Fourth dose COVID mRNA vaccines’ Immunogenicity & Efficacy Against Omicron variant of concern

WHO COVID-19 Vaccines Research
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Data not yet published
Introduction

Sheba HCW COVID-19 Cohort

15,208 HCW at the Sheba Medical Center

13,924 HCW Received a 2\textsuperscript{nd} dose

12,569 HCW Received a 3\textsuperscript{rd} dose

6597 HCW enrolled to the Sheba HCW COVID Cohort with recorded serology history
Waning of humoral immune response to 2nd vs. 3rd dose

Sheba HCW COVID-19 Cohort

15,208 HCW at the SMC

13,924 HCW Received a 2nd dose

12,569 HCW Received a 3rd dose

3972 HCW Received a 3rd dose
And participating in the Sheba COVID Cohort study

6597 HCW enrolled to the Sheba HCW COVID Cohort with recorded serology history
75 HCW with known history of SARS-CoV-2 infection
2621 HCW with recent IgG > 700 BAU

Open-label, non-randomized, controlled trial

Visit number | 1 | 2 | 3 | 4
---|---|---|---|---
Day | 0 | 7 | 14 | 21
Vaccine | BNT162b2 30 µg or mRNA1273 50 µg |
| | X |
Blood sample | IgG | X | X | X | X |
PNT | X | X | X |
microneutralization | X | X | X | X |
IgA | X | X | X |
Tcell activity | X | X |
Bcell repertoire | X | X |
Nasal/NP swab | SARS-CoV-2 PCR | X | X | X | X |
Questionnaires | Background comorbidity | X |
| | Adverse events | X |

Matched by: age, IgG, time from 3rd dose

BNT162b2 arm N=154
Dec 27, 2021

mRNA1273 arm N=120
Jan 5, 2022

Matched Control group N=426

Received the 4th dose during the follow-up period N=181
Jan 2, 2022: MOH approves 4th dose

Regev-Yochay et al. Submitted
IgG titers after 3 doses of BNT162b2 & a 4\textsuperscript{th} dose of either BNT162b2 or mRNA1273
Neutralizing ab titers after 3 doses of BNT162b2 & a 4th dose of either BNT162b2 or mRNA1273
Neutralization of live virus – before and after 4\textsuperscript{th} dose

a. 4\textsuperscript{th} dose of BNT162b2

Five months after 3\textsuperscript{rd} dose
One week after 4\textsuperscript{th} dose
Two weeks after 4\textsuperscript{th} dose

b. 4\textsuperscript{th} dose of mRNA1273

Five months after 3\textsuperscript{rd} dose
One week after 4\textsuperscript{th} dose
Two weeks after 4\textsuperscript{th} dose

Regev-Yochay et al. Submitted
Breakthrough with omicron induces neutralization of various VOCs

- Five months after 3rd dose
- One week after 4th dose
- Two weeks after 4th dose

Neutralization (titer/log2)

Vaccine: V3

Infection: Omicron, Omicron, Omicron, Omicron

VOC: WT, Alpha, Delta, Omicron

Neutralization:
- X1.3 vs. a fourth dose
- X2
- X6
Cumulative incidence of **SARS-CoV-2 infections** among BNT162b2 and mRNA1273 recipients and their matched controls

**BNT**

- VE: 30% (-9-55%)

**Moderna**

- VE: 11% (-43-43%)

### Characteristics of Breakthrough Infections

<table>
<thead>
<tr>
<th></th>
<th>BNT162b2</th>
<th>Control - B</th>
<th>mRNA1273</th>
<th>Control - M</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Breakthrough Infections</td>
<td>28</td>
<td>46</td>
<td>24</td>
<td>36</td>
</tr>
<tr>
<td>Symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>7 (25%)</td>
<td>3 (7%)</td>
<td>7 (29%)</td>
<td>3 (8%)</td>
</tr>
<tr>
<td>Mild w/o Fever</td>
<td>18 (64%)</td>
<td>30 (65%)</td>
<td>16 (67%)</td>
<td>26 (72%)</td>
</tr>
<tr>
<td>Fever&lt;48h</td>
<td>2 (7%)</td>
<td>4 (9%)</td>
<td>1 (4%)</td>
<td>5 (14%)</td>
</tr>
<tr>
<td>Fever &gt; 48h</td>
<td>0 (0%)</td>
<td>8 (17%)</td>
<td>0 (0%)</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>Required ED/Hospitalization</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Lowest N-gene Ct value</td>
<td>25.3 (23-28)</td>
<td>24.7 (23-27)</td>
<td>25.1 (22-29)</td>
<td>24.9 (23-27)</td>
</tr>
</tbody>
</table>
Conclusions

• Both mRNA vaccines induce a significant IgG and neutralizing Ab. Response.

• A 4\textsuperscript{th} dose restores the response achieved by the 3\textsuperscript{rd} dose.

• Rate of waning immune response following the 4\textsuperscript{th} dose - yet to be shown.

• Frequent breakthrough infections; mostly very mild, yet infectious

• Rigorous active surveillance & rapid spread of Omicron allowed assessing VE: Only 11-30% VE in preventing infections.

• We did not assess severe infections/hospitalizations/death.
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