Supplementary Material

Hospitalisation assessments by the Endpoint Validation Committee (EVC).

EVC members were 3 respiratory physicians independent from the sponsor and investigational sites. They independently reviewed all hospitalisation reports (unplanned admissions and subsequent nursing facility admissions, when applicable) and reviewed the list of all planned admissions with their cause. For EVC reviews, source documents were translated into English and blinded for the intervention allocated to the patients. Commercial names of medications were also replaced with their international non-proprietary names in order to mask the country. Cases were considered resolved upon unanimous agreement of the adjudication parameters. Reports not unanimously adjudicated initially were further reviewed and discussed until unanimous consensus was achieved. Hospitalisation days validated by the EVC were used in supportive analysis of the primary efficacy criterion.

Protocol amendments.

During the study, the protocol was amended to accelerate recruitment and allow study completion: inclusion criteria were expanded from COPD patients receiving LTOT to patients with severe COPD, with or without LTOT; the minimum number of patients was reduced from 520 to 306 by retaining the initial assumptions for sample size and removing a multiple comparisons adjustment; the follow-up period was reduced from 2 years to 1 year; and the contact frequency between DM patients and CMs was increased to improve patient training (either group or phone session, once per month). Prior to these changes, 72 patients on LTOT were enrolled in the study.

Table E1. Patient baseline characteristics and outcomes by country.

Baseline characteristic[a]	France (N=115)	Spain (N=89)	Germany (N=73)	Italy (N=42)	*P*[b]
Age, y	65.4 ± 9.4	70.4 ± 7.8	62.3 ± 8.3	71.9 ± 8.5	**<0.001**
Men, n (%)	72 (62.6)	76 (85.4)	39 (53.4)	35 (83.3)	**<0.001**[c]
Current smokers, n (%)	32 (27.8)	10 (11.2)	19 (26.0)	7 (16.7)	**0.020**[c]
Body mass index, kg/m^2	25.8 ± 5.8	27.8 ± 6.4	25.5 ± 6.7	26.7 ± 6.4	0.079
Number of concomitant diseases[d]	3.3 ± 1.8	3.3 ± 2.0	3.8 ± 2.2	3.6 ± 2.1	0.408
FEV_1, % of predicted	35.4 ± 12.8	39.8 ± 11.8	35.2 ± 12.4	39.2 ± 11.1	**0.024**
PaO_2 (room air), mmHg	64.1 ± 10.5	61.0 ± 10.3	58.6 ± 9.1	66.6 ± 11.4	**<0.001**
$PaCO_2$ (room air), mmHg	43.3 ± 5.9	43.2 ± 6.3	43.9 ± 7.6	44.6 ± 5.9	0.681
GOLD group D, n (%)	86 (78.9)	75 (86.2)	55 (79.7)	30 (71.4)	**<0.001**[e]
SGRQ-C total score	55.8 ± 19.2	50.1 ± 17.5	61.5 ± 18.6	51.7 ± 20.3	**0.006**
HADS total score	21.6 ± 3.1	20.8 ± 3.0	21.9 ± 3.0	19.5 ± 2.6	**<0.001**
Hospitalised exacerbations in the past 12 months	1.0 ± 0.5	1.3 ± 0.9	1.1 ± 0.6	1.1 ± 0.7	0.148
Long-term oxygen therapy, n (%)	80 (69.6)	59 (66.3)	65 (89.0)	33 (78.6)	**0.005**[c]
Home mechanical ventilation, n (%)	39 (33.9)	12 (13.5)	32 (43.8)	4 (9.5)	**<0.001**[c]
Outcomes					
Hospitalisation outcomes, mean ± SD; (median [Q1−Q3])					
Unplanned hospitalisation days/year, any cause (primary endpoint)	24.4 ± 46.4; (4 [0−259])	9.7 ± 22.7; (0 [0−123])	28.7 ± 40.9; (14 [0−203])	15.0 ± 34.8; (0 [0−163])	**0.006**[f]
All-cause, acute care wards	19.3 ± 40.3; (4 [0−259])	9.7 ± 22.7; (0 [0−123])	27.7 ± 38.9; (14 [0−203])	11.5 ± 31.9; (0 [0−163])	
AECOPD (acute care/nursing facilities)	5.6 ± 11.1; (0 [0−60])	5.5 ± 14.5; (0 [0−100])	18.4 ± 28.8; (6 [0−145])	5.3 ± 15.8; (0 [0−94])	
LTOT/HMV patients (n=243)	26.6 ± 49.8; (6 [0−259])	12.7 ± 26.3; (1 [0−123])	31.4 ± 42.6; (15 [0−203])	15.9 ± 37.1; (0 [0−163])	

Deaths, n (%, [95% CI])	8 (7.0, [3.1; 13.2])	7 (7.9, [3.2; 15.5])	6 (8.2, [3.1; 17.0])	5 (11.9, [4.0; 25.6])	

Results shown are for the intention-to-treat population. FEV_1, forced expiratory volume in 1 second, GOLD, Global Initiative for Chronic Obstructive Lung Disease; HADS, Hospital Anxiety and Depression Scale; N, number of patients in group; n, number of patients with characteristic; SGRQ-C, COPD-specific version of the Saint George's Respiratory Questionnaire.

[a]Values are means ± standard deviation (SD), unless otherwise indicated.
[b]One-way *(country)* analysis of variance for continuous variables, unless otherwise indicated.
[c]Chi-square test.
[d]In patients with ≥1 concomitant disease
[e]Fisher's exact test
[f]Country effect of two-way *(study group and country)* analysis of variance

Table E2. Primary causes for unplanned hospital admissions according to EVC assessments.

