

Supplementary Table 1. Patients' characteristics

Variables	No. (%)
No. of patients	55
Age, years, median (range)	68 (47 – 88)
Gender	
Male	33 (60)
Female	22 (40)
WHO classification at diagnosis	
MDS-MLD	4 (7)
MDS-MLD-RS	1 (2)
EB-1	19 (34)
EB-2	25 (46)
CMML	6 (11)
Hemoglobin, g/dL, median (range)	9.3 (5.2-13.8)
White blood cell count, x 10 ⁹ /L, median (range)	2.3 (0.6-46.0)
Absolute neutrophil count, x 10 ⁹ /L, median (range)	0.97 (0.05-17.00)
Lymphocyte count, x 10 ⁹ /L, median (range)	1.08 (0.24-6.98)
Platelet count, x 10 ⁹ /L, median (range)	67 (12-455)
Marrow blast, median (range)	10 (1-18)
IPSS-R cytogenetic risk	
Very good/Good	11 (20)
Intermediate	16 (29)
Poor/Very poor	28 (51)
Monosomal karyotype	
No	27 (49)
Yes	28 (51)
IPSS-R risk	
Very low/Low	4 (7)
Intermediated	12 (22)
High/Very high	39 (71)
Prior therapy	
None	39 (71)
HMA	16 (29)

MLD, multilineage dysplasia; RS, ring sideroblasts; EB-1, excess blast-1; EB-2, excess blast-2; CMML, chronic myelomonocytic leukemia; IPSS-R, Revised International Prognostic Scoring System; HMA, hypomethylating agent;

*All variables were assessed at the time of enrollment in all patients

Supplementary Table 2. The 40 most statistically significant gene expression changes between pre- and post-treatment in IMT ± HMA responders

Gene	Log2 fold change	P-value	Adjusted P-value	Gene sets
CD163	-1.57	0.000692	0.12	Phagocytosis and Degradation
LILRB5	-1.49	8.24E-05	0.0471	Adaptive Immune System
CCL2	-1.49	0.00145	0.165	Chemokine Signaling, Cytokine Signaling, Host-pathogen Interaction, Lymphocyte Activation, NLR signaling, TNF Family Signaling
TNFRSF10C	-1.48	0.000383	0.101	Apoptosis, Cytokine Signaling, Host-pathogen Interaction, Lymphocyte Activation
LILRA3	-1.47	0.000896	0.138	Adaptive Immune System, Innate Immune System
MSR1	-1.46	2.72E-05	0.0233	Phagocytosis and Degradation
CLEC7A	-1.42	0.000211	0.0702	Host-pathogen Interaction, Innate Immune System, Lymphocyte Activation, Phagocytosis and Degradation
TGFBI	-1.39	0.000496	0.102	Cell Adhesion
LILRB3	-1.35	0.00153	0.165	Adaptive Immune System, B cell Receptor Signaling
PTGS2	-1.34	0.00083	0.138	Cytokine Signaling, Host-pathogen Interaction, Immunometabolism, NF-kB Signaling, Oxidative Stress, TNF Family Signaling
MME	-1.3	0.00134	0.165	Innate Immune System
CSF3R	-1.28	0.000479	0.102	Cytokine Signaling
TLR2	-1.28	0.00185	0.186	Adaptive Immune System, Host-pathogen Interaction, Innate Immune System, MHC Class I Antigen Presentation, Phagocytosis and Degradation, TLR Signaling
CD209	-1.27	2.92E-05	0.0233	Adaptive Immune System, Host-pathogen Interaction, Innate Immune System, Lymphocyte Activation, Phagocytosis and Degradation
EGR1	-1.25	0.000143	0.0636	Cytokine Signaling, Host-pathogen Interaction, Lymphocyte Activation, Transcriptional Regulation, Type I Interferon Signaling
