Ad26 & MVA Vaccines in Acutely Treated HIV: Safety, Immunogenicity and Viral Rebound

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## Disclosure

<table>
<thead>
<tr>
<th>Relations that could be relevant for the meeting</th>
<th>Company names</th>
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<tbody>
<tr>
<td>Sponsorship or refund funds</td>
<td>• none</td>
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<tr>
<td>Payment or other financial remuneration</td>
<td>• none</td>
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<tr>
<td>Shareholder rights</td>
<td>• none</td>
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<td>Other relations</td>
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Background

• ART-free viremic control requires effective and persistent immune surveillance
  – Therapeutic HIV vaccines have failed to control viremia likely due to viral escape and immune dysfunction
  – Early treated people may be ideal candidates for HIV vaccines
    • Low HIV burden
    • Less viral diversity
    • Preserved quality of immune responses
    • Higher proportion of post-treatment controllers

De Souza, AIDS 2015; Takata, Sci Transl Med 2018; Saez-Cirion, Plos Pathog 2014
RV245 participants at Thai Red Cross, Bangkok
- 18-50 years old
- Started on ART during AHI (FI-FIV)
- HIV-1 RNA <50 copies/mL for ≥ 48 weeks
- CD4 >400 cells/mm³

ATI Criteria:
- RNA <50 c/mL x 52 wks
- CD4 >400 cells/mm³
- No clinical HIV disease

ART resumption criteria
- Confirmed VL > 1000 c/ml at least 7 days apart
- Confirmed CD4 < 350 cells/mm³
- Acute retroviral syndrome
- Pregnancy
- Participant’s request
## Characteristics at enrollment

<table>
<thead>
<tr>
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<th>Ad26MVA (n=17)*</th>
<th>Placebo (n=9)</th>
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<tbody>
<tr>
<td><strong>Median age, yrs</strong></td>
<td>24</td>
<td>25</td>
</tr>
<tr>
<td><strong>N (%) Fiebig Stage at ART initiation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>II</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>III</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>IV</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td><strong>HIV subtype</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRF01_AE</td>
<td>12</td>
<td>9</td>
</tr>
<tr>
<td>CRF01_AE/B</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Nontypeable</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td><strong>Median pre-ART VL, log_{10}c/ml</strong></td>
<td>5.9</td>
<td>6.4</td>
</tr>
<tr>
<td><strong>Median duration of ART, months</strong></td>
<td>26</td>
<td>26</td>
</tr>
<tr>
<td><strong>N (%) ART Regimens</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NNRTI (EFV)</td>
<td>15</td>
<td>9</td>
</tr>
<tr>
<td>Others</td>
<td>2</td>
<td>0</td>
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<tr>
<td><strong>Mean CD4 count, cells/mm³</strong></td>
<td>633</td>
<td>586</td>
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- All were Asian male
- 1 participant in the vaccine arm was excluded from analyses at request of the Thai MoPH IRB due to a repeat screening test
Safety: Vaccinations were well-tolerated with no safety concerns

- All solicited AEs were grades 1 and 2
- Most frequent local AEs: pain/tenderness, warmth, erythema
- Most frequent systemic AEs: fatigue, headache, myalgia

- Unsolicited AEs
  - Most common were infections
  - All AEs of grade 3 (4 cases) and grade 4 (2 cases) were unrelated to study vaccination
Immunogenicity

Week 26: post-two Ad26 and one MVA
Week 50: post-two Ad26 and two MVA

Humoral

- Higher gp140 Mos1 IgG titers in the vaccine arm

ADCC

- Higher ADCC to HIV ENV gp140.Mos 1 in the vaccine arm

Intracellular cytokine staining (ICS)

- Vaccine arm had higher CD8 and CD4 IFNγ responses to vaccine inserts (ENV, GAG and POL)

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Data from Janssen labs, A. Schuetz (AFRIMS)
Immunogenicity: T-cell response: IFN-g ELISPOT

- Subpools of 10 peptides spanning GAG, POL and ENV
- Total breadth = Number of GAG+POL+ENV positive subpools

- Higher median numbers of positive subpools by IFN-g ELISPOT in the vaccine arm at weeks 26 and 50
Viral load rebound post-ATI

Median (IQR) time to VL > 20 copies/ml for all participants: 20 (11-182) days

- Post-treatment controller was HLA B5701+¹
- No acute retroviral syndrome or new resistance mutations
- 25 of 26 participants resumed ART and had VL suppression by median of 28 (IQR 19-33) days

¹Data from R. Thomas (MHRP)
Proportion of participants who maintained viremic control post-ATI

Viral load 20 copies/ml

Median (Range)
- Ad26/MVA mos: 23 (11 - 46) days
- Placebo: 17 (13 - 182) days
Log-rank test: P = 0.26

Viral load 1000 copies/ml

Median (Range)
- Ad26/MVA mos: 28 (13 - 46) days
- Placebo: 21 (13 - 252) days
Log-rank test: P = 0.35
Conclusion: AD26 & MVA vaccines in acutely treated HIV

• Ad26.Mos prime with MVA-Mosaic boost in early treated people
  – Safe and immunogenic
  – But did not lead to ART-free viremic control
  – One post-treatment controller in the placebo arm
  – Analysis for biomarkers of viral load rebound is ongoing

• Additional therapy is needed
  – TLR7 agonist +Ad26.MVA
  – Potentially longer ATI to examine post peak viral load set point
Participants

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RV405
RV254, RV409, RV411 and RV397

ARV for RV254:
Thai GPO
ViiV Healthcare
Merck
Gilead

Acknowledgements

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