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Title: Inhaled mannitol for non-cystic fibrosis bronchiectasis: Results of a 12 month, multi-centre, double-blind, controlled study

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Body: Bronchiectasis, characterised by abnormal bronchial dilatation, is associated with increased sputum production, impaired mucocilliary clearance, mucus accumulation, cough, & recurrent bacterial infection. Inhaled dry powder mannitol (M), an osmotic agent increases mucus clearance acutely & over 24hrs in patients with bronchiectasis, however long term data are needed. Aim: The primary study aim was to evaluate the difference in pulmonary exacerbations over 12mths between M & control (C). Secondary endpoints included: Time to first exacerbation, antibiotic use, SGRQ, 24hr sputum volume, Epworth Sleepiness Scale, lung function & safety. Methods: A randomised, double-blind, multicentre, phase III study in patients (18-85yr) with a confirmed diagnosis of non-CF bronchiectasis, FEV_1 (40-85% predicted) & ≥ 1.0L. 485 patients (62.7% F), mean age (SD) 59.8 (13.6) were randomised (1:1) to M (400mg bd) or C (50 mg bd). Mean (SD) baseline FEV_1% was 62.3% (13.5). Results: There was a non-significant 8% reduction (Rate ratio 0.92, p=0.31) in the rate of defined pulmonary exacerbations for patients treated with M vs. C.

However there was a statistically significant 28% delay in time to first exacerbation (Hazard Ratio: 0.78, p=0.022) & a 24% reduction in days on antibiotics (Rate ratio 0.76, p=0.0496). SGRQ was significantly improved (-2.4, p=0.046). There was no difference in the number of patients experiencing adverse events (AEs) or serious AEs in the two groups. Conclusion: Although the primary endpoint failed to reach significance there are sufficient significant improvements in secondary endpoints to indicate the need for further evaluation of M in bronchiectasis.