

appears to increase the risk for NHL. HCV associated NHL has similar clinical characteristics to HCV-negative disease. The response to therapy is the same, with CR achieved equally. The addition of IFN to standard CHOP did not significantly increase the response rate, but decreased significantly hepatic side effects. Further cohort studies are needed to evaluate the risk of development of NHL in the natural history of HCV infection.

1214

POSTER

Thyroid toxicity after treatment of Hodgkin's disease

D. Guggenberger, C. Bokemeyer, J. Van Rhee, L. Kanz. *Department of Hematology/Oncology, Eberhard-Karls University, 72076 Tübingen, Germany*

Purpose: Thyroid disease, especially hypothyroidism, is a possible late toxicity after therapy for Hodgkin's disease (HD). We analysed the thyroid function of patients (pts) who were treated for HD according to the protocols of the German Hodgkin Study Group between 1970 and 1994 at two University centres.

Methods: 177 pts (92 men and 85 women) with median age of 38 years (range 18–74) and median time after therapy of 6 years (range 1–20) were studied. 35 pts (20%) were treated with chemotherapy alone (mainly COPP/ABVD), 44 (25%) with radiotherapy alone and 98 (55%) received combined modality. All pts were without evidence of HD for at least one year. They were evaluated for symptoms of thyroid disorder, biochemical thyroid-parameters and ultrasound imaging.

Results: Overall 48 pts (27%) were found to have subclinical (20%) or overt (7%) hypothyroidism. None of the pts with chemotherapy alone developed hypothyroidism, but 36% of pts with supradiaphragmatic radiotherapy and 34% of pts with combined supradiaphragmatic radiotherapy and chemotherapy. All pts with infradiaphragmatic radiation alone were euthyroid except one pat with hemithyroidectomy.

Conclusions: Supradiaphragmatic radiation is associated with a distinctively increased risk of hypothyroidism, chemotherapy neither alone nor in combined modality seems to enhance the risk of hypothyroidism.

1215

PUBLICATION

Prognostic factors in low grade NHL (A multivariate analysis)

G.F. El Wahidi¹, M.M. Al Awadi¹, H.A. Saker¹, A. El Shaat¹, A. Horwich². ¹Radiotherapy Dept. Mansoura, Egypt; ²Radiotherapy Dept. Royal Marsden Hospital, UK

During the period between January, 1970 and December, 1989 inclusive 278 newly diagnosed low grade NHL patients were treated and followed up at the RMH, England. The median survival and PFS was 8.75 years and 2.5 years respectively (median follow up = 8 years).

By univariate analysis, age (60 years), stage (III and IV), more than 2 sites of disease, extranodal disease, anaemia, B-symptoms, bone marrow involvement, ESR > 40 mm/h and chemotherapy treatment were adverse prognostic factors affecting survival.

By multivariate analysis, more than 2 sites of disease, age (60 years) and anaemia remained as significant adverse prognostic factors. For PFS, old age, advanced stage, more than 2 sites of disease, extranodal disease, bone marrow involvement, liver involvement, anaemia and chemotherapy treatment were univariate adverse prognostic factors.

By multivariate analysis more than 2 sites of disease and extranodal disease remained significant.

Treatment modality does not have any further significance as a prognostic factor. A pattern of continuous late relapse has been characteristic of low grade NHL.

Potentially curative treatment strategies are needed and require prospective evaluation. Only with designed clinical trials can a significant survival plateau be realized.

1216

PUBLICATION

Importance of surgery in the treatment of non-Hodgkin's lymphoma of the stomach

H.-J. Meyer, J. Jähne, E. Mössinger, H. Wilke. *Department of Surgery, Städt. Klinikum Solingen, Germany*

Purpose: Although rising incidence of non-Hodgkin's lymphoma (NHL) of the stomach could be obtained worldwide in the last years optimal treatment options remain controversial, above all the role and extent of surgery in low as well as in high grade malignancies.

Methods: Between 1969 and 1996 the postoperative course of 105 pts was analyzed retrospectively in regard to the complication rate and long term survival depending on tumor stages as well as multimodality treatment.

