VI Jornadas Interhospitalarias de Urólogos de Extremadura.

CÁNCER DE PRÓSTATA RESISTENTE A LA CASTRACIÓN NO METASTÁSICO. POSICIONAMIENTO DE LOS NUEVOS FÁRMACOS

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COMPLEJO HOSPITALARIO UNIVERSITARIO DE BADAJOZ

CONFLICTOS DE INTERESES

- COLABORACIONES PUNTUALES CON JANSSEN, IPSEN, ASTELLAS, GSK, CASEN RECORDATI, GSK, BAYER, LILLY
- INVESTIGADOR SECUNDARIO EN ENSAYO CLÍNICO DE ASTRA ZENECA
- INVESTIGADOR PRINCIPAL EN ENSAYO CLÍNICO DE BRISTOL MYERS SQUIBB

DEFINICIÓN CÁNCER DE PRÓSTATA RESISTENTE A CASTRACIÓN NO METASTÁSICO

The Prostate Cancer Clinical Trials Working Group 2 (PCWG2)

- **Rising PSA** [> 2ng/ml , higher 25% than nadir and confirmed by second PSA at 3 weeks]
- **Levels of testosterone < 50 ng/dL** or <1.7 nmol/L
- **No radiographic evidence** of metastatic disease

The Prostate Cancer Clinical Trials Working Group 3 (PCWG3)

Nonmetastatic (nmCRPC)

A rising PSA with no detectable disease in the primary site, in bone by radionuclide bone scan or CT or in visceral organs

Scher HI. Design and end points of clinical trials for patients with progressive prostate cancer and castrate levels of testosterone: recommendations of the Prostate Cancer Clinical Trials Working Group. J Clin Oncol 2008; 26:1148-59

Sher HI. Trial Design and Objectives for Castration-Resistant Prostate Cancer: Updated Recommendations From the Prostate Cancer Clinical Trials Working Group 3. J Clin Oncol 34:1402-1418.

INFORMES DE POSICIONAMIENTO TERAPEÚTICO

- ESTOS **INFORMES** TIENEN COMO OBJETIVO REALIZAR UN ANÁLISIS ACERCA DEL VALOR AÑADIDO DE LOS NUEVOS MEDICAMENTOS E INFORMAR SOBRE LA "POSICIÓN QUE EL NUEVO MEDICAMENTO OCUPA EN COMPARACIÓN CON OTROS MEDICAMENTOS O MEDIDAS DE SALUD YA EXISTENTES"
- LA **EVALUACIÓN Y AUTORIZACIÓN** DE NUEVOS MEDICAMENTOS, UNA VEZ APROBADOS POR LA AGENCIA EUROPEA DEL MEDICAMENTO (EMA), **ABRE UN PROCESO DE DECISIÓN SOBRE SU PRECIO Y FINANCIACIÓN EN EL SISTEMA NACIONAL DE SALUD, Y SU EVENTUAL INCORPORACIÓN A LA PRÁCTICA ASISTENCIAL**
- LOS IPT «CONTENDRÁN, EN UNA PRIMERA FASE, LA EVALUACIÓN DE LA EFICACIA Y LA SEGURIDAD COMPARADA, ASÍ COMO LOS CRITERIOS DE USO Y SEGUIMIENTO. OPCIONALMENTE, PODRÁ(N) INCLUIR UNA EVALUACIÓN ECONÓMICA A JUICIO DEL GCPT. EN UNA SEGUNDA FASE, TRAS EL PROCEDIMIENTO DE FIJACIÓN DE PRECIO Y FINANCIACIÓN, INCORPORARÁ(N) SIEMPRE LA VALORACIÓN ECONÓMICA Y DE IMPACTO PRESUPUESTARIO

INFORMES DE POSICIONAMIENTO TERAPÉUTICO


MINISTERIO DE SANIDAD, CONSUMO Y BIENESTAR SOCIAL

agencia española de medicamentos y productos sanitarios

INFORME DE POSICIONAMIENTO TERAPÉUTICO

Informe de Posicionamiento Terapéutico de enzalutamida (Xtandi®) en cáncer de próstata resistente a la castración no metastásico.

IPT, 31/2021. V1

Fecha de publicación: 25 de junio de 2021[*]


MINISTERIO DE SANIDAD

agencia española de medicamentos y productos sanitarios

INFORME DE POSICIONAMIENTO TERAPÉUTICO

Informe de Posicionamiento Terapéutico de darolutamida (Nubeqa®) en cáncer de próstata resistente a la castración no metastásico

IPT, 1/2021. V1

Fecha de publicación: 8 de marzo de 2021[1]


MINISTERIO DE SANIDAD

agencia española de medicamentos y productos sanitarios

INFORME DE POSICIONAMIENTO TERAPÉUTICO

Informe de Posicionamiento Terapéutico de apalutamida (Erleada®) en cáncer de próstata resistente a la castración no metastásico

IPT, 5/2021. V1

Fecha de publicación: 8 de marzo de 2021[†]

MINISTERIO DE SANIDAD

agencia española de medicamentos y productos sanitarios

INFORME DE POSICIONAMIENTO TERAPÉUTICO

Informe de Posicionamiento Terapéutico de apalutamida (Erleada®) en cáncer de próstata resistente a la castración no metastásico

IPT, 5/2021. V1

Fecha de publicación: 8 de marzo de 2021†

MINISTERIO DE SANIDAD, CONSUMO Y BIENESTAR SOCIAL

agencia española de medicamentos y productos sanitarios

INFORME DE POSICIONAMIENTO TERAPÉUTICO

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IPT, 31/2021. V1

Fecha de publicación: 25 de junio de 2021†

No se han realizado estudios que comparen directamente enzalutamida y apalutamida en el tratamiento de pacientes con CPRCnm. El grupo control de ambos estudios fue placebo. Los datos de eficacia disponibles no permiten considerar que haya superioridad de un fármaco sobre otro en eficacia.

MINISTERIO DE SANIDAD

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INFORME DE POSICIONAMIENTO TERAPÉUTICO

Informe de Posicionamiento Terapéutico de darolutamida (Nubeqa®) en cáncer de próstata resistente a la castración no metastásico

IPT, 1/2021. V1

Fecha de publicación: 8 de marzo de 2021[1]

Darolutamida se puede considerar una alternativa terapéutica a enzalutamida y apalutamida en pacientes con CPRCnm de alto riesgo de metástasis, sin que exista evidencia que muestre superioridad de uno respecto a otro.

CONSIDERACIONES FINALES DEL GC REVALMED

La Dirección General de Cartera Común de Servicios del SNS y Farmacia ha financiado Erleada® (apalutamida) para el tratamiento del cáncer de próstata resistente a la castración de alto riesgo no metastásico conforme a los siguientes criterios clínicos que deben cumplir los pacientes para su utilización:

- *Alto riesgo de metástasis (tiempo de duplicación de PSA (PSDAT) =< 6 meses)*
- *Niveles de PSA ≥ 2 ng/ml, con niveles de testosterona bajo castración =< 50 ng/dl o 1,7 nmol/l durante el tratamiento con agonista o antagonista LHRH o tras orquectomía bilateral.*
- *Sin evidencia previa o presente de enfermedad metastásica, mediante el diagnóstico recomendable por PET-TAC colina, y sobre todo por el PSMA PET/TC.*
- *Buen estado funcional (ECOG 0-1)*
- *Valoración geriátrica de los pacientes potencialmente frágiles.*
- *Análisis de las comorbilidades del paciente*
- *Consideración de la medicación concomitante*

CONSIDERACIONES FINALES DEL GC REVALMED SNS

La Dirección General de Cartera Común de Servicios del SNS y Farmacia ha financiado Nubeca® (darolutamida) para el tratamiento de hombres adultos con cáncer de próstata resistente a la castración no metastásico (CPRCnm) con alto riesgo de desarrollar cáncer con enfermedad metástastica, que cumplan los siguientes criterios:

- *alto riesgo de metástasis (tiempo de duplicación de PSA (PSDAT) < 6 meses)*
- *niveles de PSA ≥ 2 ng/ml, con niveles de testosterona bajo castración =< 50 ng/dl o 1,7 nmol/l durante el tratamiento con agonista o antagonista LHRH o tras orquectomía bilateral*
- *sin evidencia previa o presente de enfermedad metastásica, mediante el diagnóstica recomendable por PET-TAC colina, y sobre todo por el PSMA PET/TC.*
- *buen estado funcional (ECOG 0-1)*
- *valoración geriátrica de los pacientes potencialmente frágiles*
- *análisis de las comorbilidades del paciente*
- *consideración de la medicación concomitante*

CONSIDERACIONES FINALES DEL GC REVALMED SNS

La Dirección General de Cartera Común de Servicios del SNS y Farmacia ha emitido resolución de no financiación para la indicación de XTANDI® (enzalutamida) en el tratamiento de hombres adultos con cáncer de próstata resistente a la castración (CPRC) no metastásico de alto riesgo.

