Patients with intermediate-risk meningiomas who receive postoperative radiation therapy have excellent three-year progression-free survival

First analysis of RTOG 0539 trial also indicates minimal adverse events

San Antonio, October 20, 2015—Patients with intermediate meningiomas treated with radiation therapy (RT) after surgery experienced a 96 percent three-year progression-free survival rate and had minimal adverse events, according to research presented today at the American Society for Radiation Oncology’s (ASTRO’s) 57th Annual Meeting.

Meningioma, the most common type of central nervous system tumor, nearly always forms on the meninges—the membranes that surround the brain and spinal cord. Most meningiomas, approximately 75 percent, are benign (noncancerous), and may not require immediate treatment. However, many need to be removed because of proximity to or impingement of critical structures, tumor growth, or because they are not benign (in other words, they are atypical or anaplastic). Treatment decisions for patients with meningioma depend on many factors, with the more advanced meningiomas often requiring a combination of surgery and RT.
RTOG 0539, the first successfully completed cooperative group meningioma trial, enrolled 244 patients from sites throughout the U.S. and Canada. The study’s aim was to estimate patients’ three-year progression-free survival (PFS) rates in each of the study’s assigned patient groups. PFS indicates the length of time during and after the treatment of a disease that a patient lives with the disease but it does not get worse. The pathology and imaging reports of patients in the trial were all centrally reviewed and patients were assigned to three different groups depending on prognosis and management strategies, which were based upon tumor grade, recurrence status of the tumors and the extent of the surgical removal.

In this first analysis of RTOG 0539, researchers looked at the three-year PFS and adverse events for the intermediate-risk group of patients (defined as Group 2). Patients in Group 2 had either a newly diagnosed grade II meningioma (atypical, meaning neither frankly malignant nor benign), with gross total resection (GTR, Simpson I-III), or a recurrent grade I (benign) meningioma, meaning that it had been previously treated with surgery but had subsequently progressed. Any degree of surgical resection was permitted for patients with a recurrent grade I tumor. The phase II study compared the patients to a predefined historical control group of intermediate-risk meningiomas.

Of the 56 original patients classified to Group 2, 52 patients received protocol treatment (three were ineligible and one did not receive RT). Of these 52 patients, 36 (69.2 percent) were classified as having WHO grade II tumors with GTR; while 16 patients (30.8 percent) had recurrent grade I tumors. The patients received RT of 54 Gy in 30 fractions post-surgically. While 3-D CRT was permitted within the study guidelines, the majority of patients (84.6 percent) received intensity-modulated radiation therapy (IMRT). This was the first RTOG brain trial with protocol-specific IMRT parameters. Four of the 52 patients withdrew (without recurrence), so 48 patients were evaluable for the primary endpoint of three-year PFS.

Data indicated that there was no difference in PFS between the subgroups (P=.503), validating the study’s co-grouping of the patients into one prognostic category. The three-year PFS for Group 2 was 96 percent. One patient with a WHO grade II tumor died from the disease and one patient with a WHO grade I tumor died from an undetermined cause without disease progression.
Adverse events were scored using NCI common toxicity criteria, and the study specifically measured grade one or grade two adverse events. Among the 44 patients who received IMRT, four patients (9 percent) developed grade 2 acute adverse events, and 11 patients (25 percent) had grade 2 late adverse events.

“Our results have been the impetus for phase III trials and support the use of postoperative radiation for intermediate-risk meningiomas, in addition to documenting positive outcomes of using IMRT,” said lead study author Leland Rogers, MD, professor in the radiation oncology department at Virginia Commonwealth University. “We are gaining knowledge about meningiomas at a more rapid pace. This study has shown we can successfully treat meningioma patients in a large, cooperative group setting and can achieve excellent outcomes with surgery and RT.”

