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 day-time 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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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

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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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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