

Metastatic Tumor Diameter Response in patients Clear Cell Renal Cell Carcinoma Is Associated with Overall Survival

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Purpose:

Prior studies have shown that tumor shrinkage of $\geq 10\%$ with presurgical targeted molecular therapy (TMT) in renal cell carcinoma (RCC) was associated with better overall survival (OS) outcomes. To assess whether type of preoperative systemic therapy affects OS, we characterized primary and metastatic tumor diameter response and OS in patients with metastatic clear cell RCC who received preoperative therapy with TMT, immunotherapy (IO), or IO+TMT followed by deferred cytoreductive nephrectomy (dCN).

Materials and Methods:

We retrospectively reviewed our institutional database and identified 211 patients with metastatic clear cell RCC (ccRCC) who received preoperative TMT, IO, or IO+TMT followed by dCN between 2005 and 2019. Primary and metastatic tumor longest diameters from cross-sectional images obtained at initial diagnosis and before dCN were calculated using RECIST 1.1. Patient characteristics were summarized by using descriptive statistics. OS was calculated using the Kaplan-Meier method. Cox proportional hazards models were applied to assess the association between patient characteristics and OS.

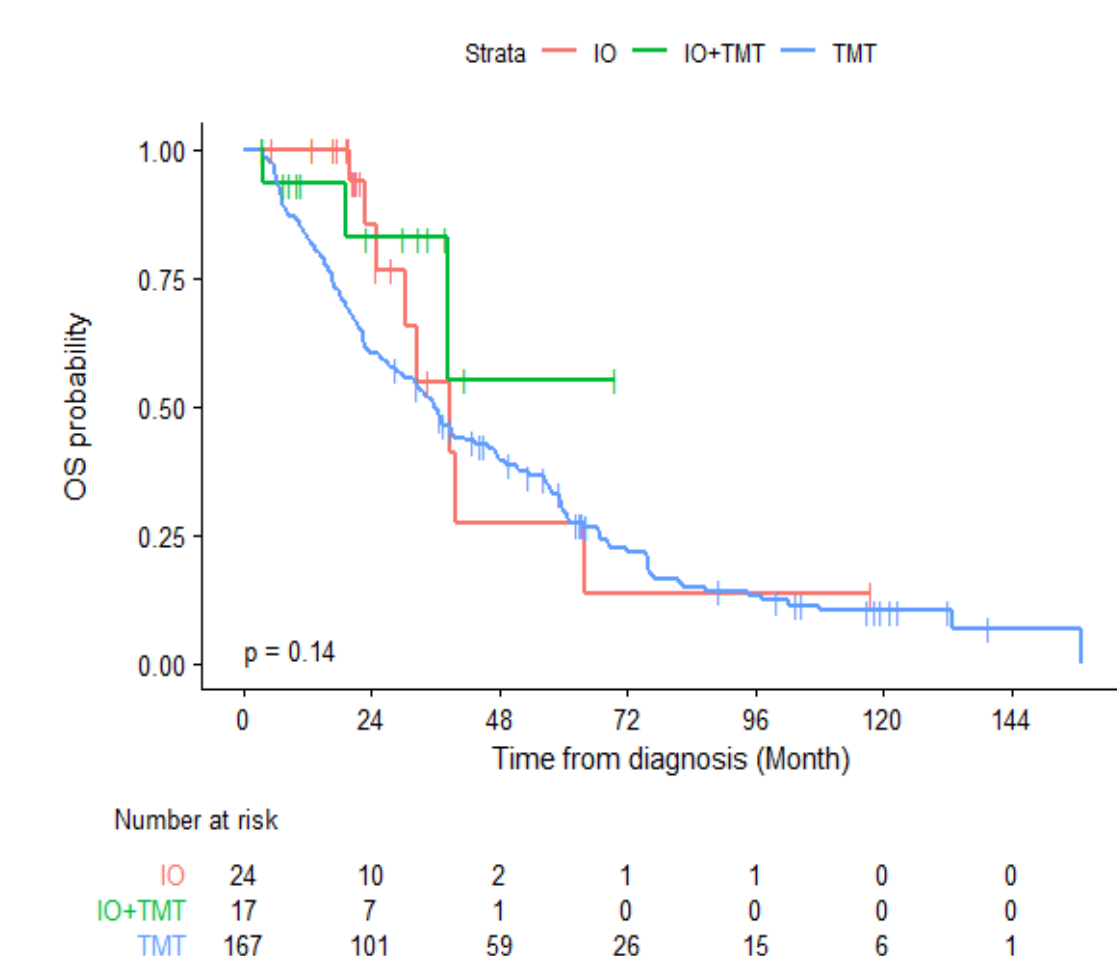
Table 1. Demographics

Patient Characteristics	Total (N=211)	IO (N=25)	IO+TMT (N=17)	TMT (N=169)	P-value
Age, y, median (IQR)	60.75 (52.9, 66.8)	62 (48, 67)	65 (59-71)	60.34 (52.8, 65.7)	0.05
Gender, No. (%)					
Female	55 (26.07%)	3 (12%)	4 (23.53%)	48 (28.4%)	0.22
Male	156 (73.93%)	22 (88%)	13 (76.47%)	121 (71.6%)	
ECOG Performance, No. (%)					
0	100 (47.39%)	18 (72%)	10 (58.82%)	72 (42.6%)	0.06
1	105 (49.76%)	7 (28%)	6 (35.29%)	92 (54.44%)	
2	5 (2.37%)	0 (0.00%)	1 (5.88%)	4 (2.37%)	
3	1 (0.47%)	0 (0.00%)	0 (0.00%)	1 (0.59%)	
Clinical T category, No. (%)					
T1a	10 (5%)	1 (4.17%)	3 (17.65%)	6 (3.77%)	0.03
T1b	35 (17.5%)	8 (33.33%)	0 (0.00%)	27 (16.98%)	
T2a	41 (20.5%)	2 (8.33%)	6 (35.29%)	33 (20.75%)	
T2b	27 (13.5%)	4 (16.67%)	1 (5.88%)	22 (13.84%)	
T3a	54 (27%)	6 (25%)	5 (29.41%)	43 (27.04%)	
T3b	31 (15.5%)	3 (12.5%)	1 (5.88%)	27 (16.98%)	
T3c	2 (1%)	0 (0.00%)	1 (5.88%)	1 (0.63%)	
Clinical N category, No. (%)					
N0	98 (46.45%)	13 (52%)	8 (47.06%)	77 (45.56%)	0.85
N1	113 (53.55%)	12 (48%)	9 (52.94%)	92 (54.44%)	
Median overall tumor diameter reduction, mm (IQR); N = 210	9.5 (-0.5, 21.5)	13.5 (2.9, 21.5)	9.75 (3.8, 13.5)	9.5 (-1, 22)	0.76
Primary tumor shrinkage $\geq 10\%$, No. (%)	87 (41.43%)	11 (44%)	10 (62.5%)	66 (39.05%)	0.18
Metastatic tumor shrinkage $\geq 10\%$, No. (%)	129 (64.18%)	18 (75%)	8 (72.73%)	103 (62.05%)	0.44

Table 2. Pathological features

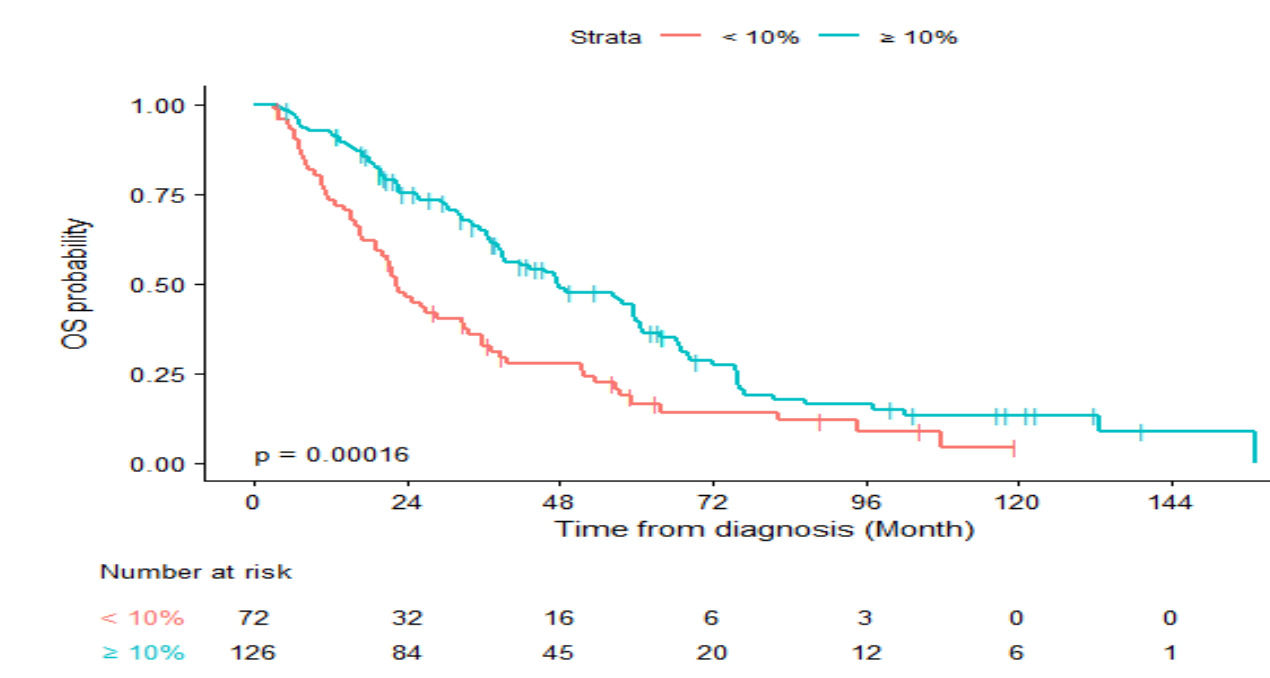
Tumor Characteristics	Total (N=211)	IO (N=25)	IO+TMT (N=17)	TMT (N=169)	P-value	
Pathologic T category, No. (%)						
T1a	4 (1.9%)	0 (0.00%)	1 (5.88%)	3 (1.78%)	0.64	
T1b	21 (9.95%)	1 (4%)	1 (5.88%)	19 (11.24%)		
T2a	8 (3.79%)	1 (4%)	1 (5.88%)	6 (3.55%)		
T2b	3 (1.42%)	0 (0.00%)	0 (0.00%)	3 (1.78%)		
T3a	127 (60.19%)	19 (76%)	11 (64.71%)	97 (57.4%)		
T3b	25 (11.85%)	3 (12%)	1 (5.88%)	21 (12.43%)		
T3c	2 (0.95%)	0 (0.00%)	1 (5.88%)	1 (0.59%)		
T4	21 (9.95%)	1 (4%)	1 (5.88%)	19 (11.24%)		
Grade, No. (%)						
2	25 (11.96%)	1 (4%)	5 (29.41%)	19 (11.38%)	0.01	
3	83 (39.71%)	14 (56%)	9 (52.94%)	60 (35.93%)		
4	101 (48.33%)	10 (40%)	3 (17.65%)	88 (52.69%)		
Sarcomatoid, No. (%)	Yes	35 (16.59%)	6 (24%)	1 (5.88%)	28 (16.57%)	0.35
Tumor thrombus, No. (%)	Yes	57 (27.01%)	7 (28%)	6 (35.29%)	44 (26.04%)	0.63
Pathologic N category, No. (%)	N1	48 (34.04%)	4 (25%)	3 (23.08%)	41 (36.61%)	0.5

FIGURE 1



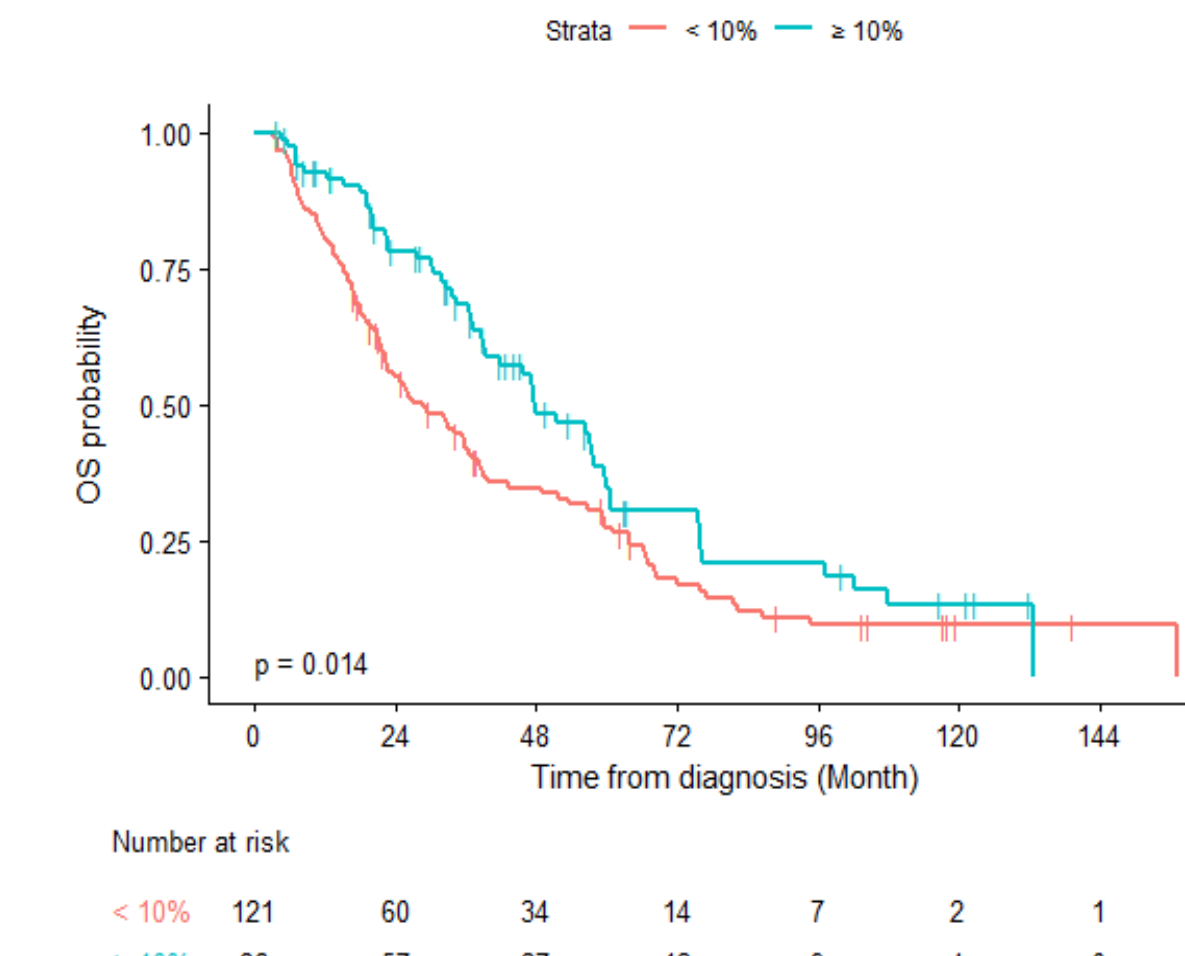
Kaplan-Meier curves of overall survival in patients who received preoperative systemic therapy with IO, IO+TMT, or TMT followed by cytoreductive nephrectomy

FIGURE 3



Kaplan-Meier curves of overall survival in patients who had metastatic tumor shrinkage of $\geq 10\%$ and $< 10\%$ after preoperative systemic therapy followed by cytoreductive nephrectomy

FIGURE 2



Kaplan-Meier curves of overall survival in patients with primary tumor shrinkage of $\geq 10\%$ and $< 10\%$ after preoperative systemic therapy followed by cytoreductive nephrectomy

Table 3. Univariable and multivariable Cox regression analysis for OS

Characteristic		Univariable		Multivariable	
		HR (95% CI)	P-value	HR (95% CI)	P-value
Age		0.99 (0.98-1.01)	0.43		
Gender	Female vs. Male	0.86 (0.59-1.25)	0.42		
Pathologic T stage	T1b vs. T1a	1.51 (0.45-5.12)	0.51		
	T2a vs. T1a	0.45 (0.1-2.09)	0.31		
	T2b vs. T1a	0.62 (0.1-3.74)	0.6		
	T3a vs. T1a	0.78 (0.25-2.47)	0.67		
	T3b vs. T1a	0.95 (0.28-3.22)	0.94		
	T3c vs. T1a	0.47 (0.05-4.58)	0.52		
	T4 vs. T1a	0.93 (0.27-3.21)	0.91		
Pathologic stage	T3-T4 vs. T1-T2	0.8 (0.53-1.2)	0.28		
Tumor thrombus	Yes vs. No	0.89 (0.62-1.27)	0.52		
Sarcomatoid	Yes vs. No	1.17 (0.77-1.76)	0.46		
Primary tumor shrinkage $\geq 10\%$	Yes vs. No	0.66 (0.47-0.92)	0.01	0.71 (0.5-1.01)	0.06
Metastatic tumor shrinkage $\geq 10\%$	Yes vs. No	0.53 (0.38-0.74)	<0.001	0.59 (0.42-0.84)	0.003
Mean overall volume reduction		0.98 (0.97-0.99)	<0.001		
Preoperative therapy	IO vs. TMT	0.62 (0.3-1.27)	0.19	0.74 (0.36-1.52)	0.41
	IO+TMT vs. TMT	0.42 (0.13-1.31)	0.14	0.71 (0.22-2.25)	0.56

Results:

- 41.4% of patients had primary tumor shrinkage (PTS) of $\geq 10\%$, and 64.1% had metastatic tumor shrinkage (MTS) of $\geq 10\%$.
- Median OS, PTS of $\geq 10\%$, and MTS of $\geq 10\%$ were similar between the 3 groups ($P=0.14$; $P=0.18$; $P=0.44$).
- In patients with MTS of $\geq 10\%$, the median OS was 47.5 months compared with 22.5 months in the group with MTS of $< 10\%$ ($P<0.001$).
- On univariable analysis, PTS and MTS of $\geq 10\%$ were associated with better OS (HR 0.66, 95% CI 0.47-0.92, $P=0.01$; HR 0.53, 95% CI 0.38-0.74, $P<0.001$).
- On multivariable analysis, MTS of $\geq 10\%$ was associated with better OS (HR 0.59, 95% CI 0.42-0.84, $P=0.003$).
- Median follow up was 37.1 months.

Conclusions:

In patients with metastatic ccRCC, MTS of $\geq 10\%$ was associated with better OS outcomes in patients who underwent dCN, independent of the type of preoperative systemic therapy.