

The 12th International Symposium on Pediatric Neuro-Oncology

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The Childhood Brain Tumor Foundation was pleased to be amongst the supporters for the 12th ISPNO, held June 6-9, at the Nara-Ken New Public Hall in Nara, Japan (the oldest capital area in Japan). Dr. Masao Matsutani, the President of the **2006 ISPNO** and Dr. Roger Packer, Vice President, provided a warm welcome to the attendees on Wednesday, June 7, 2006. The program was very comprehensive, inclusive of keynote lectures, oral and poster presentations. Many of the topics will be presented in this article, but, due to page constraints a comprehensive review will not be done.

The Pre-symposium Educational Lectures for Young Neurosurgeons was held on Tuesday, June 6. The following morning sessions included: Quality of Life in Children with Brain Tumors, Nursing and Multidisciplinary Care for Patients and Their Family; with concurrent sessions, Basic Science I and Basic Science II; and Temozolomide for Pediatric Brain Tumors.

Quality of Life Sessions:

- “*Endocrine Outcomes for Children with Medulloblastoma treated with Craniospinal and Conformal Primary Site Irradiation on the SJMB96 Trial,*” was presented by Dr. Stephen J. Laughton, St. Jude Children’s Research Hospital. The goal of the study was to determine severity of endocrine effects from irradiation. He shared that there is a relationship between radiation dose to the hypothalamus pituitary axis (HPA) and hypothyroidism, thus requiring patients to need replacement therapy. Future studies will assess minimizing HPA.
- D.J. Mabbott, Hospital for Sick Children, Toronto, Canada presented, “*White-Matter Integrity and Core Cognitive Functions in Children Treated with Cranial-Spinal Radiation: A Diffusion Tensor Study.*” Decline in intellectual outcome has been previously associated with compromised white matter after cranial spinal irradiation. Although patients had poorer working memory and attention issues when compared with controls, they were not highly significant for the overall mean. A noted difference was processing speed, considered to be associated with compromised white matter integrity, thus contributing to poorer clinical outcomes.

- The study entitled, “*Risk of Stroke Amongst Long-Term Survivors of Childhood Brain Tumors: a Report from the Childhood Cancer Survivor Study,*” presented by Daniel Bowers, University of Texas Southwestern Medical Center, addressed incidence and risk factors for stroke in pediatric brain tumor survivors = 5 years. Findings indicate that survivors, especially those who were treated with cranio-spinal irradiation are at increased risk of stroke.
- “*Measuring Health Related Quality of Life for Childhood Brain Tumor Survivors*” was presented by Dr. Stewart Goldman, Children’s Memorial Hospital, Northwestern University, Chicago, IL. The prevalence of late effects is high in pediatric brain tumor survivors, thus it is important that they are monitored throughout their life.

Nursing and Multidisciplinary Care for Patients and Their Family Sessions:

- The topic, “*Caring for Pediatric Brain Tumor Patients and their Families in the United States,*” was presented by Dianne Traynor, Pediatric Brain Tumor Foundation. She indicated that two key members of the multi-disciplinary team include the Pediatric Oncology Nurse and the Pediatric Oncology Social Worker and provided details about their involvement with families.
- Toshinobu Sato, Director of Maternal and Child Health Japanese Ministry of Health, Labor and Welfare, presented, “*Children’s Chronic Diseases support Program (CCDSP) in Japan.*” CCDSP subsidizes costs for out-of pocket expenses for medical expenses for patients in Japan, it is a national program, launched by the Ministry of Health.
- Yakiko Sasaki, parent of a child, Children’s Cancer Association at Japan, Tokyo, shared her experiences when presenting, “*My Wish as a Mother of a Child Suffered Optic Glioma.*” She commented, “What makes me sad most is that the children who have overcome painful treatment and loneliness are forced to face harder situations when they return to the normal life.” Ms. Sasaki’s wish is for society to respect the children for the battles they have fought to survive and for classmates and teachers to develop an understanding nature.
- “*Living with a Cerebellar Tumor,*” was presented by Takayuki Nakahachi, Survivor, Children’s Cancer Association of Japan. Mr. Nakahachi is a survivor of juvenile pilocytic astrocytoma, diagnosed at age 4, currently is 31-yearsold. He reflected on his treatments and related his social anxiousness and prudence to some of the socially negative experiences he endured. Due to studies and the supportive memories he had from family members and self-affirmation he has learned from others who have faced similar obstacles, he is hopeful for his adulthood.

