Work Group interpretations of data

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Prior infection
Summary of Work Group interpretation: COVID-19 vaccine and Prior infection

- Await data from Phase III trials for any possible vaccine-associated enhanced disease or reactogenicity after prior infection

- In the absence of concerning data from Phase III trials:
  - PCR +
  - Antigen +
  - Antibody +

  Not a contraindication to receive COVID-19 vaccine

- Any vaccine recommendations that rely on knowledge of prior immunity/antibody testing would be difficult to implement
Pregnant and Breastfeeding Women
Most Work Group members agreed that breastfeeding would not be a contraindication to receive a COVID-19 vaccine

- Need to be evaluated for each vaccine, especially if any live virus/vector vaccines are authorized/licensed
Summary of Work Group interpretation:
COVID-19 vaccine and Pregnant Women in Tier 1a

- Limited data on pregnancy expected from Phase III trials
- Work Group did not reach a consensus
- Majority felt that if a woman is recommended to receive the vaccine in an early allocation phase, pregnancy should be a precaution, but not a contraindication to receive a COVID-19 vaccine
  - Emphasizing need to allow women to make an informed decision, providing all current knowledge of COVID-19 vaccines/platforms with pregnancy and risk of disease
Summary of Work Group interpretation:
COVID-19 vaccine and Pregnant Women in Tier 1a

- Additional situation: Pregnancy diagnosed after receipt of first dose of COVID-19 vaccine

- Majority of Work Group felt that the second dose could be given at the recommended interval
  - Minority opinion: Postponing second dose until second trimester or until after pregnancy
  - Emphasizing need to allow women to make an informed decision
Modeling
Summary of Work Group interpretation: Modeling data

- Differences among 3 strategies is minimal
  - Ethical principles and implementation considerations may greatly contribute to selecting the optimal sequence in Phase Ib

- Largest impact in averted deaths and infections is the timing of vaccine introduction in relation to increases in COVID-19 cases
  - Emphasizes the need to continue non-pharmaceutical interventions (e.g. wearing a mask, social distancing) while we await available vaccine

- Many factors will inform interpretation of modeling data and allocation decisions
  - VE in older adults
  - Vaccine’s ability to prevent severe disease or transmission
  - If the goal is to prevent greatest number of infections or greatest number of deaths
Immunogenicity and Safety Information Reviewed by Work Group
NVX-CoV2373 (Novavax) N=131

- Immunogenicity
  - Neutralizing antibodies (wild-type neutralization assay titers) and binding antibodies (ELISA) measured 14 days post-dose 2
  - Responses similar to or exceeded convalescent sera comparison
  - Th1-biased CD4+ T-cell response
  - 5µg dose + Matrix-M1 selected for Phase III clinical trials

- Safety
  - Local and systemic symptoms followed for 7 days post-vaccination
    - Headache, fatigue and myalgia most common symptoms reported
  - Reactogenicity symptoms higher after second dose
  - No vaccine-related serious adverse events (SAEs) reported

Protein Subunit Vaccine
Immunogenicity and Safety Information Reviewed by Work Group
Ad26.COV2.S (Janssen) N=775

- **Immunogenicity**
  - Neutralizing antibodies (wild-type virus neutralization antibody titers) and binding antibodies (ELISA) measured 28 days post-dose 1
  - Responses similar to human convalescent sera
  - CD4+ and CD8+ T cell response demonstrated
  - Th1-biased CD4+ T-cell response
  - $5 \times 10^{10}$ viral particle **single** dose of Ad26.COV2.S selected for Phase III clinical trials

- **Safety**
  - Local and systemic symptoms followed after administration
    - Fatigue, headache and pain most common
  - Reactogenicity symptoms lower in older population (≥65 years)
Both vaccine candidates planning/enrolling large Phase III efficacy trials (30,000-60,000 people)

Primary endpoints: symptomatic, virologically confirmed COVID-19 disease

 Attempting to enroll diverse populations:  
   – Race and ethnicity  
   – Age (<65 years and ≥65 years of age)  
   – Underlying medical conditions
Implementation/Distribution

- Diverse cold chain, implementation requirements
- Novavax (NVX-CoV2372): 2 doses given 21 days apart, vials stored at 2-8°C
- Janssen (Ad26.COV2.S): Single dose, vials stored at -20°C long term, with 2-8°C for 3 months
Work Group Interpretation

