Grupo Português
Génito - Urinário

XXVIII Workshop
Urologia Oncológica

Carcinoma de Células Renais

Decisão terapêutica em 1ª linha

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SCHOOL OF MEDICINE AND BIOMEDICAL SCIENCES

Disclosures

Honoraria (speaker/advisory/consultant): Merck Sharp & Dohme, Ipsen, Novartis, Roche, AstraZeneca, Lilly, Gilead

Travel/logistics support: Merck Sharp & Dohme, Ipsen, Roche, AstraZeneca, Lilly, Gilead, Grünenthal

GRUPOS DE PROGNÓSTICO EM CCR

Fatores relacionados com o paciente

- Fatores clínicos
  - estado general (PS)
  - clínica
- Fatores analíticos
  - LDH, Hb, Ca^{2+}
  - parâmetros inflamatórios: neutrofilia, trombocitose, PCR

Fatores relacionados com o tumor

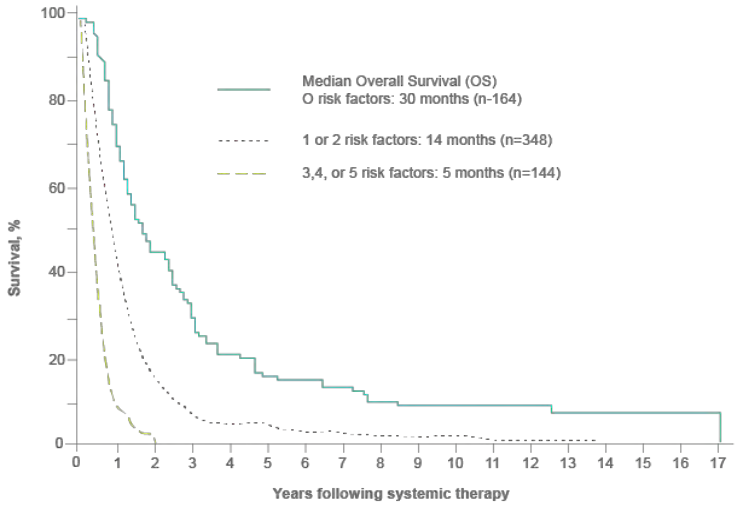
- Histologia
- Número de metástases
- Localização das metástases

Fatores relacionados com o tratamento

- Tratamentos recebidos (nefrectomia)
- Intervalo entre o diagnóstico e o início do tratamento

Motzer et al. JCO 1999.

MSKCC



KPS	<80%
Time from diagnosis to treatment with IFN-α	<12 months
Hemoglobin	<LLR
LDH	>1.5 x ULR
Corrected serum calcium	<10.0 mg/dL

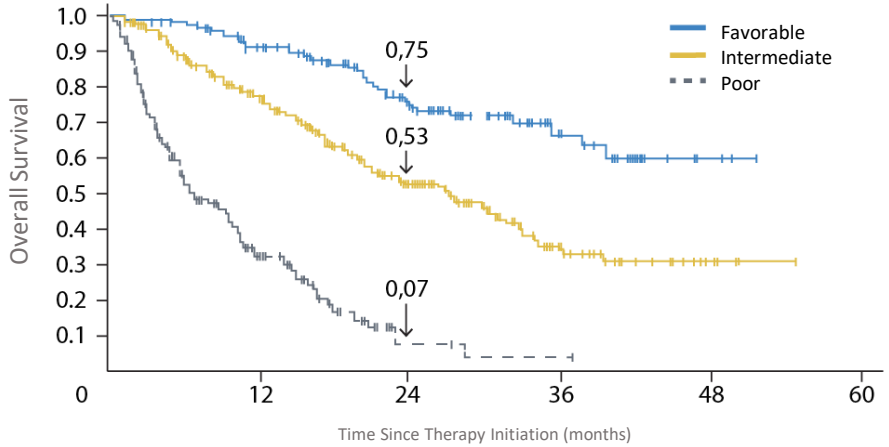
Favorable risk (18%) mOS 30m

Intermediate risk (62%) mOS 14m

Poor risk (20%) mOS 5m

Motzer et al. JCO 2002.

HENG / IMDC



Parameter	Hazard Ratio	*P*
Clinical		
KPS < 80%	2.51	< .0001
Time from diagnosis to treatment < 1 year	1.42	.0098
Laboratory		
Hemoglobin < LLN	1.72	.0001
Calcium > ULN	1.81	.0006
Neutrophil count > ULN	2.42	< .0001
Platelet count > ULN	1.49	.0121

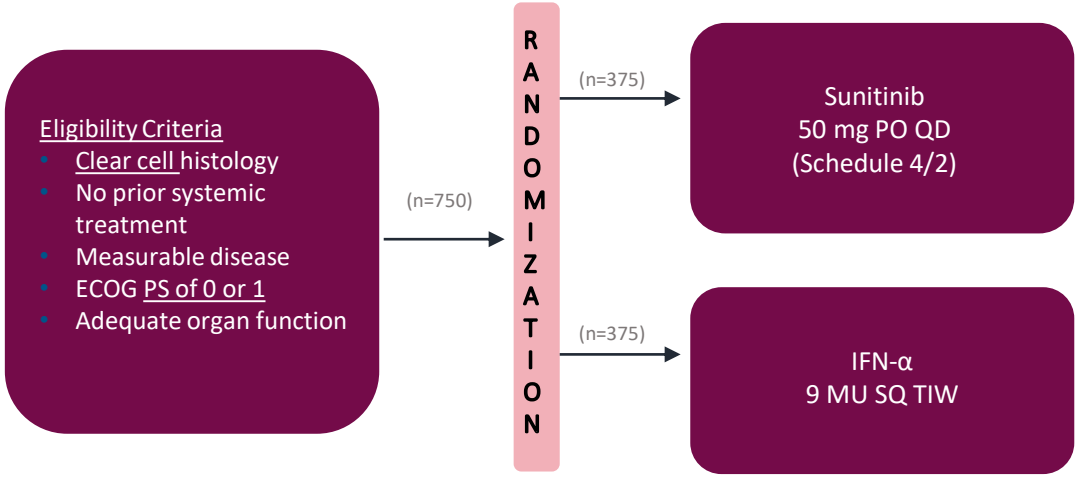
Favorable risk: 2y OS 75% | mOS 37m

Intermediate risk: 2y OS 53% | mOS 27m

Poor risk: 2y OS 7% | mOS 8.8m

Heng et al. JCO 2009.

SUNITINIB



Stratified: LDH (>1.5 vs. ≤1.5 LSN), ECOG PS (0 vs. 1) and nephrectomy (y/n)

Primary endpoint: Progression-free survival

Secondary endpoints: Response rate, overall survival, PROs, safety

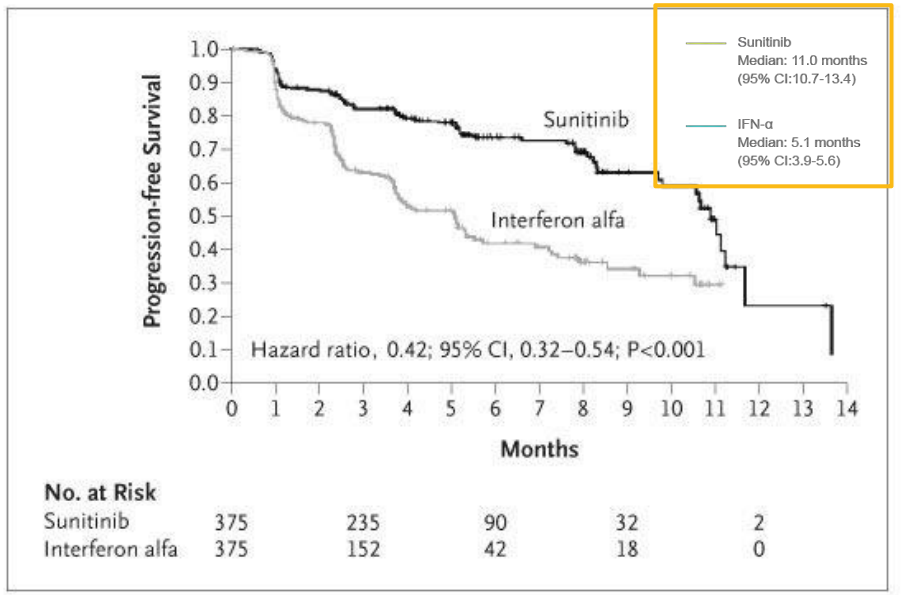


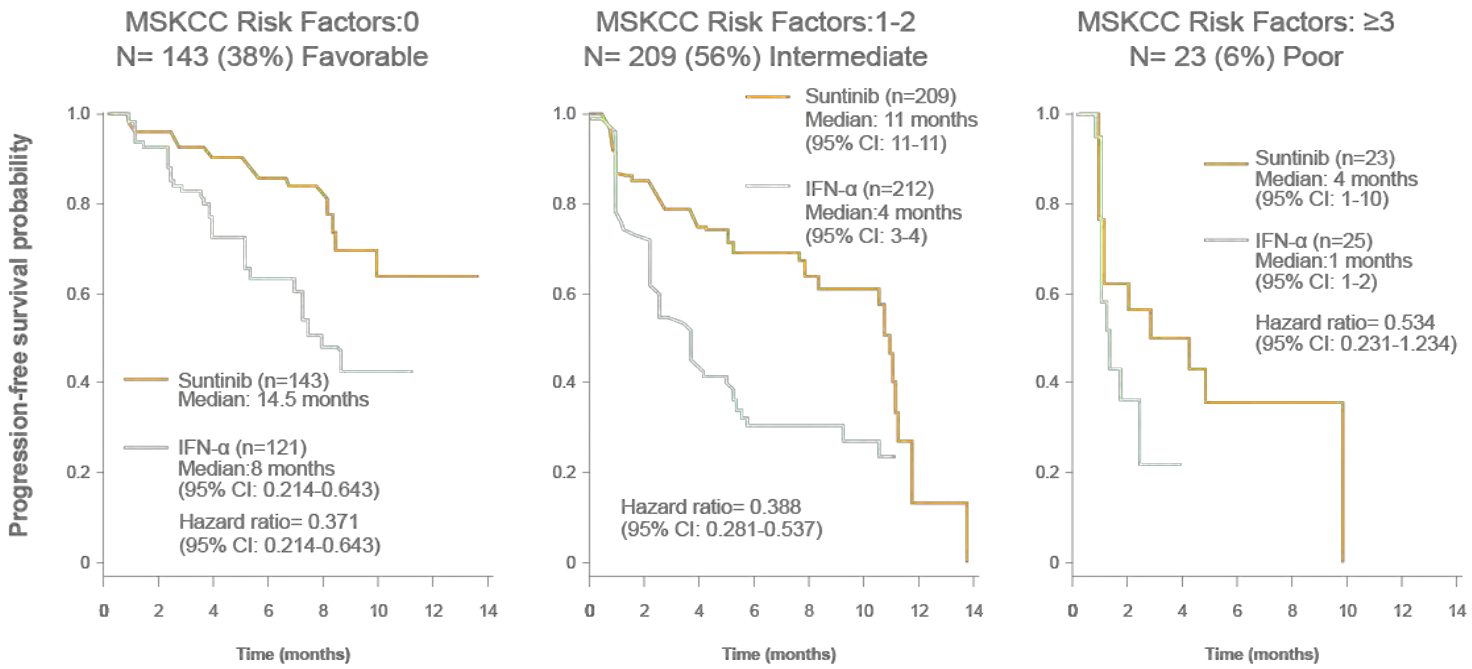
Table 3. Best Tumor Response.*

Response	Independent Central Review†		Investigator Assessment	
	Sunitinib (N=335)	Interferon Alfa (N=327)	Sunitinib (N=374)	Interferon Alfa (N=373)
	no. of patients (%)			
Objective response‡	103 (31)	20 (6)	137 (37)	33 (9)
Complete response	0	0	1 (<1)	0
Partial response	103 (31)	20 (6)	136 (36)	33 (9)
Stable disease	160 (48)	160 (49)	176 (47)	213 (57)
Progressive disease or disease could not be evaluated	72 (21)	147 (45)	61 (16)	127 (34)

Motzer et al. JCO 2007.

