CAPTAIN Study: Effects of Fluticasone Furoate/Umeclidinium/Vilanterol on FEV_1 Improvement in Asthma According to Age

Poster No. P206

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Background

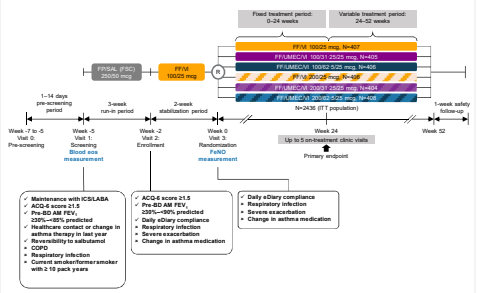
- The Phase IIIA CAPTAIN study evaluated the efficacy and safety of once-daily fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI) versus FF/VI in patients with asthma inadequately controlled on medium–high-dose inhaled corticosteroid/long-acting β_2-agonist (ICS/LABA) therapy.[1]
  - Results showed improved lung function and asthma control, and numerical reductions in the annualized rate of moderate/severe exacerbation with FF/UMEC/VI versus FF/VI.[1]
- A recently reported subgroup analysis of CAPTAIN in patients <65 years or ≥65 years indicated that the effects of different treatment strategies on absolute changes in lung function (adding UMEC or doubling FF dose) did not differ on the basis of patient age.[2] However, this dichotomous approach does not necessarily reflect potential modifications in baseline lung function that may occur with increasing age, such as decreased lung volume. As such, the clinical relevance of absolute changes from baseline may vary by age.

Objective

- This subgroup analysis of CAPTAIN aimed to build on previous findings by instead, evaluating *relative* lung function changes (relative percentage change from baseline in FEV_1) following addition of UMEC to FF/VI or doubling FF dose in additional patient age groups to address potential differences in baseline lung function by age.
- A subgroup analysis of the CAPTAIN study investigating the effects of FF/UMEC/VI on treatment outcomes in asthma according to severe exacerbation history is being presented separately at this congress (P202).

Methods

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. 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. ACQ Asthma Control Questionnaire; BID, bronchodilator; BID, twice daily; COPD, chronic obstructive pulmonary disease; DPI, dry powder inhaler; FEV_1, forced expiratory volume in 1 second; FP, fluticasone propionate; ITT, intent-to-treat; QD, once daily; R, randomization; SAL, salmeterol.

- CAPTAIN was a Phase IIIA, randomized, double-blind, 24–52-week, parallel-group study (GSK study 205715, NCT02924688). The study design is shown in **Figure 1**.
- We report post hoc analyses of relative percentage change from baseline in clinic trough FEV_1 (Week 24) in four additional patient age subgroups using the 25th, 50th, and 75th percentiles as cut points (G1:18–<44; G2:44–<54; G3:54–<63; G4:≥63 years at study entry [no upper age limit]).
  - We also present absolute change from baseline in clinic trough FEV_1 (primary endpoint) in the overall CAPTAIN ITT population as well as in the <65- vs ≥65-year age groups, as previously presented.[1,2]

Results

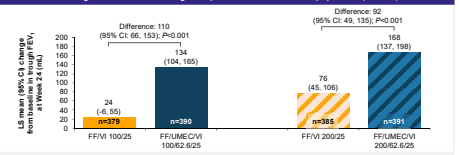
- Baseline demographics were generally similar across all age subgroups; most patients were female, overweight, and had never smoked (**Table 1**).
- Baseline lung function was greater among younger patients, than older patients (**Table 1**).
- In the overall ITT population of CAPTAIN, addition of UMEC 62.5 mcg to FF/VI significantly improved trough FEV_1 on a background of FF 100 mcg or 200 mcg (**Figure 2**).
- The previously reported CAPTAIN subgroup analysis by age (<65 vs ≥65 years) reported that the addition of UMEC to FF/VI dose led to numerical improvements in trough FEV_1, as did doubling the dose of FF, regardless of age (**Figure 3**).[2]
- Addition of UMEC 62.5 mcg to FF 100 or 200 mcg was associated with improvements in relative change from baseline in trough FEV_1, across all of the additional age subgroups assessed (**Figure 4**).
- In comparison, doubling FF dose was generally not associated with the same magnitude of improvements as observed following addition of UMEC, particularly in patients in the 54–<63 and ≥63 years categories.
- However, there was a suggestion for greater improvement in younger (18–44 years) versus older (44–<54, 54–<63, and ≥63 years subgroups) patients when doubling FF dose in dual therapy (**Figure 4**).

