Once-daily fluticasone furoate alone or combined with vilanterol in persistent asthma

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ONLINE SUPPLEMENT

Prohibited medication during the study

Any prescription or non-prescription medication that could affect the course of asthma was prohibited during the study. This included all corticosteroids (with the exception of intranasal sprays and mild topical creams), long-acting β_2 agonists (LABAs), leukotriene modifiers, slow-release bronchodilators, and any medication that could interact with corticosteroid or sympathomimetic amines.

TABLE S1 Mean change from baseline and treatment differences for the co-primary endpoints of trough forced expiratory volume in 1 s (FEV_1; last observation carried forward) and weighted mean 0–24h FEV_1 (subset of patients who performed serial FEV_1) at week 24 and the powered secondary endpoint of percentage rescue-free 24-h periods during the 24-week treatment period (sensitivity analysis population)

	FF/VI 200/25µg OD (N=197)	**FF 200µg OD (N=194)**	**FP 500µg BD (N=195)**
Trough FEV_1 (week 24)			
n	169	172	179
LS mean change from baseline, mL (SE)	329 (29.3)	165 (29.1)	156 (28.4)
Treatment difference *vs* FF 200µg OD, mL (95% CI)	164 (83, 245) p<0.001		
Treatment difference *vs* FP 500µg BD, mL (95% CI)	173 (93, 253) p<0.001	9 (–71, 89)	
0–24-h wmFEV_1 (week 24)			
n	72	69	76
LS mean change from baseline, mL	339 (44.6)	261 (46.1)	215 (43.7)
Treatment difference *vs* FF 200µg OD, mL (95% CI)	78 (–49, 205) p=0.230		
Treatment difference *vs* FP 500µg BD, mL (95% CI)	124 (1, 247) p=0.047		
Percentage rescue-free 24-h periods (weeks 1–24)			

n	176	177	183
LS mean change from baseline (SE)	38.8 (2.55)	25.6 (2.54)	31.7 (2.49)
Treatment difference *vs* FF 200µg OD (95% CI)	13.2 (6.2, 20.3) p<0.001		
Treatment difference *vs* FP 500µg BD (95% CI)	7.1 (0.1, 14.1) p=0.046		

ANCOVA model with covariates for baseline, region, age, sex and treatment.

BD: twice-daily; CI: confidence interval; FEV_1: forced expiratory volume in 1 s; FF: fluticasone furoate; FP: fluticasone propionate; LS: least squares; OD: once-daily; SE: standard error; VI: vilanterol; wm: weighted mean.

TABLE S2 Summary of percentage of trough FEV_1 (L) at week 24 relative to post-salbutamol FEV_1 at screening using the last observation carried forward method (intent-to-treat [ITT] population)

Treatment	N	n	Mean	SD	Median	Min.	Max.
FF/VI 200/25µg OD	197	193	96.1	12.78	96.8	54	136
FF 200µg OD	194	186	85.7	24.28	90.5	–100	138
FP 500µg BD	195	191	85.6	19.47	88.5	–22	131

BD: twice-daily; FF: fluticasone furoate; FP: fluticasone propionate; OD: once-daily; SD: standard deviation; VI: vilanterol.

