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Efficacy and safety of inhaled α1-antitrypsin in patients with severe α1-antitrypsin deficiency and frequent exacerbations of COPD

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ABSTRACT Patients with inherited α1-antitrypsin (AAT) deficiency (ZZ-AATD) and severe chronic obstructive pulmonary disease (COPD) frequently experience exacerbations. We postulated that inhalation of nebulised AAT would be an effective treatment.

We randomly assigned 168 patients to receive twice-daily inhalations of 80 mg AAT solution or placebo for 50 weeks. Patients used an electronic diary to capture exacerbations. The primary endpoint was time from randomisation to the first event-based exacerbation. Secondary endpoints included change in the nature of the exacerbation as defined by the Anthonisen criteria. Safety was also assessed.

Time to first moderate or severe exacerbation was a median of 112 days (interquartile range (IQR) 40–211 days) for AAT and 140 days (IQR 72–142 days) for placebo (p=0.0952). The mean yearly rate of all exacerbations was 3.12 in the AAT-treated group and 2.67 in the placebo group (p=0.31). More patients receiving AAT reported treatment-related treatment-emergent adverse events compared to placebo (57.5% *versus* 46.9%, respectively) and they were more likely to withdraw from the study. After the first year of the study, when modifications to the handling of the nebuliser were introduced, the rate of safety events in the AAT-treated group dropped to that of the placebo group.

We conclude that in AATD patients with severe COPD and frequent exacerbations, AAT inhalation for 50 weeks showed no effect on time to first exacerbation but may have changed the pattern of the episodes.