tial (PR) or complete response (CR) was achieved after induction chemotherapy, children received 2 courses of thiotepa (600mg/m²) with stem cell rescue. For patients in CR after high-dose chemotherapy, they received one course of Cyclophosphamide – Busilvex with stem cell rescue (Phase I part). The others patients (not in PR after induction or in CR after thiotepa) were treated with 2 cycles of Temozolomide-Irinotecan followed by age-adapted craniospinal irradiation and maintenance treatment. RESULTS: 28 children (2 to 4 years; median: 3.0 years) were enrolled. Group 3 MB were most common (57%). The response rate to Etoposide-Carboplatine was 60.7%. Among 20 patients treated with Thiotepa, 13 children were in CR and received Cyclophosphamide – Busilvex without radiotherapy. Out of them, 9 patients (45%) are alive in CR without craniospinal irradiation (median follow-up 5 years). Among 15 patients treated with radiotherapy, 8 patients are alive (median follow-up 3.8 years). The study was prematurely stopped for an excess of events. The median follow-up was 4 years (range 1.5 - 6.1). The 3-year EFS and OS were 42.3% [25.9 - 60.6] and 71.3% [52.7 - 84.7], respectively. CONCLUSIONS: This risk-adapted strategy did not improve EFS in young children with high-risk MB. However, the study shows that good responders to chemotherapy can be cured without recourse to irradiation.

MBCL-30. NOVEL SMO MUTATION IN DESMOPLASTIC/NODULAR MEDULLOBLASTOMA: A CASE REPORT

Avery Wright, Ana Aguilar-Bonilla, Emily Owens Pickle, and Amy A Smith; Arnold Palmer Hospital for Children, Orlando, Florida, USA

Smoothened (SMO) is a transmembrane protein which is regulated by SHH (Sonic hedgehog) protein binding to PTCH1. SMO activation controls GLI which then translocates into the nucleus and activates target genes. The SHH subtype of medulloblastoma has been extensively studied to have mutations within the SHH signaling pathway, often in PTCH1, SUFU, and SMO. We present a case of desmoplastic/nodular medulloblastoma with the mutation SMO c.1810G>A. The patient presented at 11 years old with a two-week history of headaches and morning vomiting. His neuroimaging revealed a T2 hyperintense, enhancing mass centered at the fourth ventricle. He underwent gross total resection and had no metastatic spread. There were no alterations in PTCH1, SUFU, Tp53, GLI2, MYC/MYCN, CTNNB1, or the WNT pathway. The SMO c.1810G>A alteration has not been previously identified as a somatic mutation in a CNS tumor. The functional effect of this mutation has not been studied. It is known that desmoplastic/nodular histology in medulloblastoma is associated with the SHH subtype and given the fact that SMO is regulated by SHH signaling, this patient was ultimately diagnosed with SHH subtype medulloblastoma. Findings of novel somatic mutations in patients raises the question of whether the mutation is in fact the driver of neoplasia.

MBCL-31. TREATMENT RESULTS AMONG 106 PATIENTS WITH MEDULLOBLASTOMA OF MOLECULAR SUBGROUP 3

Olga Zheludkova[1], Lyudmila Olkhova[2], Yuri Kushel'[3], Armen Melikyan[3], Marina Ryzhova[3], Lyudmila Shishkina[3], Andrey Golanov[3], Alexey Kislyakov[4], Evgeny Shultz[3], Irina Borodina[5], Svetlana Gorbatykh[4], Vladimir Popov[6], Marina Mushinskaya[7], Olga Polushkina[1], Eugenia Inyushkina[8], Natalia Yudina[9], Lyudmila Privalova[10], Lyudmila Minkina[11], Artem Zaichikov[12], Evgeny Matsekha[13], Ivan Fisyun[14], Daniil Sakun[15], Nadezhda Dunaeva[16], Svetlana Avanesyan[17], Vladislav Mitrofanov[18], Sergey Kovalenko[19], Ekaterina Grishina[20], Oleg Chulkov[21], Nadezhda Pishchaeva[22], Nikolay Vorob'ev[23], Alexey Nechesnyuk[5], Natalia Popova[24], Dmitriy Pogorelov[25], Alexander Matitsyn[26], Alexander Shapochnik[27], Valentina Timofeeva[28], Andrey Korchunov[29,30], and Elena Slobina[31]; [1]St.Luka`s Clinical Research Center for Children, Moscow, Russian Federation, [2]Russian Children Clinical Hospital, Moscow, Russian Federation, [3]Burdenko Neurosurgical Institute, Moscow, Russian Federation, [4]Morozov Children's Clinical Hospital, Moscow, Russian Federation, [5]Dmitry Rogachev National Medical Research Center of Pediatric Hematology, Oncology and Immunology, Moscow, Russian Federation, [6]SBHI of MA MRRCI n.a. M.F. Vladimirskiy, Moscow, Russian Federation. [7]Regional Oncology Center, Perm', Russian Federation, [8]Regional Oncology Center, Moscow, Russian Federation, [9]Regional Oncology Center, Voronezh, Russian Federation, [10]Regional Oncology Center, Nizhny Novgorod, Russian Federation, [11]Regional Oncology Center, Vladivostok, Russian Federation, [12]Regional Oncology Center, Ekaterinburg, Russian Federation, [13]Regional Oncology Center, Chita, Russian Federation, [14]Regional Oncology Center, Orel, Russian Federation, [15]Regional Oncology Center, Simpheropol, Russian Federation, [16]Regional Oncology Center, Vologda, Russian Federation, [17]Regional Oncology Center, Irkutsk, Russian Federation, [18]Regional Oncology Center, Arkhangelsk, Russian Federation, [19]Regional Oncology Center, Chelyabinsk, Russian Federation, [20]Regional Oncology Center, Kazan, Russian Federation, [21]Regional Oncology Center, Krasnodar, Russian Federation, [22]Regional Oncology Center, Nizhnevartovsk, Russian Federation, [23]Proton Therapy Center, Saint Petersburg, Russian Federation, [24]Regional Oncology Center, Volgograd, Russian Federation, [25]Regional Oncology Center, Lipetsk, Russian Federation, [26]Regional Oncology Center, Tambov, Russian Federation, [27]Regional Oncology Center, Orenburg, Russian Federation, [28]Regional Oncology Center, Ulyanovsk, Russian Federation, [29]Clinical Cooperation Unit Neuropathology (G380), German Cancer Research Center, Heidelberg, Germany, [30]Heidelberg University Hospital, Heidelberg, Germany, [31]Russian Scientific Center of Roentgeno-Radiology, Moscow, Russian Federation

