lung function compared with indacaterol, glycopyrronium, open-label tiotropium and placebo in patients with moderate-to-severe COPD.

Methods This 26 week, multicentre, double-blind, parallel-group, placebo and active controlled (open-label tiotropium) study randomised male or female patients ≥40 years of age with moderate-to-severe COPD (post-bronchodilator FEV_1/FVC <0.7 and FEV_1 ≥30% to <80% predicted) and smoking history ≥10 pack-years to receive once-daily QVA149 (110/50μg), indacaterol (150μg), glycopyrronium (50μg), placebo (all delivered via the Breezhaler® device) and tiotropium (18μg; delivered via the Handihaler® device) (2:2:2:1:2). The primary objective was to demonstrate superiority in trough FEV_1 (mean of 23h 15min and 23h 45min post-dose) of QVA149 versus indacaterol and glycopyrronium at Week 26. We also present results of trough FEV_1 at Day 1 and Week 12, serial spirometry for FEV_1 and forced vital capacity (FVC) at Day 1, Weeks 12 and 26.

Results Of the 2144 patients randomised, (QVA149 [n=475]; indacaterol [n=477]; glycopyrronium [n=475]; tiotropium [n=483]; placebo [n=234]), 89.1% completed the study. 75.4% were male; mean age: 63.9 years; mean post-bronchodilator FEV_1: 55.2% predicted. At Day 1, Weeks 12 and 26, QVA149 was statistically superior to indacaterol, glycopyrronium, tiotropium and placebo for mean trough FEV_1 and trough FVC (all p<0.001, table).

Serial spirometry in a subset of patients (QVA149 [n=66]; indacaterol [n=64]; glycopyrronium [n=63]; tiotropium [n=70]; placebo [n=31]) showed statistically significant improvements in FEV_1 with QVA149 versus placebo at all time-points (p<0.001) and versus indacaterol, glycopyrronium and tiotropium at almost all assessed time-points on Day 1, and Weeks 12 and 26.

Conclusion QVA149 once daily provided significant and clinically meaningful improvements in lung function versus the component monotherapies indacaterol and glycopyrronium, as well as significant improvements versus tiotropium and placebo over 26 weeks in patients with COPD.

Abstract P192 Table 1 Trough FEV_1 and FVC at Day 1, Weeks 12 and 26

	Least squares mean treatment (SE) difference in mL			
	QVA149–placebo	QVA149–indacaterol	QVA149–glycopyrronium	QVA149–tiotropium
Trough FEV_1				
Day 1	190 (11)	80 (9)	80 (9)	80 (9)
Week 12 (LOCF)	230 (16)	80 (13)	100 (13)	90 (13)
Week 26 (LOCF)	200 (17)	70 (14)	90 (14)	80 (13)
Trough FVC				
Day 1	300 (23)	130(18)	100 (18)	110 (18)
Week 12	320 (29)	110 (23)	120 (23)	110 (23)
Week 26	280 (31)	100 (24)	80 (24)	90 (24)

all p<0.001

P193 GLYCOPYRRONIUM ONCE DAILY PROVIDES RAPID AND SUSTAINED BRONCHODILATION AND IS WELL TOLERATED IN PATIENTS WITH COPD: THE SHINE STUDY

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[1]E Bateman, [2]S Hashimoto, [3]N Gallagher, [3]Y Green, [3]R Horton, [3]M Henley, [4]D Banerji.
[1]Department of Medicine, University of Cape Town, Cape Town, South Africa; [2]Nihon University School of Medicine, Itabashi Hospital, Tokyo, Japan; [3]Novartis Horsham Research Centre, Horsham, West Sussex, UK; [4]Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA

Introduction NVA237 (glycopyrronium bromide) is a once-daily inhaled long-acting muscarinic antagonist for the treatment of COPD. The SHINE study evaluated the efficacy and safety of QVA149, a fixed-dose combination of indacaterol and glycopyrronium, compared with indacaterol, glycopyrronium, open-label tiotropium and placebo in patients with COPD.

Methods This 26 week, multicentre, double-blind, parallel-group, placebo and active controlled (open-label tiotropium) study randomised male or female patients ≥40 years of age with moderate-to-severe COPD (post-bronchodilator FEV_1/FVC <0.7 and FEV_1 ≥30% to <80% predicted) and smoking history ≥10 pack-years to receive once-daily QVA149 (110/50μg), indacaterol (150μg), glycopyrronium (50μg refers to the quantity of the glycopyrronium moiety present in the capsule, which corresponds to a delivered dose of 44 μg), placebo (all delivered via the Breezhaler® device) and tiotropium (18μg; delivered via the Handihaler® device) (2:2:2:1:2). The primary efficacy endpoint was trough FEV_1 (mean of 23h 15min and 23h 45min post-dose) at Week 26. Here we report the results of the efficacy and safety of glycopyrronium versus tiotropium and placebo.

