782 POSTER

CLINICAL SIGNIFICANCE OF SOLUBLE IL-2 RECEPTORS (S-IL-2R) IN HODGKIN'S DISEASE (HD)

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To better define the clinical significance of sIL-2R in HD, from 8/88 to 6/93 we have measured serum levels of sIL-2R (U/ml) by ELISA in 175 patients (pts) with HD before treatment. Patient characteristics were: M/F: 91/84; median age 28 yrs, range 16–69; stage I + II/ III + IV: 128/47; A/B symptoms: 95/80; nodal vs extranodal disease: 140/35; number of nodal involved sites ≤ 3 vs >3:113/62; bulky No/Yes: 132/43. Sixty-nine healthy subjects were used as controls. Increased levels of sIL-2R were detected in 149/175 (85%) pts and their values (X ± SE) were significantly higher than in controls (1960 ± 174 vs 479 ± 12; $P <$ .001). Levels of sIL-2R were significantly higher in patients with either stage III–IV vs I–II (3589 ± 553 vs 1362 ± 76; $P = .0003$); "B" symptoms vs "A" (2768 ± 344 vs 1279 ± 96; $P = .0001$); nodal vs extranodal ± nodal disease (1656 ± 110 vs 3177 ± 725 $P = .0004$) or more than 3 nodal sites vs > 3 (3157 ± 424 vs 1304 ± $P = .0001$). IL-2r were also evaluated at the end of treatment in 130 pts, 128 cases achieved CR and their sIL-2R values were significantly lower compared to those at diagnosis (650 ± 25 vs 1747 ± 142, $P = 0.0001$), whereas in the patient who progressed the value increased (1900 vs 2700). After a median follow-up of 40 months, in 11 of 18 patients who relapsed sIL-2R levels were evaluated at relapse and they were higher than those detected at CR (1791 ± 554 vs 654 ± 75). However, the difference was not statistically significant. These results indicate that increase in the levels of sIL-2R is related to disease extent and their determination can be useful in monitoring the outcome of Hodgkin's disease.

783 POSTER

EVALUATION OF 487 MAGNETIC RESONANCE IMAGING (MRI) EXAMINATIONS OF THE BONE MARROW (BM) IN VARIOUS MALIGNANCIES IN THE ADULT

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MRI is the only direct *in vivo* method of BM visualisation. We have used this technique in various malignant disorders and an overall evaluation is presented. The examinations, done on a 1.5 Tesla General Electric equipment included the spine, the pelvis and the femurs. All patients had a bone marrow cytology or histology examination. The major disorders were breast cancer 12%, chronic lymphoproliferative malignancies 25%, chronic myeloproliferative disorders 14%, plasma cell disorders 16%, aplasia 3% and various others.

The images are classified as diffuse, circumscribed and diffuse circumscribed. The results were as follows: sensitivity 95%, specificity 66%, and accuracy 93%. Positive predictive value was 96%, negative predictive value 57%.

MRI of the BM gives a high quality anatomical display with high contrast details. Duration of the examination is short. For most pathologies of a wide-spread nature, especially the chronic proliferative disorders, probably an upper femur examination is sufficient. Iron overload and myelofibrosis can cause a problem in evaluation of cellularity. In BM aplasia we consider MRI as mandatory for adequate staging, the anatomical substrate showing an excellent correlation with the clinic.

784 POSTER

RESULTS OF THE CYCLOPHOSPHAMIDE, ADRIAMYCINE, VINCRISTINE, PREDNISOLON (CHOP) ± BLEOMYCINE TREATMENT AND EVALUATION OF PROGNOSTIC FACTORS IN AGGRESSIVE LYMPHOMAS

