BEST-05

SUPERIORITY OF RIC ALLOGENEIC TRANSPLANTATION OVER CONVENTIONAL TREATMENT FOR HODGKIN LYMPHOMA PATIENTS RELAPSING AFTER AUTOLOGOUS TRANSPLANTATION: A GITMO RETROSPECTIVE STUDY BASED ON TIME OF HLA-TYPING AND DONOR AVAILABILITY

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Hodgkin Lymphoma (HL) patients (pts) relapsing after autologous transplantation (auto-SCT) have a very poor outcome with no chemotherapy options able to obtain a long term disease control.Allogeneic stem cell transplantation (allo-SCT) employing reduced intensity conditioning (RIC) is increasingly used in lymphomas, but no clear data exist on the clinical role of allo-RIC as an effective salvage option. *Aims.* We investigated the role of RIC allo-SCT in HL pts relapsing or progressing after auto-SCT. Our study was structured similarly to an intent to treat analysis: only those pts undergoing a HLA-typing immediately after the failure of auto-SCT were included. The cohort of pts having a donor (donor group) was compared with the one not having a suitable donor (no donor group). *Patients and Methods. 187* pts were retrospectively evaluated. One-hundred and twenty-two pts found a donor and 104 (85%) underwent an allo-SCT: 57 identical siblings, 33 MUD,14 haploidentical family donors. Eighteen pts having a donor did not receive allo-SCT:10 for progressive disease, 5 for refusal and 3 for physician decision. Pts not having a donor (n=65) received chemo and/or radiotherapy according to the policy of each center. The two cohorts of patients were well balanced in terms of clinical features. *Results.* The patient median age was 30 years (16-59). The median follow-up was 46 months (range 1-143). For all pts, the median overall (OS) and progression free survival (PFS) were 29 and 14 months. The 2-year OS and PFS were 56% and 29% respectively. The cumulative transplant-related mortality was 14.6 % for the allo group. The 2-y OS and PFS were significantly better in the donor compared to the no donor group (OS 66% vs 41%, $p<0.001$; PFS 37% vs 12%, $p<0001$). In the univariate analysis and in multivariate analysis, PFS and OS were significantly influenced by the availability of a donor ($p<0.001$) as well as the time from autoSCT to relapse ($p<0.001$). In multivariate analysis, considering only the allo-group, PFS and OS were significantly improved by being in complete remission before allo-SCT and the occurrence of cGVHD. *Conclusions.* This is the largest study comparing RIC allo-SCT vs conventional treatment in HL patients failing an auto-SCT. These data demonstrated the efficacy of RIC-allo-SCT and provided evidence of a graft-versus-lymphoma effect. As expected, the attainment of complete remission before allo-SCT and the occurrence of cGVHD improve the outcome.

BEST-06

RELATIONSHIP BETWEEN TRANSLOCATION T(4;14)(P16;Q32) AND ACHIEVEMENT OF COMPLETE RESPONSE (CR) WITH VELCADE-THALIDOMIDE-DEXAMETHASONE AS INDUCTION THERAPY IN PREPARATION FOR AUTOLOGOUS STEM-CELL TRANSPLANTATION (ASCT) IN MULTIPLE MYELOMA: ANALYSIS OF GENE EXPRESSION PROFILE

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The recurrent immunoglobulin translocation t(4;14)(p16;q32) occurs in 15% of Multiple Myeloma patients and has been frequently associated with poor prognosis in patients treated either with conventional or high dose chemotherapy. Recently we reported that the presence of this chromosomal alteration raises a rather positive impact on the response to Velcade-Thalidomide-Dexamethasone (VTD) induction therapy (Cavo et al., ASH 2008). In the present study, 199 newly diagnosed MM patients who were randomly assigned to receive VTD in preparation for subsequent double ASCT were analyzed for the presence of t(4;14). In addition, the differential gene expression of $CD138^+$ enriched plasma cells obtained at diagnosis from patients carrying or not t(4;14) was evaluated by means of expression microarray, in order to investigate the molecular mechanisms underlying the response to therapy. Overall, 16% of patients carried t(4;14). On an intention-to-treat basis, the rate of CR and near CR (nCR) to VTD was higher in t(4;14) positive as compared to t(4;14) negative patients (46% vs. 28%, respectively; $p=0.05$). By comparing the lists of genes differentially expressed in responders (e.g. those who achieved CR+nCR) and non responders (NR) according to the presence or absence of t(4;14), we found that the differential expression of 3719 genes characterized CR+nCR vs. NR patients in the t(4;14) positive subgroup. At the opposite, the differential expression of 3182 genes characterized CR+nCR vs. NR t(4;14) negative patients. The intersection of the two lists of genes showed that only 271 genes were common to the two groups of differentially expressed genes. The presence of t(4,14) significantly affected development and differentiation signalling pathways in CR+nCR patients. These findings were associated with the deregulated expression in CR+nCR patients carrying t(4;14) of genes involved in the regulation of Wnt signalling pathway (e.g. MMP7, FZD7, WNT10A, WNT2B, WNT6 and WNT9A), cell cycle progression (e.g. MDM2, CDKN1A and SMAD2) and Hedgehog signalling pathway (GAS1, fused). We suggest that affection of pathways related to development and differentiation in patients carrying t(4;14) might predispose them to more favourably respond to VTD induction therapy. Moreover, novel prognostic factors can be identified, able to more precisely predict the response to VTD induction therapy.

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