VIII SIMPOSIO NACIONAL
de ONCOLOGÍA de PRECISIÓN
Vigo, 19 y 20 de febrero de 2026

Clínica-II: Lo mejor de 2025 en 20 diapositivas.
Tumores genitourinarios

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DISCLOSURES

- ✓ *Employment: none*
- ✓ *Consultant or Advisory Role: Astellas Pharma, Novartis AAA, Astra-Zeneca, Bayer, Bristol-Myers-Squibb, Recordati, Ipsen, Merck, Pfizer, MSD, Janssen*
- ✓ *Stock Ownership: none*
- ✓ *Research Funding: none*
- ✓ *Speaking honoraria: Novartis AAA, Almirall Pharma, Astellas Pharma, Astra-Zeneca, Bayer, Bristol-Myers-Squibb, Merck, MSD, Roche, Pfizer; Janssen*
- ✓ *Travel/Accommodations: Bristol-Myers-Squibb, Pfizer, Roche, Astellas Pharma, MSD, Merck*

XI BEST-GU 2025 VIRTUAL
11|12 FEB / 2026

CARCINOMA UROTELIAL

ctDNA
HER-2

- **ctDNA**

IMvigor010

N=809

Key eligibility[a]
- **High-risk MIUC (bladder, renal pelvis, ureter)**
- **Radical cystectomy/nephroureterectomy with LN dissection** within ≤ 14 weeks
  - **ypT2-T4a or ypN+** for patients treated with **NAC**[b]
  - **pT3-T4a or pN+** for patients **not treated with NAC**[b]
- No postsurgical radiation or AC
- If no prior NAC given, patient had to be ineligible for, or declined, cisplatin-based AC
- ECOG PS 0-2
- **Tissue sample for PD-L1 testing**

R 1:1

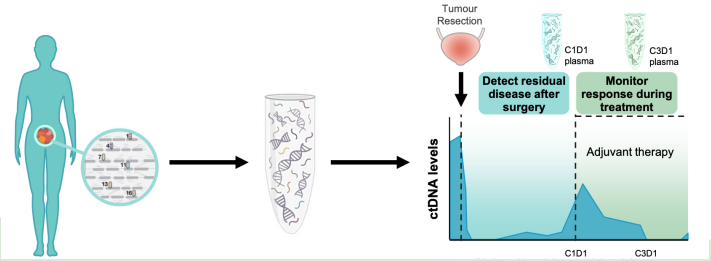
Atezolizumab 1200 mg q3w *(16 cycles or 1 year)*

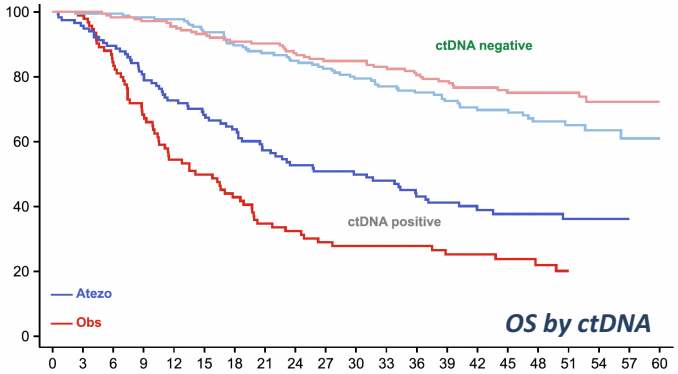
No crossover allowed

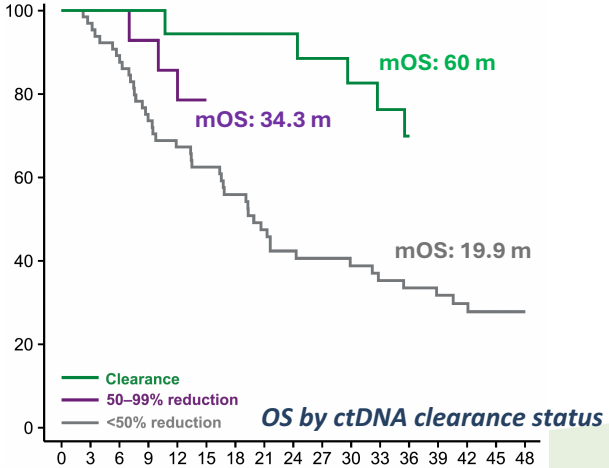
Observation[c] **q3w**

Primary endpoint: DFS

Median follow-up -> 46.8 months



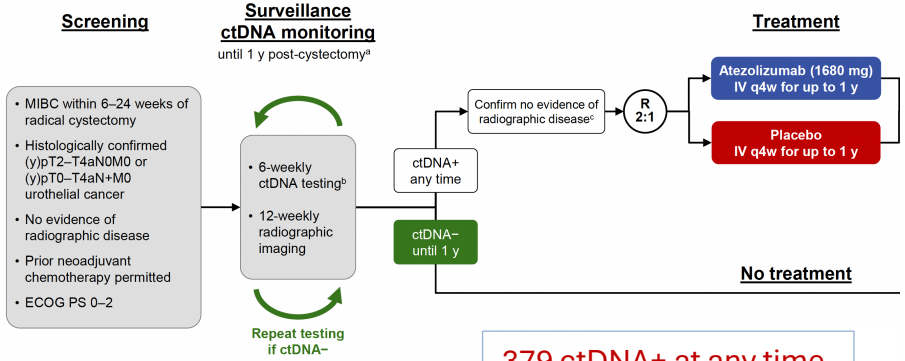




- **ctDNA**

IMvigor011

N=761



Primary endpoint: DFS

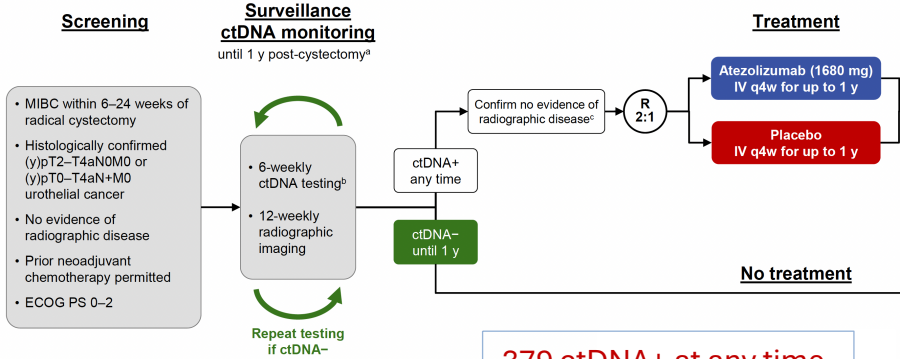
379 ctDNA+ at any time
377 persistently ctDNA-

Characteristic		Randomised ctDNA+ Atezolizumab (n=167)	Randomised ctDNA+ Placebo (n=83)	Persistently ctDNA− No treatment (n=357)
Age, median (range), y		69 (42–87)	67 (44–84)	69 (36–90)
Male, n (%)		141 (84.4)	67 (80.7)	278 (77.9)
Region, n (%)	Asia–Pacific	51 (30.5)	27 (32.5)	137 (38.4)
	Central and South America	14 (8.4)	6 (7.2)	25 (7.0)
	Europe	101 (60.5)	49 (59.0)	191 (53.5)
	North America	1 (0.6)	1 (1.2)	4 (1.1)
ECOG PS, n (%)	0	113 (67.7)	53 (63.9)	232 (65.7)
	1	52 (31.1)	29 (34.9)	110 (31.2)
	2	2 (1.2)	1 (1.2)	11 (3.1)
PD-L1 status, n (%)	IC0/1 (<5%)	108 (64.7)	53 (63.9)	189 (53.1)
	IC2/3 (≥5%)	59 (35.3)	30 (36.1)	167 (46.9)
Histological variants present, n (%)		18 (10.8)	8 (9.6)	56 (15.7)
Prior neoadjuvant chemotherapy, n (%)	Yes	80 (47.9)	33 (39.8)	168 (47.1)
	No	87 (52.1)	50 (60.2)	189 (52.9)
Tumour stage post-cystectomy, n (%)	≤T2	46 (27.5)	24 (28.9)	166 (46.8)
	T3/4	121 (72.5)	59 (71.1)	189 (53.2)
Nodal status, n (%)	Negative	71 (42.5)	35 (42.2)	285 (79.8)
	Positive	96 (57.5)	48 (57.8)	72 (20.2)
Pathological staging at cystectomy, n (%)[a]	pT2N0	8 (4.8)	3 (3.7)	62 (17.5)
	ypT2N0	15 (9.0)	5 (6.1)	61 (17.2)
	(y)pT2N+	30 (18.0)	18 (22.0)	43 (12.1)
	(y)pT3–4N0	49 (29.3)	26 (31.7)	160 (45.1)
	(y)pT3–4N+	65 (38.9)	30 (36.6)	29 (8.2)
Time from cystectomy to first ctDNA+ sample, n (%)	≤20 weeks	117 (70.1)	59 (71.1)	NA
	>20 weeks	50 (29.9)	24 (28.9)	NA
Achieved ctDNA+ status, n (%)	At initial test	99 (59.3)	49 (59.0)	NA
	At subsequent tests	68 (40.7)	34 (41.0)	NA

