AUTOLOGOUS

20

RECEIVER OPERATOR CHARACTERISTICS OF THE SYSMEX HPC MEASUREMENT USED TO INITIATE APHERESIS OF BLOOD HEMATOPOIETIC PROGENITOR CELLS

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Background: Hematopoietic progenitor cells (HPC) can be mobilized into the peripheral blood by the administration of G-CSF and/or GM-CSF and collected by apheresis for patients who are candidates for high dose chemotherapy and autologous stem cell transplantation. The initiation of apheresis is commonly based upon the number of CD34+ cells/μL in the blood, using a flow cytometric assay that typically requires 2 hours for sample preparation, acquisition, and reporting results. The availability of a new technology for rapidly measuring the content of hematopoietic progenitor cells in blood samples based upon size and impedance (Sysmex™) prompted an evaluation of how this method compares to the CD34+ flow cytometric assay. **Methods:** Prospective analysis was performed on 100 samples of cytokine mobilized peripheral blood from adult patients (ages 27-73) scheduled for collection of autologous HPC by apheresis. The HPC content was assayed using the Sysmex™ XE2100L (performed by the apheresis staff), and by the clinical lab using a dual platform BD FACScaliber™ and a modified ISHAGE protocol. The study population consisted of lymphoma (n = 32), multiple myeloma (n = 27), Hodgkin's disease (n = 9), and one patient each with CLL, germ cell cancer, and amyloidosis. **Results:** The mean number of CD34+ cells/μL determined using flow cytometry was 57.6/μL compared to 102.6/μL using the Sysmex™, with a correlation coefficient of 0.69. Of 71 patients being considered for apheresis, a mean number of 14.7 × 10^6CD34+ cells/kg were successfully collected from 62 patients (87%). An analysis of the receiver operating characteristics of the Sysmex assay, using the flow cytometric CD34+ cell assay as a "gold-standard," revealed that initiation of apheresis when the Sysmex HPC threshold was ≥31 cells/μL optimized the sensitivity and specificity of the test, and was the best predictor of when patients should begin apheresis collection (Table 1). The positive predictive value for a Sysmex™ HPC result of ≥31/μL was 80% (CD34+ cell counts of >20/μL); the negative predictive value for a Sysmex™ HPC of <31 cells/μL was 88% (12% had CD34+ cell counts of > 20/μL). **Conclusions:** Use of the Sysmex™ method for estimating HPC cell content of the peripheral blood is fast and reliable, with excellent sensitivity and specificity compared to flow cytometry. Using the Sysmex™ HPC result to initiate apheresis has reduced the average apheresis collection start time more than an hour (Table 1).

Table 1. *ROC of SysmexTM HPC Using CD34+ > 20/μL as the Standard*

HPC/μL	Sensitivity	Specificity
>10	97.3%	52.8%
>20	91.9%	69.8%
>30	83.8%	84.9%
>40	78.4%	88.7%
>50	67.6%	92.5%
>60	62.2%	94.3%
>70	59.5%	94.3%
>80	56.8%	94.3%

21

HIGH DOSE THERAPY VERSUS ORAL MAINTENANCE: RESULT OF HD-CWS 96 STUDY FOR TREATMENT OF PATIENTS WITH METASTASIZED SOFT TISSUE SARCOMA (STS)

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Objectives: We studied the efficacy of high dose (HD) versus an oral maintenance treatment (OMT) in patients with STS stage IV. **Methods:** HD consisted of a tandem cycle of thiotepa (600 mg/m^2) + cyclophosphamide (4500 mg/m^2) and melphalan (120 mg/m^2) + etoposide (1800 mg/m^2). This treatment was optionally compared with each 4 OMT cycles consisting of trofosfamide (10 days 2*75 mg/m^2/d) + etoposide (10 days 2*25 mg/m^2/d) and trofosfamide (10 days 2*75 mg/m^2/d) + idarubicin (10 days 4*5 mg/m^2). Both groups were pretreated with the CEVAIE therapy (HD 7, OMT 9 cycles) consisting of carboplatin, etoposide, vincristine, actinomycin D, ifosfamide, and epirubicin. **Results:** Overall 753 patients were registered in CWS 96. From those 96 patients fulfilled study inclusion criteria (primary stage IV, <22 years, and intent to treat with study therapy). 45 were treated with HD, 51 with OMT. Whereas the study was not randomized, in the OMT and HD groups the main risk parameters were equally distributed. In the OMT group 15/51 (29%) fulfilled highest risk criteria (age ≥10 years and bone or bone marrow involvement), in the HD group 16/45 (35%) respectively. However, in the HD-group 11/45 were alive at a median observation time of 24.6 months (24.4%), in contrast to 26/51 OMT patients (50.9.%). Kaplan-Meier analysis demonstrates an overall survival for the whole group of 0.27 (OMT group: 0.31, HD group 0.20, log rank 0.0349). The proportional hazard analysis for patients with rhabdomyosarcoma only (77.1% of all patients) demonstrates an independent benefit of oral maintenance treatment on outcome. **Conclusions:** Oral maintenance therapy instead of tandem high dose therapy in patients with soft tissue sarcoma stage IV seems to be a promising option for patients with rhabdomyosarcoma.

22

TARGETED RADIOTHERAPY IN THE CONDITIONING PRIOR TO HAEMATOPOIETIC STEM CELL TRANSPLANTATION: RESULTS OF A PHASE I TRIAL USING AN YTTRIUM-90-LABELLED ANTI-CD66 MURINE MONOCLONAL ANTIBODY DEMONSTRATING CONSISTENTLY HIGH BM UPTAKE

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We report the results of a phase I clinical trial using an yttrium-90 (Y-90) radiolabelled anti-CD66 IgG1 murine monoclonal antibody (TheraPharm GmbH) with conditioning therapy for patients receiving either an autologous or reduced intensity (RIC) allogeneic stem cell transplant (SCT) for myeloma or AML. This was a radiation dose escalation study with five patients at each radiation dose level of 5, 10, 25 and 37.5 MBq/kilogram lean body weight of recipient. Patients initially received indium-111-labelled anti-CD66 for biodistribution and dosimetry. **Patient Characteristics:** Ages 21-67 yrs (mean 56 yrs); 16 male, 4 female; disease indication for transplant: myeloma 18, poor risk AML 2. Autologous transplant 16; RIC-allogeneic 4. Patients received the therapeutic dose of radiation on day −14, for autologous SCT they also received melphalan 200 mg/m^2 on day −2; allogeneic SCT patients received a combination of fludarabine, melphalan and CAMPATH from day −8. **Results:** Excellent bone marrow targeting was seen in all patients with a 2-10 fold excess of radiation deliv-