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

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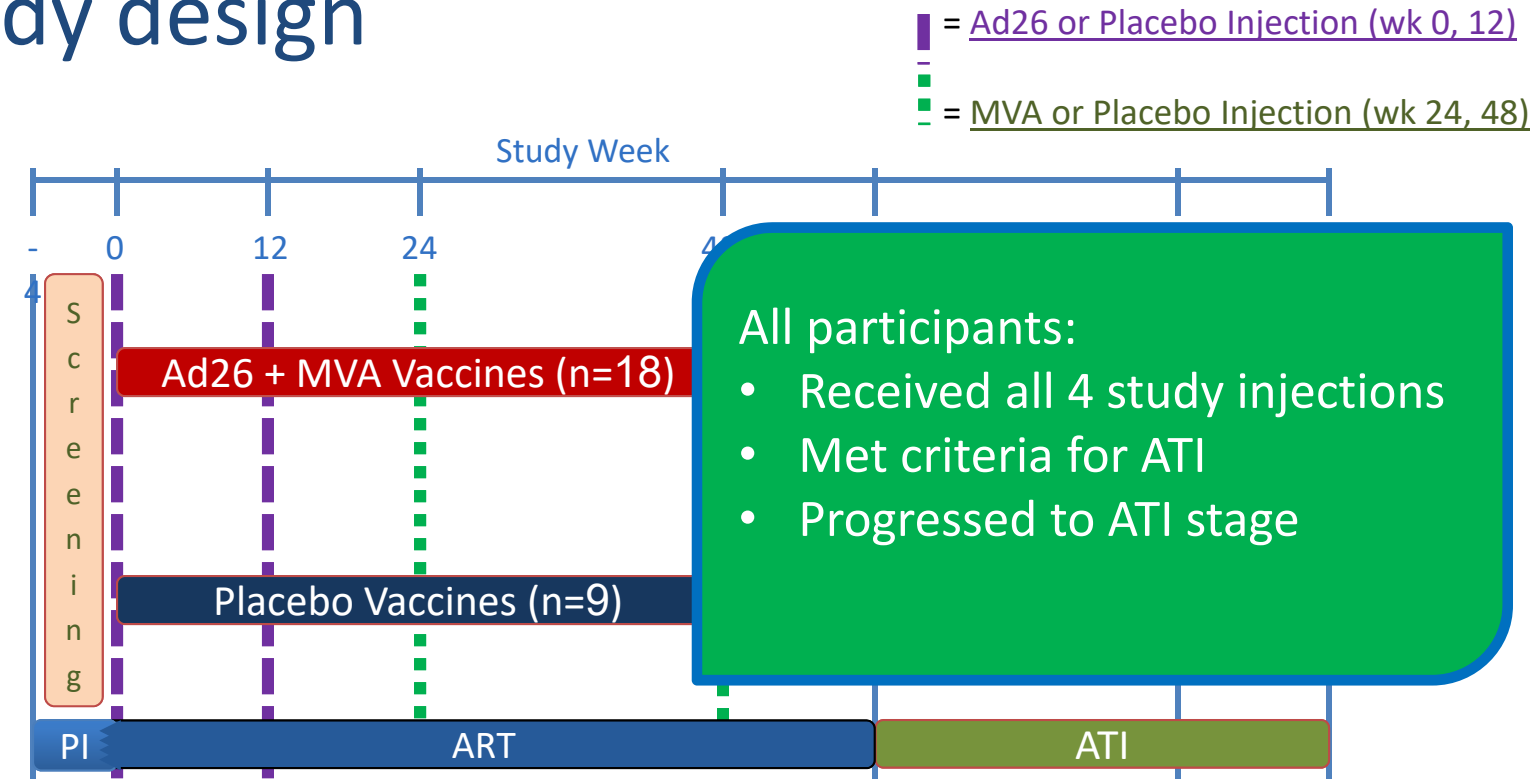
Background

- 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

Study design



RV254 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/mm^3

ATI Criteria:

