XXIII JORNADA DE REVISIÓN DEL

CONGRESO AMERICANO DE ONCOLOGÍA

Tumores genitourinarios

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Consultant or Advisory Role: BMS, MSD, Takeda, Roche, Pfizer, Roche, Ipsen, Astra-Zéneca, Boehringer, Bayer, Janssen

Speaking: Roche, Ipsen, Lilly, Astellas, Janssen, Novartis, Boehringer, Eisai, Sanofi

Grant or travelsupport: MSD, Ipsen, Roche, Janssen, Pfizer, Astellas, Takeda

Participation in clinical trials: Merck, Astellas, Pfizer, Ipsen, Roche, AZ, Mirati, PharmaMar, Gilead

TUMORES GERMINALES

SWENOTECA / COTRIMS

- Five centers: Trondheim, Oslo, Bergen, Stockholm, Gothenburg, Cologne
- 94 patients (66 SWENOTECA, 28 Cologne)
  - 58 (62%) primary CS I
  - 36 (38%) CS IIA/B
- Median age at RPLND 41.8 years (21-79)
- Median follow-up since RPLND 21 months (range 4-61)

Why primary RPLND

- No increased risk of late toxicity affecting mortality
- Many smaller series and new trials, e.g., SEMS and PRIMETEST
- COTRIMS started in 2018

Tandstad. ASCO 2023 #5008

SWENOTECA / COTRIMS

Results III: SWENOTECA

Postoperative

- Mean number lymph nodes removed 14 (5-56)
- Mean size of largest malignant lymph node 19 mm (5-49)
- Median number of malignant lymph nodes 1 (0-6)

- Pathohistology
  - Seminoma 62 (94%)
  - Nonseminoma 1 (1.5%)
  - Teratoma 1 (1.5%)
  - Benign histology 1 (1.5%)
  - Necrosis 1 (1.5%)

Results IV: SWENOTECA / COTRIMS

- Nine relapses (10%)
- Median time to relapse 6 months (range 2.5-19 months)
- All relapses good prognosis
- Overall survival 100%

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PRÓSTATA

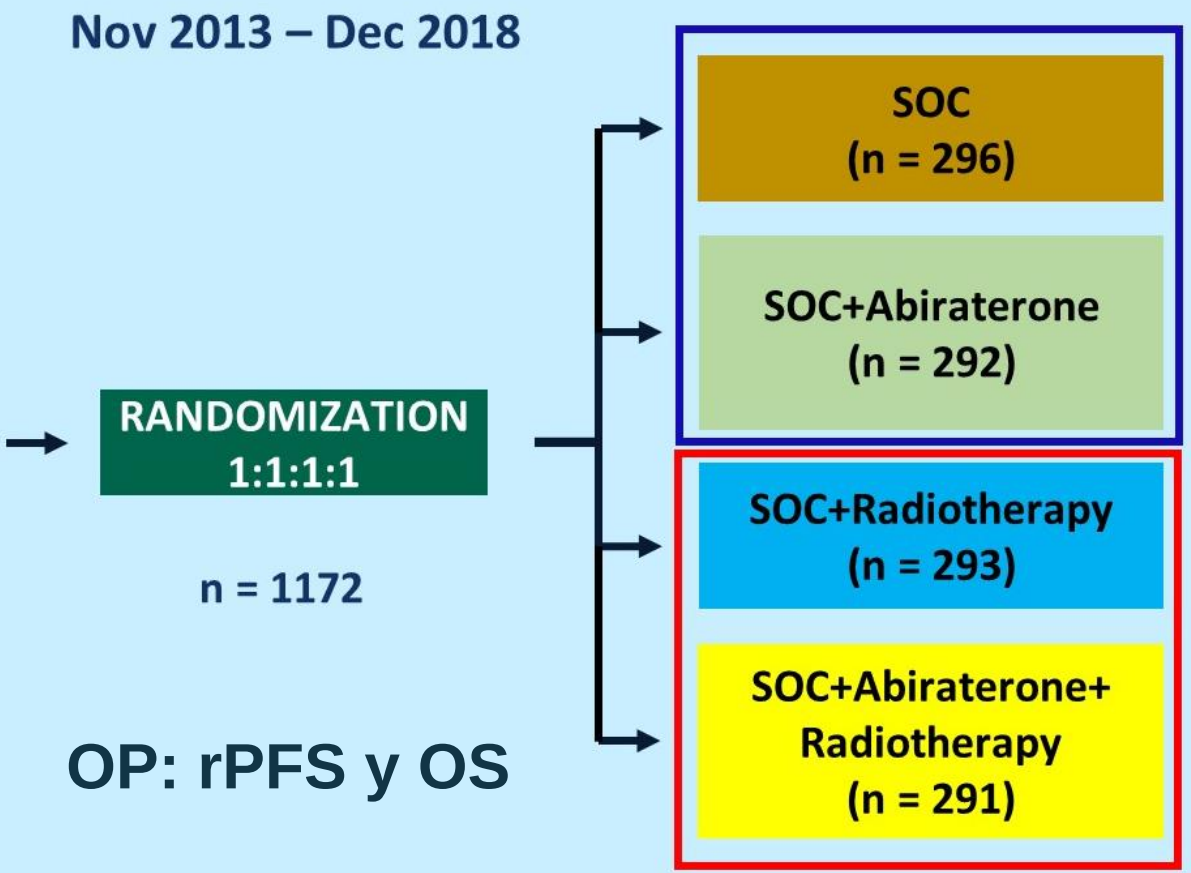
PEACE-1: radioterapia local

Key Eligibility Criteria
De novo mCSPC
Distant metastatic disease: ≥ 1 lesion on bone scan and/or CT scan
ECOG PS 0 -2

On-Study Requirement
Continuous ADT

Permitted
ADT ≤ 3 months

Stratification
ECOG PS (0 vs 1-2)
Metastatic sites (LN vs bone vs visceral)
Type of castration (orchidectomy vs LHRH agonist vs LHRH antagonist)
Docetaxel (yes vs no)



ECOG PS, Eastern Cooperative Oncology Group performance status

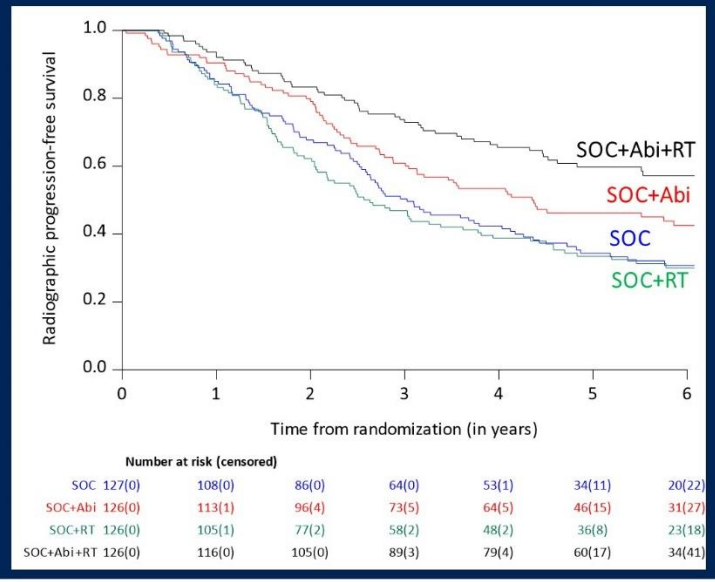
SOC: ADT +/- docetaxel x 6
RDT: 74 Gy en 37 fracciones después de docetaxel

Bajo vol: 43%
Alto vol: 57%

Bossi. ASCO 2023 #LBA5000

Resultados

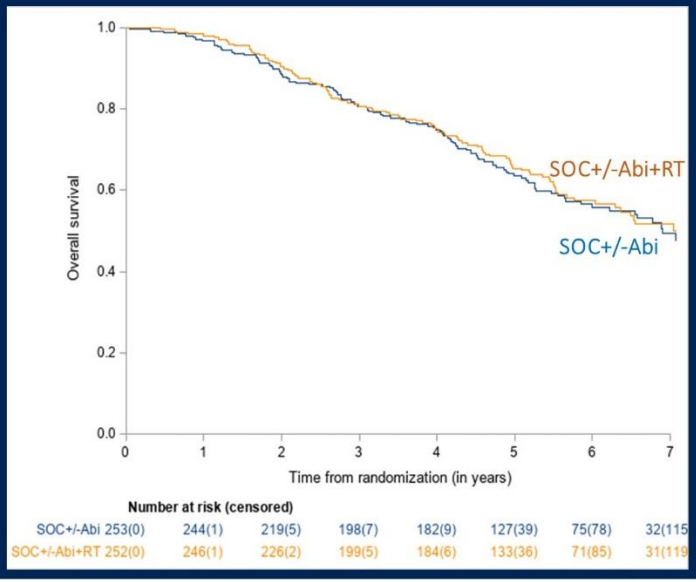
rPFS (low volume population)



	SOC (n=127)	SOC+RT (n=126)	SOC+Abi (n=126)	SOC+Abi+RT (n=126)
Median, ys. (99.9% CI)	3.0 (2.3-4.8)	2.6 (1.7-4.6)	4.4 (2.5-7.3)	7.5 (4,0-NE)
Events, n.	87	89	74	55
HR (99.9%CI)*	Ref	1.11 (0.67-1.84)	0.76 (0.45-1,28)	0.50 (0.28-0.88)
Global p-value	<0.0001			
HR (99.9% CI)*	Ref	1.08 (0.65-1.80)	Ref	0.65 (0.36-1.19)
P-values arms w/wo Abi	0.61		0.02	

*Adjusted on stratification factors (PS, type of castration, docetaxel)

OS (low volume population)



	SOC+/Abi (n=253)	SOC+/- Abi+RT (n=252)
Median, ys. (95.1% CI)	6.9 (5,9-7,5)	7.5 (6-NE)
Events, n	111	104
HR*	Ref	0.98 (0.74-1.28)
p-value	0.86	

*Adjusted on Abitraterone and stratification factors (PS, type of castration, docetaxel)

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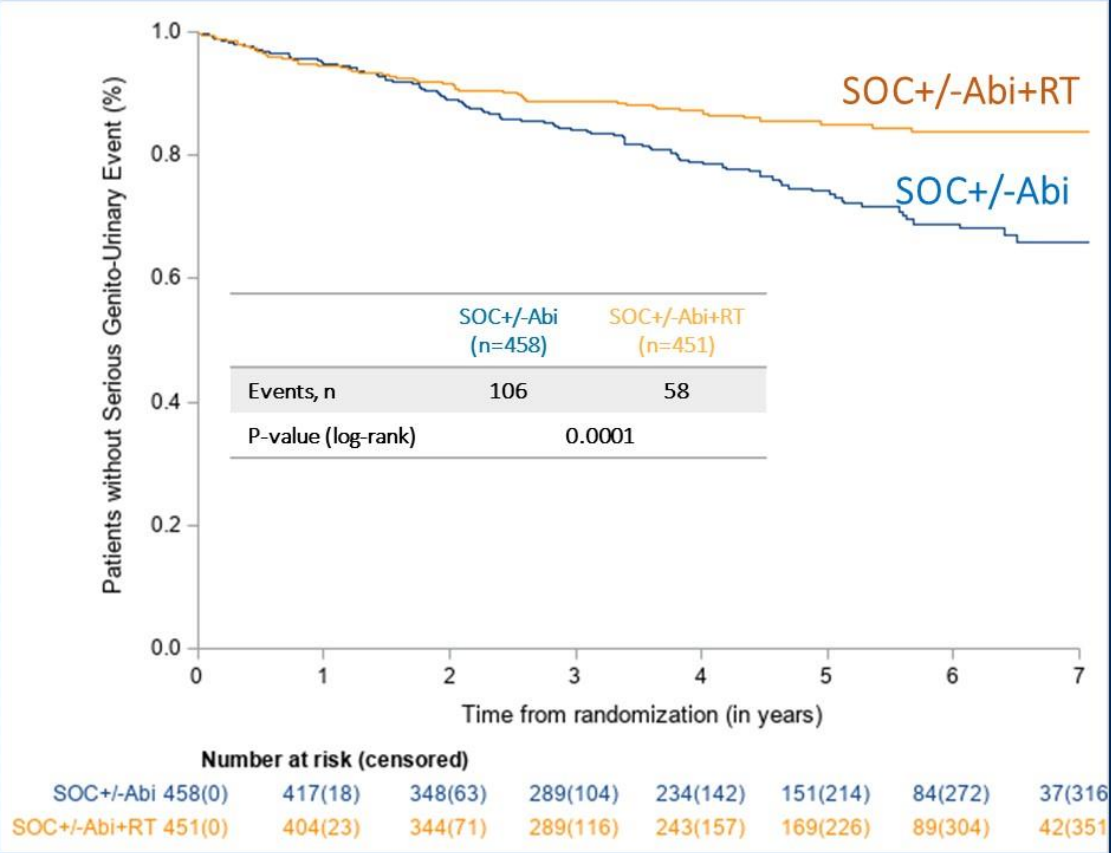
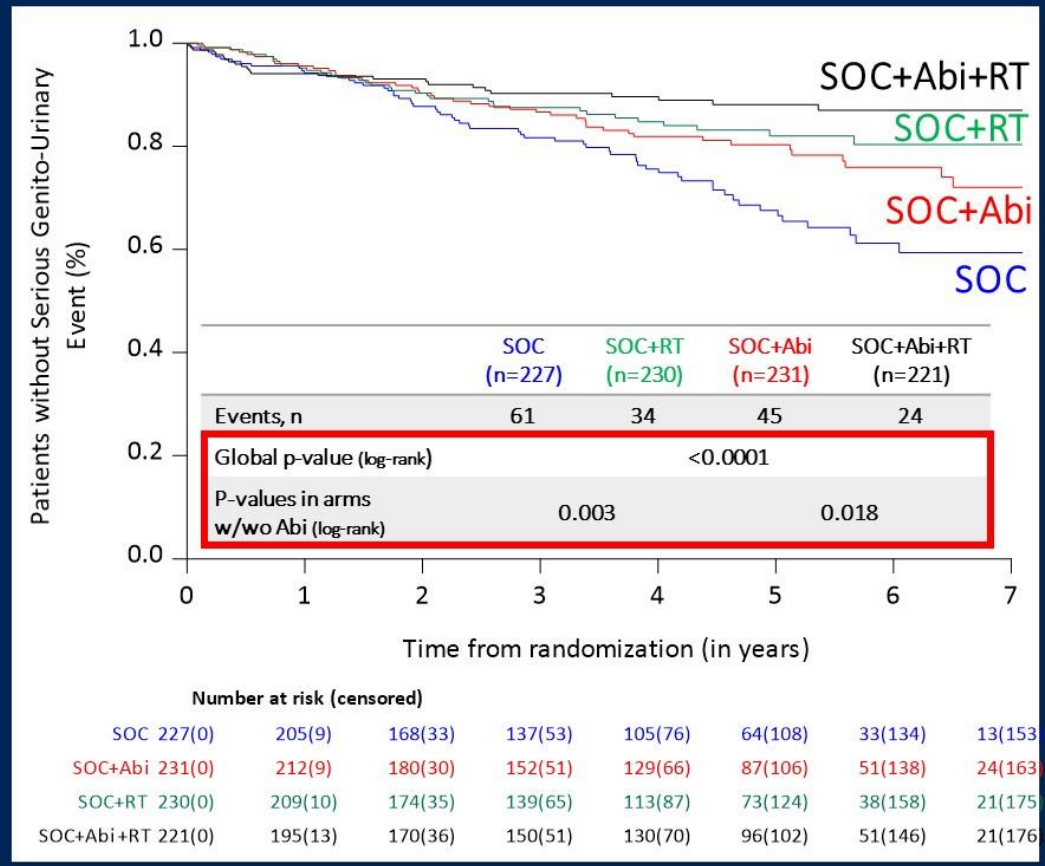
Bossi. ASCO 2023 #LBA5000

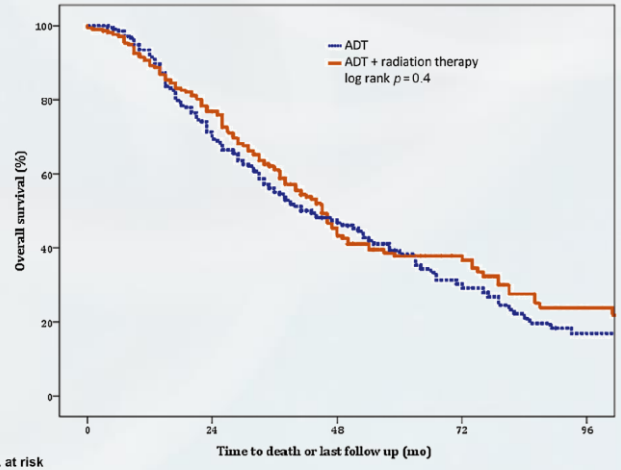
Time to Serious Genito-Urinary events (overall pop.)





