

## Online Resource 2

**Data Supplement:** Respiratory Physiologic Measures, Quality of Life, and Serum Biomarker Immunoassay Results

**Title:**

Safety and efficacy of multipotent adult progenitor cells in acute respiratory distress syndrome (MUST-ARDS): a multicentre, randomised, double-blind, placebo-controlled phase 1/2 trial

**Journal:** Intensive Care Medicine

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**Respiratory Physiologic Measures:** Mean (SD) change from baseline among ventilated subjects assessed at each timepoint. Data should be interpreted with caution because assessments are not available for all subjects at all timepoints.

	Cohort 3 Cells N = 20	Cohort 3 Placebo N = 10
<b>Peak inspiratory pressure (cm H<sub>2</sub>O)</b>		
Day 1	0.6 (5.92)	-4.0 (6.77)
Day 2	0.9 (7.48)	-1.7 (5.14)
Day 3	1.2 (6.54)	-4.5 (10.62)
Day 7	-1.6 (12.62)	-6.5 (9.03)
Day 28 <sup>1</sup>	-1.3 (14.75)	NA
<b>Plateau inspiratory pressure (cm H<sub>2</sub>O)</b>		
Day 1	1.1 (6.13)	-1.3 (3.74)
Day 2	0.7 (5.88)	0.4 (2.72)
Day 3	1.7 (5.33)	-0.6 (6.97)
Day 7	-1.6 (10.14)	-1.2 (3.83)
Day 28 <sup>1</sup>	13.0 (NA)	NA
<b>PAO<sub>2</sub>/FiO<sub>2</sub> ratio</b>		
Day 1	4.27 (48.783)	10.21 (52.455)
Day 2	24.92 (90.777)	38.28 (76.121)
Day 3	23.98 (65.691)	89.74 (109.262)
Day 7	35.03 (32.018)	87.99 (79.007)
Day 28 <sup>1</sup>	80.10 (36.846)	-127.50 (NA)
<b>PEEP (cm H<sub>2</sub>O)</b>		
Day 1	0.2 (1.80)	0.1 (2.33)
Day 2	-1.2 (2.98)	1.1 (1.91)
Day 3	-1.1 (3.28)	0.0 (4.00)
Day 7	-4.4 (4.70)	-0.5 (3.27)
Day 28 <sup>1</sup>	-1.8 (3.95)	-3.0 (NA)

<sup>1</sup> At Day 28 only a small number of subjects were still on a ventilator so the data should be interpreted with caution  
 FiO<sub>2</sub> = fraction inspired oxygen, NA = not applicable (n = 0 or 1), PaO<sub>2</sub> = arterial oxygen partial pressure, PEEP = positive end-expiratory airway pressure

## Quality of Life: EQ-5D-3L

EQ-5D-3L Index						
	Day 28		Day 90		Day 365	
	cells	placebo	cells	placebo	cells	placebo
n	9	6	11	4	10	5
Median	0.597	0.5565	0.708	0.579	0.795	0.597
Quartile 1	0.516	0.27075	0.486	0.364	0.436	0.516
Quartile 3	0.768	0.61425	0.7695	0.71025	0.796	1

VAS						
	Day 28		Day 90		Day 365	
	cells	placebo	cells	placebo	cells	placebo
n	8	6	11	4	10	5
Median	68.5	55	75	70	75	60
Quartile 1	63.75	42.5	66	66.25	66.25	55
Quartile 3	75	60	77.5	71.25	95	75

Health-related quality of life was assessed using the EQ-5D-3L instrument. The EQ-5D-3L index was calculated using the questionnaire responses. The EQ-5D-3L also includes a visual analogue scale.

