Fostemsavir

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Fostemsavir

600 mg
Attachment Inhibitor

Dose: 1 tablet twice daily with or without food
Fostemsavir is a prodrug of temsavir
Fostemsavir undergoes hydrolysis on the luminal surface of the small intestine brush border membranes.
Temsavir (Active Drug)
**HIV Entry Inhibitors**

**Fostemsavir: Attachment Inhibitor**

Illustration: David H. Spach, MD

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Fostemsavir

Temsavir

**Fostemsavir**

Binds near CD4 binding site and prevents gp120 conformational change required for attachment
- **Indication**
  - Heavily treatment-experienced adults with multidrug-resistant HIV-1

- **Drug-drug interactions**
  - Avoid: strong CYP3A4 inducers (e.g., rifampin, phenytoin, carbamazepine, St. John’s wort), grazoprevir, voxilaprevir, >30 mcg/day ethinyl estradiol
  - Use with caution if prolonged QTc or taking meds known to cause torsade de pointes
  - Consider statin dose adjustment (use lowest possible statin starting dose)

- **Use during pregnancy**
  - Insufficient data
Fostemsavir for Heavily Treatment-Experienced Individuals

BRIGHTE Study (Week 48 Data)
**Fostemsavir for Heavily Treatment-Experienced Individuals**

**BRIGHTE Study (Week 48): Background**

### Background
- Phase 3, randomized, placebo-controlled, non-inferiority trial evaluating fostemsavir (FTR) in salvage ART

### Enrollment Criteria:
- Highly ART-experienced adults
- Virologic failure on current ART
- HIV RNA >400 copies/mL
- Multiclass ART resistance
- At least one fully active agent (for randomized cohort)

*OBR = optimized background regimen

### Baseline Characteristics

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>Randomized (n = 272)</th>
<th>Non-Randomized (n = 99)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, median (range)</td>
<td>48 (18-73)</td>
<td>50 (17-72)</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>200 (74)</td>
<td>89 (90)</td>
</tr>
<tr>
<td>White, n (%)</td>
<td>184 (68)</td>
<td>74 (74)</td>
</tr>
<tr>
<td>Black/African American, n (%)</td>
<td>60 (22)</td>
<td>23 (23)</td>
</tr>
<tr>
<td>HIV RNA 1,000-100,000 copies/mL, n (%)</td>
<td>161 (59)</td>
<td>75 (76)</td>
</tr>
<tr>
<td>HIV RNA &gt;100,000 copies/mL, n (%)</td>
<td>80 (29)</td>
<td>15 (15)</td>
</tr>
<tr>
<td>CD4 count—cells/mm³, median (range)</td>
<td>99 (0-1160)</td>
<td>41 (0-641)</td>
</tr>
<tr>
<td>2 fully active agents in OBR*, %</td>
<td>42</td>
<td>0</td>
</tr>
<tr>
<td>1 fully active agent in OBR*, %</td>
<td>52</td>
<td>19</td>
</tr>
<tr>
<td>0 fully active agents in OBR*, %</td>
<td>6</td>
<td>81</td>
</tr>
</tbody>
</table>

*Most common ARV’s in OBR: dolutegravir, boosted darunavir, tenofovir DF, etravirine, maraviroc, enfuvirtide, ibalizumab

Fostemsavir for Heavily Treatment-Experienced Individuals

BRIGHTE Study (Week 48): Results

Baseline to Day 8 Change in HIV RNA Level (Randomized Cohort)

- Median change in HIV RNA from baseline (log_{10} copies/mL)
- Fostemsavir: -0.79
- Placebo: -0.17

Fostemsavir for Heavily Treatment-Experienced Individuals
BRIGHTE Study (Week 48): Results

Virologic Response Through Week 48 (HIV RNA <40 copies/mL)

Fostemsavir for Heavily Treatment-Experienced Individuals

BRIGHTE Study (Week 96 Data)
Fostemsavir for Heavily Treatment-Experienced Individuals
BRIGHTE Study (Week 96): Results

Virologic Response Through Week 96 (HIV RNA <40 copies/mL)

Participants with HIV RNA <40 copies/mL (%)

