Venetoclax-Containing Regimens Improve Outcomes of Intensive Treatment and Allogeneic Hematopoietic Stem Cell Transplantation in Patients With Extramedullary Acute Myeloid Leukemia

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Background

The optimal treatment strategy for patients with **extramedullary acute myeloid leukemia (eAML)** is questionable, especially as applied to extramedullary tumor persistence while bone marrow response is achieved.

Objective

To determine whether venetoclax-containing regimens, intensive treatment, and allogeneic hematopoietic stem cell transplantation (alloHSCT) can improve outcomes in patients with eAML.

Patients

Overall, 27 patients with verified eAML were included: 14 were male and 13 were female with a median age of 40 years (13–84). Involved sites are demonstrated on Diagram 1. Multiorgan involvement was detected in 56% cases (14/26).

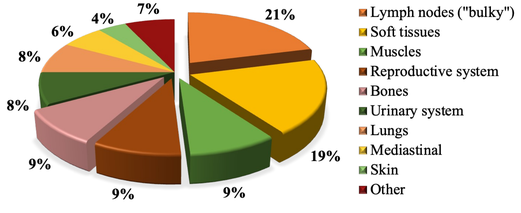


Diagram 1. Affected sites among patients with eAML

Interventions

Standard (“7+3”), high-intensity (“HiDAC”, “FLAG±Ida”), and low-intensity chemotherapy regimens were administered to all patients. Ten patients (37%) received venetoclax with 5-azacytidine (VEN-AZA) because of comorbidities or refractory disease. AlloHSCT was performed in 17 patients (63%).

Results

According to the 2017 ELN risk stratification system, 18.5% (5/27) were favorable risk, 25.9% (7/27) were intermediate risk, and 55.6% (15/27) were adverse risk. Patients with favorable genetic alterations achieved bone marrow remission more frequently (100% vs. 44%, P=0.044) but did not have advantages in the rate of complete extramedullary response (75% vs. 68%, P>0.05) (diagram 2).

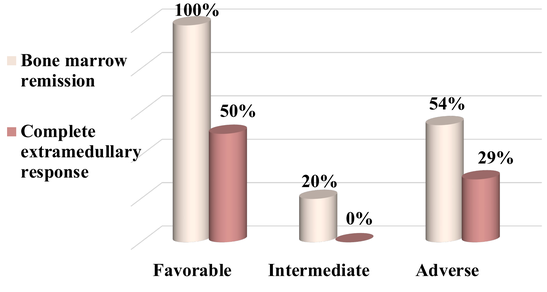


Diagram 2. Response achievement in patients of different genetic risk groups (ELN-2017) after the first induction course

Using HiDAC enabled eradication of extramedullary lesions in case of failure of standard and low-intensity regimens (85% vs. 0%, P=0.044) and decreased the rate of early (during the first 12 months) relapse (38% vs. 100%, P=0.019) (table 1).

Table 1. Efficacy of using HiDAC in patients with eAML

Type of therapy	HiDAC+	HiDAC-	P
Frequency of extramedullary response after failure of standard and low-intensity regimens	85% (11/13)	0% (0/4)	**0,044**
Early (<12 months) relapse rates	38% (5/13)	100% (5/5)	**0,019**

The overall response rate to VEN-AZA was 70% (7/10). Five patients (50%) achieved complete eradication of extramedullary tumor after venetoclax; among them, 3 still had persistent extramedullary disease after HiDAC.

Performing alloHSCT in first complete remission (CR) decreased the risk of early relapse (12% vs. 80%, P=0.015, table 2) and demonstrated better median overall survival (38.85 vs. 7.57 months, P=0.013, figure 1) and relapse-free survival (38.85 vs. 3.78 months, P=0.0021, figure 2) compared to alloHSCT performed in second and subsequent complete remissions.

Table 2. Early relapse rates depending on time of alloHSCT performing

AlloHSCT	1CR	2 and > CR	P
Early (during 12 months after alloHSCT) relapse rates	12% (1/8)	80% (4/5)	**0,015**

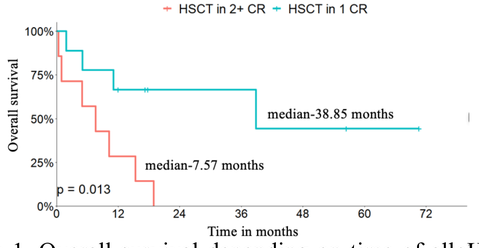


Figure 1. Overall survival depending on time of alloHSCT performing among patients with eAML

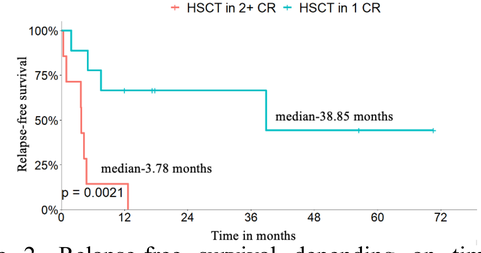


Figure 2. Relapse-free survival depending on time of alloHSCT performing among patients with eAML

Conclusions

- Favorable genetic aberrations do not increase the frequency of extramedullary response.
- Intensive treatment helps to achieve complete eradication of extramedullary tumor and reduces early relapse rate.
- Using VEN-AZA is effective among patients with eAML, including patients who were refractory to intensive treatment, and allows complete response achievement before alloHSCT.
- The best time to perform the alloHSCT among patients with eAML is the first complete remission.