GUARD CONSORTIUM

GUARD SYMPOSIUM

6-7 JULIO 2023

GU-Alliance for Research and Development

#guardsymposium2023
@GuardConsortium

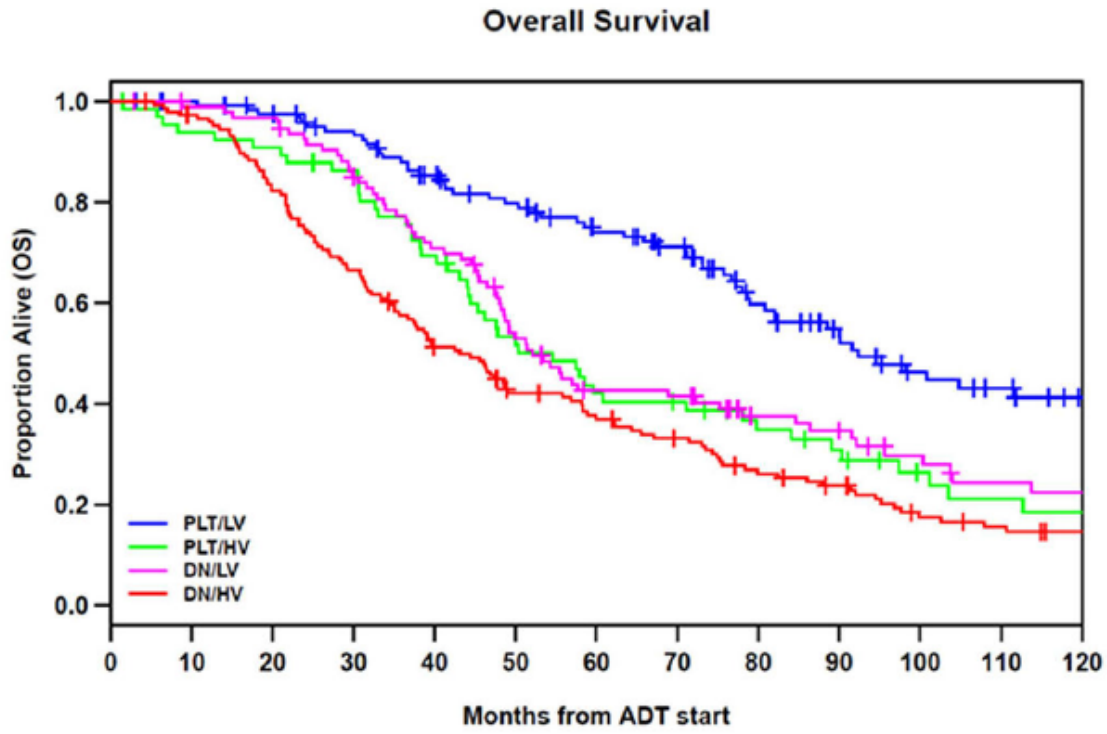
Taller: Cancer de Próstata Sensible a Castración

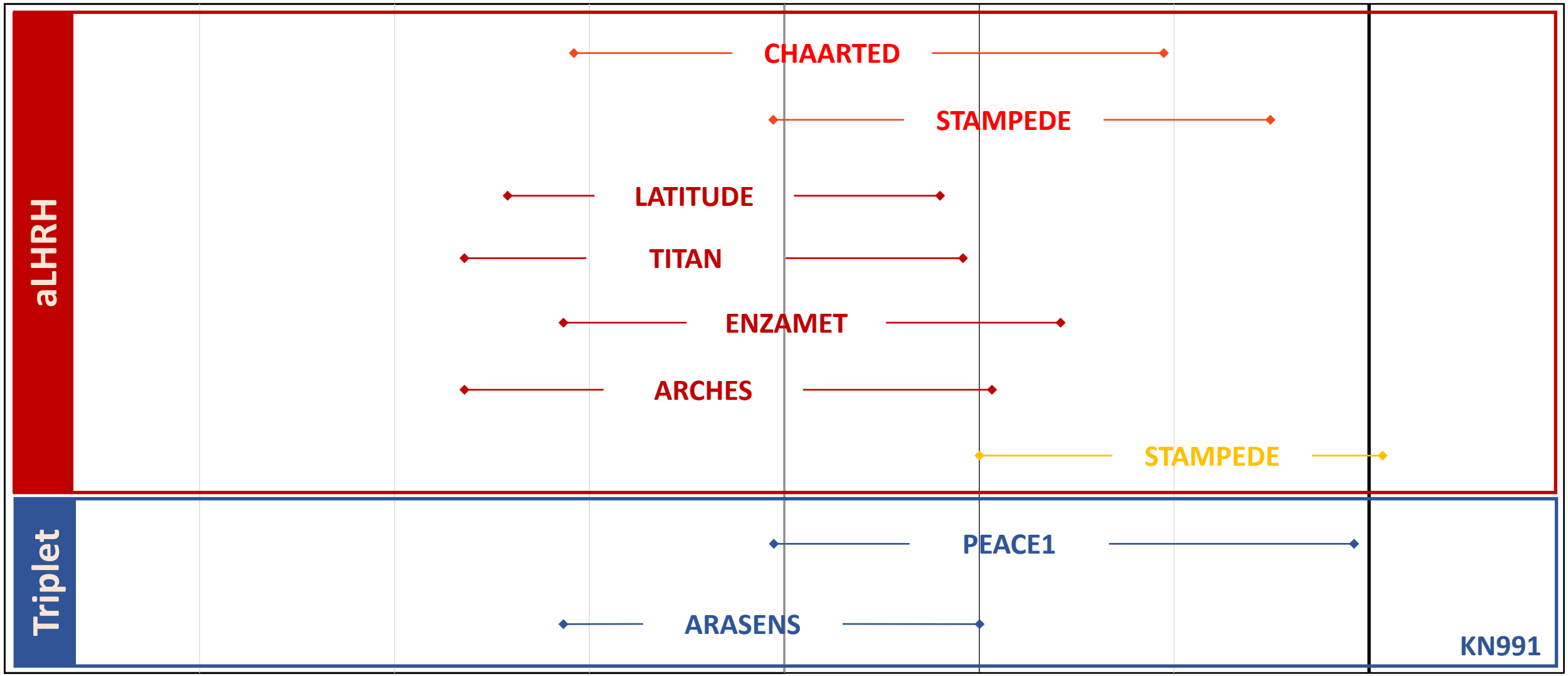
Dr. Fernando López Campos, Hospital Universitario Ramón y Cajal, Madrid

Dr. José Mª Piulats, Institut Català d'Oncologia (ICO) – IDIBELL, Barcelona

Dr. Miguel Ramírez Backhaus, Instituto Valenciano de Oncología – IVO, Valencia

	Synchronic	Metachronic
High	mOS 43.2 months mTTCR 12.2 months	mOS 55,2 months mTTCR 15 months
Low	mOS 51,6 months mTTCR 17,9 months	mOS 92,4 months mTTCR 25,6 months

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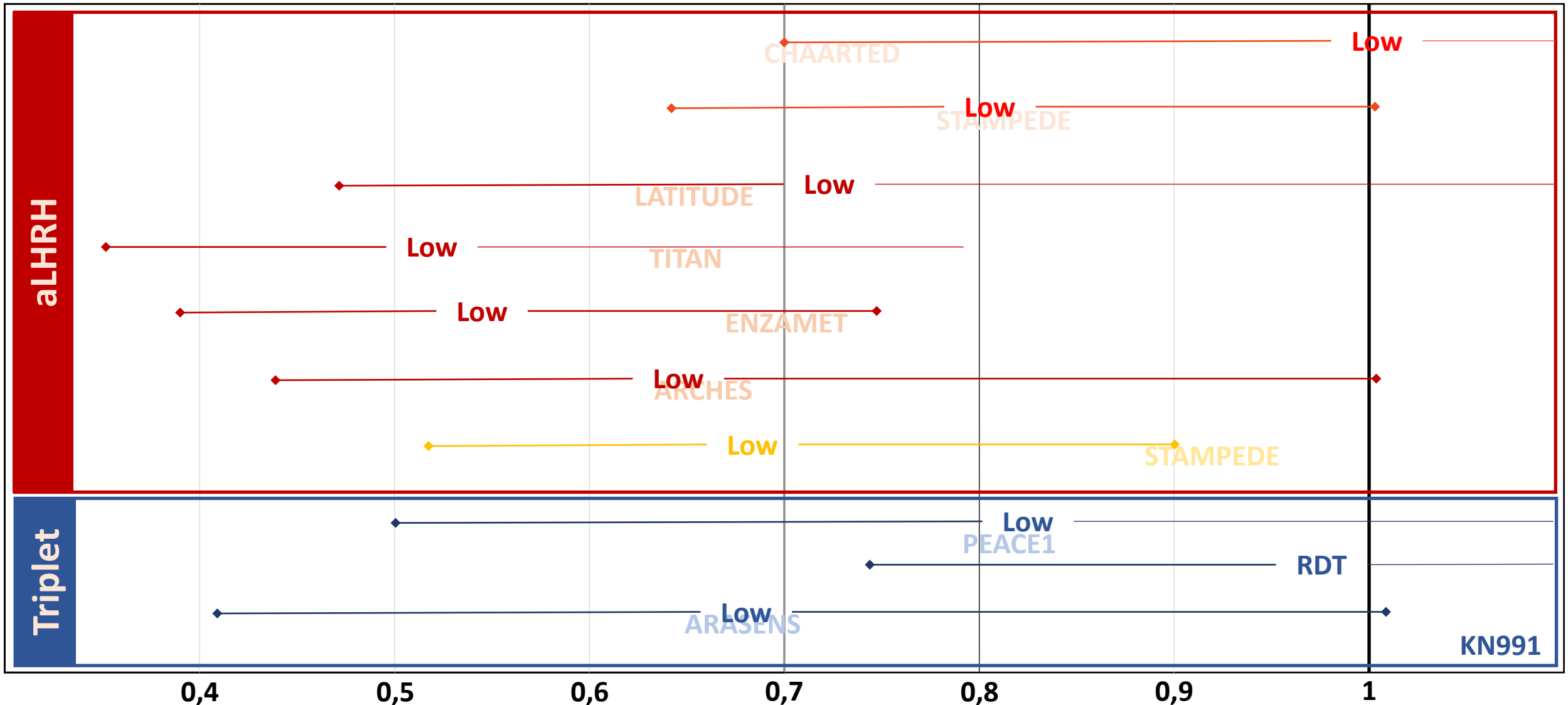
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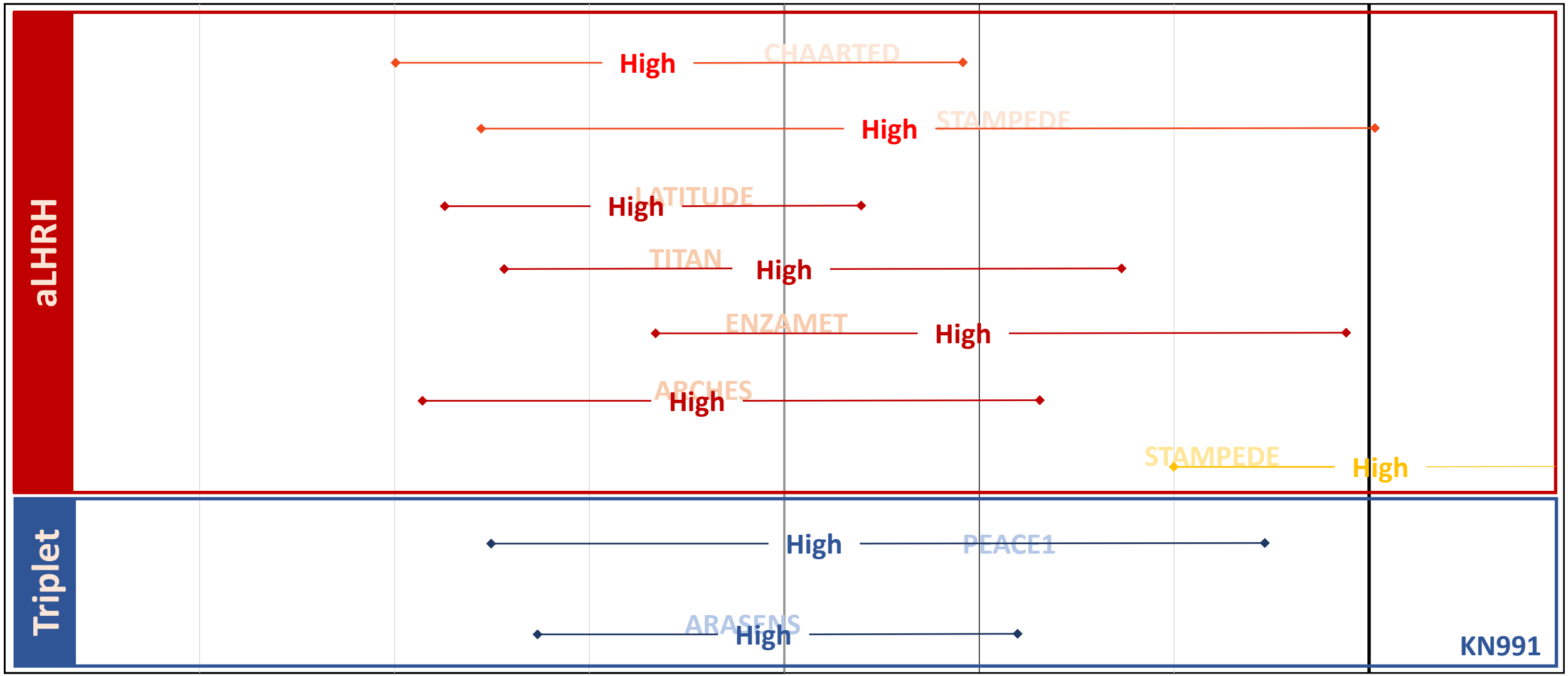
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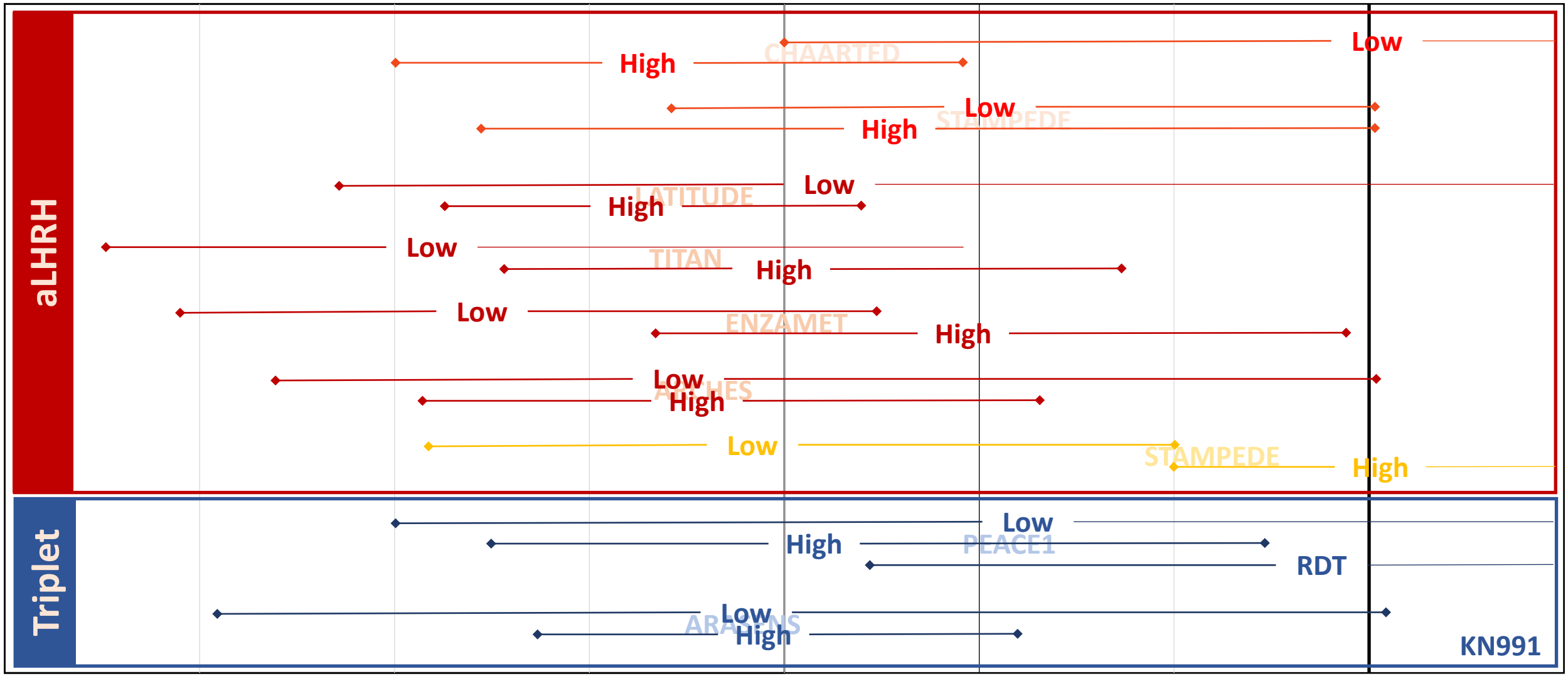
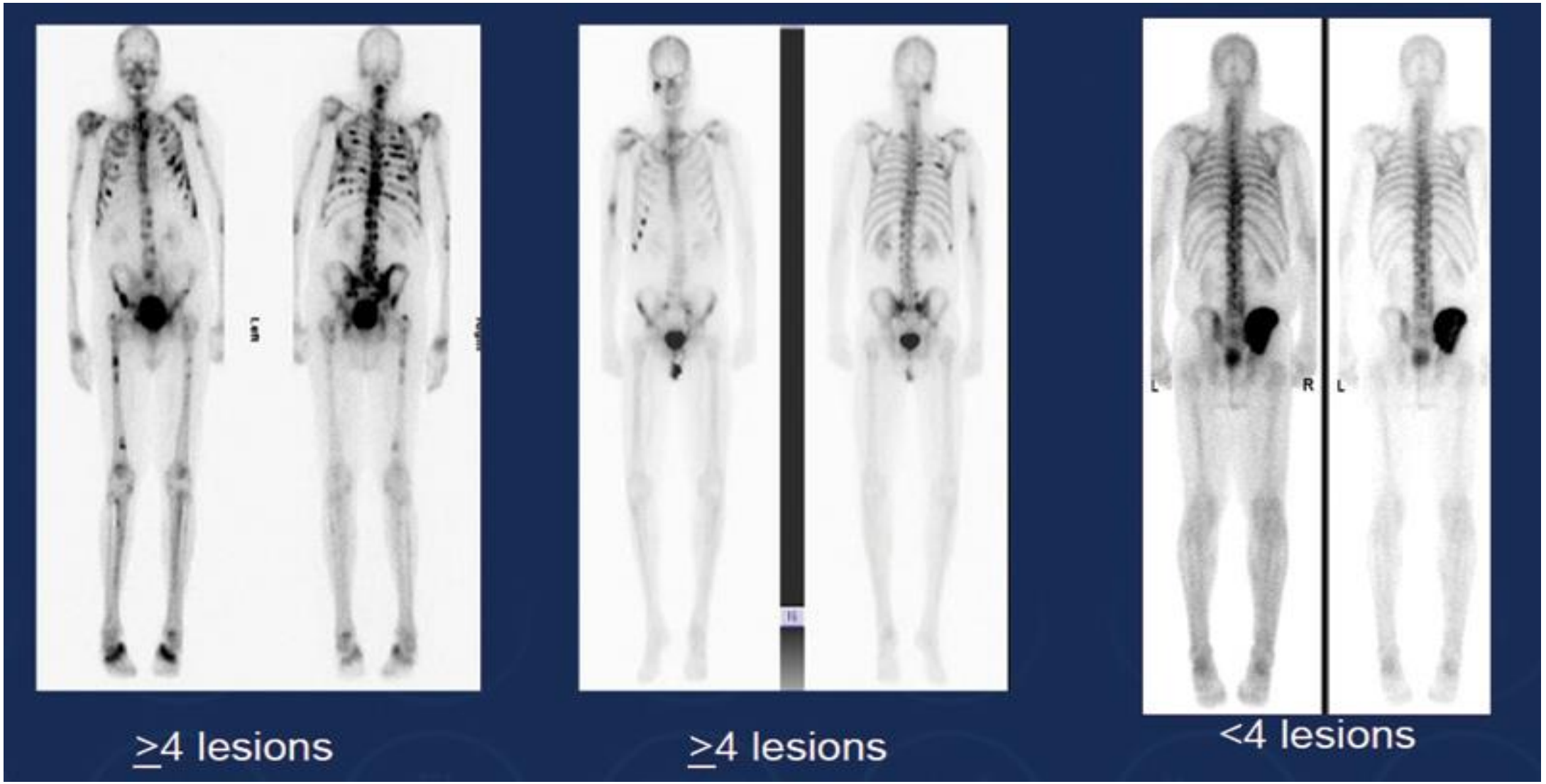
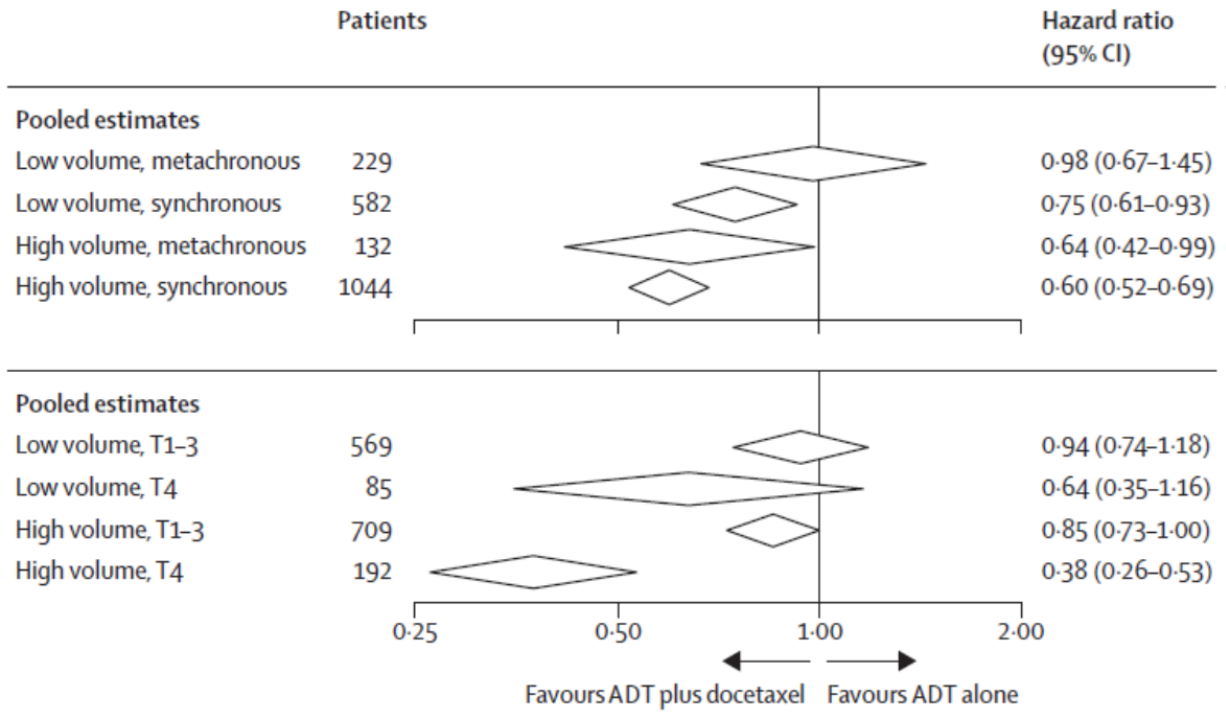
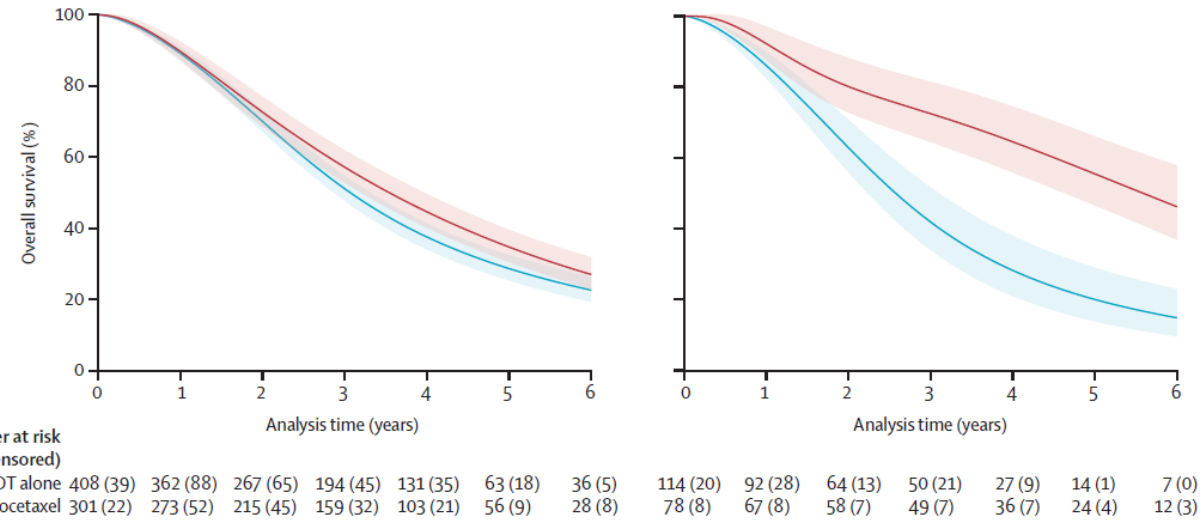
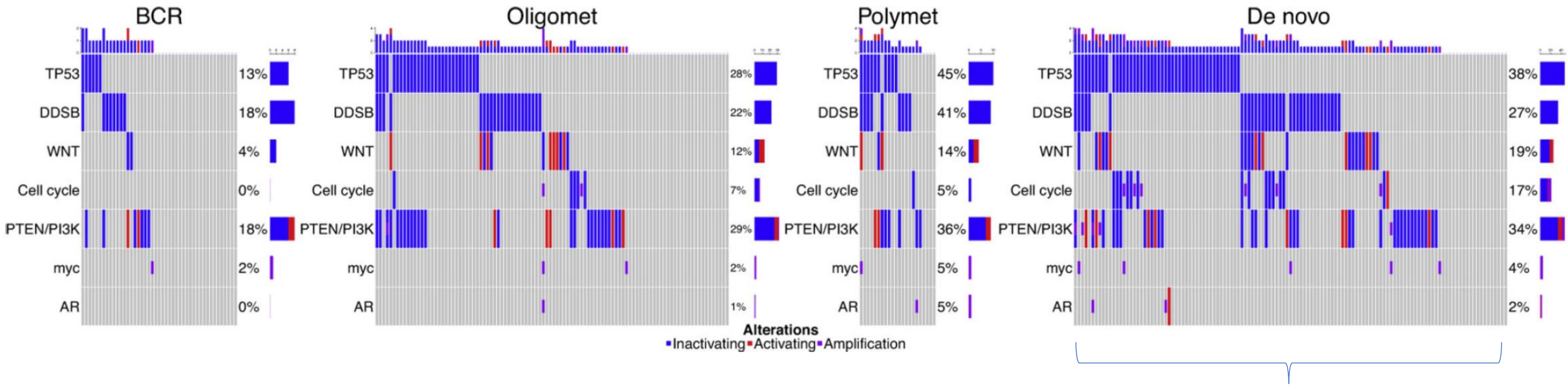



