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News Release

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Long-term results of RTOG 0236 confirm good primary tumor control and positive five-year survival rates for lung cancer patients who received stereotactic body radiation therapy (SBRT)

San Francisco, September 15, 2014—Patients with inoperable, early-stage lung cancer who receive stereotactic body radiation therapy (SBRT) have a five-year survival rate of 40 percent, according to research presented today at the American Society for Radiation Oncology's (ASTRO's) 56th Annual Meeting. Such a positive survival rate is encouraging considering that historically conventional RT resulted in poor tumor control for patients with inoperable lung cancer. This study is an update of RTOG 0236, originally published in 2010[1], and also conducted by the original researchers to evaluate tumor control rates and side effects for patients at five years post-treatment.

RTOG 0236 was a Phase II North American multicenter trial from May 2004 until October 2006 of patients age 18 and older with biopsy-proven peripheral T1-T2 N0M0 non-small cell lung cancer (early stage with no lymph node involvement or metastases). Patients in the study all had medical conditions that precluded them from surgery, so they received SBRT, a specialized type of external beam therapy that uses

1 Timmerman R, Paulus R, Galvin J, et al. Stereotactic body radiation therapy for inoperable early stage lung cancer. *JAMA: The Journal of the American Medical Association.* Mar 17 2010;303(11):1070-1076.

focused radiation beams at a tumor using detailed imaging. SBRT delivers high doses of radiation to the tumor in a decreased amount of treatment time, compared to standard RT, while minimizing exposure to surrounding healthy organs. SBRT appeared to improve tumor control, as suggested by the initial study results for RTOG 0236[2].

A total of 59 patients were accrued for the study, and 55 were evaluable (44 patients with T1 tumors and 11 patients with T2 tumors). Patients each received three fractions of 18 Gy (54 Gy total) of SBRT, and treatment lasted between one-and-a-half to two weeks.

Researchers evaluated local control, which is the rate of reoccurrence of the cancer at the site of origin, as well as disease-free survival, overall survival and toxicity (side effects). Median follow-up was four years (7.2 years for surviving patients). At five years, the rates for disease-free and overall survival were 26 percent and 40 percent, respectively, with a median overall survival of four years.

Only four patients had recurrences at the primary tumor site, resulting in an estimated five-year primary tumor failure rate of seven percent (range, 1.8 to 4.8 years after SBRT). Nine additional patients had recurrence within the involved lobe (range, 0.1 to 5.9 years after SBRT), resulting in a five-year primary tumor and involved lobe (local) failure rate of 20 percent.

The five-year local-regional failure rate was 38 percent, of which seven patients experienced a spread of the cancer to nearby lymph nodes or organs (range, 2.8 to 5.2 years after SBRT). Fifteen patients had disseminated recurrence (throughout the lung), thus the five-year disseminated failure rate was 31 percent. Treatment-related grade three and grade four side effects were reported in 15 patients and in two patients, respectively. No grade five adverse events were reported.

"Historically, when treating early lung cancer with radiotherapy, progression at the site of the primary tumor was the most common failure resulting in suffering and death," said lead study author Robert Timmerman, MD, professor and vice chair of the department of radiation oncology at the University of Texas Southwestern Medical Center in Dallas. "The initial results of RTOG 0236 showed very good tumor control; however, many physicians were concerned that treatment-related toxicity would eventually appear, so SBRT has not seen wide-spread use. This long-term analysis confirms that treated tumors did not reappear at the original site; and late toxicity, beyond what was seen in the initial report, did not appear. However, metastatic tumors continued to appear over time in untreated sites likely because those tumors were so small at initial

2 Timmerman R, Paulus R, Galvin J, et al. Stereotactic body radiation therapy for inoperable early stage lung cancer. *JAMA: The Journal of the American Medical Association.* Mar 17 2010;303(11):1070-1076.

treatment that they were not detected. These five-year results demonstrate positive tumor control and disprove the misconception that short-course treatment will result in late-appearing, unacceptable toxicities."

The abstract, "Long-term Results of RTOG 0236: A Phase II Trial of Stereotactic Body Radiation Therapy (SBRT) in the Treatment of Patients with Medically Inoperable Stage I Non-Small Cell Lung Cancer," will be presented in detail during a scientific session at ASTRO's 56th Annual Meeting at 10:45 a.m. Pacific time on Monday, September 15, 2014. To speak with Dr. Timmerman, please call Michelle Kirkwood on September 14 – 17, 2014, in the ASTRO Press Office at San Francisco's Moscone Center at 415-978-3503 or 415-978-3504, or email michellek@astro.org.

