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In a multicenter cross-sectional study we collected data on therapy and outcome of 306 patients with childhood craniopharyngioma (CP). The survival rates were $94 \pm 4\%$ in irradiated and $93 \pm 5\%$ in non-irradiated patients. The multicenter prospective study KRANIOPHARYNGEOM 2000 was initiated to collect data on relapses after complete resection and tumor progressions after incomplete resection. Since 2001 ninety-six patients with newly diagnosed CP were recruited. Complete resection was achieved in 43%, subtotal resection in 45%. XRT was performed in 22 of 96 CP patients; in 18% immediately after subtotal resection, in 53% after progression of residual tumor and in 14% after (second surgery of) relapse. Data on XRT modalities were evaluable in 17 of 22 patients. XRT was performed at a median age of 11 years (4–18 y) and after a mean interval of 10 months after first diagnosis. An interim evaluation on event-free survival rates (EFS) after three years of follow-up showed a high rate of early events (EFS: $0.22 \pm 0.06$) in terms of tumor progression after incomplete resection ($n = 48$) and relapses (EFS: $0.60 \pm 0.10$) after complete resection ($n = 37$) during the first three years of follow-up.
We conclude that progressions after incomplete resection and relapses after complete resection are frequent and early events in CP. Regular monitoring of cerebral imaging is recommended in follow-up of patients with CP. There is controversial discussion on the adequate time point of irradiation after incomplete resection. Accordingly, in the multicenter prospective study KRANIOPHARYNGEOM 2007 patients at age $> = 5$ years at diagnosis will be randomized after incomplete resection for the time point of irradiation (immediate XRT after surgery versus XRT at progression of residual tumor). Endpoints of the study will be quality of life (PEDQOL domaine: physical function), progression-free survival and overall survival. The time point of evaluation will be 3 years after randomization. Supported by Deutsche Kinderkrebsstiftung.

# O.103

## SURVIVAL AND PROGNOSTIC FACTORS OF EARLY CHILDHOOD MEDULLOBLASTOMA: AN INTERNATIONAL META-ANALYSIS

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**Purpose.** To investigate survival and prognostic factors (histologic subtype, extent of resection, staging) in young children with medulloblastoma.
**Methods.** Clinical data sets of children diagnosed 03/1987-07/2004 and treated within prospective national trials (HIT, SFOP, AIEOP.UKCCSG, Head-Start) were centrally analysed by univariable and multivariable analyses.
**Results.** Data of 253 children, median age 1.88 (0.17-4.97) years, median follow-up 8.0 (1.2–16.2) years, were collected. Rates for 8-year-EFS and OS were 39% and 57%. Survival rates were higher in 108 children with desmoplastic medulloblastoma (DMB) compared to 145 children with classical medulloblastoma (CMB) (EFS 55% versus 27%, OS 76 versus 42%; p.
**Conclusion.** Desmoplasia is a strong independent favorable prognostic factor in localized and metastatic medulloblastoma of early childhood. This should be considered for planning of future trials and treatment concepts.

# O.104

## POSTOPERATIVE CHEMOTHERAPY AND DEFERRED RADIOTHERAPY IN EARLY CHILDHOOD MEDULLOBLASTOMA: RESULTS OF THE HIT-SKK87 STUDY

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**Purpose.** Investigate prospectively the utility of postoperative chemotherapy to delay radiotherapy in children below 3 years with medulloblastoma.
**Methods.** Between 08/1987 and 07/1991, children with postoperative residual tumor or metastatic disease received i.v. procarbazine, ifosfamide, etoposide, methotrexate, cisplatin, and cytarabine (induction). Following induction or in low-risk children without induction, an interval chemotherapy with procarbazine, methotrexate, and vincristin was administered until craniospinal radiotherapy was applicated at the age of three years or at relapse.
**Results.** 8-year PFS and OS of 29 evaluable children were $50.8 \pm 9.4\%$ and $55.2 \pm 9.2\%$. Considering the postsurgical status (17, complete resection; 9, residual tumor; 3, macroscopic metastases), 8-year PFS and OS were $57.8 \pm 12.2\%$ and $58.8 \pm 11.9\%$, $55.6 \pm 16.6\%$ and $66.7 \pm 15.7\%$, 0% and 0%, respectively. The PFS and OS of 26 patients without macroscopic metastases were $56.7 \pm 9.9\%$ and $61.5 \pm 9.5\%$. Rates for 8-year PFS and OS in 9 children with desmoplastic subtype were significantly higher than in 20 children with classic medulloblastoma ($88.9 \pm 10.5\%$ and $33.0 \pm 10.8\%$; $88.9 \pm 10.5$and $40.0 \pm 11.0\%$).
**Conclusions.** Craniospinal radiotherapy was successfully delayed especially in young children with desmoplastic medulloblastoma in terms of survival, but given the pronounced neurocognitive deficits of survivors, new concepts aiming to avoid craniospinal radiotherapy have been developed subsequently.

# O.106

## ACHIEVEMENT OF TARGET CYCLOSPORINE CONCENTRATIONS AS A PREDICTOR OF SEVERE ACUTE GVHD IN CHILDREN RECEIVING CYCLOSPORINE AND METHOTREXATE PROPHYLAXIS

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**Study Objective.** To evaluate our institution's target trough cyclosporine (CSA) concentrations as a predictor of severe aGvHD in children receiving either matched related or unrelated hematopoietic stem cell transplantation (HSCT).
**Design.** Retrospective study with a mean follow-up of $3.0 \pm 1.9$ years among children who survived beyond day +100.
**Setting.** Bone marrow transplant unit at a large, university-affiliated, pediatric tertiary care hospital.
**Patients.** Eighty-seven consecutive patients who underwent allogeneic HSCT and received CSA and methotrexate as the sole intended prophylaxis against aGvHD between October 1, 1999 and September 30, 2002 were included.
**Interventions.** Target trough CSA concentrations for related and unrelated transplants were 105–155ng/mL ($n = 33$) and 155-21 0ng/mL ($n = 54$) respectively.
**Measurements and Main Results.** Three pharmacological variables were significantly associated with the development of severe aGvHD on univariate analysis: initial CSA target concentration (OR, 0.24; $p = 0.03$), proportion of time the target CSA concentration was achieved during the second week after transplant (OR, 0.16; $p = 0.02$), and proportion of time the target CSA concentration was achieved during the week before engraftment (OR, 0.22; $p = 0.0489$). Multivariable analysis demonstrated an inverse relationship between the median CSA concentration during the week before engraftment and the development of severe aGvHD (OR 0.99, $p = 0.045$). For every 10ng/mL increase in median CSA concentration during the week before engraftment, the odds of severe aGVHD was reduced by 13%.
**Conclusions.** These results suggest that achievement of our CSA target concentrations is important to aGvHD outcomes. Rapid attainment of therapeutic CSA concentrations early after transplantation may decrease the risk of severe aGvHD.