



**EBMT**

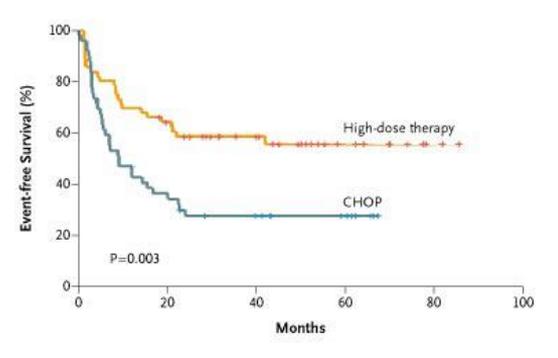
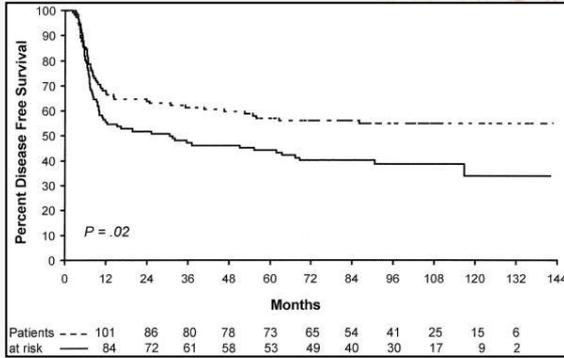
**European Society  
for Blood and Marrow  
Transplantation**

# **Chidamide, a HDAC Inhibitor, Combined with Cladribine, Gemcitabine and Busulfan with Autologous Stem Cell Transplantation in Patients with Relapsed/Refractory or High-Risk Lymphomas**

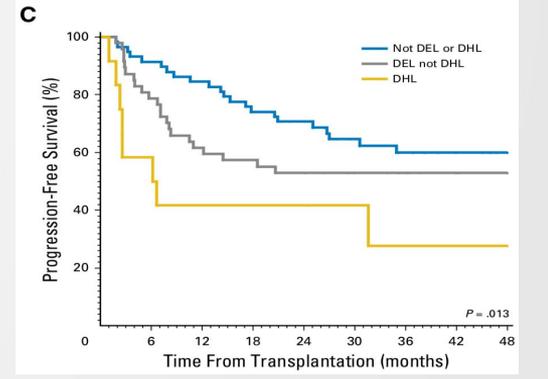
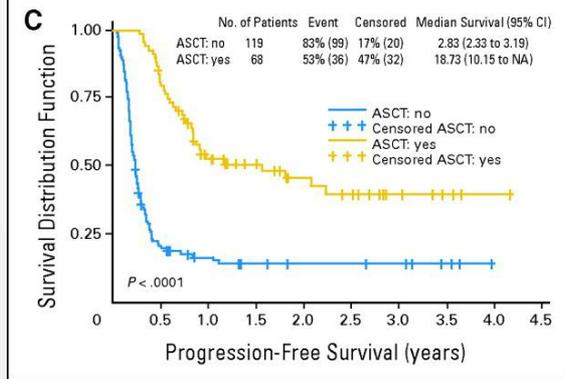
**Jie Ji, Ting Liu, Pu Kuang, Zhigang Liu, Tian Dong, Jiazhuo Liu, Li Zhang  
West China Hospital of SCU, Chengdu, China**

