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POSTER ABSTRACTS

617.ACUTE MYELOID LEUKEMIAS: BIOMARKERS, MOLECULAR MARKERS AND MINIMAL RESIDUAL DISEASE IN DIAGNOSIS AND PROGNOSIS

Measurable Residual Disease Assessment in Patients with Acute Myeloid Leukemia Aged ≥60 Years Treated with a 10-Day Decitabine Schedule Versus Intensive Chemotherapy in the AML21 Study (NCT02172872)

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Introduction

Several studies have demonstrated that patients with acute myeloid leukemia (AML) who test measurable residual disease (MRD) positive during or after treatment have a higher probability of relapse and a shorter duration of survival, as compared to those who are persistently MRD negative. Indeed, a status of MRD positivity reflects a condition of resistant disease, existing below the threshold of the morphologic evaluation of complete remission (CR). The bulk of our knowledge in terms of MRD assessment has been generated in the setting of intensive chemotherapy; much less is known for older patients receiving less intensive treatments, such as decitabine (DEC) using a 10-day schedule.

Methods

The AML21 study was a randomized open-label phase 3 clinical trial conducted by the EORTC Leukemia Group, GIMEMA, and GMDS-SG. Patients with a newly diagnosed AML, aged ≥60 years and eligible for intensive chemotherapy were randomized

1:1 to receive DEC (20mg/m2 a day) using a 10-day schedule or intensive chemotherapy regimen consisting of daunorubicin 60 mg/m2 x 3 days and cytarabine 200 mg/m2 x 7 days (3+7), followed by 1-4 additional chemotherapy cycles. Patients who had an HLA-matched donor and at least stable disease were encouraged to undergo HSCT after >1 treatment cycle. Patients from the DEC arm not receiving HSCT could continue DEC treatment. A subset of patients treated in GIMEMA sites underwent a prospectively planned MRD evaluation post cycle 3 (DEC arm)/post consolidation (3+7 arm), and at 6, 12 and 18 months after the randomization, in case they were in a first CR and had not been allografted. MRD was studied by multiparameter flow cytometry. Based on several retrospective validations in the context of former EORTC/GIMEMA protocols, the threshold for discriminating MRD negative from MRD positive cases was set at 3.5x10-4 (0.035%) residual leukemic cells, upon full blood count recovery.

Results

In total, 130 out of 154 patients treated in GIMEMA centers provided consent for participation in translational research, had leukemia associated immunophenotype suitable for MRD monitoring, and initiated the protocol treatment, DEC (N=66) or 3+7 (N=64). Median age was 68 years (range 60-78), 33% of patients were ≥70 years old, 54% were male, and 31% and 30% had good and adverse European LeukemiaNet 2017 risk profile, respectively. At the MRD evaluation post cycle 3/consolidation, 9 out of 66 (14%) patients from the DEC and 12 out of 64 (19%) patients from the 3+7 arm had documented MRD negativity. The number of patients who either had documented MRD negativity or had undergone allografting and were alive and progression-free was 12 (18%) and 17 (27%) at 6 months, 14 (21%) and 13 (20%) at 12 months, and 14 (21%) and 7 (11%) at 18 months in the DEC and 3+7 arms, respectively. The inspection of individual profiles of patients who underwent the first MRD evaluation (and were at remission at that time) indicated that all MRD-positive patients from the DEC arm who were not allografted eventually relapsed, which often occurred just after the discontinuation of DEC maintenance.

Conclusions

10-day DEC treatment can induce MRD-negativity. However, early MRD-negativity appeared more difficult to achieve with 10-day DEC than with 3+7. Among patients in whom 10-day DEC did not induce MRD-negativity, allografting or DEC maintenance appeared necessary to avoid a disease relapse.

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