with residual disease at diagnosis, 5 (36%) and 7 (50%), respectively, exhibited complete and partial response to induction. Three patients progressed on therapy, and six progressed after completion of therapy at a median of 9.7 months. In all, 18 patients completed RT (16 focal/4 CSI) and 6 pre-/12 post-consolidation). Three died of therapy-related toxicity (two in primary therapy and one in relapse therapy), and 8 died of disease. Sixteen patients (59%) are alive at a median follow up of 33 months (range 9–114). Of 17 with disease-free survival, eight (47%) had relapsed syndromes of whom three are alive. At the time of presentation, data for approximately 50 patients is expected, and we will compare outcomes to soon-to-be-published data from ACNS0333.

ATRT-31. SUCCESSFUL MULTIMODALITY MANAGEMENT OF ATRT OF THE LOWER DORSAL SPINE WITH SPINAL DROP METASTASIS
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A 6 year old boy presented with low backache for the last 5 months. MRI of the spine showed a 1.3x1.5x0.7cm intradural mass extending from D10-D12, causing compression of the conus medullaris. With a preoperative diagnosis of intradural ependymoma, a gross total resection (GTR) of tumour was performed. Post-operative histopathology showed a markedly cellular, malignant tumour with frequent mitotically active cells. Cells were round to polygonal with vesicular nuclei, prominent nucleoli and were immunopositive for CK,EMA,ps3 and immunonegative for MIC2,desmin,SMAPAP1-1(MIB1 labeling index-35-40%). The overall impression was spinal atypical teratoid rhabdoid tumour(ATRT). Post-operative neuraxis MRI revealed post-operative changes(D10-D12) with a 9 mm enhancing lesion at L5-S1 junction suggesting drop metastasis. There was no brain lesion. CSF cytology did not show any malignant cell. The metastatic work-up was normal.He was started on chemotherapy with vincristine and etoposide-2mg/m2 IV D1-D2, Carboplatin-500mg/m2 IV D3, Etoposide-100mg/m2 IV D3 D3q3weeks. Subsequently he received craniospinal irradiation (CSI)-36/Gray/2fractions/4weeks-> focal boost to primary tumour bed and spinal drop metastasis-14.4Gray/8fractions/1.5 weeks. Thereafter he received 3 more cycles of IEC regimen. End-of-treatment MRI showed post-op changes(D10-D12) and 38.5% reduction of the L5-S1 lesion suggesting partial response. Six monthly MRI spinal MRI showed serial reduction of the metastatic lesion leading to complete resolution of the lesion. On last follow up (30 months from initial diagnosis), he was neurologically intact and in CR. Multimodality management comprising GTR,CSI followed by focal boost and multiagent chemotherapy(IEC) can lead to successful outcome in patients with this rare and aggressive spinal tumour.

ATRT-32. GENOME-WIDE CRISPR AND SMALL-MOLECULE SCREENS UNCOVER TARGETABLE DEPENDENCIES IN AT/RTS
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Brain tumors are the leading cause of cancer-related deaths in children and adolescents. Embryonal brain tumors are a group of high-grade neoplasms which primarily affect young patients, and atypical teratoid rhabdoid tumors (AT/RTs) are the second most common type of tumor within this group. In spite of intensive research efforts and the knowledge of molecular mechanisms driving subgroup-specific heterogeneity within AT/RTs, survival estimates stay relatively low as compared to other tumor entities with a median survival of around 17 months. More efficacious and durable therapies are urgently needed to improve the situation of patients. We here used a combination of genome-wide CRISPR dependency screens and small-molecule drug assays to identify genetic vulnerabilities and novel therapeutic targets for this tumor entity. Here, we successfully generated a chemical library that shows preferential activity in AT/RT cell lines, thereby validating our CRISPR approach to the therapeutic testing of AT/RTs. Further, the identified dependencies seemed to be subgroup-specific, suggesting that targets identified here can be used as pan-AT/RT therapeutic avenues. Among others, these include inhibition of EGF signaling and CDK4/6. Our data provide a comprehensive map of dependencies for AT/RTs which will serve as a starting point in the development of targeted therapies for this tumor entity.

