the mediastinum. Abdominal involvement precedes upward spread via the pulmonary hili and upper mediastinum on the left side or on both sides to the cervical or axillary or inguinal nodes.

801 POSTER

SECOND AUTOGRAFTS FOR RELAPSED MYELOMA

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Forty-four pts (34–64 y, med 47.5) underwent second autografts for relapsed myeloma 10–99 mo (med 33.5) after the first. All received high-dose melphalan and BM (43 auto, 1 twin) the first time. 30 received high-dose melphalan, 10 busulfan, and 4 TBI for the second. The source of cells was BM (29 auto, 1 twin) or blood stem cells (n = 14). At the time of the second transplant, 2 pts were in CR, 21 in PR, and 21 had progressive disease. Hematologic recovery was complete in all pts after the first transplant, but not after the second. 12 pts died of toxicity at 0.5–5 mo (med 1). 16 died of progressive disease or toxicity of further therapy 2–54 mo (med 16) later. 10 pts attained CR after transplant. The probability of progression-free survival at 3 years is 8.9% (95% CI: 1.8–23.5%). 14 pts were started on IFN-α 1.5–9 mo (median 2.5) after the second transplant before any evidence of disease progression. 16 pts, 12 on IFN-α, are alive 1.5–66 mo (med 10.5) after the second transplant: 2 in continuous CR, 7 in stable PR, and 7 with progressive disease. The overall survival of this group was not different from a group of 60 relapsed patients who did not undergo repeat transplants. We conclude that although repeat autografts are feasible in relapsed myeloma, it is difficult to show an improvement in survival and the exact place of second transplants remains to be defined.

802 POSTER

DOSE INTENSITY (DI) CHEMOTHERAPY IMPROVES DISEASE FREE SURVIVAL IN ELDERLY AGGRESSIVE NON-HODGKIN'S LYMPHOMA (NHL) PATIENTS TREATED WITH CONVENTIONAL CHOP

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M.D. Instituto de Enfermedades Neoplásicas Lima, Perú 1995

Aggressive NHL in elderly pts remains a problem when are treated with suboptimal chemotherapy dosage; however the exact role of CHOP dose intensity in the outcome of these pts. has not been fully addressed.

Between 1982 and 1993, 284 pts with intermediate and inmunoblastic NHL, older than 60 years old were admitted to receive conventional CHOP for 6 courses or until progression; 171/284 were evaluable for response and toxicity.

The F/M ratio was 1:1.25 with a median age of 69 years (61–84). The histology was WF:G 95/171, WF:H 31/171 and WF:E 20/171. According to the International Index 59/171 (34%) were Low Risk; 64/171 (37%) Low-Intermediate, 34/171 (20%) High-Intermediate and 14/171 (8%) High risk group. There were 10/171 toxicity-related deaths and five deaths due to disease progression (5) during the treatment. Sixty-two percent of the pts. (107/171) achieved complete response (CR).

All patients were stratified in two groups according to a Relative dose intensity RDI (mg/m^2/week) in two groups: A) $\geq$ 80% and B) $\leq$80%. No CR rates differences were noted between two groups. With a median follow up of 30 months, the two-year disease free survival (DFS) was similar in two groups, except for the low intermediate risk in favor of the high RDI group (81% vs 45%, $P = 0.002$). A benefit in the 5 year-overall survival (DS) was also observed in both intermediate risk groups (69% vs 30% and 44% vs 0%, $P = 0.002$). These data suggest a survival benefit in at least two subsets of elderly NHL pts who received $\geq$ 80% R.D.I. of CHOP, showing the advantage of the DI concept in elderly LNH pts.

