	New Pts (24)	Previous treatment (49)	P value
Response			
CR	13 (55%)	11 (23%)	0.007
PR	9 (37%)	20 (40%)	NS
NR	2 (8%)	15 (31%)	0.03
Died	0 (0%)	3 (6%)	
Engraftment			
Pits 25 × 10^9/l	14 days	17 days	0.004
Neuts 1000/L	24 days	34 days	0.002
Inf start (Med)	55 days	68 days	0.017

The overall survival by the Kaplan Meier estimate at 2 years is 79.3% with a median follow up of 7.75 months and the progression free survival is 58% in the whole group of 73 patients. Interferon (inf) maintenance was started at a median of 61 days in 58/73 patients. We therefore conclude that the previously untreated group is a better risk group with respect to achieving remission as well as rapid engraftment. Inf was also started earlier in the untreated group. Longer follow up will be required however to comment on the efficacy of PBSCT. A CR rate of 55% in previously untreated patients is lower than our previously reported CR rate with ABMT in a comparable group of patients and the possibility of contamination of the stem cell grafts with myeloma should be borne in mind.

815 PUBLICATION

CA-125 SERUM LEVELS SIGNIFICANTLY CORRELATE WITH PROBABILITY OF RESPONSE IN MALIGNANT LYMPHOMAS

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Aim: to determine whether CA-125 serum levels correlate with disease extension and prognosis in patients with malignant lymphoma.

Methods: Ca-125 serum levels were assessed by using the OC 125 monoclonal antibody before treatment in 53 consecutive patients with malignant lymphoma (41 NHL/12 HD) and no sign of concomitant chronic hepatic disease.

Results: Increased serum levels (> 30 IU/ML) were observed in 27/53 (51%) pts. A significant difference between NHL (22/41) and HD (5/12) was not found. To date, 42 pts. are evaluable for response after the third cycle of chemotherapy. Basal abnormal CA-125 serum levels were associated with a significantly lower major response rate (14/22 vs 19/20; $P = 0.015$). At multivariate logistic analysis, presence of extranodal involvement was the only independent variable predictive of response. A further statistical estimation was made by considering a different cut-off for CA-125 (> 100 vs ⩽ 100). Only 2 of the 8 pts. with > 100 IU/ml CA-125 serum levels showed major responses, as compared to 31/34 responses in the other group ($P = 0.0004$). At logistic analysis CA-125 serum level > 100 IU/ml was the only parameter which significantly correlated with a lower response-rate ($P = 0.03$).

Conclusions: abnormal CA-125 serum levels are present in a significant rate of patients with malignant lymphoma. Our preliminary results show that very high serum levels (>100 IU/ml) correlate with a lower probability of response.

816 PUBLICATION

DEVELOPMENT OF AN ACTIVE CHOP-MODIFIED REGIMEN WHICH ALLOWS MORE CONTINUOUS AND BETTER TOLERATED TREATMENT FOR DIFFUSE AGGRESSIVE NON-HODGKIN'S LYMPHOMAS (NHL)

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A CHOP-variant regimen was developed in order to allow administration of full-doses therapy with reduced gastrointestinal and neurologic toxicity. The traditional CHOP regimen was modified as follows. Adriamycin 25 mg/m^2 iv day 1 and day 8, Cyclophosphamide 500 mg/m^2 iv day 1 and day 8, Vincristine 1.2 mg/m^2 iv day 1 and day 8, Prednison 50 mg/m^2 po days 1–8. Vincristine doses did not exceed 2.0 mg. The regimen was repeated every 21 days for 6–8 cycles. This schedule, allowing a more continuous treatment, would also adopt some of the basic concepts of the 2nd and 3rd generation regimens. Between March 1989 and March 1995 42 patients (age 25–84 yr) with stage II–IV diffuse aggressive NHL (Working Formulation F, G, H) were treated with acceptable toxicity. Most patients had grade 2 leukopenia and/or thrombocytopenia. No platelets transfusions were needed and the use of growth factors (G or GM-CSF) was not required. No life-threatening infections and no toxic deaths were observed. The regimen was safely administered also in elderly patients (17 patients had > 70 years). The large majority of patients experienced only mild nausea and vomiting. All patients had grade 3 alopecia.

The overall response rate was 85% (56% CR and 29% PR). Actuarial 3-years failure free survival is approx. 45%. These results appear to superimpose those achieved in the SWOG/ECOG trial (Fisher *et al.* NEJM, 1993).

This regimen therefore represents a CHOP variant that retains efficacy and appears easier to be administered especially in elderly patients.

Radiobiology

817 ORAL

TIME COURSE OF RADIATION-INDUCED APOPTOSIS IN THE ADULT RAT SPINAL CORD

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Radiation-induced apoptosis has been reported in thymic, lymphoid and hematopoietic cells but is infrequently documented in other adult mammalian cell types. In this study, we examined the time course of radiation-induced apoptosis in the adult cervical rat spinal cord following a single dose of 8 or 25 Gy. Apoptosis was assessed by morphological criteria under light and electron microscopy, and immunohistochemically in-situ using ApopTag to detect 3'-OH ends of DNA fragments. Little evidence of apoptosis (0.3 ± 0.3 apoptotic nuclei/spinal cord section) was observed in control un-irradiated spinal cord. A significant increase in the number of apoptotic cells was seen at 4 hr, the number peaked at 8 hr (53.7 ± 3.5 per spinal cord section after 8 Gy, and 60.7 ± 8.7 after 22 Gy) and returned to the baseline level by 24 h. A dose of 22 Gy induced apoptosis than 8 Gy at 4, 6, 10 and 12 h ($P < 0.006$), but not at 8 h. More apoptosis was observed in white matter (79 ± 3%) than in gray matter (21 ± 3%). All the apoptotic cells were observed in GFAP negative glial cells and none in vascular endothelial cells and neurons. We conclude that apoptosis in glial cells may represent a biologically relevant mechanism of radiation induced cell kill in the central nervous system. (Supported by NCIC.)

818 ORAL

RELATIONSHIP BETWEEN P53 CONSTITUTIVE/INDUCED LEVELS AND CELLULAR RESPONSE TO RADIATION

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The inhibition of replicative DNA synthesis, in which p53 has a pivotal role, is an important component of the cellular response to radiation-induced DNA damage. In this study we have examined the relationship between p53 levels before and after irradiation, radiation-induced cell cycle delays and radiosensitivity in a panel of 8 human tumour cell lines.

The cell lines differed widely in their clonogenic survival after radiation, (SF2 = 0.18–0.82). Constitutive p53 protein levels varied from 2.2 ± 0.4 to 6.3 ± 0.3 OD units per 10^6 cells. p53 after irradiation (6 Gy) also varied among the cell lines, ranging from no induction to a 1.6 fold increase in p53 levels 4 hours after treatment.