Results: The overall incidence of NHL-pts who underwent surgical treatment was 4.2% (105/2475 pts); increasing to 8% in the last decade. In 93.3% (98/105 pts) total or subtotal distal gastrectomy could be carried out with an operative mortality of 7%. The pathohistological staging determined CSI = 49, CSII = 31 and CSIV = 25; 5-year survival rate obtained for these stages was 94%, 64% and 35% resp. (p = 0.002). Compared to surgical treatment alone no statistically improved benefit was obvious after post-operative radio- and/or chemotherapy.

Conclusion: Based on the data obtained the most reliable therapy of gastric NHL is still surgery. Nevertheless, promising results of anti-H. pylori therapy of superficial low grade malignant NHL or chemo-/radiotherapy in CSI/II high grade malignant NHL must be investigated in further trials.

1217

PUBLICATION

Treatment of relapsing and refractory non-Hodgkin's lymphoma with a combination of dexamethasone, Ara-C, ifosfamide and cisplatin (DAIP)

N. Haim, M. Ben-Shahar, M. Leviov, Z. Shklar, A. Omer, R. Epelbaum. *Department of Oncology, Rambam Medical Center, Haifa, Israel*

Purpose: To evaluate the efficacy and toxicity of a novel combination of dexamethasone (D), Ara-C (A), ifosfamide (I) and cisplatin (P) – DAIP – in patients (pts) with non-Hodgkin's lymphoma (NHL) previously treated with both adriamycin and etoposide.

Methods: All medications were given over 4 consecutive days. D (40 mg/day), I (max. daily dose 1,200 mg/m²) and P (max. daily dose 20 mg/m²) were given by IV bolus. A (max. daily dose 75 mg/m²) was given by 1 hr IV infusion. Cycles were repeated every 3 wks. Adequate hydration and mesna were given.

Results: 30 pts (23 aggressive NHL, 6 low-grade NHL, 1 mantle cell) were entered in the study. Median age was 50 yrs (range, 19–69). The most common prior therapy was ProMACE/MOPP (18 pts). Nine pts received ≥ 2 prior combinations. Consolidation with high-dose chemotherapy (HDCT) was given to 6 pts. Complete response (CR) was achieved in 10 pts (33%) and partial response (PR) in 6 (20%). Median duration of PR was 4 mos; that of CR was not reached. Three pts were disease-free at 6+, 47+ and 55+ months. CR rate was higher in relapsing pts than in refractory pts (9/13 vs 1/17). Median WBC nadir was 1,050 mm³ and median platelets nadir was 26,000/mm³. Neutropenic fever developed in 13 pts (43%) and platelets transfusions were required in 6 (20%). There was one treatment-related death with sepsis and GIT bleeding.

Conclusion: DAIP is an active combination in relapsing NHL following prior exposure to adriamycin and etoposide and may be used before HDCT. Myelosuppression is the dose-limiting toxicity.

1218

PUBLICATION

Inverse relationship between apoptotic fraction and volume weighted mean nuclear volume in childhood Burkitt's versus diffuse B/T large cell lymphoma

L.M. Ball, M. Henry, K. Laybolt, C.L. Lannon, S. Murray, A. MacKay, D. Van Velzen. *Departments of Haemato-Oncology, Paediatric Pathology, Image Analysis and Quantitative Pathology, IWK/Grace Hospital, Halifax, Canada*

Purpose: Nuclear apoptosis results in nuclear size reduction and if present may cause the average nuclear appearance in histological sections to vary within lesions of the same lineage, complicating morphological classification. The accurate apoptotic fraction in most lesions is presently not appreciated.

Methods: We studied diagnostic pre-treatment tissue samples of 28 consecutive, unselected childhood MNHL (13 Burkitt's, mean age 8 y, range 4 y 2 m–14 y, 7 M, 6 F; 15 diffuse large cell lesions, mean age 9 y 9 m, range 1 y 5 m–16 y 8 m, 10 M, 5 F) for volume weighted mean nuclear volume by image analysis (Quantimet 570C) and for mean apoptotic fraction using Frag-EL DNA in-situ labelling (CalBiochem, USA). Lesions were typed as B-T cell using either immuno-cytochemistry, flow cytometry or immunoglobulin/T-cell receptor gene re-arrangements.

