Blood 142 (2023) 4276–4277

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

615.ACUTE MYELOID LEUKEMIAS: COMMERCIALLY AVAILABLE THERAPIES, EXCLUDING TRANSPLANTATION AND CELLULAR IMMUNOTHERAPIES

A Multicenter Clinical Study with Reduced Intensive Chemotherapy for Induction Remission of Pediatric Acute Megakaryoblastic Leukemia

Yixin Hu[1], *Minghua Yang, MDPhD*[2], *Ningling Wang, MD*[3], *Linhai Yang*[3], *Xiaowen Zhai, MDPhD*[4], *Hongsheng Wang, MD*[4], *Chun Li*[5], *Yufeng Liu, MDPhD*[6], *Xueju Xu*[6], *Qi An, MDPhD*[7], *Jixia Luo, MD*[8], *Liangchun Yang, MDPhD*[9], *Xiaojun Yuan, MDPhD*[10], *Qianfei Wang, PhD*[11], *Ning Liao, MD*[12], *Hua Jiang, MDPhD*[13], *Xiuli Ju, MDPhD*[14], *Xiaoming Wang*[14], *Yi Wang*[1], *Peifang Xiao*[1], *Jun Lu*[1], *Hailong He*[1], *Raul C. Ribeiro, MD*[15], *Shaoyan Hu, MDPhD*[1]

[1] Department of Hematology and Oncology, Children's Hospital of Soochow University, Suzhou, China
[2] Department of Hematology and Oncology, The Third Xiangya Hospital of Central South University, Changsha, China
[3] Department of Hematology and Oncology, The Second Affiliated Hospital of Anhui Medical University, Hefei, China
[4] Department of Hematology and Oncology, Children's Hospital of Fudan University, Shanghai, China
[5] Department of Hematology and Oncology, Anhui Provincial Hospital, Hefei, China
[6] Department of Hematology and Oncology, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China
[7] Department of Hematology and Oncology, Xuzhou Children's Hospital, Xuzhou, China
[8] Department of Hematology and Oncology, Kaifeng Children's Hospital, Kaifeng, China
[9] Department of Pediatrics, Xiangya Hospital, Changsha, China
[10] Department of Pediatric Hematology/Oncology, Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai, China
[11] CAS Key Laboratory of Genomic and Precision Medicine, Collaborative Innovation Center of Genetics and Development, Beijing Institute of Genomics, Chinese Academy of Sciences, Beijing, China
[12] Department of Pediatrics, The First Affiliated Hospital of Guangxi Medical University, Nanning, China
[13] Department of Hematology and Oncology, Guangzhou Women and Children's Medical Center, Guangzhou, China
[14] Department of Hematology and Oncology, Qilu Hospital of Shandong University, Qingdao, China
[15] Division of Leukemia/Lymphoma, Department of Oncology, St. Jude Children's Research Hospital, Memphis, TN

