relapse rate. We aimed to characterize alemtuzumab-based conditioning alloSCT patients in the Instituto Português de Oncologia do Porto (IPOP) and analyze the relation between MDC and alloSCT outcomes.
Material and Methods: Retrospective analysis of consecutive patients admitted in the IPOP for alemtuzumab-based conditioning alloSCT between 1999 and February 2011. Data on donor chimerism were obtained on months 1, 3, 9 and 12. SPSS®18 was used for statistics. Time to event data were analyzed by Kaplan-Meyer method and compared with log-rank test.
Results: We performed 40 transplants in 38 patients (45% male). Median age was 27 years. Diagnoses were acute myeloid leukemia/myelodisplastic syndrome in 47%, lymphoma in 16% and non-malignant diseases in 28%. Status pre-alloSCT was complete remission in 35%, relapse in 13%, untreated in 35% and graft failure of a previous transplant in 15%; 22% had previous alloSTC. The commonest conditioning regimens were fludarabine-based (76%%). Donor was related sibling in 14. HLA was identical in 16. Stem cell source was peripheral blood in 30 and bone marrow in 8. Immunosuppression was based in a calmoudolin inhibitor in 29. Cytomegalovirus reactivation occurred in 50%. Six patients received donor lymphocyte infusion. Median duration of follow-up was 47 months. Median time to neutrophil and platelet engraftment was 14 and 11 days. Almost 50% had MDC at all-time points; 33% and 20% had acute and chronic GvHD. Median overall survival (OS) was 3.7 years. Estimated OS at 1 and 3 years was 58% and 46%. At the last contact, 10 of the 20 alive patients were in complete remission and 16 had died of transplant-related causes, with 100 days and 1 year transplant-related mortality (TRM) of 19% and 41%. Relapse risk in malignant disorders was at 1 and 5 years 26% and 40%. Presence of MDC was associated with lower acute GvHD risk ($p = 0.47$) but found to be not related to risk of relapse, OS and TRM.
Conclusions: Alemtuzumab-based conditioning regimen wasn't related to relapse risk or OS, so it can be used in selected high risk patients. Our series differs from others in the greater diversity of diseases and conditioning regimens and higher percentage of unrelated donor transplant, non-identical HLA match and previous alloSTC. These characteristics, in association with our limited sample size, can justify the differences in results, particularly the higher TRM.

9227 POSTER

Simulation of Clinical Endpoints (Survival, PFS) in Patients With Refractory Multiple Myeloma Treated With Pomalidomide Based on Interim Week 8 M-protein Response

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Background: The aims of this project were 1) to develop a drug-independent link between tumour burden reduction (as assessed by change from baseline in serum M-Protein) and survival and PFS in multiple myeloma and 2) to simulate expected survival and PFS based on interim M-protein data of an ongoing phase 1/2 trial (CC-4047-MM02, NCT00833833) of pomalidomide (POM) in patients with relapsed and refractory multiple myeloma who have received at least 2 prior therapies including lenalidomide (LEN) and bortezomib. Similar approaches were implemented for solid tumours (Claret, J Clin Oncol 2009; Wang, Clin Pharmacol Ther 2009).
Methods: M-Protein measurements were modeled as a function of time from 704 patients included in two phase 3 clinical studies of LEN plus dexamethasone (DEX) vs. DEX (Dimopoulos, NEJM 2007 and Weber, NEJM 2007). Models for survival and PFS times as a function of model predicted change in end-of-cycle 2 (week 8) M-protein level from baseline and other prognostic factors were developed. Interim M-protein data from the ongoing MM-002 POM study (217 patients) were modeled to simulate clinical endpoints.
Results: Week 8 change in M-Protein ($p < 0.00001$), ECOG performance status ($p < 0.0009$), baseline albumin, hemoglobin and creatinine levels ($p < 0.01$) were significant independent predictors of survival when week 8 change in M-Protein ($p < 0.00001$) and baseline hemoglobin ($p < 0.001$) were significant independent predictors of PFS. Observed survival and PFS distributions over 100 weeks in lenalidomide studies and difference between the two treatments (LEN + DEX vs. DEX) were consistent with the 95% prediction intervals (PI) of the models. Model predictions (95%PIs) of median survival based on week 8 change in M-Protein following treatment with POM and POM + DEX were 78.3 weeks (53.5–116.1 weeks) and 67.8 weeks (45.8–101.3 weeks), respectively when model predicted PFS was 22.5 weeks (14.6–34.3 weeks) vs. 16.5 weeks (9.7–27.7 weeks), respectively.
Conclusions: Modeling and simulation enables the use of the change in M-protein level as a continuous longitudinal biomarker to assess drug effect in multiple myeloma studies. Current simulations indicate encouraging results for POM in a refractory multiple myeloma patient population.