≥4 lesions
≥4 lesions
<4 lesions



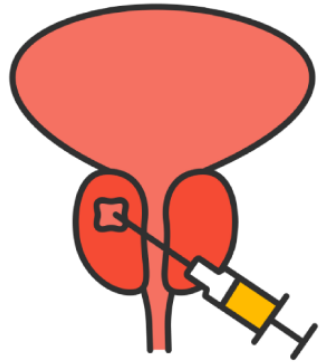


Number at risk (number censored)													
ADT alone	408 (39)	362 (88)	267 (65)	194 (45)	131 (35)	63 (18)	36 (5)	114 (20)	92 (28)	64 (13)	50 (21)	27 (9)	14 (1)	7 (0)
ADT plus docetaxel	301 (22)	273 (52)	215 (45)	159 (32)	103 (21)	56 (9)	28 (8)	78 (8)	67 (8)	58 (7)	49 (7)	36 (7)	24 (4)	12 (3)

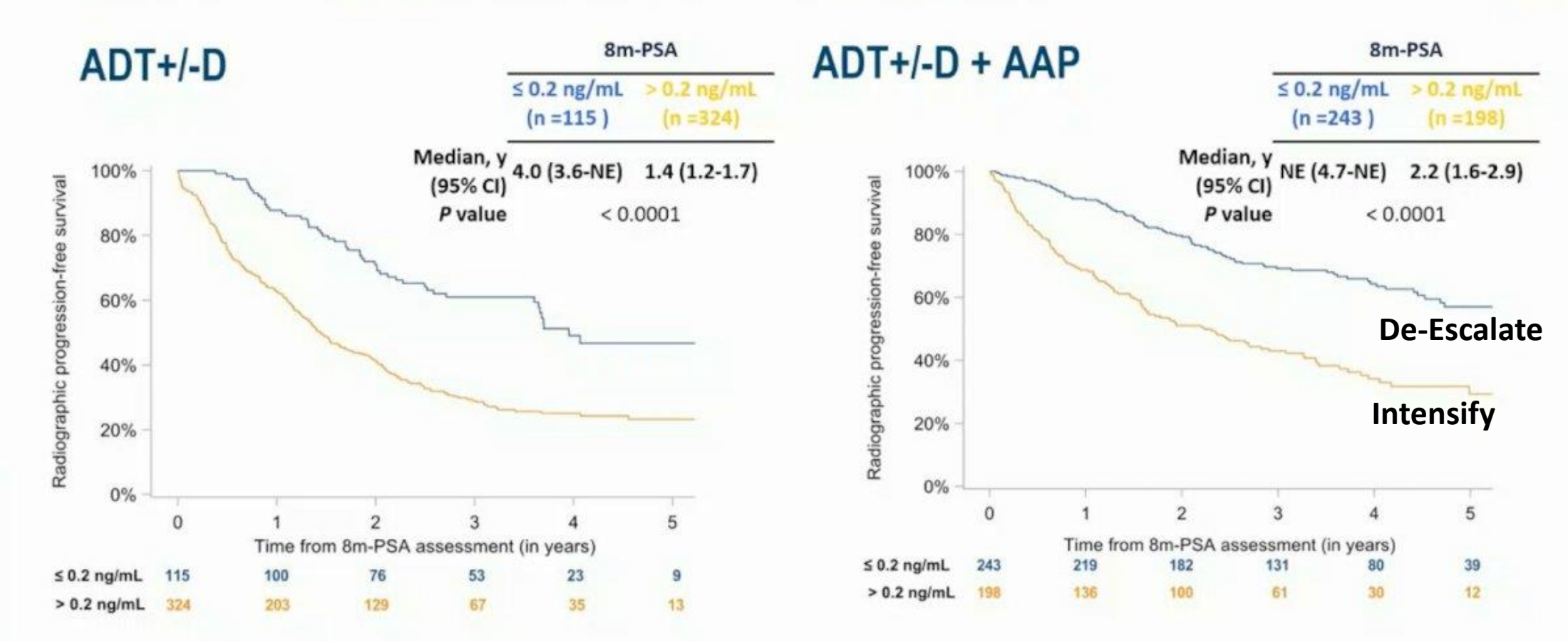


Low/High

TALAPRO3 - DDR/HRR
CAPItello - MTOR deficiency
CYCLONE3 - High Volume/High Risk



Dynamic Approach



BACKGROUND

...like pornography, she "doesn't know how to define it, but I'll know it when I see it". Prior expert consensus at the APCCC included the ability to deliver ablative therapy with curative intent"

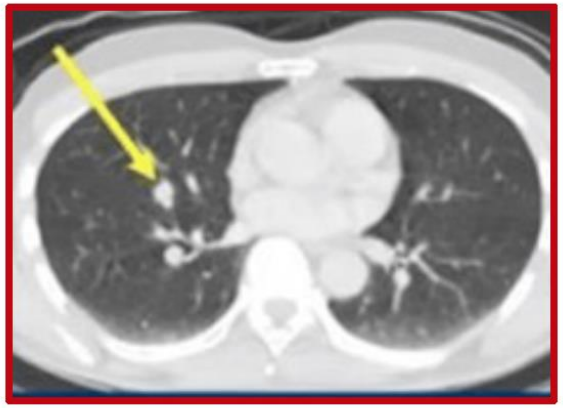
Dr Taplin. APCCC 2022

Dr. Guckenberger

Lancet Oncol 2020; 21: e18–28

OLIGOMETASTATIC ≠LOW VOLUME DISEASE

Confusing, misleading and inconsistent terminology



Major questions are un-answered: definition of Oligometastases

n=3 

n=5 

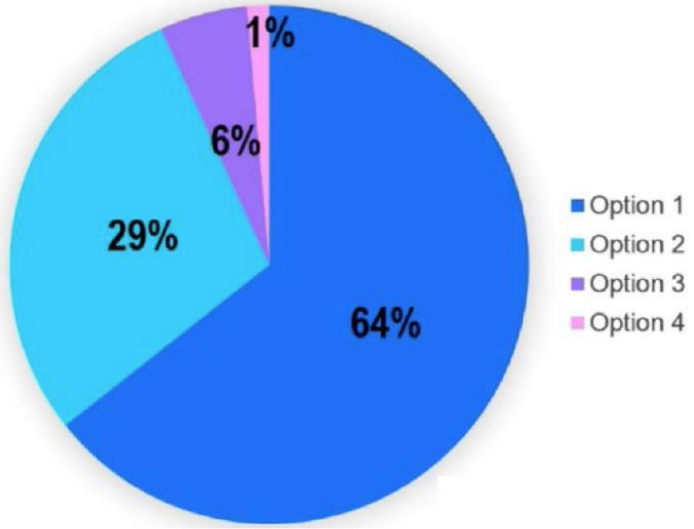
- First prime number ?
- God father, god son, holy spirit ?
- Greeks gods: Zeus, Poseidon und Hades ?
- Three Patriarchs: Abraham, Isaac and Jacob ?

➢Max. of 3 or 5 mets in one or two organs
➢No solid clinical basis, surely no biological

APCCC 2021 Conference

Question #6 asked For local treatment of the primary tumor in mHSPC, what is the cut-off of the number of bone metastases based on conventional imaging for recommending local treatment of the primary tumor?

1. 3 or less bone metastases (64% of respondents)
2. 5 or less bone metastases (29% of respondents)
3. No upper limit of bone metastases (6% of respondents)
4. I don't recommend local treatment of the primary in the metastatic setting (1% of respondents)
5. Abstain (1 respondent)



Option	Votes
Option 1	47
Option 2	21
Option 3	4
Option 4	1
Abstain	1
Total votes	74

Theme: Advances in PET offer greater detection at low PSA for PSA-recurrent disease

PSA	^{11}C-choline	^{18}F-fluciclovine	^{68}Ga-PSMA	^{18}F-DCFPyL	^{18}F-rhPSMA-7
<0.5	14-44%	31%	58%	60%	71%
0.5 to 1.0		50%	73%	78%	78%
1.0 to <2.0	29-81%	66%	93%	72%	86%
>2.0	55-89%	84%	97%	92%	95%

Choline:
Nanni *et al. Eur J Nucl Med Mol Imaging* 2016; **43**: 1601-1610.
Schwenck *et al. Eur J Nucl Med Mol Imaging* 2017; **44**: 92-101.

Fluciclovine:
Andriole *et al. J Urol* 2019; **201**: 322-331.

Ga-PSMA:
Eiber *et al. J Nucl Med* 2015; **56**: 668-674.

DCFPyL:
Rousseau *et al. J Nucl Med* 2019; **60**: 1587-1593.

rhPSMA:
Eiber *et al. J Nucl Med* 2019; [epub ahead of print].

Doctors Indefinitions

OLIGOBELIVERS

"it's always worth it"

OLIGOSCEPTIC

"it may be worth it"

OLIGOHATERS

"not worth it"

OLIGOCONVENIENCE

"I do not have technology, but I do not derive it"

"my machines are too full to treat it"

"this special case (recommended patient) I would like you to treat it"

the paradox of the search for evidence in radiation oncology

Cortesía Dr. Conde-Moreno

EUROPEAN UROLOGY 79 (2021) 565–567

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

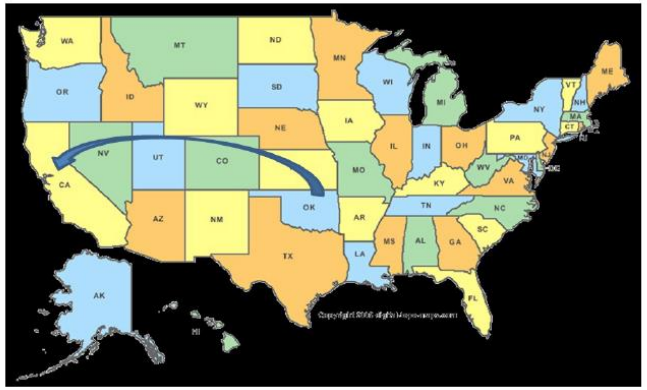
European Association of Urology

Platinum Opinion

When What You See Is Not Always What You Get: Raising the Bar of Evidence for New Diagnostic Imaging Modalities

Nora Sundahl[a,b,*], *Silke Gillessen*[c,d,e,f], *Christopher Sweeney*[g,h], *Piet Ost*[a]

Sundahl et al. Eur Urol 2021



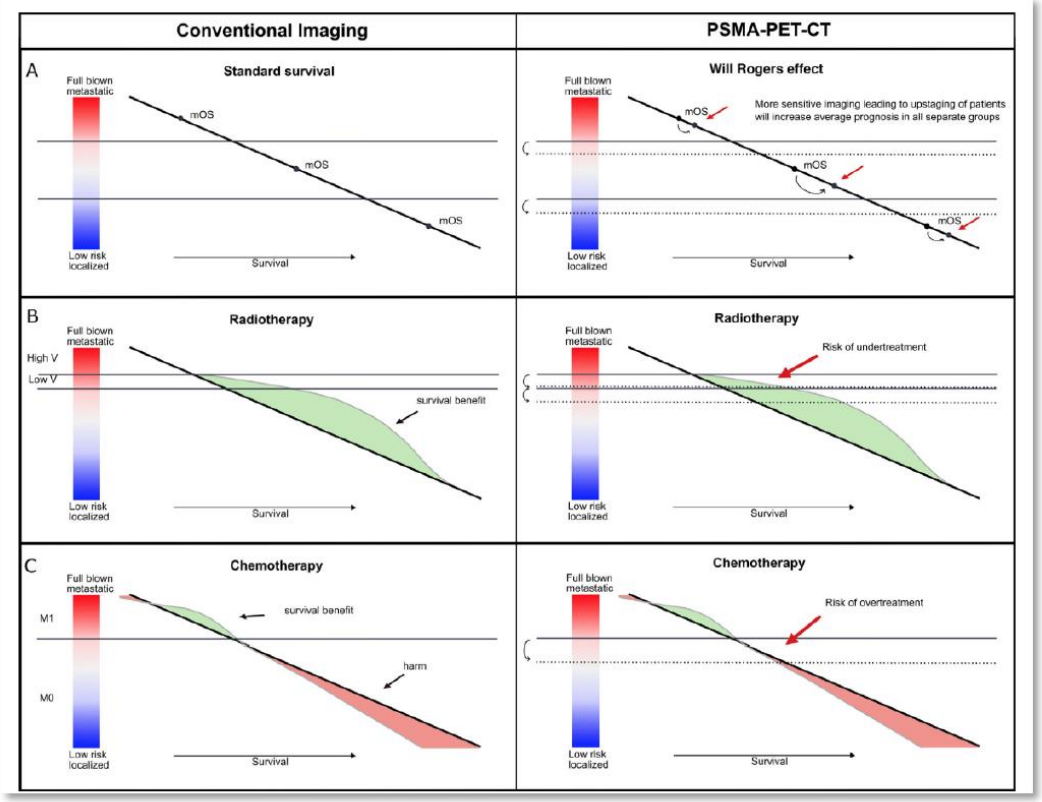
"When the Okies left Oklahoma and moved to California, they raised the average intelligence level in both states."

Will Rogers

posit that using more sensitive novel imaging may be like driving a Ferrari across London when a Mini will also get you there, but with less angst. Conversely, evidence of

PSMA

Imagen convencional



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European Association of Urology

Platinum Opinion

Modern Imaging in Prostate Cancer: Do We Treat Patients, or Their Scans?

Malcolm D. Mason[a,*], *Theodorus H. van der Kwast*[b], *Nicolas Mottet*[c], *Daniela E. Oprea-Lager*[d], *Olivier Rouvière*[e,f], *the members of the EAU-EANM-ESTRO-ESUR-ISUP-SIOG Prostate Cancer Guidelines Panel*[†]

Mason MD et al. Eur Urol 2022

Pandora's box is open: we cannot ignore modern imaging techniques and continue (re)staging and treating disease as we did in the era of conventional imaging. Instead, we must learn how to properly interpret modern imaging and how to treat patients, with an understanding of what that treatment achieves in terms of clinical outcomes such as overall survival, disease recurrence, and quality of life.

mHSPC Treatment Plans by Risk Groups##:

	Presentation of Metastases	Metastases CT/WBBS**	Main Plan Testo Suppress plus	Consider^
Good	Metachronous	3 or less bone mets (+/- NRLN#)	NHT^^	? Add SBRT
Intermediate	Metachronous	4 or more bone mets (visc mets: rare)	NHT	? Add Doc for very select pts
Intermediate	*De Novo* / Synchronous	3 or less bone mets (+/- NRLN)	NHT + **Prostate Rads***	? SBRT if Rx all ? Docetaxel if extensive LAN
Poor	*De Novo* / Synchronous	4 or more bone mets &/or visceral mets	NHT **Add docetaxel if chemofit**	Trials Trials

** CT (incl CT of CT-PET) and Tc Bone scan (future refinements to be made based on PSMA PET and biomarkers)
^trials; *awaiting PEACE-1;#non-regional LNs; ^^NHT: new hormonal therapy = abiraterone, apa- enza-, darolutamide

apccc.org

##Christopher Sweeney
April 2022 Proposal

APCCC ADVANCED PROSTATE CANCER CONSENSUS CONFERENCE

##Potent hormonal Therapy is NEW backbone

@APCCC_Lugano

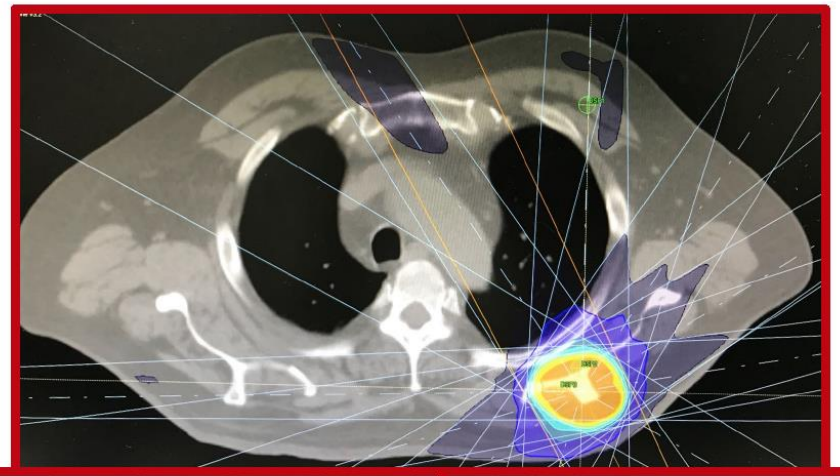
KEEP
CALM
BY
FOCUSING ON
SBRT

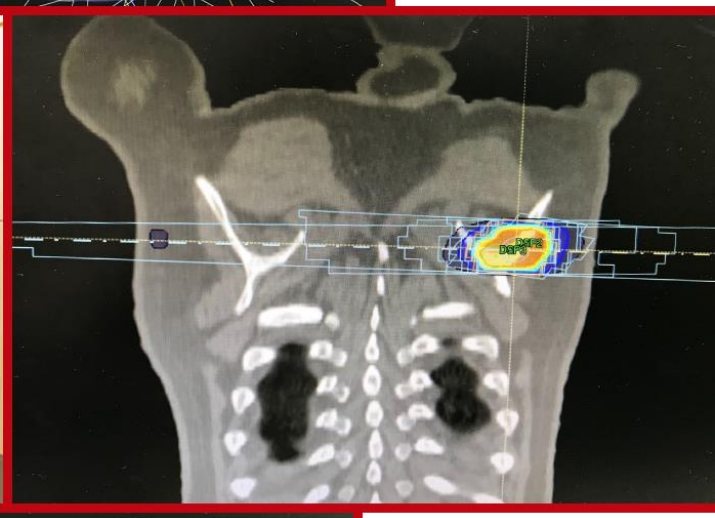
INTENCIÓN ABLATIVA

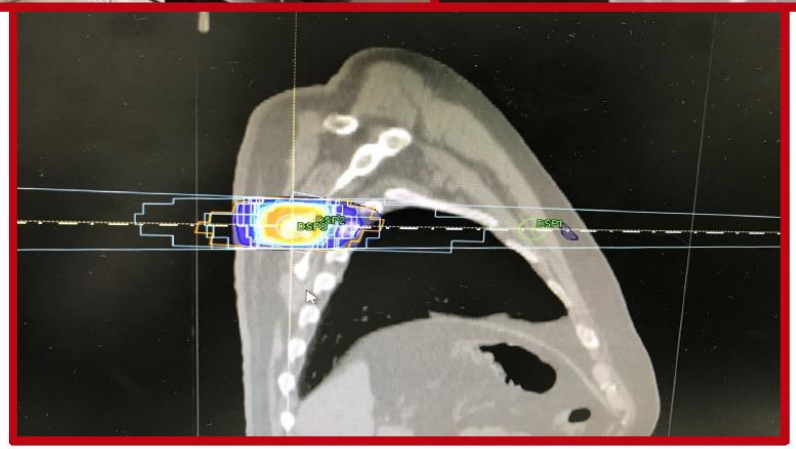
ALTA DOSIS POR FRACCIÓN

GRAN PRECISIÓN

ELEVADO GRADIENTE







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journal homepage: euoncology.europeanurology.com

European Association of Urology

Review of Prospective Trials Assessing the Role of Stereotactic Body Radiation Therapy for Metastasis-directed Treatment in Oligometastatic Genitourinary Cancers

Huynh MA R et al. Eur Urol 2022

CLINICAL TRIALS

STOMP

ORIOLE

Trial	Year	Study design	Arms (n = patients/ lesions)	Screening imaging	# Mets allowed	Concomitant ADT (%)	Lesion characteristics	MDT details	Median follow-up (mo)	Local control	PFS	Median ADT-FS	QoL	Toxicities
STOMP	2018	Phase II RCT	Metastatic-directed therapy (31/51) vs surveillance (31/65)	Choline PET-CT	1–3	0	Bone 39%, node 55%, mixed 5%, viscera 2%	PLND (n = 5), metastasectomy (n = 1), SBRT (n = 25) 30 Gy/3F, PTV = GTV + 2–5 mm	36	100 (MDT) vs 77% (OBS), at last FU, median 36 mo	PSA PFS 10 mo (MDT) vs 6 mo (OBS)	21 mo (MDT) vs 13 mo (OBS), p = 0.11	No difference	No grade ≥3
ORIOLE	2020	Phase II RCT	SABR (n = 36) vs observation (n = 18)	CT, MRI, or bone scan; PSMA-PET performed but investigators blinded	1–3	0	Bone 39%, node 61%	19.5–48 Gy/3–5F	19	98.9% (6 mo)	Progression at 6 mo—19% (SBRT) vs 61% (OBS)	NR	No difference	No grade ≥3
POPSTAR	2018	Phase I single arm	SBRT to all mets (33/50)	CT, bone scan, NaF-PET	1–3	33	Bone 61%, node 36%, bone and node 3%	20 Gy/1F prescribed to periphery at 80% of maximal dose, covering 95% target volume; PTV = GTV + 5 mm	24	97%/93% (1/2 yr)	58%/39% (1/2 yr DPFS)	2-yr ADT-FS 48%[a]	No difference	1 grade 3 (3%, vertebral fracture)
PSMA-MRgRT	2021	Phase II single arm	SBRT or surgery to all mets (37)	Negative conventional staging and positive PSMA-PET-MR/CT	1–5	0	Node 92%, bone 8%	SBRT (n = 27) 27–30 Gy/3F; surgery (n = 10)	16	22% CR (100% PSA decline, PSA <0.05 ng/ml); 38% PR (≥50% PSA decline)		17.7 mo		1 grade 3 ureter injury and 1 grade 3 DVT in surgery MDT cohort

CLINICAL TRIALS

Trial	Oligometastatic setting	Number of mets	Screening imaging	Design	Primary endpoint	Therapy
NCT03298087	De novo/synchronous	5	NaF-PET-CT or PSMA PET-CT	Single-arm phase II	PSA response	Radical prostatectomy + SABR + 6 mo of ADT (lupron, apalutamide, abiraterone)
NCT03784755 (PLATON)	De novo/synchronous	3	CT/MRI of chest/abdomen/pelvis + bone scan	Randomized phase II	FFS	SOC systemic therapy + prostate ablative therapy (if untreated low-volume) ± SBRT to all sites
NCT02742675	De novo/synchronous	5	Bone scan, CT, and/or MRI	Randomized phase II	PFS	ADT (LHRH agonist and oral antiandrogen) ± definitive surgery or radiation to the prostate
NCT05223803 (TERPS)	De novo/synchronous	5	CT/MRI and bone scan or fluciclovine, choline, or PSMA PET-CT scan	Randomized phase II	2-yr FFS	Best systemic therapy and prostate RT ± SBRT
NCT04443062 (BULLSEYE)	Synchronous or metachronous hormone sensitive (not eligible for SBRT or surgery)	5	18F-PSMA-PET-CT	Randomized phase II	6-mo PFS	SOC vs 177Lu-PSMA-617
NCT04115007 (PRESTO, GETUG AFU)	Synchronous or metachronous hormone sensitive	5	Choline-PET/CT or PSMA PET/CT or whole-body MRI	Randomized phase III	CRPC-free survival	SOC ± SBRT
NCT03361735	Synchronous or metachronous hormone sensitive	4	Any imaging	Single-arm phase II	Time to treatment failure	SBRT + ADT + radium-223
NCT04619069	Synchronous or metachronous hormone sensitive	3	Positive on PSMA-PET with no mets on conventional imaging (CT/bone scan ± MRI) within 3 mo of ADT start	Randomized phase I	Proportion of patients willing to enter RCT	Intermittent ADT ± SBRT
NCT05146973 (PROST ACT TARGET)	Synchronous or metachronous hormone sensitive	5	PSMA-PET	Single-arm phase II	PSA PFS	EBRT + radiolabeled PSMA-targeting antibody, 177Lu-TLX591
NCT05209243 (START MET)	Synchronous or metachronous hormone sensitive	5	Conventional (CT/bone scan; 1–3) or enhanced (choline or PSMA-PET; 1–5) imaging	Randomized phase III	Radiologic PFS	SOC (ADT + RT to the primary tumor (previously not treated) + second-generation hormonal treatment) + SBRT
NCT04983095 (METRO)	Synchronous or metachronous hormone sensitive	5	PSMA-PET	Randomized phase III	FFS (time to CRPC)	SOC ± SBRT
NCT03940235 (RADIOSA)	Metachronous oligorecurrence	3	Choline-PET/CT or whole-body MRI	Randomized phase II	PFS	SBRT ± 6-mo ADT
NCT04011410	Metachronous oligorecurrence	3	Not specified	Single-arm phase II	Change in prostate apoptosis response 4 level	SBRT + hydroxychloroquine
NCT04599686	Metachronous oligorecurrence	5	Ga-PSMA-PET	Randomized phase II	1 yr ADT-free survival, RT-related toxicity, time to CRPC	ADT vs SBRT
NCT04037358 (RAVENS)	Metachronous oligorecurrence	3	Conventional or PSMA-PET (number of sites must match)	Randomized phase II	PFS	SBRT ± radium-223
NCT04748042 (FAALCON)	Metachronous oligorecurrence	5	Molecular imaging (eg, 68Ga-PSMA PET/CT or Axumin, excludes FDG-PET)	Single-arm phase II	Progression at 24 mo	Abiraterone, ADT, radiation to all metastases, and olaparib
NCT04031378	Castrate-sensitive or castrate-resistant oligometastatic	3	68Ga-PSMA or 18F-choline PET/CT	Randomized phase II	PSA relapse	Single-dose radiation therapy (24 Gy × 1) ± 6 mo of adjuvant systemic therapy
NCT05053152 (NRG Promethean)	Metachronous oligorecurrence	5	Fluciclovine or PSMA-PET	Randomized phase II	Radiologic PFS	SBRT ± relugolix
NCT04641078 (DART)	Metachronous oligorecurrence	5	PSMA-PET	Randomized phase II	2-yr MFS	SBRT ± darolutamide
NCT03795207 (POSTCARD)	Metachronous oligorecurrence	5	FCH-PET CT or Ga-PSMA PET CT, not seen on conventional imaging (bone scan or CT scan)	Randomized phase II	2-yr PFS	SBRT ± durvalumab
NCT05352178 (SPARKLE)	Metachronous oligorecurrence	5	PSMA-PET	Randomized phase III (3 arm)	Polymetastatic-free survival	MDT (SBRT or surgery) vs MDT + 1-mo ADT vs MDT + 6-mo ADT + enzalutamide
NCT03902951	Metachronous oligorecurrence	5	PSMA-PET	Single-arm phase II	PSA response	SBRT + lupron, abiraterone, apalutamide
NCT02274779 (OLIGOPELVIS/ GETUG P07)	Metachronous oligorecurrent Nodes	5	18-F PET	Single-arm phase II	2-yr biochemical or clinical RFS	High-dose IMRT (50–66 Gy/30F) + 6-mo Eligard
NCT03630666 (OLIGOPELVIS2)	Metachronous oligorecurrent nodes	5	FCH-PET or PSMA-PET	Randomized phase III	PFS	Intermittent ADT ± salvage high-dose intensity modulation radiotherapy (IG-IMRT)
NCT03569241 (PEACE V-STORM)	Metachronous oligorecurrent nodes	3	FCH-PET or PSMA-PET	Randomized phase II	2-yr MFS	(MDT [salvage lymph dissection or SBRT] + 6-mo ADT) ± whole pelvis radiation
NCT04423211 (ECOG-ACRIN 8191 INDICATE)	Metachronous oligorecurrence	NA	FCH-PET with negative or equivocal extrapelvic mets on conventional imaging after prostatectomy	Randomized phase III	PFS, PFS prolongation in patients ± PET evidence of extrapelvic metastasis	Cohort 2: SOC salvage therapy and apalutamide ± MDT to PET-positive lesions

Huynh MA R et al. Eur Urol 2022

IRAD-START-MET

START-MET: SbrT Androgen Receptor Therapy METastatic HS prostate cancer.

mHSPC, non-blinded, randomized, phase III, multi center study.

