Consolidating the data on adjuvant treatment in localized renal cancer

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PROGNOSTIC FACTORS IN LOCALIZED RCC

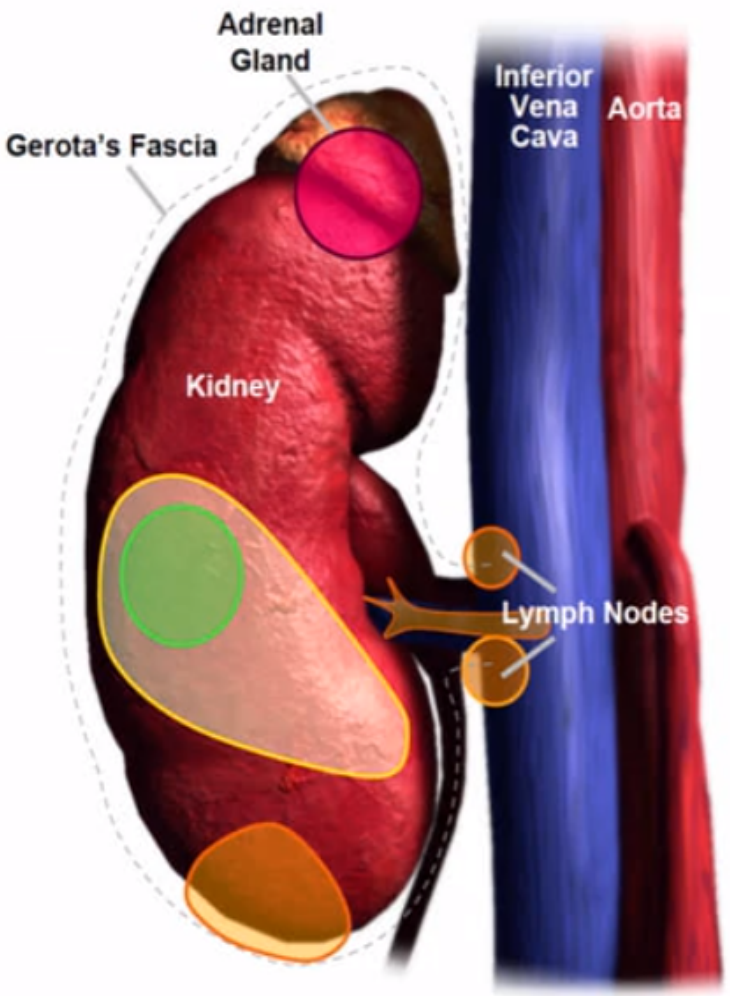
Stage I
Tumor < 7 cm in greatest dimension and limited to kidney

- **IA** < 4 cm
- **IB** > 4 to < 7 cm

Stage II
Tumor > 7 cm in greatest dimension and limited to kidney

Stage III
Tumor major veins, tumor within Gerota's fascia, or regional lymph node involved

Stage IV
Tumor invasion beyond Gerota's fascia, adrenal or distant metastases



Other prognostic factors in localized disease: tumor grade, necrosis, patients performance status

- **Primary Tumor Stage determines risk of relapse**
  - T2: 26%
  - T3: 50%;
  - T4: Virtually 100%
- **Sarcomatoid components**
- **Higher Tumor Grade**
- **Other prognostic factors?**

CLINICAL CASE

Carlos, 62 y/o man

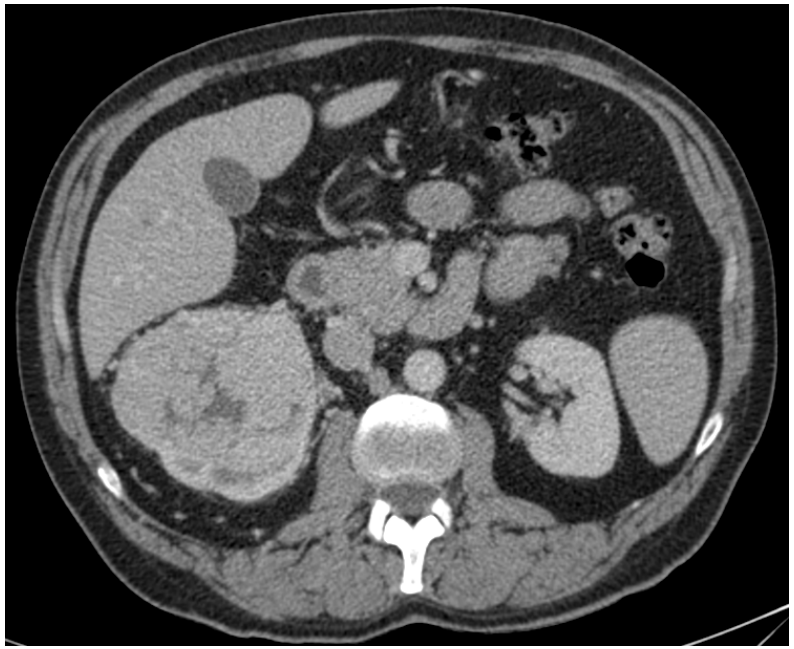
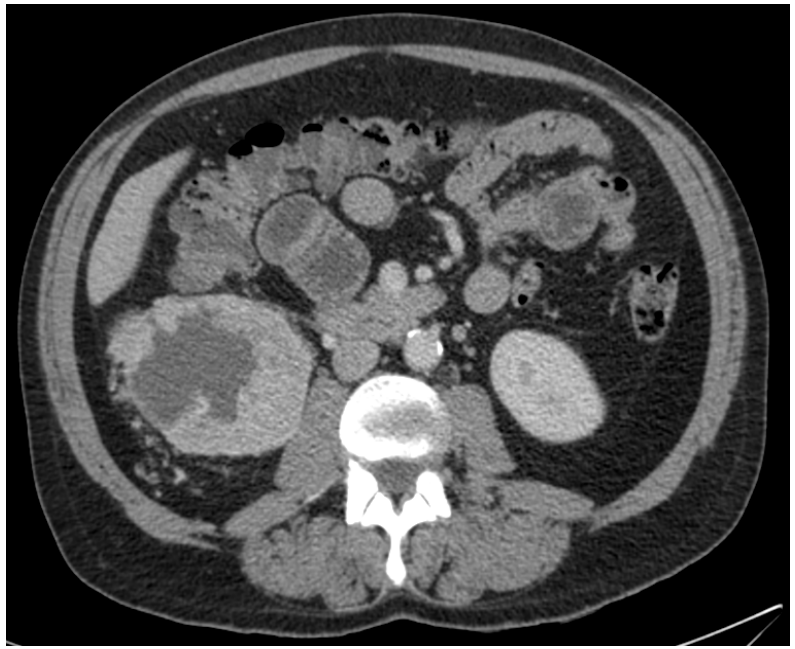
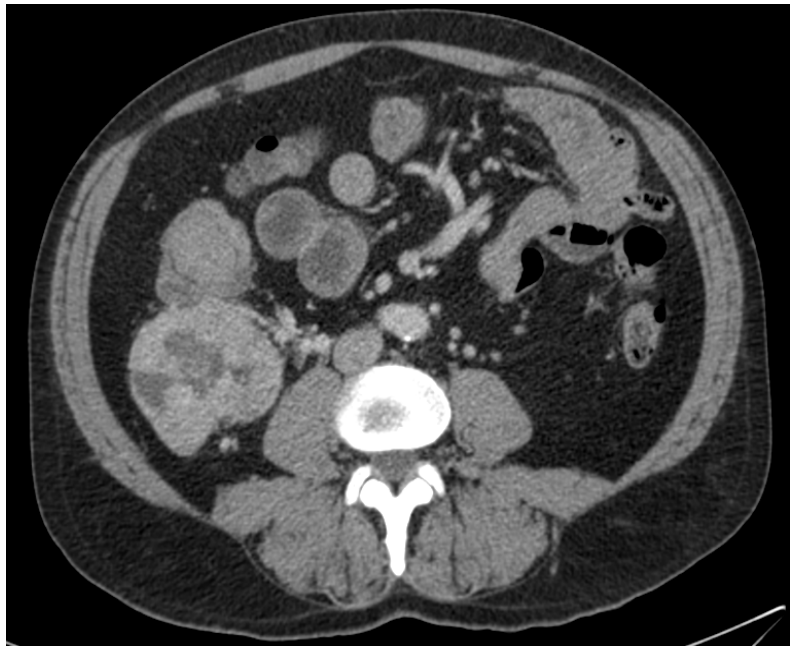
- No known drug-allergies
- Former smoker (from 15 to 35 years-old, 30cig. per day)

- **Medical history:**
- No relevant personal history
- Right inguinal herniorrhaphy

*Caso clínico ficticio

CLINICAL CASE

- **First symptom:** Hematuria
- **First diagnostic:**
    - CT SCAN: Right renal mass (111x87mm).

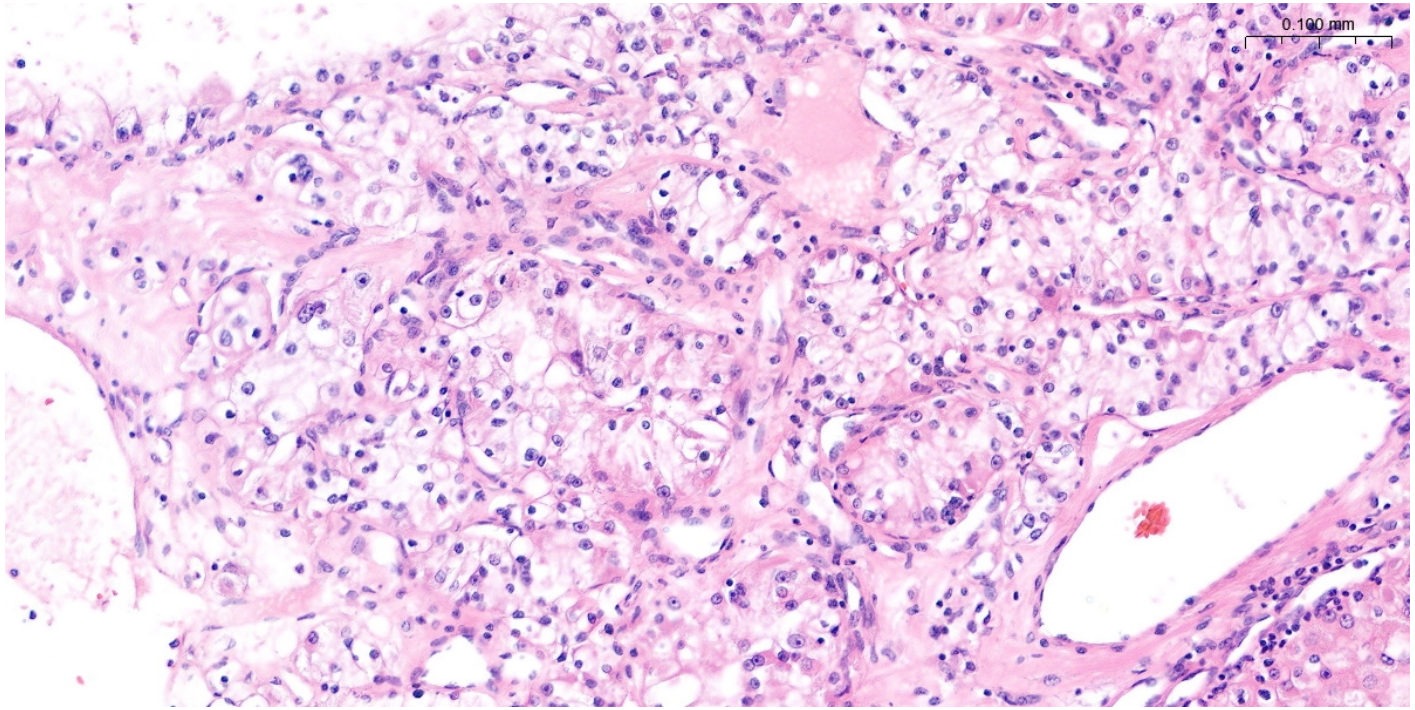




*Caso clínico ficticio

CLINICAL CASE

- Right total nephrectomy

- Clear-cell Renal Cell Carcinoma, pT3a, ISUP grade 3 with 5% of necrosis, R0



*Caso clínico ficticio

Would you treat Carlos with adjuvant therapy?

What is the risk of recurrence for Carlos?

MODELS TO PREDICT RISK OF RECURRENCE

- Around of 50% post-nephrectomy patients with high-risk features will eventually recur
- Factors such as disease stage, size, nuclear grade, regional LN involvement are associated with disease recurrence and survival

Model	RCC subtype	Factors
Kattan, Kattan M et al, J Urol 2001	Any	TNM, tumor size, histology, symptoms
SSIGN/Mayo, Frank I et al, J Urol 2002	Clear cell	TNM, tumor size, grade, tumor necrosis
Leibovich, Leibovich et al, Cancer 2003	Clear cell	TNM, N+, size, grade, tumor necrosis
UCLA/UISS, Patard JJ et al, JCO 2004	Any	TNM, grade, ECOG PS
MSKCC, Sorbellini et al, J Urol 2005	Clear cell	TNM, tumor size, grade, tumor necrosis, vascular invasion, symptoms
Karakiewicz, Karakiewicz et al, JCO 2007	Any	TNM, tumor size, grade, histology, age, symptoms
GRANT, Buti S et al, ESMO 2017	Any	Grade, age, Nodes, tumor size
VENUSS, Klatte T et al, BMC Med 2019	Papillary	TNM, Venous tumor thrombus, grade, size

Adapted from P Barata ASCO GU 2024

UCLA Integrated Staging System (UISS) for Renal Cell Carcinoma (RCC) ☆

Provides 5-year disease-free prognosis for localized and metastatic RCC.

INSTRUCTIONS

- Localized: Any T; N0; M0
- Metastatic: T>0; N>1; M>1
- For accurate staging, see the TNM Staging for RCC calculator

When to Use ⌄ | Pearls/Pitfalls ⌄ | Why Use ⌄

Type of disease present	Metastatic / **Localized**

UISS Criteria

Localized disease - T stage	T1	T2	**T3**	T4
Fuhrman nuclear grade	I	II	**III**	IV
ECOG Performance Status	**0**	≥1		

Moderate Risk

80.4% Five Year survival

UCLA Integrated Staging System (UISS) for Renal Cell Carcinoma (RCC)

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INSTRUCTIONS

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- Metastatic: T>0; N>1; M>1
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When to Use | Pearls/Pitfalls | Why Use

Type of disease present	Metastatic / **Localized**

UISS Criteria

Localized disease - T stage	T1	T2	**T3**	T4
Fuhrman nuclear grade	I	II	**III**	IV
ECOG Performance Status	**0**	≥1		

Moderate Risk

80.4% Five Year survival

SSIGN Score for Renal Cell Carcinoma (RCC)

Predicts progression of clear cell renal cell carcinoma after radical nephrectomy.

