

Abstract S68 Table 1 Overview of solicited and unsolicited adverse events

	Group 1: 140 µg F-protein-FP/2 mg BLP		Group 2: 350 µg F-protein-FP/5 mg BLP		Placebo	
	Post prime (n=18)	Post boost (n=17)	Post prime (n=18)	Post boost (n=18)	Post prime (n=12)	Post boost (n=12)
n (% of subjects with events)						
Local solicited AEs						
Loss of smell	3 (16.7)	4 (23.5)	1 (5.6)	0	2 (16.7)	0
Nasal discomfort	2 (11.1)	3 (17.6)	3 (16.7)	4 (22.2)	3 (25.0)	1 (8.3)
Nasal pain	1 (5.6)	0	1 (5.6)	2 (11.1)	1 (8.3)	0
Rhinorrhoea	8 (44.4)	4 (23.5)	6 (33.3)	4 (22.2)	3 (25.0)	2 (16.7)
stuffy nose	8 (44.4)	5 (29.4)	6 (33.3)	4 (22.2)	4 (33.3)	6 (50.0)
Sneezing	6 (33.3)	2 (11.8)	1 (5.6)	3 (16.7)	2 (16.7)	2 (16.7)
Sore throat	2 (11.1)	1 (5.9)	5 (27.8)	3 (16.7)	3 (25.0)	5 (41.7)
Solicited systemic AEs						
Arthralgia	1 (5.6)	2 (11.8)	1 (5.6)	1 (5.6)	0	0
Fatigue	9 (50.0)	7 (41.2)	6 (33.3)	6 (33.3)	7 (58.3)	5 (41.7)
Feeling feverish	2 (11.1)	1 (5.6)	1 (5.6)	1 (5.6)	1 (8.3)	1 (8.3)
Headache	8 (44.4)	4 (23.5)	8 (44.4)	8 (44.4)	4 (33.3)	2 (16.7)
Malaise	2 (11.8)	2 (11.8)	2 (11.1)	0	1 (8.3)	1 (8.3)
Myalgia	5 (27.8)	3 (17.6)	0	2 (11.1)	2 (16.7)	1 (8.3)
All unsolicited AEs						
Oro-pharyngeal pain	0	0	1 (5.6)	5 (27.8)	1 (8.3)	1 (8.3)
Cough	0	1 (5.6)	3 (16.7)	1 (5.6)	0	1 (8.3)

New approaches to characterising paediatric respiratory diseases

S69 GENETIC AND STRUCTURAL CHARACTERISATION OF OUTER DYNEIN ARM VARIANTS CAUSING PRIMARY CILIARY DYSKINESIA

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Introduction Primary ciliary dyskinesia (PCD) is a heterogeneous, recessive disease, characterised by dysfunction of motile cilia that arises from structural defects. Symptoms include chronic pulmonary disease, rhinosinusitis, otitis media, laterality defects, congenital heart disease and subfertility. The most commonly affected cilia structure is the outer dynein arm (ODA), a complex structure composed of a docking complex

and multiple heavy, light and intermediate dynein chains. An understanding of the relationship between the genetic and structural phenotype of ODA variants will allow patient stratification and improve diagnosis through verification of new candidate genes.

Methods 195 PCD patients were genotyped using next generation sequencing. Candidate variants were confirmed by Sanger sequencing and familial segregation analysis. For selected ODA mutations, electron tomography, an extension to transmission electron microscopy, was used to produce high-resolution 3D models of ciliary axonemal microtubular doublets and ODA volume ratios. The data were analysed to determine the impact of eight different gene mutations causing different structural defects of the ODAs.

Results 39% of patients had bi-allelic mutations identified which are associated with ODA structure. These include variants in known PCD genes: DNAH5 (n=39), DNAH11 (n=18), DNAI1 (n=8), DNAI2 (n=5), ARMC4 (n=3), CCDC114 (n=2), DNAL1 (n=1) and mutations in the novel candidate DNAH9. Variants in DNAH9 have been suggested as a cause of PCD previously but disregarded due to lack of phenotypic evidence. 3D models of the ODA complex identified genotype specific changes in the ODA complex in PCD. The ODA structure in PCD was different in the proximal region, in proximity to the microvilli, when compared to the distal region, towards the tip of the axoneme. A significant deficiency in the ODA volume was detected at the distal part of the axoneme in the patient with DNAH9 defects, whereas the proximal portion was unaffected, reflecting the protein position of DNAH9.

Conclusion 3D electron tomography can be used to detect subtle changes in the ultrastructure of the ODA in PCD patients with differences detected in the impact of mutations in proximal versus distal regions of the cilia.

S70 CHANGE IN LUNG CLEARANCE INDEX AND EXHALED NITRIC OXIDE AS MARKERS OF SYSTEMIC CORTICOSTEROID RESPONSE IN CHILDREN WITH SEVERE ASTHMA

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Introduction Children with severe therapy resistant asthma (STRA) have heterogeneous disease with variable response to steroids. Currently, spirometry (forced expiratory volume in 1 s (FEV₁)) is most widely used to assess treatment response. We hypothesised lung clearance index (LCI) would more sensitively assess steroid response than FEV₁ alone, using our multi-domain approach [JACI 2016;138:413–420] with the addition of LCI to measure response of distal airway disease.

Methods 39 children with STRA were recruited during a clinically-indicated admission for bronchoscopy and intramuscular triamcinolone injection. Prior to triamcinolone, they performed LCI, spirometry, FeNO, and filled in the asthma control test (ACT). They were followed up at 4 weeks and these tests repeated. ACT was considered abnormal if <20, LCI if ≥7.1, FEV₁ percent predicted below 80%, and FeNO if ≥24 parts per billion. Any domain which was abnormal at visit 2 was a non-response.