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POSTER ABSTRACTS

721.ALLOGENEIC TRANSPLANTATION: CONDITIONING REGIMENS, ENGRAFTMENT AND ACUTE TOXICITIES

Venetoclax+Azacytidine Followed By Modified BuCy Conditioning Regimen for High Risk or Refractory/Relapsed Acute Lymphoblastic Leukemia and High Risk Myelodysplastic Syndromes

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Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is the only potential curable treatment for myelodysplastic syndromes (MDS) and acute lymphoblastic leukemia (ALL). However, for patients with high-risk or refractory relapsed (R/R) B-ALL with allo-HSCT, the three-year overall survival (OS) rate is only 5-10%, more worse in T-ALL. It is widely known that MDS patients in the high-risk group do not benefit from induction chemotherapy, the five-year OS rate is 23-39% when they received allo-HSCT. Nevertheless, relapse remains a significant cause of treatment failure after allo-HSCT, highlighting the urgent need for improved conditioning regimens that can improve prognosis and reduce relapse rates. Azacytidine (AZA) combined with Venetoclax (VEN), showed a synergistic anti-tumor activity against several hematological malignancies, Therefore, we explored AZA+VEN (VA) combined with modified BuCy(mBuCy) (semustine, cytarabine, busulfan, and cyclophosphamide) conditioning regimen and assessed the safety and effectiveness.
Aims : The aim of this study is to assess the safety, and effectiveness of the VA treatment regimen followed by mBuCy as conditioning regimen for high-risk or R/R ALL(NCT05809167) and high-risk MDS(NCT03256071) .
Methods: Patients diagnosed with high-risk or R/R ALL or high-risk MDS (IPSS-R score), undergoing VA+mBuCy as conditioning regimen, and consolidation treatment with demethylating drugs every three months after transplantation, for a total of 8-12 cycles.
Results: Patients diagnosed with high-risk or R/R ALL(n=11) or high-risk MDS (IPSS-R score)(n=8) were enrolled between January 13, 2022, and June 9, 2023.
The ALL cohort comprised of 5 Ph-negative B-ALL, 2 Ph-positive B-ALL, 3 mixed phenotype leukemias (MPAL), and one T-lymphoblastic lymphoma/leukemia (T-ALL/LBL). There were 7 males and 4 females, with a median age of 33 years (17-54 years) (Table 1). Out of the eleven patients, four had previously undergone Chimeric Antigen Receptor T-Cell Immunotherapy (CAR-T) therapy, and one patient had received Blinatumomab. One patient experienced relapse, another patient was refractory, and 3 patients had extramedullary infiltration.
All patients achieved morphological complete remission prior to transplantation, and 10 patients (90.9%) achieved a MRD negative remission. Additionally, all the transplantations successfully completed, with a median time to absolute neutrophil counts (ANC) recovery of 12 days (11-15 days) and platelet (PLT) recovery of 16 days (15-21 days). The median follow-up time was 6.4 months (2.4 -13.6 months), no patient experienced relapse or death, the OS and DFS are both 100%. There were no grade 3 or higher adverse events (AEs), hepatic veno-occlusive disease (VOD),and the transplant-related mortality (TRM). Four patients who developed acute graft-versus-host disease (aGVHD) post-transplantation, all cases involved grade I/II skin aGVHD, and one of them involved grade III GI aGVHD, and no chronic graft-versus-host disease (cGVHD) were observed during the follow-up period. By the endpoint of follow-up, Cytomegalovirus (CMV) activation was 45.4% (5/11) and Epstein-Barr virus (EBV) activation was 27.3% (3/11).
The MDS cohort consisted of 7 cases of MDS-EB-I, 1 case of MDS-EB-II. There were 5 males and 3 females, with a median age of 42 years (23-57 years)(Table 2). Two patients received chemotherapy before transplantation, and the other six patients directly received allo-HSCT.
In MDS cohort, the median recovery time for ANC was 12 days (11-13 days) and PLT was 17.5 days (16-20 days). The median follow-up was 14.3 months (1.2-18.3 months), no patient had relapsed or died, both OS and DFS are 100%. There were no

grade 3 or higher AEs, and TRM. One patient developed VOD. Three patients developed aGVHD after transplantation, all involving degree I/II skin aGVHD, and there was one case of cGVHD during the follow-up period, where the patient developed a mild pulmonary cGVHD. By the endpoint of the follow-up, the rate of CMV activation was 37.5% (3/8) and EBV activation was 25% (2/8).

