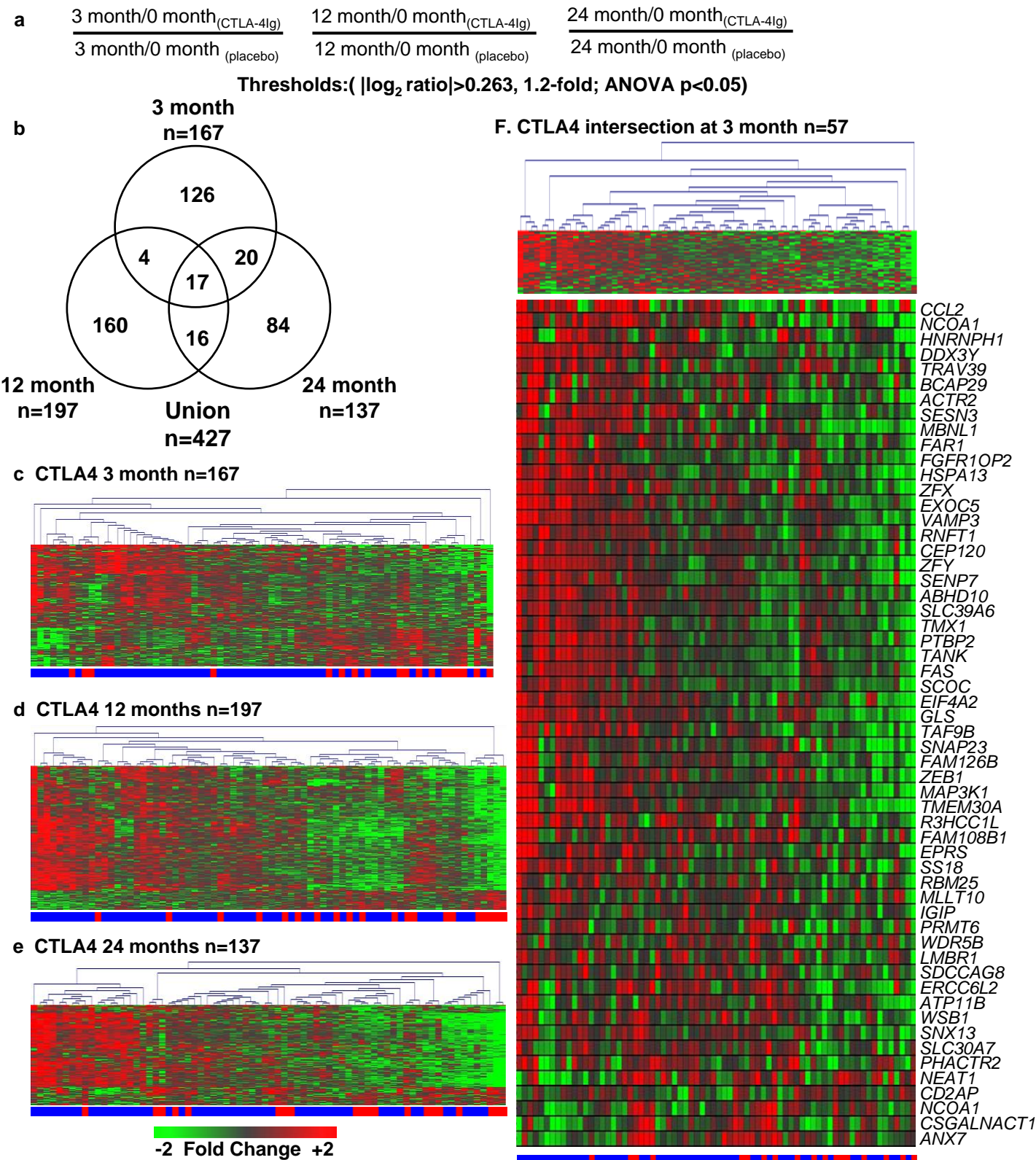


ESM TABLE 1 Subject Information TN09

Study	Treatment Arm	Subject ID	Gender	Age at diagnosis	Age at baseline visit	Duration of DM @ I.I.359	Length of Partial remission (CPEP > 0.2 nmo/L)	HbA1c at initial visit (mmol/mol)	HbA1c at initial visit (%)	Weight (kg)	Height (cm)	BMI SDS	BMI Percentile	Number of Detected Autoantibodies	HLA Risk (High: DR3 and/or DR4 positive; Low nonDR3 and nonDR4)	WGCGNA Group Assignment	Selected Treated Responder							
																	Sample and Placebo Fast Sample	Mean 2hr CPEP by min Baseline	Mean 2hr CPEP by min Day 84	Mean 2hr CPEP by min Day 196	Mean 2hr CPEP by min Day 364	Mean 2hr CPEP by min Day 560	Mean 2hr CPEP by min Day 728	
TN09	ABATACEPT	CTLA4_CT_P19002922	Male	17.91	18.21	0.30	-0.33	NA	40.3	6.5	78.6	170	1.32	91	1	high	G1	0	1.07	1.00	0.93	1.11	1.00	1.04
TN09	ABATACEPT	CTLA4_CT_P19003388	Female	21.08	21.35	0.27	-0.02	NA	32.9	5.3	81.2	182.5	0.31	62	2	high	G2	0	0.86	0.54	0.42	0.36	0.30	0.12
TN09	ABATACEPT	CTLA4_CT_P19009315	Male	11.59	11.85	0.27	-0.09	NA	39.1	6.3	38	147	-0.05	48	3	high	G2	0	0.68	0.46	0.36	0.24	0.19	0.15
TN09	ABATACEPT	CTLA4_CT_P19010058	Male	14.21	14.48	0.27	0.16	NA	32.9	5.3	68.2	180.8	0.48	68	4	high	G4	0	0.60	0.47	0.43	0.33	0.24	0.19
TN09	ABATACEPT	CTLA4_CT_P19011880	Female	9.28	9.57	0.29	-0.13	NA	45.3	7.3	36.5	134.7	1.17	88	2	high	G2	0	0.22	0.19	0.12	0.10	0.11	0.03
TN09	ABATACEPT	CTLA4_CT_P19015071	Male	16.52	16.73	0.21	-0.05	NA	39.1	6.3	67.2	174.6	0.38	65	2	high	G2	0	0.55	0.27	0.16	0.06	0.07	0.05
TN09	ABATACEPT	CTLA4_CT_P19016746	Female	8.11	8.29	0.18	0.14	NA	35.3	5.7	35.6	139	1.01	84	3	high	G4	0	1.03	0.90	0.90	0.59	0.72	0.72
