Efficacy of Bedaquiline, Pretomanid, Moxifloxacin & PZA (BPaMZ) Against DS- & MDR-TB

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Abstract

Background

Major relapses in drug-resistant TB management include long treatment duration, poor adherence, and high toxicity. Patients treated with a previously described 8-week treatment regimen (BPaZ) in South Africa and the United States demonstrated significant bactericidal activity (BA) of 5.5 log(CFU)/mL. A similar regimen including bedaquiline (B), pretomanid (Pa), and pyrazinamide (Z) in the first 8 weeks of treatment of drug-susceptible TB (DS-TB) or multi-drug resistant (MDR) TB. NC-005 is an ongoing Phase 2b trial assessing the efficacy, pharmacokinetics, and safety of BPaMZ compared to the standard 6-month regimen (HRZE) with bedaquiline in DS- and MDR-TB patients. drug-resistant TB. The BPaMZ regimen in MDR-TB patients resulted in the highest level of bactericidal activity among all treatment arms. The BPaZ regimen was better tolerated and showed significantly higher bactericidal activity in patients with MDR-TB. The BPaMZ regimen in MDR-TB patients resulted in the highest level of bactericidal activity among all treatment arms. The BPaZ regimen was better tolerated and showed significantly higher bactericidal activity in patients with MDR-TB.

Methods

Randomized, patients with DS or MDR, receive placebo or one of four regimens for 8 weeks: BPaMZ, BPa200 mg, HRZE (bedaquiline 400 mg, moxifloxacin 400 mg, and pyrazinamide 1500 mg in the first 8 weeks of treatment for both DS-TB and MDR-TB. NC-005 is an ongoing Phase 2b trial assessing the efficacy, pharmacokinetics, and safety of BPaMZ compared to the standard 6-month regimen (HRZE) with bedaquiline in DS- and MDR-TB patients. Patients with HIV to reduce the duration of treatment and minimize the burden of TB treatment. The primary outcome is bactericidal activity measured by the change in log(CFU)/mL in the sputum culture positivity (days 0-56) in the sputum culture positivity (days 0-56) in the sputum culture positivity (days 0-56) in the sputum culture positivity (days 0-56) in the sputum culture positivity (days 0-56) in the sputum culture positivity (days 0-56). Safety was assessed by monitoring the incidence and severity of treatment-emergent adverse events (TEAEs).

Results

Between 10 October 2018 and 31 May 2019, 165 patients with DS-TB and 60 patients with MDR-TB were enrolled at 11 sites in South Africa, Tanzania, and Uganda. 210 patients completed treatment and were followed up to 24 months. The mean age was 34 years, 74% were male, and 90% were Black. The majority of patients were from rural areas. 22% of patients had a CD4 count less than 50. 39% of patients were HIV positive. The primary outcome was bactericidal activity measured by the change in log(CFU)/mL in the sputum culture positivity (days 0-56) in the sputum culture positivity (days 0-56) in the sputum culture positivity (days 0-56) in the sputum culture positivity (days 0-56) in the sputum culture positivity (days 0-56). Safety was assessed by monitoring the incidence and severity of treatment-emergent adverse events (TEAEs).

The bactericidal activity for all experimental regimens was significantly better for patients receiving the experimental treatments than for patients receiving the control regimen. The hazard ratios for time to culture negativity in liquid culture for all experimental treatment groups were different from HRZE, and these differences were statistically significant. The hazard ratios for time to culture negativity in liquid culture for all experimental treatment groups were different from HRZE, and these differences were statistically significant. The hazard ratios for time to culture negativity in liquid culture for all experimental treatment groups were different from HRZE, and these differences were statistically significant.

Conclusions

The BPaMZ regimen in MDR-TB patients resulted in the highest level of bactericidal activity among all treatment arms. The BPaZ regimen was better tolerated and showed significantly higher bactericidal activity in patients with MDR-TB. The BPaMZ regimen in MDR-TB patients resulted in the highest level of bactericidal activity among all treatment arms. The BPaZ regimen was better tolerated and showed significantly higher bactericidal activity in patients with MDR-TB.