adjustment for FEV_1, age, sex, smoking pack-years, oxygen saturation, cardiovascular and respiratory admissions; cardiovascular medications and diabetes. Patients on short-acting bronchodilators only were used as the controls.

Results A total of 5048 patients were included in the study with mean age at diagnosis of 69.4 years and mean follow-up of 4.0 years. 623 were on long-acting bronchodilators only, 3510 on long-acting bronchodilator and ICS; and 915 controls. Crude hazard ratios are shown in Table 1. Adjusted HR (95%CI) for all-cause mortality for LABA only, LAMA only; and LABA + LAMA were 0.70 (0.45–1.09), 0.52 (0.37–0.73) and 0.53 (0.34–0.84) respectively. Adjusted HR for all-cause mortality for LABA + ICS, LAMA + ICS; LABA + LAMA + ICS were 0.56 (0.45 – 0.70), 0.34 (0.25 – 0.47) and 0.29 (0.24 – 0.36) respectively. Adjusted HR for cardiovascular mortality for LABA only, LAMA only; and LABA + LAMA were 0.63 (0.28–1.44), 0.41 (0.21 – 0.79) and 0.39 (0.17 – 0.90) respectively, and for LABA + ICS, LAMA + ICS; LABA + LAMA + ICS were 0.50 (0.33 – 0.75), 0.23 (0.12 – 0.45) and 0.22 (0.15 – 0.33) respectively.

Conclusions LABA monotherapy does not confer any mortality benefit but when used in combination with ICS reduces both all-cause and cardiovascular mortality. In contrast, LAMA whether given alone or in combination with a LABA and /or ICS reduces both all-cause and cardiovascular mortality. This 'real-life' study suggests that LABA should perhaps not be given as monotherapy but only in conjunction with a LAMA or ICS.

Abstract P228 Table 1.

Treatment Group	Crude hazard ratio (95% CI)*	
	All-cause mortality	Cardiovascular mortality
LABA only	1.06 (0.79-1.43)	1.06 (0.60-1.85)
LAMA only	0.71 (0.57-0.88)	0.59 (0.38-0.92)
LABA + LAMA	0.71 (0.52-0.97)	0.51 (0.26-1.00)
LABA + ICS	0.72 (0.62-0.84)	0.66 (0.50-0.89)
LAMA + ICS	0.61 (0.49-0.76)	0.48 (0.30-0.75)
LABA + LAMA + ICS	0.61 (0.53-0.69)	0.40 (0.31-0.53)

*Patients on short-acting bronchodilator only were used as the controls

Table 1: Crude hazard ratio for all-cause and cardiovascular mortality by treatment groups

P229 ADJUNCTIVE TREATMENT WITH ORAL AKL1, A BOTANICAL NUTRACEUTICAL, IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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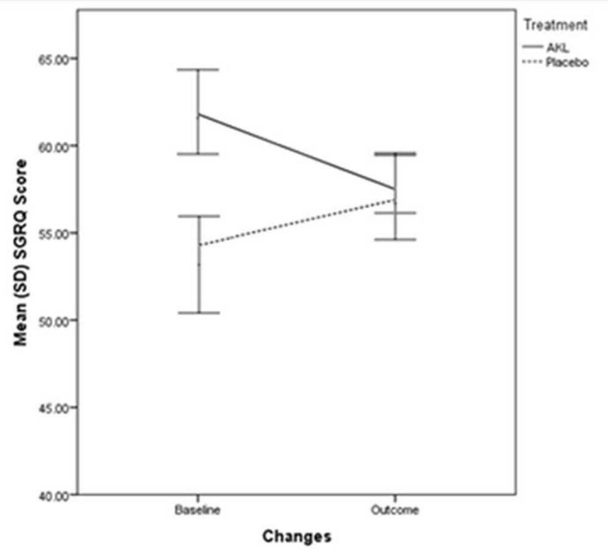
Background Treatment for chronic obstructive pulmonary disease (COPD) includes both bronchodilating and anti-inflammatory therapies. However majority of patients with COPD show corticosteroid resistance and alternative therapies are need. AKL1 is a patented botanical formulation containing extracts of *Picrorhiza kurroa*, *Ginkgo biloba*, and *Zingiber officinale* which has shown anti-inflammatory effects *in vitro*.