TN09	ABATACEPT	CTLA4_CT_P19018458	Male	8.38	8.66	0.28	0.05	NA	39.1	6.3	27.9	138.5	-1.03	15	3	low	G4	0	0.44	0.53	0.41	0.22	0.25	0.21
TN09	ABATACEPT	CTLA4_CT_P19019691	Female	6.51	6.67	0.17	0.02	NA	39.7	6.4	21.8	116.1	0.48	68	2	high	G4	0	0.27	0.36	0.10	0.10	0.03	0.01
TN09	ABATACEPT	CTLA4_CT_P19019970	Female	10.02	10.24	0.22	0.06	NA	50.2	8.1	49.5	145	1.7	96	3	high	G4	0	0.71	0.66	0.41	0.25	0.20	0.15
TN09	ABATACEPT	CTLA4_CT_P19027000	Male	14.98	15.24	0.26	0.06	NA	36.0	5.8	67.5	178.5	0.4	66	4	high	G4	0	0.81	0.85	0.85	0.63	0.48	0.50
TN09	ABATACEPT	CTLA4_CT_P19031301	Female	11.13	11.28	0.15	-0.26	NA	40.9	6.6	37.9	157.4	-1.13	13	3	high	G2	0	0.68	0.59	0.29	0.21	0.03	0.03
TN09	ABATACEPT	CTLA4_CT_P19033311	Female	8.15	8.42	0.27	0.05	NA	44.6	7.2	29.7	131.6	0.52	70	2	high	G3	0	0.35	0.24	0.21	0.09	0.05	0.02
TN09	ABATACEPT	CTLA4_CT_P19034909	Male	10.35	10.63	0.27	-0.23	NA	42.8	6.9	59.7	157.7	1.83	97	3	low	G4	0	1.29	1.39	1.10	1.23	0.98	0.87
TN09	ABATACEPT	CTLA4_CT_P19034944	Male	34.78	35.00	0.22	-0.45	NA	41.5	6.7	83	176.6	0.1	54	3	high	G1	0	0.58	0.75	0.66	0.75	0.66	0.57
TN09	ABATACEPT	CTLA4_CT_P19035621	Male	17.25	17.50	0.25	0.05	NA	36.6	5.9	86.8	175	1.61	95	2	high	G3	0	1.06	0.71	0.88	0.61	0.62	0.52
TN09	ABATACEPT	CTLA4_CT_P19039251	Male	13.45	13.66	0.21	0.17	NA	37.8	6.1	46.4	164.5	-0.8	21	3	low	G4	0	0.51	0.47	0.38	0.37	0.28	0.28
TN09	ABATACEPT	CTLA4_CT_P19040109	Female	15.85	16.06	0.21	-0.14	NA	39.7	6.4	112.1	169.9	2.33	99	2	high	G1	0	1.75	1.12	1.40	1.61	1.30	1.49
TN09	ABATACEPT	CTLA4_CT_P19041256	Female	20.18	20.44	0.26	0.03	NA	36.6	5.9	61.7	161.3	0.08	53	4	low	G1	CT_8Resp	0.53	0.39	NA	NA	NA	0.57
