PEDIATRIC LEUKEMIA CYTOGENETICS IN BOTSWANA

Lisa M. Force[1,2,3], Alan R. Anderson[1,3,4], Jennifer A. Geel[5], Michael E. Scheurer[1,4], Judith F. Margolin[1,4], Parth S. Mehta[1,4], Janet E. Poole[5], Jeremy S. Slone[1,4]

[1]Baylor College of Medicine, Houston, TX, USA, [2]Baylor International Pediatric AIDS Initiative-Texas Children's Hospital Global Health Corps, Houston, TX, USA, [3]Princess Marina Hospital, Gaborone, Botswana, [4]Texas Children's Cancer and Hematology Centers, Houston, TX, USA, [5]Wits University Donald Gordon Medical Centre, Faculty of Health Sciences, University of the Witwatersrand, Division of Paediatric Haematology-Oncology, Johannesburg, South Africa

BACKGROUND

- Acute leukemias are the most common malignancy of childhood in high-income countries (HICs) and their cytogenetics are relevant in prognosis and risk stratification.
- The majority of children diagnosed with acute leukemias live in low- and middle-income countries (LMICs), where fewer children survive. Given resource limitations there is less data on cytogenetic alterations in LMICs and whether these contribute to poorer outcomes.
- Princess Marina Hospital (PMH) is a government referral hospital with the only pediatric oncology services in Botswana, a middle-income country.
- Due to a lack of advanced diagnostics, consistent blood products and certain chemotherapeutic agents at PMH, most children with acute leukemias are referred to hospitals in South Africa (SA) for the intensive phases of treatment.

METHODS

- This retrospective cohort study reviewed pediatric patients (≤ 18 years) diagnosed with acute leukemia at PMH between January 2007 and May 2016.
- Variables assessed included age, sex, presenting leukocyte count, time between caregiver report of initial symptoms and evaluation in SA, steroid pre-treatment, HIV status, Central Nervous System (CNS) status, and cytogenetic results as well as outcome events such as survival.
- Diagnostic cytogenetic studies, including bone marrow karyotype and fluorescence in-situ hybridization (FISH), were obtained in SA.
- Standard cytogenetic testing in SA generally included karyotype analysis from a bone marrow aspirate (BMA) with FISH for prognostically relevant or cryptic translocations based on leukemia subtype.
- Patients were treated with various USA and European protocols modified for the setting; none received bone marrow transplant.

RESULTS

	Age[1] (years)	Sex	Presenting leukocyte count[1] (10^3/uL)	Time between symptom onset and evaluation in SA[1] (days)	Steroid pre-treatment	CNS positive (CNS 2 or 3)
ALL N = 30 (62.5%)	7.44 (1.30-16.11)	15 female (50%)	35.53 (2.13-517.45)	43 (3-270)	6/23 (26.1%)	2/19 (10.5%)
AML N = 14 (29.2%)	7.37 (1.42-16.61)	3 female (21.43%)	27.97 (2.26-209.50)	41 (12-86)	1/14 (7.1%)	0/10 (0%)
Other N = 4 (8.3%)	2.83 (0.44-10.50)	3 female (75%)	42.02 (22.17-57.45)	59 (10-85)	1/4 (25%)	1/3 (33.3%)
Total N = 48	7.13 (0.44-16.61)	21 female (43.75%)	35.18 (2.13-517.45)	43 (3-270)	8/41 (19.5%)	3/32 (9.4%)

Table 1: Presenting features of pediatric patients diagnosed with acute leukemias. ALL: Acute lymphoblastic leukemia, AML: Acute myeloid leukemia, Other: Mixed phenotype, ambiguous lineage, or leukemia not otherwise specified. All patients tested (96% of total patients) were HIV negative. One patient (AML) abandoned care (2.3%). [1]Median and (range).

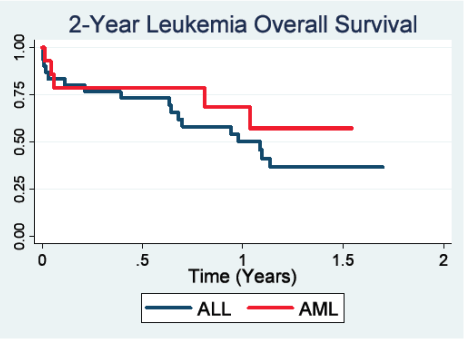
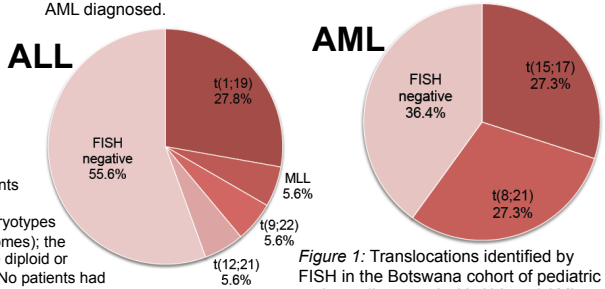


Figure 2: Kaplan-Meier overall survival estimates

ALL (N = 25)		AML (N = 12)	
Pre B-cell ALL	18 (72.0%)	M1	1 (8.3%)
T-cell ALL	6 (24.0%)	M2	4 (33.3%)
B-cell ALL (mature B)	1 (4.0%)	M3, APML	4 (33.3%)
		M7, AMKL	3 (25.0%)

Table 2: Subtypes of ALL and AML diagnosed.



*16.7% of patients with ALL had hyperdiploid karyotypes (> 50 chromosomes); the remainder were diploid or pseudodiploid. No patients had hypodiploidy (< 44 chromosomes).

Figure 1: Translocations identified by FISH in the Botswana cohort of pediatric patients diagnosed with ALL and AML.

CONCLUSIONS

- In this limited retrospective cohort study favorable translocations in AML and largely unfavorable translocations in ALL were observed.
- A substantial percentage of patients had no translocations identified by FISH; it is possible that pre-treatment prior to diagnostic BMA, sampling or laboratory challenges contributed to these negative FISH results.
- Trends suggest inferior survival for ALL compared to outcomes published in HICs, likely influenced by poor prognostic indicators at diagnosis including delay to care, steroid pre-treatment, lower percentage of hyperdiploidy and higher percentage of t(1;19).
- Survival for AML is higher than anticipated in this setting, potentially influenced by the favorable cytogenetics. However, delay of diagnosis in this setting may be selecting for favorable cytogenetics in this cohort.
- Prospective research in LMICs with regional, multinational studies is needed to best determine local cytogenetics and their prognostic and treatment implications.

Texas Children's Global HOPE (Hematology-Oncology Programs of Excellence)
@TCHGlobalHealth | globalhealth.texaschildrens.org | *Correspondence to*: Lisa.Force@stjude.org