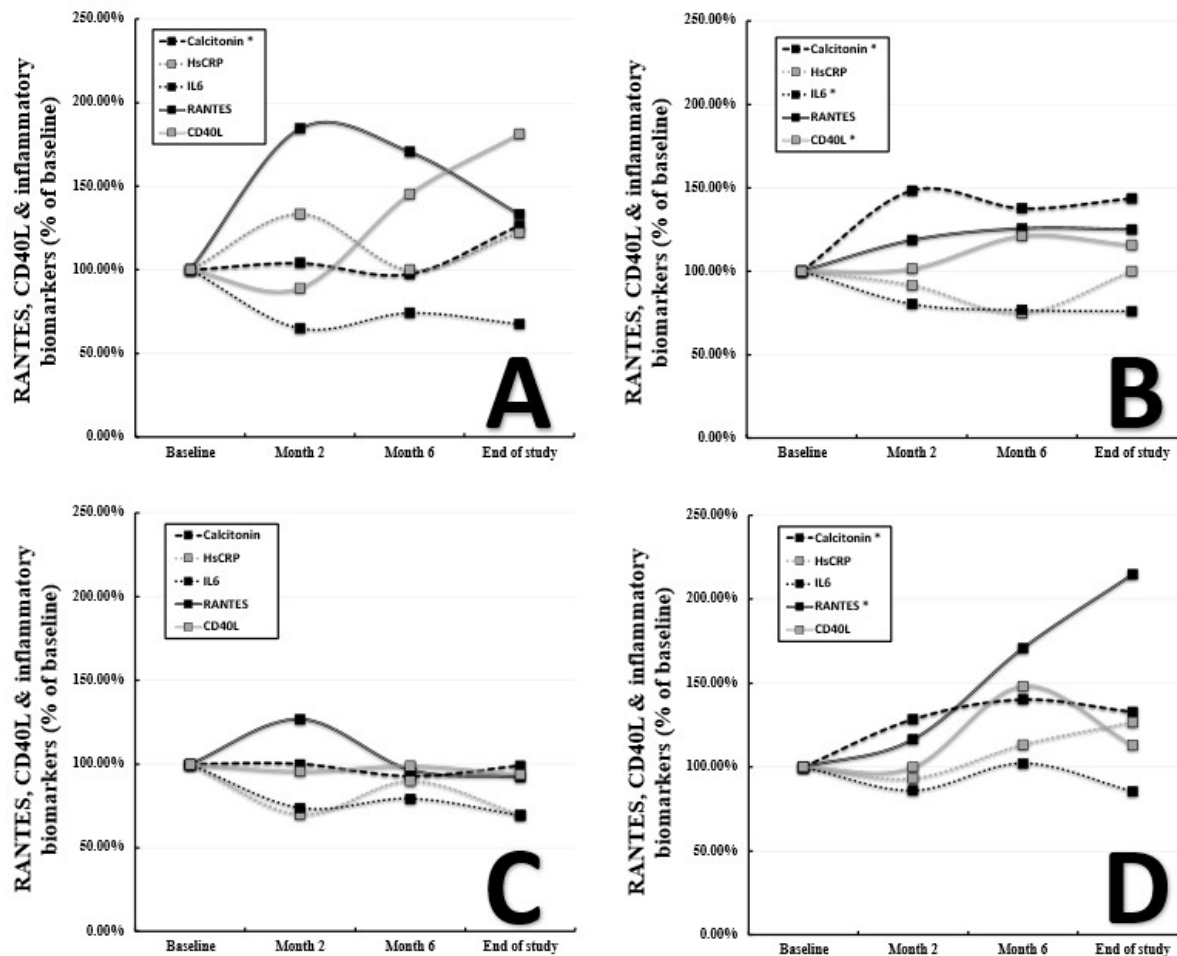
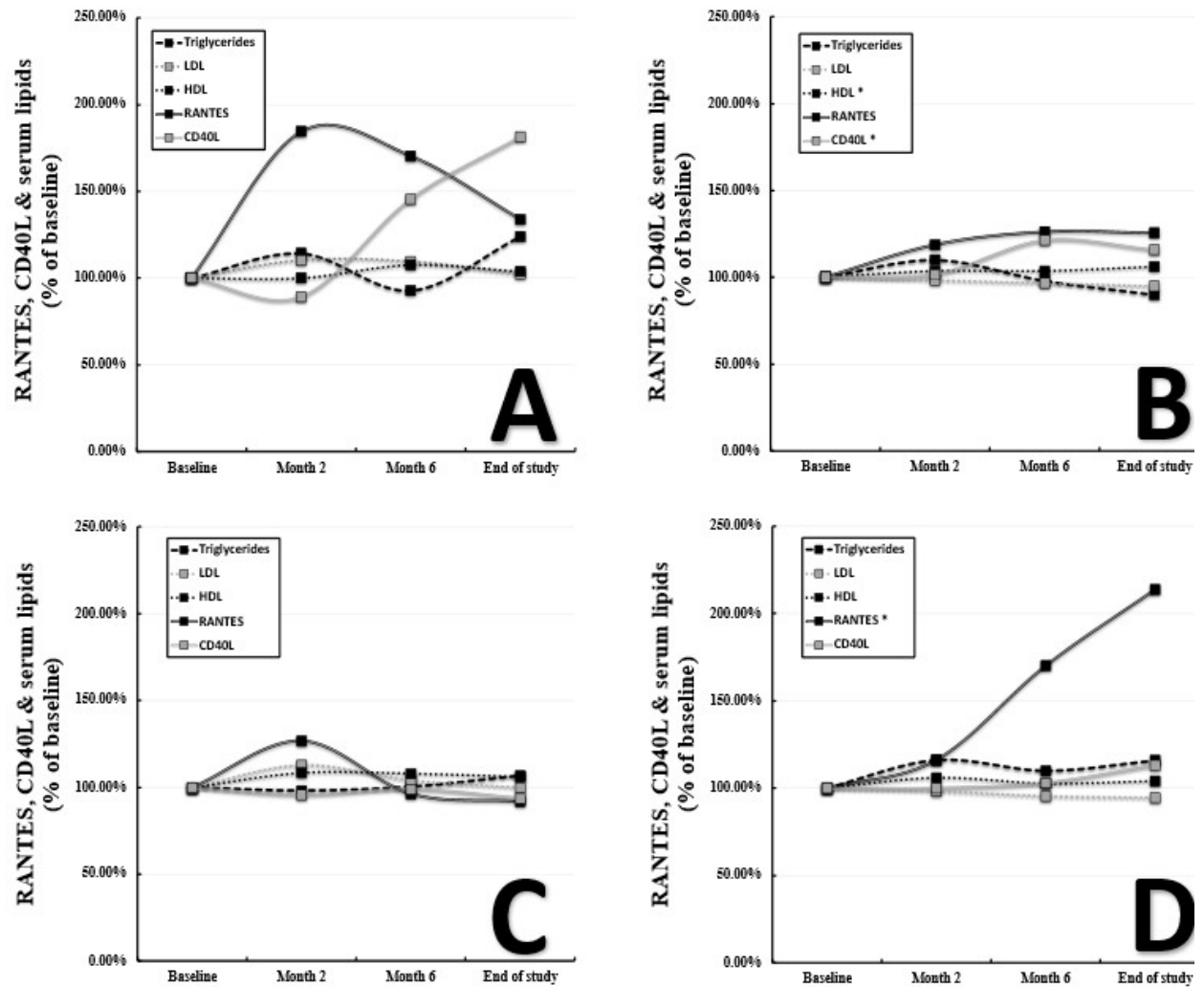