- **ctDNA**

IMvigor011

N=761

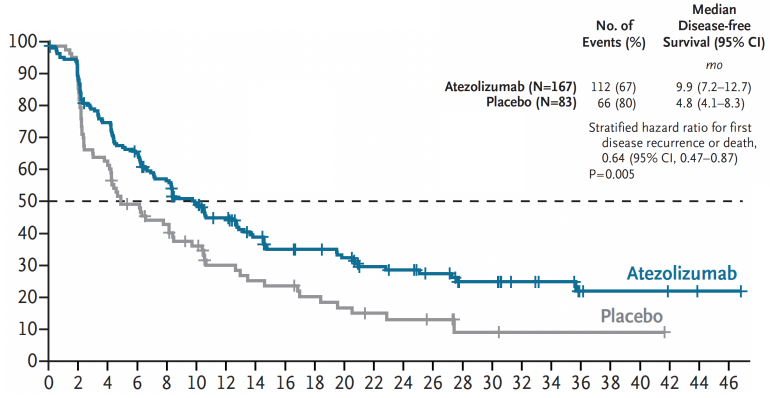


Primary endpoint: DFS

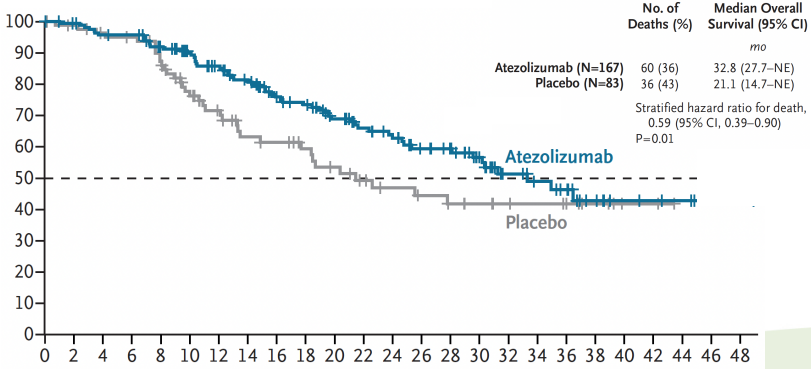
Median follow-up -> 16.1 months

379 ctDNA+ at any time
377 persistently ctDNA-

Disease-free Survival among All Patients with ctDNA-Positive Status



Overall Survival among All Patients with ctDNA-Positive Status



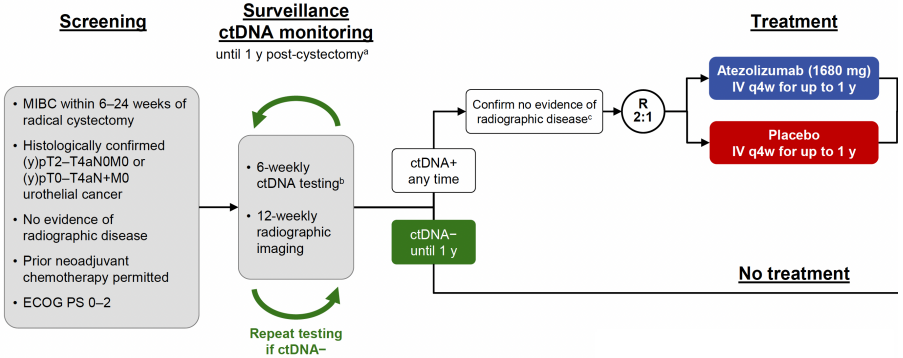
Powles T, et al. N Engl J Med 2025;393:2395.

Ca Urotelial

- ctDNA

IMvigor011

N=761



Primary endpoint: DFS

Median follow-up -> 16.1 months

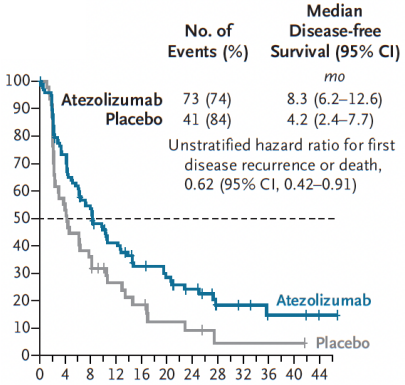
ctDNA+ at initial test

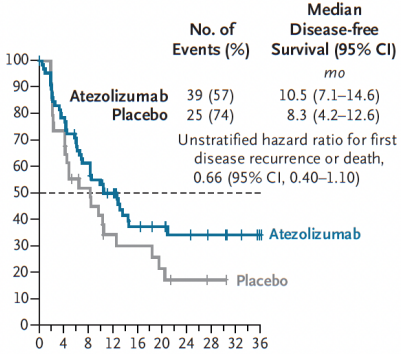
(148/250; 59.2%)

ctDNA+ at subsequent test

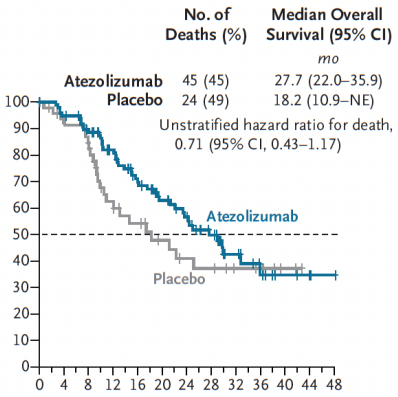
(102/250; 40.8%)

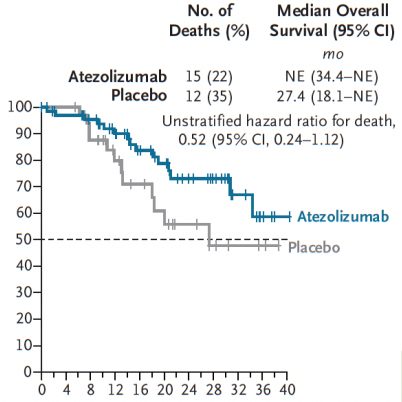
DFS





OS



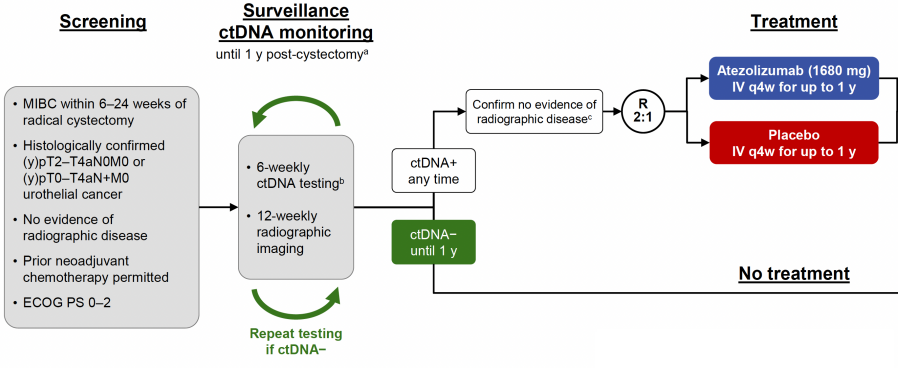


Powles T, et al. N Engl J Med 2025;393:2395.