ClinicalTrials.gov Identifier: NCT05209243

Meets following criteria

Inclusion criteria

- **Castration sensitive → Local prior treatment allowed**
- **ECOG PS 0 or 1**
- **Distant metastatic disease by ≤ 3 lesions based on CT and Bone Scan and ≤ 5 lesions based on Coline or PSMA PET/TC**

***Stratification factors*:**

- **Prior local treatment**
- **New Imaging technique (Coline vs PSMA PET/TC)**

Exclusion criteria

- **Metastases in previously irradiated areas**
- **Prior docetaxel or second generation hormonal treatments**
- **Tumor stage T4**

N = 266

Randomization 1:1

STANDARD OF CARE + SBRT (all metastatic lesions)

ADT+ RT to the primary tumor (previously not treated) + Second generation hormonal treatment

STANDARD OF CARE

ADT+ RT to the primary tumor (previously not treated) + Second generation hormonal treatment

ENDPOINTS

Primary endpoint:
- **rPFS**

Key Secondary endpoints:
- **Overall survival**
- **Time to cytotoxic chemotherapy**
- **Time to PSA progression**
- **Time to pain progression**
- **Time to castration resistance**
- **Time to skeletal-related event**
- **Quality of life and safety profile**
-

Exploratory endpoints:

- **Biomarkers assessment**
- **Local control**
- **Second progression free survival (PFS2)**
- **Time to symptomatic progression**

(ADT+ Abi/Apa/Enza/Daro)

PIs: Conde-Moreno, López-Campos, Gómez-Iturriaga.

JAMA Oncology | Original Investigation

Addition of Metastasis-Directed Therapy to Intermittent Hormone Therapy for Oligometastatic Prostate Cancer

The EXTEND Phase 2 Randomized Clinical Trial

Tang C et al. JAMA Oncol 2023

EXTEND

EXTEND intermittent prostate cancer

Major Inclusion Criteria

- Histologic diagnosis of prostate cancer
- ≤5 metastases
- ≥2 months of prior HT (either GNRH agonist/antagonist +/- 2nd generation HT)
- Untreated primaries allowed, but must be treated regardless of randomization

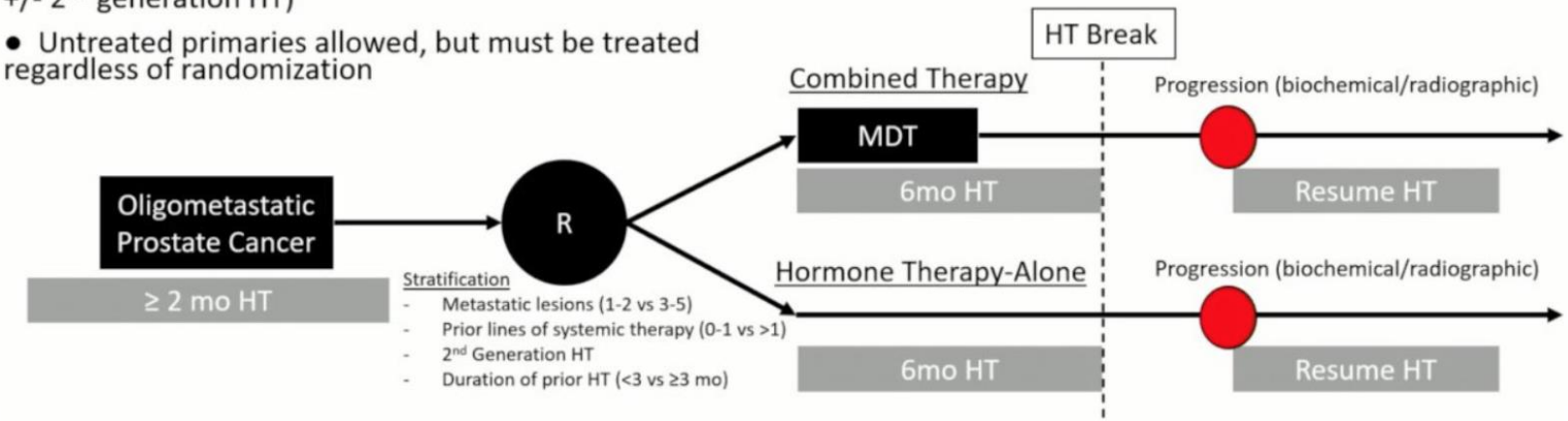


Table. Baseline Patient Characteristics (continued)

Characteristic	Participants, No. (%)[a] Combined therapy (n = 43)	Hormone therapy only (n = 44)
Second-generation androgen receptor agent use		
None	24 (56)	27 (61)
Abiraterone	15 (35)	13 (30)
Apalutamide	3 (7)	3 (7)
Enzalutamide	1 (2)	1 (2)
Metastatic lesions, No.		
1	12 (28)	21 (48)
2	18 (42)	13 (30)
3	8 (19)	4 (9)
4-5	5 (12)	6 (14)
Baseline imaging modality		
CT CAP and bone scan	33 (77)	33 (75)
Fluciclovine F 18 PET/CT	10 (23)	11 (25)

JAMA Oncology | Original Investigation

Addition of Metastasis-Directed Therapy to Intermittent Hormone Therapy for Oligometastatic Prostate Cancer

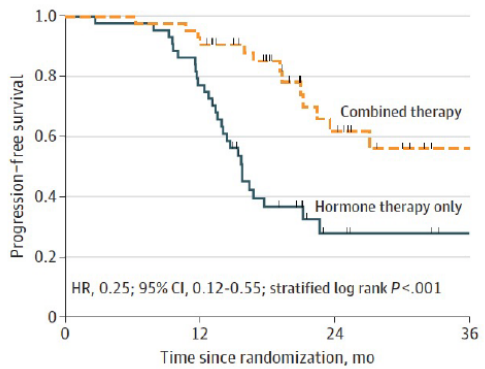
The EXTEND Phase 2 Randomized Clinical Trial

Tang C et al. JAMA Oncol 2023

EXTEND

Figure 2. Primary and Key Secondary End Points

A Progression-free survival by randomization arm

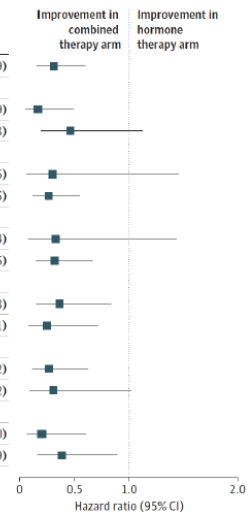


No. at risk

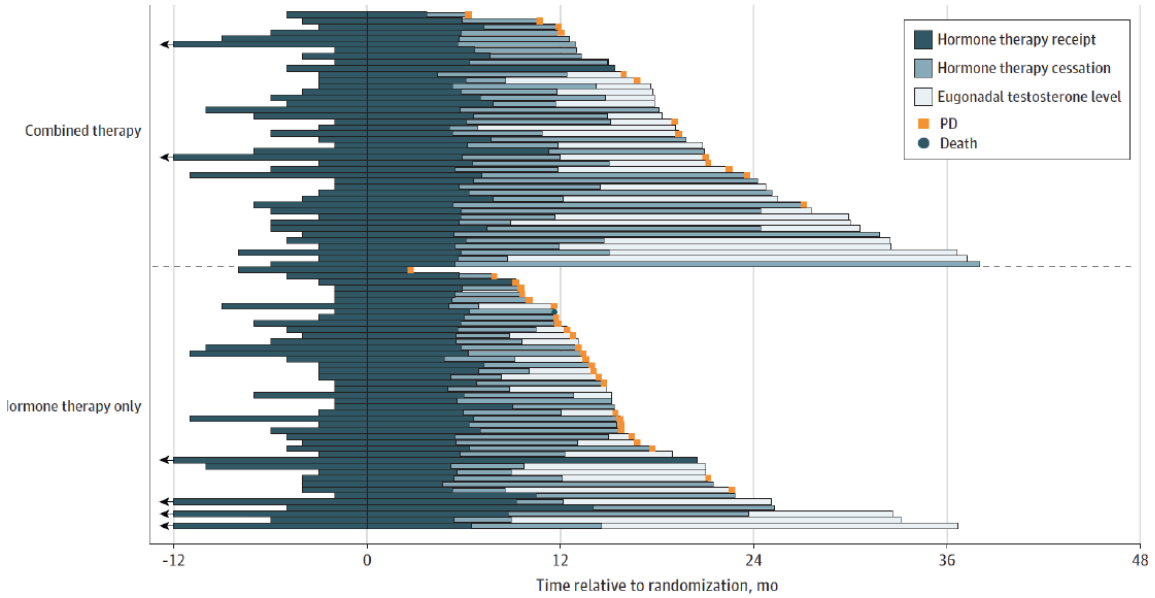
Hormone therapy only	44	34	5	1
Combined therapy	43	40	15	3

Figure 3. Analysis of Progression-Free Survival According to Key Patient Subgroups

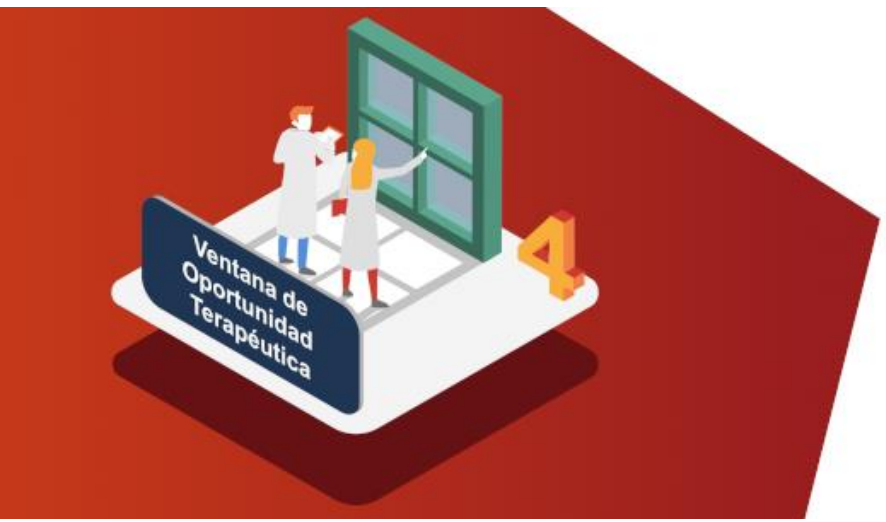
Study	Events, No./total No.	Hazard ratio (95% CI)
Overall	41/87	0.31 (0.16-0.59)
PSA level, ng/mL		
≤0.2	21/50	0.16 (0.05-0.49)
>0.2	20/37	0.46 (0.19-1.13)
Stage		
N1 and M1a	8/28	0.29 (0.06-1.46)
M1b and M1c	33/59	0.26 (0.12-0.55)
Prior primary treatment		
None	8/24	0.33 (0.07-1.44)
Any	33/63	0.31 (0.15-0.66)
Use of second-generation anti-androgens		
No	25/51	0.36 (0.15-0.83)
Yes	16/36	0.24 (0.08-0.71)
Metastatic lesions, No.		
1-2	28/64	0.26 (0.11-0.62)
3-5	13/23	0.30 (0.09-1.02)
Hormone duration before enrollment, mo ≤3		
≤3	17/35	0.20 (0.07-0.60)
>3	24/52	0.38 (0.16-0.89)



C Duration of testosterone states by randomization arm



Recidiva Bioquímica.



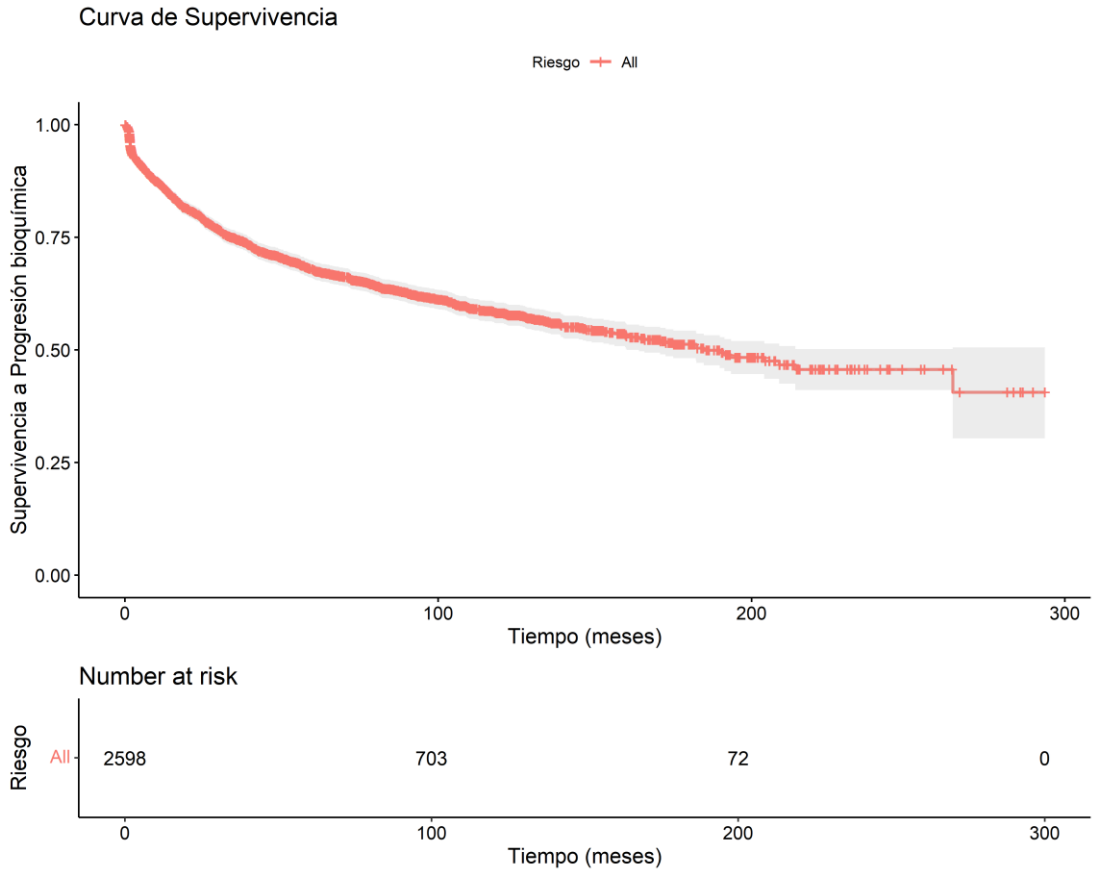
Ventana de oportunidad terapéutica

2625 pacientes

Edad mediana 63,97 (40-80)

Seguimiento mediano : 99 meses

Eventos RB. 920 (35,41%)



Datos no publicados

0,1 0,2 0,3 0,4 0,5 1 ng/ml

NCCN GUIDELINES

eau Guidelines

EMBARK

1 ng/ml

0,1 0,2 0,3 0,4 0,5

NCCN GUIDELINES

eau Guidelines

Recurrencia

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Guidelines

Review – Prostate Cancer

Prognostic Value of Biochemical Recurrence Following Treatment with Curative Intent for Prostate Cancer: A Systematic Review

Thomas Van den Broeck[a,b,1,*], *Roderick C.N. van den Bergh*[c,1], *Nicolas Arfi*[d,1], *Tobias Gross*[e], *Lisa Moris*[a,b], *Erik Briers*[f], *Marcus Cumberbatch*[g], *Maria De Santis*[h,i], *Derya Tilki*[j,k], *Stefano Fanti*[l], *Nicola Fossati*[m,n], *Silke Gillessen*[o,p,q], *Jeremy P. Grummet*[r], *Ann M. Henry*[s], *Michael Lardas*[t], *Matthew Liew*[u], *Olivier Rouvière*[v], *Jakub Pecanka*[w,x], *Malcolm D. Mason*[y], *Ivo G. Schoots*[z], *Theo H. van Der Kwast*[aa], *Henk G. van Der Poel*[c], *Thomas Wiegel*[bb], *Peter-Paul M. Willemse*[cc], *Yuhong Yuan*[dd], *Thomas B. Lam*[ee,ff], *Philip Cornford*[gg], *Nicolas Mottet*[hh]

Pacientes en Recurrencia: Grupos de Riesgo

Low-Risk BCR

- PSA-DT > 1 year

AND

- Pathological ISUP grade < 4

High risk BCP

- PSA-DT < 1 year

OR

- Pathological ISUP grade 4–5

European Association of Urology

Pacientes en Recurrencia: Grupos de Riesgo

Low-Risk BCR

- PSA-DT > 1 year

AND

- Pathological ISUP grade < 4

High risk BCP

- PSA-DT < 1 year

OR

- Pathological ISUP grade 4–5

European Association of Urology

EUROPEAN UROLOGY 75 (2019) 896–900

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

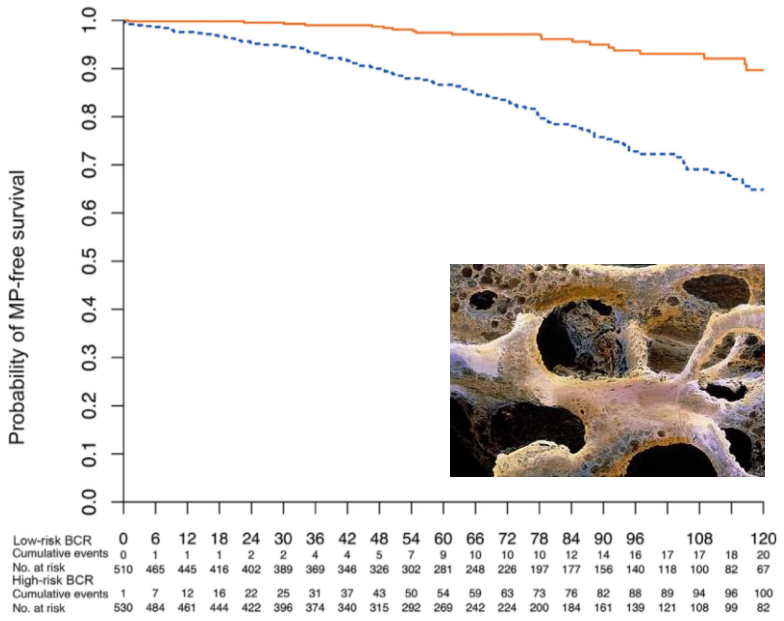
Brief Correspondence

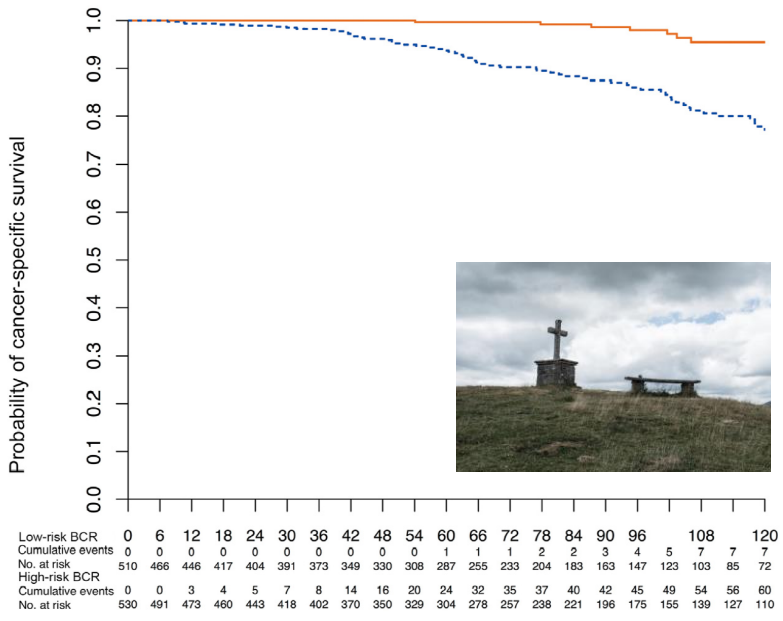
External Validation of the European Association of Urology Biochemical Recurrence Risk Groups to Predict Metastasis and Mortality After Radical Prostatectomy in a European Cohort

Derya Tilki [a,b,*], *Felix Preisser* [a], *Markus Graefen* [a], *Hartwig Huland* [a], *Raisa S. Pompe* [a,b]

[a] *Martini-Klinik Prostate Cancer Center, University Hospital Hamburg-Eppendorf, Hamburg, Germany;* [b] *Department of Urology, University Hospital Hamburg-Eppendorf, Hamburg, Germany*

Martini-Klinik
Prostatakrebszentrum
Universitätsklinikum Hamburg-Eppendorf



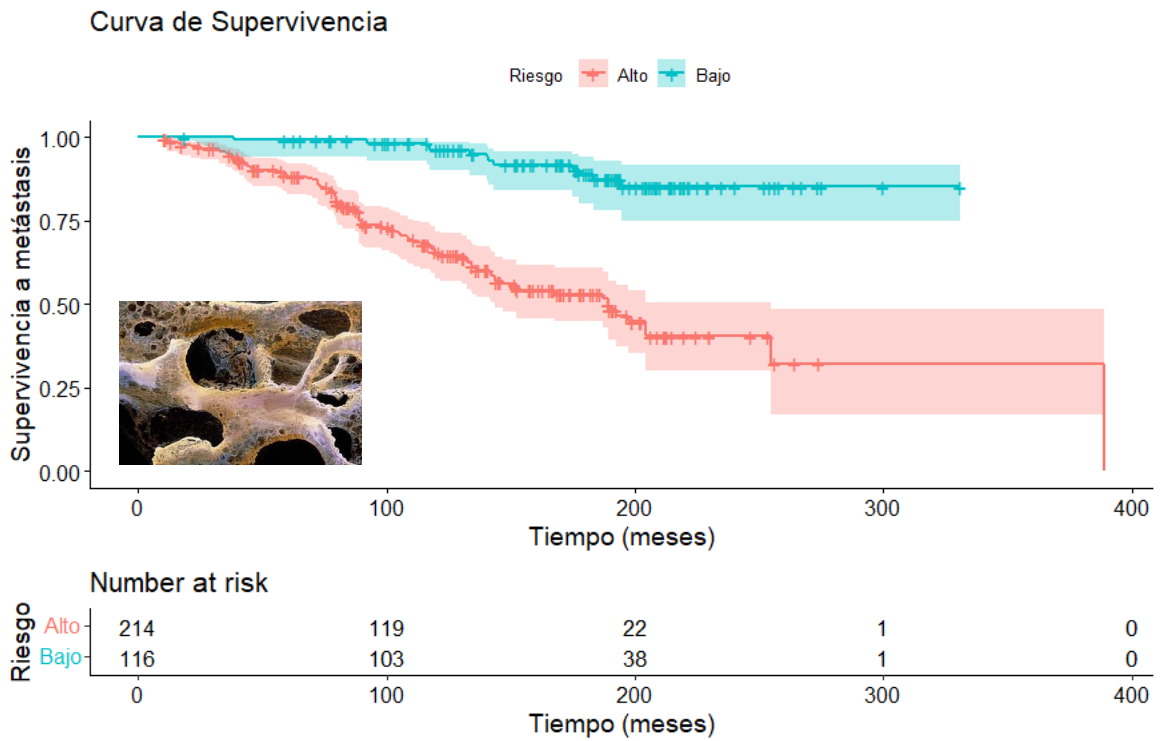


High risk BCP

- PSA-DT < 1 year or ISUP grade 4–5

Validación

ALTO RIESGO: 214 Pacientes (64.85%)
BAJO RIESGO: 116 Pacientes (35.15%)
TOTAL: 330 Pacientes



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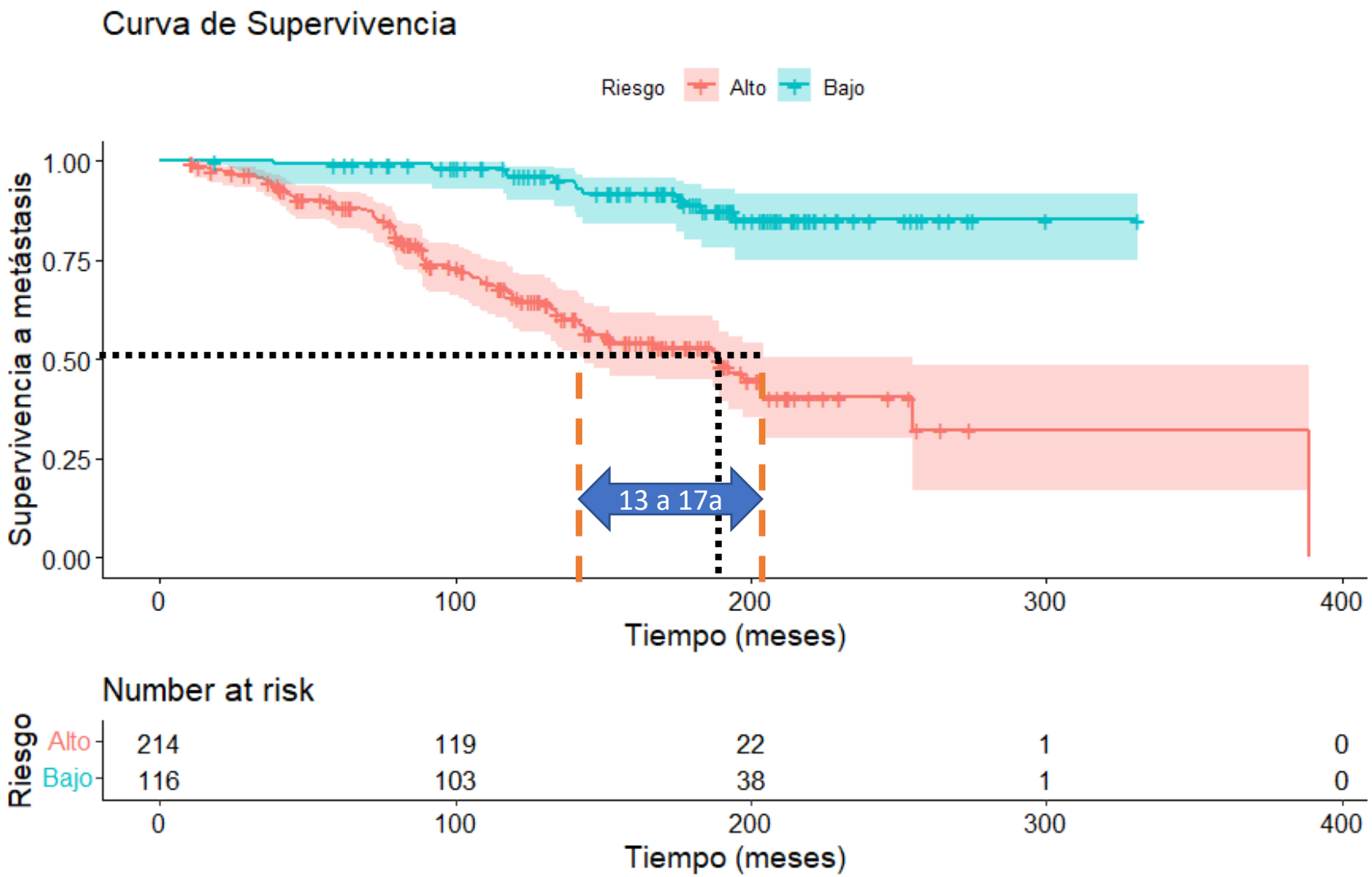
Curva de Supervivencia
Riesgo
Alto
Bajo
Supervivencia a metástasis
1.00
0.75
0.50
0.25
0.00
13 a 17a
0
100
200
300
400
Tiempo (meses)
Number at risk
Riesgo
Alto
Bajo
214
119
22
1
0
116
103
38
1
0
0
100
200
300
400
Tiempo (meses)


Erleada®
Apalutamida
Tableta
60 mg
Caja con frasco con 120 tabletas
Fórmula:
Cada tableta contiene:
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Excipiente cbp
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Xtandi
Enzalutamida
Cápsula
40 mg
Caja con 120 Cápsulas
VIA DE ADMINISTRACIÓN: Oral
ASOFARMA
astellas


LIVE
BREAKING NEWS


NUBEQA®
(darolutamide) tablets
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Oral use
50419-395-01 Rx Only
NUBEQA®
(darolutamide) tablets
300 mg
120 film-coated tablets
Bayer


