



678P: Cytoreductive nephrectomy (CN) for patients with metastatic sarcomatoid and/or rhabdoid (S/R) renal cell carcinoma (RCC) treated with immune checkpoint inhibitors (ICI)

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Introduction

- Recent clinical trials, such as CARMENA and SURTIME, have renewed the debate regarding the role of CN for patients with metastatic RCC (mRCC).^{1,2}
- Metastatic S/R clear cell RCC is an aggressive variant that historically had poor response to chemotherapy or targeted therapies.³ However, it responds well to ICI, which are the cornerstone of first-line treatment for mRCC.⁴⁻⁵
- The role of CN for metastatic S/R RCC in the checkpoint era has not been reported to date.
- Here, we evaluate CN outcomes in patients with metastatic S/R RCC treated with ICI.

Methods

- We retrospectively reviewed the records of patients with mRCC with sarcomatoid, rhabdoid, or sarcomatoid plus rhabdoid dedifferentiation who had primary renal tumor *in situ* at the time of metastatic disease and received an ICI-based regimen at MD Anderson Cancer Center.
- Clinical endpoints of interest were time on ICI therapy and OS from ICI initiation.
- A directed acyclic graph (DAG) was used to identify potential confounders to be adjusted in regression models.
- Hazard ratios (HR) and 95% confidence intervals (95% CI) were calculated using multivariable Cox regression models.

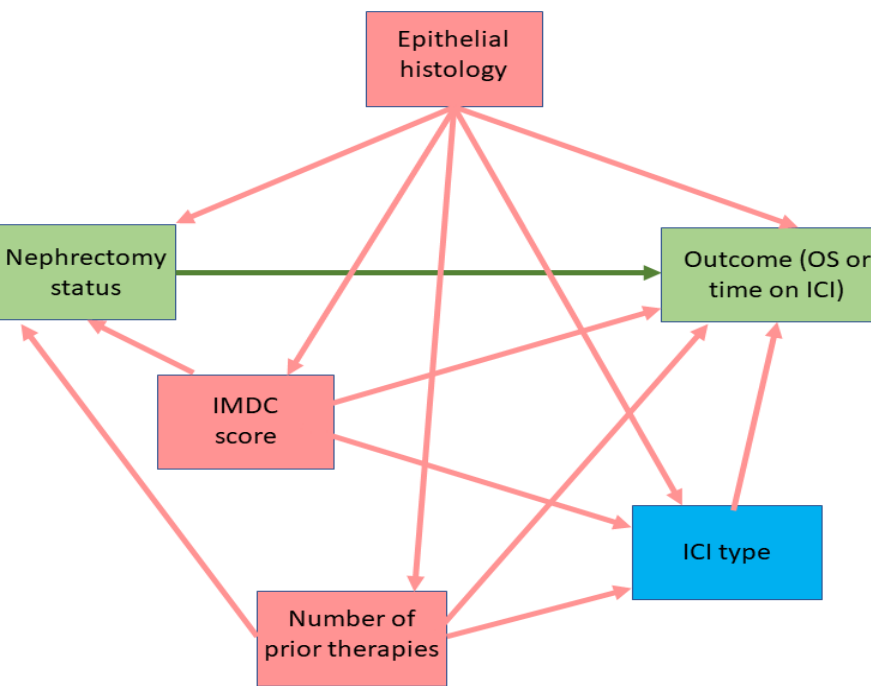


Figure 1. DAG of the causal relationships assumed in the regression models. Arrows indicate a causal interaction between two variables. The exposure of interest is nephrectomy status in metastatic S/R RCC. Red squares represent confounding variables that should be adjusted for to more accurately estimate the presumed causal effect of nephrectomy status on the outcomes of OS and time on ICI.

Results

Table 1: Multivariable analysis of clinical outcomes with ICI by CN status adjusted for epithelial histology, IMDC score and number of prior therapies.

Nephrectomy status	Median time on ICI (months)	HR (95% CI)	P value	Median OS from ICI initiation (months)	HR (95% CI)	P value
No nephrectomy (n=29)	5.1	-	-	14.0	-	-
CN (n=62)	7.7	0.59 (0.35-0.99)	0.046	29.0	0.54 (0.29-0.99)	0.048

