

## KIDNEY CANCER

### Use sorafenib first in sequential TKI regimens

A retrospective review of the efficacy and safety of sequential use of two tyrosine kinase inhibitors (TKIs) for the treatment of renal cell carcinoma has found no evidence of cross-resistance. Sablin and colleagues also observed an association between the order of drug administration and survival.

Sorafenib and sunitinib were approved in 2006 for the treatment of advanced renal cell carcinoma. The drugs have similar mechanisms of action and target similar cell surface receptors. Owing to the relatively recent approval of these drugs, the effects of sequential administration have yet to be established.

Sablin *et al.* analyzed data from 90 patients with renal cell carcinoma who were treated with both sorafenib and sunitinib at one of four medical centers in France. Disease progression or death had occurred in 60 patients at the time of

analysis. Of the 90 patients, 68 received sorafenib followed by sunitinib while 22 received sunitinib followed by sorafenib, with average washout periods of 10 weeks and 5 weeks between each drug, respectively.

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Median duration of progression-free survival was 26 weeks with sorafenib and 28 weeks with sunitinib in the former group, and 22 weeks with sunitinib and 17 weeks with sorafenib in the latter. Overall survival was longer in patients who received sorafenib first than in those who received sunitinib first (median 135 weeks versus 82 weeks,  $P = 0.04$ ). Both regimens achieved a disease control rate

(partial response or disease stability) of over 60%. Toxicity and tolerability were similar in both groups.

The researchers comment that the lack of observed cross-resistance indicates that there are clinically relevant differences in the modes of action of the two drugs. Alternatively, the washout period between cessation of the first drug and administration of the second could have facilitated resensitization of tumors to TKIs. Sablin's team suggests that sequential therapy begin with sorafenib, although they recommend prospective studies of treatment sequencing be conducted to confirm their findings.

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**Original article** Sablin, M. P. *et al.* Sequential sorafenib and sunitinib for renal cell carcinoma. *J. Urol.* **182**, 29–34 (2009).