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CAPTAIN: Effects of Asthma Onset in Childhood Versus Adulthood on Response to Triple Therapy in Patients With Inadequately Controlled Asthma on Inhaled Corticosteroid/Long-acting β_2-agonist

Busse W[1], Abbott CB[2], Chang S[2], Crawford J[3], Maselli DJ[4], Nathan R[5], Stanaland MD[2], Kerwin E[6]**

[1]University of Wisconsin School of Medicine and Public Health, Madison, WI, USA; [2]GSK, Research Triangle Park, NC, USA; [3]GSK, Brentford, UK; [4]University of Texas Health at San Antonio, San Antonio, TX, USA; [5]Asthma and Allergy Associates, P. C. and Research Center, Colorado Springs, CO, USA; [6]Crisor LLC Research, Clinical Research Institute of Southern Oregon, Medford, OR, USA. *At the time of the study

Recording by William Busse

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DISCLOSURES

- This study was funded by GlaxoSmithKline (GSK ID: 205715; NCT02924688).
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Objectives and methods

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INTRODUCTION AND OBJECTIVES

- The CAPTAIN study showed that adding umeclidinium (UMEC) to fluticasone furoate/vilanterol (FF/VI) improved lung function and symptom control in patients with uncontrolled asthma despite ICS/LABA therapy.[1]
- Response to inhaled therapy may vary according to the age at which a patient develops asthma.[2]
- We evaluated the effects of adding UMEC, increasing FF dose, or simultaneous step-up (addition of UMEC and increase in FF dose) on lung function, moderate/severe exacerbation rates, and asthma control according to the age of asthma onset (<18 vs ≥18 years [childhood- vs adult-onset]) by performing post hoc analyses of data from the CAPTAIN study (N=2436) (205715; NCT02924688).

METHODS

Week	Period	Treatment
Week −5 Weeks −5 to −2	**Visit 1: Screening** 3-week run-in period	FP/SAL 250/50 mcg
Week −2 Weeks −2 to 0	**Visit 2: Enrollment** 2-week stabilization period	FF/VI 100/25 mcg
Week 0 Weeks 0 to 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 to 52	**Primary endpoint** Variable treatment period	
	1-week safety follow-up*	

- CAPTAIN was a Phase IIIA, randomized, double-blind, 24–52 week, parallel-group study in adults with inadequately controlled asthma despite ICS/LABA therapy.†
- Here we report post hoc analyses of CAPTAIN for the overall ITT population and for subgroups defined according to age of asthma onset‡: <18 years (childhood-onset) versus ≥18 years (adult-onset). Endpoints:
  - Change from baseline in clinic trough FEV_1 at Week 24 (primary endpoint).
  - Annualized rate of moderate/severe asthma exacerbations (Weeks 1–52; key secondary endpoint).
  - Proportion of ACQ-7 responders at Week 24.
- Data for UMEC 62.5 mcg only are presented here.

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 had a safety follow-up contact approximately 7 days after the End of Study Visit (Week 24, 36, or 52) or Early Withdrawal Visit; †daily FP >250 mcg or equivalent; ‡age of asthma onset was defined as age at pre-screening – duration of asthma.
ACQ, Asthma Control Questionnaire; BID, twice daily; DPI, dry powder inhaler; FF, fluticasone furoate; FP, fluticasone propionate; FEV_1, forced expiratory volume in 1 second; ICS, inhaled corticosteroid; ITT, intent-to-treat; QD, once daily; LABA, long-acting β_2-agonist; SAL, salmeterol

1. Lee LA, et al. Lancet Respir Med 2020; 9:69–84; 2. de Nijs SB, et al. Eur Respir Rev 2013; 22:44–52.
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Baseline demographics and clinical characteristics

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- Baseline lung function was lower in the adult-onset subgroup versus childhood-onset subgroup.
- There were fewer patients with childhood-onset asthma (26.5%) versus adult-onset asthma (73.5%).

	Childhood-onset (N=645)	Adult-onset (N=1790)	Overall (N=2436)
Demographics			
Age, years, mean (SD)	44.2 (13.40)	56.4 (11.39)	53.2 (13.11)
Male, n (%)	286 (44)	636 (36)	922 (38)
BMI, kg/m^2, mean (SD)	29.8 (7.72)	29.2 (6.21)	29.4 (6.64)
Clinical characteristics			
Age of asthma onset, years, mean (SD)	7.3 (5.20)	40.9 (13.02)	32.0 (18.74)
Disease duration, years, mean (SD)	36.8 (14.14)	15.5 (11.23)	21.2 (15.31)
Pre-study ICS – medium dose*, n (%)	427 (66)	1194 (67)	1621 (67)
Pre-bronchodilator FEV_1†, mL, mean (SD)	*n=645* 2243 (755)	*n=1788* 1945 (629)	*n=2434* 2023 (677)
ACQ-7 score‡, mean (SD)	*n=631* 2.1 (0.75)	*n=1751* 2.1 (0.68)	*n=2383* 2.1 (0.70)

