CPRCnm

(CÁNCER DE PRÓSTATA RESISTENTE A LA CASTRACIÓN NO METASTÁSICO)

NUEVOS TRATAMIENTOS

Begoña Díaz Méndez

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DEL PRINCIPADO DE ASTURIAS

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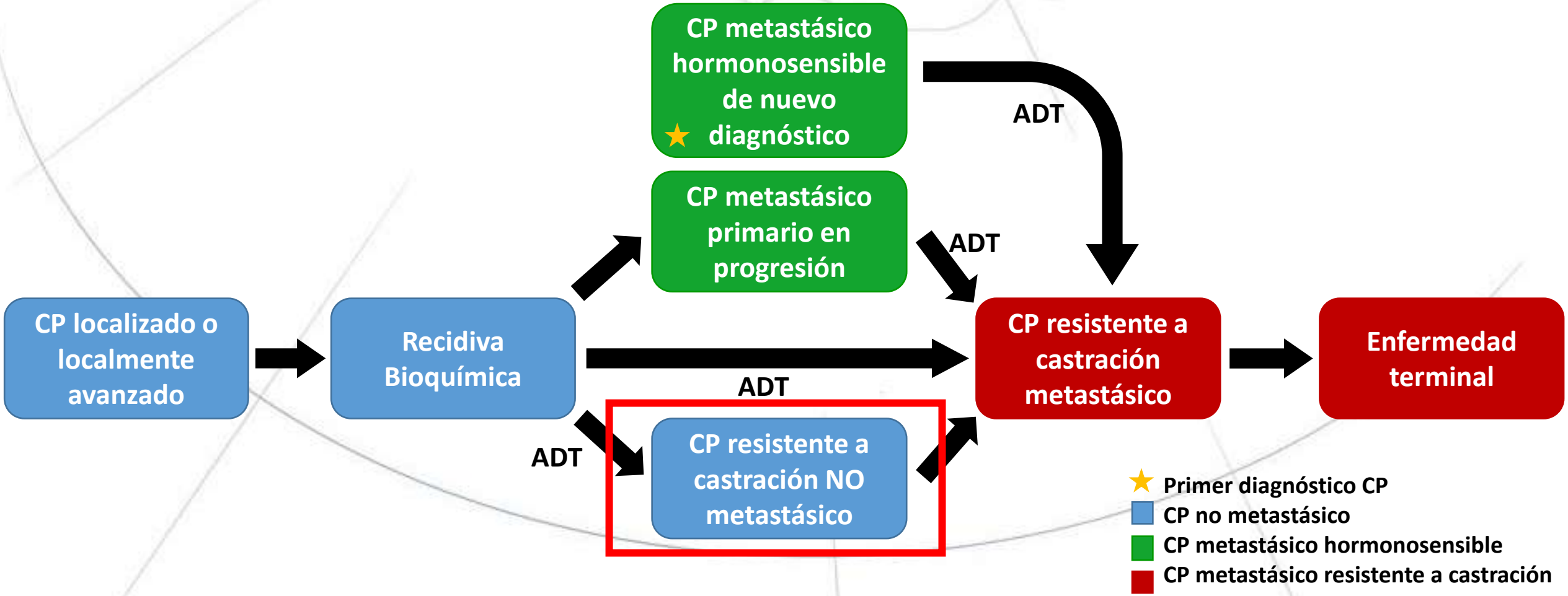
Servicio de Urología

Historia Natural del Cáncer de Próstata



Adapted from: Scher HI et al. J Clin Oncol. 2016;34(12):1402-1418; Mottet, N, et al. (2020). EAU Guidelines on Prostate Cancer; Hong JH, Kim IY. Korean J Urol. 2014 Mar;55(3):153-60

Diagnóstico de CPRCnm

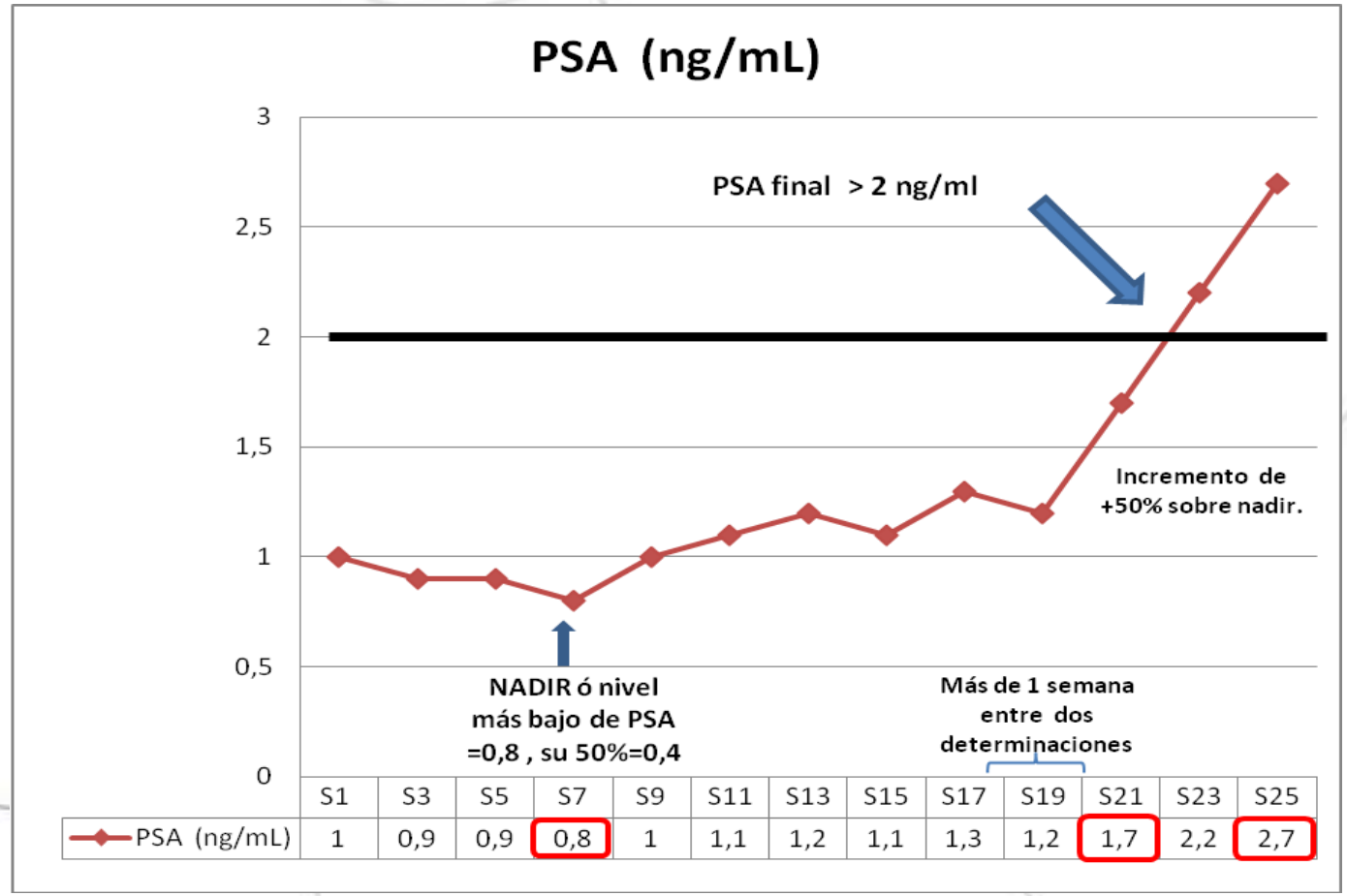
Progresión bioquímica durante TDA

+

Niveles séricos de testosterona por debajo 50 ng/dL

+

No evidencia radiológica de metástasis



	S1	S3	S5	S7	S9	S11	S13	S15	S17	S19	S21	S23	S25
PSA (ng/mL)	1	0,9	0,9	0,8	1	1,1	1,2	1,1	1,3	1,2	1,7	2,2	2,7

Incrementa el riesgo de muerte del 16-56%

La supervivencia a 5 años se reduce del 56% sin metástasis óseas, al 3% con metástasis óseas

