Background

Etravirine (ETR; TMC125) is a next-generation NNRTI with demonstrated activity in treatment-experienced HIV-infected patients, including those with NNRTI resistance. To support administration in children and in patients with swallowing difficulties, the oral bioavailability of the 100mg tablet dispersed in water and of the compositionally proportional 25mg pediatric tablet was assessed relative to the 100mg tablet swallowed whole.

Methods

In an open-label, randomized, three-period crossover trial in HIV-negative volunteers, three single doses of ETR were administered as: one 100mg tablet swallowed whole (Treatment A; reference), four 25mg tablets (Treatment B; test 1) and one 100mg tablet dispersed in 100mL water (Treatment C; test 2). All treatments were given following a meal and were separated by 14-day washout periods. Pharmacokinetics of ETR were assessed over 96 hours after each administration. Pharmacokinetic (PK) parameters were obtained by non-compartmental analysis and evaluated by a linear mixed effects model. Safety and tolerability were assessed.

Results

Thirty-seven volunteers participated (seven females). Least squares means (LSM) ratios (90% confidence interval [CI]) for ETR maximum plasma concentration (C_{max}) and area under the plasma concentration-time curve from time of administration up to the last timepoint with a measurable concentration after dosing (AUC_{0-96h}) in Treatment B compared to reference were 0.85 (0.79–0.93) and 0.91 (0.85–0.98), respectively, and in Treatment C compared to reference 0.95 (0.88–1.04) and 0.97 (0.90–1.03), respectively. ETR was generally safe and well tolerated. The most frequently reported adverse event (AE) was headache in eight volunteers. One volunteer discontinued prematurely due to grade 3 lipase increase during Treatment B. No other grade 3 or 4 AEs were reported.

Conclusions

No relevant change in the oral bioavailability of ETR was demonstrated when the drug was administered as either four 25mg tablets, or as one 100mg tablet dispersed in water, compared to the administration of a 100mg tablet swallowed whole. Patients who are looking for a different option may experience HIV-infected patients, including those with NNRTI-resistance. To support administration in children and in patients with swallowing difficulties, the oral bioavailability of the 100mg tablet dispersed in water and of the compositionally proportional 25mg pediatric tablet was assessed relative to the 100mg tablet swallowed whole.

Methods

In an open-label, randomized, three-period crossover trial in HIV-negative volunteers, three single doses of ETR were administered as: one 100mg tablet swallowed whole (Treatment A; reference), four 25mg tablets (Treatment B; test 1) and one 100mg tablet dispersed in 100mL water (Treatment C; test 2). All treatments were given following a meal and were separated by 14-day washout periods. Pharmacokinetics of ETR were assessed over 96 hours after each administration. Pharmacokinetic (PK) parameters were obtained by non-compartmental analysis and evaluated by a linear mixed effects model. Safety and tolerability were assessed.

Results

Thirty-seven volunteers participated (seven females). Least squares means (LSM) ratios (90% confidence interval [CI]) for ETR maximum plasma concentration (C_{max}) and area under the plasma concentration-time curve from time of administration up to the last timepoint with a measurable concentration after dosing (AUC_{0-96h}) in Treatment B compared to reference were 0.85 (0.79–0.93) and 0.91 (0.85–0.98), respectively, and in Treatment C compared to reference 0.95 (0.88–1.04) and 0.97 (0.90–1.03), respectively. ETR was generally safe and well tolerated. The most frequently reported adverse event (AE) was headache in eight volunteers. One volunteer discontinued prematurely due to grade 3 lipase increase during Treatment B. No other grade 3 or 4 AEs were reported.

Conclusions

No relevant change in the oral bioavailability of ETR was demonstrated when the drug was administered as either four 25mg tablets, or as one 100mg tablet dispersed in water, compared to the administration of a 100mg tablet swallowed whole. Patients who are looking for a different option may experience...