

## Motesanib Diphosphate in Progressive Differentiated Thyroid Cancer

**TO THE EDITOR:** Sherman et al. (July 3 issue)<sup>1</sup> highlight the importance of selecting patients for alternative therapies, such as motesanib diphosphate, in the treatment of progressive differentiated thyroid carcinomas. Although radiographic findings are useful criteria for predicting a response to motesanib, they can be supplemented by the microscopical findings — in particular, growth pattern, necrosis, and desmoplastic reaction — which have been correlated with progression prediction.<sup>2</sup> The genotypic alterations described in follicular-cell neoplasms control the mitogen-activated protein (MAP) kinase pathway and proliferation. Was any correlation found with proliferation markers? Which radiographic criteria were used to define progression in metastatic neoplasms? As for tumor progression, it normally refers to the acquisition of invasive capabilities in intraepithelial lesions or metastatic potential in invasive cancers.<sup>3</sup>

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2. Arif S, Patel J, Blanes A, Diaz-Cano SJ. Cytoarchitectural and kinetic features in the histological evaluation of follicular thyroid neoplasms. *Histopathology* 2007;50:750-63.

3. Diaz-Cano SJ. General morphological and biological features of neoplasms: integration of molecular findings. *Histopathology* 2008;53:1-19.

**THE AUTHOR REPLIES:** We agree with Diaz-Cano that careful selection of patients for treatment with investigational therapies for differentiated thyroid cancer is essential. As is standard in cancer-therapy trials, in our trial progression was defined by application of the Response Evaluation Criteria in Solid Tumors (RECIST) for determination of both eligibility and response.<sup>1</sup> The microscopical features referenced by Diaz-Cano may certainly be valuable in characterizing follicular neoplasms but have not yet been established as predictors of responses to therapy. Future studies of molecularly targeted therapies in thyroid cancer may well benefit from serial assessment of cellular responses to treatment, including proliferation markers and signaling intermediates, as he suggests.

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## Platelets and the Vascular Wall

**TO THE EDITOR:** In their review of the importance of platelets in maintaining the integrity of the vascular wall, Nachman and Rafii (Sept. 18 issue)<sup>1</sup> provide evidence that maintenance of the endothelial barrier depends on a reciprocal communication between endothelial cells and platelets and the formation of zipper structures at adherens junctions. A protein that is central in the activation status of platelets and endothelial zipper structures is vasodilator-stimulated phosphoprotein (VASP). VASP is crucial for the polymerization of the actin cytoskeleton and is intimately linked to

several proteins forming adherens junctions, such as  $\alpha$ -catenin. Endothelial cells deficient in VASP are leaky, and platelets lacking VASP demonstrate severe abnormalities in the platelet interaction with the endothelium.<sup>2,3</sup> Therefore, we wonder what the authors think about the role of VASP in the crosstalk between platelets and endothelial cells.

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