- **ctDNA**

IMvigor011

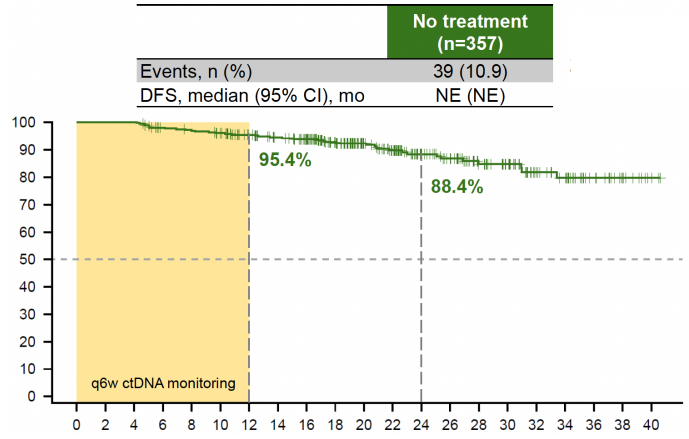
N=761



Primary endpoint: DFS

Median follow-up -> 16.1 months

DFS



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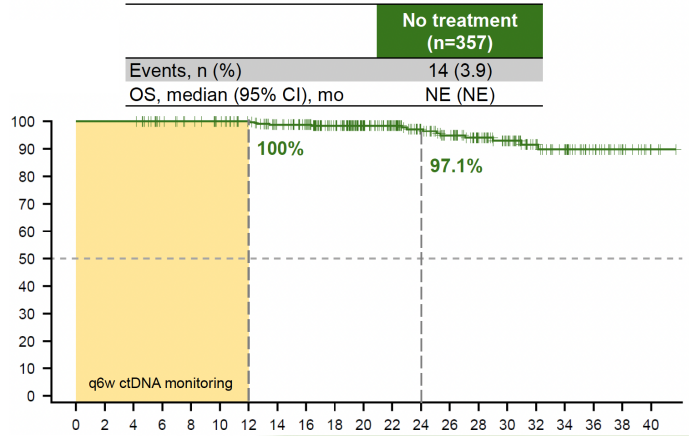


HER-2

RC48-C016

N=484

Unresectable or metastatic UC
- ECOG PS 0-1
- Previously untreated patients
- Central lab HER2 expressing (IHC ≥1+)
- Eligible for platinum

Randomization 1:1

Disitamab vedotin + Toripalimab
(2.0 mg/kg) + (3 mg/kg)
every 14 days
No set maximum cycles

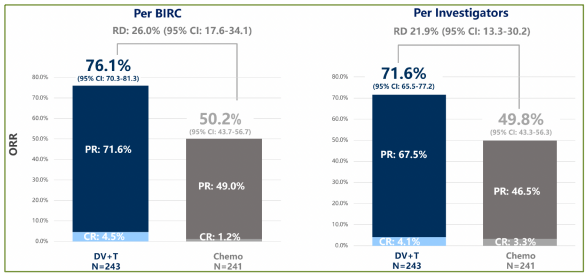
Platinum-containing regimen
Standard regimen
A maximum of 6 cycles

Primary endpoint: PFS and OS

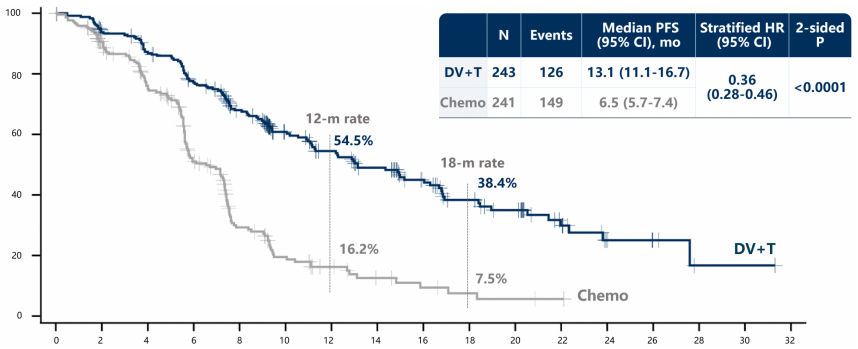
Median follow-up -> 18.2 months

82.6% HER2+
78% HER2+ (2+/3+)

47% Upper tract
52% Cis-eligible

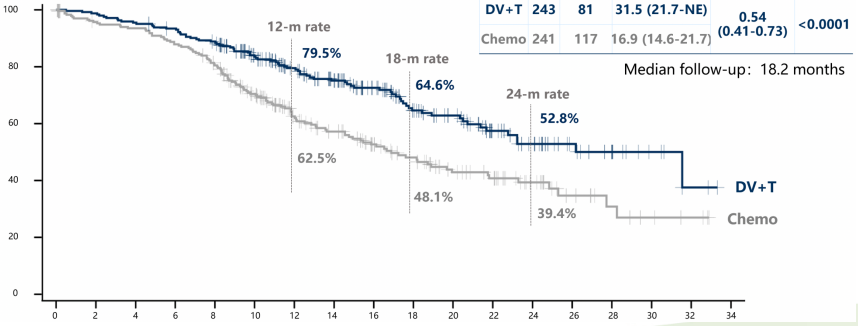


PFS



	N	Events	Median PFS (95% CI), mo	Stratified HR (95% CI)	2-sided P
DV+T	243	126	13.1 (11.1-16.7)	0.36 (0.28-0.46)	<0.0001
Chemo	241	149	6.5 (5.7-7.4)		

OS



	N	Events	Median OS (95% CI), mo	Stratified HR (95% CI)	2-sided P
DV+T	243	81	31.5 (21.7-NE)	0.54 (0.41-0.73)	<0.0001
Chemo	241	117	16.9 (14.6-21.7)		

Median follow-up: 18.2 months

XI BEST-GU 2025 VIRTUAL
11|12 FEB / 2026

CÁNCER DE PRÓSTATA

Vía HRR
Vía PI3K/Akt

- **Vía HRR**

✓ Crosstalk between androgen receptor and DDR pathway.

The rationale for combining PARPi with NHT

NHTs induce a phenotype resembling HRR deficiency

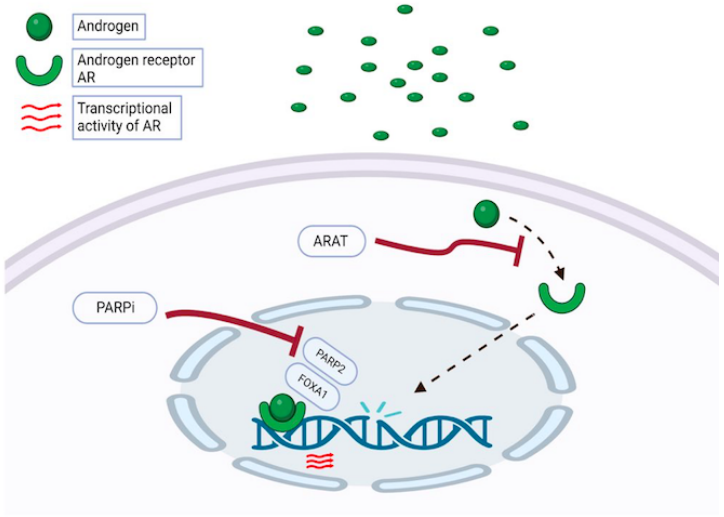
Suppressed AR function causes an upregulation of PARP

NHTs prime tumor cells for PARP inhibition

PARP augments AR activity

PARP inhibitors may attenuate resistance to NHTs

PARP inhibitors extend the benefits of NHTs



Adapted from Bin Gui et al., *PNAS* 2019 June,
DOI https://doi.org/10.1073/pnas.1908547116

Gui B, et al. PNAS 2019. Presented by N. Agarwal.