Supplementary Materials:



Supplementary Figure S1. Progression of RANTES, CD40L, hsCRP, IL6, and calcitonin serum levels in subgroups **α** (initial performance < 100%, performance gain ≤ 2.9%, n=9, Supplementary Figure 1A), **β** (initial performance < 100%, performance gain > 2.9%, n=32, Supplementary Figure 1B), **γ** (initial performance ≥ 100%, performance gain ≤ 2.9%, n=18, Supplementary Figure 1C), and **δ** (initial performance ≥ 100%, performance gain > 2.9%, n=39, Supplementary Figure 1D) over the course of 8 months. "*" indicates a two-tailed p-value of p < 0.05 comparing baseline values to those at the end of the study.



Supplementary Figure S2. Progression of RANTES, CD40L, HDL, LDL, and serum triglycerides in subgroups α (initial performance < 100%, performance gain $\leq 2.9\%$, n=9, Supplementary Figure 2A), β (initial performance < 100%, performance gain > 2.9%, n=32, Supplementary Figure 2B), γ (initial performance $\geq 100\%$, performance gain $\leq 2.9\%$, n=18, Supplementary Figure 2C), and δ (initial performance $\geq 100\%$, performance gain > 2.9%, n=39, Supplementary Figure 2D) over the course of 8 months. "*" indicates a two-tailed p-value of $p < 0.05$ comparing baseline values to those at the end of the study.

