Update on COVID-19 Vaccines

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Research America Virtual Alliance Meeting
March 8, 2021
Today’s Topics

• Accelerating vaccine development
• Three Emergency Use Authorization vaccines
• COVID-19 variants and vaccines
• Use of COVID-19 vaccines
Accelerated Vaccine Development

Compare vaccines in extensive animal studies

Human safety and efficacy studies

Emergency Use Authorization

Vaccine administration

Licensure

Post-approval surveillance

Process development, scale-up to commercial production at risk

Commercial-scale manufacturing

Establish vaccine distribution and administration infrastructure

Clinical data collection & analysis

www.fda.gov
Vaccine Development – Accelerating the Process

• Clear guidance on expectations from products
• Facilitate early conversations with regulators
• Integrating different phases into one clinical trial
• Manufacture large quantities of product at risk
• Use optimal path to facilitate product availability
Two Guidance Documents

• Development and Licensure of Vaccines to Prevent COVID-19

• Emergency Use Authorization for Vaccines to Prevent COVID-19
Biologics License Application (BLA)

• Biologics are licensed under both section 351 of the Public Health Service Act and the Federal Food Drug and Cosmetic Act
• Product must be safe, pure, potent, effective
• The standard used is that there is substantial evidence of efficacy from adequate and well-controlled clinical trials
Emergency Use Authorization (EUA)

• Put in place after 9/11 to ensure that potentially lifesaving medical products could be available to people in medical need when there is not an approved and available alternative

• The standard used is that the product “may be effective” and its “known and potential benefits outweigh the known and potential risks”
EUA for a COVID-19 Vaccine

• Must demonstrate clear and compelling efficacy in a large well-designed phase 3 clinical trial
• Careful evaluation of quality, safety, efficacy
• Public advisory committee meeting
• Enhanced post-deployment surveillance
Advanced Candidates – March 2021

• mRNA
  – BNT162b2 (Pfizer-BioNTech) – EUA granted Dec 11, 2020
  – mRNA-1273 (Moderna) – EUA granted Dec 18, 2020

• Non-Replicating Viral Vector
  – Ad26.COV2.S (Janssen) – EUA granted Feb 27, 2021
  – ChAdOx1 (Astra Zeneca-Oxford)

• Protein Subunit
  – NVX-CoV2373 (Novavax)
  – MRT55000 (Sanofi-Translate Bio)
## Vaccine Trial Demographics

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Pfizer-BioNTech (2 doses 21 d apart)</th>
<th>Moderna (2 doses 28 d apart)</th>
<th>Janssen (1 dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total patients</td>
<td>43,552</td>
<td>30,350</td>
<td>39,321</td>
</tr>
<tr>
<td>Receiving vaccine</td>
<td>21,768</td>
<td>15,180</td>
<td>19,630</td>
</tr>
<tr>
<td>Receiving placebo</td>
<td>21,784</td>
<td>15,170</td>
<td>19,691</td>
</tr>
<tr>
<td>Black/African Amer.</td>
<td>9.8%</td>
<td>9.7%</td>
<td>17.2%</td>
</tr>
<tr>
<td>Hispanic/Latino</td>
<td>26.2%</td>
<td>20.0%</td>
<td>45.1%</td>
</tr>
<tr>
<td>At least age 65</td>
<td>21.4%</td>
<td>25.3%</td>
<td>20.4%</td>
</tr>
</tbody>
</table>
Vaccine Efficacy in Phase 3

Primary efficacy was determined against moderate and severe/critical COVID-19

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Pfizer-BioNTech</th>
<th>Moderna</th>
<th>Janssen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary efficacy</td>
<td>95% (8/162)</td>
<td>94.1% (11/185)</td>
<td>d14 66.9% (116/348) d28 66.1% (66/193)</td>
</tr>
<tr>
<td>(vaccinated/placebo)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Young population</td>
<td>age 16-54</td>
<td>age 18-64</td>
<td>age 18-64</td>
</tr>
<tr>
<td></td>
<td>95.6% (5/114)</td>
<td>95.6% (7/156)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>d14 63.7% (95/260) d28 66.1% (52/152)</td>
</tr>
<tr>
<td>Older population</td>
<td>age 55+</td>
<td>age 65+</td>
<td>age 65+</td>
</tr>
<tr>
<td></td>
<td>93.7% (3/48)</td>
<td>86.4% (5/114)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>d14 76.3% (21/88) d28 66.2% (14/41)</td>
</tr>
<tr>
<td>Severe COVID-19</td>
<td>1/9</td>
<td>0*/30</td>
<td>d14 14/60; d28 5/34</td>
</tr>
</tbody>
</table>