ZYTIGA®
Abiraterona
Tabletas
250 mg
Caja con frasco con 120 tabletas
Fórmula:
Cada tableta contiene:
Acetato de Abiraterona ..... 250 mg
Excipiente csp ..... 1 Tableta
janssen

EMBARK

AUA 2023

CHICAGO ★ APR 28-MAY 1

EMBARK: A Phase 3 Randomized Study of Enzalutamide or Placebo Plus Leuprolide Acetate and Enzalutamide Monotherapy in High-Risk Biochemically Recurrent Prostate Cancer

Neal D. Shore,[1] Murilo de Almeida Luz,[2] Ugo De Giorgi,[3] Martin Gleave,[4] Geoffrey T. Gotto,[5] Gabriel P. Haas,[6] Miguel Ramirez-Backhaus,[7] Antti Rannikko,[8] Jamal Tarazi,[9] Swetha Sridharan,[10] Jennifer Sugg,[6] Yiyun Tang,[11] Ronald F. Tutrone, Jr.,[12] Balaji Venugopal,[13] Arnauld Villers,[14] Henry H. Woo,[15] Fabian Zohren,[16] Stephen J. Freedland[17]

[1]Carolina Urologic Research Center/GenesisCare US, Myrtle Beach, SC, USA; [2]Erasto Gaertner Hospital, Curitiba, Brazil; [3]IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) Dino Amadori, Meldola, Italy; [4]University of British Columbia, Vancouver, BC, Canada; [5]University of Calgary, Calgary, AB, Canada; [6]Astellas Pharma Inc., Northbrook, IL, USA; [7]Servicio de Urología, Fundación Instituto Valenciano de Oncología, Valencia, Spain; [8]University of Helsinki and Helsinki University Hospital, Helsinki, Finland; [9]Pfizer Inc., Collegeville, PA, USA; [10]Calvary Mat... NSW, Australia; [11]Pfizer Inc., San Francisco, CA, USA; [12]Chesapeake Urology Research Associates, To... USA; [13]Beatson West of Scotland Cancer Centre, University of Glasgow, Glasgow, UK; [14]University of Lille, Department of Urology, Claude Huriez Hospital, CHU LILLE, Lille, France; [15]Sydney Adventist Hospital, Sydney, NSW, Australia; [16]Pfizer Inc., Cambridge, MA, USA; [17]Samuel Oschin Comprehensive Cancer Institute, Cedars-Sinai Medical Center, Los Angeles, CA, USA

Enero 2015- Agosto 2019.
Análisis Enero 2023

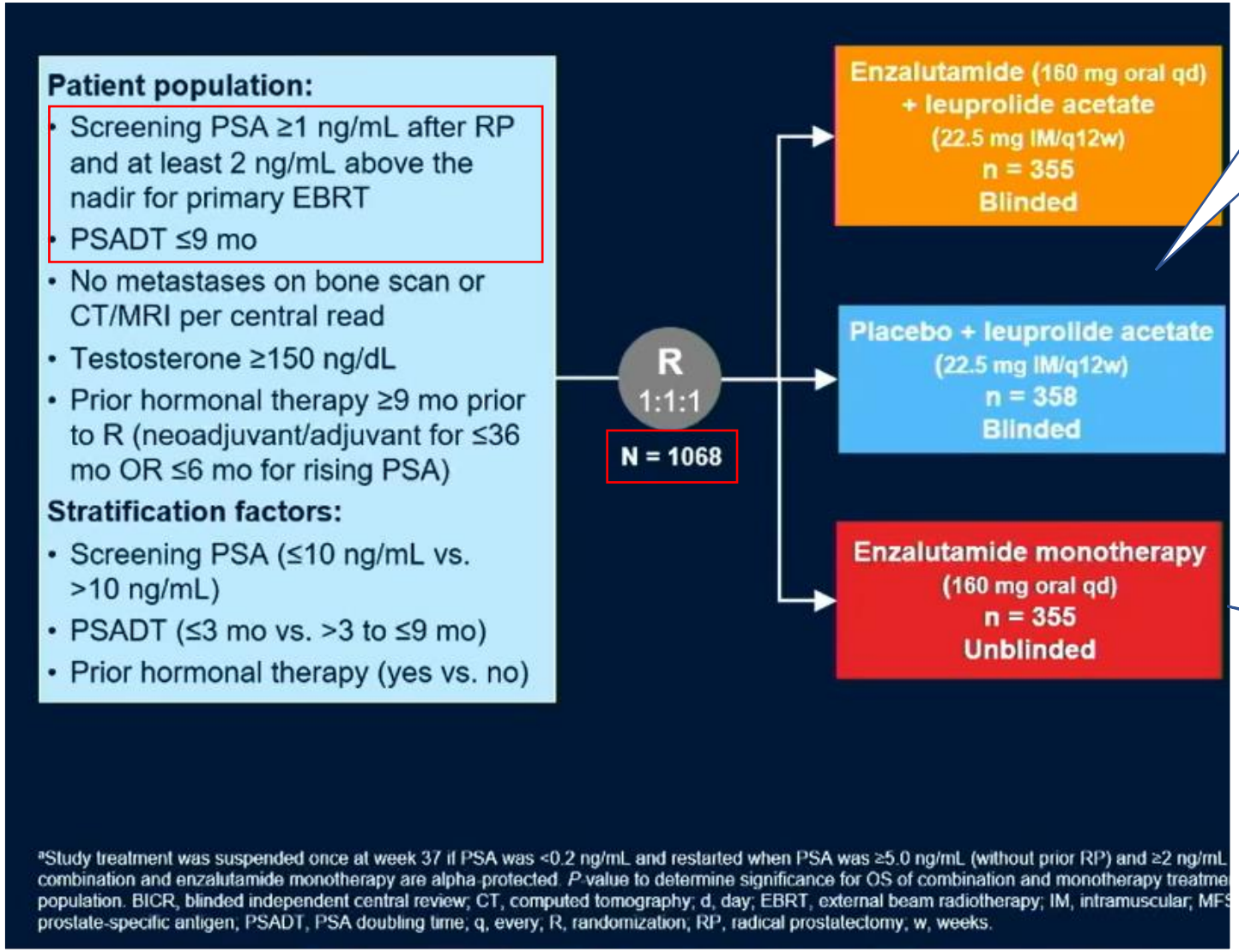
Patient population:

- Screening PSA ≥1 ng/mL after RP and at least 2 ng/mL above the nadir for primary EBRT
- PSADT ≤9 mo
- No metastases on bone scan or CT/MRI per central read
- Testosterone ≥150 ng/dL
- Prior hormonal therapy ≥9 mo prior to R (neoadjuvant/adjuvant for ≤36 mo OR ≤6 mo for rising PSA)

Stratification factors:

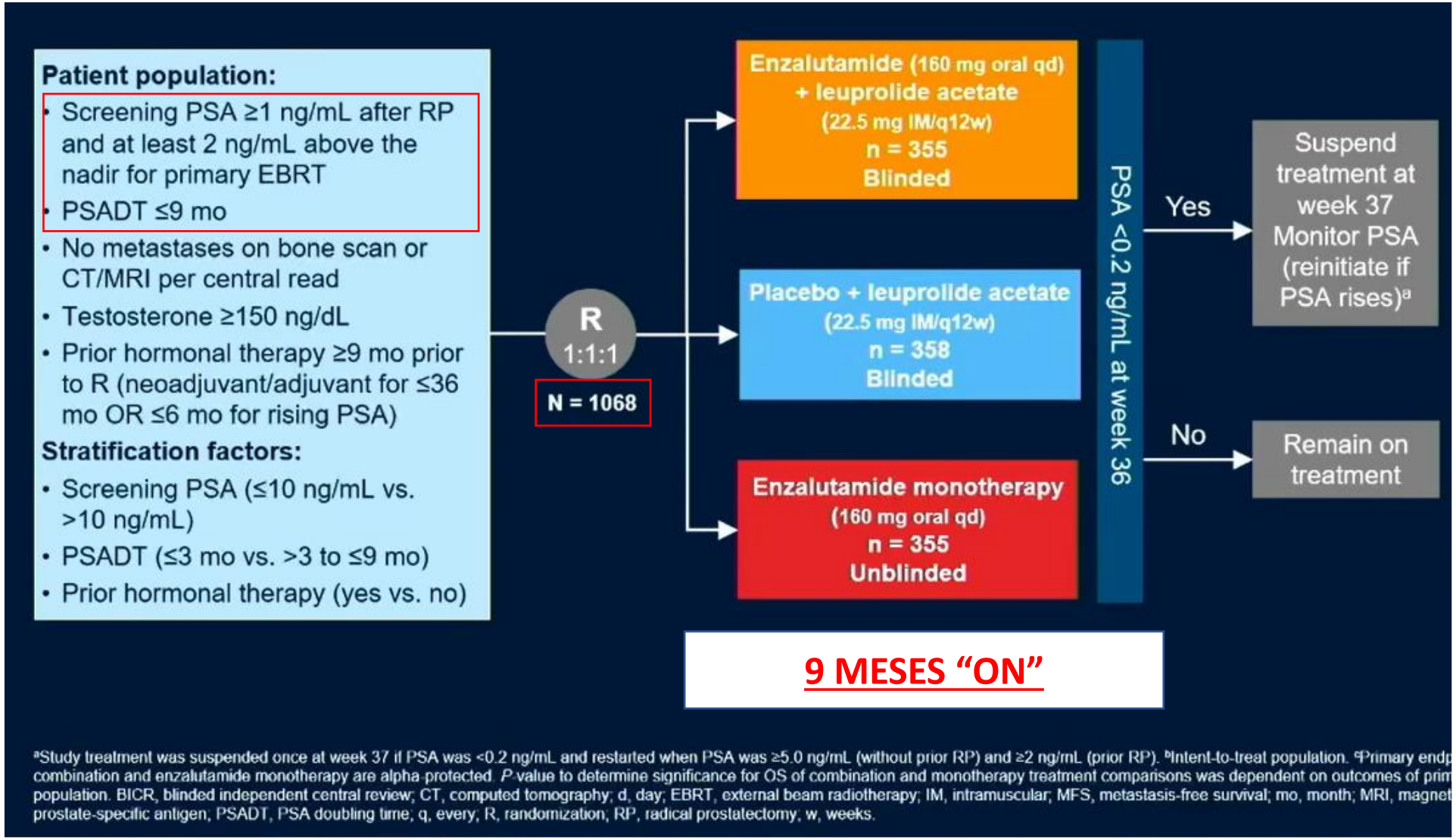
- Screening PSA (≤10 ng/mL vs. >10 ng/mL)
- PSADT (≤3 mo vs. >3 to ≤9 mo)
- Prior hormonal therapy (yes vs. no)

[a]Study treatment was suspended once at week 37 if PSA was <0
combination and enzalutamide monotherapy are alpha-protected
population. BICR, blinded independent central review; CT, comp
prostate-specific antigen; PSADT, PSA doubling time; q, every; R

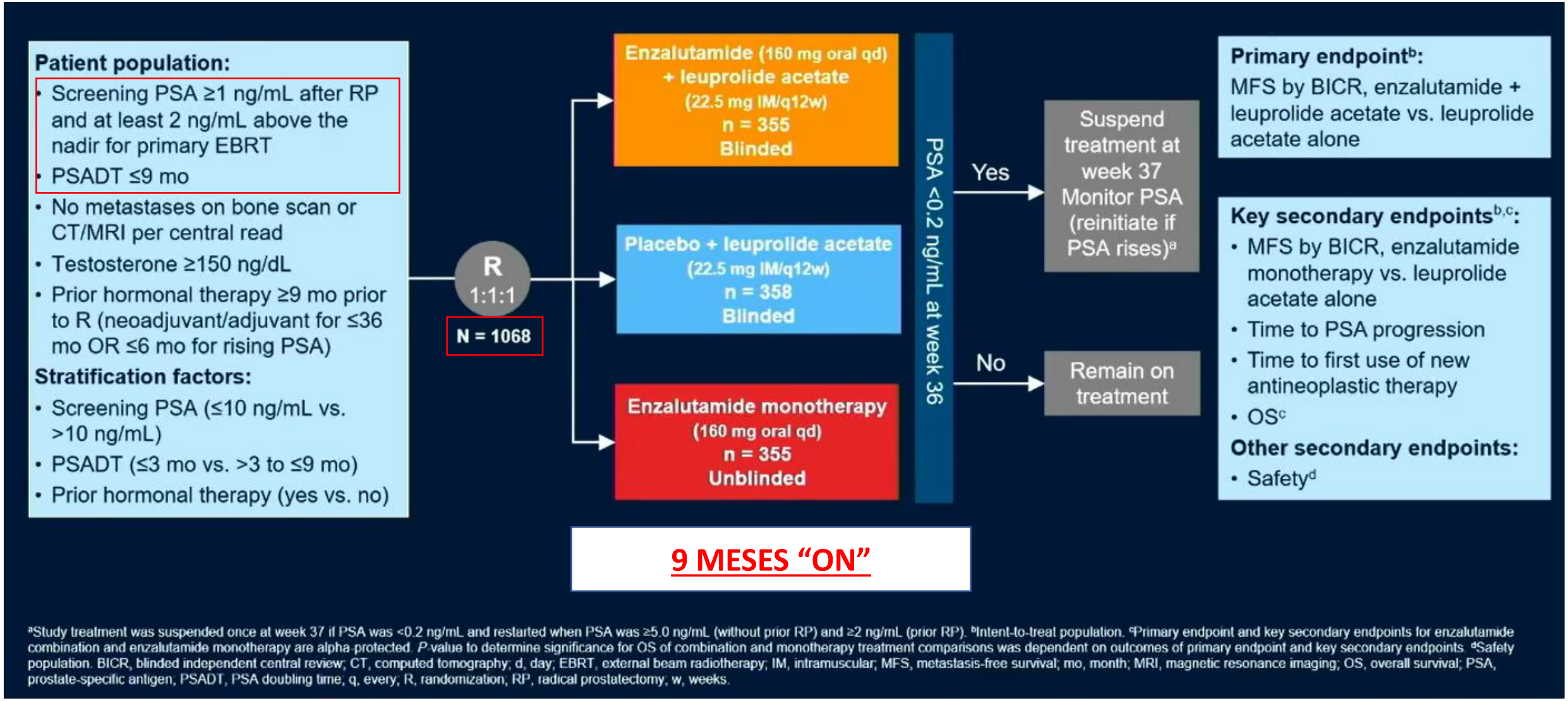


Los grupos son Ciegos

EL GRUPO NO ES Ciego



[a]Study treatment was suspended once at week 37 if PSA was <0.2 ng/mL and restarted when PSA was ≥5.0 ng/mL (without prior RP) and ≥2 ng/mL (prior RP). [b]Intent-to-treat population. [c]Primary endp combination and enzalutamide monotherapy are alpha-protected. *P*-value to determine significance for OS of combination and monotherapy treatment comparisons was dependent on outcomes of prim population. BICR, blinded independent central review; CT, computed tomography; d, day; EBRT, external beam radiotherapy; IM, intramuscular; MFS, metastasis-free survival; mo, month; MRI, magnet prostate-specific antigen; PSADT, PSA doubling time; q, every; R, randomization; RP, radical prostatectomy; w, weeks.



[a]Study treatment was suspended once at week 37 if PSA was <0.2 ng/mL and restarted when PSA was ≥5.0 ng/mL (without prior RP) and ≥2 ng/mL (prior RP). [b]Intent-to-treat population. [c]Primary endpoint and key secondary endpoints for enzalutamide combination and enzalutamide monotherapy are alpha-protected. *P*-value to determine significance for OS of combination and monotherapy treatment comparisons was dependent on outcomes of primary endpoint and key secondary endpoints. [d]Safety population. BICR, blinded independent central review; CT, computed tomography; d, day; EBRT, external beam radiotherapy; IM, intramuscular; MFS, metastasis-free survival; mo, month; MRI, magnetic resonance imaging; OS, overall survival; PSA, prostate-specific antigen; PSADT, PSA doubling time; q, every; R, randomization; RP, radical prostatectomy; w, weeks.

Characteristic	Enzalutamide combination (n = 355)	Leuprolide acetate (n = 358)	Enzalutamide monotherapy (n = 355)
Age, median (range), yr	69 (51–87)	70 (50–92)	69 (49–93)
Race, n (%)[a]			
White	293 (82.5)	301 (84.1)	295 (83.1)
Asian	26 (7.3)	26 (7.3)	26 (7.3)
Black	16 (4.5)	16 (4.5)	15 (4.2)
Other[b]	10 (2.8)	10 (2.8)	5 (1.4)
PSADT, n (%)[c]			
≤3 mo	69 (19.4)	80 (22.3)	76 (21.4)
>3 to ≤9 mo	285 (80.3)	277 (77.4)	278 (78.3)
PSADT, median, mo	4.6	5.0	5.0
Serum PSA, median, n (%), ng/mL[d]	5.0	5.5	5.3
≤10	278 (78.3)	273 (76.3)	272 (76.6)
>10	77 (21.7)	83 (23.2)	82 (23.1)
Prior hormonal therapy, n (%)	107 (30.1)	113 (31.6)	112 (31.5)
RP alone, n (%)	90 (25.4)	75 (20.9)	99 (27.9)
RT alone, n (%)	86 (24.2)	104 (29.1)	90 (25.4)
RP and RT, n (%)	179 (50.4)	179 (50.0)	166 (46.8)

[a]Not reported included: enzalutamide combination, n = 10 (2.8%); leuprolide acetate, n = 5 (1.4%); enzalutamide monotherapy, n = 14 (3.9%). [b]Includes patients who identified as multiple races (enzalutamide combination, n = 5; leuprolide acetate, n = 9; enzalutamide monotherapy, n = 5), American Indian or Alaskan Native (enzalutamide combination, n = 4; leuprolide acetate, n = 1; enzalutamide monotherapy, n = 0), Native Hawaiian or other Pacific Islander (enzalutamide combination, n = 1; leuprolide acetate and enzalutamide monotherapy, n = 0). [c]Missing included n = 1 (0.3%) for each treatment group. [d]Missing included: leuprolide acetate, n = 2; enzalutamide monotherapy, n = 1. RT, radiation therapy; yr, year.

Characteristic	Enzalutamide combination (n = 355)	Leuprolide acetate (n = 358)	Enzalutamide monotherapy (n = 355)
Age, median (range), yr	69 (51–87)	70 (50–92)	69 (49–93)
Race, n (%)[a]			
White	293 (82.5)	301 (84.1)	295 (83.1)
Asian	26 (7.3)	26 (7.3)	26 (7.3)
Black	16 (4.5)	16 (4.5)	15 (4.2)
Other[b]	10 (2.8)	10 (2.8)	5 (1.4)
PSADT, n (%)[c]			
≤3 mo	69 (19.4)	80 (22.3)	76 (21.4)
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Characteristic	Enzalutamide combination (n = 355)	Leuprolide acetate (n = 358)	Enzalutamide monotherapy (n = 355)
Age, median (range), yr	69 (51–87)	70 (50–92)	69 (49–93)
Race, n (%)[a]			
White			
Asian			
Black			
Other[b]			
PSADT, n (%)[c]			
≤3 mo			
>3 to ≤9 mo			
PSADT, median, m			
Serum PSA, media			
≤10			
>10	77 (21.7)	83 (23.2)	82 (23.1)
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Department of
UROLOGY

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Characteristic	Enzalutamide combination (n = 355)	Leuprolide acetate (n = 358)	Enzalutamide monotherapy (n = 355)
Age, median (range), yr			69 (49–93)
Race, n (%)[a]			
White			295 (83.1)
Asian			26 (7.3)
Black			15 (4.2)
Other[b]			5 (1.4)
PSADT, n (%)[c]			
≤3 mo			76 (21.4)
>3 to ≤9 mo			278 (78.3)
PSADT, median, mo			5.0
Serum PSA, median, n (%), ng/mL[d]			5.3
≤10			272 (76.6)
>10			82 (23.1)
Prior hormonal therapy, n (%)	107 (30.1)	113 (31.6)	112 (31.5)
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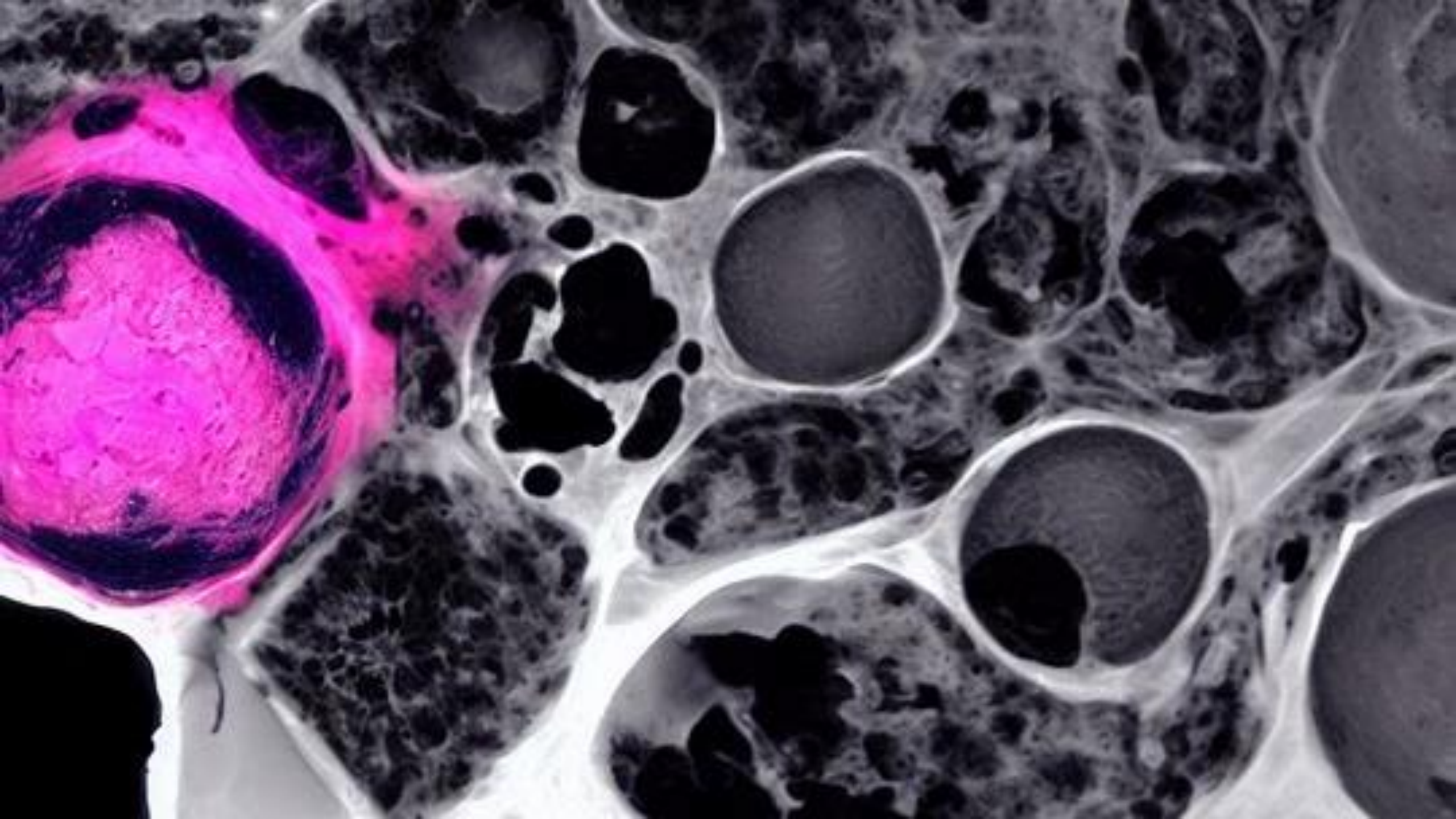
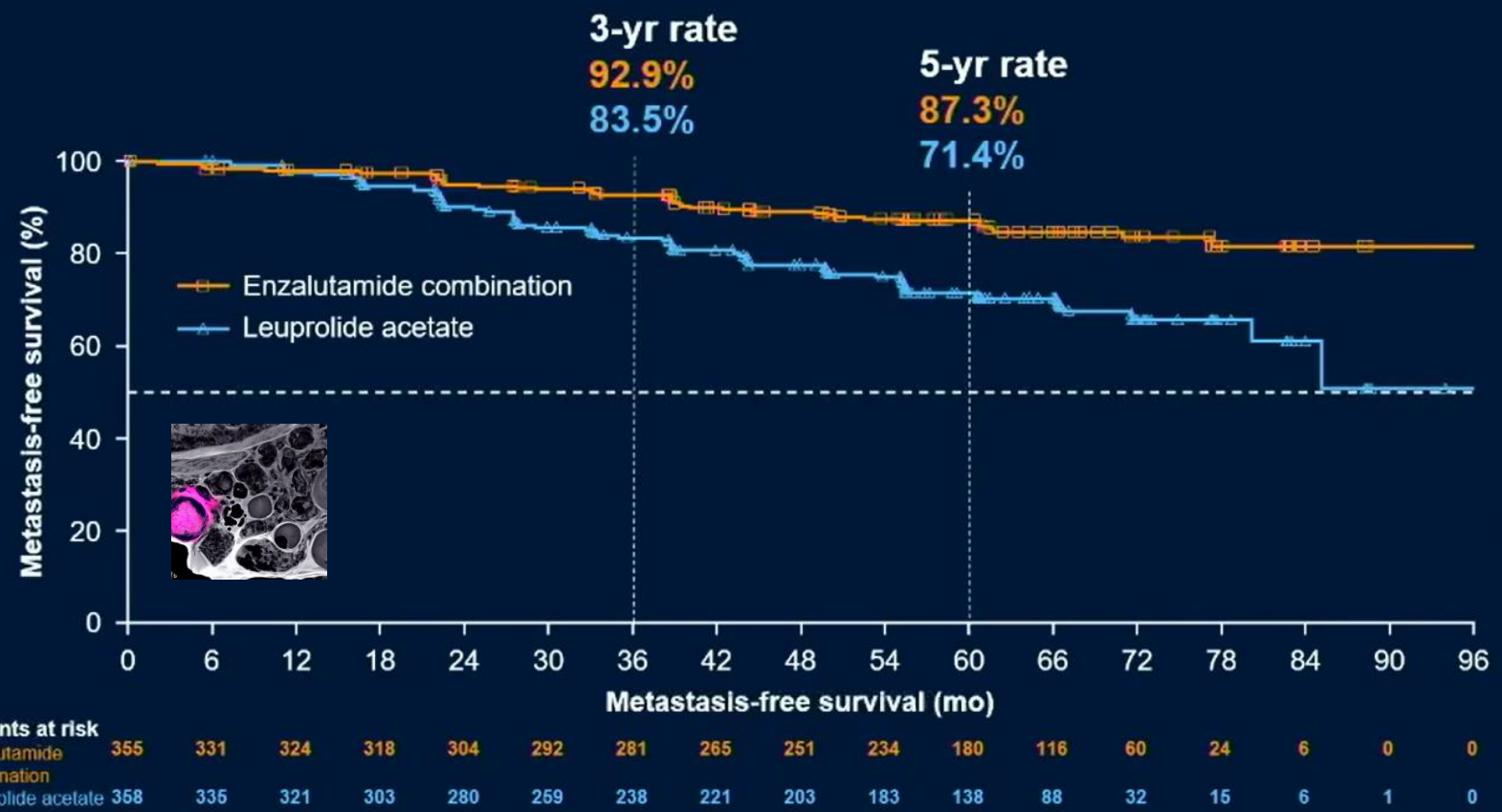




