We read with interest the article by McKay and colleagues (1) evaluating the impact of angiotensin system inhibitors (ASI) on outcomes in metastatic renal cell carcinoma (mRCC) patients treated in the targeted therapy era. They found that ASI users had improved overall survival (OS) compared with users of other antihypertensive agents and individuals receiving no antihypertensive therapy. Importantly, the benefit in OS was limited to ASI users receiving VEGF-targeted therapy and did not concern patients receiving other drugs having demonstrated survival benefit in mRCC. The authors hypothesized that this may be related to the ability of ASIs to synergize with antiangiogenics to inhibit tumor cell proliferation and angiogenesis. Yet it was reported elsewhere that ASI could favor a protumoral microenvironment and that the antiangiogenic effect of VEGF pathway inhibitors could be impeded by the use of ASI (2). Results are therefore confusing with regard to ASI action on angiogenesis, and we believe another hypothesis explaining these findings may exist.

Sarcopenia, the condition of having low muscle mass and function, is highly prevalent in mRCC patients (3, 4). Moreover, sarcopenia combined to a body mass index \(< 25 \text{ kg m}^{-2}\) predicts sunitinib-induced early dose-limiting toxicities (3) and sorafenib-induced dose-limiting toxicities (4) in mRCC patients. Interestingly, in a study of 641 noncancer patients with hypertension (61 of which had used ASI continuously, 133 intermittently, 146 never, and 301 had used other hypertensive drugs), the patients who had taken ASI continuously had a significantly lower mean 3-year decline in muscle strength (5). ASI may therefore help preserve muscle mass.

In conclusion, we propose that the action of ASI on muscle mass may result in less sarcopenia, a well-documented cause of overexposure and excessive toxicity to tyrosine kinase inhibitors. Hence, the therapeutic index of VEGF-targeted therapies may be improved by ASI, resulting in subsequent longer duration of treatments, higher dose-intensity, and finally improved efficacy.

We wonder if the authors may mention whether the patients under ASI had less early dose-limiting toxicities and less treatment interruptions.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Received August 27, 2015; accepted September 12, 2015; published online January 15, 2016.

References


Angiotensin System Inhibitors in Renal Cell Carcinoma—Letter
Olivier Huillard, Evanguelos Xylinas, Michael Peyromaure, et al.


Updated version
Access the most recent version of this article at:
http://clincancerres.aacrjournals.org/content/22/2/524

Cited articles
This article cites 5 articles, 1 of which you can access for free at:
http://clincancerres.aacrjournals.org/content/22/2/524.full#ref-list-1

E-mail alerts
Sign up to receive free email-alerts related to this article or journal.

Reprints and Subscriptions
To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions
To request permission to re-use all or part of this article, contact the AACR Publications Department at permissions@aacr.org.