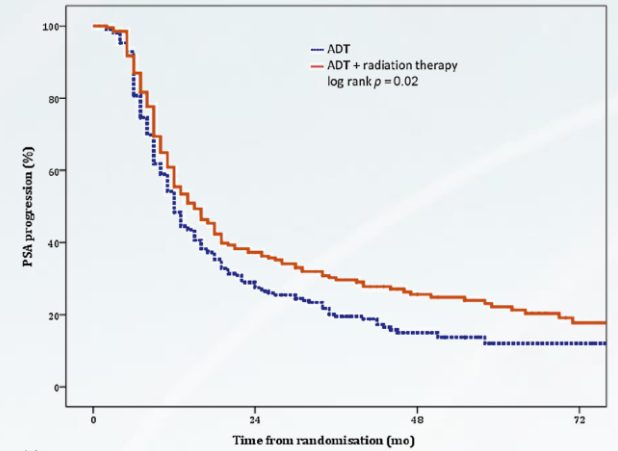
HORRAD

No datos según volumen



No. at risk

ADT	216	145	65	27	11
ADT + radiation therapy	215	161	61	33	13

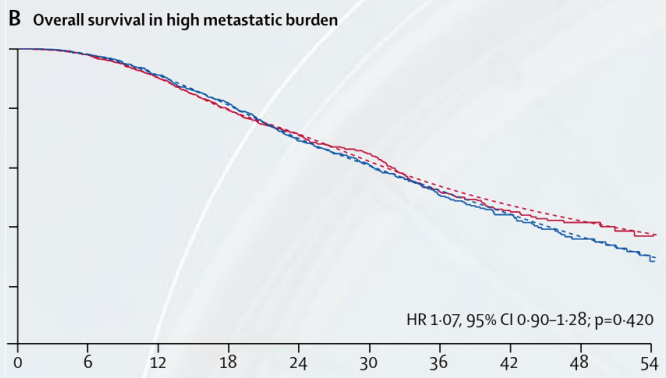


No. at risk

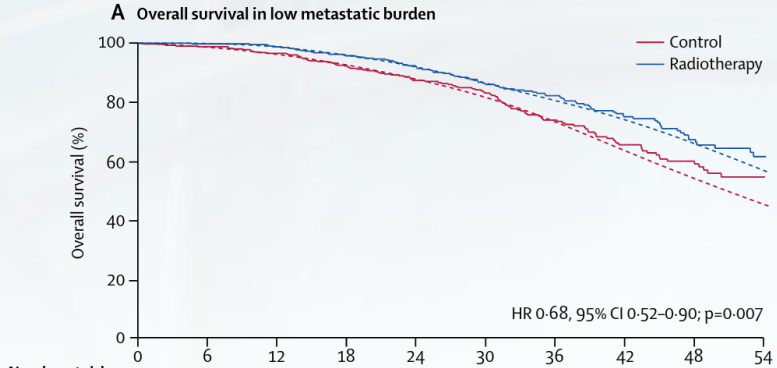
ADT	214	56	14	5
ADT + radiation therapy	210	72	32	13

Boeve. Eur Urol 2019;75:410-8

STAMPEDE (H)



567	(11)	547	(42)	500	(58)	428	(41)	312	(27)	245	(43)	161	(20)	100	(7)	48	(3)	13
553	(10)	537	(38)	487	(48)	424	(59)	282	(30)	216	(31)	146	(19)	90	(14)	44	(5)	20



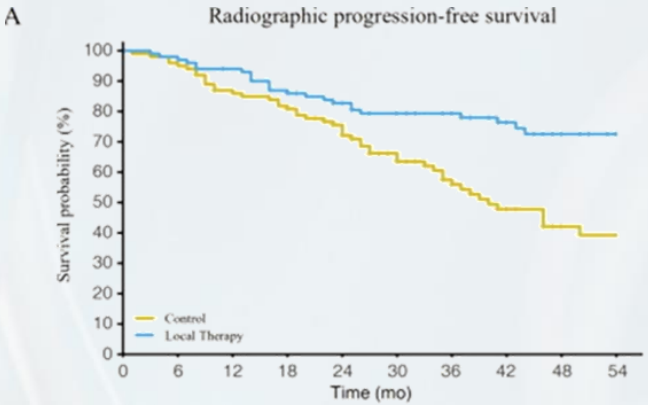
Number at risk (events)

Control	409	(5)	400	(9)	387	(17)	361	(17)	265	(12)	217	(22)	155	(16)	110	(8)	67	(5)	25
Radiotherapy	410	(1)	405	(4)	399	(12)	366	(12)	301	(19)	242	(10)	200	(15)	137	(11)	77	(5)	25

Parker. Lancet 2018;392:2353-66

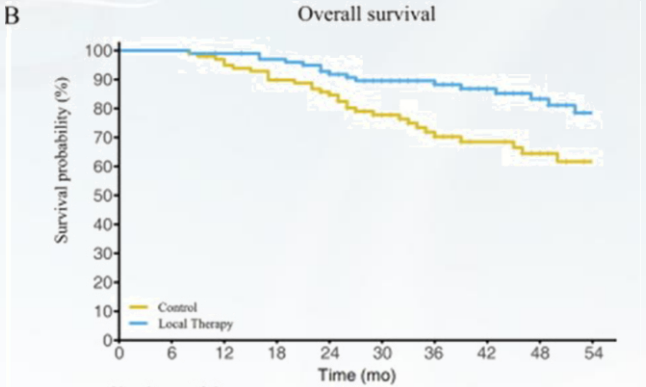
Fase II

Oligometastásico



Number at risk

Control	100	96	85	80	66	49	37	27	18	14
Local therapy	100	98	93	86	76	68	60	46	24	16

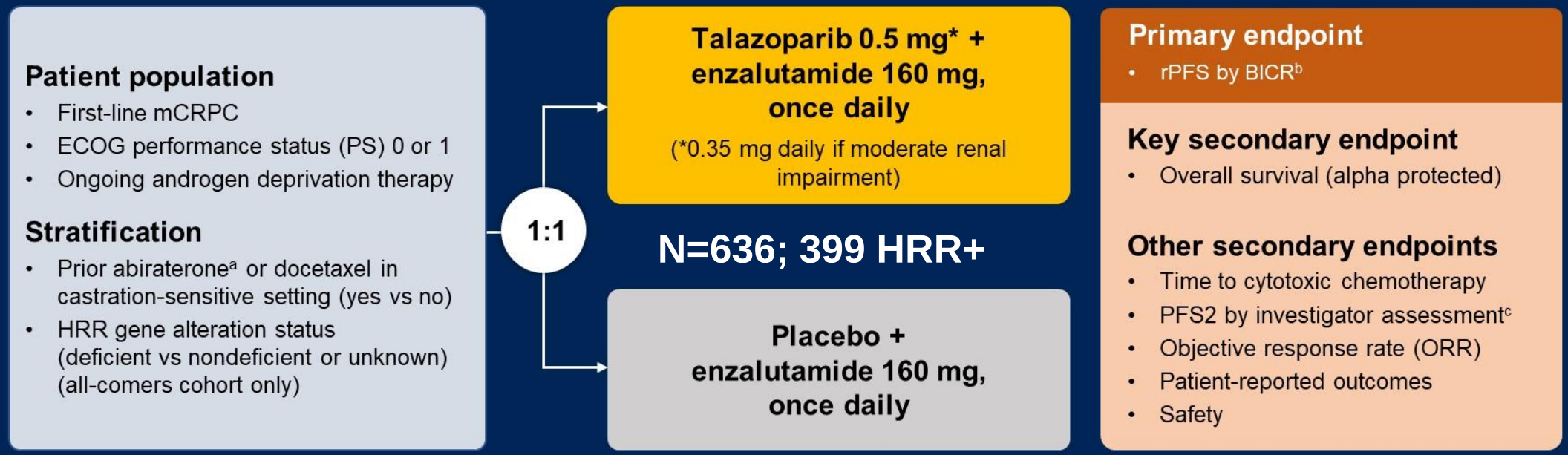


Number at risk

Control	100	100	95	88	81	61	45	36	26	20
Local therapy	100	100	98	95	88	77	68	55	42	23

Dai. Eur Urol Oncol 2022;5:519-525

TALAPRO-2: A Randomized, Double-blind, Placebo-Controlled Study



Samples prospectively assessed for HRR gene alterations (*BRCA1*, *BRCA2*, *PALB2*, *ATM*, *ATR*, *CHEK2*, *FANCA*, *RAD51C*, *NBN*, *MLH1*, *MRE11A*, *CDK12*) using FoundationOne®CDx and/or FoundationOne®Liquid CDx

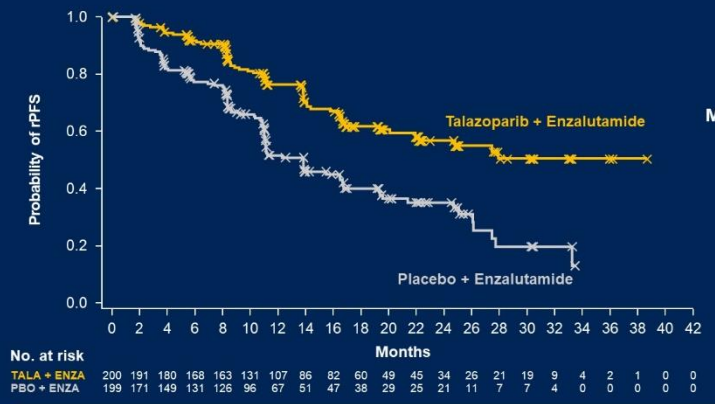
BICR=blinded independent central review; rPFS=radiographic progression-free survival.
[a]One patient in each treatment arm received prior orteronel. [b]Per RECIST version 1.1 (soft tissue disease) and Prostate Cancer Clinical Trials Working Group 3 (bone disease). [c]Time from randomization to the date of documented progression on the first subsequent antineoplastic therapy or death from any cause, whichever occurred first.

Tratamientos previos para CPHS: abiraterona 8%; docetaxel 30%

Fizazi. ASCO 2023. #5004

TALAPRO-2 HRR-Deficient Primary Endpoint: rPFS by BICR

Treatment with talazoparib plus enzalutamide resulted in a 55% reduced risk of progression or death



	TALA + ENZA (N=200)	PBO + ENZA (N=199)
Events, n	66	104
Median (95% CI), months	Not reached (NR) (21.9–NR)	13.8 (11.0–16.7)
HR (95% CI)	0.45 (0.33–0.61); *P* < 0.0001	

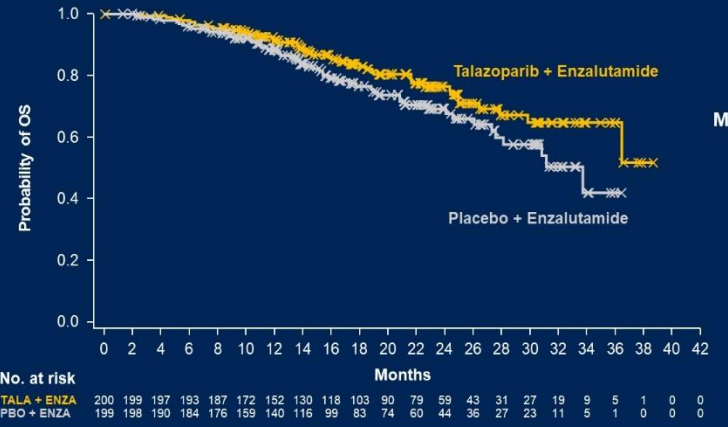
Median follow-up for rPFS was 17.5 and 16.8 months, respectively

A consistent treatment effect was seen for investigator-assessed rPFS: HR 0.48 (95% CI, 0.33–0.67); *P* < 0.0001

Stratified hazard ratios (HRs) and 2-sided *P* values are reported throughout this presentation unless otherwise stated.

TALAPRO-2 HRR-Deficient: Overall Survival (Interim Analysis)

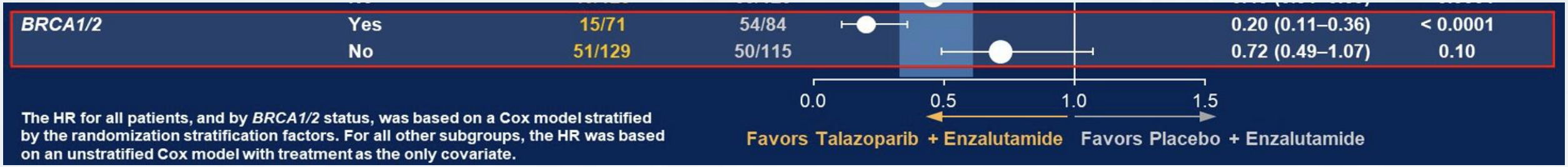
Overall survival data are immature (24% maturity overall)



	TALA + ENZA (N=200)	PBO + ENZA (N=199)
Events, n	43	53
Median (95% CI), months	NR (36.4–NR)	33.7 (27.6–NR)
HR (95% CI)	HR 0.69 (95% CI, 0.46–1.03) *P* = 0.068	

*BRCA*m HR 0.61 (95% CI, 0.31–1.23; *P* = 0.16)
non-*BRCA*m HR 0.71 (95% CI, 0.43–1.18; *P* = 0.18)

18 patients in the control arm and 3 patients in the talazoparib arm subsequently received olaparib



The HR for all patients, and by *BRCA1/2* status, was based on a Cox model stratified by the randomization stratification factors. For all other subgroups, the HR was based on an unstratified Cox model with treatment as the only covariate.

Mejoría en progresión BQ, estado de salud y en tiempo a QMT y PFS-2

Tasa de respuestas: 67 vs 40%; completas 38 vs 18%

Toxicidad grado 3-4: 66 vs 37%

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PROpel: Phase III trial design

Patient population
- 1L mCRPC
- **Asymptomatic, mildly symptomatic, symptomatic**
- No prior abiraterone
- **Other NHAs allowed if stopped ≥12 months prior to enrollment**
- ECOG 0–1

Stratification factors
- Site of distant metastases: bone only vs visceral vs other
- Prior taxane at mHSPC: yes vs no

1:1

Abiraterone 1000 mg qd* + olaparib 300 mg bid n=399
Full dose of abiraterone and olaparib

Abiraterone 1000 mg qd* + placebo n=397
Full dose of abiraterone

Primary endpoint
- rPFS by investigator assessment (sensitivity analysis by blinded independent central review)

Key secondary endpoint
- OS

Additional preplanned analyses:
- TFST
- PFS2
- HRQoL
- HRRm status (by tissue and ctDNA after randomization and before primary analysis; see supplement)
- Safety and tolerability

Analysis timeline:
- **DCO1: 30 July 2021** rPFS (primary)
- **DCO2: 14 March 2022** OS (interim)
- **DCO3: 12 October 2022** OS (final pre-specified) *current dataset*

MAGNITUDE Study Design

Patient eligibility
- L1 mCRPC
  - ≤4 months prior AAP allowed for mCRPC
- ECOG PS 0 or 1
- BPI-SF worst pain score ≤3

Stratifications
- Prior taxane-based chemotherapy for mCSPC
- Prior ARi for nmCRPC or mCSPC
- Prior AAP for L1 mCRPC
- HRR+ cohort only:
  - *BRCA1/2* vs other HRR gene alterations

Prescreening for BM status

HRR+ panel: *ATM* ***BRCA1*** ***BRCA2*** *BRIP1* *CDK12* *CHEK2* *FANCA* *HDAC2* *PALB2*

1:1 randomization

NIRA + AAP N = 212
- *BRCA1/2* n = 113
- Other HRR n = 99

PBO + AAP N = 211
- *BRCA1/2* n = 112
- Other HRR n = 99

IA2 assessments

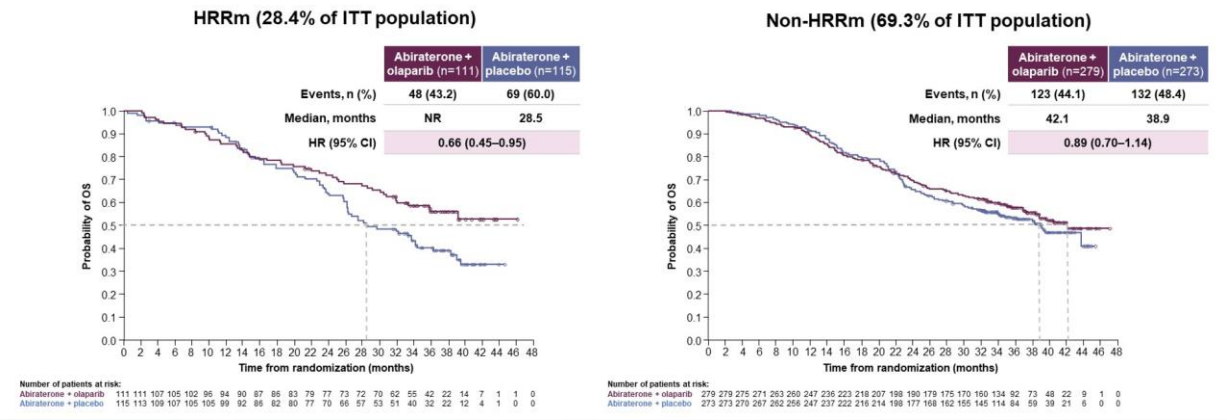
Primary endpoint[a]
- rPFS by central review

Secondary endpoints[b]
- TCC
- TSP
- OS

Other endpoints
- TTPP
- TTPI

PROpel: OS in HRRm and non-HRRm subgroups (DCO3)

A trend towards OS benefit was observed across HRRm and non-HRRm subgroups



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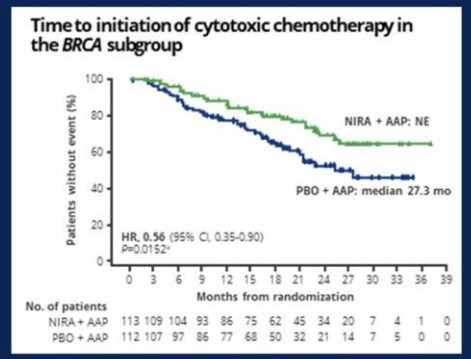
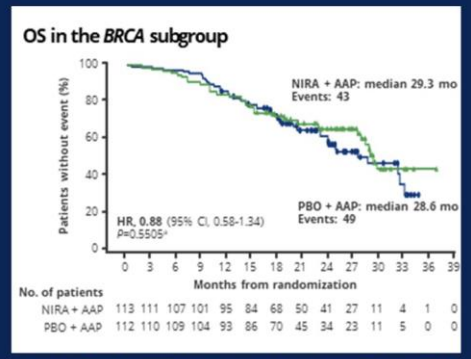
MAGNITUDE BRCA Patients: NIRA + AAP Delayed the Time to Chemotherapy with a Trend in Overall Survival



