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THYROID CANCER

Sorafenib and Sunitinib are effective in patients with progressive metastatic 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. Recently, research studies have shown that a group of drugs known as tyrosine kinase inhibitors have shown great promise in being effective in the rare patient that has metastatic thyroid cancer that does not respond to radioactive iodine. Two such tyrosine kinase inhibitor drugs that are undergoing clinical trials are Sorafenib and Sunitinib. While clinical trials are the best way to evaluate how effective a new drug is again a disease, not everyone with a disease is available to participate formally. This study examined the response of patients with widespread metastatic thyroid cancer that were treated with Sorafenib and Sunitinib outside of a clinical trial.

THE FULL ARTICLE TITLE:

Cabanillas et al. Treatment with tyrosine kinase inhibitors for patients with differentiated thyroid cancer: the M. D. Anderson experience. J Clin Endocrinol Metab 2010. jc.2009-1923;10.1210.

WHAT WAS THE AIM OF THE STUDY?

The aim of the study was to determine the response to Sorafenib and Sunitinib in patients with advanced differentiated thyroid cancer that no longer responded to radioactive iodine therapy.

WHO WAS STUDIED?

The study group included a total of 15 patients treated at MD Anderson Cancer Center with advanced differentiated thyroid cancer who had not responded to conventional treatment with surgery, radioiodine and external-beam radiotherapy and who were unable or unwilling to participate in clinical trials.

HOW WAS THE STUDY DONE?

The medical records of all patients with metastatic differentiated thyroid cancer who were treated with Sorafenib and/or Sunitinib outside of a clinical trial between 2006 and 2008, were reviewed and entered into a database. Tumor response was assessed using the Response Evaluation Criteria In Solid Tumors (RECIST). All patients but one were treated twice daily with 400 mg of sorafenib. Dose reductions occurred frequently due to side effects or toxicity. The patients treated with sunitinib received either 50 mg by mouth once daily for 4 weeks, followed by 2 weeks off drug or 50 mg daily for 2 weeks followed by 1 week off the drug.

WHAT WERE THE RESULTS OF THE STUDY?

A total of 33 patients were identified from the database, of which 15 were included in the study. The median age was 61 and 60% of the patients were women, 53% had papillary thyroid cancer, 47% had follicular thyroid cancer and 5% had poorly differentiated cancer. The most common location of metastases (73%) was in the lung, followed by bone (27%), and most patients spread of cancer to more than one site. In all of these patients the cancer was progressively growing and spreading.

Overall, 3 patients (20%) had a partial response, 9 patients (60%) had stable disease and 3 patients (20%) had progressive disease. All together, clinical benefit was seen in 80% of the patients. The response was similar for all types of cancer. Lung metastases responded better than lymph node metastases. The time before the cancers started progressing again was 3 times longer than expected in the 80% that responded to the drugs. However, side effects were common and included diarrhea, hypertension and skin problems.

This study suggests that sorafenib and sunitinib are effective in patients with widely progressive metastatic differentiated thyroid cancer. Most patients achieved stable disease or a partial response despite having progressive disease before drug therapy.

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HOW DOES THIS COMPARE WITH OTHER STUDIES?

Two other studies have also shown that these drugs are effective in treating metastatic thyroid cancer. One study (Kloos et al. *Clinical Thyroidology for Patients* August 2009) showed that 87% of patients responded to Sorafenib for an average of 15 months. Another study showed a 100% response rate to Sorafenib for an average of 21 months.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study shows that tyrosine kinase inhibitors may be a good option for treatment of patients with advanced differentiated thyroid cancer who have failed to respond to more conventional treatment modalities, such as surgery, radioiodine and external radiation.

— M. Regina Castro, 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

Follicular thyroid cancer — the second most common type of thyroid cancer.

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).

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.

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

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

Sunitanib — an anticancer tyrosine kinase inhibitor drug that has been shown to be effective in thyroid cancer.