Table 2: Baseline characteristics by dedifferentiation status

	Met. S RCC (n=42)	Met. R RCC (n=37)	Met. S+R RCC (n=12)	Met. S/R RCC (n=91)
Histology				
Clear cell	36 (85.7)	37 (100%)	12 (100%)	85 (93.4%)
Papillary	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Chromophobe	1 (2.4%)	0 (0%)	0 (0%)	1 (1.1%)
Unclassified	5 (11.9%)	0 (0%)	0 (0%)	5 (5.5%)
# metastases at ICI				
1	9 (21.4%)	7 (18.9%)	3 (25%)	19 (20.9%)
2-3	20 (47.6%)	29 (78.4%)	9 (75%)	58 (63.7%)
≥ 4	13 (31.0%)	1 (2.7%)	0 (0%)	14 (15.4%)
Systemic therapies pre-ICI				
0	26 (61.9%)	26 (70.3%)	9 (75%)	96 (67.0%)
1	14 (33.3%)	8 (21.6%)	2 (16.7%)	24 (26.4%)
≥ 2	2 (4.8%)	3 (8.1%)	1 (8.3%)	6 (6.6%)
Type of ICI				
Nivo + ipi	19 (45.2%)	14 (37.8%)	6 (50%)	39 (42.9%)
ICI + TKI	6 (14.3%)	10 (27.0%)	4 (33.3%)	20 (22.0%)
ICI monotherapy	16 (38.1%)	9 (24.3%)	2 (16.7%)	27 (29.7%)
ICI + other	1 (2.4%)	4 (10.8%)	0 (0%)	5 (5.4%)
IMDC risk score at ICI				
Favorable	1 (2.4%)	0 (0%)	0 (0%)	1 (1.1%)
Intermediate	26 (61.9%)	21 (56.8%)	7 (58.3%)	54 (59.3%)
Poor	15 (35.7%)	16 (43.2%)	5 (41.7%)	36 (39.6%)
Timing of CN				
Upfront	16 (38.1%)	17 (45.9%)	3 (25%)	36 (39.6%)
Delayed	12 (28.6%)	7 (18.9%)	7 (58.3%)	23 (25.3%)
None	14 (33.3%)	13 (35.1%)	2 (16.7%)	29 (31.9%)

