Safety and Immunogenicity of Moderna COVID-19 Vaccine (2023-2024 Formula)

Monovalent XBB.1.5 Variant Vaccine

ACIP
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Moderna
Outline of Presentation

- Overview of clinical trial of XBB.1.5 vaccine
  - Design
  - Safety data
  - Immunogenicity data
- Analysis of cross neutralization data for recent variants
- Summary
Participants previously received 4 doses of COVID-19 vaccine (primary series and booster of mRNA-1273 + booster of BA.4/BA.5 vaccine)

*Focus of today's presentation will be on the monovalent XBB.1.5 vaccine selected for 2023-2024 season*

*All analyses are descriptive*
## Demographics and Baseline Characteristics

### Study 205J, XBB.1.5 Recipients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Monovalent XBB.1.5</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>N = 50</td>
</tr>
<tr>
<td>Mean Age – Years</td>
<td>51.6</td>
</tr>
<tr>
<td>Median Age – Years (range)</td>
<td>55 (21, 84)</td>
</tr>
<tr>
<td>≥ 65 years</td>
<td>11 (22.0%)</td>
</tr>
<tr>
<td>% Female</td>
<td>30 (60.0%)</td>
</tr>
<tr>
<td>Non-White Race</td>
<td>5 (10.0%)</td>
</tr>
<tr>
<td>Months between 2(^{nd}) and 3(^{rd}) Dose, median (Q1, Q3)</td>
<td>8.2 (7.8, 9.8)</td>
</tr>
<tr>
<td>Months between 3(^{rd}) and 4(^{th}) Dose, median (Q1, Q3)</td>
<td>9.8 (8.3, 10.3)</td>
</tr>
<tr>
<td>Months between 4(^{th}) and 5(^{th}) Dose, median (Q1, Q3)</td>
<td>8.2 (8.1, 8.3)</td>
</tr>
<tr>
<td>Prior SARS-CoV-2 Infection</td>
<td>34 (68.0%)</td>
</tr>
</tbody>
</table>
Safety of Moderna COVID-19 Vaccine (2023-2024 Formula)
XBB.1.5 Monovalent Vaccine
Local Reactions Following Booster Doses in Adults
Study 205J and Study 205H, Solicited Safety Set

Within 7 days of injection; No Grade 4 events reported
Chalkias et al., medRxiv, 2022, Chu et al, Nat Med 28:1041, 2022

Local reactions similar or lower than previously authorized Moderna COVID-19 vaccines
Systemic Reactions Following Booster Doses in Adults
Study 205J and Study 205H, Solicited Safety Set

Within 7 days of injection; No Grade 4 events reported
Chalkias et al., medRxiv, 2022, Chu et al, Nat Med 28:1041, 2022

Systemic reactions similar or lower than previously authorized Moderna COVID-19 vaccines
Immunogenicity of Moderna COVID-19 Vaccine (2023-2024 Formula)
XBB.1.5 Monovalent Vaccine
Rapid Assessment of Neutralization Capacity of 2023-2024 XBB.1.5 Vaccine Against Emerging Variants

- Pre and post booster sera from XBB.1.5 vaccine recipients assessed against previously dominant and newly emerged variants
  - Duke assay (Lenti-PsVNA) – Day 29 sera assessed
  - Moderna research assay (VSV-PsVNA) – Day 15 sera assessed
  - Titers generally consistent between Day 15 and Day 29

- Sera tested against:
  - Prior strains: Ancestral (D614G), BA.4/BA.5
  - XBB-lineage: XBB.1.5, XBB.1.16
  - New strains: EG.5.1, FL.1.5.1, BA.2.86

PsVNA – pseudovirus neutralization assay; VSV – vesicular stomatitis virus
Chalkias et al. medRxiv 2023 https://doi.org/10.1101/2023.08.22.23293434
Correlation between Duke and Moderna assay described in Choi et al, Nature Medicine https://doi.org/10.1038/s41591-021-01527-y
Cross Neutralization Results (Day 29) After XBB.1.5 Vaccine in Adults – Duke Assay
Study 205J, Per-Protocol Immunogenicity Set - All Participants

Substantial fold rise demonstrated across newer variants

Pseudovirus neutralization assay
Cross Neutralization Results (Day 29) After XBB.1.5 Vaccine in Adults by Baseline SARS-CoV-2 Serostatus - Duke Assay

