Supplementary material

He L, Jin Z, Liu M, et al. Effectiveness of a modified doxorubicin-etoposide-methylprednisolone regimen for the treatment of refractory or relapsed macrophage activation syndrome in adults. Pol Arch Intern Med. 2022; 132: 16226. doi:10.20452/pamw.16226

Table S1. Criteria used in the assessment of response to therapy

Subject	Definition
Quantifiable symptoms and laboratory markers	Levels of soluble CD25 (sCD25), ferritin, and triglyceride; hemoglobin; neutrophil counts; platelet counts; alanine aminotransferase (ALT); and presence of hemophagocytosis in pathology specimens
Complete response (CR)*	Defined as the normalization of all quantifiable symptoms and laboratory markers of HLH
Partial response (PR)*	Defined as the improvement of two or more quantifiable symptoms and laboratory markers. The specific markers should meet the following criteria: 1.5-fold decrease in sCD25; ferritin and triglyceride decreases of at least 25%; an increase of at least 100% to $>0.5\times10^9$ cells/L in patients with an initial neutrophil count of $<0.5\times10^9$ cells/L; an increase of at least 100% to $>2.0\times10^9$ cells/L in patients with an initial neutrophil count of $0.5–2.0\times10^9$ cells/L; and a decrease of at least 50% in patients with initial ALT levels >400 U/L.
No response (NR)	Patients who do not meet the criteria for CR or PR

Overall response rate	The ratio of patients with CR and PR to all patients

*The body temperature must have reverted to normal ranges for either CR or PR to be diagnosed.

Abbreviations: ALT, alanine aminotransferase; CR, complete response; HLH, hemophagocytic lymphohistiocytosis; NR, no response; PR, partial response; sCD25, soluble CD25

Table S2. Baseline characteristics of patients.

Parameters, n (%) or median (minimum ~ maximum)	Result
Gender	
Male, n (%)	5 (15.2%)
Female, n (%)	28 (84.8%)
Age, years	31 (18~62)
Fever, n (%)	33 (100%)
Splenomegaly, n (%)	29 (97.9%)
Hepatomegaly, n (%)	2 (6.1%)
Skin rashes, n (%)	20 (60.6%)
Joint pain, n (%)	18 (54.5%)
Underlying diseases	
AOSD, n (%)	19 (57.6%)
SLE, n (%)	7 (21.2%)
UCTD, n (%)	5 (15.2%)
RA, n (%)	1 (3.0%)

Dermatomyositis, n (%)	1 (3.0%)
Time form autoimmune disease diagnosis to MAS diagnosis, months	2 (0.5~204)
Infection[a], n (%)	22 (66.7%)
Bone marrow suppression, n (%)	6 (18.2%)
Coronary heart disease, n (%)	2 (6.1%)
Cardiac insufficiency, n (%)	2 (6.1%)
Cardiac damage, n (%)	3 (9.1%)

a Eighteen cases (54.5%) had radiological signs of infection before the regimen was started. Infectious organisms were detected in 4 cases (12.1%).

Abbreviations: MAS, macrophage activation syndrome; AOSD, adult-onset Still's disease; SLE, systemic lupus erythematous; UCTD, undifferentiated connective tissue disease; RA, rheumatoid arthritis.