- Fostemsavir: Randomized
- Fostemsavir: Nonrandomized

Fostemsavir for Heavily Treatment-Experienced Individuals
BRIGHTE Study (Week 96): Results

Mean Change in CD4 T-Cell Count Through Week 96

### Fostemsavir for Heavily Treatment-Experienced Individuals

#### BRIGHTE Study (Week 96): Results

<table>
<thead>
<tr>
<th>Adverse Events (AEs)</th>
<th>Randomized (n = 272)</th>
<th>Non-Randomized (n = 99)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any AE, n (%)</td>
<td>249 (92)</td>
<td>98 (99)</td>
</tr>
<tr>
<td>Drug-related grade 2-4 AEs, n (%)</td>
<td>57 (21)</td>
<td>22 (22)</td>
</tr>
<tr>
<td>Nausea</td>
<td>9 (3)</td>
<td>5 (5)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>6 (2)</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Headache</td>
<td>6 (2)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>4 (1)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>3 (1)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Asthenia</td>
<td>2 (&lt;1)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Drug-related AE leading to discontinuation, n (%)</td>
<td>7 (3)</td>
<td>7 (3)</td>
</tr>
<tr>
<td>Drug-related serious AE, n (%)</td>
<td>9 (3)</td>
<td>3 (3)</td>
</tr>
</tbody>
</table>

Fostemsavir Resistance
## Fostemsavir for Heavily Treatment-Experienced Individuals

**BRIGHTE Study (Week 96): Virologic Failures**

<table>
<thead>
<tr>
<th></th>
<th>Randomized (n = 272)</th>
<th>Non-Randomized (n = 99)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of virologic failures</strong></td>
<td>69/272 (25%)</td>
<td>50/99 (51%)</td>
</tr>
<tr>
<td>With gp120 RAPs at screening (of those with genotypic data)</td>
<td>43/68 (63%)</td>
<td>26/48 (54%)</td>
</tr>
<tr>
<td><strong>Virologic failures with post-baseline data</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>With emergent gp120 (env) RAS</td>
<td>29/53 (55%)</td>
<td>33/45 (73%)</td>
</tr>
<tr>
<td>S375H/I/M/N/T</td>
<td>19/53 (36%)</td>
<td>21/45 (47%)</td>
</tr>
<tr>
<td>M426L/I</td>
<td>18/53 (34%)</td>
<td>23/45 (51%)</td>
</tr>
<tr>
<td>M434I/L</td>
<td>6/53 (11%)</td>
<td>5/45 (11%)</td>
</tr>
<tr>
<td>M475I/L/V</td>
<td>8/53 (15%)</td>
<td>5/45 (11%)</td>
</tr>
</tbody>
</table>

Abbreviation: RAPs = Resistance-associated polymorphisms; RAS = Resistance-associated substitutions

Source: Fostemsavir Prescribing Information
Fostemsavir (FTR): Resistance Testing & Cross Resistance

• FTR can be used regardless of HIV-1 tropism
• Standard genotype testing does not give FTR resistance information
• Certain viral subtypes, such as AE, may have reduced susceptibility, but are rare
• HIV with resistance mutations in the gp120 envelope subunit due to virologic failure on ibalizumab or maraviroc may have reduced susceptibility to FTR, but are rare
• Viruses resistant to the gp41 inhibitor enfuvirtide typically retain susceptibility to FTR
• Other entry inhibitors tend to retain activity in the presence of FTR resistance mutations

Source: Fostemsavir Prescribing Information
Fostemsavir: Summary

• Oral, twice-daily, CD4 attachment inhibitor

• Typically used as part of salvage antiretroviral therapy for heavily-treatment experienced individuals

• Can be combined with other entry inhibitors (ibalizumab, enfuvirtide, maraviroc if R5-tropic), other salvage antiretrovirals, and/or optimized background regimen

• Overall, well tolerated with few drug-drug interactions, though need to consider interactions with strong CYP3A4 inducers, estradiol, statins, and drugs that may prolong the QTc or cause torsade de pointes

• Resistance mutations in the gp120 envelope subunit may develop with virologic failure
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