Versión Junio de 2021

¿Y COMO NOS POSICIONAMOS?

Enzalutamida, apalutamida y darolutamida no deben utilizarse de forma secuencial tras presentar progresión a uno de ellos.

La elección entre darolutamida y las alternativas existentes se deberá basar fundamentalmente en criterios de eficiencia.

Enzalutamida, apalutamida y darolutamida no deben utilizarse de forma secuencial tras presentar progresión a uno de ellos.
La elección entre apalutamida y las alternativas existentes se deberá basar fundamentalmente en criterios de eficiencia.

EFICIENCIA EN SANIDAD

Es la ventajosa relación entre los recursos invertidos y los resultados obtenidos, o sea, definir cuál fármaco y su forma de utilización produce mejores resultados para la salud, según los recursos invertidos, una vez identificados, medidos y comparados los costos, riesgos y beneficios de los programas, servicios o terapias donde se usen

Medir la eficiencia no solo por el costo del medicamento comparado con otro sino que se trata de relacionar dichos costos con los efectos obtenidos

Y EN LA REALIDAD…

Apalutamide Treatment and Metastasis-free Survival in Prostate Cancer

Matthew R. Smith, M.D., Ph.D., Fred Saad, M.D., Simon Chowdhury, M.B., B.S., Ph.D., Stéphane Oudard, M.D., Ph.D., Boris A. Hadaschik, M.D., Julie N. Graff, M.D., David Olmos, M.D., Ph.D., Paul N. Mainwaring, M.B., B.S., M.D., Ji Youl Lee, M.D., Hiroji Uemura, M.D., Ph.D., Angela Lopez-Gitlitz, M.D., Géralyn C. Trudel, Ph.D., Byron M. Espina, B.S., Youyi Shu, Ph.D., Youn C. Park, Ph.D., Wayne R. Ruckoff, M.D., Margaret K. Yu, M.D., and Eric J. Small, M.D., for the SPARTAN Investigators*

DOI: 10.1056/NEJMoa1715546

Darolutamide in Nonmetastatic, Castration-Resistant Prostate Cancer

Karim Fizazi, M.D., Neal Shore, M.D., Teuvo L. Tammela, M.D., Ph.D., Albertas Ulys, M.D., Egils Vjaters, M.D., Sergey Polyakov, M.D., Mindaugas Jievaltas, M.D., Murilo Luz, M.D., Boris Alekseev, M.D., Iris Kuss, M.D., Christian Kappeler, Ph.D., Amir Snapir, M.D., Ph.D., Toni Sarapohja, M.Sc., and Matthew R. Smith, M.D., Ph.D., for the ARAMIS Investigators*

DOI: 10.1056/NEJMoa1815671

Enzalutamide in Men with Nonmetastatic, Castration-Resistant Prostate Cancer

Maha Hussain, M.D., Karim Fizazi, M.D., Ph.D., Fred Saad, M.D., Per Rathenborg, M.D., Neal Shore, M.D., Ubirajara Ferreira, M.D., Ph.D., Petro Ivashchenko, M.D., Eren Demirhan, Ph.D., Katharina Modelska, M.D., Ph.D., De Phung, B.S., Andrew Krivoshik, M.D., Ph.D., and Cora N. Sternberg, M.D.

DOI: 10.1056/NEJMoa1800536

The NEW ENGLAND JOURNAL of MEDICINE

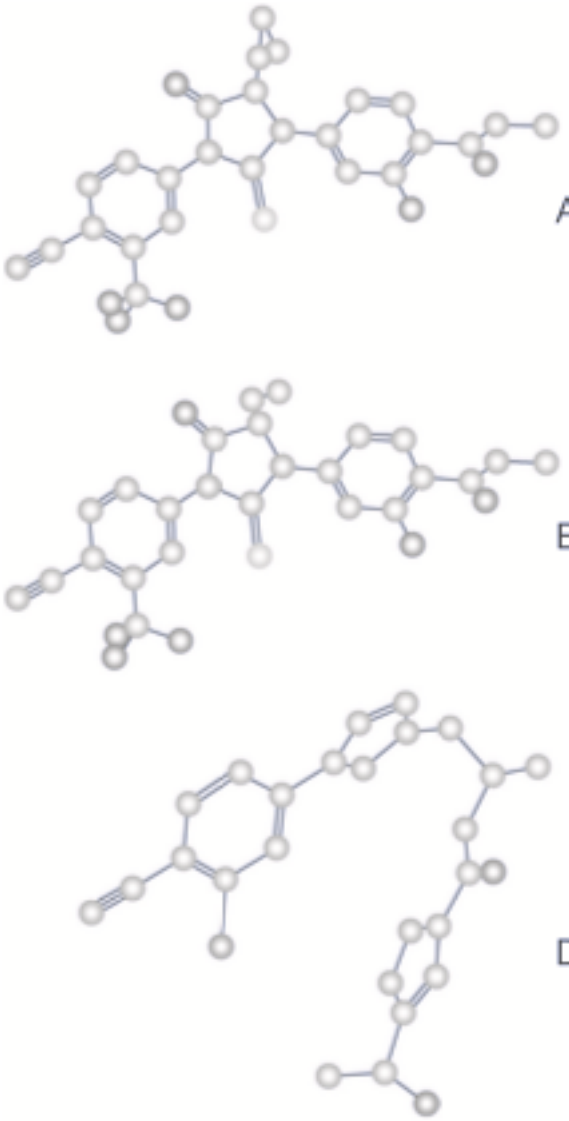

Fig. 3 The structure of apalutamide, darolutamide, and enzalutamide. Obtained from the PubChem Open Chemistry Database.

Table 1 Summary of pivotal trials for second-generation ARIs in nmCRPC

	SPARTAN (NCT01546201) [15, 49, 61]	PROSPER (NCT02003924) [14, 45, 62]	ARAMIS (NCT02200614) [16, 48, 63]
Study description	Randomized phase 3 study to evaluate the safety and efficacy of apalutamide vs. placebo in patients with nmCRPC ($N = 1207$)	Randomized phase 3 study to evaluate the safety and efficacy of enzalutamide vs placebo in patients with nmCRPC ($N = 1401$)	Randomized phase 3 study to evaluate the safety and efficacy of darolutamide vs placebo in patients with nmCRPC ($N = 1509$)
Patient population	nmCRPC with PSADT ≤ 10 months	nmCRPC with BL PSA ≥ 2 ng/mL and PSADT ≤ 10 months	nmCRPC with PSADT ≤ 10 months
	No lesions detectable by CT/MRI or bone scan	No lesions detectable by CT/MRI and bone scan and no history of seizure	No lesions detectable by CT/MRI or bone scan
Primary analysis			
Median follow up	20.3 months	Enzalutamide: 18.5 months Placebo: 15.1 months	17.9 months
Primary endpoint (drug vs. placebo)	Median MFS, assessed from randomization until radiographic progression by blinded independent central review or death	Median MFS, assessed from randomization until radiographic progression by blinded independent central review or death	Median MFS, assessed from randomization until radiographic progression by blinded independent central review or death
	40.5 vs. 16.2 months; HR 0.28; 95% CI 0.23–0.35; $P < 0.001$	36.6 vs. 14.7 months; HR 0.29; 95% CI 0.24–0.35; $P < 0.001$	40.4 vs. 18.4 months; HR 0.41; 95% CI 0.34–0.50; $P < 0.001$
Secondary endpoints evaluated in a hierarchical order (drug vs. placebo)	Median PFS: 40.5 vs. 14.7 months; HR 0.29; 95% CI: 0.24–0.36; $P < 0.001$	Median time to PSA progression 37.2 vs. 3.9 months; HR 0.07; 95% CI 0.05–0.08; $P < 0.001$	Median OS: NR vs. NR; HR 0.71; 95% CI 0.50–0.99; $P = 0.045$
	Median time to symptomatic progression: NR vs. NR; HR 0.45; 95% CI 0.32–0.63; $P < 0.001$	Median time to first use of new antineoplastic therapy: 39.6 vs. 17.7 months; HR 0.21; 95% CI 0.17–0.25; $P < 0.001$	Median time to pain progression: 40.3 vs. 25.4 months; HR 0.65; 95% CI 0.53–0.79
	Median OS: NR vs. 39.0 months; HR 0.70; 95% CI 0.47–1.04; $P = 0.07$	Median OS: NR vs. NR; HR 0.80; 95% CI 0.58–1.09; $P = 0.15$	Median time to first use of cytotoxic chemotherapy: NR vs. 38.2 months; HR 0.43; 95% CI 0.31–0.60
	Median time to first cytotoxic chemotherapy: NR vs. NR; HR 0.44; 95% CI 0.29–0.66		Median time to first SSE: NR vs. NR; HR 0.43; 95% CI 0.22–0.84
			Median PFS: 36.8 vs. 14.8 months; HR 0.38; 95% CI 0.32–0.45
			Median time to PSA progression: 33.2 vs. 7.3 months; HR 0.13; 95% CI 0.11–0.16


