Steering Board on vaccines - Meeting with Scientific Experts

6 April 2021

Summary

The pandemic is not over and will not be over soon. The issue of what is the “vaccine strategy 2.0” needs to be addressed urgently. Despite the data gaps, it is key to define the future policies toward vaccines and vaccination at the present moment even if that requires making some assumptions and predictions.

Although, the knowledge about COVID-19 disease and the SARS-CoV-2 virus and their mutations increases regarding their biological and pathological features, transmissibility and sensitivity to vaccine modulated immune responses, more data is needed to address existing gaps.

Recommendation: mRNA vaccines and probably recombinant protein based elicit the highest level of the neutralizing antibodies thus confer the highest protection against COVID-19. The experts suggested refocusing the EU vaccines portfolio on mRNA and recombinant protein-based vaccines for boosters and for variants. DNA vaccines should no longer be in the active portfolio.

1. Objective of the meeting

The objective of the meeting was to gather views of leading EU scientific experts on the approach to COVID-19 vaccines and vaccination programmes for 2022 and beyond.

2. Participants

Several key scientific experts from the leading EU based scientific institutes participated along with representatives of Member States and the European Medical Agency and the European Commission. [Chair name] chaired the meeting and the following experts contributed to the discussions:

[List of names]

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3. Discussion

The below section summarises the main takeaways from the discussion around key questions that were shared before with the group.

3.1. How do you see the future of vaccines in 2022?
Given the high global burden of Sars-Cov-2 SARS-CoV-2 transmission, viral evolution is occurring. SARS-CoV-2 and its variants will be around for some time, Covid-19 might become endemic. Due to natural and vaccine derived pressure (current vaccines do not protect against infection) concerns around the mutations and protection afforded by current vaccines will continue. Currently, the UK variant is the most dominant in Europe, but this is likely to change. New variants are likely to emerge including escape variants (those, that will escape the immunity conferred by current vaccine) for which the booster vaccination will be needed. The exact risk of the appearance of the escape variants is not easy to predict and will depend on several factors such as the rate of mutations and the rate of vaccinations. Currently, the SARS-CoV-2 mutations follow a pattern of a convergent evolution. However, with the increased pressure on the virus, new mutations will start to emerge.

The experts agreed unanimously that COVID-19 vaccines would be needed in 2022 and beyond to be used as both prime and boost doses. The focus should be on securing the access to vaccines addressing identified variants of concern (for example such as the South African variant). The currently available vaccines developed against the Wuhan SARS-CoV-2 strain could also be considered as boosters provided they elicit cross-variant neutralizing antibodies. The current pace of the viral evolution indicates that a booster vaccination could be needed as early as autumn-winter this year, especially for the most vulnerable populations.

The decision on the vaccination strategies depends on the objective of the vaccination. The experts discussed two strategies:

- **Strategy 1.0 (currently used) with an objective to prevent mortality and morbidity**

Following the outbreak of the Covid-19 pandemic, the vaccination strategy focused on the prevention of the mortality and morbidity. If such a strategy is maintained, the vaccination should focus on:

a) ensuring that the most vulnerable populations are vaccinated with vaccines effective against the identified variants of concern

b) monitoring the development of antibodies in non-vulnerable populations to define when a booster dose is needed following a declined of antibodies titres.
- **Strategy 2.0** with an objective to prevent viral transmission as much as possible in addition to the prevention of mortality and morbidity.

The new strategy will focus on both the prevention of mortality and morbidity as well as on the reduction of the viral transmission. The move to the more holistic strategy would entail:

- a) booster vaccination for everyone who received a full prime vaccination (depending on the need/identified SARS-CoV-2 variant of concern).
- b) gradual age de-escalation and the extension of prime vaccination strategies to university students, adolescents and eventually school age children.
- c) Consideration of other groups of high transmitters (frequent travellers, healthcare workers).

ECDC developed a recommendation on vaccination strategies depending on the foreseen vaccination goal.

### 3.2. What should the EU strategy be and which vaccines should be secured at this stage?

At the onset of the COVID-19 pandemic outbreak, the EU vaccine strategy focused on securing access to vaccines developed with different technologies to maximise chances of securing access to safe and effective vaccine once developed. At present, our knowledge about the safety and efficacy of Covid-19 vaccines has significantly evolved, which allows taking much more targeted choices. Experts agreed that the EU vaccines portfolio should be revisited and focused on the most effective vaccines. The group analysed vaccines developed with different technological platforms (from the EU vaccine portfolio and beyond).

Experts agreed that high titres of neutralizing antibodies is a relevant measurable indicator of vaccine efficacy. Development of persistent T cells and B cell memory is important, but studies on the effect of COVID-19 vaccines on both T cell and B cell responses are still limited. In the absence of a benchmark for the T cell mediated rate of protection, nasal cavity reactions and cross protection, the cellular responses do not currently provide a measurable indicator for the efficacy of the COVID-19 vaccines. All of the approved COVID-19 vaccines are given intramuscularly, they elicit an IgG antibody response only. It is not yet known if any of the authorized vaccines *actually prevent transmission*. However, data from Israel, where 95% of the population has received at least one dose of the mRNA BioNTech/Pfizer vaccine suggest that this may be the case.

