



Presentaciones más destacadas en cáncer de próstata

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1. **Cáncer de próstata localizado**

- Estudio PEACE-2
- MMAI-derived prognostic biomarker in CHHiP trial
- GUNS trial

2. **Cáncer de próstata metastásico hormonosensible**

- Capitello-281-PROS
- PSMAAddition health-related QoL

3. **Cáncer de próstata metastásico resistente a castración**

- Estudio PEACE-3
- Estudio BRCA Away
- Phase 1 AMX-500
- Phase 1 225Ac-PSMA, PAnTHA



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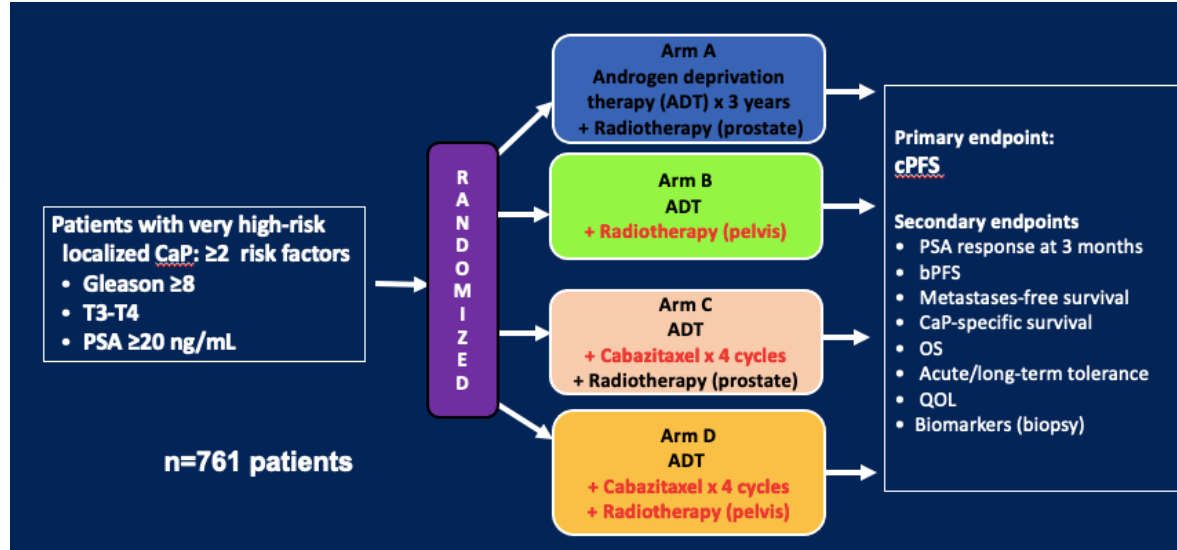
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CPL-AR. Estudio PEACE-2

Los muy alto riesgo tratados con RT + TDA larga tienen MFS <80%, los peores resultados



- Radiotherapy:
 - 74-78 Gy with 2 Gy fractions, IMRT mandatory
 - Started 3 months after ADT initiation
 - If pelvic RT: 46-50 Gy

2013-2021
mFU: 7,3 años

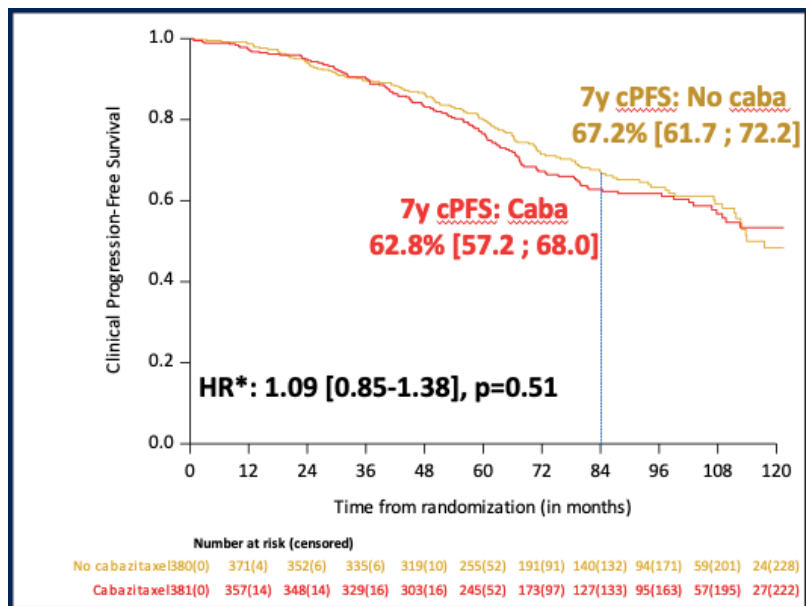
Fizazi K, et al. ASCO GU 2026

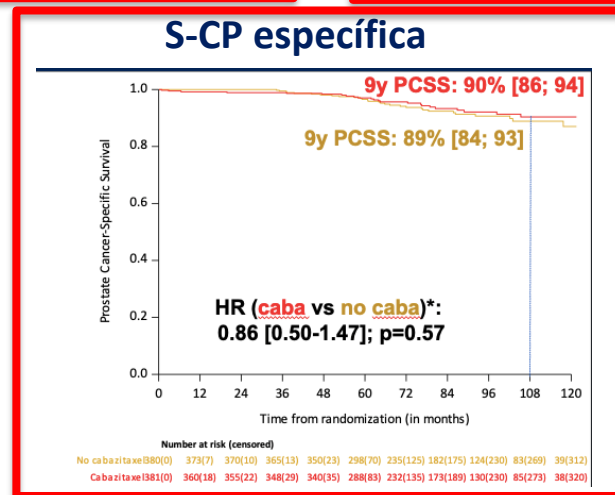
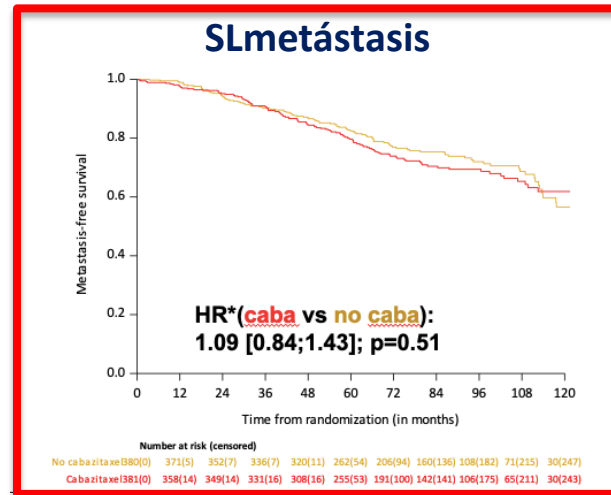
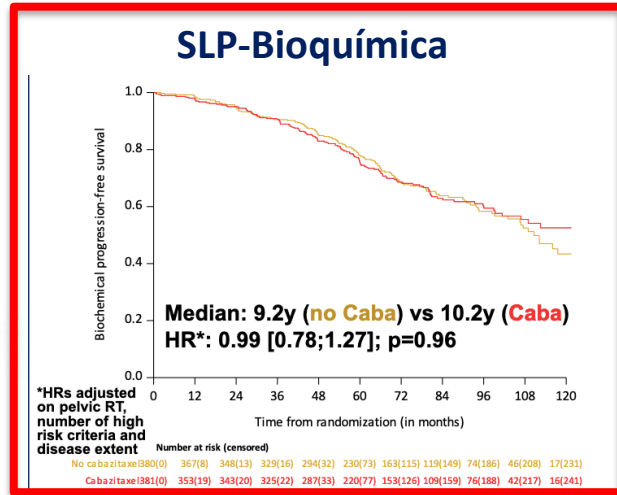
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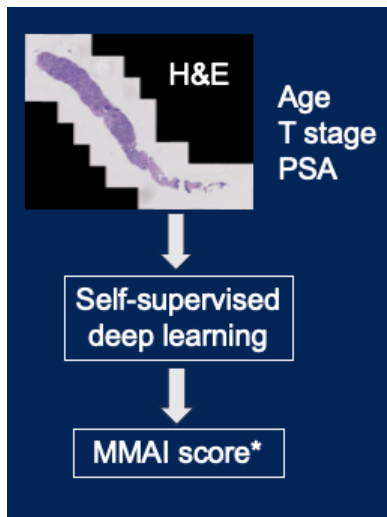
	ADT-Prostate RT (n=189)	ADT-RT Pelvis (n=191)	ADT-RT + <u>Caba</u> (n=191)	ADT-RT Pelvis + <u>Caba</u> (n=190)
<u>Median [IQR] age (years)</u>	67 [61-71]	67 [61-70]	67 [62-70]	66 [62-71]
T3-T4	166 (88%)	168 (88%)	174 (91%)	176 (93%)
<u>Gleason score 8-10</u>	145 (77%)	143 (75%)	156 (82%)	142 (75%)
<u>Median [IQR] PSA (ng/mL)</u>	22 [9-38]	23 [9-43]	19 [9-33]	22 [9-42]
<u>Risk factors:</u>				
2	149 (79%)	150 (79%)	150 (79%)	150 (79%)
3	40 (21%)	41 (21%)	41 (21%)	40 (21%)

CPL-AR. Estudio PEACE-2

SLP-clínica





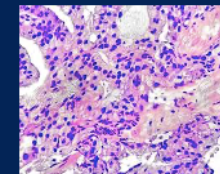


CHHiP validation cohort strengths

Recruitment period	2002-2011
Contemporary radiotherapy technique	IMRT
Consistent androgen deprivation	97% 4-6 months
Treatment quality control	✓
Robust central Gleason rescore	✓
H&E scanning quality control	✓