Incrementa el riesgo de eventos esqueléticos sintomáticos

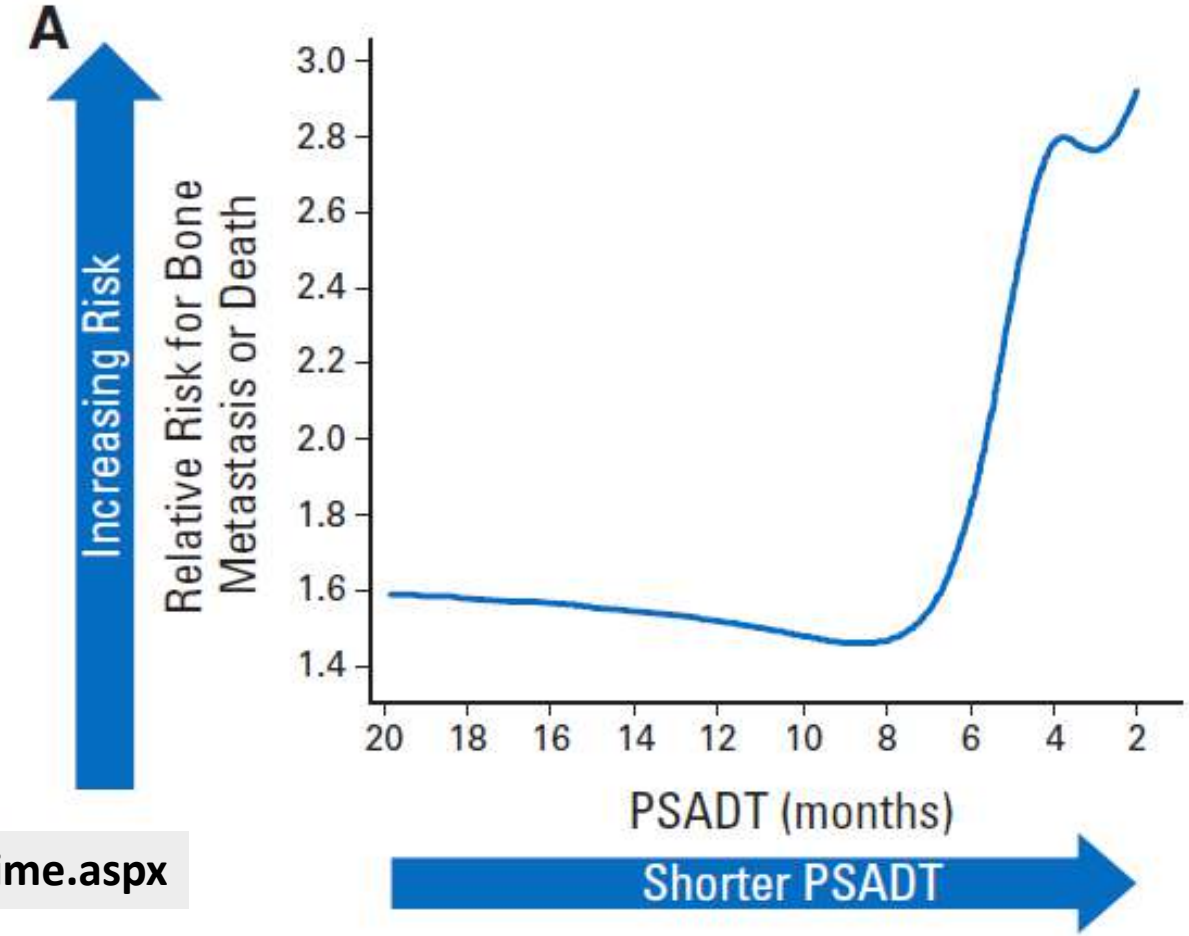
Scher HI, Solo K, Valant J, Todd MB, Mehra M. Prevalence of prostate cancer clinical states and mortality in the United States: estimates using a dynamic progression model. PLOS One. 2015;10:e01394
Hagiwara M, Delea TE, Saville MW, Chung K. Healthcare utilization and costs associated with skeletal -related events in prostate cancer patients with bone metastases. Prostate Cancer Prostatic Dis. 2013;16(1):23 -7

PSADT (Tiempo de duplicación del PSA)

Predictor de metástasis

PSA doubling time is calculated by log(2) divided by the slope of the linear regression of log(PSA) over time in months

http://nomograms.mskcc.org/Prostate/PsaDoublingTime.aspx



1. *Paller CJ et al. Clin Adv Hematol Oncol. 2013;11(1):14-23;*
2. *Smith MR, et al. J Clin Oncol. 2013 Oct 20;31(30):3800-6*
3. *Freedland SJ, et al. J Clin Oncol. 2007 May 1;25(13):1765-71*
4. *Howard LE et al. BJU Int. 2017 Nov;120(5B):E80-E86.*

PSADT (Tiempo de duplicación del PSA)

PSADT	< 3 meses	3 – 8,9 meses	9 – 14,9 meses	≥ 15 meses
SLM	9 meses	19 meses	40 meses	50 meses

PSADT, tiempo de duplicación del PSA; SLM, supervivencia libre de metástasis.
Umbrales de PSADT en hombres con CPRCnm establecidos según estudios.
Resultados tomados de Howard LE, et al.[14]

