inert negative form of GL2 indeed hampered tumorigenesis. Targeting GL2 with arsenic trioxide caused extended survival of tumor-bearing animals, indicating GL2 as a critical regulator of ZFTA fusion-positive tumorigenesis as well as a potential therapeutic vulnerability in these tumors.

EPEN-04. SIOP EPENDYMOMA I: FINAL RESULTS, LONG TERM FOLLOW-UP & PATHOLOGICAL AND MOLECULAR ANALYSIS OF THE TRIAL COHORT: A BIOMECA CONSORTIUM STUDY

Timothy A. Ritzmann1,2, Rebecca J. Chapman2, Donald Macarthur3, Conor Mallicki1, John-Paul Kilday4,5, Nicola Thorp6, Piergiorgio Modena7, Mariza Giagagcovs8, Robert Deen9,10, Timothy Jaspars11, Kristian W. Papier1,12, Thomas S. Jacques1,13, Simon M.L. Painel2,14, David W. Ellison12, Eric Bouffet1,15, and Richard G. Grundy1,16,1
1The University of Nottingham, Nottingham, UK, 2Nottingham University Hospitals NHS Trust, Nottingham, UK, 3Alder Hey Children’s NHS Foundation Trust, Liverpool, UK, 4Royal Manchester Children’s Hospital, Manchester, UK, 5The University of Manchester, Manchester, UK, 6The Clatterbridge Cancer Centre, Liverpool, UK, 7ASST Lariana General Hospital, Como, Italy, 8Hopp Children’s Cancer Center Heidelberg (KfZT), Heidelberg, Germany, 9Division of Pediatric Neurooncology, German Cancer Research Center (DKFZ) and German Cancer Consortium (DKTK), Heidelberg, Germany, 10UCL GOS Institute of Child Health, London, UK, 11Great Ormond Street Hospital for Children NHS Foundation Trust, London, UK, 12St. Jude Children’s Research Hospital, Memphis, TN, USA, 13The Hospital for Sick Children, Toronto, Canada

Introduction: Surgery and radiotherapy are established childhood ependymoma treatments. The efficacy of chemotherapy has been debated. We report final results of the SIOP Ependymoma I trial, with 12-year follow-up, in the context of a post-hoc analysis of more recently described biomarkers. Aim and Methods: The trial assessed event free (EFS) and overall survival (OS) of patients aged three to 21 years with non-metastatic intracranial ependymoma, treated with a staged management strategy targeting maximum local control. The study also assessed: the response rate (RR) of subtotally resected (STR) disease to vincristine, etoposide and cyclophosphamide, and surgical outcomes. Children with positive gross total resection (GTR) received radiotherapy of 54 Gy in 30 daily fractions over six weeks, whilst those with ST received VEC before radiotherapy. We retrospectively assessed methylation and 1q status alongside bTERT, RELA, Tenascin C, H3K27me3 and pAKT expression. Results: Between 1999 and 2007, 89 participants were enrolled, 15 were excluded with metastatic (n=4) or non-ependymoma tumours (n=11) leaving a final cohort of 74. Five- and ten-year EFS was 49.3% and 46.7%, OS was 69.3% and 60.3%. 1q gain was associated with worse EFS (p=0.002, HR=3.00, 95%CI 1.49–6.10). bTERT expression was associated with worse five-year EFS (20.0% vs 83.3%, p=0.014, HR=5.8). GTR was achieved in 33/74 (44.6%) and associated with improved EFS (p=0.006, HR=2.81, 95% confidence interval 1.35–5.84). There was an improvement in GTR rates in the latter half of the trial (1999–2002 vs 2003–2007, p=0.04). Despite the protocol, 12 participants with STR did not receive chemotherapy. However, chemotherapy RR was 65.3% (19/29, 95%CI 45.7–82.1). Conclusions: VEC exceeded the RR was 65.5% (19/29, 95%CI 45.7–82.1). Conclusions: VEC exceeded the