Pearls/Pitfalls

Pathological T category As per 2002 TNM staging guidelines	pT1	0
	pT2	+1
	pT3a-c	**+2**
	pT4	+4
Regional lymph node status As per 2002 TNM staging guidelines	**pNx or pN0**	**0**
	pN1 or pN2	+2
Metastasis category As per 2002 TNM staging guidelines	**M0 0**	M1 +4
Tumor size	<5 cm 0	**≥5 cm +2**
Tumor (nuclear) grade	1 or 2 0	**3 +1**	4 +3
Tumor necrosis present	No 0	**Yes +2**

7 points

38.6% 5-year estimated cancer-specific survival.

Copy Results | Next Steps

» Next Steps | Evidence | Creator Insights

2018 Leibovich Model for Renal Cell Carcinoma (RCC)

Predicts progression-free and cancer-specific survival in patients with renal cell carcinoma (RCC).

INSTRUCTIONS

Separate calculators are available for clear cell (ccRCC), papillary (papRCC), and chromophobe (chrRCC) histologies; always select the version that matches the surgical specimen.

When to Use | Pearls/Pitfalls | Why Use

Type of RCC

- **Clear cell RCC (ccRCC)**
- Papillary RCC (papRCC)
- Chromophobe RCC (chrRCC)

Age at surgery, years

- <60
- **≥60**

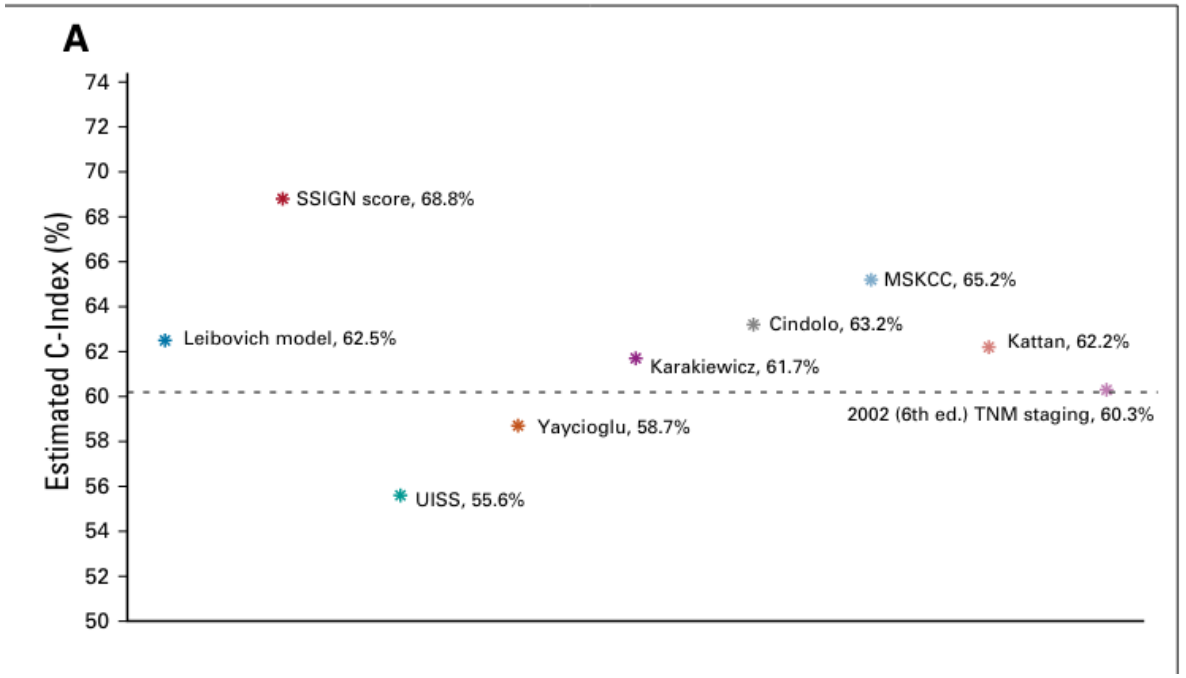
10 points	**44** %	**62** %
Progression-free survival score for ccRCC Cancer-specific survival score for ccRCC: 13 points	5-year PFS 10-year PFS: 32% 15-year PFS: 24%	5-year CSS 10-year CSS: 47% 15-year CSS: 37%

Predicting Renal Cancer Recurrence: Defining Limitations of Existing Prognostic Models With Prospective Trial-Based Validation

Andres F. Correa, MD[1]; Opeyemi Jegede, MPH[2]; Naomi B. Haas, MD[3]; Keith T. Flaherty, MD[4]; Michael R. Pins, MD[5]; Edward M. Messing, MD[6]; Judith Manola, MS[2]; Christopher G. Wood, MD[7]; Christopher J. Kane, MD[8]; Michael A.S. Jewett, MD[9]; Janice P. Dutcher, MD[10]; Robert S. DiPaola, MD[11]; Michael A. Carducci, MD[12]; and Robert G. Uzzo, MD[1]

PURPOSE To validate currently used recurrence prediction models for renal cell carcinoma (RCC) by using prospective data from the ASSURE (ECOG-ACRIN E2805; Adjuvant Sorafenib or Sunitinib for Unfavorable Renal Carcinoma) adjuvant trial.

PATIENTS AND METHODS Eight RCC recurrence models (University of California at Los Angeles Integrated Staging System [UISS]; Stage, Size, Grade, and Necrosis [SSIGN]; Leibovich; Kattan; Memorial Sloan Kettering Cancer Center [MSKCC]; Yaycioglu; Karakiewicz; and Cindolo) were selected on the basis of their use in clinical practice and clinical trial designs. These models along with the TNM staging system were validated using 1,647 patients with resected localized high-grade or locally advanced disease (≥ pT1b grade 3 and 4/pTanyN1Mo) from the ASSURE cohort. The predictive performance of the model was quantified by assessing its discriminatory and calibration abilities.

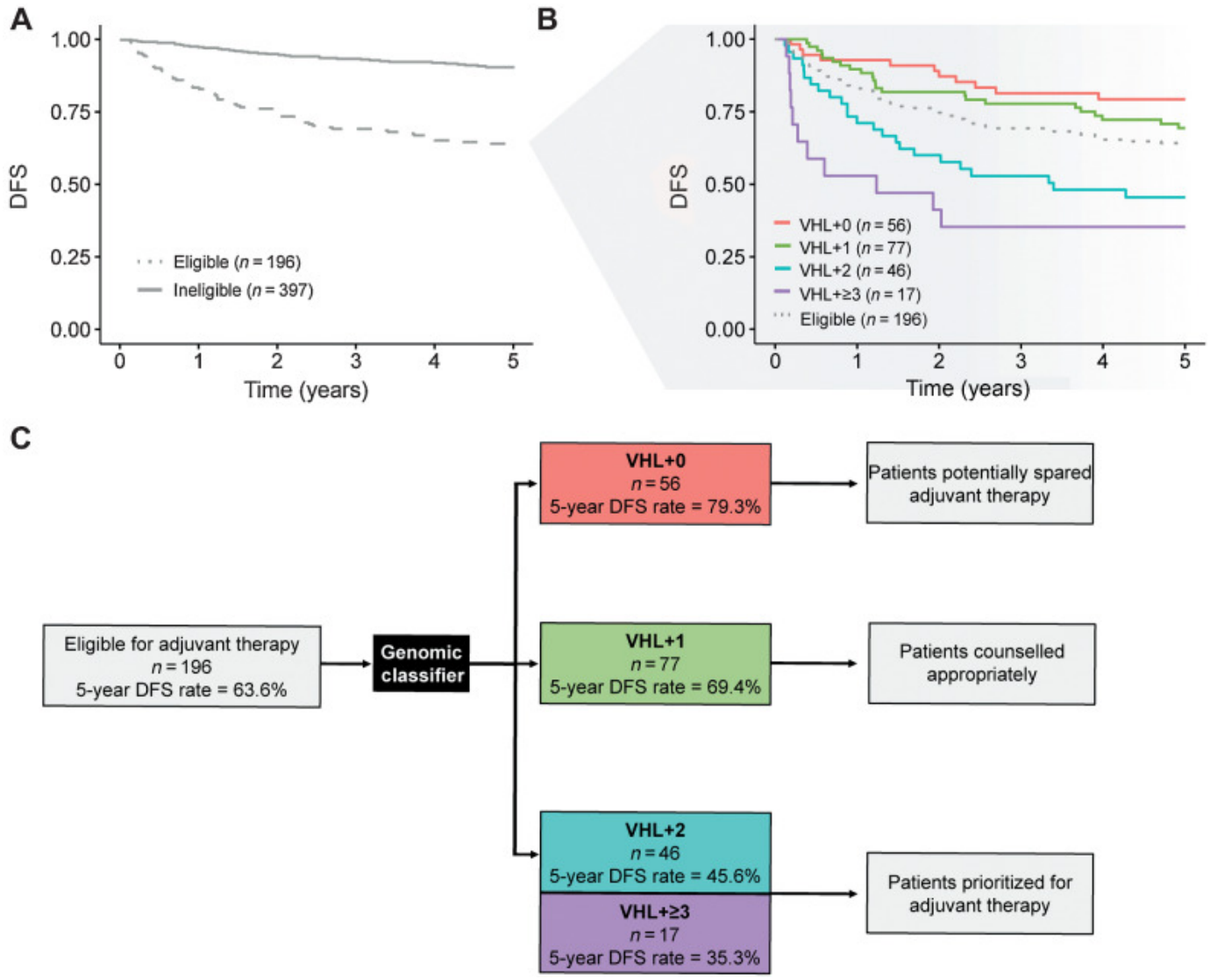


CONCLUSION In RCC, as in many other solid malignancies, clinicians rely on retrospective prediction tools to guide patient care and clinical trial selection and largely overestimate their predictive abilities. We used prospective collected adjuvant trial data to validate existing RCC prediction models and demonstrate a sharp decrease in the predictive ability of all models compared with their previous retrospective validations. Accordingly, we recommend prospective validation of any predictive model before implementing it into clinical practice and clinical trial design.

J Clin Oncol 37:2062-2071.

Riesgo de recaída en función de las mutaciones asociadas al VHL

En un estudio que investiga el papel de la secuenciación genómica en la estratificación de pacientes con **carcinoma de células renales de células claras** se observó que los pacientes que cuentan con **mutaciones añadidas al VHL (presente en 80% de los tumores)** presentan una menor supervivencia libre de enfermedad. Por tanto, **a más mutaciones añadidas al VHL mayor es el riesgo de recaída**



Naveen S et al. Application of Genomic Sequencing to Refine Patient Stratification for Adjuvant Therapy in Renal Cell Carcinoma. Clin Cancer Res. 2023 Apr 3;29(7):1220-1231.

What are the consequences of Carlos reccurring?

Para pacientes con CCR con riesgo intermedio-alto o alto de recidiva después de la nefrectomía

Es importante comprender el riesgo potencial de recidiva después de la nefrectomía.

Según un análisis observacional de datos de SEER-Medicare de 643 pacientes de 2007 a 2016

42% (n=269/643) de los pacientes con CCR con riesgo intermedio-alto o alto de recidiva experimentaron recidiva post nefrectomía.

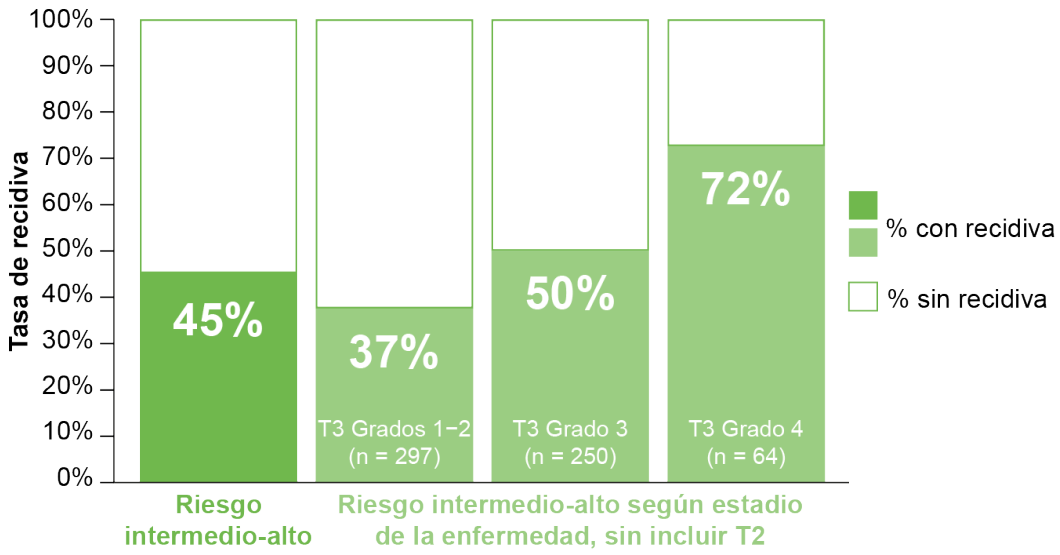
De estos pacientes **89%** (n=240/269) sufrieron recidiva con metástasis a distancia

- CCR = carcinoma de células renales; SEER = *Surveillance, Epidemiology, and End Results.*
- Sundaram M et al. J Manag Care Spec Pharm. 2022;28(10):1149–1160.

