by GOLD, on the basis of their CAT/mMRC scores and GOLD stage/Exacerbation frequency. Using CAT as the symptom grade, we compared patient distribution in the 4 categories using scores between 10 and 20 to determine the CAT threshold at which the distribution of patients in each group is proportional.

Results The proportion of patients in each of the 4 categories was consistent for each symptom score whether risk was assessed by FEV1 or exacerbation number. However the proportions using CAT 10 and mMRC 0–1, ≥2 were significantly different in each category. When the CAT threshold was changed to 13, the proportions of patients in the four groups were no longer significantly different to those using mMRC.

Conclusion We have demonstrated that in patients with AATD, using CAT score of 13 as the threshold for assessing symptoms results in a similar proportion of patients being categorised into the risk categories. This affects risk assessment and therapeutic choice. Longitudinal follow up and monitoring will enable confirmation of this threshold for patient management.

P189 REDUCED COPD EXACERBATIONS ASSOCIATED WITH ACLIDINIUM BROMIDE VERSUS PLACEBO: A POOLED ANALYSIS OF PHASE III DATA

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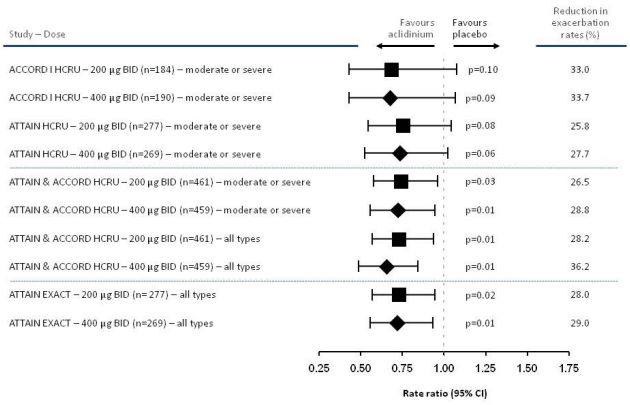
Introduction and objective Aclidinium bromide is a novel, long-acting, inhaled muscarinic antagonist indicated for the treatment of chronic obstructive pulmonary disease (COPD). COPD is characterised by periodic worsening of symptoms (exacerbations) that are associated with increased morbidity and mortality. Here, we report the results of a pooled analysis of aclidinium on exacerbations.

Methods Data from two Phase III studies (3-month ACCORD COPD I and 6-month ATTAIN) were included in this analysis. Both were designed to evaluate the efficacy and safety of aclidinium 200 μg and 400 μg (metered dose) BID versus placebo (primary endpoint: change from baseline in FEV_1). Adults (aged ≥40 years) with moderate-to-severe COPD, who were current/former smokers with a smoking history ≥10 pack-years, were included. Exacerbations (additional endpoint) were assessed in both studies using healthcare resource utilisation (HCRU) criteria (increase in symptoms for ≥2 consecutive days that required increased medication use or other medical intervention) and, in ATTAIN only, with the Exacerbations of Chronic Pulmonary Disease Tool (EXACT [daily diary card data with exacerbations defined according to the developer's criteria]). Neither study was individually powered to assess treatment differences in exacerbation frequency. In this pooled analysis, exacerbation rate ratios (per patient/year for aclidinium versus placebo) were analyzed using a Poisson regression model corrected for overdispersion; 95% confidence intervals and p-values were calculated.

Results Data for 1378 patients were included; the majority (62%) were male with a mean age of approximately 63 years. At baseline, >60% of patients were classed as GOLD stage II (moderate), and 31% reported ≥1 exacerbations in the previous 12 months. In both studies, there was a trend towards relative reduction (approximately 30%) in the rate of moderate or severe exacerbations (requiring antibiotic or corticosteroid treatment, or hospitalisation) with both aclidinium doses versus placebo (Figure). A significant reduction in moderate or severe exacerbation rate was observed with aclidinium 400 μg versus placebo when data from both studies were pooled (0.31 vs 0.44; rate ratio 0.71, p=0.01).