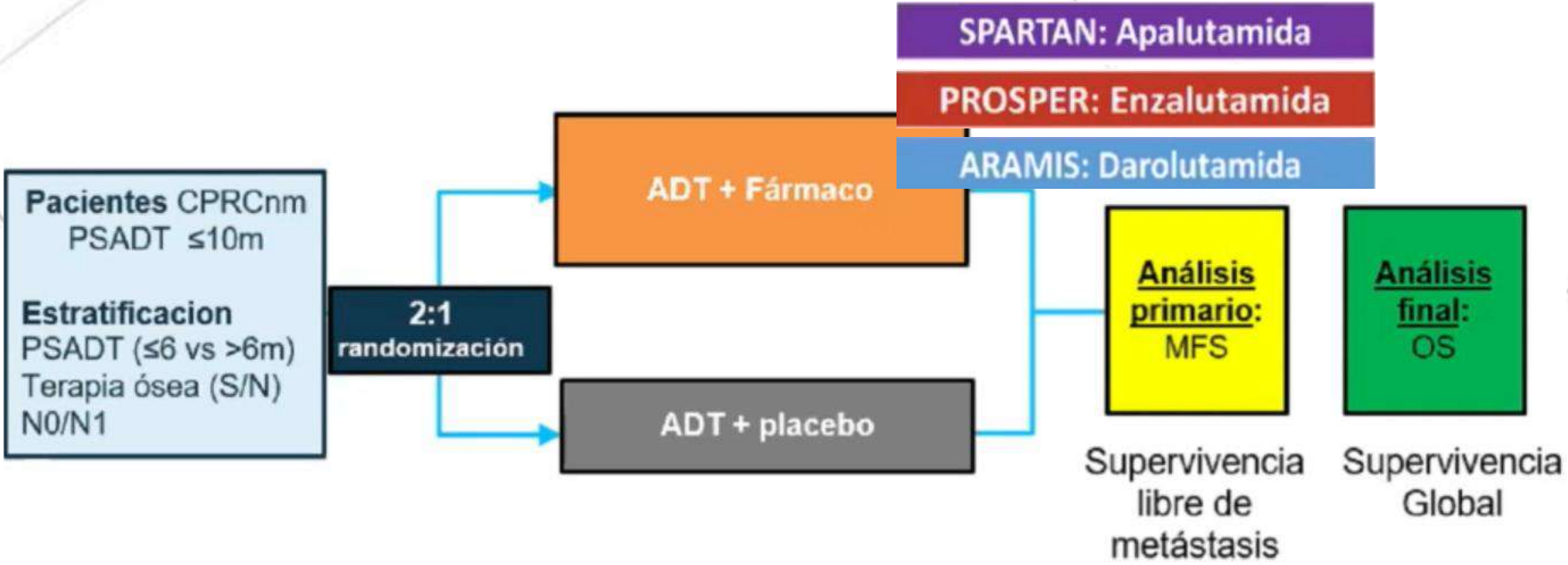
Identificar CPRC con **riesgo alto** de **metástasis**:

- PSA basal > 10 ng/ml
- PSA-DT < 6 meses

Smith MR, etal, JCO, 2005

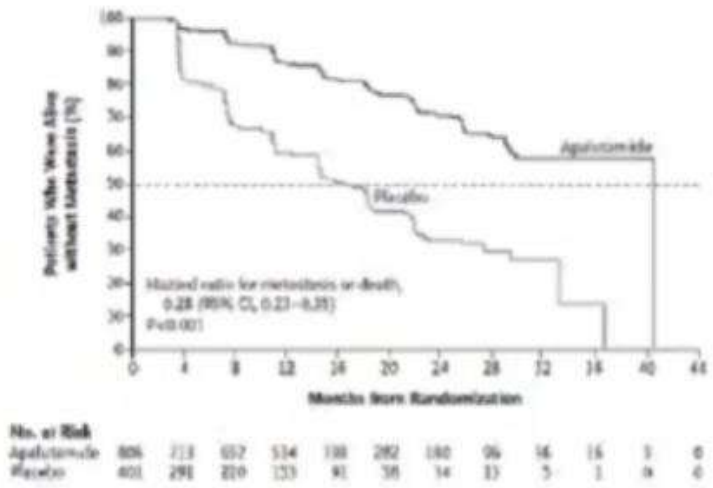
Smith MR, etal, Denosumab and bone-metastasis-free survival in men with castration-resistant prostate, the Lancet, 2013

NUEVOS TRATAMIENTOS EN CPRCnm



SPARTAN: Apalutamida

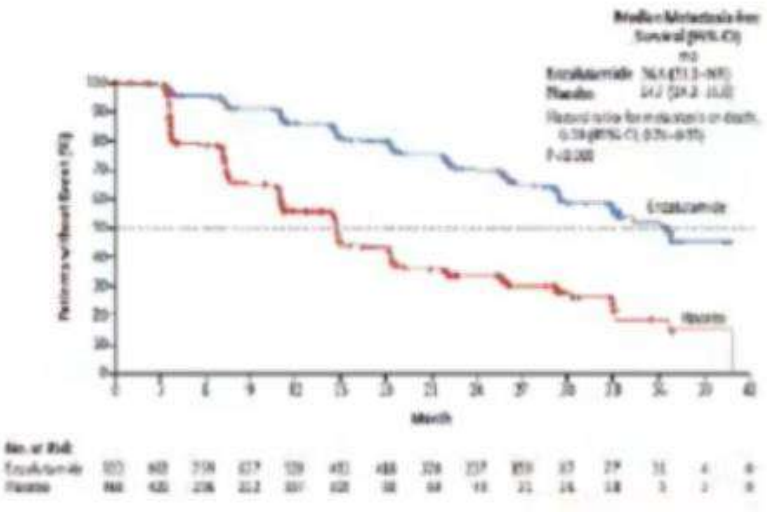
Smith et al. NEJM 2018



- **72% de reducción** de riesgo de aparición de M1 o muerte
- Mediana MFS: APA 40.5 meses vs PBO 16.2
- 24 meses de aumento en MFS

PROSPER: Enzalutamida

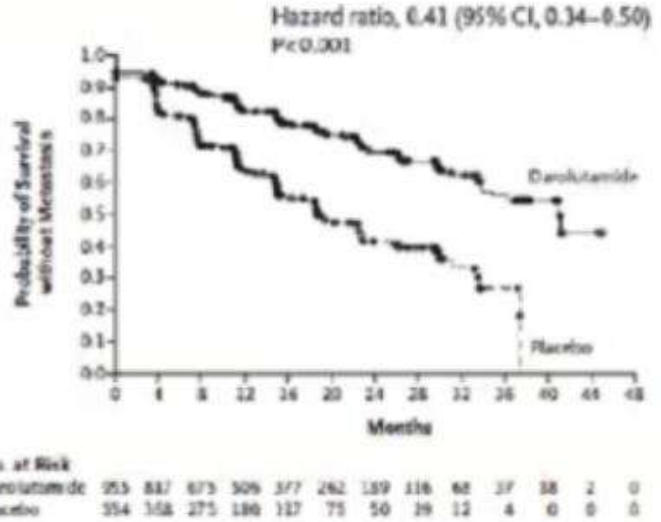
Hussain et al. NEJM 2018



- **71% de reducción** de riesgo de aparición de M1 o muerte
- Mediana MFS: ENZA 36.6 meses vs PBO 14.7
- 22 meses de aumento en MFS

ARAMIS: Darolutamida

Fizazi et al. NEJM 2019



- **59% de reducción** de riesgo de aparición de M1 o muerte
- Mediana MFS: DARO 40.4 meses vs PBO 18.4
- 22 meses de aumento en MFS

REDUCCIÓN DEL RIESGO DE APARICIÓN DE MTX 59-72%

Hussain M, et al. N Engl J Med 2018;378:2465-74
Smith MR, et al. N Engl J Med 2018;378:1408-18
Fizazi K, et al. N Engl J Med 2019; 28:380:1235-1246

