CAPTAIN Study: Daily Digital Spirometry and Symptom Data for Once-Daily, Single-Inhaler Fluticasone Furoate/Umeclidinium/Vilanterol (FF/UMEC/VI) in Asthma

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Background

- Achieving and maintaining long-term symptom control is a key goal in asthma treatment.[1]
- The addition of a long-acting muscarinic antagonist (LAMA) to inhaled corticosteroid (ICS)/long-acting β_2-agonist (LABA) therapy has been shown to improve lung function and reduce exacerbation rates in patients with asthma.[2–4]
- The Phase IIIa CAPTAIN study was designed to evaluate the efficacy and safety of once-daily fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI) in comparison to FF/VI in patients with asthma inadequately controlled on ICS/LABA; results showed improved lung function and numerical reductions in the annualized rate of moderate/severe exacerbation with FF/UMEC/VI versus FF/VI, with no new or unexpected safety findings.[4]
- Qualitative and quantitative research indicates that the Evaluating Respiratory Symptoms Questionnaire® (E-RS®), initially developed for use in chronic obstructive pulmonary disease,[5] is reliable and responsive in a symptomatic asthma population.[6,7] The E-RS: Asthma® questionnaire was included in the CAPTAIN study as a patient-reported outcome.

Aims

- To investigate the efficacy (including onset and maintenance of treatment effects) of FF/UMEC/VI versus FF/VI in CAPTAIN on daily measurements of:
  - Lung function, assessed using a home-based spirometer.
  - Symptom burden, assessed using the E-RS: Asthma questionnaire.

Methods

- CAPTAIN was a Phase IIIA, randomized, 24–52-week, parallel-group study (study 205715, NCT02924688). The study design is shown in **Figure 1.**

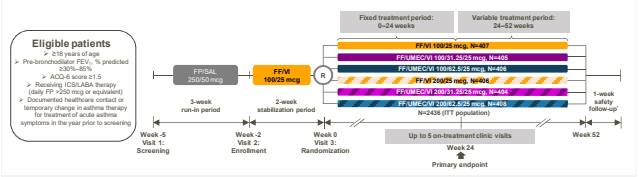
Endpoints reported in this analysis

- Change from baseline in home daily morning (AM) trough forced expiratory volume in 1 second (FEV_1) or evening (PM) FEV_1 over the first 24 weeks of the treatment period, analyzed using mixed model repeated measures (MMRM) by 4-weekly intervals.
- Change from baseline in E-RS: Asthma score and proportion of E-RS: Asthma responders (response defined as a decrease from baseline of ≥2 units) was also analyzed by MMRM over 4-weekly intervals, with the endpoint defined as Weeks 21–24 (inclusive) of the treatment period.
  - FEV_1 and E-RS: Asthma scores were measured daily using an AM3 device, which integrates a home spirometer and an electronic diary, and automatically transmits data daily to a centralized server.[6]
  - The E-RS: Asthma questionnaire was completed by the patient at home each night using the electronic diary, with a scoring range of 0–40 (with higher scores indicating more severe respiratory symptoms).[7,8]

Analysis

- Data collected post-randomization on- and post-treatment were included in these analyses; no adjustments for multiplicity were made for data reported.
- The primary analysis of non-spirometry endpoints, including E-RS: Asthma scores, was pre-specified to be performed on pooled data for both FF doses; however, unpooled spirometry and non-spirometry data are presented in this analysis to aid data interpretation.

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.
ACQ, Asthma Control Questionnaire; BID; twice daily; DPI, dry powder inhaler; fluticasone propionate; ITT, intent-to-treat; QD, once daily; R, randomization; SAL, salmeterol

Results

Study population

- 2436 participants were included in the ITT population; baseline demographics and disease characteristics were generally similar across all treatment arms.
- At screening, mean (standard deviation [SD]) % predicted pre-bronchodilator clinic FEV_1 was 58.48 (12.79), 67% of patients were on medium-dose ICS, and 63% had experienced an exacerbation in the last year requiring oral corticosteroids and/or hospitalization.
  - Baseline mean (SD) home daily morning FEV_1 (n=2430) was 1955 (699) mL and evening FEV_1 (n=2417) was 2023 (717) mL.
  - Baseline mean (SD) E-RS: Asthma total score (n=2418) was 8.30 (6.14).

