**BACKGROUND**

- Despite combination antiretroviral therapy (cART), HIV persists in anatomic sites such as the gut
- Limited ART penetration into tissue may play a role in HIV persistence with implications for:
  - Ongoing transmission
  - Barrier to HIV eradication/functional cure
- Little data available on relationship between tissue HIV viral dynamics and ART pharmacometrics

**AIMS**

AIM 1: Compare early HIV viral dynamics in blood plasma and rectal tissue following initiation of dolutegravir (DTG) – based cART

AIM 2: Explore relationships between HIV rectal tissue RNA viral load and DTG concentrations within plasma and rectal tissue

**METHODS**

**Study population:** ART-naïve HIV+ adults (≥18 years) within metropolitan Atlanta, Georgia, USA
- Normal liver and renal chemistries
- No active anal or rectal disease
- Not receiving medications with DTG interactions
- Able/willing to start 1st line DTG-based cART:
  - TDF/FTC + DTG (50 mg daily) or ABC/3TC/DTG

**Study design:** Longitudinal cohort study with serial sampling of blood and rectal tissue pre- and post- cART.

**Figure 1. Study Schema**

**BLOOD PLASMA**

**Day 0**

**Day 7, 10, or 14**

**Day 42**

**Day 84**

Blood plasma and rectal biopsies for HIV-1 RNA (Abbott Real-time PCR) and DTG quantitation (HPLC-MS/MS)

**Statistical analyses:**
- Participants grouped: Undetectable rectal HIV RNA (<40 copies/g) at any time point vs persistent detectable rectal HIV RNA
  - Median DTG plasma and rectal tissue concentrations compared between groups using Mann-Whitney non-parametric tests

**RESULTS**

**Table 1. Demographic and clinical characteristics (n = 8)**

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>N (%) or median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>39.2 (32.9 – 52.7)</td>
</tr>
<tr>
<td>Female sex</td>
<td>4 (50)</td>
</tr>
<tr>
<td>Black race</td>
<td>6 (75)</td>
</tr>
<tr>
<td>HIV risk factors</td>
<td>3 (38)</td>
</tr>
<tr>
<td>MSM</td>
<td>6 (75)</td>
</tr>
<tr>
<td>Heterosexual</td>
<td>1 (13)</td>
</tr>
<tr>
<td>IVDA</td>
<td>0.92 (0.34 – 1.82)</td>
</tr>
<tr>
<td>Time since HIV diagnosis, years</td>
<td>208 (104-320)</td>
</tr>
<tr>
<td>Baseline CD4, cells/mm³</td>
<td>24,847 (6237 – 50,269)</td>
</tr>
<tr>
<td>Receiving TDF/FTC backbone</td>
<td>6 (75)</td>
</tr>
</tbody>
</table>

**Figure 2. HIV viral dynamics in blood plasma and rectal tissue**

- All (8/8) participants achieved undetectable plasma RNA by Day 42
- 3/8 participants achieved undetectable rectal HIV RNA at any time point (circles)
- One participant had undetectable rectal RNA Day 42 & detectable RNA Day 84 (arrow)

**Figure 3. Rectal tissue DTG concentrations in undetectable and detectable rectal HIV RNA groups**

**DISCUSSION/CONCLUSIONS**

- Rectal HIV RNA persisted in most participants over the first 84 days of DTG-based cART despite rapid plasma virologic suppression
- Those with undetectable rectal HIV RNA at any time point had median steady state DTG rectal concentrations 2 times higher than those with persistent rectal HIV RNA

**IMPLICATIONS:**
- ART pharmacometrics likely play a role in tissue HIV viral dynamics
- Further studies are needed to assess implications for rectal transmission as well as barriers to HIV tissue reservoir eradication

**ACKNOWLEDGMENTS**

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