Supplementary material

Table S1. Change from baseline[a] in morning pre-dose trough FEV_1 and FEV_1 AUC_{0-4} at Week 24 by baseline blood eosinophil count (efficacy estimand; PFT sub-study mITT population[b])

Baseline eosinophil count		BGF 320/18/9.6 µg *versus* GFF 18/9.6 µg	BGF 160/18/9.6 µg *versus* GFF 18/9.6 µg	BGF 320/18/9.6 µg *versus* BFF 320/9.6 µg	BGF 160/18/9.6 µg *versus* BFF 320/9.6 µg
Morning pre-dose trough FEV_1, mL					
<100 cells/mm³	LSM	–10	–37	59	32
***n*=330**	(95% CI)	(–69, 48)	(–93, 19)	(2, 116)	(–22, 87)
	p-value	0.7323	0.1958	0.0416	0.2459
100–<300 cells/mm³	LSM	37	40	76	79
***n*=1770**	(95% CI)	(11, 63)	(15, 66)	(50, 102)	(54, 105)
	p-value	0.0052	0.0020	<0.0001	<0.0001
≥300 cells/mm³	LSM	59	62	89	93
***n*=413**	(95% CI)	(–7, 124)	(–2, 127)	(27, 151)	(32, 154)
	p-value	0.0787	0.0593	0.0047	0.0029
FEV_1 AUC_{0-4}, mL					
<100 cells/mm³	LSM	15	–25	134	94
***n*=330**	(95% CI)	(–43, 74)	(–81, 31)	(76, 192)	(38, 149)
	p-value	0.6108	0.3792	<0.0001	0.0009
100–<300 cells/mm³	LSM	51	48	115	113
***n*=1767**	(95% CI)	(23, 78)	(20, 75)	(87, 144)	(85, 141)
	p-value	0.0004	0.0006	<0.0001	<0.0001
≥300 cells/mm³	LSM	93	86	123	116
***n*=413**	(95% CI)	(23, 163)	(17, 156)	(57, 189)	(58, 181)
	p-value	0.0091	0.0149	0.0003	0.0005

[a]Baseline was defined as the mean of the 30- and 60-minute values prior to dosing on Day 1, if available; otherwise, the mean of the 30- and 60-minute pre-bronchodilator assessments at Visit 3 were used, if available; otherwise, the mean of the 30- and 60-minute pre-bronchodilator assessments at Visit 2 were used.

[b]mITT population: BGF 320/18/9.6 µg, *n*=747; BGF 160/18/9.6 µg, *n*=807; GFF 18/9.6 µg, *n*=779; BFF 320/9.6 µg, *n*=755.

AUC_{0-4}, area under the curve from 0–4 hours post-dose; BFF, budesonide/formoterol fumarate; BGF, budesonide/glycopyrrolate/formoterol fumarate; CI, confidence interval; FEV_1, forced expiratory volume in 1 second; GFF, glycopyrrolate/formoterol fumarate; LSM, least squares mean; mITT, modified intent-to-treat; PFT, pulmonary function test.

Table S2. Adjusted rate of decline in morning pre-dose trough FEV_1 and FEV_1 $AUC_{0–4}$ over 52 weeks (efficacy estimand; PFT sub-study mITT population)

	BGF 320/18/9.6 µg *versus* GFF 18/9.6 µg	**BGF 160/18/9.6 µg *versus* GFF 18/9.6 µg**	**BGF 320/18/9.6 µg *versus* BFF 320/9.6 µg**	**BGF 160/18/9.6 µg *versus* BFF 320/9.6 µg**
Morning pre-dose trough FEV_1, mL[b]				
Treatment difference (95% CI)	–5.6 (–29.8, 18.7)	–21.1 (–45.0, 2.7)	16.1 (–8.0, 40.3)	0.5 (–23.2, 24.3)
FEV_1 $AUC_{0–4}$, mL[c]				
Treatment difference (95% CI)	2.4 (–20.7, 25.6)	–14.5 (–37.2, 8.3)	11.8 (–11.2, 34.7)	–5.2 (–27.7, 17.4)

[a]Rate of the decline of pre-dose trough FEV_1 is –1 multiplied by the average of the individual slope of pre-dose trough FEV_1 over 52 weeks across patients for the treatment.

[b]Rate of the decline of FEV_1 $AUC_{0–4}$ is –1 multiplied by the average of the individual slope of FEV_1 $AUC_{0–4}$ over 52 weeks across patients for the treatment.

$AUC_{0–4}$, area under the curve from 0–4 hours post-dose; BFF, budesonide/formoterol fumarate; BGF, budesonide/glycopyrrolate/formoterol fumarate; CI, confidence interval; FEV_1, forced expiratory volume in 1 second; GFF, glycopyrrolate/formoterol fumarate; mITT, modified intent-to-treat; PFT, pulmonary function test.