwin did not particularly relate this theory to Evans syndrome. Additionally, the sequence of events and the timing in S.Y.'s particular case are more key to the outcome.

Original Decision at 18.

ii. Additional Evidence

Petitioners' expert Dr. Gershwin opines that his theory of bystander activation was "criticized as not being contemporary." Therefore, Dr. Gershwin submits the article by Lee et al.[6] on bystander activation in another model of autoimmunity, experimental autoimmune encephalitis (a surrogate of multiple sclerosis), for the proposition that "the importance of bystander activation was emphasized." Pet. Ex. 137 at 1. Dr. Matloubian responds that Lee et al. do not demonstrate the exact mechanism of bystander activation which Dr. Gershwin proposes in this case. Resp. Ex. F at 2-3. Dr. Gershwin replies that bystander activation is a viable theory, it can "amplify and/or induce immune response," and it can occur via "myriad pathways" as demonstrated by Lee et al. Pet. Ex. 138 at 1.

Lee et al. state in their abstract: "Despite the importance of antigen-specific T cells, here we show that antigen non-related, bystander memory-like CD4+ T cells also significantly contribute to autoimmune pathogenesis." Pet. Ex. 137-2 at 1. In the discussion, they state: "antigen non-related bystander-activated effector or memory CD4+ T cells are actively involved in pathogenic inflammation to amplify or initiate autoimmune disease by producing pathogenic inflammatory mediators". *Id.* at 12.

This article offers one model of bystander activation. It also reinforces the literature submitted in the earlier proceedings, to demonstrate that bystander activation is still a current concept under active investigation in the immunology research field.

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[5] I have previously accepted Dr. Gershwin's opinion – supported in part by studies in animals - that prematurity, young infancy, and the alum adjuvant used in some vaccinations all together can skew an infant's immune system so far toward a *Th-2* response which is designed to fight against bacterial infection that it cannot mount a Th-1 response against viral infection. *Barrett v. Sec'y of Health & Human Servs.*, No. 14-137V, 2017 WL 4342334 (Fed. Cl. Spec. Mstr. Sept. 6, 2017), mentioned briefly during the entitlement hearing in *Berenji* at Tr. 20-21.

[6] Lee H. et al., *Pathogenic Function of Bystander-Activated Memory-Like CD4 T Cells in Autoimmune Encephalomyelitis*, Nature Communications, Volume 10, Article Number 709 (2019) [Pet. Ex. 137-2].

I did not and still do not conclude that petitioners failed on *Loving* prong four (*Althen* prong one).

3. *Loving* Prongs Five and Six (*Althen* Prongs Two and Three)

i. Original Decision

Within this section, I discussed a key disagreement in the case. Dr. Gershwin opined that S.Y. had an extraordinarily severe case of Evans syndrome with resistance to treatment and uncommon sequelae namely autoimmune hepatitis and PVOD, "which were unusual for Evans and instead due to the contributions of the vaccines." Original Decision at 22. "Dr. Gershwin opined that he could not find cases like this in the literature." *Id.*

In contrast, Dr. Matloubian and Dr. Gill "disagreed that S.Y. had an unusually severe course of Evans syndrome." Original Decision at 22. Rather, they opined that Evans syndrome is a rare but terrible disease that can be resistant to treatment and can involve various possible immune manifestations, including autoimmune hepatitis. These opinions were based on the limited published literature on Evans syndrome and Dr. Gill's clinical experience treating this very rare condition. *Id.* at 22-24.

I concluded that the October 2011 vaccines may have caused an immune response which explained S.Y.'s initial fever, seizure, and full body rash. "However, that short-term injury, if attributed to the vaccines, did not last for more than six months." Original Decision at 24-25 (citation omitted).

However, I concluded that there was not a logical sequence of cause and effect or an acceptable temporal association for the injuries alleged. This was partly based on Dr. Matloubian's opinion that if S.Y. was experiencing an "immunological storm" that was exacerbated by the vaccines, resulting in a break of tolerance, Dr. Matloubian would have expected the manifestations of autoimmune disease to develop within a short period of time such as a few months, rather than a year later. Original Decision at 24.

