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POSTER ABSTRACTS

723.ALLOGENEIC TRANSPLANTATION: LONG-TERM FOLLOW-UP AND DISEASE RECURRENCE

Post Hematopoietic Cell Transplantation Maintenance Therapy with Low-Dose Azacitidine in a Pediatric Population with High-Risk Myeloid Neoplasms

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Patients with acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS) undergoing allogeneic hematopoietic cell transplantation (HCT) remain at risk for relapse. Children with relapsed AML and high-risk features including prior HCT, early relapse, and high-risk cytomolecular features experience survival of ≈30%. Given the even more dismal survival and limited therapy options for post-HCT relapse, azacitidine (aza) has been explored as post-HCT maintenance therapy based on potential disease targeting activity and enhancement of graft versus leukemia. Studies to date suggest that this approach is safe with signals of favorable survival. A phase 3 trial in adults did not show a survival benefit, although results were confounded by a high rate of withdrawal and a minority of patients received all intended cycles.

We performed a descriptive analysis of all patients with high-risk myeloid neoplasms who underwent allogeneic HCT at Seattle Children's Hospital (SCH) from November 2017 to January 2023 and received post-HCT maintenance aza. Patients were considered high-risk if they had undergone prior HCT, measurable residual disease at HCT, ≥CR2, or high-risk cytomolecular features. Patients received myeloablative conditioning according to standard protocols. All patients were in remission prior to aza initiation. Aza 36-50 mg/m ^{2} was administered as IV or subcutaneous infusions daily for 5 consecutive days on a 28-day cycle with intention to continue therapy with cycles beginning through 1-year post-HCT.

Nineteen patients began aza therapy at a median of 109 days (range 66-263) post-HCT. Demographics and disease information plus the primary high-risk feature for consideration of post-HCT aza are reported in Table 1. Following aza initiation, 9 (47.4%) patients continued subsequent aza cycles at their referring institution with concurrent remote management by SCH as needed. Median post-HCT follow-up was 30.4 months (range 7-66). The median number of completed aza cycles was 8 (range 3-12) and 14 (73.7%) patients received all intended cycles through 1 year following HCT. In 3 patients, aza cycles were delayed >4 weeks due to non-neutropenic fever or infection; de-escalation to 36 mg/m ^{2} for subsequent courses in the 2 patients who were receiving 50 mg/m ^{2} led to no further delays. There were no delays due to marrow suppression, no increased transfusion needs, and no hospitalizations attributed to aza.

Fourteen (73.7%) patients had grade II acute graft versus host disease (GVHD) prior to initiation of aza. Two (10.5%) of these patients subsequently developed chronic oral GVHD, 1 diagnosed incidentally during their last aza cycle and 1 diagnosed after completion of aza. Two (10.5%) patients experienced ≤ grade II acute GVHD flares while tapering systemic immunosuppressive treatment (IST) and receiving aza, prompting escalation of same systemic IST (n=1) or addition of topical IST (n=1). Seventeen of 18 patients who were in remission at 1-year post-HCT were tapering or off IST. Five (26.3%) patients discontinued aza before 1 year post-HCT: 2 due to relapse, 2 per family preference, and 1 for inflammatory process with persistent dual chimerism from double cord HCT. Three-year estimates for overall and relapse free survival were 92% (95% CI 54-99) and 76% (95% CI 46-91), respectively, and cumulative incidence of relapse was 24% (95% CI 7-48) (Figure 1). The 6 patients with history of prior HCT are all are alive with ongoing remission at ≥3 years following second HCT with aza maintenance.

Our experience demonstrates that post-HCT maintenance therapy with low-dose aza for high-risk pediatric AML/ MDS is tolerable with limited toxicity and without significant impact on marrow suppression or GVHD. The ability to successfully implement a post-HCT aza regimen in partnership with local institutions allowed families to return home, potentially reducing emotional hardship and financial toxicity due to travel/ housing and supporting feasibility. Outcomes in this cohort were

improved compared to historical controls; this was especially notable in patients undergoing 2 nd HCT and in patients ≥CR2. Our findings suggest a potential role for post-HCT low-dose aza in children with high-risk AML/ MDS but further prospective pediatric studies are needed to define optimal dosing and evaluate for benefit.

