Patient-reported outcomes provide valuable insight regarding quality of life for patients with non-small cell lung cancer

Analysis of RTOG 0617 trial evaluates the impact of high-dose radiation therapy

Atlanta, September 23, 2013 — An analysis of quality of life (QOL) data of stage III lung cancer patients who received higher doses of radiation therapy (with chemotherapy) shows a significantly lower quality of life at 3 months after treatment compared to patients who received a standard dose of radiation (with chemotherapy), according to research presented today at the American Society for Radiation Oncology’s (ASTRO’s) 55th Annual Meeting. The study also suggests that lung cancer patients who received intensity modulated radiation therapy (IMRT) reported less decline in their QOL compared to those receiving three-dimensional conformal radiation therapy (3-D CRT).

Patient data was compiled from the RTOG 0617 study, a phase III, randomized clinical trial of patients with locally advanced non-small cell lung cancer (NSCLC) conducted from 2007 to 2011. The randomized study compared a high-dose (HD) of 74 Gy to a standard dose (SD) of 60 Gy. All enrolled patients received concurrent chemotherapy of carboplatin/paclitaxel, and they were also randomized to be treated with or without cetuximab (C225). The radiation was administered with two types of radiation therapy (RT): 3-D CRT, in which beams of radiation are shaped to match the tumor, or IMRT, a more sophisticated technique that uses a computer-controlled algorithm to modify
the intensity of each beam to further spare normal tissue. While the study was not randomized for the radiation treatment technique (3-D CRT or IMRT), the pretreatment characteristics were not significantly different for these techniques except that higher stage tumors were treated with IMRT. Prior results of a planned analysis of the trial determined that the higher dose of radiation therapy was associated with lower overall survival (OS), and, at that point, the high-dose radiation therapy arms of the study were closed.

Because the RTOG study indicated that OS rates were lower with higher doses of radiation, despite few differences in provider-reported toxicity between the study’s arms, researchers evaluated if patient-reported outcomes had any bearing on the results of the RTOG 0617 trial. Patient QOL scores were compared between the treatment arms, as well as between the RT techniques. QOL information was collected using the Functional Assessment of Cancer Therapy-Trial Outcome Index (FACT-TOI), which is a compilation of physical well being (PWB), functional well being (FWB), and lung cancer subscale (LCS) results. Results were studied at baseline, at the end of chemoradiation, and at three months and 12 months post-treatment. Two-sample t-tests—the Wilcoxon-Mann-Whitney test and the Chi-Square test—compared QOL between arms and between technologies (3-D CRT vs. IMRT) via two-sided p values and effect sizes (ES).

Baseline FACT-TOI were completed from each arm on 88 percent of patients, with no difference in patient demographics, baseline QOL scores or C225 use. Seventy-one percent of patients completed QOL data at three months, of whom approximately 60 percent of patients (225) completed it at 12 months.

The primary QOL hypothesis was that there would be a significant difference between arms at 3 months using the LCS, which focuses on key symptoms of lung cancer. A clinically meaningful decline (CMD) in LCS for patients receiving 74 Gy was significantly higher at three months post-treatment (46 percent) than for patients receiving 60 Gy (31 percent, p=0.024, ES 0.4); yet these differences resolved by 12 months, with the 74 Gy dose producing a CMD of 36 percent, and the 60 Gy dose producing a CMD of 39 percent (p=0.7, ES<0.1).
Additionally, the results suggested that IMRT, which was administered to 45 percent of patients in each arm, was associated with a much lower decline in QOL compared to those who received 3-D CRT, even a year after treatment. Indeed, at 12 months post-treatment, 23 percent of the IMRT patients in either arm had a CMD in LCS, as opposed to 47 percent of 3-D CRT patients \( (p=0.005, \text{ ES 0.3}) \).

“This study further emphasizes the critical importance of patient-reported outcomes,” said Benjamin Movsas, MD, FASTRO, the lead author of the study and chairman of the department of radiation oncology at the Henry Ford Health System in Detroit. “The fact that the QOL scores were initially lower in the high-dose radiation arm was illuminating because few differences in toxicity between the arms were noted by the health care providers. Thus, the patient-reported outcomes help tell ‘the rest of the story.’ Another intriguing discovery with our analysis was that QOL was significantly improved with the use of more sophisticated technology, i.e. IMRT (relative to 3-D CRT), suggesting that advanced radiation treatment techniques may provide meaningful QOL benefits for patients with non-small cell lung cancer.”

The abstract, “Quality of Life (QOL) Analysis of the Randomized Radiation (RT) Dose Escalation NSCLC Trial (RTOG 0617): The Rest of the Story,” will be presented in detail today in the Plenary session at ASTRO’s Annual Meeting at 2:00 p.m. Eastern time, on Monday, September 23, 2013. To speak with Dr. Movsas, contact Michelle Kirkwood on September 22-25, 2013, in the ASTRO Press Office at the Georgia World Congress Center in Atlanta at 404-222-5303 or 404-222-5304, or email michellek@astro.org.

