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POSTER ABSTRACTS

906.OUTCOMES RESEARCH-MYELOID MALIGNANCIES

Survival Disparities By Frontline Clinical Trial Enrollment Status for Treatment of Pediatric Acute Myeloid Leukemia

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Introduction: Studies have suggested superior outcomes for patients enrolled on clinical trials for their cancer treatment. While sociodemographic disparities in trial enrollment are well established in adults, the literature in children is mixed and limited. A deeper understanding of disparities in pediatric clinical trial enrollment and potential survival differences is critical to ensure the generalizability of trial results and equitable outcomes. In a cohort of children with AML, we sought to examine

(1) differences in sociodemographic and clinical characteristics by trial enrollment status, (2) the impact of trial enrollment on survival, and (3) the potential drivers of survival differences.

Methods: A retrospective cohort including all pediatric (age <19 years) patients with AML treated at 10 institutions in the United States from 2011-2018 was established and is being actively expanded to include diagnoses through 2023. Chart abstraction by trained study personnel collected detailed demographic and clinical information. Resource utilization data from the Pediatric Health Information System was merged to ascertain patient acuity. Higher acuity was defined as requiring ICU-level resources for 2 or more organ systems within 72 hours of diagnosis. Only patients who had a frontline therapeutic trial option available at their treating institution were included. This was operationalized as a center-level restriction to patients initiating therapy while any frontline trial was enrolling at the center. We additionally included only patients with complete data for all covariates in this analysis.

Statistical Analysis: Demographic and clinical characteristics by trial enrollment status were compared using t-test or Fisher's exact test as appropriate. Cox proportional hazards regression estimated hazard ratios (HR) with a doubly robust estimator (adjusted models only) of 4-year OS and EFS by trial enrollment status. A stepwise propensity score (PS) approach assessed the impact of potential drivers of the associations between trial enrollment and overall survival (OS) and event-free survival (EFS). PS were computed by logistic regression and generated stabilized inverse probability weights used for adjustment. First, a Base PS model including a predefined set of potential confounders (age, sex, weight category, preferred language, risk classification, mean annual hospital AML volume) was created. Additional variables of interest were then sequentially added to the PS. The change in adjusted HR relative to the unadjusted comparison was used to quantify the proportion of the association explained at each step.

Results: 342 pediatric patients diagnosed with AML with representation from three distinct frontline clinical trials (AAML1031, AML08, and AML16) were included. Patients who were Black (11% vs. 24%), Hispanic (24% vs. 28%), publicly insured (44% vs. 55%), higher acuity (3% vs. 8%), and high-risk classification (29% vs. 34%) were underrepresented in the trial enrollment group compared to non-trial enrolled (Table 1). In unadjusted analyses, trial enrollment was significantly associated with superior OS (HR=0.69, 95% CI 0.47-0.99, p=0.04); there was no significant difference in EFS (HR=0.95, 95% CI 0.69-1.31, p=0.75). Adjustment for the Base PS accounted for 23% of the observed association between trial enrollment and OS (Figure 1). Acuity explained an additional 7% of the association. Inclusion of race/ethnicity and insurance did not result in further adjustment. In fully adjusted analysis, the association was substantially attenuated (HR=0.93, 95% CI 0.59-1.46, p=0.76).

Conclusions: Significant sociodemographic and clinical differences exist in frontline trial enrollment for pediatric AML, which may contribute to worse overall survival outcomes for patients not enrolled on trials. Acuity at diagnosis may be a potential modifiable driver of survival differences. These findings support the need to evaluate enrollment patterns across pediatric clinical trials, including how enrollment disparities impact generalizability of clinical trial results, as well as a critical need for interventions designed to improve equity in healthcare access.

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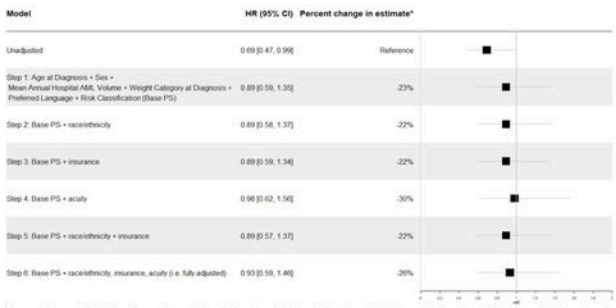
Table 1. Sociodemographic and clinical characteristics of pediatric AML patients by frontline trial enrollment status

	Overall	Trial Enrolled	Not Enrolled on Frontline Trial	*P* value
	N=342	N=189	N=153	
Age at Diagnosis (mean (SD))	8.11 (6.11)	7.90 (6.06)	8.37 (6.17)	0.48
Sex (%)				0.91
Female	49.7%	49.2%	50.3%	
Male	50.3%	50.8%	49.7%	
Risk Classification				<0.001
Low	51.8%	60.8%	40.5%	
Intermediate	3.5%	5.3%	1.3%	
High	31.3%	29.1%	34.0%	
Not risk stratified/Unknown	13.4%	4.8%	24.2%	
Weight Category[b] at Diagnosis				0.11
Underweight	7.3%	4.3%	11.1%	
Healthy Weight	60.8%	61.9%	59.5%	
Overweight	16.1%	16.9%	15.0%	
Obese	15.8%	16.9%	14.4%	
Acuity at Diagnosis (%)				0.09
Lower Acuity	94.7%	96.8%	92.2%	
Higher Acuity	5.3%	3.2%	7.8%	
Race/Ethnicity (%)				0.003
White	44.7%	52.4%	35.3%	
Black/African American	16.7%	11.1%	23.5%	
Hispanic	25.7%	23.8%	28.1%	
Other	12.9%	12.7%	13.1%	
Insurance Status (%)				0.05
Public Only	48.8%	43.9%	54.9%	
Any Private	51.2%	56.1%	45.1%	
Preferred Language (%)				0.27
English	85.1%	87.8%	81.7%	
Spanish	9.1%	7.4%	11.1%	
Other	5.8%	4.8%	7.2%	
Mean Annual Hospital AML Volume of Treating Institution[c] (mean (SD))	7.44 (2.48)	7.27 (2.50)	7.66 (2.45)	0.14

[a] Not risk stratified/unknown includes patients who died during Induction I and/or did not have formal documentation of their risk classification. These were not considered missing data given potential differences by trial enrollment status.
[b] Body mass index (BMI) percentiles for age at diagnosis and gender were computed from reported weight and height based on 2000 Centers for Disease Control (CDC) growth chart data (patients aged 2 to 20 years) and the World Health Organization reference (patients aged <2 years) and were classified into weight categories as follows: obese (≥95th percentile), overweight (85th to <95th percentile), healthy weight (5th to <85th percentile), and underweight (<5th percentile).
[c] Calculated as average annual number of AML diagnoses for each center over the study period

Figure 1. OS hazard ratios for patients enrolled vs. not enrolled on frontline pediatric AML clinical trials



*Percent change with adding of specific covariates outlined in each step relative to unadjusted model. Calculated as $((HR_{unadjusted} / HR_{adjusted}) - 1) \times 100$.

Figure 1

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