CAPTAIN Study: Evaluating the Efficacy of Once-Daily, Single-Inhaler Fluticasone Furoate/Umeclidinium/Vilanterol (FF/UMEC/VI) Versus FF/VI in Inadequately Controlled Asthma Using Change in Asthma Control Questionnaire and the Relationship With Trough FEV_1

Poster No. P788 (A5626)

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*At the time of the study

Background

- Achieving and maintaining symptom control over the long term is a key goal for asthma treatment according to the Global Initiative for Asthma 2019 guidelines.[1]
- Approximately 30%–50% of patients with moderate/severe asthma remain symptomatic with poorly controlled disease despite adherence to inhaled corticosteroid (ICS)/long-acting β_2-agonist (LABA) therapy.[2–5]
- The addition of a long-acting muscarinic antagonist (LAMA) to ICS/LABA therapy improves lung function and reduces exacerbation rates in patients with asthma; improvements in symptoms are less consistent.[6,7] There is therefore an unmet need for a step-up therapy to provide effective symptom control.
- Fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI) is widely approved as a once-daily treatment for chronic obstructive pulmonary disease (COPD).[8,9]
- The Phase IIIA CAPTAIN study was designed to evaluate the efficacy (primary endpoint: lung function) and safety of once-daily FF/UMEC/VI in comparison to FF/VI in patients with asthma inadequately controlled on ICS/LABA.[10]

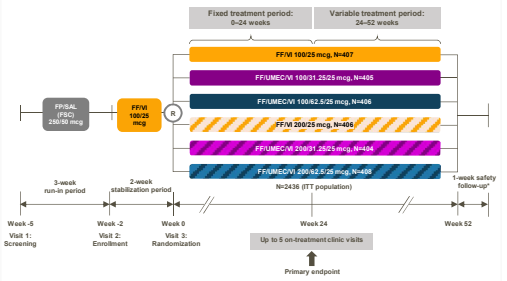
Aims

- To report Asthma Control Questionnaire (ACQ) data from the CAPTAIN study, and explore the relationship between changes in ACQ-7 score and trough forced expiratory volume in 1 second (FEV_1).

Methods

- CAPTAIN was a Phase IIIA, randomized, 24–52-week, parallel-group study (study 205715, NCT02924688), enrolling adults with asthma on maintenance ICS/LABA therapy with a pre-bronchodilator FEV_1 of ≥30% and <85% of predicted, with an increase in FEV_1 of ≥12% and ≥200 mL following albuterol inhalation, and an ACQ-6 score of ≥1.5 (**Figure 1**).
  - Patients with COPD or other respiratory disorders and pneumonia/pneumonia risk factors were excluded.
- Following run-in and stabilization periods, patients were randomized to one of two FF/VI or one of four FF/UMEC/VI dose combinations administered once daily via the Ellipta dry powder inhaler (**Figure 1**).
- We report treatment differences when UMEC 62.5 mcg or 31.25 mcg was added to FF/VI for the following pre-specified endpoints:
  - Change from baseline in trough FEV_1 and ACQ-7 score at Week 24.
  - Proportion of ACQ-7, -6, and -5 responders (defined as reaching a minimally clinically important difference [MCID] of ≥0.5 points improvement [decrease] from baseline)[11] at Week 24.
- ACQ-7 includes five symptoms and impact questions which are completed by patients (ACQ-5) and measures of rescue medication use and lung function. ACQ-6 comprises ACQ-5 plus measures of rescue medication use.[11]
- To increase power and precision of analyses, FF doses were pooled for each UMEC dose for ACQ endpoints. Here, we also report pooled analysis of lung function data for comparison.
  - For all analyses reported, *P*-values were not adjusted for multiplicity.
- The influence of change from baseline in trough FEV_1 on ACQ-7 responders at Week 24 was assessed post hoc using Pearson's correlation coefficient.

Figure 1. CAPTAIN study design



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.
*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
BID, twice daily; DPI, dry powder inhaler; FP, fluticasone propionate; QD, once daily; R, randomization; SAL, salmeterol

Results

- 2436 patients were included in the ITT (intent-to-treat) population.
- Baseline demographics and clinical characteristics were similar between treatment groups (**Table 1**).
- Greater improvements in least squares (LS) mean change from baseline in trough FEV_1 were observed in the pooled analysis of FF/UMEC 62.5 mcg/VI versus FF/VI (101 mL [95% confidence interval (CI): 70, 132]) at Week 24 (**Figure 2A**).
  - Improvements were seen as early as Week 4 (64 mL [95% CI: 39, 90]).
- Similarly, all treatment groups showed decreases (improvements) greater than or equal to the MCID of 0.5 points for LS mean change from baseline in ACQ-7 score at Week 24 (**Figure 2B**).
  - At Week 24, numerically greater improvements were observed for FF/UMEC 62.5 mcg/VI versus FF/VI (mean difference [95% CI]: 0.089 [0.023, 0.156]), with improvements seen as early as Week 4 (0.070 [0.012, 0.129]).
- A higher proportion of ACQ responders was observed with FF/UMEC 62.5 mcg/VI versus FF/VI at Week 24, with a higher odds of response with the triple therapy (**Figure 3**). Greater proportions of ACQ-7 responders were seen with FF/UMEC 62.5 mcg/VI versus FF/VI as early as Week 4 (50% vs 42%; odds ratio: 1.45 [95% CI: 1.18, 1.79]).
- Regardless of treatment, a modest correlation between trough FEV_1 and ACQ-7 score change from baseline was observed across the study population at Week 24 (correlation: -0.37) (**Figure 4**).