*At screening, medium dose defined as >250 to ≤500 µg/day FP (or equivalent); †the last acceptable/borderline acceptable pre-dose FEV_1 prior to randomized treatment start date; ‡at randomization.
ACQ, Asthma Control Questionnaire; BMI, body mass index; FEV_1, forced expiratory volume in 1 second; FP, fluticasone propionate; ICS, inhaled corticosteroid; SD, standard deviation

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Adding UMEC to FF/VI or increasing FF dose led to numerical improvements in trough FEV_1 in both subgroups

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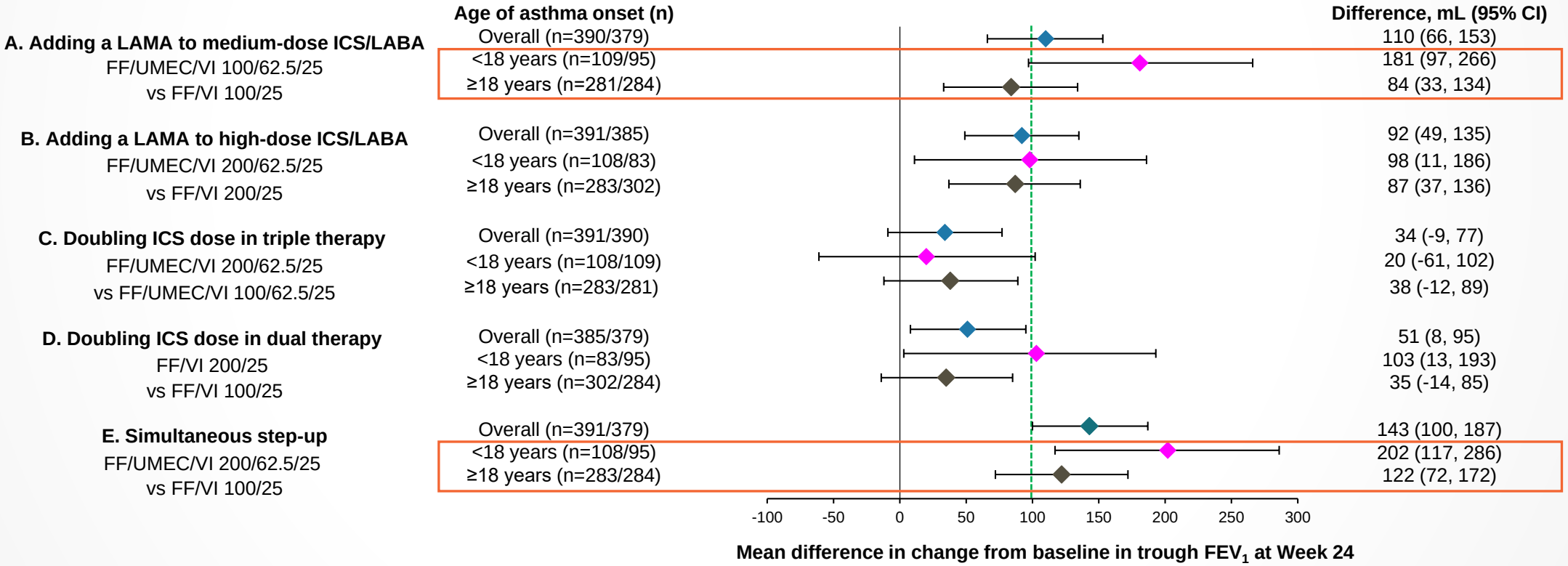
- Addition of UMEC to FF/VI 100/25 mcg (**A**) and simultaneously adding UMEC and doubling FF dose (**E**) led to the largest numerical improvements in airflow in the childhood-onset subgroup (181–202 mL).
- The same treatment approaches also led to airflow improvements of 84–122 mL in the adult-onset subgroup.



Analysis performed using a mixed-model repeated measures (MMRM) model. All doses are mcg. n = number of patients with analyzable data at Week 24 by treatment. Differences meeting the MCID in the positive direction (≥100 mL) are indicated by the vertical dashed green line.

