Impact of baseline NNRTI mutations on the virological response to TMC125 (etravirine; ETR) in the DUET-1 and DUET-2 Phase III clinical trials

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Abstract

Background: TMC125 is a next-generation NNRTI, active against wild-type and NNRTI-resistant HIV-1, with a high genetic barrier to the development of resistance. Here, we identified baseline genotypic determinants of decreased virological response to TMC125 in the Phase III, double-blind, placebo-controlled DUET trials.

Methods: Effect of baseline genotype on virological response (<50 HIV-1 RNA copies/mL) to TMC125 was assessed in patients not using enfuvirtide or maraviroc, and excluding discontinuations for reasons other than virological failure (n=406). The presence of K103N was not associated with decreased virological response (<50 copies/mL). The number of total baseline NNRTI RAMs correlated with the virological response (<50 copies/mL) to TMC125 (TMC125 RAMs): V90I, A98G, L100I, K101E/P, V106I, V179D/F, Y181C/I/V and G190A/S. These patients had K103N mutations from previous genotype RT mutations were included in the analysis if they were present at baseline in five or more patients.

Conclusions: Thirteen mutations, mainly occurring within other NNRTI RAMs, were associated with a decreased response to TMC125. The decrease was a function of the number of baseline TMC125 RAMs, with the largest impact in the subgroup of patients with ≥3 TMC125 RAMs.

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