- **Vía HRR**

TALAPRO-2

N=805

Elegibility
Metastatic CRPC
No prior therapy for mCRPC
ADT + Docetaxel in mHSPC allowed

Cohort-1: all comers

Enzalutamide 160 mg/24h + Talazoparib 0.5 mg (n=399)

Enzalutamide 160 mg/24h + Placebo/12h (n=397)

Primary endpoint: PFS IN ITT

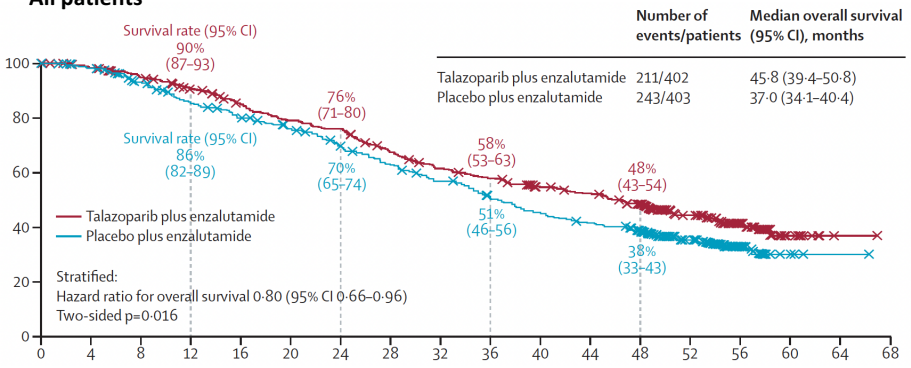
29% docetaxel
8% prior ARPi

Median follow-up -> 52.5 months

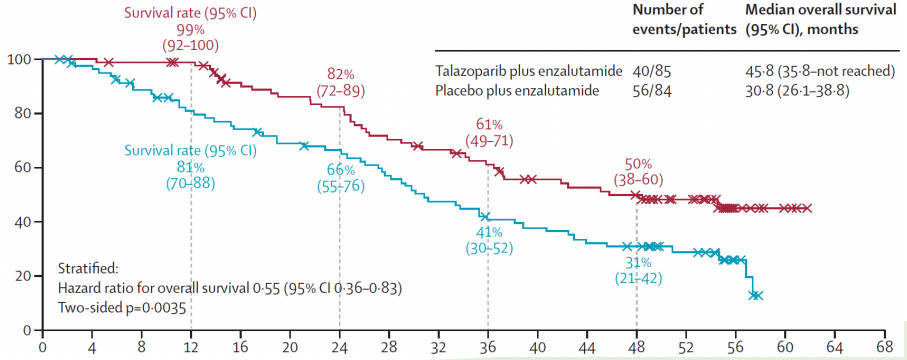
Prospective genomic assessment:
BRCA1, BRCA2, PALB2, ATM, ATR, CHEK2, FANCA RAD51C, NBN, MLH1, MRE11A, CDK12

OS

All patients



Deficient HRR gene alteration status by randomisation stratification



Agarwal N, et al. Lancet 2025;406:447.

- **Vía HRR**

TALAPRO-2

N=805

Elegibility
Metastatic CRPC
No prior therapy for mCRPC
ADT + Docetaxel in mHSPC allowed

Cohort-2: HRR-

Enzalutamide 160 mg/24h + Talazoparib 0.5 mg (n=399)

Enzalutamide 160 mg/24h + Placebo/12h (n=397)

Primary endpoint: PFS IN ITT

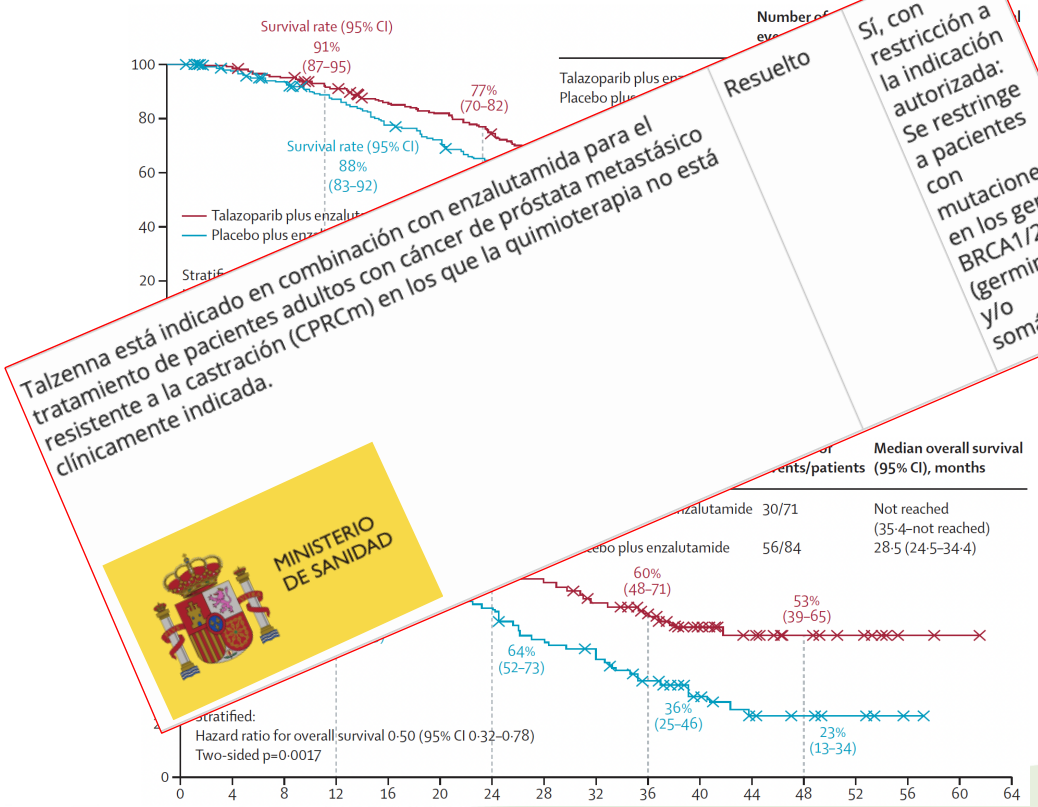
Median follow-up -> 52.5 months

5.5% BRCA1
33% BRCA2

Prospective genomic assessment:
BRCA1, BRCA2, PALB2, ATM, ATR, CHEK2, FANCA RAD51C, NBN, MLH1, MRE11A, CDK12

OS

Any HRR gen alteration



Fizazi K, et al. Lancet 2025;406:461.

Vía HRR

AMPLITUDE

N=696

- mCSPC
- Alteration in ≥ 1 HRR eligible gene: *BRCA1, BRCA2, BRIP1, CDK12, CHEK2, FANCA, PALB2, RAD51B, RAD54L*
- ECOG 0-2
- No prior PARPi nor ARPi other than AAP

Prior allowed treatments in mCSPC:

- ADT ≤6 months
- Docetaxel ≤6 cycles
- AAP ≤45 days
- Palliative RT

Randomization 1:1

Niraparib (200 mg QD)
AAP (1000 mg QD + 5 mg QD)
ADT

Placebo
AAP (1000 mg QD + 5 mg QD)
ADT

16% docetaxel

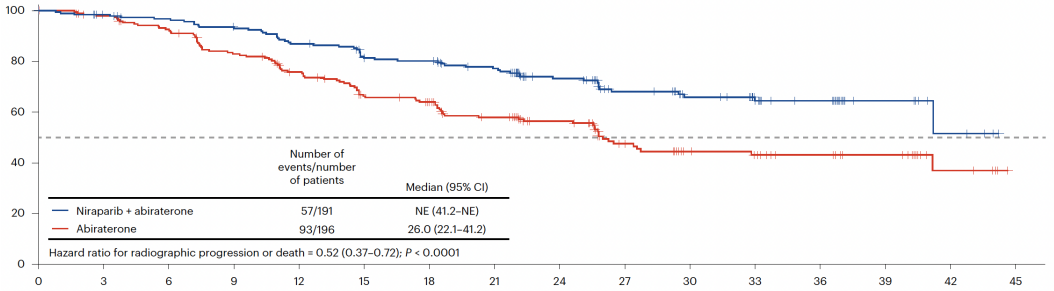
Primary endpoint: rPFS

Median follow-up -> 30.8 months

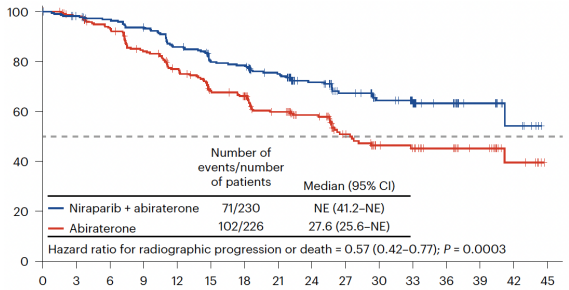
HRR effector subgroup:
BRCA1/2 (56%)
BRIP1, PALB2, RAD51B, RDA54L

