

SUPPLEMENTARY TABLES

Table S1. Subject listing of demographics, pulmonary function, symptoms, and imaging measurements

Subject	Group	Tmt days	Age (yrs)	Sex	BMI (kg/m ²)	Pack- years	FEV ₁ % _{pred}	FVC % _{pred}	FEV ₁ /FVC	RV/TLC % _{pred}	DL _{CO} % _{pred}	6MWD (m)	SGRQ Total	PEQ Cough Frequency ^a	PEQ Cough Severity ^a	PEQ Chest Discomfort ^a	PEQ Dyspnea ^a	PEQ Need for BD ^a	RA ₉₅₀	VDP (%)
1	SP	28	74	M	27	56	40	56	52	173	59	384	60	3.75	3.75	3.50	3.75	3.25	9	27
2	SP	28	76	M	31	72	82	96	61	124	84	369	31	1.50	1.50	1.50	2.00	1.50	2	8
3	SP	28	73	M	34	20	63	76	60	156	76	399	25	3.00	3.00	1.75	2.00	2.50	3	18
4	SP	21	66	M	27	63	52	98	40	140	55	513	50	2.67	2.33	2.67	2.33	3.00	22	28
5	SP	21	67	F	31	12	96	101	73	112	110	399	28	3.67	2.00	1.00	1.00	3.00	0	3
6	SP	21	77	M	27	94	79	135	42	100	50	570	42	3.00	2.00	3.00	2.00	NA	13	22
7	SP	22	72	F	21	68	32	58	42	152	63	315	66	2.00	2.00	1.00	2.00	2.00	7	19
8	SP	28	79	F	27	39	67	97	52	109	35	243	61	2.33	3.00	3.33	3.33	1.00	18	14
9	SP	28	79	M	28	20	71	97	53	132	62	204	55	1.50	1.50	2.50	2.67	NA	5	23
10	SP	21	62	F	35	90	37	54	52	183	36	NA	57	3.00	2.33	1.33	2.00	2.33	2	20
11	SP	21	56	F	26	35	59	89	52	122	57	387	32	5.00	2.50	2.00	2.00	4.00	3	28
12	SP	21	68	M	32	126	68	85	59	124	59	336	58	3.00	3.33	2.67	2.33	2.00	6	31
13	SP	21	61	M	28	30	41	74	42	165	93	450	44	3.67	2.00	2.00	2.00	3.00	5	16
14 ^c	SP	20	60	M	32	96	44	62	54	189	97	360	58	2.00	2.00	2.33	3.00	3.00	4	-
15 ^b	SP	-	61	F	20	53	30	63	37	178	30	NA	NA	NA	NA	NA	NA	NA	25	36
16 ^b	SP	-	58	M	38	113	49	87	43	160	67	NA	72	NA	NA	NA	NA	NA	NA	NA
17	NSP	28	80	M	22	52	58	107	38	147	42	447	20	1.50	1.50	1.50	2.00	1.00	32	19
18	NSP	28	66	M	30	50	57	102	42	122	82	423	47	3.25	2.25	1.25	2.00	1.75	5	22
19	NSP	28	65	F	23	28	71	103	53	116	69	495	28	2.50	2.25	1.50	2.50	2.25	4	9
20	NSP	28	69	F	24	52	62	103	46	95	46	464	46	1.50	1.25	3.25	2.75	1.33	17	15
21	NSP	21	71	F	32	88	62	83	56	113	50	279	39	3.00	3.00	1.75	2.00	2.50	5	5
22	NSP	22	80	M	24	128	81	112	52	119	35	456	32	1.33	1.33	1.00	1.00	1.00	16	21
23	NSP	28	77	F	21	40	47	82	43	127	15	174	44	3.00	2.25	1.50	2.50	1.50	38	43
24	NSP	28	69	F	32	52	84	97	66	117	65	327	52	3.00	3.00	2.75	3.00	3.00	2	7
25	NSP	28	72	F	26	23	64	84	57	113	57	427	38	1.00	1.00	3.00	2.75	1.00	9	8
26	NSP	27	62	F	20	39	48	106	35	111	48	452	18	2.00	2.00	1.00	2.00	1.00	29	22
27	NSP	21	62	M	29	38	89	99	68	130	64	465	13	1.00	1.00	1.00	2.00	1.00	2	4
28	NSP	26	51	M	25	30	28	100	22	165	32	402	67	3.00	2.00	1.00	2.00	1.00	31	37
29	NSP	21	75	F	23	41	46	89	39	139	29	402	41	2.00	1.00	2.67	2.67	1.00	26	36
30 ^b	NSP	-	77	M	29	70	33	83	29	158	46	216	NA	NA	NA	NA	NA	NA	17	36
31 ^b	NSP	-	74	M	20	17	27	63	31	169	24	114	68	NA	NA	NA	NA	NA	37	14
32 ^b	NSP	-	75	F	29	58	100	103	73	101	41	390	29	NA	NA	NA	NA	NA	7	5
Intent-to-treat Population (n=32)																				
Mean (±SD)		69(8)	17M/15F		27(5)	56(31)	58(20)	89(19)	49(12)	136(27)	56(22)	375(106)	44(16)	-	-	-	-	-	13(12)	20(11)
Efficacy Population (n=27)																				
Mean (±SD)		69(8)	14M/13F		27(4)	55(31)	60(18)	91(19)	50(11)	133(25)	58(22)	390(93)	43(15)	2.53(0.96)	2.11(0.73)	1.99(0.83)	2.28(0.60)	2.00(0.92)	12(11)	20(11)
P-value		0.99	-		0.99	0.84	0.70	0.73	0.71	0.65	0.66	0.57	0.74	-	-	-	-	-	0.67	0.95

