Philadelphia Chromosome-Positive Acute Lymphoblastic Leukemia: Risk Factors for Development of Chronic Myeloid Leukemia-Like Subtype

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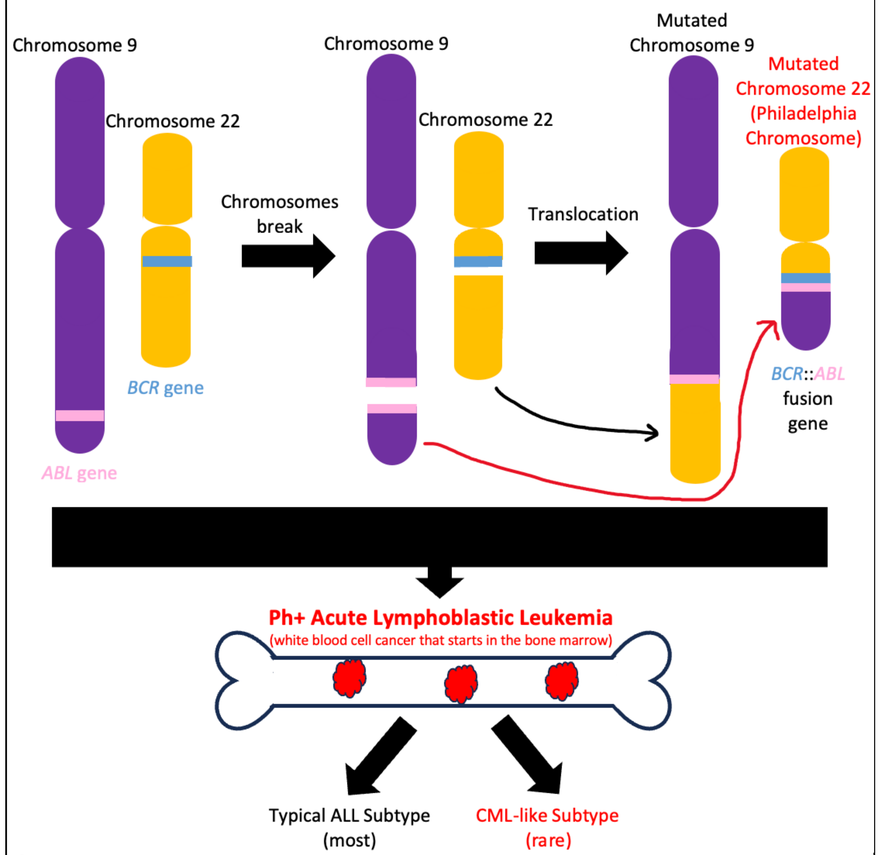
Introduction

- Acute Lymphoblastic Leukemia (**ALL**) is the **most common childhood cancer**
- Philadelphia chromosome-positive **(Ph+) ALL** is a rare, **high-risk subtype** of ALL
- A small percentage of Ph+ ALL patients develop a **Chronic Myeloid Leukemia (CML)-like subtype**, which resembles the **dangerous blast crisis phase of CML**, after receiving ALL treatment
- The risk factors, characteristics, and outcomes of this population **have not been well characterized**



Objectives

- Characterize parameters that can be used to **predict predisposition** toward developing the Ph+ ALL CML-like subtype

BCR::ABL Protein Isoforms

- The Philadelphia chromosome (i.e., the *BCR*::*ABL* fusion gene) generates the **BCR::ABL fusion protein,** which takes one of **two isoforms: p190 or p210**

Demographics

- Patients were **well-balanced** in baseline characteristics

Baseline Characteristic	CML-Like (n=8)	Others (n=35)	p-value
Age at Diagnosis, median (IQR)	12.5 (8.3, 14.6)	11.9 (5.7, 14.6)	0.66
Sex, n (%)			1.00
Female	3 (37.5)	14 (40.0)	
Male	5 (62.5)	21 (60.0)	
Race, n (%)			0.14
White	4 (50.0)	27 (77.1)	
Black	4 (50.0)	6 (17.1)	
Other	0 (0.0)	2 (5.7)	

Abbreviations
CML = Chronic Myeloid Leukemia. IQR = Interquartile Range.

Table 1. Baseline characteristics. There were no statistically significant differences between the CML-like group and Others group in baseline characteristics.

Results: Early Risk Factor Identification

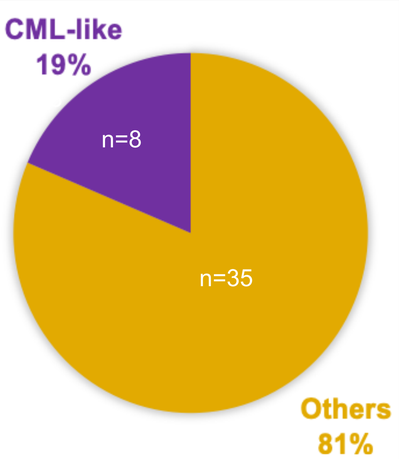
Patient Characteristic	CML-Like (n=8)	Others (n=35)	p-value
WBC Dx (x10e3), median (IQR)	181 (63.9, 271.8)	21 (5.5, 67.6)	**0.006**
CNS status Dx, n (%)			**0.007**
CNS1	1 (12.5)	24 (68.6)	
CNS2	6 (75.0)	10 (28.6)	
CNS3	1 (12.5)	1 (2.8)	
BCR::ABL isoform (n, %)			**0.011**
p190 (ALL-like)	4 (50.0)	31 (88.6)	
p210 (CML-like)	4 (50.0)	4 (11.4)	

Abbreviations
WBC = White Blood Cell count. Dx = Diagnosis. CNS = Central Nervous System. RBC = Red Blood Cell count.
CNS status is defined by cerebrospinal fluid findings as follows: CNS1 (≤5 WBCs/μL, <10 RBCs/μL, leukemic blasts absent); CNS2 (≤5 WBCs/μL, <10 RBCs/μL, leukemic blasts present); CNS3 (>5 WBCs/μL, <10 RBCs/μL, leukemic blasts present).

Table 2. Patient characteristics. There were statistically significant differences between the CML-like group and Others group in several patient characteristics at diagnosis, including WBC, CNS status, and BCR::ABL fusion protein isoform.

Study Design and Methods

- **Retrospective chart review** of **43 pediatric patients with Ph+ ALL** treated at St. Jude Children's Research Hospital between 2000 and 2023
- Divided into **two groups**: those who developed CML-like disease (**CML-like**) and those who did not (**Others**)
- **Analyzed characteristics, treatment, and outcomes**



Conclusion and Future Studies

Conclusion

- We reviewed clinical and laboratory characteristics of a sample of **43 Ph+ ALL patients**
- **8 out of the 43 patients (19%) developed the CML-like subtype**
- We identified three **parameters at diagnosis that predict predisposition** toward developing the Ph+ ALL CML-like subtype:
  - ***Higher WBC*** *(median 181k vs. 21k)*
  - ***CNS status of 2 or higher*** *(87.5% vs. 31.4%)*
  - ***p210 BCR::ABL isoform*** *(50.0% vs. 11.4%)*
- **Ability to predict development of CML-like subtype** in these high-risk patients will ultimately help clinicians **implement more aggressive treatment strategies**

Future Studies

- **Genomic analysis** may be able to shed light on potential different genetic mutation patterns at diagnosis in patients at risk for developing the CML-like subtype