9228 POSTER

Chemotherapy With Artificial Hyperglycemia in Treatment of Recurrent or Refractory Follicular Non-Hodgkin's Lymphomas

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Background: We conducted trial to evaluate the therapeutic efficacy and toxicity of CHOEP regimen under artificial hyperglycemia in patients with relapse or refractory follicular non-Hodgkin's lymphomas. It is stated that under hyperglycemia antitumour effect of chemotherapeutic agents is considerably increased.
Methods: Eligible for this study was 163 patients with recurrent or refractory follicular non-Hodgkin's lymphomas from 2002 to 2007 in our institute. Patients received under hyperglycemia regimen CHOEP. Hyperglycemia is carried out by introduction of 20% solution of glucose in quantity 1200vl. Chemotherapeutic agents dissolved and entered into each bottle of glucose (400 ml); infusion of glucose is spent at the rate of 140–170 drops to a minute. Insulin not entered into glucose solution.
Results: There were 40 CR and 64 PR, for an overall response rate 63.3%. The median time to attainment of CR was after four courses (range, one to six); all CR patients had achieved at last a PR after four courses (median, two). For those whose maximum response was a PR, the median time to PR were two courses (range, one to five). The median duration of CR was 21 months (range, 4 to 25+). The median duration of PR was 9 month (range, 4 to 25+). Among PR patients, 26 developed progressive disease early (within 9 months), 6 within 1 month of discontinuation of CHOEP under hyperglycemia, 13 while on chemotherapy under hyperglycemia, and 7 after early discontinuation of four courses. 23 of these 26 patients with early progression after CHOEP did subsequently stabilize. Three died of progressive lymphoma within 6 months. Only 19 patients did not achieve at least a PR. With a median follow-up duration of 20months, the median survival and failure-free survival times from the time of entry onto the CHOEP+ hyperglycemia study were 34 and 14 months, respectively.
Conclusions: The CHOEP regimen under artificial hyperglycemia achieved a high rate of response in this group of patients with recurrent or relapsed follicular non-Hodgkin's lymphomas. 33% of this 160 patients responded to the CHOEP regimen under artificial hyperglycemia, and there was a CR rate of 25%. Several of the CRs have been durable, lasting up to 2 years. The CHOEP regimen under artificial hyperglycemia was well tolerated.

9229 POSTER

Severe Central Nervous System (CNS) Graft Versus Host Disease (GVHD) in a Patient Without Any Other GvHD Symptoms After Allogeneic Stem Cell Transplantation

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Background: Although graft versus horst disease (GvHD) is the most relevant complication of allogeneic stem cell transplantation (SCT), it rarely affects the central nervous system. Recently, a consensus conference proposed criteria of diagnosis for cerebral GvHD including the obligatory manifestation of chronic GvHD at other organs [Grauer et al., Brain, 133: 2852, 2010]. We observed a 41 y old women, who developed spastic paralysis and fell into coma 2.5 years after having an allogeneic peripheral blood stem cell stem cell transplantation (PBSCT) for acute myeloblastic leukemia from an unrelated HLA 9/10-matched donor. The patient presented with a history of several month of headache supposed to be caused by migraine. She had a history of acute GvHD stage III (skin and intestinal) but no signs of chronic GvHD. In addition she had no history of an independent autoimmunopathy or migraine prior to SCT.
Material and Methods: MRI scan was performed, cerebrospinal fluid was analyzed to exclude CNS relapse and infectious agents, and finally CNS biopsy was obtained by open brain surgery.
Results: MRI scan showed disseminated severe leucencephalopathy without established sign of CNS relapse, lymphoma or typical infection. The cerebrospinal fluid analysis was normal. Toxoplasmosis and viral infection

