EMBR-03. PINEOBLASTOMA: A POOLED OUTCOME STUDY OF NORTH AMERICAN AND AUSTRALIAN THERAPEUTIC DATA

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Background: Pineoblastoma (PB) is a rare embryonal brain tumour most often diagnosed in young children. To date, no clinical trials have been conducted specific to pediatric PB. Collaborative studies performed over the past 30 years have included PB in studies accruing for other embryonal tumours, primarily medulloblastoma (MB), but also included the entity formerly known as CNS-PNET and atypical teratoid rhabdoid tumors. Each of these studies have included only a small number of children with PB, making clinical features difficult to interpret and determinants of outcome difficult to ascertain. Patients and Methods: Published centrally reviewed series with sufficient clinical and outcome data from PB were pooled. To investigate associations between variables, Fisher’s exact and Wilcoxon-Mann-Whitney tests, and Spearman correlations were used as appropriate. Kaplan-Meier plots, log-rank tests, and Cox proportional hazards models were used in survival analysis. Results: We describe a 30-year review of the reported clinical features of PB and a pooled centrally reviewed, cohort series and Additional supportive evidence are still warranted.

EMBR-05. THE TENTATIVE APPLICATION OF EN BLOC CONCEPT IN THE PEDIATRIC BRAIN TUMOR: EXPERIENCE FROM A LARGE PEDIATRIC CENTER IN CHINA

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Background: The less allowable blood loss and tolerance of intraoperative blood loss of children lead to the high rate of massive blood transfusion in the treatment of brain tumor. The surgical concepts of en bloc resection may contribute to the improvement of brain tumor resection. Objective: To investigate the effects of en bloc concept on short-term outcomes of pediatric brain tumors and factors associated with the application of en bloc concept. Methods: According to the surgical concept involved, the patients were divided into three subgroups-complete en bloc concept, partial en bloc concept, and piecemeal concept. The machine comparison (preoperative HCT levels, blunting EPHA2 overexpression and mitigating the excessive AKT signaling) was performed based on age, tumor location, lesion volume, and pathological diagnosis to investigate the effect of the en bloc concept on the short-term outcomes. Then the patient data after January 2018, when the en bloc concept was routinely integrated into brain tumor surgery in our medical center, were reviewed and analyzed to find out the predictors associated with the application of en bloc concept. Results: In the en bloc group, the periproductive outcome including hospital stay(p=0.001), PICU stay(p=0.003), total blood loss(p=0.015), transfusion rate(p=0.005) and complication rate(p=0.039), were all significantly improved. The multinomial logistic regression analysis showed that tumor volume and imaging features, like bottom vessel, encasing nerve or pass-by vessel, finger-like attachment, ratio of “limited line” and ratio of “clear line” remained independent factors for the application of en bloc concept in our medical center. Conclusion: This study supports the application of complete or partial en bloc concept in the pediatric brain tumor surgery referring to the preoperative imaging features, and confirms the advantages of piecemeal concept in children and en bloc technique in the short outcomes without significant increases in neurological complication. Large series and Additional supportive evidence are still warranted.

EMBR-06. EFFECTIVE INHIBITION OF MYC-AMPLIFIED GROUP 3 MEDULLOBLASTOMA BY FACT-TARGETED CURAXIN DRUG CBL0137

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Medulloblastoma (MB) is the most common malignant pediatric brain tumor that can be categorized into four major molecular subgroups. Group 3 MB with MYC amplification (MYCamp-G3-MB) has been shown to be highly aggressive and exhibited worst prognosis, indicating the need for novel effective therapy most urgently. A few epigenetic targeted therapeutic strategies have recently been proven to effectively treat preclinical models of MYCamp-G3-MB, including BET inhibition, HDAC inhibition and SETDB8 inhibition, unveiling a promising direction for further investigation. In this study, we carried out systemic bioinformatic analyses of public-available MB datasets as well as functional genomic screening datasets of primary MYCamp-G3-MB lines to search for other potential therapeutic targets within epigenetic modulators. We identified SSRP1, a subunit of histone-chaperone FACT complex, to be the top drug target candidate as it is highly cancer-dependent in whole-genome CRISPR-Cas9 screening across multiple MYCamp-G3-MB lines; significantly up-regulated in MYCamp-G3-MB compared to normal cerebellum and most of the rest MB subtypes; its higher expression is correlated with worse prognosis; and it has a blood-brain-barrier penetrable targeted drug that has entered early phase human clinical trials already. Then we utilized RNA-interference approach to verify the cancer-dependency of SSRP1 in multiple MYCamp-G3-MB lines and further confirmed the therapeutic efficacy of FACT-targeted curaxin drug CBL0137 on treating preclinical models of MYCamp-G3-MB in vitro and in vivo, including an orthotopic intracranial xenograft model. Mechanistically, transcriptome analyses showed