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ASSESSMENT OF PROGNOSTIC FACTORS FOR SURVIVAL AND TREATMENT OUTCOMES OF PATIENTS WITH SECONDARY ACUTE MYELOID LEUKEMIA

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INTRODUCTION

Secondary acute myeloid leukemia (sAML) is associated with shorter overall survival (OS) compared to de novo AML and remains an ongoing challenge in hematooncology [1]. The pathogenetic spectrum of sAML is heterogeneous and until now accounts for 18-28% of overall AML cases [2]. Among sAML, therapy-related AML (tAML) arises from prior cytotoxic, radiation, or immunosuppressive therapy, while MDS/MPN-AML develops from the previous clonal disorder of hematopoiesis [3]. However, the independent prognostic value of sAML itself has been questioned, as the diagnosis is often connected with older age, severe comorbidities, and an unfavorable cytogenetic and molecular profile [4].

AIM

To characterize MDS/MPN-AML and tAML patients treated at our center and evaluate relevant prognostic factors for survival, as well as treatment outcomes in these subtypes of AML.

METHOD

- We performed the single-center retrospective analysis of sAML patients diagnosed based on ELN2017 classification in the Hematology Department in Lodz, Poland [5].
- Simultaneously, the demographic data, clinical factors, and laboratory findings were collected (Table 1).
- The patients were treated according to the guidelines of the Polish Adult Leukemia Group (PALG).
- The median follow-up was 3.2 months (95%CI: 2.5-5.3).
- For statistical analysis, we used Cox proportional hazard models, the Kaplan-Meier method, log-rank, and Chi^2 tests.

Table 1. Patients' characteristics.

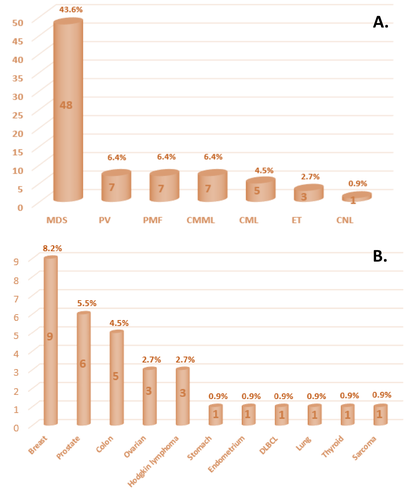
	MDS/MPN-AML	tAML
Patients, n	78	32
- **Female, n (%)**	32 (41)	19 (59)
- **Male, n (%)**	46 (59)	13 (41)
Age at diagnosis, median (Me) (IQR)	66 (60-71.75)	67.5 (62.75-72)
Primary disease, n (%)	MDS 48 (62) MPN 30 (38)	breast 9 (28) prostate 6 (19) other 17 (53)
Cytogenetic risk profile, n (%)		
- **1**	2 (3)	2 (6)
- **2**	28 (36)	5 (15)
- **3**	16 (21)	13 (41)
- **No data**	32 (41)	12 (37)
WBC at dgn. [G/l], Me (IQR)	6 (1.9-42)	6.21 (1.98-66.66)
ANC at dgn. [G/l], Me (IQR)	1.25 (0.5-11.2)	1.22 (0.27-9.91)
PB Blasts at dgn. [%], Me (IQR)	14 (4-45)	2.5 (0-30)
Plt at dgn. [G/l], Me (IQR)	45.5 (21.2-107)	45 (21.5-80)
Hb at dgn. [g/dl], Me (IQR)	8.3 (7.4-9.2)	8.4 (6.9-9.6)
LDH at dgn. [U/l], Me (IQR)	282 (230-559)	350.5 (222.7-506)
Uric acid [mg/dl], Me (IQR)	6.1 (4.6-8.2)	5.5 (4.7-7.2)
Albumin [g/dl], mean ± SD	3.6 ± 0.67	3.8 ± 0.61
BM blasts at dgn. [%], Me (IQR)	35 (25-55)	45 (27.5-63.2)
Intensive treatment, n (%)	22 (28)	5 (16)
Time since primary disease dgn. to AML dgn., Me (IQR) [months (m)]	13.5 (4.3-30)	90 (38.5-112.0)
OS since primary disease dgn., Me (IQR) [m]	26 (11-48.7)	94 (44.0-119.0)
OS since AML dgn., Me (IQR) [m]	4.1 (1.1-13.7)	2.8 (1.4-8.2)

AML – acute myeloid leukemia, MDS – myelodysplastic syndrome, MPN – myeloproliferative neoplasm, MDS/MPN-AML – AML secondary to MDS/MPN, tAML – therapy-related AML, n – number, dgn. – diagnosis, WBC – white blood count, ANC – absolute neutrophil count, PB – peripheral blood, PLT – platelets, Hb – hemoglobin, LDH – lactate dehydrogenase, BM – bone marrow, IQR – interquartile range, SD – standard deviation, OS – overall survival.