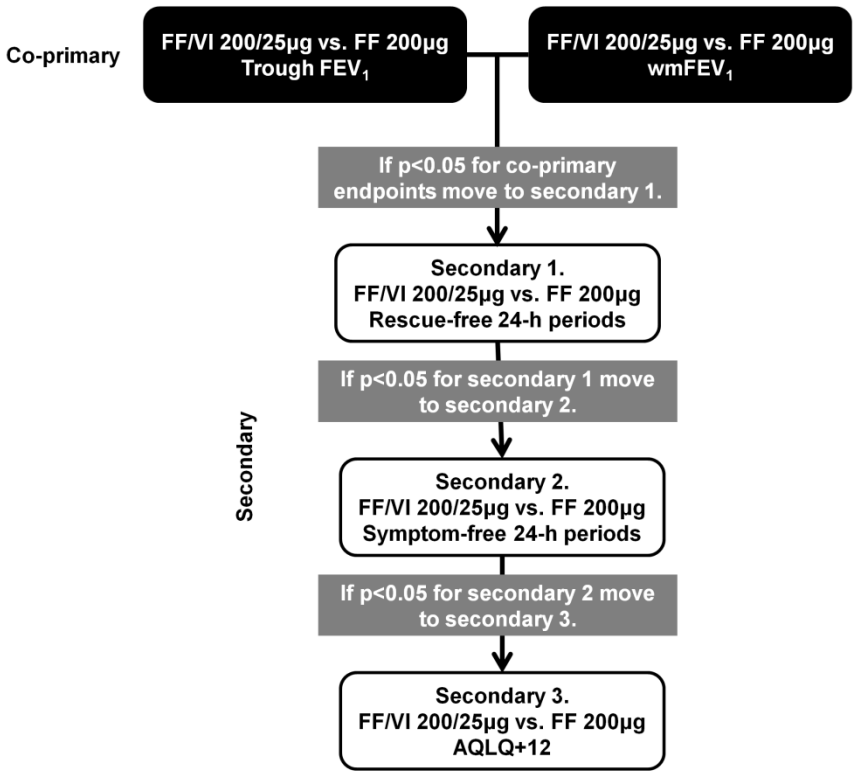
TABLE S3 Summary of adverse events by treatment group (ITT population)

	FF/VI 200/25µg OD (N=197)	FF 200µg OD (N=194)	FP 500µg BD (N=195)
AEs, n (%)			
On-treatment	92 (47)	90 (46)	97 (50)
Treatment-related AEs	17 (9)	8 (4)	16 (8)
AEs leading to permanent discontinuation of study drug or withdrawal from study	7 (4)	3 (2)	2 (1)
Most frequent on-treatment AEs, n (%)[a]			
Nasopharyngitis	25 (13)	27 (14)	39 (20)
Headache	11 (6)	13 (7)	15 (8)
Cough	3 (2)	6 (3)	13 (7)
Respiratory tract infection, viral	7 (4)	7 (4)	7 (4)
Influenza	5 (3)	8 (4)	7 (4)
Bronchitis	7 (4)	6 (3)	6 (3)
Oropharyngeal pain	4 (2)	8 (4)	7 (4)
Sinusitis	3 (2)	7 (4)	4 (2)
Dysphonia	6 (3)	2 (1)	4 (2)
Pharyngitis	4 (2)	2 (1)	6 (3)
Rhinitis	1 (<1)	2 (1)	7 (4)
Oropharyngeal candidiasis	5 (3)	1 (<1)	2 (1)

[a]Occurring in ≥3% of patients in any treatment group.