*One severe case reported 2 months after vaccination
# Vaccine Safety in Phase 3

## Second dose

<table>
<thead>
<tr>
<th>Reaction (2nd injection)</th>
<th>Placebo*</th>
<th>&lt;55</th>
<th>55+</th>
<th>&lt;65</th>
<th>65+</th>
<th>&lt;60</th>
<th>60+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injection site pain</td>
<td>14%</td>
<td>78%</td>
<td>66%</td>
<td>90%</td>
<td>83%</td>
<td>57%</td>
<td>33%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>22%</td>
<td>59%</td>
<td>50%</td>
<td>68%</td>
<td>58%</td>
<td>44%</td>
<td>30%</td>
</tr>
<tr>
<td>Headache</td>
<td>21%</td>
<td>52%</td>
<td>39%</td>
<td>63%</td>
<td>46%</td>
<td>44%</td>
<td>30%</td>
</tr>
<tr>
<td>Muscle pain</td>
<td>10%</td>
<td>38%</td>
<td>29%</td>
<td>61%</td>
<td>47%</td>
<td>39%</td>
<td>24%</td>
</tr>
<tr>
<td>Chills</td>
<td>4%</td>
<td>35%</td>
<td>23%</td>
<td>48%</td>
<td>31%</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Joint pain</td>
<td>8%</td>
<td>21%</td>
<td>19%</td>
<td>45%</td>
<td>35%</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Fever</td>
<td>0.4%</td>
<td>16%</td>
<td>11%</td>
<td>17%</td>
<td>10%</td>
<td>13%</td>
<td>3%</td>
</tr>
</tbody>
</table>

*Average value across all studies, all doses, all ages*
Safety Monitoring by CDC and FDA

• Passive monitoring through the Vaccine Adverse Event Reporting System (VAERS) and the v-safe text monitoring system for COVID-19 vaccine safety

• Active monitoring through Vaccine Safety Datalink, the Clinical Immunization Safety Assessment, and large databases such as the CMS Medicare Database and Sentinel/BEST covering ≥100 million lives
  – Combination of claims data and EHR data
  – Monitoring about 15 safety outcomes of interest
Vaccine Severe Allergic Reactions

• Anaphylaxis with the Pfizer-BioNTech and Moderna vaccines
  – Heightened surveillance in place in collaboration with CDC
• These vaccines should not be administered to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine
• Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration
COVID-19 Variants

• UK variant (B.1.1.7)
• South Africa variant (B.1.351)
• Brazil variant (P.1)
• California variant of interest (B.1.427/B.1.429)
• Others...
Adapting COVID-19 Vaccines

- Repeat dose toxicity studies or development and reproductive toxicology studies may not be necessary
- Animal studies are encouraged
  - Prototype and modified COVID-19 vaccine directed against SARS-CoV-2 variant(s)
  - Subsequently challenged with wild-type viruses representing clinically relevant circulating variants, including the variant(s) of interest, are encouraged
Adapting COVID-19 Vaccines

• Effectiveness of a modified COVID-19 vaccine can be evaluated based on the efficacy of the manufacturer’s authorized prototype COVID-19

• A determination of effectiveness should be supported by conducting clinical immunogenicity studies

• Sponsors should conduct a booster study in which the modified COVID-19 vaccine is administered to persons who previously received the prototype COVID-19 vaccine
Vaccine Dose and Schedule

• With deployment of vaccines in other countries and challenges in vaccine deployment in this country, questions of alternative dosage and administration schedules have been raised
  – Delay in administration of second doses
  – Single doses of two dose vaccines
  – Half doses of certain vaccines
  – Mix and match of vaccines

• If you don’t have time to do it right, what makes you think you’ll have the time to do it over – Seth Godin
COVID-19 Vaccine Development

• Vaccine development timelines shortened without compromising vaccine safety and efficacy standards
• Vaccine authorization or approval will follow a process that is as open to the public as possible
• The focus on the evaluation of safety and effectiveness through a transparent process is likely to improve confidence in any approved or authorized vaccine