
Thirty-nine patients (32 male and 7 female) with histologically proven diffuse histiocytic lymphoma were treated with the MACRO-B regimen (Klimo and Connors, 1985). Sixteen patients had stage IV, 5 stage I11, 15 stage I1, and 5 less than stage I1 disease. Constitutional (B) symptoms were reported by 15 patients. Results of the treatment could be evaluated in 36 patients. Nineteen patients (52.7%) achieved complete remission (CR), 15 (41.6%) partial remission (PR), 1 patient (2.7%) showed no change (NC), and 1 patient (2.7%) had progressive disease (PD). Of all patients who achieved CR and PR (n=34) 70.5% are currently alive (CR: 17/19 and PR: 7/15; median follow up: 16 months). WHO grade IV toxicities were observed in 7 patients, anemia in 1 patient, and thrombocytopenia in 1 patient. One patient died due to sepsis during myelosuppression. Two patients died from intestinal perforations resulting in acute respiratory distress syndrome. The pretherapeutic thrombocytic dehydrogenase (PDH) level proved to be a highly significant prognostic marker for achieving CR. The 52.7% CR rate observed in diffuse histiocytic lymphoma does not appear to be superior to that induced by a variety of other treatment regimens for this lymphoma. The long-term remission and survival rate for this regimen cannot be compared favorably to the ones reported for the original protocol. Therefore, MACRO-B is an efficacious treatment for the diffuse histiocytic lymphomas. We caution, however, against the use of this considerably toxic regimen without intensive and constant toxicity surveillance.

T 74 INTENSIVE TREATMENT OF STAGE III-IV AGGRESSIVE NON-HODGKIN Lymphoma. J. B. R. D. (TUMORFOUR), Universitätshämatologie und Hämatologie, Fakultät für Medizin, Universität Heidelberg, Germany.

In the past decade, treatment strategies have been developed that have achieved a cure of approximately 20% of patients with aggressive non-Hodgkin's lymphoma (NHL). In addition to the use of alternating regimens and autologous bone marrow transplantation (ABMT), 183 patients with stage III-IV NHL were treated in a multicenter protocol (TIP protocol) according to age, histology, and tumor stage. Of all patients who achieved CR and PR (n=34) 70.5% are currently alive (CR: 17/19 and PR: 7/15; median follow up: 16 months). WHO grade IV toxicities were observed in 7 patients, anemia in 1 patient, and thrombocytopenia in 1 patient. One patient died due to sepsis during myelosuppression. Two patients died from intestinal perforations resulting in acute respiratory distress syndrome. The pretherapeutic thrombocytic dehydrogenase (PDH) level proved to be a highly significant prognostic marker for achieving CR. The 52.7% CR rate observed in diffuse histiocytic lymphoma does not appear to be superior to that induced by a variety of other treatment regimens for this lymphoma. The long-term remission and survival rate for this regimen cannot be compared favorably to the ones reported for the original protocol. Therefore, MACRO-B is an efficacious treatment for the diffuse histiocytic lymphomas. We caution, however, against the use of this considerably toxic regimen without intensive and constant toxicity surveillance.

T 75 ADRIABLASTINE-TENCEPOSIDE-CYCLOPHOSPHAMIDE (T-CAM) VERSUS EPIRUBICIN-TENCEPOSIDE-CYCLOPHOSPHAMIDE (T-CAM) FOR PATIENTS WITH INTERMEDIATE OR HIGH GRADE NON-HODGKIN'S LYMPHOMA. S. G. N. K. J. M. L. R. (TUMORFOUR), Universitätshämatologie und Hämatologie, Fakultät für Medizin, Universität Heidelberg, Germany.

119 patients with intermediate grade NHL lymphoma (Working formulation) clinical stage II-IV entered the study. 62 received T-CAM (Adriamycin 50 mg/m², d1; Cyclophosphamide 300 mg/m², d2; d3; d4; d5; d6; d7; d8). 57 received T-CAM (Epirubicin 50 mg/m², d1; d2; d3; d4; d5; d6; d7; d8). All patients received dexamethasone 40 mg/m², d1; d2; d3; d4; d5; d6; d7; d8. All patients received 16 cycles of MTHP for a total of 192 cycles. 119 patients with stage II-IV NHL were treated in a randomized trial comparing Adriamycin (d1) vs. Epirubicin (d1) and cyclophosphamide (d1, d2, d3, d4, d5, d6, d7, d8) and further randomized to 3 epirubicin doses (d1, d2, d3, d4, d5, d6, d7, d8) and T-CAM (d1, d2, d3, d4, d5, d6, d7, d8). All patients received dexamethasone 40 mg/m², d1; d2; d3; d4; d5; d6; d7; d8. All groups were matched regarding age and sex. The complete response rates (CR) and overall response rates (ORR) were: T-CAM: CR 35/62, RR 56/62. T-CAM: CR 35/62, RR 56/62. T-CAM: CR 35/62, RR 56/62. T-CAM: CR 35/62, RR 56/62. T-CAM: CR 35/62, RR 56/62.


Preliminary results of a prospective study of pts with NHL of intermediate or high grade NHL of the Working formulation, 1982 treated by a slightly modified MACRO-B regimen are presented. Compared to historically treated pts (Ann. Int. Med. 102: 595, 1985) the dose escalation of doxorubicin and cyclophosphamide as well as the antibiotic prophylaxis against bacterial and Pneumocystis carinii infections were omitted. Histologies of the individual patient (T-cell lymphoma, NHL, NHL, NHK, and KI1-99) were evaluated by the WHO classification of NHL by age of 44 years (range 24-72) presented with the following stages (acc. to the Ann Arbor classification criteria): IIIA (n=1), IIIB (n=5), IIIA (n=1), IIIIB (n=2), IV A (n=2) and V (n=5). All pts achieved 10 pts (53%) presented clinical complete (CR) and additional 7 pts (37%) partial remission. ACR in pts with stage 1 and 2 achieved 10 pts (53%) presented clinical complete (CR) and additional 7 pts (37%) partial remission. ACR in pts with stage 1 and 2 achieved 10 pts (53%) presented clinical complete (CR) and additional 7 pts (37%) partial remission.
T 77 "I-VEGAS" RILISER FOR INTERMEDIATE AND HIGH GRADE NON-HODGKIN Lymphoma.
M. Antei, M. Reis, M. Rimilia, F. Pinelli, G. de Paolis and G. Papi. Chair of Haematology, 2nd University of Rome, Ospedale S. Eugenio, 00144 Rome - Italy.

The actual 3rd generation regimens for the treatment of high grade NHL see a phase of swift intensification by cycle-specific drugs, followed, during myeloablation, by a sequential supply of non-myelotoxic agents: in this way it was registered the highest percentage of complete response, (over the 65%), with more than 2/3 of patients in complete remission (CR), disease free at 4-5 years; the toxicity of these schemes tends to be high, especially for patients (pts) with obesity, diabetes, and liver and kidney failure. To reduce the toxicity of a triade scheme as F-MACHOP, we have modified the sequence in this way: VCR 0.5 mg/m² d.1, d. 4 - 10; CDDP 750 mg/m², EMA-C 1 g/m², ADR 60 mg/m² d. 2, h.6-8, without fluorouracil. MTH 500 mg/m² d. 1-4 and folic acid rescue 30 mg bid were consecutively infused on day 12 and 13. In 20 pts were treated, 26 male and 4 female, (range 26-77 yrs) 3 F -stage II E - IV 9, 17 pts showed the following presentation: gastrointestinal; 4, skin; 3, bone marrow; 3; bulky disease; medisternal; 2, abdomen; 2, 18 pts achieved CR (68%). 7 PR (partial response) (23%) and 5 experienced progressive disease; 7/30 pts favor of unknown origin; exceptionally pulmonary and urogenital events. No case of toxic death, no available hemmorhagic syndrome resulted, as well as nausea, vomiting, hepatocellular damage or mucositis. Grade II-IIII esophageal was constant but reversible. 93% of pts showed granulocytic and platelet nadir between 10 to 15 d, and 8 to 15 respectively. This regimen was mostly performed in out patient setting. The median overall survival and the event free survival haven't been reached yet 32 months after the start of the therapy, and 35% of pts are alive and disease free even at 27 months after CR.

In conclusion we registered a less percentage of CR most aggressive regimens (60% vs > 85%) but the complete response seems to be lasting. The treatment seems to be effective and moderately toxic: it can be tolerated by elderly pts too and could represent, in our opinion, a good therapeutic alternative for pts unbearable by the actual intensification regimens.

T 78 A Phase II study with CHOP (C - Cyclophosphamide, E - Epirubicin, O - Vincretinase, P - Prednisolone) in stage III-IV Non-Hodgkin's lymphoma.

(1) Dept. of Haematology, University Hospital, Ghent, Belgium (2) Medical Dept. Parmatica Carlo Erbe, Nivelles, Belgium.

Thirty-one patients with stage III (n = 6) and stage IV (n = 25) Non-Hodgkin's lymphomas were enrolled in a first line phase II clinical trial treating a combination chemotherapy with C 750 mg/m² I.V. d.1, E 60 mg/m² I.V. d.1, O 3 mg/kg I.V. d.1, P 100 mg/m² p.o. d.1 to d.5. The median follow-up of the study is 33 months. The mean age of the patients was 56 ± 11 years (range 28 - 74 years). Of the 31 patients, 18 were male and 13 female. At entry, 19 patients presented with a performance status (PS) 0 and 2 a PS 1. No CNS prevention was performed. Response (WHO) to treatment was as follows CR: 15, PR: 10 and NC: 6 (Response Rate: 81%). In stage III, 5 CR's out of 6 were observed while in stage IV 10 CR's out of 25 were recorded. Median time to the best response was 71 days (range 21 - 279 days). The median duration of response is not yet reached. The median time to progression is 21 months (range 6 - 60 months). The median survival of patients while for stage IV it was 29 months. The median of the number of administrated cycles was 14 (range 4 - 17). The median cumulative dose of E was 695 mg/m² (range 582 - 990 mg/m²) 12 patients received more than 800 mg/m². Treatment delays and dose reductions were applied in 70, 81 cycles respectively, on a basis of cumulative chemotherapoy. Toxicities per patient (WHO grade 2 or more) were as follows: anemia grade 2: 1; thrombocytopenia grade 2: 1; neutropenia grade 2: 9, grade 3: 1; nausea and vomiting grade 2: 16; grade 3: 3; mucositis grade 2: 1; infection grade 2: 2; grade 3: 2; allopnea grade 3: 1; grade 3: 1; neurotoxicity grade 2: 1; grade 3: 1.

One patient died from untreated cardiac failure and generalisation of the lymphoma in 100 days (WHO grade IV). While one patient developed a drop in ICBP of more than 20% (cumulative dose of E 695 mg/m²).

In conclusion, the results achieved with this treatment are comparable with more aggressive regimens, with very acceptable toxicity.


Between December 1986 and September 1989, 38 patients with intermediate and high grade NHL were treated with oral prednisolone 75mg daily for 12 weeks; cyclophosphamide 350mg/m² iv and mitozonast 10mg/m² on days 1,15,29,43,57 and 71; vindesine 1 mg/m² on days 8, 22, 36, 50, 64 and 78; mitoxantrone 40mg/m² iv on days 8, 36 and 64; bleomycin 15mg/m² iv on days 22, 30 and 78. None had received previous chemotherapy. One had received previous radiotherapy.

Age range was 14-66 years (median 53). 19 were male. At diagnosis 4 patients had stage II, 9 patients stage III, and 25 patients had stage IV disease. Histological classification according to the International Working Formulation placed 1 patient in category D, 1 in E, 7 in F, 17 in G, 8 in H, 1 in I, 3 in J. Performance status ranged from 0-4.

22 patients achieved CR (58%) including 3 patients who received local radiotherapy and one who had a partial gastrectomy after P-COMP-B. 6 patients achieved PR (16%) 6 showed progressive disease (16%), and 4 were unavailable for response (10%). Product limit estimates of overall survival and relapse-free survival at 2 years are 45% and 46% respectively. The most severe toxicity has been neutropenia (WHO grade III-IV in 23%). Proximal nephropathy confined 4 patients to a wheelchair bed temporarily. Mucositis, peripheral neuropathy and nausea were frequent but rare. There were no chemotherapy-related deaths.

P-COMP-B offers effective first-line chemotherapy in advanced aggressive NHL with acceptable toxicity.

T 80 CAVBP/DEP ALTERNATING CHEMOTHERAPY FOR THE TREATMENT OF HIGH-RISK NON-HODGKIN'S LYMPHOMA. G.Palmieri, R.V. Laffioli, F. Caponigora, A.Contelegiacomo, R.Lauria, C.Pagliarulo, V.Montesarchio, S.De Placido, F.Muzzo, A.R.Bianco. Division of Oncology, University of Naples, Medical School II.
ABSTRACTS - Fourth International Conference on Malignant Lymphoma, Lugano

T 81 RESULTS OF SEQUENTIAL COMBINATION CHEMOTHERAPY (CABOPP/VIM) IN HIGH-GRADE MALIGNANT NON-HODGKIN Lymphoma.
M.H. Nowroussian, C.R. Meier, B. Schötenass, C. Anders, N. Niederle, R. Osięka, K. Rößken, B. Sieber, C.G. Schaumlöffel, West German Tumor Centre, Department of Internal Medicine (Cancer Research), University of Essen, 4300 Essen, F.R.G.

A new treatment program was used in 42 patients with high-grade malignant lymphomas in an attempt to improve the results without increasing toxicity. Two effective, relatively well tolerated and non-cross resistant drug combinations were given sequentially according to the response of disease. Therapy was started with a combination consisting of Cyclophosphamide, Adriamycin, Bleomycin, Vincristin, Procarbazine, and Prednisone (CABOPP). In patients who achieved complete remission with CABOPP, this program was continued for a total of 6 cycles. In patients with progressive disease or with only a partial remission after a maximum of 4 cycles of CABOPP, therapy was switched to a combination consisting of Etoposide, Ifosfamide, and Methotrexate (VIM). Complete remission was achieved in 68% of the patients. 69% of the patients obtained complete remission with CABOPP alone and 71% after changing to VIM. The complete remission rate was 100% in patients with stage I or II of disease, 91% in patients with stage III, and 59% in patients with stage IV. The projected survival at 2 years is 66%. 56% of patients with complete remission are predicted to have continued complete remission at 2 years. Thus, CABOPP/VIM appears to be an effective and well tolerated program for the treatment of aggressive lymphomas. However, this program compares with other newly developed protocols, can only be established in prospective randomized studies.

T 82 LONG-TERM FOLLOW-UP OF CHOP-TREATED NON-HODGKIN Lymphoma OF HIGH-GRADE MALIGNANCY. R. Hein, B. Schneider, 3rd Med.Dept. and Ludwig Boltzmann Institute for Leukaemia Research and Haematology, Hanusch Hospital, A-1140 Vienna, Austria.

The longterm outcome of 116 high grade malignancy NHL patients 18 CB, 33 IB, 24 LB, 11 high grade unclassified, 14 pseudolymphomas, and 14 Ki-1 lymphomas according to the modified Kiell classification (for the modified Kiell classification) treated with age adjusted CHOP between 1980 - 1985 was evaluated. The median age was 66 years. Of these patients 28% had a significant comorbidity. 35% of all patients are alive after a median followup of 5 years. CB patients had the best outcome; median survival has not been reached after 110 months, however the differences between all histologic entities are not significant (p=0.8). Risk factors were balanced between the histologic entities. 58% of the patients had localized disease after clinical staging. CR rate was 47%. 9 out of 12 relapses occurred within 2 years. Median time to relapse was 9 months. Salvage therapy was usually not successful, none of LB and LB patients achieved CR. Five CB had remissions with secondline therapy, four of these patients had PR after induction treatment, one patient had relapse after 30 months. 15% of CR patients developed second (or third) neoplasms. Only one acute myeloblastic leukemia was seen. According to our results age adjusted CHOP is a well tolerated and effective treatment for elderly patients and patients with localized disease. New therapeutic approaches are necessary for advanced disease and patients with an accumulation of risk factors. The future value of ABMT in selected patients will be discussed.