TN09	ABATACEPT	CTLA4_CT_P19042186	Female	13.76	13.98	0.22	-0.50	NA	47.1	7.6	42.5	159	-1.06	15	3	high	G1	0	0.49	0.57	0.61	0.56	0.50	0.38
TN09	ABATACEPT	CTLA4_CT_P19043824	Male	17.75	18.02	0.27	0.77	NA	34.7	5.6	72.5	169	0.98	84	3	high	OL	CT_8Resp	2.42	2.03	2.19	1.90	1.87	2.53
TN09	ABATACEPT	CTLA4_CT_P19045146	Female	7.50	7.77	0.27	0.08	NA	44.6	7.2	34.2	129.7	1.63	95	3	high	G1	0	0.53	0.52	0.54	0.38	0.23	0.28
TN09	ABATACEPT	CTLA4_CT_P19048858	Male	8.93	9.18	0.25	-0.28	NA	34.1	5.5	30.8	129.2	0.91	82	4	high	G1	0	0.67	0.49	0.34	0.34	0.34	0.20
TN09	ABATACEPT	CTLA4_CT_P19051989	Male	7.48	7.73	0.25	0.04	NA	40.9	6.6	28.8	122	1.54	94	4	low	G4	0	0.36	0.17	0.11	0.03	0.01	0.01
TN09	ABATACEPT	CTLA4_CT_P19052289	Female	23.78	24.04	0.26	0.24	NA	30.4	4.9	60.5	160.1	0.2	57	1	high	G4	0	0.91	0.92	0.71	0.55	0.40	0.22
TN09	ABATACEPT	CTLA4_CT_P19053269	Male	11.10	11.36	0.25	-0.34	NA	33.5	5.4	44.9	142.9	1.37	92	2	high	G1	0	1.08	0.96	0.76	0.52	0.27	0.24
TN09	ABATACEPT	CTLA4_CT_P19055573	Male	17.08	17.35	0.27	-0.19	NA	40.9	6.6	93	181	1.63	95	3	high	G1	0	1.20	1.01	1.17	1.09	0.82	0.77
TN09	ABATACEPT	CTLA4_CT_P19059514	Female	17.74	17.99	0.25	-0.47	NA	37.8	6.1	55.2	166.3	-0.46	32	4	low	G1	0	0.71	0.70	0.63	NA	NA	0.25
TN09	ABATACEPT	CTLA4_CT_P19060795	Male	17.02	17.29	0.27	-0.28	NA	34.7	5.6	79.5	174	1.27	90	2	high	G1	0	0.56	0.74	0.96	0.90	0.68	0.49
TN09	ABATACEPT	CTLA4_CT_P19060824	Female	11.18	11.40	0.23	0.20	NA	NA	NA	42.1	154.9	-0.06	48	3	low	G3	0	0.78	0.86	0.40	0.26	0.14	0.04
TN09	ABATACEPT	CTLA4_CT_P19064499	Male	33.43	33.70	0.27	0.17	NA	32.2	5.2	70.5	172.1	-0.44	33	2	low	G3	CT_8Resp	0.75	1.01	1.23	0.97	0.74	0.71
