



HYPOTHYROIDISM

Hypothyroidism during cancer therapy with tyrosine kinase inhibitors.

BACKGROUND

Thyroid function can be affected by cancer chemotherapy drugs given to treat non-thyroid cancers. Hypothyroidism is more common than hyperthyroidism. This is especially true with some of the newer drugs that affect the immune system. One class of cancer chemotherapy drugs is tyrosine kinase inhibitors (TKI), of which there are >20 TKI drugs. TKI drugs are active against a variety of solid cancers, especially kidney cancers and some GI cancers. They are also active against progressive thyroid cancer, although thyroid cancer patients are already hypothyroid after thyroidectomy and radioactive iodine therapy. Interestingly, the development of hypothyroidism during cancer treatment of non-thyroid cancer may be linked to improved survivals.

This study examined the development of hypothyroidism in patients receiving TKI drugs for non-thyroid cancer and the effect on survival.

THE FULL ARTICLE TITLE

Lechner MG et al. 2018. Hypothyroidism during tyrosine kinase inhibitor therapy is associated with longer survival in patients with advanced nonthyroidal cancers. *Thyroid* 28:445–453. PMID: 29652597.

SUMMARY OF THE STUDY

Data on more than a 1000 patients who received one of 6 TKI drugs was collected and reviewed. Almost half of the patients studied had renal cell cancer. Those patients who had TSH levels done before and within 6 months after the day the TKI was started were included. Patients with pre-existing thyroid disease or thyroid cancer were not included in the study. Data was also collected regarding treatment with levothyroxine for those patients who did develop hypothyroidism.

Women were more likely to become subclinically or overtly hypothyroid (53%) compared to men (34%). Of the 538 patients in the study, subclinical hypothyroidism developed in 71 (13%), and overt hypothyroidism in 144

(27%). Hyperthyroidism was detected in 18 patients who subsequently became hypothyroid. Most cases of hypothyroidism developed within 6 months but some took up to 18 months. The average survival time for those who remained with normal thyroid function was 685 days, but for those who became subclinically hypothyroid, it was 1005 days, and for those who became overtly hypothyroid it was 1643 days. Almost all the patients had advanced disease and about half had been treated with at least two TKIs. Hypothyroidism was also more frequent in patients with renal-cell cancer and GI stromal cancers.

More than 90% of those with overt hypothyroidism received levothyroxine replacement therapy (132 of 144). Patients who were given levothyroxine for a TSH above 5 and below 10 mIU/L generally had symptoms such as fatigue, depression, or worsening functional status. The 27 patients given replacement levothyroxine for a TSH between 5 and 10 mIU/L survived longer than the 83 patients who were not treated.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study showed that new hypothyroidism—sometimes preceded by a hyperthyroid phase—developed after TKI drugs in ~40% of patients, and they survived longer. Hypothyroid patients treated with levothyroxine seemed to have a longer overall survival than those not given levothyroxine. It is not clearly understood as to why many patients who receive the TKI therapy for non-thyroidal cancer develop hypothyroidism. However, this study suggests that thyroid function tests should be measured before treatment with TKIs and then periodically after for at least for the first 6 months and especially in women. However, it appears that patients who develop this condition may have an improved survival. Further studies are needed to better understand the survival benefit and to determine if thyroid function on TKIs are a real prognostic factor.

—Vibhvasu Sharma, MD





HYPOTHYROIDISM, continued

ATA THYROID BROCHURE LINKS

Hyperthyroidism (Overactive): <https://www.thyroid.org/hyperthyroidism/>

Hypothyroidism (Underactive): <https://www.thyroid.org/hypothyroidism/>

ABBREVIATIONS & DEFINITIONS

TSH: thyroid stimulating hormone — produced by the pituitary gland that regulates thyroid function; also the best screening test to determine if the thyroid is functioning normally.

Hypothyroidism: a condition where the thyroid gland is underactive and doesn't produce enough thyroid hormone. Treatment requires taking thyroid hormone pills.

Subclinical Hypothyroidism: a mild form of hypothyroidism where the only abnormal hormone level is an increased TSH. There is controversy as to whether this should be treated or not.

Overt Hypothyroidism: clear hypothyroidism an increased TSH and a decreased T_4 level. All patients with overt hypothyroidism are usually treated with thyroid hormone pills.

Thyroid hormone therapy: patients with hypothyroidism are most often treated with Levothyroxine in order to return their thyroid hormone levels to normal. Replacement therapy means the goal is a TSH in the normal range and is the usual therapy. Suppressive therapy means that the goal is a TSH below the normal range and is used in thyroid cancer patients to prevent growth of any remaining cancer cells.

Hyperthyroidism: a condition where the thyroid gland is overactive and produces too much thyroid hormone. Hyperthyroidism may be treated with antithyroid meds (Methimazole, Propylthiouracil), radioactive iodine or surgery.

Tyrosine kinases: proteins that are overactive in many of the pathways that cause cells to be cancerous. Inhibiting these proteins with drugs known as tyrosine kinase inhibitors are effective chemotherapy drugs for cancers, including advanced thyroid cancer

