who had been prescribed ≥12 SABA inhalers without an asthma review (as coded by QOF) were identified.

Results 94,955 asthma patients met the inclusion criteria, of which 12661 (13%) were children. LABAs with no ICS had been prescribed to 402 patients (0.4%). A total of 5032 patients (5.3%) had been prescribed ≥ 12 SABA inhalers, ranging from 13–136 inhalers of which 1965 (39%) had not had an asthma review. Among these, 117 were children, 0.92% of the total.

Conclusion These data, covering a large GP population, suggest evidence of non-guideline recommended prescribing which might contribute to increased risk to asthma patients. Prescribers should consider implementing system alerts to identify and review such prescribing behaviours.

REFERENCE

1 Lee C, Corren J. Budesonide/formoterol in the treatment of asthma. *Expert Rev Respir Med* 2008;**2**:551–64

P148 ONCE-DAILY TIOTROPIUM RESPIMAT® ADD-ON TO AT LEAST ICS MAINTENANCE THERAPY REDUCES EXACERBATION RISK IN PATIENTS WITH UNCONTROLLED SYMPTOMATIC ASTHMA

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Background A reduction in the risk of asthma exacerbation may provide improvements in clinical burden, patient experience and healthcare costs. In Phase III trials, once-daily tiotropium Respimat® add-on to at least ICS improved lung function in patients with symptomatic asthma. We investigated exacerbation risk in each trial.

Methods Five Phase III, double-blind, placebo-controlled, parallel-group trials in patients with symptomatic asthma. Patients received tiotropium Respimat® 5 µg or placebo Respimat® each as add-on to at least ICS maintenance therapy (Table 1). Pre-planned co-primary or secondary end points were time to first severe exacerbation and time to any asthma worsening.

Results Mean baseline% of predicted FEV_1, ACQ-7 score and ICS dose (µg) were: 56.0 ± 13.1, 2.6 ± 0.7 and 1198 ± 539 in PrimoTinA-asthma® (two replicate trials); 75.1 ± 11.5, 2.2 ± 0.5 and 660 ± 213 in MezzoTinA-asthma® (two replicate trials); and 77.7 ± 11.9, 2.1 ± 0.4 and 381 ± 78 in GraziaTinA-asthma®. Tiotropium Respimat® 5 µg reduced risk of severe asthma exacerbation by at least 21% in all three severity cohorts (Table 1) and risk of asthma worsening versus placebo Respimat® in all trials, with a statistically significant reduction in PrimoTinA-asthma®.

Conclusion Once-daily tiotropium Respimat® 5 µg add-on to at least ICS maintenance therapy consistently reduced exacerbations across asthma severities and so may be a beneficial add-on option to reduce current and future exacerbation risk.

Abstract P148 Table 1 Risk of severe asthma exacerbation in PrimoTinA-asthma®, MezzoTinA-asthma® and GraziaTinA-asthma®

		Severe asthma exacerbations, proportion of patients (%)			
Trial	**Background medication**	**Tiotropium Respimat® 5 µg**	**Placebo Respimat®**	**HR[a] (95% CI)**	**p value**
PrimoTinA-asthma®[b]	ICS + LABA (>800 µg budesonide or equivalent)	122/453 (26.9)	149/454 (32.8)	0.79 (0.62, 1.00)	0.034
MezzoTinA-asthma®[c]	ICS (400–800 µg budesonide or equivalent)	31/513 (6.0)	43/518 (8.3)	0.72 (0.45, 1.14)	0.164
GraziaTinA-asthma®[d]	ICS (200–400 µg budesonide or equivalent)	1/151 (0.7)	4/151 (2.6)	0.25 (0.03, 2.24)	0.216

[a]Hazard ratio, time to first severe exacerbation (vs placebo, <1 favours tiotropium Respimat®); [b]Baseline to Week 48, NCT00776984/NCT00772538; [c]Baseline to Week 24, NCT01172808/NCT01172821; [d]Baseline to time of last event, NCT01316380.

P149 ONCE-DAILY TIOTROPIUM RESPIMAT® ADD-ON TO AT LEAST ICS IN ADULT PATIENTS WITH SYMPTOMATIC ASTHMA: POOLED SAFETY ANALYSIS

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Background A high proportion of patients with asthma are symptomatic despite at least ICS maintenance therapy. Five trials aimed to evaluate the safety of tiotropium Respimat® compared with placebo Respimat®, each as add-on to at least ICS in adult patients with symptomatic asthma.

Methods Five Phase III and one Phase II randomised, double-blind, placebo-controlled, parallel-group trials. PrimoTinA-asthma® (48 weeks): tiotropium Respimat® 5 µg add-on to ICS + LABA (≥800 µg budesonide or equivalent); MezzoTinA-asthma® (24 weeks): tiotropium Respimat® 5 µg or 2.5 µg add-on to ICS (400–800 µg budesonide or equivalent); GraziaTinA-asthma® (12 weeks): tiotropium Respimat® 5 µg or 2.5 µg add-on to ICS (200–400 µg budesonide or equivalent); Study 342 (16 weeks): tiotropium Respimat® 5 µg add-on to ICS (400–800 µg budesonide or equivalent). Pooled safety data are presented.

Results 1929 patients received tiotropium Respimat® (PrimoTinA-asthma®, n = 456; MezzoTinA-asthma®, n = 1036; GraziaTinA-asthma®, n = 309; Study 342, n = 128). Frequency

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