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POSTER ABSTRACTS

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

Chidamide-Based Pre-Emptive Treatment for High-Risk AML Patients after Hematopoietic Stem Cell Transplantation: A Real-World Experience from Chinese Single-Center

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Background: The treatment of relapsed or refractory acute myeloid leukemia (AML) remains challenging. Measurable residual disease (MRD) persistence at transplantation or post-transplantation has been identified as the strongest risk factor for relapse and poor outcomes for patients with hematological malignancies (HMs). Chidamide, a novel oral histone deacetylase inhibitor, has shown potential therapeutic effects in various types of HMs by inducing cell apoptosis and regulating immunity. This study aimed to evaluate the efficacy and safety of Chidamide-based prophylactic or pre-emptive treatment for patients who are MRD positive before or who have sustained MRD positive after transplantation.

Aim: The rate of 6 months of conversion to MRD- and relapse-free survival of high-risk AML after Chidamide-based treatment.

Methods: From December 2020 to July 2023, 50 patients with high-risk HMs received chidamide-based therapy after allo-HSCT. 39 patients were diagnosed with AML (4 secondary AML), 2 with myelodysplastic syndromes, 6 with acute lymphoid leukemia, and 3 with mixed-phenotype acute leukemia. 46 patients (92%) with relapsed/refractory status or detectable MRD (MRD+) at transplantation or after allo-HSCT received chidamide as pre-emptive, and the remaining 4 high-risk patients with MRD− conducted as prophylactic intervention. Patients with detectable MRD before transplantation and those who remained positive for MRD after transplantation were defined as very high-risk AML (VHR-AML). Chidamide was administered at a dose of 5 mg per day orally, 6 times per week, lasting at least 1 year after engraftment. Additional agents included hypomethylating agents (HMAs), donor lymphocyte infusion (DLI) or tyrosine kinase inhibitor (TKI) in patients with Philadelphia chromosome-positive. In this study, 28 patients received chidamide monotherapy, 13 received chidamide combined with HMAs, and 9 cases with other therapy.

Results: The median age of all patients was 38 years old (range 17-67), comprising 24 males and 26 females. Up to 1st July 2023, with a median follow-up period of 376 days (25-984d), the overall rate of MRD negative showed 64%. The rate of MRD- survival, Relapse-free survival (RFS) and overall survival (OS) were 56%, 66% and 76%, respectively. The 6 months MRD negative rate, RFS and OS rate were 86%, 82%, 86% and 88%, which maintained at 82%, 82% and 86% with 12 months follow-up, respectively.

In 46 cases of the pre-emptive intervention arm, the overall MRD- rate was 61.7%. Among them, 83.3% of patients (20/24) who received chidamide monotherapy exhibited a much higher conversion to MRD− than those combined with HMAs (7/13, 53.8%) or other drugs (2/9, 22.2%) (P=0.004). In 4 cases who received chidamide monotherapy as prophylactic intervention, 3 patients sustained MRD negativity up to the last follow-up, except for one patient diagnosed with MPAL(B+M) relapsed after 1 year of HSCT with taking chidamide for 6 months.

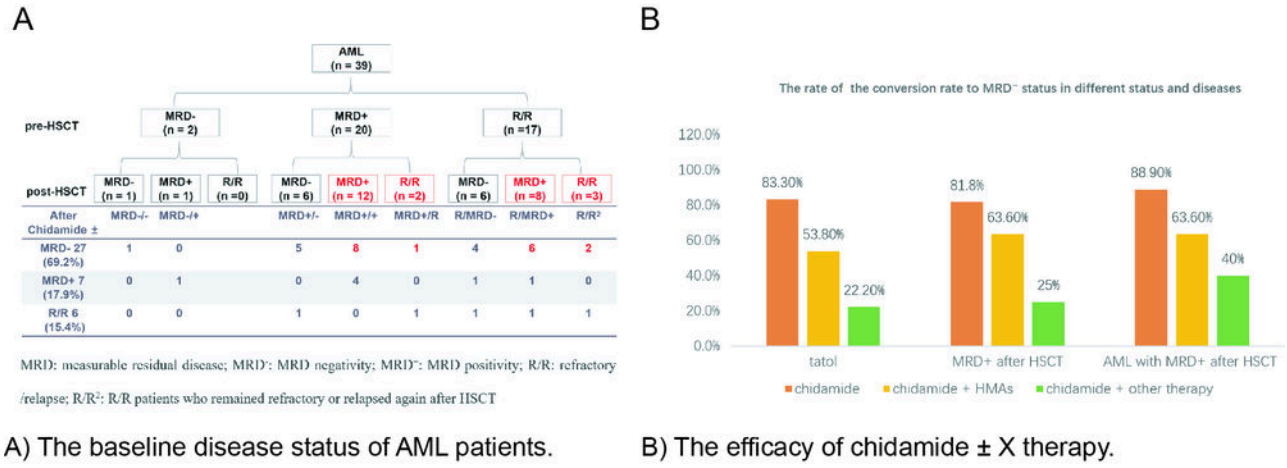
A total of 30 patients (including 25 AML) with VHR diseases remained in a status of MRD+ or non-remission after transplantation. Eighteen patients (60%) achieved MRD− and sustained for a median of 251 days (range 31-531 d). VHR-AML patients account for 94.4% (17/18) of MRD- responders(Figure 1A). Similarly, the results showed a higher rate of conversion from MRD+ to MRD− in chidamide monotherapy than the combination groups (Chidamide monotherapy, 81.8%; Chidamide + HMA, 63.6% and Chidamide + others, 25%, P=0.042,Figure 1B). It highlighted that treatment with chidamide resulted in increased MRD− response, especially for AML. On the contrary, of 7 patients with B-cell malignancy, including 5 B-ALL and 2 MPAL (B + M) patients, only 2 (28.6%) patients converted to MRD−.

Reversible grade 3/4 neutropenia occurred in 38% of patients, and thrombocytopenia was observed in 24% during the first four treatment cycles. Five patients experienced grade 1/2 non-hematological adverse events, such as fatigue, gastrointestinal

reaction, pneumonia and infection. No new-onset GvHD was reported in patients without a prior history of GvHD during chidamide treatment.

Conclusion: The chidamide-based regimen is safe and effective in pre-emptive treatment for patients with high-risk relapsed AML after transplantation. Whether as a monotherapy or combined with HMA, chidamide shows significant efficacy in eliminating MRD, warranting further clinical research.

Disclosures No relevant conflicts of interest to declare.



A) The baseline disease status of AML patients.

B) The efficacy of chidamide ± X therapy.

Figure 1

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