TN09	ABATACEPT	CTLA4_CT_P19066427	Female	7.30	7.47	0.17	-0.21	NA	42.8	6.9	24.2	123.3	0.18	57	2	high	G1	0	0.45	0.49	0.65	0.50	0.42	0.37
TN09	ABATACEPT	CTLA4_CT_P19068024	Male	10.54	10.81	0.27	0.40	NA	45.9	7.4	46.5	141.5	1.68	95	1	high	G3	CT_8Resp	0.22	0.24	0.22	NA	NA	0.11
TN09	ABATACEPT	CTLA4_CT_P19068424	Male	34.29	34.50	0.21	0.24	NA	34.1	5.5	84.4	191.4	-0.64	26	2	low	G3	CT_8Resp	1.35	1.55	1.74	1.56	1.36	1.43
TN09	ABATACEPT	CTLA4_CT_P19072101	Male	9.61	9.77	0.16	-0.06	NA	42.2	6.8	29.1	141.5	-1.3	10	1	high	G1	0	0.44	0.70	0.76	0.64	0.49	0.46
TN09	ABATACEPT	CTLA4_CT_P19074578	Female	12.21	12.46	0.25	-0.12	NA	32.2	5.2	44.3	147	0.66	75	3	high	G1	0	1.60	1.58	1.33	1.28	NA	0.99
TN09	ABATACEPT	CTLA4_CT_P19082597	Male	26.93	27.19	0.26	0.12	NA	28.5	4.6	87	190.9	-0.18	43	3	high	G3	0	0.94	0.57	0.67	0.81	0.33	0.52
TN09	ABATACEPT	CTLA4_CT_P19083384	Male	10.42	10.69	0.27	0.10	NA	40.3	6.5	40	141.2	1.08	86	3	high	G3	CT_8Resp	0.47	0.60	0.75	0.51	0.48	0.43
TN09	ABATACEPT	CTLA4_CT_P19084943	Male	15.40	15.67	0.27	0.34	NA	36.6	5.9	74.3	175	1.11	87	4	high	G3	0	0.67	0.87	0.66	0.32	0.59	0.56
TN09	ABATACEPT	CTLA4_CT_P19084986	Female	10.55	10.76	0.21	0.36	NA	36.6	5.9	61.5	155.3	1.87	97	4	high	G3	0	1.27	1.48	1.79	1.74	1.52	1.03
TN09	ABATACEPT	CTLA4_CT_P19086296	Male	12.88	13.07	0.19	0.15	NA	36.6	5.9	51.5	158	0.072	76	4	high	G4	0	1.45	1.28	1.19	0.92	0.98	0.80
TN09	ABATACEPT	CTLA4_CT_P19087810	Male	8.77	9.03	0.26	0.04	NA	36.0	5.8	28	131.1	0.07	53	2	high	G2	0	0.50	0.53	0.46	0.53	0.40	0.49
TN09	ABATACEPT	CTLA4_CT_P19088623	Male	11.32	11.58	0.27	-0.88	NA	45.3	7.3	31.1	136.6	-0.41	34	2	high	G1	0	0.51	0.42	0.28	0.16	0.10	0.06