I found most persuasive Dr. Matloubian's opinion that approximately 99% of the B cells present at the time of the October 2011 vaccines were wiped out by a course of Rituximab in February – March 2012. Afterwards, S.Y.'s bone marrow – specifically the plasma – produced new replacement B cells which were observed in February 2013. "Only afterward did S.Y. become positive for antinuclear (ANA) antibodies and antiphospholipid antibodies and developed PVOD and giant cell hepatitis." Original Decision at 24. Dr. Matloubian opined that the activation of these new B cells and the development of hepatitis and PVOD could not be attributed to the vaccines. *Id.* Furthermore, in early 2015, S.Y. received Velcade, which eliminated the *plasma cells* which produce the B cells which produce antibodies. *Id.* Velcade was largely successful in treating his Evans syndrome. *Id.* (Although it wiped out his preexisting immunity, which necessitated continuing IVIg treatment. *Id.*) Accordingly, I concluded that "there is not a logical sequence of cause and effect or an acceptable temporal association between the vaccinations and S.Y.'s long term course." Original Decision at 25. That dictated the outcome in this case.

ii. Additional Evidence

As noted above, there is no doubt that S.Y. has suffered tremendously in connection with his Evans syndrome. This is undoubtedly a very rare, not well understood, and often debilitating condition. The published literature on this condition is limited, but it continues to be a subject of active research and investigation. As such, I find that it is reasonable and "in the interest of justice" to review the article by Hadjadj et al. which examines the potential genetic bases and manifestations of this syndrome.

Regarding this article, Dr. Gershwin states:

> [T]here is now data that there are several genes that predispose to Evans syndrome; activation of genetic pathways would significantly impact the manifestations of Evans syndrome. I had argued during the hearing that such predisposition existed but could not provide more than generic data on such predisposition.

Pet. Ex. 137 at 1.

Dr. Gershwin also states:

> In the hearing, I argued that there was a genetic predisposition, in other words, [S.Y.] was a promiscuous host, highly susceptible to aberrant immune activation. [The Hadjadj et al. article] confirms such a predisposition.
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> In the hearing, my opinions and mechanism was based on the concept of bystander activation… to amplify and/or induce immune responses. In this case, the result was that the clinical manifestations in [S.Y.] were exceedingly severe and far worse than the overwhelming number of cases in the literature or in the experience of any of the experts at this hearing.

Pet. Ex. 138 at 1.[7]

The Hadjadj et al. article was pre-published online in the journal *Blood* in April 2019. It was a study of the potential genetic bases for Evans syndrome. It utilized an extensive French database of patients diagnosed with Evans syndrome.[8] In Hadjadj et al.'s study, from the French database of approximately two hundred patients, eighty non-selected consecutive individuals underwent genetic testing. That resulted in two groups. First, the M+ group contained 52 patients (65%) who received a genetic diagnosis (49 patients had germline mutations and the

[7] In this reply, Dr. Gershwin raises two other points. The first is that this case has never involved an allegation that the vaccines can or did cause Evans syndrome, only that the vaccines can and did significantly aggravate that condition. He is correct; this has been the posture of the case from the start. The remaining point (listed as fourth in his reply) is that Dr. Matloubian referred to bystander activation as an anachronism. That was never taken seriously in the original opinion, as discussed above under *Loving* prong four (*Althen* prong one). Pet. Ex. 138 at 1.

[8] This same database was utilized by Al-Adjidi et al., whose research is discussed in my original decision.

remaining 3 patients had somatic variants). Of the M+ group, 32 patients carried mutations in one of 9 genes known to be involved in primary immunodeficiencies. The other 20 patients carried probable pathogenic variants in 16 genes that had not previously been reported in the context of autoimmune disease. All but one of the "probable" pathogenic variants had CADD scores above 20, indicating that they are among the top 1% of deleterious variants in the human genome. The second group, the M- group, contained 28 patients (35%) in which no genetic abnormalities were found.