T 83 RESULTS OF THE COP-CHOP-L 1 REGIMENT IN 30 PATIENTS WITH INTERMEDIATE AND HIGH GRADE NON-HODGKIN'S Lymphomas.
Santos R. de Jongh, C. Acquatella G., Desenre J., Caldera L., Soya A., Toivar E., Rossas Urriol A., Rodriguez I.J.U., Unidad de Linfomas Hospital Universitario, Unidad de Hematologo y Oncologia MIN-SAS, Caracas. FUNDACION BADAN.

Between January 1986 and May 1989, 30 patients with intermediate and high grade non hodgkin's lymphomas were treated. The average age was 57 years (18-75), the relatio males/females was 10/20. The histologic distribution was the following: NHL 19 (63%), DL0M 3 (10%), DLDPM 3 (10%), CLL 3 (10%). Clinical stages were as follows: stage I: 11 (36%); II: 8 (26%); III: 11 (36%); IV: 9 (29.6%); all stages III and IV were B. 15 cases (50%) had bulky disease. A correlation study showed that 52% of patients with B symptoms had high IMM and all asymptomatic patients had normal values (P<0.01). The group we studied had 4 high risk factors: advanced stage, B symptom, bulky disease, high LDH values. The lymph node areas involved in stages I and II and III were iliacum 10 (33%), retroperitoneal area 11 (36%), cervical area 7 (18%). In stage IV patients, the affected organs were: lungs 6 (50%), bone marrow 3 (27%) and soft tissues 2 (18%).

Patients were treated with de COP-CHOP-L 1 regimen, after 6 cycles remission was evaluated. In 21 patients (70%) complete remission (CR) was obtained with an average duration of 26 months. In 9 patients 30% partial remission was reached. The total survival at 12 months was 83% and disease free survival was 78% at 18 months, total survival 64%, disease free survival 41%, both values were maintained up to 38 months. The average observation period was 16 months. We recommend the COP-CHOP-L 1 regimen as a National protocol in Venezuela. We thank to Dr. Schmidt for his high effectively (70% of CR with a 2 year total survival of 63%), and low toxicity.

T 84 ETOPOSIDE, CYCLOPHOSPHAMIDE, MITOXANTRONE AND PREDNISONE (VEMP) IN THE TREATMENT OF NON-HODGKIN'S LYMPHOMAS: PRELIMINARY RESULTS OF A PHASE III STUDY. T. Chiesi, L. Ramon, G. Samboni, G. Bertolino and V. Bontoli Hospital, Vicenza (Italy).

Considering both satisfactory therapeutic results achieved for advanced aggressive NHL refractory or relapsed to optimal first-line therapy we utilized the same schedule in previously untreated pts with NHL. A pilot study has been performed in our Department to evaluate these polichemotherapeutic regimen as first-line therapy for pts presenting one or more of following criteria: P.S. 2-3, aggressive histology at stage I-II, low grade histology B-symptoms stage III-IV, age over 65. Up to today 38 pts entered this study. Median age in 64 years (range 34-72), most of pts (68%) were in stage III-IV; B-symptoms were present in 30/72 (26%) and extranodal disease in 24 (63%). Pts at stage I-II received 3 cycles plus involved field radiotherapy while pts at stage III-IV received a minimal of 3 cycles (when responding). At present 24 pts are evaluable for response: CR was obtained in 20/26 (77%), PR in 2/26 (8%) and 4 in 26 (15%). Five pts relapsed within one year after the CR. Hematologic, cardiac or hepatic toxicity was low and the therapy was generally well tolerated. These data suggest that VEMP is safe and effective as more aggressive regimens and it is also indicated for pts not eligible for anthracycline-including protocols.
ABSTRACTS - Fourth International Conference on Malignant Lymphoma, Lugano


Achieving a rapid and complete remission is the most important goal in the treatment of aggressive lymphomas. In order to overcome early resistance and regrowth of lymphoma in treatment-free intervals we chose a 9-drug regimen with weekly therapy. We combined a non-cross-resistant regimen, CEOP (Cyclophosphamide 780 mg/m² d 1, Etoposide 70 mg/m² d 1, Oncovin 1,4 mg/m² d 1 and Prednisolon 100 mg d 1-5) and IMVP-DAXA (Ifoflamide 2 g/m² weekly, trimethoprim 960 mg/m² d 1-5, VP-16 160 mg/m² d 1-7, Dexamethasone 40 mg d 1-5 and Methotrexate 800 mg/m² with Ca-folinol rescue d22) and gave them every 4 weeks, 3 to 6 times according to response. Dose reductions were not applied as long as granulocyte counts were over 0,5x10⁹/L. Therapy was withheld if counts dropped below 0,2x10⁹/L. Patients with untreated histologic proven high and intermediate grade Non-Hodgkin lymphoma and measurable disease were treated if they gave an informed consent. To date 8 Austrian centers entered 37 patients in this multicenter trial. Data are available from 33 pts. 3 were excluded, two because of pretreatment, one because of wrong histology. Male/female ratio was 1:2, age between 25 and 72 years, median 56.6 years. Histology was centroblastic 16, immunoblastic lymphoma 1, lymphoblastic lymphoma 3, 2H-N, 3, undifferentiated 3, plasmablastic 1 and diffuse centro-blastocellular in 1. 5 patients were stage I, 11 stage II, 3 stage III and 11 stage IV, 13 patients had B-symptoms. Karnovsky status at presentation was between 100 and 60, median 85. Observation time was 0.4-23.8 months, median 8.8 months.

Toxicity was primarily hematologic with 53.3% of patients having granulocytopenia nadir below 0,5x10⁹/L, 33.3% under 0,1x10⁹/L. Although 60% of patients had infections, there was only one life threatening infection in an AIDS patient. Other important toxicities were nausea/vomiting, stomatitis and hair loss. 6 patients died, 4 of lymphoma and 2 of sepsis, 2 of AIDS after 22 and 33 weeks and two were early deaths within 10 days after registration. 25 patients were evaluable for response; 21 had a complete and 3 a partial remission, two of them entered a complete remission after radiotherapy to residual disease, resulting in a complete remission rate of 92%. Only one patient progressed during therapy. Until now 3 patients were progressive after achieving a remission. Median time to treatment failure, to relapse and median survival are not reached.

CEOP-IMVP-DAXA can be given safely even in smaller hematologic centers and is able to achieve a high rate of complete responses in patients with high and intermediate grade malignant Non-Hodgkin lymphomas.

T 87 ACTIVITY OF MITOXANTRONE, CYTOSINE ARABINOSIDE, AND PREMISOLONE IN PRETREATED PATIENTS WITH HIGH GRADE MALIGNANT NON-HODGKIN'S LYMPHOMAS. B. Steinke, M.E. Heim, K. P. Schalk Medizinische Universitätsklinik, 740 Tübingen, FRG

Between 1986 and 1988, 10 patients with heavily pretreated high grade malignant NHL were treated with Mitoxantrone 8 mg²/m² iv days 1-2, Cytosine Arabinoside 100 mg/m² sc days 1-5 and Prednisolon 80 mg/m² po days 1-5 (MAP). Treatment cycles were repeated beginning on day 29. According to the Kiel-classification, 5 patients had a centroblastic, 2 an immunoblastic and 3 a high grade malignant lymphoma, which could not be further classified. All patients were pretreated with CHOP and VIM-Elo, a modification of the IMVP-16 protocol. 4 patients had had additional radiotherapy. With this pretreatment, 6 patients had achieved a complete remission for 1 - 10, median 6 months. 3 patients had achieved only a partial remission and 1 patient stable disease. All but one patient with a partial remission had a relapse and progressive disease at the time of start of the MAP-protocol. 2 patients had stage II disease as massive initial involvement, 3 stage III and 5 stage IV disease. Treatment resulted in a complete remission (CR) in 3 patients, 1 patient had a partial remission, 3 a minor response and 3 progressive disease. CR is still stable in 2 patients at 24 and 2 months so far, the third patient with CR re-lapsed 15 months after start of MAP therapy. Main toxicity was hematotoxicity with leukopenia < 1000 /µl in 7 patients. 1 patient developed thrombopenia < 20000 /µl. Leukopenia resulted in infections in 4 patients (WHO grade 2: 3 patients, WHO grade 3: 1 patient). Other toxicity was mild. We conclude that MAP is an active regimen in heavily pretreated NHL which has considerable hematotoxicity but can produce stable CR in some patients.


There is a need to identify alternative chemotherapy for patients with active high grade non-Hodgkin's lymphoma (NHL) and Hodgkin's disease (HD) who have previously received most of the principal effect agents. Fifty-five patients, initially treated for advanced high grade NHL or HD, refractory to first-line treatment or in relapse, were given an ifosfamide-mitoxantrone combination (I-M). Ifosfamide 6g/m² was infused over 48 hours. Mms, such as prophylaxis against hemorrhagic cystitis, was given as a prophylaxis bolus at 0 hours with additions of 2g to the infusion at 12 hourly intervals. Mitoxantrone 120mg/m² was given over 31 minutes, following completion of the ifosfamide infusion. The regimen was repeated at three weekly intervals, the total duration of treatment being determined by response. Patient details were: 35 NHL, ages 15-76 (median 52), M:22:13, primarily refractory 5, relapsed 24, relapsed and refractory 2, 20 HD, ages 21-45 (median 31), M:14:1, primarily refractory 7, relapsed 11, relapsed and refractory 2.

Overall, 207 complete courses have been given to date, 8 being the maximum received by any patient. Delays in treatment or dosage modification were mainly due to myelosuppression. Neutropenia ≥ grade 3 occurred following 70% of courses, whereas thrombocytopenia ≥ grade 3 occurred in only 15% of courses. There were 11 instances of post-chemotherapy neutropenia required hospitalisation and 17 antibiotic treatments. Ten patients showed evidence of CNS toxicity and decreased levels of consciousness in the early post-treatment period. Two of those patients, there was only one treatment-related death, due to septicemia.

Of 32 patients with NHL evaluable for response; 10 (31%) achieved CR and 5 (overall response rate 47%); in 5, disease was static and so a plateau was maintained. 20% of CR did not achieve CR and 6 PR (median response rate 70%); in 2 disease was static and in 3 progressive. Two patients (one CR and one PR) went on to subsequent ABMT. Responses in both NHL and HD were predominantly in patients with relapsed as opposed to primarily refractory disease.

In conclusion, the I-M regimen shows useful activity in both high grade NHL and HD, with acceptable toxicity given the output of the patient categories. This combination is clearly of value in relapsed patients, especially where therapeutic options are limited because of previous multiagent treatment.

T 89 METHYL-GAG, IFOSFAMIDE, METHOTREXATE AND ETOPOSIDE (MIME) AS SALVAGE THERAPY FOR MALIGNANT LYMPHOMAS. G. Gobbi, B. Palmellis, H. Hamburger and C. Lindemulva for the Swedish Lymphoma Study Group, Department of Oncology, University of Uppsala, Akademiska sjukhuset, Uppsala, Sweden

Patients with Hodgkin's disease (HD) or high grade malignant non-Hodgkin's lymphoma (NHL) who fail to respond to or who relapse after first-line chemotherapy have a poor prognosis. A combination designated MIME was recently evaluated in Sweden for HD after initially positive reports from the group at MD Anderson Hospital, Houston, USA, and it became increasingly used for NHL. A retrospective study was initiated in order to evaluate the therapeutic effect and toxicity when given on a routine basis in a general number of hospitals.

Retrospective study: One hundred and three patients with HD and NHL treated with MIME at 26 hospitals in Sweden between October 1987 and July 1988 were evaluated. All patients were heavily pretreated. Thirty-seven of the 44 patients with HD, 34/47 with high grade malignant and 9/12 with low-grade malignant NHL were evaluable for response. Twelve (43%) patients with HD achieved complete remission (CR) and 4 partial remission (PR), giving a total response rate of 58%. Five patients with high-grade NHL achieved CR and 8 PR, giving a response rate of 38%. Of 9 evaluable patients with low-grade NHL, 2 achieved CR. The main toxicity was leukopenia, thrombocytopenia and infections. Twenty-six percent of the patients developed septicemia, which was fatal in 6 cases. In conclusion, MIME could induce remissions in heavily pretreated lymphoma patients, particularly in HD, and it was relatively well tolerated.

Prospective study: The promising results of the retrospective study led to the initiation of a prospective study of MIME as second-line therapy for malignant lymphomas. Patient inclusion started in July 1988. Until December 1988, 68 patients in total (47 high-grade NHL, 11 low-grade NHL after failure on adriamycin-containing regimen) NHL and 11 HD. Preliminary results from this study will be presented.
ABSTRACTS - Fourth International Conference on Malignant Lymphoma, Lugano

T 91  
SALVAGE CHEMOTHERAPY WITH MITOXANTRONE, ETOPOSIDE, VINDEINE AND PREDEXISOLONE (MEVP THERAPY) FOR REFRACTORY OR RELAPSED MALIGNANT LYMPHOMA. 

Twenty-two patients with refractory or relapsed malignant lymphoma were treated with a combination chemotherapy with mitoxantrone, etoposide, vindesine and prednisolone (MEVP therapy). In the patients who had been previously treated with doxorubicin-based combination chemotherapy, 18 with CHOP, 1 with MOPP, and 2 with VERA regimen. Nine patients had the refractory lymphoma and 13 had relapsed lymphoma. MEVP therapy consisted of 10 mg/m² of mitoxantrone (IV on day 1), 2 mg/m² of vindesine (IV on day 1), 200 mg/m² of etoposide (PO on days 1-3) and 40 mg/m² of prednisolone (PO on days 1-5). Of the 20 evaluable patients, 6 (30.0%) attained CR and 7 (35.0%) PR according to WHO criteria. 4 CRs were obtained in 5 patients who were refractory to previous CHOP or VCP-TPH regimen. Further investigations are needed for determining the historical types in the five patients obtaining CR were B cell lymphoma of low, intermediate or high grade malignancy and included was one patient with AIL (BL-T cell lymphoma). CD duration ranged from 6 to 70 (median 59) weeks.

T 92  
PHASE II-TRIAL OF IFOSFAMIDE AND MESNA IN PREVIOUSLY TREATED PATIENTS WITH NON- 

Ifosfamide (IF), an analog of cyclophosphamide, has demonstrated promising activity in early studies of lymphoma and multiple myeloma. Its clinical activity has been a significant complicating factor limiting its utility. A CALGB phase II trial was initiated to evaluate the therapeutic potential of IF, by studying the possible prevention of the urotoxicity of IF by mesna, a sulfhydryl reagent. A non-genitourinary detoxification of the oxysphorine derivatives, IF at an initial dose of 1.25g/m² was given I.V. over 4 hours/day X5 days every 21 days (over 5 minutes) 15 minutes prior to each dose of IF and 4g/h on days 1-5. Urinary output was maintained with diuretics if necessary. Therapy was given for a minimum of 2 cycles unless rapid progression. In responding patients (ps) therapy was continued 3 cycles beyond maximum response. Forty-six previously treated patients with non-
Hodgkin's lymphoma have been treated on this protocol. Median age was 41 years (range 18-93), performance status 1 (0-2), and number of prior regimens 3 (1-11). Responses were observed in 94% with a median duration of remission of 2.5 months (range 1-12 months). Responses were seen in favorable and unfavorable histologies. Myelosuppression was the dose-limiting toxicity. Median nadir WBC 4000/mmc (range 2000-33,500) and platelets 140,000/mmc (range 150,000-500,000). Treatment was discontinued in 65% of patients and was usually mild/ 
moderate. Alopecia was observed in 39%. Grades of xerostomia and nausea were noted. Complete anaphylaxis were observed. Hematemia was observed in 3 patients. In 2 patients gross weight loss occurred while in the 3rd patient complete alopecia was observed. One patient with microscopic hematuria tolerated a reduced dose of ifosfamide without further blood loss. This agent is active as a single agent in non-Hodgkin's lymphoma.
An acceptable toxicity either hematologic or cardiac or hepatic was registered. Nausea and vomiting were observed more common but generally well tolerated and less important than using Anthracyclines, with the exception of the combination including Cisplatin. The results of our Phase II study indicate that Mitoxantrone-containing regimens can play a role in the treatment of refractory or relapsed NHL. Moreover the low toxicity, with particular care for cardiac adverse effects suggests that these regimens might be recommended also in the old pts.

