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Arterial hypertension and clinical benefit of sunitinib, sorafenib and bevacizumab in first and second-line treatment of metastatic renal cell cancer

The paper by Bono et al. [1] suggests that treatment-related hypertension may predict a gain in response rate to antiangiogenics used to treat metastatic renal cell carcinoma (MRCC) [1, 2].

We confirm that occurrence of hypertension is predictive of a clinical benefit (objective response + stable disease) in this setting. Moreover, in our prospective follow-up of blood pressure in the treatment of 94 consecutive patients with MRCC, hypertension was predictive of clinical benefit whatever the antiangiogenic (sunitinib, sorafenib and/or bevacizumab) and whatever the line of treatment.

Sixty-six, 25 and four patients received, respectively, one, two or three antiangiogenics. The majority of patients received them in first-line (42.6%) or second-line (43.6%) treatment. Thirty-seven patients were given bevacizumab (39.4%), 42 sorafenib (44.7%) and 48 sunitinib (51%) [3].

All the patients were seen at initiation by the same oncologist (AR). All underwent cardiovascular evaluation before initiation and had normal blood pressure of 140/90 mmHg maximum with a recommendation for stabilisation at ≤130/80 mmHg before treatment. Thirty-seven patients had controlled hypertension at initiation. All patients measured their own blood pressure three times in a row, twice daily, every day, in the case of previous hypertension, or three times a week for the others. When patients had hypertension ≥150/90 mmHg, the antihypertensive treatment was modified to normalise blood pressure, whereas when blood pressure reached 170/100 mmHg, the patient had to stop antiangiogenic treatment for at least the time required to obtain normal blood pressure for 48 h before resuming the antiangiogenics.

In our cohort, whatever the drug or treatment line, 17 assessable patients had ≥ grade 2 hypertension according to the National Cancer Institute—Common Toxicity Criteria grading system. Fifteen of these had a clinical benefit (88.2%) and nine (52.9%) benefited for at least 6 months. For patients with no significant change in blood pressure, 58 of 106 assessable patients (a patient who received several drugs could be studied several times, each time exposed to a different antiangiogenic drug) had a clinical benefit (54.7%) and 37 patients (34.9%) benefited for ≥6 months. Comparison of clinical benefit among patient with ≥ grade 2 or < grade 2 arterial hypertension was carried out using chi-squared statistics. A significant hypertension (≥ grade 2) predicted clinical benefit ($\chi^2 = 6.82$; $P = 0.009$), as well as a trend in gain for prolonged benefit ≥6 months ($\chi^2 = 1.79$; $P = 0.18$) when compared with the outcome of patients with no significant change in blood pressure (< grade 2). There was no significant difference between sunitinib, sorafenib or bevacizumab or between first- or second-line treatment.

In conclusion, conducting a clearly defined survey of blood pressure and hypertension management in patients with MRCC treated with sunitinib, sorafenib or bevacizumab confirms that a significant hypertension predicted clinical benefit. Confirmation of this important clinical implication underlines our recommendation for a standard definition of arterial hypertension in studies [4], along with continued management of hypertension. The predictive nature of drug-induced hypertension also merits more prospective studies to investigate prolonged clinical benefit and/or survival [5].

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