Allogeneic hematopoietic cell transplantation outcomes in patients with Richter's transformation

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SUPPLEMENTARY MATERIAL

Table S1. Baseline Characteristics

	N	%		N	%
Total, N	28	100	Conditioning Intensity		
Age, median (range)	61 (41, 73)		MAC (Cy/TBI1400)	2	7.1
Sex			RIC	26	92.9
Male	24	85.7	Flu/Bu1	9	32.1
Female	4	14.3	Flu/Bu2	11	39.3
Patient-Donor Sex match			Flu/Cy/TBI200	4	14.3
Male ← Female	4	14.3	Flu/Mel	1	3.6
Pathology at HCT			Flu/Mel/ATG	1	3.6
DLBCL	27	96.4	Flu/Mel/TBI200		
HD	1	3.6	HLA type (at A, B, C, DRB1)		
Time from CLL DX to Transformation			8/8 MRD	6	21.4
median (range) (in years)	4.5 (0, 24.4)		8/8 MUD	15	53.6
Time from Transformation to HCT			7/8 MUD	3	10.7
median (range) (in years)	0.6 (0.2, 3.1)		5/8 MUD	1	3.6
Time from CLL DX to HCT			Haplo	3	10.7
median (range) (in years)	5 (0.7, 24.7)		GVHD Prophylaxis		
Disease Status at HCT			CI/Sir/MTX	11	39.3
CR1	14	50	CI/Sir+/-Oth	6	21.4
CR2	2	7.1	CI/MTX	3	10.7
CR3 or later	1	3.6	CI/MTX+oth	1	3.6
PR	9	32.1	CI+/-oth	5	17.9
Relapse	1	3.6	Other	2	7.1
Induction Failure	1	3.6	WBC count ($x10^9$/L) at HCT		
ECOG PS			<2	6	20.7
0	6	21.4	2-10	22	75.9
1	12	42.9	>10	1	3.5
2	9	32.1	median(range)	4.5 (1, 14)	
3	1	3.6	platelet count ($x10^9$/L) at HCT		
HCT-comorbidity score			<100	4	14.3
0	5	17.9	≥100	24	85.7
1	3	10.7	median(range)	147 (35, 442)	
2	3	10.7	LDH at HCT		
>=3	17	60.8	median(range)	187 (111, 333)	
median (range)	3 (0, 8)		High LDH	7	25
No. of prior therapies			Bulky Disease at HCT		
median (range)	3 (1, 7)		≥10 cm	0	0
1	3	10.7	≥5 cm	4	14.3
2-3	17	60.7	PET at HCT		
>=4	8	28.6	Positive	7	25
No. of therapies for RT prior to HCT			Negative	16	57.2
median (range)	2 (1, 5)		UNK	5	17.9
Prior Therapy			Year HCT		

CIT	19	67.9	2010-2012	8	28.6
CIT+Targeted therapy	9	32.1	2013-2015	8	28.6
Type of Targeted therapy			2016-2019	12	42.9
Ibrutinib	4		FISH		
Ibrutinib/Idelalisib			Del17p		
Ibrutinib/Venetoclax	1		No	14	50
AVL292	1		Yes	8	28.6
Venetoclax	3		UNK	6	21.4
Cell source			Complex karyotype		
BM	2	7.1	(>=5 abnormalities)		
PBSC	25	89.3	No	14	50
UCB	1	3.6	Yes	5	17.9
Pt-Dnr CMV sero status			UNK	9	32.1
R-/D-	11	39.3			
R-/D+	5	17.9			
R+/D-	7	25			
R+/D+	5	17.9			

RT: Richter's transformation. DLBCL: diffuse large B-cell lymphoma. HL: Hodgkin's lymphoma. CLL: chronic lymphocytic leukemia without RT. PS: performance status. Targeted: prior targeted thearpy. CIT: prior chemoimmunotherapy. CART19: CD19-directed chimeric antigen receptor T cells. CR: complete remission. PR: partaila remission. Pt-dnr: patient and donor. MRD: matched related donor. MUD: matched unrelated donor. BM: bone marrow. PBSC: peripheral blood stem cell. UCB: Umbilical cord blood. MAC: myeloablative conditioning. RIC: rediced intensity conditioning. CI: calcineurin inhibitor. MTX: methotrexate. Flu: fludarabine. Sir: sirolimus. Bu1: busulfan 3.2 mg/kg, Bu2: busulfan 6.4 mg/kg, Mel: melphalan. ATG: anti-thymocyte globulin. LDH: lactate dehydrogenase.