Disclosures Thakar: *Proteios Technology:* Other: Scientific Advisory Board; *ImmunoVec:* Other: Scientific Advisory Board. **Carpenter:** *Incyte, Janssen, AbbVie, and Sanofi:* Research Funding. **Petrovic:** *Horizon Therapeutics:* Other: Scientific Advisory Board ; *Allovir:* Other: Scientific Advisory Board . **Bleakley:** *Orca Bio:* Consultancy; *Miltenyi Biotec:* Research Funding.

OffLabel Disclosure: Azacitidine is a nucleoside analog approved for use in treatment of myeloid neoplasms including myelodysplastic syndrome, acute myeloid leukemia, and juvenile myelomonocytic leukemia. Low dose azacitidine has been investigated as post-HCT maintenance therapy for its potential disease targeting activity and enhancement of graft versus leukemia in populations with myeloid neoplasms at high risk of relapse, as is used in this study. This use is not approved in the United States.

Table 1. Characteristics and clinical course in patients receiving post-HCT azacitidine

Male, n (%)		8 (42.1%)
Age at HCT in years, median (range)		11.3 (0.7-19.3)
High-risk disease features, n (%)	AML (n=12)	
	History of prior HCT	5 (41.7%)
	Primary refractory, detectable at HCT	1 (8.3%)
	High-risk MLLT10 fusions	2 (16.7%)
	≥CR2 without prior HCT	4 (33.3%)
	MDS (n=6)	6 (31.5%)
	High-risk cytomolecular features	2 (33.3%)
	Excess Blasts, undetectable at HCT	1 (16.7%)
	Excess blasts, detectable at HCT	2 (33.3%)
	tMDS with history of prior HCT	1 (16.7%)
	CMML (n=1)	
	Disease at HCT	1 (100%)
Donor source, n (%)	Matched sibling	4 (21.0%)
	Matched unrelated	9 (47.4%)
	Mismatched unrelated	1 (5.3%)
	Haploidentical	1 (5.3%)
	Cord blood	4 (21.0%)
Conditioning regimen, n (%)	BU CY MEL	6 (31.6%)
	BU CY	3 (15.8%)
	BU FLU	1 (5.3%)
	BU FLUE 4Gy TBI	2 (10.5%)
	FLU CY 13.2Gy TBI	3 (15.8%)
	FLU CY Thiotepa 4Gy TBI	1 (5.3%)
	CY 13.2Gy TBI	1 (5.3%)
	Treosulfan FLU 2Gy TBI	1 (5.3%)
	TBI 13.2Gy, post-transplant CY	1 (5.3%)
Acute GVHD at time of azacitidine initiation, n (%)	No GVHD	5 (26.3%)
	Grade I acute GVHD	0 (0.0%)
	Grade II acute GVHD	14 (73.7%)
	Grade III or IV acute GVHD	0 (0.0%)
Days from HCT to initiation of azacitidine, median (range)		109.4 (66-263)
Number of azacitidine cycles completed, median (range)		8 (3, 12)
Azacitidine course delayed >4 weeks due to toxicity, n (%)		3 (15.8%)
Received all planned azacitidine up to 1 year post HCT, n (%)		14 (73.7%)
Reason for discontinuing azacitidine, n (%)	Relapse	2 (10.5%)
	Family preference	2 (10.5%)
	Inflammatory process	1 (5.3%)

Abbreviations: Hematopoietic Cell Transplantation (HCT), Busulfan (BU), Cyclophosphamide (CY), Fludarabine (FLU), Melphalan (MEL), Total Body Irradiation (TBI)

Figure 1. Overall survival, Relapse free-survival, and Cumulative Incidence of Relapse for patients receiving post-HCT azacitidine

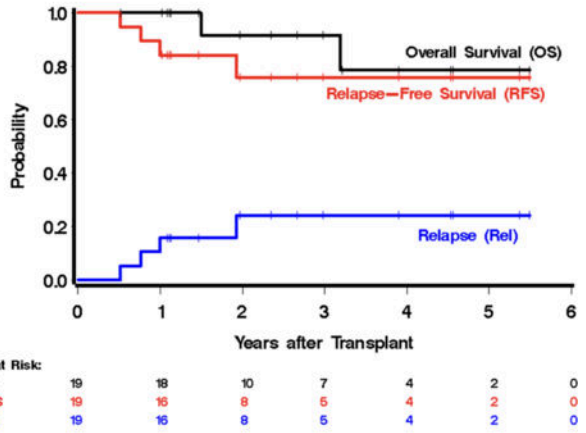

Figure 1

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