TLR4	-1.19	0.00186	0.186	Adaptive Immune System, Apoptosis, Host-pathogen Interaction, Innate Immune System, Lymphocyte Activation, MHC Class I Antigen Presentation, NF-kB Signaling, NLR signaling, Phagocytosis and Degradation, TLR Signaling
CCR1	-1.18	0.000205	0.0702	Chemokine Signaling, Cytokine Signaling
FCGR2A	-1.17	0.00051	0.102	Host-pathogen Interaction, Innate Immune System, Phagocytosis and Degradation
FCGRT	-1.07	0.000192	0.0702	Hemostasis
TNF	-1.06	0.000549	0.105	Apoptosis, Cytokine Signaling, Host-pathogen Interaction, Lymphocyte Activation, NF-kB Signaling, NLR signaling, Oxidative Stress, T Cell Receptor Signaling, TGF-b Signaling, Th17 Differentiation, TLR Signaling, TNF Family Signaling
CARD9	-0.975	0.00149	0.165	Host-pathogen Interaction, Innate Immune System, NLR signaling
POU2F2	-0.931	0.00103	0.152	Lymphocyte Activation, Transcriptional Regulation
SYK	-0.746	0.00145	0.165	Adaptive Immune System, B cell Receptor Signaling, Cytokine Signaling, Hemostasis, Host-pathogen Interaction, Innate Immune System, Lymphocyte Activation, NF-kB Signaling
TNFRSF1B	-0.695	0.00158	0.167	Cytokine Signaling, Innate Immune System, TNF Family Signaling
PTPN6	-0.566	0.000101	0.0507	Adaptive Immune System, B cell Receptor Signaling, Cytokine Signaling, Hemostasis, Host-pathogen Interaction, Innate Immune System, Lymphocyte Activation, T Cell Receptor Signaling, Type I Interferon Signaling, Type II Interferon Signaling
PML	-0.404	0.00134	0.165	Cytokine Signaling, Host-pathogen Interaction, Oxidative Stress, Type II Interferon Signaling
CD28	0.923	0.00114	0.157	Adaptive Immune System, Cell Adhesion, Host-pathogen Interaction, Lymphocyte Activation, T Cell Receptor Signaling
CD96	1.01	0.000316	0.0973	Adaptive Immune System
CD3D	1.07	0.00111	0.157	Adaptive Immune System, Host-pathogen Interaction, Lymphocyte Activation, T Cell Receptor Signaling
SH2D1A	1.12	0.00139	0.165	Adaptive Immune System, Host-pathogen Interaction, Lymphocyte Activation
CD8B	1.16	0.000466	0.102	Adaptive Immune System, Cell Adhesion, Lymphocyte Activation, T Cell Receptor Signaling
GATA3	1.23	0.000591	0.108	Cytokine Signaling, Hemostasis, Lymphocyte Activation, Th2 Differentiation, Transcriptional Regulation
GZMK	1.26	0.000403	0.101	Apoptosis, Lymphocyte Activation
FOXP3	1.31	0.000868	0.138	Lymphocyte Activation, Transcriptional Regulation, Treg Differentiation
IFNG	1.35	0.00145	0.165	Cytokine Signaling, Host-pathogen Interaction, Lymphocyte Activation, T Cell Receptor Signaling, TGF-b Signaling, Th1 Differentiation, Type II Interferon Signaling
DUSP4	1.48	0.000354	0.101	Cytokine Signaling, Innate Immune System, TLR Signaling
KLRK1	1.6	5.90E-05	0.0394	Host-pathogen Interaction, Lymphocyte Activation
sCTLA4	1.95	9.77E-06	0.0188	Adaptive Immune System, Cell Adhesion, Lymphocyte Activation, T Cell Receptor Signaling

