post-diagnosis. RESULTS: The ATRT- vs. LGG-cohorts were comparable for median age at diagnosis, sex-ratio and tumor-localization, though they differed slightly in median age at assessment (9.5/7.2 years (±2.5/1.1)). Results of age-appropriate tests showed increased impairments for ATRT-patients in fluid intelligence (FI) (p=.006, d=1.214) and in visual-spatial processing (VSP) (p<.001, d=2.233) compared to LGG-patients. The median for neuropsychological test results of ATRT-patients spanned from considerably below the normal to the lower normal range (median=65-90), while results of LGG-patients were mostly in the lower normal range (median=83-103). Results for psychomotor speed abilities (PMS) were distinctly below the norm for both patient groups (p=.002-.007). **CONCLUSION:** Infant ATRT- and LGG-patients develop significant impairments in PMS abilities following multimodal treatment. Long-term survivors of ATRT suffer from additional FI and VSP deficits. Our data suggest that high malignancy requiring multimodal treatment determines the inferior cognitive outcome for the ATRT-cohort. Long-term neuropsychological monitoring (and treatment options) should be implemented as standard of care in ATRT- and LGG-trials.

ATRT-03. ADAPTED TREATMENT PROTOCOL: SYNCHRONOUS ATYPICAL TERATOID/RHABDOID CNS TUMOR AND EXTRA CNS DISEASE

Nicole Jackson, Marleni Torres, Eva Glenn Lecea, Candelaria O'Farrell, Ziad Khatib, Ossama Maher; Nicklaus Children's Hospital, Miami, FL, USA

Atypical teratoid/rhabdoid tumors (AT/RTs) of the central nervous system (CNS) are rare, aggressive, early childhood tumors with unfavorable prognosis. There have been 31 cases reported of children with AT/RT of the CNS and extra CNS primary tumors. In addition to its aggressive tendencies, malignant rhabdoid tumors (MRTs) of the kidney have also shown a common genetic abnormality-inactivating mutation of SMARC B1/INI-gene. We report a 22-month-old male who presented at 15 months of age with metastatic AT/RT of the posterior fossa and synchronous malignant rhabdoid tumor of the left kidney. MRI of the brain demonstrated a midline posterior fossa mass and left renal mass was noted incidentally on imaging of spine. Pathology was consistent with MRT of the kidney and pathogenic variant was found in the tumor sample, specifically SMARCB1 homozygous/biallelic deletion. Patient underwent a subtotal resection of the posterior fossa tumor and subsequent radical resection of the mass on kidney rhabdoid tumor. He was treated as per ACNS033 protocol with 2 cycles of induction with high-dose methotrexate followed by vincristine, cyclophosphamide, cisplatin, and etoposide with complete response followed by three tandem stem cell transplants with thiotepa and carboplatin for which he has been tolerating and responding favorably. Focal radiation therapy to the brain and flank area is planned at end of therapy. In a large series of synchronous AT/RTs reported in 2017 only 3 of the 31 patients were considered long-term survivors. All received a combination of high dose intrathecal or intravenous chemotherapy, total resection of at least one of the tumors, focal radiation, and autologous peripheral blood stem cell transplant. We demonstrated a case with a favorable response with our treatment. Treatment continues to be challenging given the tumor's rarity and mortality as there are no standardized protocols or randomized controlled trials.

ATRT-04. CLINICAL AND (EPI)GENETIC CHARACTERISATION OF PATIENTS WITH ATYPICAL TERATOID/RHABDOID TUMOR (ATRT) AND EXTRACRANIAL MALIGNANT RHABDOID TUMOR CONCEIVED FOLLOWING ASSISTED REPRODUCTION TECHNOLOGIES (ART)