<u>RANTES</u>	Group α	Group β	Group γ	Group δ	Total cohort
Risk factors:	Gain $\leq 2.9\%$ (n=9)	Gain $> 2.9\%$ (n=32)	Gain $\leq 2.9\%$ (n=18)	Gain $> 2.9\%$ (n=39)	(n=98)
Packyears	0.397	0.262	0.965	0.569	0.851
Diabetes mellitus	0.272	0.786	0.644	0.630	0.326
Hypertension	0.638	0.355	0.113	0.107	0.775
Dyslipidemia	0.815	0.535	0.633	0.255	0.327
Overweight	0.946	0.822	0.042 (-0.484)*	0.378	0.555
Positive family history	0.638	0.444	0.833	0.231	0.697
<u>sCD40</u>	Group α	Group β	Group γ	Group δ	Total cohort
Risk factors:	Gain $\leq 2.9\%$ (n=9)	Gain $> 2.9\%$ (n=32)	Gain $\leq 2.9\%$ (n=18)	Gain $> 2.9\%$ (n=39)	(n=98)
Packyears	0.388	0.875	0.414	0.277	0.226
Diabetes mellitus	0.635	0.094	0.303	0.289	0.185
Hypertension	0.730	0.067	0.654	0.248	0.083
Dyslipidemia	0.323	0.494	0.829	0.120	0.255
Overweight	0.901	0.609	0.179	0.669	0.977
Positive family history	0.051	0.527	0.524	0.810	0.296

Supplementary Table S1. RANTES and CD40L and pre-existing risk factors at baseline. "*" indicates a two-tailed p-value of $p < 0.05$.

<u>RANTES</u>	Group α baseline	Group β baseline	Group γ baseline	Group δ baseline
Parameters:	Gain ≤2.9% (n=9)	Gain> 2.9% (n=32)	Gain ≤2.9% (n=18)	Gain> 2.9% (n=39)
Calcitonin	0.036 (+0.700)*	0.421	0.824	0.151 (+0.275)
IL6	0.013 (-0.783)*	0.155	0.651	0.090 (+0.275)°
hsCRP	0.008 (-0.814)*	0.067 (+0.328)°	0.996	0.668
<u>RANTES</u>	Group α end of study	Group β end of study	Group γ end of study	Group δ end of study
Parameters:	Gain ≤2.9% (n=9)	Gain> 2.9% (n=32)	Gain ≤2.9% (n=18)	Gain> 2.9% (n=39)
Calcitonin	0.221 (-0.006)	0.973	0.441	0.014 (+0.392)*
IL6	0.347 (-0.087)	0.634	0.596	0.232 (-0.196)
hsCRP	0.559 (+0.108)	0.556 (+0.108)	0.577	0.470
<u>sCD40</u>	Group α baseline	Group β baseline	Group γ baseline	Group δ baseline
Parameters:	Gain ≤2.9% (n=9)	Gain> 2.9% (n=32)	Gain ≤2.9% (n=18)	Gain> 2.9% (n=39)
Calcitonin	0.551	0.936	0.272	0.151 (+0.235)
IL6	0.205	0.482	0.225	0.090 (+0.275)°
hsCRP	0.695	0.060 (+0.336)°	0.993 (-0.022)	0.668
<u>sCD40</u>	Group α end of study	Group β end of study	Group γ end of study	Group δ end of study
Parameters:	Gain ≤2.9% (n=9)	Gain> 2.9% (n=32)	Gain ≤2.9% (n=18)	Gain> 2.9% (n=39)
Calcitonin	0.660	0.168	0.154	0.015 (+0.386)*
IL6	0.179	0.705	0.121	0.217 (-0.196)
hsCRP	0.342	0.224 (+0.221)	0.019 (+0.545)*	0.691

Supplementary Table S2. Correlations of RANTES and CD40L with hsCRP, IL6, and calcitonin serum levels throughout the study period. "*" indicates a two-tailed p-value of $p < 0.05$. "°" indicates a borderline significance of $p = 0.05$, $p = 0.1$.

