Azacitidine in Combination with Venetoclax Maintenance Post Allogeneic Hematopoietic Cell Transplantation in T-Cell Acute Lymphoblastic Leukemia

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Background

- T-cell acute lymphoblastic leukemia (T-ALL) with high risk features including ETP TALL ,patients who remain MRD +ve post induction and Patients who relapse have few available salvage options and most require Allo Transplant
- Allogeneic hematopoietic stem cell transplantation (allo-HSCT) efficacy in T-ALL remains problematic, as up to half of patients will relapse post allo-HSCT.
- Post-transplant maintenance in acute myeloid leukemia (AML) has long been debated, with recent implementation by transplant centers, especially the use of hypomethylating agents (HMAs) and targeted agents such as FLT3 inhibitors.
- In T-ALL, this concept has not been explored yet

Objective

The aim of this case series is to present a novel approach for post-transplant maintenance in patients with high risk T-ALL

Materials & Methods

This is a case series including 4 patients with T-ALL who underwent allo-HSCT at the American University of Beirut Medical Center and received post-transplant maintenance with low-dose 5-azacitidine and venetoclax

Disease Subtype	Status at transplant	Transplant type	Conditioning Regimen	Days to azacitidine treatment	Status at last F-up	CR duration post allo-SCT
T-ALL 30 yo male	CR2 molecular MRD negative	Full Match related donor	Clofarabine-TBI 4 Gy	42 days	Alive and in CR MRD negative	+ 25 months
ETP -ALL 31 y.o male	CR1,molecular MRD positive for TCR	Haplo-SCT	Fludarabine-TBI-8GY	53 days	Alive in CR MRD negative	+17 month
T-ALL 45 yo male	CR1 molecular MRD positive for TCR	Full Match related donor	Clofarabine-TBI 8 Gy	115 days	Alive and in CR MRD positive	+13 months
Near ETP-ALL – 37 yo male	CR1 molecular MRD negative	Full Match related donor	Fludarabine- TBI 8 Gy	46 days	Alive and in CR MRD negative	+ 12 months

Summary for the four patients who received 5-azacitidine and venetoclax maintenance post-transplant.

Results

- We identified four adult patients diagnosed with high-risk T-ALL
- Three patients with mature T-ALL and one with early T-precursor [ETP] ALL) with a median age of 35 years (range, 31–45 years).
- Patient disease status at transplant :2 of our Patients where in CR1 MRD positive, one was in CR2 MRD negative ,and one was in CR1 MRD negative.
- All received post-allo-HSCT maintenance with 5 days of low dose 5-azacitidine at 32 mg/m^2 daily with venetoclax 100 mg orally daily for 5 days with voriconazole every 28 days.
- The median duration of maintenance treatment was 12.75 months (range, 9.5–23.5 months).
- 3 patients remain in continuous complete remission with undetectable measurable residual disease and one remains in CR but MRD positive after a median follow-up of 15 months from the date of allo-HSCT (range, 12–25 months)

Summary

- Both HMAs and venetoclax possess significant antitumor activity effects against AML/myelodysplastic syndrome, and their efficacy in R/R T-ALL has been demonstrated in multiple case series.
- These encouraging results along with our case series of successful maintenance treatment with azacitidine with venetoclax in T-ALL are worth exploring in larger prospective trials.

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