- RNA <50 c/mL x 52 wks
- CD4 >400 cells/mm^3
- No clinical HIV disease

ART resumption criteria

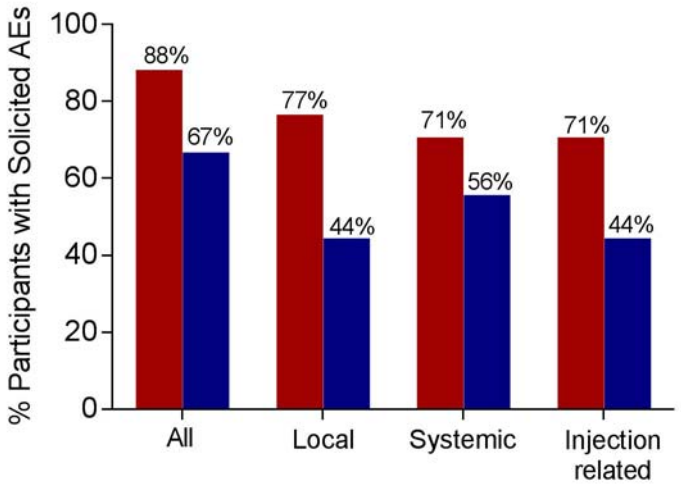
- **Confirmed VL > 1000 c/ml at least 7 days apart**
- Confirmed CD4 < 350 cells/mm^3
- Acute retroviral syndrome
- Pregnancy
- Participant's request

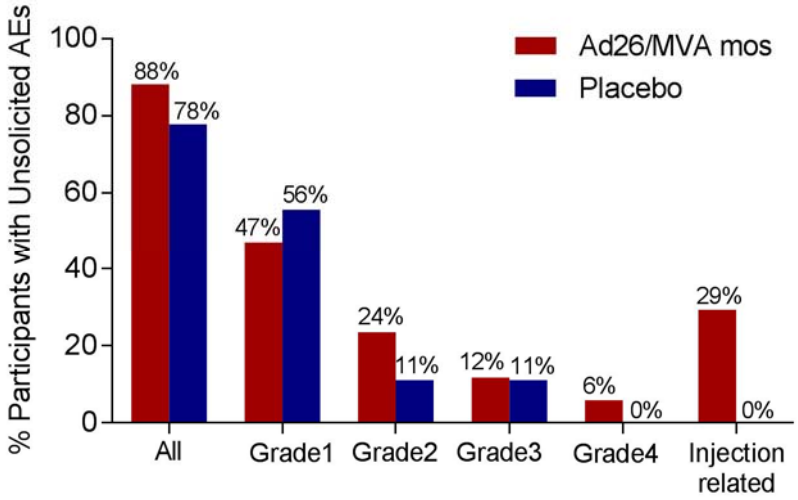
Characteristics at enrollment

	Ad26MVA (n=17)*	Placebo (n=9)
Median age, yrs	24	25
N (%) Fiebig Stage at ART initiation		
I	0	1
II	6	4
III	6	4
IV	5	0
HIV subtype		
CRF01_AE	12	9
CRF01_AE/B	3	0
Nontypeable	2	0
Median pre-ART VL, log_{10}c/ml	5.9	6.4
Median duration of ART, months	26	26
N (%) ART Regimens NNRTI (EFV)	15	9
Others	2	0
Mean CD4 count, cells/mm^3	633	586

- 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





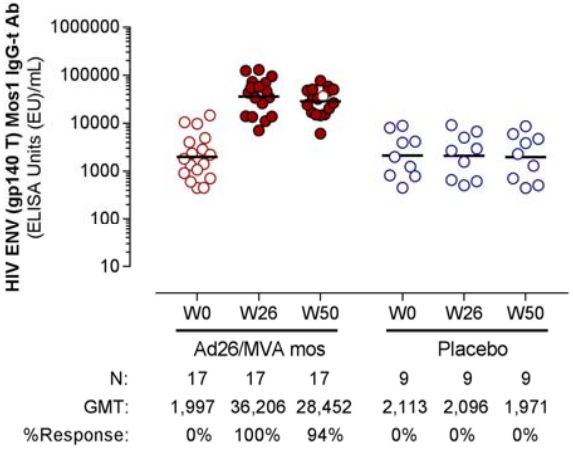
- All solicited AEs were grades 1 and 2
- Most frequent local AEs: pain/tenderness, warmth, erythema
- Most frequent systemic AEs: fatigue, headache, myalgia

