Researchers investigate a less toxic radiation treatment for HPV-Positive oropharynx cancer

May 31 2013

Researchers from Fox Chase Cancer Center and other institutions have completed a phase II clinical trial that may help identify those patients with HPV-positive oropharyngeal cancer who do not require the full radiation dose given in a standard regimen of Intensity-Modulated Radiation Therapy (IMRT). Preliminary findings will be presented by Shanthi Marur, first author on the study and an oncologist at the Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, at the 49th Annual Meeting of the American Society of Clinical Oncology on Sunday, June 2.

Patients enrolled in the trial received an initial regimen of chemotherapy followed by treatment with the targeted therapy cetuximab, a monoclonal antibody. In the study, a patient's response to those initial treatments determined the dose during radiation treatment.

"Those patients who had a really good response to chemotherapy might also be more responsive to radiation," says Barbara Burtness, senior author on the study and chief of head and neck medical oncology at Fox Chase. "Therefore, the use of a full dose of radiation for those patients might represent overtreatment."

Burtness is also chair of the Eastern Cooperative Oncology Group (ECOG), which sponsors this ongoing trial. ECOG is a a National Cancer Institute-funded team of researchers who organize and carry out

clinical trials.

According to the National Cancer Institute, more than 40,000 people will be diagnosed with cancer of the oropharynx—a swath of tissue at the back of the throat—in 2013, and nearly 8,000 will die from the disease. Between 60 and 80 percent of cases are associated with infection by Human Papilloma Viruses, or HPVs.

"Patients with HPV-associated oropharyngeal cancer tend to be younger than other oropharyngeal cancer patients, and would be living with the aftereffects of treatment for more years," says Burtness. A patient who undergoes standard radiation to the back of the throat—usually between 66 and 70 Gy—may suffer serious side effects like dry mouth and disfunction in swallowing.

The investigators suspected a subset of HPV-associated oropharyngeal cancer patients, identified by their response to chemotherapy, may be suitable for trials of lower radiation.

Burtness and her co-investigators enrolled 90 patients in the trial, 80 of whom were analyzable. Of those patients, 95 percent were men, and the median age was 57. The researchers reported that most patients tolerated the induction chemotherapy and treatment with cetuximab, and 96 percent completed all three cycles. Forty-six patients had a complete clinical response, which meant all signs of the primary tumor had disappeared following treatment. These patients went on to receive a lower-than-standard dose of radiation, at 54 Gy.

The researchers report that most patients tolerated the treatment with low incidence of high-grade side effects, but other data are premature. The primary endpoint of the study is two-year progression-free survival, the fraction of patients whose diseases have not worsened after two years. The investigators say that if the two-year progression-free survival

rate is at least 85 percent, further studies on lower-dose radiation are warranted.

"We do not expect that anyone would want to lower the dose of radiation based on this study, which is very much a developmental study," says Burtness. "We've never had a comparative trial of low dose versus standard dose IMRT."

Burtness notes among patients who received a lower dose of radiation, "what seemed to predict for a slightly worse outcome was either a heavy smoking history (more than 10 pack years), or those with larger tumors."

She says that although it's too early to draw definitive conclusions, the early results "may justify further study of deintensifying radiation among nonsmokers with HPV-associated oropharyngeal cancers."

Provided by Fox Chase Cancer Center