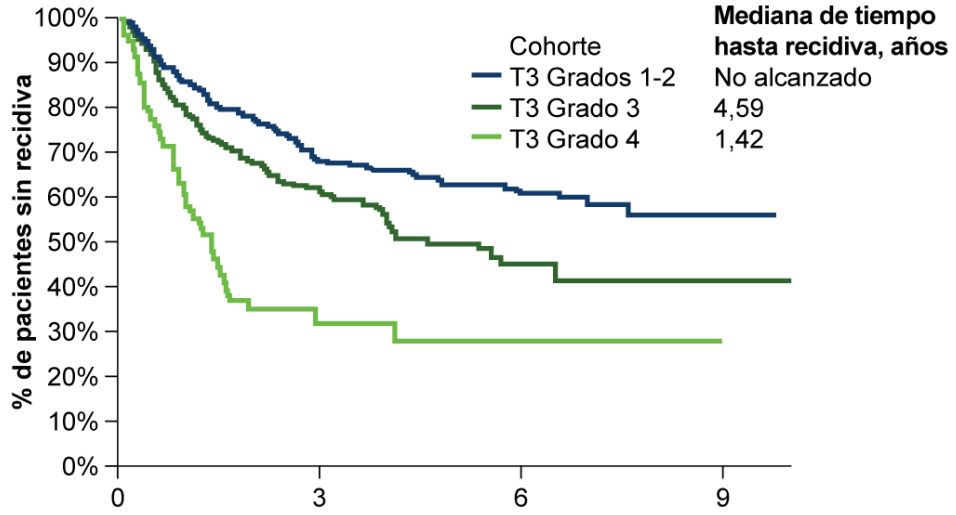
Riesgo de recidiva posnefrectomía en pacientes con tumores T3N0

- Este fue un análisis observacional retrospectivo de los datos de SEER-Medicare de EE. UU. de pacientes que tenían ≥66 años de edad cuando se les diagnosticó CCR por primera vez. Los datos se basan en un subconjunto de pacientes con CCR con riesgo intermedio-alto de recidiva después de la nefrectomía.[1,2]

Tasas de recidiva post nefrectomía a 5 años[1,2]



Tiempo hasta recidiva post nefrectomía[2]



Pacientes en riesgo		Años desde la nefrectomía		
T3 Grado 1-2	297	149	62	n[a]
T3 Grado 3	250	99	32	n[a]
T3 Grado 4	64	11	n[a]	n[a]

Basado en un análisis observacional de los datos de SEER-Medicare de EE. UU. (2007-2016)

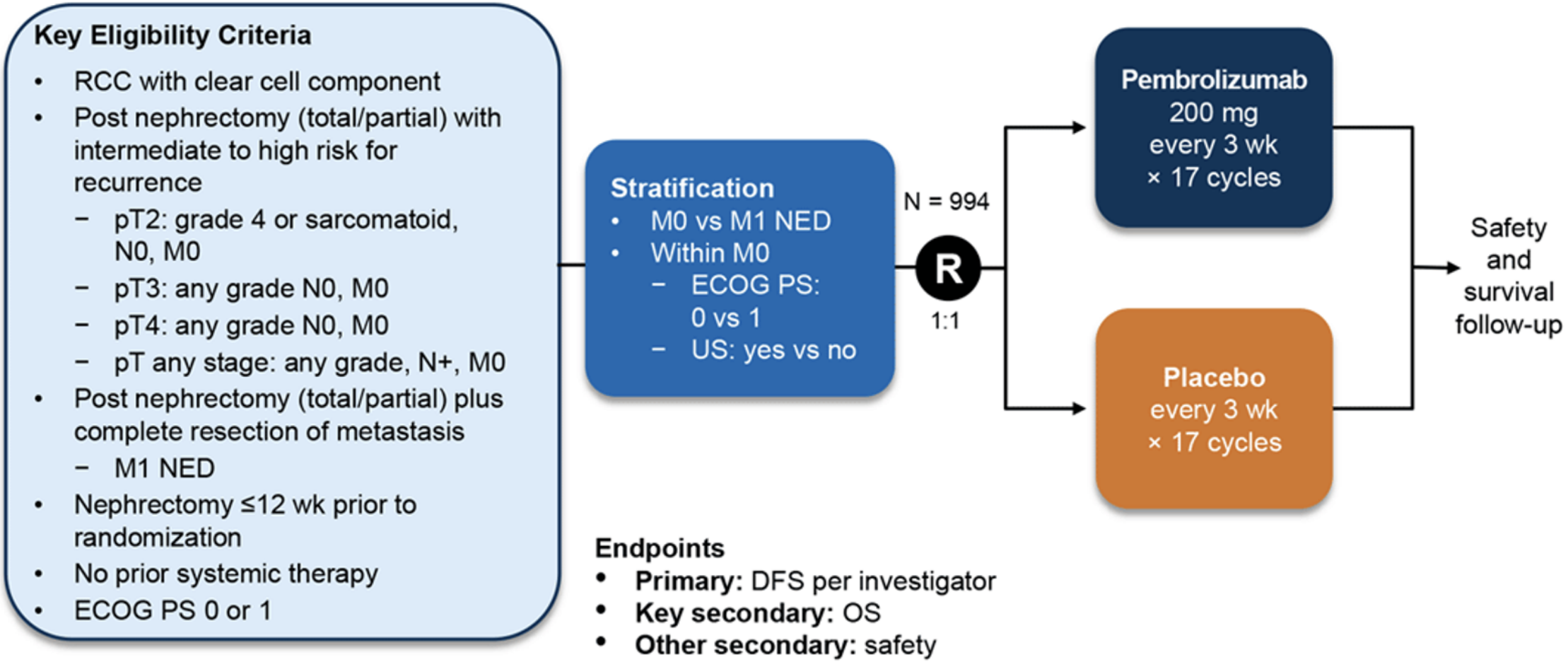
[a]Indica que la N de tamaño de muestra es <11 pacientes.

CCR = carcinoma de células renales; M0 = sin metástasis a distancia[3]; N0 = sin metástasis a ganglio linfático regional[3]; SEER = *Surveillance, Epidemiology, and End Results*;
T = tumor primario; T2 = tumor >7 cm en su mayor dimensión, limitado al riñón[3]; T3 = el tumor se extiende a las venas principales o a los tejidos perinéfricos, pero no a la glándula suprarrenal ipsilateral ni más allá de la fascia de Gerota[3].

1. Sundaram M et al. J Manag Care Spec Pharm. 2022;28(10):1149–1160. **2.** Supplementary to: Sundaram M et al. J Manag Care Spec Pharm. 2022;28(10):1149–1160 **3.** Gallardo E, et al. Clin Transl Oncol. 2018 Jan;20(1):47-56

What data do we have for adjuvant treatment in RCC?

Keynote-564: Study design



1.- Choueiri T, et al .NEJM 2021; 2.- Powles T, et al. Lancet Oncol 2022

KEYNOTE-564: Prespecified disease risk categories

Intermediate-High Risk		High Risk		M1 NED
pT2	pT3	pT4	Any pT	NED after resection of oligometastatic sites ≤1 year from nephrectomy
Grade 4 or sarcomatoid	Any grade	Any grade	Any grade	
N0	N0	N0	N+	
M0	M0	M0	M0	

86,1%

8,1%

5,8%

M0 = sin metástasis a distancia; M1 = con metástasis a distancia[3]; N0 = sin compromiso ganglionar[3]; NED = sin evidencia de enfermedad[3]. p = patológica.

1. Ficha técnica de Keytruda. **2.** Choueiri TK et al. *N Engl J Med.* 2021;385(8):683–694. **3.** Gallardo E, et al. Clin Transl Oncol. 2018 Jan;20(1):47-56

Keynote-564: Baseline Characteristics

Baseline Characteristics, ITT Population

	Pembro Arm (N = 496)	Placebo Arm (N = 498)
Age, median (range)	60 (27–81)	60 (25–84)
Male	347 (70.0%)	359 (72.1%)
ECOG PS 1	75 (15.1%)	72 (14.5%)
Geographic location		
North America	133 (26.8%)	125 (25.1%)
European Union	188 (37.9%)	187 (37.6%)
Rest of world	175 (35.3%)	186 (37.3%)
Disease risk category		
M0 intermediate-high	427 (86.1%)[a]	433 (86.9%)
M0 high risk	40 (8.1%)	36 (7.2%)
M1 NED	29 (5.8%)	29 (5.8%)
Sarcomatoid features[b]		
Present	52 (10.5%)	59 (11.8%)
Absent	414 (83.5%)	415 (83.3%)
PD-L1 CPS[c,d]		
<1	124 (25.0%)	113 (22.7%)
≥1	365 (73.6%)	383 (76.9%)

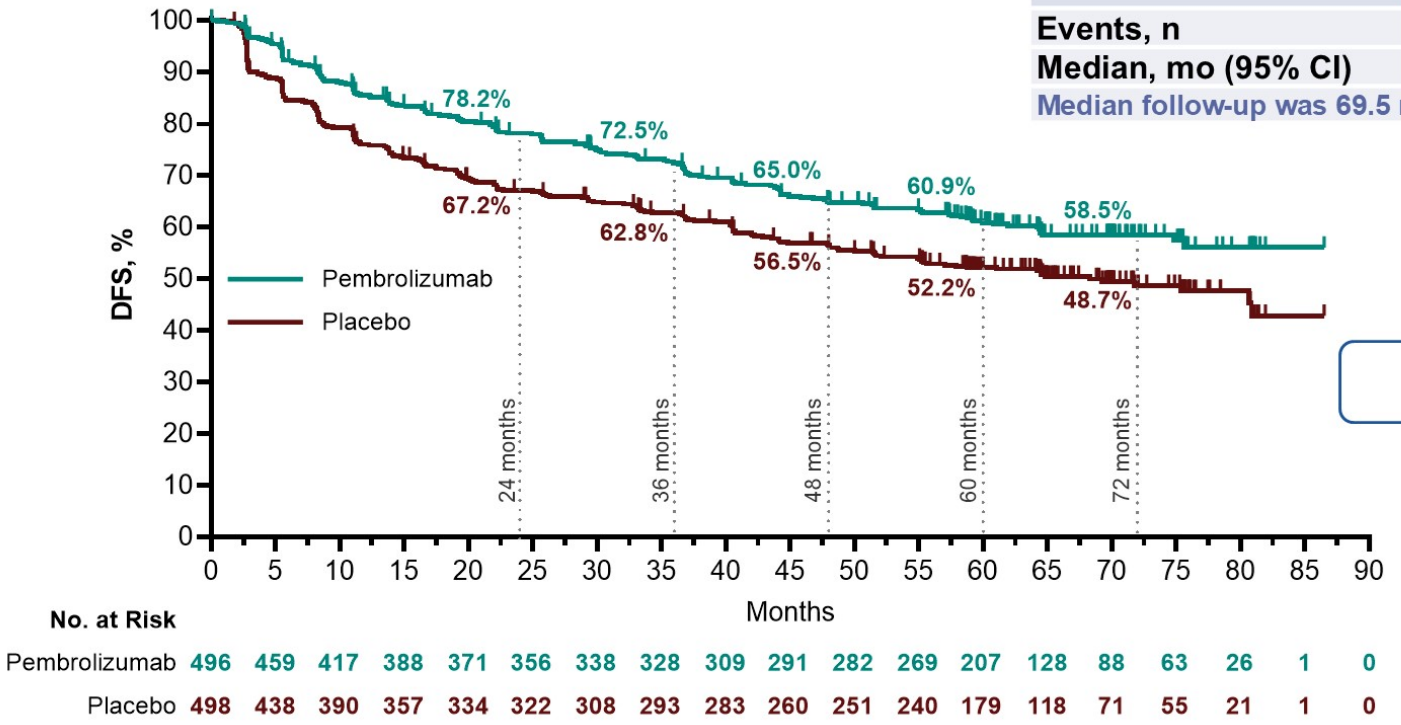
	Pembro Arm (N = 496)	Placebo Arm (N = 498)
Primary tumor stage		
T1	11 (2.2%)	15 (3.0%)
T2	27 (5.4%)	33 (6.6%)
T3	444 (89.5%)	437 (87.8%)
T4	14 (2.8%)	13 (2.6%)
Tumor nuclear grade[e]		
Grade 1	19 (3.8%)	16 (3.2%)
Grade 2	153 (30.8%)	150 (30.1%)
Grade 3	219 (44.2%)	213 (42.8%)
Grade 4	103 (20.8%)	119 (23.9%)
Lymph node stage		
N0	465 (93.8%)	467 (93.8%)
N1	31 (6.3%)	31 (6.2%)
Metastatic stage		
M0	467 (94.2%)	469 (94.2%)
M1 NED	29 (5.8%)	29 (5.8%)

[a]Included 5 participants with T2, grade ≤3, N0, M0 or T1, N0, M0. [b]30 additional participants in the pembro arm and 24 in the placebo arm had unknown sarcomatoid status. [c]Assessed using the PD-L1 IHC 22C3 pharmDx assay. CPS (combined positive score) is the number of PD-L1–staining cells (tumor cells, lymphocytes, and macrophages) divided by the total number of viable tumor cells, multiplied by 100. [d]7 additional participants in the pembro arm and 2 in the placebo arm had missing PD-L1 CPS. [e]2 additional participants in the pembro arm had missing tumor grade.
ITT population included all randomized participants. Data cutoff date: June 14, 2021.

1. Ficha técnica de Keytruda. **2.** Choueiri TK et al. *N Engl J Med*. 2021;385(8):683–694.

Keynote-564: Disease free survival
5 year follow up

Updated DFS by Investigator, ITT Population



	Pembro (N = 496)	Placebo (N = 498)
Events, n	188	241
Median, mo (95% CI)	NR (NR–NR)	68.3 (51.7–NR)

Median follow-up was 69.5 months (range, 60.2–86.9)

HR 0.71 (95% CI 0.59–0.86)

NR, not reported.
Primary DFS endpoint was met at IA1 and was not formally statistically tested thereafter.

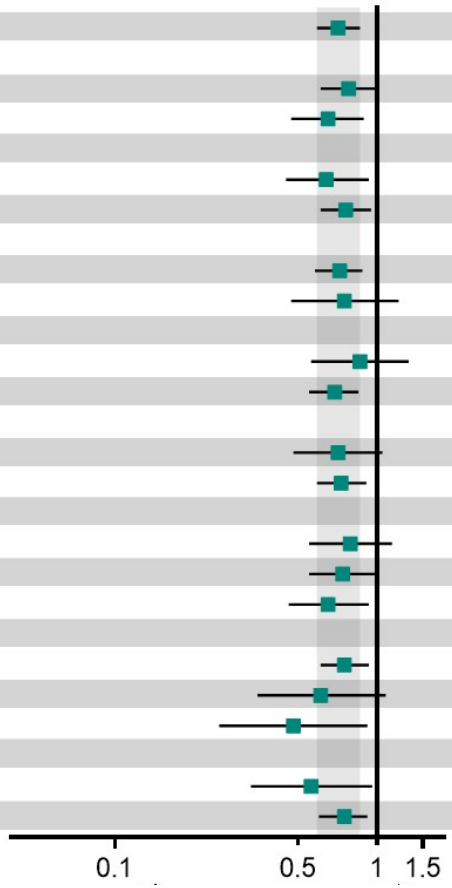
Data cutoff date: September 25, 2024.

