University of Vienna, Vienna, Austria, [5]The Center for Oncology at the University Children's Hospital Zurich, Department of Oncology, Zurich, Switzerland, [6]Department of Clinical Oncology, Cambridge University Hospitals, Cambridge, United Kingdom, [7]Department of Radiology, University of Newcastle, Newcastle, United Kingdom, [8]Department of Radiology, Cambridge University Hospitals, Cambridge, United Kingdom, [9]Department of Neuropathology, DGNN Brain Tumor Reference Center, University of Bonn, Bonn, Germany, [10]Academic Neuropathology, University of Edinburgh, Edinburgh, United Kingdom, [11]Dept for Children and Adolescents, St, Olav University Hospital of Trondheim, Trondheim, Norway, [12]Dept, Pediatric Oncology, BOND Linköping University Hospital, Linköping, Sweden, [13]Unit of Neurooncology, Department of Haemato-Oncology Gaslini Children's Hospital, Genova, Italy, [14]Imaging Department, Institut Curie, Paris, France, [15]Department of Pediatric Hematology/Oncology, Hannover Medical School, Hannover, Germany, [16]Department of Radiation Oncology, Leipzig, Germany, [17]Radiation Oncology Department Institut Curie, Paris & Proton Centre, Orsay, Paris, France, [18]Department of Paediatric Oncology, Cambridge University Hospitals, Cambridge, United Kingdom

SIOP CNS GCT II aimed to establish if 24Gy Whole Ventricular Radiotherapy (WVRT) in localised germinoma is sufficient for tumour control. After central review of radiological response after 'CarboPEI' chemotherapy, patients in complete remission (CR) were consolidated with 24Gy WVRT. Between 2/2012 and 7/2018, 182 patients from 8 European countries with histologically-confirmed fully-staged localised germinoma were registered. 70 patients were in CR after chemotherapy, 98 in partial remission (PR), seven had stable disease, two progressive disease, and in five no response data were documented. Of the 70 patients in CR, 58 received 24Gy WVRT alone; two of these relapsed, one local and one disseminated, two and six years after diagnosis. Of the 98 patients in PR after chemotherapy, 86 received 24Gy WVRT and 16Gy boost, of which five relapsed (three local, two distant) 12–24 months from diagnosis. Twelve patients in each of the CR/PR groups received non-protocol or undocumented radiotherapy fields/doses. Median follow-up was 3.7 years. Event-free survival (EFS) for patients in CR and with WVRT only (n=58) was 98% at 4 years. 4-years EFS of patients with PR and WVRT 24Gy and 16Gy tumor boost (n=86) was 95%. Localised germinoma in CR after chemotherapy had an excellent outcome with 24Gy WVRT alone; 24GY WVRT can therefore be considered standard consolidation treatment in this group. International consensus on radiological response criteria is of utmost importance to avoid over- and undertreatment of such patients and to pave the way for further treatment reduction in this group of patients.

HIGH GRADE GLIOMA

HGG-01. ENTRECTINIB IN RECURRENT OR REFRACTORY SOLID TUMORS INCLUDING PRIMARY CNS TUMORS: UPDATED DATA IN CHILDREN AND ADOLESCENTS

Giles Robinson[1], Ami Desai[2], Ellen Basu[3], Jennifer Foster[4], Karen Gauvain[5], Amit Sabnis[6], Suzanne Shusterman[7], Margaret Macy[8], Luke Mease[9], Janet Yoon[10], Thomas Cash[11], Mohamed Abdelbaki[12], Kellie Nazemi[13], Christine Pratilas[14], Brian Weiss[15], Saibah Chohan[16], Alison Cardenas[17], Katherine Hutchinson[17], Guillaume Bergthold[18], and Amar Gajjar[1]; [1]St. Jude Children's Research Hospital, Memphis, TN, USA, [2]University of Chicago Medical Center, Chicago, IL, USA, [3]Memorial Sloan Kettering Cancer Center, New York, NY, USA, [4]Texas Children's Hospital, Houston, TX, USA, [5]Washington University School of Medicine, St, Louis, MO, USA, [6]University of California San Francisco, Benioff Children's Hospital, San Francisco, CA, USA, [7]Dana Farber Cancer Institute, Boston Children's Cancer and Blood Disorders Center, Boston, MA, USA, [8]Children's Hospital Colorado, Department of Hematology- Oncology & Bone Marrow Transplantation, Aurora, CO, USA, [9]University of Utah/Huntsman Cancer Institute, Primary Children's Hospital, Salt Lake City, UT, USA, [10]Rady Children's Hospital, San Diego, CA, USA, [11]Aflac Cancer & Blood Disorders Center, Children's Healthcare of Atlanta, Emory University School of Medicine, Atlanta, GA, USA, [12]Nationwide Children's Hospital, Columbus, OH, USA, [13]Oregon Health & Science University, Doernbecher Children's Hospital, Portland, OR, USA, [14]Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine, Baltimore, MD, USA, [15]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA, [16]F. Hoffmann-La Roche Limited, Mississauga, ON, Canada, [17]Genentech, South San Francisco, CA, USA, [18]F. Hoffmann-La Roche, Basel, Switzerland

