

# transplantation

## 540 THE STUDY OF RELATIVITY BETWEEN THE EXPRESSION OF KI-67, P53, BCL-2 AND PROGNOSIS OF PATIENTS WITH MALIGNANT LYMPHOMA AFTER THE AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION

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**Introduction:** 1. To evaluate the expression of Bcl-2, Ki-67, P53 in Malignant lymphoma (ML). 2. To study the relationship between the expression of Bcl-2, Ki-67, P53 and prognosis for patients given autologous hematopoietic stem cell transplantation (AH SCT) for malignant lymphoma (ML).

**Material and methods:** Bcl-2, Ki-67, P53 were measured by immunohistochemistry (IHC) on paraffin-embedded slices in 33 cases of ML who received AH SCT. Survival analysis was done by the Kaplan-Meier method and log-rank test. Multivariate analysis was carried out using Cox proportional hazard model.

**Results:** For patients with ML who received AH SCT, the 3-year disease free survival (DFS) of Bcl-2(+) group was 35.71%, while that Bcl-2(-) group was 88.89%. There was significant difference of DFS between the two groups. Meanwhile, for these patients, the 3-year DFS of Ki-67(+) and Ki-67(-) were 43.75% and 85.71%, respectively ( $P < 0.05$ ). Multivariate analysis showed that the expression of Bcl-2 and Ki-67 were the independent prognostic factors.

**Conclusions:** The expression of Bcl-2 and Ki-67 were closely related with relapse after AH SCT in patients with ML. They were useful molecular makers for predicting the prognosis of patients with ML after AH SCT.

## 541 CHEMOTHERAPY COMBINED WITH RITUXIMAB DOES NOT ADVERSELY AFFECT THE PERIPHERAL STEM CELL MOBILIZATION AND ENGRAFTMENT AFTER HIGH-DOSE THERAPY AND AUTOLOGOUS STEM CELL TRANSPLANTATION IN PATIENTS WITH DIFFUSE LARGE-B-CELL LYMPHOMA

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**Introduction:** Previous studies indicated that rituximab (R) with chemotherapy does not compromise the mobilization and engraftment of autologous peripheral blood stem cells (PBSC) in lymphoma. In our study, we analyzed the effect of prior combined R and chemotherapy (CT) administration on PBSC mobilization, post-transplant engraftment, relapse rate and survival in DLBCL pts.

**Materials and methods:** From May 1999 to August 2007, 69 ASCTs were performed in poor-risk DLBCL patients younger than 65 years who achieved CR and PR after induction CT (31 pts.) or rituximab with CT (38 pts). PBSC were mobilized after cyclophosphamide and etoposide in 6 pts or after cytosine-arabioside and mitoxantrone in 63 pts followed by 5 mg/kg body weight of rhG-CSF from day 8. The BEAM conditioning regimen was given to all 69 patients.

**Results:** CT with R did not significantly affect CD34+ stem-cell mobilization ( $7.81 \times 10^6$ /kg after R-CT vs  $13.8 \times 10^6$ /kg after CT;  $p = 0.11$ ), number of CFU-GM ( $76.55 \times 10^4$ /kg vs  $98.1 \times 10^4$ /kg;  $p = 0.07$ ) and number of mononuclear cells ( $5.24 \times 10^8$ /kg vs  $3.77 \times 10^8$ /kg;  $p = 0.8$ ), but lowered number of BFU-E ( $31.3 \times 10^4$ /kg vs  $90.9 \times 10^4$ /kg;  $p = 0.01$ ). There was no significant difference in the recovery of neutrophils (median 11 days in both groups) and platelets (median 10 days in both groups), number of neutrophils and platelets at day +100 after ASCT and post-transplant complications between R-CT and CT groups. The number of relapses (29% vs 5%;  $p = 0.009$ ) and deaths (19% vs 3%;  $p = 0.04$ ) was significantly higher in CT group. Estimated EFS at 3 year was 90% in R-CT pts., but only 67% in CT pt. ( $p = 0.04$ ), OS at 3 years was not significantly different (R-CT 95% vs CT 84%,  $p = 0.18$ ).

**Conclusions:** R combined with CT has no adverse effect on the mobilization and engraftment of PBSC, minimizes relapse rate and improves EFS in DLBCL pts. after ASCT.

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## 542 PLASMA LEVEL OF INFLAMMATORY CYTOKINES AND ASSOCIATED PROTEIN EXPRESSION PROFILING IN RELAPSED NON-HODGKIN'S LYMPHOMA PATIENTS BEFORE HIGH DOSE THERAPY

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**Background:** Prognostic evaluation of patients with relapsed and refractory non-Hodgkin's lymphoma (NHL) before high dose therapy (HDT) and autologous stem cell transplantation (ASCT) is mainly based on clinical variables and tumour response following reinduction. Prognostic parameters are likely to reflect the underlying pathogenesis and several biomarkers or molecular signatures have been reported as predictors of outcome in *de novo* NHL (1, 2). We hypothesized that individual protein expression identified by cytokine levels and global protein analyses may identify new prognostic markers in relapsed NHL.

