



# Impact of Genetic Alterations and Types of Therapy on Outcomes of Patients with Extramedullary Acute Myeloid Leukemia and Myeloid Sarcoma: A Single-Center Experience

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## Background

**Myeloid sarcoma (MS)** and **extramedullary acute myeloid leukemia (eAML)** are characterized by proliferation of immature myeloid cells in extramedullary sites with or without effacing of the tissue architecture. Extramedullary lesions identify among **9% of AML patients**. Isolated MS is rare and occurs with frequency of about **2 cases per 1 million people**.

Nowadays, such relevant questions as the prognostic impact of genetic alterations among patients, choosing the optimal treatment strategy, the role of radiation therapy (RT), and allogeneic bone marrow transplantation (alloBMT) are discussed.

## Objective

To identify the **prognostic importance** of genetic aberrations and different types of therapy among patients with MS/eAML.

## Patients

The study included 23 eAML/MS patients: 12 males and 11 females with an age range of 13 to 78 years (median 38 years). They were classified according to the WHO criteria.

### Inclusion criteria:

- Patients diagnosed with MS/eAML;
- Patients were treated with standard AML-type chemotherapy (“7+3”, “HiDAC”, “FLAG+/-Ida”) with or without subsequent radiotherapy (RT) and allogeneic bone marrow transplantation.

### Exclusion criteria:

- The involvement of the liver, spleen, lymph nodes (except “bulky”) as well as tissue infiltration (e.g. gums), blast presence in effusions (e.g. pleural, pericardial) and cerebrospinal fluid (CSF).

## Results

- 20 patients (87%) had extramedullary lesions at the onset of the disease and 3 patients (13%) had an extramedullary relapse of AML;
- Isolated MS was verified in 3 patients (17%);
- The most common sites were lymph nodes (21%), soft tissues (17%), bones (11%), and reproductive system (11%) (*Diagram 1*);
- 57% (13/23) of patients had multiorgan involvement.

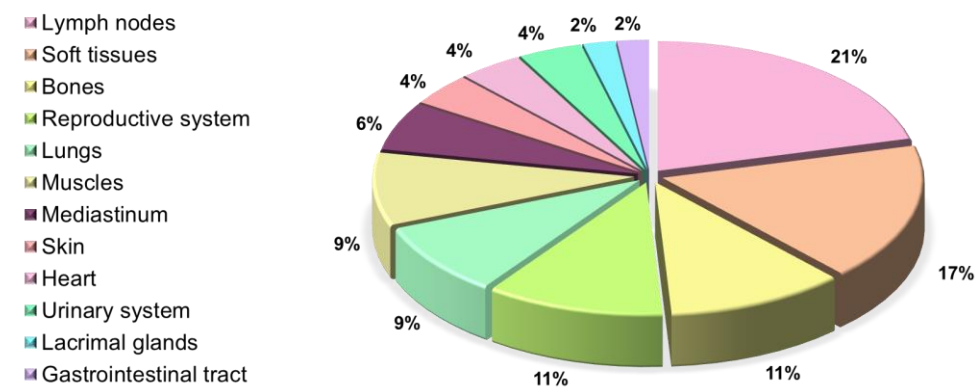


*Diagram 1. Anatomic sites affected among patients with MS/eAML*

Genetic and molecular aberration of patients with MS/eAML are presented at *Diagrams 2 and 3*. 17% (4/23), 26% (6/23), and 57% (13/23) of the patients were attributed to favorable, intermediate, and adverse risk categories, respectively (according to ELN-2017).

**There were no significant correlations between ELN-2017 risk stratification and CR rates and frequency of early (during the first 12 months) relapse ( $p>0.05$ ).**

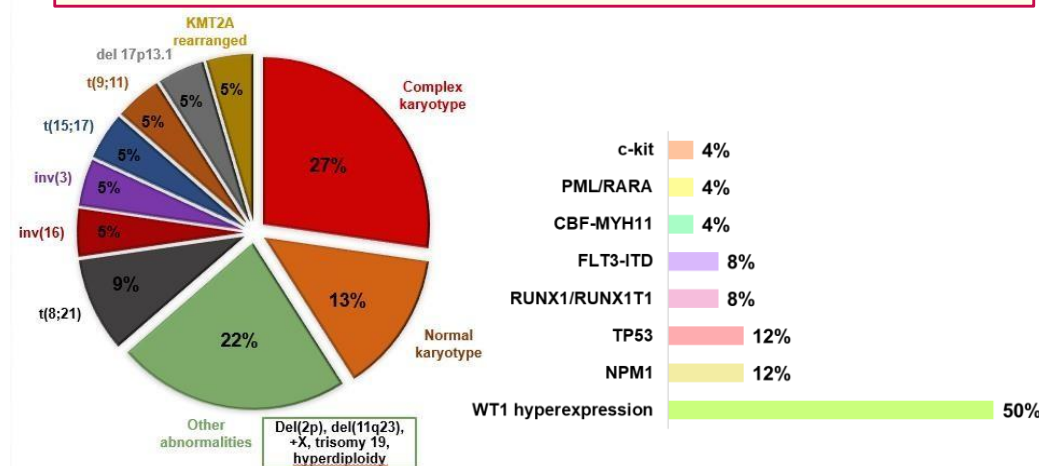


*Diagram 2. Results of cytogenetic evaluation*

*Diagram 3. Molecular markers*

Most of the patients with bone marrow involvement achieved CR (78%, 14/18), of whom 71% (10/14) achieved CR only after over 2 cycles of chemotherapy, mostly because of persistent extramedullary disease (60%, 6/10) (*Diagrams 4 and 5*).

