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Letter to the Editor

Nivolumab plus ipilimumab as neoadjuvant treatment in primary advanced renal cell tumors: Cutting edges for cutting-edge surgery

With great interest we have read the article entitled *"Pathologic response and surgical outcomes in patients undergoing nephrectomy following receipt of immune checkpoint inhibitors for renal cell carcinoma"* by Singla et al. In their article, Singla et al report that cytoreductive nephrectomy following systemic treatment with immune checkpoint inhibitors (ICI) appears safe in patients with advanced or metastatic renal cell carcinoma (RCC) [1]. In their cohort, pathological responses of primary RCC to nivolumab ± ipilimumab were observed. As these pathological responses are remarkable for primary RCC, the question rises whether ICIs could be effective as neoadjuvant therapy.

To answer this question, we here illustrate the efficacy of nivolumab plus ipilimumab in unresectable primary RCC. In a 74-year old patient, cT3aN1M0 RCC of clear cell histology was considered unresectable due to regional lymphadenopathy compressing the tumor thrombus in the renal vein (Fig. 1). First-line nivolumab (3 mg/kg) and ipilimumab (1 mg/kg) was started and after four 3-week cycles, a partial response according to RECIST v1.1 [2] was observed with disappearance of lymphadenopathy, 42% reduction of the primary tumor and a near-complete response of the tumor thrombus. As the primary tumor was considered resectable, open radical nephrectomy was performed. No vital tumor cells could be detected by histopathological examination (ypT0N0). After nephrectomy, systemic therapy was discontinued and active surveillance was started. Until now, at 5 months after nephrectomy, there is no evidence of disease.

Since the introduction of ICIs, the treatment strategies in RCC patients are dramatically changing. As an increasing number of RCC patients will experience durable tumor responses in both primary tumor and metastases after ICIs, delayed nephrectomy will be considered more often [3–5]. During first-line combination treatment with ICIs, the rate and depth of primary tumor response is significantly improved as compared with first-line monotherapy tyrosine kinase inhibitors [3,4]. For the first time, we have illustrated that ICIs even facilitate nephrectomy by transforming unresectable to resectable primary RCC [1] and induce complete pathological responses in primary RCC. As ICIs obviously have neoadjuvant potential for the treatment of primary RCC, treatment with ICIs should be considered prior to cytoreductive nephrectomy.

Conflicts of interest

Karlijn de Joode: nothing to declare.

Jolanda I. de Ruig-Spakman: nothing to declare.

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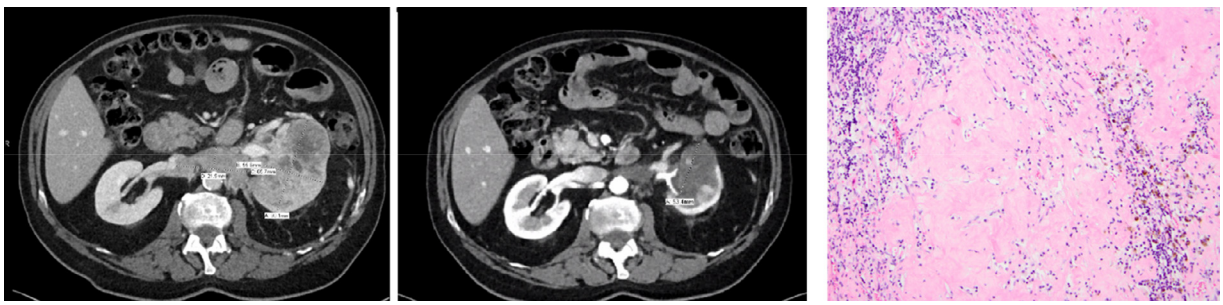

Fig. 1. Primary RCC in the left kidney with enlarged regional lymph nodes and tumor thrombus up to the inferior vena cava at baseline (left) and after 4 cycles of nivolumab and ipilimumab (middle). Histopathological examination of the nephrectomy specimen after treatment with nivolumab and ipilimumab shows sclerotic connective tissue with hemosiderin pigment and lymphocytic infiltration, without any vital tumor cells (right, H&E, 10×). RCC = renal cell carcinoma.

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References

[1] Singla N, Elias R, Ghandour RA, Freifeld Y, Bowman IA, Rapoport L, et al. Pathologic response and surgical outcomes in patients undergoing nephrectomy following receipt of immune checkpoint inhibitors for renal cell carcinoma. Urol Oncol 2019;37:924–31.
[2] Eisenhauer EA, Therasse P, Bogaerts J, Schwartz LH, Sargent D, Ford R, et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). Eur J Cancer 2009;45:228–47.
[3] Motzer RJ, Rini BI, McDermott DF, Aren Frontera O, Hammers HJ, Carducci MA, et al. Nivolumab plus ipilimumab versus sunitinib in first-line treatment for advanced renal cell carcinoma: extended follow-up of efficacy and safety results from a randomised, controlled, phase 3 trial. Lancet Oncol 2019;20:1370–85.
[4] Motzer RJ, Tannir NM, McDermott DF, Aren Frontera O, Melichar B, Choueiri TK, et al. Nivolumab plus ipilimumab versus sunitinib in advanced renal-cell carcinoma. N Engl J Med 2018;378:1277–90.
[5] Cella D, Grunwald V, Escudier B, Hammers HJ, George S, Nathan P, et al. Patient-reported outcomes of patients with advanced renal cell carcinoma treated with nivolumab plus ipilimumab versus sunitinib (CheckMate 214): a randomised, phase 3 trial. Lancet Oncol 2019;20:297–310.