(52% versus 48%), 3-year EFS was the same in both arms (53%) in salvage treatment. Individual treatment with stem cell rescue as upfront treatment offers a survival benefit.

Methods: Autologous stem cell rescue was provided in our center, from September 1997 to February 2007 to 54 patients. High dose chemotherapy was indicated to 32 patients in salvage setting after 2nd line of treatment (VeIP) and to 22 patients as upfront treatment after 1st line treatment (BEP). Median age was 29 years and tumor markers were elevated: HCG in 10 pts, AFP in 13pts.

Stem cell mobilization was performed after the 3rd cycle of VeIP or BEP in combination with G-CSF. The amount of CD34+ cell/kg b.w. was $2.0-13.4\times10^6$. High-dose conditioning regimen CARBOPEC (carboplatin 1,600−2,200 mg/m^2, etoposide 1,800 mg/m^2, cyclophosphamide 6,400 mg/m^2) was used. The treatment was well tolerated without transplant-related mortality.

Result: WHO criteria non-hematological toxicity was predominantly grade 2 to 3. Engraftment was rapid, recovery of hematopoiesis in neutrofils over 1.0×10^9/l and platelets over 50×10^9/l was reached an average on days +10 and +13 respectively. Additional post-transplant treatment for persistence, progression or relapse had 20 patients (9 pts had 2nd line treatment VEIP, 12 pts had 3rd line treatment with paclitaxel + gemcitabine and 5 pts had retroperitoneal lymphadenectomy).

The follow-up period ranging from 3 to 107 months, at present 40 (74%) patients are alive, 14 (26%) pts died. Median TTP of all pts is 10 months, median OS of all pts is 39 months. Median DFS of surviving pts is 38 months.

Conclusion: high-dose chemotherapy with autologous stem cell rescue in patients with poor risk germ cell tumors is feasible and beneficial method of the individual treatment. High-dose chemotherapy as upfront treatment for poor prognosis germ cell tumors and as salvage treatment in good risk pts seems to be good possibility of the individual treatment.

Supported by Internal Grant Agency of The Czech Ministry of Health, Grant No.8442-3/2005

4531 POSTER

Prognostic significance of primary tumor morphology on progression-free survival (PFS) in patients (pts) with metastatic nonseminomatous germ cell tumors (NSGCT)

M. Fedianin[1], A. Tryakin[1], T. Zakharova[2], I. Fainstein[3], K. Figurin[4], B. Polckii[5], Y. Sergeev[3], A. Garin[1], S. Tjulandin[1]. *[1]N.N. Blokhin Russian Cancer Research Center, Department of clinical pharmacology and chemotherapy, Moscow, Russian Federation; [2]N.N. Blokhin Russian Cancer Research Center, Department of morphology, Moscow, Russian Federation; [3]N.N. Blokhin Russian Cancer Research Center, Department of surgical oncology, Moscow, Russian Federation; [4]N.N. Blokhin Russian Cancer Research Center, Department of urological oncology, Moscow, Russian Federation; [5]N.N. Blokhin Russian Cancer Research Center, Department of thoracic oncology, Moscow, Russian Federation*

Purpose: IGCCCG classification is currently used to determine prognosis of pts with metastatic germ cell tumors. One of the limitations of IGCCCG classification is the absence of data about histological subtypes of primary tumor. We studied the prognostic significance of histological subtypes in pts with metastatic NSGCT.

Patients and Methods: We analyzed data of 693 chemotherapy-naive pts with advanced NSGCT treated in our department from 1987 to 2005 with etoposide- and cisplatin-based regimens (EP, BEP, C-BOP-3BEP and T-BEP). Median follow-up time was 32 months (range 3–215); 181 (26%) pts relapsed. 35 of 250 (19.3%) pts, 51 of 257 (28.3%) pts and 95 of 186 (52.4%) pts from good, intermediate and poor prognostic groups relapsed, respectively. Multivariate Cox regression analysis was performed to determine independent factors, which influenced on progression-free survival (PFS) inside IGCCCG prognostic groups.

