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POSTER ABSTRACTS

617.ACUTE MYELOID LEUKEMIAS: BIOMARKERS, MOLECULAR MARKERS AND MINIMAL RESIDUAL DISEASE IN DIAGNOSIS AND PROGNOSIS

Recommendations on Minimal Residual Disease Monitoring in Acute Promyelocytic Leukemia Treated with Combination of All-*Trans* Retinoic Acid and Arsenic Trioxide

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Background

All- *trans* retinoic acid (ATRA)-arsenic trioxide (ATO) combination therapy significantly reduces acute promyelocytic leukemia (APL) relapse compared to ATRA combined with chemotherapy, leading to a cure rate of 80-90% in APL patients. The ideal frequency and duration of minimal residual disease (MRD) monitoring needs to be identified in the era of ATO.

Methods

A total of 1072 APL patients were enrolled in this study, comprising 855 from the APL2012 trial (NCT01987297) and 217 from our center between January 2018 to June 2022 (APL2018 study). The APL2018 protocol was adjusted for consolidation and maintenance therapy based on APL2012 (Chen et. al. PNAS 2021): In consolidation therapy, low-, intermediate-, and high-risk patients were performed following the ATO-group scheme of corresponding risk stratification in the APL2012 study. From December 2019, chemotherapy was no longer administered to high-risk group during consolidation phase. In maintenance treatment, ATO was replaced with oral arsenic realgar-indigo naturalis formula, and methotrexate was removed. RT-PCR or RQ-PCR was routinely used for MRD monitoring, detecting *PML::RARA* fusion genes in bone marrow before each consolidation and maintenance therapy. MRD testing was conducted every 3 months within the first year, every 6 months within the second year, and annually from 3 to 5 years after treatment.

Results

A total of 993 patients achieved complete remission (CR) after induction therapy. The negative MRD rates were observed in 61.7% of patients before 1 st consolidation , 95.4% before 2 nd consolidation, 99.3% before 3 rd consolidation, and 99.5% before maintenance therapy , respectively. The median time to achieve negative MRD was 57 (22-301) days with no significant difference between relapsed and non-relapsed patients (p=0.166).

A total of 34 patients (30 in the APL2012 trial and 4 in the APL2018 study) relapsed, including 5 at low risk, 9 at intermediate risk, and 20 at high risk. The median recurrence time was 13.5 (3.5-49.0) months after achieving CR, with 94% (32/34) relapsing within 3 years of achieving CR. After induction remission, the risk of relapse decreased with time (44% occurred within the first year, 29% within the second year, 21% within the third year, and only 6% after three years, Figure 1).

The median follow-up for the 179 evaluable patients after achieving CR was 39.7 (3.5 -64.6) months in the APL2018 group. The estimated 5-year disease-free survival (DFS) rates were 95.8% (95% CI 92.8-98.9). Prior to the 1 st, 2 nd, and 3 rd consolidation treatment, and before maintenance therapy, the estimated 5-year DFS rates for MRD positive and negative patients were 92.4% (95% CI 86.1-99.2) versus 97.8% (95% CI 94.8-100), p=0.100; 57.1% (95% CI 30.1-100) versus 97.3% (95% CI 94.7-100), p<0.001; 0 versus 96.5% (95% CI 93.1-100), p<0.001; 0 versus 96.8% (95% CI 94.0-99.6), p<0.001, respectively. The results of the APL2012 study were similar to those of APL2018.

In the APL2018 study, the estimated 5-year cumulative incidence of relapse (CIR) was 2.51% (95% CI 2.48-2.54), which was 0%, 1.16% (95% CI 1.13-1.19), and 7.83% (95% CI 7.44-8.22) in the low-risk, intermediate-risk, and high-risk patients, respectively (p=0.057). The estimated 5-year CIR for the low to intermediate risk group was 0.74% (95% CI 0.73-0.75), which was statistically different from high-risk patients (p=0.019). The estimated 5-year CIR for MRD positive and negative patients prior to the 1 st and 2 nd consolidation treatments was 4.92% (95% CI 4.76-5.08) versus 1.10% (95% CI 1.08-1.12), p=0.194; 14.29% (95% CI 10.30-18.28) versus 2.08% (95% CI 2.05-2.11), p=0.010, respectively.

