

This article was written for the Childhood Brain Tumor Foundation, Germantown, MD.

## The 11th International Symposium on Pediatric Neuro-Oncology

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The 11<sup>th</sup> International Symposium on Pediatric Neuro-Oncology (ISPNO) was held on June 13-16, 2004 at the Westin Copley in Boston, MA. The Childhood Brain Tumor Foundation (CBTF) was pleased to be amongst the sponsors for this comprehensive conference organized by neuro-oncology professionals for medical professionals dealing with the many various aspects of neuro-oncology in children. Experts from around the world convened to share treatment and research results. This year's ISPNO was chaired by Dr. Mark Kieran and co-chaired by Dr. Peter Black. Attendees were warmly welcomed by Drs. Kieran and Black, as well as Drs. Archie Bleyer and Roger Packer. This article covers only a small fraction of the topics discussed.

On Saturday, June 13 the first session was co-chaired by Drs. Mark Kieran and Peter Phillips on the topic of New Therapeutics. Dr. Xiao-Nan Li (Baylor College of Medicine, Texas Children's Hospital) discussed his research, "*Anti-medulloblastoma effects of Valproic Acid as a histone deacetylase (HDAC) inhibitor,*" a study partially funded by the CBTF. Dr. Li shared his data and indicated by inhibiting HDACs valproic acid has shown potent anti-medulloblastoma effects; promoting apoptosis (programmed cell death) and inhibiting proliferation of medulloblastoma cells grown in culture. Another speaker for the morning session was Dr. Birgit Geoerger (Institute Gustave-Roussy, Villejuif, France). Dr. Geoerger presented, "*Conditionally Replicating Adenoviruses Express p53 or Targeted Toward EGFR Exhibit Enhanced Oncolytic Potency in Malignant Gliomas.*" Conditionally replicative adenoviruses show enhanced oncolytic capacity due to CRA-independent infectivity through EGFR targeting and/or restoration of p53 dependent cell death and may be promising agents for treatment of malignant gliomas in the future.

A session entitled, "*Epidemiology of Pediatric Brain Tumors*" was co-chaired by Drs. Archie Bleyer and Faye Davis. Dr. Anne Berdel (Children's Hospital and Clinics, Minneapolis, MN and Children's Oncology Group, Arcadia, CA) presented "*CNS Tumor Epidemiology and Outcome in Adolescents and Young Adults in the US, 1975-1998.*" Dr. Berdel reported the incidence of astrocytomas were 64% of CNS neoplasms, with "other gliomas" being 19%, primitive neuroectodermal tumors 8%, and ependymomas 5%. The 20-year survival rate for astrocytoma was reported to be 65% for children ages 15-19 years of age, 40% for 20-24 years of age and 25% for survivors 24-25 years of age.

Dr. Monika Drogasiewicz (Children's Memorial Health Institute, Warsaw, Poland) presented "*The Pre-diagnostic Problems in Children with Primary Brain Tumors.*" The study investigators determined that more education is needed for the basic levels of health care to create a better understanding about the epidemiology of brain tumors. In addition, further studies are needed to understand the signs and symptoms of brain tumors.

On Monday, June 14, the morning session focused on the "*Biology of Medulloblastoma,*" co-chaired by Drs. Richard Gilbertson, Tobey MacDonald and Scott Pomeroy. "*Molecular Genetics of Medulloblastoma*" was presented by Dr. Hai Yun (Duke University Medical Center, Durham, NC). Dr. Yun reported that genome-wide evaluations of genetic alterations in medulloblastoma will provide improvements in molecular classification and new therapeutic targets. Dr. Tobey MacDonald (from Children's National Medical Center, Washington, DC) discussed "*PDGFR Inhibition in Medulloblastoma Cells Induces Apoptosis and Alters Gene Expression,*" a study that has shown that overexpression of platelet-derived growth factor receptor (PDGFR) is associated with metastatic medulloblastoma. Dr. MacDonald reports the drug Gleevec inhibits PDGFR activation and mediated responses in medulloblastoma cells.

Concurrently, a session titled, *Nursing Update – Part 1* was Co-Chaired by Christine Chordas, Kristen Graham and Mary Ann Lefrancois. "*Paediatric Oncology Health Information on the Internet: a Survey of Usage by Families*" was presented by Kristina Hardy. Her findings indicated that most caregivers utilize

the Internet as one of the sources of health information.

