Abstract P201 Table 1 Predicted vs observed impact of anti-inflammatory treatments in patients with a baseline blood eosinophil count $\geq 0.15 \times 10^9$ cells/L or FeNO ≥ 25 ppb

Annual severe asthma attack rate		Included trial: control vs active interventions (n)				Weighted mean% reduction
		Novel START ²	CAPTAIN ³	QUEST ^{4,5}	DREAM ⁵	Control
		Salbutamol (n=201) vs	FF100	Placebo	Placebo	(n=1763) vs
		Any ICS	(n=903) vs	(n=514) vs	(n=145) vs	Active
		(n=377) *†	FF200	Dupi 200	Any Mepo	(n=2162)
			(n=909)*	(n=484)	(n=392)	
Observed	Control arm	0.05	0.40	1.07	2.46	
	Active arm	0.03	0.24	0.41	1.19	
	% Reduction	35%	38%	62%	52%	46%
Predicted	Control arm	0.13	0.32	0.93	1.28	
	Active arm	0.07	0.19	0.53	0.74	
	% Reduction	42%	42%	42%	42%	42%

*For both the Novel START and CAPTAIN studies, data of patients with a baseline FeNO of <20 ppb were regrouped into the <25 ppb group, as the difference of 5 ppb in FeNO is not clinically relevant. †For Novel START, only the percentage of patients with one or more severe attacks(s) in the 52-weeks of follow-up was reported so a rate was imputed as $-\log_{10}(1 - \% \text{incidence})$. Dupi 200, dupilumab 200 mg/2w; FF, fluticasone furoate; ICS, inhaled corticosteroid; Mepo, mepolizumab. ²Pavord *et al.* Lancet Respir Med 2020;8:671–80; ³Lee *et al.* Lancet Respir Med 2021;9:69–84; ⁴Busse *et al.* Lancet Respir Med 2021: in press; ⁵Shrimanker *et al.* Am J Respir Crit Care Med 2019;200:1308–12.

inflammatory treatment benefits. For the 3925 patients with at least one type-2 biomarker high at baseline, the observed vs predicted frequency-weighted mean rate ratios were 0.54 vs 0.58 (table 1); the corresponding percentages reduction in asthma attacks were 46% and 42%, respectively. In contrast, the 814 patients with both biomarkers low at baseline had observed vs predicted rate ratios of 0.86 vs 1.00; the corresponding percentages reduction in asthma attacks were 14% and 0%, respectively. The relative risk associated with biomarkers was consistent across populations, but the absolute risk and the treatment benefit conferred by type-2 biomarkers was greater in a population at higher background risk.

Conclusion The prototype ORACLE scale predicts the excess risk conferred by raised biomarkers which is removed by anti-inflammatory therapy in trial populations.

REFERENCE

1. Couillard, *et al.* <https://ats2021.info/qybelSJ>

Please refer to page A193 for declarations of interest related to this abstract.

P202

REAL LIFE EXPERIENCE WITH MEPOLIZUMAB AND COMPARISON WITH OMALIZUMAB IN CHILDREN WITH SEVERE ASTHMA

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Introduction Mepolizumab (anti-IL-5) and omalizumab (anti-IgE) are the only biologics licensed for asthma in children from age 6. Omalizumab is of known effectiveness, but mepolizumab lacks paediatric efficacy data. We hypothesised that mepolizumab and omalizumab are equally effective treatments for paediatric severe asthma.

Methods Single-centre, observational study of children 5–18 years with severe asthma, confirmed following multi-disciplinary (MDT) assessment, started on mepolizumab (since 2019) or omalizumab (since 2008). Baseline exacerbations

before biologic initiation were collected retrospectively. Prospective monthly assessments recorded exacerbations (≥ 3 days systemic steroid or hospital attendance), lung function with spirometry, exhaled Nitric Oxide (FeNO), Asthma Control Test (ACT) or childhood ACT (cACT) and mini-Paediatric Asthma Quality of Life Questionnaire (mini-PAQLQ). MDT assessed response to mepolizumab 6-monthly and omalizumab 4-monthly including comparison to their 6 or 4-monthly baseline exacerbations.

Results Seventy-six children initiated mepolizumab (n=16) or omalizumab (n=60). Both groups had similar baseline treatment, clinical assessments and exacerbations. A greater proportion of mepolizumab group were female (81% vs 35%).

56.7% of children continued omalizumab following 4-month trial and 75% continued mepolizumab after 6-month trial.

Median (IQR) monthly exacerbations/person decreased significantly after 4-month omalizumab trial compared to 4-months pre-treatment (baseline: 0.75 (0.438–1), 4-month: 0.25 (0–0.5), $P=0.0003$); median (IQR) monthly exacerbations/person non-significantly decreased in the mepolizumab group after 6-month trial (baseline: 0.333 (0.167–0.792), 6-months: 0 (0–0.333), $P=0.2344$).

A subgroup of 6 children experienced no exacerbations after 6 months of mepolizumab and reduced monthly exacerbations after 1-year ($P=0.007$). Pre-treatment exacerbations and measures of eosinophilic airway inflammation did not distinguish mepolizumab responders and non-responders.

Children prescribed omalizumab experienced significant reduction in FeNO and improved mini-PAQLQ scores and proportion of patients with controlled ACT/cACT after 4-months. Children prescribed mepolizumab experienced non-significant improvements in mini-PAQLQ scores and proportion of patients with controlled ACT/cACT scores after 6-month trial (table 1).

