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PERIPHERAL BLOOD PROGENITOR CELL (PBPC) TRANSPLANTATION WITH A SINGLE APHERESIS. R Pettengell, DP Deakin, D Crowther for the Manchester Lymphoma Group, Christie Hospital, Manchester, UK

We have used PBPC harvested with a single apheresis to transplant 34 high grade NHL (N) and 10 Hodgkin's disease (H) patients. Following 7 weekly cycles of VAPEC-B chemotherapy, rhG-CSF 300μg/day sc was given and patients leukapheresed after 5-9 days. A median (range) of $2.1x10^8$ (0.22-9.7) (N) and $1.7x10^8$ (1.3-2.8) (H) mononuclear cells/kg were obtained, comprising $11.6x10^6$ (0.6-180) (N) and $4.6x10^6$ (1.9-2.8) (H) CD34 positive cells/kg and $1.18x10^6$ (0.23-5.2) (N) and $0.5x10^6$ (0.13-1.8) (H) GM-CFC/kg.

9 Hodgkin's disease patients proceeded directly to ablative therapy (cyclophosphamide 50mg/kg iv daily x 4, BCNU 600mg/m^2 iv). 20 NHL patients had consolidation chemotherapy (ifosfamide 3g/m^2, Ara-C 800mg/m^2 iv x 4 day infusion q 3 wks x 3 cycles) then ablative therapy (busulphan 4mg/kg, cyclophosphamide 50mg/kg each x 4 days). PBPC alone were reinfused and G-CSF 300μg sc daily started. Recovery times were median days (range) to ANC> 0.5 $x10^9$/l, 9 (8-14) (N) and 9 (8-18) (H); platelets≥20$x10^9$/l, 9 (6-15) (N) and 13 (8-68) (H); antibiotic days, 8 (0-22) (N) and 9 (7-19) (H); hospital days 13 (10-35) (N) and 14 (11-55) (H); blood units transfused 3.5 (0-9) (N) and 6 (7-19) (H); platelet units transfused 16 (1-101) (N) and 46 (8-215) (H). There have been no graft failures.

In both the NHL and heavily pretreated Hodgkin's disease group, routine chemotherapy and G-CSF enable sufficient PBPC to be harvested at a single leukapheresis for haemopoietic rescue after myeloablative therapy. This approach improves the therapeutic index of tranplantation.

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COMBINED MODALITY THERAPY FOR PRIMARY GASTRO-INTESTINAL NON-HODGKIN'S LYMPHOMA (GI-NHL). Tondini C, Giardini R, Valagussa P, Santoro A, Bertulli R, Balzarotti M, Rocca A and Bonadonna G. Division of Medical Oncology, Istituto Nazionale Tumori, Milano, Italy

Clinical features and outcome of 135 pts with primary GI-NHL referred since 1972 to the Milan Cancer Institute were reviewed. 114 (84%) presented with Ann Arbor stage I-II, while 21 had widespread abdominal disease (stage IV). Primary was in the stomach in 73%, 15% in the small intestine and 9% in the colon ; multiple GI localizations occurred in 5 pts. Median age was 50 years, with 25% of pts older than 60. According to Kiel classification, 61% had pure high grade lymphoma, 9% had high-grade NHL with evidence of residual low grade NHL, and 30% had low-grade NHL. Complete surgical removal of all measurable tumor was feasible in 101 patients (75%). 22 patients were managed with surgery alone (12 pts) or with post-operative RT (10 pts) because they had very superficial low-grade NHL, while 83% were treated with CT, followed by local-regional RT in stage I-II disease. Of patients with stage I-II, 99% achived CR. After a median follow-up of 73 mos, 10-yr FFP and OS were 84% and 86%, respectively. Aside from age and a trend in favor of low grade histology (FFP 97% vs 79%), no other factor had a statistically significant impact on outcome. Of patients with advanced abdominal disease, 48% achieved CR and 10-yr FFP and OS were 44% and 42%, respectively. In conclusion, present study shows the good results obtained in a wide and unselected population of patients with stage I-II primary GI-NHL using a combined approach that includes surgical debulking and systemic chemotherapy. Surgery alone could be considered adequate treatment for those patients with low-grade NHL that does not infiltrate beyond the submucosa. Patients with advanced GI-NHL showed a long-term outcome similar to that of patients with advanced NHL arising outside the gastrointestinal tract.

