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POSTER ABSTRACTS

613.ACUTE MYELOID LEUKEMIAS: CLINICAL AND EPIDEMIOLOGICAL

Outcome of Risk- and Response-Adapted Post-Remission Therapy in Patients with NPM1 AML Treated Intensively

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Introduction: Molecular assessment of measurable residual disease (MRD) is a powerful prognostic tool to identify high risk of relapse. Specifically, large studies have shown that MRD negativity of NPM1 after two cycles of intensive chemotherapy (IC) predicts long term remission. The translation of MRD results to treatment decisions such as treatment augmentation (MRD erasing) and referral to an allogeneic stem cell transplant (allo-SCT) is still lacking. The purpose of this study is to report the outcome of AML patients with NPM1 mutation who received IC and achieved remission, in whom NPM1 MRD post cycle 2 of IC, combined with FLT3-ITD status, were used systematically to decide whether patients were to complete intensive consolidations or refer to alloSCT.

Methods: This is a retrospective analysis from 3 large hospitals in Israel. Patients were treated with 7+3 for induction and a repeat induction based on day 14 marrow. Midostaurin was added for FLT3mut leukemia since 2018. Consolidation consisted of 3-4 HiDAC cycles at doses of 1-3 g/msqrX6. Gemtuzumab ozogamicin and maintenance with FLT3 inhibitors or CC486 could be added. NPM1 transcript levels (normalized to ABL copies) were collected at diagnosis, after 2 cycles of IC, at the end of IC cycles and during follow-up. Patients were transplanted if a donor was available and any of the following: NPM1 transcript level was not reduced by 3 logs by the end of second cycle chemotherapy, absolute level was >1%, poor risk AML (ELN 2017 guidelines) or high AR FLT3-ITD mutation was present. Patients were followed for relapse (type and timing) and whether a second remission was achieved, as well as for EFS and overall survival.

Results: A database search yielded 90 patients with NPM1 AML who were treated according the abovementioned protocol between 5/2015 and 11/2022 and achieved remission, with a median follow-up of 872 days (range 103-2751). Forty-seven patients were to receive consolidation cycles without transplantation in CR1, based on the aforementioned criteria. All but one patient (death from sepsis) completed treatment cycles. During follow-up, 21 (45%) patients relapsed at a median of 343 days. Two patients died while in CR1 during follow-up (extensive burns; sudden death at home). In a subgroup analysis of patients <60y (N=28), there were 11 events (9 relapses and 2 deaths), whereas in patients >60y (N=19) there were 13 events (12 relapses and 1 death during follow-up). Of note, 4 patients >60y were treated with CC486, of whom only 1 relapsed.

Of the 18 patients who relapsed and received further treatment (3 had palliative care only), only 1 patient did not enter CR2 (died during salvage). The other 17 patients entered CR2 after salvage regimen (N=7, 4 were qPCR MRDneg, 5 were subsequently transplanted in CR2) or after upfront alloSCT without any salvage regimen (N=10, 4 were qPCR MRDneg). Forty-three patients were planned for alloSCT at CR1 (27 - inadequate molecular response, 16 - ELN risk group). Only one of these patients failed to undergo alloSCT in CR1 as she relapsed. The other 42 patients underwent alloSCT at CR1. In this group of patients, the median progression-free survival was 5 years, with no difference in patients above or below the age of 60. One half of the events (9/18) were relapses and the other half were deaths in remission, almost all were GVHD associated (figure1).

Discussion: NPM1 mut AML without FLT3 is still considered by the ELN to have favorable outcome and most patients are not being transplanted at CR1. Yet, many relapse. This study evaluated the outcome of AML patients according to molecular risk stratification and alloSCT consideration by the end of cycle 2 of IC. In line with previous publications, younger patients with standard-risk AML and with adequate molecular response had a favorable outcome, with >60% of them having a disease-free

long-term survival without transplantation. Moreover, even in a case of relapse, patients can achieve CR2 with MRDneg and attain long-term remission (90% OS in long-term follow-up).
Older patients have a less favorable outcome even when they achieve adequate molecular response with two thirds of them experiencing relapse. Hence, the potential long-term outcome without transplantation needs to be balanced by the high risk of relapse. Nevertheless, even these patients can be successfully treated with either a salvage regimen or immediate transplantation, and >40% of them can be long-term survivors.

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Figure 1: Progression-free survival of patients who were planned for alloSCT at CR1

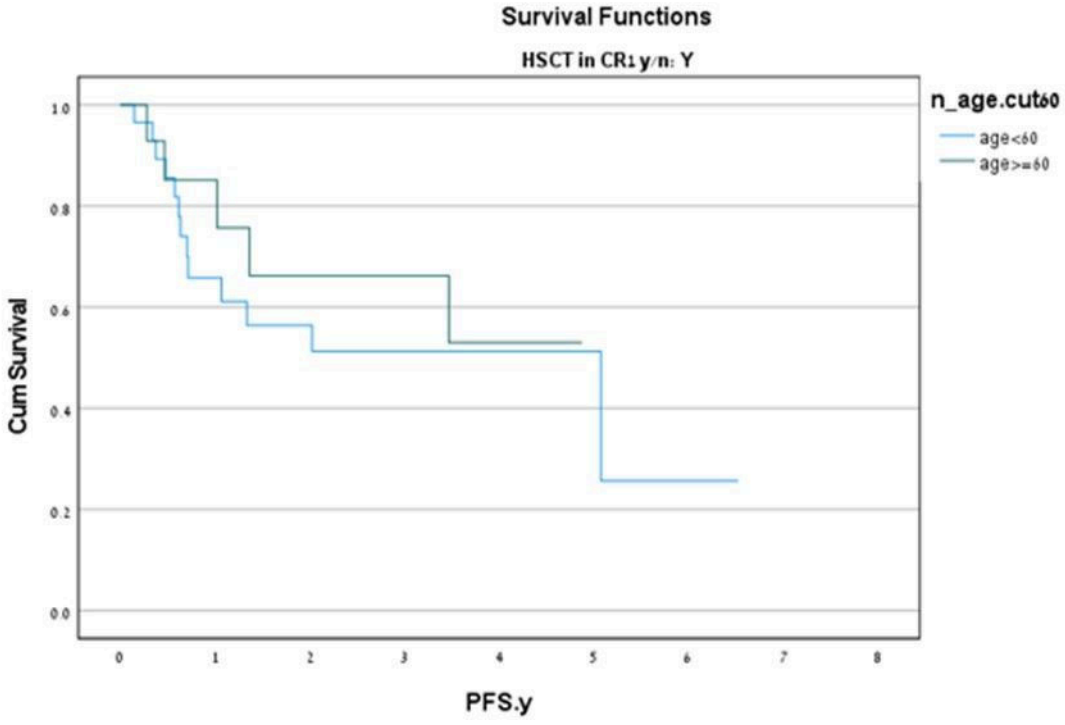

Figure 1

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