Conclusions This pooled analysis provides evidence to support a reduction in moderate or severe COPD exacerbations with aclidinium 200 μg and 400 μg BID compared with placebo.



Abstract P189 Figure 1

P190 QVA149 ONCE DAILY PROVIDES SIGNIFICANT IMPROVEMENTS IN LUNG FUNCTION OVER 1 YEAR IN PATIENTS WITH COPD: THE ENLIGHTEN STUDY

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Introduction QVA149 is a novel inhaled once-daily dual bronchodilator, containing a fixed-dose combination of the long-acting β_2-agonist indacaterol and the long-acting muscarinic antagonist NVA237 (glycopyrronium) in development for the treatment of COPD. This study evaluated the long-term effect of QVA149 on lung function in patients with COPD.

Methods This was a multicentre, double-blind, parallel group, placebo-controlled study in which patients with moderate-to-severe COPD were randomised (2:1) to receive QVA149 (110/50μg) or placebo once daily via the Breezhaler® device for 52 weeks. Treatment was taken in the morning at the same time of day. Lung function was measured as forced expiratory volume in 1 second (FEV_1) and forced vital capacity (FVC) at 30 and 60 minutes post-dose at clinic visits over 52 weeks.

Results 339 patients (77% male, mean age 63 years; mean post-salbutamol FEV_1 57% predicted, FEV_1/FVC 54%) were randomised to receive QVA149 (n=226) or placebo (n=113); 86% and 79% of patients respectively completed treatment, respectively. QVA149 significantly increased FEV_1 and FVC versus placebo at all assessment points (table).

Conclusion QVA149 once daily provided rapid and clinically meaningful bronchodilation compared with placebo. No tachyphylaxis was observed and the bronchodilator effect was sustained over the 52 week treatment period.

Ronal Dahl: he participated in advisory boards for Novartis, AstraZeneca, Boehringer-Ingelheim, Pfizer, ALK-Abello, UCB, Nycomed, Dainippon and ONO.

Kenneth R Chapman: he holds the GSK-CIHR Research Chair in Respiratory Healthcare Delivery at the University Health Network, has served as a consultant to CSL Behring, GlaxoSmithKline, Novartis, Nycomed (Takeda), and Talecris (Grifols), and has received payment for lectures or service on speakers bureaus from Boehringer-Ingelheim, GlaxoSmithKline, Grifols, Nycomed (Takeda), Family Physicians Airways Group of Canada, Canadian Network for Respiratory Care, and Talecris.

Abstract P190 Table 1 QVA149 versus placebo least squares mean (LSM) differences in FEV_1 and FVC

	QVA149-placebo LSM treatment difference (SE) in mL			
Visit	FEV1		FVC	
	30 min post-dose	60 min post-dose	30 min post-dose	60 min post-dose
Day 1	156 (14.2)	200 (16.9)	221 (29.7)	255 (35.8)
Week 3	255 (24.8)	275 (25.1)	342 (43.3)	335 (44.7)
Week 6	266 (26.2)	275 (27.2)	341 (47.3)	342 (46.5)
Week 12	236 (25.4)	260 (26.7)	277 (43.2)	294 (44.1)
Week 26	265 (31.5)	270 (29.6)	345 (49.7)	331 (48.1)
Week 39	240 (32.4)	286 (32.7)	296 (51.0)	340 (51.7)
Week 52	247 (33.3)	255 (33.6)	289 (52.9)	317 (56.9)

all $p<0.001$

Michael Rudolf: he has been reimbursed by the following companies for speaking at educational meetings, for consultancy work, or for attending scientific conferences: Almirall, Astra-Zeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Merck Sharp and Dohme, Napp, Novartis, Pfizer, Schering-Plough, and Teva.

Rajendra Mehta: he has no conflicts of interest.