T 95 MITOXANTRONE AS SINGLE AGENT OR IN COMBINATION: SECOND LINE CHEMOTHERAPY IN REFRATORY OR RELAPSED NON-HODGKIN'S LYMPHOMAS. REPORT OF THE NON-HODGKIN'S LYMPHOMA CO-OVERATIVE STUDY GROUP (NHLCOSG). A. Congiu (Genova)*, T. Chiesi (Vicenza), A. Cottu (Sassari), V. Rizzoli (Parma), P. Coser (Bolzano), A. Porcellini (Cremona), L. Salvaggio (Padova), C. Minarelli (Novara), E. Endrizzi (Ravenna), M.R. Sartori (Genova), A. Rossi, T. DiAntico and G. Santini (Genova). *Department of Haematology, Ospedale S. Martino, Genova, Italy.

The failure to cure first line chemotherapy resistant leukemias and lymphomas, must incite to experiment with new and more active agents.

In 1988 the NHLCOSG began a phase II study in vicin patients, come out or not partially responders to a 2nd or 3rd generation regimen, were treated by Mitoxantrone. In the first phase Mitoxantrone was administered as a bolus injection (30 minutes) at 15mg/m2 i.v., repeated every 21 days for 6 courses as maximum (range 2-6). Fifteen patients with non-Hodgkin's lymphomas in advanced stage (K. C. Group II,III, and IV, and with a median age of 57 years (range 41-72) entered this study: of these, 9 were relapsed and 6 were refractory to the first line chemotherapy (CHOP, MACOP-B, etc.). Four patients obtained a CR (27%), 4 a PR (27%) and 7 were not responders or showed a progression of the disease (CR+PR=56%). Of the 4 patients in CR, 3 relapsed at 4,5,13 months respectively, while the fourth one is still alive and well treated with Mitoxantrone.

NHLCOSG employed in association with VP 16-213 and Prednisone (VP) with the following schedule, repeated every 28 days for 6 cycles as maximum (range 2-6): MITOXANTRONE 10mg/m2 i.v. days 1,2,3, VP 16-213 100mg/m2 i.v. days 1,2,3; PREDNISONE 60mg/m2 i.v. day 1,2-5. Twenty patients with the same characteristics of the first group (Histology, median age, stage), entered the second phase and presently eleven are evaluable for response and toxicity. A complete remission (CR) was obtained in 5 out of 11 patients (45%), while 6 did not respond to the treatment. The five patients in whom a CR obtained, were still now alive and well treated with Mitoxantrone and etoposide with the most frequent hematological toxicities (grade 2-4), while nausea, vomiting, myalgias, hair-loss and fever were mild. Cardiologic toxicity of grade 2 was observed only in one case.

In conclusion Mitoxantrone appears to be an active and safe-utilization drug. The first results suggest that a further employment of this drug in more organised regimens, could have an important role in the therapy of non-Hodgkin's lymphomas.


Various salvage regimens have been proposed for resistant NHL: results are heterogeneous and optimal treatment has not yet been defined. Cisplatin (P), Etoposide (E) and Mitoxantrone (M) have been found active both as single agents and in combination in NHL. Phase I-II studies have established Mitoxantrone (M) as active in refractory NHL as single agent, a lack of cross-resistance between Doxorubicin and M has been demonstrated in human lung cancer cell line. Based on these observations we initiated a study to assess the efficacy of MEPE combination as salvage chemotherapy (CT) in pts with resistant NHL (not responders to primary CT or relapsing after first line CT). From June 1988 through September 1992, 20 pts received MEPE with the following schedule: M 10 mg/m2 i.v. on day 1, E 70 mg/m2 days 1-3, P 60 mg/m2 on day 1 and D 40 mg/m2 days 1-5. Treatment was repeated every 4-6 weeks. Intense hydration with saline and mannitol was given on day 1 during P administration. There were 9 males and 11 females, median age was 54 yrs (range 27-68). 10 pts had intermediate grade NHL and 10 diffuse large cell lymphoma (DLCL). 17 pts were in advanced stage (IV, III and 3 stage II bulky. All pts were previously treated with Doxorubicin and E. 10 pts achieved a CR, 3 (25%) a PR, 2 a minor response. 7 (35%) were disease free or stable and 10 pts were progressive. The overall response to MEPE was therefore 50% with relapsing lymphomas responded better than those with primary refractory NHL as follows:

<table>
<thead>
<tr>
<th>Pt</th>
<th>CR</th>
<th>PR</th>
<th>Refractory</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>2</td>
<td>1</td>
<td>8</td>
</tr>
</tbody>
</table>

The main serious toxicity was myelosuppression, but only 3 pts had fever due to neutropenia. Nausea and/or vomiting were present in most of the pts. However 13 pts were given MEPE on an outpatient basis. MEPE was reasonably well tolerated and proved to be effective as salvage CT in resistant NHL.

T 93 MITOXANTRONE-CONTAINING REGIMENS IN REFRATORY OR RELAPSED NON-HODGKIN'S LYMPHOMAS: RESULTS OF A PHASE II STUDY. T. Chiesi, L. Rinaldi, G. Caprini, Department of Hematology, S. Bortolo Hospital, Vicenza, Italy.

In the aim of finding out a more effective salvage drug-combination for patients (pts) with intermediate/high grade NHL refractory or relapsed to front-line treatment of second or third generation a study is being performed by using Mitoxantrone in association with conventional agents to assess both the efficacy in inducing a response and clinical and hematological toxicities. The treatment schedule was as follows: A) Mitoxantrone (12mg/m2 i.v. on day 1) + Etoposide (150mg/m2 i.v. on day 1) + Cyclophosphamide (650 mg/m2 i.v. on day 1) + Prednisone (60mg/m2 i.v. or i.m. on days 1-5); B) Mitoxantrone (4mg/m2 i.v. on day 1) + Etoposide (150mg/m2 i.v. on day 1) + Cisplatin (20mg/m2 i.v. on days 1-5) + Prednisone (40mg/m2 i.v. or i.m. on days 1-5); Therapy was repeated every 21 days for a minimum of 4 cycles in responding pts. Preliminary data on the therapeutic results with these regimens are summarized in the table:

<table>
<thead>
<tr>
<th>N° of evaluable patients</th>
<th>CR</th>
<th>PR</th>
<th>None</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>2</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>B</td>
<td>1</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

T 96 PTY-119 PROTEIN IN PATIENTS WITH NON-HODGKIN LYMPHOMAS (NHL) LOW AND INTERMEDIATE GRADE: TRAIL OF AN ACTIVE NEW AGENT. Antia M., Nisi M., Minnelli M., Piselli F., Del Pozzo G. and G. Papi - Hematology department, I. Eugenio Hospital, University of Rome, Italy.

PTY-119 Protein, (sericin of Lycopersicon esculentum), is a new tripotent anti-cancer protein with anti-cancerous and anti-inflammatory action. PTY-119 was assayed to test the in vitro and in vivo antileukemic activity of PTY-119 on HL-60 cells. The results are promising: 60 mg of PTY-119 administered to leukemia-bearing mice caused a 50% reduction in tumor growth. In a phase II, 32 patients (pts) with stage IV, A, were studied. 5 pts were given an initial dose of PTY-119, while 20 pts were given a therapeutic dose of 50 mg. The results were consistent with the in vivo experiments. In conclusion, PTY-119 is an active and relatively not much toxic agent for Low and Intermediate grade NHL. Further trials studying this drug as a single agent or in combination therapy are indicated.
ABSTRACTS - Fourth International Conference on Malignant Lymphoma, Lugano

T 97 CARBOPlatin Phase II STUDY IN RESISTANT MALIGNANT LYMPHOMA
Institut Gustave Roussy, 94805 Villejuif Cédex, FRANCE.

Thirteen patients (pts) with malignant lymphoma were entered in a phase II trial of Carboplatin between January 89 and December 89. Carboplatin was administered in the day hospital at 400 mg/m² in 500 ml of 0.9% dextrose over one hour by intravenous infusion at 28 day intervals. Median age was 42 years (24-63). Histological diagnosis was 6 Hodgkin's disease (HD) and 7 non-Hodgkin Lymphoma (NHL) of intermediate type (3 F, 4 G). All pts had progressive disease (2 relapsed in P19 therapy and had previously received combination chemotherapy. Median number of drugs administered before Carboplatin was 12 (4-14). Eight pts received previously ≥ 3 different regimens and 7 pts were irradiated.

The interval between diagnosis and Carboplatin treatment ranged from 10 to 60 months (median = 12 months). WHO performance status was 2. All pts had measurable disease. Toxicity and response were evaluated according WHO criteria. A total number of 21 Carboplatin cycles was administered.

Hematological toxicity is shown in the table:

<table>
<thead>
<tr>
<th>WHO GRADE</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>7</td>
<td>6</td>
<td>6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>RBC</td>
<td>9</td>
<td>4</td>
<td>4</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Platelets</td>
<td>5</td>
<td>4</td>
<td>3</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

Nausea and vomiting (≥ 2) were noted during 12 cycles. No significant nephrotoxicity or neurotoxicity was encountered. There were 2 partial responses (1 HD, 1 NHL). The first patient died 4 months later of hemmorhage after high dose therapy followed by autologous bone marrow transplantation and the second patient is alive in complete remission 10 months later after consolidation by radiotherapy. These preliminary results merit further investigation and patient accrual should be continued.

T 98 SIS-BMP CHEMOTHERAPY FOR LYMPHOMAS WITH BONE MARROW FAILURE
E. GILLES, M. OSTRONOFF, P. BRAULT, E. ZAKBE, J.-L. PICO, M. HAYAT.
Institut Gustave ROUSSY - 94805 Villejuif, FRANCE.

Despite progress in curative treatment of lymphomas, there is a category for whom only palliative therapy can be offered for the relief of pain or symptoms, or psychosocial support. However, when effective drugs have already been used and bone marrow is often involved or irradiated. From 1/89 to 9/89, 15 patients (pts) were treated with a combination of SIS-BMP chemotherapy. All pts had only a mild aplastic effect: CISPLATIN 100 mg/m² d1 (day), BLEOMYCINE 15 mg Total Dose (TD) d1 d2 and d15, METHYL-DEOOG 500 mg/m² d2 and d15, MELPHY-DENDROISOLE 120 mg/m² d1 and d2, 240 mg/m² d2. Disease was given regardless of the blood counts. Second cycle at d28 if 28 blood counts were compatible. The patients' characteristics were as follows: 12 males, median age 57 years, (range 34 - 76). Others: one hemorrhage related death due to autoimmune thrombopenia. Hair generally regrew after treatment.

T 100 AUTOLOGOUS BONE MARROW TRANSPLANTATION IN RELAPSED B CELL NON-HODGKIN'S LYMPHOMAS: VERY LOW TREATMENT RELATED MORTALITY IN 130 UNIFORMLY TREATED PATIENTS

High dose ablative therapy and ABMT has been shown to be the only potentially curative modality in relapsed patients (pts) with relapsed NHL. More widespread use of this therapeutic approach has been limited by significant fatal toxicity and irradiation of the bone marrow (BM) by lymphoma cells. One hundred thirty pts with B cell NHL in second relapse or incomplete first remission (13 pts) were uniformly treated with high dose chemoradiotherapy and anti-B cell monoclonal antibody treated ABMT. All of these pts demonstrated good performance status with Karnofsky score of ≥ 80%. However, the majority of these pts had one or more adverse prognostic features including a failure to achieve a complete remission with conventional combination chemotherapy (52 pts), BM involvement (96 pts), a history of extranodal disease other than BM involvement (56 pts), and histologic conversion from a low to intermediate grade NHL (16 pts). At the time of ABMT, only 64 pts were in CR; however, all pts had achieved a minimal disease state (≤ 2 cm lymph node masses and BM involvement of ≥ 20%) following conventional intensive chemotherapy.

Following high dose ablative therapy (cyclophosphamide 60 mg/kg x 2 and 200 mg/m² x 6), two acute in-hospital toxic deaths occurred (1 CNS bleed, 1 VOD). Four late non-infectious deaths were observed, not due to recurrent NHL. All patients achieved hematologic engraftment with a median of 26 days for granulocytes (> 500 PMN/mm³) and 27 days for platelets (> 40,000/mm³). The late complications have been limited with 16 pts with pneumonia (3 PMN, 1 CMV, and 12 culture negative), and 27 pts with H. zoster (25 dermatomal, 2 disseminated). Of the remaining 12 pts, 7 pts were unengrafted with a median follow-up of 17.9 months. Of the 13 pts undergoing ABMT in incomplete first remission, only 2 have relapsed. The majority of relapses were in sites of previous disease (22 old sites vs 7 new sites) while 7 occurred on new sites. When relapsed, only 7 pts had a prior history of BM infiltration, and 9 of whom had BM involvement at harvest. BM infiltration was limited with NHL either historically or at harvest.

The study demonstrates that high dose chemotherapy and ABMT can be employed with very low treatment related mortality and in pts with persistent BM involvement at harvest. This low mortality has now permitted us to employ high dose chemoradiotherapy and monoclonal antibody purged ABMT as consolidative therapy for patients with both low and intermediate/high grade lymphoma who are not considered curable with conventional therapy.

Conclusion: CIS-BMP gives thus promising results in this context.

T 100 AUTOLOGOUS BONE MARROW TRANSPLANTATION (ABMT) in the treatment of lymphomas with emphasis on cardiac complications. S. MEYER, D. BRON, P. RECOLUX, L. DEBUSSCHER, C. JARRY and P. STRYKMAN. Dept of Internal Medicine, Inst J. Bordet, Brussels, Belgium.

High dose chemotherapy (HDCT) followed by ABMT offers one way to circumvent treatment resistance of patients (pts) with lymphoma. From December 81 to December 89, 32 patients (15 males, 17 females), median age of 31 (range 16 - 57) years underwent ABMT. 16 pts had relapsed NHL and 16 had Hodgkin's disease. HDCT was BEAC (BCNU 300 mg/m² d1, cyclophosphamide (CPA) 60 mg/kg d2-3, VP16 500 mg/m² d2-3, ASA-C 400 mg/m² d2-5) for 22 pts, CPA 60 mg/kg d1-2 and total body irradiation in 5 pts, AV (ADR 135 mg/m² d1, CPA 300 mg/m² d1, VP16 250 mg/m² d1-2) in 4 pts and ABM (BCNU 550 mg/m² d1, ANSA 150 mg/m² d2-5) in 1 pt. 20 pts were in relapsing relapse, 11 pts were in resistant relapse (RR) or progressive disease (PD) and 1 pt with poor prognostic lymphoclastic lymphomas was in complete remission (CR).

Some of the pts with RR or PD are alive and the median survival was 2 (0-80) months. Among the 20 pts grafted in relapsing relapse, 9 (45%) are alive and 6 (30%) are disease-free with a median follow-up of 20 (3-96) months. The pt grafted in CR is alive, in continuous CR. All pts had a normal cardiac function before ABMT (isotopic ejection fraction and/ or routine bidimensional echocardiography).

We observed 3 non-fatal pericarditis and 4 fatal myocarditis. Nephrotoxic-related manifestations included daily weight gain, decrease of the GFR complexes, altered left ventricular function and presence of pericardial effusion. Three 6 pts had all previous mentioned modalities. Cardiotoxicity was associated with cyclophosphamide and ifosfamide, cisplatin and/or etoposide and high dose therapy. Myocarditis-related manifestations included daily weight gain, decrease of the GFR complexes, altered left ventricular function and presence of pericardial effusion.
ABSTRACTS - Fourth International Conference on Malignant Lymphoma, Lugano

T 101 PARMA INTERNATIONAL PROTOCOL: EARLY NON-RANDOMIZED PILOT STUDY OF DHAP FOLLOWED BY INVOLVED FIELD RADIOTHERAPY AND BEAC WITH ADMT: REVIEW OF A GROUP OF 60 PATIENTS WITH A MINIMUM FOLLOW-UP OF 3 YEARS.

Fifty patients with intermediate or high grade non-hodgkin's lymphoma who had not received any previous therapy were randomized to a complete remission induced by an Adriamycin containing chemotherapy regimen participated in this pilot study. The patients ranged in age from 16-60 years (mean 40 yr). All patients received Dexamethasone, high dose Cytarabine, and Cisplatin (DHAP) for two courses at 3-4 week intervals. Patients achieving a partial or complete response received involved field radiotherapy and high dose Carmustine, Etoposide, Cytarabine, and Cyclophosphamide (BEAC). The response to DHAP in 48 evaluable patients (i.e. one was lost to follow up and one had no measurable disease) was complete response in 78 patients, partial response in 21 patients, and no response in 3 patients. Twenty patients died during treatment for related toxicity and five others declined autologous bone marrow transplantation. The patient with non measurable disease did not progress on DHAP and was submitted to ABMT. Twenty-two patients underwent autologous bone marrow transplantation. Two patients received Cyclophosphamide plus total body irradiation and 20 received the BEAC protocol. Of these 20 patients, 11 are alive (7 patients are disease-free) and two (9%) died from toxicity; event free survival is 42% at 24 months. This prospective multicentric trial documents the ability of DHAP followed by autologous bone marrow transplantation to produce durable complete remission in a significant proportion of patients with relapsed or refractory lymphoma unselected at time of relapse from a conventional protocol.


