WS5.5  A randomised, open label phase 3 study to evaluate the efficacy and safety of a dry powder formulation of inhaled colistimethate sodium (Colobreathe®) versus tobramycin nebuliser solution (TNS) in cystic fibrosis subjects with chronic Pseudomonas aeruginosa lung infection

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Objectives: To compare the efficacy and safety of a novel dry powder formulation of inhaled colistimethate sodium, Colobreathe®, versus tobramycin nebuliser solution (TNS) in an open-label multi-center, randomised study.

Methods: 380 subjects (aged ≥6 years) from 66 CF centres in EU countries, Russia and Ukraine were randomized to Colobreathe® 125 mg twice daily or TNS 300 mg twice daily. The primary endpoint was non-inferiority of Colobreathe® for change in FEV₁% predicted after 24 weeks, pre-specified ≤-3%. Secondary endpoints were changes in antibiotic resistance and the safety and convenience of Colobreathe®, using a quality of life (QoL) questionnaire.

Colobreathe® was as safe and as well tolerated as TNS in adult and paediatric subjects with CF. After logarithmic transformation based on non-normal value distribution, the adjusted mean difference between Colobreathe® and TNS groups in the change in FEV₁% predicted at week 24 was −0.97% (95% CI: −2.74%, 0.86%) for the ITT population (n=374), while it was −0.56% (95% CI: −2.71%, 1.70%) for the PP population (n=261). In the Colobreathe® and TNS groups, the proportion of colistin-resistant isolates during the 24-week period was low (≤1.1%) compared to 11.0–19.7% of tobramycin resistant isolates. At week 24, the QoL assessments were in favour of Colobreathe® in ITT and PP populations.

Conclusions: Colobreathe® demonstrated non-inferiority to TNS in lung function over 24 week treatment and CF subjects favoured Colobreathe® over TNS. We conclude that Colobreathe is as effective and was similarly tolerated as TNS in the management of chronic P aeruginosa infection in CF.

WS5.6  A challenging double-blind, placebo-controlled study of tobramycin inhalation powder in cystic fibrosis: results of the EDIT trial

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Objective: EDIT (Establish tobramycin Dry powder efficacy in Cystic fibrosis; NCT00918957) was conducted to confirm the efficacy of tobramycin inhalation powder (TIP) produced with a modified manufacturing process.

Methods: A randomized, double-blind trial of a single cycle of 28 days on/28 days off treatment with twice-daily TIP 112 mg or placebo in patients with cystic fibrosis and Pseudomonas aeruginosa (Pa) lung infection, aged 6–21 years, and naive to inhaled anti-pseudomonal therapy (at least for past 4 months). Primary endpoint was relative change in mean FEV₁% predicted from baseline to Day 29. Other assessments included change in spumt Pa density, safety and tolerability.

Results: 62 patients were randomized (n=32 TIP, n=30 placebo), falling short of the planned target of 100. Mean treatment differences (TIP-placebo) for relative and absolute change in FEV₁% predicted were 5.9% (p=0.148) and 4.4% (p=0.0496) respectively. Statistical significance for the primary endpoint was achieved in sensitivity analyses when excluding an outlier patient and when excluding invalid screening spirometry measures. TIP significantly decreased Pa sputum density by 1.2 log₁₀ colony forming units vs placebo (p=0.002). TIP was well tolerated with a safety profile consistent with previous findings.

Conclusion: Placebo control and use of treatment-naive patients led to significant recruitment challenges and an underpowered study. However, EDIT demonstrates TIP to be effective in improving lung function and reducing Pa bacterial load.