**Lisbon, 19/03/2018**

- ASCT has been standard of care for R/R or high risk lymphomas



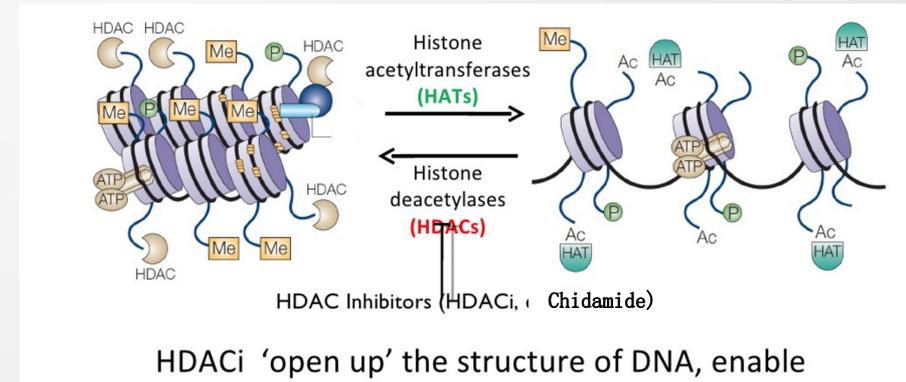
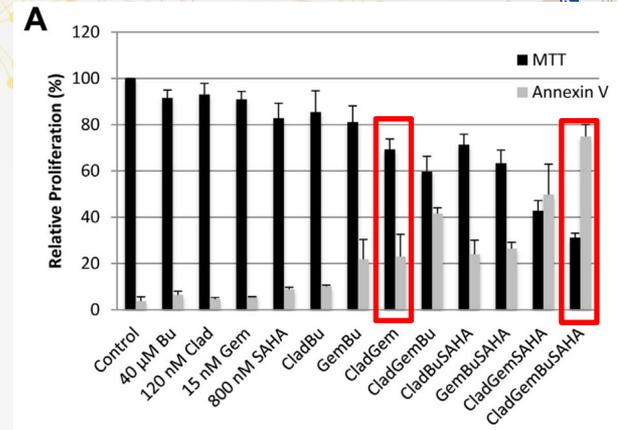
- In the era of immuno-chemotherapy, patients relapsed or refractory to 1st line therapy benefit less from ASCT



Haioun, C., et al., J Clin Oncol, 2000. 18(16): p. 3025-30  
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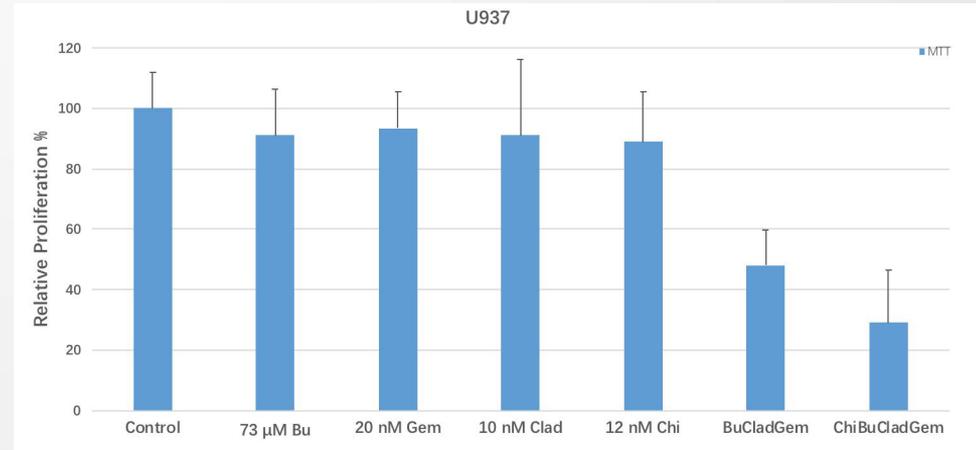
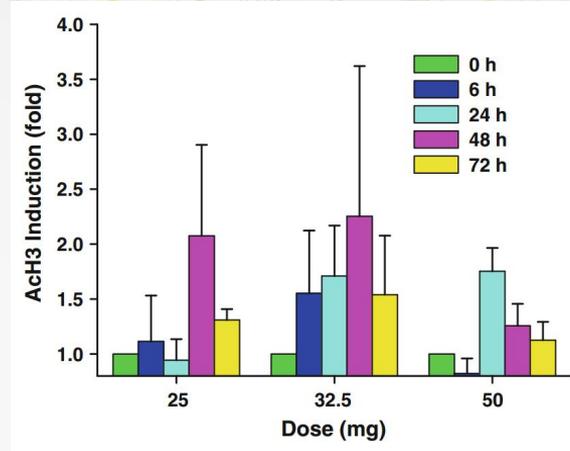
- Our pre-clinical data confirmed the antitumor efficacy of Cladribine, Gemcitabine combined with Busulfan
- Introducing HDAC inhibitor, increases sensitivity of lymphoma cells to CGB combination