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In this study, we presented the results of the CHOP ± bleomycine treatment and evaluation of prognostic factors in 93 patients with aggressive lymphoma. Mean age was 43 (15–82) years; male/female ratio was 55/38. Primary extranodal lymphoma, most frequently gastric and intestinal, was found in 19 (20%) patients. Distributions of patients according to the clinical stages were: 15% in stage I, 44% in stage II, 24% in stage III and 17% in stage IV. Performance status (PS) (ECOG) of the patients were: 15% in PS 0, 53% in PS 1, 21% in PS 2 and 11% in PS 3. Serum LDH levels were elevated in 41 patients (49.4%). Seven patients with primary extranodal lymphoma received adjuvant chemotherapy following surgery. Excluding these patients, the overall response rate was 83% (69% complete remission (CR)). Three-year-disease-free and overall survivals were 67% and 57%, respectively. Ninety percent or over dose intensity was achieved in 50% of the patients. Treatment toxicities were within acceptable limits with 10% of patients having grade 3–4 hematologic toxicity. Age, PS, stage, number of the extranodal involvement sites (NEIS), B symptoms and LDH were examined as prognostic factors. PS (0–1 vs 2–4) and stage were found to be significant in complete remission rate ($P = 0.025$ and $P = 0.040$, respectively). LDH, stage, NEIS (≤ 1 vs >1)and PS were determined to be significant factors for overall survival in univariate analysis ($P = 0.0345$, $P = 0.0005$, $P = 0.0030$, and $P = 0.0027$, respectively). Multivariate analysis yielded PS and NEIS as independent factors ($P = 0.019$ and $P = 0.018$, respectively). Only NEIS was found to be the independent factor in our patients younger than 60 ($P = 0.009$) in contrast to the international prognostic index. A modified age adjusted index including stage, LDH, PS and NEIS was found to be an important factor for both complete remission rate ($P = 0.017$) and overall survival ($P < 0.00001$) in this study.

785 POSTER

RADIOTHERAPY IN THE MANAGEMENT OF CUTANEOUS EPIDEMIC KAPOSI'S SARCOMA

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Patients treated for AIDS-associated skin Kaposi's sarcoma from October 1992 to June 1994, by localized irradiation using 100 Kv x-ray energy were reviewed. Given dose was 800 cGy/1 fr for small (less than 1.5 cms) lesions and non-edematous lesions and 3000 cGy/10 fr for the rest. All fields were treated daily. Twenty-two patients received treatment to 251 lesions. Median age was 38 years old (2859). According to Mitsuyasu's staging, 2 pts were stage I, 8 pts were stage II, 1 pts stage III, and 11 pts stage IV. One hundred and ninety lesions were localized in the face, 28 in lower extremities, 24 in superior extremities, and 9 in the thorax. Palliation of pain was the main justification for treatment in all feet lesions, while cosmesis was the rational for the facial lesions. 84% of lesions had some degree of associated edema, and 1% were ulcerated. CR with or without residual pigmentation was achieved in 95.2%, while 4.4% had a PR, and 0.4% NR. Pain was completely relieved in all patients. The overall tolerance was acceptable. Radiotherapy is useful and recommended as a palliative treatment to relieve pain, cosmetic and physical discomfort for those patients with AIDS related Kaposis's sarcoma. Long term control with doses ranging from 800 cGy/1 fr to 3000 cGy/10 fr tailored to the individual patient's needs.

786 POSTER

PRIMARY NON-HODGKIN'S LYMPHOMA OF THE BONE (PLB): MANAGEMENT OF 21 CASES

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A retrospective series of 21 pts with PLB treated between 1980 and 1994 is presented. Median age was 55 ys (34–84). Eight were male and 13 female. Almost all pts had pain as initial symptom, while pathologic fracture was observed in 5 cases. Most common site was toraco-lumbar spine (14 cases). Twelve cases had stage I–II disease and 9 had stage IV (multiple bony sites without systemic parenchymal nor bone marrow involvement). Two pts had systemic symptoms (stage IV). Bulky lesions were observed in 25% of pts with limited disease (LD) and in 56% of pts with advanced disease (AD). Adjacent soft tissue involvement was observed in 72% of cases. The commonest histology was diffuse large cell lymphoma (13 cases).

Three pts with LD are not assessable for response and survival because they died during therapy (not iatrogenic causes). Seven out of 9 evaluable pts with LD were treated with adriamycin (ADM)-containing CT plus RT to involved bony and locoregional nodal sites with a mean dose of 43 Gy (36–45 Gy), while 2 were treated with CT alone (one pt received ADM and one did not). All of them achieved CR. Only the pt that did not receive ADM relapsed but is yet alive after 69 mo. Seven pts with LD are alive and disease free after median follow-up of 43 mo. Remaining pt died in free of disease at 20 mo of myocardial infarction. Median survival of evaluable pts is 34+ mo.

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

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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

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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

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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

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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