

Simvastatin as a Treatment for Pulmonary Hypertension Trial (SiPHT)

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Online Data Supplement

Table E1 - Plasma cytokines and growth factors

pg/ml	Placebo W0		Placebo W24		Sig.	Statin W0		Statin W24		Sig.
	Mean	SEM	Mean	SEM		Mean	SEM	Mean	SEM	
Hu IL-1b	2.6	.8	2.3	.6	0.68	1.8	.4	1.7	.4	0.77
Hu IL-1ra	297.8	94.2	237.7	49.8	0.44	113.3	19.6	139.1	35.4	0.48
Hu IL-2	6.9	1.6	5.4	1.5	0.64	4.2	1.7	4.7	1.3	0.79
Hu IL-4	2.4	.3	2.4	.3	0.39	1.8	.5	2.0	.3	0.61
Hu IL-5	1.7	.3	1.6	.4	0.85	1.2	.3	1.1	.2	0.94
Hu IL-6	16.6	5.5	15.1	5.2	0.67	8.6	2.4	8.7	2.2	0.94
Hu IL-7	4.6	.9	3.6	.5	0.72	5.4	1.4	3.7	.7	0.13
Hu IL-8	7.2	1.4	6.1	1.2	0.79	5.2	1.5	4.3	.9	0.48
Hu IL-9	48.1	10.6	36.3	6.7	0.24	51.2	11.9	87.1	42.8	0.42
Hu IL-10	10.2	2.0	11.5	3.2	0.47	23.6	13.7	15.7	9.6	0.16
Hu IL-12(p70)	32.0	3.7	27.5	3.7	0.26	36.9	7.7	36.1	6.9	0.87
Hu IL-13	5.8	.9	5.7	1.2	0.81	12.4	5.5	10.6	4.9	0.11
Hu IL-15	15.8	4.0	13.8	3.9	0.69	11.9	2.2	13.4	2.4	0.44
Hu IL-17	88.0	27.7	58.7	7.6	0.79	67.1	18.5	57.3	13.4	0.51
Hu Eotaxin	94.0	19.5	82.0	11.5	0.35	71.7	8.9	69.3	8.0	0.78
Hu FGF basic	20.8	7.3	20.7	7.0	0.80	24.8	8.3	20.8	6.6	0.56
Hu G-CSF	29.6	4.4	26.8	4.3	0.14	30.6	5.3	27.3	4.3	0.22
Hu GM-CSF	83.2	12.0	78.3	10.8	0.87	67.0	13.5	72.1	11.0	0.71
Hu IFN- γ	319.4	113.9	247.3	58.7	0.42	122.1	47.7	115.9	18.3	0.88
Hu IP-10	2018.5	474.5	1848.1	554.0	0.73	1284.7	236.5	1337.8	324.5	0.79
Hu MCP-1	33.5	4.6	25.6	3.3	0.09	33.3	5.8	27.4	2.3	0.32
Hu MIP-1a	15.5	5.3	7.5	3.3	0.09	8.1	3.9	4.4	2.0	0.34
Hu MIP-1b	88.1	8.0	83.1	8.4	0.76	312.7	236.8	384.1	307.6	0.33
Hu PDGF bb	2896.8	472.2	2734.2	329.8	0.58	3306.7	1502.4	2530.8	538.3	0.65
Hu RANTES	2553.4	1192.8	1635.1	175.9	0.08	3138.6	1292.2	1577.4	110.9	0.25
Hu TNF- α	73.9	12.4	75.7	8.6	0.11	96.7	20.0	80.9	17.1	0.36
Hu VEGF	50.4	10.9	40.9	4.8	0.99	51.8	15.2	35.0	5.3	0.30

Data are presented as mean \pm SEM for plasma concentrations (picograms per millilitre) at baseline

(W0) and 6 months (W24) in patients receiving placebo or simvastatin. Statistics shown are paired t-

tests. Hu, human; IL, interleukin; IL-1ra, IL-1 receptor antagonist; MCP-1 monocyte chemoattractant protein 1; MIP-1 β , macrophage inflammatory protein 1 β ; MIP-1 α , macrophage inflammatory protein 1 α ; RANTES, regulated on activation, normal T-cell expressed and secreted; IFN- γ , interferon- γ , G-CSF, granulocyte-colony stimulating factor; GM-CSF, granulocyte macrophage-colony stimulating factor ; FGF basic, fibroblast growth factor basic; IP-10, interferon-inducible protein 10; TNF- α , tumour necrosis factor- α ; PDGFbb, platelet-derived growth factor bb; VEGF, vascular endothelial growth factor.

Plasma cytokines and growth factors were measured using a Bio-Plex Human Group I 27-plex Panel, with a detection range of 1.95-32,000 pg/ml (171-A11127; Bio-Rad Laboratories Ltd, Hemel Hempstead, Herts, UK).

No significant differences in circulating cytokines and growth factors were observed over the 6 month period, in either group. Nonetheless, when compared with independent data from subjects with no known cardiovascular disease(1) it is apparent that the circulating levels of several cytokines and growth factors were raised in the patients who took part in this study. These include factors that are implicated in the pathophysiology of PAH, such as RANTES, PDGFbb, TNF- α and VEGF (2), as well as other cytokines.

Reference List

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2. Hassoun, P. M., L. Mouthon, J. A. Barbera, S. Eddahibi, S. C. Flores, F. Grimminger, P. L. Jones, M. L. Maitland, E. D. Michelakis, N. W. Morrell, et al. Inflammation, growth factors, and pulmonary vascular remodeling. *J Am Coll Cardiol* 2009;54:S10-S19.