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CAPTAIN: Effects of Adding the Long-acting Muscarinic Antagonist Umeclidinium to Inhaled Corticosteroid/ Long-acting β_2-agonist Therapy on Symptoms in Patients With Inadequately Controlled Asthma

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Recording by Neil Barnes

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DISCLOSURES

- This study was funded by GlaxoSmithKline (GSK ID: 205715; NCT02924688).
- ELLIPTA and DISKUS are owned by or licensed to the GSK group of companies.
- On behalf of all authors, an audio recording of this poster was prepared by Neil Barnes, who did not receive any payment for this recording.
- The presenting author declares the following real or perceived conflicts of interest during the last 24 months in relation to this presentation: Neil Barnes is an employee of GSK and holds stocks or shares in GSK.
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Objectives and methods

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INTRODUCTION AND OBJECTIVES

- E-RS®: Asthma is an 11-item patient-reported daily diary derived from E-RS®: COPD, which has been shown to be reliable and responsive in assessing respiratory symptoms in patients with moderate/severe asthma.[1]
- E-RS: Asthma captures respiratory symptoms experienced by patients through three symptom domains (RS-Breathlessness, RS-Chest Symptoms, RS-Cough and Sputum) and provides a total score ranging from 0 to 40 (with higher scores representing greater symptom burden).[1]
- The E-RS: Asthma questionnaire was completed by patients throughout the CAPTAIN study[2] via an eDiary. Here we present a pre-specified pooled analysis of CAPTAIN to evaluate the effects of adding UMEC to the ICS/LABA combination of FF/VI on symptom burden as measured by the E-RS: Asthma and its three subscales: RS-Breathlessness, RS-Chest Symptoms, and RS-Cough and Sputum.

METHODS

Week	Period	Treatment
Week -5 Weeks -5 to -2	**Visit 1: Screening** 3-week run-in period	FP/SAL 250/50 mcg
Week -2 Weeks -2 to 0	**Visit 2: Enrollment** 2-week stabilization period	FF/VI 100/25 mcg
Week 0 Weeks 0 to 24	**Visit 3: Randomization** Fixed treatment period	FF/VI 100/25 mcg (N=407) FF/UMEC/VI 100/31.25/25 mcg (N=405) FF/UMEC/VI 100/62.5/25 mcg (N=406) FF/VI 200/25 mcg (N=406) FF/UMEC/VI 200/31.25/25 mcg (N=404) FF/UMEC/VI 200/62.5/25 mcg (N=408)
Week 24 Weeks 24 to 52	**Primary endpoint** Variable treatment period	
	1-week safety follow-up*	

- CAPTAIN was a Phase IIIA, randomized, double-blind, 24–52 week, parallel-group study in adults with inadequately controlled asthma despite ICS/LABA therapy.†
- Patients completed the E:RS: Asthma questionnaire at home using an eDiary during the run-in period and throughout the study; data were analyzed in 4-weekly intervals.
- Endpoints reported here, for pooled FF/UMEC/VI (UMEC 62.5 mcg only) versus pooled FF/VI data:
  - LS mean change from baseline‡ at Weeks 21–24 in E:RS: Asthma total and domain scores.
  - Proportion of patients achieving the minimally important within-patient change for E-RS: Asthma total score (-2.0 units) at Weeks 21–24.

FP/SAL provided BID as a fixed dose via the DISKUS DPI; FF/VI and FF/UMEC/VI provided QD as a fixed dose via the ELLIPTA DPI. Patients had up to 5 on-treatment clinic visits. *All patients in the study had a safety follow-up contact approximately 7 days after the End of Study Visit (Week 24, 36, or 52) or Early Withdrawal Visit; †daily FP >250 mcg or equivalent; ‡baseline period is defined as the mean of E-RS total or domain scores over the last 14 days prior to the randomized treatment start. BID, twice daily; COPD, chronic obstructive pulmonary disease; DPI, dry powder inhaler; E-RS, Evaluating Respiratory Symptoms; FEV_1, forced expiratory volume in 1 second; FF, fluticasone furoate; FP, fluticasone propionate; ICS, inhaled corticosteroid; LABA, long-acting ß$_2$-agonist; LS, least squares; QD, once daily; SAL, salmeterol; UMEC, umeclidinium; VI, vilanterol

1. Tabberer M, et al. Am J Respir Crit Care Med 2020;201:A5624; 2. Lee LA, et al. Lancet Respir Med 2020;9:69–84.

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Baseline demographics and clinical characteristics were similar in the two pooled treatment groups

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- E-RS: Asthma total and domain scores were low at baseline and similar in the two pooled treatment groups.

