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EDITORIAL

Cytoreductive nephrectomy in primary metastatic clear cell renal cell carcinoma

Nephrectomy for patients with primary metastatic clear cell renal cell carcinoma (MccRCC) has been discussed for decades. Just after the millennium, two studies demonstrated a survival advantage for upfront cytoreductive nephrectomy (CN) in the interferon/interleukin era [1,2]. With the introduction of targeted therapies (TTs), the role of CN again was put under debate. Several large retrospective registry or consortium-based studies indicated a positive impact of upfront CN before TT. The results of the randomized controlled trial (RCT) CARMENA contradicted this [3]. However, how to interpret the results of CARMENA has been a topic in a lot of papers and at most conferences since the study was presented at ASCO in 2018.

Surgical voices have been raised claiming CN to have an advantageous impact on MccRCC outcome that CARMENA did not capture due to selective inclusion of poor-risk participants.

In this issue of the *Scandinavian Journal of Urology*, two studies with different angles on this topic are presented. Based on their single-center series, Roussel et al. [4] claim that patients with oligometastatic disease, $\leq$2 evaluable IMDC prognostic criteria and the lung as only metastatic site may achieve a long treatment free period after a CN. From the National Kidney Cancer Registry in Sweden, Ljungberg et al. [5] demonstrate an overall survival benefit for patients treated with upfront CN before systemic treatment.

There seems to have developed a misunderstanding about the intention of CARMENA. CARMENA never intended to include all patients with MccRCC. The patients should be in need of TT, as stated in the study protocol attached to the original paper [3]. Furthermore, there was a requirement of a minimum two metastases present for inclusion [6]. Thus, patients with single metastases or low-volume oligometastatic disease without an urgent need of TT were not offered inclusion in CARMENA, as they did not fulfill the inclusion criteria. Most likely these patients were treated with nephrectomy and metastasectomy or surveillance.

The results in the present paper from Roussel et al. [4] underscore the role of nephrectomy in this group of patients. Moreover, it is also likely that this patient group is driving the results in the paper from Ljungberg et al. [5], but unfortunately data on metastatic burden and performance status is lacking in this study.

Both studies are important as real-world data supporting the present guidelines from the European Association of Urology, recommending upfront CN in cases where all metastases may be completely resected or systemic therapy is not needed immediately [7].

For patients with a larger metastatic burden in need of immediate systemic therapy, upfront CN is not recommended [7] and the two presented papers do not challenge this.

As suggested by the SURTIME trial [8], deferred CN is an option to consider if the patient responds to the TT treatment. Whether deferred CN will remain a viable option after the introduction of immunotherapy in first-line treatment for MccRCC is currently being investigated in the Danish initiated ongoing NORDIC-SUN trial (Clinicaltrials.gov Identifier: NCT03977571).

Disclosure statement

No potential conflict of interest was reported by the author(s).

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