- A clinically meaningful improvement in time to initiation of cytotoxic chemotherapy was observed in the niraparib + AAP group compared with the placebo + AAP group
- Substantially more BRCA patients in the PBO + AAP arm (22) received subsequent PARPi with or without chemo treatment relative to the NIRA + AAP arm (1)



- IPCW analysis of OS showed a 46% reduction in the risk of death with niraparib + AAP compared with placebo + AAP (HR, 0.54 [95% CI, 0.33-0.90])
- The OS stratified analysis HR was 0.88 (95% CI, 0.58-1.34), with a trend toward improvement in OS observed in the IPCW analysis (HR=0.54 [95% CI, 0.33-0.90])

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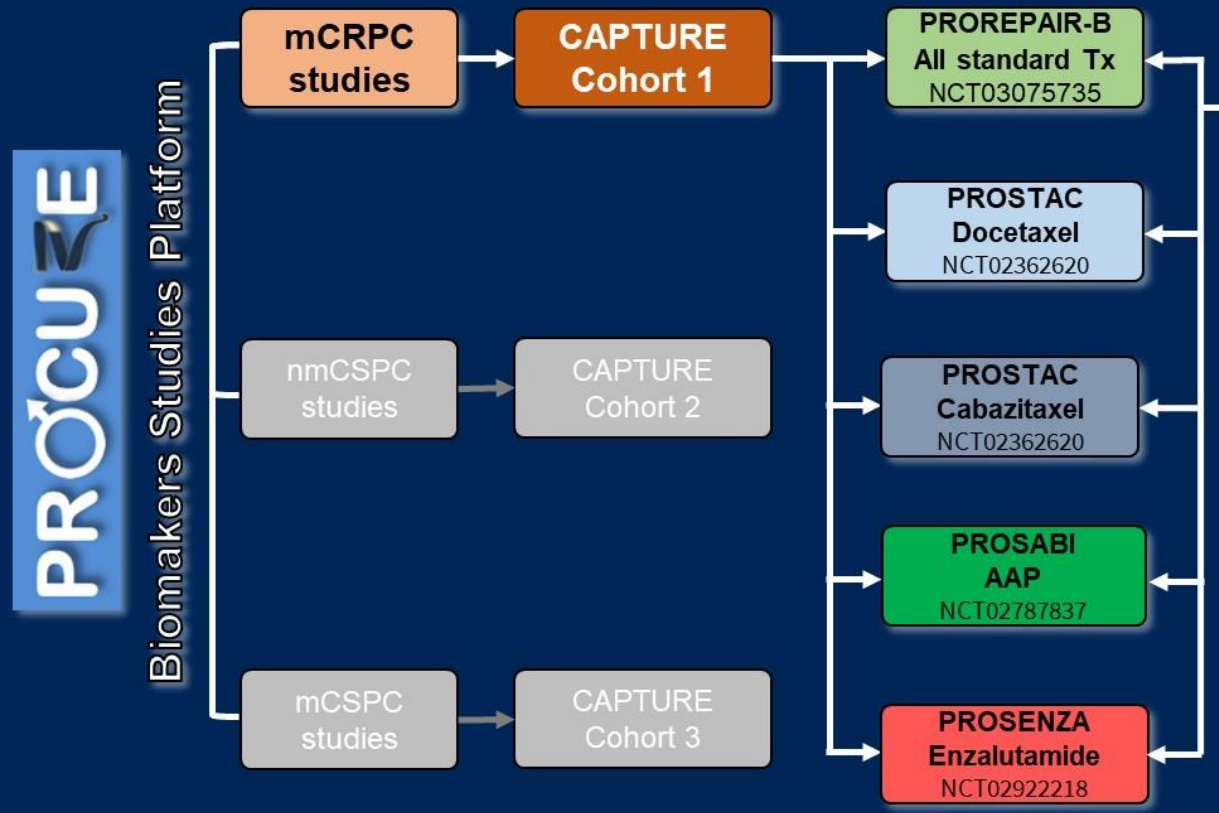
rPFS + en población ITT

rPFS + en HRR+

CAPTURE: Study design



Patient eligibility

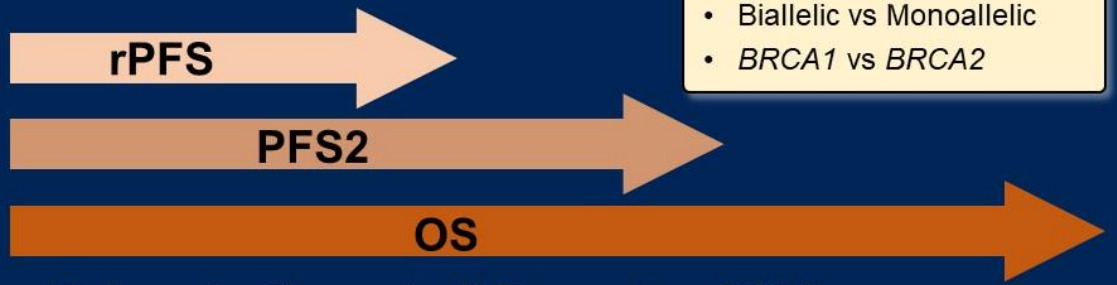
- Enrolled prospectively in any PROCURE study at 1L mCRPC
- 1L with standard dose of docetaxel, cabazitaxel, AAP* or enzalutamide
- Availability of a DNA sample for germline variants analysis
- Archived FFPE sample with tumor tissue amenable for molecular analysis according to central pathologist
- No Prior PARPi or Alkylating agents
- ECOG 0-2
- Adequate Bone Marrow function

Gene Panel

ATM	***FANCA***
BRCA1	***HDAC2***
BRCA2	***PALB2***
BRIP1	***RAD51B***
CDK12	***RAD54L***
CHEK2	

Planned analyses groups

- *BRCA1/2* vs non-BRCA
- *BRCA1/2* vs HRR non-BRCA
- 1L NHT vs Taxane
- Germline vs Somatic
- Biallelic vs Monoallelic
- *BRCA1* vs *BRCA2*

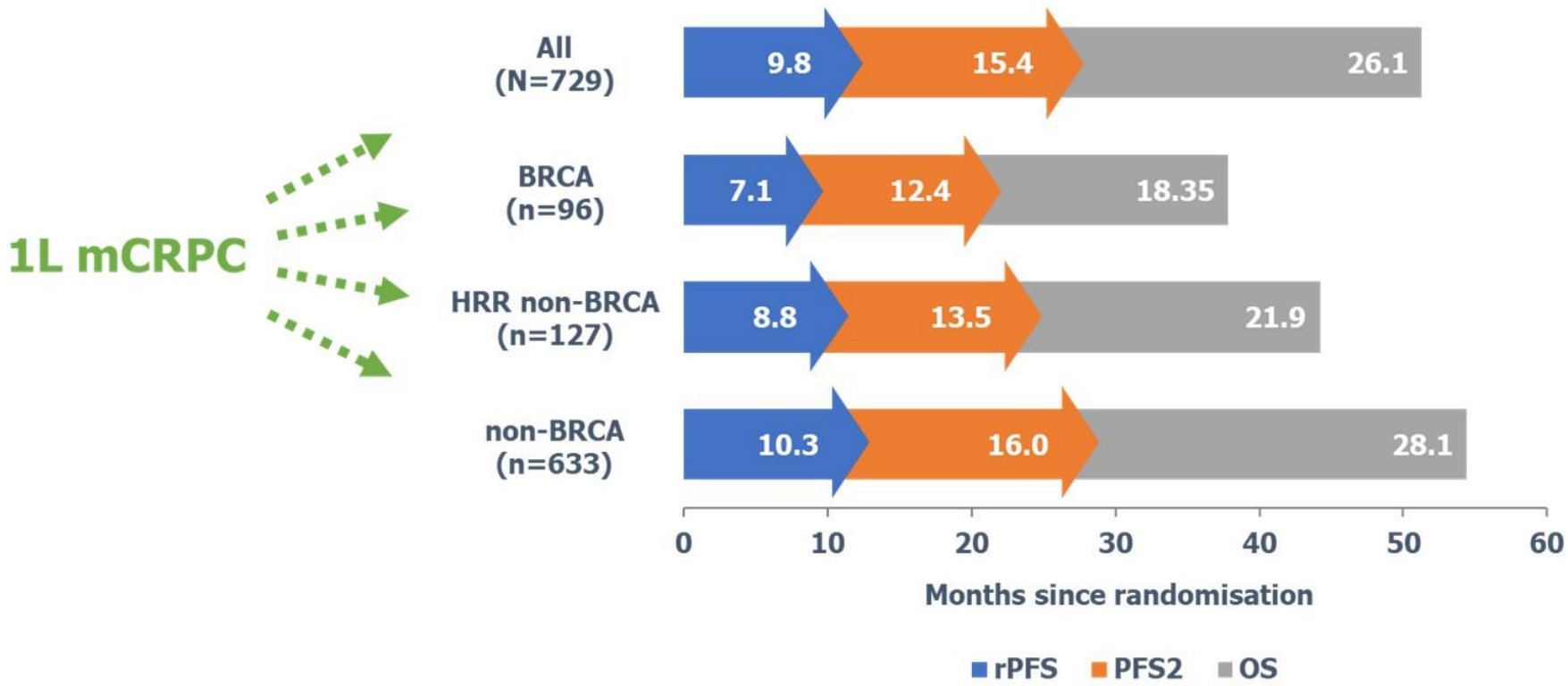


Data collection cut-off December 2021

FFPE: Formalin-Fixed Paraffin Embedded

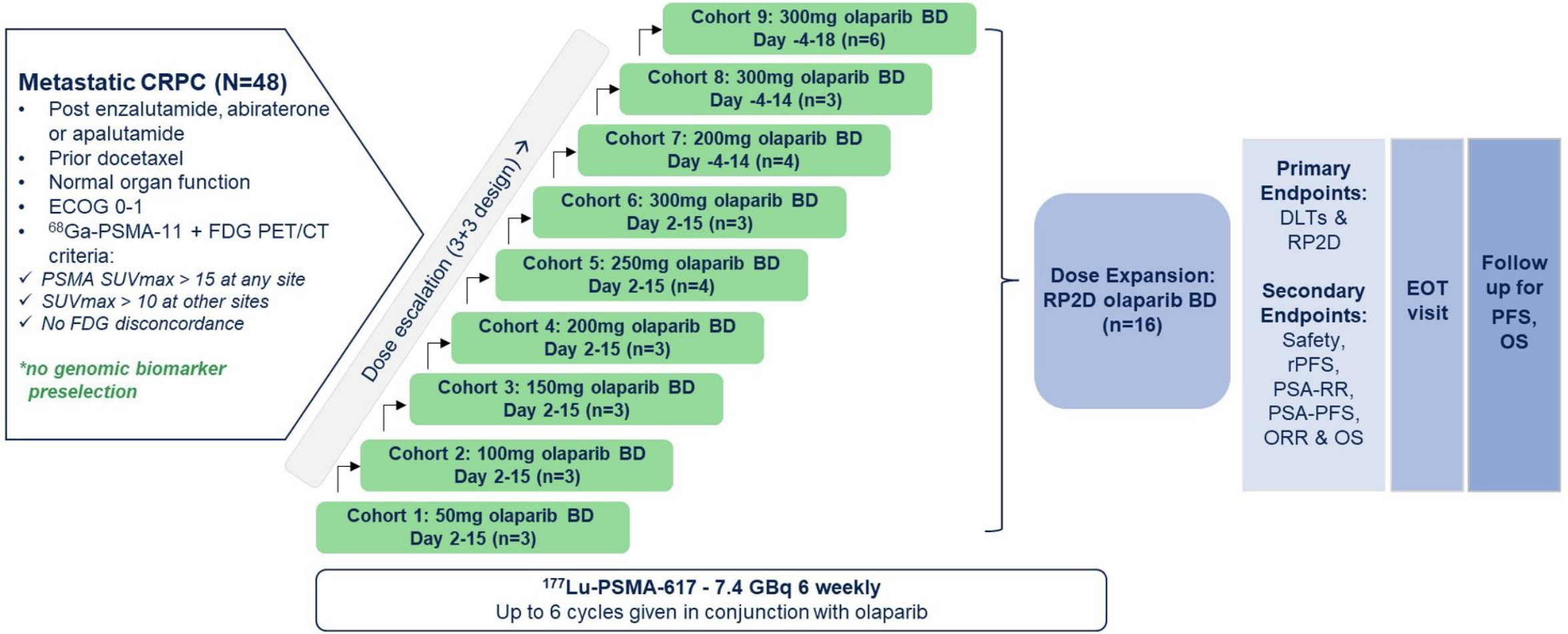
**Abiraterone Acetate plus prednisone*

Summary of outcomes by subgroup



NOTE: naïve, non-adjusted, median survival outcomes

LuPARP: Phase 1 Trial Schema



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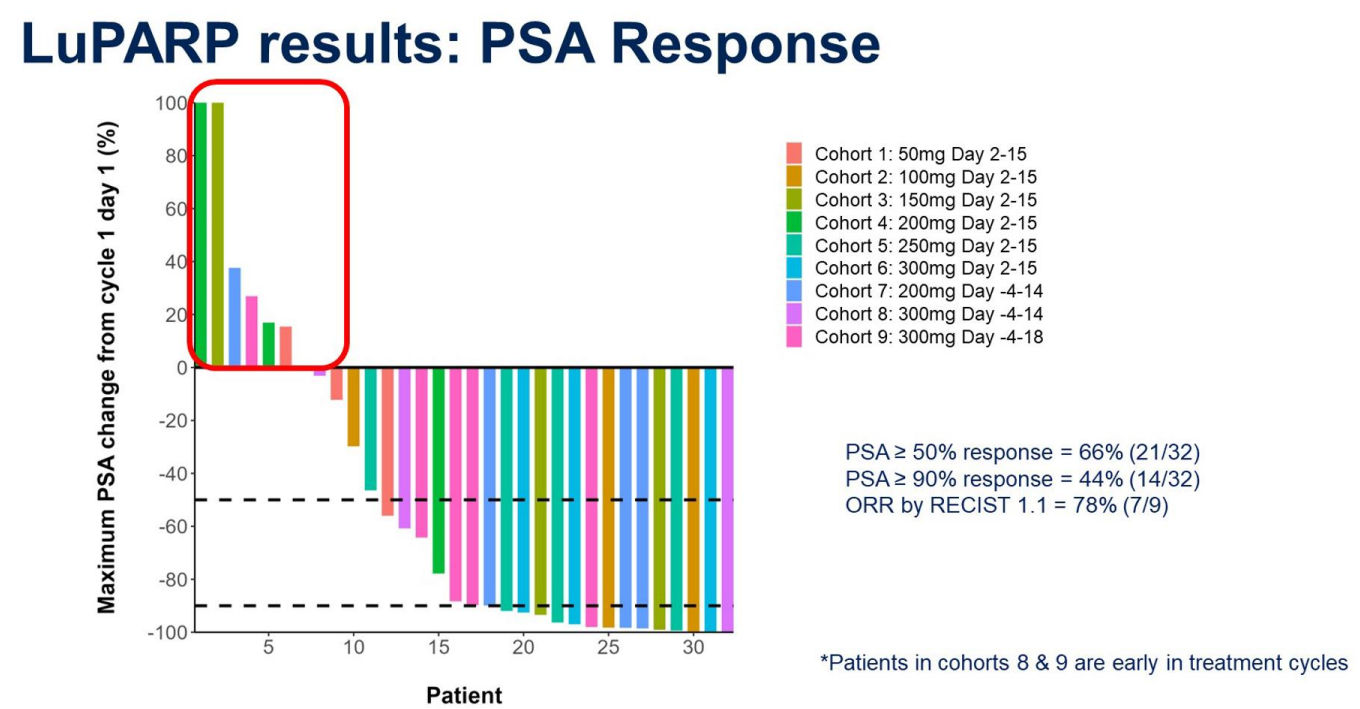
No DLTs entre los diferentes niveles de dosis

No AEs grado 4



PSA RR: 66%

PSA≥90% response: 44% (most notable at higher dose levels)

RR 78%

RP2D: 7.4 Gb LuPSMA + olaparib 300 mg BD days -4 to 18 of each 6-w cycles

Sandhu. ASCO 2023 #5005

VEJIGA

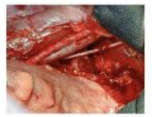
LDN extendida

N=591

S-1011 Study Design

T2-T4a Urothelial ca
Radical Cystectomy
Neoadjuvant Ctx allowed
N1,2 allowed

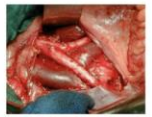
RANDOMIZE



Standard PLND
External/internal iliac, obturator nodes

pT3-4N0, pTanyN+
Adjuvant Chemotherapy

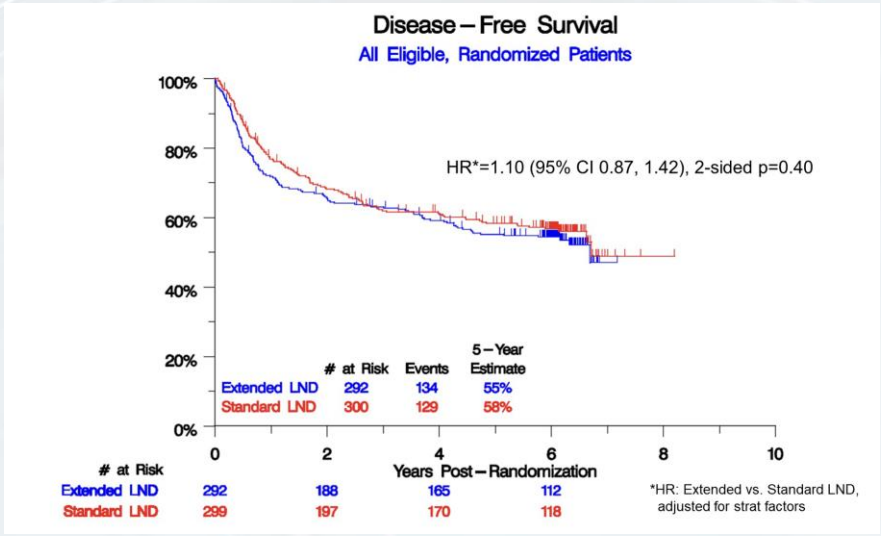
Extended LND
Standard + CI, pre sacral, distal IVC and aorta

