Scientific Update by CureVac Representatives to Member State Experts Nominated by the Joint Negotiation Team and [redacted] with Follow-up Discussion to the Scientific Presentation

3 November 2020

12:00 – 13:30 CET

Subject: CureVac's mRNA based vaccine candidate CVnCoV against SARS-CoV2 – Pre-Clinical and available Phase I Data Update

The Chair opened the meeting and welcomed all participants, the representatives of CureVac and the experts nominated by the Joint Negotiation Team and [redacted]

CureVac provided the update as per the post-read slides, [redacted]

The Chair opened the Q&A session.

[redacted] referred to the immunogenicity data on the [redacted] group presented in the last iteration. [redacted] these results are encouraging.

[redacted] highlighted that temperature stability is a real advantage if the vaccine can be kept at 2-8° C for a considerable period of time instead of deep freeze capacity storage. In terms of NAbs, recent readings show improved data to previous ones. With most mRNA vaccines, the maximum titers reached the order of magnitude of convalescent plasma. Comparisons will be possible only when there is a standardised assay or measure. The temperature stability is a great asset. Two questions were asked: a) in addition to testing by PCR (Polymerase Chain Reaction) in animals, is there a possibility to also detect / test infectious virus titers in animals (are animals able to spread the virus or not), and b) in the well-functioning hamster model, has CureVac thought of taking the serum of immunised hamsters and testing whether this would protect hamsters from challenge. CureVac replied in relation to the first question that they measure live virus (done in hamsters) [redacted]. The intention is to do so at similar endpoints as in the hamster study. [redacted]

. In relation to the second question, CureVac explained that they have just started a pilot study to test the model itself and also looking into a mouse model that they could use with a view to obtaining more confidence/ support on efficacy data for Phase III CT data.

commended CureVac on the considerable improvement for the higher dose regimen and all the immune assays and reactogenicity profiles. Questions were asked on new data: for reactogenicity, Spike-specific multifunctional CD4+ T-cells were measured, but is CureVac also measuring the type 2 cytokines for a balanced response and whether they would expand those data for the 12µg group. A second question on the upfront prescription of paracetamol was asked in view of addressing more prolonged severe effects after the second dose in the 12µg reactogenicity group. CureVac concurred with the suggestions of the speaker for both questions and confirmed that T-cell analysis is underway in the cytokine panel; expansion to 12µg is ongoing. Based on previous rabies data, no signs of biased Th2 responses were observed. On the prophylactic use of paracetamol, CureVac explained that whilst recommended (posology 500 mg), the company do not wish to impose it.

A question was asked on the chosen locations for the roll-out of the Phase III study. CureVac replied that the latter would take place in .

Another question was asked about the reactogenicity profile in seropositives as the latter appears to be lower with a response even after the first dose. CureVac explained that the recent data gives a lot of hope with respect to the induction of memory cells in patients. .

A further question was asked regarding the increase in IgG titers. CureVac replied that for the dose, an increase for all subjects was observed. provides further data on NAbs, also for IgG (binding antibodies), for which a similar increase is observed. The increase is more pronounced for subjects that have low antibody titers. The reactogenicity also seems to be lower compared to the naïve persons. In the Phase III trial, proportion of seropositive subjects may well be higher. For IgG, the picture is very similar.

asked whether testing of 16µg and 20µg in humans was planned. CureVac explained that these assays are ongoing. Safety of those higher dosages is being monitored. Whilst there are not many vaccinees in the 16µg and 20µg group (under 20 vaccinees) amounting to a relatively small sample, the observation that reactogenicity increases with the dose is of note. Consensus around the 12µg dose exists in view of a balanced human response reactogenicity.

enquired about regulatory approvals for a Phase III start in . CureVac was asked whether they have considered how their plans can be modified just in case

other vaccines obtain regulatory approval before them and how their Phase III trials could be adjusted in this light. A question was also asked about the use of more than two doses. CureVac replied that Phase IIb/ III trials are indeed planned in [redacted] CureVac further explained that it is predictable that other vaccines would be on the market. Some vaccines might obtain approval whilst CureVac Phase III study is ongoing – in this case CureVac has an obligation to inform the vaccinees, as these developments might impact their willingness to continue the study. Subjects eligible to participate might indeed leave the study as information from competitors comes in, hence adjustments in the study planning may well be needed. With respect to the prospect of having three doses, CureVac informed that [redacted] The company further explained that the [redacted]

A question on publication timelines was raised. CureVac informed that in the coming week the work would be presented at an mRNA Conference and a publication would be prepared in parallel. Regarding the NHP data, the partnership with PHE for the manuscript is expected to result in a publication in [redacted].

[redacted] requested the final version of the presented slides and referred to the reactogenicity in the older group and whether expectations for immunogenicity and reactogenicity in this group would not be for lower read-outs. CureVac replied that the point was well taken and in view of the few subjects [redacted], more data would be needed for an assessment. CureVac also clarified that these were a subset of adults and not 60+ adults. As the studies are in Europe and Latin America, the perception of side effects can be different from country to country. Whilst fever is objectively measured, all other symptoms (myalgia, fatigue, etc) are subjective and can change with age and country.

[redacted]

The Chair thanked once again the representatives of CureVac and the company signed off, allowing for more discussion amongst the experts.

[redacted]

[redacted] expressed a minor reservation regarding reactogenicity which might jeopardise the acceptance of the second dose. He added that the role of prophylactic paracetamol was also not very clear. The key aspect compared to other mRNA vaccines is the storage conservation, i.e. the stability of the CureVac candidate vaccine.

[redacted] remarked that the company was making good progress on many aspects that were previously not clear [redacted]. Overall, the development is positive for CureVac and data on paracetamol can still be used in relation to reactogenicity. The profile chosen by their Data monitoring board is appropriate.

[redacted] explained that reactogenicity in the case of mRNA vaccines is to be expected. Low fever is a characteristic of these types of vaccines, with a recent paper by BioNTech/ Pfizer pointing to high to moderate fever and chills. This is a question of risk/ benefit. AstraZeneca also used Paracetamol, hence not uncommon.

In reply to a question from the Chair, [redacted] explained [redacted].

The Chair remarked that the situation may improve with the second wave of vaccines. [redacted] agreed that [redacted]% efficacy is needed for vaccines to render them appropriate for deployment.

[redacted]

[redacted] enquired about views on a possible third dose and reactogenicity. As data on 16 and 20µg is still being collected (for the elderly the 12µg dosage may not be enough), a third dose may be of interest.

[redacted] confirmed that logistics can be very complicated with three doses.

[redacted].

[redacted] expanded that in nursing homes this can be done. In Latin America, a dose reduction is being tested for improved immunity. If there is a marked improvement, this is doable – however, if the improvement is marginal, then such a reduction and dosage may not be worth the effort.

The Chair thanked all experts for their independent views and expertise and concluded that logistics will likely be key in the choice of vaccines by Member States. The Chair thanked all for their active engagement and closed the meeting.

Participants

CureVac:

[redacted] Managing [redacted]

[redacted] Technology Officer

[redacted] [redacted] Infectious Diseases

[redacted] COVID-19 Programme Lead

[redacted] Area Head Infectious Diseases

[redacted] Supervisory Board

Member States:

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European Commission:

Sandra Gallina (EC, Chair)

[redacted] (EC)

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[redacted] (EC)

[redacted] (EC, Minutes)