SUNITINIB

PROGRESSION-FREE SURVIVAL BY MSKCC RISK STATUS*



toxicidade G3-4:

neutropenia, trombocitopenia,

hiperamilasemia, diarreia, SPP e HTA

50% com necessidade de

redução de dose ou descontinuação

Motzer et al. JCO 2007.

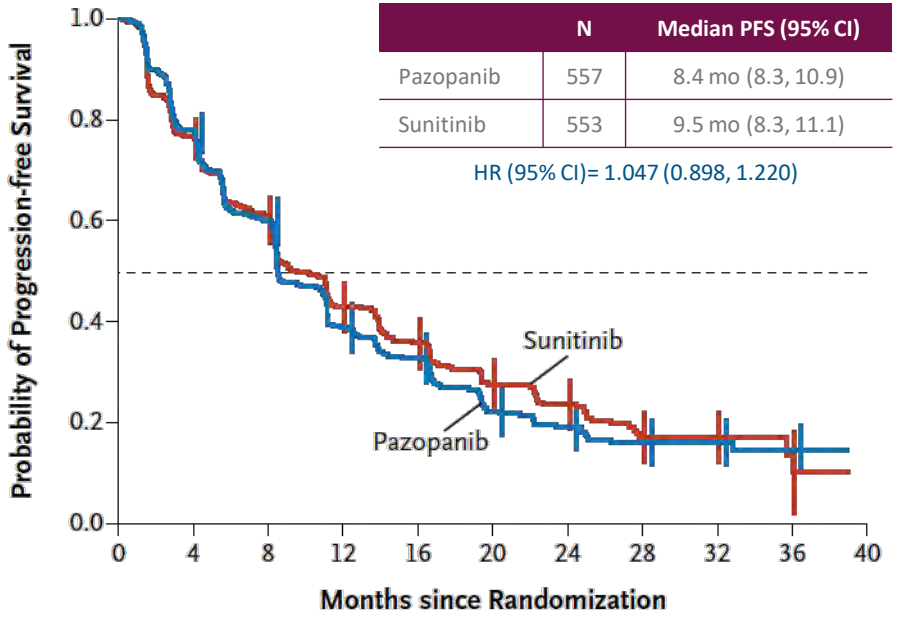
PAZOPANIB

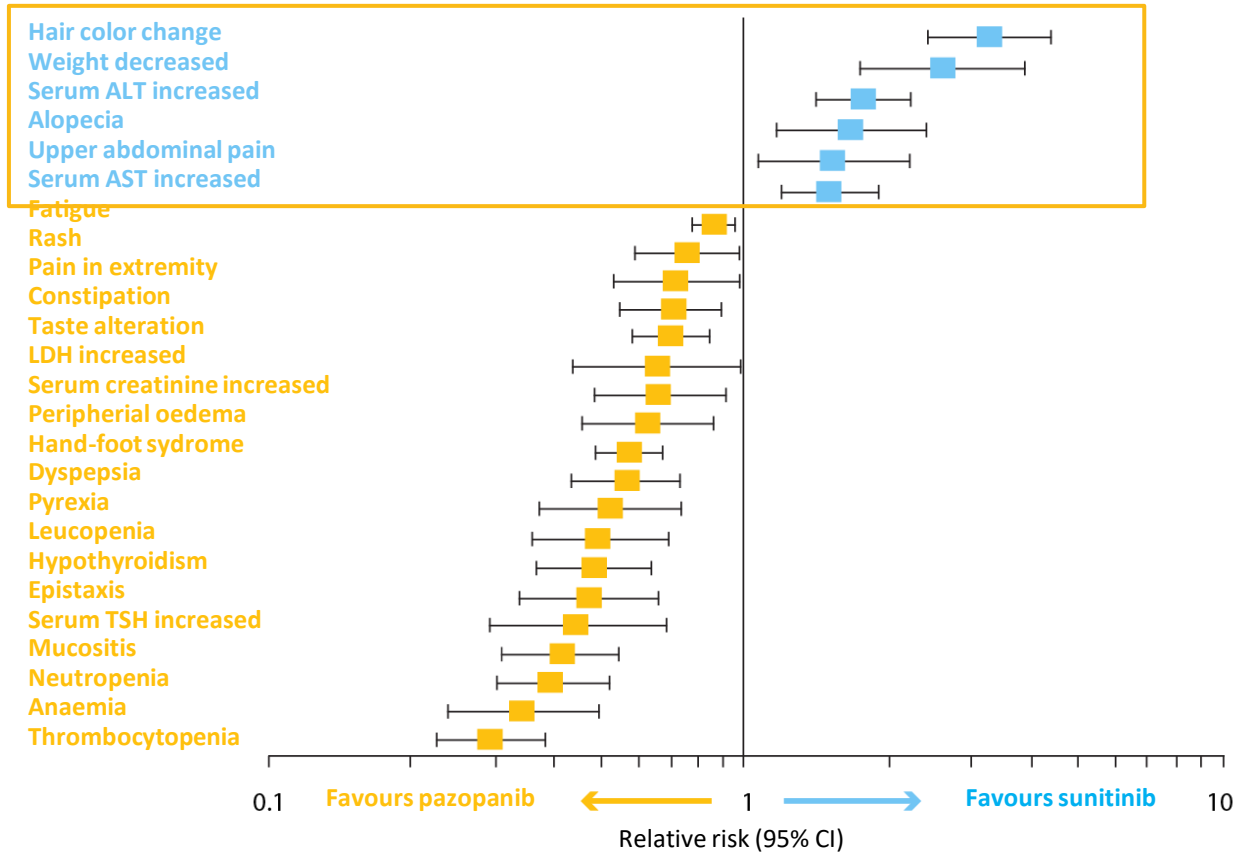
COMPARZ

Pazopanib não inferior a Sunitinib

	N	Median PFS (95% CI)
Pazopanib	557	8.4 mo (8.3, 10.9)
Sunitinib	553	9.5 mo (8.3, 11.1)

HR (95% CI)= 1.047 (0.898, 1.220)

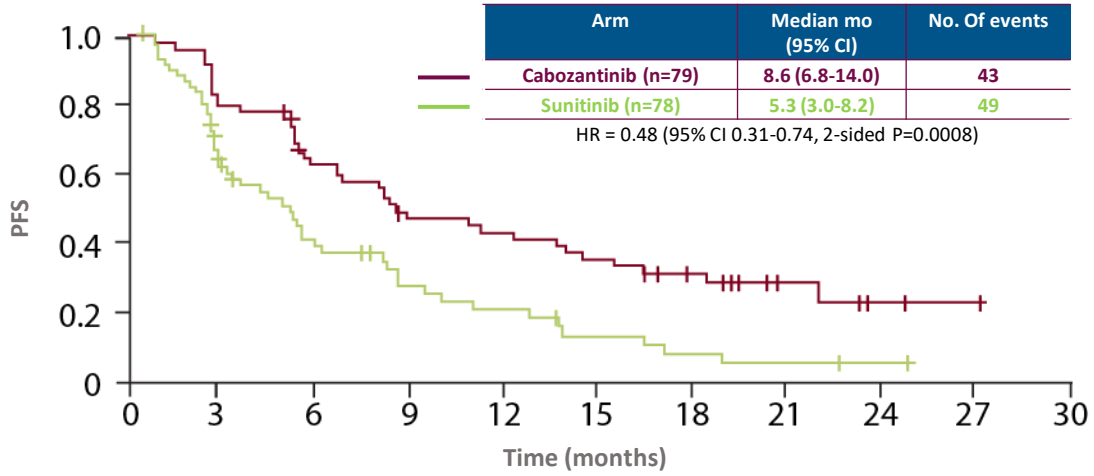




Motzer RJ. N Engl J Med. 2013 Aug 22;369(8):722–31.

CABOZANTINIB

CABOSUN phase 2

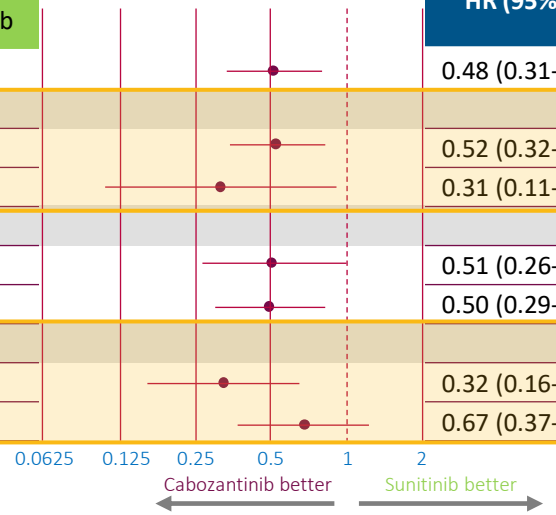


Arm	Median mo (95% CI)	No. Of events
Cabozantinib (n=79)	8.6 (6.8-14.0)	43
Sunitinib (n=78)	5.3 (3.0-8.2)	49

HR = 0.48 (95% CI 0.31-0.74, 2-sided P=0.0008)

No. of patients at risk									
Cabozantinib	79	51	37	24	22	18	12	5	2
Sunitinib	78	38	21	12	9	5	3	2	1

	N	Median PFS (months)		HR (95% CI)
		Cabozantinib	Sunitinib	
All patients	157	8.6	5.3	0.48 (0.31-0.74)
IMDC risk group				
Intermediate	127	11.4	6.1	0.52 (0.32-0.82)
Poor	30	6.8	2.7	0.31 (0.11-0.92)
Bone metastases				
Yes	57	5.5	3.3	0.51 (0.26-0.99)
No	100	11.4	5.7	0.50 (0.29-0.85)
MET status*				
Positive	62	13.8	3.0	0.32 (0.16-0.63)
Negative	69	6.9	6.1	0.67 (0.37-1.23)

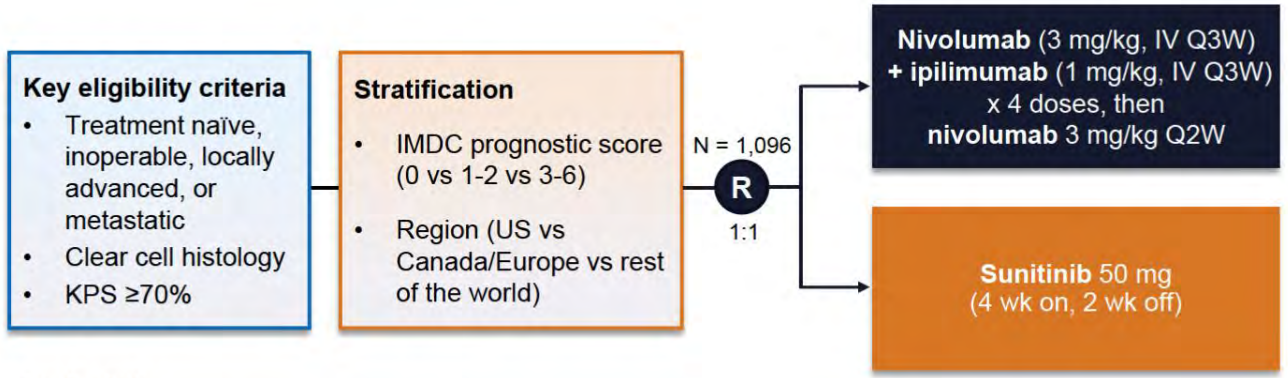


toxicidade G3-4 e
taxa de descontinuação semelhantes

Choueiri TK, et al. Eur J Cancer 2018;94:115–25.