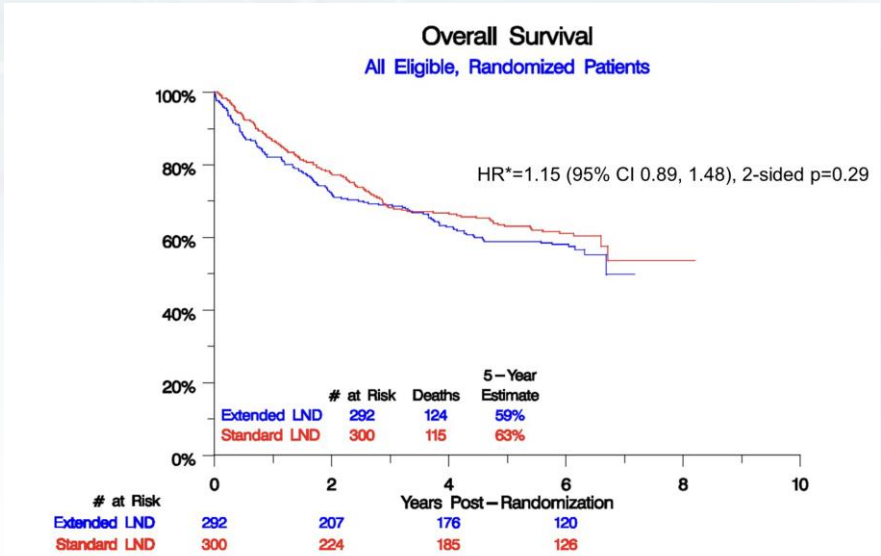


Stratification factors:
NAC – cisplatin v carboplatin v other v none
cT stage – T2 v T3/4a
PS – 0-1 v 2

- Assume 55% 3-yr DFS in standard LND group (based on review of 8 surgical series 2000-2009 including 7957 patients)
- 85% power to detect 10-12% improvement in 3-yr DFS with extended LND, clinically significant (HR=0.72)
- Sample size of 564 eligible patients (282 per arm)

30-day mortality 9 (1.5%); SLND - 1 (0.3%) vs ELND - 8 (2.7%)
90-day mortality 26 (4.4%); SLND - 9 (3%) vs ELND - 16 (5.5%)





Lerner ASCO 2023 #4508

VESPER: OS a 5 años

N=500 (88% NA)

Trial design (1)

Chemotherapy

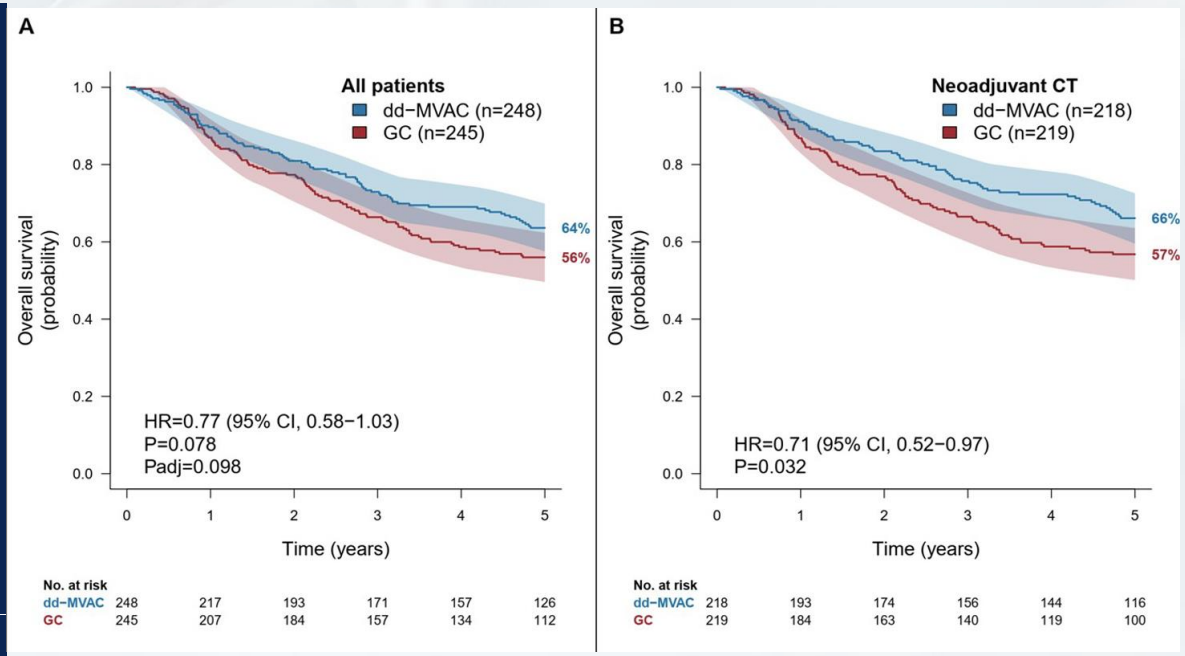
- **4 cycles of GC** — Gemcitabine 1250 mg/m² d1 and d8; Cisplatin 70 mg/m² d1 — **every 3 weeks**
- **6 cycles of ddMVAC** — Methotrexate 30 mg/m² d1; Vinblastine 3 mg/m² d2; Doxorubicin 30 mg/m² d2; Cisplatin 70 mg/m² d2; ***+ G-CSF support from d3 to d9*** — **every 2 weeks**

Inclusion criteria

- Pure or mixed urothelial bladder cancer *(neuroendocrine excluded)*
- ECOG PS < 2 and all criteria for cisplatin eligibility
- Written informed consent

AND

- ≥ T2, N0 *(LN ≤ 10 mm on CT scan)*, M0 (Neoadjuvant CT)
- > pT2 or pN+ and M0 (Adjuvant CT)



Subgrupo neoadyuvante

60% recibieron 6 ciclos de ddMVAC

Cistectomía radical en >90%

Más astenia, anemia y tox GI en ddMVAC

Pfister. ASCO 2023 #LBA4507

IMVIGOR-130: la respuesta inicial a la inducción no impacta en la OS

Trial design

- Locally advanced or metastatic UC
- No prior systemic therapy for mUC
- ECOG PS 0-2
- Eligible for 1L plt-based chemo

R[a] 1:1:1

- **Arm A: Atezo + plt/gem**
- Arm B: Atezo monotherapy
- **Arm C: Placebo + plt/gem**

Co-primary efficacy endpoints

- PFS and OS (Arm A vs C ITT)
- OS (Arm B vs C ITT and PD-L1 IC2/3, hierarchical approach)

Post-hoc analysis

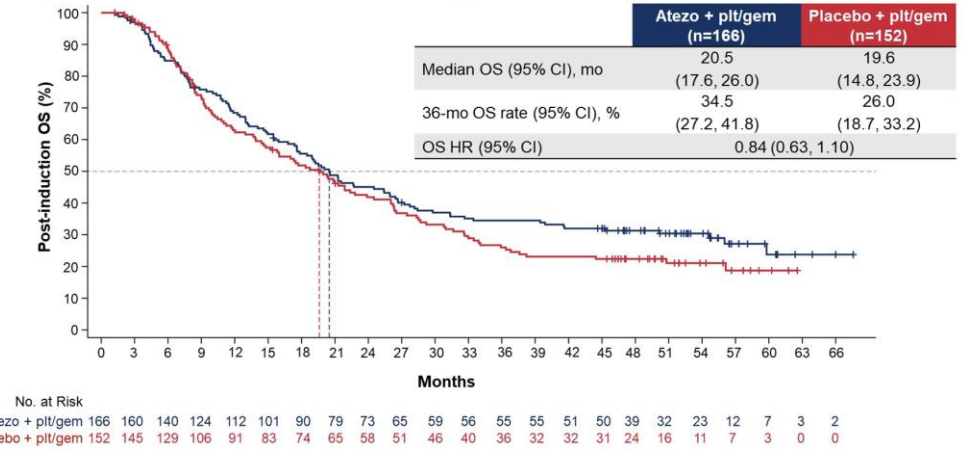
1) No PD subgroup (CR, PR or SD without PD at/before Week 18): *Evaluate post induction OS[b] (since week 18)*

Induction period
Atezo/placebo + 4-6 cycles of chemotherapy

Maintenance period
≥1 dose atezo/placebo monotherapy

2) PD subgroup (PD at/before week 18): *Evaluate OS[b] (since PD)*

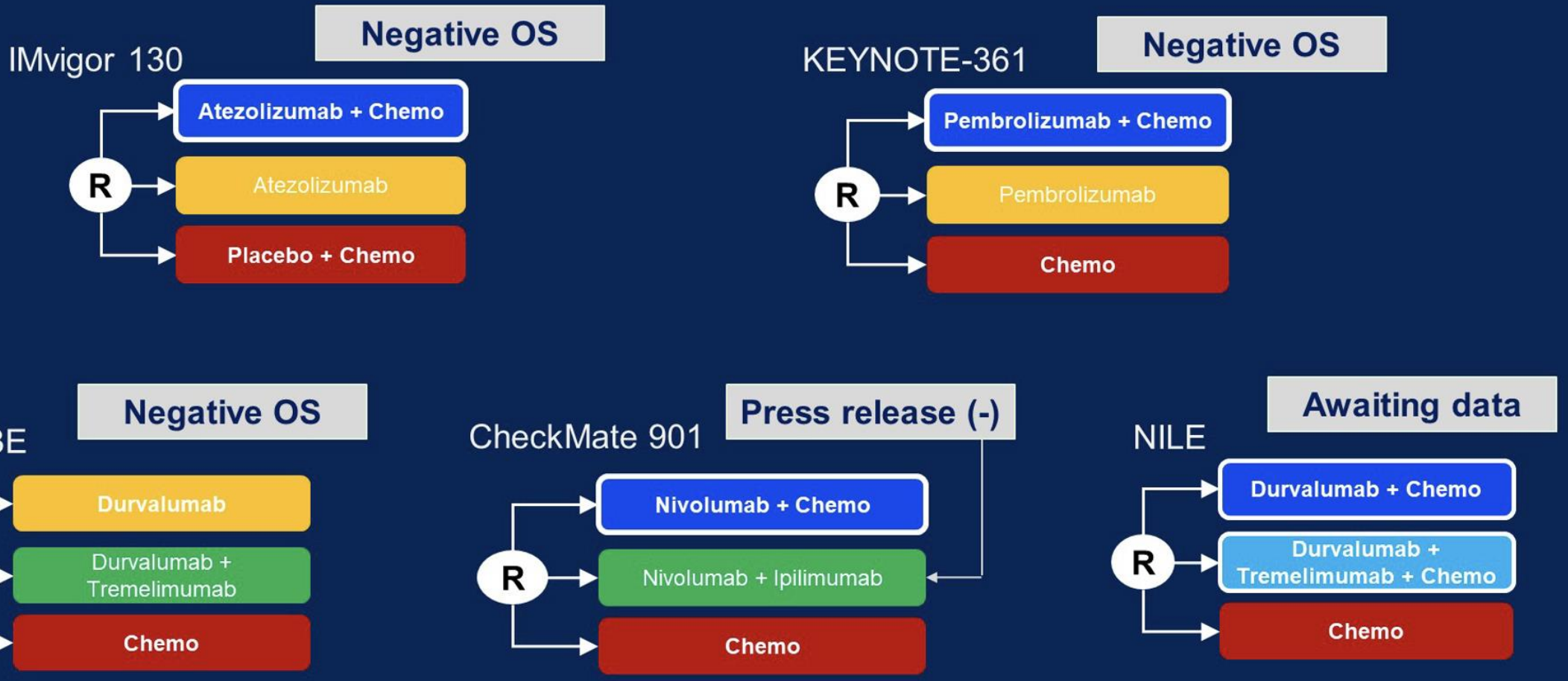
Post-induction (week 18) OS in patients with no PD during induction: OS during maintenance



	Atezo + plt/gem (n=166)	Placebo + plt/gem (n=152)
Median OS (95% CI), mo	20.5 (17.6, 26.0)	19.6 (14.8, 23.9)
36-mo OS rate (95% CI), %	34.5 (27.2, 41.8)	26.0 (18.7, 33.2)
OS HR (95% CI)	0.84 (0.63, 1.10)	

Grande. ASCO 2023 #4503

COMBINATIONS in 1L treatment in mUC



Apolo, AB. Oral abstract discussion, GU ASCO 2023

THOR

Cohort 1

Key eligibility criteria

- Age ≥18 years
- Metastatic or unresectable UC
- Confirmed disease progression
- Prior tx with anti–PD-(L)1
- 1-2 lines of systemic tx
- Select *FGFR3/2alt* (mutation/fusion)[a]
- ECOG PS 0-2

1:1
N=266[b]

R

Erdafitinib
(n=136)
Once-daily erdafitinib 8 mg with pharmacodynamically guided uptitration to 9 mg

Chemotherapy of Choice
(n=130)
docetaxel or vinflunine once every 3 weeks

Stratification factors: region (North America vs European Union vs rest of world), ECOG PS (0 or 1 vs 2), and disease distribution (presence vs absence of visceral [lung, liver, or bone] metastases)

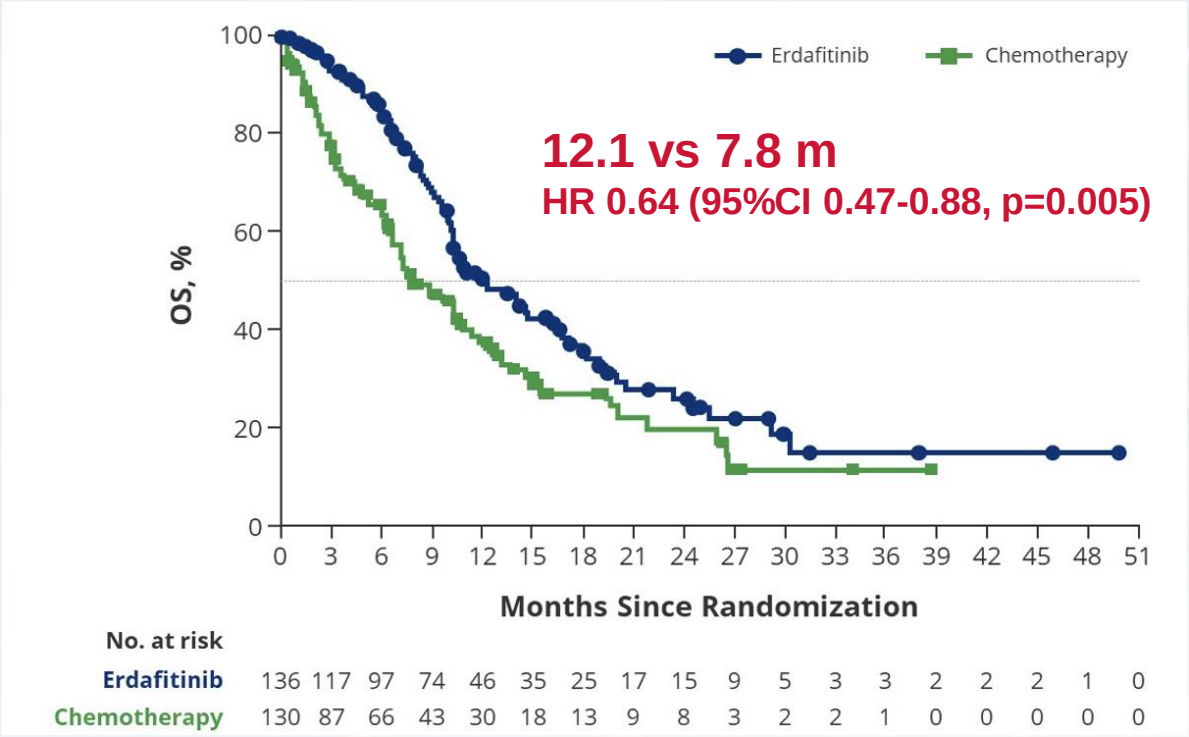
Primary end point:
- OS

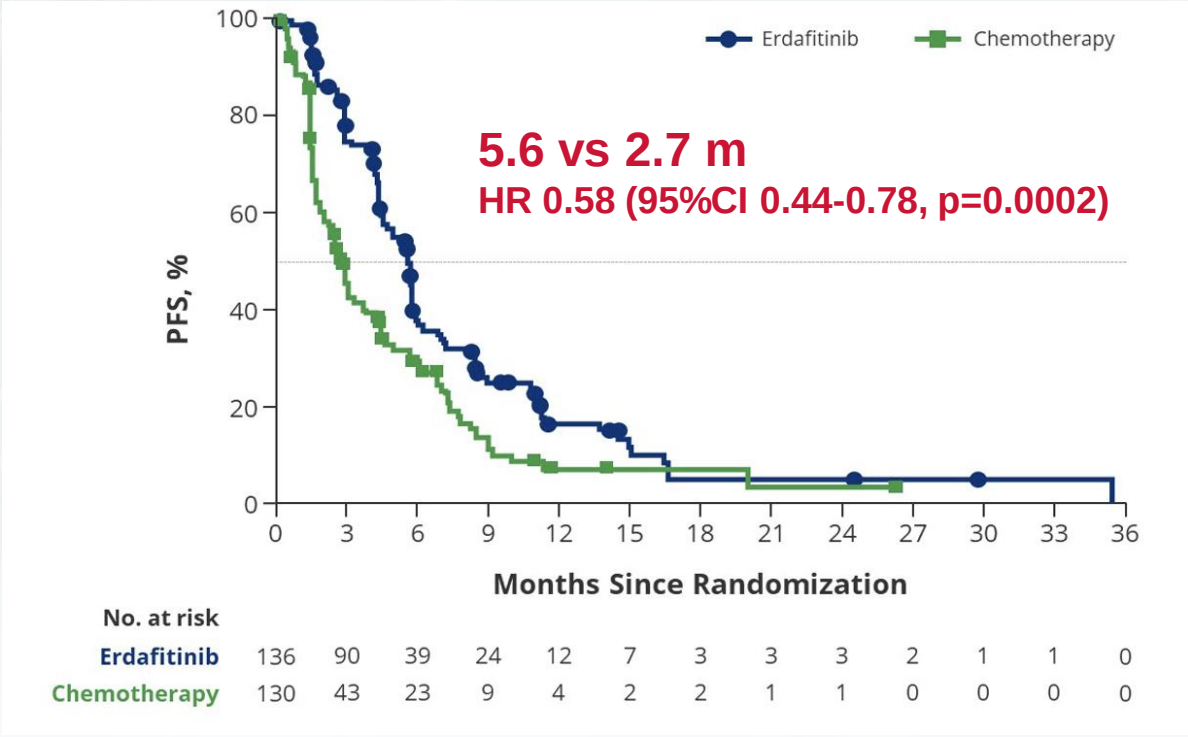
Key secondary end points:
- PFS
- ORR
- Safety

