Materials and Methods: Data on the entire Norwegian married population aged 17−69 with children under the age of 20 in 1974–2001 (N = 1.04 million couples) was retrieved from the Cancer Registry, the Central Population Register, the Directorate of Taxes, and population censuses. Divorce rates for 4524 couples with a child with cancer were compared to those of otherwise similar couples by means of discrete-time hazard regression models.
Results: Cancer in a child was not associated with an increased risk of parental divorce overall, or for any of the more common cancer forms among children. A tendency towards an increased divorce risk (OR 1.34, CI 1.00−1.81) was observed for parents' of children with renal cancers (primarily Wilm's tumor). Neither age, time from diagnosis, nor prognosis influenced the estimates adversely. The death of a child with cancer did not influence the divorce rates significantly in either direction. Couples with mothers with an education above high school level did, however, display significantly increased divorce rates (OR 1.19, CI 1.05−1.36). The risk was particularly high shortly after diagnosis. Other risk factors for these couples were CNS cancer, age 5−9 years, and death of a child.
Conclusions: This large registry-based study has shown that contrary to existing myths, cancer in a child is not associated with an increase in parental divorce risk. An exception exists for couples with highly educated mothers. This may relate to these mothers' wish to work outside the home, which may be difficult given an increased care burden at home. Shared parental responsibility for children and thus a shared provision of care is more common among women with a high education versus a low education in Norway. Further studies are, however, clearly warranted to understand the background for the observed increase in divorce risk for these couples.

4105 ORAL

Is institution a prognostic factor in adolescent and young adult patients with osteosarcoma?b

D. Carrle[1], B. Blank[1], M. Paulussen[2], P. Reichardt[3], S. Bielack[1]. *[1]Klinikum Stuttgart, Olgahospital – Pediatrics (Oncology Hematology Immunology), Stuttgart, Germany; [2]Universitätskinderspital beider Basel, Pediatric Oncology and Hematology, Basel, Switzerland; [3]HELIOS-Klinikum Bad Saarow, Sarkomzentrum Berlin-Brandenburg, Bad Saarow, Germany*

Background: Compared to paediatric cancer patients adolescents and young adults may have disadvantaged access to care. Therefore we investigated the correlation of patient, tumour and institutional characteristics with the outcome of osteosarcoma in this age group.
Material and Methods: Analysis of consecutive patients aged 15−24 years with newly diagnosed high-grade osteosarcoma entered into the Cooperative Osteosarcoma Study Group (COSS) registry 1980–2004 and treated in pediatric (PO) or medical oncology institutions (MO). Standardised multimodal therapy according to a COSS-protocol. Event-free survival rates (EFS) evaluated in relation to patient demographics and registering institution (MO vs PO and treatment volume as: $\leqslant$3 or >3 osteosarcoma/year).
Results: 944 patients identified (median age: 17.35 years; range: 15.01−24.99; 79% aged <20 years). Patients $\geqslant$20 years were more likely than younger patients to be treated in centers with low treatment volume ($p < 0.0001$) and MO ($p < 0.0001$) but otherwise comparable. After a median follow-up of 5.59 years (range: 0.12−27.92) for all patients and 8.08 years (range: 0.19−27.92) for 617 survivors, actuarial 5/10 year event-free survival probability (EFS) was 58%/54%. Upon univariate analysis of the total cohort neither of the institutional variables correlated significantly with EFS. There was a correlation between treatment in PO and improved EFS for patients $\geqslant$20 years ($p = 0.001$) and for those with primary metastases ($p = 0.009$). Upon multivariate testing type of center (odds ratio: 1.26; $p = 0.022$) but not treatment volume were significant.
Conclusions: Within a framework of standardised regimens and consultation support by our group's infrastructure, similar EFS-probabilites were obtained regardless of institutional treatment volumes. Observed variations in outcome between PO and MO may be partly due to different distributions of presenting factors but deserve further investigation.
Acknowledgement: Supported by Deutsche Krebshilfe, Thanks to M. Kevric and E. Hallmen for data management.

