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MINE REGIMEN IN NON-HODGKIN'S LYMPHOMA (NHL)

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Current treatment programs for NHL are based on both the histopathologic classification and on the stage or extent of the disease. We used MINE regimen containing Mesna (1.3 gr/m2 iv over 8 h on days 1,2,3); Ifosfamide (1.3 gr/m2 iv over 8 h on days 1,2,3); Mitoxantrone (12 mg/m2 iv over 24 h on day 1); Etoposide (100 mg/m2 iv over 1 h on days 1,2,3) as first line treatment for patients with intermediate and high-grade NHL. There were 21 patients in the study group. The mean age was 45.7 year (range 19-65), 18.1% of the patients had ECOG performance status >1, 50.0% had B symptoms, 45.4% had Ann Arbour stage III or IV disease, and 50.0% had bulky disease. 13 (59.1%) patients achieved complete response with a median disease free-survival of 9 months (range 3+ - 16+). Mild myelosupression was observed in all patients which was tolerable except one. In spite of the the high response rates reported with MINE as a salvage-regimen, we did not observe any superiority of this combination to the current therapies as first line treatment of NHL.

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PEG-L-ASPARAGINASE - NEW ANTICANCER AGENT FOR TREATMENT OF RELAPSES OR RESISTANT MALIGNANT NON-HODGKIN'S LYMPHOMA IN ADULTS

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PEG-L-asparaginase (ONCASPAR - ENZON, Inc., USA) is a new anticancer drug with a prolonged action for treatment of Hemoblastosis. OCASPAR is L-asparaginase produced from E.coli and connected with polyethylenglucol (PEG) for prolonged circulation in blood. PEG-L-asparaginase was tested for treatment of 25 patients with relapsed or resistant high-grade Non-Hodgkin's lymphoma: immunoblastic 40%, lymphoblastic 60%, T-cell lymphoma 12% of them. LOP and LOAP schemes were used in which PEG-L-asparaginase was a basic agent: ONCASPAR in dosage increasing from 500 to 2500 IU/m^2 on days 1,15 und 22 and then once in 2 weeks. If the partial remission was not registered to day 15, we added adriamycin 50 mg/m^2 on days 15 and 22 (LOAP).

The patients included 14 males and 11 females; median age was 34 (range 17 - 66). 6 cases were in their first, 5 cases in their second relapse, 4 cases had resistant disease. Efficacy of treatment was 68% (CR 40%, PR 28%). The fact that treatment of the second relapse was as effective as treatment of the first relapse, is very important. Bone marrow leukemisation was highly sensitive.

The tolerance of PEG-L-asparaginase was satisfactory. Side effects on ONCASPAR and L-asparaginase are almost the same. We noticed moderate hepatotoxicity and very rarely allergic reactions, nausea, vomiting and toxic pancreatitis. The grade of toxicity didn't depend on the dosage of ONCASPAR.

The results prove that PEG-L-asparaginase is a very effective new anticancer agent for the treatment of patients with malignant Non-Hodgkin's lymphoma.

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PERIPHERAL T-CELL LYMPHOMA (PTCL): THE MILAN CANCER INSTITUTE EXPERIENCE.

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Retrospective sorting of all cases of PTCL treated and followed at our Instiution identified 57 patients. All histology slides were reviewed and diagnosis formulated according to updated 1988 Kiel classification. Median age was 45 years (range 18-80), with M/F ratio 1.6. Ann Arbor stage was I in15 pts, II in 12, III in 17 and IV in 12. Extranodal disease was present in 26 pts. Twenty pts. had high grade and 37 low-grade PTCL. Stage I-II disease was more common in high-grade PTCL (13/20 cases) while stage III-IV in low-grade PTCL (23/35). All pts except one received systemic treatment with antracycline-containing regimens in most cases (82%), followed by involved field RT in patients with limited stage. After a median follow-up of 58 months, 34 pts. have relapsed and 18 have died of lymphoma. Actuarial 6-yr freedom from progression (FFP) shows a better outcome for pts. with stage I-II disease (57% vs. 24% in stage III-IV, p=.03), with similar overall survival (OS) (62 vs.60%). According to histology, there was a trend towards a poorer outcome for patients with low-grade as opposed to patients with high-grade PTCL (FFP 30 vs 53%, OS 54 vs 74%). This difference between low- and high-grade was more evident for patients with stage I-II disease (FFP 45 vs 68%, OS 49 vs71%) than for patients with stage III-IV disease (FFP 26 vs 21%, OS 55 vs 83%). These observations suggest that low grade PTCL as defined by the Kiel classification shows an aggressive clinical behaviour, with long term success rate in stage I-II disease that is lower than in those with high grade histology. Prospective studies with larger series of patients should focus on better characterizing the clinical course of PTCL and on improving therapeutic strategies, especially for low-grade subgroups.

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OXALIPLATIN (L-OHP®) : A NEW PLATINUM ANALOG : ACTIVE IN REFRACTORY/RELAPSED INTERMEDIATE AND LOW GRADE NON-HODGKIN LYMPHOMA (NHL) : A PHASE I-II STUDY. Gastiaburu J., Brienza S., Rotarski M., Musset M., Di Palma M., Lemonnier M.P., Itzhaki M., Jasmin C. and Misset J.L. - SMST Hôpital Paul Brousse - Villejuif - France.