ASTRO's 56th Annual Meeting, to be held at the Moscone Center in San Francisco, September 14-17, 2014, is the nation's premier scientific meeting in radiation oncology. The 2014 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 G. Haffty, MD, FASTRO, a radiation oncologist specializing in breast cancer, the theme of the 2014 Meeting is "Targeting Cancer: Technology and Biology," and the Presidential Symposium, "Local-regional Management of Breast Cancer: A Changing Paradigm," will feature Jay R. Harris, MD, FASTRO, and Thomas A. Buchholz, MD, FASTRO, to highlight recent practice-changing, landmark studies and current developments in the local-regional management of breast cancer. ASTRO's four-day scientific meeting includes presentation of up to four plenary papers, 360 oral presentations, 1,862 posters and 144 digital posters in more than 50 educational sessions and scientific panels for 20 disease-site tracks. Three keynote speakers will address a range of topics including oncologic imaging, biology and targeting in oncology, and human error and safety concerns: Hedvig Hricak, MD, PhD, Chair of the Department of Radiology and the Carroll and Milton Petrie Chair at Memorial Sloan Kettering Cancer Center; Frank McCormick, PhD, FRS, DSc (hon), Professor Emeritus and the David A. Wood Distinguished Professor of Tumor Biology and Cancer Research of the University of California at San Francisco Helen Diller Family Comprehensive Cancer Center; and Sidney Dekker, PhD, MA, MSc, Professor and Director of the Safety Science Innovation Lab at Griffith University, Brisbane, Australia.

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 two medical journals, International Journal of Radiation Oncology • Biology • Physics (www.redjournal.org) and Practical Radiation Oncology (www.practicalradonc.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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2014 American Society for Radiation Oncology (ASTRO) 56th Annual Meeting
News Briefing, Tuesday, September 16, 2014, 7:00 a.m. Pacific time

Scientific Session: Monday, September 15, 2014, 10:45 a.m. – 12:15 p.m. PT, the Moscone Center

56 Long-term Results of RTOG 0236: A Phase II Trial of Stereotactic Body Radiation Therapy (SBRT) in the Treatment of Patients with Medically Inoperable Stage I Non-Small Cell Lung Cancer

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Purpose/Objective(s): Patients with early stage but medically inoperable lung cancer historically had poor primary tumor control and high mortality with conventional radiotherapy. SBRT appeared to improve outcomes, as suggested by the initial published results of RTOG 0236. Herein, we update those results with longer follow-up.

Materials/Methods: The study was a Phase 2 North American multicenter study of patients aged 18 years or older with biopsy-proven peripheral T1-T2N0M0 non-small cell tumors (measuring ≤5 cm in diameter) and medical conditions precluding surgical treatment. The prescription dose was 18 Gy per fraction X 3 fractions (54 Gy total) with entire treatment lasting between 1½ and 2 weeks. The study opened May 26, 2004, and closed October 13, 2006; data were analyzed through October 15, 2013. The primary end point was 2-year actuarial primary tumor control; secondary end points were disease-free survival (i.e., primary tumor, involved lobe, regional, and disseminated recurrence), treatment-related toxicity, and overall survival.

Results: A total of 59 patients accrued, of which 55 were evaluable (44 patients with T1 tumors and 11 patients with T2 tumors) with a median follow-up of 4.0 years (7.2 years for surviving patients). Four patients had an in-field/marginal (primary) tumor failure (range, 1.8-4.8 years after SBRT); the estimated 5-year primary tumor failure rate was 7%. Nine additional patients had recurrence within the involved lobe (range 0.1-5.9 years after SBRT); the 5-year primary tumor and involved lobe (local) failure rate was 20%. Seven patients experienced regional failure (range, 2.8-5.2 years after SBRT); the 5-year local-regional failure rate was 38%. Fifteen patients experienced disseminated recurrence; the 5-year disseminated failure rate was 31%. The rates for disease free and overall survival at 5 years were 26% and 40%, respectively. The median overall survival was 4 years. Protocol treatment-related grade 3 and 4 adverse events were reported in 15 patients and in 2 patients, respectively, modestly more than was described in the previous 3-year report. No grade 5 adverse events were reported.

Conclusions: Patients with inoperable non-small cell lung cancer treated with SBRT had a survival rate of 40% at 5 years. While tumor control rates remain high compared to conventional fractionation results, late failures were observed particularly in the involved (untreated) residual lobe. However, an excess of late-appearing toxicity was not observed.

Author Disclosure Block: R.D. Timmerman: E. Research Grant; Varian Medical Systems. **C. Hu:** None. **J. Michalski:** None. **W. Straube:** None. **J. Galvin:** None. **D. Johnstone:** None. **J. Bradley:** None. **R. Barriger:** None. **A. Bezjak:** None. **G.M. Videtic:** None. **L. Nedzi:** None. **M. Werner-Wasik:** None. **Y. Chen:** None. **R.U. Komaki:** None. **H. Choy:** None.