disease (large cell - anaplastic histology, *MYC/MYC-N* gene amplification, Iso17q and *TP53* gene mutation) were absent in this tumor samples. We have also achieved 100% PFS in patients with desmoplastic tumor histology and in patients, who were treated with thiphosphamide - based chemotherapy regimen. Molecular - biological characteristics analysis of tumor cells showed a negative effect on PFS of DNMT - positive status (Score 4 and>, by 3 markers) and presence of *MYC-N* gene amplification (SHH molecular subgroup).

MBCL-06. RISK STRATIFICATION IMPROVEMENT OF THE HIT2000 AND I-HIT-MED COHORTS USING MOLECULAR SUBTYPES I-VIII OF GROUP 3/4 MEDULLOBLASTOMAS

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OBJECTIVE: Molecular subtypes of Group 3/4 medulloblastoma have been identified by unsupervised clustering methods in different studies. We hypothesized that risk stratification using these subtypes I-VIII improves outcome prediction. PATIENTS AND METHODS: n=340 patients with Group 3 or Group 4 medulloblastoma defined by DNA methylation array profiling enrolled into the HIT2000 study and HIT-MED registries were subtyped by the Heidelberg Medulloblastoma Classifier. The discovery cohort consisted of n=162 previously published samples, the validation cohort of n=178 newly analyzed samples. RESULTS AND DISCUSSION: n=300/340 (88%) MBs could be assigned to one of the subtypes with confidence (score >0.8; Heidelberg Medulloblastoma classifier). Subtype II,III and V showed a poor PFS and OS and were classified as HR (discovery:5y-PFS 45%[95%-CI:33–62], 5y-OS 50%[37–67]; validation:5y-PFS 32%[20–50], 5y-OS 40%[27–61]). Subtypes I, IV, VI-VIII fared better (discovery:5y-PFS 67%[58–77], 5y_OS 84%[77–91]; Validation:5y-PFS 70%[58–83], 5y-OS 89%[81–99]). Survival prediction by subtype-based risk assessment was improved compared to Group 3 versus 4 differentiation in both cohorts in univariate and multivariable Cox regression models (PFS:Hazard ratio HR versus LR 2.474, p<0.001; Group 3 versus Group 4 1.842, p=0.003; adjustment for anaplasia, age and metastatic disease). Patients older than 4 with subtype IV tumors (mainly Group 3) treated with radiotherapy achieved a 100% PFS, while subtype V patients (mainly Group 4) had poor survival. CONCLUSION: We showed that molecular subtypes I-VIII improved risk stratification of Group 3/4 medulloblastomas. Group 3 subtype IV MB treated with RT had very high cure rates.

MBCL-07. NON-METASTATIC MEDULLOBLASTOMA OF EARLY CHILDHOOD: RESULTS FROM THE PROSPECTIVE CLINICAL TRIAL HIT-2000 AND AN EXTENDED VALIDATION COHORT

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OBJECTIVE: To avoid craniospinal irradiation (CSI) in children younger than four years with non-metastatic medulloblastoma by chemotherapy, intraventricular methotrexate and risk-adapted local radiotherapy. PATIENTS AND METHODS: Eighty-seven patients received systemic chemotherapy and intraventricular methotrexate. Until 2006, CSI was reserved for non-response or progression. After 2006, local radiotherapy was introduced for non-responders or classic (CMB), anaplastic or large-cell medulloblastoma (LCA). Infantile SHH-activated medulloblastomas (SHH_INF) were subdivided by DNA-methylation profiling. Survival in SHH_INF subtypes were also assessed in a val-