The afternoon session was Co-Moderated by Dr. T-R Wong (Taiwan) and Jeanne Young, (Childhood Brain Tumor Foundation, MD, USA). (photo right)



- “*Study on Psychosocial status of Families and Children Treated of Central Nervous System Tumors,*” was presented by B. Dembowskia-Baginska, The Children’s Memorial Health Institute, Warsaw, Poland. He concluded that in Warsaw patients were often neglected by social services and received inadequate attention in the school setting.

- “*Quality of Family Life for Children with Brain Tumors,*” was presented by Adrienne Witol, Stollery Children’s Hospital and was an international study (Edmonston, Canada, and the USA). The study outcome results indicated quality of life and family support for the child’s needs are influenced by many factors; treatment phase, tumor type, and logistics of the treatment center during school.
- “*Maternal and Familial Stress, and their Determinants Early after Diagnosis in Children with Brain Tumors,*” was presented by A Penn, Frenchay Hospital, Bristol. The conclusion showed that stress in mothers of these children is increased over the controls. The associated stress levels are related to dependency, family functioning and family support. Interestingly, they found no relationship between the child’s emotional or behavioral state and the mother’s emotional health or family stress.
- M. Voltz-Fleckenstein, Pediatric Oncology, Regensburg, discussed, “*Developing a Palliative Care Program in Pediatric Oncology.*” In Germany, palliative care for patients was underdeveloped and a program was developed in 2001-2003. They found that the program developments have influenced choices at end of life, often is now in the home environment.

Basic Science I Sessions:

- “*Screening for Candidate Genes Reveals RASSF1A as the Only Consistently Methylated Gene in Malignant Childhood Brain Tumors.*” - Michael Fruhwald, Pediatric Oncology, University Children’s Hospital Muenster, Germany, presented data from a study evaluating gene methylation in malignant childhood brain tumors. His group found that *RASSF1A* is the only consistently methylated gene in medulloblastomas and supratentorial PNET’s. Aberrant methylation contributes to the development of childhood brain tumors. Identifying these genes may play a role in early detection and development of new treatments.
- “*DNA Copy Number Alterations of Cell Cycle Regulated Loci in Pediatric Primitive Neuroectodermal Brain Tumors*” was presented by Annie Huang, M.D. and her colleagues from the Hospital for Sick Children in Toronto, Canada. Dr. Huang et al found that there were multiple new areas of genetic loci in addition to more well-known genetic alterations, such as the *c-myc* that has previously been reported. This study identified several other areas of interest, such as gains at the *cyclin D1-D3* and *cdk4* loci and high level gene amplification of the *cdk6* locus. *CDK6* was highly expressed in Medulloblastoma and PNET compared to normal brain tissue suggesting that *CDK6* may play an important role in the etiology of these tumors. This may provide important clues to developing molecular targeted therapies to knock out the *cdk6* receptors.
- “*Genomics Identifies Medulloblastoma Subgroups that are Enriched for Specific Genetic Alterations*” was presented by a group from St. Jude’s Children’s Research Hospital, Texas Children’s Hospital, Royal Children’s Hospital (Australia), The Children’s Hospital at Westmead (University of Sydney, Australia), and Hospital for Sick Children (Canada). This group presented their findings of gene expression profiles for 46 tumor samples of Medulloblastoma. They were able to identify five different subgroups of Medulloblastoma. They found specific subgroup mutations in the Wingless (WNT) pathway and deletion of chromosome 6 (subgroup B), and mutations in the Sonic Hedgehog (SHH) pathway (subgroup D) in 31 of these samples. The conclusion was that gene expression profiles can further classify the larger group of Medulloblastoma tumors

into smaller subgroups which may assist in treatments for specific molecular targeted therapies.

