



THYROID CANCER

Lenvatinib increases survival in patients with metastatic radioiodine-resistant thyroid cancer

BACKGROUND

Treatment of thyroid cancer involves surgery to remove the thyroid and any lymph nodes that may contain cancer. This is followed by radioactive iodine therapy in some patients. In addition, patients take thyroid hormone pills for suppression to prevent cancer recurrences. Most people have excellent outcomes; however about 5-10% of patients have worsening thyroid cancer even though they have been treated with surgery, radioactive iodine and thyroid hormone suppression. Often times, the cancer cells do not take up iodine anymore and become “refractory to radioactive iodine”. Treatment options are limited for these patients. Newer chemotherapeutic drugs target the proteins (tyrosine kinases) that cause cells to become cancer cells. These drugs are called tyrosine kinase inhibitors (TKI) and some of them help kill thyroid cancer cells. This study was done to see whether Lenvatinib, a TKI drug, works to delay the growth of thyroid cancer that cannot be removed surgically or is refractory to radioactive iodine. They also looked at overall survival of patients and the side effects.

THE FULL ARTICLE TITLE

Schlumberger M et al. Lenvatinib versus placebo in radioiodine-refractory thyroid cancer. *N Engl J Med* 2015;372:621-30.

SUMMARY OF THE STUDY

This is a Phase III clinical study of 392 patients with thyroid cancer refractory to radioactive iodine that demonstrated cancer growth within 12 months of entering the study. Patients were from multiple centers throughout the world and then divided in 2 groups: those that received Lenvatinib and those that received a placebo. Neither the treating doctor, nor the patient knew which pill they were taking. A total of 261 patients received

Lenvatinib and 131 patients got the placebo. Of these patients, 51% had papillary thyroid cancer, 13% poorly differentiated cancer, 18% follicular thyroid cancer, and 18% Hurthle cell carcinoma.

The results showed that fewer patients taking the Lenvatinib showed progression of the thyroid cancer (35%) compared to those on placebo (83.2%). Patients in the Lenvatinib group showed progression of their cancer at 18.3 months compared to 3.6 months in the placebo group. Side effects occurred in 97% of the patients taking Lenvatinib and significant side effects occurred in 30% of the Lenvatinib group compared to 10% in the placebo group. The main side effects of the drug noted in the study include: high blood pressure, diarrhea, fatigue, decreased appetite, skin rash, kidney problems and blood clots. There were 6 deaths in the Lenvatinib group.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Because of the excellent results shown in this study, Lenvatinib was approved by the FDA earlier this year for the treatment of progressive thyroid cancer refractory to radioactive iodine. There are now 2 approved targeted chemotherapeutic agents for treating metastatic thyroid cancer refractory to iodine: Sorafenib and Lenvatinib. These drugs can delay progression of thyroid cancer, but also have significant side effects. Therefore, the risks and benefits of TKI treatments such as these drugs must be carefully reviewed with patients before starting them.

—Wendy Sacks, MD

ATA THYROID BROCHURE LINKS

Thyroid cancer: <http://www.thyroid.org/cancer-of-the-thyroid-gland>

ABBREVIATIONS & DEFINITIONS

Cancer metastasis: spread of the cancer from the initial organ where it developed to other organs, such as the lungs and bone.

Thyroid hormone therapy: Suppressive therapy means that the goal is a TSH below the normal range and is used in thyroid cancer patients to prevent growth of any remaining cancer cells.



THYROID CANCER, continued

Radioactive iodine (RAI): this plays a valuable role in diagnosing and treating thyroid problems since it is taken up only by the thyroid gland. I-131 is the destructive form used to destroy thyroid tissue in the treatment of thyroid cancer and with an overactive thyroid. I-123 is the non-destructive form that does not damage the thyroid and is used in scans to take pictures of the thyroid (Thyroid Scan) or to take pictures of the whole body to look for thyroid cancer (Whole Body Scan).

Cancer recurrence: this occurs when the cancer comes back after an initial treatment that was successful in destroying all detectable cancer at some point.

Clinical trials: when a new drug is developed, it must undergo an extensive series of steps, called phases, to prove that it is more effective in patients than the drugs

that are currently available to treat the condition. A Phase I trial tests a new drug or treatment in a small group of people for the first time to evaluate its safety, determine a safe dosage range and identify side effects. A Phase II trial gives the drug to a larger group of people to see if it is effective and to further evaluate its safety. A Phase III trial gives the drug to large groups of people to confirm its effectiveness, monitor side effects, compare it to commonly used treatments and collect information that will allow the drug or treatment to be used safely.

Placebo: A placebo is a pill that has no effect on any disease process. In a clinical trial, a placebo is used as a way to determine whether a drug being studied can cause an improvement in a disease.