ACIP Meeting: COVID-19 Vaccines

October 30, 2020
Today’s agenda

**Vaccine Development & Regulatory**
- Update from VRBPAC meeting:
  Dr. Doran Fink (FDA)
- NVX-CoV2373 Vaccine Candidate:
  Dr. Filip Dubovsky (Novavax)
- Janssen’s SARS-CoV-2 Vaccine Program:
  Dr. Jerry Sadoff (Janssen)

**Implementation**
- Update on vaccine implementation planning:
  Dr. Janell Routh (CDC)
- Vaccinate with Confidence:
  Dr. Amanda Cohn (CDC)

**Safety**
- FDA safety surveillance systems:
  Dr. Steven Anderson (FDA)
- Post-authorization safety monitoring plans:
  Dr. Tom Shimabukuro (CDC)

**Allocation and Epidemiology**
- Modeling strategies for the initial allocation of COVID-19 vaccines:
  Dr. Matthew Biggerstaff (CDC)
- Updates to immunity and epidemiology to inform COVID-19 vaccine policy:
  Dr. Megan Wallace (CDC)
- Ethical principles for early vaccine allocation:
  Dr. Mary Chamberland (CDC)

**Work Group Interpretation**
- Work Group interpretation of data:
  Dr. Sara Oliver (CDC)
- Policy questions, Evidence to Recommendation Framework, and outcomes:
  Dr. Kathleen Dooling (CDC)
Vaccine Update: Phase III clinical trials in the U.S.

- AZD1222 vaccine (AstraZeneca) announced removal of FDA hold 10/23, resuming Phase III trials

- Ad26.COV2.S vaccine (Janssen) announced lifting of safety pause 10/23, resuming Phase III trials

- BNT162b2 vaccine (Pfizer/BioNtech)
  - 42,133 participants enrolled as of 10/26/2020
  - 35,771 participants have received their second vaccination
  - 30% of U.S. participants enrolled have “diverse backgrounds”

- mRNA-1273 vaccine (Moderna): Enrollment Complete
  - 30,000 participants enrolled as of 10/22/2020
  - 25,654 participants have received their second vaccination

Sources:
- https://www.modernatx.com/cove-study
- https://connect.trialscope.com/studies/34986a8ab779-4169-a350-5d929149d428
Vaccine Update: Phase III clinical trials in the U.S.

Race and ethnicity

- 63% White
- 20% Hispanic/Latinx
- 10% Black/AA
- 4% Asian
- 3% All others

27% of participants living with comorbidities: including diabetes, cardiac disease, lung disease, obesity

22% healthcare personnel

Age and gender

Sources: https://www.modernatx.com/sites/default/files/content_documents/2020-COVE-Study-Enrollment-Completion-10.22.20.pdf
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
**Possible groups for Phase 1 vaccination**

From prior ACIP Discussions:

**Phase 1a:**
- HCP

**Phase 1b:**
- Essential Workers
- High Risk Med Conditions
- Adults ≥ 65 years old

- HCP
- Essential Workers
- High Risk Medical Conditions
- Adults ≥ 65 years old

High Risk Medical Conditions
>100M

Essential workers
~80M

Healthcare personnel
~20M

Adults ≥ 65 years old
~53M
75% of the healthcare workforce are women.

Women are a majority among the largest healthcare personnel groups

- **Registered Nurses**: 88%
- **Healthcare support workers**: Nursing, psychiatric, and personal and home health aides (86%)

From 2019 Census Data
Increased risk for ICU admission, mechanical ventilation and death during pregnancy

<table>
<thead>
<tr>
<th>Outcomes of Interest</th>
<th>No. (%)*</th>
<th>Crude RR (95% CI)</th>
<th>aRR (95% CI)†</th>
<th>Previously Published¶ aRR (95% CI)†</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pregnant women</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICU Admission</td>
<td>225 (0.9)</td>
<td>2.4 (2.2-2.9)</td>
<td>2.2 (1.9-2.5)</td>
<td>1.5 (1.2-1.8)</td>
</tr>
<tr>
<td>Mechanical Ventilation</td>
<td>79 (0.3)</td>
<td>3.0 (2.4-3.8)</td>
<td>2.5 (2.0-3.2)</td>
<td>1.7 (1.2-2.4)</td>
</tr>
<tr>
<td>ECMO¶</td>
<td>17 (0.1)</td>
<td>1.9 (1.1-3.4)</td>
<td>2.0 (1.2-3.4)</td>
<td>--</td>
</tr>
<tr>
<td>Death</td>
<td>41 (0.2)</td>
<td>1.4 (1.1-2.0)</td>
<td>1.6 (1.1-2.2)</td>
<td>0.9 (0.5-1.5)</td>
</tr>
<tr>
<td><strong>Nonpregnant women</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICU Admission</td>
<td>1,551 (0.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mechanical Ventilation</td>
<td>451 (0.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>486 (0.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Percentages calculated among total in pregnancy status group; those with missing data on outcomes were counted as not having the outcome
† Adjusted for age, race/ethnicity, and presence of underlying conditions. Nonpregnant women are the referent group.
Extracorporeal membrane oxygenation
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
Population-Wide Averted Infections: Infection-Blocking Vaccine, Older Adults Receive Full Protection