## Chidamide



- New member of the benzamide
- Inhibits Class I HDAC(1-3) and HDAC10
- Long half life: 16.8–18.3 h
- Long-lasting histone H3 acetylation response





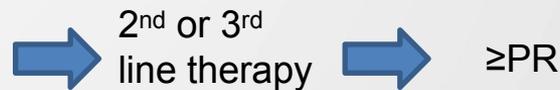
- To evaluate effect of ChiCGB as conditioning therapy with ASCT in high risk and relapsed/refractory lymphomas
- Single arm, prospective, phase II clinical trial

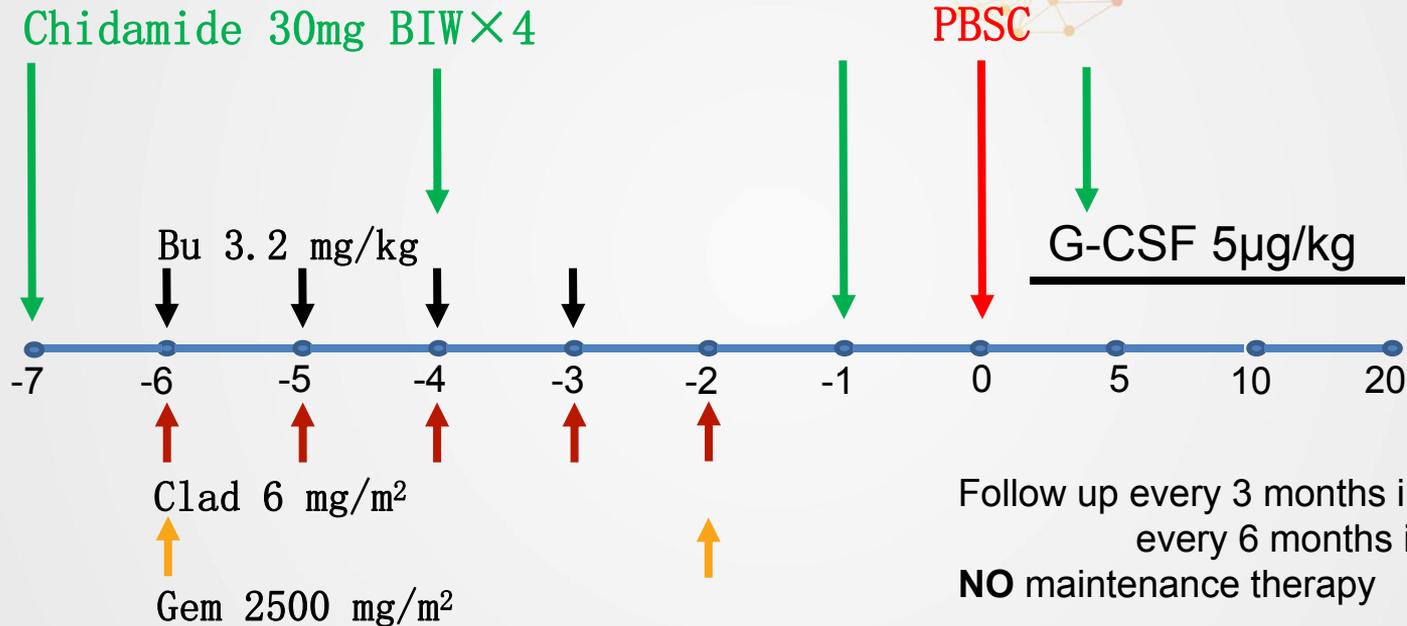


- Inclusion criteria
  - Patients with high-risk or R/R lymphomas
  - Patient age 16-65 at ASCT
  - Preserved function of major organs (heart, liver, kidney and lung)
- Exclusion criteria
  - Relapse from transplantation
  - Active bacteria or fungal infection required systemic therapy
  - HIV infection, active HBV or HCV infection



