

Figure S1. Response and survival outcomes at interim and final evaluation

Kaplan Meier curves showed (A) progression-free survival and (B) overall survival in terms of response at interim evaluation, (C) progression-free survival and (D) overall survival in terms of response at EOT. CR = complete response, PR = partial response, NR = no response, EOT = end of treatment.

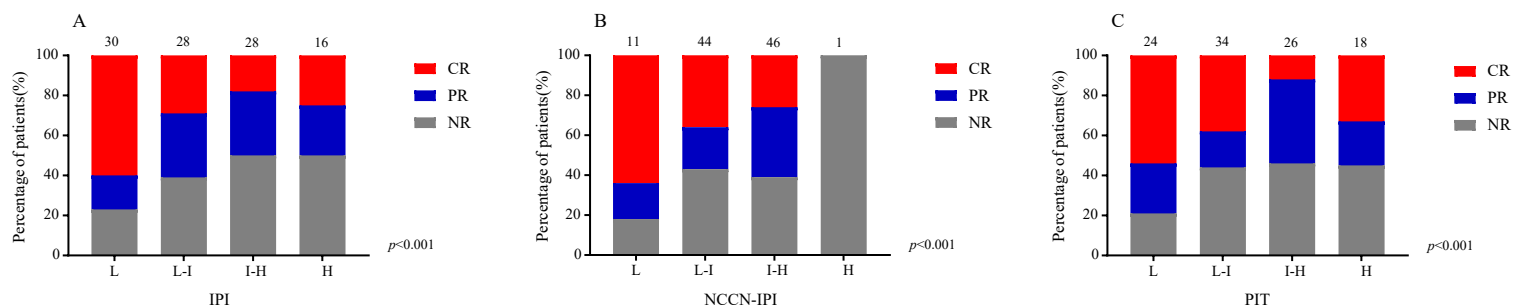


Figure S2. Response at EOT and prognostic index

Response according to (A) IPI, (B) NCCN-IPI, (C) PIT prognostic system. CR=complete response, PR=partial response, NR=no response, L=Low risk, L-I=Low-intermediate risk, I-H=Intermediate-high risk, H=High risk, IPI=International prognostic index, NCCN-IPI=National Comprehensive Cancer Network- International prognostic index, PIT = Prognostic Index for T cell lymphoma.