Results: Volume weighted mean nuclear volume of Burkitt's lymphoma (mean 250, range 134–411 μm³) was smaller than that of large cell diffuse lesions (mean 285, range 168–489 μm³). However this difference is based on selective increase of B-cell lesions only (n = 7, mean 350, range 260–489 μm³) in contrast to T-cell lesions (n = 8, mean 228, range 168–350 μm³). Conversely, mean apoptotic fraction of large cell, B-cell lesions (40.2, range

30.5–47%) was the lower than that of large cell, T-cell lesions (54.9, range 5–80.5%) whilst Burkitt's lymphoma lesions had the highest mean apoptotic fractions (68.5, range 48.5–87%).

Conclusions: Apoptotic fraction of MNHL in childhood affects mean nuclear volume and may explain difficulties in classifying lesions on nuclear size and appearance only. However, the relationship between the mean, although somewhat variable, apoptotic fractions of Burkitt's lymphoma versus large cell lesions and present treatment outcome (75–85 versus 50–70% survival) justifies further study.

1219

PUBLICATION

Bendamustine – Relapse therapy in patients with low grade non Hodgkin's lymphoma (NHL)

A. Heider, F. Steffens, J. Koch, N. Niederle. *Department of Oncology and Hematology, Klinikum Leverkusen, Germany*

Purpose: Low grade NHL rarely are showing complete and sustained remissions after first line cytostatic therapy making new options for relapse therapy necessary.

Methods: Since January 1995, 27 patients (pts) with advanced and refractory low grade NHL (lymphocytic 13, cbcc 10, immunocytic 2, centrocytic 2) were included in this monoinstitutional trial. Pts were pretreated with 1–4 (median 2) cytostatic combinations. Bendamustine was given dependant on weight (<50 kg: 100 mg, >50 kg: 200 mg) as an one-hour infusion on two consecutive days every three weeks until stable disease (NC), partial (PR) or complete remission (CR) could be documented. In case of further progression, treatment was stopped.

Results: So far, 23 pts are evaluable for response and toxicity. 2 pts (9%) achieved CR, 14 pts (61%) PR and 3 pts (13%) NC, while 4 pts (17%) showed PD. The preliminary median remission duration is 8 months (range, 2–14). Side effects were mild and restricted to nausea and myelosuppression WHO-grade 1 and 2.

Conclusions: Bendamustine is an active and well-tolerated cytostatic drug in relapsed low grade NHL. Further controlled investigations are warranted.

1220

PUBLICATION

Magnetic resonance imaging of bone marrow versus biopsy in malignant lymphoma

M. Özgüroğlu¹, G. Ersavaş², G. Demir¹, F. Demirelli¹, N. Tüzüner³, K. Kanberoğlu², N. Mandel¹, E. Büyükcünal¹, S. Serdengeçti¹, B. Berkarda¹. ¹Dept. of Medical Oncology; ²Dept. of Radiology; ³Dept. of Pathology, Univ. of Istanbul, Cerrahpaşa Medical School, Istanbul, Turkey

Purpose: Bone marrow biopsy of the posterior iliac crest is routinely performed for staging of malignant lymphoma. Abnormal magnetic resonance imaging (MRI) signals of bone marrow is also reported to be indicative of bone marrow involvement. In this study, we aimed to evaluate the role of MRI in detecting bone marrow infiltration in patients with malignant lymphoma.

Methods: 60 patients with malignant lymphoma were studied. Patients were evaluated prior to initiation of the treatment. Unilateral bone marrow biopsy of the posterior iliac crest and MRI of lumbar spine were performed. Analysis of the results were based on the assumption that histologic examination of core biopsies of the posterior iliac crest is the ultimate method of detecting bone marrow involvement.

Results: Among 60 patients evaluated, MRI findings of 52 patients were deemed to be positive or negative for radiologic evidence of unequivocal tumor involvement by 3 radiologists. MRI intensity were suspicious in 8 patients. The sensitivity and specificity of MRI of 52 patients were found to be 86% and 90% respectively.

Conclusion: Although limited in number, these results suggest that MRI of bone marrow is a fairly sensitive, noninvasive method and might be of potential value in detecting bone marrow infiltration in malignant lymphoid neoplasms and can be utilised, as a useful adjunct to standard staging procedures.

1221

PUBLICATION

Initial clinical features in patients of various age with non-Hodgkin's lymphomas

M.V. Robu, I.T. Corchmaru, L.Z. Mustyats, V.G. Mustyats. *Institute of Oncology, Republic of Moldova*

Purpose: The initial clinical features of non-Hodgkin's lymphomas (NHL) were studied in 606 patients of various age.