Dx, diagnosis; Tmt, treatment; yrs, years; BMI, body mass index; FEV₁, forced expiratory volume in 1 second; %_{pred}, percent predicted; FVC, forced vital capacity; RV, residual volume; TLC, total lung capacity; DL_{CO}, diffusion capacity of the lung for carbon monoxide; 6MWD, six-minute walk distance; SGRQ, St. George's Respiratory Questionnaire; PEQ, Patient Evaluation Questionnaire; BD, bronchodilator; RA₉₅₀, relative area of the lung with attenuation values below -950 Hounsfield units; VDP, whole lung ventilation defect percent; SD, standard deviation; SP, sputum-producer; NSP, non-sputum producer; COPD, chronic obstructive pulmonary disease; F, female; M, male; NA, data not acquired; ^a, Mean data acquired off-oPEP; ^b, Withdrew from the study prior to completion; ^c, ³He MRI signal-to-noise ratio <10.

Table S2. Subject listing of pulmonary function, symptoms, and imaging measurements pre-and post-oPEP

Subject	Group	Tmt days	Daily Tmt frequency	Tmt Adherence (%)	Pre-oPEP							Post-oPEP							Post-oPEP Difference (Pre-Post)								
					FEV ₁ (L)	FEV ₁ (% _{pred})	FVC (L)	FVC (% _{pred})	6MWD (m)	SGRQ Total	VDP (%)	FEV ₁ (L)	FEV ₁ (% _{pred})	FVC (L)	FVC (% _{pred})	6MWD (m)	SGRQ Total	VDP (%)	FEV ₁ (L)	FEV ₁ (% _{pred})	FVC (L)	FVC (% _{pred})	6MWD (m)	SGRQ Total	PEQ-ease-bringing-up-sputum	PEQ-patient-global-assessment	VDP (%)
1	SP	28	4.0	100	1.20	40	2.32	56	384	60	27	1.26	42	2.78	67	390	65	24	-0.06	-2	-0.46	-11	-6	-4	2.50	2.50	3
2	SP	28	3.9	93	2.49	82	4.05	96	369	31	8	2.48	82	4.43	106	389	32	18	0.01	0	-0.38	-10	-20	-1	-0.75	0.25	-10
3	SP	28	3.8	93	1.67	63	2.79	76	399	25	18	1.50	57	2.87	79	426	32	16	0.17	6	-0.08	-3	-27	-7	1.25	0.00	2
4	SP	21	3.9	90	1.58	52	3.98	98	513	50	28	1.55	51	4.23	104	540	42	29	0.03	1	-0.25	-6	-27	8	1.33	1.00	-1
5	SP	21	4.0	95	2.04	96	2.81	101	399	28	3	2.18	103	3.02	109	411	22	2	-0.14	-7	-0.21	-8	-12	6	0.67	0.00	1
6	SP	21	3.4	57	2.06	79	4.94	135	570	42	22	2.26	86	4.88	134	588	28	24	-0.20	-7	0.06	1	-18	14	2.67	2.67	-2
7	SP	22	3.7	76	0.61	32	1.47	58	315	66	19	0.73	38	2.05	82	339	47	15	-0.12	-6	-0.58	-24	-24	19	1.67	0.00	4
