

# Effect of Multiple Doses of ALX-009, a Novel Combination of Hypothiocyanite and Lactoferrin, on Microbial Load in Cystic Fibrosis (CF) Sputum

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# Aim & Methods

- Treatment of sputum from CF patients with a single dose of ALX-009 results in a significant decrease in *P. aeruginosa* load. However, when *P. aeruginosa* is present at a high load, regrowth is apparent.
- **Aim:** to determine if treatment of sputum from CF patients with two doses of ALX-009, 12 hours apart, resulted in a significant decrease in microbial load of *P. aeruginosa* and total sputum microbial load.
- **Methods:** Sputum samples, excess to clinical requirements, were collected from CF patients chronically colonised with *P. aeruginosa* (n=10).
- Sputum plugs were homogenised by repeated passage through a 1 ml syringe.
- ALX-009 or phosphate buffered saline (PBS) were added at 0 and 12 hours, with total viable counts (TVC) performed at 0, 6, 12, 18, 24 and 34 hours.
- A reduction of the original inoculum by  $\geq 3 \log_{10}$  CFU/g sputum was considered bactericidal.

# Results

## ALX-009: single dose

- Bactericidal activity against *P. aeruginosa* was apparent at 6h (8/10 samples), 12h (8/10 samples), 18h (6/10 samples), 24h (5/10 samples) and 34h (3/10 samples) (Figure 1).

## ALX-009: two doses

- Bactericidal activity was apparent for all samples (n=10) at 18, 24 and 34h (Figure 1).
- No regrowth of *P. aeruginosa* was apparent in 6/10 samples at 24 or 34h.

