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HIGH-DOSE CHEMOTHERAPY WITH AUTOLOGOUS STEM CELL TRANSPLANTATION IN 61 PATIENTS WITH LIGHT CHAIN AMYLOIDOSIS: A SINGLE CENTRE EXPERIENCE

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Introduction: High-dose chemotherapy (HDC) with autologous hematopoietic stem cell transplantation (ASCT) is currently the treatment which induces the highest rates of remission in patients (pts) with light chain amyloidosis (AL). Due to impaired organ function in these pts a high treatment-related mortality (TRM) up to 40% has been published. A high TRM was also noted in a French multicenter phase III study which compared melphalan / dexamethasone chemotherapy with HD melphalan. As a consequence no advantage of HDC could be observed in this trial so far (ASH 2005).

Methods: We have retrospectively analyzed all pts with AL who received HDC (HD melphalan median 200 mg/m^2, range 70-200 in 60 pts and HD-BEAM in 1pt) and ASCT in our centre from 1998 until 2006.

Results: We report on 61 patients (median age 57 years, range 35-69; n=7 with multiple myeloma stage I and 1 pt with Waldenstroms disease) treated with HDC and ASCT in our institution with a follow up of more than 3 months. Exclusion criteria were age >70 years, symptomatic heart involvement > NYHA stage II and WHO performance status >2. The median number of involved organs was 2 (1-5). 5 pts had end stage renal failure at time of transplant. The median follow-up is 23 months (range, 9 days - 100 months). Complete hematological remission was obtained in 26 out of 54 (48%) and organ response in 22 out of 56 evaluable patients (39%). In further 31 patients organ function has stabilized (55%). 48 out of 61 pts are alive (79%), 2 pts died of TRM (3%). Estimated overall survival at 2 and 4 years is 80% and 66%, respectively. Hematological relapse or progression occurred in 10 patients (19%) at a median of 27 months. There was a significant difference regarding OS between pts in CR vs. non-CR ($p<0.001$). Organ progression was noted only in 5 pts with CR and in 15 pts not reaching CR and occurred later in CR pts ($P<0.001$).

Discussion: HDC is in our view currently the treatment of choice for pts who are highly selected to be eligible for this treatment. Here we confirm that high overall response and survival rates can be achieved with a low TRM in a single institution with a large experience in AL amyloidosis. The main goal remains achievement of a CR as organ progression can be prevented in these pts. Further therapeutic strategies have to focus on non-CR pts using new drugs effective in the treatment of multiple myeloma.

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IMPLICATIONS OF BODY WEIGHT CALCULATIONS FOR AUTOLOGOUS PERIPHERAL BLOOD STEM CELL TRANSPLANTATION

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Background: BMI varies greatly among autologous stem cell transplantation (SCT) recipients. Stem cell collection targets are usually determined using actual body weight (ABW). Conditioning chemotherapy doses usually use corrected ideal body weight (IBW). Since stemcells home to bone marrow, the IBW being based on the height may better indicate stemcell numbers required than ABW. Since chemotherapy doses are calculated based on corrected IBW, and the volume of distribution is higher in obese patients, these patients may have decreased drug exposure and higher progression risk.

Methods: Retrospective, single institution evaluation of engraftment kinetics and outcomes of 306 SCTs done between 1998 and 2001 was performed. SCT reasons were myeloma (46%), NHL (34%), HD (6%) and AL amyloidosis (14%). The stem cell doses were calculated based on ABW and IBW and correlated with time to WBC and platelet engraftment. We also evaluated the effect of BMI on the PFS after SCT using various cutoffs.