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

Immunogenicity

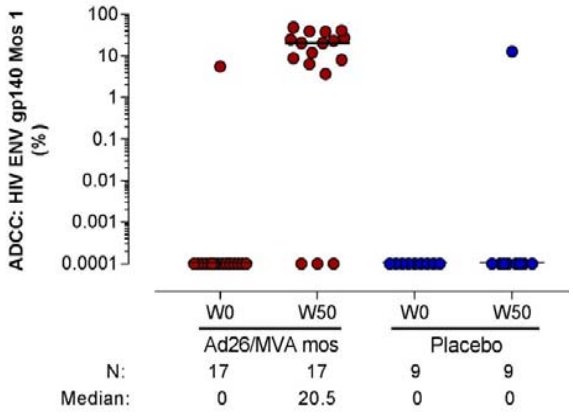
Week 26: post-two Ad26 and one MVA
Week 50: post-two Ad26 and two MVA

Humoral



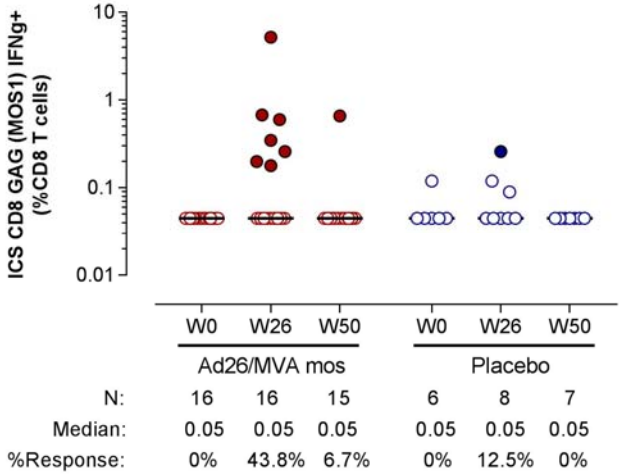
- Higher gp140 Mos1 IgG titers in the vaccine arm

ADCC



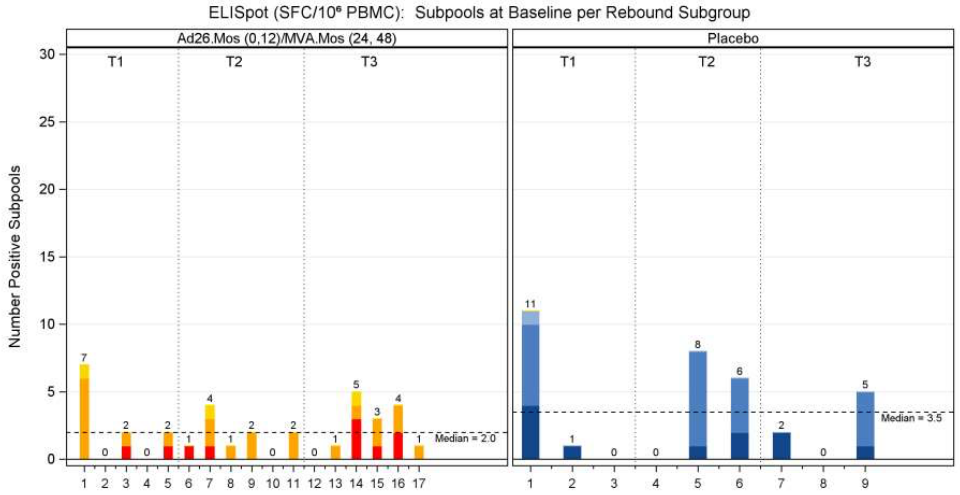
- Higher ADCC to HIV ENV gp140.Mos 1 in the vaccine arm

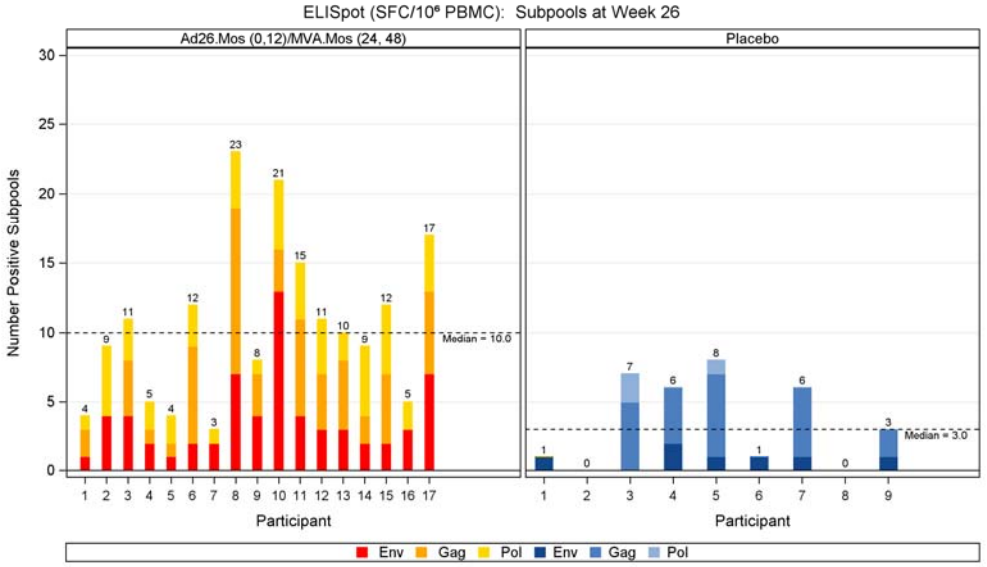
Intracellular cytokine staining (ICS)