CTLA4_all	2.03	1.41E-05	0.0188	Adaptive Immune System, Cell Adhesion, Lymphocyte Activation, T Cell Receptor Signaling
CTLA4-TM	2.24	2.93E-07	0.00117	Adaptive Immune System, Cell Adhesion, Lymphocyte Activation, T Cell Receptor Signaling

Supplementary Table 3. The 40 most statistically significant gene expression changes between pre- and post-treatment in IMT ± HMA non-responders

Gene	Log2 fold change	P-value	Adjusted P-value	Gene sets
CCRL1	-3.31	4.26E-06	0.00582	Chemokine Signaling
IL12B	-2.57	2.48E-07	0.000991	Cytokine Signaling, Host-pathogen Interaction, Lymphocyte Activation, Th1 Differentiation, Th17 Differentiation, TLR Signaling
IRGM	-2.17	1.28E-05	0.0109	Host-pathogen Interaction
IFNA2	-2.1	0.000133	0.024	Cytokine Signaling, Hemostasis, Host-pathogen Interaction, Innate Immune System, Lymphocyte Activation, NLR signaling, TLR Signaling, Type I Interferon Signaling
LILRA4	-1.96	5.04E-05	0.0152	Adaptive Immune System
EOMES	-1.91	9.88E-05	0.0197	Lymphocyte Activation, Transcriptional Regulation
CCL8	-1.84	3.00E-04	0.0353	Chemokine Signaling, Cytokine Signaling
ICOS	-1.82	1.91E-05	0.0109	Cell Adhesion, Lymphocyte Activation, T Cell Receptor Signaling
ARG2	-1.82	0.000449	0.046	Host-pathogen Interaction, Immunometabolism
IL18R1	-1.77	0.000444	0.046	Cytokine Signaling, Lymphocyte Activation, TNF Family Signaling
KLRC2	-1.56	0.000143	0.024	Innate Immune System, Lymphocyte Activation
TNFRSF8	-1.56	0.000192	0.0271	Cytokine Signaling
KIR3DL2	-1.53	6.48E-05	0.0162	Adaptive Immune System, Lymphocyte Activation
CR1	-1.5	5.29E-05	0.0152	Complement System, Host-pathogen Interaction, Innate Immune System
CD274	-1.46	0.00035	0.0388	Adaptive Immune System, Cell Adhesion, Lymphocyte Activation
CRADD	-1.33	5.33E-05	0.0152	Apoptosis
CCR6	-1.33	0.000121	0.023	Chemokine Signaling, Cytokine Signaling, Innate Immune System
KLRG1	-1.33	0.000197	0.0271	Adaptive Immune System, Lymphocyte Activation
CD1A	-1.33	0.000377	0.0407	Adaptive Immune System
CCL5	-1.3	2.95E-05	0.0113	Chemokine Signaling, Cytokine Signaling, Host-pathogen Interaction, Lymphocyte Activation, NLR signaling, Oxidative Stress, TLR Signaling, TNF Family Signaling
IRAK2	-1.3	6.14E-05	0.0162	Cytokine Signaling, Host-pathogen Interaction, Innate Immune System, NLR signaling, TLR Signaling
ITGB1	-1.22	2.80E-05	0.0113	Adaptive Immune System, Cell Adhesion, Cytokine Signaling, Hemostasis, Host-pathogen Interaction, Lymphocyte Activation, Lymphocyte Trafficking, Phagocytosis and Degradation
ICOSLG	-1.21	8.99E-05	0.0189	Adaptive Immune System, Cell Adhesion, Lymphocyte Activation
TIGIT	-1.17	0.000238	0.0297	Cell Adhesion, Lymphocyte Activation
ABCB1	-1.15	0.000173	0.0264	Immunometabolism
ATG12	-1.14	2.97E-05	0.0113	Autophagy, Innate Immune System, NLR signaling
IL6ST	-0.996	0.000237	0.0297	Cytokine Signaling, Lymphocyte Activation, Th17 Differentiation
SLC2A1	-0.987	0.000342	0.0388	Host-pathogen Interaction, Immunometabolism
TRAF4	-0.971	7.71E-05	0.0171	NF-κB Signaling, TNF Family Signaling
ATG5	-0.823	1.65E-05	0.0109	Autophagy, Host-pathogen Interaction, Innate Immune System, Lymphocyte Activation, NLR signaling
GFI1	-0.82	3.12E-05	0.0113	Transcriptional Regulation
CD59	-0.76	0.00015	0.024	Complement System, Innate Immune System, Lymphocyte Activation

MAPK1	-0.699	4.37E-06	0.00582	Apoptosis, Autophagy, B cell Receptor Signaling, Chemokine Signaling, Cytokine Signaling, Hemostasis, Host-pathogen Interaction, Innate Immune System, Lymphocyte Activation, NLR signaling, T Cell Receptor Signaling, TGF- β Signaling, TLR Signaling, TNF Family Signaling
GPI	0.536	7.41E-05	0.0171	Immunometabolism, Innate Immune System
ILF3	1.01	0.00015	0.024	Transcriptional Regulation
HLA-DPA1	1.08	0.000509	0.0495	Adaptive Immune System, Cell Adhesion, Cytokine Signaling, Host-pathogen Interaction, Lymphocyte Activation, MHC Class II Antigen Presentation, Phagocytosis and Degradation, T Cell Receptor Signaling, Type II Interferon Signaling
FCGR2B	1.39	1.43E-05	0.0109	Adaptive Immune System, B cell Receptor Signaling, Host-pathogen Interaction, Phagocytosis and Degradation
CD24	1.61	0.000179	0.0264	Lymphocyte Activation
NFKBIA	1.78	0.000207	0.0275	Adaptive Immune System, Apoptosis, B cell Receptor Signaling, Chemokine Signaling, Cytokine Signaling, Host-pathogen Interaction, Innate Immune System, NF- κ B Signaling, NLR signaling, T Cell Receptor Signaling, TLR Signaling, TNF Family Signaling, Transcriptional Regulation
S100A9	1.9	0.000264	0.0319	Innate Immune System, TLR Signaling

Supplementary Table 4. The 40 most statistically significant differential expression results between pre- and post-samples in the patients treated with α CTLA4 \pm HMA

