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## Summary of animal studies with intermittent PrEP and rectal virus exposures

<table>
<thead>
<tr>
<th>ORAL DOSING SCHEDULE</th>
<th>No. ANIMALS PROTECTED*</th>
<th>RISK REDUCTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily</td>
<td>4/6 (p=0.0004)</td>
<td>9.9, p=0.002</td>
</tr>
<tr>
<td>Intermittent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-22h/+2h</td>
<td>5/6 (p&lt;0.0001)</td>
<td>16.7, p=0.006</td>
</tr>
<tr>
<td>-3days/+2h</td>
<td>5/6 (p&lt;0.0001)</td>
<td>15.4, p=0.008</td>
</tr>
<tr>
<td>-7days/+2h</td>
<td>4/6 (p&lt;0.0001)</td>
<td>9.3, p=0.003</td>
</tr>
<tr>
<td>-3days/no post</td>
<td>1/6</td>
<td>2.0, p=0.16</td>
</tr>
<tr>
<td>-2h/+22h</td>
<td>3/6 (p=0.0004)</td>
<td>4.1, p=0.02</td>
</tr>
<tr>
<td>+2h/+24h</td>
<td>3/6 (p=0.0004)</td>
<td>4.0, p=0.03</td>
</tr>
<tr>
<td>-24h/+24h</td>
<td>3/6 (p=0.0004)</td>
<td>6.6, p=0.0024</td>
</tr>
</tbody>
</table>

*14 rectal exposures
Drug Correlates in iPrEx

- Cases matched to controls by site and time on study
- Drug Detection Correlated with Seronegative Status (OR 12.9, P<0.001)
  - 92% reduction in HIV risk
  - 95% if controlled for Unprotected Receptive Anal Intercourse
Premise

• Non-daily dosing of oral FTC/TDF may
  – Increase tolerance
  – Increase convenience
  – Decrease costs

• Dosing pre and post sex may
  – Provide guidance on when to start and stop
  – Motivate planning for sex

• Drug levels in hair, PBMCs and blood plasma
  – May be helpful for monitoring PrEP programs
  – More information about population variance needed
Primary Objective

• To test the hypothesis that recommending intermittent (non-daily) usage of oral FTC/TDF chemoprophylaxis, compared with recommending daily usage, will be associated with:
  – Equivalent coverage of sex events
  – Lower number of pills needed for coverage
  – Decreased self-reported side effects
Secondary Objectives

• To characterize the variance of drug levels in DOT
• To assess safety outcomes
• To identify regimen preferences
• To evaluate differences by arm in adherence
• Evaluate the potential influence of PrEP usage on:
  – sexual behavior
  – planning for sex
  – prediction of risky situations
  – and recognition of possible HIV exposure
  – Social relationships that bear on prevention choices
HPTN 067 Design

- 6-week DOT phase to establish baseline for PK analysis
- Randomization to 3 dosage groups (1:1:1) at Week 6:
  - daily dosing
  - time-driven dosing (2X weekly and post sex)
  - event-driven dosing (pre and post sex)
- 24-weeks of self-administered dosing (Weeks 6 - 30)
  - Adherence (Next Step) and RR counseling
  - Weekly phone calls
  - 4 week visits HIV testing, safety and data collection
- Post Week 34 Qualitative Component
Study Sites:

- Silom Community Clinic in Bangkok, Thailand for HIV uninfected, high risk MSM (N=180)
  - Anticipated start date: late 3rd QTR 2011.
- Emavundleni Centre, in Cape Town, South Africa for HIV uninfected, high risk WSM (N=180)
  - Anticipated start date: early 3rd QTR 2011.

Study Duration:

- Less than two years
  - Enrollment ~ 8 months
  - 34 weeks on study
Estimated Timelines

Enrollment
- July 2011
- to Mar 2012

34 weeks on study
- Dec 2012

Qualitative Component
- Ongoing
- Final in Jan 2013

Study close out
- Early 2013
Methogological Development

Monitoring
- Wisepill device for real time assessment of pill access
- Dose – drug level relationships during 6 week DOT phase
- Weekly telephone contact to improve sexual recall

Counseling
- Adapt Next Step Counseling for non-daily dosing

Social and Behavioral Determinants of Prevention Choices
- CASI assessment of IMB parameters for condoms and PrEP
- Focus Groups and Interviews on Engagement in Prevention