**Methods:** 50 EDTA blood specimens from patients with relapsed NHL, after completion of induction chemotherapy and 1-6 days before HDT and ASCT were collected and stored at  $-80^\circ\text{C}$  until analysis. Specific cytokine analysis was performed by ELISA. Surface-enhanced laser desorption/ionization time-of-flight mass spectrometry (SELDI-TOF-MS) were performed on prefractionated samples. Data analysis was assessed individually by conventional biostatistics.

**Results:** Plasma levels of TNF $\alpha$  and YKL-40 predicted clinical response to the pretransplant reinduction therapy (CR contra non-CR), however did not predict survival post transplant. A range of distinct MS peaks were significant correlated to the level of YKL-40. Plasma samples from patients in complete remission (CR) were compared with non-responding patients. Distinct MS peaks were identified in the poor responding group. Furthermore a range of low molecular peaks were predictive for survival.

**Conclusion:** Preliminary data indicate that inflammatory cytokine measurements do not predict outcome, however, circulating biomarkers identified before high dose therapy may be predictors for posttransplant outcome in relapsed NHL.

**References:** 1: Pedersen LM, et al., Br J Haematol. 2005 Mar; 128(6): 813-9. 2: Pedersen LM, et al., Ann Hematol. 2005 Aug; 84(8): 510-6.

## 543 R-CHOP PROTOCOL PLUS GRANULOCYTE COLONY STIMULATING FACTOR FOR MOBILIZATION OF PERIPHERAL BLOOD STEM CELLS IN NON HODGKIN'S LYMPHOMA: OUR EXPERIENCE OF TWO YEARS

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**Introduction:** The current method for mobilization of peripheral blood stem cells (PBSC) consists in use of the chemotherapeutic regimen plus granulocyte colony stimulating factor (G-CSF). We have studied the mobilization of PBSC following CHOP plus rituximab (R-CHOP) therapy plus G-CSF in patients with non Hodgkin's lymphoma (LnH).

**Material and methods:** From January 2006 to December 2007 we have effected leukapheresis for PBSC in 12 patients with LnH after treatment with R-CHOP regimen + G-CSF (lenograstim). We mobilized PBSC after R-CHOP regimen plus G-CSF in 13 patients with LnH (2 mantle cells and 10 large cells; three patients were in IV stage for bone marrow involvement; the mean age was 43 years; range 29-55 years). All patients were at first treatment for LnH and at the time of PBSC mobilization were in partial or completeremission and at fourth or fifth sequence of R-CHOP. Every one patient was administered 5 micrograms/Kg of G-CSF starting from day 4 after R-CHOP therapy. The CD 34+ blood cell count were performed before of the cycle of chemotherapy, before the beginning of the G-CSF at day 4 and subsequently daily.

**Results:** The increase of the CD 34 has daily been progressive with doubling then of the value around the 10 -11° daypost R-CHOP. The single leukapheresis was performed in all patients when the values of cells CD34+ were over 20/microlitres. The leukapheresis product was forever over 5 cells CD34 $\times 10^6$ /Kg.

**Conclusion:** The R-CHOP protocol + lenograstim at dose of 5  $\mu\text{g}/\text{Kg}$  once daily in LnH patients produce a good mobilization of the PBSC and of course offers the possibility to recuperate the PBSC with the standard treatment for the LnH, economize and in addition is feasible preventative procedure for refractory or relapse of disease.

## 544 STUDY OF THE EFFECT OF INTERMEDIATE-DOSE OR HIGH-DOSE CYTARABINE COMBINING HUMAN GRANULOCYTE COLONY-STIMULATING FACTOR FOR LYMPHOMA TREATMENT

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**Introduction:** High-dose therapy plus autologous stem cell transplantation (HDT/ASCT) plays an important role in the treatment of lymphoma. We conducted a clinical trial to compare the efficacy of peripheral stem cell mobilization with  $6\text{g}/\text{m}^2$  (intermediate-dose, ID) or  $10\text{g}/\text{m}^2$  (high-dose, HD) cytarabine in lymphoma.

**Material and methods:** 33 patients in remission with induction or salvage chemotherapy or chemoradiotherapy have received peripheral stem cell mobilization with cytarabine plus rhG-CSF from 1997 to 2006. The dose of cytarabine was  $6\text{g}/\text{m}^2$  in intermediate-dose (ID) group ( $n=13$ ) and  $10\text{g}/\text{m}^2$  in high-dose (HD) group ( $n=20$ ).  $5\mu\text{g}/\text{m}^2/\text{day}$  of rhG-CSF was administered to all patients.