Methods We undertook a randomised double-blind, placebo-controlled trial to determine the safety and efficacy of AKL1 in patients with a clinical labelled diagnosis of COPD and Leicester Cough Questionnaire (LCQ) score of <17. The 10-week study period comprised a 2-week single-blind placebo run-in period followed by add-on treatment with AKL1 or placebo twice daily for 8 weeks. The primary study end-point was the change from week 0 to week 8 in cough-related health status, as assessed by the LCQ. Secondary endpoints were St. George's Respiratory Questionnaire, MRC dyspnea score, forced expiratory volume in 1 second (FEV1) and 6 minute walk test.



Abstract P229 Figure 1.

Results Of 33 (19 male) patients mean (SD) age of 67 (9.4) years 57.9 (17.2) FEV1% predicted enrolled into the study, 15 (45%) patients were smokers and 16 (49%) were ex-smokers. Twenty patients were randomised to AKL1 and 13 to placebo. The mean (SD) change from baseline in LCQ score at 8 weeks was 2.3 (4.9) in the AKL1 group and 0.6 (3.7) in the placebo group ($p = 0.43$). The St. George's Respiratory Questionnaire score improved significantly more in the AKL1 treatment group (mean [SD], -7.7 [11.7]) than in the placebo group (+ 1.5 [9.3]; $p = 0.042$). There were no significant differences between treatment groups in change from baseline to week 8 in other patient-reported measures, lung function, or the 6-minute walk distance. Five patients reported adverse events. Chest infections were diagnosed in one patient in each treatment allocation group. In the AKL1 group, one patient reported nightmares and one patient had right shoulder pain at the baseline visit; and one patient had influenza at the final visit.

Conclusion Further study is needed with a larger patient population and over a longer duration to better assess the effects of add-on therapy with AKL1 in COPD

P230 SYMPTOMATIC BENEFIT OF OLODATEROL QD DELIVERED VIA RESPIMAT® VS PLACEBO AND FORMOTEROL BID IN PATIENTS WITH COPD: COMBINED ANALYSIS FROM TWO 48-WEEK STUDIES

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Background The novel LABA olodaterol has 24-h bronchodilator activity.
Objective To evaluate the symptomatic benefit of olodaterol QD in patients with GOLD 2–4 COPD.
Methods In replicate, randomised, double-blind, placebo-controlled, parallel-group studies, patients with post-bronchodilator FEV_1 <80% predicted normal and FEV_1/FVC <70% received olodaterol (5 or 10 g) QD via Respimat®, formoterol (12 µg) BID via Aerolizer® or placebo for 48 weeks (Study A: NCT00793624; Study B: NCT00796653). Patients continued to receive usual care background COPD maintenance therapy, including SAMA, LAMA, ICS and xanthines. In addition to FEV_1-based primary end points, TDI and SGRQ after 24 weeks were identified as co-primary and key secondary symptomatic end points, respectively.
Results 904 (Study A) and 934 (Study B) patients were treated. In the primary analysis using a mixed model for repeated measures (MMRM; combined dataset), there was no significant difference in TDI focal score after 24 weeks for olodaterol or formoterol vs placebo. A post hoc analysis using pattern mixture modelling (PMM) to account for discontinued patients demonstrated statistical significance for olodaterol vs placebo. There were significant improvements in SGRQ total score with olodaterol, but not formoterol, vs placebo after 24 weeks using MMRM and PMM.
Conclusions Lung function improvements with olodaterol QD translated into symptomatic benefit in COPD patients receiving usual care background therapy.

