spirometry to predict exacerbations and to indicate subsequent worsening of lung function resulting from a previous COPD exacerbation.

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Please refer to page A273 for declarations of interest in relation to abstract P297.

REFERENCE

1 Magnussen H, *et al*. *N Engl J Med* 2014;**371**:1285–1294.

P298 TIOTROPIUM/OLODATEROL THERAPY PROVIDES SYMPTOMATIC BENEFITS IRRESPECTIVE OF PRIOR MAINTENANCE TREATMENT: POST HOC ANALYSES OF THE OTEMTO® STUDIES

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Rationale The combination of tiotropium (T), a long-acting muscarinic antagonist (LAMA), plus olodaterol (O), a long-acting β_2-agonist (LABA), is approved for once-daily maintenance treatment of COPD. The randomised, double-blind, Phase IIIb OTEMTO® 1 and 2 studies (NCT01431274; NCT01431287) showed improvements in quality of life and lung function after 12 weeks' treatment with T/O compared to T alone or placebo in patients with moderate to severe COPD. This *post hoc* analysis investigated whether previous maintenance treatment with a long-acting bronchodilator or inhaled corticosteroid (ICS) influenced symptomatic benefits of T/O.

Methods Patients aged ≥40 years received T/O 2.5/5 µg, T/O 5/5 µg, T 5 µg or placebo once daily for 12 weeks via Respimat® inhaler. St George's Respiratory Questionnaire (SGRQ) total score was a primary end point, alongside lung function (FEV_1 area under the curve from 0–3 hours and trough FEV_1 responses). Secondary end points included Mahler Transition Dyspnoea Index (TDI) focal score. Salbutamol/albuterol was provided as rescue medication and use was recorded in an e-diary. We report comparisons between T/O 5/5 µg, T 5 µg and placebo.

Results Of the 1621 patients evaluated, 943 had received prior maintenance treatment (66.7% LABA; 59.4% LAMA; 64.5% ICS) and 678 had not. Similar improvements in mean SGRQ total score were observed with T/O compared to T and placebo, respectively, in patients receiving prior maintenance treatment (−2.02 and −4.59 units) and those without (−2.20 and −4.78 units) (Table). TDI focal scores improved with T/O compared to T and placebo, respectively, in patients receiving prior maintenance treatment (0.60 and 1.87 units) and those without (0.60 and 1.33 units) (Table). Patients with and without prior maintenance treatment demonstrated similar improvements in daytime and night-time rescue medication use and lung-function improvements with T/O compared to T and placebo.

Conclusions T/O provides symptomatic benefits as demonstrated by improvements in SGRQ score, TDI focal score and decreased rescue medication use compared to placebo and T, independent of previous maintenance treatment. These findings suggest T/O is beneficial over monotherapy when used as first COPD maintenance treatment.

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Please refer to page A273 for declarations of interest in relation to abstract P298.

Abstract P298 Table 1

Treatment comparison	Prior maintenance treatment	No prior maintenance treatment
SGRQ total score		
T/O 5/5 µg – placebo	−4.59 (−10.23, 1.06)	−4.78** (−6.93, −2.63)
T/O 5/5 µg – T	−2.02 (−5.42, 1.37)	−2.20* (−4.34, −0.07)
Mahler TDI focal score		
T/O 5/5 µg – placebo	1.87** (1.36, 2.39)	1.33** (0.76, 1.90)
T/O 5/5 µg – T	0.60* (0.09, 1.10)	0.60* (0.04, 1.17)

Adjusted mean (95% confidence interval) **p<0.001, *p<0.05

P299 EFFECTS OF SYMPTOM SEVERITY AT BASELINE ON LUNG-FUNCTION AND SGRQ RESPONSES IN THE OTEMTO® STUDIES

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Rationale In the randomised, double-blind, Phase IIIb OTEMTO® 1 and 2 studies (NCT01431274; NCT01431287), the combination of tiotropium (T), a long-acting muscarinic antagonist, plus olodaterol (O), a long-acting β_2-agonist, showed meaningful improvements in quality of life (St George's Respiratory Questionnaire [SGRQ]) and lung function in patients with moderate to severe COPD after 12 weeks' treatment compared to T alone or placebo. This *post hoc* analysis investigated whether symptomatic status at inclusion, as measured by the modified Medical Research Council (mMRC) dyspnoea scale and the Baseline Dyspnoea Index (BDI), influenced lung-function and SGRQ responses.

Methods Patients aged ≥40 years received T/O 2.5/5 µg, T/O 5/5 µg, T 5 µg or placebo once daily for 12 weeks via Respimat® inhaler. SGRQ total score and lung function (FEV_1 area under the curve from 0–3 hours [AUC_{0-3}] and trough FEV_1 responses) were primary end points. Patients completed the mMRC and BDI scales at baseline. We report comparisons between T/O 5/5 µg, T 5 µg and placebo.

Results 1621 patients were evaluated: 736 patients (45%) had mMRC scores <2, 883 patients (54%) ≥2 (scored from grade 0–5, lower is better); 418 patients (26%) had BDI scores <6, 1201 patients (74%) ≥6 (scored from 0–12, higher is better). Patients were distributed evenly across treatment arms with respect to mMRC and BDI scores, and baseline characteristics were consistent across treatment arms. Improvements in FEV_1 $AUC_{0–3}$ and trough FEV_1 were observed with T/O compared to T and placebo in patients with mMRC score <2 and ≥2, as well as in patients with BDI score ≥6 and <6 (Table). All BDI and mMRC groups demonstrated improvements in SGRQ with T/O compared to placebo above the minimal clinically important difference.

Conclusions There was a trend towards better lung-function improvement with T/O versus T or placebo in less symptomatic patients assessed by baseline BDI. More severe dyspnoea by mMRC category was associated with improved SGRQ with T/O versus T or placebo, but did not affect lung-function improvement. Overall, T/O provided lung-function and quality of life benefits regardless of symptomatic status prior to treatment.

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Abstract P299 Table 1

Dyspnoea severity	Less severe	More severe	Less severe	More severe
Treatment comparison	mMRC score < 2	mMRC score ≥ 2	BDI score ≥6	BDI score <6
FEV_1 $AUC_{0–3}$, L				
T/O 5/5 µg – placebo	0.30*** (0.26, 0.34)	0.32*** (0.28, 0.36)	0.32*** (0.29, 0.35)	0.28*** (0.22, 0.35)
T/O 5/5 µg – T	0.11*** (0.07, 0.14)	0.11*** (0.07, 0.15)	0.11*** (0.08, 0.14)	0.10** (0.04, 0.15)
Trough FEV_1, L				
T/O 5/5 µg – placebo	0.16*** (0.13, 0.20)	0.16*** (0.13, 0.20)	0.18*** (0.15, 0.21)	0.12*** (0.07, 0.18)
T/O 5/5 µg – T	0.05* (0.01, 0.08)	0.02 (−0.01, 0.06)	0.040** (0.01, 0.07)	0.01 (−0.04, 0.06)
SGRQ total score				
T/O 5/5 µg – placebo	−4.20*** (−6.11, −2.29)	−5.11*** (−7.24, −2.97)	−4.78*** (−6.33, −3.23)	−4.38 (−8.95, 0.19)
T/O 5/5 µg – T	−0.71 (−2.57, 1.16)	−3.44** (−5.47, −1.41)	−1.87* (−3.43, −0.32)	−2.96* (−5.84, −0.09)

Adjusted mean (95% confidence interval) ***p <0.0001; **p <0.01; *p <0.05

Please refer to page A274 for declarations of interest in relation to abstract P299.