	FF/VI (N=813)	FF/UMEC 62.5/VI (N=814)	Total (N=2436)
Demographics			
Age, years, mean (SD)	53.6 (13.16)	53.3 (12.95)	53.2 (13.11)
Male, n (%)	307 (38)	308 (38)	922 (38)
BMI, kg/m^2, mean (SD)	29.3 (6.19)	29.5 (6.79)	29.4 (6.64)
Clinical characteristics			
E-RS: Asthma score, mean (SD)*	*n=805*	*n=807*	*n=2418*
Total score	8.16 (6.174)	8.35 (6.069)	8.30 (6.137)
Breathlessness score	3.90 (3.231)	4.00 (3.170)	3.94 (3.201)
Cough and Sputum score	2.19 (1.701)	2.23 (1.690)	2.23 (1.699)
Chest score	2.07 (1.835)	2.12 (1.796)	2.12 (1.814)
Total number of exacerbations, n (%)†			
0	124 (15)	107 (13)	364 (15)
1	470 (58)	469 (58)	1390 (57)
≥2	219 (27)	238 (29)	682 (28)
ACQ-7 score, mean (SD)‡	*n=793* 2.1 (0.70)	*n=795* 2.1 (0.69)	*n=2383* 2.1 (0.70)

*Mean of E-RS total or domain scores over the last 14 days prior to the randomized treatment start; †in the 12 months prior to the screening visit; ‡at randomization.
ACQ, asthma control questionnaire; BMI, body mass index; E-RS, Evaluating Respiratory Symptoms; FF, fluticasone furoate; SD, standard deviation; UMEC, umeclidinium; VI, vilanterol
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E-RS: Asthma total score was reduced beyond the minimally important difference with a greater reduction for FF/UMEC/VI versus FF/VI

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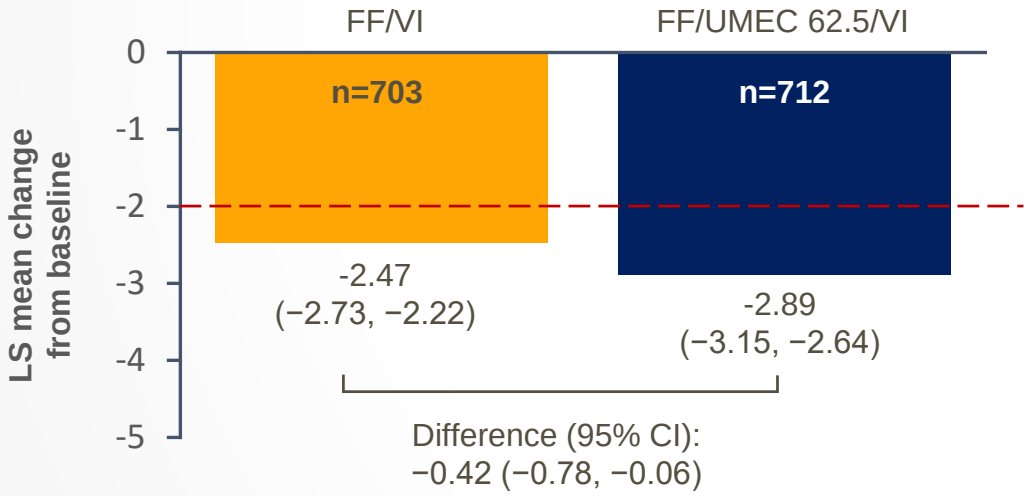
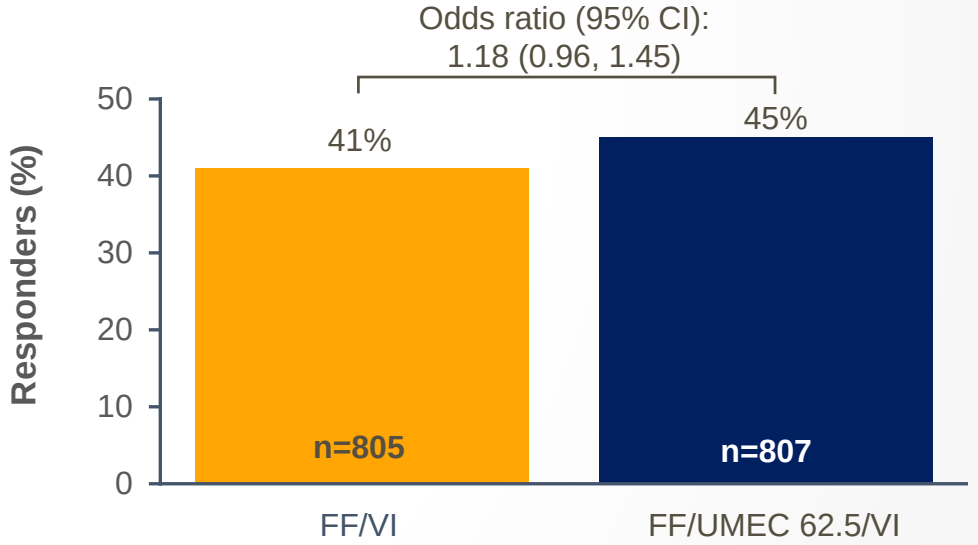
- At Weeks 21–24, E-RS: Asthma total scores were reduced in both pooled treatment groups, with changes exceeding the minimally important within-patient change (−2.0) (**A**).
- The reduction in E-RS: Asthma total score was greater with FF/UMEC 62.5/VI versus FF/VI (**A**), with a corresponding greater proportion of E-RS: Asthma responders in the triple therapy group (**B**).

