IX CONGRESO de la
SOCIEDAD GALLEGA DE NEFROLOGÍA
27-28 OCTUBRE 2023

# Toxicidad renal de los inhibidores del *checkpoint*: La Importancia de Trabajar en Equipo

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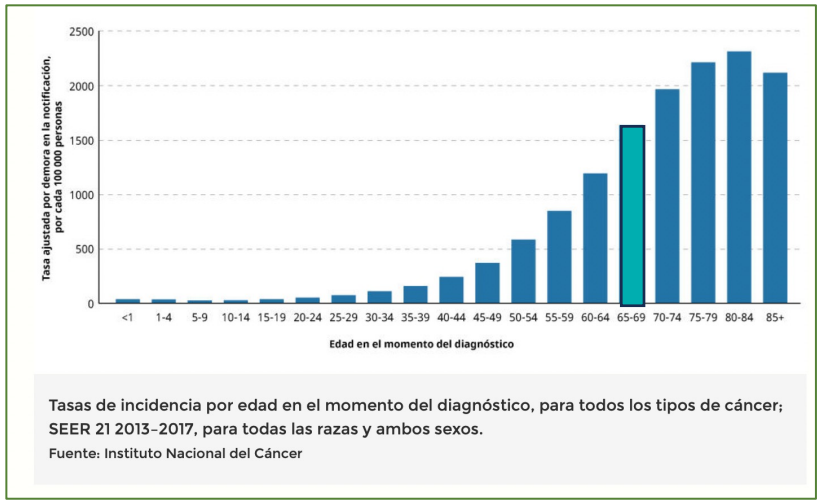
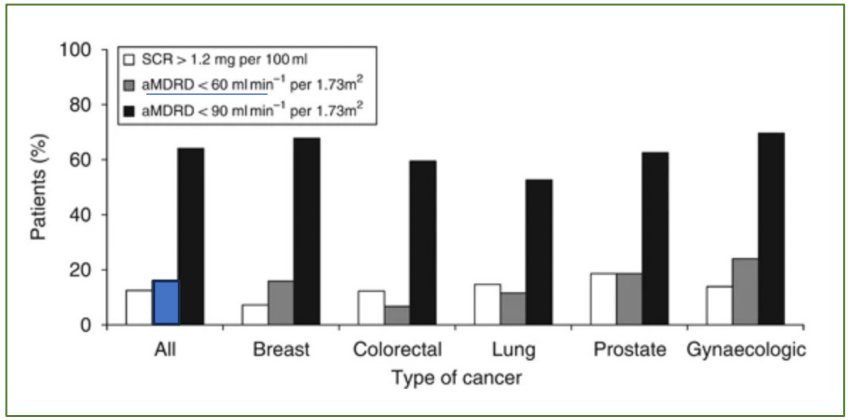
FEA Nefrología H.U. Marqués de Valdecilla (Santander)

# Relación bi-direccional Onco-Nefrología

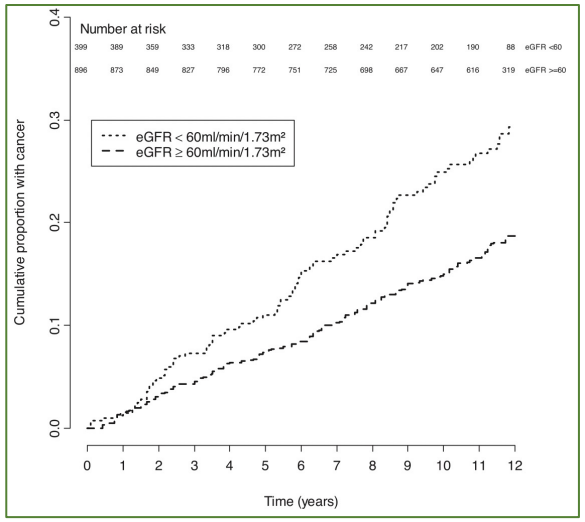
# Relación bi-direccional Onco-Nefrología



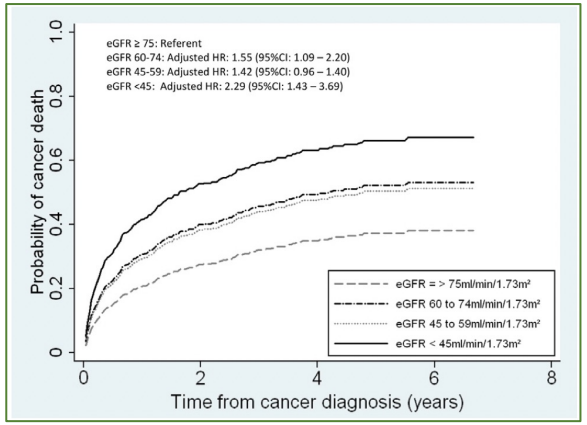

Tasas de incidencia por edad en el momento del diagnóstico, para todos los tipos de cáncer; SEER 21 2013–2017, para todas las razas y ambos sexos.
Fuente: Instituto Nacional del Cáncer




Cancer and renal insufficiency results of the BIRMA study. N Janus et al. British Journal of Cancer (2010) 103(12), 1815 – 1821




Association of CKD and cancer risk in older people. Wong et al. Am Soc Nephrol 2009;20:1341-1350.



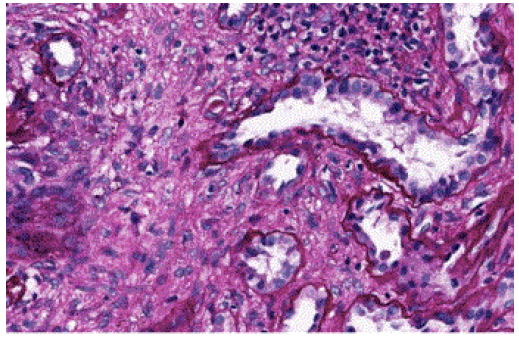

Reduced estimated GFR and cancer mortality. Iff et al. Am J Kidney Dis. 2014;63(1)23-30.

# La importancia de trabajar en equipo…

**Table 1. Food and Drug Administration–approved immune checkpoint inhibitors and timing of approval**

| Immune Checkpoint Inhibitor | Year of Approval | Indication |
|---|---|---|
| **CTLA-4 inhibitor** | | |
| Ipilimumab | 2011 | Melanoma, renal cell carcinoma; in combination with nivolumab in CRC |
| **PD-1 inhibitor** | | |
| Nivolumab | 2015 | Melanoma, nonsmall-cell lung cancer, small cell lung cancer, renal cell carcinoma, urothelial carcinoma, squamous cell carcinoma of the head and neck, Hodgkin lymphoma, hepatocellular carcinoma, colorectal carcinoma with microsatellite instability/mismatch repair |
| Pembrolizumab | 2015 | Melanoma, nonsmall-cell lung cancer, squamous cell carcinoma of the head and neck, Hodgkin lymphoma, renal cell carcinoma, urothelial carcinoma, gastric cancer, cancers with microsatellite instability, mismatch repair, cervical cancer, primary mediastinal B cell lymphoma |
| Cemiplimab | 2018 | Cutaneous squamous cell cancer |
| **PD-L1 inhibitor** | | |
| Atezolizumab | 2016 | Nonsmall-cell lung cancer, urothelial carcinoma |
| Avelumab | 2017 | Merkel-cell carcinoma, urothelial carcinoma |
| Durvalumab | 2018 | Urothelial carcinoma, nonsmall-cell lung cancer |

CRC, colorectal carcinoma; CTLA-4, cytotoxic T lymphocyte–associated protein 4; PD-1, programmed cell death protein 1; PD-L1, PD-ligand 1.



Curación del cáncer

Progresión del daño renal

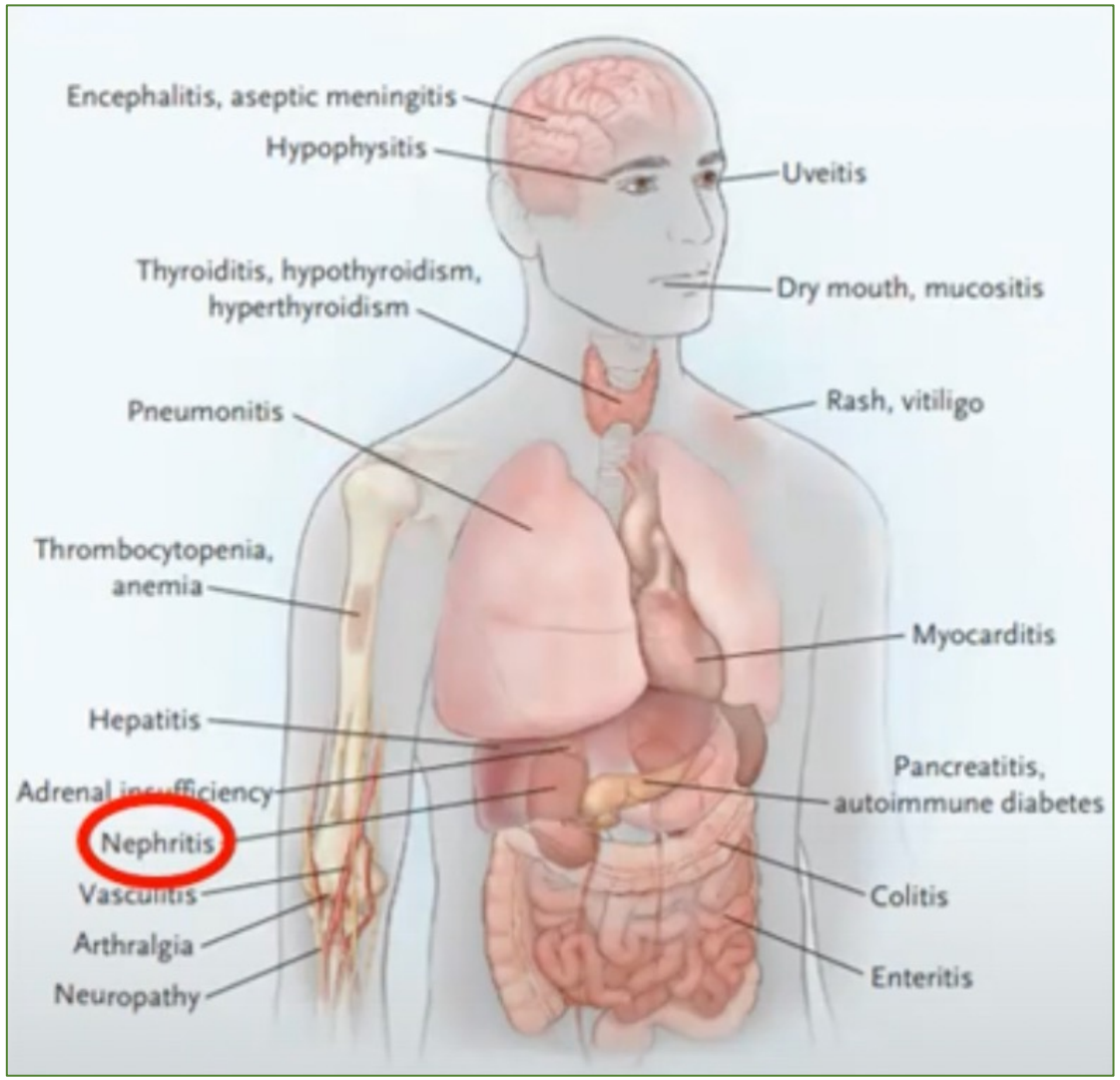
Tratamiento personalizado

Pérdida de oportunidades

Immune checkpoint inhibitor nephrotoxicity. Gupta et al. Kidney360 2020;1:130-140.

# Toxicidad renal de los ICP

No es la más grave




Ni la más frecuente

Immune-related adverse events associated with immune checkpoint blockade. Postow et al. NEJM 2018;378:158-168.

# Toxicidad renal de los ICP

Onconephrology: update in anticancer drug-related nephrotoxicity. García-Carro et al. Nefron 2022; DOI: 10.1159/000525029.

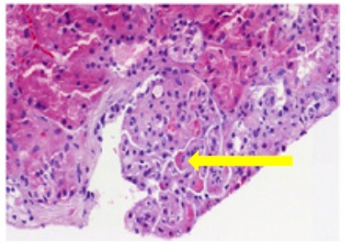
- Cualquier compartimento (TI > glomerular)
- Impredecible (marcadores?)

