A Phase 3, Randomized, Controlled Clinical Trial of Bictegravir in a Fixed-Dose Combination, B/F/TAF, vs DTG/ABC/3TC in Treatment-Naive Adults at Week 96

Wohl, David; Yazdanpanah, Yazdan; Baumgarten, Axel; Clarke, Amanda; Hagins, Debbie; Ramgopal, Moti N; White, Kirsten; Collins, Sean; Chirino, Ruby; Silva, Fernando; Martin, Hal

University of North Carolina at Chapel Hill Chapel Hill, NC USA; Hôpital Bichat Claude Bernard Paris France; Zentrum für Infektionologie Berlin Prenzlauer Berg (ZIBP) Berlin Germany; Royal Sussex County Hospital Brighton UK; Central Texas Clinical Research Austin, TX USA; Midway Immunology Center Fort Pierce, FL USA; Gilead Sciences Inc Foster City, CA USA; Public Health & Medical Affairs Gilead Sciences Inc Mexico City Mexico

Introduction

- Bictegravir, a novel, potent INSTI with a high barrier to resistance, was formulated with emtricitabine and tenofovir alafenamide into a single-tablet regimen (B/F/TAF) and is approved in the US, Europe, Australia, and Canada as Biktarvy® - Unboosted, once daily dosing without regard to food - B/F/TAF was noninferior at Week 48 to standard-of-care comparators, with no treatment-emergent resistance, and was well tolerated in five randomized phase 3 studies in adults, including a study of 470 women.10

- The current trial compares B/F/TAF to cotrimoxazole dolutegravir, abacavir, and lamivudine (DTG/ABC/3TC) in treatment-naive adults and is ongoing in a double-blind design through Week 96.

- B/F/TAF is associated with significantly fewer ‘bothersome’ symptoms, particularly GI and neurologic, than DTG/ABC/3TC by patient reported outcomes (PRO)35 - Similar bone and renal profiles were observed at Week 4831

- We now report cumulative efficacy and safety results through Week 96

Results

- Resistance Analysis Population

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>B/F/TAF 314</th>
<th>DTG/ABC/3TC 315</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resistance analysis population</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Emergent resistance</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

- Virologic Rebound at or after Week 8

- Confirmed virologic failure without resuppression

- Two consecutive HIV-1 RNA tests ≥ 50 c/mL, after achieving < 50 c/mL and HIV-1 RNA ≥ 200 c/mL at the confirmation test

- ≥1 log10 copies/mL increase in HIV-1 RNA from nadir

- HIV-1 RNA ≥ 200 c/mL at Week 96 or last visit on study drug (did not require confirmation)

- The second, confirmatory sample was sent for resistance analysis, unless there was no follow-up sample

- All Grade Adverse Events (≥10%) Through Week 96

<table>
<thead>
<tr>
<th>AEs</th>
<th>B/F/TAF 314</th>
<th>DTG/ABC/3TC 315</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>15</td>
<td>16</td>
</tr>
<tr>
<td>Headache</td>
<td>13</td>
<td>16</td>
</tr>
<tr>
<td>Nausea</td>
<td>11</td>
<td>24</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>11</td>
<td>12</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>11</td>
<td>16</td>
</tr>
<tr>
<td>Fatigue</td>
<td>9</td>
<td>11</td>
</tr>
<tr>
<td>Sjogren’s Syndrome</td>
<td>9</td>
<td>12</td>
</tr>
<tr>
<td>Back pain</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>Influenza</td>
<td>7</td>
<td>10</td>
</tr>
</tbody>
</table>

- None of the AEs were considered to be fatal

- The second, confirmatory sample was sent for resistance analysis, unless there was no follow-up sample

- B/F/TAF was associated with significantly fewer “bothersome” symptoms,

- 2 deaths were reported in the B/F/TAF arm:

- – Virologic rebound at or after Week 8

- – Confirmed virologic failure without resuppression

- – Two consecutive HIV-1 RNA tests ≥ 50 c/mL, after achieving < 50 c/mL and HIV-1 RNA ≥ 200 c/mL at the confirmation test

- – ≥1 log10 copies/mL increase in HIV-1 RNA from nadir

- – HIV-1 RNA ≥ 200 c/mL at Week 96 or last visit on study drug (did not require confirmation)

- – The second, confirmatory sample was sent for resistance analysis, unless there was no follow-up sample

- Virologic Outcome at W96

- Confirmed virologic failure without resuppression

- HIV-1 RNA ≥ 200 c/mL at Week 96 or last visit on study drug (did not require confirmation)

- There were small differences in the change in median TC, LDL, and TC/HDL ratio; however, there was no difference in the proportion of participants initiating lipid-lowering agents between the two arms

- These results provide further evidence of longer-term safety, efficacy, and high barrier to resistance of B/F/TAF in people living with HIV-1

References

2. Daar ES, Sax PE, Gallant JE, et al. A Randomized, Double-Blind, Double-Dummy, Non-Inferiority Trial Comparing 88.9% Bictegravir/Tenofovir/Emtricitabine (B/F/TAF) to 89.8% Dolutegravir/Abacavir/Lamivudine (DTG/ABC/3TC) Once Daily in Treatment-Naive Adults. 2018; 70(Suppl 3):C303.