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REVIEW ARTICLE

Treatment of nonmetastatic castration-resistant prostate cancer: focus on second-generation androgen receptor inhibitors

Fred Saad[1] · Martin Bögemann[2] · Kazuhiro Suzuki[3] · Neal Shore[4]

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Final analysis	(*N* = 1707)	(*N* = 1401)	(*N* = 1509)
Median follow-up	52.0 months	48.0 months	29.0 months
Secondary endpoints (drug vs. placebo)	Median OS: 73.9 vs. 59.9 months; HR 0.78; 95% CI 0.64–0.96; *P* = 0.016	Median OS: 67.0 vs. 56.3 months; HR 0.73; 95% CI 0.61–0.89; *P* = 0.001	Median OS: NR vs. NR; HR 0.69; 95% CI 0.53–0.88; *P* = 0.003
	Median time to cytotoxic chemotherapy: NR vs. NR; HR 0.63; 95% CI 0.49–0.81; *P* = 0.0002	Median time to use of cytotoxic chemotherapy: NR vs. NR; HR 0.54; 95% CI 0.44–0.67	Median time to first cytotoxic chemotherapy: NR vs. NR; HR 0.58; 95% CI 0.44–0.76; *P* < 0.001
	Median time to symptomatic progression: NR vs. NR; HR 0.57; 95% CI 0.44–0.73; *P* < 0.0001	Median time to first use of new subsequent antineoplastic therapy: 56.7 vs. 19.1 months; HR 0.29; 95% CI 0.25–0.34	Median time to pain progression: 40.3 vs. 25.4 months; HR 0.65; 95% CI 0.53–0.79; *P* < 0.001
	Median time to PSA progression: 40.5 vs. 3.7 months; HR 0.07; 95% CI 0.06–0.09; *P* < 0.0001	Chemotherapy free survival: 58.3 vs. 41.6 months; HR 0.67; 95% CI 0.53–0.72	Median time to first SSE: NR vs. NR; HR 0.48; 95% CI 0.25–0.82; *P* = 0.005
	Median time to second progression: 55.6 vs. 41.2 months; HR 0.55; 95% CI 0.46–0.66; *P* < 0.0001		
HRQoL outcomes at primary analysis (drug vs. placebo)[a]	Change from baseline in mean ± SE FACT-P total score: −0.99 ± 0.98 vs. −3.29 ± 1.97	BPI-SF (pain severity): time to progression 36.8 months vs. NR; HR 0.75; 95% CI 0.57–0.97; *P* = 0.028	BPI-SF (LSM time-adjusted AUC mean changes from baseline): pain interference: 1.1 vs. 1.3 points; difference −0.2; 95% CI −0.3 to −0.1
	Change from baseline in mean ± SE EQ-VAS score: 1.44 ± 0.87 vs. 0.26 ± 1.75	FACT-P total score: time to deterioration 22.1 vs. 15.4 months; HR 0.83; 95% CI 0.69–0.99; *P* = 0.037	Pain severity: 1.3 vs. 1.4 points; difference −0.2; 95% CI −0.3 to −0.1
		EORTC QLQ-PR75: time to deterioration	FACT-P total score (LSM time-adjusted AUC mean changes from baseline): 112.9 vs. 111.6 points; difference 1.3; 95% CI 0.4–2.1
		Bowel symptoms and function: 33.2 vs. 25.9 months; HR 0.72; 95% CI 0.59–0.88; *P* = 0.0013	FACT-P PCS total score: time to deterioration 11.1 vs. 7.9 months; HR 0.80; 95% CI 0.70–0.91; *P* = 0.0005
		Hormonal treatment related symptoms: 33.2 vs. 36.8 months; HR 1.29; 95% CI 1.02–1.63; *P* = 0.035	EORTC QLQ-PR25: time to deterioration
		Urinary symptoms: 36.9 vs. 25.9 months; HR 0.58; 95% CI 0.46–0.72; *P* < 0.0001	Bowel symptoms: 18.4 vs. 11.5 months; HR 0.78; 95% CI 0.66–0.92; *P* < 0.01
			Urinary symptoms: 25.8 vs. 14.8 months; HR 0.64; 95% CI 0.54–0.75; *P* < 0.01

ADT androgen-deprivation therapy, *AUC* area under the curve, *BL* baseline, *BPI-SF* Brief Pain Inventory Short Form, *CFB* 28-item core questionnaire, *CI* confidence interval, *CRPC* castration-resistant prostate cancer, *CT* computerized tomography, *EORTC QLQ* European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire, *EQ-VAS* European Quality of Life Visual Analogue Scale, *FACT-P* Functional Assessment of Cancer Therapy-Prostate, *FACT-P PCS* Functional Assessment of Cancer Therapy-Prostate, prostate cancer subscale, *HR* hazard ratio, *HRQoL* health-related quality of life, *LSM* least squares mean, *mCSPC* metastatic castration-sensitive prostate cancer, *MFS* metastasis-free survival, *mHSPC* metastatic hormone-sensitive prostate cancer, *mPC* metastatic prostate cancer, *MRI* magnetic resonance imaging, *nmCRPC* nonmetastatic castration-resistant prostate cancer, *nmPC* nonmetastatic prostate cancer, *NE* not estimable, *NR* not reached, *OS* overall survival, *PBO* placebo, *PC* prostate cancer, *PFS* progression-free survival, *PR25* prostate cancer-specific 25-item questionnaire, *QoL* quality of life, *rPFS* radiographic progression-free survival, *SSE* symptomatic skeletal event.

[a]Key exploratory results are reported in this table.

Prostate Cancer and Prostatic Diseases (2021) 24:323–334
https://doi.org/10.1038/s41391-020-00310-3

REVIEW ARTICLE

Treatment of nonmetastatic castration-resistant prostate cancer: focus on second-generation androgen receptor inhibitors

Fred Saad[1] · Martin Bögemann[2] · Kazuhiro Suzuki[3] · Neal Shore[4]

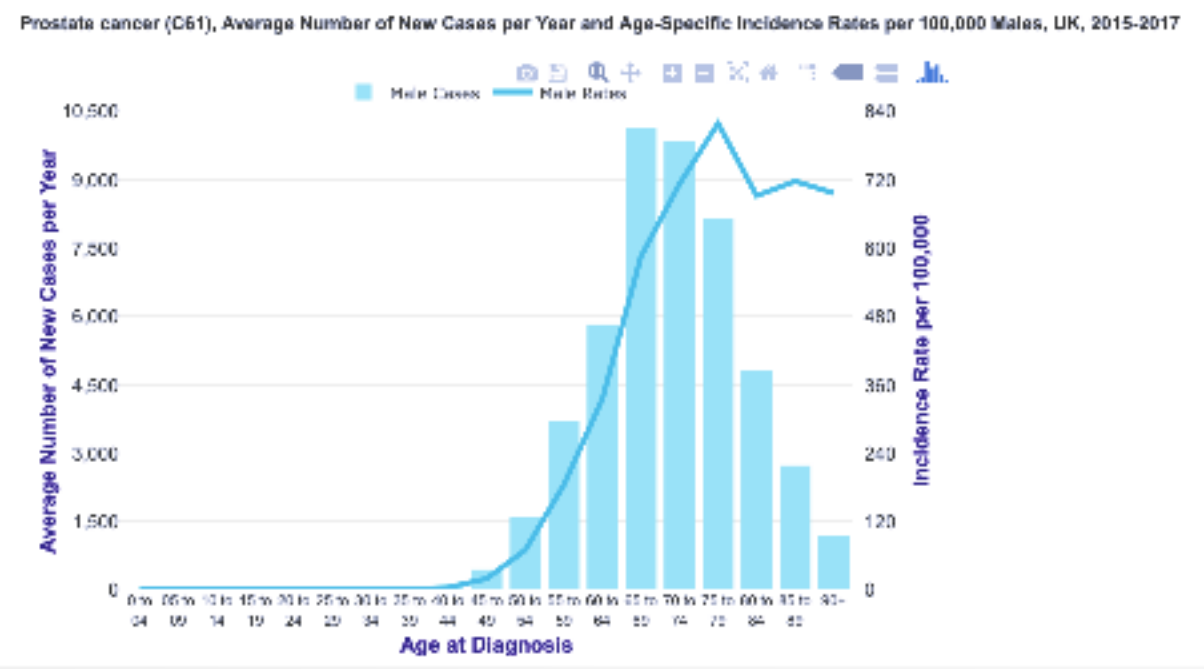
Received: 2 September 2020 / Revised: 27 November 2020 / Accepted: 4 December 2020 / Published online: 8 February 2021

