Abstract P199 Table 1

Mean VAS(0 to 100mm)	Standard group (n=10)	ICNB group (n=10)	P value
1 hour post LAT	64	23	0.002
2 hour post LAT	64	23	0.002
Day 1	55	17	0.001
Day 2	34	NA	NA
Length of stay (Mean/Median, days)	2.4/2	1/1	0.009
Total analgesia use (mean)			
Oral morphine,mg	38.5	23	0.347
Codeine,mg	34.4	38.6	0.912
Paracetamol,g	3.4	1.5	0.006

In this small cohort, ICNB potentially has a role in reducing pain, LOS and analgesia use and allows LAT to be more tolerable, and may widen the scope of procedures possible during LAT.

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Asthma: phenotyping and the response to biologics

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URINARY LEUKOTRIENE E4 AS A BIOMARKER IN NSAID EXACERBATED RESPIRATORY DISEASE (N-ERD): A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction NSAID exacerbated respiratory disease (N-ERD) - formerly aspirin-induced asthma (AIA), is an asthma phenotype characterised by increased leukotriene production. Urinary Leukotriene E4 (uLTE₄) indicates cysteinyl leukotriene production and activity.

Objectives To evaluate whether baseline uLTE₄ in N-ERD are different from post-aspirin challenge uLTE₄ in N-ERD and whether baseline uLTE₄ in N-ERD are different from aspirin-tolerant-asthma (ATA) patients and healthy controls (HC).

Methods A systematic literature search (Medline, EMBASE, EMCARE, CINAHL, PsychINFO) was performed from database inception to January 2021, to identify 1) studies reporting baseline uLTE₄ in both AIA/N-ERD and ATA asthmatics, and 2) uLTE₄pre- and post-aspirin challenge tests. Meta-analysis was performed (i.e. pooled standardised mean difference (SMD) with 95% confidence intervals (95% CI)) and risk of bias assessed (implementing Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy).

Results Of 522 study records reviewed, qualitative synthesis and meta-analysis were performed on $n=36$ and $n=33$ studies respectively (Meta-analysis; $n=1273$ AIA, 1305 ATA, and

582 HV across 8 countries). Criteria for aspirin intolerance were (i) positive aspirin challenge alone ($n=26$), (ii) convincing clinical history ($n=2$), and (iii) either challenge or history ($n=8$). Methodologies used for uLTE₄ analysis were (i) Amer-sham-enzyme immunoassay (A-EIA) ($n=8$), (ii) Cayman-enzyme immunoassay (C-EIA) ($n=18$), (iii) mass spectrometry (MS) ($n=5$), and (iv) radioimmunoassay (RIA) ($n=6$). uLTE₄ was higher in AIA vs ATA (SMD: 0.80; 95% CI: 0.71–0.89) and distinguished ATA from HC (SMD: 0.52; 95% CI: 0.23–0.81). For studies reporting uLTE₄ at baseline and post-challenge, uLTE₄ increased following aspirin challenge in AIA ($n=12$, SMD: 0.56; 95% CI: 0.26–0.85) but not ATA ($n=8$, SMD: 0.12; CI: -0.08–0.33). Risk of bias was acceptable across all studies, however 30.6% of quality assessment items were unfulfilled.

Conclusions This comprehensive systematic review and meta-analysis showed that uLTE₄ is significantly higher in N-ERD than ATA or HC. Likewise, people with N-ERD have greater increases in uLTE₄ following aspirin challenge. Because of heterogeneity, and lack of original data point reporting, diagnostic accuracy evaluation for uLTE₄ was not possible. In patients not fit to undergo confirmatory challenge tests for N-ERD, uLTE₄ can serve as a useful adjunct to diagnostic process.

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

P201

TO WHAT EXTENT DOES THE PROTOTYPE ORACLE SCALE PREDICT TREATMENT BENEFITS? PREDICTED VERSUS OBSERVED IMPACT OF ANTI-INFLAMMATORY TREATMENTS

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Background We have derived a prototype asthma attack risk scale (ORACLE)¹ centred on the peripheral blood eosinophil count and exhaled nitric oxide (FeNO). We speculate that the excess risk identified by raised biomarkers would be equivalent to the benefits of specific anti-inflammatory treatment.

Objective To assess whether the treatment effect conferred by raised blood eosinophils and FeNO is predicted by ORACLE.

Methods Observed biomarker-stratified annualised severe asthma attack rates of patients randomised to control and anti-inflammatory treatment arms were extracted from the Novel START (as needed salbutamol vs low dose regular or as needed ICS), CAPTAIN (fluticasone furoate (FF) 100 vs 200µg/d-containing arms), QUEST (placebo vs Dupilumab 200mg/2w), and DREAM (placebo vs any mepolizumab) studies. Observed rate ratios were calculated between control and active arm attack rates in patients with any raised type-2 biomarker at baseline (blood eosinophils $\geq 0.15 \times 10^9/L$ or FeNO ≥ 25 ppb) and those with none (blood eosinophils $< 0.15 \times 10^9/L$ and FeNO < 25 ppb). The predicted biomarker-stratified attack rates were calculated based on our hypothesis that type-2 high asthma has an anti-inflammatory treatment effect equal to moving from any biomarker high stratum's predicted risk to the biomarker low stratum's predicted risk.

Results The Table shows the observed vs ORACLE-predicted biomarker-stratified annual asthma attack rates and anti-

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