INTRODUCTION: Therapeutic strategies for patients with intracranial germ cell tumors of poor prognosis remain controversial. In particular, mixed germ cell tumors including various malignant elements show a 3-year survival rate of only 9.3%. Establishment of effective chemotherapies for such tumors is needed. Here we report a case of mixed germ cell tumor mainly comprising undifferentiated mesenchymal cells that was successfully managed using a sarcoma-type chemotherapeutic regimen.

CASE REPORT: A 11-year-old boy was referred to our institute with double vision, headache and nausea. Magnetic resonance imaging revealed a large pineal tumor with heterogeneous enhancement extending to the left thalamus. Surgical subtotal removal of the tumor was performed, and the patient received 16 courses of ICE chemotherapy (cisPlatin/Ifosfamide/cisplatin). After a period of 8 months, the patient was without disease progression.

DISCUSSION: Intracranial germ cell tumors of poor prognosis include choriocarcinomas, yolk sac tumors, embryonal carcinomas, immature teratomas, and mixed tumors with these malignant elements. Immediate teratomas have various pathological features, including neuroepithelial, endodermal, and mesenchymal elements. Biological characteristics of undifferentiated mesenchymal tumors resemble those of sarcoma. Chemotherapeutic regimens used for sarcoma might be worthwhile for mixed germ cell tumors refractory to platinum-based chemotherapies.

GC-03. RELAPSED CENTRAL NERVOUS SYSTEM GERMINOMAS FOLLOWING STANDARDISED FIRST-LINE TREATMENT: EXPERIENCE FROM UK AND GERMANY

Matthew Murray1, Juliet Hale1, Katja Heinemann1, Frank Saran1, Gabrielle Calaminus1, and James Nicholson1; 1Addenbrooke’s Hospital, Cambridge, UK; 2Royal Victoria Infirmary, Newcastle, UK; 3University of Muenster, Muenster, Germany; 4Royal Marsden Hospital, Surrey, UK

BACKGROUND: Since 1997, European patients with intracranial germ cell tumors have been treated according to SIOP-CNS-GCT-96, with standardised diagnostics/treatment. Survival was excellent, whether patients were treated with standard platinum-based chemotherapy followed by 40Gy focal-RT (Option-B). However, there is no uniform treatment strategy for relapse. SIOP-CNS-GCT-96 provides a significant cohort of patients suitable for retrospective study, to inform future treatment approaches.

RESULTS: The 13 cases (9 male; 4 female) had a median age at initial diagnosis of 12y (range 4y-16y); initial disease-sites were pineal (5), suprasellar (4), and bital ganglia (1). 7 patients were treated on Option-A, 6 on Option-B. Overall, 6 of 12 patients received high-dose-therapy of which 1 is AND at 43m follow-up. Of 4 patients treated with high-dose-therapy, 1 is AND at 21m follow-up. All other patients died of disease (DOD) or died of complications. Both survivors had relapsed at extracranial sites. For the 6 Option-B patients, overall time-to-relapse was 27m and median survival 34m. Three were treated without high-dose-therapy of which 2 are AND (after 30 and 114m follow-up) and 1 DOD. For the 3 patients who received high-dose-therapy, 2 are AND (after 60 and 162m) and 1 DOD. CONCLUSIONS: Salvages are seen for relapsed intracranial germinomas, with and without high-dose-therapy. Combined chemo-radiotherapy for primary disease (Option-B) did not compromise salvageability. The use of high-dose-therapy is supported, but remains unproven.

GC-04. RELAPSED CENTRAL NERVOUS SYSTEM NON-GERMINOMATOUS GERM CELL TUMOURS (NGGCTs) FOLLOWING STANDARDISED FIRST-LINE TREATMENT: EXPERIENCE FROM UK AND GERMANY

Matthew Murray1, Katja Heinemann1, Juliet Hale1, Frank Saran1, James Nicholson1, and Gabrielle Calaminus1; 1Addenbrooke’s Hospital, Cambridge, UK; 2University of Muenster, Muenster, Germany; 3Royal Victoria Infirmary, Newcastle, UK; 4Royal Marsden Hospital, Surrey, UK

BACKGROUND: Since 1997, European patients with intracranial non-germinomatous germ-cell tumors (NGGCTs) have been treated according to SIOP-CNS-GCT-96, with standardised diagnostics/treatment. Survival was excellent, whether patients were treated with standard platinum-based chemotherapy followed by 40Gy focal-RT, with additional 30Gy craniospinal-RT if metastatic. However, there is no uniform treatment strategy for relapse. SIOP-CNS-GCT-96 provides a significant cohort of patients suitable for retrospective study, to inform future treatment approaches.

RESULTS: Of 4 cases, 2 were AND (21 and 43m follow-up) and 2 DOD. The 3 cases (3 male; 1 female) had a median age at initial diagnosis of 14y (range 1y-29y). Initial disease-sites were pineal (4), suprasellar (8), and bital ganglia (1). Two patients were treated on Option-A, 4 on Option-B. Overall, 6 of 12 patients received high-dose-therapy of which 1 is AND at 43m follow-up. Of 4 patients treated with high-dose-therapy, 1 is AND at 21m follow-up. All other patients died of disease (DOD) or died of complications. Both survivors had relapsed at extracranial sites. For the 6 Option-B patients, overall time-to-relapse was 27m and median survival 34m. Three were treated without high-dose-therapy of which 2 are AND (after 30 and 114m follow-up) and 1 DOD. For the 3 patients who received high-dose-therapy, 2 are AND (after 60 and 162m) and 1 DOD. CONCLUSIONS: Salvages are seen for relapsed intracranial germinomas, with and without high-dose-therapy. Combined chemo-radiotherapy for primary disease (Option-B) did not compromise salvageability. The use of high-dose-therapy is supported, but remains unproven.
were embryonal carcinoma (marker-negative). Time-to-relapse from initial diagnosis was 10m (range 5-86m). Seventeen relapses were localised, 20 distant, 5 combined, 3 non-specified. Twenty-five cases were inside RIR. Diagnosis was made on ACCS 0232 protocol therapy. Four patients were treated with teratoma only, treated with surgery alone; 5 patients were treated with palliative-intent; 5 patients received non-specified-treatment. Of the 31 patients treated with known curative-intent, 11 received non-high-dose-therapy, all of whom died of disease (DOD; range: 3-48m) except 1 patient alive-with-stable disease (AUD; 20m). Three patients were planned for high-dose-therapy but progressed prior to this and DOD (9-13m). Of the 17 patients receiving high-dose-therapy, 14 DOD (3-35m), 1 is alive-with-progress disease (APD; 38m) and 2 are alive-with-no-evidence-of-disease (AUD; 41 and 127m). In summary, only 2/10 (20%) of patients with intention to treat using high-dose-therapy are AND. CONCLUSIONS: Salvage-rates for patients with relapsed intracranial NGGCTs who have received optimal first-line-therapy are very poor, and no patient is AND without high-dose-therapy.

