Brooklyn Methodist Hospital, Brooklyn, NY, USA, [2]Nationwide Children's Hospital, Columbus, OH, USA

BACKGROUND: Patients with relapsed CNS NGGCTs experience poor outcomes. Our aim to explore prognostic factors that may guide future clinical trials. METHODS: A review of clinical trials that included patients with relapsed CNS NGGCTs was performed. RESULTS: Seventy-four patients were identified; only 14 patients (19%) were long-term survivors. Patients who relapsed >24 months after initial diagnosis had a survival rate of 47% compared with 15% of patients who relapsed in <24 months after initial diagnosis (p= 0.015). Patient with serum/cerebrospinal fluid (CSF) alpha-fetoprotein (AFP) level <25 ng/ml at relapse had a survival rate of 40% compared with 0% among patients with serum/CSF AFP level >25 ng/ml at relapse (p= 0.0015). Patients who achieved complete response/continued complete response (CR/CCR) by the end of therapy had a survival rate of 59% compared with 3% among patients who had less than CR/CCR by the end of therapy (p= 0.0001). Patients who received marrow-ablative chemotherapy followed by autologous hematopoietic cell rescue (HDCx/AuHCR) at relapse had a survival rate of 33% compared with 9% of patients who did not receive HDCx/AuHCR at relapse (p=0.056). The extent of surgical resection, receiving radiotherapy, and beta-human chorionic gonadotropin levels at relapse were not statistically associated with improved outcomes. CONCLUSION: Timing of relapse (>24 months after initial diagnosis), serum/CSF AFP <25 ng/ml at relapse, achieving CR/CCR after treatment were associated with a positive impact on survival. Receiving HDCx/AuHCR at relapse was associated with an improved outcome trend among the patients.

GCT-41. RESPONSE-BASED RADIATION THERAPY IN PATIENTS WITH NEWLY DIAGNOSED CENTRAL NERVOUS SYSTEM LOCALIZED GERMINOMA: A CHILDREN'S ONCOLOGY GROUP (COG) PROSPECTIVE PHASE 2 CLINICAL TRIAL

Ute Bartels[1], Jason Fangusaro[2], Dennis Shaw[3], Aashim Bhatia[4], Arzu Omar-Thomas[5], Shengjie Wu[5], Shannon MacDonald[6], Erin Murphy[7], Mark Souweidane[8], Maryam Fouladi[9], Amar Gajjar[5], Girish Dhall[10], and Soumen Khatua[11]; [1]The Hospital for Sick Children, Toronto, ON, Canada, [2]Aflac Cancer Center, Emory University and Children's Healthcare of Atlanta, Atlanta, GA, USA, [3]Seattle Children's Hospital, Seattle, WA, USA, [4]Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA, USA, [5]St. Jude Children's Research Hospital, Memphis, TN, USA, [6]Massachusetts General Hospital, Boston, MA, USA, [7]Taussig Cancer Institute, Cleveland Clinic, Cleveland, OH, USA, [8]Weill Cornell Medical College and Memorial Sloan-Kettering Cancer Center, New York, NY, USA, [9]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA, [10]The Alabama Center for Childhood Cancer and Blood Disorders at Children's of Alabama, Alabama, AL, USA, [11]MD Anderson Cancer Center, Houston, TX, USA

