were mild. By intention-to-treat analysis, 12 pts (40%) showed stable disease and 11 (36%) showed a partial response while 5 (16%) showed treatment failure. For two pts evaluation of efficacy was impossible due to early withdrawn from the study: in one case the pt refused to continue the treatment and in one case we registered an early progression. 1-year survival probability was 68%; median time to progression was 6.1 months. Median survival has not been reached yet.
Conclusion: At this dose and schedule the combination of GEM and CDDP appears to be active considering that response rate and survival stand in the range of the most active regimens. Considering toxicity, the schedule appears safe even in this special subset of elderly patients. Complete data will be available for the congress.

1311 POSTER

Adjuvant radiotherapy of the cervical carcinoma in elderly patients

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Background: In older cancer patients, comorbidity can have an influence on survival and can enhance the risk of treatment complications. The purpose of the study was to analyze survival and late complications according to performed surgery and postoperative radiotherapy in elderly cervix cancer patients.
Material and Methods: We retrospectively reviewed the medical records of 44 cervix cancer patients older than 60 years, treated by postoperative radiotherapy between 1996–1997 year. Radiotherapy for all patients included doses of 36−45 Gy of 6−10 MV external photons to pelvis in 18−22 fractions and concomitant brachytherapy with ^{192}Ir HDR. Brachytherapy was delivered in 4−5 fractions and 6−7.5 Gy to a dose of 28−35 Gy. The mean age of all patients was 65.5 years (range 60−74). The majority of patients, 39/44, had Stage Ib and the remainder, 5/44, had Stage IIa or IIb. Twenty-nine patients (65.9%) were treated by radical hysterectomy with lymphadenectomy (group I) while 15 (34.1%) by simple hysterectomy (group II).
Results: After a median follow-up of 48 months (range 2−60 months) the actuarial overall survival for all patients was 70.43%. Late gastrointestinal (GI) complications were determined in 40.9% and on urinary (UR) tract in 25%. The doses of external beam irradation were equalized in both groups, while increased brachytherapy dose of 7.5 Gy per fraction was more represented in group I. A larger percent of late GI complications was found in group I vs group II (44.8% vs 33.3%) and also on UR tract (31.03% vs 13.3%).
Conclusions: Postoperative radiotherapy in elderly patients is good tolerated and late complications rate is acceptable with higher complications rate in a case of increased brachytherapy dose and after a more radical surgical procedure.

1312 POSTER

Radiotherapy for nasopharyngeal carcinoma in elderly: a retrospective review of 22 patients

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Background: The incidence of nasopharyngeal carcinoma (NPC) varies extensively with age, ethnic and geographical origin. Radiotherapy (RT) is the standard treatment. The elderly population is increasing in recent years, and the need for cancer care and treatment for the elderly is growing. This retrospective study aimed to evaluate the disease characteristics and outcome of radiotherapy in the elderly with nasopharyngeal carcinoma.
Materials and Methods: Between 1998 and 2002, 22 patients aged 75 and older with pathologically confirmed nasopharyngeal carcinoma were treated with radiotherapy in Taipei Veterans General Hospital. The median age was 77 years (range: 75−87). All patients were male. Clinical stage (UICC 1997) was stage I in 1, II in 4, III in 8, and IV in 9 (IVC in 4), respectively. Eighteen patients (82%) had nodal metastasis. Fourteen patients (64%) had non-keratinizing squamous cell carcinoma. Kaplan-Meier curves were used for evaluation of prognostic factors and were compared using the log-rank test with SPSS 13.0 software. Statistical tests were considered significant at $p < .05$.
Results: The median follow-up time for all patients was 17.1 months (range, 2.4−60.5 months). Twenty (91%) patients received RT alone and two patients received concurrent chemoradiotherapy. Nineteen (86%) patients received curative RT (range: 68−74 Gy), among which 16 completed RT. Three patients received palliative RT (range: 36−54 Gy) and all completed RT. Seventeen (77%) patients received more than 60 Gy. Four (5%) patients experienced grade 3−4 acute side effects and one treatment-related mortality. There are 2 patients with grade 3−4 late side effects (one with nasopharyngeal necrosis and one with radiation encephalopathy) and 6 patients with grade 2 Xerostomia. The 1- and 3-year overall survival rates were 59.1% and 36.4%, respectively. The 1- and 3-year disease free survival rates were 61.1% and 27.8%, respectively. Age $\geqslant$80 years ($p < .001$), M1 stage ($p < 0.001$), stage IV ($p = 0.019$), palliative intent RT ($p = 0.017$), and RT dose <60 Gy ($p = 0.009$) had a poor impact on overall survival.
Conclusions: High dose RT can be achieved in the majority of elderly patients with nasopharyngeal carcinoma and is associated with a low complication rate. Very old age, distant metastasis, and RT dose were important prognostic factors.

