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-blind 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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Introduction Chronic obstructive pulmonary disease (COPD) is a progressive chronic inflammatory disease of the lungs. Exercise testing is a sensitive way to assess disease severity and patient outcome and to evaluate the efficacy of interventions. The COPD Assessment Test (CAT) is a validated assessment tool that has been shown to be as sensitive as exercise duration in COPD.

Methods In the TIOLOD study, a phase 3, randomised, double-blind, placebo-controlled, parallel-group, multicentre study, patients with moderate to severe COPD (GOLD stage 2–4) were randomised 2:1 to daily tiotropium 18 μg via the Respimat inhaler (132 μg/actuation) or placebo for 12 weeks. Exercise endurance was assessed using the 6-minute walk test (6MWT) and CAT at study entry, week 6 and 12.

Results At week 12, exercise endurance (both 6MWT and CAT) was significantly improved from baseline in both tiotropium and placebo groups. However, tiotropium was associated with greater improvements in exercise endurance compared with placebo. Patients on tiotropium had a mean increase in exercise endurance of 126 m and 1.9 points in CAT score compared to 71 m and 1.1 points in placebo group, respectively. These improvements were maintained at week 12. Tiotropium was well tolerated and no serious adverse events (AEs) were reported. There was no significant difference in laboratory values, ECG or pulmonary function tests between treatment groups.

Conclusion The results of this study confirm that tiotropium improves exercise endurance in patients with COPD. The improvement seen with tiotropium was greater than that seen in the placebo group and the effects were maintained over the 12-week study period. The results of this study provide further evidence for the use of tiotropium as an effective treatment for exercise intolerance in COPD.

Background Both tiotropium (T) and olodaterol (O) mono-therapies 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 endpoints 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 < 0.0001). No safety concerns were identified.

Conclusions T+O 5/5 μg improved endurance time during cycle ergometry versus placebo.