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AUTOLOGOUS BONE MARROW TRANSPLANTATION (ABMT) FOR NON-HODGKIN'S LYMPHOMA (NHL) AND HODGKIN'S DISEASE (HD): THE ROLE OF IMMUNOTHERAPY

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Between 10/83 and 11/92 we have transplanted 90 patients (pts) with malignant lymphoma (NHL-52, HD-38). Of the NHL pts fifteen were transplanted at > second PR, 14 at progressive disease stage while 23 were transplanted during complete remission (first-9, second-10, third-4). Of the HD pts., 8 during CR (first-1, second-4, third-2, fourth-1), seventeen were transplanted at progressive stage, 11 at > second PR. Conditioning regiments included BCNU (300 mg/m^2 x 1 day), etoposide (200 mg/m^2 x 4 days), cytosar (200 mg/m^2 x 4 days), cyclophosphamide (60 mg/kg x 1 day) and thiotepa (0.6 mg/kg x 3 days) (BECAM) (NHL 17, HD 20); 9 NHL and 12 HD pts had the identical protocol w/o thiotepa (BECAM); 16 NHL 3 HD pts had the identical protocol w/o BCNU (TECAM). 8 pts (NHL 6, HD 2) were conditioned with total body irradiation and cyclophosphamide and 5 NHL pts with other polychemotherapy regiments. In addition to the chemotherapy involved field radiation was administrated to the site of the bulky disease. Transplant related toxicity was 11.5%. At 3 month post ABMT 32 pts.(NHL 19, HD 13) received immunotherapy with Interlukin-2 (IL-2) and interferon alpha (IFN α), while 45 (NHL 26, HD 19) recieved no immunotherapy. No significant difference in grade, stage or disease status at time of transplant was observed between the two groups of pts. Overall 25 (NHL 16, HD 9) (32%) relapsed 4.3 (0.8-33) month post ABMT. Relapse rate was higher for BECAM conditaioning (50%) in comparison to BECTAM (24%) or TECAM (25%) ($p<0.05$). Of the pts. with no immunotherapy 23 (NHL 14, HD 9) (51%) relapsed ($p<0.05$). Overall 52 pts (NHL 29, HD 23) (58%), 30/32 (94%) w/immunotherapy, 22/43 (51%) w/o immunotherapy are alive with no evidence of disease 19.2 (3-48) and 33.8 (3-84) month post ABMT, recpectively. In conclusion immnnotherapy may reduce relapse rate and increase survival for lymphoma pts. post ABMT.

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ON THE INFLUENCE OF ALPHA-2 INTERFERON (ROFERON-A) ON REMISSION DURATION IN PATIENTS WITH STAGES III AND IV LOW GRADE MALIGNANT NON-HODGKIN'S LYMPHOMA. J.H. Meerwaldt, A. Hagenbeek, on behalf of the EORTC Lymphoma Cooperative Group.

