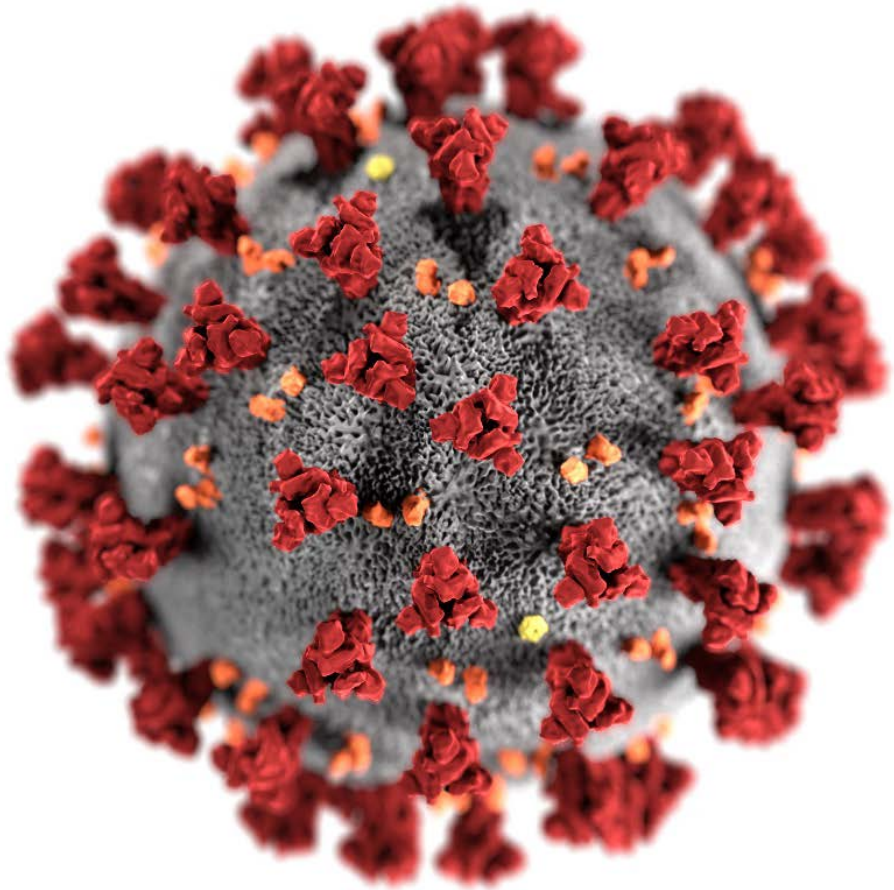
ACIP COVID-19 Vaccines



Work Group interpretations of data

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ACIP Meeting

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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

Summary of Work Group interpretation:
COVID-19 vaccine and Breastfeeding Women in Tier 1a

- 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

Clinical Trial Data

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
  - **$5x10^{10}$** 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)

Plans for Phase III

- 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^{o}C
- Janssen (Ad26.COV2.S): Single dose, vials stored at -20^{o}C long term, with 2-8^{o}C for 3 months

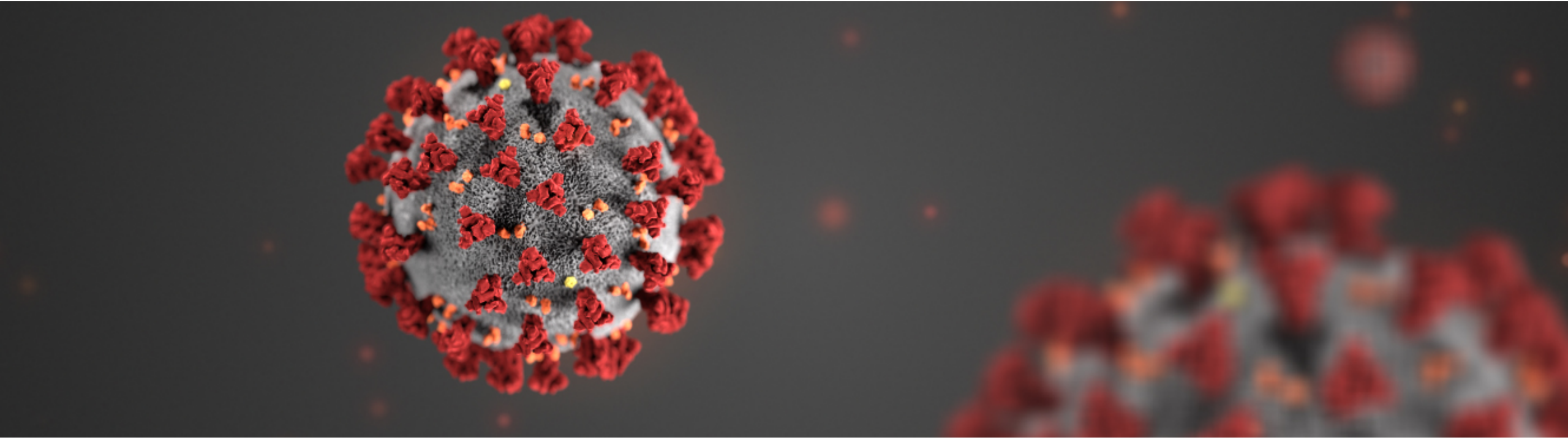
Work Group Interpretation

- 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)
TTY: 1-888-232-6348 www.cdc.gov

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

	moderna	janssen	University of Oxford AstraZeneca	NOVAVAX	gsk SANOFI	BIONTECH Pfizer
Platform/ Design	mRNA: encodes 2P-stabilized Spike, TM, FI	Replication Incompetent Ad26; Stab. Spike; △F; TM	Replication incompetent ChAdOx1 wild type Spike; △F; TM	Baculovirus Expressed trimeric Stabilized Spike, △F; TM + Matrix M	Baculovirus Expressed trimeric Stabilized Spike, △F; TM + AS03	mRNA: encodes stabilized SARS-CoV-2 Spike
Dose/ Schedule	2 doses 100 µg (0,28 days)	1 dose at 5 x 10^{10}/ 2 doses separate trial (0-56 days)	2 doses at 5 × 10^{10} 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.