NIVOLUMAB + IPILIMUMAB

CHECKMATE 214



Endpoints

- **Coprimary (intermediate/poor risk):** PFS, OS, ORR
- **Secondary:** safety

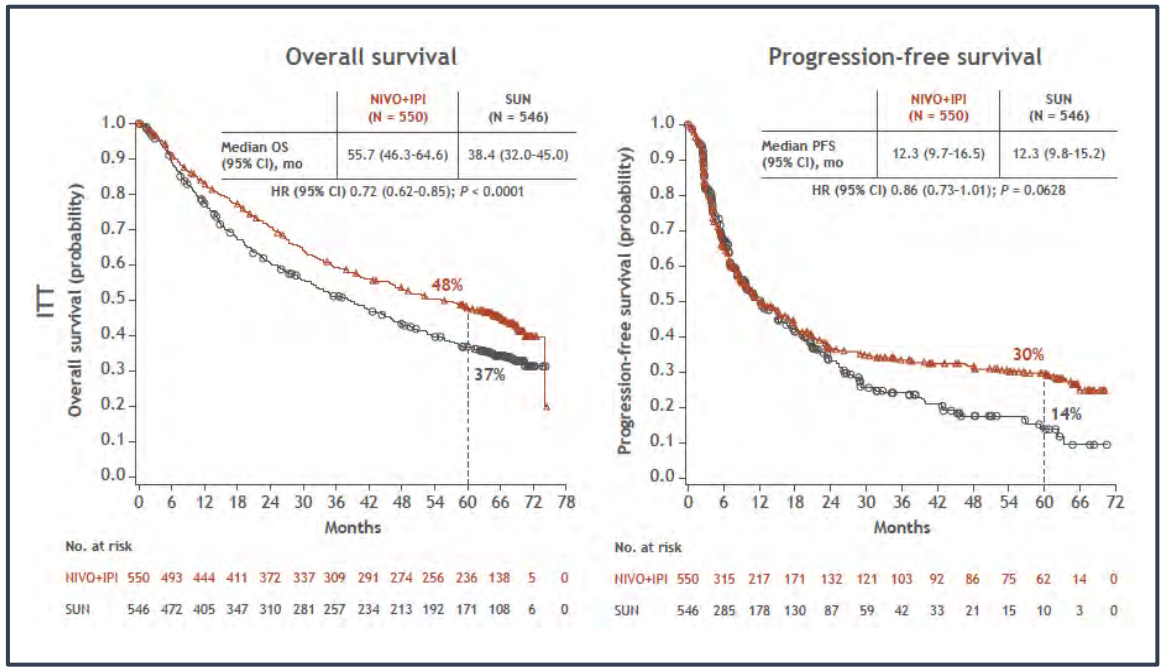
Table 1. Baseline Demographic and Clinical Characteristics of the Patients Who Underwent Randomization.*

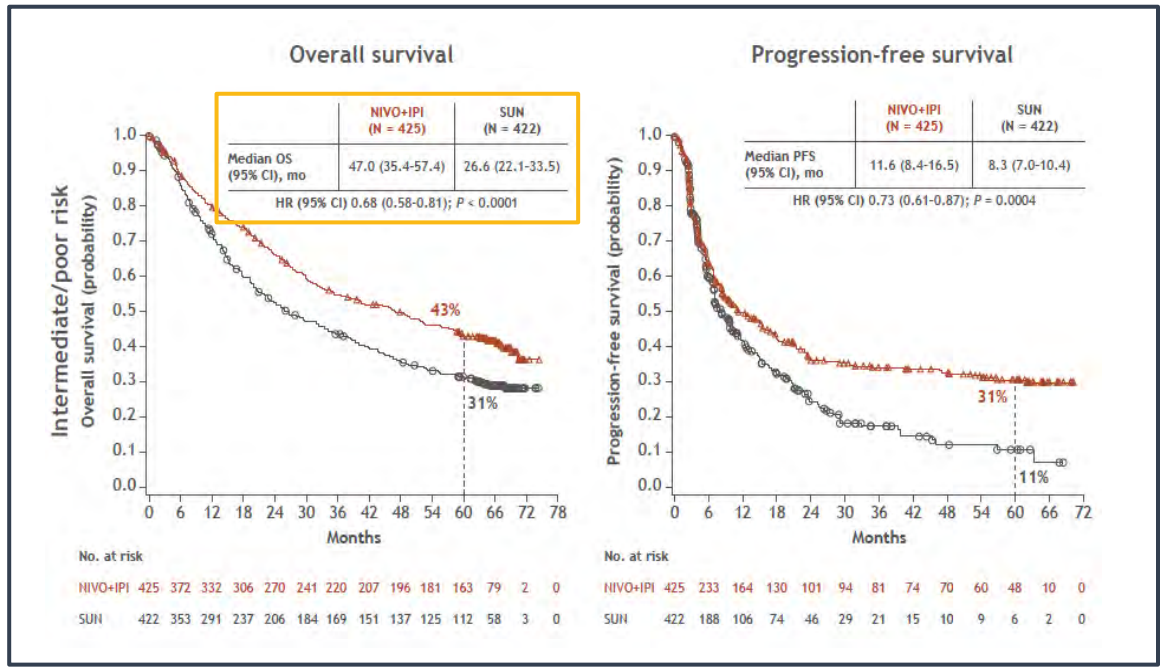
Characteristic	IMDC Intermediate- and Poor-Risk Patients		Intention-to-Treat Population	
	Nivolumab plus Ipilimumab (N=425)	Sunitinib (N=422)	Nivolumab plus Ipilimumab (N=550)	Sunitinib (N=546)
Median age (range) — yr	62 (26–85)	61 (21–85)	62 (26–85)	62 (21–85)
Sex — no. (%)				
Male	314 (74)	301 (71)	413 (75)	395 (72)
Female	111 (26)	121 (29)	137 (25)	151 (28)
IMDC prognostic risk — no. (%)†				
Favorable	0	0	125 (23)	124 (23)
Intermediate	334 (79)	333 (79)	334 (61)	333 (61)
Poor	91 (21)	89 (21)	91 (17)	89 (16)
Geographic region — no. (%)				
United States	112 (26)	111 (26)	154 (28)	153 (28)
Canada and Europe	148 (35)	146 (35)	201 (37)	199 (36)
Rest of the world	165 (39)	165 (39)	195 (35)	194 (36)
Quantifiable tumor PD-L1 expression — no./ total no. with evaluable data (%)				
<1%	284/384 (74)	278/392 (71)	386/499 (77)	376/503 (75)
≥1%	100/384 (26)	114/392 (29)	113/499 (23)	127/503 (25)
Previous radiotherapy — no. (%)	52 (12)	52 (12)	63 (11)	70 (13)
Previous nephrectomy — no. (%)	341 (80)	319 (76)	453 (82)	437 (80)
No. of sites with target or nontarget lesions — no. (%)‡				
1	90 (21)	84 (20)	123 (22)	118 (22)
≥2	335 (79)	337 (80)	427 (78)	427 (78)
Most common sites of metastasis — no. (%)				
Lung	294 (69)	296 (70)	381 (69)	373 (68)
Lymph node	190 (45)	216 (51)	246 (45)	268 (49)
Bone§	95 (22)	97 (23)	112 (20)	119 (22)
Liver	88 (21)	89 (21)	99 (18)	107 (20)

Motzer et al. at ESMO 2021.

NIVOLUMAB + IPILIMUMAB

CHECKMATE 214 (FU 5 anos)





Motzer et al. at ESMO 2021.

NIVOLUMAB + IPILIMUMAB

	NIVO + IPI		SUNITINIB	
Treratment-related event, %	**Any grade**	**Grade 3-4**	**Any grade**	**Grade 3-4[a]**
AEs in ≥25% of patients	**93**	**46**	**97**	**63**
Fatigue	37	4	49	9
Pruritus	28	<1	9	0
Diarrhea	27	4	52	5
Nausea	20	2	38	1
Hypothyroidism	16	<1	25	<1
Decreased appetite	14	1	25	1
Dysgeusia	6	0	33	<1
Stomatitis	4	0	28	3
Hypertension	2	<1	40	16
Mucosal inflammation	2	0	28	3
Hand-foot síndrome	1	0	43	9
Aes leading to discontinuation, %	**22**		**12**	
Deaths	**n=7[b]**		**n=4[c]**	

[a]Two patients had grade 5 cardiac arrest. [b]Pneumonitis, immune mediated bronchitis, lower GI hemorrhage, hemophagocytic síndrome, sudden death, liver toxicity, lung infection. [c]Cardiac arrest (n=2), heart failure, multiple organ faulire.

Motzer et al. NEJM 2018.

PEMBROLIZUMAB + AXITINIB

KEYNOTE 426

Key Inclusion Criteria

- Newly diagnosed or recurrent stage IV clear-cell renal-cell carcinoma.
- ≥ 1 measurable lesion per RECIST V1.1.
- No prior systemic therapy for advanced renal cell carcinoma.
- Karnofsky performace status ≥70.

Stratification factors

- IMDC risk group (favorable vs intermediate vs por).
- Geographic región (North America vs Western Europe vs Rest of World).

