Status of HIV vaccine development
Update on advanced projects

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2017 WHO Product Development for Vaccines Advisory Committee Consultation
22 June, 2017
Geneva
### HIV/AIDS Continues to Devastate

<table>
<thead>
<tr>
<th>78 million infected</th>
<th>HALF of all people living with HIV don’t know they have it</th>
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<tbody>
<tr>
<td>since discovery in early 1980s</td>
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<thead>
<tr>
<th>35 million deaths</th>
<th>20 million don’t have access to treatment</th>
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<tr>
<td>since discovery in early 1980s</td>
<td>Many of those who do, don’t adhere well</td>
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<tr>
<td>Leading killer of women in reproductive age</td>
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<tr>
<th>37 million live with HIV</th>
<th>2.1 million new annual HIV infections</th>
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UNAIDS, 2015
Number of New HIV infections globally – all ages

Source: http://aidsinfo.unaids.org/
A vaccine could prevent millions of additional HIV infections on top of scale-up of existing interventions

Projected reductions of new annual HIV infections (millions) in low- and middle-income countries in years after vaccine introduction

“Without an AIDS vaccine we will not end AIDS.”

Peter Piot, BMGF Global Health Forum 2015

Illustrative vaccine with an assumed efficacy of 70%, not representative of any specific candidate. Coverage in generalized epidemics: routine 10 years old 70%, catch-up 11-14 years old 60%, 15-17 years old 55%, 18-49 years old 50%; in high risk populations in concentrated epidemics: 50%
## AIDS Vaccine Development Efficacy Trials: Summary of Past Trials

<table>
<thead>
<tr>
<th>Year</th>
<th>Vaccine Candidate</th>
<th>Prevention of HIV Infection</th>
<th>Control of HIV Infection</th>
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<tbody>
<tr>
<td>2003</td>
<td>VaxGen: gp120</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>2007</td>
<td>STEP Merck rAd5: Gag, Pol, Nef</td>
<td>No – more infections in vaccinees than placebo</td>
<td>No</td>
</tr>
<tr>
<td>2009</td>
<td>RV144 (Sanofi/Vaxgen) Canarypox Gag, Pol, Env/gp120 boost</td>
<td>31% efficacy - first signal in humans for benefit by HIV vaccine</td>
<td>No</td>
</tr>
<tr>
<td>2013</td>
<td>HVTN 505 NIAID-VRC: DNA + Ad5 gag-pol-nef; Env A, B, C</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>
RV-144: Evidence that an AIDS Vaccine Can Prevent HIV-1 Infection in Humans

Vaccination with ALVAC and AIDSVAX to Prevent HIV-1 Infection in Thailand.


- Modest 31% reduction in infection
- Limited duration

Proof of concept for a protective vaccine
Lessons from RV144

- Protection from HIV infection is possible
  - Highest protection in first 6-12 months
  - Antibody titers appear to wane in line with protection
  - Specific antibodies against the HIV envelope V1/V2 region are associated with protection
  - Assess similar approach in Sub-Saharan Africa with improved vaccine, adapted to clade C

In South Africa...

Even if other prevention options are scaled up, 60% coverage with a vaccine like the one used in RV 144 would still result in:

- 773,000 infections averted
- 34% reduction in incidence
- 1 life saved every 162 vaccinations

With a more effective vaccine, these numbers could be even higher.
Progress in HIV vaccines/prevention

• HIV Vaccine Pipeline
  o HVTN 702: ALVAC + gp120/MF59 efficacy– Nov 2016 (follow-on to RV144)
  o Janssen/HVTN 705: Ad26 mosaic + gp140/alum phase 2b - late 2017

• HIV Monoclonal Antibodies for Prevention
  o HVTN/HPTN AMP trial of single VRC01 BNAb - April 2016
  o Other BNAbs in phase 1 (3BNC117, 101074, PGT121, VRC-07 LS)

• Other HIV Prevention Technologies
  o ASPIRE and the Ring dapivirine studies with modest efficacy results
  o Long-acting injectable ARV advances (Cabotegravir LA - HPTN 083, HPTN 084)
**Population**: South African adults at risk for HIV infection, HIV seronegative

**Objective**: Efficacy, safety, immunogenicity, correlates of protection discovery, disease modulation

**Two stages:**
- Stage 1 assesses efficacy 0-24 months (primary objective)
- Stage 2 assesses efficacy up until 36 months post first vaccination

### Primary Vaccine Regimen

<table>
<thead>
<tr>
<th>N (total 5400)</th>
<th>Primary Vaccine Regimen</th>
<th>Booster</th>
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<tbody>
<tr>
<td></td>
<td>Month 0</td>
<td>Month 1</td>
</tr>
<tr>
<td>2700</td>
<td>ALVAC-HIV (vCP2438)</td>
<td>ALVAC-HIV (vCP2438)</td>
</tr>
<tr>
<td>2700</td>
<td>Placebo</td>
<td>Placebo</td>
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High Level Target Product Profile Goal:
Prophylactic vaccine offering protection against all clades of HIV-1 through an heterologous prime boost regimen