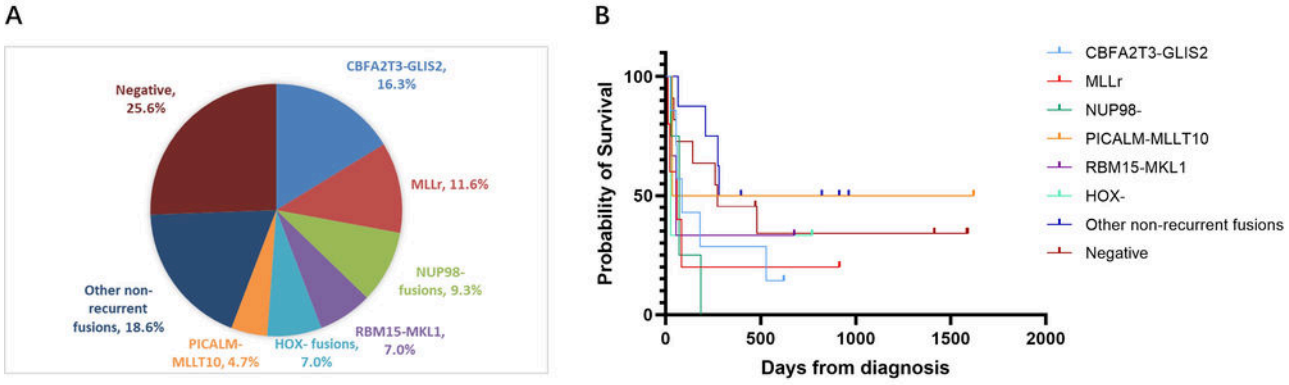
Bcakground: Pediatric acute megakaryoblastic leukemia (AMKL) without Down syndrome (DS) is a genetically heterogenous myeloid malignancy and with dismal prognosis. Refractory and relapse remains a major challenge. Given to the young age distribution of AMKL and high frequency of abandonment in middle-income countries, we conducted a multicenter clinical trial (ChiCTR1800015875) in aims to lower the intensity of induction while without compromise the remission rate and survival.
Methods: From June 2018 to December 2022, there were consecutively 43 cases with de novo non-DS AMKL, which accounted for 7.6% cases of acute myeloid leukemia (AML) during the same period, enrolled in this trial. All the patients received at least one cycle of low-dose induction with HAG regimen (homoharringtonine 1 mg/m ^{2}, intravenous daily, days 1-7; cytarabine 10 mg/m ^{2}, subcutaneously every 12 hours, 20 doses, and G-CSF 5μ/kg subcutaneous, daily, 10 doses) followed by 3 to 4 courses of intensive chemotherapy or HSCT as post-remission consolidation. Besides conventional molecule testing, RNA-sequencing and whole exon sequencing (WES) were performed as well to reveal underlying genetic landscape of this type of disease.
Results: The median age of the 43 patients at diagnosis was 18.5 (range 4-114) months. The median while blood cell (WBC) counts and platelet at diagnosis were 17.2×10 ^{9}/L (range 1.8-105.7 ×10 ^{9}/L) and 36.5×10 ^{9}/L (range 4-472 ×10 ^{9}/L), respectively. Among them, 39.5% of cases exhibited hepatosplenomegaly. A diversity of genetic fusions and mutations were uncovered. The recurrent fusions in this cohort include CBFA2T3-GLIS2 (16.3%), MLLr (11.6%), NUP98-(9.3%), RBM15-MKL1 (7.0%), HOX fusions (7.0%) and PICALM-MLLT10 (4.7%). Other non-recurrent fusions accounted for 18.6% (Figure 1A). The common mutations detected in our pediatric AMKL were JAK2, NRAS, MPL, BCOR, CTCF, KRAS and PTPN11. Regarding treatment response, 20 of 43 cases (46.5%) attained complete remission (CR) or complete remission with incomplete blood cell recovery (CRi) after one cycle of induction. Among the 20 cases, 9 of them got minimal residual disease (MRD) negative by flow cytometry. Ten patients (23.2%) achieved partial remission (PR) while 13 patients (30.2%) showed no response (NR) to treatment.

Thirty-one patients continued with another cycle of the same regimen and 21 of the 28 cases who were available for evaluation (75.0%) attained CR/CRi. Disease relapse was observed in 16/43 (37.2%) cases, with 7/43 (16.2%) patients relapsed after transplantation. The 3-year overall survival (OS) and event-free survival (EFS) were 49.6±8.2% and 29.5±7.1%, respectively (Figure 1B). In total, more than half of patients (22/43, 51.5%) underwent HSCT. The 3-year OS of transplant group and chemotherapy group were 57.9±11.7% versus 39.5±11.2%, P=0.036. As genetic characteristics often predict treatment response and prognosis, we wonder which subgroup could benefit from the reduced intensive induction. We further compared the features of patients who got CR/CRi after induction I with those achieved PR/NR. Interestingly, we found more patients with adverse fusions in PR/NR group, such as CBFA2T3-GLIS2 (26.0% vs. 5.0%), NUP98- (17.4% vs. 0%), MLLs (13.0% vs. 10.0%), and RBM15-MKL1 (8.7% vs. 5.0%); while other non-recurrent fusions were more common in CR/CRi group (4.3% vs. 35.0%). Two thirds of patients (67.4%) experienced refractory or relapse and almost half of them harbored adverse fusions or mutations such as CBFA2T3-GLIS2, MLLr, NUP98- fusions, NRAS and PTPN11. On the other hand, 14 patients without refractory or relapse had genetic features with more JAK2 and MPL mutations. No treatment-related mortality (TRM) occurred during induction. Only one patient with KRAS mutation died of infection after consolidation III.

Conclusion: Insight into the genetic and molecular landscape improved our understanding of pediatric AMKL. Distinct molecular features can serve as a tool to tailor the therapy. Though treatment still lags behind and novel therapy is urgent for the adverse subgroups, our low-dose induction with HAG regimen could benefit for a subgroup with non-recurrent fusions, which showed efficiency while is tolerable for the young age group. Based on our results, we provide an induction option for these AMKL patients, especially for those in the middle-income countries.

Disclosures No relevant conflicts of interest to declare.

Figure 1. Genetic characteristics and Survival of pediatric acute megakaryoblastic leukemia patients.



(A) Heterogenous genetic fusions of pediatric AMKL without Down syndrome.
(B) Event-free survival (EFS) of different pediatric AMKL subgroups.

Figure 1

https://doi.org/10.1182/blood-2023-190821