The abstract, “Intermediate-Risk Meningioma: Initial Outcomes from Nrg Oncology/RTOG-0539,” will be presented in detail during a scientific session at ASTRO’s 57th Annual Meeting at 1:15 p.m. Central time on Wednesday, October 21, 2015. To speak with Dr. Rogers, 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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INTERMEDIATE-RISK MENINGIOMA: INITIAL OUTCOMES FROM NRG ONCOLOGY/RTOG-0539

Author Block: L. Rogers, P. Zhang, M. A. Vogelbaum, A. Perry, L. Ashby, A. Alleman, J. M. Galvin, D. Brachman, J. M. Jenrette, J. DeGroot, J. A. Bovi, M. Werner-Wasik, J. P. S. Knisely, and M. P. Mehta; 1Virginia Commonwealth University, Richmond, VA, 2NRG Oncology Statistics and Data Management Center, Philadelphia, PA, 3Cleveland Clinic, Cleveland, OH, 4University of California, San Francisco, San Francisco, CA, 5Barrow Neurological Institute, Phoenix, AZ, 6Yale University, New Haven, CT, 7University of Oklahoma, Oklahoma City, OK, 8IROC Philadelphia RT, Philadelphia, PA, 9St. Joseph’s Hospital and Medical Center accruals for Arizona Oncology Services Foundation, Phoenix, AZ, 10Medical University of South Carolina, Charleston, SC, 11MD Anderson Cancer Center, Houston, TX, 12Medical College of Wisconsin, Milwaukee, WI, 13Sidney Kimmel Medical College of Thomas Jefferson University, Philadelphia, PA, 14Hofstra North Shore-LIJ School of Medicine, Lake Success, NY, 15University of Maryland School of Medicine, Baltimore, MD

Purpose/Objective(s): This is the first report of RTOG-0539, outlining 3-year progression free survival (3y PFS) compared to a predefined historical control of intermediate-risk meningiomas, and secondarily evaluating prospectively scored adverse events (AEs) from intensity modulated radiation therapy (IMRT).

Materials/Methods: RTOG-0539 allocated meningioma patients to 1 of 3 prognostic groups and management strategies according to WHO grade, recurrence status, and resection extent. For the intermediate-risk group (Group 2), eligible patients had either newly diagnosed WHO grade 2 meningioma with gross total resection (GTR, Simpson I-III) or recurrent WHO grade 1 of any resection extent. Pathology and imaging were centrally reviewed. Patients were treated with radiation therapy (RT), either IMRT or 3D conformal (3DCRT), 54 Gy in 30 fractions. Three-year PFS for Group 2 was estimated a priori at 70% with GTR alone, and 90% GTR + RT. This is the first RTOG brain trial with protocol-specific IMRT parameters. Although 3DCRT was permitted, the majority (44, 84.6%) received IMRT. Of 56 patients enrolled, 3 were ineligible, and 1 did not receive RT. Fifty-two received protocol treatment, 4 of whom withdrew without recurrence before 3y; thus, 48 were evaluable for the primary endpoint, 3y PFS. Adverse events were scored using NCI common toxicity criteria.

Results: Of these 52 patients, 36 (69.2%) were WHO 2 with GTR, and 16 (30.8%) recurrent WHO 1. There was no difference in PFS between the subgroups (P=.503), validating our co-grouping of these entities in 1 prognostic category. Fifty (96.2%) were treated per protocol or with acceptable variation, with no statistical association between tumor dose or volume and progression risk. Three-year PFS was 96.0%. At 3y, there were 2 events: 1 WHO grade 2 patient died from disease, and 1 recurrent WHO 1 died from undetermined cause without progression. Three-year local failure was 2.0%, and 3y overall survival 96.0%. After 3y, 2 additional patients progressed, 1 recurrent WHO 1 and the other WHO 2; both remain alive. According to the prespecified analysis, AEs (definitely, probably or possibly related to protocol treatment) were limited to grade 1 or 2, with no grade 3 events; however, when evaluating all AEs, 2 patients had late grade 3 subjective hearing loss, without categorical evidence of audiometric loss. Per the prespecified analysis, among 44 receiving IMRT, 4 (9%) developed grade 2 acute AEs, and 11 (25%) grade 2 late AEs.

Conclusion: This is the first completed cooperative group meningioma trial. Patients with intermediate-risk meningioma treated with RT experienced excellent 3y PFS of 96.0%, with local failure 2.0%, and minimal acute or late AEs above grade 2. These results support postoperative RT for gross totally resected WHO grade 2, or recurrent WHO grade 1 meningioma irrespective of resection extent. They also document minimal toxicity and high rates of tumor control with IMRT.