Background We evaluated the effect of once-daily tiotropium Respimat® 5 µg on lung function, asthma exacerbation and asthma symptom control among patients with symptomatic asthma receiving inhaled corticosteroids (ICS; ≥800 µg/day budesonide or equivalent) + long-acting β_2-agonist (LABA).
Methods Data were pooled from two replicate, double-blind, placebo-controlled, 48-week, parallel-group studies of once-daily tiotropium 5 µg versus placebo, both delivered via the Respimat® SoftMist™ inhaler (PrimoTinA-asthma®: NCT00772538, NCT00776984). Eligible patients had: ≥5-year history of asthma diagnosed before the age of 40 years; seven-question Asthma Control Questionnaire (ACQ-7) score of ≥1.5; experienced ≥1 exacerbation during the previous year. Patients were either lifelong non-smokers, or ex-smokers (<10 pack-years) who quit smoking ≥1 year before study enrolment. Exclusion criteria included diagnosis of chronic obstructive pulmonary disease. Co-primary end points in individual trials: peak forced expiratory volume in 1 second (FEV_1) within 3 h post-dose (0–3 h) and trough FEV_1. A co-primary end point in pooled data was time to first severe exacerbation; secondary end points included time to first episode of asthma worsening and ACQ-7 response. *Post hoc* efficacy analyses were performed.
Results 912 patients were randomised to receive tiotropium Respimat® (n = 456) or placebo Respimat® (n = 456). At Week 48, tiotropium Respimat® was associated with statistically significant improvements versus placebo Respimat® in peak $FEV_{1(0–3h)}$ (adjusted mean difference 100 mL; 95% confidence interval: 52, 148; $p < 0.0001$) and trough FEV_1 (adjusted mean difference 62 mL; 95% confidence interval: 18, 106; $p = 0.006$). Time to first severe asthma exacerbation was significantly longer with tiotropium Respimat® versus placebo Respimat® (282 vs 226 days, respectively; hazard ratio 0.79; $p = 0.034$), as was time to first episode of asthma worsening (315 vs 181 days, respectively; hazard ratio 0.69; $p < 0.0001$). At Week 24, ACQ-7 responder rate was significantly higher with tiotropium Respimat® (53.9%) versus placebo Respimat® (46.9%; odds ratio 1.32; $p = 0.0427$).
Conclusion Once-daily tiotropium Respimat® add-on to ICS + LABA improves lung function, reduces risk of severe asthma exacerbation and asthma worsening, and significantly improves asthma symptom control compared with placebo Respimat® in patients with symptomatic asthma.

S92 EFFICACY OF ONCE-DAILY TIOTROPIUM RESPIMAT® 5 µG FROM FIVE PHASE III TRIALS IN ADULTS WITH SYMPTOMATIC ASTHMA

[1]D Price, [2]ED Bateman, [3]P Paggiaro, [4]A Kaplan, [5]M Engel, [5]H Schmidt, [5]P Moroni-Zentgraf, [6]HAM Kerstjens. *[1]Institute of Applied Health Sciences, University of Aberdeen, Aberdeen, UK; [2]University of Cape Town, Cape Town, South Africa; [3]University of Pisa, Pisa, Italy; [4]Family Physician Airways Group of Canada, Ontaria, Canada; [5]Boehringer Ingelheim Pharma GmbH and Co. KG, Biberach an Der Riss, Germany; [6]University Medical Center Groningen, Groningen, The Netherlands*

10.1136/thoraxjnl-2014-206260.98

Background Recent clinical trials have indicated that the long-acting antimuscarinic agent tiotropium, a once-daily long-acting bronchodilator, may provide benefit to patients with symptomatic asthma. We investigated primary efficacy data (lung function, risk of severe exacerbation and seven-question Asthma Control Questionnaire [ACQ-7] response) from five Phase III, randomised, double-blind, parallel-group trials that evaluated the efficacy and safety of once-daily tiotropium add-on versus placebo add-on (all tiotropium doses delivered via the Respimat® SoftMist™ inhaler) in adults with symptomatic asthma on inhaled corticosteroid (ICS) ± long-acting β_2-agonist (LABA) maintenance therapy.