STARTRK-NG (phase 1/2) is evaluating entrectinib, a CNS-penetrant oral, TRK/ROS1/ALK tyrosine kinase inhibitor, in patients <21 years with recurrent/refractory solid tumors, including primary CNS tumors. After determining the recommended dose, 550mg/m^2/day, in all-comers, expansion cohorts with gene-fusion-positive CNS/solid tumors (*NTRK1/2/3*, *ROS1*) are being enrolled. As of 5Nov2019 (data cut-off), 39 patients (4.9m–20y; median 7y) have been evaluated for response, classified as complete (CR) or partial response (PR), stable (SD) or progressive disease (PD) using RANO (CNS), RECIST (solid tumors), or Curie score (neuroblastoma). Responses in patients with fusion-positive tumors were Investigator-assessed (BICR assessments are ongoing) and occurred at doses ≥400mg/m^2. Best responses in fusion-positive CNS tumors (n=14) were: 4 CR (*GKAP1-NTRK2, ETV6-NTRK3* [n=2], *EML1-NTRK2*); 5 PR (*KANK1-NTRK2, GOPC-ROS1, ETV6-NTRK3, TPR-NTRK1, EEF1G-ROS1*); 3 SD (*BCR-NTRK2, ARHGEF2-NTRK1, KIF21B-NTRK1*); 2 PD (*PARP6-NTRK3, EML4-ALK*); and in fusion-positive solid tumors (n=8) were: 3 CR (*ETV6-NTRK3* [n=2], *DCTN1-ALK*); 5 PR (*EML4-NTRK3, TFG-ROS1* [n=3], *KIF5B-ALK*). Responses (Investigator-assessed) in non-fusion tumors (n=17) were: 1 CR (*ALK F1174L* mutation), 3 SD, 10 PD, 3 no data/unevaluable. The objective response rate (CR+PR/total) in patients with fusion-positive tumors was 77% (17/22) versus 6% (1/17) in those with non-fusion tumors. All 39 patients experienced ≥1 adverse event (AE); the most frequent AEs included weight gain and anemia (both 48.7%); increased ALT, increased AST, cough and pyrexia (all 46.2%); increased creatinine and vomiting (both 43.6%); and bone fractures (n=10, in 9 patients). Entrectinib has produced striking, rapid, and durable responses in solid tumors with target gene fusions, especially high-grade CNS neoplasms.

HGG-02. ADOLESCENT AND YOUNG ADULT (AYA) GLIOMA WITH BRAF V600E-MUTANTATION

Yui Kimura[1,2], Yukitomo Ishi[3], Yuko Watanabe[4], Yoshiko Nakano[1], Shigeru Yamaguchi[3], Yoshitaka Narita[5], and Koichi Ichimura[1]; [1]Division of Brain Tumor Translational Research, National Cancer Center Research Institute, Chuo, Tokyo, Japan, [2]Unit of Comprehensive Oncology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Nagasaki, Japan, [3]Department of Neurosurgery, Hokkaido University Graduate School of Medicine, Sapporo, Hokkaido, Japan, [4]Department of Pediatric Oncology, National Cancer Center, Chuo, Tokyo, Japan, [5]Department of Neurosurgery, National Cancer Center, Chuo, Tokyo, Japan

BACKGROUND: Biological features of pediatric glioma differ significantly from those of adult glioma, and limited data are available on those of AYA patients. Here, we focused on AYA patients with glioma, especially those harboring BRAF V600E mutation, and investigated their clinical and genetic features. METHOD: We retrospectively analyzed AYA patients with brain tumors harboring BRAF V600E, who were treated in two hospitals in Japan. RESULTS: Clinical information was available for 14 patients. The median age at diagnosis was 25 years (range: 15–38). Five patients were diagnosed with glioblastoma (GBM), including one epithelioid type. These patients were over 25. Although one patient with GBM died of the disease 6.9 years after initial diagnosis, the remaining patients were alive. Two patients were alive without recurrence at 38 and 51 months after the treatment. The patient with epithelioid glioblastoma experienced early recurrence. The remaining nine patients (64%) were diagnosed with low-grade glioma, including ganglioglioma, pilocytic astrocytoma, diffuse astrocytoma, oligodendroglioma, pleomorphic xanthoastrocytoma, and polymorphous low-grade neuroepithelial tumor of the young. No patients died of the disease, and four patients are alive without recurrence after initial operation without adjuvant treatment. Two patients are (epithelioid glioblastoma and ganglioglioma) currently undergoing treatment with a BRAF inhibitor for recurrent tumors. DISCUSSION: Although the number of this study is limited, our study suggested that the prognosis of AYA patients with BRAF-V600E positive GBM may not be as dismal as that of children or adults.