Eleven patients with relapsed or progressive non-Hodgkin's lymphomas were treated with an innovative scheme, recently developed at Istituto Nazionale Tumori of Milan, including the sequential administration (9-3 weeks interval) of cyclophosphamide (7 g/m²), methyltrexate (8 g/m²) and Vinristine (1.5 g/m²) followed by autologous bone marrow transplantation (ABMT). The response to DHAP in 48 evaluable patients (i.e. one was lost to follow up and one had no measurable disease) was complete response in 78 patients, partial response in 21 patients, and no response in 3 patients. Twenty patients died during treatment for related toxicity and five others declined autologous bone marrow transplantation. The patient with non measurable disease did not progress on DHAP and was submitted to ABMT. Twenty-two patients underwent autologous bone marrow transplantation. Two patients received Cyclophosphamide plus total body irradiation and 20 received the BEAC protocol. Of these 20 patients, 11 are alive (7 patients are disease-free) and two (9%) died from toxicity; event free survival is 42% at 24 months. This prospective multicentric trial documents the ability of DHAP followed by autologous bone marrow transplantation to produce durable complete remission in a significant proportion of patients with relapsed or refractory lymphoma unselected at the time of relapse from a conventional protocol.

T 103 RESULTS OF COLLECTION OF PERIPHERAL BLOOD STEM CELLS IN PAIRED RAPING MALIGNANT LYMALIGNANT LYM

Histology, Hôpital Cochin, ** Hematology, Hôpital Pitié Salpêtrière, Paris, France.

Peripheral blood stem cells (PBSC) were collected from 10 patients (pts) with high grade, stage IV non hodgkin lymphomas (NHL) in second or third relapse. The conditioning regimen prior PBSC collection included AMONIDRINE (200 mg/m² x 3 days) and CYTOSINE-ARABINOSID (ARAC) = 500 mg/m² twice a day x 4 days (n=5) or ARAC 1g/m² twice a day x 5 days (n=4). One patient received AMONIDRINE 200 mg/m² x 3 days and ARAC 3 g/m² x 12 h x 6 days. Median aplastic phase duration was 18 days (range = 9 - 26). PBSC collection began after leukocytes count reached 1500/mm³ at day 21 (range = 18 - 29) to 5 apheresis were performed in all cases. A median number of 5 x 10⁹/kg (range = 1.5 - 10) nucleated cells were collected per apheresis corresponding to 12.10⁶/kg CD34⁺ cells (range = 0 - 88.8). In 3 cases, we didn't obtain sufficient number of CD34⁺ cells. In one patient a second phase of ARAC induced aplasia allowed us to collect enough CD34⁺ cells. No toxic related death was reported during the apheresis phase. After high dose chemotherapy and radiotherapy, 5 patients have already been transplanted with leukapheresis products. The engraftment was observed in every case.

Our results suggest that chemotherapy with AML and/or ARAC is a potential and safe conditioning regimen in order to collect PBSC in heavy treated lymphoma.

PBSC collected can induce hematopoietic reconstitution after myeloablative chemotherapy. Currently the follow up after PBSC autograft remains too short to evaluate the usefulness of such therapeutic approach in malignant lymphoma.


38 patients (28 male, 10 female, mean age 28 yrs. [17 - 62] yrs) with ALL and AUL have been included in this trial. 6 months have been treated for relapsed ALL and AUL. A first induction phase was performed with prednisone, daunorubicine and second and third phase cut off after 6 months. 10 ALL and 16 AUL patients in CR at end of induction phase 1, 8 after phase II. The median survival 6.6 mo. Patients with a preceding CR of less than 18 months had a 47% CR. Those with a preceding CR more than 18 months had a complete remission rate of 76%, however (p = 0.06).

Patients with short preceeding CR had a higher disease-free survival (not significant). Side effects of induction phase I consisted predominantly in hematotoxicity and subsequent infections and gastrointestinal toxicity. The median duration of critical granulopenia <0.5 x 10³/µl of 13 days phase I. Among some patients experienced additional cutaneous, ocular and hepatic toxicity. Granulopenia lasted about 15 days and thrombocytopenia <20,000/µl for 11 days. Four patients died during induction. Nine patients had allogeneic and seven autologous BMT. 5 patients allogeneic and 1 with autologous BMT remain disease-free. The treatment regimens is effective in remission induction, but the remissions are short. The duration of the preceding remission is the main prognostic factor.
ABSTRACTS - Fourth International Conference on Malignant Lymphoma, Lugano

T 106

NASAL Lymphoma - A CLINICO-PATHOLOGICAL STUDY. R. Liang1, D. Toda2, D. Chey3, T.K. Chan1, E. Chi1, F. Ho1.

University Departments of Medicine1 and Pathology2 and the Institute of Radiotherapy and Oncology3, Queen Mary Hospital, Hong Kong

Between 1975 and 1988, sixty adult Hong Kong Chinese patients were diagnosed to have nasal lymphomas which comprised 6.5% of all cases of lymphomas. Only cases involving the nasal cavity and nasal sinuses were included. There were 42 males and 18 females. The median age was 69 years. 31 patients had stage I disease, 10 stage II, 3 stage III and 16 stage IV disease. According to the Working Formulation, there were 1 case of SL, 1 FSC, 2 FM, 1 DSC, 5 DM, 14 DGC, 5 DIB, 1 DMB, 1 DMBG, 16 unclassifiable and 13 polyosepnic reticulosis. Immunophenotype was known in 18 cases. There were 12 T-cell, 4 B-cell and 2 were inconclusive. Twenty seven patients with stage I/II disease received radiotherapy alone and the remaining 33 patients had chemotherapy (m-BACOD 10, BACOP 2, CHOP 12, COPP 4, COP 6). 11 patients had additional radiotherapy following chemotherapy. Ann Arbor Staging was the only significant prognostic factor. Patients with stage I/II disease had a 5-year survival of 55% and chemotherapy did not appear to be more effective than radiotherapy alone in treating these patients. Stage III/IV patients had significantly (p < 0.005) poorer prognosis with a 3 year survival of only 17%.

T 107


A considerable number of lymphomas arise from extranodal sites. Primary Hodgkin and non-Hodgkin lymphomas of the breast are a rare occurrence. Their incidence is 0.05-0.5% of all breast neoplasms. Our aim was to evaluate the primary lymphomas of breast we had in our clinics, where a large population of breast cancer patients had been studied. The incidence of HD and non-HD was found of the order of 0.05%. Nine patients presented with localized disease to the breast (stage IE) or the breast and ipsilateral axillary lymph nodes (stage IIE). In this series is included a case presented with brain involvement due to breast lymphoma. The pathological material was classified according to the Working Formulation classification and all patients were evaluated with physical examination, laboratory investigation including CT abdominal and in a few cases brain CT or r-ray, bone scan and bone marrow biopsy. No patient underwent staging laparotomy. Treatment included chemotherapy in a few cases, chemotherapy and radiation therapy. Our results indicated complete remission in 5/9 (60%) of patients within 5 months since the diagnosis. Partial remission was obtained in 3/9 and one failure to combined treatment in the case with brain involvement (CHOP plus RT). Localized RT was given to 2/9 and chemotherapy only with CHOP in 3/9 cases. Bulky disease (tumor size > 5 cm and LDH high) was treated with combined chemoradiation. Prognostic factors like bulky disease and high LDH were the more useful parameters. We cannot draw any firm conclusion at the present time, because of the rarity of the primary breast lymphomas and the optimum management require further evaluation.

T 108

PRIMARY EXTRA-MEDULLARY NON-HODGKIN LYMPHOMAS (PENNL): REPORT OF A CLINICAL STUDY OF 104 PATIENTS. R. Sambion1, A. Ambrosiotti1, A. Perini1, G. Todeschini1, F. Pavani1, D. Veneri1, T. Franceschi1, G. Peroni1, G.L. Catto1. Institute of Medical Pathology, Division of Hematology (1) and Medical Oncology (2). University of Verona, Italy.

Non-Hodgkin Lymphomas (NHL) which arise out of central lymphoid system (lymph nodes, spleen, thymus) without (stage IE) or with involvement of regional lymph nodal (IE) are classified as PENNL. From 1973 to 1989, 695 patients (pts) with NHL were referred to our Institutions: 104 of these (14.9%) fulfilled the criteria mentioned above: 60 were males and 44 females (ratio 1.3:1), median age was 57 years (range 12-84), seventy-two (69%) were staged as IE and thirty-two (31%) as IIE. The sites involved were gastroduodenal tract in 52 pts (50%), head and neck region in 17 pts (16.3%), skin in 10 pts (9.6%), central nervous system in 8 cases in 6, bone in 4, lung in 2, and uterus in 1.

Histologically, the diffuse pattern (90/104) was more frequently observed, compared to the nodular one (14/104). According to the Working Formulation, the prevalence of the high grade malignancy subtype (56/104) was detected, compared to those of the intermediate (42/104) and the low grade (6/104). Highly pts (77%) underwent surgery; in 51/80 chemotherapy was performed and in 15/51 involved field radiotherapy was associated to the chemotherapy. In the 24/104 pts, who did not undergo surgery, treatment was chemotherapy in 11 pts, radiotherapy in 4 pts, and chemotherapy plus radiotherapy in 9 pts. Complete remission (C.R.) was achieved in 100/104 pts (95.2); at date, 74/104 are still alive and 68 are in C.R., with a median follow-up of 32 months (range 3-142), 36 pts survived more than 5 years. The overall median survival is 121 months.

Our data, outlined the good results in terms of C.R. and long term survival in PENNL, suggesting the importance of an integrated therapeutic approach.
ABSTRACTS - Fourth International Conference on Malignant Lymphoma, Lugano


Involvement of the stomach is the second most common extranodal site after Waldeyer's ring, accounting for 9% of all NHLs in our experience. Despite this fact, the disease is relatively uncommon and it is difficult for large numbers of pts to be accrued into single centre trials. To date, the majority of the reported series are about results of treatment of pts with primary gastric lymphoma have been based on retrospective analyses. Our study refers to 39 cases of primary gastric lymphoma (20 m. and 19 f.m. mean age 56 yrs, range 27-78 yrs). At the onset, the most common symptoms were epigastric pain (56%), weight loss (33%) and dyspepsia. Hematemesis was observed in two cases. In the majority of instances the disease was localized at gastric body (41%), followed by antrum (35%) and fundus. In six cases (16%) a multicentric involvement of the stomach was observed. Ulcerating lesions surrounded by elevated borders or infiltrating the gastric wall(66%), as well as lesions diffusely infiltrating (16%) were the macroscopic appearance more frequently observed. According to the Working Formulation, intermediate and high grade NHLs were found in 79% of cases (16 8, IG 17, HS 14). The Musshoff Staging - Lymphoma (M-HL) in stage 1, 13 in II (III Ipts, III 2pts), and 7 pts in stage III/IV.

Treatment consisted, whenever possible, in surgery followed by cyclic chemotherapy (CVP for low grade or 6-8 pts more than 65 yrs; CHOP/CHOEP- Bleo/CHOEP for intermediate-high grade). CR was achieved in 33 pts (84,6) and PR in 2 pts (6,82). 4 pts with advanced disease and high grade NHL died within few months from diagnosis (surgery not possible 2 pts, gastrointestinal bleeding or re- fused therapy in the other 2 cases). Four relapses were observed in 31, +18,18+ and 2þ6 months (2 local and 2 nodal); one of these pts, relapsed after surgery, achieved 2nd CR by chemotherapy. The remaining 3 pts died with progressive disease.

At present time, 31 pts (79,4%) are alive and well with a follow-up from 4 to +110 months (mean 38 months).


108 patients (pts) with stage I-II primary gastric non-Hodgkin’s lymphoma (NHL) observed from 1975 to 1987 in seven onc-hematological Units in Northern Italy have been retrospectively analyzed. Mean age was 56 yrs (range 20-81); male-female ratio was 1:1.7. Symptoms were similar to those of gastric carcinoma. The most frequent gastric location was the antrum (21%), followed by lesser curve and greater curve. Stage was IE in 63 pts, IIE in the remaining 45. According to Kiel Classification, 50 pts had a high grade lymphoma, 30 pts an intermediate grade lymphoma, 22 pts a low grade lymphoma. In 6 pts, histology was unclassifiable. The treatment consisted of radical surgery alone in 31 pts, surgery + chemotherapy (CT) in 39 pts, surgery and radiotherapy (RT) in 15 pts, surgery+CT+RT in 9 pts, CT only in 12 pts, CT and RT in 2 pts. Median follow-up is 49 months. Complete remission (CR) was achieved in 86 pts (80%); 9 pts relapsed, 8 of them locally. In univariate analysis, significant prognostic factors were: histological grading (low or intermediate grade vs. high grade), infiltration of sieroasc, and the accomplishment of radical surgery. In a multivariate analysis, only radical surgery resection maintained its prognostic significance. Data coming from this series suggest that radical surgical resection is recommended as first-line treatment in all the pts with stage I-II primary gastric NHL, possibly being adjuvant chemotherapy in stage I pts without unfavourable prognostic factors. In stage I pts with unfavourable prognostic factors and stage II pts an adjuvant treatment with RT or CT is advisable.


We have evaluated 695 cases of NHL observed in our Institutions from 1973 to 1989. We considered as PIGINH the Ron Hodgkin Lymphomas (NHL) which arise from gut-intestinal tissue without (stage IE) or with involvement of regional lymph nodes (IIE). Only 52 patients (7,5%) can be defined as PIGINH, (34 males, 18 females, ratio 1:1;1), the median age was 58 years.

The stomach was the most frequent localization (45/52). Thirty patients were staged as IE, 20 as IIE of the disease. Histologically we observed a prevalence of a diffuse pattern (43/52) compared to a nodular one (9/52) and a prevalence of high and intermediate grade malignancy (respectively 23 and 25) versus low grade (4 patients), according to the Working Formulation.

The treatment was not homogenous. Forty-nine patients underwent surgery; and 15 of these had surgery alone. The remaining 34 patients had chemotherapy (38), radiotherapy (1) or both (5) after surgery. Only 3 patients were treated with chemotherapy alone.

Complete remission was achieved in 50/52 patients (96%); in two patients the disease progressed; 9/50 (18%) relapsed; 42/52 are alive to date with a median follow-up of 30 months (range 3-142). Median survival is still not reached (60% of survivors at 93 months).

The encouraging results obtained confirm the better prognosis of PIGINH as compared to other NHL, irrespective of histology, and suggest the opportunity for an integrated approach (surgery plus chemotherapy).

T 112 GASTROINTESTINAL NON-HODGKIN’S LYMPHOMA (NHL) A RETROSPECTIVE STUDY ON SURVIVAL PROGNOSTIC FACTORS. M. Sarafidou, A. Trabulsi, N. Tsavara, M. Bakoyannis, N. Droutz, S. Tselentis, D. Liauzou, L. Kymiadis. Second Dept. of Medical Oncology, Hematology Dept., Metaxa Cancer Hospital Botsali 51 - Piraeus - Greece

Gastrointestinal (GI) tract is the most common site of primary extranodal lymphomas. Although the lymphomas of this anatomic region are in their majority of diffuse aggressive type, several other prognostic factors affect the evolution of disease.

Our aim was to retrospectively study the survival of patients with primary GI lymphoma, in relation to possible prognostic factors and type of treatment.