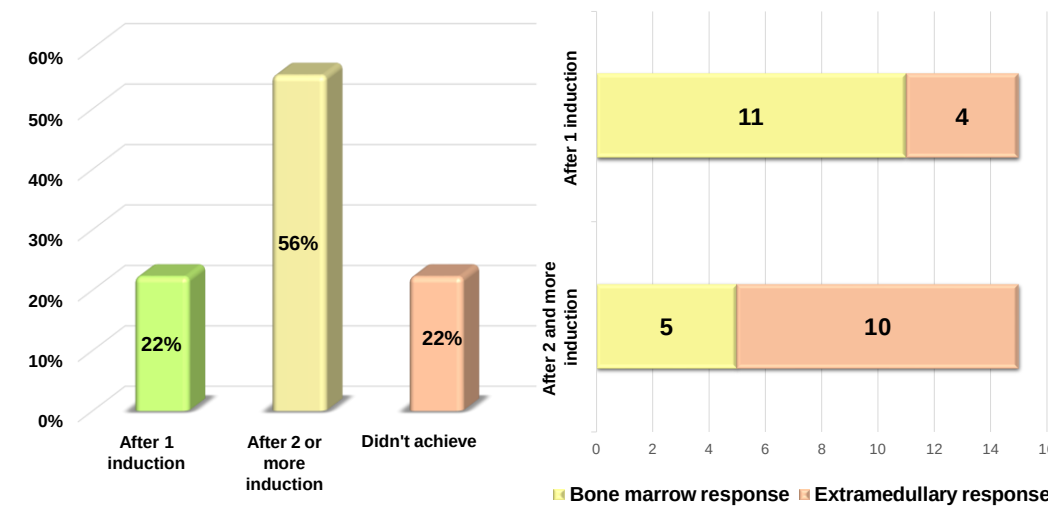


*Diagram 4. Achievement of CR after induction chemotherapy*

*Diagram 5. Achievement of bone marrow and extramedullary responses*

- Type of induction chemotherapy didn't influence on CR rates.
- Using HiDAC in consolidation therapy significantly decreased the rate of early relapse (38% vs 100%,  $p=0.019$ ) (*Table 1*).

*Table 1. Frequency of CR rates and early relapse rates depending on the different types of chemotherapy*

| Types of chemotherapy                                                                | With HiDAC    | Without HiDAC | p     |
|--------------------------------------------------------------------------------------|---------------|---------------|-------|
| All patients                                                                         | 17            | 6             |       |
| Frequency of CR rates depending on the type of induction                             | 76,5% (13/17) | 83% (5/6)     | 0.727 |
| Frequency of early relapse (<12 months) rates depending on the type of consolidation | 38,5% (5/13)  | 100% (5/5)    | 0.019 |

RT received 22% (5/23) patients. RT adding **didn't impact outcomes ( $p>0.05$ )**.

Allogeneic stem cell transplantation was performed in 74% (17/23) patients. The patients who received alloBMT at first CR had a **lower risk of early relapse (12% vs 80%,  $p=0.015$ )** (*Diagram 6, Table 2*).

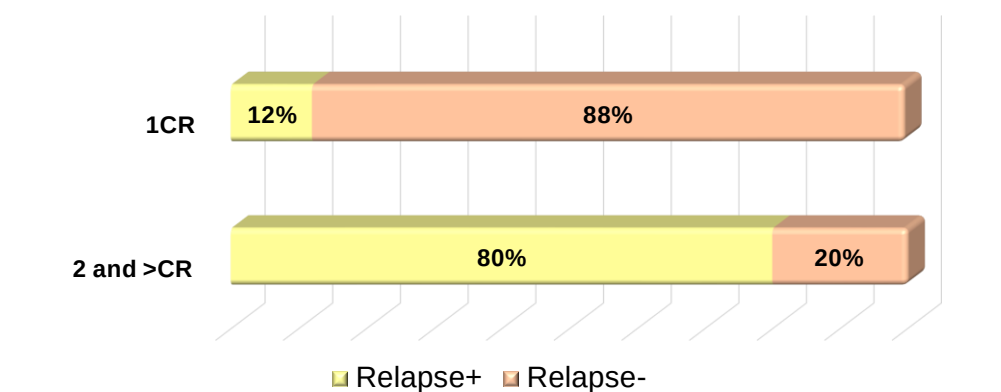


*Diagram 7. Development of relapse among patients received allogeneic stem cell transplantation*

*Table 2. Frequency of early relapses depending on the allogeneic bone marrow transplantation timing*

| Allogeneic bone marrow transplantation | 1CR       | 2 or more CR | p     |
|----------------------------------------|-----------|--------------|-------|
| All patients                           | 8         | 5            |       |
| Early relapse rates                    | 12% (1/8) | 80% (4/5)    | 0.015 |

## Conclusion

1. The most common cytogenetic and molecular abnormalities among patients with eAML/MS were complex karyotype, t(8;21), inv(16), WT1 hyperexpression, NPM1 mutation and TP53 mutation.
2. During the analysis of a very limited series of patients with eAML/MS, the ELN-2017 stratification risk group doesn't influence the outcomes.
3. Using HiDAC in consolidation therapy reduces early relapse rate.
4. The best time to perform the alloBMT among patients with eAML/MS is the first CR.