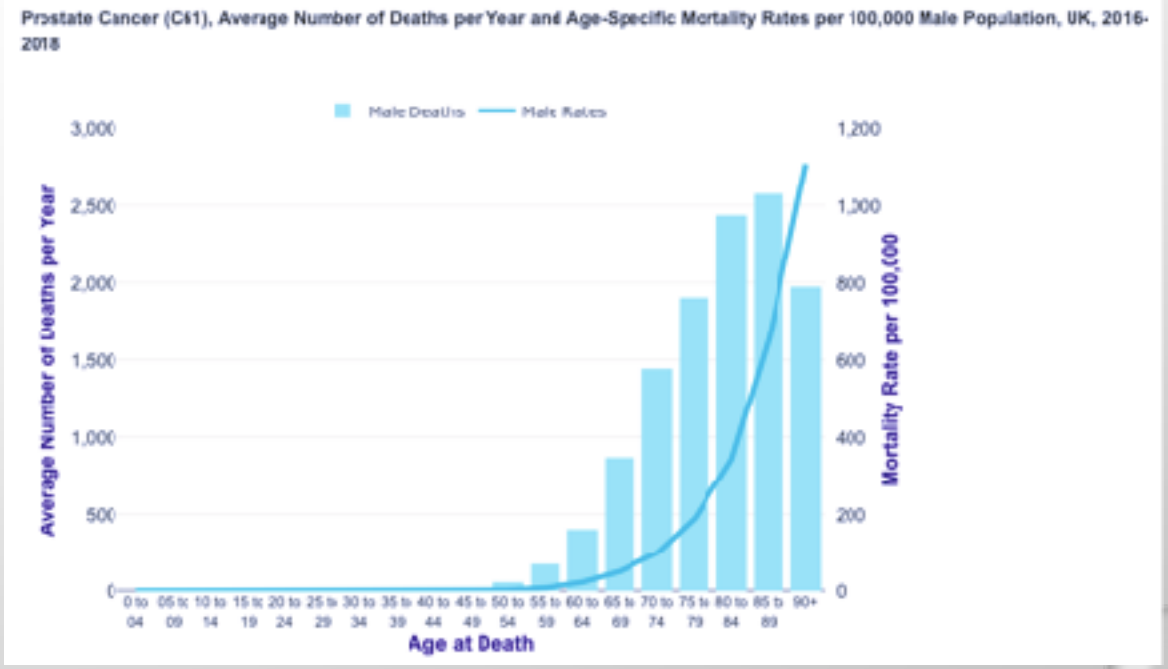
TEMAS A DEBATE

- ¿HAY EDAD LÍMITE PARA INICIAR EL TRATAMIENTO?
- QUE HACER EN EL CASO DE TENER UN CASO DE CPRC NO METASTÁSICO PERO CON TIEMPO DE DUPLICACIÓN DE PSA ENTRE 6 Y 10 MESES

EDAD

ES UNA ENFERMEDAD “ASOCIADA” A EDAD



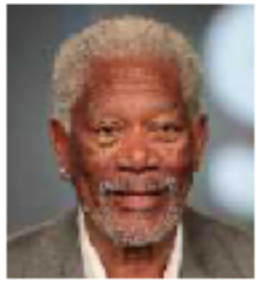


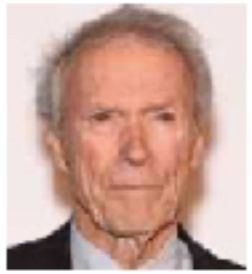
CONSIDERACIONES DEL PACIENTE ANCIANO

- DISFUNCIÓN ORGÁNICA
- DIFERENTE METABOLISMO Y ACLARAMIENTO DEL FÁRMACO
- AUMENTO RELATIVO DE LA GRASA CORPORAL
- CONTENIDO REDUCIDO DE AGUA
- MENOR MASA MUSCULAR
- PRESENCIA DE COMORBILIDADES
- TRATAMIENTOS CONCOMITANTES

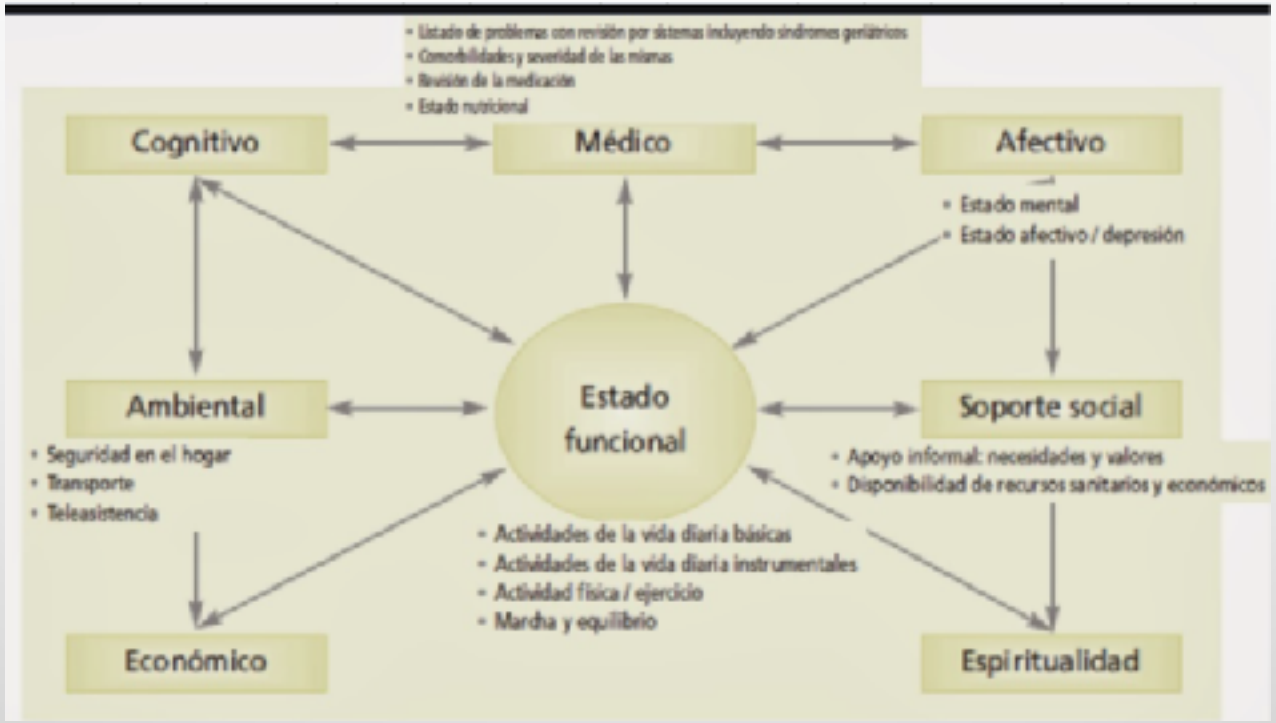
DEFINICIÓN PACIENTE ANCIANO

- Guias NCCN
  - Anciano joven (65-75 años)
  - Anciano (76-85 años)
  - Anciano mayor (>85 años)





VALORACIÓN GERIÁTRICA INTEGRAL



Functional status	Performance status
	Activities of daily living (ADL)
	Instrumental ADL (IADL)
Comorbidities	Cumulative Illness Rating Scale for Geriatrics (CIRS-G)
	Charlson Comorbidity Index (CCI)
	Adult Comorbidity Evaluation 27 (ACE-27)
	OARS Multidimensional Functional Assessment Questionnaire
Polypharmacy status	Beers criteria
	Medication Appropriateness Index (MAI)
	Screening Tool of Older Persons' Prescriptions (STOPP) criteria
	Screening Tool to Alert Doctors to Right Treatment (START) criteria
Nutritional status	Mini-Nutritional Assessment (MNA)
	Body mass index (BMI)

Cognitive function	Mini-Mental State Examination (MMSE)
	Montreal Cognitive Assessment (MoCA)
	Blessed Orientation-Memory-Concentration (BOMC) test
Socioeconomic issues	Living conditions
	Caregiver
Psychological status	
• Depression	Geriatric Depression Scale (GDS)
• Distress	Distress Thermometer (DT)
Geriatric syndromes	
• Delirium	Confusion Assessment Method (CAM)
• Frailty	Fried frailty criteria, Balducci frailty criteria
• Fatigue	Screening questionnaire to rate the severity of fatigue
• Falls	Multifactorial risk assessment
• Osteoporosis	Fracture risk assessment