**Tabla 5:** Revisión sistemática de las nefropatías glomerulares asociadas a ICP (n,%) [36].

| | |
|---|---|
| GN pauci-inmune/ vasculitis | 12[26,7%] |
| Lesiones glomerulares mínimas | 9[20%] |
| GN C3 | 5[11%] |
| IgA | 4 [8,9%] |
| Amiloidosis amiloide A | 4 [8,9%] |
| Anti GBM | 3[6,7%] |
| Hialinosis segmentaria focal | 2[4,4%] |
| GN inmunocomplejos (MP) | 2[4,4%] |
| MAT | 2[4,4%] |
| GN Membranosa | 1[2,2%] |
| GN lupus-like | 1[2,2%] |
| Nefritis túbulo intersticial asociada | 17[40,5%] |

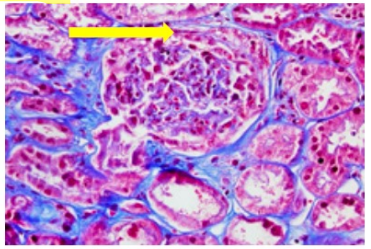
**Glomerular patterns**

- **Thrombotic microangiopathy**: platinum compounds, gemcitabine, mitomycin C, anti VEGF, tyrosine kinase inhibitors, interferon, check-point inhibitors

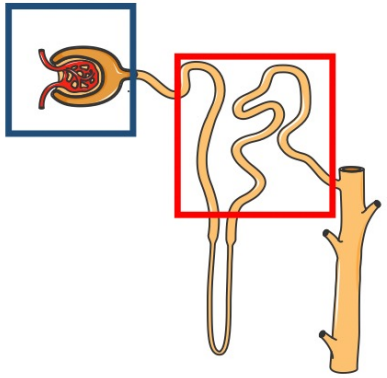


Bevacizumab-induced TMA (arrow: intraglomerular thrombi)

- **Focal segmental glomerulosclerosis**: tyrosine kinase inhibitors, interferon
- **Minimal change disease**: check-point inhibitors
- **Lupus-like nephritis**: check-point inhibitors
- **Necrotizing glomerulonephritis/vasculitis**: check-point inhibitors

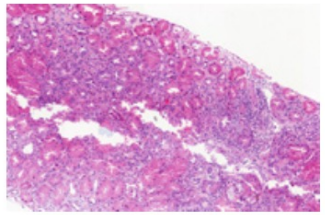


Pauciimmune extracapillar glomerulonephritis related to check-point inhibitrs (arrow: epothelial crescent)



**Tubulointerstitial patterns**

- **Acute/chronic interstitial nephritis**: tyrosine kinase inhibitors, BRAF inhibitors, check-point inhibitors



Dabrafenib – related acute tubulointerstitial nephritis

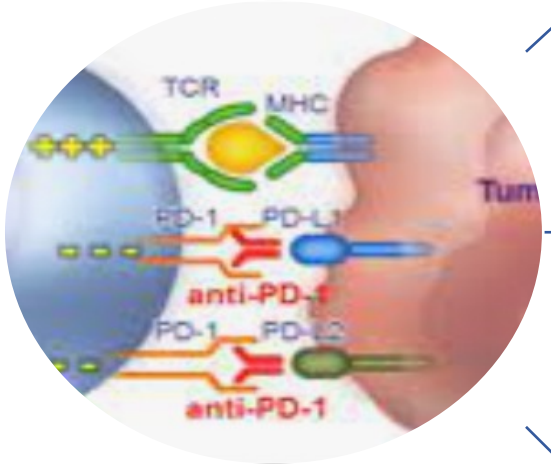
- **Acute tubular injury**: platinum compounds, methotrexate, pemetrexed, tyrosine kinase inhibitors, BRAF inhibitors, BRC-Abl tyrosine kinase inhibitors, CAR-T cells
- **Interstitial fibrosis and tubular atrophy**: pemetrexed
- **Uric acid nephropathy**: rituximab, CAR-T cells
- **Cristally nephropathy**: methotrexate

Histological diagnosis of immunecheckpoint inhibitor induced acute renal injury in patients with metastatic melanoma. Hultin S et al. BMC Nephrol. 2020;21:391.37

# Toxicidad renal de los ICP

**AKI**

Hasta un 17% otras causas (AINES, prerrenal…)
**3% NIA**




Daño glomerular

40% asociados a NIA

T. electrolíticos

> HipoNa
Multifactorial

AKI in patients on checkpoint inhibitor therapy. Seethapathy et al. CJASN 2019;14:1692-1700.

# Toxicidad renal de los ICP: No todo es Cr…

**Tabla 6: Alteraciones electrolíticas posible inducidas por tratamiento con ICP**

| |
|---|
| HIPONATREMIA |
| • SIADH<br>• Hipofisitis- deficiencia aislada de ACTH<br>• Insuficiencia suprarrenal<br>• Hipo-hipertiroidismo<br>• Síndrome de liberación de citoquinas (fuga capilar) |
| HIPERCALCEMIA |
| • Hipofisitis<br>• Adrenalitis<br>• Granulomas "like" sarcoideos<br>• Producción de PTHrp |
| HIPOCALCEMIA |
| • Hipoparatiroidismo<br>• Síndrome de lisis tumoral |
| HIPOKALIEMIA |
| • Acidosis tubular (proximal, distal)<br>• Síndrome de liberación de citoquinas (fuga capilar)<br>• Colitis |
| HIPERKALIEMIA |
| • Síndrome de lisis tumoral |
| HIPOFOSFATEMIA |
| • Acidosis tubular (proximal, distal)<br>• Síndrome de liberación de citoquinas (fuga capilar) |

Efectos renales adversos de la inmunoterapia. ALM de Francisco et al. Nefrología al día.

# NIA: Presentación clínica y características

**Brief Communication**

Kidney360

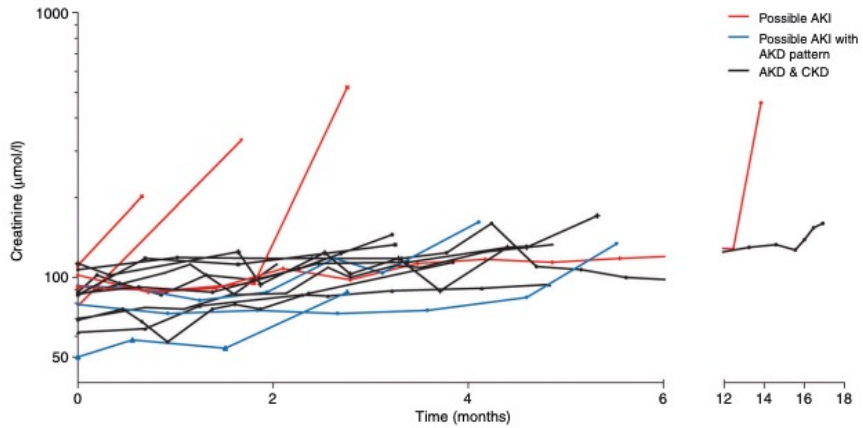
## Kidney Injury in Patients Treated with Immune Checkpoint Inhibitors Does Not Meet KDIGO-AKI Criteria

*Maartje F.A. Verploegen,[1] Marye J. Boers-Sonderen,[2] Berber Piet,[3] and Jack F.M. Wetzels[1]*

**Key Points**

- Kidney injury in patients treated with immune checkpoint inhibitors develops gradually and often does not meet the Kidney Disease Improving Global Outcomes criteria for AKI.
- Proper classification of kidney injury could prevent the development of CKD and improve continued oncologic treatment.

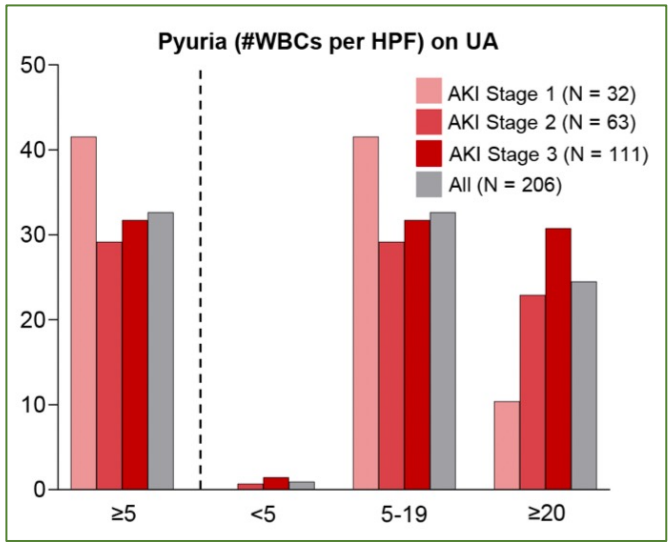
*KIDNEY360* 3: 524–529, 2022. doi: https://doi.org/10.34067/KID.0006752021

