NOT FOR PUBLICATION

COMMISSION ON HUMAN MEDICINES

Minutes of the Ad Hoc Videoconference Meeting held on Saturday 27th March 2021 at 10:30 via MS Teams.

Commissioners Participated

Professor Sir M Pirmohamed (Chair)
Ms S Bradford
Dr J Fraser
Professor J S Friedland
Professor R J C Gilson
Professor M R Macleod
Dr R Mann
Dr S Misbah
Professor P M Patel
Professor S Price
Professor M Turner
Dr M Wilson

Apologies

Professor J Coleman
Professor C Weir

Invited Experts

Professor G Dougan
Professor N French
Professor D Goldblatt
Professor S Meredith
Professor T Solomon
Professor K M G Taylor
Professor C Toh
Mrs H Ward

Observers

Dr N Andrews
Professor WS Lim
Dr M Ramsay
Dr NR
Professor J Van-Tam

Professional Staff of MHRA Participated

Principal Assessor for this meeting[1]

Dr S Branch – VRMM
NR

VRMM Presenters[1]

NR

Internal Observers

NR – MHRA-Policy
NR - VRMM
NR – VRMM
NR - COMMS
NR - VRMM
NR - VRMM
VRMM
Dr J Raine – MHRA CEO
Dr C Schneider - NIBSC
NR - VRMM
Mr P Tregunno - VRMM

Secretariat

NR

Personal Data

24 January 2022

Key

LD = Licensing Division
VRMM = Vigilance & Risk Management of Medicines
NIBSC = National Institute for Biological Standards & Control
MHRA CEO = Chief Executive

1 Supported specific items

a currently unknown other factor(s). Nevertheless, the Commission noted that it could take a long time to identify a mechanism.

2.11 The Commission concluded that while there was a temporal association between vaccination and the reported events, the mechanism had not been confirmed and thus a causal association with the AstraZeneca vaccine could not be established. The Commission considered that useful information could be gleaned from data from 2nd doses, however, there currently was not sufficient 2nd dose data to analyse any potential risks.

2.12 The Commission heard that no UK cases of thromboembolic events with thrombocytopenia had been reported following the Pfizer vaccine. However, one case had been reported in Italy (of cerebral venous thrombosis with thrombocytopenia), as well as a Slovenian report of M2 branch thrombus with a low platelet count and an Italian case of pulmonary embolism with thrombocytopenia. Non-UK cases were also validated with the criteria described above. MHRA highlighted a US publication of a series of cases reporting thrombocytopenia within 2 weeks of vaccine with mRNA COVID-19 vaccines. Two cases reported thrombotic events with thrombocytopenia following Pfizer vaccine. MHRA also reported on 1 case from clinical trials and another from post-marketing use with the Janssen vaccine in the US.

2.13 The Commission was presented with statistics on the cumulative exposure to the AstraZeneca and Pfizer vaccines, broken down by age. Estimates of the incidence rates of CVST with thrombocytopenia and of all thromboembolic events with thrombocytopenia were provided. The incidence rates broken down by age and gender were also provided.

2.14 The Commission heard the MHRA review of an analysis from PHE of the events of interest associated with the AZ and Pfizer vaccine from hospital admissions data in the UK. The presentation highlighted that there was no indication of raised risk of thromboembolic events with either of the vaccines. There was no increased risk identified with the exception of 'Intracranial and intraspinal phlebitis and thrombophlebitis' for which there was indication of a small increased risk for AZ in the under 65 years age group; it was noted that unadjusted confounding could be present and that the numbers were small. The Commission was also informed about an analysis of the benefit of COVID-19 vaccination based on a PHE review. The number of cases of hospitalisation, death and long-COVID prevented per 1 million vaccinations per age group was presented, along with the number of cases and fatal cases of thromboembolic events expected to be reported per 1 million doses.

2.15 Finally, MHRA's work on opportunities for further epidemiological analysis was presented.

2.16 When discussing the benefit risk in different age groups, the Commission again commented that there could be under reporting of events in elderly people due to a less thorough investigation of neurological symptoms. That being said, the

Commission noted that the age distribution seen is typical for CVST events in the non-vaccinated population.

2.17 The Commission discussed whether risk mitigation was needed due to the presence of an alternative vaccine where these events are not seen at the same level, however it was agreed that risk benefit evaluations should be made without consideration of other vaccines.

2.18 The Commission considered that the overall risk of thrombosis with thrombocytopenia remains low but there is concern of significant harm for individual patients. In younger age groups, the risk of COVID-19 and associated complications might not be as high and so the benefit risk from the vaccine in these groups may be different to older groups. It was however noted that while Long COVID is still not well understood, that this is an important risk in young people and a decrease in the risk would be an additional benefit of vaccination.

2.19 The Commission was not able to identify any specific risk factors but did note that cases with confounding factors should be further investigated to determine any populations at risk.

2.20 The Commission concluded that based on current data it not possible to establish an age group where the benefit risk was negative but recognised that irrespective of causality, early identification of such events and correct treatment were needed.

2.21 The Commission commented that the gender bias usually seen with CVST has not been established in the reported cases, which could also suggest a causal link. It was agreed that simple and clear messaging on warning signs is needed so that cases could be identified early, reported in detail and managed clinically.

2.22 The Commission was presented with an overview of planned and ongoing pregnancy studies for the Pfizer and AstraZeneca vaccine, as well as initiated paediatric studies.

2.23 The Commission heard that there was clear support from the Paediatric Medicines Expert Advisory Group for vaccine studies in children with careful evaluation of safety in this population. The Commission considered it reasonable to suggest that children will be at lower risk of these events as thromboembolic risk factors are much lower in children and also there were no documented cases of HIT in children.

2.24 The Commission concluded that paediatric and pregnancy trials should not be stopped at this point, but there needs to further evaluation of the pregnancy trials, and pregnancy exposure to date.

2.25 The CHM advised that the benefit/risk is still overwhelmingly positive, however younger age groups may have risk minimisation needs. Further work is needed on case definition and case ascertainment will be important. Understanding the background rate of these thromboembolic events with concurrent low platelets will be critical as it is not currently clear if or how much higher above background rates