Scan the QR code or click on
http://tago.ca/CHEST_14 to access a
downloadable version of these slides

CHEST®

CAPTAIN Study: Association of Moderate and Severe Asthma Exacerbations With Lung Function and Patient-reported Outcomes in a Large Randomized Phase III Clinical Trial

Sule N[1], Fowler A[2], Kerstjens HA[3], Kerwin E[4], Lee L[1]*, Nathan R[5]*, Oppenheimer J[6], Pavord ID[7], Peachey G[2], Tabberer M[2], Zarankaite A[2], Manning ME[8], Mannino D[9]*, **Hanania NA[10]**

[1]GSK, Collegeville, PA, USA; [2]GSK, Stockley Park West, Uxbridge, Middlesex, UK;
[3]University of Groningen and University Medical Center Groningen, Groningen, the Netherlands;
[4]Crisor LLC Research, Clinical Research Institute of Southern Oregon, Medford, OR, USA;
[5]Asthma & Allergy Associates, P.C. and Research Center, Colorado Springs, CO, USA;
[6]Rutgers New Jersey Medical School, Newark, NJ, USA; [7]University of Oxford, Oxford, UK;
[8]Allergy, Asthma and Immunology Associates, Scottsdale, AZ, USA; [9]GSK Research Triangle Park, NC, USA;
[10]Baylor College of Medicine, Houston, TX, USA
*Affiliation at time of study

Disclosures and acknowledgments

- The presenting author, Nicola A Hanania, 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

- The authors wish to thank Dr Mark Millard for his contributions to the development of the associated abstract and contributions to data acquisition. Editorial support in the form of writing assistance (including assembling tables and figures, and slide formatting) was provided by Lucia Correia, PhD, at Fishawack Indicia Ltd, UK, and was funded by GSK

- The CAPTAIN study was funded by GSK (205715; clinicaltrials.gov ID: NCT02924688)

Introduction

- Approximately 10%–25% of patients classified as GINA Step 3 or higher experience an exacerbation within a 1-year period[1–3]
- Asthma exacerbations are adversely associated with patients' lung function, symptom control, HRQoL; whether the extent of this association differs according to exacerbation severity is poorly understood[4,5]
- Moderate exacerbations have been reported to occur more frequently, and individually, may have higher mean unit costs than non-hospitalized severe exacerbations[6,7]; additionally, severe exacerbations are often preceded by moderate events, suggesting that early intervention may be valuable[6]
- The Phase IIIA CAPTAIN study evaluated single-inhaler FF/UMEC/VI in patients with uncontrolled asthma on ICS/LABA[8]
  - Dose-related numerical reductions in the annualized rate of moderate and/or severe asthma exacerbations were observed in patients given FF 100/UMEC 62.5 or 31.25/VI 25 mcg compared with those given FF/VI 100/25 mcg

The objective of the descriptive summaries of the CAPTAIN study presented here was to assess lung function, disease control, and HRQoL associated with patients' experience of post-randomization asthma exacerbations over a 24-week period

FF, fluticasone furoate; GINA, Global Initiative for Asthma; HRQoL, health-related quality of life; ICS, inhaled corticosteroid; LABA, long-acting β_2-agonist; UMEC, umeclidinium; VI, vilanterol

1. Global Initiative for Asthma (GINA) 2020 report. Available at: https://ginasthma.org/gina-reports/ [last accessed September 2020]; 2. Suruki RY, et al. *BMC Pulm Med* 2017;17:74; 3. Zeiger RS, et al. *J Allergy Clin Immunol Pract* 2014;2:741–50; 4. Virchow JC, et al. *Respir Med* 2015;109:547–56; 5. Reddel HK, et al. *Am J Respir Crit Care Med* 2009;180:59–99; 6. Lane SJ, et al. *J Asthma* 2013;50:642–8; 7. Gutiérrez JFA, et al. *BMC Pulm Med* 2017;17:77; 8. Lee L, et al. *Lancet Respir Med* 2020 [Epub ahead of print]