Haas NB, ASCO 2025

Keynote-564: Disease free survival
5 year follow up

DFS by Subgroups

	Events/Participants	Hazard Ratio (95% CI)
Overall	429/994	0.71 (0.59-0.86)
Age		
<65 yrs	271/664	0.78 (0.61-0.99)
≥65 yrs	158/330	0.65 (0.47-0.89)
Sex		
Female	118/288	0.64 (0.45-0.93)
Male	311/706	0.76 (0.61-0.95)
ECOG performance status		
0	360/847	0.72 (0.58-0.88)
1	69/147	0.75 (0.47-1.21)
PD-L1 status[a]		
CPS <1	83/237	0.86 (0.56-1.32)
CPS ≥1	341/748	0.69 (0.55-0.85)
Regions		
United States	101/231	0.71 (0.48-1.05)
Outside United States	328/763	0.73 (0.59-0.91)
Tumor grade		
1-2	116/338	0.79 (0.55-1.14)
3	185/432	0.74 (0.55-0.98)
4	127/222	0.65 (0.46-0.93)
Risk category		
M0 int/high	342/855	0.75 (0.61-0.93)
M0 high	49/77	0.61 (0.35-1.08)
M1 NED	37/57	0.48 (0.25-0.92)
Sarcomatoid features		
Present	59/111	0.56 (0.33-0.96)
Absent	339/829	0.75 (0.60-0.92)

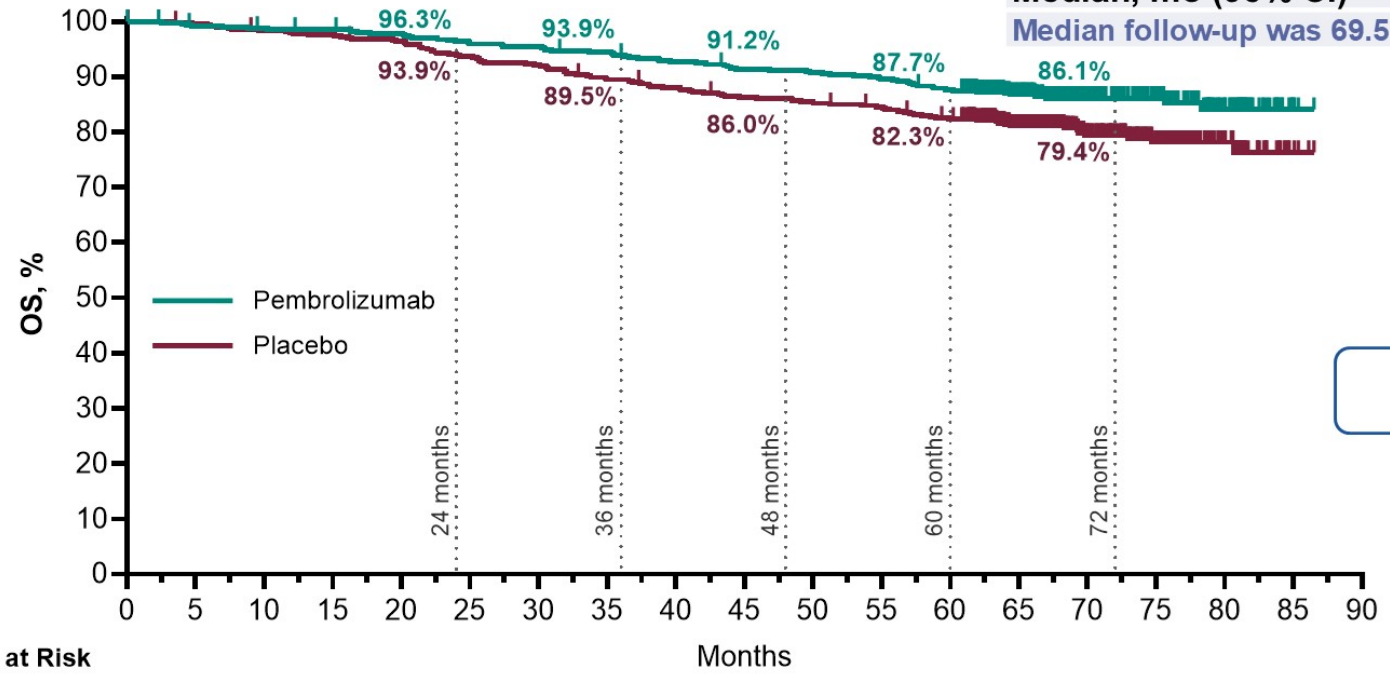


Haas NB, ASCO 2025

Keynote-564: Overall survival
5 year follow up

Updated OS, ITT Population

	Pembro (N = 496)	Placebo (N = 498)
Events, n	68	99
Median, mo (95% CI)	NR (NR–NR)	NR (NR–NR)
Median follow-up was 69.5 months (range, 60.2–86.9)		



HR 0.66 (95% CI 0.48–0.90)

No. at Risk																			
Pembrolizumab	496	489	486	484	479	470	468	462	452	445	442	436	426	310	198	121	50	3	0
Placebo	498	494	487	483	476	463	455	441	433	423	419	413	400	284	177	111	46	4	0

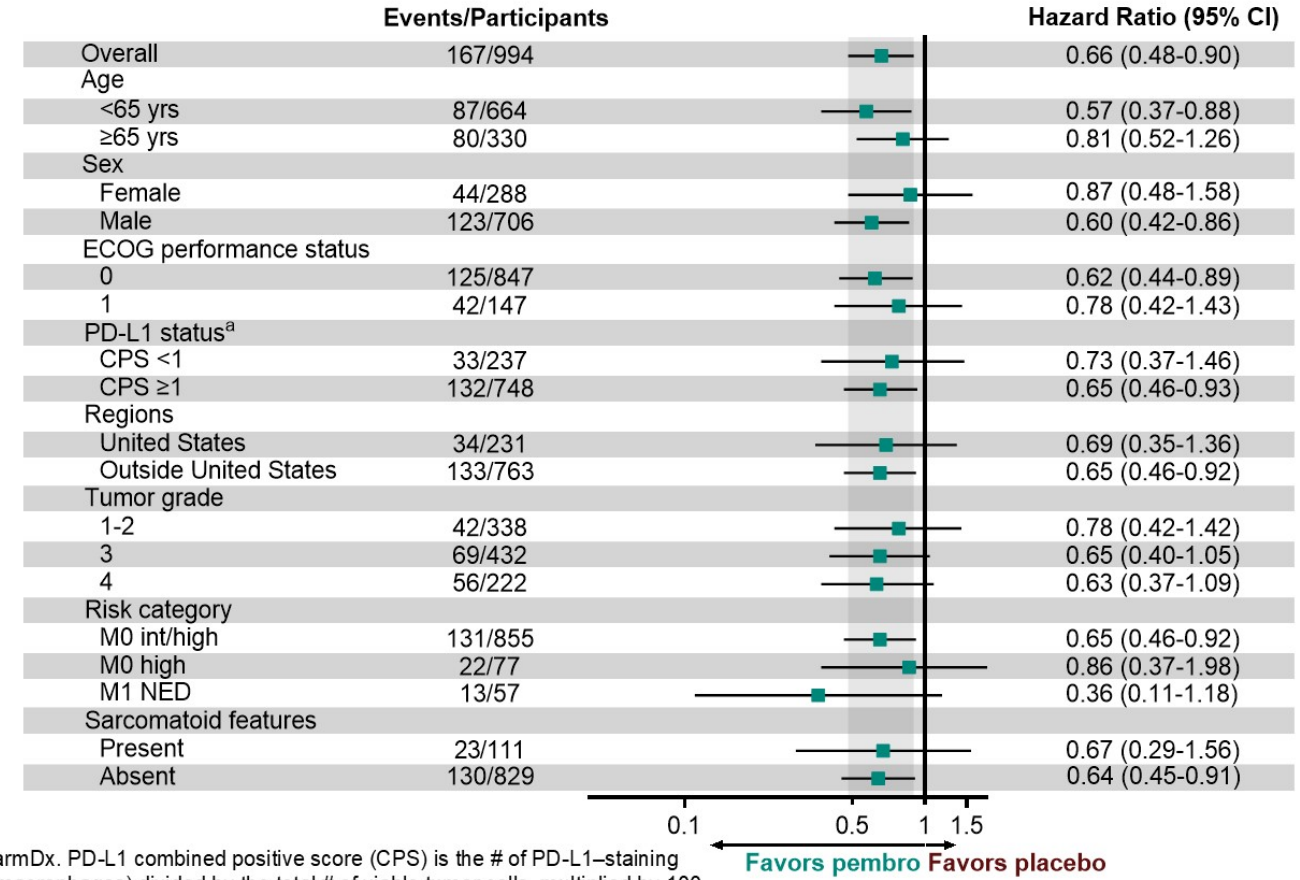
Key secondary OS endpoint was met at IA3 and was not formally statistically tested thereafter.

Data cutoff date: September 25, 2024.

Haas NB, ASCO 2025

Keynote-564: Overall survival
5 year follow up

OS by Subgroups



[a]Assessed with PD-L1 IHC 22C3 pharmDx. PD-L1 combined positive score (CPS) is the # of PD-L1–staining cells (tumor cells, lymphocytes, and macrophages) divided by the total # of viable tumor cells, multiplied by 100. The 95% CI boundary for overall OS is indicated by the shaded column.

Median follow-up to data cutoff (Sept 25, 2024): 6

Haas NB, ASCO 2025

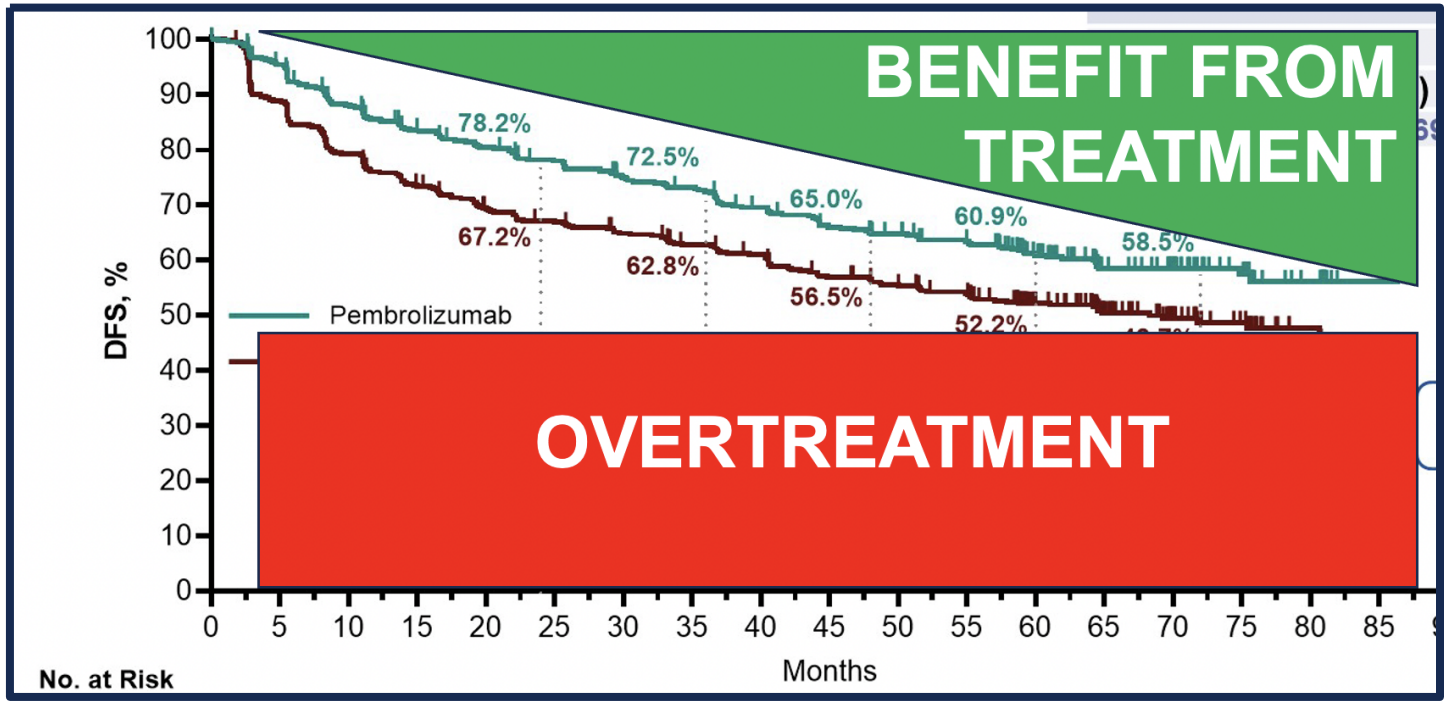
Keynote-564: Adverse events
5 year follow up

Summary of Updated Safety Findings, As-Treated Population

	IA3 (57.2 mo follow-up)		IA4 (69.5 mo follow-up)	
	Pembro (N = 488)	Placebo (N = 496)	Pembro (N = 488)	Placebo (N = 496)
Duration of therapy, median (range), months	11.1 (0.03–14.3)	11.1 (0.03–15.4)	11.1 (0.03–14.3)	11.1 (0.03–15.4)
Any-cause AEs[a]	470 (96.3%)	453 (91.3%)	470 (96.3%)	453 (91.3%)
Grade 3 to 5	156 (32.0%)	88 (17.7%)	156 (32.0%)	88 (17.7%)
Led to treatment discontinuation	103 (21.1%)	11 (2.2%)	103 (21.1%)	11 (2.2%)
Led to death	2 (0.4%)	1 (0.2%)	2 (0.4%)	1 (0.2%)
Any-cause serious AEs[a]	101 (20.7%)	57 (11.5%)	101 (20.7%)	57 (11.5%)
Led to treatment discontinuation	49 (10.0%)	5 (1.0%)	49 (10.0%)	5 (1.0%)
Treatment-related AEs[a]	386 (79.1%)	263 (53.0%)	386 (79.1%)	263 (53.0%)
Grade 3 to 4	91 (18.6%)	6 (1.2%)	91 (18.6%)	6 (1.2%)
Led to treatment discontinuation	89 (18.2%)	4 (0.8%)	89 (18.2%)	4 (0.8%)
Led to death	0	0	0	0
Treatment-related serious AEs[a]	59 (12.1%)	1 (0.2%)	58 (11.9%)	1 (0.2%)
Immune-mediated AEs and infusion reactions[b,c]	178 (36.5%)	36 (7.3%)	179 (36.7%)	36 (7.3%)
Grade 3 to 4	46 (9.4%)	3 (0.6%)	47 (9.6%)	3 (0.6%)
Led to death	0	0	0	0

Haas NB, ASCO 2025

What is the “real” benefit of adjuvant treatment?