Karolina Nemes[1], Martin Benesch[2], Julia Kolerova[3], Pascal Johann[1,4], Martin Hasselblatt[5], Christian Thomas[5], Susanne Bens[3], Olga Liaugaudiene[6], Alireza Sadeghipour[7], Nicolas von der Weid[8], Irene Schmid[9], Corrie Gidding[10], Anat Erdreich-Epstein[11], Claudia Khurana[12], Georg Ebetsberger-Dachs[13], Andreas Lemmer[14], Carmen Hernández Marqués[15], Ziad Khatib[16], Jane Pears[17], Franz Quehenberger[18], Jaclyn A. Biegel[19], Reiner Siebert[3], Michael C. Frühwald[1]; [1]Swabian Children's Cancer Center, Paediatric and Adolescent Medicine, University Medical Center Augsburg, Augsburg, Germany. [2]Division of Pediatric Hematology and Oncology, Department of Pediatrics and Adolescent Medicine, Medical University of Graz, Graz, Austria. [3]Institute of Human Genetics, Ulm University & Ulm University Medical Center, Ulm, Germany. [4]Division of Pediatric Neurooncology, German Cancer Consortium (DKTK), German Cancer Research Center (DKFZ), Heidelberg, Germany. [5]Institute of Neuropathology, University Hospital Münster, Münster, Germany. [6]Department of Genetics and Molecular Medicine, Hospital of Lithuanian University of Health Sciences, Kauno Klinikos, Kaunas, Lithuania. [7]Department of Pathology, Rasoul Akram Medical Complex, Iran University of Medical Sciences, Tehran, Iran, Islamic Republic of. [8]Department of Pediatric Hematology and Oncology, University Children's Hospital Basel (UKBB), Basel, Switzerland. [9]Department of Pediatric Hematology and Oncology, Dr. von Haunersches Kinderspital, München, Germany. [10]Princess Máxima Center for Pediatric Oncology, Utrecht, Netherlands. [11]Children's Center for Cancer and Blood Diseases, Children's Hospital Los Angeles, Keck School of Medicine, University of Southern California, Los Angeles, USA. [12]Children's Center, Evangelisches Krankenhaus Bielefeld, Bielefeld, Germany. [13]Kepler University Hospital Linz, Department of Pediatrics, Linz, Austria. [14]Children's Hospital, HELIOS Klinikum Erfurt, Erfurt, Germany. [15]Department of Pediatric Oncology, Hospital Infantil Universitario Niño Jesús, Madrid, Spain. [16]Department of Pediatric Hematology and Oncology, Miami Children's Hospital, Miami, USA. [17]Children's Health Ireland at Crumlin, Dublin, Ireland. [18]Institute for Medical Statistics, Medical University of Graz, Graz, Germany. [19]Department of Pathology and Laboratory Medicine, Children's Hospital Los Angeles, Keck School of Medicine, University of Southern California, Los Angeles, USA

INTRODUCTION: Anecdotal case reports suggest an association between assisted reproduction technologies (ART) and malignant rhabdoid tumors (MRT). We performed a multi-institutional retrospective analysis of the EU-RHAB database, complemented by additional cases outside of EU-RHAB to compile clinical, (epi)genetic characteristics and outcome data of children with MRT following ART. METHODS: Data of 14 patients (from 311 patients with MRT) from 9 countries were analyzed (2010-2018). Tumors and matching blood samples were examined for *SMARCB1* mutations using FISH, MLPA and sequencing. Molecular subgroups were determined using DNA methylation arrays and correlated with a validation cohort (n=22, tumor samples of MRT; n=39 blood samples of patients small for gestational age). RESULTS: The median age at diagnosis of the 13 girls and 1 boy was 9 months (0 – 66). 8 patients with ATRT, 3 with extracranial, extrarenal-, 1 with renal rhabdoid tumor and 2 with synchronous tumors were identified. Distant metastases at diagnosis were present in 6 patients. A germline mutation (GLM) was detected in 5 patients. In 11 tumors complete data on SMARCB1 mutational status were available. DNA methylation subgrouping was available in 10 tumors and 6 blood samples. A female predominance was noted as compared to the EU-RHAB cohort with MRT born without ART (n=213, p=0.009). A total of 8 patients received gross total resection, n=12 patients received conventional chemotherapy (EU-RHAB=9, Head Start II=2, IRS III=1). Radiotherapy was applied to 6 patients. 10 patients achieved CR, and 5 remain in continuing CR. Significant genome-wide DNA methylation differences (including imprinted genes) between patients born after ART and patients born without ART could not be demonstrated. CONCLUSIONS: Long-term survival is achievable in patients who develop MRT after ART, even in cases with GLM, metastatic disease at diagnosis, or relapse. Larger epidemiological studies are needed to confirm a potential association between MRT and ART.