Trans-CHHiP

1854 patients



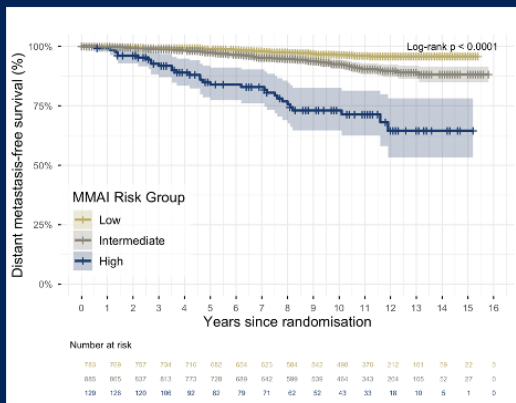
FINAL n = 1797

Two risk stratification systems in localized prostate cancer

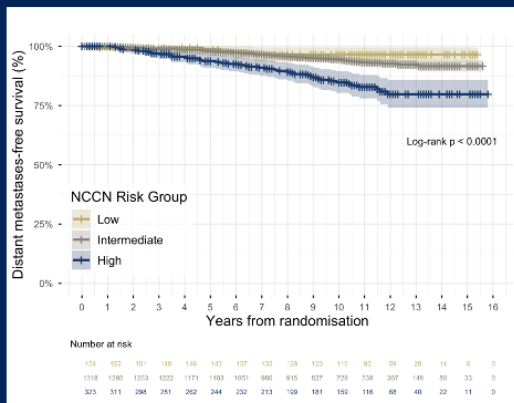
National Cancer Comprehensive Network		Cambridge Prognostic groups	
Risk group	Criteria	Risk group	Criteria
Low	Clin T1b/c or T2a & PSA ≤10 & Gleason ≤6	1	T1-T2 & PSA ≤10 & Gleason 6
Intermediate	T2B/C or PSA 10-20 or Gleason 7	2	T1-T2 & PSA 10-20 OR Gleason 3+4
		3	T1-T2 & PSA 10-20 & Gleason 3+4 or T1-T2 & Gleason 4+3
High	T3A or PSA >20 or Gleason ≥8	4	T3 or PSA >20 or Gleason 8
		5	≥ 2 of T3, PSA >20, Gleason 8 or Gleason 9-10 OR T4

Distant metastasis-free survival per MMAI risk group

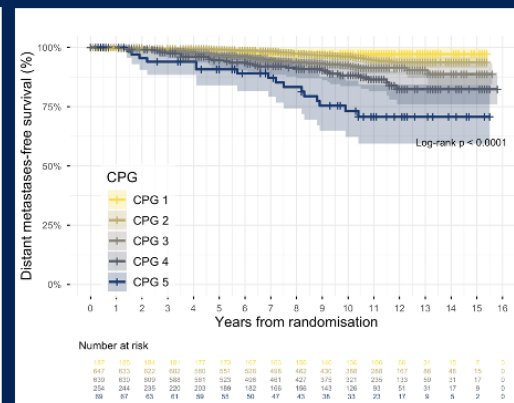
MMAI Risk Groups



NCCN Risk Groups



CPG Risk Groups



10 year distant metastases-free survival by:

- MMAI Low: 96.4%
- MMAI Intermediate: 92.5%
- MMAI High: 73.1%

10 year distant metastases-free survival by:

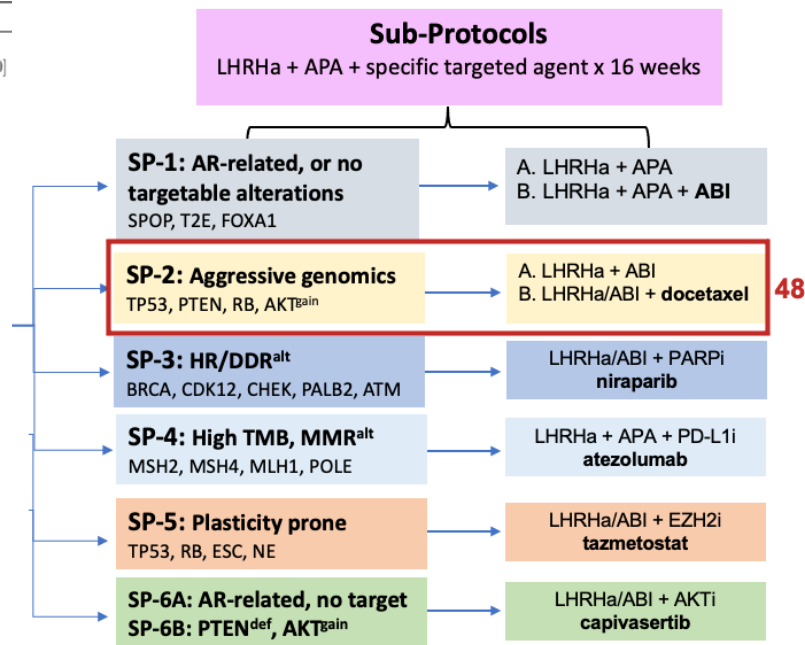
- NCCN Low: 96.5%
- NCCN Intermediate: 94.5%
- NCCN High: 84.8%

10 year distant metastases-free survival by:

- CPG1: 97.1%
- CPG2: 96.1%
- CPG3: 92.0%
- CPG4: 88.2%
- CPG5: 73.2%

GUNS: Genomic Umbrella Neoadjuvant Study in High Risk PCA

		SP 2a	SP 2b	Cohort
n		24	24	234
Age, years (median [IQR])		64.00 [58.50, 69.00]	63.00 [58.00, 67.00]	65.00 [60.00, 71.00]
Race (%)	Asian	1 (4.2)	1 (4.2)	30 (12.8)
	Black or African American	1 (4.2)	2 (8.3)	13 (5.6)
	White	22 (91.7)	21 (87.5)	190 (81.2)
	Unknown			1 (0.4)
PSA, ng/mL (%)	< 10	6 (25.0)	8 (33.3)	76 (32.5)
	10 ≤ PSA < 20	8 (33.3)	6 (25.0)	72 (30.8)
	20 ≤ PSA < 40	5 (20.8)	3 (12.5)	45 (19.2)
	40 ≤ PSA < 80	5 (20.8)	5 (20.8)	37 (15.8)
	≥ 80		2 (8.3)	4 (1.7)
Grade group (%)	2	1 (4.2)	1 (4.2)	5 (2.1)
	3	3 (12.5)	4 (16.7)	21 (9.0)
	4	3 (12.5)	3 (12.5)	37 (15.8)
	5	17 (70.8)	16 (66.7)	171 (73.1)
	IDC (%)	No	6 (33.3)	7 (46.7)
	Yes	12 (66.7)	8 (53.3)	59 (39.6)
Cribriform (%)	No	9 (50.0)	4 (26.7)	77 (52.0)
	Yes	9 (50.0)	11 (73.3)	71 (48.0)
cT stage (%)	T1	2 (8.3)	3 (12.5)	38 (16.2)
	T2	15 (62.5)	12 (50.0)	123 (52.6)
	T3	7 (29.2)	9 (37.5)	69 (29.5)
	T4			1 (0.4)
	TX			3 (1.3)
	cN stage (%)	N0	20 (83.3)	17 (70.8)
N1		4 (16.7)	7 (29.2)	21 (9.0)
NX				2 (0.9)
Tempus xT (%)	No			32 (13.7)
	Yes	24 (100.0)	24 (100.0)	202 (86.3)
Tempus RNA-seq (%)	No	7 (29.2)	4 (16.7)	85 (36.3)
	Yes	17 (70.8)	20 (83.3)	149 (63.7)



ETS fusions, *FOXA1*^{alt}, *TP53*^{alt}, *PTEN*^{alt}, and *SPOP*^{alt} dominate the genomic landscape of diagnostic tumor biopsies in GUNS

202/234 pre-Tx biopsies
(14% non-evaluable)

T2E fusions (30%)
***FOXA1*^{alt} (23%)**
***SPOP*^{alt} (13%)**



TP53* -19%** ***TP53
PTEN* - 16%** ***PTEN/AKT pathway
RB1, cell cycle genes

***BRCA2* (6%)**

DDR genes (*BRCA2, ATM, ...*) & *CDK12*

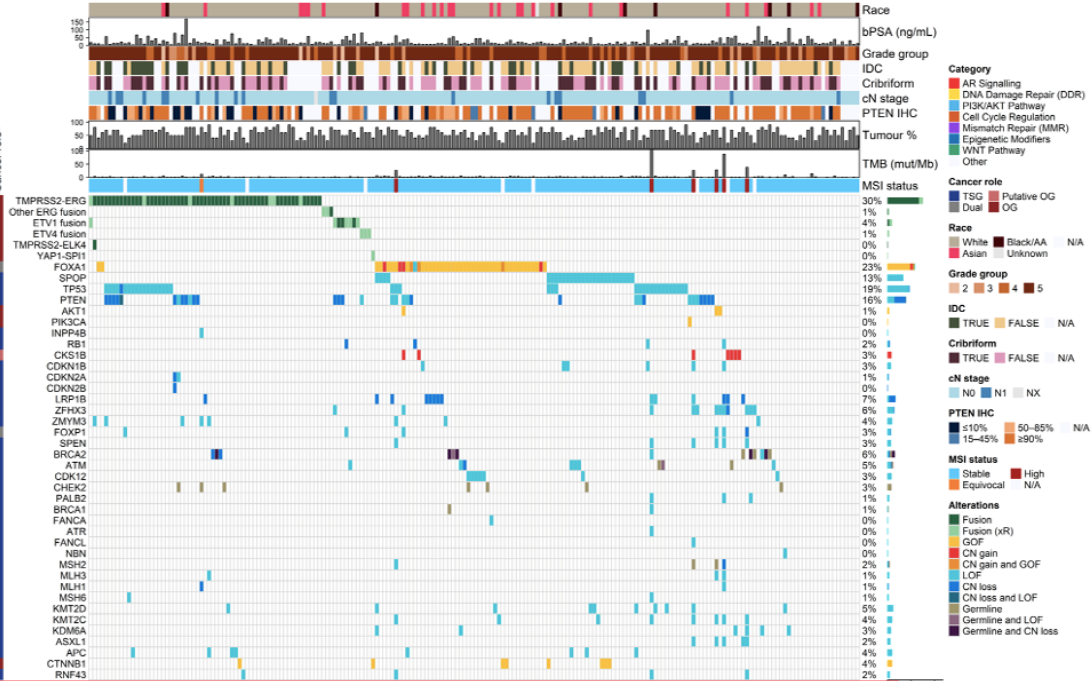
MMR genes

Epigenetic modifiers

WNT pathway genes



Josh Scurl



SP-2 genomics: 65/202 (32%) of evaluable tumours had *TP53*^{alt}, *PTEN*^{alt}, *AKT1*^{GOF}, or *RB1*^{alt}