Paediatric Oncology

SIOP Europe special session

(Tue, 25 Sep, 09.00−11.30)

1400 ORAL

Late mortality among five-year survivors of cancer in teenagers and young adults in England

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Background: We have previously shown that survival to five years after a diagnosis of cancer in teenagers and young adults (TYAs) has greatly improved during recent decades, but little is known about subsequent mortality. We have analysed mortality in the next five years among five-year survivors of cancer in TYAs diagnosed during 1979–1998 in England.
Materials and Methods: 19,223 cancer patients aged 13−24 years diagnosed in 1979–1998, who had survived at least five years in England, have been included in the analysis. Cancer diagnosis and vital status for each patient were obtained from national cancer registrations for England. Patients were grouped using a specialized TYA diagnostic classification. Cumulative excess mortality for all causes in the next five years after surviving five years from diagnosis was calculated by taking into account of the sex, age, deprivation index and calendar year specific national mortality rates. Cumulative excess mortality in patients diagnosed during 1990–1998 was compared with a corresponding cohort diagnosed in 1979–1989 using Poisson regression (Dickman et al, 2004), allowing for sex, age at diagnosis and socioeconomic deprivation.
Results: Overall, the excess risk of dying of all causes in the next five years after surviving five years from diagnosis during 1979–1989 and 1990–1998 fell from 6.4% to 4.8% ($p < 0.001$). The decrease in cumulative excess mortality was most pronounced in patients with leukamia (14.5% to 7.5%), lymphoma (6.5% to 3.4%), and germ cell tumours (1.8% to 0.7%) (in all groups, $p < 0.01$). There were non-significant reductions for bone tumours (9.4% to 7.9%), melanoma(5.8% to 4.6%), and carcinomas (4.1% to 3.3%). There were non-significant increases for central nervous system (11.6% to 14.9%) and soft tissue sarcomas (9.2% to 10.4%).
Conclusions: Overall, the improvements in five year survival have been accompanied by a reduction in the risk of death during the subsequent five years. However mortality is high compared with the general population. Causes of late mortality should be investigated.

1401 ORAL

The biological basis of ploidy as a genetic marker for the distinct clinical behaviour of neuroblastic tumours

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Background: Neuroblastic tumors (NBTs) are biologically very heterogeneous and may display radically different clinical behavior. Ploidy has been correlated with clinically relevant subgroups of NBTs. Favorable NBTs are characterized by near-triploid DNA content whereas unfavorable NBTs are

