Designs under Discussion for “Unmet Prevention Need”

Ideas emerging from Seattle Workshop “HIV Prevention Efficacy Trial Designs of the Future” Nov 5, 2018

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Goal: Regulatory Approval of New Product

1. **Safe**
   - Sufficient total person years of experience
   - Safety established with 12+ months of use

2. **Effective**
   - Unequivocal evidence of prevention of HIV infection

**Standard for evidence**
- Randomized Clinical Trial
- In populations at highest need

**Current Era**: FTC/TDF PrEP
- Current approved market leader is highly effective
- Dependent on daily adherence to pill taking
Data accumulating about PrEP non-persistence

• HPTN 067: < 2 pills/week (daily arm)
  At 30 weeks
  • Young women in Capetown: 46%
  • MSM in Thailand: 4%
  • MSM in Harlem, US: 50%

• HPTN 073: < 4 days/week
  • Black MSM at 26 weeks: 36%

• HPTN 082: Undetectable DBS at 13 weeks
  • Young women in Africa: 16%

• US PrEP user pharmacy refills (Coy, 2019, JAIS)
  • At year 1: 44%
  • At year 2: 37%
With an effective product, three choices in future RCTs

1. **Compare**
   Compare experimental product (EXP) to existing prevention (FTC/TDF)

2. **Layer**
   Compare EXP to placebo (PBO) on top of use of existing prevention

3. **Combine**
   Compare existing prevention combined with EXP product

HPTN 083/084

- FTC/TDF
- EXP
- Placebo
- EXP
- FTC/TDF + Placebo
- FTC/TDF + EXP
The Prevention Mosaic
The Prevention Mosaic

Condoms
Oral PrEP
Abstinence
Still Unprotected
Ring
Condoms
Abstinence
Potential new approach

PrEP initiation

PrEP success?

Yes

Continue PrEP

No

PrEP access

Placebo

EXP

PrEP
Sample size implications

- Incidence in those with unmet need is probably higher
- Difference between incidence placebo and active is projected to be bigger

<table>
<thead>
<tr>
<th>Percentage on PrEP</th>
<th>Type: Powered for 60% efficacy of EXP</th>
<th>Total number of infections</th>
<th>Number of participants (Assuming 4% incidence)</th>
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<tbody>
<tr>
<td>100%</td>
<td>Non-inferiority</td>
<td>980</td>
<td>17,754</td>
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<tr>
<td>75%</td>
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<tr>
<td>0%</td>
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Potential new approach

PrEP initiation

PrEP success?

High

Continue PrEP

No

Low

Continue PrEP

PrEP access

Placebo

EXP

Placebo

EXP
Explore innovative design ideas

• Challenge of advancing new products for prevention when existing products are very successful
• Need community, stakeholder and scientists engaged in robust discussion of prevention need, to discern a path forward together