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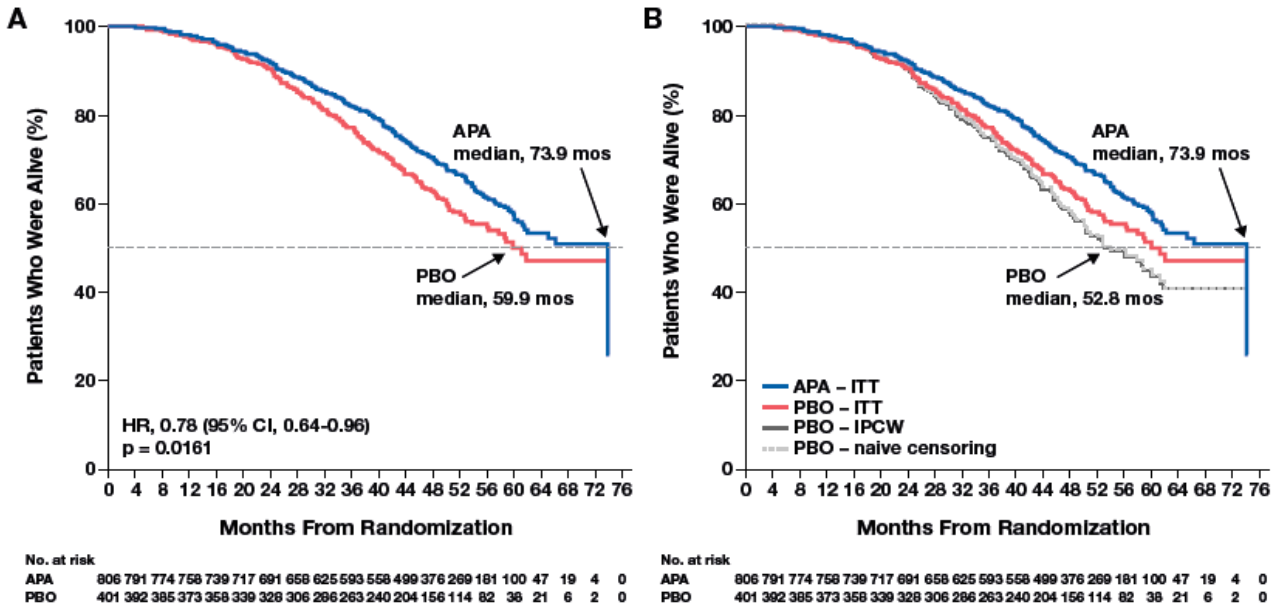
SPARTAN – RESULTADOS FINALES

Overall Survival

- APA significantly increased median OS by 14 months compared with PBO (Figure 4A).
- When adjusted for crossover effects using the naive-censoring and IPCW sensitivity analyses, APA increased median OS by 21.1 months compared with PBO (Figure 4B).
- Treatment effect of APA was generally consistent in study subpopulations (Figure 4C).

Figure 4. Kaplan-Meier Estimate of OS (A), and of OS Adjusted for Patient Crossover From PBO to APA (B), and Forest Plot Subgroup Analysis for OS by Baseline Patient Characteristics (C)



Mediana seguimiento: 52 m
Mediana SG: +14 m
Mediana SG (ajustada crossover): +21 m
SG 74 m (APA) / 60 m (PBO)

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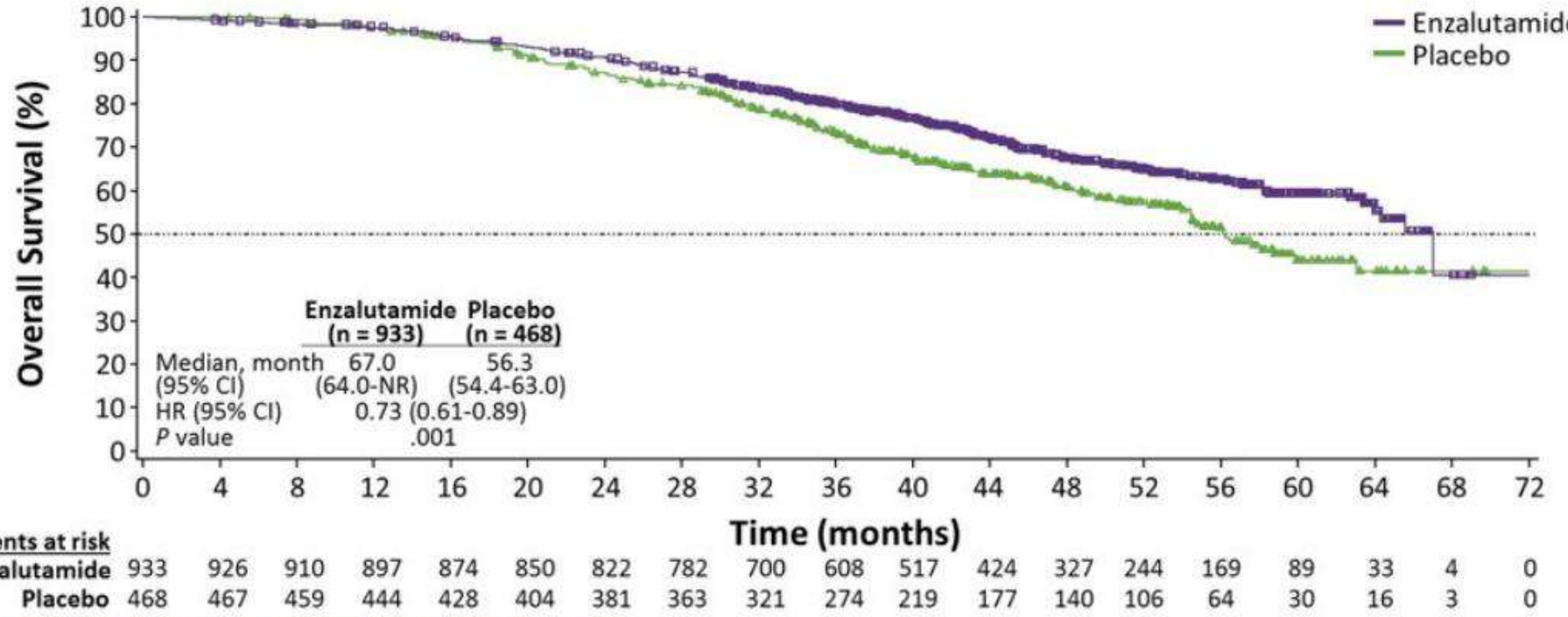
Final Survival Results From SPARTAN, a Phase 3 Study of Apalutamide Versus Placebo in Patients With Nonmetastatic Castration-Resistant Prostate Cancer. ASCO 2020. Poster 5516

PROSPER Final Overall Survival Analysis

Enzalutamide was associated with a statistically significant 27% reduction in the risk of death



Patients at risk																			
Enzalutamide	933	926	910	897	874	850	822	782	700	608	517	424	327	244	169	89	33	4	0
Placebo	468	467	459	444	428	404	381	363	321	274	219	177	140	106	64	30	16	3	0

CI, confidence interval; HR, hazard ratio; NR, not reached.

