BACKGROUND

- Treating Late Tuberculosis Infection (LTBI) is important for TB elimination. In the Prevent TB trial, the 12- dose isoniazid-rifapentine (3HP) regimen had a higher completion rate than the 9-month isoniazid regimen (9H). 3HP had less hepatotoxicity than 9H, but possible hypersensitivity reactions occurred in 4% of the 3HP group.
- A post marketing assessment identifying factors associated with treatment discontinuation during programmatic use of 3HP has been published (Sondul et al., CID 2017). Among 3288 patients who received ≥1 dose of 3HP, 2867 (87%) completed treatment. Project sites and patient profiles of people who started on 3HP is shown in Figure 1 and 2.
- Median age was 36 years (range 5 to 91); equally divided by gender and majority were non-white. 421 (12.8%) patients discontinued treatment. 246 (8%) patients stopped treatment after symptoms began.
- The primary objectives of this analysis of INH-RPT were 1) to describe the adverse events (AEs) associated with INH-RPT and treatment discontinuation, 2) to identify patient risk factors that may be associated with AEs, and 3) to identify factors associated with serious AEs (SAEs) during programmatic use of 3HP.

METHODS

- We followed patients who received 3HP prospectively at 16 U.S. program sites between 06/2011 and 12/2012. Sites were divided into 3 groups: 1) those that reported demographics, weekly symptoms while on 3HP, and treatment outcomes. Ten sites also reported co-morbid conditions and concomitant medications.
- We performed descriptive analyses, and did multivariable logistic regression to identify factors independently associated with treatment discontinuation.
- AEs were defined as symptoms. AEs are symptoms or laboratory abnormalities that occurred during the course of therapy, SAEs are inpatient hospitalization or ED visit.

RESULTS

- A total of 1174 (36%) reported symptoms at least once during course of therapy (Table 1).
- Frequent symptoms and the relative risk of treatment discontinuation are identified in Table 1.
- Relative risk association of 10 most frequent adverse events with demographic, TB risk factors, and medical conditions shown in Table 2. No single symptom by itself was significantly associated with treatment discontinuation.
- Likelihood of stopping 3HP did not increase with the number of times a patient reported any adverse events (Table 3) but was associated with the number of adverse events reported at a given dose (Table 4).
- 14 (0.4%) patients had hepatitis (Table 5), 8 (0.24%) had hypotension (SBP<90mmHg); 3 (0.09%) reported hypersensitivity symptoms. 26 (0.8%) patients were hospitalized for any reason; no permanent sequelae or deaths were reported.

CONCLUSIONS

- Discontinuation due to symptoms while on therapy, and possible hypersensitivity reactions occurred at rates similar to those previously reported.
- Most patients taking INH-RPT tolerated the regimen well. Low rates of hepatitis was observed.
- Because of high rates of reported AEs in a few patients with certain characteristics, more data will be needed to evaluate tolerability of INH-RPT among those with non-HIV immunosuppression or on certain medications such as TNF-a inhibitors or SNRIs.
- TB programs should strongly consider use of the 3HP regimen for treatment of TB infection.