Abstract S85 Table 1 Baseline Characteristics

	Whole cohort n=116	Plugged n=69	No Plugging n=47	Plugging low n=29	Plugging High n=40	P value plugged vs unplugged	P value across plugging groups
Female	73	44	29	14	30	0.82	0.07
N (%)	(62.9)	(63.8)	(61.7)	(48.3)	(75)		
Age	52.3	53.94	49.96	55	53.18	0.10	0.22
Mean (SD)	(12.8)	(13.2)	(11.8)	(12.9)	(13.6)		
BMI	31.3	31.0	31.7	30.5	31.3	0.59	0.78
Mean (SD)	(7.2)	(6.6)	(8.0)	(6.4)	(6.7)		
AER	4.8	4.7	4.9	4.6	4.8	0.67	0.83
Mean (SD)	(3.3)	(3.0)	(3.9)	(3.0)	(3.0)		
mOCS	64	39	25	17	22	0.72	0.90
N (%)	(55.2)	(56.5)	(53.2)	(58.6)	(55.0)		
Peak Eosinophil Count	0.6 (0.4 - 0.9)	0.6 (0.5–0.9)	0.6 (0.4–0.8)	0.6 (0.5–0.7)	0.7 (0.5–1.0)	0.40	0.45
Median (IQR)							
FENO ppb	44	44	47	62	38.5	0.74	0.3
Median (IQR)	(25–78)	(27–83)	(23–67)	(26–93)	(27.5–58.5)		
Adult onset	59	37	22	15	22	0.47	0.74
N (%)	(50.9)	(53.6)	(46.8)	(51.7)	(55.0)		
Atopy	86	47	39	18	29	0.07	0.12
N (%)	(74.1)	(68.1)	(83.0)	(62.1)	(72.5)		
Nasal Polyps	35	25	10	7	18	0.08	0.04
N (%)	(30.2)	(36.2)	(21.3)	(24.1)	(45.0)		
FEV1 Litres	1.7	1.6	1.86	1.6	1.6	0.06	0.17
Mean (SD)	(0.7)	(0.6)	(0.7)	(0.7)	(0.7)		
FEV1 % Predicted	61.7	59.6	64.8	58.5	60.4	0.20	0.42
Mean (SD)	(21.6)	(19.8)	(30.0)	(21.3)	(18.9)		
ACQ-6	2.9	2.8	3.2	2.9	2.7	0.12	0.26
Mean (SD)	(1.4)	(1.4)	(1.3)	(1.4)	(1.4)		
Mini-AQLQ	3.3	3.3	3.2	3.0	3.6	0.68	0.25
Mean (SD)	(1.7)	(1.7)	(1.8)	(1.8)	(1.5)		
Non-Smokers	77	42	35	15	27	0.19	0.24
N (%)	(66.4)	(60.9)	(74.5)	(15.7)	(67.5)		
Ex-Smokers	37	26	11	14	12		
N (%)	(31.9)	(37.7)	(23.4)	(48.3)	(30)		
Current Smokers	1	1	0	0	1		
N (%)	(0.9)	(1.4)			(2.5)		

For normally distributed data, number quoted is mean (standard deviation). For non-parametric variables, number quoted is median (inter-quartile range).

Abbreviations: ACQ6 = Asthma Control Questionnaire 6; Receptor; BMI = Body Mass Index; FeNO = Fractional exhaled Nitric Oxide; FEV1 = Forced Expiratory Volume in 1 second; mOCS = maintenance Oral Corticosteroid; Mini-AQLQ = Mini Asthma Quality of Life Questionnaire; ppb = parts per billion;

S86

LONG-TERM ASSESSMENT OF EXACERBATIONS AND LUNG FUNCTION IN THE LIBERTY ASTHMA TRAVERSE STUDY, STRATIFIED BY LUNG FUNCTION IMPROVEMENTS AT THE END OF THE PHASE 3 LIBERTY ASTHMA QUEST PARENT STUDY

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Introduction and Objectives Low pre-bronchodilator FEV₁ in asthma patients is associated with increased exacerbations and lung function decline. Dupilumab, a fully human monoclonal antibody, blocks the shared receptor component for interleukin-4 and interleukin-13, key and central

drivers of type 2 inflammation in multiple diseases. TRAVERSE (NCT02134028), a single-arm, open-label extension study, evaluated long-term safety, tolerability, and efficacy of dupilumab added to standard of care in adult/adolescent patients continuing from a previous dupilumab asthma study. Post-hoc analysis of TRAVERSE patients enrolled from QUEST (NCT02414854) with baseline blood eosinophils ≥ 150 cells/ μ L or FeNO ≥ 25 parts per billion assessed the relationship of lung function (characterized by baseline and change in pre-bronchodilator FEV₁ and FEV₁:forced vital capacity [FVC] ratio) on severe exacerbation rate (AER).

