Supplementary data

TABLE 1. Overall patient disposition (ITT population)

	Placebo n=68	UMEC 62.5 mcg n=69	UMEC 125 mcg n=69
Completion status			
Completed[a]	50 (74)	62 (90)	56 (81)
Withdrawn	18 (26)	7 (10)	13 (19)
Primary reason/sub-reason for withdrawal[b]			
Adverse event	0	1 (1)	3 (4)
Lack of efficacy	8 (12)	5 (7)	4 (6)
COPD exacerbation	6 (9)	5 (7)	2 (3)[c]
Protocol deviation	0	0	0
Patient reached protocol-defined stopping criteria	6 (9)	0	5 (7)
ECG abnormality	6 (9)	0	5 (7)
Lab abnormality	0	0	0
Study closed/terminated	0	0	0
Lost to follow-up	0	0	1 (1)
Withdrew consent	4 (6)	1 (1)	0
Burden of procedures	3 (4)	0	0
Frequency of visits	0	1 (1)	0
Other	1 (1)	0	0

ECG: electrocardiogram; ITT: intent-to-treat; UMEC: umeclidinium bromide.

[a]Patients were considered to have completed if they completed the last clinic visit (Visit 8).
[b]Patients were not required to indicate sub-reasons.
[c]Although the primary reason for withdrawal was reported as a COPD exacerbation (lack of efficacy) for two UMEC 125 mcg patients, an additional patient in the UMEC 125 mcg treatment group was withdrawn because of a COPD exacerbation which was reported as a serious adverse event. The primary reason for the third patient is, therefore, reported here as an adverse event.

TABLE 2. Trough FEV_1 (mL) at day 85 (ITT population)

Day 85	Placebo n=68	UMEC 62.5 mcg n=69	UMEC 125 mcg n=69
n[a]	67	69	66
n[b]	50	61	55
LSM (SE)	1235 (28.0)	1363 (25.7)	1388 (26.8)
LSM change (SE)	-7 (28.0)	120 (25.7)	145 (26.8)
Column vs. placebo difference		127	152
95% CI		(52–202)	(76–229)
p-value		<0.001	<0.001

CI: confidence interval; FEV_1: forced expiratory volume in 1 second; ITT: intent-to-treat; LSM: least squares mean; SE: standard error; UMEC: umeclidinium bromide.

Note: analysis performed using a repeated measures model with covariates of treatment, baseline (mean of the two assessments made 30 and 5 min pre-dose on day 1), smoking status, centre group, day, day by baseline and day by treatment interactions.
[a]Number of patients with analysable data for one or more visits.
[b]Number of patients with analysable data at the current visit.

TABLE 3. Trough FVC (mL) at day 85 (ITT population)

Day 85	Placebo n=68	UMEC 62.5 mcg n=69	UMEC 125 mcg n=69
n[a]	67	69	66
n[b]	50	61	55
LSM (SE)	2699 (44.6)	2892 (41.1)	2935 (42.8)
LSM change (SE)	47 (44.6)	241 (41.1)	283 (42.8)
Column vs. placebo difference		193	236
95% CI		(74–313)	(114–358)
p-value		0.002	<0.001

CI: confidence interval; FVC: forced vital capacity; ITT: intent-to-treat; LSM: least squares mean;
SE: standard error; UMEC: umeclidinium bromide.

Note: analysis performed using a repeated measures model with covariates of treatment, baseline
(mean of the two assessments made 30 and 5 min pre-dose on day 1), smoking status, centre group,
day, day by baseline and day by treatment interactions.
[a]Number of patients with analysable data for one or more visits.
[b]Number of patients with analysable data at the current visit.

TABLE 4. 0–6 h weighted mean FVC (mL) at day 84 (ITT population)

Time point	Placebo n=68	UMEC 62.5 mcg n=69	UMEC 125 mcg n=69
Day 84			
n[a]	66	69	69
n[b]	49	60	56
LSM (SE)	2691 (44.8)	2934 (41.0)	3009 (42.3)
LSM change (SE)	42 (44.8)	285 (41.0)	360 (42.3)
Column vs. placebo difference		243	318
95% CI		(123–363)	(196–439)
p-value		<0.001	<0.001

CI: confidence interval; FVC: forced vital capacity; ITT: intent-to-treat; LSM: least squares mean; SE: standard error; UMEC: umeclidinium bromide.

Note: analysis performed using a repeated measures model with covariates of treatment, baseline (mean of the two assessments made 30 and 5 min pre-dose on day 1), smoking status, centre group, day, day by baseline and day by treatment interactions.
[a]Number of patients with analysable data for one or more visits.
[b]Number of patients with analysable data at the current visit.

TABLE 5. Analysis of proportion of responders according to TDI focal score (ITT population)

Time point	Placebo n=68	UMEC 62.5 mcg n=69	UMEC 125 mcg n=69
Day 84			
n	53	64	60
Responder, n (%)[a]	8 (15)	24 (38)	23 (38)
Non-responders, n (%)	45 (85)	40 (63)	37 (62)
Column vs. placebo			
Odds ratio		3.4	3.4
95% CI		(1.3–8.4)	(1.4–8.6)
p-value		0.009	0.009

BDI: Baseline Dyspnoea Index; CI: confidence interval; ITT: intent-to-treat; TDI: Transitional Dyspnoea Index; UMEC: umeclidinium bromide.

Note: analysis performed using a separate logistic regression model at each visit with covariates of treatment, BDI focal score, smoking status and centre group.

[a]Response was defined as a TDI focal score of at least 1 unit. Non-response was defined as a TDI focal score of less than 1 unit or a missing TDI focal score with no subsequent non-missing TDI assessments. The classification was not derived if the TDI focal score was missing but subsequent non-missing TDI assessments were present.