**Results:** 30 patients had non-Hodgkin's lymphoma. The ratio of male to female was 8:5 in ID group and 17:3 in HD group. The median age was 34 and 21.5 years in ID and HD groups, respectively. 4 patients in ID group failed mobilization while there was no such case in HD group. Median number of peripheral mononuclear cells were 6.245 and  $6.045 \times 10^6/\text{kg}$  in ID and HD group, respectively, and median number of peripheral CD34+ cells were 20.12 and  $39.14 \times 10^6/\text{kg}$  in the ID and HD groups, respectively. 29 patients received HDT/ASCT. Median time of leukocyte engraftment ( $\geq 1.5 \times 10^9/\text{L}$ ) was 11.5 days in ID group versus 12 days in HD group ( $p=0.501$ ), median time of platelet engraftment ( $\geq 50 \times 10^9/\text{L}$ ) was 10 days in ID group versus 13 days in HD group ( $p=0.232$ ). There was no treatment related death during mobilization and HDT/ASCT. The key factors for successful mobilization were patient gender as female ( $p=0.002$ ), high-dose cytarabine ( $p=0.019$ ) and less than 3 chemotherapy regimens before mobilization ( $p=0.049$ ). HD group patients had longer time-to-treatment failure (TTF) than those in ID group did ( $p=0.020$ ). And the only factor influenced TTF was successful mobilization by Cox regression analysis ( $p=0.001$ ).

**Conclusions:** HD cytarabine could mobilize stem cell more efficiently than ID in lymphoma. Toxicities were tolerable in both groups.

#### 545 ETOPOSIDE $1.0\text{G}/\text{M}^2$ OR $1.5\text{G}/\text{M}^2$ COMBINED WITH G-CSF FOR MOBILIZATION OF PERIPHERAL BLOOD STEM CELLS IN PATIENTS WITH MALIGNANCY: EFFICACY AND TOXICITY

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**Background:** Although cyclophosphamide combined with G-CSF is a standard regimen for peripheral blood stem cell (PBSC) mobilization, several authors reported failure of standard mobilization regimens in 10% to 30% of patients with certain malignancies. And this figure will be further increased if patients were heavily pretreated. Etoposide alone or combined with other agents, as another effective initial or salvage mobilization regimen, have been widely studied in recent years. In most studies, the recommended dose of etoposide as a single mobilization agent ranged from 1.6 to  $2.0\text{g}/\text{m}^2$ . Based on these positive results, we designed a nonrandomized study to observe the effectiveness and toxicity of etoposide at two relative low dose levels for PBSC mobilization according to the constitution of oriental population, and evaluate their anti-tumor activity at the same time. Furthermore, factors that may correlate with the yield of CD34+ cells were explored. Material and

**Methods:** Totally, 38 consecutive patients received etoposide  $1.0\text{g}/\text{m}^2$  (group A) or  $1.5\text{g}/\text{m}^2$  (group B) followed by G-CSF  $300\mu\text{g}/\text{d}$  for PBSC mobilization in a nonrandomized manner. Each group had 19 patients.

**Results:** The median number of CD34+ cells collected totally was  $17.33 \times 10^6/\text{kg}$  (range  $4.85\text{--}89.00 \times 10^6/\text{kg}$ ) in the group A and  $26.54 \times 10^6/\text{kg}$  (range  $1.85\text{--}108.00 \times 10^6/\text{kg}$ ) in the group B. Altogether, 34/38 (89.5%) patients obtained the target total collection of at least  $4 \times 10^6$  CD34+ cells/kg by a single leukapheresis. Vomiting was the most common grade 3/4 non-hematological toxicity. Response can be seen in 4 out of 19 (21.1%) evaluable patients. All parameters between two groups did not reach the significant level. The most predictive factor for CD34+ yield of the first leukapheresis was the percentage of CD34+CD38- cells in peripheral blood.

**Conclusions:** These results indicate that etoposide combined with G-CSF is an effective and tolerable regimen for PBSC mobilization, either given at a dose of  $1.0\text{g}/\text{m}^2$  or  $1.5\text{g}/\text{m}^2$ .

#### 546 STUDY ON EFFECT OF GINSENOSE Rg3 ON IMMUNOLOGICAL RECOVERY AFTER PERIPHERAL BLOOD STEM CELL TRANSPLANTATION IN ANIMAL EXPERIMENTS

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**Introduction.** To study the effect of ginsenoside Rg3 on immunological recovery in mice after peripheral blood stem cell transplantation (PBSTCT).

