Supplementary

Tiotropium/olodaterol delays clinically important deterioration compared with tiotropium monotherapy in patients with early COPD: A post hoc analysis of the TONADO® trials

Klaus F. Rabe,[1] James D. Chalmers,[2] Marc Miravitlles,[3,4] Janwillem W.H. Kocks,[5–7] Ioanna Tsiligianni,[8] Alberto de la Hoz,[9] Wenqiong Xue,[10] Dave Singh,[11] Gary T. Ferguson,[12] Jadwiga Wedzicha[13]

Supplementary methods – key inclusion and exclusion criteria

Patients were aged ≥40 years, with a smoking history of ≥10 pack-years and a diagnosis of moderate-to-very severe chronic obstructive pulmonary disease (COPD; Global Initiative for Chronic Obstructive Lung Disease [GOLD] 2–4). Patients were required to have a post-bronchodilator forced expiratory volume in 1 second (FEV_1) <80% of predicted normal, and a post-bronchodilator FEV_1/forced vital capacity ≤70%. Key exclusion criteria included a history of asthma or a significant disease other than COPD. Patients were also excluded if they had any clinically relevant abnormal baseline laboratory parameters, myocardial infarction within 1 year of screening, unstable or life-threatening cardiac arrhythmia, known active tuberculosis, clinically evident bronchiectasis, cystic fibrosis, or a life-threatening pulmonary obstruction. In addition, patients were excluded if they had been hospitalised for heart failure within the past year, had a diagnosis of thyrotoxicosis or paroxysmal tachycardia, had previously had a thoracotomy with pulmonary resection, regularly used daytime oxygen and were unable to abstain during clinic visits, or were currently enrolled in a pulmonary rehabilitation programme (or completed in the 6 weeks before screening).

Supplementary Table 1. Demographic and baseline patient characteristics (treated population)

Characteristic	Tiotropium (5 µg)	Tiotropium/olodaterol (5/5 µg)
Participants, n	1,033	1,029
Male	755 (73.1)	733 (71.2)
Age, years	63.9 ±8.6	63.8 ±8.3
Smoking status		
Ex-smoker	663 (64.2)	629 (61.1)
Current smoker	370 (35.8)	400 (38.9)
Comorbidities	902 (87.3)	890 (86.5)
Cardiac	219 (21.2)	213 (20.7)
Vascular	513 (49.7)	496 (48.2)
Pre-bronchodilator screening FEV_1, L	1.200 (±0.504)	1.180 (±0.493)
Post-bronchodilator screening FEV_1 L	1.370 ±0.521	1.344 ±0.505
Change from pre- to post-bronchodilator FEV_1, L	0.171 ±0.146	0.164 ±0.148
FEV_1/FVC %	45.0 ±12.0	45.1 ±11.6
FEV_1 % pred	49.7 ±15.7	49.3 ±15.3
GOLD stage[a]		
1 (FEV_1 ≥80% pred)	1 (0.1)	0 (0.0)
2 (FEV_1 50–<80% pred)	517 (50.0)	502 (48.8)
3 (FEV_1 30–<50% pred)	387 (37.5)	408 (39.7)
4 (FEV_1 <30% pred)	128 (12.4)	119 (11.6)
Baseline pulmonary medication		
SAMA[b]	131 (12.7)	125 (12.1)
LAMA[c]	346 (33.5)	378 (36.7)
SABA[d]	401 (38.8)	400 (38.9)
LABA[e]	450 (43.6)	486 (47.2)
ICS[f]	466 (45.1)	506 (49.2)
Xanthines[g]	109 (10.6)	108 (10.5)
Baseline cardiovascular medication	596 (57.7)	581 (56.5)
β-blockers	109 (10.6)	110 (10.8)

Data are presented as n (%) or mean±SD, unless otherwise stated.

[a]Based on post-bronchodilator FEV_1 percentage predicted.

[b]Including ipratropium, ipratropium/fenoterol or ipratropium/salbutamol, and oxitropin.

[c]Tiotropium.

[d]All patients received SABAs as rescue medication.

[e]Including arformoterol, formoterol, indacaterol, fenoterol and salmeterol.

[f]Including beclomethasone, budesonide, ciclesonide, mometasone furoate/formoterol fumarate hihydrate, fluticasone, formoterol/beclomethasone, formoterol/budesonide, mometasone, mometasone furoate and salmeterol/fluticasone.

[g]Including aminophylline and theophylline.

FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease; ICS, inhaled corticosteroid; LABA, long-acting β_2-agonist; LAMA, long-acting muscarinic antagonist; pred, predicted; SABA, short-acting β_2-agonist; SAMA, short-acting muscarinic antagonist.