Advisory board review 12 October 2020

Advanced Purchase Agreement with Janssen Vaccines

Post meeting Fiche

1. Administrative data

- Vaccine: **Ad26.COV2.S** (Janssen Vaccines & Prevention B.V.)
- Type: non replicating viral vector (Adenovirus 26)
- Administration: 0,5 ml , either two doses, given with a time interval of a few weeks, or one single dose.
- Route of administration: The vaccine is administered intramuscularly (IM).
- Clinical development phase: Phase III initiated in US on 21 Sept 2020
- Marketing Authorization: Expected approval date on [redacted].

2. Scientific evaluation

This report is mainly based on published data.

CLINICAL DEVELOPMENT

Janssen is developing a SARS-CoV-2 viral vector vaccine, based on their Adenovirus 26 platform encoding the full-length Spike protein. The first-in-human trial (FIH) started (Belgium and the US) in July 2020 and assessed a 'low' and a 'high' dose level according to a single or a two-dose schedule. A phase 3 efficacy trial assessing a single 'low' dose regimen is now starting in the US based on the interim results of this FIH.

NON CLINICAL IMMUNOGENICITY AND CHALLENGE STUDIES

The nonclinical pharmacology studies performed by Janssen support the selection of the final construct currently tested in clinical trials. [redacted] the final choice was based on desirable immune response and protection after challenge in NHP. The final candidate elicits immune responses in mice, rabbits, monkeys and hamsters. Hamsters were used as a model for more severe COVID-19 disease, and the final candidate demonstrated reduced tissue viral load, reduced weight loss and minimal to no evidence of pneumonia and no mortality as compared to sham controls. This confirms previous results in the monkey, where all 6 vaccinated animals were protected from LRT infection and 5/6 animals had no detectable viral load in the URT.

From nonclinical point of view, this vaccine candidate is promising. The above results should now be confirmed in human.

Limitations of the NHP challenge study are as follows: number of animals per group limited inherent to species choice, this species is less sensitive to the COVID disease than human, studies are performed in young healthy adults, the duration of response in vaccinated animals is not addressed. Nonetheless, these data are complemented by challenge studies in Syrian hamsters, a model for more severe disease.

CLINICAL IMMUNOGENICITY AND EFFICACY

In general, adenovirus based vaccines are considered able to induce robust neutralising antibody responses, as well as CMI responses (including CD4 Th1 and CD8 responses). Such responses were observed in different clinical trials testing various Adenovirus-based vector vaccines with various antigens.

Although a large number of subjects have been vaccinated with Ad26-based vaccines, published data are limited. These data indicate that an Ad26-based vaccines is able to induce antigen-specific humoral (binding and neutralizing Ab) and Th1 specific immune responses to the transgene in naïve and (RSV) pre-immune individuals after a single dose (IFN-gamma secretion or production by/in CD4+ and CD8+ T cells). A single dose of the Ad26.ZIKA vaccine was able to induce neutralizing responses as early as 14 days following vaccination.

The level of Ad26-pre-existing immunity in BE is currently not known, but is likely low given data available [redacted]. The impact of pre-existing immunity to the vector on vaccine-induced immune responses, when present, is uncertain given the lack of published data. Data from HIV vaccine candidate suggest that it might be limited.

It is uncertain what are the implications of immunity to the vector induced by a first dose on immunogenicity of subsequent vaccination with the same vaccine/vaccine platform. However, a second dose of the Ad26 based zika vaccine was able to increase the immune response.

Data from the interim analysis of the Ad26 COVID-19 vaccine candidate have been published a few days ago and demonstrated that Spike-specific humoral and cellular immune responses were induced following 1 dose, including antibodies neutralizing the wild type viruses and Th1 cytokine producing CD4+ T cells.

Data in the elderly are currently too limited to draw conclusion on the potential of this vaccine candidate and other candidates to overcome immunosenescence.

There is currently no efficacy data (i.e. protection against disease) available for this vaccine candidate, as for any of the COVID-19 vaccine candidates.

All the vaccine candidates reaching Phase 3 in Europe or the US can be assumed 'sufficiently promising' in terms of the limited data suggesting benefit, as they should have demonstrated sufficiently robust immune responses (at least nAb and Th1 responses) and an acceptable safety profile on a limited safety database in the earlier development phases. However, in this particular case of COVID-19, the absence of a correlate of protection makes early development not predictive of the efficacy.

NON CLINICAL SAFETY

No nonclinical issues were identified in the platform data submitted to support the clinical trials, there are no insert-specific toxicity study results available to date (will be submitted during MAA).

CLINICAL SAFETY

Very limited safety data from the FIH are available for the Ad26 COVID 19 vaccine. No safety concern has been raised as of today. The safety profile of the vaccine will be driven both by the antigen and the vector platform.

The Janssen Pharmaceutical Ad26-based vaccine is based on a non-replicating adenovirus vector. Non-replicating adenovirus vectors are in general considered safe platforms that in principle could be used in immunocompromised individuals and pregnant women.

Ad26-based vaccines against various infectious disease were evaluated (RSV, HIV, Ebola, Malaria, Filo, Zika) in thousands on individuals, mainly in young adults, but also elderly people and children without raising safety issues. One Ad26-based vaccine has been licensed (Zabdeno, indicated for active immunisation for prevention of disease caused by Ebola virus in individuals ≥1 year of age).

