Fostemsavir (Rukobia)

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Fostemsavir (Rukobia)

Rukobia
[rue-KOH-bee-ah]

Source: Photograph courtesy of ViiV Healthcare
Fostemsavir (*Rukobia*)

*Rukobia*  
[rue-KOH-bee-ah]
Fostemsavir (*Rukobia*)

- **Indication:**
  - Heavily treatment-experienced adults with multidrug resistant HIV-1 failing their current antiretroviral regimen

- **Dosing:**
  - 600 mg orally twice daily, with or without food

- **Contraindications**
  - Hypersensitivity to fostemsavir
  - Coadministration with strong cytochrome P450 (CYP) 3A inducers

- **Use During Pregnancy**
  - Insufficient data

- **Common Adverse Events (≥5%)**
  - Nausea (10%)

Source: *Rukobia* Prescribing Information
HIV Cell Entry

HIV

CD4 binding site

CD4

gp120

CCR5

Intracellular Space

Host Cell
HIV Cell Entry
HIV gp120 Attachment to Host Cell CD4 Receptor

HIV

Intracellular Space
Host Cell

CD4

CCR5

CCR5
HIV Entry Inhibitors: Attachment Inhibitors

Fostemsavir—prodrug converted to Temsavir

Temsavir
Binds near CD4 binding site and prevents gp120 conformational change required for attachment

Intracellular Space
Host Cell
Fostemsavir in Treatment-Experienced Patients

BRIGHTE Study (Week 48 Data)
Fostemsavir (FTR) for Heavily Treatment Experienced BRIGHTE Study (Week 48): Background

**Study Design: BRIGHTE**

- **Background:**
  - Phase 3, randomized, multicenter, placebo-controlled, non-inferiority trial evaluating attachment inhibitor fostemsavir (FTR) in salvage ART

- **Enrollment Criteria:**
  - Highly ART-experienced adults
  - Failing current ART regimen
  - HIV RNA >400 copies/mL
  - Multiclass ART resistance
  - At least one fully active agent
  - Unable to construct viable regimen

**Randomized Cohort**

- FTR 600 mg BID + failing regimen (n = 203)
- FTR 600 mg BID + OBR (n = 272)

**Nonrandomized Cohort**

- Placebo BID + failing regimen (n = 69)
- FTR 600 mg BID + OBR (n = 99)

*Also a cohort with 0 remaining active agents; all given Fostemsavir 600 mg BID + OBR (n = 99)

*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, darunavir, tenofovir DF, etravirine, maraviroc, enfuvirtide, ibalizumab

Baseline to Day 8 Change in HIV RNA Level

<table>
<thead>
<tr>
<th></th>
<th>Median Change in HIV RNA from Baseline (Log10 copies/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fostemsavir</td>
<td>-0.79</td>
</tr>
<tr>
<td>Placebo</td>
<td>-0.17</td>
</tr>
</tbody>
</table>

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

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

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

Adverse Events

Conclusion: “In patients with multidrug-resistant HIV-1 infection with limited therapy options, those who received fostemsavir had a significantly greater decrease in the HIV-1 RNA level than those who received placebo during the first 8 days. Efficacy was sustained through 48 weeks.”

Fostemsavir in Treatment-Experienced Patients
BRIGHTE Study (Week 96 Data)
Fostemsavir (FTR) for Heavily Treatment Experienced BRIGHTE Study (Week 96): Results

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

Fostemsavir (FTR) for Heavily Treatment Experienced BRIGHTETE Study (Week 96): Results

Mean Change in CD4 T-Cell Count Through Week 96

Fostemsavir (FTR) for Heavily Treatment Experienced 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 (30)</td>
</tr>
</tbody>
</table>

**Interpretation**: “In heavily treatment-experienced individuals with advanced HIV-1 disease and limited treatment options, fostemsavir-based antiretroviral regimens were generally well tolerated and showed a distinctive trend of increasing virological and immunological response rates through 96 weeks; these findings support fostemsavir as a treatment option for this vulnerable population.”
Fostemsavir (BMS-663068) Dose-Ranging Study
AI438-006 Study
Fostemsavir (BMS-663068) Dose-Ranging Study AI438-011: Results

GS-US-141-1219: Study Design

- **Background**: Randomized, open-label, multiple-dose, parallel phase IIa study

- **Inclusion Criteria (n = 50)**
  - Adults with subtype B HIV-1
  - Treatment-naïve or experienced,
  - If treatment experienced, off ART ≥8 weeks
  - HIV RNA >5,000 copies/mL
  - CD4 count ≥200 cells/mm³
  - Not pregnant; no hepatitis B or C
  - No prior exposure to an HIV attachment inhibitor

- **Treatment Arms**
  - 8 days of fostemsavir (BMS-663068) +/- ritonavir
  - Participants randomized to various dosing arms

FTR 600 mg q12h + RTV 100 mg q12h (n = 10)
FRT 1200 mg qhs + RTV 100 mg qhs (n = 10)
FTR 1200 mg q12h + RTV 100 mg q12 hrs (n = 10)
FTR 1200 mg q12h + RTV 100 mg qam (n = 10)
FTR 1200 mg qhs (n = 10)

Fostemsavir (BMS-663068) Dose-Ranging Study AI438-011: Results

Baseline to Day 8: Change in Baseline HIV RNA Level

Interpretation: “Administration of BMS-663068 for 8 days with or without ritonavir resulted in substantial declines in plasma HIV-1 RNA levels and was generally well tolerated. Longer-term clinical trials of BMS-663068 as part of combination antiretroviral therapy are warranted.”
Fostemsavir in Treatment-Experienced Patients
AI438-011 Study
Fostemsavir in Treatment-Experienced Patients
AI438-011: 24 Week Results

Fostemsavir in Treatment-Experienced Patients AI438-011: 24 Week Results

Proportion with HIV RNA <50 copies/mL at 24 weeks (FDA snapshot analysis)

All regimens given in combination with a backbone of raltegravir + tenofovir DF

**Interpretation:** “In a comparison with ritonavir-boosted atazanavir, efficacy and safety of BMS-663068 up to the week 24 analysis support continued development of BMS-663068, which is being assessed in a phase 3 trial in heavily treatment-experienced individuals.”
Fostemsavir in Treatment-Experienced Patients

AI438-011 Study: Week 48 Results
Fostemsavir in Treatment-Experienced Patients AI438-011: 48 Week Results

Proportion with HIV RNA <50 copies/mL at 48 weeks (FDA snapshot analysis)

<table>
<thead>
<tr>
<th>Regimen</th>
<th>HIV RNA &lt; 50 copies/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fostemsavir 400 mg BID</td>
<td>40/50</td>
</tr>
<tr>
<td>Fostemsavir 800 mg BID</td>
<td>34/49</td>
</tr>
<tr>
<td>Fostemsavir 600 mg QD</td>
<td>39/51</td>
</tr>
<tr>
<td>Fostemsavir 1200 mg QD</td>
<td>36/50</td>
</tr>
<tr>
<td>Atazanavir + Ritonavir QD</td>
<td>38/51</td>
</tr>
</tbody>
</table>

All regimens given in combination with a backbone of raltegravir + tenofovir DF

Fostemsavir in Treatment-Experienced Patients AI438-011: 48 Week Conclusions

**Interpretation:** “Through week 48, fostemsavir continued to be well tolerated and showed similar efficacy to ATV/r. These results support the ongoing Phase III trial in heavily treatment-experienced adults with limited therapeutic options (≤2 classes of active antiretrovirals remaining).”

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