Poster presentations (Thu, 24 Sep, 09:00−12:00)
Paediatric oncology

4106 POSTER

Atypical Teratoid and Rhabdoid tumours in children: the French experience since 1998

A. Beaugrand[1], M. Quidot[2], P. Varlet[3], F. Bourdeaut[4], P. Leblond[5], J. Grill[1], M.C. Le Deley[2], C. Dufour[1]. *[1]Institut Gustave Roussy, Paediatrics, Villejuif, France; [2]Institut Gustave Roussy, Biostatistics, Villejuif, France; [3]Sainte-Anne Hospital, Neuropathology, Paris, France; [4]Institut Curie, Inserm U509 Laboratoire Pathologie Moléculaire des Cancers, Paris, France; [5]Centre Oscar Lambret, Paediatrics, Lille, France*

Background: To describe clinical features and therapeutic approaches and to identify prognostic factors in children with ATRT of the CNS.
Material and Methods: Observational study including all patients aged less than 18 years, diagnosed with CNS ATRT in France between January 1998 and July 2008, identified from hospital files and French Pediatric Cancer registry. Pathology review included histological and immunohistochemical analysis, including INI-1 staining. Impact of clinical characteristics (age, sex, site of primary tumor and metastatic status) on the overall survival (OS) was assessed using Cox models.
Results: seventy out of the 71 patients identified with ATRT over this 10-year period were included in the study (1 patient excluded due to incomplete clinical data). Median age was 2.8 years (range, 15 days – 12.8 years). Primary tumor site was supratentorial (ST) in 34, posterior fossa (PF) in 30, mixed (ST+PF) in 2 and medullar in 4 patients. The disease was disseminated at diagnosis in 22 patients. Five patients had non-CNS disease associated with CNS disease. Surgical resection was complete in 41 patients. Adjuvant therapy included chemotherapy in 55 cases and radiotherapy in 20 patients. Chemotherapy regimens were not standardized more than the study period: ATRT04, PNET High Risk and BB SFOP protocols were most frequently used. Median follow-up was 52 months (range, 13 months – 10 years). Disease progression or relapse occurred in 51 children. Median time to progression/relapse was 4.4 months. Median survival time was 9.9 months. One-year progression-free survival and OS were 21% and 42%, respectively. Metastatic status at diagnosis was the only prognostic factor (Hazard ratio for death: 2.1, 95%CI: 1.2−3.8, $p = 0.01$).
Conclusion: Children with ATRT of the CNS have a dismal prognosis. Innovative therapeutic are urgently needed.

4107 POSTER

Extended low-dose temozolomide induces severe lymphopenia in children with brain tumours: a phase II clinical trial

V. Ridola[1], G. Barone[1], I. Lazzareschi[1], A. Ruggiero[1], D. Rizzo[1], R. Riccardi[1]. *[1]"A. Gemelli" Hospital UCSC, Department of Pediatric Oncology, Roma, Italy*

Background: Standard schedule temozolomide (TMZ) with oral daily doses 200 mg/m^2 for 5 days every 4 weeks, has been utilized in children with progressive or relapsed brain tumours or with high grade glioma (HGG) at diagnosis. With this schedule manageable hematological toxicity and limited antitumor activity have been observed. Clinical and preclinical studies have shown that TMZ activity is highly schedule dependent. Extended TMZ dosing regimens may be more effective that standard regimens resulting in an higher cumulative dose over time.
Patients and Methods: We assessed the toxicity of a new extended low-dose schedule of TMZ in children with progressive or relapsed brain tumours or with HGG at diagnosis. Seventeen children were considered eligible for the study. Median age at diagnosis was 12.5 years (1 y-17 y). A total of 156 courses were administered, with a median number of 6 courses per patient (range: 2−22). TMZ was administered at 70 mg/m^2/day orally for 21 days every 28 days, as reported in adults studies. Heavily pre-treated patients started at a dose of 50 mg/m^2/day. Histological diagnosis showed 5 Ependymomas, 3 Low Grade Gliomas, 9 High Grade Gliomas.
Results: No toxic deaths or extra-haematological toxicity occurred. Grade IV and III lymphopenia occurred in 22.4% and 10.8% of courses, respectively. Grade III thrombocytopenia occurred in 0.6% of courses. Grade IV and III neutropenia occurred in 1.9% and 0.6% of courses, respectively. Among the patients showing lymphopenia, we observed 1 case of disseminated Zoster (meningoencephalitis and cutaneous involvement), 1 case of prolonged Rotavirus gastroenteritis, and 2 cases of herpetic stomatitis. The objective response rate was 11.8%. Overall, 82.3% of patients showed stable disease.
Conclusion: Our extended schedule was safe and well tolerated. No further cases of neutropenia or thrombocytopenia were observed despite the higher cumulative dose of the drug. Nevertheless, the prolonged

exposure to TMZ at a low dose induced lymphopenia and might be responsible for a higher rate of viral infections.

