Introduction

- The efficacy and safety of the protease inhibitor (PI) darunavir (DRV) with low dose ritonavir (RTV) at a dose of 800/100 mg tid in treatment-naive patients has been demonstrated in the ODIN trial. DRV 800/100mg tid is approved in combination with other antiretrovirals (ARVs) for the treatment of HIV-1 infection in adults in the USA, Europe, and other countries.

- IDCN (TMC114-229): Once-daily Darunavir in Treatment-experienced Patients 48- and 24-week, confirmatory, open-label trial, compared the efficacy, safety and tolerability of DRV 800/100 mg tid versus DRV/RTV 600/100mg tid in treatment-experienced, HIV-1-infected patients with or without DRV resistance-associated mutations (RAMs) at screening.

- The primary objective of the ODIN trial was to demonstrate non-inferiority in virological response of once-daily versus twice-daily DRV at 48 weeks. At Week 48, 72.1% of once-daily DRV and 70.9% of twice-daily DRV patients achieved HIV-1 RNA <50 copies/mL, the response difference was 1.2% (95% confidence interval (CI): 4.1 ± 5.9; p = 0.61), establishing non-inferiority of once-daily DRV.

Methods

Study design

- Treatment-experienced, HIV-1 infected patients on a stable highly active ARV therapy regimen for >12 weeks with no DRV RAMs at screening and with HIV-1 RNA <1,000 copies/mL at baseline, were randomised to receive either DRV 800/100 mg tid or DRV 800/100 mg bid.

- Based on ARV history and resistance testing, patients also received an investigator-selected optimised background regimen consisting of 2 NRTIs.

Efficacy and safety assessments

- The intention-to-treat (ITT) population was used for the safety analysis. Patients failed for at least 1 hour prior to each blood sample being taken for toxicokinetic testing.

- Laboratory abnormalities and incidence and severity of AEs (determined by the investigator) were assessed during each visit.

Adherence assessments

- Mean adherence (Weeks 4–48) was assessed during the last 30 days prior to study visits over 48 weeks using:
  - the Medication Adherence Self-Report Inventory (MASRI).
  - Questionnaires.

- Plasma DRV concentrations were assessed at baseline, Week 8, 24, 36 and 48.

- Safety data were collected at screening, baseline, Weeks 4, 12, 24, 36 and 48.

- Adherence as measured by pill count was performed using the Fishers' exact test.

Results

Patient disposition and baseline characteristics

- In the ODIN trial, a total of 519 treatment-experienced, HIV-1 infected patients were randomised to receive either DRV 800/100 mg tid or DRV 600/100 mg bid (n=254) or DRV 800/100 mg bid (n=265) plus 2 NRTIs.

- At baseline, demographic and disease characteristics were generally well balanced between treatment arms (Table 1).

Adherence

- Across the three methods used, the percentage of patients who were adherent over the whole treatment period ranged from 57.3% to 83% for twice-daily DRV and 54% to 80% for daily DRV.

- Based on the M-MASRI, the percentage of adherent patients was numerically greater in the once-daily DRV group (ranging between 57.9% and 83.2%) compared with the twice-daily DRV group (ranging from 59.2% to 66.2%) at all measured timepoints (Figure 1), but not significantly so (p=0.18).

- Adherence rates were numerically, but not significantly higher in the once-daily DRV group than in the twice-daily DRV group.

- Adherence rates were generally lower when calculated by pill count than by M-MASRI (Figure 1).

Conclusions

- Adherence was numerically, but not significantly higher in the once-daily DRV group than in the twice-daily DRV group.

- Fewer AEs were reported in the once-daily versus twice-daily DRV group in both adherent and suboptimally adherent patients.

- Overall, the incidence of gastrointestinal (GI) disorders was higher in suboptimally adherent patients than adherent patients in both treatment groups (Figure 4).

- GI disorders decreased over time in both treatment groups for both adherent and suboptimally adherent patients.

Acknowledgements and disclosures

References