803 POSTER

RADIOTHERAPY SALVAGE FOR HODGKIN'S DISEASE AFTER CHEMOTHERAPY FAILURE

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A retrospective study was performed at the PMCI to assess the effectiveness of radiotherapy (RT) as sole salvage treatment for relapsed Hodgkin's disease (HD). Between 1978 and 1992, 52 patients with relapsed/ refractory HD following chemotherapy (CT) received RT with curative intent. Patient characteristics at diagnosis: median age 26, with 32% > 40 years old; M/F 31/21; stage I-4,II-16, III-25, IV-7. Initial CT was MOPP- 31 patients, ABVD-1, both-16. A median 6 cycles of CT was given per regimen. Prior to salvage RT, 26/52 patients had received both MOPP and ABVD, either as sequential regimens, or as alternating or hybrid protocols. The response to initial CT was: CR-30, PR/SD-18, PD-4. Duration of initial CR was < 12 months in 8/30 patients. Salvage treatment consisted of radiotherapy to all known areas of disease. Doses ranged from 3600–4000 cGy. Twenty three patients (45%) achieved CR. With a median follow-up of 70 months (range 4.8–166), actuarial median failure free survival (FFS) and overall survival (OS) are 22 months and 83 months respectively. Actuarial 5 year FFS and OS are 26% and 57% respectively. Patients with CR duration >12 months following initial CT, only one CT regimen prior to salvage RT, and anatomically limited relapse had a significantly longer FFS. These factors, and age <40 were associated with significantly longer OS. Only 6% of patients failed solely in the irradiated volume as first site of relapse. Salvage RT was well tolerated and resulted in no treatment-related deaths. RT is of benefit in selected patients, and should be considered as a treatment option for patients with HD who fail CT.

804 POSTER

EPSTEIN-BARR VIRUS AND HODGKIN'S DISEASE: COMPARISON BETWEEN ALGERIAN AND FRENCH PATIENTS

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The prevalence of Epstein-Barr virus (EBV) markers in nodal lesions from Algerians (Al) patients (n = 68) was compared to French (Fr) patients (Pts) (n = 21) with Hodgkin's disease. Initial characteristics were: males Fr 57%, Al 53%; median age Fr 29, Al 25; histologic subtypes: lymphocytic predominance (LP) Fr 1, Al 3; nodular sclerosis (NS) Fr 16, Al 33; mixed cellularity (MC) Fr 4, Al 30; lymphocytic depletion (LD) Al 2.

The latent membrane protein (LMP) expression was founded in Reed-Sternberg cells (RSC) in 26 cases Al (1 PL, 8 NS, 17 MC) and 4 Fr (2 NS, 2 MC). All cases LMP-positive were also by DNA or RNA *in situ* hybridization (ISH). ISH was positive in RSC of 29% of Fr and 66% of Al Pts ($P < 0.02$); the positivity was more frequent in MC (80%) than in other histologic types (39%). EBV genome was detected by PCR on DNA in 84% of Fr and 95% of Al patients (100% of MC and 86% of other histologic types).

More pronounced ISH positivity in Al young adult cases ($P < 0.05$) can result from the age at primary EBV infection, which occurs earlier in Algeria than in France.

805 POSTER

VINCRISTINE, ETOPOSIDE, MITOXANTRONE AND PREDNISONE (VEMP) AS FIRST-LINE CHEMOTHERAPY FOR HODGKIN'S DISEASE (HD)

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Etoposide and mitoxantrone were combined with vinca alkaloid and steroid in order to evaluate the activity of a new combination, VEMP, whilst avoiding the long term complications related to MOPP and ABVD. 30 consecutive patients (pts) with *de novo* HD were treated between Jan. 1992 and Dec. 1994. 21 were males, median age was 34 years (range 18–67). 3 patients were HIV+. 18 had nodular sclerosis, 8 mixed cellularity, 3 lymphocytic predominance, 1 lymphocyte depletion. 2 pts were IA, 6 IIA, 3 IIB, 5 IIIA, 3 IIIB, 2 IVA, 9 IVB. 4 pts had lung involvement, 2 bone marrow, 1 liver, 1 bone, 3 both liver and bone marrow. VEMP was given on a 21-day (D) cycle basis for a median of 6 courses as follows: vincristine 1.4 mg/m^2 iv D1 and 8, etoposide 100 mg/m^2 iv D1 to 4, mitoxantrone 10 mg/m^2 D1 and prednisone 100 mg po D1 to 5. Toxicity data are available for 25 pts. 6 pts had grade (G) 4 WHO leucopenia, 18 G2, 2 G1. 1 pt had G4 infection, 2 G2, 1 G1. 1 pt had G4 thrombocytopenia, 7 G1. Peripheral neuropathy G1 occurred in 10 pts, G2 in 6. 1 pt had cutaneous erythema, 1 toxic hepatitis, 1 myocardial infarction, 1 fatigue. Response rate was 100% with 42% complete remission (CR), 20% CR unconfirmed (CRu) and 38%

