### GCT-16. MANAGEMENT OF PATIENTS WITH METASTATIC CENTRAL NERVOUS SYSTEM (CNS) GERMINOMA; A LITERATURE REVIEW

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BACKGROUND: Outcomes of patients with primary metastatic CNS Germinoma are excellent. There is no global consensus over the optimal irradiation doses and fields to reduce long-term radiotherapy side effects. Our literature review explores the different treatment modalities utilized for patients with metastatic CNS germinoma. METHODS: A literature review of studies that included patients with primary metastatic CNS germinoma via PubMed database. RESULTS: Sixty-eight patients (male: 48, female: 13, not specified: 7) were identified. At presentation, the median age was 14.4 years (range: 1.5–47 years). Primary tumor location included the following: pineal (n=15), suprasellar (n=11), bifocal (suprasellar and pineal) (n=21), other (n=9), not specified (n=12). Metastasis sites included the following: multifocal intracranial with/without ventricular metastasis (n=18), ventricular metastasis only (n=21), spinal metastasis only (n=8), CSF cytology dissemination only (n=3), and not specified (n=18). Seventeen patients received radiotherapy only, and 51 received radiochemotherapy. Radiotherapy modalities included the following: craniospinal irradiation (n=36) with a mean whole-brain dose of 23.3 Gy (range:10.8-40.5 Gy) and spinal dose of 21.6 Gy (range: 10.8 – 30.6 Gy), whole-brain irradiation (n=13) with a mean dose of 24.2 Gy (range: 18 - 40 Gy), whole ventricular irradiation (n=16) with a mean dose of 24.7 Gy (range: 23.4 – 30 Gy), Focal irradiation only (n=1) with a dose of 40 Gy, and not specified (n=2). Four patients died of disease progression or relapse. Two patients were alive with relapse/residual disease. Sixty-two patients were alive with no evidence of disease with a mean follow of 77 months (range: 10.3 – 256 months). Further analysis is underway and will be presented at the meeting. CONCLUSION: The role of neoadjuvant chemotherapy in reducing the dose and field of radiation therapy remains unclear. Further analysis is pending which may highlight the role of neoadjuvant chemotherapy in managing patients with metastatic germinoma.

### GCT-17. RECURRENCE OF CNS GERM CELL TUMORS (GCTS) ALONG BIOPSY AND VENTRICULOSTOMY TRACTS

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BACKGROUND: Central nervous system (CNS) germinoma relapses are rare. However, the latest Children's Oncology Group (COG), ACNS1123 stratum 2, described three relapses along the biopsy tract out of eight total relapses; two along the biopsy and endoscopic third ventriculostomy (ETV) tract and one along the biopsy tract and external ventricular drain. Given these findings, we sought to describe other cases of GCT recurrence along surgical tracts. METHODS: We performed a literature review from 1980-2021 to identify cases of GCT recurrence along biopsy and ventriculostomy tracts. RESULTS: Three patients with pineal lesions were identified (13, 14, and 34-years old). All underwent ETV, cerebrospinal fluid (CSF) sampling, and tumor biopsy. Two patients had uncomplicated postoperative courses. One developed persistent hydrocephalus and underwent repeat ventriculostomy. Two were diagnosed with pure germinoma and treated with focal radiotherapy of 45 Gy alone or chemotherapy and radiation (50.4 Gy to the tumor volume and 36 Gy to adjacent high-risk area). The third was treated with methotrexate and corticosteroids. All three had recurrence on surveillance MRI (1-3 years after diagnosis). One had recurrence at the ventriculostomy bur hole site, and two had recurrence along the ventriculostomy tract. On biopsy, all three lesions were germinomas. One received pre-radiation chemotherapy and palliative radiation (36 Gy to surgical bed and 30.6 Gy to surrounding high-risk area). Another received chemotherapy and craniospinal radiation of 15 Gy. The third had a complicated post-biopsy course. He ultimately underwent chemotherapy and radiation (24 Gy). All were still alive at time of report. Two were disease free at 12 and 18 months, while one was still receiving chemotherapy. **CONCLUSION:** Recurrence along the biopsy or ventriculostomy tract is rarely reported in the literature. Future evaluation to determine the incidence could inform if biopsy and ventriculostomy tracts should be included in the radiation therapy field.

