GUARD CONSORTIUM

GUARD SYMPOSIUM

6-7 JULIO 2023

GU-Alliance for Research and Development

#guardsymposium2023

@GuardConsortium

Taller de trabajo: Ca. Renal Localizado

Óscar Rodríguez Faba

Javier Molina

Marian Gómez

T - Primary tumour			
TX	Primary tumour cannot be assessed		
T0	No evidence of primary tumour		
T1	Tumour ≤ 7 cm or less in greatest dimension, limited to the kidney		
	T1a Tumour ≤ 4 cm or less		
	T1b Tumour > 4 cm but ≤ 7 cm		
T2	Tumour > 7 cm in greatest dimension, limited to the kidney		
	T2a Tumour > 7 cm but ≤ 10 cm		
	T2b Tumours > 10 cm, limited to the kidney		
T3	Tumour extends into major veins or perinephric tissues but not into the ipsilateral adrenal gland and not beyond Gerota fascia		
	T3a Tumour extends into the renal vein or its segmental branches, or invades the pelvicalyceal system or invades perirenal and/or renal sinus fat*, but not beyond Gerota fascia*		
	T3b Tumour grossly extends into the vena cava below diaphragm		
	T3c Tumour grossly extends into vena cava above the diaphragm or invades the wall of the vena cava		
T4	Tumour invades beyond Gerota fascia (including contiguous extension into the ipsilateral adrenal gland)		
N - Regional Lymph Nodes			
NX	Regional lymph nodes cannot be assessed		
N0	No regional lymph node metastasis		
N1	Metastasis in regional lymph node(s)		
M - Distant metastasis			
M0	No distant metastasis		
M1	Distant metastasis		
pTNM stage grouping			
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1, T2, T3	N1	M0
Stage IV	T4	Any N	M0
	Any T	Any N	M1

T1 Guidelines 2023:

The Panel concluded that the current data are inadequate to reach conclusions regarding the clinical effectiveness of TA as compared with PN. Given these uncertainties in the presence of only low-quality evidence, TA can only be recommended to frail and/or comorbid patients with SRMs.

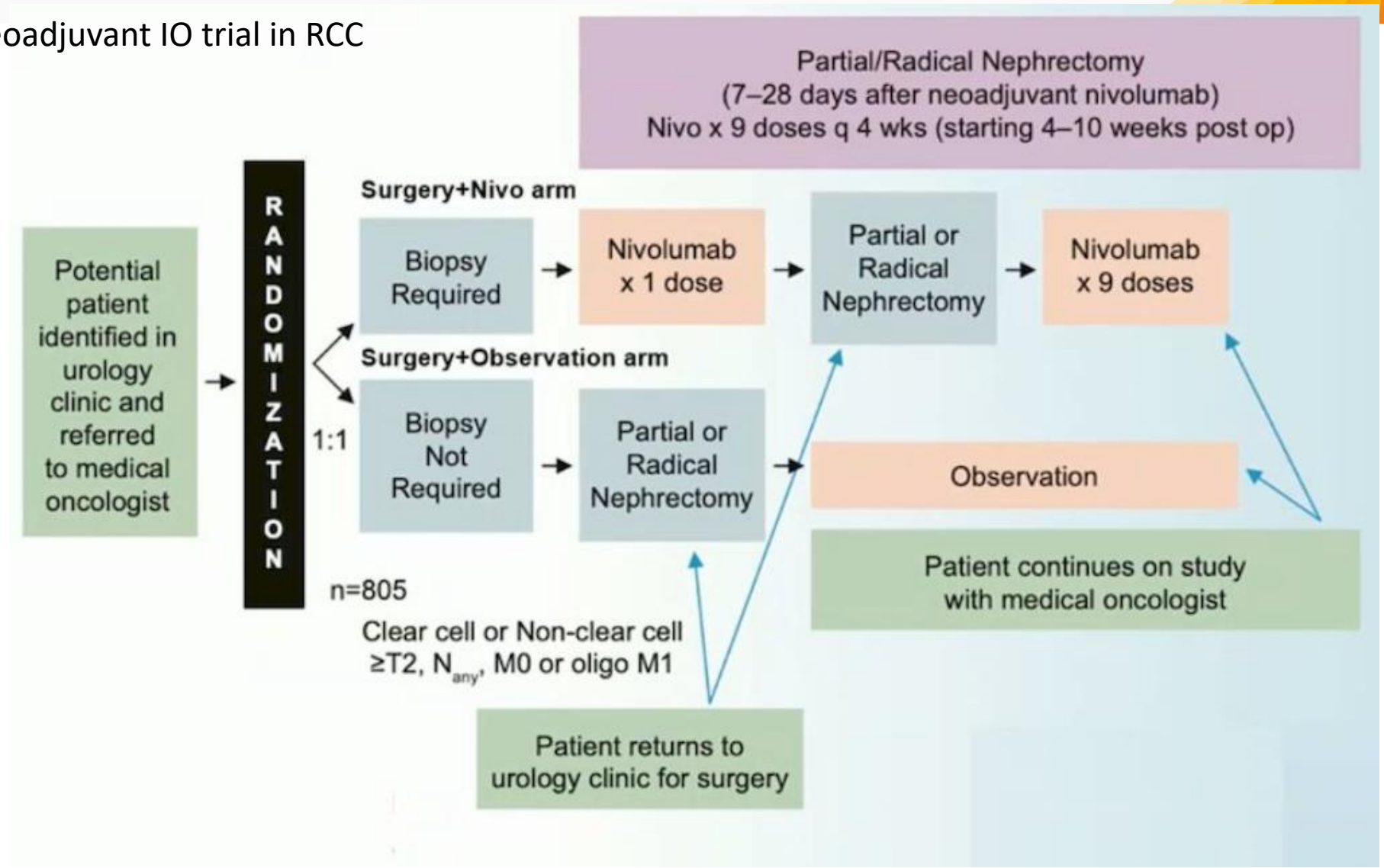
Estudios retrospectivos, observacionales (sin controles).
Heterogeneidad metodológica.
No claros “endpoints.