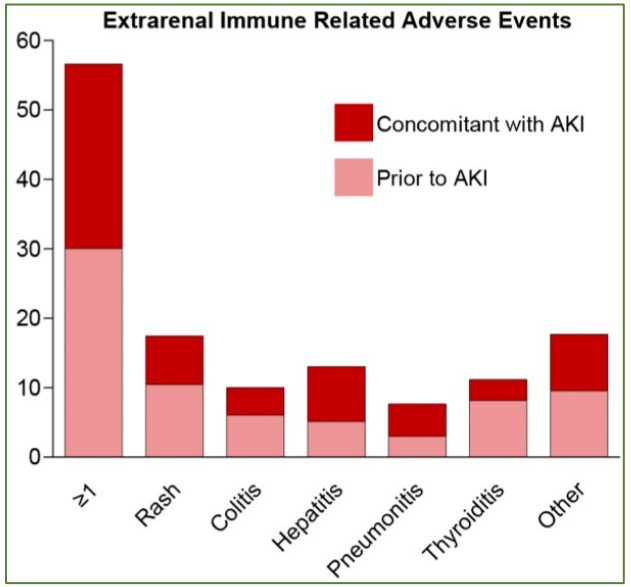


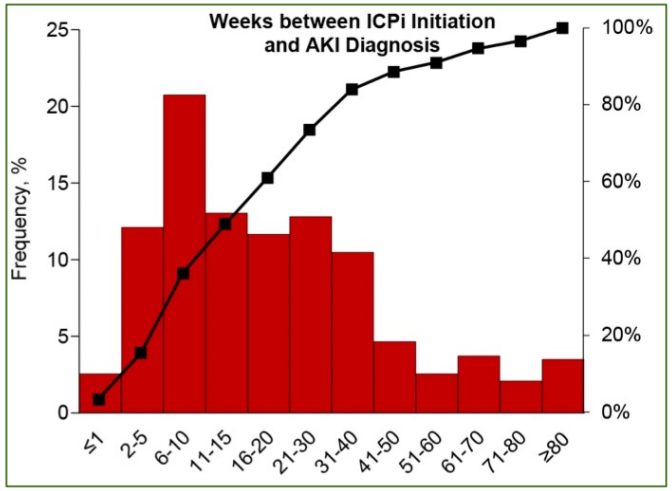

39.7% microhematuria
56.2% piuria
58.7% CPC ≥0.3 g/g

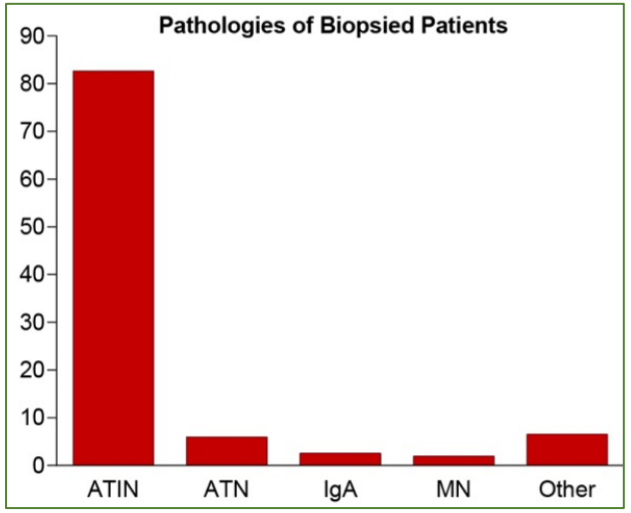
16.5% eosinofilia

# NIA: Presentación clínica y características



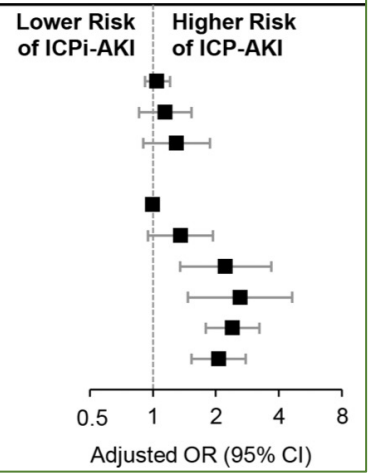



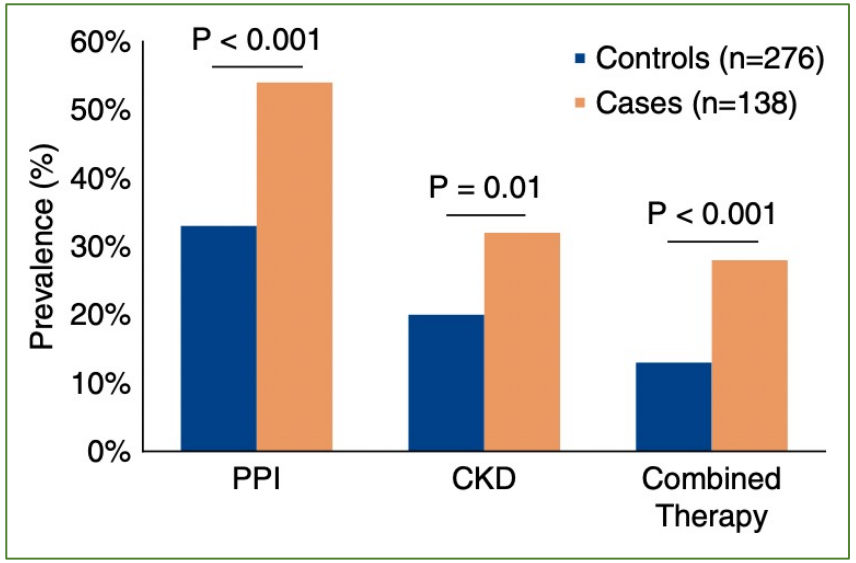




AKI in patients treated with immune checkpoint inhibitors. Gupta et al. Journal for Immunotherapy of cancer 2021;9:e003467.

# NIA: Presentación clínica y características

| Variable | Unadjusted OR (95% CI) | Adjusted OR (95% CI) |
|---|---|---|
| Age (per 10 years) | 1.17 (1.04-1.31) | 1.05 (0.92-1.21) |
| Male sex | 1.16 (0.88-1.52) | 1.15 (0.86-1.53) |
| Combination ICPi therapy | 1.42 (1.01-1.98) | 1.30 (0.90-1.87) |
| Baseline eGFR (ml/min/1.73m²) | | |
| ≥90 (REF) | 1 | 1 |
| 60-89 | 1.54 (1.13-2.10) | 1.36 (0.95-1.94) |
| 45-59 | 2.48 (1.59-3.87) | 2.23 (1.35-3.68) |
| <45 | 1.92 (1.74-4.89) | 2.62 (1.47-4.65) |
| PPI use* | 2.55 (1.92-3.40) | 2.40 (1.79-3.23) |
| Prior or concomitant extrarenal irAEs** | 2.19 (1.65-2.91) | 2.07 (1.53-2.78) |



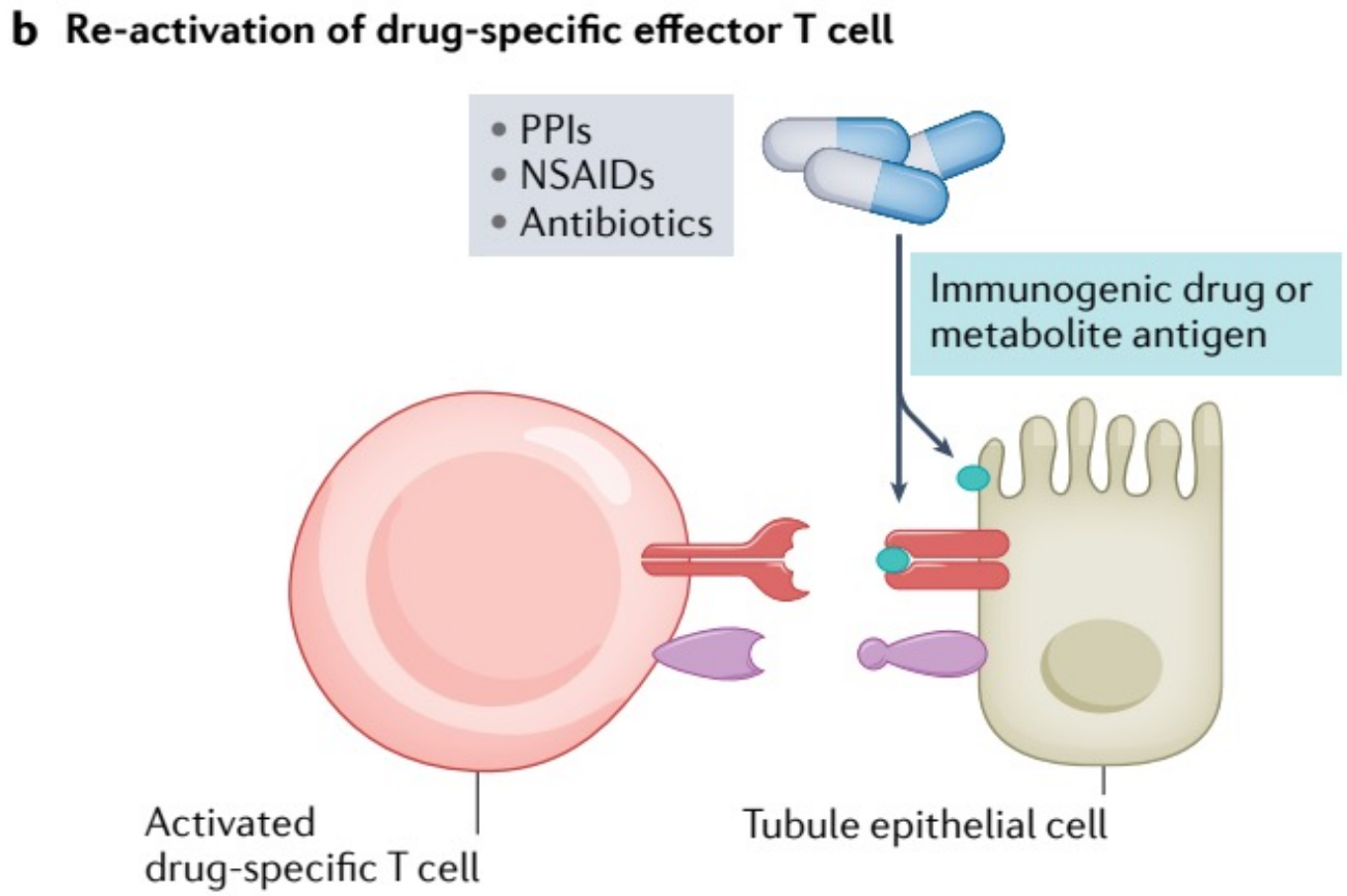

| Characteristics | Odds ratio (95% confidence interval) | P-value |
|---|---|---|
| Male | 1.05 (0.72–1.53) | 0.8073 |
| Age at notification, years | 1.02 (1.00–1.04) | **0.0135** |
| BMI | 0.75 (0.26–2.18) | 0.5951 |
| Chronic kidney disease | 2.50 (1.22–5.14) | **0.0125** |
| Hypertension | 1.02 (0.66–1.56) | 0.9451 |
| Renal cancer | 1.42 (0.67–3.00) | 0.3610 |
| Concomitant drugs | | |
| NSAIDs | 3.18 (1.07–9.4) | **0.0368** |
| Thiazide diuretic | 1.56 (0.77–3.19) | 0.2192 |
| Loop diuretic | 1.37 (0.65–2.89) | 0.4052 |
| PPI | 2.18 (1.42–3.34) | **0.0004** |
| Hypouricemic | 1.81 (0.66–4.99) | 0.2489 |
| Fluindione | 6.53 (2.21–19.31) | **0.0007** |

Gérard AO, et al. Clin Kidney J 2022;15:1881-1887.

Clinical features and outcomes of immune checkpoint inhibitor-associated AKI: a multicenter study. Cortazar et al. JASN 2020;31:435-446.

AKI in patients treated with immune checkpoint inhibitors. Gupta et al. Journal for Immunotherapy of cancer 2021;9:e003467.

# NIA: Presentación clínica y características




Ben Sprangers et al. Nat Rev Nephrol 2022;18:795-805.

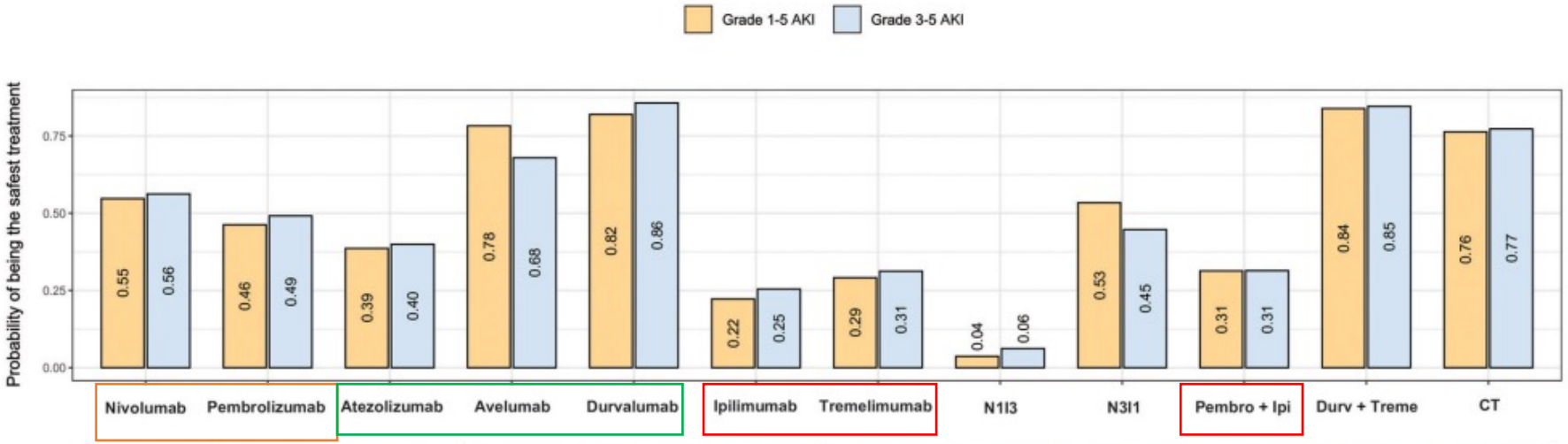
# NIA: Presentación clínica y características

- Mayor probabilidad de toxicidad:
  - 1. Anti-CTLA-4 (solo o en combinación a dosis ALTAS)
  - 2. Anti-PD-1
  - 3. Anti-PD-L1

Received: 13 May 2022 | Revised: 22 October 2022 | Accepted: 2 December 2022
DOI: 10.1002/cac2.12396
REVIEW
CANCER COMMUNICATIONS

**Comparative risk of acute kidney injury among cancer patients treated with immune checkpoint inhibitors**

Fei Liu[1,2,3,#] | Zixian Wang[4,#] | Xiaofan Li[5] | Zhen Zhang[4] | Yue Yang[5] |