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

Immunogenicity: T-cell response: IFN-g ELISPOT





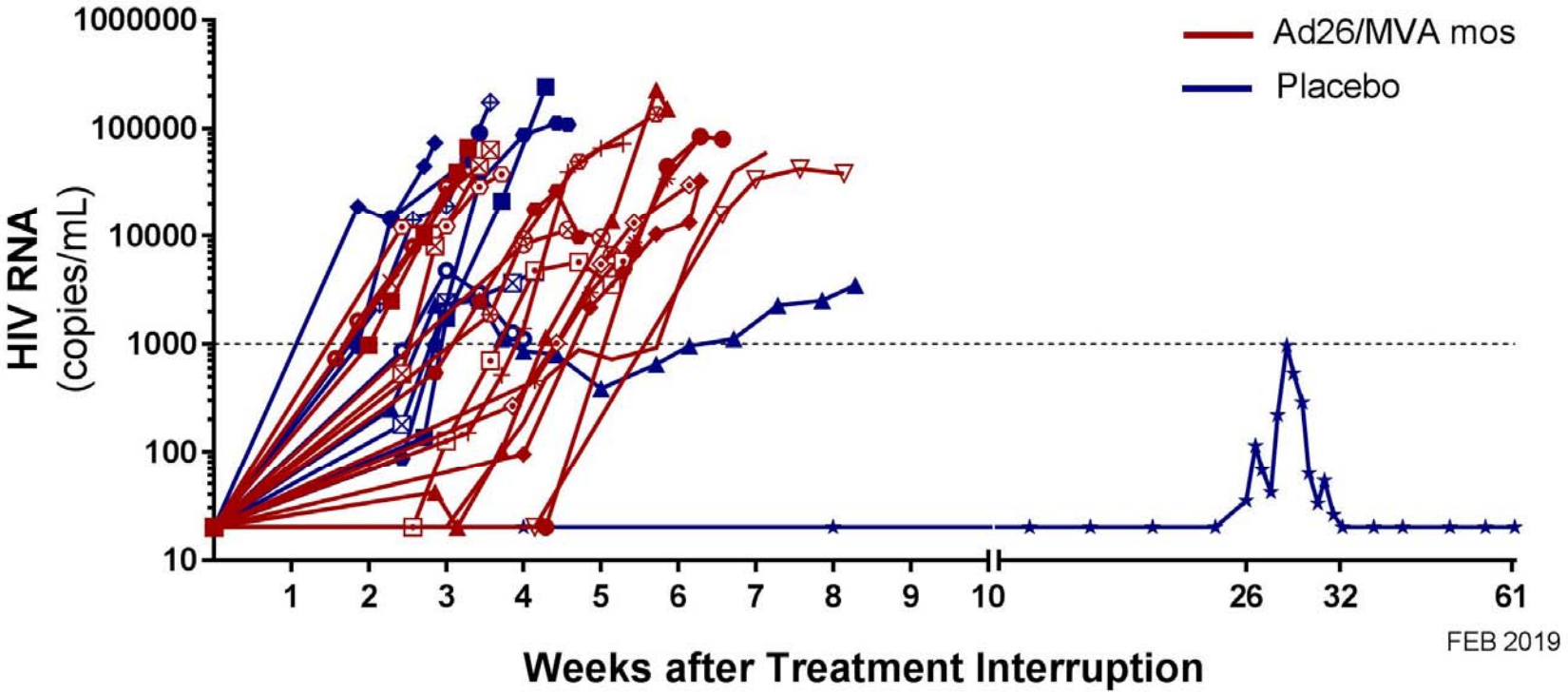
- Subpools of 10 peptides spanning GAG, POL and ENV
- Total breadth = Number of GAG+POL+ENV positive subpools