Results Of the 1192 patients randomised (glycopyrronium [n=475]; tiotropium [n=483]; placebo [n=234]); 88.3% completed the study with the mean age in glycopyrronium, tiotropium and placebo groups being 64.3, 63.5 and 64.4 years, respectively. At Week 26, glycopyrronium was superior to placebo for mean trough FEV_1 (treatment difference: 120mL; p<0.001). A similar significant improvement was observed with tiotropium versus placebo (treatment difference: 130mL; p<0.001). Significant improvement was also seen with glycopyrronium compared with placebo in other outcome measures evaluating lung function (table).

Serial spirometry in a subset of patients (glycopyrronium [n=63]; tiotropium [n=70] and placebo [n=31]) showed statistically significant improvements in FEV_1 with glycopyrronium and tiotropium versus placebo at all assessed time-points on Week 26. The incidence of adverse events was similar between groups (61.3% glycopyrronium; 57.3% tiotropium and 57.8% placebo).

Conclusion Glycopyrronium 50μg once daily provided rapid and sustained bronchodilation over 26 weeks and was well tolerated. The onset of action of glycopyrronium was faster than tiotropium on Day 1 and the FEV_1 AUC 0–12h, 12–24h and 0–24h profiles at Week 26 were similar, thereby showing good 24-hour efficacy.

Abstract P193 Table 1 Least squares mean (LSM) treatment difference on Day 1 and Week 26

	Total number of patients (n)	LSM treatment difference (SE) in mL		
		Glycopyrronium–placebo	Tiotropium–placebo	Glycopyrronium–tiotropium
Day 1				
FEV_1 $AUC_{0–4h}$	1165	190 (9)*	140 (9)*	50 (8)*
FEV_1 $AUC_{0–12h}$	164	180 (25)*	130 (25)*	50 (20)†
Week 26				
FEV_1 $AUC_{0–12h}$	152	210 (41)*	210 (41)*	–10 (33)NS
FEV_1 $AUC_{12–24h}$	152	200 (43)*	210 (42)*	–10 (33)NS
FEV_1 $AUC_{0–24h}$	152	200 (41)*	210 (40)*	–10 (32)NS

*p<0.001; † p<0.05; NS=not significant.

Prof Eric Bateman has served on advisory boards for Boehringer Ingelheim, AstraZeneca, Elevation Pharma, Napp Pharma, Novartis, Almirall, Forest, and Merck and Takeda; has served as a consultant to Navigant Consulting, IMS consulting group, ALK-Abello, Almirall, Hoffman la Roche, and ICON; has been paid lecture fees by AstraZeneca, ALK-Abello, Chiesi, Boehringer Ingelheim, GlaxoSmithKline, Nycomed/Takeda, Novartis, Pfizer, and Indegene Lifesciences Ltd.

Prof Shu Hashimoto has no conflicts of interest.

P194 ONCE-DAILY QVA149 PROVIDES SUPERIOR BRONCHODILATION AND IMPROVES LUNG FUNCTION VERSUS TWICE-DAILY FLUTICASONE/SALMETEROL IN COPD PATIENTS: THE ILLUMINATE STUDY

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[1]C Vogelmeier, [2]E Bateman, [3]J Pallante, H Bryant[4], [3]V Alagappan, [3]P D'Andrea, [3]E He, [3]D Banerji. *[1]Department for Respiratory Diseases, University of Marburg, Marburg, Germany; [2]Department of Medicine, University of Cape Town, Cape Town, South Africa; [3]Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; [4]Novartis Horsham Research Centre, Horsham, West Sussex, UK*

Introduction QVA149 is a novel inhaled once-daily dual bronchodilator containing a fixed-dose combination of the long-acting β_2-agonist (LABA) indacaterol and the long-acting muscarinic antagonist (LAMA) glycopyrronium, in development for the maintenance treatment of COPD. This study evaluated the superiority of QVA149 once daily in terms of efficacy over fluticasone/salmeterol twice daily in patients with COPD.

Methods In this 26 week, multicentre, double-blind, double-dummy, parallel-group study patients aged ≥40 years with moderate-to-severe COPD (post-bronchodilator FEV_1/FVC <0.7 and FEV_1 ≥40% to <80% predicted), no history of exacerbations in the previous year and smoking history ≥10 pack-years, were randomised (1:1) to receive QVA149 110/50μg (via the Breezhaler® device) or fluticasone/salmeterol 500/50μg (via the Accuhaler® device). The primary efficacy end point was standardised FEV_1 area under the curve (FEV_1 $AUC_{0–12h}$) at Week 26. The pre-dose trough FEV_1 on Week 12 and 26 and peak FEV_1 on Day 1, Week 12 and Week 26 were also measured.