- Initially vaccinating high-risk adults or essential workers in Phase 1B averts approximately 1–5% more infections, compared to targeting age 65+
  - This difference is greatest in the scenario where the vaccine is introduced before incidence rises
- Findings are robust to assumptions of reduced VE in older populations

Initial Phase 1B Target:
Age 65+
High-Risk Adults
Essential Workers

<table>
<thead>
<tr>
<th>Vaccine Introduction Time</th>
<th>% Infections Averted by Phase 1 Vaccination (6 Months Following Introduction)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before Incidence Rises</td>
<td>~5%</td>
</tr>
<tr>
<td>As Incidence Rises</td>
<td>~3%</td>
</tr>
<tr>
<td>As Incidence Falls</td>
<td>~1%</td>
</tr>
</tbody>
</table>
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 Iб

- 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
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)
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
ACIP Policy Questions
Should COVID-19 vaccine ‘A’ be recommended?

Evidence to Recommendation Framework
GRADE

To whom should early allocation of COVID-19 vaccine ‘A’ be recommended?

Scientific Evidence Ethical Principles Implementation

ACIP RECOMMENDATION

FDA approval
- Licensure
- Emergency use Authorization
- Expanded Access

ACIP Pathway to Recommendation

ACIP RECOMMENDATION
## PICO for Vaccine Policy Question #1

<table>
<thead>
<tr>
<th>Population</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>COVID-19 vaccine “A”</td>
</tr>
<tr>
<td>Comparison</td>
<td>No vaccine (Placebo, including saline or non-COVID-19 vaccine)</td>
</tr>
</tbody>
</table>

### Outcomes

<table>
<thead>
<tr>
<th>Category</th>
<th>Benefits (prevention of)</th>
<th>Harms (possible risks)</th>
</tr>
</thead>
</table>
| Critical | • Symptomatic COVID-19 (PCR* conf)  
• Hospitalization due to COVID-19 | • Serious Adverse Events (including vaccine-associated enhanced disease) |
| Important | • Death (all cause)  
• SARS-CoV-2 Seroconversion (non-spike)  
• Serial PCRs for asymptomatic infection | • Reactogenicity |

*PCR= Polymerase chain reaction*
## Outcomes under study in clinical trials

<table>
<thead>
<tr>
<th>Outcome</th>
<th>In clinical Protocols?</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic COVID-19 (PCR+)</td>
<td>✓</td>
<td>Primary outcome, consistent definition</td>
</tr>
<tr>
<td>Hospitalization due to COVID-19</td>
<td>✓</td>
<td>Exploratory aim (or as adverse event)</td>
</tr>
<tr>
<td>Serious Adverse Events</td>
<td>✓</td>
<td>Unsolicited, consistent definition</td>
</tr>
<tr>
<td>Death (all cause)</td>
<td>✓</td>
<td>Exploratory aim (or as adverse event)</td>
</tr>
<tr>
<td>Reactogenicity</td>
<td>✓</td>
<td>Solicited symptoms 7d</td>
</tr>
<tr>
<td>SARS-CoV-2 Seroconversion (non-spike)</td>
<td>✓</td>
<td>Differences in timing &amp; assay</td>
</tr>
<tr>
<td>Serial PCRs for asymptomatic infection</td>
<td>X</td>
<td>? Outside U.S.</td>
</tr>
</tbody>
</table>
COVID-19 Vaccine Work Group next steps

Policy Question #1: **Vaccine Recommendations**
- Populate the Evidence to Recommendation Framework
- Start GRADEing vaccine evidence and incorporate Phase III data when available
- Discuss clinical guidance (special populations/concomitant administration/scheduling)

Policy Question #2: **Allocation Recommendations**
- Publish ethical principles manuscript
- Incorporate latest information regarding science, implementation, and ethics to further refine Phase 1 allocation
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.