# CAPTAIN Study: Effect of Baseline Lung Function on Response to Triple Therapy in Patients With Asthma Inadequately Controlled on Inhaled Corticosteroid/Long-acting $\beta_2$-agonist Therapy

**Poster No. P1483**


Nathan R[1*], Boulet L-P[2], Kerstjens HA[3], Papi A[4], Pavord ID[5], Hanania NA[6], Oppenheimer J[7], Maselli DJ[8], Liu MC[9], Weinstein S[10], Mannino D[11*], Peachey G[12], Zarankaite A[12], Sule N[13], Fowler A[12], Lee L[13*], Kerwin E[14]

[1]Asthma and Allergy Associates, P. C. and Research Center, Colorado Springs, CO, USA; [2]Laval University, Quebec, Canada; [3]University of Groningen and University Medical Center Groningen, Groningen, the Netherlands; [4]University of Ferrara, Ferrara, Italy; [5]University of Oxford, Oxford, UK; [6]Baylor College of Medicine, Houston, TX, USA; [7]Rutgers New Jersey Medical School, Newark, NJ, USA; [8]University of Texas Health at San Antonio, San Antonio, TX, USA; [9]Johns Hopkins Asthma and Allergy Center, Baltimore, MD, USA; [10]Allergy and Asthma Specialists Medical Group and Research Center, Huntington Beach, CA, USA; [11]GSK Research Triangle Park, NC, USA; [12]GSK, Stockley Park West, Uxbridge, Middlesex, UK; [13]GSK, Collegeville, PA, USA; [14]Crisor LLC Research, Clinical Research Institute of Southern Oregon, Medford, OR, USA

*Affiliation at time of study


## Background

- Approximately 30%–50% of patients with asthma remain uncontrolled, despite adherence to inhaled corticosteroid/long-acting $\beta_2$-agonist (ICS/LABA) therapy.[1–4]
- Adding a long-acting muscarinic antagonist (LAMA) to ICS/LABA has been shown to improve lung function and reduce exacerbation rates in patients with asthma.[5,6]
- The CAPTAIN study showed improved lung function and asthma control, and numerical reductions in the annualized rate of moderate/severe asthma exacerbations with fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI) versus FF/VI in patients with asthma inadequately controlled on medium–high-dose ICS (daily fluticasone propionate >250 mcg or equivalent)/LABA.[7] There were no new or unexpected safety findings.
- Data from the CAPTAIN study also suggested that treatment outcomes may differ according to patient characteristics at baseline, including the presence of type 2 inflammation.[7]
- The evidence regarding the influence of baseline lung function on response to LAMA therapy is not consistent[8,9], hence this analysis was conducted to investigate the effect of adding UMEC to FF/VI on asthma outcomes for patient subgroups defined according to baseline lung function.

## Aims

- The objective of this prespecified subgroup analysis of CAPTAIN was to investigate the effects of adding UMEC 62.5 mcg to FF (100 and 200 mcg)/VI 25 mcg on lung function, moderate/severe exacerbations and asthma control according to subgroups defined by baseline lung function.

## Methods

- CAPTAIN was a Phase IIIA, randomized, 24–52-week, parallel-group study (GSK study 205715, NCT02924688; **Figure 1**).

**Figure 1. CAPTAIN study design**

**Key inclusion criteria**

- ≥18 years of age
- Pre-bronchodilator $FEV_1$ predicted ≥30%–<85% at screening
- ACQ-6 score ≥1.5 at screening
- Receiving ICS/LABA therapy (daily FP >250 mcg or equivalent)
- Documented healthcare contact or temporary change in asthma therapy for treatment of acute asthma symptoms in the year prior to screening

**Key exclusion criteria**

- Patients with COPD or other respiratory disorders, including pneumonia and pneumonia risk factors
- Current smokers and former smokers with a smoking history of ≥10 pack years

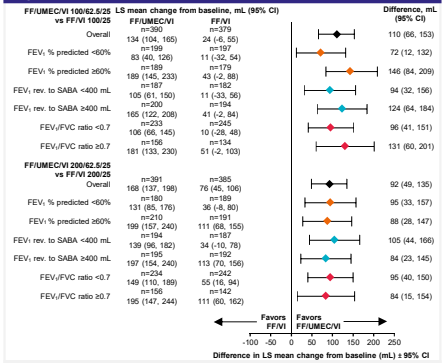
| Week | Period | Treatment |
|---|---|---|
| **Week -5**<br>Weeks -5–-2 | **Visit 1: Screening**<br>3-week run-in period | FP/SAL 250/50 mcg |
| **Week -2**<br>Weeks -2–0 | **Visit 2: Enrollment**<br>2-week stabilization period | FF/VI 100/25 mcg |
| **Week 0**<br>Weeks 0–24 | **Visit 3: Randomization**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