Results A total of 523 patients (35.1% on inhaled corticosteroids use) were randomised [QVA149, n=259; fluticasone/salmeterol, n=264; male (70.9%); mean age: 63.3 years; mean post-bronchodilator FEV_1: 60.2% predicted], 82.6% completed. FEV_1 $AUC_{0–12h}$ was found clinically meaningful and statistically significant in favour of QVA149 compared to fluticasone/salmeterol on Day 1, Week 12 and Week 26 (Least squares mean [LSM] treatment difference=70mL, 120mL, 140mL, respectively; all p<0.001). Pre-dose trough FEV_1 was significantly (p<0.001) higher for QVA149 compared with fluticasone/salmeterol at Week 12 and 26 (LSM treatment difference=90mL and 100mL, respectively; p<0.001). The LSM treatment difference for peak FEV_1 was also statistically significant for QVA149 compared with fluticasone/salmeterol on Day 1 (70mL), Week 12 (150mL) and Week 26 (150mL), all p<0.001.

Conclusion QVA149 once daily provided superior bronchodilation at all time-points compared to fluticasone/salmeterol twice daily and showed clinically meaningful improvements in lung function for a sustained period of 26 weeks. In moderate-to-severe COPD patients without a history of exacerbations in the previous year, LABA/LAMA dual bronchodilation with once-daily QVA149 proves a superior alternative to twice-daily fluticasone/salmeterol.

Prof Claus Vogelmeier has served on scientific advisory boards for AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Janssen, Novartis, Pfizer, Almirall, Takeda, and Sterna Biologicals; has been paid lecture fees by AstraZeneca, Chiesi, GlaxoSmithKline, Janssen, Talecris, Novartis, Boehringer Ingelheim, Takeda, and Pfizer.

Prof Eric Bateman has served on advisory boards for Boehringer Ingelheim, AstraZeneca, Elevation Pharma, Napp Pharma, Novartis, Almirall, Forest, and Merck and Takeda; has served as a consultant to Navigant Consulting, IMS consulting group, ALK-Abello, Almirall, Hoffman la Roche, and ICON; has been paid lecture fees by AstraZeneca, ALK-Abello, Chiesi, Boehringer Ingelheim, GlaxoSmithKline, Nycomed/Takeda, Novartis, Pfizer, and Indegene Lifesciences Ltd.

Lung cancer investigation, treatment and survival

P195 CASE SERIES: HOW USEFUL ARE FLEISCHNER GUIDELINES FOR NODULE SURVEILLANCE IN A DISTRICT GENERAL HOSPITAL?

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RW Lee, KE Millward, FE Ossai, D Ellis, M Townsend, S Lohani Darent Valley Hospital, Dartford, Kent, United Kingdom

Background Surveillance of pulmonary nodules aims to identify early-stage lung cancers where radical therapy can offer cure. Interval CT scans track nodule characteristics with Fleischner criteria commonly used in an attempt to standardise care. There remains debate regarding the applicability of Fleischner guidance in populations of UK patients that can differ substantially from those included in existing studies that define the Fleischner recommendations.

Objectives

- Audit compliance of pulmonary nodule follow up with Fleischner Guidelines.
- Compare local outcomes with those used to create Fleischner guidelines.
- Compare local compliance with published compliance.

Methods Patients referred to a specialist respiratory nurse service for pulmonary nodule surveillance since 2008 (including patients already under surveillance) with opportunity for 2 years of completed follow-up were included with retrospective review of the nodule database/electronic records and imaging. Patients were risk stratified according to nodule size and Fleischner risk category (e.g. smoking).

Results 111 patients under surveillance were identified of whom 56 were Male and 55 Female with median age 67 (34–91) years. 67 were solitary and 44 were multiple. Patients were stratified to Low- and High-risk groups according to main nodule size: (L1–4 or H1–4 respectively). Each group included; High-risk: H1 (<=4mm)10, H_2 (>4–6mm) 25, H3 (>6–8mm) 19 and H4 (>8mm) 36 cases and Low-risk: L1 (<=4mm) 0, L2 (>4–6mm) 5, L3 (>6–8mm) 4 and L4 (>8mm) 3 cases.

89 patients completed standard follow-up and were discharged. Positive scans included Lung tumours (3) - (two underwent lobectomy); Aspergilloma (1); Rectal carcinoma (1)- discovered by non-Fleischner abdominal CT. Surveillance was discontinued for: Patient choice/co-morbidity (8); Nodule resolution (3); Not documented/lost (6).

Conclusion Fleischner guidelines were well adhered to and were also utilised where their application is less well defined e.g. development of a new nodule during follow-up prompted either re-initiation or more commonly continued/modified trajectory of Fleischner - an area notably not well covered in current guidance. Furthermore principals of Fleischner recommendations were applied to multiple nodules but management of such patients is often not as easily followed as solitary nodules.

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