

Table E1 of the online supplement. Median sputum concentrations of IL-8, MPO, LTB4 and neutrophils and macrophages in individual patients with A1ATD and their matched usual COPD control

Patient	Biomarker	A1ATD	COPD
1	IL-8	11.8 (9.7 - 13.8)	14.3 (11 - 15.4)
	MPO	1.7 (1.0 - 1.9)	7.2 (6.3 - 9.4)
	LTB4	14.5 (7.7 - 37.8)	91.2 (37.2 - 94.2)
	Neutrophils	3.3 (1.5 - 7.8)	4.45 (4.1 - 6.2)
	Macrophages	0.4 (0.2 - 0.8)	0.12 (0.04 - 0.17)
2	IL-8	20.6 (12.0 - 23.5)	4.8 (3.8 - 6.0)
	MPO	0.4 (0.4 - 0.6)	1.8 (1.7 - 1.8)
	LTB4	20.6 (14.2 - 30.8)	1.1 (0.8 - 1.6)
	Neutrophils	1.0 (0.6 - 1.4)	6.1 (5 - 6.8)
	Macrophages	0.62 (0.2 - 0.9)	0.18 (0.13 - 0.2)
3	IL-8	2.22 (1.6 - 3.8)	1.4 (1.2 - 1.4)
	MPO	1.58 (1.47 - 1.8)	1.7 (1.6 - 1.9)
	LTB4	2.04 (1.6 - 2.9)	5.9 (5.3 - 6.4)
	Neutrophils	1.2 (0.8 - 2.3)	6.4 (5.2 - 7.8)
	Macrophages	0.7 (0.27 - 1.39)	0.08 (0.06 - 0.11)
4	IL-8	24.6 (20 - 34.6)	25.8 (22 - 27.3)
	MPO	4.2 (3.9 - 4.4)	3.1 (1.7 - 4.1)
	LTB4	33.8 (27.9 - 46.8)	28.7 (20.8 - 40.4)
	Neutrophils	6.1 (4.9 - 9.8)	7.8 (5.9 - 17.6)
	Macrophages	1.2 (0.5 - 1.3)	0.13 (0.12 - 0.44)
5	IL-8	11.3 (7.5 - 17.7)	5.4 (4.9 - 6.9)
	MPO	3.3 (3.2 - 3.9)	4.1 (3.4 - 12.3)
	LTB4	65.3 (46.8 - 73.9)	11.6 (2.2 - 17.6)
	Neutrophils	5.3 (2.9 - 8.6)	6.23 (5.9 - 6.9)
	Macrophages	0.87 (0.6 - 3.02)	0.4 (0.3 - 1.02)
6	IL-8	22.4 (20.5 - 32.6)	6 (1.8 - 40.1)
	MPO	2.4 (2.3 - 2.6)	2.4 (1.6 - 4.2)
	LTB4	4.9 (2.9 - 7.8)	11.4 (8.3 - 49.0)
	Neutrophils	5.8 (3.9 - 6.3)	5.15 (3.8 - 6.5)
	Macrophages	1.9 (1.8 - 3.7)	0.28 (0.2 - 0.3)
7	IL-8	0.4 (0.2 - 0.5)	1.0 (0.5 - 2.6)
	MPO	0.2 (0.1 - 0.3)	1.9 (1.1 - 2.4)
	LTB4	3.2 (0.1 - 4.0)	0.5 (0.3 - 0.6)
	Neutrophils	4.9 (2.2 - 7.8)	7.3 (6.3 - 11.9)
	Macrophages	1.1 (0.3 - 1.6)	0.37 (0.3 - 0.7)

Legend

Presented data are the median concentrations (with interquartile range in parentheses) of the nine visits for a single patient. Individual A1ATD patients were matched with patients with usual COPD by the presence of chronic bronchitis, FEV₁, gas transfer, pack year smoking history and smoking status, medications and gender.