Results: Multivariate analysis revealed the following negative prognostic factors as independent: in the IGCCCG good prognostic group – mature and immature teratoma complex in primary tumor (hazard ratio [HR] 3.384; 95% CI 1.534−7.463), absence of embryonal cancer component (HR 2.136; 95% CI 1.251−3.649), number of metastatic sites (HR 2.806; 95% CI 1.487−5.296). In patients with the intermediate prognosis: presence of immature teratoma (HR 1.738; 95% CI 1.132−2.669). In IGCCCG poor prognostic group: presence of non-pulmonary visceral metastases (HR 1.45; 95% CI, 1.056−1.992).

Conclusion: In good and intermediate prognostic groups, morphology of NSGCT has an independent prognostic value. It should be taken in to account while defining the prognosis and choice of treatment.

4532 POSTER

Bone abnormalities in male germ-cell cancer survivors

P.M. Willemse[1], L. van Wulften[1], J. van Steijn[1], N.A.T. Hamdy[2], S. Osanto[1]. *[1]Leiden University Medical Center, Clinical Oncology, Leiden, The Netherlands; [2]Leiden University Medical Center, Endocrinology and Bone metabolism, Leiden, The Netherlands*

Background: Survival of men with testicular cancer is long due to successful therapeutic intervention, which usually includes orchidectomy. Therefore, we studied the prevalence of osteoporosis in a single center cohort of long term survivors of germ cell cancer.

Methods: In a cross-sectional study design, we studied 225 male patients with a mean age of 39.9 years (range 18.2−66.9), who were treated between 1977 and 2006 for germ cell cancer. 223 (99.1%) patients underwent an unilateral orchidectomy and in 2 (0.9%) patients no orchidectomy but retroperitoneal or mediastinal tumor biopsy was performed to confirm the diagnosis. 159 (70.7%) patients received cisplatin-based combination chemotherapy for metastases or primary extra-gonadal tumor at a mean age of 30.9 years (range 14.2−61.1). Between 2003 and 2007, bone mineral density (BMD) was measured at the lumbar spine and femoral neck by DXA and Z-scores calculated. Vertebral deformities were evaluated by a semi-quantitative measurement on lateral x-rays of the spine. Non-vertebral fractures were evaluated by questionnaire and confirmed by x-ray. All patients had normal total testosterone, estradiol, parathyroid hormone, 25(OH)-vitamin D and 1,25$(OH)_2$-vitamin D concentrations, evaluated by fasting blood samples.

Results: BMD was low in 73 (32.4%) patients; 59 (26.2%) patients had Z-scores between −1 and −2 SD, while fourteen (6.2%) had Z-scores below −2 SD. Vertebral deformities were present in 73 of 190 (38.4%) evaluated patients, twenty-five of whom also had low BMD. There was no relationship between vertebral deformities and either age, chemotherapy or testosterone/estradiol levels. No correlation was found between vertebral deformities and low BMD. Nine of 182 (4.9%) patients who responded to the questionnaire had non-vertebral fractures at a mean age of 39.1 years (range 21−51); 1−17 years after the initial diagnosis of testicular cancer.

Conclusions: More than one third of the eugonadal male survivors of germ cell cancer have vertebral abnormalities which are not related to age, chemotherapy or genital hormone concentrations. The underlying mechanism remains unknown. This high prevalence of bone abnormalities indicates that screening should be advocated in all germ cell cancer survivors.

4533 POSTER

Combination of gemcitabine and doxorubicin in sarcomatoid and/or rapidly progressive metastatic renal cell carcinoma (MRCC)

G. Roubaud, M.S. Dilhuydy, G. Pasticier, H. de Clermont, D. Smith, A. Ravaud. *Hôpital Saint André, Department of medical oncology and radiotherapy, urology, nuclear medicine, Bordeaux, France*

Background: Clinical presentation of MRCC could be rapidly aggressive especially when tumor exhibit sarcomatoid or Furhman's grade 4 profile. In 2004, Nanus et al. reported efficacy of the association of Gemcitabine (G) and Doxorubicin (D) in sarcomatoid or rapidly progressive MRCC (Cancer). In this retrospective study, we evaluated G+D in this setting.

