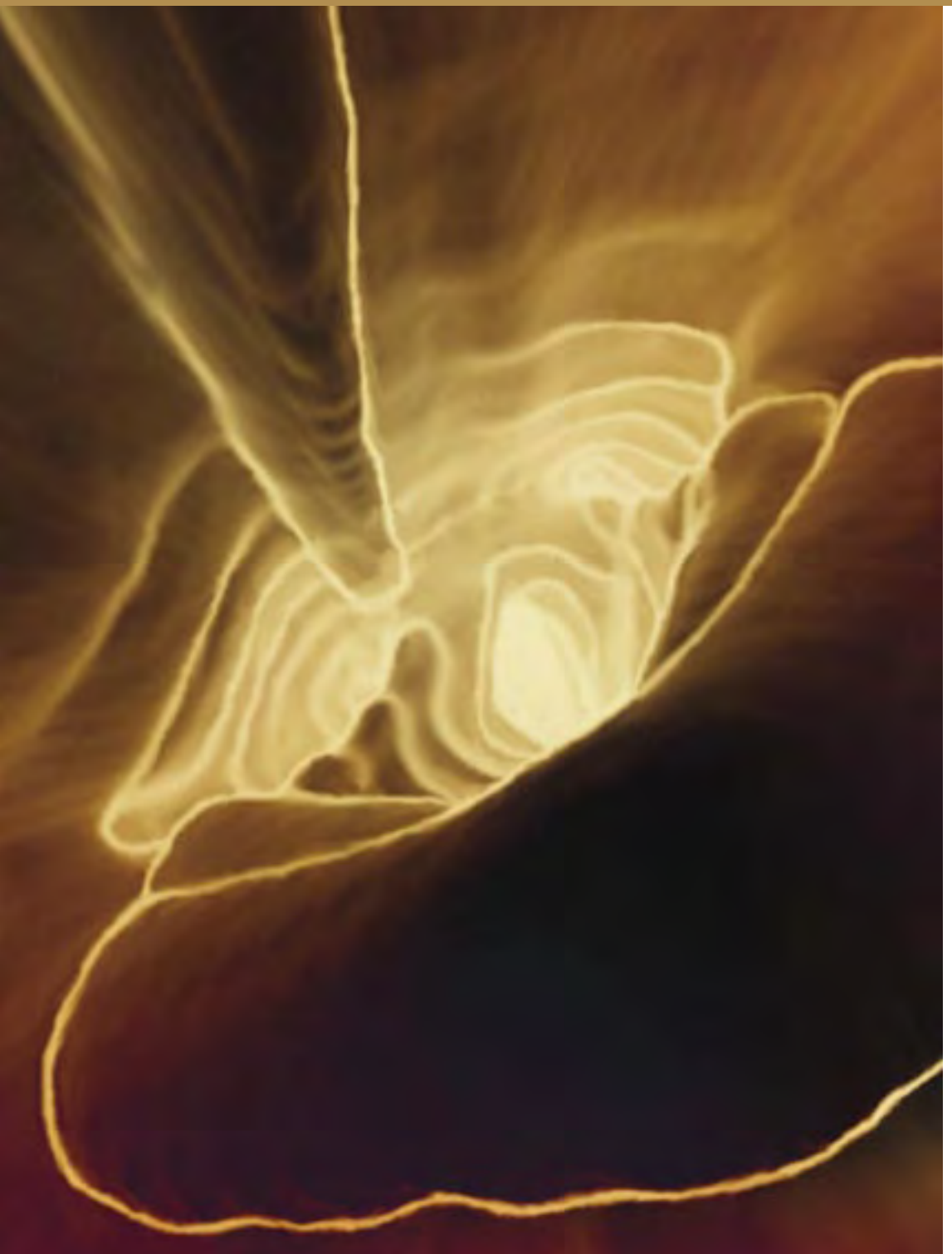

A Report From the American Society of Clinical Oncology 2007 Annual Meeting

Head and Neck Cancers

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◀ Vocal cords in the larynx

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Head and neck cancers account for about 5 percent of all cancers in the United States. Each year, roughly 40,000 people are diagnosed with these cancers. Most head and neck cancers are caused by smoking. As you'll learn in the first study we describe in this chapter, the **human papillomavirus (HPV)** is also linked to head and neck cancers. These cancers begin in the cells that line the surfaces of the mouth, nose, and throat. These tissue surfaces contain cells that look like scales (squamous) under the microscope, so head and neck cancers are often referred to as **squamous cell carcinomas**. Some head and neck cancers begin in other types of cells. For example, cancers that begin in glandular cells of the salivary or thyroid glands are called adenocarcinomas. Cancers of the head and neck are further identified by the area in which they begin, such as the oral cavity, salivary glands, or nasal cavity, for example.

