insertion. Mean follow up was 12 months and mean survival 27.2 months. These results compare very favourably with a historical comparator group of the last 10 patients who received MS between 2009 and 2012 who required an average of 15.3 bronchoscopies after MS insertion and who had an overall mean drop in FEV1 of 0.59 L. SEMS have been used for a longer period of time, so follow up in this group was 30.5 months and mean survival 34.7 months (Table 1).

Conclusion Our data add to the limited literature that BS can be a safe alternative to MS for airway stenosis, and may also represent a useful treatment for anastamotic bronchomalacia.

Improving patient therapies in COPD

P248 CURRENT COPD DISEASE BURDEN ASSOCIATED WITH MAINTENANCE MONOTHERAPY IN THE UK

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Introduction and objectives National Institute for Health and Care Excellence (NICE) recommends long–acting bronchodilators, including β2-agonists (LABAs) or muscarinic antagonists (LAMAs) as first line maintenance treatment for patients with COPD. The aim of this descriptive study was to characterise a cohort of COPD patients who were on maintenance bronchodilator monotherapy for at least six months to establish their disease burden, measured by healthcare utilisation.

Methods Data were extracted from the UK Clinical Practice Research Datalink (CPRD) which also linked to Hospital Episode Statistics (HES). The monotherapy period spanned the first prescription of a LABA or LAMA until the end of the study period (31/12/2013) or until step-up to dual/triple therapy; for example the addition of another long acting bronchodilator, an ICS or ICS/LABA. A minimum of four consecutive prescriptions and six months on continuous monotherapy were required for study entry. Patients <50 years old at time of first COPD diagnosis or with another significant respiratory disease prior to the start of monotherapy were excluded. Disease burden was evaluated by measuring patients' rate of consultations with a healthcare professional (HCP), COPD-related exacerbations, hospitalisations and referrals to key specialities.

Results A cohort of 8,811 COPD patients (94% GOLD stage A or B) on maintenance monotherapy was identified between 2002 and 2013; 45% (N=3,947) of these patients were still on monotherapy by the end of the study period. The median time from first COPD diagnosis to first monotherapy prescription was 56 days while the median time on maintenance bronchodilator monotherapy was 748 days. The median number of prescriptions during this period was 14. Patients had a median of 19 HCP consultations and a mean of 0.1 (95% CI 0.1, 0.2, N= 8,811) COPD exacerbations and 0.02 (95% CI 0.01, 0.02, N=4,848) COPD hospitalisations per year.

Conclusion In summary, COPD patients who are on maintenance bronchodilator monotherapy for at least six months appear to remain on this therapy for over two years despite having a disease burden that requires healthcare resources, particularly HCP consultations, at a cost to the NHS.

P249 EFFECT SIZE OF OPEN-LABEL VERSUS DOUBLE-BLIND ADMINISTRATION OF TIOTROPIUM IN TRIALS INVESTIGATING HEALTH-RELATED QUALITY OF LIFE IN COPD

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Introduction Effects of interventions on patient-reported outcomes may be subjective and modulated by patients' expectations regarding treatment efficacy. The 'gold standard' for minimising such biases are double-blind randomised controlled trials. We analysed the effects of tiotropium on health-related quality of life in chronic obstructive pulmonary disease (COPD) in placebo-controlled trials and assessed whether trial design (double-blind versus open-label) is a relevant modifier of the effects of tiotropium.

Methods Trials of ≥6 months' duration investigating the effect of tiotropium versus placebo on health-related quality of life in COPD (assessed using St George's Respiratory Questionnaire [SGRQ]) were identified from the Boehringer Ingelheim clinical trial database and by a systematic literature search in MEDLINE, with a cut-off date of 30 November 2011. As a clinical end point, the mean difference between treatment groups in SGRQ total score was assessed. Trials were grouped according to double-blind or open-label design. We performed a network meta-analysis including standard methodology to test for interaction to evaluate whether trial design is a potential modifier of effect size or its direction.

Results We identified 12 trials in which tiotropium had been administered double-blind and three trials with open-label application. The overall effect for mean difference versus placebo in SGRQ total score was -2.98 units (95% confidence interval [CI]: -3.49, -2.47). For the double-blind trial subgroup, mean difference versus placebo was -3.20 (95% CI: -3.75, -2.65) compared to -1.67 (95% CI: -3.02, - 0.32) for open-label trials. The p-value for interaction between subgroup and effect on SGRQ total score was 0.04.

Conclusions In patients with COPD, trial design (double-blind versus open-label) was a statistically significant modifier of the effect of inhaled tiotropium on health-related quality of life. The modification was quantitative, resulting in a substantial underestimation of the effect of tiotropium on SGRQ total score when the administration had been open-label compared to the 'gold standard' double-blind. A subjective end point such as quality of life is particularly susceptible to bias due to patients' expectations towards the efficacy of an intervention. Therefore, the validity of studies using non-blinded designs to investigate such end points must be questioned.