4108 POSTER

Reduced intensity conditioning regimen and allogeneic stem cell transplantation from related or unrelated HLA identical donor in high risk neuroblastoma

A. Prete[1], R. Rondelli[1], F. Locatelli[2], E. Lanino[3], C. Favre[4], M. Rabusin[5], A. Pession[6], F. Fagioli[7]. [1]*Ospedale S. Orsola Malpighi, Oncology and Hematology Pediatric Department, Bologna, Italy;* [2]*IRCCS S. Matteo, Oncology and Hematology Pediatric Department, Pavia, Italy;* [3]*G. Gaslini Institute, Oncology and Hematology Pediatric Department, Genova, Italy;* [4]*Clinica Pediatrica, Oncology and Hematology Pediatric Department, Pisa, Italy;* [5]*IRCCS Burlo Garofaolo, Oncology and Hematology Pediatric Department, Trieste, Italy;* [6]*S. Orsola-Malpighi, Oncology and Hematology Pediatric Department, Bologna, Italy;* [7]*Ospedale S. Anna, Oncology and Hematology Pediatric Department, Torino, Italy*

Background: To evaluate the feasibility and efficacy of a reduced intensity conditioning regimen (RIC) followed by allogeneic stem cell transplantation (SCT) from related or unrelated HLA identical donor (MUD) in neuroblastoma (NB) poor responder to front line therapy or relapsed after a previous autologous stem cell transplantation.
Methods: 19 patients (pts), aged 3−17 years, affected by resistant (5) or relapsed (14) NB were enrolled and submitted to an SCT after a RIC consisting of Thiotepa 15 mg/kg and Melphalan 140 mg/sqm. The donor was an identical sibling in 11 cases or a MUD in 8. At time of transplant 14 pts were in any kind of remission of disease and 5 in progressive disease. Graft versus host disease (GVHD) prophylaxis consisting of Cyclosporin A $\pm$ Anti-lymphocytic serum and short term methotrexate in MUD setting. Stem cell sources were bone marrow in 15 cases and peripheral blood in 4.
Results: The reconstitution of bone marrow function was obtained in all the 19 pts after a median time of 12 and 17 days for PMN and PLT respectively in sibling setting, and 14 and 17 days in MUD setting. Acute GVHD of grade II-III occurred in 7 pts and a complete marrow donor chimerism was observed after 40 and 60 days in sibling and MUD setting respectively. After a median follow-up of 25 (6−41) months, 9 pts relapsed, 6 dead for progressive disease and 10 are alive and well. The median time of relapse from SCT was 9 (3−25) months. No pts dead for treatment related causes (TRM). The 3 years probability of overall survival (OS) and event free survival (EFS) of the entire cohort of pts were respectively 0.58 (0.13) and 0.30 (0.13), with a better SUR and EFS for pts who developed grade II-III acute GVHD (SUR 0.67 versus 0.44; EFS 0.30 versus 0.22), were in any kind of stable disease (SUR 0.62 versus 0.53; EFS 0.41 versus 0 p = 0.041), received a MFD graft (SUR 0.62 versus 0.50; EFS 0.32 versus 0.25).
Conclusions: Our experience show the feasibility and efficacy of a RIC with SCT from HLA MFD or MUD in the treatment of relapsed or refractory NB. In fact no patient suffered TRM. Moreover in a setting of pts who the 3 years probability of survival is nearly to zero, in our experience more than 50% are alive and well. The observation that the develop of acute GVHD is related to a better outcome may offer the evidence of graft-versus-tumour in NB.

4109 POSTER

Rodent parvovirus H1 induces lytic infection in human neuroblastoma cells and down-regulates N-myc expression in N-myc amplified neuroblastoma cell lines

J. Lacroix[1], J. Li[1], B. Leuchs[1], H.E. Deubzer[2], O. Witt[2], J. Rommelaere[1], J.R. Schlehofer[1]. [1]*German Cancer Research Center, FS Infection and Cancer, Heidelberg, Germany;* [2]*University Children's Hospital, Paediatric Hematology Oncology and Immunology, Heidelberg, Germanyi*

With about 15% of all deaths in pediatric oncology advanced localized and high risk neuroblastoma remains a main therapeutic issue. Thus, despite applying multimodal therapeutic concepts, new modalities for the treatment of neuroblastoma are urgently required. H1-PV is an oncolytic wildtype Parvovirus in rodents. So far, no relevant pathogenic effects have been observed in laboratory animal populations, widely infected with H1-PV. Additionally, no pathogenicity and low immunogenicity of H1-PV infection have been observed in humans. Here, we investigated, whether the oncolytic H1-PV is cytotoxic for neuroblastoma cells.
Neuroblastoma cell lines with different MYCN status as well as normal primary cells of different origin were infected with H1-PV. We determined infection efficacy, viral replication, lytic activity and cell viability and effects of H1-PV on N-myc expression in vitro.
Non-neoplastic infant cells (myocardial myocytes, glia cells, astrocytes and neuronal cells in short term culture) could be shown to be unaffected in viability and morphology by H1-PV. In contrast, all 11 neuroblastoma cell lines analyzed were infectable with H1-PV, and H1-PV actively replicated in neuroblastoma cells with virus titres increasing up to 10.000-fold within 48 to 96 hours after infection. Parvovirus H1 induced lytic infection in all 11 neuroblastoma cell lines after application of MOIs between 0.001 and 1 pfu/cell. The lytic effect of H1 was independent of MYCN oncogene amplification or differentiation status of the respective cell line. Moreover, H1-infection could be demonstrated to down-regulate the protein level of N-myc in N-myc amplified neuroblastoma cell lines.
The application of H1-PV appears to be a promising treatment option for neuroblastoma. The treatment efficiency is currently analyzed in a rat xenotransplant model.