CI, confidence interval; FEV_1, forced expiratory volume in 1 second; FF, fluticasone furoate; ICS, inhaled corticosteroid; LABA, long-acting β_2-agonist; LAMA, long-acting muscarinic antagonist; MCID, minimal clinically important difference; UMEC, umeclidinium, VI, vilanterol

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Adding UMEC and/or increasing FF dose led to decreases in the rate of moderate/severe exacerbations* in the adult-onset group

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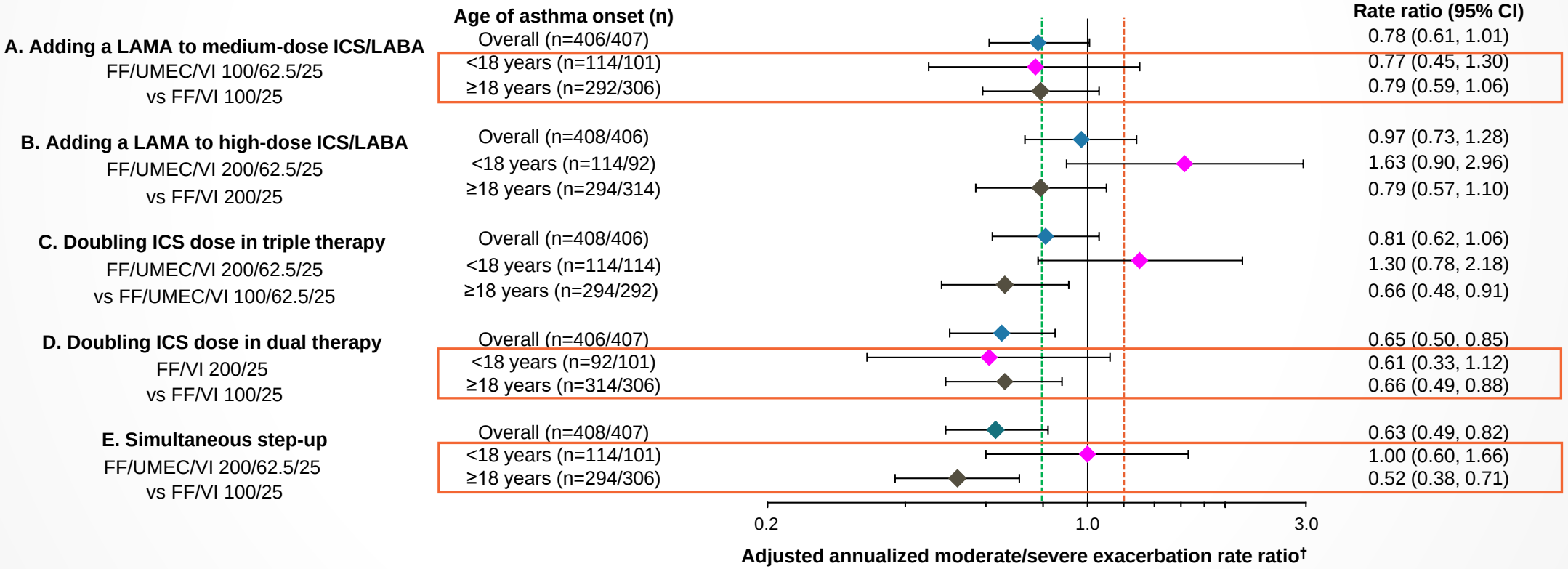
- In the adult-onset subgroup, all treatment strategies led to reductions in exacerbation rates, with simultaneous step-up (**E**) having the greatest impact.
- In the childhood-onset subgroup, adding UMEC to FF/VI 100/25 (**A**) or increasing FF dose in FF/VI 100/25 (**D**) led to reductions in exacerbation rates.



*Moderate asthma exacerbation: a deterioration in either asthma symptoms or lung function, or increased rescue bronchodilator use, that required a physician-directed temporary change in maintenance treatment in order to prevent it from becoming a severe exacerbation; severe asthma exacerbation: a hospitalization or emergency department visit due to asthma requiring systemic corticosteroids, or asthma deterioration requiring systemic corticosteroid use (or doubling of the current maintenance systemic corticosteroid dose) for ≥3 days; †note: the x-axis is on a log scale. Analysis performed using a negative binomial model. All doses are mcg. n = number of patients with analyzable data at Weeks 1–52 by treatment. Differences meeting the MCID in the positive direction (rate ratio ≤0.80) and the negative direction (rate ratio >1.2) are indicated by the vertical dashed green and orange lines, respectively.

CI, confidence interval; FF, fluticasone furoate; ICS, inhaled corticosteroid; LABA, long-acting β_2-agonist; LAMA, long-acting muscarinic antagonist; MCID, minimal clinically important difference; UMEC, umeclidinium, VI, vilanterol

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A greater odds of achieving an ACQ-7 response* was seen with the majority of treatment strategies in both subgroups