- “*b-Catenin Status Predicts Favourable Prognosis in Childhood Medulloblastoma*” was presented by physicians from the University of Newcastle and the University of Swansea in the United Kingdom. This group found that nuclear accumulation of *b-Catenin* appears to be a marker of favorable outcome in Medulloblastoma. All children in this trial who had *b-Catenin* positive cells, even those with high risk disease such as anaplastic large cell Medulloblastomas or metastatic disease, were alive at least five years after diagnosis.

- “*Clinical and Molecular Characteristics of Malignant Transformation of Low-Grade Glioma in Children: The St. Jude Children’s Research Hospital Experience*” was presented by Dr. Alberto Broniscer. St. Jude’s reviewed clinical, radiology and pathology of all patients with Grade II Astrocytomas less than 22 years of age who were treated at St. Jude’s from 1985-2004. The treatment of this group included radiation and/or chemotherapy. Available tumor tissue was sent for molecular analysis (FISH, immunohistochemistry, and *TP53* sequencing. The St. Jude’s group did find similar molecular abnormalities associated with primary and secondary adult glioblastomas but they did not find that previous treatment, especially radiation therapy, was associated with malignant transformation in children.

- “*Characterization and Therapeutic Targeting of the Brain Tumor Stem Cell Niche*” was presented by the St. Jude’s Children’s Research Hospital. Their data indicated that glial and neuroectodermal tumors were maintained by stem cells that express CD133 and Nestin. Cancer stem cells in the brain and endothelial cells were found close together and cooperated in regenerating cancer stem cells but not other cells. Specifically, ERBB2 signaling in Medulloblastoma cells, which is associated with a poor prognosis, promotes this regeneration. Inhibiting the ERBB2 signaling prolonged survival of mice with ERBB2 positive Medulloblastoma. This data is significant as it represents a new target for therapy.

- “*Characterization of Stem Cell-Like Cells in Cancer Cell Lines*” was presented by Dr. Toro Kondo from Kobe, Japan. Dr. Kondo’s laboratory identified stem cell-like cells in rats Gliomas and human breast cancer cell lines. Tumors that have these stem cell-like cells were much more malignant than those that did not have these types of cells. The cancer stem cell may be an important target for newer molecular targeted therapies in the futures.

Basic Science II Sessions:

- “*The Neurofibromatosis Type 1 Gene Product Neurofibomin Enhances Cell Motility by Regulating Actin Filament Dynamics via the Rho-ROCK-LIMK2-COPFILIN Pathway*” was presented by physicians from Kumamoto University in Kumamoto, Japan. This group found that neurofibomin, an NF 1 tumor suppressor gene, induces morphological changes and play an important role in regulating cell growth and affecting cell motility and adhesion. These findings may explain, in part, the mechanism of formation of multiple neurofibromas in NF1 patients.

- “*Spectrum of Mutations in the Tumor Suppressor Gene, Patched-1, in Patients with Nevoid Basal Cell Carcinoma Syndrome*” was presented by Dr. Toshiyumi Miyashita from Tokyo, Japan. Basal cell nevoid syndrome, commonly known as Gorlin syndrome,

is characterized by developmental abnormalities and development of tumors such as basal cell carcinoma and Medulloblastoma. Dr. Miyashita's laboratory found mutations in 15 of 19 patients. They discovered that the *patched-1* gene undergoes complicated mutation sequences in these patients. Diagnosis during childhood is often challenging because signs develop over time so diagnosis may be delayed. Early genetic diagnosis by identifying these mutations is important for early detection and prevention.

- “*Brain Pathology of Tuberous Sclerosis: Pathogenesis of Dysplastic and Neoplastic Lesions*” was presented by Dr. Masashi Mizuguchi from the University of Tokyo, Japan. Tuberous sclerosis is an autosomal dominant genetic disorder in which various types of dysplastic and neoplastic lesions may develop in various organs, including the brain. These researchers investigated the Tsc2 gene in rats that had brain lesions. They found that the pathogenesis of dysplasia is different from the tuberous sclerosis associated tumors. These findings may aid in early detection and prevention of tumor in patients with tuberous sclerosis.

