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Introduction/Aim: BOREAS (NCT03930732) and NOTUS (NCT04456673) are 52-week, phase 3, randomized, double-blind, placebo-controlled trials demonstrating dupilumab efficacy and safety data in patients with COPD. The objective of this analysis was to evaluate the efficacy and safety of dupilumab in a pooled analysis combining both BOREAS and NOTUS.

Methods: Patients with moderate-to-severe COPD and type 2 inflammation (blood eosinophils ≥300 cells/μL at screening) on triple therapy (ICS +LABA+LAMA) received add-on dupilumab 300 mg q2w vs. placebo for 52 weeks. The pooled primary endpoint was annualized rate of moderate or severe exacerbations and the key secondary endpoint was pre-BD FEV_1; safety is also reported.

Results: 1874 participants were randomized (936 to placebo and 938 to dupilumab). There was a 31% reduction in the annualized rate of moderate-to-severe exacerbations (nominal $p < 0.0001$). At Week 12, change from baseline in pre-BD FEV_1 was greater with dupilumab (LS mean difference 83 mL, nominal $p < 0.0001$) compared with placebo. This improvement was maintained at Week 52 (LS mean difference 73 mL, nominal $p < 0.0001$). Dupilumab was well tolerated; treatment-emergent adverse events (TEAEs) were balanced between arms across both groups (proportion of participants with any TEAE: dupilumab, 72.1%; placebo, 71.0).

Conclusion: Dupilumab reduces moderate-to-severe exacerbations, improves lung function, and had safety consistent with the known safety profile in patients with COPD and type 2 inflammation.

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Keywords: COPD, type 2 inflammation, dupilumab, efficacy, safety, phase 3 trials

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TO038

HIGH-RISK COPD PATIENT MANAGEMENT OPPORTUNITIES: AUSTRALIA, US AND UK COMPARISONS

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Introduction/Aim: Identifying COPD patients as high-risk based on exacerbation history provides opportunities for targeted care to reduce adverse outcomes. Previous international studies using primary care datasets highlighted management opportunities for high-risk COPD patients.[1,2] Understanding corresponding Australian data may illustrate similar opportunities.

Aim: To review management opportunities, aligned with guidelines and CONQUEST Quality Standards,[3] for high-risk COPD patients in Australia, compared to the US and UK. **Methods:** We compared Australian primary healthcare data with recent US and UK data. Electronic health record (EHR) databases were used to identify diagnosed COPD patients, aged ≥40 years, who were considered high-risk based on exacerbation history in the previous 12-24 months. EHR data on therapy, non-pharmacological interventions and follow-up were reviewed per country for COPD patients who met high-risk criteria on January 1st, 2019.

Results: In Australia, 24.9% of COPD patients were identified as high-risk, compared to 10.7% and 37.2% in the US and UK respectively (Table 1). Of high-risk patients, 44.3% were on no therapy or reliever therapy only in Australia, versus 65.9% in the US and 12.3% in the UK. Dual or triple agent inhaled maintenance therapy was prescribed for 46.7% of Australian patients; US and UK proportions were 25.2% and 76.8% respectively. Approximately one third of smokers had recorded smoking cessation support in Australia and the US, compared to 91.6% in the UK. Record of cardiac risk assessment was below 10.0% in Australia and the US, and 18.0% in the UK. Only 30.1% had a recorded COPD review in Australia, compared to over 70% in the US and the UK.

Conclusion: For Australian high-risk patients, substantial opportunities to enhance COPD management aligning with guidelines and CONQUEST Quality Standards were identified, as in the US and UK. Inter-country variations in opportunity exist, with COPD review and smoking cessation support emerging as key areas for improvement in Australia.

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Table 1. Identification and Recorded Management of High-risk COPD Patients across Australia, the United States (US) and United Kingdom (UK).

	Australia	United States	United Kingdom
Eligible already diagnosed COPD patients*, *N*	5922	73,111	48,063
High-risk Patients†; *n* (%)	1476 (24.9%)	7827 (10.7%)	17,858 (37.2%)
Therapy‡; %			
No therapy	39.5%	53.9%	6.6%
Reliever only	4.8%	12.0%	5.7%
ICS	1.4%	2.7%	1.3%
LAMA	7.1%	3.7%	8.5%
LABA	0.4%	0.3%	1.1%
ICS/LABA	15.0%	11.0%	12.7%
ICS/LAMA	0.8%	0.3%	0.8%
LAMA/LABA	5.8%	4.1%	10.2%
ICS/LABA/LAMA	25.1%	9.8%	53.1%
Other§	0.1%	2.2%	0.0%
Smoking cessation support,‖ %	36.5%	36.3%	91.6%
Cardiac risk assessment,¶ %	7.1%	2.1%	18.0%
COPD review, ** %	30.1%	70.9%	77.7%

* Aged ≥40 years, with a COPD diagnosis recorded at least 1 year prior to January 1st, 2019.