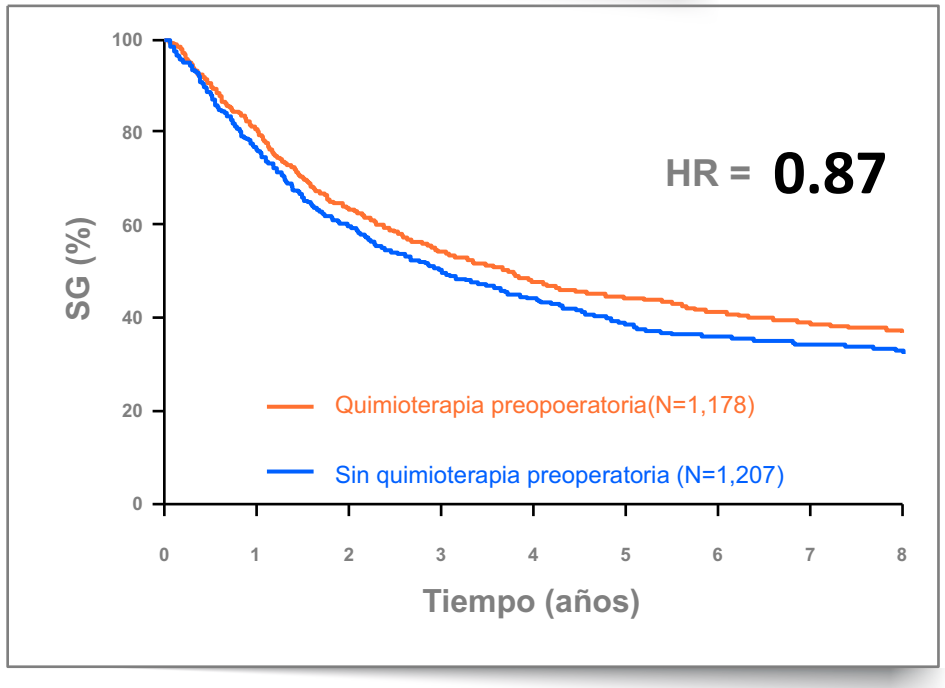


Outcome	Pembrolizumab	Placebo	Absolute Benefit	Hazard Ratio (HR)	Number Needed to Treat (NNT)
Disease-Free Survival (DFS)	60.9% (5-year)	52.2% (5-year)	8.7%	0.71 (95% CI: 0.59–0.86)	~12
Overall Survival (OS)	87.7% (5-year)	82.3% (5-year)	5.4%	0.66 (95% CI: 0.48–0.90)	~19

Are we overtreating Carlos?

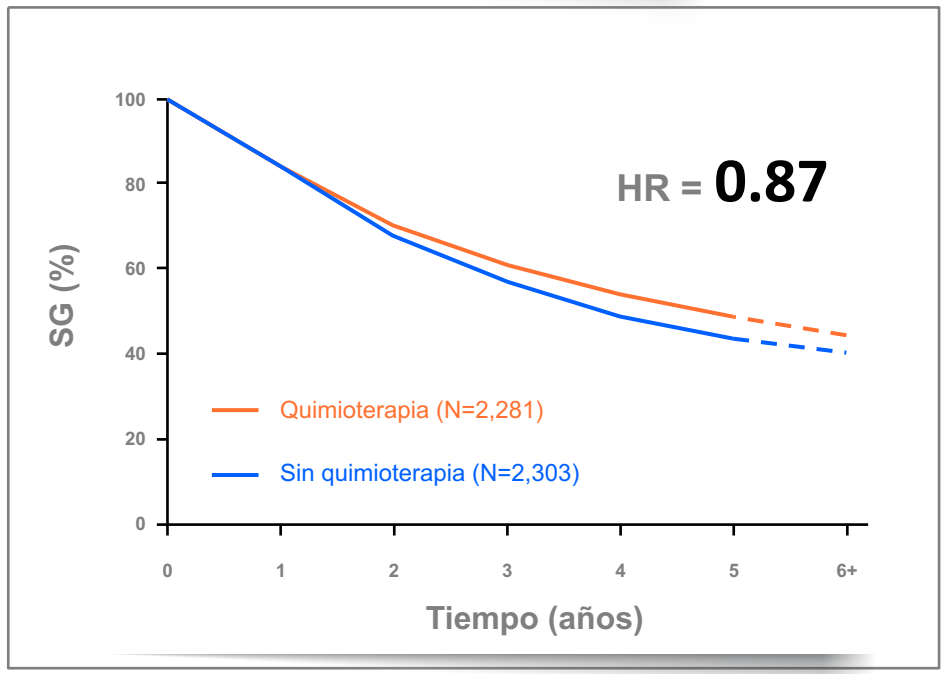
La quimioterapia adyuvante y neoadyuvante mejoran la supervivencia global en NSCLC

Quimioterapia neoadyuvante[1]



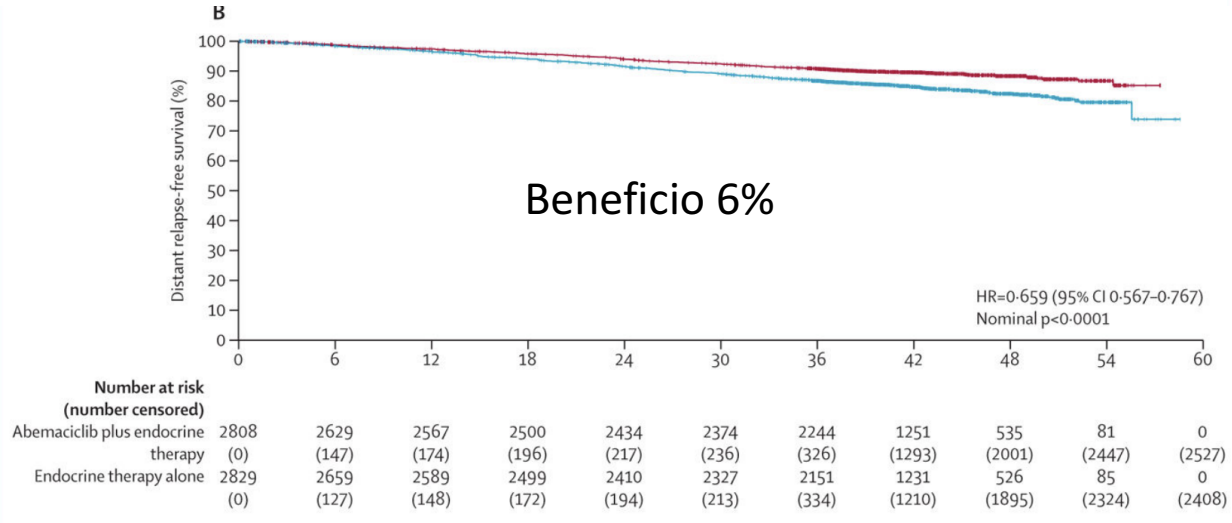
5%
de mejora en la SG a 5 años[1,2]

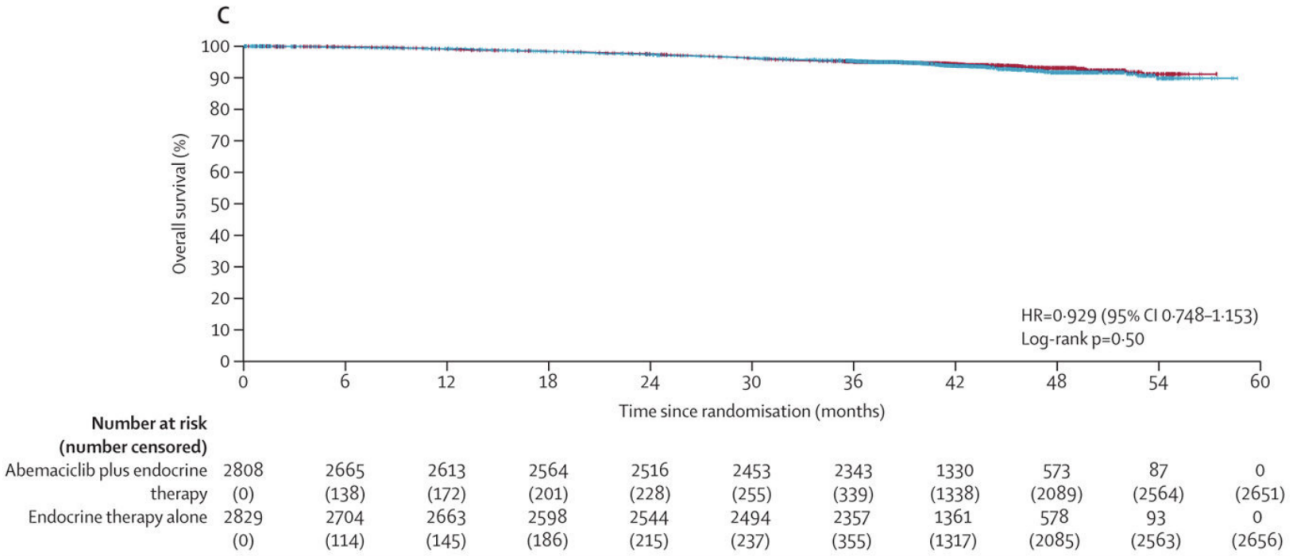
Quimioterapia adyuvante[2]



1. NSCLC Collaborative Group. Lancet 2014. 2. Pignon, et al. J Clin Oncol 2008. 3. Postmus, et al. Ann Oncol 2017.

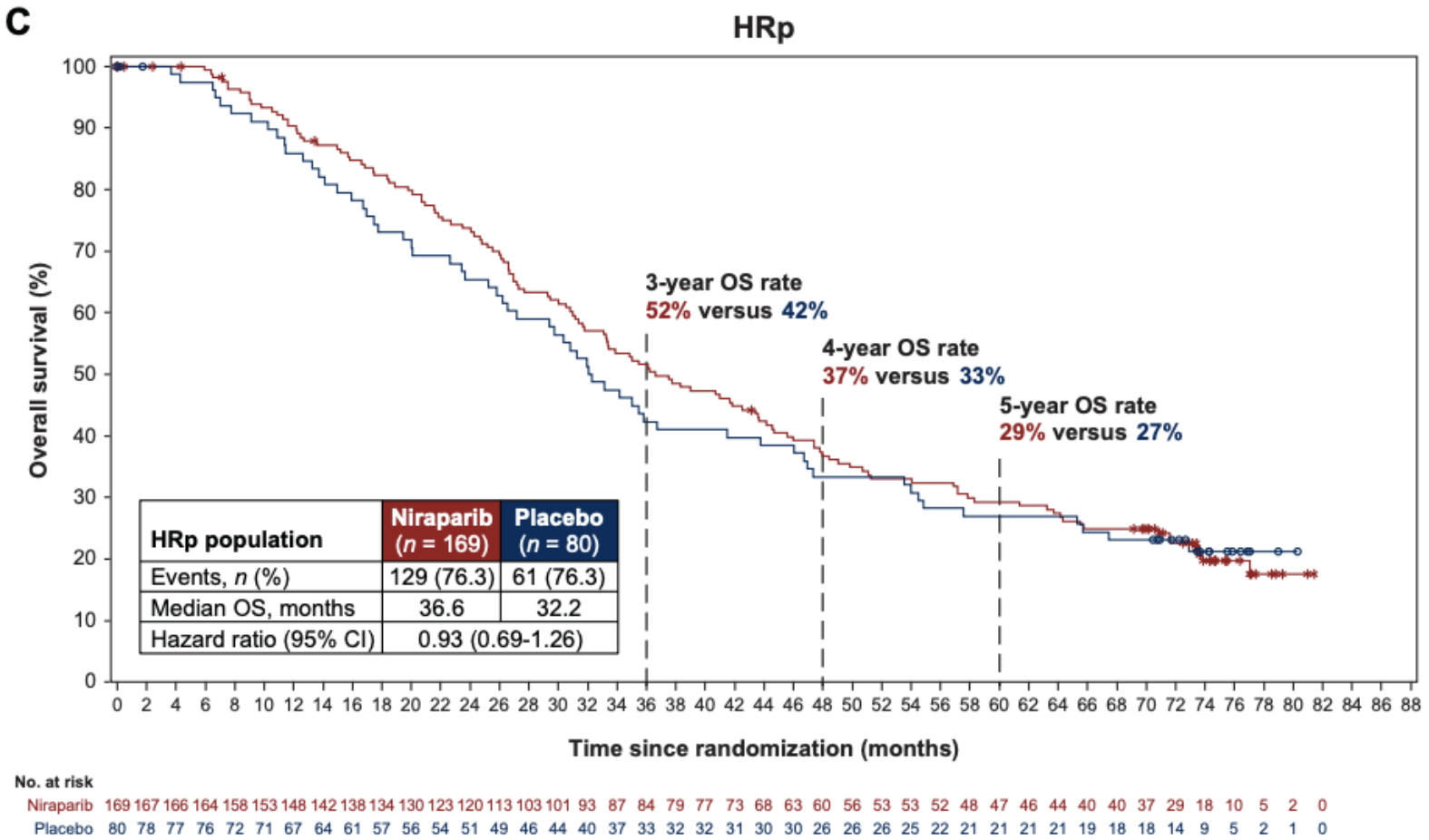
Abemaciclib plus endocrine therapy for hormone receptorpositive, HER2-negative, node-positive, high-risk early breast cancer (monarchE): results from a preplanned interim analysis of a randomised, open-label, phase 3 trial





Johnston. Lancet Oncol. 2023 January ; 24(1): 77–90

Niraparib first-line maintenance therapy in patients with newly diagnosed advanced ovarian cancer: final overall survival results from the PRIMA/ENGOT-OV26/GOG-3012 trial



2%
de mejora en la SG a 5 años

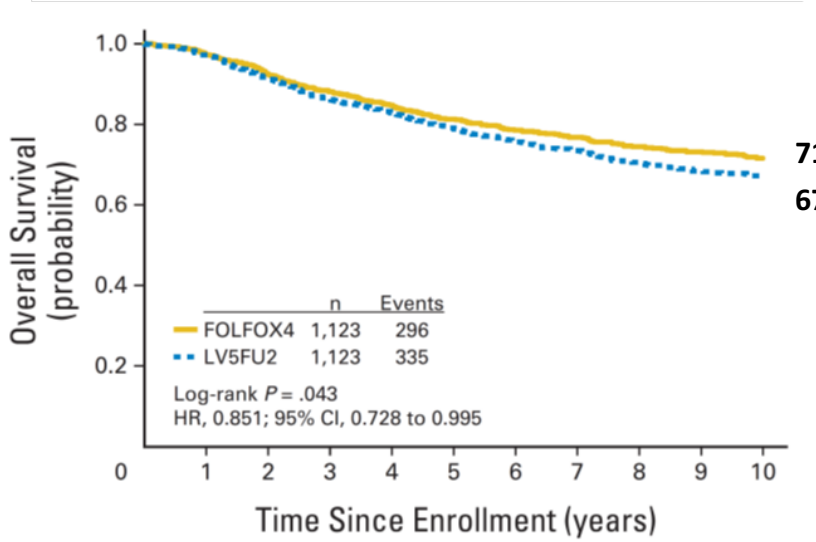
El laboratorio titular de la autorización de comercialización de Niraparib es Glaxosmithkline (Ireland) Limited.