rPFS

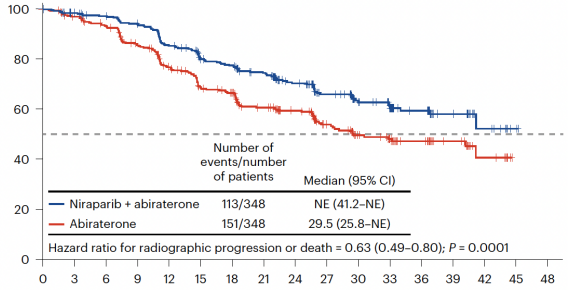
BRCA1/2 gen alteration



HRR effector subgroup



All ITT



Vía HRR

AMPLITUDE

N=696

- mCSPC
- Alteration in ≥ 1 HRR eligible gene: *BRCA1, BRCA2, BRIP1, CDK12, CHEK2, FANCA, PALB2, RAD51B, RAD54L*
- ECOG 0-2
- No prior PARPi nor ARPi other than AAP

Prior allowed treatments in mCSPC:

- ADT ≤6 months
- Docetaxel ≤6 cycles
- AAP ≤45 days
- Palliative RT

Randomization 1:1

Niraparib (200 mg QD)
AAP (1000 mg QD + 5 mg QD)
ADT

Placebo
AAP (1000 mg QD + 5 mg QD)
ADT

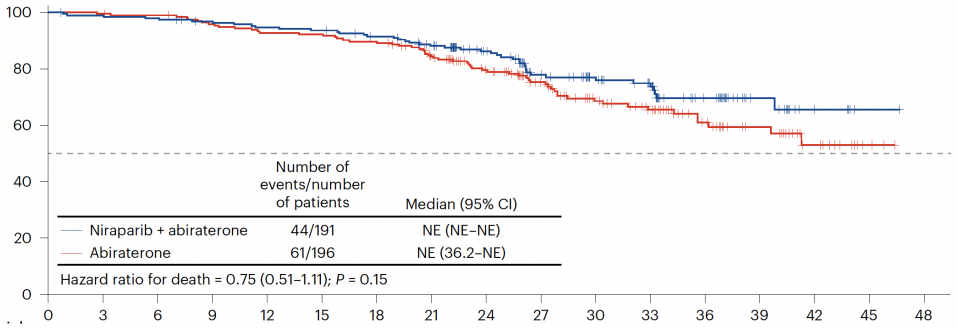
Primary endpoint: rPFS

Median follow-up -> 30.8 months

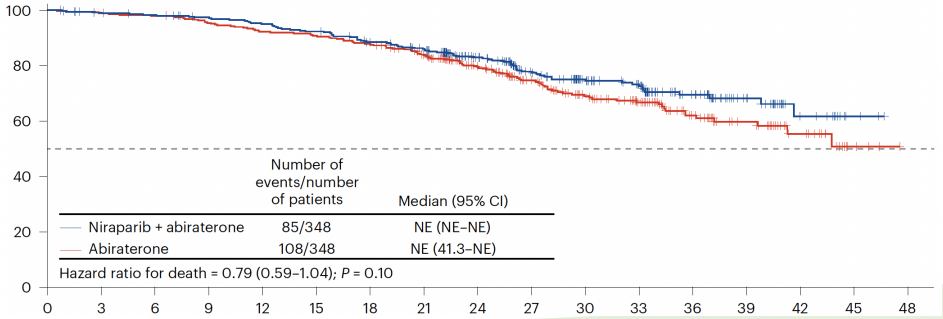
HRR effector subgroup: BRCA1/2, BRIP1, PALB2, RAD51B, RDA54L

OS

BRCA1/2 gen alteration



All ITT

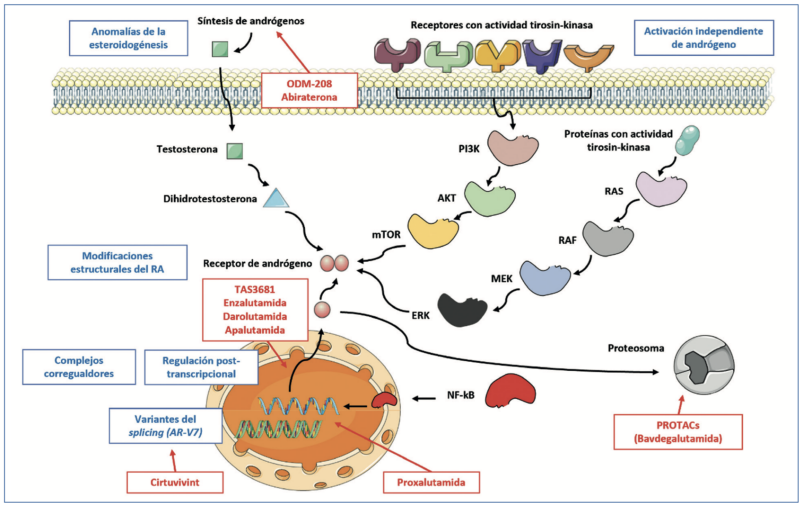


Attard G, et al. Nature Med 2025;31:4109.

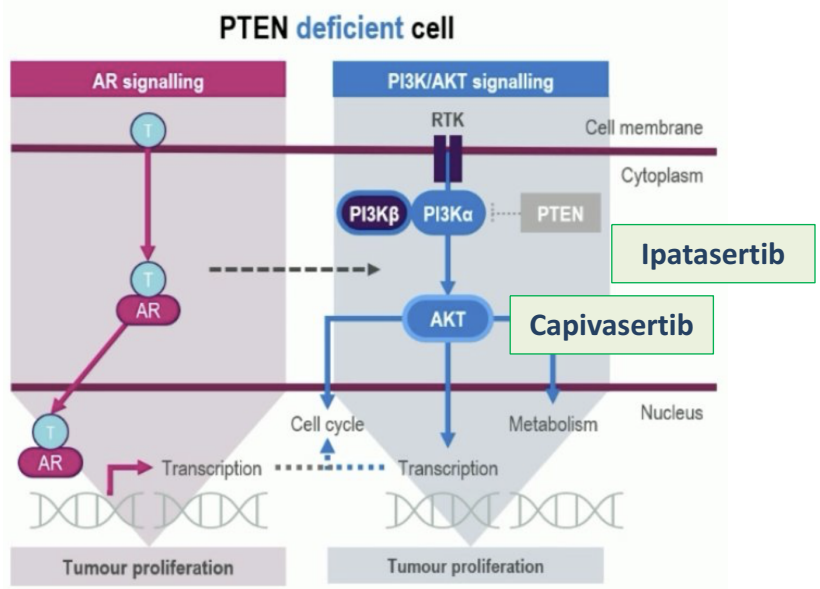
- ## Vía PI3K/Akt

✓ The androgen receptor remains relevant on progression to hormone therapy

Mechanisms of androgen resistance and targets of second-generation ISRAs and new hormonal therapies



30-50% CaP



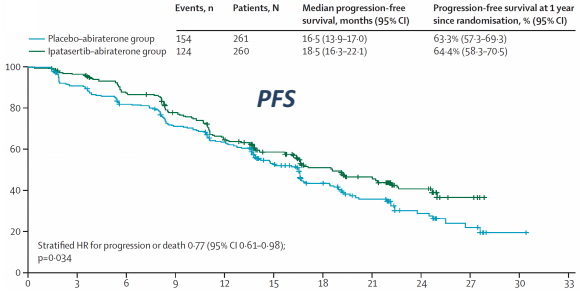
González Merino C,, et al. Rev Cancer 2023;ISSN: 0213-8573.
Fizazi K, et al. ESMO 2025.