NCT03390504

Characteristic	Erdafitinib (n=136)	Chemotherapy (n=130)
ECOG PS 0-1, n (%)	124 (91.2)	117 (90)
Primary tumor upper tract, n (%)	41 (30.1)	48 (36.9)
PD-L1 low (CPS <10), n (%)	89 (92.7)[a]	68 (86.1)[a]
FGFRalt, n (%)[b]	(n=135)	(n=129)
Mutations	108 (79.4)	107 (82.3)
Fusions	25 (18.4)	19 (14.6)
Mutations and fusions	2 (1.5)	3 (2.3)
Prior lines of systemic therapy[c]		
1 line	45 (33.1)	33 (25.4)
2 lines	90 (66.2)	97 (74.6)

THOR





RR: 45.6 vs 11.5%

Loriot ASCO 2023 #LBA4610

THOR

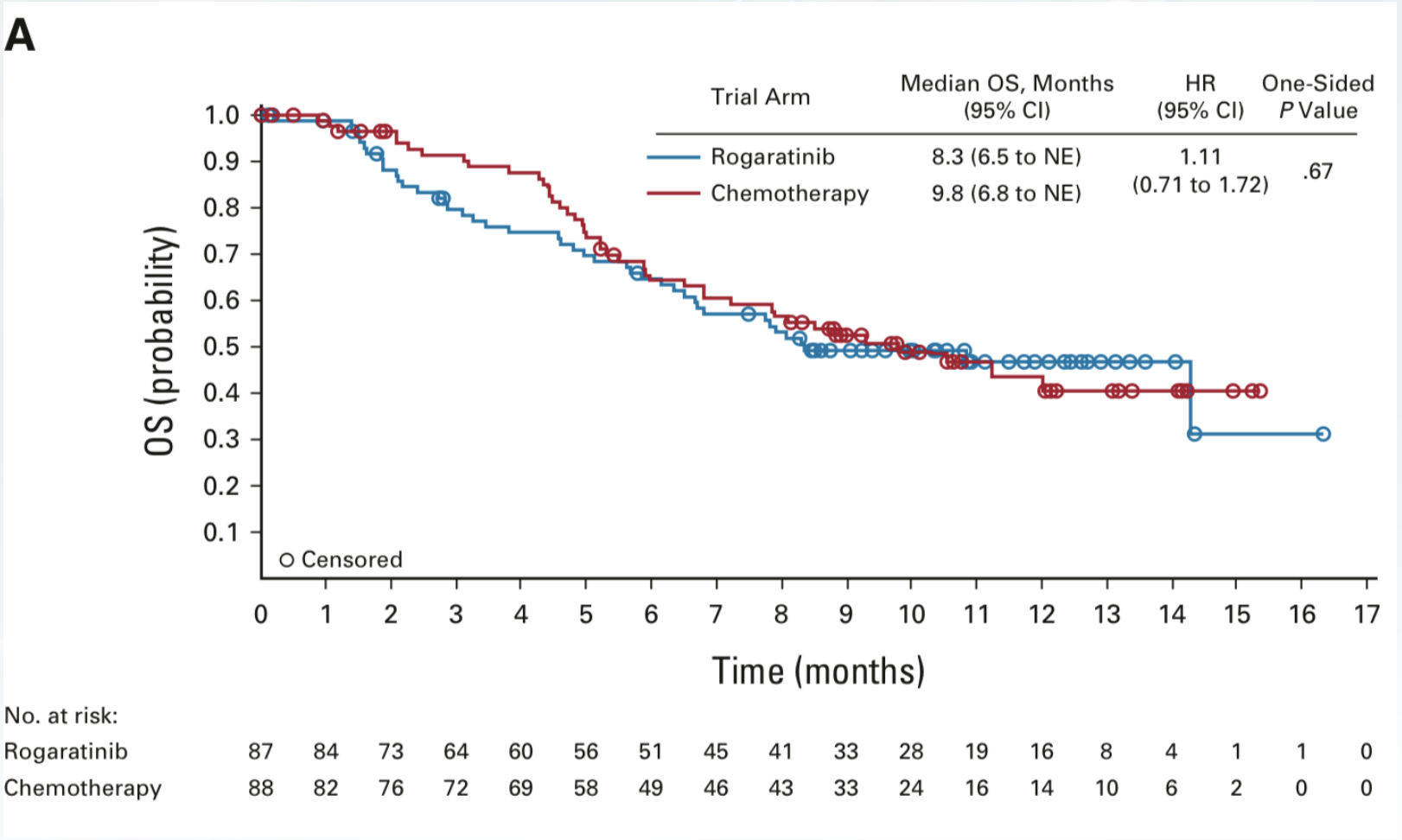
Patients with AEs, n (%)[a]	Erdafitinib (n=135)	
	Any grade	Grade 3-4
≥1 treatment-related AE	131 (97.0)	62 (45.9)
Hyperphosphatemia	106 (78.5)	7 (5.2)
Diarrhea	74 (54.8)	4 (3.0)
Stomatitis	62 (45.9)	11 (8.1)
Dry mouth	52 (38.5)	0
PPE syndrome	41 (30.4)	13 (9.6)
Onycholysis	31 (23.0)	8 (5.9)
Patients who discontinued study treatment, n (%)		
Discontinuation due to treatment-related AEs	11 (8.1%)[b]	

- **In the erdafitinib group:**
  - 18 patients (13.3%) had treatment-related serious AEs
  - 1 treatment-related death occurred[c]
  - AEs with erdafitinib were mostly manageable with dose modifications and supportive care
- **In the chemotherapy group:**
  - 27 patients (24.1%) had treatment-related serious AEs
  - 6 treatment-related deaths occurred[d]

Patients with AEs, n (%)[e]	Chemotherapy (n=112)	
	Any grade	Grade 3-4
≥1 treatment-related AE	97 (86.6)	52 (46.4)
Anemia	31 (27.7)	7 (6.3)
Alopecia	24 (21.4)	0
Nausea	22 (19.6)	2 (1.8)
Neutropenia	21 (18.8)	15 (13.4)
Leukopenia	13 (11.6)	9 (8.0)
Febrile neutropenia	9 (8.0)	10 (8.9)
Patients who discontinued study treatment, n (%)		
Discontinuation due to treatment-related AEs	15 (13.4)[f]	

Patients with AEs of interest, n (%)	Erdafitinib (n=135)		Chemotherapy (n=112)	
	Any grade	Grade 3-4	Any grade	Grade 3-4
Nail disorders[a]	90 (66.7)	15 (11.1)	6 (5.4)	0
Skin disorders[b]	74 (54.8)	16 (11.9)	14 (12.5)	0
Eye disorders (excluding central serous retinopathy)[c]	57 (42.2)	3 (2.2)	6 (5.4)	0
Central serous retinopathy[d]	23 (17.0)	3 (2.2)	0	0

FORT-1: rogaratinib



Sternberg. J Clin Oncol 2022;41:629

THOR, EV-301 y TROPHY: pacientes

	Tracto superior %	Vejiga %	Mets hepáticas %	QMT previa 1-2 %
THOR	30	70	23%	100
EV-301	32	67	32	87
TROPHY-U-01	NR	NR	34	47

Mod de Petrylak ASCO 2023

Loriot ASCO 23; Powles NEJM 2021; Tagawa JCO 2021

EFICACIA: THOR, EV-301 y TROPHY

	OS (m)	PFS (m)	Resp compl %	Resp parc %
THOR	12.1	5.6	6.6	39
EV-301	12.9	5.5	4.9	36
TROPHY-U-01	10.9	5.4	5.3	22

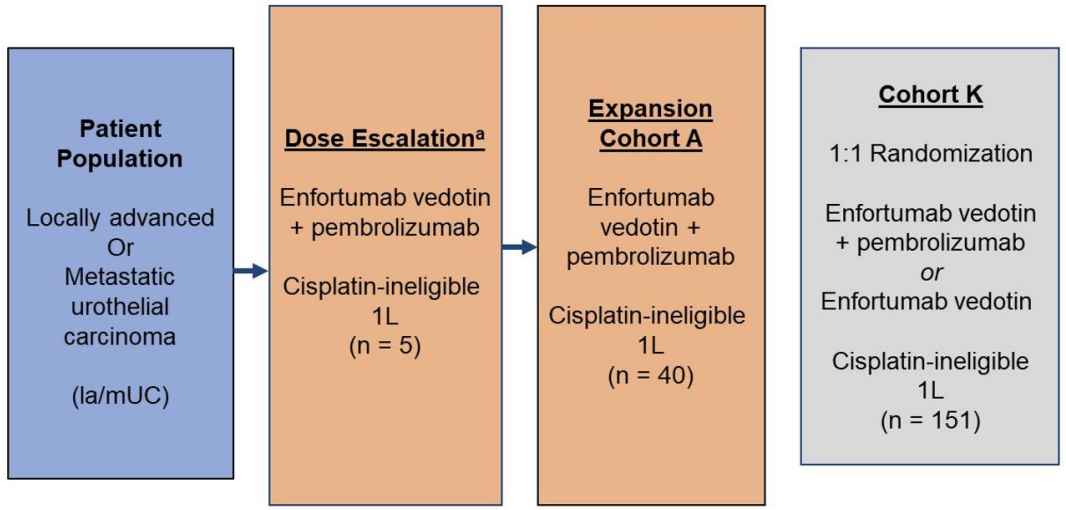
Mod de Petrylak ASCO 2023

Loriot ASCO 23; Powles NEJM 2021; Tagawa JCO 2021

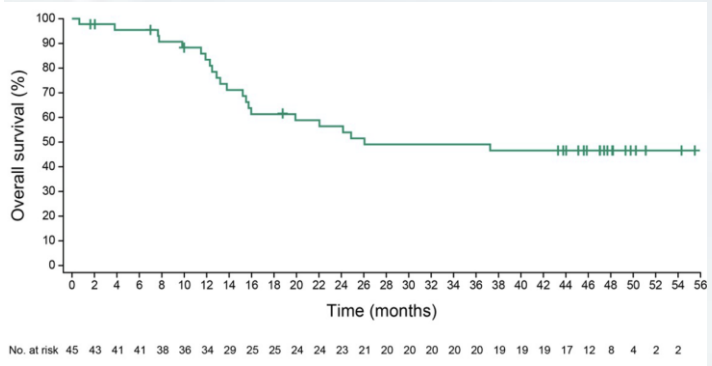
EV-103: seguimiento a largo plazo

Study Design – EV+P Cohorts

EV-103 is an open-label, multiple cohort, phase 1b/2 study



- **Dosing:** EV 1.25 mg/kg IV on Days 1 and 8, and P 200 mg IV on day 1 of every 3-week cycle
- **Primary endpoints:** AEs, lab abnormalities
- **Key secondary endpoints:** confirmed ORR, DOR, DCR, and PFS per RECIST v1.1 by BICR[b] and investigator; OS, plasma/serum PK of EV



	Dose Escalation + Cohort A (N = 45)
	≥ Grade 3[a] n (%)
Overall	29 (64.4)
Lipase increased[b]	8 (17.8)
Rash maculo-papular	5 (11.1)
Fatigue	5 (11.1)
Neutropenia	4 (8.9)
Anemia	4 (8.9)
Hyperglycemia	4 (8.9)
Amylase increased	4 (8.9)
Transaminases increased	3 (6.7)

Razones inelegibilidad

	Dose Escalation + Cohort A (N = 45)
Patient meeting at least one of the following Galsky criteria	44 (97.8%)
CrCL <60 and ≥30 mL/min[a]	25 (55.6)
ECOG PS of 2	6 (13.3)
≥ grade 2 hearing loss	5 (11.1)
CrCL <60 and ≥30 mL/min[a] and ≥ grade 2 hearing loss	5 (11.1)
CrCL <60 and ≥30 mL/min[a] and ECOG PS of 2	2 (4.4)
ECOG PS of 2 and ≥ grade 2 hearing loss	1 (2.2)
Patient considered cisplatin-ineligible by the investigator although not meeting Galsky criteria[b]	1 (2.2)

RR: 73%
OS 26 m

Gupta ASCO 2023 #4505

NORSE

Key eligibility criteria
- Age ≥18 years
- mUC diagnosis
- Ineligible for cisplatin[b]
- Select *FGFR* alterations (mutation/fusion)[c]
- Measurable disease
- No prior systemic therapy for mUC

Patients with any PD-L1 status could be enrolled

1:1
N=89
R

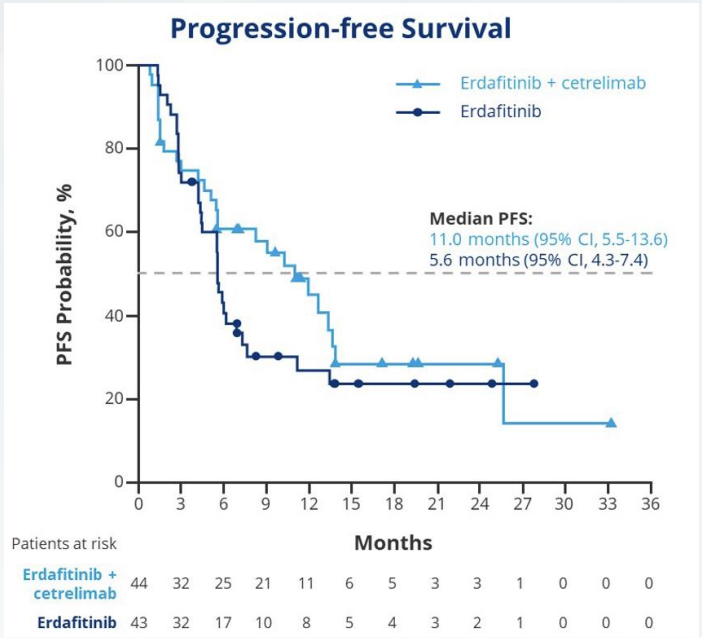
Erdafitinib
(n=44)
Once-daily erdafitinib 8 mg with pharmacodynamically guided uptitration to 9 mg

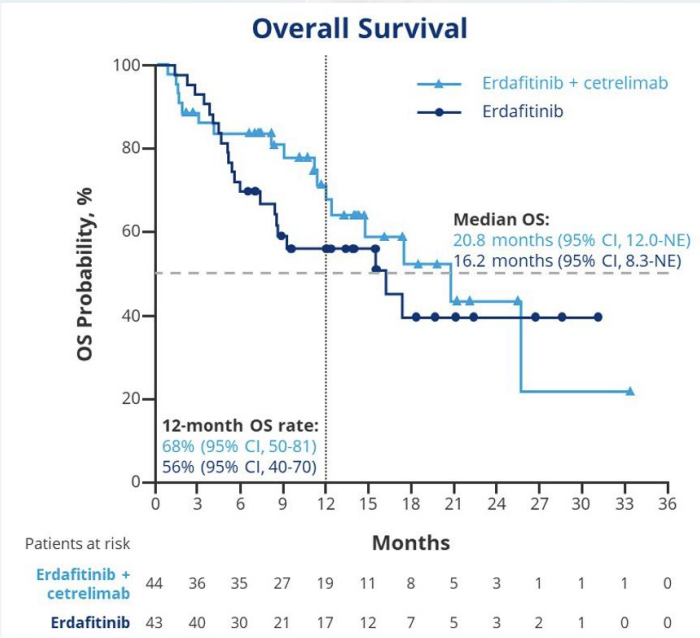
Erdafitinib + cetrelimab[d]
(n=45)
Once-daily erdafitinib 8 mg + cetrelimab