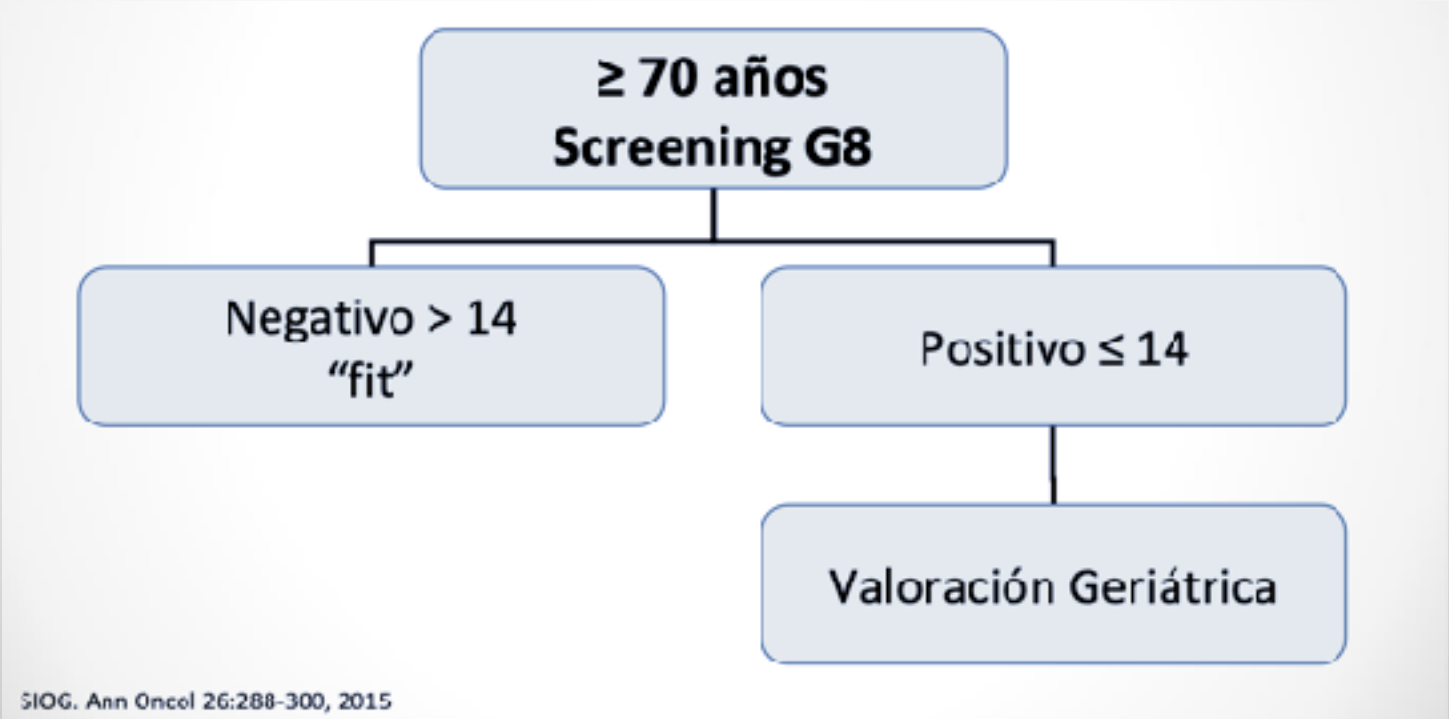
VALORACIÓN GERIÁTRICA INTEGRAL

- PROCESO DE DIAGNÓSTICO (Y TRATAMIENTO) PARA IDENTIFICAR (Y CORREGIR) LAS NECESIDADES DEL PACIENTE PARA MEJORAR SU EVOLUCIÓN.
  - EL PERFORMANCE STATUS (ECOG) NO ES SUFICIENTE
- ES MULTIDIMENSIONAL Y MULTIDISCIPLINAR. SE CONSENSUA CON EL
- PACIENTE (EXPECTATIVAS) Y SU UNIDAD FAMILIAR O DE SOPORTE.
  ES UNA APROXIMACIÓN SIMILAR A PROPIA DE LA ATENCIÓN PALIATIVA

APROXIMACIÓN: ESCALA G8

	Items	Possible answers (score)
A	Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties?	0 : severe decrease in food intake
		1 : moderate decrease in food intake
		2 : no decrease in food intake
B	Weight loss during the last 3 months	0 : weight loss > 3 kg
		1 : does not know
		2 : weight loss between 1 and 3 kgs
		3 : no weight loss
C	Mobility	0 : bed or chair bound
		1 : able to get out of bed/chair but does not go out
		2 : goes out
E	Neuropsychological problems	0 : severe dementia or depression
		1 : mild dementia or depression
		2 : no psychological problems
F	Body Mass Index (BMI (weight in kg) / (height in m^2)	0 : BMI < 19
		1 : BMI = 19 to BMI < 21
		2 : BMI = 21 to BMI < 23
		3 : BMI = 23 and > 23
H	Takes more than 3 medications per day	0 : yes
		1 : no
P	In comparison with other people of the same age, how does the patient consider his/her health status?	0 : not as good
		0.5 : does not know
		1 : as good
		2 : better
	Age	0 : >85
		1 : 80-85
		2 : <80
	TOTAL SCORE	**0 – 17**

ESCALA G8



SIOG. Ann Oncol 26:288-300, 2015

¿SE BENEFICIARAN DE INICIAR TRATAMIENTO ?

THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Darolutamide in Nonmetastatic, Castration-Resistant Prostate Cancer

Karim Fizazi, M.D., Neal Shore, M.D., Teuvo L. Tammela, M.D., Ph.D., Albertas Ulys, M.D., Egils Vjaters, M.D., Sergey Polyakov, M.D., Mindaugas Jievaltas, M.D., Murilo Luz, M.D., Boris Alekseev, M.D., Iris Kuss, M.D., Christian Snapkie, Ph.D., Amir Snapir, M.D., Ph.D., Toni Sarapohja, M.Sc., and Matthew R. Smith, M.D., Ph.D., for the ARAMIS Investigators*

Table 1. Patient Demographic and Clinical Characteristics at Baseline.*

Characteristic	Darolutamide (N=955)	Placebo (N=554)
Median age (range) — yr	74 (48–95)	74 (50–92)

Age			
<65 yr	197		0.59 (0.37–0.95)
65–74 yr	589		0.35 (0.26–0.47)
75–84 yr	593		0.43 (0.31–0.60)
≥85 yr	130		0.51 (0.27–0.96)

THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Apalutamide Treatment and Metastasis-free Survival in Prostate Cancer

Matthew R. Smith, M.D., Ph.D., Fred Saad, M.D., Simon Chowdhury, M.B., B.S., Ph.D., Stéphane Oudard, M.D., Ph.D., Boris A. Hadaschik, M.D., Julie N. Graff, M.D., David Olmos, M.D., Ph.D., Paul N. Mainwaring, M.B., B.S., M.D., Ji Youl Lee, M.D., Hiroji Uemura, M.D., Ph.D., Angels Lopez-Gitlitz, M.D., Geralyn G. Trardel, Ph.D., Byron M. Espina, B.S., Youyi Shu, Ph.D., Youn C. Park, Ph.D., Wayne R. Ricklin, M.D., Margaret K. Yu, M.D., and Eric J. Small, M.D., for the SPARTAN Investigators*

Table 1. Demographic and Disease Characteristics at Baseline.*

Characteristic	Apalutamide (N=806)	Placebo (N=401)
Age — yr		
Median	74	74
Range	48–94	52–97
Median time from initial diagnosis to randomization — yr	7.95	7.85

	median metastasis-free survival (mo)			
All patients	40.5	16.2		0.30 (0.24–0.36)
Age				
<65 yr	NR	7.3		0.14 (0.08–0.27)
65 to <75 yr	NR	14.6		0.25 (0.18–0.34)
≥75 yr	40.5	18.5		0.42 (0.31–0.56)

EUROPEAN UROLOGY 79 (2021) 150–158

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

European Association of Urology

Prostate Cancer

Apalutamide and Overall Survival in Prostate Cancer

Matthew R. Smith[a,*], *Fred Saad*[b], *Simon Chowdhury*[c], *Stéphane Oudard*[d], *Boris A. Hadaschik*[e], *Julie N. Graff*[f], *David Olmos*[g], *Paul N. Mainwaring*[h], *Ji Youl Lee*[i], *Hiroji Uemura*[j], *Peter De Porre*[k], *Andressa A. Smith*[l], *Sabine D. Brookman-May*[m,n], *Susan Li*[l], *Ke Zhang*[o], *Brendan Rooney*[p], *Angela Lopez-Gitlitz*[m], *Eric J. Small*[q]

C

Subgroup	Median overall survival (mo)		Hazard ratio (95% CI)	Events/*N*	
	Apalutamide	Placebo		Apalutamide	Placebo
All patients	73.9	59.9	0.79 (0.65–0.96)	274/806	154/401
Age					
<65 yr	NR	NR	0.39 (0.19–0.78)	18/106	14/43
≥65 yr	61.5	58.7	0.86 (0.70–1.06)	256/700	140/358

The NEW ENGLAND JOURNAL of MEDICINE

JUNE 28, 2018

Enzalutamide in Men with Nonmetastatic, Castration-Resistant Prostate Cancer

Maha Hussain, M.D., Karim Fizazi, M.D., Ph.D., Fred Saad, M.D., Per Rathenborg, M.D., Neal Shore, M.D., Ubirajara Ferreira, M.D., Ph.D., Petro Ivashchenko, M.D., Eren Demirhan, Ph.D., Katharina Modelska, M.D., Ph.D., De Phung, B.S., Andrew Krivoshik, M.D., Ph.D., and Cora N. Sternberg, M.D.