Methods Patients with increased type 2 inflammatory biomarkers who participated in QUEST (52 weeks) and continued to TRAVERSE (up to 96 weeks) were stratified by pre-bronchodilator FEV₁ improvement at Week 52 of QUEST. Endpoints assessed were exacerbation history in the year before QUEST; annualized AER during QUEST and

Spoken sessions

TRAVERSE; change from QUEST baseline in pre-bronchodilator FEV₁ in QUEST and TRAVERSE and FEV₁:FVC in TRAVERSE; and proportion of patients who maintained pre-bronchodilator FEV₁ improvements at Week 52 in QUEST during TRAVERSE.

Results Of 1,227 type 2 QUEST patients, 102 (8%) and 661 (54%) achieved <100 and ≥100mL improvement in pre-bronchodilator FEV₁ at Week 52, respectively. Of these, 556

patients achieved improvements of ≥200mL. Patients with greater improvements in pre-bronchodilator FEV₁ by the end of QUEST experienced long-term enhanced AER reductions (≥100mL: 0.202; ≥200mL: 0.180) and FEV₁ and FEV₁:FVC improvements during Weeks 48–96 in TRAVERSE. Patients with <100mL improvement in QUEST also showed benefits of dupilumab treatment during TRAVERSE (unadjusted AER: 0.216, Weeks 48–96) (table 1). Dupilumab-treated patients

Abstract S86 Table 1 Efficacy endpoints during QUEST and TRAVERSE in type 2 QUEST patients stratified by level of pre-bronchodilator FEV₁ improvement at Week 52 of QUEST

	<100mL improvement		≥100mL improvement		≥200mL improvement	
	Combined PBO	Combined DPL	Combined PBO	Combined DPL	Combined PBO	Combined DPL
Number of severe asthma exacerbations ^a experienced in the year prior to QUEST (exacerbation history)						
N	32	70	199	462	158	398
Mean (SD)	2.19 (1.97)	1.96 (1.71)	2.27 (1.97)	2.09 (2.00)	2.20 (1.85)	2.12 (2.10)
Adjusted annualized event rate of severe exacerbation ^a during 52-week treatment period of QUEST ^b						
Patients with ≥1 severe exacerbation events, n (%)	12(37.5)	18 (25.7)	72(36.2)	109 (23.6)	53 (33.5)	94(23.6)
Estimate	0.690	0.481	0.679	0.331	0.704	0.331
Relative risk (95% CI) vs matching placebo	0.697 (0.291, 1.667)		0.487 (0.355, 0.669)		0.471 (0.330, 0.673)	
	P = 0.4134		P < 0.0001		P < 0.0001	
Unadjusted annualized event rate of severe exacerbation ^a by year during treatment period of TRAVERSE ^c						
	PBO/DPL	DPL/DPL	PBO/DPL	DPL/DPL	PBO/DPL	DPL/DPL
Patients with ≥1 severe exacerbation events, Weeks 0–48, n/N (%)	8/32 (25.0)	17/70 (24.3)	31/198 (15.7)	74/463 (16.0)	19/157 (12.1)	60/399(15.0)
	0.417	0.360	0.222	0.257	0.188	0.239
Patients with ≥1 severe exacerbation events, Weeks 48–96, n/N (%)	5/29 (17.2)	6/58 (10.3)	17/167 (10.2)	35/387 (9.0)	13/127 (10.2)	27/335(8.1)
	0.359	0.216	0.186	0.202	0.175	0.180
	Combined PBO	Combined DPL	Combined PBO	Combined DPL	Combined PBO	Combined DPL
Pre-bronchodilator FEV ₁ (L) at baseline in QUEST						
Mean (SD)	1.65 (0.36)	1.82 (0.65)	1.76 (0.58)	1.78 (0.60)	1.79 (0.60)	1.78 (0.60)
Change from baseline in pre-bronchodilator FEV ₁ (L) in QUEST ^d						
Week 12: LS mean (SE)	0.16 (0.03)	0.16 (0.02)	0.34 (0.03)	0.51 (0.02)	0.40 (0.03)	0.57 (0.02)
Difference vs PBO (95% CI)	0.01 (–0.07, 0.08)		0.17 (0.10, 0.23)		0.16 (0.09, 0.24)	
	P = 0.8792		P < 0.0001		P < 0.0001	
Week 52: LS mean (SE)	0.06 (0.03)	0.07 (0.02)	0.47 (0.03)	0.60 (0.02)	0.55 (0.03)	0.67 (0.02)
Difference vs PBO (95% CI)	0.01 (–0.07, 0.08)		0.13 (0.07, 0.19)		0.12 (0.06, 0.18)	
	P = 0.8170		P < 0.0001		P = 0.0002	
Change from baseline in pre-bronchodilator FEV ₁ (L) in TRAVERSE ^d						
	PBO/DPL	DPL/DPL	PBO/DPL	DPL/DPL	PBO/DPL	DPL/DPL
Week 48: LS mean (SE)	0.22 (0.04)	0.04 (0.03)	0.58 (0.03)	0.60 (0.02)	0.65 (0.03)	0.66 (0.02)
P vs PBO/DPL	P = 0.0009		P = 0.6657		P = 0.7457	
Week 96: LS mean (SE)	0.22 (0.06)	0.03 (0.04)	0.54 (0.03)	0.56 (0.02)	0.60 (0.04)	0.61 (0.03)
P vs PBO/DPL	P = 0.0063		P = 0.6242		P = 0.7336	
	Combined PBO	Combined DPL	Combined PBO	Combined DPL	Combined PBO	Combined DPL
Pre-bronchodilator FEV ₁ /FVC (%) at baseline in QUEST						
Mean (SD)	59.31 (10.94)	64.16 (9.37)	62.27 (9.92)	62.74 (10.80)	62.19 (9.89)	62.41 (10.96)
Change from baseline in pre-bronchodilator FEV ₁ /FVC (%) in TRAVERSE ^e						
	PBO/DPL	DPL/DPL	PBO/DPL	DPL/DPL	PBO/DPL	DPL/DPL
Week 48: LS mean (SE)	4.91 (1.02)	1.53 (0.75)	7.06 (0.46)	6.69 (0.31)	7.64 (0.53)	7.40 (0.34)
P vs PBO/DPL	P = 0.0055		P = 0.4869		P = 0.6877	
Week 96: LS mean (SE)	6.00 (0.97)	2.10 (0.72)	7.13 (0.52)	6.83 (0.35)	7.48 (0.58)	7.44 (0.37)
P vs PBO/DPL	P = 0.0008		P = 0.6147		P = 0.9564	

