Keep an eye on the HPV p16 protein in head and neck cancer

At the 2014 Multidisciplinary Head and Neck Cancer Symposium in Scottsdale, Arizona, experts presented their findings on novel therapies and surgical and radiotherapeutic techniques with a view to improving outcomes, refining supportive care, and easing toxicity. Neil Osterweil reported from the symposium, which was sponsored by the American Society for Radiation Oncology, the American Society of Clinical Oncology, and the American Head & Neck Society.

Better survival with concurrent chemoradiation for HNSCC

Major finding At a median follow-up of 30 months, actuarial rates of 2-year overall survival of patients treated with concurrent chemoradiation were 81%, compared with 62% for patients treated with accelerated radiation. *Data source* A randomized trial comparing accelerated radiotherapy with concurrent chemoradiation with standard fractionation radiation in 101 patients with head and neck cancers. *Disclosures* The study was supported by the Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology. Dr Skladowski reported having no financial disclosures. Dr Harari has received research funding from Amgen.

Concurrent chemoradiation offered better overall survival (OS) and disease-free survival (DFS) than did accelerated radiotherapy in patients with moderately advanced head and neck squamous cell carcinomas (HNSCC), reported Dr Krzysztof Skladowski of the Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology in Gliwice, Poland. Actuarial rates of 2-year OS and DFS in patients treated with concurrent chemoradiation (CCR) were significantly better than the rates for patients treated with accelerated radiotherapy alone, he noted.

"CCR with conventional 7 weeks of fractionation and at least 2 courses of high-dose cisplatin is more effective than 6 weeks of accelerated radiotherapy alone," he said.

Even if patients can tolerate only a single course of cisplatin, CCR is still superior to accelerated radiation, he added. The findings suggest that accelerated radiation protocols should be reserved for patients with more favorable prognosis, such as those with stage T2 disease with limited nodal involvement, and those who are positive for the human papillomavirus (HPV) p16 protein, Dr Skladowski said.

Dr Paul Harari of the University of Wisconsin, Madison, and the invited discussant, said the findings are "concordant with data that has been emerging now over the last 10-14 years of the value of concurrent chemoradiation in head and neck cancer for a substantial cohort of patients over radiation alone."

Although findings in a previous meta-analysis (Lancet. 2006;368:843-854) suggested that accelerated or hyperfractionated radiotherapy was associated with a 3.4% advantage in OS, compared with conventional radiotherapy over 5 years, there have been no randomized studies comparing accelerated radiotherapy protocols with concurrent chemoradiation in this population, Dr. Skladowski said.

He and his colleagues compared the 2 modalities in 101 patients with moderately advanced cancers of the oropharynx (46 patients), hypopharynx (19), and larynx (36). They defined moderately advanced cancers as stage T2N1-2, T3N0-2, or T4AN0-2 if the involved nodes were not larger than 3 cm in diameter. Patients with oropharyngeal cancers were tested for expression of the HPV p16 protein.

Patients were randomly assigned to receive either concurrent chemoradiation with intensity-modulated radiation therapy-delivered doses of 66-70 Gy divided into 33-35 daily fractions over 45-49 days plus cisplatin 100 mg/m^2, delivered on days 1, 2, and 43, or to accelerated radiotherapy delivered via intensity-modulated radiation therapy in 1.8 Gy fractions 7 days a week to a total dose of 66.2-72 Gy. Five patients in the CCR arm received only 1 dose of cisplatin, 30 received 2 doses, and 13 received the planned 3 doses.

At a median follow-up of 30 months, actuarial rates of 2-year OS of patients treated with CCR were 81%, compared with 62% for patients treated with accelerated radiation (P = .02). DFS rates were 75% and 60%, respectively (P = .05).

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Acute adverse events were similar, with about 80% of patients in each treatment arm experiencing confluent mucositis, and about 10% having grade 3 dysphagia. There were no grade 4 toxicities. Most of the treatment failures in each group were local, occurring in 21 of 52 patients treated with radiation alone, and in 11 of 49 patients treated with CCR (P = .03). Significantly more deaths occurred in the radiation alone arm: 20, compared with 9 (P =.02).

The 2-year DFS rate among patients in the CCR arm was dose dependent, at 60% of patients who received 1 course of cisplatin, 77% of those who received 2 courses, and 79% for those who received all 3. At the time of the analysis, all of the patients with oropharyngeal cancer who were positive for HPV p16 (5 treated with accelerated radiation, 6 with CCR) were alive with no treatment failure. The OS rate for HPV-positive patients was 60% in the radiation-only arm, and 80% in the CCR arm.

HPV+ patients with recurrent disease survive longer

Major finding Two years after a diagnosis of recurrence of oropharyngeal cancer, 54.6% of HPV-positive patients were alive, compared with 27.6% of HPV-negative patients. *Data source* Retrospective analysis of 181 patients with known HPV status in the RTOG 0129 and 0522 trials. *Disclosures* The study was supported by the National Cancer Institute and Bristol-Myers Squibb. Dr Fakhry reported having no financial disclosures. Dr Cohen disclosed serving as a consultant and adviser to BMS.

Patients who are positive for the human papillomavirus have nearly twice the OS rate from recurrent oropharyngeal cancers as HPV-negative patients, according to Dr Carole Fakhry. Two years after a diagnosis of recurrence, 54.6% of HPV-positive patients were alive, compared with 27.6% of HPV-negative patients ($P \leq .001$), according to a retrospective analysis of data from 2 clinical trials of 181 patients with stage III-IV oropharyngeal squamous cell carcinomas and known HPV status (measured by p16 protein expression).

"Tumor p16 status is independently associated with OS among oropharyngeal cancer patients with disease progression," said Dr Fakhry of Johns Hopkins Medicine in Baltimore.

The analysis shows that "unquestionably, HPV-positive patients have a different molecular disease than their HPV-negative, tobacco-related counterparts. They are different in respect to specific tumor suppressor genes, and they are different in respect to specific activating oncogenes," noted Dr Ezra Cohen of the University of California San Diego Moores Cancer Center, who was the invited discussant.

Dr Fakhry and her colleagues looked at data on patients treated in the RTOG 0129 and 0522 trials.

Median time to progression was similar between the groups (8.2 months for HPV-positive patients and 7.3 months for HPV-negative; P = .67), with most disease progressions occurring within the first year (65% and 63%, respectively), reported Dr Fakhry.

Factors associated with better OS in multivariate analysis included HPV-positive status, salvage surgery, local-regional versus distant progression, lower T stage at enrollment, and less than 20 smoking pack-years.