CLINICAL THYROIDOLOGY **FOR THE PUBLIC**

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THYROID CANCER

Sorafenib prolongs progression-free survival of metastatic thyroid cancer patients

BACKGROUND

Thyroid cancer is the fasting rising cancer in women. The vast majority of patients do very well after initial therapy with surgery and, occasionally, radioactive iodine therapy and their prognosis is excellent. However, some patients (<10%) have relentlessly progressive cancer that becomes resistant to radioactive iodine and is very difficult to treat – these are the patients that are at risk of dying from thyroid cancer. Fortunately, a new class of anticancer drugs, known as tyrosine kinase inhibitors (TKI), have shown to be effective in these patients. Several phase I and phase II trials of TKIs for the treatment of metastatic and progressive thyroid cancer unresponsive to radioactive iodine therapy have been published in the past few years. This paper reports the results of the first phase III trial, which established the utility of the TKI sorafenib for the treatment of thyroid cancer and was the basis for the approval of this drug by the FDA.

THE FULL ARTICLE TITLE

Brose MS et al on behalf of the DECISION investigators. Sorafenib in radioactive iodine-refractory, locally advanced or metastatic differentiated thyroid cancer: a randomized, double-blind, phase 3 trial. Lancet. April 23, 2014 [Epub ahead of print]. pii: S0140-6736(14)60421-9. doi: 10.1016/S0140-6736(14)60421-9. PMID:24768112

SUMMARY OF THE STUDY

This study included 416 patients from 77 centers in 18 countries. Patients were > 18 years, with locally advanced or metastatic radioactive iodine-resistant thyroid cancer that had progressed within the past 14 months and had not received any other chemotherapy. Patients were randomly assigned to receive either 400-mg sorafenib twice daily (total of 207 patients) or matching placebo tablets (209 patients). Of these patients, 409 had distant metastases—86% in the lungs, 51% in lymph nodes, and 27% in bone. Treatment was continued until there was progression of disease or unacceptable drug side effects. The primary end point was progression-free survival (PFS) based on evaluations every 8 weeks. The secondary end points were overall survival, time to progression, disease control rate, complete or partial objective response, stable disease for ≥4 weeks and duration of response. Serum thyroglobulin was used as a biomarker of the cancer.

The sorafenib group had a PFS of 10.8 months, versus 5.8 months for the placebo group, although the overall survival was similar in both groups. At disease progression, 71% of patients in the placebo group crossed over to receive open-label sorafenib. Twenty percent of patients in the sorafenib group received other cancer therapy after the trial.

The objective response rate, based on CT or MR imaging was significantly better with sorafenib than with placebo. Stable disease for 6 months or longer occurred more frequently in sorafenib than placebo groups (42% versus 33%). The median time to progression was 11.1 months with sorafenib versus 5.7 months with placebo.

Of the 207 patients in the sorafenib group, 31 (15%) discontinued the drug because of an adverse event. The most frequent adverse events in the active drug group were hand–foot syndrome in 76%, diarrhea in 69%, hair loss in 67%, rash in 50%, weight loss in 47%, hypertension in 41%, anorexia in 32%, oral mucositis in 23%, and pruritus in 20%.

The thyroglobulin concentration decreased significantly in the sorafenib group but not in the placebo group.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Sorafenib significantly improved PFS as compared with placebo in patients with progressive, radioactive iodine-resistant thyroid cancer, although it did not improve overall survival. However, sorafenib has frequent, intolerable side effects that need to be considered before starting this therapy, particularly in older patients who enjoy a good quality of life despite the presence of metastatic disease in lymph nodes and lungs. The criteria for initiating therapy with a TKI such as sorafenib have not been clearly defined. It seems therefore, reasonable to reserve therapy with a TKI for patients with significant disease burden and progressive, life-threatening disease.

— M. Regina Castro, MD

THYROID CANCER, continued

ATA THYROID BROCHURE LINKS

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

Radioactive Iodine Therapy: http://www.thyroid.org/radioactive-iodine

ABBREVIATIONS & DEFINITIONS

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

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 in patients that do not have thyroglobulin antibodies.

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).

Lymph node: bean-shaped organ that plays a role in removing what the body considers harmful, such as infections and cancer cells.

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

Tyrosine kinases inhibitors (TKI): drugs that block the effect of proteins (tyrosine kinases) that are overactive in many of the pathways that cause cells to be cancerous.

Progression free survival (PFS): duration of time that metastatic cancer remains stable

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.