thickening/enhancement after chemotherapy was to be classified as partial-remission (PR). Patients with less than CR after chemotherapy received a boost. RESULTS: Shortly before trial closure (2018), it was noted that national CR rates were discrepant across the largest recruiting countries. For German patients, CR rates were ~80%, compared with ~30–40% for UK and France. A formal neuroradiology review was therefore convened. A total of 59 cases were randomly selected (UK, n=32; France, n=14 and Germany, n=13), including those deemed to be in CR and PR. Cases included those with disease at pituitary, pineal and bifocal sites. Both diagnostic scan and scan after induction chemotherapy were used for assessment. Detailed analysis is ongoing and will be presented. CONCLUSION: Residual changes at both pituitary and pineal sites of uncertain significance may remain after chemotherapy. This process should facilitate consensus to define the best response criteria allowing treatment reduction for CNS germinoma for future clinical trials.

GCT-21. CENTRAL NERVOUS SYSTEM GERMINOMA - PONDERING THE NEXT STEPS

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Central nervous system germinoma (CNS) represents one successful example where the introduction of chemotherapy into the treatment allowed significant and meaningful reductions in the volume and dose of radiation therapy while maintaining excellent outcomes. However, the long-term toxicities and morbidities of the current therapies, in addition to their substantial negative impact on the social wellbeing of germinoma patients, should clearly indicate that the current achievements are not enough. While stepwise cutback of the radiation therapy needs to be commended, real progress must be achieved in the exploration and investigation of biological and molecular markers. Furthermore, the differences that still exist between the several working groups around the globe in determining the tumor marker cut-offs that help diagnose these tumors illustrate their shortcomings, and therefore the need for newer and more reliable methods. Additionally, efforts should focus on the inclusion of metastatic and basal ganglia/thalamic germinomas in future prospective clinical trials given the lack of evidence on the best treatment strategy for these patients. A comprehensive review of all major CNS germinoma clinical trials will be presented aiming to lay a foundation for researchers and clinicians alike who are currently working on designing innovative approaches for this group of patients. This review also details the current issues of debate, and provides suggestions which may assist in the design of future prospective clinical trials for children with CNS germinomas.

GCT-22. PROTEIN DEUBIQUITINATION PATHWAY IS A NOVEL THERAPEUTIC TARGET AGAINST MALIGNANT NON-GERMINOMATOUS CNS GERM CELL TUMORS

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Central nervous system germ cell tumors (CNSGCTs) are rare intracranial neoplasm usually developed in adolescents and young adults. However, in East Asia including Japan, incidence of CNSGCTs is considerably higher compare with other regions of the world. Whereas germinomas generally respond to chemo-radiotherapy well, malignant subtypes of non-germinomatous germ cell tumors (NGGCT) are refractory, and development of novel therapy against NGGCTs is urgently needed. To develop a new therapeutic strategy against aggressive NGGCTs, we have investigated novel molecular targets for NGGCT treatment. We screened a total of 120 CNSGCT tumor tissues (including 55 NGGCT), which were registered to the Intracranial Germ Cell Tumor Consortium (iGCT), and discovered multiple mutations of a molecule that regulates protein ubiquitination and degradation specifically in NGGCT cases (5 of 55 cases; 1 immature teratoma, 3 mixed gem cell tumors, and 1 embryonal carcinoma). An in vitro ubiquitination assay revealed the mutations of this molecule discovered in NGGCT cases were loss of function mutations. Reduced expression of this molecule by knockdown in an established human seminoma cell line Tcam2 or a human yolk sac tumor cell line YST1, which was recently established in our institute, resulted in enhanced proliferation as well as upregulation of MEK-ERK activation. Importantly, treatment of these two GCT cell lines with reduced expression of this molecule by MEK inhibitor trametinib suppressed augmented proliferation of these cells. Taken together, these results suggest that protein ubiquitination-related pathways as well as MEK-ERK cascade may serve as a novel therapeutic target against NGGCTs.

GCT-23. MULTI-INSTITUTIONAL ANALYSIS OF TREATMENT MODALITIES IN BASAL GANGLIA AND THALAMIC GERMINOMA

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BACKGROUND: Central nervous system (CNS) germinomas are radiotherapy (RT)-sensitive tumors with excellent survival. Current treatment strategies combine chemotherapy with RT to reduce the field and dose of RT. There is no standard treatment for germinomas originating in the basal ganglia/thalami (BGTG) given their rarity and poorly-defined imaging characteristics. Craniospinal (CSI), whole brain (WBI), whole ventricle (WVI), and focal RT have been previously utilized; however, the optimal strategy remains unclear. METHODS: Retrospective multi-institutional analysis was conducted across 18 institutions in four countries. RESULTS: For 46 cases with non-metastatic BGTG, the event-free survival (EFS) was 86.9% at both 5 and 10 years, while overall survival (OS) was 100%, and 95.7% respectively at 5 and 10 years. Median RT dose and range for the various treatment volumes were as follows: CSI (n=10): 2340 cGy (1980–3060 cGy), WBI (n=8): 2340 (1800–3000 cGy), WVI (n=14): 2340 cGy (1800–2550 cGy), focal (n=9): 3600 cGy (3060–5400 cGy). There was no statistically significant difference in the EFS based on RT modality (p=0.57), but EFS for subjects with CSI and WBI were both 100%. The three subjects who received chemotherapy alone had significantly lower EFS than those who received chemotherapy and RT (p=0.001), but were salvageable with RT. CONCLUSION: In the largest study to date for BGTG, there were no significant differences in outcomes between patients who received CSI, WBI, WVI or focal RT. This group of patients should be included in future prospective clinical trials, and a more limited RT field may be considered.

GCT-24. RELAPSE PATTERN AND QUALITY OF LIFE IN PATIENTS WITH LOCALIZED GERMINOMA ORIGINATING FROM BASAL GANGLIA REGION

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BACKGROUND: The optimal radiation field in localized basal ganglia (BG) germinoma was not well defined, mostly due to unknown relapse patterns. In our institute, both focal radiotherapy (FR) and craniospinal irradiation (CSI) plus boost were considered in this population until whole-brain radiotherapy (WBRT) plus boost became an option in 2008. Thus, a retrospective study was conducted to address the issue. Furthermore, the health-related quality of life (HRQOL) was also evaluated. METHODS: Patients who were diagnosed as localized BG germinoma between 2000 and 2017 were studied. HRQOL was evaluated by PedsQL 4.0 (≤15 years) and SF-36 (>15 years) questionnaires based on the age at last follow-up. RESULTS: Among 161 patients included, 35 patients received FR, 109 patients