Trial watch

TARGETING THYROID ANGIOGENESIS

Promising results from two phase II trials that assess the use of the anti-angiogenesis drugs sorafenib and axitinib in patients with advanced thyroid cancer were published recently in the *Journal of Clinical Oncology*. Patients with thyroid cancer are usually treated with radioactive iodine (^{131}I) or surgery, but those patients for whom these strategies are not appropriate or successful have limited treatment options.

Sorafenib has numerous targets, including RAF kinase, vascular endothelial growth factor receptors (VEGFRs) and platelet-derived growth factor receptor. Gupta-Abramson and colleagues treated 30 patients with ^{131}I-refractory metastatic thyroid carcinoma with 400 mg sorafenib twice daily for at least 16 weeks. Responses were measured by radiography at 2–3 month intervals and the endpoints included response rate, progression-free survival (PFS) and best response according to Response Evaluation Criteria in Solid Tumors (RECIST). They found that partial responses lasting 18–84 weeks occurred in 7 patients (23%; 95% confidence interval (CI) 0.10–0.42) and 16 patients (53%; 95% CI 0.34–0.72) had stable disease for 14–89+ weeks. The median PFS was 79 weeks and the overall clinical benefit rate was 77%, indicating that sorafenib has clinically relevant effects in these patients. Importantly, toxicity in these patients was comparable to previous clinical testing of sorafenib, although one patient died of treatment-related liver failure.

Axitinib is a selective inhibitor of VEGFR1, VEGFR2 and VEGFR3 and Cohen and colleagues tested this drug at a dose of 5 mg twice daily in 60 patients with advanced thyroid cancer of any histology for which ^{131}I or surgery was not appropriate. Using the RECIST-defined objective response rate as the primary endpoint and PFS, duration of response, overall survival, safety and effects on soluble VEGFRs as secondary endpoints, the authors found that partial responses were observed in 18 patients, an objective response rate of 30% (95% CI 13.9–43.2). Twenty-three patients (38%) had stable disease for at least 16 weeks and the median PFS was 18.1 months (95% CI 12.1–unknown), providing evidence that axitinib is also a clinically relevant drug for the treatment of patients with refractory thyroid cancer. Moreover, axitinib was generally well-tolerated, although 8 patients (13%) discontinued treatment because of treatment-related adverse events.

Although the prognosis of thyroid cancer is generally good, patients with refractory thyroid cancer do not always have such a promising future and advances in the treatment of these patients have not been forthcoming. Therefore, as discussed in the accompanying editorial, these two trials might provide a significant step forward in the treatment of this disease.

ORIGINAL RESEARCH PAPERS Gupta-Abramson, V. *et al.* Phase II trial of sorafenib in advanced thyroid cancer. *J. Clin. Oncol.* 9 Jun 2008 (doi: 10.1200/JCO.2008.16.3279) | Cohen, E. E. W. *et al.* Axitinib is an active treatment for all histologic subtypes of advanced thyroid cancer: results from a phase II study. *J. Clin. Oncol.* 9 Jun 2008 (doi: 10.1200/JCO.2007.15.9566)
FURTHER READING Pfister, D. G. & Fagin, J. A. Refractory thyroid cancer: a paradigm shift in treatment is not far off. *J. Clin. Oncol.* 9 Jun 2008 (doi: 10.1200/JCO.2008.17.3682)