Abstract Presentations

2. Peter Calverley, UK

The effect of tiotropium/olodaterol versus tiotropium on COPD exacerbation rates in patients with/without frequent exacerbation history: pooled analysis of DYNAGITO® and TONADO® trials

J.A. Wedzicha, R. Buhl, A. de la Hoz, F. Voß, P.M.A. Calverley[1]

27 June 2020

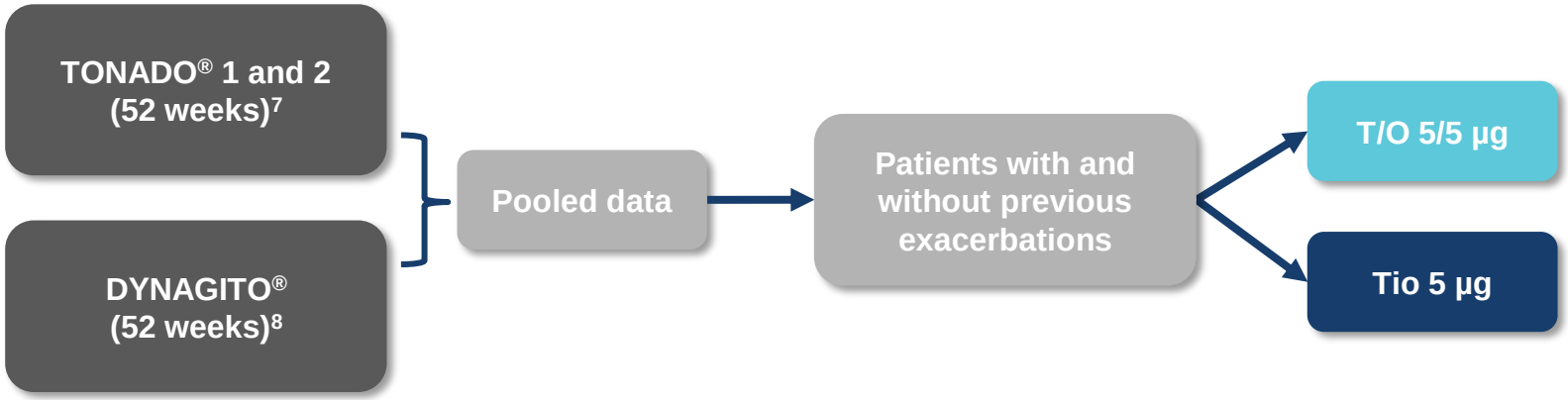
Disclosure: Dr. Calverley reports grants and personal fees from GlaxoSmithKline, personal fees from AstraZeneca, Boehringer Ingelheim, Recipharm and Zambon and personal fees and other from Boehringer Ingelheim outside the submitted work.

[1]Clinical Science Centre, Institute of Ageing and Chronic Disease, University of Liverpool, Liverpool, UK

Introduction, Aim and Methods

- Compared with placebo, tio has been shown to reduce the total number of exacerbations and the proportion of subjects experiencing at least one exacerbation, and also prolong the time to first exacerbation[1–3]
- Tio significantly increased time to first moderate/severe exacerbation compared with LABA alone[3–5] and had a similar effect on exacerbation rate compared with LABA/ICS combination[6]

Aim: To investigate the relative effect of T/O versus tio on exacerbations in a large COPD population from the DYNAGITO® and TONADO® trials in a variety of patient subgroups



At Week 52, the following subgroups were analysed:

- Low and high exacerbation history
- GOLD stage 2–4
- ICS use

COPD, chronic obstructive pulmonary disease; GOLD; Global Initiative for Chronic Obstructive Lung Disease; ICS, inhaled corticosteroid; LABA, long-acting β_2-agonist; SGRQ, St. George's Respiratory Questionnaire; T/O, tiotropium/olodaterol; tio, tiotropium.

1. Dusser D, et al. Eur Respir J 2006; 27:547–555; 2. Niewoehner DE, et al. Ann Intern Med 2005; 143:317–326; 3. Tashkin DP, et al. N Engl J Med 2008; 359:1543–1554; 4. Vogelmeier C, et al. N Engl J Med 2011; 364:1093–1103; 5. Decramer ML, et al. Lancet Respir Med 2013; 1:524–533; 6. Wedzicha JA, et al. Am J Respir Crit Care Med 2008; 177:19–26; 7. Calverley PMA, et al. Lancet Respir Med 2018; 6:337–344; 8. Buhl R, et al. Eur Respir J 2015; 45:969–979.

