Evaluation of First-Line Sorafenib Treatment for Metastatic Renal Cell Carcinoma in Kidney Transplant Patients: A Single-Center Experience With Four Cases

Evaluation of first-line sorafenib treatment for metastatic renal cell carcinoma in kidney transplant patients: A single-center experience with four cases

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Main text

The risk of developing renal cancers is reportedly 3−5% among patients with end-stage renal disease pre- and post-transplantation, which is 100-fold higher than that among the general population (1). Immunosuppressive therapies, which are administered to prevent graft rejection, increase the risk of developing cancers or accelerate tumor cell growth (2). Currently, the treatment strategy for metastatic renal cell carcinoma (mRCC) consists of molecular-targeted therapy. Sorafenib is one of first-line tyrosine kinase inhibitors, and its efficacy has been demonstrated in a previous clinical trial (3). However, clinical information on the use of sorafenib in patients with renal dysfunction, such as those with end-stage renal disease or those who have undergone kidney transplantation, has been limited, because such patients were excluded from the aforementioned trial. We previously reported the efficacy and safety of sorafenib in 20 patients with mRCC undergoing dialysis therapy (1). Our former study indicated that sorafenib treatment seemed feasible (median time to progression: 6.3 months; overall survival: 14.2 months), although careful monitoring of severe adverse events (AEs) was required（4 of 20 patients［20.0%］ discontinued treatment because of ≥grade 3 AEs). Thus, we believe that sorafenib treatment is effective for patients with renal dysfunction. Herein, we describe our single-center experience with first-line sorafenib treatment in 4 kidney transplant patients with mRCC.

Patient characteristics and outcomes are shown in Table 1. All cancers originated from native kidneys. Three patients were pathologically diagnosed as having clear-cell carcinoma. All patients received the same immunosuppressive regimen, including tacrolimus, mycophenolate mofetil, and methylprednisolone at

the time of diagnosis. Conversion to a different regimen (i.e., mycophenolate mofetil to everolimus) was performed in 3 patients. All patients experienced disease progression and died of the cancers. The median times to disease progression and to death were 8.98 and 15.1 months, respectively. AEs were observed in 3 patients; ≥grade 3 AEs were observed in 1 patient (25%). During treatment, graft function was stable, and no patient required a major adjustment in the dose of tacrolimus.

Previous studies have indicated that the median progression-free survival ranges from 5–9 months (3, 4), and the median overall survival is 12.5 months in the general population (4). Thus, an equivalent effect of prolonging survival in kidney transplant patients was shown in this study. However, physicians need to pay attention to frequent AEs in these patients compared to the general population (3, 4). Moreover, sorafenib treatment had a similar efficacy and toxicity in kidney transplant patients compared to patients with hemodialysis (1).

Finally, the present study's findings may suggest that sorafenib does not affect immunosuppression, because we did not need to modify the dose of tacrolimus. This may be because sorafenib, which is a multi-targeted tyrosine kinase inhibitor of Raf, the vascular endothelial growth factor receptor, and platlet-derived growth factor receptor, is not associated with the mechanism of immunosuppression caused by tacrolimus. However, there may be a possible pharmacokinetic correlation between the two different agents, thus further investigations are needed.

In summary, first-line sorafenib treatment seems feasible in kidney transplant patients with mRCC; nevertheless, careful monitoring for AEs is required.

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Conflicts of interest

No conflict of interest is declared.

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Table 1: Patients' characteristics and outcomes

Case	Sex	Dialysis duration before KTx (month)	Immunosuppressive agents at diagnosis mRCC	Age at diagnosis (year)	MSKCC	Pathology	Time from KTx to diagnosis (month)	Initial/maintenance dose (mg)	Conversion	Time to disease progression/death (month)	AEs	FK dose at treatment initiation/end (mg)
1	Male	192	FK, MMF, MP	55	Intermediate	CCC	26.1	400/800	MMF to EVL	6.67/15.6	None	1/1
2	Male	48	FK, MMF, MP	73	Intermediate	CCC	126.8	400/400	MMF to EVL	11.3/14.6	Anemia G3	N/A
3	Male	192	FK, MMF, MP	52	Intermediate	CCC with sarcomatoid	67.2	600/600	None	3.42/6/67	Gastrointestinal disorder G2	1/1
4	Male	57	FK, MMF, MP	70	Favorable	CCC	37.6	400/600	MMF to EVL	23.1/29.1	Gastrointestinal disorder G2	2/1
Mean (median, range)		122,3 (124.5, 48.0 – 192)		62.5 (62.5, 52 – 73)			64.4 (52.4, 26.1 – 126.8)			11.1 (8.98, 3.42 – 23.1)/16.5 (15.1, 6.67 – 29.1)		

KTx, kidney transplantation; mRCC, metastatic renal cell carcinoma; MSKCC, Memorial Sloan-Kettering Cancer Center; AEs, adverse events; FK, tacrolimus; MMF, mycophenolate mofetil; MP, methylprednisolone; CCC, clear-cell carcinoma; EVL, everolimus; G, grade; N/A, not applicable;