been included and we report the safety results on 29 patients enrolled in the first 5 dose levels:

C/D (mg/m^2)	Nb of pts	Nb of eval. cycles (cy)	Neutropenia G4 (% cy)	Febrile neutropenia (% cy)	Non-hematol. toxicity G3 except alopecia (% cy)
1000/60	6	36	80.5	8.3	0
1000/66	7	38	57.8	10.5	10.5
1200/66	7	42	61.9	4.7	14.2
1000/75	6	33	69.6	6.0	9.0
1200/75	3	13	92.3	0	15.3

No grade 4 non-hematological toxicity was reported. The maximum tolerated dose is not yet reached. Regarding the efficacy results from 24 evaluable pts, 14 pts responded (1 CR and 13 PR), 9 were in stable disease and 1 pt progressed during the treatment. We are continuing to explore the dose level D 75 mg/m^2 and C 1200 mg/m^2. Antitumoral efficacy of this combination is encouraging (ORR = 58%).

1326 PUBLICATION

The responsivness of bone metastases in breast cancer patients to radiotherapy: Prospective study comparing six different fractionation schedules

N. Borojević, I. Golubičić, Lj. Radošević-Jelić. *Institute for Oncology and Radiology of Serbia, Yugoslavia*

Aim: The aim of this paper was assesment of values of different regimens of radiotherapy fractionation, determining radiologically assessed response, as well as analysis of effect of further evolution of the disease with impact on quality of life and on overall survival.

Materials and Methods: Prospective nonrandomised clinical trial was performed during the period: 1.1988.–12.1996., in the Institute for oncology and radiology of Serbia (Belgrade, Yugoslavia), to evaluate the effectivness of six different radiotherapy schedules of bone metastases irradiation. Thise schedules were: (A) short – 14 Gy/2 fractions, 48 hours interval between them and 16 Gy/4 fractions; (B) median 18 – Gy/6 fractions and 20 Gy/8 fractions; and (C) long ones – 30 Gy/10 fractions and 40 Gy/20 fractions. A total of 386 patients (441 irradaiated lesions) with breast cancer and osteolytic bone metastases as a first and sole relaps of the disease, were included in this trial. The responese quality was evaluated radiographicaly, 2 and 4 months after completition of irradiation.

Results: Looking at the relation between response rate and subjection to treatment arms A, B and C no statistical differences were notable. For short and median irradaition regimens better response is achived at the second than at the first radiological control. The probability of five years survival of patients with bone metastases and first and sole relaps was 45.01%, with median overall survival of 31 months. Response quality to undertaken treatment by irradaition is not predictor of overall survival.

Conclusion: It is concluded hat short fractionation radiotherapy regimens is as effective as median and long ones in palliation of bone metastases in breast cancer patients with this form of metastatic disease.

1327 PUBLICATION

Improved survival for patients with metastatic breast cancer treated with high dose chemotherapy compared with matched controls who received conventional treatment

P. Donnellan[1], P. Dillon[1], S. Hoey[1], A. Baker[1], M. Smith[1], D. Cameron[1], R. Leonard[1]. *Western General Hospital, Dept of Clinical Oncology, Edinburgh, United Kingdom*

We have examined the survival of 2 groups of patients with metastatic breast cancer who were treated between 1988 and 1997; one group had conventional anthracycline combination chemotherapy and the other high dose (HDC) as first line treatment. The study was performed to test Rahman's hypothesis (ASCO 1995) that selection of patients largely explains the survival (S) benefit claimed for HDC in non-randomised studies. This study has matched the presenting characteristics of patients treated with conventional therapy (Conv.) against those of a series of 50 patients treated with HDC. For this study patients with non-visceral metastases were excluded. HDC comprised cyclophosphamide 4 gr/m^2 followed by GCSF/PBSC harvesting then melphalan 140 mg/m^2 plus thiotepa 600 mg/m^2.

Characteristics: HDC: n = 48, Age 41 [27–56], ECOG 1 [0–4], DFI 86 wk [0–240] Conv: n = 190, Age 48 [28–57], ECOG 1[0–4], DFI 94 wk [0–684]

Results: (No treatment associated mortality for HDC) HDC: Median S 24 mo [7–116]; 1, 3, 5 yr S 81%, 27%, 15% Conv.: Median S 15 mo [0–89]; 1, 3, 5 yr S 53%, 13%, 2.6%

The HDC results are similar to those reported by us and others earlier. The Conv. results are at least as good as the outcomes reported elsewhere. The study suggests that the benefit of HDC in this group of patients with visceral mets is not entirely explained by patient selection.