Primary end point
- ORR
- Safety

Secondary end points
- DCR
- DOR
- Time to response
- PFS
- OS

RR: 44 vs 54.5%



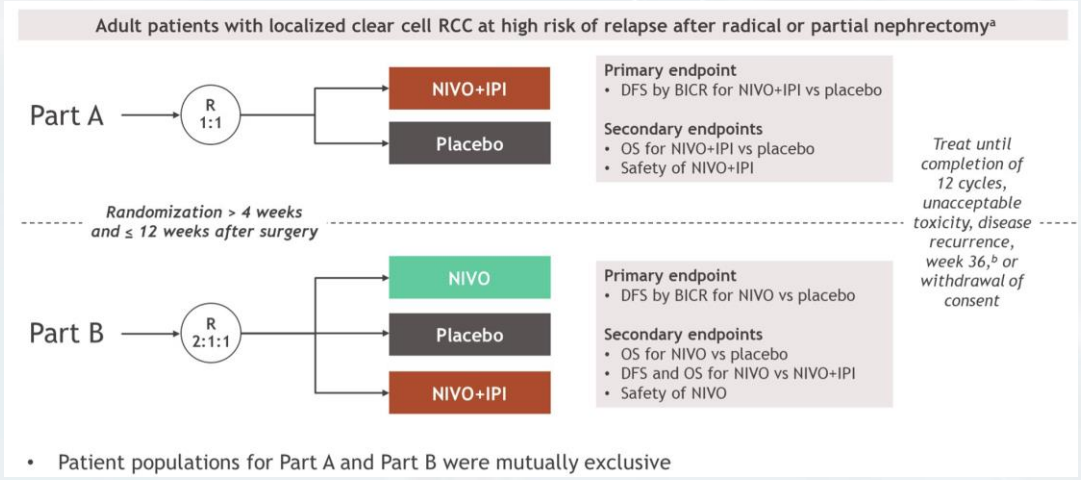


Patients with treatment-related AEs, n (%)[c]	Erdafitinib (N=43)		Erdafitinib + Cetrelimab (N=44)	
	Any grade	Grade 3-4	Any grade	Grade 3-4
≥1 treatment-related AE	41 (95.3)	20 (46.5)	43 (97.7)	20 (45.5)
Hyperphosphatemia	36 (83.7)	3 (7.0)	30 (68.2)	0
Stomatitis	30 (69.8)	7 (16.3)	25 (56.8)	4 (9.1)
Dry mouth	16 (37.2)	0	25 (56.8)	1 (2.3)
Diarrhea	18 (41.9)	2 (4.7)	13 (29.5)	1 (2.3)
Dry skin	14 (32.6)	0	16 (36.4)	0
Patients who discontinued study treatment, n (%)	**Erdafitinib**	**Cetrelimab**	**Erdafitinib**	**Cetrelimab**
Discontinuation due to treatment-related AEs	6 (14.0)	NA	9 (20.5)[d]	6 (13.6)[d]

Siefker-Radtke. ASCO 2023 #4504

RENAL

CM 914 (parte A): análisis de subgrupos



N = 816

Key inclusion criteria[1,2]

- Radical or partial nephrectomy
- Predominant clear cell histology
- Pathologic TNM staging:
  - pT2a, G3 or G4, N0 M0/pT2b, G any, N0 M0
  - pT3, G any, N0 M0
  - pT4, G any, N0 M0/pT any, G any, N1 M0
- No evidence of residual disease or metastases after nephrectomy, confirmed by BICR

Stratification factors:
- *Pathologic TNM staging*[a]
- *Type of nephrectomy*

Expected treatment duration of 24 weeks[b]

R 1:1

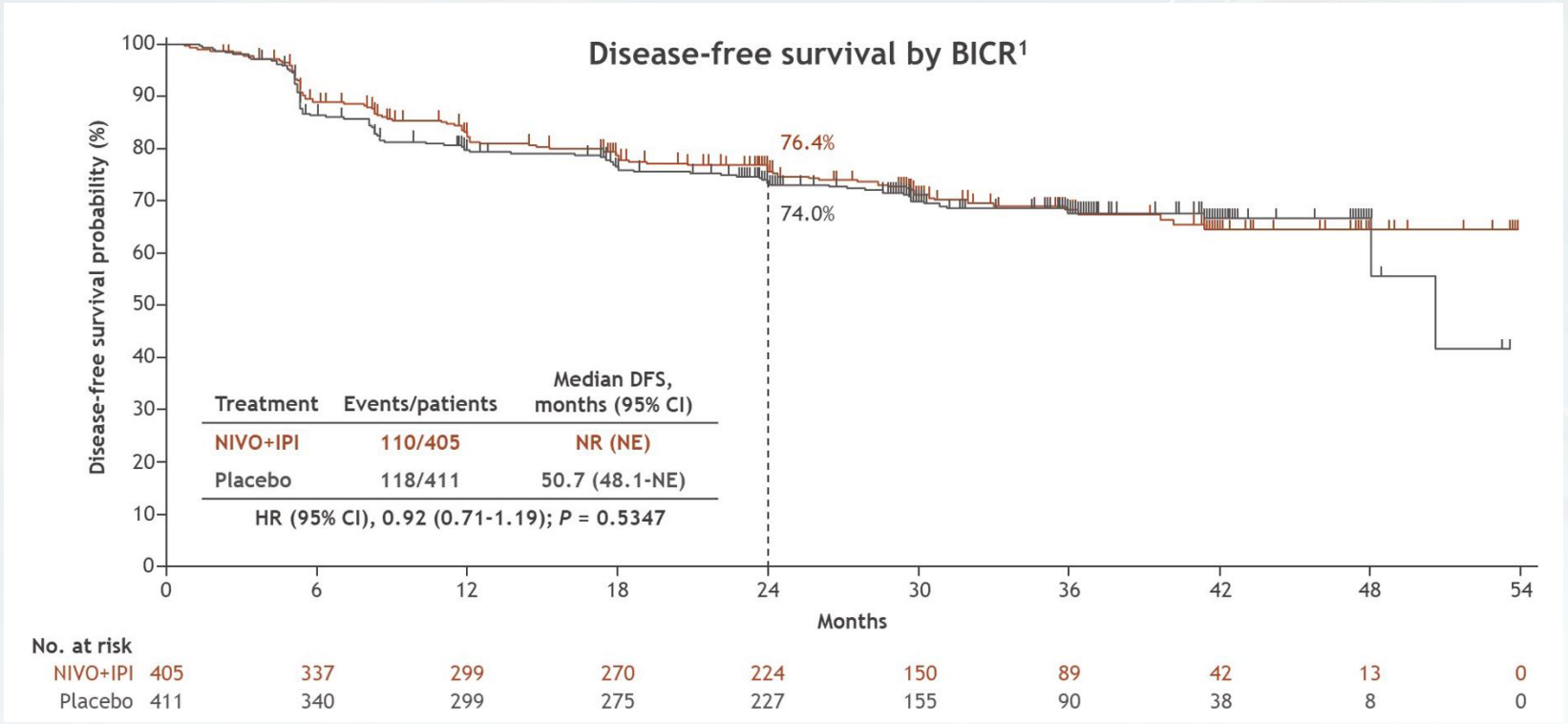
NIVO 240 mg IV Q2W (× 12 doses) + **IPI** 1 mg/kg IV Q6W (× 4 doses) **N = 405**

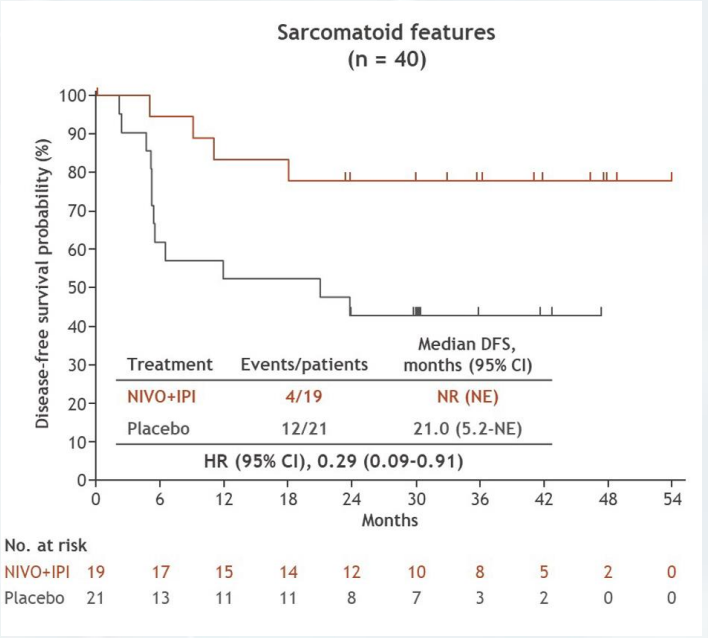
Placebo IV Q2W (× 12 doses) + **Placebo** IV Q6W (× 4 doses) **N = 411**

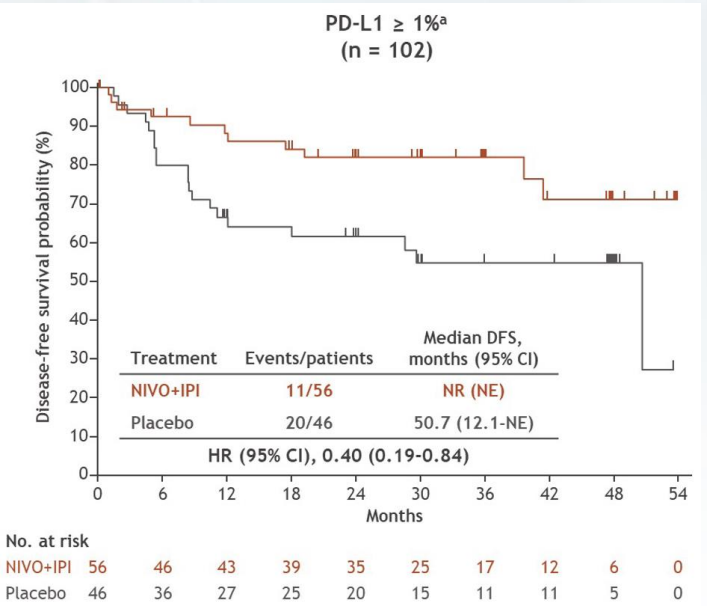
Randomization > 4 weeks and ≤ 12 weeks after surgery

Primary endpoint: DFS by BICR for NIVO+IPI vs placebo
Secondary endpoints: OS for NIVO+IPI vs placebo, safety of NIVO+IPI

Motzer. ASCO 2023 #4506

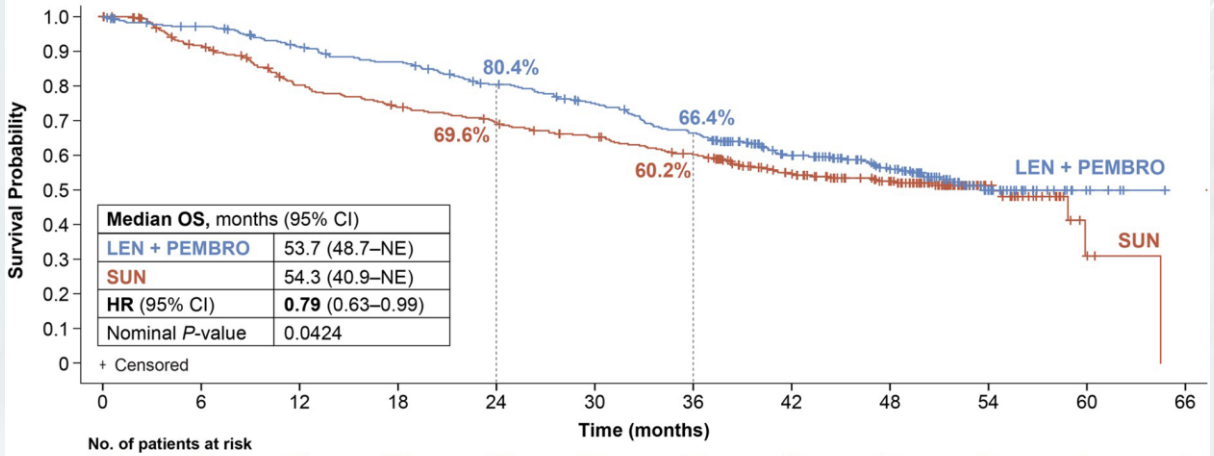

Disease-free survival by BICR[1]
Disease-free survival probability (%)
100
90
80
70
60
50
40
30
20
10
0
76.4%
74.0%
Treatment | Events/patients | Median DFS, months (95% CI)
NIVO+IPI | 110/405 | NR (NE)
Placebo | 118/411 | 50.7 (48.1-NE)
HR (95% CI), 0.92 (0.71-1.19); P = 0.5347
0 6 12 18 24 30 36 42 48 54
Months
No. at risk
NIVO+IPI 405 337 299 270 224 150 89 42 13 0
Placebo 411 340 299 275 227 155 90 38 8 0


Sarcomatoid features
(n = 40)
Disease-free survival probability (%)
100
90
80
70
60
50
40
30
20
10
0
Treatment | Events/patients | Median DFS, months (95% CI)
NIVO+IPI | 4/19 | NR (NE)
Placebo | 12/21 | 21.0 (5.2-NE)
HR (95% CI), 0.29 (0.09-0.91)
0 6 12 18 24 30 36 42 48 54
Months
No. at risk
NIVO+IPI 19 17 15 14 12 10 8 5 2 0
Placebo 21 13 11 11 8 7 3 2 0 0

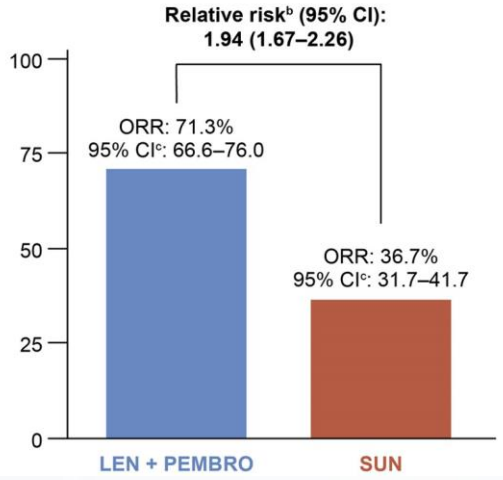

PD-L1 ≥ 1%[a]
(n = 102)
Disease-free survival probability (%)
100
90
80
70
60
50
40
30
20
10
0
Treatment | Events/patients | Median DFS, months (95% CI)
NIVO+IPI | 11/56 | NR (NE)
Placebo | 20/46 | 50.7 (12.1-NE)
HR (95% CI), 0.40 (0.19-0.84)
0 6 12 18 24 30 36 42 48 54
Months
No. at risk
NIVO+IPI 56 46 43 39 35 25 17 12 6 0
Placebo 46 36 27 25 20 15 11 11 5 0

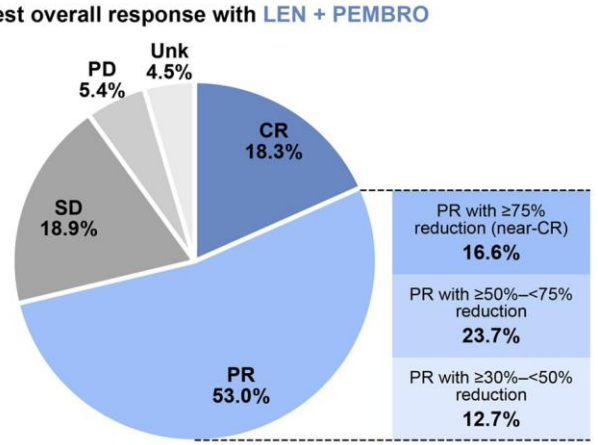
CLEAR

Final OS analysis



Objective response rate per independent review[a]

