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DRUG THERAPY

A new standard for thyroid cancer?

Patients with advanced-stage medullary thyroid cancer (MTC) have a poor prognosis, and treatment options are limited because neither radiotherapy nor chemotherapy are effective at producing durable responses. Around 40% of patients have sporadic mutations in the oncogene *RET*, with most of these patients harboring the M918T substitution. As a follow up to a phase II study that showed convincing activity of the RET multikinase inhibitor, vandetanib, a large-scale randomized trial has now provided clear evidence of efficacy of this drug in patients with advanced-stage inoperable MTC. These data prompted the FDA to approve this drug for this indication.

Samuel Wells and colleagues conducted a randomized, placebo-controlled trial in 331 patients, and demonstrated that the primary end point of progression-free survival (PFS) was significantly improved with the use of vandetanib. Douglas Ball, an expert in the field who discussed the trial with us, elaborates "this is a landmark study—it is the first large-scale randomized phase III study in thyroid cancer, and provides a clear indication of efficacy for vandetanib in patients with advanced inoperable MTC".

Patients with the M918T alteration had better response rates and prolonged PFS compared with those lacking this mutation. "A major limitation of the study is that overall survival data have not fully matured," explains Ball. Owing to the crossover effect, once disease progression occurs in patients taking placebo, they will be allowed to receive vandetanib. However, Ball cautions, "given the significant side effect of cardiac QT prolongation caused by vandetanib, there's a potential for harm if oncologists 'jump the gun' when using this drug in patients with early-stage or non-progressive disease".

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Original article Wells, S. A. Jr *et al*. Vandetanib in patients with locally advanced or metastatic medullary thyroid cancer: a randomized, double-blind phase III trial. *J. Clin. Oncol*. doi:10.1200/JCO.2011.35.5040