ATRT-05. INFANTS AND NEWBORNS WITH ATYPICAL TERATOID/RHABDOID TUMORS (ATRT) AND EXTRACRANIAL MALIGNANT RHABDOID TUMORS: A UNIQUE AND CHALLENGING POPULATION

Karolina Nemes[1], Pascal D. Johann[1,2], Mona Steinbügl[1], Miriam Gruhle[1], Susanne Bens[3], Denis Kachanov[4], Margarita Teleshova[4], Hauser Peter[5], Thorsten Simon[6], Stephan Tippelt[7], Wolfgang Eberl[8], Martin Chada[9], Vicente Santa-Maria Lopez[10], Lorenz Grigull[11], Pablo Hernáiz-Driever[12], Matthias Eyrich[13], Jane Pears[14], Till Milde[15,16], Harald Reinhard[17], Alfred Leipold[18], Marianne v. de Wetering[19], Maria João Gil-da-Costa[20], Georg Ebetsberger-Dachs[21], Kornelius Kerl[22], Andreas Lemmer[23], Heidrun Boztug[24], Rhoikos Furtwängler[25], Uwe Kordes[26], Reiner Siebert[3], Christian Vokuhl[27], Martin Hasselblatt[28], Brigitte Bison[29], Thomas Kröncke[29], Patrick Melchior[30], Beate Timmermann[31], Joachim Gerss[32], Michael C. Frühwald[1]; [1]Swabian Children's Cancer Center, Paediatric and Adolescent Medicine, University Medical Center Augsburg, Augsburg, Germany. [2]Division of Pediatric Neurooncology, German Cancer Consortium (DKTK), German Cancer Research Center (DKFZ), Heidelberg, Germany. [3]Institute of Human Genetics, Ulm University & Ulm University Medical Center, Ulm, Germany. [4]Dmitry Rogachev National Medical Research Center of Pediatric Hematology, Oncology and Immunology, Moscow, Russian Federation. [5]BAZ County Hospital and University Teaching Hospital, Velkey László Child's Health Center, Miskolc, Hungary. [6]Department of Pediatric Hematology and Oncology, University Children's Hospital of Cologne, Cologne, Germany. [7]Department of Pediatric Hematology and Oncology, Pediatrics III, University Hospital of Essen, Essen, Germany. [8]Department of Hematology and Oncology, Center for Child and Adolescent Medicine, Städtisches Klinikum Braunschweig gGmbH, Braunschweig, Germany. [9]Department of Pediatric Oncology and Hematology, Center of Child and Adolescent Medicine, University Hospital Erlangen, Erlangen, Germany. [10]Department of Pediatric Oncology, Hospital Sant Joan de Déu Barcelona, Esplugues de Llobregat, Barcelona, Spain. [11]Department of Pediatric Hematology and Oncology, Children's Hospital of Hannover, Hannover, Germany. [12]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, Department of Pediatric Oncology and Hematology, Berlin, Germany. [13]Department of Pediatric Hematology and Oncology, University Würzburg, Würzburg, Germany. [14]Children's Health Ireland at Crumlin, Dublin, Ireland. [15]Hopp Children's Cancer Center (KiTZ), Heidelberg, Germany; Clinical Cooperation Unit (CCU) Pediatric Oncology, German Cancer Research Center (DKFZ) and German Consortium for Translational

