Imagine a world without AIDS

Safety and immunogenicity of DNA and MVA HIV-1 subtype C vaccine prime-boost regimens: A Phase I trial in HIV-uninfected Indian volunteers

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ABSTRACT

With over 2.5 million HIV-infected people and evidence of ongoing transmission, the search for a preventive HIV vaccine for India is high priority. We previously reported moderate immunogenicity of an MVA-based HIV vaccine in Indian volunteers. Other studies suggest that a superior immunogenicity can be achieved by heterologous adjuvanted regimens. We assessed the safety and immunogenicity of HIV-1 subtype C-based DNA and MVA prime-boost regimens in Indian adults. Volunteers were randomly assigned to receive 2 doses of DNA followed by 2 doses of MVA [Group A] or 3 doses of MVA [Group B].

Safety, local and systemic reactogenicity profiles were comparable between groups, and were mostly mild and transient. No serious adverse events were reported.

Immunogenicity: In group A, vaccine recipients’ IFN-γ ELISPOT responses were detected in 0%, 25%, 100%, and 100% participants post 1st, 2nd, 3rd and 6th vaccinations, and 70%, 92%, and 70% of group B participants post 1st, 2nd, and 3rd vaccinations, respectively. Responses were directed to multiple-HIV proteins (mean magnitude of 144 – 295 EIU/TFC (PRMO) in most volunteers. HIV-specific Tetramer positive responses were detected in 3/11 and 4/12 volunteers at week 1 and 2, respectively.

RESULTS

Table 2. IFN-γ ELISPOT responses

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<tbody>
<tr>
<td></td>
<td>ADVAX</td>
<td>DNA-MVA</td>
<td>AVDAX</td>
<td>MVA</td>
<td>AVDAX</td>
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<tr>
<td>TFC (median ± SD)</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5 ± 0.5</td>
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- * A number of positive responses / number of subjects after each vaccination.
- Each and every volunteers consist of ADVAX in Group A and TBC-M4 in Group B.
- ** T-cell vaccination consisted of TBC-M4 in Group A and TBC-M4 in Group B, while fourth vaccination consisted of TBC-M4 in Group B.
- A subject was counted as positive if the response was positive at week 1 and/or 2.

**Table 1. Trial Design**

<table>
<thead>
<tr>
<th>Group</th>
<th>Study Sites</th>
<th>N/A</th>
<th>ADVAX (100 µg)</th>
<th>ADVAX (100 µg)</th>
<th>TFC-M4 (0.5 µL) in 0.5 mL</th>
<th>TFC-M4 (0.5 µL) in 0.5 mL</th>
<th>TFC-M4 (0.5 µL) in 0.5 mL</th>
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<tbody>
<tr>
<td>A</td>
<td>N/A</td>
<td>0/2</td>
<td>0/2</td>
<td>1/2</td>
<td>0/1</td>
<td>0/1</td>
<td>0/1</td>
</tr>
<tr>
<td>B</td>
<td>N/A</td>
<td>0/2</td>
<td>0/2</td>
<td>1/2</td>
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<td>0/1</td>
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**Figure 1. Magnitude of IFN responses in trial participants**

**Figure 2. Anti HIV antibodies (frequency and breadth) in trial participants**

**Figure 3. Flow Cytometry**

**Figure 4. HIV neutralization**

**SUMMARY**

- No major safety concerns were reported and both vaccine candidates were well tolerated.
- All 12 volunteers from group A and 11 of 12 volunteers from group B showed presence of IFN-γ ELISPOT responses at 14 day following last vaccination.
- Nine of 12 vaccines from group B and 7 of 12 vaccines from group A showed presence of neutralizing antibodies at 14 days following the last vaccination.

**CONCLUSIONS**

- Both DNA and MVA vaccines were found to be safe and were well tolerated.
- Heterologous DNA-MVA prime boost strategy elicited comparable T-cell immune responses to the homologous MVA strategy.