Craniospinal irradiation with concurrent temozolomide for primary metastatic pediatric high-grade or diffuse intrinsic pontine gliomas. A first report from the GPOH-HIT-HGG Study Group.

High-grade (HGG) and diffuse intrinsic pontine gliomas (DIPG) with primary metastatic spread are extremely rare and have a dismal prognosis. Analogous to simultaneous radiochemotherapy in non-metastatic HGG and DIPG, concurrent craniospinal irradiation (CSI) and metronomic temozolomide (metroTMZ) may represent a reasonable therapeutic approach. However, the antitumor efficacy and toxicity of this treatment still have to be investigated. Between March 2007 and December 2012, six children with primary metastatic HGG (n = 4) or DIPG (n = 2) received CSI and concurrent metroTMZ based on individual treatment recommendations and, in some cases, within the HIT-HGG 2007 multicenter trial. Outcome and treatment-related toxicities were evaluated. All patients received irradiation to the entire craniospinal axis (35.2 Gy, n = 5; 36 Gy, n = 1:) and 5 received a local boost to macroscopic tumor deposits. Simultaneously, metroTMZ (75 mg/m\(^2\)/day, n = 5; 60 mg/m\(^2\)/day, n = 1) was administered. Additionally, 1 patient received nimotuzumab once per week. Within a median follow-up of 10.0 months (range 6.5-18.7 months), all patients
experienced disease progression and 5 patients died. Median progression-free survival was 4.0 ± 0.8 months (range 2.4-10.7 months) and median overall survival was 7.6 ± 3.5 months (range 4.0-17.6 months). Acute myelosuppression most severely limited application of this aggressive treatment strategy. Severe hematotoxicities (≥ grade 3) occurred in all patients and metroTMZ had to be interrupted or discontinued in 4 out of 6 cases. Concurrent CSI and metroTMZ might represent a feasible treatment approach for primary metastatic HGG and DIPG. On the basis of our experience, severe but manageable acute hematotoxicity has to be expected. An international effort is warranted to reassess the efficacy and toxicity of this approach within a prospective study.