OBJECTIVE: To evaluate the treatment results among 106 patients of molecular subgroup 3 and to determine the factors affecting the prognosis. PATIENTS AND METHODS: In all the patients, initial removal of the tumor was performed. All the patients got chemoradiotherapy according to the HIT protocol. There were 34girls and 72boys. Most patients were over 3 years:74 compared to 32 younger than 3. The majority of the patients had stage M+: 65; in 38 stage M0 was determined; in 3patients, stage was not specified, Mx.MYC amplification was found in 20 patients; MYCN amplification, in 4 patients. Classic medulloblastoma was predominant: 65, and 41 patients had anaplastic/large cell medulloblastoma. RESULTS: The five-year progression-free survival was 0.51±0.05, the five-year overall survival was 0.52±0.04.The median survival was 82months,and the median progression-free survival was 37 months. There were no significant variations of PFS depending on the sex and age. The treatment results depended on the histological subtype: for classic medulloblastoma, the five-year PFS was 0.57; for the anaplastic/largecell,0.38(p = 0.02030). The presence of metastases significantly affected the survival: PFS for stage M0 was 0.77; for stage M+,0.35(p = 0.00062). Patients with MYC amplification had a significantly worse survival compared to MYCN patients and those without MYC amplification: 0.1, 0.75, and 0.58, respectively (p = 0.00002). Three patients with MYC amplification are alive: two patients had MGMT methylation detected. CONCLUSIONS: The results of treatment among the patients with molecular subgroup 3 depended on the tumor subtype, presence of metastases, MYC amplification and MGMT methylation. In the absence of unfavorable factors, the survival was the same as in molecular subgroup 4.

MBCL-32. HIGH-DOSE CHEMOTHERAPY WITH STEM CELL RESCUE FOR RECURRENT PREVIOUSLY IRRADIATED MEDULLOBLASTOMA

Ekaterina Salnikova, Irina Vilesova, Artur Merishavyan, Alexander Druy, Ludmila Yasko, Andrey Sysoev, Alexey Nechesnyuk, Irina Borodina, Alexander Karachunsky, Galina Novichkova, and Ludmila Papusha; Dmitry Rogachev National Medical Research Center of Pediatric Hematology, Oncology and Immunology, Moscow, Russian Federation

BACKGROUND/OBJECTIVES: Relapse of medulloblastoma (MB) is highly lethal in previously irradiated patients. As one of therapeutic options for recurrence MB, high-dose chemotherapy with stem cell rescue (HDSCR) is suggested. The aim of our work was to evaluate the effectiveness of this therapy. DESIGN/METHODS: We retrospectively analyzed the data of 8 pts with previously irradiated relapse MB using HDSCR. Initially, M0-stage was verified in 4 cases. Histological diagnoses were desmoplastic (2 pts), classic (2 pts), anaplastic (2 pts) and MB NOS (2 pts). Molecular genetic analyses was performed in 6 cases: Group 3 was verified in 2 cases (1-classic, 1-anaplastic), Group 4 – in 3 cases (1-classic, 1-anaplastic, 1-desmoplastic). Time to first PD was from 15 to 86 months (median=29,4 months). Local relapse was revealed in 1 pt, metastatic – in 5 pts, mixed – in 2 pts. RESULTS: All pts were treated according HIT-REZ 2005 (3–5 cycles without/with intraventricular etoposide), with CR achieved in 3 pts and PR in 5 pts. HDCT regimens consisted of carboplatin, etoposide, thiotepa and temozolomide. 2 pts received re-irradiation – focal RT (1) and CSI (1). 7/8 patients died, 1 pt alive with PD. Time from HDCT to death was 5–15 months (median=9,6 months). CONCLUSIONS: HDSCR for recurrent previously irradiated MB is ineffective. Use of other methods should be considered in these cases.

MBCL-33. RARE PULMONARY TOXICITY IN THREE MEDULLOBLASTOMA PATIENTS UNDERGOING ANTIANGIOGENIC METRONOMIC COMBINATION THERAPY

Alicia Lenzen[1,2], Daniel Gryzlo[2], Irene McKenzie[1], Stewart Goldman[1,2], and Natasha Pillay-Smiley[3,4]; [1]Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, USA, [2]Northwestern University Feinberg School of Medicine, Chicago, IL, USA, [3]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA, [4]University of Cincinnati College of Medicine, Cincinnati, OH, USA

BACKGROUND: Metronomic and targeted anti-angiogenesis therapy (MEMMAT) has emerged as a promising treatment for recurrent/progressive medulloblastoma. This treatment includes bevacizumab, oral agents (thalidomide, celecoxib, fenofibrate, etoposide & cyclophosphamide) and intrathecal chemotherapy (etoposide & cytarabine). Common toxicities include myelosuppression, nausea, and infection. Mild respira-