Abstract P156 Table 1 Peak $FEV_{1(0–3\ h)}$, trough FEV_1,FEV_1 $AUC_{(0–3\ h)}$, and Peak $FVC_{(0–3\ h)}$ responses at Week 24 (full analysis set); and overall AEs in treated set

Responses at Week 24			
		Tiotropium Respimat® 5 µg[a] n = 135	Tiotropium Respimat® 2.5 µg[a] n = 135
		Adjusted mean difference versus placebo Respimat®[a] ± standard error[1]	
Background maintenance therapy		Medium-dose ICS (200–400 µg budesonide or equivalent) alone or in combination with another controller medication	
Peak $FEV_{1(0–3h)}$ response, mL		164 ± 31 P < 0.0001 n = 134	170 ± 31 P < 0.0001 n = 131
Trough FEV_1 response, mL[b]		118 ± 36 P = 0.0010 n = 134	116 ± 36 P = 0.0012 n = 131
FEV_1 $AUC_{(0–3h)}$ response, mL		157 ± 30 P < 0.0001 n = 134	154 ± 30 P < 0.0001 n = 131
Peak $FVC_{(0–3h)}$ response, mL		91 ± 37 P = 0.0152 n = 134	110 ± 38 P = 0.0036 n = 131
Adverse Events (AEs)[2]			
	Placebo Respimat®[a] n = 131	Tiotropium Respimat® 5 µg[a] n = 135	Tiotropium Respimat® 2.5 µg[a] n = 135
		n (%)	
Patients with any AE	89 (67.9)	82 (60.7)	86 (63.7)
Patients with investigator-defined drug-related AEs	2 (1.5)	0	0
Patients with AEs leading to discontinuation	0	0	0
Patients with serious AEs	6 (4.6)	1 (0.7)	3 (2.2)

[1]Full analysis set. Placebo Respimat®, N = 131; Placebo Respimat®, Week 24, n = 126. Mean baseline values (± standard deviation): ICS dose, 310.0 ± 112.0 µg; ACQ-IA total score, 1.87 ± 0.31; FEV_1, 1629 ± 393 mL; FVC, 2121 ± 564 mL.
[a]Add-on to background maintenance therapy.
[b]Measured 10 minutes before next dose of trial medication.
ACQ-IA, interviewer-administered Asthma Control Questionnaire
[2]Treated set. Percentages calculated using total number of patients per treatment group as denominator.

daily tioR add-on therapy, a Phase III trial was carried out in patients aged 6–11 years with moderate symptomatic asthma.

Methods This 48-week, Phase III, randomised, double-blind, placebo-controlled, parallel-group study (CanoTinA-asthma®; NCT01634139) was performed in patients aged 6–11 years with moderate symptomatic asthma. Patients received once-daily tioR 5µg (2 puffs, 2.5 µg), tioR 2.5 µg (2 puffs, 1.25 µg) or placebo Respimat® (pboR; 2 puffs) as add-on to maintenance treatment of at least medium-dose inhaled corticosteroid (ICS) (200–400 µg budesonide or equivalent) alone or in combination with another controller medication. The primary end point was peak FEV1 within 3 hours post-dosing (FEV1(0–3 h)). Secondary end points included trough FEV1 (key end point), FEV1 area under the curve (AUC) (0–3 h), and peak FVC (0–3 h); all measured as response (change from baseline) at Week 24. Adverse events (AEs) were analysed descriptively.

Results Of 403 patients randomised, 401 were treated. Baseline demographics and disease characteristics were balanced between treatment groups. TioR 5 µg and 2.5 µg provided statistically significant improvements in lung function versus pboR at Week 24 (Table) with adjusted mean difference ± standard error peak FEV1 (0–3 h) improvements of 164 ± 31 ml ($p < 0.0001$) and 170 ± 31 ml ($p < 0.0001$), respectively. The frequency of patients with AEs was similar across treatment arms, with a low incidence of drug-related and serious AEs (Table); no deaths occurred. The most common AEs were asthma worsening/exacerbation (lower incidence in tioR 5µg and 2.5 µg [34.1% and 36.3%] vs pboR [43.5%]), decreased peak expiratory flow rate (21.5% and 23% vs 20.6%), nasopharyngitis (8.9% and 11.1% vs 9.9%) and respiratory tract infection (9.6% and 8.1% vs 12.2%).

Conclusion In patients aged 6–11 years with moderate symptomatic asthma, once-daily tioR add-on to ICS with or without other maintenance therapy significantly improves lung function compared with pboR. The safety profile of tioR was similar to that of pboR.

REFERENCE

1 Vogelberg C, *et al. Respir Res* 2015;***16***(1):20.

Please refer to page A272 for declarations of interest in relation to abstract P156.

P157 SEASONAL VARIABILITY OF SEVERE ASTHMA EXACERBATIONS AND CLINICAL BENEFIT FROM LEBRIKIZUMAB

DF Choy, TL Staton, JR Arron, J Olsson, CTJ Holweg, S Grey, A Chai, JG Matthews. *Genentech, Inc., South San Francisco, USA*