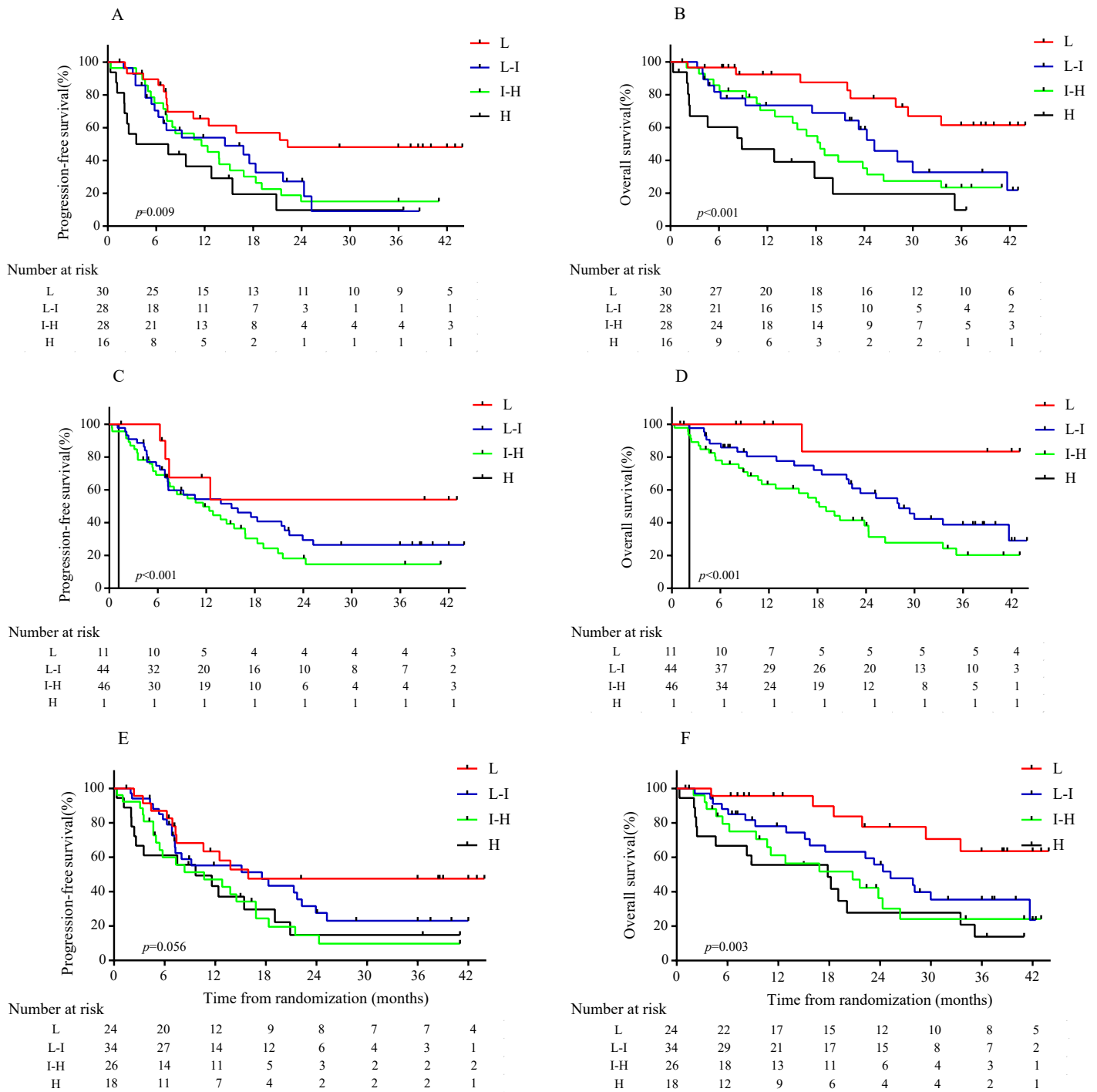


Figure S3. Survival curves and prognostic index  
Survival curves according to (A) IPI, (B) NCCN-IPI and (C) PIT prognostic systems

Table S1. Recruiting centers

<b>Site</b>	<b>P.I.</b>	<b>Patients recruited (N)</b>
State Key Laboratory of Medical Genomics, Shanghai Institute of Hematology, Shanghai Rui Jin Hospital	Weili Zhao	46
Department of Hematology, Shandong Provincial Hospital Affiliated to Shandong University, Jinan, China	Xin Wang	24
Fujian Institute of Hematology, Fujian Medical University Union Hospital, Fuzhou, China	Jianda Hu	23
Department of Hematology, The Affiliated Cancer Hospital of Zhengzhou University, Henan Cancer Hospital, Zhengzhou, China	Yongping Song	13

