The 9 pts with polyostotic disease received a combined therapy. Pts were irradiated to bulky lesions or to sites with high risks of fracture, with a mean dose of 37 Gy (30–45 Gy). Five pts were treated with ADM containing CT (4 CR and 1 PR). Two of them relapsed and died after 15 and 131 mo, while 3 pts are alive and disease-free after a median follow-up for the entire group of 80 mo. Four pts that did not receive ADM did not achieve CR and died of disease progression. Survival rate is 80% with a median follow-up of 43 mo for pts with LD and 34% with a median follow-up of 80 mo for pts with AD.

Neither bulky lesions, soft tissue involvement, pathologic fracture nor systemic symptoms were associated to worse prognosis. The use of ADM was associated to a lower incidence of local or systemic relapse in all pts and to a higher survival rate among pts with AD. A high CR rate was obtained with a radiation dose >40 Gy, while all treatment failures were observed in the group treated with a dose <40 Gy. Pts treated with a partial irradiation of the bone did not relapse. The impact of local lymph nodes irradiation and the advantage of whole bone irradiation or partial bone irradiation remain undefined.

Although the small number of cases, we can conclude that the use of ADM-containing CT and a radiation dose > 40 Gy on involved sites is mandatory in the treatment for PLB, independently of stage.

787 POSTER

MULTIPLE CYCLES OF AGGRESSIVE CHEMOTHERAPY FOR RELAPSED LYMPHOMA

G. Goss, J. Szer, A. Grigg
Bone Marrow Transplant Service, Royal Melbourne Hospital, Melbourne 3050, Australia

Patients with non-Hodgkin's lymphoma and advanced Hodgkin's disease who relapse after first line therapy have a poor prognosis. Around 30–40% of patients with disease sensitive to salvage chemotherapy achieve long term survival after subsequent high dose chemotherapy (HDCT) and autologous bone marrow transplantation (ABMT). In addition, for patients undergoing HDCT, the use of peripheral blood progenitor cells (PBPC) results in faster neutrophil and platelet recovery compared with bone marrow.

Based on the premise that a single cycle of HDCT may be suboptimal, we piloted a regimen combining 5 days of infusional ara-C and etoposide with bolus doses of cyclophosphamide and methotrexate and high dose oral dexamethasone (MADEC) as a salvage therapy for patients with relapsed lymphoma. Following MADEC all patients received granulocyte colony stimulating factor to assist in mobilisation of PBPC, and to reduce the incidence of febrile neutropenia.

Twenty-five patients with relapsed lymphoma (19 with intermediate grade non-Hodgkin's lymphoma, 6 with Hodgkin's disease) received a total of 45 cycles of MADEC. All had demonstrated response to prior induction chemotherapy (22 CR, 3 PR) with median duration of response of 6 months (1–60 mos). There was one toxic death. The MADEC regimen was intensely myelosuppressive. All patients had nadir granulocyte counts of $>0.5 \times 10^9$/l, resulting in hospitalisation for febrile neutropenia after 35 of 45 cycles. Platelet and packed cell transfusions were required after the majority of cycles. Non-haematological toxicity was mainly mucositis and was generally mild.

Of 24 evaluable patients 8 achieved CR after MADEC and 10 achieved PR (6 pts with residual masses had gallium scans, 5 were negative). Patients responding following cycle 1 underwent leukapheresis after the neutrophil nadir. Median number of leukaphereses was 2 (1–4). Median number of CD34+ cells mobilised was 2.75×10^6/kg ($0.5–22.8 \times 10^6$/kg) and median number of CFU-GM was 68.4×10^4/kg ($0.5–697.5 \times 10^4$/kg). In responding patients a second course of MADEC was given to achieve maximal reduction of disease bulk prior to transplantation. Sixteen patients proceeded to HDCT with PBPC support. All patients engrafted successfully with median days to ANC $< 0.5 \times 10^9$/l of 12 days (9–16 days) and to platelets 20×10^9/l independent of transfusion of 10 days (7–42 days). Overall median survival of the entire group and of patients undergoing HDCT has not been reached, with median follow up 14 months (6–44 mos.) Disease free survival in the HDCT group is median 13 months (6–44 mos).

Conclusion: The MADEC regimen was useful for identifying patients with chemosensitive disease who may benefit from HDCT and for maximal reduction of disease bulk prior to the procedure. Combination with G-CSF resulted in mobilisation of adequate numbers of PBPC to support engraftment after HDCT. The therapeutic benefits of this regimen relative to less intensive regimens prior to transplant warrants evaluation.

