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POSTER ABSTRACTS

613.ACUTE MYELOID LEUKEMIAS: CLINICAL AND EPIDEMIOLOGICAL

Improving Prediction of Early Death in Acute Promyelocytic Leukemia: External Validation Study from Italian Single Center Experience

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Background: Despite significant advancements in treatment efficacy of acute promyelocytic leukemia (APL), early death (ED) - mainly related to major hemorrhagic and thrombotic events occurring within 30 days from diagnosis - remains a prominent hurdle to therapeutic success. In this regard, *Österroos et al.* very recently developed a score which stratifies the risk of ED of patients (pts) with APL in three categories (low [score 0-2], high [score 3-4], very high [score 5-7]) according to age (<50 years, 50-59 years, 60-69 years and ≥70 years), white blood cell count (<3.0x10 ^{9}/L, 3.0-5.0x10 ^{9}/L and >5.0x10 ^{9}/L), and platelet count (≥30x10 ^{9}/L and <30x10 ^{9}/L), all of which are readily available, real-world variables. However, the presence of specific comorbidities, or diseases characteristics, such as the presence of *FLT3*-ITD mutation, CD2 expression and bcr3 *PML::RARA* transcript were not evaluated, even if they could potentially further improve the risk stratification (*Österroos et al.* Haematologica 2022;107(7):1528-1537).
Aims: The aims of this study were to integrate the score proposed by *Österroos et al.* and evaluate the role of pts comorbidities and disease biological data in modifying risk stratification.
Methods: Data were retrospectively collected from 127 consecutive pts diagnosed at our Center from January 2000 to May 2023. Patients had been treated according to the AIDA protocol (n = 76, 60%) or with the combination of *all-trans* retinoic acid (ATRA) and arsenic trioxide (ATO) (n = 39, 31%) (*Lo-Coco et al.* N Engl J Med 2013;369:111-121); 10 pts received ATRA; only 2 pts did not receive any treatment.
Results: Table 1 summarizes the main clinical characteristics of the 127 pts included in this study. Overall, ED rate was 11% (n = 14, 12 died within 7 days from diagnosis); the cause of death was a hemorrhagic event in 11 pts. The score identified low- (n = 79, 64%), high- (n = 39, 31%) and very high-risk (n = 6, 5%) categories; ED rates for each category were 3.8%, 20.5% and 0%, respectively. Despite no ED events were registered in our small very-high risk cohort (n = 6), a third of these pts (n = 2) experienced cerebral hemorrhage at disease onset and eventually survived. We confirmed that the score proposed by *Österroos et al.* was better at predicting ED risk than the Sanz score, with the Area Under the Receiver Operating Characteristic (AUROC) curve of 0.73 (95% CI 0.60-0.87) vs 0.66 (95% CI 0.51-0.81). The AUROC of the reference study cohort was 0.77 (95% CI 0.72-0.83).
The presence of specific biological characteristics of the disease, such as *FLT3*-ITD mutation, bcr3 *PML::RARA* transcript or CD2 expression were not associated with an increased risk of ED (Table 2). Similarly, the presence of comorbidities (i.e. cardiovascular diseases, hypertension, chronic kidney disease, diabetes mellitus, dyslipidemia, and smoking) were not associated with an increased risk of ED (data not shown). By univariate analysis the presence of fever at diagnosis and male sex showed a trend toward an increased risk of ED (OR 3.77, 95% CI 0.88-19.26, P = 0.08 and OR 3.13, 95% CI 0.92-14.36, P = 0.09, respectively).
Conclusions: Our data support the use of the score developed by *Ö sterroos et al.* to better predict the risk of ED in APL and to select the pts who may benefit from more aggressive supportive care. The presence of fever at diagnosis and male sex

seems to be associated with a further increase in the risk of ED but this association needs to be confirmed in a larger study. The integration of biological characteristics of disease and comorbidities does not improve the risk stratification of ED.

Disclosures Frigeni: *AbbVie:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Jazz Pharmaceutical:* Honoraria. **Galli:** *Amgen:* Honoraria; *BMS:* Honoraria; *GSK:* Honoraria; *Janssen:* Honoraria; *Menarini:* Honoraria; *Sanofi:* Honoraria; *Takeda:* Honoraria. **Lussana:** *Incyte:* Speakers Bureau; *Bristol Myers Squibb:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *AbbVie:* Membership on an entity's Board of Directors or advisory committees; *Clinigen:* Membership on an entity's Board of Directors or advisory committees; *Pfizer:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Amgen:* Speakers Bureau. **Rambaldi:** *Abbvie:* Honoraria.

Table 1. Patients characteristics (N=127)

Characteristics	N (%)
Age at diagnosis, median (range)	48 (19-81)
Sex	
male	72 (57)
female	55 (43)
PML RARA isoform	
bcr 1-2	76 (61)
bcr 3	49 (39)
CD2 positivity	31 (25)
FLT3-ITD*	18 (28)
White blood cells x10^9/L, median (range)	2 (0-176)
Hemoglobin g/dl, median (range)	9 (4-15)
Platelets x10^9/L, median (range)	30 (1-260)
Sanz Risk score	
Low	36 (28)
Intermediate	60 (47)
High	31 (24)
Early Death Risk score#	
low	79 (64)
high	39 (31)
very high	6 (5)
Fever§	39 (33)

* 62 missing data;
# 3 missing data;
§ 8 missing data

Table 2: univariate analysis on death within 30 days

Factors	No ED, N=113	ED, N=14	OR (95% CI)	P
Age at diagnosis	49 (21-81)	39 (19-62)	0.96 (0.92-0.99)	0.0344
Sex				
female	52 (46)	3 (21)	1	
male	61 (54)	11 (79)	3.13 (0.92-14.36)	0.0928
PML RARA isoform				
bcr 1-2	70 (62)	6 (50)	1	
bcr 3	43 (38)	6 (50)	1.63 (0.48-5.52)	0.4236
CD2 positivity				
no	85 (75)	9 (75)	1	
yes	28 (25)	3 (25)	1.01 (0.21-3.67)	0.9865
FLT3-ITD				
no	44 (73)	3 (60)	1	
yes	16 (27)	2 (40)	1.83 (0.23-12.06)	0.5271
White blood cells x10^9/L	2 (0-72)	27 (2-176)	1.04 (1.02-1.07)	0.0003
Hemoglobin g/dl	9 (4-15)	9 (4-12)	0.88 (0.66-1.17)	0.3874
Platelets x10^9/L	31 (1-260)	27 (13-86)	1 (0.97-1.01)	0.6150
Sanz Risk score				
Low	34 (30)	2 (14)	1	
Intermediate	55 (49)	5 (36)	1.55 (0.31-11.21)	0.6146
High	24 (21)	7 (50)	4.96 (1.09-35.28)	0.0581
Early Death Risk score				
low	76 (67)	3 (27)	1	
high	31 (27)	8 (73)	6.54 (1.76-31.36)	0.0082
very high	6 (5)	0 (0)	NA	0.9929
Fever				
no	77 (69)	3 (37)	1	
yes	34 (31)	5 (63)	3.77 (0.88-19.26)	0.0800

Figure 1

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