A discutir:
Desarrollo de estudios prospectivos randomizados NP vs TA/SABR
Documento de consenso multidisciplinar del manejo de masas renales T1a

Phase III trial of PD-1 immune checkpoint inhibitors in adjuvant RCC						
Study	**N**	**Experimental arm**	**Primary endpoint**	**Risk groups**	**DFS (mo) Median (95% CI) HR**	**OS (mo.) Median (95% CI) HR**
Keynote-564 NCT03142334 Median follow-up of 30.1 mo. [440]	994	PEMBRO 200 mg IV Q3W (17 cycles) vs. placebo	DFS in the ITT by IR	**Intermediate-high:** pT2 grade 4 or sarcomatoid; pT3 any grade **High:** pT4 any grade, pN1 **M1 NED:** cM0 after resection of oligometastatic disease < 12 mo.	(ITT) PEMBRO: NR (NE) PLACEBO: NR (NE) HR: 0.63 (95% CI: 0.50–0.80) p < 0.002 DFS at 24 mo.: PEMBRO: 78.3% PLACEBO: 67.3%	(ITT) PEMBRO: NR (NE) PLACEBO: NR (NE) HR: 0.52 (95% CI: 0.31–0.86) not significant alive at 30 mo.: PEMBRO: 95.7% PLACEBO: 91.4%
IMmotion010 NCT03024996 Median follow-up of 44.7 mo. [442]	778	ATEZO 1200 mg IV Q3W (16 cycles or 1 yr.) vs. placebo	DFS in the ITT by IR	**By TNM:** pT2 grade 4 or sarcomatoid; pT3 a grade 3–4; pT3b/c/T4 any grade, pN1 M1 NED: cM0 after resection of oligometastatic disease (synchronous or ≥ 12 mo.)	(ITT) ATEZO: 57.2 (44.6–NE) PLACEBO: 49.5 (47.4–NE) HR: 0.93 (95% CI: 0.75–1.15) p = 0.4950 DFS at 24 mo.: NR	(ITT) ATEZO: NE (59.8–NE) PLACEBO: NE (NE–NE) HR : 0.97 (95% CI: 0.67–1.42) alive at 24 mo.: NR
CheckMate 914 NCT03138512 Median follow-up of 37.0 mo. [443]	816	NIVO 240 mg IV Q2W (× 12 cycles) + IPI 1 mg/kg IV Q6W (× 4 cycles vs. placebo)	DFS in the ITT by BICR	**By TNM:** pT2a grade 3–4; pT2b/T3/T4 any grade, pN1	(ITT) NIVO + IPI: NR (NE) PLACEBO: 50.7 (48.1–NE) HR: 0.92 (95% CI: 0.71–1.19) p = 0.5347 DFS at 24 mo.: NIVO + IPI: 76.4% PLACEBO: 74.0%	NR