**Material and methods.** A murine model of PBSTCT was established. Ninety recipient mice were divided into 6 groups after transplantation: A, B, C, D, E, F groups, 15 mice each. They were intra-abdominally injected with Rg3  $3\text{mg}/\text{kg}$ , Rg3  $6\text{mg}/\text{kg}$ , Rg3  $9\text{mg}/\text{kg}$ , IL-2 and normal saline (NS), respectively. They were injected began from day 15 after PBSTCT, daily for successive 15 days per month, for a total of 3 months. The functional recovery of T and B lymphocytes was observed by the lymphocyte transformation test; and

formation test of antibody, respectively, and the functional recovery of NK cell was observed by the killing test. The changes in number of T cell subpopulations, B cells and NK cells were observed by Flow cytometry (FCM).

**Results.** For the influence of Rg3 on cyto-immunity the action of  $6\text{mg}/\text{kg}$  and  $9\text{mg}/\text{kg}$  Rg3 was much better than that of NS ( $P<0.01$ ) but not difference from that of IL-2. Only the combined group showed a good synergistic effect on immunological recovery. For the influence of Rg3 on humoral immunity, the effect of Rg3  $3\text{mg}/\text{kg}$  was stronger than NS but weaker than IL-2. The effect of Rg3  $6\text{mg}/\text{kg}$  and  $9\text{mg}/\text{kg}$  was similar to that of IL-2 ( $P>0.05$ ). Only the combined group showed a good synergistic effect which was much better than that of other groups. For the influence on cytotoxic activity, the test groups were all better than NS group at the first month after PBSTCT ( $P<0.05$ ), but in the second month the cytotoxic activity of all test groups reduced gradually. However, in the third month the activity gradually recovered again, especially in Rg3  $6\text{mg}/\text{kg}$ ,  $9\text{mg}/\text{kg}$  and  $9\text{mg}/\text{kg}+\text{IL-2}$  groups ( $P<0.01$ ).

**Conclusion.** The combined use of ginsenoside Rg3 (high dose) and biological response modifier (BRM) improves greatly the immunological recovery of transplanted mice, and enhances greatly the immune function. The effect of combined therapy is much better than single IL-2 or Rg3 treatment.

#### 547 FEASIBILITY OF DEXAMETHASONE, ETOPOSIDE, IFOSFAMIDE AND CISPLATIN AS AN EFFECTIVE PERIPHERAL BLOOD STEM CELL MOBILIZATION REGIMEN FOR TRANSPLANTATION-ELIGIBLE PATIENTS WITH NON-HODGKIN LYMPHOMA

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**Background:** Although DVIP regimen (dexamethasone, etoposide, ifosfamide and cisplatin) was very effective as salvage regimen in the management of relapse or refractory non-Hodgkin lymphoma (NHL), the efficacy of DVIP as a peripheral blood stem cell (PBSC) mobilization regimen remained unclear.

**Material and Methods:** Forty-one consecutive transplant-eligible patients with relapse or refractory NHL were treated with DVIP for salvage treatment and peripheral blood stem cell mobilization. Patients subsequently received high-dose chemotherapy (HDC) and autologous peripheral blood stem cell transplantation (APBSCT) if they achieved a complete response (CR) or partial response (CR) to chemotherapy.

**Results:** Forty-one patients received a total of 99 cycles of DVIP regimen. The median DVIP chemotherapy was two cycles when they proceeded on to peripheral blood stem cell mobilization. Thirty-three patients were available for response in 41 patients. The objective response following DVIP chemotherapy was observed in 73% of patients (CR 34%, PR 39%). Of 41 patients, 67 leukapheresis procedures were performed with a median of two leukapheresis (range 1–3). The median yield of CD34+ cells was  $6.04 \times 10^6/\text{kg}$  (range,  $1.82\text{--}32.7 \times 10^6/\text{kg}$ ) for all patients and the median yield of CD34+ cells was  $8.75 \times 10^6/\text{kg}$  (range,  $2.38\text{--}21.35 \times 10^6/\text{kg}$ ) in patients with single collection. Correlation analysis indicated that the yield of CD34+ cells ( $\times 10^6/\text{kg}$ ) showed a strong correlation with the count of pre-apheresis CD34+ cells in peripheral blood cell on the harvest day ( $r=0.778$ ,  $P<0.001$ ). Neutropenia (Grade 4, 46%) and thrombocytopenia (Grade 3/4, 54%) were commonly seen in hematological toxicities. Nausea and vomiting (Grade 1/2, 59%; Grade 3, 5%) and elevated transaminase (Grade 1/2, 7%) were observed in non-hematological toxicities. All patients received successful haemopoietic and immunological reconstitution following HDC and APBSCT.