788 POSTER

COMPARISON OF LIPOSOMAL ENTRAPPED DOXORUBICIN (LED) WITH BLEOMYCIN AND VINCRISTINE (BV) IN THE TREATMENT OF AIDS-RELATED KAPOSI'S SARCOMA

M. Harrison[1], D. Tomlinson[1], M. Spittle[2], S. Stewart[1]
[1]*Department of Oncology, St Mary's Hospital, London, U.K.*
[2]*Department of Oncology, Middlesex Hospital, London, U.K.*

Between July 91 and Sept 94 106 patients were commenced on treatment with BV or LED (Dox SL LTI) on 123 occasions. Treatment was initiated with LED on 68 occasions with 56 patients and with BV on 55 occasions with 51 patients.

Both groups of patients were comparable in terms of age, Karnofsky score and ACTG poor prognosis criteria (JCO: 7(9). 1201–1207. 1989).

In total 585 cycles of chemotherapy were given (BV-268, LED-317). Median number of cycles for BV is 5 (1–15) and median number for LED is 4 (1–14). Overall response rate for BV is 65.4% (36/55) with 58.2% (32/55) partial responses (PRs) and 7.2% (4/55) complete responses (CRs). Overall response rate for LED is 72% (49/68) with 64.7% (44/68) PRs and 7.3% (5/68) CRs. There is no statistical difference in response rate between the two groups (Chi squared test).

Median response duration measured from completion of chemotherapy is 8 weeks for BV (4–48) and 8 weeks for LED (1–24). (Kaplan Meier and Log Rank assessment). Median cycle to response is 3 for BV (1–6) and 2 for LED (2–4).

In summary LED offers an equivalent response rate and duration of response to conventional chemotherapy for AIDS related KS.

789 POSTER

ORIGIN, FUNCTION, AND PROGNOSTIC SIGNIFICANCE OF SOLUBLE CIRCULATING CD44

R. Ristamäki, S. Jalkanen, K. Grön-Virta, M. Salmi, H. Hagberg, K.-M. Kälkner, H. Joensuu
National Public Health Institute, Department of Oncology and Radiotherapy, University of Turku, Finland
Department of Oncology, University of Uppsala, Sweden
Department of Oncology and Radiotherapy, University of Helsinki, Finland

The serum level of soluble CD44 (s-CD44) has been reported to change in parallel with response to treatment in lymphoma, but its origin, function, and prognostic value have not been known. Both peripheral blood and tumour lymphocytes were able to secrete s-CD44 in a cell culture. When Burkitt lymphoma cells were transfected with human CD44 and transplanted into SCID-mice, human s-CD44 appeared in the blood circulation. s-CD44 was able to adhere to hyaluronate and fibronectin, suggesting that it retains biological activity. S-CD44 was measured from the sera of 123 patients with non-Hodgkin's lymphoma by dotblotting, and high levels of s-CD44 turned out to be associated with high serum levels of lactate dehydrogenase and thymidine kinase, high histological grade of malignancy, and poor outcome. In conclusion, s-CD44 is biologically active and partially originates from lymphoma cells.

790 POSTER

REHABILITATION OF LONG-TERM SURVIVORS AFTER HODGKIN'S DISEASE: A CROSS-SECTIONAL STUDY IN CALVADOS, FRANCE

F. Joly[1], M. Henry-Amar[1], A. Tanguy[1], O. Reman[2], A.M. Peny[1], B. Vié[1], J.Y. Génot[1], X. Troussard[2], A. Busson[1], M. Leporrier[2]
[1]*Registre Général des Tumeurs, France*
[2]*C.H.R.U. Hématologie Clinique, 14021 Caen, France*

With the growing number of patients surviving cancer, there is an increasing concern with their long-term adaptation. A cross-sectional study was performed in 1995 focusing on physical, psychological, social and familial sequelae in Hodgkin's disease patients who survived 4 years or more from initial treatment. Patients were selected from the Calvados General Cancer Registry if they were treated during the 1978–1990 period, did not develop a second malignancy, remained free of disease since 01.01.1991, and were aged 18 years or more at interview. Information was taken from a self questionnaire sent by mail. The EORTC QLQ-C30 core questionnaire was used to evaluate the quality of life. Clinical data were obtained from medical records.

