reached), and corresponding figures for those with 1–2 previous regimes were 50% and 3 yrs, and ≥3 previous regimes 13% and 0.8 yrs.

Responding patients may achieve a prolonged remission and survival, but response is less likely in heavily pretreated patients.

396 ORAL

The role of lung function measurements before allogenic BMT to anticipate long term lung failure

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Background: Lung function often deteriorates after allogenic BMT for hematological malignancies, and lung failure is the most important cause of death after grafting. To test whether pre-BMT lung function impairment is associated with long term lung deterioration, we prospectively measured lung function parameter of 80 consecutive patients with AML (n = 23), CML (n = 38) and ALL (n = 19) before allogenic BMT, after 6 months, and thereafter annually until 5 years after grafting.

Results: Pretransplant forced expiratory volume in one second (FEV1), diffusing capacity for carbon monoxide (TLco) and vital capacity (VC) were significantly decreased in the ALL subgroup (FEV1 85% pred, TLco 79% pred, VC 83% pred, ECCS normal values). In contrast, no pre-BMT lung impairment was detectable in CML and AML patients. During the first 6 months after BMT lung function parameter decreases in all patient groups in a similar way (FEV1 15 ± 7.3%, TLco 23 ± 11.2%, VC 19 ± 9.8%). Further, all lung parameter at least partially recovered within one year. Long-term decline in FEV1, TLco and VC happened in all patients groups without significant differences. No association was detectable between pre-BMT, 6 months after BMT and long term lung function decrease.

Conclusion: Pretransplant lung function impairment is not associated with increased relative risk for long term lung failure in allogenic BMT patients.

397 ORAL

Platelet recovery after high-dose (HD) chemotherapy (C) is superior with peripheral blood stem cells (PBSC) mobilized by C + G-CSF compared to G-CSF alone

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Collection of PBSC mobilized with G-CSF is often more predictable and easier to perform than mobilization using C. We evaluated two mobilization strategies to support women receiving cyclophosphamide 6 g/m^2, mitoxantrone 64 mg/m^2, carboplatin 0.8–2.0 g/m^2 over 4 days (d) for C-sensitive metastatic breast cancer. 35 consecutive pts received FAC (cyclo 2 g/m^2) d1 + G-CSF 10 μg/kg d4–14, with leukapheresis (10–12 L) × 4 d12–15 (C + G, n = 16); or G-CSF 10 μg/kg d1–7 with leukapheresis d5.6 ± 7.8, depending on CD34 recovery (target > 2 × 10^6/kg) (G, n = 19). Number of collections/pt: C + G 3:2pts, 4:12, 5:2; G 2:5 pts, 3:5, 4:8, 5:1. CD34+ cell recovery (× 10^6/kg) was greater for C + G: median 12.9 vs 3.5 (p = 0.009), whereas CFU-GM, total cell number were similar. Mean D to ANC > 0.5 × 10^9/L were similar (C + G: 10.9, G: 12.4, p = 0.15), but mean d to plts > 20 × 10^9/L was less for pts collected after C + G (12.8 vs 24.4, p = 0.03). Plt recovery and time to hospital discharge (DC) were significantly shorter for C + G pts (logrank p = 0.02 and 0.001 respectively), with similar ANC recovery (p = 0.14). Prior adjuvant C did not affect apheresis yield, engraftment or time to DC. For women receiving HDC for MBC, PBSC mobilized with C + G may be superior to G alone, at least with respect to plt recovery.

398 ORAL

Treatment of patients with relapsed or refractory acute myeloid leukemia (AML) with recombinant engineered human anti-CD33 antibody-calicheamicin drug conjugate

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CMA-676 is a conjugate of the potent cytotoxic agent calicheamicin linked to a recombinant engineered human antibody directed against the CD33 antigen, which is commonly expressed on AML blast cells. The lack of CD33 antigen expression on hematopoietic stem cells allows for selective delivery of the cytotoxic calicheamicin to the tumor target, while sparing normal stem cells. Patients with CD33-positive relapsed or refractory AML received CMA-676 as a single 2-hour IV infusion per treatment cycle every 14 days for up to 3 cycles at the same dose, contingent upon a lack of leukemic progression and significant toxicity. Three to 6 patients were treated at escalating dose levels of CMA-676. Between April 1995 and December 1996, 36 patients from 23 to 73 years of age, were entered. CMA-676 was well-tolerated at all dose levels. Fever and chills occurred in 26 (74%) patients. Three patients experienced Grade III hepatic toxicity. Dose-limiting toxicity was not observed, and only one patient discontinued the study due to fever and hypotension. Marrow morphologic remissions were achieved in 5 patients, two of whom recovered normal blood counts for 6 months before experiencing relapse. Three other patients achieved morphologic remission; however one died of fungal sepsis, one remained transfusion dependent in morphologic remission for 70 days when bone marrow relapse occurred, and one experienced CNS relapse after a morphologic remission of 40 days. We conclude that single-agent therapy with CMA-676 safely induces remission in some patients with relapsed or refractory AML.

399 ORAL

Transplant-related morbidity (TRM) in patients undergoing bone marrow transplantation (BMT): The role of preparative regimens (PR)

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Purpose: This retrospective analysis evaluated acute and late toxicities after BMT according to PR.

Methods and Materials: From January 1984 to December 1994, 229 patients with acute leukemia (AL, n = 114), chronic myelogenous leukemia (CML, n = 53), lymphoma (51) and aplastic anemia (11) were transplanted (171 allogeneic BMT, 58 autologous BMT). Preparative regimens were combining cytotoxic drugs (cyclophosphamide) with TBI (TBI group, n = 146) or without TBI (cyclophospamide, busulfan) (CHE group, n = 83). Median age was 32.4 years. Median follow-up was 36 months (0.3–121).

Results: There was no difference in term of white blood cell count recovery, engraftment, veno-occlusive disease and hemorrhagic cystitis between the 2 groups. The CHE group presented an increased incidence of second malignancies. The TBI group showed an higher incidence of platelets and red blood cell transfusion, cataracts (especially with cobalt irradiation), aseptic necrosis of bone and interstitial pneumonitis (IP). IP occurred in 25% of TBI group, especially in patients with graft-vs-host disease. Survival according to the type of preparative regimens was similar (Cox model). According to the BMT type, survival was better with allogeneic BMT even if TRM was higher in this group (especially with TBI, 73% vs 12%).

Conclusion: Although patients treated with TBI experienced more late toxicity, survival remains the same. This could be explained by the higher rate of relapses in the CHE group. Therefore TBI keeps its place as first intent treatment choice.

400 POSTER

Development of a "myeloma risk score" for patients with a paraproteinaemia

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Purpose: Diagnostic systems for monoclonal gammopathies use bone marrow and X-ray examinations to exclude multiple myeloma (MM). Data from a population-based registry of unselected patients with paraproteinaemia indicate that these tests are frequently not performed. We therefore evaluated the possibility of estimating the risk for MM in patients with paraproteinaemia using only standard laboratory tests.

Methods: We used 441 randomly selected patients to develop a simple four point "Myeloma Risk Score" based only on paraprotein type and concentration. One point was given for concentrations ≥10 g/l, one point for IgG and IgA, and two points for IgD and light chains only. A score of 0 or 1 indicated a low risk for MM, with scores of 2 and 3 signifying high risks.

Results: Sensitivity, specificity, positive and negative predictive value (PV) for the Myeloma Risk Score in the training sample were 92%, 88%,

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