99 Early eradication therapy for *Pseudomonas aeruginosa*: impact of prior clinical status and choice of antibiotic regimen on eradication rates

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Aims: Early eradication therapy may delay chronic infection with *Pseudomonas aeruginosa* in patients with CF. We assessed the impact of prior clinical status (as determined by Leeds Criteria [1]) and antibiotic regimen on success rates of eradication therapy.
Methods: The study was conducted at the Regional Paediatric CF Unit in Leeds, UK. We reviewed all episodes of eradication therapy between 1st January 2000 and 31st December 2004. Patients were classified by Leeds Criteria as 'never', 'free' or 'intermittent'. Success for each eradication therapy episode was determined using the Artimino consensus. Results were analyzed using Fisher's Exact test.
Results: Data was complete on 223 episodes of eradication therapy in 118 patients. Fifty-five episodes were classified as 'never', 88 as 'free' and 80 as 'intermittent'. Success rates were 71%, 70% and 54% respectively. Rates were significantly higher in 'never'/'free' categories compared to intermittent ($p = 0.05/0.04$ respectively). There were no statistically significant differences between regimens, but there was a trend towards higher rates by using intravenous antibiotics for two weeks (as compared to not using them) in conjunction with aerosolized and oral antibiotics for three months (74% versus 62%, $p = 0.1$)
Conclusion: Prior clinical status can be used to predict successful outcome of eradication therapy for early *P. aeruginosa* colonization. The optimum regimen is unknown but the addition of two weeks of intravenous antibiotic therapy to existing 'oral/aerosolized antibiotics for three months' protocols may improve success rates.

References

[1] T Lee et al, J Cystic Fibrosis 2003; 2: 29–34.

100 Safety of inhaled tobramycin nebuliser solution for treatment of early *Pseudomonas aeruginosa* infection: First results from the ELITE study

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The primary objective of the ELITE study (EarLy Inhaled Tobramycin for Eradication), an open-label, randomized, multi-centre study at 21 European CF centres, was to estimate duration of eradication of Pa following 28 or 56 days of twice-daily inhaled tobramycin nebuliser solution (TNS). Secondary objectives were to assess the proportion of subjects free from Pa 1 month after the end of treatment and safety profile of the two treatment arms. An unplanned interim safety evaluation was undertaken due to potentially relevant serum tobramycin levels in three subjects identified as AEs by the investigator. 90 patients (8 months to 30 years old, 51% male) were enrolled at the time of analysis of which 66 were randomised to either 28 or 56 days of TNS. 13/34 subjects in the 28 d group were withdrawn early from the study compared to 7/32 subjects in the 56 d group. The majority of withdrawals were due to recurrence or lack of eradication of Pa. Four subjects experienced SAEs during the study, including two 28 d TNS subjects (severe constipation and moderate Stenotrophomonas infection) and two 56 d TNS subjects (severe gastroenteritis with exsiccosis and Varicella infection). Only the Stenotrophomonas infection was considered to be related to TNS treatment by the investigator. No changes in serum creatinine were observed. 4 patients had serum peak tobramycin levels >4 µg/mL of which one had a transient hearing loss on audiometry that had completely resolved after 4 weeks. In conclusion, these results demonstrate that TNS 300 mg twice daily for 28 and 56 days was safe and well tolerated by CF patients including patients <6 years of age.

101* Effect of TOBI® on the eradication of *Pseudomonas* colonisation

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Aim: to investigate the effects of TOBI® on the eradication of *Pseudomonas aeruginosa* (PA) first isolation in CF.
Methods: Our study is part of a TOBI® post-marketing surveillance involving 21 Italian CF centers. 621 CF patients were enrolled: 104 had a first PA infection, 517 a chronic colonisation. All patients were followed-up at 1 year before, at the start, at 6 and 12 months of TOBI® treatment. Eradication was defined as the absence of PA in 2 subsequent expectorate cultures after PA new isolation.
Results: Out of 104, 100 patients completed the follow-up. 43%used only TOBI®,57% TOBI® in association with another antibiotic (95%oral ciprofloxacine). Overall 68% eradicated PA: 59 patients after 6 months (of whom 3 had a PA recurrent infection); 19 patients after 12 months. Univariate analyses showed a higher probability of eradication when TOBI® was associated with another antibiotic (OR 5.2, 95%CI 1.4–19.2) and when macrolides were used in the 12 months after TOBI® start (OR 3.7, 95% CI 1.1–12.2); a lower probability with administration of intravenous (iv) antibiotics (OR 0.1, 95% CI 0.04–0.5), of DNAse (OR 0.1, 95% CI 0.03–0.4) and with hospitalization (OR 0.1, 95% CI 0.03–0.3). At multivariate analyses (on 43 patients) only the use of iv antibiotics was associated with PA eradication (OR 0.1, 95% CI 0.02–0.8).
Conclusions: 68% of CF patients with first infection eradicated PA. The association between TOBI® and another antibiotic may be more efficient although this association was present only at univariate analyses. The negative association between iv antibiotics and eradication may be attributed to TOBI® inefficacy in patients with a more severe clinical condition.

102* Treatment of intermittent *Pseudomonas aeruginosa* colonization with colistin and ciprofloxacin result in very low antibiotic resistance – 15 years follow up

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Methods: Since 1989, CF-patients with intermittent *P. aeruginosa* colonization have been treated with inhaled colistin and oral ciprofloxacin (cipro). 146 CF-patients without chronic *P. aeruginosa*-infection have been followed for 15 years (1501 patient years). 36 patients became chronically infected and were excluded from the study at the time of chronic infection.
Results: 1125 *P. aeruginosa* isolates were studied. (7.7 isolates/patient): 966 non-mucoid, 159 mucoid strains. 618 courses of colistin and cipro, 121 courses of i.v. antibiotics and 61 courses of other combinations of inhaled and oral antibiotics were given (5.5 treatments/patient). 154 isolates found during treatment indicated treatment failure (14.7% of colistin/cipro treatments, 42.3% of other combinations). 176 isolates were not treated – found before early treatment was routine, or in patients with other chronic, G-negative infections.
No colistin-resistant isolates were found. 45 cipro-resistant isolates were found (4% of all isolates) in 31 patients; 8 patients had recurrent growth of cipro-resistant isolates, while 23 patients had no more cipro-resistant isolates. 1st resistant strain occurred after a median of 24 weeks of cipro-treatment (range 0 – 99), and a median of 1.7 years after first cipro-treatment (range 0–13.9). 40 isolates were non-mucoid (4.3% of all non-mucoid isolates) and 5 were mucoid (3.2% of all mucoid isolates). Percentage of cipro-resistant strains did not increase in the study period.
Conclusion: Inhaled colsitin and oral cipro as treatment of intermittent *P. aeruginosa* colonization in CF-patients can lead to a small percentage of cipro-resistant isolates, which tend to occur after several weeks of treatment.