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POSTER ABSTRACTS

613.ACUTE MYELOID LEUKEMIAS: CLINICAL AND EPIDEMIOLOGICAL

Poor Outcome of Patients with Acute Myeloid Leukemia in First Relapse Underscores the Need for Effective Initial Treatment

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Introduction: The incorporation of novel targeted agents into combination regimens used in the treatment of patients with acute myeloid leukemia (AML) has improved their outcomes. However, disease relapse is still challenging and associated with a poor response rate, limited therapeutic options and poor outcome. Predictors of outcome for patients in first relapse include the duration of first remission, cytogenetic risk at diagnosis, age and whether they underwent an allogeneic stem cell transplantation (alloSCT) in first remission. The incorporation of genetic aberrations detectable at diagnosis has been useful in further stratifying prognosis, but their predictive value at the time of relapse is not well established. Herein we analyze a large cohort of frontline-treated AML patients, focusing on the outcomes of patients presenting a first disease relapse.
Methods: This is a retrospective single-center study including patients diagnosed with AML from April 2017 to October 2022. Risk assessment and response to treatment were defined according to the ELN 2022 guidelines. Mutations were assessed using an 81-gene NGS panel. Survival analyses were estimated with the Kaplan-Meier method, using the log-rank test for comparison. Univariate and multivariate analysis were performed using Cox proportional hazards regression.
Results: A total of 875 patients with AML were included in the study, with a median age of 65 years old (range,18-95). According to the ELN risk category, 171 (20%) patients had favorable disease, 200 (23%) patients intermediate and 473 (54%) adverse. Patients received intensive treatment (IT; 40% of patients, 41% of whom with the addition of venetoclax) or low intensity treatments (LIT; 60% of patients, 72% with venetoclax). The overall response rate including complete remission (CR)/CR with incomplete hematologic recovery (CRi) was 73%. Among responding patients, 201 (32%) underwent alloSCT in first remission. After a median follow-up of 25 months, the median OS was 53 months for patients receiving IT and 11 months for patients receiving LIT (Figure 1). The median OS for favorable, intermediate and adverse risk patients was not achieved, 24 and 11 months, respectively. During this follow up time, 337 patients were alive and maintaining CR.
197 patients have relapsed after having achieved CR/CRi, 36 of them after undergoing alloSCT. Available data for analysis was available in 164 of these patients. The median age at relapse was 67 (21-95) and 57 (35%) received prior IT whereas 107 (65%) received LIT. At diagnosis, 15%, 16% and 69% were favorable, intermediate and adverse risk, respectively. The median time from best response to relapse was 7.5 (range,1-35) and 6.3 (range, 1-49) months for patients treated with IT and LIT, respectively. At the time of relapse, 36% of patients had a complex karyotype, 4% had *MECOM* gene rearrangement and 3% had *KMT2A* gene rearrangement. The most common mutations at time of relapse were *TP53* (34%), *DNMT3A* (34%), *TET2* (23%) and *RUNX1* (19%).
After relapse, 32 (20%) and 132 (80%) received salvage IT and LIT treatment, respectively. The CR/CRi rate for IT and LIT were 31% and 27%, respectively. The mOS from relapse was 3.4 and 5.5 months for patients with salvage IT and LIT, respectively (p=0.6). Age at relapse (mOS of 6.5 vs 5.1 months for patients age <60 and ≥60, respectively [p=0.1]), type of induction therapy (mOS of 6.6 vs 4.9 for patients receiving IT and LIT, respectively [p=0.07]), or risk classification at relapse (mOS of 4.9, 6.3 and 5.1 months for favorable, intermediate and adverse risk, respectively [p=0.7]) did not stratify patients. Duration of first remission longer than 12 months was associated with a better OS (mOS 8.1 vs 4.3 months, p=0.008). Univariate and

multivariate analysis was performed, including clinical and biological variables at diagnosis and relapse (Table 1). Importantly, high white blood cell count at relapse (HR 2.1), short first remission (HR 1.6), complex karyotype at relapse (HR 1.7) and *KMT2A* rearrangement at relapse (HR 3.8) were independent predictors of outcome after relapse.

Conclusion: Although outcomes of patients with AML have improved, disease relapse remains a major obstacle with poor outcomes despite the availability of new salvage strategies. Highly effective induction and maintenance regimens are needed to reduce the risk of relapse.

