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KIDNEY CANCER

New approaches for high-risk disease

Despite substantial improvments in our ability to treat patients with clear-cell renal cell carcinoma (RCC), several important questions, including how to manage patients with high-risk disease following surgery and how best to delay disease progression in those with metastatic disease, remain unanswered. Data from two clinical trials presented at the 2016 ESMO annual meeting, provide further insight into these important issues.

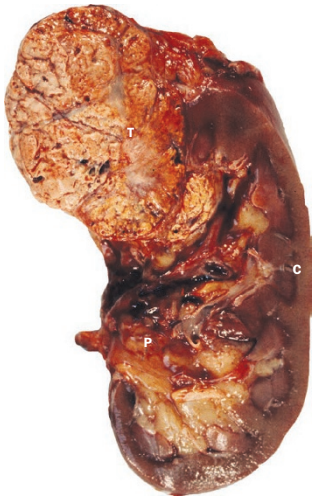

Figure from Vladimir A. Valera & Maria J. Merino. *Nat. Rev. Urol.* **8**, 321-333 (2011), Nature Publishing Group.

A substantial majority of patients with RCC will undergo nephrectomy, and around 40% of these patients are likely to have disease recurrence after surgery. Despite this considerable level of risk, postoperative management is currently limited to surveillance for signs of recurrence. Now, data from a double-blind, randomized phase III trial demonstrate the value of the multi tyrosine-kinase inhibitor sunitinib, in the adjuvant setting in these patients.

A total of 615 patients with high-risk RCC were randomly assigned to receive either sunitinib, or placebo following nephrectomy; all patients were monitored for signs of recurrence. Patients receiving sunitinib had a significant increase in median progression-free survival (PFS) duration (6.8 years) compared with that of the placebo group (5.6 years). However, this increase in PFS duration was accompanied by a significant increase in the risk of adverse events, including grade ≥3 adverse events. This increased risk of adverse events reflects a moderate decrease in patients' quality of life and might affect the use of sunitinib in this setting. Investigators commented that further follow-up monitoring of this cohort is required because almost 40% of patients undergoing nephrectomy will survive for 10 years afer surgery.

In a second study, researchers compared the efficacy of sunitinib versus that of cabozantinib, an agent that inhibits a broader range of tyrosine kinases than sunitinib, in 157 patients with metastatic RCC. In this randomized phase II trial, patients received either drug, and .patients in the cabozantinib group had a significant increase in median PFS duration (8.6 months) compared with the sunitinib group (5.6 months), which probably reflects the significantly more-favourable rate of responses to cabozantinib. Both groups of patients had similar risks of adverse events; however, patients receiving sunitinib had a greater risk of haematological toxicites, while those receiving cabozantinib had an increased risk of hypertension.

Data from both trials provide an improved level of evidence, which will likely enable clinicians to make better judgements on the most-appropriate treatment for patients with high-risk RCC.

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ORIGINAL ARTICLES Rayvaud, A. *et al.* Adjuvant sunitinib in high-risk renal-cell carcinoma after nephrectomy. *N. Engl J. Med.* http://dx.doi.org/10.1056/NEJMoa1611406 (2016) | Choueiri, T. K. *et al.* CABOzantinib versus SUNitinib (CABOSUN) as initial targeted therapy for patients with metastatic renal cell carcinoma (mRCC) of poor and intermediate risk groups. [abstract LBA30_PR]. Presented at ESMO (2016)