EDCTP Third Forum

PARTNERSHIP AND AFRICAN LEADERSHIP IN VACCINE RESEARCH AND HIV/AIDS DRUG

MBOUP Souleymane
HIV VACCINE IN AFRICA

• In 2005, 13 new trials of preventive AIDS vaccine candidates began in 9 countries around the world.
• Two of these involved vaccine candidates that entered Phase II trials, an intermediate stage of clinical evaluation.
• Several of those newly initiated trials involved novel vaccination strategies
• Participation by Africa in those trials is continuously increasing with
• Rwanda started its first AIDS vaccine and South Africa began the country’s first Phase II AIDS vaccine trial
PROGRESS IN NUMBER OF COUNTRIES PARTICIPATING IN VACCINE TRIALS

2000: 1 country

2006: 8 countries participating in vaccine trials
PROGRESS IN NUMBER OF COUNTRIES PARTICIPATING IN VACCINE TRIALS

2000

2006

Countries currently involved in vaccine trials

Countries preparing for vaccine trials
# COMPLETED TRIALS IN AFRICA*

<table>
<thead>
<tr>
<th>Phase</th>
<th>Trial Name/Sponsor</th>
<th>Country</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ALVAC205 (Pasteur Merieux): <strong>Gag, pol, env (Subtype B)</strong></td>
<td></td>
<td></td>
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<tr>
<td>Phase I</td>
<td>DAIDS</td>
<td>Uganda</td>
<td>Complete</td>
</tr>
<tr>
<td>(40)</td>
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<td></td>
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<tr>
<td></td>
<td>DNA Plasmid (Polyepitope Pharmexa – Epimmune): <strong>Polyepitope</strong></td>
<td></td>
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<tr>
<td>Phase I</td>
<td>HVTN/DAIDS</td>
<td>Botswana</td>
<td>Complete</td>
</tr>
<tr>
<td>(42)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>DNA MVA (Oxford / IAVI): <strong>Gag, polyepitope (Subtypes A)</strong></td>
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<tr>
<td>Phase II</td>
<td>IAVI</td>
<td>Kenya, Uganda, South Africa</td>
<td>Complete</td>
</tr>
<tr>
<td>(238)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>VEE Replicon (AlphaVax): <strong>Gag (Subtype C)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase I</td>
<td>HVTN/DAIDS</td>
<td>South Africa, Botswana</td>
<td>Complete</td>
</tr>
<tr>
<td>(88)</td>
<td></td>
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<tr>
<td></td>
<td>Ad 5 (Merck): <strong>Gag (Subtype B)</strong></td>
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<td></td>
</tr>
<tr>
<td>Phase II</td>
<td>HVTN/DAIDS</td>
<td>South Africa, Malawi</td>
<td>Complete</td>
</tr>
<tr>
<td>(120)</td>
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*follow-up still ongoing
## PREVENTIVE VACCINE CONCEPTS IN TRIAL IN AFRICA

<table>
<thead>
<tr>
<th>Phase</th>
<th>Trial Name/Sponsor</th>
<th>Country</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase II (90)</td>
<td>Adeno Associated (TG, IAVI): Gag-Pr-RT (Subtype C)</td>
<td>IAVI Uganda, Zambia, South Africa</td>
<td>Enrolling</td>
</tr>
<tr>
<td>Phase II (114)</td>
<td>DNA prime/ Ad5 boost (VRC): Gag, Pol, Nef, Env (Subtypes A,B,C)</td>
<td>IAVI V001, VRC/DAIDS Rwanda, Kenya</td>
<td>Enrolling</td>
</tr>
<tr>
<td>Phase II (240)</td>
<td></td>
<td>HVTN 204, VRC/DAIDS South Africa</td>
<td>Enrolling</td>
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<tr>
<td>Phase II (324)</td>
<td></td>
<td>RV172,WRAIR VRC/DAIDS Uganda, Kenya, Tanzania</td>
<td>Enrolling</td>
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</table>
# PREVENTIVE VACCINE CONCEPTS IN TRIAL IN AFRICA

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<tr>
<th>Phase</th>
<th>Trial Name/Sponsor</th>
<th>Country</th>
<th>Status</th>
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<tbody>
<tr>
<td>IIb</td>
<td>Ad5 (Merck): Gag-Pol-Nef (Subtype B)</td>
<td>South Africa</td>
<td>Pending</td>
</tr>
<tr>
<td></td>
<td>HVTN503, Merck/DAIDS</td>
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<td></td>
</tr>
<tr>
<td>DNA, MVA: Gag, RT, env, pol (Subtype A, E)</td>
<td>Tanzania</td>
<td>Pending</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>DNA, MVA: Gag, RT, env, pol (Subtype A, E)</td>
<td>Tanzania</td>
<td>Pending</td>
</tr>
<tr>
<td></td>
<td>SIIDC, Karolinska, EU, Sida/SARE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALVAC-HIV vCP1521: Gag, Pro, Env (Subtype B, E)</td>
<td>Uganda</td>
<td>Pending</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>ALVAC-HIV vCP1521: Gag, Pro, Env (Subtype B, E)</td>
<td>Uganda</td>
<td>Pending</td>
</tr>
<tr>
<td></td>
<td>HPTN027/DAIDS</td>
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</table>
FIRST “TEST OF CONCEPT TRIAL” IN AFRICA (Q4 2006):
MRKAd5 Trivalent Vaccine

1:1:1 mixing of 3 vectors

G. Gray, PHRU, SA
FIRST “TEST OF CONCEPT TRIAL”: HVTN 503

A South African Study to test subtype B vaccine (Ad5 gag, pol, nef) in subtype C region (similar to STEP HVTN502 in MSM in USA):

- Will subtype B vaccine be efficacious against subtype C heterosexual infection
- Markedly enhance the information on efficacy in women
- Refine the assessment of the impact of pre-existing Ad5 titers
- More than double the number of endpoints to enhance the evaluation of correlates of protection.