RESULTS

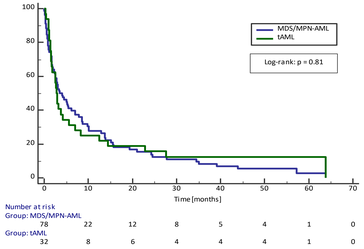
- The study included 110 patients with either MDS/MPN-AML (n=78) and tAML (n=32), with a median age of 66 (range 31-86).
- The most common hematological disorder preceding sAML was MDS (n=48) (Figure 1A), while the most frequent neoplasm previous to tAML was breast cancer (n=9) (Figure 1B).

Figure 1(A-B). Disorders previous to sAML – number of cases (% of both MDS/MPN-AML and tAML cases at the top of columns).



- The median OS for MDS/MPN-AML patients was 4.1 months (95%CI: 2.5-7.0) and for tAML 2.8 months (95%CI: 1.6-5.6). There were no differences in OS between MDS/MPN-AML and tAML (p=0.81) (Figure 2).

Figure 2. Kaplan-Meier plot for OS comparing sAML subgroups.



- Intensively treated patients had longer median OS – 13.9 months, as compared to patients receiving non-intensive therapy – 2.5 months (95%CI: 1.6-3.0 (*P<0.0001*).
- Only few patients (n=8) were eligible for alloHSCT, and it was the reason for difficulties in assessment of the role of this procedure. No difference was observed in patients treated intensively with and without alloHSCT (*P=0.14).*
- The complete or partial remission has been achieved in 39% of patients, non-response or progressive disease was noted in 41%, and early death (within 28days of diagnosis/treatment onset) occured in 20%. The ouctomes did not vary between MDS/MPN- and tAML groups.

- In the multivariate Cox regression model for OS the factors like age at diagnosis, higher ECOG score (interpreted as 2/3/4 vs. 0/1), hypoalbuminemia, and percentage of bone marrow blasts infiltration were independent predictors of poorer survival for the whole cohort. On the other hand, the intensive treatment approach was related to longer survival in both groups considered together (Table 2, Figure 3(A-E)).

Figure 3(A-E). Kaplan-Meier plots for OS in sAML comparing each predictor.

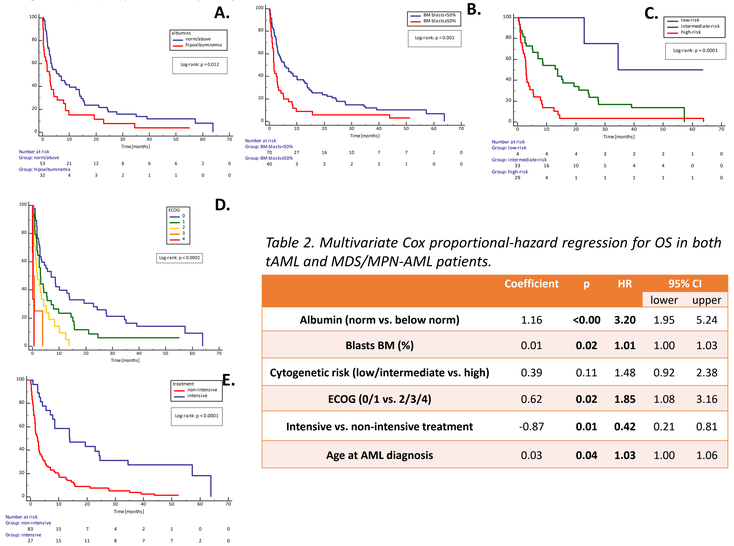


Table 2. Multivariate Cox proportional-hazard regression for OS in both tAML and MDS/MPN-AML patients.

	Coefficient	p	HR	95% CI	
				lower	upper
Albumin (norm vs. below norm)	1.16	**<0.00**	**3.20**	1.95	5.24
Blasts BM (%)	0.01	**0.02**	**1.01**	1.00	1.03
Cytogenetic risk (low/intermediate vs. high)	0.39	0.11	1.48	0.92	2.38
ECOG (0/1 vs. 2/3/4)	0.62	**0.02**	**1.85**	1.08	3.16
Intensive vs. non-intensive treatment	-0.87	**0.01**	**0.42**	0.21	0.81
Age at AML diagnosis	0.03	**0.04**	**1.03**	1.00	1.06

CONCLUSIONS

- **The poor outcomes of sAML treatment are compounded by factors such as low response rates and high early mortality, as well as older age and a history of previous neoplasm.**
- **Both the MDS/MPN-AML and tAML groups showed similar clinical characteristics, a high rate of unfavorable cytogenetics, and comparable OS.**
- **Clinical and laboratory variables, like age, ECOG, blasts level infiltration, and albumins have proven to be independent prognostic factors of OS in sAML patients.**
- **A more intensive therapeutic approach is associated with a survival benefit.**

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