Subject: Scientific Considerations and Recommendations on adenovirus vector-based COVID-19 vaccine candidates

From: Dutch Scientific Committee-COVID-19 vaccines (22-07-2020)

This Note was provided to the Ministry of Public Health, Welfare and Sport and the Task Force of the Dutch Government on Covid-19 vaccine initiatives, 22 July 2020

Considering that:

- Three teams are currently most advanced in the development of COVID-19 vaccines based on the Spike protein and adenoviral platforms,
- these teams being:
  i. The CanSino team (CS) developing a product based on human Adenovirus 5 (Ad5) which is in phase 2,
  ii. The Oxford/AstraZeneca team (AZ) developing the AZD1222 vaccine based on the ChAdOx1 chimpanzee adenovector which is in Phase 3, and
  iii. The Janssen team (JJ) developing a vaccine based on human Ad26 expected entering Phase 1 on 22 July
- The committee has seen publications for the CS product (phase 1 and phase 2) and for the AZ product (preclinical and phase 1, 2);
- The chair of the Dutch Science Committee has interviewed representatives and reviewed unpublished preclinical data from JJ on June 19th under confidentiality;
- The Dutch Science Committee has seen recommendations from the French scientific committee COVID-19 vaccines and the comments on these recommendations from the Spanish Agency from Medicines and Medical Devices;
- The deputy chair of the Dutch committee has participated in the science discussion during the July 21 meeting of the scientific board of France, Spain and NL with their JNT-members.

The Dutch Scientific Committee-COVID-19 vaccines

- Agrees with the French and Spanish experts that the CS product is not considered optimal for vaccination against COVID-19 because of pre-existing immunity to the ad5 vector;
- Considers the other two adenovirus-vector-based AZ and JJ products as serious candidates in the covid-19 vaccine landscape, based on shown or expected safety profiles (phase 1/ 2 data published for the AZD122 product, clinical data for the JJ Ad26 vector) and their immunogenicity data in the clinic (AZ) and in preclinical 5.1.1c model (AZ and JJ);
- Acknowledges that the AZ and JJ platforms and products have intrinsic differences, including the vector and precise sequence and conformation of the Spike protein antigen expressed;
- Acknowledges that the human adenovirus 26 vector from the JJ product may encounter pre-existing immunity, which is absent for the ChAdOx1 chimpanzee adenovector;
- Acknowledges that the safety records for the AZ vector are more limited than for the JJ product;
- Acknowledges that a 1:1 comparison of the (pre)clinical for the AZ and JJ products is not fully possible due to the absence of standardized covid-19 antibody and T-cell test platforms and differences in the design of the preclinical challenge models used.

Furthermore the Dutch Scientific Committee-COVID-19 vaccines:

- Recommends that both the AZ and JJ products are serious COVID-19 vaccine candidates, 'horses with legs', and should be continued for development;
- Recommends that apart from adenovirus vector-based COVID-19 vaccine candidates it is important to include candidates based on other technologies, especially the innovative mRNA/DNA and the more traditional subunit/protein based technologies, in the COVID-19 vaccine candidate portfolio;
- Recommends to include the time of delivery of sufficient doses of vaccines as a selection criterion
- Recommends to intensify efforts to establish a pharmacovigilance program for COVID-19 vaccines
- Recommends standardization of test platforms independent of companies