8	SP	28	1.4	36	1.25	66	2.41	95	171	63	12	1.22	64	2.35	92	234	61	15	0.03	2	0.06	3	-63	2	-0.50	0.00	-3
9	SP	28	3.7	79	2.04	66	3.92	91	237	47	33	2.05	66	4.10	95	217	47	24	-0.01	0	-0.18	-4	20	0	1.75	1.00	9
10	SP	21	3.8	90	0.69	31	1.32	46	NA	46	20	0.79	36	1.42	50	NA	39	14	-0.10	-5	-0.10	-4	NA	7	0.00	0.00	6
11	SP	21	3.8	95	1.14	43	2.24	67	321	54	28	1.41	54	2.69	80	399	34	22	-0.27	-11	-0.45	-13	-78	20	3.00	3.00	6
12	SP	21	2.7	62	1.96	63	3.15	75	348	54	31	1.97	64	3.30	79	321	47	23	-0.01	-1	-0.15	-4	27	7	3.00	1.67	8
13	SP	21	3.7	86	1.27	43	2.71	70	363	50	14	1.15	39	2.55	66	384	35	17	0.12	4	0.16	4	-21	15	0.67	1.00	-3
14*	SP	20	0.9	10	1.50	43	3.30	72	426	65	-	1.65	47	3.46	75	414	35	-	-0.15	-4	-0.16	-3	12	30	0.00	-1.00	-
17	NSP	28	3.8	89	1.43	58	3.72	107	447	20	19	1.35	55	3.59	103	428	26	29	0.08	3	0.13	4	19	-6	0.00	0.00	-10
18	NSP	28	3.9	96	1.87	57	4.51	102	423	47	22	1.51	46	4.29	97	392	55	30	0.36	11	0.22	5	31	-8	0.00	-1.25	-8
19	NSP	28	4.0	100	1.44	71	2.73	103	495	28	9	1.45	71	2.74	103	541	26	6	-0.01	0	-0.01	0	-46	2	0.75	0.00	3
20	NSP	28	1.7	4	1.40	62	3.05	103	464	46	15	1.31	58	2.98	100	452	44	20	0.09	4	0.07	3	12	2	-0.50	-1.00	-5
21	NSP	21	3.9	95	1.25	62	2.22	83	279	39	5	1.20	59	2.07	77	258	48	6	0.05	3	0.15	6	21	-9	1.25	0.00	-1
22	NSP	22	3.7	81	2.30	81	4.44	112	456	32	21	2.12	75	4.23	107	468	21	25	0.18	6	0.21	5	-12	11	0.00	0.00	-4
23	NSP	28	4.0	100	0.92	45	2.41	88	234	42	41	0.96	47	2.44	90	222	41	40	-0.04	-2	-0.03	-2	12	2	0.00	0.00	1
24	NSP	28	2.5	50	1.91	87	2.90	100	360	46	7	1.91	87	2.89	100	400	41	7	0.00	0	0.01	0	-40	5	0.25	0.25	0
25	NSP	28	3.5	68	1.45	64	2.54	85	428	33	9	1.55	69	2.53	85	446	36	5	-0.10	-5	0.01	0	-18	-3	0.00	0.00	3
26	NSP	27	3.4	68	1.52	50	4.12	106	480	18	23	1.46	49	4.02	103	499	21	27	0.06	1	0.10	3	-19	-3	0.00	0.00	-5
27	NSP	21	3.0	76	2.84	81	4.13	89	450	12	3	2.91	83	4.31	93	450	9	5	-0.07	-2	-0.18	-4	0	3	0.67	0.00	-2
28	NSP	26	1.8	19	1.12	27	4.87	93	402	53	35	1.16	28	4.93	94	408	64	36	-0.04	-1	-0.06	-1	-6	-11	0.67	0.00	-1
29	NSP	21	4.0	100	0.98	44	2.47	83	432	42	37	1.00	44	2.48	83	411	37	34	-0.02	0	-0.01	0	21	6	1.67	0.00	3

