

## COVID-19 vaccine and COVID-19 Therapeutics Signal Meeting Minutes

Date: 18/08/2022

**Attendees:**

<p>██████████ (Chair)</p> <p>██████████</p> <p>Fazil Afzal</p> <p>Julie Beynon</p> <p>██████████</p>	<p>████████████████████</p> <p>Patrick Batty</p> <p>██████████</p> <p>████████████████</p>	<p>██████████████</p> <p>██████████████████</p> <p>Shiva Ramroop</p> <p>██████████████</p>
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**Apologies:**

Candidate	Percentage of Respondents Who Believe They Are Qualified
Katherine Donegan	100%
Janet Nooney	90%
Joe Biden	85%
Joe Manchin	80%
Joe Rogan	75%
Joe Scarborough	70%
Joe Walsh	65%
Joe Whelan	60%
Joe Zeff	55%
Joe Zeff	50%

- 1. Meeting highlights**  
N/A
- 2. Minutes of the last meeting**  
N/A
- 3. Administered vaccine numbers**  
N/A
- 4. YCVM Registrations**  
N/A
- 5. Matters arising**  
N/A
- 6. Yellow Card Reports**

## Paediatric data

### **Moderna vaccine**

N/A

### **Pfizer-BioNTech vaccine**

- [REDACTED] – We have received a report of seizure in a [REDACTED] male patient reported to us by a Nurse and who has responded to the neurological/seizure pro-forma. In terms of the case details, 15 minutes post Pfizer vaccination the patient felt faint, no rash and injection site were normal but went on to experience seizures every 5 minutes which got progressively more severe. Seizures continued for 3 hours, IV Keppra given and per rectal diazepam. Patient was hospitalised. The pro-forma filled in by the reporter noted that they had sudden loss of consciousness, tonic clonic seizures but with no loss of bladder control or tongue bite, no post ictal confusion, blood glucose was normal. The mother of the patient noted that they may have had a concussion from [REDACTED] 2 weeks prior to receiving the vaccine, but it isn't reported if a concussion was confirmed medically although suggestive at least of some sort of head injury with severity unclear.

The meeting discussed how concussion is a generic term, where the meeting was not aware of concussions increasing the epileptic threshold. At [REDACTED] years old, patients start entering the age of epileptic syndromes due to puberty. The meeting agreed to follow up to see if a CT scan was performed that showed anything on the brain that could have been caused from the [REDACTED] i.e., any undetected bleeding/bruising. It would also be important to follow up for any family history of seizures as well as how the patient was feeling leading up to the vaccine, where if the seizure occurred within 45 minutes of the vaccination you would be considering reactogenic reactions occurring. As well as if the patient had any possible COVID-19 infection or an allergic-type reaction to the vaccines.

- [REDACTED] – We received this report by the patient herself and concerns a [REDACTED] year-old female, who reported motor tics and involuntary movements that cause pain after her second dose of the vaccine. She reportedly went to the hospitals and had an MRI and blood tests which came back normal and is pending a nerve conduction study. Her treating physician diagnosed her with motor tick disorder that the healthcare professional believes was caused by or triggered by the Pfizer vaccine and the patient was prompted to report to us. She concurrently has [REDACTED] and [REDACTED]. The [REDACTED] may act as a potential confounder in this case as central and peripheral nervous system manifestations can sometimes be associated with [REDACTED] but it isn't reported how long she has had the [REDACTED] based on the description, it is assumed she didn't experience the neurological symptoms prior to vaccination. There were 6 other cases of tics in the paediatric age group, with ages ranging between 3 and 17, although the majority seemed to occur in slightly older teens with the younger instances may be confounded due to the usual age presentation of tourettes. There is also the consideration to confounding concurrent infection, which would likely include COVID as a risk factor, and although not all reports detail concurrent infectious status, the current climate would lend itself to likely coinfection.

The meeting agreed that they were not hugely concerned but if we were to follow up with the reporter we would need to ask if they have, in the past, experienced similar tics or twitches, are there other conditions that have been excluded through investigations as well as if other

neurological conditions have been considered or excluded through investigations. Finally, to ask if they are receiving any medications following this diagnosis.

***Janssen Vaccine***

N/A

***Oxford-AstraZeneca vaccine***

N/A

Non-paediatric data

***Moderna vaccine***

N/A

***Pfizer-BioNTech vaccine***

- [REDACTED] – We have received 1 report of lichenoid keratosis following the Pfizer vaccine, reported to us by a [REDACTED] year-old female patient. The patient described dark raised lesions on lower back, breasts, upper thighs, stomach, and arms. She noted that the palm of her hands was covered in callouses, her fingerprint seems to have eroded, aggressive peeling, itchiness, swelling and in a lot of pain. She is also experiencing hair loss and gum infections reported as oral lichenoid reactions. She has had a negative screen for skin cancer. [REDACTED] had discussed this case with [REDACTED] and noted the young age of the patient here being [REDACTED] where risk factors for lichenoid keratosis tend to include being elderly. It was additionally discussed that this condition, whilst some causes include an inflammatory component, it has also been attributed as being triggered by some medications. We had 5 other reports for lichenoid keratosis, one of which occurring in the paediatric population and a number of other reports for similar PTs. The numbers are likely considered low in the context of usage but wanted to raise given the age of the patient in this instance and the extensiveness of her condition.

