Clinical outcomes of patients with metastatic renal cell carcinoma with or without sarcomatoid differentiation treated with systemic therapies in real-world Canadian setting

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INTRODUCTION

- In 2020[1]
  - ❖431 288 new cases of kidney cancer
  - ❖179 368 deaths due to kidney cancer
- 15% of RCC are diagnosed as metastatic[2]
- 20% of metastatic RCC (mRCC) patients have sarcomatoid features[3]
  - ❖Contain features such as spindle cells, high cellularity and cellular atypia
  - ❖Aggressive form of RCC and associated with poor prognosis
- Systemic treatment for mRCC
  - ❖Targeted Therapy (TT)
    - ➢Tyrosine Kinase Inhibitors (TKI) and mTOR inhibitors
  - ❖Immunotherapy (IO)
    - ➢Used alone or in combination of IO-IO or IO-TKI
- TT was the standard systemic therapy for mRCC[4,5]
- In recent studies, it has been reported that sarcomatoid mRCC (smRCC) patients have better outcomes when treated with IO compared to TT[5]
  - ❖Checkmate 214 (Post-hoc analysis)[6]
  - ❖Keynote 426 (Post-hoc analysis)[7]
  - ❖Checkmate 9ER (Post-hoc analysis)[8]

OBJECTIVE

- Evaluate the impact of first-line systemic therapies on survival of mRCC patients with or without sarcomatoid features using real-world data

METHODS

- The Canadian Kidney Cancer information system (CKCis) database was used to identify patients diagnosed with mRCC between January 2011 and April 2022
- Criteria of selection (all criteria must have been met to be included)
  - ❖Patients with synchronous disease (metastases found within 3 months of primary tumor diagnosis or between 4 to 6 months)
  - ❖Intermediate or high-risk International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) criteria
  - ❖Confirmed histology of RCC with documentation of presence/absence of sarcomatoid features
- Included patients were separated in 2 groups
  - ❖TT-based treatment group
    - ➢ Presence of sarcomatoid features
    - ➢ Absence of sarcomatoid features
  - ❖IO-based treatment group
    - ➢ Presence of sarcomatoid features
    - ➢ Absence of sarcomatoid features
- Inverse probability of treatment weighting (IPTW) using propensity scores was used to balance the groups for:
  - ❖Sex
  - ❖Age
  - ❖Charlson comorbidity score
  - ❖Clear cell histology
  - ❖Cytoreductive Nephrectomy (before or after systemic treatment)
  - ❖IMDC risk category
  - ❖Sites and number of organs with metastasis
  - ❖Synchronous disease
- Cox proportional hazards models were used to assess the Overall Survival (OS) between TT and IO in patients with and without sarcomatoid features
- Analysis period started from the date of first treatment received to end of follow-up, which was the earliest between date of death, loss to follow-up or end of study period (April 30, 2022)
- The median of percentage sarcomatoid in the cohort is 10%

RESULTS

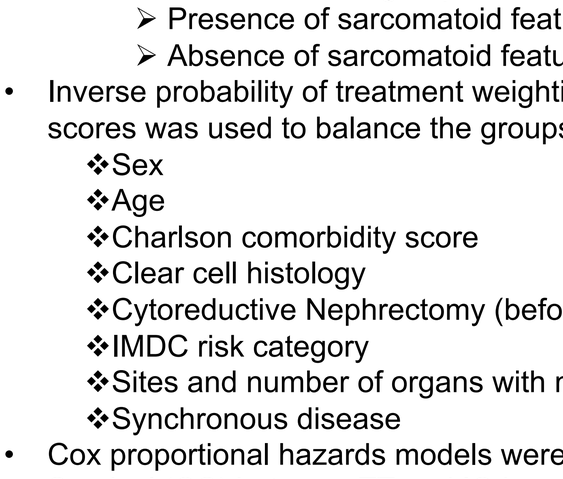


Figure 1. Number of included patients

- 90% of patients, treated with IO, were on combination treatment
- 1.3% of patients, treated with TT, were on combination treatment
- 63% of patients, treated with IO, were treated with Ipilimumab+Nivolumab
- 99% of patients, treated with TT, were treated with sunitinib or pazopanib

RESULTS (Continuation)

