The impact of background regimen on virologic response to etravirine: pooled 48-week analysis of DUET-1 and DUET-2

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Abstract

Background

DUET-1 and DUET-2 are ongoing, Phase III, randomized, double-blind, placebo-controlled trials investigating the efficacy, safety and tolerability of the next-generation NNRTI etravirine (ETR) (TMC125) in HIV-1-infected, treatment-experienced patients.

Methods

Patients with documented NNRTI resistance, ≥3 primary protease inhibitor (PI) mutations and viral load ≥1000 copies/mL, were randomized 1:1 to receive ETR 200mg bid or placebo bid with a background regimen (BR) consisting of darunavir with low-dose ritonavir (DRV), optimized NNRTI (oNNRTi) and optional enfuvirtide (ENF). The primary endpoint was the percentage of patients with a confirmed viral load <50 copies/mL. Baseline antiretroviral (ARV) sensitivity was determined by phenotypic sensitivity score (PSS). Subgroup analyses were conducted on the pooled DUET trial data to determine the impact of the BR on virologic response to ETR.

Results

ETR or placebo were administered to 599 and 604 patients, respectively. Baseline characteristics were comparable between the ETR and placebo groups with regards to median baseline viral load (both 4.8 log10 copies/mL), CD4 cell count (99 cells/mm3), overall ENF use (45.4% vs 46.7%), DRV sensitivity, NRTI sensitivity and median number of sensitive ARVs (2 sensitive ARVs 78 vs 76; sensitive NRTIs 76 vs 70). Baseline DRV resistance and PSS were significant predictors of response in both treatment groups. ETR was classed as sensitive if a FC ≥10 was observed; FC = fold change.

Conclusions

ETR + BR Placebo + BR Difference vs p value
ETR or placebo were administered to 599 and 604 patients, respectively. Baseline characteristics were comparable between the ETR and placebo groups with regards to median baseline viral load (both 4.8 log10 copies/mL), CD4 cell count (99 cells/mm3), overall ENF use (45.4% vs 46.7%), DRV sensitivity, NRTI sensitivity and median number of sensitive ARVs (2 sensitive ARVs 78 vs 76; sensitive NRTIs 76 vs 70). Baseline DRV resistance and PSS were significant predictors of response in both treatment groups. ETR was classed as sensitive if a FC ≥10 was observed; FC = fold change.

Conclusions

- Superior virologic responses were achieved with ETR + BR versus placebo + BR, irrespective of ENF use, DRV FC and NRTI sensitivity, baseline DRV/RAMs and PSS.
- The 40% response rate in patients with PSS ≤2 is comparable with the expected response rate from treatment-naïve patients when ETR FC ≤3.
- Even when given with no active drugs, ETR produced a significant virologic response compared with placebo.
- In line with treatment guidelines, at least two active ARVs should be used in ARV regimens.

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DUET-1