Intensification of the Regimen Fludarabine Melphalan with the Addition of 400 cGy of Total Body Irradiation in Allogeneic Stem Cell Transplantation. It Is Feasible, Has a Good Anti-Leukemic Effect and a Low Toxicity

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Introduction
Fludarabine 120-160 mg/m2 plus melphalan 140 mg/m2 (Flu-Mel) is a well known reduced intensity conditioning protocol used in allogeneic transplantation, however it can be no enough intense to treat high risk acute leukemia, specially in the relapse setting. On the other hand, 400 cGy of total-body irradiation (TBI 400) has been successfully added to myeloablative dose of fludarabine busulfan without excessive toxicity. We designed a regimen adding TBI 400 to usual dose of Flu-Mel with the idea to increase its anti-leukemic activity. Below we present our experience.

Methods and Patients
Peripheral blood stem cells were mobilized with figrastin for 5 days, later, 1 or 2 apheresis were done to achieve a minimum of 3 million of CD34+ cells/kg. The conditioning consisted of fludarabine 30-40 mg/m2 for four days, melphalan 140 mg/m2 one dose, and, on day – 1, TBI 400 was administered split in 2 fractions. The prophylaxis against graft versus host disease (GVHD) was done with cyclosporine and methotrexate, all patients were given pegfilgrastim.

Results I
Twenty two patients were transplanted, median age 26.5 years (range 8-49), the diagnosis were; acute lymphoblastic leukemia (13), acute myeloid leukemia (6), chronic myeloid leukemia (1), high risk myelodisplasia (1), mixed acute leukemia (1), 32% were in first remission, 41% in second, 27% were in third remission or they had active disease. The discrimination according CIBMTR disease risk index (CIBMTR-DRI) was: 54% high risk, 41% intermediate and 5% low.

Fludarabine 30-40mg/m2 TBI 400 cGy PBSC

Results II
With a median follow up of 11 months (range 6-30) the overall survival (OS) at 24 and 36 months is 69 and 55%. Six patients have died, one due to sepsis and five secondary to relapse. The OS according to CIBMTR-DRI at 36 month was 75 and 46% for intermediate and high risk groups.

Conclusion
The addition of TBI 400 cGy to Flu- Mel regimen is feasibly, the main toxicity is mucositis, the non- relapse mortality is very low and the incidence of GVHD, acute and chronic, is not higher than expected. This combination shows an encouraging anti leukemic effect, as it is demonstrated by an OS of 75 and 46% in patients classified in intermediate and high risk CIBMTR DRI groups.

This preparative protocol can be a low toxicity alternative to more conventional myeloablative regimen. It warrants further studies.

There are not relevant conflicts of interest to disclose