Monk. Ann Oncol. 2024 Nov;35(11):981-992

Beneficio de la quimioterapia sistémica adyuvante en cáncer de colon

10-year Overall Survival

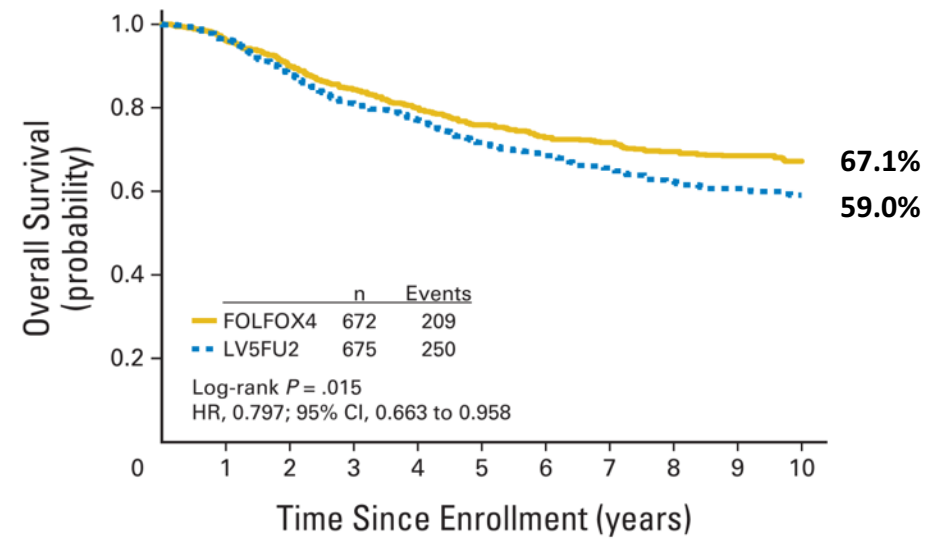
ITT population



71.7%
67.1%

5%
de mejora en la SG a 10 años

Stage III population



67.1%
59.0%

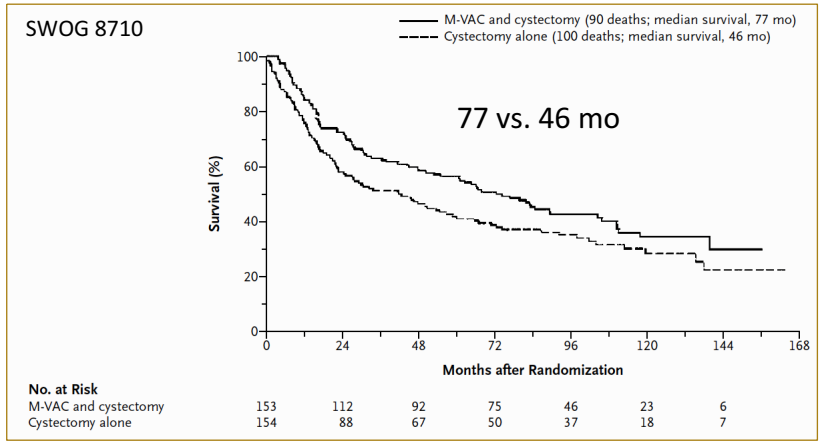
FOLFOX4											
No. at risk	1,123	1,082	1,024	971	923	881	815	638	479	445	349
Events	0	31	84	133	170	207	236	252	269	277	285
LV5FU2											
No. at risk	1,123	1,081	1,006	949	898	846	781	595	434	393	301
Events	0	31	97	150	190	231	264	286	307	320	327

FOLFOX4											
No. at risk	672	637	592	553	519	491	457	356	279	262	205
Events	0	28	68	104	133	158	178	185	195	199	203
LV5FU2											
No. at risk	675	642	581	533	499	454	417	324	241	219	163
Events	0	25	81	126	153	186	206	223	238	244	249

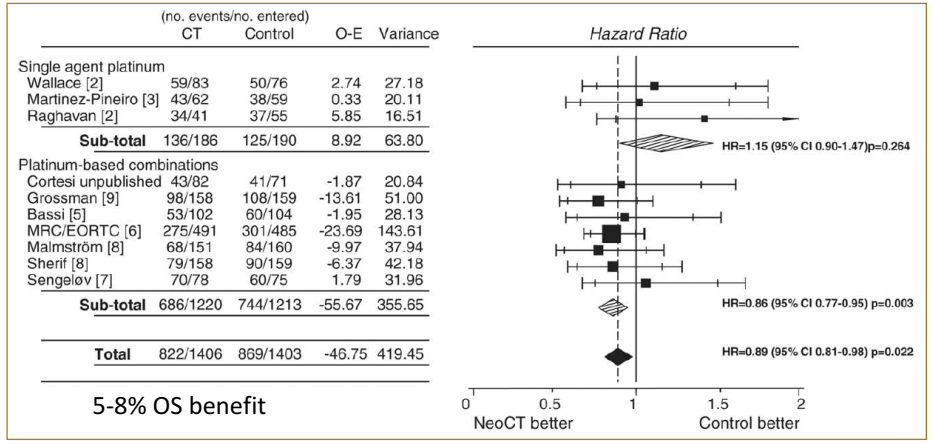
André T, et al. J Clin Oncol 2015;33:4176-4187

Beneficio del tratamiento sistémico perioperatorio en cáncer urotelial

Neoadjuvant chemotherapy



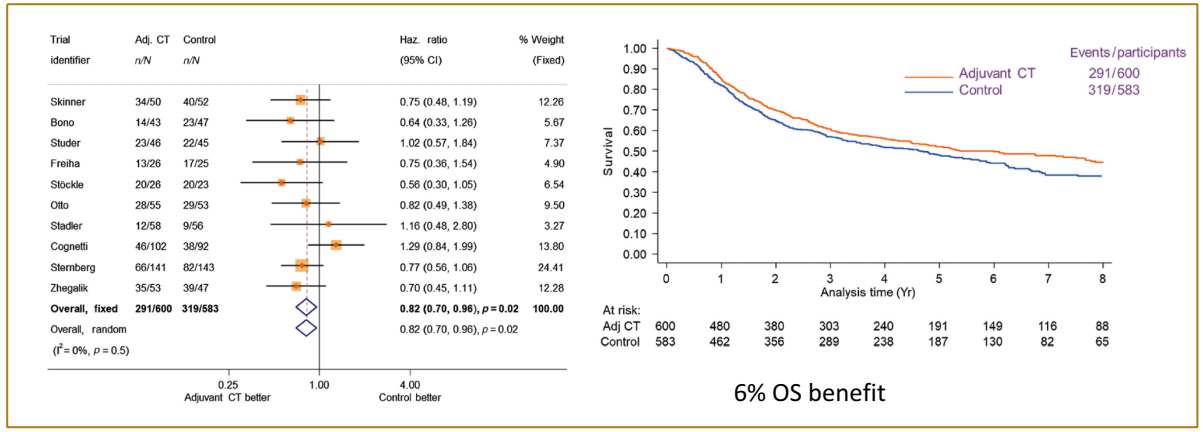
N = 317



5-8% OS benefit

N = 3005

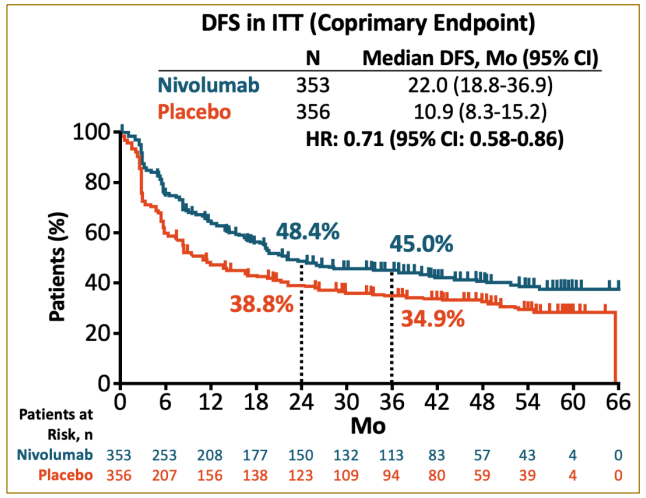
Adjuvant chemotherapy



6% OS benefit

N = 1183

Adjuvant nivolumab



N = 709

Grossman HB, et al. N Engl J Med 2003;349:859-866
ABC Metaanalysis. Eur Urol 2005;48:202-206
ABC Metaanalysis. Eur Urol 2022;81:56-61

Bajorin DF, et al. N Engl J Med 2021;384:2102-2114
Galsky M, et al. J Clin Oncol 41, 2023 (suppl 6; abstr LBA443)

Do we have any biomarker that can help us with the decision?

2024 ASCO ANNUAL MEETING

Circulating kidney injury molecule-1 (KIM-1) biomarker analysis in IMmotion010, a randomized Phase 3 study of adjuvant atezolizumab vs placebo in patients with renal cell carcinoma at increased risk of recurrence after resection

Laurence Albiges,[1] Axel Bex,[2] Cristina Suarez,[3] Robert Uzzo,[4] Xiaobin Tang,[5] Zoe June Assaf,[5] Sarita Dubey,[5] Erik Goluboff,[5] Corey Carter,[5] Romain Banchereau,[5] Mahrukh Huseni,[5] Sumanta Pal,[6] Brian Rini[7]

Key eligibility criteria

- Resected intermediate- to high-risk[a] RCC
  - T2 Grade 4
  - T3a Grade 3/4
  - T3b/c or T4 any Grade
  - TXN+ any Grade
  - M1 NED[b]
- Clear cell and/or sarcomatoid component

R 1:1

N=778

Atezolizumab 1200 mg IV q3w for 16 cycles or 1 year[c]

Placebo IV q3w for 16 cycles or 1 year[c]

Stratification factors

- **Disease stage**
  T2/T3a vs T3b/c/T4/N+ vs M1 NED
- **PD-L1 expression on IC[d]**
  IC0 (<1%) vs IC1/2/3 (≥1%)
- **Region**
  North America[e] vs rest of world

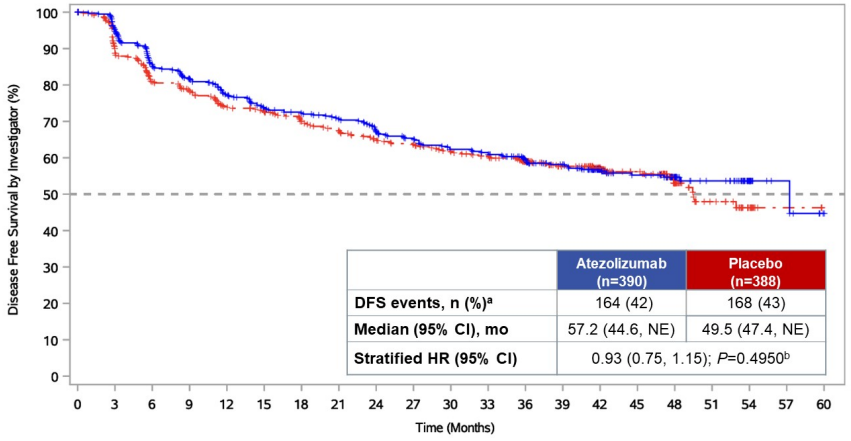
Primary endpoint

- Investigator-assessed DFS in ITT population

Key secondary endpoints

- OS in the ITT population
- Investigator-assessed DFS in the IC1/2/3 population
- IRF-assessed DFS in the ITT and IC1/2/3 populations
- IRF-assessed EFS in the ITT population
- Safety

Investigator-assessed DFS in the ITT population



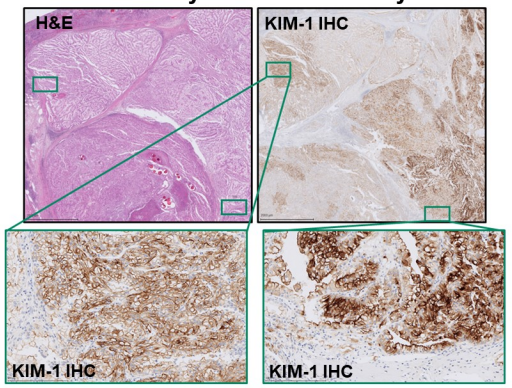
	Atezolizumab (n=390)	Placebo (n=388)
DFS events, n (%)[a]	164 (42)	168 (43)
Median (95% CI), mo	57.2 (44.6, NE)	49.5 (47.4, NE)
Stratified HR (95% CI)	0.93 (0.75, 1.15); *P*=0.4950[b]	

KIM-1 (Kidney injury molecule-1) is a tumor associated protein and may be a useful circulating biomarker in RCC

10

- KIM-1, a type 1 membrane glycoprotein, has been identified as a marker of unresected clear-cell RCC and as a marker for early detection of RCC[1,2,3]
- In the ASSURE trial of adjuvant sunitinib, sorafenib, or placebo, higher levels of KIM-1 in post-nephrectomy, pre-treatment **plasma samples** were associated with worse DFS and OS[4]
- KIM-1 can be measured **in plasma or serum** and is stable under different storage conditions, suggesting suitability to serve as a **peripheral blood circulating biomarker**[5]

KIM-1 IHC analysis in RCC Primary Tumor



Circulating kidney injury molecule-1 (KIM-1) biomarker analysis in IMmotion010, a randomized Phase 3 study of adjuvant atezolizumab vs placebo in patients with renal cell carcinoma at increased risk of recurrence after resection

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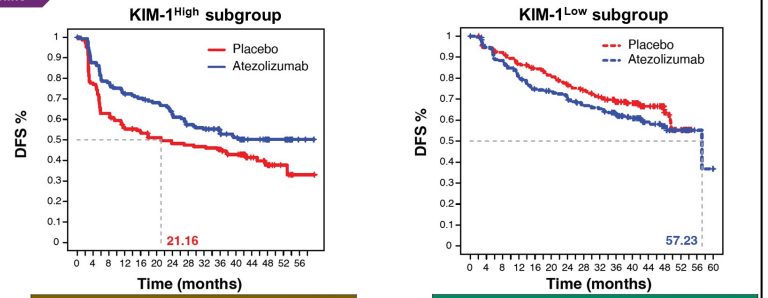
Atezolizumab improved DFS vs Placebo in the baseline KIM-1^{High} subgroup

