Dolutegravir with tenofovir disoproxil fumarate-emtricitabine as HIV post-exposure prophylaxis in gay and bisexual men

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Introduction

- Antiretroviral drugs as HIV nonoccupational postexposure prophylaxis (NPEP) is recommended by the World Health Organisation.
- Up to one-third of gay or bisexual men (GBM) do not complete 28 days of NPEP.
- Adverse events (AEs) are the likely primary cause of NPEP non-completion.
- Co-formulated TDF/FTC (Truvada; TVD) is the preferred NRTI backbone for NPEP.
- Choices for a 3rd drug include PIs, integrase inhibitors, NNRTIs and entry inhibitors.
- 3-drug NPEP discontinuation due to pill fatigue, drug-drug interactions and after HIV integrase.
- RAL can cause acute muscle toxicity and twice-daily dosing is required.
- RPV must be taken with food.
- Dolutegravir (DTG) is an attractive 3rd drug for NPEP.

Methods

- Open-label, single-arm study at 3 sexual health clinics and 2 emergency departments in Australia.
- One hundred HIV-uninfected GBM requiring 3-drug PEP received DTG plus TVD for 28 days.
- The primary endpoint was PEP failure (pregnancy cessation or primary HIV infection through Week 12).
- Additional endpoints were: adherence by self-report (n=98); pill count (n=55); plasma tenofovir levels (n=82); plasma DTG levels (n=80); and safety (clinical and laboratory adverse events [AEs]).
- Adherence and adverse events (laboratory & clinical) assessed at Week 1, 2 and 4.

Adherence

<table>
<thead>
<tr>
<th>Self-report % (n=98)</th>
<th>Pill count % (n=55)</th>
<th>Day-28 plasma drug level</th>
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<tbody>
<tr>
<td>TVD 98%</td>
<td>TVD 98%</td>
<td>TNV 85%</td>
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<tr>
<td>DTG 98%</td>
<td>DTG 98%</td>
<td>DTG 99%</td>
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# measured a mean 15 (SD 8) hrs after last dose of DTG or TVD

Safety / adverse events

Clinical AEs (n=98)

- 67 (68%) reported 144 subjective AEs possibly attributable to study drug
- 98% of AEs were grade 1-2
- There were no unexpected AEs and no serious AEs
- 1 pt ceased NPEP because of grade-3 headache

Conclusions

- DTG + TVD were well tolerated as NPEP with high levels of completion (90%) and adherence.
  - Rates similar to those using single-tablet NPEP with TDF-FTC-RLV
  - Adherence 98% by self report and pill count, but only 85% had plasma tenofovir ≥40ng/mL at Day 28

References