



THYROID CANCER

Motesanib Shows Promise as a New Treatment for Widespread Medullary Thyroid Cancer

WHAT IS THE STUDY ABOUT?

Medullary cancer is a rare form of thyroid cancer, accounting for <10% of all thyroid cancers. Unlike the more common papillary and follicular thyroid cancer, medullary thyroid cancer does not respond to radioactive iodine, so the main treatment option is surgery. When medullary thyroid cancer has spread throughout the body (becomes metastatic), there has been little to offer these unfortunate patients as there has been no effective chemotherapy drugs. Recent studies have identified vascular endothelial growth factor receptor (VEGFR) as a target for cancer therapy. VEGFRs are a family of proteins (called tyrosine kinase) that sit on the surface of cells and trigger chemical signals to grow new blood vessels and make existing blood vessels bigger. Drugs that block VEGFRs cause blood vessels to shrink and kills off cancer cells that are supplied by these blood vessels. Motesanib blocks VEGFRs and preliminary reports have shown this drug to be effective in patients with metastatic medullary thyroid cancer. This study reports the results of a Phase II clinical trial of Motesanib in patients with metastatic medullary thyroid cancer.

THE FULL ARTICLE TITLE:

Schlumberger et al. Phase II Study of Safety and Efficacy of Motesanib in Patients with Progressive or Symptomatic, Advanced or Metastatic Medullary Thyroid Cancer. *J Clin Oncol* 2009; 27:3794-3801.

WHAT WAS THE AIM OF THE STUDY?

The objective of the study was to test whether an experimental new treatment, motesanib, was an effective treatment for metastatic medullary thyroid cancer.

WHO WAS STUDIED?

The study group included 91 patients from around the world with advanced medullary thyroid cancer. These patients either had evidence of cancer progression within the 6 months prior to treatment or symptoms caused by medullary thyroid cancer.

HOW WAS THE STUDY DONE?

The patients took Motesanib (125 mg) by mouth once daily for 48 weeks unless they had worsening of their

cancer or severe side effects. Detailed imaging studies and cancer symptoms were assessed every 8 weeks, or earlier, if there were signs of cancer progression. Blood tests for markers of medullary thyroid cancer (calcitonin and CEA) were measured every 4 weeks.

WHAT WERE THE RESULTS OF THE STUDY?

Tumor response was assessed using the Response Evaluation Criteria in Solid tumor (RECIST). A total of 54 (59%) patients stopped Motesanib prior to 48 weeks: 30 had progression of medullary thyroid cancer, 13 had side effects, 3 died and 8 stopped for other reasons. No patients were cured over the course of the study. In 2 patients (2%), the medullary thyroid cancer responded with a significant decrease in size. A smaller decrease in the size of the cancer was seen in 69 patients (76%). 83% of patients had a decrease in the level of the medullary cancer marker, calcitonin, while 75% had a decrease in the level of CEA. 74 patients (81%) did not improve or worsen while they were on treatment. The average cancer progression-free period was 48 weeks and overall survival at 12 months was 75%. Twenty-four patients died during the study period. An extension study was created for 34 patients who completed the 48-week therapy protocol.

The most common side effects thought to be related to Motesanib were diarrhea (41% of patients), feeling tired (41%), hypothyroidism (29%), elevated blood pressure (27%) and decreased eating (27%). Eight patients experienced gallbladder problems, including gallbladder infections, gallstones and gallbladder enlargement.

HOW DOES THIS COMPARE WITH OTHER STUDIES?

A similar experimental drug that blocks VEGFR showed an improvement of medullary thyroid cancer in 20% of patients and stable cancer in 30%. Yet another similar experimental drug showed stable disease in 87% of patients. The studies suggest new medicines that interfere with the growth of new blood vessels which feed cancers by blocking VEGFR may be useful for preventing spread of medullary thyroid cancer.

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WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Motesanib was generally well tolerated by patients with advanced medullary thyroid cancer and resulted in shrinkage of the cancer in rare patients (2%). For the majority of the patients (81%), Motesanib caused the cancer to stop growing for a period of time. Further testing may show that treatments blocking blood vessel

growth may prove helpful for treating medullary thyroid cancer.

— Ruth Belin, MD

ATA THYROID BROCHURE LINKS

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

ABBREVIATIONS & DEFINITIONS

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.

Medullary thyroid cancer — a relatively rare type of thyroid cancer that also may be inherited. Medullary cancer arises from the C-cells in the thyroid.

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.

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

Calcitonin — a hormone that is secreted by cells in the thyroid (C-cells) that has a minor effect on blood calcium levels. Calcitonin levels are increased in patients with medullary thyroid cancer.

Carcinoembryonic antigen (CEA) — a protein that can be made by certain cancers such as colorectal cancer and medullary thyroid cancer. CEA may be measured with a blood test.

Vascular endothelial growth factor receptors (VEGFR) — family of proteins (called tyrosine kinase) that sit on the surface of cells and, in response to other proteins (VEGF), trigger chemical signals to grow new blood vessels and make existing blood vessels bigger. Cancers cannot grow beyond a limited size without blood supply; cancers with working VEGF and VEGFRs are able to grow and spread.