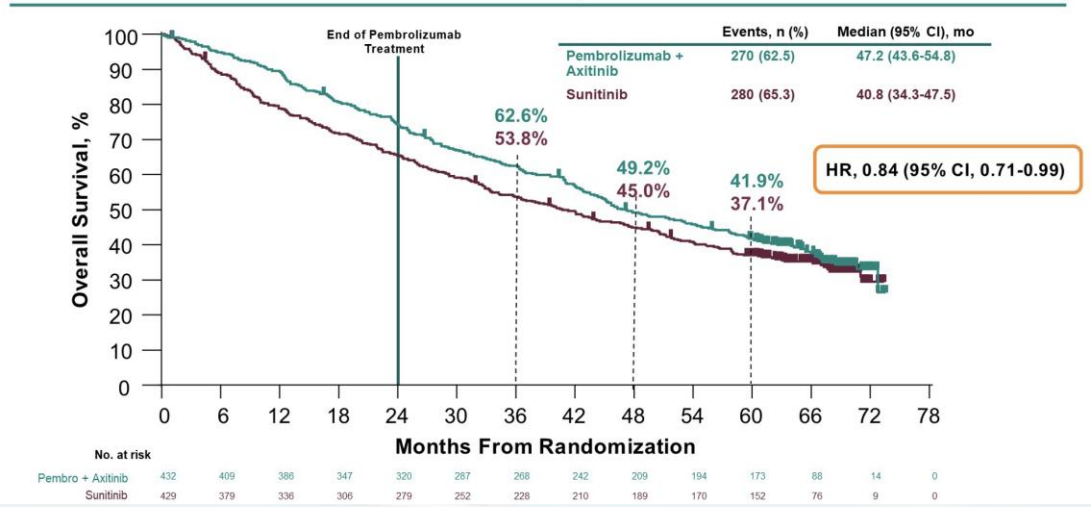




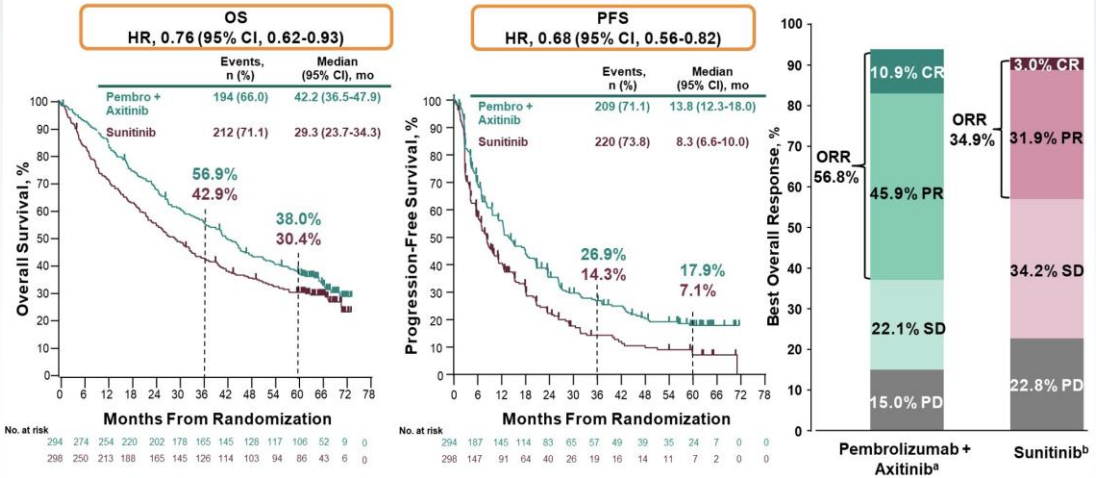
Motzer. ASCO 2023 #LBA4502

KN-426

Overall Survival in the ITT Population

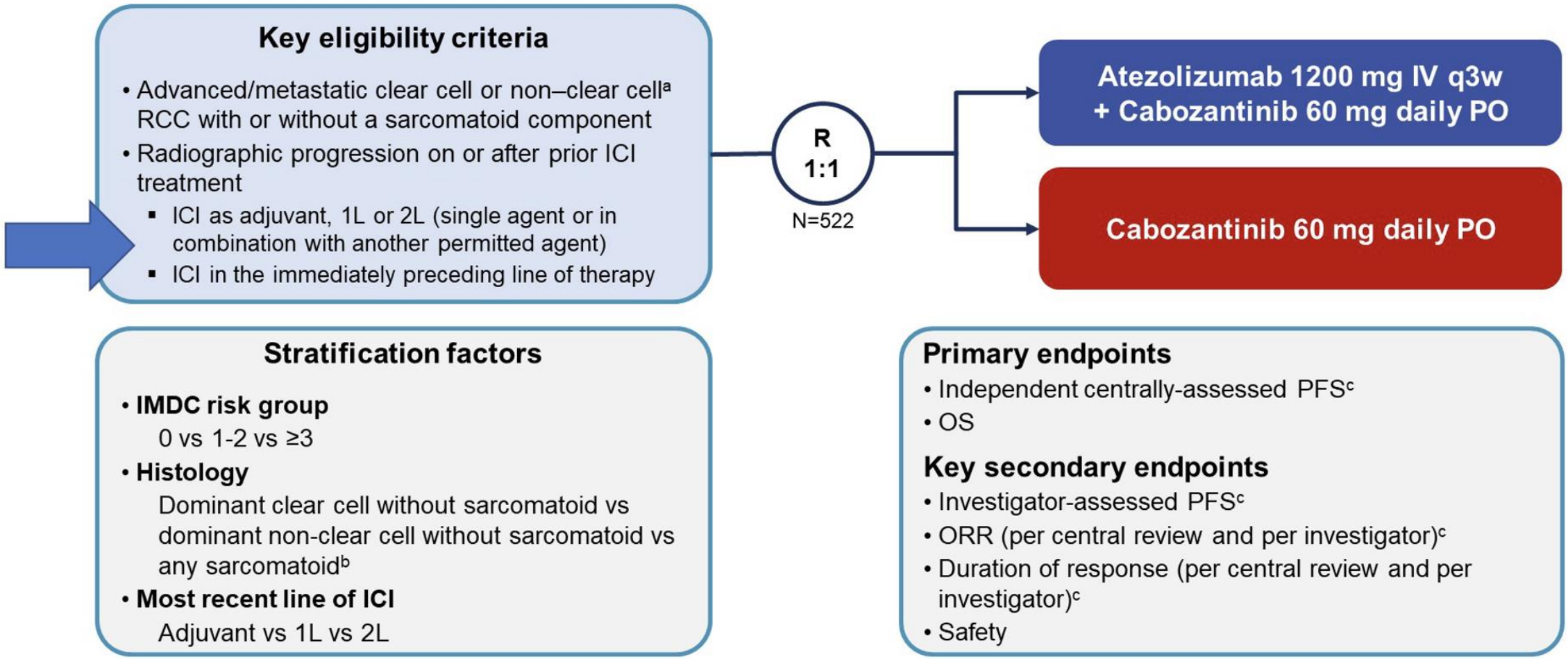


IMDC Intermediate/Poor Risk: OS, PFS, ORR



Rini. ASCO 2023 #LBA4501

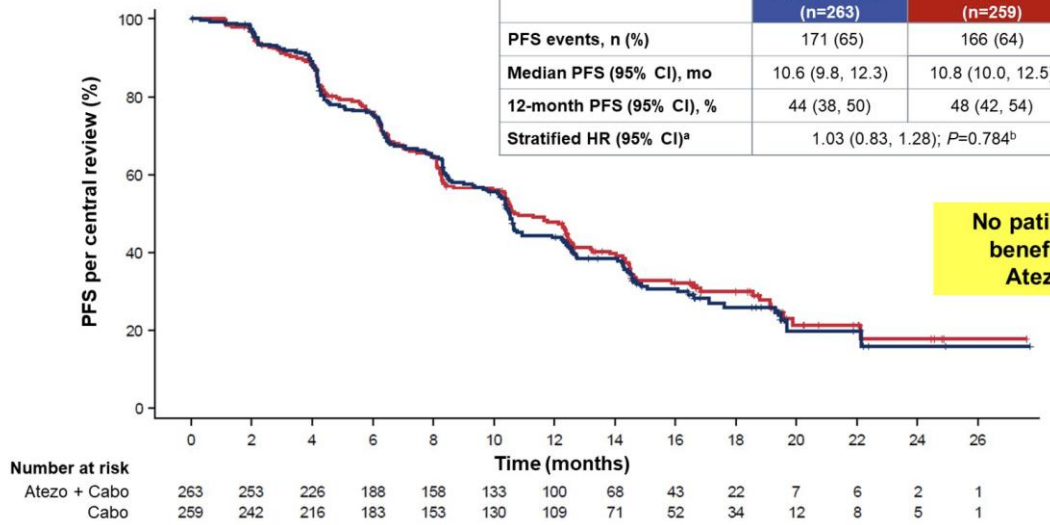
The global, Phase III CONTACT-03 study



Estudio negativo

Primary analysis of centrally reviewed PFS (primary endpoint)

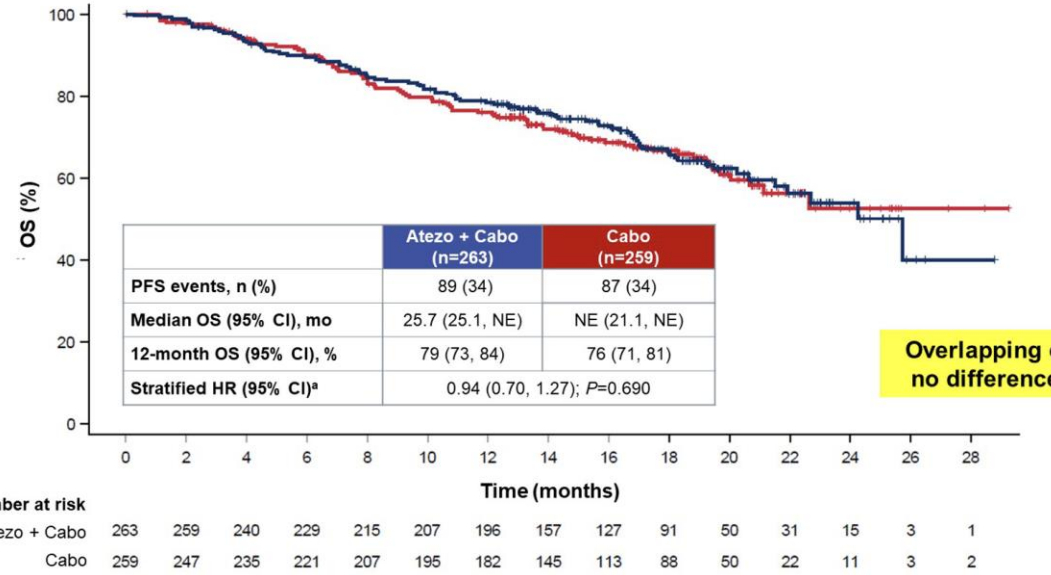
	Atezo + Cabo (n=263)	Cabo (n=259)
PFS events, n (%)	171 (65)	166 (64)
Median PFS (95% CI), mo	10.6 (9.8, 12.3)	10.8 (10.0, 12.5)
12-month PFS (95% CI), %	44 (38, 50)	48 (42, 54)
Stratified HR (95% CI)[a]	1.03 (0.83, 1.28); *P*=0.784[b]	



No patient subset benefited from Atezo/Cabo

Interim analysis of OS (primary endpoint)

	Atezo + Cabo (n=263)	Cabo (n=259)
PFS events, n (%)	89 (34)	87 (34)
Median OS (95% CI), mo	25.7 (25.1, NE)	NE (21.1, NE)
12-month OS (95% CI), %	79 (73, 84)	76 (71, 81)
Stratified HR (95% CI)[a]	0.94 (0.70, 1.27); *P*=0.690	



Overlapping curves: no difference in OS

Grade 3 or 4 AE	177 (67.6)	158 (61.7)
Grade 3 or 4 treatment-related AE	145 (55.3)	121 (47.3)
Death due to AE	17 (6.5)	9 (3.5)
Death due to treatment-related AE	3 (1.1)[a]	0
Serious AE	126 (48.1)	84 (32.8)
Serious treatment-related AE	63 (24.0)	30 (11.7)

Choueiri. ASCO 2023 #LBA4500

No células claras

KN-B61

Key Eligibility Criteria

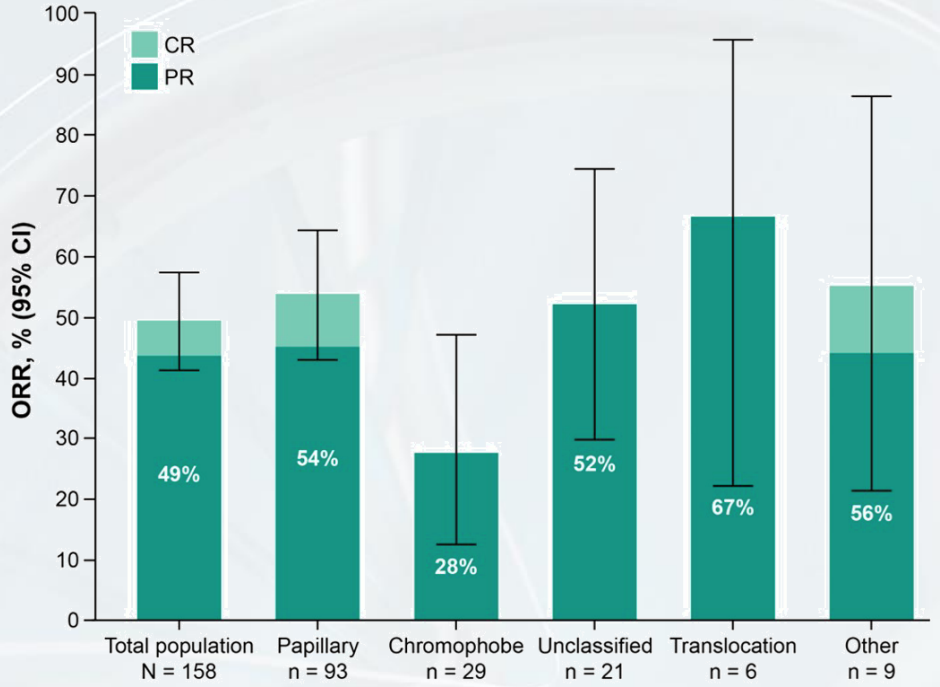
- Histologically confirmed diagnosis of nccRCC (per investigator)
- Locally advanced/metastatic disease
- No prior systemic therapy
- Measurable disease per RECIST v1.1
- KPS ≥70%

N = 158

Pembrolizumab 400 mg IV Q6W for ≤18 cycles[a] (~2 years) + Lenvatinib 20 mg PO QD

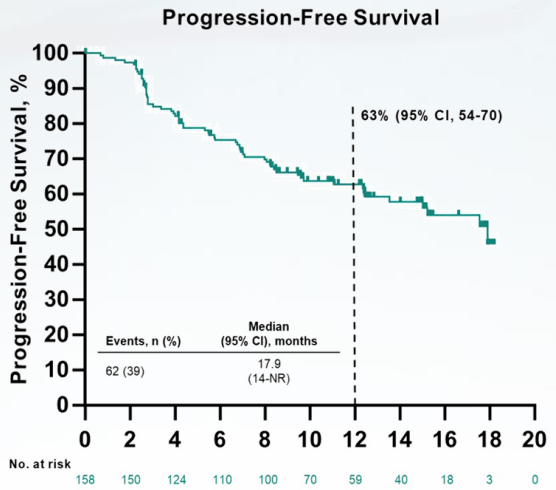
End Points

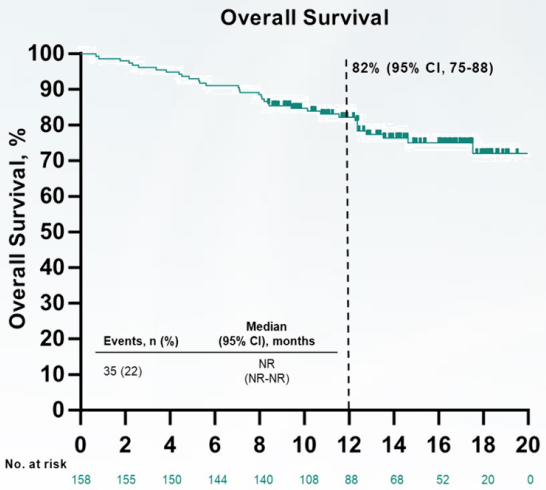
- Primary: ORR per RECIST v1.1 by BICR
- Secondary: CBR, DCR, DOR, and PFS per RECIST v1.1 by BICR; OS; safety and tolerability



44%: riesgo favorable

	Pembrolizumab + lenvatinib N = 158
ORR (CR + PR), % (95% CI)	49 (41-57)



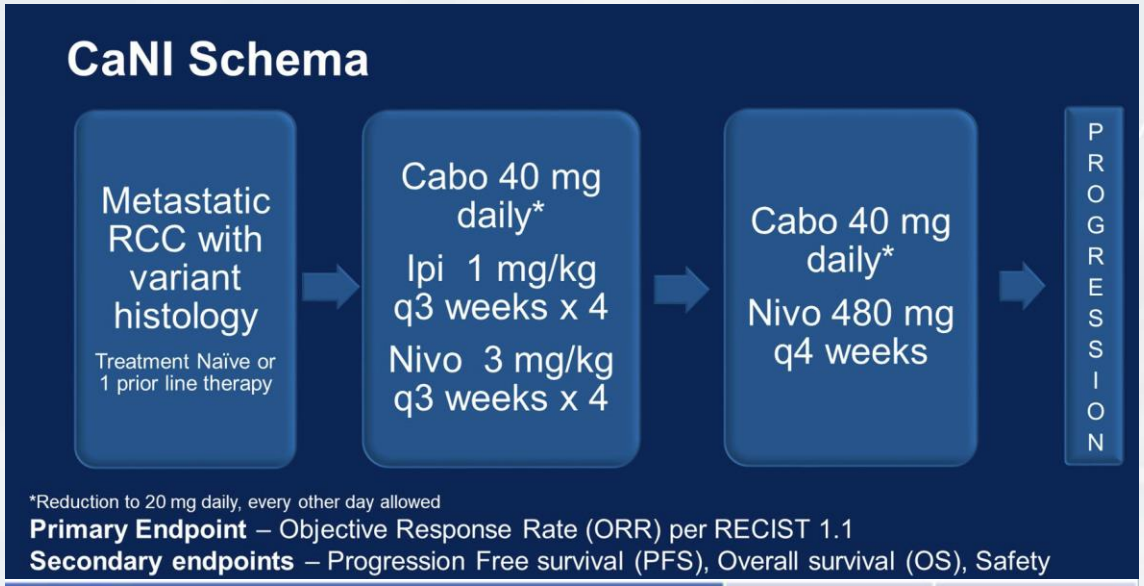


Lee. ASCO 2023 #4518

No células claras

CaNI

CaNI Schema

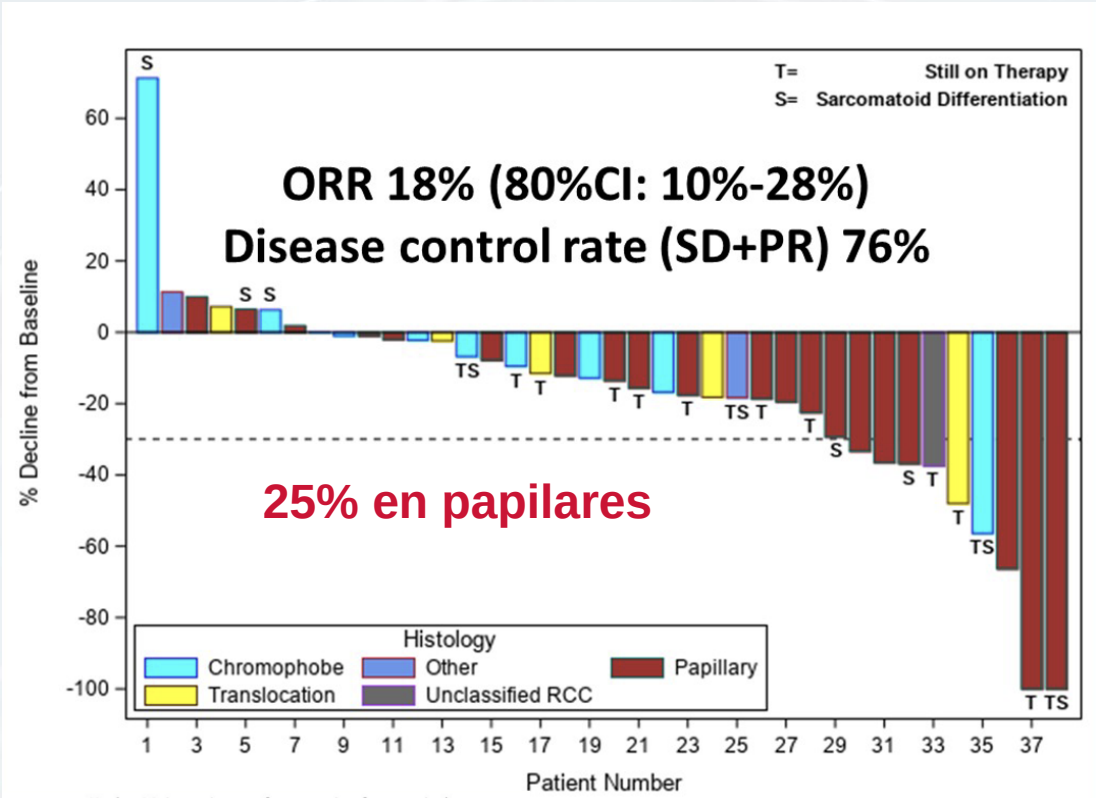


*Reduction to 20 mg daily, every other day allowed

Primary Endpoint – Objective Response Rate (ORR) per RECIST 1.1

Secondary endpoints – Progression Free survival (PFS), Overall survival (OS), Safety