HGG-04. ZINC ENHANCES TEMOZOLOMIDE CYTOTOXICITY IN PEDIATRIC GLIOBLASTOMA MULTIFORME MODEL SYSTEM

Amos Toren, Michal Yalon, Aner Dafni, and Ruty Mehrian-Shai; Sheba Medical Center, Ramat Gan, Israel

BACKGROUND: Temozolomide (TMZ) is an alkylating agent that has become the mainstay treatment of the most malignant brain cancer, glioblastoma multiforme (GBM). Unfortunately only a limited number of patients respond to it positively. We have shown that zinc metal reestablishes chemosensitivity in adult GBM in vitro and also in vivo but this effect has not been tested with pediatric GBM. METHODS: Using Human pediatric glioblastoma cell lines- KNS42 (mutant p53/ MGMT [+]) and SF188 (mutant p53/ MGMT [-]), we investigated whether addition of zinc to TMZ enhances its cytotoxicity against GBM. RESULTS: *In vitro* cell viability analysis showed that the cytotoxic activity of TMZ was substantially increased with addition of zinc and this response was accompanied by an elevation of p21, PUMA, BAX and a decrease in growth fraction as manifested by low ki67. Beta gal analysis showed that most of the remaining cells after the combination therapy are in senescence state. In order to eliminate the senescent population created as a result of the combined treatment of TMZ and Zinc, we decided to use a senolytic agent Navitoclax (ABT-263) that was demonstrated to be effective in reducing senescent cells by specific in-

hibition of Bcl-2, Bcl-XL and Bcl-w. Following the addition of Navitoclax to the combined treatment, SF188 cells, but not KNS42, show a significance reduction in viability compare to the combination treatment. CONCLUSIONS: Our results suggest that zinc may serve as a potentiator of TMZ therapy in pediatric GBM patients and using a second hit with senolytic drug in some cases may be even more beneficial.

HGG-05. REGRESSION OF RECURRENT GLIOBLASTOMA AFTER BORON NEUTRON CAPTURE THERAPY AND CHIMERIC ANTIGEN RECEPTOR T-CELL THERAPY IN A CHILD

Hsin-Hung Chen[1,2], and Yi-Wei Chen[1,2]; [1]Taipei Veterans General Hospital, Taipei, Taiwan, Taiwan, [2]National Yang-Ming University, Taipei, Taiwan, Taiwan

A 6 y/o girl with recurrent multifocal glioblastoma received 3 times of boron neutron capture therapy (BNCT) and chimeric antigen receptor (CAR)–engineered T cells targeting the tumor-associated antigen HER2. Multiple infusions of CAR T cells were administered over 30 days through intraventricular delivery routes. It was not associated with any toxic effects of grade 3 or higher. After BNCT and CAR T-cell treatment, regression of all existing intracranial lesions were observed, along with corresponding increases in levels of cytokines and immune cells in the cerebrospinal fluid, but new lesions recurred soon after the treatment. This clinical response continued for 14 months after the initiation of first recurrence.

HGG-06. REMARKABLE RESPONSE TO BRAF INHIBITOR IN AN INFANT WITH DISSEMINATED DIFFUSE LEPTOMENINGEAL GLIONEURONAL TUMOR (DLGNT)