Drs. Roger J. Packer and Giorgio Perilongo co-chaired the *Standard-Risk Medulloblastoma Forum*. Dr. Packer provided an overview about standard-risk medulloblastoma and presented “*Preliminary Report of A9961: A Phase II Randomized Study of Craniospinal Radiotherapy (CSRT) followed by One of Two Adjuvant Chemotherapy Regimens with Newly Diagnosed Average-risk Medulloblastoma.*” In summation, he concluded that the preliminary results (pending eligibility) of 2340cGY of CSRT and chemotherapy during and after radiation is a reasonable approach to treatment. Many issues, such as posterior fossa mutism, high incidence of ototoxicity, and several other factors, will need to be addressed in these patients. As part of this session, Dr. Kenneth Cohen (Johns Hopkins Medical Center, Baltimore, MD) presented an interesting historical perspective on the past use of vincristine in cancer therapy and led a stimulating discussion of its future use in the treatment of childhood brain tumors.

Other sessions included topics such as, “*High-Risk Medulloblastoma/PNET Forum*; and *Relapsed Medulloblastoma Forum, Minimally Invasive/Innovative Techniques for Neurosurgery.*”

On Monday afternoon, co-chairs Drs. David Osoba and Susan Parsons introduced “*The Quality of Life Forum.*” Pamela Wolters (Medical Illness Counseling Center and HIV and AIDS Malignancy Branch, Bethesda, MD) presented “*Development of Quality of Life Scale for Children with Chronic Illness with CNS Involvement; Preliminary Data.*” Based on the Impact of Pediatric Illness Test (IPIT) that was developed by Dr. Wolters, et.al., preliminary findings indicated that, in regard to quality of life, the most impaired area of functioning is adaptive functioning. A “*Leptomeningeal Disease Forum*” was chaired by Dr. Susan Blaney (Baylor College of Medicine). Dr. Blaney opened with experimental agents for intrathecal use. Dr. Udo Bode, et.al., from the University of Bonn, Bonn, Germany, presented “*Experiences with Intraventricular Etoposide in Neoplastic Meningitis of Relapsed Metastatic Brain Tumors.*” Dr. Bode stated that treatment options are limited mainly to craniospinal irradiation for patients with metastatic brain tumors, and reported that the long-term side effects of this treatment included impairment of concentration, short term memory and verbal fluency issues. She stated that Etoposide chemotherapy administered intrathecally was well-tolerated and should be evaluated in the future as a potential alternative therapy.

“*Current Topics in Neurofibromatosis (NF)*” was co-chaired by Drs. Roger Packer and Brigitte Widemann (NCI). Dr. Widemann discussed “*Current clinical Trials in Neurofibromatosis Type-1.*” It is estimated that approximately 25% of NF-1 patients will have disfigurement and functional impairments. Dr. Bryan C. Oh (Children’s Hospital of Los Angeles) shared the topic “*Neurofibromatosis 3: A Report of Patients Meeting Diagnostic Criteria for both Neurofibromatosis 1 and 2.*” Three patients have met diagnostic criteria for both NF1 and NF2, one female and two males. NF can be quite variable, ranging from mild cases that present in adulthood to others that are severe and that develop serious complications. Although the investigators felt that a diagnostic category called NF3 might be of consideration, after some group discussion others concluded that a genetic test might be advisable before creating a NF3 category.

On Tuesday, June 15, Dr. M. Judiah Folkman (Surgery and Chief, Emeritus, Children’s Boston) gave a keynote address, “*Research and the Mechanisms of Angiogenesis Research.*” Dr. Folkman explained that solid tumors are dependent on blood vessels, and he described the applications of angiogenesis in cancer research and how principles of angiogenesis apply to brain tumors. He stated that p53, which is often mutated in cancer, normally increases expression of thrombospondin-1, a natural angiogenesis inhibitor. He mentioned Thalidomide, an example of an angiogenesis inhibitor, is currently under investigation. Thirty clinical trials with various anti-angiogenesis inhibitors are being conducted in the United States today. Dr. Folkman proposed the question: Can angiogenesis inhibitors treat cancer years before it become visible? He indicated it may be possible, if guided by forecasting biomarkers in blood and urine.