Results: The mean (range) of ABW, IBW and BMI were 46.6 kg to 189 Kg; 45.5 kg to 94 kg; and 17.5 to 55.8 respectively. Using logistic regression, we estimated the CD34 cell dose by ABW and IBW that best predicts platelet engraftment (50,000) by day 21 post transplant. The coefficients for both doses were similar (Ideal 0.391; Actual 0.361).Using ROC analysis; we determined the stem cell dose cutoff that best predicted for failure to engraft neutrophils by 21 days post transplantation, median CD34 dose by ABW of 3.6 million/Kg and by IBW of 4.2 million/Kg. Similarly, for failure to engraft platelets by day 30 the cutoffs were 2.89 million/Kg by ABW and 3.77 million/kg by IBW. Among the individuals with ABW more than 25% of IBW(n=122, 40%), we calculated the optimal total CD34 dose required and compared to the actual dose infused using both cutoffs (286 million vs. 446 million, $P < 0.001$ using ANC cutoff and 251 million vs. 446 million using the platelet cutoff, $P < 0.001$). The PFS and OS post transplant was similar for patients with BMI over 30 kg/m^2 compared to those below this cutoff. There was no difference when patients with myeloma or lymphoma were studied separately.

Conclusion: This study confirms prior studies that IBW determined stem cell dose is comparable to that by ABW. In patients significantly above IBW, it is reasonable to use a target based on IBW which will allow for collection of less CD34 cells. In SCT using corrected IBW does not compromise outcomes.

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POOR OUTCOME OF AUTOLOGOUS-BONE MARROW TRANSPLANT (AUTO-BMT) FOLLOWING FAILED PERIPHERAL BLOOD STEM CELL (PBSC) MOBILIZATION

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BACKGROUND: Auto-PBSC transplant has replaced auto-BMT. 10-30% of patients (pts) fail to mobilize adequate PBSCs. Auto-BMT is typically considered in these pts. The results of such an approach are not well studied.

METHODS: Consecutive pts undergoing high-dose chemotherapy (HDC) and auto-BMT after failed PBSC mobilization were evaluated. Nucleated cell (NC) dose, CD34+ cell dose, time to neutrophil (ANC) and platelet (Plt) engraftment were reviewed. Overall survival (OS) and progression free survival (PFS) were evaluated.

RESULTS: 22 pts failed to mobilize PBSCs and underwent marrow harvest followed by HDC and auto-BMT from 2001 to 2006. 3 and 19 pts failed G-CSF and cyclophosphamide/G-CSF mobilization. The median age was 56 yrs (range, 9-69). Diagnoses included Non-Hodgkin lymphoma (14,64%), Hodgkin lymphoma (4,18%), and acute myeloid leukemia (3,14%). The median number of salvage regimens before attempted PBSC mobilization was 1 (range, 0-4). The median NC and CD34+ cell doses of the marrow infused were 3.7×10^8/kg (range, 1.4-6.8) and 1.0×10^6/kg (range, 0.3-3.0). All pts achieved ANC engraftment with G-CSF support at a median of 20.5 days (range, 13-43). 55% (12/22) of the pts achieved Plt engraftment at a median of 46.5 days (range, 23-92). The NC and CD34+ cell dose did not differ significantly in patients with ANC engraftment (20 days or >20 days), Plt engraftment (45 days or >45 days) or number of salvage regimens (1 or >1). There was no correlation between NC dose or CD34+cell dose and time to either ANC engraftment (NC, rho=-0.05, P=0.8; CD34, rho=-0.2, P=0.4) or Plt engraftment (NC,rho=0.6, P=0.9; CD34, rho=- 0.2, P=0.4).Median follow up was 322 days (range, 53 to 1700). 59% (13/22) patients have relapsed at a median of 155 days (range, 13-882). Median overall survival (OS) and median PFS were 1140 and 509 days (95% CI, 368 to 649). Overall mortality was 36% (8/22). Causes of death were progressive disease (6/8,75%) and treatment related mortality (2/8,25%). 9/22 (41%) pts are alive without post-transplant relapse (PTR) at a median follow-up time of 276 (range, 53 to 649). 6 of these 9 pts continue to have Plt counts $<100\times10^9$/L.

CONCLUSIONS: The relapse rate after auto-BMT in pts who