# Diagnóstico invasivo: biopsia renal

## Presentación histológica indistinguible de otras causas de NIA

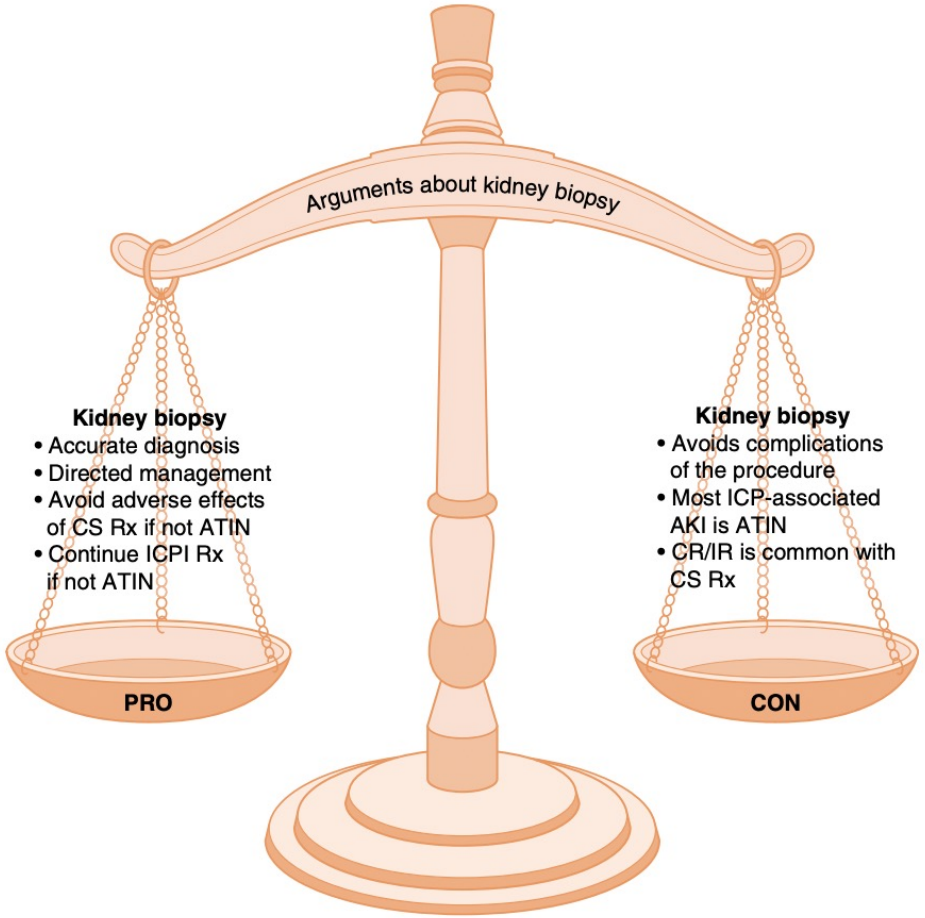
**Table 2.** Histologic findings in ICI-related and non-ICI related AIN

| Finding | ICI-related $n = 11$ | Non-ICI related $n = 12$ | *P*-value |
|---|---|---|---|
| Cortical tissue affected (%) | 50 (50–60) | 25 (20–25) | < 0.001 |
| Interstitial inflammatory cells other than lymphocytes | | | |
| Eosinophils | 7 (64%) | 6 (50%) | 0.41 |
| Plasma cells | 5 (45%) | 3 (25%) | 0.40 |
| Histiocytes | 5 (45%) | 3 (25) | 0.40 |
| Tubulitis moderate and severe | 7 (64%) | 3 (25) | 0.09 |
| IFTA <25% | 8 (72%) | 10 (83%) | 0.64 |
| IHC | | | |
| PD1 | 10 (91%) | 1 (9%) | < 0.001 |
| PDL1PD-L1 | 10 (91%) | 1 (9%) | < 0.001 |

AIN, acute tubulointerstitial nephritis; ICI, immune checkpoint inhibitors; IFTA, interstitial fibrosis and tubular atrophy; IHC, immunohistochemistry

Kidney International Reports (2023) **8,** 672–675

# ¿Biopsiar o no biopsiar?




KIDNEY360 1: 166–168, March, 2020

TABLE 1 Pro and con arguments for kidney biopsy in ICPI-AKI.

| Kidney biopsy | Empiric steroids |
|---|---|
| • More specific to detect culprit lesion than non-invasive testing | • Majority of lesions are ATIN which can be treated with corticosteroids |
| • Accurate diagnosis guides appropriate management (including cases of ATIN, glomerular disease, or tubular injury) | • Early initiation of corticosteroids can improve renal recovery |
| • Potential to spare patients long and possibly harmful corticosteroid courses | • Avoids potential complications of kidney biopsy |
| • Can continue ICPI if lesion is not irAE | • Presence of extrarenal irAEs prompts corticosteroid therapy irrespective of kidney lesion |
| • Useful for future research to better understand and treat ICPI-AKI | |

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TYPE Mini Review
PUBLISHED 10 August 2022
DOI 10.3389/fmed.2022.964335

The role of kidney biopsy in immune checkpoint inhibitor nephrotoxicity

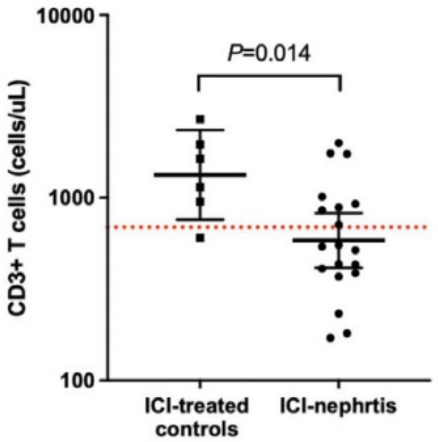
Emily M. Moss[1]* and Mark A. Perazella[2,3]

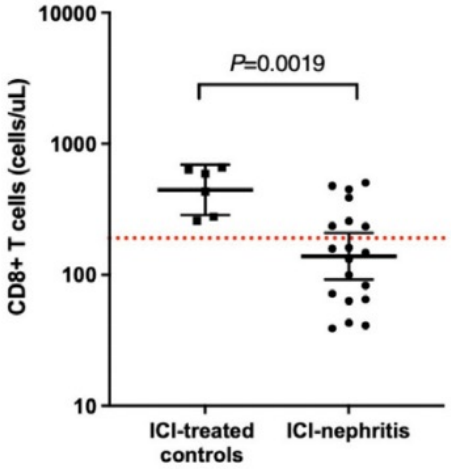
# ¿Biopsiar o no biopsiar?

| Valoración de prueba empírica con corticoides antes de la biopsia renal | Necesaria la biopsia renal desde el primer momento |
|---|---|
| 1. Uso concomitante de otras medicaciones asociadas a NTIA (IBPs, AINEs, antibióticos). Retirar estos fármacos.<br>2. Presencia previa o simultánea de otros eventos adversos inmunomediados<br>3. Ausencia de otras posibles etiologías que pudieran justificar el daño renal (contraste intravenoso reciente, otros fármacos con toxicidad tubular como platino).<br>4. Ausencia de datos que hagan sospechar nefropatía glomerular: Albuminuria de nueva aparición (>1 gr/día), sedimento urinario atípico para NTIA (cilindros hemáticos, dismorfia glomerular)<br>5. Paciente en estado muy avanzado de su enfermedad neoplásica, terminal. | En cualquier paciente que debute con daño renal grave (IRA KDIGO2 o 3) o en el que no se cumplan las condiciones anteriores. |

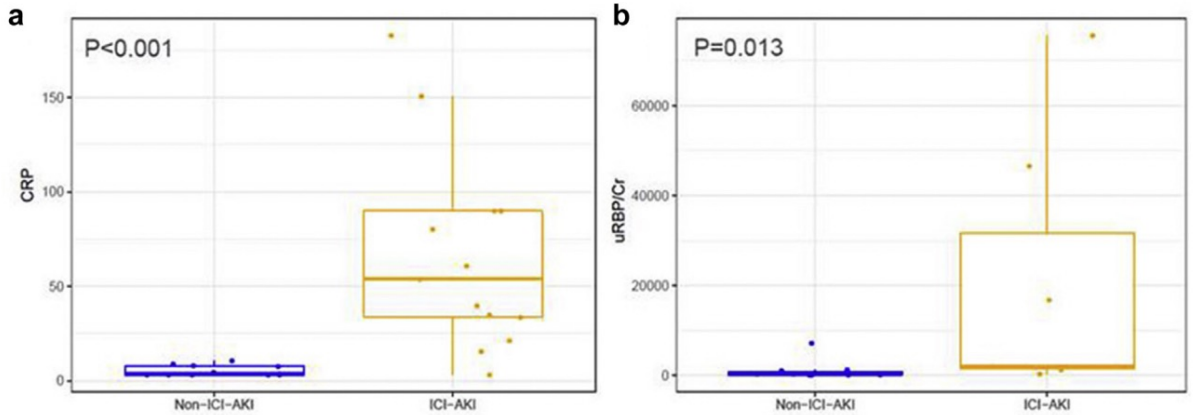
Alonso F, et al. Efectos renales adversos por inhibidores del *check-point* (ICP) en pacientes con cáncer. Recomendaciones del grupo de Onconefrología de la Sociedad Española de Nefrología (SEN). Nefrologia. 2023. https://doi.org/10.1016/j.nefro.2022.12.004

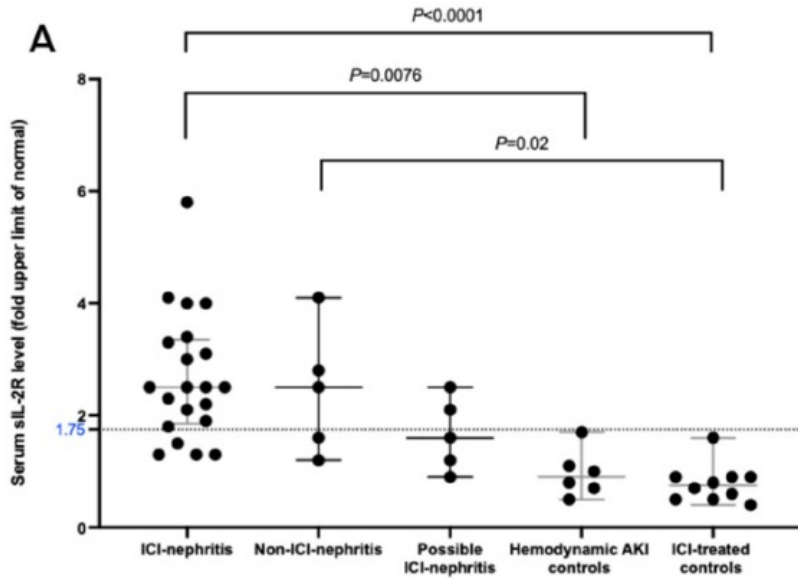
# NIA: diagnóstico no invasivo






Sise ME, *et al. J Immunother Cancer* 2023;**11**:e006222. doi:10.1136/jitc-2022-006222

# NIA: diagnóstico no invasivo

- Estudio prospectivo multicéntrico en marcha: ICITOX

- H. Virgen Macarena (Sevilla)
- H.U. Marqués de Valdecilla(Santander)
- Dr. Peset (Valencia)
- H. 12 de Octubre (Madrid)
- Hospital de la Princesa (Madrid)
- H. Virgen de la Candelaria (Tenerife)
- H. Clínico Universitario de Valencia
- Clinic Barcelona
- Hospital de Ciudad Real
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GRUPO DE TRABAJO
Sociedad Española de Nefrología
ONCONEFRO

