Cancer patients with malignant spinal cord compression experienced preserved mobility when administered one high-dose of radiation therapy compared to more frequent lower doses of RT

San Francisco, September 15, 2014—Mobility is equally preserved in cancer patients suffering from malignant spinal cord compression (MSCC) who receive a single dose of 10 Gy of radiation therapy (RT), compared to patients who receive five daily doses of 4 Gy of RT each, according to research presented today at the American Society for Radiation Oncology’s (ASTRO’s) 56th Annual Meeting.

Malignant spinal cord compression (MSCC) is a complication of metastatic cancer mostly with bone involvement that occurs when a tumor’s secondary deposit presses on the spinal cord and nerves. This pressure exposes patients to neurological damage that can result in pain, loss of muscle strength and function of one or more of the senses. In some cases, the neurological damage can lead to paralysis of the entire body below the neck or paralysis of one or more limbs.

Although the standard of care for patients with MSCC is a combination of direct decompressive surgery and radiation therapy, sometimes surgery is not an option and patients receive only therapeutic radiation therapy. Currently, there is not a defined, optimal radiation therapy technique, or dose and schedule for patients with MSCC who do not undergo surgery.

This ICORG (All Ireland Co-operative Oncology Research Group) prospective, randomized, non-

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inferiority, Phase III trial compared two radiation therapy fractionation schedules in patients with MSCC who had not undergone surgery. From 2006 to 2014, five centers in Ireland and the United Kingdom accrued 116 patients with pathologically proven metastatic cancer. The study included 42 women and 74 men, with a median age of 69. The patients’ median Karnofsky performance status (KPS) score was 60 out of a possible 100. (KPS is a standard scale used to assess patients’ ability to perform ordinary tasks).

The patients’ main primary tumor sites (initial locations of the patients’ cancer) were 24 percent prostate cancer (28 patients); 20 percent breast cancer (23 patients); and 19 percent lung cancer (22 patients).

The patients’ MSCC sites included 4.3 percent cervical (five patients); 67 percent thoracic (78 patients); 23.5 percent lumbar (27 patients); 2.6 percent sacral (three patients) and 2.6 percent two synchronous occurring in more than one area at the same time (three patients).

Patients were randomized into two groups, with baseline characteristics balanced between both groups. Group One (the control group) received 20 Gy of EBRT, delivered over five treatment days. Group Two received an experimental high-dose of 10 Gy of EBRT, delivered in one single treatment.

The study measured the change in the patients’ mobility at five weeks based on a modified Tomita scoring system. The modified Tomita score evaluated patient mobility using a three-class scale, with class I indicating the patient was mobile and unaided; class II indicating the patient was mobile with a walking aid; and Class III indicating the patient was bed-bound (which corresponds to the original Tomita scale class III and IV).

The study also evaluated patients’ changes in bladder function at five weeks, using an in-house scoring scale, acute and long-term side effects (based on the Radiation Therapy Oncology Group, or RTOG scale) and overall survival (OS).

At five weeks post-treatment, 76 patients—38 patients in Group One and 38 patients in Group Two were evaluable. Analysis of the evaluable patients showed no statistically significant difference in overall mobility score change at five weeks post-treatment, with an overall response (improvement/stability) rate of 68.4 percent (10.5 improvement/57.9 percent stability) for Group One; and 78.9 percent (10.5 percent improvement/68.4 percent stability) for Group Two. Additionally, there wasn’t a significant difference in mean mobility score changes, with a difference of -0.29 for Group One and a difference of -0.08 for Group Two (difference = -0.21, 95%CI: -0.56 to 0.14, +0.4 non-inferiority margin outside 95%CI), confirming the non-inferiority statistical hypothesis.

No significant differences were also detected in patients’ bladder function score changes at five weeks
post-treatment, with an overall response (improvement/stability) rate of 75.7 percent (10.8 percent improvement/64.9 stability) for Group One; and 86.8 percent (2.6 percent improvement/84 percent) for Group Two. The groups’ mean sphincter score changes were -0.22 for Group One and -0.16 for Group Two (difference = -0.06, 95%CI: -0.44 to 0.32).

The neurological deterioration-free survival and overall survival median durations were similar in both groups, with a median neurological deterioration free survival time of 1.4 months and a median overall survival time of four months.

Additionally, the reported overall toxicity (side effect rate) for the entire group of patients was low; there was one, Grade 3 acute side effect reported and two Grade 3 long-term side effects reported.

