undergoing lap-assisted anterior resection (but not abdomino-perineal resection) but this is not currently supported by the 3-year disease free survival data.

44 Abstract not received

Scientific Symposium
Brain tumours in childhood – problems and new concepts

45 INVITED

Hyperfractionated radiotherapy for PNET

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Background: In children with standard risk PNET (medulloblastoma) hfx-RT may allow a higher local total dose (68–72 Gy) in order to improve tumour control within the posterior fossa (PF) and reducing long-term toxicity in normal brain compared with conventionally fractionated RT (36 Gy). In high risk PNET hfx-RT (40 Gy CSA/68–72 Gy tumour site) results in increased tumour cell kill without increasing normal tissue toxicity. The rationale for hyperfractionated radiotherapy (hfx-RT) is to try to reduce delayed effects of radiation injury and to prevent tumour repopulation by giving more than one radiation fraction per day in smaller doses per fraction.allowing a redistribution of proliferating tumour cells with some cells entering a radiosensitive stage. Other non-proliferating or dose-limiting tissue, such as normal brain, will potentially be spared.
Methods: Results from retrospective and prospective series and present observations of ongoing phase II trials were analysed.
Results: *In standard risk disease* 5 year PFS was 76 and 79% (Ricardi et al., 1997, Prados et al., 1993). In the recent SFOP study (1.0 Gy bid. 36 Gy CSA/68 Gy tumour) the 3 year PFS was 81% (overall survival 89%) without chemotherapy. No decrease in intelligence was observed in 22 children tested during the first 2 years (Carrie et al., 2005). The SIOP–HIT PNET IV study is currently investigating this concept in a prospective randomized study and compares hfx-RT (1.0 bid./CSA 36 Gy/PF 60 Gy tumour 68 Gy) with conventionally fractionated RT (CSA 23.4 Gy/PF 54 Gy) followed by 8 courses Cisplatin, CCNU, VCR. *In high risk disease* 14 of 15 patients (93%) remained disease free for a median of 68 months (Allen et al., 1997). In the Milan study, hyperfractionated-accelerated RT (1.3 Gy bid. 39 Gy CSI/1.5 Gy bid. 21 Gy PF boost) was delivered to 31 pts (median age 9 yrs) combined with high-dose sequential postoperative CT. 5 yrs PFS, EFS, and OS were 75%, 72%, and 76% respectively. The UKCCSG phase 1study investigates hyperfractionated accelerated RT (HART) with cisplatin, vincristine and CCNU chemotherapy. In the ongoing HIT 2000 study (intensive chx. followed by hfx-RT 1.0 Gy bid. CSA 40 Gy, boost, 60–68 Gy) only 18/110 patients (16.4%) (0–51 months) showed progressive disease. Data on late effects are not yet available.
Conclusion: Hfx-RT is a novel approach to improve tumour control and survival in standard and high risk PNET. Results of phase II studies are promising. In standard risk PNET a preservation of neurocognitive function might be possible. Quality of life as an endpoint is of increasing importance.

46 INVITED

Treatment of PNET in children without radiotherapy

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Young children with medulloblastoma have a dismal prognosis and morbidity is high with standard therapy including craniospinal irradiation (CSI). Two recently published national trials (one from Germany and one from France) have shed some light on the possibility to treat some children without using CSI. To analyse these results, three groups of patients can be defined a priori: R0M0 (no residue, no metastasis), R1M0 (radiological residue only) and RXM+ (presence of metastasis whatever the residue). Despite the use of completely different chemotherapy regimens and salvage strategy, both trials have shown that more than 70% of children with R0M0 disease can be cured without craniospinal irradiation. In the German trial, these results were obtained after an intensive methotrexate-containing chemotherapy while in the French trial two third of the survivors required a salvage regimen with high-dose chemotherapy. Patients with RXM+ and R1M0 diseases have a poorer prognosis when treated with conventional chemotherapy only. In both trials, desmoplasia was an indicator of better prognosis. In addition, in the French trial, a poorer outcome was observed for patients with subtotal resection (ie surgical report indicating microscopic tumor remnants despite the absence of radilogic residue on early postoperative scans). Both trials claimed an improved intellectual outcome albeit different scales were used for neuropsychologic assessment. Concurrent trials still ongoing or recently completed in the USA and in UK seem to have similar results for R0M0 patients with protocols including early posterior fossa irradiation together with conventional chemotherapy.The brain tumor comittees of the International Society of Pediatric Oncology (SIOP) and the Children's Oncology Group (USA, Canada, Australia) have started the process to build up a common randomized trial in this category of patients (localized medulloblastomas) to compare the different strategy both in terms of survival and in terms of cognitive outcome. The progresses of this endeavour will be presented at this meeting.

47 INVITED

Modern approach to childhood low grade glioma

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The treatment of childhood low grade glioma (LGG), if not amenable to complete resection, quite often is a relevant clinical challenge. LGG in many instances are indeed slow growing tumours, which, if not controlled, can cause severe morbidity and ultimately jeopardize life. Most of the time children bearing an unresectable LGG can be considered affected by a chromic disease, deserving protracted cures. The treatment philosophy, which has dictated the treatment of malignant cancers, has also inspired the therapeutic concepts for managing childhood LGG. However, it is getting more and more evident that different strategies are needed for them. LGG represent a highly heterogeneous group of neoplasm and comprehensive treatment concepts rarely meet the individual patient's needs. After more than 20 years of clinical research it can be stated with confidence that for unresectable, progressive LGG, chemotherapy (CT) represents an effective treatment modality. It delays tumour growth and postpones the use of radiotherapy (RT), thus sparing the deleterious effects of irradiation on a developing brain. However, CT rarely cures LGG and definitively obviates the need of RT or aggressive surgery. Furthermore, little is known on the actual impact of CT on patients' overall health status. Recent progresses in RT delivering techniques, which allow reducing the safety margins, are tempering the concerns related to the use of this treatment modality in children. While waiting for more biological based therapeutic approaches, CT and RT (other than surgery) are the present tools for treating childhood LGG, which seems to be working best if guided by expert and dedicated multidisciplinary neuro-oncology teams

48 INVITED

New approaches for high-grade gliomas

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High grade glioma are characterized by there heterogenic molecular and histological appearence, and their poor prognosis. With the improvement of radiation and with more radical surgery, survival times have increased. In addition, large phase II studies have shown significant but limited survival benefits with chemotherapy in high grade glioma with temozolomide and nitrosurea. However, numerous clinical trials have been published previously with smaller patient numbers and no control groups. A small positive effect could be missed this way resulting in premature rejection of possible beneficial treatment.
Expanding our former database (Hauch 2005), we analyzed the glioma literature 1997 to 2005 in order to compare treatment results. In this database, one record represents a cohort of patients treated in the same way. Various patient cohort characteristics such as median age, and outcome measures such as median overall survival times (mOS), were documented. Patient population factors influencing the outcome of a cohort were analyzed. Based on those, a predicted outcome for each cohort was calculated. The measured outcome was compared with the predicted outcome to calculate the survival gain archived by the treatment, and treatments were ranked according to their survival gain.
24023 patients are reported in 503 cohorts in 362 publications. The male to female ratio was 1.55 to 1. The median age was 45 years, 9% of the studies included children only. The grade IV to grade III ratio was 3.3 to 1. Supratentorial to infratentorial: 7.1 to 1. Newly diagnosed to recurrent tumors: 1.9 to 1. The median overall survival was 14.5 months.