P250 EFFECTS OF 12 WEEKS OF ONCE-DAILY TIOTROPIUM AND OLODATEROL FIXED-DOSE COMBINATION ON EXERCISE ENDURANCE IN PATIENTS WITH COPD

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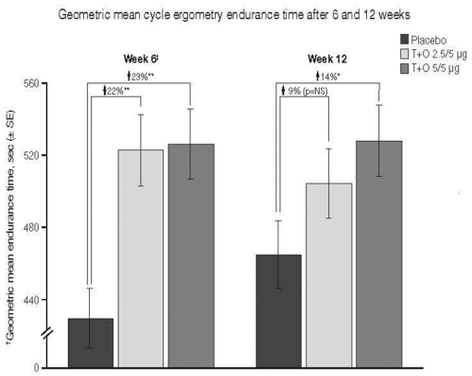
Background Both tiotropium (T) and olodaterol (O) monotherapies improve exercise endurance in patients with chronic obstructive pulmonary disease (COPD).
Objective To evaluate the effects of T+O fixed-dose combination on exercise endurance in patients with Global initiative for chronic Obstructive Lung Disease (GOLD) 2–3 COPD after 12 weeks.
Methods TORRACTO (NCT01525615) was a 12-week, double-blind, parallel-group, placebo-controlled, Phase III study. Patients with GOLD 2–3 COPD received T+O (5/5 µg or 2.5/5 µg) or placebo once daily via Respimat® Soft Mist™ inhaler. Primary end point was endurance time during constant work-rate cycle ergometry to symptom limitation after 12 weeks. Endurance time during endurance shuttle walking to symptom limitation after 12 weeks was also assessed in a subset of 165 patients. Other end points included pre-exercise inspiratory capacity.
Results 404 patients (269 men) were randomised (full analysis set n = 385). Mean post-bronchodilator forced expiratory volume in 1 second was 1.66 L (58.6% predicted). Endurance time during cycle ergometry was significantly increased by 14% with T+O 5/5 µg versus placebo at 12 weeks. Increases in endurance time during endurance shuttle walking were observed for both T+O doses versus placebo at 12 weeks (21% increase, nominal p = 0.06 for each dose). Both T+O doses increased pre-exercise inspiratory capacity versus placebo at 12 weeks (T+O 5/5 µg, 234 mL; T+O 2.5/5 µg, 207 mL; nominal p < 0.0001). No safety concerns were identified.
Conclusions T+O 5/5 µg improved endurance time during cycle ergometry versus placebo.



Abstract P250 Figure 1 Geometric mean cycle ergom.etry endurance time after 6 and 12 weeks
†Geometric mean results reported as primary analysis based on log_{10}-transformed data ‡No
t included in hierarchical testing sequence; to be considered descriptive only
Geometric mean baseline endurance time: 443.0 sec
Patient numbers: placebo = 121; T+O2.5/5 µg = 129; T+O5/5 µg = 135
*p < 0.05; **nominal p < 0.0005 for difference from placebo
SE, standard error; NS, not significant

P251 EFFICACY AND SAFETY OF ONCE-DAILY INDACATEROL/MOMETASONE COMPARED WITH TWICE-DAILY SALMETEROL/FLUTICASONE IN PATIENTS WITH MODERATE TO VERY SEVERE COPD

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Introduction QMF149 is an investigational inhaled fixed-dose combination of indacaterol acetate and mometasone furoate via the Breezhaler® device for once daily maintenance treatment of asthma and COPD. This double-blind, 12-week study compared QMF149 (150/160µg) o.d. with salmeterol 50µg/fluticasone 500µg, (Seretide®; SFC) b.i.d. in patients with moderate to very severe COPD.
Objectives Primary objective of the study was to demonstrate the non-inferiority of QMF149 vs SFC in terms of trough FEV_1 at Week 12. Main secondary objectives were to compare the efficacy of QMF149 vs SFC in terms of dyspnoea via Transition Dyspnoea Index (TDI), health status via St. George Respiratory Questionnaire (SGRQ), rescue medication, exacerbations and safety during the treatment period.
Results 629 patients (mean FEV_1 46.51% predicted, QMF149 n = 316; SFC n = 313) were randomised. The primary objective was met. QMF149 showed significant improvement in trough FEV_1 vs SFC (LSM treatment difference [LSMTD] 56mL; p < 0.001). QMF149 improved significantly TDI (LSMTD 0.5; p < 0.026) and numerically SGRQ (-1.66, p = 0.093) vs SFC. QMF149 significantly prolonged the time to first moderate or severe exacerbation with a 49% reduction in hazard ratio (hazard ratio [HR] 0.51; CI 0.298, 0.855; p = 0.011) and was associated with 44% reduction in the number of moderate or severe exacerbations (rate ratio [RR] 0.56; CI 0.331, 0.937; p = 0.028). A significantly greater percentage of days with no rescue medication (LSMTD 6.26%; p = 0.007) and significantly fewer rescue medication use was observed with QMF149 (daily number of puffs LSMTD -0.47; p = 0.003). Both treatments were well tolerated with low incidence of AEs.
Conclusion When compared with SFC, QMF149 significantly improves trough FEV_1 and dyspnoea, reduces exacerbations and rescue medication use in patients with moderate to very severe COPD.

P252 GOLD CATEGORY AND OPTIMAL MANAGEMENT : A CANADIAN PERSPECTIVE

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Hypothesis Current Canadian guidelines and GOLD strategy for COPD management provide a treatment algorithm based on current symptoms and exacerbation history. We wished to assess COPD patient current objective, subjective symptoms, quality of life and exacerbation history of a random sample in primary