TN09	ABATACEPT	CTLA4_CT_P19088950	Female	12.55	12.82	0.27	-0.17	NA	38.4	6.2	56.8	157.4	1.14	87	2	high	G1	0	0.90	0.81	1.03	1.14	0.78	0.47
TN09	ABATACEPT	CTLA4_CT_P19088997	Male	NA	15.85	NA	0.07	NA	36.0	5.8	81.7	170.7	1.73	96	3	low	G3	CT_8Resp	1.75	1.65	1.45	1.75	1.69	2.63
TN09	ABATACEPT	CTLA4_CT_P19090498	Female	6.37	6.54	0.17	-0.30	NA	44.0	7.1	25.6	126.1	0.46	68	4	high	G2	0	0.31	0.11	0.12	0.02	0.02	0.01
TN09	ABATACEPT	CTLA4_CT_P19091454	Male	10.95	11.19	0.25	-0.40	NA	36.0	5.8	44.1	148	0.99	84	2	high	G1	0	1.24	0.86	0.73	0.62	0.58	0.44
TN09	ABATACEPT	CTLA4_CT_P19092010	Male	13.36	13.59	0.23	0.03	NA	34.7	5.6	54.6	162.3	0.63	74	1	low	G3	0	1.65	0.32	1.28	0.95	1.11	0.64
TN09	ABATACEPT	CTLA4_CT_P19092037	Female	11.84	12.07	0.23	-0.03	NA	32.2	5.2	38.8	143	0.3	62	4	high	G4	0	0.60	0.38	0.13	0.39	0.19	0.13
TN09	ABATACEPT	CTLA4_CT_P19092765	Male	18.04	18.28	0.24	0.12	NA	42.8	6.9	73.54	176	0.52	72	2	high	G4	0	0.55	0.48	0.36	0.34	0.25	0.21
TN09	ABATACEPT	CTLA4_CT_P19093838	Female	26.68	26.95	0.27	0.16	NA	NA	NA	52.8	159.4	-0.77	22	2	high	G4	0	0.70	0.48	0.59	0.40	0.43	0.43
TN09	ABATACEPT	CTLA4_CT_P19095979	Female	10.53	10.81	0.27	-0.01	NA	40.3	6.5	31.3	144.9	-1.24	11	3	high	G4	0	0.40	1.22	0.39	0.27	0.14	0.14
TN09	ABATACEPT	CTLA4_CT_P19097442	Female	10.10	10.35	0.26	0.08	NA	42.8	6.9	33.2	135.8	0.37	64	2	high	G4	0	0.44	0.36	0.38	0.33	0.21	0.06
TN09	ABATACEPT	CTLA4_CT_P19098085	Male	27.86	28.12	0.26	-0.26	NA	38.4	6.2	80.9	187	-0.15	44	2	high	G1	0	0.64	0.74	0.73	1.02	0.93	0.69
TN09	PLACEBO	CTLA4_PL_P19001411	Male	8.98	9.23	0.25	0.11	0.2	39.1	6.														

