are at risk of late effects of therapy. The major aim of a prospective study was to evaluate health consequences from radiation therapy (RT), including those to thyroid gland.

Methods: Since 1996 130 early stage HD patients in long-term remission were contacted; 39 persons (26 women, 13 men) gave informed consent to participate in the study. All of them were administered 40 Gy RT to the neck lymph nodes using 60 Co source. Median remission duration was 21 (range 16-34) years, median age at evaluation - 45 (range 35-73) years.

Thyroid exploration included 131 iodine scintigraphy; TTG and T4 levels; ultrasound and, if necessary, UG-FNAB; thyroid antibodies; morphology.

Results: After complex examination thyroid enlargement was found in 9 (23%) cases, chronical autoimmune thyreoiditis - in 16 (41%), nodular lesions - in 29 (74%), follicular adenomas - in 8 (20%), papillary thyroid cancer -in 1(2.3%). Complaints at referral were presented by two pts with minor swallowing disturbances. Only 4 (10%) pts were found free from any thyroid pathology. Due to combination of different pathologies its total number was higher than overall proportion (90%) of patients with thyroid disorders.

Conclusion: High total rate (90%) of thyroid pathology and 23% rate of neoplasias were revealed in HD patients randomly examined in 20 years and more after RT to the neck area. These findings attract attention to necessity of more systematic follow-up of otherwise cured HD patients.

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The combination of Gemcitabine plus vinorelbine as salvage treatment in non-Hodgkin's Lymphoma. A Hellenic Cooperative Oncology Group study

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Purpose: To evaluate the response rate, toxicity and time to progression of the combination of Gemcitabine + Vinorelbine as salvage treatment in pri-mary refractory or relapsed lymphoma.

Methods: Twenty-five patients with primary refractory disease (five patients), in first relapse (14 patients) and 6 in subsequent relapses were treated with the combination of gemcitabine 1000 mg/m2 and vinorelbine 30 mg/m2

D1+D8 in cycles of three weeks with the support of GCSF 5 μg/kg D2-D6 and D10-D16. Two patients had small cell lymphocytic lymphoma, 2 patients mantle cell lymphoma and 21 patients high grade lymphoma.

Results: Two patients were not evaluable for response, one because refused further treatment after the first cycle and one because of neurotoxicity gr 4 after the first cycle. They were evaluable for toxicity.

Of twenty three evaluable patients, 4 patients (17%), (95% CI;12-32%) achieved CR, seven patients (30%) (95% CI;11-49% achieved PR, six patients (26%) had strabilization of their disease and six patients (26%) progressed, for an overall response rate of 47% (95% CI; 27-68%). The median time to progression was 5 months. Toxicities grade three, four were leucopenia in 6 (27%), neutropenia in 7 (30%), anemia in (17%) thrombocytopenia in 3 (13%) and neurotoxicity in1 (4%) patients.

Conclusions: The combination of gemcitabine + vinorelbine is active in the treatment of refractory or relapsed lymphomas with an overall response rate of 47% and acceptable toxicities

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Prevalence of Anemia in Intermediate Grade Non-Hodgkin's Lymphoma (IGNHL)

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Purpose: To evaluate the prevalence of anemia at baseline (pre-chemotherapy) in IGNHL patients and its association with other clinical characteristics.

Methods: A retrospective sample of 591 patients diagnosed between 1993 and 1999 and subsequently treated with CHOP chemotherapy was used. Data were collected from twelve different oncology practice sites. Anemia was defined as a hemoglobin (Hb) value < 12 g/dL at baseline.

Results: Anemia was present in 193/546 (35.3%) of the patients. Baseline Hb values were not available for 45 patients. Of the 193 anemic patients, 131 (67.9%) patients had Hb values between 10-11.99 (NCI Grade 1; mild), 53 (27.5%) had Hb values between 8-9.99 (NCI Grade 2; moderate), and 9 (4.7%) had Hb values <8 g/dl (NCI Grade 3 & 4; severe to life-threatening). Anemia was significantly associated with age over 60 (38.8% vs. 29.9%, p=.035), extranodal sites > 2 (43.5% vs. 31.5%, p=.035), Ann Arbor stage III or IV (41.8% vs. 28.7%, p=.003), elevated LDH (51.5% vs. 23.3%, p<.001) and B-symptoms (51.3% vs. 31.3%, p<.001). Histology data were available for 473 patients, and anemia was most frequently observed in large cell-immunoblastic (56%) and large cleaved or non-cleaved cell (38.9%). Bone marrow involvement data were only partially available and are not reported here.

Conclusion: The results support previous finding of a high prevalence of anemia prior to cytotoxic therapy in chemo-naive lymphoma patients. Whether the implementation of early anemia management, especially in poor prognostic patients, improves clinical outcomes will need further evaluation.

