Dose-adjusted EPOCH regimen as first-line treatment for non-Hodgkin lymphoma-associated hemophagocytic lymphohistiocytosis: a single-arm, open-label, phase II trial

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Table S1. The eligible and exclusionary criteria:

Patients were eligible if:
(1) they were histologically confirmed NHL;
(2) patients whose clinical findings satisfy HLH 2004 standard [1];
(3) newly-diagnosed and untreated;
(4) understand and voluntarily sign an informed consent form, able to adhere to the study visit schedule and other protocol requirements;
Exclusion criteria were:
(1) primary HLH;
(2) HLH from rheumatic disorder (such as systemic Lupus Erythematosus, adult onset still disease, antiphospholipid antibody syndrome);
(3) pregnancy (as determined by serum or urine test) or active breast feeding;
(4) concomitant malignancy other than NHL and need to treat;
(5) concomitant with other hematologic diseases (such as leukemia, hemophilia primary myelofibrosis) which investigators considered it unsuitable to be enrolled into this clinical trial;
(6) any potential drug abuse, medical, psychological or social conditions which may disturb this investigation and assessment;
(7) in any conditions which investigator considered ineligible for this study.

[1] HLH 2004 standard.

At least 5 criteria out of the following:
(4) Fever ≥38.5℃for ≥ 7 days;
(5) hepatosplenomegaly;
(6) Cytopenias affecting ≥2 of 3 lineages in peripheral blood: Hb<90g/L, Platelet<100x10^9/L, ANC<1.0 x 10^9/L;
(7) Hypertriglyceridemia and/or hypofibrinogenemia: fasting triglycerides ≥265 mg/dL, fibrinogen ≤1.5 g/L;
(8) Hemophagocytosis in bone marrow or spleen or lymph nodal;
(9) Low or absent NK-cell activity (according to local laboratory reference);
(10) Serum-ferritin ≥500 ug/L ;
(11) Soluble CD25 (sIL-2 receptor) ≥2,400 U/mL ;

Abreviations: ANC=absolute neutrophil count; Hb=hemoglobin; HLH=hemophagocytic lymphohistiocytosis; NHL=non-Hodgkin's lymphoma; NK=natural killer; PD=progressive disease.