NAG
KIM-1
NGAL
IL-9
TNF-alfa
GM2AP…

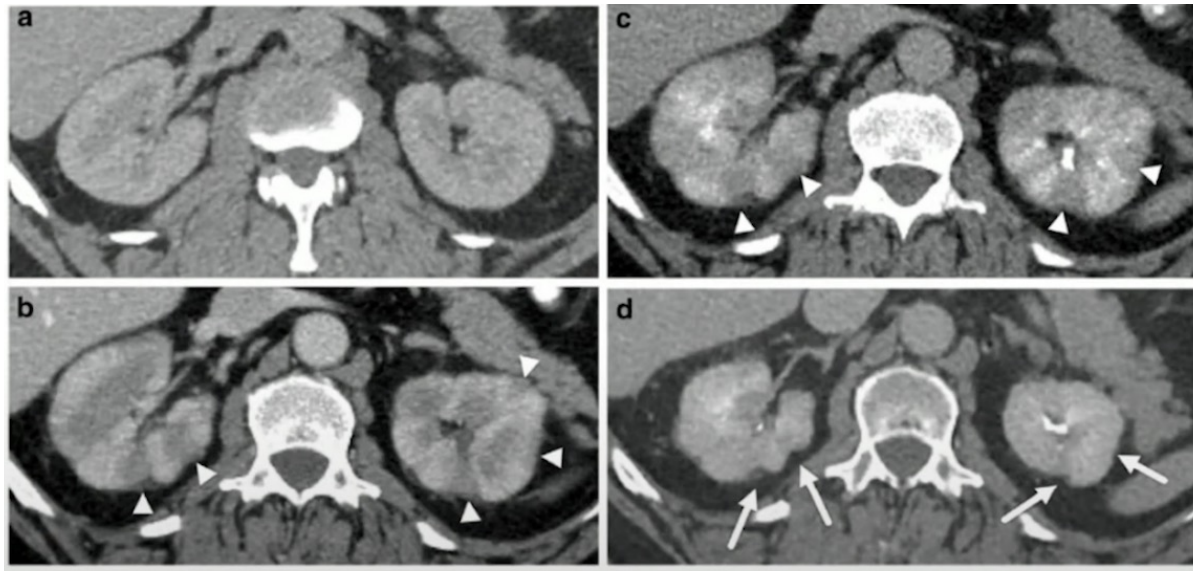
# NIA: diagnóstico no invasivo

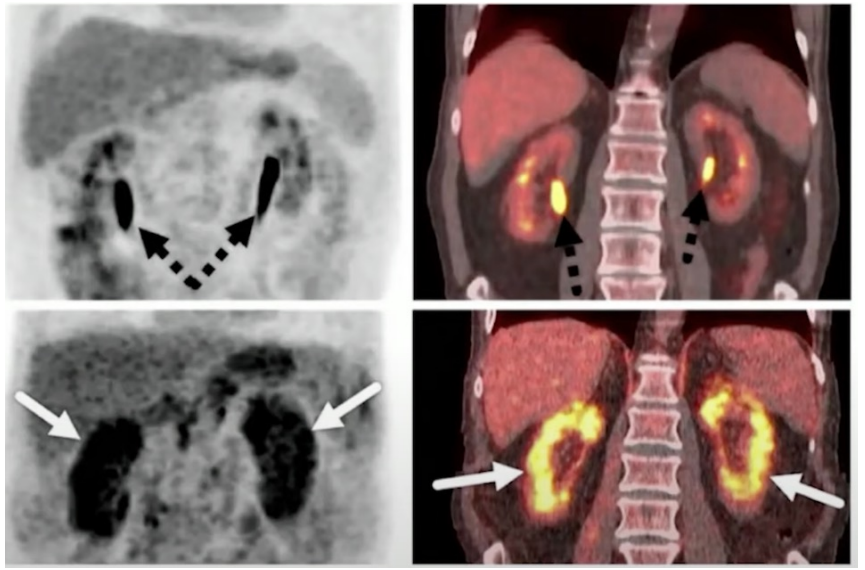
> Eur Radiol. 2023 Mar;33(3):2227-2238. doi: 10.1007/s00330-022-09158-8. Epub 2022 Oct 18.

**Imaging features of immune checkpoint inhibitor-related nephritis with clinical correlation: a retrospective series of biopsy-proven cases**

Muhammad O Awiwi [1], Ala Abudayyeh [2], Noha Abdel-Wahab [3] [4], Adi Diab [5], Migena Gjoni [6], Guofan Xu [7], Raghu Vikram [8], Khaled Elsayes [8]

- Aumento de tamaño renal
- Aumento de realce periférico
- PET captación cortical incrementada de radiotrazador



# Manejo de la toxicidad renal: ONCO vs NEFRO

Table 1 | **CTCAE and KDIGO criteria (based on serum creatinine) for acute kidney injury**

| Grade | CTCAE | KDIGO |
|---|---|---|
| 1 | SCr > 1–1.5 × baseline | SCr 1.5–1.9 × baseline |
| 2 | SCr > 1.5–3 × baseline | SCr 2–2.9 × baseline |
| 3 | SCr > 3 × baseline | SCr ≥ 3 × baseline or initiation of RRT |
| 4 | SCr > 6 × baseline | NA |

AKI, acute kidney injury; CTCAE, Common Terminology Criteria of Adverse Events; KDIGO, Kidney Disease: Improving Global Outcomes; NA, not applicable; RRT, renal replacement therapy; sCr, serum creatinine.

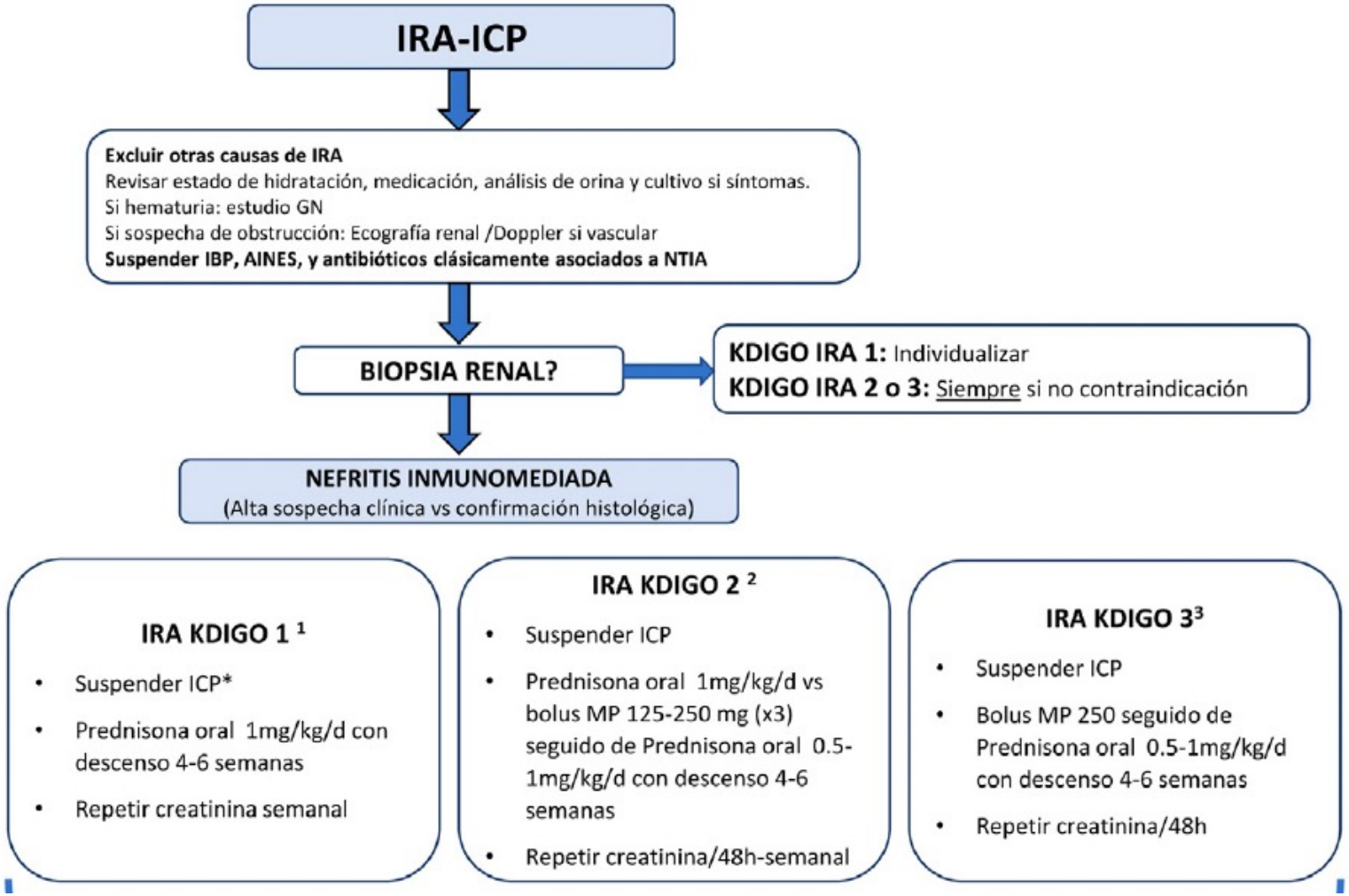
Ben Sprangers et al. Nat Rev Nephrol 2022;18:795-805.

# Manejo de la toxicidad renal: ONCOLOGÍA

| **Grado 1**<br>Creatinina 1.5 x basal<br>o >1.5 x UPL * | **Grado 2**<br>Creatinina >1.5-3 x basal<br>o >1.5 x UPL * | **Grado 3**<br>Creatinina >3 x basal<br>o >3-6 x UPL * | **Grado 4**<br>Creatinina >6 x UPL * |
|---|---|---|---|
| Revisar estado de hidratación,medicación, análisis de orina y cultivo si síntomas<br>Proteina /creatinina ratio<br>Si sospecha de obstrucción Ecografia renal / o Doppler si vascular | Revisar estado de hidratación,medicación, análisis de orina y cultivo si síntomas<br>Proteina /creatinina ratio<br>Si sospecha de obstrucción Ecografia renal / o Doppler si vascular<br>Si hematuria estudio GN según opinión de Nefrología<br>Avisad al paciente de notificar oliguria | Igual que grado 1-2 | Igual que grado 1-2 |
| Continuar ICP<br>Repetir creatinina semanal<br>Si empeora seguir indicaciones grado 2 | Suspender ICP;Hidratación y revisar creatinina en 48-72h. Si no mejora consensuar con Nefrología necesidad de biopsia. Si se atribuye a IrAE **: esteroides (prednisolona oral 0.5-1 mg/kg) y creatinina/48h<br>Si vuele a G1/ basal reanudar ICP (si con esteroides solo cuando prednisonola < 10mg) .Si no se atribuye a IrAE continuar ICP | Suspender ICP. Monitorización balance de liquidos<br>Repetir creatinina /24 h<br>Consenso inmediato con Nefrología sobre biopsia renal<br>Si empeora Metilprednisolona IV 1-2 mg/kg | Como grado 3<br>Ingreso en hospital con servicio de Nefrologia (dialisis ) |

Management of Immune-Related Adverse Events in Patients Treated With Immune Checkpoint Inhibitor Therapy: ASCO Guideline Update. Schneider et al. J Clin Oncol. 2021 Dec 20;39(36):4073-4126

# Manejo de la toxicidad renal: NEFROLOGÍA




Alonso F, et al. Efectos renales adversos por inhibidores del *check-point* (ICP) en pacientes con cáncer. Recomendaciones del grupo de Onconefrología de la Sociedad Española de Nefrología (SEN). Nefrologia. 2023. https://doi.org/10.1016/j.nefro.2022.12.004

# Tratamiento con corticoides: Pauta ORAL

## KDIGO 1-2 (pauta oral)

- **1ª semana**: 1 mg/kg/d (máx 80mg/d)
- **2ª semana**: 40-60mg/d
- **3ª semana**: 20-40mg/d
- **4ª semana**: 10-20mg/d.
- **5ª semana**: 5-10mg/d
- **6ª semana**: SUSPENDER

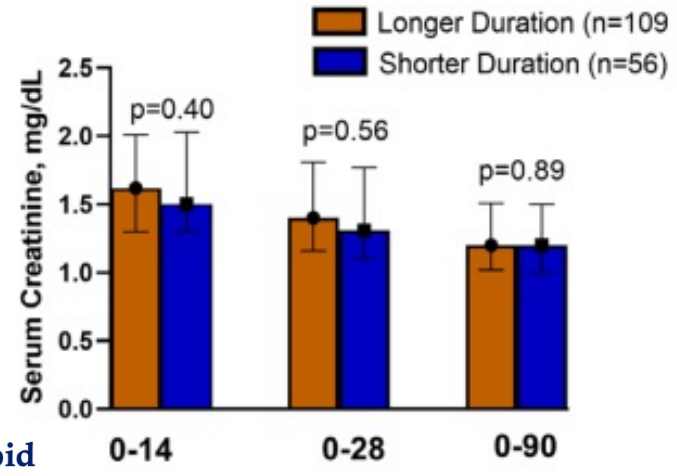
## KDIGO 2-3 (pauta iv+vo)

