ADYUVANCIA EN CARCINOMA DE CELULAS RENALES: PASADO, PRESENTE Y FUTURO

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INTRODUCCION

- Gold standard → CIRUGÍA

IL-2 e INF-α

Table 1. Randomized trials of adjuvant immunotherapy in RCC

Author [reference]	Experimental arm	Control arm	N	Primary endpoint	Details
Pizzocaro et al. [18]	IFN-α	Observation	247	5-year DFS	• Eligibility: pT3-4aN0M0 or pTxN1-3M0 RCC • No difference in 5-year DFS (control: 67.1% vs. IFN-α: 56.7%; $p = .107$) • No difference in 5-year OS (control: 66.5% vs. IFN-α: 66.0%; $p = .861$)
Messing et al. [19]	IFN-α	Observation	283	5-year OS	• Eligibility: pT3-4aN0M0 or pTxN1-3M0 RCC • No difference in 5-year DFS (control: 56% vs. IFN-α: 51%; $p = .33$) • No difference in 5-year OS (control: 62% vs. IFN-α: 57%; $p = .07$)
Clark et al. [20]	IL-2	Observation	138	2-year DFS	• Eligibility: pT3b-4NxM0 or pTxN1-3M0 or M1 (s/p complete metastasectomy) RCC • No difference in 2-year DFS (control: 55% vs. IL-2: 48%, $p = .431$) • No difference in 2-year OS (control: 88% vs. IL-2: 86%)
Atzpodien et al. [23]	IL-2/IFN-α/5-FU	Observation	203	2-year DFS	• Eligibility: pT3b-4N0M0 or pTxN1-3M0 RCC • No difference in 2-year DFS (control: 62% vs. IL-2/IFN-α/5-FU:54%) • No difference in 2-year OS (control: 91% vs. IL-2/IFN-α/5-FU: 81%)

1. Estos tratamientos puede que no ejerzan adecuado efecto antitumoral→ Las antiguas estrategias inmunoterápicas pueden no ser tan efectivas para eliminar bajos volúmenes de enfermedad → Inclusión de pacientes con mayor riesgo.

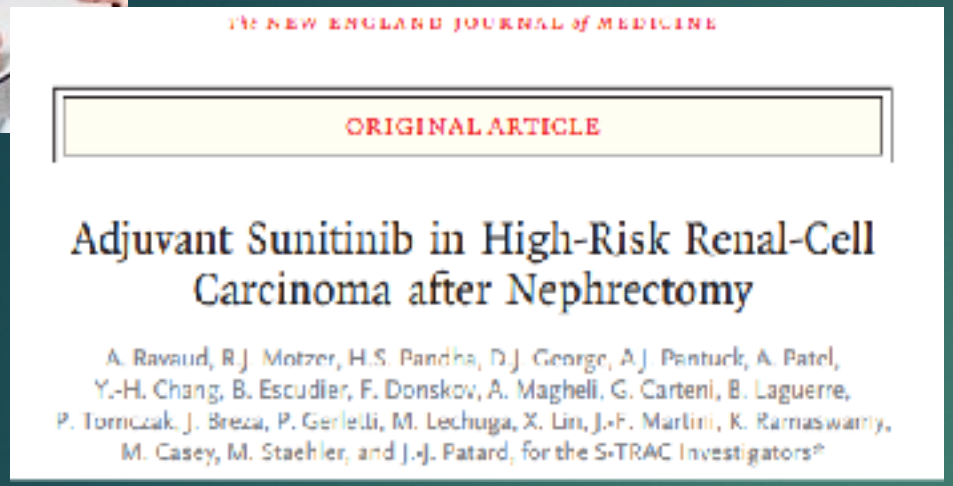
2. En futuras estrategias inmunes se busca → Inclusión de pacientes con factores biológicos definidos que predispongan a la respuesta hacia un fármaco especifico.