Adapted from G. Gray, PHRU, Soweto
VRC DNA PRIME RAD5 BOOST

- Currently largest trial concept being tested in Africa

- Enrolling into 3 trials /6 countries in Africa >600 participants

- Involving 3 major vaccine initiatives /networks.
  - HIV Vaccine Trials Network (HVTN)
  - US Military HIV Research Program (USMHRP)
  - International AIDS Vaccine Initiative (IAVI)

- PAVE 100 (in planning for 2007/8) will be next proof of concept trial in Africa planning to enrol ~12,000 globally and ~8,000 in Africa
# Therapeutic Vaccine Concepts in Trial in Africa

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</tr>
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<tbody>
<tr>
<td>DNA Plasmid: Tat, rev, nef, gag, pol, env (Subtype B)</td>
<td>FIT Biotech</td>
<td>South Africa</td>
<td>Enrolling</td>
</tr>
<tr>
<td>Phase II (60)</td>
<td>AVIP /ISS</td>
<td>South Africa</td>
<td>Enrolling</td>
</tr>
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E. Vardus, PHRU, SA
PLANNED VACCINE TRIALS

- PAVE 100: DNA /Ad5; ~12,000 participants; 8,000 in Africa; multiple sites; multiple partners.
- Mrk Ad5: Adolescent trial in SA (HVTN/DAIDS)
- SAAVI DNA /MVA: Phase I trial in SA (SAAVI / HVTN /DAIDS)
- EuroVac (NYVAC)
- Chiron (Subtype C Env)
- Tat Vaccine (AVIP /ISS)
INCREASING PARTICIPATION BY AFRICA

2000

50 volunteers
1 country

2006

400 volunteers
8 countries
15 trial sites

2008

> 4000 volunteers
? 12 countries

2010

>10 000 volunteers
SCIENTIFIC CHALLENGES SPECIFIC TO AFRICA

- Vaccine Pipeline is too narrow
- Pre-existing immunity to vaccine vector
- Genetic Diversity
Regional distribution of HIV-1 subtypes and recombinants in 2004

Osmanov, pers. comm
ARV therapy in sub saharan Africa:
- Complicated combination regimens
- Expensive and dangerous
- Severe side effects
- Rapid development of drug resistance in the community

Instead of promoting expensive and dangerous ARV therapies...
PREVENTION

Lancet, 1998
SHORT TERM EVALUATION ON THE FIRST 175 PATIENTS

- Virological and immunological results similar to Western countries
- Excellent Adherence
- Good Accessibilty and Acceptability
CLINICAL TRIALS IN AFRICA

- Access to ARV for HIV-infected individuals in resource-poor settings
  - Efficacy?
  - Safety?
  - Adherence?
- Potent, safe, inexpensive simplified regimen
Once a day DDI/3TC/EFV regimen in treatment naive HIV-1 infected adults in Senegal

ANRS 12-04 / IMEA_011 study (1999)
Once a day HAART regimen in treatment naive HIV-1 infected adults in Senegal

ANRS 12-04 / IMEA 011 study

Evolution from baseline of viral load and CD4 count
CLINICAL TRIALS in Africa

1. First trial in Africa of a simplified regimen
2. effective through treatment period among severely immuno-compromised individuals in resource-poor settings
3. ARV clinical trial in resource-poor settings feasible
4. Introduction et validation of new ARV Drug in SENEGAL
ONGOING TRIAL

• ANRS 1207/IMEA 025:

  Once a day
  Tenofovir/Emtricitabine/Efavirenz
  regimen (3 pills)
Viral load
ANRS 1207/IMEA 025

Série 1

JO (N=40) | M1 (N=39) | M3 (N=37) | M6 (N=32)
---|---|---|---
0 | -2.8 | -3.6 | -3.6
Preliminary results: ANRS 1207/IMEA 025

- Good virological and immunological efficacy
- Good adherence to treatment
- More simplified regimen

2 daily pills
Truvada (TDF/FTC)+EFV

1 daily pill
TDF/FTC/EFV
ATRIPLA®: TDF+FTC+EFV 1 daily pill
Research Clinical Center, Fann
HIV LABORATORIES AT LE DANTEC
CONCLUSION (1)

- Increased African participation in vaccine trials
- Increased funding to address scientific questions
- Increased partnerships to accelerate the field

Increased success rate at an accelerated pace
(Results of first IIb trials in Africa still 3 - 5 years)
CONCLUSION (2)

• ARV scaling up in developing countries
• Host, viral, environmental factors (logistical, operational etc.)
• Affordable second line regimen required
• Need of increasing African participation in ARV clinical trials
• Impact in developing and developed countries
ACKNOWLEDGEMENTS

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