partial remission (PR). 12 pts received additional radiation therapy and 3 pts high dose chemotherapy with peripheral stem cell rescue in first complete remission. 1 HIV+ pt relapsed at 6 months and died. 4 pts (2 HIV+) progressed at 3, 4, 6 and 9 months and died. Probability of survival in remission is 88% (95% CI 56–97%) at 18 months: (excluding the 3 HIV patients). VEMP is well tolerated and is highly active in most HD. VEMP can be combined with radiation therapy. VEMP can also be used as an induction regimen in selected cases proceeding immediately to high dose chemotherapy. VEMP is devoid of pulmonary toxicity. Despite a short follow-up, VEMP should not be as leukemogenic as the alkylating agent containing regimen and should neither sterilize men nor advance menopause in women.

806 PUBLICATION

PRIMING FOR KILLING: CAN THE ASSOCIATION GM-CSF-CYTARABINE HAVE ANY ROLE IN THE TREATMENT OF CHRONIC MYELOGENOUS LEUKEMIA (CML)?

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Except for bone marrow (BM) transplant, current therapies fail to cure CML because Ph'clone cannot be eradicated. *In vitro*, exposing blast-crisis CML blasts to CM-CSF results in a three fold increment of cells in S phase and cell killing is 34% higher when GM-CSF+cytabarine are added simultaneously.

This *in vitro* experience deals with the likelihood of priming CML BM cultures with GM-CSF followed by exposure to Cytarabine to evaluate Ph'clone depletion. The BMs of 12 CML pts (3 newly diagnosed, 6 chronic phase, 3 hematological/cytogenetic complete remission) were cultured during the 24 hrs as follows: 1. controls; 2: GM-CSF (Leukomax, Schering Plough) 0.2 μg/ml; 3. Cytarabine (Ara-C, Rontag) 0.1 μg/ml 6 hrs before harvesting; 4. GM-CSF + cytarabine (as in 2 and 3). Colchicine 0.1 μg/ml was added 1 hr before harvesting. Mitotic index (MI) was expressed as X ± SE for all cultures (Table 1).

Table 1: Mitotic index mean values according to cultures:

Culture	MI (X ± SE)	
1.Controls	4.50 ± 120*	*$P < 0.05$
2.GM-CSF	6.75 ± 1.80*$^{\approx}$	
3.Cytarabine	3.00 ± 0.78	
4. GM-CSF + Cytabarine	3.50 ± 0.77	*$P < 0.01$

According to these data, MI in CML BMs exposed to GM-CSF. Is higher than MI of controls (*$P < 0.05$), and is lower in BMs exposed to GM-CSF and treated with Cytarabine 6 hrs before harvesting compared to BMs only exposed to GM-CSF ($P < 0.01$). *In vitro*, more Ph' + CML cells can be killed with cyterabine in BMs previously exposed to GM-CSF. Could this experience be useful to develop new therapeutic strategies for Ph' + CML pts?

807 PUBLICATION

COMBINATION THERAPY WITH CYTOSTATIC DRUGS AND A POLYENZYME PREPARATION DECREASES CONCENTRATION OF SOLUBLE TUMOR NECROSIS FACTOR RECEPTORS P55 AND P75 IN SERUM OF PATIENTS WITH MULTIPLE MYELOMA

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Conventional chemotherapy with drug combinations is still the preferred treatment for multiple myeloma. Immuno-chemotherapy with Wobe-Mugos (a polyenzyme preparation) and MOCCA/VMPC of MM patients results in a prolongation of clinical remission and a significant prolongation of survival time in comparison to MM patients who received chemotherapy only (Sakalova and Stauder *et al.* in prep.).

In the present study we measured the serum levels of β2microglobulin (β2M) and of soluble tumor necrosis factor receptors (sTNF-R: p55 and p75) in serum of 169 patients to determine their value as a monitor of diseases status in untreated, chemotherapy treated and immuno-chemotherapy treated MM patients. Serum levels of p55 and p75 as well as β2M were elevated in parallel with the clinical stage in untreated patients. sTNF-R and β2 M correlate (β2m/p55: 0.7162 $P < 0.0001$; β2M/p75: 0.7221 $P < 0.0001$—Spearman correlation coefficients). The mean levels of p55 receptors (control:2339 pg/ml) were increased to 4866 ± 2067 pg/ml ($P < 0.0001$ v normal) in stage II and to 8196 ± 4185 ($P < 0.0001$ v normal) in stage III. The mean levels (control: 3542 pg/ml) of p75 were increased to 6248 ± 2278 ($P < 0.0001$ v normal) in stage II and to 13873 ± 6229 ($P < 0.0001$ v control) in stage III.

