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POSTER ABSTRACTS

613.ACUTE MYELOID LEUKEMIAS: CLINICAL AND EPIDEMIOLOGICAL

The ELN 2022 Risk Stratification Has No Impact on the Dismal Prognosis of Patients with Acute Undifferentiated Leukemia

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Introduction: Acute undifferentiated leukemia (AUL) is a rare subtype of acute leukemia. It is characterized by lack of expression of myeloid or lymphoid lineage markers, frequently expressing CD56 or CD7. The dismal prognosis of AUL was reported in small studies; the largest previously reported group with this disorder included 24 patients (Weinberg, Mod Pathol, 2019). Furthermore, data are lacking regarding cytogenetic and molecular patterns of AUL. In this study, the cytogenetic and molecular changes of AUL patients are described, together with the clinical outcome.
Methods: AUL was defined, in accordance with the WHO classification, as an acute leukemia that does not qualify for myeloid, B- or T-cell lineage. Immunophenotyping of BM cells at diagnosis was performed using 8-color flow cytometry. Multi-parameter Cytognos acute orientation tube (ALOT) and the combination of the following antigens were used: CD34/CD117/CD14/CD56/CD36/CD123/HLA-DR/CD45/CD64/CD11c. (Weinberg, Mod Pathol, 2019).
Results: Three hundred and eighty-five patients with acute myeloid leukemia (AML) were diagnosed at Rambam Health Care Campus in Haifa, Israel between April 2015 and April 2021, of whom 30 (8%) were defined as AUL. The baseline characteristics are presented in Table 1. The median age was 62 years, none of the patients harbored NPM1 mutation, with 1 patient expressing FLT3-ITD mutation. Cytogenetic analysis was completed for all patients: 9 (30%) had adverse-risk cytogenetics by ELN 2022 criteria. A comprehensive molecular study using molecular inverted probe was performed on all patients, with final results available on 17. Nine of these 17 (53%) had high-risk mutations; RUNX1 was found in 4 patients. Notably, 4 other patients had JAK2 mutation, with or without previous myeloproliferative neoplasm. Only 3 patients had mutations characterizing secondary AML (Lindsley, Blood, 2015). Only 2 patients in this cohort had TP53 mutation or del17p. Fourteen patients were classified as adverse-risk AML by ELN 2022 using cytogenetic and molecular markers, while 15 were classified as intermediate risk. Only 4 patients in this adverse-risk cohort were not allogeneic hematopoietic stem cell transplant (HSCT) candidates due to age or comorbidity limitations.
The outcome of the cohort is presented in Table 2. Twenty-two fit patients received 7+3 intensive chemotherapy, of whom 10 achieved complete remission (CR) after induction. Four of the 10 patients needed reinduction chemotherapy due to a high blast count on the bone marrow performed at day 14. Five patients were treated with low-intensity therapies such as hypomethylating agents ± novel agents; 2 achieved CR. One patient received FLAG-Ida chemotherapy and another patient was treated with ECOG1910 protocol due to clinical presentation more compatible with acute lymphoid leukemia; both achieved CR. Of the 14 patients achieving CR, 4 relapsed before HSCT and needed further salvage therapy. Eventually, 13 (50% of the transplant-eligible candidate cohort) patients proceeded to HSCT. Relapse occurred in 14 patients (10 post-HSCT and 4 before HSCT), none of them achieved long-term survival. Four of the 30 patients are alive, all in remission. The median overall survival of the entire cohort is 1 year (Fig 1). The outcome of patients with adverse or intermediate risk according to the ELN risk classification did not differ. The CR rate and relapse rate and median overall survival (OS) were similar in both groups (Table 2; Fig 1).
Discussion: These data emphasize the dismal outcome of patients diagnosed with AUL, with the 5-year OS of 7.5%, far lower than the survival of other types of acute leukemia. In this cohort, 15 patients were classified as intermediate risk AML; yet, their CR rate and long-term survival were not different from the whole cohort. The CR rate achieved with the widely used

7+3 protocol, was inferior, raising the question whether this protocol should be the "standard of choice" in such patients. A limitation of this study is that not all patients were evaluated by the NGS panel, bringing about the issue whether more patients had high-risk mutations, who would then be classified as adverse risk.
Conclusion: The unique subtype of AUL is associated with a particularly adverse risk genotype, irrespective of known prognostic determinants, as in the 2022 ELN classification.

Disclosures Zuckerman: *Novartis:* Honoraria, Speakers Bureau; *Janssen:* Honoraria, Speakers Bureau; *Cellect Biotechnology:* Honoraria, Speakers Bureau; *BioSight Ltd:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Gilead:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Orgenesis:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau.

Table 1: Patient characterestics

	All (n=30)	Intemediate (n=15)	Adverse (n=14)
Age (range)	62 [22-94]	59 [40-75]	63 [22-82]
FLT3-ITD or TKD	1	0	1
NPM1	0	0	0
JAK2	4	2	2
Secondary type mutations*	3	0	3

* SRSF2, SF3B1, U2AF1, ZRSR2, ASXL1, EZH2, BCOR, STAG2

Table 2: Response assessment

	All (n=30)	Intemediate (n=15)	Adverse (n=14)
Induction 7+3 Low intensity Other	29 22 4 3	15 11 2 2	14 11 2 1
CR1 (%)	15 (52)	8 (53)	7 (50)
HSCT at any time	13	7	6
Relapse rate (%) Pre-transplant Post-trasnplant	14 (48) 4 10	7 (47)	7 (50)
Survival [n]	4	2	2
Median OS [years]	1	1.3	0.7

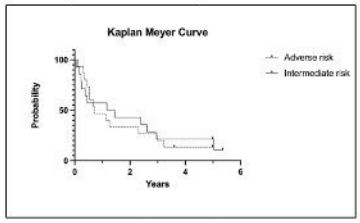

Figure 1: Overall survival

Figure 1

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