Tandem autologous hematopoietic stem cell transplantation for treatment of adult T-cell lymphoblastic lymphoma: a multiple center prospective study in China

Yao Liu,[1*] Jun Rao,[1,2*] Jiali Li,[1*] Qin Wen,[1,2] Sanbin Wang,[3] Shifeng Lou,[4] Tonghua Yang,[5] Bin Li,[6] Lei Gao,[1,2] Cheng Zhang,[1,2] Peiyan Kong,[1,2] Li Gao,[1,2] Maihong Wang,[1,2] Lidan Zhu,[1,2] Xixi Xiang,[1,2] Sha Zhou,[1,2] Xue Liu,[1,2] Xiangui Peng,[1,2] Jiangfan Zhong,[1,2,7] and Xi Zhang[1,2]

[1]Medical Center of Hematology, Xinqiao Hospital, Army Medical University, Chongqing, China; [2]State Key Laboratory of Trauma, Burns and Combined Injury, Army Medical University, Chongqing, China; [3]Department of Hematology, General Hospital of Kunming Military Region of People's Liberation Army, Kunming, China; [4]Department of Hematology, Second Affiliated Hospital of Chongqing Medical University, Chongqing, China; [5]Department of Hematology, Yunan Provincial People's Hospital, Kunming, China; [6]Department of Hematology, Second Yunnan Provincial Peoples Hospital, Yunnan, China and [7]Department of Pathology, University of Southern California, Keck School of Medicine, Los Angeles, CA, USA

**YL, JR and JL contributed equally as co-first author.*

 doi:10.3324/haematol.2019.226985

Received: June 18, 2019.

Accepted: November 26, 2019.

Pre-published: November 28, 2019

Correspondence: *YAO LIU/XI ZHANG*

648283926@qq.com/zhangxxi@sina.com

Supplementary methods

1. Patients

Eligible adults (n=181) 18 to 59 years of age with stage III/IV, newly diagnosed T-LBL patients were enrolled in this study from Feb. 2005 to Nov. 2013. Patients were diagnosed by lymph node/bone marrow histopathology, cytohistochemistry, immunohistochemistry, flow cytometry, and cytogenetics according to the World Health Organization classification criteria, and the stage was evaluated based on the Ann Arbor system, also bone marrow infiltration was assessed in each patient to distinguish T-ALL. Patients were excluded for contraindication to anthracyclines, general or visceral contraindications to intensive treatment, infection with HIV, previous treatment with chemotherapy, lymphoblastic blast crisis of chronic myeloid leukemia, or malignant tumors of other systems. Women of childbearing age required a negative pregnancy test.

2. Stem cell mobilization and collection

The source of hematopoietic progenitor cells was peripheral blood in all patients. Peripheral stem cell collection was performed after 3 cycles of chemotherapy, the PBSCs were mobilized using MOED regimens (6-8 mg/m^2 mitoxantrone on days 1-3, 1.4 mg/m^2 vincristine on day 1, 100 mg/m^2 etoposide on days 1-3, 2 mg/kg prednisone on days 1-5). We began treatment with granulocyte-colony stimulating factor (filgrastim, 10 μg/kg, day 1-4) when the leukocyte count began to recover. Leukapheresis was successfully performed on all the patients on day 5 or 6. MNC > 4 $\times 10^8$/kg and CD34+ cells > 2×10^6/kg were required for each transplantation. For the patients in the tandem auto-HSCT group, sufficient stem cells were collected at harvest for use in both the first and second transplantations.

3. Responses criteria

CR was defined as the disappearance of clinical symptoms, marrow infiltration and extramedullary lesions of lymphoma as revealed by physical examinations and PET-CT. PR was defined as greater than 50% reduction in the product of the diameters of

the two largest tumors, lasting for more than 4 weeks. Relapse/progression was defined as the occurrence of any new lesions or a ≥50% increase from the lowest lesion level. OS was defined as the time from diagnosis until death or the last follow-up. PFS was defined as the time from CR (achieved through induction therapy) until relapse / progression or death from any cause. All the analyses were carried out for patients who were qualified for therapeutic effect evaluation.

Supplementary Table 1 Patients' demographic and clinical characteristics in the chemotherapy and auto-HSCT group

Characteristics	Before match			After match		
	Chemo(n)	HSCT(n)	*P*	Chemo(n)	HSCT(n)	*P*
Median age (Range)	34(18-53)	28(18-50)	0.803	32(18-51)	31(19-50)	0.451
Gender						
Male	47	44	0.503	36	36	1
ECOG scroe						
0-1	44	40	0.422	32	33	0.868
2	45	52		42	41	
Stage						
III	39	28	0.062	24	26	0.728
IV	50	64		50	48	
B Symptom	40	35	0.346	30	29	0.867
aaIPI score						
2	36	29	0.211	23	24	0.86
3	53	63		51	50	
Bone marrow involvement	32	32	0.869	27	26	0.864
Mediastinal masses	26	42	0.022	26	28	0.733
CNS involvement	4	3	0.667	2	2	1
Remission status						
CR	47	46	0.705	34	30	0.507
PR	42	46		40	44	

