

Supplementary Table S1. Summary of patient-reported outcome measures used to capture symptoms in each clinical trial and corresponding endpoints

	ATTAIN	ACCORD COPD I	Active-comparator study	Endpoints
EXACT E-RS				
Total score	X		X	Change from baseline in E-RS total score
Cough and sputum domain	X			Change from baseline in E-RS cough and sputum domain
SYMPTOM QUESTIONNAIRES				
6-item nighttime and morning symptoms of COPD questionnaire	X			Percentage of days with morning or nighttime symptoms
9-item COPD morning symptoms questionnaire			X	Change from baseline in: % days without morning symptoms; severity of morning cough; difficulty bringing up phlegm
11-item COPD nighttime symptoms questionnaire		X		Change from baseline in COPD nighttime symptoms

Supplementary Table S2. Baseline E-RS scores, E-RS cough and sputum domain score, nighttime symptoms questionnaire, nighttime and morning symptoms of COPD questionnaire and COPD questionnaire results in ACCORD COPD 1, ATTAIN and active-comparator studies

	ACCORD COPD I		ATTAIN		Active-comparator study		
	Placebo	Aclidinium 400 µg BID	Placebo	Aclidinium 400 µg BID	Placebo	Aclidinium 400 µg BID	Tiotropium 18 µg QD
	(N=185)	(N=190)	(N=273)	(N=269)	(N=85)	(N=171)	(N=158)
<i>E-RS scores^a</i>							
Total, mean (SD)			13.6 (6.6)	14.1 (6.4)	13.4 (6.0)	13.6 (5.8)	12.5 (5.8)
Cough and sputum domain, mean (SD)			3.8 (1.9)	3.9 (1.8)	3.7 (1.8)	3.9 (1.6)	3.6 (1.5)
<i>COPD nighttime symptoms questionnaire</i>							
Frequency of nighttime cough ^b mean (SD)	2.06 (1.50)	1.92 (1.61)					
Frequency of nighttime sputum production ^b mean (SD)	1.33 (1.43)	1.35 (1.55)					
Severity and impact of nighttime cough ^c mean (SD)	1.49 (0.88)	1.39 (0.97)					
<i>Nighttime and morning symptoms of COPD questionnaire</i>							
Mornings with any COPD symptoms, ^d %, mean (SD)			89.3 (22.6)	89.5 (23.2)			
Mornings with any cough symptoms, ^d %, mean (SD)			70.8 (34.2)	68.9 (37.0)			
Mornings with any bringing up phlegm or mucus symptoms, ^d %, mean (SD)			63.9 (36.6)	64.9 (37.7)			
Nights with any COPD symptoms, ^d %, mean (SD)			84.2 (26.4)	84.0 (27.3)			
Nights with any cough symptoms, ^d %, mean (SD)			65.3 (35.3)	63.2 (37.5)			
Nights with any bringing up phlegm or mucus symptoms, ^d %, mean (SD)			56.0 (37.1)	57.7 (37.1)			
<i>COPD symptoms questionnaire</i>							
Days without morning COPD symptoms, ^e %, mean (SD)					10.2 (22.3)	11.1 (23.1)	14.0 (24.9)
Days without morning cough symptoms, ^e %, mean (SD)					27.2 (34.3)	27.1 (33.7)	30.5 (35.9)
Days without morning difficulty bringing up phlegm symptoms, ^e %, mean (SD)					68.9 (38.5)	59.9 (37.3)	69.7 (35.7)
Overall severity of morning symptoms, ^f mean (SD)					2.30 (0.61)	2.36 (0.61)	2.25 (0.62)
Severity of morning cough symptoms, ^f mean (SD)					1.20 (0.76)	1.29 (0.74)	1.15 (0.73)
Severity of morning difficulty bringing up phlegm symptoms, ^e mean (SD)					0.62 (0.82)	0.86 (0.88)	0.60 (0.78)

^aE-RS total score ranged from 0 to 40; E-RS cough and sputum domain score ranged from 0 to 11. Higher scores indicate more severe symptoms

^bAssessed on a 5-point scale: 0 = 'never' to 4 = '7 or more times'

^cAssessed on a 5-point scale: 0 = 'no symptoms' to 4 = 'severe symptoms that interfered with normal daily activities'

^dAssessed as the average proportion of days during the run-in period

^eAssessed as the average proportion of days during the run-in period

^fAssessed on a 5-point scale: 0 = 'no symptoms' to 4 = 'very severe symptoms'

BID, twice daily; COPD, chronic obstructive pulmonary disease; E-RS, Evaluating Respiratory Symptoms, formerly known as EXAcerbations of Chronic pulmonary disease Tool; ITT, intent-to-treat; QD, once daily; SD, standard deviation