†High-risk defined differently in each country.

UK: ≥2 moderate or ≥1 severe exacerbations in the previous 12 months.

US: ≥2 moderate or ≥1 severe exacerbations in the previous 24 months, with 1 occurring in the last 12 months.Australia: ≥2 exacerbations in the previous 24 months.

‡In the 12-month period **before** January 1st, 2019, as a proportion of high-risk patients.

§'Other' therapy refers to Theophylline, Leukotriene receptor antagonist monotherapies.

‖Within12 months **either side** of January 1st, 2019, as a proportion of the high-risk patients who were current smokers.

¶Within 12 months **either side** of January 1st, 2019, as a proportion of high-risk patients. Indicators of cardiac risk assessment varied per country according to relevant risk scores. In the US, risk assessment is reported irrespective of existing cardiac diagnosis.

In the 12-month period **after January 1st, 2019, as a proportion of high-risk patients. COPD Review identified in each country according to recorded evidence of.

UK: Annual Review, MRC Dyspnoea scale, COPD Assessment Test, Spirometry, Self-Management, Exacerbation Count.

US: Clinical COPD Review, Inhaler Technique Review.

Australia: Review, Medication Review, Spirometry, Respiratory Symptoms.

Josephine Samuel-King, Bruce Willet, Lisa Sugg, Ondrej Rejda, Ian Miles, Ying Liu, Majella Soumakiyan, Rob Campbell, Marion Magee, Sheryl Bradley, Nicole O'Sullivan of the OPCA High-risk COPD in Australia Research Group for their valuable contributions.

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Key Words: COPD; exacerbations; high-risk; management; CONQUEST.

TO039

BENRALIZUMAB FOR EOSINOPHILIC ASTHMA AND/OR COPD EXACERBATIONS (ABRA TRIAL)

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Introduction/Aim: Exacerbations of asthma and COPD are important events. Despite routine treatment with systemic glucocorticoids, there is a high risk of treatment failures and harm. Eosinophilic inflammation is common during acute exacerbations. We hypothesised that for patients with eosinophilic exacerbations, a single injection of benralizumab alone or in combination with prednisolone will improve clinical outcomes compared to prednisolone.

Methods: In a phase 2 double-blind double-dummy multicentre randomised trial, patients with an exacerbation of asthma or COPD with blood eosinophil counts ≥300 cells/μL were assigned: (1) prednisolone 30 mg once daily for 5 days+100 mg benralizumab subcutaneous injection once; (2) placebo tablets once daily for 5 days+100 mg benralizumab subcutaneous injection once; (3) prednisolone 30 mg once daily for 5 days+placebo subcutaneous injection once. The co-primary outcomes were proportion treatment failures over 90 days and total visual analogue scale (VAS) symptoms at day 28. Secondary endpoints included time to treatment failure and lung function.

Results: 158 patients were randomised at acute eosinophilic exacerbation. At 90 days treatment failures occurred in 39/53 (73.6%) and 47/105 (44.8%) in the prednisolone only and pooled benralizumab group respectively (OR 0.264, 95% CI 0.125–0.556, $p < 0.001$). The 28-day total VAS mean difference (95% CI) was 49 mm (14-84), $p = 0.006$, favouring the pooled benralizumab group. The time to treatment failure was longer in the pooled benralizumab group (HR 0.393, 95% CI 0.252–0.612, log-rank p-value < 0.001). Post-hoc analysis showed no difference between benralizumab alone or benralizumab and prednisolone treated groups. There was no difference in lung function between treatments. Benralizumab was well tolerated.

Conclusion: Benralizumab can be used as a treatment of eosinophilic exacerbations with better outcomes than systemic glucocorticoids alone.

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TO040

DEFINING TRAJECTORIES IN HEALTH STATUS WITH CHRONIC AIRWAYS ASSESSMENT TEST (CAAT) IN PATIENTS WITH ASTHMA AND/OR COPD IN NOVELTY

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