A. Change from baseline in E-RS: Asthma total score at Weeks 21–24*



B. Proportion of E-RS: Asthma responders at Weeks 21–24†



*The minimal clinically important difference for E-RS: Asthma is defined as an improvement (decrease) of ≥2 points from baseline, as depicted by the red dashed line;[1] †E-RS: Asthma responders had an improvement in E-RS: Asthma score of ≥2 points from baseline.

CI, confidence interval; E-RS, Evaluating Respiratory Symptoms; FF, fluticasone furoate; LS, least square; UMEC, umeclidinium; VI, vilanterol

1. Tabberer M, et al. Am J Respir Crit Care Med 2020;201:A5624.

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Breathlessness and Chest scores were also improved with FF/UMEC 62.5/VI versus FF/VI

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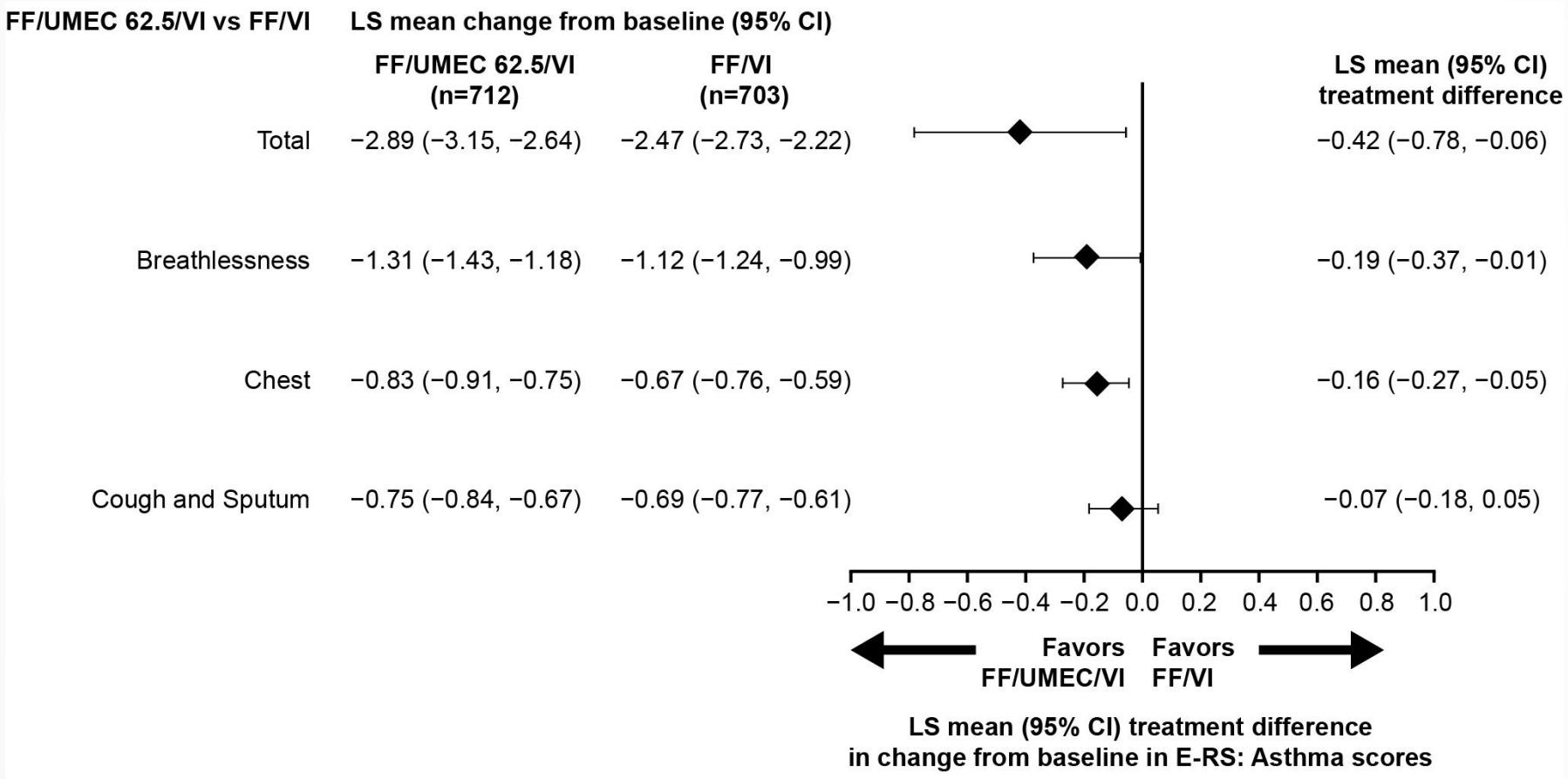

