Abstract

Objectives: TMC125 is a next-generation NNRTI with potent activity against HIV-1, including viruses with NNRTI-resistance-associated mutations (RAMs). DUET-1 and DUET-2 are ongoing, randomised, placebo-controlled, double-blind, Phase III trials designed to show superiority of TMC125 plus background regimen (BR) over placebo plus BR in treatment-experienced HIV-infected patients. Our report efficacy findings from planned, pooled analyses when patients reached Week 24 (or discontinued).

Methods: Patients with documented HIV-1 at study entry and ≥3 primary protease inhibitor (PI) mutations were randomised to TMC125 (200mg) plus BR or placebo twice-daily with BR of darunavir/ritonavir (DRV)+ritonavir, optimized NRTIs and optional enfuvirtide (ENF). The primary endpoint was proportion of patients with confirmed viral load <50 copies/mL at Week 24 (intent-to-treat population (ITT) vs time to loss of virologic response imputation algorithm (TLOVR)). Primary analysis was according to ENF use (de novo versus reusing or not using).

Results: Baseline characteristics were generally similar across treatment arms. Overall, TMC125 was superior to placebo for efficacy endpoints (viral load <50 copies/mL: 59% vs 41%). TMC125 demonstrated a high barrier to resistance, with ≥2 TMC125 RAMs (selected NNRTI-RAMs) required to substantially reduce virologic responses.

Conclusions: As 24 weeks, in patients with NNRTI-resistant virus, TMC125 plus BR provided superior virological and immunological response versus placebo plus BR.

References

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DUET-1
Argentina: VA Araya, M Baxa, F Chrea, R González, LA Hinojosa, CA Palma, CA Rincón, CA Soto, CA Vela.
France: J-brice Daul, C Marnere, M Monerris, M Mounier, C Pene, M Planchot, M Samii, F Yameogo.
USA: A Balane, J Ballesteros, R Northland.

DUET-2
Argentina: VA Araya, M Baxa, F Chrea, R González, LA Hinojosa, CA Palma, CA Rincón, CA Soto, CA Vela.
France: J-brice Daul, C Marnere, M Monerris, M Mounier, C Pene, M Planchot, M Samii, F Yameogo.
USA: A Balane, J Ballesteros, R Northland.

Viral load reduction from baseline (ITT NC=F)

Response (<50 copies/mL) according to number of DRV RAMS

Response (<50 copies/mL) according to number of ENF RAMS

Change in CD4 cell count from baseline (ITT NC=F)

Table. Baseline characteristics and efficacy endpoints in the overall population

DUET study design and major inclusion criteria

Baseline characteristics and background ARVs

Patients with viral load <50 copies/mL at Week 24 (primary endpoint; ITT TLOVR)

Response (<50 copies/mL) according to number of active background ARVs

Response (<50 copies/mL) according to baseline viral load and CD4 cell count

Response (<50 copies/mL) according to ENF use (primary analysis)

The greatest added benefit in the TMC125 plus BR group was seen in patients with 3 TMC125 RAMs. 86% of patients had <3 TMC125 RAMs.

TMC125 demonstrated significant activity and provides a new treatment option for patients with resistance to other NNRTIs.