Reviewer's report

Title: Safety and treatment patterns of multikinase inhibitors in patients with metastatic renal cell carcinoma at a tertiary oncology center in Italy

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Reviewer: Takeshi Yuasa

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Safety and treatment patterns of multikinase inhibitors in patients with metastatic renal cell carcinoma at a tertiary oncology center in Italy
Camillo Porta, MD et al.

The primary objective of this study was to examine the safety profiles of sunitinib and sorafenib and the frequency of treatment modifications, including treatment discontinuation, treatment interruptions and dose changes in the clinical practice at a tertiary oncology center. In this study, they retrospectively analyzed 145 patients including 85 sunitinib and 60 sorafenib administered patients. Median treatment duration was 6.6 (sunitinib) and 5.8 (sorafenib) months. Treatment discontinuation, interruption, and dose reduction due to adverse effects occurred in 11.8%, 23.5%, and 30.6%, respectively, of patients receiving sunitinib, and 5.0%, 23.3%, and 36.7%, respectively, of patients receiving sorafenib. This study is interesting for us clinical urologists as well as medical oncologists. However, it might be difficult for us to find out what the author would like to tell us from this study.

Major points

I understand the authors' statement that the statistical comparisons between groups are not likely to be meaningful. However, I also think that it is difficult to understand the difference between them and the expand access trials. In the sunitinib expand access trials, the median progression-free survival was 10.9 months (95% CI 10.3–11.2) and overall survival was 18.4 months (17.4–19.2). However, in this study, the median treatment duration was 6.6 (sunitinib) and 5.8 (sorafenib) months. Do they recommend that the patients should not be treated at a tertiary oncology center? Please describe the cause of this difference and the opinion from these results.

Because the progressive disease was the most frequently reported reason for treatment discontinuation in both groups (62.4% for sunitinib and 58.3% for sorafenib), I think that the results of the PFS and the OS of the respective patients are necessary.

I think the conclusion that these results suggest a need for additional effective and more tolerable treatments for mRCC, is strange. I think that the conclusion should be extracted from the differences between the PFS, OS, or AEs of the previous studies and their studies.
Minor points
In Table 1, which described the patients’ characteristics, tumor histology and classifications (favorable, intermediate, and poor) by MSKCC score are necessary.

Among these patients, 24 patients have brain metastases. I think that they underwent gamma-knife therapy for brain lesion. After RTx, sunitinib or sorafenib were administered? Otherwise, they were administered during RTx? None had cerebro-vascular bleeding? Please describe it. Some clinical doctors cautioned that we should be cautious regarding the concomitant use of sunitinib with radiation to the brain, so as to avoid potentially serious adverse effects. (Paul J. Kelly et al “Sunitinib-Induced Pseudoprogression After Whole-Brain Radiotherapy for Metastatic Renal Cell Carcinoma”)

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.