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THYROID CANCER

Dabrafenib increases radioactive iodine uptake in patients with radioactive iodine-resistant thyroid cancer with BRAF-mutation

BACKGROUND

Most patients with thyroid cancer do well, are at low risk and are often cured of their cancer after surgery. Those with higher risk cancers (large cancers that spread outside the thyroid) can be treated with radioactive iodine, which acts as a "magic bullet" to destroy thyroid cancer cells as it is taken up and concentrated within the cells. However, in some patients, the thyroid cancers stop taking up radioactive iodine and are, thus, more difficult to treat as they become resistant to radioactive iodine. In particular, cancers that contain the BRAF-mutation are more likely to become radioactive iodine-resistant. Treatment options are limited for these patients. Newer chemotherapeutic drugs (tyrosine kinase inhibitors, TKI) target essential proteins in thyroid cancer cells and have been shown to be effective in treating these cancer. In particular, dabrafenib is a TKI that can block the BRAF-mutation, possibly allowing the thyroid cancer cells to take up radioactive iodine again. This study was done to determine if dabrafenib could increase the uptake of radioactive iodine in radioactive iodine-resistant thyroid cancer.

THE FULL ARTICLE TITLE

Rothenberg SM et al. Redifferentiation of iodine-refractory BRAF V600E-mutant metastatic papillary thyroid cancer with dabrafenib. Clin Cancer Res. December 30, 2014 [Epub ahead of print].

SUMMARY OF THE STUDY

All patients included in this study were older than 18 years of age (6 males and 4 females) and had thyroid cancer that could not be removed by surgery or was radioactive iodine-resistant. All patients had already received 1-4 previous radioactive iodine treatments. All patients were treated with dabrafenib. A diagnostic radioiodine scan was performed after 25 days in all patients. Dabrafenib treatment was stopped if there was no sign of increased radioactive iodine uptake in the diagnostic scan and was continued for 2 weeks only in patients with increased radioiodine uptake in diagnostic whole-body scan. After 2 weeks, the patients were treated with radioactive iodine and a whole body scan was performed. A total of 6 of 10 patients with dabrafenib treatment showed increased radioactive iodine uptake. Cancer size was reduced in 5 of 6 treated patients. The thyroid cancer marker thyroglobulin was decreased in only in 3 of 6 treated patients. Dabrafenib also caused several significant side effects such as skin lesion, fatigue, weight loss, headache, and hypocalcemia.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Dabrafenib increases radioactive iodine uptake in patients with metastatic radioactive iodine-resistant thyroid cancer with BRAF-mutation. This offers another option for treating these patients with high risk thyroid cancers. However, dabrafenib also causes significant side effects. Therefore, the risks and benefits of treatment with this drug should be carefully reviewed with patients.

— Jamshid Farahati, MD

ATA THYROID BROCHURE LINKS

Thyroid Cancer: http://www.thyroid.org/thyroid-cancer/

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

Thyroid Surgery: http://www.thyroid.org/thyroid-surgery/

ABBREVIATIONS & DEFINITIONS

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

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THYROID CANCER, continued

pictures of the whole body to look for thyroid cancer (Whole Body Scan).

Radioactive iodine uptake (RAIU): this is a measurement of activity of the thyroid gland and is reported as the percent of a dose of radioactive iodine that is retained in the thyroid gland 24 h after the dose is given. An increase in RAIU usually indicates hyperthyroidism.

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

Cancer-associated genes: these are genes that are normally expressed in cells. Cancer cells frequently have mutations in these genes. It is unclear whether mutations in these genes cause the cancer or are just associated with the cancer cells. The cancer-associated genes important in thyroid cancer are BRAF, RET/PTC and RAS.

BRAF gene: this is gene that codes for a protein that is involved in a signaling pathway and is important for cell growth. Mutations in the BRAF gene in adults appear to cause cancer.

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.