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POSTER ABSTRACTS

613.ACUTE MYELOID LEUKEMIAS: CLINICAL AND EPIDEMIOLOGICAL

Identification of Characteristics and Prognostic Impact of *FUS-ERG* and *AML1-MTG16* Fusion Genes in Adult AML Patients

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Background

FUS-ERG and *AML1-MTG16* are two rare fusion genes in acute myeloid leukemia (AML), characterized by similar karyotypic abnormalities, namely t(16;21)(p11;q22) and t(16;21)(q24;q22), respectively. A previous research has demonstrated that *FUS-ERG* represents a high-risk subtype associated with an extremely poor prognosis, while *AML1-MTG16* has favorable outcomes in pediatric cohort. Despite this valuable insight, a comprehensive systematic review of these fusion genes in the adult population remains absent.

Method

In this study, we conducted an extensive collection of AML patients with *FUS-ERG* or *AML1-MTG16* fusion genes, who were reported in Mitelman Database of Chromosome Aberrations and Gene Fusions in Cancer, PubMed and China national knowledge infrastructure (CNKI) from 1988 to 2023. Patients lacking detailed survival data or those who did not receive treatment were excluded. Additionally, patients diagnosed and treated in our institution between 2018 and 2023 were included if they were identified as carrying *FUS-ERG* or *AML1-MTG16* fusion genes.

The reference cohort comprised of 669 adult AML patients (excluding the t(16;21) cases and acute promyelocytic leukemia) admitted to our institution from 2016 to 2021. All patients within the cohort were classified into 3 categories based on the 2022 ELN genetic risk classification, namely favorable (F), intermediate (I) and adverse (A) risk. These patients were then compared with the *FUS-ERG* and *AML1-MTG16* groups to explore their respective clinical features and prognosis.

Results

A total of 800 patients were included for analysis (Table 1). Patients with *FUS-ERG* (n=111) exhibited significant distinctions, including a younger onset age (34 years vs. 59 years), lower platelet count (30×10^{9}/L vs. 51×10^{9}/L), higher bone marrow blasts proportion (80.0% vs. 60.0%), a higher relapse rate (78.6% vs. 44.7%) and a higher incidence of trisomy 8 (16.4% vs. 9.0%), trisomy 10 (9.1% vs. 0.3%) and complex karyotype (37.8% vs. 11.6%), when compared to the reference cohort ($p<0.01$). Meanwhile, patients with *AML1-MTG16* (n=20) primarily presented as the secondary AML (70.0%), and displayed a higher prevalence of trisomy 8 (40.0%) and complex karyotype (35.0%) than reference cohort ($p<0.01$).

The *FUS-ERG* patients had a less median overall survival (OS) when compared to the reference cohort (13 vs. 35 months, $p<0.001$). The median OS in subgroups with ELN 2022 F-risk vs. ELN 2022 I-risk vs. *FUS-ERG* was not reached (NR) vs. 33.6 months vs. 13.0 months ($p<0.001$) and the median OS of *FUS-ERG* group was even inferior to ELN 2022 A-risk group (13.0 vs. 16.8 months, $p=0.015$). Furthermore, the *FUS-ERG* patients also displayed a less median disease-free survival (DFS) than the reference cohort (7.5 vs. 20.5 months, $p<0.001$). The median DFS in subgroups with F-risk vs. I-risk vs. A-risk vs. *FUS-ERG* was NR vs. 19.8 vs. 13.3 vs. 7.5 months ($p<0.001$).

In contrast, patients with *AML1-MTG16* had a median OS of 18.7 months and a median DFS of 16 months, presenting a relatively unfavorable OS trend and indistinctive DFS, when compared to the reference cohort (OS: $p=0.083$, DFS: $p=0.612$), F-risk (OS: $p<0.001$, DFS: $p=0.128$), I-risk (OS: $p=0.162$, DFS: $p=0.835$) and A-risk (OS: $p=0.877$, DFS: $p=0.731$). Moreover, the *AML1-MTG16* group had a better DFS than the *FUS-ERG* group (14.0 vs. 7.5 months, $p=0.016$), but their OS was comparable (16.0 vs. 7.5 months, $p=0.219$).

For adult patients with *FUS-ERG* (Table 2) multivariate analysis revealed that age >60 years (HR=2.96, 95%CI: 1.14-7.73, p=0.026), WBC >100×10^9/L (HR=2.98, 95%CI: 1.24-7.13, p=0.014) and the presence of monosomy (HR=2.61, 95%CI: 1.21-5.66, p=0.015) were independent risk factors for OS, while monosomy was associated with poor DFS (HR=3.72, 95%CI: 1.69-8.20, p=0.001). However, receiving HSCT could significantly improve both OS (HR=0.22, 95%CI: 0.11-0.42, p<0.001) and DFS (HR=0.31, 95%CI: 0.16-0.57, p<0.001).

Pediatric *FUS-ERG* patients presented similar clinical features, exhibiting a better median OS (19.5 vs.13 months, p=0.014) and a comparable median DFS (9.5 vs. 7.5 months, p=0.496), when compared to the adult population.