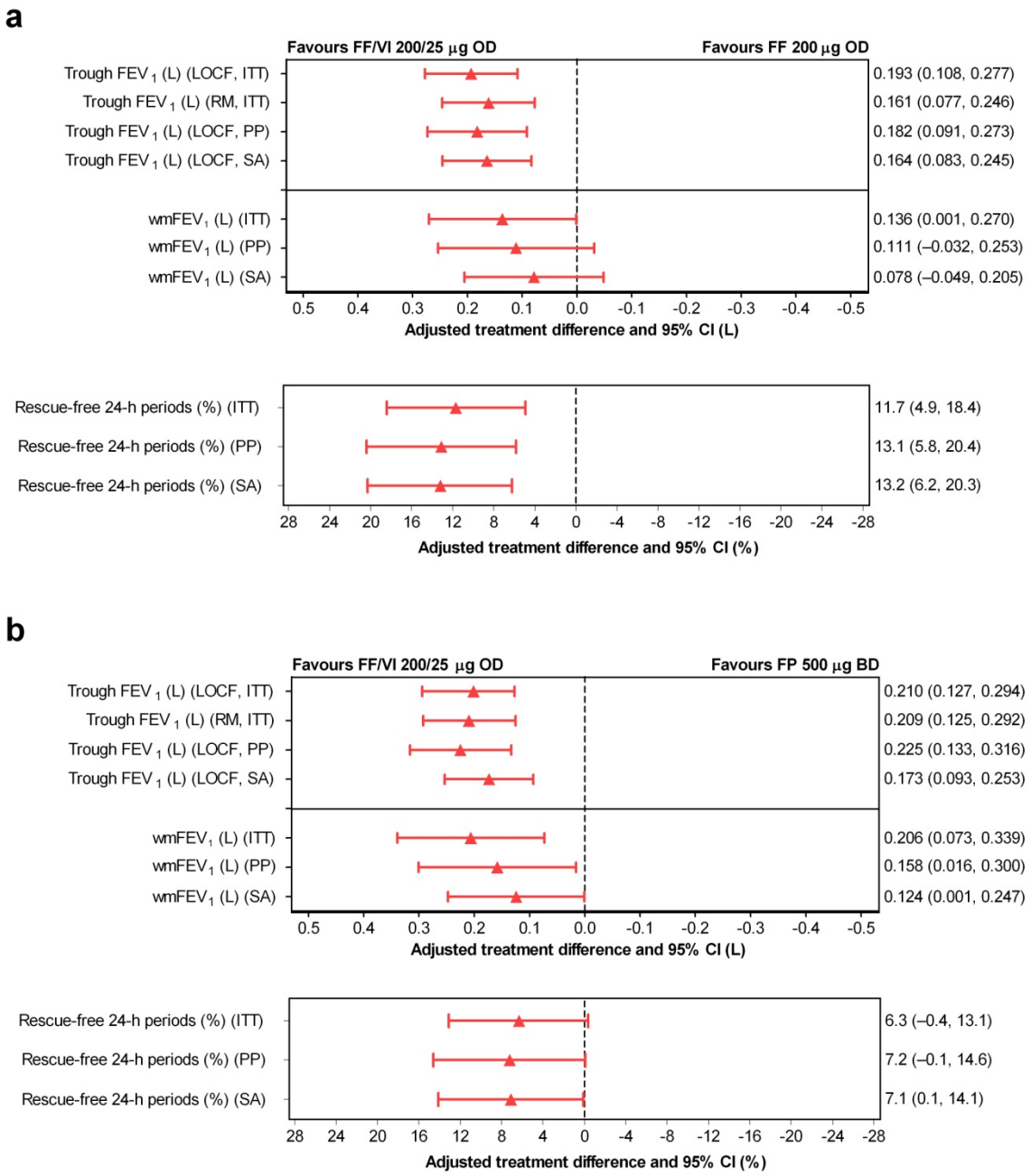
AEs: adverse events; BD: twice-daily; FF: fluticasone furoate; FP: fluticasone propionate; OD: once-daily; VI: vilanterol.

FIGURE S1. Statistical hierarchy.



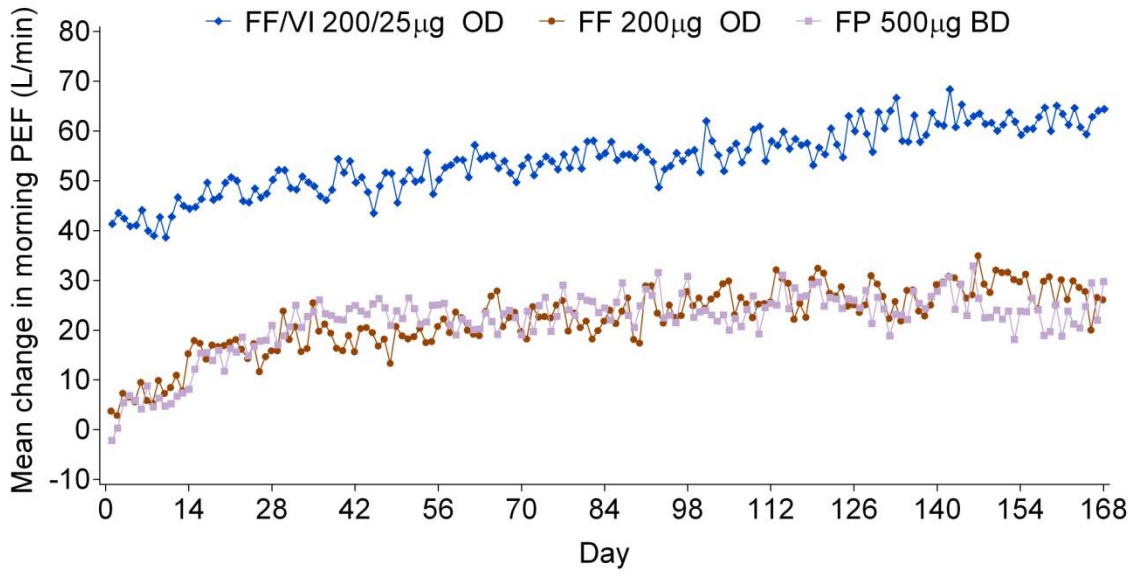
AQLQ+12: Asthma Quality of Life Questionnaire; FEV_1: forced expiratory volume in 1 s; FF: fluticasone furoate; FP: fluticasone propionate; VI: vilanterol; wm: weighted mean.

