SOHO ANNUAL MEETING 2024

‘PROGNOSTIC GENE ALTERATIONS AND MRD POSITIVITY IN PH-LIKE B-LINEAGE ALL IN RESOURCE-LIMITED SETTINGS’

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INTRODUCTION

“B-lymphoblastic leukaemia/lymphoma, Ph-like acute lymphoblastic leukaemia (ALL)” has been considered an entity in the revised World Health Organization (WHO) (2022) classification of Haematolymphoid neoplasms. The unique gene expression profile (GEP) of this entity resembles *BCR::ABL1*-positive ALL cases without the presence of t(9:22)(q34;q11.2) translocation. Early detection of Ph-like ALL is crucial for improving treatment and survival rates. This high-risk subtype, characterized by genomic alterations triggering the activation of cytokine receptors & kinase signaling, is challenging to detect in developing countries due to the lack of specialized assays.

AIM

To identify Ph-like ALL cases using our in-house PHi-RACE classifier and characterize associated genomics alterations in recurrent gene abnormalities negative (RGA^{neg}) B-ALLs.

METHODS

This study utilized the PHi-RACE classifier, developed from 1024 B-ALL cases, to detect Ph-like ALL, followed by characterization of genetic alterations in 108 RGA^{neg} (Recurrent gene abnormalities negative) B-ALL samples. Genetic alterations were characterized, focusing on *TSLPR*/*CRLF2* expression, *IKZF1* deletion, chimeric gene fusions, and aberrant myeloid markers. MRD positivity was compared between Ph-like and non-Ph-like ALL cases.

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RESULTS

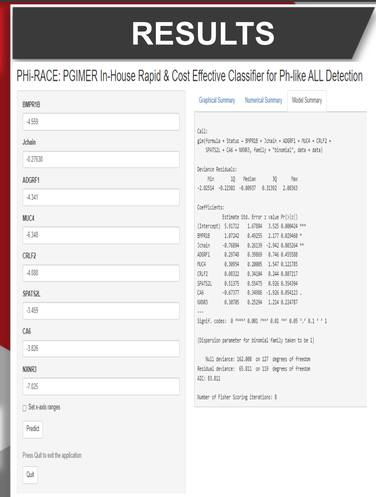


Figure 1: The PHi-RACE classifier identified 34.25% of cases among RGA-negative B-ALL patients.

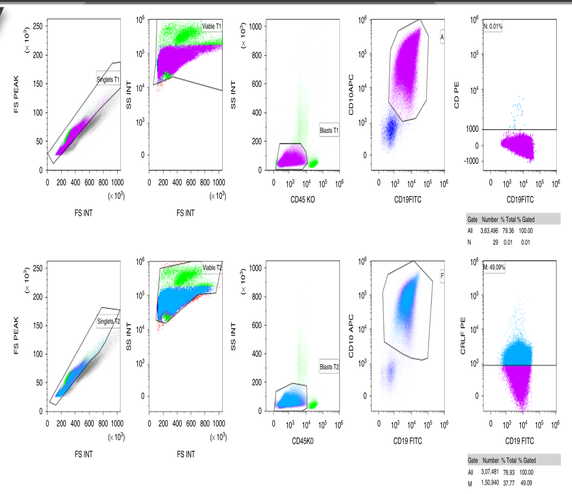
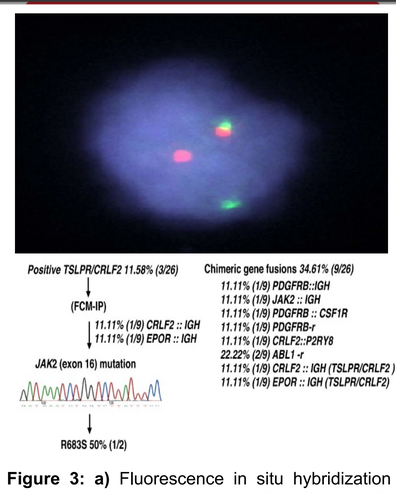


Figure 2: Flow cytometry (FCM) analysis revealed ***TSLPR*/*CRLF2*** expression in 11.58% of blasts in Ph-like ALL cases.



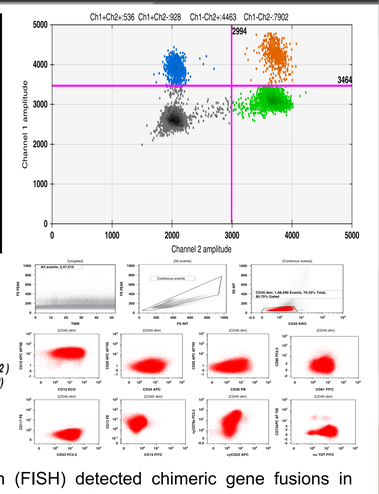


Figure 3: a) Fluorescence in situ hybridization (FISH) detected chimeric gene fusions in 34.61% of Ph-like ALL cases. b) Digital droplet PCR (ddPCR) identified *IKZF1* (Δ4-7 deletion) in 18.9% of Ph-like ALL cases. c) Flow cytometry (FCM) identified aberrant expression of myeloid markers CD13 (18.91%) and CD33 (27.02%) in Ph-like ALL cases.

CONCLUSIONS

The PHi-RACE classifier revealed a high occurrence of Ph-like ALL and a lower occurrence of *CRLF2* alterations and associated chimeric gene fusions. Early identification at diagnosis is essential for optimizing personalized treatment, especially in low-middle-income countries lacking specialized assays.

ACKNOWLEDGMENT

I sincerely thank the faculty of Hematology, Clinical Hematology & Internal Medicine, technical staff, and clerical staff for providing valuable support for this study. I would like to extend my sincere thanks to Dr Monika, Dr. Sarki Abba Abdulkadir (Roberts H. Lurie Cancer Centre, Northwestern University) & Aarohan Puri (DePaul University) for their valuable support/suggestions.

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