of AEs in >2% of patients was comparable in the tiotropium Respimat® 5 μg, tiotropium Respimat® 2.5 μg and placebo Respimat® groups (Table 1). No deaths occurred. 110 (5.7%) and 55 (4.4%) patients receiving tiotropium Respimat® and placebo Respimat®, respectively, reported drug-related AEs (cardiac AEs were rare: tiotropium Respimat®, 7 [0.4%]; placebo Respimat®, 3 [0.2%]). One drug-related serious AE (asthma) was reported with tiotropium Respimat®.

Abstract P149 Table 1 Frequency of AEs occurring in >2% of patients

	AEs occurring in >2% of patients, n (%)[a]		
	Tiotropium Respimat® 5 μg (n = 1256)	Tiotropium Respimat® 2.5 μg (n = 673)	Placebo Respimat® (n = 1260)
Exposure, patient-years	705.42	271.08	708.04
Any AE	732 (58.3)	350 (52.0)	772 (61.3)
Serious AEs	51 (4.1)	12 (1.8)	56 (4.4)
AEs by preferred term			
Asthma	326 (26.0)	106 (15.8)	384 (30.5)
Decreased PEF rate	158 (12.6)	58 (8.6)	207 (16.4)
Nasopharyngitis	98 (7.8)	51 (7.6)	118 (9.4)
Upper respiratory tract infection	49 (3.9)	29 (4.3)	67 (5.3)
Bronchitis	43 (3.4)	9 (1.3)	27 (2.1)
Headache	41 (3.3)	19 (2.8)	49 (3.9)
Sinusitis	31 (2.5)	17 (2.5)	33 (2.6)
Influenza	29 (2.3)	1 (0.1)	25 (2.0)

[a]Treated set. PrimoTinA-asthma®: NCT00776984/NCT00772538; MezzoTinA-asthma®: NCT01172808/NCT01172821; GraziaTinA-asthma®: NCT01316380; Study 342: NCT00350207.

Conclusion Once-daily tiotropium Respimat® add-on to at least ICS maintenance therapy in adult patients demonstrates a safety profile comparable with that of placebo and is well tolerated across severities of symptomatic asthma.

P150 ONCE-DAILY TIOTROPIUM RESPIMAT® REDUCES RISK OF SEVERE ASTHMA EXACERBATION AND ASTHMA WORSENING IN SYMPTOMATIC ASTHMA, INDEPENDENT OF ALLERGIC AND INFLAMMATORY STATUS

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Background Four trials explored whether tiotropium Respimat® add-on to at least ICS is effective in the T_H2 phenotype, determined by high serum immunoglobulin E (IgE) and blood eosinophil values, in reducing risk of severe asthma exacerbation and asthma worsening in adult patients with moderate or severe symptomatic asthma.

Methods Four Phase III, double-blind, placebo-controlled, parallel-group trials. PrimoTinA-asthma® (two 48-week trials; NCT00776984/NCT00772538; n = 912): tiotropium Respimat® 5 μg or placebo Respimat® add-on to ICS + LABA (≥800 μg budesonide or equivalent); MezzoTinA-asthma® (two 24-week trials; NCT01172808/NCT01172821; n = 2100): tiotropium Respimat® 5 μg, tiotropium Respimat® 2.5 μg or placebo add-on to ICS (400–800 μg budesonide or equivalent). Patients had symptomatic asthma requiring treatment with at least ICS for ≥4 weeks before screening; COPD was excluded. Subgroups of allergic and inflammatory status (IgE and eosinophils) were used to analyse risk of severe exacerbation and asthma worsening, *post hoc*. Cox regression modelling analyses, adjusted for treatment, IgE or eosinophils and treatment by IgE or eosinophil interaction, were applied to calculate hazard ratios and 95% confidence intervals across IgE (2–2000 μg/L) and eosinophil (0.05–7.00 × 10^9/L) values.

Results Severe exacerbation: in PrimoTinA-asthma®, tiotropium Respimat® 5 μg reduced risk in terms of hazard ratio versus placebo Respimat® up to an IgE level of ~1000 μg/L, and consistently across all eosinophil values. In MezzoTinA-asthma®, tiotropium Respimat® 5 μg and 2.5 μg reduced risk versus placebo consistently across all IgE and eosinophil levels. Asthma worsening: in PrimoTinA-asthma®, tiotropium Respimat® 5 μg reduced risk in terms of hazard ratio versus placebo Respimat®, independent of IgE and eosinophils. In MezzoTinA-asthma®, tiotropium Respimat® 5 μg reduced risk versus placebo across all IgE and eosinophil values. Tiotropium Respimat® 2.5 μg reduced risk versus placebo across all IgE values and at eosinophil values <3.00×10^9/L.

Conclusion Tiotropium Respimat® add-on to ICS ± LABA reduces risk of severe exacerbation and asthma worsening in patients across severities of symptomatic asthma and a broad range of IgE and eosinophil values, suggesting efficacy independent of underlying allergic/eosinophilic inflammation. Once-daily tiotropium Respimat® may have potential as add-on to at least ICS maintenance therapy in patients with symptomatic asthma, independent of T_H2 phenotype.

P151 TIOTROPIUM RESPIMAT® ADD-ON THERAPY REDUCES EXACERBATION RISK IN PATIENTS WITH MODERATE OR SEVERE SYMPTOMATIC ASTHMA, INDEPENDENT OF TH2 STATUS

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Background Phase III studies have demonstrated reduced exacerbation rates with tiotropium Respimat® (tioR) add-on to ICS + LABA in patients with symptomatic asthma (Kerstjens *et al*. NEJM 2012;367:1198–207). There are currently no reported specific treatments for asthma that work equally well in both T_H2-low and T_H2-high phenotypes. We explored, in patients with moderate or severe symptomatic asthma, whether T_H2 status influenced tioR responses, assessed by time to first exacerbation.

Methods In two 48-week trials (PrimoTinA-asthma®: NCT00776984/NCT00772538), patients on ICS + LABA (≥800