Hypofractionated radiation therapy can halve treatment time for poor performance status lung cancer patients

Survival rates from accelerated treatment equivalent to conventional RT with limited severe toxicities for poor performance status stage II and III NSCLC patients

BOSTON, September 26, 2016 -- For patients with stage II and III non-small cell lung cancer (NSCLC) unable to receive standard treatments of surgery or chemoradiation (CRT), hypofractionated radiation therapy (RT) results in similar overall survival (OS) and progression-free survival (PFS) rates, limited severe side effects and shorter treatment times when compared to conventional RT, according to research presented today at the 58th Annual Meeting of the American Society for Radiation Oncology (ASTRO).

NSCLC is responsible for the most cancer-specific deaths globally, and many of these deaths are associated with the high percentage of patients who present with stage III cancer upon diagnosis. Additionally, due to other medical issues or poor performance status (a measure that considers a patient’s quality of life and ability to function during treatment), some stage III NSCLC patients are unable to receive the standard treatment of concurrent chemotherapy and RT.

“These patients have limited disease-specific survival with conventional radiation alone, suggesting a need for changing treatment approaches and paradigms for this group,” said Puneeth Iyengar, MD, PhD, lead author of the study and an assistant professor of radiation oncology at the University of Texas Southwestern Medical Center in Dallas. “In an earlier phase I clinical study, our group has shown that increasing the dose of radiation delivered daily with high precision and using image guidance may offset the need for chemotherapy in improving survival, and it may also improve quality of life measures by reducing treatment periods in half. The earlier work established that treatment with
hypofractionated radiation was as tolerable as historical treatment with standard, conventional courses of radiation.”

While the focus of this phase III trial was to assess differences in OS among patients receiving hypofractionated versus conventional RT, researchers also measured several secondary endpoints, including PFS (an indicator that the cancer is still present but has not spread), toxicities, quality of life and cost effectiveness of the treatment.

The study enrolled patients from 15 centers based in Texas. Eligible patients had stage II or stage III NSCLC, indicating that their cancer had spread to the lymph nodes. All of the patients with stage II NSCLC could not undergo surgery, and all of the stage III patients were not candidates to receive RT and chemotherapy concurrently.

This interim analysis included 60 patients, with an average age of 68 years. The vast majority of enrolled patients (88 percent, or 53 of 60) presented with stage III NSCLC, and seven patients presented with stage II disease. The majority of the patients’ lesions (53 percent) had squamous cell carcinoma, and the remaining 47 percent had adenocarcinoma. Patients were randomized to one of two treatment arms. The conventional RT group (n = 28 patients) received 60 to 66 Gy over the course of 30 to 33 treatment sessions, and the hypofractionated RT group (n = 32 patients) received 60 Gy over the course of 15 treatment sessions.

A follow-up of the 48 patients who were evaluable at a median time of 24 months indicated no statistical differences between the two groups in terms of overall or progression-free survival. Kaplan-Meier analysis of the two treatment arms found a median OS of 14 months and median PFS of 11.5 months. Treatment approach (i.e., 30-33 vs. 15 treatments) did not significantly impact either survival rate.

While researchers did not find differences in survival rates, they did find differences in side effects between the treatment arms at this interim analysis. Patients who received accelerated RT experienced fewer grade 3 toxicities (10 reported for conventional RT vs. six for hypofractionated RT) and a lower rate of death from hypoxia (two for conventional RT vs. one for hypofractionated RT). No grade 4 side effects were attributed to RT in either group.

“The use of advanced technologies may allow radiation therapy to be delivered in larger doses per treatment safely and potentially translate into an overall survival difference in NSCLC patient populations while improving patient quality of life through an acceleration of treatment courses,” said Dr. Iyengar. “The patients in the study who were treated with hypofractionation were able to finish therapy in three weeks, compared to the six weeks needed for the conventionally treated patients. Additionally, I predict that at the completion of our study, despite the higher doses given per treatment in the experimental...
accelerated, hypofractionated RT arm, there will be no increased toxicity with this regimen. If hypofractionated radiation with curative intent can reduce the treatment time for lung cancer patients by half with no greater toxicity, and with equivalent—if not better—tumor control and survival outcomes, this research could result in a change in the paradigm of how a large subset of locally advanced NSCLC patients are treated."

The abstract, “A Phase III Randomized Study of Image Guided Conventional (60Gy/30fx) vs Accelerated, Hypofractionated (60Gy/15fx) Radiation for Poor Performance Status Stage II and III NSCLC Patients – An Interim Analysis,” will be presented in detail during the poster session at ASTRO’s 58th Annual Meeting beginning at 10:00 a.m. Eastern time on Sunday, September 25, 2016. To speak with Dr. Iyengar, please contact ASTRO’s media relations team on-site at the Boston Convention and Exhibition Center on September 25-28, by phone at 703-286-1600 or by email at press@astro.org.