N=432

Randomization 1:1

N=429

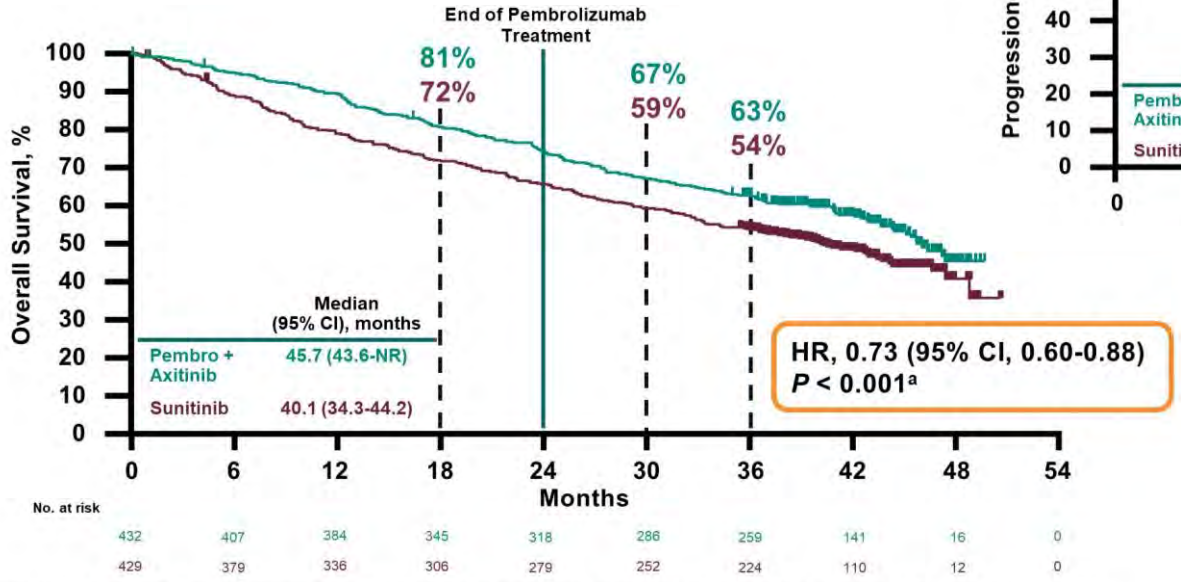
Table 1. Demographic and Disease Characteristics at Baseline.*

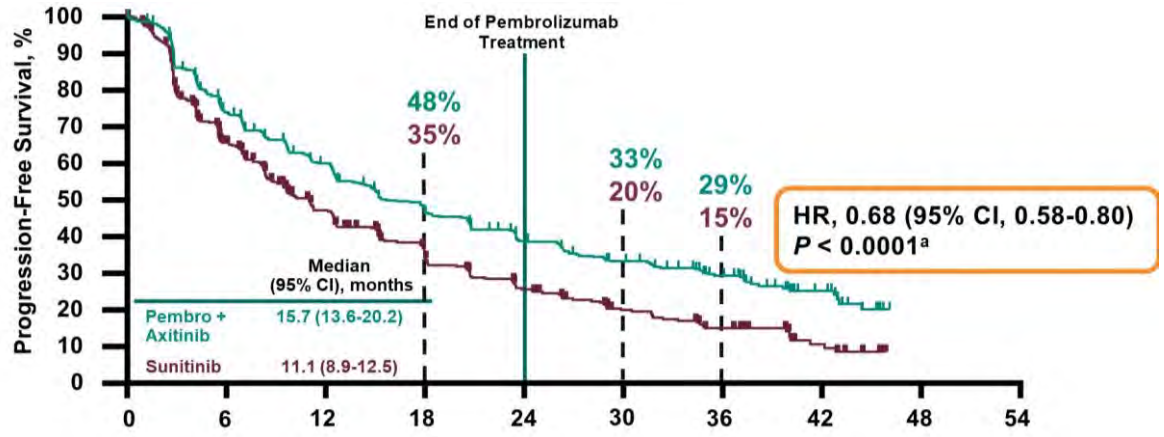
Characteristic	Pembrolizumab–Axitinib (N=432)	Sunitinib (N=429)
Age		
Median (range) — yr	62 (30–89)	61 (26–90)
<65 yr — no. (%)	260 (60.2)	278 (64.8)
Male sex — no. (%)	308 (71.3)	320 (74.6)
Region of enrollment — no. (%)		
North America	104 (24.1)	103 (24.0)
Western Europe	106 (24.5)	104 (24.2)
Rest of the world	222 (51.4)	222 (51.7)
IMDC prognostic risk — no. (%)†		
Favorable	138 (31.9)	131 (30.5)
Intermediate	238 (55.1)	246 (57.3)
Poor	56 (13.0)	52 (12.1)
Sarcomatoid features — no./total no. with known status (%)	51/285 (17.9)	54/293 (18.4)
PD-L1 combined positive score — no./total no. with data (%)‡		
≥1	243/410 (59.3)	254/412 (61.7)
<1	167/410 (40.7)	158/412 (38.3)
No. of organs with metastases — no. (%)§		
1	114 (26.4)	96 (22.4)
≥2	315 (72.9)	331 (77.2)
Most common sites of metastasis — no. (%)¶		
Lung	312 (72.2)	309 (72.0)
Lymph node	199 (46.1)	197 (45.9)
Bone	103 (23.8)	103 (24.0)
Adrenal gland	67 (15.5)	76 (17.7)
Liver	66 (15.3)	71 (16.6)
Previous radiotherapy — no. (%)	41 (9.5)	40 (9.3)
Previous nephrectomy — no. (%)	357 (82.6)	358 (83.4)

Thomas Powles at 2019 Genitourinary Cancers Symposium.

PEMBROLIZUMAB + AXITINIB

KEYNOTE 426 (ITT)

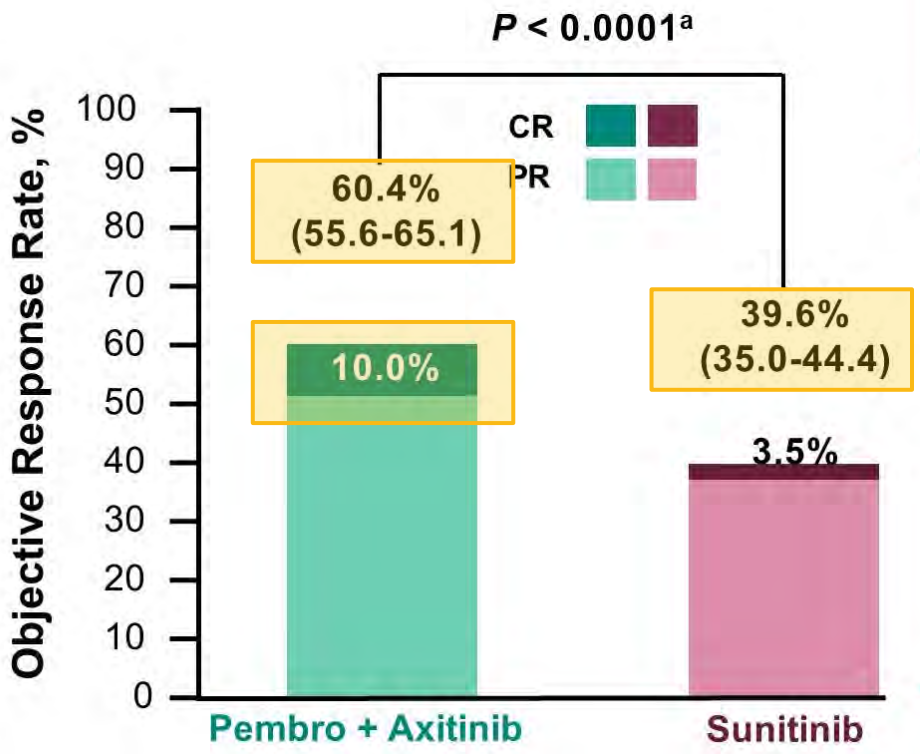




aBecause superiority of pembrolizumab + axitinib was shown at the first interim analysis, no alpha was allocated to OS; only nominal *P* values are reported. Data cutoff: January 11, 2021.

PEMBROLIZUMAB + AXITINIB

KEYNOTE 426 (ITT)



	Pembro + Axitinib n = 432	Sunitinib n = 429
Best response, n (%)		
CR	43 (10.0)	15 (3.5)
PR	218 (50.5)	155 (36.1)
SD	99 (22.9)	152 (35.4)
PD	49 (11.3)	73 (17.0)
NE[b]	7 (1.6)	6 (1.4)
NA[c]	16 (3.7)	28 (6.5)

Brian Rini at 2021 ASCO.

PEMBROLIZUMAB + AXITINIB

KEYNOTE 426

Parameter	ITT		Favorable Risk		Intermediate/Poor Risk	
	Pembro + Axitinib n = 432	Sunitinib n = 429	Pembro + Axitinib n = 138	Sunitinib n = 131	Pembro + Axitinib n = 294	Sunitinib n = 298
OS, HR (95% CI)	**0.73 (0.60-0.88)**		**1.17 (0.76-1.80)**		**0.64 (0.52-0.80)**	
42-month rate, %	57.5	48.5	72.3	73.0	50.6	37.6
PFS, HR (95% CI)	0.68 (0.58-0.80)		0.76 (0.56-1.03)		0.67 (0.55-0.81)	
Median, months	15.7	11.1	20.7	17.8	13.8	8.2
ORR, %	60.4	39.6	68.8	50.4	56.5	34.9
CR, %	10.0	3.5	11.6	6.1	9.2	2.3
PR, %	50.5	36.1	57.2	44.3	47.3	32.6

Data cutoff: January 11, 2021.

Brian Rini at 2021 ASCO.

PEMBROLIZUMAB + AXITINIB

KEYNOTE 426

	Pembro + Axi (N= 429)		Sunitinib (N= 425)	
	Any grade	Grade 3-5	Any grade	Grade 3-5
Any	51.3%	10.7%	36.2%	1.9%
Hypothyroidism	35.4%	0.2%	31.5%	0.2%
Hyperthyroidism	12.8%	1.2%	3.8%	0
Adrenal insufficiency	3.0%	0.7%	0.2%	0
Hepatitis	2.8%	2.3%	0.5%	0.2%
Pneumonitis	2.8%	0.5%	0.2%	0
Thyroiditis	2.8%	0.2%	0.5%	0
Colitis	2.6%	1.9%	0.7%	0
Severe skin reactions	1.9%	1.2%	1.4%	0.7%
Infusion reactions	1.6%	0.2%	0.9%[a]	0.2%[a]
Nephritis	1.4%	0.2%	0.2%	0
Hypophysitis	1.2%	0.9%	0	0

Brian Rini at 2021 ASCO.

NIVOLUMAB + CABOZANTINIB

CHECKMATE 9ER

Key inclusion criteria[1,2]

- Previously untreated advanced or metastatic RCC
- Clear cell component
- Any IMDC risk group

R
1:1

Median study follow-up, 18.1 months (range, 10.6–30.6 months)

Table 1. Demographic and Disease Characteristics at Baseline.*

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Age		
Median (range) — yr	62 (30–89)	61 (26–90)
<65 yr — no. (%)	260 (60.2)	278 (64.8)
Male sex — no. (%)	308 (71.3)	320 (74.6)
Region of enrollment — no. (%)		
North America	104 (24.1)	103 (24.0)
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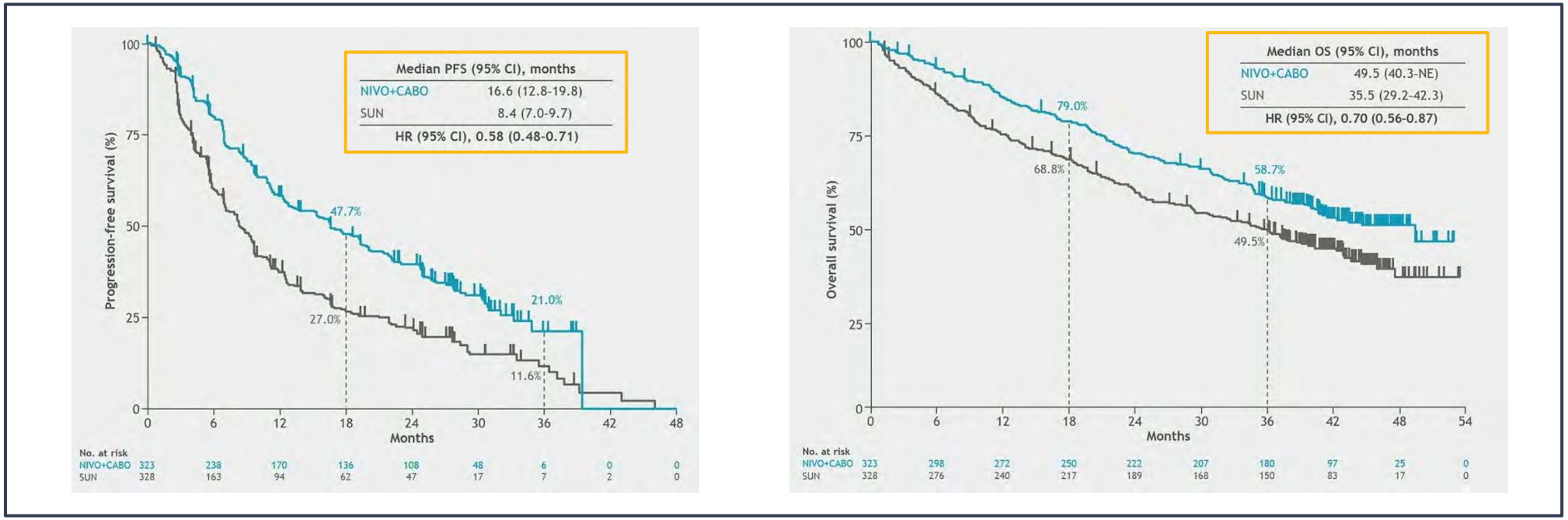
NIVOLUMAB + CABOZANTINIB

CHECKMATE 9ER



Burotto at ASCO GU 2023.