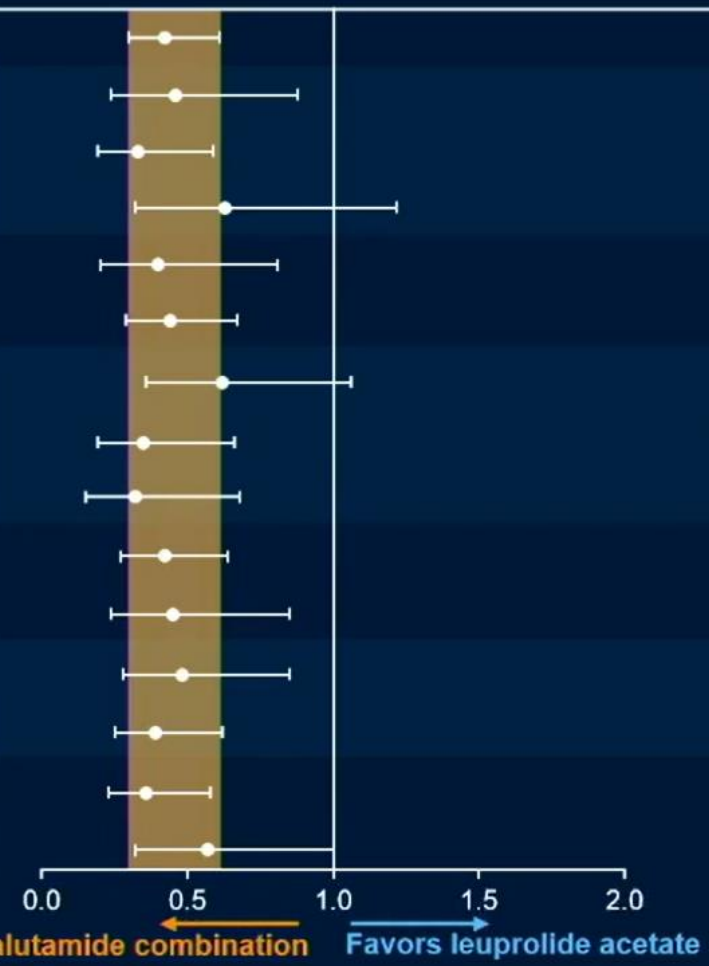
	Enzalutamide combination (n = 355)	Leuprolide acetate (n = 358)
Median follow-up, mo	60.7	60.6
Events, n (%)	45 (13)	92 (26)
Per BICR, median MFS (95% CI), mo	NR (NR)	NR (85.1–NR)

HR (95% CI): 0.42 (0.31–0.61); *P*<0.0001[a]

A consistent treatment effect was seen for investigator-assessed MFS: HR (95% CI): 0.47 (0.37–0.67); *P*<0.0001

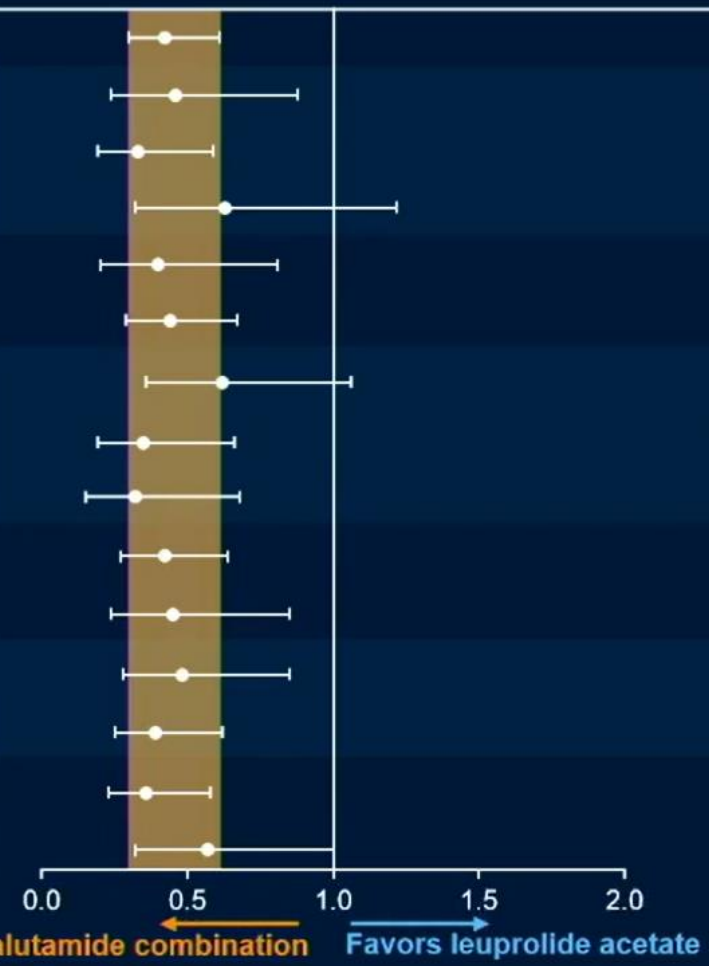
Data cutoff: January 31, 2023. Symbols indicate censored data. [a]HR was based on a Cox regression model with treatment as the only covariate stratified by screening PSA, PSADT, and prior hormonal therapy as reported in the IWRS; relative to leuprolide acetate <1 favoring enzalutamide combination; the two-sided *P*-value was based on a stratified log-rank. CI, confidence interval; HR, hazard ratio; IWRS, interactive web response system; NR, not reached.

Subgroup		Enzalutamide combination Events, n /patients, n	Leuprolide acetate Events, n /patients, n	MFS HR (95% CI)
All patients		45/355	92/358	0.42 (0.30–0.61)
PSADT	≤3 mo	14/69	30/80	0.46 (0.24–0.88)
	>3 to ≤6 mo	18/187	35/142	0.33 (0.19–0.59)
	>6 to ≤9 mo	13/98	27/135	0.63 (0.32–1.22)
Baseline age	≤65 years	11/81	28/91	0.40 (0.20–0.81)
	≥65 years	34/274	64/267	0.44 (0.29–0.67)
Geographic region	North America	22/144	32/137	0.62 (0.36–1.06)
	Europe	14/130	33/128	0.35 (0.19–0.66)
	ROW	9/81	27/93	0.32 (0.15–0.68)
Baseline PSA	≤10 ng/mL	31/278	64/273	0.42 (0.27–0.64)
	>10 ng/mL	14/77	28/83	0.45 (0.24–0.85)
Prior hormonal therapy	Yes	19/107	34/113	0.48 (0.28–0.85)
	No	26/248	58/245	0.39 (0.25–0.62)
Prior RP	Yes	26/269	61/254	0.36 (0.23–0.58)
	No	19/86	31/104	0.57 (0.32–1.00)



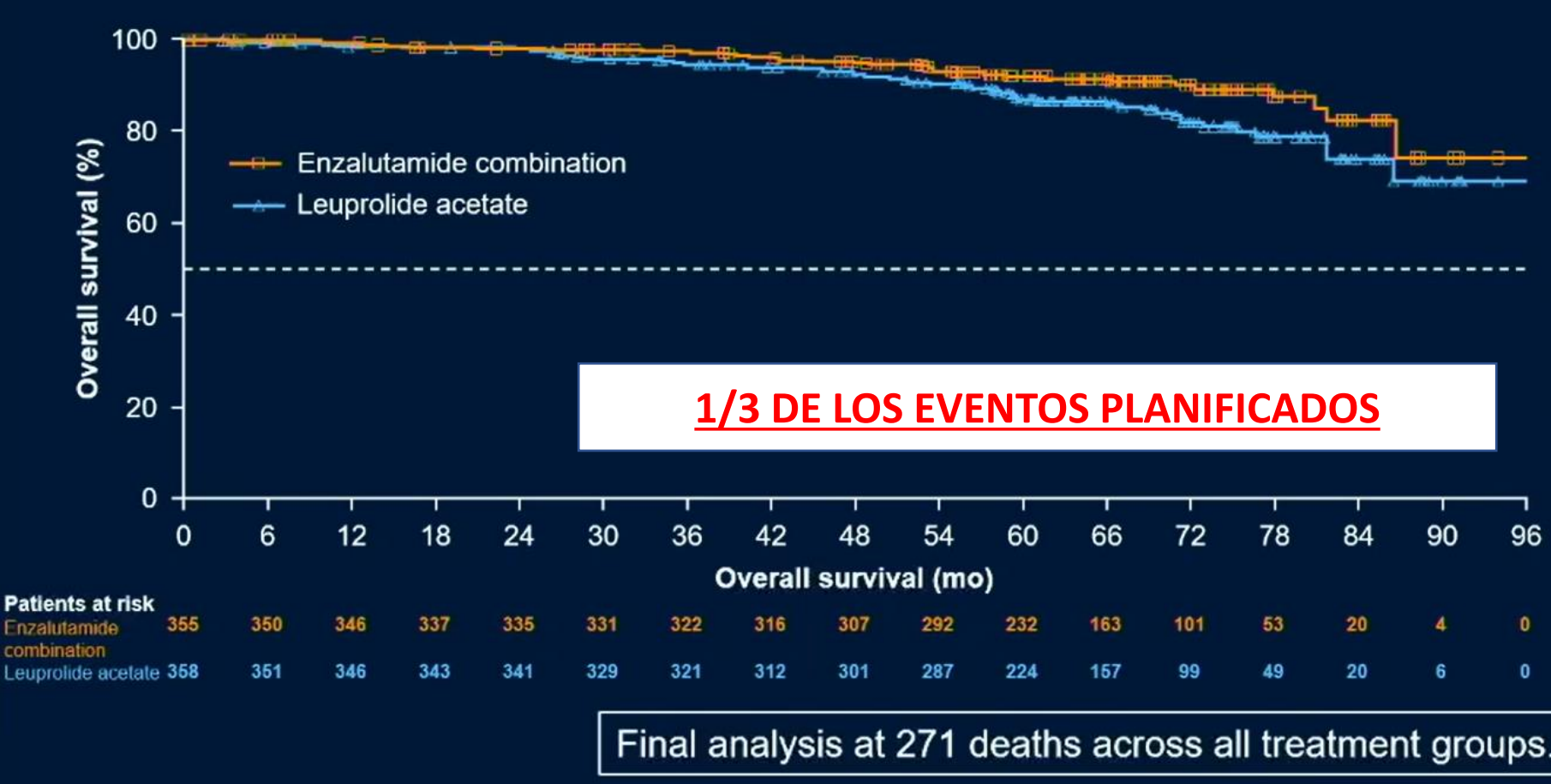
Data cutoff: January 31, 2023. For all patients, HR and 95% CI are based on stratified Cox regression model stratified by randomization stratification factors; for subgroups, HR and 95% CI are based on unstratified Cox regression model.

Subgroup		Enzalutamide combination Events, n	Leuprolide acetate /patients, n	MFS HR (95% CI)
All patients		45/355	92/358	0.42 (0.30–0.61)
PSADT	≤3 mo	14/69	30/80	0.46 (0.24–0.88)
	>3 to ≤6 mo	18/187	35/142	0.33 (0.19–0.59)
	>6 to ≤9 mo	13/98	27/135	0.63 (0.32–1.22)
Baseline age	≤65 years	11/81	28/91	0.40 (0.20–0.81)
	≥65 years	34/274	64/267	0.44 (0.29–0.67)
Geographic region	North America	22/144	32/137	0.62 (0.36–1.06)
	Europe	14/130	33/128	0.35 (0.19–0.66)
	ROW	9/81	27/93	0.32 (0.15–0.68)
Baseline PSA	≤10 ng/mL	31/278	64/273	0.42 (0.27–0.64)
	>10 ng/mL	14/77	28/83	0.45 (0.24–0.85)
Prior hormonal therapy	Yes	19/107	34/113	0.48 (0.28–0.85)
	No	26/248	58/245	0.39 (0.25–0.62)
Prior RP	Yes	26/269	61/254	0.36 (0.23–0.58)
	No	19/86	31/104	0.57 (0.32–1.00)



¿El Gleason?

Data cutoff: January 31, 2023. For all patients, HR and 95% CI are based on stratified Cox regression model stratified by randomization stratification factors; for subgroups, HR and 95% CI are based on unstratified Cox regression model.



	Enzalutamide combination (n = 355)	Leuprolide acetate (n = 358)
Events, n (%)	33 (9)	55 (15)
Median time to death (95% CI), mo	NR (NR)	NR (NR)

HR (95% CI): 0.59 (0.38–0.90) *P*=0.0142[a]

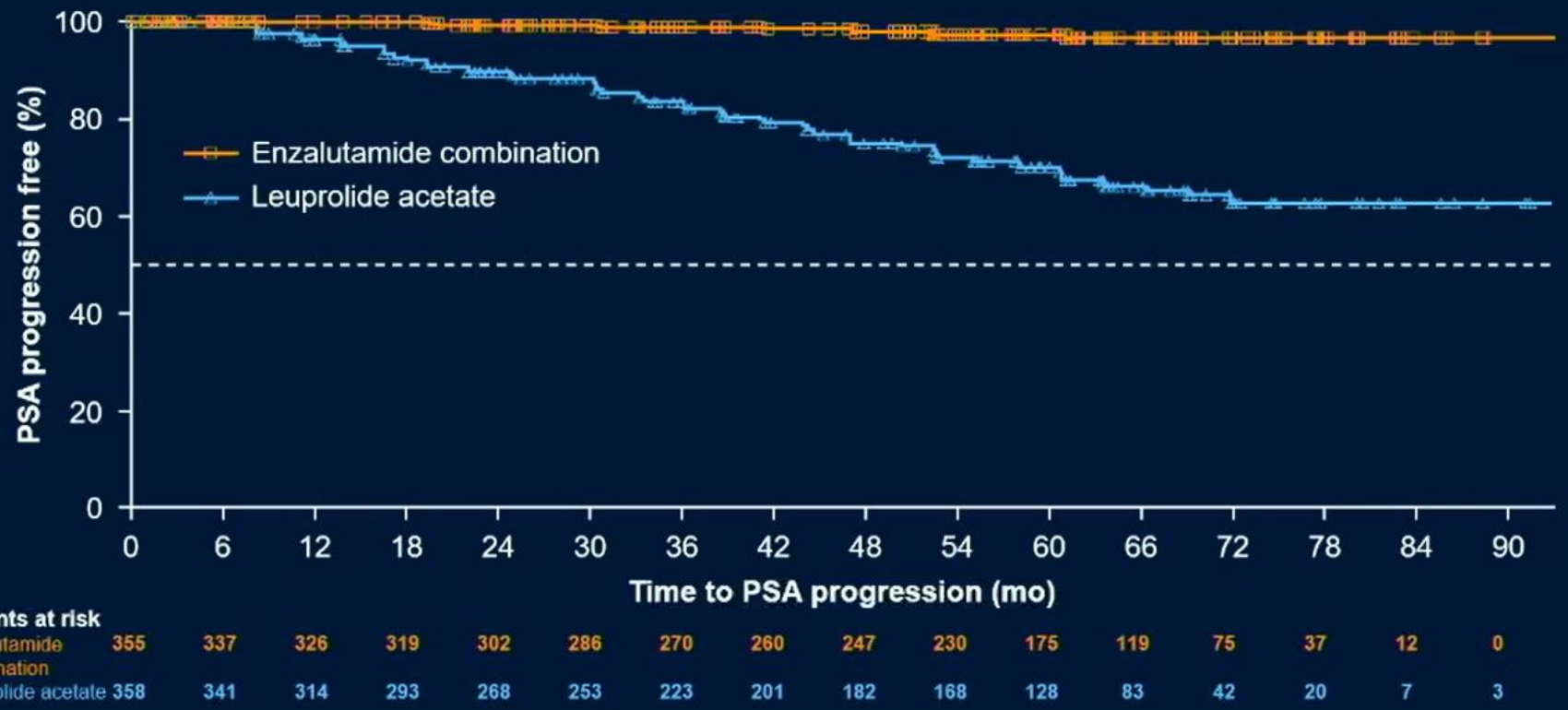
(Pre-specified efficacy boundary, *P*<0.0001)

1/3 DE LOS EVENTOS PLANIFICADOS

Final analysis at 271 deaths across all treatment groups.

Data cutoff: January 31, 2023. Symbols indicate censored data. [a]The HR was based on a Cox regression model with treatment as the only covariate stratified by screening PSA, PSADT, and prior hormonal therapy as reported in the IWRS; relative to leuprolide acetate <1 favoring enzalutamide combination; the two-sided *P*-value is based on a stratified log-rank test.

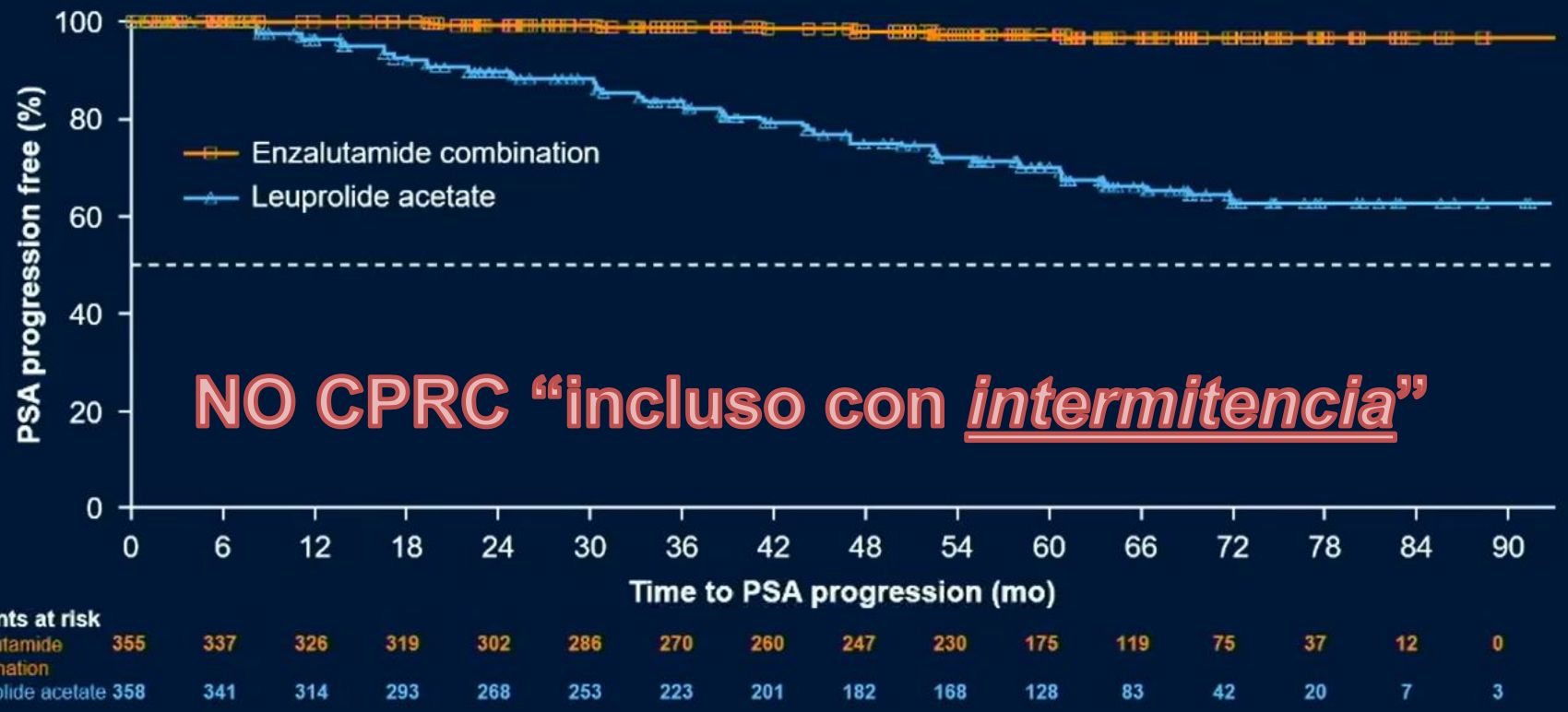
		Previous result	May 11 update
OS: Combo Comparison	HR, 95% CI	0.59 (0.38 ,0.90)	0.59 (0.38, 0.91)
	p-value	0.0142	0.0153



	Enzalutamide combination (n = 355)	Leuprolide acetate (n = 358)
Events, n (%)	8 (2)	93 (26)
Median time to PSA progression (95% CI), mo	NR (NR)	NR (NR)

HR (95% CI): 0.07 (0.03–0.14); *P*<0.0001[a]

Data cutoff: January 31, 2023. Symbols indicate censored data. [a]The HR was based on a Cox regression model with treatment as the only covariate stratified by screening PSA, PSADT, and prior hormonal therapy as reported in the IWRS; relative to leuprolide acetate <1 favoring enzalutamide combination; the two-sided *P*-value is based on a stratified log-rank test.

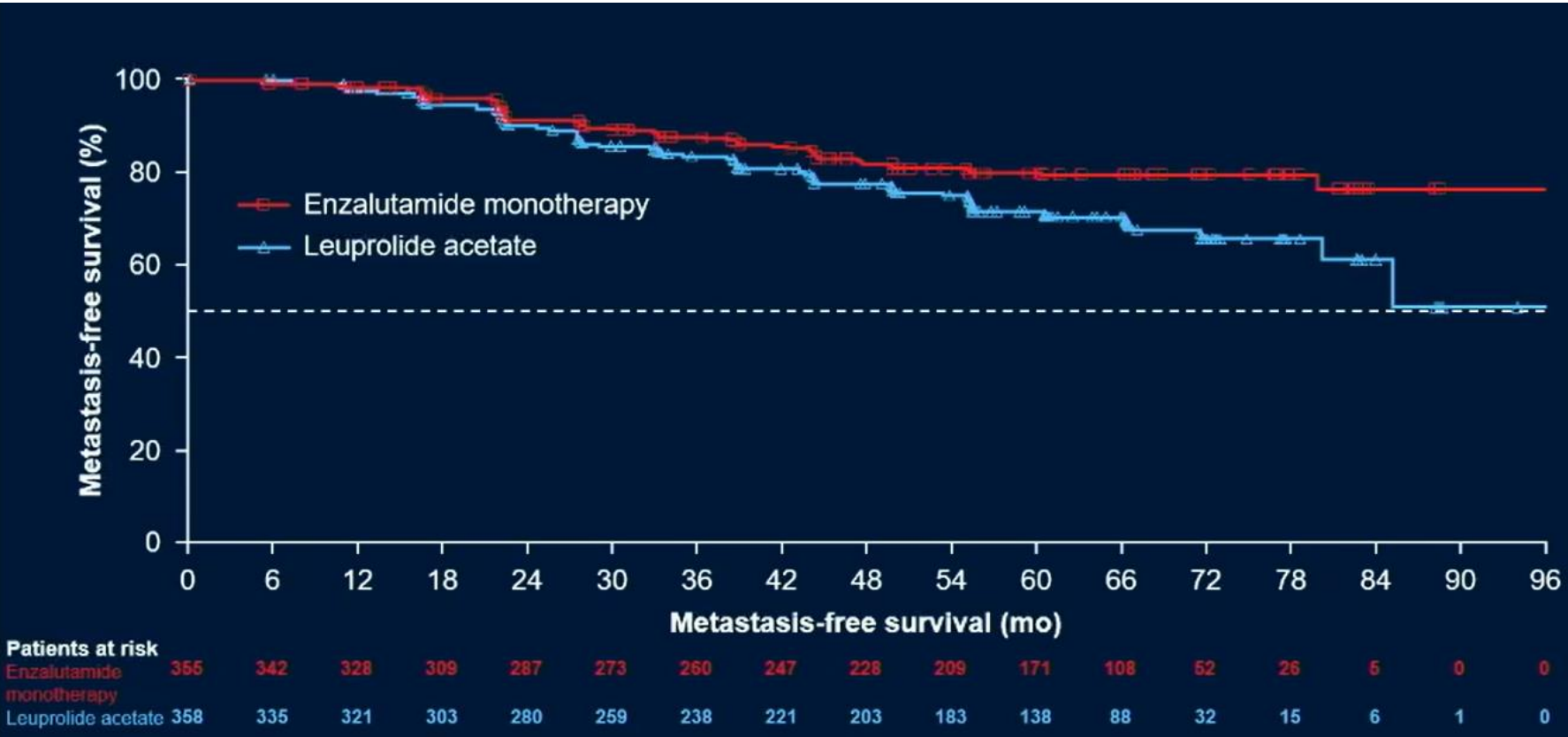


NO CPRC "incluso con *intermitencia*"

	Enzalutamide combination (n = 355)	Leuprolide acetate (n = 358)
Events, n (%)	8 (2)	93 (26)
Median time to PSA progression (95% CI), mo	NR (NR)	NR (NR)

HR (95% CI): 0.07 (0.03–0.14); *P*<0.0001[a]

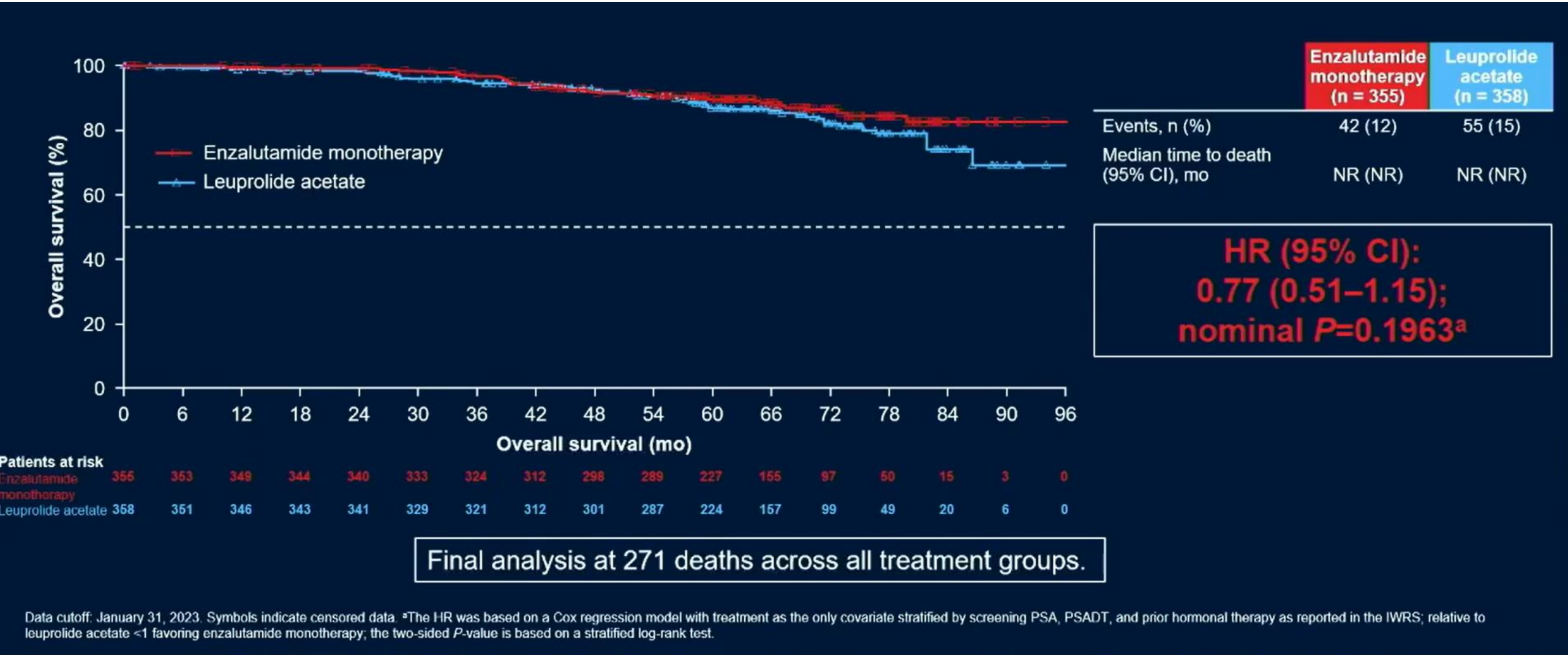
Data cutoff: January 31, 2023. Symbols indicate censored data. [a]The HR was based on a Cox regression model with treatment as the only covariate stratified by screening PSA, PSADT, and prior hormonal therapy as reported in the IWRS; relative to leuprolide acetate <1 favoring enzalutamide combination; the two-sided *P*-value is based on a stratified log-rank test.



