【参考資料３】

International Coalition of Medicines Regulatory Authorities SARS-CoV-2 Variant Workshop

Thursday 30 June 2022, 13:00 - 15:30 CET

Co-chairs: Dr Peter Marks (US FDA) and Dr Marco Cavaleri (EMA)

Welcome and objectives of workshop

Following-up on the January ICMRA Omicron variant workshop, the objectives of this workshop were to discuss the emerging evidence and preliminary data shared by vaccine developers on adapted vaccines addressing emerging variants, with the aim of ensuring global alignment on the criteria for the selection of adapted vaccines and regulatory requirements to address new waves of COVID-19. Emer Cooke, Executive Director of the EMA opened the ICMRA SARS-CoV-2 variant workshop.

Latest developments on virus evolution, adapted SARS-CoV-2 vaccines and host responses induced.

Peter Marks (FDA) and Rogerio Gaspar (WHO), on behalf of The Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC), presented the latest developments regarding SARS-CoV-2 virus evolution, vaccine effectiveness against Omicron and cross-neutralization data against Omicron, including Omicron descendent lineages.

Since the identification of Omicron as a Variant of Concern (VOC) in November 2021, Omicron has continued to evolve, leading to increased viral diversity, with Omicron descendent lineages BA.4/BA.5 currently the dominant variant in many locations. Mutations present in these Omicron descendent lineages may be associated with higher infectivity and escape from existing immunity. Omicron is displacing other variants in all six WHO regions. Antigenic cartography has shown

that the Omicron lineages are clearly antigenically distinct from earlier VOCs. Omicron BA.4/BA.5 are associated with additional immune escape based on published data in individuals either vaccinated or vaccinated and previously infected.

Currently used mRNA vaccines based on the ancestral (index) virus still perform well against severe disease, but waning efficacy is observed, most noticeably for protection against infection and symptomatic disease. Vaccine efficacy has decreased with time since last dose administered and against recent VOCs, particularly Omicron. Booster doses largely restore protection, especially against severe disease and death and potentially against serious complications like long COVID-19.

Waning immunity in the population together with the ongoing emergence of novel variants deviating from the ancestral virus results in an increased risk of significant COVID-19 outbreaks. A vaccine composition update would be expected to provide additional protection against current and future variants, some of which are now rather distant from the ancestral (index) virus.

Repeated exposure to SARS-CoV-2 antigens (vaccination/infection) enhances not only the magnitude but also the breadth of the antibody response. In addition, Moderna and Pfizer both presented preliminary data on neutralizing antibodies induced by their mRNA vaccines to contain Omicron. Vaccination of previously uninfected adults with a bivalent mRNA vaccine (encoding for ancestral as well as the Omicron BA.1 S protein) appears to result in titers of neutralizing antibodies against Omicron BA.1 that are 1.5 to 2-fold higher than with the ancestral virus-based mRNA vaccine currently used. A monovalent vaccine as a booster can produce robust immunity especially against the homologous strain included in the vaccine, but in a primary series clinical study a monovalent BA.1 vaccine showed a narrow breadth of immunity across other strains. Data in animals can provide additional insight into the type of immunity induced by different vaccine compositions ahead of results from clinical trials. More data with respect to

neutralization of Omicron BA.4/BA.5 from the ongoing clinical trials with monovalent or bivalent mRNA vaccines incorporating a BA.1 Omicron and ancestral strain, as well as data from different types of vaccines, such as subunit Beta variant booster vaccines, are awaited.

Conclusions and next steps

Based on the data presented, there was agreement that currently approved COVID-19 vaccines are still recommended for primary series and booster doses as they offer protection against severe disease and death, especially following the administration of booster doses. In this context, new vaccines including the ancestral, or a close-to ancestral, strain are currently still valid candidates for booster vaccination. However, continuous viral evolution is expected, likely resulting in reduction in protection, especially from infection and symptomatic disease. Independent from the strain included in the vaccine, current vaccines are designed to provide protection primarily against symptomatic and severe disease.

With the further evolution of Omicron descendent lineages, regulatory agencies have requested safety and immunogenicity clinical studies be conducted by vaccine developers, and those data are now being assessed to determine the suitability of Omicron adapted vaccines to protect against recently emergent and existing VOCs. Based on emerging clinical data with investigational vaccines incorporating the Omicron BA.1 variant in mRNA vaccines, and as Omicron and its subvariants remain dominant, an Omicron variant strain should be included in adapted versions of currently approved vaccines to offer increased protection that would ideally be longer lasting.

To expand upon this recommendation, the objective of adapted vaccines is to provide a larger breadth of immunity against SARS-CoV-2 strains including Omicron, as it is currently unknown which strains will be circulating next. With the increasing circulation of Omicron-descendent lineages, bivalent vaccines incorporating an Omicron descendent lineage and ancestral (index) virus would be preferred for adapted versions of vaccines already in use, as they may provide

an improved level of cross-neutralization against previous VOCs as well as current Omicron and possibly future Omicron sublineages in the Northern hemisphere winter season of 2022. While initial recommendations might be restricted to booster doses, additional data may enable using adapted vaccines also to be used for primary series in the future.

In addition, there might be a possibility that vaccines with a different VOC included, e.g. Beta, could still provide an adequate immune response to Omicron and its subvariants and could be considered for regulatory approval. Moreover, it is not excluded that different types of strains could be prevalent among regions, which might require some regional flexibility for selection of variants incorporated in vaccines.

Effectiveness studies with variant-adapted vaccines should be conducted to determine the level of protection conferred over time in real-life conditions against different clinical endpoints such as disease, hospitalization and death. Furthermore, depending on vaccine availability and national recommendations, as a general principle, elderly and vulnerable populations should be prioritized in the vaccination campaigns ahead of the Northern hemisphere winter season. Finally, regulatory strategies for approval of variant vaccines will be fine-tuned in the future considering the experience gathered so far with various vaccine compositions and across different platform technologies.