We studied 29 patients (15 male, 14 female), treated between 1/80 and 5/89. The median follow-up was 17 months. The primary site included stomach 22 patients, small bowel 3 and large bowel 4. The depth of tumor invasion was in 3 patients superficial, in 7 transmural and in 19 there was senescent penetration. Involvement of lymph nodes had 20 patients, of these 7 contiguous only, 13 and/or not contiguous. Right patients presented with stage Ig, 14 stage Ig, 9 Ig. 7 Stage IV. Low grade (LG) histology had 2 intermediate (IG) 4, high grade (HG) 20. Twenty five patients underwent surgical procedures, 11 complete resection of disease, 14 laparotomy and biopsies only. All patients received chemotherapy (6 cycles at least), mainly GITOP (GI). At a median follow-up of 41 months (6-109), 20 of 29 patients remained alive. The projected 5-year survival for the entire group is 71.6%, 96.2% for lymphoma of the stomach have better 5-year probability of survival (89.0%) compared to those of bowel (42.9%) (P<0.05). For Stage I gi and II gi to IV the projected 5-year survival is 100% and 30% respectively (P<0.005). Although the rejected over the remaining group 100% vs 60% respectively (P<0.05).

These results suggest that localized in the stomach disease and early stage are favorable prognostic factors. Also completeness of disease prior to chemotherapy, influences positively the survival.
ABSTRACTS - Fourth International Conference on Malignant Lymphoma, Lugano

T 113 THE PRIMARY GASTRIC NON-HODGKIN LYMPHOMA : A RETROSPECTIVE STUDY.
Divisione di Chirurgia Generale, Ospedale San Martino, Genova, Italy.

eCattedra di Chirurgia Toracica - Università di Genova. "Cattedra di Oncologia Universitaria di Genova."

A retrospective study was carried out on the survival of 54 patients with primary gastric non-Hodgkin Lymphoma (G-HL) hospitalised at various departments of San Martino Regional Hospital of Genova from 1976 to 1989. 9 patients were excluded from the analysis due to incomplete data. The remaining 45 patients, 18 females and 27 males, median age 66 years (range 21-84), were staged according to Ann Arbor staging system and graded according to the International Working Formulation for clinical usage (stage I, II and III; stage I/II: I/III: 17:1:12; stage III=17:4:5.). Among the classified Lymphomas, low grade G-HLs were encountered in 5 pts, intermediate grade in 21, high grade in 12. Out of 45 pts 22 underwent surgery alone (9 at I and II; 8 at IV; 5 at III); 11 surgery+chemotherapy (3 pts at I and II; 1 at II; 5 at III; 1 at IV). 5 chemotherapy alone (3 pts at I and II; 1 pt at II; 1 pt at III); 1 radiotherapy alone (1 pt at II); 3 surgery+chemotherapy+radiotherapy (1 pt at I and II; 1 pt at III; 1 pt at IV). 3 pts were not treated (1 pt at I and II; 2 pts at III). The median survival was 86 months in early stages (I-I/II) and 6 months (range 1-20) in stages III-IV. Statistical analyses showed a significant survival advantage (P value 0.004) Mantel-Cox test in pts in stages I-I/II compared to stages III-IV. No significant difference in survival was found among the different treatment groups (Kaplan-Meier function). Age, sex and histologic grade (low + intermediate grade versus high grade) all were nonsignificant factors.

CONCLUSIONS: The initial clinical stage is an important prognostic covariate. According to literature, the study failed to demonstrate a significant prognostic value for the WF in primary G-HL. The best treatment for these neoplasms still remains uncertain and it is a matter of active debate. It is then important to design prospective randomized clinical trials on the basis of the results provided by prognostic classifications. To this aim, optimal management of patients with primary G-HL can be investigated by conducting multicentric prospective trials.

T 114 MEDIALSTINAL & LARGE CELL LYMPHOMA IN ADULTS. A CLINICAL AND PROGNOSTIC STUDY OF 16 PATIENTS TREATED BY CHEMOTHERAPY ALONE.LNH 84 REGIMEN. B. DUPRIET, P. MOREL, A. WURTZ, P. PENAUX, B. BAUTERS. Maladiere du Sang, 1, Chirurgie, CHU, LILLE, France.

Between January 1983 and June 1989, we diagnosed mediastinal large cell lymphoma (non-hodgkin lymphoma and revealed symptoms related to a mediastinal mass) in 16 adult pts (9 females, 7 males, median age 36 yrs, range 25-60 yrs). 6 pts (37%) were classified as adult aggressive NHL. Symptoms concerning symptoms were dyspnoea (4), cough (7), dysphonia (3), hemoptysis (2), chest pain (1), and tachycardia (1). CT features included: para-teresophageal (3), pericardial effusion (4) and symptoms related to pericardial involvement (2). 4 pts had radiodensite lesions. The chest X-ray showed a large anterior mediastinal mass, whose minimal diameter, measured by CT-scan, was 10 cm in all cases. There was massive extramedullary spread in 13 pts (pleura: 7, but only 4 pts had large effusions), lymph nodes (6,3, 2 pts and pericardial effusion and 1 diffuse pericardial and mediastinal effusion). 7/10 pts had subcutaneous pleural effusion (3). 6/10 pts had pericardial involvement: 5/10 pts had a median sternotomy (2) followed by subtotal pericardectomy and 2 pts had an anterior mediastinoscopy.

The patients were treated with the LNH 84 regimen (6 courses of CVP + BOP at higher doses of Adri (75 mg/m2) and Cytoxan (120 mg/m2) for induction, followed by sequential CHOP and 5-fluorouracil). The response was complete in 5 pts, 3 pts achieved a partial remission and 1 pt had no response. The median time to progression was 17 months (range 2-42) and the median time to death was 24 months (range 2-51).

Centre Aesle Vauluis, Brabant, 54511 Vaudreuil-D'Xy-Nancy Cedex, France.

Fourteen (6 females and 8 males) with primary lymphomas of the central nervous system were treated at the Centre Aesle Vauluis between 1971 and 1988. The median age was 52 years. We observed no disturbance of the immune system and no development outside the CNS.

The mean duration of symptoms prior to presentation was 8 weeks with a range of 0-24 weeks. The most common symptoms were headaches, mental impairment and focal neurological signs. Evidence of raised intracranial pressure was present in 4 cases. Two patients presented diabetes insipidus with a severe hyponatraemia and coma in one case. There were also two cases of primary spinal localisation.

Histological diagnosis was performed by surgical biopsy (5 cases) and by stereotactic biopsy (8 cases) with excellent results. In one case no biopsy was made because regression had occurred with corticosteroid treatment. This patient is still alive with 8 months follow-up.

We recorded 3 total regressions with corticosteroid treatment. Chemotherapy with different protocols was administered in 6 patients followed by radiotherapy. Radiotherapy alone was used in 6 other patients and 2 were treated with surgery and corticosteroids only. The dose range was 30-50 Gy. The brain plus boost a total dose of between 37,5 and 50 Gy in 4-6 weeks.

Median survival was 7 months (range 1-22 months). The median survival of patients treated with chemotherapy plus radiotherapy (6 cases) was 9 months (range 1-17 months), with radiotherapy alone (5 cases) 7 months (range 1-22 months). Four patients are still alive (4 - 24 months), 3 in complete regression and 1 with tumor.

T 116 Four cases of Non-Hodgkin's lymphoma of the soft tissue adjacent to a long-standing Pythorax.
T. IBOKA, T. SAKAI, K. IMAI, Y. SAKAI and K. KAMAUCHI.
Dept. of Thoracic and Cardiovascular Surgery and Pathology, Tokyo Metropolitan Komagome Hospital.

It is well known that malignant pleural tumors develops in patients with pythorax resulting from therapeutic pneumothorax for pulmonary tuberculosis (the pneumothorax). In the past 7 years we have encountered four cases of Non-Hodgkin's Lymphoma (NHL), diffuse large-cell type, which developed in the soft tissue adjacent to a long-standing pneumothorax. Immunohistological studies revealed 3 cell nature of lymphoma cells in the two cases (Case 1 and Case 2).

Case 1 was a 63-year-old male. At the age of 24, he received the pneumothorax on the right side. Initial symptom was the right shoulder pain. The main tumor was in the right lateral hand arm and was growing to the axilla with a rapid growth rate. On CT-scan there was a large tumor in the right upper abdomen. The tumor invaded the pancreas, spleen, aorta, inferior vena cava, pericardium, inferior vena cava, diaphragm, stomach and right lower leg vein.

Case 2 was a 61-year-old male. At the age of 21, he received the pneumothorax on the right side. Initial symptom was the right shoulder pain and the left lower back pain. The main tumor was in the right upper abdomen. The tumor invaded the right lower abdomen, right lower hand arm and was growing to the axilla with a rapid growth rate. On CT-scan there was a large tumor in the right upper abdomen. The tumor invaded the right lower abdomen, right lower hand arm and was growing to the axilla with a rapid growth rate.

These four cases have a common feature with the other 40 cases reported in literature (37 cases are Japanese) and are regarded as a group with a common etiology, a long-standing pneumothorax.

From November 1985 to March 1989, patients with Mycosis Fungoides (MF) or Sézary Syndrome (SS) were treated with recombinant interferon-alpha 2a (ROFERON A). The protocol design consisted of a dose escalation from 3 MU/day for 3 months. After this, all patients underwent other 9 months of therapy with 18 MU three times weekly. Twenty patients entered the study (18 MF and 2 SS); 15 were previously treated by other conventional therapies including PUVA, chemotherapy or both and 5 were not. There were 12 males and 8 females. The median age was 53 years: range of 28 to 75 years. Five patients (25%) achieved a complete clinical remission, 10 (50%) obtained more than 50% reduction of detectable skin lesion or circulating Sézary’s cells, 4 (20%) reached a minor response, and one patient (5%) resulted resistant. The clinical side effects included fever (20/20), flu-like syndrome (18/20), nausea (17/20), itching (17/20), paraesthesia (17/20), stomatitis (4/20). Haematological toxicity included thrombocytopenia (1/20) and neutropenia (15/20). No treatment-related deaths occurred. Protocol violations included 3 definitive interuptions, 8 reductions of scheduled dose and 4 temporary interruptions.

The median follow-up is 28 months. The projection of survival shows 80% of patients alive at 48 months; the freedom from progression is 50% at the same interval. In conclusion, the daily administration of interferon-alpha 2a has been shown to be highly effective in patients with advanced or refractory MF and SS; the improvement was well documented after a few weeks and continued during the consolidation therapy. We correlated the most part of side effects to the advanced age of the patients and those pretreated with systemic therapy. Since patients over 60 years did not tolerate more than 9 MU dose, we suggest to give dose more than that dose to such patients in the future trials.


A series of 4 Ki-1+ clonal T-cell lines were established from 2 patients with a history of spontaneously regressing skin lesions. Patient 1 had a 17 year history of papulonodular skin lesions beginning in 1972 and mixed cutaneous HD in 1975. He developed erythroderma and circulating Sézary cells in 1985. Two years later the skin lesions became larger and more persistent, suggesting that tumor progression had occurred. Tumor cells (Ki-1+ clonal T-cell line established from malignant cells in the blood (1986) and each of two skin lesions (1987). Each cell line has a clonal rearrangement of TCR beta chain genes but a germline configuration of TCR gamma chain genes. All cell lines have a stem line CD4+ and additional additional CD8+ T-cells. The cell lines express the CD40 antigen and can induce in vitro proliferation. The cell lines produce IL-2 constitutively. The blood cell line expresses IL-2R; expression of IL-2R is suppressed by phorbol ester or TGFβ which down regulates IL-2R.

T 120 THE NATURAL HISTORY OF LYMPHOMA IN PRIMARY SJOGREN'S SYNDROME. N.A. Pavlidis, A.A. Drosos, N. Talai, H.M. Moutsopoulos. Medical School, University of Ioannina, GRECE, and University of Texas, San Antonio, USA.

The purpose of this study was to analyse the incidence, histology, primary site and course of lymphomas in 75 pts. Eighty of 120 pts with PSS followed over the past 7 years developed non-Hodgkin's lymphoma (NHL). Incidence was 6.6%. All 83 pts were female with a median age of 55 years. Median time from PSS diagnosis to NHL development was 6.5 yrs. NHL were diagnosed according to the Kiel classification. Six pts had immunoblastic, one had diffuse centrocytic-centroblast (CC-CB) and one nodular and diffuse CC-CB. Most pts had monoclonal k light chains. In 9 of the 14 malignancies the lesion was located at the minor salivary glands, 3 in the cervical lymph nodes and one in the nasopharynx. No immunocytoma pts were treated and they remain well, while the nasopharyngeal lymphoma underwent complete remission following local radiotherapy. It was interesting the fact that in two immunocytoma pts the malignancy lesions were reported spontaneously 6 and 18 months after diagnosis.

CONCLUSIONS: Lymphomas in PSS: 1) represent mainly low grade NHL and especially immunocytoma, 2) can arise primarily at the site of the autoimmune lesion, 3) usually have a benign course, thus conservati-ve approach to treatment is indicated, and 4) spontaneous regression can be seen.
ABSTRACTS - Fourth International Conference on Malignant Lymphoma, Lugano

T 121. THE CLINICO-PATHOLOGIC SPECTRUM OF VASCULITIS IN PATIENTS WITH NHL AND CLL.

Department of Medicine, School of Medicine, University of Ioannina, Ioannina, Greece

Vasculitis (VC) in lymphoma patients (pts) has been very scanty described in the literature.

Between Jan 80-Jan 90, 9 cases of skin VCS were diagnosed among 70 NHL and 60 CLL pts, treated and followed in our Department (an incidence of 11%). Mean age was 59 y+i, 5 were male and 4 female. Four patients had low and 2 had intermediate grade B cells NHL, while 3 others had CLL. Skin biopsies revealed lymphocytic VCS (ly VCS) in 7 leukemicosis VCS (It VCS) in 1 and a mixed form in 1. Median time from NHL diagnosis to first episode of VCS was 10 months (1-6).

Painful erythematous nodules with burning or stinging sensation was the main clinical picture in 2 pts with ly VCS, while all the rest presented with palpable purpurae over the extremities end/or the trunk.

Pruritus was present in 3 pts. One patient developed CNS involvement and peripheral neuropathy. The lesions were spontaneously regressed. Recurrence of the lesions was noticed in 4 pts. Neither chemotherapy or steroid induced the course of VCS.

Full immunologic and autoimmune profile including cryoglobulins and anti-cardiolipin antibodies were performed.

CONCLUSIONS: VCS in NHL and CLL pts: 1) is not a rare phenomenon, 2) lymphocytic VCS is the most frequent type, 3) it affects mainly the skin, 4) very rarely can become systemic, 5) the lesions can "wax end wane" spontaneously and 6) treatment doesn't seem to alter its course.

T 122. THE PATHOGENETIC MECHANISMS OF LOW SERUM ALBUMIN GAP IN MULTIPLE MYELOMA PATIENTS.
M. Ellis, K. C. Siamopoulos, K. Bourantas, N. Pavlidis.

Department of Internal Medicine, Medical School, University of Ioannina, Greece

It has been reported that in IgG multiple myeloma patients (MM pts), the serum albumin gap (SAG) is lower compared to normal controls. However, the pathogenetic mechanisms of this electrolyte disturbance are still uncertain. In this study, we determined the SAG in IgG MM pts with a median age of 48 years, and we correlated it with the amount of serum monoclonal protein as well as with serum albumin. Some of the MM pts had renal failure, hypercalcemia and hyperuricemia or any other disease affecting acid base balance and serum electrolytes levels. In none of the patients diuretics were given. Ten normal individuals were used as controls. The SAG in MM pts was 6.02±2.7 (mean ± SD) mmol/L, and it was significantly lower as compared to the controls (11.5±1.2; mean ± SD, p<0.01). There was a significant correlation between the values of SAG and the amount of serum monoclonal protein (r=0.993, p<0.01). In most of the MM pts the serum sodium was in the lower normal limits (136±3.9 mmol/L, mean ± SD) and it was correlated significantly with the amount of serum monoclonal protein (r=0.66, p<0.05). No correlation between SAG and serum albumin as well as between serum monoclonal protein and serum CT or HCO3 was found. However, most MM pts had high serum CT (106±4±2; mean ± SD), whereas serum HCO3 was within normal limits (22.6±2.6 mmol/L, mean ± SD). On the other hand, serum albumin was significantly lower in the MM pts (3.8±0.4; mean ± SD) as compared to normal controls (4.5±0.2; mean ± SD), p<0.05.

CONCLUSIONS: 1) SAG is low in IgG MM pts, 2) this finding is directly associated with the amount of serum paraprotein, 3) hypobulminemia could also be an additional factor in the pathogenesis of this electrolyte disturbance, 4) the study is still in progress.