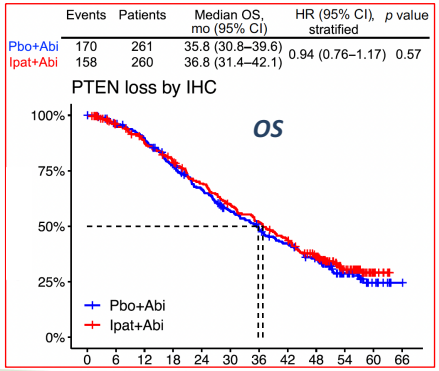
- **Vía PI3K/Akt**

IPATential150

N=1611 with mCRPC

Ipatasertib





Capivasertib

Trial (Pha					
ProCAID (Ph II)					0 mo =0.32)
RE-AKT (Ph II)					mo =0.33)
CAPItello-280 (Ph III)	mCRPC 1st-line chemo	None	Capivasertib + docetaxel *vs.* Placebo + docetaxel	Trial halted, no benefit	No benefit
CAPItello-281 (Ph III)	De novo mHSPC PTEN loss	PTEN loss required	Capivasertib + abiraterone *vs.* Placebo + abiraterona	OS maturing	rPFS improved (primary endpoint met)

AstraZeneca is discontinuing the CAPItello-280 Phase III trial evaluating the efficacy and safety of *Truqap* (capivasertib) in combination with docetaxel and androgen-deprivation therapy (ADT) compared to docetaxel and ADT with placebo in patients with metastatic castration-resistant prostate cancer (mCRPC).

This decision is based on the recommendation of the Independent Data Monitoring Committee (IDMC) following their review of data from a pre-specified interim analysis, which concluded that the *Truqap* combination was unlikely to meet the dual primary endpoints of radiographic progression-free survival (rPFS) and overall survival (OS) versus the comparator arm upon trial completion. The safety profile for *Truqap* was consistent with previous trials.

Sweeney C, et al. Lancet 2021;398:131.
De Bono JS, et al. Euro Urol 2025;87:672
Crabb SJ, et al. J Clin Oncol 2021;39(3):190.
Crabb SJ, et al. Eur Urol 2022;82(5):512.
Rescigno P, et al. Eur Urol Cancer 2024;205:114103.
https://www.astrazeneca.com/media-centre/press-releases/2025/update-on-capitello-280-phase-iii-trial.html.
https://www.astrazeneca.com/media-centre/press-releases/2024/truqap-improved-rpfs-in-advanced-prostate-cancer.html.

Vía PI3K/Akt

CAPItello-281

N=1012

Patients with PTEN deficient *de novo* mHSPC

- PTEN deficiency: (diagnostic cut-off of ≥90% of viable malignant cells with no specific cytoplasmic staining by IHC)*

Of ~6,200 patients submitting tumour tissue, **97%** had a valid IHC result and **25%** were **PTEN deficient**

Primary endpoint: PFS

Median follow-up -> 18.4 months

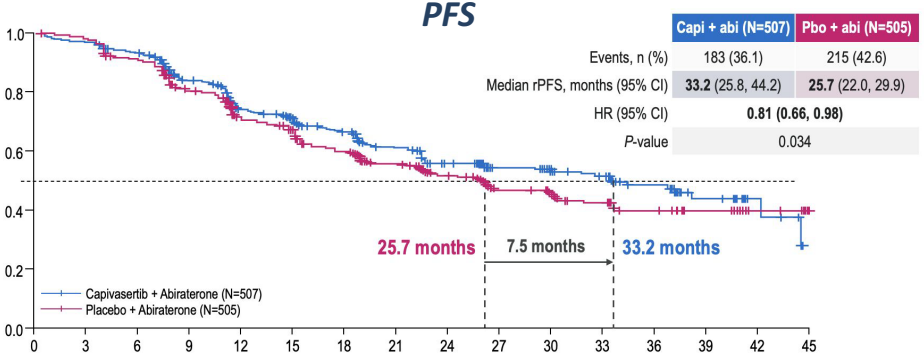
1,012 patients randomised (1:1)

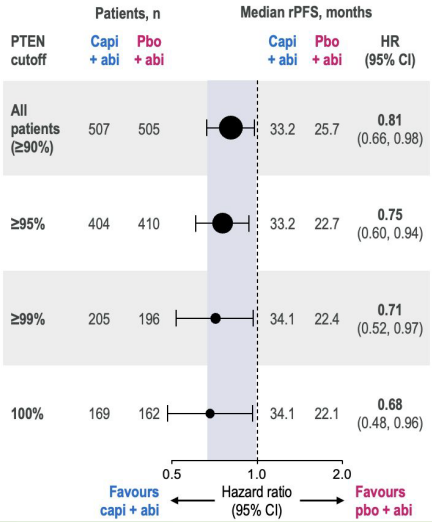
Capivasertib	400 mg BID 4 days on, 3 days off
Abiraterone/pred + ADT	1000 mg QD + ADT
Placebo	400 mg BID 4 days on, 3 days off
Abiraterone/pred + ADT	1000 mg QD + ADT

Stratification factors:†

- M1 volume (CHAARTED criteria) and visceral mets
- Geography

PFS





Fizazi K, et al. Ann Oncol 2026;37(1):53.

Vía PI3K/Akt

CAPItello-281

N=1012

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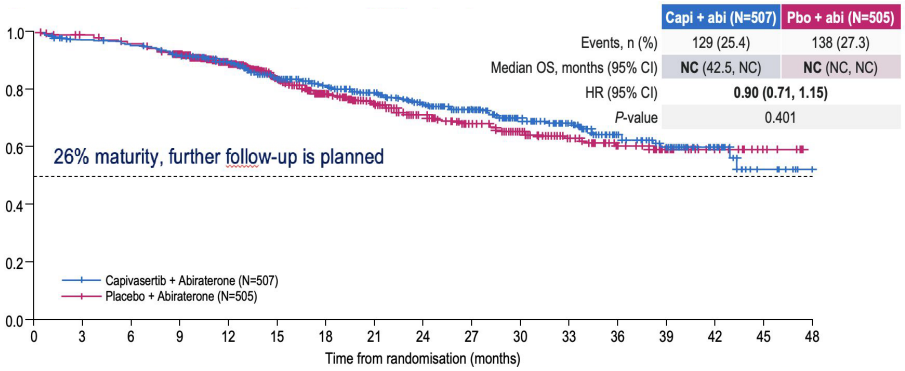
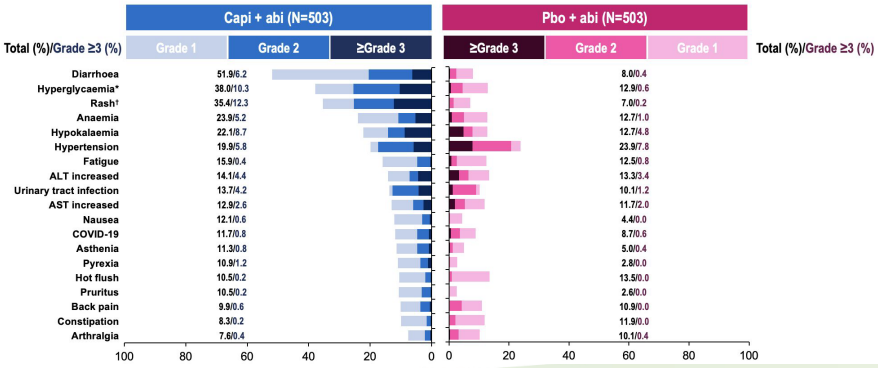
OS



Adverse events (≥10% of patients)



XI BEST-GU 2025 VIRTUAL
11|12 FEB / 2026

CÁNCER RENAL

Subtipos moleculares
KIM-1

Ca Renal

Subtipos moleculares

IMmotion-151

N=915

Key eligibility
- Treatment-naive advanced or metastatic RCC
- Clear cell and/or sarcomatoid histology
- KPS ≥ 70
- Tumor tissue available for PD-L1 staining

