Embargoed until Wednesday, February 15 at 3:00 pm US EST / Wednesday, February 15 at 20:00 GMT

THE NIX-TB TRIAL OF PRETOMANID, BEDAQUILINE AND LINEZOLID TO TREAT XDR TB

Conradie F, Diacon A, Everitt D, Mendel C, van Niekerk C, Howell P, Comins K, Spigelman M

Background: Patients with Extensively Drug Resistant (XDR) tuberculosis (TB) have had limited options for treatment and high mortality. Nix-TB is an ongoing open label study in South Africa of bedaquiline (400 mg qd for 2 weeks followed by 200 mg tiw), pretomanid (200 mg qd) and linezolid (1200 mg qd) given orally for 6 months.

Methods: Participants are required to have documented XDR-TB, or MDR TB treatment intolerance or failure (TI or Fr). The primary endpoint is bacteriologic failure, relapse or clinical failure at 6 months after treatment. Participants who are culture positive at 4 mos treatment may extend treatment for 3 mos. Clinical, laboratory and sputum liquid culture evaluations are performed at baseline and wks 1, 2, 4, 6, 8 and then every 4-6 wks through treatment. Eye examinations with slit lamp are made 3 times. Participants who complete treatment are followed for 24 mos after treatment end with repeat clinical assessments and sputum cultures.

Results: Since April 2015 61 participants have been enrolled as of 15 December 2016 at 2 sites. 49% of the participants are HIV positive, 79% have XDR-TB and 21% have MDR TI or Fr to prior therapy. 34 have completed the 6 months of therapy with the drug regimen and 20 have been followed to the primary endpoint at 6 months after treatment. All surviving patients were culture negative by 4 mos, with 74% negative at 8 wks. 4 participants died within the first 8 wks of therapy; 3 had multi-organ TB on autopsy and 1 had a GI bleed due to erosive esophagitis. 27% had serious adverse events (AE). No surviving participants have withdrawn from the study due to any clinical AE or lab abnormalities. The expected linezolid toxicities of peripheral neuropathy (PN) and myelosuppression (MSPN) were common but manageable. 71%, of participants had at least one linezolid dose interruption (22% of all participants due to MSPN and 28% due to PN), during the 6 mos of treatment. One had peak ALT and AST > 3 X ULN and total bili > 2X ULN, but these improved and treatment restarted without a recurrence. There were 7 cases of grade 3 or 4 transaminitis and all resolved and allowed the study regimen to be continued. There were no cases of optic neuritis. As of 15 December, 2016, there has been 1 microbiological relapse.

Conclusions: Current results of this greatly simplified and shortened all-oral regimen for drug resistant TB are encouraging in terms of both efficacy and safety.

Session at CROI:

Session: TB and Other Opportunistic Infections
Date: Wednesday, February 15
Time: 10:00AM-12:00PM PST
Presenter: Dr. Francesca Conradie, University of the WItswatersrand, Johannesburg, South Africa
Presentation time: 11:00AM-11:15AM
Link to agenda page (page 48)