Effects of longstanding antiretroviral therapy on semen HIV viral load

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Treatment as prevention (TASP) is the most effective HIV prevention method to date

- HPTN 052 (heterosexuals)\(^1\)
- Partner (heterosexuals and MSM)\(^2\)

PI monotherapy may reduce NRTI related toxicities

- MONET\(^3\) and MONOI\(^4\) report non inferiority
- PIVOT\(^5\) found more blips particularly in first year of switch
- Concerns include poor penetration into sanctuary sites including the brain and genital tract\(^6\)

1. Rodger et al Abs 153LB CROI 2014
5. Paton et al Abs 550LB CROI 2014
HIV infected individuals stable on Atripla
HIV VL < 100 copies/ml for ≥6 months

N = 64

1:1 randomisation, open label

Remain on Atripla
N = 32

Switch to darunavir/ritonavir monotherapy (DRV/r)
N = 32

48 week study
Primary outcome: vitamin D 25(OH)D
Primary outcome: Vitamin D & Bone

P71 Hamzah et al

- At 48 week Darunavir was associated with:
  - Higher vitamin D levels
  - Improved bone mineral density
  - Lower ALP
To investigate whether:

Long term virological suppression in the plasma is associated with virological suppression in semen in those:

a. on long-term stable Atripla
b. switching to DRV/r monotherapy
**Methods**

**HIV semen substudy**

- N=22

- **Remain on Atripla**
  - N=11

- **Switch to DRV/r**
  - N=11

- Semen samples taken at baseline and at week 48
- Semen VL measured using Roche COBAS Taqman 48 system
- Lower limit of quantification = 34 HIV RNA copies/ml
Results: Overall

- 6 participants had unquantifiable semen VLs due to inhibition of assay at baseline and/or week 48 (4 samples at baseline, 3 at week 48)
- 1 participant had inhibition at both baseline and week 48
- 3 participants had no useful data (either inhibition or sample missing)
Results: Baseline

- **Baseline characteristics (N=19)**
  - Median exposure Atripla 3.5 yrs (IQR 2.5, 3.9yrs)
  - All had plasma HIV VL< 50 cps/ml
  - All asymptomatic for STIs

- **Baseline seminal VL (N=19)**
  - 14 (74%) had undetectable semen VL
  - 4 (21%) had detectable semen VL
    - Mean 337 cps/ml
    - Range 89-831 cps/ml

<table>
<thead>
<tr>
<th>Patient</th>
<th>Plasma HIV VL cps/ml</th>
<th>ARV</th>
<th>Semen HIV VL cps/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient A</td>
<td>34</td>
<td>DRV/r</td>
<td>89</td>
</tr>
<tr>
<td>Patient B</td>
<td>&lt;20</td>
<td>Atripla</td>
<td>127</td>
</tr>
<tr>
<td>Patient C</td>
<td>&lt;20</td>
<td>Atripla</td>
<td>301</td>
</tr>
<tr>
<td>Patient D</td>
<td>&lt;20</td>
<td>Atripla</td>
<td>831</td>
</tr>
</tbody>
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Results: Week 48

* At week 48, 18 subjects had plasma HIV VLs < 50 cop/ml
  * N=1 plasma VL=63 (on Atripla)
  * All were asymptomatic for STIs

* 4 samples had usable data
  * 2 (50%) had undetectable semen VLs
  * 2 (50%) had detectable semen VL
  * Range 80-879 cps/ml

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<th>Semen HIV VL cps/ml</th>
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<tr>
<td>Patient C</td>
<td>&lt;20</td>
<td>Atripla</td>
<td>879</td>
</tr>
<tr>
<td>Patient E</td>
<td>20</td>
<td>DRV/r</td>
<td>80</td>
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<td>(inhibition at baseline)</td>
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<tr>
<td>Patient F</td>
<td>&lt;20</td>
<td>DRV/r</td>
<td>&lt;34</td>
</tr>
<tr>
<td>Patient G</td>
<td>&lt;20</td>
<td>Atripla</td>
<td>&lt;34</td>
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Paired results: Baseline and Week 48

- 6 participants provided samples at baseline and week 48
- 18 valid samples at baseline
- 4 valid samples at week 48
- Only 3 had valid paired samples
  - DRV/r n=1
  - Atripla n=2
- All reported 100% adherence to ART

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<tr>
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<tr>
<td></td>
<td>Baseline</td>
<td>Week 48</td>
</tr>
<tr>
<td>Patient C</td>
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<td>879</td>
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<tr>
<td>(Atripla)</td>
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Long standing plasma virological suppression with Atripla conferred virological suppression in semen in 74% individuals.

- The highest semen detected was VL 879 copies/ml
- Supports TASP clinical trial data (PARTNER, 052)

Switch to DRV/r monotherapy did not appear to increase viral load in the semen in our limited group of subjects
Limitations

- Small sample size
- Inhibition of PCR in semen - known to occur
Our Patients

Lisa Hamza, Juan Tiraboschi, Martina Toby, Alistair Teague, Sinead Costello, Siobhan O’Shea, Ranjababu Kulasegaram, Frank Post, Julie Fox

Staff at Harrison Wing, St Thomas’ Hospital