GC-05. MARKER (+) CNS GERM CELL TUMORS IN REMISSION: ARE SURVEILLANCE MRI SCANS NECESSARY? Sybil Martinez1, Yasmin Khakoo2, Stephen Gilheeney1, Kim Kramer1, Suzanne Wodicka3, and Surovendean,3; 1University Hospital, Portland, OR, USA; 2New York Presbyterian Weill Cornell, New York, NY, USA.

BACKGROUND: Patients with marker (+) CNS germ cell tumors are usually followed with both surveillance MRI scans and serum tumor markers. We hypothesized that patients with elevated serum tumor markers at diagnosis who achieve a complete biochemical and radiological remission may not need surveillance MRI scans. METHODS: We retrospectively identified 31 patients with CNS germ cell tumors who presented with an elevated serum AFP and/or beta-HCG at the time of diagnosis. We reviewed the records of those patients who (1) achieved a complete biochemical and radiological remission and (2) later suffered tumor recurrence to determine whether the recurrence was detectable biochemically, radiologically, or via both modalities. RESULTS: Nine of the 31 patients suffered tumor recurrence following initial remission. All 9 had elevated serum tumor markers at diagnosis and MRI evidence of recurrence. The 1 patient presenting biochemically and radiologically evidence of recurrence developed MRI evidence of recurrence 15 months later without intervening treatment. One other patient (not one of the 9) had a secondary malignancy (anaplastic astrocytoma) identified by brain MRI scan. CONCLUSION: Patients with CNS germ cell tumors who present with elevated serum tumor markers at diagnosis and achieve a complete biochemical and radiological remission may not need surveillance MRI scans to monitor for recurrence, but MRI scans may be considered to monitor for secondary malignancy. If other series replicate these findings, surveillance via monitoring of serum tumor markers only could be done and omission or reduction of the frequency of surveillance MRI scans could save a significant amount of money and effort.

GC-06. CHORIONIC GONADOTROPHIN PRODUCING BRAIN GERMINOMA AS A CAUSE OF PREOCIOUS PSEUDOPUBERTY Eva Brichova1, Zdenek Pavelka2, Andrea Bobekova2, Olga Magnova1, Leos Krein1, Tomas Svoboda1, Alena Sprlakova1, Pavel Slampa1, Karel Zitterbart2, and Jaroslav Sterba2; 1Department of Pediatric Oncology, University Hospital Brno and Faculty of Medicine, Masaryk University, Brno, Czech Republic; 2Department of Neurosurgery, University Hospital Brno and Faculty of Medicine, Masaryk University, Brno, Czech Republic.

A 6-year-old boy with history of Langerhans cell histiocytosis with subsequent brain germinoma, clinically manifested by precocious pseudopuberty on the basis of chorionic gonadotrophin ectopic secretion. The germinoma was verified histologically after stereotactic biopsy and classified as "pure germinoma". The biopsy was performed due to atypical and rare, but possible tumor localization in basal ganglia on the right and serum chorionic gonadotrophin values below the diagnostic level for secretory non-germinomas. Due to the presence of two different malignancies, the patient underwent genetic examination including suppressor and DNA repair genes mutations screening. The child started treatment according to the Children's Cancer Group Study. Four patients were treated with high-dose non-cyclophosphamide cycles followed by response differentiated radiotherapy. To blockade testosterone effect on target receptors, antiandrogen cyproterone acetate was deployed. Due to the association with gonadal tumor, we performed genetic examination including teratoma only, treated with surgery alone; 5 patients were treated with palliative-intent; 5 patients received non-specified-treatment. Of the 31 patients treated with known curative-intent, 11 received non-high-dose-therapy, all of whom died of disease (DOD; range: 3-48m) except 1 patient alive-with-stable disease (AUD; 20m). Three patients were planned for high-dose-therapy but progressed prior to this and DOD (9-13m). Of the 17 patients receiving high-dose-therapy, 14 DOD (3-35m), 1 is alive-with-progress disease (APD; 38m) and 2 are alive-with-no-evidence-of-disease (AUD; 41 and 127m). In summary, only 2/10 (20%) of patients with intention to treat using high-dose-therapy are AND. CONCLUSIONS: Salvage-rates for patients with relapsed intracranial NGGCTs who have received optimal first-line-therapy are very poor, and no patient is AND without high-dose-therapy.

GC-07. PSYCHIATRIC SYMPTOMS IN SURVIVORS OF CHILDHOOD GERM CELL TUMORS Cynthia J. Campen1, Dejune Ashley1, Paul G. Fisher1, and Michelle Monge1; Stanford University, Stanford, CA, USA; 2Oregon Health and Science University, Portland, OR, USA.

