

## Abstract: P508

### Title: THE PROGNOSTIC SIGNIFICANCE OF THE MEASURABLE RESIDUAL DISEASE STATUS WITHIN THE THREE AML ELN2022 RISK GROUPS

**Abstract Type:** Poster Presentation

**Session Title:** Acute myeloid leukemia - Clinical

#### Background:

The 2022 updated European LeukemiaNet (ELN) risk classification for acute myeloid leukemia (AML) includes risk adjustments during disease course by measurable residual disease (MRD) assessment. While the ELN2022 classification suggests MRD adjustment in patients (pts) with favorable (fav) or intermediate (int) risk, studies with regard to the utility of MRD also including the adverse (adv) risk group are pending.

#### Aims:

To evaluate the clinical value of the MRD status at allogeneic hematopoietic stem cell transplantation (HSCT) within all three diagnostic ELN2022 risk groups.

#### Methods:

We analyzed 229 AML pts who could be unambiguously classified according to the ELN2022 risk classification at diagnosis and underwent consolidating HSCT (median age 61.5, range 16.3-76.4 years) in first (78%) or second (22%) complete remission (CR) or CR with incomplete peripheral count recovery (CRi). Conditioning regimens were non-myeloablative (77%), reduced-intensity (7%), or myeloablative (16%). At diagnosis, cytogenetics, as well as the mutation status of 54 recurrently mutated genes were evaluated. All pts had blood or bone marrow remission material up to 28 days prior to HSCT available for MRD analysis based on *NPM1* mutations or *BAALC*, *MN1*, or *WT1* expression. MRD positivity was defined as being positive for any of the analyzed markers, and outcomes were analyzed for each ELN2022 risk group separately. Median follow up after HSCT was 3.9 years.

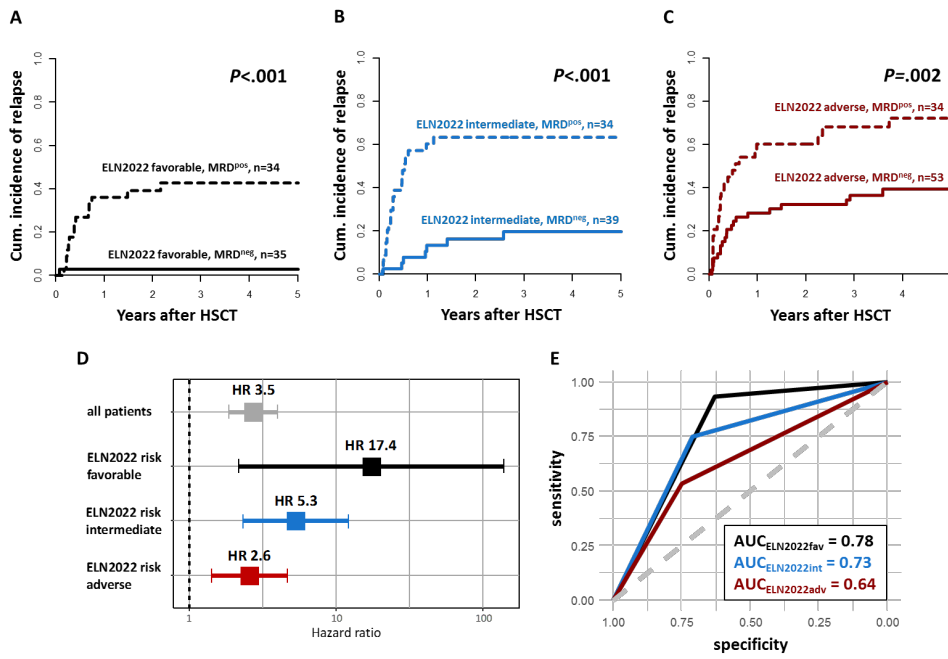
#### Results:

ELN2022 risk at diagnosis was fav (n=69), int (n=73), or adv (n=87). The percentage of pts attaining a MRD-negative (neg) remission did not differ significantly according to ELN2022 risk at diagnosis (fav 51% vs int 53% vs adv 61%,  $P=.40$ ). A total of 38% of pts relapsed after HSCT with a significantly higher risk of relapse in MRD-positive (pos) than in MRD-neg pts ( $P<.001$ , Hazard Ratio [HR] 3.5 [range 2.2-5.5]) in the whole cohort. Regarding the diagnostic ELN2022 groups, the MRD status at HSCT significantly impacted the cumulative incidence of relapse (CIR) in all three groups (fav:  $P<.001$ , int:  $P<.001$ , adv:  $P=.002$ , Figure 1A-C). However, the relative risk of relapse for MRD-pos vs MRD-neg pts decreased with higher diagnostic ELN2022 risk: the HR for relapse was highest in ELN2022 fav (HR 17.4, range 2.2-139), lower in int (HR 5.3, range 2.3-12.1), and lowest in adv risk pts (HR 2.6, range 1.4-4.7, Figure 1D). Similarly, the c-statistics was highest in ELN2022 fav (0.78), lower in int (0.73) and lowest in adv risk pts (0.64, Figure 1E).

While overall, the risk of relapse after HSCT increased with higher ELN2022 risk at diagnosis, this was especially seen in MRD-neg pts at HSCT (at 5 years, fav vs int vs adv: 3% vs 20% vs 39%) and less in MRD-pos pts at HSCT (43% vs 63% vs 72%). Similar results were observed when we excluded *NPM1* based MRD from the analysis. In contrast, the time to relapse did not differ significantly between the three ELN2022 risk groups in MRD-neg (one pts after 27 vs median 346 vs median 131 days,  $P=.24$ ) or MRD-pos (median 138 vs 93 vs 83 days,  $P=.25$ ) pts suffering relapse.

**Summary/Conclusion:** Although the MRD status at HSCT was a significant factor for CIR in all ELN2022 risk groups, the relative risk of relapse between MRD-neg and MRD-pos pts at HSCT depended on the ELN2022 risk at diagnosis and was lowest in ELN2022 adv risk pts. Especially MRD-neg pts with adverse diagnostic ELN2022 risk still had a high risk of relapse, most likely due to a higher "background" relapse risk of a more aggressive AML

phenotype. This should be taken into account during clinical surveillance after HSCT.



**Keywords:** AML, Clinical outcome, ELN, HSCT