TERAPIAS DIANA VEGF y mTOR

Table 2. Trials of adjuvant targeted therapy for localized renal cell carcinoma

Trial (sponsor)	Randomization	Duration of therapy (years)	N	Start date	End date*	Primary endpoint	Clear cell required?	Details
ASSURE (ECOG)	Sunitinib vs. sorafenib vs. placebo	1	1,943	April 2005	September 2010	DFS	No	• Eligibility: pT1bN0M0 (grades 3–4) or pT2-4N1-3M0 RCC • Histology: Any • Cardiac safety substudy reported
ATLAS (Pfizer)	Axitinib vs. placebo	3	592	April 2012	June 2017	DFS	Yes	• Eligibility: pT2-4N0M0 or pTxN1M0 RCC
EVEREST (SWOG)	Everolimus vs. placebo	1	1,218	April 2011	October 2021	DFS	No	• Eligibility: pT1bN0M0 (grades 3–4) or pT2-4N1-3M0 RCC • Histology: Any • Accrual >50% complete
PROTECT (GSK)	Pazopanib vs. placebo	1	1,500	November 2010	April 2016	DFS	Yes	• Eligibility: pT2N0M0 (grades 3–4) or pT3-4N0M0 or pTxN1M0 RCC
SORCE (MRC)	Sorafenib vs. placebo	3	1,420	June 2007	December 2012	DFS	No	• Eligibility: Intermediate- or high-risk RCC (Leibovich score, 3–11)
S-TRAC (Pfizer)	Sunitinib vs. placebo	1	720	July 2007	November 2015	DFS	Yes	• Eligibility: High-risk RCC (modified UISS criteria) pT2N0M0 (grades 3–4) or pT3-4N0M0 or pTxN1M0 RCC

*Study completion date reflects estimated primary completion date cited at http://www.clinicaltrials.gov or actual date of complete enrollment. Abbreviations: DFS, disease-free survival; ECOG, Eastern Cooperative Oncology Group; VEGF, vascular endothelial growth factor; GSK, GlaxoSmithKline; MRC, Medical Research Council; OS, overall survival.

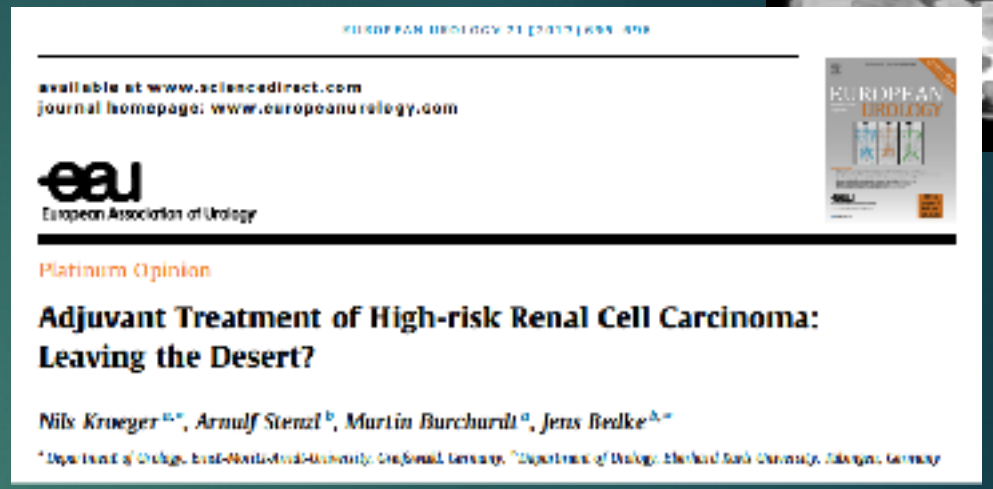


THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Adjuvant Sunitinib in High-Risk Renal-Cell Carcinoma after Nephrectomy

A. Ravaud, R.J. Motzer, H.S. Pandha, D.J. George, A.J. Pantuck, A. Patel, Y.-H. Chang, B. Escudier, F. Donskov, A. Magheli, G. Carteni, B. Laguerre, P. Tomczak, J. Breza, P. Gerletti, M. Lechuga, X. Lin, J.-F. Martini, K. Ramaswamy, M. Casey, M. Staehler, and J.-J. Patard, for the S-TRAC Investigators*



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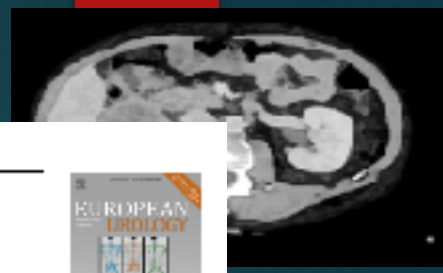
Platinum Opinion

Adjuvant Treatment of High-risk Renal Cell Carcinoma: Leaving the Desert?