Study design

Week	Period	Treatment
Week -5 Weeks -5–-2	**Visit 1: Screening** 3-week run-in period	FP/SAL 250/50 mcg
Week -2 Weeks -2–0	**Visit 2: Enrollment** 2-week stabilization period	FF/VI 100/25 mcg
Week 0 Weeks 0–24	**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 24–52	**Primary endpoint** 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. Ellipta and Diskus are owned by or licensed to the GSK group of companies. 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
BID; twice daily; DPI, dry powder inhaler; FF, fluticasone furoate; FP, fluticasone propionate; QD, once daily; SAL, salmeterol, UMEC, umeclidinium; VI, vilanterol

Descriptive summaries

Here we report the occurrence and severity of post-randomization asthma exacerbations (none, moderate only, severe only), on- and post-treatment, in relation to clinic trough FEV_1, FEV_1 % predicted, ACQ-6, and SGRQ at Weeks 12 and 24*

- Moderate exacerbations defined as asthma worsening requiring physician-directed temporary change in maintenance therapy;† severe exacerbations defined as requiring systemic steroids for ≥3 days, or an ED visit or hospitalization requiring systemic steroids†
- All summary data presented here were produced independent of treatment and summarized the overall CAPTAIN population according to the patient's experience of post-randomization, on- and post-treatment, asthma exacerbations, over Weeks 1–24

Eligibility criteria

Key inclusion criteria[1]

- ≥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/temporary change in therapy for treatment of acute asthma symptoms in the year prior to screening

Key exclusion criteria[1]

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

*Summaries for trough FEV_1, ACQ-6, and SGRQ were all pre-specified; summary of FEV_1 % predicted was performed post hoc; †consistent with ATS/ERS guidelines[2,3]

ACQ, Asthma Control Questionnaire; COPD, chronic obstructive pulmonary disease; ED, emergency department; FEV_1, forced expiratory volume in 1 second; FP, fluticasone propionate; ICS, inhaled corticosteroid; LABA, long-acting β_2-agonist; SGRQ, St George's Respiratory Questionnaire

1. Lee L, et al. *Lancet Respir Med* 2020 [Epub ahead of print]; 2. Virchow JC, et al. *Respir Med* 2015;109:547–56; 3. Reddel HK, et al. *Am J Respir Crit Care Med* 2009;180:59–99

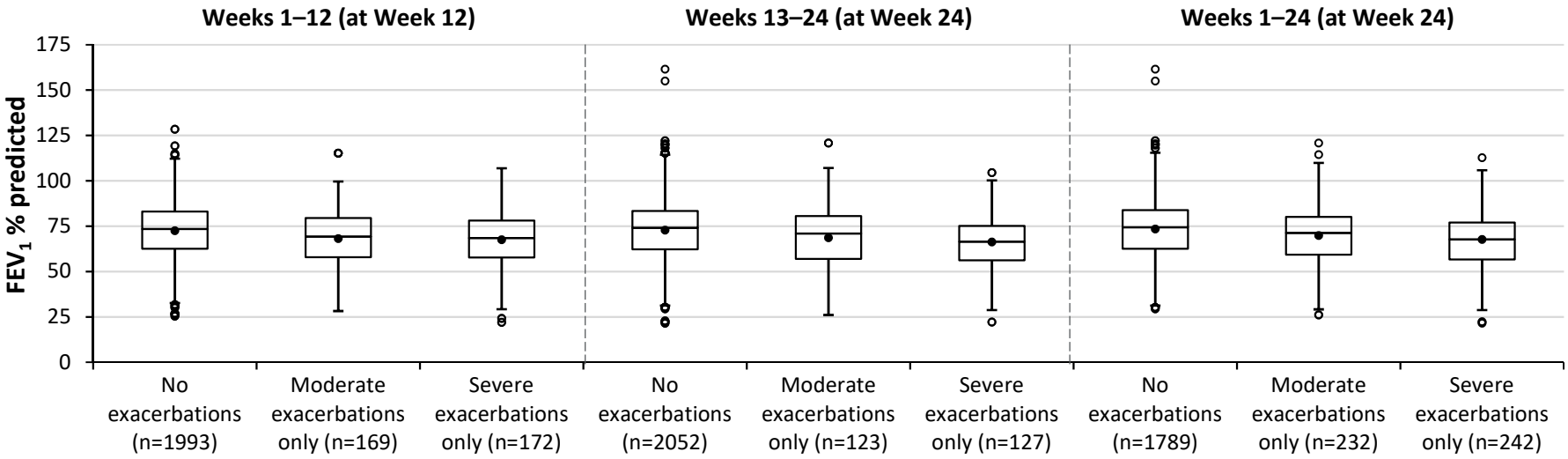
Baseline characteristics according to on- and post-treatment exacerbations over Weeks 1–24 (ITT population)