DYNAGITO/TONADO inclusion criteria

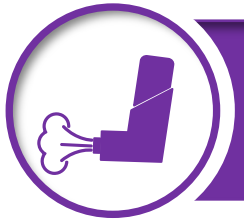
Aged ≥40 years

Diagnosed with moderate to very severe COPD

≥1 moderate/severe exacerbation in previous year (DYNAGITO only)

Smoking history of >10 pack-years

FEV_1 <60% predicted (DYNAGITO)
FEV_1 <80% predicted (TONADO)

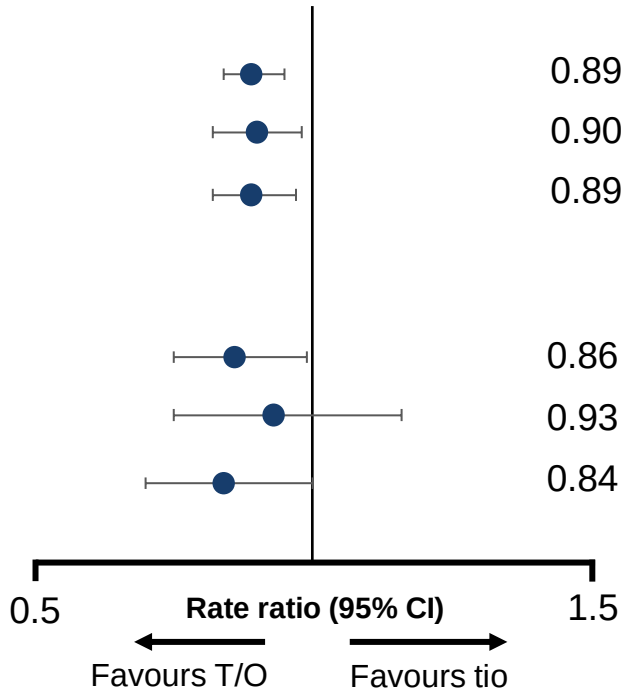


ICS was not withdrawn in patients receiving ICS at baseline

FEV_1, forced expiratory volume in 1 second.

Exacerbation rates in all patients and by exacerbation history

	N	Rate of events per patient-year (SE)		Rate ratio T/O versus tio (95% CI)
	Tio / T/O	Tio	T/O	
Moderate/severe exacerbations				
All patients[a]	4,974/4,968	0.77 (0.023)	0.68 (0.023)	0.89 (0.84, 0.95)
0 to 1 moderate exacerbation	2,988/2,959	0.60 (0.032)	0.54 (0.033)	0.90 (0.82, 0.98)
≥2 moderate or ≥1 severe exacerbation	1,985/2,008	1.09 (0.032)	0.97 (0.032)	0.89 (0.82, 0.97)
Exacerbations leading to hospitalisation				
All patients[a]	4,974/4,968	0.13 (0.053)	0.11 (0.054)	0.86 (0.75, 0.99)
0 to 1 moderate exacerbation	2,988/2,959	0.07 (0.084)	0.07 (0.084)	0.93 (0.75, 1.16)
≥2 moderate or ≥1 severe exacerbation	1,985/2,008	0.24 (0.066)	0.20 (0.067)	0.84 (0.70, 1.00)



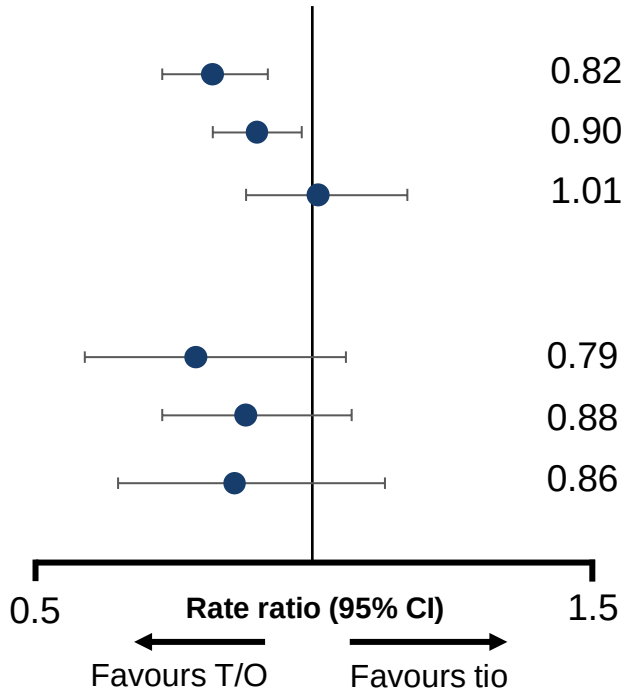
[a]Includes patients with missing exacerbation history

T/O was associated with a lower rate of moderate/severe exacerbations and exacerbations leading to hospitalisation compared with tio

CI, confidence interval; SE, standard error.