Study 205J, Per-Protocol Immunogenicity Set

Cross neutralization demonstrated regardless of prior SARS-CoV-2 infection

Pseudovirus neutralization assay
Cross Neutralization Results (Day 15) After XBB.1.5 Vaccine in Adults - *Moderna Assay*

*Study 205J, Subset Analysis (N = 20)*

- **XBB.1.5**
  - Pre-Boost: 116
  - D15: 1207
  - 10.4-fold rise

- **XBB.1.16**
  - Pre-Boost: 144
  - D15: 1393
  - 9.7-fold rise

- **EG.5.1**
  - Pre-Boost: 118
  - D15: 1264
  - 10.7-fold rise

- **FL.1.5.1**
  - Pre-Boost: 93
  - D15: 1057
  - 11.4-fold rise

- **BA.2.86**
  - Pre-Boost: 162
  - D15: 1406
  - 8.7-fold rise

**Consistent cross neutralization demonstrated for newer variants, including BA.2.86**

Pseudovirus neutralization assay; PB - pre boost
Cross Neutralization Results (Day 15) After XBB.1.5 Vaccine in Adults by Baseline SARS-CoV-2 Serostatus - Moderna Assay

Study 205J, Subset Analysis (N=20)

Cross neutralization demonstrated regardless of prior SARS-CoV-2 infection

Neutralizing Antibody Titer (ID<sub>50</sub>)

<table>
<thead>
<tr>
<th></th>
<th>No Prior Infection</th>
<th>Prior Infection</th>
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<tbody>
<tr>
<td></td>
<td>XBB.1.5</td>
<td>XBB.1.6</td>
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<tr>
<td></td>
<td>13.6-fold rise</td>
<td>10.6-fold rise</td>
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<tr>
<td></td>
<td>1158</td>
<td>1158</td>
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<tr>
<td></td>
<td>EG.5.1</td>
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<tr>
<td></td>
<td>11-fold rise</td>
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<td></td>
<td>1065</td>
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<td></td>
<td>FL.1.5.1</td>
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<tr>
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<td>14.8-fold rise</td>
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<td>964</td>
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<tr>
<td></td>
<td>BA.2.86</td>
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<tr>
<td></td>
<td>14-fold rise</td>
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<td>1237</td>
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**Pseudovirus neutralization assay**
Cross Neutralization Results (Day 29) in Adults after **Bivalent BA.4/BA.5 Vaccine**

*Study 205H – Duke Assay*

- **Ancestral**
  - Pre-Boost: 1151
  - Day 29: 9961
  - 8.7-fold rise

- **BA.4/BA.5**
  - Pre-Boost: 123
  - Day 29: 3355
  - 27.3-fold rise

- **XBB.1.5**
  - Pre-Boost: 16
  - Day 29: 298
  - 12.3-fold rise

- **XBB.1.16**
  - Pre-Boost: 24
  - Day 29: 468
  - 19.3-fold rise

- **XBB.2.3.2**
  - Pre-Boost: 17
  - Day 29: 276
  - 15.8-fold rise

- **EG.5**
  - Pre-Boost: 13
  - Day 29: 148
  - 11.6-fold rise

Limited cross neutralization to newer variants after previously authorized BA.4/BA.5 bivalent vaccine

Pseudovirus neutralization assay; PB - pre boost
Summary
Safety and Immunogenicity of Moderna COVID-19 Vaccine (2023-2024 Formula)
*XBB.1.5 Vaccine*

**Clinical Study of XBB.1.5 Vaccine**
- Safety profile of XBB.1.5 vaccine consistent with previously authorized vaccines
- Robust neutralizing antibody titers against XBB.1.5, XBB.1.16, EG.5.1, FL.1.5.1, and BA.2.86 measured in sera from recipients of XBB.1.5 vaccine
- XBB.1.5 vaccine is anticipated to be effective against current SARS-CoV-2 variants

**Moderna’s Vaccine Preparedness**
- Moderna will supply an XBB.1.5 vaccine for Fall 2023
- Moderna will continue its ongoing variant monitoring and risk assessment of emerging variants
THANK YOU to Our Study Collaborators, Investigators, and Participants

- All investigators
- Study site personnel
- Laboratory personnel
- Most importantly, the individuals who participated in these trials