DTG Versus LPV/r in Second Line (DAWNING): Outcomes by WHO-Recommended NRTI Backbone

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Introduction

There needs to optimize second-line antiretroviral therapy (ART) in resource-limited settings. DAWNING is a noninferiority study comparing dolutegravir (DTG) plus 2 nucleoside reverse transcriptase inhibitors (NRTIs) with a current World Health Organization (WHO)-recommended regimen of lamivudine/tenofovir (2 NRTIs) plus 2 NRTIs in HIV-1–infected adults failing first-line therapy (HIV 1 RNA ≤100,000 c/mL) or with a non-nucleoside reverse transcriptase inhibitor (NNRTI) plus 2 NRTIs (ClinicalTrials.gov identifier, NCT02272388). We report the outcome of this study, including all study participants.

Methods

Patients were randomized (1:1) to 52 weeks of open-label, treatment-reconduit investigation. The study included 968 patients screened for the study, 627 (DTG group, n=312; LPV/r group, n=315) were randomly assigned to receive study medication, with 92% retention at Week 52. Patients were randomized to receive study medication, with 92% retention at Week 52. There were no significant differences across groups (Table)

Table. Prior ART and Background NRTIs Received at Day 1

<table>
<thead>
<tr>
<th>NRTIs</th>
<th>EFV (n=312)</th>
<th>LPV/r (n=315)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EFV</td>
<td>242 (78)</td>
<td>242 (78)</td>
</tr>
<tr>
<td>ART</td>
<td>181 (58)</td>
<td>186 (60)</td>
</tr>
<tr>
<td>FDC</td>
<td>89 (29)</td>
<td>89 (29)</td>
</tr>
<tr>
<td>TDF</td>
<td>123 (39)</td>
<td>123 (39)</td>
</tr>
<tr>
<td>ABC</td>
<td>10 (3)</td>
<td>10 (3)</td>
</tr>
</tbody>
</table>

In the DAWNING study, response rates were highest in participants taking first-line NRTIs. Fifty participants not taking WHO-recommended first-line NRTIs were excluded. WHO-recommended second-line NRTIs were defined as tenofovir disoproxil fumarate (TDF) + cleveland t2 (FTC) or tenofovir (TDF) and stavudine (AZT) or stavudine (AZT) + 3TC (AZT) = stavudine (AZT) + 3TC (AZT) + TDF = FTC + TDF (FTC). All patients had an HIV-1 RNA of ≤100,000 c/mL or >100,000 c/mL, a CD4 cell count <350 cells/µL, and no previous genotypic resistance testing at screening.

WHO-recommended NRTIs in the investigator-selected study background regimen (9/6 2 NRTIs included 11 fully active NRTIs based on known genotypic resistance testing at screening) (Figure 1).

At Week 24, DTG + 2 NRTIs was superior to LPV/r + 2 NRTIs, with 82% (257/312) and 86% (315/312) of participants, respectively, achieving HIV-1 RNA <400 c/mL (adjusted difference, 13.4% [95% confidence interval (CI), 7.3–20.5]; P<0.001). The difference was mainly driven by lower rates of failure and snapshot virologic nonresponse in the DTG group compared with the LPV/r group.

Overall, 90% of participants in the DTG group and 84% in the LPV/r group achieved the secondary efficacy endpoint of plasma HIV-1 RNA <400 c/mL at Week 52. The proportion of participants without WHO-recommended second-line NRTIs was 76/115 (66%) in the LPV/r group and 70/115 (61%) in the DTG group.

Conclusions

DTG is a safe and effective ART treatment option for patients who failed first-line ART. The DAWNING study provides important information to help guide second-line treatment decisions in resource-limited settings.

Discussions

Participants, %

<table>
<thead>
<tr>
<th>Treatment group</th>
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</tr>
</thead>
<tbody>
<tr>
<td>LPV/r</td>
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</tr>
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