plus GM-CSF in patients with HER2-positive, hormone refractory prostate cancer.

Patients and Methods: Patients were treated with GM-CSF 5 μg/kg/day by subcutaneous injection for 4 days plus MDX-H210 15 mg/m^2 by intravenous infusion on day 4, repeated weekly for 6 weeks.

Results: 25 patients entered the trial, 1 received no treatment and 20 were assessable for response. Toxicity was generally NCI-CTG 0–2. There were 2 grade 4 adverse events (nausea and vomiting, spinal cord compression, probably related to disease progression). 7 of 20 (35%) evaluable patients had a partial PSA response (reduction of >50%), ranging from 51% to 99%, of duration 71, 83, 89, 122, 128, 160+ and 184+ days. A further 6 patients experienced minor PSA responses (reduction <50%, >25%) of 41, 89+, 131, 140, 152 and 165 days duration. 5 of 16 (31%) patients with evaluable pain had improvements in pain scores. The PSA relative velocity (rate of change of the natural logarithm of the PSA level) on therapy was compared to the period prior to study entry and decreased in 16/18 (89%) assessable patients. Median duration of follow up was 105+ days (range 21–188 days) with 6 patients continuing on treatment.

Conclusions: The combination of GM-CSF and MDX-H210 is active in hormone refractory prostate carcinoma. Toxicity was generally mild to moderate and mostly manageable on an outpatient basis. Further studies in prostate cancer are indicated.

1389 POSTER DISCUSSION

Effect of high dose Rhenium 186 HEDP with stem cell support on skeletal metastases in prostate cancer

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Introduction: Isotope treatment has an established role in the treatment of prostate cancer bone metastases. The activity given is limited by bone marrow suppression. We have explored the use of Rhenium 186 HEDP in a phase I dose escalation protocol using peripheral stem cell support.

Patients and Methods: 14 patients with hormone resistent advanced prostate cancer with skeletal metastases were given activities of 1400 to 3488 MBq of Rhenium 186 HEDP. Seven received activities above 3000 Mbq. Following growth factor stimulation peripheral stem cells were harvested pre-treatment and returned at day 12 post-treatment. Metastases on whole body scans pre-treatment were compared with these on average 10 weeks post-treatment and activity scored as: not visible, decreased, no change, increased.

Results: Treatment was well tolerated and peripheral blood counts recovered to the normal range in all patients. No patients developed clinically significant thrombocytopenia or neutropenia. The total number of metastases (areas of increased uptake on pre-treatment scan) ranged from 10–70 per patient in the >3000 MBq group and 7 to 31 in the <3000 MBq group. The change in appearance of metastases after treatment was documented. Of the 223 metastases identified in the >3000 MBq group 26%, 16%, 13% and 46% were in "not visible", "decreased", "no change" and "increased" categories respectively post-treatment compared to 6%, 7%, 57% and 31% respectively for the 106 metastases in the <3000 MBq group. Compared with the the number of metastases in the pre-therapy examination there were 3% new metastases in the >3000 MBq group and 49% in the <3000 MBq group at the time of the second scintigram. There was no obvious relationship between the number of metastases nor their size and the reponse to therapy.

Conclusion: These results demonstrate that some metastases can be successfully ablated by therapeutic activities of Rhenium 186 and higher activities are more effective.

1390 POSTER

Increase in stage at presentation in prostate cancer: Have thresholds for referral risen?

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Screening and case finding for early prostate cancer has been much debated in the United Kingdom and widely practiced in Europe and North America. The UK has adopted a case finding approach rather than screening. After running a TRUS clinic in a 'Quick Early Diagnostic Unit' for 5 years we were concerned that we were not seeing any increase in low stage disease.

Patients: Over the last three years 785 patients were seen and biopsied. Criteria for being seen have remained unchanged and only patients with a raised PSA (>4 ng/l) or a suspicious rectal exam were seen.

Results: Total referrals, total number of cancers and cancer stage are shown. There was a trend towards increasing PSA and age over the three years, though this did not reach statistical significance.

Variable	1996	1997	1998
Total referrals	274	237	274
Total Cancers (% of total referrals)	99 (36%)	84 (35%)	115 (42%)
Stage			
T1cM0 (% of all cancers)	33 (33%)	27 (32%)	21 (18%)
T2M0 (% of all cancers)	23 (23%)	21 (25%)	29 (24%)
T3–4M0 (% of all cancers)	19 (19%)	20 (24%)	44 (38%)
M1 (% of all cancers)	18 (18%)	11 (13%)	32 (28%)

Conclusion: Despite the increase awareness of prostate cancer among doctors and public, the case finding approach adopted in our practice has not seen any increase in early disease. This is unexpected and cause for concern. A more aggressive approach to the detection of prostate cancer within the UK is required.

1391 POSTER

Metastatic transitional cell carcinoma: Evaluation of prognostic factors and change in prognosis during the last 20 years

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Purpose: To investigate patients with metastatic urothelial cancer and propose the most appropriate combination of prognostic variables describing the outcome, and to analyse changes in overall survival during the past two decades.

Methods: Between 1992 and 1997, a total of 156 patients with recurrent locally advanced disease (non-resectable, radio-resistant) and/or metastatic transitional cell carcinoma of the urothelial tract were included in a protocol evaluating prognostic factors and pattern of metastases.

Results: Distant metastases were diagnosed in 86% with lymph nodes (57%) and bones (40%) as the most frequent localizations. Liver metastases were found in 21%. Median survival after recurrence was 5.8 months. Multivariate analysis showed that good performance status (PS), normal alkaline phosphatase (AP), absence of liver metastases and chemotherapy were independent prognostic factors for long survival. Comparison was made with 240 patients treated in the period from 1976–1992. A significant increase in survival in the present period was found.

Conclusion: PS, AP and liver metastases are the major important prognostic factors. Stage migration and increased use and efficacy of chemotherapy has resulted in increased survival in metastatic urothelial cancer.

1392 POSTER

Length of follow-up influences biochemical control rates after treatment for prostate cancer

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To determine whether biochemical control (bNED) rates following treatment for prostate cancer are dependent on the length of post-treatment follow-up (f/u), we reviewed 437 patients with clinically localized prostate cancer treated with conformal radiotherapy without neoadjuvant androgen deprivation (AD). Biochemical failure was defined as three consecutive PSA increases or an increase large enough to prompt salvage AD. The date of failure was back-projected to the midpoint between the PSA nadir and the first PSA increase (or between the nadir and the initiation of salvage therapy). The analysis was performed by censoring patients with longer f/u in a step-wise fashion, thus creating smaller subgroups with shorter f/u. Subgroup 1 (N = 191) and Subgroup 2 (N = 273) were defined to include those patients followed for up to 2 years and up to 3 years, respectively. No significant differences were seen in pre-treatment prognostic factors among the three groups. The 2-year bNED of Subgroup 1 (median f/u = 1.1 years), Subgroup 2 (median f/u = 1.5 years), and the original population (median f/u = 2.5 years) were 86.3%, 77.4%, and 73.4% (p = 0.05). No differences in clinical recurrence rates were seen between any of the three groups. In conclusion, bNED rates are highly dependent on the length of f/u. This appears to result from the back-projection of failure dates, which is a component of commonly used bNED definitions. This has important implications