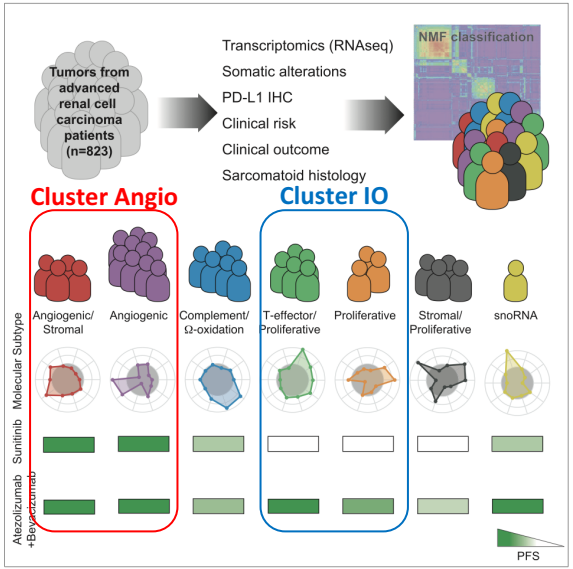
Stratification
- MSKCC risk score
- Liver metastases
- PD-L1 IHC status (< 1% vs ≥ 1%)[a]

N = 915 → R 1:1

- Atezolizumab 1200 mg IV q3w[b] + bevacizumab 15 mg/kg IV q3w[b]
- Sunitinib 50 mg/day orally (4 wk on, 2 wk off)

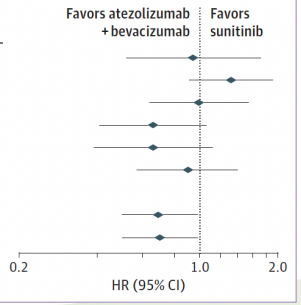
Primary endpoint: PFS in PD-L1 and OS in ITT

Minimum follow-up -> 40 months



C HRs for OS

Cluster	HR (95% CI)	Atezolizumab + bevacizumab	Sunitinib
Cluster 1: Angiogenic/stromal (n = 98)	0.94 (0.52-1.72)	NR	48.2
Cluster 2: Angiogenic (n = 245)	1.32 (0.91-1.91)	46.2	NR
Cluster 3: Complement/Ω-oxidative (n = 156)	0.99 (0.64-1.54)	35.0	36.6
Cluster 4: T-effector/proliferative (n = 116)	0.66 (0.41-1.06)	38.7	23.3
Cluster 5: Proliferative (n = 74)	0.66 (0.39-1.12)	21.7	15.5
Cluster 6: Stromal/proliferative (n = 106)	0.90 (0.57-1.40)	15.9	12.7
Cluster 7: snoRNA (n = 28)	NC	NR	42.1
Clusters 4 + 5 (n = 190)	0.69 (0.48-0.98)	34.0	19.5
Clusters 4, 5, and 7 (n = 218)	0.70 (0.50-0.98)	35.4	21.2



Motzer RJ, et al. Cancer Cell 2020;38: 803.

Subtipos moleculares

OPTIC-RCC

N=101

Key Eligibility Criteria
- ECOG 0 or 1
- Metastatic clear cell RCC without prior systemic therapy in any setting
- Available tumor tissue for RNA-sequencing/cluster prediction

Primary endpoint: ORR

Clusters 1/2 → **Nivolumab/Cabozantinib (N=26)**
- H_0: ORR ≤ 55%
- H_A: ORR > 75%

Stage I (N=12) ≥7/12 responders → **Stage II (N=14) ≥18/26**

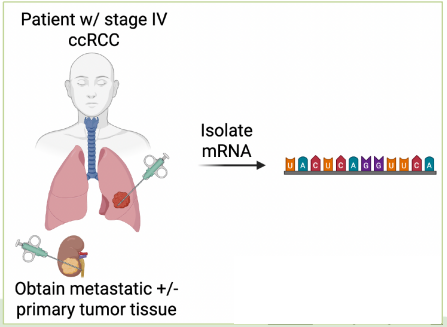
Clusters 4/5 → **Ipilimumab/Nivolumab (N=28)**
- H_0: ORR ≤ 40%
- H_A: ORR > 60%

Stage I (N=16) ≥7/16 responders → **Stage II (N=12) ≥15/28**

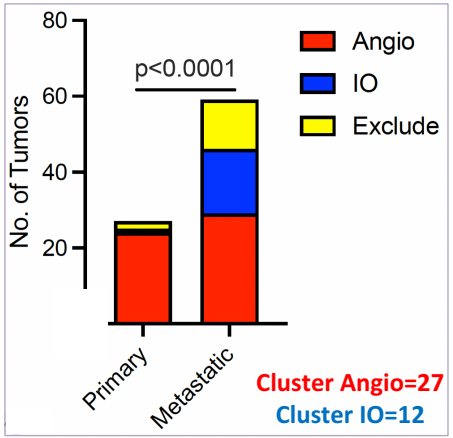
Remains open to accrual

Clusters 3/6/7 → Excluded from trial

Median follow-up -> 11.1 months



IMDC prognostic risk group – Favorable/Intermediate/Poor (%)	41/52/7
Source of RNA – Primary/Metastatic (%)	22/78

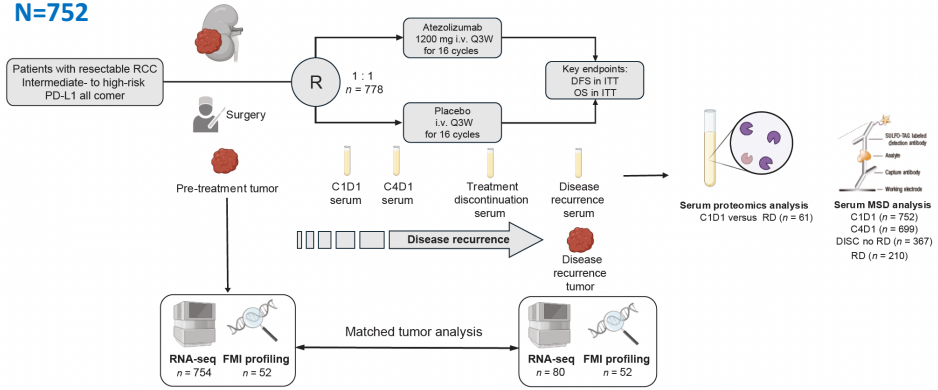


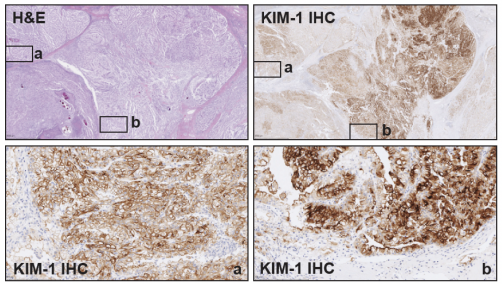
	Cluster 1/2 (n=25)*
Objective response – no. (%)	19 (76)
Best overall response – no. (%)	
Complete response	2 (8)
Partial response	17 (68)
Stable disease	6 (24)
Progressive disease	0 (0)
Patients with tumor burden reduction – no. (%)	25 (100)
% tumor shrinkage – median (range)	42 (5-100)