FIGURE S2 Summary of adjusted treatment differences for the co-primary endpoints of trough FEV_1 and weighted mean (wm) FEV_1, and powered secondary endpoint of percentage rescue-free 24-h periods for (**a**) fluticasone furoate/vilanterol (FF/VI) 200/25µg *versus* FF 200µg and (**b**) FF/VI 200/25µg *versus* fluticasone propionate (FP) 500µg in the ITT last observation carried forward population, ITT repeat measures population (trough FEV_1 only), per protocol population and sensitivity analysis population.



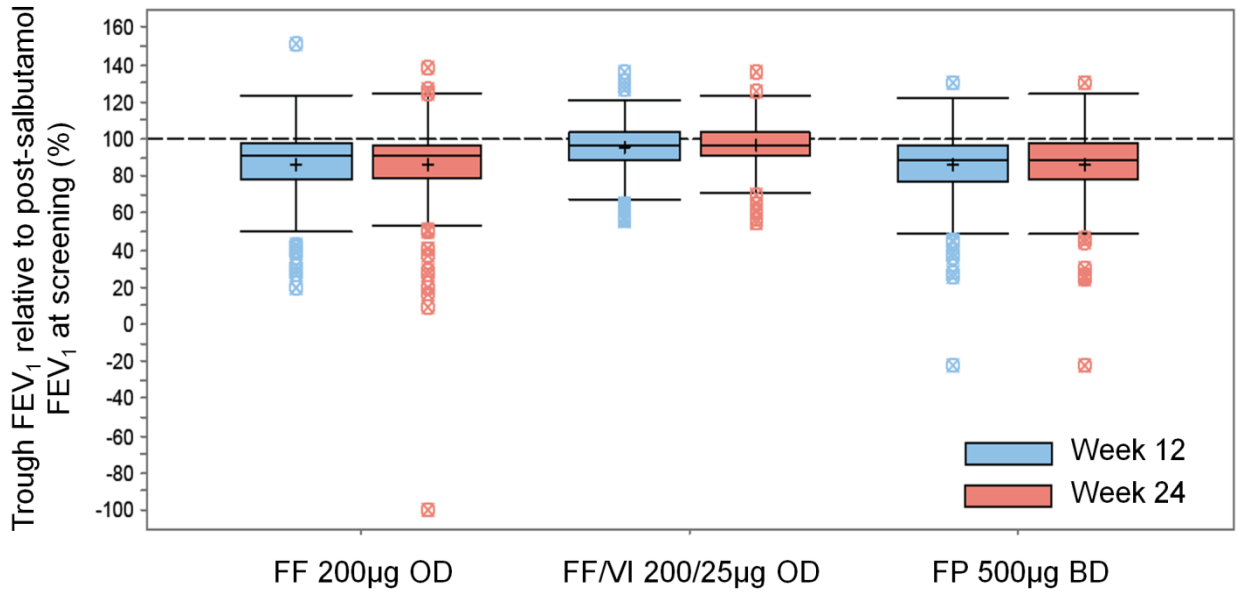
BD: twice-daily; CI: confidence interval; FEV_1: forced expiratory volume in 1 s; FF: fluticasone furoate; FP: fluticasone propionate; ITT: intent to treat; LOCF: last observation carried forward; LS: least squares; OD: once-daily; PP: per protocol; RM: repeat measures; SA: sensitivity analysis; VI: vilanterol; wm: weighted mean.