Abstract P230 Table 1.

Adjusted mean difference vs placebo after 24 weeks (combined dataset)

	TDI focal score		SGRQ total score	
	MMRM	PMM	MMRM	PMM
Olodaterol 5µg	0.3*	0.5†	-2.8†	-2.3†
Olodaterol 10µg	0.2*	0.5†	-3.4†	-3.1†
Formoterol 12µg	0.2*	0.4*	-1.2*	-1.2*

*p=ns; †p<0.05

P231 THE IMPACT OF INDACATEROL (ONBREZ®) ON THE DAILY LIVES AND HEALTH STATUS OF PATIENTS WITH COPD: INTERIM RESULTS

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Introduction The GOLD guidelines recommend that the COPD Assessment Test (CAT)[1] can be used in guiding and optimising therapy, however there is little evidence on its use in monitoring treatment. Aim We have conducted a 6-month prospective observational study describing the impact of COPD on daily life, following the initiation of maintenance indacaterol, a once-daily long-acting beta-agonist.
Method Subjects from 39 UK GP practices (April 2012 to May 2013) with a diagnosis of COPD and were newly-prescribed indacaterol for routine COPD management, either as maintenance mono-therapy or add-on therapy to long-acting muscarinic antagonists (LAMA) were recruited. Here we present interim results of completed CAT and a descriptive Daily Life Impact Questionnaire (DLIQ), developed for specifically for the study, at treatment initiation and 6–8 weeks. Further assessments will be made at 6 months, when treatment changes in addition to indacaterol will be recorded.
Results One hundred and three subjects (61 males, 42 females), with a mean age of 67 years (range 44–86) and a median baseline FEV1% predicted of 61% (n = 100; IQR 51–70%) were recruited. Median time from diagnosis to indacaterol initiation was 6 months (IQR 0–37). Of the 86 (83.5%) subjects evaluated for change in CAT score, 65 (76%) had a reduction (i.e. improved health status), 18 (21%) increased and 3 (3%) remained the same (Figure 1); with a mean overall change of -4.1 (SD ± 5.6; p < 0.001). Fifty-nine (69%) subjects had a ≥2 point (clinically significant) reduction in CAT score. Ninety-two patients completed the DLIQ; 42 (46%) patients reported an improved ability to perform activities important to them, which had previously been rated as being challenging (e.g. walking, gardening, housework).
Conclusion The CAT appears responsive to treatment for COPD with indacaterol when assessed in routine practice and the average size of improvement was large. Alongside this mean improvement, nearly half of patients reported the ability to do more activities that previously they had found difficult. These initial results require further confirmation when full results are available at 6 months.

REFERENCES

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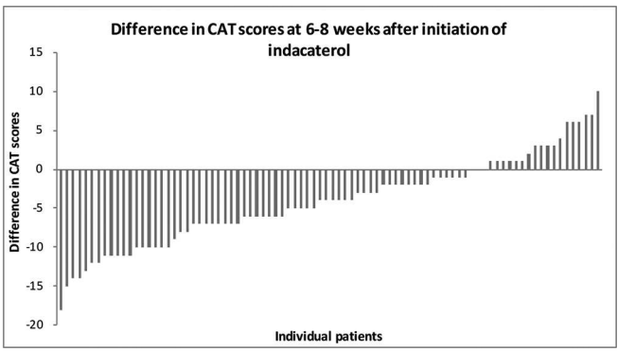

Abstract P231 Figure 1. The impact of indacaterol (Onbrez) on the daily lives and health status of patients with COPD: interim results.

P232 ONCE-DAILY CO-ADMINISTRATION OF GLYCOPYRRONIUM AND INDACATEROL VIA BREEZHALER® DEVICE IMPROVES LUNG FUNCTION AND SYMPTOMS IN PATIENTS WITH COPD VERSUS INDACATEROL ALONE: THE GLOW6 STUDY

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