Gene	Log2 fold change	P-value	Adjusted P-value	Gene sets
EDNRB	-1.73	0.00222	0.467	Hemostasis
IL1A	-1.64	0.00739	0.8	Cytokine Signaling, Host-pathogen Interaction
CCL8	-1.62	0.00233	0.467	Chemokine Signaling, Cytokine Signaling
FN1	-1.61	0.00713	0.8	Cytokine Signaling, Hemostasis, Host-pathogen Interaction, Oxidative Stress
PPARG	-1.58	0.000686	0.365	Immunometabolism, Transcriptional Regulation
IL10	-1.31	0.000644	0.365	Cytokine Signaling, Host-pathogen Interaction, Lymphocyte Activation, T Cell Receptor Signaling, Treg Differentiation
MSR1	-1.28	0.00143	0.443	Phagocytosis and Degradation
HFE	-1.24	0.00182	0.443	Lymphocyte Activation
IL1R1	-1.23	0.00792	0.8	Cytokine Signaling, Host-pathogen Interaction, NF-kB Signaling, Oxidative Stress, Th17 Differentiation
CD1D	-1.14	0.00485	0.695	Adaptive Immune System, Host-pathogen Interaction, Lymphocyte Activation
HAVCR2	-1.13	0.00268	0.486	Cytokine Signaling, Lymphocyte Activation
CD209	-1.12	0.000738	0.365	Adaptive Immune System, Host-pathogen Interaction, Innate Immune System, Lymphocyte Activation, Phagocytosis and Degradation
BST2	-1.01	0.00185	0.443	Cytokine Signaling, Innate Immune System, Lymphocyte Activation, Type I Interferon Signaling
CD4	-0.885	0.00552	0.763	Adaptive Immune System, Cell Adhesion, Cytokine Signaling, Innate Immune System, Lymphocyte Activation, T Cell Receptor Signaling
AHR	-0.848	0.0042	0.648	Immunometabolism, Lymphocyte Activation, Th17 Differentiation, Transcriptional Regulation
BCL3	-0.735	0.00291	0.486	Lymphocyte Activation, TNF Family Signaling, Transcriptional Regulation
SYK	-0.711	0.00188	0.443	Adaptive Immune System, B cell Receptor Signaling, Cytokine Signaling, Hemostasis, Host-pathogen Interaction, Innate Immune System, Lymphocyte Activation, NF-kB Signaling
TLR1	-0.646	0.00288	0.486	Adaptive Immune System, Host-pathogen Interaction, Innate Immune System, MHC Class I Antigen Presentation, TLR Signaling
ITGA5	-0.636	0.000867	0.365	Hemostasis, Host-pathogen Interaction, Phagocytosis and Degradation
IRF7	-0.596	0.00798	0.8	Cytokine Signaling, Hemostasis, Host-pathogen Interaction, Innate Immune System, NLR signaling, TLR Signaling, Transcriptional Regulation, Type I Interferon Signaling, Type II Interferon Signaling
MCL1	-0.567	0.0072	0.8	Apoptosis, Cytokine Signaling, Oxidative Stress
BCL10	-0.502	0.00164	0.443	Adaptive Immune System, B cell Receptor Signaling, Host-pathogen Interaction, Innate Immune System, Lymphocyte Activation, NF-kB Signaling, T Cell Receptor Signaling
HLA-DRA	-0.493	0.00737	0.8	Adaptive Immune System, Cell Adhesion, Cytokine Signaling, Host-pathogen Interaction, Lymphocyte Activation, MHC Class II Antigen Presentation, Phagocytosis and Degradation, T Cell Receptor Signaling, Type II Interferon Signaling
CD44	-0.429	0.000419	0.355	Cytokine Signaling, Hemostasis, Host-pathogen Interaction, Immunometabolism, Innate Immune System, Type II Interferon Signaling
TNFSF8	-0.429	0.00722	0.8	Cytokine Signaling, Lymphocyte Activation
SMAD5	-0.423	0.00679	0.8	TGF- β Signaling
CD164	-0.385	7.42E-05	0.149	Phagocytosis and Degradation
IFIH1	-0.364	0.00731	0.8	Host-pathogen Interaction, Innate Immune System
STAT3	-0.355	0.000241	0.322	Chemokine Signaling, Cytokine Signaling, Host-pathogen Interaction, Th17 Differentiation, Transcriptional Regulation, Treg Differentiation
HLA-B	-0.344	0.00468	0.695	Adaptive Immune System, Cell Adhesion, Cytokine Signaling, Host-pathogen Interaction, Innate Immune System, Lymphocyte Activation, MHC Class I Antigen Presentation, Phagocytosis and Degradation, Type I Interferon Signaling, Type II Interferon Signaling
TRAF2	0.376	0.00705	0.8	Apoptosis, Cytokine Signaling, Host-pathogen Interaction, Innate Immune System, Lymphocyte Activation, NF-kB Signaling, NLR signaling, Oxidative Stress, TNF Family Signaling
MBP	0.779	0.00184	0.443	Lymphocyte Trafficking
CD96	0.815	0.00184	0.443	Adaptive Immune System
IL18RAP	0.897	0.00233	0.467	Cytokine Signaling, Oxidative Stress
IL32	1.05	0.00779	0.8	Cytokine Signaling
CTLA4_all	1.19	0.00248	0.473	Adaptive Immune System, Cell Adhesion, Lymphocyte Activation, T Cell Receptor Signaling
IL20	1.27	0.00345	0.554	Cytokine Signaling
sCTLA4	1.33	0.000911	0.365	Adaptive Immune System, Cell Adhesion, Lymphocyte Activation, T Cell Receptor Signaling
CTLA4-TM	1.48	7.55E-07	0.00303	Adaptive Immune System, Cell Adhesion, Lymphocyte Activation, T Cell Receptor Signaling
KLRK1	1.76	0.000443	0.355	Host-pathogen Interaction, Lymphocyte Activation