SupplementaryTable 2 complication occurred in single auto-HSCT and tandem auto-HSCT

Complication	1st HSCT		2st HSCT		P vavle
	Grade 1-2	Grade 3-4	Grade 1-2	Grade 3-4	
Haematological events					
Anemia	1	45	0	46	1
Neutropenia	2	44	1	45	1
Thrombocytopenia	0	46	0	46	1
Non-haematological events					
Infection	12	4	10	6	0.704
Alimentary symptoms	5	9	2	5	0.743
Hepatic injury	1	0	0	0	1
Mucositis	4	2	4	1	0.621
Cystitis	0	2	0	0	1

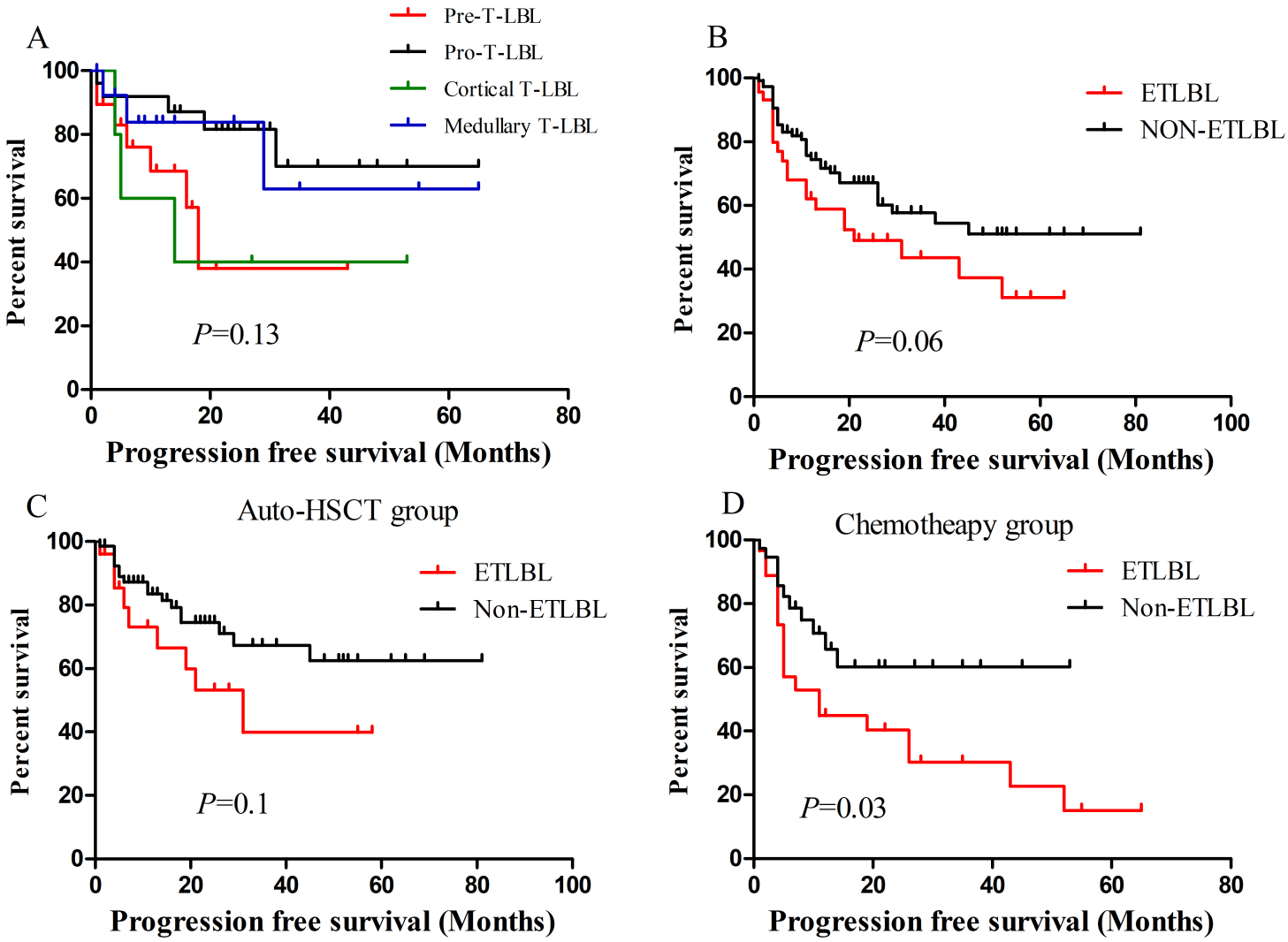

Fig. S1 Progression-free survival of patients based on immunotyping. Kaplan-Meier estimated progression-free survival of patient with EGIL classification (A). Kaplan-Meier estimated progression-free survival of patient with immunophenotype by immunohistochemical surface marker (B). Kaplan-Meier estimated progression-free survival of patient with immunophenotype by immunohistochemical surface marker in chemotherapy group (C). Kaplan-Meier estimated progression-free survival of patient with immunophenotype by immunohistochemical surface marker in auto-HSCT group (D).