HPV-positive tumor status indicates better survival in patients with oropharyngeal cancer

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Oropharyngeal cancer patients whose tumors in the upper part of the throat test positively for the human papillomavirus (HPV) have better overall survival than patients with HPV-negative disease, researchers from The University of Texas MD Anderson Cancer Center report in a study published in the *New England Journal of Medicine*.

The study - the largest and most definitive to date completed in a joint effort with the Radiation Therapy Oncology Group (RTOG) - shows that tumor HPV status is a strong and independent prognostic factor for survival for these patients. Follow-up data from the study were presented today at the 44th annual meeting of the American Society of Clinical Oncology.

"This is the strongest prognostic factor we have ever identified for head and neck cancer patients," said K. Kian Ang, M.D., Ph.D., professor in MD Anderson's Department of Radiation Oncology and lead author on the paper. "Its value is stronger than other prognostic factors we have used such as the size of the tumor or presence of tumor in lymph nodes. Knowing that the tumor is associated with HPV is telling the patient that the prognosis is excellent with currently available treatments."

The Phase III clinical trial established by the RTOG examined overall survival and progression-free survival in 323 patients with stage III-IV oropharyngeal cancer treated with a combination of radiation therapy

and chemotherapy. Of these patients, 206 had HPV-positive tumors and 117 were HPV-negative. The three-year overall survival rate for patients with HPV-positive tumors was 82.4 percent compared to 57.1 percent with HPV-negative cancer. Progression-free survival rates were 73.7 percent and 43.4 percent, respectively.

When researchers adjusted for other significant determinants of survival, including patient age, race, tumor and nodal stage and tobacco use, patients with HPV-positive cancer had a 58 percent reduction in risk of death relative to patients with HPV-negative tumors. The study noted tobacco use substantially increased risk of death. Results will allow physicians to stratify patients enrolled in clinical trials into low, intermediate or high-risk of death based on HPV status, tobacco use and cancer stage. This information can then be used to better determine which patients are candidates for more intensive investigational therapies.

Oropharyngeal cancer develops in the part of the throat just behind the mouth. The American Cancer Society estimates that 28,500 people in the United States are diagnosed with cancer of the oral cavity and oropharynx each year. While the incidence of head and neck cancer has been declining during the past 30 years, the rate of HPV-positive oropharyngeal cancer is rapidly rising. Today, nearly 70 percent of oropharynx cancer cases are HPV-positive.

Ang credits the strength of the study to its size and the importance of collaboration among investigators. "Even large cancer centers like MD Anderson cannot do these types of studies alone. Working with our collaborators including, Maura Gillison, M.D., Ph.D., professor of medicine, epidemiology and otolaryngology at The Ohio State University, an experienced investigator on the role of HPV in head and neck cancer and co-author on the study, we were able to build on what smaller studies have suggested and produce numbers large enough to

examine HPV status together with other prognostic factors."

Head and neck tumors are routinely tested for HPV at MD Anderson and other large institutions. While it remains unclear why patients with HPV-positive tumors have better outcomes than those with HPV-negative tumors, researchers speculate it may be due to biologic and immunologic properties that render HPV-positive cancers inherently less malignant or better able to respond to treatment. Ang notes future studies are warranted to determine how the HPV vaccine, made available to the public in 2006, affects the incidence of HPV-related head and neck cancers.

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