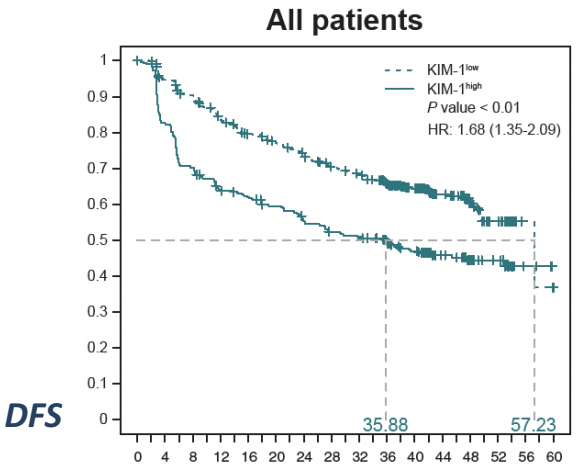
- **KIM-1**

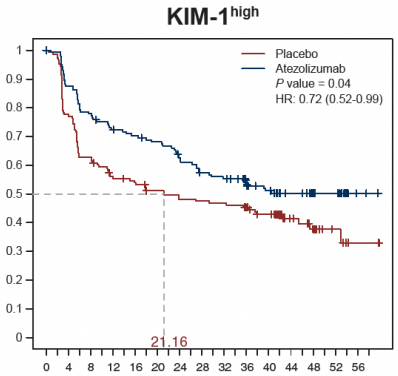
IMmotion010

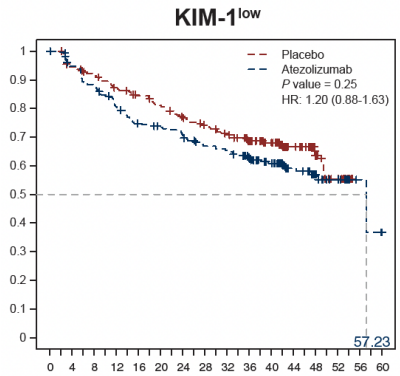
N=752











Ca Renal

- **KIM-1**

CheckMate-214

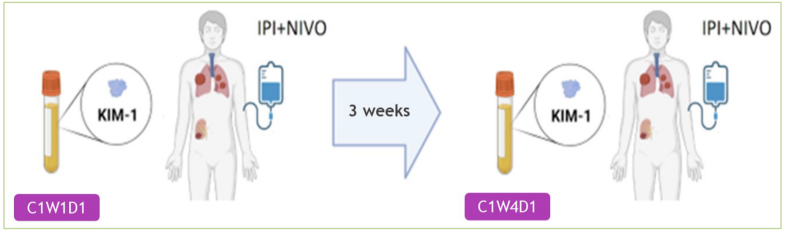
N=1096

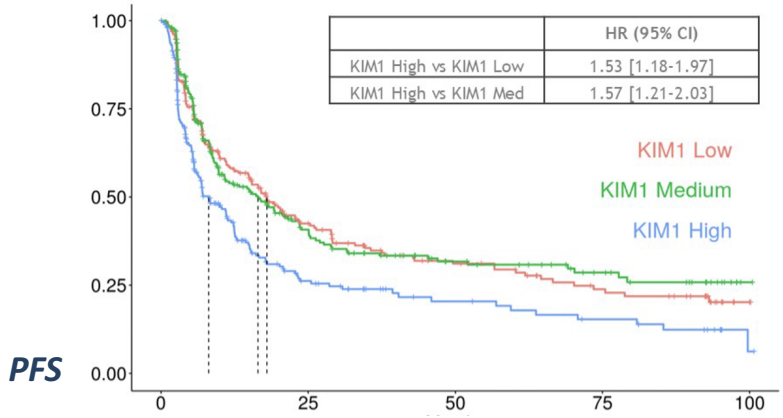
Key inclusion criteria[1]
- ≥ 18 years old
- Treatment-naïve aRCC
- Clear cell component
- Measurable disease per RECIST v1.1
- KPS ≥ 70%

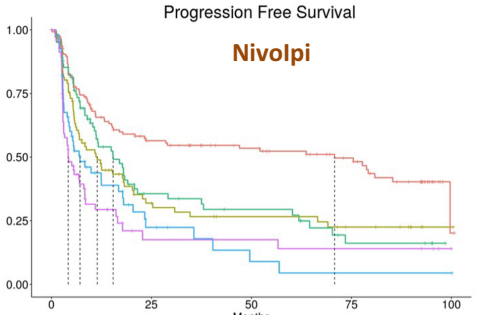
R 1:1

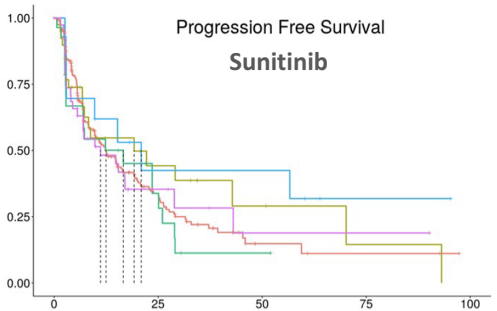
Nivolumab 3 mg/kg IV
+ **Ipilimumab** 1 mg/kg IV Q3W (× 4 doses)
followed by **Nivolumab** 3 mg/kg Q2W
Patients receiving NIVO monotherapy could switch to NIVO 240 mg Q2W or 480 mg Q4W flat dosing[6]

Sunitinib 50 mg PO QD
for 4 weeks on, 2 weeks off
(6-week cycles)
Crossover from SUN to NIVO+IPI was permitted for IMDC intermediate/poor-risk patients[6]









Xu W, et al. ASCO GU 2025;abstr437.

- **KIM-1**

COSMIC-313

N=676

Advanced RCC (N ~676)
- Clear-cell component
- Intermediate or poor risk per IMDC
- Measurable disease per RECIST v1.1

R1:1

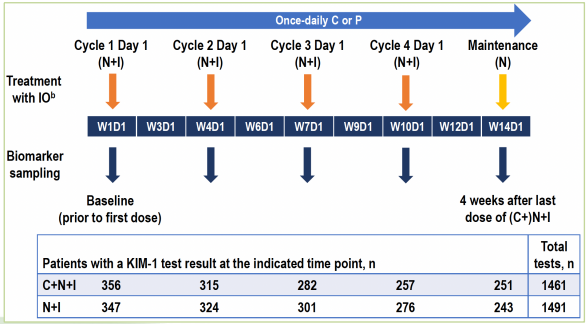
Stratification
- IMDC score
- Region

Cabozantinib + Nivo-Ipi
Cabozantinib 40 mg PO QD
Nivo 3 mg/kg IV Q3W x 4
Ipi 1 mg/kg IV Q3W x 4

Cabozantinib 40 mg PO QD
Nivo 480 mg IV Q4W*

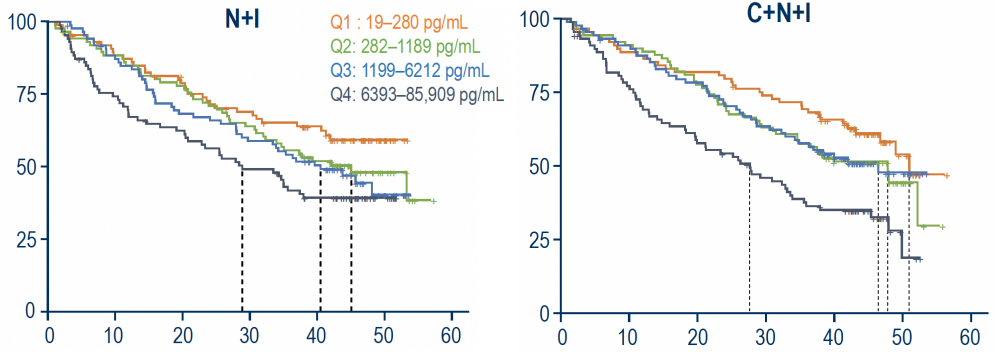
Placebo + Nivo-Ipi
Placebo PO QD
Nivo 3 mg/kg IV Q3W x 4
Ipi 1 mg/kg IV Q3W x 4

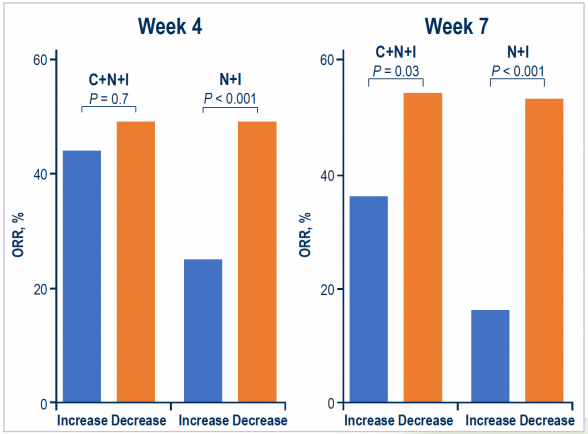
Placebo PO QD
Nivo 480 mg IV Q4W*



Patients with a KIM-1 test result at the indicated time point, n						Total tests, n
C+N+I	356	315	282	257	251	1461
N+I	347	324	301	276	243	1491

Kaplan-Meier OS analyses stratified by quartiles of baseline circulating KIM-1





No me dejan más diapos para conclusiones -> DEBATE

¡Mil gracias!

Begoña Pérez Valderrama
Hospital Universitario Virgen del Rocío. Sevilla