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Topic area: Transplant-specific topics
Topic: 15. Conditioning regimen
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Myeloablative, reduced toxicity versus standard conditioning in AML: a randomized clinical trial from Gruppo Italiano Trapianto di Midollo Osseo (GITMO)

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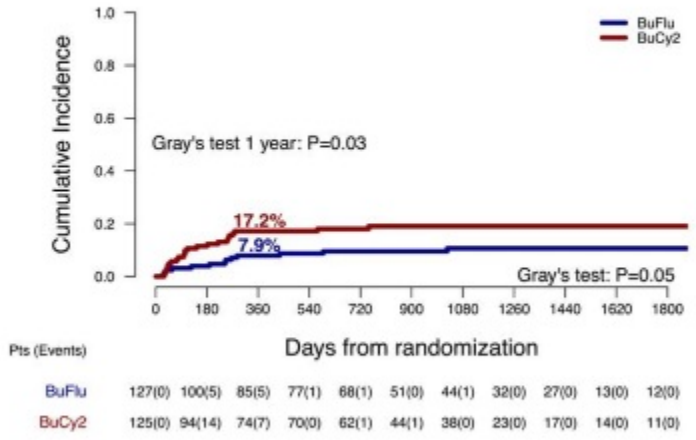
Preferred Method of Presentation: Oral Presentation
Introduction: The combination of a myeloablative dose of intravenous (iv) busulfan with cyclophosphamide (BuCy2) is the standard conditioning regimen for allogeneic hematopoietic stem cell transplantation in AML. In patients older than 40 years, it can be associated to high non relapse mortality (NRM). The same myeloablative dose of busulfan combined to fludarabine (BuFlu) may be associated to a lower NRM
Materials (or patients) and methods: The standard conditioning with iv busulfan at a dose of 0.8 mg/kg/6h for 4 consecutive days for a total dose of 12.8 mg/kg, in combination with cyclophosphamide at the dose of 60 mg/kg/day for 2 consecutive days for a total dose of 120 mg/kg (BUCY2 arm) was randomly compared to the same dose of busulfan combined with fludarabine at the dose of 40 mg/m^2/day for 4 consecutive days, for a total dose of 160 mg/m2(BUFLU arm). Eligible were patients with a diagnosis of AML in 1st or 2nd complete remission (CR) with an age ≥40 and ≤ 65 years, and the availability of an HLA compatible sibling or unrelated donor. The GvHD prophylaxis was based on

conventional Cyclosporine A and Methotrexate. In case of unrelated donors, ATG was given at a total dose of 5 mg/kg. The primary study end-point was the one-year NRM using an intent-to-treat analysis.
Results: 252 patients were assessed for eligibility: 125 were randomized to BuCy2 (121 received the allocated intervention, 3 withdrew consent and 1 relapsed before conditioning) while 127 were randomized to BuFlu (124 received the allocated intervention and 3 relapsed before conditioning).Patients were stratified according to donor type and remission (1st vs. 2nd or more). The main clinical and transplant characteristics were well balanced between the randomization arms. The median age was 51 years, 85% of patients was in 1st remission and the ELN risk subgroups were good (11%), intermediate-1 (49%), intermediate-2 (16%) and adverse (25%). The donor was a sibling related (45%) or matched unrelated (55%) while the stem cell graft was the peripheral blood in the majority of cases. On an intent to treat basis, at 1 year, the NRM in the BUCY2 arm was 17.2% vs. 7.9% in the BUFLU (Gray Test P=0.03). At 2 years and throughout the study, the same significantly different NRM was observed between study arms being respectively 18.2% vs. 8.9% and 19% vs. 9.7% (Gray Test P=0.05) (Figure 1). By forest plots analysis the experimental treatment was better in all strata and particularly in patients in CR1. A non-significant lower incidence of relapse was documented in the BUCY2 vs. the BUFLU arm being 22.1% vs. 25.2% at 1 year, respectively (Gray test 0.47) and no difference could be detected by forest plot analysis in any strata. At 4 year, in the BuFlu and the BuCy2 arm respectively, the leukemia free survival was 51% vs. 42% and the overall survival 55% vs. 54%. The overall (grade II-IV) cumulative incidence of acute GVHD was slightly higher in the BuCy2 arm and this difference was significant (p= 0.0083) when only grade III and IV were considered.
Image / Graph:



Conclusion: The conditioning regimen based on Busulfan and Fludarabine was associated with a lower non-relapse mortality and less acute GvHD (grade III-IV), with a similar incidence of relapse and comparable LFS and OS. This myeloablative, albeit reduced toxicity program is a valid alternative for older AML patients.

Disclosure of Interest: A. Grassi Conflict with: Pierre Fabre, Pharma, C. Micò: None Declared, E. Oldani: None Declared, C. Boschini: None Declared, A. Busca: None Declared, B. Benedetto: None Declared, I. Cavattoni: None Declared, S. Santarone: None Declared, R. Raimondi: None Declared, M. Montanari: None Declared, G. Milone: None Declared, P. Chiusolo: None Declared, G. Specchia: None Declared, S. Guidi: None Declared, F. Patriarca: None Declared, A.

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