Table S3. Genes variations in MAS Patients

Patient ID	Gender	Age	AID	Gene	Variants type	Genotype	Pathogenicity*	DNA coding	Protein	Identifier
1	Female	48	RA	UNC13D	SNV	Homozygous	No	c.2599A>G	p.K867E	rs1135688
2	Female	26	AOSD	UNC13D PRF1	SNV SNV	Heterozygosity Homozygous	No No	c.2599A>G c.900C>T	p.K867E p.H300H	rs1135688 rs885822
3	Female	62	AOSD	UNC13D PRF1	SNV SNV	Homozygous Heterozygosity	No No	c.2599A>G c.900C>T	p.K867E p.H300H	rs1135688 rs885822
4	Female	23	AOSD	UNC13D	SNV	Heterozygosity	No	c.2599A>G	p.K867E	rs1135688
5	Male	56	AOSD	STX11	SNV	Heterozygosity	No	c.313 C >A	p.R105S	cosv62449047
6	Male	27	AOSD	UNC13D	SNV	Heterozygosity	Likely	c.3134C>T	p.T1045M	rs201146973
7	Female	25	AOSD	LYST	SNV	Heterozygosity	Likely	c.7586T>A	p.M2529K	-
8	Female	31	AOSD	STX11	SNV	Heterozygosity	Likely	c.799 G >A	p.V267M	rs45574234
9	Female	22	AOSD	LYST	SNV	Heterozygosity	Likely	c.7994 A >G	p.D2665G	rs562418362
10	Female	32	AOSD	UNC13D STX11	SNV SNV	Heterozygosity Heterozygosity	No No	c. 1228 A >C c. 326 A >G	p.I410L p.E109G	rs117221419 -

11	Female	29	AOSD	UNC13D	SNV	Heterozygosity	Yes	c. 2588 G >A	p.G863D	rs140184929
12	Female	32	UCTD	UNC13D LYST	SNV SNV	Heterozygosity Heterozygosity	Yes Yes	c.680 G >A c.8368 A >C	p.R227H p.K2790Q	rs751394792 rs138506576
13	Female	20	AOSD	UNC13D	Frame shift	Heterozygosity	Yes	c.3229_3235del	p.R1077fs	rs76652119
14	Female	20	AOSD	SH2D1A	SNV	Heterozygosity	Yes	c.7G>T	p.A3S	rs148554414
15	Male	18	SLE	LYST	SNV	Heterozygosity	Unknown	c.10833A> T	p.H3611Q	-

*Pathogenicity was evaluated by SIFT and PolyPhen2.

Abbreviations: SNV, single nucleotide variants.

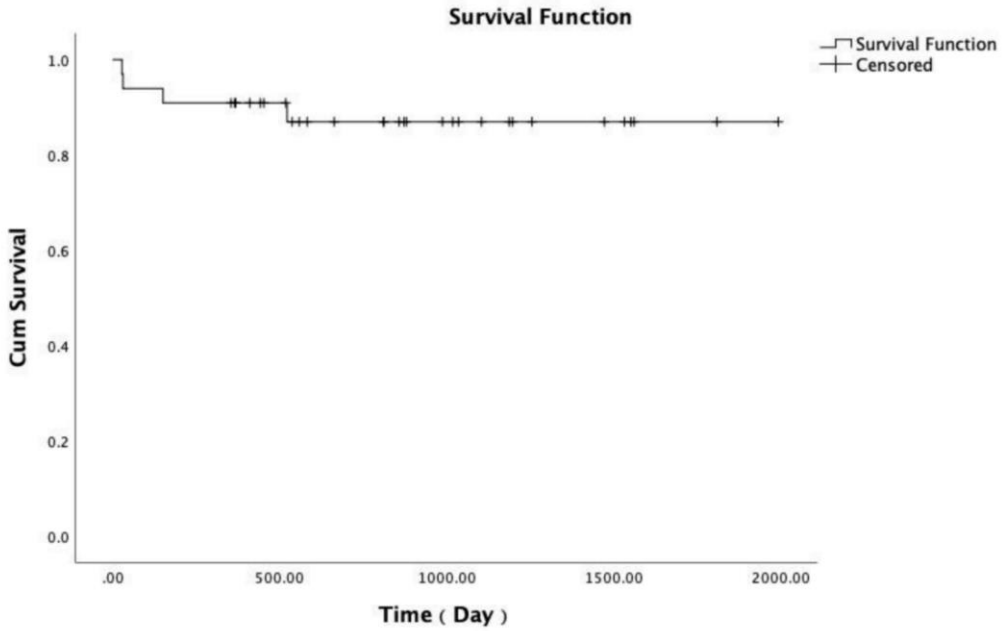

Figure S1. Kaplan-Meier analysis of patient survival.