L (T+O 2.5/5 µg) and 0.140 L (T+O 5/5 µg). SGRQ total scores improved by 5.1 (O 5 µg), 5.7 (T 2.5 µg), 5.6 (T 5 µg), 6.2 (T+O 2.5/5 µg) and 6.8 points (T+O 5/5 µg); differences between T+O 5/5 µg and O 5 µg and T 5 µg were statistically significant (p

Conclusions T+O 5/5 µg significantly improved lung function and provided symptomatic benefit over O 5 µg and T 5 µg.

P255 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 asthma exacerbation risk may provide improvements in clinical burden, patient experience and healthcare costs. In Phase III trials, once-daily tiotropium (delivered via the Respimat® SoftMist™ inhaler) added on to at least inhaled corticosteroids (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 as add-on to at least ICS maintenance therapy (Table). 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 forced expiratory volume in 1 second, seven-question Asthma Control Questionnaire score and ICS dose (µg) were: 56.0 ± 13.1, 2.6 ± 0.7, 1198 ± 539 (PrimoTinA-asthma®); 75.1 ± 11.5, 2.2 ± 0.5, 660 ± 213 (MezzoTinA-asthma®); 77.7 ± 11.9, 2.1 ± 0.4, 381 ± 78 (GraziaTinA-asthma®). Tiotropium Respimat® 5 µg reduced severe asthma exacerbation risk by at least 21% in all three severity cohorts (Table) and asthma worsening risk versus placebo in all trials, with a statistically significant reduction in the PrimoTinA-asthma® trial.

Abstract P255 Table 1

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

^aHazard ratio; time to first severe exacerbation (versus placebo, <1 favours tiotropium Respimat®); ^bBaseline to Week 48; ^cBaseline to Week 24; ^dBaseline to time of last event

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.

P256 SAFETY OF ONCE-DAILY TIOTROPIUM AND OLODATEROL FIXED-DOSE COMBINATION VIA THE RESPIMAT IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN TWO 1-YEAR STUDIES

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Introduction The fixed-dose combination (FDC) of tiotropium (T), a once-daily long-acting muscarinic antagonist, and olodaterol (O), a once-daily long-acting β₂-agonist, is currently being evaluated in chronic obstructive pulmonary disease (COPD).

Two 52-week, Phase III replicate pivotal studies were conducted to assess the efficacy and safety of FDCs of T and O (T+O) delivered via Respimat® Soft Mist™ inhaler in patients (pts) with GOLD Stage 2–4 COPD. Pooled safety data from the two studies are presented here.

Methods These were double-blind, randomised, parallel-group studies with 5 arms: O 5 µg, T 2.5 µg, T 5 µg, T+O 2.5/5 µg, T+O 5/5 µg. Key inclusion criteria were: age ≥40 years, diagnosis of COPD, smoking history >10 pack-years. Pts with a history of asthma or significant disease other than COPD were excluded. Adverse events (AEs) were reported throughout the studies.

Results A total of 5162 pts were randomised and treated. In general, AEs, serious AEs and fatal AEs were balanced across treatment groups. In particular, frequencies of AEs in the cardiac disorders System Organ Class (SOC) and respiratory disorders SOC were similar.

Abstract P256 Table 1

	Pts with AE, %				
	O 5 µg n = 1038	T 2.5 µg n = 1032	T 5 µg n = 1033	T+O 2.5/5 µg n = 1030	T+O 5/5 µg n = 1029
Total AEs	76.6	73.4	73.3	74.7	74.0
Serious AEs	17.4	15.1	16.7	16.3	16.4
Fatal AEs	1.3	1.2	1.6	1.4	1.7
Cardiac disorders*	5.7	5.8	5.3	5.8	4.5
Respiratory, thoracic and mediastinal disorders*	45.3	43.9	42.7	38.2	39.4

*MedDRA SOC