Le Le Aung; Parkway Cancer Centre, Singapore, Singapore

INTRODUCTION: Diffuse Leptomeningeal Glioneuronal Tumor (DLGNT) are rare CNS tumors and in infants, they can be lethal. There are several anecdotal reports in infants with low grade gliomas (LGG) with treated with BRAF inhibitors. METHODS: A six-month old baby girl presented with a 2-week history of absent visual contact and vomiting. Imaging revealed a large 4.7 X 4.2 X 2.8 cm suprasellar charismatic region mass and multiple small extra-axial plaques in spinal canal. The child developed significant ascites post VP shunt requiring shunt externalization, extensive protein infusion support and hospitalization for six weeks. Immunohistochemical staining revealed Olig-2 and S-100, GFAP and synaptophysin positive. EMA showed patchy cytroplasmic reactivity in stromal cells and CD99 showed diffuse reactivity in stromal and lesional cells. INI-1, IDH-1, and CD117 were negative. Ki-67 proliferation index was 8–10%. PCR for BRAF V600E/E2/D was detected and KIAA1549-BRAF fusion as negative. This was confirmed by Genome Wide Next Generation Sequencing. While waiting for GNS testing results, the baby received one dose of Vinblastine. However, within seven days of initiating Debrafenib, significant clinical and radiological responses were observed. CONCLUSION: The baby continues safely on Debrafenib with continued dramatic radiological response. This suggest that there may be a role in early initiation of targeted therapy such as *BRAF* inhibitors rather than giving standard chemotherapy such as Vinblastine or Carboplatin-Vincristine in extremely ill infants with low grade gliomas.

HGG-07. CYCLIN-DEPENDENT KINASES AS TARGET STRUCTURES FOR CANCER THERAPY – A COMPARATIVE IN VITRO ANALYSIS ON PATIENT-DERIVED GLIOBLASTOMA CELL CULTURE MODELS

Christin Riess, Carl Friedrich Classen, and Claudia Maletzki; University Medicine, Rostock, Mecklenburg-Vorpommern, Germany

INTRODUCTION: Current therapeutic approaches have limited clinical success for Glioblastoma patients, making novel strategies urgent. Cyclin-dependent kinases (CDK) are crucial in cell cycle, oncogenic transcription, DNA repair, and stem-cell renewal. Glioma cells frequently show genomic alterations in CDKs. Here, we evaluated the antitumoral activity of selective CDK inhibitors (CDKI) abemaciclib (CDK4/6), palbociclib (CDK4/6), and dinaciclib (CDK1/2/5/9) alone and in combination with chemo-/radiotherapy. MATERIALS/METHODS: Low passage glioblastoma cell lines (N=5) with different molecular characteristics were cultured in 2D and 3D (neurospheroids (NSPs), glioma stem-cells (GSCs). The impact of CDKI alone or in combination with TMZ and radiation (2Gy) was examined. Viability was measured using Calcein-AM and 3D-Glo assays; DNA double-strand breaks by γ-H2AX immunofluorescence. Functional analyses were performed from a 2D culture (72h treatment). RESULTS: Dinaciclib significantly affected viability of GBM cell lines even shortly after low-dose treatment. CDK 4/6 inhibitors were less effective. Abemaciclib and dinaciclib acted radio-sensitizing. Dinaciclib combined with different substances (72h, dose: IC_{20}), synergistically potentiated antitumoral effects. In a scratch assay, abemaciclib decelerated wound healing; dinaciclib even induced cell death. Microarray analysis revealed altered gene expression: Genes mediating cell adhesion, division, DNA-binding, apoptosis (*Casp3*,*Casp8*), senescence (*ASF1A,CENPA,FBXO31*), and autophagy (*ATG4D,ATG2A,SOGA1*) were upregulated. Chemotaxis-mediating *(CXCL8,CCL20)* and proto-oncogenes like *JUNB* and *FOS* were strongly down-regulated. Long-term treatment induced dinaciclib resistance in 1/5 cases, and none abemaciclib-treated cells. This was reversed when dinaciclib was combined with TMZ. CONCLUSION: Our results demonstrate strong anti-GBM activity of dinaciclib and abemaciclib, with additive effects of chemotherapy and radiosensitization, encouraging to move forward this strategy.

HGG-09. FIRST LINE THERAPY OF PEDIATRIC GLIOBLASTOMA WITH LAROTRECTINIB

Musa Alharbi[1], Nahla Ali Mobark[1], Ali Abdullah O. Balbaid[2], Fatmah A. Alanazi[3], wael abdel Rahman Aljabarat[1], Eman A.K. Bakhsh[4], Murad Turkistani[5], and Malak Abedalthagafi[6]; [1]Department of Paediatric Oncology Comprehensive Cancer Centre, King Fahad Medical, Riyadh, Saudi Arabia, [2]Radiation Oncology Department Comprehensive Cancer Centre, King Fahad Medical City, Riyadh, Saudi Arabia, [3]Department of Clinical Pharmacy, King Fahad Medical City, Riyadh, Saudi Arabia, [4]Radiology Department King Fahad Medical CITY, Riyadh, Saudi Arabia, [5]Department of Pathology, King Abdulaziz University Hospital, Jeddah, Saudi Arabia, [6]Genomics Research Department, Saudi Human Genome Project, King Fahad Medical City and King Abdulaziz City for Science and Technology, Riyadh, Saudi Arabia