Table 1. Baseline demographics and clinical characteristics

	G1: 18–<44 (N=569)	G2: 44–<54 (N=579)	G3: 54–<63 (N=650)	G4: ≥63 (N=638)	Overall (ITT) (N=2436)
Baseline demographics					
Age, years, mean (SD)	34.8 (6.7)	48.8 (2.8)	57.9 (2.5)	68.7 (4.7)	53.2 (13.1)
Male, n (%)	250 (44)	199 (34)	228 (35)	245 (38)	922 (38)
BMI (kg/m^2), mean (SD)	29.33 (7.98)	29.87 (6.88)	29.41 (6.18)	28.83 (5.44)	29.35 (6.64)
Never smoked, n (%)	483 (85)	468 (81)	505 (78)	510 (80)	1966 (81)
Clinical characteristics					
Pre-bronchodilator FEV_1, mL, mean (SD)*	n=569 2573 (720)	n=578 2097 (571)	n=650 1867 (537)	n=637 1625 (492)	n=2434 2023 (677)
Percent-predicted FEV_1 pre-dose, %, mean (SD)†	n=561 72.33 (14.52)	n=575 68.64 (14.80)	n=648 66.47 (14.69)	n=636 65.84 (14.22)	n=2420 68.18 (14.76)
Pre-dose FEV_1/FVC ratio, mean (SD)†	n=561 0.70 (0.12)	n=575 0.66 (0.11)	n=648 0.63 (0.12)	n=636 0.61 (0.12)	n=2420 0.65 (0.12)
ACQ-7 score, mean (SD)†	n=564 2.02 (0.72)	n=563 2.09 (0.74)	n=634 2.20 (0.69)	n=622 2.16 (0.66)	n=2383 2.12 (0.70)
Pre-study ICS – patients on medium dose at screening*, n (%)	395 (69)	376 (65)	421 (65)	429 (67)	1621 (67)

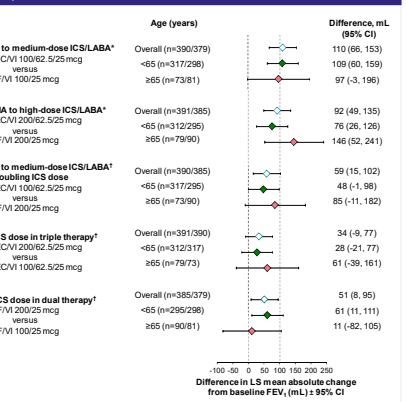
N numbers include patients in 31.25 mcg UMEC-containing groups. *The last acceptable/borderline acceptable pre-dose FEV_1 prior to randomized treatment start date; †at randomization; ‡medium dose defined as >250 to ≤500 µg/day FP (or equivalent). BMI, body mass index; FVC, forced vital capacity; SD, standard deviation.

Figure 2. LS mean change from baseline in trough FEV_1 at Week 24 in overall ITT population (N=2436)



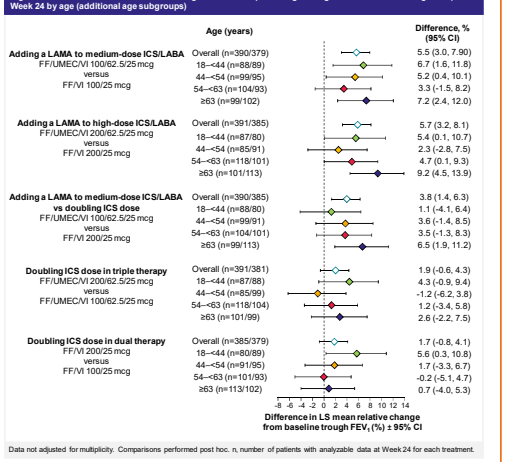
P-values were adjusted for multiplicity. Baseline values were the last acceptable/borderline acceptable pre-dose FEV_1 prior to randomized treatment start date. n=patients with analyzable data at Week 24. All doses are mcg. All analyses were prespecified.
CI, confidence intervals; LS, least squares. Modified from Lee et al. 2020.[1]