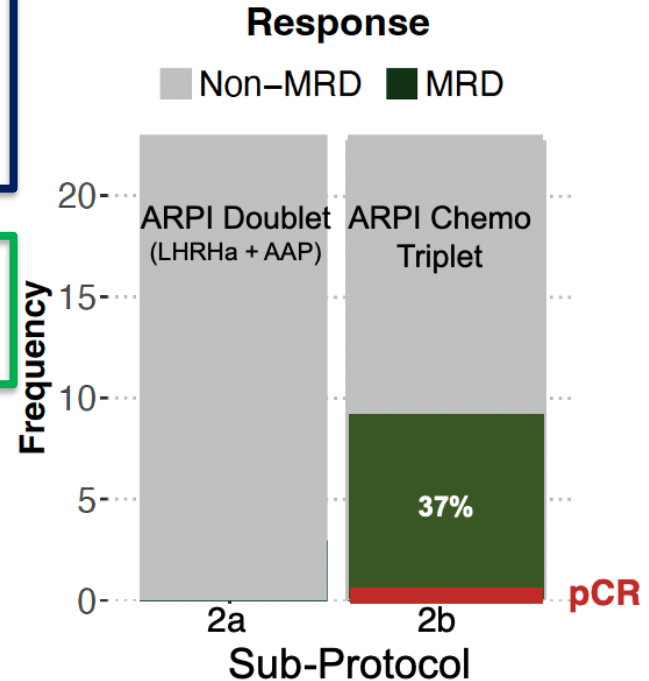
Hypothesis:

Do ARPI-docetaxel triplets, in cancers with aggressive TSG loss, increase depth of pathologic response

- 24 pts/arm enrolled – Stage 1 of Simon’s 2-stage design

MRD rate higher in ARPI-chemo triplet than doublet

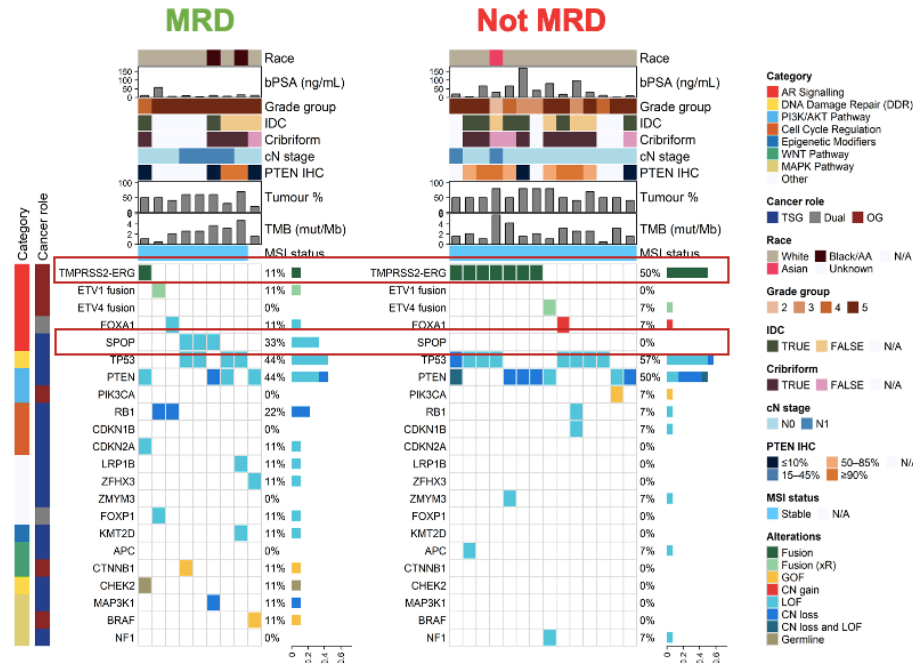
- 0/24 (0%) vs 9/23 (39%), p=0.016
- One pCR in SP2B
 - Degenerative scores averaged higher in SP-2B vs SP-2A
 - Similar +ve margin (17%) or LN (37% vs 28%)



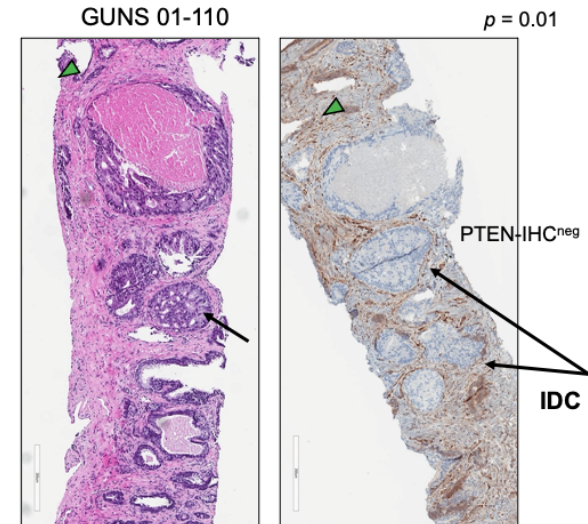
*01-097 (SP-2B) Grade 3 SAE, CVA; non-surgical candidate

**MRD = < 5mm total tumor content:
%Tumor cellularity x diameter of ROI¹+ROI²+ROI³...**

SPOP^{mut} associates with MRD, T2E fusions with non-MRD, to ARPI-docetaxel triplets in SP-2B



PTEN^{def} or TP53^{mut}, especially combined with ETS fusion, associated with intra-ductal cancer (IDC)



Heterogeneidad intragrupal que puede modular la sensibilidad terapéutica



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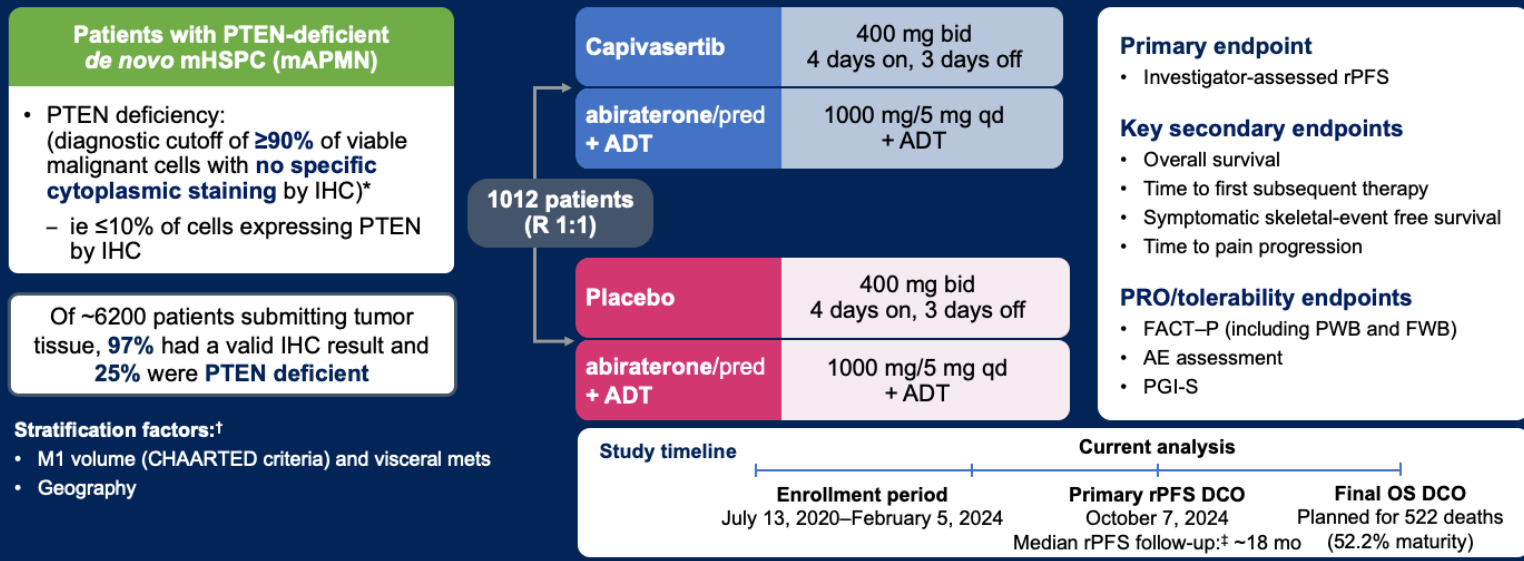
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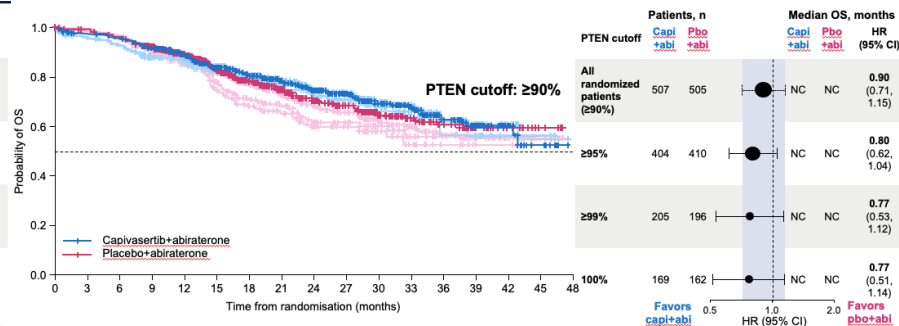
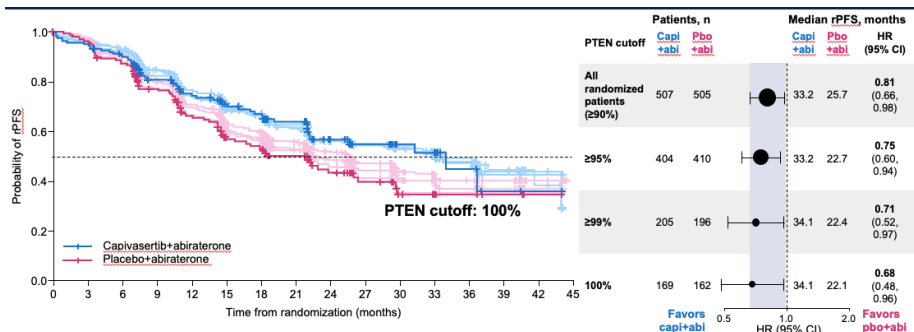
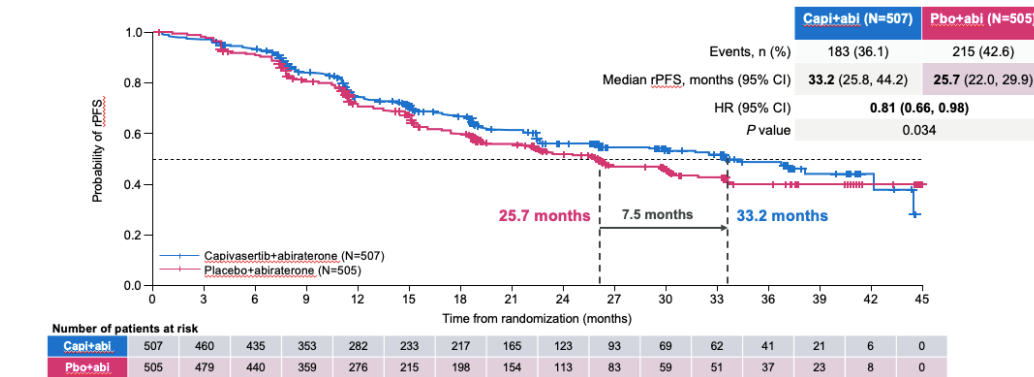
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CAPITello-281 study design