1. Viral vectors that elicit optimal immune responses
2. Mosaic inserts for global coverage (Gag-Pol-Env)
3. Trimeric env proteins for improved humoral immunity
Proof-of-Concept Study
HPX2008/HVTN 705

Design: Multicenter, randomized, parallel group, placebo-controlled, double-blind clinical trial

Countries: South Africa, Zambia, Zimbabwe, Malawi, Mozambique

Target N: 2,600

Population: Sexually active HIV-1 uninfected women (born female), age 18-35 years
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Antibody Mediated Prevention
Two Phase 2B Studies

- HVTN 703/HPTN 081 will enroll 1,500 women in sub-Saharan Africa
- HVTN 704/HPTN 085 will enroll 2,700 MSM and transgender persons in the Americas
- Randomized to receive VRC01 (IV) 10 mg/kg or 30 mg/kg or placebo every 8 weeks for 10 doses

www.ampstudy.org

Slide courtesy of Ken Mayer
Broadly Neutralizing Antibodies to HIV

Structure of HIV Trimer Detailed

- Multi-laboratory collaboration.
- Achieved decade-long goal.
- Clear picture of trimer and how it interacts with bNAb provides targets for HIV vaccine design.
Progress in HIV vaccines/prevention

- **HIV Vaccine Pipeline**
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  - ASPIRE and the Ring dapivirine studies with modest efficacy results
  - Long-acting injectable ARV advances (Cabotegravir LA - HPTN 083, HPTN 084)
Summary of progress – Anticipated data

Preventive vaccine
- HVTN 702 ALVAC/gp120 w/MF59 – July 2021 (Final data collection date for POM)
- Janssen POC : Ad26.Mos4.HIV/Clade C gp140 – November  2020 (Final data collection date for POM)

Antibody VRC01
- AMP (HVTN 704/HPTN 085) - July 2020 (Final data collection date for POM) data by 2021
- AMP (HVTN 703/HPTN 081 – Data by 2021

Other bNAb and combinations planned - later

Concurrent with 5 ARV-based prevention efficacy trials: vaginal ring (2), oral Prep F/TAF, long-acting injectable Cabotegravir (2)
What next if efficacy is demonstrated?

- Repeat efficacy trials (larger, different population, modified product)
- Licensure by one or more countries
- Request for WHO policy recommendations
- Request for WHO prequalification
- Request for purchase by governments, GAVI, others
- Demonstration/roll-out projects
Readiness depends on substantial planning and preparation

- International policy based on product characteristics
- Procurement
- Delivery
- Financing

**Objective:** Begin discussions with vaccine developers and public health decision making organizations to identify gaps and needs, and determine a roadmap for further action.
WHO Consultation: Q1-2, 2018

Being Prepared for Success:

From Proof of Efficacy to **Policy, Access** and **Use** of HIV Immunization Tools for Prevention
“Immunization is a cornerstone of global health security in an interconnected world where diseases do not respect national borders.”

Dr Margaret Chan, WHO; Chris Elias, Gates Foundation; Anthony Fauci, NIAID; Anthony Lake, UNICEF; Seth Berkley, GAVI. - WHO Commentary, February 25 2017
THANK YOU
Back-up Slides
WHO Consultation Topics (1\textsuperscript{st} day)

- Burden of disease and medical need for immunization strategies
- HIV vaccines and antibodies for prevention, state of the art
- WHO pathways from proof of concept to broad use
- Licensure, access and use: regulatory pathways, country perspectives, end-user expectations, financing delivery
WHO Consultation Topics (2nd day)

- Advanced program plans of developers
- Industry perspective
- Public Health Benefits
  - Value proposition for the development of immunization platforms against HIV
- End-to-end view: path forward and recommendations
- Publish meeting report
- Recommendations to WHO
Heterologous prime-boost HIV-1 vaccine regimen aiming at global coverage: tested in parallel in humans (ph. 1/2a study HIV-V-A004/ IPCAVD009/APPROACH) and in NHP challenge study.

**Prime**
- Ad26.Mos.HIV
  - Ad26 vectors with Mosaic gag-pol or env inserts
    - Ad26.Mos2.Gag-Pol
    - Ad26.Mos1.Env

**Boost**
- Ad26.Mos.HIV
  - gag-pol-env
- gp140 Clade C
  - Soluble trimeric gp140 env protein
- MVA-Mosaic
  - MVA vectors with Mosaic gag-pol-env inserts
    - VA-Mosaic 1
    - VA-Mosaic 2

Regimen to be selected after Phase 1/2a
Expanding Breadth of Immune Responses:
Tetravalent Ad26 and Mosaic gp140

**Prime**
- Ad26.Mos4.HIV
  - Ad26 vectors with Mosaic gag-pol or env inserts
- Ad26.Mos2.Gag-Pol
- Ad26.Mos1.Env
- Ad26.Mos2S.Env

**Boost**
- Ad26.Mos4.HIV
  - gag-pol-env
  + gp140 Clade C
    - Soluble trimeric gp140 env protein
  OR
  - gp140 Clade C+Mosaic
    - Soluble trimeric gp140 env proteins

Regimen to be selected after Phase 1/2a