Histology	N=58	
Papillary	20	51.3
Chromophobe	11	28.2
Translocation	5	12.8
Other	2	5.1
Unclassified RCC	1	2.6



Tox grado 3-4: 74% (21% disc)

McGregor. ASCO 2023 #4520

No células claras

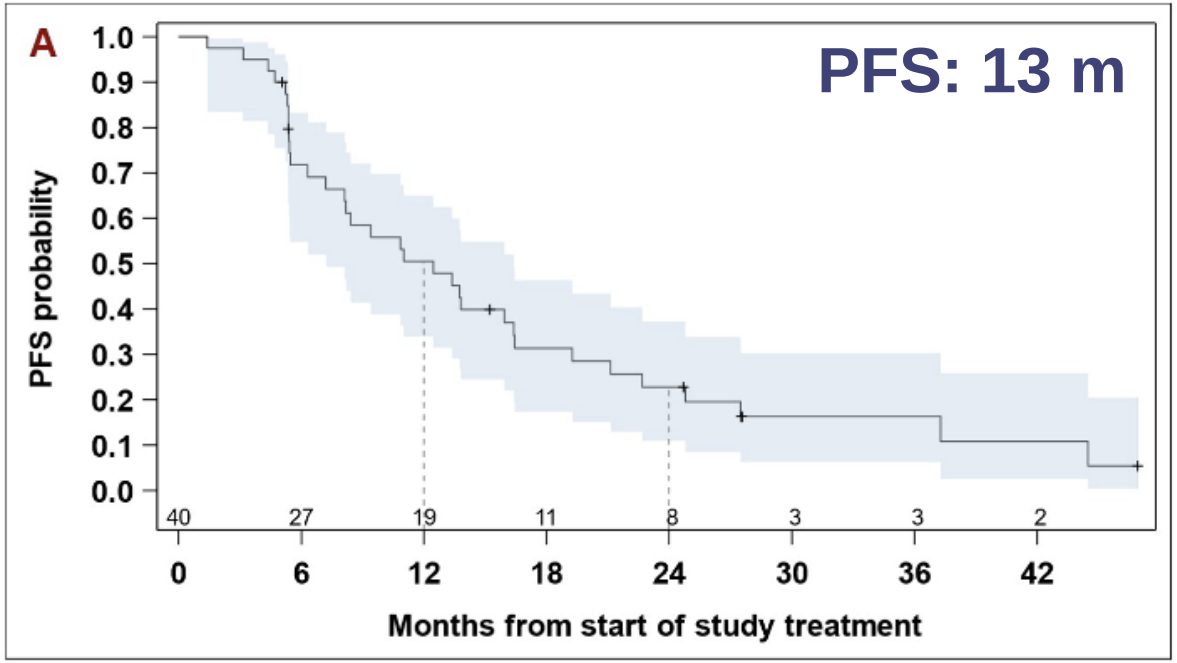
Cabo-nivo

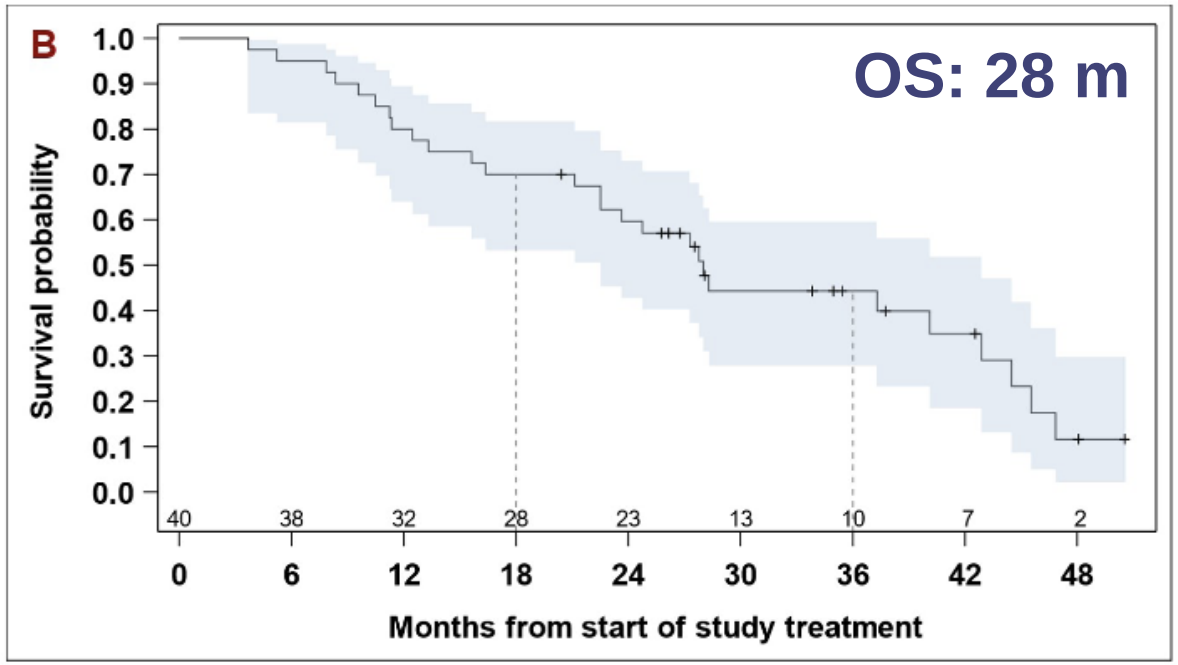
	1st line (any histology, N=26)	2nd line (any histology, N=14)	Papillary* (32)	Unclassified w/o papillary features (6)	Translocation-assoc. (2)
ORR	54% (33, 73)	36% (13, 65)	47% (30, 64)	50% (12, 88)	50% (1, 99)
CR	1 (4%)	0	1 (3%)	0	0
PR	13 (50%)	5 (36%)	14 (44%)	3 (50%)	1 (50%)
SD	12 (46%)	7 (50%)	16 (50%)	2 (33%)	1 (50%)
PD	0	2 (14%)	1 (3%)	1 (17%)	0
Med. PFS, months (95% CI)	11 (7, 19)	13 (5, 16)	13 (7, 16)	8 (1, *NE*)	14 (5, 23)
*Includes 16 unclassified with papillary features, 11 high grade papillary and 5 FH-deficient RCC.					

Lee. ASCO 2023 #4537

No células claras

Cabo-nivo

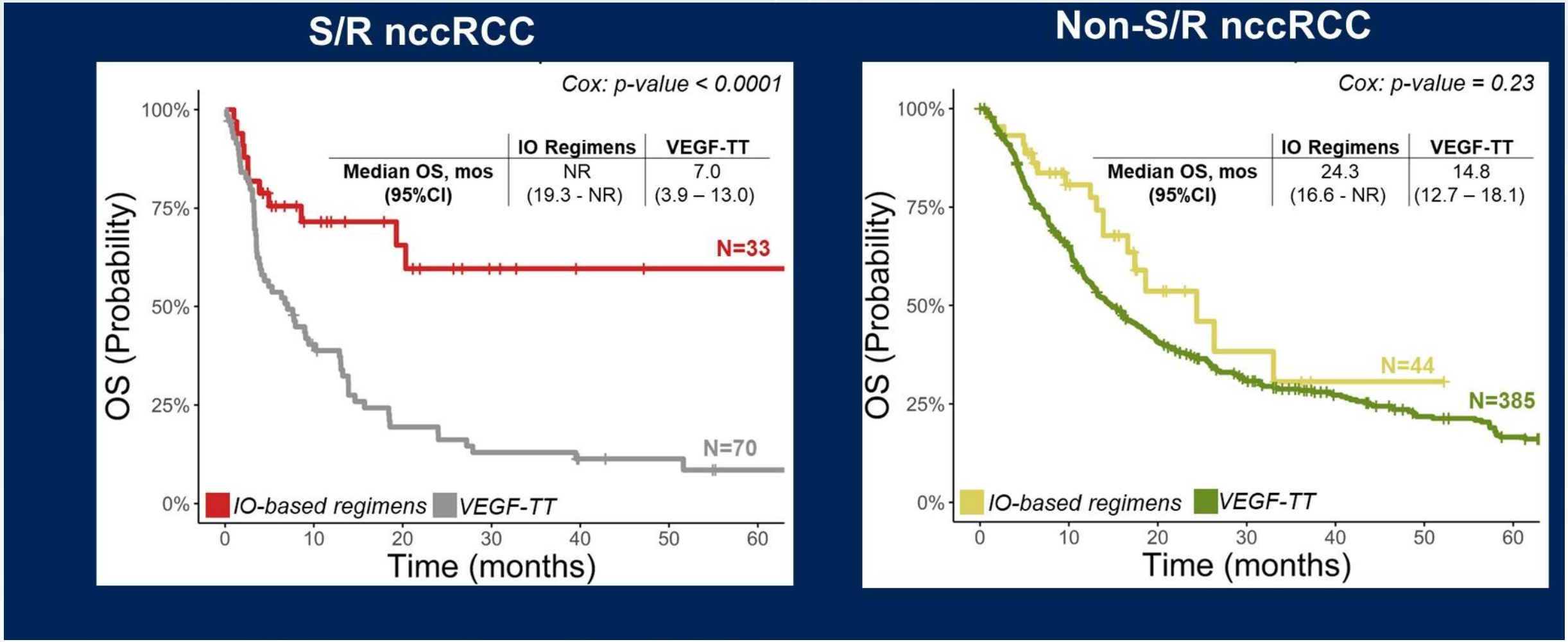




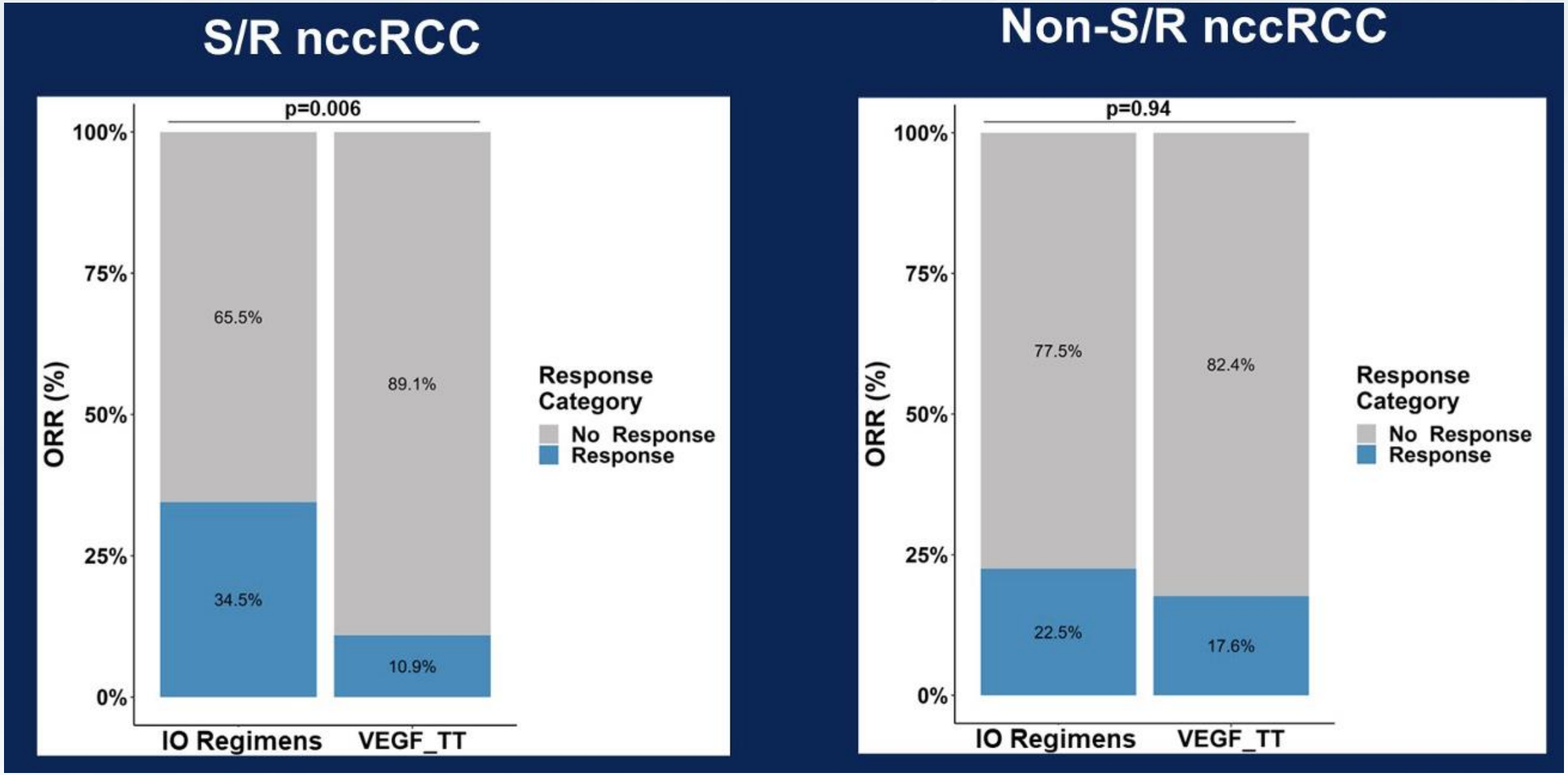
Lee. ASCO 2023 #4537

Eficacia del tratamiento en 1ª línea basado en inmunoterapia en pacientes con componente sarcomatoide y/o rabdoide: Datos del IMDC

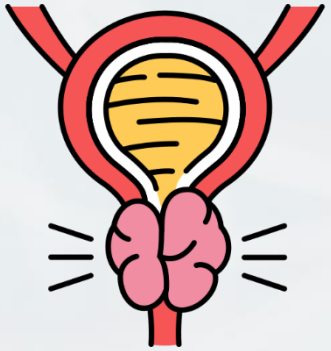
103 patients withS/R nccRCC were included, of whom 33 (32%) received 1L IO regimens



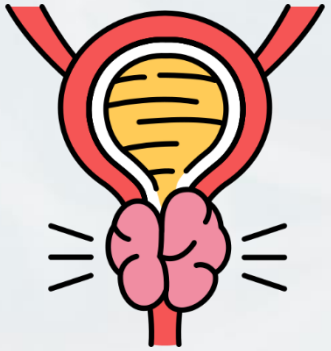
Labaki. ASCO 2023



Labaki. ASCO 2023



- La combinación de RDT con trat° sistémico intensificado mejora rPFS en CPSCm de bajo volumen (PEACE-1)
- Talazoparib + AA mejora rPFS en pacientes HRR+; OS pendiente (TALAPRO-2)



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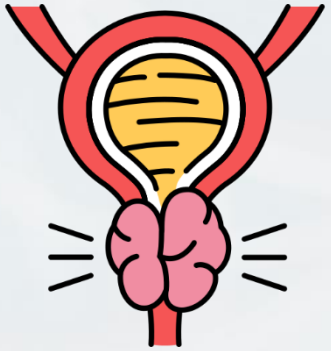
- LDNA extendida no mejora DFS ni OS
- VESPER: ddMVAC
- EV-103: importante ORR que ha llevado a su aprobación por la FDA
- THOR: erdafitinib mejora resultados en 2-3 L FGFR+



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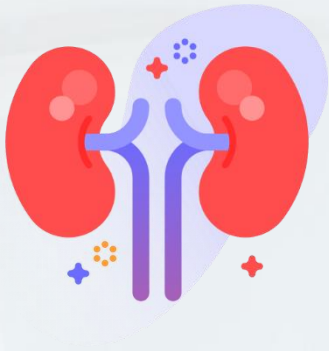

- Nivo-ipi: no debe usarse en adyuvancia; mejoría en subgrupos en SLE
- CONTACT-03: en ocasiones más no es mejor
- CLEAR y KN-426 mantienen beneficio
- No células claras: KN-B61; sarcomatoide

XXIII JORNADA DE REVISIÓN DEL

CONGRESO AMERICANO DE ONCOLOGÍA

Muchas gracias