Baseline

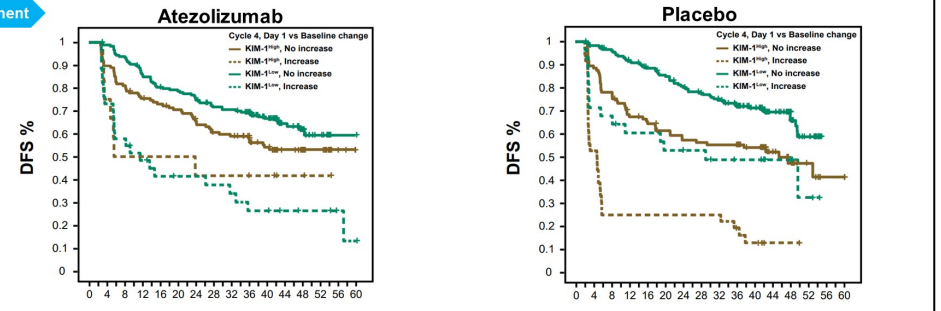


	n	Median DFS	HR[a] (95% CI)
Atezolizumab	151	NE	0.72 (0.52, 0.99)
Placebo	149	21.16	

	n	Median DFS	HR[a] (95% CI)
Atezolizumab	229	57.23	1.12 (0.88, 1.63)
Placebo	223	NE	

On-treatment increase in KIM-1 was associated with worse DFS in both KIM-1^{High} and KIM-1^{Low} subgroups

On Treatment



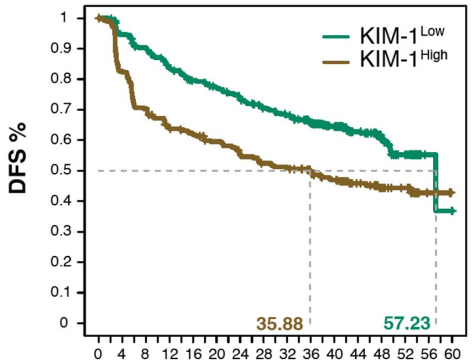
Baseline	On-treatment	n	Median DFS	HR (95% CI)
KIM-1^{High}	Increase[a]	12	14.8	1.68 (0.77, 3.69)
	No increase	126	NE	
KIM-1^{Low}	Increase[a]	34	11.5	3.56 (2.21, 5.75)
	No increase	179	NE	

Baseline	On-treatment	n	Median DFS	HR (95% CI)
KIM-1^{High}	Increase[a]	36	4.8	3.53 (2.24, 5.58)
	No increase	105	45.4	
KIM-1^{Low}	Increase[a]	28	29.0	2.51 (1.42, 4.44)
	No increase	179	NE	

KIM-1^{High} status at baseline was associated with worse DFS in IMmotion010

15

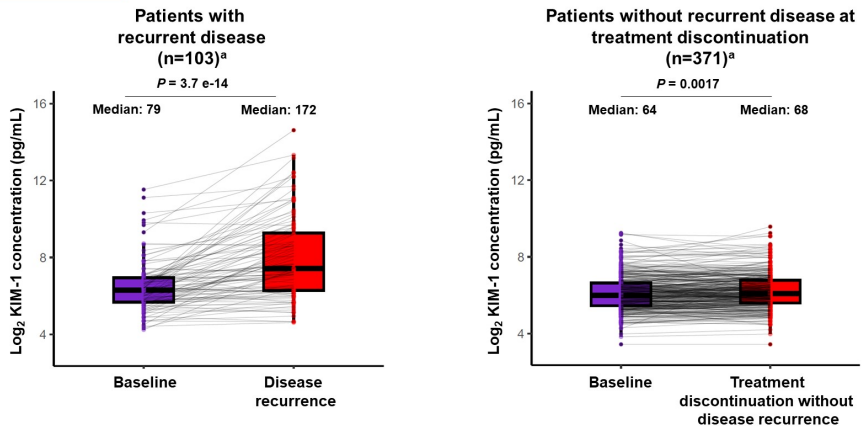
Baseline



	n	Median DFS (months)	HR[a] (95% CI)
KIM-1^{High}	300	35.88	1.75 (1.40, 2.17)
KIM-1^{Low}	452	57.23	

Serum KIM-1 levels increased at time of disease recurrence vs baseline

Disease Recurrence/ Treatment Discontinuation

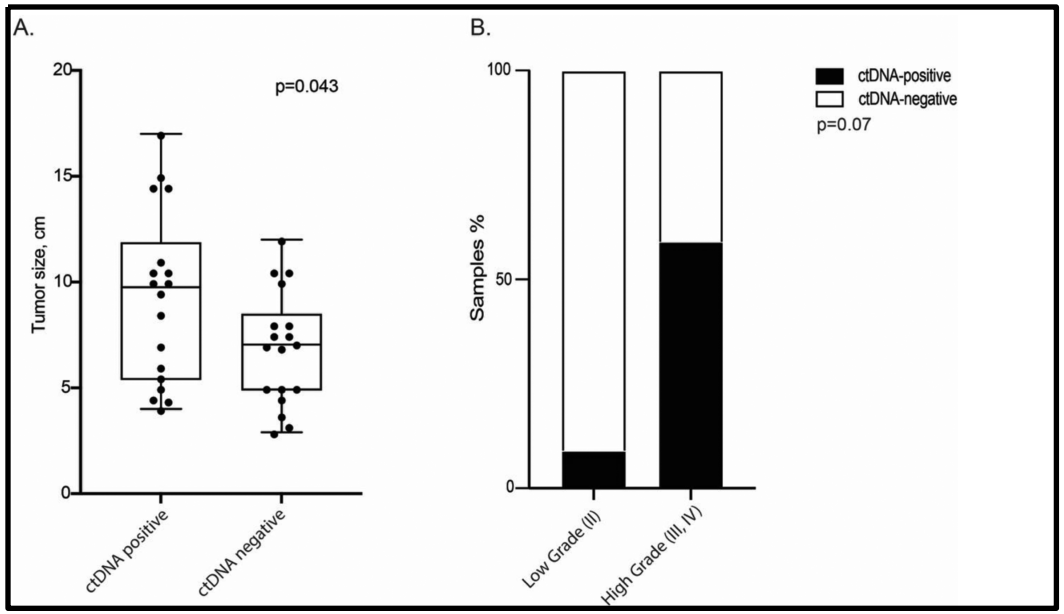


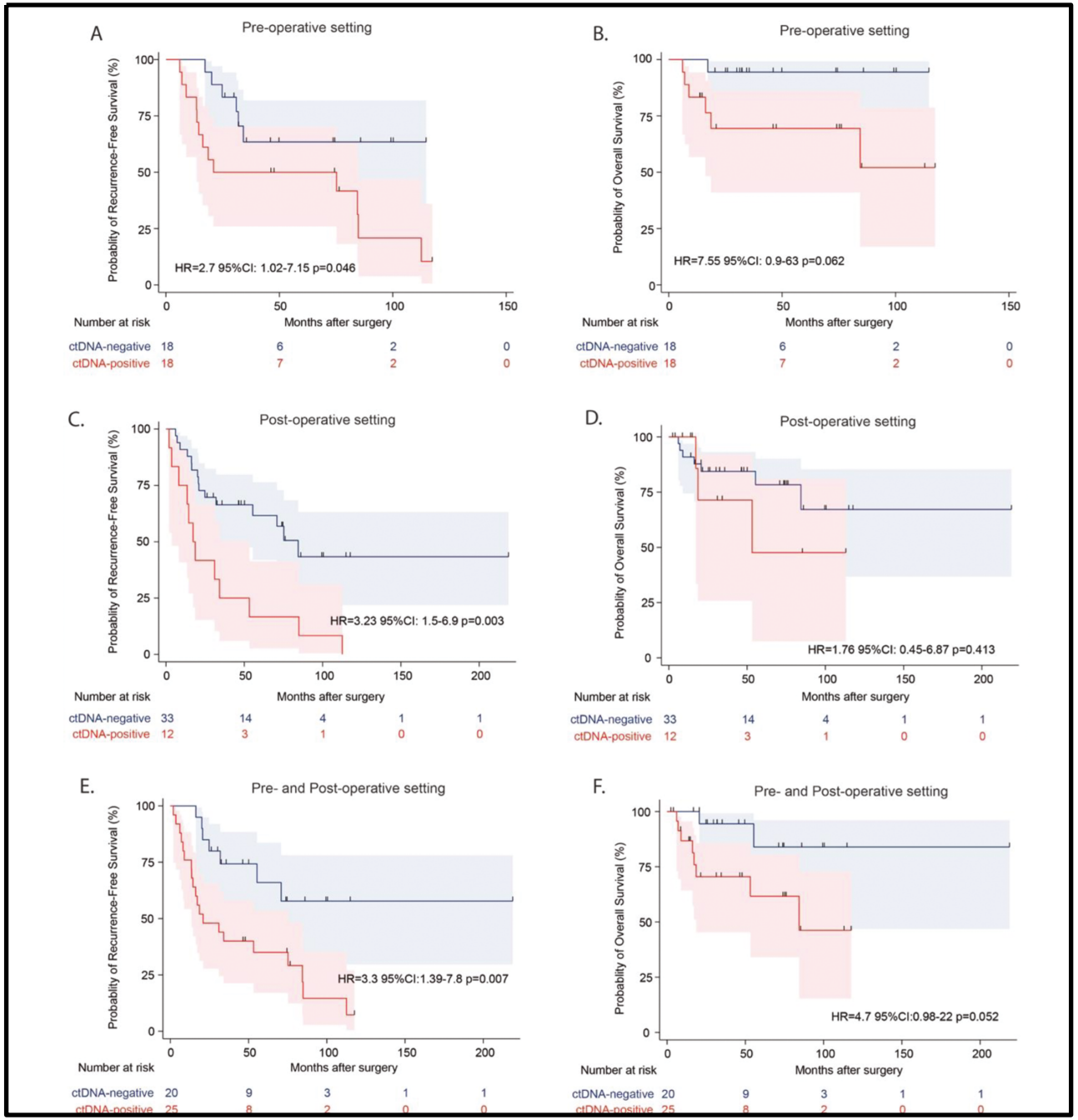
The Oncologist, 2024, **29**, 887–893
https://doi.org/10.1093/oncolo/oyae180
Advance access publication 16 July 2024
Original Article

OXFORD

Association of circulating tumor DNA with patient prognosis in surgically resected renal cell carcinoma

Andres F. Correa[1], Ekaterina Kalashnikova[2], Hsin-Ta Wu[2], Ryan M. Winters[3,4], Mustafa Balcioglu[2], Sumedha Sudhaman,[2] Denise C. Connolly[3,5], Yulan Gong[6], Robert G. Uzzo[1], Himanshu Sethi[2], Adam C. ElNaggar[2], Alexey Aleshin[2], Minetta C. Liu,[2] Philip H. Abbosh[*,5,7]



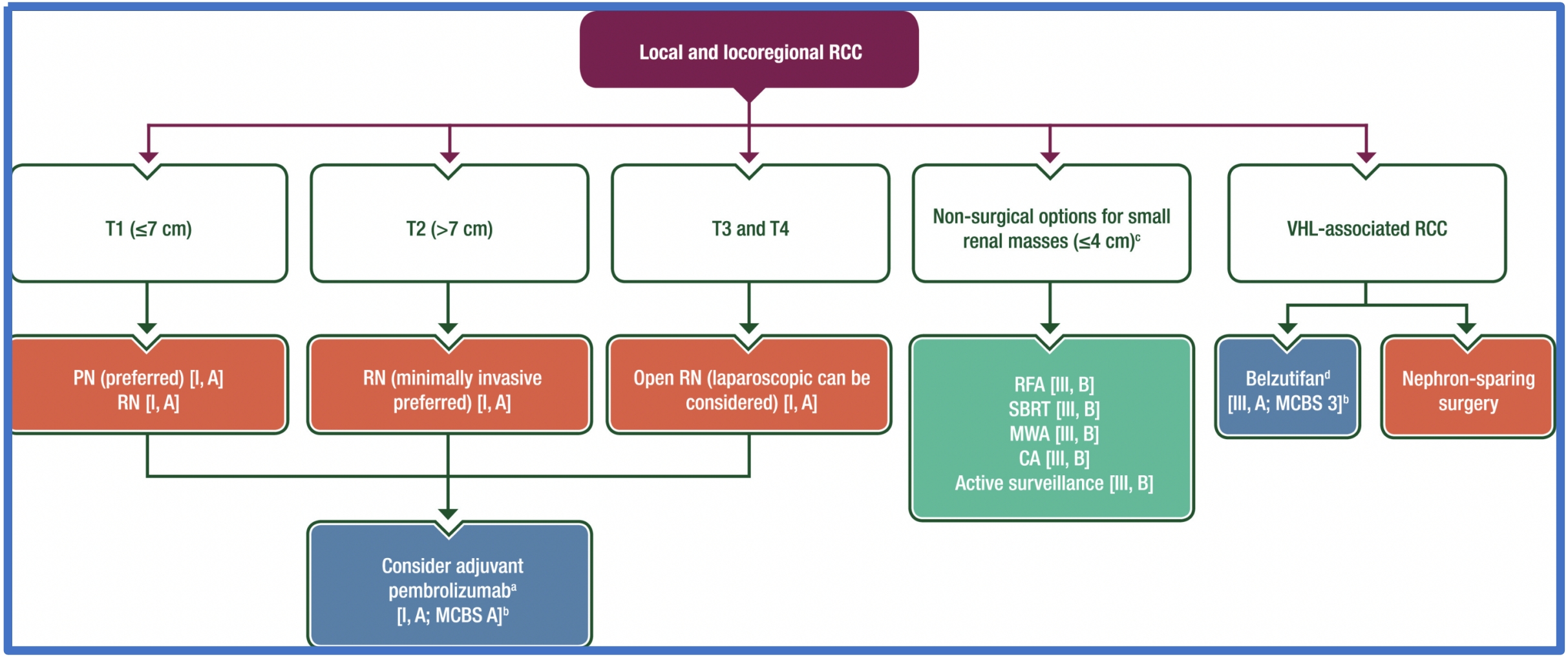


ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

SPECIAL ARTICLE

Renal cell carcinoma: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up☆



Powles T, *et al.* Ann Oncol. 2024;35(8):692-706.