Table S2. List of prior and post HCT therapy

Subject	Age group	High risk	Prior therapy for CLL	Prior therapy for RT	Post HCT therapy
27	70+	N	1. CVP-R, 2. BR	1. CHOP	CHOP, DLI
26	60-69	N		1. R-CHOP	
25	50-59	N	1. FCR	1. ABVD 2. BR	
24	40-49	N	R-Flud 2. CVP	1. R-CHOP 2. CHOP	
23	50-59	N	1. ABVD 2. ICE 3. Brentuximab	1. R-EPOCH	
22	70+	N	1. Rituximab **2. Ibrutinib**	1. DA+R-EPOCH	
21	60-69	N	1. Rituximab 2. BR	1. R-CHOP 2. R/ICE 3. R-GemOx 4. R-ESHAP 5. R-ESHAP	
20	60-69	N	1. **AVL292 (BTKi)**	1. R-CHOP	XRT
19	50-59	Y	1. PCR	1. R-CHOP 2. R/ICE	XRT
18	50-59	N		1.EPOCH+V	
17	60-69	N		1. R-CHOP	Venetoclax, Rituximab
16	50-59	N		1. R-CHOP 2. **Ibrutinib** + Pembrolizumab	
15	50-59	N		1.RCHOP 2. Radiation	
14	60-69	Y	1. alloHCT 2. FR 3. FCR 4. BR	1. R-CHOP	
13	60-69	N	1. FCR	1. DA R-EPOCH + **Veneotclax**	
12	60-69	N		1.RCHOP 2. Radiation	
11	60-69	N	1. FCR	1. R-EPOCH 2. R-CHOP	
10	60-69	N		1.RCHOP 2. Pembro**/Ibrutinib** 3. **Venetoclax**	Venetoclax
9	50-59	Y	1. FCR	1. **Venetoclax** + R-EPOCH	
8	50-59	N		1. RCHOP 2. FCR x 2	
7	60-69	Y		1.R-EPOCH 2.RGDP	
6	60-69	N	1. FCRx1 2. **Ibrutinib** x 3 weeks 3. CRD x6	1. R-CHOP	
5	60-69	Y	1. FCR 2. BR	1. R-CHOP 2. **Ibrutinib**	
4	40-49	Y	1. Radiotherapy 2. FCR 3. Rituximab 4. CHOP	1. Radiation 2. RICE conditioning	Campath
3	50-59	Y		1. R-EPOCH 2. Rituximab + Solumedrol	
2	60-69	Y	1. FCR 2. **Ibrutinib** 3. **Venetoclax**	1. R-CHOP	
1	70+	Y	1. Chlorambucil 2. R-CHOP 3. FCR 4. BR	1. R-ESHAP 2. Focal XRT	XRT

High risk is defned as having LDH≥205 or platelet count ≤100x10^9/L
CHOP: cyclophosphamide+doxorubicin+vincristine+prednisone, F (Flud): Fludarabine, C: cyclophosphamide, R: Rituxan, B: Bendamustine, ICE: ifosfamide+carboplatin+etoposide, DLI: donor lymphocyte infusion, CVP
CVP: Cyclophosphamide, Vincristine, and Prednisolone.
ABVD: Adriamycin, Bleomycin, Vinblastine, Dacarbazine.
EPOCH: Etoposide, Prednisolone, Vincristine, Cyclophosphamide, and Doxorubicin.
DA: Dose Adjusted.
R-GemOx: Rituximab, Gemcitabine, and Oxaliplatin.
ESHAP: Etoposide, Methylprednisolone, High-Dose Cytarabine, Cisplatin.
XRT: Radiotherapy.
Prior therapy in boldface indicates targeted therapy.
Subject 1: R-CHOP was given for the treatment of CLL prior to diagnosis of RT.
Subject 4: Both Rituximab and CHOP were given prior to diagnosis of RT and for the treatment of CLL. There was initial concern for possible transformation prior to starting the Rituximab but a biopsy showed no evidence of RT so Rituximab and CHOP were given to treat a suspected aggressive recurrence of CLL B-Symptoms. Then, several months later, another biopsy confirmed RT and Radiation and RICE were initiated.

Figure S1. Association between risk factors and outcome. (A) Progression-free survival and (B) cumulative incidence of relapse according to age (Age≥65 vs Age<65). Cumulative incidence of (C) NRM and (D) relapse according to the risk group