	No exacerbations (N=1881)	Moderate exacerbations only (N=244)	Severe exacerbations only (N=260)	Both moderate and severe exacerbations* (N=51)	Total (N=2436)
Age (years), mean (SD)	52.8 (13.38)	53.2 (12.52)	55.3 (12.03)	56.0 (9.56)	53.2 (13.11)
Total number of exacerbations 1 year prior to screening, n (%) 0 1 ≥2	 307 (16) 1098 (58) 476 (25)	 25 (10) 130 (53) 89 (36)	 27 (10) 136 (52) 97 (37)	 5 (10) 26 (51) 20 (39)	 364 (15) 1390 (57) 682 (28)
Clinic trough FEV_1 (mL), mean (SD)	(n=1879) 2065 (692)	(n=244) 1936 (612)	(n=260) 1861 (604)	(n=51) 1722 (535)	(n=2434) 2023 (677)
FEV_1 % predicted, mean (SD)	(n=1879) 69.0 (14.64)	(n=244) 66.2 (14.68)	(n=260) 65.5 (14.59)	(n=51) 61.6 (15.46)	(n=2434) 68.2 (14.74)
ACQ-6 total score, mean (SD)	(n=1867) 1.9 (0.73)	(n=244) 1.9 (0.75)	(n=259) 1.9 (0.74)	(n=51) 2.3 (0.73)	(n=2421) 1.9 (0.73)
SGRQ total score, mean (SD)	(n=1865) 38.5 (17.74)	(n=244) 40.8 (17.18)	(n=257) 43.7 (18.21)	(n=51) 53.1 (16.02)	(n=2417) 39.5 (17.88)

*Encompasses patients who had ≥1 moderate and ≥1 severe asthma exacerbation during the treatment period

ACQ, Asthma Control Questionnaire; FEV_1, forced expiratory volume in 1 second; ITT, intent-to-treat; SD, standard deviation; SGRQ, St George's Respiratory Questionnaire