“*Outcomes and Survivorship, Neuropsychology-Part 1: Neuropsychology*” was chaired by Dr. Raymond Mulhern. Shawna Palmer (Memphis, TN) presented “*Age at Diagnosis. A Prominent Risk Factor when Evaluating Cognitive Performance following Risk-adapted Treatment for Medulloblastoma.*” The most prominent risk factor for neurocognitive issues is young age at diagnosis. Children with averrisk and high risk disease experience greater difficulty with phonological analysis skills. “*Part II: Multidisciplinary Care*” was chaired by Dr. Christopher Turner. Incidence and trends of overweight and at-risk for overweight among pediatric central nervous system tumor patients was presented by Dr. Della Howell (Emory University, Atlanta). A study was conducted by Dr. Howell, et al, regarding the trend and

etiologies in regard to patients who are overweight and are at risk for becoming overweight. Data indicates that patients with tumors in certain regions tend to have a greater association with being overweight or risk of becoming overweight, those with higher association were craniopharyngioma and hypothalamic area tumors.

Biology of Pediatric CNS Tumors included many informative sessions. “*Genomic imbalances in high and low-grade paediatric astrocytomas*,” was presented by Dr. Richard Grundy (Birmingham, UK). Gene analysis may aid in diagnosis and stratification of tumors. According to the study results there was evidence of novel chromosomal imbalances in paediatric astrocytomas.

In the afternoon, *High-Grade Gliomas* was co-chaired by Drs. Henry Friedman and Peter Phillips. Dr. Stewart Goldman, Children’s of Chicago presented ‘*Thalidomide and carboplatin for the treatment of brain stem gliomas*.’ Ten percent of pediatric CNS tumors are brain stem gliomas. A protocol incorporating carboplatin with thalidomide (an antiangiogenic agent) was paired as a clinical trial for brain stem glioma patients. The regimen was considered feasible, well tolerated by most and may be incorporated into future trials.

“*Microvessel density (MD) predicts behavior in pediatric optic pathway/hypothalamic gliomas (OPHG)*,” was presented by Dr. Ute Bartels, Toronto, Canada. OPHGs are typically low-grade tumors, however, they may exhibit unpredictable behavior. Dr. Bartels investigated the angiogenic features for prognostic factors. Finding indicated that angiogenesis is important in low-grade gliomas with microvessel density having prognostic value. Dr. Eric Bouffet, Toronto, Canada presented, “*Pilot study of vinblastine in patients with recurrent and refractory low-grade glioma*.” In conclusion, he reported that vinblastine is tolerable and shows promising activity in recurrent low-grade gliomas. When patients, especially young children are given prolonged treatments of vinblastine (12 months or more), it appears to help delay the need for radiation.

Dr. Stewart Goldman chaired the session “*Current Treatments for Ependymoma. Childhood Ependymoma: Improved survival for patients with incompletely resected tumors with the use of pre-irradiation chemotherapy*” was presented by Dr. James Garvin (Columbia University, NY, NY). The survival rate for children with incompletely resected ependymomas is approximately 35%, where survival is approximately 75% for patients that have had total resection. Post operative radiation increases survival in patients that have had partial resection. Chemotherapy could improve outcome in infants and those with recurrent tumors. The study results suggest that pre-RT chemotherapy should be incorporated into the treatment plan for pediatric ependymomas.

On Wednesday, June 16 the session entitled “*Neuropathology Update and Platform Presentations*” was co-chaired by Drs. Peter Burger, David Louis and Lucy Rourke. “*What’s in a name?*” was presented by Dr. Floyd H. Giles. He stated that the current schemes for classifying tumors results in subsets of diagnoses and grades. These diagnoses often have varying survival expectations. In summation Dr. Giles stated that tumors must be separated using reliable histology and statistical methods that recognize patterns in tumors in a reproducible manner.

Unfortunately, as space is limited it is impossible for us to summarize a great deal of the excellent information presented at the medical symposium. However, we have tried to highlight many of the symposium presentations and hope that you have found this overview of the symposium informative, interesting, and useful.