^aDefined as any treatment with ≥1 systemic (oral or parenteral) steroid bursts for worsening asthma or hospitalization or an emergency/urgent medical care visit for worsening asthma. ^bDerived using negative binomial model with the total number of events onset from randomization up to Visit 18 or last contact date as the response variable; with treatment group, age, region (pooled country), baseline eosinophil strata, baseline ICS dose level, and number of severe exacerbation events within 1 year prior to the study as covariates; and log-transformed standardized observation duration as an offset variable. ^cTotal number of events that occurred during the observational period divided by the total patient-years followed in the observational period. ^dDerived using mixed-effect models with repeated measures with change from baseline in pre-bronchodilator FEV₁ values up to Week 52/96 as the response variable; and treatment, age, sex, baseline height, region, baseline eosinophil strata/levels subgroups (<0.3 Giga/L, ≥0.3 Giga/L), baseline ICS dose level, visit, treatment-by-visit interaction, baseline pre-bronchodilator FEV₁ value, and baseline-by-visit interaction as covariates. ^eDerived using mixed-effect models with repeated measures with change from baseline in FEV₁/FVC values up to Week 96 as the response variable; and treatment, age, sex, baseline height, region, baseline eosinophil strata/levels subgroups (<0.3 Giga/L, ≥0.3 Giga/L), baseline ICS dose level, visit, treatment-by-visit interaction, baseline FEV₁/FVC value, and baseline-by-visit interaction as covariates. CI, confidence interval; DPL, dupilumab; FVC, forced vital capacity; ICS, inhaled corticosteroid; LS, least square; PBO, placebo; SD, standard deviation; SE, standard error.

with higher pre-bronchodilator FEV₁ improvement at end of QUEST experienced fewer exacerbations during both studies. Over 80% of patients who achieved $\geq 100\text{mL}$ or $\geq 200\text{mL}$ pre-bronchodilator FEV₁ improvements at the end of QUEST maintained these improvements in TRAVERSE.

Conclusions Greater improvements in pre-bronchodilator FEV₁ in QUEST led to long-term enhanced benefits of dupilumab treatment; patients maintained these improvements and had fewer exacerbations during TRAVERSE.

Please refer to page A189 for declarations of interest related to this abstract.

S87 SEVERE ASTHMA OUTCOMES WHEN SWITCHING FROM MEPOLIZUMAB TO BENRALIZUMAB IN NON-RESPONDERS WITH PERSISTENT SPUTUM EOSINOPHILIA

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Background Anti-IL-5 monoclonal antibodies reduce systemic corticosteroid use and exacerbation rate in severe eosinophilic asthma. Although their specific mechanisms of action differ, there is as yet no guidance on whether to choose mepolizumab or benralizumab for any given patient.