### GCT-18. ENDOSCOPIC THIRD VENTRICULOSTOMY (ETV) AND TUMOR BIOPSY ARE NOT ASSOCIATED WITH RELAPSE RATE OR PATTERNS IN PRIMARY CENTRAL NERVOUS SYSTEM (CNS) GERM CELL TUMOR (GCT)

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BACKGROUND: ETV and tumor biopsy are central to the surgical management of children with primary CNS GCT. An ETV creates a communication between the intraventricular compartment and the subarachnoid spaces and decompartmentalizes the ventricular system. "Tumor spill" or shedding may result from surgical interventions, such as biopsy. ETV with simultaneous biopsy may impart a greater tendency for dissemination and possible distant relapse. This is a concern in CNS GCT given the attempts of irradiation field and dose reduction following chemotherapy. METHODS: We performed a retrospective review of the prospective database for the Children's Oncology Group (COG) ACNS1123 study. Possible associations were explored among ETV, endoscopic biopsy, and combined ETV+biopsy with relapse, distant relapse, progression free survival (PFS), and time to distant relapse. RESULTS: Among 244 eligible patients, 97 ETV+/-biopsies were performed, and 30 relapses occurred. There were no associations among ETV and/or biopsy with relapse (Cochran-Mantel-Haenszel [CMH] test, with histology (germinoma vs. nongerminomatous germ cell tumor (NGGCT)) as stratification variable: ETV: p=0.3167, biopsy: p=0.3375, combined: p=0.3066), distant relapse (CMH test, ETV: p=0.4631, ETV+biopsy: p=0.6795), PFS (log-rank test, ETV: NGGCT p=0.1632, germinoma p=0.9288; biopsy: NGGCT p=0.1682, germinoma p=0.9701; ETV+Biopsy: NGGCT p=0.1306, germinoma p=0.7758), or time to distant relapse with death/local relapse as competing risk (Gray's test, ETV: NGGCT p=0.5694, germinoma p=0.2327; biopsy: NGGCT p=0.3505, germinoma p=0.5747; ETV+Biopsy: NGGCT p=0.3988, germinoma p=0.6839). CONCLUSIONS: Based on a secondary analysis of prospective data from the ACNS1123 trial, ETV and biopsy did not impart a greater likelihood of relapse in children with primary CNS GCT treated with combined chemotherapy and irradiation. However, three tract recurrences did occur (all germinoma), suggesting that they may affect pattern of relapse. Current and future prospective trials should continue to explore associations among these variables and relapse, including patterns of relapse.

### GCT-19. TOWARD UNDERSTANDING OF THE PATHOGENESIS OF CENTRAL NERVOUS SYSTEM GERM CELL TUMORS

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Central nervous system germ cell tumors (CNSGCT) are the most enigmatic brain tumors that arise predominantly in children and young adults. CNSGCTs are rare in Europe and North America, while they are rather common in East Asia. The genetic basis of the distinct regional prevalence is yet to be elucidated. The WHO Classification of Central Nervous System Tumours recognizes 6 subtypes of CNSGCT, however multiple subtypes are often present as a mixed tumor, and the subtype may change at the recurrence. In 2012, we organized the Intracranial Germ Cell Tumor Genome Analysis Consortium of Japan (iGCT Consortium) and have collected nearly 300 frozen tumor specimen and patients' information for CNSGCT cases since then to comprehensively investigate the genomic/epigenomic mechanism of CNSGCT development. We found that alterations of the MAPK and/or PI3K pathways were present in approximately 50% of all subtypes of CNSGCTs, KIT mutations being the most common. Germinomas are characterized by global hypomethylation, indicating that their cell of origin may be primordial germ cells. Transcriptomic profiling suggested that germinomas and non-germinomatous germ cell tumors (NGGCTs) developed from the common cell of origin and then diverted at some stage. We also showed that components of mixed CNSGCT shared the identical somatic mutation while having distinct methylation profiles, supporting the common cell-of-origin theory. In this paper, we will present an overview of our investigation in the iGCT Consortium as well as some of the ongoing projects, single cell RNA sequencing among others.

### GCT-20. MULTI-INSTITUTIONAL ANALYSIS OF PEDIATRIC RELAPSED/REFRACTORY CENTRAL NERVOUS SYSTEM GERM CELL TUMORS

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Central nervous system (CNS) germ cell tumors (GCTs) constitute ~ 4% of primary pediatric brain tumors in the United States. While multimodality therapy approaches have ensured >80% survival benefit, these patients still