Nils Krueger, Arnulf Stenzl, Martin Burchardt, Jens Bedke



- Mayores reducciones de dosis máximas en ASSURE que en S-TRAC (25 vs 37.5 mg)
- Diferente paciente poblaciones (RCC vs ccRCC)
- Diferentes evaluaciones métodos (evaluación centralizada frente a investigador)
- Parece que la interrupción de los TKI después de 1 año→ Crecimiento Metástasico
- Uso hasta recaída ?

DESAFÍOS EN LOS DISEÑOS DE ENSAYOS

- TNM
- Nomogramas de pronostico postquirúrgico
- Mayor numero de paciente pero mejor selec

Table 3. Risk of metastasis by clinical stage using several validated nomograms

		5-year DFS (%)			
Stage	Fuhrman grade	Leibovich	Karakeiwicz	Kattan	Sorbellini
pT2N0	2	80.8	80.2	66	76.9
pT3aN0	2	85.4	84.5	74	86.2
pT3bN0	2	85.4	84.5	56	76.9
pT3cN0	2	85.4	84.5	56	—
pT4N0	2	94.6	81	—	—
pT2N0	4	72.3	74.4	66	20
pT3aN0	4	50	64.8	74	42.3
pT3bN0	4	50	64.8	56	20
pT3cN0	4	50	64.8	56	—
pT4N0	4	74.9	55.2	—	—
pT2N1	2	74.9	79.6		
pT3N1	2	72.3	72.4		
pT4N1	2	85.4	64.8		
pT2N1	4	24.7	51.5		
pT3N1	4	24.7	40.9		
pT4N1	4	50	33.4		

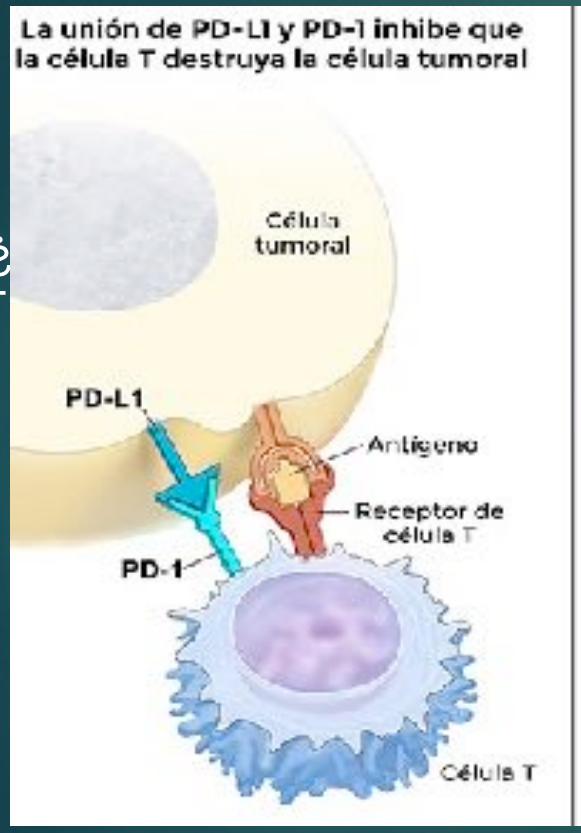
Abbreviations: —, not available; DFS, disease-free survival.