Conclusion

Our results show that MRD after one course of consolidation treatment, rather than before, is a crucial predictive factor for APL relapse. Patients with positive MRD after 1 st consolidation therapy have a high risk of relapse. ATRA-ATO based treatment has significantly reduced APL relapse, so the value of frequent MRD monitoring may be limited. It is recommended to implement an optimized MRD monitoring for risk stratification. For low to intermediate-risk patients and those with negative MRD after a consolidation treatment, the frequency and duration of MRD testing can be minimized. For high-risk patients with sustained MRD negativity for more than 3 years, MRD testing can be considered for discontinuation.

Disclosures No relevant conflicts of interest to declare.

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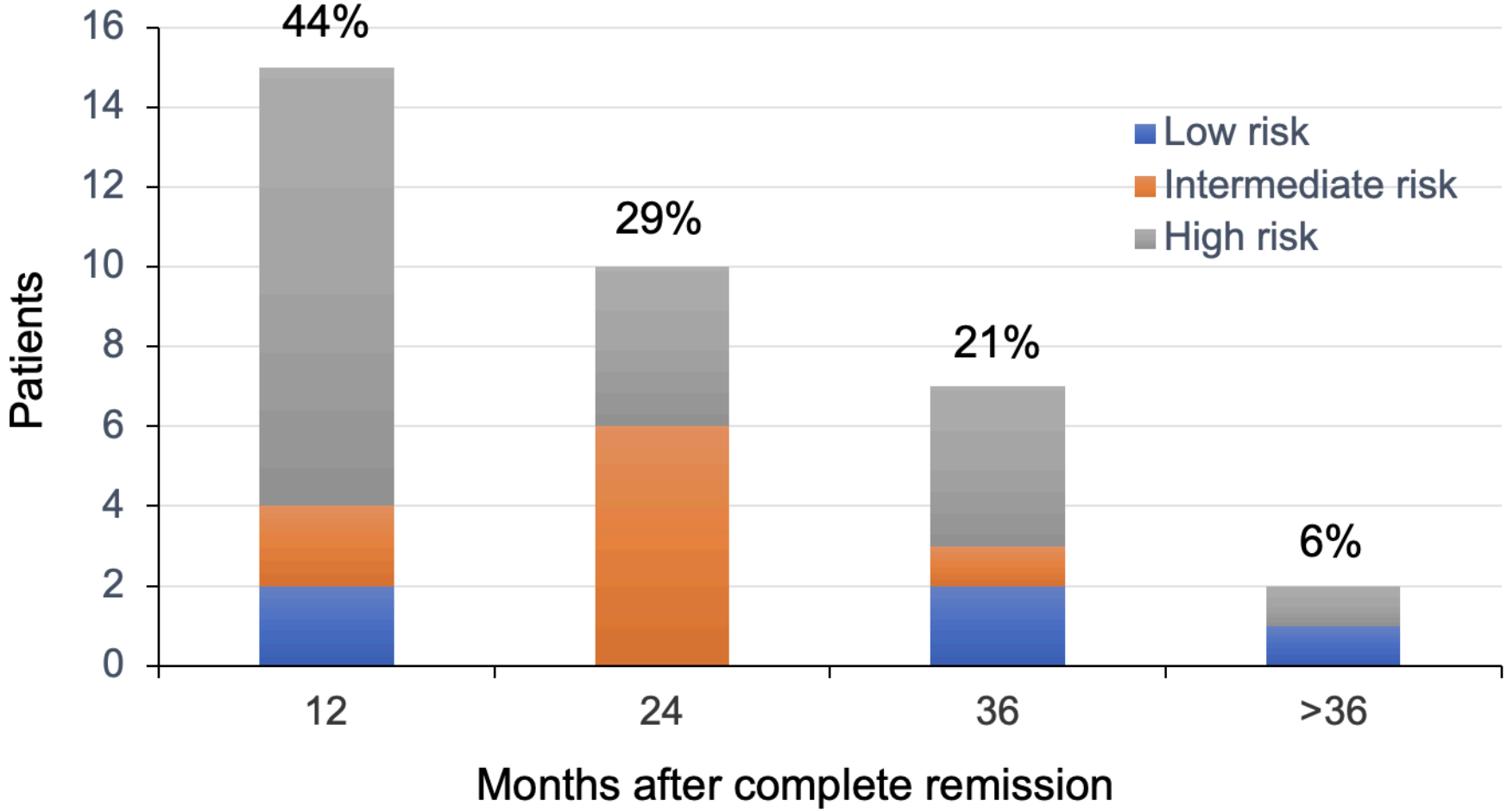

Figure 1. Number of relapsed patients per year from time of complete remission.

Figure 1