such as HSV, VZV, ADV, EBV, CMV, HHV-6 and HIV was excluded by PCR. The blood lymphocyte subset showed lymphopenia, however with normal CD4/CD8 ratio. Finally CNS biopsy revealed T-cells close to blood vessels, a pattern typical for cerebral GvHD. Immunosuppressive treatment was started with high dose steroids in combination with mycophenolatmofetil (MMF). She recovered rapidly and became completely awake within one week. After 9 months of immunosuppression the patient is competent in activities of daily living.
Conclusions: GVHD of the central nervous system (CNS) is a rare disease after allogeneic stem cell transplantation. The absence of lymphocytes in the cerebrospinal fluid and normal CD4/CD8 ratio in peripheral blood does not exclude GvHD of the CNS. CNS biopsy should be considered to confirm the diagnosis. This case demonstrates that CNS involvement can be the only manifestation of chronic GvHD. Immunosuppressive therapy may provide an impressive benefit in these patients.

9230 POSTER

Can Allogeneic Peripheral Blood Stem Cells Be Safely Cryopreserved for Use in Patients Undergoing Transplant

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Background: Peripheral blood cells (PBC) are now widely used over bone marrow transplantation in patients with haematological malignancy. To date, there has been no analysis as to whether cryopreservation is associated with delayed stem cell engraftment. We therefore decided to perform a retrospective study to observe the outcomes of patients post PBC transplantation.
Materials and Methods: 154 patients who underwent PBC transplantation over a 5 year period at the Queen Elizabeth Hospital were divided according to the type of stem cell transplantation; fresh allogeneic or cryopreserved allogeneic. Data was sourced from an automated Patient Information Communication System (PICS). The main outcome measure was defined as the time taken for primary stem cell engraftment (neutrophil count recovery to 1×10^9/l and platelet count recovery to 30×10^9/l). Any differences were compared whilst adjusting for age, diagnosis, transplant intensity and stem cell number.
Results: The mean time taken for neutrophil count to reach 1×10^9/l was greater in the cryopreserved group (14.5 days, 95% CI 11.9–12.9) when compared to the fresh group (12.4 days, 95% CI 13.6–15.4) ($p < 0.05$ for difference). The mean time taken for platelet count to reach 30×10^9/l was also greater in the cryopreserved group (19.36, 95% CI 16.2–22.6) when compared to the fresh group (11.72, 95% CI 10.9–12.5) ($p < 0.05$ for difference). Similar results were found when adjusting for age, diagnosis, transplant intensity and stem cell number.
Conclusions: For the first time, we have shown that cryopreservation of haemapoeitic stem cells does delay both platelet and neutrophil engraftment. We recommend that a cautious approach should be considered when choosing cryopreservation over fresh stem cell transplants. In patients requiring such methods there may be a delay in engraftment; increasing hospital associated morbidity and the necessity for greater supportive care.

9231 POSTER

BEACOPP-14 Vs. BEACOPP-esc in Patients With Hodgkin's Disease From Poor-prognosis Group − Updated Results of Prospective Randomized Multicenter Study

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Background: The efficacy and toxicity of the treatment with beacopp-14 and beacopp-esc regimens in patients with Hodgkin's disease (HD) from high risk group are compared in prospective randomized study.
Materials and Methods: Since September 2008 81 patients in 6 Ukrainian centers from 18 to 65 years old (median 28 years), 38 male and 43 female with stage IIB with $\geqslant$1 unfavorable factors and stage III-IV were randomized to receive the treatment with beacopp-14 (36 pts, 5.88 cycles per patient) and beacopp-esc (45 pts, 5.61 cycles per patient). The treatment efficacy in both groups was evaluated after 4, 6 and 8 cycles by Cheson criteria (1999, 2007). Toxicity rate was evaluated with NCI-CTC. After completion of chemotherapy patients with initial sites >5 cm, residual lymph nodes >2 cm and PET-positive sites received radiotherapy (30−36 Gy). The similar group of patients, who received the therapy with ABVD, was selected for the historical control.
Results: The therapy efficacy in both groups was higher than in the group of ABVD treatment; the difference in the efficacy in the groups of beacopp-14 and beacopp-esc was insignificant (Table). 2 patients after the treatment with beacopp-esc have early relapse (after 3 months and 1 year). There were no relapses detected in the group of beacopp-14; $p > 0.05$. All patients are alive; maximal observation period is 26 mnths. In the group of historical control overall response rate (ORR) after the completion of the treatment was 80.39%; that is significantly lower than in the both groups treated with beacopp-esc or beacopp-14. The most frequent toxicity type in both groups was hematological toxicity (Table) of different grades. In 7.5% the beacopp-14 cycles were not completed due to neutropenia of 4 grade. The most frequent nonhematologic complications were nausea and vomiting.
Conclusion: Both comparative regimens show almost equal treatment efficacy and toxicity rate in patients with HD of the poor prognosis group (100% ORR after 6−8 cycles). The efficacy of ABVD treatment in the similar group of patients with HD was significantly lower. However, the results are preliminary and should be confirmed in larger number of patients and with a longer follow-up.