Table 1. Demographic and Clinical Characteristics of the Patients at Baseline.*

Characteristic	Enzalutamide Group (N=933)	Placebo Group (N=468)
Age — yr		
Median	74	73
Range	50–95	53–92

Age at baseline						
≤Median	489	267	126	97		0.64 (0.49–0.84)
>Median	444	201	162	81		0.81 (0.62–1.05)

THE LANCET
Oncology
Volume 22, Issue 9, September 2021, Pages 1290-1299

Articles

Survival outcomes in older men with non-metastatic castration-resistant prostate cancer treated with androgen receptor inhibitors: a US Food and Drug Administration pooled analysis of patient-level data from three randomised trials

- 4117 patients were assigned to androgen receptor inhibitor (apalutamide, enzalutamide, or daralutamide; n=2694) or placebo (n=1423) across three randomised trials
- The median follow-up duration for metastasis-free survival was 18 months (IQR 11–26) and for overall survival was 44 months (32–55).
- In patients aged 80 years or older (n=1023):

In patients aged 80 years or older (n=1023):
-The estimated median **metastasis-free survival** was **40 months** (95% CI 36–41) in the androgen receptor inhibitor groups and **22 months** (18–29) in the placebo groups (adjusted hazard ratio [HR] 0·37 [95% CI 0·28–0·47])
-The median **overall survival** was **54 months** (50–61) versus **49 months** (43–58), respectively (adjusted **HR 0·79** [0·64–0·98]).
-In patients aged 80 years or older, grade 3 or worse adverse events were reported in 371 **(55%)** of 672 patients in the androgen receptor inhibitor groups and 140 **(41%)** of 344 patients in the placebo groups, compared with 878 **(44%)** of 2015 patients in the androgen receptor inhibitor groups and 321 (30%) of 1073 patients in the placebo groups among patients younger than 80 years

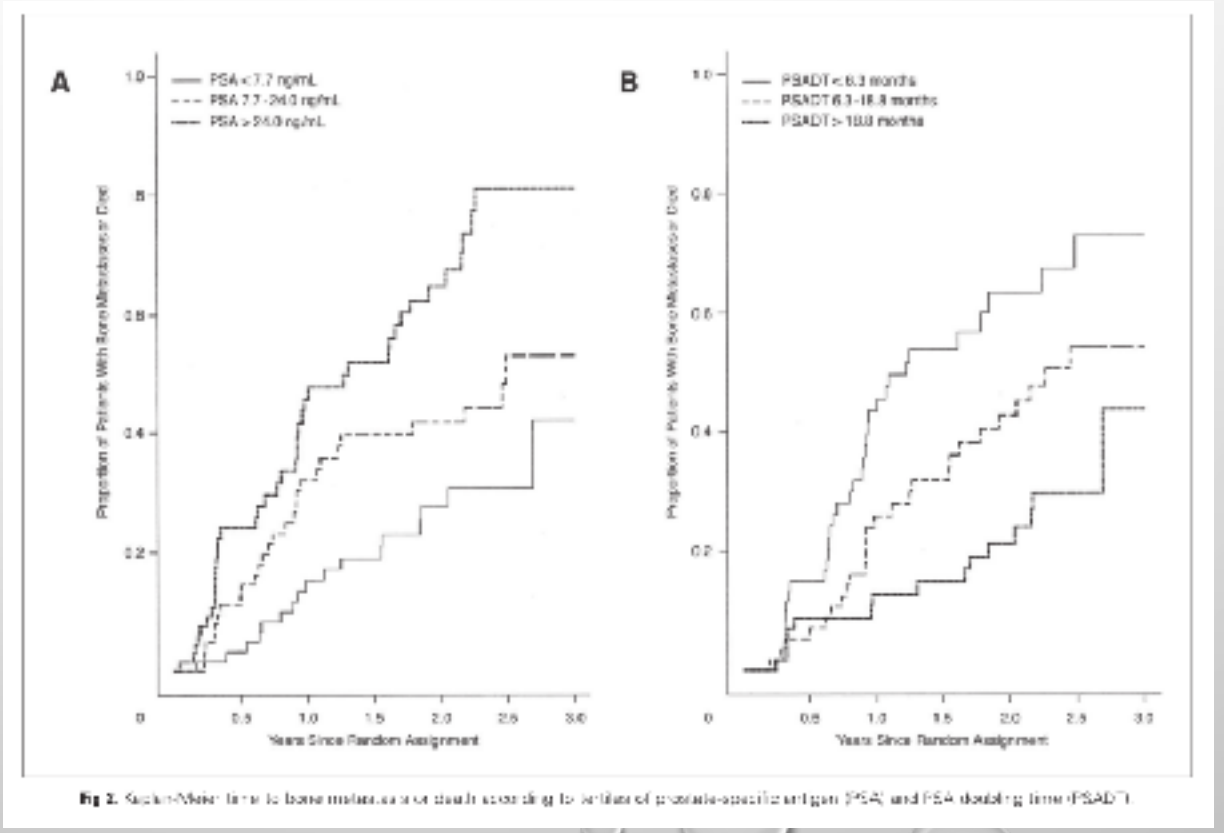
¿Que hacer en el caso de tener un caso de CPRC no Metastásico pero con tiempo de duplicación de PSA entre 6 y 10 meses?

VOLUME 23 · NUMBER 13 · MAY 1 2005

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Natural History of Rising Serum Prostate-Specific Antigen in Men With Castrate Nonmetastatic Prostate Cancer

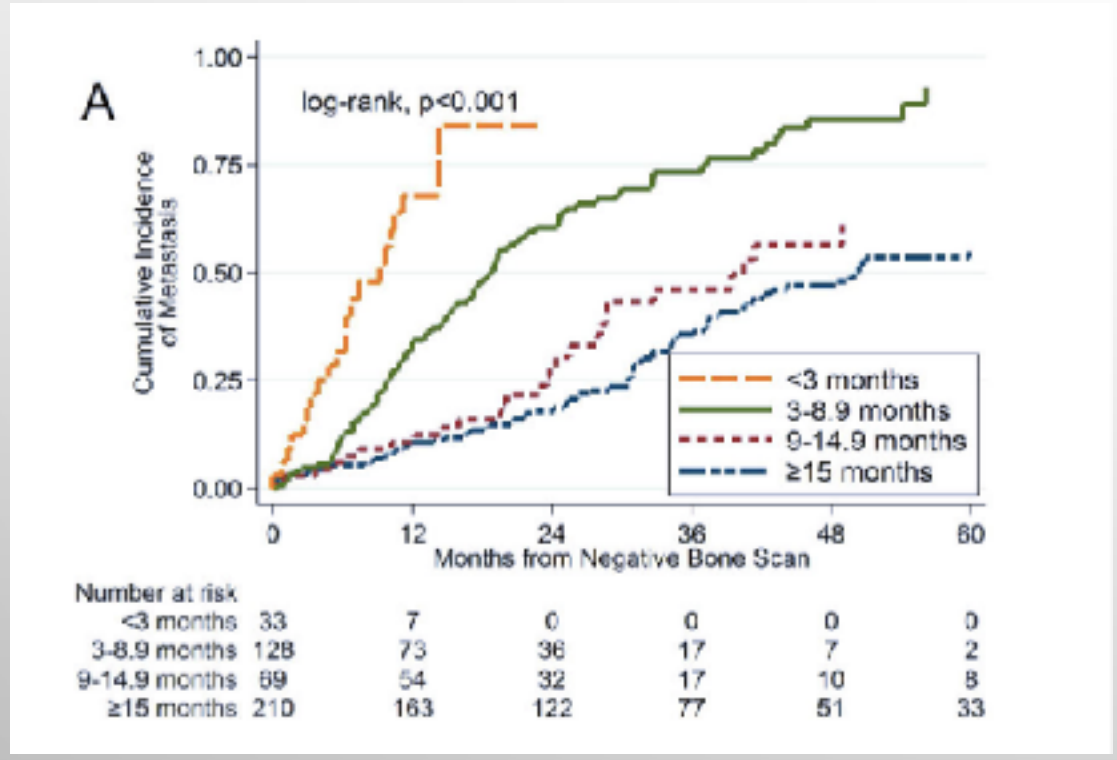
Matthew R. Smith, Fairooz Kabbinavar, Fred Saad, Arif Hussain, Marc C. Gittelman, David L. Bilhartz, Chris Wynne, Robin Murray, Norman K. Zinner, Claude Schulman, Ronald Lieuwen, Ming Zheng, Carsten Goessl, Yong-Sang Hei, Eric J. Small, Richard Cook, and Celestia S. Higano