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Table 1

		Univariate analysis		Multivariate analysis	
Variable	Category	HR	pval	HR	pval
Sex	Male	0.97 (0.7-1.35)	0.860		
Venetoclax	Yes	1.16 (0.84-1.6)	0.380		
Previous HSCT	Yes	0.87 (0.59-1.28)	0.483		
trAML	Yes	1.1 (0.75-1.62)	0.614		
Type of treatment	LIT	1.38 (0.98-1.95)	0.066		
Age at diagnosis	Continuous	1.01 (1-1.02)	0.193		
WBC at relapse	> 20x10^9/L	**2.37 (1.38-4.08)**	**0.001**	**2.06 (1.09-3.89)**	**0.026**
Hgb at relapse	Continuous	**0.86 (0.77-0.96)**	**0.007**	0.91 (0.8-1.03)	0.13
Platelets at relapse	Continuous	1 (0.99-1)	0.443		
BM blasts at relapse	Continuous	**1.01 (1-1.01)**	**0.027**		
Complex karyotype	Complex	**1.83 (1.29-2.6)**	**<0.001**	**1.72 (1.07-2.77)**	**0.025**
Abn Chr5	Yes	**1.66 (1.16-2.37)**	**0.005**		
Abn Chr7	Yes	**1.72 (1.19-2.49)**	**0.003**	1.45 (0.88-2.38)	0.15
Abn Chr17	Yes	1.32 (0.88-1.98)	0.182		
Inv16	Yes	0.94 (0.39-2.32)	0.901		
KMT2A rearrangement	Yes	**3.87 (1.54-9.69)**	**0.003**	**3.81 (1.46-9.97)**	**0.006**
Diploid karyotype	Yes	**0.62 (0.43-0.91)**	**0.015**		
t(6;9)	Yes	0.32 (0.04-2.29)	0.256		
ELN Risk2022 at relapse	Intermediate Adverse	1.01 (0.53-1.91) 1.38 (0.82-2.32)	0.985 0.218		
ELN Risk 2017 at relapse	Intermediate Adverse	0.98 (0.54-1.77) 1.44 (0.91-2.27)	0.946 0.120		
Age at relapse		1.01 (1-1.02)	0.252		
Age at relapse	>60 years old	1.36 (0.93-1.99)	0.115	1.38 (0.89-2.13)	0.15
Time in remission	Continuous	0.98 (0.95-1)	0.054		
Time in remission	<12 months	**1.8 (1.22-2.64)**	**0.002**	**1.58 (1.02-2.43)**	**0.039**
ASXL1	Mutated	1.26 (0.81-1.96)	0.310		
BCOR	Mutated	1.01 (0.52-1.99)	0.968		
BCORL1	Mutated	0.82 (0.33-2)	0.657		
CBL	Mutated	1.12 (0.49-2.54)	0.792		
CEBPA	Mutated	0.65 (0.24-1.78)	0.406		
DDX41	Mutated	0.7 (0.29-1.72)	0.435		
DNMT3A	Mutated	0.81 (0.57-1.15)	0.235		
ETV6	Mutated	0.69 (0.22-2.17)	0.525		
EZH2	Mutated	1.03 (0.46-2.35)	0.936		
FLT3_TKD	Mutated	1.78 (0.83-3.83)	0.137		
FLT3_ITD	Mutated	0.95 (0.55-1.62)	0.849		
GATA2	Mutated	0.73 (0.32-1.65)	0.447		
IDH1	Mutated	0.57 (0.28-1.17)	0.125		
IDH2	Mutated	0.75 (0.46-1.22)	0.245		
KIT	Mutated	0.9 (0.13-6.48)	0.919		
KRAS	Mutated	1.56 (0.76-3.21)	0.227		
NPM1	Mutated	1.05 (0.66-1.68)	0.827		
NRAS	Mutated	1.09 (0.69-1.72)	0.707		
PHF6	Mutated	1.55 (0.67-3.55)	0.303		
PTPN11	Mutated	1.93 (0.78-4.77)	0.153		
RAD21	Mutated	1.28 (0.47-3.49)	0.629		
RUNX1	Mutated	0.84 (0.55-1.27)	0.397		
SETBP1	Mutated	1.01 (0.25-4.11)	0.983		
SF3B1	Mutated	0.61 (0.28-1.31)	0.207		
SMC1A	Mutated	2.2 (0.8-6.03)	0.125		
SMC3	Mutated	0.17 (0.02-1.24)	0.081		
SRSF2	Mutated	1.12 (0.72-1.73)	0.611		
STAG2	Mutated	1.01 (0.47-2.17)	0.970		
TET2	Mutated	1.12 (0.76-1.64)	0.566		
TP53	Mutated	**1.72 (1.21-2.45)**	**0.002**		

Figure 1

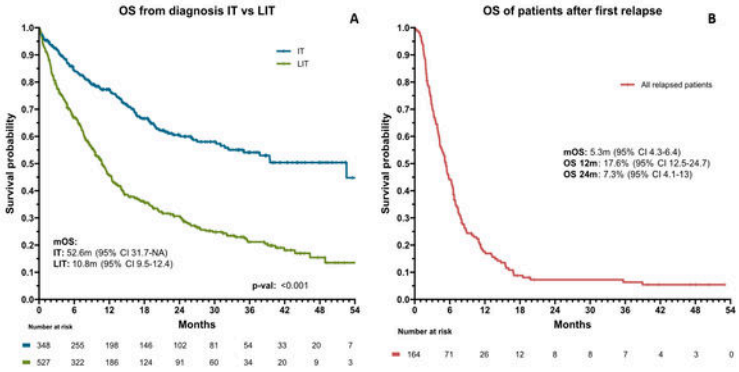

Figure 1

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