HPTN081/HVTN703/AMP Study Lessons Learnt

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Study Design and Duration

• A phase 2b double blind Placebo controlled study to evaluate the efficacy of VRC01 broadly neutralizing monoclonal antibody in reducing acquisition of HIV-1 infection
**Study Rationale**

- Passive administration of VRC01 antibody will reduce acquisition of HIV infection in high risk populations;
- Doses selected will determine the activity of the antibody across a range of serum concentration in diverse populations across multiple geographic regions of the world;
- Level of VRC01 antibody required for protection will vary by type of sexual exposure;
- Concentration of antibody in serum will be directly associated with the rate of protection; that is, higher levels of antibody will give greater rates of protection than lower levels; and
- Breakthrough isolates will have greater resistance to neutralization and will exhibit molecular signatures associated with escape from neutralization.
Study Objectives

- Safety & Tolerability of VRC01 infusion
  - Reactogenicity, AEs, SAEs, discontinuation rates
- Efficacy to prevent HIV infection
  - HIV infection by week 80 in those HIV-negative at enrollment

- Develop a marker(s) of VRC01 that correlates with the level and antigenic specificity of efficacy
  - Serum VRC01 concentration
  - Serum mAb effector functions
  - Breakthrough HIV viral sequences in infected people
  - VRC01 neutralization sensitivity of, & effector functions against, HIV strains from infected trial participants
# Study Population and Size

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Antibody (VRC 01) 10mg/kg</th>
<th>Antibody (VRC 01) 30mg/kg</th>
<th>Placebo</th>
<th>Total Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Americas*: United States, Peru &amp; Brazil</td>
<td>800</td>
<td>800</td>
<td>800</td>
<td>2,400*</td>
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<tr>
<td>MSM &amp; TG people (Clade B)</td>
<td></td>
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<tr>
<td>Southern Africa: Botswana, Kenya, Malawi, Mozambique, South Africa, Tanzania, Zimbabwe</td>
<td>500</td>
<td>500</td>
<td>500</td>
<td>1,500</td>
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<tr>
<td>Heterosexual women (Clades A, C, D, &amp; CRFs)</td>
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<tr>
<td>Total*</td>
<td>1,300</td>
<td>1,300</td>
<td>1,300</td>
<td>3,900*</td>
</tr>
</tbody>
</table>
Clinical Research Sites

- Gabarone, Botswana
- Kisumu, Kenya
- Blantyre, Malawi
- Lilongwe, Malawi
- Maputo, Mozambique
- Harare (3 clinics), Zimbabwe
- Mbeya, Tanzania

- Cape Town, RSA
- Durban (4 clinics), RSA
- Johannesburg, RSA
- Soweto, RSA
- Vulindlela, RSA
- Rustenberg
- Klerksdorp
- Pretoria
- Tembisa
Gaborone CRS

- Started screening - 21 July 2016
- First Enrolment - 16 Aug 2016
- Screened to date - 141 (March 30, 2017)
- Enrolled to date - 52 (March 30, 2017)
- Average screenings per week - 3.6
- Average enrolments per week - 1.5
Recruitment

• First contact?
  - utilized existing established relationships with clinics
  - contacted participants from previous studies
  - visited tertiary institutions
  - collaborations with HTC organizations
Challenges and Solutions

- Some participants willing to join study but partners/parents not too sure
  - we are open to participant bringing in significant others
  - more information dispels myths about research
Challenges and Solutions

Contraception

- women not on hormonal contraception
  - fear of side effects

- we partnered with an organization which provides FP services
Challenges and Solutions

- Women come as group
  - If one decides not to enroll, ALL go
  - To about individual
Retention Strategies

- All our participants still on study
  - Bringing significant others
  - Bringing babies
  - Wifi
  - Snack
  - Television??
  - Small talk about how study going
  - CAB members interaction with study participants
Community Engagement

- Continuous CE with various stakeholders
- Use of recruitment material
- Piggy back on national/local events
- Maintenance of established referral system with HTC organizations and advocacy groups
  - Periodic updates including successes and challenges
  - Effort recognition of individual organization
ACKNOWLEDGEMENTS

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Stakeholders – MoH, Clinics
Community Members
HTC and other service organizations
Community and Religious leaders