		Group α baseline	Group β baseline	Group γ baseline	Group δ baseline
Parameters:		Gain $\leq 2.9\%$ (n=9)	Gain > 2.9% (n=32)	Gain $\leq 2.9\%$ (n=18)	Gain > 2.9% (n=39)
Triglycerides		0.898	0.766	0.743	0.888
HDL		0.651	0.364	0.284	0.468
LDL		0.050 (-0.667) ^o	0.615	0.395	0.013 (+0.393)*
<u>RANTES</u>		Group α end of study	Group β end of study	Group γ end of study	Group δ end of study
Parameters:		Gain $\leq 2.9\%$ (n=9)	Gain > 2.9% (n=32)	Gain $\leq 2.9\%$ (n=18)	Gain > 2.9% (n=39)
Triglycerides		0.898	0.884	0.261	0.486
HDL		0.589	0.882	0.645	0.199
LDL		0.460 (+0.283)	0.308	0.416	0.875 (+0.026)
<u>CD40L</u>		Group α baseline	Group β baseline	Group γ baseline	Group δ baseline
Parameters:		Gain $\leq 2.9\%$ (n=9)	Gain > 2.9% (n=32)	Gain $\leq 2.9\%$ (n=18)	Gain > 2.9% (n=39)
Triglycerides		0.575	0.349	0.768	0.521
HDL		0.814	0.503	0.269	0.226
LDL		0.546	0.028 (+0.389)*	0.456 (+0.194)	0.078 (+0.286) ^o
<u>CD40L</u>		Group α end of study	Group β end of study	Group γ end of study	Group δ end of study
Parameters:		Gain $\leq 2.9\%$ (n=9)	Gain > 2.9% (n=32)	Gain $\leq 2.9\%$ (n=18)	Gain > 2.9% (n=39)
Triglycerides		0.154	0.626	0.510	0.165
HDL		0.284	0.894	0.714	0.270
LDL		0.406	0.077 (+0.317) ^o	0.037 (+0.494)*	0.472 (+0.119)

Supplementary Table S3. Correlations of RANTES and CD40L with HDL, LDL, and serum triglycerides throughout the study period. "*" indicates a two-tailed p-value of $p < 0.05$. "^o" indicates a borderline significance of $p = 0.05$, $p = 0.1$.