PRESENTED AT: 2020 ASCO ANNUAL MEETING #ASCO20 Slides are the property of the author, permission required for reuse. PRESENTED BY: Cora N. Sternberg, MD, FACP 4

Mediana seguimiento: 48 m
Mediana SG: +10,7 m
SG 67 m (ENZA) / 56 m (PBO)

SERVICIO DE SALUD DEL PRINCIPADO DE ASTURIAS

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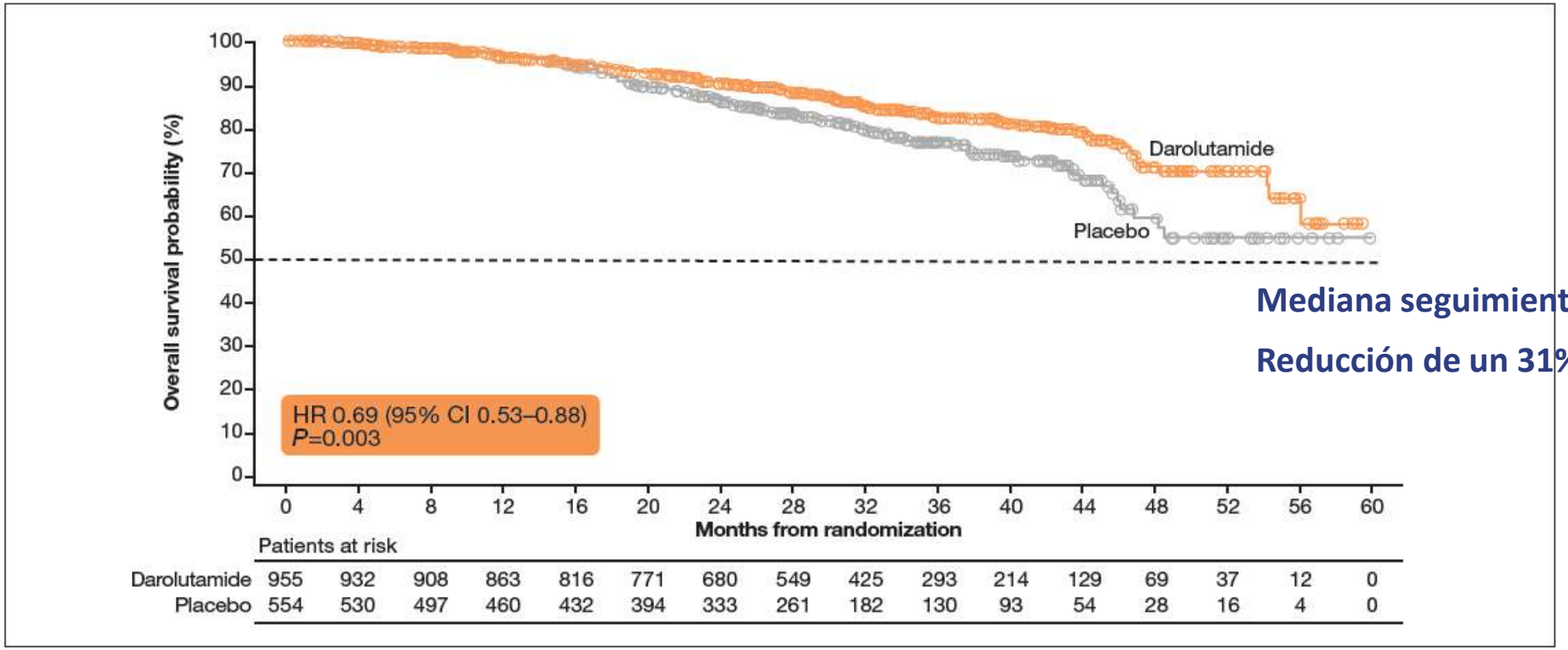
Final overall survival (OS) from PROSPER: A phase III, randomized, double-blind, placebo (PBO)-controlled study of enzalutamide (ENZA) in men with nonmetastatic castration-resistant prostate cancer (nmCRPC).ASCO 2020. Presentation by Cora N. 5515

ARAMIS- RESULTADOS FINALES



Mediana seguimiento: 29 m

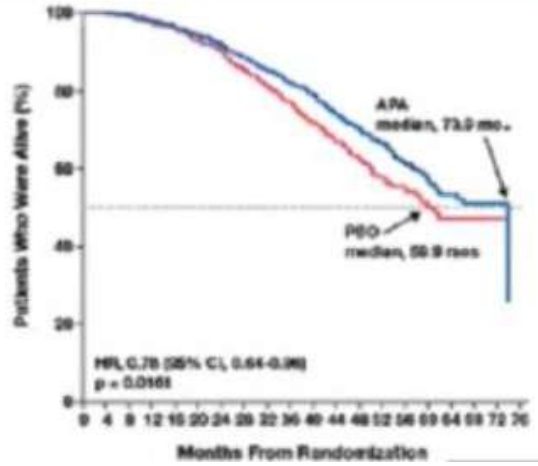
Reducción de un 31% del riesgo de muerte

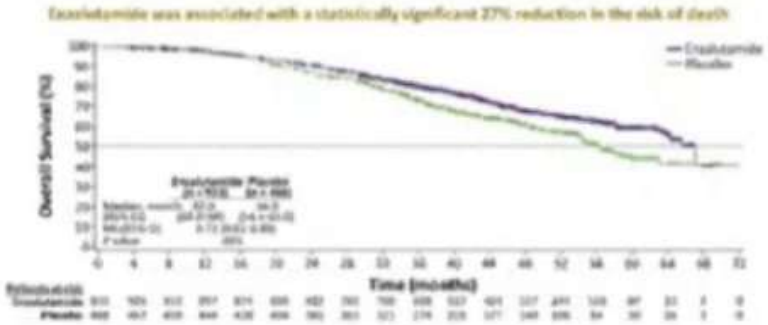
Efficacy

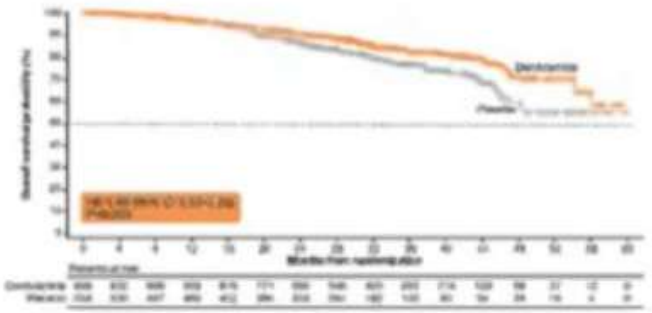
- Final analysis was conducted after 254 deaths were observed (148/955=15.5% of patients receiving darolutamide and 106/554=19.1% of patients receiving placebo).
- Darolutamide was associated with a statistically significant 31% reduction in the risk of death compared with placebo (HR 0.69; 95% CI 0.53–0.88; two-sided *P*=0.003; **Figure 2**).
  - The OS rate at 3 years was 83% (95% CI 80–86%) in the darolutamide group and 77% (95% CI 72–81%) in the placebo group.
  - OS benefit was observed despite more than half of patients in the placebo group receiving subsequent darolutamide or other life-prolonging therapy.
- The treatment effect for OS consistently favored darolutamide in prespecified subgroups, although the confidence intervals in some subgroups with smaller sample size did cross 1.

Fizazi K, et al. N Engl J Med. 2020;383:1040-1049.

