INTREPID: Clinical Effectiveness of Once-Daily Single-Inhaler Fluticasone Furoate/Umeclidinium/Vilanterol Versus Multiple-Inhaler Triple Therapy in Usual Clinical Practice

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Halpin DMG[1], Worsley S[2], Ismaila AS[3,4], Astrom J[5], Beeh KM[6], Brintziki D[7], Di Boscio V[8], Kocks JWH[9,10,11], Marin JM[12], Tabberer M[7], Snowise NG[8*,13], Compton C[8]

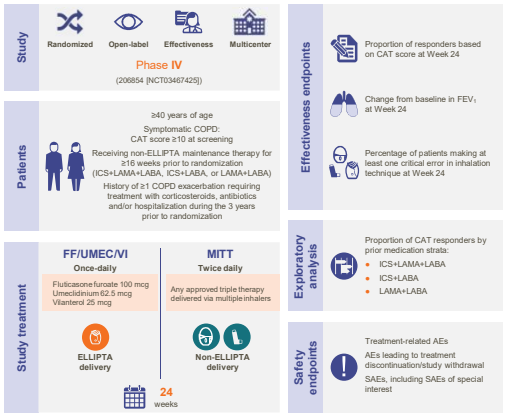
*At the time of the study

[1]University of Exeter Medical School, College of Medicine and Health, University of Exeter, Exeter, UK; [2]GSK, Stevenage, Hertfordshire, UK; [3]GSK, Collegeville, PA, USA; [4]McMaster University, Hamilton, ON, Canada; [5]GSK, Värmdö, Stockholm, Sweden; [6]insaf Respiratory Research Institute, Wiesbaden, Germany; [7]GSK, Stockley Park West, Uxbridge, Middlesex, UK; [8]GSK, Brentford, Middlesex, UK; [9]General Practitioners Research Institute, Groningen, the Netherlands; [10]University of Groningen, University Medical Center Groningen, GRIAC Research Institute, Groningen, the Netherlands; [11]Observational and Pragmatic Research Institute, Singapore; [12]University Hospital Miguel Servet, Zaragoza, Spain; [13]King's College, London, UK

Introduction

- In patients with chronic obstructive pulmonary disease (COPD) who remain symptomatic or continue to experience exacerbations while receiving dual therapy, triple therapy with an inhaled corticosteroid (ICS), long-acting β_2-agonist (LABA), and long-acting muscarinic antagonist (LAMA) is recommended.[1]
- Single-inhaler triple therapy is a recent development for the treatment of COPD and could provide a more practical option for patients, and improve treatment adherence and outcomes, compared with multiple-inhaler triple therapy (MITT).[2,3]
- Recently, single-inhaler triple therapy with fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI) delivered by the ELLIPTA inhaler has shown more sustained lung function benefit throughout the dosing interval compared with MITT, and similar health status improvements in the randomized controlled trial (RCT) environment.[4] However, real-world effectiveness data on single-inhaler versus multiple-inhaler regimens on health status and symptoms in COPD are currently lacking.
- The INTREPID (**IN**vestigation of **TR**eley **E**ffectiveness: Usual **P**ract**I**ce **D**esign) study evaluated the impact of once-daily single-inhaler triple therapy with FF/UMEC/VI versus non-ELLIPTA MITT on health status in patients requiring triple therapy within the real-world clinical setting.

Methods



AE, adverse event; CAT, COPD Assessment Test; FEV_1, forced expiratory volume in 1 second; SAE, serious adverse event

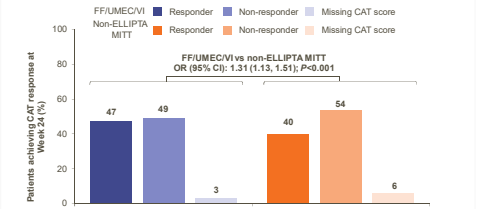
Results

Table 1. Patient characteristics at screening

Characteristic	FF/UMEC/VI (N=1545)	Non-ELLIPTA MITT (N=1547)
Age, mean (SD) years	67.8 (8.78)	67.8 (8.59)
Male, n (%)	837 (54)	818 (53)
BMI (kg/m²), mean (SD)	n=1536 27.84 (5.93)	n=1538 28.05 (6.05)
COPD exacerbation history in the prior 12 months, n (%)		
Moderate		
0	409 (26)	405 (26)
1	639 (41)	645 (42)
≥2	497 (32)	497 (32)
Severe		
0	1349 (87)	1361 (88)
1	155 (10)	139 (9)
≥2	41 (3)	47 (3)
CAT score, mean (SD)	n=1543 20.8 (6.76)	n=1547 20.5 (6.62)
Post-bronchodilator FEV_1 (L), mean (SD)*	n=825 1.474 (0.5653)	n=827 1.462 (0.5840)
Actual prior medication use strata, n (%)		
ICS + LAMA + LABA	1226 (79)	1235 (80)
ICS + LABA	126 (8)	126 (8)
LABA + LAMA	192 (12)	183 (12)
Missing†	1 (<1)	3 (<1)

