1 and 15 of 28-day cycles. RESULTS: Between 2015 and 2020, 10 subjects were enrolled at MBZ 50mg/kg/day (n=3), 100mg/kg/day (n=4), and 200mg/kg/day (n=3). One subject assigned to 100mg/kg/day was not evaluable. Seven subjects had a diagnosis of diffuse midline glioma, 1 subject had anaplastic astrocytoma, and 1 subject had a spinal HGG. All subjects received radiation. There were no dose limiting toxicities. The most frequent G3/G4 adverse events were neutropenia (n=3), and lymphopenia (n= 4). The overall response rate was 33% with 2 subjects achieving a partial response and 1 subject achieving a complete response sustained for 10 months. The PFS and OS from the start of study treatment were 4.7 months and 11.4 months, respectively. CONCLUSION: MBZ was safe and well tolerated when administered with BVCZ and CPT-11 at doses up to 200mg/kg/day. Further studies are needed to determine the efficacy of this treatment.

EPCT-03. WORKING TOGETHER TO ACCELERATE THE PRECLINICAL TO CLINICAL TRANSLATION OF DRUG DELIVERY SYSTEMS FOR CHILDREN'S BRAIN TUMOURS

Emma Campbell[1], Kristian Aquilina[2], Madhumita Dandapani[1], David Walker[1], Ruman Rahman[1]; [1]The University of Nottingham, Nottingham, United Kingdom. [2]Great Ormond Street Hospital, London, United Kingdom

Children's brain tumours are the biggest cancer killer in children and young adults. Several techniques, such as intra-cerebrospinal fluid chemotherapy, ultrasound-mediated blood-brain barrier disruption, convection enhanced delivery, polymer delivery systems, electric field therapy, and intra-arterial and intra-nasal chemotherapy, have the potential to transform the treatment of brain tumours in children. However, there have been very few clinical trials to evaluate these. In 2021, the CBTDDC (Children's Brain Tumour Drug Delivery Consortium) and the ITCC (Innovative Therapies for Children with Cancer) brain tumour group established a Clinical Trials Working Group comprising international researchers and clinicians to address this issue. This partnership highlighted the main challenges in preclinical to clinical translation of paediatric CNS drug delivery as: (1) a lack of specific funding for prototype development and/or scale-up for clinical trials; (2) difficulties in navigating the regulatory landscape; (3) lack of accurate preclinical models; and (4) increased need for multi-centric working. In response to this, we ran a hybrid workshop in November 2021 on 'Clinical Trial Readiness for CNS Drug Delivery'. At this workshop, around 50 delegates (comprising clinicians, researchers, trial regulatory experts, policy makers, and representatives from funding organisations, brain tumour charities and industry) came together to discuss issues around funding, preclinical models and regulatory processes. We have established speciality-specific working groups to build on the workshop discussions, with the aim of producing recommendations around the use of preclinical models and drug delivery techniques according to brain tumour type. We have also used the workshop presentations and discussions to create a 'Roadmap' document for preclinical to clinical translation, which will be freely shared with the neuro-oncology research community. We continue to liaise with funders and regulatory bodies to address the changes that are needed in these areas. If you would like to join our network, contact: cbtddc@nottingham.ac.uk

EPCT-04. STEREOTACTIC BIOPSY SPLIT-COURSE RADIATION THERAPY FOR DIFFUSE MIDLINE GLIOMA OF THE PONS (SPORT-DMG): EARLY PHASE II ENROLLING CLINICAL TRIAL

Danielle Cunningham, Jonathan Schwartz, Julie Guerin, Derek Johnson, Soumen Khatua, Nadia Laack, Safia Ahmed, Victoria Michelle Silvera, Debra Brinkmann, Deanna Pafundi, Gesina Keating, Aditya Raghunathan, Caterina Giannini, David Daniels, Anita Mahajan; Mayo Clinic, Rochester, MN, USA

Diffuse midline glioma (DMG) of the pons remains the leading cause of death among pediatric patients with brain tumors, despite numerous attempts to intensify treatment. While standard treatment includes 54Gy in 30 fractions of radiation over six weeks of time, nearly all patients progress within the treatment field, and many experience symptomatic radionecrosis with steroid dependence. Symptom improvement typically begins after 20Gy to the tumor. Both hypofractionation and reirradiation after recurrence have been found to be safe for patients with DMG. Our study aims to enroll patients with newly diagnosed pontine DMG aged >1 year (no maximum age), and collect molecular information about DMG via stereotactic biopsy, followed by a short 2 week course of 25Gy in 10 fractions of radiation, with volumes guided by MRI with tractography reconstruction and FDOPA PET radiotracer uptake. Patients are followed closely and can complete the 25Gy in 10 fraction radiation course up to 3 times total for meeting radiographic and clinical progression criteria. Our primary endpoint is to estimate the time to progression from diagnosis to after receiving the second 25Gy course, and to compare this to the historical 7 month standard from diagnosis to progression after one 54Gy course. We aim to improve the time interval where patients are asymptomatic at home while minimizing time receiving daily treatments. Other endpoints will include the patient quality of life, caregiver quality of life, PFS intervals after each course, overall survival, and toxicity.