At March 1st, 1995, 107 patients (male/female ratio 1.4; mean age 32 years, range 3 to 78) were selected of whom 67% presented with early stages, 38% with B symptoms. Initial therapy consisted of irradiation (RT) in 29%, combination RT and chemotherapy (CT, mostly MOPP) in 66%, and CT alone in 5%. The mean follow-up was 123 months

(57 to 203). Overall, 59% of patients developed mild (27%), moderate (25%) or severe (7%) clinical complications. Complications did not correlate with follow-up, clinical stage and RT extent. In contrast, complications correlated with CT ($P = 0.058$), independently of RT.

Results concerning the survey and the quality of life in these patients will be presented.

791 POSTER

CNS INVOLVEMENT IN NON-HODGKIN'S LYMPHOMA (NHL)

N. Keldsen, W. Michalski, S. M. Bentzen, K. Thorling

Department of Oncology and Danish Cancer society, Department of Experimental Clinical Oncology, Aarhus University Hospital, Denmark

Twenty-seven cases of CNS involvement were found among 498 consecutive patients with NHL. Only 3 of 96 patients with low grade lymphomas (Working formulation) had CNS involvement, in all 3 cases occurring after transformation into high grade lymphoma.

In univariate analysis of 402 patients with intermediate or high grade lymphoma lymphoblastic histology (LB), age <35 years, B-symptoms, stage IV disease, testis involvement (2 of 6 patients), and bonemarrow (BM) involvement were significant. When LB was excluded BM became insignificant ($P = 0.65$). Sex, extranodal disease and LDH >400 U were insignificant. In multivariate analysis only LB, Stage IV disease and B-symptoms were significant.

It is concluded that other risk factors such as young age and BM involvement are connected with LB histology and do not constitute true independent risk factors.

792 POSTER

INCREASED GLUCOSE METABOLISM IN NON-HODGKIN'S LYMPHOMA AS STUDIED WITH FDG PET

M. Lapela, S. Leskinen, H. Minn, P. Lindholm, P. Klemi, K.-O. Söderström, M. Haaparanta, H. Joensuu, E. Nordman

Department of Oncology and Radiotherapy, Turku University Cyclotron, PET Center, Turku University, FIN-20520 Turku, Finland

Glucose metabolism has been demonstrated to be increased in neoplastic tissue, and to reflect the grade of malignancy of human cancer. We studied *in vivo* glucose metabolism in 22 pts with untreated non-Hodgkin's lymphoma with fluorine-18-fluorodeoxyglucose (FDG) and positron emission tomography (PET). FDG uptake in lymphoma deposits was measured as standardized uptake values (SUVs) of the tracer, and compared with histological classification and proliferative activity.

Results: The median SUV of the lymphomas was 8.5. A high FDG uptake in tumors was associated with high histological degree of malignancy by the Working Formulation ($P = 0.005$) or by the Kiel classification ($P = 0.003$). A high FDG accumulation was also associated with a high S-phase fraction ($r = 0.786$, $P = 0.002$).

Conclusion: FDG PET may find application in assessing the grade of aggressiveness of lymphoma in clinically problematic cases.

793 POSTER

RAG1 AND 2 EXPRESSION IN THE GENESIS OF HIV ASSOCIATED NON-HODGKIN'S LYMPHOMAS (NHL)

R. Levy[1], J.M. Cayuela[2], J. Brière[1], D. Israel Biet[1], F. Sigaux[2], J.M. Andrieu[1]

[1]Oncology Unit, Laennec Hospital 75007 Paris, France

[2]Haematology Laboratory, U93 St Louis Hospital, 75010 Paris, France

The mechanisms responsible for the high incidence of NHL during HIV infection remain unclear. We test the hypothesis that an abnormal expression (a normal one is necessary for the physiological recombination in lymphoïd cells) of the RAG1 and 2 genes, induced by HIV infection, could be involved in the chromosomal translocations leading to NHL. We investigate their expression in various lymphoid tissues of HIV infected patients (pts). *Material:* peripheral blood mononuclear cells (PBMC) (5 pts), lymph nodes (3 pts), bone marrow (1 pt), spleen (3 pts) from HIV infected pts, and benign hyperplastic lymph nodes from 3 non HIV infected subjects as well as normal PBMC infected *in vitro* with HIV1, (with or without PHA treatment) were analyzed. *Methods:* total cellular RNA was isolated, reverse transcribed with 3′ primers of RAG 1, RAG 2 and actin primers. PCR was then performed on cDNA with adequate RAG1, 2, and actin (control) primers (JC Bories Blood, 1991, 78). RNA from REH cells, a RAG expressing cell line, and from Hela (non expressing cell line) were used as controls. This method allows detection of 10000 RAG expressing cells and discriminates illegitimate transcription (J.C. Bories, *Blood*, 1991, 78). PCR products were run on agarose gel to detect specific PCR bands. *Results:* No RAG 1 and 2 expression was detected in any sample tested except REH. *Conclusion:* These results do not favor the hypothesis that deregulated RAG 1 and 2 expression participates in the lymphomagenesis of HIV associated NHL. However, we cannot exclude that an abnormal RAG 1 and 2 expression exists, if it occurs in a very limited number of cells, which would have be undetectable in our system.

