Consistency of Dolutegravir Treatment Difference in HIV Positive Treatment Naives at Week 96


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Introduction

- Dolutegravir (DTG, GSK1349572), an INSTI not requiring boosting, is approved in 53 countries for HIV-1 infected patients. It has shown good efficacy and safety in treatment-naive patients.1-3
- We present subgroup results from the efficacy analyses of the phase III/IV studies ING113086 (SPRING-2), ING114467 (SINGLE) and ING114915 (FLAMINGO) up to Week 96 (and Week 144 for SINGLE) in antiretroviral-naive adults with HIV-1 infection.1-3

Methods: DTG treatment naive study designs

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Comparator</th>
<th>Outcomes</th>
<th>Participants</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>SINGLE</td>
<td>Treatment-naive</td>
<td>DTG + ABC/3TC vs EFV/TDF/FTC</td>
<td>Proportion of individuals with &lt;50 c/mL HIV-1 RNA</td>
<td>N=833</td>
<td>Week 96: 8.0% (2.3, 13.8), 12.4% (4.7, 20.2)</td>
</tr>
<tr>
<td>SPRING-2</td>
<td>Treatment-naive</td>
<td>DTG vs EFV/TDF/FTC</td>
<td>Virologic success</td>
<td>N=822</td>
<td>Week 96: 80% (74%, 85%)</td>
</tr>
<tr>
<td>FLAMINGO</td>
<td>Treatment-naive</td>
<td>DTG vs RAL</td>
<td>Virologic success</td>
<td>N=632</td>
<td>Week 96: 85% (68%, 92%)</td>
</tr>
</tbody>
</table>

Methods: Efficacy Analysis - Overall Response (Snapshot) and Virologic Response (ERDF)

- In the Snapshot analysis (1st endpoint in each study), a switch or discontinuation for any reason was treated as a treatment failure. The adjusted difference in the proportions was based on a stratified analysis using Cochran-Mantel-Haenzel weights.
- In the efficacy-related discontinuations = failure (ERDF) analysis, only virologic failure or withdrawal due to lack of efficacy were counted as failure. Participants who discontinued for other reasons were censored.
- Time to ERDF was analysed using the Kaplan-Meier method to allow for censoring.

FDA SNAPSHOT 96-Week Subgroup Response RATES

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>DTG</th>
<th>RAL</th>
<th>EFV/TDF/FTC = Dolutegravir</th>
<th>ORAL</th>
<th>FLAMINGO</th>
</tr>
</thead>
<tbody>
<tr>
<td>INDIVIDUALS WITH HIGH BASELINE VL BY BACKGROUND REGIMEN</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABC/3TC</td>
<td>27/57</td>
<td>47/77</td>
<td>25/49</td>
<td>67/77</td>
<td>60/85</td>
</tr>
<tr>
<td>TDF/FTC</td>
<td>62/77</td>
<td>47/77</td>
<td>94/131</td>
<td>103/131</td>
<td>25/49</td>
</tr>
<tr>
<td>INDIVIDUALS WITH LOW BASELINE VL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;200 c/mL</td>
<td>38/5</td>
<td>28/50</td>
<td>39/27</td>
<td>45/27</td>
<td>28/50</td>
</tr>
<tr>
<td>&lt;50 c/mL</td>
<td>116/144</td>
<td>103/139</td>
<td>113/139</td>
<td>113/139</td>
<td>70/72</td>
</tr>
</tbody>
</table>
ERDF by Baseline (BL) VL and Randomised Treatment: SPRING-2

A) SPRING-2: Time to ERDF by BL VL and treatment

- Group (events/N):
  - ≤100k, DTG + NRTI (12/297)
  - ≤100k, RAL + NRTI (11/295)
  - >100k, DTG + NRTI (11/154)
  - >100k, RAL + NRTI (17/116)

Pooled Analysis: ERDF Kaplan-Meier Estimates at Week 96 by BL VL and Third Agent

- DTG vs Comparator

Conclusions

- By Snapshot analysis, DTG showed superiority over comparator in 2 of the 3 naive studies
- Inconsistencies in Snapshot treatment differences were observed in smaller subgroups but not observed consistently across studies, endpoints or time points
- The efficacy-related endpoint (ERDF) did not show the same inconsistencies, enabling pooled analyses
- These pooled analyses suggested no evidence of a difference in long-term virologic efficacy between DTG and third agents or between ABC/3TC and TDF/FTC at low or high viral load
Acknowledgements

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  • The study teams and the numerous contributors from ViiV Healthcare and GSK