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Etravirine protects the activity of darunavir in the DUET trials

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Purpose of the study

It has been shown in the TITAN study that darunavir/ritonavir (DRV/r) was more effective than lopinavir/ritonavir in protecting against the emergence of NRTI mutations. The protective effect of etravirine (ETR) on the development of DRV resistance was studied in patients experiencing virologic rebound in the ETR and placebo arms of the DUET trials.

Methods

In this analysis, patients with a virologic rebound were defined as those who showed a virologic response at earlier time-points but rebounded to >50 copies/ml in the DUET week 48 dataset. Phenotyping and genotyping at baseline and end-point were performed with the Antivirogram™ and Virco® TYPE HIV-1 assays, respectively, if viral load (VL) was >1000 copies/ml. Emerging mutations were those present at end-point (i.e. the last available resistance test on treatment) but not at baseline. Patients who discontinued the trial for non-virologic reasons were excluded.

Summary of results

Baseline DRV susceptibility was balanced across treatment arms: overall median (range) number of primary protease inhibitor (PI) mutations: 4 (0–8), DRV resistance associated mutations (RAMs): 2 (0–8), DRV fold change (FC): 6.40 (0.2–908.9), and 64% of patients had DRV FC ≤ 10 at baseline. ENF use and NRTI susceptibility were balanced between arms.

Virologic rebound occurred in 57 (11%) and 119 (22%) patients in the ETR and placebo arms, respectively. Among those experiencing a rebound, fewer patients in the ETR arm developed DRV RAMs (63% vs. 96% in placebo, $p < 0.0001$). The median number of emerging DRV RAMs was one and two in the ETR and placebo arms, respectively. The most frequently emerging DRV RAMs in the ETR and placebo arms were V32I (32% vs. 60%), I54L (16% vs. 34%) and I47V (11% vs. 8%). DRV FC at rebound vs. baseline increased 2.8-fold and 10.1-fold in the ETR and placebo arms, respectively ($p < 0.0001$). Among the patients with virological rebound that had a DRV FC ≤ 10 at baseline, 47% in the ETR arm vs. only 7% in the placebo arm still had a DRV FC ≤ 10 at end-point.

Conclusion

In the DUET studies, ETR-treated patients experienced less virologic rebound and loss of DRV susceptibility than those in the placebo arm. Among those with virologic failure, ETR-treated patients showed less emergence of resistance to DRV.