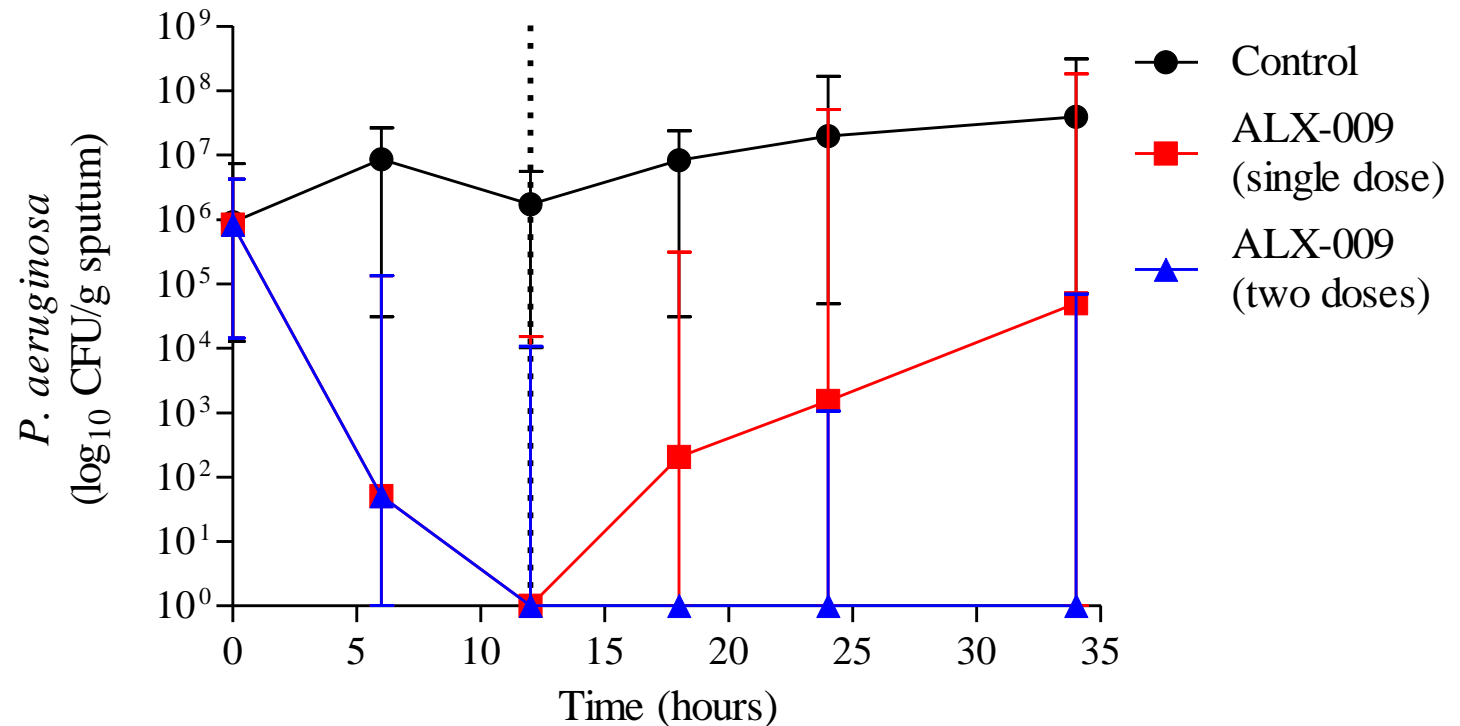


Figure 1. Time-kill assay demonstrating the effect of ALX-009 against *P. aeruginosa* in sputum (n=10); median CFU/g sputum with range.

# Results & Conclusions

## ALX-009: single dose

- Bactericidal activity against total microbial load was apparent at 18h (5/10 samples) and 34h (2/10 samples) (Figure 2).

## ALX-009: two doses

- Bactericidal activity against total microbial load was apparent at 18h (9/10 samples) and 34h (7/10 samples) (Figure 2).

## Conclusions

- A second dose of ALX-009, added within a similar time-frame to administration of currently used inhaled antibiotics, resulted in enhanced activity against *P. aeruginosa*.
- Further work to evaluate the effect of prolonged treatment with ALX-009 on *P. aeruginosa* airway burden is required.

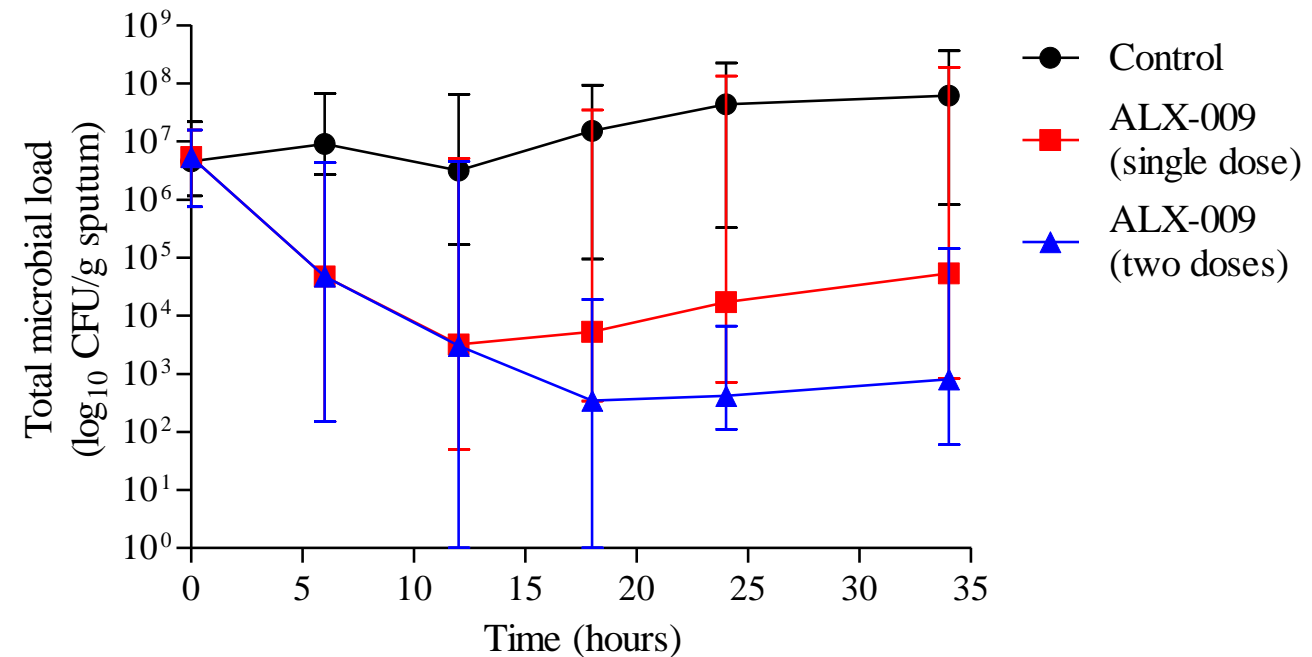


Figure 2. Time-kill assay demonstrating the effect of ALX-009 against total bacterial load in sputum (n=10); median CFU/g sputum with range.

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