P. I. =Principle Investigator

Table S2. Mutation information of 62 patients with PTCL

Category	Genes	Pt No.	Sequencing	Transcription ID	Ref	Alt	AAChange.ref Gene	ExonicFunc.ref Gene
Histone modification	<i>KMT2D</i>	P1	Target	NM_003482	G	A	p.R3508Q	nonsynonymous
	<i>KMT2D</i>	P3	Target	NM_003482	G	-	p.P2738fs	frameshift
	<i>KMT2D</i>	P4	Target	NM_003482	A	G	p.T2228A	nonsynonymous
	<i>KMT2D</i>	P5	WES	NM_003482	C	T	p.R5224H	nonsynonymous
	<i>KMT2D</i>	P6	WES	NM_003482	C	T	p.R5224H	nonsynonymous
	<i>KMT2D</i>	P8	Target	NM_003482	C	T	p.P2382S	nonsynonymous
	<i>KMT2D</i>	P10	WES	NM_003482	T	C	p.T2228A	nonsynonymous
	<i>KMT2D</i>	P11	WES	NM_003482	A	C	p.V1561G	nonsynonymous
	<i>KMT2D</i>	P12	Target	NM_003482	T	A	p.L4551X	stopgain
	<i>KMT2D</i>	P15	Target	NM_003482	A	AGCT	p.Q3919fs	frameshift
	<i>KMT2D</i>	P21	WES	NM_003482	C	G	p.A3676P	nonsynonymous
	<i>KMT2D</i>	P23	Target	NM_003482	C	T	p.S186L	nonsynonymous
	<i>KMT2D</i>	P25	Target	NM_003482	G	A	p.G2881S	nonsynonymous
	<i>KMT2D</i>	P34	Target	NM_003482	T	TTGC	p.0	frameshift
	<i>KMT2A</i>	P14	WES	NM_001197104	T	A	p.N2347K	nonsynonymous
	<i>KMT2A</i>	P24	Target	NM_001197104	C	A	p.P3914H	nonsynonymous
	<i>SETD2</i>	P22	WES	NM_001349370	C	T	p.S2278N	nonsynonymous
	<i>EP300</i>	P7	WES	NM_001429	G	C	p.Q63H	nonsynonymous
	<i>EP300</i>	P13	Target	NM_001429	A	G	p.I997V	nonsynonymous
	<i>EP300</i>	P16	WES	NM_001429	C	T	p.P847S	nonsynonymous
	<i>EP300</i>	P17	Target	NM_001429	G	C	p.Q1455H	nonsynonymous
	<i>EP300</i>	P19	Target	NM_001429	G	C	p.W1466C	nonsynonymous
	<i>CREBBP</i>	P9	Target	NM_004380	A	G	p.Y1450C	nonsynonymous
<i>CREBBP</i>	P18	WES	NM_001079846	A	G	p.M250T	nonsynonymous	
<i>CREBBP</i>	P20	Target	NM_004380	C	T	p.R1446C.	nonsynonymous	
DNA	<i>TET2</i>	P1	Target	NM_001127208	T	C	p.F125S	nonsynonymous

methylation	<i>TET2</i>	P5	WES	NM_001127208	C	T	p.Q960X	stopgain
	<i>TET2</i>	P5	WES	NM_001127208	-	A	p.N837fs	frameshift
	<i>TET2</i>	P6	WES	NM_001127208	T	G	p.Y1659X	stopgain
	<i>TET2</i>	P7	WES	NM_001127208	C	T	p.H1380Y	nonsynonymous
	<i>TET2</i>	P7	WES	NM_001127208	A	C	p.N1387H	nonsynonymous
	<i>TET2</i>	P12	Target	NM_001127208	C	G	p.P29R	nonsynonymous
	<i>TET2</i>	P17	Target	NM_001127208	C	G	p.R1216G	nonsynonymous
	<i>TET2</i>	P17	Target	NM_001127208	G	C	p.C1289S	nonsynonymous
	<i>TET2</i>	P27	WES	NM_001127208	C	-	p.Y1421X	stopgain
	<i>TET2</i>	P27	WES	NM_001127208	AA	-	p.Q770fs	frameshift
	<i>TET2</i>	P28	WES	NM_001127208	CAGT	-	p.P1520fs	frameshift
	<i>TET2</i>	P29	Target	NM_001127208	4634delA	4634delA	p.Q1545fs	frameshift
	<i>TET2</i>	P32	WES	NM_001127208	A	G	p.K1299E	nonsynonymous
	<i>TET2</i>	P32	WES	NM_001127208	-	G	p.D1143fs	frameshift
	<i>TET2</i>	P37	WES	NM_001127208	C	G	p.Y1679X	stopgain
	<i>TET2</i>	P37	WES	NM_001127208	-	A	p.I750fs	frameshift
	<i>TET2</i>	P38	WES	NM_001127208	C	T	p.A1355V	nonsynonymous
	<i>TET2</i>	P38	WES	NM_001127208	A	G	p.K1310E	nonsynonymous
	<i>TET2</i>	P39	Target	NM_001127208	C	T	p.Q790X	stopgain
	<i>TET2</i>	P39	Target	NM_001127208	C	T	p.Q916X	stopgain
<i>TET2</i>	P39	Target	NM_001127208	C	T	p.T444I	nonsynonymous	
<i>TET2</i>	P44	WES	NM_001127208	A	-	p.S1059fs	frameshift	
					ATCATCTC			
	<i>DNMT3A</i>	P5	WES	NM_001320893	CCTCCTTG	-	p.588_596del	frameshift
					GGCCGCG			
					CATC			
	<i>DNMT3A</i>	P7	WES	NM_001320893	G	C	p.R619G	nonsynonymous
	<i>DNMT3A</i>	P16	WES	NM_001320892	C	T	p.G10R	nonsynonymous
	<i>DNMT3A</i>	P26	WES	NM_001320893	C	T	p.R730H	nonsynonymous