Methods: All patients (pts) had MRCC, with sarcomatoid feature or a significant progression in previous 4 months. G: 1500 mg/m^2 and D: 50 mg/m^2 were given every 2 weeks with G-CSF support. Pts were evaluated bimonthly for toxicity using NCI/CTCAE scale and every 4 cycles for efficacy using RECIST criteria.

Results: From June 2003 to August 2005, 29 pts were treated. Five (17%), 19 (65%) and 4 (14%) pts had an ECOG performance status of 0, 1 and 2, respectively. Twenty-one pts (86%) had at least 2 metastatic sites. Sarcomatoid feature was predominant in 6 pts (20%) while 6 pts had papillary tumor. Clear-cell histology was pure in 17 pts (59%) and mixed in 5 pts, while Furhman's grade 4 was predominant. All pts had progressive MRCC in the last 4 months. Twenty-five pts had received a previous systemic therapy. A median of 4 courses of G+D was given. Only 4 pts (14%) had a dose reduction or a time delay for subsequent course. No grade 4 toxicity or drug-related death was reported. One pt had grade 3 vomiting and reversible grade 3 renal insufficiency. No febrile neutropenia was seen. One pt had a partial response (7 months), one pt had a mixed response and 14 pts had a stable disease for at least 4 months for 9 pts. No response was seen in sarcomatoid tumors. The median disease-free survival was 3.7 months, including 8 pts (28%) with a time to progression $\geqslant$6 months and median overall survival was 7.1 months including 6 pts (21%) leaving more than 12 months.

Conclusion: In this study, the combination of D+G in sarcomatoid and/or rapidly growing MRCC showed a lower response rate than previously reported (Nanus. Cancer 2004). Nevertheless, some patients

had prolonged progression free-survival and/or survival, despite an initial unfavorable clinical and/or histopathological presentation. The toxic profile consisted in infrequent grade 3 toxicity and was easily manageable. So far G+D associated with G-CSF could be an option in first line treatment for sarcomatoid tumors where anti angiogenics have no efficacy or when rapid progressions, whatever the histopathologic types, occur following targeted therapies.

4534 POSTER

Phase II study of single-agent vinflunine in platinum-refractory transitional cell carcinoma of the urothelium (TCCU)

C. George[1], D.J. Vaughn[2], D. Petrylak[3], S. Srinivas[4], R. Pili[5], W. Stadler[6], S. De Marco[7], D.C. Smith[8], S. Nason[9], E. De Wit[9]. *[1]Pharmaceutical Research Institute, Global Development, Princeton NJ, USA; [2]University of Pennsylvania, Division of Hematology/Oncology, Philadelphia PA, USA; [3]Columbia University, Medical Oncology, New York NY, USA; [4]Stanford University, Medical Oncology, Stanford CA, USA; [5]Johns Hopkins University, Medical Oncology, Baltimore MD, USA; [6]University of Chicago, Medical Oncology, Chicago IL, USA; [7]San Camillo Forlanini Hospital, Medical Oncology, Rome, Italy; [8]University of Michigan, Medical Oncology, Ann Arbor MI, USA; [9]Bristol-Myers Squibb, Medical Oncology, Wallingford CT, USA*