ATRT-33. ENABLING RAPID CLASSIFICATION OF ATRT WITH NONSTRING NCounter PLATFORM
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In recent years, using gene expression and methylation array platforms, multiple research groups have reported the presence of at least three major Atypical Teratoid Rhabdoid Tumor (ATRT) subtypes that exhibit distinct epigenetic, transcriptomic and clinical features. Yet, utilizing ATRT subtypes in a clinical setting remains challenging due to a lack of suitable biological markers, limited sample quantities and relatively high cost of current assays. To address this gap between research and clinical practice, we have designed a assay that utilizes a custom 53 signature genes panel for the NanoString nCounter System and have created a flexible machine learning classifier package for ATRT tumour subtyping. We have analyzed 71 ATRT primary tumours with matching gene expression data using the 53 genes panel. 60% of the data was used for models training (10 repeats of 30-fold cross validation with subgroup balanced sample splitting) resulting in overall 94.6% training accuracy. The remaining 40% of the samples were used for model validation and the assay was able to achieve 92-100% accuracy with no subgroup existentiality of the workflows, we have tested it again over other transcriptome-based methods such as gene expression array and RNAseq. We have also demonstrated its use in samples that were not classifiable by methylation-based method. We are presenting here a rapid and accurate ATRT subtyping assay for clinical usage that is compatible with archived ATRT tissues.

COVID-19 AND PEDIATRIC NEURO-ONCOLOGY

COVID-01. VINBLASTINE MONOTHERAPY INDUCTION FOR LOCALISED CNS GERMINOMA DURING THE COVID-19 PANDEMIC
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INTRODUCTION: Patients with localised CNS-germinoma have excellent survival. More recently, intensive inpatient chemotherapy (carboPEI=carboplatin/etoposide/Ifosfamide in Europe) has been effectively employed to reduce radiotherapy fields and/or dose. Current research priorities focus on reducing treatment burden and long-term sequelae. Of note, outpatient-based single-agent carboplatin chemotherapy is associated with excellent outcomes in metastatic testicular seminoma (an identical pathology) [Alifrangis,ECOJ,2020]. Recently, successful inpatient vinblastine monotherapy was utilised in localised CNS-germinoma [Murray,Neuromanol-Adv,2020]. METHODS: Due to the COVID-19 pandemic, adapted UK guidelines for germ-cell-tumour management were distributed, including potential non-standard treatment options that would reduce hospital visits and admissions. A 30-year-old patient presented with a 32mmx30mmx35mm diameter solid+multi-cystic localised pineal CNS lesion, consistent radiologically with a germ-cell tumour with prominent teratoma component. Investigation revealed negative AFP/HCG markers and biopsy-proven pure germinoma. After appropriate consent, the patient commenced a 12-week induction with weekly vinblastine monotherapy (low-grade-gloma dosing [Lassaleta,ECOJ,2016]), with wk6&12 MRI re-assessment prior to definitive radiotherapy. RESULTS: Vinblastine was well-tolerated. After initial 4mg/m2 test-dosing (wk1), standard 6mg/m2 was delivered for wk2, but resulted in asymptomatic neutropenia (nadir 0.3×10⁹/L) and missed dosing at wk3. Subsequent doses were 4mg/m2, with no further neutropenia. As expected, MRI showed moderate 40% tumour volume reduction by wk12. Surgical resection of the residual, preserved teratoma component was undertaken prior to radiotherapy. CONCLUSION: Patients with CNS-germinoma have excellent outcomes and reduction of treatment-effects remains a priority. The exquisite chemosensitivity of germinoma, excellent results from monotherapy for metastatic testicular disease, and early promise of vinblastine monotherapy lend itself to further exploration for CNS-germinoma.

COVID-02. COVID-19 AND CHILDHOOD CANCER CARE: THEMATIC ANALYSIS OF PUBLISHED SCIENTIFIC AND CLINICAL LITERATURE
Chris Barton1, NHS, Liverpool, United Kingdom

INTRODUCTION: The SARS-CoV-2 pandemic has affected modern medicine and healthcare provision profoundly. National and regional ex-
Abstracts

EXPERIENCES WITH COVID-19 HAVE BEEN HUGELY VARIABLE ACROSS THE GLOBE, REFLECTING ETHNIC, GOVERNMENTAL, CULTURAL, ECONOMIC AND HEALTHCARE DIFFERENCES. THIS THEMATIC ANALYSIS WAS PERFORMED TO IDENTIFY SCIENTIFIC AND CLINICAL EXPERIENCES WITH COVID-19 IN CHILDREN WITH CNS TUMORS AND TREATMENT. METHODS: THE NHS EVIDENCE PORTAL WAS USED TO CONDUCT A HEALTHCARE DATABASE ADVANCED SEARCH. Duplicates were removed. Remaining results were screened using clear inclusion and exclusion criteria. RESULTS: 172 results were identified and data extracted. Literature was identified from all 5 continents, with lower and middle income countries well represented. Key themes identified included: 1) Impact of patients already diagnosed, including decreased treatment regimens, impact on outpatient clinics, COVID susceptibility and travel restrictions; 2) Delays in presentation and diagnosis, and national screening programs; 3) The impact of COVID on healthcare professionals; 4) Impact on current and future research; 5) Consequence of global economic crisis on childhood cancer care; 6) Impact on long-term survivorship, late effects and surveillance monitoring. CONCLUSION: COVID-19 has had a profound effect on healthcare, and the literature reflects the extent to which communities involved in childhood cancer care have worked together to minimise the impact. It is inevitable that there have been consequences of the pandemic on the treatment of existing patients, and the diagnosis of new ones, but evidence suggest these effects in the short term are minimal. The greatest concerns are for immediate and short-term research conduct.