	<i>DNMT3A</i>	P27	WES	NM_001320893	C	G	p.R479T	nonsynonymous	
	<i>DNMT3A</i>	P37	WES	NM_001320893	C	T	p.W449X	stopgain	
	<i>DNMT3A</i>	P45	Target	NM_022552	C	T	p.R882C	nonsynonymous	
	<i>IDH2</i>	P38	WES	NM_001290114	C	T	p.R42K	nonsynonymous	
	<i>IDH2</i>	P39	Target	NM_002168	G	T	p.R172M	nonsynonymous	
	<i>IDH2</i>	P46	Target	NM_002168	G	A	p.R172K	nonsynonymous	
	<i>TET1</i>	P38	WES	NM_030625	T	C	p.I173T	nonsynonymous	
Chromatin remodeler	<i>ARID1B</i>	P5	WES	NM_001346813		GGAGGAG GAGGA	-	p.321_324del	frameshift
	<i>ARID1B</i>	P6	WES	NM_001346813	-		GC	p.Q121fs	frameshift
	<i>ARID1B</i>	P6	WES	NM_001346813	-		ACAG	p.Q121fs	frameshift
	<i>ARID1B</i>	P12	Target	NM_017519	G		A	p.V1503I	nonsynonymous
	<i>ARID1B</i>	P14	WES	NM_001346813	-		GGC	p.V339delinsVA	frameshift
	<i>ARID1B</i>	P15	Target	NM_001346813	CAG		-	p.114_114del	frameshift
	<i>ARID1B</i>	P26	WES	NM_017519	C		G	p.Q1393E	nonsynonymous
	<i>ARID1B</i>	P38	WES	NM_001346813	-		AGGAGC	p.G327delinsG GA	frameshift
	<i>ARID1B</i>	P39	Target	NM_020732	A		G	p.M1578V	nonsynonymous
	<i>ARID1B</i>	P41	Target	NM_020732	C		T	p.P737S	nonsynonymous
	<i>ARID1A</i>	P2	Target	NM_006015	G		A	p.A339T	nonsynonymous
	<i>ARID1A</i>	P13	Target	NM_006015	G		A	p.V1982I	nonsynonymous
	<i>ARID1A</i>	P31	WES	NM_006015	-		A	p.P421fs	frameshift
	<i>ARID1A</i>	P40	WES	NM_006015	C		T	p.R1335X	stopgain
	<i>ARID1A</i>	P42	Target	NM_006015	T		G	p.Y1012X	stopgain
	<i>ARID1A</i>	P43	Target	NM_006015	C		T	p.A1872V	nonsynonymous
	<i>ARID2</i>	P36	WES	NM_001347839	C		T	p.P536S	nonsynonymous
	<i>CHD8</i>	P14	WES	NM_001170629	G		A	p.S2069L	nonsynonymous
Tumor suppressor	<i>TP53</i>	P3	Target	NM_000546	C		T	p.R273C	nonsynonymous
	<i>TP53</i>	P26	WES	NM_000546	C		T	p.V31I	nonsynonymous