**Conclusions:** DVIP has potential to be utilized as an effective mobilization regimen in patients with refractory and relapsed lymphoma for the reason of acceptable toxicity and excellent PBSC mobilizing characteristics.

#### 548 EVALUATION OF PEGFILGRASTIM EFFICACY IN PERIPHERAL BLOOD STEM CELL MOBILIZATION OF PATIENTS WITH LYMPHOMA

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Twenty four patients (pts) with planned autologous stem cell transplantation for lymphoma diseases (Hodgkin's disease=4; NHL=20) received chemotherapy (CT) (Induction CT=3 and salvage CT= 21) followed by a fixed single dose (6 mg) and well tolerated administration of Pegfilgrastim (PF) after the last day of CT for peripheral blood stem cell collection (PBSC) (target cell dose of  $>2 \times 10^6$  CD34+/kg). Median age was 53 yrs (24-68) and median weight was 72, 5 kg (45-98). Among the 24 pts, 7 received more than 2 lines of CT regimens. Median time interval between day 1(D1) of the cycle of CT mobilization and first leukapheresis session was 14 days (10-18) while the median time interval between injection of PF and first leukapheresis session was 9 days (6-13). Stem cell collection was started when the absolute number of circulating CD34+ cells was  $>10 \times 10^6/\text{L}$  and performed with standard volume leukapheresis. Median CD34+ cells level at D1 of leukapheresis was  $35.5/\text{mm}^3$  (11-320) and interestingly, more than 35% of pts could reach this median level of CD34+ early after PF injection (D6). Notably, 22 pts reached the target cell dose in 2 sessions of

leukapheresis or less (10 pts after 1 session, 10 other pts after 2 sessions, 2 pts after 3 and 4 sessions respectively). The median number of leukapheresis sessions was 2(1-4) and the median CD34<sup>+</sup> cells harvested was 4x10<sup>6</sup>/kg (0.8-26.6). Two pts (DLBCL=1 and FL=1) could not reach the level of CD34<sup>+</sup> required to start leukapheresis, and both became secondary refractory to CT. In univariate analysis, PBSC collection of >4x10<sup>6</sup>/kg was highly correlated with pts who started their collection at D9 of PF administration (P=0.01) and with those presenting a CD34<sup>+</sup> cells level >35.5/mm<sup>3</sup> at D1 of leukapheresis (P=0.033). White blood cells level higher than 9 G/l was also predictive of circulating CD34<sup>+</sup> cells >35.5/mm<sup>3</sup> (P=0.033).

These data suggest that PF may represent an attractive option for PBSC mobilization in pts with lymphoma when optimal compliance of sequential regimens of CT is required. We also emphasize that PBSC mobilization is effective even in pts in second or subsequent salvage CT. Importantly, the circulating CD34<sup>+</sup> count should be performed from D6 of PF administration.

#### 549 EFFICACY OF SINGLE-DOSE PEGFILGRASTIM COMPARED WITH DAILY FILGRASTIM TO MOBILIZE AUTOLOGOUS PERIPHERAL BLOOD STEM CELLS AFTER CHEMOTHERAPY IN MALIGNANT LYMPHOMAS

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**Introduction:** Autologous stem cell transplantation (ASCT) improves the outcome in patients (pts) with relapsed or refractory Hodgkin's (HD) and aggressive non-Hodgkin's lymphomas (NHL). Peripheral blood stem cells (PBSC) are usually harvested after the administration of daily granulocyte-colony stimulating factor (G-CSF) with or without chemotherapy (CT). Pegfilgrastim (Peg), the covalent conjugate of G-CSF to a polyethylene glycol molecule, has proved to be as effective as G-CSF in recovering neutrophil count after CT, whereas its efficacy in PBSC mobilization is still an open issue.

**Materials and methods:** 41 consecutive pts with refractory/relapsed NHL or HD eligible for ASCT were treated at our institution since July 2003 to December 2007 and received a cisplatin-cytarabine-based regimen (ESHAP), to reduce the tumour burden and mobilize PBSC. 19 pts received 5 microg/kg daily G-CSF, whilst the other 22 pts underwent a 6 mg single dose of Peg. The two groups were similar for their characteristics: 50% of pts were refractory to front-line chemotherapy and about 40% of them were at relapse.

**Results:** we observed a difference in the median CD34+ cells count (104 cells/microL with G-CSF and 51/microL with Peg) and in the median yield of CD34+ cells collected (15.3x10<sup>6</sup>/Kg with G-CSF and 8.47x10<sup>6</sup>/Kg with Peg), but in both groups 95% of pts harvested successfully. A single apheresis was performed in all pts who received G-CSF and in 90% of pts treated with Peg. The cost analysis suggested a possible 20% of reduction in terms of growth factor cost (Peg 1489,49 Euros vs 1811 Euros in G-CSF cohort for a median of 14 vials pro patient in our analysis). No significant differences were observed in terms of toxicity: all pts presented grade 3-4 neutropenia (with a median duration of 3 days); no difference in febrile episode were reported (5 in each group). All patients had a grade 3-4 thrombocytopenia.

