INTRODUCTION

- Liposomal amikacin for inhalation (LAI) is a novel formulation of amikacin currently in development for the treatment of patients with CF who have chronic lung infections caused by Pseudomonas aeruginosa and non-tuberculous mycobacteria (NTM).
- The Clinical Evaluation of ARIKAYCE™ (CLEAR)-308 study compared the efficacy, safety, and tolerability of 3 cycles of LAI once daily (QD) with tobramycin inhalation solution (TIS) twice daily (BID) in patients with CF and chronic P. aeruginosa infection.
- LAI was generally safe and well tolerated, with no unexpected adverse events.
- Eligible patients who completed CLEAR-308 were enrolled in CLEAR-310, a 2-year open-label extension study, in which all patients received LAI.

STUDY OBJECTIVE

- To determine the long-term safety, tolerability, and efficacy of LAI in patients with CF and chronic P. aeruginosa infection previously treated with LAI or TIS.

METHODS

- Figure 1 shows the CLEAR-108-110 study design.
- CLEAR-108 was a phase 3, multicenter, multicenter study.
- CLEAR-110 was the phase 3, multicenter, multicenter extension study of CLEAR-108.
- Key eligibility criteria for CLEAR-108 included a confirmed diagnosis of CF, chronic infection with P. aeruginosa age 18 years (FEV1 ≥50% predicted), or at least 30 days off previous anti-P. aeruginosa therapy, and a history of exacerbations in the prior year.
- Eligible patients in CLEAR-108 were randomized 1:1 to receive treatment with LAI QD or TIS BID for 28 days, followed by a 28-day off-treatment period, to assess the impact of LAI on the frequency of exacerbations.
- Patients who completed CLEAR-108 fulfilled criteria to enroll in CLEAR-110 to receive up to 12 additional treatment cycles (each cycle 28 days on/28 days off) of LAI 590 mg QD via PulmoAide L Pulse Nebulizer System, and stratified by age and FEV1 predicted.
- Patients who completed CLEAR-108 on-study medication could consent to enroll in CLEAR-110 to receive up to 12 treatment cycles (on-treatment, 28 days on/28 days off) of LAI 590 mg QD once daily (QD) with tobramycin inhalation solution (TIS) 500 mg BID via PulmoAide PLUS+ Nebulizer system, and stratified by age and FEV1 predicted.
- Monthly efficacy and safety evaluations included pulmonary function tests, P. aeruginosa colony-forming unit (CFU) sputum assays, and adverse event (AE) assessments.

RESULTS

- Results are presented for patients who received at least one dose of LAI and completed up to 12 cycles of LAI treatment.
- Of 206 patients overall (Figure 2), 134 completed through Year 2 of 66 of 92 patients in the CLEAR-108 LAI group (prior LAI), and 60 of 114 patients in the CLEAR-110 TIS group (prior TIS).

SAFETY SUMMARY

- The majority (64%) of patients in CLEAR-108 had ≥3 treatment-emergent AE and, as in CLEAR-108, most AEs were respiratory in nature.
- Reported AEs in both CLEAR-108 and CLEAR-110 were consistent with those expected in a population of patients with CF.
- In both treatment groups, similar trends in treatment-emergent adverse events (TEAEs) were observed in CLEAR-108 and CLEAR-110 (Table 2).
- Upper respiratory tract infection, dyspnea, hemoptysis, and cough decreased from Cycle 1 to Cycle 12 in both treatment groups (Figure 3).
- Most TEAEs were mild or moderate in severity.
- 20% of 92 (22.7%) patients in the prior LAI group and 32 (28.8%) of the prior TIS group had TEAEs related to the study drug.
- 14 (15.2%) patients in the prior LAI group and 17 (14.9%) in the prior TIS group discontinued study drug because of an AE.

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REFERENCES


CONCLUSIONS

- LAI was generally safe and well tolerated, with no unexpected adverse events.
- In patients with CF and chronic P. aeruginosa infection who continued treatment with LAI for 12 cycles or who switched from TIS to LAI for 12 cycles had similar changes in FEV1 (L) and FEV1 percent predicted, regardless of the prior treatment.
- Changes from baseline in P. aeruginosa sputum density were similar, regardless of prior treatment.

Figure 4. Mean relative change (%) in FEV1 (L) from baseline to end of study over 3 cycles in CLEAR-108 and over 12 cycles in CLEAR-110 (mITT population)

Figure 5. Mean relative change in FEV1, percent predicted from baseline to the end of the study (mITT population)

Figure 6. Mean change from baseline in Pseudomonas aeruginosa sputum density in CLEAR-108 and CLEAR-110 (mITT population)