T 123. HYPERTHYROIDISM FOLLOWING HODGKIN'S DISEASE (IN CASES).- B. Desaleksh, B. Lofan, A. Le Mavel, N. Vlahi, M. Coz, J. M. Andre, M. Malinau, S. S. Cz, M. T. A. Cz, A. Nantes, C. A. V. Cz, Czennes Cz, Bogun Cz, Hopital Laennec Paris France.

Association between hyperthyromia and Hodgkin's disease is rare since less than 30 cases have been reported. We report 8 new cases noted among 407 patients treated by the Hodgkin POP 88/92 and 87/34 trials from October 1981 to September 1988. The incidence is 2.0% among our patients, 1.3% among men and 2.8% among women (NS).


Case 8: 56-year-old man - Splenic IB - CR in July 1986 - Biological hypothyroidism in March 1986 with high levels of anti-thyroid antibodies: Hashimoto's autoimmunity - spontaneous hypothyroidism 2 months later.

As reported by other authors, our data suggests that the clinical aspects of hyperthyroidism following Hodgkin's disease are heterogeneous (typical Graves' disease; Graves' disease-like hyperthyroidism and that several etiologic factors may be considered (immuneological substitution; iodine overload; cervical radiotherapy...). (Work supported by APRES).


Studies of possible dominant inheritance of leukemia and lymphoma have shown that familial occurrence of these diseases is exceptional either in the same generation or in first degree relatives. The authors have investigated cancer in family members of children with Hodgkin's disease, but primarily the occurrence of malignancy in first degree relatives. The study involved 50 children treated at the Belgrade University Children's Hospital between 1974-1989. The results showed a high frequency of positive family history regarding the presence of cancer in other family members of children with Hodgkin's disease. In 4 children the presence of cancer was discovered in their parents; of these, the parents of 2 patients had cancers at the same time as their children. Familial aggregation of hematologic malignancies was also disclosed. It was concluded that further studies are necessary because familial factors are significant in the pathogenesis of malignant lymphoproliferative diseases, particularly of Hodgkin's disease.
ABSTRACTS - Fourth International Conference on Malignant Lymphoma, Lugano

T 125 HODGKIN’S DISEASE: A RETROSPECTIVE STUDY OF TRENDS IN KENYA (1968 - 1987)
A.G. Kungo, H.A. Abinoy, and L. Nyabola
Departments of Human Pathology, Medicine and Community Medicine, University of Nairobi, Nairobi, Kenya

Title name only: Type author's name(s) here.

In order to show changes (if any) in Hodgkin's disease pattern in Kenya with the onset of AIDS, a retrospective study of the disease was undertaken using Kenya Cancer Registry material covering the period between 1st January, 1968 to 31st May, 1987 (19.5 years).

A total of 695 cases (520 males and 175 females) were found; the annual age-standardized incidence rate for males from 11 in 1968 to 53 in 1969 with a mean of 34.8. 345 (49.6%) cases were under the age of 20 years with 135 (19.4%) being under 10. Only 86 (12.2%) were over 40. The age groups with the highest frequency of cases was between 10 and 19 years; representing 30% of all cases. The male: female ratio decreased over the years: 4.8:1 in 1968-72 period to 2.4:1 in 1983 – 87 period. The overall ratio was 2.9:1. Distribution according to districts showed a predilection for high altitude and tea-growing areas (Kisii, Kericho, Rachakos, Meru, Kiambu, Nyahurir) as opposed to low-lying, non tea-growing areas.

No clusters were seen in areas supposed to have high AIDS transmissions rates. 265 (38.1%) were not histologically subclassified. 201 (28.9%) were of mixed cellularity type, 58 (8.2%) were nodular sclerosis, 57 (8.2%) were lymphocyte predominant type and 116 (16.7%) were lymphocyte depleted type.

With respect to age-groups, sex ratio and histologic types the disease reveals a different pattern from that seen in western countries. It seems that the disease prevalence has not changed with onset of AIDS although serology could not be employed in our study. There is an increase in prevalence among females during the study period. There appears to be an association with tea growing areas. These areas may also represent high-income, other cash-crop growing and good nutrition populations. There may also show exposure to a low environmental pollutant. Epidemiological studies in this areas are urgently called for. Since those under 10 years of age are significantly affected a maternal related phenomenon needs to be further investigated. Connection with AIDS cannot be completely ruled out at this time. Since Hodgkin's disease has been associated with immunodeficiency for a long time additional studies to rule out a connection with AIDS in our areas are necessary.

T 128 TREATMENT IN HODGKIN'S DISEASE: A REVIEW OF 1024 CASES
Radiotherapy of Florence, University (**) and Hospital (*)
Radiotherapy of Arezzo, Hospital (**) Radiotherapy of Chieti, University (**)

We reviewed the records of 1024 patients affected by Hodgkin's lymphoma and treated at our institution from 1960 to 1987 and followed by us till now. About 64% of patients received, as initial therapy, radiotherapy alone (RT). Apart of the pts. treated with RT before 1970 (who were irradiated on several volumes) the majority received total nodal irradiation (TNI) or subtotal nodal irradiation (as mandible plus lumbar bar or similar). The total tumor dose ranged between 36 and 44 Gy/4-5 weeks. About 21% of patients received, as initial therapy, RT and adjuvant chemotherapy (CT). Apart of few cases treated with RT + CT in the late sixties, the majority, treated after 1970, were submitted to MOPP or ABVD polychemotherapy. In this group the volume treated and the dose delivered with RT was the same as that used in RT group. The remaining 15% of patients received chemotherapy alone (CT) as initial therapy. 477 pts (after 1971) were submitted to laparoscopy: 75% of those received RT whereas the others received CT + RT.

The disease-free period before relapsing was examined according to the clinical characteristics at the onset of the disease: age, sex, histologic clinical stage, systemic symptoms, mediastinal involvement, "bulky" disease and number of involved areas. The clinical stages I and II was furthermore divided in I and II and III, I11, I111 according to the suggestion of Tabi and others. (Cancer, 54: 885-894, 1984). The time elapsed from the primary treatment and the onset of the first relapse and the patterns of relapses were evaluated. The Kaplan - Meier method for overall and disease free survival and the Cox regression model for the evaluation of independent effects of variables were adopted. The results show that, apart a little difference in III2 pts, the overall survival is not implemented by the RT + CT association whereas relapses occur much more in RT group. As far as concern the relapses those occurring within the first year may be related to more "aggressive biology" of the disease; those occurring between the second and the fifth year after treatment may be related to "treatment failure"; and then the relapses, occurring later than seven years could represent a new Hodgkin's disease rather than a relapse of the previous disease.
ABSTRACTS - Fourth International Conference on Malignant Lymphoma, Lugano

T 129 PROGNOSTIC VALUE OF ESR IN PATIENTS WITH LOW STAGE HODGKIN'S DISEASE TREATED BY RADIOTHERAPY ALONE

sa, P. Gavarotti, L. Depaoli and G.L. Sannazzari

For the PHSG C/O Dep. of Radiotherapy, University of Torino,

Between January 1982 and June 1987, 74 patients (43 males and 31 females) with Hodgkin's disease stage IA (29), II A (38) or II A (7), were treated by radiotherapy in the course of their initial staging.

PHSG: 66 had supradiaphragmatic and 8 infra diaphragmatic disease; no patient with bulky lesions was included in this series. Age ranged between 15 and 72 years (median 30); staging included laparotomy in all cases except 5 patients with stage I, upper neck presentation and 3 patients with stage I l muscular neck presentation. Patients with supradiaphragmatic lesions received mantle field plus upper parafield area with an optional radiation in whom parafield irradiation was omitted, and patients with infra diaphragmatic disease received chestfield alone. Median follow-up was 5 years.

Complete remissions (CR) were obtained in all cases; 11 patients relapsed: 5 within the radiation field, 2 in non irradiated diaphragmatic area and 4 with systemic dissemination. All responded to salvage chemotherapy and achieved a CR. Factors influencing the DFS rates were analysed: age, sex, type of presentation, stage, type of RT (whether mantle or mantle plus parafield), number of involved sites and mediastinal involvement did not significantly affect DFS. Patients with NS involved sites had a worse DFS (versus 40% for patients with CR, p<0.0001). The most significant prognostic indicator in patients with 'favorable' Hodgkin's disease is patients with high ESR need aggressive treatment.

T 131 Radiotherapy alone of stage I and II clinical stages Hodgkin's disease


Division of Radiotherapy and Nuclear Medicine of Padua, Italy.

** Division of Radiotherapy and Nuclear Medicine of Padua, Italy.

Staging laparotomy, including splenectomy, liver and abdominal lymph node biopsy, remains the most accurate method for determining involvement of the spleen in clinical stages I and II Hodgkin's disease. However, in some institutions, the routine laparotomy is not performed because of its high incidence of complications. Therefore, some centers have investigated the safety and feasibility of standardizing the staging procedures. This study analyses the possibility to spare laparot-
omy for a selected subgroup of patients with clinical stages I and II.

From January 1985 to November 1985, 41 previously untreated patients, with clinical stages IA (14 pts) and IIA (26 pts) non bulky disease, entered into the study. They were 28 males and 13 females, median age of 45 years (range 18-74). Other clinical features of the patients will be discussed. The clinical staging was based on a complete histo-

T 132 Risk adapted combined radio-chemotherapy in Hodgkin's disease

M. Herold, K. Keiner and G. Anger

Department of Internal Medicine and Department of Radiology, Medical Academy Erfurt, Nordhäuser Str. 74, Erfurt, 30110, Germany

In an open pilot study we tested a program of reduced dosages of combined radio- and chemotherapy in Hodgkin's disease in limited stages (I-II) presenting with risk factors and in advanced stages (III-IV). The aim of the study was to reduce the delayed complications of CHM while preserving its effectiveness.

From May 1985 to December 1987, 45 previously untreated patients entered into the treatment consisted of alternating chemotherapy (CVP/DMSO) and low dose (25 Gy) involved field radiotherapy between the 6 cycles of chemotherapy. At present, 16.80 patients are evaluable for response to treatment. Primary CR reached 35/40 (88.3%) pts.. PR/SD 5/40 (7.5%). Three out of the five PR patients had a CR after salvage treatment, so total CR rate amounted 35/40 (87.5%). After a median observation of 29 months 26/32 (81.3%) resp. 30/35 (85.7%) patients are in first CR. The survival data after one and two years are as follows: RFS 1 y 32/32 (100%), RFS 2 y 25/27 (92%) overall survival 1 y 39/40 (97.5%) and 2 y 30/33 (90%). So far 4 pts. died, 2 after primary CR, three had a new relapse (after 14, 27 and 30 months), one a bone marrow relapse (after 12 months). In two of the three patients a second CR was achieved by salvage therapy. Acute toxicity of the treatment program was acceptable, whereas it is important to report about long-term side effects.

In conclusion we regard our treatment approach useful and the results of the pilot-study encourage us to continue this study with only minor modifications as a multicenter trial.
T 133 HODGKIN'S DISEASE (HD) STAGE IA AND IIA. EFFECTIVE THERAPY WITH MOPP COMBINATION AND INVOLVED FIELD RADIATION. DOSE AND TIME RESPONSE ANALYSIS. V.A. Boussiotis, P. Panayiotis, A. Pavessesiliou, G.A. Papanis. Hematology Unit, Lymphoma Clinic and Radiotherapy Department, University of Athens School of Medicine, Athens 115 27, Greece.

Early stages HD (IA and IIA) treated with radiation, have a relapse rate of approximately 31%. From January 1981 to December 1987 we have treated 48 HD stage IA and IIA patients with MOPP chemotherapy combined with involved field radiation at a dose of 2500 rads. The treatment schedule had as follows: Three cycles of MOPP/Involved field radiation/three cycles of MOPP. All patients were prospectively followed in the same unit. Twenty eight of them were men and 20 women, with a mean age of 36y (18-77). Their mean follow up time from diagnosis was 43 mo (20-94). Twenty patients had stage IA and 28 stage IIA disease, with the histologic subtypes: lymphocyte predominance 2, nodular sclerosis 29, mixed cellular 16 and lymphocyte depletion 1. Complete remission (CR) was achieved in 45 patients (94%). The mean time of CR was 38.1 mo (4-82). Ten patients (20%) subsequently relapsed in a mean time of 0.20 mo (0-56) from the documentation of CR. Factors which could be considered responsible for relapse, such as the clinical stage, the histologic subtype, the presence of mediastinal mass, the mean total nitrogen mustard (NM) and procarbazine (PCZ) dose as well as the mean time deviation from the scheduled drug administration, were analysed in the relapsed and nonrelapsed patients. The only parameter which was found to be significant in this comparison, was the mean total NM dose (p<0.05). Thus patients who relapsed, received a mean total NM dose of 80mg as compared to the nonrelapsed who received a mean total NM dose of 35mg. These doses represent the 66.2% and 77.5% of the anticipated 120mg mean total NM protocol dose, respectively. The main reason for dose reduction was myelotoxicity, frequently expressed with neutropenia. We concluded from our analysis that a reduced NM dose in early stages HD it is still effective, although its significant reduction may result in an increased number of relapses, whether this dose reduction in the nonrelapsed patients will result to a lower frequency of second neoplasia of our patients remains to be seen.

T 134 LOPP/ABE HYBRID PROGRAM: A COMBINATION CHEMOTHERAPY IN ADVANCED HODGKIN'S DISEASE: PRELIMINARY RESULTS. C. Gimm, T. Cerny, K.W. Brunner Institute of Medical Oncology, Inselspital, 3010 Bern, Switzerland.

26 patients (pts) with advanced Hodgkin's disease (III-IVB) were treated with a new seven-drug regimen (CT). 4 pts with II A were included because of their risk factors, especially bulky disease. Chlorambucil 6mg/m^2 i.v. d 1, vinristine 1.2mg/m^2 i.v. d 1, procarbazine 100mg/m^2 i. p.o. d 1-7, Adriamycin 75mg/die i. p. d 1-10 were given in a hybrid treatment plan with adriablastin 30mg/m^2 i. d 8, bleomycin 5mg/m^2 i.v. d 8-10 and etoposide 100mg/m^2 i. v. d 8-10 (LOPP/ABE). Cycles were repeated at 28-day intervals. 15 pts received consolidation radiotherapy (RT). Of the 26 evaluable pts 23 (88%) achieved a complete remission (CR). 20 pts went into CR with CT alone. From the 5 pts in partial remission (PR) 3 converted in CR with additional RT. 1 pt had a progression of his disease under CT. The 3 non responding pts showed a noticeable frequency of bad prognostic factors (stage, B-symptoms, bulky disease, high sedimentation rate and age).

2 pts relapsed after 2 and 7 months, although no definitive statement can be made about relapse-free survival for the 21 pts still in CR because of the short median follow-up of 20 months (range 8-53 months).

<table>
<thead>
<tr>
<th>number of pts</th>
<th>CR</th>
<th>PR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>after CT alone</td>
<td>26</td>
<td>20</td>
<td>5</td>
</tr>
<tr>
<td>conversion of PR to CR with RT</td>
<td>5</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>total</td>
<td>26</td>
<td>23</td>
<td>2</td>
</tr>
</tbody>
</table>

The treatment was well tolerated with no cardiotoxicity, neuropathy WHO grade 1 in 5 pts and 2 pts with pneumopathy grade 2. The treatment delivery was excellent as 93% of the treated pts received at least 75% and 60% pts got more than 90% of the calculated dosage. The median nr of cycles was 7.19. These preliminary results indicate that LOPP/ABE for pts with advanced Hodgkin's disease is an effective and well tolerated schema.

T 135 TREATMENT OF ADVANCED HODGKIN'S DISEASE WITH CCNU, ETOPOSIDE AND PREDNISOLONE (CEP). J.G. Saal, B. Steinke & R.V. Hirschhausen Medizinische Universitätsklinik, Abt. II, 74-Tübingen, FRG

Patients with Hodgkin's disease (HD) who do not respond to COPP/ABV or radiotherapy present serious and still unsolved therapeutic problems. For such cases Santoro and coworkers suggested in 1983 a chemotherapeutic salvage protocol with CCNU, etoposide and predniplusone (CEP). At our institution this regimen was administered to 26 patients with advanced, chemotherapy resistant HD. In a retrospective study the outcome of CEP therapy was analyzed.

