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

success with RT only. One pt that refused further RT, died, with relapse, after radical surgical excision. The 2 pts with eyelid lesions were in DFS for more than 13 months. They were treated with RT. CH, as initial treatment after RT, has been done in one of our last pts that had lachrymal gland lymphoma because the MR after RT showed perhaps residual disease.

We conclude that surgery, if done, must always be followed by local RT. Local RT provides a good and almost permanent local control of the disease. Doses of 30–35 Gy controlled our low grade lymphomas with no late complications, when good shielding of the lens of the eye is possible. The prognosis for pts with small-cell lymphoma in the ocular adnexa seems difficult to predict, mainly for the orbit.

The role of adjuvant Ch with CVP or CHOP-like regimen, after local RT need to be investigated for pts with bad prognosis factors as retro-orbital lymphoma, bulky tumour and high grade malignancy histology.

810 PUBLICATION

DEXAMETHASONE, ETOPOSIDE, IFOSFAMIDE AND CISPLATIN AS SECOND-LINE CHEMOTHERAPY IN INTERMEDIATE OR HIGH GRADE NON-HODGKIN'S LYMPHOMA

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The combination of dexamethasone, etoposide (VP-16), ifosfamide and cisplatin (DVIP) was evaluated as a second line after adriamycin-containing combinations in intermediate or high grade non-Hodgkin's lymphoma (NHL). 39 patients (pts) (median age 68 years) entered the study. Objective responses were seen in 29 pts (74%) and included complete response (CR) in 14 (36%). Median duration of CR was 12 months (mos) and that of partial response was 3.5 mos. 13/25 (52%) pts who responded with CR to adriamycin-based combinations responded with CR to DVIP (vs 1/14 who failed to respond with CR). Durable remissions (24 ± 57+ mos) continue in 4 pts who responded with CR to front-line therapy. Main toxicity was myelosuppression. Median WBC nadir was 1100/mm^3 and median platelets nadir was 66,000/mm^3. There was no treatment-related mortality. We conclude that DVIP is an effective second line in histologically aggressive NHL, associated with acceptable toxicity, and has a curative potential in pts with relapsing disease.

811 PUBLICATION

SEQUENTIAL HIGH-DOSE THERAPY OF ADULT ACUTE LYMPHOBLASTIC LEUKEMIA

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We have developed a sequential treatment strategy for intensive post-remission management of adult ALL. Patients ⩾ 15 y in CR1 receive melphalan (200 mg/m^2) followed by peripheral blood stem cells mobilized with G-CSF (Neupogen, Amgen). On hematologic recovery, 2-year maintenance chemotherapy with daily 6-MP and weekly MTX is started. In case of relapse, an allograft is performed with etoposide (60 mg/kg) and TBI (1050 cGy) in CR2. 13 patients (6 M, 7 F; 32 y, 19–58) underwent PBSCT between 1/93 and 6/94. Toxicity of PBSCT was minimal with 2 d (0–5) of fever and 18 d (17–23) in hospital. Neutrophils reached 0.5 × 10^9/L on d 15 (12–27), and platelets 50 × 10^9/L on d 16 (12–77). 6-MP was started in 12 patients on day 32 (15–132). The median dose of 6-MP tolerated, averaged over the entire post-PBSCT follow-up period, was 45.4 mg/m^2/d. 10 patients (76.9%) are alive and well on chemotherapy in first CR at 18 mo (8–26). Of 3 patients relapsing at 4–7 mo, 2 are alive and well 7 and 8 mo after BMT from HLA-matched siblings in CR2. The third declined ABMT in CR2 and died of relapsed disease. We conclude that melphalan-PBSCT and maintenance chemotherapy have minimal toxicity and significant anti-leukemic activity in adult ALL, and patients relapsing after PBSCT can be salvaged by a second BMT with acceptable toxicity.

812 PUBLICATION

NON-HODGKIN'S LYMPHOMA OF INTERMEDIATE DEGREE. 13-YEAR FOLLOW-UP OF 89 PATIENTS TREATED WITH CHOP

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From January 1981 to January 1993, 89 patients with non-Hodgkin's lymphoma of intermediate degree were treated with 6 courses of CHOP chemotherapy. The median age of these patients was 57 years and male/female ratio was 1.53. 8 of the patients were large-cell follicular lymphomas, 33 diffuse small-cell, 25 diffuse mixed and 22 diffuse large-cell. The lymphatic areas most affected were: para-aortic 16%, left cervical 14%, right cervical 13% and mesenteric 11%. The number of lymphatic areas affected were: 1 (31%) 2 (29%) and 3 (16%). 24% of the patients were Stage I, 19% Stage II, 17% Stage III and 28% Stage IV. Bulky disease was present in 19% of the patients. The extra-nodal localizations most frequently affected were: Waldeyer ring 22%, followed by Spleen, Liver and Bone. Marrow with the percentage in each been 11%. 70% CR was achieved and 12% PR. More than 50% of the patients have had more than an 8-year follow-up and the disease-free survival rate at 13 years is 32%. A multivariant analysis, according to histological degree, primary localization and stage, will be presented.

813 PUBLICATION

TREATMENT OF PH+ CHRONIC MYELOGENOUS LEUKEMIA (CML) WITH INTERFERON ALFA 2B R(IFN)

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In 1988 and 1990 2 randomized IFN-based (Intron A, Schering Plough) pilot trials on CML were activated. The first trial (20 untreated pts, 18 evaluated, follow-up 56 months range 10–80) compared IFN versus IFN + cytoreductive chemotherapy to evaluate time to hematological/cytogenetic responses (HR, CR), event -free/overall survivals (EFS, OS); all pts received IFN for maintenance. Except for slight advantage in time to HR (P = NS) in low risk pts (compared to intermediate/high risk), no difference was observed between arms in CR/EFS/OS. Two low risks pts (1 from each arm) are currently BCR-ABL (−) (PCR) at 50/61 mos f-up. The second trial (23 untreated pts, 20 evaluated, f-up 44 mos range 7–59) compared 5 versus 3 days-a-week IFN maintenance after daily IFN until HR, to evaluate the impact on CR, EFS, OS. Four low risk pts (3 with IFN 5 days-a-week) remain BCR-ABL (−) at 22, 39, 45, 49 mos f-up (2 pts no current therapy). Six hematological relapses (3 in each arm) occurred in 2 intermediate, 4 high risk pts. Pts at low risk under IFN 5 days-a-week showed better CR and survived longer (median survival not achieved at 42 mos f-up), than intermediate/high risk pts. Side effects and toxicity did not limit therapy with IFN. According to these data, IFN at higher doses during induction/maintenance induces sustained HR and CR in low risk Ph+ CML pts. On this basis, in 1993 a new stratified multicentric (GATLA) trial (IFN at higher dose plus more intensive chemotherapy for induction/maintenance) was activated.

814 PUBLICATION

PERIPHERAL BLOOD TRANSPLANTS FOLLOWED BY MAINTENANCE INTERFERON IN MYELOMA

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Between November 1992 and November 1994, 73 myeloma patients were treated with high dose Melphalan (200 mg/m^2) followed by rescue with peripheral blood stem cells. All patients had received induction treatment with C-VAMP until maximum response. 24 patients were newly diagnosed while 49 patients had received some form of previous treatment. Response and engraftment details are shown in the table below.