Savolitinib for *MET*-driven papillary renal cell carcinoma

Patients with advanced papillary renal cell carcinoma harbouring *MET* alterations could respond to treatment with the selective MET tyrosine kinase inhibitor savolitinib, according to the results of a recent clinical trial.

Papillary renal cell carcinoma has few effective treatment options. *MET* alterations (kinase domain mutations or gene amplification) are uncommon in these carcinomas, and the associated activation of the MET pathway is thought to drive tumour growth. In the single-arm, international, phase 2 study by Toni Choueiri (Dana-Farber Cancer Institute, Boston, MA, USA) and colleagues, 109 patients with locally advanced or metastatic papillary renal cell carcinoma were given savolitinib (600 mg orally once daily); clinical tumour samples from each patient were assessed for *MET* alterations with a next-generation sequencing assay.

The activity of savolitinib was strongly associated with the presence of *MET* alterations in the tumour. Eight (18%) of the 44 patients with *MET*-driven tumours achieved objective responses (all confirmed partial responses) to savolitinib, whereas no responses were recorded in the 46 patients whose tumours were *MET*-independent (p=0·002). Furthermore, patients with *MET*-driven tumours had a longer median progression-free survival than those with *MET*-independent tumours (6·2 months [95% CI 4·1–7·0] *vs* 1·4 months [1·4–2·7]; hazard ratio 0·33 [95% CI 0·20–0·52]; log-rank p<0·001). Savolitinib had a tolerable safety profile, with the most frequent drug-related adverse events being nausea, vomiting, and peripheral oedema.

Choueiri commented on savolitinib: "Perhaps this drug makes the most sense in a subset of papillary renal cell cancer patients with *MET* alterations. Molecular characterisation by *MET* status was more predictive of response to savolitinib than pathology." Choueiri added that an international, phase 3 trial is planned to test sunitinib versus savolitinib only in patients with *MET* alterations.

Hans Hammers (UT Southwestern Medical Center, Dallas, TX, USA) said the study results were encouraging: "The problem with kidney cancer is that we really have not had a good biomarker to select for treating patients." Although the results will need confirmation in a phase 3 trial, he added: "For the first time, we would identify a molecularly identifiable subset of patients, and we can deliver a therapy that may be more effective in this population than the current standard of care."

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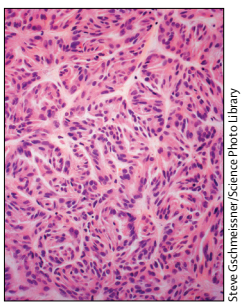

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For the **study by Choueiri and colleagues** see *J Clin Oncol* 2017; published online June 23. http://dx.doi.org/10.1200/JCO.2017.72.2967