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

Data from L. Peter and D. Barouch (BIDMC)

Viral load rebound post-ATI

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

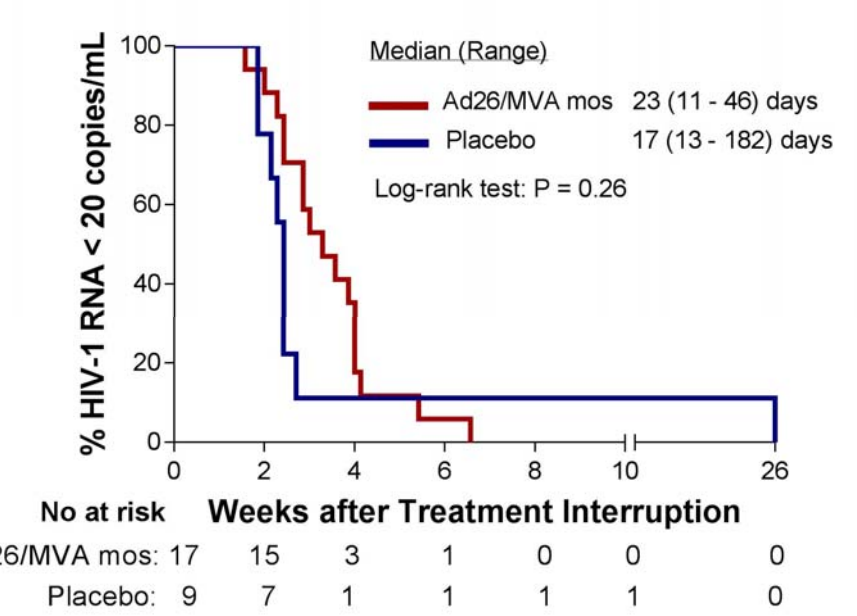


- Post-treatment controller was HLA B5701+[1]
- No acute retroviral syndrome or new resistance mutations
- 25 of 26 participants resumed ART and had VL suppression by median of 28 (IQR 19-33) days

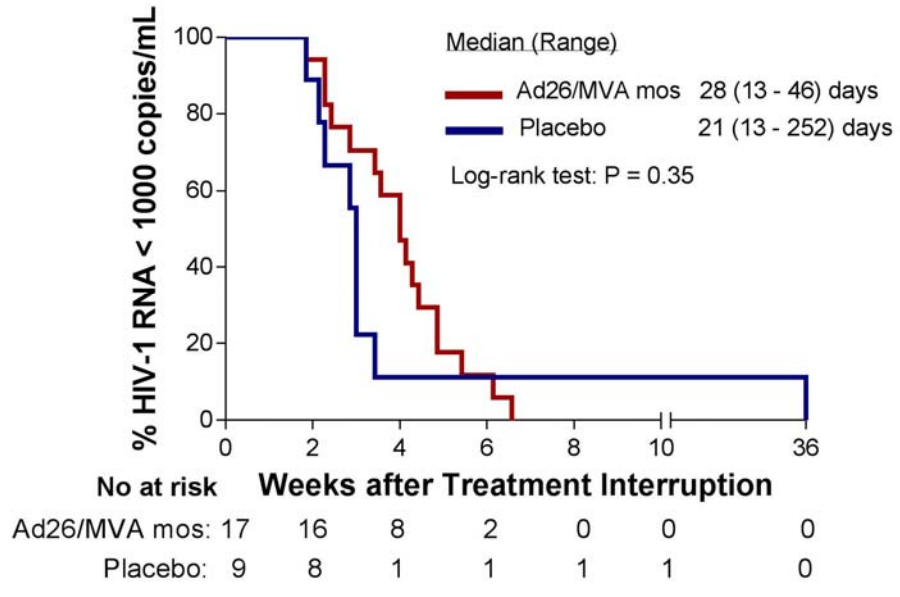
[1]*Data from R. Thomas (MHRP)*

Proportion of participants who maintained viremic control post-ATI

Viral load 20 copies/ml



Viral load 1000 copies/ml



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

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Participants

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