significantly higher relapse rate compared to ctx ± rtx, but those pts were salvaged by effective ctx.

1384 POSTER DISCUSSION

Radiotherapy for stage I testicular seminoma – A prospective trial

J. Classen, H. Schmidberger, R. Souchon, M. Bamberg. *Dep. of Radiooncology, University of Tuebingen, Germany*

Purpose: With high cure rates of 95–98% for radiotherapy (XRT) of stage I (CS I) testicular seminoma it is the aim of modern treatment strategies to reduce the intensity of adjuvant XRT without compromising locoregional tumour control. We therefore conducted a multicenter prospective trial for limited XRT of CS I seminoma with reduced treatment portals and small total doses. Data on the "per protocol" population have been reported previously. We now present updated results including data of those patients with protocol violations.

Method: Patients with histologically proven pure CS I seminoma received adjuvant XRT to the paraaortic lymph nodes only. Treatment portals stretched from the upper border of thoracic vertebra 11 (T11) to the lower border of lumbar vertebra 4. The total dose was 26 Gy in 2 Gy daily fractions. Acute and late side effects of treatment were prospectively scored using the EORTC score.

Results: Between 4/91 and 3/94 721 patients were enrolled for the trial. 670 patients were eligible for an interim analysis in 1/99. 483 patients were treated strictly per protocol (PP), 187 patients showed protocol violations (PV). Mean follow up was 55 months. There have been 24 cases of relapse, 18 (3.7%) in the PP and 6 (3.2%) in the PV group. There was no in-field recurrence. 22/24 patients were salvaged with two cases of disease-realted death. Statistical analysis showed no differences in relapse rate nor survival between the study populations. Acute side effects of adjuvant XRT were moderate.

Conclusions: Limited volume XRT for CS I seminoma yields high cure rates with moderate acute side effects.

1385 POSTER DISCUSSION

$E_{400}P$ in good prognosis advanced seminoma. The Spanish germ-cell cancer group experience

J.A. Arranz, X. García del Muro, J. Gumà, J. Aparicio, R. Salazar, A. Saenz, J. Carles, M. Sánchez, J.R. Germà. *On behalf of the Spanish Germ-Cell Cancer Group, Spain*

Objective: To analyse response, toxicity, time to treatment failure (TTF) and survival (OS) in patients (p) with IGCCG good-prognosis advanced seminoma treated with $E_{400}P$ (cisplatin 25 mg/m^2/d and etoposide 100 mg/m^2/d × 4 d).

Methods: Since 1994 63 p with were included, 48 p with advanced disease at diagnosis (76%) and 15 p who relapsed after stage I (13 p follow-up, 1 p RT and 1 p carboplatin × 2 after orchiectomy). Mean age was 38 y (19–83), Metastatic sites were retroperitoneum (89%), mediastinum (10%), other lymph nodes (19%) and lung (2%). Royal Marsden stages were II: 84%, III: 14% and IV: 2%. Sixteen p (25%) had high BHCG levels, 16 p had LDH > 2 × N, and 61 p (97%) were classified as MIRC good-prognosis (*Fosse et al, Eur J Cancer 33: 1380–87*). Number of cycles administered were 3 (7%), 4 (80%), 5 (10%) or 6 (3%); 3 p are still on treatment.

Results: Grade 3–4 toxicities were anemia (3%), thrombocytopenia (3%), neutropenia (32%), mucositis (3%), neurotoxicity (2%), alopecia (96%) and emesis (4%). Twenty-one p (33%) received prophylactic filgastrim and 53/60 p (85%) received ≥80% of the maximum dose intensity. All p responded (72% CR, 28% residual disease). After a median follow-up of 26 m, treatment failed in 4 p (6%). Failure was defined as viable tumor after CT (1 p), regrowth of a residual mass (0 p), relapse (3 p) or unacceptable toxicity (0 p). These 4 p had MRC good-prognosis and normal BHCG; 3 of them were IIa–b. One p is on 2nd CT, the other 3 p achieved a 2nd CR (1RT, 2CT). One p died after a 2nd relapse. Median TTF and OS have not been reached. Three-year TTF and OS are 92.5% (95%CI: 85.4–99.6%) and 97% (95%CI: 91–100%) respectively. All IIc–IV p are alive and their 3-year TTF is 96%.

Conclusion: In our experience, $E_{400}P$ is a safe regimen for patients with good prognosis advanced seminoma. This regimen could reduce acute and late toxicities observed with the more standard $E_{500}P$ or BEP regimens.

1386 POSTER DISCUSSION

Identification of prognostic subgroups in patients (PTS) with poor risk germ cell cancer (GCT): A cart analysis

C. Kollmannsberger[1], C. Nichols[2], C. Meisner[1], J. Beyer[3], A. Harstick[4], J.T. Hartmann[1], L. Kanz[1], C. Bokemeyer[1]. [1]*University of Tuebingen, Germany;* [2]*Health Science University Oregon, United States;* [3]*University of Berlin;* [4]*University of Essen, Germany*

Purpose: Only a few data exist about prognostic criteria within the group of pts who exhibit poor prognostic criteria according to the IGCCCG classification.

