Benefits of tiotropium/olodaterol over tiotropium alone in delaying clinically significant deterioration in patients with COPD

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INTERACTIVE

Rabe et al. CID TONADO poster with audio summary

BACKGROUND

- A once-daily combination of T/O has previously been demonstrated to improve lung function, breathlessness and quality of life in patients with COPD[1–3]
- Whether more patients with mild-to-moderate disease or fewer symptoms could benefit from earlier treatment with LAMA/LABA combination therapy is under debate[4–5]
- The aim of this analysis was to determine whether combination treatment with T/O was more effective than tio alone at delaying CID in COPD patients, in patients with GOLD stage 2 COPD, and in those not previously receiving COPD maintenance therapy (treatment-naïve)

STUDY DESIGN

Post hoc analysis in patients treated with either T/O 5/5 µg or tio 5 µg (delivered via Respimat®) in two replicate, 52-week, parallel-group, double-blind studies (TONADO® 1 [NCT01431274] and TONADO® 2 [NCT01431287])

Three analyses were performed
- Overall patient population (n=2,055)
- GOLD stage 2 COPD patients (n=1,017)
- Treatment-naïve patients (n=733)

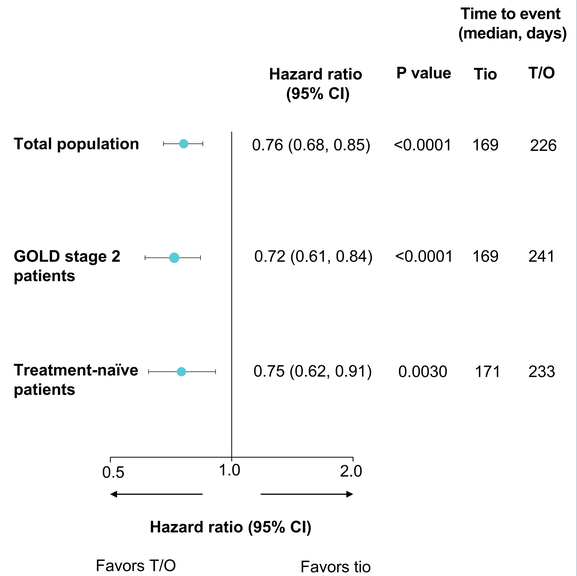
CID ≥1 of the following:

- ⬇ Trough FEV_1 ≥100 mL
- ⬆ SGRQ score ≥4 units
- Moderate or severe exacerbation

- The time to first occurrence of one of these events was recorded as the time to clinical deterioration

RESULTS

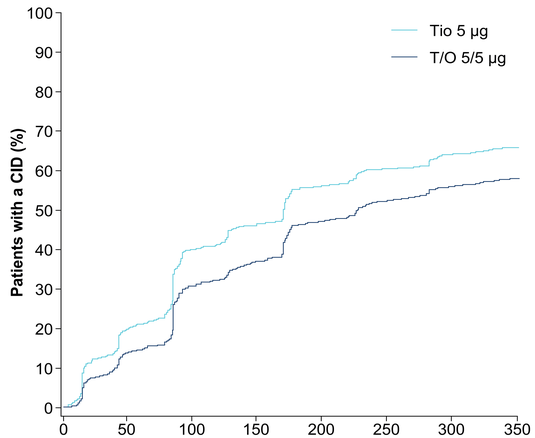
Treatment comparison and time to event for T/O versus tio by CID composite endpoint score



HRs were determined using a Cox proportional hazard model with study, inhaled corticosteroid use at baseline, region, GOLD stage and smoking status as fixed effects, and with baseline SGRQ score and number of exacerbations in the previous year as covariates. P values were based on CIs assuming normal distribution for log (HR).

There was a reduction in the risk of CID with T/O compared with tio in the overall patient population and in both patient subsets

Kaplan–Meier estimate of the probability of an event in patients treated with T/O versus tio in the overall patient population



Number of patients at risk								
Tio 5 µg	1029	797	582	509	412	368	326	310
T/O 5/5 µg	1026	863	677	612	505	451	410	389

The Kaplan–Meier estimate shows that the time to an event is longer with T/O versus tio, with clear separation between the two treatment arms

Individual components of the composite endpoint: event rates and time to first event (25th percentile) in the total patient population

Endpoint	Tio 5 µg		T/O 5/5 µg		Time to first event treatment comparison (T/O–tio)	
	Event rate, n/N (%)	Time to first event (25th percentile), days	Event rate, n/N (%)	Time to first event (25th percentile), days	HR (95% CI)	P value
Trough FEV_1 decline from baseline ≥100 mL	386/1,026 (37.6)	132	305/1,023 (29.8)	279	0.69 (0.59, 0.80)	<0.0001
SGRQ score increase from baseline ≥4 units	339/955 (35.5)	172	290/979 (29.6)	365	0.80 (0.68, 0.93)	0.0046
Moderate or severe exacerbation	297/1,029 (28.9)	270	285/1,026 (27.8)	293	0.86 (0.73, 1.02)	0.0749

Improvements in each component of the composite endpoint contributed to the delay in reaching CID with T/O versus tio

CONCLUSIONS

T/O reduced the risk of CID compared with tio alone in the overall trial population, and in GOLD stage 2 and treatment-naïve patients

- Our results suggest that early treatment with T/O may be more effective than tio in preventing CID in these patient populations
- These results support clinically established data on patient outcomes, with greater improvements observed with T/O versus tio

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Abbreviations
CI, confidence interval; CID, clinically important deterioration; FEV_1, forced expiratory volume in 1 second; HR, hazard ratio; LABA, long-acting β_2-agonist; LAMA, long-acting muscarinic antagonist; SGRQ, St. George's Respiratory Questionnaire; T/O, tiotropium/olodaterol; tio, tiotropium.

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