79%, and 96% respectively. Similar results were obtained for the validation sample, including 215 patients. In the total population, 90% of patients with a monoclonal gammopathy could be classified correctly as having MM or a non-myeloma condition.

Conclusion: The Myeloma Risk Score can identify patients with a paraproteinaemia at risk for MM. These patients are candidates for bone marrow and X-ray examination.

401 POSTER

Treatment of peripheral blood progenitor (PBPC) harvests by two-stage immunomagnetic selection: Yields comparable to positive selection alone

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Purpose: To determine the feasibility of sequential positive and negative selection to enrich haemopoietic progenitors and deplete tumour cells from PBPC's for rescue following high-dose chemotherapy.

Methods: Aliquots of 9 PBPC harvests (0.59–2.3 × 1010 cells) were processed by immunomagnetic selection using antibodies (Ab's) to CD34 for enrichment of haemopoietic precursors, followed by depletion of tumour cells using a cocktail of Ab's to either 5 lymphoid or 3 epithelial antigens for lymphoma (5 pts) or breast cancer (4 pts) respectively. Numbers of CD34+ cells were measured by flow cytometry and CFU-GM enumerated in the apheresis product and at each stage of the procedure.

Results: Initial mean concentration of CD34+ cells was 1.73% (±0.81), increased to 90.8% (±8.25) following enrichment and 92.6% (±7.05) after both stages. CFU-GM were enriched a mean 241-fold (±132) in the final product. For the enrichment step the mean yield of CD34+ cells was 34.5% (±11.8), for depletion 92.1% (±6.7). Overall mean yield of CD34+ cells was 33.6% (±9.15). By projecting numbers of CD34+ cells from the total harvest on 2 days apheresis, all 5 patients with lymphoma and 1 patient with breast cancer would have had sufficient numbers (>2 × 106/kg) for rescue after both stages. The proportion of CD34+ cells in the apheresis product was a good predictor of adequate numbers of cells remaining after processing, with a cut-off at 1%.

Conclusion: Two-stage selection of PBPC gives yields of early progenitors very similar to single stage enrichment, suggesting that this is a feasible method for in vitro treatment to remove tumour cells.

402 POSTER

Treatment of multiple myeloma with short-term infusion of liposomal daunorubicin in combination with vincristine and dexamethason

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The continuous infusion of vincristine and doxorubicin over 96 h in combination with oral dexamethason (VAD) is one of the most effective treatment options for patients with relapsed or primary refractory multiple myeloma. On the other hand, a retrospective analysis of quality of life in patients treated with VAD in our clinic showed that this regimen which requires a central venous catheter and hospitalization in most cases is associated with considerable inconvenience. We have initiated a phase I/II trial with a modification of this protocol by replacing doxorubicin with short-term infusion of liposomal encapsulated daunorubicin, which provides sustained intracellular anthracycline levels. Furthermore, the rate of alopecia and cardiotoxicity of liposomal daunorubicin seems to be substantially lower. Patients receive a bolus injection of vincristine 1 mg/m^2 on day 1, and 40 mg dexamethason on d1–4, 9–12 p.o. The starting dose of liposomal daunorubicin is 40 mg/m^2 and will be escalated interindividually in 10 mg/m^2 steps. The treatment courses are repeated every three weeks.

Quality of life is assessed with special emphasis on bone pain and preliminary results indicate an advantage over VAD. Multiple clinical and laboratory parameters of disease activity, number and immuno-phenotype of the myeloma cells in the bone marrow, P-glycoprotein expression, functional assays of the multidrug resistance are measured before and during the chemotherapy course to identify subgroups of patients with different probabilities of remission and survival within this protocol.

403 POSTER

Correlation between the number of CD34+ cells reinfused and complications and mortality of high-dose chemotherapy with stem cell support

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Reinfusion of peripheral blood autologous stem cells (PBSCs) allows hematologic recovery after high-dose chemotherapy (HD-CHT). There is an inverse correlation between the number of CD34+ cells and the duration of aplasia. There is little information as to the clinical correlates of this observation, that is, are the severity of complications (comp) and the mortality affected by the number of CD34+ cells infused?. The severity of comp in 45 consecutive patients (pts) treated with HD-CHT+PBSC at our institution (1995–6) was evaluated by an investigator unaware of the CD34+ counts, and subsequently correlated with the number of CD34+ cells reinfused. Pts with mild comp were those with fever lasting <48 hours, grade 0–2 mucositis and diarrhoea and no need of total parenteral nutrition. Pts with severe comp were those with grade 4 diarrhoea plus either peritonitis or sepsis of intraabdominal origin, and those who required admission in the Intensive Care Unit. All others were labeled intermediate comp. Eighteen pts had mild comp, 19 had intermediate comp and 8 had severe comp. The median numbers of CD34+ cells × 10^{-6}/Kg infused were 4.3 (range 2.3–18.5), 3.7 (2.2–16.5) and 2.9 (2–5.3) respectively ($p < 0.05$ mild vs severe). Since the evaluation of comp is subjective, we then compared CD34+ cell numbers in pts with toxic death (5 pts) vs those who survived (40 pts). Medians were 2.6 (2–5.3) and 3.7 (2.2–18.5) ($p < 0.05$). None of 12 pts who received >5.5 × 10^6 CD34+ cells had severe comp vs 24% of those who received <5.5. Infusion of high numbers of CD34+ PBSCs not only results in shorter aplasia but also in milder extrahematologic comp and lower mortality

404 POSTER

High-dose therapy with peripheral blood progenitor cell (PBPC) autografting in multiple myeloma (MM)

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Purpose: Dose-escalated therapy combined with autografting improves the response rates and survival in patients (pts.) with MM (Attal et al. 1996).

Methods: In a prospective study we treated MM-pts. with high-dose cyclophosphamide or ifosfamide/mitoxantrone followed by filgrastim (R-metHuG-CSF, 300 μg/day) and myeloablative therapy consisted of total body irradiation (TBI) + Melphalan (MEL) or MEL alone.

Results: 131 pts. have been transplanted. Autografts contained a median of 3.3 × 10^6 CD34$^+$ cells/kg BW (range 2.0–29.0). A neutrophil count of 0.5 × 10^9/l and an unsubstituted platelet count of >20 × 10^9/l was reached after a median of 14 days (range 9–22) and 11 days (range 5–157), respectively. Two pts. died of transplantation-related complications. As a result of HD-therapy, the remission status (EBMT criteria) in 60 pts. was improved. The median event free survival period was 23 months. The median overall survival (OS) has not yet been reached. We found no difference in EFS and OS between the two high-dose treatment regimens (TBI + MEL vs. MEL).

Conclusion: >2.0 × 10^6 CD34$^+$ cells/kg BW predicts a rapid hematopoietic reconstitution in MM patients. The functional capacity of CD34$^+$ cells is not influenced by treatment before PBPC mobilization. To improve the results of HD-therapy, we have started a multicenter protocol using CD34$^+$ selected PBPC for tandem autografting followed by α-interferon maintainance therapy.

405 POSTER

Apoptosis induction by fludara and anti-Fas monoclonal antibodies on B-chronic lymphocytic leukemia cells

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Purpose: Apoptosis occurs in responce to many different stimuli. We examined the induction of apoptosis by Fludara (Fludarabine phosphate) in vitro against freshly isolated B-chronic lymphocytic leukemia (B-CLL) cells