Introduction Blood eosinophil counts (BEC) are used to direct ICS therapy in COPD. BEC are variable and can move across treatment thresholds over time. Multiple factors can influence the stability of BEC. Identification and assessment of potential surrogate markers for stable state BEC over time would be helpful.

Aims The blood eosinophils in COPD (BECCOPD) study is assessing whether the highest of ≥3 BEC within 24 months is a suitable surrogate for stable state BEC. We compared the stability of the highest and second highest BEC over 10 years.

Methods Patients with spirometry confirmed COPD, stable at baseline, were recruited from primary and secondary care. BEC over the first and last 3 years within the previous 10 years were captured and converted to 1 decimal place for reporting consistency. Only patients with 3 or more BEC within both time periods were included. The highest and second highest BEC between both time frames were compared using a paired t-test.

Results 145/235 (62%) of participants were included in this analysis. Mean age 71 (7), mean FEV1% predicted 57 (22), 58% female, median eMRCD 4 (3–4). When comparing the highest BEC between the two groups, 101/145 (69.66%) were in the same GOLD guideline threshold, 20/145 (13.79%) moved into a lower threshold and 24/145 (16.55%) into a higher threshold.

The mean and SD values are shown in table 1. The intraclass correlation coefficient between the two groups for highest BEC was 0.555 and 0.670 for the second highest BEC indicating moderate reliability for both.

Conclusion Blood eosinophil endotype varied over a ten-year period. The ICC for both measures of BEC showed a moderate correlation but was better when comparing the second highest BEC. This shows promise as a surrogate marker of eosinophil endotype.

Acknowledgements The BECCOPD study is funded by GSK via the supported studies program.

Abstract S30 Table 1 Comparison of mean highest and second highest BEC in BECCOPD participants in the first and last 3 year time periods.

<table>
<thead>
<tr>
<th></th>
<th>First 3 years</th>
<th>Last 3 years</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Highest BEC</td>
<td>0.3 (0.3)</td>
<td>0.3 (0.2)</td>
<td>0.04</td>
</tr>
<tr>
<td>Second highest BEC</td>
<td>0.3 (0.2)</td>
<td>0.2 (0.2)</td>
<td>0.08</td>
</tr>
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</table>

Rationale Chronic obstructive pulmonary disease (COPD) is characterized by progressive lung function decline and worsening symptoms, accelerated by recurrent exacerbations. Type 2 (T2) inflammation may play a significant role in a subset of patients with COPD. Dupilumab, a fully human monoclonal antibody, blocks the shared receptor component for interleukin (IL)-4 and IL-13, key and central drivers of T2 inflammation.

Methods BOREAS (NCT03930732) was a 52-week, phase 3, placebo-controlled trial of the efficacy and safety of subcutaneous add-on dupilumab 300 mg qw2 vs placebo in COPD patients with moderate-to-severe airflow limitation with T2 inflammation (blood eosinophils ≥300 cells/µL at screening) on triple therapy with inhaled corticosteroids (ICS), long-acting β2-agonists (LABA), and long-acting muscarinic antagonists (LAMA) (or LABA/LAMA if ICS was contraindicated). Primary endpoint: annualized rate of moderate or severe exacerbations (AECOPD). Secondary/other endpoints: change from baseline in pre-bronchodilator FEV1 at Weeks 12/52; change from baseline in St. George’s Respiratory Questionnaire (SGRQ) total score and E-RS: COPD RS-Total Score at Week 52; SGRQ responders with ≥4-point improvement from baseline at Week 52; blood eosinophil levels over time; and safety.

Results 939 participants were randomized to placebo (N=471) or dupilumab (N=468). Treatment groups were balanced at baseline. Dupilumab met all multiplicity-adjusted endpoints. Dupilumab demonstrated a 30% reduction in the annualized rate of AECOPD (p=0.0005). In the entire study population, dupilumab vs placebo significantly increased pre-BD FEV1 at Week 12 (least squares mean (LSM) difference vs placebo: 83 mL, p<0.0001); through Week 52 (83 mL, p=0.0003). Dupilumab demonstrated greater improvement from baseline in pre-BD FEV1 at Week 52 in the subgroup of patients with baseline blood eosinophils ≥300 cells/µL (table 1). Median change from baseline in blood eosinophils was 3c (30.00 cells/µL in both groups at Week 52. Safety was similar in the dupilumab and placebo groups. TEAEs were balanced between placebo and dupilumab groups. No clinically symptomatic eosinophilia was observed.

Conclusions Dupilumab is the first biologic to significantly improve exacerbations, lung function, health-related quality-of-life, and symptoms in COPD patients with T2 inflammation.