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Poster presentation

Phase III TITAN week 96 final analysis: efficacy/safety of darunavir/r (DRV/r) vs. lopinavir/r (LPV/r) in LPV-naïve, treatment-experienced patients

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Background

The primary and secondary end-points of TITAN were met: at week (wk) 48, significantly more DRV/r than LPV/r patients (pts) had VL <400 cp/mL (77 vs. 68%; diff. 9%, 95% CI 2 – 16%; PP non-inferiority p < 0.001; ITT superiority p = 0.008). Final wk 96 data are shown.

Methods

Treatment-experienced, LPV-naïve, HIV-1-infected pts (VL>1,000 cp/mL) on stable HAART or off-treatment for ≥12 wks were randomised to DRV/r 600/100 mg BID, or LPV/r 400/100 mg BID, + OBR (≥2 NRTIs/NNRTIs) for 96 wks.

Summary of results

595 pts enrolled (79% male; median 40 yrs; mean baseline VL 4.30 $\log_{10}$cp/mL; median CD4 232 cells/mm^3); 31.4% were PI-naïve; 81.8% susceptible to ≥4 PIs. At wk 96, significantly more DRV/r than LPV/r pts achieved VL<400 cp/mL (66.8% vs. 58.9% [ITT-TLOVR]; diff. 7.9%, 95% CI 0.1 – 15.6), confirming non-inferiority (p < 0.001) and superiority of DRV/r over LPV/r (p = 0.034). At wk 96, 60.4% of DRV/r pts achieved VL<50 cp/mL compared to 55.2% of LPV/r pts (ITT-TLOVR; diff. 5.2%, 95% CI -2.8 – 13.1). Virologic failure (VF; defined as >400 cp/mL) was less frequent with DRV/r compared to LPV/r (13.8 vs. 25.6%). Median CD4 increase was 81 and 93 cells/mm^3 for DRV/r and LPV/r groups, respectively. Significantly more DRV/r than LPV/r pts with ≥1 baseline primary PI mutation achieved VL<50 cp/ml (68.0 vs. 37.6%; diff 30.4%, 95% CI 16.4 – 43.3; p < 0.001). The same was true in pts with previous use of ≥1 PI (62.3 vs. 49.0%; diff 13%, 95% CI 3.6 – 22.6; p < 0.007). The incidence of treatment-related diarrhea of at least moderate intensity (≥Grade 2) was lower in DRV/r pts compared with LPV/r pts (8.1 vs. 15.2%, p = 0.007). Rash was more common in DRV/r pts (3.4 vs. 1.0%) but infrequently led to discontinuation (1%). Most Grade 2 to 4 adverse events (AEs), at least possibly related to DRV/r or LPV/r, occurring in ≤1% pts during therapy, were comparable between groups. Serious AEs were reported for 13.8% (DRV/r) and 16.5% (LPV/r) of pts. The incidence of AEs leading to discontinuation was low (8.1% both groups). Changes in triglycerides and total cholesterol from baseline were less pronounced in DRV/r pts.

Conclusion

In this final 96-wk analysis, the primary end-point was maintained, showing non-inferiority and superiority to LPV/r in virologic response. DRV/r pts were half as likely

to experience virologic failure and showed more favourable GI and lipid profiles than LPV/r pts. Rash was more common in DRV/r pts than LPV/r pts, but infrequently led to discontinuations.