The outcome of the assessments for each vaccine platform is as follows:

- a) **Messenger RNA (mRNA) vaccines** - Two authorized mRNA vaccines might prevent SARS-CoV-2 infection in real-world conditions. They elicit neutralizing antibodies to the Wuhan strain and currently circulating variants and a good level of cellular responses. Due to high potential to elicit cross-variant neutralizing antibodies, smaller doses of booster mRNA vaccine could be examined and considered, thus reducing the time and manufacturing costs. Studies to assess the duration of the response are ongoing. Pfizer press release confirmed no decrease in the duration of the response within 6 months after vaccination. The **mRNA vaccine platforms can be quickly modified to produce booster doses that target new variants**. Both Pfizer and Moderna have also announced plans for clinical trials of boosters identical to their original vaccines. They are a good choice for the booster.
b) **Recombinant protein based vaccines** - Data from the first clinical studies with protein vaccine front-runners are highly encouraging. The Novavax recombinant protein vaccine showed high titers of total as well as neutralizing antibodies. They can be a good choice for the booster and also provide a fallback in case of issues with mRNA.

c) **Viral vector vaccines** - the viral vectors vaccines provide a solution for the current phase of the pandemic. However, adenovirus vaccines do not elicit high neutralizing antibodies titres. Moreover, due to immunity to the adenovirus vector and the potential neutralizing effect, the adenovirus vaccines are not considered a relevant choice for the boost vaccination.

d) **Inactivated virus vaccines** - The peer reviewed scientific publications for the inactivated virus COVID-19 vaccines are very limited. At present, it is difficult to reach any meaningful conclusions that would justify taking these vaccines into account. Data published by Sinovac shows much lower efficacy than other COVID-19 vaccines. Sinopharm claims that their vaccine has high efficacy, but to date they have not open their data for the scientific scrutiny. The Commission is in negotiations with Valneva developing such a format.

e) **Virus like particles (VLP) vaccines** - these vaccines are currently mainly developed based on an outdated technology. VLPs are highly immunogenic and are able to elicit both the antibody- and cell-mediated immune responses. However, the response is less targeted and specific with low titres of neutralizing antibodies. There are also technical challenges such as getting the molecules to display on the particle surface properly.

f) **DNA vaccines** - still upstream in the development phase. The most advanced ones as Inovio (if efficacious), present the delivery challenges due to an electric shock needed to facilitate the uptake of the DNA into the nucleus of muscle cells. Additional delivery devices are needed which impacts the costs and availability.

3.3 **What is the vaccination rate that would work in the population?**

More data is needed to define the needed vaccination rate. The ongoing studies, especially the one from Israel, where a significant part of the population has been vaccinated, will provide some indications. Additional data is available from the UK.

Importantly, the efficacy of the vaccines is a key factor to consider along the percentage of the vaccinated population. Moreover, despite the substantial advances in data collection, calculation of the risk of reinfection has proved difficult but is important to consider. However, the protection from natural immunity cannot be fully included in the calculation of the vaccination rate.

Despite the several unknowns, countries and regions in the world are already defining targeted vaccination rate. The African Union, for example, is helping to vaccine 60% of the African population. The numbers for the EU would be well above 80%.
3. 4. Do we need to vaccinate children and with which vaccines?

The vaccination of children has to be considered if the objective of the vaccination strategy is to avoid the viral transmission as adolescents and school children are among the high transmitters. The communication with parents focused on the safety and vaccination incentives is key to ensure support. Moreover, the vaccines used in children should have reduced reactogenicity compared to currently used vaccines to provide incentive of vaccination over the effects from the actual infection, which is most often asymptomatic in children.

3. 5. What do we need to do to react to emerging variants?

The molecular epidemiology should be used to detect variants quickly. Reducing emergence of variants might be an objective of the vaccination strategy 2.0. Efficacious vaccines need to cover emerging variants. The mRNA vaccines seem to be adjustable to variants.

3. 6. Is COVID-19 becoming endemic? Which volumes do we need in the years to come to boost vaccinations? Which groups most likely need a boost?

Although it is difficult at this stage to predict the behaviour of the virus, there is a scientific consensus that SARS-CoV-2 might become in some way endemic with potential periodic outbreaks. Murray et al.\(^1\) discusses the prospect that COVID-19 could become a recurrent seasonal disease like influenza and proposes strategies to mitigate the consequences for communities and health systems, including changes in surveillance, medical and public health response, and socioeconomic programs.

Concerning the boost vaccination, more studies are needed to define the duration of the protection and the timeline when a booster dose will be needed for specific populations (protection in the elderly is declining faster than in the younger adults). Comparing to the SARS 2003 outbreak, individuals infected in 2003 continue to have a robust T cells responses, however, their antibodies levels have declined.

In the UK, the government announced a mass boost vaccination in autumn this year. However, it is unclear at this stage which vaccine will be used and what is the vaccination objective. The protection of the existing vaccines to emerging variants is a key factor that should be considered, especially the more and more present South African variant, for which the currently authorized vaccines do not provide the same level of protection as for the Wuhan strain.

3. 7. Are heterologous vaccinations a solution to overcome potential shortages?

Sheward et al.\(^2\) discusses the neutralization of a SARS-Cov-2 variant of concern with a heterotypic boost (using a different antigen). The results show that a single adjuvants dose of protein extracted from a variant virus drives an extremely potent neutralizing antibody response capable of cross-neutralizing both Wuhan and another variant in rhesus macaques previously immunized with Wuhan strain spike protein. Thus provides a promising evidence for the heterologous vaccination.

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\(^1\) JAMA. Published online March 3, 2021. doi:10.1001/jama.2021.2828

\(^2\) https://www.biorxiv.org/content/10.1101/2021.04.03.438330v1
On a different note, the multivalent vaccines, especially combining the influenza and COVID-19 vaccines should be considered (especially for a most vulnerable populations) as a potent tool to manage the likely co-existing future outbreaks of COVID-19 and influenza.