Activity of etravirine on different HIV-1 subtypes: Week 48 data of the pooled DUET trials and in-vitro susceptibility in treatment-naive patients

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Abstract
Etravirine (ETR; TMC125) has shown good in-vitro activity against primary HIV-1 group M isolates from different subtypes and has demonstrated durable efficacy in treatment-experienced, HIV-1-infected patients in the Phase III DUET trials. In-vivo efficacy and in-vitro activity of ETR against different HIV-1 subtypes was further investigated.

DUET patients were randomised 1:1 to ETR (200mg bid) or placebo, both with a background regimen (BR) of NRTIs, darunavir (DRV) with low-dose ritonavir (DRV/r) and optional enfuvirtide (ENF). Subgroup analyses of the effect of HIV-1 subtype on the proportion of patients with viral load <50 HIV-1 RNA copies/mL (time-to-loss of virological response [TLOVR] imputation algorithm) were conducted on pooled Week 48 data. Genotype/subtype and phenotype determinations were performed using the virco® TYPE HIV-1 and Antivirogram® assays, respectively. The effect of HIV-1 subtype on ETR fold-change in EC50 (FC) values was analysed in HIV-1 recombinant clinical isolates from treatment-naive patients enrolled in other Tibotec trials (n=872) that included 49% of HIV-1 subtype non-B (18% CRF01_AE; 16% C; 5% A1; 3% CRF12_BF; 2% CRF02_AG; 1% F; 3% others).

In DUET, HIV-1 subtype was available for 594 and 595 patients in the ETR and placebo arms, respectively. The majority of these (80.8%) harboured HIV-1 subtype B. Among the non-B subtypes, CRF12_BF (2.1%), F1 (1.2%), and CRF02_AG (0.8%) were most prevalent.

Baseline disease characteristics (viral load, CD4, ETR FC, DRV FC) were similar between patients with different subtypes, except for a higher number of sensitive NRTIs used in those with HIV-1 subtype non-B. Baseline disease characteristics (viral load, CD4, ETR FC, DRV FC) were similar between patients with different subtypes, except for a higher number of sensitive NRTIs used in those with HIV-1 subtype non-B.

In the DUET studies, ETR was equally effective in suppressing viral replication in patients infected with HIV-1 subtype B or non-B. Furthermore, both subtype B and non-B HIV-1 recombinant clinical isolates from treatment-naive patients exhibited comparable levels of in-vitro phenotypic susceptibility to ETR. These results confirmed the broad activity of ETR against HIV-1.

Conclusions
ETR was equally effective in suppressing viral replication in patients infected with HIV-1 subtype B or non-B. Furthermore, both subtype B and non-B HIV-1 recombinant clinical isolates from treatment-naive patients exhibited comparable levels of in-vitro phenotypic susceptibility to ETR. These results confirmed the broad activity of ETR against HIV-1.

Supported by Tibotec