Outlook

# Fwd: MIS follow-up

Forwarded message
From: [redacted]
Date: Thu, Sep 15, 2022 at 9:26 AM
Subject: Fwd: MIS follow up
To: Marks, Peter <Peter.Marks@fda.hhs.gov>
Cc: Brianne Dressen <[redacted]>

Dear Dr.Marks,
In lieu of our upcoming meeting next week, I wanted to resend you my email below which was a summary of questions I had asked at our last meeting in May regarding the CDC data published in the Lancet earlier this year that identified multiple children with vaccine induced MIS. Because of the high acuity of these patients with ICU care often required, unique treatment for this illness, and potential for this illness to be fatal, our discussion about whether the current evidence is enough to justify adding this adverse reaction to the Pfizer COVID vaccine package insert is an important one.

Thank you and I am looking forward to speaking with you soon!
Best Regards,
[redacted]

Forwarded message
From: [redacted]
Date: Wed, May 25, 2022 at 7:02 PM
Subject: MIS follow up
To: Marks, Peter <Peter.Marks@fda.hhs.gov>, Brianne Dressen [redacted]

Hi Dr.Marks,
Thank you again for meeting with us today. For your convenience, below are the questions I had regarding the CDC published investigation into multiple inflammatory syndrome (MIS) and its association with COVID 19 vaccination.

Here is the link to the article:
https://www.thelancet.com/journals/lanchi/article/PIIS2352_4642(22)00028_1/fulltext#tbl3

Questions/Points of concerns:

1. On page 304, the panel on the right hand side with the CDC definition for MIS, on the bottom it indicates the following: "the exposure criterion was not used in this investigation" specifically for "suspected or confirmed COVID-19 case within 4 weeks before onset of symptoms." *Why was the MIS case definition of 4 week time frame not fully followed when investigating possible vaccine related MIS?*

- This is problematic because with the definition of 4 week timeline not followed, children with previous COVID infection were all lumped together no matter the timeline of previous covid infection compared to their vaccine timeline to MIS
- Examples: page 308, table 3: patient 4 had *39 days from previous covid infection to onset of illness but 24 hours from 1st dose of vaccine* to onset of MIS; second example: patient 13 had *191 days from covid infection to MIS diagnosis but only 5 days from 2nd dose of vaccine to diagnosis*. There are a total of five cases listed in this table where they are temporally closer related to the vaccine administration then their COVID infection and their previous COVID infections were >4weeks. *Why were these patients considered COVID related MIS instead of from the vaccine?*

2. Page 307 in the results section, it states "three (12%) of patients met MIS-C clinical and inflammatory criteria and did not have alternative diagnosis, but did not meet the case definition in absence of a positive SARS-COV-2 test" and later on page 310 it further clarifies that "we identified three individuals others who met clinical and inflammatory criteria and did not have evidence of SARS-CoV2 infection but did not meet MIS-C case definition because an anti-spike antibody test was not obtained (although presumably would have been positive from vaccination)". *Why wasn't confirmed vaccine administration from the patient's medical records considered a surrogate marker for inclusion in this study?*

3. Page 308, right hand last paragraph the authors write: "of the 21 individuals with MIS-C, 6 had positive anti-spike antibody test alone and were classified as not having laboratory evidence of SARS-COV-2 infection. None of the individuals had a history of a positive SARS-COV-2 test before MIS-C illness and all had a negative SARS-COV2 NATT and anti-nucleocapsid test during evaluation of MIS-C illness....all six individuals received BNT162b2...median time to onset from vaccination with the second dose to MIS0C onset was 14 days"

- This confirms that for 6 individuals, the authors could not attribute their MIS to anything other than the vaccine
- If we include the five individuals from above who had COVID >4 weeks and closer temporal relationship to vaccine with MIS onset; this brings our number of patients to 11. If we also add the 3 excluded patients with assumed confirmed vaccine administration on documentation but no formal anti spike protein testing, our patient number is now 14.

4. I also argue we should additional include patients (in table 3 page 308) who did not have current active infection, timing of previous COVID infection is reported as unknown (assume no documented clinical infection previously which is why no documented previous positive test result) but had positive anti-nucleocapsid testing, this is an additional 6 patients. Example patient for reference here is *patient 2 who had a positive anti-nucleocapsid test, negative NAAT, no documented positive COVID infection, and has MIS onset within 24 hours of 1st dose of vaccine*. The timing of 24 hours from vaccine to onset is pretty concerning, especially since anti-nucleocapsid tests take a minimum of 7 days to return positive from time of initial infection. Thus in this case, the vaccine timing is clearly closer linked to illness onset. Of these six patients, the median time of onset from vaccine to symptom onset is 10 days. Three of these six cases presented within 24 hours from vaccine administration. Adding these patients brings a grand total of **20 patients** with vaccine induced MIS.

- 20 patients makes the incidence of this to be 1.06 per million cases. This less then the case incidence of .75 per million cases of TTS that resulted in a brief pause on the Johnson and Johnson roll out https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-limits-use-janssen-covid-19-vaccine-certain-individuals.

The discussion of the paper on page 309 states that "although no direct comparatory background rate exists, the reporting rate of illness meeting the MIS C diagnosis in individuals who had received a COVID 19 vaccine is substantially lower then the previously published incidence of MIS C among unvaccinated individuals". I do not dispute this. The risk appears to be less from the vaccine as compared to COVID virus itself. But, the risk of this illness arising from the vaccine itself has been demonstrated by this paper. They could not find any evidence of current or previous COVID infection in multiple patients, there's a clear temporal link to the vaccine, and the disease does not exist in the background population otherwise. Thus, the question of *how many cases of MIS are needed before MIS is listed on the vaccine safety label?* This paper only included VAERS cases through November of 2021, I would suspect more cases have since been reported.

I very much appreciate your time and willingness to look further into this. Thank you again for meeting with us and discussing this with us.

Sincerely,

[redacted]