Exacerbation rates by GOLD stage (2 versus 3 versus 4)

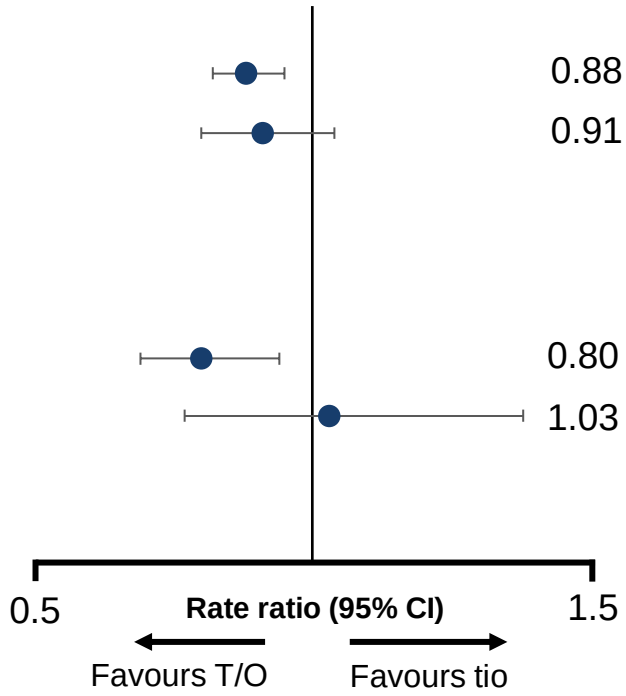
	N	Rate of events per patient-year (SE)		Rate ratio T/O versus tio (95% CI)
	Tio / T/O	Tio	T/O	
Moderate/severe exacerbations				
GOLD stage 2	1,974/1,877	0.60 (0.039)	0.49 (0.042)	0.82 (0.73, 0.92)
GOLD stage 3	2,398/2,436	0.84 (0.032)	0.76 (0.032)	0.90 (0.82, 0.98)
GOLD stage 4	595/644	1.12 (0.056)	1.14 (0.051)	1.01 (0.88, 1.17)
Exacerbations leading to hospitalisation				
GOLD stage 2	1,974/1,877	0.07 (0.107)	0.06 (0.116)	0.79 (0.59, 1.06)
GOLD stage 3	2,398/2,436	0.16 (0.071)	0.14 (0.071)	0.88 (0.73, 1.07)
GOLD stage 4	595/644	0.30 (0.107)	0.26 (0.104)	0.86 (0.65, 1.13)



T/O was associated with reduced exacerbation rates in patients with GOLD stage 2 and GOLD stage 3 compared with tio. T/O was also associated with reduced rates of exacerbations leading to hospitalisation in all GOLD stages compared with tio, although the differences were not statistically significant

Exacerbation rates by baseline ICS use

	N	Rate of events per patient-year (SE)		Rate ratio T/O versus tio (95% CI)
	Tio / T/O	Tio	T/O	
Moderate/severe exacerbations				
Baseline ICS use	3,229/3,277	0.90 (0.026)	0.79 (0.026)	0.88 (0.82, 0.95)
No baseline ICS use	1,745/1,691	0.56 (0.047)	0.51 (0.048)	0.91 (0.80, 1.04)
Exacerbations leading to hospitalisation				
Baseline ICS use	3,229/3,277	0.16 (0.059)	0.13 (0.061)	0.80 (0.69, 0.94)
No baseline ICS use	1,745/1,691	0.08 (0.113)	0.08 (0.110)	1.03 (0.77, 1.38)



T/O reduced the rate of moderate/severe exacerbations for patients with and without baseline ICS use, and exacerbations leading to hospitalisations in patients with baseline ICS, compared with tio

Conclusions

Treatment with T/O decreases moderate/severe exacerbations and exacerbations leading to hospitalisation compared with tio. These reductions were seen across a range of patient subgroups

This analysis of a heterogeneous population of over 9,900 patients with COPD reflects patients seen in clinical practice

These results support the use of dual bronchodilation with T/O in a broad range of patients