Background: Vinflunine (VFL) is a new microtubule inhibitor of the vinca alkaloid class with clinical activity in TCCU (S. Culine, BJC 2006). This trial was conducted to define VFL activity in platinum-refractory TCCU patients (pts).
Methods: Global, multicenter, single-arm study. Primary endpoint: response rate (Independent Review; modified WHO criteria). Planned sample size: 150 pts. Main pt eligibility: at least one measurable lesion; documented progression within 12 months of last dose of platinum-containing regimen; calculated creatinine clearance (Cr Cl) >20 mL/min. VFL (320 mg/m^2 IV infusion over 20 minutes) was administered every 3 weeks. In pts with poor performance status, prior pelvic irradiation, or renal impairment (Cr Cl 20−60 mL/min), initial dose (ID) was 280 mg/m^2, escalated to 320 mg/m^2 if well tolerated.
Results (first 114 pts treated; 7 [5 PR, 2 SD] treatment ongoing): Baseline pt characteristics: Male 77%; female 23%. Median age: 66 years (range 40−83). Renal impairment: 40%. Prior chemotherapy: cisplatin: 66%; carboplatin: 44%, gemcitabine: 89%. Refractory status: 77%. Total of 425 VFL cycles administered (range: 1−14+). 320 mg/m^2 ID: 34 pts; 280 mg/m^2 ID: 80 pts. Main toxicity was hematologic (Grade [G] 3/4): neutropenia: 20%/39%; thrombocytopenia: 4%/0%; anemia: 16%/1%; febrile neutropenia: 7% (no pts withdrawn from study). Main non-hematologic toxicities (G 3/4): constipation: 13%/1%; fatigue: 11%/0%. Severe diarrhea or vomiting was infrequent. Only 1 atypical G3 peripheral neuropathy was noted (no G4). IRC response rate was 14.9% (95% CI: 8.9%-22.8%) with median duration of response: 6.8+ months. Stable disease in 42% of pts.
Conclusions: VFL has demonstrated activity and a manageable toxicity profile in pts with platinum-refractory TCCU.

4535 POSTER

Pronostic factors in seminoma

S. Neciosup[1], S. Quintana[1], L. Casanova[1], L. Mas[1], J. Esquerra[2], C. Samanez[1], J. León[1], K. Robles[1], C. Flores[3], H. Gómez[1]. *[1]Instituto de Enfermedades Neoplásicas, Deparment of Medical Oncology, Lima, Peru; [2]Instituto de Enfermedades Neoplásicas, Research Deparment, Lima, Peru; [3]Instituto de Enfermedades Neoplásicas, Statistics Deparment, Lima, Peru*

Purpose: To determine the prognostic factors and to assess the relationship between selected pretreatment characteristics and survival in patients with seminoma.
Patients and Methods: 714 patients with seminoma diagnosed at INEN, Lima-Peru from 1990 to 2005 and were the subjects of the study. We describe the clinic behavior, response to treatment, follow up and survival. The overall patterns were compared in relation to clinical characteristics with Logrank/Breslow test. We identified the prognostic factors through the Cox model. The statistical evaluation was performed with 5% significance level. The results were processed with SPSS v. 12.0 program.
Results: The median age was 33 years (15−80y). The presentation of the primary site was testicular (97.2%), mediastinum (2.2%) and retroperitoneum (0.6%). 54.6% of them were CS I, 29.6% CS II, 15.8% CS III. The involved sites were lungs (4.2%), liver (2.4%) and Central Nervous System (0.6%). According to the IGCCCG risk classification, 83% were low risk (LR) and 17% intermediate risk (IR). The median follow up was 65 months. The patients with CS I, who received para-aortic radiotherapy (RT), had overall survival (OS) at 10 years of 98% in relation to 85% in patients with observation ($p \leqslant 0.001$). In CS II−III patients who received chemotherapy (CT), the OS at 5 and 10 years were 98% and 86% in LR, 73% and 72% in IR respectively. The prognostic factors for the OS were: age >50 years ($p = 0.023$, RR = 2.8), CS II ($p < 0.001$, RR = 19.3), CS III ($p < 0.001$, RR = 54.0) and liver metastasis ($p = 0.025$, RR = 3).
Conclusions: In our study the survival was related with prognostic factors such as age, clinical stage and liver metastasis. The risk qualification was not prognostic factor in our population. We observe that in CS I, radiotherapy was significant in relation to observation in survival. Further studies of tumor biology, including genetic analysis are required to identify other parameters that may correlate with survival.