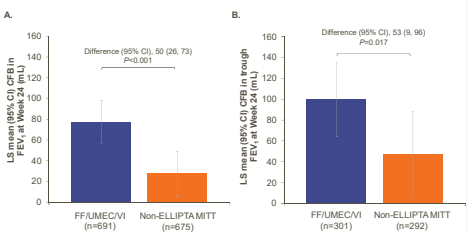
*FEV_1 population included all members of ITT population for whom a spirometry assessment was performed at any of Visit 1 or Visit 2; FF/UMEC/VI N=910; non-ELLIPTA MITT N=904. †Stratum is considered missing if the combination of maintenance treatments taken in the 14 days prior to randomization did not meet any of the 3 defined strata groups. BMI, body mass index; ITT, intent to treat; SD, standard deviation

Figure 1. Proportion of CAT responders at Week 24



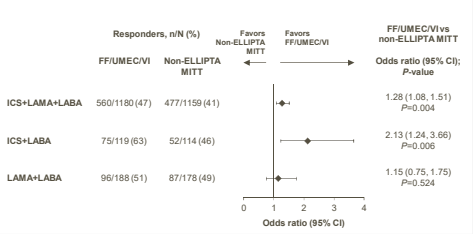
Response is defined as a CAT score ≥2 units below baseline. Patients who modified their randomized treatment, changed pulmonary rehabilitation status, or started oxygen therapy were considered as non-responders. CAT data for patients who discontinued randomized treatment without receiving another COPD maintenance therapy during the study was used. Missing data was imputed using multiple imputation based on the randomized treatment arm characteristics assuming MAR. Analysis performed using a logistic regression model with covariates of treatment group, baseline CAT score, number of exacerbations in the prior year, actual prior medication use strata, and country. CI, confidence interval; MAR, missing at random

Figure 2. LS mean change from baseline in (A) FEV_1 and (B) trough FEV_1 at Week 24



Week 24 data was used regardless of whether patients discontinued/modified their randomized treatment, changed pulmonary rehabilitation status, or started oxygen therapy. Missing Week 24 FEV_1 data were not imputed. Missing trough FEV_1 data were imputed based on randomized treatment arm characteristics assuming MAR. Analyses performed using (A) an analysis of covariance model with covariates of treatment group, baseline FEV_1, actual prior medication use strata, country, and timing of spirometry; and (B) an analysis of covariance model with covariates of treatment group, baseline trough FEV_1, actual prior medication use strata, and country. CFB, change from baseline; LS, least squares; MAR, missing at random

Figure 3. Proportion of CAT responders at Week 24 by prior therapy strata



Response is defined as a CAT score ≥2 units below baseline. Patients who modified their randomized treatment, changed pulmonary rehabilitation status, or started oxygen therapy were considered as non-responders. CAT data for patients who discontinued randomized treatment without receiving another COPD maintenance therapy during the study were used. Missing Week 24 data were not imputed. Analysis performed using a separate logistic regression model for each subgroup with covariates of treatment group, baseline CAT score, number of exacerbations in the prior year, and country. N denotes number of patients in the analysis.

Table 2. On-randomized treatment adverse events

Outcome	FF/UMEC/VI (N=1545)	Non-ELLIPTA MITT (N=1547)
Total duration at risk (patient-years)	636.7	685.8
	n (%)	n (%)
Any AE*	250 (16)	151 (10)
Any treatment-related AE	145 (9)	44 (3)
Any AE leading to treatment discontinuation/study withdrawal	115 (7)	32 (2)
Any SAE	114 (7)	114 (7)
Any treatment-related SAE	13 (<1)	6 (<1)
Any fatal SAE	8 (<1)	8 (<1)
Any treatment-related fatal SAE	0	0
Serious AESIs		
Cardiovascular effects	29 (2)	23 (1)
Decreased BMD and associated fractures	6 (<1)	4 (<1)
Infective pneumonia	27 (2)	32 (2)
LRTI excluding infective pneumonia	7 (<1)	10 (<1)

*Only treatment-related AEs, SAEs, and AEs leading to study treatment discontinuation or study withdrawal were collected in the study. AESI, adverse event of special interest; BMD, bone mineral density; LRTI, lower respiratory tract infection

- The ITT population comprised 3092 patients (FF/UMEC/VI N=1545; MITT N=1547). Characteristics at screening were similar between the two treatment groups (**Table 1**).
- The odds of being a CAT responder at Week 24 were significantly greater with FF/UMEC/VI than non-ELLIPTA MITT (**Figure 1**).
- FF/UMEC/VI significantly improved lung function versus non-ELLIPTA MITT at Week 24 (**Figure 2**).
- The percentage of patients with ≥1 critical error in inhalation technique at Week 24 was 6% in the FF/UMEC/VI treatment group and 3% in the non-ELLIPTA MITT group (odds ratio: 1.99; P=0.103).
- The odds of being a CAT responder at Week 24 were significantly greater with FF/UMEC/VI versus non-ELLIPTA MITT in patients previously on ICS-containing therapy. In patients previously on LAMA+LABA, there was a numerical improvement in favour of FF/UMEC/VI but this was not statistically significant. Interpretation is limited due to the smaller subgroup sizes (**Figure 3**).
- Both treatments had a similar safety profile (**Table 2 – Serious AESIs**).

Conclusions

- In the usual clinical care setting, treatment with single-inhaler FF/UMEC/VI resulted in significantly more patients achieving health status improvement and greater lung function benefit versus non-ELLIPTA MITT, with a similar safety profile.
- This pragmatic study broadens the understanding of the effectiveness of FF/UMEC/VI beyond the traditional RCT setting, into real-world clinical practice.

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Disclosures

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