PrEPVacc: A Phase IIb three-arm, two-stage HIV prophylactic vaccine trial with a second randomization to compare TAF/FTC to TDF/FTC as pre-exposure prophylaxis

IAVI G003 Protocol
A Phase 1, Randomized, Open-label Study of eOD-GT8 60mer mRNA in HIV-1 Uninfected Adults in Good General Health

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AVAC HVAD Webinar 24th May 2022
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Other Lab Activities
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Jill Schwartz (CONRAD, US)
- To assess the efficacy of two HIV-1 prophylactic vaccine regimens, each compared to placebo in preventing acquisition of HIV

- To determine the effectiveness of Descovy PrEP as a function of the effectiveness of Truvada PrEP and hypothetical placebo

- To determine the safety of (i) each vaccine combination regimen compared to placebo and (ii) Descovy compared to Truvada
Vaccine A

Vaccine B

Placebo

Factorial

- Descovy = A+D
- Truvada = A+T
- Descovy = B+D
- Truvada = B+T
- Descovy = placebo+D
- Truvada = placebo+T

Randomised Placebo-controlled vaccine trial

Randomised Open-label PrEP trial
Study schema

**Injection visits**
- **Vaccine A**: DNA-HIV-PT123 plus AIDSVAX B/E at Visits 2, 4, 8, 12 (wks 0,4,24,48)
- **Vaccine B**: DNA-HIV-PT123 plus CN54gp140/MPLA at visits 2 and 4, MVA-CMDR/CN54gp140/MPLA at visits 8 and 12
- **Placebo**: Salty water at visits 2, 4, 8 and 12 = placebo

**Descovy or Truvada**

Blood for haematology/biochemistry at visits 1, 4, 6, 9, 13

Blood for HIV testing/store at visits 1, 2, 4, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, every 12 week during long-term FU

Larger blood draw for immune responses and store at visits 2, 6, 9, 13, 15 and at a new HIV infection visit
Primary Outcome Measures – Vaccine Trial

**Efficacy:** HIV acquisition by a participant who had completed the first three immunizations and was HIV negative *at the visit 2 weeks after the third immunization*

- **Final analysis assumptions**
  - Target *efficacy of 70%* relative to placebo
  - Target HIV incidence: 4/100 person-years
  - Loss to follow-up: 10%
  - Power: 90%
  - Sample size: ≥556 per comparison group

**Safety:** A clinical decision to discontinue the vaccine regimen for an adverse event that is considered related to product
Primary Outcome Measures – PrEP Trial

- **Effectiveness:** HIV acquisition at or before the visit 2 weeks after the third immunisation by a participant who was HIV negative at enrolment.
  - **Averted Infections Ratio**
    - Measures the proportion of infections that would be averted by using Descovy rather than Truvada.
    - Takes account of background incidence (obtained through PrEPVacc registration cohort & follow-up of trial participants after 26 week).

- **Safety:** A clinical decision to discontinue the PrEP regimen for an adverse event that is considered related to product.

Trial Communities

- General population, MSM, Female Sex Workers, Maputo, Mozambique
- General population, Durban, South Africa
- Female bar workers, Mbeya, Tanzania
- Bar workers and Female Sex Workers, Dar Es Salaam, Tanzania
- Fisherfolk and key populations in Masaka, Uganda
Screening/enrolment progress (N=1668)

<table>
<thead>
<tr>
<th>Site</th>
<th>Screened</th>
<th>Enrolled (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Masaka, Uganda</td>
<td>502</td>
<td>325 (65)</td>
</tr>
<tr>
<td>Mbeya, Tanzania</td>
<td>226</td>
<td>145 (64)</td>
</tr>
<tr>
<td>Dar es Salaam, Tanzania</td>
<td>189</td>
<td>108 (57)</td>
</tr>
<tr>
<td>Durban, South Africa</td>
<td>171</td>
<td>137 (80)</td>
</tr>
<tr>
<td>Overall</td>
<td>1088</td>
<td>715 (66)</td>
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IAVI G003 Phase I Trial — launch in Africa

A Phase 1, Randomized, Open-label Study of eOD-GT8 60mer mRNA in HIV-1 Uninfected Adults in Good General Health (Rwanda and South Africa)

Key Aims of the trial:

1. Evaluate safety and immunogenicity of the vaccine
2. Test eOD-GT8 60mer mRNA priming — will mRNA generate similar VRC01-class responses as in G001, and G002 in an African population where HIV vaccine is most needed?
3. Increase capacity for novel sampling methods and cutting-edge immunological analyses in Africa — analysis to be conducted by African scientists in country
G003 Background and Study Rationale

• This is a phase 1 clinical trial to assess the safety, tolerability, and ability to induce a desired immune response to eOD-GT8 60mer mRNA Vaccine in a small number of HIV-1 uninfected adults in good general health.
• This is the first time this immunogen is being tested in Africa; it is also being concurrently tested in the USA in a separate study.
• The inclusion of African populations at this stage of the development phase provides an opportunity for early safety and immunological readouts that can inform the applicability of this strategy in the continent most affected by HIV.
• eOD-GT8 60mer mRNA Vaccine is a nanoparticle composed of 60 recombinant protein subunits engineered to represent the outer domain (OD) of the HIV-1 gp120 envelope fused to a bacterial enzyme, Lumazine synthase (LS), through a 15-amino acid Glycine-Serine linker. eOD-GT8 60mer will be delivered using an mRNA-based vaccine platform (eOD-GT8 60mer mRNA Vaccine).
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Establishment of New Clinical Capacity

Fine Needle Aspiration (Aurum and CFHR)

- Allows “real-time” monitoring of B-cells responses in germinal centers

  - 2 weeks post immunization

Leukapheresis (Aurum only)

- Allows in depth characterization of B-cell responses with lower overall blood volume

  - Week 16 (8 weeks post 2nd dose)
Final remarks

- These two studies are examples of innovative trial designs and approaches that can quickly ask and answer key questions with African leadership.
- PrEPVacc is an adaptive phase 2b trial testing a combined regimen of PrEP plus two combination HIV vaccines.
- G003 is an Experimental Medicine HIV Vaccine Trial aimed at answering important questions around inducing the desired B-cell responses while at the same time building the required capacity in African centers.
THANK YOU
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