To: [redacted] [redacted]@rivm.nl]
From: [redacted].
Sent: Tue 11/3/2020 9:36:55 AM
Subject: FW: VAED/VMED operationalization in observational studies
Received: Tue 11/3/2020 9:37:07 AM
Vaccine Associated Enhanced Disease VM questions 14 Oct 2020_v 0.5.docx
WHO Ordinal scale.pdf

Ter info

Van: [redacted].
Verzonden: maandag 19 oktober 2020 16:48
Aan: [redacted]. <[redacted]@cbg-meb.nl>; [redacted] <[redacted]@cbg-meb.nl>; [redacted] <[redacted]@cbg-meb.nl>; [redacted] <[redacted]@cbg-meb.nl>; [redacted] <[redacted]@lareb.nl>
Onderwerp: FW: VAED/VMED operationalization in observational studies

Ter info, ongoing discussies over de Vaccine-mediated enhanced disease.

Mvg
[redacted]

Van: [redacted]. <[redacted]@cbg-meb.nl>
Verzonden: vrijdag 16 oktober 2020 09:00
Aan: [redacted]. <[redacted]@cbg-meb.nl>; [redacted] <[redacted]@cbg-meb.nl>; [redacted]. <[redacted]@cbg-meb.nl>
CC: [redacted]. <[redacted]@cbg-meb.nl>; [redacted]. <[redacted]@cbg-meb.nl>; [redacted] van der <[redacted]@cbg-meb.nl>; [redacted]. <[redacted]@cbg-meb.nl>
Onderwerp: FW: VAED/VMED operationalization in observational studies

Beste collega's,

Gisteren ben ik op verzoek van [redacted] aangesloten bij een gesprek over het volgen van het risico op vaccine induced enhanced disease na uitrol van de vaccins. De klinische studies zullen hier naar aller waarschijnlijkheid geen uitsluitsel over geven (tenzij er een duidelijk risico is natuurlijk) omdat de lange termijns follow up niet mogelijk is als er efficacy wordt gedetecteerd. En dus moet het na registratie voor alle vaccins gevolgd worden. Maar de hoe is uitdagend; hoe weet je of iets een simpele vaccin falen is en of het echt enhanced disease betreft. Wat voor informatie moet je ten minste hebben om dit vast te stellen (om ernst van ziekte vast te stellen heb je toegang nodig tot de ziekenhuis gg van een persoon). En waar en hoe zou je het makkelijkst een signaal kunnen toetsen?

Hieronder een kort verslag van [redacted] van deze meeting, en het uiteindelijke doel; over twee weken is er een vervolg. Ik zal jullie op de hoogte houden, wellicht ook goed om deze discussie in de ETF in te brengen. Als er van jullie kant ideeën en suggesties zijn hoor ik dat graag. Een brainstorm moment kan volgens mij ook geen kwaad.

Als er vragen zijn hoor ik dat graag,

Groet,

[redacted]

Van: [redacted] <[redacted]@vac4eu.org>
Verzonden: donderdag 15 oktober 2020 18:11
Aan: [redacted]@sanofipasteur.com; [redacted] <[redacted]@gmail.com>; [redacted] <[redacted]@gmail.com>; [redacted], [redacted]. <[redacted]@umcutrecht.nl>; [redacted]. <[redacted]@umcutrecht.nl>; [redacted] <[redacted]@bcm.edu>; [redacted] [redacted] <[redacted]@gmail.com>; [redacted]. <[redacted]@cbg-meb.nl>; [redacted] <[redacted]@rti.org>
CC: [redacted] /CA <[redacted]@sanofi.com>
Onderwerp: Re: VAED/VMED operationalization in observational studies

Dear all,

Thank you for those who could join today during this follow-up of the joint VAC4EU-SPEAC working group on how to monitor VAED. We had a good initial discussion between 5.1.2e , 5.1.2e 5.1.2e 5.1.2e 5.1.2e and myself

We explored and agreed
1) this is a complex issue
2) no one has a solution yet, there are several groups who start to think
Complicating issues:

- we do not yet know what the natural history of disease is fully, and this may change over time and be affected by treatments
- there is no marker that distinguishes between vaccine failure and enhanced disease
- WHO severity score is based on respiratory, how to build in multi organ severity? (NB BC definition has this in VAED)

3) Our group should come up with some guidance/a table with different scenarios of how VAED can be studied, each with its assumptions/limitations, this would then be shared with a larger audience for discussion

The following initial options to monitor were shared
1) Follow-up of a clinical trials and assessing whether the distribution of severity of COVID is different between vaccinated and non-vaccinated COVID-19 cases. We cannot just compare rates as you assume VE
Main advantages: well controlled and monitored group where data collection on severity and vaccine status would be known
Issues: need for long term follow-up (2 to 3 years) loss to follow-up, costs, but mostly infeasibility if vaccines are available, controls have the right to be vaccinated. So seems a good scenario for only short-term follow-up

2) Case control design including severe COVID-19 cases in hospital where you would be able to look at detailed charts. VE spoke about test negative designs,

While thinking about this after the meeting I personally feel we would need a test positive design: a control that is also positive for COVID-19 but with a severity score that is low. As being a severe case is conditional on having COVID-19. Then the vaccine history should be compared and this can be done over a long time, and we would need to deal with confounding. Having an opportunity to review in detail the medical history of a non-severe case may be difficult, but I feel we could think of persons close to the case. Stratification by key groups to persons with limited co-morbidity and high risk of vaccination may help first (HCW). This idea needs to be further explored

3) O/E: calculate a personalized score on what you would expect the severity to be

We agreed that we will meet in 2 weeks again, 5.1.2e will find someone to start a table. 5.1.2e shared the current thoughts of VE (see attached) which lay down clearly what a document may address
We also agreed we need FDA on board 5.1.2e whom to ask permission?)

We discussed we would also like 5.1.2e on board

Suggested date for next call is: Oct 29, 4-5.30 PM
We will share a document beforehand to go through

Best wishes and thank you,

5.1.2e

From: 5.1.2e

Sent: Wednesday, October 14, 2020 4:04 PM
To: 5.1.2e @sanofipasteur.com <5.1.2e @sanofipasteur.com>; 5.1.2e <5.1.2e @gmail.com>; 5.1.2e 5.1.2e 5.1.2e @gmail.com>; 5.1.2e . <5.1.2e @umcutrecht.nl>; 5.1.2e . <5.1.2e @umcutrecht.nl>; 5.1.2e 5.1.2e <5.1.2e @bcm.edu>; 5.1.2e <5.1.2e @gmail.com>; 5.1.2e . <5.1.2e @cbg-meb.nl>; 5.1.2e <5.1.2e @rti.org>
Cc: 5.1.2e /CA <5.1.2e @sanofi.com>
Subject: VAED/VMED operationalization in observational studies
When: Thursday, October 15, 2020 4:00 PM-5:30 PM.
Where:

Dear all,
Through mail we polled who can join this meeting. Not everybody can join tomorrow but we would like to make a start with the attempt to create a draft for a consensus document on how to assess VAED/VMED in observational studies as a follow-up of the webinar we had.
This document should help to create a consensus meeting. If you have certain documents to share please do with this group.

See enclosed the dial in.

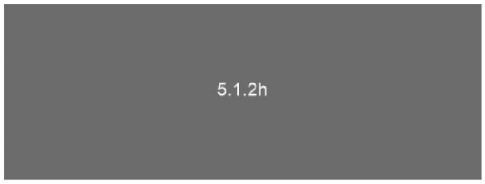
Operationalization of VAED/VMED in observational studies
Thu, Oct 15, 2020 4:00 PM - 5:30 PM (CEST)

Please join my meeting from your computer, tablet or smartphone.
5.1.2h

You can also dial in using your phone.
United States: 5.1.2h

Access Code: 5.1.2h

More phone numbers:
5.1.2h



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