Dx, diagnosis; Tmt, treatment; Daily Tmt frequency, the average number of times oPEP treatment was performed daily; Tmt Adherence, percent of days that in which oPEP treatment was performed four-times; FEV₁, forced expiratory volume in 1 second; %_{pred}, percent predicted; FVC, forced vital capacity; 6MWD, six-minute walk distance; SGRQ, St. George’s Respiratory Questionnaire; VDP, whole lung ventilation defect percent; PEQ, Patient Evaluation Questionnaire; SP, sputum-producer; NSP, non-sputum producer; COPD, chronic obstructive pulmonary disease; NA, data not acquired;

a, ³He MRI signal-to-noise ratio <10.

Table S3. Pre- and Post-oPEP measurements for the On-Off and Off-On Group

Parameter (±SD)	On-Off Group n=13 (SP n=7, NSP n=6)				Off-On Group n=14 (SP n=7, NSP n=7)				Δ ^a
	Pre	Post	Δ	p/p ^b	Pre	Post	Δ	p/p ^b	p/p ^b
FVC % _{pred}	95(22)	98(17)	-3(9)	0.25/0.75	83(16)	85(14)	-2(4)	0.14/0.42	0.67/1.00
6MWD (m)	424(80)	432(89)	-8(23)	0.21/0.84	358(94) ^d	370(92) ^d	-12(33) ^d	0.39/0.39	0.76/1.00
SGRQ total-score	40(13)	37(14)	2(9)	0.44/0.88	45(15)	39(14)	-6(10)	0.07/0.28	0.34/1.00
PEQ-ease-bringing-up-sputum ^c	3.82(0.85)	2.99(0.83)	0.83(1.07)	0.02 /0.10	4.07(0.27)	3.27(1.10)	0.80(1.13)	0.01 /0.05	0.83/0.83
PEQ-patient-global-assessment ^c	3.62(0.93)	3.29(1.17)	0.32(1.14)	0.89/0.89	4.00(0.00)	3.58(0.97)	0.42(0.97)	0.16/0.32	0.65/1.00

On-Off Group, patients randomized to oPEP and crossed-over to baseline care; Off-On Group, patients randomized to baseline care and crossed-over to oPEP; SP, sputum-producers; NSP, non-sputum-producers; SD, standard deviation; Δ, pre – post; FVC, forced vital capacity; %_{pred}, percent predicted; 6MWD, six-minute walk distance; SGRQ, St. George's Respiratory Questionnaire; PEQ, Patient Evaluation Questionnaire; **Bold** p-values=significant; ^a, Significance of difference between the change following oPEP therapy for the On-Off Group and Off-On Group; ^b, Holm-Bonferroni adjusted significance values; ^c, Mean data acquired Off- and On-oPEP; ^d, n=13.