Temozolomide for Pediatric Brain Tumors:

This session was moderated by Dr. Ian Pollack and Dr. Masao Matsutani and included five discussions with physicians from Italy, the US, and Germany.

- “*Antitumor Activity of Temozolomide in Medulloblastoma-PNET*” was presented by Dr. R. Riccardi, Catholic University, Rome, Italy. Dr. Riccardi presented findings from a Phase II study of children and young adults including 34 patients with relapsed or refractory Medulloblastoma. The observed response rate (including 6 complete responses, 7 partial responses and 3 minor responses) was 47% with no unexpected toxicities. Progression-free survival was 67% at 6 months. Their study showed that Temozolomide is a safe and effective agent in children and young adults who have previously intensive therapy. They suggest that Temozolomide should be included in treatment for newly diagnosed patients with Medulloblastoma/PNET.

- “*Should Temozolomide be the Standard of Care for Children with Newly Diagnosed High Grade Gliomas? Results of the Children's Oncology Group ACNS0126 Study*” was presented by Dr. Ken Cohen, Johns Hopkins's University, USA. This was a single-arm Phase II trial investigating the combination of radiation therapy and Temozolomide (daily during radiation and ten cycles of monthly 5 day pulses following completion of radiation). The overall one year survival was $68 \pm 5\%$, which was less than the historical control (CCG-945 study) where the overall one year survival was $68 \pm 4\%$. This was particularly significant for those patients with Anaplastic Astrocytoma where the one year event-free survival was $31 \pm 8\%$ for the current study as compared to $45 \pm 6.5\%$ seen in the CCG-945 study. For those patients with Glioblastoma, the one year event-free survival was $36 \pm 7\%$ for the current study as compared to $32 \pm 6\%$ seen in the CCG-945 study. Those patients with GBM seemed to do better with the ACNS0126 study. These findings may be related to the methylated AGT expression in tumors which is linked to increased event-free survival. There is ongoing analysis of tumor specimens for MGMT and MMR to determine if individual patient specimens would have predicted sensitivity or resistance to Temozolomide.

- “*Temozolomide (TMZ) as Part of Combination Chemotherapy for Pediatric Brain Tumors: The Children's Oncology Group Experience*” was presented by Dr. Regina Jakacki, Children's Hospital of Pittsburgh, USA. Dr. Jakacki discussed the COG

ADVL0011 Phase I study of Temozolomide in combination with CCNU for newly diagnosed patients with unresectable high-grade gliomas. This study utilized two cycles of Temozolomide prior to radiation therapy and six cycles of Temozolomide following completion of radiation therapy. She also discussed COG ADVL0214 which evaluated the oral EGFR inhibitor, Erlotinib, given as a single agent for 28 days and then in combination with Temozolomide given for 5 days. The ADVL0011 study included patients with glioblastoma, anaplastic astrocytoma and anaplastic oligodendroglioma. Thirteen patients were treated on this study for two or more courses with an overall one year survival of $59 \pm 13\%$ and an overall two year survival of $25 \pm 12\%$. The ADVL0214 study treated sixteen patients including diagnoses of brain stem glioma, ependymoma, medulloblastoma/PNET and a few other tumor types. There were two responses noted and the most common side effects were rash and diarrhea. These results are encouraging in a small sample size and warrant further study.

- “*Molecular Predictors of Outcome in Childhood Malignant Gliomas: The Children’s Oncology Group Experience*” was presented by Dr. Ian Pollack, University of Pittsburgh, USA. The COG examined tumor samples from patients enrolled on the CCG-945 study for malignant gliomas. Tumors were assessed for *p53* overexpression/mutations, EGFR expression/amplification, PTEN deletions, 1p and 19q chromosomal deletions, drug resistance markers, and other genetic alterations. Amplification of EGFR and mutations of PTEN were rare in gliomas (< 5%) and not correlated with prognosis. However *p53* mutations were frequent and were an adverse prognostic indicator. Chromosome 1p and 19q deletions, common in adults, were only present in a few childhood gliomas and were not associated with prognosis. MGMT overexpression occurred in 10-20% of tumors and was indicative of poor outcome as it is associated with resistance to certain types of chemotherapy agents (alkylators). Overexpression of *p53* and MGMT were particularly adverse indicators. These observations will be helpful in the development of new molecular targeted therapy approaches.

