changes and the occurrence and distribution of tumour-infiltrating mononuclear cells.

Results: Among patients with regional disease, 50% showed a high degree of regressive changes (more than 75 percent of the section area) after biochemotherapy. Patients with histopathological response could be identified pretreatment by analysing the numbers of tumour infiltrating CD4+ lymphocytes in FNA. There was a statistically significant correlation between the occurrence of these cells and a high degree of regressive changes post treatment, p=0.01. A Kaplan-Meyer analysis of patients with regional metastses showed a tendency to a longer overall survival in patients with a high degree of regressive changes. Similar results were found in a smaller group of patients with systemic disease.

Conclusion: Biochemotherapy showed a remarkable efficacy with a high degree of tumour regression in 50% of the patients with regional disease. There was a close correlation between extensive regressive tumour changes and the amount of tumour infiltrating CD4+ lymphocytes pre-treatment. Patients with regressive changes of more than 75% of the analysed biopsies were also found to have a tendency to a longer overall survival. Thus immunohistochemical analysis of tumour biopsies shortly after immunotherapy seems to be a good surrogate endpoint and this technique also allows a detailed analysis of anti-tumour reactivity and escape mechanisms.

109 ORAL

Immunomagnetic detection of micrometastatic cells in bone marrow predicts survival of patients with malignant melanoma and osteosarcoma

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Purpose: We have previously reported simple and sensitive methods for detection and characterization of micrometastatic tumor cells, based on the use of immunomagnetic and fluorescent microparticles. The aim of this work was to relate results obtained with our method on samples from patients with advanced malignant melanoma and with osteosarcoma to clinical parameters to examine the clinical potential of the method for predicting prognosis.

Methods: The methods were used on blood and bone marrow samples obtained from 152 melanoma patients and from 39 patients with primary osteosarcoma. Twentyfive (16.3%) melanoma patients had positive samples. This group showed a significantly shorter survival, both from primary operation (p = 0.031) and from time sampling (p = 0.042), than those without micrometastasis. Multiple variat analysis revealed that presence of melonoma cells was, together with the number of metastatic sites, the most important parameter of survival. In osteosarcoma, 50–100% of 39 patients had tumor cells in their bone marrow, increasing with disease stage. In a number of the patients the findings in repeated samples correlated to the effect of preoperative chemotherapy. The malignant nature of the immunomagnetically selected cells could be confirmed by binding of fluorescent antibody-coated particles targeting other tumor-associated antigens, and in a few cases by culturing the cells in vitro and in nude mice.

Conclusion: The results demonstrate the validity and clinical potential of using these methods for prognostication and response monitoring in these type of malignancies.

110 ORAL

Sentinel node biopsy improves regional node staging in melanoma patients

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Elective lymph node dissection (ELND) has been performed widely in the past for patients with melanoma who have been considered to be at high risk for local or systemic recurrence. Sentinel node biopsy (SNB) has largely replaced this technique in many major cancer centres in order to reduce postoperative morbidity and to minimise unnecessary dissections. Whether SNB, with subsequent lymph node dissection when micrometastatic disease is found in a SN, has any benefit in terms of survival remains unclear. Whilst some SNs are not removed due to technical failures, SNB has been shown to improve staging in breast cancer patients when compared to standard axillary lymphadenectomy. In melanoma patients such an improvement has never been demonstrated, therefore a large matched-paired patient study was conducted to compare nodal staging accuracy and survival in patients treated with either SNB or ELND.

All patients treated at the Sydney Melanoma Unit (SMU) between 1983 and 2000 for a primary tumour ~ 1.5 mm in thickness and who underwent a SNB (n=775) or an ELND (n=1026) were evaluated. Two groups of 659 ELND and 659 SNB patients treated over the same time period were matched for age, sex and thickness of the primary melanoma, and compared for node involvement.

The most important predictors of node positivity in multivariate analysis of the matched pairs were tumour thickness (p<0.0001), ulceration (p=0.001), and age (p=0.002). The overall number of patients with positive nodes after ELND was 11.4% and after SNB 16.1%, which was a statistically significant difference (p=0.004). Overall survival after 3 years of follow-up was comparable for both groups.

Thus it is concluded that SNB identifies proportionally more lymph nodes containing metastatic melanoma than ELND in this retrospective matched-paired cohort analysis. Detailed pathological examination, recent improvements in immunohistochemical techniques and accurate identification of the lymph node field(s) by preoperative lymphoscintigraphy are all likely to be responsible for this increased accuracy. Irrespective of any effects on survival which may be demonstrated by presently ongoing clinical trials, SNB in combination with preoperative lymphoscintigraphy is desirable for all patients entering trials of adjuvant therapy in order to create more closely equivalent patient groups.

111 ORAL

Histamine dihydrochloride administered with Interleukin-2 increases survival duration in patients with ocular melanoma with liver metastases

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Background: Ocular melanoma (OM) is the most common intra-ocular malignancy, and it metastasizes to the liver in about two-thirds of patients (pts). This portends a poor prognosis and a median survival of only 2 to 7 months. Therapy for metastatic cutaneous melanoma (CM) has been largely ineffective in pts with OM, and these pts are usually excluded from clinical trials for metastatic CM. Results of a large, randomized phase III trial of a novel combination of IL-2 and histamine dihydrochloride (HDC) compared with IL-2 alone have recently been reported [Agarwala et al. Cancer Invest 19 (suppl 1): 81, 2001], and a significant survival benefit in pts with melanoma metastatic to the liver treated with the combination of HDC and IL-2 was noted. Methods: To examine the potential role of IL-2 and HDC specifically in pts with OM with liver metastases (OM-LM), a retrospective analysis of 35 pts with OM-LM enrolled in a randomized trial and in on-going phase II trial of combination IL-2 and HDC was performed. Pts received IL-2 (9 MIU/m2, bid, sc, days 1-2, weeks 1,3; and 2 MIU/m2, bid, sc, days 1-5, weeks 2, 4) with or without HDC (1.0 mg, bid, sc, days 1-5, weeks 1-4) for 4 weeks of a 6-week cycle. Results: 13 pts received IL-2 alone, and 22 pts received the combination of IL-2 and HDC. In the group receiving HDC + IL-2, the median age was 55 years (range 31-79), 7 (32%) pts were male, and high LDH levels (> ULN) were present in 6/15 (40%) pts. In the group receiving IL-2 only, median age was 64 years (range 25-75), 9 (69%) pts were male, and high LDH levels were present in 6/12 (50%) pts. The median survival for pts with OM-LM receiving IL-2 + HD was 229 days compared to 119 days for pts receiving IL-2 alone (p=0.0051). Conclusions: These results suggest that the benefit noted for pts with CM metastatic to the liver in the randomized phase III trial of IL-2 + HDC vs IL-2 alone was not restricted to CM but extended to those with OM-LM. Further trials in this subset of patients are planned.

112 ORAL

Early evaluation of tumour response to STI 571 with FDG-PET in patients with soft tissue sarcomas (STS)

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Evaluation of treatment response is currently based on changes in tumour volume measured on CT. New anti-cancer drugs often induce tumour growth