occurring among 8 cases who were treated with electron energy of 12 MeV or higher.

Conclusions: Local RT for PONHL is very effective in achieving local control, and close long-term follow-up is warranted considering late distant relapse and morbidity. Lens shielding and use of electron energy lower than 12 MeV are important technical factors to be kept in mind to decrease late morbidity risk.

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Antileukemic and cytogenetic effects of two chemotherapeutic schemes CHOP and AHOP (A= aza-steroidal alkylating ester)

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Purpose: CHOP is one of the most well established and widely used chemotherapeutic schemes against lymphomas. Although CHOP has been proved highly effective, its genotoxic activity produces a high percentage of secondary tumors. Our previous studies on the antileukemic activity of an homo-aza-steroidal alkylating ester (ASE), showed good results, lower genotoxicity than cyclophosphamide and synergism with anthracycline activity. In this study we adjusted CHOP on mice for the treatment of P388 and L1210 leukemias and comparatively we adopted ASE in CHOP in replacement of cyclophosphamide, creating a new experimental treatment scheme (AHOP).

Methods: BDF1 mice were used for the evaluation of the antileukemic activity. Experiments were initiated on day 0 by implanting i.p. of 10^5 and 10^6 ascites cells of lymphoid L1210 and lymphocytic P388 leukemias. Administration was begun either on day 1 as a single injection of CHOP(C= 112, H=7.5, O= 0.21, P= 15 mg/kg) and AHOP (A= 13, H= 7.5, O= 0.21, P= 15 mg/kg) or on day 5 for P388. The antitumor activity was assessed from the oncostatic parameter T/C%. For the cytogenetic experiments 1 h before i.p. injection of 5-bromodeoxyuridine adsorbed to activated charcoal P388 tumor bearing mice treated i.p. with either CHOP or AHOP, at 1/10 of the dose giving for the surviving testing, were investigated for sister chromatid exchange (SCE) rates and proliferation rate indices (PRI).

Results: Three groups of P388 and L1210 leukemias were treated with CHOP and AHOP. Both treatment schemes were highly effective, causing 100% cures (6/6), when leukemias P388 and L1210 were treated on day 1 post transplantation. They, also, showed significant antileukemic effect producing T/C values of 308 and 257% for CHOP and AHOP, respectively, when advanced P388 leukemia on day 5 was treated. Both schemes produced significant increases in SCE-s however AHOP induced higher SCE frequencies and lower PRI levels than CHOP in P388 leukemic cells in vivo.

Conclusion: Both treatment schemes were determined to be extremely effective and the therapeutic activity depends on the treatment schedule (day 1, day 5) where CHOP was slightly more effective than AHOP in advanced P388 leukemia. However, the most effective scheme in inducing cytogenetic effect was CHOP. This study is in progress and these preliminary results should be investigated furthermore as a potential antitumor scheme.

339 POSTER

Incidence of anemia in CHOP-treated intermediate-Grade Non-Hodgkin's Lymphoma (IGNHL)

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Purpose: To evaluate the CHOP therapy-induced anemia rates and associated factors in IGNHL.

Methods: A practice pattern study was conducted at twelve community and academic oncology sites. Data on 591 IGNHL patients treated with CHOP chemotherapy were retrospectively collected. Data on patients with available baseline chemotherapy hemoglobin (Hb) value were analyzed (546 patients).

Results: The overall mean drop in Hb from baseline to the lowest value measured during chemotherapy was 2.3 g/dl (95% confidence interval, 2.18, 2.46). Of the 353 patients who had a normal Hb (> 12.0) at baseline, 28.3% (100 patients) developed moderate to severe anemia (< 10 g/dL) during chemotherapy and patients 60 years and older had a significantly higher risk (odds ratio 2.5) of developing anemia. Examining the persistence of anemia throughout all chemotherapy cycles shows that of the 62/546 patients with baseline Hb <10 g/dl, 47.5% of the patients failed to recover to a ≥ 10 level during chemotherapy. Anemia treatment data were not available. Similarly, 131/546 patients whose baseline Hb was between 10-12 g/dl dropped below the Hb level of 10. In addition, anemia and neutropenia were found to be significantly associated. Among patients who developed anemia, there was a higher incidence of patients with febrile-neutropenia (FN). FN was documented in patient charts by their treating physician. The following table summarizes the distribution of patients with anemia (chemotherapy-induced) and documented FN.

NCI Anemia Scale	Hb (g/dL)	Total N (%)	Documented FN n (% of N)
Grade 0 (WNL)	> 12.0	95 (17.4)	7 (7.4)
Grade 1 (mild)	10 - 11.9	209 (38.3)	43 (20.6)
Grade 2 (moderate)	8 -9.9	181 (33.2)	74 (40.9)
Grade 3 & 4 (serious to life-threatening)	< 8.0	61 (11.2)	32 (52.5)

NCI Anemia Scale: National Cancer Institute anemia grading scale. WNL: Within normal limits. N: No. of patients in each anemia grade. n: No. of patients in each grade anemia grade with documented FN

Conclusion: Treatment of IGNHL patients with CHOP chemotherapy results in anemia. Also, there is an association between CHOP induced anemia and FN.

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Modified ESHAP as salvage chemotherapy for recurrent or refractory non-Hodgkin's lymphoma: experience at Hacettepe university and a review of the literature

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We have evaluated the clinical efficacy and toxicity of a modified etoposide, methylprednisolone, cytarabine and cisplatin (ESHAP) chemotherapy regimen that has been used by the Hacettepe University Department of Medical Oncology (Ankara, Turkey) since 1993. Thirty-two patients (18 men and 14 women) with refractory or recurrent non-Hodgkin's lymphoma (NHL) were enrolled in this study. The median age of patients were 39 years (range, 21-66 years). Patients were hospitalized during therapy. On the first day, 2 g/m2 cytarabine was given, followed on days 2-5 by 60 mg/m2 etoposide, 500 mg methylprednisolone, and 25 mg/m2 cisplatin. After two cycles of chemotherapy clinical efficacy was assessed by clinical examination, chest radiography, ultrasonography and/or computed tomography. The complications were assessed on the basis of the WHO criteria. Nine patients (28.1%) had a complete response (CR), and 8 (25%) had partial response (PR). In responders, the median duration of remission was 6 months. By the end of the first year, 27% of the patients were still disease-free, and 66% were alive. High serum levels of lactate dehydrogenase had an adverse effect on disease-free survival (DFS), but no effect on overall survival (OS). The only unfavorable prognostic factor for OS was the presence of bulky disease. Neutropenia developed in 59% of patients, and febrile neutropenia developed in 74% of these patients, requiring hospitalization for an average of 8 days. Three patients died of neutropenia-associated sepsis despite broad-spectrum antibacterial and antifungal treatment. Thrombocytopenia was detected in 10 patients and anemia in three patients; among these, seven patients with thrombocytopenia and one patient with anemia required transfusions. The modified ESHAP regimen induced remission in more than half of the patients with refractory or recurrent NHL. However, the duration of remission was brief. Moreover, significant myelotoxicity was common, and the risk of treatment-related death was 9%.

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Thyroid pathology among long-term survivors from Hodgkin's disease (HD)

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Purpose: As a result of the high cure rates and relatively young age of HD patients at the time of diagnosis there are many long-term survivors who

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).