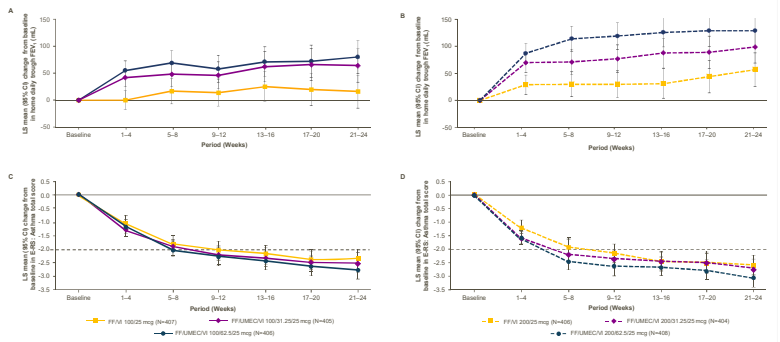
Daily lung function

- Greater improvements from baseline in home daily morning trough FEV_1 were observed with all doses of FF/UMEC/VI versus FF/VI; improvements were seen as early as Weeks 1–4 and were maintained to the end of the treatment period (**Figures 2A and 2B**).
- Differences from baseline in mean home daily morning trough FEV_1 and evening FEV_1 were numerically greater with all doses of FF/UMEC/VI versus FF/VI for the overall 24-week treatment period, and were also greater in the UMEC 62.5 mcg-containing groups versus the UMEC 31.25 mcg groups (**Figure 3**).

Symptom control

- E-RS: Asthma total score improved from baseline in all treatment groups at all 4-weekly intervals assessed until Weeks 21–24, with a ≥2-point improvement from baseline observed as early as Weeks 5–8 for FF/UMEC/VI 100/62.5/25 mcg and for both FF 200 mcg-containing triple therapies (**Figures 2C and 2D**).
- Improvements in E-RS: Asthma total score with triple therapy were numerically greater than those for dual therapy, giving rise to small dose-ordered effects in favor of UMEC 62.5 mcg at both FF doses (**Figures 2C and 2D**).
- A greater proportion of patients on FF/UMEC/VI versus FF/VI therapy were E-RS: Asthma responders by Weeks 21–24, with the exception of the FF/UMEC/VI 200/31.25/25 mcg versus FF/VI 200/25 mcg comparison (**Figure 4**).

Figure 2. Change from baseline in home daily morning trough FEV_1 (top) and E-RS: Asthma scores (bottom) with FF 100 mcg- (A) and (C), and FF 200 mcg-(B) and (D) containing therapies, respectively

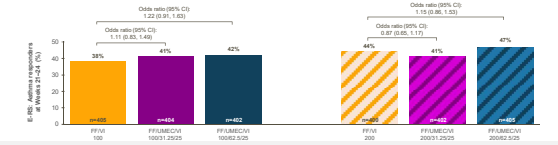


The minimal clinically important difference for E-RS: Asthma is defined as an improvement (decrease) of ≥2 points from baseline, as depicted by the dashed line.[7,8]
CI, confidence interval; LS, least squares

Figure 3. Change from baseline in (A) home daily morning trough FEV_1 and (B) evening FEV_1 over 24 weeks

LS, least squares mean; FEV_1 forced expiratory volume in 1 second

Figure 4. Percentage of E-RS: Asthma responders* at Weeks 21–24



*Responders had an improvement (decrease) in E-RS: Asthma score of ≥2 points from baseline.

Conclusions

- Addition of both doses of UMEC to FF/VI resulted in early and sustained improvements in lung function (FEV_1, measured on daily basis).
- Early and sustained improvements in symptoms were also seen with the addition of UMEC (measured using E-RS: Asthma).
- Observed trends across the endpoints assessed favored the higher dose of UMEC.
- Home daily spirometry results and improvements in E:RS Asthma scores are consistent with improvements observed in clinic-based measurements of lung function and other patient-reported outcomes observed with once-daily FF/UMEC/VI triple therapy in CAPTAIN.

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Disclosures

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