BACKGROUND: Cranial irradiation disturbs new cell production in the hippocampus and in the white matter tracts of the developing frontal lobe, areas critical for memory, learning, and behavior. Furthermore, the germ cell tumor (GCT) predilection for midline, subcortical structures may disrupt frontal-basal-ganglion-subcortical circuitry and thalamo-cortices thought to be involved in psychiatric disease. METHODS: Patients were identified via the LPCH Pediatric Brain Tumor Database and were included if they were aged 20 years or younger at the time of diagnosis of their incident brain tumor, and diagnosed between 1/1/1997 - 6/1/2011. RESULTS: GCTs were identified in 28 patients (germinoma: 21, non-germinomatous germ cell tumor (NGGCT): 7), in whom 11 (39.2%) had psychiatric symptoms, including hallucinations: 4 (14.3%), and mood/anxiety disorders: 7 (25.0%). Gender and age at diagnosis did not predict development of psychiatric symptoms (p = 0.7, p = 0.69 respectively). Median time to first mood or psychotic symptom was 18.5 and 32 months, respectively. Higher radiation dosage was a predictor of psychiatric symptoms (median with psychiatric symptoms: 30.4 Gy vs. 30.6 Gy [without], p = 0.0001), as was receiving more cycles of chemotherapy (median with psychiatric symptoms: 4 vs. 2 [without], p = 0.0043). As a control group, subjects treated for medulloblastoma were similarly evaluated and none were found to exhibit psychotic symptoms. CONCLUSIONS: Psychiatric sequelae of brain-tumor therapy are under-recognized and poorly understood. We note that patients with GCTs have a high risk for late psychiatric disorders, particularly psychotic disorders, with risk factors including higher radiation doses and more chemotherapy. The delayed development of the psychiatric disorders suggests the underlying etiology may be one of disrupted neurodevelopment. Understanding the mechanism of these psychiatric sequelae of midline brain tumor therapy will be critical not only for patients requiring such therapy, but may help to elucidate the pathophysiology and neural substrate for psychiatric disorders in general.
she received identical treatment as Patient C with complete response, fol-
lowed by irradiation to the ventricular field and primary site boost; sixteen
months later, she continues in remission. DISCUSSION: Down syndrome patients with CNS GCT can tolerate inten-
sive, including marrow-ablative, chemotherapy with complete, durable
tumor responses.

GC-09. RESPONSE OF REFRACTORY AND RECURRENT CNS GERM CELL TUMOURS TO PROLONGED LOW-DOSE ORAL ETOPOSIDE
Takaki Yanagisawa1, Kohei Fukuoka1, Tomonari Suzuki1, 
Tomoaki Kogawa2, Kenji Wakiya3, Junich Adachi3, Kazushiko Mishima2, 
Tamayumi Fujimaki2, Masao Matsutani3, and Ryo Nishikawa2, 
1Division of Paediatric Neuro-Oncology, Department of Neuro-Oncology/ 
Neurosurgery, Saitama International Medical Center, Saitama Medical 
University, Hidaka, Japan; 2Department of Neuro-Oncology/Neurosurgery, 
Saitama International Medical Center, Saitama Medical University, Hidaka, 
Japan

PURPOSE: The outcome for patients with recurrent germ cell tumor is sometimes very poor, even with aggressive treatment with high-dose chemother-
apy and/or re-irradiation. Here we report on six cases with recurrent germ cell tumor, all heavily pretreated with a variety of chemotherapeutic agents, 
including parenteral etoposide(VP-16), who showed responses to the 
repeated course of low-dose oral VP-16. PATIENTS AND METHODS: Six patients age 10 to 31 years were treated with VP-16 after 
neuro-radiographic and clinical evidence of tumor progression. All had 
received prior irradiation and four of them received re-irradiation. All had been pretreated with various chemotherapy regimens, with two of them 
receiving regimens, with two of them having prior irradiation. Of six patients, 
response(PR) and the remaining two had stable disease. Response in tumor 
tumor marker(beta-HCG and 

GC-10. MULTI-INSTITUTIONAL, PROSPECTIVE PHASE 2 STUDY FOR PRIMARY INTRACRANIAL GERM CELL TUMORS Masao Matsutani1; Saitama International Medical Center, Saitama Medical 
University, Hidaka, Saitama, Japan

OBJECTIVE: After summarizing the 1st mult-institutional clinical study 
for intracranial germ cell tumors (1995 - 2003), we started a multi-institutional, prospective Phase 2 study for primary intracranial germ cell 
tumors. METHODS: In the first study, we evaluated 10 years OS and PFS of 
histology-verified 228 patients with the median follow-up period of 8.2 
years. They were classified into 3 therapeutic groups; germoma, intermedi-
ate prognosis group (IPG), and poor prognosis group (PPG). In the 2nd study, 
we selected 197 protocol patients were 

Time since international closure of SIOP CNS GCT 96 is 

GC-11. RISK ADAPTED IRRADIATION IS FEASIBLE IN INTRACRANIAL NON-GERMINOMATOUS GERM CELL TUMOURS (NGGCT): FINAL RESULTS OF SIOP CNS GCT 96
Gabrielle Calaminus1, Didier Frappaz2; Rolf Dieter Kortmann3, 
Claire Alapetite4, Maria Luisa Garre5, Umberto Ricardi6, Frank Hans Saran7, and Didier Frappaz8; 1University Hospital, Muenster, 
Germany; 2Addenbrookes Hospital, Cambridge, UK; 3Institute Curie, Paris, 
France; 4University Hospital, Leipzig, Germany; 5Gaslini Childrens 
Hospital, Genova, Italy; 6University Hospital, Turin, Italy; 7Royal Marsden 
NHS Trust, London, UK; 8Centre Leon Béard, Lyon, France

OBJECTIVE: The SIOP CNS GCT 96 protocol standardised diagnostics 
treatment and intracranial Non-Germ Cell Tumors (NGGCT). Diagnosis was made by imaging/markers in serum and CSF (AFP and 