A global, multicenter, randomized, double-blind, Phase III study



Estudio CAPITELLO-281



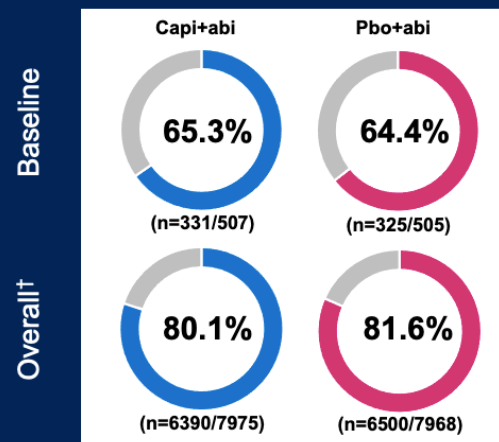
FACT-P total score includes five subscales:

- **Physical wellbeing**
 - Includes side effects such as energy, nausea and pain
- **Functional wellbeing**
 - Includes ability to work, sleep quality and ability to enjoy life
- Emotional wellbeing
- Social/family wellbeing
- Prostate cancer symptoms

Assessments until earliest of:

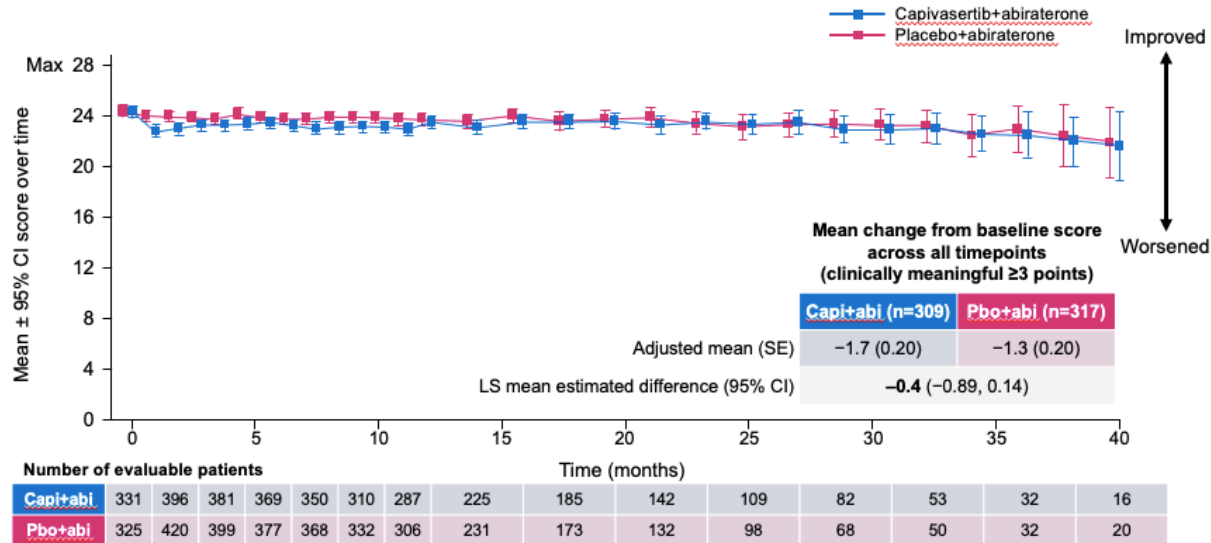
- Subsequent anticancer treatment
- 12 months post radiographic progression

FACT-P compliance*



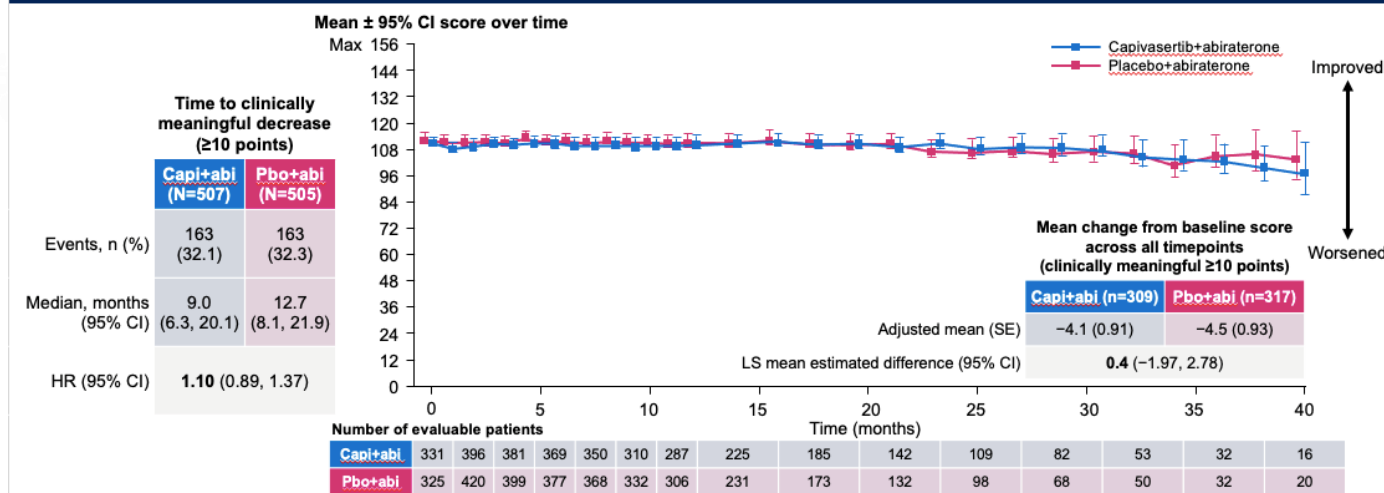
CAPitello-281: FACT-P physical wellbeing (PWB)

PWB includes outcomes such as side effects, energy, nausea and pain

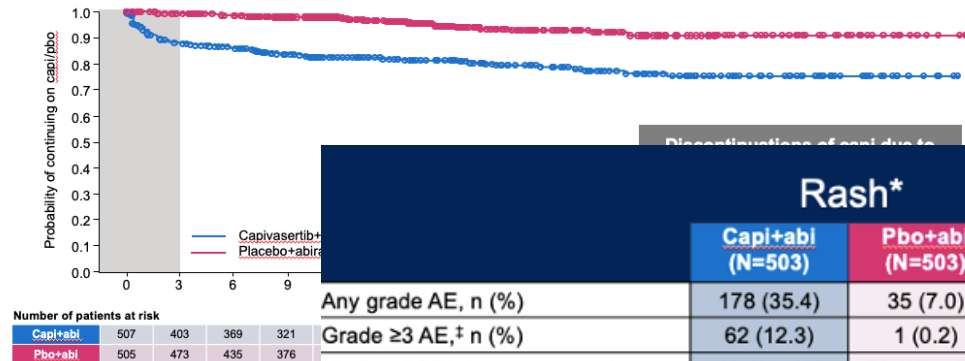


CAPITello-281: FACT-P total score

FACT-P total score includes physical, functional and emotional wellbeing, as well as prostate cancer symptoms

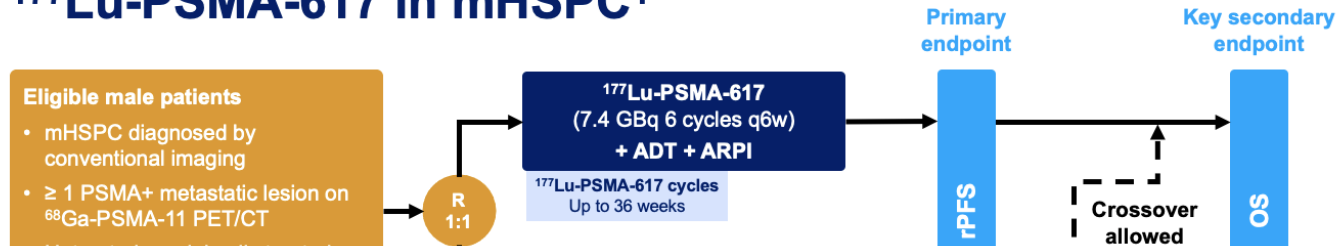


CAPITello-281: Discontinuations due to AEs



	Rash*		Diarrhea		Hyperglycemia†	
	Capi+abi (N=503)	Pbo+abi (N=503)	Capi+abi (N=503)	Pbo+abi (N=503)	Capi+abi (N=503)	Pbo+abi (N=503)
Any grade AE, n (%)	178 (35.4)	35 (7.0)	261 (51.9)	40 (8.0)	191 (38.0)	65 (12.9)
Grade ≥3 AE,‡ n (%)	62 (12.3)	1 (0.2)	31 (6.2)	2 (0.4)	52 (10.3)	3 (0.6)
Median (IQR) time to onset, days	13 (11–43)	78 (37–195)	12 (3–43)	142 (28–339)	54 (15–114)	114 (71–326)
AE leading to, n (%)						
Interruption of capi/pbo	85 (16.9)	3 (0.6)	63 (12.5)	1 (0.2)	55 (10.9)	4 (0.8)
Reduction of capi/pbo	43 (8.5)	2 (0.4)	22 (4.4)	0	33 (6.6)	1 (0.2)
Discontinuation of capi/pbo	24 (4.8)	0	5 (1.0)	0	5 (1.0)	0
Supportive treatment given, n (%)	146 (29.0)	20 (4.0)	167 (33.2)	19 (3.8)	127 (25.2)	23 (4.6)
Outcome at time of DCO, n (%)						
Recovered/recovering	164 (32.6)	28 (5.6)	238 (47.3)	36 (7.2)	140 (27.8)	43 (8.5)
Not recovered	24 (4.8)	8 (1.6)	45 (8.9)	4 (0.8)	65 (12.9)	25 (5.0)