BJU Int. 2017 November ; 120(5B): E80–E86. doi:10.1111/bju.13856

Cut-points for PSA doubling time in men with non-metastatic castration-resistant prostate cancer

Lauren E. Howard, MS[a,b], Daniel Moreira, MD[c], Amanda De Hoedt, MS[b], William J. Aronson, MD[c,e], Christopher J. Kane, MD[f], Christopher L. Amling, MD[g], Matthew R. Cooperberg, MD[h], Martha K. Terris, MD[i,j], and Stephen J. Freedland, MD[b,k]



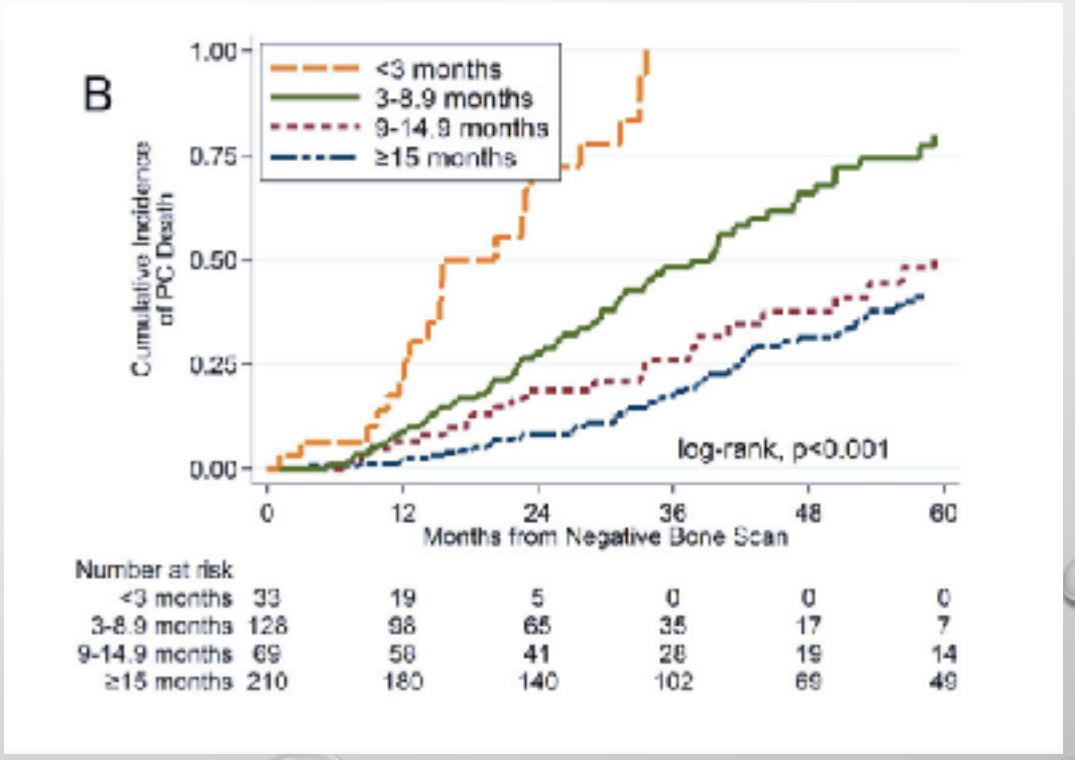


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Table 2

PSADT at M0 CRPC as a predictor of metastases

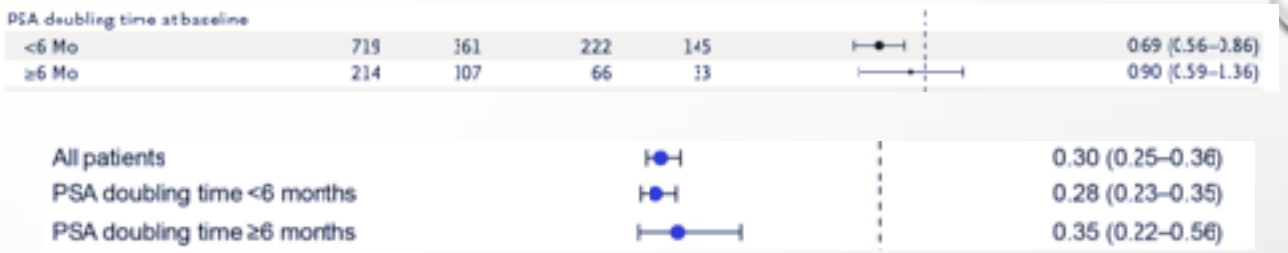
		Univariable			Multivariable*		
	n	HR	95% CI	P-value	HR	95% CI	P-value
PSADT **, months (continuous)	223/441	1.68	1.48-1.90	<0.001	1.59	1.40-1.80	<0.001
PSADT				<0.001			<0.001
≥15 months	37/210	*Ref.*			*Ref.*		
9-14.9 months	29/69	1.33	0.87-2.02		1.31	0.86-2.00	
3-8.9 months	86/129	3.30	2.41-4.51		2.85	2.06-3.94	
<3 months	21/53	10.0	5.93-16.9		8.63	5.07-14.7	

THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Enzalutamide and Survival in Nonmetastatic, Castration-Resistant Prostate Cancer

Cora N. Sternberg, M.D., Karim Fizazi, M.D., Ph.D., Fred Saad, M.D., Neal D. Shore, M.D., Ugo De Giorgi, M.D., Ph.D., David F. Penson, M.D., M.P.H., Ubirajara Ferreira, M.D., Ph.D., Eleni Efstathiou, M.D., Ph.D., Katarzyna Madziarska, M.D., Ph.D., Michael P. Kolinsky, M.D., Daniel G. Cubero, M.D., Ph.D., Bettina Noerby, M.D., Fabian Zohren, M.D., Ph.D., Xun Lin, Ph.D., Katherine Modelska, M.D., Ph.D., Jennifer Sugg, M.S., Joyce Steinberg, M.D., and Maha Hussain, M.D., for the PROSPER Investigators*



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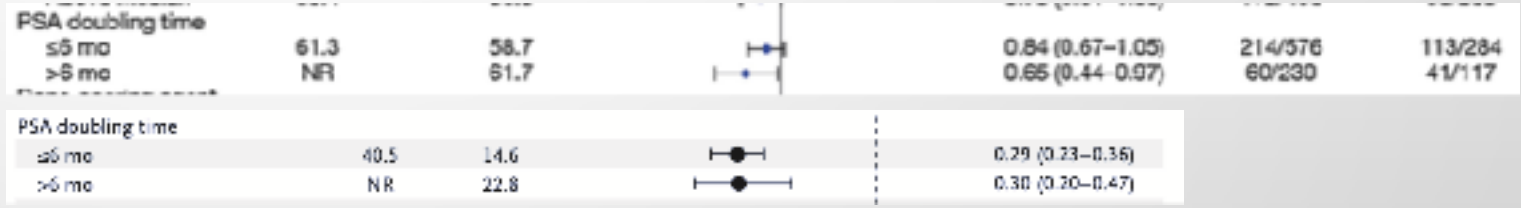