Results: Only high-grade NHL were diagnosed in childhood. Lymphomas of high-grade malignancy were predominating in adults too, but the frequency of low-grade NHL was increasing with the age. Fifty-five per cent of cases NHL in children originated in extranodal tissue. Primary NHL of various lymph nodes were present in most adult patients. Favoured extranodal sites in adults and children included the digestive tract and Waldeyer's ring. The most frequent sites of primary NHL of digestive tract were the stomach in adult and the intestines in children. Primary NHL of the spleen were more frequent in adults, especially over 60 years. Retroperitoneal and mesenteric lymph nodes were most often involved in children, mediastinal lymph nodes in teen-agers, peripheral lymph nodes – in adults.

1222

PUBLICATION

Combined chemotherapy-radiotherapy in I-II stage of non-Hodgkin's lymphomas

L.Z. Mustyats, I.T. Korchmaru, M.V. Robu, I.A. Iakovleva, A.E. Tkachenko. *Institute of Oncology, Republic of Moldova*

Purpose: We have reported the results of combined chemotherapy-radiotherapy in 98 previously adult patients with localized non-Hodgkin's lymphomas (NHL; stage I-II-48, stage II-II-50). There were 78 patients with high- and intermediate-grade and 20 patients with low-grade NHL.

Methods: All patients received 3 courses of CHOP in I phase, involved radiotherapy in II phase, and final 3 courses of CHOP chemotherapy in III phase with following maintenance therapy.

Results: Thirty seven (92.5%) patients had a complete response and 2 (5.0%) had a partial response in I-II stage of high- and intermediate-grade NHL. Twenty two (57.3%) patients from unfavorable group had a complete response and seven (18.4%) had a partial response in II-II stage. The complete remission rate was achieved in all patients with low-grade NHL in I-II stage and in 11 (91.7%) cases with II-II stage. The actuarial survival at five years in unfavorable group was 79.4% in I-II stage and 40.0% – in II-II stage. The actuarial survival at five years for favorable group was 100% in I-II stage and 73.3% – in II-II stage.

1223

PUBLICATION

Relationship between rate of "in-field" bone marrow regeneration and radiation dose in patients with Hodgkin's disease

S.V. Kanayev, S.N. Novikov, L.A. Jukova. *Department of Radiooncology and Nuclear Medicine, Research Institute of Oncology, St.-Peterburg, Russia*

Purpose: To evaluate relationship between absorbed dose and rate of irradiated BM regeneration after combined modality treatment (CMT) of patients with Hodgkin's disease (HD).

Materials: BM scanning was performed 1–84 months after CMT of 69 patients with HD. Absorbed doses ranged from 28–32 Gy to 38–45 Gy. BM activity was estimated semiquantitatively: grades 1–2 – no or some activity, grades 3–4 – partial or complete regeneration.

Results: Irrespective of absorbed dose (in the range of 28–45 Gy) during 1–5, 9 months after CMT hematopoietic activity was reduced in 70 of 71 irradiated regions. 6–12 months after radiotherapy scintigraphic signs of BM regeneration (grades 3–4 of tracer uptake) were mentioned in 12 of 17 areas (71%) irradiated with 28–32 Gy and in only 5 of 16 (28%) – with 38–45 Gy ($p < 0.05$). Thirteen and more months after the end of CMT percent of BM regeneration was still dose dependant: 77% (in 44 of 57 areas) – after 28–32 Gy and 51% (in 36 of 71 areas) after 38–45 Gy ($p < 0.05$).

Conclusion: After irradiation with 28–32 Gy rate of in-field BM regeneration is higher than after irradiation with 38–45 Gy. BM recovery after conventional CMT of patients with HD is dose dependant.

1224

PUBLICATION

Results of mantle irradiation alone in adult patients with clinical stage (CS) I and II Hodgkin's disease (HD) with low probability of abdominal involvement and good prognostic factors

C.A. Regueiro, G. Aragón, M. Martín, F.J. Valcárcel, A. de la Torre, P. González, J. Romero, E. Polo, R. Magallón. *Dept. of Radiation Oncology, Clínica Puerta de Hierro, Madrid, Spain*

Background: Since 1988 we have used mantle irradiation alone for patients with CS I or II HD with low probability of abdominal involvement at laparotomy