Stability and Consistency of Treatment Effect With Liposomal Amikacin for Inhalation (LAI) as Add-on Therapy in Patients With Nontuberculous Mycobacterial (NTM) Lung Disease

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INTRODUCTION

 Recent reports suggest that the incidence and prevalence of nontuberculous mycobacterial (NTM) lung disease and its healthcare impacts are increasing in some regions of the world, with a higher prevalence among women, older age groups, and the minority races and ethnicities. Clinical improvement and prolonged culture conversion outcomes of 2-months of negative cultures for patients with NTM lung disease is now generally considered. Liposomal amikacin for inhalation (LAI) is a novel, manufactory product intended for development for the treatment of non-tuberculous mycobacterial (NTM) lung disease. LAI was developed to improve the stability and consistency of treatment effect with LAI, over the double-blind and open-label periods of the study.

METHODS

• Patients with treatment-naïve NTM lung disease (MAC and M. abscessus) were enrolled in a double-blind study. Eligibility criteria were as follows: 1) a confirmed positive sputum culture for fast-growing aerobic/anaerobic organisms, 2) history of at least one sputum culture positive for MAC lung disease, with a score of 1 representing a negative culture.

RESULTS

The mean rate of negative sputum culture over the double-blind study period for the liposomal amikacin for inhalation (LAI) and placebo (95% CI: 4.26-5.02) with adjustment for baseline SQS score (P = .060). During the open-label period, numeric differences in the rate of negative sputum culture between LAI and placebo were smaller than during the double-blind period. The difference in rates of negative sputum culture between the prior LAI and prior placebo groups was 15% (95% CI: 1.8%-28.2%; P < .05). The majority (~90%) of patients in both groups eventually were both administered LAI during the open-label phase. The study reports post hoc analytic results from a randomized, placebo-controlled, phase 2 clinical trial; there were no significant differences in clinical outcomes or rate of negative sputum cultures compared to those in the LAI group during the double-blind period.

DISCUSSION

The placebo clinical trial was conducted with a relatively small study sample and was of short duration. Though statistical testing in the post hoc analysis is valid, the study data suggested trends of consistency and stability in treatment regimens over time and between understanding double-blind treatment effect with LAI in the double-blind and placebo periods of the study.

CLINICAL IMPLICATIONS

• LAI 590 mg once daily appears to have a stable and consistent effect in reducing mycobacterial burden in patients with MAC or Mab lung disease, with a potentially flexible time window for drug initiation, in patients who eventually were both administered LAI during the open-label phase.

CONCLUSIONS

• These post hoc analyses support the stability and consistency of effect with LAI add-on therapy, for rifampin NTM lung disease (MAC and M. abscessus) 5 month study period.

REFERENCES


RIFAMPIN AND SUBSEQUENT RIFAMPIN-CONTAINING TREATMENT REGIMEN

In the study, post hoc analysis of patients treated with a rifampin-containing regimen, was performed. The study reports that rifampin treatment did not affect the above findings. The results are consistent with a previously published article reporting a 34% (13/38) vs. 0% (0/13) 1-year mortality rates in patients with macrolide-resistant NTC lung disease, suggesting that patients treated with rifampin experience more severe disease and higher mortality.

CAVEATS AND LIMITATIONS

• The study reports post hoc analysis results from a randomized, placebo controlled, phase clinical trial; there were no significant differences in clinical outcomes or rate of negative sputum cultures compared to those in the LAI group during the double-blind period.

• To maintain transparency, confidence intervals are reported and statistical P-values should be considered as exploratory, since the study was not powered for the proposed outcome end point and many other variables were not assessed (Table 1).

• All patients’ outcomes were ascertained prospectively but were assessed from study safety reports.

Mycobacterium avium complex (MAC) being the most common organism (MAC lung disease).

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