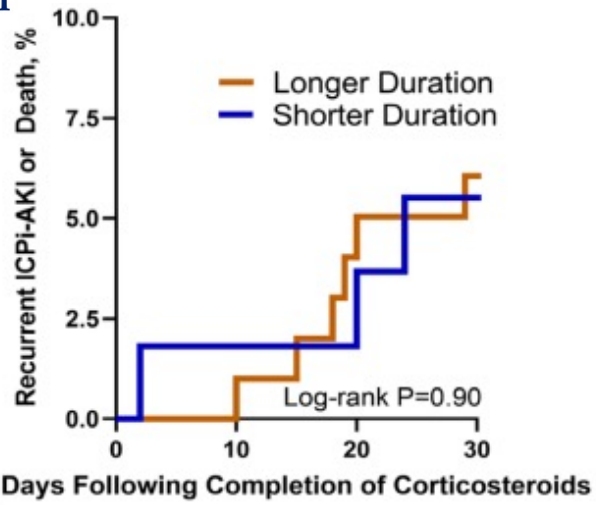
- **INICIO**: MPS 125-250 mgx3d
- **1ª semana**: 30-40mg/d
- **2ª semana**: 20-30mg/d
- **3ª semana**: 10-20mg/d
- **4ª semana**: 5-10 mg/d
- **5ª semana**: 0-5mg/d
- **6ª semana**: SUSPENDER

Alonso F, et al. Efectos renales adversos por inhibidores del *check-point* (ICP) en pacientes con cáncer. Recomendaciones del grupo de Onconefrología de la Sociedad Española de Nefrología (SEN). Nefrologia. 2023. https://doi.org/10.1016/j.nefro.2022.12.004

# Tratamiento con corticoides: Duración

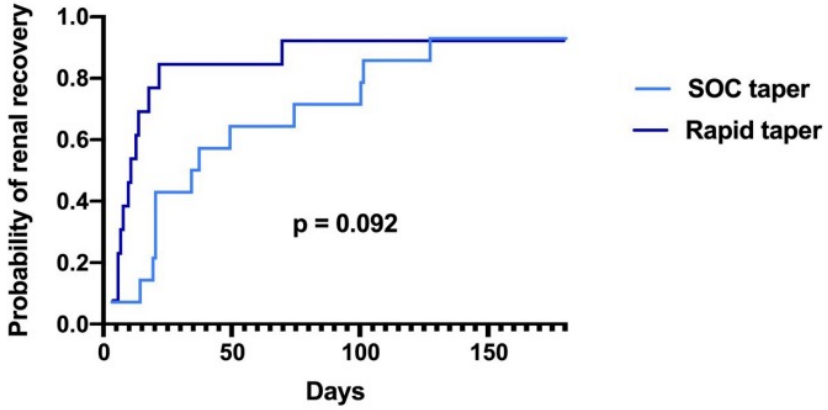
**Shorter versus longer corticosteroid duration and recurrent immune checkpoint inhibitor-associated AKI**



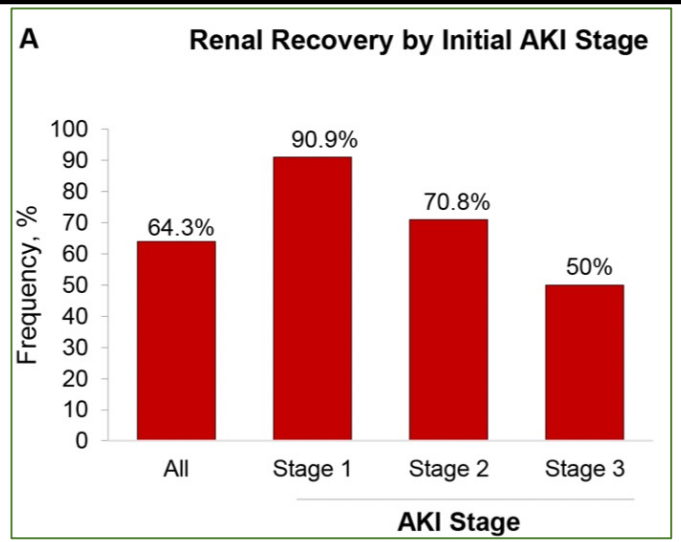

Gupta S, *et al. J Immunother Cancer* 2022;**10**:e005646. doi:10.1136/jitc-2022-005646

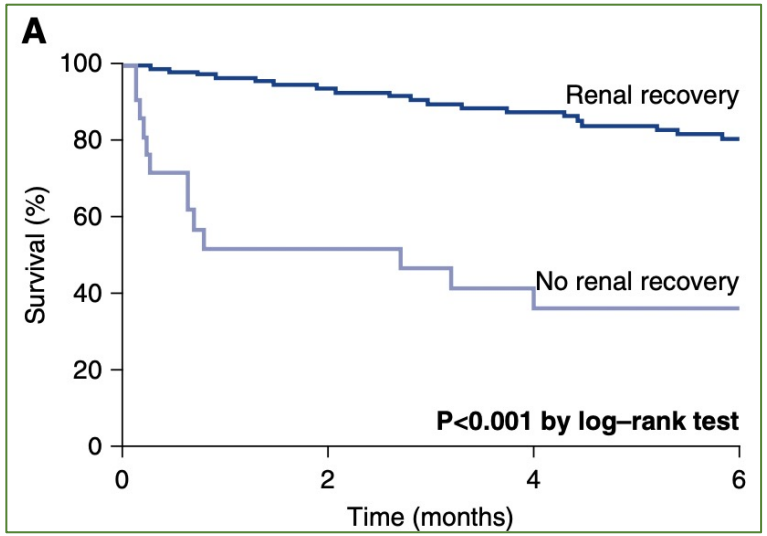
**Rapid corticosteroid taper versus standard of care for immune checkpoint inhibitor induced nephritis: a single-center retrospective cohort study**




Lee MD, *et al. J Immunother Cancer* 2021;**9**:e002292. doi:10.1136/jitc-2020-002292

# Respuesta renal




| Variable | Overall ($N=63$) |
|---|---|
| Baseline serum creatinine, µmol/L | 96 ± 23 |
| Cures to onset, N° | 6.3 ± 6.6 |
| Time to onset, days | 105.5 ± 98.6 |
| Peak serum creatinine, µmol/L | 288 ± 138 |
| Maximum creatinine increase, % of baseline | 220.8 ± 201.7 |
| Last Known Serum Creatinine, µmol/L | 163 ± 74 |
| Last known serum creatinine, % of baseline | 70.7 ± 69.5 |
| Outcome, *N* (%) | |
| Complete recovery[a] | 17 (27.0) |
| Partial recovery[b] | 34 (54.0) |
| No recovery[c] | 8 (12.7) |
| Death | 1 (1.6) |
| Unknown | 3 (4.8) |

Clin Kidney J 2022;15:1881-1887

**Table 4. AKI and mortality.**

| | | Hazard ratio (95% CI) | |
|---|---|---|---|
| | | Crude | |
| No AKI | N = 580 | 1 | (reference) |
| AKI | N = 96 | 2.18 | (1.62–2.93) |
| ICPi-AKI | N = 32 | 1.17 | (0.68–2.03) |
| Non-ICPi-AKI | N = 64 | 2.83 | (2.03–3.93) |

PLOS ONE | https://doi.org/10.1371/journal.pone.0252978 June 8, 2021

Clinical features and outcomes of immune checkpoint inhibitor-associated AKI: a multicenter study. Cortazar et al. JASN 2020;31:435-446.

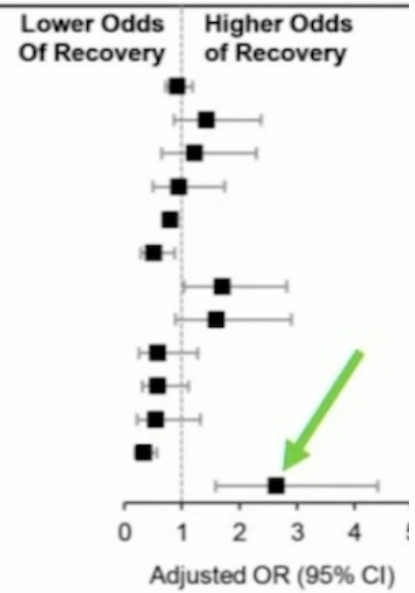
AKI in patients treated with immune checkpoint inhibitors. Gupta et al. Journal for Immunotherapy of cancer 2021;9:e003467.

# Respuesta renal

## Predictores de recuperación

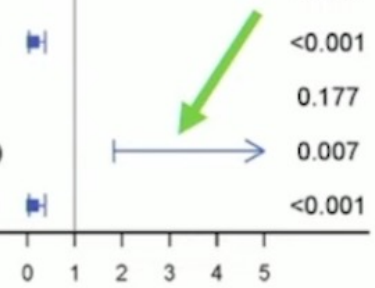
| Variable | Unadjusted OR (95% CI) | Adjusted OR (95% CI) |
|---|---|---|
| Age (per 10 years) | 1.10 (0.92-1.34) | 0.92 (0.71-1.18) |
| Male sex | 1.80 (1.18-2.75) | 1.43 (0.86-2.38) |
| White | 1.57 (0.93-2.67) | 1.22 (0.64-2.30) |
| Combination Therapy | 1.65 (0.98-2.77) | 0.94 (0.50-1.75) |
| Baseline eGFR (per 10 points) | 0.74 (0.66-0.82) | 0.79 (0.69-0.91) |
| Lung cancer | 0.38 (0.25-0.60) | 0.51 (0.29-0.87) |
| Concomitant ATIN-causing medication* | 1.50 (0.98-2.29) | 1.70 (1.03-2.82) |
| Concomitant extrarenal irAEs** | 2.01 (1.20-3.39) | 1.60 (0.88-2.90) |
| ≥2+ Blood on urinalysis | 0.49 (0.26-0.90) | 0.58 (0.26-1.28) |
| ≥2+ Leukocyte esterase on urinalysis | 0.42 (0.24-0.73) | 0.58 (0.31-1.12) |
| ≥1 g/g UPCR | 0.40 (0.20-0.81) | 0.54 (0.22-1.32) |
| Stage 3 AKI | 0.30 (0.20-0.47) | 0.33 (0.19-0.57) |
| Treated with corticosteroids*** | 2.27 (1.48-3.48) | 2.64 (1.58-4.41) |

***inicio corticoides en los primeros 14 días




Odds Ratio (95% CI) for risk factor with kidney outcome

| Variable | Univariate | Multivariable | P value |
|---|---|---|---|
| Age | 1.044(1.010,1.080) | 1.046(1.000,1.095) | 0.051 |
| Male | 0.445(0.171,1.159) | | 0.538 |
| ATIN/AIN | 4.990(2.193,11.352) | | 0.855 |
| Systematic disease | 0.072(0.028,0.184) | 0.119(0.038,0.376) | <0.001 |
| AKD grade | 1.689(0.999,2.856) | | 0.177 |
| Corticosteroid | 5.240(1.563,17.568) | 9.429(1.823,48.779) | 0.007 |
| RRT | 0.085(0.033,0.215) | 0.111(0.033,0.374) | <0.001 |




XU Ly, et al. J Clin Med 2023; 12:1349.

AKI in patients treated with immune checkpoint inhibitors. Gupta et al. Journal for Immunotherapy of cancer 2021;9:e003467.

# Respuesta renal

*Clinical Kidney Journal*, 2023, vol. 16, no. 5, 817–826

https://doi.org/10.1093/ckj/sfac194
Advance Access Publication Date: 31 August 2022
CKJ Review

CKJ REVIEW

**The association between acute kidney injury and outcomes in cancer patients receiving immune checkpoint inhibitor therapy: a systematic review and meta-analysis**

Mehmet Kanbay[1], Sidar Copur[2], Dimitrie Siriopol[3], Abdullah Burak

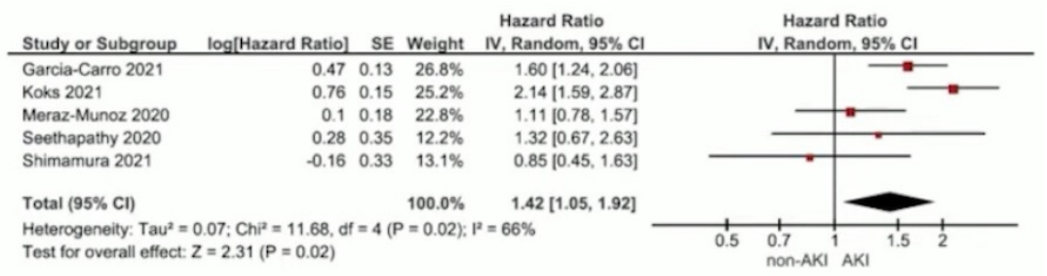



Figure 2: Forest plot of association between outcomes of AKI and non-AKI in patients on ICPI.