- High-risk
  - Peripheral T cell lymphomas
  - Stage IV ENKTCL
  - Aggressive mantle cell lymphoma
  - Transformed large B cell lymphoma
  - EBV(+) large B cell lymphoma
  - MYC and BCL-2  $\pm$  BCL-6 expresser B cell lymphoma
  - Aggressive intravascular large B cell lymphoma
  - DLBCL, NOS with IPI $\geq$ 3
- Refractory
  - Fail to achieve CR after standard 1<sup>st</sup> line therapy
- Relapse



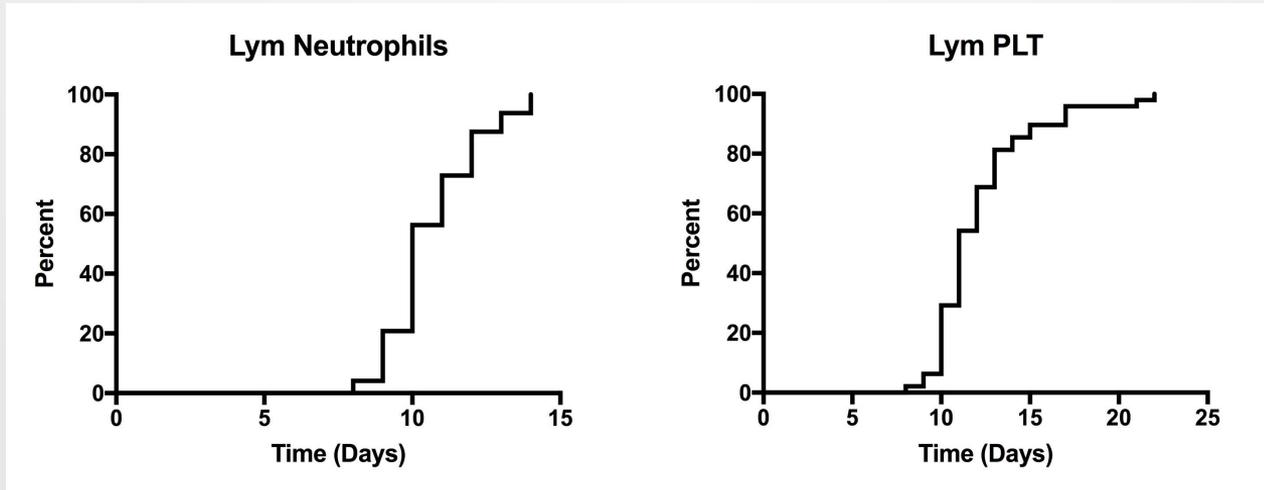


Clad : cladribine ; Gem : gemcitabine Bu : busulfan ; PBSC : peripheral-blood stem cells

Characteristics	Value	Characteristics	Value	Characteristics	Value
Cases	60	Sub-type		Sub-type	
Age (range)	35 (16-63)	<b>B-NHL</b>	28 (46.7%)	<b>T &amp; NK</b>	28 (46.7%)
Sex		relapse/refractory	10/4	relapse/refractory	4/4
Male	36 (60%)	poor-risk	14	poor-risk	20
Female	24 (40%)	DEL/TEL	14 (4 with single hit)	ENKCL	22
Disease status		IVLBL	3	ALCL ALK(-)	2
R/R	26 (43.3%)	EBV(+) DLBCL	3	T lymphoblastic	3
Poor-risk	34 (56.7%)			ANKL	1
PET+	10 (16.7%)			<b>HL</b>	4 (6.6%)
Median CD34+	2.13 × 10 <sup>6</sup> /kg			relapse/refractory	4
Median follow-up	15.1 M				