near-diploid/tetraploid. In this study we approached the biological basis of ploidy in order to unveil the genetics behind each relevant subgroup of NBT.
Material and Methods: 49 NBTs with available ploidy data were evaluated by microarray gene expression analysis. Genes with high expression variability were selected by determining standard deviations higher than a factor 2- and 3-fold the sample means. Differential gene expression was validated on 46 independent primary NBTs using quantitative real-time PCR (qPCR). Concomitant gene copy number analysis was performed on 27 out of these 46 NBTs by qPCR to ascertain the correlation between gene expression level and DNA copy number.
Results: Pair wise comparison analysis of near-triploid versus near-diploid/tetraploid NBTs revealed 254 statistically differentially expressed genes capable of significantly discriminate between the 2 groups. A large set of these genes mapped to chromosomal regions with described recurrent abnormalities in NBTs; chromosome 1, 36/254 genes ($p = 0.01$); chromosome 17, 33/254 genes ($p < 0.0001$); and chromosome 19, 26/254 genes ($p = 0.05$).
To validate microarray gene expression data, 13 genes on chromosomes 1 and 17 were analyzed in 46 NBTs by qPCR. The expression levels identified by qPCR confirmed the microarray data; 77% of the analyzed genes maintained statistically significant differences between groups.
Four genes on chromosomes 1 and 17 were further analyzed for gene copy number by DNA qPCR. Gene copy number results in near-triploid NBTs were suggestive of tri- or tetrasomies, while near-diploid/tetraploid NBTs displayed normal somies.
Comparison between DNA copy number and gene expression levels revealed a higher expression in near-triploid NBTs in contrast to a lower expression in near-diploid/tetraploid NBTs than expected according to gene copy number.
Conclusions: Gene expression profile analysis of NBTs with different DNA content revealed a relevant list of genes differently expressed mapping at specific chromosomal regions. No correlation between gene expression levels and DNA copy number was found, suggesting specific tumorigenic transcriptional regulation mechanisms other than gene dosage effect.

1402 ORAL

Body mass index in adult childhood cancer survivors after treatment with potential cardiac and vascular toxicity

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Background: We performed a cross-sectional study on cardiovascular status in childhood cancer survivors (CCS) who received treatment with potential cardiac and vascular toxicity. Since overweight is considered an important risk factor for cardiovascular disease, we evaluated body mass index (BMI; weight/height^2) at several timepoints post-treatment and assessed the relation between under-/overweight and cancer treatments.
Patients and Methods: Inclusion criteria: treatment with anthracyclines (A+/A−), platinum (P+/P−) and/or radiotherapy; age at diagnosis $\leqslant$21 yrs; current age $\geqslant$18 yrs; no evidence of disease and $\geqslant$5 yrs post-treatment. Heights and weights were collected at 4−6 yrs (T5), 9−11 yrs (T10) and $\geqslant$15 yrs post-treatment ($T \geqslant 15$). In adults, BMI < 18.5 kg/m^2 was defined as underweight and BMI $\geqslant$ 25 kg/m^2 as overweight. For children, BMI-equivalents were used according to Cole et al (2000) and Van Buuren et al (2004). Logistic regression was used to study the relation between under-/overweight and the several treatment modalities with adjustment for age at diagnosis.
Results: The inclusion criteria were met by 372 CCS (212 males). Median (range) age at diagnosis was 9.3 (0−21.3) yrs.
At T5 ($n = 301$; age 15.2±4.9 yrs), underweight was found more frequently in A+ CCS versus A− CCS (OR 2.30; CI 1.03−5.16), especially if also treated with alkylating agents (AA) (OR 3.11; 1.05−9.26).
At T10 ($n = 250$; age 19.6±4.7 yrs), the risk of underweight in A+ was not different from A−, however in A+ the effect was dose-related: OR 1.43 (1.07−1.92) per 100 mg/m^2 increase. CCS with cranial or craniospinal radiotherapy (CRT) had less frequently underweight versus CRT− CCS (OR 0.46; 0.21−0.99), but after CRT and steroids the risk of overweight was increased (OR 2.82; 1.17−6.80).
At $T \geqslant 15$ ($n = 198$; age 28.7±6.9 yrs), the risk of underweight in A+ CCS was increased after A$\geqslant$300 mg/m^2 (OR 3.73; 1.11−12.57) or after A in combination with AA (OR 10.72; 1.33−86.46). The risk of overweight was increased in CCS who received CRT (OR 2.83; 1.50−5.34) and in CCS who received CRT in combination with steroids (OR 4.45; 2.01−9.86).
At T5, T10 and T$\geqslant$15, P+ CCS had no more under-7sol;overweight versus P− CCS.
Conclusions: In a CCS-cohort treated with potential cardiac and vascular toxic treatment, A+ CCS were at increased risk of underweight, especially if A dose was higher and if treatment was combined with AA. Furthermore, CRT+ CCS were at increased risk of overweight, especially if CRT was combined with steroids.

