μg budesonide or equivalent) received once-daily tioR 5 μg or placebo Respimat®. In two 24-week trials (MezzoTinA-asthma®: NCT01172808/NCT01172821), patients on ICS (400–800 μg budesonide or equivalent) received once-daily tioR 5 μg or 2.5 μg, twice-daily salmeterol 50 μg via hydrofluoroalkane metered-dose inhaler (active comparator) or placebo (identical devices in a double-dummy protocol). Pre-planned analyses (pooled data) of time to first severe exacerbation and time to first episode of asthma worsening were performed in T_H2-low and T_H2-high subgroups: total serum immunoglobulin (IgE) ≤ or >430 μg/L (179.2 IU/L); blood eosinophils ≤ or $>0.6 \times 10^9$/L (600/μL).

Results 912 patients with severe asthma received tioR 5 μg or placebo Respimat®: 205/182 were reported with IgE >430 μg/L and 99/87 with an eosinophil count of $>0.6 \times 10^9$/L. 2100 patients with moderate asthma received tioR 5 μg or 2.5 μg, salmeterol or placebo: 319/320/319/326 were reported with IgE >430 μg/L and 104/103/111/107 with an eosinophil count of $>0.6 \times 10^9$/L. Time to first severe exacerbation was longer with tioR versus placebo (Table 1) in patients with severe or moderate asthma, independent of IgE and eosinophils (interaction p values [Cox regression] 0.169 and 0.754, respectively, for PrimoTinA-asthma®; analyses not performed for MezzoTinA-asthma® because of low incidence of severe exacerbations). Time to first asthma worsening was longer with tioR versus placebo (Table 1) in patients with moderate or severe asthma, independent of IgE (interaction p values 0.998 [PrimoTinA-asthma®] and 0.041 [MezzoTinA-asthma®]) and eosinophils (interaction p values 0.251 [PrimoTinA-asthma®] and 0.125 [MezzoTinA-asthma®]).

Abstract P151 Table 1 Risk of severe asthma exacerbation and asthma worsening in PrimoTinA-asthma® and MezzoTinA-asthma®

	All comparisons versus placebo Respimat® or placebo HFA-MDI, hazard ratio			
	Serum IgE (μg/L)		Eosinophils ($\times 10^9$/L)	
	≤430	>430	≤0.6	>0.6
Time to first severe asthma exacerbation				
PrimoTinA-asthma® (ICS + LABA)				
TioR 5 μg	0.75	1.07	0.81	0.75
QD	p = 0.162	p = 0.692	p = 0.162	p = 0.218
MezzoTinA-asthma® (ICS)				
TioR 5 μg	0.86	0.61	0.65	1.04
QD[b]	p = 0.691	p = 0.107	p = 0.099	p = 0.953
TioR 2.5 μg	0.51	0.50	0.41	1.25
QD[b]	p = 0.119	p = 0.033	p = 0.003	p = 0.715
Salmeterol[c]	0.82	0.68	0.62	1.76
	p = 0.594	p = 0.189	p = 0.066	p = 0.310
Time to first episode of asthma worsening[a]				
PrimoTinA-asthma® (ICS + LABA)				
TioR 5 μg	0.73	0.73	0.65	0.85
QD	p = 0.030	p = 0.017	p < 0.001	p = 0.360
MezzoTinA-asthma® (ICS)				
TioR 5 μg	0.88	0.83	0.90	0.70
QD[b]	p = 0.495	p = 0.220	p = 0.410	p = 0.170
TioR 2.5 μg	0.45	0.81	0.60	0.91
QD[b]	p < 0.001	p = 0.157	p < 0.001	p = 0.691
Salmeterol[c]	0.60	0.84	0.71	0.92
	p = 0.009	p = 0.231	p = 0.009	p = 0.714

[a]Defined as either a progressive increase in symptoms or a decline of ≥30% in best morning PEF for ≥2 consecutive days; [b]Plus placebo HFA-MDI BID; [c]Salmeterol HFA-MDI 50 μg BID plus placebo Respimat® QD.
BID, twice-daily; HFA-MDI, hydrofluoroalkane metered-dose inhaler; QD, once-daily; tioR, tiotropium Respimat®.

Conclusion Once-daily tiotropium Respimat® add-on to at least ICS reduced the risk of severe exacerbation and asthma worsening in patients with moderate or severe symptomatic asthma, independent of T_H2 phenotype.

P152 FLUTICASONE FUROATE (FF)/VILANTEROL (VI) ONCE DAILY REDUCES ASTHMA SYMPTOMS BOTH DAY AND NIGHT

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Introduction and objectives FF/VI is the first once daily inhaled corticosteroid/long-acting b_2-agonist combination available for the treatment of asthma. Results from five phase III studies that have previously been presented demonstrated a sustained 24 h improvement in lung function and improvement in symptom-free 24 h periods.

Methods Post-hoc analyses of diary card data from these studies were performed to examine whether there was any difference in the contribution of the day and night time symptom-free period to the 24 h symptom-free period. The diary card scale used is described below.

Day-time Symptom Score:

0 = No symptoms during the day

1 = Symptoms for one short period during the day

2 = Symptoms for two or more short periods during the day

3 = Symptoms for most of the day which did not affect my normal daily activities

4 = Symptoms for most of the day which did affect my normal daily activities

5 = Symptoms so severe that I could not go to work or perform normal daily activities

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 day or night the patient needed to record a score of 0.

Results The post-hoc analyses demonstrated that the improvements in day and night time symptom –free periods were similar to the 24 h symptom free periods. See Figure 1 below.

Conclusions In general benefits in symptom free days and symptom free nights contributed to the benefit of FF/VI over comparator groups in terms of 24 h symptom free periods.

P153 FLUTICASONE PROPIONATE/FORMOTEROL PRESSURISED METERED-DOSE INHALER '2–3–4' TRAINING PARADIGM AIDS CORRECT INHALER TECHNIQUE

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Background Inhaler technique is crucial to effective disease control. Amongst the most frequent mistakes made with all inhalers are the failure to exhale adequately, an insufficient breath-hold