Three Months of Weekly Rifapentine + INH for *M. tuberculosis* Infection in HIV-Infected Persons

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**Background:** Three months of once-weekly rifapentine 900 mg + INH 900 mg under direct observation (3HP) is at least as effective as 9 months of daily self-administered INH (9H) in HIV-uninfected persons, but there are limited data on the effectiveness of 3HP in HIV-infected populations.

**Methodology:** We enrolled HIV-infected persons ≥2 years old who were tuberculin skin test positive or close contacts of TB cases, into a prospective, randomized, open-label non-inferiority trial of 3HP (directly observed) vs. 9H (self-administered). HIV-infected participants were enrolled from the U.S., Brazil, Spain, Peru, and Canada between June 2001 and December 2010. Participants were followed 33 months from enrollment, and could not receive antiretroviral therapy (ART) until > 90 days after enrollment. The endpoint was culture-confirmed TB in adults and culture-confirmed or clinical TB in children. The non-inferiority margin was 0.75%.

**Results:** There were 399 eligible HIV-infected persons enrolled (MITT population): 193 in the 9H arm and 206 in the 3HP arm. There was no significant difference in the proportion of children < 18 years (0.5 vs. 1.5%), history of injection drug use (17 vs. 13%), history of hepatitis C virus infection (14 vs. 11%), median baseline CD4 (524 vs. 496), or receipt of ART > 90 days after enrollment (13 vs. 19%) in the 9H vs. 3HP arms, respectively (P > 0.10 for all). There were 6 TB cases in 471 patient-years (p-y) of follow-up from enrollment in the 9H arm (1.27 per 100 p-y) vs. 2 TB cases in 511 p-y of follow-up in the 3HP arm (0.39 per 100 p-y). Cumulative TB rates were 3.69% vs. 1.01% in the 9H vs. 3HP arms, respectively (difference in cumulative TB rate: -2.68%; upper bound of the 95% CI of the difference: 0.55%). In the per-protocol population, cumulative TB rates were 1.90% vs. 0.56% in the 9H vs. 3HP arms, respectively. Of the 8 TB cases, 6 were pan-susceptible, one was resistant to rifampin + pyrazinamide (*M. bovis*; 3HP arm) and one was resistant to INH + rifampin (9H arm). Among those with CD4+ lymphocyte counts at study entry, the median CD4 was 344 (IQR 271-460) among those who developed TB vs. 512 (IQR 398-704) in those who did not (P = 0.06). Treatment completion was higher in the 3HP (88%) than the 9H (64%) arm (P < 0.001); drug discontinuation due to an adverse drug reaction was similar (3.4% vs. 4.2%; P = 0.80) in 3HP vs. 9H.

**Conclusions:** In this study conducted in countries with diverse TB prevalence, among HIV-infected persons who did not receive ART for at least the first 3 months, 3HP was non-inferior to 9H. 3HP had higher treatment completion rates and was well-tolerated. 3HP should be considered for treatment of latent *M. tuberculosis* infection in HIV-infected persons.