Pediatric patients with ependymoma have favorable outcomes with immediate post-surgical radiation therapy
Large Children’s Oncology Group trial reports five-year event free survival

San Antonio, October 18, 2015—Outcomes for pediatric patients as young as 12 months old with ependymoma who are treated with immediate post-operative radiation therapy are favorable and consistent based upon the patients’ tumor surgical resection and tumor grade, according to research presented today at the American Society for Radiation Oncology’s (ASTRO’s) 57th Annual Meeting.

The Children’s Oncology Group ACNS0121 trial was a prospective study for childhood ependymoma (EP)—a rare type of brain and spinal cord tumor that arises from the ependyma, a tissue of the central nervous system. This was the largest prospective trial for childhood ependymoma ever conducted and the first cooperative group trial for ependymoma to target the post-operative tumor bed and to use three-dimensional conformal radiation therapy (3-D CRT) and intensity-modulated radiation therapy (IMRT). In addition, this study is significant in that it was the first to systematically use immediate post-operative radiation therapy in children under the age of
three with this type of brain tumor. Many children diagnosed with ependymoma are younger than three years old. Prior studies did not include the use of radiation therapy in frontline management for very young children with ependymoma.

The study was conducted from 2003 to 2007 to determine the rate of tumor control in children with ependymoma who were treated with conformal radiation therapy using a 1cm clinical target volume margin surrounding the post-operative tumor bed. The underlying goals were to reduce the volume of radiation therapy and decrease the risk of side effects without affecting the rate of tumor control.

The trial included 378 patients from 115 institutions. The average patient age was 5.3 years (range 1.01-21.01 years), and each patient had been newly diagnosed. There were 216 patients with World Health Organization (WHO) grade II tumors and 140 with WHO grade III tumors. Patients were enrolled in the study within 56 days of initial surgical resection (removal of part or all of the tumor).

Researchers categorized the patients into non-overlapping subgroups or strata. The study was designed to observe patients with WHO grade II; supratentorial ependymoma (tumors in the upper part of the brain) after microscopically complete (GTR1) surgical resection (stratum 1); administer chemotherapy with optional second surgery prior to conformal radiation therapy (CRT) for patients with subtotal (STR) resection at the time of protocol enrollment (stratum 2); administer immediate post-operative CRT for patients with either near-total (NTR defined as < 5mm residual thickness) or macroscopic gross-total (GTR2) resection (stratum 3) or with WHO grade III, supratentorial or any infratentorial ependymoma (tumors in or around the fourth ventricle) after GTR1 (stratum 4).

Stratum 2 patients were treated with pre-CRT chemotherapy consisting of two three-week cycles of vincristine, carboplatin, and cyclophosphamide (cycle 1) and etoposide (cycle 2); and some of the stratum 2 patients had a second surgery prior to CRT. Stratum 3 and stratum 4 patients received post-operative CRT. Radiation was administered using a 1.0 cm clinical target volume margin. The cumulative total dose was 59.4 Gy, except for patients younger than 18 months after GTR.
One endpoint the study measured to evaluate the effectiveness of treatment was the rate of patients’ five-year event free survival (EFS). In cancer, EFS refers to a length of time after primary treatment that the patient remains free of certain complications or events (such as the return of the cancer or onset of symptoms) that the treatment was intended to prevent or delay.

Data indicated that progression (meaning the cancer was spreading or getting worse) was observed in five of the 11 eligible stratum 1 patients, and the five-year EFS rate for patients in stratum 1 was 61.4 percent ± 14.4 percent. In stratum 2, a second surgery was performed in 25 of the 64 patients, and GTR was achieved in 14 patients. There was no difference in EFS comparing the 25 patients that underwent a second surgery to the 39 patients that did not (log-rank test: P=0.0790). The EFS rate for stratum 2 patients was 39.2 percent ± 7.0 percent. The EFS rate for patients in stratum 3 was 67.3 percent ± 4.5 percent; and 69.5 percent ± 3.8 percent for patients in stratum 4. Among the 281 patients treated on stratum 3 and 4, EFS was 74.6 ± 3.6 percent for those with WHO grade II tumors and 60.7 percent ± 4.7 percent for those with WHO grade III tumors, according to central pathology review (log-rank test: P=0.0047).

“These results indicate that radiation therapy may be safely administered to children of all ages with ependymoma and high-rate of tumor control may be achieved for the majority of children,” said Thomas E. Merchant, DO, PhD, lead author of the study and Baddia J. Rashid Endowed Chair in Radiation Oncology at St. Jude Children’s Research Hospital. “All children with ependymoma should receive expert care and treatment teams should follow protocol guidelines similar to those used in this study with consideration given to the importance of gross-total tumor resection and advances in radiation therapy methods. Other treatments, in addition to surgery and radiation therapy, should be investigated to further increase the rate of tumor control.”

The abstract, “A Phase II Trial of Conformal Radiation Therapy for Pediatric Patients With Localized Ependymoma, Chemotherapy Prior to Second Surgery for Incompletely Resected Ependymoma and Observation for Completely Resected, Differentiated, Supratentorial Ependymoma” will be presented in detail during the clinical trials session at ASTRO’s 57th Annual Meeting at 3:15 p.m. Central time on Sunday, October 18, 2015. To speak with Dr. Merchant, please
call Nancy Mayes in ASTRO’s Press Office at the Henry B. González Convention Center, in San Antonio on October 18 – 21, 2015 at 210-258-8104 or 210-258-8105, or email press@astro.org.