Cancer Research (DKTK), Heidelberg, Germany. [16]Pediatric Oncology, Hematology and Immunology, Center for Child and Adolescent Medicine, Heidelberg University Hospital, Heidelberg, Germany. [17]Department of Pediatric Hematology and Oncology, Asklepios Hospital Sankt Augustin, Sankt Augustin, Germany. [18]Children's Hospital Karlsruhe, Karlsruhe, Germany. [19]Princess Máxima Center for pediatric oncology, Utrecht, Netherlands. [20]Pediatric Oncology Department, University Hospital S. João, Alameda Hernani Monteiro, Porto, Portugal. [21]Department of Paediatrics and Adolescent Medicine, Kepler University Hospital, Linz, Austria. [22]Department of Pediatric Hematology and Oncology, University Children's Hospital Münster, Münster, Germany. [23]Pediatric Oncology Center, Helios Klinikum, Erfurt, Germany. [24]St. Anna Kinderspital and Children's Cancer Research Institute, Department of Paediatrics, Medical University of Vienna, Vienna, Austria. [25]Department of Pediatric Hematology and Oncology, University of Saarland, Homburg, Germany. [26]Department of Pediatric Hematology and Oncology, University Hospital Hamburg-Eppendorf, Hamburg, Germany. [27]Department of Pathology, Section of Pediatric Pathology, University Hospital Bonn, Bonn, Germany. [28]Institute of Neuropathology, University Hospital Münster, Münster, Germany. [29]Department of Diagnostic and Interventional Radiology and Neuroradiology, University Medical Center Augsburg, Augsburg, Germany. [30]Department of Radiation Oncology, University of Saarland, Homburg, Homburg, Germany. [31]Department of Particle Therapy, University Hospital Essen, West German Proton Therapy Centre Essen (WPE), West German Cancer Center (WTZ), Germany, German Cancer Consortium (DKTK), Essen, Germany. [32]Institute of Biostatistics and Clinical Research, University of Münster, Münster, Germany

INTRODUCTION: Malignant rhabdoid tumors (MRT) predominantly affect infants. Patients below six months represent a particularly challenging group: intensity of therapy is limited by toxicity to developing organs. Information on prognostic factors, toxicity and long term outcome is sparse. METHODS: Clinical, genetic, and treatment data of 100 patients (less than 6 months at diagnosis) from 13 European countries were analyzed (2005-2020). Tumors and matching blood samples were examined for SMARCB1 mutations using FISH, MLPA and Sanger sequencing. DNA-methylation subgroups (ATRT-TYR, ATRT-SHH, and ATRT-MYC) were determined using DNA methylation arrays. RESULTS: A total of 45 patients presented with ATRT, 29 with extracranial, extrarenal (eMRT) and 9 with renal rhabdoid tumors (RTK). Seventeen patients demonstrated synchronous tumors (SYN). Distant metastases at diagnosis (M+) were present in 27% (26/97). A germline mutation (GLM) was detected in 55% (47/86). Methylation subgroup status was available in 50% (31/62) of ATRT or SYN (SHH=13, TYR=13, MYC=4, SHH+TYR=1). The 5-year overall- (OS) and event free survival (EFS) rates were 23.5±4.6% and 19±4.1%, respectively. Male sex (11±5% vs. 35.8±7.4%), M+ (6.1±5.4% vs. 36.2±7.4%), presence of SYN (7.1±6.9% vs. 26.6±5.3%) and -GLM (7.7±4.2% vs. 45.7±8.6%) were significant prognosticators of 5-year OS, in univariate analysis. Molecular subgroup and survival analyses confirmed the previously described survival advantage of ATRT-TYR. In an adjusted multivariate model clinical factors that influence prognosis were: male sex [HR: 2.1 (1.2 – 3.6)], M+ [3.3 (1.8 – 6)], GLM [HR: 2 (1.1 – 3.6)] and maintenance therapy [HR: 0.3 (0.1 – 0.8)]. CONCLUSION: In this large cohort of homogenously treated infants with MRT, significant predictors of outcome were sex, M+, GLM and maintenance therapy. We confirm the need to stratify which patient group benefits from multimodal treatment, and which patients need novel therapeutic strategies. Biomarker-driven tailored trials may be a key option.