All doses are mcg. n=number of patients with analyzable data at Weeks 21–24.
CI, confidence interval; E-RS, Evaluating Respiratory Symptoms; FF, fluticasone furoate; LS, least squares; UMEC, umeclidinium; VI, vilanterol

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Conclusions

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- Among patients with uncontrolled asthma, addition of UMEC 62.5 mcg to FF/VI produces improvements in the E-RS: Asthma total and domain scores related to breathlessness and chest symptoms, but has no effect on those related to cough and sputum.
- The reason for the lack of differentiation for FF/UMEC/VI on RS-Cough and Sputum is not clear.
  - This may relate to the fact that this domain comprises one cough and two sputum items and may therefore be less responsive in asthma.
- Further research on effects of FF/UMEC/VI on cough may be warranted.

E-RS, Evaluating Respiratory Symptoms; FF, fluticasone furoate; UMEC, umeclidinium; VI, vilanterol

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CO-AUTHORS' DISCLOSURES

- Z Bailes, A Fowler, F Gardiner, E Pizzichini, and D Slade and are employees of GSK and hold stocks or shares in GSK.
- M Tabberer was an employee of GSK at the time of the study and holds stocks or shares in GSK.
- G Brusselle has received speaker fees from and served on advisory boards for AstraZeneca, Boehringer Ingelheim, Chiesi, GSK, Novartis, and Teva, and has served on advisory boards for Amgen and Sanofi.
- H Inoue has received research/educational grants from Boehringer Ingelheim, Chugai, GSK, Kyorin, MSD, Novartis, Ono, Pfizer, Sanofi, Shionogi, Taiho, and Teijin-Pharma, and has received speaker's honoraria and/or fees for advisory boards from Astellas, AstraZeneca, Boehringer Ingelheim, Chugai, GSK, Kyorin, MSD, Novartis, and Sanofi.
- H Kerstjens has received research/educational grants and served on advisory boards for Boehringer Ingelheim, GSK, and Novartis, and has served on advisory boards for Chiesi and AstraZeneca.
- J Oppenheimer has served on adjudication committees/data and safety monitoring boards for AstraZeneca, GSK, Novartis, and Sanofi/Regeneron, and has received grants/personal fees from GSK.
- A Papi has received research grants and personal fees from AstraZeneca, Chiesi, GSK, Menarini, and Teva, and personal fees from Boehringer Ingelheim, Edmond Pharma, Mundipharma, Novartis, Sanofi, and Zambon.
- I Pavord is an employee of the University of Oxford; has received research grants, speaker fees, fees for advisory boards and travel expenses for attending international meetings/advisory boards from Chiesi and Afferent; has received speaker's honoraria, travel expenses and honoraria for attending advisory boards from AstraZeneca, Boehringer Ingelheim, GSK, and Teva; and has received speaker fees/fees for advisory boards from Circassia, Knopp, Merck, Mundipharma, Novartis, Roche/Genentech, and Sanofi/Regeneron.