Table E1 of the online supplement (continued). Median sputum concentrations of IL-8, MPO, LTB4 and neutrophils and macrophages in individual patients with A1ATD and their matched usual COPD control

Patient	Biomarker	A1ATD		COPD	
8	IL-8	1.6	(1.0 - 2.1)	8.3	(0.2 - 0.4)
	MPO	0.3	(0.2 - 0.4)	7.1	(1.0 - 1.3)
	LTB4	1.8	(1.7 - 2.1)	10	(7.0 - 14.0)
	Neutrophils	0.4	(0.3 - 0.6)	13.6	(12.5 - 16.2)
	Macrophages	0.34	(0.03 - 0.46)	0.8	(0.08 - 0.3)
9	IL-8	10.6	(6.2 - 12.5)	3.4	(2.8 - 4.2)
	MPO	0.7	(0.6 - 0.7)	0.9	(0.7 - 1.0)
	LTB4	24.8	(13.5 - 45.1)	2.8	(2.2 - 3.7)
	Neutrophils	0.5	(0.3 - 4.6)	5.6	(4.9 - 6.6)
	Macrophages	0.4	(0.21 - 0.99)	0.31	(0.2 - 0.5)
10	IL-8	12.0	(7.3 - 15.7)	2.1	(1.1 - 2.8)
	MPO	0.5	(0.46 - 0.51)	1.9	(1.3 - 2.0)
	LTB4	10.3	(6.5 - 12.6)	8.0	(3.3 - 11.4)
	Neutrophils	1.5	(0.7 - 2.3)	4.1	(3.6 - 4.9)
	Macrophages	0.28	(0.15 - 0.31)	1.7	(1.3 - 2.1)
11	IL-8	32.6	(25.2 - 39.4)	1.8	(1.5 - 2.6)
	MPO	1.8	(0.7 - 0.9)	0.8	(0.3 - 0.9)
	LTB4	75.9	(26.6 - 107.8)	1.4	(0.4 - 1.9)
	Neutrophils	2.8	(1.8 - 4.5)	4.5	(4.3 - 5.2)
	Macrophages	1.39	(0.6 - 2.1)	0.42	(0.09 - 0.9)
12	IL-8	1.4	(0.7 - 1.71)	22.2	(19.1 - 36.7)
	MPO	0.5	(0.4 - 0.6)	4.3	(2.1 - 6.1)
	LTB4	11.5	(7.3 - 14.0)	10.5	(7.8 - 21.9)
	Neutrophils	1.6	(0.9 - 3.4)	13.7	(8.2 - 12.7)
	Macrophages	0.3	(0.1 - 0.7)	2.57	(1.8 - 5.3)

Legend

Presented data are the median concentrations (with inter-quartile range in parentheses) of the nine visits for a single patient. Individual A1ATD patients were matched with patients with usual COPD by the presence of chronic bronchitis, FEV₁, gas transfer, pack year smoking history and smoking status, medications and gender.

Table E2 Intra-patient variability of sputum inflammatory mediators and cell counts in matched stable patients with usual COPD and A1ATD: the effect of a rolling mean.

Days	IL8		MPO		LTB4		Neutrophil		Macrophage	
	A1ATD	COPD	A1ATD	COPD	A1ATD	COPD	A1ATD	COPD	A1ATD	COPD
1	28.9	45.1	36.0	72.2	32.0	45.5	69.4	23.0	111.2	71.4
3	17.2 **	32.2 **	13.5**	34.1**	14.5 **	30.7*	47.1**	11.7*	47.3**	26.0 *
5	10.9** ^	13.8**^^	6.3**^^	20.2**^^	6.9 **^^	18.5**^^	20.1** ^	7.9** ^	24.7** ^	16.8 *

Legend

Data is the intra-patient variability, expressed as the median co-efficient of variance (CV) as a percentage. The median coefficient of variation has been derived from the mediator specific CV from each patient. Differences in CVs were assessed using the Wilcoxon's matched pairs signed rank test. * = significant reduction in mean CV from raw data ($p < 0.05$), ** ($p < 0.01$) ^ = significant reduction in mean CV from 3 day rolling mean ($p < 0.05$), ^^ ($p < 0.01$)

Table E3. A comparison of the numbers needed in a parallel study design when one day's data, the mean of three days' data or the mean of five days' data are used for calculations in A1ATD and usual COPD

Days	IL8		MPO		LTB4		Neutrophil		Macrophage	
	A1ATD	COPD	A1ATD	COPD	A1ATD	COPD	A1ATD	COPD	A1ATD	COPD
1	59	106	537	143	30	89	172	32	186	56
3	8	17	71	37	9	10	110	8	129	27
5	7	12	50	17	9	13	79	6	96	18

Legend

Numbers required to provide an 80% chance of detecting a 50% decrease in mediators or cells at the 5% level of significance. For 1 day's data, power calculations were performed for each mediator or cell using data from the first study visit. For three and five days' data; power calculations were performed using data collected on the first three days (visit 1 to 3) or first five days respectively.