**Introduction**

The protease inhibitor (PI) darunavir (DRV; TMC114) with low-dose ritonavir (DRV/r) at a dose of 600/100mg tid has been approved in Europe, the USA and other countries for the treatment of HIV-1 infection in treatment-experienced adults.

POWER 1 and 2 (TMC14-C123 and C202) are randomised, controlled, Phase III, 144-week trials designed to evaluate the efficacy and safety of DRV/r in comparison with currently available PIs (PIs) in treatment-experienced patients, in combination with an optimised background regimen (OBR):— at week 48, 45% of patients receiving DRV 600/100 mg bid had significantly greater virological and immunological responses than patients receiving CPIs:**1** 45% of DRV/r patients versus 10% of CPI patients achieved a viral load <50 copies/mL.

**POWER 3 is an analysis of two open-label, non-randomised trials (TMC14-C123 and C202) evaluating the efficacy and safety of DRV 600/100 mg bid plus an OBR in a larger set of treatment-experienced patients.**

At Week 48, 45% of patients achieved a viral load <50 copies/mL, and DRV/r was generally well tolerated, with a similar safety and tolerability profile to that observed in POWER 1 and 2.

These findings are supported by recent 48-week clinical data from Phase III trials, where lower incidences of gastrointestinal-related AEs were observed with DRV/r compared with ritonavir-boosted lopinavir (LPV/r).**2,3**

This pre-planned combined analysis of POWER 1, 2 and 3 evaluated the long-term safety and tolerability of DRV/r 600/100 mg bid, when all patients had reached Week 96 or discontinued earlier.

**Methods**

Patients

- Patients were male or female, aged ≥18 years, with HIV-1 RNA >1,000 copies/mL and ≥1 primary PI mutation (based on the IAS-USA 2003 list for POWER 1 and 2 and the IAS-USA 2004 list for POWER 3) at screening.
- Patients had received a PI-containing regimen for at least 8 weeks prior to screening, and patients were clinically stable and would not require treatment, but such patients were excluded from POWER 1.

- All exclusion criteria were active AIDS-defining illness, use of a treatment interruption schedule at screening, previous randomisation to a DRV treatment arm, and use of investigational antiretroviral therapy at screening.

- The study protocols were reviewed and approved by the appropriate institutional ethics committee(s) and health authorities, and were conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all patients.

**Study design**

In POWER 1 and 2, randomisation at baseline was to either DRV/r (53·[11%] were considered at least possibly related to DRV/r).

The mean duration of treatment was 90·5 weeks (SD 32·1). At the time of analysis, 149 patients (32%) had discontinued the treatment— the most common reasons for discontinuation were virological failure (63 patients, 13% and AEs (39 patients, 8%)—leading to permanent treatment discontinuation reported as at least possibly related to DRV/r were reported in 1·7% of patients.

**Adverse events**

In general, the safety and tolerability observations at Week 96 confirmed the findings at Week 48. DRV/r was not associated with any new safety concerns.

The majority of the AEs reported were grade 1–2 in severity. Apart from entrapment/associate reaction site injection (166 patients, 25%), the most common individual treatment-emergent AEs were diarhoea, nausea, nephropathy, and headache (Table 2). A total of 196 patients (42%) reported at least one grade 3 or 4 AE, of which most were considered unrelated or doubtfully related to DRV/r (53 [11%] were considered at least possibly related to DRV/r).

**Conclusions**

- Treatment with DRV/r 600/100mg bid was generally well tolerated by treatment-experienced patients over 96 weeks, with no new safety concerns identified.
- The most frequently reported treatment-emergent AEs (regardless of severity and causality) were diarhoea, nausea, nephropathy, and headache, each of which occurred in no more than 25% of patients.
- The majority of AEs were grade 1 or 2 in severity. Discontinuation due to AEs was infrequent.
- Results of the clinical laboratory evaluations confirmed those of the previous analyses. Most graded laboratory abnormalities were grade 1 or 2 in severity.
- The results of this analysis confirm and extend the safety and tolerability findings at Weeks 24 and 48. The safety findings for DRV/r from the POWER trials are also confirmed by the results of Phase III studies, where DRV/r treatment was generally well tolerated in treatment-experienced (600/100mg bid) and treatment-naïve 1800/1000 mg qd patients.

**References**


