

Study design

	Visit-4	Visit-5
PFT	✓	✓
MRI	✓	✓
CT	✓	✓
ACQ/AQLQ/SGRQ	✓	✓

Figure 1. Open-extension Study design PFT=Pulmonary Function Test; MRI=Magnetic Resonance Imaging; ACQ=Asthma Control Questionnaire; AQLQ=Asthma Quality-of-life Questionnaire; SGRQ=St. George's Respiratory Questionnaire

Participant Flow

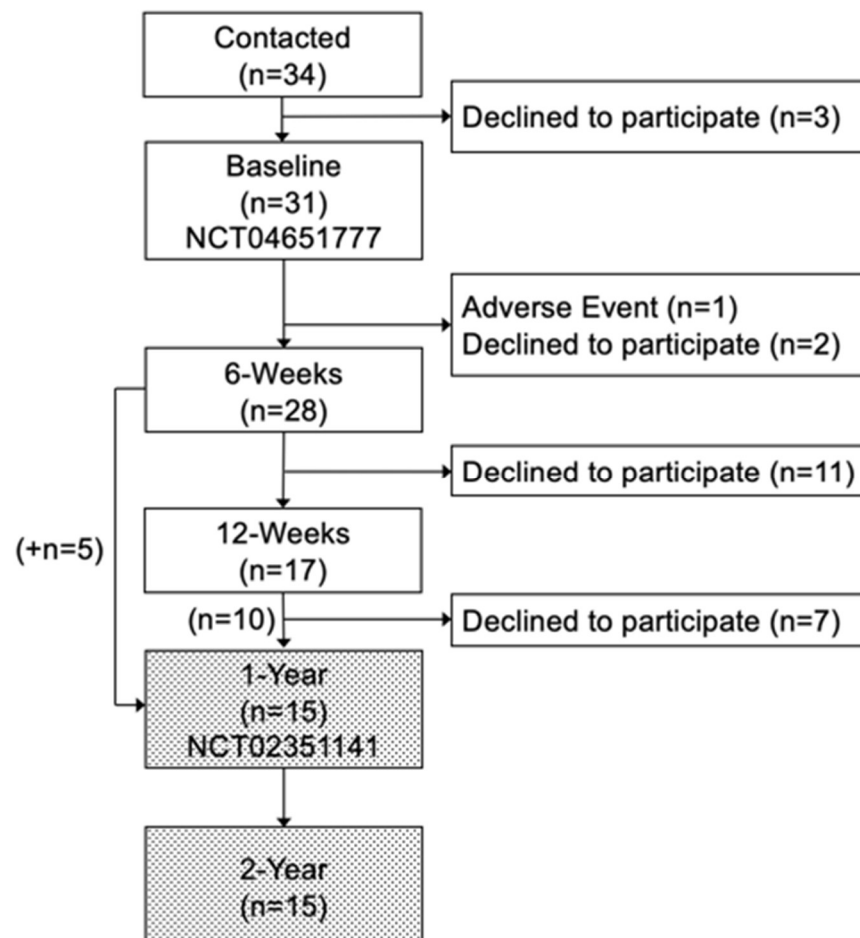


Figure 1. CONSORT Diagram of Study enrollment and Participation

Baseline Characteristics

Table 1. Baseline participant demographic characteristics and other markers

Parameter Mean ($\pm$ SD)	Completed V1 (n=31)	Completed V4 and V5 (n=15)	<i>P</i>
Age years	54 (15)	56 (14)	ND
BMI kg/m ²	31 (7)	33 (8)	ND
Female n (%)	24 (77)	11 (73)	ND
Pre-BD FEV ₁ L	2.1 (0.7)	2.2 (0.8)	.8
Post-BD FEV ₁ L	2.4 (0.8)	2.5 (1.0)	.8
Pre-BD FEV ₁ % _{pred}	72 (19)	73 (15)	.8
Post-BD FEV ₁ % _{pred}	81 (19)	84 (16)	.6
Pre-BD FEV ₁ /FVC %	65 (12)	67 (10)	.5
Post-BD FEV ₁ /FVC %	68 (12)	71 (8)	.3
Pre-BD R ₅ cm H ₂ O·sec/L	5.7 (1.7)	5.5 (1.8)	.7
Post-BD R ₅ cm H ₂ O·sec/L	4.9 (1.5)	4.5 (1.4)	.4
Pre-BD R ₁₉ cm H ₂ O·sec/L	3.7 (1.2)	3.6 (1.1)	.8
Post-BD R ₁₉ cm H ₂ O·sec/L	3.5 (1.0)	3.3 (1.0)	.4
Pre-BD R ₅₋₁₉ cm H ₂ O·sec/L	2.0 (1.0)	1.9 (1.0)	.7
Post-BD R ₅₋₁₉ cm H ₂ O·sec/L	1.4 (0.9)	1.2 (0.8)	.6
ACQ-6	2.1 (1)	1.6 (1.1)	.2
AQLQ	4.5 (1.2)	4.9 (1.3)	.3
SGRQ	49 (16)	45 (20)	.5
Pre-BD VDP %	13 (11)	11 (8)	.8
Post-BD VDP %	9 (10)	6 (4)	.4

P=Significance values for independent samples t-test for participants who only completed V1 vs those who completed V4+V5. BMI=body mass index; BD=bronchodilator; FEV₁=forced expiratory volume in 1 second; %_{pred}=percent of predicted value; FVC=forced vital capacity; ACQ=Asthma Control Questionnaire; AQLQ=Asthma Quality-of-Life Questionnaire; SGRQ=St. George's Respiratory Questionnaire; VDP=Ventilation Defect Percent.