BACKGROUND: The objective of stratum 2 of COG ACNS1123 was to evaluate children and young adults (3–21 years) with localized central nervous system (CNS) germinoma and investigate whether simplified pre-irradiation chemotherapy followed by response based dose-reduced whole ventricular irradiation (WVI) would maintain a high progression-free survival (PFS) while reducing long term treatment burden. METHODS: Pre-irradiation chemotherapy consisted of 4 cycles of carboplatin and etoposide every 21 days followed by response-based irradiation (XRT). Patients with a complete response (CR) to pre-XRT chemotherapy received 18Gy WVI + 12Gy boost to the tumor bed. Patients with partial response (PR) but less than 1.5 cm residual proceeded to 24Gy WVI + 12Gy boost. All patients were also enrolled on COG ALTE07C1 to prospectively evaluate and longitudinally model the cognitive, social and behavioral functioning. RESULTS: During a total accrual time of 45.5 months from 05/2012 to 06/2018, 137 eligible patients were enrolled. Median age was 14.09 years (4.95–21.46), 73% were male, and 45.26% had elevated βhCG in serum and/or cerebrospinal fluid. Twenty-nine patients (21.17%) did not have tissue biopsy. Eleven patients underwent second-look surgery; 7 had mature teratoma and 4 had non-viable tumor. Eighty-one patients (59.13%) had a CR. There were 4 relapses in patients receiving 18Gy WVI + boost, but no deaths. No unexpected treatment-related events were observed. The estimated 3-year PFS was 94.4 ±2.7% among 74 evaluable subjects. CONCLUSION: This study shows promise in XRT reduction for patients with localized CNS germinoma and CR. Long-term survival outcomes and ALTE07C1 data are being evaluated.

GCT-42. CLINICAL CHARACTERISTICS OF LOCALIZED CENTRAL NERVOUS SYSTEM NON-GERMINOMATOUS GERM CELL TUMORS (NGGCT) PATIENTS ENROLLED ON ACNS1123 WITH RELAPSE: A CHILDREN'S ONCOLOGY GROUP (COG) STUDY

Girish Dhall[1], Shengjie Wu[2], Arzu Onar-Thomas[2], Dennis Shaw[3], Shannon MacDonald[4], Erin Murphy[5], Soumen Khatua[6], Ute Bartels[7], and Jason Fangusaro[8]; [1]University of Alabama at Birmingham, Birmingham, AL, USA, [2]St. Jude Children's Research Hospital, Memphis, TN, USA, [3]Seattle Children's Hospital, Seattle, WA, USA, [4]Massachusetts General Hospital, Boston, MA, USA, [5]Cleveland Clinic, Cleveland, OH, USA, [6]M,D, Anderson Cancer Center, Houston, TX, USA, [7]Hospital for Sick Children, Toronto, ON, Canada, [8]Emory University, Atlanta, GA, USA

ACNS1123 was a Children's Oncology Group Phase 2 study that was undertaken to determine whether irradiation could be safely reduced without impacting survival in a subgroup of NGGCT patients. Between May 2012-Jan 2017, 107 eligible patients were accrued to Stratum 1 (NGGCT stratum). Sixty-six (61.7%) patients achieved a complete/partial response (CR/PR) to induction chemotherapy and received 30.6Gy whole ventricular field irradiation followed by 54Gy tumor-bed boost achieving a 2-year progression-free survival rate of 89% (95% CI:81%-97%) and overall survival rate of 92% (95% CI:86%- 99%). Eight patients progressed; 6 had a spinal relapse and 2 patients had a local plus spinal relapse. Seven of eight patients had marker elevation at relapse and data was not available in one patient. At diagnosis, location was pineal in six cases, suprasellar in one, and bifocal in one case. Four patients had beta HCGβ and AFP elevation and two each had HCGβ and AFP elevation alone at diagnosis. Only two patients had HCGβ or AFP >1000 (HCGβ 3550 in one patient and AFP of 1340 in another). All eight patients were CR by markers; four had radiographic CR and four had a PR. Five patients had surgery at diagnosis: two had embryonal carcinoma, one germinoma, and two mixed germ cell tumor with malignant elements on histology. A consistent significant risk factor could not be identified to explain excess of spinal failures seen in our cohort.

