Scientific Update by AstraZeneca Representatives to Member State Experts
Nominated by the Steering Board + Norway and Iceland

15 December 2020
16:00 – 17:00 CET

Subject: Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK (Interim combined analysis of trials of AZD1222)

The Chair opened the meeting and welcomed all participants, the representatives of AstraZeneca and the experts nominated by the Steering Board + Norway and Iceland.

The slides were presented as per the post-read slides, focusing on Phase III data of COV001, COV002, COV003, and COV005 studies. The important take-away is that efficacy is 70% overall (average result from the pooling of efficacy data). More immunogenicity studies are expected. Great interest in the dosing regimen going forward. The rolling submission to FDA, MHRA and EMA (receiving a series of clinical data packages) will continue over the next weeks and months.

The Chair thanked for the presentation and opened the Q&A session.

In the Q&A session, enquired about data on subjects aged 70+, pointing out that it is limited – asked whether AstraZeneca would go for an age cut-off for the indication or whether it would be broad.

AstraZeneca replied that they observed comparable immunogenicity across the age groups and that they would be submitting all data to regulators. Studies are not powered to look at specific age groups, but more at safety in older participants – the latter should allow to show trends more accurately.

enquired which dosing regimen AstraZeneca is putting forward for EMA authorisation: LD (low dose) - SD (standard dose) or SD - SD.

AstraZeneca replied that they would be providing all data. More data cuts will come through in due course. They are primarily submitting SD-SD regimen but that so far, no downside has been

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1 https://doi.org/10.1016/S0140-6736(20)32661-1
observed to giving LD-SD.

further asked when AstraZeneca expects EMA to have sufficient data to review and provide the conditional approval.

AstraZeneca replied that they would be submitting packages in clinical and in chemistry, manufacturing and controls (CMC). In the coming weeks, EMA would be able to provide some timelines.

enquired about data on SARS-COV-2 seropositives at baseline.

AstraZeneca replied that this is part of the ongoing analysis but that the numbers are small. The seropositives at baseline are also excluded from the primary analysis.

asked about the pooling of efficacy data. A vaccine is a combination of a product and a schedule, therefore would the time interval between doses (12 weeks) not be problematic for the pooling of the data?

AstraZeneca explained that other immunologists offered similar feedback and they agree that duration is key. One of the hypotheses was that if cleared quicker, there would be a better boost response. The decision to pool was based on the fact that comparable immunogenicity (antibody titers) were observed. When considering duration, the latter does not appear to be the clear driver (Brazil 9 weeks, LD-HD 12 weeks). More cases are needed. Subgroup analysis seems appropriate but indeed, hypotheses remain to be tested. SD-SD regimen (one month or three months apart) gives 60-65% efficacy. There is no evidence that it wouldn’t protect fully against the diseases. More data will be gathered.

remarked that data on asymptomatic transmissibility seems to be better for LD-SD regimen.

also enquired about AstraZeneca’s explanation for the higher efficacy of the LD-SD scheme: higher quality of immune mechanisms to the S protein, or less interference of anti-vector immunity?

AstraZeneca replied that thus far there is no reliable immunological explanation. There may be another explanation that would be provided with more data emerging.

asked whether AstraZeneca measured anti-vector (CdAdOx1) antibodies in vaccinated participants that had been infected with COVID-19.

AstraZeneca replied that no difference was observed when performing such operations.

asked when AstraZeneca expect data on their cooperation with the Gamaleya Institute and whether the latter would concern immunogenicity or also vaccine efficacy.

AstraZeneca replied that they are in conversations with key protagonists: the Gamaleya Institute, Pfizer and Moderna. There are a number of prospective studies that they would need to set up and carry out over the next few months.
enquired whether AstraZeneca expect using another vector in the second dose would make the vaccine more efficacious regarding the outcome of infection.

AstraZeneca replied that they do not know – it remains to be investigated.

enquired how confident AstraZeneca is regarding the protection provided by the first dose if the interval for boosting is increased.

AstraZeneca replied that one of the advantages conferred by this variability (two to three months between administrations) is the window where one can start looking at protection after a single dose. Yes, in summary, AstraZeneca confirms seeing protection after a single dose.

enquired whether heterologous boosting wouldn’t complicate the traceability of potential adverse events.

AstraZeneca replied that the primary safety dataset would be built on a two dose regimen of the same vaccine. The heterologous boosting is not intended to optimise a dosing, but to assure globally that if individuals receive different doses of different vaccines, they would not stand a safety issue.

Evolutions will be observed over time.

asked about data on subjects already infected that received the vaccine – whether neutralising antibodies for evidence of infection at baseline sera were checked.

AstraZeneca replied that they had not looked at all that data yet but they expect numbers to be very small. For example, SD-SD data indicate 62% vaccine efficacy. However, if pooled data is used, efficacy after a single dose indicates 70%. AstraZeneca will endeavour to optimise the dosing schedule but the vaccine at hand is already an effective vaccine, even if one does not consider the pooled data.

enquired about the recommended needles and syringes. Would AstraZeneca recommend extra needles for withdrawal of the vaccine from the multi-dose vial or would the needle used for administration have to be used? also asked about the type of recommended needle.

AstraZeneca replied that multi-dose vials (10 doses) are used. Local pharmacy site procedures for IM vaccine dose preparation and administration should be followed, but to prevent needle dulling and pain upon injection, site procedures may recommend that the needle be switched after dose withdrawal, with a new needle used for administration.

remarked that there seem to be a lot of unknowns in the current dataset. While AstraZeneca is submitting the current data generated so far, more important data from further studies will be collected and submitted. enquired about the longer-term strategy for submission of new data. also asked if it is plausible that initial schedules/doses will be adapted at a later stage.
AstraZeneca replied that they would submit more of this type of data in due course. Regulators across the world expressed a strong interest in the half dose, which would allow them to vaccinate more subjects. Having two different doses adds some complexity. While the majority of the existing data would be in the SD regimen, more data would be obtained.

AstraZeneca replied that it would take some time for the vaccines to roll out. As the latter process unfolds, AstraZeneca has the responsibility to ensure that subjects do get vaccinated. Individuals become eligible for an approved vaccine – at that point, if they receive two doses of the AstraZeneca vaccine, there is no further need to be vaccinated. If they receive one dose only or are in the control group, they can get vaccinated with other vaccines.

The Chair thanked AstraZeneca and all participants for the update and closed the meeting.

Participants

AstraZeneca

- Oncology/ Infection
- Medical and Regulatory
- Respiratory and Immunology
- Development

- BioPharmaceuticals R&D
- Europe and Canada
- Global Government Affairs & Policy Strategy, Europe, Canada
- AZ Germany
- Customer Account Manager
Independent experts:

(London School of Hygiene and Tropical Medicine)

European Commission:

Sandra Gallina (EC, Chair)