EPCT-05. PHASE IB STUDY OF UNESBULIN (PTC596) IN CHILDREN WITH NEWLY DIAGNOSED DIFFUSE INTRINSIC PONTINE GLIOMA (DIPG) AND HIGH-GRADE GLIOMA (HGG): A REPORT FROM THE COLLABORATIVE NETWORK FOR NEURO-ONCOLOGY CLINICAL TRIALS (CONNECT)

Margot A. Lazow[1,2], Patricia Baxter[3], Joseph Stanek[1], Adam Lane[4], Diana P. Rodriguez[1,2], Shiva Senthil Kumar[1,2], James L. Leach[4,5], Leonie Mikael[1], Christine Fuller[6], Daniel R. Boué[1,2], Christopher R. Pierson[1,2], Diana Thomas[1,2], John Breneman[4,5], Joshua Palmer[7,1], Xiao-Nan Li[8], Ralph Salloum[1,2], David Ashley[9], Peter de Blank[4,5], Eugene Hwang[10], Sarah E. S. Leary[11], Ashley Plant[8], Dorothy Crabtree[1], Mona Wahba[12], Marla Weetall[12], John Baird[12], Jeffrey Leonard[1,2], Clinton F. Stewart[13], Elaine Mardis[1,2], Maryam Fouladi[1,2], Rachid Drissi[1,2]; [1]Nationwide Children's Hospital, Columbus, OH, USA. [2]The Ohio State University, Columbus, OH, USA. [3]Texas Children's Hospital, Houston, TX, USA. [4]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA. [5]University of Cincinnati, Cincinnati, OH, USA. [6]Upstate Medical University, Syracuse, NY, USA. [7]The James Cancer Hospital at the Ohio State University, Columbus, OH, USA. [8]Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, USA. [9]Duke Children's Hospital, Durham, NC, USA. [10]Children's National Medical Center, Washington, DC, USA. [11]Seattle Children's Hospital, Seattle, WA, USA. [12]PTC Therapeutics, South Plainfield, NJ, USA. [13]St. Jude Children's Research Hospital, Memphis, TN, USA

BACKGROUND: The B-cell-specific Moloney murine leukemia virus integration site-1 (BMI-1) protein, implicated in self-renewal and DNA-damage signaling, is highly expressed in DIPG and HGG. Preclinically, BMI-1 modulation by unesbulin (PTC596 [which mediates hyperphosphorylation and subsequent degradation of BMI-1]) leads to DIPG/HGG cell proliferation blockade, mitotic abnormalities, and tumor cell sensitization to radiation-induced DNA damage. METHODS: This phase Ib study sought to determine the maximally tolerated dose/ recommended phase 2 dose (RP2D) of unesbulin administered concurrently with radiotherapy and adjuvantly in children with newly diagnosed DIPG or HGG. Patients were enrolled according to a Rolling-6 design and received oral unesbulin twice weekly during radiotherapy and as maintenance therapy. RESULTS: Twenty-seven patients enrolled (median age: 8.5 years [range: 2-18]), including 18 patients with DIPG and nine patients with HGG. Unesbulin was administered in capsule formulation in the first nine patients, then tablet formulation for subsequent patients. Within the capsule formulation group, three dose-limiting toxicities (DLTs) were observed in two patients on dose level 2 (grade 4 neutropenia). Within the tablet formulation group, four DLTs were experienced by three patients on dose level 2 (grade 3 ALT elevation, grade 3 dehydration/vomiting, grade 3 decreased ejection fraction, grade 4 neutropenia). Dose level 1 was declared the RP2D, and six additional patients enrolled in the expansion cohort at this dose without DLTs. Most common drug-related grade 3/4 toxicities were neutropenia (48%), leucopenia (35%), and elevated ALT (26%). Similar pharmacokinetic profiles were observed for capsule and tablet formulations, consistent with adult data. Survival outcomes and genomics results will be shared at time of presentation. CONCLUSIONS: The RP2D of unesbulin in children newly diagnosed with DIPG or HGG is 200mg/m2 twice weekly, concurrent with and following radiotherapy. The recently opened surgical cohort will assess intratumoral pharmacokinetics and inhibition of tumor BMI-1 signaling, with results forthcoming.

EPCT-06. PHASE I STUDY OF RIBOCICLIB AND EVEROLIMUS POST-RADIOTHERAPY IN CHILDREN WITH NEWLY DIAGNOSED DIFFUSE INTRINSIC PONTINE GLIOMA (DIPG) AND HIGH-GRADE GLIOMA (HGG): UPDATED REPORT FROM THE COLLABORATIVE NETWORK FOR NEURO-ONCOLOGY CLINICAL TRIALS (CONNECT)

Margot A. Lazow[1,2], Mariko DeWire[3,4], Olivia Campagne[5], James L. Leach[3,4], Christine Fuller[6], Shiva Senthil Kumar[1,2], Joseph Stanek[1], Peter de Blank[3,4], Trent R. Hummel[3,4], Natasha Pillay-Smiley[3,4], Ralph Salloum[1,2], Charles B. Stevenson[3,4], Patricia Baxter[7], David Gass[8], Stewart Goldman[9], Sarah E. S. Leary[10], Adam Carle[3,4], Adam Lane[3,4], Rachid Drissi[1,2], Clinton Stewart[5], Maryam Fouladi[1,2]; [1]Nationwide Children's Hospital, Columbus, OH, USA. [2]The Ohio State University, Columbus, OH, USA. [3]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA. [4]University of Cincinnati, Cincinnati, OH, USA. [5]St. Jude Children's Research Hospital, Memphis, TN, USA. [6]Upstate Medical University, Syracuse, NY, USA. [7]Texas Children's Hospital, Houston, TX, USA. [8]Atrium Health Levine Children's Hospital, Charlotte, NC, USA.