INTRODUCTION

- Non-tuberculous mycobacteria (NTM) infection is associated with significant morbidity and mortality, and its treatment can be a global emerging health concern.
- The management of NTM is complicated by lengthening multidrug regimens often associated with drug toxicity and poor adherence.
- Achieving persistent negativity (PNT) NTM sputum cultures is a clinically relevant microbiologic endpoint for patients with NTM lung disease.
- Liposomal amikacin (LAI) is novel, once-daily formulation of amikacin that is currently in development for the treatment of NTM-MAC lung disease.

STUDY DESIGN

- TRD-02-112 was a placebo-controlled clinical trial of patients with NTM-MAC lung infection who had thought both their microbiology and their symptoms had improved with multidrug MAC regimens and in whom cultures remained positive. The primary endpoint of the trial was to determine if first-line LAI multidrug conversion regimens compared with multidrug alone in 12 months were non-inferior for achieving PNT patients with NTM-MAC, while minimizing toxicity.

- The efficacy of LAI was shown to treat patients with PNT NTM-MAC. Although not the main endpoint of the study, comparing LAI with multidrug alone for the primary endpoint of the study, toxicity from LAI was assessed. The apparent microbiologic efficacy of LAI is important in the population of patients with NTM-MAC, where disease burden was highest at the time of initial treatment.

- TRD-02-112: patients receiving LAI also had significant improvement in the 6-minute walk test (6MWT; distance a patient can walk in 6 minutes compared with patients receiving placebo with PNT NTM-MAC.

STUDY OBJECTIVES

- To evaluate the efficacy of LAI (590 mg) administered once daily (QD), when added to a multidrug MAC treatment regimen, for achieving PNT NTM-MAC.
- To evaluate the efficacy of LAI (590 mg) administered once daily (QD), when added to a multidrug regimens, for achieving PNT MAC for the treatment of NTM-PD.
- The management of NTM-PD is complicated by lengthy multidrug regimens that often are associated with drug toxicity and poor adherence.
- A need exists for new and better treatments for the effective management of NTM-PD that have less toxicity/complex.

STUDY ENDPOINTS

- Primary objective: the proportion of patients achieving culture conversion (CVR) at the end of the 84-day treatment period. Although there was a trend in favor of the LAI arm compared with placebo, at the end of the 84-day treatment period, there were no differences in culture negativity between the LAI arm and the placebo arm.

- Secondary objectives: to evaluate:
  - Cultures collected monthly without relapse or recurrence) by Month 6 in the LAI arm compared with a multidrug regimen alone
  - Time to culture conversion in the LAI arm compared with a multidrug regimen alone at Month 6
  - Change in 6MWT distance at end of treatment (EOT) in the LAI arm compared with a multidrug regimen alone
  - Number of patients who achieve negative MAC sputum cultures compared with placebo

REFERENCES


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DISCUSSION

- A new area of need for better treatments for the effective management of NTM-PD that has less toxicity/complex.
- LAI is novel, study formulations of amikacin, that when added to multidrug regimens in a proportionality higher than 30% of the patients, added to a multidrug regimen, for achieving PNT NTM-MAC, was more effective than a multidrug regimen alone for microorganisms' role in patients who achieve negative NTM sputum cultures compared with placebo.
- The management of NTM-PD is complicated by lengthy multidrug regimens that often are associated with drug toxicity and poor adherence. A need exists for new and better treatments for the effective management of NTM-PD that have less toxicity/complex.