## Reconstruction of hematopoiesis

- Median recovery of neutrophils: 11 days
- Median recovery of platelets: 11.5 days

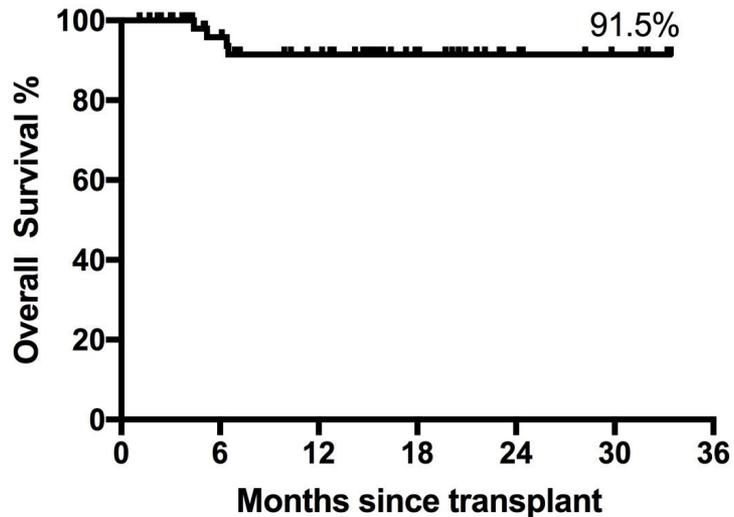
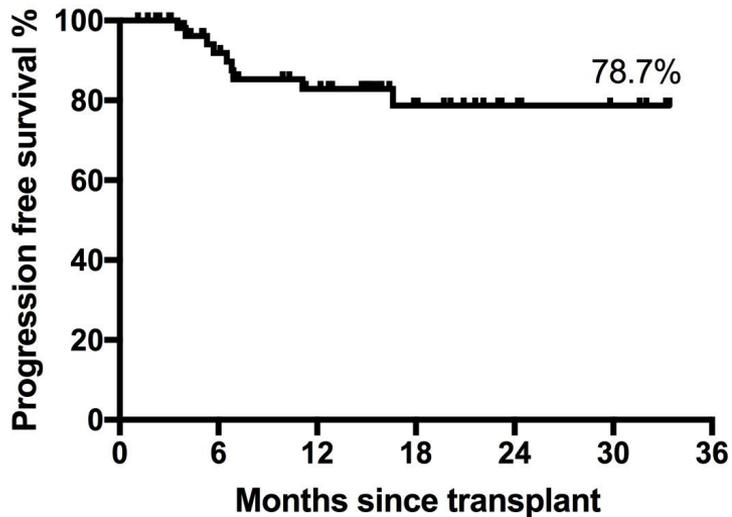


## Adverse events (AEs)

- **NO** transplant related mortality
- Major non-hematologic AEs:
  - Febrile neutropenia: 73.3%
  - Documented infections:
    - 2 cases of *E. coli* bacteremia
    - 1 case of herpes zoster infection 1 month after transplant
  - Grade 2 diarrhea: 38.3%
  - Grade 2 mucositis: 15%
  - Seizure: 1.7% (1 case with history of seizure)
- All of these AEs were fully recovered