From 7/88 to 8/92, 22 patients(pts) with refractory or relapsed NHL, non suitable for high dose chemotherapy were treated with single agent L-OHP®, a 3rd generation platinum compound. Patients characteristics : 12 males, 10 females. Median age : 58 yrs (36 - 79), PS (W.H.O.) grade(gr.) 0 = 10 ; gr.1 = 8 ; gr.2 = 3 ; gr.3 = 1. Previous treatment : Refractory : 19 Relapse : 3. Number of prior therapeutic regimens : median : 3 (1-5). 4 pts were previously treated with CDDP, 19pts with Vinca Alcaloids. Prognostic factors : B symptoms in 7/22 pts, LDH >n= 1.5 X N in 4/22 pts, bone marrow infiltration in 14/22 pts Histologic grade : 1/22 pts high gr., 6/22 pts intermediate gr., 15/22 pts low gr. (CLL:3). Treatment : starting dose was 65 mg/s.q.m. then up to 130mg/s.q.m every 3 weeks, (intrapatient dose escalation when toxicity was lower than gr.2). 65-99 mg/s.q.m.: 2 pts., 100-129 mg /s.q.m.: 5 pts.130mg/s.q.m.: 15 pts. 133 cycles were delivered. Median no. of cycles/pt : 4 (1-26). Median total dose : 390mg/s.q.m (100-3290). Results: Major responses were observed at all dose levels. Overall response (CR+PR) : 9/22 pts (41%). CR: 2/22 pts (both low gr.), PR: 7/22 pts (4/intermediate gr., 3/low gr.). Response duration: Median : 14 mos.(3-40) Progression free survival : 12 months (median). No responses were seen in CLL nor in the high grade NHL pt. PRs were observed in 3/4 pts with primary gastro-intestinal NHL and in 1/4 pts pretreated with CDDP. Toxicity (W.H.O.): gr 3 : neurologic : reversible dysesthesia in 4/133 cycles, gr. 3-4 : hematologic : Leucopenia, thrombocytopenia in 3/133 cycles. 1 pt presented a reversible anaphylactoid reaction, 1 pt refused to continue the treatment Conclusion : L-OHP® is an active agent in relapsed/refractory intermediate and low gr. NHL. Its safety profile (devoid of renal toxicity and minimal hematologic toxicity) makes of L-OHP® a good therapeutic alternative in heavily pretreated patients and a potential compound for first line combination chemotherapy.

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MIM (MITOXANTRONE, IFOSFAMIDE, METHOTREXATE) SALVAGE CHEMOTHERAPY FOR RESISTANT/RELAPSED INTERMEDIATE GRADE NHL

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Nineteen pts (M/F=9/10; median age=61 yrs, range,20-69; Resistant=2, Relapsed=17) affected by intermediate grade NHL according to W.F. (E=5,F=10,G=3) received a median (range,3-6) of 6 cycles of MIM combination chemotherapy : Mitoxantrone 12 mg/m^2 i.v. day 1, Ifosfamide 1 g/m^2 i.v. days 1-5 plus MESNA 20% of IFO dose delivered i.v. immediately before, 4 and 8 hours after each IFO dose, Methotrexate 30 mg/m^2 i.v. day 3. Each cycle was repeated every 21 days. Six (32%; 95% C.I.13-57%) pts attained a CR, 5(26%) a PR, 3(16%) a MR, giving 58% of major responses. Five (26%) pts had progressive disease and died within a median interval of 7(range,5-13) mos. The projected OS after 5-22(median,9) mos was 21%, with a difference (p<0.001) between pts with abnormal (n=9) and those with normal (n=10) LDH values. Median duration of TTF (Time to Treatment Failure) of CRs was 9.5+ (range,6-21+) mos. Toxicity included grade 1-3 alopecia (89%), vomiting (74%) and leukopenia (54%) and grade 2 hematuria (5%).

The CR rate, overall survival and response duration of MIM are comparable to other previous salvage protocols for resistant/relapsed intermediate grade NHL. Likewise in other studies, present results confirm the prognostic relevance of LDH and the need for further alternative therapeutic approaches.

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TREATMENT OF LOW-GRADE NON-HODGKIN'S LYMPHOMAS (NHL) WITH CVP ± INTERFERON ALFA-2B (IFN). A MULTICENTER RANDOMIZED PROSPECTIVE TRIAL. PRELIMINARY RESULTS.

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OBJECTIVE: to determine the ability of IFN to increase the complete response rate and survival of patients with low-grade NHL treated with CVP.

PATIENTS AND METHODS: From february 1990 to August 1992, 62 patients with low-grade NHL who had not received previous chemotherapy or radiotherapy were included in the study. There were 38 males and 24 females, with a median age of 62 years (20-79). Stages: I and II 17.8%, III 8% and IV 74.2%. Fifty-eight percent of the patients had bulky nodal or extranodal disease and 14% had and elevated serum LDH.

CVP chemotherapy was given every 21-28 days up to the maximal response. Randomisation was made with regard to IFN, 3MU/m2 subcutaneous three times per week, 36 doses. Radiotherapy was administered for bulky or residual disease. Afterwards, a second randomisation determined if the patient should receive maintenance IFN.

RESULTS: (first randomisation) 32 patients received IFN (group A) and 30 did not(group B). There were not significant differences between the groups with regard to diagnosis, stage, presence of bulky disease, LDH and age.

	GLOBAL	GROUP A	GROUP B	
CR and good PR	31(50.1%)	19(59.4%)	12(40%)	NS
PR	6(9.7%)	3(9.4%)	3(10%)	
Minimal response/NR	7(11.3%)	3(9.4%)	4(13.3%)	NS
Non evaluable	18(29.1%)	7(21.9%)	11(36.6%)	NS

Toxicity: hematologic toxicity appeared in 175 courses (65.8%), 154 in group A and 84 in group B (p=0.001): there were 22 episodes of grade IV hematologic toxicity (12 in group A and 10 in group B). Twenty-eight patients in group A had flu-like symptoms.

CONCLUSION: there seems to be a higher percentage of responses in the group treated with IFN, although the difference was not significant. The global toxicity was also greater in this group, but not the severe toxicity.