Single-Inhaler Triple Therapy Fluticasone Furoate/Umeclidinium/Vilanterol Compared With Tiotropium Monotherapy in Chronic Obstructive Pulmonary Disease: A Post Hoc Analysis by Airflow Limitation

Poster No. P1440

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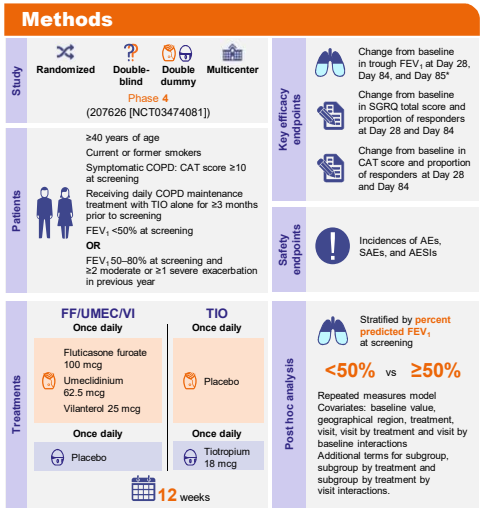
Introduction

- Study 207626 (NCT03474081) demonstrated significant improvements in lung function and health status in patients with symptomatic chronic obstructive pulmonary disease (COPD) and moderate-to-very severe airflow limitation who received inhaled corticosteroid/long-acting muscarinic antagonist/long-acting β_2-agonist (ICS/LAMA/LABA) triple therapy with single-inhaler fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI) versus LAMA monotherapy with tiotropium (TIO).[1]
- These results support previous studies that demonstrated improvements in lung function, health status, and exacerbations in patients with symptomatic COPD receiving ICS/LAMA/LABA triple therapy compared with LAMA monotherapy.[2-8]
- To assess the effect of patients' airflow limitation on clinical outcomes, a post hoc analysis of the 207626 study was conducted comparing once-daily single-inhaler FF/UMEC/VI therapy versus once-daily TIO monotherapy in patients with COPD stratified by patients' airflow limitation (as assessed by percent predicted forced expiratory volume in 1 second [FEV_1]) at screening.

Methods



*Day 85: primary endpoint; Days 28 and 84: secondary endpoints. AE, adverse event; AESI, adverse event of special interest; CAT, COPD Assessment Test; SAE, serious adverse event; SGRQ, St George's Respiratory Questionnaire.

Results

Patients

- In total, the ITT population comprised 800 patients (FF/UMEC/VI, n=400; TIO, n=400). Of these, 795 patients had FEV_1 % predicted data available and were included in this analysis: 415 patients had FEV_1 <50% predicted at screening (FF/UMEC/VI, n=212; TIO, n=203) and 380 patients had FEV_1 ≥50% predicted at screening (FF/UMEC/VI, n=185; TIO, n=195).
- Demographics were generally similar across FEV_1 subgroups, although lung function parameters differed as expected after stratification by FEV_1 values (**Table 1**). Patients in the FEV_1 ≥50% predicted subgroup had a higher frequency of moderate exacerbations in the previous 12 months, as dictated by inclusion criteria.

Efficacy

- Mean change from baseline in trough FEV_1 was significantly greater with FF/UMEC/VI versus TIO at Days 28, 84, and 85 in both the FEV_1 <50% and ≥50% subgroups (**Figure 1**).

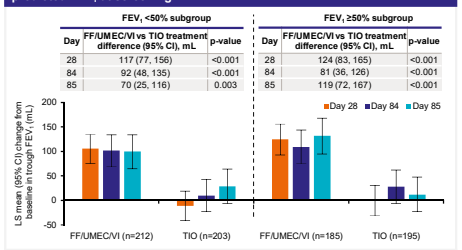
Table 1. Baseline characteristics by predicted FEV_1 at screening

	FEV_1 <50% predicted at screening (N=415)		FEV_1 ≥50% predicted at screening (N=380)	
	FF/UMEC/VI (n=212)	TIO (n=203)	FF/UMEC/VI (n=185)	TIO (n=195)
Age, years, mean (SD)	65.9 (8.0)	65.2 (7.4)	66.7 (8.2)	67.0 (8.1)
Male, n (%)	149 (70)	129 (64)	123 (66)	139 (71)
BMI, kg/m^2, mean (SD)	27.4 (6.4)	27.0 (5.8)	27.6 (5.7)	27.4 (4.8)
Current smoker at screening, n (%)	104 (49)	100 (49)	82 (44)	91 (47)
Lung function at screening, mean (SD)				
Post-bronchodilator FEV_1, mL	1137 (314)	1097 (290)	1775 (437)	1803 (420)
Post-bronchodilator FEV_1, % predicted	39.2 (7.8)	38.6 (7.6)	62.1 (8.2)	62.4 (7.8)
Post-bronchodilator FEV_1/FVC ratio	0.437 (0.099)	0.445 (0.097)	0.557 (0.081)	0.561 (0.079)
Reversibility to salbutamol, %*	10.9 (14.9)	9.8 (12.1)	6.3 (11.0)	7.4 (10.9)
Moderate COPD exacerbations in previous 12 months, n (%)				
0	117 (55)	115 (57)	27 (15)	36 (18)
1	39 (18)	32 (16)	4 (2)	8 (4)
≥2	56 (26)	56 (28)	154 (83)	151 (77)
Severe COPD exacerbations in previous 12 months, n (%)				
0	168 (79)	163 (80)	148 (80)	147 (75)
1	41 (19)	37 (18)	31 (17)	40 (21)
≥2	3 (1)	3 (1)	6 (3)	8 (4)
CAT score at screening, mean (SD)†	21.6 (5.6)	21.2 (5.4)	19.7 (4.7)	19.8 (4.8)
SGRQ total score at baseline, mean (SD)‡	53.3 (15.4)	50.0 (15.6)	46.4 (15.6)	45.5 (14.2)