Immuno-chemotherapy significantly reduced serum levels of p55, p75 and β2M in stages I and II in comparison to chemotherapy alone (p55: 2970 ± 1095 $P < 0.01$ v. chemotherapy p75: ± 4345 ± 1497 $P < 0.05$ v. chemotherapy—stage II).

In stage III the serum concentrations of p55 and p75 were reduced by chemotherapy (p55: $P < 0.05$; p75: $P < 0.02$ v. untreated stage III) but to a higher degree by Immuno-chemotherapy (p55:$P < 0.001$; p75:$P < 0.0001$ v. untreated stage III).

Our results suggest that p55 and p75 concentrations in serum of MM patients correlate well with β2M and may be potential markers for both disease progression and response to therapy.

808 PUBLICATION

ABVD OR EBVD AS FIRST LINE CHEMOTHERAPY IN HODGKIN'S DISEASE (HD)

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Forty consecutive patients with HD were treated with ABVD or EBVD (doxorubicin 25 mg/m^2 or 4-epi-doxorubicin 37.5 mg/m^2, bleomycin 10 mg/m^2, vinblastine 6 mg/m^2 and dacarbazine 375 mg/m^2 day 1 and 14 every 28 days). Patients (pts) obtaining a complete remisión (CR) after 4 cycles received up to 8 cycles, and pts obtaining a partial remission (PR) received up to 10 cycles. Two pts did not respond after 4 cycles and received a second line regimen.

Twenty-two pts were male and 18 female. Median age was 36 years (13–77). 56% had nodular sclerosis, 19% mixed cellularity, 14% lymphocyte depletion and 11% lymphocyte predominance. Staging showed IE-A to III-A: 20 pts, III-B to IV-A, B: 20 pts. 12 received ABVD or EBVD after radiotherapy (RT) failure.

With 4 cycles of CT 75% of pts achieved a CR (67% ABVD, 82% EBVD), this rate was increased to 95% (89% ABVD, 100% EBVD) after 8 or 10 cycles. With a median follow-up of 81 m (21–141) the freedom for progression (FFP) survival at 12 years is 86%.

ABVD (or EBVD) is as or perhaps more effective and less toxic than MOPP as first line therapy in HD. In our series previous RT did not influence the results.

809 PUBLICATION

PRIMARY ORBITAL AND ADNEXAL NON-HODGKIN LYMPHOMA (POAL): A SINGLE CENTRE STUDY OF 20 CASES

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The clinical behaviour, the prognosis and the treatment of the POAL are subject to some controversies. We define POAL as a localised lymphoma in the orbital and adnexal structures (I E), lasting at least one month after a diagnosis and complete staging procedure used in NHL. We studied 20 patients (pts) with lymphoproliferative lesions, from 1974 to 1994, finding 14 with POAL (orbit 6; lachrymal gland 4; conjunctive 2; eyelids 2), 1 patient had bilateral lesions. For the recent pts we studied the immunophenotype the beta2 microglobulin, LDH, abdominal ecography or CT, orbital CT or MRI. We applied the up-dated Kiel Classification (1 high grade and 13 low grade, most of them lymphoplasmocytic or diffuse centrocytic type cells). They was 2.5% of our NHL. The median age was 68 years (range 16–87) and there were a female predominance (M/F 1:2.5). No patients had monoclonal gammopathy or immune disorder. The initial presentation was ocular tumour or proptosis in all pts.

Treatment was: (1) surgery 2 (1 relapsed, 1 maintained CR); (2) radiotherapy (RT): 9 (7 of them with doses of 30–40 Gy, with the following late complications of RT (EORTC): G0 = 6, G1 = 3, G2 = 1; all pts but one attained CR; (3) RT plus chemotherapy (CH):3.

Four of the 6 orbital lesions had elapsed (66.6%); 4 of them were treated only with RT. The 2 pts with conjunctive lesions have been treated with RT; 1 is in CR 24 months (m.) after treatment.

Three of the 4 pts with lachrymal lymphoma had a disease free survival (DFS) of 5, 12 and 32 m; one of them was treated only with surgery; in this group was the only pt with high grade lymphoma treated with