PSMAddition: randomized phase 3 trial of ¹⁷⁷Lu-PSMA-617 in mHSPC¹



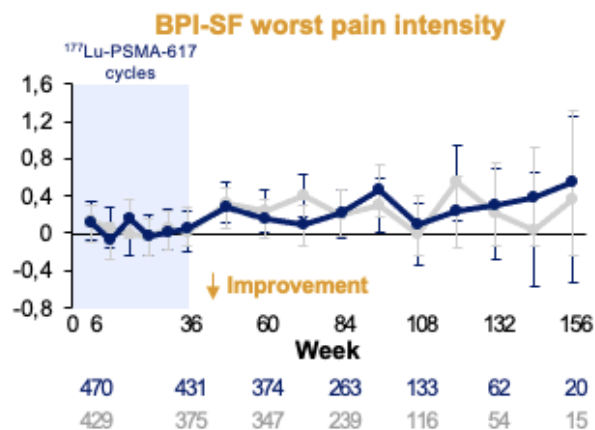
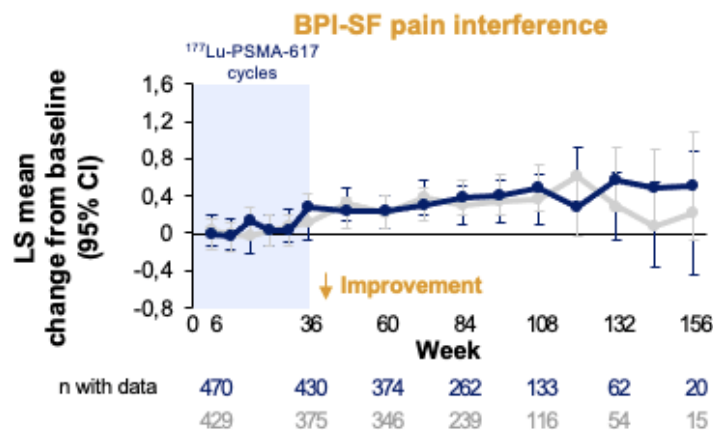
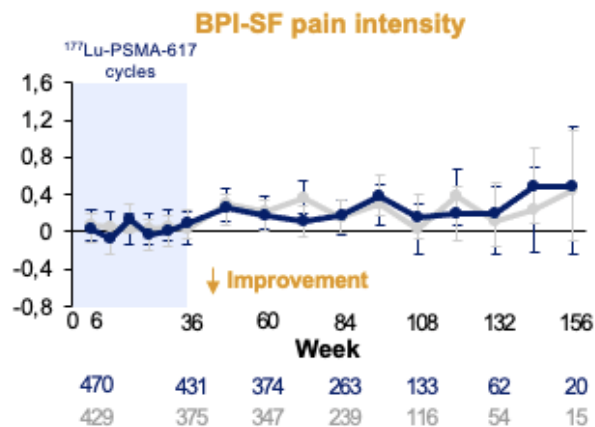
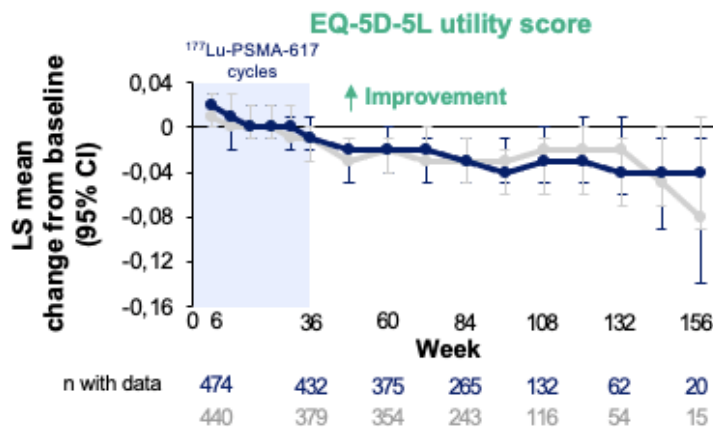
Patient-reported outcomes and SSE endpoints

High compliance with HRQoL and pain questionnaires at baseline

Baseline questionnaire completed and score calculable – n (%)	¹⁷⁷ Lu-PSMA-617 + ADT + ARPI (n = 572)	ADT + ARPI (n = 572)
FACT-P total score	511 (89.3)	483 (84.4)
EQ-5D-5L utility score	512 (89.5)	487 (85.1)
BPI-SF worst pain intensity	509 (89.0)	481 (84.1)

¹ OS, overall survival; rPFS, radiographic progression-free survival; rPFS, radiographic progression-free survival; SSE, symptomatic skeletal event. 1. Tagawa SI, et al. *Ann Oncol* 2023;36:31–36 (ESMO 2023)

— $^{177}\text{Lu-PSMA-617}$ + ADT + ARPI — ADT + ARPI

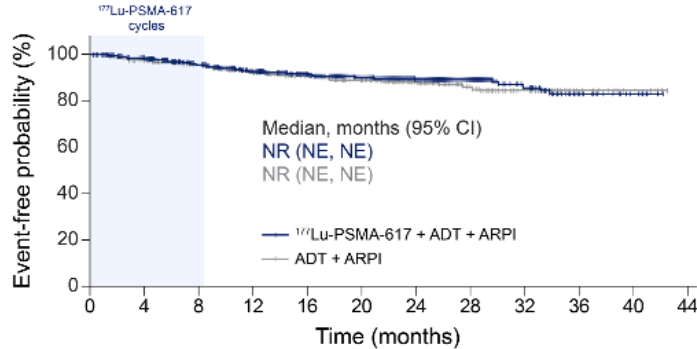


- Se emplea modelo lineal de efectos mixtos

Time to first SSE or death

Composite time to first SSE or death

HR 0.89 (95% CI: 0.62, 1.26)

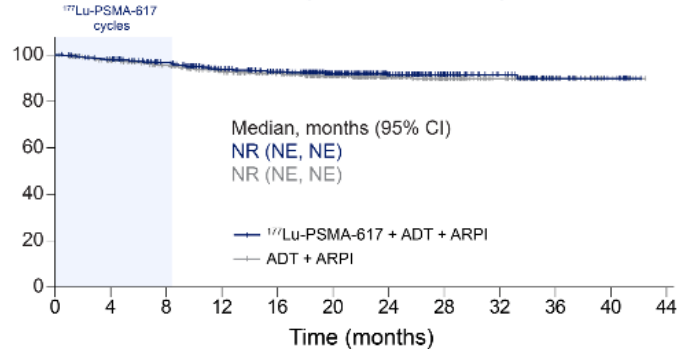


Number of patients still at risk

572 561 550 529 511 484 457 440 420 403 312 245 186 151 108 79 70 55 28 15 10 1 0
572 549 533 508 489 462 443 418 397 373 286 223 166 136 100 70 58 40 21 15 7 2 0

Time to first SSE (excluding death)

HR 0.87 (95% CI: 0.58, 1.31)



Number of patients still at risk

572 561 550 529 511 484 457 440 420 403 312 245 186 151 108 79 70 55 28 15 10 1 0
572 549 533 508 489 462 443 418 397 373 286 223 166 136 100 70 58 40 21 15 7 2 0

Bone protective agent use	¹⁷⁷ Lu-PSMA-617 + ADT + ARPI (n = 564)	ADT + ARPI (n = 565)
Denosumab	65 (11.5)	89 (15.8)
Bisphosphonates	46 (8.2)	50 (8.8)



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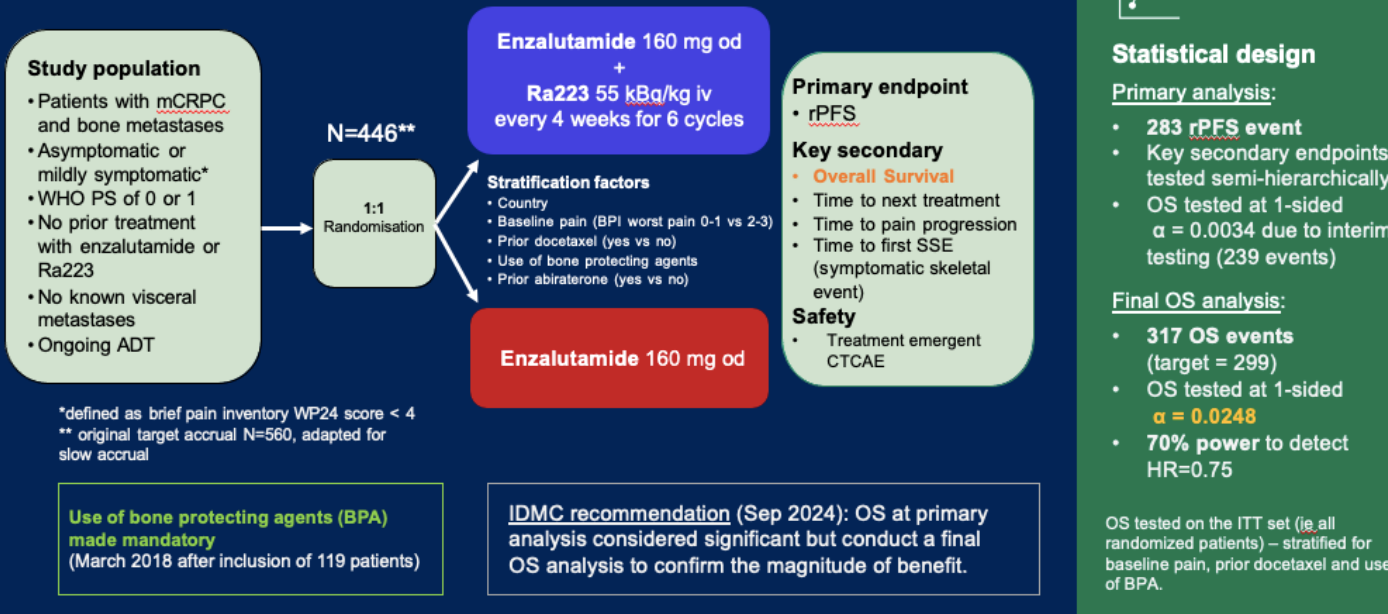
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CPMRC. Estudio PEACE-3

Methods – Study design



Baseline characteristics

	Enza+Ra223 (N=222)	Enza (N=224)
	N (%)	N (%)
Age, Median (range) years	70.0 (43.0 - 90.0)	70.0 (47.0 - 90.0)
PSA, Median (Q25-Q75) ng/mL	24.5 (7.8-68.8)	21.2 (7.9-53.1)
WHO Performance status 0	153 (69)	154 (69)
Prior docetaxel ⁽¹⁾	67 (30.2)	66 (30)
Prior abiraterone ⁽¹⁾	4 (2)	7 (3)
Bone lesions⁽²⁾		
<10	109 (49)	105 (47)
≥10	93 (42)	99 (44)
Missing or diffuse lesions	20 (9)	20 (9)
Alkaline phosphatase		
≤ULN	127 (57)	109 (49)
>ULN	82 (37)	109 (49)
Missing	13 (6)	6 (3)
Extra-skeletal disease at baseline	77 (35)	73 (33)

(1) Prior docetaxel or abiraterone was allowed for mHSPC.