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; twice daily; COPD, chronic obstructive pulmonary disease; DPI, dry powder inhaler; $FEV_1$, forced expiratory volume in 1 second; FP, fluticasone propionate; QD, once daily; SAL, salmeterol.

- Here we report pre-specified analyses of CAPTAIN for the overall population and for subgroups defined according to baseline lung function ($FEV_1$ <60/≥60% predicted; $FEV_1$ reversibility to short-acting $\beta_2$-agonist (SABA) <400/≥400 mL; $FEV_1$/forced vital capacity (FVC) ratio <0.7/≥0.7).
- Endpoints reported here are:
  - Change from baseline in trough $FEV_1$ at Week 24 (primary endpoint) analyzed using a mixed model repeated measures model
  - Annualized rate of moderate/severe asthma exacerbations (Weeks 1–52; key secondary endpoint) analyzed using a negative binomial model. *P*-values were not adjusted for multiplicity
  - Percentage of ACQ-7 responders at Week 24 analyzed using a generalized linear mixed model with a logit link function.
- For the overall analyses of the primary and key secondary endpoints, a step-down closed-testing hierarchy was used to account for multiplicity across endpoints and UMEC doses.
  - The overall ACQ-7 responder analysis and the subgroup analyses were not adjusted for multiplicity.
  - Data for UMEC 62.5 mcg only are shown here.

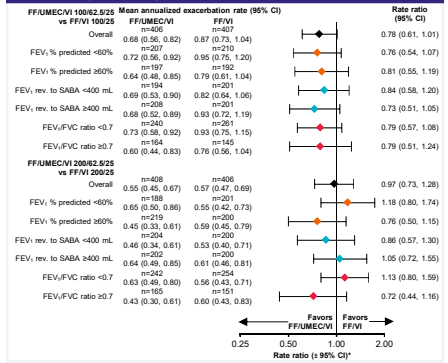
## Results

**Figure 2. Effects of adding UMEC to FF/VI on trough $FEV_1$ at Week 24, by baseline lung function**



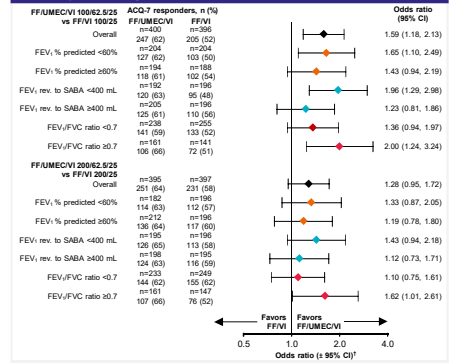

n = number of patients with analyzable data at Week 24 by treatment.
CI, confidence interval; LS, least squares.

**Figure 3. Effects of adding UMEC to FF/VI on annualized rate of moderate/severe asthma exacerbations by baseline lung function**




*Note that the x-axis has been log transformed. n = number of patients with analyzable data by treatment.

**Figure 4. Effects of adding UMEC to FF/VI on percentage of ACQ-7 responders* at Week 24, by baseline lung function**




*Defined as a ≥0.5-point improvement (decrease) from baseline in ACQ-7 total score; †note that the x-axis has been log transformed. n = number of patients with analyzable data at Week 24 by treatment.