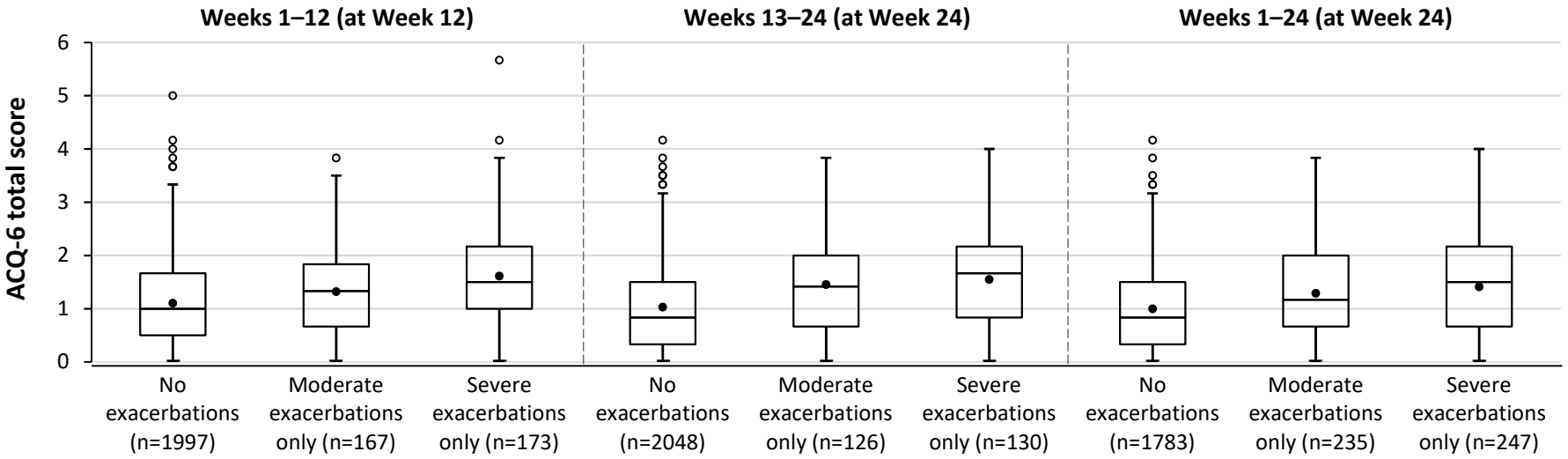
FEV_1 % predicted by patients' experience of post-randomization asthma exacerbations



- Mean FEV_1 % predicted appeared to be slightly higher in patients with no exacerbations compared with those who experienced moderate exacerbations only or severe exacerbations only
- Similar patterns were also seen with respect to clinic trough FEV_1 (L):
  - Median (IQR) at Week 24: 2.10 L (1.67, 2.66) for patients with no exacerbations vs 1.99 L (1.61, 2.39) and 1.84 L [1.50, 2.24]) for patients with moderate exacerbations only or severe exacerbations only, respectively

FEV_1, forced expiratory volume in 1 second; n corresponds to the number of subjects with analyzable data at the given time point for each group. Box plot displays the mean (filled circle), median (center line) and interquartile range (IQR). Whiskers are shown at the maximum/minimum observation within 1.5*IQR of the upper/lower quartiles, respectively, with open circles denoting observations outside this range.
Note: the same set of subjects is included in each time period

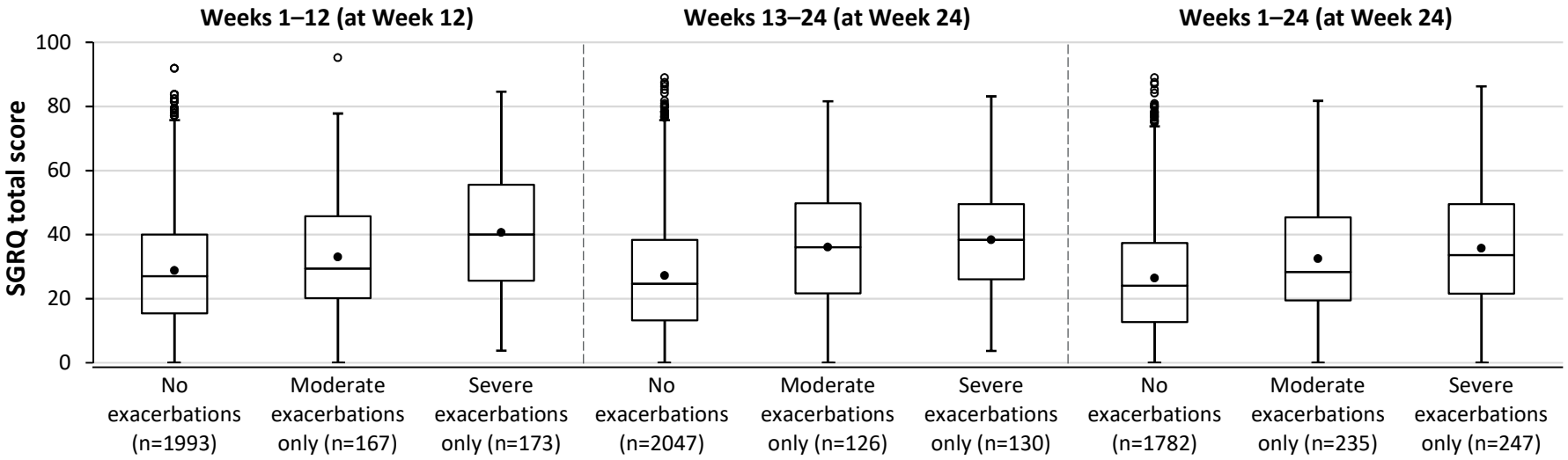
ACQ-6 total score by patients' experience of post-randomization asthma exacerbations