ATRT-06. ATYPICAL TERATOID RHABDOID TUMORS (ATRT): RESULTS FROM A SINGLE INSTITUTION IN BRAZIL - SÃO PAULO UNIVERSITY

Juliana Silveira Barreto[1], Karen Nirit Melo Gomez[2], Alvaro Pimenta Dutra[2], Alessandra Milani Prandini De Azambuja[1], Lilian Maria Cristofani[1], Felipe Hada Sanders[3], Carlo Petito[3], Helena Espindola Baraldi[4], Eduardo Weltman[4], Suely Fazio Ferraciolli[5], Fernando Pereira Frassetto[6], Leandro Tavares Lucato[5], Sérgio Rosemberg[6], Vicente Odone Filho[1]; [1]ITACI - USP, São Paulo, SP, Brazil. [2]ITACI - USP, São Paulo, SP, Brazil. [3]Fac Medicina USP - Neurocirurgia, São Paulo, SP, Brazil. [4]Fac Medicina USP - Radioterapia, São Paulo, SP, Brazil. [5]Fac Medicina USP - Radiologia, São Paulo, SP, Brazil. [6]Fac Medicina USP - Patologia, São Paulo, SP, Brazil

OBJECTIVES: Atypical teratoid/rhabdoid tumor (AT/RT) is a rare, highly malignant tumor of the central nervous system with poor prognosis. Nowadays, multimodal management, including surgery, chemotherapy (CMT), radiation therapy (RT) and Bone Marrow Transplantation (BMT). The aim of this study was to assess the experience and survival in a center of reference of treatment in childhood cancer in Brazil. PATIENTS AND METHODS: Medical records of AT/RT patients who underwent surgery from 2008 to 2020 at a center of childhood cancer treatment (ITACI) in São Paulo University were retrospectively reviewed and statistically analyzed. RESULTS: Eight patients (2 males and 6 females) were presented with AT/RTs. Median age during presentation was 22 months (range, 0 - 6 years). Seven patients (88%) were < 18 months and one patient were >18 months. Tumor location was supratentorial in four patients, infratentorial in 2 patients. Kidney disease as the primary diagnosis in 2 patients (25%). Surgical treatment was performed in 4 patients. Seven children underwent total CMT and 3 children were treated with RT. Only 3 patients underwent Autologous Bone Marrow Transplantation (ABMT). The chemotherapy management protocol of the patients was variable: 2 patients received the EU-RHAB protocol, 2 patients received the HEAD START III protocol, 3 patients received chemotherapy in the ICE regimen (Ifosfamide + Carboplatin + Etoposide) and 1 patient received chemotherapy in the CDDP+CTX+VCR (Cyclophosphamide + Cisplatin + Vincristine) regimen. All patients had episodes of neutropenic fever when they received chemotherapy, requiring hospitalization and use of an antibiotic treatment. Among the 8 patients analyzed, all died. CONCLUSIONS: Despite progress in treatment, AT/RT of the CNS disease or primary kidney disease associated with a lack of standardization in a regimen contributes to the dismal prognosis. There is a high mortality in patients with AT/RT, similar to that found in the literature.