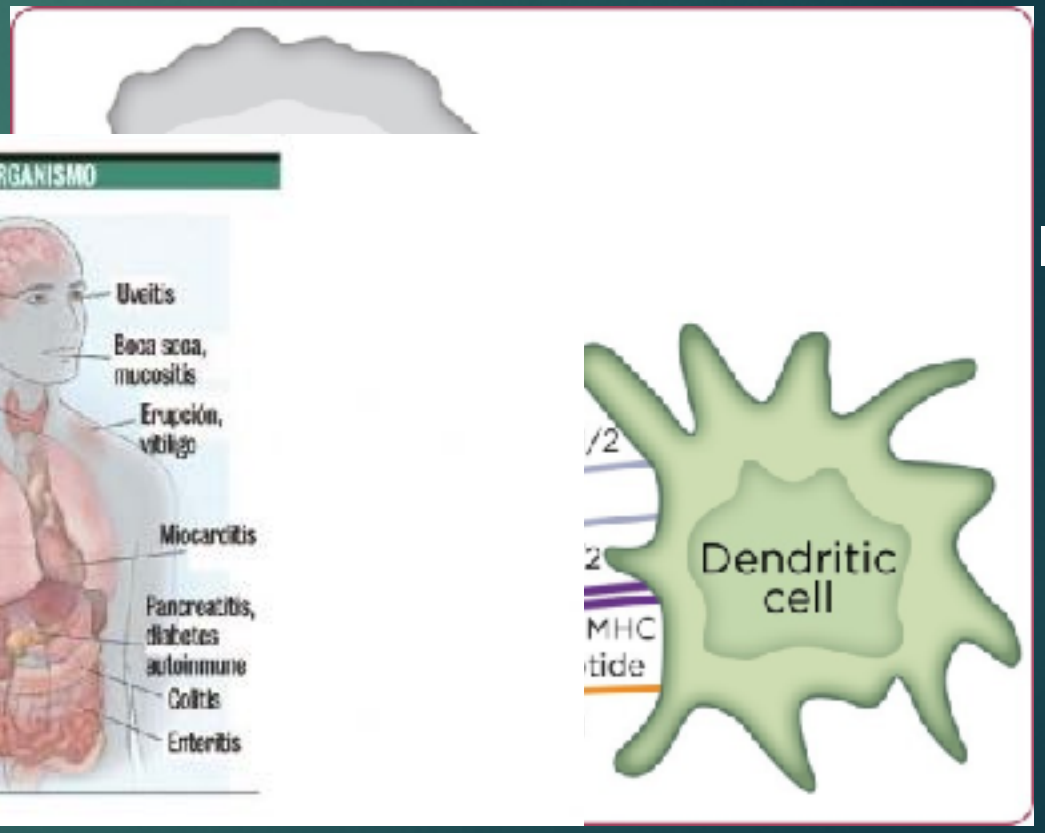
OTROS CAMINOS

- Anhidrasa carbonica IX (CAIX) → Girentuximab
- HSPP-96 (Heat -shock protein peptide complex)
- Vacunas autologas de células tumorales → 76% celulas claras frente 68% en el brazo control
- Otras vacunas actualmente en desarrollo en el entorno metastásico (por ejemplo, AGS-003 y IMA-901)

ESTRATEGIAS ACTUALES: ANTI PD-1, PD-L1 y CTLA-4

- ¿ las T





NOSOTROS

- Ensayo Nivolumab e Ipilimumab
- CCR tipo células claras o con diferenciación sarcomatoide tras Nefrectomia radical o parcial.
- Alto riesgo: PT2-4N0-N1
- Cirugía realizada hace menos de 4 semanas
- ECOG 0-1

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Approved Drugs

Hematology/Oncology (Cancer)