EAU Guidelines on Renal Cell Carcinoma

A. Bex (Chair), L. Albiges, J. Bedke (Vice-Chair), U. Capitanio, S. Dabestani, M. Hora, T. Klatte, T. Kuusk, L. Lund, L. Marconi, G. Pignot, T. Powles, M. Tran, A. Volpe
Patient Representative: S. Bonn
Guidelines Associates: Y. Abu-Ghanem, R. Campi, C. Palumbo
Guidelines Office: N. Schouten

Table 2 – Summary of recommendations from the European Association of Urology RCC Guidelines Panel on the use of adjuvant ICI and subsequent therapy for RCC

Recommendation	Strength rating
Offer adjuvant pembrolizumab to patients with clear-cell RCC, preferably within 12–16 wk after nephrectomy, with recurrence risk as defined in the KEYNOTE-564 trial: **Intermediate-high risk:** • pT2, grade 4 or sarcomatoid differentiation, N0, M0 • pT3, any grade, N0, M0 **High risk:** • pT4, any grade, N0, M0 • Any pT, any grade, N+, M0 **M1 NED:** • NED after resection of oligometastatic sites within 1 yr after nephrectomy	Strong
If adjuvant therapy is planned: • Discuss the contradictory results available from adjuvant ICI trials with the patient to facilitate shared decision-making • Inform the patient about the potential risk of overtreatment and immune-related side effects if adjuvant therapy is considered	Strong
Do not offer ICI monotherapy or combination therapy to patients with recurrence during or within 6 mo after adjuvant pembrolizumab	Weak

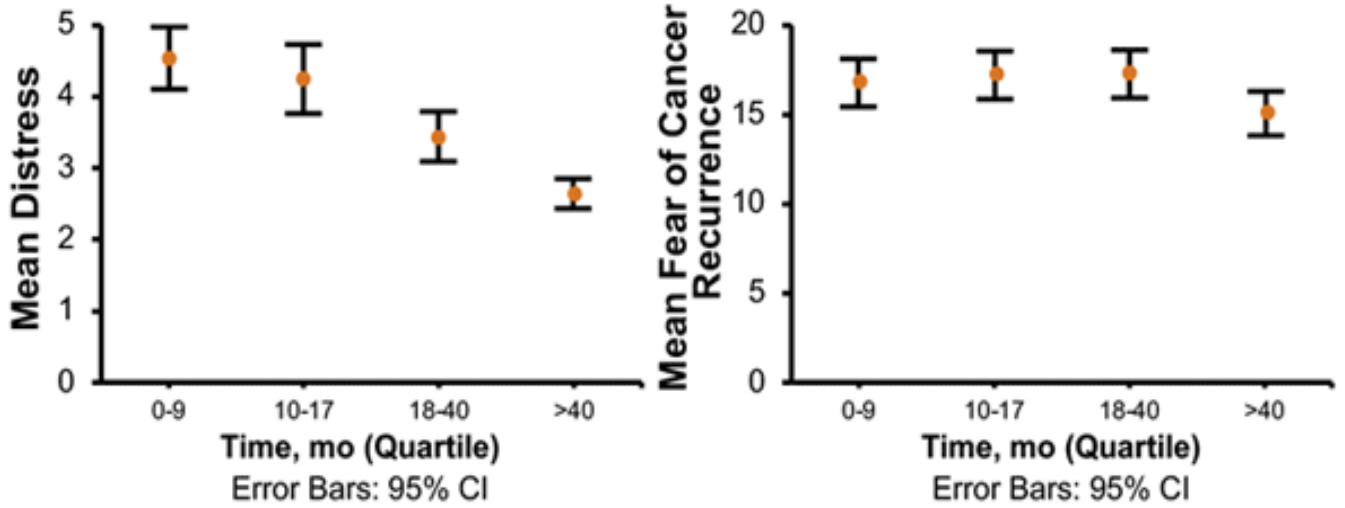
ICI = immune checkpoint inhibitor; NED = no evidence of disease; RCC = renal cell carcinoma.

Bedke, J. et al. Updated European Association of Urology Guidelines on the Use of Adjuvant Immune Checkpoint Inhibitors and Subsequent Therapy for Renal Cell Carcinoma, European Urology. Eur Urol. 2025 Apr;87(4):491-496.

What if Carlos is not convinced of receiving adjuvant treatment?

Patient perspectives: fear of cancer recurrence

Emotional Well-Being and Time Since Diagnosis[1,a]



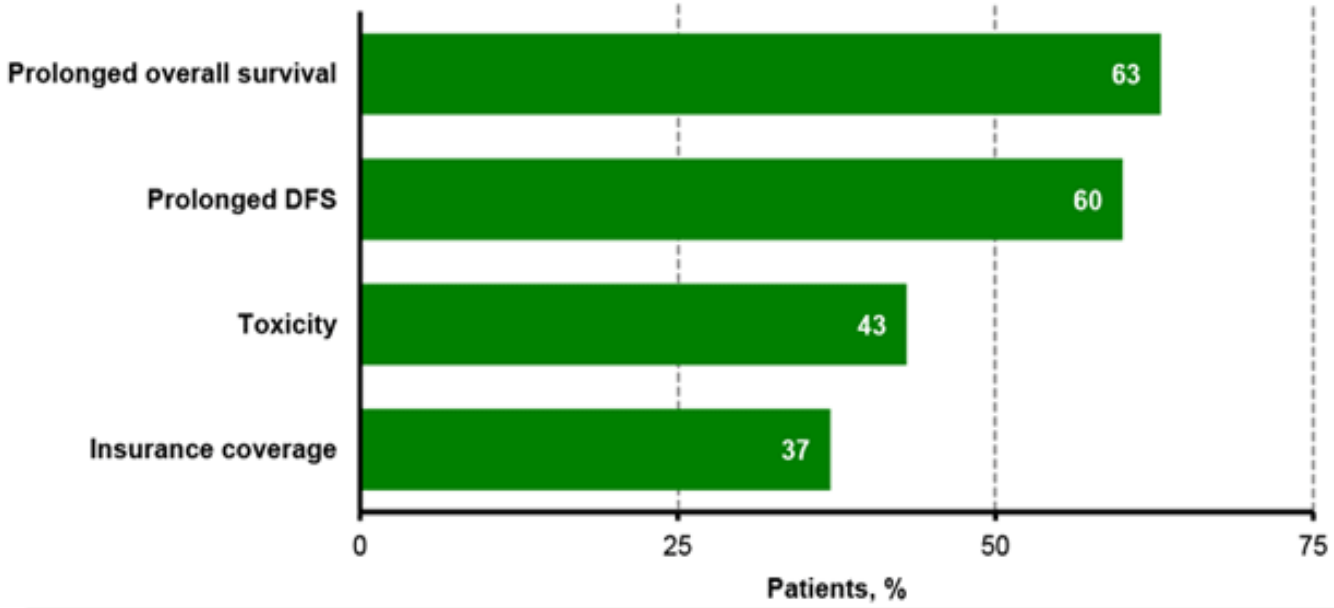
Whereas rates of distress lessened as patients moved further from treatment, fear of cancer recurrence did not seem to dissipate over time

Providers should be aware of these patient perspectives and know they may contribute to a patient's decision about therapy choice

1.-Bergerot CD, et al. JCO Oncol Pract 2020

Patient perspectives: adjuvant therapy

Q. If you were able to get treatment to prevent recurrence of your kidney cancer, what would be important for you?[1,2,a]



- Patient surveys indicate that patients are willing to use adjuvant therapy if the treatment prolongs OS or DFS
- Toxicity of treatment is less important than efficacy endpoints

[a] N = 450 patients with RCC.

kccure
Research Begins Here

Patient Voices[3]

"I wondered why, following the surgery, that some sort of adjuvant therapy was not instituted, but was told that if there is no other cancer detectable, then there is nothing to compare over time to know if the meds are working. I scratched my head on that one because if the adjuvant is working the scans would continue to show NED which would be more than good enough for me."

1.-Battle D, et al. J Clin Oncol 2018 (suppl 644 & 4571); Http://kccure.org/category/patient-stories

Factors impacting patient's decision on adjuvant therapy

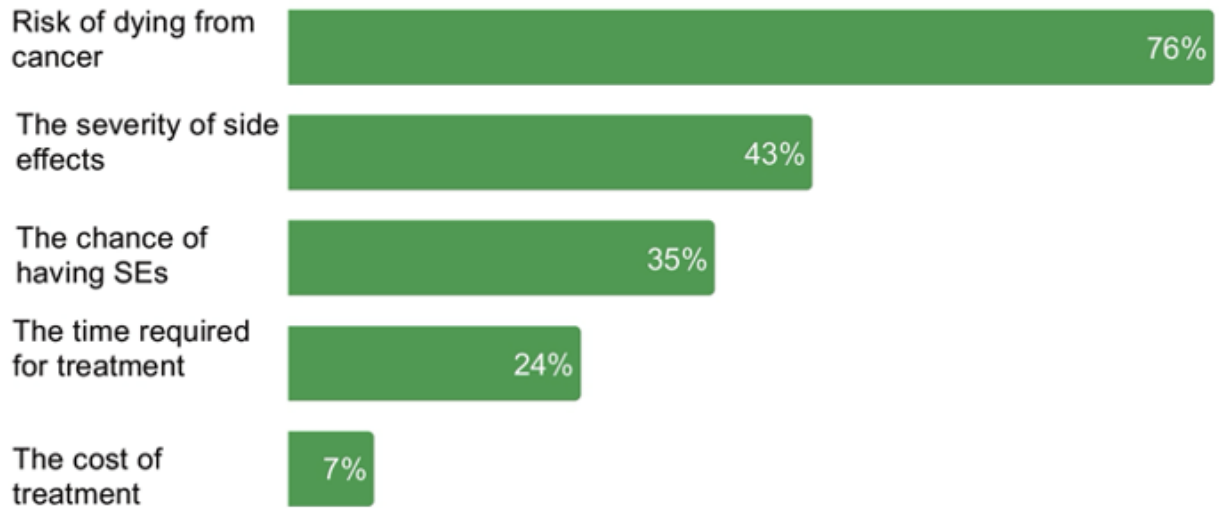


Figure 3: Factors impacting patients' decision on adjuvant therapy

Online survey:
639 patients with RCC in 2022

Battle D, et al. 2023 ASCO GU Cancers Symposium, Abstr #633. J Clin Oncol 41, 2023 (suppl 6; abstr 663)

What if Carlos hipothetically relapses after adjuvant treatment?

FOLLOW-UP

National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2025
Kidney Cancer

FOLLOW-UP
(category 2B)

Stage I
Follow-up After a Partial or Radical Nephrectomy[1]
- H&P annually
- Laboratory tests annually, as clinically indicated
- Abdominal imaging:
  - Baseline abdominal CT or MRI (preferred) both with and without IV contrast (unless otherwise contraindicated) within 3–12 months of surgery, then annually for up to 5 years or longer as clinically indicated
  - A more rigorous imaging schedule can be considered if there are positive margins or adverse pathologic features (such as sarcomatoid, high-grade [grade 3/4])
- Chest imaging:
  - Chest x-ray or CT annually for at least 5 years, then as clinically indicated
  - A more rigorous imaging schedule (CT preferred) can be considered if there are positive margins or adverse pathologic features

Stage II
Follow-up After a Partial or Radical Nephrectomy[1]
- H&P annually
- Laboratory tests annually, as clinically indicated
- Abdominal imaging:
  - Baseline abdominal CT or MRI (preferred) both with and without IV contrast (unless otherwise contraindicated), every 6 months for 2 years, then annually for up to 5 years or longer as clinically indicated
  - A more rigorous imaging schedule can be considered if there are positive margins or adverse pathologic features (such as sarcomatoid, high-grade [grade 3/4])
- Chest imaging:
  - Chest x-ray or CT annually for at least 5 years, then as clinically indicated
  - A more rigorous imaging schedule (CT preferred) can be considered if there are positive margins or adverse pathologic features

Follow-up for Stage III[1,11]
- H&P every 3–6 months for 3 years, then annually for up to 5 years, and as clinically indicated thereafter
- Comprehensive metabolic panel and other tests as indicated every 3–6 months for 3 years, then annually for up to 5 years, and as clinically indicated thereafter
- Abdominal imaging:
  - Baseline abdominal CT or MRI both with and without IV contrast (unless otherwise contraindicated) within 3–6 months, then CT or MRI (preferred), or US (US is category 2B for stage III), every 3–6 months for at least 3 years and then annually for up to 5 years
  - Imaging beyond 5 years: as clinically indicated
- Chest imaging:
  - Baseline chest CT within 3–6 months with continued imaging (CT preferred) every 3–6 months for at least 3 years and then annually for up to 5 years
  - Imaging beyond 5 years: as clinically indicated based on individual patient characteristics and tumor risk factors
- Additional imaging (ie, bone scan, brain imaging):
  - As symptoms warrant

Follow-up After Adjuvant Therapy
- **Patients who received adjuvant therapy should receive clinical follow-up as for stage III disease**

NCCN	1-3 years	4-5 years	> 5 years
TC + LT	3-6 months	Annual	Clinically indicated

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Renal cell carcinoma: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up☆

FOLLOW-UP, LONG-TERM IMPLICATIONS AND SURVIVORSHIP

There is no robust evidence to guide recommendations regarding the frequency of follow-up imaging in early- or advanced-stage RCC.

Resectable disease

It is reasonable to use follow-up imaging based on the risk factors for recurrence and available treatment options upon diagnosis of recurrence. For patients with high-risk disease, CT scans of the thorax and abdomen should be carried out every 3-6 months for the first 2 years, regardless of whether adjuvant pembrolizumab is used. For patients with low-risk disease, annual CT scans are likely sufficient. Radiological examination after 2 years is less strongly recommended, although continuation for up to 5 years after surgery can be considered. The possibility of long-term relapses should be taken into account when planning follow-up.

NCCN	1-3 years	4-5 years	> 5 years
TC + LT	3-6 months	Annual?	-----

What if Carlos hipothetically relapses after adjuvant treatment?

WHAT TO DO ON AN HIPOTHETICAL RELAPSE?

Subsequent Therapies, Participants with Documented Recurrence

	Participants with Documented Recurrence, n	
	Pembrolizumab (n = 171)	Placebo (n = 226)
Systemic therapy only	73 (42.7%)	100 (44.2%)
Systemic + surgery/radiation therapy	37 (21.6%)	54 (23.9%)
Surgery/radiation therapy only	33 (19.3%)	30 (13.3%)
No subsequent therapy reported[a]	28 (16.4%)	42 (18.6%)
VEGF/VEGFR inhibitor[b]	101 (59.1%)	133 (58.8%)
Anti–PD-(L)1 therapy[b]	49 (28.7%)	109 (48.2%)

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Thank you very much for your attention