NIVOLUMAB + CABOZANTINIB

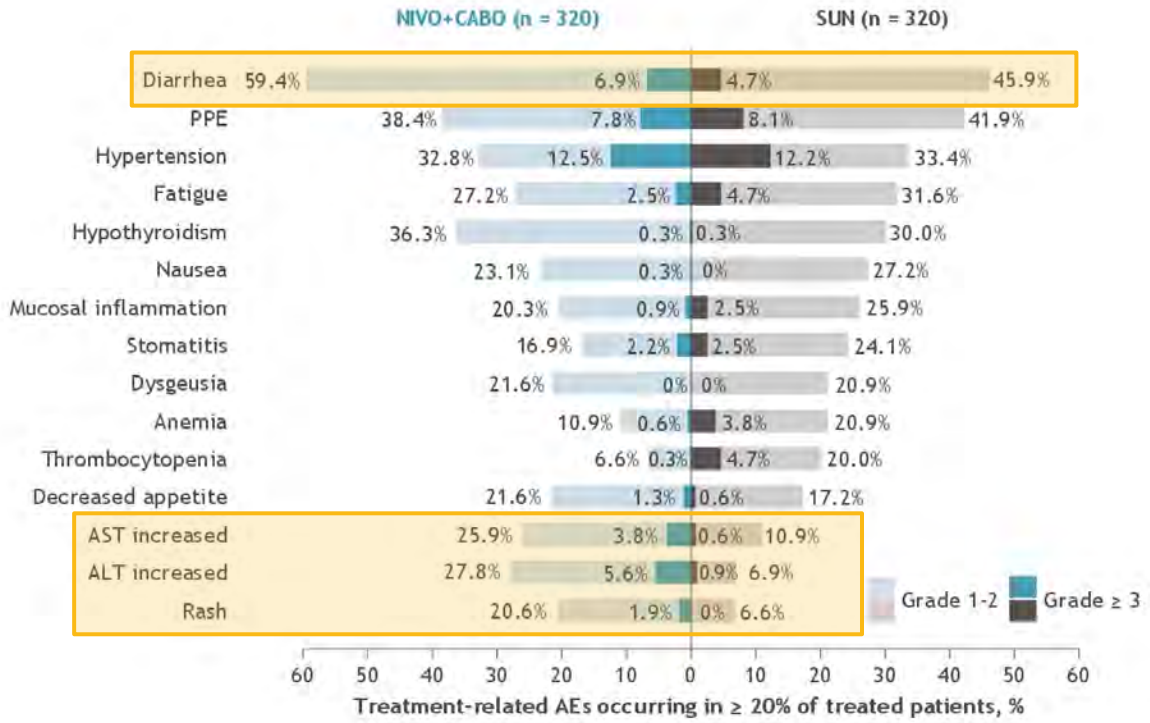
CHECKMATE 9ER

Variable[a]	Nivo+Cabo (n = 323)	Sun (n = 328)
Confirmed ORR (95% CI), %	55.7 (50.1–61.2)	28.4 (23.5–33.6)
Confirmed BOR, n (%)		
Complete response	40 (12.4)	17 (5.2)
Partial response	140 (43.3)	76 (23.2)
Stable disease	105 (32.5)	134 (40.9)
Progressive disease	20 (6.2)	45 (13.7)
Unable to determine	18 (5.6)	55 (16.8)
Not reported	0	1 (0.3)
mTTR (range), mo	2.8 (1.0–22.3)	4.2 (1.7–30.4)
mDOR (95% CI), mo	23.1 (20.2–27.9)	15.1 (9.9–20.5)

Thomas Powles et al. ASCO GU 2022.

NIVOLUMAB + CABOZANTINIB

CHECKMATE 9ER



Variable, % of pts	Nivo+Cabo (n = 320)	Sun (n = 320)
All-cause AEs	99.7	99.1
Treatment-related AEs	97.2	93.1
Grade 3 or higher	65.0	54.1
Leading to discontinuation	7.5 (Nivo+Cabo) 10.6 (Nivo only) 9.1 (Cabo only)	10.3
Treatment-related deaths	1	3

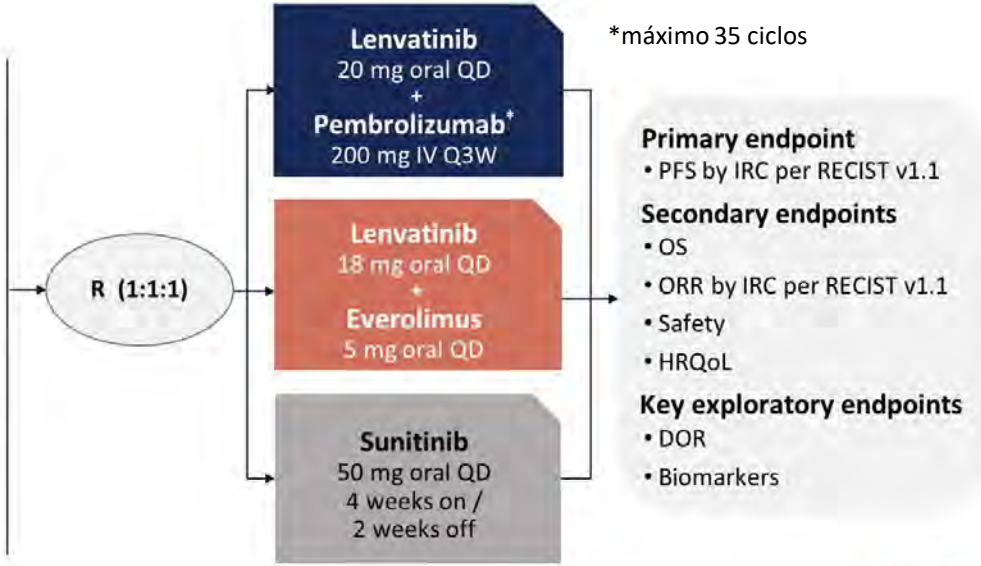
Thomas Powles et al. ASCO GU 2022.

PEMBROLIZUMAB + LENVATINIB

CLEAR

Key eligibility criteria
- Advanced clear-cell RCC
- Treatment-naïve
- Karnofsky performance status ≥70
- Measurable disease
- Adequate organ function

Stratification factors
- **Geographic region:** Western Europe and North America vs Rest of the World
- **MSKCC risk category:** Favorable, Intermediate, or Poor



*máximo 35 ciclos

Primary endpoint
- PFS by IRC per RECIST v1.1

Secondary endpoints
- OS
- ORR by IRC per RECIST v1.1
- Safety
- HRQoL

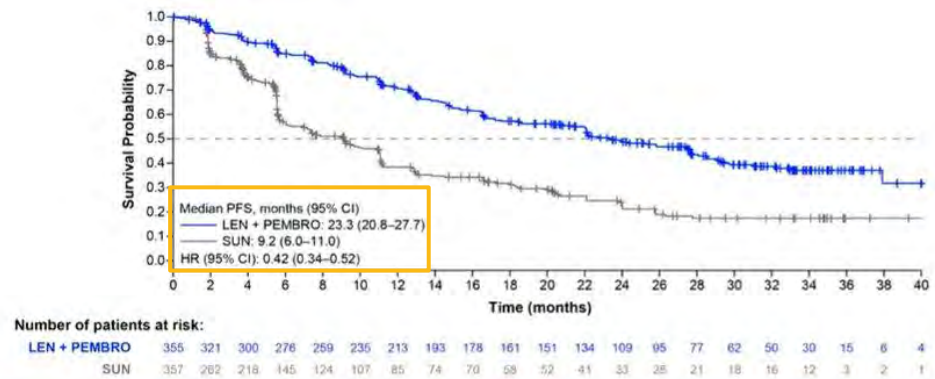
Key exploratory endpoints
- DOR
- Biomarkers

	LEN + PEMBRO (n = 355)	LEN + EVE (n = 357)	SUN (n = 357)
IMDC risk group — % Favorable / Intermediate / Poor	31.0 / 59.2 / 9.3	31.9 / 54.6 / 11.8	34.7 / 53.8 / 10.4
Sarcomatoid features — %	7.9	6.7	5.9
PD-L1 expression — % ≥ 1 / < 1 / not available	30.1 / 31.5 / 38.3	32.5 / 33.1 / 34.5	33.3 / 28.9 / 37.8

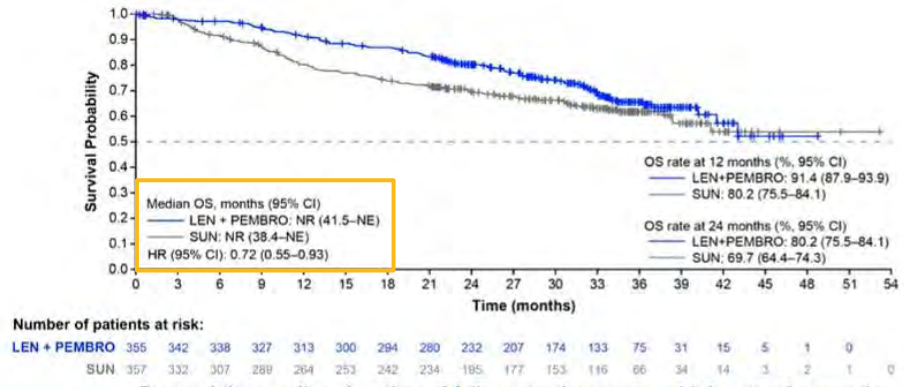
Motzer at 2021 Genitourinary Cancers Symposium.

PEMBROLIZUMAB + LENVATINIB

CLEAR



	MSKCC			IMDC		
	Poor risk	Intermediate risk	Favorable risk	Poor risk	Intermediate risk	Favorable risk
LEN +PEMBRO vs SUN HR (95% CI)	0.18 (0.08–0.42)	0.46 (0.35–0.60)	0.43 (0.29–0.64)	0.30 (0.14–0.62)	0.41 (0.30–0.54)	0.47 (0.32–0.69)



	MSKCC			IMDC		
	Poor risk	Intermediate risk	Favorable risk*	Poor risk	Intermediate risk	Favorable risk*
LEN +PEMBRO vs SUN HR (95% CI)	0.50 (0.25–1.02)	0.71 (0.52–0.97)	1.00 (0.51–1.96)	0.39 (0.20–0.77)	0.72 (0.52–1.00)	1.22 (0.66–2.26)*

Porta at 2022 ESMO.

