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Case Report

Long-Term Control of Metastatic Renal Cell Carcinoma Using Pazopanib

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Keywords
Pazopanib · Nivolumab · Metastatic renal cell carcinoma

Abstract
COMPARZ study revealed no marked differences in terms of the progression free survival and overall survival between sunitinib and pazopanib treatment. Regarding the quality of life and early tumor shrinkage, pazopanib showed more favorable results than sunitinib treatment. A 70-year-old man underwent right nephrectomy in 2015. In 2017, iliac bone metastasis was found and consequently lung metastasis was developed. Pazopanib (200 mg × 4 tablets) was introduced. He showed no abnormal liver function markers during pazopanib treatment for more than two years and the size and number of lung metastases decreased. We herein report a case of successful control of metastatic renal cell carcinoma for more than two years using pazopanib treatment.

Introduction

For primary advanced or recurrent metastatic renal cell carcinoma (mRCC), sunitinib and pazopanib are recommended treatment options, especially for favorable and intermediate-

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risk RCC, according to the NCCN and EAU guidelines [1–4]. Recently, combination therapy of ipilimumab and nivolumab has prolonged both the progression-free survival (PFS) and overall survival (OS) compared to sunitinib treatment in mRCC and is available for clinical application in Japan [5]. However, despite its effectiveness, ipilimumab and nivolumab combination treatment has a high rate of immune reactive adverse events (irAEs), and around 60% of treated patients must take steroids to manage these irAEs. We herein report a case of successful control of mRCC for more than two years using pazopanib treatment.

Case Presentation

A 70-year-old man underwent chemo-radiotherapy for T4N1M0 lung cancer in October 2014. Follow-up computed tomography (CT) showed a right renal tumor 5.2 cm in size, so he was referred to our hospital for a further examination. Contrast-enhanced CT suggested RCC, so laparoscopic nephrectomy was performed in October 2015 (Fig. 1). A pathological examination revealed clear cell carcinoma, Furman grade 2. In December 2015, fluorodeoxyglucose-positron emission tomography (FDG-PET)-CT showed the uptake of FDG at his left iliac bone, so a bone biopsy was performed (Fig. 2). The pathological diagnosis was bone metastasis from RCC.

Due to the lack of other metastatic lesions, radiotherapy and denosumab treatment were performed. Follow-up CT revealed multiple lung metastases in August 2016, so pazopanib (200 mg × 4 tablets) was introduced. He showed no abnormal liver function markers, including AST, ALT, and gamma GTP, during pazopanib treatment for more than two years, and the size and number of lung metastases decreased (Fig. 3, 4). CT showed no marked changes on his iliac bone metastasis (Fig. 4). We also assessed the PD-L1 expression using immunohistochemistry found expression.

Discussion

The CheckMate-214 study showed that the combination of ipilimumab and nivolumab prolonged the PFS comparing to sunitinib treatment (11.6 vs. 8.4 months, $p = 0.033$) [5]. While ipilimumab with nivolumab combination therapy and sunitinib treatment have almost the same side effects (Grade ≥3), ipilimumab with nivolumab requires additional steroid treatment for managing irAEs in around 60% of treated patients [5].

The SU11248 study revealed that sunitinib prolonged the PFS compared with interferon alpha (11 vs. 5 months, $p < 0.001$) [10]. The VEG105192 study showed that pazopanib prolonged the PFS, although no significant difference in the OS was noted (9.2 vs. 4.2 months, $p < 0.001$ and 22.9 vs. 20.5 months $p = 0.224$). The COMPARZ study revealed no marked differences in terms of the PFS or OS between sunitinib and pazopanib treatment [6]. Regarding the quality of life and early tumor shrinkage, pazopanib showed more favorable results than sunitinib treatment.

In the CheckMate-214 study, the group with a high PD-L1 expression showed more favorable results when ipilimumab with nivolumab treatment was administered, but even in the low-PD-L1-expression group, ipilimumab with nivolumab showed favorable efficacy [5, 7]. The present case showed a positive expression of PD-L1. In the COMPARZ study, the high-PD-L1-expression group showed a poorer outcome than the low-PD-L1-expression group [8]. While there are no useful biomarkers for predicting whether or not an immune checkpoint

inhibitor will be effective in a given patient, the PD-L1 expression plays an important role in mRCC patients.

In the present case, the patient was able to take a full dose of pazopanib without experiencing any side effects for more than two years, achieving successful cancer control. The VEG105192 studies found median PFS values of 9.2 months [6, 9]. Thus, a PFS exceeding two years is relatively rare. While the combination of ipilimumab and nivolumab has shown a more favorable outcome than treatment with sunitinib in a number of studies, tyrosine kinase inhibitors – including pazopanib and sunitinib – still play an important role in the first-line treatment of mRCC.

Availability of Data and Material

Due to ethical restrictions, the raw data underlying this paper are available upon request to the corresponding author.

Statement of Ethics

Written informed consent to participate in this study and for the publication of this report was obtained from the patient. A copy of the written consent form is available for review from the Editor-in-Chief of this journal. The present study received ethical approval.

Disclosure Statement

The authors declare no conflicts of interest in association with the present study.