**Table 1. Baseline demographics and disease characteristics**

| | Overall N=2436 | $FEV_1$ % predicted | | $FEV_1$ reversibility to SABA | | $FEV_1$/FVC ratio | |
|---|---|---|---|---|---|---|---|
| | | <60% N=1235 | ≥60% N=1188 | <400 mL N=1175 | ≥400 mL N=1243 | <0.7 N=1475 | ≥0.7 N=955 |
| **Demographics** | | | | | | | |
| **Age, years, mean (SD)** | 53.2 (13.11) | 54.6 (12.51) | 51.7 (13.55) | 57.3 (11.72) | 49.4 (13.17) | 55.8 (12.11) | 49.2 (13.55) |
| **Male, n (%)** | 922 (38) | 477 (39) | 440 (37) | 324 (28) | 590 (47) | 633 (43) | 286 (30) |
| **BMI, kg/m², mean (SD)** | 29.4 (6.64) | 29.9 (6.82) | 28.8 (6.40) | 29.5 (7.11) | 29.2 (6.15) | 28.9 (6.25) | 30.0 (7.12) |
| **Disease characteristics** | | | | | | | |
| **Pre-study ICS dose*** | | | | | | | |
| Medium dose, n (%) | 1621 (67) | 759 (61) | 851 (72) | 745 (63) | 861 (69) | 926 (63) | 691 (72) |
| High dose, n (%) | 815 (33) | 476 (39) | 337 (28) | 430 (37) | 382 (31) | 549 (37) | 264 (28) |
| **Reversibility to salbutamol*, %, mean (SD)** | (n=2418) 29.92 (18.12) | (n=1234) 36.70 (20.60) | (n=1184) 22.86 (11.43) | (n=1175) 20.45 (7.39) | (n=1243) 38.88 (20.55) | (n=1471) 30.48 (17.49) | (n=947) 29.05 (19.03) |
| **Pre-bronchodilator $FEV_1$, mL, mean (SD)†** | (n=2420) 2023 (678) | (n=1232) 1764 (610) | (n=1177) 2289 (639) | (n=1169) 1730 (505) | (n=1236) 2293 (704) | (n=1471) 1860 (624) | (n=945) 2273 (682) |
| **Pre-bronchodilator $FEV_1$, % predicted, mean (SD)†** | (n=2420) 68.18 (14.76) | (n=1232) 60.27 (13.55) | (n=1177) 76.39 (11.03) | (n=1169) 64.83 (14.11) | (n=1236) 71.26 (14.72) | (n=1471) 63.46 (14.11) | (n=945) 75.48 (12.63) |
| **Pre-bronchodilator $FEV_1$/FVC ratio, mean (SD)†** | (n=2420) 0.65 (0.12) | (n=1232) 0.60 (0.12) | (n=1177) 0.70 (0.10) | (n=1169) 0.63 (0.12) | (n=1236) 0.66 (0.12) | (n=1471) 0.58 (0.09) | (n=945) 0.75 (0.08) |
| **ACQ-7 score, mean (SD)†** | (n=2383) 2.1 (0.70) | (n=1206) 2.3 (0.70) | (n=1165) 1.9 (0.66) | (n=1144) 2.2 (0.68) | (n=1223) 2.1 (0.72) | (n=1444) 2.2 (0.70) | (n=935) 2.0 (0.68) |

*At screening; medium dose defined as >250 to ≤500 mcg/day FP (or equivalent), high dose defined as >500 mcg/day FP (or equivalent); †at randomization. BMI, body mass index; SD, standard deviation.

- A total of 2436 participants were included in the overall intent-to-treat population. The mean age and proportion of patients on high-dose ICS before the start of the study were higher in the subgroups with poorer baseline lung function or bronchodilator response. In contrast, ACQ-7 score did not differ markedly across subgroups (**Table 1**).
- Similar improvements in trough $FEV_1$ to the overall population were observed following the addition of UMEC to FF/VI 100/25 mcg or 200/25 mcg in all subgroups (**Figure 2**).
- FF/UMEC/VI 100/62.5/25 mcg was associated with numerical reductions in the annualized rate of moderate/severe asthma exacerbations versus FF/VI 100/25 mcg in all subgroups. For the FF 200 mcg dose comparisons, there was no reduction in the overall population and no clear pattern of response in the subgroups (**Figure 3**).
- For ACQ-7 response, trends were seen favoring the addition of UMEC to FF/VI 100/25 mcg or 200/25 mcg in the overall population and across all subgroups (**Figure 4**).

### Conclusions

- The pattern of response observed in the subgroups was consistent with that seen in the overall population.
- Improvements in trough $FEV_1$ and trends for increases in ACQ-7 response following addition of UMEC to FF/VI 100/25 mcg or 200/25 mcg, and numerical reductions in the annualized rate of moderate/severe asthma exacerbations following addition of UMEC to FF/VI 100/25 mcg, were independent of baseline lung function and bronchodilator response.
- These data suggest that patients whose asthma is inadequately controlled on ICS/LABA benefit from the addition of UMEC in FF/UMEC/VI triple therapy irrespective of baseline lung function.


