HIV WITH TRANSMITTED DRUG RESISTANCE IS DURABLY SUPPRESSED BY B/F/TAF AT WEEK 144

Rima K. Acosta
Gilead Sciences, Inc., Foster City, CA

Disclosure: Ms. Acosta and all authors are employees and stock holders of Gilead Sciences, Inc.
Objective and Study Design

- To assess the effect of preexisting, transmitted drug resistance mutations (TDR) on treatment outcomes, virologic failure, and emergent resistance to B/F/TAF, DTG/ABC/3TC, or DTG + F/TAF.

**Treatment-Naive Adults**

**Study 1489 (NCT02607930)**
- HLA B*5701 negative
- Negative for chronic HBV
- eGFR_{cr} ≥50 mL/min

Key inclusion criteria for both: no known resistance to study NRTIs; HIV-1 RNA ≥500 c/mL

- Resistance to study NRTIs was excluded at screening
  - Study 1489 excluded resistance to FTC, TAF, ABC, and 3TC
  - Study 1490 excluded resistance to FTC and TAF

**Study 1490 (NCT02607956)**
- Chronic HBV or HCV infection allowed
- eGFR_{cr} ≥30 mL/min

- TDR was assessed by population sequencing of HIV-1 PR/RT performed at screening and retrospectively at baseline by next-generation sequencing of PR/RT and IN, analyzed at a ≥15% cutoff
- Treatment outcomes were assessed at Week 144 using LOCF
- Resistance analyses performed on participants with confirmed viral rebound of HIV-1 RNA ≥200 c/mL through Week 144 or last visit who did not resuppress to <50 c/mL while on study drug

LOCF: Last Observation Carried Forward, which assigns outcomes of HIV-1 RNA <50 c/mL or ≥50 c/mL at the last on-treatment timepoint of each participant's follow up.
## Frequency of Preexisting Baseline Resistance Substitutions

<table>
<thead>
<tr>
<th>Participants With Resistance Substitutions at Baseline, n (%)</th>
<th>B/F/TAF n=634</th>
<th>DTG/ABC/3TC n=315</th>
<th>DTG + F/TAF n=325</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary NRTI associated</td>
<td>21 (3)</td>
<td>8 (3)</td>
<td>6 (2)</td>
</tr>
<tr>
<td>1–2 TAMs</td>
<td>19 (3)</td>
<td>6 (2)</td>
<td>6 (2)</td>
</tr>
<tr>
<td>K65E/R</td>
<td>2 (&lt;1)</td>
<td>1 (&lt;1)</td>
<td>0</td>
</tr>
<tr>
<td>Primary INSTI associated</td>
<td>7 (1)</td>
<td>4 (1)</td>
<td>6 (2)</td>
</tr>
<tr>
<td>T97A</td>
<td>6 (&lt;1)</td>
<td>4 (1)</td>
<td>6 (2)</td>
</tr>
<tr>
<td>Q148H</td>
<td>1 (&lt;1)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Secondary INSTI associated</td>
<td>326 (52)</td>
<td>152 (48)</td>
<td>161 (50)</td>
</tr>
<tr>
<td>Primary NNRTI associated</td>
<td>82 (13)</td>
<td>53 (17)</td>
<td>45 (14)</td>
</tr>
<tr>
<td>K103N/S</td>
<td>42 (7)</td>
<td>27 (9)</td>
<td>23 (7)</td>
</tr>
<tr>
<td>E138A/G/K/Q</td>
<td>28 (4)</td>
<td>17 (5)</td>
<td>14 (4)</td>
</tr>
<tr>
<td>Primary PI associated</td>
<td>19 (3)</td>
<td>13 (4)</td>
<td>12 (4)</td>
</tr>
</tbody>
</table>

- Primary NRTI- and INSTI-associated substitutions were infrequent in this treatment-naïve population
- Primary NNRTI-R was frequent at 13% for B/F/TAF

TAM, thymidine analogue mutation.
No Impact of Preexisting Resistance Substitutions on Treatment Outcome at Week 144

>99% of B/F/TAF participants with preexisting resistance substitutions had virologic suppression at Week 144 or last visit

*LOCF outcome analysis did not include 7 B/F/TAF participants and 1 DTG/ABC/3TC participant who had no on-treatment postbaseline HIV-1 RNA data; 1 of these B/F/TAF participants had a primary PI-associated resistance substitution.
## Virologic Resistance Results at Week 144

<table>
<thead>
<tr>
<th>Participants, n, (%)</th>
<th>B/F/TAF n=634</th>
<th>DTG/ABC/3TC n=315</th>
<th>DTG + F/TAF n=325</th>
</tr>
</thead>
<tbody>
<tr>
<td>Met criteria for resistance testing*</td>
<td>8 (1.3)</td>
<td>6 (1.9)</td>
<td>7 (2.2)</td>
</tr>
<tr>
<td>NRTI resistance detected</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>INSTI resistance detected</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*Resistance testing performed for participants with confirmed HIV-1 RNA ≥200 c/mL or ≥200 c/mL at last visit, with no resuppression of HIV-1 RNA to <50 c/mL while on study drug.

- No resistance to any components of the treatment regimens occurred in any treatment group
- In these studies, participants could remain on study drug if they had virologic failure without resistance
  - 2/8 B/F/TAF, 6/6 DTG/ABC/3TC, and 4/7 DTG + F/TAF participants had multiple confirmed virologic rebounds during the studies, and none developed drug resistance
Conclusions

- Overall, treatment with B/F/TAF, DTG/ABC/3TC, or DTG + F/TAF led to high rates of durable virologic suppression in HIV-1 treatment-naïve participants.
- The presence of transmitted, preexisting resistance substitutions did not affect treatment outcomes in these clinical trial settings:
  - For B/F/TAF participants with NRTI-, NNRTI-, and PI-resistance substitutions, high treatment efficacy was seen at Week 144 or last visit.
  - For B/F/TAF participants with study drug resistance to BIC or TAF (1 with Q148H+G140S in IN and 2 with K65E in RT), high efficacy was also seen; however, use of B/F/TAF is not generally recommended in these cases.
- No participant had treatment-emergent resistance to study drugs detected through Week 144.
- B/F/TAF has broad clinical utility as an initial or switch regimen, including in people with HIV-1 with or without resistance substitutions.

We extend our thanks to the participants and their families, study investigators and staff.

We acknowledge our co-authors Grace Q. Chen, Silvia Chang, Ross Martin, Xinxin Wang, Hailin Huang, Diana M. Brainard, Jason Hindman, Sean E. Collins, Hal Martin, Kirsten L. White.

These studies were funded by Gilead Sciences, Inc. For questions: Rima.Acosta@Gilead.com