**Efficacy and Safety of Fostemsavir Plus Optimized Background Therapy in Heavily-Treated Adults Exposed to HIV-1: Week 240 Results of the Phase 3 BRIGHT3 Study**

**Introduction**

Fostemsavir is the prodrug of temsavir, a first-in-class CCR5 antagonist. It binds to the HIV-1 receptor CXCR4, preventing attachment and entry into host T cells and other immune cells.

**Objective**

The Week 240 interim analysis was conducted to evaluate the efficacy and safety of fostemsavir + OBT in HIV-1-infected participants who remained in the study.

**Methods**

- **Randomization Cohort**
  - 1 or 2 ARV classes remaining and no remaining approved non-nucleoside reverse transcriptase inhibitors

- **Non-randomized**
  - 0 ARV classes remaining and no remaining approved non-nucleoside reverse transcriptase inhibitors

**Randomized Cohort**

- 1 or 2 ARV classes remaining with at least 1 ARV should be active

- 40% of participants discontinued/ withdrew

**Non-randomized**

- No ARV classes remaining and no remaining approved non-nucleoside reverse transcriptase inhibitors

**Week 240**

- 12 participants had completed the study by transitioning to locally approved fostemsavir (the first approved CCR5 antagonist) in the Non-randomized Cohort.

**Immunologic Response**

- **CD4+ T-cell counts** increased steadily from baseline through Week 240 (Figure 4)

- **Mean CD4+CD8+ ratio** also increased steadily from baseline (0.2) to Week 240 (0.6)

**Safety**

- The safety profile was consistent with earlier findings across both cohorts (Table 3)

**Conclusions**

- **Through 5 years of treatment with fostemsavir-based regimens, durable virologic responses, clinically meaningful improvements in CD4+ T-cell counts, and a favorable safety and tolerability profile were observed in HIV-1 patients with multidrug-resistant HIV-1.**

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**Table 1: Baseline Disease Characteristics**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Non-randomized (N=272)</th>
<th>Randomized Cohort (N=272)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4+ T-cell count, cells/mm&lt;sup&gt;3&lt;/sup&gt;</td>
<td>219 (51)</td>
<td>194 (57)</td>
<td>0.01</td>
</tr>
<tr>
<td>Any CDC class C event</td>
<td>6 (2)</td>
<td>2 (1)</td>
<td>0.12</td>
</tr>
<tr>
<td>Any AE leading to D/C</td>
<td>1 (0)</td>
<td>1 (0)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

**Figure 2: Participant Disposition Through the Week 240 Database Lock**

- **ITT** - Intent to Treat

**Figure 3: HIV-1 RNA Load, Through Week 240 by Snapshot Analysis (ITT-E) and Observed Analysis**

- **ITT-E** - Intent to Treat-Early

**Figure 6: Change in CD4+ T-Cell Count From Baseline to Week 240 by Virologic Response During the Same Time Point (Randomized Cohort, Observed Analysis)**

**Figure 7: CD4+CD8+ Ratio Through Week 240 (Observed Analysis)**

- **Non-randomized (N=98)**

**Figure 8: Change in CD4+ T-Cell Count From Baseline to Week 240 (Observed Analysis)**

- **Non-randomized (N=98)**

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**Table 2: Virologic Outcomes and Protocol-Defined Virologic Failure Through Week 240 by Snapshot Analysis (ITT-E)**

- **Randomized Cohort**
- **Non-randomized Cohort**

**Table 3: Cumulative Summary of Safety**

- **Any AE**
- **Any grade 3-4 AE**
- **Drug-related grade 3-4 AE**
- **Any SAE**
- **Drug-related SAE**

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**References**

1. Lataillade et al. (2022).
5. HVTN 100 study team (2021).
7. Lataillade et al. (2022).