Supplementary Table 5. The 40 most statistically significant differential expression results between pre- and post-samples in the patients treated with α PD1 \pm HMA

Gene	Log2 fold change	P-value	Adjusted P-value	Gene sets
CD86	-3.92	0.00153	0.279	Adaptive Immune System, Cell Adhesion, Cytokine Signaling, Lymphocyte Activation, TLR Signaling
LILRA6	-3.81	0.00148	0.279	Adaptive Immune System, MHC Class I Antigen Presentation
TLR7	-3.66	0.00212	0.279	Host-pathogen Interaction, Innate Immune System, TLR Signaling
LTF	-3.56	0.000793	0.279	Innate Immune System
CLEC7A	-3.46	0.000373	0.279	Host-pathogen Interaction, Innate Immune System, Lymphocyte Activation, Phagocytosis and Degradation
CD14	-3.46	0.00269	0.279	Adaptive Immune System, Apoptosis, Host-pathogen Interaction, Innate Immune System, MHC Class I Antigen Presentation, NF-kB Signaling, Phagocytosis and Degradation, TLR Signaling
TLR1	-3.18	0.00229	0.279	Adaptive Immune System, Host-pathogen Interaction, Innate Immune System, MHC Class I Antigen Presentation, TLR Signaling
LILRA1	-3.09	0.00244	0.279	Adaptive Immune System
TLR4	-3.08	0.00223	0.279	Adaptive Immune System, Apoptosis, Host-pathogen Interaction, Innate Immune System, Lymphocyte Activation, MHC Class I Antigen Presentation, NF-kB Signaling, NLR signaling, Phagocytosis and Degradation, TLR Signaling
TNFRSF10C	-3.03	0.000508	0.279	Apoptosis, Cytokine Signaling, Host-pathogen Interaction, Lymphocyte Activation
TGFBI	-2.91	0.000643	0.279	Cell Adhesion
TYK2	-2.74	0.00113	0.279	Cytokine Signaling, Host-pathogen Interaction, NLR signaling, Th1 Differentiation, Th17 Differentiation, Treg Differentiation, Type I Interferon Signaling
TNFRSF13B	-2.67	0.00107	0.279	Cytokine Signaling, Lymphocyte Activation
FCER1A	-2.55	0.00172	0.279	Innate Immune System
CCR1	-2.55	0.00288	0.279	Chemokine Signaling, Cytokine Signaling
CEBPB	-2.51	0.00224	0.279	Host-pathogen Interaction, Lymphocyte Activation, TNF Family Signaling, Transcriptional Regulation
TNFRSF8	-2.51	0.00249	0.279	Cytokine Signaling
LILRA4	-2.48	0.00161	0.279	Adaptive Immune System
LILRB3	-2.46	0.00209	0.279	Adaptive Immune System, B cell Receptor Signaling
TFRC	-2.31	0.00256	0.279	Phagocytosis and Degradation
LTBR	-2.31	0.00264	0.279	Cytokine Signaling, Host-pathogen Interaction, NF-kB Signaling
TLR2	-2.24	0.00245	0.279	Adaptive Immune System, Host-pathogen Interaction, Innate Immune System, MHC Class I Antigen Presentation, Phagocytosis and Degradation, TLR Signaling
IL18	-2.23	0.00203	0.279	Cytokine Signaling, Host-pathogen Interaction, Lymphocyte Activation, NLR signaling
LILRA3	-2.18	0.000864	0.279	Adaptive Immune System, Innate Immune System
ARG2	-2.07	0.000494	0.279	Host-pathogen Interaction, Immunometabolism
CAMP	-2.06	0.00276	0.279	Host-pathogen Interaction, Innate Immune System, NLR signaling
SRC	-2.04	0.00049	0.279	Chemokine Signaling, Host-pathogen Interaction, Lymphocyte Activation, Oxidative Stress
TLR9	-1.99	0.000909	0.279	Host-pathogen Interaction, Innate Immune System, TLR Signaling
FCGRT	-1.52	0.00277	0.279	Hemostasis
LILRA5	-1.52	0.00285	0.279	Adaptive Immune System
TNFRSF13C	-1.42	0.00182	0.279	Cytokine Signaling, Host-pathogen Interaction, Lymphocyte Activation, NF-kB Signaling
TAL1	-1.36	0.000592	0.279	Transcriptional Regulation
MAP4K2	-1.19	0.00219	0.279	TNF Family Signaling
IL1RAP	-0.925	0.00125	0.279	Cytokine Signaling, Th17 Differentiation