- ACQ-6 total scores were lower in patients with no exacerbations vs those who experienced moderate exacerbations only or severe exacerbations only
- ACQ-6 total scores were generally higher in patients with severe exacerbations only vs those who experienced moderate exacerbations only
- Observations were generally similar across Weeks 1–12 and Weeks 13–24

ACQ-6, Asthma Control Questionnaire; n corresponds to the number of subjects with analyzable data at the given time point for each group. Box plot displays the mean (filled circle), median (center line) and interquartile range (IQR). Whiskers are shown at the maximum/minimum observation within 1.5*IQR of the upper/lower quartiles, respectively, with open circles denoting observations outside this range.
Note: the same set of subjects is included in each time period

SGRQ total score by patients' experience of post-randomization asthma exacerbations



- SGRQ total scores were lower in patients with no exacerbations vs those who experienced moderate exacerbations only or severe exacerbations only
- SGRQ total scores were generally higher in patients with severe exacerbations only vs those who experienced moderate exacerbations only
- Observations were generally similar across Weeks 1–12 and Weeks 13–24

SGRQ, St George's Respiratory Questionnaire; n corresponds to the number of subjects with analyzable data at the given time point for each group. Box plot displays the mean (filled circle), median (center line) and interquartile range (IQR). Whiskers are shown at the maximum/minimum observation within 1.5*IQR of the upper/lower quartiles, respectively, with open circles denoting observations outside this range. Note: the same set of subjects is included in each time period

Conclusions

- Patients who experienced a moderate only or severe only exacerbation appeared to have poorer lung function, symptom control, and HRQoL compared with patients who did not experience an exacerbation
- At baseline, the group of patients with both at least one moderate **and** at least one severe asthma exacerbation (on- or post-treatment) had the poorest lung function, asthma control, and HRQoL. However, this subgroup was small (n=51), and requires additional investigation in a larger population
- Both moderate and severe exacerbations, comprised of both clinical and functional changes, negatively impact HRQoL and asthma control

Scan the QR code or click on http://tago.ca/CHEST_14 to access a downloadable version of these slides

Note: A separate analysis evaluating the influence of lung function impairment at baseline (defined according to FEV_1/FVC ratio) on treatment outcomes in the CAPTAIN study will also be reported at this CHEST Annual Meeting[1]

FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; HRQoL, health-related quality of life

1. Nathan R, et al. CAPTAIN Study: Effect of baseline lung function on response to triple therapy in patients with asthma inadequately controlled on inhaled corticosteroid/long-acting β_2-agonist therapy; presented at the CHEST Annual Meeting, October 18–21 2020

Co-author disclosures

- NS, AF, MT, and AZ are employees of GSK and hold stocks/shares in GSK; GP is an employee of GSK and holds stocks/shares in GSK and Novartis; LL and DM were employees of GSK at the time of the study and hold stocks in GSK; 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; 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 multicenter clinical research trials for approximately 40 pharmaceutical companies; 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; 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; 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; MEM received research grant support from Aimmune, BioCryst, CSL Behring, Dyax, Genentech, GSK, Merck, Novartis, Sanofi, Shire, Takeda, and Teva; and consultant/advisor/speakers bureau for Aimmune, AstraZeneca, BioCryst, CSL Behring, Genentech, GSK, Pharming, Sanofi/Regeneron and Takeda