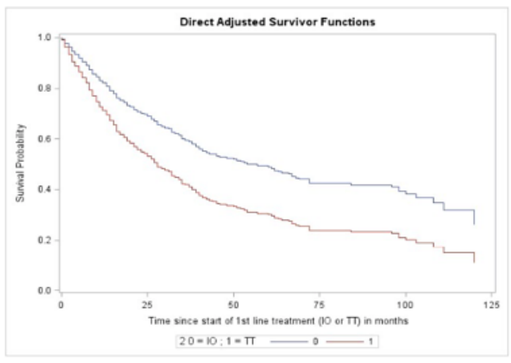
Table 1. Weighted cohort baseline characteristics for all patients

Variables	Treated with TT	Treated with IO	ASD
Number of organs with metastases; mean (sdev)	1.70 (1.00)	1.67 (0.96)	0.032
Sex; men	74	75	0.012
Age; 65 and older	39	38	0.033
Cytoreductive Nephrectomy; before systemic treatment	85	87	0.043
Sarcomatoid; yes	25	24	0.013
Charlson comorbidity; more than 1	57	59	0.028
IMDC; intermediate risk	66	66	0.0068
Clear cell histology; yes	85	84	0.053
Metastases in lungs; yes	62	62	0.0043
Metastases in brains; yes	3	3	0.0098
Metastases in liver; yes	11	10	0.021
Metastases in bones; yes	22	21	0.017
Synchronous disease; within 3 months	78	77	0.015

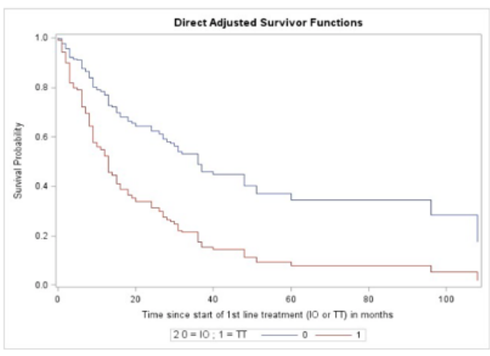
Data are presented in percentage unless otherwise noted. ASD: Absolute Standardized Difference; sdev: Standard Deviation; IMDC: International Metastatic Renal Cell Carcinoma Database Consortium

Table 2. Risk of death and Median Overall Survival

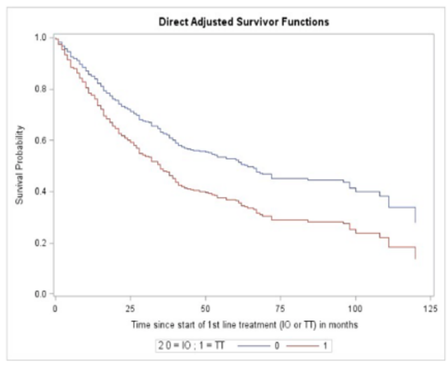
Assessments	Hazard Ratio	95% Confidence Interval	
All patients			
IO vs TT	0.58	0.43-0.78	60 vs 36 months in favor of IO
Sarcomatoid vs Non-sarcomatoid	2.07	1.66-2.58	
Patients with sarcomatoid features			
IO vs TT	0.40	0.23-0.69	36 vs 18 months in favor of IO
Percentage sarcomatoid (>10% vs ≤10%)	1.71	1.10-2.66	
Patients without sarcomatoid features			
IO vs TT	0.64	0.45-0.92	72 vs 36 months in favor of IO



A. All patients



B. Patients with sarcomatoid features



C. Patients without sarcomatoid features

Figure 2 (A-C). Direct Adjusted Survival Curves in the weighted cohorts

CONCLUSION

- mRCC patients with or without sarcomatoid features, who received IO-based treatments, **have longer survival** compared to patients who received TT-based treatments
- mRCC patients with sarcomatoid features **have 2.07 times the risk of death** compared to non-sarcomatoid mRCC patients
- smRCC patients with a percentage sarcomatoid >10% **are 71% more likely to die** compared to smRCC patients with a percentage sarcomatoid ≤10%

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POTENTIAL CONFLICTS OF INTEREST

Naveen S. Basappa: Honoraria/Advisory Board-Ipsen, Pfizer, BMS, Merck, Eisai, Janssen, Bayer, AstraZeneca, Roche/Travel grant-Eisai
Aly-Khan Lalani: Honoraria/Advisory Meetings-AbbVie, Astellas, Bayer, BMS, Eisai, Ipsen, Janssen, Merck, Novartis, Pfizer, Roche, TerSera, BMS (Inst), BioCanRx (Inst), Novartis (Inst), Roche (Inst), Ipsen (Inst), EMD Serrono (Inst)
Vincent Castonguay: Consultant-BMS, Ipsen, Esai, Merck