GC-12. COMBINED TREATMENT WITH LOCAL IRRADIATION IS NOT SUFFICIENT TO CONTROL SUBCLINICAL DISEASE IN LOCALISED INTRACRANIAL GERMINOMA. FINAL RESULTS OF SIOP CNS GCT 96
Gabrielle Calaminus1, James Nicholson2, Claire Alapetite3, Rolf 
Dieter Kortmann4, Maria Luisa Garre5, Umberto Ricardi6, Frank 
Hans Saran7, and Didier Frappaz8; 1University Hospital, Muenster, 
Germany; 2Addenbrookes Hospital, Cambridge, UK; 3Institute Curie, Paris, 
France; 4University Hospital, Leipzig, Germany; 5Gaslini Childrens 
Hospital, Genova, Italy; 6University Hospital, Turin, Italy; 7Royal Marsden 
NHS Trust, London, UK; 8Centre Leon Béard, Lyon, France

OBJECTIVE: SIOP CNS GCT 96 standardised diagnostics/treatment for 

Patients with localised disease received 4 courses of Cisplatin 
/ 
Etoposide/Hosamide (PEI) followed by focal radiotherapy of 45 Gy. 
Patients with metastases after chemo received 30 Gy craniospinal radiother-
apy (CSI) and 24 Gy boost to tumor and macropatic metastatic sites. 
RESULTS: Progression-free survival (PFS) of patients with localised disease 
and chemo + focal radiotherapy was 0.69 + 0.04 (median follow-up 53 months) and OS: 0.78 + 0.04; (median follow-up 41 months) and of those 
with dissemination and chemo and CSI 0.67 + 0.08 (median follow-up 55 months). 
OS: 0.70 + 0.09; (median follow-up 36 months), 13 relapsed 
after CSI (n = 43), including 7 local, 2 distant and 4 combined. There were 
10 focal relapses after chemo + radiotherapy in 18 patients, which is 0.44. 
A total of 48 patients received chemo (of those 24 were treated with 
Radiotherapy) and 22 received chemo + radiotherapy and 26 received 
radiotherapy alone. Of the 48 patients, 21 received chemotherapy alone, 
13 received chemo + radiotherapy and 14 received radiotherapy alone. 
The overall response rate (ORR) was 0.70 (95% CI: 0.55 - 0.83), with 0.68 + 0.13 (median follow-up 75 months) OS: 0.95 + 0.03.

resulted in high rate of recurrence. CONCLUSIONS: From the analysis of 
treatment failure in the 1st clinical study, we planed the 2nd multi-
institutional, prospective Phase 2 study for primary intracranial germ cell 
tumors. The basic design of the study is to follow the protocol in the 1st 
study with stricter treatment plan and the objective is to evaluate the efficacy 
and safety of post-operative histology-oriented radiotherapy and chemother-
apy proposed by the 1st study.
Unfortunately she developed severe persistent lower limb motor and sensory neurotoxicity and high frequency hearing loss. This occurred despite pharmacokinetic monitoring ensuring the target AUC was achieved. CONCLUSIONS: It is possible to salvage multiple relapses of CNS germ-cell tumour even when within a radiation field. Current ventricular radiation strategies may have prevented the first relapse. Caution is needed with HD carboplatin, especially in the context of prior platinum exposure, as neurotoxicity can be idiosyncratic.

GC-15. CHARACTERISTICS OF CENTRAL NERVOUS SYSTEM GERMINOMAS INVOLVING THE BASAL GANGLIA
Tomoyuki Koga, Tomonari Suzuki, Ryo Nishikawa, Takakai Yangasawa, Kohiti Fukukura, and Masao Matsutani; Department of Neuro-Oncology, Saitama Medical University International Medical Center, Saitama, Japan

PURPOSE: Because of the rarity of germinomas involving the basal ganglia (BG), clinical characteristics and outcomes of this disease are not well studied. The purpose of this study was to review the characteristics of BG germinomas and to discuss treatment consideration. METHOD: Retrospective chart review of BG germinoma was performed. RESULTS: Data of ten patients with germinoma involving the BG was available. Age at diagnosis ranged from four to 22 years (median 14 years) and nine patients were younger than 20 years of age. All of these patients were male. Presenting symptoms were dysarthria in one patient, hemiparesis in eight patients, hemiparesis and precocious puberty in one patient. Interval between onset and diagnosis ranged from four to 26 months (median 9 months). Serum or cerebrospinal fluid beta-human chorionic gonadotropin level was elevated in six among eight patients who were evaluated. Seven of 10 patients underwent combination of radiation therapy (RT) and chemotherapy, two patients underwent RT only and one patient chemotherapy only as initial treatment. The patient who was treated by chemotherapy only underwent RT at recurrence. Morality of RT was whole brain RT in seven patients, whole ventricle RT in one patient and local RT in two patients. The follow-up period ranged from 45 to 130 months (median 103 months). One patient died at 96 months and another patient was lost to follow-up. All the other patients are still alive and five-year overall survival rate was 100%. CONCLUSIONS: Germinomas of the BG predominantly affected male in first and second decades of life. Although presenting symptoms were specific, period between first onset and diagnosis was relatively long. Majority of the patients received WRBT and survival outcomes were acceptable. Longer follow-up and multi-institutional study is necessary to evaluate the best treatment of choice for BG germinomas.

GC-16. VENTRICULAR TUMOR MARKERS IN CNS GERM CELL TUMORS - HELP OR HINDRANCE?
Genevieve Legault and Jeffrey Allen; NYU Langone Medical Center, New York, NY, USA