- Phase I/II data from the vaccines show induction of binding and neutralizing antibodies as well as T-cell responses, favorable safety/reactogenicity profile, supporting advance to Phase III trials

- Both platforms with prior experience from other vaccines

- Safety pauses are expected with large clinical trials, indicate the process is working appropriately
Work Group Interpretation:
Current Phase III Clinical Trials

- Importance of enrolling diverse study participants
- Importance of harmonizing safety and efficacy endpoints across all Phase III trials to the extent possible
- Need to report maternal and fetal outcomes for women who become pregnant during the clinical trials
- Support FDA’s guidance for ensuring that Phase III trials conduct ongoing assessment of long-term safety and efficacy, and that issuance of an EUA is not grounds to unblind follow-up in an ongoing clinical trial
For more information, contact CDC
1-800-CDC-INFO (232-4636)

Thank you

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.
# OWS Supported SARS-CoV-2 Vaccines

<table>
<thead>
<tr>
<th>Platform/Design</th>
<th>Moderna</th>
<th>Janssen</th>
<th>AstraZeneca</th>
<th>Novavax</th>
<th>GSK</th>
<th>Sanofi</th>
<th>BioNTech</th>
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</thead>
<tbody>
<tr>
<td>mRNA: encodes 2P-stabilized Spike, TM, F1</td>
<td>Replication Incompetent Ad26; Stab. Spike; ΔF; TM</td>
<td>Replication incompetent ChAdOx1 wild type Spike; ΔF; TM</td>
<td>Baculovirus Expressed trimeric Stabilized Spike, ΔF; TM + Matrix M</td>
<td>Baculovirus Expressed trimeric Stabilized Spike, ΔF; TM + AS03</td>
<td>mRNA: encodes stabilized SARS-CoV-2 Spike</td>
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| Dose/Schedule | 2 doses 100 µg (0,28 days) | 1 dose at 5 x 10⁹/2 doses separate trial (0-28 days) | 2 doses at 5 x 10⁹ vp, (0-28 days) | 2 doses at 5 µg + Matrix M (0,21 days) | 5/15 µg +AS03 (0, 21 days) | 2 doses X 30 µg (0, 21 days) |

| Current Status | Phase 3 US (start date July 27th) | Phase 3 international (includes US) | Phase 3 International (includes US) | Phase 2 International | Phase 1 | Phase 2-3 International (start date July 27th) |

| Phase 3 Est. Start Date | Finished recruiting | Ongoing | Ongoing | November 2020 | December 2020 | Ongoing (close to completing recruitment) |

| DART | Ongoing-Report expected Q1 2021 | Ongoing-Report expected Q1 2021 | Expected to start Q4 2020 | Ongoing-Report expected Q1 2021 | Expected to start Q4 2020 | Will complete DART study. Date unknown |

| Pregnancy Exposure | NO; Platform has been tested in adults | Yes, Ad26+ Ebola (1000 patients) Current pregnancy trials ongoing | NO; Platform has been tested in adults | Baculovirus Expression YES; Adjuvant has been tested in adults | Baculovirus expression YES; Adjuvant in commercial vaccine (Pandemrix, Arepanrix) | NO |

| Comments | DART with previous formulations; no concerns | Recruiting lactating women in their Phase 3 | Extensive experience with pregnancy trials (RSV+Alum) | GSK conducting pregnancy trials (Phase 2) for RSV vaccine | Pfizer conducting pregnancy trials (Phase 3) for RSV vaccine |  |
Precautions:
General Best Practices Guidelines

- **Precaution**: A condition in a recipient that might increase the risk for a serious adverse reaction, might cause diagnostic confusion, or might compromise the ability of the vaccine to produce immunity.

- In general, vaccinations should be deferred when a precaution is present. However, a vaccination might be indicated in the presence of a precaution if the benefit of protection from the vaccine outweighs the risk for an adverse reaction.
Vaccination during Pregnancy: General Best Practices Guidelines

- “No evidence exists of risk to the fetus from vaccinating pregnant women with inactivated virus or bacterial vaccines or toxoids”

- Live vaccines administered to a pregnant woman pose a theoretical risk to the fetus; therefore, live, attenuated virus and live bacterial vaccines generally are contraindicated during pregnancy

- Pregnancy is a contraindication for smallpox vaccine, MMR and varicella-containing vaccines.