

Five-year outcome of CD19 followed by CD22 chimeric antigen receptor T-cell therapy in B-cell acute lymphoblastic leukemia patients who relapsed after allo-transplantation

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Table S1. Patient characteristics

Characteristics	No. (n=30)	% of patients
Age (years)		
Median	20.5 (range, 1.6-55)	
Children (<18)	10	33
Adults	20	67
Sex		
Male	17	57
Female	13	43
Type of transplant		
HID	22	73
MSD	4	13
MUD	3	10
UCB	1	3
Interval between HCT and relapse (months)		
Median	9 (range, 3-32)	
< 6	8	27
6-12	12	40
>12	10	33
Disease status at enrollment^a		
High disease burden (blasts in BM/blood \geq 20% or with EMD ^b)	21	70
Low disease burden (isolated BM blasts < 20%)	9	30
EMD distribution		
Overall	11	37
Multiple sites ^c	5 (1 with CNSL)	17
Single site	6	20
CNS	4	
Others (breast, mediastinum)	2	
High-risk genetic changes		
Complex karyotype	7 (1 with BCR/ABL)	23
Fusion gene	8	27
BCR/ABL	7 (3 with T315I mutation)	
MLL/AF4	1	
Pre-existing mild cGVHD		
Yes	4	13
No	26	87

^aDisease status was no longer evaluated in most patients before CD19 CAR-T cell infusion because all infusions were performed within a month (80% \leq 15 days) since enrollment (it only took 5-8 days to produce CAR-T cells); and debulking chemotherapy was short-term and non-intensive. ^bInvolved sites of EMD included central nervous system (CNS), lymph nodes, bones, soft masses, breast, mediastinum, pharynx and kidney. ^cMultiple sites were defined as \geq 2 sites of EMD.

Abbreviations: HID, haploidentical donor; MSD, matched sibling donor; MUD, matched unrelated donor; UCB, unrelated cord blood; HCT, hematopoietic cell transplantation; BM, bone marrow; EMD, extramedullary disease; CNSL, central nervous system leukemia; cGVHD, chronic graft versus host disease.

Table S2. Basic information of individual patients at enrollment (*n* =30)

Pt.No.	Age(years)	Sex	Type of transplant	Duration from HCT to relapse(months)	Blasts in BM(%) ^a	EMD	Complex karyotype	Fusion gene	pre-existing cGVHD
2	9	M	HID	4	66	-	-	BCR/ABL(with T315I mutation)	
3	10	M	MUD	6	14.5	-	+	-	
4	18	M	MSD	12	-	Multiple ^b	-	-	mild(mouth)
5	21	F	HID	12	11	-	-	BCR/ABL(with T315I mutation)	
6	27	F	HID	12	75.5	Breast	-	-	
7	15	M	HID	6	36.5	-	-	-	mild(skin and liver)
9	29	M	HID	12	28	-	-	-	mild(skin and liver)
10	29	F	HID	15	0.38	Multiple	-	-	
11	18	M	HID	6	19	-	+	E2A/PBX1	mild(skin)
12	28	F	MUD	7	2.66	Multiple	-	-	
13	29	M	HID	3	86.5	-	+	-	
15	43	M	HID	9	-	CNS	-	BCR/ABL	
16	20	M	HID	31	-	Multiple(with CNS)	-	-	
17	16	F	HID	9	0.85	Mediastinum	-	TEL/AML1	
18	55	F	HID	30	32	-	-	BCR/ABL	
19	31	F	HID	9	15.5	-	-	-	
20	18	F	HID	4	91	-	+	-	
21	5	F	MUD	11	55(PB)	-	+	-	
22	1.6	M	HID	3	13	CNS	N/A	MLL/AF4	
23	6	M	HID	18	54	-	-	-	
25	12	F	HID	5	0.41	CNS	-	-	
26	9	F	HID	11	85.5	-	N/A	-	
27	31	F	MSD	4	-	Multiple	-	-	
28	38	M	HID	4	16	-	+	-	
29	41	F	MSD	8	81	CNS	+	BCR/ABL(with T315I mutation)	
31	31	F	UCB(5/6)	9	17	-	-		
32	22	M	HID	3	21.5	-	-	-	
M1	20	M	MSD	13	0.04	-	-	BCR/ABL(with T315L mutation)	
M2	9	M	HID	9	0.98	-	-	BCR-ABL(with F317L mutation)	
M3	22	M	HID	32	0.8	-	-		

^a Blasts were determined by flow cytometry when morphologic count was <5%. ^bMultiple was defined as ≥ 2 sites of EMD, involved sites included central nervous system (CNS), lymph nodes, bones, soft masses, breast, mediastinum, pharynx and kidney.