There is increasing reliance on oncoprotein assays such as the β subunit of human chorionic gonadotropin (HCG) and alpha-fetoprotein (AFP) for diagnosis or confirmation of histology of central nervous system (CNS) germ cell tumours (GCT), but the relative diagnostic sensitivity and reliability of assays from serum(S), lumbar(L) and ventricular(V) cerebrospinal fluid (CSF) are uncertain. A total of 69 patients with CNS GCT were identified from a retrospective chart review to determine the value of ventricular CSF oncoprotein assays in CNS GCT. Our study group consisted of 11 patients who had contemporaneous HCG and/or AFP assays available in serum, ventricular and lumbar CSF at diagnosis (n = 10) or relapse (n = 1). Their primary tumour sites were: pineal (n = 6), suprasellar (n = 1) or both (n = 4). Their mean age at diagnosis was 15.4 years (range 9.1-21.6) and the male/female ratio was 10/1. For the histologically confirmed germinoma patients (n = 8), the median HCG values (S/L/V) were 0.7/8.1/12.2 μIU/ml. For the mixed malignant GCT (MMGCT) patients (n = 2), the median HCG values (S/L/V) were 0.3/3.6/6.1 μIU/ml and the median AFP values were 24.1/2.0/7.0 ng/ml. One patient with an inconclusive pathology had AFP values of 1.6/0/0 and HCG values of 0.10/0/0.15.0 and was treated as a germinoma. Lumbar CSF HCG levels exceeded those in ventricular CSF or serum in 7 of 8 cases (87.5%) and the median serum HCG levels were higher in lumbar than in ventricular CSF, but lower than in serum. One patient with histologically confirmed germinoma with serum and ventricular CSF HCG < 100 was treated as a MMGCT because lumbar HCG level > 100 was obtained. In conclusion, the role of ventricular CSF oncoprotein assays is evolving but lumbar CSF remains the most sensitive and reliable source of fluid for clinical guidance in the management of CNS GCT.

GC-13. PATIENTS WITH INTRACRANIAL NON-GERMINOMATOUS GERM CELL TUMOURS (NGGCT): BENEFIT FROM DELAYED SURGERY AFTER NEOADJUVANT CHEMOTHERAPY. FINAL RESULTS OF SIOP CNS GCT 96

Background: Many patients with non-germinomatous germ cell tumours (NGGCT) benefit from neoadjuvant chemotherapy. However, the value of delayed surgery after chemotherapy concurrently with radiotherapy is controversial and the optimal strategy is not well established.

PATIENTS AND TREATMENT: 197 protocol patients with NGGCT between 0-30 years (median 12 years) were registered, 150 were boys. 154 were localised (86 pineal, 40 suprasellar, 13 hypothalamus, 13 other), 43 metastatic. Patients with localised disease received 4 cycles Cisplatin /Etoposide/Ifosfamide (PEI) followed by focal radiotherapy of 54 Gy. Patients with metastases received 4xPEI followed by 30 Gy craniospinal radiotherapy (CSI) and 24 Gy boosts to tumor and macroscopic metastatic sites. RESULTS: Biopsy: 30 patients were only biopsied, 7 were resected after chemotherapy; 2 relapses occurred. 23 were biopsied with no further surgical excision with 7 relapses in follow-up. Resection: 71 patients received primary resection, which was complete in only 31 cases; 12 of these patients relapsed after the end of treatment. 38 were incompletely resected; in 2 patients extend of resection was not reported. 6 of 38 patients underwent second surgery before RT; no relapse occurred. Of the 32 without resection 10 relapsed. Marker at diagnosis: 96 diagnoses were based on markers, 28 underwent chemotherapy and delayed surgery prior to irradiation. 2/28 developed relapse during follow up. 68 patients received chemotherapy with no surgery although only 36 were stated to be in CR after irradiation; 20 of these patients relapsed. CONCLUSION: It is apparent that patients given upfront chemotherapy and delayed surgery before RT have the best outcome. Those who had incomplete resection upfront and delayed surgery after chemotherapy also benefited from excision of residual tumour as no relapses occurred in this group. In SIOP CNS GCT II therefore radiological/ marker diagnosis, if feasible, followed by delayed surgery before RT is favoured. Supported in part by Deutsche Krebshilfe.

GC-14. SUCCESSFUL SALVAGE OF MULTIPLE RELAPSED CNS GERMINOMA BUT WITH CARBOPLATIN NEUROTOXICITY
Rodnick Walker and Juliet Hale; Paediatric and Adolescent Haematology and Neurology, RVI, Newcastle upon Tyne Hospitals Trust, Newcastle upon Tyne, UK

BACKGROUND: CNS germinomas have a cure rate of > 90% but after relapse they have an overall survival (OS) < 60%. There are few reports of survival following multiple relapse. High dose (HD) carboplatin is often part of the treatment of relapse. The known neurotoxicities are usually transient. CASE REPORT: A 4 year, 10 month old girl presented with growth failure and diabetes insipidus. MRI showed a bifocal tumour (serum HCG 4IU/L, CSF HCG 8IU/l) and histology confirmed germinoma. She was treated according to SIOP CNS GCT 96, Arm B with carboplatin /etoposide /ifosfamide followed by 40 Gy involved field radiotherapy. She remained disease free for 17 months until a 4th relapse was noted followed by carboplatin /etoposide /ifosfamide followed by further radiotherapy. She remained disease free for 9 months before relapsing for the second time in the pineal primary site. She was retreated with high dose carboplatin (AUC 21) /thiotepa /etoposide with stem cell support. She is currently disease free more than 3.5 years following salvage therapy.

i52 • JUNE 2012 NEURO-Oncology
GC-17. RESULTS OF TREATMENT AND PROGNOSIS OF PEDIATRIC INTRACRANIAL GERMINOMA (IG): MULTICENTR RETROSPECTIVE ANALYSIS OF 44 PATIENTS
Olga Geludkova1, Marina Mushinskaya2, Yuri Kushnel, Anton Korshunov3, Armen Melikyan1, Ludmila Shishkina1, Valentina Oserova1, Sergey Oserov1, Nadezhda Mase尔kina1, Irina Borodina1, Ella Kumirova1, Nataliya Boyarchuk1, Svetlana Gorbatyh4, Evgeniy Popova1, Oleg Sherbeyov1, Yuliya Zelinsкая1, Rostislav Shemyakin1, Ludmila Privalova1, Oleg Chulkov4, and Yuliya Kose1,5,6

