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Survival and Prognostic Factors of Early Childhood Medulloblastoma: An International Meta-Analysis

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Abstract: *PURPOSE*: To assess the prognostic role of clinical parameters and histology in early childhood medulloblastoma. *PATIENTS AND METHODS*: Clinical and histological data from 270 children younger than five years diagnosed with medulloblastoma between March 1987 and July 2004 and treated within prospective trials of five national study groups were centrally analyzed. *RESULTS*: 260 children with medulloblastoma and specified histological subtype were eligible for analysis (median age 1.89 years, median follow-up 8.0 years). Rates for 8-year event-free survival (EFS) and overall survival (OS) were 55% and 76% in 108 children with desmoplastic / nodular medulloblastoma (DNMB) or medulloblastoma with extensive nodularity (MBEN), 27% and 42% in 145 children with classic medulloblastoma (CMB), and 14% and 14% in seven children with large cell / anaplastic medulloblastoma (LC/A); p<0.001. Histology (DNMB/MBEN HR 0.44, CI 0.31-0.64; LC/A HR 2.27, CI 0.95-5.54; p<0.001 compared to CMB), incomplete resection and metastases (M0R1 HR 1.86, CI 1.29-2.80, M+ HR 2.28, CI 1.50-3.46, p<0.001 compared to M0R0) and national group were independent prognostic factors for EFS. The hazard ratios for OS ranged from 0.14 for localized M0–DNMB/MBEN to 13.67 for metastatic LCA in different national groups *CONCLUSION*: Our results confirm the high frequency of desmoplastic variants of medulloblastomas in early childhood and histopathology as a strong independent prognostic factor. A controlled de-escalation of treatment may be appropriate for young children with DNMB and MBEN in future clinical trials.

Statement: In this study original data of 260 young children with medulloblastoma, treated within 5 different national trials were evaluated. In this by far largest analysis on prognostic factors of early childhood medulloblastoma, histological subtypes have been confirmed as strong and significant independent risk factors across different treatment regimens. This study has a relevant impact on planning of future treatment of early childhood medulloblastoma patients, who due to their young age are at high risk for treatment induced late effects as severe neurocognitive impairments. This is the first international co-operative metaanalysis on this disease, and it encourages treatment stratification based on histological findings, which has important clinical implications. Its results perfectly match the recent literature on medulloblastoma biology, where it has been shown, that this disease represents different biological subtypes. It contributes to the rationale for a controlled treatment de-escalation within a European randomized trial for young children with desmoplastic medulloblastoma under sponsorship of the UKE, which is currently under preparation.

Prof. Rutkowski is trial chairman of the HIT-2000 study of the German Society for Pediatric Hematology and Oncology (GPOH), funded by the German Childrens Cancer Foundation (Deutsche Kinderkrebsstiftung), by the Federal Ministry of Education and Research (BMBF), and by the “Fördergemeinschaft Kinderkrebs-Zentrum Hamburg e.V.”. This study is a prospective, multicentre study for treatment of infants and children with different brain tumors. Prof. Rutkowski and his team have significantly contributed to the elucidation of medulloblastoma treatment (see Rutkowski et al. 2005, NEJM), he holds a professorship for Pediatric Oncology at UKE, Department of Pediatric Hematology and Oncology since he joined UKE in 2009. Dr. med. Katja v. Hoff is working within the study team since 2005, and joined UKE in 2010 as trial coordinator.