PURPOSE: In this case report, we document new recommendations for the treatment of pediatric glioblastoma based on a genetic understanding of the disease. PATIENTS AND METHODS: A Saudi girl aged 18 months presented with a history of right sided weakness and partial seizures. MRI revealed the presence of large complex left frontal tumor. Craniotomy and gross total resection were performed. post-operatively The patient showed excellent recovery with no neurological deficits. Pathology reports confirmed glioblastoma (GBM). Due to the expected poor survival, the patient's family declined standard therapy, including chemotherapy and/or radiation therapy. RESULTS: Molecular analysis showed positive fusion mutations for ETV6-NTRK3 making the patient an ideal candidate for larotrectinib, an oral tyrosine kinase (TRK) inhibitor. Unfortunately, follow-up MRI showed local tumor recurrence at 3-months post-surgery. The family agreed to the initiation of oral larotrectinib as a less invasive therapy. The patient tolerated Larotrectinib very well with no reported side effects. Follow up MRI was performed 8-weeks post-larotrectinib treatment and showed significant tumor regression, indicating an excellent treatment response. CONCLUSION: This case highlights how TRK-inhibitors can be integrated as a first-line therapy for pediatric high grade GBMs harboring TRK-fusions. We also highlight the need for the integration of genomic profiling and molecular analysis into the routine histopathologic analyses of pediatric patients with malignant primary intracranial tumors, to detect any genetic mutations that can be targeted with available therapies to avoid the morbidity associated with non-precision conventional therapies.

HGG-11. HIGH-GRADE GLIOMAS IN ADOLESCENTS AND YOUNG ADULTS HIGHLIGHT HISTOMOLECULAR DIFFERENCES WITH THEIR ADULT AND PAEDIATRIC COUNTERPARTS

Alexandre Roux[1,2], Johan Pallud[1,2], Raphaël Saffroy[3], Myriam Edjlali-Goujon[4,2], Marie-Anne Debily[5], Nathalie Boddaert[6], Marc Sanson[7,8], Stéphanie Puget[9], Steven Knafo[10], Clovis Adam[11], Thierry Faillot[12], Dominique Cazals-Hatem[13], Emmanuel Mandonnet[14], Marc Polivka[15], Georges Dorfmüller[16], Aurélie Dauta[17], Mathilde Desplanques[18], Albane Gareton[18], Mélanie Pages[18,2], Arnault Tauziède-Espariat[18,2], Jacques Grill[19,5], Franck Bourdeaut[20], François Doz[20], Frédéric Dhermain[21], Karima Mokhtari[22,7], Fabrice Chrétien[18], Dominique Figarella-Branger[23], and Pascale Varlet[18]; [1]Department of Neurosurgery, GHU Paris, Sainte-Anne Hospital, University of Paris, Paris, France, [2]INSERM UMR 1266, IMA-Brain, Institute of Psychiatry and Neurosciences of Paris, Paris, France, [3]Department of Biochemistry, Paul-Brousse Hospital, AP-HP, Villejuif, France, [4]Department of Neuroradiology, GHU Paris, Sainte-Anne Hospital, University of Paris, Paris, France, [5]INSERM U981, «Biomarqueurs and New Therapeutic Targets in Oncology», Team «Genomics and Oncogenesis of Brain Tumors", Paris-Sud University, Paris-Saclay University, Villejuif, France, [6]Department of Neuroradiology, Necker Enfants-Malades Hospital, AP-HP, University of Paris, Paris, France, [7]Brain and Spine Institute (ICM), Experimental Neuro-Oncology Department, Inserm U1127, CNRS UMR 7225, Sorbonne University, UPMC University Paris 06, Paris, France, [8]Department of Neurology [2], Mazarin Unit, Pitié-Salpêtrière Hospital, AP-HP, Paris, France, [9]Department of Neurosurgery, Necker Enfants-Malades Hospital, AP-HP, University of Paris, Paris, France, [10]Department of Neurosurgery, Bicêtre Hospital, AP-HP, Paris-Sud University, Kremlin-Bicêtre, France, [11]Department of Pathology, Bicêtre Hospital, AP-HP, Paris-Sud University, Kremlin-Bicêtre, France, [12]Department of Neurosurgery, Beaujon Hospital, AP-HP, Clichy, France, [13]Department of Pathology, Beaujon Hospital, AP-HP, Clichy, France, [14]Department of Neurosurgery,