794 POSTER

CLONAL EVOLUTION IN PROGRESSIVE LYMPHOMAS

R. Rosenquist[2], D. Holmberg[3], A. Lindström[2], G. Roos[2], J. Lindh[1]

[1]Inst. of Oncology, [2]Inst. of Pathology, [3]Cell and Molecular Biology Umeå, Sweden

Introduction: Alterations in clinical behaviour, morphological appearance and immunophenotype are frequently observed in relapsing non-Hodgkin's lymphoma (NHL). The aim of this study was to analyse a material of relapsing or progressive lymphomas with respect to clonality changes, using the immunoglobulin heavy-chain (IgH) as a marker of clonality.

Material and methods: 52 samples taken during the course from 19 NHL cases were investigated with *RFLP analysis* of the IgH locus, *VH gene family specific PCR-SSCP* and in five selected cases by *sequence analysis* of VH gene fragments. Seven cases showed transformation or discordant lymphomas during the course.

Results: In 10 cases no alteration of the IgH locus could be detected by the methods used, By *RFLP* 5/7 cases with transformed/discordant lymphomas and 3/12 with unchanged morphology showed altered IgH patterns. Three cases showed evidence of oligoclonality (> 2 rearranged bands) on RFLP. Altered VH gene *PCR-SSCP pattern* and/or *VH gene family utilization* was observed in 7 cases, 6 of these also showing altered IgH-RFLP. In two cases, a rearrangement involving an additional VH family was amplified at relapse. In two other cases the VH rearrangement from diagnosis was not detected at relapse. *Sequence analysis* revealed point-mutations in the 4 cases (4, 4, 6, 20 mutations, respectively) with altered PCR-SSCP pattern. In one of the two cases with a novel VH gene family utilization at relapse, a VH gene replacement was detected. In the other case, no sequence homology was found between the samples.

Conclusion: Alterations of the clonal IgH rearrangements during the course occurred in about half of the cases, mainly in the transformed/discordant lymphomas and were due to point mutations as well as to presence of different clones of malignant cells.

795 POSTER

EARLY STAGE HODGKIN'S DISEASE (HD): AN ANALYSIS OF PROGNOSTIC FACTORS IN A LARGE SERIES FROM A SINGLE INSTITUTION

S.M. Magrini, E. Cellai, M.G. Papi, M. Portici, P. Ponticelli[1], R. Bagnoli, G.P. Biti

Radiotherapy, Florence

[1]Radiotherapy, Arezzo, Italy

Considerable progresses have been made in the treatment of HD in the last 25 years: cause specific survival rate for HD patients (pts) treated in Florence (all stages combined) is much higher for those treated after 1970 then in those treated before (74% vs 46% at 20 years). Results are even better for early stage HD. However, the analysis of prognostic factors in early stage HD is crucial to the definition of "high risk" groups, to be treated more aggressively, and of "low risk" subsets of patients, for whom the "therapeutic burden" could be reduced, to avoid long term sequelae. We present the results of an analysis on 841 Clinical Stage I–II HD pts (472 of whom have been submitted to staging laparotomy) consecutively treated 1960 through 1991, at the Florence Radiotherapy Department. Data from a single Institution are more homogeneous; moreover, our cases have been submitted to unlimited follow up and long term results have therefore a sound basis. Twenty-years cause specific survival rates are higher in patients: without "B" symptoms (77% vs 59%); with favourable histology (PL, NS); in the younger ones; in the females (78% vs 70%); in patients with CS I (84% vs 71%); in patients without lung hilar involvement (76% vs 65%); in patients presenting with high neck or subdiaphragmatic involvement only. Conversely, bulky mediastinal disease does not seem to adversely affect prognosis. The use of more aggressive treatment options (including chemotherapy) seems to ameliorate prognosis in patients with "B" symptoms. Results of uni- and multivariate analysis of the different factors affecting cause specific and relapse free survival will be discussed.