COVID-03. IMPACT OF COVID-19 ON THERAPY PROVISION FOR CHILDREN WITH CNS TUMOURS
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INTRODUCTION: The COVID-19 pandemic has led to widespread changes in the delivery of rehabilitation. The Teenage Cancer Trust reported that 69% of young people with cancer saw their physiotherapist less than usual during the pandemic raising concerns about physiotherapy input. METHODS: Retrospective analysis of all children’s therapy input recorded using the Teenage Cancer Trust Neuro Oncology Rehabilitation Team (NOTRT) system between 1st April and 30th July 2020. Descriptive analysis of change to physiotherapy provision during this time period by Tertiary and local community services. RESULTS: 49 children were managed under the NOTRT Therapy team and 9 children were newly diagnosed with CNS tumours. There was no impact on inpatient therapy provision, 3 had delayed local therapy provision on discharge requiring increased virtual input by the Tertiary centre. 40 children were outpatients managed under the NOTRT therapy team. 16 children were also receiving regular local physiotherapy input prior to the COVID-19 pandemic. 13 of these children subsequently had their local physiotherapy input suspended during this time period, 8 children were offered virtual input as an alternative by the Tertiary centre, 2 children received increased face to face appointments at the Tertiary centre. 14 of the 24 children managed solely under the Tertiary NOTRT Therapy Team changed to virtual therapy reviews. DISCUSSION: There is a clear change in therapy provision as a result of the COVID-19 pandemic. Future research should consider the effectiveness of neurorehabilitation conducted virtually and the impact on physical function of reduced local therapy provision in children with CNS tumours.

COVID-04. CHARACTERISTICS OF SARS-COV-2 IN 64 CHILDREN WITH CNS TUMORS: A REPORT FROM THE SIOP/ST, JUDE CHILDREN’S RESEARCH HOSPITAL (SJRCH) GLOBAL COVID-19 CHILDHOOD CANCER REGISTRY
Daniel Moreira1,2, Eric Beuker,3 Nickhil Bhakta,1 Guillermo Chantada,1 Yichen Chen,1 Lane Laughman,1 Yuvanesh Vedaraju,1 Maghana Avula,1 Maysam Hamori,1 Paula Naidu,1 Andrew Pappas,1 Radhikesh Rana,1 Victor Santana,1 Michael Sullivan,1 Lorenza Baroni,1 Miguela Camza,1 Meenakshi Devidas,1 Kathy Pritchard-Jones,1 Carlos Rodriguez-Galindo,1 and Sheena Mukkada1
1St. Jude Children’s Research Hospital, Memphis, TN, USA, 2The Hospital for Sick Children, Toronto, ON, Canada, 3Hospital de Pediatría S.A.M.I.C. Prof Dr Juan P Garrahan, Buenos Aires, Argentina, 4Royal Hospital for Sick Children, Glasgow, Scotland, 5Royal Children’s Hospital, Melbourne, Australia, 6UCL Great Ormond Street Institute of Child Health, London, United Kingdom