- “*Aberrant Methylation of O⁶-MGMT in Pediatric High Grade Glioma (HGG) – A Surrogate Marker for Response to Temozolomide*” was presented by Dr. Michael Fruhwald, University Children’s Hospital Muenster, Germany. Dr. Fruhwald presented results from analysis of 26 tumor specimens from children with high grade gliomas who had received Temozolomide therapy at the time of relapse. The findings showed aberrant methylation of O⁶-MGMT in 8/24 specimens. Preliminary results suggest a longer time to progression in those patients with methylation. O⁶-MGMT methylation may be a useful marker for response to Temozolomide in children with high grade gliomas.

On Thursday, June 8 sessions included, Medulloblastoma/PNET; Epidemiology; AT/RT & Pineoblastoma, Surgery, Craniopharyngioma; High_dose Chemotherapy & New Treatment Trial; and Glioma

Medulloblastoma/PNET Sessions:

- “*Brain Tumours in Very Young Children – Challenges and Controversies*” was presented by Dr. Antony Michalski, Great Ormond Street Hospital for Children, London, England. A review of previous treatment approaches and future directions for treatment of primitive neuroectodermal tumors in infants were discussed. Of particular interest

were treatment approaches that minimized neuropsychological and endocrine effects and maximize quality of life.

- *“Treatment of Early Childhood Medulloblastoma by Postoperative Chemotherapy: Results of the HIT-SKK’92 Study”* was presented by Dr. Stefan Rutkowski, University Children’s Hospital, Wuerzburg, Germany. Dr. Rutkowski discussed the outcomes of 43 children with Medulloblastoma who were treated with combination chemotherapy including intravenous and intraventricular Methotrexate as well as other IV antineoplastic agents. The overall 5-year event free survival was $93.6 \pm 6\%$ for those patients who had a complete resection, $56 \pm 14\%$ for those with residual tumor and $38 \pm 15\%$ for those with macroscopic metastases. These investigators concluded that this chemotherapy regimen was highly effective for those children without metastasis or residual tumor and allowed radiation to be omitted, thereby preserving neurocognitive functioning and maximizing quality of life.

- *“Non-Disseminated Medulloblastoma < 3 years of Age: Final Report of the Head Start I and II Protocols”* was presented by Dr. Jonathan Finlay, Children’s Hospital of Los Angeles, USA. This session discussed the 5 year outcomes for 21 children with Medulloblastoma treated on these two intensive chemotherapy protocols. The overall survival was $75 \pm 10\%$. The overall survival for those patients with desmoplastic histology was $78 \pm 14\%$. Those patients who had a gross total resection at diagnosis did the best with an overall survival of $86 \pm 9\%$ compared to $57 \pm 19\%$ for those who did not have gross total resections. Seven patients did develop tumor recurrence but became long term survivors with radiation therapy. The remaining patients who did not receive radiation therapy had near normal neurocognitive functioning and quality of life.

- *“Final Results of COG 9961: A Prospective Randomized Study of 2340 cGy of Craniospinal Radiation Therapy and Adjuvant Chemotherapy for Average-Risk Medulloblastoma”* was presented by Dr. Roger Packer, Children’s National Medical Center, USA. This large Phase III clinical trial treated 421 children with non-disseminated Medulloblastoma. The overall survival was $86 \pm 9\%$ at 5 years. Nearly 25% of patients had posterior fossa mutism syndrome. These are encouraging results using a reduced dose of craniospinal radiation therapy. Evaluation of neurocognitive and other late effects is ongoing.