(2) Per imaging guidelines, the type of bone lesions is reported by a radiologist and classified into focal, diffuse or equivocal. Only focal bone lesions can be counted.

N = 446 patients

- Nov 2015 → Mar 2023
- 56 centres from 12 countries

• Database lock = 12 Jan 2026
(cutoff date = 1MAY2025)

- Median follow-up = 4.8 years (3.4 yrs at primary analysis)

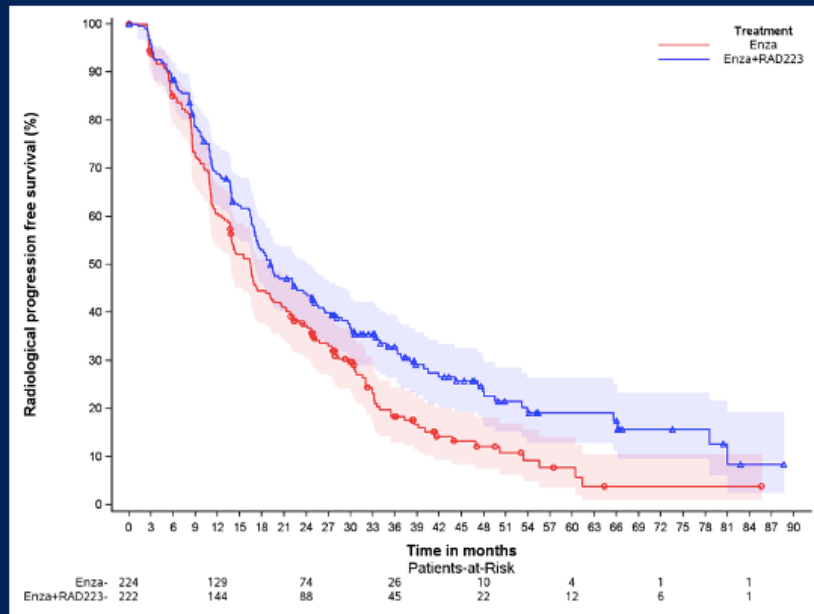
Intergroup trial led by EORTC (EU)

Collaborating groups:

- LACOG (Brazil)
- CTI (Ireland)
- CUOG (Canada)
- UNICANCER-GETUG (France)

The method used (inversed censoring) censors at death. It attempts to estimate what follow-up would have been if patients had not died.

Final rPFS results



Database locked on 12 January 2026 (cut off date: 01 May 2025)

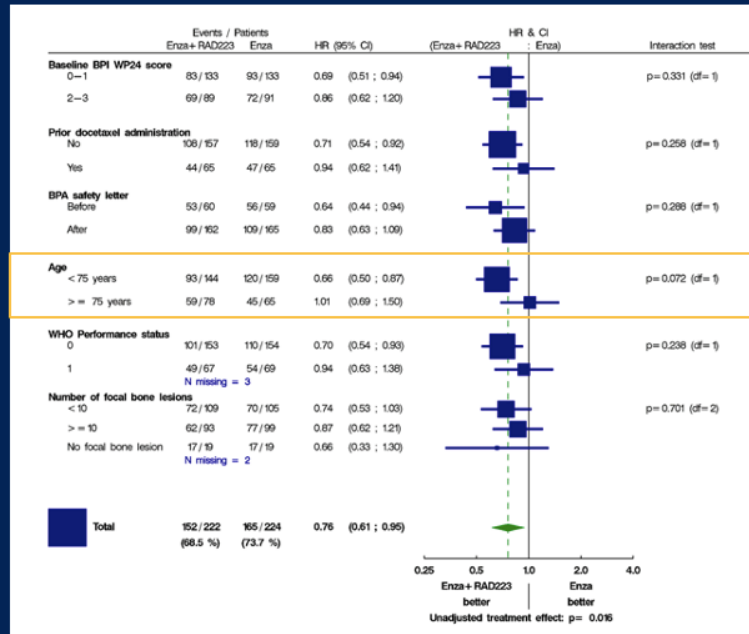
Treatment	Event/ Total	Median (95%CI) (months) ¹	Hazard Ratio (95% CI) ²
Enza	176/224	16.43 (13.77-19.15)	Reference
Enza+Ra223	156/222	19.19 (16.92-24.57)	0.71 (0.57-0.89)

¹Kaplan-Meier method; ²Cox model

	Enza+RAD223 (N=222)	Enza (N=224)
	(95% CI)	(95% CI)
6 months	88.4 (83.3-92.0%)	84.6 (79.1-88.8%)
12 months	68.9 (62.2-74.7%)	60.6 (53.8-66.8%)
18 months	52.9 (45.9-59.4%)	44.5 (37.7-51.0%)
24 months	44.1 (37.2-50.7%)	37.2 (30.7-43.7%)

rPFS results confirmed with longer follow-up and appear little changed from primary analysis.

Final OS – Subgroup analysis



Treatment effect is reduced in older patients (≥ 75 years)

<75 yrs: HR = 0.66
≥ 75 yrs: HR = 1.01

Similar but less pronounced effect for:

- Prior docetaxel administration
- WHO performance status

Reduced treatment effect may be linked with lower prognosis although small number of patients avoid a conclusion.

Survival status and reasons of death over 12 months

Died within 12 months			Died after 12 months		
Enza+Ra223 (N=22)	Enza (N=16)	Total (N=38)	Enza+Ra223 (N=130)	Enza (N=149)	Total (N=279)
N (%)	N (%)	N (%)	N (%)	N (%)	N (%)

If death, give main cause

- progression of disease (PD)	15 (68.2)	11 (68.8)	26 (68.4)	95 (73.1)	108 (72.5)	203 (72.8)
- PD or toxicity indistinguishable	0 (0.0)	1 (6.3)	1 (2.6)	1 (0.8)	1 (0.7)	2 (0.7)
- cardiovascular disease (no toxicity or PD)	2 (9.1)	0 (0.0)	2 (5.3)	5 (3.8)	8 (5.4)	13 (4.7)
- non malignant disease (no toxicity or PD)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (2.0)	3 (1.1)
- new malignancy (≠ prostate cancer)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	2 (1.3)	4 (1.4)
- other (no toxicity or PD)	5 (22.7)	1 (6.3)	6 (15.8)	9 (6.9)	8 (5.4)	17 (6.1)
- unknown	0 (0.0)	3 (18.8)	3 (7.9)	18 (13.8)	19 (12.8)	37 (13.3)

Before the curves cross, the OS difference is observed at 12 months and is only 6 patients.

Regarding deaths due to PD before 12 months, the difference is only 4 patients.

After 12 months, more deaths were observed in the Enza alone arm at any time point.

Safety Summary: TEAE grade ≥ 3

Number of patients (%) with grade 3-5 TEAE	Enza+RAD223 (N=218)	Enza (N=224)
	N (%)	N (%)
All	151 (69.3%)	129 (57.6%)
Hypertension	78 (35.8)	80 (35.7)
Fatigue	12 (5.5)	4 (1.8)
Fracture	12 (5.5)	3 (1.3)
Anemia	13 (6)	5 (2.2)
Neutropenia	10 (4.6)	0
Bone pain	13 (6)	12 (5.4)
Weight decreased	10 (4.6)	2 (0.9)
Spinal cord compression	7 (3.2)	8 (3.6)
Drug-related	63 (28.9%)	42 (18.8%)
Hypertension	26 (11.9)	27 (12.1)
Fatigue	9 (4.1)	3 (1.3)
Anemia	6 (2.8)	0
Neutropenia	7 (3.2)	0

Side effects of special interest:

- 1 MDS
- 1 AML
- 1 CML (drug-related)

All 3 in the combination arm

- 17 osteonecrosis of the jaw:
 - 14 in the combo (5 grade 3)
 - 3 in the enza arm

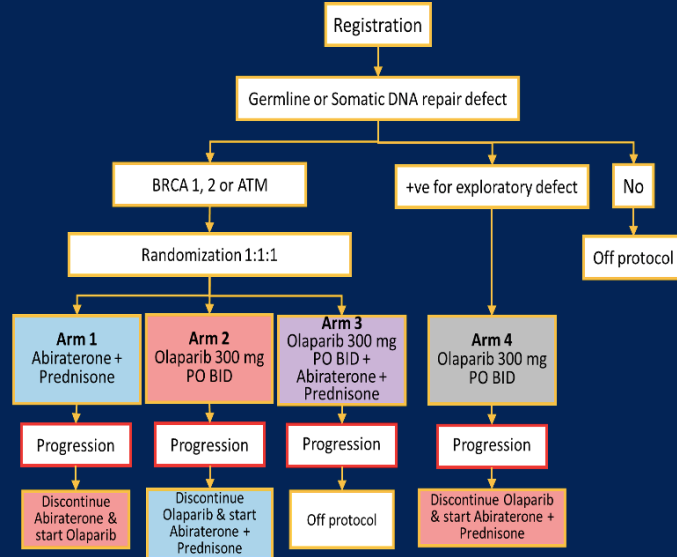
No individual TEAE \geq grade 3 has increased by more than 5% in the combination compared to the enzalutamide alone arm.