Figure 2: Adjusted survival curves for OS by CN status

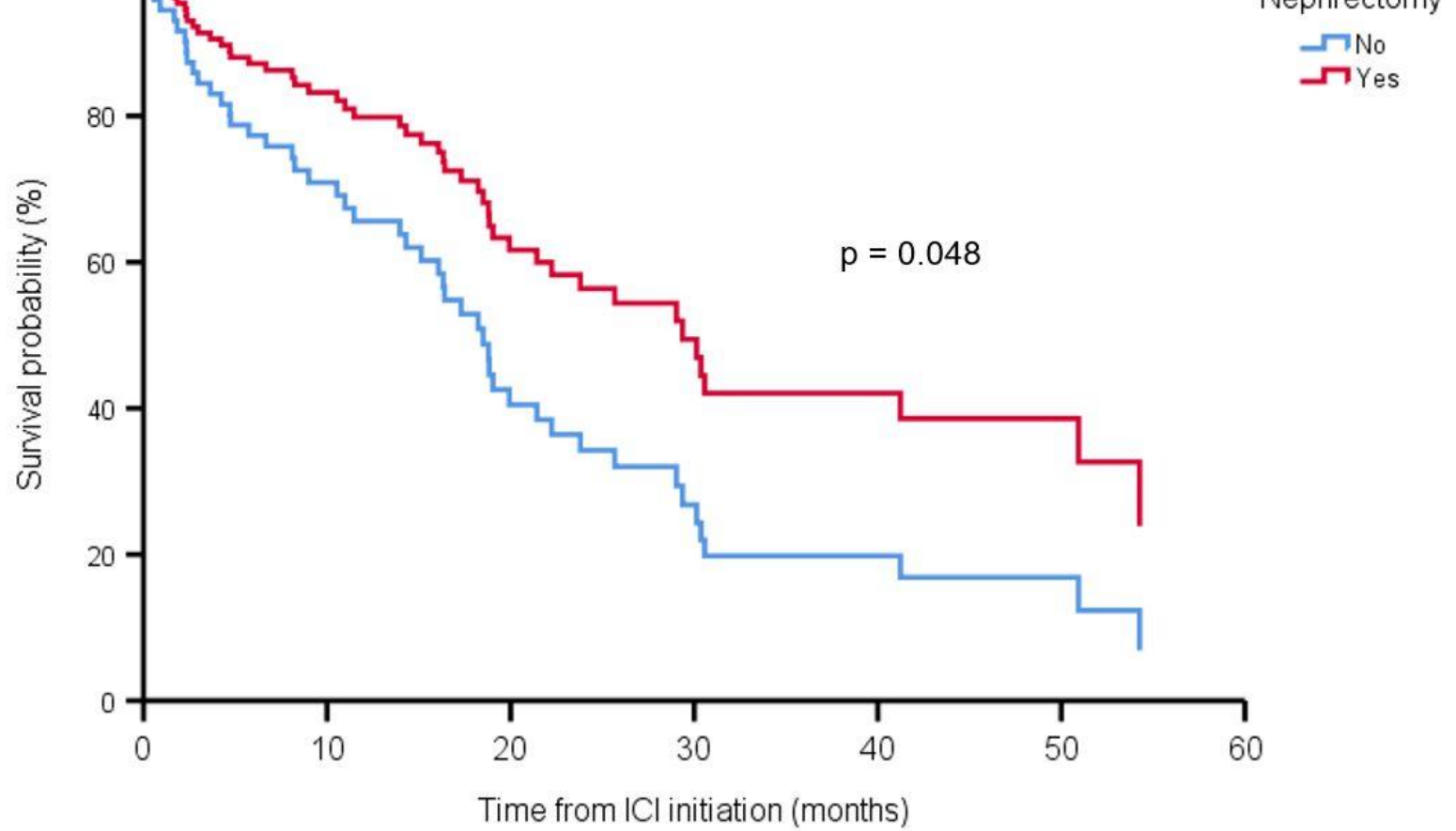
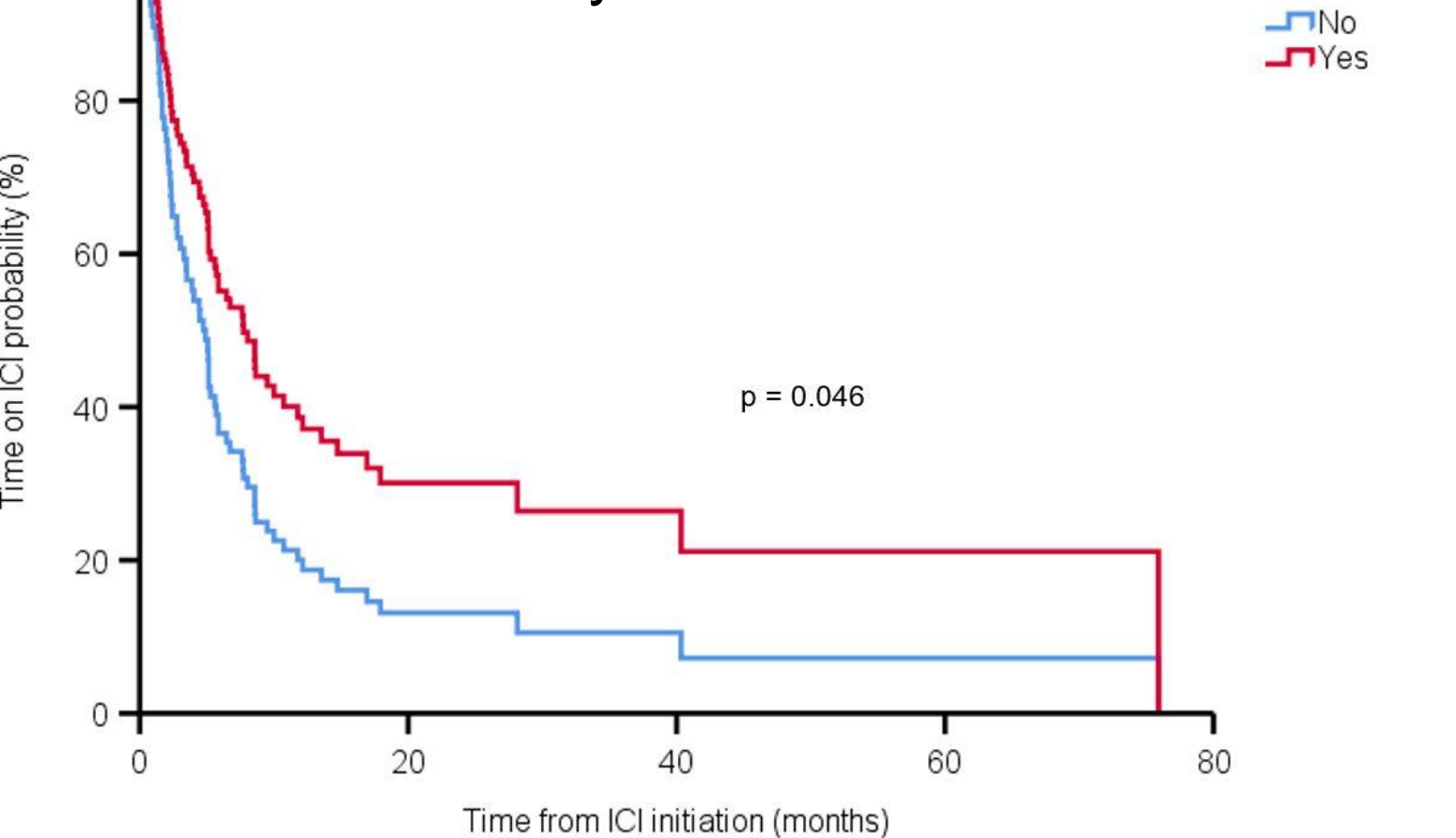


Figure 3: Adjusted survival curves for time on ICI by CN status



Conclusions

- Under the assumed analysis model, CN was independently associated with improved OS and time on ICI compared to not receiving a nephrectomy in patients with S/R RCC.
- This hypothesis-generating study suggests that CN should be considered in select patients with S/R RCC who respond to ICI.

Limitations/COI

- This retrospective analysis is based on the assumption that dedifferentiation subtype does not change the effect of CN on outcomes.
- Tumor response to ICI prior to CN is not reported, and this information could influence the results of the current analysis.
- Additionally, we do not report individual patient comorbidities and how these impacted the decision to perform CN.
- COI statement: Andrew W. Hahn has no conflicts of interest to disclose.

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