When median change/person was compared between biologics, there was no significant difference for any parameter.

Conclusion There were significant improvements in asthma outcomes with omalizumab but not mepolizumab. This may be due to sample size however these data underscore the need

Abstract P202 Table 1 Multidomain assessment for children before and after 6-month mepolizumab trial and 4-month omalizumab trial

Domain assessed		Mepolizumab	Omalizumab	Comparison between biologics: P-value
Monthly exacerbation rate	Baseline	0.333 (0.167 - 0.792) n=12	0.75 (0.5 - 1) n=31	0.218
	End of biologics trial	0 (0 - 0.333) n=12	0.25 (0 - 0.5) n=31	
	Paired comparison of baseline and end of trial P-value	0.234	0.0001***	
	Median (IQR) change/person	-0.167 (-0.583 - 0)	-0.5 (-0.5 - 0)	0.328
Mean $\pm$ SD% predicted Forced Expiratory Volume in 1 second	Baseline	86.9 $\pm$ 24.8 n=7	81.2 $\pm$ 19.9 n=53	0.3
	End of biologics trial	91.9 $\pm$ 25.7 n=7	82.4 $\pm$ 18.6 n=53	
	Paired comparison of baseline and end of trial P-value	0.381	0.607	
	Median (IQR) change/person	1 (-4 - 8)	3 (-8 - 12.8)	0.949
Median (IQR) Fractional exhaled Nitric Oxide - parts per billion	Baseline	65 (18.5 - 101) n=5	44 (21.8 - 77.8) n=38	0.698
	End of biologics trial	26 (15 - 54) n=5	27 (14 - 50) n=38	
	Paired comparison of baseline and end of trial P-value	0.438	0.0499*	
	Median (IQR) change/person	-11 (-80 - 16))	-6.68 (-35.2 - 8.78)	0.755
Median (IQR) Mini-Paediatric Asthma Quality of Life Questionnaire score	Baseline	6.04 (3.56 - 7) n=8	4.19 (3.23 - 5.42) n=32	0.083
	End of biologics trial	6.69 (4.57 - 7) n=8	6.05 (4.11 - 6.59) n=32	
	Paired comparison of baseline and end of trial P-value	0.188	0.0008***	
	Median (IQR) change/person	0.115 (0 - 1.75) n=8	0.885 (-0.263 - 2.11) n=32	0.550
Proportion of patients with Asthma Control Test or childhood Asthma Control Test $\geq$ 20 - No. (%n)	Baseline	3 (20) n=15	8 (14) n=57	0.277
	End of biologics trial	5 (55.6) n=9	15 (34.9) n=43	
	Change from baseline P-value	0.0994	0.0175*	

Normality tested with Shapiro-Wilkes.

Normal data compared with paired t-test, non-normal with Wilcoxon signed-rank and categorical data with Fisher's exact test.

[†]mepolizumab and omalizumab exacerbation baselines are the 6 and 4 months before treatment initiation respectively.

*denotes $P \leq 0.05$, ** denotes $P \leq 0.001$ and *** denotes $P \leq 0.0001$.

for large-scale paediatric mepolizumab studies, especially given evidence of low Type-2 cytokines in children with severe asthma.

P203 EFFECTIVENESS OF ANTI-IL4R THERAPY FOLLOWING SUBOPTIMAL RESPONSE TO ANTI-IL5/5R THERAPY IN SEVERE EOSINOPHILIC ASTHMA

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Introduction Dupilumab is an anti-IL4R monoclonal antibody (mAb) with proven efficacy in severe eosinophilic asthma (SEA). We previously reported that a suboptimal response to the eosinophil-targeting anti-IL5/5R mAbs mepolizumab and benralizumab is seen in 27% and 14% of patients with SEA respectively.^{1,2} The mechanism of this is not well-understood. It is unknown whether such patients respond in a clinically meaningful way following a switch to dupilumab.

Methods We performed a retrospective analysis of the clinical effectiveness of dupilumab (minimum 6 months treatment) in patients with SEA at our tertiary severe asthma centre who had failed to adequately respond to at least one of the anti-IL-5/5R mAbs. Change in the annualised exacerbation rate (AER), maintenance oral corticosteroids (mOCS) requirements and ACQ-6 was recorded.

Results Twenty-one patients (mean age 43.5, 71% female, 70% atopic) were included in the analysis. 9/21(42.9%) had co-morbid nasal polyposis and 3/21(14.3%) had eczema. The baseline FeNO was 62.5(38-87)ppb. 15/21 were switched from benralizumab (including 7/15 who had previously failed mepolizumab); 5/21 from mepolizumab and 1/21 from reslizumab. 3/21 had previously failed omalizumab prior to a switch to an anti-IL5/5R mAb. Fifteen patients were receiving mOCS at the time of commencing dupilumab.

At six months, the daily median mOCS dose fell from 10mg (6.25-22.5mg) to 3mg (0-7.5mg), $P < 0.002$. ACQ-6 improved by 1.04 units from 2.94 ± 1.31 to 1.90 ± 1.40 , $p = 0.037$. There was a trend towards improvement in AER from 1.56 ± 1.50 to 0.75 ± 1.24 , $p = 0.063$. Median blood eosinophil count rose from 0.0(0-0.2) to 0.5(0.3-1.2), $p < 0.001$.