BACKGROUND: The GCCCR is a collaboration between SIOP and SJRCH to describe the natural history of SARS-CoV-2 in children with cancer across the world. METHODS: The GCCCR is a deidentified registry of patients <19 years of age with cancer or recipients of a hematopoietic stem cell transplant. Data were collected from laboratory-confirmed cases of SARS-CoV-2 infection. Demographic data, cancer diagnosis, cancer-directed therapy, and clinical characteristics of SARS-CoV-2 infection were collected. Outcomes were collected at 30-days and 60-days post infection. RESULTS: As of August 10th 2020, the GCCCR included 730 cases from 35 countries, including 64 children with CNS tumors (8.8%) from 17 countries. The most frequent diagnoses were embryonal tumors (31.2%) and low-grade glioma (17.2%). Thirty-nine (60.9%) children were asymptomatic from infection, while 19 (29.7%) patients required hospital admission and 2 (6.3%) transferred to the intensive care unit. There was an associated increase in COVID-19 severity and ANC <500 (p=0.04). At the time of infection, 44 (68.8%) patients were undergoing cancer-directed therapy. Thirty-two cases have follow-up data. No modification in cancer-directed therapy occurred in 11 (34.4%) patients, while chemotherapy was modified in 6 (18.8%), radiotherapy delayed in 2 (6.3%), and surgery postponed in 1 (3.1%). No patients died from SARS-CoV-2 infection, although 2 died from non-COVID-19 related causes. CONCLUSION: The frequency and severity of COVID infection among children with CNS tumors appears to be proportionally lower compared to other children with cancer. Although this is the largest cohort of patients reported to date, additional insight is needed, including the effects of treatment modifications on outcomes.

DRUG DELIVERY/PHARMACOKINETICS

DDEL-01. ENHANCING DRUG DELIVERY WITH MRGFSUS FOR DIFFUSE INTRINSIC PONTINE GLIOMA MODEL
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Diffuse intrinsic pontine glioma (DIPG) is a surgically unresactable and devastating tumor in children. To date, there have been no effective chemotherapeutics despite a myriad of clinical trials. The intact blood-brain barrier (BBB) in part is responsible for the limited clinical response to chemotherapeutics. MRI guided focused ultrasound (MRgFUS) is a promising non-invasive tissue ablative method for CNS tumors. Moreover, MRgFUS allows for the temporary disruption of BBB. Our first objective was to determine the feasibility and safety of temporary BBB disruption within the brainstem using MRgFUS following intravenous (IV) administration of microbubbles in vivo. Our second objective was to select effective chemotherapeutics against DIPG cell lines, and to examine their therapeutic effects with MRgFUS in a mouse model of DIPG which exhibits an intact BBB. The non-invasive opening of the BBB was determined in the brainstem of normal rodents using physiological monitoring and histological analysis. Doxorubicin was selected from a drug screen consisting of conventional chemotherapeutics using SU-DIPG4 and SU-DIPG17 cell lines. We established SU-DIPG17 xenografts which demonstrated diffuse infiltrative tumor growth similar to human DIPG. By LC-MS/MS analysis, MRgFUS led to 4-fold increase in doxorubicin concentrations within the brainstem tumors following IV administration when compared to IV administration alone. We demonstrated feasibility and safety of MRgFUS in the rodent brainstem model, and have shown that MRgFUS increases doxorubicin concentration in the brainstem of a rodent model of DIPG. These preclinical data will be helpful in designing clinical trials of BBB disruption using MRgFUS for DIPG in children.

DDEL-02. DECREASED TOXICITY OF CONVENTIONAL DOSE CHEMOTHERAPY UTILIZING BODY WEIGHT INSTEAD OF BODY SURFACE AREA FOR DOZING IN YOUNG CHILDREN <6 YEARS OLD ENROLLED ON THE “HEAD START” 4 CLINICAL TRIAL
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Metabolism of drugs in infants and young children is significantly different from older individuals due to differences in distribution, protein-binding capacity, hepatic metabolism and renal excretion. To be consistent with Children’s Oncology Group (COG) guidelines, body surface area (BSA) was used for dose chemotherapeutics in children <3 years old enrolled on “Head Start” 4 clinical trial (HS 4). Four of 30 patients enrolled on HS 4 developed sinusoidal obstruction syndrome (SOS) while receiving induction chemotherapy with cisplatin, etoposide, vincristine, cyclophosphamide and high-dose AraC. In contrast, the same chemotherapeutics were used without toxicity in 15 patients of median age 1.3 years old enrolled on “Head Start” 4 clinical trial (HS 4). To address this issue, a biweekly dose regimen for all conventional chemotherapeutics using SU-DIPG4 and SU-DIPG17 cell lines. We established SU-DIPG17 xenografts which demonstrated diffuse infiltrative tumor growth similar to human DIPG. By LC-MS/MS analysis, MRgFUS led to a 4-fold increase in doxorubicin concentrations within the brainstem tumors following IV administration when compared to IV administration alone. We demonstrated feasibility and safety of MRgFUS in the rodent brainstem model, and have shown that MRgFUS increases doxorubicin concentration in the brainstem of a rodent model of DIPG. These preclinical data will be helpful in designing clinical trials of BBB disruption using MRgFUS for DIPG in children.