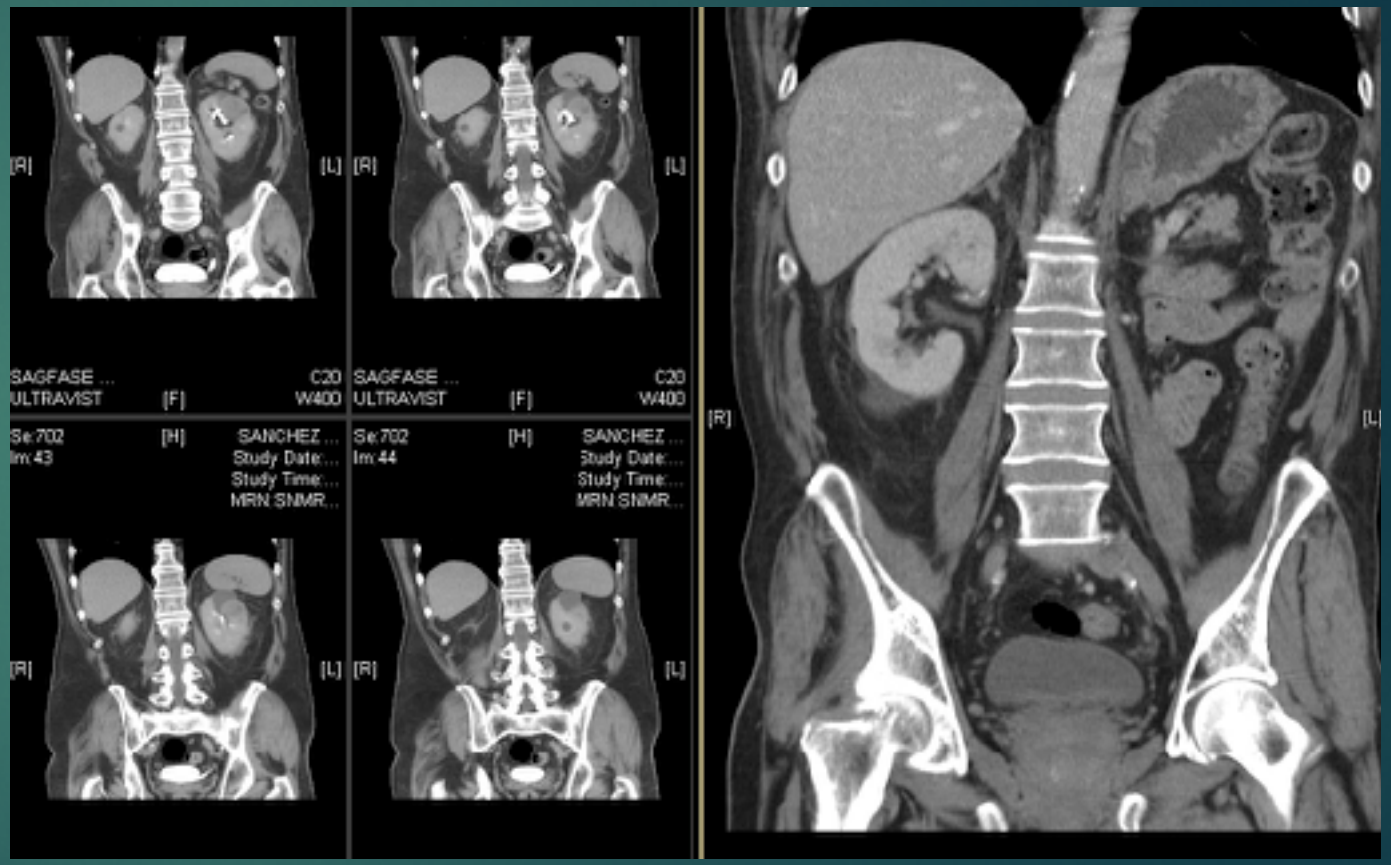
FDA approves sunitinib malate for adjuvant treatment of renal cell carcinoma

Adjuvant cytokines cannot improve survival after nephrectomy.	1b
Adjuvant sunitinib improved disease free survival in one of the two available studies, but not overall survival, after nephrectomy in selected high risk patients.	1b

Recommendations	grade	
Do not offer adjuvant therapy with sorafenib.	strong	↓↓
Do not offer adjuvant sunitinib following surgically resected high-risk clear-cell renal cell cancer.	weak	↓

NOSOTROS

- 71 años
- Carcinoma Celulas Renales tipo células claras
- NRL izquierda + linfadenectomia inter aoto-cava
- pT1N2
- Adyuvancia Sunitinib 50 mg durante 1 año



¿ POR QUÉ NO?
GRACIAS