

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 β_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 (FEV₁) over IND (least squares mean treatment difference [Td]: 64 mL; p < 0.001). Significantly greater improvements in FEV₁ area under curve from 30 min to 4h (FEV₁AUC_{30min-4h}) 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 (≥ 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.

P233 EFFICACY AND SAFETY OF ONCE-DAILY GLYCOPYRRONIUM COMPARED WITH BLINDED TIOTROPIMUM IN PATIENTS WITH COPD: THE GLOW5 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).¹ The GLOW5 study compared the efficacy and safety of glycopyrronium with blinded tiotropium.

Methods In this multicentre, 12-week, blinded study, patients ≥ 40 years with moderate-to-severe COPD (post-bronchodilator FEV₁ $\geq 30\%$ and $< 80\%$ of the predicted normal, post-bronchodilator FEV₁/FVC < 0.70) and a smoking history of ≥ 10 pack-years were randomised to glycopyrronium 50 μ g (via Breezhaler[®] device) or tiotropium 18 μ g (via HandiHaler[®] device). The primary objective was to demonstrate non-inferiority of glycopyrronium versus tiotropium for trough FEV₁ at Week 12 (non-inferiority margin: -50 mL). Other endpoints included FEV₁ area under the curve from 0 to 4 hours (AUC_{0-4hr}) 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 FEV₁: 53.5% predicted), 95.9% completed the study. Glycopyrronium demonstrated non-inferiority to tiotropium for trough FEV₁ 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 FEV₁ AUC_{0-4hr} 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.

P234 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 β_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