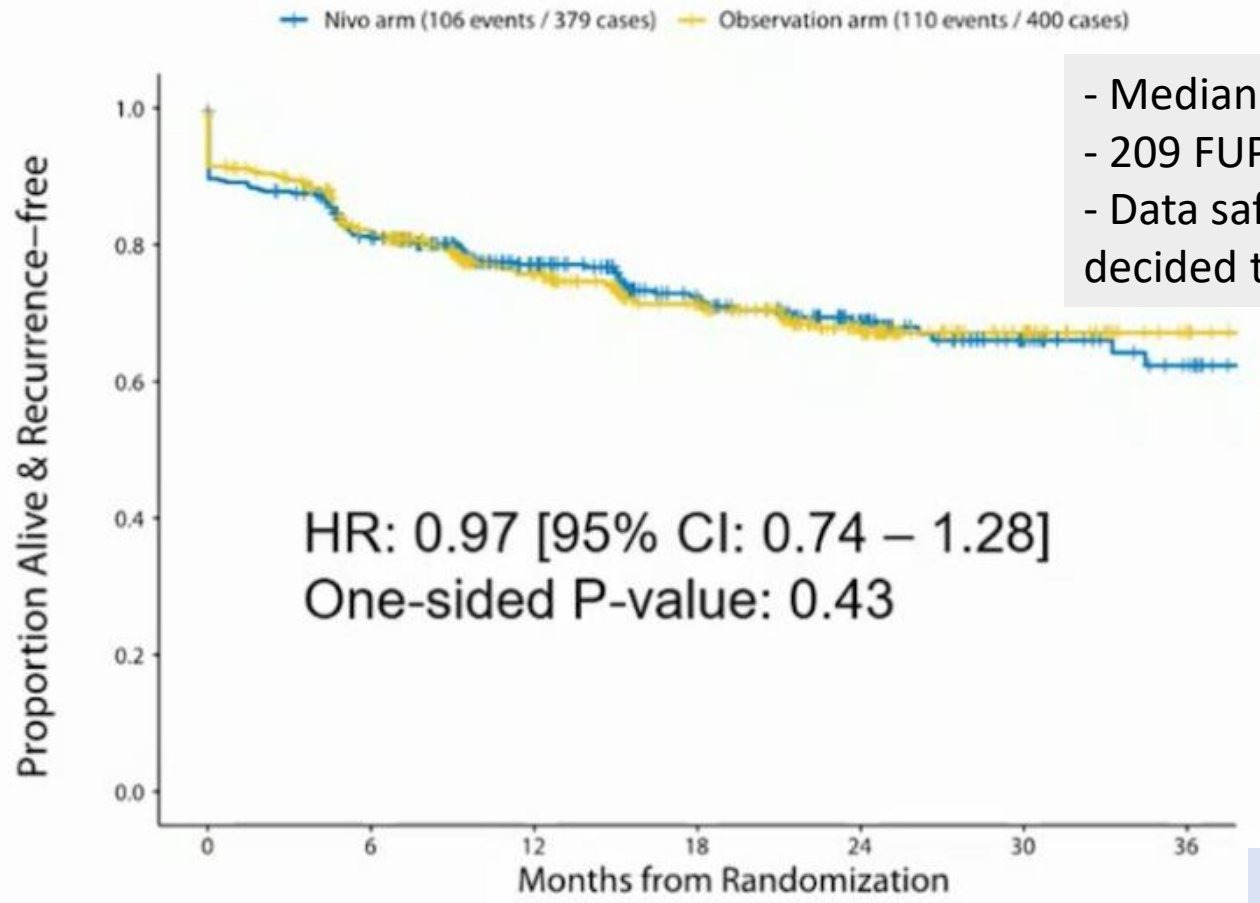
Adyuvancia:
Identificación correcta de pacientes con márgenes negativos post nefrectomía.
Propuesta a desarrollar:
Pacientes con TC negativo post nefrectomía: Realizar estudio con PET- Zirconium Zr89 Girentuximab y valorar correlación TC/ PET Zirconium de cara a la selección de pacientes para adyuvancia