FIGURE S3. Mean change from baseline in morning peak expiratory flow (ITT population).



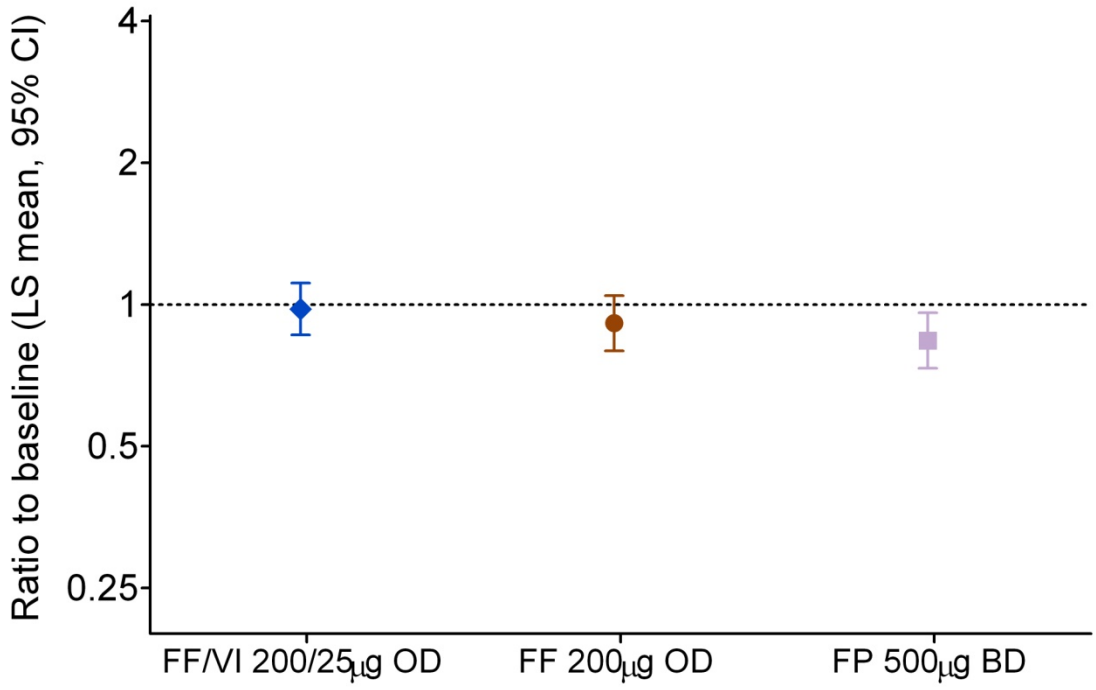
BD: twice-daily; FF: fluticasone furoate; FP: fluticasone propionate; LS: least squares; OD: once-daily; PEF: peak expiratory flow; VI: vilanterol.

FIGURE S4. Box plot of percentage of trough FEV_1 at week 24 relative to post-salbutamol FEV_1 at screening using last observation carried forward method (ITT population)



BD: twice-daily; FEV_1: forced expiratory volume in 1 s; FF: fluticasone furoate; FP: fluticasone propionate; OD: once-daily; VI: vilanterol.

FIGURE S5. Adjusted LS mean ratio to baseline 24-h urinary cortisol (UC) excretion by treatment group at week 24 (UC population).



BD: twice-daily; CI: confidence interval; FF: fluticasone furoate; FP: fluticasone propionate; LS: least squares; OD: once-daily; VI: vilanterol.