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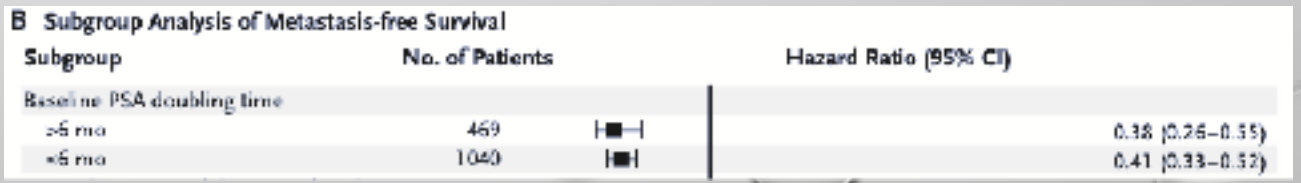
- 0.55 (95% CI = 0.35–0.88) among 469 patients with baseline PSA doubling time > 6 months and 0.73 (95% CI = 0.54–0.99) among 1,040 with PSA doubling time ≤ 6 months



THE JOURNAL OF UROLOGY®

Vol. 201, 882-892, April 2019

A Clinician's Guide to Next Generation Imaging in Patients With Advanced Prostate Cancer (RADAR III)

E. David Crawford,*† Phillip J. Koo,‡ Neal Shore,§ Susan F. Slovin,¶ Raoul S. Concepcion,‖ Stephen J. Freedland,** Leonard G. Gomella,†† Lawrence Karsh,‡‡ Thomas E. Keane,§§ Paul Maroni, David Penson,¶¶ Daniel P. Petrylak,‖‖ Ashley Ross,*** Vlad Mouraviev,††† Robert E. Reiter, Chaitanya Divgi and Evan Y. Yu‡‡‡ for the RADAR III Group

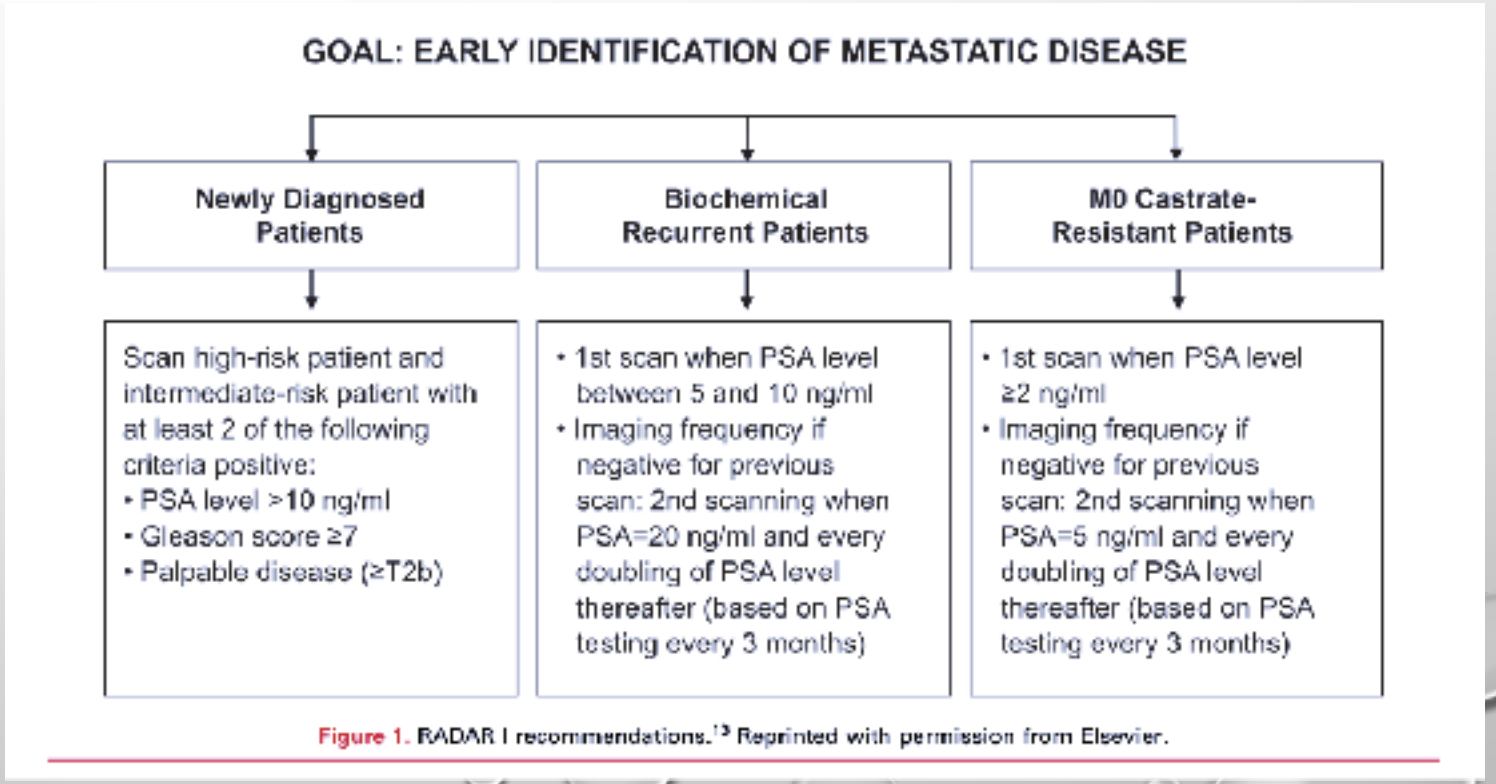


Figure 1. RADAR I recommendations.[13] Reprinted with permission from Elsevier.

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RADAR III suggests followup imaging every 6 to 12 months or more frequently based on less than 6-month PSADT and/or symptoms in patients undergoing therapy for M0 CRPC. If traditional imaging fails to detect metastatic disease, NGI can be performed only if approved therapies in the M1 space are being considered. RADAR III cautions against ceasing therapy for a PSA rise alone.

M0 Castrate-Resistant Patients

1st conventional scan when PSA level ≥2 ng/ml

Imaging frequency if negative for previous conventional scan:

2nd conventional scan when PSA=5 ng/ml and every doubling of PSA level thereafter (based on PSA testing every 3 months)

Only consider NGI in the setting of PSADT <6 months, when M1 therapies would be appropriate

¿QUÉ OPCIONES TENEMOS SI TENEMOS UN PACIENTE CON CPRC M0 CON PSA DT ENTRE 6-10 MESES?

- CONTROL PSA CADA 3 MESES PARA VALORAR CINÉTICA DE PSA
- HACER PRUEBAS DE IMAGEN DE NUEVA GENERACIÓN PARA VALORAR SI ES METASTÁSICO
- ¿Y SI TRATAMOS LOCALMENTE LA PRÓSTATA?

Original Article Published: 19 March 2018

Long-term outcomes of definitive external-beam radiotherapy for non-metastatic castration-resistant prostate cancer

Rihito Aizawa, Kenji Takayama, Kiyonao Nakamura, Takahiro Inoue, Takashi Kobayashi, Shusuke Akamatsu, Toshinari Yamasaki, Osamu Ogawa & Takashi Mizowaki

International Journal of Clinical Oncology **23**, 749–756 (2018) | Cite this article

565 Accesses | **3** Citations | **1** Altmetric | Metrics

-Retrospectively evaluated 31 NM-CRPC patients consecutively treated with definitive EBRT.
-The median prostate dose was 70.4 Gy
-The median follow-up duration after EBRT was 66.6 months.
-The 5- and 8-year overall survival rates were 74.6 and 49.8%, respectively
-The 5- and 8-year prostate cancer-specific survival rates were 77.4 and 51.7%, respectively.
-The 5- and 8-year relapse-free survival rates were 32.3 and 25.8%, respectively

Original Paper | Published: 22 September 2013

May non-metastatic clinically localized castration-resistant prostate cancer after primary androgen ablation benefit from salvage prostate radiotherapy?

Angela Botticella ✉, Alessia Guarneri, Andrea Riccardo Filippi, Niccolò Giaj Levra, Fernando Munoz, Riccardo Ragona, Paolo Gontero & Umberto Ricardi

Journal of Cancer Research and Clinical Oncology **139**, 1955–1960 (2013) | Cite this article

-Forty-two patients presenting a non-metastatic castration-resistant prostate cancer after PADT were referred to our institution and underwent RT between June 2003 and July 2011.
-Median follow-up after EBRT was 53 months
- Five-year biochemical disease-free survival (bDFS), distant metastases-free survival (DMFS) and cancer-specific survival (CSS) were, respectively, 39.4, 60 and 65 %

CONCLUSIONES

- LOS INFORMES DE POSICIONAMIENTO SON DOCUMENTOS INFORMATIVOS DE AUTORIZACIÓN
- NO DIFERENCIAS EN POSICIONAMIENTO
- EDAD COMO FACTOR DE RIESGO
- RESULTADOS CONSISTENTES EN PACIENTES DE EDAD AVANZADA
- ALTERNATIVAS A LA SITUACIÓN DE CPRC M0 EN CASOS DE NO TENER PRECIO REEMBOLSO

Muchas gracias

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