

**Table S9. Heterogeneity in the relative treatment effects.**

	Relative treatment effect of combination therapy vs. comparator (SD) <sup>¶</sup>	Between-trials standard deviation <sup>†</sup>
Change from baseline in FEV1 (L) at 3 months (vs. placebo, LABA, and LAMA)	0.21 (0.01) 0.10 (0.01) 0.06 (0.01)	0.01
Change from baseline in (L) FEV1 at 6 months (vs. placebo, LABA, and LAMA)	0.17 (0.01) 0.08 (0.01) 0.05 (0.01)	0.02
Change from baseline in FEV1 (L) at 12 months (vs. placebo and LAMA)	0.24 (0.05) 0.07 (0.04)	0.05
Change from baseline in SGRQ at 3 months (vs. placebo, LABA, and LAMA)	-4.50 (0.69) -2.16 (0.54) -2.12 (0.33)	0.34
Change from baseline in SGRQ at 6 months (vs. placebo, LABA, and LAMA)	-3.63 (0.63) -1.44 (0.55) -1.53 (0.44)	0.82
Proportion of SGRQ responders at 6 months (vs. placebo, LABA, and LAMA)	0.20 (0.07) 0.21 (0.07) 0.21 (0.05)	0.09
TDI at 3 months (vs. placebo, LABA, and LAMA)	1.22 (0.14) 0.37 (0.12) 0.41 (0.10)	0.08
TDI at 6 months (vs. placebo, LABA, and LAMA)	1.18 (0.16) 0.40 (0.13) 0.35 (0.11)	0.05
Proportion of TDI responders at 6 months (vs. placebo, LABA, and LAMA)	0.74 (0.09) 0.29 (0.07) 0.26 (0.07)	0.08
Moderate-to-severe exacerbations (vs. placebo, LABA, and LAMA)	0.66 (0.06) 0.82 (0.05) 0.92 (0.04)	0.06
Severe exacerbations (vs. placebo, LABA, and LAMA)	-0.29 (0.23) 0.07 (0.20) -0.06 (0.13)	0.25
Mortality (vs. placebo, LABA, and LAMA)	0.69 (0.58) -0.07 (0.33) -0.26 (0.24)	0.33
Total serious adverse events (vs. placebo, LABA, and LAMA)	0.10 (0.11) -0.03 (0.08) -0.04 (0.06)	0.07
Cardiac serious adverse events (vs. placebo, LABA, and LAMA)	0.49 (0.36) -0.21 (0.27) -0.14 (0.19)	0.37

Dropouts due to adverse event(vs. placebo, LABA, and LAMA)	-0.04 (0.15) -0.08 (0.13) 0.03 (0.10)	0.22
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<sup>¶</sup>The results of dichotomous outcomes are presented in log-odds or log-hazard ratio. † If the between-trials SD approximates the size of treatment effect, heterogeneity is likely very high so that a 95% predictive interval of a future trial of infinite size could span zero effect. FEV1= forced expiratory volume in 1 second; SD= standard deviation; SGRQ=St. George's Respiratory Questionnaire; TDI=Transitional Dyspnea Index