**Conclusions:** Pegfilgrastim showed to be as effective as G-CSF in the PBSC mobilization setting, not only for the practical advantage to the pts (single vs daily administration) but also for the possible cost reduction.

#### 550 FEASIBILITY AND EFFICACY OF BEAM AS A FRONTLINE HIGH DOSE CHEMOTHERAPY SUPPORTED BY AUTOLOGOUS PBSC IN ELDERLY PATIENTS WITH DLBCL

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Limited data is available concerning feasibility and efficacy of high dose therapy (HDT) with autoPBSC in elderly patients with DLBCL. In young patients with poor prognosis intensification as a part of first-line treatment suggests survival benefit. It is not clear if the same strategy is applicable to the older patients. The Institute Paoli-Calmettes database was reviewed for DLBCL patients who received BEAM followed by PBSC in patients ≥60 y.o. between 01.1998 and 12.2006 (9 y). All patients received BEAM as a part of front-line treatment and were in a complete response after CHOP±R induction. Twenty seven auto-transplanted patients were identified (median age 63 y, range 60-68). This cohort was compared with closely matched 37 patients of same age range, who received first-line CHOP±R regimen without intensification in the same 9-years interval. Only patients in complete response were included. As frontline autoPBSC was performed in high-risk patients, the group without HDT was naturally privileged in the terms of stage and aIPI. There was significant difference in the localised vs disseminated disease (stage I-II: 54% in no-HDT vs 26% in HDT group, p=0.03) and aIPI (0-I: 66% in no-HDT vs 37% in HDT, p=0.046). Factors evaluated included treatment-related mortality (TRM), overall survival (OS) and event-free survival (EFS). TRM in the HDT group (1/27 pts (3.7%)) was comparable with

previously published data. The estimated 5-y OS was 75.5% (52-90%) for HDT group compared to 79.9% (58-92%) in the no-HDT group. There were 8 events in the HDT group and 11 events in no-HDT (5-y EFS 49.4% vs 64.2%).

The front-line intensification can be safely performed in patients ≥60 y.o. with DLBCL. There was no difference in OS and EFS between cohorts with and without intensification even if the HDT was reserved for the high risk patients. The first-line HDT in older patients with high-risk IPI score might improve survival in this group and produce results similar to those in the low-risk group.

#### 551 TREATMENT OF MALIGNANT LYMPHOMA BY AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION COMBINED WITH HIGH DOSE RADIOTHERAPY AND CHEMOTHERAPY

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**Introduction:** To investigate the effects of treatment of malignant lymphoma (ML) by autologous hematopoietic stem cell transplantation (AH SCT) combined with high dose radiotherapy and chemotherapy.

**Material and Methods:** From June 1991 to October 2002, 56 patients, aged 9~65 years, with ML, 44 non-Hodgkin's lymphoma (NHL) and 12 Hodgkin's disease (HD) were treated with AGSCT combined with high dose radiotherapy and chemotherapy. Among them, 12 received autologous bone marrow transplantation (ABMT) and 44 received autologous peripheral blood stem cell transplantation (APBSCT). In the latter the APBSCTs were mobilized by carboplatin and etoposide (CE) or CHOP (CTX, ADM, VCR, PDN) plus granulocyte-colony stimulating factor (G-CSF) and/or granulocyte-macrophage colony stimulating factor (GM-CSF) 10/kg/kg/d. Pretreatment included BEAM (BCNU, Vp-16, AraC, MEL) or MEL 140 mg/m<sup>2</sup>+Vp-16 200 mg/L total body irradiation (TBI) 8 Gy.

**Results:** The patients were flowed up for 40~4310 days with a median of 1 820 days.

**Results:** Hematopoietic reconstruction was observed in all patients. The 1, 2, and 5-year disease-free survival rates were 87.5%, 60.7%, and 57.1% respectively, with the longest survival of 11 years. Fourteen patients developed relapse. No transplantation related death was seen.

**Conclusion:** Autologous hematopoietic stem cell transplantation combined with high dose radiotherapy and chemotherapy is effective on ML. AH SCT shows a more rapid effect on hematopoietic reconstruction than ABMT.

#### 552 THE CLINICAL RESEARCH OF IMPROVED EFFECT FOR IMMUNE RECONSTITUTION OF GINSENSINOSIDE RG3 FOR PATIENTS AFTER AUTOLOGOUS PERIPHERAL BLOOD STEM CELL TRANSPLANTATION (APBSCT)

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**Introduction:** To study the improvement of immune reconstitution of ginsenoside Rg3 for patients after autologous peripheral blood stem cell transplantation (APBSCT).