## **Serum Biomarkers:**

Serum biomarkers multiplex immunoassays (Aeirtec - Newcastle upon Tyne, UK) measured at baseline, and days 1, 2, 3, and 7 after cell product or placebo administration included angiopoietin 1 (ANG1), angiopoietin 2 (ANG2), C-X-C Motif chemokine ligand 10 (CXCL10), Interferon (IFN) gamma, interleukin 1 beta (IL-1b), interleukin 1 receptor 2 (IL-1R2), interleukin 1 receptor antagonist (IL-1RA), interleukin 6 (IL-6), interleukin 8 (IL-8), interleukin 10 (IL-10), interleukin 12 (IL-12), keratinocyte growth factor (KGF), matrix metalloproteinase 2 (MMP-2), programmed cell death protein (PD-1), receptor for advanced glycation end-products (RAGE), regulated on activation, normal T cell expressed and secreted (RANTES), surfactant protein D (SP-D), tumour necrosis factor alpha (TNF alpha), soluble TNF receptor 1 (sTNFR1) and thrombospondin 1 (TSP-1). Table presents median with quartile 1 and quartile 3 information. The table provides baseline data for all subjects including those who do not have day 7 information. This differs from figure 2 which compares baseline with day 7 data so only those with both data sets.

Biomarkers for Cohort 3										
Patients, n=	Cell Group					Placebo Group				
	20	20	20	19	19	10	10	9	10	7
	Baseline	Day 1	Day 2	Day 3	Day 7	Baseline	Day 1	Day 2	Day 3	Day 7
ANG1 (ng/mL)	0.27	0.26	0.28	0.32	0.40	0.13	0.14	0.17	0.15	0.41
Q1	0.12	0.12	0.16	0.06	0.30	0.07	0.10	0.05	0.10	0.19
Q3	0.39	0.45	0.47	0.51	0.70	0.45	0.93	0.51	0.41	1.65
ANG2 (ng/mL)	4.00	4.00	3.44	2.03	1.32	6.12	3.79	1.79	3.01	0.62
Q1	0.90	1.73	0.81	0.68	0.39	0.70	0.22	0.03	0.41	0.32
Q3	7.42	10.38	7.48	5.66	4.28	18.91	5.74	4.01	5.05	2.37
CXCL10 (pg/mL)	223.85	187.78	140.00	119.17	147.00	214.12	154.81	209.18	195.73	193.76
Q1	57.45	73.91	74.80	77.57	98.57	122.58	83.52	72.59	125.57	132.33
Q3	1902.59	1152.57	452.43	285.11	245.66	1922.52	611.60	337.45	420.71	672.66
IFN (pg/mL)	35.31	45.75	48.94	34.73	31.23	39.57	35.50	23.81	29.87	66.24
Q1	26.62	24.64	20.06	22.92	18.28	28.65	27.92	20.26	17.48	46.52
Q3	71.80	104.27	78.31	74.01	55.80	57.00	47.06	31.62	34.34	105.23
IL1 beta (pg/mL)	5.24	5.08	5.05	6.78	6.61	8.20	7.41	4.40	5.86	18.76
Q1	3.49	3.32	2.62	2.49	3.07	2.91	4.92	2.35	3.01	9.07
Q3	13.11	17.47	12.61	10.22	9.37	13.02	12.98	7.79	7.16	27.32
IL1-R2 (ng/mL)	1.00	0.73	0.48	0.41	0.38	1.09	1.16	1.46	1.61	0.37
Q1	0.26	0.24	0.23	0.22	0.24	0.44	0.33	0.27	0.49	0.26
Q3	2.21	2.89	3.82	2.21	0.61	5.15	4.99	3.45	2.81	1.30
IL1-RA (ng/mL)	0.05	0.06	0.06	0.09	0.05	0.16	0.11	0.02	0.08	0.04
Q1	0.02	0.02	0.02	0.01	0.01	0.02	0.03	0.02	0.02	0.02
Q3	0.13	0.15	0.20	0.21	0.46	0.31	0.12	0.09	0.15	0.10