Cause of hospitalisation, n (%)	Disease Management (N=157 hospital admissions)	Usual Management (N=160 hospital admissions)
COPD exacerbation	116 (73.9)	103 (64.4)
Pneumonia	14 (8.9)	16 (10.0)
Acute cardiac failure	4 (2.5)	10 (6.3)
Urinary tract infection	3 (1.9)	0
Gastroenteritis	2 (1.3)	1 (0.6)
Traumatic pneumothorax	0	2 (1.3)
Epistaxis	2 (1.3)	0
Lobar pneumonia	2 (1.3)	0
Atrial fibrillation	1 (0.6)	1 (0.6)
Fall	1 (0.6)	1 (0.6)
Lung cancer	1 (0.6)	1 (0.6)
Normochromic normocytic anaemia	0	1 (0.6)
Coronary artery disease	0	1 (0.6)
Colitis	0	1 (0.6)
Colitis ulcerative	0	1 (0.6)
Epigastric discomfort	0	1 (0.6)
Rectal haemorrhage	0	1 (0.6)
Upper gastrointestinal haemorrhage	0	1 (0.6)
Asthenia	0	1 (0.6)
Condition aggravated	0	1 (0.6)
Jaundice	0	1 (0.6)
Sepsis	0	1 (0.6)

Thermal burn	0	1 (0.6)
Back pain	0	1 (0.6)
Bile duct cancer	0	1 (0.6)
Cerebrovascular accident	0	1 (0.6)
Hypoxic-ischaemic encephalopathy	0	1 (0.6)
Neuralgia	0	1 (0.6)
VIIth nerve paralysis	0	1 (0.6)
Anxiety	0	1 (0.6)
Acute renal failure	0	1 (0.6)
Bronchopneumonia	0	1 (0.6)
Haemoptysis	0	1 (0.6)
Pulmonary arterial hypertension	0	1 (0.6)
Femoral artery occlusion	0	1 (0.6)
Septic shock	0	1 (0.6)
Acute coronary syndrome	1 (0.6)	0
Left ventricular failure	1 (0.6)	0
Diarrhoea	1 (0.6)	0
Intestinal obstruction	1 (0.6)	0
Chest pain	1 (0.6)	0
Appendicitis	1 (0.6)	0
Toxicity to various agents	1 (0.6)	0
Syncope	1 (0.6)	0
Delirium	1 (0.6)	0
Urosepsis	1 (0.6)	0
Arm amputation	1 (0.6)	0

COPD, chronic obstructive pulmonary disease; N, number of patients in group; n, number of causes of hospitalisation.

Table E3. Components of educational & exercise program practices routinely available at study start to COPD patients (both groups) by country in the 33 study centres.

	Spain (N=7)	France (N=12)	Germany (N=8)	Italy (N=6)	Total (N=33)
Educational booklets/sheets	3 (42.9)	2 (16.7)	2 (33.3)	0 (0.0)	7 (22.6)
Specific educational sessions	1 (14.3)	1 (8.3)	2 (28.6)	2 (33.3)	6 (18.8)
Specific exercise program	4 (57.1)	5 (41.7)	2 (28.6)	2 (33.3)	13 (40.6)

%, (n row / n non-missing)*100; COPD, chronic obstructive pulmonary disease; N, number of centers; n, number of centers with non-missing data.

Table E4. Baseline characteristics and number of hospital days for patients who died during the study.

Baseline characteristic[ab]	**Deaths (N=26)**
Age, y	69.2 ± 9.0
Men/Women, n	17/9
Current smokers, n (%)	6 (23.1)
Pack-years	47.3 ± 20.8
Body mass index, kg/m^2	25.5 ± 7.8
6-min walking distance, m	219 ± 121
FEV_1, % of predicted	35.2 ± 11.7
PaO_2 (room air), mmHg	62.7 ± 11.5
$PaCO_2$ (room air), mmHg	44.4 ± 7.2
Total exacerbations in the past 12 mo	1.2 ± 0.6
GOLD group A-D combined severity, n (%)[c]	
A - Low risk, less symptoms	1 (3.8)
B - Low risk, more symptoms	0 (0.0)
C - High risk, less symptoms	3 (11.5)
D - High risk, more symptoms	22 (84.6)
BODE index	6.2 ± 2.3
BODE index of 7−10, n (%)	12 (54.5)
COPD treatments, n (%)	
Long-term oxygen therapy	22 (84.6)

Home mechanical ventilation	12 (46.2)
SGRQ-C total score (0 best - 100 poorest)[d]	63.7 ± 20.3
HADS, total score (0 best - 42 poorest)[d]	21.2 ± 2.8
Age-adjusted Charlson comorbidity index score	4.88 ± 2.05
Number of concomitant diseases[e]	4.3 ± 2.8
Living with partner, n (%)	17 (65.4)
Outcomes	
Unplanned hospitalisation days/year, any cause (primary endpoint), median [Q1−Q3]	68 [21−110]

BODE index, body mass index, airflow obstruction, dyspnea, and exercise index; COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 second; GOLD, Global Initiative for Chronic Obstructive Lung Disease; HADS, Hospital Anxiety and Depression Scale; N, number of patients in group; n, number of patients with characteristic; $PaCO_2$, arterial blood carbon dioxide partial pressure; PaO_2, arterial blood oxygen partial pressure; Q1−Q3, interquartile range; SGRQ-C, COPD-specific version of the Saint George's Respiratory Questionnaire.

[a]Values are means ± standard deviation (SD), unless otherwise indicated.

[b]One patient who died prior to randomisation is not included.

[c]GOLD A-D stage was determined using modified Medical Research Council dyspnea scale.

[d]SGRQ-C and HADS scores were collected after the run-in period in which patients in the DM group had already received four home-coaching sessions. HADS scores of 11−21 indicate moderate-to-severe anxiety or depression.

[e]In patients with ≥1 concomitant disease.