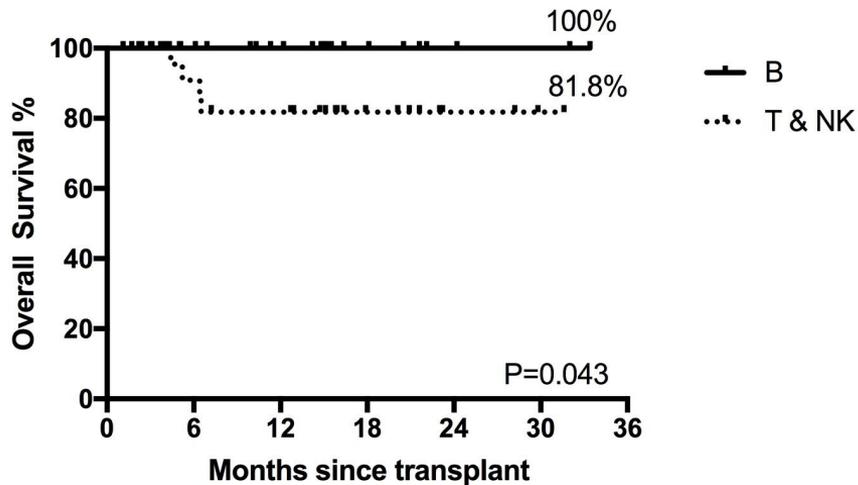
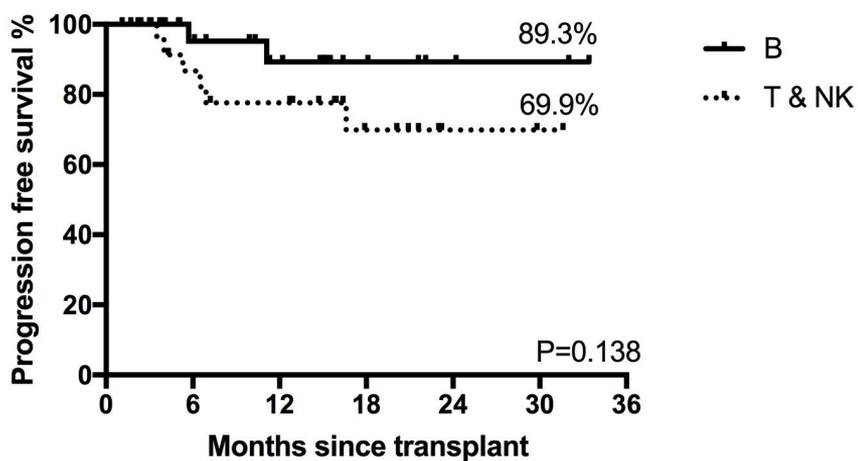
## Survival

