

## Poster sessions

**Introduction** To benefit symptomatic patients with moderate-to-severe COPD not managed by single bronchodilator, COPD management strategies recommend combining bronchodilators with different mechanisms. We compared, once-daily dual bronchodilation by co-administration of the long-acting muscarinic antagonist (LAMA) glycopyrronium 50 g (GLY) and the long-acting  $\beta_2$ -agonist (LABA) indacaterol 150 g (IND), with IND 150 g monotherapy.

**Methods** In this randomised, multicentre, placebo-controlled, double-blind, parallel-group study, patients with moderate-to-severe COPD were administered with GLY + IND or IND + placebo (1:1; all delivered via Breezhaler® device) for 12 weeks. We assessed lung function, dyspnoea (via the transition dyspnoea index [TDI]), patient-reported symptoms, and safety and tolerability over 12 weeks.

**Results** Of the 449 patients randomised (GLY + IND [ $n = 226$ ]; IND [ $n = 223$ ]), 94.0% completed the study. At Week12, GLY + IND demonstrated a statistically significant improvement in mean trough forced expiratory volume in one second ( $FEV_1$ ) over IND (least squares mean treatment difference [Td]: 64 mL;  $p < 0.001$ ). Significantly greater improvements in  $FEV_1$  area under curve from 30 min to 4h ( $FEV_1 AUC_{30\text{min}-4\text{h}}$ ) and trough forced vital capacity were observed with GLY + IND vs IND on Day1 (Td: 105 mL, 112 mL, respectively) and at Week12 (Td: 111 mL, 93 mL, respectively), all  $p < 0.01$ . GLY + IND demonstrated significant improvements in inspiratory capacity versus IND at most timepoints on Day1 and Week12 (Td: 59 to 159 mL). GLY + IND significantly improved TDI total score versus IND (Td: 0.49,  $p = 0.037$ ) and a higher proportion of patients on GLY + IND achieved a clinically meaningful improvement ( $\geq 1$  point) versus IND at Week12 (odds ratio 1.97 favouring GLY + IND;  $p = 0.004$ ). GLY + IND was also associated with significantly greater improvements in mean daytime respiratory symptom score and the percentage of days being able to perform usual daily activities vs IND over 12 weeks of treatment (Td: -0.1 and 6.2, respectively; both  $p < 0.05$ ). The overall incidence of adverse events (AEs) and serious AEs (SAEs) was comparable for the GLY + IND and IND groups (AEs: 37.6% vs 34.1%; SAEs: 2.2% vs 2.3%, respectively).

**Conclusion** In patients with moderate-to-severe COPD, compared with indacaterol monotherapy, once-daily co-administration of glycopyrronium and indacaterol delivered via Breezhaler® device provided superior improvements lung function and early post-dose bronchodilation (from Day1), dyspnoea, symptoms and activities, without adversely affecting safety and tolerability.

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### EFFICACY AND SAFETY OF ONCE-DAILY GLYCOPYRRONIUM COMPARED WITH BLINDED TIOTROPIUM IN PATIENTS WITH COPD: THE GLOWS STUDY

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10.1136/thoraxjnl-2013-204457.385

**Background** Glycopyrronium, a once-daily long-acting muscarinic antagonist (LAMA), has demonstrated a similar efficacy and safety profile to open-label tiotropium in patients with

moderate-to-severe chronic obstructive pulmonary disease (COPD).<sup>1</sup> The GLOW5 study compared the efficacy and safety of glycopyrronium with blinded tiotropium.

**Methods** In this multicentre, 12-week, blinded study, patients  $\geq 40$  years with moderate-to-severe COPD (post-bronchodilator  $FEV_1 \geq 30\%$  and  $< 80\%$  of the predicted normal, post-bronchodilator  $FEV_1/FVC < 0.70$ ) and a smoking history of  $\geq 10$  pack-years were randomised to glycopyrronium 50 µg (via Breezhaler® device) or tiotropium 18 µg (via HandiHaler® device). The primary objective was to demonstrate non-inferiority of glycopyrronium versus tiotropium for trough  $FEV_1$  at Week 12 (non-inferiority margin: -50 mL). Other endpoints included  $FEV_1$  area under the curve from 0 to 4 hours ( $AUC_{0-4\text{hr}}$ ) on Day 1, Transition Dyspnoea Index (TDI), St George's Respiratory Questionnaire (SGRQ), rescue medication use, exacerbation rate, safety and tolerability.

**Results** Of the 657 patients randomised, (glycopyrronium [ $n = 327$ ]; tiotropium [ $n = 330$ ]; mean age: 63.5 years, mean post-bronchodilator  $FEV_1$ : 53.5% predicted), 95.9% completed the study. Glycopyrronium demonstrated non-inferiority to tiotropium for trough  $FEV_1$  at Week 12 (Least Squares Mean [LSM] = 1.41L for both the groups; 95% confidence interval [CI]: -0.032, 0.031L). Glycopyrronium had a rapid onset of bronchodilation in the morning as demonstrated by a higher  $FEV_1 AUC_{0-4\text{hr}}$  on Day 1 compared to tiotropium (LSM treatment difference [Td] = 58mL;  $p < 0.001$ ). At Week 12, TDI total score (Td = -0.188;  $p = 0.385$ ), SGRQ total score (Td = 0.65;  $p = 0.488$ ) and percentage of days with no rescue medication use (Td = -1.5;  $p = 0.528$ ) were comparable between the groups. No significant treatment difference was observed with respect to rate of moderate/severe COPD exacerbations per year (glycopyrronium 0.38 versus tiotropium 0.35 [rate ratio = 1.10, 95% CI: 0.62, 1.93];  $p = 0.754$ ). Overall, the incidence of adverse events was similar in the glycopyrronium (40.4%) and tiotropium (40.6%) groups.

**Conclusion** Glycopyrronium and blinded tiotropium showed similar improvements in lung function, dyspnoea, health status, exacerbation rate and rescue medication use, with a similar safety and tolerability profile. Onset of bronchodilation with glycopyrronium was significantly more rapid following the first dose.

## REFERENCE

1. Kerwin, E. et al. Eur Resp J 2012;40:1106–1114.

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### QVA149 ONCE DAILY IMPROVES LUNG FUNCTION, DYSPNOEA AND HEALTH STATUS INDEPENDENT OF PRIOR MEDICATIONS AND DISEASE SEVERITY: THE SHINE STUDY

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10.1136/thoraxjnl-2013-204457.386

**Introduction** QVA149 is a novel, inhaled, once-daily, fixed-dose combination of the long-acting  $\beta_2$ -agonist (LABA) indacaterol and the long-acting muscarinic antagonist (LAMA) glycopyrronium (NVA237) in development for the maintenance treatment of chronic obstructive pulmonary disease (COPD). The SHINE study compared the effects of QVA149 110/50 g, indacaterol 150 g, glycopyrronium 50 g, tiotropium 18 g and placebo in