	<i>TP53</i>	P31	WES	NM_001126118	-	G	p.P8fs	frameshift
	<i>TP53</i>	P37	WES	NM_001126115	A	C	p.V41G	nonsynonymous
	<i>ATM</i>	P9	Target	NM_000051	T	C	p.I1688T	nonsynonymous
	<i>ATM</i>	P11	WES	NM_000051	C	T	p.P2974L	nonsynonymous
	<i>ATM</i>	P32	WES	NM_000051	G	A	p.D520N	nonsynonymous
	<i>MGA</i>	P10	WES	NM_001164273	G	A	p.V1699I	nonsynonymous
	<i>MGA</i>	P11	WES	NM_001080541	A	G	p.T338A	nonsynonymous
	<i>NF1</i>	P33	WES	NM_001128147	G	C	p.R574S	nonsynonymous
JAK-STAT	<i>SOCS1</i>	P31	WES	NM_003745	G	A	p.Q131X	stopgain
pathway	<i>SOCS1</i>	P34	Target	NM_003745	506_529del	506_529del	p.169_177del	frameshift
	<i>SOCS1</i>	P35	Target	NM_003745	106_122del	106_122del	p.P36fs	frameshift
	<i>JAK3</i>	P33	WES	NM_000215	C	T	p.M511I	nonsynonymous
	<i>STAT3</i>	P32	WES	NM_003150	C	T	p.G421R	nonsynonymous
Transcriptional	<i>ASXL3</i>	P8	Target	NM_030632	C	G	p.P1457R	nonsynonymous
regulation	<i>PRDM1</i>	P26	WES	NM_001198	G	A	p.G11D	nonsynonymous
Others	<i>RHOA</i>	P5	WES	NM_001313943	C	A	p.G17V	nonsynonymous
	<i>RHOA</i>	P6	WES	NM_001313943	C	A	p.G17V	nonsynonymous
	<i>RHOA</i>	P26	WES	NM_001313943	G	T	p.G17V	nonsynonymous
	<i>RHOA</i>	P27	WES	NM_001313943	C	A	p.G17V	nonsynonymous
	<i>RHOA</i>	P28	WES	NM_001313943	C	A	p.G17V	nonsynonymous
	<i>RHOA</i>	P29	Target	NM_001664	G	T	p.G17V	nonsynonymous
	<i>RHOA</i>	P30	WES	NM_001313943	C	A	p.G17V	nonsynonymous
	<i>NOTCH1</i>	P7	WES	NM_017617	C	T	p.R2263Q	nonsynonymous



Table S3. Univariable analysis of factors associated with progression-free survival and overall survival

