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

for studies comparing patient cohorts that have different lengths of f/u. It is particularly pertinent in the case of radiation dose escalation protocols, wherein higher dose levels are not offered until lower dose levels have been proven safe.

1393 POSTER

Analysis of the prognostic factors in germ cell tumours of the testis (GCTT)

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Purpose: Analysis of the selected variables in patients (pt) with GCTT and their prognostic value for the risk of failure of the standard treatment.

Material and Methods: Nine hundred forty one pt with GCTT was treated in Maria Sk"odowska-Curie Memorial Cancer Center in Warsaw from January 1980 to December 1995: 374 pt with seminoma of the testis (244 in clinical stage [CS] I, 109 in CS II, 21 in CS III) and 567 with nonseminomatous GCTT (189 in CSI, 202 in CSII, 176 in CS III). Median age was 31 years (14–83), median follow-up – 61 months (1–209) and 788/941 pt (84%) were observed longer than 2 years. Probability of survival was assessed using Kaplan-Meier method and multivariate analysis was performed using the Cox model of proportional risk. Following variables were analysed: CS, age, level of alphafetoprotein (AFP) and human chorion gonadotrophin (HCG), presence of brain, liver, bone and mediastinal metastases, number and volume of lung metastases, volume of retroperitoneal tumour, histological type.

Results: One hundred sixty four pt (17%) died. The probability of 5-year survival was 82%. The multivariate analysis revealed the following statistically significant variables: CS – $p < 0.00005$, age > 50 years – $p < 0.00005$, brain metastases – p 0.0022, diameter of the retroperitoneal tumour at least 10 cm – p 0.0063, elevated AFP – p 0.42, elevated HCG – p 0.039.

Conclusions: Clinical stage III, retroperitoneal metastatic tumour diameter at least 10 cm, presence of brain metastases, elevated AFP of HCG level, age of the patient more than 50 years are independent risk factors for the patient with GCTT.

1394 POSTER

Health-related quality of life following high dose rate brachytherapy and external beam radiation for prostate cancer

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Purpose: To measure the health-related quality of life (HRQoL) after combined high dose rate (HDR) 192Iridium-brachytherapy (BT) and external beam radiation (EBR) for localized prostate cancer.

Material and Methods: Hundred and eighty-nine patients were analized. The HRQoL of the 145 (76.7%) surviving patients at time of analisis was assessed with the core questionnaire QLQ-C30 of the EORTC and a new developed prostate-specific instrument. The reliability of boths protocols was tested.

Results: The mean Cronbach's-Alpha value for the QLQ-C30 module was 0.81, and for the prostate-specific protocol 0.74, respectivelly. Univariate analysis of variance of the variables T-stage, grading, PSA and tumor status after therapy, and adjuvant hormonal treatment revealed that PSA elevation after radiation therapy, and adjuvant hormonal treatment were associated with significant lower level of HRQoL. T-stage and grading had no significant influence on HRQoL. In multivariate analyses only adjuvant hormonal treatment had negative impact on HRQoL without survival benefit. However, the stratification for adjuvant hormonal treatment was not according to random.

Conclusion: The HRQoL assessment with QLQ-C30 protocol and the new developed prostate-specific instrument was reliable. Survival following HDR-BT combined with EBR in men with localized prostate cancer is associated with good quality of life.

1395 POSTER

Geographic clustering of testicular cancer incidence in the northern part of The Netherlands

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Geographic variations in testicular cancer (TC) incidence may be caused by differences in environmental factors, genetic factors, or both. In this study, geographic patterns of TC incidence rates (IRs) in the 12 provinces in The Netherlands in the period 1989–1995 were analyzed. Geographic variations within the rural North were analyzed in more detail. Incidence data were obtained from the Netherlands Cancer Registry and the Comprehensive Cancer Centre North-Netherlands. In addition, the occurrence of TC by degree of urbanisation was evaluated.

The overall annual age-adjusted IR of TC in The Netherlands between 1989–1995 was 4.4 per 100,000 men. The province Groningen in the North showed the highest annual IR with 5.8 per 100,000 men, which was significantly higher ($P < 0.05$) than the overall IR in The Netherlands (incidence rate ratio (IRR) 1.3, 95% CI 1.1–1.6). Friesland, also in the North, showed the second highest IR with 5.3 per 100,000 men (IRR 1.2, 95% CI 1.0–1.5, not significant). Analysis of IRs in 9 smaller survey areas within the 3 northern provinces Groningen, Friesland and Drenthe demonstrated 4 areas with annual IRs that were significantly higher than the IR in The Netherlands: Friesland-Southwest (IR 6.7, IRR 1.5, 95% CI 1.0–2.3), Groningen-East (IR 6.5, IRR 1.5, 95% CI 1.0–2.0), Friesland-Southeast (IR 6.1, IRR 1.4, 95% CI 1.0–1.9) and Groningen-West (IR 5.6, IRR 1.3, 95% CI 1.0–1.6). Analysis of the occurrence of TC by degree of urbanisation in The Netherlands showed no urban-rural differences by analyses of all histologic types, nor by separate analyses of the main histologic types seminomas and nonseminomas.

This study demonstrated geographic clustering of TC in the rural North of The Netherlands with some stable founder populations, which are likely to share a relatively high frequency of genes from common ancestors including possible disease related genes. Although this finding does not exclude the involvement of shared environmental factors, it may also lend support to a genetic susceptibility to TC development. TC cases in stable founder populations seem particularly suitable for searching possible disease genes predisposing to TC.

1396 POSTER

The optimal cut off value of the percentage of free PSA to enhance differentiation of prostate cancer and benign prostate disease: A prospective blind study

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Purpose: The percentage of serum free PSA (% fPSA) has been shown to improve the specificity of PSA testing for early detection of prostate cancer. However, the reported cut off value vary greatly depends on different study design, test essay and sensitivity criterion.

Methods: From Sept 1995 to Feb 1999, 476 men with serum PSA level between 4 and 25 ng/ml underwent transrectal ultrasonography (TRUS) and sextant biopsies of prostate. The age ranged from 46 to 84 with a mean age of 68.7. Just before TRUS guide biopsy, a second serum sample was obtained and stored in −70 degree freezer. The serum free and total PSA were measured with FPSA-RIACT kit and TPSA-RIACT kit (cis bio international, France).

Results: The mean % fPSA of 113 patients with prostate cancer was 18.0 ± 8.7 and was significantly ($p = 0.001$) lower than that of 363 men who were histologically benign, which mean % fPSA was 27.0 ± 10.3. The sensitivity, specificity, and avoid biopsy rate (AVB) were shown as following table:

	Cut off value of % fPSA				
%	15	20	25	30	35
Sensitivity	47.8	69.9	83.2	92.9	96.5
Specificity	91.5	79.6	60.9	34.7	19.3
AVB	82.1	67.9	50.4	28.2	15.6

If the cut off value was set on 25%, then 19 patients (17%) of cancer would be missed, and 11 of these patients were clinical significant cancer. However, using 30% fPSA as cut off could eliminate 28% negative biopsy