4536 POSTER

Salvage chemotherapy in patients with recurrent germ cell tumors (GCT)

M. Foldyna, J. Abrahámová, J. Nepomucká, Z. Donátová, E. Vorilková, D. Kordíková. *Thomayer Teaching Hospital, Dep. of. oncology, Prague 4, Czech Republic*

Background: Patients (pts) with relapsed or refractory GCT may be cured by salvage chemotherapy with gemcitabine and paclitaxel. Optimal treatment is unknown.
Methods: Retrospective review of 35 consecutive pts treated with gemcitabine and paclitaxel at Thomayer Teaching Hospital in Prague from 1999 to 12/2006. Highly pretreated patients (chemoterapy BEP – average 4 cycles per patient, chemotherapy VeIP – average 3 cycles per patient, high-dose MTX was applied in 5 pts, high dose chemotherapy Carbopec in 24 pts) were treated with paclitaxel 175 mg/m^2 D1 and gemcitabine 1000 mg/m^2 D1+5, int. 3−4w.
Results: toxicity was quite low, hematological toxicity was manageable with growth factors and replacement of platelets, neurological toxicity grade III was observed in 3 patients, ototoxicity grade III was observed in 1 patient. 9 pts attained CR, 6 pts PR, 11 patients had stable disease, progressive disease was observed in 9 pts. Median OS was 16.2 months.
Conclusion: salvage chemotherapy with paclitaxel and gemcitabine is effective treatment with acceptable toxicity in highly pretreated patients with recurrent germ-cell tumors.
Supported by Internal Grant Agency of The Czech Ministry of Health, Grant No.8442−3/2005.

4537 POSTER

Late recurrences (LR) in germ cell testicular tumours (GCTT): a population-based experience over 23 years

D. Argirovic. *Clinic of Urology Special Urologic office "Cvijiceva", Division of Urologic Chemotherapy, Belgrade, Serbia*

Background: Sparse data are available with regard to incidence, clinical characteristics, therapeutic management and prognosis of pts with GCTT, who relapsed >2 years (y) after initial treatment.
Methods: A review of 1633 pts treated from 1980 to 2003 was conducted. 1504 of 1633 pts (92.1%) who received 1st line treatment were relapse free at 2 y. Among these 1504 pts [710 seminoma (S), 794 nonseminoma (NS)], 37 pts (2.5%) developed LR [10 S (1.4%), 27 NS (3.4%)].
Results: Median age at 1st presentation was 34 y and 27.2 y in S and NS, respectively. Intervals to LR were 31.8 months (mo) (range 25−48) in S and 59.6 mo (range 25–180) in NS. A total of 74.1 of NS but only 40% of S had disseminated disease (ds) at 1st presentation ($p < 0.01$). 25 pts (92.6%) with NS had initially received chemotherapy (cht) vs only 4 pts (40%) with S ($p < 0.01$). AFP was the dominant serum tumor marker elevated. Lymphogenic spread was the predominant pathway of LR metastasis [symptomatic in 17 pts (45.9%)]. The majority of pts presented with far advanced metastatic ds (80% and 88.9% in S and NS, respectively). Of 10 pts with S alive with NED are 7 pts (70%) for MFU of 84.4 mo (range 27–138), whereas 1 pt is alive with stable ds and 2 pts died of ds. Management included radiotherapy (2), cht (5) and surgery (3, combined with CHT in 2 pts) [1 teratoma (T), 2 vital carcinoma (VC)] (multiple procedures in 1 pt). 14 pts (51.8%) with NS are alive and free of ds (AFD) after treatment of LR at MFU of 82.6 mo (range 6–204). 13 pts died (11 of ds, 2 of cht related toxicity). Only 1 of 8 pts (12.5%) managed with CHT alone (PEB, PVI/PEI, CARBOPEC, paclitaxel combined regimens, oral VP 16) is AFD at 36 mo. 13 pts underwent successful surgery for LR, following previous salvage cht in 3 pts, for MFU of 82.6 mo (range 6–204). Cure failed in 1/13 pts (7.7%) with T and in 5/6 pts (87%) with VC (log rank test = 0.0015). Salvage surgery included RPLA (8), redo RPLA (11), neck dissection (1), lung (3) and liver (2) metastasectomy (multiple procedures in 3 pts).Overall AFD are 21/37 pts (56.8%) at MFU of 84.4 mo (range 6–204). Predictive factors for long term CR/NED included extent of ds, AFP < 100 ng/ml, no