Safety

Table 3. Asthma exacerbations and oral OCS use across follow-up periods

P#	Baseline to 1-Year follow-up period		1-Year to 2-Year follow-up period	
	Exacerbations?	OCS?	Exacerbations?	OCS?
001	X	X	X	X
002	✓	✓	✓	✓
006	X	X	X	X
007	X	X	✓	X
008	X	X	✓	✓
010	X	X	✓	✓
013	✓	✓	✓	✓
018	X	X	X	X
021	X	X	✓	✓
023	X	X	X	X
027	X	X	✓	✓
028	✓	✓	X	X
029	✓	✓	✓	✓
030	X	X	X	X
033	X	X	X	X
<i>Total</i>	4	4	8	7

X indicates no event or requirement; (✓) indicates ≥ 1 exacerbation or ≥ 1 OCS course.

Outcome Measures

Table 4. Pulmonary Function and other clinical Markers

Parameter Mean ($\pm$ SD)	Baseline (n=15)	1-Year (n=15)	2-Years (n=15)	P	P*
Age years	56 (14)	57 (14)	58 (14)	ND	ND
BMI kg/m ²	32 (8)	33 (8)	32 (8)	ND	ND
Female n (%)	11 (73)	11 (73)	11 (73)	ND	ND
FEV ₁ L	2.2 (0.8)	2.4 (0.8)	2.3 (0.8)	.001	.1
FEV ₁ % _{pred}	73 (15)	83 (16)	78 (15)	.005	.2
FVC L	3.3 (1.2)	3.4 (1.2)	3.4 (1.2)	.8	.1
FVC % _{pred}	85 (9)	90 (12)	89 (11)	.5	.2
FEV ₁ /FVC %	67 (10)	72 (8)	68 (9)	.002	.9
R ₅ cm H ₂ O·sec/L	5.5 (1.8)	4.5 (1.3)	4.3 (1.2)	.5	.03
R ₁₉ cm H ₂ O·sec/L	3.6 (1.1)	3.5 (1.0)	3.2 (0.9)	.3	.2
R ₅₋₁₉ cm H ₂ O·sec/L	1.9 (1.0)	1.1 (0.8)	1.1 (0.7)	.9	.01
FeNO ppb	36 (37)	47 (71)	33 (31)	.8	.8
ACQ-6	1.6 (1.1)	1.2 (0.8)	1.3 (1.2)	.5	.3
AQLQ	4.9 (1.3)	5.8 (1.2)	5.2 (1.1)	.02	.2
SGRQ	45 (20)	29 (16)	35 (22)	.2	.048

P=Significance determined using paired samples t-test between 1-year and 2-year visits; P*=Significance determined using paired samples t-test between baseline and 2-year visits. BMI=body mass index; FEV₁=forced expiratory volume in 1 second; %_{pred}=percent of predicted value; FVC=forced vital capacity; R₅=total airway resistance; R₁₉=central airway resistance; R₅₋₁₉=peripheral airway resistance; Eos=blood eosinophil count; FeNO=fraction of exhaled nitric oxide; ppb=parts per billion; ACQ=Asthma Control Questionnaire; AQLQ=Asthma Quality-of-Life Questionnaire; SGRQ=St. George's Respiratory Questionnaire.

Table 5. Imaging Measurements

Parameter Mean ($\pm$ SD)	Baseline (n=15)	1-Year (n=15)	2-Years (n=15)	P	P*
Pre-BD VDP %	11 (8)	8 (8)	8 (9)	.9	.08
Post-BD VDP %	6 (4)	6 (6)	-	-	-
TBV mL	278 (65)	271 (64)	270 (63)	.9	.4
BV ₅ mL	147 (37)	149 (31)	147 (32)	.6	1
BV ₅₋₁₀ mL	46 (15)	45 (16)	45 (15)	.9	.6
BV ₁₀ mL	84 (28)	77 (24)	78 (25)	.8	.2
BV ₅ /TBV %	53 (8)	55 (6)	55 (7)	.6	.7
BV ₅₋₁₀ /TBV %	17 (4)	16 (3)	16 (3)	.7	.7
BV ₁₀ /TBV %	30 (6)	28 (4)	29 (5)	.6	.4
Total airway count n	200 (46)	218 (46)	201 (49)	.4	1
Wall thickness %	18.1 (0.6)	18.0 (0.7)	17.6 (0.8)	.08	.04
Wall area %	68 (1)	67 (1)	66 (2)	.01	.005
Lumen area %	32 (1)	33 (1)	34 (2)	.01	.005
Mucus-count	4 (3)	2 (3)	3 (5)	.4	.6
Mucus-score	3 (3)	1 (2)	2 (3)	.2	.6

P=Significance determined using paired samples t-test between 1-year and 2-year visits; P*=Significance determined using paired samples t-test between baseline and 2-year visits. CT=computed tomography; TBV=total blood volume; BV₅=blood volume of vessels with cross-sectional area <5 mm²; BV₅₋₁₀=blood volume of vessels with cross-sectional area 5-10 mm²; BV₁₀=blood volume of vessels with cross-sectional area >10 mm²; BD=bronchodilator; VDP=ventilation defect percent; TAC=total airway count.