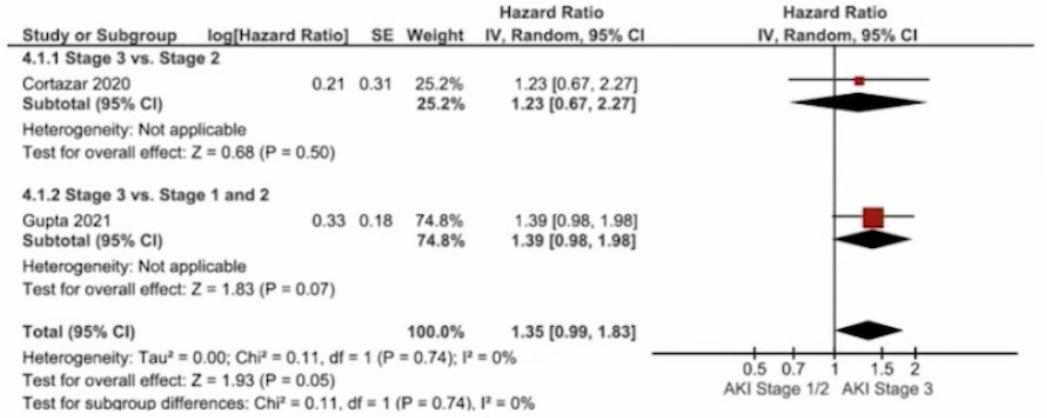
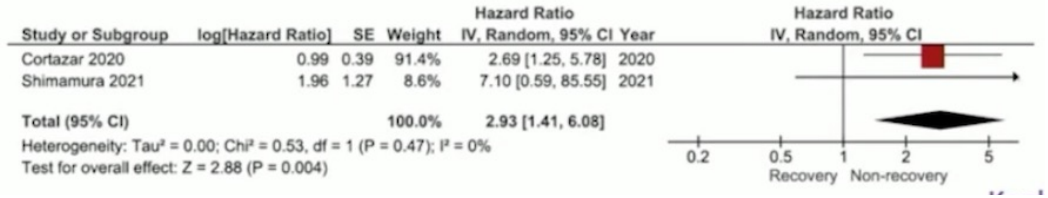



Figure 3: Forest plot of association between Stage 1, 2 AKI and Stage 3 AKI in patients on ICPI.



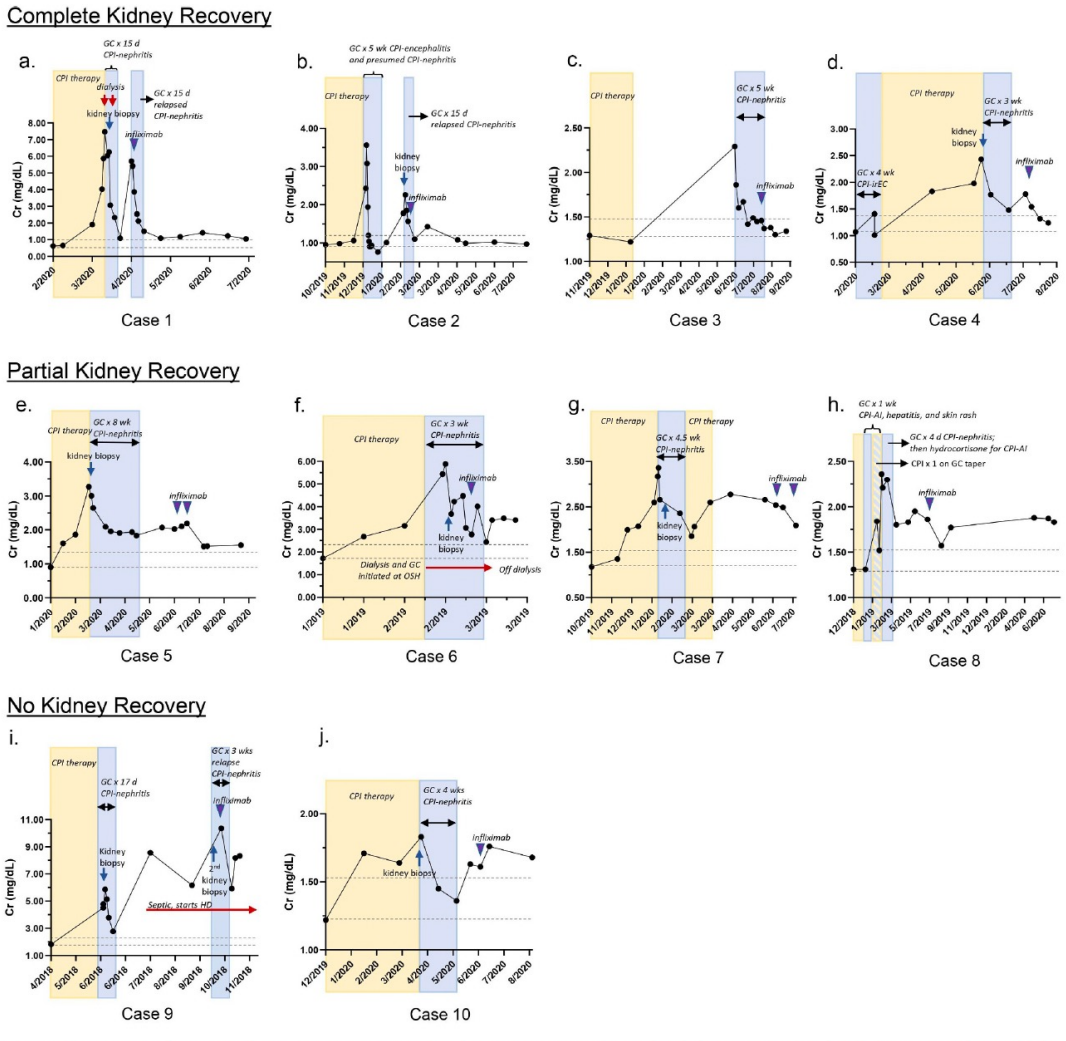

Mayor mortalidad:

1. Pacientes con AKI

2. AKI más grave

3. No recuperación de función renal

# Tratamiento de “rescate”




**Infliximab for the treatment of patients with checkpoint inhibitor–associated acute tubular interstitial nephritis.** Jamie S. Lina et al. ONCOIMMUNOLOGY 2021, VOL. 10, NO. 1, e1877415 (11 pages) https://doi.org/10.1080/2162402X.2021.1877415

# *Rechallenge*

**Tabla 10.** Reanudación ICP después de IRA -ICP: recurrencia de IRA

| | n ICP-IRA | n retratados | % con IS en el momento de la reanudación | Recurrencia ICP-IRA |
|---|---|---|---|---|
| Isik et al [47] | 37 | 16 | 81% | 3 (19%) |
| Cortazar et al [22] | 138 | 31 | 39% | 7 (23%) |
| Dolladille et al [58] | 276 | 78 | NA | 4 (5%) |
| Hultin et al [62] | 23 | 5 | NA | 0% |
| Espi et al [61] | 13 | 5 | 20% | 20% |
| Gupta et al [21] | 429 | 121 | 49% | 17% |

Efectos renales adversos de la inmunoterapia. ALM de Francisco et al. Nefrología al día.

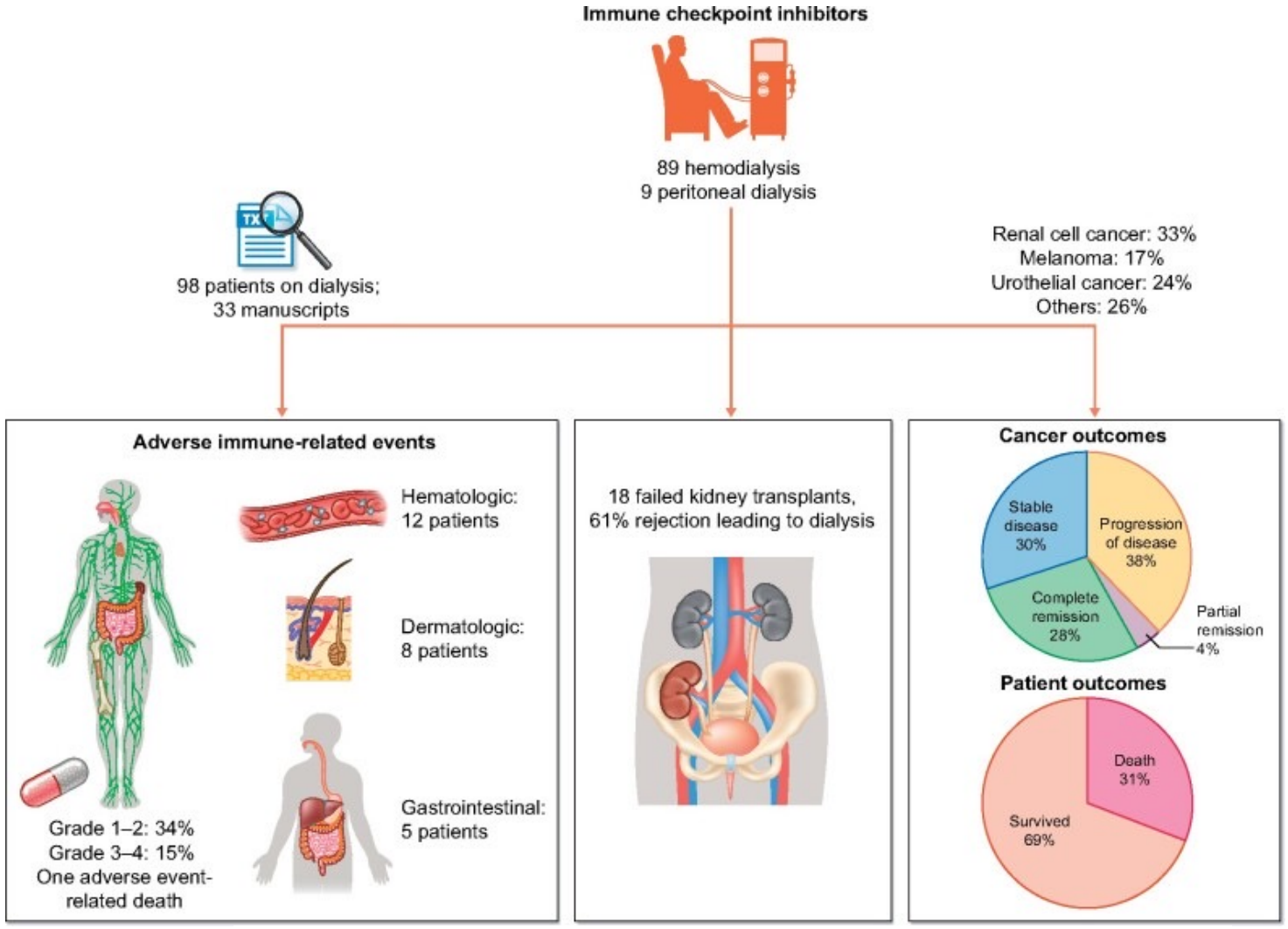
# *Rechallenge*

- Posicionamiento del grupo de Onconefrología de la SEN:

| A FAVOR | EN CONTRA |
|---|---|
| Cáncer no controlado | Buena respuesta tumoral |
| Buena respuesta a CE | Mala respuesta a CE |
| Fármacos inductores (IBP, AINEs) | Eventos inmunomediados graves |
| Combinación -> monoterapia | Opciones terapéuticas alternativas |
| Reiniciar con prednisona < 20-10 mg/d | Sospecha de glomerulonefritis |