- *“Impact of Anaplasia on Outcome for Metastatic (M+) Medulloblastomas (MB) Treated with Carboplatin as a Radiosensitizer During Radiotherapy (RT) Followed by Adjuvant Cyclophosphamide (CPM) and Vincristine (VCR): Preliminary Results of COG 99701”* was presented by Dr. Regina Jakacki, Children’s Hospital of Pittsburgh, USA. This study had 58 eligible patients with an overall survival rate of $89 \pm 6\%$ at 3 years for patients without anaplasia versus $64 \pm 12\%$ for those with anaplasia. The presence of anaplasia on pathology review is a significant predictor of poorer outcome for patients with metastatic Medulloblastoma.

- *“Prognostic Relevance of Clinical and Biological Risk Factors in Childhood Medulloblastoma: Results of Patients Treated in the Prospective Multicenter Trial HIT’91”* was presented by Dr. Stefan Rutkowski, University Children’s Hospital of Wuerzburg, Germany. These researchers found three risk groups defined by clinical criteria and mRNA expression. Patients whose tumors had very high TrkC mRNA expression or high TrkC/low C-MYC did not relapse regardless of metastatic disease (100% event-free survival at 7 years). Those with metastatic disease and high C-

MYC/low TrkC levels relapsed (33% event-free survival at 7 years). The remaining patients (intermediate risk) had an event-free survival of 63%. These findings are significant in planning treatment strategies based upon risk groups.

- “A Phase II Study of Oxaliplatin in Children with Recurrent or Refractory Medulloblastoma (MB), Supratentorial Primitive Neuroectodermal Tumors (SPNET) and Atypical Teratoid Rhabdoid Tumors (ATRT): A Pediatric Brain Tumor Consortium Study” was presented by Dr. Maryam Fouladi, St. Jude’s Children’s Research Hospital, USA. Oxaliplatin was well tolerated in children. For children with first recurrence of Medulloblastoma, the observed response rate was 6.7%.
- “Supratentorial Primitive Neuroectodermal Tumors (sPNET): Final Outcome for Children Enrolled on Head Start I and II” was presented by Dr. J. Fangusaro, Children’s Hospital of Los Angeles, USA. This approach with intensive chemotherapy and hematopoietic stem cell rescue, for children under the age of 10 years, provided an overall survival of $49 \pm 8\%$ at 5 years. This is an improved outcome over historical treatments and often eliminates the need for radiation therapy in the majority of patients.

Epidemiology

Although, pediatric brain tumors are the second cause of cancer death in children, they are the most common solid tumors in children. Large population studies are used to define the incidence of primary brain tumors. The US study indicated that although pediatric brain tumors are rare, the incidence is approximately 4.3 per 100,000. Three presenters shared statistics regarding incidence of pediatric brain tumors. The first presenter was from the Central Brain Tumor Registry of the United States; second was from Tokyo, and the third presenter was from Hong Kong. Dr. Soichiro Shibui, National Cancer Center Hospital, Tokyo, Japan, presented, “*Pediatric Brain Tumor in Japan based on the Data of Brain Tumor Registry of Japan.*” Dr. Shibui concluded that craniospinal radiotherapy and platinum-based chemotherapies improve survival in patients with Medulloblastoma and germinoma. However, in patients with craniopharyngioma improved survival was attributed to improved microsurgical techniques and patient management.

Dr. Paul Fisher, neurologist, Stanford University Hospital, presented three topics in regard to Epidemiology. One topic, “*Do Children and Adults Differ in Survival from Medulloblastoma? A Study from the San Francisco Oakland SEER Registry.*” concluded that children and adult Medulloblastoma patient survival does differ overall, however, infants tend to fare significantly worse. Study outcomes showing some similarities suggest that there may be some justification to including some adults in pediatric cooperative trials, specifically for Medulloblastoma.

