Week 48 Resistance Analyses of the Once-daily, Single-tablet Regimen Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide (D/C/F/TAF) in Adults Living with HIV-1 from the AMBER and EMERALD Phase 3 Trials

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INTRODUCTION

• Boosted darunavir (DRV) containing regimens have demonstrated a high, durable virologic response, a high genetic barrier to resistance, and long-term safety in a broad range of patients,1,2 and are included in international HIV-1 treatment guidelines — DRV is also recommended for naïve and in situations when resistance test results are not available.3

• In Phase 3 randomised trials, darunavir (DRV)/cobicistat (CBI)/emtricitabine (FTC)/tenofovir alafenamide (TAF) QD was non-inferior efficacy and favorable renal and bone safety versus the control arms.

AMBER and EMERALD Studies

• AMBER (double-blind) included ART-naïve adults with a screening plasma VL ≥50 copies/mL, CD4+ cell count ≥200 cells/mm³ and genotypic sensitivity to DRV, emtricitabine (FTC) and TAF4 1Janssen Research & Development, Pennington, NJ, USA

• EMERALD (open-label) included ART-experienced, virologically-suppressed adults and

– VL ≥50 copies/mL for 12 months before screening, allowing one VL ≤50 copies/mL

– ART history

Previous ART virologic failure (VF) was defined, with no history of VF or DRV-based regimen and absence of D/C + F/TDF failure

• No restriction on F/TDF or VF failures or any other ARVs.

Virology Assessments

• For both studies (AMBER and EMERALD)

– Plasma HIV-1 RNA was quantified at screening, baseline, Weeks 2, 4, 8, 12, and every 12 weeks thereafter

– Standard resistance testing was done when HIV-1 RNA >400 copies/mL and

– All patients had HIV-1 virus that remained susceptible to all drugs in the regimen

METHODS

AMBER and EMERALD Studies

• AMBER (double-blind) included ART-naïve adults with a screening plasma VL ≥50 copies/mL, CD4+ cell count ≥200 cells/mm³ and genotypic sensitivity to DRV, emtricitabine (FTC) and TAF4

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Virology Assessments

• For both studies (AMBER and EMERALD)

– Plasma HIV-1 RNA was quantified at screening, baseline, Weeks 2, 4, 8, 12, and every 12 weeks thereafter

– Standard resistance testing was done when HIV-1 RNA >400 copies/mL (resistance assay cut-off).

• For AMBER (ART-naïve patients)

– Genotypic resistance testing was performed using GenoSure® (Invitrogen), a high-resolution genotyping assay for measuring resistance to HIV-1 reverse transcriptase (RT) and protease and standard (core) resistance test (post-baseline genotypes). No archived geno-archive data were available for genotypic analysis

– All other patients had HIV-1 virus that remained susceptible to all drugs in the treatment regimen.

RESULTS

AMBER: ART-naive Patients

Baseline Resistance

• The majority of all patients in both treatment arms were infected with HIV-1 subtype B (71%).

• There was no effect of HIV-1 subtype (B, non-B), presence of previous primary PI and/or DRV RAMs, or N(t)RTI RAMs on baseline geno-archive data. None had archived RAMs to DRV, FTC and TAF.

Post-baseline Resistance

• Through 48 weeks, eight (D/C/F/TAF) and six (control) patients had PDV centres (Figure 1), paired screening and post-baseline antiretroviral treatment genotypes were available for seven and two patients, respectively (Table 1).

• No DRV, primary PI, or TFV RAMs emerged in any patient

• One patient receiving D/C/F/TAF had a minor (VF) DRV mutation (K65R) at baseline

• No DRV, primary PI, or TFV RAMs emerged in any patient

• Overall, 91.4% vs 88.4%, respectively, with viral suppression of VF on DRV-based regimens and absence of DRV RAMs

• All INIs 86 (88) 39 (93) 125 (89)

• All NNRTIs 56 (57) 29 (69) 85 (61)

Table 1. Prevalence of Baseline RAMs12 in HIV-1 Proviral DNA from Patients with PDV centres during Treatment through 48 Weeks

<table>
<thead>
<tr>
<th>Baseline geno-archive data</th>
<th>patients (n=%)</th>
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<th>patients (n=%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Archived RAMs to DRV, FTC and TAF</td>
<td>4 (4)</td>
<td>0</td>
<td>4 (3)</td>
</tr>
<tr>
<td>Archived RAMs to DRV, FTC, and TFV</td>
<td>4 (4)</td>
<td>0</td>
<td>4 (3)</td>
</tr>
<tr>
<td>Archived RAMs to DRV, FTC, All INIs and All NNRTIs</td>
<td>4 (4)</td>
<td>0</td>
<td>4 (3)</td>
</tr>
</tbody>
</table>

Figure 1. AMBER: Individual Virologic Load Profiles for Patients with PDV centres (19/763 patients, 2% with PDV centres)

Table 2. Prevalence of Baseline RAMs12 in Patients with HIV-1 Proviral DNA from patients with prior VF in EMERALD.

<table>
<thead>
<tr>
<th>Baseline geno-archive data</th>
<th>patients (n=%)</th>
<th>patients (n=%)</th>
<th>patients (n=%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Archived RAMs to DRV, FTC and TAF</td>
<td>20 (20)</td>
<td>7 (17)</td>
<td>27 (19)</td>
</tr>
<tr>
<td>Archived RAMs to DRV, FTC, All INIs and All NNRTIs</td>
<td>5 (5)</td>
<td>1 (2)</td>
<td>6 (4)</td>
</tr>
</tbody>
</table>

CONCLUSIONS

• Through Week 48 in AMBER and EMERALD (252 patients receiving D/C/F/TAF and 629 patients receiving boosted DRV in control) with (12/88) and (2/629) treatment-emergent DRV, primary PI or TFV RAMs were observed

– In one patient, an FTC RAM (M184V) was identified post-VF (AMBER: D/C/F/TAF arm).

– In all patients with archived DRV, FTC and TAVs (archived <45 copies/mL at Week 48 or on treatment VL).

– In addition 24 (D/C/F/TAF and 7 control) patients with PDV centres had baseline geno-archive data. None had archived RAMs to DRV, FTC and TAV.

REFERENCES

5. 7. 89% to all INIs

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