	Enzalutamide monotherapy (n = 355)	Leuprolide acetate (n = 358)
Median follow-up, mo	60.7	60.6
Events, n (%)	63 (18)	92 (26)
Per BICR, median MFS (95% CI), mo	NR (NR)	NR (85.1–NR)

HR (95% CI): 0.63 (0.46–0.87); *P*=0.0049[a]

A consistent treatment effect was seen for investigator-assessed MFS: HR (95% CI): 0.56 (0.40–0.78); *P*=0.0006



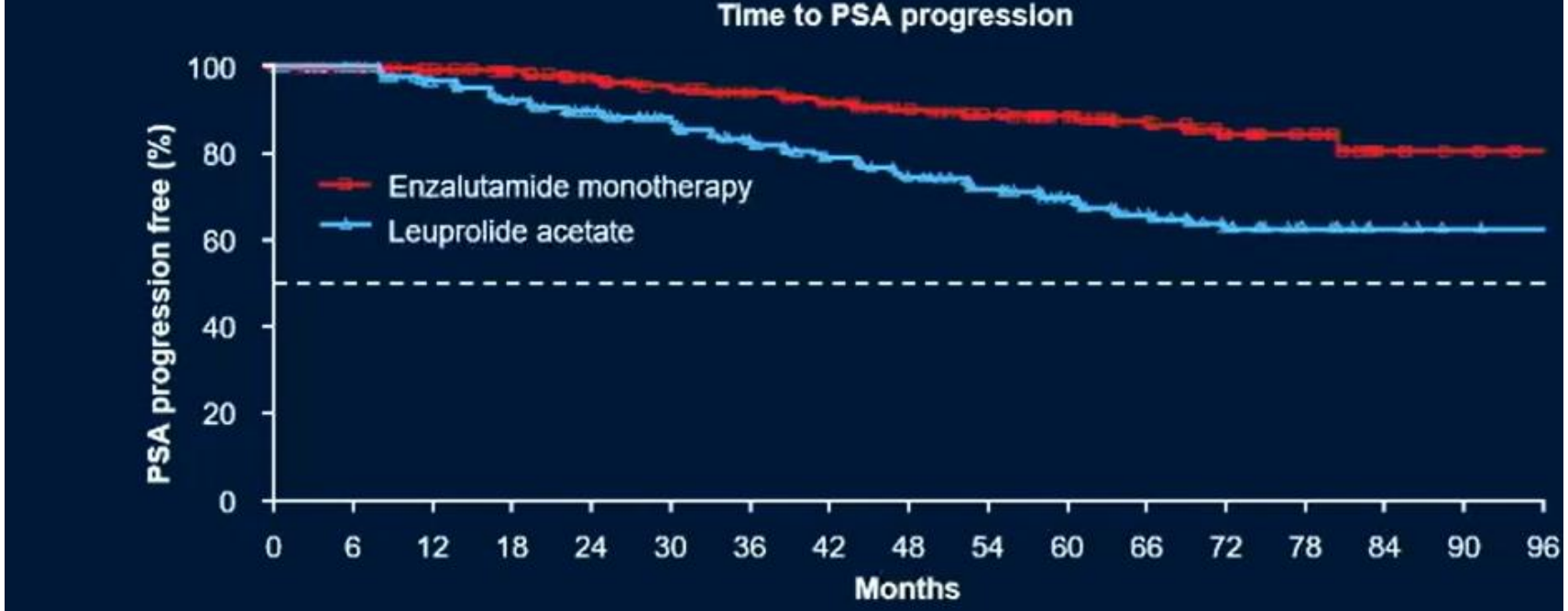
	Enzalutamide monotherapy (n = 355)	Leuprolide acetate (n = 358)
Events, n (%)	42 (12)	55 (15)
Median time to death (95% CI), mo	NR (NR)	NR (NR)

HR (95% CI): 0.77 (0.51–1.15); nominal *P*=0.1963[a]

Final analysis at 271 deaths across all treatment groups.

Data cutoff: January 31, 2023. Symbols indicate censored data. [a]The HR was based on a Cox regression model with treatment as the only covariate stratified by screening PSA, PSADT, and prior hormonal therapy as reported in the IWRS; relative to leuprolide acetate <1 favoring enzalutamide monotherapy; the two-sided *P*-value is based on a stratified log-rank test.

OS: Mono Comparison	HR, 95% CI	0.77 (0.51 , 1.15)	0.78 (0.52 , 1.17)
	p-value	0.1963	0.2304



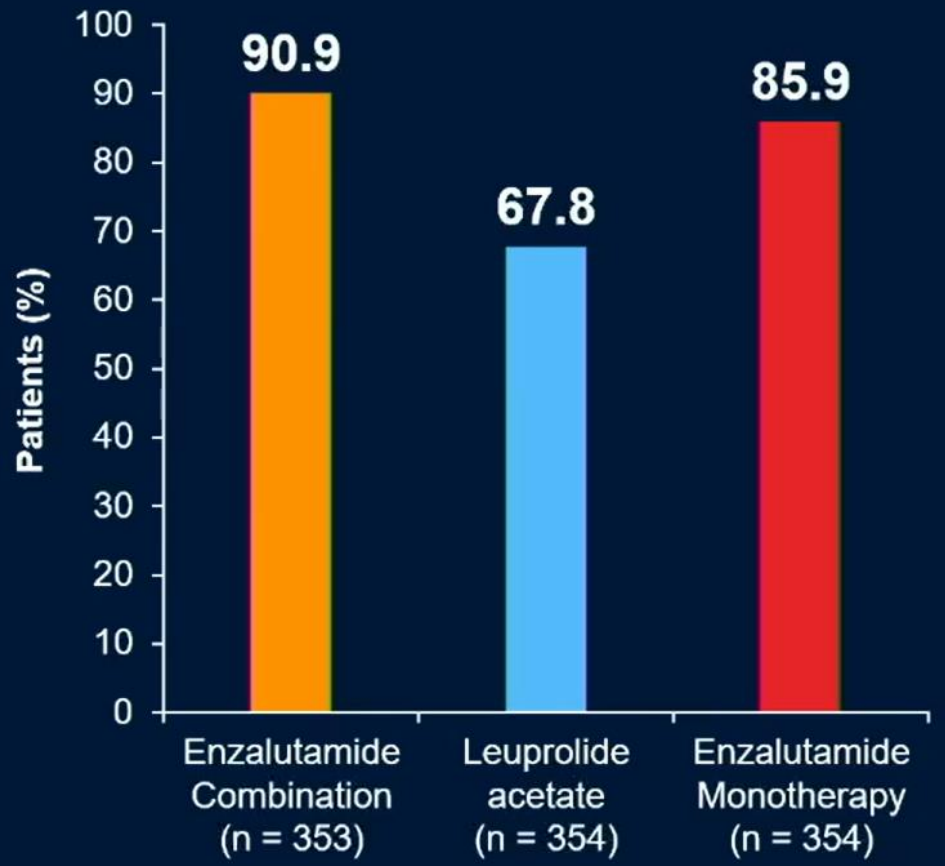
Patients at risk

Enzalutamide monotherapy	355	346	328	311	291	279	262	246	228	213	168	108	63	37	8	3	0
Leuprolide acetate	358	341	314	293	268	253	223	201	182	168	128	83	42	20	7	3	0

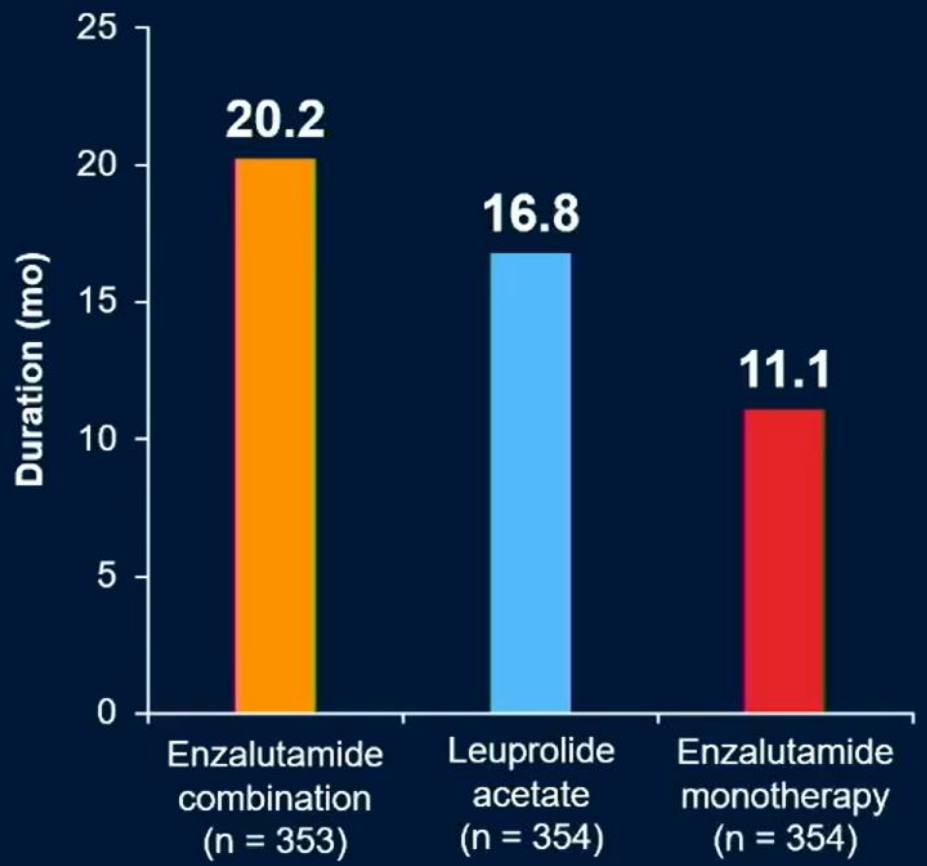
	Enzalutamide monotherapy (n = 355)	Leuprolide acetate (n = 358)
Events, n (%)	37 (10)	93 (26)
Median time to PSA progression (95% CI), mo	NR (NR)	NR (NR)

HR (95% CI): 0.33 (0.23–0.49); *P*<0.0001[a]

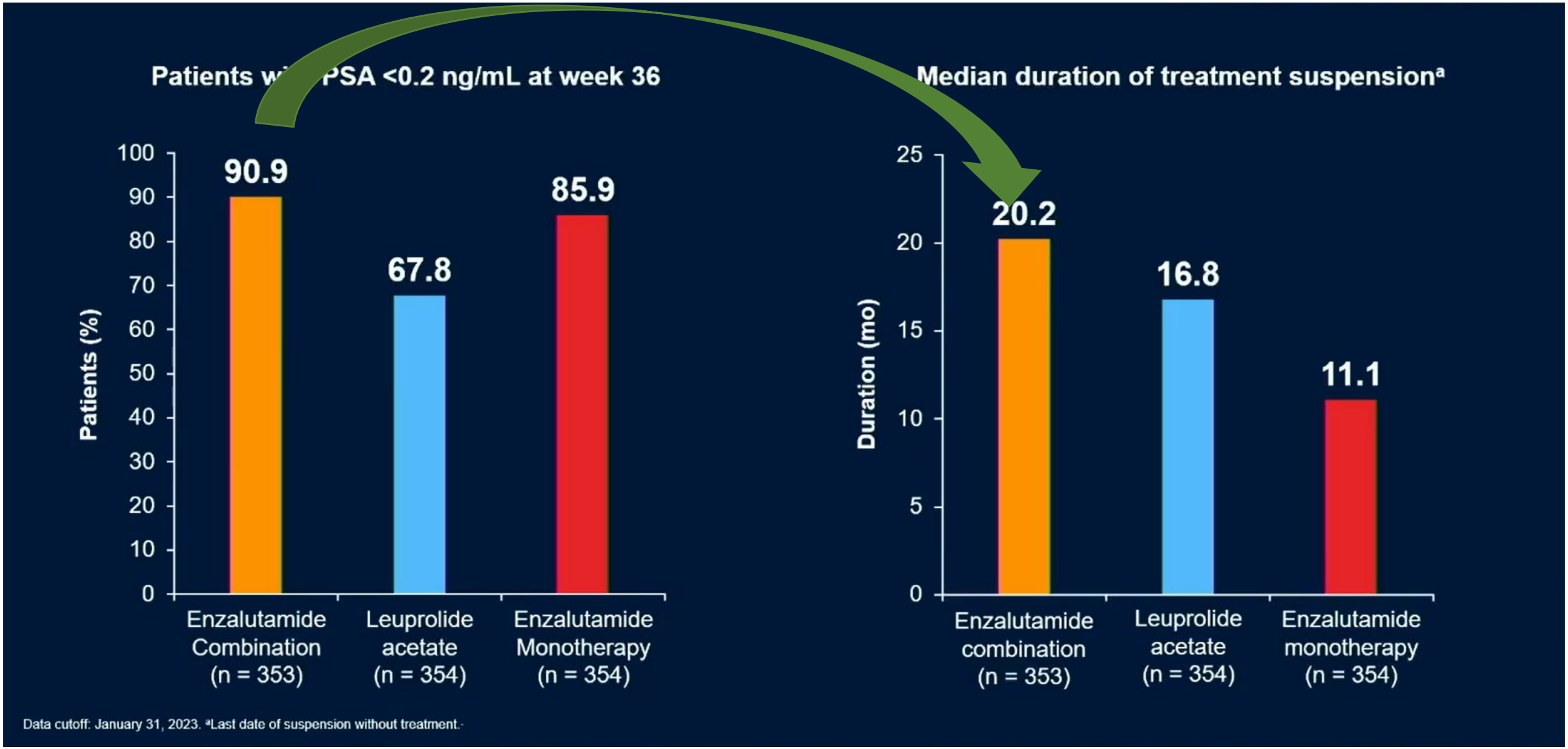
Patients with PSA <0.2 ng/mL at week 36



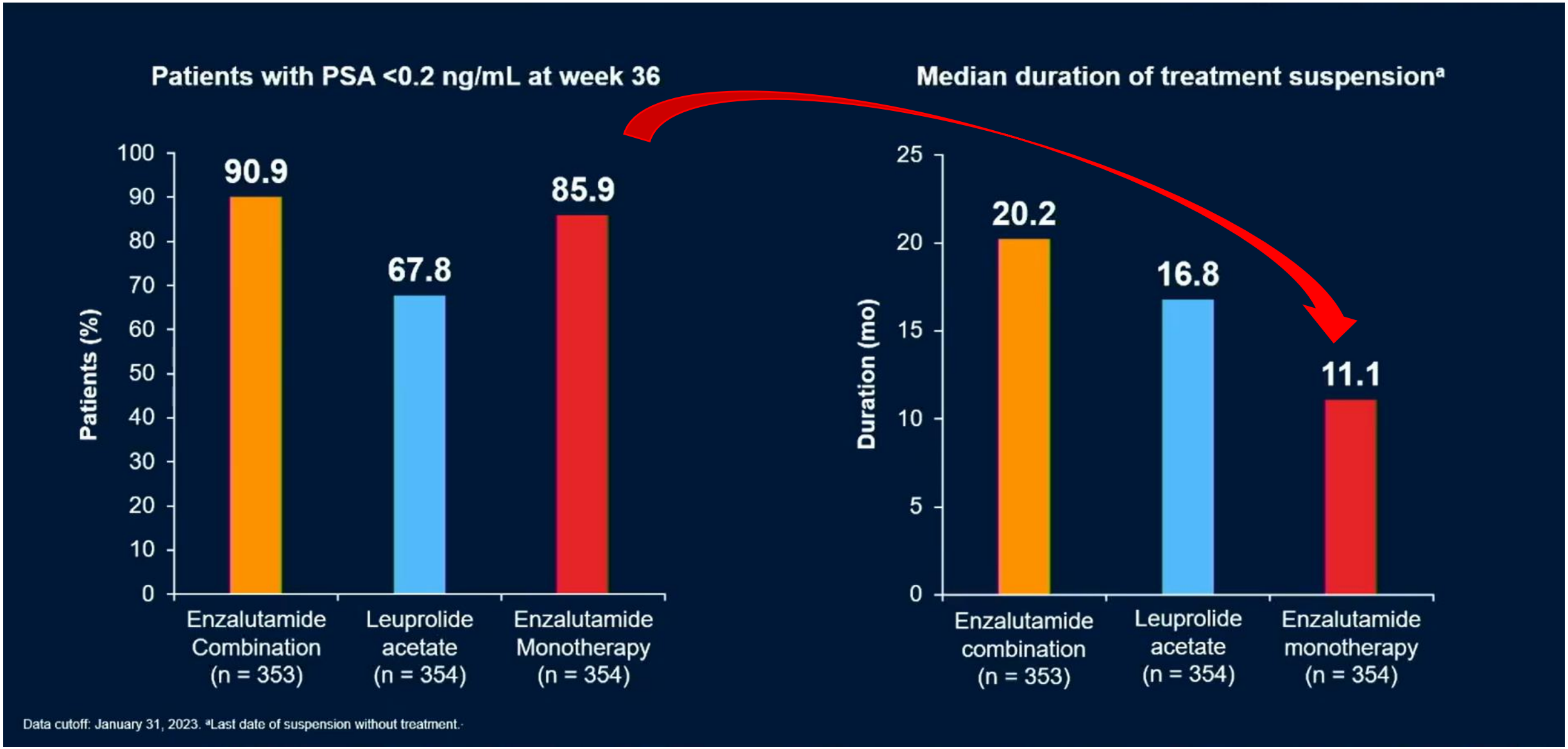
Median duration of treatment suspension[a]



Data cutoff: January 31, 2023. [a]Last date of suspension without treatment.



Data cutoff: January 31, 2023. [a]Last date of suspension without treatment.


Patients with PSA <0.2 ng/mL at week 36
Patients (%)
100
90
80
70
60
50
40
30
20
10
0
90.9
67.8
85.9
Enzalutamide Combination (n = 353)
Leuprolide acetate (n = 354)
Enzalutamide Monotherapy (n = 354)
Median duration of treatment suspension[a]
Duration (mo)
25
20
15
10
5
0
20.2
16.8
11.1
Enzalutamide combination (n = 353)
Leuprolide acetate (n = 354)
Enzalutamide monotherapy (n = 354)
Data cutoff: January 31, 2023. [a]Last date of suspension without treatment.

Event, n (%)[a]	Enzalutamide combination (n = 353)		Leuprolide acetate (n = 354)		Enzalutamide monotherapy (n = 354)	
	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3
Any AE	343 (97.2)	164 (46.5)	345 (97.5)	151 (42.7)	347 (98.0)	177 (50.0)
Treatment-related AE	305 (86.4)	62 (17.6)	283 (79.9)	31 (8.8)	312 (88.1)	57 (16.1)
Serious AE	123 (34.8)	110 (31.2)	112 (31.6)	100 (28.2)	131 (37.0)	116 (32.8)
Treatment-related serious AE	26 (7.4)	22 (6.2)	8 (2.3)	7 (2.0)	17 (4.8)	17 (4.8)
AE leading to dose reduction	25 (7.1)	11 (3.1)	16 (4.5)	5 (1.4)	56 (15.8)	14 (4.0)
AE leading to permanent discontinuation	73 (20.7)	31 (8.8)	36 (10.2)	19 (5.4)	63 (17.8)	34 (9.6)
AE leading to death	6 (1.7)[b]	–	3 (0.8)[b]	–	8 (2.3)[b]	–

- Median treatment duration excluding treatment suspension was 32.4 mo (range, 0.1–83.4 mo) for enzalutamide combination, 35.4 mo (range, 0.7–85.7 mo) for leuprolide acetate, and 45.9 mo (0.4–88.9 mo) for enzalutamide monotherapy.
- The most common AE leading to study drug discontinuation was fatigue (enzalutamide combination, 3.4% [n = 12]; leuprolide acetate, 1.1% [n = 4]; enzalutamide monotherapy, 2.3% [n = 8]).

Data cutoff: January 31, 2023. [a]Percentages may not total 100 because of rounding. Shown are AE that occurred from the time of first dose of study treatment through 30 days after permanent discontinuation. AE were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03. [b]Grade 5 AE; none were considered treatment-related. AE, adverse event.


Erleada®
Apalutamida
Tableta
60 mg
Caja con frasco con 120 tabletas
Fórmula:
Cada tableta contiene:
Apalutamida 60 mg
Excipiente cbp
© J-C 2019


Xtandi
Enzalutamida
Cápsula
40 mg
Caja con 120 Cápsulas
VIA DE ADMINISTRACIÓN: Oral
ASOFARMA
astellas


NDC 50419-395-01
Rx Only
NUBEQA®
(darolutamide) tablets
300 mg
120 film-coated tablets
Oral use


ZYTIGA®
Abiraterona
Tabletas
250 mg
Caja con frasco con 120 tabletas
Fórmula:
Cada tableta contiene:
Acetato de Abiraterona ..... 250 mg
Excipiente csp ..... 1 Tableta
janssen


Erleada®
Apalutamida
Tableta
60 mg
Caja con frasco con 120 tabletas
Fórmula:
Cada tableta contiene:
Apalutamida 60 mg
Excipiente cbp
© J-C 2019


Xtandi
Enzalutamida
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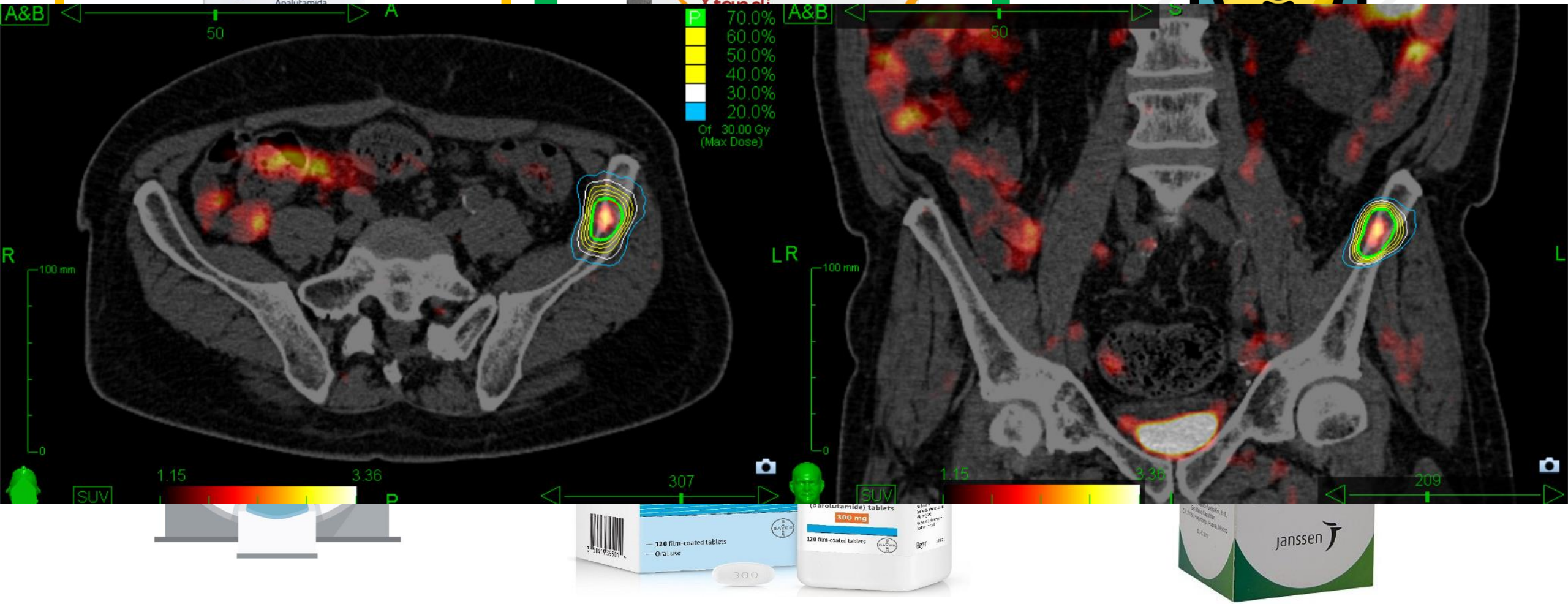
Excipiente csp ..... 1 Tableta
janssen


A&B
50
A
P
70.0%
60.0%
50.0%
40.0%
30.0%
20.0%
Of 30.00 Gy
(Max Dose)
A&B
50
S
R
100 mm
0
LR
100 mm
0
L
SUV
1.15
3.36
P
307
SUV
1.15
3.36
209
Erleada®
Apalutamida
300 mg
120 film-coated tablets
Oral use
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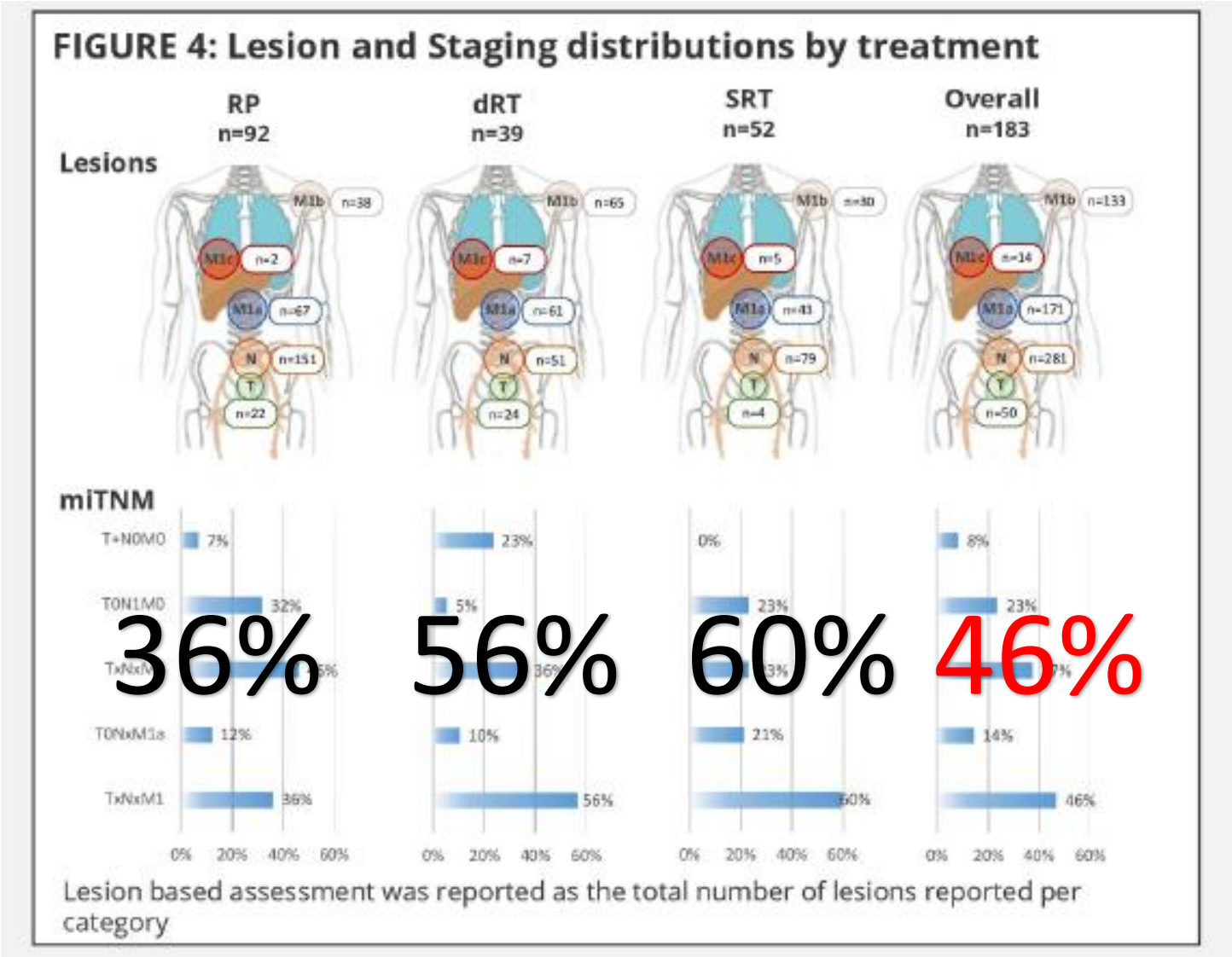
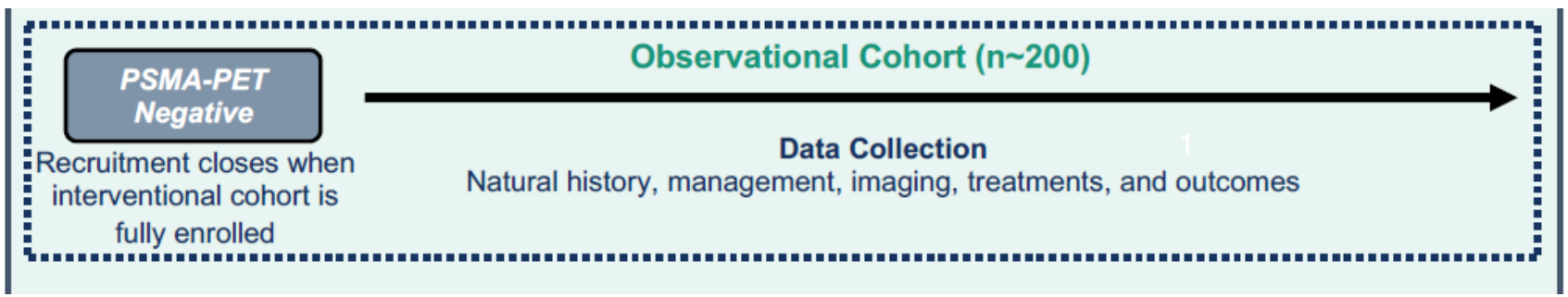
Perfil EMBARK. Rendimiento del PET