AT/RT & Pineoblastoma Sessions:

- “*Combined Multi-Modality Therapy for Pediatric Central Nervous System (CNS) Atypical Teratoid/Rhabdoid Tumor (ATRT): An Interim Analysis of the German ATRT-CNS Pilot Study*” was presented by Dr. O. Peters, University of Regensburg, Germany. This treatment regimen contains novel agents for brain tumors, using traditional chemotherapy along with intraventricular chemotherapy and radiosensitizers during radiation therapy. The overall survival at 2 years was 94% which is a significant

improvement from previous German clinical trials, although the number of patients is small. There was significant toxicity with increased incidences of mucositis and infection (48-42%). This regimen appears effective but there is significant toxicity.

- “*Atypical Teratoid/Rhabdoid Tumor of the CNS – A Retrospective Analysis of Outcome Depending on Initial Diagnosis and Treatment Received in 12 Consecutive Patients*” was presented by Dr. T. Czech, Medical University of Vienna, Austria. This study investigated accurate diagnosis of ATRT tumors by applying the INI1 antibody to all highly malignant pediatric brain tumors treated at the institution. Twelve patients were found to be INI1 positive, correlating with a diagnosis of ATRT. Only five of these patients had been diagnosed as ATRT originally. Because historically ATRT tumors have a poor outcome and a median survival of 6-19 months with conventional therapies, proper diagnosis at the time of original presentation is essential.
- “*Outcome for Patients with Pineoblastoma Treated with Carboplatin as a Radiosensitizer during Radiotherapy (RT) Followed by Adjuvant Cyclophosphamide (CPM) and Vincristine (VCR): Preliminary Results of COG 99701*” was presented by Dr. Regina Jakacki, University of Pittsburgh, USA. The overall survival at 3 years was 84 ± 11%. Outcome was not significantly different for those with metastatic disease. The use of carboplatin as a radiosensitizer followed by six months of adjuvant chemotherapy is a promising treatment for patients with pineoblastoma.
- “*Childhood Pineoblastoma: Experiences from the Prospective Multicenter Trials HIT-SKK92 and HIT 91*” was presented by Dr. Stefan Rutkowski, University Children’s Hospital of Werzburg, Germany. Combination chemotherapy and radiation therapy was feasible for children older than 3 years of age, leading to prolonged remissions, however tumor biology appeared to be more aggressive in younger children. More intensive treatment regimens should be explored.
- “*Pineoblastoma in the Pediatric Population – Review of a Single Institution Experience*” was presented by Dr Stephen Gilheeney, Dana-Farber Cancer Institute, USA. This institution did a retrospective medical record review of 18 patients treated between 1985 and 2005. There was an overall survival rate of 70% at 7 years. Extent of surgical resection, specific histological features and radiation/chemotherapy treatments were all found to be predictive of outcome.

Surgery

“*Cerebellar Injury After Posterior Fossa Tumors: Anatomic-Functional Correlations in 61 Children,*” was presented by Jacques Grill, Gustave Roussy Institut, France. Cognitive functioning is strongly impacted if there is direct damage to the cerebellum caused by tumor and/or surgery. The impact of damage and neuropsychologic effects in children with posterior fossa tumors was assessed. The goal of cure with minimal damage is priority, therefore surgical risk for tumors of the posterior fossa should be balanced with the need for aggressive adjuvant therapies.

Craniopharyngioma Sessions:

- “*Current Management of Craniopharyngiomas*” was presented by Dr. Concezio Di Rocco, Catholic University Medical School, Rome, Italy. “*Lessons from Attempted Radical Total Resection of Childhood Craniopharyngiomas*” was presented by Dr. Byung-Kyu Cho, Seoul National University Children’s Hospital, Korea. “*Surgical*

Strategy of Pediatric Craniopharyngiomas Based on the Long Term Follow-up Results” was presented by Dr. Shigetoshi Yano, Kumamoto University, Japan. These sessions presented a review of the current strategies for diagnosing and treating craniopharyngiomas. Total tumor removal is associated with higher rates of complications, both short term and long term. Radical tumor resection was found not to prevent tumor recurrence and this presentation suggested that more conservative surgical approaches be the standard of care.