IRF8	-0.733	0.00084	0.279	Cytokine Signaling, Host-pathogen Interaction, Transcriptional Regulation, Type I Interferon Signaling, Type II Interferon Signaling
HLA-DPB1	-0.651	0.000183	0.279	Adaptive Immune System, Cell Adhesion, Cytokine Signaling, Host-pathogen Interaction, Lymphocyte Activation, MHC Class II Antigen Presentation, Phagocytosis and Degradation, T Cell Receptor Signaling, Type II Interferon Signaling
STAT5A	-0.581	0.00261	0.279	Cytokine Signaling, Host-pathogen Interaction, Th2 Differentiation, Transcriptional Regulation
CD96	0.858	0.00259	0.279	Adaptive Immune System
CXCR4	1.29	0.000681	0.279	Chemokine Signaling, Cytokine Signaling, Lymphocyte Trafficking
DUSP4	2.24	0.00162	0.279	Cytokine Signaling, Innate Immune System, TLR Signaling

Supplementary Table 6. The 40 most statistically significant differential expression results between pre- and post-samples in the patients treated with α CTLA4/ α PD1 \pm HMA

Gene	Log2 fold change	P-value	Adjusted P-value	Gene sets
CCRL1	-3.14	3.26E-05	0.028	Chemokine Signaling
C6	-2.79	3.16E-05	0.028	Complement System, Innate Immune System
EDNRB	-2.39	0.000949	0.206	Hemostasis
CDH5	-2.15	0.000741	0.194	Cell Adhesion, Lymphocyte Trafficking
IL6	-1.92	2.33E-05	0.028	Cytokine Signaling, Host-pathogen Interaction, Lymphocyte Activation, NLR signaling, Oxidative Stress, Th17 Differentiation, Th2 Differentiation, TLR Signaling, TNF Family Signaling
IL12B	-1.9	0.00289	0.382	Cytokine Signaling, Host-pathogen Interaction, Lymphocyte Activation, Th1 Differentiation, Th17 Differentiation, TLR Signaling
IFNA1/13	-1.86	0.000939	0.206	Cytokine Signaling, Host-pathogen Interaction, Lymphocyte Activation, NLR signaling, TLR Signaling, Type I Interferon Signaling
MBL2	-1.82	0.00279	0.382	Complement System, Host-pathogen Interaction, Innate Immune System, Oxidative Stress, Phagocytosis and Degradation
DEFB103A	-1.73	0.000371	0.106	Innate Immune System
CCL8	-1.72	0.000777	0.194	Chemokine Signaling, Cytokine Signaling
RAG2	-1.71	0.00125	0.227	Cytokine Signaling, Lymphocyte Activation
CD209	-1.63	0.00205	0.356	Adaptive Immune System, Host-pathogen Interaction, Innate Immune System, Lymphocyte Activation, Phagocytosis and Degradation
MME	-1.62	0.00217	0.362	Innate Immune System
IFNA2	-1.61	0.00409	0.419	Cytokine Signaling, Hemostasis, Host-pathogen Interaction, Innate Immune System, Lymphocyte Activation, NLR signaling, TLR Signaling, Type I Interferon Signaling
IRGM	-1.6	0.000275	0.0848	Host-pathogen Interaction
ITLN1	-1.58	0.00379	0.408	Innate Immune System
SLC2A1	-1.55	0.000117	0.0609	Host-pathogen Interaction, Immunometabolism
IL28A	-1.54	0.00229	0.367	Cytokine Signaling, Lymphocyte Activation
CCRL2	-1.38	0.00306	0.382	Chemokine Signaling
TNFSF15	-1.31	0.00372	0.408	Cytokine Signaling
TNF	-1.3	0.000194	0.0647	Apoptosis, Cytokine Signaling, Host-pathogen Interaction, Lymphocyte Activation, NF-kB Signaling, NLR signaling, Oxidative Stress, T Cell Receptor Signaling, TGF-b Signaling, Th17 Differentiation, TLR Signaling, TNF Family Signaling
TNFRSF8	-1.29	0.00368	0.408	Cytokine Signaling
LILRA4	-1.28	0.00304	0.382	Adaptive Immune System
CCL11	-1.27	0.00281	0.382	Chemokine Signaling, Cytokine Signaling
IL1B	-1.2	0.00388	0.408	Cytokine Signaling, Host-pathogen Interaction, Innate Immune System, Lymphocyte Activation, NF-kB Signaling, NLR signaling, Oxidative Stress, Th17 Differentiation, TLR Signaling, TNF Family Signaling
CR1	-1.18	0.000174	0.0631	Complement System, Host-pathogen Interaction, Innate Immune System
CD36	-1.03	0.0036	0.408	Adaptive Immune System, Cytokine Signaling, Hemostasis, Host-pathogen Interaction, Immunometabolism, Innate Immune System, MHC Class I Antigen Presentation, Oxidative Stress, Phagocytosis and Degradation, TLR Signaling
IL6ST	-0.893	2.00E-05	0.028	Cytokine Signaling, Lymphocyte Activation, Th17 Differentiation
TRAF4	-0.862	0.000135	0.0609	NF-kB Signaling, TNF Family Signaling
MAPK1	-0.636	0.000152	0.0609	Apoptosis, Autophagy, B cell Receptor Signaling, Chemokine Signaling, Cytokine Signaling, Hemostasis, Host-pathogen Interaction, Innate Immune System, Lymphocyte Activation, NLR signaling, T Cell Receptor Signaling, TGF-b Signaling, TLR Signaling, TNF Family Signaling
CTSC	0.383	0.00348	0.408	Adaptive Immune System, Apoptosis, Innate Immune System, MHC Class II Antigen Presentation, Phagocytosis and Degradation
HLA-DPB1	0.65	0.000977	0.206	Adaptive Immune System, Cell Adhesion, Cytokine Signaling, Host-pathogen Interaction, Lymphocyte Activation, MHC Class II Antigen Presentation, Phagocytosis and Degradation, T Cell Receptor Signaling, Type II Interferon Signaling