*FEV_1 <50% predicted: FF/UMEC/VI, n=207, TIO, n=197; FEV_1 ≥50% predicted: TIO, n=194. †FEV_1 <50% predicted: TIO, n=202. ‡FEV_1 <50% predicted: FF/UMEC/VI, n=210; FEV_1 ≥50% predicted: FF/UMEC/VI, n=184, TIO, n=194.
BMI, body mass index; CAT, COPD Assessment Test; FVC, forced vital capacity; SD, standard deviation.

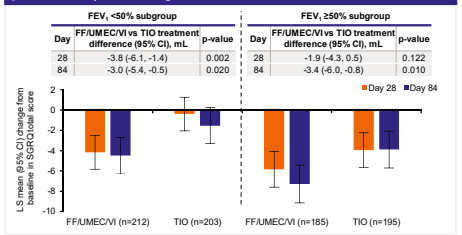
- Significantly greater improvements in SGRQ total score were observed with FF/UMEC/VI versus TIO at Days 28 and 84 for the FEV_1 <50% subgroup (**Figure 2**).
  - FF/UMEC/VI also significantly improved SGRQ total score versus TIO at Day 84 in the FEV_1 ≥50% subgroup; the point estimate favored FF/UMEC/VI over TIO at Day 28 but was not statistically significant (**Figure 2**).
  - Improvements in SGRQ total score were numerically greater in the FEV_1 ≥50% subgroup compared with the FEV_1 <50% subgroup.
- Significantly greater improvements in CAT scores were seen with FF/UMEC/VI versus TIO at Days 28 and 84 for the FEV_1 <50% subgroup (**Figure 3**).
  - No statistically significant between-treatment difference was seen in the FEV_1 ≥50% subgroup at either time point (**Figure 3**).

Figure 1. Change from baseline in trough FEV_1 according to percent predicted FEV_1 at screening



CI, confidence interval; LS, least squares.

Figure 2. Change from baseline in SGRQ total score according to percent predicted FEV_1 at screening



Safety

- In the ITT population, the incidence of AEs, SAEs, and AESIs was similar between treatment groups, including cardiovascular effects (**Table 2**).
  - The incidence of pneumonia was low in both treatment groups (<1%) (**Table 2**).

Figure 3. Change from baseline in CAT score according to percent predicted FEV_1 at screening

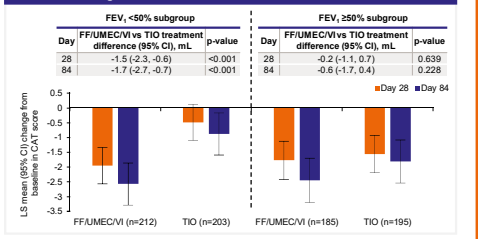


Table 2. Incidence of on-treatment adverse events (ITT population)

	FF/UMEC/VI (N=400) n (%)	TIO (N=400) n (%)
Any adverse events	127 (32)	115 (29)
Any serious adverse events	13 (3)	10 (3)
Fatal	2 (<1)	1 (<1)
Adverse events of special interest		
Cardiovascular effects	11 (3)	11 (3)
Decreased BMD and associated fractures	2 (<1)	0
LRTI excluding pneumonia	0	1 (<1)
Pneumonia	3 (<1)	3 (<1)

BMD, bone mineral density; LRTI, lower respiratory tract infection.

Conclusions

- Treatment with once-daily single-inhaler FF/UMEC/VI triple therapy significantly improved lung function compared with TIO monotherapy, regardless of airflow limitation at baseline, with a similar safety profile.
- Improvements in health status between FF/UMEC/VI and TIO were more pronounced at Day 28 in patients with more severe baseline airflow limitation.
- These results indicate that FF/UMEC/VI is a viable step-up option for patients with symptomatic COPD at risk of exacerbations who are currently receiving LAMA monotherapy.

Disclosures

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