Effects of once-daily darunavir/ritonavir versus lopinavir/ritonavir on lipid parameters and anthropometrics in treatment-naive, HIV-1-infected ARTEMIS patients at Week 96

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Introduction

The efficacy and safety of the protease inhibitor (PI) darunavir (DRV) combined with low-dose ritonavir (RTV) has been assessed in the Phase II, open-label, randomized ATTAIN (TMC114-C11; Acronym: Trizivir Therapy with TMC114) study. In this study, 498 treatment-naive adults were randomized to receive DRV/RTV 800/100 mg twice daily (BID) or placebo (PBO) BID. The primary endpoint was the Abel Assessment of Treatment-Induced Lipodystrophy (AA-TILDY) score at 48 weeks. In this present study, we compare the changes in lipid parameters and anthropometrics in treatment-naive, HIV-1-infected ARTEMIS patients at Week 96.

Methods

Study design

The ARTEMIS study methodology has been reported in detail previously.1,2 Treatment-naive, HIV-1-infected adult patients with HIV-1 RNA >5000 copies/mL were randomised in a 1:1 ratio to receive DRV/RTV 800/100 mg or PBO 200/200 mg (total daily dose) or PBO 200/200 mg (total daily dose or PBO).3 All patients received a fixed-dose background regimen of TDF 300 mg and FTC 200 mg.4 Assessments and endpoints

Safety assessments were performed at screening, baseline, Week 2 and every 4 weeks until Week 16, at Weeks 24 and every 12 weeks thereafter to Week 96. Patients were required to fast for at least 10 hours prior to blood sampling for biochemistry tests. The ITT population was used for the safety analysis. Incidence and severity of adverse events (AEs) and laboratory abnormalities were evaluated throughout the study. Lipid parameters assessed included triglycerides, total cholesterol, low-density lipoprotein (LDL) calculated and high-density lipoprotein (HDL). Results

Patient disposition and baseline characteristics

In total, 498 patients were randomised to receive DRV/RTV 800/100 mg (n=249) or PBO 200/200 mg (total daily dose) of PBO (n=249).5 All patients received a fixed-dose background regimen of TDF 300 mg and FTC 200 mg.6 Assessments and endpoints.

Lipid-associated AEs were reported in fewer DRV/r than LPV/r patients over time. DRV/r patients achieved HIV RNA <50 copies/mL (50.0%; 95.0%; NS) vs LPV/r patients (68.0%; 95.0%; 4.0%; NS). The change in median levels to Week 96 are shown for all lipid parameters.7 The median percentage increase in triglycerides and total cholesterol from baseline to Week 96 was significantly lower with DRV/r than with LPV/r. At Week 96, fewer DRV/r than LPV/r patients had grade 2–4 treatment-related lipid AEs.8 Few lipodystrophy- or anthropometric-associated AEs were reported in either group.9

Anthropometric measurements

Medium mid-waist ratio at Week 96 was comparable to both DRV/r and LPV/r treatment groups (baseline: 59.0%; median increase: 0.0%; 0.0%).10 Mean exposure, weeks 95.0 91.4 – – – – Mean HIV RNA, log10 copies/mL 4.86 (0.64) 4.84 (0.60) 1.68 (0.53) 1.69 (0.68) 1.70 (0.58) 1.70 (0.68) Change in median lipid levels up to Week 96

At Week 96, fewer DRV/r than LPV/r patients had grade 2–4 treatment-emergent abnormalities of triglycerides (4.0% vs 13.0%; p=0.005) or total cholesterol (18% vs 28%; p=0.0019; Table 3) – these differences were not thought to be attributable to the use of lipid-modifying drugs, which were used similarly in both groups. The proportion of patients with increases in LDL and decreases in HDL was similar between the treatment groups.11

Conclusions

No clinically relevant changes were seen with other anthropometric measurements. There were small and not considered to be clinically relevant.

Changes in median lipid levels up to 96 weeks

The changes in median levels to Week 96 are shown for all lipid parameters.12 The median percentage increase in triglycerides from baseline to Week 96 was lower for DRV/r (12% compared with LPV/r: 50%; p=0.001) – in the DRV/r group, median levels remained within the NCEP cut-offs; in the LPV/r group, triglyceride levels exceeded cut-offs as early as Week 2 and remained above the cut-off throughout (Figure 1). For total cholesterol, the median percentage increase was lower for DRV/r (15% compared with LPV/r: 33%; p<0.001) – despite higher median levels of total cholesterol over the time period in the LPV/r group, median levels were within the recommended NCEP limits (Figure 1). The changes for HDL and LDL calculated at Week 96 were less pronounced relative to the other lipid parameters (Figure 1).

References