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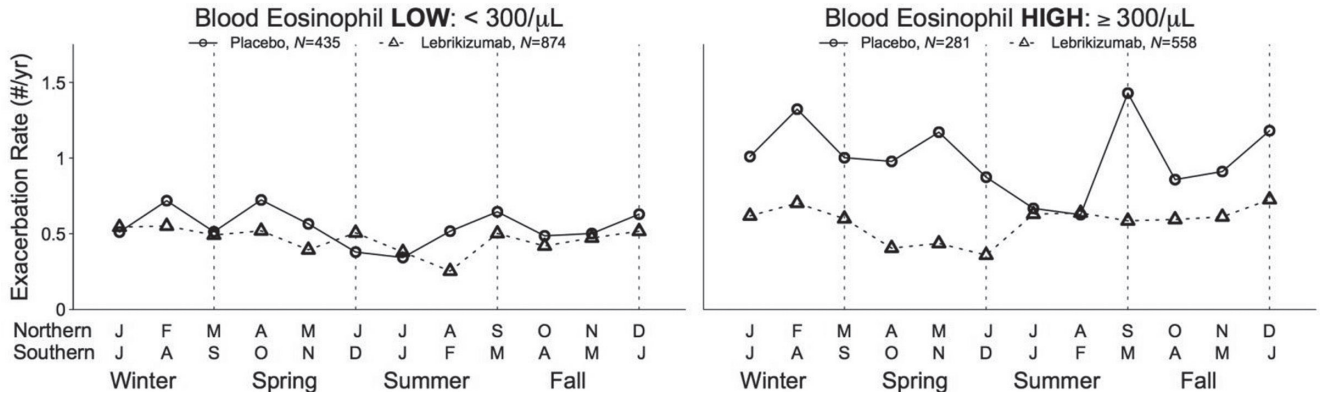
Introduction and objectives Epidemiologic studies have implicated aeroallergens and respiratory infections as triggers underlying seasonal increases in asthma exacerbations in spring and autumn months. These seasonal factors may trigger or amplify airway inflammation in atopic, Type 2 high asthma patients that precipitates acute worsening of symptoms. Biologic therapies targeting Type 2 cytokine pathways have demonstrated efficacy in reducing the rate of severe asthma exacerbations, particularly in patients selected on the basis of Type 2 biomarkers. In children with asthma, increased inhaled corticosteroid or anti-IgE therapy has been found to reduce the rate of seasonal exacerbations. We hypothesised that lebrikizumab (anti-IL-13) therapy would likewise be effective in reducing seasonal exacerbations in adults with asthma.

Methods We conducted *post-hoc* analyses of the Phase III LAVOLTA studies (NCT01867125 and NCT01868061) to assess the seasonal dependence of exacerbations and efficacy of lebrikizumab in 2,148 adults with moderate to severe asthma. We employed Poisson regression utilising linear mixed models to estimate the per-month (normalised by hemisphere) annualised exacerbation rate and treatment effect of lebrikizumab in reducing exacerbations (percent rate reduction).

Results Per-month exacerbation rates in placebo treated eosinophil-low (<300/µL) patients were lower and less variable (0.34 to 0.72 per year) than in eosinophil-high (≥300/µL) patients; (0.63/



Abstract P157 Figure 1 Seasonal analysis of exacerbations in subjects defines by baseline blood eosinophil counts. Unadjusted exacerbation rates are plotted as a function monthe normalised by hemisphere. The month for corresponding hemispheric season are annotated in plot margins. Analyses for subject with baseline blood eosinophils < 300/μL or > 300/μL are plotted on left and right panels respectively.

year in August to 1.43/year in September). The 95% confidence intervals for the per-month lebrikizumab treatment effect overlapped with zero in eosinophil-low patients for all calendar months. The maximum per-month treatment effects for eosinophil-high patients were observed during the autumn and spring months (62.7 [10.1, 84.5]% for September and 65.1 [8.6,86.7]% for May). The minimum per-month treatment effects were observed in the summer months (11.3[−148.7, 68.4]% for July and 6.6[−166.0, 67.2]% for August).

Conclusions We conclude that seasonal spikes in exacerbations may be primarily dependent on Type 2 inflammatory processes. The molecular pathways underlying asthma exacerbations are heterogeneous and therapeutic strategies targeting Type 2 biology alone may have the greatest efficacy in limiting seasonal spikes in exacerbation rates. Overall, these data highlight that a significant proportion of asthma exacerbations may be independent of seasonal influences and/or Type 2 biology and that increased therapeutic efficacy may require targeting multiple distinct pathways in asthma.

P158 FLUTICASONE FUROATE(FF)/VILANTEROL (VI) ONCE DAILY IMPROVES NIGHT-TIME AWAKENINGS IN ASTHMA

[1]N Barnes, [1]L Yates, [1]MR Gibbs, [2]R Forth. *[1]GlaxoSmithKline Respiratory Global Franchise, London, UK; [2]PAREXEL International, Research Triangle Park, USA*

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Introduction and objectives FF/VI, the first once daily inhaled corticosteroid/long-acting ß2-agonist combination available for the treatment of asthma, has demonstrated a sustained 24 hour improvement in lung function and improvement in symptom-free 24 hour periods.

Methods Post-hoc analyses of diary card data from three Phase III studies were performed to examine whether there was an improvement in night-time awakening during the studies for those patients treated with the addition of vilanterol to fluticasone furoate. The diary card scale used is described below. Changes in night-time awakenings over the duration of the studies were analysed for percentage of patients with ≥50% symptom-free nights, including the time taken for 50% of patients to achieve 7 nights without symptoms.

Night-time Symptom Score:

0 = No symptoms during the night

1 = Symptoms causing me to wake once (or wake early)

2 = Symptoms causing me to wake twice or more (including waking early)

3 = Symptoms causing me to be awake for most of the night

4 = Symptoms so severe that I did not sleep at all

To be counted as symptom-free during the night the patient needed to record a score of 0.

Results The percentage of patients with ≥50% symptom-free nights was generally higher in patients treated with FF/VI compared to either FF or FP alone (Table below). The time (in days) for 50% of patients to achieve 7 nights without symptoms was achieved sooner with patients treated with FF/VI compared to FF alone (Table).

Conclusions In general, night-time awakenings improved over time in asthma patients with FF/VI and improved faster with FF/VI compared with FF or placebo.