



## THYROID CANCER

### WHAT IS THE STUDY ABOUT?

Motesanib diphosphate can induce partial remissions in patients with progressive advanced metastatic DTC unresponsive to surgery, external beam radiotherapy and <sup>131</sup>I.

**THE FULL ARTICLE TITLE:** Sherman SI, Wirth LJ, Droz JP, Hofmann M, Bastholt L, Martins RG, Licitra L, Eschenberg MJ, Sun YN, Juan T, Stepan DE, Schlumberger MJ. Motesanib diphosphate in progressive differentiated thyroid cancer. *N Engl J Med* 2008;359:31-42. <http://www.ncbi.nlm.nih.gov/pubmed/18596272?dopt=Citation>

### WHAT IS KNOWN ABOUT THE PROBLEM BEING STUDIED?

Differentiated thyroid cancers such as papillary or follicular thyroid cancer, as well as other thyroid cancers express vascular endothelial growth factor (VEGF) and tyrosine kinases and other genetic features that regulate the growth and invasion of malignant tumors. This is a study of a new drug that appears to be helpful in patients with advanced cancer that is unresponsive to standard therapy.

### WHAT WAS THE AIM OF THE STUDY?

The study was done to evaluate the efficacy and tolerability of motesanib diphosphate in patients with progressive, locally advanced or metastatic differentiated thyroid cancer.

### WHO WAS STUDIED?

The study subjects were 93 patients who had progressive, locally advanced, or metastatic, radioactive iodine-resistant papillary, follicular, Hürthle cell, or other forms of thyroid cancer that were not amenable to standard therapeutic measures.

### HOW WAS THE STUDY DONE?

The patients were treated with 125 mg of motesanib diphosphate, administered orally once daily. The main end point of the study was an objective response as assessed by an independent radiographic review using the RECIST Criteria as well as additional end points including the duration of the response, progression-free survival and safety.

### WHAT WERE THE RESULTS OF THE STUDY?

The objective response rate was 14%. Stable disease was achieved in 67% of the patients, and was maintained for 24 weeks or longer in 35%; 8% had progressive disease as the best response. The most common treatment-related complications were diarrhea (59%) high blood pressure (56%) fatigue (46%) and weight loss (40%). There are other complications (see the website link above under the full title of the article).

### HOW DOES THIS COMPARE WITH OTHER STUDIES?

There are no published studies to compare with this excellent study published in the *New England Journal of Medicine*. The full study information can be retrieved at the following web link: <http://content.nejm.org>

### WHAT ARE THE LIMITATIONS OF THIS STUDY?

The decrease in serum thyroglobulin levels and its correlation with the tumor response, although consistent with other findings with radioiodine therapy, probably underestimated the efficacy of the study because thyroglobulin secretion and treatment with motesanib diphosphate caused increases in serum thyrotropin (TSH).

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This new drug can induce partial responses in patients with advanced tumor disease.

### ABBREVIATIONS & DEFINITIONS

**VEGF** is vascular endothelial growth factor. VEGF has been shown to be responsible for the development and maintenance of a vascular network that promotes tumor growth and metastasis. A large and growing body of evidence indicates that both VEGF gene expression and VEGF production are associated closely with poor prognosis of thyroid cancer.

**Motesanib diphosphate (AMG 706)** is a novel oral inhibitor of VEGF receptors, platelet-derived growth-factor receptor, and KIT, all of which are involved in tumor growth and invasion

**RECIST** is Response Evaluation Criteria in Solid Tumors. Which is recommended for National Cancer Institute sponsored trials and involves formalized rules for measurement of tumor target lesions. Further explanation can be found at the NCI website: <http://imaging.cancer.gov/clinicaltrials/imaging/>

Web links are provided to provide further information