

**Scientific Presentation by Johnson & Johnson Representatives to Experts
from EU27 Nominated by the Steering Board**

4 September 2020

15:00-16:00 CET

Subject: Scientific Update on Janssen's SARS-CoV-2 Vaccine Development Program

The Chair opened the meeting and welcomed all participants, including the participant from Iceland who joined this format of meetings for the first time. [REDACTED]

[REDACTED] gave the presentation, indicating that their candidate Ad26 COVS1 is a non-replicative recombinant human Ad26-based vaccine. The choice of Ad26 is based on the low prevalence of type 26 adenovirus immunity in the human population globally. In terms of the antigen, after tests of several variants, a full stabilised SARS-CoV-2 Spike protein was chosen. Regarding clinical development, Phase I/II started on July 22nd 2020 in Belgium and the United States. 400 (Phase I) participants + 270 (Phase 2) participants (18-55 years of age). A cohort extension of 375 participants over 65 years of age is planned. Two doses to be tested in a single-dose or homologous prime-boost schedule (56-day interval between prime and boost vaccine administrations). The data are coming now, with an estimated efficacy of at least 40%, with the lower limit 20%. The intention is to demonstrate that high dose-high dose equals low dose-low dose. Phase IIb/III starts in the second half of September 2020. Countries involved include United States, South Africa, Latin America (Brazil, Argentina, Mexico), Italy, Germany. Participants: 18-65 years old to start, then extensions to >65. Vaccination schedule: one high dose (10^{11} pv) or two low doses (5×10^{10} pv) with an interval of 56 days. Production is an

[REDACTED] The recent article¹ published in Nature magazine was referred to – only one in six rhesus macaques had traces of detectable virus in the upper respiratory tract (i.e. nose), none having traces in the lower respiratory tract (i.e. lungs). For further details, the reader is referred to the PPT/post-read presentation.

Q&A:

The Chair thanked for the lively presentation and opened the floor to questions from the audience. In the Q&A session, [REDACTED] enquired about the expected registration with

¹ <https://www.nature.com/articles/s41586-020-2607-z>

EMA. [REDACTED] confirmed that the company is in touch with [REDACTED] and that they are seeking to align their registration with the equivalent process for the US-based FDA.

[REDACTED] asked about the NHP studies. With respect to the 3R rules and animal welfare, six rhesus macaques per group does not seem a sufficient sample size to provide valid results. [REDACTED] replied that in the preclinical trials for the Ebola vaccine, more animals were involved. Hence, the sample size of six animals gives a certain level of comfort but not to substitute for an efficacy trial. That number would need to be beefed up.

[REDACTED] enquired about any plans for participation in the WHO Solidarity trial. [REDACTED] replied that this action point is under serious consideration and that the read-out of the Phase I CT would be decisive.

[REDACTED] enquired about how the EU population and seroprevalences would be represented in Phase III studies. [REDACTED] replied that in past studies on Ebola, no interference with the vaccine take or the immune response was found (the titers were substantially lower).

[REDACTED] asked about the injection devices for administration and [REDACTED] replied that these would be syringes.

[REDACTED] informed that for the Ebola vaccine, the second dose is Modified Vaccinia Virus Ankara (MVA) vector. He wondered whether this could be an advantage for the COVID-19 vaccine candidate. [REDACTED] asked about immune response to the vector when used in humans on other indications. [REDACTED] replied that the answer lies in the antibodies observed in response to the vector.

[REDACTED] enquired about potential paediatric plans and the data regarding >65 cohort. [REDACTED] confirmed that such a plan is in place and that registration would follow comparison studies on children. The company highlighted their intention to have the paediatric indication as well. For >65, the assay on the dedicated cohort to >65 started two weeks after the assay on the 18-25 cohort and hence the data would only become available on 12 September – full immunogenicity data as of September 28th.

[REDACTED] and [REDACTED] enquired about final formulation, number of doses/vial, storage conditions (room temperature?) and administration equipment. [REDACTED] replied that storage is 2-8°C for 2-3 months, central warehouse at -20°C (no need for -70°C). Real-time stability data is being accumulated, with hopes to expand shelf life (NB for the Ebola vaccine it is shorter than for the Zika vaccine).

[REDACTED] asked about waning immunity/ diminishing NABs and how quickly these can be observed. [REDACTED] replied that good persistence in antibodies is observed for the platform, more so than in inactivated viral approaches. The company is monitoring this very closely in real-time, also in light of the evolving epidemiological situation.

██████████ asked about the volume being administered. ██████████ replied that 1ml was used in Phase I, which went down to 0.5 ml in Phase III. A multi-dose presentation is being considered; in case of single regimen vaccine a high dose shall be needed.

██████████ enquired about Phase III endpoints. ██████████ also asked about the level of NABs deemed protective in clinical studies and whether it would be compared to convalescents' sera levels. ██████████ replied that in reality this is very difficult to pin down and remains largely an unknown: dosing down, antibody levels can go down significantly before breakthroughs can be seen. Faster breakthrough infections can be observed at the level of the nose – via passive protection tests. The company is also doing efficacy studies to identify the threshold that would be protective. Trials comparing to convalescents' serum are not standardised and fully conclusive since certain panels score high and others score low. After vaccination, monkeys had titers that were higher than in the convalescent US panel. Monkeys had a factor of 4. CDH responses might be important in controlling the infection and severity of the disease.

██████████ asked about the age range of the Phase III study population and if there is a minimum number of elderly individuals to be included. ██████████ further asked whether diabetic patients would be enrolled in Phase II/III trials. ██████████ answered that patients with comorbidities would be enrolled and the company would then start to focus more specifically on comorbidities. The minimal threshold (25-40%) should be over 65 years of age and comorbidities.

██████████ asked whether the vaccine Ad26 COVS1 could be given as a second dose if a person has been vaccinated with a potential approved vaccine from AstraZeneca. ██████████ replied that for Ebola, a mix and match approach did work but this remains to be seen in this case.

██████████ asked whether the asymptomatic state is assessed as an endpoint in Phase III serology (with many young vaccinees, the asymptomatic state could be indicative of the majority). ██████████ replied that using an assay that considers this element would help to make that assessment. ██████████ added that this being an event-driven trial, it is difficult to predict when a statistically significant protection would be achieved. If the vaccine Ad26 COVS1 is 65% efficacious, it could be established somewhere in the March-April 2021 timeframe. If the vaccine is more efficacious, the finalisation could even be possible at the end of December 2020. ██████████ stressed that very often a selection bias is observed – those who volunteer to receive the vaccine take more cautious approaches. It is not unlikely that the real incidence one observes in a placebo group is lower than in the normal population as subjects take extra precautions. This has also been seen in HIV trials, with risk behaviour starting to change.

The Chair thanked ██████████ and Johnson & Johnson for their detailed and vivid presentation and closed the meeting thanking participants for their attention.

Participants

Johnson & Johnson:



Member States:





