## Supplemental Materials

Patient #	Age (years)	Sex	Prior nephrectomy	Histology	IMDC risk group	Sites of metastasisª
1	62	Male	Yes	Clear cell + rhabdoid and sarcomatoid	Intermediate	Lungs, lymph
1	02	Male	165	transformation	intermediate	nodes
				Clear cell + rhabdoid		Lungs honos
2	54	Male	Yes	and sarcomatoid	Intermediate	Lungs, bones, brain
				transformation		
3	39	Male	Yes	Clear cell + rhabdoid	Poor	Lungs, liver
5	39	Male	165	transformation		
						Lungs, lymph
4	63	Male	Yes	Clear cell	Intermediate	nodes,
						nephrectomy bed
						nodule
						Lungs, lymph
5	56	Male	Yes	Clear cell	Poor	nodes, brain,
						bones, adrenal
						glands
6	63	Male	No	Clear cell	Poor	Lungs, Bones,
						Brain
7	57	Male	Yes	Clear cell with sarcomatoid changes	Intermediate	Lymph nodes, Bones

Supplemental Table 1. Patient characteristics

<sup>a</sup>At the time of initiation of lenvatinib plus everolimus treatment.

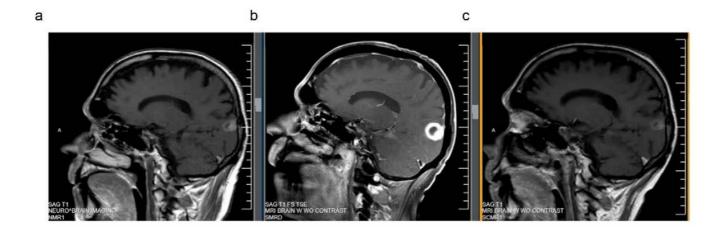
IMDC, International Metastatic renal cell carcinoma Database Consortium.

Patient #	Genomic variants	Copy number variations	PD-L1 expression	
	PBRM1 LOF		Not assessed	
	VHL LOF			
1	PTEN LOF	None		
	ARID1A LOF			
	LIFR frameshift			
2	Not assessed	Not assessed	Not assessed	
	VHL LOF		Negative	
3	SETD2 LOF	CDKN1B CNG		
	ARID2 GOF			
4	VHL LOF	None	Negative	
5	PBRM1 LOF	None	Positive	
	VHL LOF	PTEN CNL		
6	PIK3R1 LOF	CDKN2A CNL	Negative	
0	KDM5C LOF	CDKN2B CNL		
	KDIVI3C LOF	MTAP CNL		
		CDKN2A CNL		
7	None	CDKN2B CNL	Negative	
		MTAP CNL		

## Supplemental Table 2. Genomic and PD-L1 data

CNG, Copy Number Gain; CNL, Copy Number Loss; GOF, gain of function; LOF, loss of function; PD-L1, programmed death ligand-1.

**Supplemental Figure 1.** Imaging results for Patient 1 with mRCC who received lenvatinib plus everolimus treatment. The first image (MRI of the brain) shows the tumor size (mid-right side of the brain) after treatment for 2 weeks (a); the patient then discontinued treatment due to toxicity and experienced a rapid progression 5 days later (b; tumor regrowth ); after which, the patient resumed lenvatinib plus everolimus treatment and experienced a rapid improvement (as indicated by the brain MRI taken approximately 2 weeks later) (c).



MRI, magnetic resonance imaging; mRCC, metastatic renal cell carcinoma.