We analyzed 44 pts with IG from 1997 to 2011 (11 girls and 33 boys). Median age was 13 years (range, 3-17). In 39 pts the diagnosis was confirmed histologically. M0-stage was detected in 16 pts, M+ in 13, Mx in 15. 42 pts received RT (18 pts – 24 Gy CSF, 16 – 40 Gy local RT, 8 – 24 Gy ventricular RT), including 38 pts in combination with CHT (according SIOP CNS GCT protocol (n=33), male: female ratio (M:F) 1:2). CSF tumor markers were measured in 32 pts. Median of observing was 36 months (range, 6-120). 10y OS/ESF was 0.91 ± 0.07 and 0.57 ± 0.1 respectively (5y OS/ESF – 0.91/0.66). EFS in pts after surgery + CHT + RT and after CHT + RT had no differences (0.57 ± 0.62 respectively, p = 0.38). EFS of pts after RT without CHT was 0.38 ± 0.2. PD was detected in 6 and 43 months in 2 pts without RT. Pts after CTH or ventricular RT demonstrated better results of EFS, in compare with those pts, who received it locally: 5y-ESF was 0.86 ± 0.53 (p = 0.02) respectively. Relapse detected in 8 pts after local RT with median of time 24 months (range, 11 – 63), in 1 with CTH after 36 month of observing. Ventricular metastasis we detected more often, in 2 pts there were spinal metastasis. The survival rate in pts with local and metastatic IG did not have a statistical difference, but it was higher than in pts with M-stage: 5y-ESF was 0.69; 0.83 and 0.22 (p = 0.13) respectively. In localized IG the effective treatment is ventricular RT in combination with CHT, in metastasis IG and M-stage – CSH. Complete diagnostic procedure is very important for reduction of the RT in M0 pts.

GC-18. TREATMENT OF INTRACRANIAL GERMINOMA: EXPERIENCE OF A BRAZILIAN INSTITUTION
Andrea M. Cappellano, Priscila Paiva, Sergio Cavalheiro, Patricia Dátilo, Marla Teresa Seixas, and Nasja S. Silva; IOP/GRAACC/UNIFESP, Sao Paulo, Brazil

INTRODUCTION: Primary central nervous system germ cell tumor (CNS-GCT) account for 2-3% of all brain tumors in children and adolescent in western hemisphere. Based on the histological components, the classification has been divided into germinomas and non-germinomatous germ cell tumors. The aim of this study is to evaluate the results of an institutional protocol in patients with CNS germinoma. MATERIAL AND METHODS: Since 1998, 41 patients were treated at IOP/GRAACC/UNIFESP with diagnosis of CNS-GCT. 17 were germinoma receiving 4 cycles of carboplatin (300mg/m2 D1-2) and etoposide (200mg/m2 D1-2) followed by ventricular field irradiation of 24-30 Gy and a primary site(s) boost of 36-45 Gy. RESULTS: The mean age at diagnosis was 14 years, 13 males. Primary tumor location was pineal (6), suprasellar (6) and bifocal (3), 3 patients with periventricular dissemination at diagnosis. Elevated HCG levels (< 200mU/ml) was observed in 5 patients (serum) and in 9 pts after 10 (CSF). Surgical procedure was performed in 11 patients. After 2 cycles of chemotherapy, 10 patients achieved radiographic complete response (CR) and 7 partial responses, 1 patient had persistent positive HCG. After 4 cycles, all patients had controlled CR (radiographic and HCG). In this present study, we report 44 patients with IG. Complete diagnostic procedure is very important for reduction of the RT in M0 pts.

GC-19. BEP AND SFOP PROTOCOLS IN THE TREATMENT OF CHILDHOOD CENTRAL NERVOUS SYSTEM GERM CELL TUMOR
Goddard Chi-Chun Chan1, Matthew Ming-Kong Shing2, Hui-Leung Yuen1, Rever Cheau-Ho Lai1, Chi-Keung Li1, Shau-Yin Ha1, and Chi-Kong Li2,3

OBJECTIVE: Germ cell tumors (GCT) are more common among East Asian children. In our locality, the most commonly used protocols were BEP (bleomycin, etoposide, cisplatin) or SFOP which consisted of alternated cycle of CE-IE (carboplatin, etoposide, ifosfamide). We compared the efficacy of these 2 protocols in our patients cohort. MATERIALS AND METHODS: CNS-GCTs were diagnosed either by histological proof or imaging with positive serum/CSF tumor markers. All patients were treated with either BEP or SFOP chemotherapy protocols + irradiation. There were 5 hospitals in our locality involved in treating children with cancer and all the patients’ data were captured by 3 data managers. In general, BEP was the standard protocol before 2003 and it was gradually changed to SFOP since then. RESULTS: From Jan 1999 to Dec 2009 (11 yrs), 76 cases of childhood (≤18 yrs) CNS-GCT were diagnosed. Their median age was 12.9 yrs (ranged 0 to 18yrs) and M:F was 4.5:1. Excluding 17 patients age > 15yrs, the incidence of CNS-GCT was 5.3/million in 15yrs children/yr. Teratoma was relatively more in infant and germinoma was more among adolescents. Overall, 55/76 (72%) patients had germinoma, 9/76 (12%) had malignant or immature teratoma and other non-germinomatous GCT accounted for 12/76 (16%). The 5y OS was 92% for germinoma and 65% for non-germinoma. Comparing the 2 treatment protocols (BEP n = 25 vs SFOP n = 41), it was 90% vs 88% for 5y OS and 85% vs 82% for 5y EFS respectively for the 2 protocols. They were not significantly different in statistical analysis and the minimal follow-up was 2 years. More therapy related complications such as electrolytes disturbances and hearing impairment were noted in the BEP group. CONCLUSION: Germinoma, has good outcome if treated with either BEP or SFOP protocol plus irradiation. But the outcome of non-germinomatous GCT remains suboptimal with these 2 approaches.