Vaccine induced enhanced disease (VED) is considered as a theoretical risk with SARS-COV-2 vaccines based on non-clinical data generated with inactivated SARS-COV-1 and other coronaviruses vaccines in animals.

COMPARISON TO OTHER VACCINE CANDIDATES

-There is a large experience with adenovirus vectored vaccines. The level of uncertainties is considered lower with this platform compared to mRNA vaccines which is a newer technology.

- [redacted]
side-by-side comparison of protection studies between vaccine candidates from different companies is hampered by differences in design, such as challenge dose, and absence of standardized assays to measure the immune response, and should as such be interpreted with caution. In addition, clinical data are very limited at this stage and in the absence of a correlate of protection, it is not possible to rank vaccines based on their potential vaccine efficacy. Both candidates are considered promising at this stage.

-Although a few months behind the Moderna and the Astra Zeneca vaccine candidates in terms of the start of the phase 3 trial, the Janssen vaccine is one of the most advanced COVID-19 vaccine candidates.

-Immunogenicity data observed in humans cannot be compared across vaccine candidates, due to the absence of a correlate of protection, and the lack of standardisation of assays.

-The Oxford/AZ vaccine candidate is based on a simian (chimpanzee) adenovirus. Consequently, there seems to be no appreciable level of immunity to this adenovirus in human populations. Although there is more uncertainties about pre-existing immunity to the Ad26, which is a human adenovirus, the magnitude of the humoral immune response to Ad26 seems low in most population.

- There is a large amount of data available for the Ad26-platform with various antigens; the safety database is larger compared to the ChAdOx1. The Ad26 platform is the only adenovirus platform for which a vaccine has been licensed (Zabdeno).

-In terms of insert choice, no comparison can be made since this information is not available for competitors. However, for the insert used by Janssen, they have provided justification of their final choice, with a wild type signalling peptide and prefusion stabilizing mutations.

CONCLUSION

Overall, based on the data we had available at the time of assessment, we consider the Ad26-Cov2-S as a promising vaccine candidate. We did not identify concerns that would render this candidate a lesser choice from scientific point of view. There are currently no data available that could justify the selection of one adenoviral vector-based vaccine over the other.

There are no critical issues requiring not to proceed with J&J contract.

3. Manufacturing considerations

Janssen plans to deliver 200 million regimens in 3 phases:

- o [redacted]

Possibility to purchase an additional volume of 200 million regimens [redacted]

- o [redacted]

Delivery will be allocated based on population binding allocation key (around 2.5% for Belgium): this represent a total of 5,1 millions of regimens for Belgium.

Vaccine presentation and storage condition:

- o Vaccine Volume will be delivered [redacted]
- o all Vaccine Regimens comprised in a vial should be used within four (4) to six (6) hours after administration of the first dose of the vial
- o [redacted] Based on clinical trials data, vaccine can be stored at -20° (during 24m) and 2-8°C (during 3m). Those storage condition might evolve based on generation of stability data.

Distribution and delivery : delivery of the vaccine volume according [redacted]

Other manufacturing consideration: [redacted].

4. Legal considerations

Conclusion on the assessment of contract by Deloitte Legal/ IUS Famhp (see detailed assessement in annex)

Aansprakelijkheid ten aanzien van derden en schadevergoedingen [redacted]

- [redacted]

5. Financial considerations

- Estimated Price per regimen: [redacted] (excluding VTA)
- European Commission contribution: [redacted] per Vaccine Regimen (=> contribution per MS: [redacted] (TVA included) [redacted] ([redacted])
- [redacted]
- Each Participating Member State shall submit a Vaccine Order Form in respect of its Allocated portion of the Base Volume Commitment in writing to Contractor [redacted]. Member States shall pay to Contractor the Price Balance for such Vaccine Volume within [redacted].
- Additional consideration:
  - [redacted]

6. Advisory Board recommendation

Considering the strong non clinical supportive package ; the large amount of data available for this platform with various antigens, including safety data; the fact that this is the only platform for which a vaccine has been licensed; the experience of the company in manufacturing at large scale; the [redacted] ; the standard storage/distribution condition (2 to 8 degree); and the probability to have a one dose regimen,

Taking also into consideration the clinical unknowns (phase 3 study has just started, limited data available in human) , [redacted], the specific labelling requirement, [redacted],

The advisory board considers that in the current context, based on available data, there are no critical issues requiring not to proceed with contract. The list of experts having participated to this advisory board is listed below:

Name	Expertise
Yves Van Laethem (per mail)	Infectiologue et président du groupe vaccination du CSS
Charlotte Martin	Infectiologue (ULB)
Laura Piraprez	Représentant de la communauté germanophone
Geert Top	Agentschap Zorg en Gezondheid
Paloma Carillo	Responsable programme vaccination, ONE

M. Lardennois	Représentant de la communauté bruxelloise
Pierrette Melin	Representant de la communauté Wallone
Stéphanie Mali	Coordinateur centre d'excellence vaccins (Afmps)
Steven Hippe	Responsable du département légal (Afmps)
Xavier De Cuyper	CEO AFMPS et membre du Steering Board vaccin
Greet Musch	Directeur Général, DG Pre (Afmps)