

## **Online Supplement**

### **The Short-term Impact of Symptom-defined COPD Exacerbation Recovery on Health Status and Lung Function**

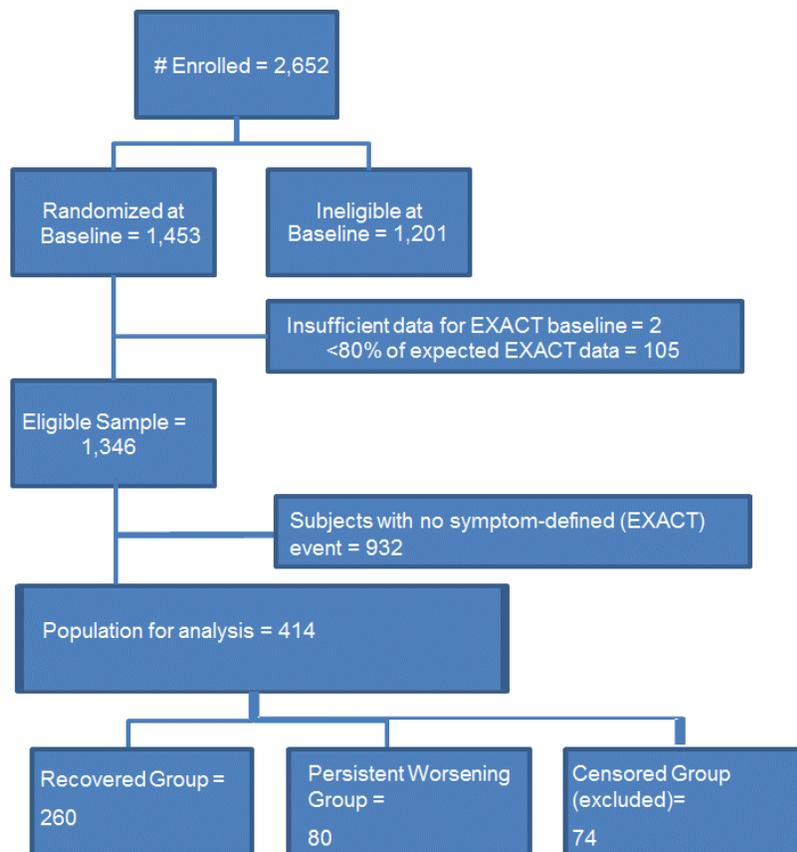
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#### **Patient Disposition**

The patient disposition is presented in Figure S1. The final analysis population was 340 patients, comprised of the 260 patients in the recovered group and 80 patients in the persistent worsening group. Patients with censored-only events were excluded from the analysis.

**Figure S1. Patient Disposition**



**Patient Characteristics by Symptom-Defined Exacerbation Status**

Patients in the study sample (N=340) were similar to those with no symptom-defined events in terms of age, gender, race, airflow obstruction, history of acute exacerbations, and other baseline characteristics (Table S1). Study inclusion criteria ensured all patients had moderate to severe COPD, a history of  $\geq 1$  HCRU event in the last 12 months, and were symptomatic at the time of enrollment.

**Table S1. Baseline Sociodemographic and Clinical Characteristics by Symptom-defined Exacerbation Status**

	<b>Recovered (N=260)</b>	<b>Persistent Worsening (N=80)</b>	<b>No Events (N=932)</b>
Age, mean (SD)	61.7 (8.06)	61.4 (6.89)	62.1 (8.37)