**Material and methods:** We selected 30 patients who received high-dose chemotherapy and APBSCT from June 2000 to May 2003. These patients were randomly divided 4 groups: IL-2 group, ginsenoside Rg3 group, the combination group and control group. We observed the number changes of T cell subpopulation and NK cell by Flow cytometry (FCM), observed the functional recovery of T lymphocyte by the lymphocyte transformation test, the functional recovery of NK cell by the killing test and the functional recovery of humoral immunity by the mensurate of antibody in peripheral blood by ELISA.

**Results:** The combination of ginsenoside Rg3 and IL-2 can greatly improved the recovery of the number of CD3, CD4 and the ratio of CD4/CD8, enhanced the rate of the lymphocyte transformation. The effect of immune improvement of the combination group was better than the other groups.

**Conclusion:** The combination of ginsenoside Rg3 and IL-2 can greatly improved the immune improvement for patients after APBSCT and had the enhanced effect for immune function. The effect of the combination was better than the single drug for ginsenoside Rg3 or IL-2.

#### 553 YTTRIUM-90 IBRITUMOMAB TIUXETAN COMBINED WITH HIGH-DOSE BEAM CHEMOTHERAPY AND AUTOLOGOUS STEM CELL TRANSPLANTATION FOR RELAPSED/REFRACTORY B-CELL NON-HODGKIN'S LYMPHOMA

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**Background:** High-dose chemotherapy followed by autologous stem cell transplantation is an established treatment option for patients with relapsed or refractory non-Hodgkin's lymphoma (NHL). Recently, radioimmunotherapy has emerged as a new treatment modality for B-cell NHL with the combined benefits of immunotherapy and radiotherapy. The incorporation of Yttrium-90 ibritumomab tiuxetan into a high-dose chemotherapy conditioning regimen promises to improve the outcome after autologous stem cell transplantation for relapsed or refractory NHL.

**Materials and Methods:** A phase II trial to evaluate the safety and efficacy of combining Yttrium-90 ibritumomab tiuxetan with high-dose carmustine, cytarabine, etoposide, and melphalan (BEAM) conditioning chemotherapy and autologous stem-cell transplantation in patients with relapsed or refractory NHL. Patients with either relapsed, refractory or transformed follicular lymphoma (FL) or relapsed, refractory diffuse large B cell lymphoma (DLBCL) were eligible. All patients received a sequential high-dose regimen including rituximab as salvage chemotherapy. Results for the first 10 out of a planned 20 patients are reported.

**Results:** The median age was 57 years. 7 patients had DLBCL, 2 had FL, and 1 patient had a transformed FL. The median number of relapses was 1 (range 1-3). After a median time of follow up of 11 months (range 1 to 26 months) 2 patients relapsed. Interestingly, both patients had central nervous system relapse. One of these patients died. Adverse events were similar to those seen historically with high-dose BEAM alone. There were no treatment-related deaths or secondary malignancies.

**Conclusions:** These preliminary results suggest that the combination of Yttrium-90 ibritumomab tiuxetan and BEAM followed by autologous stem cell transplantation is safe and effective for the treatment of patients with relapsed or refractory NHL.

**554 HEMATOLOGICAL RECOVERY AND EARLY POST-TRANSPLANT TOXICITY OF Z-BEAM REGIMEN – A PAIR MATCHED ANALYSIS**

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**Background:** Z-BEAM allows to combine Zevalin (Ibritumomab tiuxetan) guided "total tumor radiotherapy" and the efficiency of standard BEAM conditioning regimen. It's clinical efficiency remains to be determined in a randomized studies.

**Methods:** Pair match comparison of Z-BEAM and 2 other transplant conditioning regimens (Cy-TBI and BEAM) was performed. Patients were matched according to age, diagnosis and the number of pre-transplant chemotherapy lines. Early post transplant toxicity (until day +100) and hematological reconstitution was assessed.

**Results:** Hematological recovery is summarized in a table. Neither the time of WBC or Plts recovery nor required transfusions or G-CSF support were different. Infection rate was comparable, both during and after discharge from the transplant ward (until day +100) only 4 patients developed serious infections: 2 Z- BEAM, 1 BEAM, 1 TBI). There were also no differences in other organ toxicities.

