P127 SUPERIORITY OF GLYCOPYRRONIUM VERSUS TIOTROPIUM IN EARLY ONSET OF BRONCHODILATION IN PATIENTS WITH MODERATE TO SEVERE COPD – THE FAST STUDY

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10.1136/thoraxjnl-2015-207770.264

Background Glycopyrronium (GLY) has demonstrated efficacy similar to open-label and single-blinded tiotropium (TIO) in the treatment of COPD and fast onset of bronchodilation action.[1,2] The double-blinded FAST study compared the efficacy of GLY with TIO in serial spirometry and bodyplethysmography measurements to allow for a more intensified characterisation of the earlier onset of action.

Methods In this multicenter, randomised, double-blinded, double-dummy, cross-over study patients (pts) with moderate-to-severe COPD received single-dose of both once- daily GLY 44 µg and TIO 18 µg via the Breezhaler® and Handihaler® devices respectively. Primary endpoint was the forced expiratory volume in one second (FEV_1) AUC_{-2h}. Other endpoints included inspiratory capacity (IC), residual volume (RV), functional residual capacity (FRC) and specific airway resistance (sRaw), all measured by bodyplethysmography.

Results Of 152 pts randomised (mean age: 61.8 yr, mean post-bronchodilator FEV_1: 52.1%) 99.3% completed the study. After inhalation of the single dose, GLY demonstrated superiority to TIO in early bronchodilation i.e. FEV_1 AUC_{-2h} (least squares mean (LSM) = 0.037 L, p = 0.0006). Both treatments showed similar improvements in IC, RV, and FRCpleth. Over the first 90 min after dosing, GLY also showed statistically significant improvement in sRaw compared to TIO with a difference of 0,184 kPa*s at the time point 90 min (LSM, p = 0.006).

Conclusion GLY showed effective bronchodilation and was superior to double-blinded TIO in terms of early onset of bronchodilation. Both GLY and TIO showed similar improvements in static lung volume parameters; however GLY was superior in reduction of sRaw early after inhalation.

REFERENCES

1 Kerwin E, *et al*. *Eur Resp J* 2012;**40**:1106–1114
2 Chapman, *et al*. *BMC Pulm Med*. **2014**;14:4

P128 POOLED SAFETY ANALYSIS OF ADJUDICATED SERIOUS ADVERSE EVENTS WITH THE COMBINATION OF TIOTROPIUM + OLODATEROL

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10.1136/thoraxjnl-2015-207770.265

Rationale This analysis aimed to obtain a comprehensive and objective safety assessment of the combination of tiotropium (T), a long-acting muscarinic antagonist, with olodaterol (O), a long-acting β_2-agonist, (T+O) in patients with moderate to very severe chronic obstructive pulmonary disease (COPD).

Methods Data from two, 52-week, pivotal Phase III trials investigating T+O 5/5 µg and T+O 2.5/5 µg versus T 2.5 µg, 5 µg and O 5 µg were pooled, and patient narratives and profiles of serious adverse-event (SAE) reports were reviewed by an independent Adjudication Committee. The committee members independently assessed all SAEs to determine if any deaths, hospitalisations or intubations were respiratory-related, cardiovascular-related, cerebrovascular-related or other event-related. For an SAE adjudicated as respiratory-related, determination was made if it was related to COPD or pneumonia. For an SAE adjudicated as cerebrovascular-related, determination was made if it was related to stroke or other cerebrovascular events. Incidences of the composite end point (death, hospitalisation and intubation for respiratory-, cardiovascular-, cerebrovascular- or other-related events) and the individual components of this end point were evaluated.

Results The safety population for the primary analysis included patients from two trials (NCT01431274 and NCT01431287) in which 799/5162 (15.5%; range across treatments: 14.3–16.5%) had any adjudicated event of interest. As expected in a moderate to very severe COPD population, most SAEs were respiratory-related (8.1%; 420 patients). Eighty-three (1.6%) patients had cardiovascular-related SAEs and 27 (0.5%) had cerebrovascular-related SAEs; 363 (7.0%) had SAEs that were adjudicated as non-respiratory-, non-cardiovascular- or non-cerebrovascular-related. Most adjudicated SAEs (763 patients; 14.8%) were hospitalisations, while there were 26 (0.5%) patients with intubation and 75 (1.5%) with fatal SAEs (86 [1.7%] had fatal SAEs when including vital status follow-up).

Conclusions The adjudicated analysis of SAEs demonstrated that the risk of having an event (composite end point of hospitalisations, intubations and death whether related to respiratory, cardiovascular, cerebrovascular or other cause) was similar for T+O 5/5 µg compared to T+O 2.5/5 µg or any of the monotherapy components. Similar conclusions can be drawn for the individual events of hospitalisations, intubations and death.

Abstract P128 Table 1 Summary of adjudicated SAEs: combined data (n [%])

	O 5 µg	T 2.5 µg	T 5 µg	T+O 2.5/5 µg	T+O 5/5 µg
Total number of patients	**1038**	**1032**	**1033**	**1030**	**1029**
SAEs					
Any adjudicated	171 (16.5)	148 (14.3)	162 (15.7)	157 (15.2)	161 (15.6)
Any respiratory-related	85 (8.2)	82 (7.9)	84 (8.1)	78 (7.6)	91 (8.8)
Key respiratory-related	78 (7.5)	74 (7.2)	70 (6.8)	69 (6.7)	83 (8.1)
COPD-related	67 (6.5)	63 (6.1)	65 (6.3)	53 (5.1)	71 (6.9)
Pneumonia-related	15 (1.4)	15 (1.5)	9 (0.9)	22 (2.1)	18 (1.7)
Other respiratory-related	7 (0.7)	10 (1.0)	17 (1.6)	11 (1.1)	11 (1.1)
Cardiovascular-related	15 (1.4)	13 (1.3)	19 (1.8)	17 (1.7)	19 (1.8)
Any cerebrovascular	6 (0.6)	6 (0.6)	5 (0.5)	5 (0.5)	5 (0.5)
Stroke-related	3 (0.3)	3 (0.3)	5 (0.5)	4 (0.4)	2 (0.2)
Other cerebrovascular-related	4 (0.4)	3 (0.3)	0	1 (0.1)	3 (0.3)
Non-respiratory, non-cardiovascular or non-cerebrovascular-related	78 (7.5)	67 (6.5)	74 (7.2)	73 (7.1)	71 (6.9)