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P505 GIMEMA AML1819 TRIAL: GEMTUZUMAB OZOGAMICIN PLUS INTENSIVE CHEMOTHERAPY IMPACTS ON THE LEVEL OF POST-CONSOLIDATION MEASURABLE RESIDUAL DISEASE (MRD) IN ACUTE MYELOID LEUKEMIA

Topic: 4. Acute myeloid leukemia - Clinical

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Background:

Following the experience of the GIMEMA AML1310 protocol (*Venditti A et al, Blood 2019*), in which the choice between autologous (AuSCT) or allogeneic hematopoietic stem cell transplant (ASCT) was risk-adapted (for favorable- and adverse-risk categories) or MRD-driven (for patients in the intermediate-risk category), we designed a next generation, multicenter trial named AML1819 (NCT04168502). This trial recruits young patients (≤ 60 years of age) belonging to the ELN2017 favorable-and intermediate-risk categories, with the exception of cases FLT3 positive and relies on the addition of gemtuzumab ozogamicin (GO) to intensive chemotherapy (*Castaigne S et al, Lancet 2012 – Lambert J et al, Haematologica 2019*). AML1819 trial, likewise AML1310, is inspired to a MRD-oriented post-remission approach.

Aims:

The primary outcome measures of AML1819 are to determine (1) the percentage of MRD negativity after

consolidation in patients treated in induction and consolidation with GO; (2) the efficacy of a post-transplant maintenance with glasdegib vs clinical observation in terms of disease free survival improvement. The present report illustrates the preliminary results of the post-consolidation MRD analysis.

Methods:

In AML1819, patients are to receive 1 induction and 1 consolidation with the addition of gemtuzumab ozogamicin (GO) and then, based on the level of post-consolidation MRD, they are submitted to an AuSCT (MRD neg) or ASCT (MRD pos). Following the transplant, the patients are randomized between observation or a maintenance with glasdegib, for 12 months. MRD is assessed by Reverse-Trascriptase quantitative-Polimerase Chain Reaction (RT-qPCR) for patients with a molecular marker (*NPM1* mutation or *CBF* rearrangements) or by multiparametric flow cytometry (MFC) in those lacking a traceable molecular signature (Fig. n.1

Results:

Of 171 patients enrolled, 145 patients (85%) are evaluable, median age 53 (18-61), 52% males and 48% females; 76 patients (52%) belonged to the ELN2017 favorable-risk (FR) category and 69 (48%) to the intermediate-risk (IR) one. Of 145 patients, 107 (74%) achieved a CR/CRi. In the FR and IR category, 63 of 76 (83%) and 44 of 69 (64%) achieved CR/CRi, respectively. Of 107 patients, 105 (98%) received the consolidation course and 96 (91%) [58 FR (60%) and 38 IR (40%)] are evaluable for post-consolidation MRD assessment. Overall, 74% (71) of 96 were MRD neg and 26% (25) MRD pos. When the analysis was split as per risk category, 81% (47) of 58 patients with FR AML became MRD neg after consolidation and 19% (11) were MRD pos. In the IR category, of 38 patients 63% (24) achieved a MRD neg status whereas 37% (14) remained MRD pos. The post-consolidation frequency of MRD negativity for patients belonging to the IR category of the AML1310 protocol was 46% (42 patients out of 92). With a median follow-up of 17.4 months, 1-year overall survival of FR and IR patients is 83.1% (SD 69.2%, 99.8%) and 72.1% (53.0%, 98.0%), respectively.

Summary/Conclusion:

In the AML1819 trial, the preliminary analysis of the MRD status after consolidation indicates that a remarkable proportion of patients become negative when GO is added to intensive chemotherapy. With all the limits of such a comparison, we also found that the proportion of patients being MRD negative after consolidation was higher in AML1819 trial than in AML1310 one, in which no GO was added to chemotherapy. Such a finding has practical implications since, in AML1819 trial, a lower fraction of patients is submitted to ASCT. These figures need confirmation in a more advanced phase of trial development, showing that the high frequency of MRD negativity translates into a survival benefit.

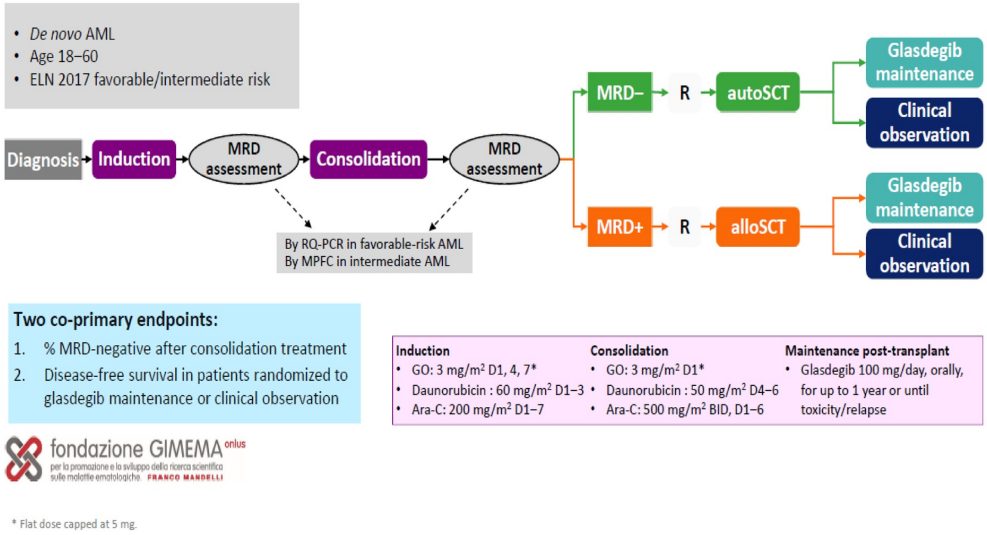

Fig. 1. GIMEMA AML1819 Trial Design