ELSEVIER

Blood 142 (2023) 2836–2837

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

612.ACUTE LYMPHOBLASTIC LEUKEMIAS: CLINICAL AND EPIDEMIOLOGICAL

Prognostic Features of CD9 in Childhood Acute Lymphoblastic Leukemia - a Retrospective Analysis of a Nation-Wide Multicenter Study in China

Kathy Yuen Yee Chan, PhD[1], Jiaoyang Cai, PhD[2], Yu Liu, PhD[3], Jun J. Yang, PhD[4], Ching-Hon Pui, MD[4], Shuhong Shen, MD PhD[3], Chi Kong Li[5], Kam Tong Leung[5]

[1]Department of Paediatrics, The Chinese University of Hong Kong, Shatin, Hong Kong
[2]Key Laboratory of Pediatric Hematology & Oncology of the Ministry of Health of China, Department of Hematology & Oncology, Shanghai Children's Medical Center, Shanghai, China
[3]Key Laboratory of Pediatric Hematology & Oncology of the Ministry of Health of China, Department of Hematology & Oncology, Shanghai Children's Medical Center, School of Medicine, Shanghai Jiao Tong University, Shanghai, China
[4]Department of Oncology, St. Jude Children's Research Hospital, Memphis, TN
[5]Department of Paediatrics, The Chinese University of Hong Kong, Shatin, Hong Kong

Background and objectives: The outcomes of children with acute lymphoblastic leukemia (ALL) have been incrementally improved with risk-directed chemotherapy but therapy responses remain heterogeneous in clinically defined risk groups. Parameters with added prognostic values are therefore warranted to refine the current risk stratification system and inform appropriate management. CD9, a cell surface protein presented on malignant lymphoblasts, may have such predictive characteristics as shown by our previous single-center study conducted in Hong Kong (Leung *et al*, Leukemia, 2020). This study aims to determine the precise prognostic features of CD9 in a nation-wide, multicenter childhood ALL cohort in China, and deliver algorithms for identification of patients who may benefit from early interventions.
Study design and outcome measures: This multicenter cohort study included childhood ALL patients (aged <18 years) enrolled into the Chinese Children Cancer Group (CCCG)-ALL-2015 study from January 2015 to December 2019, with 7,640 patients from 20 tertiary hospitals in China treated with a uniform protocol. A total of 3,781 subjects (49.5%) from 16 sites had flow cytometry data on lymphoblast CD9 at diagnosis. The final study cohort comprised 3,395 B-ALL and 386 T-ALL patients with a median follow-up of 53.9 months. The primary outcomes were 5-year overall survival (OS), event-free survival (EFS), and cumulative incidence of relapse (CIR) for patients with $CD9^+$ or $CD9^-$ phenotypes (positivity defined by the presence of ≥20% $CD9^+$ blasts evaluated through a univariate analysis demonstrating the highest odds for adverse events or relapse at this cut-off). The secondary outcomes were 5-year OS, EFS, and CIR rates of $CD9^+$ and $CD9^-$ patients after inclusion of known prognostic factors, including risk assignment, cytogenetic anomalies, and minimal residual disease (MRD) status. Survival benefits of $CD9^+$ subjects from treatment intensification or hematopoietic stem cell transplantation (HSCT) were analyzed.
Results: CD9 was expressed in 88.5% of B-ALL and 27.9% of T-ALL cases. It conferred a dismal EFS (82.1% *vs.* 89.3%, P=0.001) and a higher CIR (15.5% *vs.* 7.8%, P<0.001) in B-ALL but not T-ALL patients. The prognostic impact of CD9 is much more prominent in subjects with adverse presenting features or poor early treatment responses, as best exemplified in those assigned to the intermediate/high-risk arms (EFS: 72.8% vs. 83.2%, P=0.028; CIR: 23.1% *vs.* 10.2%, P=0.003) or those with positive MRD at day 19 (EFS: 65.2% *vs.* 82.0%, P=0.053; CIR: 30.3% *vs.* 9.7%, P=0.007). The adverse impact of CD9 is confined to specific cytogenetics, including *BCR-ABL1* (CIR: 39.5% *vs.* 0%, P=0.019) and normal karyotype (CIR: 15.0% *vs.* 6.8%, P=0.034). In multivariate analyses, CD9 remains an independent factor predicting event-free survival (HR=1.917, P=0.001) and relapse (HR=2.208, P<0.001). The time to and site of relapse did not differ between $CD9^+$ and $CD9^-$ patients. For $CD9^+$ patients with MRD at the end of induction, treatment upstaging only benefited initial low-risk subjects. HSCT at first remission did not improve the outcomes of high-risk subjects with a $CD9^+$ phenotype.
Conclusions: This is the largest study to evaluate the significance of CD9 in childhood ALL. We confirmed the results of our previous single-center study with this multicenter national study. CD9 positivity is definitively associated with a higher relapse probability particularly for patients with intermediate/high risk diseases, MRD positivity or specific cytogenetic background. *BCR-ABL1* $^+$ patients with a $CD9^-$ phenotype had excellent outcomes and HSCT may not be required. Whereas MRD $^+$ patients who were $CD9^+$ had poor outcomes, and therefore should have early interventions with innovative treatments to

reduce the risk of relapse. With these, we propose to incorporate CD9 into the diagnostic immunophenotyping panel to inform risk stratification and management of childhood ALL.

Disclosures Yang: *Takeda Pharmaceutical Company:* Research Funding.

https://doi.org/10.1182/blood-2023-191098