Conclusions: The hepatic biopsy change the NHL stage in an important number of patients (5) even in those without clinical or analytic hepatic abnormalities. In these group of patients the value of hepatic biopsy was similar to bone marrow biopsy also with a greater morbidity.

Multiple myeloma

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Incidence and prognostic significance of deletions of tumor suppressor genes and aneuploidies in multiple myeloma: an interphase FISH study

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Recent studies indicate that chromosome aberrations are important prognostic factors in patients with multiple myeloma. In the present study, we performed interphase fluorescence in situ hybridization (FISH) in consecutively ascertained samples from 32 patients with multiple myeloma treated in our department from 1990 to 1999. In each case, a panel of 10 different FISH probes hybridizing to the chromosomal regions 8q24/CMYC 9p21/P16, 11q13/CyclinD1, 11q22, 13q14/D13S25, 17p13/P53 and to the centromeres of chromosomes 3, 7, 9, and 11 was applied. A simultaneous applied control probe served as an internal control for the hybridization efficiency. In addition to the patients' samples, 8 normal control samples were analyzed to define the cut-off levels for the probes under investigation. The FISH results were correlated with clinical data and the overall survival of the patients.

The majority of cases showed alterations of at least one locus analyzed (28 of 32 cases). The following abnormalities were detected: monosomies of 17p13/P53 in 11 of 31 cases (35%), monosomies of 13q14/D13S25 in 10 of 31 cases (32%), trisomies of 8q24/CMYC in 10 of 31 cases (32%), trisomies of 11q13/CyclinD1 in 10 of 32 cases (31%), trisomies of 11q22 in 7 of 31 cases (23%), trisomies of 9p21/P16 in 7 of 32 cases (22%), and trisomies of centromeres 3, 7, 9, and 11 in 11 of 32 (34%), 6 of 31 (19%), 4 of 29 (14%), and 10 of 32 cases (31%), respectively.

Deletions of D13S25 (18 vs. 30 months median survival, p 0,017) and P53 (20 vs. 32 months median survival, p 0,03), and overrepresentations of CMYC (16 vs. 30 months median survival, p 0,005) were associated with a significantly shorter overall survival as compared to patients without these aberrations.

The present study underlines the importance of chromosomal abnormalities in the assessment of the prognosis of patients with multiple myeloma.

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Spontaneous secretion of matrix metalloproteinases, urokinase plasminogen activator, its receptor and cytokines in primary long-term bone marrow cultures of multiple myeloma patients

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Purpose: Matrix metalloproteinases (MMP's), urokinase plasminogen activator (uPA), its receptor (uPAR) play a key role in dissemination of several cancers, and cooperate with cytokine network. There are only very limited report on their involvement in pathology of multiple myeloma (MM), a bone devastating neoplasia. We investigated spontaneous secretion of MMP's, uPA, uPAR, and cytokines by myeloma marrow microenvironment in primary long-term bone marrow cultures (LTBMC) in MM patients.

Methods: LTBMC's were established from bone marrows of 19 newly diagnosed myeloma patients, and 18 donors without any malignancy and any skeletal disease. Conditioned media from LTBMC's were analysed by gelatine zymography. Total MMP-1, MMP-2, MMP-3, MMP-9, uPA, uPAR, IL-6, IL-1beta, IL-10, IL-11 and TNF-alpha were measured by ELISA.

Results: The proteolytic activity corresponding to proMMP-2, proMMP-9 and their active forms was found by gelatine zymography in all cultures. Myeloma cultures secreted significantly more MMP-2, IL-6 and IL-10 than control cultures, but less MMP-3, MMP-1, IL-11 and TNF-alpha. MMP-1, MMP-9, uPAR, IL-6, IL-1beta levels were positively correlated with percentages of malignant plasma cells in bone marrows, however there were no differences in MMP-9, uPA, uPAR and IL-1beta levels between cultures. Further MMP-1 and MMP-9 levels in myeloma LTBMC's were positively correlated with uPAR and IL-1beta.

Conclusion: Spontaneous secretion of MMP's by bone marrow microenvironment is significantly disturbed in MM and could reflect angiogenic potential of malignant plasma cells. The study gives reason for introduction of synthetic selective matrix metalloproteinase inhibitors into therapy of multiple myeloma.

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The Antwerp experience with thalidomide in relapsed/refractory multiple myeloma

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Background: Barlogie and coworkers showed the marked anti-tumor effect from thalidomide in high risk refractory multiple myeloma (MM) in 1998.

Aim of the study: To evaluate in a retrospective way the effect of thalidomide in patients with relapsed/refractory MM.

Patients: Since 12.07.1999 51 patients with relapsed/refractory MM have been treated; 50 are evaluable. The mean age is 69 years with the youngest being 45, the oldest 87; 26 are males, 24 are females. Before the start of thalidomide, patients were treated with an average of 4 different schemes of chemotherapy and/or irradiation (1-18). Fifteen patients underwent an autologous transplant; one patient was transplanted twice. The distribution of the different subtypes is as follows: IgG k (24), IgG l (11),IgA k (6), IgA l (4), light chain k (2), light chain l (1) and unknown (2).

Treatment: Ten patients were treated for 14 days or less at the moment of evaluation and are not included for further evaluation. The mean duration of treatment in the other patients is 176 days, with a minimum of 15 and a maximum of 448 days. The average oral dosage was 200 mg daily (100-400).

Results: Of the 40 evaluable patients, 15 reached a partial response (PR) (37.5%), 3 a good PR (GPR) (7.5%), 13 had stable disease (32.5%) and 9 developed progressive disease (PD) (22.5%).

Discussion: The effect of thalidomide can be quite dramatic in a positive sense. Moreover, the majority of patients only complained of mild side-effects.

Bone marrow transplantation/cytokines

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Dose intensified chemotherapy with growth factors, in patients with advanced cancer

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Background: Inadequate drug dose is a major factor responsible for the failure of chemotherapy (CT). Carboplatin (CBDCA), Cyclophosphamide (CTX) and Etoposide (VP-16) are active drugs in many solid tumors. In a previous phase I study (Clin Ter 148:201-207,1997) we found the maximum tolerated dose of the three drugs given in combination with growth factors. In another study we ascertained the value of the sequential administration of G-CSF and GM-CSF (Am J Clin Oncol 20:209-214,1997) after dose intensified (HD) CT. Aim of this phase II study was to find the activity and toxicity of HDCT in a group of patients with advanced tumors.

Patients and Methods: A group of 48 patients, were entered in this phase II study of HDCT from 1-93 to 11-99. Patient's characteristics: median age was 52 years (range 18-75). Patients had been treated previously as follows: surgery-37, radiotherapy-7, all had received CT (total 330 courses, median-6 courses/patient, range 4-13). Diagnosis: 26-breast cancer, 13-lung cancer, and 9 miscellaneous tumors. 21 patients had metastatic disease at the diagnosis, 16 patients had a median disease free interval of 18.5 months before developing metastases, while 11 patients had inflammatory breast cancer. Patients received two consecutive courses of the same CT, over 3 days, with CTX and VP-16 (1500 mg/m2 and 400 mg/m2 respectively). CBDCA was administered at the AUC of 8. After CT patients received a sequential combination of growth factors (G-CSF and GM-CSF, both at the