Human Papillomavirus and Head and Neck Cancers

HPV, which also has been linked to cervical cancer and genital warts, is responsible for between 15 and 35 percent of head and neck cancers in North America. HPV is associated with about 50 percent of squamous cell cancers of the tonsils and base of the tongue. According to the National Cancer Institute, the number of squamous cell cancers of the head and neck possibly related to HPV has been on the rise over the past 30 years in the United States, particularly in white men and women between the ages of 30 and 50.

Researchers have believed that the presence of HPV may predict which people with squamous cell cancers of the head and neck are more likely to respond to treatment. Recent findings from a clinical trial conducted by the Eastern Cooperative Oncology Group (ECOG) seem to confirm this. ECOG is a large research group funded by the National Cancer Institute.

What's New, What's Important

- People with head and neck cancer who have the human papillomavirus (HPV) may respond better to both chemotherapy and chemoradiation than people who do not have HPV.
- Alternating radiation and chemotherapy offers no advantage over the standard sequence of chemotherapy for people with cancer of the larynx or hypopharynx.
- Cetuximab (Erbitux) combined with chemotherapy may help people with recurrent or advanced head and neck cancer to live longer and may possibly change the way these patients are treated.
- A new drug called axitinib appears to slow the growth of and/or shrinks tumors in people with advanced thyroid cancer. This class of drugs, which blocks vascular endothelial growth factor, appears to be useful for thyroid cancers.
- Motesanib diphosphate, also known as AMG 706, has shown promise and may eventually be used to treat people with advanced thyroid cancer.

In this clinical trial, nearly 100 people who took part had newly diagnosed, advanced-**stage** squamous cell cancer of the oropharynx (the mouth and throat) or **larynx** (voice box). HPV was found in 40 percent of these patients. All of them were then treated with paclitaxel (Taxol) and carboplatin (Paraplatin) followed by paclitaxel plus radiation. (The latter treatment is known as chemoradiation.)

People who were HPV positive responded better to the original chemotherapy, as well as to the chemoradiation, than did those without HPV. The growth of the tumor was stopped in more than 80 percent of HPV-positive patients compared with only about 55 percent of those who were HPV negative. More than three years after treatment, the risk of the squamous cell cancer growing was about 70 percent lower in HPV-positive patients

than in those who were HPV negative. The risk of death was also about 80 percent lower in the HPV-positive group.

Researchers think HPV may be more responsive to chemotherapy and radiation, perhaps explaining the improved outlook for people with this type of head and neck cancer who are HPV positive.

Chemotherapy for Cancer of the Larynx and Hypopharynx

Surgery has long been the standard treatment for cancers of the larynx or **hypopharynx** (the entrance to the "food pipe," or esophagus). But surgical removal of part or all of these areas can be disabling, leaving a person unable to speak.

During the past few years, doctors have been using chemotherapy, often combined with radiation, as an alternative to surgery. Two medications—cisplatin (Platinol) and 5-fluorouracil (5-FU)—are typically used to treat cancer of the larynx or hypopharynx. Researchers wondered whether the way in which they gave these drugs would affect the results of treatment for people with these types of head and neck cancer.

In a clinical trial conducted by the Head and Neck Group of the European Organization for Research and Treatment of Cancer, researchers compared two different approaches to providing chemotherapy and radiation. They wanted to see whether they could improve results and preserve the larynx. A total of 450 patients who had advanced cancer of the larynx or hypopharynx that had not been treated before were split almost evenly into two groups. One group received the standard treatment of chemotherapy with cisplatin plus 5-FU followed by radiation treatment. The second group received cisplatin plus 5-FU alternating with radiation treatment.

The alternating treatment approach provided no significant advantage over the standard sequence of treatment, chemotherapy followed by radiotherapy. Thus, researchers do not recommend a shift to alternating radiation treatment and chemotherapy for cancer of the larynx or hypopharynx.