IRAK3	0.987	0.00594	0.582	Cytokine Signaling, Innate Immune System, TLR Signaling
CD45RB	1.06	0.00299	0.382	Adaptive Immune System, Cell Adhesion, Innate Immune System, Lymphocyte Activation, T Cell Receptor Signaling
MUC1	1.14	0.00113	0.222	Cytokine Signaling, Innate Immune System
IFI35	1.26	0.000142	0.0609	Cytokine Signaling, Type I Interferon Signaling
FCGR2B	1.3	0.000105	0.0609	Adaptive Immune System, B cell Receptor Signaling, Host-pathogen Interaction, Phagocytosis and Degradation
BTLA	1.4	0.00275	0.382	Adaptive Immune System, Lymphocyte Activation
sCTLA4	2.02	0.00116	0.222	Adaptive Immune System, Cell Adhesion, Lymphocyte Activation, T Cell Receptor Signaling
CTLA4-TM	3.21	3.50E-05	0.028	Adaptive Immune System, Cell Adhesion, Lymphocyte Activation, T Cell Receptor Signaling

Supplementary Table 7. The 40 most statistically significant differential expression results between pre- and post-samples in the patients treated with HMA alone

Gene	Log2 fold change	P-value	Adjusted P-value	Gene sets
S100A8	-3.03	2.28E-05	0.00368	Innate Immune System, TLR Signaling
IL32	-2.91	3.09E-05	0.00411	Cytokine Signaling
CD74	-2.82	1.24E-05	0.00253	Adaptive Immune System, Hemostasis, Host-pathogen Interaction, Lymphocyte Activation, MHC Class II Antigen Presentation
CD45RA	-2.33	7.45E-06	0.00192	Adaptive Immune System, Cell Adhesion, Innate Immune System, Lymphocyte Activation, T Cell Receptor Signaling
PECAM1	-2.26	4.69E-05	0.00482	Cell Adhesion, Hemostasis, Host-pathogen Interaction, Innate Immune System, Lymphocyte Trafficking
GPR183	-2.25	2.80E-05	0.00388	Lymphocyte Activation
MYD88	-2.12	1.66E-05	0.00307	Adaptive Immune System, Cytokine Signaling, Host-pathogen Interaction, Innate Immune System, Lymphocyte Activation, MHC Class I Antigen Presentation, NF-kB Signaling, NLR signaling, TLR Signaling
IL2RB	-1.96	4.76E-05	0.00482	Cytokine Signaling, Hemostasis, Host-pathogen Interaction, Lymphocyte Activation, Th2 Differentiation
CD164	-1.16	4.75E-05	0.00482	Phagocytosis and Degradation
TAGAP	1.62	2.46E-06	0.00106	NF-kB Signaling
GNLY	2.28	2.51E-05	0.00385	Innate Immune System
LCP2	2.48	4.86E-05	0.00482	Adaptive Immune System, Hemostasis, Innate Immune System, Lymphocyte Activation, T Cell Receptor Signaling
CD79A	2.6	4.85E-06	0.00134	Adaptive Immune System, B cell Receptor Signaling, Lymphocyte Activation
TNFRSF14	2.61	3.51E-05	0.00413	Adaptive Immune System, Cytokine Signaling, Host-pathogen Interaction, Lymphocyte Activation
GZMB	2.7	2.58E-05	0.00385	Apoptosis, Lymphocyte Activation
IRF8	2.74	3.39E-05	0.00411	Cytokine Signaling, Host-pathogen Interaction, Transcriptional Regulation, Type I Interferon Signaling, Type II Interferon Signaling
IL10RA	2.83	4.07E-05	0.00451	Cytokine Signaling, Host-pathogen Interaction, Treg Differentiation
ADA	2.97	3.45E-06	0.00112	Immunometabolism, Lymphocyte Activation, Oxidative Stress