1403 ORAL

Fenretinide enhances the antitumour efficacy of bortezomib on human neuroblastoma cells

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Background: Neuroblastoma (NB) is the most common and deadly extracranial solid tumour of childhood and so far is still refractory to conventional therapy. The proteasome inhibitor bortezomib was able to inhibit cell growth and angiogenesis in neuroblastoma (Brignole et al., JNCI 98:16, 2006). Moreover, bortezomib has been shown to induce additive or synergistic activity when combined with several other antineoplastic agents. Here, we assayed a putative increased antitumour activity of bortezomib if delivered to NB cells together with fenretinide, a synthetic retinoic acid used as potential therapeutic agent in a variety of cancers, including NB.
Materials and Methods: Different NB cell lines were tested for sensitivity to bortezomib and fenretinide, when both of the drugs were given to the cells alone or in different dose-and time-dependent combination schedules. Cell proliferation, cell viability and apoptosis were evaluated by measuring 3H-thymidine incorporation, trypan blue staining, DNA fragmentation and western-blot analysis. A mouse xenograft model that mimics the growth and spread of NB in humans was set up to examine in vivo sensitivity of NB to bortezomib and fenretinide. Histologic analysis of mouse orthotopic tumours was performed.
Results: A short (1−4 hours) pre-incubation with 2.5 μM fenretinide caused >50% inhibition of cell growth when NB cells were treated with 5nM bortezomib at 24 hours: these values correspond to at least the half concentration necessary to have the same results when both drugs were administred alone. These results were not obtained when bortezomib was administred to NB cells at the same time or before fenretinide. Preliminary experiments seem to suggest that NB cell death, triggered by the combination of the two drugs, occurs with apoptosis features via ER stress and suppression of the unfolded protein response, that is translated in the activation of different genes, related to these precesses. Furthermore, mice treated with fenretinide followed by bortezomib lived statistically significantly longer than either control mice or mice treated with each single drug.
Conclusions: Our findings provide the rationale for design a new therapeutic strategy to treat pediatric neuroblastoma, based on this pharmacological combination.

1404 ORAL

Proton beam therapy for children with sarcomas: The University of Tsukuba experience

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Background: Proton beam therapy has an excellent dose-localization capability because the beams have a finite range of penetration. It is expected to reduce treatment-related morbidities especially for children who are growing. We reviewed children with various sarcomas irradiated with proton beams to examine its feasibility and efficacy.
Methods and Materials: Between 1984 and 2005, 31 children with typical childhood sarcomas, aged 1 to 15 years, were treated with proton beam therapy at University of Tsukuba. There were 17 boys and 14 girls. Of the 31 children, 13 had rhabdomyosarcoma, 4 PNET, 3 neuroblastoma, 3 hepatoblastoma, 2 osteosarcoma, and 6 miscellaneous. All 13 children with rhabdomyosarcoma had IRS Group III tumors. Sites of irradiation were head and neck for 21 children, abdomen and pelvis for 6, and miscellaneous for 4. Thirty-one children also received chemotherapy prior to proton beam therapy. Of the 31 children, 1 had osteosarcoma of the left arm for which 100 Gy of proton dose in 5 fractions was given. For another 26 children, median 45 Gy (range, 18−73.2 Gy) in median 35 days with median daily dose being 2.0 Gy (1.8−4.2 Gy) were given using proton beams alone. Remaining 5 children were irradiated with a combination of