4110 POSTER

Survivors after childhood malignant lymphoma (MLCSs): what do they know about their diagnosis and treatment?

S. Hess[1], H. Hamre[1], C. Kiserud[1], J.H. Loge[1], S.D. Fossâ[1]. [1]*Rikshospitalet – Radiumhospitalet Trust, Clinical Cancer Research, Oslo, Norway*

Background: MLCSs are at risk for long term effects, but need to have knowledge about their diagnosis, treatment and possible late effects in order to take responsibility for their own health.
Methods: 215 adult MLCSs were invited to participate, 145 (67%) responded. So far 115 MLCSs have completed physical examination, blood sampling, cardiopulmonary tests and responding to a questionnaire evaluating health problems. Before the clinical examination, they were interviewed about their awareness of their malignancy and treatment. Their responses were compared with medical record data.
Results: Sixty-two were males (54%), 53 females (46%). Median observation time was 21 years (range: 7−37 years). The median age at diagnosis was 13 years (2−18), the median age at survey was 34 years (19−55). 71 (62%) had Hodgkin lymphoma (HL), 44 (38%) had non-Hodgkin lymphoma (NHL). 108 (94%) reported their diagnosis correctly, 7 (6%) reported that they had cancer, but did not identify malignant lymphoma. 28 (26%) could not differentiate HL vs NHL.
103 patients (90%) had been treated with chemotherapy (CT), of whom 37 with CT only. 78 patients (76%) had undergone radiotherapy (RT), 12 with RT only. 66 patients (64%) had been treated with both CT and RT.
109 of 115 (95%) reported their treatment modalities correctly. Among the 103 treated by chemotherapy, 73 (71%) did not know the name of any cytostatic drug. Of the 78 who had received radiotherapy, 73 (94%) described the radiation site precisely. Only 13 (11%) had – on request – received a written summary of their disease and treatment, and 96 (84%) reported that they were not regularly followed as to long-term effects. 75 (65%) were not aware of the risks for long-term effects and consequences of their treatment.
Conclusion: MLCSs in Norway seem to have a sufficient level of knowledge about their diagnosis and treatment modality. But they have a low level of knowledge about consequences and long-term toxicity. In general they have received verbal, but not written information about their disease and treatment. Improved communication seems necessary between MLCSs and the responsible health care team, both at the end of oncological follow-up and during subsequent years.

4111 POSTER

Esthesioneuroblastoma in children and adolescents: experience on 11 cases with literature review

O. Oberlin[1], J.L. Habrand[2], F. Janot[3], L. Amoroso[1], D. Couanet[4], M. Elkababri[1]. [1]*Institut Gustave Roussy, Paediatrics, Villejuif, France;* [2]*Institut Gustave Roussy, Radiotherapy, Villejuif, France;* [3]*Institut Gustave Roussy, Surgery, Villejuif, France;* [4]*Institut Gustave Roussy, Radiology, Villejuif, France*

Background: Esthesioneuroblastoma (ENB) is an uncommon malignancy developing from the olfactory placode, in the superior nasal vault. Purpose of this study was to review the cases of paediatric ENB treated at the Pediatric Department of the Institute Gustave Roussy (IGR).
Material and Methods: Between 1982 and 2002, eleven children and adolescents with histologically proven olfactory neuroblastoma were treated at IGR. Therapy included chemotherapy, administered before surgery, and radiotherapy.
Results: 10 out of 11 patients received chemotherapy. Only one patient underwent surgery before radiation therapy and did not receive chemotherapy. All patients underwent radiotherapy. The response to chemotherapy could be assessed in 10 patients of whom 7 achieved complete or partial response. One patient achieved complete response by chemo- and radiation therapy alone. After an 8.8 years median follow-up (range, 3.9−16.4 y), 10 patients were survivors. Only one patient relapsed locally and at distant sites 9 months after the diagnosis, and died after few