ASTRO’s 57th Annual Meeting, being held at the Henry B. González Convention Center in San Antonio, October 18-21, 2015, is the nation’s premier scientific meeting in radiation oncology. The 2015 Annual Meeting is expected to attract more than 11,000 attendees including oncologists from all disciplines, medical physicists, dosimetrists, radiation therapists, radiation oncology nurses and nurse practitioners, biologists, physician assistants, practice administrators, industry representatives and other health care professionals from around the world. Led by ASTRO President Bruce D. Minsky, MD, FASTRO, a radiation oncologist specializing in gastrointestinal cancers, Professor of Radiation Oncology, and the Frank T. McGraw Memorial Chair at The University of Texas MD Anderson Cancer Center, Houston, the theme of the 2015 Meeting is “Technology Meets Patient Care.” Dr. Minsky’s Presidential Symposium, “Multidisciplinary Management of Esophageal and Rectal Cancers,” will feature Leonard L. Gunderson, MD, MS, FASTRO, and Joel E. Tepper, MD, FASTRO, to highlight imaging, staging, genomics and data mining approaches, as well as the latest advances in esophageal and colorectal cancer treatment. ASTRO’s four-day scientific meeting includes presentation of more than 2,100 abstracts: five plenary papers, 351 oral presentations, 1,609 posters and 171 digital posters in more than 53 educational sessions and 26 scientific panels for 20 disease-site tracks. Three keynote speakers will address a range of topics including cancer biology in radiation oncology, the essential roles of a physician, and patient safety: Arul Chinnaiyan, MD, PhD, Professor and Director, Michigan Center for Translational Pathology; Francisco G. Cigarroa, MD, Past President and Chancellor, University of Texas; and Gerald B. Hickson, MD, Senior Vice President and Assistant Vice Chancellor, Vanderbilt University Medical Center.

ABOUT ASTRO

ASTRO is the premier radiation oncology society in the world, with more than 10,000 members who are physicians, nurses, biologists, physicists, radiation therapists, dosimetrists and other health care professionals that specialize in treating patients with radiation therapies. As the leading organization in radiation oncology,
the Society is dedicated to improving patient care through professional education and training, support for clinical practice and health policy standards, advancement of science and research, and advocacy. ASTRO publishes three medical journals, International Journal of Radiation Oncology • Biology • Physics (www.redjournal.org), Practical Radiation Oncology (www.practicalradonc.org) and Advances in Radiation Oncology (www.advancesradonc.org); developed and maintains an extensive patient website, www.rtanswers.org; and created the Radiation Oncology Institute (www.roinstitute.org), a non-profit foundation to support research and education efforts around the world that enhance and confirm the critical role of radiation therapy in improving cancer treatment. To learn more about ASTRO, visit www.astro.org.

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A Phase II Trial of Conformal Radiation Therapy for Pediatric Patients With Localized Ependymoma, Chemotherapy Prior to Second Surgery for Incompletely Resected Ependymoma and Observation for Completely Resected, Differentiated, Supratentorial Ependymoma

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Purpose/Objective(s): The Children’s Oncology Group ACNS0121 trial was designed to observe patients with WHO grade II, supratentorial ependymoma (EP) after microscopically complete (GTR1) resection (stratum 1), administer chemotherapy with optional second surgery prior to conformal radiation therapy (CRT) for patients with subtotal (STR) resection at the time of protocol enrollment (stratum 2) and immediate post-operative CRT for patients after near-total (NTR defined as < 5mm residual thickness) or macroscopic gross-total (GTR2) resection (stratum 3) and WHO grade III, supratentorial or any grade, infratentorial after GTR1 (stratum 4).

Materials/Methods: Newly diagnosed patients were enrolled within 56 days of initial resection. Stratum 2 patients were treated with pre-CRT chemotherapy – two 3 week cycles of vincristine, carboplatin and cyclophosphamide (cycle 1) and etoposide (cycle 2); second surgery prior to CRT was optional. Stratum 3 and 4 received post-operative CRT. Radiation was administered using a 1.0cm clinical target volume margin. The cumulative total dose was 59.4Gy except for age <18 months after GTR. Patients were enrolled October 2, 2003 through September 28, 2007.

Results: 378 patients and 115 institutions participated. Median age was 5.3 years (range 1.01 -21.01 years). There were 216 WHO grade II and 140 grade III tumors. Stratum 1: progression was observed in 5 of the 11 eligible stratum 1 patients. The 5 year event-free survival (EFS) was 61.4% + 14.4%. Stratum 2: second surgery was performed in 25 of 64 patients, GTR was achieved in 14. There was no difference in EFS comparing the 25 patients that underwent second surgery to 39 patients that did not (log-rank test: P=0.0790). Stratum 2 EFS was 39.2% + 7.0%. EFS was 67.3% + 4.5% for stratum 3 and 69.5% + 3.8% for stratum 4. Among the 281 patients treated on stratum 3 and 4, EFS was 74.6 + 3.6% for WHO grade II and 60.7 + 4.7% for WHO grade III tumors according to central pathology review (log-rank test: P=0.0047).

Conclusion: The concept of immediate post-operative radiation therapy for patients with ependymoma as young as 12 months of age was supported by investigators in the Children’s Oncology Group. The outcome for patients with ependymoma treated with immediate post-operative radiation therapy on a cooperative group trial appear to be favorable, consistent with single institution benchmarks, and associated with the known prognostic factors of extent of resection and tumor grade. There remains opportunity for further improvement in all patient groups.