	Progression-free survival				Overall survival		
	<i>N</i>	Median (95% CI)	HR (95% CI)	<i>p</i> - value	Median (95% CI)	HR (95% CI)	<i>p</i> - value
<b>Age</b>							
≤ 60 years	61	13.8 (7.4-20.2)			25.2 (15.5-34.9)		
> 60 years	41	11.6 (5.8-17.4)	1.30 (0.81-2.09)	0.279	23.8 (14.8-32.8)	1.56 (0.92-2.65)	0.098
<b>Gender</b>							
Male	66	13.8 (6.9-20.7)			24.3 (15.1-33.6)		
Female	36	7.3 (0.2-14.5)	1.08 (0.66-1.78)	0.750	22.3 (9.2-35.3)	1.12 (0.64-1.95)	0.701
<b>Pathology type</b>							
PTCL*	52	12.4 (7.8-16.9)		<b>0.005</b>	21.9 (15.7-28.1)		<b>0.029</b>
AITL	34	7.5 (3.4-11.6)	1.16 (0.71-1.90)	0.573	23.3 (15.8-30.7)	1.15 (0.66-2.00)	0.615
ALCL	16	Not reached	0.23 (0.80-0.65)	<b>0.003</b>	Not reached	0.25 (0.08-0.83)	<b>0.016</b>
<b>IPI</b>							
0-1	30	Not reached		<b>0.004</b>	Not reached		<b>0.000</b>
2	28	14.5 (1.7-27.3)	2.08 (1.02-4.23)	<b>0.034</b>	25.2 (19.8-30.7)	2.58 (1.09-6.12)	<b>0.019</b>
3	28	11.6 (4.9-18.3)	2.28 (1.15-4.51)	<b>0.021</b>	18.5 (14.4-22.7)	3.54 (1.54-8.11)	<b>0.002</b>
4-5	16	3.5 (0.0-13.1)	3.59 (1.65-7.83)	<b>0.003</b>	8.8 (0.0-18.6)	6.67 (2.69-16.57)	<b>0.000</b>
<b>Treatment</b>							
CEOP/IVE/GDP	51	15.4 (9.4-21.5)			24.3 (17.1-31.6)		
CEOP	51	9.2 (4.2-14.2)	1.36 (0.85-2.19)	0.199	23.3 (9.6-37.0)	1.44 (0.84-2.47)	0.178
<b>EBV-DNA (N=87)</b>							
Undetectable	65	15.1 (11.0-19.3)			29.4 (20.1-38.7)		
Detectable	22	5.3 (2.1-8.6)	1.76 (1.00-3.10)	<b>0.046</b>	8.8 (2.3-15.3)	2.43 (1.30-4.53)	<b>0.004</b>
<b>Gene Mutation (N=62)</b>							
<i>KMT2D</i> positive	14	6.9 (6.5-7.3)	2.00 (0.99-4.01)	<b>0.047</b>	28.1 (0.0-64.1)	0.94 (0.39-2.29)	0.890
<i>KMT2A</i>	2	4.6 (NA)	1.33 (0.32-5.54)	0.690	6.1 (NA)	2.29 (0.54-9.66)	0.248
<i>EP300</i>	5	25.2 (NA)	0.51 (0.12-2.11)	0.343	25.2 (NA)	0.36 (0.05-2.67)	0.298
<i>CREBBP</i>	3	4.3 (3.0-5.6)	4.89 (1.41-16.89)	<b>0.005</b>	4.3 (3.1-5.5)	7.27 (2.04-25.84)	<b>&lt;0.001</b>
<i>TET2</i>	14	8.0 (0.0-22.2)	0.90 (0.45-1.82)	0.768	24.3 (8.2-40.4)	1.22 (0.55-2.70)	0.631
<i>DNMT3A</i>	7	25.2 (8.5-41.9)	0.49 (0.18-1.38)	0.167	25.2 (18.4-32.0)	1.13 (0.40-3.23)	0.821
<i>IDH2</i>	3	3.5 (3.3-3.7)	8.21 (2.21-30.42)	<b>&lt;0.001</b>	8.9 (1.2-16.4)	7.29 (1.99-26.74)	<b>&lt;0.001</b>
<i>ARID1B</i>	9	5.0 (3.8-6.2)	2.31 (1.07-5.01)	<b>0.028</b>	9.3 (8.0-10.6)	2.91 (1.30-6.51)	<b>0.006</b>
<i>ARID1A</i>	6	10.6 (3.9-17.3)	1.26 (0.49-3.21)	0.626	29.4 (17.4-41.4)	0.69 (0.21-2.26)	0.436
<i>TP53</i>	4	7.4 (NA)	0.54 (0.13-2.25)	0.392	Not reached	0.44 (0.06-3.19)	0.398
<i>ATM</i>	3	8.0 (6.7-9.3)	1.96 (0.59-6.51)	0.258	15.7 (7.6-23.8)	2.70 (0.80-9.06)	0.094
<i>MGA</i>	2	6.9 (NA)	2.03 (0.48-8.56)	0.322	10.67 (NA)	4.16 (0.94-18.49)	0.061
<i>SOCS1</i>	3	7.4 (5.6-9.2)	1.51 (0.47-4.90)	0.487	15.6 (4.6-65.7)	0.74 (0.18-3.09)	0.672
<i>RHOA</i>	7	15.9 (0.0-35.1)	0.96 (0.41-2.32)	0.957	24.3 (0.8-47.8)	1.32 (0.46-3.78)	0.604

\* PTCL subtype includes PTCL, NOS and other types.

NA= not available. CEOP = cyclophosphamide, epirubicin, vincristine, and prednisone. IVE = ifosmide, epirubicin, and etoposide. GDP = gemcitabine, cisplatin, and dexamethasone. LDH = lactate dehydrogenase. IPI = International Prognostic Index.

