

**Supplementary Table 1 - Literature review of ESC RCC cases**

	Author, year	Gender	Age	tumor size	metastase	stage/clinical outcome	PAX-8/CK20/CK7	genetic changes	Notes
1	Trpkov, 2016	16 females	Median 57 (31-75 y)	Median 38.5mm (15-135mm)	None	13 pT1, 2 pT2, 1 pT3a; 13/14 patients were alive and without evidence of disease progression, 1 died of other causes	PAX-8(+); 14/16 CK20(+) (11/14 diffuse, 3/14 focal); 4/16 CK7(+) focal	CN gains: 1p, 7p-q, 10q, 13q, 16p-q (2/3 cases); CN losses: 19p, 19q, Xp, Xq (2/3 cases); LOH: 16p and Xq (3/3 cases), 11p (2/3 cases). (3 cases Molecular Karyotyping)	
2	Trpkov, 2017	19 females (16 cases were reported previously)	Median 55 (32-79 y)	Median 31mm (12-135mm), 1/19 multifocal	None	17 pT1, 1 pT2a, 1 pT3a; 15/16 patients were alive and without evidence of disease progression, 3 died of other causes	PAX-8(+); 14/19 CK20(+) (11/14 diffuse, 3/14 focal); 6/9 CK7(+) focal	CN gains: 16p13-16q23, 7p21-7q36, 13q14 and 19p12; CN losses: Xp11.21 and 22q11; LOH: 16p11.2-11.1, Xq11-13, Xq13-21, 11p11, 9q21-22, and 9q33; LOH alterations at TSC1 and CN gains at TSC2. (12 cases Molecular Karyotyping)	
3	Li, 2018	6 females, 4 males	Median 27 (14-35 y)	Median 24mm (5-90mm), 4/10 multifocal ( 1 bilateral)	1 patient with the lung and liver metastases	8 pT1, 1 pT2, 1 pT4; 2/10 without evidence of disease progression	10/10 CK20(+) focal	N/A	2/10 patients had a history of a prior malignancy (bladder and CNS)

4	McKenney, 2018	1 female	69	150mm	1/3 hilar lymph nodes metastase	N/A	PAX-8(+), CK20(+), CK7(-)	N/A	
5	Parilla, 2018	2 females	65 and 33	115mm and 17mm	None	no tumor progression	PAX-8(+); CK20(+) diffuse; 1/2 CK7(+) variable	TSC2 mutations (somatic confirmed in one case) (NGS)	
6	Palsgrove, 2018	12 females, 4 males (10 cases were reported by Li <i>et al</i> )	Median 46.5 (42-66 y) (new cases)	Median 38mm (18-115mm) (new cases), 5/10 multifocal ( 1 bilateral) (prior cases)		N/A	4/6 CK20(+) focal (new cases)	14/15 TSC mutations (somatic confirmed in one case) (NGS)	Liver metastases in a case responded to mTOR inhibitor and the patient remains stable with no evidence of disease 8 yr later (comment by Pedram Argani).
7	Tretiakova, 2018	3 females, 1 male	Median 46 (27-50 y)	Median 50mm (15-205mm)	1 patient with two bone metastases and 1 patient with invasion of adrenal gland and retroperitoneum	1 pT1N0M1, 1 pT4N0Mx, 2 pT1N0M0; 2 younger patients had no signs of tumor recurrence	PAX-8(+); 4/4 CK20(+) (3/4 diffuse, 1/4 focal); 1/4 CK7(+) focal	0/1 TSC mutation (NGS)	
8	Mehra, 2018	6 females, 1 male	Median 63 (37-76 y)	Median 44mm (19-75mm)	None	3 pT1a, 3 pT1b, 1 pT2a	N/A	6/7 somatic bi-allelic loss of TSC1 or TSC2 genes	mTOR activation by immunohistochemistry.

9	Cho, 2019	1 female	46	50mm	None	pT1b	CK20(-), CK7(-)	TSC1 mutation (germline)	TSC-associated ESCRCC, with 2 synchronous angiomyolipomas including 1 AMLEC. mTOR activation by immunohistochemistry
10	Mohaghegh Poor, 2021	2 females	38 and 44	35mm and 40mm	None	2 T1N0M0, no evidence of ecurrent tumor or distant metastases	PAX-8(+), CK20(+) focal, CK7(-)	N/A	the 38-year-old patient with a concurrent clear cell RCC
11	Lerma, 2021	2 females, 3 males	Median 51.5 (49-54 y)	Median 19mm (11-50mm), 2/5 multifocal	None	3 pT1, 1 pT2, 1 pT3;3 patients with no evidence of disease, 1 died of other causes, 1 with follow-up not available	4/4 CK20(+) (3/4 diffuse, 1/4 rare), 1/4 CK7(+) focal	3/5 TSC1 mutation (2 germline and 1 somatic) (NGS)	co-existence of ESCRCC, EVT, LOT, RCC-FMS, and AML as synchronous and metachronous tumors
12	Kamboj, 2021	1 female	55	27mm	None	T1aNx, no evidence of disease	PAX-8(+), CK20(-), CK7(-)	N/A	
13	Wang, 2021	1 female	52	40mm	N/A	N/A	CK20(+), CK7(-)	N/A	

14	Sakhadeo, 2021	2 females, 1 male	55, 62, 61	155mm, 106mm, 87mm	1 patient with the liver and omentum metastases, 1 patient with the perinephric space and perihilar nodes metastases, 1 patient with invading the renal sinus and extending into the left renal vein.	3 M1	3/3 CK20(+) (1/3 diffuse, 2/3 focal), 1/3 CK7(+) focal	N/A	Two patients were referred for oral tyrosine kinase inhibitor (TKI) therapy.
15	Munari, 2022	4 females	Median 61 (50-74 y)	Median 31.5mm (20-50mm)	None	3 pT1a, 1 pT1b, no evidence of disease	PAX-8(+), 4/4 CK20(+) focal, 4/4 CK7(-)	4/4 TSC1 mutations (germline confirmed in one case) (NGS)	the MTOR mutation in one case
16	Aldera, 2022	1 male	19	N/A	None	N/A	PAX-8(+), CK20(+) diffuse, CK7(-)	TSC2 mutation (NGS)	
17	Lobo, 2022	6 females	Median 57.5 (6-83 y)	Median 45.5mm (10-73mm)	None	4 pT1, 1 pT2, 1 localised	PAX-8(+), 6/6 CK20(+) focal, 2/6 CK7(+) single cells	1/5 TSC1 mutations, 1/5 TSC2 mutation (NGS)	
18	Sharma, 2022	1 female	67	195mm	None	pT2bN0	PAX-8(+), CK20(+) focal, CK7(-)	N/A	Sarcomatoid differentiation in the form of spindling (10%) and areas of necrosis (40%) were seen.

Abbreviations: CN, copy number; LOH, loss of heterozygosity; NA, not available; FISH, fluorescence in-situ hybridization; IHC, immunohistochemistry.