Conclusion: The VA combined with the mBuCy proves to be a effective and safe conditioning regimen for high-risk ALL and MDS patients. However, more patients are needed for follow-up and validation.

Disclosures No relevant conflicts of interest to declare.

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Table 1:Clinical information on patients in the ALL cohort.

Patient No.	Gender	Age(y)	Diagnosis	High Risk Factor	Type of donor	Pretransplant state	Time of enrolment	ANC recovery(d)	PLT recovery(d)	Current disease state	OS(m)	DFS(m)
1	Female	54	B-ALL	MLL-AF4/Relapse	Haplo	CR2	2022/6/20	13	21	CMR	13.60	13.60
2	Female	19	Ph+ALL	Extramedullary infiltration	Haplo	CR1	2022/7/11	13	18	CMR	12.93	12.93
3	Male	42	Ph+ALL	BCR-ABL1	Haplo	CR1	2022/10/14	13	18	CMR	9.73	9.73
4	Male	17	B-ALL	Extramedullary infiltration	Haplo	CR1	2023/1/6	12	16	CMR	7.03	7.03
5	Male	33	T-LBL/ALL	Extramedullary infiltration/Hyperleukocytemia	Haplo	CR1	2023/2/24	12	16	CMR	5.33	5.33
6	Female	50	B-ALL	UQCC3-KMT2A/complex karyotype	Haplo	CR1	2023/2/28	12	16	CMR	5.27	5.27
7	Male	46	B-ALL	Complex karyotype/TP53	URD	CR1	2023/4/11	11	15	CMR	3.70	3.70
8	Male	29	B-ALL	MLL-AF4/TP53	Haplo	CR1	2023/5/23	12	16	CMR	2.40	2.40
9	Male	27	T/B-MPAL	Refractory	Haplo	CR1	2022/4/26	12	16	CMR	3.10	3.10
10	Female	25	M/B-MPAL	BCR-ABL1/Hyperleukocytemia	Haplo	CR1	2022/6/30	13	17	CMR	13.27	13.27
11	Male	36	T/M-MPAL	Mixed phenotype	Haplo	CR1	2023/1/28	15	19	CMR	6.27	6.27

Haplo:Haploidentical Transplant,URD:Unrelated Donor;ANC:absolute neutrophil counts,PLT:platelet,CMR:complete molecular remission,OS:Overall Survival time,DFS:Disease-free Survival time

Table 2:Clinical information on patients in the MDS cohort.

Patient No.	Gender	Age(y)	Diagnosis	IPSS-R	Type of donor	Pre-transplant chemotherapy	Time of enrolment	ANC recovery(d)	PLT recovery(d)	Current disease state	OS(m)	DFS(m)
1	Female	23	MDS-EB-I	High-Risk	Haplo	N	2022/2/10	11	16	CR	18.33	18.33
2	Female	36	MDS-EB-I	High-Risk	MSD	Y	2022/4/8	13	17	CR	16.03	16.03
3	Male	57	MDS-EB-I	High-Risk	Haplo	Y	2022/4/15	13	20	CR	15.83	15.83
4	Male	43	MDS-EB-I	High-Risk	Haplo	N	2022/5/10	12	17	CR	14.97	14.97
5	Male	40	MDS-EB-II	High-Risk	Haplo	N	2022/5/16	13	19	CR	14.80	14.80
6	Male	35	MDS-EB-I	High-Risk	Haplo	N	2022/11/25	11	18	CR	8.33	8.33
7	Female	55	MDS-EB-I	Very High-Risk	Haplo	N	2023/3/24	12	17	CR	4.40	4.40
8	Male	55	MDS-EB-I	High-Risk	Haplo	N	2023/6/19	13	19	CR	1.27	1.27

IPSS-R:Revised International Prognostic Scoring System,Haplo:Haploidentical Transplant,MSD:Matched Sibling Donor;ANC:absolute neutrophil counts,PLT:platelet,CR:complete remission,OS:Overall Survival time,DFS:Disease-free Survival time

Figure 1