ATRT-07. LOW-GRADE DIFFUSELY INFILTRATIVE TUMOR, SMARCB1-MUTANT: A CLINICAL AND HISTOPATHOLOGICAL DISTINCT ENTITY SHOWING EPIGENETIC SIMILARITY WITH ATRT-MYC

Christian Thomas[1], Aniello Federico[2,3], Susanne Bens[4], Mats Hellström[5], Olivera Casar-Borota[5,6], Uwe Kordes[7], Julia E. Neumann[8,9], Matthias Dottermusch[8,9], Fausto E. Rodriguez[10], Andrea C. Lo[11], Sylvia Cheng[12], Glenda Hendson[13], Juliette Hukin[12], Christian Hartmann[14], Arend Koch[15], David Capper[15,16], Reiner Siebert[4], Werner Paulus[1], Karolina Nemes[17], Pascal D. Johann[17], Michael C. Frühwald[17], Marcel Kool[2,18], Martin Hasselblatt[1]; [1]Institute of Neuropathology, University Hospital Münster, Münster, Germany. [2]Hopp Children´s Cancer Center (KiTZ), Heidelberg, Germany. [3]Division of Paediatric Neurooncology, German Cancer Research Center (DKFZ) and German Cancer Consortium (DKTK), Heidelberg, Germany. [4]Institute of Human Genetics, Ulm University & Ulm University Medical Center, Ulm, Germany. [5]Dept. of Immunology, Genetics and Pathology, Rudbeck Laboratory, Uppsala University, Uppsala, Sweden. [6]Dept. of Clinical Pathology, Uppsala University Hospital, Uppsala, Sweden. [7]Dept. of Pediatric Hematology and Oncology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany. [8]Institute of Neuropathology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany. [9]Center for Molecular Neurobiology Hamburg (ZMNH), University Medical Center Hamburg-Eppendorf, Hamburg, Germany. [10]Dept. of Pathology, The Johns Hopkins University School of Medicine, Baltimore, MD, USA. [11]Radiation Oncology, British Columbia Cancer and University of British Columbia, Vancouver, BC, Canada. [12]Division of Hematology, Oncology & BMT, Department of Pediatrics, University of British Columbia, Vancouver, BC, Canada. [13]Dept. of Pathology, BC Women and Children's Hospital, Vancouver, BC, Canada. [14]Dept. of Neuropathology, Institute of Pathology, Hannover Medical School, Hannover, Germany. [15]Charité - Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Dept. of Neuropathology, Berlin, Germany. [16]German Cancer Consortium (DKTK), Partner Site Berlin, German Cancer Research Center (DKFZ), Heidelberg, Germany. [17]Swabian Children's Cancer Center, Paediatric and Adolescent Medicine, University Medical Center Augsburg, Augsburg, Germany. [18]Princess Máxima Center for Pediatric Oncology, Utrecht, Netherlands

Most atypical teratoid/rhabdoid tumors (ATRTs) occur in infants, but children and adolescents may also be affected. ATRTs occurring in older patients often comprise the molecular subgroup ATRT-MYC. Recently, central nervous system low-grade diffusely infiltrative tumor with INI1 deficiency (CNS LGDIT-INI1) has been described as a rare low-grade lesion (Nobusawa et al. Am J Surg Pathol 2020;44:1459-1468). Little is known on the molecular relationship of CNS LGDIT-INI1 and ATRT. We therefore further explored a series of six CNS LGDIT-INI1. The median age of the four males and two females was 16 years (range: 10-28 years). All tumors were of supratentorial location and showed low to moderate cellularity, diffuse growth of inconspicuous small SMARCB1-deficient tumor cells and reactive pleomorphic neuronal and glial cells with retained SMARCB1-staining in the background. In addition, two cases also displayed a high-grade rhabdoid component. After DNA isolation, purification and bisulfite conversion, samples were subjected to DNA methylation profiling (MethylationEPIC BeadChip array). Using DNA methylation-based classification and the Heidelberg Brain Tumor Classifier (version v11b4), all tumors were classified as ATRT-MYC (median calibrated score: 0.97). On t-SNE analysis, DNA methylation profiles grouped closely together in proximity to ATRT-MYC. Follow-up information was available for four cases (including the two cases with a high-grade component). Patients received heterogeneous treatments (including chemotherapy according to AT/RT protocols) and experienced stable disease or complete remission after an observation time of three to 56 months. In conclusion, CNS LGDIT-INI1 is a clinically and histologically