Incidence and severity of nervous system and psychiatric events are similar with etravirine versus placebo: pooled 48-week data from the Phase III DUET studies

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Abstract

Background
Neuropsychiatric events have been associated with other NNRTIs. The next-generation NNRTI etravirine (ETR; TMC125) provided durable and statistically superior efficacy versus placebo over 48 weeks in treatment-experienced patients in the Phase III DUET trials. This preplanned, pooled analysis of DUET-1 and DUET-2 focuses on a comparison of nervous system and psychiatric events observed with ETR versus placebo after patients had received at least 48 weeks of treatment or discontinued.

Methods
Patients with documented NNRTI resistance and ≥3 primary protease inhibitor (PI) mutations received ETR 200mg or placebo, both bid, with a background regimen (BR) of darunavir/low-dose ritonavir (DRV/r), investigator-selected NNRTI(s) ± enfuvirtide (ENF). Specific events were identified by a physician blinded to treatment assignment, prior to database lock, based on the type of events commonly reported with NNRTIs, specifically efavirenz.

Results
The intent-to-treat population included 1203 patients: 599 vs 604 patients received ETR versus placebo, respectively (median age 45 years, 10.7% female, median baseline viral load 4.9 log10, copies/mL, median CD4 cell count 105 cells/mm3). Incidences of nervous system (17.2% vs 19.7%, p=0.066) and psychiatric disorders (16.7% vs 19.5%, p=0.204) with ETR were comparable to placebo. The most frequent nervous system events were headache (10.9% ETR vs 12.7% placebo), dizziness (3.2% vs 4.3%) and somnolence (1.8% vs 2.5%). Most frequent psychiatric events were insomnia (7.2% vs 8.3%), depression (4.2% vs 6.6%), anxiety (3.8% vs 4.1%), and psychiatric disorders (16.7% vs 19.5%, p=0.2042) with ETR.

Conclusions
The incidence and severity of neuropsychiatric events observed with ETR was similar to placebo over 48 weeks in the DUET trials. The incidence and severity of neuropsychiatric events of interest, incidences were comparable – headache and insomnia were the most commonly reported nervous system and psychiatric events, respectively, and occurred at similar instances in both treatment groups.

• Over 48 weeks, the incidence and severity of neuropsychiatric events of interest with ETR was similar to placebo; events decreased over time – headache and insomnia were the most commonly reported nervous system and psychiatric events, respectively, and occurred at similar instances in both treatment groups.
• Incidences of grade 3 neuropsychiatric events of interest were low and similar between treatment groups.
• No grade 4 neuropsychiatric events of interest were reported with ETR.
• ETR was associated with low discontinuation rates and incidence of serious AEs.

Although psychiatric history was associated with an increased frequency of neuropsychiatric events of interest, incidences were comparable between the ETR and placebo groups.

Conclusions

Acknowledgments

• We acknowledge all of the patients, investigators, and sites participating in the studies, as well as the study center staff, for their
• safety, and monitoring board, clinical event adjudication panels, Virco, Tibotec personnel and the following principal

DUET-1

• Argentina: HA Ariza, J Benetucci, P Cahn, LM Calanni, LI Cassetti, J Corral, DO David, A Krolewiecki, MH Losso,
• Brazil: AA Alvilés Montoya, G Herrera Martinez,
• Canada: RJ Myers Jr, G Richmond, K Sathasivam, S Schneider, H Schrager, P Shalit, FP Siegal, L Sloan, K Smith, S Smith, AE Greenberg, C Hicks, DT Jayaweera, S Kerkar, N Markowitz, C Martorell, C McDonald, D McMahon, M Mogyoros, J Baxter, G Beatty, D Berger, C Borkert, C Cohen, M Conant, J Ernst, C Farthing, T File, M Frank, JE Gallant, J López-Aldeguer, D Podzamczer;
• Chile: AA Alvilés Montoya, G Herrera Martinez,
• USA: J Andrade-Villanueva, G Reyes-Terán, J Sierra-Madero;
• The Netherlands: PHJ Frissen, JM Prins, BJA Rijnders;
• Mexico: LA Álvarez, A Colorado;
• The Netherlands: PHJ Frissen, JM Prins, BJA Rijnders;
• Spain: S Martin de la Torre, P del Río;