GCT-43. GAIN OF SHORT ARM OF CHROMOSOME 12 IS A MOLECULAR MARKER TO PREDICT PROGNOSIS AND REPRESENTS AN EARLY EVENT IN TUMORIGENESIS IN INTRACRANIAL GERM CELL TUMORS

Kaishi Satomi[1,2], Hirokazu Takami[2,3], Shintaro Fukushima[2], Yoichi Nakazato[4], Shota Tanaka[3], Nobuhito Saito[3], Masayuki Kanamori[5], Toshihiro Kumabe[5], Keiichi Kobayashi[6], Motoo Nagane[6], Toshihiko Iuchi[7], Koji Yoshimoto[8], Masahiro Mizoguchi[8], Kaoru Tamura[9], Taketoshi Maehara[9], Keiichi Sakai[10], Kazuhiko Sugiyama[11], Kiyotaka Yokogami[12], Hideo Takeshima[12], Masahiro Nonaka[13], Akio Asai[13], Ryo Nishikawa[14], Masao Matsutani[15], and Koichi Ichimura[2]; [1]Department of Diagnostic Pathology, National Cancer Centre Hospital, Chuo, Tokyo, Japan, [2]Division of Brain Tumour Translational Research, National Cancer Center Research Institute, Chuo, Tokyo, Japan, [3]Department of Neurosurgery, Faculty of Medicine, The University of Tokyo, Bunkyo, Tokyo, Japan, [4]Department of Pathology, Hidaka Hospital, Takasaki, Gumma, Japan, [5]Department of Neurosurgery, Tohoku University Graduate School of Medicine, Sendai, Miyagi, Japan, [6]Department of Neurosurgery, Kyorin University Faculty of Medicine, Mitaka, Tokyo, Japan, [7]Department of Neurosurgery, Chiba Cancer Center, Chiba, Chiba, Japan, [8]Department of Neurosurgery, Graduate School of Medical Sciences Kyusyu University, Fukuoka, Fukuoka, Japan, [9]Department of Functional Neurosurgery, Tokyo Medical and Dental University, Bunkyo, Tokyo, Japan, [10]Department of Neurosurgery, Shinshu Ueda Medical Center, Ueda, Nagano, Japan, [11]Department of Clinical Oncology and Neuro-oncology Program, Cancer Treatment Center, Hiroshima University Hospital, Hiroshima, Hiroshima, Japan, [12]Department of Neurosurgery, Faculty of Medicine, University of Miyazaki, Miyazaki, Miyazaki, Japan, [13]Department of Neurosurgery, Kansai Medical University Hospital, Hirakata, Osaka, Japan, [14]Department of Neuro-Oncology/Neurosurgery, Saitama Medical University International Medical Center, Hidaka, Saitama, Japan, [15]Gotanda Rehabilitation Hospital, Shinagawa, Tokyo, Japan

Gain of short arm of chromosome 12 (12p) is commonly observed in testicular germ cell tumors (tGCTs) and also seen in intracranial GCTs (iGCTs). However, little is known about the clinical significance of 12p gain in iGCTs. We have collected over 200 fresh frozen tissue samples of iGCTs through the Intracranial Germ Cell Tumor Genome Analysis Consortium in Japan. Firstly, we analyzed DNA methylation profile in 83 iGCTs, 3 tGCTs (seminomas) and 6 normal control samples using Infinium Human Methylation 450K BeadChip array (Illumina, CA, USA) in order to determine 12p gain status. Then, fluorescence in situ hybridization (FISH) study was carried out on 3 mixed iGCT cases using 12p/CEP12 probe (Abbott Molecular, Abbott park, IL, USA). Lastly, 58 iGCTs with clinicopathological information were analyzed for progression-free survival (PFS) and overall survival (OS). Gain of 12p was observed in 100% (3/3) of seminoma, 14% (3/22) of germinoma, 17% (1/6) of mature teratoma, 25% (1/4) of immature teratoma, 55% (11/20) of mixed germ cell tumor, 100% (4/4) of yolk sac tumor, 100% (1/1) of embryonal carcinoma, and 100% (1/1) of choriocarcinoma. In total, 45% (37/83) of iGCT showed 12p gain. Different histological components in each mixed GCT shared the same 12p copy number status within each mixed GCT case. Both PFS and OS were significantly worse in iGCTs with 12p gain (PFS: P=0.027, OS: P=0.0012). Gain of 12p can be a molecular marker to predict prognosis and represents an early event in tumorigenesis prior to histological differentiation in iGCTs.