Haematological malignancies

1328 ORAL

Genes and rearrangements in 3q21 relevant to leukemia

A. Rynditch. *Institute of Molecular Biology and Genetics, 150 Zabolotnogo Str., UKR-252627 Kiev, Ukraine*

Rearrangements of the long arm of human chromosome 3, in particular of bands 3q21 and 3q26, are well documented in leukemia. In 3q26 the EVI1 gene, a zinc finger transcription factor not normally expressed in hematopoietic tissues, has been implicated, but the role od sequences in 3q21 remains poorly understood. The breakpoints within 3q21 are clustered within a 30 kb region which appears to be extremely gene rich as we previously identified up to nine novel genes in an 80 kb P1 clone that spans 10 different breakpoints& These putative genes are of unknown function, are generally expressed at low levels in normal tissues and in a set of cancer cell lines, and breakpoints are dispersed among them. Most recently, examination of a leukemia derived cell line and nine patient samples carrying t(3;3)(q21;q26) and inv(3)(q21;q26) has demonstrated activation of expression of some of these genes. In addition, some activated genes are involved in complex alternative and/or intergenic splicing. For example, formation of a fusion transcript between the 3q21 gene Ribophorin I and the 3q26 gene EVI1 is a common event in t(3;3)(q21;q26) observed both in s leukemic cell line and in several patients. Fusion between the 3q21 gene GR6 and EVI1 has been more rarely observed, and reflects a less common 3q21 breakpoint location. Each of these fusions splice the 5'-end of the 3q21 gene into exon 2 of the EVI1 gene, altering the translational start site and potentially producing EVI1 proteins with altered transcriptional activator properties. These data suggest that sequences in 3q21 play a role in leukemia development or progression.

1329 ORAL

DNA fingerprinting of low-grade extranodal marginal zone B-cell lymphoma (of MALT type)

F. Bertoni[1,2], R. Müllenbach[3], E. Roggero[1], M. De Boni[4], F. Cavalli[1], F.E. Cotter[3], E. Zucca[1]. [1]*Ospedale S. Giovanni, Istituto Oncologico della Svizzera Italiana, Bellinzona, Switzerland;* [2]*Istituto Mario Negri, Oncologia, Milan, Italy;* [3]*Institute of Child Health, LRF Dep. of Haematology and Oncology, London, United Kingdom;* [4]*Ospedale di Feltre, Gastroenterologia, Feltre, Italy*

Introduction: DNA amplification by PCR with primers designed on the widely distributed Alu sequences allows the production of specific inter Alu DNA-fingerprints. Amplification of tumour and matched normal DNA can show differences due to genetic alterations within tumour genome. Thus, molecular events responsible for the malignant growth pattern might be identified. We applied this approach to study low-grade extranodal marginal zone B-cell lymphoma (of MALT type).

Methods: DNA was extracted from frozen MALT lymphoma and from matched peripheral blood samples. After separate digestion with 2 restriction enzymes, DNA samples were amplified by PCR with 3 different primers. A comparison between the fingerprint pattern for lymphoma and Pb samples was made. Inter-Alu (ITA) bands differing between the two samples were excised from the gel, cloned and sequenced. The obtained DNA sequences were analysed for homologies in the GenBank database, using the BLAST software.

Results: Six cases of low-grade MALT-lymphomas have been already analysed. 17 differing bands (range 400–800 bp) were excised from gels. Nine bands were absent in the tumour, 7 in the Pb, and 1 appeared apparently amplified in the lymphoma sample. The combination of ALU-I restriction enzyme and ALU-IV primer was the most informative. DNA sequences analysis showed highly significant homologies for three ITA bands (with chromosome 9p21, chromosome 22q11, and chromosome 16p12). Additional cases are going to be studied.

Conclusions: Since homology with chromosome 9p21 region fell within the p16 gene locus, already known to be involved in the MALT lymphoma progression, Alu-PCR technique appears as an useful tool to compare tumour and normal DNA from MALT-lymphoma patients and may provide insights into the genetic events leading to tumorigenesis.