PEMBROLIZUMAB + LENVATINIB

CLEAR

	LEN + PEMBRO (n = 355)	LEN + EVE (n = 357)	SUN (n = 357)
Objective response rate (95% CI) — %	71.0 (66.3–75.7)	53.5 (48.3–58.7)	36.1 (31.2–41.1)
Best overall response — %			
Complete response	16.1	9.8	4.2
Partial response	54.9	43.7	31.9
Stable disease	19.2	33.6	38.1
Progressive disease	5.4	7.3	14.0
Unknown / not evaluable	4.5	5.6	11.8
Relative risk versus SUN (95% CI)	1.97 (1.69–2.29)	1.48 (1.26–1.74)	--
P-value	< 0.001	< 0.001	--

Motzer at 2021 Genitourinary Cancers Symposium.

PEMBROLIZUMAB + LENVATINIB

CLEAR

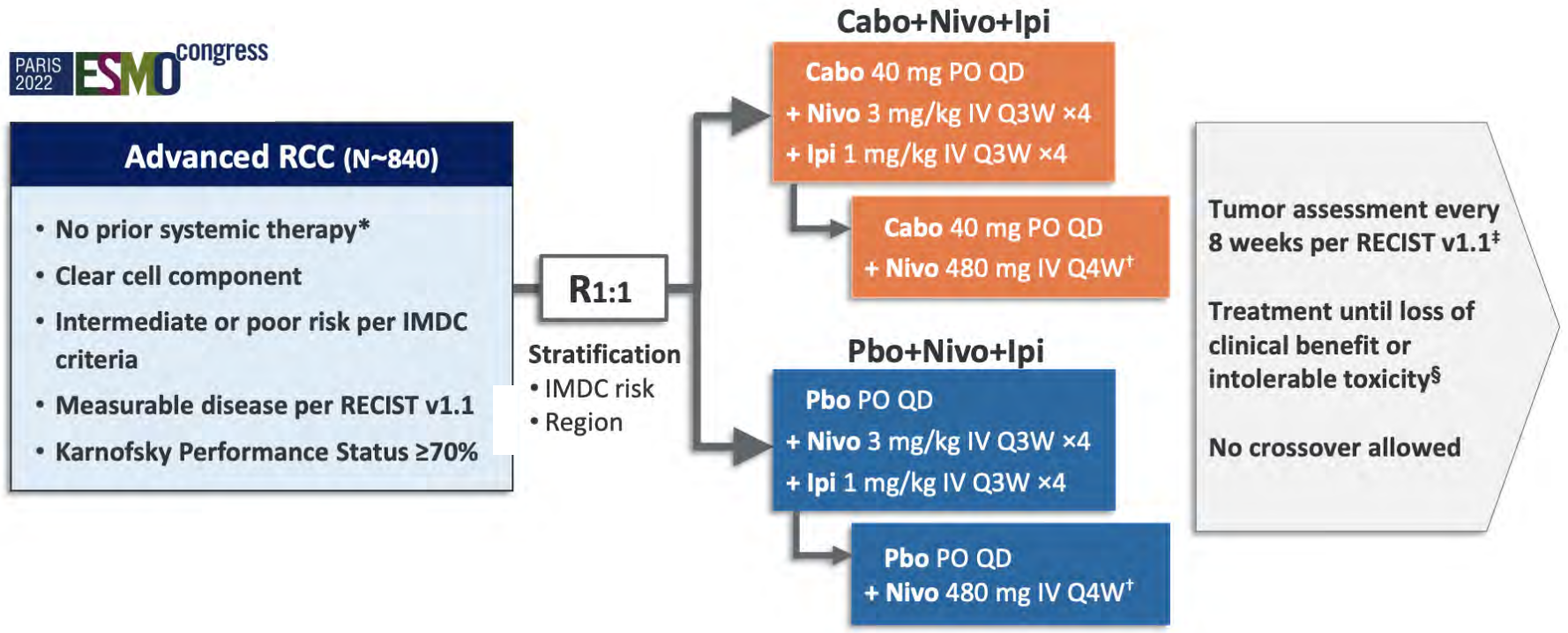
	LEN + PEMBRO (n = 352)	LEN + EVE (n = 355)	SUN (n = 340)
Median duration of treatment, months (range)	17.0 (0.1–39.1)	11.0 (0.1–40.0)	7.8 (0.1–37.0)
Patients with any TRAEs (%)	96.9	97.7	92.1
Grade ≥ 3*	71.6	73.0	58.8
Patients with any TRAEs leading to dose reductions (LEN or SUN) (%)	67.3	69.3	49.7
Patients with any grade TRAEs leading to discontinuation (%)			
LEN or SUN	18.5	16.1	10.0
PEMBRO or EVE	25.0	19.2	--
LEN + PEMBRO or LEN + EVE	9.7	13.5	--

*Grade 5 TRAEs were observed in 1.1% of patients in the LEN + PEMBRO arm, 0.8% of patients in the LEN + EVE arm, and 0.3% of patients in the SUN arm.
TRAE, treatment-emergent adverse event.

Motzer at 2021 Genitourinary Cancers Symposium.

NIVOLUMAB + IPILIMUMAB + CABOZANTINIB

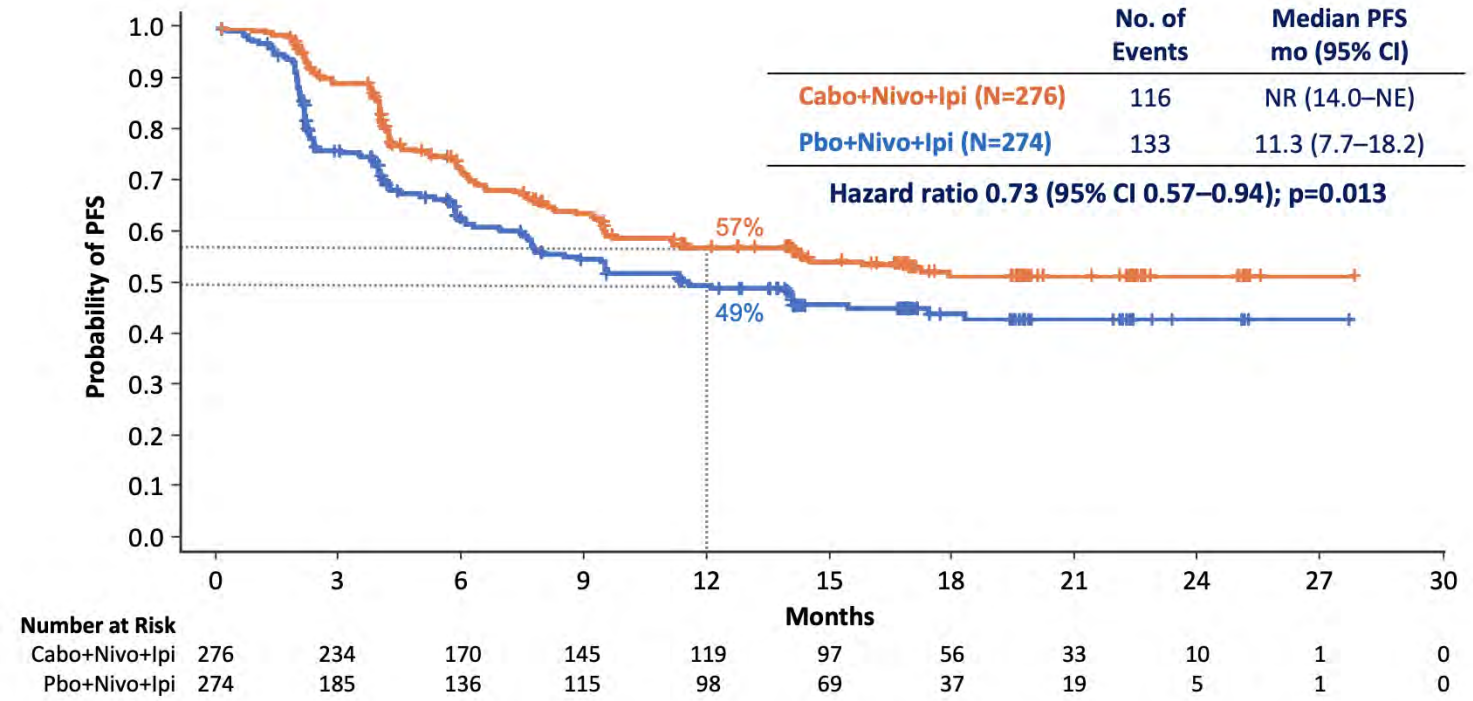
COSMIC 313



Toni Choueiri at 2022 ESMO Presidential Symposium.

NIVOLUMAB + IPILIMUMAB + CABOZANTINIB

COSMIC 313 (ITT)



Toni Choueiri at 2022 ESMO Presidential Symposium.

NIVOLUMAB + IPILIMUMAB + CABOZANTINIB

COSMIC 313

	Cabo+Nivo+Ipi (N=426)		Pbo+Nivo+Ipi (N=424)	
	Any Grade	Grade 3–4	Any Grade	Grade 3–4
Treatment-related adverse events				
Any event,* %	99	73	91	41
Alanine aminotransferase increased	46	26	17	6
Aspartate aminotransferase increased	44	20	16	5
Diarrhea	41	4	18	3
Palmar-plantar erythrodysesthesia	28	3	4	0
Hypothyroidism	24	<1	15	0
Hypertension	23	8	5	2
Fatigue	22	2	21	1
Lipase increased	22	9	13	6
Amylase increased	20	5	12	2
Rash	20	2	20	1
Pruritus	20	0	26	<1

