Abstract: P529

Title: THE EFFECT OF AGE AND TREATMENT ON THE PREDICTIVE VALUE OF MEASURABLE RESIDUAL DISEASE: IMPLICATIONS FOR THE CLINICAL MANAGEMENT OF ADULT PATIENTS WITH ACUTE MYELOID LEUKEMIA

Abstract Type: Poster Presentation

Session Title: Acute myeloid leukemia - Clinical

Background:

Measurable residual disease (MRD) is a powerful predictor of outcome in acute myeloid leukemia (AML). In the early phases of treatment, MRD refines risk stratification and is used for the allocation to allogeneic transplant. However, the universal successful application of MRD is challenged by a not negligible fraction of patients who relapse albeit achieving MRD_{neg} status.

Aims:

The aim of our work was to assess the influence of baseline features and treatment intensity on the predictive value of MRD_{neg} status after first consolidation (MRD2).

Methods:

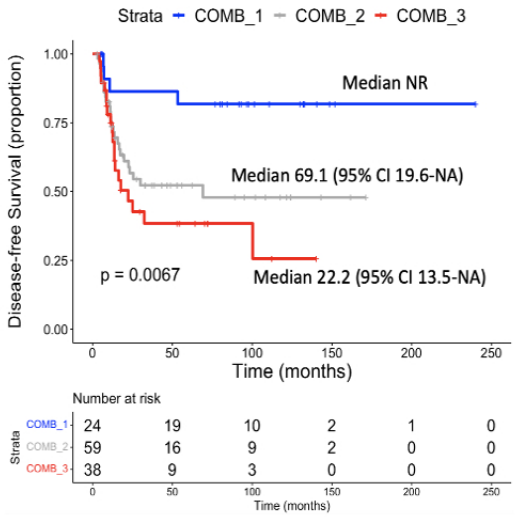
Patients in study had untreated AML and were intensively treated. For the purpose of the study, the first two chemotherapy cycles were categorized for treatment intensity according to cytarabine (ARA-C) dose: standard (SDAC) included regimens sharing a single dose infusion of 100-200 mg/m^2 and a cumulative dose up to 1.400 mg/m^2; high (HDAC) included schedules sharing a single dose infusion of at least 1.000 mg/m^2 and a cumulative dose of at least 8.000 mg/m^2. For CBF-related and *NPM1*-mutated AML, MRD categorization based on PCR data. For the remaining cases, multi-parameter flow cytometry (MFC) was used. To validate our findings on treatment effect, we carried out an in-silico analysis by extracting survival data from Kaplan-Meier curves through the commercial graph digitizer software (DigitizeIt 2.1; Bormisoft) and applying a previously published algorithm to reconstruct survival data for MRD_{pos} and MRD_{neg} cases.

Results:

From 2004 to 2022, 194 AML patients met the inclusion criteria. After first consolidation, 121 (62.4%) cases reached $MRD2_{neg}$ status, whereas 73 (37.6%) patients were $MRD2_{pos}$. We searched for interactions between $MRD2_{neg}$ and baseline features: age (< 55 y and ≥ 55 y), WBC and ELN (favorable and intermediate). Younger (<55y) $MRD2_{neg}$ patients showed a significantly longer DFS than their older counterpart (P=0.013, HR=2.08). No significant differences emerged for WBC- (P=0.29) and ELN-(P=0.1) related strata. As regards treatment, we first analyzed the impact of MRD according to treatment group: we observed significant difference in DFS between $MRD2_{neg}$ and $MRD2_{pos}$ in patients who received SDAC at induction and first consolidation (HR=3.87, P<0.0001). Conversely, MRD2 status failed to significantly discriminate DFS in patients treated with at least one HDAC-containing cycle (HR=1.60, P=0.066). When comparing patients reaching $MRD2_{neg}$ status after SDAC vs HDAC, significantly different DFS (P=0.048, HR=1.80) and OS (P=0.049, HR=1.94) emerged, with DFS rate diverging at 12 months (83.4% vs 71.5%) and at 24 months (70.6% vs 51.7%). The impact of treatment intensity was confirmed on data extracted from in-silico analysis of AML patients unselected for disease subset (P=0.014), after exclusion of CBF AML (P<0.0001) and with intermediate-risk karyotype (P=0.0018). Then we stratified $MRD2_{neg}$ patients according to the combination of age and treatment. Twenty-four (19.8%) patients (<55y, SDAC-treated; COMB_1) showed a DFS rate of 86.4% at 3 years (Fig.1) compared to a DFS rate of 46.6% in 38 (31.4%) elderly and HDAC-treated patients (COMB_3). The remainder patients (elderly or HDAC-treated, COMB_2) displayed an intermediate behavior.

Summary/Conclusion:

Our data showed variable prognostic impact of MRD in different AML categories as defined by age and treatment intensity prior to MRD evaluation. Overall, these findings call for a multidimensional application of MRD data, that include variables such as age and dose intensity, to tailor consolidation therapy on adequately estimated relapse rates.



Keywords: Measurable residual disease, Acute myeloid leukemia, Chemotherapy