GUARD CONSORTIUM

GUARD SYMPOSIUM

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GU-Alliance for Research and Development

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Cáncer Renal avanzado: 1ª línea

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Summary of evidence	LE
Deferred CN with pre-surgical sunitinib in intermediate-risk patients with cc-mRCC shows a survival benefit in secondary endpoint analyses and selects out patients with inherent resistance to systemic therapy.	2b
Sunitinib alone is non-inferior compared to immediate CN followed by sunitinib in patients with MSKCC intermediate and poor risk who require systemic therapy with VEGFR-TKI.	1a
Cytoreductive nephrectomy in patients with simultaneous complete resection of a single metastasis or oligometastases may improve survival and delay systemic therapy.	3
Patients with MSKCC or IMDC poor risk do not benefit from CN.	1a
Patients with their primary tumour in place treated with IO-based combination therapy have better PFS and OS in exploratory subgroup analyses compared to treatment with sunitinib.	2b

EAU Guidelines 2023

Recommendations	Strength rating
Do not perform cytoreductive nephrectomy (CN) in MSKCC poor-risk patients.	Strong
Do not perform immediate CN in intermediate-risk patients who have an asymptomatic synchronous primary tumour and require systemic therapy.	Weak
Start systemic therapy without CN in intermediate-risk patients who have an asymptomatic synchronous primary tumour and require systemic therapy.	Weak
Discuss delayed CN with patients who derive clinical benefit from systemic therapy.	Weak
Perform immediate CN in patients with a good performance status who do not require systemic therapy.	Weak
Perform immediate CN in patients with oligometastases when complete local treatment of the metastases can be achieved.	Weak

EAU Guidelines 2023

Table 1 – Patient characteristics at the initiation of immune checkpoint inhibitors or targeted therapy stratified by CN status

	Immune checkpoint inhibitors		Targeted therapy	
	CN (*N* = 234)	No CN (*N* = 203)	CN (*N* = 2326)	No CN (*N* = 1876)
Age at systemic therapy initiation (yr), median (IQR)	60 (53–66)	63 (56–70)	61 (54–68)	63 (56–71)
Months from CN to systemic therapy initiation, median (IQR)	3.0 (1.8–7.4)		2.5 (1.4–6.2)	
Gender, *n* (%)				
Female	61 (26)	57 (28)	621 (27)	532 (28)
Male	172 (74)	146 (72)	1705 (73)	1344 (72)
Missing	1			
KPS, *n* (%)				
≥80	215 (95)	159 (82)	1678 (83)	1107 (68)
<80	11 (4.9)	34 (18)	338 (17)	519 (32)
Missing	8	10	310	250
IMDC, *n* (%)				
Favorable (0 risk factor)	18 (9.0)	1 (0.60)	106 (6.5)	22 (1.6)
Intermediate (1–2 risk factors)	143 (72)	78 (47)	983 (60)	612 (46)
Poor (≥3 risk factors)	39 (19)	88 (53)	547 (33)	707 (53)
Missing	34	36	690	535
Histology, *n* (%)				
Clear cell	204 (89)	110 (73)	1926 (85)	1167 (80)
Non–clear cell	26 (11)	41 (27)	351 (15)	293 (20)
Missing	4	52	49	416
Sarcomatoid features, *n* (%)				
No	137 (72)	111 (84)	1399 (75)	1035 (89)
Yes	53 (28)	21 (16)	476 (25)	127 (11)
Missing	44	71	451	714
Sites of metastasis, *n* (%)				
1	52 (23)	39 (20)	735 (32)	431 (24)
≥2	171 (77)	155 (80)	1528 (68)	1341 (76)
Missing	11	9	63	104
Presence of bone, brain, or liver metastases, *n* (%)				
No	108 (55)	48 (29)	921 (45)	576 (36)
Yes	87 (45)	120 (71)	1116 (55)	1032 (64)
Missing	39	35	289	268

CN = cytoreductive nephrectomy; IMDC = International Metastatic Renal Cell Carcinoma Database Consortium; IQR = interquartile range; KPS = Karnofsky Performance Scale.