Aims To investigate clinical outcomes of patients switching to benralizumab after non-response to mepolizumab associated with persistent sputum eosinophilia.

Methods We recruited patients who failed to respond to mepolizumab over 12 months (no meaningful reduction in maintenance steroid use and/or exacerbation rate), with sputum eosinophils above the threshold of 2%.

Over the subsequent 12 months of benralizumab treatment we recorded daily prednisolone dose, ACQ6, AQLQ, and sputum & blood eosinophils. Lung function and FeNO testing was severely impacted by the COVID pandemic.

Results Fifty-three of 165 (32%) mepolizumab patients were identified as candidates for a switch of therapy with residual positive sputum eosinophils, of which 36 have completed 12 months of treatment, 20 with available sputum eosinophil results. Five patients stopped therapy before a full year (two for failure to respond to treatment at 6–9 months, one allergic reaction, two unspecified).

Abstract S87 Table 1

Clinical parameter Median (IQR) or mean (SD)	n	Prior to benralizumab	12 months benralizumab	Paired test p value
OCS δ mg/d, median (IQR)	33	4 (10)	5 (7.5)	0.101
Annual exacerbations δ , mean (SD)	25	4.5 (5.5)	2 (5)	0.010
Sputum % eosinophils δ , median (IQR)	20	8.5 (15)	0 (0)	<0.001
ACQ6 δ , mean (SD)	33	2.8 (1.7)	2.3 (1.5)	0.046
AQLQ β , mean (SD)	28	3.3 (1.8)	4.0 (2.1)	0.033
ICS δ mcg BDP equivalent / d, median (IQR)	33	2000 (1200)	1840 (400)	0.753
Blood eosinophils β 10 ⁹ cells/ml- median (IQR)	30	0.09 (0.11)	0 (0.00)	0.001

Clinical parameters measured at time of decision to switch from mepolizumab or benralizumab (δ) or benralizumab baseline visit (β) and after 12 months on benralizumab.

After 12 months on benralizumab, all patients had negative sputum eosinophils as well as improvements in ACQ6, AQLQ, blood eosinophils and reduced exacerbation rate compared to before switching (table 1).

Conclusions Around a third of patients failed to respond to mepolizumab and displayed persistent airway eosinophilia. All of these patients had complete suppression of sputum eosinophils on benralizumab with significant clinical improvements in exacerbation rate, blood eosinophils, asthma control and quality of life. These real-life observations in our severe asthma patient population confirm the results of the SIROCCO and Calima trials.

S88 USE OF A CONNECTED INHALER SYSTEM IN THE PRE-BIOLOGIC ASSESSMENT OF PATIENTS WITH SEVERE ASTHMA

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Background Sub-optimal adherence is a significant factor in patients with difficult to treat asthma. Aligning adherence to maintenance inhaled corticosteroid (ICS) treatment with digital inhaler monitoring and measurement of fractional exhaled nitric oxide (FeNO suppression) can rapidly differentiate patients with poor adherence from those who require treatment escalation with type-2 biologic therapy.¹

Objectives To assess the feasibility and utility of monitoring adherence using a digital connected inhaler system (CIS) embedded within the patient pathway as a service evaluation, to rapidly identify patients for initiation of biologic therapies in UK specialist severe asthma clinics (n=7).

Methods Using a CIS (Propeller Health) patients completed adherence monitoring/biomarker profiling for 1 month as part of a pre-biologic assessment followed by clinical decision (initiate biologic therapy or continue monitoring – figure 1). Patients had the following assessments at baseline and 1 month follow-up: spirometry, FeNO, peripheral blood eosinophil count and asthma control questionnaire (ACQ-7).

Results To date, 104 patients have been initiated on the CIS with 43 having outcome data at 3 months. In FeNO-high subjects (FeNO ≥ 45 ppb, n=26) median adherence was 100% (range 57 – 100%) and there were significant reductions in ACQ-7 (2.88 vs 2.14, p = 0.03) and FeNO (63ppb vs 32ppb, p < 0.001) between baseline and 1 month follow-up. In patients with positive FeNO suppression¹ (n=16), 14 maintained good adherence with no rescue prednisolone, 2 were commenced on a biologic therapy and 2 had persistent poor adherence. In those with negative FeNO suppression¹ (n=10), 6 were commenced on a biologic therapy at 3 months, with 4 having good adherence with ongoing monitoring. In FeNO-low subjects (FeNO<45 ppb, n=17), median adherence was 100% (range 85 – 100%) but no differences in parameters were seen at 1 month, consistent with previous data supporting this 'cut-point' to identify difficult to treat asthma patients with poor ICS adherence.¹

Conclusion Using a CIS in conjunction with FeNO monitoring is a useful method for assessing adherence to ICS when