	Primer análisis		*Análisis final*		
	Mediana MFS	Seg.	Mediana SG	Seg./ nº eventos	M en tto
APA	40,5 meses vs. 16,2 (HR: 0,28; IC95%: 0,23-0,35; p<0,001)	20,3 meses	73,9 meses vs. 59,9 (HR: 0,784; IC95%: 0,64-0,96; p = 0,0161)	52 m/428	32,9 meses vs. 11,5
ENZ	36,6 meses vs. 14,7 (HR: 0,29; IC95%: 0,24-0,35; p<0,0001)	18,5meses vs. 15,1	67,0 meses vs. 56,3 (HR: 0,73; IC95%: 0,61-0,89; p = 0,0011)	48 m/466	33,9 meses vs. 14,2
DARO	40,4 meses vs. 18,4 (HR: 0,41; IC95%:0,34-0,50; p<0,001)	17,9 meses	NR vs. NR (HR: 0,69; IC95%:0,53-0,88; p = 0,003)	29,1m/254	25,8 meses vs 11,6

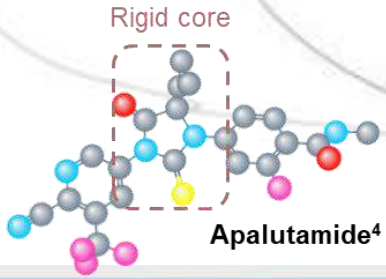




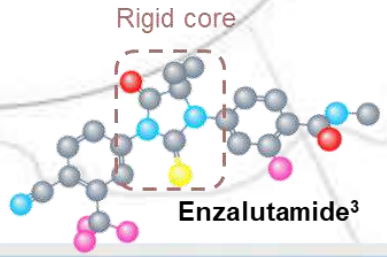


REDUCCIÓN RIESGO MUERTE 22-31%

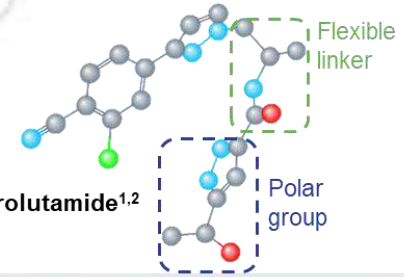
Hussain M, et al. N Engl J Med 2018;378:2465-74; Smith MR, et al. N Engl J Med 2018;378:1408-18; Fizazi K, et al. N Engl J Med 2019; 28;380:1235-1246; Fizazi K, et al. ASCO 2020 (Abstract 5514), Fizazi K, et al. NEJM 2020 Small E, at al. ASCO 2020 (abstract 5516), Smith M, et al. EurUrol 2020



Apalutamide[4]



Enzalutamide[3]



Darolutamide[1,2]

	APALUTAMIDA	ENZALUTAMIDA	DAROLUTAMIDA
Indicación	CPHSm / CPRCM0	CPRCM0/M1	CPRCM0
Dosis	4x60mg (240mg) c/24h	4x40mg (160mg) c/24h	2x300mg (600mg) cada 12h
Posología	1 vez al día con o sin alimentos	1 vez al día con o sin alimentos	2 veces al día con alimentos
Método	Los comprimidos deben tragarse enteros; no se deben partir, triturar, ni disolver en agua		
Dosis olvidada	Tomarla lo antes posible ese mismo día y volver al horario normal al día siguiente. No tomar dosis adicional para compensar la olvidada		
Castración	Mantener castración química con análogo RHLH		
Edad avanzada	Sin ajuste	Sin ajuste	Sin ajuste
Insuficiencia renal	Leve o moderada sin ajuste Grave: no recomendada	Leve o moderada sin ajuste Grave: no recomendada	Leve o moderada sin ajuste Grave: 300 mg/12h
Insuficiencia hepática	Leve o moderada sin ajuste Grave: no recomendada	sin ajuste	Leve: sin ajuste Moderada o grave: 300 mg/12h

https://www.ema.europa.eu/en/documents/producto-information/erleada-epar-producto-information_en.pdf
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https://www.ema.europa.eu/en/documents/producto-information/nubeqa-epar-producto-information_en.pdf

APALUTAMIDA, ENZALUTAMIDA Y DAROLUTAMIDA
REVISIÓN SISTEMÁTICA Y META-ANÁLISIS EN RED

Table 1 Study characteristics

Trial	PROSPER	SPARTAN	ARAMIS
Author	Hussain	Smith	Fizazi
Year	2018	2018	2019
Agents	Enzalutamide+ADT	Apalutamide+ADT	Darolutamide+ADT
Dosage	160mg	240mg	600mg
Control	Placebo+ADT	Placebo+ADT	Placebo+ADT
Inclusion criteria	M0N0CRPC, PSADT < 10 months, PSA >2 ng/ml	M0N0-N1CRPC, PSADT <10 months	M0N0-N1CRPC, PSADT < 10 months, PSA >2 ng/ml
Number	1401	1207	1509
Number (Treatment)	933	806	955
Number (Control)	468	401	554
Median Age (range)	74 (50–95) vs. 73 (53–92)	74 (48–94) vs. 74 (52–97)	74 (48–95) vs. 74 (50–92)
Median PSA at baseline (ng/ml)	11.1 vs. 10.2	7.78 vs. 7.96	9.0 vs. 9.7
Median PSADT (months)	3.8 vs. 3.6	4.4 vs. 4.5	4.4 vs. 4.7
Proportion of N1	0% vs. 0%	16.5% vs. 16.2%	17% vs. 29%
Metastasis free survival	36.6 vs. 14.7, HR 0.29 95% CI 0.24-0.35	40.5 vs. 16.2, HR 0.28 95% CI 0.23-0.35	40.4 vs. 18.4, HR 0.41 95% CI 0.34-0.5
PSA progression free survival	37.2 vs. 3.9, HR 0.07 95% CI 0.05-0.08	NR vs. 3.7, HR 0.06 95% CI 0.05-0.08	33.2 vs. 7.3, HR 0.13 95% CI 0.11-0.16
Overall survival	67 vs. 56.3, HR 0.73 95% CI 0.61-0.89	NR vs. NR, HR0.75 95% CI 0.59-0.96	NR vs. NR, HR 0.71 95% CI 0.5-0.99
Any grade AE rate	87% vs. 77%	96.5% vs. 93.2%	83.2% vs. 76.9%
Grade 3 or 4 AE rate	31% vs. 23%	24.8% vs. 23.1%	24.7% vs. 19.5%
Grade 5 AE rate	3% vs. 1%	1.2% vs. 0.3%	3.9% vs. 3.2%
Discontinuation rate	9% vs. 6%	10.6% vs. 7.0%	8.9% vs. 8.7%
Median follow up (months)	48	41	17.9

ADT androgen deprivation therapy, *CRPC* castration-resistant prostate cancer, *PSA* prostate-specific antigen, *PSADT* PSA doubling time, *NR* not reached, *HR* hazard ratio, *CI* confidential interval, *AE* adverse event

Cohortes homogéneas de pacientes (edad, riesgo de mtx, pronóstico…)

Mori K, Mostafaei H, Pradere B, Motlagh RS, Quhal F, Laukhtina E, Schuettfort VM, Abufaraj M, Karakiewicz PI, Kimura T, Egawa S, Shariat SF. Apalutamide, enzalutamide, and darolutamide for non-metastatic castration-resistant prostate cancer: a systematic review and network meta-analysis. Int J Clin Oncol. 2020 Nov;25(11):1892-1900. doi: 10.1007/s10147-020-01777-9. Epub 2020 Sep 14.