	<b>Recovered (N=260)</b>	<b>Persistent Worsening (N=80)</b>	<b>No Events (N=932)</b>
Gender, % male	191 (73.5%)	59 (73.8%)	714 (76.6%)
Race/ethnicity			
White	227 (87.3%)	68 (85.0%)	767 (82.7%)
Asian	31 (11.9%)	11 (13.8%)	158 (17.0%)
Hispanic or Latino	0 (0.0%)	1 (1.3%)	3 (0.3%)
FEV <sub>1</sub> (L), mean (SD)	1.6 (0.52)	1.6 (0.52)	1.6 (0.50)
FEV <sub>1</sub> % predicted, mean (SD)	55.4 (14.56)	56.7 (15.49)	57.2 (13.85)
GOLD stage (spirometry only), n (%)			
I	10 (3.9%)	4 (5.0%)	29 (3.2%)
II	137 (52.7%)	46 (57.5%)	577 (63.8%)
III	101 (38.9%)	27 (33.8%)	284 (31.4%)
IV	4 (1.5%)	1 (1.3%)	15 (1.7%)
# of HCRU exacerbations in past 12 months, mean (SD)	1.4 (0.79)	1.4 (0.75)	1.3 (0.89)
SGRQ total score, mean (SD) <sup>a</sup>	55.4 (17.46)	55.8 (16.25)	53.0 (17.91)
EXACT baseline score, mean (SD) <sup>a, b</sup>	43.5 (9.97)	39.6 (10.93)	44.4 (9.02)
E-RS baseline scores, mean (SD) <sup>b, c</sup>			
RS – Total	16.8 (6.41)	14.3 (6.84)	17.2 (5.84)
RS – Breathlessness	8.3 (3.43)	7.1 (3.61)	8.5 (3.03)
RS – Cough & Sputum	4.4 (1.68)	3.7 (1.56)	4.5 (1.55)
RS – Chest Symptoms	4.1 (1.92)	3.5 (2.09)	4.2 (1.95)
Study, n (%) AZ 1	148 (56.9%)	45 (56.3%)	508 (54.5%)

*Abbreviations:* AZ = AstraZeneca; EXACT = Exacerbations of Chronic Pulmonary Disease Tool; E-RS = Evaluating Respiratory Symptoms tool; FEV<sub>1</sub> = forced expiratory volume in one second; GOLD = Global Initiative for Obstructive Lung Disease; HCRU = healthcare resource utilization; SGRQ = St. George's Respiratory Questionnaire.

<sup>a</sup> Scores can range 0–100, higher scores are worse.

<sup>b</sup> Baseline days -7 to -1.

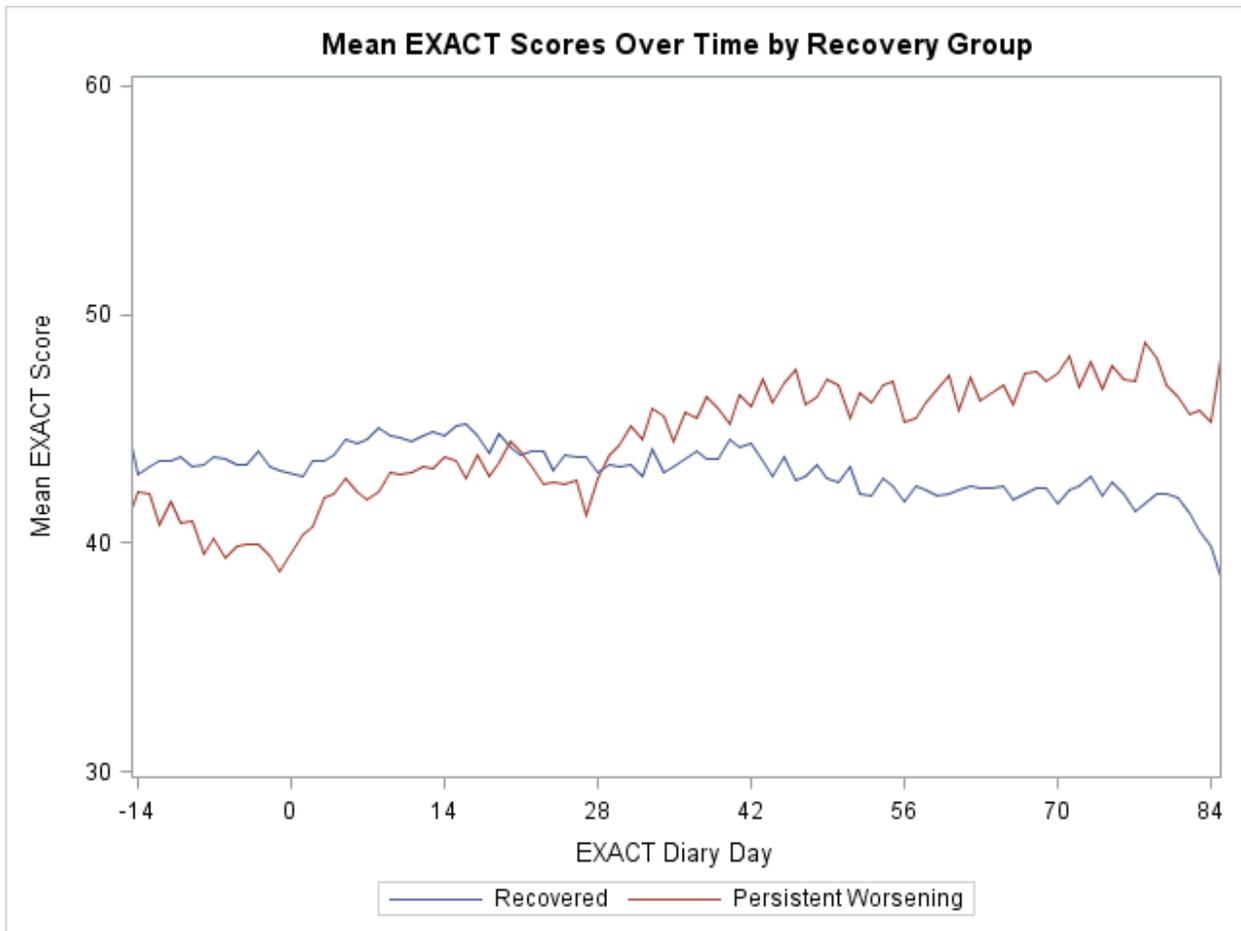
<sup>c</sup> Scores can range as follows: RS – Total 0-40, RS – Breathlessness 0-17, RS – Cough and Sputum 0 – 11 and RS – Chest Symptoms 0 – 12, higher scores are more severe.

