(PF541) LOW-DOSE INDUCTION CHEMOTHERAPY IS ASSOCIATED WITH VERY LOW EARLY MORTALITY IN PEDIATRIC ACUTE MEGAKARYOBLASTIC LEUKEMIA: A PROSPECTIVE MULTICENTER STUDY

Topic: 04. Acute myeloid leukemia - Clinical

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Background

Pediatric non–Down syndrome acute megakaryoblastic leukemia (non-DS AMKL) is a rare, highly aggressive subtype of acute myeloid leukemia (AML) with poor outcomes despite intensive therapy. Early death and treatment-related mortality (TRM) are major barriers to improving survival, particularly in high-risk genetic cases, underscoring the need for improved induction regimens.

Aims

This study aimed to evaluate the safety and efficacy of low-dose HAG (homoharringtonine, low-dose cytarabine, and G-CSF priming) as an induction therapy for children with newly diagnosed non-DS AMKL. The primary goal was to assess the complete remission (CR) rate after two induction courses. Secondary objectives included overall survival (OS), event-free survival (EFS), cumulative incidence of relapse (CIR), and the role of measurable residual disease (MRD) in predicting outcomes. Additionally, the study evaluated the safety of low-dose HAG and its potential to reduce early mortality and TRM.

Methods

This was a prospective, phase II, multicenter clinical trial (CALD-AMKL-18) conducted across 9 pediatric centers in China. Between June 2018 and December 2022, 51 children aged <18 years with newly diagnosed non-DS AMKL were enrolled. Patients received a low-dose chemotherapy regimen (HAG: homoharringtonine, low-dose cytarabine, and G-CSF priming) as induction therapy, followed by risk-adapted consolidation and post-remission therapy. The primary endpoint was complete remission (CR) after two induction courses, and secondary endpoints included OS, EFS, CIR, MRD status, and treatment-related toxicities.

Results

The median age at diagnosis was 40 months (range 2–114), with 26 (51%) male patients. Twenty-seven patients underwent allogeneic hematopoietic stem cell transplantation (allo-HSCT). No early deaths occurred during induction, and only one patient (2%) died due to severe infection during consolidation. After the second induction, the CR rate was 76.5% (26/34). The two-year overall survival (OS) was 48.7%, and event-free survival (EFS) was 49.0%, with a 2-year cumulative incidence of relapse (CIR) of 31.3%. Fusion-negative and *KMT2A*-rearranged patients demonstrated relatively favorable survival, while *CBFA2T3::GLIS2* or *NUP98::KDM5A* fusions were associated with poor long-term outcomes. MRD ≥0.1% after Induction II identified a high-risk subgroup with significantly worse OS (12.5% vs 64.5%, $P < 0.01$) and EFS (12.5% vs 63.0%, $P < 0.01$). MRD ≥0.1% after Induction II, but not after Induction I, was strongly associated with inferior outcomes. Pre-transplant MRD negativity predicted better post-HSCT outcomes.

Summary/Conclusion

Low-dose HAG induction reduces early mortality and significantly lowers TRM, providing a well-tolerated backbone for risk-adapted strategies. This approach supports the incorporation of targeted therapies guided by fusion profiles and MRD status, offering a promising treatment for pediatric non-DS AMKL. Further studies are needed to validate these findings and explore the long-term benefits of combining low-dose chemotherapy with targeted therapies in high-risk populations.