Journal of
Clinical Medicine

MDPI

Supplement 1 Inflammatory marker levels in therapy responders and non-responders.

Protein	----- Pre-treatment comparison -----				----- Post-treatment comparison -----			
	Responder		Non-responder		Responder		Non-responder	
	lg-mean	SD	lg-mean	SD	lg-mean	SD	lg-mean	SD
TNFα	0.289	0.108	0.348	0.303	0.108	0.338	0.123	0.111
IL-6	-0.318	0.286	-0.170	-0.298	0.298	-0.079	0.299	0.276
CRP	6.201	0.539	6.388	6.172	0.506	6.599	0.568	0.557
IL-10	-0.732	0.407	-0.675	-0.652	0.289	-0.567	0.259	0.304
IL-8	0.951	0.182	0.979	1.012	0.130	1.081	0.175	0.165
IL-12	1.307	0.163	1.305	1.359	0.144	1.415	0.180	0.181
IL-7	1.967	0.222	1.968	1.970	0.200	1.937	0.264	0.278
IL-15	0.447	0.105	0.439	0.481	0.115	0.530	0.105	0.127
IL-16	2.325	0.177	2.329	2.300	0.147	2.334	0.163	0.162
IL-17	0.256	0.390	0.199	0.309	0.347	0.288	0.279	0.303
MCP1	2.457	0.152	2.470	2.467	0.168	2.549	0.218	0.172
MCP4	2.170	0.189	2.182	2.142	0.151	2.272	0.220	0.226
Mip1b	2.089	0.193	2.145	2.115	0.159	2.117	0.135	0.179
Eotaxin	2.296	0.208	2.326	2.317	0.213	2.359	0.254	0.223
sICAM1	6.481	0.415	6.546	6.413	0.468	6.646	0.332	0.353
sVCAM 1	5.668	0.097	5.717	5.684	0.100	5.758	0.124	0.111
SAA	5.775	0.097	5.785	5.782	0.092	5.825	0.114	0.085
TARC	2.472	0.226	2.526	2.451	0.266	2.720	0.336	0.297
Tie2	3.625	0.192	3.703	3.607	0.223	3.682	0.231	0.176
IP-10	2.326	0.154	2.368	2.332	0.151	2.383	0.191	0.241
IFNγ	0.707	0.285	0.592	0.701	0.316	0.538	0.320	0.249
Eotaxin 3	0.742	0.491	0.795	0.743	0.496	0.916	0.404	0.442
TNFβ	-0.725	0.541	-0.663	-0.664	0.469	-0.578	0.388	0.428

Protein levels before and after therapy in responders and non-responders.
lg-mean = log-transformed mean value in pg/ml (except for CRP which was converted into mg/L), SD = standard deviation.

Supplement 2: Post-hoc analyses adjusting for other potentially important confounders

Elevated IL-6 at baseline predicted non-response. Baseline IL-6 was also associated with age and physical illness, so a post-hoc logistic regression including these two variables was conducted. In the absence of indicated multi-collinearity, IL-6 (and neither other variable) remained significant: OR = 0.153 [95% CI 0.027, 0.861], p = 0.033.

Elevated TNFa at baseline predicted non-response. Baseline TNFa was also associated with age, physical illness and the number of comorbidities. A post-hoc logistic regression including these three variables indicated that, without significant multi-collinearity, TNFα remained a significant predictor of non-response (OR = 0.009 [95% CI 0.000, 0.698], p = 0.034 while none of the other variables appeared significantly associated.

Attenuated IFNy at baseline predicted non-response. Baseline IFNy was also negatively associated with early life stress (CTQ score). In the post-hoc logistic regression containing these two variables, IFNy was only associated with response at a trend level (OR = 5.178 [95% CI 0.974, 27.536], p = 0.054) while CTQ was not a significant predictor.

After treatment, non-response was cross-sectionally associated with elevated CRP; CRP was positively associated with age (already adjusted for in a priori logistic regression) and therefore a subsequent regression was not conducted.

After treatment, non-response was cross-sectionally associated with elevated MCP4, which was also correlated with age and physical illness. A post-hoc logistic regression including these factors suggested that only MCP4 was independently associated with non-response (OR = 0.020 [95% CI 0.000, 0.942], p = 0.047).

After treatment, non-response was cross-sectionally associated with elevated TARC. TARC was also positively associated with physical illness. A post-hoc logistic regression including these two variables indicated that TARC (but not physical illness) remained associated with non-response (OR = 0.030 [95% CI 0.002, 0.520], p = 0.016) although poor model fitting was indicated (Hosmer and Lemeshow Chi-square statistic 17.359, p = 0.027).

After treatment, non-response was cross-sectionally associated with attenuated IFNy. At this timepoint, IFNy was also negatively associated with number of psychiatric comorbidities. The post-hoc logistic regression including these two variables rendered IFNy a non-significant contributor (OR = 2.716 [95% CI 0.283, 26.075], p = 0.387) whereas the number of comorbidities was higher in non-responders (OR = 0.640 [95% CI 0.423, 0.969], p = 0.035).

When not adjusting for age, gender and BMI, IL-6 was significantly higher in non-responders. IL-6 was indeed positively associated with age, but in the post-hoc logistic regression containing only IL-6 and age, IL-6 remained weakly significant (OR = 0.062 [95% CI 0.004, 0.924], p = 0.044) while age was not significantly associated with response.

Similarly, when not adjusting for age, gender and BMI, sICAM1 was significantly higher in non-responders. sICAM was also associated with age as well as physical illness. The post-hoc logistic regression including these three factors suggested that none of the variables were significantly and independently associated with response (sICAM1 being the strongest contributor with OR = 0.002 [95% CI 0.000, 1.540), p = 0.066).