p-values based on t-test or  $\chi^2$ , as appropriate

## Exact Scores Over Time

Group mean EXACT scores by recovery group during the run-in period through the end of the study are presented in Figure S2. The persistent worsening group had consistently lower group mean EXACT scores than the recovered patients up until approximately Day 28 (corresponding to the median time to first event) when their scores increased in an exacerbation event and remained elevated for the remainder of the study period.

**Figure S2. Mean EXACT Scores Over Entire Study Period (Days -14 to 84) by Recovery Group**



Higher scores are worse.

Recovered Group n=260; Persistent Worsening Group n=80

## Health Status and Lung Function Change Over Time

Change scores in SGRQ and FEV<sub>1</sub> from baseline to Week 12 are summarized in Table S2. The proportion of patients in each group whose health status improved, did not change, or deteriorated was also compared across recovery groups, with groups defined by SGRQ total score thresholds for clinically meaningful change. Between-group differences in SGRQ total and symptoms scores were statistically significant. No differences in lung function deterioration or the proportion of patients who improved, did not change or deteriorated was identified.

**Table S2. Summary of Change Scores in SGRQ, and FEV<sub>1</sub> from Baseline to Week 12 by Recovery Group**

	Recovered (N=260)	Persistent Worsening (N=80)	p-value
SGRQ score change, n mean (SD) <sup>a, b</sup>			
Total change	250 -2.1 (13.87)	77 1.5 (13.41)	0.04
Symptoms change	255 -4.8 (15.41)	77 0.5 (14.27)	0.01
Activity change	251 -1.5 (17.84)	77 -0.3 (16.26)	0.60
Impacts change	254 -1.5 (16.75)	77 2.9 (17.85)	0.05
SGRQ Total change groups, n (%) <sup>b</sup>			
Improvement (-4 points)	103 (39.6%)	27 (33.8%)	0.46
No Change	74 (28.5%)	22 (27.5%)	
Worsened (+ 4 points)	73 (28.1%)	28 (35.0%)	
FEV <sub>1</sub> change (L), n mean (SD)	255 -0.03 (0.21)	77 -0.04 (0.29)	0.89

<sup>a</sup> Scores can range 0–100, higher scores are worse.

<sup>b</sup> Includes only patients with non-missing SGRQ scores at Week 12.

p-values based on student's t-test or  $\chi^2$ , as appropriate