First phase III neoadjuvant IO trial in RCC



Allaf M, et al. ESMO 2022

Recurrence-free survival



Number at risk

Nivo arm	379	291	208	151	99	50	30
Observation arm	400	300	214	161	100	47	22

- Median FUP 16 months
- 209 FUP events
- Data safety monitoring committee decided to stop early due to futility

Perioperative nivolumab did not improve RFS in RCC patients at high risk for recurrence

Allaf M, et al. ESMO 2022

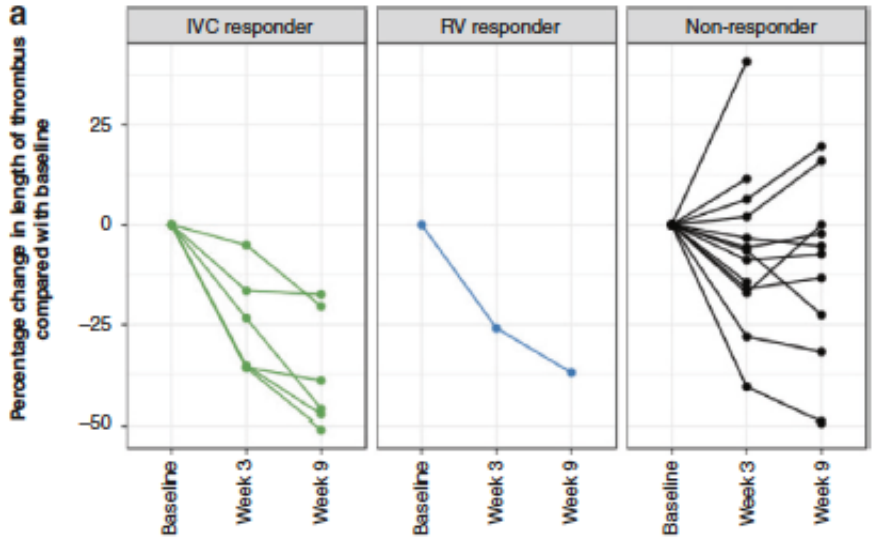
ONGOING PHASE III TRIALS

Name of the study	Drug	N	Inclusion Criteria	Primary Endpoint
NCT03288532 **RAMPART** Recruiting	Durvalumab or Durvalumab + Tremelimumab (vs monitoring)	1750	Leibovich score 3–11 All cell types except for pure oncocytoma, collecting duct, medullary and transitional cell cancer	Disease-free survival Overall Survival
NCT05239728 **MK-6482-022** **LITESPARK-022** Recruiting	Pembrolizumab +/- belzutifan	1600	pT2N0M0 Grade 4 or sarcomatoid pT3N0M0 any Grade pT4N0M0 any Grade pT any N + M0 any Grade M1 NED	Disease-free survival

IL-2,… potential role for vaccines in this setting such as melanoma?

A Phase II study of neoadjuvant axitinib for reducing the extent of venous tumour thrombus in clear cell renal cell cancer with venous invasion (NAXIVA)

Grant D. Stewart[1,2], Sarah J. Welsh[1,2], Stephan Ursprung[1], Ferdia A. Gallagher[1,2], James O. Jones[1,2,3], Jacqui Shields[3,14], Christopher G. Smith[4], Thomas J. Mitchell[1,2,5], Anne Y. Warren[1,2], Axel Bex[6], Ekaterini Boleti[6], Jade Carruthers[7], Tim Eisen[1,2], Kate Fife[2], Abdel Hamid[8], Alexander Laird[9,10], Steve Leung[9], Jahangeer Malik[9], Iosif A. Mendichovszky[1,2], Faiz Mumtaz[6], Grenville Oades[11], Andrew N. Priest[1,2], Antony C. P. Riddick[2], Balaji Venugopal[11,12], Michelle Welsh[7], Kathleen Riddle[7], Lisa E. M. Hopcroft[7,15], NAXIVA Trial Group* and Robert J. Jones[11,12]



Factibilidad de neoadyuvancia en T3b-c

RESULTS: In all, 35% (7/20) patients with VTT had a reduction in Mayo level with axitinib: 37.5% (6/16) with IVC VTT and 25% (1/4) with RV-only VTT. No patients had an increase in Mayo level. In total, 75% (15/20) of patients had a reduction in VTT length. Overall, 41.2% (7/17) of patients who underwent surgery had less invasive surgery than originally planned. Non-responders exhibited lower baseline microvessel density (CD31), higher Ki67 and exhausted or regulatory T-cell phenotype.