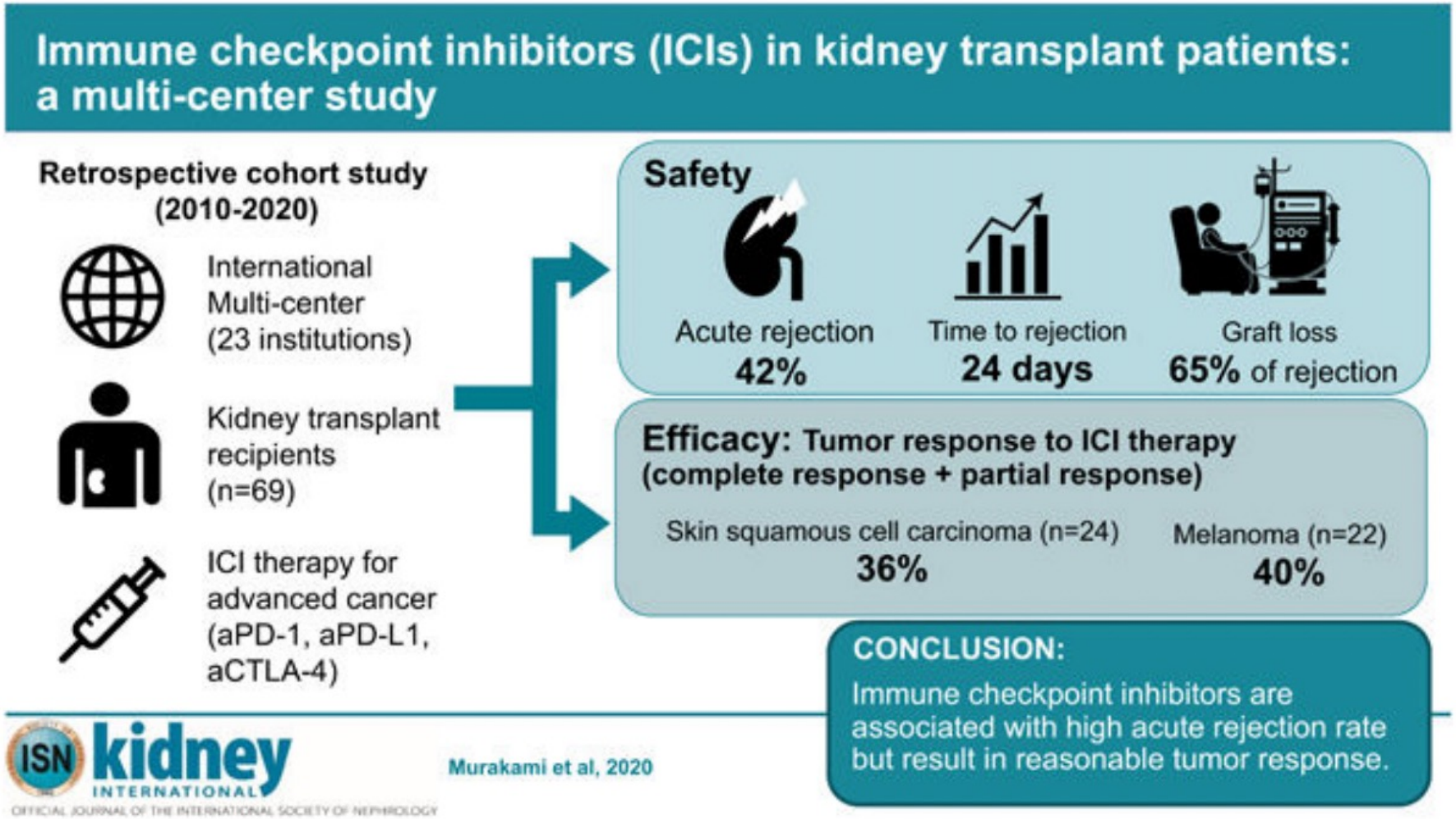
Alonso F, et al. Efectos renales adversos por inhibidores del *check-point* (ICP) en pacientes con cáncer. Recomendaciones del grupo de Onconefrología de la Sociedad Española de Nefrología (SEN). Nefrologia. 2023. https://doi.org/10.1016/j.nefro.2022.12.004

# ICIs y diálisis




*Clinical Kidney Journal*, 2021, vol. 14, no. 9, 2012–2022

# ICIs y trasplante renal



# ICIs y trasplante renal

**Tabla 11:** Características clínicas de IRA asociada a tratamiento con ICP comparando pacientes trasplantados vs. no t

| | Pacientes no- Tx | Pacientes con Tx renal |
|---|---|---|
| Frecuencia | 2-3% | 30-40% |
| Tiempo de ICP a IRA | 14 semanas | 24 días |
| Histología biopsia renal | Infiltración celular (T,B,Eosinófilo)<br>NTIA | Infiltración celular T y B<br>Rechazo celular y humoral |
| Respuesta a esteroides | Buena (85%) recuperación | Refractaria |
| Diálisis | 5-10% | 60-70% |
| Factores de riesgo | Función renal disminuida, IBP | imTOR y 3 inmunosup (menor riesgo) |

Efectos renales adversos de la inmunoterapia. ALM de Francisco et al. Nefrología al día.

# La importancia de trabajar en equipo…

GRUPO DE TRABAJO
Sociedad Española de Nefrología
ONCONEFRO

NEFROLOGIA (2021);41(2):154–164

Sociedad Española de Nefrología

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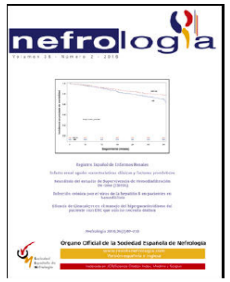

Artículo especial

## Consulta monográfica de onconefrología. Justificación y puesta en marcha

*Fabiola Alonso*[a,*], *Pilar Auñón*[b], *Teresa Cavero*[b], *Mercedes Salgueira*[a], *Manuel Praga*[b], *Borja Quiroga*[c], *Ángel L.M. de Francisco*[d], *Manuel Macía*[e]
*y Grupo Español de Onconefrología (ONCONEFRO)*

# La importancia de trabajar en equipo…

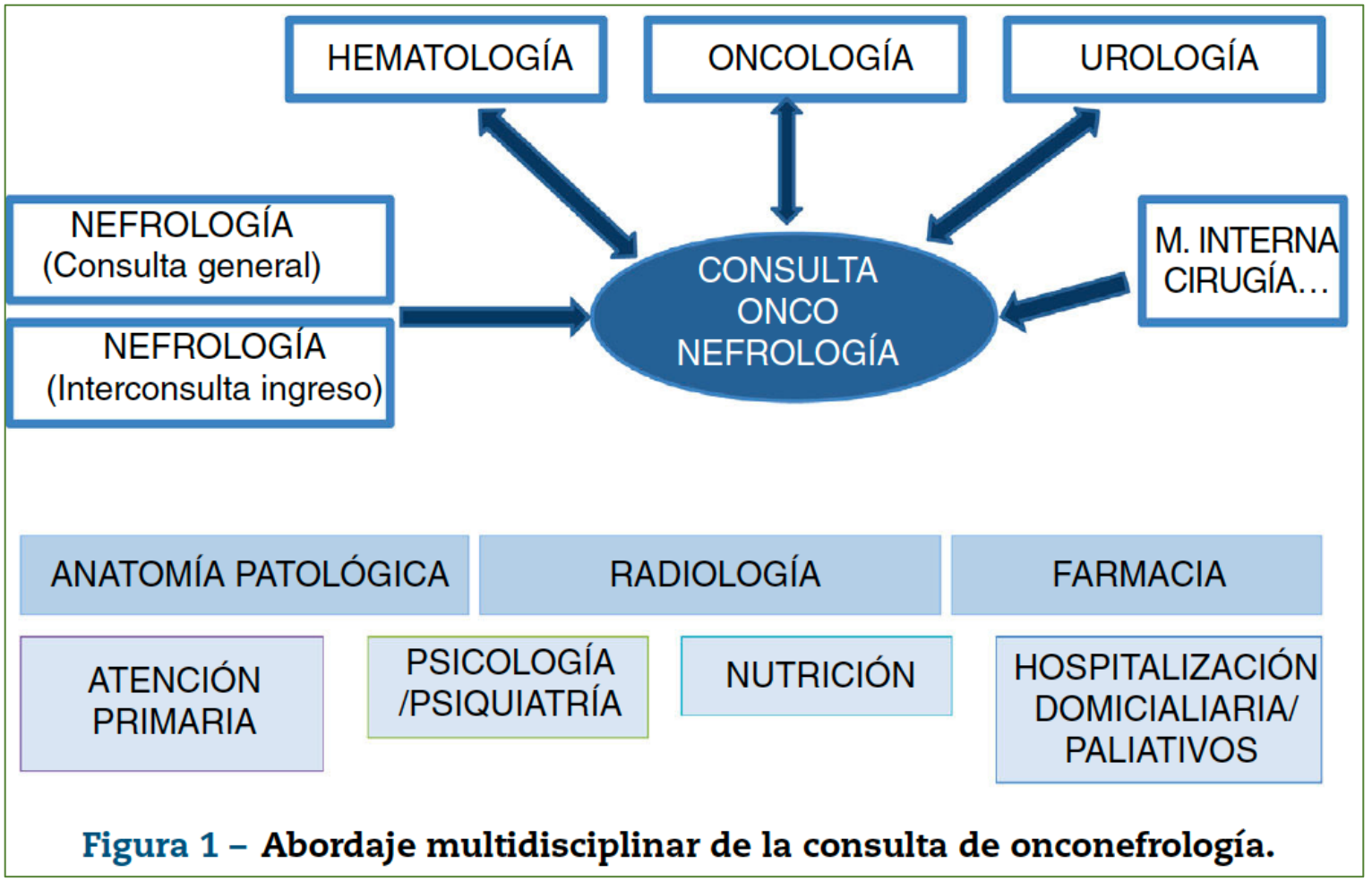


**Figura 1 – Abordaje multidisciplinar de la consulta de onconefrología.**

# Consulta Onconefrología: Profesionales implicados en el HUMV

- Mara Serrano Soto. FEA **Nefrología**, HUMV.
- Gema Fernández Fresnedo. FEA Nefrología, HUMV.
- Luis Martín Penagos. FEA Nefrología, HUMV.
- Milagros Heras Vicario. FEA Nefrología, HUMV.
- Juan Carlos Ruiz San Millan. Jefe de Servicio de Nefrología, HUMV.
- Fernando Rivera Herrero. Jefe de Servicio de **Oncología**, HUMV.
- Ignacio Duran Martínez. FEA Oncología, HUMV.
- Diego Cacho Lavín. FEA Oncología, HUMV.
- Enrique Maria Ocio San Miguel. Jefe de Servicio de **Hematología**, HUMV.
- Javier Núñez Céspedes. FEA Hematología, HUMV.
- Jose Luis Gutierrez Baños, Jefe de Servicio de **Urología**, HUMV.
- Sara Barbadillo Villanueva. FEA **Farmacia Oncológica**, HUMV.

Consulta 138
Todos los martes
Extensión 72555
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Correo electrónico

# EFECTO RENAL ADVERSO PARA CONSIDERAR DERIVACION A NEFROLOGIA

## 1. HTA

- **HTA Grado III como primera toxicidad** *(PA > 180/110 mmHg)*
- **HTA resistente***

* HTA que no se controla con 3 fármacos a dosis máxima tolerada incluyendo un diurético

## 2. FRACASO RENAL AGUDO

- **GRADO 2 o superior** *(Creatinina basal x 2-2.9)*
- **CUALQUIER GRADO CON COMPLICACIONES ASOCIADAS**
  - **HEMATURIA de causa no justificada** (no urológica)
  - **PROTEINURIA (> 300mg/g)**
  - **HIPERPOTASEMIA > 5.5 mEq/L sin respuesta a tto convencional**
  - **ASOCIADO A HTA SEVERA**

## 3. TNOS ELECTROLÍTICOS

- **SODIO < 130 mEq/L**
- **POTASIO > 6 mEq/L**
- **MAGNESIO < 1 mEq/L**
- **CALCIO < 7 mg/dl ó > 11 mg/dl**
- **FÓSFORO > 6 ó < 2 mg/dl**

## 4. PROTEINURIA

***[Cociente Prot/Creat > 1000 mg/g]***

**En caso de indicar ingreso hospitalario por sospecha de nefritis inmunomediada, comentar primero telefónicamente 72555** (horario laboral)- 64733 (horario de guardia o festivo)

# Gracias, equipo ;-)

mara.serrano@scsalud.es