Complete remissions (CR) with a median duration of 16+ months were reached in 42% of the patients. Partial remissions (PR) were seen in 19%. Thus even after failure of a number of previous chemotherapeutic and radiotherapeutic approaches, CEP had the potential of inducing long lasting CR. The protocol showed no cross resistance with COPP/ABVD. Its efficacy did not correlate with the extent of Hodgkin's disease at the beginning of CEP treatment. The median duration of CR lasted mainly longer than that achieved with primary or first relapse therapies. Because of its low toxicity outpatient treatment was possible.

In view of the similarity of CEP to the BMT-conditioning protocol with BCNU/etoposide, CEP seems useful to test sensitivity of HD relapses for possible autologous bone marrow transplantation.

T 136 TREATMENT FOR HODGKIN’S DISEASE RELAPSING AFTER CHEMOTHERAPY: A REPORT OF THE FIRST 18 PTS RECEIVING VAPEC-B. A WEEKLY SCHEDULE COMPRISING 5 CYTOTOXIC DRUGS AND PREDNISOLONE WITH PROPHYLACTIC CO-TRIMOXAZOLE AND KETOCONAZOLE. J A Radford, D Crowther. CRC Dept Medical Oncology, Christie Hospital, Manchester, UK

A total of 18 pts (12 male, 6 female; median age 29 yrs) have received VAPEC-B chemotherapy for relapsed HD. Six pts were treated in first relapse, seven pts in second relapse and five pts in third or subsequent relapse. All patients had received at least one previous adjuvant containing regimen and 17 of 18 pts had also received radiotherapy. Initial stage was I, II, III, IV, I, II, III, IV, I, II, III, IV and histology was nodular sclerosing 10 pts, mixed cellular 2 pts, lymphocyte predominance 3 pts and HD unclassified 3 pts.

A median of 8 weeks of VAPEC-B were administered (range 6-11) and 8/18 pts (44%) achieved CR or equivocal CR (minimal residual abnormality on CXR or CT scan but no palpable disease and BM (biochemistry normal). A further 5 pts achieved PR, 3 had stable disease, 1 pt progressed and 1 pt with extensive lung disease died of sepsis after week 3. The CR/equivocal CR rate was the same for pts treated in 2nd or subsequent relapse as for those in 1st relapse (both 4 of 9, 44%) but overall response (CR & PR) was greater in this latter group (6 of 9, 66%) against 3 of 9, 33%). After 4 VAPEC-B, 12 pts proceeded to high dose cyclo and BCNU followed by ABMR. For reasons of massive disease, advanced age, psychological unsuitability or no autologous source of BM, 5 pts did not and of these 2 continue in CR at 12 and 15 mths (1 had nodal disease in 2nd relapse, 1 had nodal disease and heavy BM involvement in 3rd relapse). Apart from 1 septic death after week 3, toxicity has been easily manageable and subjectively the regimen is well tolerated.

We conclude that weekly cytotoxic therapy is effective in relapsed HD and should be considered as a possible alternative to standard three or four weekly treatment in this disease.

VAPEC-B is Adr 35mg/m^2 weeks 1, 3, 5, 7, 9, 11; Cyclo 350mg/m^2 i.v. weeks 1, 3, 5, 7, 9, 11; Etop 100mg/m^2 i.v. given daily for 5 days weeks 3, 7, 11; Vinc 1.4mg/m^2 weeks 2, 4, 6, 8, 10; Bleo 10mg/m^2 i.v. weeks 2, 6, 10 plus prednisolone 30mg p.o. days 1-5, 23mg days 6-11 then tailed to zero, and prophylactic co-trimoxazole 2 tabs 12 hourly and ketoconazole 200mg daily 12 hourly, both for 12 weeks.
T 137  

**ABSTRACTS - Fourth International Conference on Malignant Lymphoma, Lugano**

**T 137  ABDC SALVAGE CHEMOTHERAPY FOR REFRACTORY/RELAPSED HODGKIN'S DISEASE (HD). M. Smith, A. Al-Kaib, C. Dwyer, V. Ratanatharathorn, L. Sensenbrenner. Division of Hematology and Oncology, Wayne State University, Detroit, MI.**

We report the results of salvage treatment with ABDC in 10 patients (pts) with advanced refractory/relapsed HD. The ABDC regimen is based on Rodgers et al (1982 46:2349-55). For continuous infusion (CI) by Hagermeier (personal communication), and consists of doxorubicin 25mg/m² CI daily x 2, DTIC 200 mg/m² CI daily x 5, bleomycin 5 mg/m² IV qd and d5, CCNU 40 mg/m² orally daily I and prednisone 40 mg/m² days 1-5, repeated each 28 days. However, 4 pts did not receive bleomycin due to prior pneumonitis(1) or planned bone marrow transplantation (BMT/3).

At the time of ABHD treatment, the pts had a mean age of 27 (range 13-52); eight were stage IVB and 2 IIIB. All pts had received previous treatment, with the mean number of prior regimens being 3.4 (range 2-6), and all had failed at least MOPP and ABVD type regimens. The mean time from diagnosis to ABHD was 6.2 years (range 9 months-14 years). Three pts had never achieved CR, while 2 had CR<1 year.

Responses included 1 CR (7-4 months off therapy), 6 PR (5 ongoing on therapy, I having a BMT after 2 cycles), 1 with a brief response but then progression of disease before the third cycle could be given, I too early to evaluate, and one with no response. Overall response rate was 71/0 or 70%. Toxidity was primarily bone marrow suppression and mild nausea. Four pts who had been extremely non-compliant with other regimens tolerated ABHD well. One patient died of a dilated cardiomyopathy with onset after the fifth ABDC cycle; she had received prior TNI.

We conclude that ABDC with doxorubicin and DTIC by CI is an active regimen in our heavily pretreated population. It may have a role in reducing tumor burden of HD in preparation for BMT. It may also be a basis for developing more active combination chemotherapy regimens based on CI as second line therapy for HD.

---


Thirty patients with advanced Hodgkin's disease (stages III B to IV) were randomly treated with low-dose nitrocydole (Nature): 5 mg/kg or 4 mg doxorubicin (ADRI); 25 mg/m², on days 1 and 14, to a total of 150, 6 cycles. Clinical and histological characteristics were similar in both regimens. Complete response (CR) was observed in 12 of 15 patients treated with 6 IPI (60%) Similar results were observed in 1 out of 5 patients who were treated with 3 IPI. Side effects were minimal and well tolerated. No cardiotoxicity, assessed by the left radiocathode angiocardiography, was observed with doses between 250 to 420 mg for EPI and 55 to 85 mg for Mx. The median survival time was 11 months, and all the patients remained in CR and, probably they will have long survival, although, the follow-up is short. The results observed with use of these new drugs in the treatment of advanced Hodgkin's disease were similar to the achieved with therapeutic approaches, and we believe that the treatment in question, in a limited number of patients, is accompanied of lesser side effects and the effectiveness of the chemotherapy remain to be useful.

We feel that new programs with these type of therapy will be performed in patients with advanced Hodgkin's disease.

---

**T 139  EARLY DEATH IN HODGKIN'S DISEASE: INDICATOR OF AGGRESSIVE DISEASE? J. N. Burgaño, A. Maland, R. Suen, E. Van Horn. The Methodist Cancer Institute, Amsterdam.**

In the period 1977-1986 333 patients (pts) with previously untreated Hodgkin's disease were treated in our institute. 30 (9%) died within 2 years of diagnosis. It was found that 10 pts (3% of pts) had a progressively course of disease, 8 pts (2.4%) died of complications or cancerous other disease, in 6 pts (2% of pts) relapse after initial remission could not be salvaged and 6 pts (2%) never defined if old age and/or cancerous other disease.

For these pts division over stage and histology was not different from the total group. Despite the cellular type of nodular sclerosis occurred in 5 pts of whom 1 in group A, compared to 10 pts in the total group. In the study group 30% of pts were > 50 yrs, 22% 31-60 yrs, 27% 61-70 yrs and 20% > 70 yrs, compared to 80%, 9%, 7% and 44% for the total group. In the study group 21 pts had concomitant disease. Liver abnormalities were documented in 24/30 pts, 12 had hepato-megaly, 19 had disturbed liver function, 16 had both; however only in 7 pts this might have been considered at 3Y on clinical grounds. In 11 pts liver biopsy was done and 2 only were positive. For comparison all pts > 50 yrs of the total group were studied and 12/38 had liver abnormalities, of which 1 only was interpreted as stage IV. In the 10 pts of gr. A with progressive disease, 6 pts had an E3 of > 50%, compared to 2/30 pts in group A. Only 4 of these pts were > 50 yrs. Dubious liver functions were present in 9, liver biopsy was done in 7 pts and positive only in 2 pts. Concomitant disease was restricted to skin problems in 4 pts.

Conclusion: early death within 2 yr of diagnosis of Hodgkin's disease occurred in 9% of pts, in 3% due to aggressive Hodgkin's disease, in the other due to old age, concomitant disease, or complications.

---

**T 140  INFECTIONS IN PATIENTS WITH NON-HODGKIN LYMPHOMA: REPORT OF 110 EPISODES. G. Todescini, G. Benato, A. Ambrosetti, V. Negri, R. Bonini, E. Benefetti, G. Vincenzi, F. Zanotti and G. Perona. Cattedra di Ematologia, Università di Verona, Italy.**

One hundred and ten infectious episodes in 73 pts (42 males; 31 median age 51 range 10-78) occurred in our Institution. The infection-related death were 12/110 (11%) in 6 more pts (4%) died because of the combined effect of infection and other causes. In 88/110 (80%) cases the infections occurred in pts with lymphoma in progression or in relapse, the remaining 22 episodes occurred at diagnosis or during induction therapy. Before the onset of infection, in 78 episodes the pts received polychemotherapy, in 9 single agent therapy and in 3 surgery. In 1 (alpha 1%) and 1 (beta 1%) in 18 cases the pts had not been previously treated; 4 pts are not evaluable. During the study, the majority of infections were microbiologically or clinically documented, FUD ring 2%. There were 77 bacteremias (Gram-positive 39, Gram-negative 28, polyvalent 10) and 1 Candidaemia; 37 out of these 78 episodes were associated with pneumonia. Pneumonia alone was 11. Overall, pneumonia was then observed in 48/110 (44%) episodes. Other infections were: soft tissue infections (4), gastrointestinal tract infections (2), abscesses (1), chest infection (1), abscesses (1). Infectious deaths were observed in presence of Gram-negative bacteremia (9/28 32%), Gram-positive bacteremia (4/10 40%), polyvalent bacteremia (4/10 40%), pneumonia (1/10 10%), FUD (1/10 10%). During bacteremia, the infectious mortality was three times more frequent when pneumonia was associated.

Conclusions:

1) The infections were often severe (in the majority of cases bacteremia associated pneumonia).
2) The frequency of pneumonia was particularly high, as compared to that commonly observed in other hematologic malignancies.
3) The majority of infections occurred when the lymphoma was in relapse or progression, but the disease status was not important for the outcome of the infectious episode.
4) Pneumonia, persistent neutropenia and age over 50 years seem to be important poor prognostic factor for the outcome of infection.
T 141 SECOND CANCERS AFTER TREATMENT IN PATIENTS WITH Hodgkin’S DISEASE
Sobič V., Bančić B., Ruvičić R., Bošković B., Golubić I., Frič O.
Institute of Oncology and Radiology, Belgrade, Yugoslavia

In the recent 20 years, the survival of patients with Hodgkin’s disease (HD) has increased due to extensive treatment with radiotherapy (RT) and chemotherapy (CT). However, extensive treatment has its price and there is evidence in the literature that modern aggressive treatment may induce severe complications such as secondary cancers (SC). The aim of this study was to compare the risk of SC in two randomized, sequential cohorts of patients with HD of clinical stages I and II that were followed for 5 to 20 years after the end of their initial treatment. From 1970 to 1985 were treated 338 patients with Hodgkin’s disease in clinical stages. All patients were treated with chemotherapy and radiotherapy. Nine secondary tumors have been discovered in this group with varicous localizations in period from 5 to 15 years. Three solid tumors (ST), one non-Hodgkin’s lymphoma and 5 acute leukemias were also discovered. The authors discuss the risk and interval of secondary tumors appearance in relation to applied therapy, age of patient and duration of the remission follow-up.

T 142 TREATMENT INTENSIONS AMONG PRACTISING MEDICAL ONCOLOGISTS AND ONCOLOGICAL SENIOR HOSPITAL STAFF IN SWITZERLAND FOR ELDERLY PATIENTS WITH AGGRESSIVE NON-HODGKIN’S LYMPHOMA. R. Ohlert, Div. of Oncology, Dept of Internal Medicine of the University, Kantonspital, CH-4031 Basel, Switzerland (for the SAKK lymphoma Group)

The treatment of Elderly Patients with advanced aggressive NHL (EPANHL) is a controversial issue. Treatment outcome seems to be related to the thorough application of treatment schedules such as CHOP, and dose reductions or delays are detrimental. Elderly patients (pts) are more susceptible to side effects of aggressive chemotherapy and often handicapped with numerous concomitant internal diseases. Apart from objective contraindications to aggressive therapy, subjective contraindications may prevent the application of potentially curative therapy. In 1989 a questionnaire was sent to all practising medical oncologists (PMO, n=34) and to all known senior hospital staff (SNS, n=36) in the divisions of medical oncology in Switzerland. A detailed therapy schedule for the systemic treatment of EPANHL was asked for, as well as measures in dose or dose intensity. 35 forms were returned (50%), 15 (44%) from PMO and 12 (34%) from SNS, in 8 cases no identification was possible. 12 of the answering doctors documented the following for treatment (34%), 13 a rather more aggressive, second or third generation regimens (37%) and only 9 (26%) a clearly less aggressive schedule, such as CVP or COP. One PMO did not treat EPANHL himself. No difference was seen in PMO and SNS as to the aggressivity of the proposed schedules, 22 (63%) intending to give a fully dosed regimen without delays, 3 a delayed (9%) and 7 a reduced (20%) regimen. However, only 21 (60%) suggested irradiation of bulk disease, whereas 9 (26%) rejected any irradiation therapy. The most chosen regimen was CHOP. The data indicate that treatment of EPANHL may be influenced by personal biases than postulated. To test the real behaviour a prospective and controlled registration of treatment intentions and given treatment in EPANHL is currently under way in Switzerland (SAKK study 39/89).

T 143 IFOSFAMIDE CONTINUOUS INFUSION AND ETOPOSIDE IN THE TREATMENT OF ELDERLY PATIENTS WITH AGGRESSIVE LYMPHOMA. A PHASE II TRIAL. B. Coiffier, S. Demolombe, Y. Baston, J.D. Tignaud, D. Espinoise, P.A. Bryon. Centre Hospitalier Lyon-Sud, Pierre Benite, France.

Ifosfamide (IFM) is an alkylating agent used in salvage regimens in lymphomas. Pharmacokinetics studies showed that its alkylating activity was increased by divided doses or continuous infusion. Its dose-limiting toxicity is urotoxic and could be prevented by the administration of mesna. The better administration scheme is not known for this drug. A potentialisation of its activity in lymphomas has been observed when associated with etoposide. For these reasons we decided to conduct of phase II trial of IFM 1500 mg/m²×d in continuous infusion for 3 days, mesna 500 mg/m²×d×3/d for 4 days, and etoposide 100 mg/m²×d×3/d in one infusion of 3 hours. This treatment was administered every 4 weeks. 16 patients (pts) aged 70 or more presenting an aggressive lymphomas were enrolled in this study either following failure of a previous chemotherapy (9 pts) or due to a contraindication to anthracyclins (7 pts).

11 pts were male and 5 female. Median age was 75 y (70 to 81 y). Performance status ranged from 0 to 3. According to the Working Formulation, histologic types were E: 1 pts, F: 3 pts, G: 6 pts, H: 5 pts, J: 1 pts. At time of treatment, 1 pt had stage III and 15 stage IV.

Toxicity was very mild: 2 pts experience vomiting; out of 65 courses, only 3 episodes of hyperthermia and 2 grade 2 neurotoxicity; one grade 3 thrombocytopenia; one cystitis; 16 pts grade 3 alopecia. 1 pt with myocardial infarction history died suddenly during treatment. 2 had to be hospitalized after courses for toxicity.