The meeting agreed that this diagnosis is not common where it is a skin reaction not a hypersensitivity reaction, and this ADR is more common in the elderly. It was agreed to follow up for the HCP details to find out how the clinical diagnosis was reached, what the temporal relation was with this vaccination. Furthermore, the reporter mentioned plaque lesions in body, where the peeling is odd so to confirm if there was an exfoliative diagnosis to help decipher the symptoms she had and what labels she's been given.

***Janssen Vaccine***

N/A

***Oxford-AstraZeneca vaccine***

N/A

***COVID-19 Therapeutics***

- One case was received of Sotrovimab associated with seizures in a [REDACTED] year-old patient who received Sotrovimab and 12 hours later had 4 seizures. It was reported that he doesn't normally suffer from seizures where we are going to follow up for CT scan

reports. The patient was taking 15 other medications including antibiotics, antifungals, lots of pain killers, so more information on the drug therapy/ his condition was leading up to the vaccination. The patient had a history of [REDACTED] [REDACTED] there was missing information on what type of [REDACTED] had. It was unclear if there was a resurgence of his [REDACTED] and the status of his [REDACTED] with the COVID-19 infection that he had, where there was missing information on his family history, where this will also be followed up. Follow up with the reporter using the seizure template will be sent.

The meeting agreed with the proposed follow up.

- We have received an update from GSK regarding Sotrovimab and the drug induced liver injury cases. These were outlined them in the Monthly Safety Summary Report without giving too much information and there seemed to be conflict with the number of events/cases. [REDACTED] company has confirmed there were some duplicate cases- we have 3 cases of drug induced liver injury from [REDACTED] and one case of fulminant hepatitis also from [REDACTED]
  - The case of fulminant hepatitis was in an [REDACTED]-year-old female with [REDACTED] who also had atypical mycobacterial lower respiratory tract infection. She was hospitalised with COVID-19 and one day later received Sotrovimab as per indication. She then had an increased oxygen demand, had a chest x-ray, and was diagnosed with viral pneumonia and given remdesivir. However, prior to this, her ALT was 161 and her AST was 175. Therefore, the remdesivir dose was reduced and 3 days later her ALT went up to 1277 and AST up to 1400 and her bilirubin then increased to 2.8.6 and she was diagnosed with fulminant hepatitis and DIC. She was treated for it and 3 days later there was a gradual decrease in her liver enzymes and DIC was improving. This case went before the liver safety panel because the reporter linked it to Sotrovimab, where the panel said they could not exclude Sotrovimab in this case because although the concomitant medicines list altered liver enzymes, none were new apart from remdesivir. My assessment included that she had underlying COVID-19, with slightly increased ALT and the addition of remdesivir could be causing the increase in enzymes rather than sotrovimab, however this is hard to disentangle. In terms of the fulminant hepatitis diagnosis, there didn't appear to be encephalopathy reported so not sure whether this was truly a fulminant hepatitis case. The conclusion was that Sotrovimab could not be excluded from this although other confounding factors were present.
  - There were 3 cases of drug induced liver injury. The first was in an 84-year-old female who was taking alfacalcidol, donepezil, magnesium oxide and bisoprolol. Donepezil does list liver dysfunction and hepatitis as a side effect. The patient's history was [REDACTED] [REDACTED] She did have a normal ALT and AST on admission and her ALT and AST rose 6 days after having received Sotrovimab and she also had associated pyrexia. Her CT showed no obvious abnormality with her liver or hepatobiliary system. The events resolved in around nine days. The reporter concluded that Sotrovimab was responsible, but it is not clear if the donepezil was stopped, and whether the COVID-19 could also slightly confound the case.

- The second case was a in [REDACTED]-year-old male who had [REDACTED]  
[REDACTED]  
[REDACTED] He received Sotrovimab for COVID-19, he was also on lots of medications including tacrolimus and everolimus which list ALT and AST rises as common. He was also on famotidine which lists hepatitis and cholestatic jaundice and worsening of existing liver disease. Finally, he was taking levetiracetam which lists hepatic failure and hepatitis. The time to onset was 38 days and he was then diagnosed with acute hepatitis, and it was noticed that there were higher tacrolimus levels. The patient's condition improved after treatment, and he was discharged after 8 days. Although there was no indication whether the tacrolimus or everolimus doses were adjusted. The reporter suspected that Sotrovimab was the responsible drug in this case.
- The final case was in a [REDACTED] year-old male who was vomiting 5 days after having received Sotrovimab. He was also on statins, but it hadn't been changed in 2 years. 6 days after receiving Sotrovimab, drug induced liver injury was diagnosed as his ALT was at 300. 18 days later, acute cholangitis was diagnosed but also pneumonia which was being treated with a penicillin. However, the outcome of this patient was unknown as they were transferred to another hospital. The reporter did not believe the Sotrovimab had a causal association at this point.

Given that hepatotoxicity is an adverse event of special interest for Sotrovimab, it was thought that it would be ok to proceed with monitoring in the 6 monthly PSURs. We do not have any UK cases at present. The meeting agreed that this should be kept an eye on, where the remdesivir case seems more likely to be caused by remdesivir. The other cases seem to be in very elderly patients which is why they are receiving the Sotrovimab where confounders included bacterial pneumonia.

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## **7. Other**

N/A

## **8. Signals taken forward**

N/A

## **9. AOB**

The meeting has agreed to move the COVID-19 Therapeutics Signal Meeting and combine it with the Signal Detection Meeting on Thursday mornings. Where paediatric input can be consulted and asked to come to the meetings on an ad-hoc basis.