Methods: We retrospectively analyzed the data of 332 pts with 'IGCCCG' poor risk GCT using the classification-and-regression-tree model (CART). The following variables were included: primary localization, presence of visceral or lung metastases (met.), presence of an abdominal tumor, number of metastatic sites, levels of β-HCG, AFP and LDH. All patients had been treated with cisplatin/etoposide-based CTx within randomized clinical trials.

Results: Patient characteristics: gonadal/retroperitoneal (G/R) primary tumor 260 pts (78%), mediastinal primary, tumor 72 pts (22%), visceral met. 205 pts (62%), lung met. 247 pts (74%), abdominal tumor 241 pts (73%), elevated AFP, β-HCG or LDH levels 235 (71%), 253 (76%) and 275 (83%) of pts, respectively. Pts with primary, mediastinal disease and lung met. exhibited the worst 3-year PFS (28%), whereas pts with primary G/R disease and without visceral met. showed the longest 3-year PFS (75%). Pts without visceral met and primary G/R tumor had the most favourable 3-year OS (79%). In contrast, pts exhibiting visceral met. from a primary mediastinal tumor displayed the worst 3-year OS (40%).

Conclusion: Different prognostic subgroups can be identified within the group of poor risk GCT. These data may help to estimate detailed individual prognoses and to identify subgroups of high risk pts that may, in turn, be included in new treatment strategies.

1387 POSTER DISCUSSION

Acute and late sequelae in conventionally fractionated and hyperfractionated conformal radiotherapy in prostate cancer. Preliminary evaluation

R. Valdagni[1], C. Italia[1], P. Montanaro[1], A. Lanceni[1], P. Lattuada[1]. [1]*Casa di Cura S. Pio X, Radiation Oncology, Milan, Italy*

Purpose: To evaluate acute and late toxicities in patients affected by prostate cancer treated with conformal radiotherapy using conventional (STD) or pure hyperfractionated (HFX) regimens.

Method: One hundred patients (pts) were treated with 5-field conformal radiotherapy to prostate and seminal vesicles; 85 were evaluable for this analysis. Forty-two pts were treated with STD-CRT at a total dose (ICRU p.p.) of 73.5–75.5 Gy (median: 75.5 Gy; mean: 74.7 Gy); 43 were treated with HFX-CRT at a total dose of 78.3–82 Gy (median: 80.7 Gy; mean: 80.2 Gy). Acute and late toxicities according to RTOG-EORTC criteria were evaluated weekly during CRT, one month after CRT and 3–4 times yearly afterwards.

Results: No significant worsening of acute toxicities was observed using HFX-CRT (grade 2 max. incidence with HFX vs STD: G.I.: 56% vs 62%; G.U.: 33% vs 31%; grade 3 max. incidence with HFX vs STD: G.I.: 0% vs 0%; G.U.: 9% vs 17%). Actuarial probability at 20 months of grade 2 G.U. toxicity was 13% with HFX and 23% with STD, while grade 2 G.I. toxicity was 20% with HFX and 19% with STD. Only one pt, belonging to the STD-CRT group, experienced a grade 3 toxicity (G.U.). Erectile function in pre-radiotehrapy potent patients was maintained at one year in 86% of HFX and 69% of STD pts.

Conclusion: HFX-CRT seems to favourably compare with lower dose STD-CRT with respect to treatment feasibility and acute/late sequelae.

1388 POSTER DISCUSSION

Immunotherapy with the bispecific antibody MDX-H210 (anti-HER2 × anti-CD64) combined with GM-CSF in HER2 positive hormone resistant prostatic cancer

N.D. James[1], P.J. Atherton[1], A.J. Howie[1], S. Tchekmedyian[2], R.T. Curnow[3]. [1]*CRC Institute for Cancer Studies, University of Birmingham, Birmingham, United Kingdom;* [2]*Pacific Shores Medical Group, Long Beach;* [3]*Medarex Inc, Annandale, United States*

Purpose: Treatment of hormone resistant cancer is palliative in nature and new therapies are urgently needed. We report results following treatment with the bispecific antibody MDX-H210 (anti-HER2 × anti-CD64)

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

A. Al-Deen[1], V.R. McCready[2], D.P. Dearnaley[1], J. Treleaven[3]. [1]*Institute of Cancer Research, Academic RT, Sutton;* [2]*Royal Marsden NHS Trust, Nuclear Medicine, Sutton;* [3]*Royal Marsden NHS Trust, Haematology Sutton, United Kingdom*

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?

J. Dawson[1], E. Elves[1], D. Wallace[1]. [1]*University Hospital, Urology, Birmingham, United Kingdom*

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

L. Sengelov[1], C. Kamby[1], H. von der Maase[2], L.I. Jensen[3], F. Rasmussen[4], T. Horn[3], S.L. Nielsen[3], K. Steven[3]. [1]*Herlev University Hospital, Department of Oncology, Copenhagen;* [2]*Aarhus University Hospital, Department of Oncology, Aarhus;* [3]*Herlev University Hopital, Copenhagen;* [4]*Aarhus University Hospital, Aarhus, Denmark*

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

S. Vijayakumar, P.P. Connell, L. Ignacio, R. McBride, R.R. Weichselbaum. *University of Chicago Hospitals, Radiation and Cellular Oncology, Chicago, United States*

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