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Study of the role of hepatitis c virus in overt b-cell non-Hodgkin's lymphoma

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Several studies from different parts of the world have indicated a potential association between Hepatitis C virus (HCV) and a variety of lymphoproliferative disorders. In the present study we examined whether HCV RNA sequences can be found in paraffin sections from patients with B-cell NHL using the most sensitive technique RT-PCR for detecting 5 untranslated sequences of HCV. Forty patients with B-NHL were investigated for serum HCV-antibodies (ELISA-Ver.4), HCV-RNA sequences in formalin fixed paraffin embedded tumor tissues by using RT-PCR. In addition 10 cases with Hodgkin's disease (HD), and 10 cases with metastatic lymphadenopathy from non-lymphoproliferative malignancies were taken as a control. HCV-RNA was detected in 6/40 patients (15%) with NHL studied from paraffin-embedded lymphoma tissue, negative strands were detected in five of them indicating viral replication within lymphoid tissues. All cases of the HD & control groups were found to be negative for HCV-RNA. To rule out the most common other viral cause of NHL & HD, these cases were also investigated for EBV-DNA in tumor tissues by PCR. Ninety percent of these cases were positive for EBV & all were polyclonal & type 2, which had no role in lymphoma in Egypt. From our study we concluded that the HCV may play a role in the pathogenesis of B-NHL, & it needs careful studying. Paraffin-embedded tissue can be tested for HCV RNA and this technique allows retrospective and prospective analysis of tissue of HCV.

345 POSTER

Value of hepatic biopsy in the Non-Hodgkin Lymphomas (NHL)

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Introduction: Hepatic biopsy in patients (pts) with NHL is indicated when laboratory measurements are elevated or hepatic enlargement is found. This result can change the therapeutic approach. The purpose of this study is to determinate the contribute of this biopsy in the staging of NHL.

Patients and Methods: Descriptive study about 52 patients included in a staging, that were submitted to hepatic biopsy at the diagnosis of NHL.

Results: Thirty were male and 22 were female. Thirteen patients had extranodal NHL. The histology subtypes found were diffuse large cell (DLC)(25 pts), follicular centre cell (FC)(11 pts), mantle cell(MCL) (4pts), marginal zone(MZL) (3 pts) and others (9 pts). Eight patients had clinical hepatomegaly or liver enlargement in CT scan, and 6 pts had analytic hepatic abnormalities. Thirteen patients (25%) had positive hepatic biopsy and 2 of these are extranodal NHL. From these, 6 patients had liver enlargement, 2 analytic hepatic abnormalities and 7 no clinical or analytic liver alterations Liver is the only extranodal involvement in 5 patients (9,6%). Eight also had organic involvement at others sites and/or positive bone marrow biopsy. Three patients had liver enlargement with negative liver biopsy. Thirteen patients had bone marrow invasion and this is the only extranodal involvemegnt in 6 of them. One patient had a hepatic hematoma and another an self-limited hemoperitoneu, both requiring hospitalisation The patients with positive hepatic biopsy had the DLC (4 pts), MCL (3 pts), CF (1 pts), MZL (1 pts) other histology's (5 pts).

Conclusions: The hepatic biopsy change the NHL stage in an important number of patients (5) even in those without clinical or analytic hepatic abnormalities. In these group of patients the value of hepatic biopsy was similar to bone marrow biopsy also with a greater morbidity.

Multiple myeloma

346 POSTER

Incidence and prognostic significance of deletions of tumor suppressor genes and aneuploidies in multiple myeloma: an interphase FISH study

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Recent studies indicate that chromosome aberrations are important prognostic factors in patients with multiple myeloma. In the present study, we performed interphase fluorescence in situ hybridization (FISH) in consecutively ascertained samples from 32 patients with multiple myeloma treated in our department from 1990 to 1999. In each case, a panel of 10 different FISH probes hybridizing to the chromosomal regions 8q24/CMYC 9p21/P16, 11q13/CyclinD1, 11q22, 13q14/D13S25, 17p13/P53 and to the centromeres of chromosomes 3, 7, 9, and 11 was applied. A simultaneous applied control probe served as an internal control for the hybridization efficiency. In addition to the patients' samples, 8 normal control samples were analyzed to define the cut-off levels for the probes under investigation. The FISH results were correlated with clinical data and the overall survival of the patients.

The majority of cases showed alterations of at least one locus analyzed (28 of 32 cases). The following abnormalities were detected: monosomies of 17p13/P53 in 11 of 31 cases (35%), monosomies of 13q14/D13S25 in 10 of 31 cases (32%), trisomies of 8q24/CMYC in 10 of 31 cases (32%), trisomies of 11q13/CyclinD1 in 10 of 32 cases (31%), trisomies of 11q22 in 7 of 31 cases (23%), trisomies of 9p21/P16 in 7 of 32 cases (22%), and trisomies of centromeres 3, 7, 9, and 11 in 11 of 32 (34%), 6 of 31 (19%), 4 of 29 (14%), and 10 of 32 cases (31%), respectively.

Deletions of D13S25 (18 vs. 30 months median survival, p 0,017) and P53 (20 vs. 32 months median survival, p 0,03), and overrepresentations of CMYC (16 vs. 30 months median survival, p 0,005) were associated with a significantly shorter overall survival as compared to patients without these aberrations.

The present study underlines the importance of chromosomal abnormalities in the assessment of the prognosis of patients with multiple myeloma.