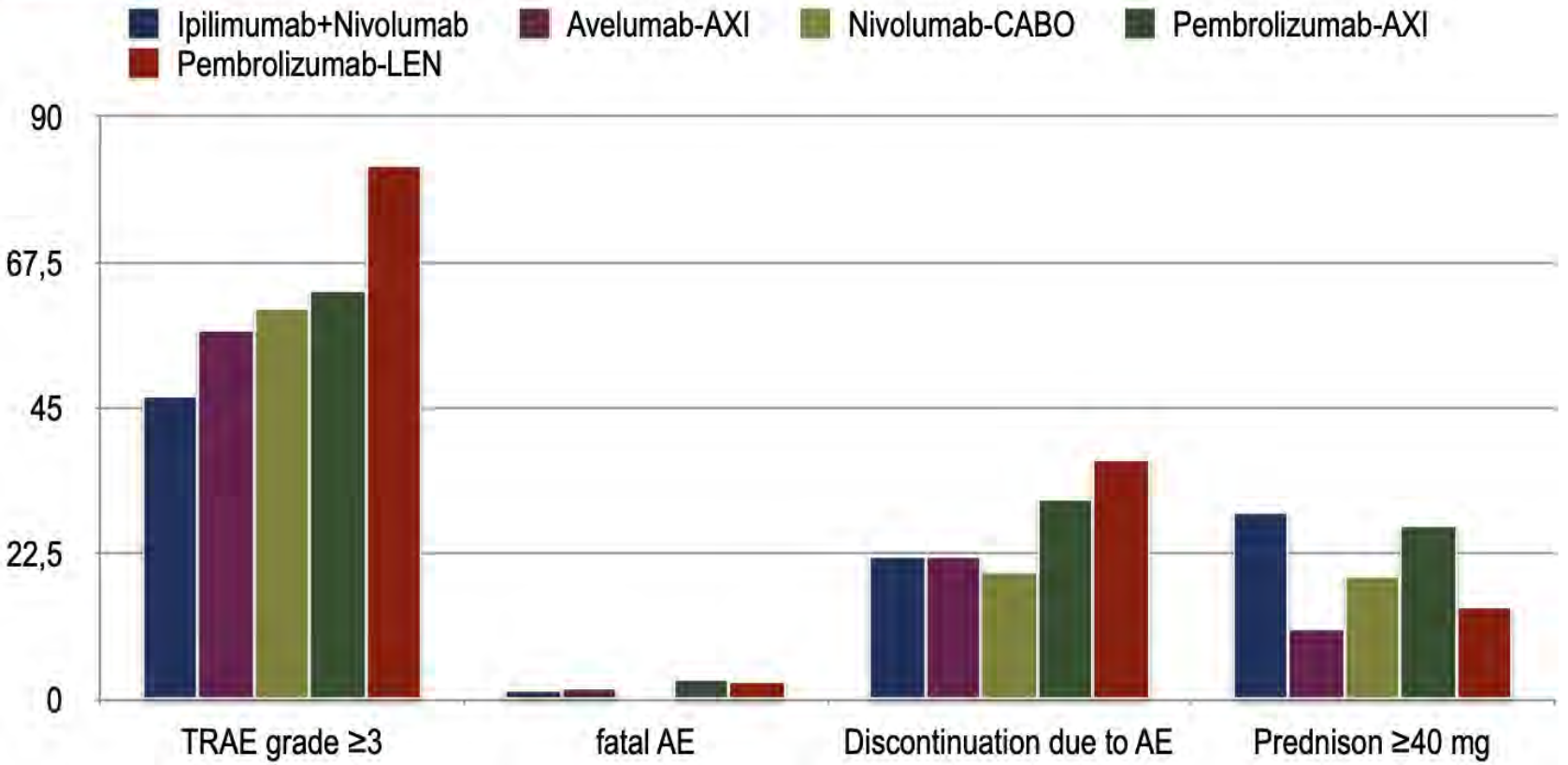
- Grade 5 TRAEs occurred in 3 patients (1%) with Cabo+Nivo+Ipi (gastrointestinal hemorrhage, hepatic failure, and respiratory failure) and 3 patients (1%) with Pbo+Nivo+Ipi (renal failure, myocarditis, and sudden death) ≤30 days after last dose; through 100 days after last dose, two additional patients had grade 5 TRAEs with Cabo+Nivo+Ipi (immune-mediated hepatitis and acute hepatic failure) and one additional patient with Pbo+Nivo+Ipi (perforated ulcer)
- Use of high-dose corticosteroids (≥40 mg of prednisone or equivalent) for AEs was 58% with Cabo+Nivo+Ipi and 35% with Pbo+Nivo+Ipi

Toni Choueiri at 2022 ESMO Presidential Symposium.

CCRcc estadio IV – tratamento em 1ª linha

Como selecionar?

Safety parameter vary between IO combinations



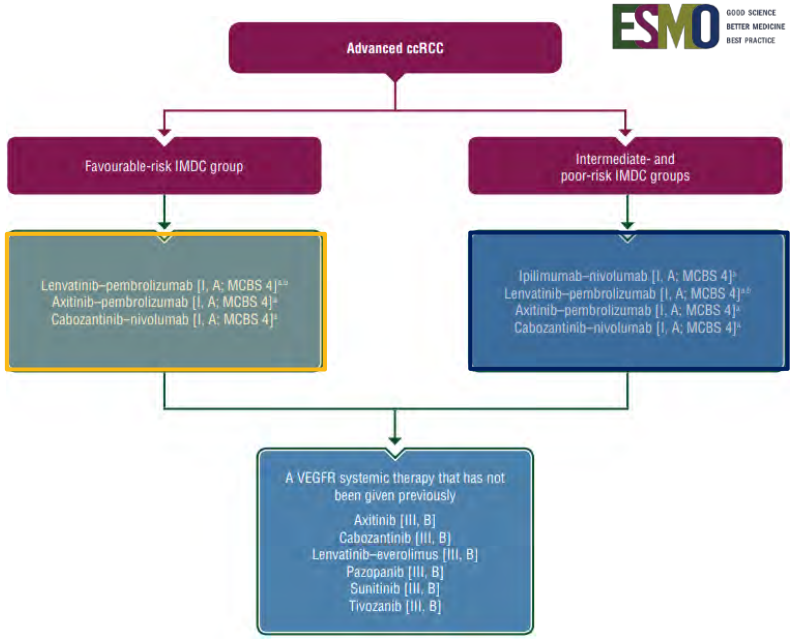
Motzer et al. Lancer Oncol 2019 http://dx.doi.org/10.1016/S1470-2045(19)30413-9. Motzer et al. N Engl J Med NEJMoa1816047 (2019). doi:10.1056/NEJMoa1816047. Rini, B. I. *et al. N Engl J Med* NEJMoa1816714–12 (2019). Motzer, R. *et al. New Engl J Med* (2021) doi:10.1056/nejmoa2035716.

CCRcc estadio IV – tratamento em 1ª linha

O que dizem as guidelines?

National Comprehensive Cancer Network®

FIRST-LINE THERAPY FOR CLEAR CELL HISTOLOGY			
Risk	**Preferred Regimens**	**Other Recommended Regimens**	**Useful in Certain Circumstances**
Favorable[a]	• Axitinib + pembrolizumab[b] (category 1) • Cabozantinib + nivolumab[b] (category 1) • Lenvatinib + pembrolizumab[b] (category 1)	• Axitinib + avelumab[b] • Cabozantinib (category 2B) • Ipilimumab + nivolumab[b] • Pazopanib • Sunitinib	• Active surveillance[c] • Axitinib (category 2B) • High-dose IL-2[d] (category 2B)
Poor/ intermediate[a]	• Axitinib + pembrolizumab[b] (category 1) • Cabozantinib + nivolumab[b] (category 1) • Ipilimumab + nivolumab[b] (category 1) • Lenvatinib + pembrolizumab[b] (category 1) • Cabozantinib	• Axitinib + avelumab[b] • Pazopanib • Sunitinib	• Axitinib (category 2B) • High-dose IL-2[d] (category 3) • Temsirolimus[e] (category 3)

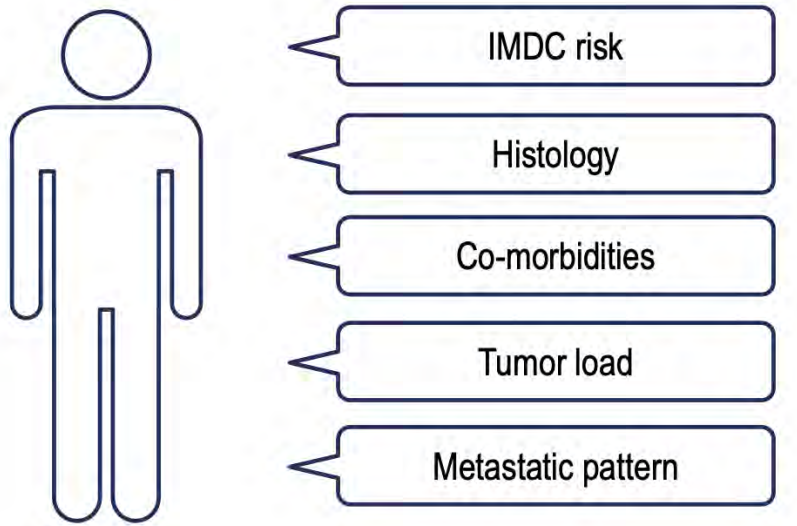


European Association of Urology	Standard of Care	Alternative in patients who can not receive or tolerate immune checkpoint inhibitors
IMDC favourable risk	nivolumab/cabozantinib [1b] pembrolizumab/axitinib [1b] pembrolizumab/lenvatinib [1b]	sunitinib* [1b] pazopanib* [1b]
IMDC intermediate and poor risk	nivolumab/cabozantinib [1b] pembrolizumab/axitinib [1b] pembrolizumab/lenvatinib [1b] nivolumab/ipilimumab [1b]	cabozantinib* [2a] sunitinib*[1b] pazopanib* [1b]

NCCN Guidelines Version 4.2023 Kidney Cancer. ESMO Guidelines eUpdate Sept. 2021. EAU 2022.

Tratamento 1ª linha de CCRcc estadio IV – panorama atual

- Combinações IO-IO ou IO-TKI são o tratamento preferencial
- IO-IO com FU 5 anos: dados maduros e efeito a longo prazo
- IO-TKI com melhor ORR (+20%)
- dif. sarcomatóide com melhor resposta com IO-IO e IO-TKI
- toxicidade e descontinuação maior com IO-TKI
- PDL1 preditivo de maior resposta mas fraco marcador de seleção



Grupo Português
Génito - Urinário

XXVIII Workshop
Urologia Oncológica

Obrigada pela atenção .

Joana Simões

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Caso clínico

Carcinoma de Células Renais

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Caso clínico

Homem de 71 anos.

ECOG 0, excelente estado geral.

Antecedentes médicos: # Adenocarcinoma da próstata Gleason 8 (4+4), submetido a prostatectomia radical e linfadenetomia pélvica em Janeiro de 2018, estadio pT2N1R0, fez depois RT pélvica de salvação em Novembro de 2019, sem evidência de recidiva (PSA <0.006 ng/mL); # Pancreatite aguda de etiologia litiásica, com trombocitopenia sequelar (80-100.000); # IVP.

Sem medicação atual. Sem alergias medicamentosas.

Hábitos pessoais: # Ex-fumador (112 UMAs).

Informação consentida pelo doente.

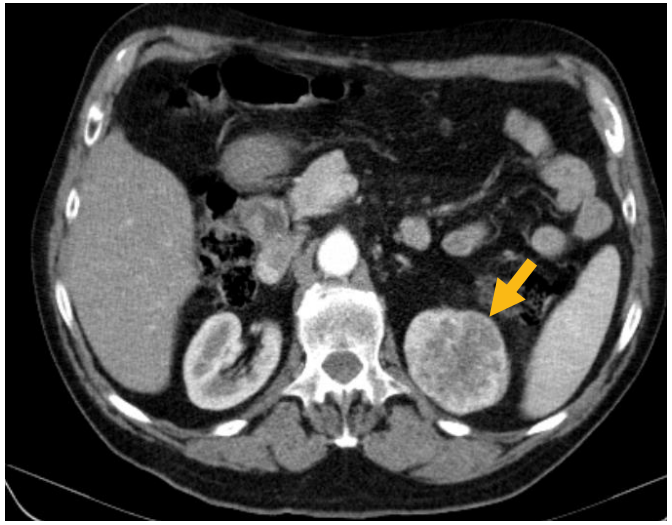
Caso clínico

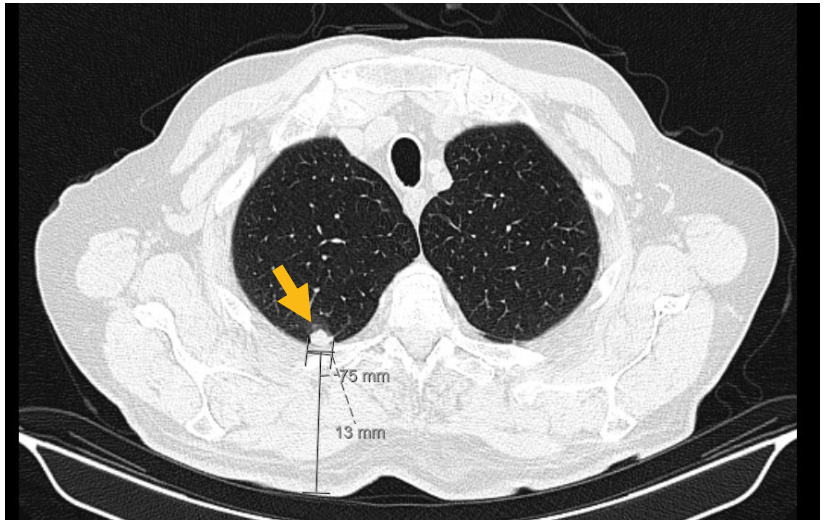
Maio de 2021 → hematúria

Necessidade de internamento no serviço de Urologia

TAC com **massa no pólo superior do rim esquerdo** com 6 cm e **nódulos pulmonares** (maior no LSD com 13 mm).