Table. Efficacy and toxicity rate

	BEACOPP-14, %	BEACOPP-esc, %	p-value
ORR, 6 cycles	100	97.4	>0.05
ORR, 8 cycles	100	100	>0.05
CRR, 8 cycles	82.8	86.8	>0.05
CRR, 8 cycles	88.9	87.5	>0.05
Relapses	2 pts	0 pts	>0.05
Hematological toxicity	72.8	67.6	>0.05
Anemia	25	12.5	<**0.05**
Neutropenia	35.5	37.3	>0.05
Febrile neutropenia	8.5	6.7	>0.05
Nausea and vomiting	31.3	44.6	>0.05
Mucositis	11.8	6.1	>0.05

9232 POSTER

B Cell-activating Factor of TNF Family (BAFF) Signaling Pathway is Associated With Helicobacter Pylori-independent Growth of Gastric MALT Lymphoma Without T(11;18)(q21;q21)

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Background: We have recently discovered that nuclear expression of BCL10 or NF-κB is closely associated with *Helicobacter pylori* (HP)-independent status of low-grade gastric mucosa-associated lymphoid tissue (MALT) lymphoma with or without t(11;18)(q21;q21) (Blood. 2005;106:1037–1041). In this study, we examined the role of B cell-activating factor belonging to the TNF family (BAFF) in mediating BCL10 nuclear translocation and in activating NF-κB, and HP-independence of gastric MALT lymphoma without t(11;18)(q21;q21).
Materials and Methods: Sixty-six patients who underwent successful HP eradication for localized low-grade gastric MALT lymphomas were included. Status of t(11;18)(q21;q21) was determined by reverse transcriptase polymerase chain reaction for API2-MALT1 transcript, while expression of BCL10, NF-κB, and BAFF was detected by immunohistochemistry. The primary MALT lymphoma cell was obtained from fresh marrow aspiration-derived lymphoma of a t(11;18)(q21;q21)- and t(1;14)(p22;q32)-negative gastric MALT lymphoma patients who had failed antibiotics treatment and standard chemotherapy. Phospho-Akt (Ser473 and Thr308), BCL3, BCL10, NF-κB (p65), NF-κB (p52), cyclin D3, c-Myc, and BAFF protein expression were assessed by immunoblotting. Transactivity of NF-κB was measured by electromobility shift assay,
Results: Fifty-two (78.8%) patients were negative for t(11;18)(q21;q21); among them, 34 (65.4%) were HP-dependent and 18 (34.6%) were HP-independent. Furthermore, in t(11;18)(q21;q21)-negative patients, BAFF expression was significantly higher in HP-independent than in HP-dependent tumours (13 of 18 [72.2%] vs 10 of 34 [29.4%]; $P = .003$). BAFF overexpression was associated with nuclear expression of BCL3 ($P = .014$), BCL10 ($P = 0.006$), and NF-κB ($P = 0.008$). In MALT lymphoma cell line, BAFF activated NF-κB and AKT; the activated NF-κB up-regulated BCL10, c-Myc, and cyclin D3, and the activated AKT caused formation of BCL10/BCL3 complexes that translocated to the nucleus. Inhibition of AKT by LY294002 (a PI3K inhibitor) blocked BCL10 and BCL3 nuclear translocation, NF-κB transactivity, and BAFF expression. The BCL3 nuclear translocation and NF-κB activation were inhibited by silencing BCL10 (BCL10 SiRNA). In addition, knockdown of BCL3 expression by SiRNA influenced the nuclear translocation of BCL10.