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

while still detecting 93% of carcinoma and the majority of missed cancer were low grade and low stage.

Conclusions: Measurement of % fPSA can reduce 28% of unnecessary biopsies in patients with PSA level between 4 and 25 ng/ml with a reasonable sensitivity in detecting prostate cancer. The optimal cut off value of 30% fPSA may apply to the cis bio PSA assay for reference.

1397 POSTER

Cisplatin versus carboplatin based chemotherapy as induction chemotherapy of bladder cancer

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Purpose: To compare combinations of the 2 platinum analogues as induction chemotherapy for invasive or locally advanced bladder cancer.

Methods: Patients (pts) with T2-4 N0/+ M0 transitional cell bladder cancer are randomized to either 3 cycles of combination Cisplatin 70 mg/m^2 (Day 1), Epirubicin (E) 50 mg/m^2 (Day 1) and Methotrexate (M) 50 mg/m^2 (Days 8, 15) (Arm A) or Carboplatin 300 mg/m^2 (Day 1) plus E and M at the same doses (Arm B) given every 3 weeks. Consequently all complete responders and pts not feasible or refusing cystectomy are treated with local radiotherapy (60 Gy).

Results: A total of 96 pts (52 in arm A, 44 in arm B) entered the study. The median age is 66 years, while the majority of pts (73) had T2-3 disease. Toxicity was mild. Anemia and thrombocytopenia were more frequent in arm B, while nausea/vomiting was more evident in arm A. Relative dose intensity was higher in Cisplatin arm. There was not statistically significant differences in term of overall response rate (75% vs 60%), complete response rate (44% vs 50%), time to progression (19.6 vs 21.7 months) and survival (51.8 vs 58.1 months), between the two arms..

Conclusions: Carboplatin based chemotherapy appears to demonstrate comparable activity to cisplatin as induction chemotherapy for invasive or locally advanced bladder cancer.

1398 POSTER

Loss of p27Kip1 expression correlates with tumor grade and with reduced disease-free survival in primary superficial bladder cancers

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p27Kip1 is a member of the Cip1/Kip1 family of cyclin-dependent kinase inhibitors and is a potential tumor suppressor gene. The expression level of p27Kip1 has been reported as an important prognostic factor in primary lung, breast, colon, gastric and prostate cancers. This study was undertaken to assess the prognostic value of p27Kip1 in human bladder cancer. The expression of p27Kip1 protein was evaluated by immunostaining in a series of 96 superficial (Ta-1) human bladder carcinomas. p27Kip1 protein was expressed at high (>50% positive cells), moderate (25–50%) and low (<25%) level in 39 (41%), 19 (20%) and 38 (39%) out of the 96 primary superficial bladder cancers, respectively. Decreased p27Kip1 staining correlated with higher tumor grade ($p = 0.0005$). A significant correlation was also observed between high expression of p27Kip1 and increased disease-free survival ($P = 0.003$ by log-rank test) and overall survival ($P = 0.01$ by log-rank test). On multivariate analysis low p27Kip1 protein expression was an independent predictor of reduced disease-free survival second only to tumor stage. These data indicate that p27Kip1 protein is frequently expressed at high level in well differentiated tumors and suggest that this protein might represent a useful prognostic marker for disease recurrence in primary superficial bladder carcinomas.

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1399 POSTER

Prognostic value of growth fraction measurement with MIB-1 in bladder cancer

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Introduction: Prognosis in transitional cell cancer (TCC) of the bladder is usually assessed with the TNM staging system and a grading system (e.g. WHO). We evaluated the prognostic value of growth fraction in TCC with the monoclonal antibody MIB-1 (Ki-67), which suffers less from inter-observer variation.

Methods: Histological tumour specimens of 301 patients diagnosed between 1979 and 1991 were stained with monoclonal antibody MIB-1 and the fraction of positively stained cells was counted. All patients were staged and graded by classical methods and the mitotic index was counted on conventionally stained histological material. Follow-up data from a prospective database were used to calculate crude survival, recurrence free survival (for Ta and T1 tumours) and progression free survival.

Results: In univariate analysis crude survival, recurrence free survival and progression free survival were strongly related to all analysed prognostic factors after an median follow-up of 60 months. In multivariate analysis however, crude survival and progression free survival were only determined by stage ($p = 0.0001$) and recurrence free survival was determined by mitotic index ($p = 0.0246$) and MIB-1 index ($p = 0.0319$).

Conclusion: In this series stage was the most important prognostic factor for crude survival and progression free survival in TCC, while in superficial tumours MIB-1 and mitotic index determined recurrence

1400 POSTER

Bladder preservation with sequential chemotherapy (CT) and radiotherapy (RT)

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Purpose: To evaluate the effectiveness of combined induction chemotherapy and local radiotherapy for invasive or locally advanced bladder cancer.

Methods: Patients (pts) with T2-4 M0/+ M0 transitional cell bladder cancer are treated initially with platinum based chemotherapy, either Cisplatin 75 mg/m^2 or Carboplatin 300 mg/m^2 (day 1) plus Epirubicin 50 mg/m^2 (Day 1) and Methotrexate 50 mg/m^2 (Days 8, 15). Consequently complete responders (CR) are treated with RT (60 Gy). Partial responders (PR) were treated with RT in case cystectomy was not feasible or they refused cystectomy.

Results: A total of 96 pts entered the study. The CR rate after chemotherapy was 47% and the overall response rate was 71%. 71 pts (37 CRs, 34 PRs) underwent radiotherapy. The CR rate after RT was increased by 10%. After median follow-up of 33 months, median time to progression for patients treated with sequential CT and RT is 26.5 months and median survival 58 months. The 5-year survival is 49% and the 5-year survival with intact bladder 42.7%.

Conclusions: Comparable results to radical cystectomy in terms of survival can be achieved with the above combination of CT and RT with high rate of bladder preservation.

1401 POSTER

Technetium-99m labelling of monoclonal antibody, C595 for bladder cancer immunoscintigraphy – Pre-clinical evaluation

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Introduction: Current radiological techniques for staging bladder cancer are inaccurate in up to 40% of cases. We have previously reported on the results of Indium-111 labelled C595 monoclonal antibody immunoscintigraphy and showed that it may offer additional information to current staging techniques prior to radical therapy for invasive bladder cancer. Technetium-99m offers advantages over 111In in terms of cost, availability and quality of imaging. The direct reduction mediated method is a reliable technique for labelling antibodies with 99mTc.