EPEN-06. CELL ECOSYSTEM AND SIGNALING PATHWAYS OF PRIMARY AND METASTATIC PEDIATRIC POSTERIOR FOSSA EPIENDYMOMA

Rachael Aujun, Emma Troisi, Adam Algahlith, MacLean Nasrahall, Naeema Sani, and Bruno Camara; University of Pennsylvania, Philadelphia, PA, USA

Childhood ependymoma is an ependymoma of the central nervous system with a chronic relapsing pattern. In children, 90% of pediatric ependymoma occur intracranially where prognosis is grim. Standard care for this disease includes surgical resection followed by radiation. Despite several clinical trials, adjuvant chemotherapies have yet to extend patient survival, highlight the need for novel therapeutic options. Ependymoma tumors have been stratified into nine molecular subgroups based on their DNA methylation profile. The most prevalent and aggressive pediatric subgroup is known as posterior fossa ependymoma type A (PFA) which represents approximately 60% of pediatric cases and has a 5-year progression free survival rate of 30%. Whole genome sequencing studies have revealed that PFA tumors rarely harbor recurrent mutations. To inform the potential development of new treatment options for this disease, we sought to decipher the specific mechanisms leading to the tumorigenesis, progression, and metastasis of PFA tumors. By means of single-nuclei RNA-seq and an array of computational methods, we show that the expression profile of PFA tumor cells recapitulates the developmental linages of radial glia in neurogenic niches, and is consistent with an origin in LGR+ stem cells and a pro-inflammatory environment. In addition, our analysis reveals the abundance of a mesenchymal cell population expressing TGF-β signaling, reactive gliosis, and hypoxia-related genes in distal metastases from PFA tumors. Taken together, our results uncover the cell ecosystem of pediatric posterior fossa ependymoma and identify WNTβ/b-catenin and TGF-β signaling as candidate drivers of tumorigenesis for this cancer.

EPEN-07. SINGLE-CELL RNA SEQUENCING IDENTIFIES A UNIQUE MYELOID SUBPOPULATION ASSOCIATED WITH MESENCHYMAL TUMOR SUBPOPULATION IN POOR OUTCOME PEDIATRIC EPIENDYMOMA

Andrea Griesinger,E,1 Kent Riemondy1, Andrew Donson1,2, Nicholas Willard1,2, Eric Prince1,2, Fahri Hariri1,2, Vladimir Amani1,2, Enrique Grimaldo1,2, Todd Hancock1,2, Richard Grundy3, Andrew Jackson1, Nicholas Forrest4,5, and Timothy Ritzmann1,6
1UC Anschutz Medical Campus, Aurora, CO, USA, 2Children’s Hospital Colorado, Aurora, CO, USA, 3University of Nottingham, Nottingham, UK

We have previously shown immune gene phenotype variations between posterior fossa ependymoma subgroups. PFA1 tumors chronically secrete IL-6, which induces secretion of myeloid cell IL-8 and pushes the infiltrating myeloid cells to an immune suppressive function. In contrast, PFA2 tumors have a more immune activated phenotype associated with a better prognosis. The objective of this study was to use single-cell (sc) RNAseq to descriptively characterize the infiltrating myeloid cells. We analyzed approximately 8300 cells from 21 PFA patient samples. Using advanced machine learning, we identified eight myeloid cell subpopulations with unique gene expression profiles. Interestingly, only one subpopulation was significantly enriched in PFA1 tumors. This subpopulation, denoted as the hypoxia myeloid subpopulation, was defined by genes associated with osteoclast activation and response to oxygen levels. These myeloid cells also share similar gene expression profile to a mesenchymal tumor subpopulation (MEC) enriched in PFA1 and associated with poor outcome in EPN patients. This tumor subpopulation was the only population expressing IL-6. Using immunohistochemistry, we found the hypoxia myeloid located in regions of tumor necrosis and perivascular niches. The MEC cells were also more abundant in these regions. In an independent single-cell cytokine re-