



THYROID CANCER

WHAT IS THE STUDY ABOUT?

In general, thyroid cancer grows slowly and is usually responds very well to treatment. Most patients with thyroid cancer can be treated with a combination of surgery, radioactive iodine therapy and thyroid hormone therapy. Unfortunately, some patients are not cured with these treatments and have cancers that spread and continue to grow. Frequently, these cancers no longer take up iodine and, thus, no longer respond to radioactive iodine. In the past, there was little to offer these unfortunate patients as there had been no effective chemotherapy drugs. External Beam Radiation, with the aim of keeping the cancer stable, is an option but has significant side effects. Recently, research studies have shown that proteins known as tyrosine kinases are overactive in thyroid cancer cells. Because of this finding, a group of drugs known as tyrosine kinase inhibitors have been studied and have shown great promise in being effective in the rare patient that has metastatic thyroid cancer that does not respond to radioactive iodine. In particular, Sorafenib is a tyrosine kinase inhibitor that has been shown to be effective in these patients and is currently being studied in clinical trials. This study reports the results of a Phase II clinical trial of Sorafenib in patients with metastatic thyroid cancer.

THE FULL ARTICLE TITLE: Kloos RT, Ringel MD, Knopp MV, Hall NC, King M, Stevens R, Liang J, Wakely PE Jr, Vasko VV, Saji M, Rittenberry J, Wei L, Arbogast D, Collamore M, Wright JJ, Grever M, Shah MH. Phase II trial of sorafenib in metastatic thyroid cancer. *J Clin Oncol* 2009;27:1675–84.

WHAT WAS THE AIM OF THE STUDY?

The aim of the study is to investigate the effectiveness of Sorafenib in the treatment of advanced, metastatic thyroid cancer.

WHO WAS STUDIED?

In total, 56 patients with advanced, progressive metastatic thyroid cancer that no longer responded to radioactive iodine therapy were enrolled in this clinical trial. These patients had Papillary (73 %), Follicular (4%), Hurtle cell (16%) and Anaplastic (7%) subtypes of thyroid cancer. There were 31 men and 22 women in this study.

HOW WAS THE STUDY DONE?

The patients in the study were treated with Sorafenib 400 mg twice per day. They were monitored every 4 weeks for one year. After a year, they were seen in clinic every 12 weeks. Blood and imaging studies were obtained every 8 weeks to determine cancer response. Sorafenib therapy was stopped if: 1) the cancer did not respond to the therapy, 2) the patient's health deteriorated, 3) the patient had severe side effects, or 4) the patient decided to withdraw from the study. Side effects of Sorafenib include severe hand and feet skin rash, severe fatigue, muscle and joint pains, recurrent diarrhea, weight loss, elevated blood pressure and mouth pain. If severe side effects developed, the drug was stopped then re-started at a lower dose after the side effect resolved. The dose was then increased back to full dose if tolerated.

WHAT WERE THE RESULTS OF THE STUDY?

Tumor response was assessed using the Response Evaluation Criteria in Solid tumor (RECIST). In this study, 6 of the patients with Papillary thyroid cancer had a partial response (decrease in the cancer size) that lasted up to 7.5 months. None of the other thyroid cancer types decreased in size. In more than half of the patients, the cancer remained stable (did not increase in size) for more than 6 months. In most of the patients where it was measured, the level of thyroglobulin decreased up to 25 % on Sorafenib.

Severe side effects were common including severe hand and feet skin rash, severe fatigue, and muscle and joint pains. The Sorafenib dose had to be decreased in more than half of the patients in this study.

HOW DOES THIS COMPARE WITH OTHER STUDIES?

Another study used Sorafenib for treating advanced metastatic Papillary thyroid cancer at the same dose for a shorter period of time (16 weeks compared to up to 14 months in the current study). Close to 25% of the treated patients had a decrease in cancer size (compared to only 15 % in this study). Similar to this study, a little over half of the patients had stable disease and the Thyroglobulin level decreased in almost all patients. Side effects were similar in both studies, although one patient died of liver failure in the other study, probably due to Sorafenib therapy.

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THYROID CANCER, continued

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Sorafenib offers some hope for patients with advanced, progressive metastatic Papillary thyroid cancer. The drug is relatively well tolerated and is effective in slowing the progression of disease. However, patients need to be followed closely for significant side effects of the drug.

— Mona Sabra, MD

ATA THYROID BROCHURE LINKS

Thyroid cancer: http://thyroid.org/patients/patient_brochures/cancer_of_thyroid.html

ABBREVIATIONS & DEFINITIONS

Papillary thyroid cancer — the most common type of thyroid cancer.

Thyroglobulin — a protein made only by thyroid cells, both normal and cancerous. When all normal thyroid tissue is destroyed after radioactive iodine therapy in patients with thyroid cancer, thyroglobulin can be used as a thyroid cancer marker.

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.

RECIST: Response Evaluation Criteria in Solid Tumors — this is a set of published rules that define when cancer patients improve (“respond”), stay the same (“stable”) or worsen (“progression”) during treatments.

Sorafenib — an anticancer drug that has been shown to be effective in thyroid cancer.

Tyrosine kinases — proteins that are overactive in many of the pathways that cause cells to be cancerous.