### Disclosures

- This study was funded by GlaxoSmithKline (GSK; study number 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 Robert Nathan, who did not receive any payment for this recording.
- AF, AZ and NS are employees of GSK and hold stocks/shares in GSK. GP is an employee of GSK and holds stocks/shares in GSK and Novartis. DM and LL were employees of GSK at the time of the study and hold stocks in GSK. RN is a non-paid instructor and clinical professor at the University of Colorado Health Sciences Center (Denver CO, USA); was an employee of Asthma and Allergy Associates, PC and Research Center at the time of the study; and has received speaker's fees and honoraria for advisory boards for GSK and Boehringer Ingelheim. L-PB has received research grants for participation to multicenter studies from AstraZeneca, Boston Scientific, GSK, Hoffman La Roche, Novartis, Ono Pharma, Sanofi, and Takeda, and support for research projects introduced by the investigator from AstraZeneca, Boehringer Ingelheim, GSK, Merck, and Takeda. L-PB has also received fees for consulting and advisory boards from AstraZeneca, Novartis, and Methapharm, non-profit grants for the production of educational materials from AstraZeneca, Boehringer Ingelheim, GSK, Merck, and Novartis, conference fees from AstraZeneca, GSK, Merck, and Novartis, and support for participation in conferences and meetings from Novartis, Takeda, and Teva. HAK has received research or educational grants and served on advisory boards for Boehringer Ingelheim, GSK, and Novartis, and has served on advisory boards for Chiesi, AstraZeneca, and Fluidda. AP has received research grants and personal fees from Chiesi, GSK and Teva, and personal fees from AstraZeneca, Boehringer Ingelheim, Menarini, Merck Sharp & Dohme, Mundipharma, Novartis, Sanofi, and Zambon. IDP 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 and 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 also received speaker fees or fees for advisory boards from Circassia, Knopp, Merck, Mundipharma, Novartis, Roche/Genentech, and Sanofi/Regeneron. NAH reports personal fees from AstraZeneca, Boehringer Ingelheim, Genentech, GSK, Mylan, Novartis, Regeneron and Sanofi Genzyme for serving as an advisor or consultant. He also received research support from AstraZeneca, Boehringer Ingelheim, Gossamer Bio, Genentech, GSK, Sanofi Genzyme, and Novartis. JO has served on adjudication committees or data and safety monitoring boards for AstraZeneca, GSK, Novartis, and Sanofi/Regeneron, and has received grants and personal fees from GSK. DJM reports fees from AstraZeneca, GSK, Novartis, Sanofi/Regeneron and Sunovion for advisory boards and speaking. MCL received research grants from GSK, Boehringer Ingelheim, and Gossamer Bio and served on advisory boards for GSK. SW received research grants from AstraZeneca, Boehringer Ingelheim, Chiesi, GSK, Novartis, and Teva. EK is an employee of Crisor Research; has served on advisory boards, speaker panels, or received travel reimbursement from Amphastar, AstraZeneca, Boehringer Ingelheim, Cipla, Chiesi, Forest, GSK, Mylan, Novartis, Pearl, Sunovion, Teva, and Theravance; and has also conducted multicentre clinical research trials for approximately 40 pharmaceutical companies.

### Acknowledgements

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 Fishawack Indicia Ltd, UK, and was funded by GSK.



### References

1. Bernstein DI, et al. *J Asthma* 2015;52:1073–83.
2. Lee LK, et al. *J Asthma* 2018;55:208–19.
3. Sulaiman I, et al. *Eur Respir J* 2018;51:1701126.
4. Davis J, et al. *J Asthma* 2019;56:332–40.
5. Virchow JC, et al. *Lancet* 2019;394:1737–49.
6. Kerstjens HA, et al. *N Engl J Med* 2012;367:1198–207.
7. Lee LA, et al. *Lancet Respir Med* 2020 [Epub ahead of print].
8. Peters SP, et al. *J Allergy Clin Immunol* 2013;132:1068–74.
9. Casale TB, et al. *Respir Med* 2019;158:97–109.


Scan the QR code or click on http://tago.ca/CHEST_15 to access a downloadable version of this poster, a version that has been formatted for online viewing, and the associated audio recording.


Prepared for the American College of Chest Physicians Congress (2020)