ATTRIBUTION TO THE AMERICAN SOCIETY OF RADIATION ONCOLOGY (ASTRO) ANNUAL MEETING REQUESTED IN ALL COVERAGE.

Full study abstract available on the final page of this release.

ABOUT ASTRO’S ANNUAL MEETING
ASTRO’s 58th Annual Meeting, the nation’s premier scientific meeting in radiation oncology, will be held September 25-28, 2016, at the Boston Convention and Exhibition Center in Boston. The 2016 Annual Meeting is expected to attract more than 11,000 attendees from across the globe, including oncologists from all disciplines and members of the entire radiation oncology team. Led by ASTRO president David C. Beyer, MD, FASTRO, the 2016 meeting will feature keynote addresses from Kathleen Sebelius, former U.S. Secretary of Health and Human Services; Thomas James Lynch Jr., MD, Chair and CEO, Massachusetts General Physicians Organization; and Jason Ragogna, general manager, SMS and Safety Alliances, Corporate Safety, Security, and Compliance, Delta Air Lines, Inc. The Presidential Symposium, “Prostate Cancer: Defining Value and Delivering It,” highlights the meeting’s theme of “Enhancing Value, Improving Outcomes” and will feature recent practice-changing studies and current developments in value-based care for prostate cancer. ASTRO’s four-day scientific meeting will feature a record number of abstracts, including 368 oral presentations, 1,760 posters and 180 digital posters in more than 50 educational sessions and 20 scientific panels for 20 disease-site tracks. For more information about ASTRO’s 58th Annual Meeting, visit www.astro.org/AnnualMeeting. For press registration and news briefing information for ASTRO’s 58th Annual Meeting, visit www.astro.org/AMPress.

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 who 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.practicaradonc.org) and Advances in Radiation Oncology (www.advancesradonc.org); developed
and maintains an extensive patient website, RT Answers (www.rtanswers.org); and created the Radiation Oncology Institute (www.roinstitute.org), a nonprofit 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.
A Phase III Randomized Study of Image Guided Conventional (60Gy/30fx) vs Accelerated, Hypofractionated (60Gy/15fx) Radiation for Poor Performance Status Stage II and III NSCLC Patients – An Interim Analysis

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Purpose/Objective(s): To evaluate overall survival (OS) in a comparison of image guided conventional versus accelerated, hypofractionated radiation delivered to poor performance status (PS) stage II and III non-small cell lung cancer (NSCLC) patients in a randomized phase III study.

Materials/Methods: All patients with stage II NSCLC not candidates for surgery or stage III NSCLC not candidates for chemoradiation due to diminished PS (Zubrod PS 2 or greater) were eligible for this phase III randomized trial of radiation alone comparing conventional regimes of 60-66Gy/30-33fx (Arm A) versus accelerated, hypofractionated 60Gy/15fx (Arm B). Overall survival was the primary endpoint with several secondary endpoints including toxicity assessment, progression free survival (PFS), quality of life, and cost effectiveness. Chemotherapy was permissible sequentially either as induction or in the adjuvant setting. The study was open at more than 10 institutions across the state of Texas.

Results: To date, 60 patients have been enrolled on the study (28 to Arm A and 32 to Arm B), with a median age of 68y in both cohorts. There is an equal M:F ratio in Arm B but a 4:1 M:F ratio in Arm A. 53% of all lesions are squamous cell carcinoma, with the rest adenocarcinoma, equally weighted in the cohorts. 53/60 patients presented with stage III disease, 7/60 with stage II. 48/60 patients were evaluable due to adequate length of follow-up at this time. 56% of patients (27/48) were alive at last follow-up. By Kaplan-Meier analysis, median OS for the 48 patients evaluable was 14 months, with no statistical difference between conventional vs hypofractionated radiation treatment arms. PFS was 11.5 months with again no statistical difference between treatment arms. In Arm A, 2 deaths from hypoxia were possibly related to conventional radiation, 1 death in Arm B from hypoxia was possibly related to hypofractionated radiation. No grade 4 toxicities were attributed to radiation. There were 10 (Arm A) vs 6 (Arm B) grade 3 toxicities.

Conclusion: A curative approach with accelerated, hypofractionated radiation alone is equivalent in OS and PFS to conventional radiation in a population of poor PS patients, with less grade 3-5 toxicity, and a treatment course of half the time. Completion of this study will potentially change the paradigm of treatment of poor PS stage III NSCLC patients who cannot receive chemoradiation.