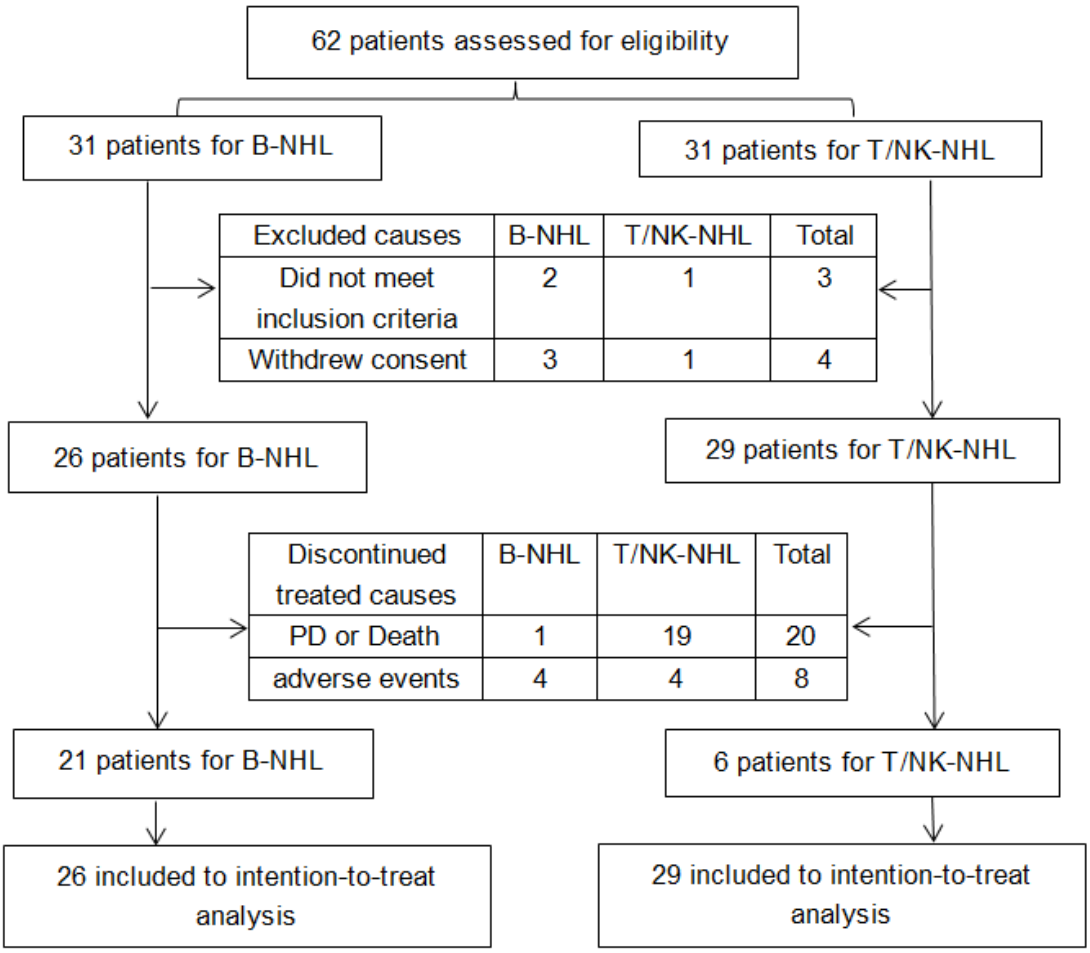

Figure S1. Trial profile

Abreviations: HLH=hemophagocytic lymphohistiocytosis; NHL=non-Hodgkin's lymphoma; NK=natural killer; PD=progressive disease.

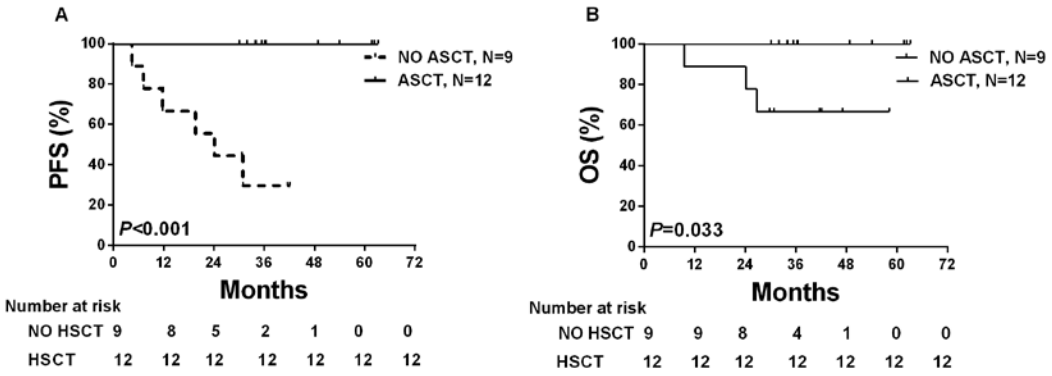

Figure S2. Progression-free survival (A) and overall survival (B) for the 21 patients who achieved ≥PR receive with or without ASCT

Abreviations: SCT= stem cell transplantation; CR/CRu=complete response/completed response unconfirmed; OS=overall survival; PFS=progression-free survival; PR=partial response; NHL=non-Hodgkin's lymphoma.

Table S2. Percent of each dose level administered over treatment cycles.

		B-NHL with HLH						T/NK-NHL with HLH					
Dose level	Change relative to dose level	1 (n=26)	2 (n=21)	3 (n=21)	4 (n=21)	5 (n=21)	6 (n=21)	1 (n=29)	2 (n=17)	3 (n=13)	4 (n=6)	5 (n=5)	6 (n=4)
-1	80		8	5	5	4	3		8	4			
1	100	26	13	8	9	10	11	29	9	9	5	4	2
2	120			8	7	7	6				1	1	1
3	144						1						1

Abreviations: HLH=hemophagocytic lymphohistiocytosis; NHL=non-Hodgkin's lymphoma; NK=natural killer.