Higher-Dose RT Does Not Result in Improved Survival in Patients With Stage III Lung Cancer

Philadelphia, PA—Results of a randomized phase III clinical trial demonstrated that treatment with higher-dose (74 Gy) radiotherapy (RT) compared with standard-dose (60 Gy) RT, and the addition of cetuximab to concurrent chemoradiotherapy, did not extend the lives of patients with inoperable, stage III non-small cell lung cancer (NSCLC). Results of the trial conducted by the Radiation Therapy Oncology Group (RTOG), now conducting research as NRG Oncology, were published online ahead of print in The Lancet Oncology on January 16, 2015.

Lung cancer is the country’s leading cause of cancer-related death, and the majority of newly diagnosed patients (75 to 80 percent) have NSCLC histology. Approximately 40 percent of these patients have locally advanced disease (stage IIIA or IIIB) with nearly 85 percent expected to experience cancer progression within the chest cavity. According to the RTOG 0617 Principal Investigator Jeffrey D. Bradley, M.D., a professor in radiation oncology at Washington University in St. Louis, Mo., a basic principle of radiotherapy for decades in lung cancer treatment has been the higher the achievable dose, the more tumor cell kill and, accordingly, the greater likelihood of longer survival. “This principle led several research groups, including the RTOG, to investigate in early phase trials the maximum tolerated radiotherapy dose that could be given with concurrent chemotherapy and still be safe. The results of these investigations led to a consensus to test 74 Gray in a randomized trial,” explains Bradley. The RTOG developed the phase III, randomized RTOG 0617 trial to establish whether 74 Gy, (the investigational high-dose arm) as compared with 60-Gy (the standard arm as established by prior research) would result in improved overall survival for patients with stage III, NSCLC.

“In the setting of concurrent chemotherapy with daily radiation therapy for stage III lung cancer, the results showed that survival with 60 Gray is numerically higher than with 74 Gray, with a potential statistically significant detriment associated with the higher radiation dose,” says Bradley. Median follow-up time of the trial’s 419 evaluable patients was 22.9 months, with a median survival time of 28.7 vs. 20.3 months for the 60 Gy and 74 Gy arms, respectively. As for the 60 Gy arm, these survival results are amongst the best reported outcomes for this patient population to date.

Based on promising research data, the trial additionally tested the hypothesis that the addition of cetuximab, a monoclonal antibody that targets the epidermal growth factor receptor (EGFR) pathway and has radiation-sensitizing properties, to chemoradiotherapy would lead to improved survival. However, the authors report “The use of cetuximab had no meaningful effect on overall survival in our trial.”

For next steps, Bradley points to new research directions currently under investigation by NRG Oncology that benefit from the RTOG 0617 research results, “With the identification of a number of genetic driver mutations, targeted therapy is clearly the next phase of treatment for NSCLC,” says Bradley. RTOG 1306 is an example of a phase II study evaluating newly developed agents that block EGFR mutations or anaplastic lymphoma kinase (ALK) translocations.
“Patients will receive either a targeted agent for a few months followed by chemoradiotherapy or chemoradiotherapy alone, which represents the standard arm in RTOG 0617,” he explains.

“These results stand as an excellent example of the importance of rigorously testing new therapeutic strategies and of NRG Oncology’s essential role in conducting clinical trials to provide the evidence to guide clinical care,” says Walter J. Curran, Jr. M.D., an NRG Oncology Group Chair and Executive Director of the Winship Cancer Institute of Emory University in Atlanta.