Figure 3. Effects of different treatment strategies on absolute change from baseline in trough FEV_1 at Week 24 by age (<65, ≥65 years)



Data were not adjusted for multiplicity. *Comparison was pre-specified for trough FEV_1; †comparison was performed post hoc.
Data were not adjusted for multiplicity. n, number of patients with analyzable data at Week 24 by treatment. LAMA, long-acting muscarinic antagonist. Figure modified from Boulet et al. ERS 2020.[2]

Figure 4. Effects of different treatment strategies on relative percentage change from baseline in trough FEV_1 at Week 24 by age (additional age subgroups)



Data not adjusted for multiplicity. Comparisons performed post hoc. n, number of patients with analyzable data at Week 24 for each treatment.

Conclusions

- Adding UMEC to FF/VI improved lung function regardless of age.
- Doubling the dose of FF appeared to have less of an impact than adding UMEC in older patients, whilst younger patients (18–<44) saw similar benefits from both treatment strategies.
- These findings are consistent with the previous subgroup analysis,[2] with the additional findings that younger patients appear to have greater improvements in lung function from doubling their dose of ICS than their older counterparts.
- Furthermore, these data suggest that younger patients may benefit from either a step up to triple therapy or doubling their ICS dose, whilst older patients may benefit more from triple therapy.
- Overall, this subgroup analysis of the CAPTAIN study suggests that patient age could be considered when tailoring treatment via a personalized medicine approach.

Disclosures

- This study was funded by GlaxoSmithKline GSK (205715/NCT02924688).
- Ellipta and Diskus are owned by or licensed to the GSK Group of Companies.
- Figure 1 is reprinted from *The Lancet Respiratory Medicine*, Lee LA et al. Efficacy and safety of once-daily single-inhaler triple therapy (FF/UMEC/VI) versus FF/VI in patients with inadequately controlled asthma (CAPTAIN): a double-blind, randomised, phase 3A trial [Epub ahead of print]. Copyright (2020), with permission from Elsevier.
- On behalf of all authors, a video recording of this poster was prepared by Nicola Hanania, who did not receive any payment for this recording.
- NAH: reports receiving personal fees from AstraZeneca, Genentech, Sanofi Genzyme, GSK, Mylan, Novartis, and Regeneron for serving as an advisor or consultant. He also received research support from AstraZeneca, Boehringer Ingelheim, Novartis, Sanofi Genzyme, Genentech, and GSK. KS: advisory board for BioCryst, clinical trial payments from Biocryst, AstraZeneca, GSK, Pearl, 3M, and Watson. VM: has received speaker honorarium fees from AstraZeneca, Boehringer Ingelheim, GSK, Regeneron, and Sanofi Genzyme. He has also received clinical trial payments from AstraZeneca, GSK, Novartis, Regeneron, and Sanofi Genzyme. DN: has received personal fees from GSK and Mylan for serving on advisory boards, and as speaker. Has participated in paid pharmaceutical research with GSK, AstraZeneca, Novartis, Boehringer Ingelheim, Mylan, Genentech, and Sanofi Genzyme. NL: has attended advisory boards for AstraZeneca, GSK, Genentech, Novartis, Teva, and Sanofi. She has participated in clinical trials for which the institution received funding from AstraZeneca, GSK, and Sanofi. She has a consultancy agreement with AstraZeneca. ZB, NB, and FG are employees of and own stocks and shares in GSK. DM is a former employee of GSK and owns stocks and shares in GSK. HAMK: his institution has received research/educational grants and fees for serving on advisory boards for Boehringer Ingelheim, GSK, Novartis, Chiesi, and AstraZeneca.

Acknowledgments

Editorial support (in the form of writing assistance, including development of the initial draft based on author direction, assembling tables and figures, collating authors' comments, grammatical editing, and referencing) was provided by Rebecca Dawson, PhD, at Fishawack Indicia Ltd, and was funded by GSK.

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CAPTAIN TRIAL

Prepared for the American College of Allergy, Asthma & Immunology Annual Meeting (2020)