Among the 7 pts in first line chemotherapy there were 3 CR, 2 good PR, 1 pr and 1 PR in second line. Among the 6 pts who progressed on-therapy after an anthracycline regimen there was only 1 PR. Overall response rate is 50%. 3 out of the 4 PR pts progressed to 6 months later and 3 out of the 5 CR pts at 4, 6 and 7 months after treatment.

This regimen is active and well tolerated in aged pts but probably not enough active for younger pts.


This is a retrospective evaluation of select treatment given according to stage, histology and performance status to 53 previously untreated pts with NHL aged over 70 years (range 70-92, median age 72 y). Distribution of pts into risk categories of Working Formulation (WF) was as follows: low grade,27 cases; intermediate grade,16 cases; high grade,10 cases. As far as first-line treatment is concerned,10 pts received a single chemotherapeutic agent (SA) and 43 a combination polychemotherapy regimen (Pol-CT) including Adriamycin (Pol-CT + ADM) in 14 of them. The three therapeutic groups were alike with regard to age, sex and clinical stage. However, pts of intermediate-risk high grade categories of WF more frequently were treated with combination Pol-CT (P<0.05). Eleven (20.6%) of 53 evaluable pts obtained CR. No difference emerged among different treatment groups when CR rates were analyzed according to both stage and grade of malignancy. Furthermore, CR was associated with a significant better prognosis (P<0.001).

A higher incidence of significant toxicity was found in pts treated with combination Pol-CT regimens (P<0.005). It should be stressed, however, that the incidence of adverse events is mainly due to an excess of lethal and severe toxicity observed in pts treated with Pol-CT schema not including ADM. Twenty-one of 53 pts included in this study were submitted to second-line treatments. Therefore, a total of 15 pts received SA or we first submitted on-therapy, a total of 30 pts were submitted to Pol-CT without ADM as first or second-line treatment (18 pts received Pol-CT without ADM both as first and second-line therapy whereas a total of 20 pts were received Pol-CT with ADM as first or second-line treatment (1 pt received Pol-CT + ADM both as first and second-line). In the overall group of 50 pts treated with combination Pol-CT regimens a total of 5 (10%) treatment-related deaths could be detected. The incidence of lethal toxicity not being increased by the addition of ADM.

In conclusion, our data suggest that severe and lethal side effects are not associated with Pol-CT regimens. Devised aggressive treatment for elderly pts should be sought.
T 145 NON-HODGKIN'S LYMPHOMA IN THE ELDERLY PATIENT.

A study of 593 consecutive cases aged more than 70.
F. D'Amore for the Danish Lymph-group.

ABSTRACT

Five hundred and ninety-three cases of non-Hodgkin's lymphoma (NHL) in patients aged 70 or older were studied. The representation was 37.9% of all cases (n=1568) of NHL prospectively registered during 6 years in a Danish semi-national lymphoma centre. Localized disease (stage I and II) was found in 45%, disseminated disease (stage III and IV) in 50% while clinical staging was not done in 5% of the patients. Fifty-two % of cases were nodal and 41% extranodal. 7% of cases were insufficiently defined as to the clinical stage. The 4% of all cases that were localized (stage I, or II) were the most frequently involved extranodal sites being the stomach (65 cases). Bone marrow infiltration was present in 134 (23%) cases and mostly associated with plasmacytoid histology. One hundred and seventy-six (32%) patients had low-grade (12% intermediate and 245 (41%) high-grade histology. Diffuse large cell lymphoma was the most common histological subtype. Overall median survival was 2 years. Of the 322 deceased patients 55% were due to lymphoma, 4% to treatment-related causes and 25% to other causes. The cause of death was uncertain in 15% of the cases. Statistically significant adverse influence on survival was seen for age, stage IV and for elevated serum lactate dehydrogenase (LDH), hyperuricemia and hypercalcemia. Serum levels of LDH were elevated in 30% and those of uric acid in 17% while hypercalcemia occurred in 4%. Paraproteinemias, mostly of IgM type, was found in 8%.

T 146 P-ABEC CHEMOTHERAPY IN ELDERLY HIGH-GRADE NON-HODGKIN'S LYMPHOMA (NHL) IN THE ELDERLY.


Biopathology, Ugin, Uhin' La sapiens via Benvendo 8, 60185 Roma, Italy.

A new weekly alternating six drugs chemotherapy regimen (C-flair) was applied to 26 previously untreated high-grade NHL patients (pts) aged <60 yrs starting on October 1985 to August 1989. This schedule consisted of Adriamycin 100mg/m² sq-ad. on day 1, cyclophosphamide 50mg/m² sq/ad. on day 1, vincristine 1.2mg/m² sq/ad. on day 1, bleomycin 5mg/m² sq/ad. on day 1 were administered. The entire treatment schedule was given in 4 repeated cycles. Adverse effects were not severe. Twenty-two of 26 pts had a clinical stage 3 and 24 stage IV. The overall performance status according to WHO criteria was 2 or worse in all pts, a bulky disease in 10 pts. Complete remission (CR) was present in 11 pts, a LDR high levels in 2 pts. A complete response (CR) was obtained in 14/26 pts, partial remission (PR) in 4/30 (13)%. Both CR and PR pts were responders. After a median follow-up of 7 months (range 1-14), 5 pts relapsed at 1,2,3,3,6 months respectively. One patient died in CR for cerebrovascular stroke. Hematological toxicity was moderate in all patients. In particular platelet counts <50x10^9/ml and/or white blood cell counts <5x10^9/ml were not observed. However, for the other toxicities two pts died for infection complications (1 hepatic and 1 pulmonary) and 2 pts had a severe leukopenia (<2x10^9/ml). Neuropathy was observed in 3 pts. The present study was closed. A suitable first line treatment for elderly NHL patients is needed to evaluate the CHOP duration.

T 147 HODGKIN'S DISEASE IN THE ELDERLY.

F. de Reijke, M. Boebel, L. Bosch, J.M. Beemsen. Department of Internal Medicine, Catharina hospital, HS/IEO-comprehensive cancer centre southern, Eindhoven, The Netherlands.

We analysed the influence of age on the prognosis of Hodgkin's disease(ND) in a prospective cohort of 182 patients. Between 1972 and 1983 40 patients(22% aged 50 year or older were diagnosed and treated in,from 1979 cooperating, community hospital in the Southeastern part of The Netherlands. Staging procedures and treatment at that time were not uniform.

Results(table 1): Overall 5- and 10-year survival rates for the whole group were 73% and 55%, resp. Survival curves showed a significant decrease of overall survival after 50 years of age (p<0.001). Male-free survival rates of the old and young patients (p<0.01). 13 patients received incomplete therapy (Chemotherapy only) because of toxicity and only involved field radiotherapy was given to 6 patients. Survival rates were significantly lower for patients over 50years, who had incomplete therapy (p<0.01). Failure to achieve CR occurs mainly in patients with advanced CS (table 2) and incomplete therapy. In this study salvage therapy was equally effective in both groups but the group 50 years included only 5 patients of those achieved 4 another CR Treatment related, which is compatible with the group 50year<28/30 patients(71%) ,7 treatment related.

Table 1: 5-year S 10-year S CR
<50year 142 77% 68% 83%
50year 40 47% 60% 83%
<50year,CR 25 67% 87% 83%
n=number, Survival, CR=complete remission, CT=complete therapy

Table 2: CS1-IIA CstLII-IV
<50year, CR 92% (103/112) 83% (24/29)
50year, CR 65% (17/26) 45% (5/51)

Conclusion: Significant decrease in overall survival above 50 years of age was not significant in long-term survival.

T 148 NON-HODGKIN'S LYMPHOMA (NHL) IN THE ELDERLY: A RETROSPECTIVE STUDY. E. Scheurer, S. Levyraz, J. Bauer, P. Capasso, L. Barret, Centre Fluoridoclinique d'Oncologie, University Hospital, Lausanne, Switzerland.

The elderly comprise a group at highest risk for cancer and represent an increasing challenge for oncologists, mainly because of poor tolerance to potentially aggressive chemotherapy. We reviewed our experience in the treatment of NHL in 57 patients >65 yrs. using data from May 1975 to June 1987. Twenty-one patients (37%) presented with low grade NHL but our study focused on the 36 patients (63%) with intermediate and high grade NHL according to IWF. There were 15 males and 21 females with a median age of 75 yrs old (65-87). Eight patients were more than 80 yrs. Twenty-three had an intermediate grade and 13 a high grade histology. Twenty-four median survival (66%) was observed for a group I and 12 (24%) a stage III IV disease. Nine patients had an extranodal presentation (Tonsil=4, bowel=2, 2: stomach 1, skin 2).

A complete clinical and radiological work-up, with bone marrow biopsy was done in 25 patients (69%). Bone marrow biopsy was omitted in 11 cases (31%) among whom 6 were >80 yrs. Curative treatments were foreseen in 24 patients and palliative ones in 12 patients. Treatment choice was independent of age, performance status or extent of disease. Patients undergoing curative therapy received tailored regimens with anthracyclines (diced doses, less than 6 cycles, or anthracyclines analogues), except for one who received a full dose of CHOP. Overall, 33% patients achieved complete remission, that was obtained in 18/24 (75%) patients treated curatively. The overall actuarial median survival for the whole group was 32 months, with 30% surviving at 5 years. Five patients died in complete remission.

Leucopenia was seen in 15 patients (mean 1.2 G/l (0.2 - 2.9). Infection developed in 9 patients and gastrointestinal bleeding in 2 patients without thrombocytopenia. Heart failure was clearly treatment related. Eleven patients developed WHO grade I peripheral neuropathy related to Vincristine. Toxic death was diagnosed in 4 patients (11%) (1 lymph syndrome, 2 pneumonia, 1 heart failure).

In conclusion, the treatment of the elderly was heterogeneous and based on medical appreciation. Toxicity was severe when aggressive therapy was chosen. Anthracycline regimens showed a treatment response rate similar to that seen in younger patients with a 30% five year survival. In the future, adapted treatment protocols for the elderly should be designed and studied prospectively.
A NEW PERSPECTIVE IN CANCER TREATMENT: NAVALBINE®

Its differences are its potential.

NAVELBINE® (Vinorelbine) is the first semi-synthetic 5’ Nor-Vinca-Alkaloid.

The structural modification of the Catharanthere ring makes its chemically unique.

Because its affinity is greater for mitotic microtubules than for axonal microtubules, it has a selective mechanism of action.

Extensive tissue distribution and high pulmonary concentration are its pharmacokinetic characteristics.

These differences make NAVALBINE®, a spindle poison with great potential expressed by:
- demonstrated efficacy in non small cell lung cancer
- good systemic tolerance
- short-duration leukocytopenia, allowing for weekly dosing
- and most importantly, less neurotoxicity.

Incorporating NAVALBINE® to non small cell lung cancer treatment opens new therapeutic perspectives by offering patients a good quality of life.

PIERRE FABRE ONCOLOGIE.

NAVALBINE® 50 mg and 10 mg are already registered and available in France since September 1989.

FORM AND PRESENTATION: Predicted injectable solution ready for use. * 1 ml vial containing 10 mg of vinorelbine base. 5 ml vial containing 50 mg of vinorelbine base. PHARMACOLOGIC PROPERTIES: NAVALBINE® is an antineoplastic cytostatic of the Vinca-Alkaloids family. The molecular target of its activity is the dynamic equilbrium between tubulin and microtubules. THERAPEUTIC INDICATIONS: non small cell lung cancer. CONTRAINDICATIONS: * Pregnancy. * Breast feeding. * Severe Hepatic Insufficiency. WARNING: NAVALBINE® should only be given intravenously. PRECAUTIONS FOR USE: Treatment should be given under strict hemostatic control (complete blood count, before all injections). In case of granulocytopenia (< 2000/mm³) stop administration until normalization and keep the patient under close surveillance. In case of liver failure the dose should be reduced. Due to the lack of studies concerning renal insufficiency, caution is highly recommended to be taken when used in such patients. Avoid all accidental eye contamination: risk of severe irritation, conjunctival ulceration if the product is injected under pressure. In case of accidental contact, rinse the eye immediately with water or isotonic solution. NAVALBINE® should not be administered at the same time as radiotherapy if it is being given to the liver or surrounding areas. SIDE EFFECTS: hematologic toxicity: * The limiting toxicity is granulocytopenia. * Anemia is frequent but of a moderate intensity. NEUROTOXICITY: * Peripheral: generally limited to the abduction of deep tendinous reflexes. Paraesthesiae are rare. After prolonged treatment, weakness in lower limbs may be observed. * Vegetative: The main symptoms are bowel hypomotility and constipation. Infrequent cases of paralytic ileus have been observed. DIGESTIVE TOXICITY: * Constipation. * Nausea. * Vomiting; severity and incidence are low. VENTRICULAR TOXICITY: NAVALBINE® may bring on dyspnea and bronchial spasms; reactions occur usually a few minutes or a few hours after injection. OTHER SIGNS: * Alopecia (progressive or moderate), jaw pain. All extravasation of the product during intravenous injection can cause local reactions (which may even lead to necrosis). DOSE AND USAGE INSTRUCTIONS: Strictly intravenously. As a single agent the usual dose is 25 to 30 mg/m² given weekly. In polychemotherapy the dose and frequency is controlled by the protocol. The injected dose should be diluted in an isotonic solution (125 ml for example) and administered by an IV perfusion of short duration (15 to 20 min.) Drug administration should be followed by a vein washout using isotonic solution. The rate of administration and dose should be adjusted for patients with granulocytopenia, hepatic or renal insufficiency (see Precautions for Use). OVERDOSE: Appearance of severe granulocytopenia with risk of infection can seriously endanger vital prognosis. STORAGE PRECAUTIONS: This product should be conserved under refrigeration at 4°C (39°F) and should not be exposed to light. This drug has been registered in the complete specialties dictionary. List I (Table A) APMS (1989) 331 904-4 carton containing 10 vials of 10 mg. APMS (1989) 331 845-8 carton containing 10 vials of 50 mg. Accepted by the General Public Administration Department. PIERRE FABRE MEDICAL, 125, rue de la Faisanderie, 75116 Paris. For further medical information write to: Laboratoires Pierre Fabre Oncologie, 192, rue Lecourbe, 75015 Paris or telephone: 45.30.19.79 (Paris, France).
AUTHOR INDEX

Abstract number

Abdyldaev, R.A. ............... T-130
Aiello, A. ....................... P-I/8
Alavaikko, M.J. ............... P-II/4
Anand, S. ....................... T-51
Anderson, H. .................... 13
Anderson, J.R. .................. 16
Andrieu, J.M. .................. P-II/11
Ansell, S.M. .................... P-I/40
Anselmo, A.P. .................. P-II/22
Antimi, M. .................... T-77, T-96
Antonopoulos, M. .............. T-107
Armitage, J. .................. 48, 52
Aviles, A. .................... T-60, T-138
Baglin, T. ................... P-II/32
Balan, M. ..................... T-29
Belanger, C. ............... T-103
Ben-Shahar, M. ............. 77
Benedetti, F. ............... P-II/12
Bennett, M.H. .................. 4
Bernier, M. ......... P-I/15
Bertini, M. ................... T-94
Betta, P.G. ............... P-I/11
Bianco, A.R. .................. T-62
Bocchini, M. ............. P-II/21
Bodis, S. .................. P-II/26
Bonadonna, G. .............. 11
Borisch Chappuis, B. .... T-24
Bosly, A. ..................... P-I/39
Botto, F. ................... T-113
Brada, M. ................. 18
Brice, P. ............. 14, P-II/31
Broder, S. ................... 7
Brons, P.P.T. .............. P-I/6
Bucsky, P. .................. 34
Burgers, J.M.V. .......... 17, P-II/27, P-III/4, T-139
Býlykûnal, E. .............. T-68
Carpe, P. ................... 56
Carella, A.M. .............. P-II/30
Case, D.C. .................. T-92
Child, J.A. .................. T-86
Chisesi, T. ........... P-III/20, P-III/23, T-4, T-45, T-84, T-93
Cogliatti, S.B. ........... 75
Coiffier, B. .............. 53, 82, T-41, T-61, T-143
Comella, P. ................ P-II/20, T-66
Cometti, B. .............. P-III/14
Conroy, T. .................. T-115
Cosset, J.M. .................. 12
Cotter, F.E. ............... 28
Cowan, R.A. ............. 86
Croce, C.M. .................. 9
Crowther, D. .................. 66
D'Agay, M.F. .............. 73, P-I/9

P - Poster Presentation
T - Presentation by Title Only