1330 ORAL

Anaplastic large cell lymphoma: Clinical features and prognosis in a retrospective series of 72 patients treated in a single institution

V. Boulanger[1], P. Soubeyran[1], I. Soubeyran[2], I. de Mascarel[2], H. Eghbali[1]. [1]*Institut Bergonié, Department of Medicine, Bordeaux;* [2]*Institut Bergonié, Department of Pathology, Bordeaux, France*

Purpose: ALCL represent a heterogeneous group of lymphomas differing in their histology, phenotype, clinical course and even cytogenetics. This entity is unfrequent and information about its clinical behaviour and prognosis is limited. We reviewed clinical, histologic and immunologic features of 72 cases of primary ALCL retrospectively diagnosed and treated in our institution.

Methods: There was a majority of male and median age was 43. B symptoms were present for 29 patients (40%). There was a predominance of localized stages (60%).

Results: Thirty-seven patients had extra-nodal localizations (52%). Skin involvement was the most frequent extra-nodal site (18%). Among histologic types, common type was the most frequent (65%). Tumour cell phenotype was B, T, and Null in respectively 28%, 28% and 29% of cases. Complete remission rate was 73%. Five and ten years overall survival were 55% and 45% respectively. Nineteen patients relapsed (26%). Five and ten years relapse-free survival were 62% and 58% respectively. Complete remission rate was 74% after salvage treatment. Five years overall survival after relapse was 38%. For overall survival, in multivariate analysis, favourable independent prognostic factors were respectively: negative immunostaining for CD45 ($p = 0.0032$), localized stage ($p = 0.0064$), good performance status ($p = 0.031$) and hemoglobin level (Hb superior or equal to 12 g/dl) ($p = 0.036$). For relapse-free survival, in multivariate analysis, only negative immunostaining for CD45 was a favorable independent prognostic factor ($p = 0.012$).

Conclusion: In this series, prognosis of ALCL appears sensibly better than diffuse large B-cell NHL may be due to young and response to chemotherapy. Besides other factors, immunostaining for CD45 appears an independent prognostic factor in ALCL and should be confirmed in further studies.

1331 ORAL

Anemia associated with non-platinum chemotherapy (CT) for Hodgkin's lymphoma (HL) or non-Hodgkin's lymphoma (NHL)

B. Coiffier[1]. [1]*Hospices Civils de Lyon, Lyon, France*

Purpose: Anemia is a common but treatable condition in cancer patients (pts). Treatment options have included blood transfusions (TFs) and, more recently, epoetin alfa. This agent increases hemoglobin (Hb) levels while decreasing the need for TFs, which have been associated with a number of serious side effects. To identify pts who might benefit most from epoetin alfa, the prevalence of anemia, Hb levels, TF requirements, and predictive factors for anemia and TFs were determined in pts with HL or NHL who had undergone cyclic non-platinum CT.

Methods: Hematologic and TF data obtained retrospectively from the hospital records of 93 HL and 220 NHL pts were analyzed. The pts were a diagnostic subset of a previously described group of pts with selected cancers treated at 24 centers in France between Jan 1, 1994 and Dec 31, 1995.

Results: At baseline, mean Hb levels for all HL and NHL pts receiving CT were 12.2 (range, 7.9–15.4) g/dL and 12.3 (range, 6.2–18.5) g/dL, respectively. At this time, 45% of HL pts and 42% of NHL pts were anemic (Hb, 12 g/dL or less). The prevalence of anemia tended to increase with succeeding CT cycles, reaching 76.5% for HL pts and 65.8% for NHL pts by cycle 6; mean Hb levels for all pts receiving CT at cycle 6 were 10.6 g/dL and 11.7 g/dL, respectively. TF requirements were 20.4% for HL pts and 33.2% for NHL pts from cycle 1 onward (vs 0% and 5.9% at baseline). More pts with Hb levels less than 10.5 g/dL received TFs than did those with Hb levels of 10.5 g/dL or greater (HL: 35.7% vs 15.3% and NHL: 76.1% vs 22.6%). Anemia and TFs were associated with baseline Hb level and duration of CT.