ASTRO’s 55th Annual Meeting, held in Atlanta, September 22-25, 2013, is the premier scientific meeting in radiation oncology and brings together 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. The theme of the 2013 meeting is “Patients: Hope • Guide • Heal” and will focus on patient-centered care and the importance of the physician’s role in improving patient-reported outcomes and the quality and safety
of patient care. The four-day scientific meeting includes presentation of four plenary papers, 363 oral presentations, 1,460 posters and 144 digital posters in 70 educational sessions and scientific panels for 19 disease sites/tracks. Keynote and featured speakers include: William B. Munier, director of the Center for Quality Improvement and Patient Safety at the Agency for Healthcare Research and Quality; Darrell G. Kirch, MD, president and CEO of the Association of American Medical Colleges; James Cosgrove, PhD, director of the U.S. Government Accountability Office; Otis W. Brawley, MD, chief medical officer of the American Cancer Society; and Peter Friedl, MD, PhD, of St. Radboud University Nijmegen Medical Centre at the University of Nijmegen and MD Anderson Cancer 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 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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2013 American Society for Radiation Oncology (ASTRO) 55th Annual Meeting  
News Briefing, Wednesday, September 24, 2013, 8:30 a.m. Eastern time

Scientific Session: Monday, September 23, 2013, 2:00 – 3:10 p.m. ET, Georgia World Congress Center

2 Quality of Life (QOL) Analysis of the Randomized Radiation (RT) Dose Escalation NSCLC Trial (RTOG 0617): The Rest of the Story

1Henry Ford Health System, Detroit, MI, 2RTOG, Philadelphia, PA, 3Mayo Clinic, Rochester, NY, 4Washington University, St. Louis, MO, 5USON-Texas Oncology-Sugar Land, Sugarland, TX, 6Michigan Cancer Research Consortium CCOP, Ann Arbor, MI, 7Florida Radiation Oncology Group - Baptist Regional, Jacksonville, FL, 8Southwestern University, Dallas, TX

Purpose/Objective(s): The lower survival on the high-dose (HD) RT arm (74 vs 60 Gy) of RTOG 0617 is perplexing, particularly as no significant differences in provider-reported toxicity were found. Could patient-reported outcomes (PROs) shed light on the results of this study?

Materials/Methods: RTOG 0617 was a phase III study of 74 vs 60 Gy RT with concurrent & consolidation carboplatin/paclitaxel +/- cetuximab (C225) in patients with stage III NSCLC using a 2x2 design & stratified by RT technique (3D vs IMRT). QOL was collected prospectively via Functional Assessment of Cancer Therapy-Trial Outcome Index (FACT-TOI), equaling Physical Well Being (PWB) + Functional Well Being (FWB) + Lung Cancer Subscale (LCS). Data are presented at baseline, 3 months and 12 months via minimal clinically meaningful changes of >2 points for PWB, FWB or LCS or >5 points for TOI (per Cella et al Clin Epidemiol 55: 285, 2002). Two-sample t-tests, Wilcoxon-Mann-Whitney test, and chi-square compared QOL between arms and between technologies via 2-sided p values and effect sizes (ES; moderate ES~0.3-0.4). The 1st QOL hypothesis predicted a clinically meaningful decline (CMD) in LCS in the HD arm at 3 months.

Results: Of 419 eligible patients randomized, 357 (85%) consented to QOL, of whom 88% completed baseline FACT-TOI on each arm, with no difference in demographics or QOL scores and equal use of C225. 71% completed QOL at 3 months, of whom 63% did so at 12 months. The clinically meaningful decline (CMD) in LCS for 74Gy was significantly higher at 3 months (46%) than for 60 Gy (31%, p=0.024, ES 0.4) and resolved at 12 months (36% vs 39%, p=0.7, ES<0.1). IMRT (used in 45% of patients in each arm) was associated with significantly less QOL decline than 3D. On the 60 Gy arm, fewer patients receiving IMRT had a CMD in LCS (14%) at 3 months vs 3D (42%, p=0.002, ES 0.4). At 12 months, fewer patients on both arms who received IMRT (vs 3D) had CMDs in PWB (41% vs 58%, p=0.045, ES 0.2), LCS (23% vs 47%, p=0.005, ES 0.3) and TOI (36% vs 57%, p=0.016, ES 0.3). Beyond RT level, baseline PWB, FWB, & TOI also predicted for survival, as well as in multivariate analysis (MVA), p<0.02.

Conclusions: Despite no significant differences in provider-reported toxicity bwn arms, the PROs tell the “rest of the story”, the patient perspective, by showing significantly worse QOL on the HD arm (74 Gy) at 3 months, confirming the 1st QOL hypothesis. Baseline QOL significantly predicted for survival on MVA. This analysis raises an intriguing question of whether the decline in QOL on the HD arm may help account for the survival decrement in this arm over time. The clinically meaningful decline in QOL was significantly reduced with the use of IMRT (vs 3D), suggesting that improved RT treatment techniques may help enhance the therapeutic window for patients with lung cancer.

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