TBAJ-876 CL001: Pharmacokinetics and safety data from a Phase 1 trial of TBAJ-876, a novel 2nd generation diarylquinoline, in healthy participants

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Type selection
Category: Scientific research
Prefered presentation type: Oral abstract presentation

Track selection
Track: B3: Clinical trials and operational research for new treatments for TB (for adults and children)

Title

Scientific Research Abstract Text
Background: TBAJ-876 is a diarylquinoline with greater antimycobacterial potency and a potentially better safety profile than bedaquiline.
Design/Methods: 3-part study: Single ascending dose (SAD) of 68 participants [13 on placebo, 55 on TBAJ-876 10-800 mg in the fasted state or 100 mg in the fed state to evaluate food effect; multiple ascending dose (MAD) of 39 participants (12 on placebo, 25 on TBAJ-876 25, 75, and 200 mg daily for 14 days in the fed state); bioavailability part of 30 participants (3 groups receiving a single tablet of 100 mg in either the fasted or fed state, or 4 tablets of 25 mg in the fasted state) to compare PK/exposures of the suspension and tablet formulations.
Results: The concentrations of TBAJ-876 increased proportionally with dose. Administration with food increased the AUC of TBAJ-876 by 60% and 90% for the single 100 mg doses of suspension and tablet formulations, respectively. The bioavailability of the oral suspension and tablet formulations was similar. Mean half-lives were 4.4 – 11 weeks across cohorts. There were no serious AEs; most of the AEs were mild, and all resolved. There were very few clinically significant changes in safety laboratory tests, and all resolved. In both the SAD and MAD portions, the AE profile was generally similar in the TBAJ-876 and placebo groups. There was no evidence of treatment related myocardial, musculoskeletal, hepatic, or pancreatic toxicity. There were also no clinically significant QT prolongations based on ECG review. In the third part of the trial, the tablet formulation was also generally safe and well tolerated.
Conclusions: TBAJ-876 was dose proportional, with similar bioavailability of oral suspension and tablet formulations. Food increased exposure by 60% - 90%. Mean half-lives of 4.4 – 11 weeks support once daily dosing. TBAJ-876 was generally safe and well tolerated in healthy participants, and no safety signals were identified.

Summary
Summary: TBAJ-876, a diarylquinoline with greater antimycobacterial potency and a potentially better safety profile than bedaquiline, was studied in healthy participants at single (10 to 800 mg oral suspension, 100 mg of a tablet formulation) and multiple doses (25 to 200 mg/day of an oral suspension for 14 days).

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