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.