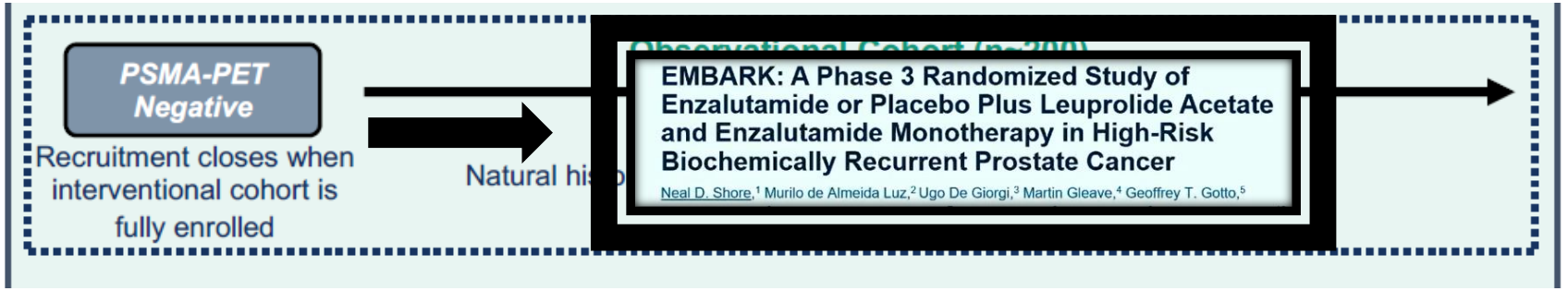
PRIMORDIUM

56021927PCR3015; NCT04557059



PRIMORDIUM

56021927PCR3015; NCT04557059



PRIMORDIUM

56021927PCR3015; NCT04557059

Study Design

Interventional Cohort (n~412)

Treatment Phase: 6 months

RT: whole pelvic salvage radiotherapy ± SBRT
LHRHa: 2x3-monthly or 1x6-monthly depot
Apalutamide: 240 mg/day orally

PSMA-PET Positive

1:1

- **RT + LHRHa**
- **RT + LHRHa + Apalutamide**

Post-treatment Phase (until PSMA-PET progression)

Assessments
PSA, testosterone, patient-reported outcomes

Unblinded at baseline,
BICR at 6, 12, and q12 months (until PSA ≥0.2 ng/mL, then immediately and q6 months)

Post-PSMA-PET Progression Phase

Assessments
Bone scan, CT/MRI, patient-reported outcomes

Brazo obsoleto

PSMA-PET Negative

Recruitment closes when interventional cohort is fully enrolled

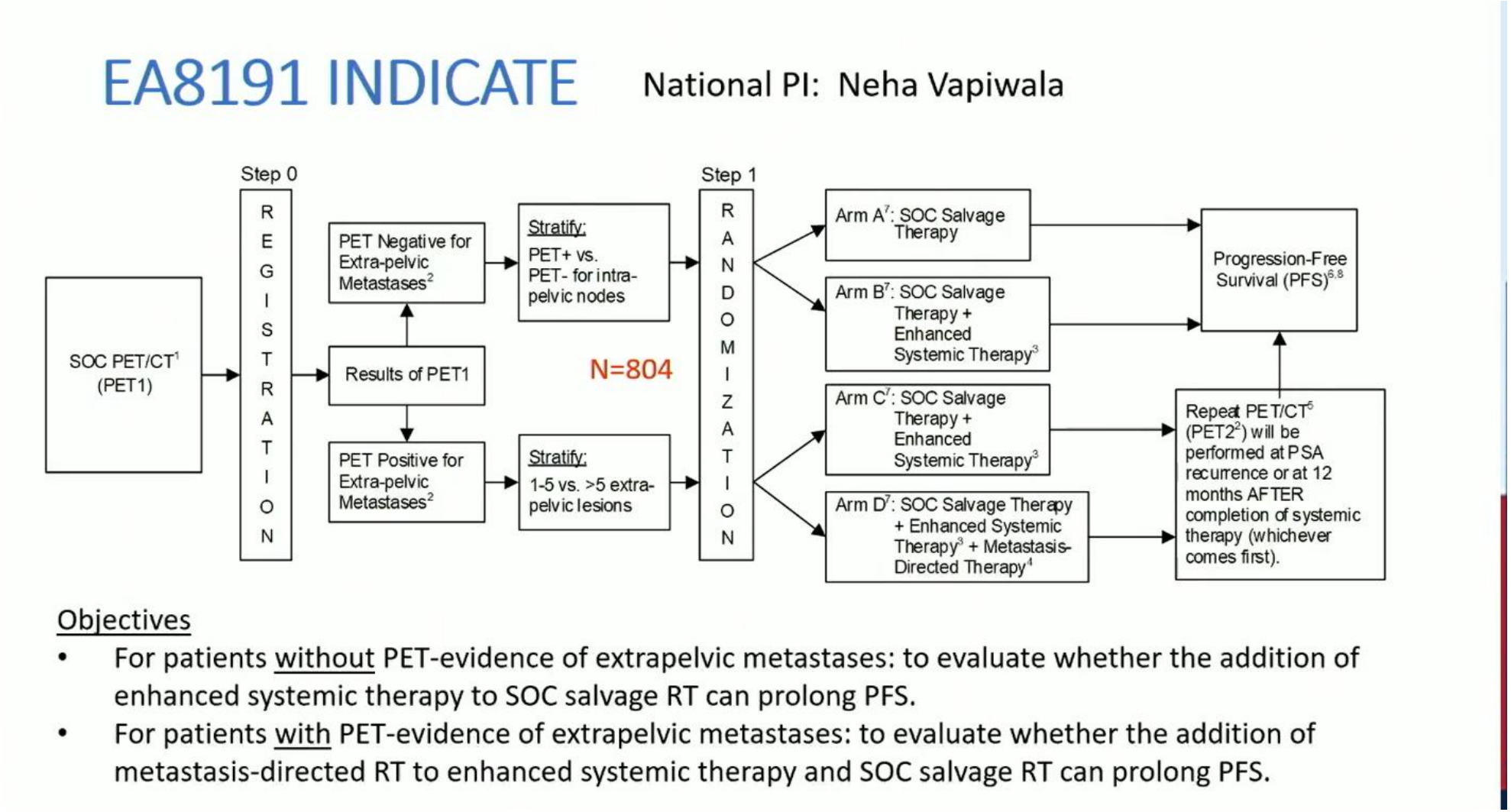
Natural his

Observational Cohort (n~200)

EMBARK: A Phase 3 Randomized Study of Enzalutamide or Placebo Plus Leuprolide Acetate and Enzalutamide Monotherapy in High-Risk Biochemically Recurrent Prostate Cancer

Neal D. Shore,[1] Murilo de Almeida Luz,[2] Ugo De Giorgi,[3] Martin Gleave,[4] Geoffrey T. Gotto,[5]

Futuro referido en AUA



Objectives

- For patients without PET-evidence of extrapelvic metastases: to evaluate whether the addition of enhanced systemic therapy to SOC salvage RT can prolong PFS.
- For patients with PET-evidence of extrapelvic metastases: to evaluate whether the addition of metastasis-directed RT to enhanced systemic therapy and SOC salvage RT can prolong PFS.

CPHSm

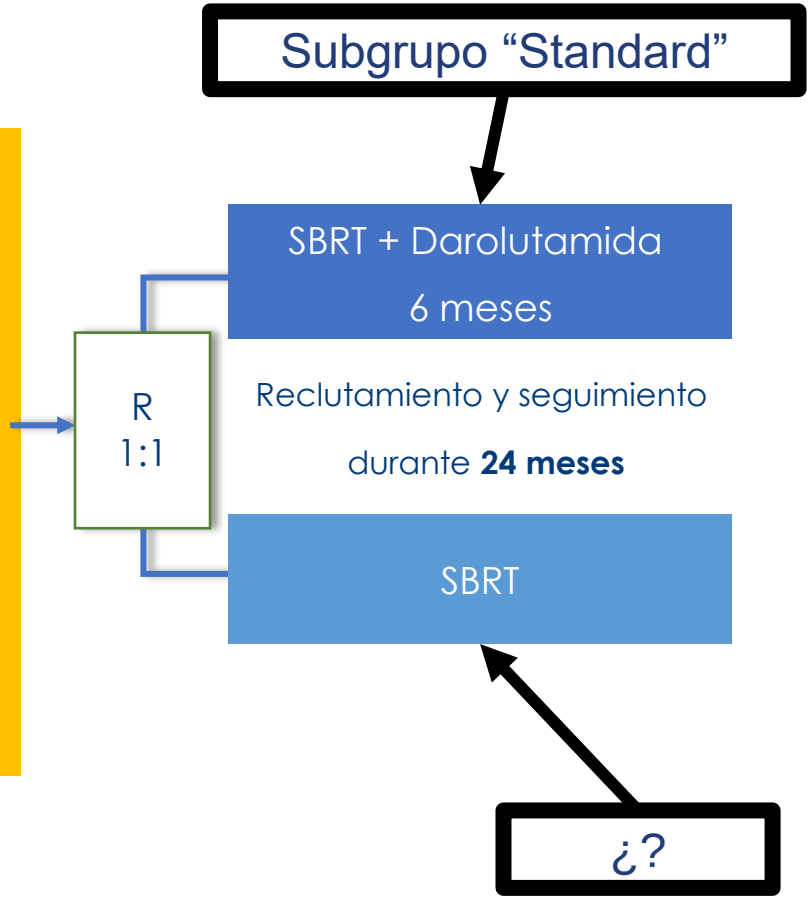
DART: Radioterapia estereotáctica corporal con o sin darolutamida para el cáncer de próstata oligorrecurrente

FASE 2 aleatorizado que compara darolutamida con SBRT

Patrocinador: **Hospital Universitario, Gante**
PI: Piet Ost
Fecha estimada de finalización: 2024
Países: Bélgica
Recruiting

N=128

- CPHS con recurrencia bioquímica después de la terapia primaria
- Hasta 5 metástasis en PET-CT
- Estratificación:
Hasta 5 metástasis en PSMA PET-CT
- Tiempo de duplicación del PSA (</=6 frente a 6-12 meses)



Objetivo primario:
- **Supervivencia libre de metástasis (SLM)**

Objetivos secundarios:
- Seguridad
- Supervivencia libre de recaída bioquímica
- Supervivencia libre de progresión clínica
- Tiempo hasta la próxima terapia sistémica
- Supervivencia libre de CRPC
- Supervivencia global y específica del cáncer de próstata
- Calidad de vida

SLM = Tiempo entre la aleatorización y la aparición de una nueva recurrencia metastásica (cualquier M1) según lo sugerido por PET-CT o muerte por cualquier causa

SBRT: Radioterapia corporal estereotáctica; CPRC: cáncer de próstata resistente a la castración

Clinical Trials Identifier: NCT04641078. https://clinicaltrials.gov/ct2/show/NCT04641078

IRAD START-MET

START-MET: SbrT Androgen Receptor Therapy METastatic HS prostate cancer.

mHSPC, non-blinded, randomized, phase III, multi center study.

Meets following criteria

Inclusion criteria

- **Castration sensitive → Local prior treatment allowed**
- **ECOG PS 0 or 1**
- **Distant metastatic disease by ≤ 3 lesions based on CT and Bone Scan and ≤ 5 lesions based on Coline or PSMA PET/TC**

***Stratification factors*:**

- **Prior local treatment**
- **New Imaging technique (Coline vs PSMA PET/TC)**

Exclusion criteria

- **Metastases in previously irradiated areas**
- **Prior docetaxel or second generation hormonal treatments**
- **Tumor stage T4**

N = 266

Randomization 1:1

STANDARD OF CARE + SBRT (all metastatic lesions)

ADT+ RT to the primary tumor (previously not treated) + Second generation hormonal treatment

STANDARD OF CARE

ADT+ RT to the primary tumor (previously not treated) + Second generation hormonal treatment

ENDPOINTS

Primary endpoint:
- **rPFS**

Key Secondary endpoints:
- **Overall survival**
- **Time to cytotoxic chemotherapy**
- **Time to PSA progression**
- **Time to pain progression**
- **Time to castration resistance**
- **Time to skeletal-related event**
- **Quality of life and safety profile**
-

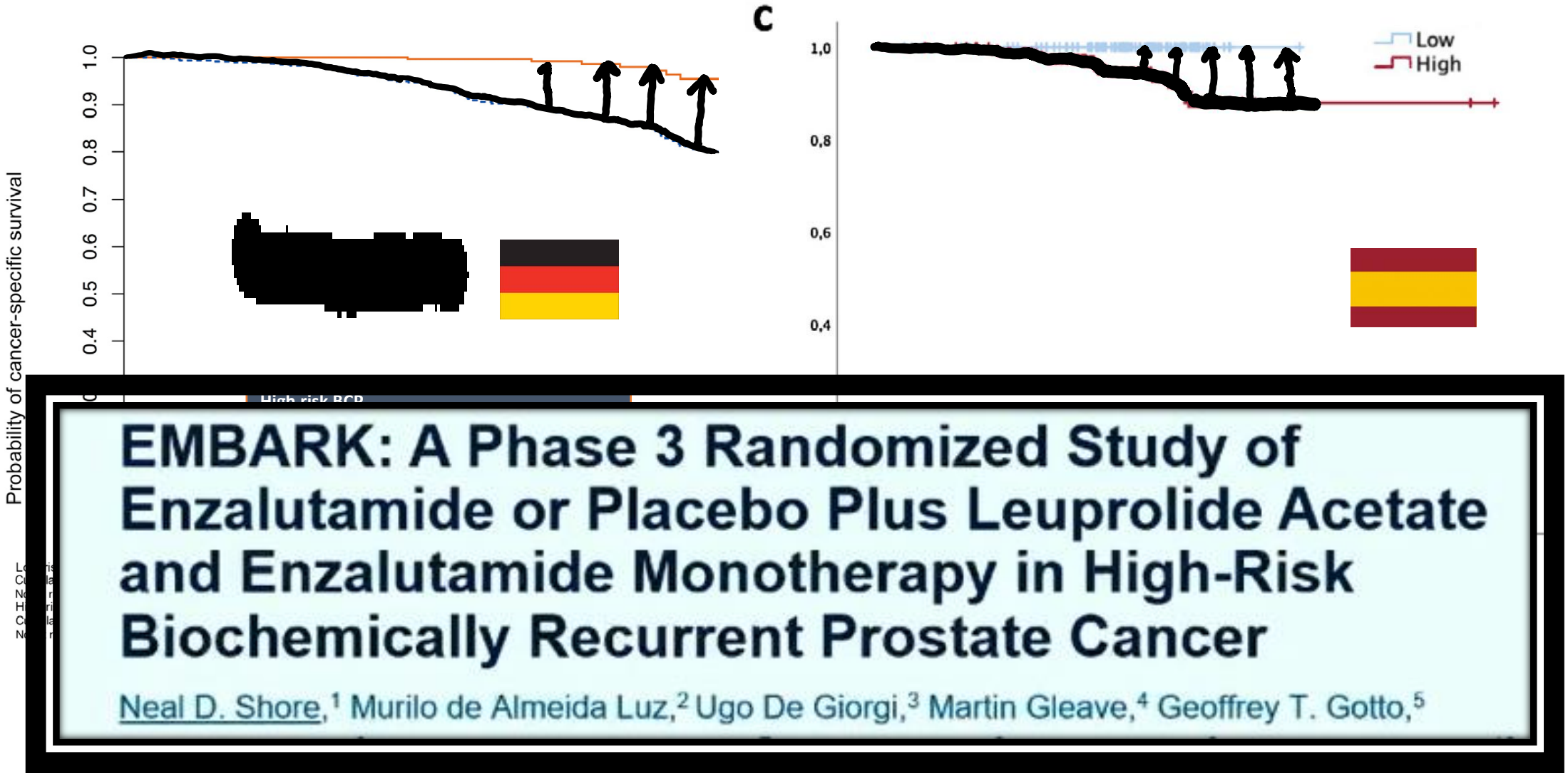
Exploratory endpoints:

- **Biomarkers assessment**
- **Local control**
- **Second progression free survival (PFS2)**
- **Time to symptomatic progression**

(ADT+ Abi/Apa/Enza/Daro)

PIs: Conde-Moreno, López-Campos, Gómez-Iturriaga

Conclusiones.



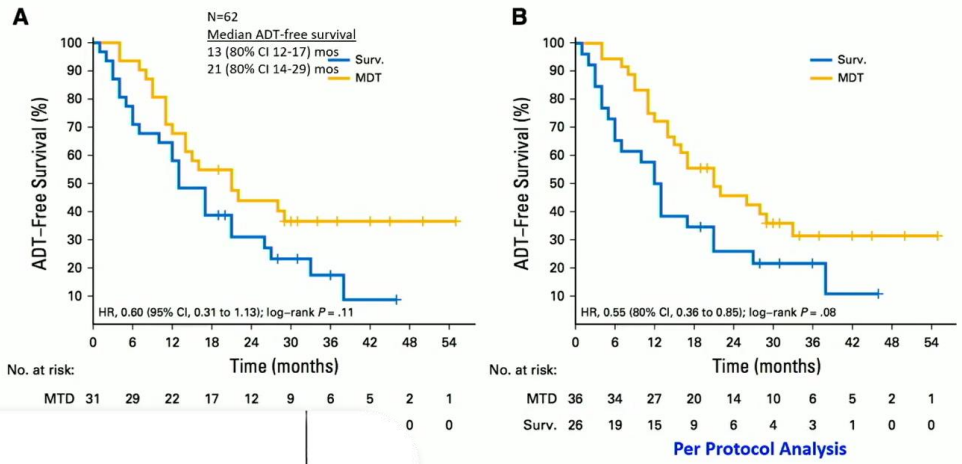
Virtudes de una Fase OFF:

OLIGO 

SU perfil. Radio/URO que piensa que el PSMA da la oportunidad de rescatar y curar algunos POCOS pacientes.

¿Cómo acaban los PIVOTALES de los oligobelievers?

Metastasis-Directed Therapy Improves ADT-free Survival



al. J Clin Oncol. 2018; 36:446-53.

Surveillance or Metastasis-Directed Therapy for Oligometastatic Prostate Cancer Recurrence: A Prospective, Randomized, Multicenter Phase II Trial

Piet Ost, Dries Reynders, Karel Decaestecker, Valérie Fonteyne, Nicolaas L Lambert, Louke Delrue, Renée Bultijnck, Tom Claeys, Els Goetghebeur, Geer Ignace Billiet, Steven Joniau, Friedl Vanhaverbeke, and Gert De Meerleer

Ost P et al. J Clin Oncol. 2018; 36:446-53.

Outcomes of Observation vs Stereotact for Oligometastatic Prostate Cancer
The ORIOLE Phase 2 Randomized Clinica

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Phillips R et al. JAMA Oncol 2020; 6:650-59.

0 0

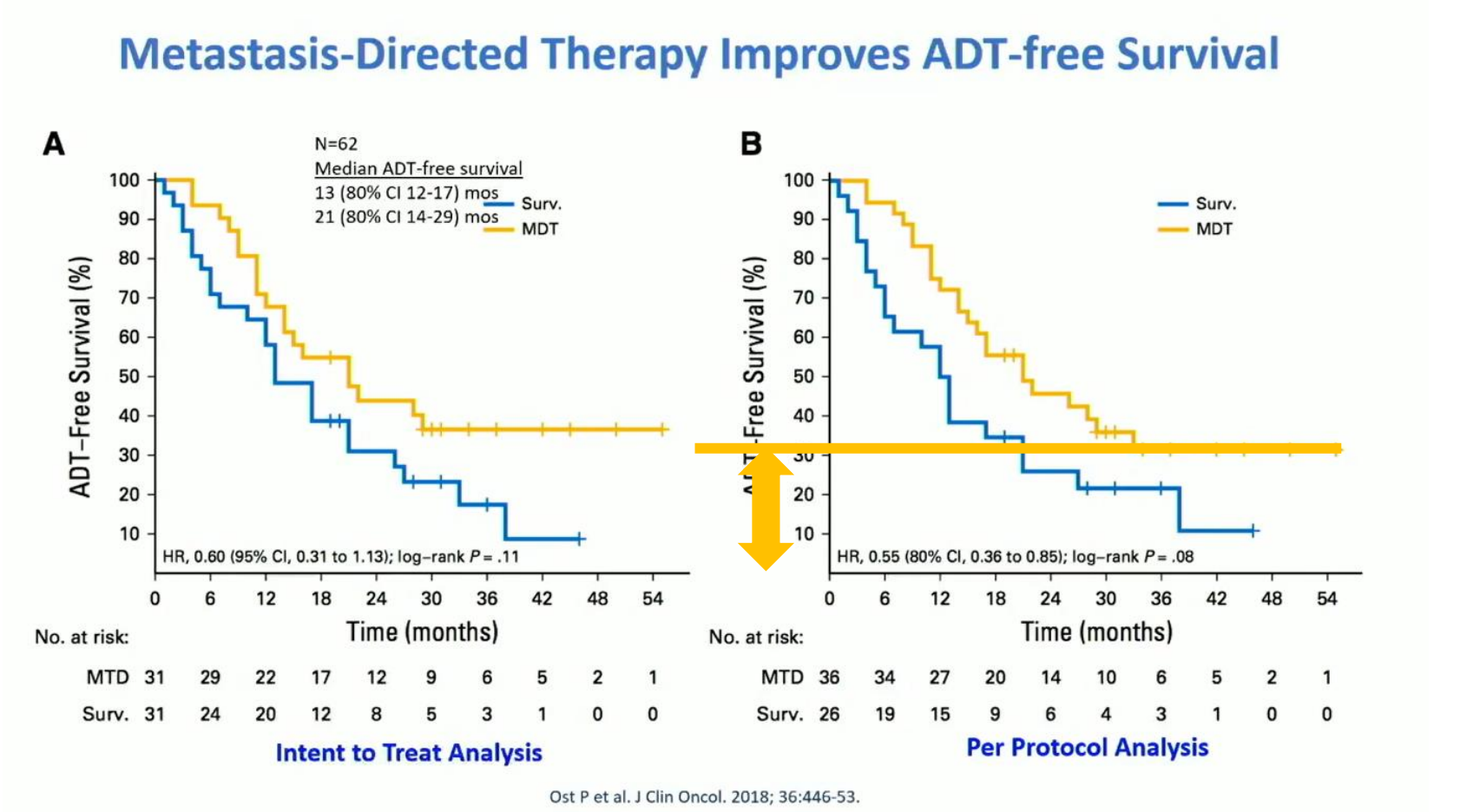
pecific antigen (PSA) after 3 months and (B) the best response. (C) Kaplan-Meier plot comparing tion-to-treat analysis. (*) Indicates patients who were randomly assigned to the surveillance (Surv) arm , hazard ratio.

IDT a treat-
te only ret-
series tried
etrospective
ulting in an
onths) after

ent because
nts received
SBRT. This
the better
he addition

of temporary ADT to radiotherapy is known to prolong progression-free survival and overall survival in both high-risk and biochemical recurrent PCa.[2] Consequently, we believe it is worthwhile to investigate the addition of a temporary systemic drug to MDT in future trials. The synergistic approach might improve the therapeutic ratio by eradicating microscopic disease, which is still often missed by choline PET-CT. This is demonstrated clearly by the current trial—30% of patients treated with MDT progressed to polymetastatic disease within the first year. Advances in imaging, such as ^{68}Ga prostate-specific membrane antigen (PSMA) PET-CT, might also improve patient selection for MDT.[27] PSMA-PET, which is widely available and has a better sensitivity and specificity than does

Pero….. ¿Cuál es la única manera de reconocer a este subgrupo?



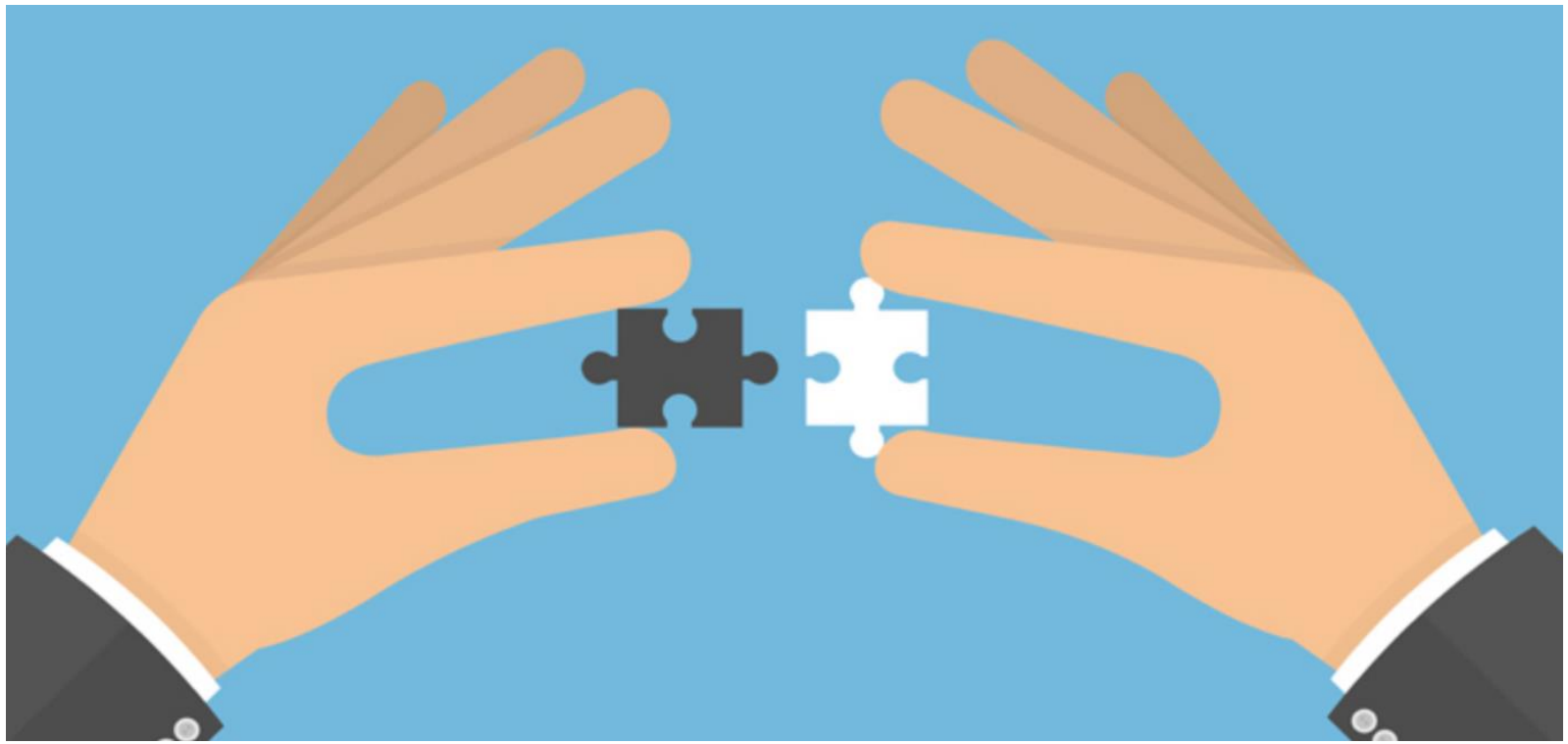
Ost P et al. J Clin Oncol. 2018; 36:446-53.