Conclusion

Both *FUS-ERG* and *AML1-MTG16* were identified as high-risk subgroups in adult AML anddiffered from the results in pediatric cohort. Several factors including age, WBC count, HSCT and monosomy influenced the prognosis of adult AML patients with *FUS-ERG*.

Disclosures No relevant conflicts of interest to declare.

Table 1 Clinical characteristics of adult AML patients with *FUS-ERG* and *AML1-MTG16*

Characteristics	N	*FUS-ERG* (n=111)	p-value*	*AML1-MTG16* (n=20)	p-value*	Reference Cohort (n=669)
Sex: Female (%)	800	48/111 (43.2)	0.18	13/20 (65.0)	0.19	335/669 (50.1)
Median age (range), years	800	34.0 (18.0-81.0)	**<0.01**	51.0 (19.0-76.0)	0.11	59.0 (18.0-93.0)
Hematological tests						
Median WBC (range), $\times10^9$/L	765	14.6 (0.5-168.6)	0.39	5.4 (1.0-78.8)	0.42	11.1 (0.2-531.8)
Median Hb (range), g/L	741	82.0 (34.0-147.0)	0.60	84.0 (10.0-114.0)	0.68	82.0 (36.0-175.0)
Median PLT (range), $\times10^9$/L	741	30.0 (2.0-219.0)	**<0.01**	34.0 (17.0-109.0)	0.13	51.0 (3.0-552.0)
Median PB blasts (range), %	70	78.0 (3.0-99.0)		37.0 (1.0-81.0)		
Median BM blasts (range), %	747	80.0 (20.8-99.0)	**<0.01**	67.5 (32.0-94.5)	0.32	60.0 (10.0-98.0)
FAB-type (%)	800		**<0.01**		**<0.01**	
M0		1/111 (0.9)		0/20 (0.0)		29/669 (4.3)
M1		27/111 (24.3)		3/20 (15.0)		30/669 (4.5)
M2		22/111 (19.8)		10/20 (50.0)		266/669 (39.8)
M4		12/111 (10.8)		2/20 (10.0)		44/669 (6.6)
M5		37/111 (33.3)		2/20 (10.0)		291/669 (43.5)
M7		2/111 (1.8)		0/20 (0.0)		0/669 (0.0)
NOS		8/111 (7.2)		3/20 (15.0)		9/669 (1.3)
Special		2/111 (1.8)		0/20 (0.0)		0/669 (0.0)
Secondary (%)	131	3/111 (2.7)		14/20 (70.0)		
Cytogenetics (%)						
Sole abnormality	131	42/111 (37.8)		5/20 (25.0)		
Trisomy 8	731	18/110 (16.4)	**<0.01**	8/20 (40.0)	**<0.01**	54/601 (9.0)
Trisomy 10	731	10/110 (9.1)	**<0.01**	0/20 (0.0)	0.80	2/601 (0.3)
Monosomy	731	19/110 (17.3)	0.14	3/20 (15.0)	0.70	73/601 (12.1)
Complex karyotype	732	42/111 (37.8)	**<0.01**	7/20 (35.0)	**<0.01**	70/601 (11.6)
Treatment (%)						
CR obtained	790	85/101 (84.2)	0.39	15/20 (75.0)	0.54	539/669 (80.6)
Refractory	106	59/88 (67.0)		13/18 (72.2)		
Relapsed	638	66/84 (78.6)	**<0.01**	5/15 (33.3)	0.38	241/539 (44.7)
HSCT	125	38/105 (36.2)		7/20 (35.0)		
Survival (%)						
3-year-DFS (95% CI)	632	9.5 (4.3-21.3)	**<0.01**	20.4 (4.3-96.6)	0.61	42.6 (37.5-48.4)
3-year-OS (95% CI)	800	11.4 (5.9-22.3)	**<0.01**	12.9 (2.4-68.7)	0.08	48.7 (43.6-54.3)

※N is the number of non-missing value; WBC: white blood cell; Hb: hemoglobin; PLT: platelet; PB: peripheral blood; BM: bone marrow; FAB: French–American–British; CR: complete remission; HSCT: hematopoietic stem cell transplantation; DFS: disease-free survival; OS: overall survival.
*Compared with the reference cohort.

Table 2 Multivariate analysis of OS and DFS among the adult patients with *FUS-ERG*

Variable*	OS (N=68)		DFS (N=69)	
	HR [95%CI]	p-value	HR [95%CI]	p-value
Age (>60 years)	2.96 [1.14-7.73]	0.026		
WBC (>100×10^9/L)	2.98 [1.24-7.13]	0.014		
Received HSCT	0.22 [0.11-0.42]	<0.001	0.31 [0.16-0.57]	<0.001
Monosomy	2.61 [1.21-5.66]	0.015	3.72 [1.69-8.20]	0.001

※N is the number of non-missing value; WBC: white blood cell; HSCT: hematopoietic stem cell transplantation; DFS: disease-free survival; OS: overall survival.
*The variables whose P-value <0.20 in univariate analysis were included into multivariate analysis.

Figure 1

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