Table S4. Multivariate analysis of factors associated with progression-free survival and overall survival

	Progression-free survival				Overall survival		
	<i>N</i>	HR	95% CI	<i>p</i> -value	HR	95% CI	<i>p</i> -value
Pathology type							
PTCL*	37	1.0		(0.410)	1.0		(0.551)
AITL	18	0.81	0.29-2.21	0.673	0.80	0.27-2.42	0.564
ALCL	7	0.35	0.07-1.65	0.183	0.31	0.12-0.76	0.062
IPI							
0-1	16	1.0		(0.336)	1.0		(0.120)
2	20	0.68	0.26-1.78	0.437	1.50	0.39-5.84	0.558
3	17	1.37	0.52-3.61	0.530	2.80	0.79-9.90	0.111
4-5	9	1.71	0.60-4.89	0.319	4.48	1.20-16.76	0.026
EBV-DNA							
Undetectable	45						
Detectable	14	1.34	0.53-3.40	0.544	1.50	0.54-4.16	0.435
Gene Mutation							
<i>KMT2D</i> positive	14	3.12	1.50-6.50	<b>0.002</b>	/	/	/
<i>ARID1B</i>	9	1.43	0.39-5.22	0.592	3.16	0.82-12.23	0.096
<i>CREBBP</i>	3	11.13	2.91-42.51	<b>&lt;0.001</b>	10.27	2.75-38.35	<b>0.001</b>
<i>IDH2</i>	3	19.61	4.66-82.44	<b>&lt;0.001</b>	10.44	2.69-40.61	<b>0.001</b>

\* PTCL subtype includes PTCL, NOS and other types.

CEOP = cyclophosphamide, epirubicin, vincristine, and prednisone. IVE = ifosmide, epirubicin, and etoposide. GDP = gemcitabine, cisplatin, and dexamethasone. LDH = lactate dehydrogenase. IPI = International Prognostic Index.

Table S5. Progression-free survival and overall survival between two study groups in terms of IPI, NCCN-IPI and PIT

	N	Median progression-free survival			Median overall survival		
		CEOP/IVE/GDP	CEOP	p-value	CEOP/IVE/GDP	CEOP	p-value
<b>IPI</b>							
0-1	30	Not reached	Not reached	0.713	Not reached	Not reached	0.565
2	28	16.8 (2.8-30.8)	14.5 (1.0-28.0)	0.917	25.2 (14.4-35.0)	30.0 (20.3-39.6)	0.616
3	28	15.1 (10.7-19.7)	7.3 (1.1-13.5)	0.210	20.8 (12.3-29.2)	12.9 (5.1-20.7)	0.328
4-5	16	15.4 (1.3-29.6)	2.6 (1.0-4.2)	0.089	20.1 (15.4-24.8)	4.6 (0.0-11.3)	<b>0.012</b>
<b>NCCN-IPI</b>							
0-1	11	Not reached	Not reached	0.553	Not reached	Not reached	0.987
2-3	44	13.8 (2.0-25.6)	15.9 (0.0-32.0)	0.229	22.3 (15.6-28.9)	41.7 (26.1-57.3)	0.141
4-6*	47	16.8 (10.1-23.5)	5.8 (3.1-8.5)	<b>0.024</b>	23.8 (18.6-29.0)	9.4 (5.8-12.9)	<b>0.028</b>
<b>PIT</b>							
0	24	Not reached	Not reached	0.881	Not reached	Not reached	0.515
1	34	15.1 (1.7-28.6)	9.2 (0.0-30.9)	0.698	24.3 (13.2-35.5)	27.9 (17.0-38.8)	0.880
2	26	16.8 (0.7-32.9)	7.3 (0.0-16.3)	0.465	23.8 (20.7-26.9)	11.1 (7.1-15.1)	0.401
3-4	18	15.4 (7.7-23.2)	2.6 (0.3-4.9)	<b>0.026</b>	20.1 (15.3-24.9)	4.6 (0.0-13.8)	<b>0.021</b>

\*Including NCCN-IPI of 6 because of only 1 patient in this category

IPI=International prognostic index, NCCN-IPI= National Comprehensive Cancer Network- International prognostic index, PIT= Prognostic Index for T cell lymphoma.