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Safety analysis of darunavir/r (DRV/r): combined data from randomised Phase II and Phase III studies

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Purpose of the study

DRV/r has been evaluated in a large-scale clinical program in a broad range of HIV-1-infected antiretroviral-naïve and -experienced patients (pts). This analysis examines the safety profile of DRV/r in pts in these studies administered DRV/r 600/100 mg BID or 800/100 mg QD, as part of combination therapy.

Methods

All available safety data at 48 weeks were analysed from 1,376 pts recruited to the DRV/r 600/100 mg BID and 800/100 mg QD arms of Phase IIb POWER 1 + 2 trials and Phase III ARTEMIS, TITAN and DUET trials. In ARTEMIS, treatment-naïve pts received 800/100 mg QD (n = 343) or lopinavir/r (LPV/r) 800/200 mg (total daily dose; n = 346); all pts received tenofovir/emtricitabine. In TITAN, treatment-experienced, LPV-naïve pts received DRV/r 600/100 mg BID (n = 298) or LPV/r 400/100 mg BID (n = 297) + OBR. In POWER 1 + 2, highly treatment-experienced pts who only received DRV/r 600/100 mg BID + OBR (n = 131) were included. Only pts from the control arm of DUET 1 + 2 (n = 604) receiving DRV/r 600/100 mg + OBR and etravirine (ETR) placebo were analysed.

Summary of results

Most common adverse events (AEs) (regardless of causality or severity) were diarrhoea and nausea. Comparing across all trials, there was a lower incidence of overall AEs, serious AEs, discontinuations due to AEs and lipid AEs in naïve pts receiving DRV/r 800/100 mg QD than in treatment-experienced pts using DRV/r 600/100 mg BID. The lower incidence of grade 2–4 at least possibly treatment-related diarrhoea with DRV/r compared to LPV/r was seen in both ARTEMIS and TITAN (see table in Figure 1). No apparent differences were seen with gender, race or age.

Conclusion

In conclusion, DRV/r was consistently well tolerated and caused significantly less grade 2–4 diarrhoea than LPV/r. In ARTEMIS, the incidence of grade 2–4 diarrhoea and nausea with DRV/r 800/100 mg QD was half that reported with DRV/r 600/100 mg BID in TITAN; this could be related to population, background regimen and/or dosing differences.

AEs during treatment, n (%)	ARTEMIS		TITAN		POWER 1+2	DUET 1+2 (ETR placebo arms)
	DRV/r (n=343)	LPV/r (n=346)	DRV/r (n=298)	LPV/r (n=297)	DRV/r (n=131)	DRV/r (n=604)
Dose (mg)	800/100 qd	800/200 (as bid or qd)	600/100 bid	400/100 bid	600/100 bid	600/100 bid
Mean exposure (weeks)	55	53	54	52	62	51‡
Serious AEs	25 (7)	41 (12)	28 (9)	31 (10)	26 (20)	141 (23)
Discontinuations due to AEs	17 (5)	27 (8)	20 (7)	20 (7)	11 (8)	34 (6)
Grade 2–4 AEs (at least possibly treatment-related)						
Diarrhoea	14 (4)*	34 (10)	23 (8)*	43 (15)	3 (2)	22 (4)
Nausea	6 (2)	10 (3)	12 (4)	13 (4)	2 (2)	8 (1)

*p<0.01 fewer events compared with LPV/r control; ‡median

Figure 1

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