APALUTAMIDA, ENZALUTAMIDA Y DAROLUTAMIDA REVISIÓN SISTEMÁTICA Y META-ANÁLISIS EN RED

Conclusion

In this systematic review and network meta-analysis of first-line systemic therapies for patients with nmCRPC, based on an indirect comparison of data from placebo controlled phase 3 clinical trials, apalutamide was identified as having a higher likelihood of providing the maximum benefits in terms of MFS and PSA PFS. Darolutamide appeared to have the most favorable tolerability. These findings may provide guidance to patients and clinicians with regards to treatment decisions in conjunction with other aspects that drive personalized medicine strategies for nmCRPC.

Mori K, Mostafaei H, Pradere B, Motlagh RS, Quhal F, Laukhtina E, Schuettfort VM, Abufaraj M, Karakiewicz PI, Kimura T, Egawa S, Shariat SF. Apalutamide, enzalutamide, and darolutamide for non-metastatic castration-resistant prostate cancer: a systematic review and network meta-analysis. Int J Clin Oncol. 2020 Nov;25(11):1892-1900. doi: 10.1007/s10147-020-01777-9. Epub 2020 Sep 14.

EFECTOS ADVERSOS

	SPARTAN (Apalutamida)	PROSPER (Enzalutamida)	ARAMIS (Darolutamida)
Any grade	+3,2%	+10%	+6,1%
Grado 3-4	+10,9 %	+8%	+5,2%
EA discontinuación tto	+3,6 %	+3%	+0,2%
Fatiga grado 3-4	+0,6%	+2%	-0,5%
HTA	+5%	+6,7%	+1,4%
Rash	+18,3%	-	+2%
Caídas	+6,6%	+7%	-0,5%
Fracturas	+5,2%	-	+0,6%
Alteraciones mentales	+2,1	+3%	+0,2%
Hipotiroidismo	+6,1%	-	+0,2%
Mareos	+3%	+6%	+0,5%

**M. Rodrigo, Curso AEU 2020.Fizazi K, et al. ASCO 2020 (Abstract 5514), Fizazi K, et al. NEJM 2020 Small E, at al. ASCO 2020 (abstract 5516), Smith M, et al. EurUrol 2020 Sternberg C, et al. ASCO 2020, Sternberg C, et al. NEJM 2020

SEGURIDAD DE APALUTAMIDA, ENZALUTAMIDA Y DAROLUTAMIDA

Table 2. AE recording and reporting, risks of AEs in the placebo arms, and relative risks of AEs when comparing drug vs placebo arm, by trial

	nmCRPC			mCSPC		mCRPC	
AE recording, reporting, and risks	SPARTAN	PROSPER	ARAMIS	ARCHES	TITAN	PREVAIL	AFFIRM
AE methods							
CTCAE version	4.0	4.03	4.03	4.03	4.03	4.0	4.0
Risk cutoff for AEs[a]	≥15%	≥5%	≥5%	≥5%	≥10% or grade 3 in n ≥ 10 per arm	≥10% and drug arm ≥2% points higher than placebo arm	>10% and drug arm ≥2% points higher than placebo arm
AEs of interest,[b] No.	5	7	14	17	5	7	4
AEs reported,[c] No.	13	23	26	27	19	20	10
Placebo arm	Yes	No	Yes	No	No	Yes	No
	Yes	No	No	No	No	No	No
Fatigue, absolute risk (95% CI), %	21.1 (17.4 to 25.4)	13.8 (10.9 to 17.2)	8.7 (6.6 to 11.3)	15.3 (12.6 to 18.5)	16.7 (13.8 to 20.1)	25.8 (23.0 to 28.9)	29.1 (24.8 to 33.7)
Hypertension, absolute risk (95% CI), %	19.8 (16.2 to 24.0)	5.2 (3.5 to 7.6)	5.2 (3.7 to 7.4)	5.6 (4.0 to 7.8)	15.6 (12.7 to 18.9)	4.1 (3.0 to 5.7)	3.3 (1.9 to 5.5)
Any AE, absolute risk (95% CI), %	93.2 (90.3 to 95.3)	77.4 (73.4 to 81.0)	76.9 (73.2 to 80.2)	85.9 (82.8 to 88.5)	96.6 (94.7 to 97.8)	93.2 (91.4 to 94.8)	97.7 (95.8 to 98.8)
Any grade 3-4 AE, absolute risk (95% CI), %	34.2 (29.7 to 39.0)	23.4 (19.8 to 27.5)	19.5 (16.4 to 23.0)	25.6 (22.2 to 29.3)	40.8 (36.7 to 45.0)	37.1 (33.9 to 40.4)	53.1 (48.2 to 58.0)
Relative risk of all grade 3-4 AEs[f] (95% CI)	1.00 (Referent)	0.44 (0.22 to 0.88)	0.45 (0.23 to 0.86)	0.45 (0.23 to 0.88)	1.22 (0.69 to 2.17)	0.86 (0.48 to 1.54)	1.66 (0.71 to 3.91)
AEs by drug vs placebo							
Fatigue, relative risk (95% CI)	1.44 (1.16 to 1.79)	2.37 (1.85 to 3.03)	1.39 (1.01 to 1.92)	1.28 (0.99 to 1.65)	1.18 (0.91 to 1.52)	1.38 (1.19 to 1.59)	1.16 (0.96 to 1.39)
Hypertension, relative risk (95% CI)	1.25 (0.99 to 1.58)	2.32 (1.51 to 3.56)	1.26 (0.82 to 1.93)	1.44 (0.93 to 2.23)	1.14 (0.87 to 1.49)	3.24 (2.25 to 4.67)	2.00 (1.11 to 3.61)

Drago JZ, Gönen M, Thanarajasingam G, Sacks CA, Morris MJ, Kantoff PW, Stopsack KH. Inferences about drug safety in phase 3 trials in oncology: Examples from advanced prostate cancer. J Natl Cancer Inst. 2020 Aug 28:djaa134. doi: 10.1093/jnci/djaa134.

SEGURIDAD DE APALUTAMIDA, ENZALUTAMIDA Y DAROLUTAMIDA

- No son comparables entre si: heterogenicidad en la recogida de datos.
- Comparar con su brazo placebo.
- Apalutamida recoge EAs cada 4 s, el resto cada 16 s