IL6 (pg/mL)	57.35	64.99	46.92	42.79	29.46	35.07	32.67	27.42	29.44	33.20
Q1	21.23	32.73	17.42	26.51	17.22	16.72	14.95	12.99	23.28	27.84
Q3	103.88	82.71	69.88	64.54	40.19	88.31	71.74	36.42	54.06	44.78
IL8 (pg/mL)	12.01	11.98	8.45	6.93	8.63	18.13	18.67	12.62	12.97	12.33
Q1	4.29	6.32	5.95	4.44	4.70	7.64	10.39	12.44	10.57	9.79
Q3	19.38	18.51	17.33	16.12	23.86	27.28	26.09	24.94	31.81	15.20
IL10 (pg/mL)	25.65	27.34	29.08	21.30	36.34	37.55	34.66	30.51	32.13	79.97
Q1	15.86	14.30	13.53	11.98	21.95	17.43	25.84	20.65	20.69	37.71
Q3	65.68	73.57	58.95	43.45	44.98	57.70	67.20	34.51	49.12	120.72
IL12 (pg/mL)	99.58	99.60	88.69	72.45	52.71	161.45	114.98	67.15	87.56	225.52
Q1	22.24	30.50	19.00	0.63	0.63	30.83	47.12	26.67	19.34	100.73
Q3	158.09	232.09	186.90	154.53	91.68	252.27	188.03	90.57	91.33	361.43
MGF (pg/mL)	77.23	74.33	41.69	43.48	44.18	68.57	62.50	63.25	42.19	60.54
Q1	33.99	37.07	29.01	29.53	31.54	44.62	34.37	51.35	33.53	41.75
Q3	148.45	102.39	87.52	69.00	79.26	115.55	116.68	83.32	200.35	82.53
MMP2 (ng/mL)	4709.75	4998.77	7223.41	6660.45	7709.82	5462.57	8126.23	4040.75	4074.14	2763.60
Q1	3016.76	3035.27	3436.69	2920.48	3684.42	3423.79	3555.03	1600.04	2594.39	1916.39
Q3	9417.63	13931.81	14189.17	11080.05	14684.17	8222.99	11973.75	7500.46	7657.20	5980.80
PD1 (ng/mL)	1.65	1.86	1.61	1.81	1.34	2.41	2.14	1.78	1.78	3.45
Q1	1.21	1.33	1.36	1.15	1.20	1.75	1.47	1.30	1.27	2.06
Q3	2.94	3.87	2.55	2.63	2.47	2.91	2.41	2.21	2.32	4.48
RAGE (ng/mL)	0.31	0.21	0.01	0.01	0.01	0.43	0.20	0.01	0.06	0.01
Q1	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
Q3	0.62	0.44	0.22	0.01	0.01	0.94	0.55	0.19	0.27	0.11
RANTES (pg/mL)	87.30	179.34	192.57	114.31	309.23	178.85	172.40	101.21	50.55	268.12
Q1	36.38	46.52	49.82	44.83	87.81	71.69	63.93	63.36	36.79	213.32
Q3	221.67	265.60	416.16	451.72	405.31	298.78	308.95	217.07	171.20	302.93
SP-D (ng/mL)	10.91	18.41	17.07	10.39	12.25	31.37	27.61	37.27	28.63	15.35
Q1	7.42	10.42	9.88	7.19	7.86	13.25	14.29	20.35	14.79	9.02
Q3	25.91	39.94	34.57	33.21	19.11	59.06	49.85	55.17	37.41	27.83
sTNFR1 (pg/mL)	998.04	896.03	850.90	713.36	730.29	1731.84	1976.03	2497.07	1867.87	612.43
Q1	484.46	457.52	444.00	411.67	417.35	729.64	618.49	699.71	577.91	457.96
Q3	1539.44	1901.07	2018.57	1613.32	1573.37	3340.52	2862.76	2732.72	2776.66	1481.74
TNF (pg/mL)	4.87	5.81	5.41	4.61	4.68	7.24	6.04	4.59	5.08	6.79
Q1	3.52	4.22	3.83	3.44	2.81	4.61	3.93	3.49	3.47	3.11
Q3	10.42	11.24	8.31	6.70	6.87	9.62	8.06	6.40	6.01	10.41
TSP1 (ng/mL)	1461.11	2088.23	3935.94	2986.04	445.18	2487.46	1877.58	1044.44	1607.69	2745.29
Q1	984.88	865.51	1387.27	1093.75	1527.87	1617.95	1356.74	901.32	958.65	1954.58
Q3	4367.06	5478.67	5267.75	4770.33	5441.82	4177.24	2361.55	2711.14	2206.62	3614.97