TNFRSF13C	3.1	3.74E-07	0.000255	Cytokine Signaling, Host-pathogen Interaction, Lymphocyte Activation, NF-kB Signaling
CD48	3.11	3.80E-05	0.00433	Hemostasis, Lymphocyte Activation
RUNX1	3.12	8.80E-06	0.00201	Transcriptional Regulation
JAK1	3.15	3.20E-05	0.00411	Cytokine Signaling, Hemostasis, Host-pathogen Interaction, NLR signaling, Th1 Differentiation, Th17 Differentiation, Treg Differentiation, Type I Interferon Signaling, Type II Interferon Signaling
JAK3	3.19	2.72E-05	0.00388	Chemokine Signaling, Cytokine Signaling, Hemostasis, Host-pathogen Interaction, Lymphocyte Activation, Th17 Differentiation, Th2 Differentiation
IL8	3.2	3.33E-05	0.00411	Chemokine Signaling, Cytokine Signaling, Host-pathogen Interaction, NF-kB Signaling, NLR signaling, TLR Signaling
CTNNB1	3.28	3.28E-06	0.00112	Host-pathogen Interaction, Innate Immune System, Lymphocyte Activation, Lymphocyte Trafficking
KLRK1	3.5	4.97E-05	0.00482	Host-pathogen Interaction, Lymphocyte Activation
IFI16	3.56	1.31E-05	0.00253	Innate Immune System, NLR signaling
HLA-A	3.57	9.28E-08	0.000144	Adaptive Immune System, Cell Adhesion, Cytokine Signaling, Host-pathogen Interaction, Lymphocyte Activation, MHC Class I Antigen Presentation, Phagocytosis and Degradation, Type I Interferon Signaling, Type II Interferon Signaling
PTPN2	3.78	1.27E-05	0.00253	Cytokine Signaling, Lymphocyte Activation
CD46	3.82	8.32E-06	0.00201	Complement System, Host-pathogen Interaction, Innate Immune System, Lymphocyte Activation
BTLA	3.91	3.87E-06	0.00115	Adaptive Immune System, Lymphocyte Activation
KLRD1	4.03	3.21E-06	0.00112	Adaptive Immune System, Innate Immune System, Lymphocyte Activation
LGALS3	4.06	1.85E-05	0.00326	Innate Immune System, Lymphocyte Activation

NFKBIA	4.54	6.66E-08	0.000144	Adaptive Immune System, Apoptosis, B cell Receptor Signaling, Chemokine Signaling, Cytokine Signaling, Host-pathogen Interaction, Innate Immune System, NF-kB Signaling, NLR signaling, T Cell Receptor Signaling, TLR Signaling, TNF Family Signaling, Transcriptional Regulation
CASP8	4.92	8.07E-07	0.000447	Apoptosis, Host-pathogen Interaction, Innate Immune System, Lymphocyte Activation, NLR signaling, TLR Signaling, TNF Family Signaling
NOTCH2	5.07	1.83E-06	0.000884	Host-pathogen Interaction, Lymphocyte Activation, Th2 Differentiation
CD97	5.82	3.95E-07	0.000255	Innate Immune System
HLA-DPA1	5.99	1.51E-07	0.000147	Adaptive Immune System, Cell Adhesion, Cytokine Signaling, Host-pathogen Interaction, Lymphocyte Activation, MHC Class II Antigen Presentation, Phagocytosis and Degradation, T Cell Receptor Signaling, Type II Interferon Signaling
CD58	6.4	2.07E-05	0.0035	Cell Adhesion, Hemostasis, Host-pathogen Interaction, Innate Immune System
STAT1	6.82	1.12E-07	0.000144	Chemokine Signaling, Cytokine Signaling, Host-pathogen Interaction, NLR signaling, Th1 Differentiation, TLR Signaling, Transcriptional Regulation, Type I Interferon Signaling, Type II Interferon Signaling