DMID 21-0012 - Heterologous Platform Boost Study

Mix and Match

Advisory Committee on Immunization Practices
October 21, 2021

Robert L. Atmar, MD representing Mix and Match Study Team
Baylor College of Medicine
Disclosures:

The speaker receives grant funding from NIAID/IDCRC as co-Chair and site PI for the MixNMatch and as an investigator on the Moderna and Novavax Phase III studies.
<table>
<thead>
<tr>
<th>Group</th>
<th>Sample Size</th>
<th>EUA Vaccine</th>
<th>Interval (weeks)</th>
<th>Delayed Booster Vaccination</th>
<th>Strategy Tested</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50</td>
<td>Previously dosed Janssen – Ad26.COV2-S</td>
<td>≥12</td>
<td>Moderna- mRNA-1273</td>
<td>Same Strain Heterologous platform</td>
</tr>
<tr>
<td>2</td>
<td>50</td>
<td>Previously dosed Moderna – mRNA-1273</td>
<td>≥12</td>
<td>Moderna- mRNA-1273</td>
<td>Control - Same Strain &amp; platform</td>
</tr>
<tr>
<td>3</td>
<td>50</td>
<td>Previously dosed Pfizer/BioNTech – BNT162b2</td>
<td>≥12</td>
<td>Moderna- mRNA-1273</td>
<td>Same Strain Similar platform</td>
</tr>
<tr>
<td>4</td>
<td>50</td>
<td>Previously dosed Janssen – Ad26.COV2-S</td>
<td>≥12</td>
<td>Janssen – Ad26.COV2.S</td>
<td>Control - Same Strain &amp; platform</td>
</tr>
<tr>
<td>5</td>
<td>50</td>
<td>Previously dosed Moderna – mRNA-1273</td>
<td>≥12</td>
<td>Janssen – Ad26.COV2.S</td>
<td>Same Strain Heterologous platform</td>
</tr>
<tr>
<td>6</td>
<td>50</td>
<td>Previously dosed Pfizer/BioNTech – BNT162b2</td>
<td>≥12</td>
<td>Janssen – Ad26.COV2.S</td>
<td>Same Strain Heterologous platform</td>
</tr>
<tr>
<td>7</td>
<td>50</td>
<td>Previously dosed Janssen – Ad26.COV2-S</td>
<td>≥12</td>
<td>Pfizer/BioNTech – BNT162b2</td>
<td>Same Strain Heterologous platform</td>
</tr>
<tr>
<td>8</td>
<td>50</td>
<td>Previously dosed Moderna – mRNA-1273</td>
<td>≥12</td>
<td>Pfizer/BioNTech- BNT162b2</td>
<td>Same Strain Similar platform</td>
</tr>
<tr>
<td>9</td>
<td>50</td>
<td>Previously dosed Pfizer/BioNTech – BNT162b2</td>
<td>≥12</td>
<td>Pfizer/BioNTech – BNT162b2</td>
<td>Control - Same Strain &amp; platform</td>
</tr>
</tbody>
</table>

Study Visits: Days 1, 8 (safety call), 15, 29, Months 3, 6, 12
Blood for immunogenicity studies

Atmar et al. ACIP Oct 21, 2021
Volunteer Characteristics
**N = 458**

2 Participants
- Group 4 (n = 1)
- Group 6 (n = 1)
- High N protein antibody (D1) suggestive of prior infection

1 Participant
- Group 5 (n = 1)
- Covid-19 Study Day 27

---

### Table 1. Characteristics of the Participants at Enrollment

<table>
<thead>
<tr>
<th>Group</th>
<th>Booster</th>
<th>Primary EUA Immunization Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Janssen mRNA-1273</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Ad26.COV2-S</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>mRNA-1273</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>BNT162b2</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>Janssen</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>Moderna</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>Pfizer/BioNTech</td>
</tr>
</tbody>
</table>

#### Total Number
- Female: 26 (49.1), 32 (62.7), 29 (58.0)
- Male: 27 (50.9), 19 (37.3), 21 (42.0)

#### Age – years
- Mean (s.d.): 56.8 (14.5), 53.1 (16.2), 54.8 (17.4)
- Range: 24-81, 24-76, 22-85

#### Race – no. (%)
- Asian: 4 (7.5), 5 (9.8), 4 (8.0)
- Hawaiian or Pacific Islander: 0 (0.0), 0 (0.0), 0 (0.0)
- Black/African American: 1 (1.9), 2 (3.9), 3 (6.0)
- White: 46 (86.8), 41 (80.4), 43 (86.0)
- Multi-racial: 1 (1.9), 3 (5.9), 0 (0.0)
- Other: 1 (1.9), 0 (0.0), 0 (0.0)