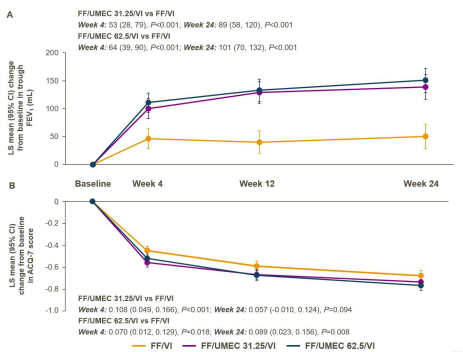
Results

Table 1. Baseline demographics and clinical characteristics (ITT population)

	FF/VI 100/25 (N=407)	FF/UMEC/VI 100/31.25/25 (N=405)	FF/UMEC/VI 100/62.5/25 (N=406)	FF/VI 200/25 (N=406)	FF/UMEC/VI 200/31.25/25 (N=404)	FF/UMEC/VI 200/62.5/25 (N=408)	Total (N=2436)
Baseline demographics							
Age, years, mean (SD)	53.3 (13.03)	51.7 (13.27)	52.9 (13.39)	53.9 (13.30)	53.5 (13.12)	53.7 (12.50)	53.2 (13.11)
Male, n (%)	153 (38)	143 (35)	158 (39)	154 (38)	164 (41)	150 (37)	922 (38)
BMI (kg/m²), mean (SD)	29.3 (6.08)	29.1 (6.80)	29.2 (6.65)	29.4 (6.29)	29.4 (7.07)	29.7 (6.93)	29.4 (6.64)
Former smokers, n (%)	69 (17)	78 (19)	81 (20)	69 (17)	80 (20)	93 (23)	470 (19)
Clinical characteristics at randomization							
Pre-bronchodilator FEV_1, mL, mean (SD)	n=405 2008 (681)	n=401 2073 (675)	n=402 2073 (678)	n=405 1987 (674)	n=401 2011 (667)	n=406 1984 (693)	n=2420 2023 (678)
ACQ-7 score, mean (SD)	n=396 2.1 (0.67)	n=399 2.1 (0.73)	n=400 2.1 (0.73)	n=397 2.1 (0.73)	n=396 2.2 (0.71)	n=395 2.1 (0.65)	n=2383 2.1 (0.70)

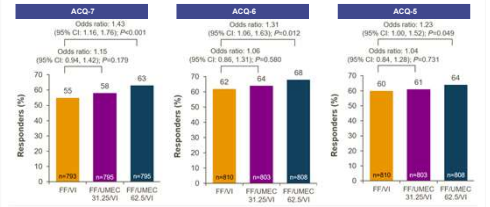
All doses are mcg. BMI, body mass index; SD, standard deviation

Figure 2. LS mean change from baseline in (A) trough FEV_1 and (B) ACQ-7 score over time (ITT population; FF doses pooled for each UMEC dose)



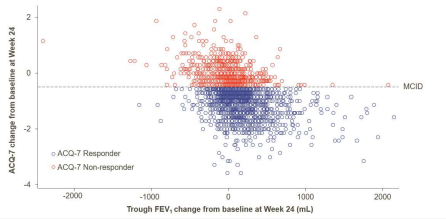
Note: Baseline FEV_1 was last value prior to randomization and baseline ACQ was value at randomization visit. *P*-values are not adjusted for multiplicity.
All doses are mcg.

Figure 3. ACQ responder rates at Week 24 (ITT population; FF doses pooled for each UMEC dose)



Note: Responders are defined as meeting the MCID of ≥0.5 points improvement (decrease) from baseline. *P*-values are not adjusted for multiplicity. All doses are mcg.

Figure 4. Modest correlation (-0.37) between change from baseline in ACQ-7 score and trough FEV_1 at Week 24 (ITT population)



Conclusions

- In addition to improving lung function, FF/UMEC/VI improved asthma control compared with FF/VI as measured by change from baseline in ACQ-7 score and the proportion of responders across all ACQ measures, as early as Week 4 and sustained until Week 24.
- The limited correlation between changes in lung function (FEV_1) and disease control (ACQ-7) indicates that improvements in disease control are driven by symptom improvement as well as changes in lung function.

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Disclosures

- This study was funded by GlaxoSmithKline (GSK study 205715, NCT02924688).
- AF, GP, MT, NB, and ZB are employees of GSK hold stocks or shares in GSK. LAL was an employee of GSK at the time of the study. HAMK has received research/educational grants and served on advisory boards for Boehringer Ingelheim, GSK, and Novartis, and has served on advisory boards for Chiesi, AstraZeneca, and Fluidda. JO has served on an adjudication committees/data and safety monitoring boards for AstraZeneca, GSK, Novartis, and Sanofi/Regeneron, and has received grants/personal fees from GSK.
- Editorial support in the form of preparation of the first draft based on input from all authors, and collation and incorporation of author feedback to develop subsequent drafts, was provided by Chloe Stevenson, MSci, of Fishawack Indicia Ltd, UK, and was funded by GSK.
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Prepared for the American Thoracic Society Annual Meeting (2020)