

Additional safety data for online submission

No significant changes in serum creatinine concentrations were observed in either group. In the 56-day TIS group, there was no difference between serum tobramycin levels at Day 28 and 56 (mean [SD; minimum–maximum] 1.4 [1.2; 0–5.8] µg/mL versus 1.3 [1.1; 0–3.7] µg/mL) suggesting no accumulation of tobramycin over time. In addition, the serum tobramycin levels were not influenced by the age of the patients. There were two cases of an AE ‘drug level increased’ reported in the 28-day TIS group. Neither of the cases was serious, one was reported to be mild and the other moderate in severity. Both cases were reported as probably related to study medication. No action was taken and both patients recovered.

None of the 65 patients (53% of the safety population) with audiology measurements exhibited ototoxicity, defined as a bilateral increase of ≥ 15 dB in hearing threshold at two consecutive frequencies between 2 and 8 kHz. There were, however, minor increases measured sporadically in two patients in the 56-day group, which were reported as an AE of ‘deafness’ or hearing loss, one mild and one moderate-to-severe in severity. Both events were reported as probably related to study medication, but no action was taken and both patients’ hearing returned to normal.

Additional figures for online submission

Figure. Kaplan-Meier plot of time to recurrence of any strain of *Pseudomonas aeruginosa* using expectorated sputum in patients with cystic fibrosis treated with tobramycin inhalation solution twice daily (efficacy evaluable population).

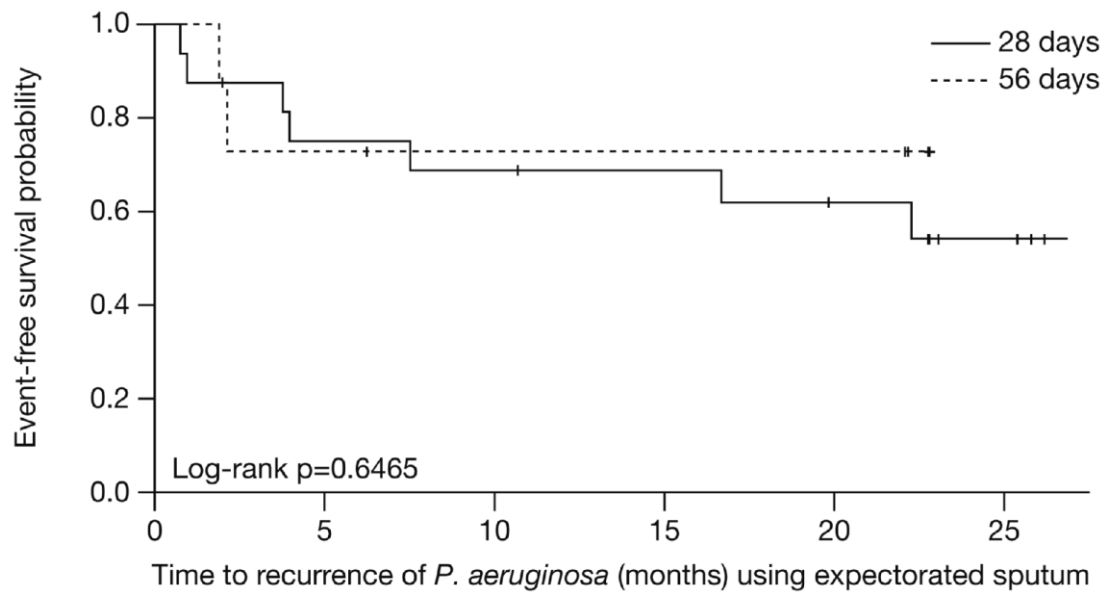


Figure. Kaplan-Meier plot of time to recurrence of any strain of *Pseudomonas aeruginosa* using deep throat swab in patients with cystic fibrosis treated with tobramycin inhalation solution twice daily (efficacy evaluable population).