“Our study shows that while radiotherapy alone provides only short-term neurological stabilization, the single treatment, high-dose experimental treatment was as effective as the current standard of care,” said lead author Pierre Thirion, MD, consultant radiation oncologist at St. Luke’s Radiation Oncology Network in Dublin, Ireland. “Sometimes less treatment is as effective, and our research can help reduce the burden of treatment and frequency of hospital visits for this patient population, while maintaining the same clinical outcome and quality of care, as well as the treatment cost. The study also highlights the poor overall outcome for MSCC patients, both in terms of daily living and overall survival, since less than half of these patients survived four months. These findings confirm the importance of further clinical research to improve patient outcome and the essential role of cooperative clinical research group, such as ICORG, to lead it.”

The abstract, “ICORG 05-03: Prospective Randomised Non-Inferiority Phase 3 Trial Comparing Two Radiation Schedules in Malignant Spinal Cord Compression not Proceeding with Surgical Decompression,” will be presented in detail during the plenary session at ASTRO’s 56th Annual Meeting at 2:15 p.m., Pacific time on Monday, September 15, 2014. To speak with Dr. Thirion, please call Michelle Kirkwood on September 14 – 17, 2014, in the ASTRO Press Office at the Moscone Center in San Francisco 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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LBA2 ICORG 05-03: Prospective Randomised Non-Inferiority Phase 3 Trial Comparing Two Radiation Schedules in Malignant Spinal Cord Compression not Proceeding with Surgical Decompression

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Purpose / Objective(s): To prospectively compare two External Beam Radiation Therapy (EBRT) Fractionation Schedules (FS) in patients (pts) with Malignant Spinal Cord Compression (MSCC) not proceeding with surgical decompression.

Materials / Methods: An ICH-GCP compliant prospective (1.1) randomised non-inferiority phase 3 trial compared two EBRT-FS: arm 1 (control): 20 Gy / 5 fractions (#) vs. arm 2 (experimental): 10 Gy / 1 #, with 90% power, 5% significant level and +0.4 non-inferiority margin. The primary end-point was the change in mobility at 5 weeks (Modified Tomita score); the secondary end-points were change in bladder function at 5 weeks (in-house score), acute and long-term toxicity (RTOG scale), and overall survival (OS). Eligible pts had pathologically proven metastatic cancer, excluding haematological/ germ cell malignancies, and diagnosed with a MRI documented treatment naive symptomatic MSCC.

Results: From 2006 to 2014, 5 institutions accrued 116 pts (1 non-eligible pt, no treatment allocation violation), 76 pts alive at 5 weeks were evaluable. The baseline characteristics were balanced between arms [♀/♂ ratio: 36/64, median age: 69 (range: 30-87), median baseline KPS: 60 (range: 30 - 100)]. The main primary tumour sites were prostate (24%), breast (20%) and lung (19%). The MSCC sites were cervical (4.3%), thoracic (67%), lumbar (23.5%), sacral (2.6%) and two synchronous levels (2.6%, 3 pts treated with same FS). Analysis of evaluable pts showed no statistically significant differences in 1) overall mobility score change at 5 week [Overall response (Improvement/Stability) rate: arm 1: 68.4% (10.5/57.9) vs. arm 2: 78.9% (10.5/68.4); mean mobility score change: arm 1: -0.29 vs. arm 2: -0.08, difference= -0.21, 95%CI: -0.56 to 0.14, +0.4 non-inferiority margin outside 95%CI] or 2) bladder function score change at 5 weeks [Overall response (Improvement/stability) rate: arm 1: 75.7% (10.8/ 64.9) vs. arm 2: 86.8% (2.6/84.); mean sphincter score change: arm 1: -0.22 vs arm 2: -0.16, difference = -0.06, 95%CI: -0.44 to 0.32]. The mobility deterioration free survival and overall survival median durations were similar in both arms respectively 1.4 months and 4 months. Independent favourable prognostic factors were 1) for 5 week mobility overall response: preserved baseline mobility, and 2) for OS: preserved baseline mobility, high baseline KPS, young age and non-lung primary. The reported overall toxicity was low with 1 G3-acute and 1 G3-long-term toxicity events (arm 2) and no higher grade toxicity reported.

Conclusions: With respect to mobility preservation, 10 Gy / 1 # is at least equivalent to 20 Gy / 5#. When using EBRT in similar pts, a single fraction schedule should be considered.