- “*Craniopharyngioma Cystic: Intratumoral Therapy with Interferon Alpha*” was presented by Patricia Dastoli, Universidade Federal de Sao Paulo, Brazil. Interferon Alpha proved to be an effective agent in the control of cystic craniopharyngiomas. Nineteen patients were treated and showed tumor shrinkage and low neurotoxicity. Further studies are needed to determine the optimal dose in the treatment of these tumors.

High-Dose Chemotherapy & New Treatment Trial Sessions:

- “*Is There a Role for Myeloablative Chemotherapy with Autologous Hematopoietic Progenitor Cell Rescue (AHPCR) in Children with Malignant Gliomas?*” was presented by Dr. Jonathan Finlay, Children’s Hospital of Los Angeles, USA. This presentation reviewed the current approaches for treatment of malignant gliomas and compared them to historical data. Although neither high-dose BCNU or Thiotepa alone has been effective, multidrug regimens have produced responses in a small subset of patients. The most important factor predictive of a favorable outcome with myeloablative chemotherapy/stem cell support regimens is the extent of the initial surgical resection. The use of tandem intensive chemotherapy regimens with stem cell support and the addition of post-transplant biological agents (Cis-retinoic acid, Avastin, Tarceva, metronomic dose Temozolomide) may be next steps in treatment for these high risk patients to improve outcome.

- “*Factors Affecting Event Free Survival (EFS) After Myeloablative Chemotherapy with Autologous Hematopoietic Progenitor Cell Rescue (HDC/AUHPER) in Children with Malignant Brain Tumors*” was presented by Dr. J.A. Teplick, Children’s Hospital of Los Angeles, USA. Fifty three patients, ages 4 months to 18.1 years, were treated with a high dose chemotherapy regimen including thiotepa and/or etoposide and/or carboplatin followed by stem cell rescue. The 3 year EFS for patients with Medulloblastoma/PNET was $53 \pm 9\%$ and $40 \pm 15.5\%$ for all other tumor types. Children most likely to benefit from this approach are those less than 3 years of age with newly diagnosed Medulloblastoma/PNET (no metastatic disease) and those with other tumor types who have had a gross total resection of the tumor.

- “*Pilot Phase II Study of Metronomic Oral Cyclophosphamide (CTX) Plus Thalidomide (THAL) in Children with Recurrent Malignant Brain Tumors*” was presented by Dr. Sri Gururangan, Duke University Medical Center, USA. Treatment included once daily low dose CTX and THAL without interruption in 21 patients. In this cohort of patients, this treatment approach had modest activity with manageable toxicities and warrants further study in larger patient cohorts.

- “*Phase I/II Study with Pegylated Liposomal Doxorubicin in Combination with Oral Topotecan in Children with Progressive High-Grade Glioma: An Interim Analysis*” was presented by Dr. Sabine Wagner, Department of Pediatric Oncology of Regensburg, Germany. PEG-DOxo was individually dosed per patient every 2 weeks over 6 weeks,

increasing the dose depending upon toxicity to a maximum dose. Topotecan was given orally twice a day as maintenance chemotherapy. Some responses were seen in this group of 10 patients but further study is needed.

Glioma

“Phase 3 Randomized Study of Two Chemotherapy Regimens for Treatment of Progressive low Grade Glioma in Young Children: Preliminary Report from the Children’s Oncology Group Protocol A9952, was presented by Dr. Joan Ater. The study goal was to compare event free survival in patients diagnosed with hypothalamic optic pathway or brainstem tumors when in randomized trials. Regimen A included (carboplatin/vincristine) and Regimen B, a combination of thioguanine, procarbazine, CCNU and vincristine. In conclusion, further investigations are warranted, there was no significant difference in the two protocols.

This article only reflects excerpts from the International Symposium on Pediatric Neuro-oncology. Very informative presentations were given throughout the conference and the poster presentations were outstanding. In addition, there was an art show featuring drawings from children diagnosed with brain tumors, leukemia, and Hodgkins Lymphoma. The pictures were very expressive of how the children relate to diagnosis, treatment, and family life. It was a very compelling display, enjoyed by all.