	WBC > 1500/ul days	PLTS >20 000/ul days	G-CSF days	PLTs transfusions units	RBCs transfusions units
Z-BEAM N= 11	14,27 (11-20)	19,18 (10-36)	3 (0-11)	6,91 (0-14)	4,91 (0-12)
BEAM N=11	15,09 (10-23)	18,64 (10-37)	5,09 (0-17)	5,91 (2-13)	4,36 (0-13)
TBI N=11	15,91 (13-19)	13,23 (10-15)	1,18 (0-5)	4,27 (1-12)	1,64 (0-5)

**555 ALLOGENEIC STEM CELL TRANSPLANTATION IN LYMPHOPROLIFERATIVE DISEASES**

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Allogeneic stem cell transplantation (alloSCT) is considered a therapeutic option for poor-prognosis lymphoproliferative diseases (LPDs), especially after failure of an autoSCT. We retrospectively analyzed the outcomes of this procedure in patients (pts) who received alloSCT with a myeloblative or a reduced intensity conditioning (RIC) regimen at our center. Between 1992-2007, 44pts (34M/10F), with median age of 46 (range 19-63) years, underwent alloSCT for LPDs. The diseases were: 8 Hodgkin's lymphoma (HL), 8 mantle cell lymphoma (MCL), 4 follicular lymphoma (FL), 12 B-CLL, 8 peripheral T cell lymphoma (PTCL), 4 other. The median interval from diagnosis to alloSCT was 26 (range 5-156) months. Donors were identical siblings (n=34) or matched unrelated (n=10). A RIC regimen was used in 31pts. Twelve pts had received an autoSCT at a median interval of 11 months prior to alloSCT. At transplant, the disease was chemosensitive in 23, and chemoresistant in 21pts. Acute GVHD occurred in 24 (grade III/IV, n=9), and extensive chronic GVHD in 17 pts. CR was achieved in 18 pts after alloSCT, including 14/23 with chemoresistant disease. Transplant-related mortality (TRM) at 3 and 12 months was 20% and 32%, respectively. Early TRM was significantly lower with RIC regimens (13% vs 38%). Twelve pts had disease progression at a median of 11 (range 8-23) months post alloSCT. Donor lymphocyte infusions DLI were administered to 7 pts, either for disease recurrence (n=5) or for persistent mixed chimerism (n=2) and only 2 pts (1 CLL, 1 FL) achieved CR. Overall survival (OS) at 3 years was 48%, and progression-free survival (PFS) was 52%. Among subtypes of LPDs, 3-year OS and PFS were for: FL 75% and 100%, MCL 62% and 72%, B-CLL 59% and 45%, HL 28% and 21%, PTCL 24% and 40%. Better outcome was noted for pts with chemosensitive compared to chemoresistant disease (3-year PFS: 61% vs 42% and OS: 68% vs 2%, p=0.03). Age, type of conditioning regimen and previous autoSCT did not seem to influence OS and PFS. In conclusion, alloSCT, especially with a RIC regimen, can be a tolerable and curative modality for certain advanced-phase LPDs. The efficacy of this approach is clearly superior in pts with chemosensitive disease.

**556 THE EUROPEAN BONE MARROW WORKING GROUP (EBMWG) TELE HEMATOLOGY, A SUPPORT NETWORK**

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**Background:** Hematopathology, has been severely neglected in emerging countries, resulting that local pathologists are not prepared for the high level of diagnostic precision demanded by modern therapies.

**Objectives:** To raise the level of hematopathology in emerging countries and Eastern Europe by providing an internet forum for discussion of difficult cases, and alleviate the isolation of our colleagues through online contact with experts in the field. Advice is also offered how to improve, laboratory techniques, in order to achieve the highest possible standards with a minimum of means. In exceptional cases, locally not available special investigations are performed in laboratories of our members.

**Methods:** 'iPath', a soft ware developed specifically for telepathology (\*) serves for data transfer. Each case consists of three sections: a clinical, a gallery of microscopic images and a third for comments. Each case is discussed by several members of the group, case submitters are actively participating in the discourse.

**Results:** 23 hematologists and hematopathologists from 10 countries (Australia, Canada, France, Germany, Greece, Italy, Sweden, Switzerland, UK and US) act as consultants. 189 cases from 15 countries (Argentina, Armenia, Bosnia, Cambodia, Egypt, Estonia, India, Iran, Kenya, Latvia, Lithuania, Solomon Islands, UAE, Ukraine, and Uzbekistan) have been submitted during the period between 2005 and 2007. The majority are lymph nodes, and bone marrows followed by extra nodal lymphoproliferations. Sporadically other hematologic questions such as transfusion related problems were submitted.

**Conclusion:** The positive feedback from submitters reflects the need for a support network as ours, trying to cater for individual needs. Our activities could also help to establish new professional contacts, which might lead to fruitful scientific collaboration between the various parties. In addition online conferences are planned for the near future. Our project started off as a pilot of uncertain outcome, consequently it turned out to meet a great need.

\* Brauchli et al., Telemicroscopy by the internet revisited. J. Pathol. 2002; 196: 238.

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