Si los autores reconocen que a la sbrt hay que añadir TDA…

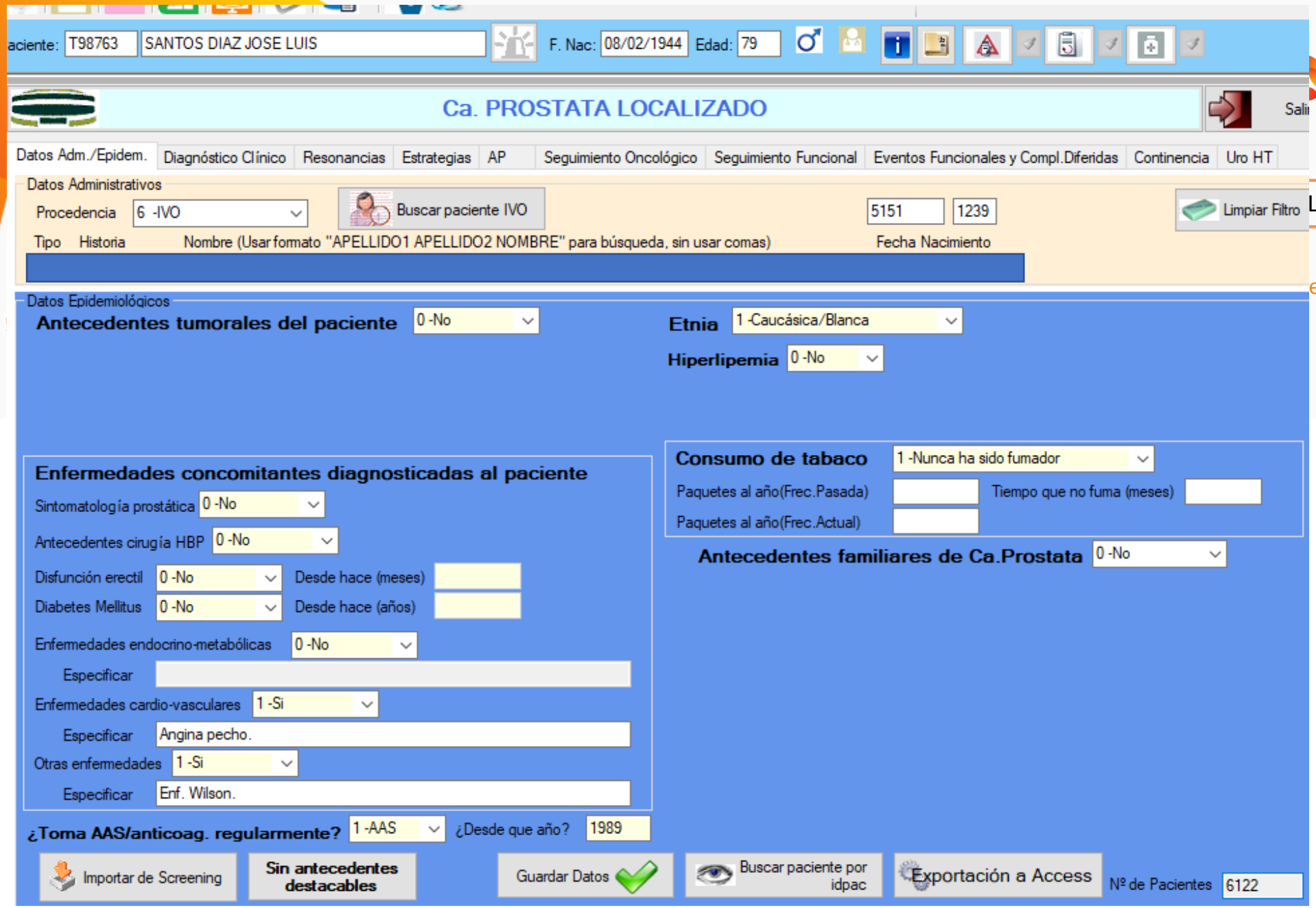
Sin embargo, refieren que hay un 30% de pacientes que gracias a la SBRT EVITAN LA TDA?....

La Solución es LA INTERMITENCIA


Buenas Ideas y Proyectos
Bases de Datos
Compañeros/amigos y Jefes Inspiradores
GUARD



1. Proyectos Ambiespectivos.



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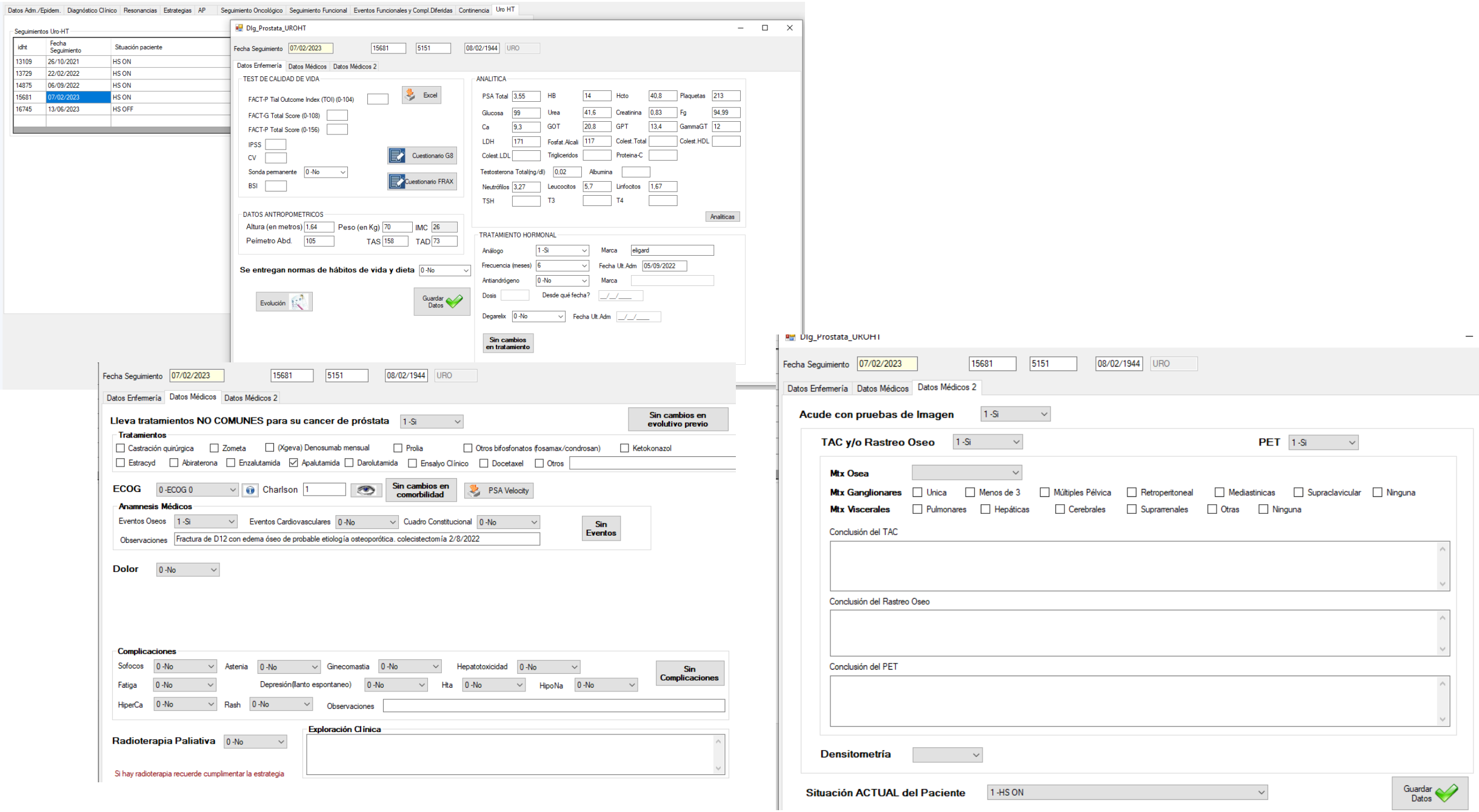
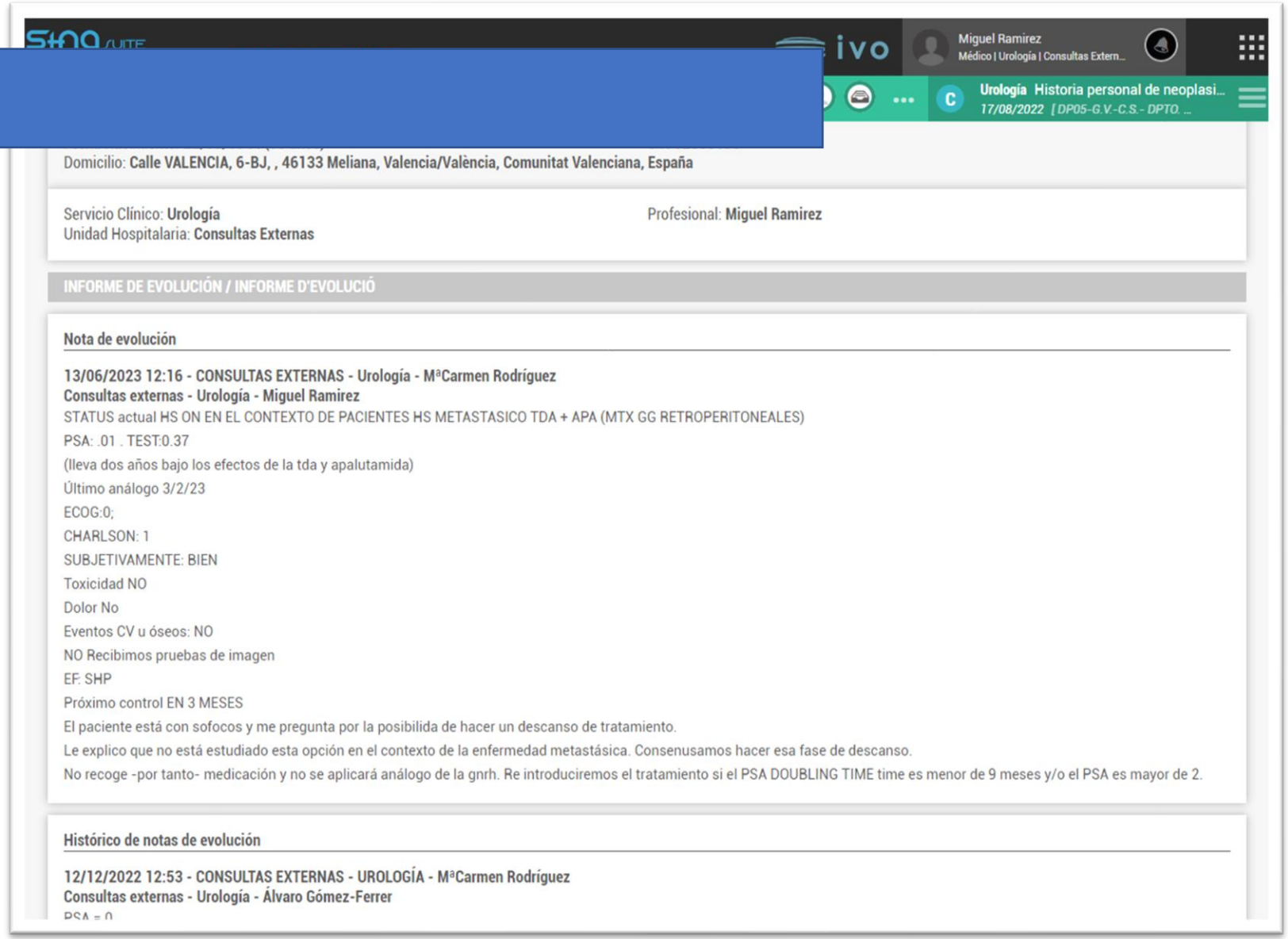
e for Research
Development


Datos Adm./Epidem.
Diagnóstico Clínico
Resonancias
Estrategias
AP
Seguimiento Oncológico
Seguimiento Funcional
Eventos Funcionales y Compl.Diferidas
Continencia
Uro HT
Seguimientos Uro-HT
idht
Fecha Seguimiento
Situación paciente
13109 26/10/2021 HS ON
13729 22/02/2022 HS ON
14875 06/09/2022 HS ON
15681 07/02/2023 HS ON
16745 13/06/2023 HS OFF
Dlg_Prostata_UROHT
Fecha Seguimiento 07/02/2023
15681
5151
08/02/1944
URO
Datos Enfermería
Datos Médicos
Datos Médicos 2
TEST DE CALIDAD DE VIDA
FACT-P Tial Outcome Index (TOI) (0-104)
FACT-G Total Score (0-108)
FACT-P Total Score (0-156)
IPSS
CV
Sonda permanente
0 -No
BSI
Excel
Cuestionario G8
Cuestionario FRAX
ANALITICA
PSA Total 3,55
HB 14
Hcto 40,8
Plaquetas 213
Glucosa 99
Urea 41,6
Creatinina 0,83
Fg 94,99
Ca 9,3
GOT 20,8
GPT 13,4
GammaGT 12
LDH 171
Fosfat.Alcali 117
Colest.Total
Colest.HDL
Colest.LDL
Triglicéridos
Proteina-C
Testosterona Total(ng/dl) 0,02
Albumina
Neutrófilos 3,27
Leucocitos 5,7
Linfocitos 1,67
TSH
T3
T4
Analíticas
DATOS ANTROPOMETRICOS
Altura (en metros) 1,64
Peso (en Kg) 70
IMC 26
Peímetro Abd. 105
TAS 158
TAD 73
TRATAMIENTO HORMONAL
Análogo 1 -Si
Marca eligard
Frecuencia (meses) 6
Fecha Ult.Adm 05/09/2022
Antiandrógeno 0 -No
Marca
Dosis
Desde qué fecha?
Degarelix 0 -No
Fecha Ult.Adm
Sin cambios en tratamiento
Se entregan normas de hábitos de vida y dieta 0 -No
Evolución
Guardar Datos
Lleva tratamientos NO COMUNES para su cancer de próstata 1 -Si
Sin cambios en evolutivo previo
Tratamientos
Castración quirúrgica
Zometa
(Xgeva) Denosumab mensual
Prolia
Otros bifosfonatos (fosamax/condrosan)
Ketokonazol
Estracyd
Abiraterona
Enzalutamida
Apalutamida
Darolutamida
Ensalyo Clínico
Docetaxel
Otros
ECOG 0 -ECOG 0
Charlson 1
Sin cambios en comorbilidad
PSA Velocity
Anamnesis Médicos
Eventos Oseos 1 -Si
Eventos Cardiovasculares 0 -No
Cuadro Constitucional 0 -No
Observaciones Fractura de D12 con edema óseo de probable etiología osteoporótica. colecistectomía 2/8/2022
Sin Eventos
Dolor 0 -No
Complicaciones
Sofocos 0 -No
Astenia 0 -No
Ginecomastia 0 -No
Hepatotoxicidad 0 -No
Fatiga 0 -No
Depresión(llanto espontaneo) 0 -No
Hta 0 -No
HipoNa 0 -No
HiperCa 0 -No
Rash 0 -No
Observaciones
Sin Complicaciones
Radioterapia Paliativa 0 -No
Exploración Clínica
Si hay radioterapia recuerde cumplimentar la estrategia
Dlg_Prostata_UROHT
Fecha Seguimiento 07/02/2023
15681
5151
08/02/1944
URO
Datos Enfermería
Datos Médicos
Datos Médicos 2
Acude con pruebas de Imagen 1 -Si
TAC y/o Rastreo Oseo 1 -Si
PET 1 -Si
Mtx Osea
Mtx Ganglionares
Unica
Menos de 3
Múltiples Pélvica
Retroperitoneal
Mediastinicas
Supraclavicular
Ninguna
Mtx Viscerales
Pulmonares
Hepáticas
Cerebrales
Suprarrenales
Otras
Ninguna
Conclusión del TAC
Conclusión del Rastreo Oseo
Conclusión del PET
Densitometría
Situación ACTUAL del Paciente 1 -HS ON
Guardar Datos


ivo
Miguel Ramirez
Médico | Urología | Consultas Extern...
Urología Historia personal de neoplasi...
17/08/2022 [DP05-G.V.-C.S.- DPTO. ...
Domicilio: Calle VALENCIA, 6-BJ, , 46133 Meliana, Valencia/València, Comunitat Valenciana, España
Servicio Clínico: Urología
Unidad Hospitalaria: Consultas Externas
Profesional: Miguel Ramirez
INFORME DE EVOLUCIÓN / INFORME D'EVOLUCIÓ
Nota de evolución
13/06/2023 12:16 - CONSULTAS EXTERNAS - Urología - MªCarmen Rodríguez
Consultas externas - Urología - Miguel Ramirez
STATUS actual HS ON EN EL CONTEXTO DE PACIENTES HS METASTASICO TDA + APA (MTX GG RETROPERITONEALES)
PSA: .01 . TEST:0.37
(lleva dos años bajo los efectos de la tda y apalutamida)
Último análogo 3/2/23
ECOG:0;
CHARLSON: 1
SUBJETIVAMENTE: BIEN
Toxicidad NO
Dolor No
Eventos CV u óseos: NO
NO Recibimos pruebas de imagen
EF: SHP
Próximo control EN 3 MESES
El paciente está con sofocos y me pregunta por la posibilida de hacer un descanso de tratamiento.
Le explico que no está estudiado esta opción en el contexto de la enfermedad metastásica. Consenusamos hacer esa fase de descanso.
No recoge -por tanto- medicación y no se aplicará análogo de la gnrh. Re introduciremos el tratamiento si el PSA DOUBLING TIME time es menor de 9 meses y/o el PSA es mayor de 2.
Histórico de notas de evolución
12/12/2022 12:53 - CONSULTAS EXTERNAS - UROLOGÍA - MªCarmen Rodríguez
Consultas externas - Urología - Álvaro Gómez-Ferrer
PSA = 0

Intermitencia con NAH

CPHS oligometastásico sincrónico:

- ✓ Candidato a tratamiento de la próstata.
- ✓ <5 metástasis por PET (Colina o PSMA).

CPHS oligorecurrente M1a.

Relugolix 120mg/día

+

Apa/Dari/Enza.

PSA ≤ 0.2 ng/ml

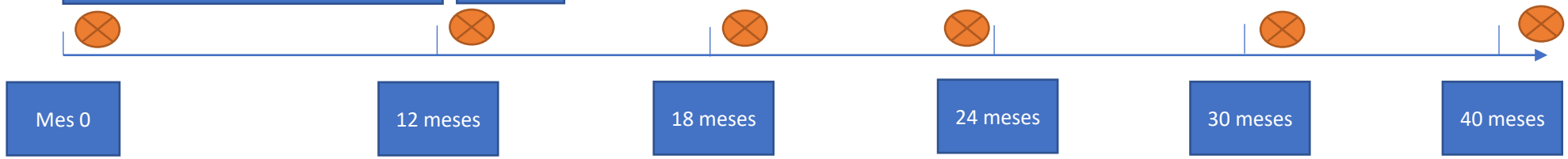
Si: Inicio Fase OFF.

Si PSA > 2ng/ml: Reinicio fase ON

Reiniciar fase OFF si PSA ≤ 0.2 ng/ml

Si PSA > 2ng/ml en fase ON : Diagnóstico de CPRC

NO: Continuar tratamiento hasta CPRC



- Cuestionarios (FACT-P, EORTC QLQ-PR25, IIEF-5...)
- Evaluación masa muscular (Impedanciometría, dinamometría)
- Evaluación masa ósea (densitometría, eventos esqueléticos)

PERFILES DE RESPUESTA

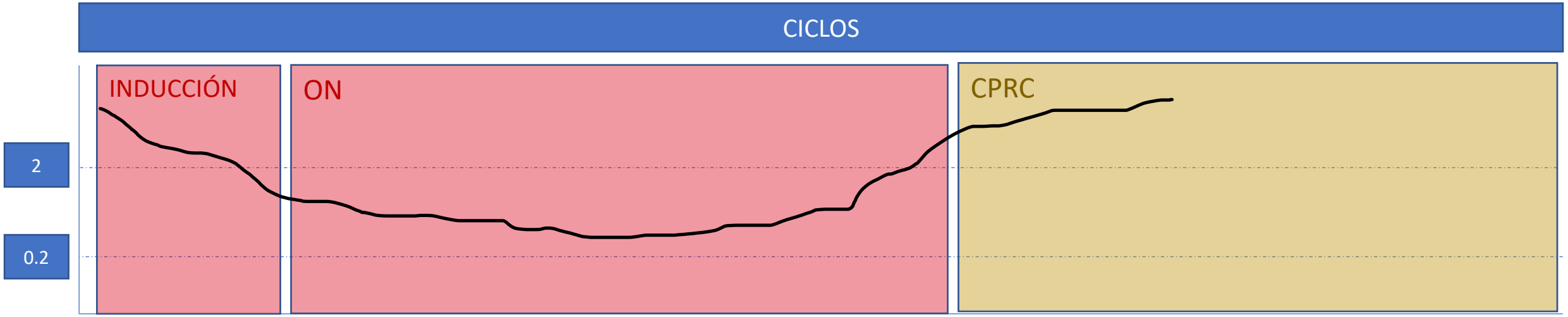
NO respondedor: No responde a la inducción

Mal respondedor: Menos de 2 años en OFF

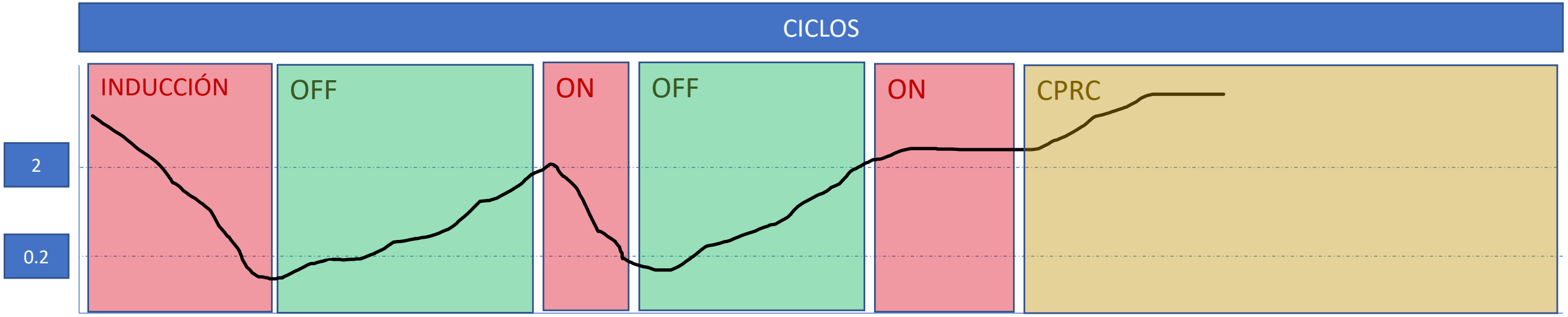
Buen respondedor: Más de 2 años en OFF

Excelente respondedor: Termina el estudio o fallece en OFF

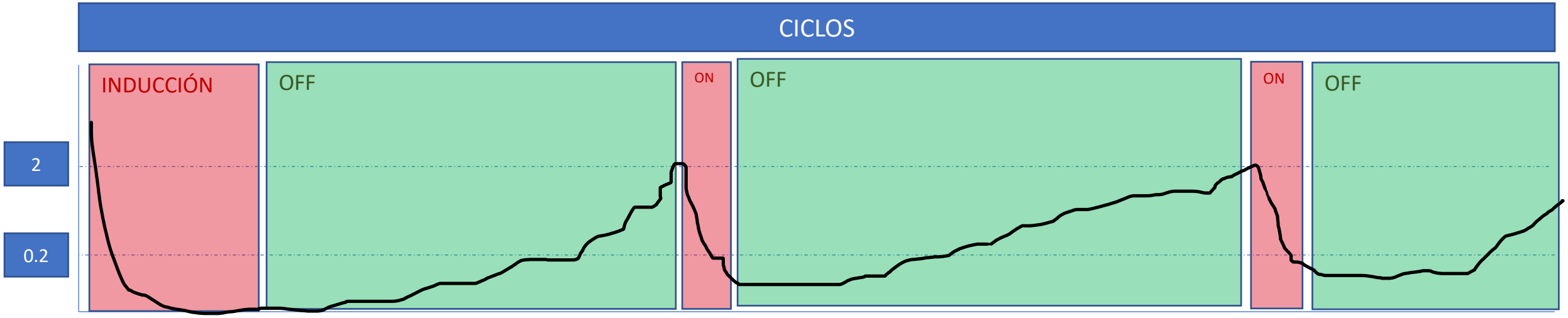
NO respondedor: No responde a la inducción



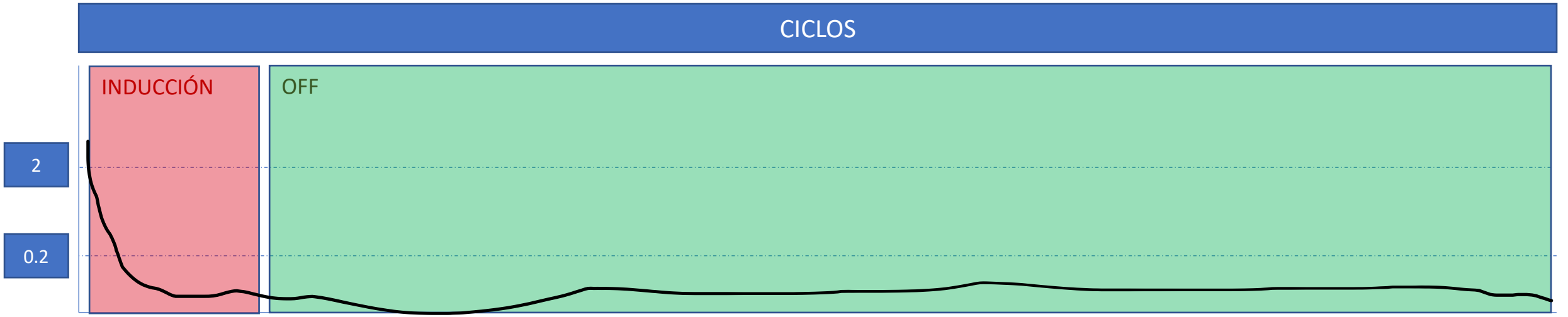
Mal respondedor: Menos de 2 años en OFF



Buen respondedor: Más de 2 años en OFF



Excelente respondedor: Termina el estudio o fallece en OFF



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6-7 JULIO 2023

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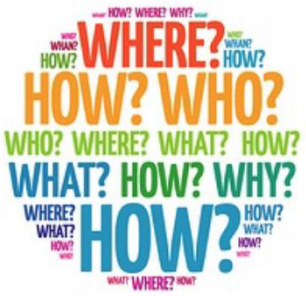

2024