Cistoscopia sem alterações. Citologia urinária negativa.





Caso clínico

Discutido o caso em **Reunião de Grupo Oncológico de Urologia** e, atendendo ao difícil acesso para biópsia percutânea dos nódulos pulmonares assim como à hematúria persistente, foi decidido realizar nefrectomia radical esquerda.

Nefrectomia radical esquerda laparoscópica transperitoneal (Agosto de 2021): carcinoma de células renais, variante células claras, com 5.5 cm, grau 3, limitado ao rim, com focos de diferenciação sarcomatóide (<5%) - estadio pT1bNx.

Repetiu **TAC** que mostrou **progressão dimensional das lesões pulmonares**.

Realizou biópsia pulmonar à lesão subpleural do LSD que revelou carcinoma compatível com **metástase de CCR claras.**

Carcinoma de células renais, variante células claras, estadio IV (pT1bNxM1 – metastização pulmonar), risco intermédio (1 FR).

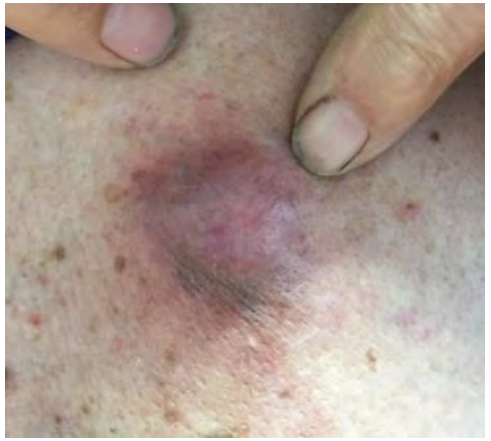
Rediscutido o caso em **Reunião de Grupo Oncológico de Urologia** e decidido tratamento sistémico com TKI.

Caso clínico

1ª consulta de OM em Dezembro de 2021: **nódulo subcutâneo no QSI da mama esquerda** com 11 mm.

Pedida biópsia: **metástase de carcinoma de células renais**, variante células claras.

Dezembro de 2021: início de tratamento com Pazopanib **800 mg id**.



Dezembro 2021.

Toxicidade com agravamento da trombocitopenia (G3), mesmo com **Pazopanib 400 mg** (50% dose), com múltiplos adiamentos.

Pedida autorização para **Pembrolizumab e Axitinib** (coincidente com reembolso em Portugal).

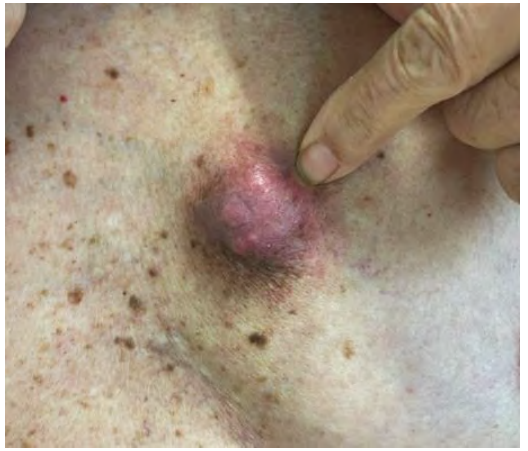
Em **Março de 2022**, iniciou Pembrolizumab **200 mg 3/3 semanas** e Axitinib **5 mg 2id** → por trombocitopenia G2-3, com necessidade de redução de dose para **2 mg 2id**, tendo mantido estabilidade de valor plaquetário.

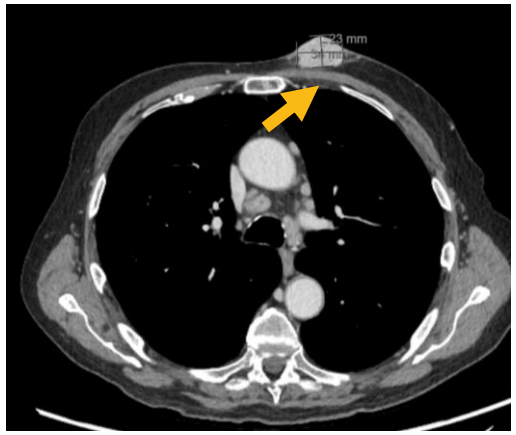
Primeira reavaliação imagiológica em Junho de 2022 com **DE**.

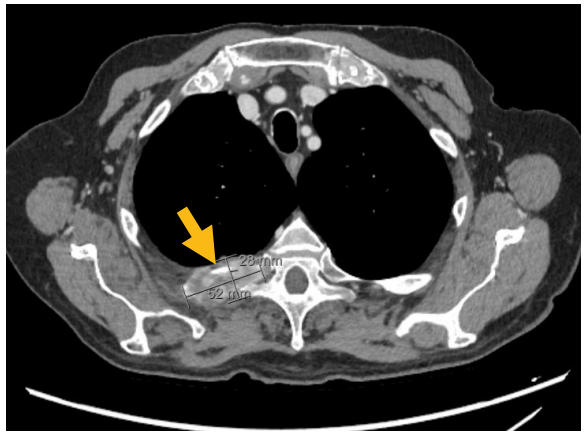
Caso clínico

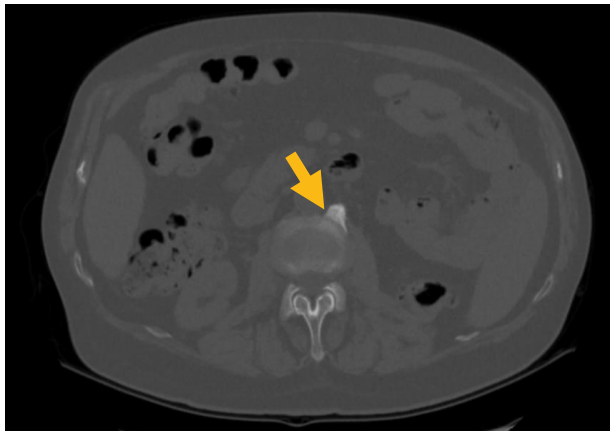
TAC de Novembro de 2022: PD após 13 ciclos de Pembro/Axitinib

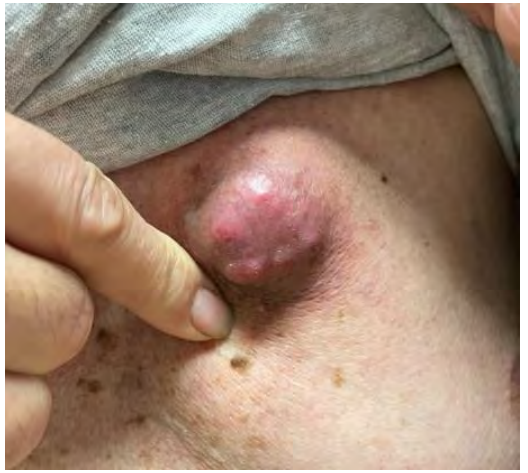
- Progressão da lesão sólida no QSI da ME, com 34 mm
- Metástase no arco posterior da 4ª costela direita, com componente de partes moles, de novo
- Metástase sagrada com 20 mm, de novo
- Lesão nodular na apófise unciforme do pâncreas com 8 mm, de novo
- Estabilidade dos nódulos pulmonares







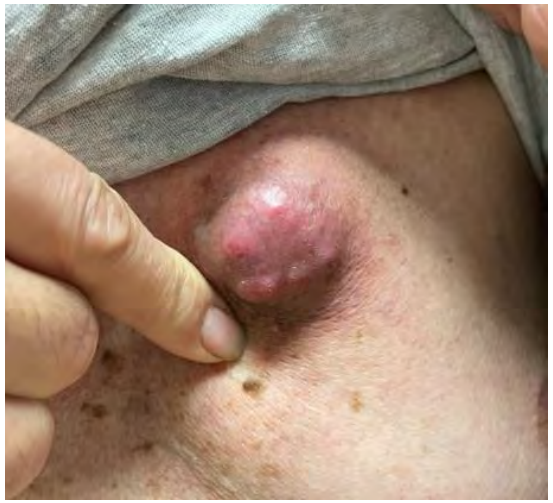


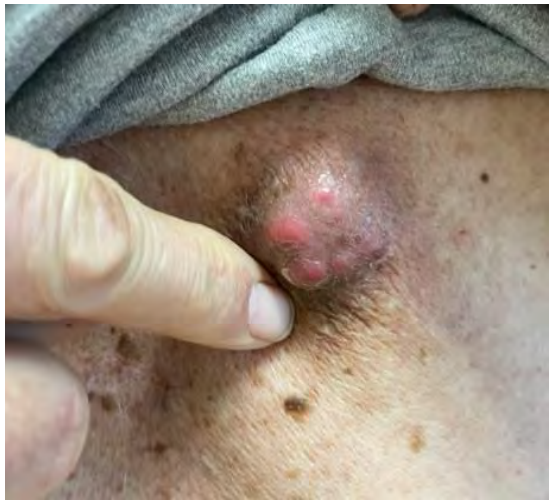


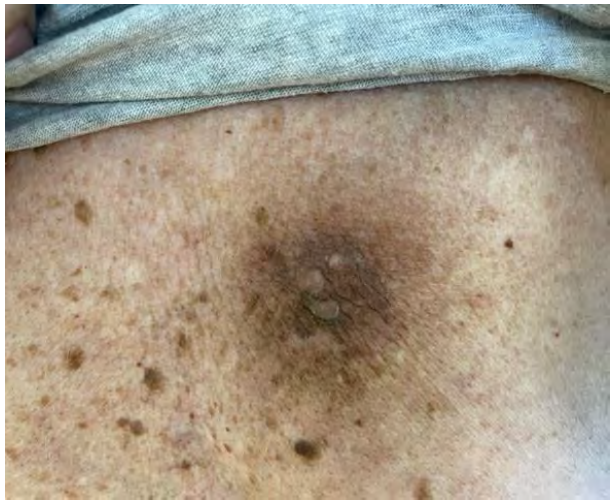
Caso clínico

Dezembro 2022: início de 2ª linha com Cabozantinib **40 mg id** (1 nível de redução de dose basal). Associado tratamento com **AZ mensal**.

Boa tolerância. Trombocitopenia basal sem agravamento.







Janeiro de 2023: úlcera anal com fístula. **Biópsia de leito ulceroso: exuberante processo inflamatório com lesões de vasculite focais.**

Suspenso TKI e medicado com metronidazol e ciprofloxacina 10 dias. Resolução completa com cicatrização.

Retomou Cabozantinib com **+1 nível de redução de dose (20 mg id).**

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