Results There were 20 patients analysed (SAFS, $n = 11$) and (ABPA $n = 9$), M: F = 8:12, median age 65.5 yrs (range = 24–78). The median duration of therapy was 30 days (IQR, 0.0–142). Clinical benefit was observed in 2 (10%) in which mean ACQ score improved from 6 to 2, overall mean AQLQ score improved by 0.95 and mean FEV1 improved by 1.2 L (63.1%). Seven (35%) failed the challenge due to bronchospasm. 11 (55%) discontinued within 12 months of therapy due to delayed bronchospasm ($n = 3$, within 4 weeks), equipment problems ($n = 4$) and lack of clinical benefit ($n = 4$) (fig 1). There were no significant changes in immunological and radiological outcomes.

Conclusion Our data suggests that the overall efficacy of nebulised amphotericin in this group of patients may be poor and is associated with high frequency of adverse events. However, the responses were excellent in 2 (10%) patients. It is not clear which patients are likely to respond. Further studies need to be conducted to establish the optimal dose range (dose, frequency), nebulizer type, pressures and identification of patients who may respond.

Abstract S92 Figure 1. Reason for treatment failure in patients treated with non-liposomal, nebulised Amphotericin B (Fungisone). Na = Not applicable (ie no failure observed).

S93 LARYNGEAL OBSTRUCTION DURING EXERCISE IS PREVALENT IN SEVERE ASTHMA

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10.1136/thoraxjnl-2013-204457.100

Introduction Reduced exercise capacity is a common problem for patients with severe asthma, yet the reason for this remains unclear. Exercise induced laryngeal obstruction (EILO) is now recognised to cause dyspnoea on exertion but has never been studied in patients with severe asthma. We therefore undertook this study, utilising a gold standard endoscopic visualisation technique, to evaluate laryngeal function during exercise, in a well-characterised cohort of patients with severe asthma.

Methods Adult patients with severe asthma were recruited following a systematic assessment of their disease. All subjects reported impairment of activities of daily living despite treatment. Subjects underwent a symptom-limited continuous

laryngoscopy during exercise (CLE) test. Laryngeal function / EILO was graded against a validated score. Measures of asthma control, perceived dyspnoea, lung function and procedure tolerability were recorded.

Results 32 patients ($n = 25$; female) completed CLE evaluation (Table 1). All patients were prescribed step 4/5 BTS treatment; 75% were prescribed maintenance oral corticosteroid. Despite this, patients reported poor disease control and high perceived dyspnoea (Table 1). EILO of at least moderate severity (graded ≥ 2 from max 3) was evident in 14 (44%) patients. The pattern and respiratory phase of EILO varied; inspiratory phase predominant ($n = 7$; 22%), expiratory phase predominant ($n = 5$, 16%), present in both phases ($n = 2$). Subjects with expiratory predominant EILO were more likely to have obstruction at the glottic level (i.e. vocal cord abduction) and poorer lung function. The CLE test was well tolerated; majority of subjects reported no/minimal procedural discomfort.

Conclusion Exercise induced laryngeal obstruction is highly prevalent in patients with severe asthma and is associated with dyspnoea. This abnormal laryngeal function was not evident at rest and may impair physical exercise capacity. Further work is required to explore underlying mechanisms and relationships with dyspnoea during activities of daily living.

Abstract S93 Table 1. Subject characteristics.

	All (n = 32)	Expiratory EILO (n = 5)	Inspiratory EILO (n = 7)
Age (yr)	43 (12)	47 (11)	39 (15)
BMI (kg/m ²)	29.8 (6.4)	27.1 (4.1)	29.1 (7.8)
FEV ₁ (% predicted)	68 (18)	47 (18)	74 (17)*
FEV ₁ /FVC	0.63 (0.14)	0.52 (0.17)	0.70 (0.14)
Asthma Control test (x/25)* [§]	12 (6–23)	12 (7–20)	9 (6–15)
Nijmegen Score (x/64)* [§]	23 (6–45)	23 (10–45)	25 (12–45)

Data presented as Mean (SD) or Median (range).

*P<0.05 difference between subgroups

Mechanisms of lung injury

S94 TUMOUR NECROSIS FACTOR RECEPTOR 1 INHIBITION USING A NOVEL INHALED HUMAN ANTIBODY REDUCES INFLAMMATION IN A HUMAN MODEL OF LUNG INJURY INDUCED BY INHALED LIPOPOLYSACCHARIDE; A RANDOMISED PLACEBO-CONTROLLED CLINICAL TRIAL

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10.1136/thoraxjnl-2013-204457.101

Introduction and Objectives Tumour Necrosis Factor receptor 1 (TNFR1) transduces the pro-inflammatory activity of TNF- α , whereas signalling through TNFR2 may contribute to tissue repair. Attenuation of TNFR1 signalling, whilst simultaneously preserving the effects of TNFR2 signalling, may be beneficial in management of acute lung injury (ALI). GSK1995057 is a novel, fully human antibody fragment (domain antibody) that selectively binds TNFR1 and antagonises signalling of TNF- α via TNFR1.