Abstract S92 Table 1

	Adjusted mean of difference in response from placebo (mL)		
	PrimoTinA-asthma® (Week 24)	MezzoTinA-asthma® (Week 24)	GraziaTinA-asthma® (Week 12)
	Tiotropium Respimat®5 µg[a] (n = 456)	Tiotropium Respimat®5 µg[a] (n = 517)	Tiotropium Respimat®5 µg (n = 155)
Peak $FEV_{1(0–3h)}$	110 ($p < 0.0001$)	185 ($p < 0.0001$)	128 ($p = 0.0005$)
Trough FEV_1	93 ($p = 0.0058$)	146 ($p < 0.0001$)	122 ($p = 0.0010$)
FEV_1 $AUC_{(0–3h)}$	107 ($p < 0.0001$)	182 ($p < 0.0001$)	125 ($p = 0.0003$)
Peak $FVC_{(0–3h)}$	87 ($p = 0.0050$)	95 ($p < 0.0001$)	57 ($p = 0.1714$)

[a]Pooled data
AUC, area under the curve; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity

Methods Two 48-week trials of tiotropium Respimat® 5 µg (PrimoTinA-asthma®: NCT00776984, NCT00772538) in patients on high-dose ICS (≥800 µg budesonide or equivalent) + LABA; two 24-week trials of tiotropium Respimat® 5 µg and 2.5 µg (MezzoTinA-asthma®: NCT01172808, NCT01172821) in patients on moderate-dose ICS (400–800 µg budesonide or equivalent); one 12-week trial of tiotropium Respimat® 5 µg and 2.5 µg (GraziaTinA-asthma®: NCT01316380) in patients on low-dose ICS (200–400 µg budesonide or equivalent).
Results 3476 patients were treated, of whom 1128 received tiotropium Respimat® 5 µg. Once-daily tiotropium Respimat® 5 µg significantly improved lung function (Table) in patients with not fully controlled asthma receiving low- to high-dose ICS. In addition, tiotropium Respimat® 5 µg reduced the risk of severe exacerbations versus placebo (co-primary end point) in patients on high-dose ICS + LABA (hazard ratio 0.79; $p = 0.0343$), and there was an increase in ACQ-7 responder rate (co-primary end point) with the5 µg dose (odds ratio 1.32; $p = 0.0308$) compared with placebo in patients on moderate-dose ICS.
Conclusion Once-daily tiotropium Respimat® significantly improves lung function in adult patients with symptomatic asthma receiving a range of doses of ICS, including even high-dose ICS + LABA, suggesting a potential role for this treatment as add-on to ICS in adults with symptomatic asthma.

S93 A PROSPECTIVE STUDY INVESTIGATING EXACERBATIONS, HEALTHCARE UTILISATION AND HEALTH ECONOMIC INDICATORS IN OMALIZUMAB TREATED SEVERE ALLERGIC ASTHMA PATIENTS – RESULTS FROM AN INTERIM ANALYSIS OF THE APEX II STUDY

[1]M Masoli, [2]A Menzies-Gow, [3]L Dobson, [4]JB Morjaria, [5]R Allcock, [6]R Niven. *[1]Derriford Hospital, Derriford, UK; [2]Royal Brompton Hospital, London, UK; [3]Torbay Hospital, Torbay, UK; [4]Hull Royal Infirmary, Hull, UK; [5]Queen Elizabeth Hospital Gateshead, Gateshead, UK; [6]University Hospital of South Manchester, Manchester, UK*

10.1136/thoraxjnl-2014-206260.99

Background A previous retrospective study of UK clinical practice demonstrated that omalizumab was associated with reduced exacerbations and healthcare utilisation in severe allergic asthmatics.