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Spontaneous secretion of matrix metalloproteinases, urokinase plasminogen activator, its receptor and cytokines in primary long-term bone marrow cultures of multiple myeloma patients

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Purpose: Matrix metalloproteinases (MMP's), urokinase plasminogen activator (uPA), its receptor (uPAR) play a key role in dissemination of several cancers, and cooperate with cytokine network. There are only very limited report on their involvement in pathology of multiple myeloma (MM), a bone devastating neoplasia. We investigated spontaneous secretion of MMP's, uPA, uPAR, and cytokines by myeloma marrow microenvironment in primary long-term bone marrow cultures (LTBMC) in MM patients.

Methods: LTBMC's were established from bone marrows of 19 newly diagnosed myeloma patients, and 18 donors without any malignancy and any skeletal disease. Conditioned media from LTBMC's were analysed by gelatine zymography. Total MMP-1, MMP-2, MMP-3, MMP-9, uPA, uPAR, IL-6, IL-1beta, IL-10, IL-11 and TNF-alpha were measured by ELISA.

Results: The proteolytic activity corresponding to proMMP-2, proMMP-9 and their active forms was found by gelatine zymography in all cultures. Myeloma cultures secreted significantly more MMP-2, IL-6 and IL-10 than control cultures, but less MMP-3, MMP-1, IL-11 and TNF-alpha. MMP-1, MMP-9, uPAR, IL-6, IL-1beta levels were positively correlated with percentages of malignant plasma cells in bone marrows, however there were no differences in MMP-9, uPA, uPAR and IL-1beta levels between cultures. Further MMP-1 and MMP-9 levels in myeloma LTBMC's were positively correlated with uPAR and IL-1beta.

Conclusion: Spontaneous secretion of MMP's by bone marrow microenvironment is significantly disturbed in MM and could reflect angiogenic potential of malignant plasma cells. The study gives reason for introduction of synthetic selective matrix metalloproteinase inhibitors into therapy of multiple myeloma.

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The Antwerp experience with thalidomide in relapsed/refractory multiple myeloma

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Background: Barlogie and coworkers showed the marked anti-tumor effect from thalidomide in high risk refractory multiple myeloma (MM) in 1998.

Aim of the study: To evaluate in a retrospective way the effect of thalidomide in patients with relapsed/refractory MM.

Patients: Since 12.07.1999 51 patients with relapsed/refractory MM have been treated; 50 are evaluable. The mean age is 69 years with the youngest being 45, the oldest 87; 26 are males, 24 are females. Before the start of thalidomide, patients were treated with an average of 4 different schemes of chemotherapy and/or irradiation (1-18). Fifteen patients underwent an autologous transplant; one patient was transplanted twice. The distribution of the different subtypes is as follows: IgG k (24), IgG l (11),IgA k (6), IgA l (4), light chain k (2), light chain l (1) and unknown (2).

Treatment: Ten patients were treated for 14 days or less at the moment of evaluation and are not included for further evaluation. The mean duration of treatment in the other patients is 176 days, with a minimum of 15 and a maximum of 448 days. The average oral dosage was 200 mg daily (100-400).

Results: Of the 40 evaluable patients, 15 reached a partial response (PR) (37.5%), 3 a good PR (GPR) (7.5%), 13 had stable disease (32.5%) and 9 developed progressive disease (PD) (22.5%).

Discussion: The effect of thalidomide can be quite dramatic in a positive sense. Moreover, the majority of patients only complained of mild side-effects.

Bone marrow transplantation/cytokines

349 POSTER

Dose intensified chemotherapy with growth factors, in patients with advanced cancer

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Background: Inadequate drug dose is a major factor responsible for the failure of chemotherapy (CT). Carboplatin (CBDCA), Cyclophosphamide (CTX) and Etoposide (VP-16) are active drugs in many solid tumors. In a previous phase I study (Clin Ter 148:201-207,1997) we found the maximum tolerated dose of the three drugs given in combination with growth factors. In another study we ascertained the value of the sequential administration of G-CSF and GM-CSF (Am J Clin Oncol 20:209-214,1997) after dose intensified (HD) CT. Aim of this phase II study was to find the activity and toxicity of HDCT in a group of patients with advanced tumors.

Patients and Methods: A group of 48 patients, were entered in this phase II study of HDCT from 1-93 to 11-99. Patient's characteristics: median age was 52 years (range 18-75). Patients had been treated previously as follows: surgery-37, radiotherapy-7, all had received CT (total 330 courses, median-6 courses/patient, range 4-13). Diagnosis: 26-breast cancer, 13-lung cancer, and 9 miscellaneous tumors. 21 patients had metastatic disease at the diagnosis, 16 patients had a median disease free interval of 18.5 months before developing metastases, while 11 patients had inflammatory breast cancer. Patients received two consecutive courses of the same CT, over 3 days, with CTX and VP-16 (1500 mg/m2 and 400 mg/m2 respectively). CBDCA was administered at the AUC of 8. After CT patients received a sequential combination of growth factors (G-CSF and GM-CSF, both at the