Hadjadj et al. followed those patients for a median of 9.1 years. Thirty-eight patients (47%) had "various autoimmune/autoinflammatory manifestations (mainly liver, digestive tract, and lung manifestations." Pet. Ex. 137-1 at 15. "The M+ group displayed more severe disease than the M- group, with a greater frequency of additional immunopathologic manifestations and a greater median number of lines of treatment." *Id.* at 4 (abstract). "Six patients (all from the M+ group) died during the study." *Id.*

During the prior proceedings in this case, the experts agreed that there is likely a genetic component to Evans syndrome. There was discussion about identified and yet-to-be identified genetic factors. At the hearing, Dr. Matloubian noted that in 2014, S.Y. underwent whole-exome sequencing. Dr. Matloubian explained that this kind of testing examines the parts of the gene which eventually become protein, but not the parts of the gene that regulate how much protein is made. This is in comparison to whole-*genome* sequencing examines all parts of the genes, but that is more expensive and time-consuming. In S.Y.'s case, the whole-*exome* sequencing did identify a heterozygous variant for a mitochondrial disorder, which he shared with his mother. Since this was a heterozygous variant, the significance was unclear. Tr. 182-86. The particular variant found in S.Y. is not mentioned by Hadjadj et al. Pet. Ex. 137-1.

Hadjadj et al. concluded that pediatric Evans syndrome is "potentially genetically determined in at least 65% of cases." Pet. Ex. 137-1 at 4. They noted, in reference to the M- group, that they could not rule out the role of currently unidentified genetic variants or mutations. *Id.* They also could not rule out the role of somatic mutations. *Id.* They argued that their results supported the provision of "wide-ranging genetic screening" for children with multi-lineage cytopenias such as Evans syndrome "because the findings have prognostic significance and may thus influence treatment choices." *Id.* at 18.

Dr. Gershwin opines that on the date of vaccination, S.Y.'s Evans syndrome was in a promiscuous stage, but had not yet been discovered. The coincidental administration of the vaccines caused activation of cytokines, which led to bystander activation of dormant cells. This caused S.Y. to experience a more severe course of Evans syndrome than he otherwise would have experienced. Dr. Gershwin opines that S.Y.'s Evans syndrome is more severe than the overwhelming number of cases of Evans syndrome. Dr. Gershwin opines that the two additional articles further support his opinion.

First, as noted above, I agree that the Lee et al. article reinforces that bystander activation is a recognized concept that is still under active investigation in the field of immunology. However, I recognized that concept in my original decision.

With regard to the key problems in this case, first, Hadjadj et al. report that 47% of the patients with pediatric Evans syndrome developed severe secondary manifestations mainly including the liver, digestive tract, and lungs. This would appear to reinforce Dr. Matloubian and Dr. Gill's opinions that Evans syndrome is a terrible condition that in its normal course, is resistant to treatment and develops seemingly unrelated complications such as those experienced by S.Y. (anti-nuclear antibodies, anti-phospholipid antibodies, hepatitis, and PVOD).

Second and particularly problematic for petitioners, Dr. Gershwin opined that in October 2011, S.Y. was in a crucial early stage of Evans syndrome during which the vaccines activated bystander cells, which significantly aggravated his condition. But his severe secondary complications (antinuclear antibodies, antiphospholipid antibodies, PVOD, and hepatitis) did not occur for 16 – 22 months. It remains difficult to understand how the vaccines could cause or contribute to complications occurring this much later.

Additionally, Dr. Matloubian opined that of the B cells present at the time of the vaccines in October 2011, 99% were wiped out by a course of Rituximab in early 2012. S.Y. then generated new replacement B cells that were observed in February 2013. S.Y. developed his severe secondary complications afterwards. It remains difficult to understand how B cells and antibodies generated in response to the vaccines could cause the severe secondary complications, when nearly all of those B cells were wiped out before those complications developed.

Petitioners' motion for reconsideration does not address these issues. Thus, there is still not a logical sequence of cause and effect or an acceptable temporal association between the vaccines and the long-term course of S.Y.'s Evans syndrome.

III. Conclusion

I remain acutely aware that S.Y. and his family have experienced significant suffering and stress in connection with his Evans syndrome. I again express my sympathy to them. However, I cannot award compensation unless the evidence favors vaccine causation, even after consideration of the new evidence. For the aforementioned reasons, petitioners' Motion for Reconsideration is hereby **DENIED**. The Original Decision will be reinstated and considered filed as of today's date, August 30, 2019.

IT IS SO ORDERED.

s/ Thomas L. Gowen
Thomas L. Gowen
Special Master