GC-20. BASAL GANGLIA GERM CELL TUMORS: A REPORT OF 43 CASES
Hsin-Hung Chen1, Feng-Chu Chang1, Yi-Wei Chen1, and Tai-Tong Wong2

OBJECTIVE: Germ cell tumors (GCTs) originating in the basal ganglia (BG) are rare. It is notorious for the diagnostic difficulty and the majority of the patients present symptoms similar to multiple sclerosis or stroke. MATERIALS AND METHODS: We retrospectively reviewed the clinical features, neuroimaging studies, tumor markers, management, and outcome of these 43 patients from 1985 to 2011 in Taipei Veterans General Hospital. RESULTS: 39 of them were boys and 4 were girls. The mean age of onset of symptoms was 11.5 years. 27 patients presented with progressive hemiparesis, 7 with headache, 13 with opsoclonus and 6 with precocious puberty. 6 patients had bilateral BG tumors. We classified them into 3 groups by mainly involved locations: medial group (10, 20%), lateral group (27, 35%), and diffuse group (12, 25%). The medical group involved thalamostriate junction (groove) and/or caudate nucleus. The size were bigger and the major presenting symptoms were mainly headache. The lateral group involved lenticular nucleus and more than 80% of the patients in this group presented progressive hemorrhages and/or dystonia when the lesion is < 5cm in diameter. The diffuse group was difficult to trace the origin and the tumor size is big to involve both medial and lateral areas of BG, which represented delayed diagnosis and poor functional outcome. All of the six patients suffered from behavior and mood disorder before and after treatment. The outcome was somewhat better among cases than in extracranial locations. 3 patients survived, and 3 patients died. CONCLUSION: The BG is a significant locus for intracranial germ cell tumor and can be bilateral. The initial image finding may be subtle and it should be highly suspicious when hemiparesis or precocious puberty is seen. Treatment of GCTs in specific location is similar to GCTs in other intracranial locations.
Intracranial germinoma is a rare malignant intracranial tumor comprising only 0.5-2.0% of all intracranial tumors. It accounts for almost 60% of all central nervous system germ cell tumors and is highly sensitive to chemoradiotherapy. The incidence of germinoma, which may originate from primordial germ cells in the yolk sac wall, is higher in males and in Asian populations. It usually occurs in children and adolescents, most commonly in a midline location, favouring either pineal or suprasellar sites. In this series, we describe clinical and MRI findings of four sequential patients, all adolescent males of non-Asian descent, who presented to McMaster Children’s Hospital over a two-year period, diagnosed with biopsy-confirmed germinoma occurring in an atypical location. Patient 1, a twelve-year old boy previously successfully treated for intracranial teratoma, presented with left arm and leg motor tics, memory loss and diffuse periventricular disease on MRI. Patient 2, a fifteen-year old boy, presents with right facial numbness, headache and disseminated germinoma arising in the pineal gland, extending along the spine and multiple cranial nerves bilaterally. Patient 3 is a 17-year old boy presenting with diplopia, upper extremity dysesthesia and a unilateral thalamic mass on MRI. Patient 4, a 17-year-old boy, presents with headache, vomiting, diplopia and signs of panhypopituitarism, with a biofocial germinoma on MRI. All patients were diagnosed by CSF/blood sampling for germ cell markers and histology, and were treated successfully with radiation and chemotherapy as per the Japanese CARE protocol. Our case series documents an unusual clinic-radiological presentation of four sequential patients with intracranial germinoma, prompting consideration of this diagnosis for even atypical, non-midline lesions visualized on MRI investigations of adolescent males being investigated for potential CNS neoplasia.

Growing teratoma syndrome (GTS) is a rare condition among patients with intracranial germ cell tumors. It is important to differentiate growing teratoma syndrome from tumor recurrence in the setting of an enlarging residual mass present after treatment of intracranial germ cell tumors (GCT). We report the history of 7-years old boy, who manifested with the next symptoms: visual acuity decrease, polyuria, polydipsia, precocious puberty (pubic hair, genital development, gynecomastia and change of a timbre of a voice). His initial evaluation included MRI of the brain where the thickening of a stalk of a hypophysis was detected. Later 5 months he had serum elevation of alpha-fetoprotein and AFP, up to 26,67 and human chorionicgonadotropin (beta-HCG) up to 200,1 ng/ml. Repeated MRI has revealed formation substantial growth in chiasma-sellar region; with the signs of obstructive hydrocephalus and normal MRI-spiral exams. CSF cytology was not evaluated. Patient underwent 2 cycles of CHT (PEI) according to the protocol “SIOP GCT”. The tumor markers were normalized after 2 cycles of CHT, but with regrowing tumor cystic mass on MRI. 1 cycle of CHT (VP-16 and etoposide) was added without any positive MRI-response. Ten months after the tumor was performed, histopathology revealed mature teratoma. Patient underwent RT of the brain up to 30 Gy. He is clinically well about 12 months; continue to receive the replaceable therapy by c-kit, OCT4 and partially PLAP immunohistochemically.

CONCLUSION: Spontaneous regression of intracranial germinomas can be not so rare. It is difficult to expect regression clinically and histopathologically. Shrinkage at biopsies or before treatment should be taken care of.

Background: Germinal Brain tumors is a rare cancer in children but its prognosis is good with multimodal treatment. They are heterogeneous tumors that vary in presentation, treatment and outcome. METHODS: A retrospective review of all children less than 14 years of age with the diagnosis of germinal brain tumors treated at our institution from January 1990 till December 2011, was performed. Data collected included demographic, clinical, neuroradiologic, pathologic, treatment and outcome. RESULTS: Over the study period there were 6 patients with the diagnosis of germinal brain tumors treated at our hospital of 2300 children with cancer. Their median age was 10 years (range 6-12 years). There were 1 boy and 5 girls. The main signs were headache, polyuria and hyponipidemia (100%), diplopia (75%) and 25% ptosis. Five tumors were located at suprasellar region and one at infundibulum. At initial, all cases underwent partial surgery resection. The histopathology results were disgerminome in four cases (67%) and immature teratome in two cases (33%). The first case was assessed in 1990 and he was treated only with radiotherapy after surgery but this patient died after six months of survival because of relapsing. In addition to radiotherapy, the other 5 cases undergo chemotherapy; cyclophosphamide + etoposide alternated with cytoplatin, for 4 courses of treatment. At his time these five patients (83%) are alive with no evidence of disease, with a median follow-up of 96 months. CONCLUSIONS: Gonads germinal cancer is a frequent condition in children in our country but is rare in brain the germinal tumors. The “sandwich method” (chemotherapy/radiotherapy/chemotherapy), after partial surgery resection, showed a good response and the patients did not need the second-look surgery.