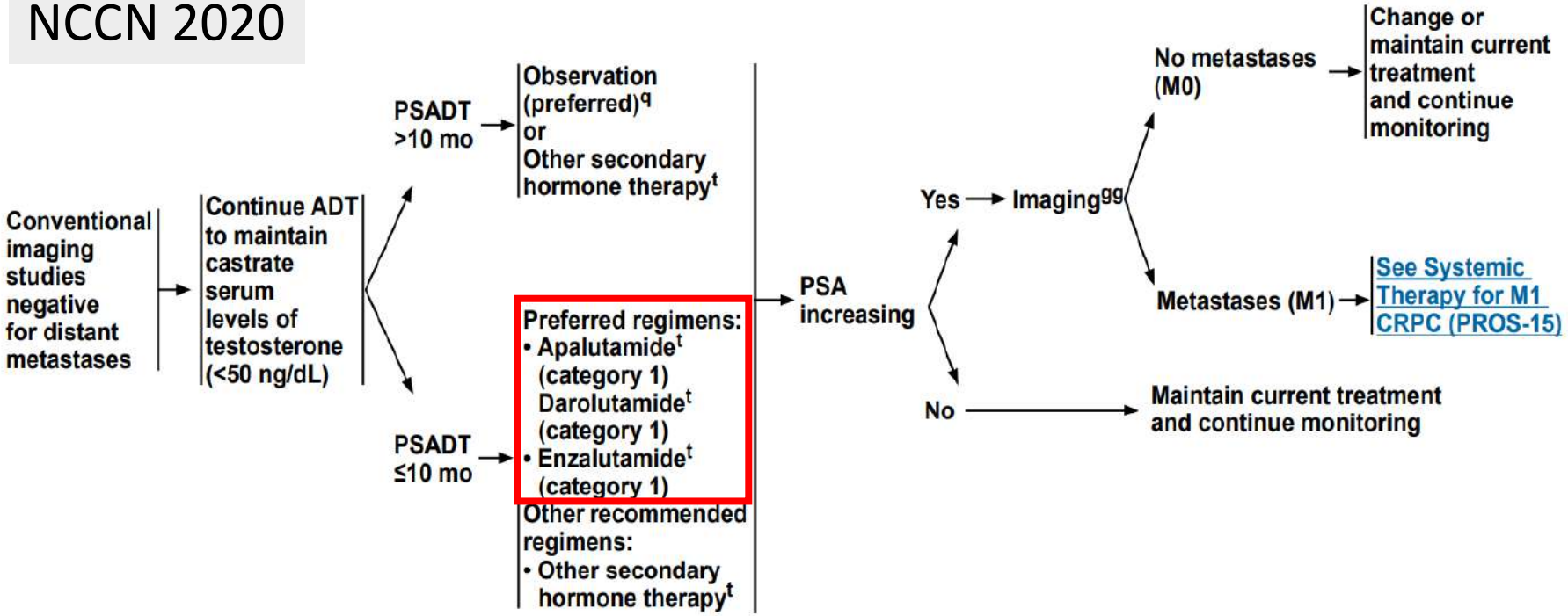
¿Qué dicen las guías?

EAU 2020

Recommendation	Strength rating
Offer apalutamide, darolutamide or enzalutamide to patients with M0 CRPC and a high risk of developing metastasis (PSA-DT < 10 months) to prolong time to metastases.	Strong

NCCN 2020

SYSTEMIC THERAPY FOR M0 CASTRATION–RESISTANT PROSTATE CANCER (CRPC)[jj]



CONCLUSIONES

- Intervención precoz en pacientes de alto riesgo de progresión (PSADT <10 m). Beneficio en supervivencia libre de metástasis y supervivencia global (calidad de vida)

- **APALUTAMIDA, ENZALUTAMIDA Y DAROLUTAMIDA:** 3 fármacos que reducen el riesgo de aparición de Mtx (59-72%) y el riesgo de muerte (22-31%)

- Tienen buena tolerabilidad y perfil de toxicidad favorable

RECORDAD TRATAMIENTOS CPHSm

(CÁNCER DE PRÓSTATA HORMOSENSIBLE METASTÁSICO)

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DEL PRINCIPADO DE ASTURIAS

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Servicio de Urología

TRATAMIENTO CPHSm

ADT ha sido el estándar de tratamiento durante 75 años…

Selected randomized controlled trials of androgen deprivation therapy in patients with metastatic prostate cancer

Data source	Population		Intervention	Follow-up, yr, median	Key findings *
	Clinical stage **	*n*			
Crawford et al. [57]	100% M+	603	CAB (leuprolide + flutamide) compared with leuprolide plus placebo	–	The addition of flutamide resulted in longer PFS (16.5 vs 13.9 mo, $p = 0.039$), OS (35.6 vs 28.3 mo, $p = 0.035$), and reduced disease flare expressed as pain at first week ($p = 0.019$) and fourth week ($p = 0.013$).
Eisenberger et al. [59]	100% M+	1387	CAB (orchiectomy plus flutamide) compared with orchiectomy plus placebo	–	PSA response was improved in men receiving flutamide ($p < 0.001$); OS was not significantly different ($p = 0.14$).
Dijkman et al. [58]	100% M+	457	CAB (orchiectomy plus nilutamide) compared with orchiectomy plus placebo	8.5	At 8.5 yr, CAB resulted in better PFS (21.2 vs 14.7 mo, $p = 0.002$), CSS (37.0 vs 29.8 mo, $p = 0.013$), and OS (27.3 vs 23.6 mo, $p = 0.033$).
Boccardo et al. [56]	35% M0 and 65% M+	373	CAB (goserelin plus flutamide) compared with goserelin plus placebo	2	At 2 yr, CAB vs monotherapy resulted in no PFS or OS difference.
Tyrrel [71]	T3–T4, M0 and M+	589	Bicalutamide 150 mg compared with monotherapy ***	2	At 2 yr, in M+ men bicalutamide compared with monotherapy resulted in worse OS (HR: 1.30 for time to death); data immature for evaluation of M0 men.
PCTCG [60]	Meta-analysis of 27 RCTs; population composed of 12% M0 and 88% M+	8275	CAB (orchiectomy or LHRH-A plus flutamide, nilutamide, or CPA) compared with monotherapy ***	5	At 2 or 5 yr, CAB compared with monotherapy resulted in no OS difference. However, CAB with nilutamide or flutamide resulted in better OS (27.6% vs 24.7%, $p = 0.005$), while CAB with CPA resulted in worse OS (15.4% vs 18.1%, $p = 0.04$).
Collette et al. [61]	Reanalysis of PCTCG excluding trials without disease flare protection; population composition not specified	4764	Orchiectomy compared with CAB (11 trials) or monotherapy *** plus ST-AA compared with CAB (4 trials)	–	Exclusion of trials without disease flare protection from PCTCG meta-analysis results in no survival benefit of maximal androgen blockade over monotherapy (0.95 [0.89–1.02]; $p = 0.15$).

CAB = combined androgen blockade; CPA = cyproterone acetate; CSS = cancer-specific survival; HR = hazard ratio; LHRH-A = luteinizing hormone–releasing hormone agonist; OS = overall survival; PCTCG = Prostate Cancer Trialists' Collaborative Group; PFS = progression-free survival; PSA = prostate-specific antigen; RCT = randomized controlled trial; ST-AA = short-term antiandrogens.

* Unless specified differently, results are presented as hazard ratios or relative risks (treatment compared with control), with the associated 95% confidence intervals and *p* values, whenever available.

** Based on the 1992 American Joint Committee on Cancer tumor category [103].

*** Monotherapy: orchiectomy or LHRH-A.

Guía NCCN 2019
Pagliarulo V, et al. Eur Urol 2012 Jan;61(1):11-25
Etheridge T et al. Asian Journal of Urology 2019

Hoy en día…

- CPHSm ALTO RIESGO:
  - 2015 (Chaarted y Stampede): DOCETAXEL
  - 2017 (Latitude y Stampede): ABIRATERONA

- CPHSm (ALTA Y BAJA CARGA, TRATAMIENTOS PREVIOS)
  - 2019 (Stampede): ABIRATERONA
  - 2019 (Titan): APALUTAMIDA
  - 2019 (Enzamet y Arches): ENZALUTAMIDA

MUCHAS GRACIAS