ESM TABLE 1 Subject Information LOCAL

Study	Sample Identifier	Gender	Age at diagnosis	Age at visit	Duration of DM @ visit	Length of Partial Remission		HbA1C at Diagnosis (mmol/mol)	HbA1C at Diagnosis (%)	Weight (kg)	Height (cm)	BMI SDS	BMI Percentile	Number of Detected Autoantibodies	Used for: Treg (T) enumeration or CTLA4Ig Addback (A)	HLA Risk (High: DR3 and/ or DR4 positive; Low nonDR3 and nonDR4)
						I.I.359	IDAA1C > 9									
LOCAL	RO2350	Female	7.25	7.56	0.3123	NA	0.33	72.5	11.7	25.9	126.1	0.35	64	4	T	high
LOCAL	RO2527	Male	10.97	11.29	0.326	NA	0.86	57.7	9.3	39.7	148	0.32	63	4	T	high
LOCAL	RO2973	Female	13.92	14.05	0.1342	NA	1.1	86.8	>14	70.1	161.8	1.58	94	4	T	high
LOCAL	RO3291	Female	6.35	6.83	0.4767	NA	0.28	71.9	11.6	31.2	134.9	0.89	81	4	T	high
LOCAL	RO3325	Male	9.66	10.12	0.4575	NA	1.01	78.7	12.7	43.5	145.9	1.29	90	4	T	high
LOCAL	RO3373	Female	6.79	7.17	0.3808	NA	0.29	86.8	>14	25.9	129.3	-0.01	50	0	T	high
LOCAL	RO3593	Female	11.44	11.56	0.1233	NA	0.74	85.6	13.8	34.7	148.5	-0.95	17	2	T	NA
LOCAL	RO3664	Female	15.73	16.08	0.3534	NA	0.4	NA	NA	53.6	151.1	0.79	79	1	T	low
LOCAL	RO3676	Male	11.45	11.78	0.3342	NA	0.82	64.5	10.4	80	172.8	1.99	98	4	T	high
LOCAL	RO3757	Male	5.64	6.08	0.4438	NA	0.74	42.2	6.8	26.6	124.4	1.11	87	2	T	low
LOCAL	RO3775	Female	16.97	17.14	0.1726	NA	1.1	54.6	8.8	65.6	169.3	0.55	71	3	T	low
LOCAL	RO3803	Female	10.40	10.85	0.4548	NA	0.87	86.8	>14	36.6	148.5	-0.33	37	3	T	low
LOCAL	RO3810	Female	16.65	17.06	0.4082	NA	1.1	81.2	13.1	57.1	172	-0.61	27	4	T	low
LOCAL	RO3887	Male	7.27	7.34	0.0712	NA	0.3	52.7	8.5	24.8	127	-0.15	44	4	T	NA
LOCAL	RO3940	Female	10.82	11.15	0.3205	NA	0.34	86.8	>14	41.5	142	0.93	82	4	T	NA
LOCAL	RO253	Male	10.38	10.74	0.3616	0.73	0.53	49.6	8	60.2	157.5	1.83	97	4	NA	low
LOCAL	RO946	Female	10.68	10.84	0.1562	-0.05	0.3	74.4	12	49.2	148.5	1.37	91	4	NA	high
LOCAL	RO949	Male	9.81	10.34	0.5315	0.40	0.53	71.3	11.5	38.7	133.5	1.5	93	0	T	high
LOCAL	RO972	Male	11.47	11.75	0.2822	0.36	0.28	77.5	12.5	38.5	142.5	0.5	69	4	NA	low
LOCAL	RO1123	Female	13.12	13.34	0.2219	0.41	0.95	73.2	11.8	54	166	0.22	59	0	NA	low
LOCAL	RO1964	Female	9.75	9.84	0.0849	0.71	0.34	69.4	11.2	43.6	155.5	0.5	69	4	NA	high
LOCAL	RO1997	Male	12.75	12.98	0.2274	0.14	0.8	86.8	>14	49.8	153.2	0.88	81	3	T	high
LOCAL	RO2034	Male	5.82	5.96	0.137	0.43	0.83	49.0	7.9	25.2	126.2	0.32	63	4	NA	low
LOCAL	RO2130	Male	15.39	15.62	0.2274	0.77	0.32	68.8	11.1	82	188	0.88	81	2	NA	low
LOCAL	RO2348	Female	9.38	9.65	0.2685	0.71	0.55	67.6	10.9	27.3	136.8	-1.16	12	4	NA	low
LOCAL	RO2359	Female	11.88	12.04	0.1589	0.01	2.41	86.8	>14	45.1	160.7	-0.25	40	3	NA	high
LOCAL	RO2559	Male	11.39	11.8	0.4055	0.52	1.08	72.5	11.7	41.6	150	0.31	59	4	NA	high
LOCAL	RO2808	Male	9.39	9.55	0.1644	0.75	0.59	86.8	>14	48.5	145.1	1.87	97	4	A	high