Purpose: Some cases of spontaneous regression of primary intracranial germinomas have ever been reported in the literature. But the frequency of spontaneous regression and hypersensitivity of intracranial germinomas are not well known. We report clinical outcome and histopathological characteristics in cases of spontaneous regression. MATERIALS AND METHODS: Twenty-four cases with primary intracranial pure germinomas or HCG-producing germinomas were treated in Osaka University Hospital from 1994 to 2011. In three (12.5%) of twenty-four cases, tumors appeared to shrink spontaneously on MRI. Patient’s age in these cases ranged from 16 to 19 years. All cases were male. About tumor location, MRI revealed mass of pineal region in two, bifocal lesion in one. Endoscopic tumor biopsies including CSF samplings were performed in all, endoscopic third ventriculostomies were done in two. In one case, tumor sample was not obtained because of marked shrinkage. Serum markers (HCG, HCG-beta, AFP) in serum or cerebrospinal fluid (CSF) were measured in all cases. All serum markers and HCG in CSF were normal, but HCG-beta in CSF were slightly elevated from 0.4 to 1.4ng/ml. RESULTS: Diagnostic radiation dose before treatment in shrinking germimomas were from 0.05Gy to 0.926Gy and they were not significantly different from that in cases of non-shrinking germinoma. Administration dose of steroid hormone, time from onset to treatment (3-12 days) and initial tumor maximal diameter (10-30mm) did not influence tumor regression. In cases with spontaneous regression, no recurrence was seen during follow up (9-69months, median: 49months). Histopathologically, small infiltrating lymphocytes in the specimens diminished in two. MIB1 labeling index was 40-60%. Tumor cells were positive for c-kit, OCT4 and partially PLAP immunohistochemically.

CONCLUSION: Spontaneous regression of intracranial germinomas can be not so rare. It is difficult to expect regression clinically and histopathologically. Shrinkage at biopsies or before treatment should be taken care of.
GC-25. PINERAL NON GERMINOMATOUS GERM CELL TUMOUR RELAPSE FOLLOWING FOCAL RADIOTHERAPY - 3 CASES
M. Trivedi, A. Tyagi, J. Goodden, P. Chumas, M. Elliott, and S. Picton; Leeds General Infirmary, Leeds, West Yorkshire, UK

The standard treatment for intracranial non germinomatous germ cell tumours (NGGCT) has not yet been established. The SIOP CNS GCT 96 trial emphasised on focal radiotherapy (RT) following chemotherapy and surgical resection for intracranial NGGCT. We present a case series of three male patients who were diagnosed with secreting germ cell tumours and treated as per the SIOP CNS GCT 96 phase III trial protocol. All the three patients relapsed either at follow up or during focal RT, with metastases outside the treated tumour bed. This raises a question over whether craniospinal rather than focal RT should be considered in this group of patients, and certainly suggests a need to revisit the current treatment protocols. Further research to study the efficacy of focal RT and its relationship with subsequent progression to metastatic disease outside the treated tumour bed may be helpful.

GC-26. EVALUATION OF PITUITARY STALK THICKENING IN CHILDREN AND ADOLESCENTS
Nathan Robison1, Sanjay Prabhu2, Pengling Sun1, Susan Chi1, Mark Kieran1, Peter Manley1, Laurie Cohen2, Liliana Goumnerova2, Edward Smith2, Michael Scott2, Wendy London1, and Nicole J. Ullrich2; 1Dana Farber Cancer Institute, Boston, MA, USA; 2Children’s Hospital Boston, Boston, MA, USA

BACKGROUND: The significance of pituitary stalk thickening >2-3mm on magnetic resonance imaging (MRI) is often unclear. We evaluated the presenting symptoms, MRI findings, clinical course, and outcome predictors of patients with pituitary stalk thickening. METHODS: We used a computerized search of the medical record from 1995-2008 to identify patients with pituitary stalk >2.6 mm on coronal or sagittal measurements and without pituitary mass. Baseline and follow-up MRIs were reviewed in a blinded fashion. Relevant clinical data was abstracted. RESULTS: 83 patients with reported pituitary stalk thickening were identified; 42 of these had adequate imaging for review and met study criteria. Median age at first abnormal MRI was 13.6 years (range: 0.8 - 19.7); 57% were female. Median follow-up was 3.4 years (range 0 - 12.8). Patients with diabetes insipidus (DI) were significantly more likely to have a neoplastic process than those without (p = 0.0008). Of 16 patients who presented with diabetes insipidus (DI), 8 (50%) were ultimately found to have a neoplastic process, including germ cell tumor (n = 4), Langerhans cell histiocytosis (LCH, n = 3), and lymphoma (n = 1). Among patients with DI, seven (44%) also developed anterior pituitary hormone dysfunction (APD), either at presentation or on pre-biopsy follow-up, including 6/8 patients with stalk neoplasm and only 1/8 patients without (p = 0.04). 26 patients presented without DI; none were found to have neoplasm of the stalk except one patient with craniopharyngioma. Degree of stalk thickening at presentation had no prognostic significance. However, >15% increase in pituitary stalk measurement on follow-up imaging was significantly associated with a subsequent neoplastic diagnosis (p = 0.04). CONCLUSION: These results suggest an increased likelihood of neoplasm in patients with pituitary stalk thickening and DI, especially in patients who also develop APD or progressive stalk increase, for whom biopsy may be indicated. Observation alone may be appropriate for most cases without DI.