Background and Rationale

- A single-tablet antiretroviral regimen (STR) for switch has demonstrated improved adherence
- Reduced pill burden
- Eliminated risk of partial non-adherence

M184V/I
- Most common NRTI mutation in patients treated with 3TC and FTC
- Occurs in up to 64% of treated patients with prior virologic failure
- Confers resistance to FTC and decreases susceptibility to ABC, but increases susceptibility to TFV
- M184V/I mutations may not preclude response to E/C/F/TDF or E/C/F/TAF

TAF, with 4-fold higher intracellular TFV-DP than TDF, may have additional activity against viruses with resistance mutations including M184VI

3TC, lamivudine; ABC, abacavir; C, cobicistat; E, elvitegravir; FTI or F, emtricitabine; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; TFV, tenofovir; TFV-DP, tenofovir diphosphate.

Study Design

Ongoing, multicenter, international, open label, single arm study in HIV-1-infected adults with HIV-1 RNA <50 copies/mL receiving FTC/TDF or ABC/3TC + third agent

Part 1
- Week 12 (Primary) and Week 24 PVR Analyses:
  - No virological failures or emergence of new resistance
  - Absence of confirmed virologic failure (HIV-1 RNA ≥ 50 copies/mL on 2 consecutive visits) before Week 12 or Week 24

Part 2
- Extending participants who develop virologic failure after switching to E/C/F/TAF
- To determine the durability at Weeks 24 and 48 in maintaining virologic suppression

M184V/I only n=15
M184I/NNRTI-R only n=14
M184V/I + NNRTI-R only n=2

Baseline Characteristics

<table>
<thead>
<tr>
<th>E/C/F/TAF (n=37)</th>
<th>Related to Study Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-1 RNA &gt;50 copies/mL</td>
<td>4 (11%)</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>27 (73%)</td>
</tr>
<tr>
<td>White</td>
<td>7 (19%)</td>
</tr>
</tbody>
</table>
| Female | 9 (36%)
| Hispanic/Latino ethnicity | 6 (16%)
| Median CD4 count, cells/mm³ | 724 (143-1562) |
| Median estimated GFR, mL/min (range) | 94 (38-215) |

Screening Regimen: FTC/TDF as NRTI backbone

To evaluate the emergence of new resistance mutations in patients switching to E/C/F/TAF: M184V/I

Baseline Resistance (n=37)

- HIV-1 RNA <50 copies/mL harboring the M184V and/or M184I mutation, switching to E/C/F/TAF: Approximately half of participants also have NNRTI-R HIV-1
- Proviral DNA: M184V/I detected in less than half of patients
- Proviral DNA-resistance testing failed to detect known M184V and NNRTI-R seen on historical genotype

Conclusions

- In this open-label study of participants with HIV RNA < 50 copies/mL harboring the M184V and/or M184I mutation, switching to E/C/F/TAF:
  - Maintained virologic suppression (100%) using the Week 12 and Week 24 PVR analyses
  - Well tolerated with no SAE or Grade 3/4 adverse events that were study-drug related, and one discontinuation due to adverse events
  - Compared to historical genotype, proviral DNA resistance testing only detected M184V/I and NNRTI-R in approximately half of participants
  - Switching to E/C/F/TAF may be considered for patients with pre-existing M184V and/or M184I mutations
  - Part 2 of the study with M184V/I and up to 2 TAMs is currently enrolling

References


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