Abbreviations: Pt.No., patient number, M1-M3 were three cases only with minimal residual disease; HCT, hematopoietic cell transplantation; BM, bone marrow; EMD, extramedullary disease; cGVHD, chronic graft-versus-host disease; HID, haploidentical donor; MUD, matched unrelated donor; MSD, matched sibling donor; UCB, unrelated cord blood; CNS, central nervous system.

Table S3. CAR-T treatments, late adverse effects and long-term outcomes

Pt.No.	First CD19 CAR-T(n=30)					Second CD22 CAR-T(n=24)				B-cell aplasia(months after CD19 CAR-T)	Survival/relapse/death
	Disease burden at enrollment*		Treatment response on day 30	Months after cell infusion		Disease status before CAR-T	Treatment response on day 30	Months after cell infusion			
	Blasts in BM(%)	EMD		Blood cell count recovery	Severe infections (site, grade)			Blood cell count recovery	Severe infections (site, grade)		
2	66	-	CR			MRD+	PD				died of disease progression
3	14.5	-	CRi	2.0		CR	CR			6.2	relapsed and alive
4	-	Multiple	CR		3.5(lung, III)	CR	CR		7.0(lung, III)	7.6	relapsed and died
5	11	-	CR		3(skin VZV, III)	CR	CRi	3.0		3.9	relapsed and alive
6	75.5	Breast	CRi	1.4		CR	CRi	3.0		4.8	CCR
7	36.5	-	CRi	5.5(not yet before death)	4.9(lung, III)		N/A			5.5	died of extensive GVHD
9	28	-	CRi	1.8	4.1(lung, III)		N/A			10.8	relapsed and died
10	0.38	Multiple	PR	1.0	3.9(lung, III)	PR	CR			6	relapsed and died
11	19	-	CRi	5(not yet before 2nd CAR-T)		CRi	CRi	5	6.5(skin VZV, III); 21.5(lung, III)	60(no further data)	CCR
12	2.66	Multiple	CRi	2.5(not yet before 2nd CAR-T)		CRi	CRi	6.7	16.2(lung, III)	30.8	CCR
13	86.5	-	CRi	2.3	6.5(lung, III)#		N/A			20.1(no further data)	died of acute respiratory failure associated with lung GVHD and infection
15	-	CNS	CRi	3.4			N/A			27.5	CCR
16	-	Multiple(with CNS)	PR	1.0		PR	CRi	1.6		2	relapsed and died
17	0.85	Mediastinum	CR			CR	CR			6.3	CCR
18	32	-	CRi	2.0		CR	CR			28.3	relapsed and alive
19	15.5	-	CRi	1.5		CR	CR			16	CCR
20	91	-	CRi	2.0		BM blasts 11.5%	CRi	2.5(not yet before 2nd relapse)			relapsed and died
21	55(PB)	-	CRi	2.0		CR	CR			15.3	relapsed and alive
22	13	CNS	CR			CR	CR		5.3(lung, III)	12	CCR
23	54	-	CRi	1.3		CR	CRi	2.0		51	CCR
25	0.41	CNS	CRi	1.6(not yet before 2nd CAR-T)		CRi	CRi	4.0	6.1(lung, III)	34.6(no further data)	CCR
26	85.5	-	CRi	1.5(not yet before 2nd CAR-T)		CRi	CR			9.6	relapsed and alive
27	-	Multiple	PR	1.6		PR	CR			6.4	CCR
28	16	-	CR		2.2(lung, IV)		N/A			12.9(no further data)	CCR
29	81	CNS	Died				N/A				died of severe CRS(on day 17)
31	17	-	CR			CR	CR			12.6	relapsed and alive

32	21.5	-	CRi	4.7(not yet before 2nd CAR-T)		CRi	CRi	4.0		47	CCR
M1	0.04	-	CR			CR	CR			9	CCR
M2	0.98	-	CR			CR	CR			6.8	relapsed and died
M3	0.8	-	CR			CR	CRi	2.0		11.3	CCR

*Disease status was no longer evaluated before CD19 CAR-T cell infusion since all infusions were finished in a month (80% \leq 15 days) since enrollment.

#Patient 13 had another twice severe infections related to lung GVHD (he developed lung GVHD from 9-month on), we only count this isolated infection here.

Abbreviations: Pt.No., patient number, M1-M3 were three cases only with minimal residual disease; BM, bone marrow; EMD, extramedullary disease; CR, complete remission; MRD, minimal residual disease; PD, progressive disease; CRi, CR with incomplete blood count recovery; VZV, varicella-zoster virus; CCR, continuous complete remission; N/A, not applicable; GVHD, graft-versus-host disease; PR, partial response; CNS, central nervous system; CRS, cytokine release syndrome.