#### Ethnicity – no. (%)
- Non-Hispanic: 49 (92.5), 46 (90.2), 47 (94.0)
- Hispanic/Latino: 4 (7.5), 4 (7.8), 3 (6.0)
- Unknown/Not reported: 0 (0.0), 1 (2.0), 0 (0.0)

#### Boost Interval
- Weeks: 15.4 wks, 18.4 wks, 21.5 wks
- Mean (s.d.): 13.7 (1.0), 16.4 (1.9), 16.8 (2.2)
- Range: 12.0-15.9, 12.4-20.0, 12.0-20.9

---

Atmar et al. ACIP Oct 21, 2021
Immunogenicity
Summary of Available Immunogenicity through D15/D29

Duke (Montefiori Lab): PsVN  (ID50, ID80 and in IU50/mL, IU80/mL)
   • D614G  N=~450 (50/arm)
   • VoCs N=60, 20/arm, 10/age group
     • Beta, Delta - In process

VRC (McDermott Lab): IgG Antibody Binding
   • 4-plex (validated) (AU/mL)
     • S-2P (Wa-1 and Beta) N=~450 (~50/arm) (AU/mL)
       • S-2P Wa-1: Binding Antibody Units/mL (BAU/mL) (International Standard)
   • 10-plex Fit for Purpose (FFP)
     • S-2P (Alpha, Beta, Gamma, Delta, Wa-1) (AUC/m)

Atmar et al. ACIP Oct 21, 2021
Immunogenicity of all three boosters - IgG binding Antibody (A-C) and Neutralizing Antibody (D-F) Through Days 15/29

A. Boost: mRNA-1273
B. Boost: Ad26.COV2.S
C. Boost: BNT162b2

D. Boost: mRNA-1273
E. Boost: Ad26.COV2.S
F. Boost: BNT162b2

Study Day: Day 1, Day 15, Day 29
All 3 vaccines

IgG Serum Binding Antibody Response to S-2P-Wa-1 (control), B.1.1.7 (alpha), and B.1.617.2 (delta)

FFP 10-plex ECLIA, by Group and Timepoint
Results are reported as Area Under Curve (AUC)
Safety
Two SAEs
1. Acute renal failure due to rhabdomyolysis from a fall - Unrelated
   30 days after mRNA-1273 vaccination
2. Acute cholecystitis - Unrelated
   24 days after Ad26.COV2.S vaccination.

No pre-specified study-halting rules were met
No new onset chronic medical conditions occurred (through study D29)
One related AESI
• Severe vomiting that led to a medically attended visit the day after vaccination: Ad26.COV2.S boost
Unsolicited AEs (deemed related to boost) of any severity grade

- mRNA-1273: 24/154 (15.6%)
- Ad26.COV2.S: 18/150 (12.0%)
- BNT162b2: 22/154 (14.3%)

Most related AEs were Grade 1 or 2 severity

Four related Grade 3 AEs:

- Vomiting in one participant - mRNA-1273 booster group
- Vomiting in one participant - Ad26.COV2.S booster group
- Fatigue in one participant - Ad26.COV2.S booster group
- Insomnia in one participant - Ad26.COV2.S booster group
Booster Solicited AEs

Local and Systemic Reactogenicity – Through Day 8
Limitations -

• Non-randomized, open label design
• Study not designed to compare between boosts
  - Didn’t control for intervals between primary vaccine and boosts
• Correlates of protection are not completely elucidated
• Correlates for severe disease and death are even less well understood
• This is only antibody data
  - Cellular immune responses are still being analyzed
• These data represent only early timepoints from the trial
  - Vaccines may differ in time to reach peak responses, and may have different durability of the responses
Conclusions -

1. Use of mRNA-1273, Ad26.COV2.S and BNT162b2 as booster vaccines led to anamnestic serologic responses in all 3 EUA-dose vaccine groups.

2. For a given primary EUA Covid-19 vaccine, heterologous boosts elicited similar or higher serologic responses as compared to their respective homologous booster responses.

3. mRNA vaccines resulted in higher antibody titers in the first 28 days after the boost.

4. No safety concerns identified.

Preprint: https://www.medrxiv.org/content/10.1101/2021.10.10.21264827v2
The “MixNMatch” Study Team

Clinical Sites
- Kaiser Permanente
- Washington Health Research Institute
- Fred Hutch / SCHARP
- The University of Washington

Labs
- Cincinnati Children's Hospital
- University of Pittsburgh
- University of Rochester
- New York University
- University of Maryland
- VRC
- Duke University
- Emory University
- FHI360

Regulatory, Data and Statistical Centers
- Moderna, Inc.
- Johnson & Johnson / Janssen
- Pfizer / BioNTech

University of Texas Medical Branch
Baylor College of Medicine
Questions?