P191 QVA149 ONCE DAILY IMPROVES EXERCISE TOLERANCE AND LUNG FUNCTION IN PATIENTS WITH MODERATE TO SEVERE COPD: THE BRIGHT STUDY

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Introduction QVA149 is a novel once-daily fixed-dose combination of the long-acting β_2-agonist indacaterol and the long-acting muscarinic antagonist glycopyrronium (NVA237) in development for the treatment of chronic obstructive pulmonary disease (COPD). The BRIGHT study evaluated the effects of QVA149 versus placebo and tiotropium on exercise tolerance and lung function in patients with moderate-to-severe COPD.

Methods In a double-blind, double-dummy, 3-period crossover study, patients with moderate-to-severe COPD were randomised to QVA149 110/50 μg, placebo or tiotropium 18 μg once daily for 3 weeks. The primary endpoint was exercise endurance time for QVA149 versus placebo during a submaximal exercise tolerance test (SMETT) via cycle ergometry at Day 21. Dynamic inspiratory capacity (IC) at isotime during exercise, trough IC, trough FEV_1 and trough forced vital capacity (FVC) were also measured.

Results Eighty five patients were randomised; mean age was 62 years, mean post-bronchodilator FEV_1 56% predicted. 86% patients completed the study. At Day 21, QVA149 significantly improved exercise endurance time by 59.5 seconds versus placebo ($p=0.006$), which was of a similar magnitude to the improvement seen with tiotropium versus placebo (66.3 seconds; $p=0.002$). More patients stopped exercise due to dyspnoea with placebo (43% versus 36% with both QVA149 and tiotropium) and due to muscle fatigue with QVA149 and tiotropium (44–46% versus 38% with placebo). QVA149 also produced significant and clinically meaningful improvements in trough FEV_1, dynamic IC at exercise isotime, trough IC and trough FVC versus placebo and tiotropium (table).

Conclusion QVA149 once daily provided significant and clinically meaningful improvements in exercise tolerance and lung function in patients with moderate-to-severe COPD. Despite superior bronchodilation demonstrated by QVA149 versus tiotropium, improvements seen in exercise endurance were similar, perhaps due to extra-pulmonary factors (muscle fatigue, ceiling effect). There were no safety concerns.

P192 QVA149 ONCE DAILY PROVIDES SUPERIOR BRONCHODILATION VERSUS INDACATEROL, GLYCOPYRRONIUM, TIOTROPIUM AND PLACEBO: THE SHINE STUDY

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Introduction QVA149 is a novel inhaled once-daily dual bronchodilator containing a fixed-dose combination of the long-acting β_2-agonist indacaterol and the long-acting muscarinic antagonist NVA237 (glycopyrronium) in development for the maintenance treatment of COPD. This study evaluated the effect of QVA149 on

Abstract P191 Table 1

	Treatment differences on Day 21 Least squares means (95% Confidence interval)		
	QVA149–Placebo	QVA149–Tiotropium	Tiotropium–Placebo
Exercise endurance time (seconds)	59.5 (17.7, 101.3)**	–6.7 (–47.5, 34.0)	66.3 (24.8, 107.7)**
IC at isotime (L)‡	0.32 (0.23, 0.40)***	0.14(0.05, 0.22)**	0.18(0.10.0.27)***
Trough IC (L)	0.19 (0.09, 0.29)***	0.15 (0.06, 0.25)**	0.04 (–0.06, 0.13)
Trough FEV_1 (L)	0.20 (0.15, 0.26)***	0.10 (0.05, 0.15)***	0.10 (0.05, 0.15)***
Trough FVC (L)	0.28 (0.19, 0.37)***	0.11 (0.02, 0.20)*	0.17 (0.08, 0.27)***

***$p<0.001$; **$p<0.01$; *$p<0.05$; ‡Isotime is the latest matching point during exercise at which for all periods for a patient there is an IC assessment; IC: inspiratory capacity; FEV_1: forced expiratory volume in 1 sec; FVC: forced vital capacity.