

Can high-dose rifampicin be an option to shorten tuberculosis treatment for tuberculosis and HIV co-infected patients?

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Background

Ongoing trials are evaluating high-dose rifampicin (R) regimens to shorten tuberculosis (TB) treatment duration. The risk of drug interaction with some antiretroviral precludes the inclusion of HIV-infected patients. We assessed the effect of high-dose R on the efavirenz (EFV) metabolism in co-infected patients.

Methods

RIFAVIRENZ was a phase-2, randomized, open-label trial conducted in Uganda between 2014 and 2017. Pulmonary TB and antiretroviral therapy (ART)-naïve patients were randomized to 2-study regimens (SR) using high-dose R (20mg/Kg) with ART initiation 2-4 weeks later with 600mg/day (SR₁) or 800mg/day (SR₂) EFV; or to 1-control regimen (CR) using R10mg/Kg and EFV600mg/day. At 8 weeks, all patients were switched to standard R and EFV doses. All patients had intensive pharmacokinetic sampling 4 weeks after EFV-R co-administration, and 4 weeks after R discontinuation. HIV and TB treatment response and safety were monitored.

Preliminary results

Of 97 included patients (SR₁: 31; SR₂: 33; CR: 33), 26.8% were females and median age, weight and CD4 count were 33 years, 53.6 kg and 141 cells/L, respectively. Under R, the median of the EFV minimum concentration (C₂₄) was 1188, 1064 and 1078ng/mL for SR₁ (N=27), SR₂ (N=30) and CR (N=28),

respectively. Five (18.5%), 6 (20.0%) and 8 (28.6%) patients had C₂₄ < 750ng/mL. At 12 weeks post-ART initiation, 92.6%, 86.2% and 92.6% of patients had HIV

viral load < 400 copies/mL. Week 8 TB culture conversion was 88.5% (SR₁), 88.9% (SR₂) and 90.3% (CR). During first 8 weeks, 6 (2 per arm) and 4 patients (SR₁: 1; SR₂: 2; CR: 1) had transaminase increase ≥ grade 3 and neuropsychiatric events ≥ grade 2, respectively.

Conclusions

Doubling the R dose does not seem to affect the EFV concentrations. These preliminary results need confirmation with the comparison of the EFV pharmacokinetics parameters with and without R.

Trials evaluating high-dose rifampicin short regimens exclude HIV-infected patients due to risk of drug interaction with antiretroviral. Based on the preliminary RIFAVIRENZ trial results, doubling the rifampicin dose does not seem to affect the efavirenz concentrations.