

➔ KIDNEY CANCER

SAVOLITINIB — A SAVIOUR FOR PAPILLARY RCC?

Savolitinib, a selective inhibitor of the MET tyrosine kinase pathway, demonstrates activity and tolerability in patients with papillary renal cell cancer (pRCC), according to data published in the *Journal of Clinical Oncology*.

Although clear cell RCC is the most common histological subtype of renal tumour, the papillary variant comprises ~40% of non-clear cell tumours, with an estimated incidence of ~6,400 cases per year in the USA. The papillary subtype can be further subclassified; type 1 pRCC tumours are characterized by mutations in the *MET* receptor tyrosine kinase gene. Activation of the MET pathway promotes tumour growth, angiogenesis, and metastasis; thus, inhibition of this pathway could offer a therapeutic target for this hard-to-treat disease.

Choueiri and colleagues carried out a single-arm, multicentre, global, phase II study to evaluate the efficacy and tolerability of savolitinib in patients with pRCC. Participants ($n = 109$) received 600 mg of oral savolitinib daily, until RECIST-defined progression or discontinuation criteria were met.

Using next-generation sequencing with a 400-gene panel, tumours were confirmed as *MET*-positive if *MET* copy number gain, *HGF* gene amplification, or *MET* kinase domain mutations were identified ($n = 44$). *MET*-driven pRCC was strongly associated with response to savolitinib: eight partial responders were observed in the *MET*-driven group, versus none in the *MET*-independent group ($P = 0.002$). Median progression-free survival for patients with *MET*-driven pRCC was 6.2 months, versus 1.4 months for those with *MET*-independent pRCC. 75% of the patients who showed a partial response were still responsive at the study cut-off point, demonstrating an enduring response. 88% of participants experienced ≥ 1 adverse effect of therapy, but most events were low-grade, including nausea and vomiting, fatigue, and peripheral oedema.

Overall, these data support the further study of savolitinib for pRCC driven by *MET* and, indeed, a phase III trial has recently been launched.

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ORIGINAL ARTICLE Choueiri, T.K. *et al.* Biomarker-based phase II trial of savolitinib in patients with advanced papillary renal cell cancer. *J. Clin. Oncol.* <http://dx.doi.org/10.1200/JCO.2017.72.2967> (2017)

FURTHER READING Fenner, A. Diving into the genome of papillary RCC unearths therapeutic pearls. *Nat. Rev. Urol.* <http://dx.doi.org/10.1038/nrurol.2017.100> (2017)