- Median follow-up time: 15.1 months

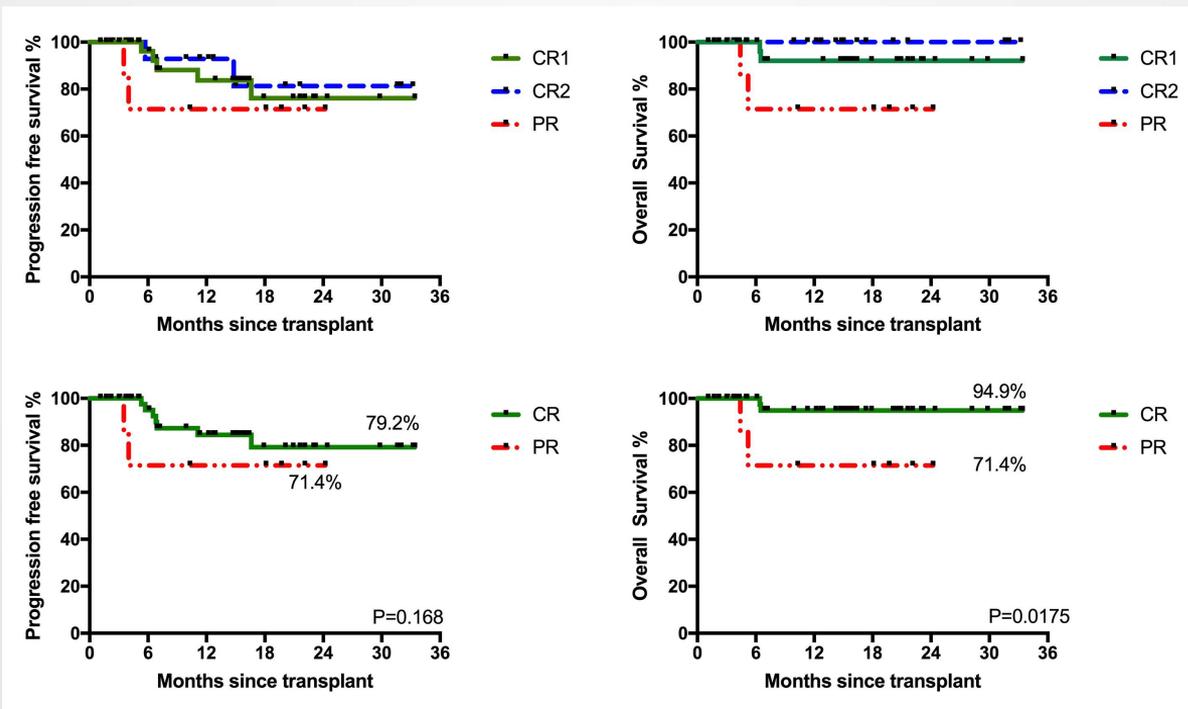


## Survival--Subtypes

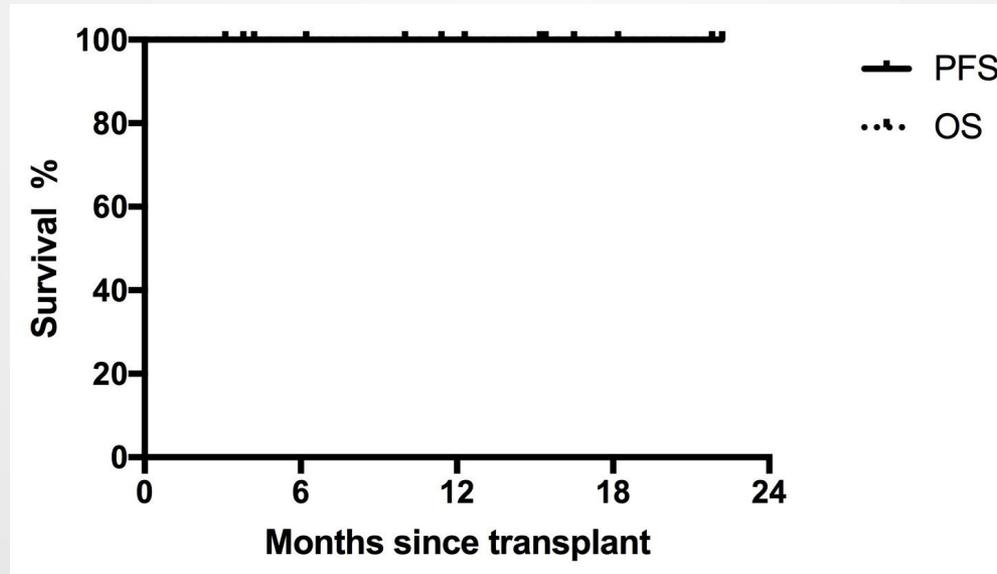
- B-NHL vs T&NK



## Survival--Disease status before ASCT



## Survival – Double/triple expresser B cell lymphoma



## Relapse

- 9 relapses: median relapse time 6.5M (3.5-16.6)
  - 4 ENKTCLs:
    - 2 relapsed with HLH and died
    - 2 local relapse ,1 salvaged by radio therapy **in CR** , the other is on radio therapy
  - 2 IVLBLs:
    - 1 salvage by rituximab + ibrutinib **in CR**
    - 1 salvage by rituximab + ibrutinib & allo-SCT **in CR**
  - 1 ALCL alk(-)
    - Died
  - 1 Lymphoblastic T cell lymphoma
    - Died
  - 1 HL
    - On anti-PD-1 therapy

- ChiCGB conditioning regimen is well tolerated
- ChiCGB with ASCT may be an option for consolidation therapy for patients with R/R or High-risk lymphoma
- The efficacy of ChiCGB with ASCT in DEL/TEL lymphoma need more data to confirm

## Thank You:

All patients and their family to make this trial possible and our collaborators:

- WCH Pathology
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