Treatment-emergent AEs are all AEs arising from start of treatment until 28 days after last dose of any study drug

Fase II aleatorizado, biomarcador-dirigido

Methods & Study Design

- **Eligibility:** mCRPC (first line: no prior exposure to PARP-I, AR-I, or chemotherapy for mCRPC)
- Eligible pts underwent tumor next-generation sequencing (NGS) & germline testing
- Pts with *BRCA1/2* and/or *ATM* alterations were randomized 1:1:1 to:
 - **Arm I:** abiraterone (1000 mg QD) + prednisone (5mg BID),
 - **Arm II:** olaparib (300 mg BID)
 - **Arm III:** olaparib + abiraterone/prednisone
- Crossover at progression was permitted in Arm I and II pts.
- **Arm IV:** Pts with other HRRm received olaparib (300 mg BID) and switched to *abi/pred* at progression

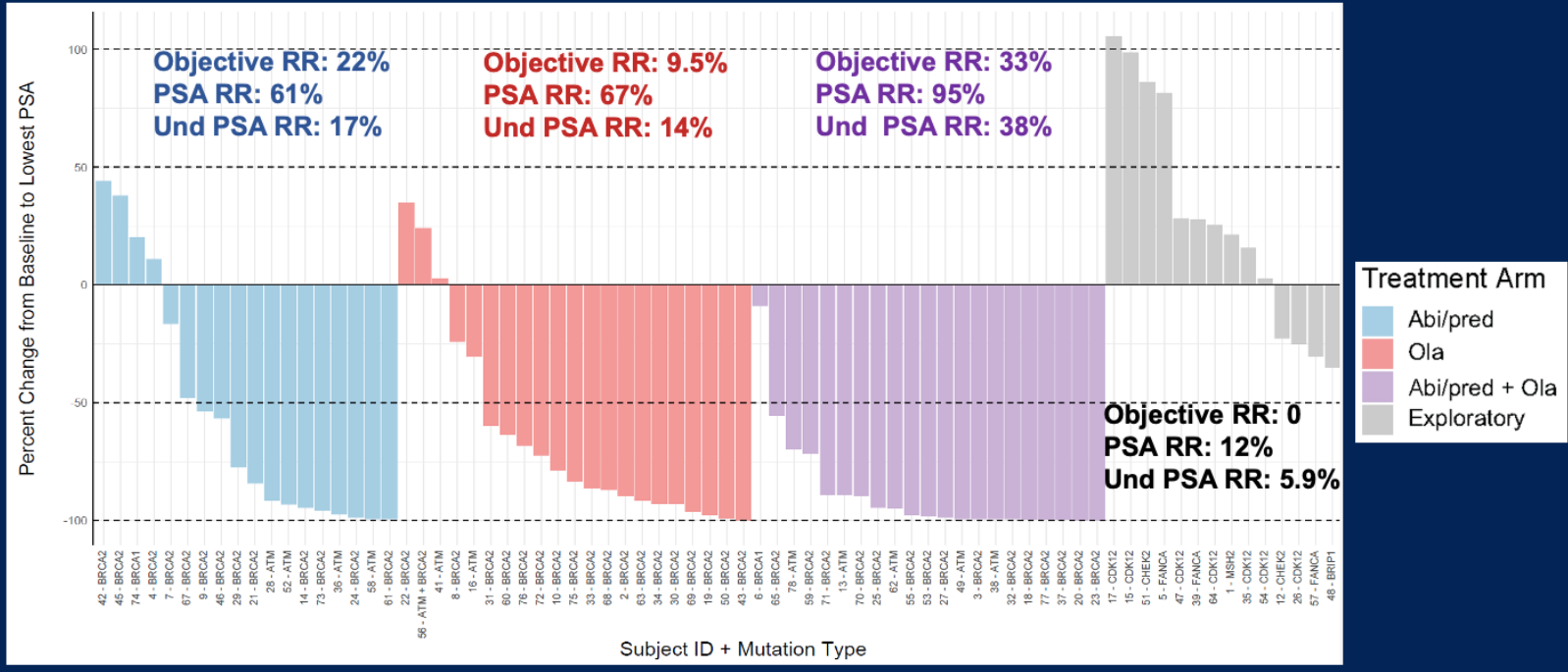


- Primary endpoint: rPFS
- Secondary endpoints: OS, RR, PSA-RR, toxicity

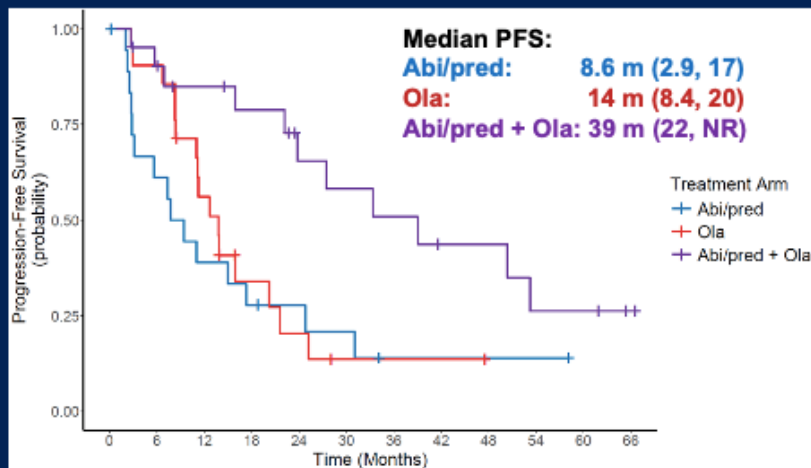
CPMRC. Estudio BRCAAway

	Arm I: Abi/pred (n = 19)	Arm II: Ola (n = 21)	Arm III: Abi/pred + Ola (n = 21)	Arm IV: Exploratory (n = 17)
Age, Median (IQR)	63 (60-69)	68 (66-72)	69 (62-74)	70 (63-78)
Race, N (%)				
Black	2 (11%)	2 (9.5%)	2 (9.5%)	2 (12%)
Hispanic or Latino	0	0	1 (4.8%)	0
Non-Hispanic White	17 (89%)	19 (90%)	18 (86%)	15 (88%)
ECOG PS, N (%)				
0	10 (53%)	15 (71%)	16 (76%)	9 (53%)
1	9 (47%)	6 (29%)	5 (24%)	8 (47%)
Baseline PSA (ng/mL), Median (IQR)	14 (3.7-133)	14 (7.7-33)	15 (6.3-39)	9.3 (5.2-69)
Sites of Metastatic Disease, N (%) ¹				
Bone	16 (84%)	13 (62%)	16 (76%)	13 (76%)
Lymph node	9 (47%)	12 (57%)	10 (48%)	10 (59%)
Visceral ²	2 (11%)	3 (14%)	7 (33%)	5 (29%)
Other ³	1 (5.3%)	2 (9.5%)	0	3 (18%)
Measurable Disease, N (%)	8 (42%)	11 (52%)	9 (43%)	8 (47%)
Genetic Mutation, N (%)				
Germline	9 (47%)	13 (62%)	11 (52%)	-
Somatic	10 (53%)	8 (38%)	10 (48%)	-
Canonical Mutation, N (%) ¹				
ATM	4 (21%)	3 (14%)	5 (24%)	-
BRCA1	2 (11%)	0	1 (4.8%)	-
BRCA2	13 (68%)	19 (90%)	15 (71%)	-
Previous Treatments, N (%) ^{1,4}				
Docetaxel	8 (42%)	4 (19%)	4 (19%)	5 (29%)
Darolutamide/Enzalutamide	1 (5.3%)	0	1 (4.8%)	-
Sipuleucel-T	3 (16%)	4 (19%)	2 (9.5%)	4 (24%)
Other Agent(s) ⁵	2 (11%)	2 (9.5%)	0	1 (5.9%)

Efficacy Summary: Objective and PSA Response Rates



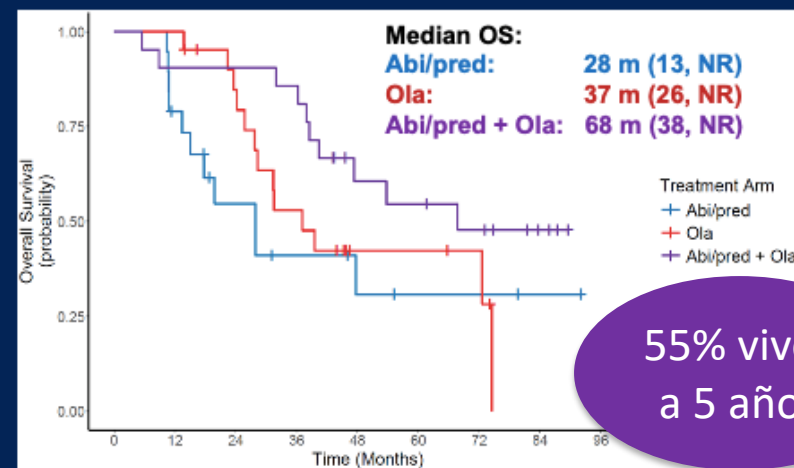
CPMRC. Estudio BRCAAway



HRs:

Abi/pred + Ola vs Abi/pred: 0.33 (0.15, 0.72)

Abi/pred + Ola vs Ola: 0.37 (0.17, 0.84)



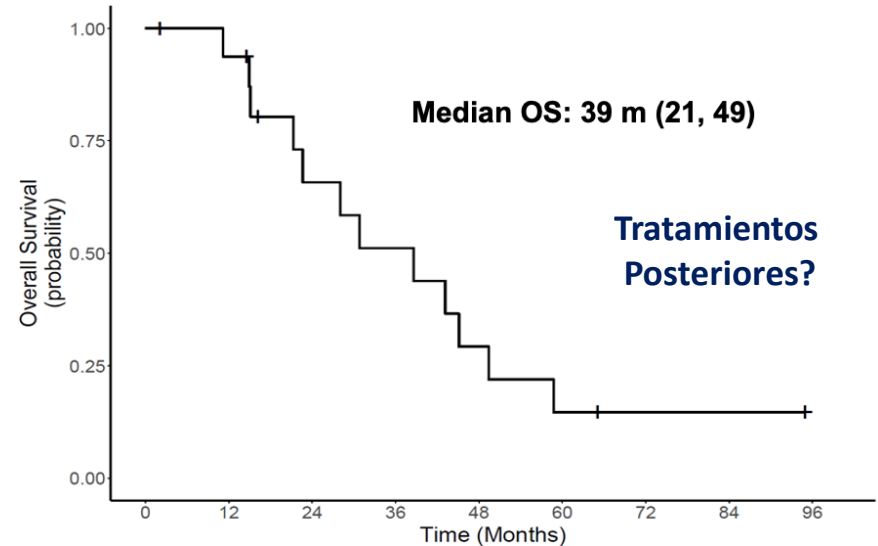
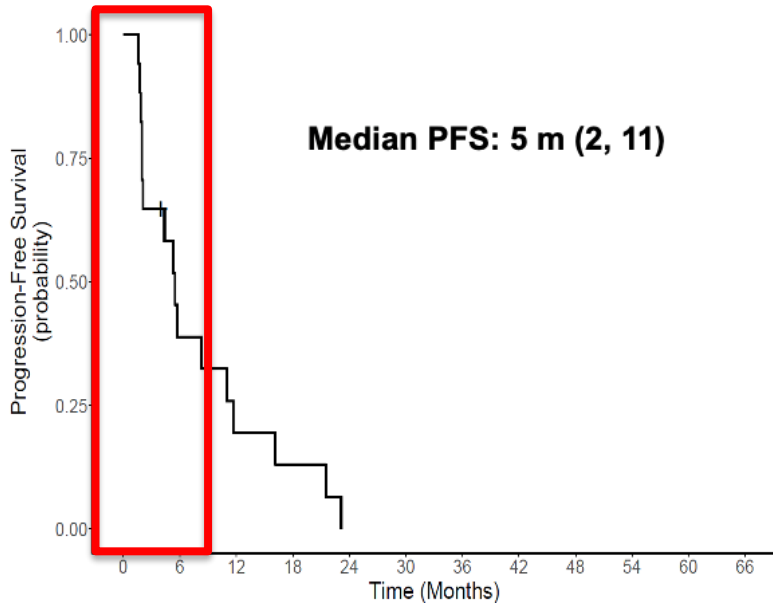
HRs:

Abi/pred + Ola vs Abi/pred: 0.39 (0.16, 0.93)

Abi/pred + Ola vs Ola: 0.51 (0.22, 1.18)

55% vivos
a 5 años

Brazo exploratorio descriptivo no randomizado

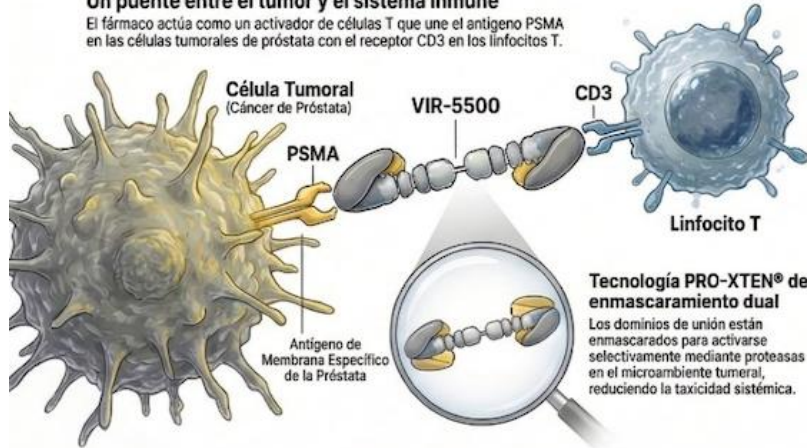


VIR-5500 (AMX-500): Un Nuevo Horizonte en el Tratamiento del Cáncer de Próstata Metastásico Resistente a la Castración (mCRPC)

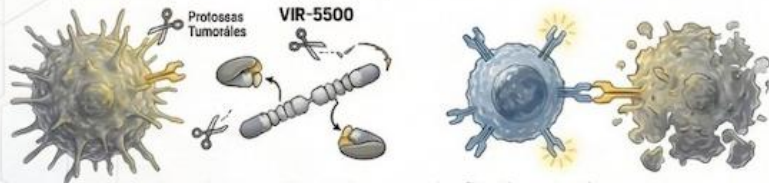
1 MECANISMO DE ACCIÓN – ACTIVADOR DE CÉLULAS T “DUAL-MASKED”

Un puente entre el tumor y el sistema inmune

El fármaco actúa como un activador de células T que une el antígeno PSMA en las células tumorales de próstata con el receptor CD3 en los linfocitos T.



Activación dirigida de linfocitos T



Al unirse a ambos objetivos, provoca la infiltración y activación de células T dentro del tumor para destruir las células cancerosas.

2 DISEÑO DEL ESTUDIO, EFICACIA Y SEGURIDAD

DISEÑO DEL ESTUDIO DE FASE 1 (PART 1 MONOTERAPIA)

Población de pacientes con mCRPC - Mediana de 4 líneas de terapia previas (98% tratados con taxanos y 100% con ARPI) avanzado

Estrategia de escalada de dosis

QW
(Semanal)
Q3W
(Cada tres semanas)

Cohortes de dosis Q3W
(Enfoque en dosis altas)
Escaladas hasta alcanzar niveles críticos de $\times 3000 \mu\text{g/kg}$ para maximizar la respuesta terapéutica.

RESULTADOS PRINCIPALES DE EFICACIA (Dosis $\geq 3000 \mu\text{g/kg}$)

82% PSA50

Una gran mayoría alcanzó una reducción del PSA de al menos el 50%

53% PSA90

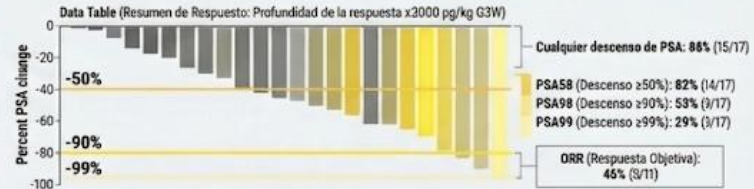
Más de la mitad superó el 90% de reducción

45% ORR

Tasa de Respuesta Objetiva según criterios RECIST v1.1

Respuestas rápidas y duraderas

Descensos profundos de PSA tan pronto como el Ciclo 1 Día 8, con evidencia de durabilidad radiográfica.



PERFIL DE SEGURIDAD Y TOLERABILIDAD

SIN DLTs

Todas las cohortes completaron el estudio sin DLTs significativas.

SRC principalmente de Grado 1

Síndrome de Liberación de Citoquinas (50%) mayoritariamente fiebre leve, sin necesidad de profilaxis con esteroides o anti-IL-6.

12.1% Eventos Adversos Grado ≥ 3

Baja incidencia de eventos adversos graves relacionados con el tratamiento.

AUSENCIA DE ICANS

No se reportaron casos de síndrome de neurotoxicidad asociada a células efectoras inmunes.

No requirement of prophylactic steroids or IL-6 therapy except for exploratory analysis in high dose cohort (n=3)

Pacientes con mCRPC pretratados (ARPI y 1-2 taxanos). Sin terapia previa con radionúclidos.

Escalamiento de Dosis: 75, 100, 125, 150 kBq/kg

Ciclos de 6 semanas (Máximo 4 ciclos)

Objetivos primarios: Evaluar seguridad, eficacia y establecer la Dosis Recomendada para Expansión (RDE).

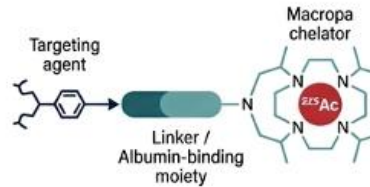
mFU: 7.2 m

Estudio PANThA Fase 1: Resumen Ejecutivo de ²²⁵Ac-PSMA-Trillium en mCRPC

Diseño Molecular Trifuncional

²²⁵Ac-PSMA-Trillium (BAY 3563254) presenta una estructura diferenciada para maximizar eficacia y seguridad:

- **Quelante Macropa™:** Permite un marcaje estable y eficiente con ²²⁵Ac.
- **Unión a albúmina:** Aumenta el tiempo de residencia en plasma, optimizando la exposición tumoral.



Perfil de Seguridad Manejable

0 DLTs (Toxicidades Limitantes de Dosis)

0 Casos de xerostomía Grado 3

Tratamiento bien tolerado. Los eventos adversos (TEAEs) de grado ≥ 3 más comunes fueron linfopenia y anemia, sin reportes de interrupción permanente por toxicidad limitante inmanejable.

Eficacia Excepcional en RDE (125 kBq/kg)

La Dosis Recomendada de Expansión (RDE) demostró respuestas bioquímicas y radiográficas profundas.

83%

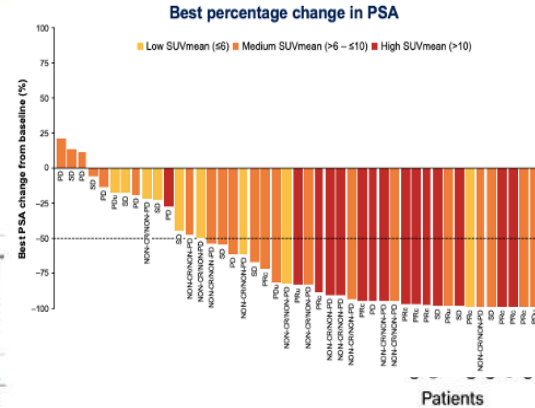
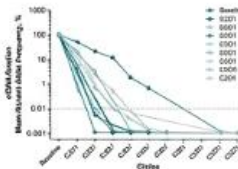
PSA50 (Tasa de respuesta de declive de PSA ≥ 50%)

71%

ORR (Tasa de respuesta objetiva, confirmada y no confirmada)

Validación Biológica Independiente

- **SUVmean basal:** Las respuestas PSA50 ocurrieron en todos los niveles, alcanzando un 93% de respuesta en pacientes con alta captación (SUVmean >10).
- **Dinámica de ctDNA:** Disminución >50% del ctDNA en el 100% de los pacientes con respuesta PSA50 en la dosis RDE. Se observó aclaramiento de ctDNA en el 36% (C2D1).






PSA50 response rate, %	Baseline SUVmean		
	≤6 (N=10)	>6 - ≤10 (N=25)	>10 (N=19)
	22	57	93

PSA50 responses were observed across all baseline SUVmean groups, with greatest response in patients with high SUVmean



Transición a Fase 3

Basado en la ausencia de DLTs, la preservación de las glándulas salivales y una eficacia sin precedentes (ORR 71% en 125 kBq/kg), el estudio transita exitosamente a ensayos de Fase 3 para pacientes con mCRPC. Expansión de dosis actualmente en curso en tres cohortes estratégicas.






1. Cáncer de próstata localizado

- Estudio PEACE-2 
- MMAI-derived prognostic biomarker in CHHiP trial 
- GUNS trial 

2. Cáncer de próstata metastásico hormonosenible

- Capitello-281-PROS 
- PSMAAddition health-related QoL 

3. Cáncer de próstata metastásico resistente a castración

- Estudio PEACE-3 
- Estudio BRCA Away  
- Phase 1 AMX-500 
- Phase 1 225Ac-PSMA 



Actualizaciones tras el Congreso
Americano de Oncología Clínica GU