Bakouny Z, Eur Urol. 2023; 83(2): 145

European Association of Urology

imdc

Platinum Priority – Kidney Cancer

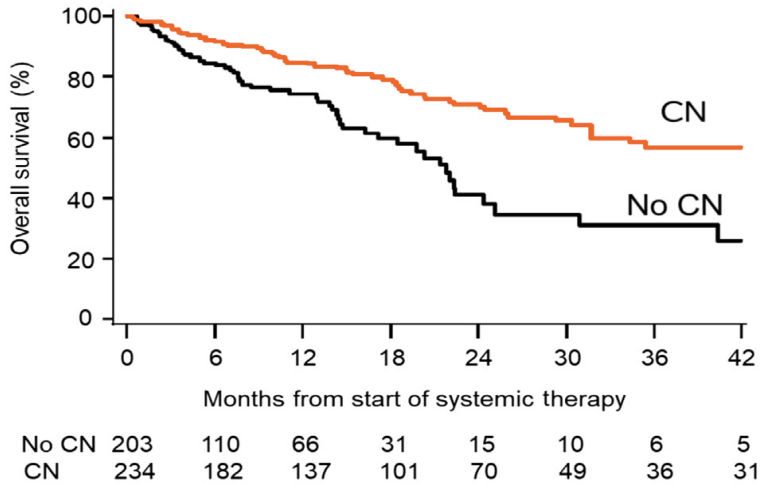
Editorial by Ithaar H. Derweesh, Rana R. McKay, Aditya Bagrodia on pp. 152–153 of this issue

Upfront Cytoreductive Nephrectomy for Metastatic Renal Cell Carcinoma Treated with Immune Checkpoint Inhibitors or Targeted Therapy: An Observational Study from the International Metastatic Renal Cell Carcinoma Database Consortium

With the recent approval of **immune checkpoint inhibitors for the treatment of mRCC**, the **impact of CN on clinical outcomes remains largely unknown**. Herein, we leveraged the **IMDC** to carry out a retrospective analysis of patients with mRCC who received either targeted therapies or immune checkpoint inhibitor–based regimens, to **examine the benefit of upfront CN in both settings.**

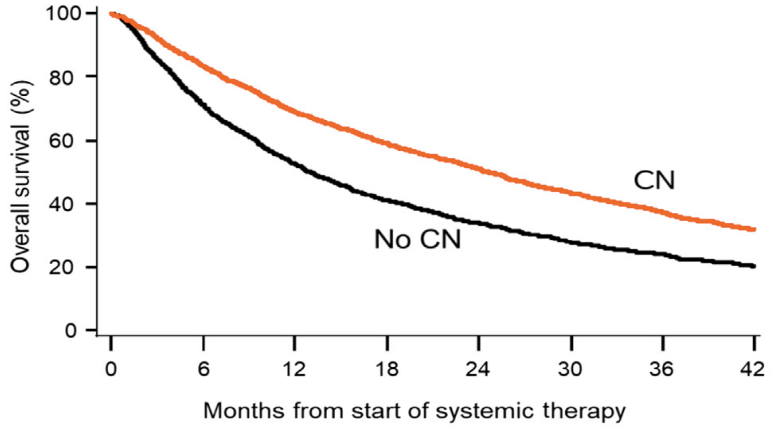
Bakouny Z, Eur Urol. 2023; 83(2): 145

(A) ICI based



No CN	203	110	66	31	15	10	6	5
CN	234	182	137	101	70	49	36	31

(B) TT based



No CN	1876	1263	861	616	462	349	274	202
CN	2326	1856	1444	1164	920	706	532	415

Bakouny Z, Eur Urol. 2023; 83(2): 145

- **Age**

- **IMDC**
  - ***Favorable (0 risk factors)***
  - ***Intermediate (1-2 risk factors)***
  - ***Poor (>3 risk factors)***

- **Not adverse metastases (liver, brain, bone)**

- **Good PFS**

- **Ongoing RCTs:**
  - ***NORDIC-SUN (NCT03977571):*** **nivo-ipi + deferred CN**
  - ***SWOG-1931 / PROBE (NCT04510597)*****: effect of CN in nivo-ipi / pembro-axi / avelu-axi**
  - ***CYTOSHRINK (NCT04090710)*****: nivo-ipi + cytoreductive SBRT**