A prospective, randomised phase III study was initiated 6½ years ago in the EORTC Lymphoma Group. The objective of the study was to investigate whether alpha-2-interferon (IFN)administration in the phase of "minimal residual disease" will increase relapse-free survival or postpone progression of disease. Previously untreated patients older than 15 years with NHL (Working Formulation class B,C) were eligible. All patients recieved 8 courses of combination chemotherapy (Cyclophosphamide 300 mg/m^2 per os, days 1-5; Vincristine 1.4 mg/m^2 i.v. day 1, and Prednisone 40 mg/m^2 per os, days 1-5). After CVP all patients were evaluated and submitted to iceberg radiotherapy. Thereafter, ranomisation to either IFN $3x10^6$ IU s.c. three times per week for a period of 12 months or to "no further treatment". 346 patients were registered of which 262 are now evaluable for response to CVP with a total response rate of 85%, i.e. 125/262 (48%) complete remission, CR, and 98/262 (37%) partial remission, PR. A total of 101 patients were eligible for iceberg irradiation, 32 in CR and 69 in PR after 8 courses of CVP. Of the 69 PR patients, 28 (41%) reached a CR after irradiation. So far, 228 patients have been randomised: 114 to IFN, 114 to "no further treatment". IFN was well tolerated. The overall and progression free 3-years survival (PFS-3Yr) are estimated at 84% and 43%, respectively (median follow-up: 2.5 years). The median for PFS for all patients is 116 weeks. When the two curves are compared, the PFS-3Yr is 48% in the IFN maintenance group versus 40% in the control group. However, there is a significant difference in the duration of the PFS, i.e. 140 weeks in the IFN maintenance group versus 87 weeks in the control group ($p=0.03$). It is still too early to comment on possible differences in overall survival. In conclusion: in this randomised, study IFN maintenance treatment in the phase of "minimal residual disease" of low grade malignant NHL significantly prolongs progression free survival.

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PATTERNS OF RELAPSE AND SURVIVAL IN PATIENTS WITH NON HODGKIN LYMPHOMAS. A MULTIVARIATE STUDY

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Optimun treatment for NHL is a matter of controversy where the role of RT needs to be defined with a higher precision. The present study has been carried out aiming to know the reasons of failure and define clear indications for RT. The records of 143 NHL patients long followed after treatment have been reviewed. The majority of them were patients with diffuse (77%), extranodal (60%) and stages I/II (59%) lymphomas. Treatment was performed as follows: 1) radical or debulking surgery for primary extranodal presentations (followed by CT/CT + RT); 2) CT alone (53%) or CT + RT (47%) for nodal presentations. QT regimes used (COP, CHOP, BACOP) changed according to grade and stage. EF-RT in low grade I/II stages and IF-RT in all stages of high grade lymphomas were used as basic schedules. Univariate and multivariate analysis for survival were performed in order to find some predictive parameters and to establish different risk groups. Important results are the following: i) RT improved (91%) the rate of CR observed in nodular lymphomas stages I/II treated by CT alone (22%) ($p<0.01$); ii) RT lessened (5%) the local relapsing rate observed in diffuse lymphomas stages I/II treated by CT alone (87%) ($p<0.01$); iii) survival figures of patients with stages I/II of both nodular and diffuse lymphomas (treated by RT) were satisfactory (RFS 66% and 54% at 10 years, respectively) while survival figures of stage III nodular lymphomas (treated by CT alone) were under standard levels (RFS 11% at 10 years); iv) tumor size, number of tumor sites, LDH levels and surgery turned out to be other factors predicting for RFS; v) three risk groups of patients with probabilities of survival of about 74%, 36% and 0% at 10 years were defined.

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SALVAGE CHEMOTHERAPY FOR NON-HODGKIN'S LYMPHOMA [NHL] AND HODGKIN'S DISEASE [HD] WITH DEXAMETHASONE, ETOPOSIDE, IFOSFAMIDE AND CISPLATIN [DVIP].

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Fifty-four patients [pts] with refractory or relapsing NHL [n=42] and HD [n=12], aged 18-89 years, were treated with DVIP. Prior therapy included adriamycin and cyclophosphamide in all NHL pts and MOPP + ABV [or their variants] in all HD pts. Objective responses were noted in 29/42 [69%] NHL pts and in 5/10 [50%] evaluable HD pts. Seventeen NHL pts [40%] achieved CR for 2.5-29+ months. The following pre-treatment factors were associated with a higher CR rate in NHL pts: 1] aggressive histology, 2] low tumor burden, 3] CR to previous chemotherapy, 4] prior therapy with one combination only. Only one HD pt [10%] achieved CR for 14+ months. The main toxicity of DVIP was myelosuppression. Grades 3 and 4 leukopenia developed in 37 [69%] pts and grades 3 and 4 thrombocytopenia in 16 [30%] pts. Drug-related death occurred in one HD pt. Non-hematological toxicity was mild to moderate. We conclude that DVIP is an effective and relatively safe salvage therapy in lymphoma.