<i>Table 1</i>	Group α	Group β	Group γ	Group δ	Total cohort
<u>Parameters:</u>	Gain $\leq 2.9\%$ (n=9)	Gain $> 2.9\%$ (n=32)	Gain $\leq 2.9\%$ (n=18)	Gain $> 2.9\%$ (n=39)	(n=98)
RANTES 0 (ng/mL)	1.65 \pm 5.02	2.14 \pm 1.61	2.60 \pm 4.05	1.88 \pm 1.37	2.08 \pm 2.13
RANTES 2 (ng/mL)	3.05 \pm 1.10	2.54 \pm 1.97	3.29 \pm 2.88	2.19 \pm 1.44	2.59 \pm 1.95
RANTES 6 (ng/mL)	2.82 \pm 1.42	2.70 \pm 1.57	2.50 \pm 1.80	3.21 \pm 2.64	2.87 \pm 2.06
RANTES 8 (ng/mL)	2.21 \pm 0.70	2.69 \pm 1.76	2.39 \pm 1.59	4.03 \pm 3.12	3.12 \pm 2.42
CD40L 0 (pg/mL)	320.83 \pm 234.02	323.10 \pm 585.66	213.49 \pm 100.38	199.25 \pm 75.73	253.47 \pm 348.78
CD40L 2 (pg/mL)	285.82 \pm 263.52	328.48 \pm 561.47	204.75 \pm 82.96	199.38 \pm 76.94	250.18 \pm 335.38
CD40L 6 (pg/mL)	465.83 \pm 553.75	392.96 \pm 912.44	211.93 \pm 108.78	205.67 \pm 54.51	293.08 \pm 548.11
CD40L 8 (pg/mL)	580.89 \pm 1155.99	374.19 \pm 615.96	200.32 \pm 65.54	225.11 \pm 79.13	301.91 \pm 497.90
HsCRP 0 (mg/dL)	0.09 \pm 0.04	0.23 \pm 0.20	0.20 \pm 0.30	0.14 \pm 0.15	0.18 \pm 0.20
HsCRP 2 (mg/dL)	0.11 \pm 0.06	0.21 \pm 0.22	0.13 \pm 0.10	0.13 \pm 0.17	0.16 \pm 0.17
HsCRP 6 (mg/dL)	0.08 \pm 0.04	0.17 \pm 0.13	0.17 \pm 0.20	0.37 \pm 1.24	0.24 \pm 0.78
HsCRP 8 (mg/dL)	0.10 \pm 0.06	0.24 \pm 0.29	0.14 \pm 0.12	0.19 \pm 0.53	0.19 \pm 0.38
Calcitonin 0 (pg/mL)	1.24 \pm 1.35	2.14 \pm 3.10	3.01 \pm 3.41	2.30 \pm 1.83	2.27 \pm 2.59
Calcitonin 2 (pg/mL)	1.28 \pm 1.49	3.18 \pm 3.92	3.00 \pm 2.93	2.97 \pm 2.22	2.88 \pm 2.97
Calcitonin 6 (pg/mL)	1.21 \pm 1.29	2.96 \pm 3.31	2.79 \pm 2.98	3.23 \pm 2.72	2.86 \pm 2.88
Calcitonin 8 (pg/mL)	1.56 \pm 1.71	3.09 \pm 3.82	2.98 \pm 2.82	3.06 \pm 2.29	2.92 \pm 2.93
IL6 0 (pg/mL)	2.71 \pm 1.22	3.06 \pm 2.16	2.48 \pm 2.41	2.23 \pm 0.85	2.59 \pm 1.74
IL6 2 (pg/mL)	1.76 \pm 1.17	2.46 \pm 1.78	1.82 \pm 1.38	1.93 \pm 1.31	2.07 \pm 1.49
IL6 6 (pg/mL)	2.01 \pm 1.47	2.35 \pm 1.40	1.96 \pm 1.31	2.29 \pm 1.85	2.22 \pm 1.57
IL6 8 (pg/mL)	1.84 \pm 1.49	2.33 \pm 1.57	1.72 \pm 1.12	1.92 \pm 1.96	2.01 \pm 1.66
Triglycerides 0 (mg/dL)	154.00 \pm 85.85	149.09 \pm 99.70	110.52 \pm 72.02	119.30 \pm 62.20	130.81 \pm 80.67
Triglycerides 2 (mg/dL)	176.33 \pm 118.08	164.93 \pm 98.09	108.38 \pm 28.07	138.63 \pm 80.80	144.98 \pm 85.96
Triglycerides 6 (mg/dL)	143.00 \pm 54.42	146.21 \pm 81.08	110.88 \pm 79.07	131.27 \pm 77.14	133.24 \pm 76.71
Triglycerides 8 (mg/dL)	191.55 \pm 87.74	134.25 \pm 70.68	118.00 \pm 70.76	138.28 \pm 80.73	138.13 \pm 77.50
LDL 0 (mg/dL)	126.20 \pm 50.35	117.02 \pm 32.24	111.65 \pm 28.67	116.26 \pm 34.96	116.62 \pm 34.36
LDL 2 (mg/dL)	139.43 \pm 48.48	115.85 \pm 35.60	125.98 \pm 40.46	114.43 \pm 28.40	119.40 \pm 35.57
LDL 6 (mg/dL)	138.40 \pm 56.19	113.43 \pm 32.06	116.29 \pm 33.36	111.06 \pm 33.15	115.54 \pm 35.10
LDL 8 (mg/dL)	129.35 \pm 43.28	111.21 \pm 30.95	111.62 \pm 25.165	110.06 \pm 33.152	112.49 \pm 32.12
HDL 0 (mg/dL)	52.22 \pm 19.46	56.09 \pm 21.65	61.94 \pm 11.97	60.46 \pm 14.99	58.51 \pm 17.47
HDL 2 (mg/dL)	52.66 \pm 20.60	58.06 \pm 23.01	67.94 \pm 11.97	64.07 \pm 17.81	61.65 \pm 19.32
HDL 6 (mg/dL)	56.667 \pm 19.83	58.35 \pm 19.83	66.94 \pm 12.82	62.05 \pm 15.37	61.28 \pm 16.98
HDL 8 (mg/dL)	54.88 \pm 20.42	59.46 \pm 19.57	65.77 \pm 13.45	62.92 \pm 17.09	61.58 \pm 17.68

Supplementary Table S4. Mean \pm standard deviation of the analyzed parameters throughout the study period. HsCRP, high-sensitivity C-reactive protein; IL6, interleukin 6; LDL, low-density lipoprotein; HDL, high-density lipoprotein.