LOCAL	RO2936	Male	11.55	11.85	0.2959	0.12	1.34	56.4	9.1	31.5	134	-0.07	47	3	NA	high
LOCAL	RO2944	Female	6.36	6.49	0.1315	0.76	0.28	>86.8	>14	25.4	127.2	0.24	59	4	NA	low
LOCAL	RO2953	Female	8.92	9.12	0.2027	1.27	0.29	52.7	8.5	30.6	135.2	0.18	57	3	A	low
LOCAL	RO3052	Female	8.38	8.98	0.6027	0.10	1.86	78.1	12.6	39	145	0.87	81	3	A	high
LOCAL	RO3139	Female	12.03	12.47	0.4329	0.01	0.89	69.4	11.2	40.8	150.7	-0.17	43	4	T	high
LOCAL	RO3309	Female	6.91	7	0.0904	0.70	0.29	56.4	9.1	19.5	119.1	-1.32	9	1	T	high
LOCAL	RO3367	Male	5.19	5.48	0.2904	0.90	0.56	53.9	8.7	18.5	114	-1.1	14	2	T	high
LOCAL	RO3521	Male	5.91	6.13	0.2137	0.31	0.84	57.7	9.3	21.3	114	0.68	75	3	T	high
LOCAL	RO3527	Female	4.47	4.86	0.3836	-0.02	1.23	49.0	7.9	18	109.2	-0.05	48	4	T	high
LOCAL	RO3555	Male	10.68	10.9	0.2219	0.46	0.29	67.6	10.9	56.9	156	1.68	95	3	A	low
LOCAL	RO3572	Male	4.88	5.16	0.2767	0.62	0.63	56.4	9.1	20.6	112.4	0.69	75	4	T	high
LOCAL	RO3585	Male	5.78	6.26	0.474	0.27	0.5	76.3	12.3	23.6	125.9	-0.42	34	4	NA	high
LOCAL	RO3621	Female	8.61	8.91	0.2932	0.52	0.34	78.1	12.6	28.2	128.6	0.35	64	3	NA	low
LOCAL	RO2598	Male	6.21	6.71	0.4959	0.54	0	67.6	10.9	22.1	113.8	0.95	83	4	A	high
Mean TN09 Subset (n=74)			14.71	14.99	0.24					55.04	154.82	0.46	64.23	2.69		
SD TN09 Subset (n=74)			6.81	6.73	0.04					21.52	26.24	0.93	27.5	0.91		
Mean Local (n=42)			9.72	10.02	0.3					39.44	141.67	0.45	63.79	3.14		
SD Local (n=42)			3.27	3.26	0.14					16.45	18.57	0.83	25.23	1.22		
p-value (2 sample ttest)			2.05E-05	1.68E-05	1.14E-03					8.79E-05	5.00E-03	0.98	0.93	0.02		



ESM Figure 1. This analysis of the TN-09 trial included 54 CTLA4-Ig-treated patients and 20 placebo-treated patients. Plasma induced transcription was conducted at the baseline, 3 month, 12 month, and 24 month time points. **(a)** Analysis strategy. For each subject, gene expression measured at 3, 12, and 24 months was baseline normalized. **(b)** Venn diagram illustrating the total of 427 probe sets that were differentially induced ($|\log_2 \text{ratio}| > 0.263$, 1.2-fold; ANOVA $p < 0.05$) between the treatment and placebo arms at ≥ 1 time point. **(c-e)** Two-way hierarchical clustering (probe sets and subjects) for the regulated probe sets respectively identified between CTLA4-Ig-treated (blue bar) and placebo-treated (red bar) subjects at 3 ($n=167$ probe sets), 12 ($n=197$ probe sets), and 24 months ($n=137$ probe sets) was conducted. There was heterogeneity in both study arms, as evidenced the imperfect clustering observed at each time point. **(f)** An intersection of 57 probe sets, regulated between the two arms at all time points was identified. Well annotated transcripts of the intersection are shown.