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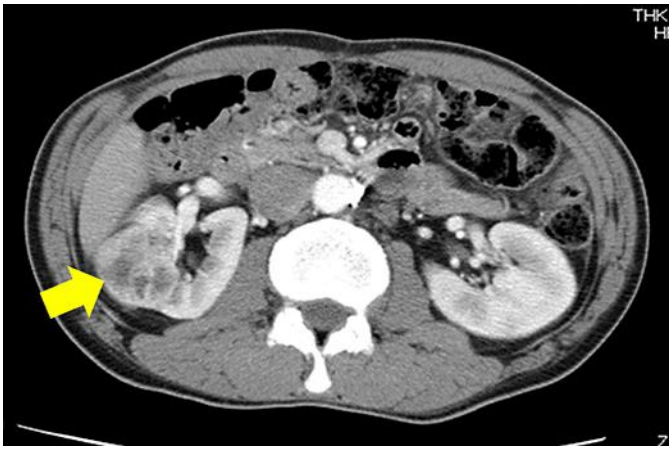


Fig. 1. CT in initial right renal tumor.

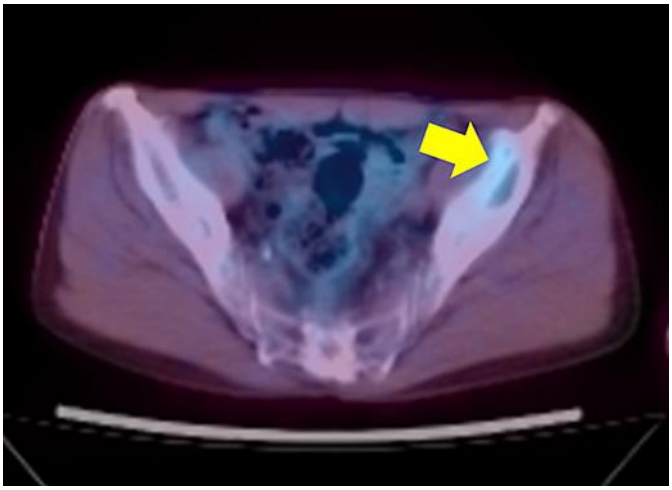
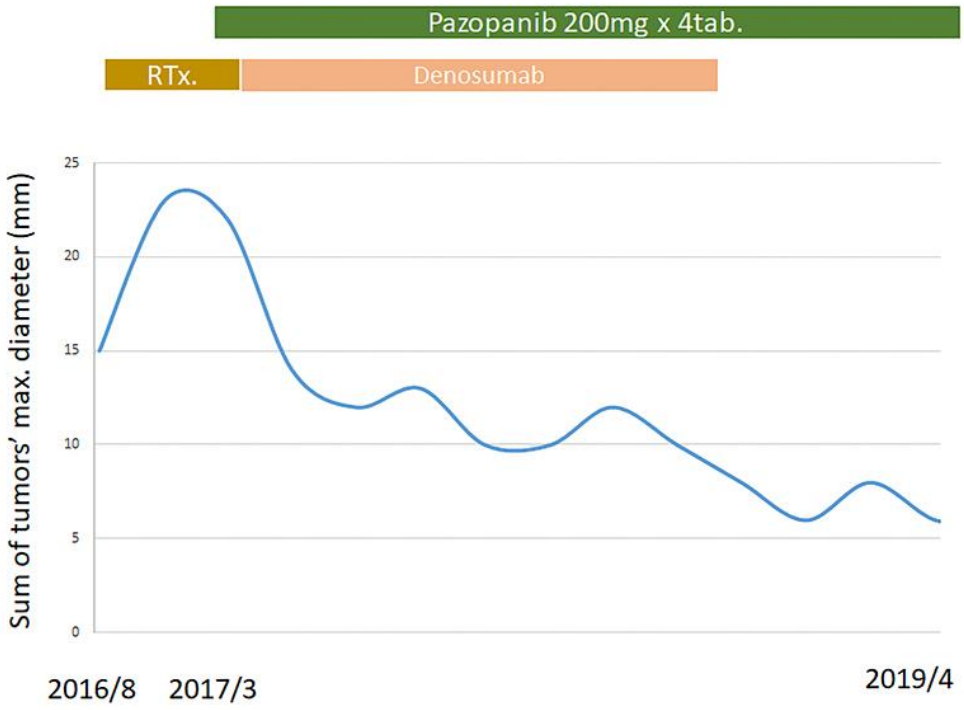


Fig. 2. Left iliac bone metastasis in PET-CT.



AST (IU/L)	22	31	23	22	20	15
ALT (IU/L)	14	23	13	14	10	8
γ-GTP (IU/L)	28	18	32	28	209	17

Fig. 3. Clinical course.

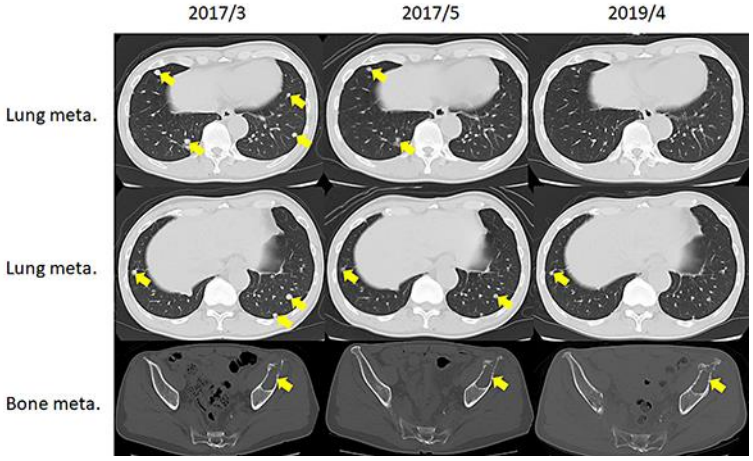


Fig. 4. CT before initial pazopanib treatment (2017/3) as well as 2 months (2017/5) and 2 years (2019/4) after initial pazopanib treatment.