Conclusion: Baseline Hb levels and duration of CT were associated with anemia development and TFs, and thus may help identify pts likely to benefit from epoetin alfa. Because anemia can have detrimental effects on the pt's physical and emotional well-being, as well as therapeutic intervention and outcome, epoetin alfa therapy has the potential for providing substantial benefits.

1332 ORAL

Allogeneic, autologous bone marrow transplantation and chemotherapy in first remission of adult acute lymphoblastic leukemia. Prospective study LALA87. Long term results

D. Fière, L. Degos, J. Reiffers, J.L. Harousseau, J.P. Vernant, M. Michallet, C. Sebban, E. Lepage. *Université Claude Bernard, Lyon1, Lyon, France*

In this prospective study patients 15–60 years with de novo ALL, except L3 FAB subtype have been included between November 1986 and July 1991. Two randomized arms for induction Daunorubicin or Zorubicin associated with Vincristine Cyclophosphamide and Prednisone were followed if complete remission (CR) was not achieved at day 28 by a common salvage regimen with Amsacrine and Aracytine. In CR a stratification took place.

– patients over 50 y: chemotherapy arm with 3 courses of consolidation, cranial irradiation and maintenance

– patients 15–40 with an identical sibling were included in allogenic bone marrow transplantation (BMT) arm performed after one course of CVP (Cyclophosphamide, Vincristine, Prednisone) as soon as possible. Other patients were randomized during the second consolidation course in chemotherapy arm or auto BMT arm.

Analysis of Results: Allo BMT was compared to a control group of patients 15–40 y, in CR with at least one sibling and HLA typed but without any identical donor. Auto BMT arm was compared with randomized chemotherapy arm. In each arm, patients were stratified in high and standard risk group according Hoelzer,s criteria. Analysis was performed on an intention to treat basis.

572 out of 634 included patients were evaluable, 562 with an initial immuno phenotyping, and, 274 an initial cytogenetic analysis.

Results: 76% (436 patients) achieved CR. There were 9% of death during induction and 15% of failure. No statistical difference between the DNR and ZRB arms in term of remission rate or survival.

At ten years, the overall disease free survival (DFS) and survival (S) are 30% and 27% and survival for partients over 50 y is 23%.

– in allo BMT study, overall survival of allo arm (116) and control group (141) is 46% versus 31% ($p = 0.04$). In high risk, survival is 44% in allo arm versus 11% in control group (p: 0.009), in standard risk, survival is 49% versus 43% (p: 0.6). For auto BMT arm survival is 34% in auto versus 29% in chemo arm (p: 0.65) There is not difference for standard or high risk group.

1333 ORAL

FDG-PET following treatment is a valid predictor for disease-free survival in Hodgkin's disease

M. de Wit[1], K.H. Bohuslavizki[2], M. Clausen[2], D.K. Hossfeld[1]. [1]*Department of Oncology and Haematology;* [2]*Department of Nuclear Medicine, University Hospital Eppendorf, Hamburg, Germany*

Purpose: The value of FDG-PET to predict outcome after chemotherapy or combined radio/chemotherapy is compared to conventional morphological staging and erythrocyte sedimentation rate (ESR).

Methods: 50 whole-body FDG-PET were performed in 37 patients with Hodgkin's disease undergoing either CT or MRI at the same time. ESR was evaluated 32 times after treatment was completed. Median follow-up after PET was 25.6 months. Patients presented at primary diagnosis at stage I (4), stage II (17), stage III (11) and stage IV (5) according routine morphological methods.

Results: 39 residual masses were observed with radiological methods resulting in 8 relapses. 3 recurrences occurred in 11 patients with radiological complete remission. FDG-PET was positive in 22 examinations with 10 recurrent lymphoma. In the group of 28 patients without FDG-uptake 1 patient relapsed 4 years after PET. For predicting recurrence overall accuracy for PET was 74%, sensitivity 91% and specificity 69%. Overall accuracy for CT/MRI was 34%, sensitivity 72% and specificity 23%, while accuracy for ESR was 66%, sensitivity 50% and specificity 71%. In addition only PET was able to predict disease-free survival statistically significant ($p < 0.001$).

Conclusion: FDG-PET is the best method to predict relapse respectively disease-free survival in Hodgkin's lymphoma. FDG-PET was the only statistically significant examination.