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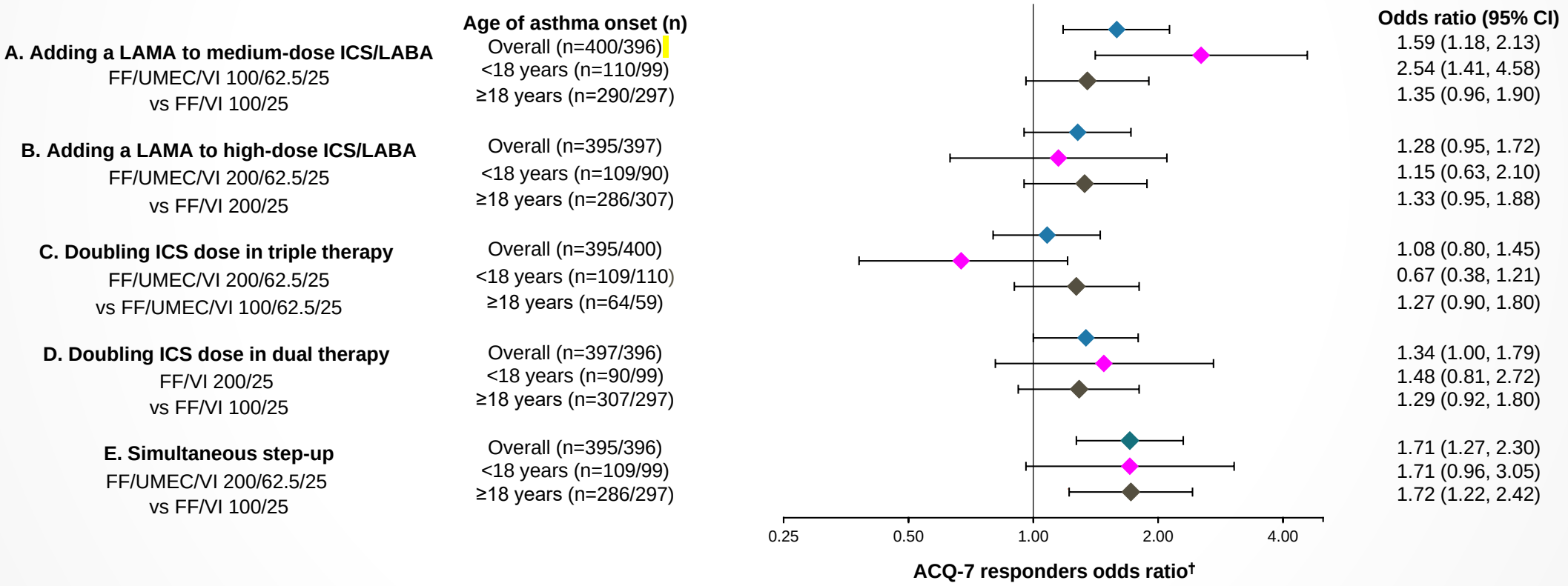
- The only exception was increasing FF dose in triple therapy (**C**) in the childhood-onset subgroup.



*Defined as a ≥0.5-point improvement (decrease) from baseline in ACQ-7 total score; †note: the x-axis is on a log scale. Analysis performed using a generalized linear mixed model with a logit link function. All doses are mcg.
n = number of patients with analyzable data at Week 24 by treatment.
ACQ, Asthma Control Questionnaire; CI, confidence interval; FF, fluticasone furoate; ICS, inhaled corticosteroid; LABA, long-acting β_2-agonist; LAMA, long-acting muscarinic; UMEC, umeclidinium, VI, vilanterol
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Conclusions

- For patients with uncontrolled asthma on ICS/LABA, adding UMEC and/or increasing FF dose was generally associated with improved lung function and greater odds of ACQ-7 response regardless of age of asthma onset.
- These treatment strategies also led to improvements in exacerbation rates in patients with adult-onset asthma, while outcomes were less consistent in the childhood-onset subgroup.
- Overall, adding UMEC to FF/VI 100/25 mcg led to pronounced improvements in lung function, exacerbation rates, and asthma control in the childhood-onset subgroup.
- Simultaneous step-up to FF/UMEC/VI 200/62.5/25 mcg led to the greatest improvements in these outcomes in the adult-onset subgroup.

ACQ, Asthma Control Questionnaire; FF, fluticasone furoate; ICS, inhaled corticosteroid; LABA, long-acting β_2-agonist; UMEC, umeclidinium, VI, vilanterol

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CO-AUTHORS' DISCLOSURES

- CB Abbott, S Chang, J Crawford and MD Stanaland are employees of GSK and hold stocks/shares in GSK. E Kerwin was an employee of Crisor LLC Research and has served on advisory boards, speaker panels, or received travel reimbursement from Amphastar, AstraZeneca, Boehringer Ingelheim, Cipla, Connect Biopharma, Chiesi, Forest, GSK, Mylan, Novartis, Pearl, Sunovion, Teva, and Theravance. DJ Maselli received personal fees from AstraZeneca, GSK, Novartis, Regeneron/Sanofi, and Sunovion. R Nathan 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 from GSK and Boehringer Ingelheim.