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Once-daily darunavir (DRV) used in routine clinical care produces trough DRV drug concentrations in excess of 30× the protein-corrected (PC) EC_{50} for wild-type HIV

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Purpose of the study

In clinical practice measured drug concentrations often exhibit significant differences to those published in clinical trials. This can impact on virological efficacy and drug toxicity. We aimed to describe DRV concentrations achieved in a cohort of HIV-positive individuals using a non-standard dose of DRV 900 mg OD with RTV 100 mg OD.

Methods

HIV-positive patients with no DRV resistance-associated mutations were commenced on antiretroviral therapy (ART) regimens with DRV/RTV 900/100 mg OD. Trough [DRV] (C_{24})actual and predicted were measured and compared to published protein-corrected (PC)EC_{50} values for wild-type (WT) HIV (55 ng/ml) and (PC)EC_{50}

Summary of results

69 patients (pts) commenced OD DRV/RTV and have reached a median of 23 weeks of therapy (range 4–83; IQR 12–31); 15 pts started DRV/RTV as their first PI-based regimen. Others changed for: ART simplification/move to OD ART (n = 17), GI side-effects (n = 15), low level viraemia (n = 6), jaundice (n = 6), lipid abnormalities (n = 6), perceived potency (n = 4). PI-based regimens changed from were: LPV/r (n = 25), ATZ/r (n = 20), FAPV/r (n = 2), double-boosted PI (n = 7). 51 trough [DRV] were obtained. Twenty-nine pts provided actual trough samples (23–26.5 hrs post-drug; median = 24 hrs). Median trough [DRV] was 1,738 ng/ml (range 414–3,582; IQR 1085–2497); this was 31× the PCEC50 for WT HIV. A further 22 pts provided blood samples a median of 15 hrs (range 12.5–21 hrs) post-drug ingestion. Using a t1/2 of 15 hrs the projected C24 was 2026 ng/ml (range 772–4,558; IQR 1420–2638), representing 37× the PCEC50 for WT HIV. Furthermore 50/51 samples were above the PCEC50 for Res HIV. No patients have exhibited virological failure to date. All six swapping for low level viraemia reached an HIV viral load of <40 copies/ml. There was no incidence of rash and only one grade 1 LFT abnormality. Multivariate analysis of factors affecting DRV concentrations, and metabolic parameters, will be presented.

Conclusion

Once-daily darunavir used in routine clinical care produces trough DRV drug concentrations in excess of 30× the PCEC50 for WT HIV. This is in keeping with data from randomised controlled trials.

References

1. Sekar V, *et al.*: *15th Conference on Retroviruses and Opportunistic Infections, Boston, MA, USA; February 3–6, 2008* . Abstract 769.