Chemotherapy and Cetuximab (Erbitux) for Head and Neck Cancer

In 2006, the U.S. Food and Drug Administration approved the drug cetuximab (Erbitux) as a treatment, along with radiation, for head and neck cancers that cannot be removed with surgery. It also approved the drug for use alone in people whose cancer continues to grow despite chemotherapy. Now, the findings of a new study suggest that cetuximab plus chemotherapy may help people with recurrent or advanced head and neck cancer to live longer.

Referred to as the EXTREME clinical trial, this study included more than 400 patients in 35 European medical centers. Cetuximab, combined with either 5-FU and cisplatin or 5-FU and carboplatin, was given to half the patients. The other half received only the chemotherapy treatments. Patients who received the cetuximab combination lived an average of 10 months, whereas those who did not receive the combination lived for an average of seven months. Researchers say that the length of time patients in the first group survived is among the longest ever seen in a large clinical trial of head and neck cancer patients.

Cetuximab belongs to a class of drugs called **targeted treatments**, which zero in on cell mechanisms that supply blood to tumors and promote their growth. Rather than killing

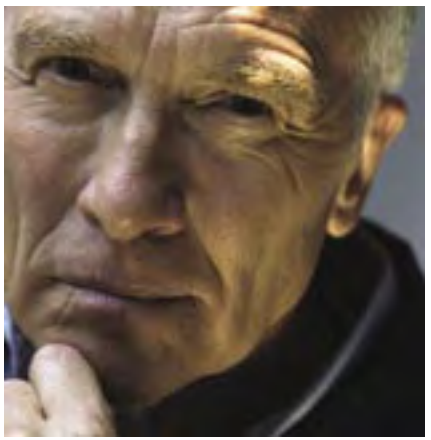
both healthy and unhealthy cells, targeted treatments attack cancer cells primarily, sparing healthy tissues and causing less severe side effects. Cetuximab works by blocking **epidermal growth factor receptor (EGFR)**, one of the key substances involved in head and neck cancer. The drug prevents EGFR from starting a chain reaction in the cells that leads to cancer.

On the Horizon

AXITINIB FOR ADVANCED THYROID CANCER

Many people with thyroid cancer are effectively treated with surgery and/or radioactive iodine treatment. But there are few options for those whose cancer does not respond to these standard methods. So researchers are searching for newer medications to help these patients.

At the University of Chicago, researchers studied a new drug called axitinib in patients with advanced thyroid cancer. Axitinib belongs to a class of drugs that blocks **vascular endothelial growth factor (VEGF)**. People with thyroid tumors tend to have an increased level of VEGF. This substance plays an important role in the growth of blood vessels feeding cancerous tumors, a process called angiogenesis.



Sixty people whose thyroid cancer had not responded to other treatments were given axitinib, which was taken by mouth. The tumors shrank by about one-third to nearly three-quarters in almost 20 percent of patients treated with this drug. This effect lasted from one to 16 months. In another 50 percent of people treated with axitinib, the tumors stopped growing altogether. There were few serious side effects with this drug, but almost half the patients said they felt extremely tired during treatment.

Axitinib and other drugs in this class may become important treatments for people with advanced thyroid cancer. Other clinical trials of this drug are being planned.

MOTESANIB DIPHOSPHATE (AMG 706) FOR ADVANCED THYROID CANCER

Motesanib diphosphate (AMG 706) is another encouraging drug being studied in people with advanced thyroid cancer. Like axitinib, AMG 706 also blocks VEGF, among other substances.

In a clinical trial, researchers gave this drug to nearly 100 people with advanced thyroid cancer that was resistant to standard treatment with radioactive iodine. More than eight months after treatment, the tumor had shrunk in approximately 12 percent of patients treated with AMG 706. In nearly 70 percent of patients, the cancer neither grew nor shrank. Also, 85 percent of the people were still alive more than eight months after starting treatment with AMG 706.

Everyone who received this new drug experienced some type of side effect related to treatment. Common but manageable problems included diarrhea, tiredness, high blood pressure, headache, and nausea.

Please note: *Although the treatments discussed in this chapter are showing promise, most are still in clinical trials—some in earlier phases of research—and may not be available yet to the general public. Your doctor can help guide you as to which new medications could be right for you and whether you are eligible to take part in the clinical trials of these new treatments.*