Immune Responses Post COVID-19 Vaccination: Possible Implications for the Omicron Variant

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Immunogenicity of Ad26.COV2.S vaccine against SARS-CoV-2 variants in humans


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Immunogenicity of Ad26.COV2.S Against SARS-CoV-2 Variants: Neutralizing Antibody Responses

Placebo

Ad26.COV2.S

Day 57

Day 71

Neutralizing Antibody Titer

No observed titer differences between Placebo and Ad26.COV2.S groups for WA-1/2020, BMG, B.1.1.7, CK-02, P.1, and B.1.529 variants.
Immunogenicity of Ad26.COV2.S Against SARS-CoV-2 Variants: Fc Functional Antibody Responses
Immunogenicity of Ad26.COV2.S Against SARS-CoV-2 Variants: CD8 and CD4 T Cell Responses
Immunogenicity of Ad26.COV2.S Against SARS-CoV-2 Variants

- NAb responses reduced 5-fold to B.1.351 and 3.3-fold to P.1 variants
- Less impact of variants on binding and Fc functional antibodies
- No impact of variants on CD8 T cell responses
- It is likely that cellular immune responses will be more preserved against SARS-CoV-2 variants that partially escape NAb responses

Alter et al. Nature, June 9, 2021
Differential Kinetics of Immune Responses Elicited by Covid-19 Vaccines
Magnitude and Durability of BNT162b2, mRNA-1273, and Ad26.COV2.S Antibody Responses Against SARS-CoV-2

Live Virus nAb

Pseudovirus nAb

RBD IgG

<table>
<thead>
<tr>
<th>BNT162b2</th>
<th>mRNA-1273</th>
<th>Ad26.COV2.S</th>
</tr>
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<tbody>
<tr>
<td>n</td>
<td>27</td>
<td>29</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Peak</th>
<th>6mo</th>
<th>8mo</th>
<th>Peak</th>
<th>6mo</th>
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<td>133</td>
<td>146</td>
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</table>

Fold Change (Peak to 8 months)

- 34
- 44
+4.3

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<tr>
<td>700</td>
<td>262</td>
<td>160</td>
<td>1569</td>
<td>414</td>
<td>273</td>
<td>391</td>
<td>185</td>
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</table>

Fold Change (Peak to 8 months)

- 4.5
- 5.7
- 2.11

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<tr>
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<td>2432</td>
<td>755</td>
<td>25677</td>
<td>4346</td>
<td>1546</td>
<td>1361</td>
<td>843</td>
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</tbody>
</table>

Fold Change (Peak to 8 months)

- 28.6
- 16.6
- 1.6

Collier et al. NEJM. October 15, 2021
Magnitude and Durability of BNT162b2, mRNA-1273, and Ad26.COV2.S Antibody Responses Against Variants

- **WA1/2020**
  - NT50
  - BNT162b2
  - mRNA-1273
  - Ad26.COV2.S
  - n: 29, 30, 23, 20, 21, 20, 8, 8
  - Peak 6mo 8mo Peak 6mo 8mo Peak 6mo 8mo
  - 700 262 160 1569 414 273 391 185

- **Delta (B.1.617.2)**
  - NT50
  - BNT162b2
  - mRNA-1273
  - Ad26.COV2.S
  - n: 29, 30, 23, 20, 21, 20, 8, 8
  - Peak 6mo 8mo Peak 6mo 8mo Peak 6mo 8mo
  - 191 80 67 274 115 76 53 107

- **Alpha (B.1.1.7)**
  - NT50
  - BNT162b2
  - mRNA-1273
  - Ad26.COV2.S
  - n: 29, 30, 23, 20, 21, 20, 8, 8
  - Peak 6mo 8mo Peak 6mo 8mo Peak 6mo 8mo
  - 378 128 89 786 223 107 60 148

- **Beta (B.1.351)**
  - NT50
  - BNT162b2
  - mRNA-1273
  - Ad26.COV2.S
  - n: 29, 30, 23, 20, 21, 20, 8, 8
  - Peak 6mo 8mo Peak 6mo 8mo Peak 6mo 8mo
  - 130 63 54 293 103 86 33 62
Magnitude and Durability of BNT162b2, mRNA-1273, and Ad26.COV2.S T Cell Responses Against SARS-CoV-2

<table>
<thead>
<tr>
<th></th>
<th>CD4</th>
<th>CD8</th>
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<tbody>
<tr>
<td>BNT162b2</td>
<td>mRNA-1273</td>
<td>Ad26.COV2.S</td>
</tr>
<tr>
<td>n</td>
<td>3 24 20</td>
<td>8 9 8</td>
</tr>
</tbody>
</table>

%IFN+ / CD4+CD3+ T Cells

<table>
<thead>
<tr>
<th></th>
<th>6mo</th>
<th>8mo</th>
<th>6mo</th>
<th>8mo</th>
<th>Peak</th>
<th>6mo</th>
<th>8mo</th>
<th>Peak</th>
<th>8mo</th>
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<tbody>
<tr>
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<td>0.021</td>
<td>0.027</td>
<td>N/A</td>
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<tr>
<td>CD8 Peak</td>
<td>0.017</td>
<td>0.035</td>
<td>0.016</td>
<td>N/A</td>
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<td>0.017</td>
<td>0.12</td>
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</tbody>
</table>
Differential Kinetics of Immune Responses Elicited by BNT162b2, mRNA-1273, and Ad26.COV2.S

- mRNA vaccines induce high initial antibody titers, but these responses decline sharply by 6 months and even further by 8 months.

- Ad26.COV2.S induces lower initial antibody titers, but these responses are durable and show minimal decline for 8 months.

- Ad26.COV2.S induces higher CD8+ T cell responses than mRNA vaccines.
Ad26.COV2.S vs. BNT162b2 Boosting in Individuals Vaccinated with BNT162b2: NAb Responses

Time Following Boost Immunization

Tan et al. medRxiv December 5, 2021
Ad26.COV2.S vs. BNT162b2 Boosting in Individuals Vaccinated with BNT162b2: CD8 T Cell Responses

Time Following Boost Immunization

Tan et al. medRxiv December 5, 2021
Ad26.COV2.S vs. BNT162b2 Boosting in Individuals Vaccinated with BNT162b2

- Ad26.COV2.S and BNT162b2 boost antibody titers similarly by week 4 in individuals vaccinated with BNT162b2 but with different kinetics

- Ad26.COV2.S is more potent than BNT162b2 at boosting CD8 T cell responses

- “Mix-and-match” and homologous boosts increase immune responses that will likely provide cross-reactivity against SARS-CoV-2 variants
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