QUIMIOTERAPIA EN EL CÁNCER DE PRÓSTATA METASTÁSICO ENFERMEDAD HORMONOSENSIBLE. CUÁNDO APLICARLA.

ORGANIZA

GUA urología andrología

SCU Sociedad Canaria de Urología

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Disclosures

BMS, Astellas, Ipsen, Roche, Lilly, Novartis, Merck, Pfizer, Servier

INTRODUCCIÓN

- TUMOR MÁS INCIDENTE EN LA POBLACIÓN MASCULINA
- 3º en mortalidad en España.
- EDAD MEDIA: 65 años.
- 15% to 40% of patients develop recurrent disease (biochemical recurrence and metastatic disease) within 10 years of initial treatment
  - Median time to biochemical recurrence: 2-3 years

American Cancer Society. Cancer Facts & Figures 2021. Pound. JAMA. 1999;281:1591. Higano. Uro Oncol. 2011;29(6 Suppl):S1. Toussi. J Urol. 2016;195:1754. Freedland. JAMA. 2005;294:433.

LANDSCAPE

ESCENARIO: CANCER DE PRÓSTATA SENSIBLE A LA CASTRACIÓN M1 (mCPSH)

- ESTUDIOS:
  - **CHAARTED**
  - LATITUDE
  - **STAMPEDE**
  - **TITAN**
  - **ARCHES**
  - **ENZAMET**
  - **ARASENS**
  - **PEACE-1**

TABLE 1. BASELINE CHARACTERISTICS OF THE INCLUDED TRIALS

Study	Treatment arms		Total participants	Median age (years)	Volume of disease (%)		Metastatic Presentation (%)		Docetaxel
Year	Experimental	Control			High	Low	Synchronous	Metachronous	
GETUG-AFU1 2013	Docetaxel + ADT	ADT	385	Rx: 63;	48	52	71	29	Yes (100%)
CHAARTED 2015	Docetaxel + ADT	ADT	790	Rx: 64; Control: 63	65	35	73	27	Yes (100%)
STAMPEDE[a] 2016, 2017, 2022	Docetaxel + ADT	ADT	1086	65	43	33	~95	~5	Yes (100%)
	Abiraterone + ADT	ADT	1002	67	56	45	97	3	No
	Abiraterone + Enzalutamide + ADT	ADT	916	68	NA	NA	94	6	Yes (54)
LATITUDE 2017	Abiraterone + ADT	ADT	1199	Rx: 68; Control: 67	80	20	100	0	No
ENZAMET 2019	Enzalutamide + ADT	NSAA + ADT	1125	69	53	47	67	33	Yes (Concurrent 45%)
ARCHES 2019	Enzalutamide + ADT	ADT	1150	70	63	37	67	15	Yes (Prior 18%)
TITAN 2019	Apalutamide + ADT	ADT	1052	Rx: 69; Control; 68	63	37	76	19	Yes (Prior 11%)
SWOG 1216 2022	TAK + ADT	NSAA + ADT	1279	68	NA	NA	NA	NA	No
PEACE1 2022	Abiraterone + Docetaxel + ADT	Docetaxel + ADT	1172	Rx: 67; Control: 66	57	43	100	0	Yes (Concurrent 61%)
ARASENS 2022	Darolutamide + Docetaxel + ADT	Docetaxel + ADT	1305	Rx: 67; Control: 67	77	23	86	13	Yes (Concurrent 100%)

https://www.urotoday.com/conference-highlights/asco-2023/asco-2023-prostate-cancer/144863-asco-2023-the-role-of-volume-of-disease-for-treatment-selection-in-patients-with-mcspc-a-living-meta-analysis.html

CONCEPTOS DE LOS ESTUDIOS.

	High-Volume Disease[1,2] (n = 1005/1305 [77%])	High-Risk Disease[1,2] (n = 912/1305 [70%])
Definition	**CHAARTED Criteria[3]** ▪Visceral metastases ▪≥4 bone metastases (≥1 beyond vertebral column/pelvis*)	**LATITUDE Criteria[4]** ≥2 risk factors: ▪Gleason score ≥8 ▪≥3 bone metastases ▪Visceral metastasis

***ARASENS:** Análisis retrospectivo usando Alto volumen y alto riesgo.

- **PEACE-1:** Alto y bajo volumen

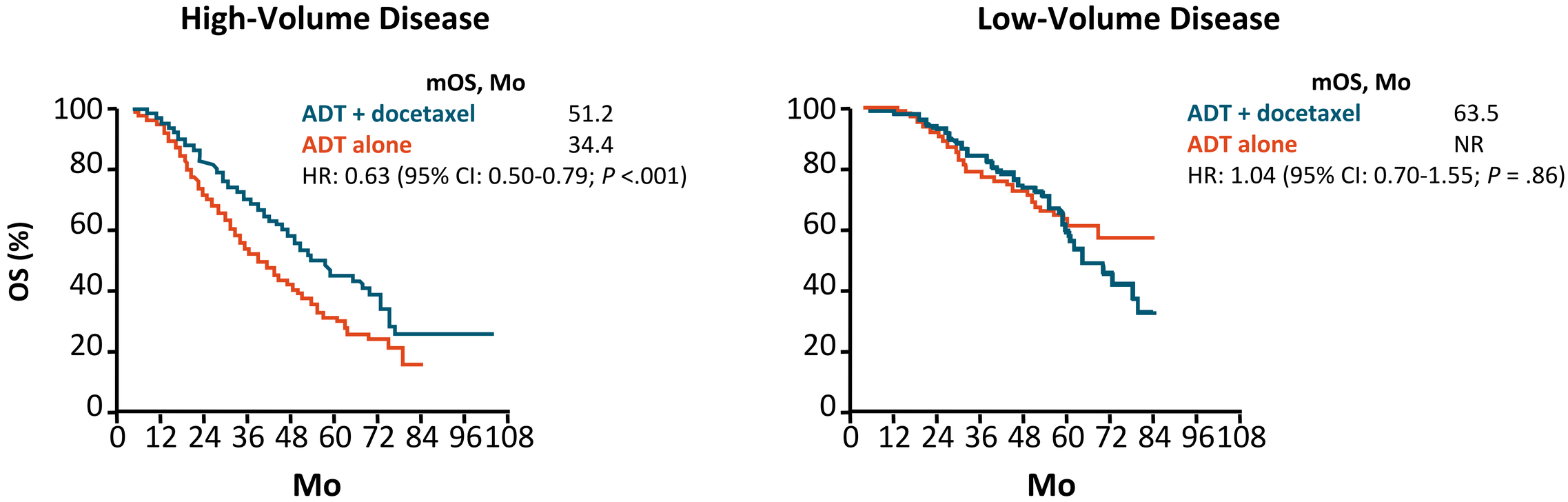
ENFERMEDAD SINCRÓNICA Y METACRÓNICA

DOCETAXEL SECUENCIAL O CONCURRENTE

1. Hussain. ASCO GU 2023. Abstr 15. 2. Hussain. JCO. 2023;[Epub].
3. Sweeney. NEJM. 2015;373:737. 4. Fizazi. NEJM. 2017;377:352.

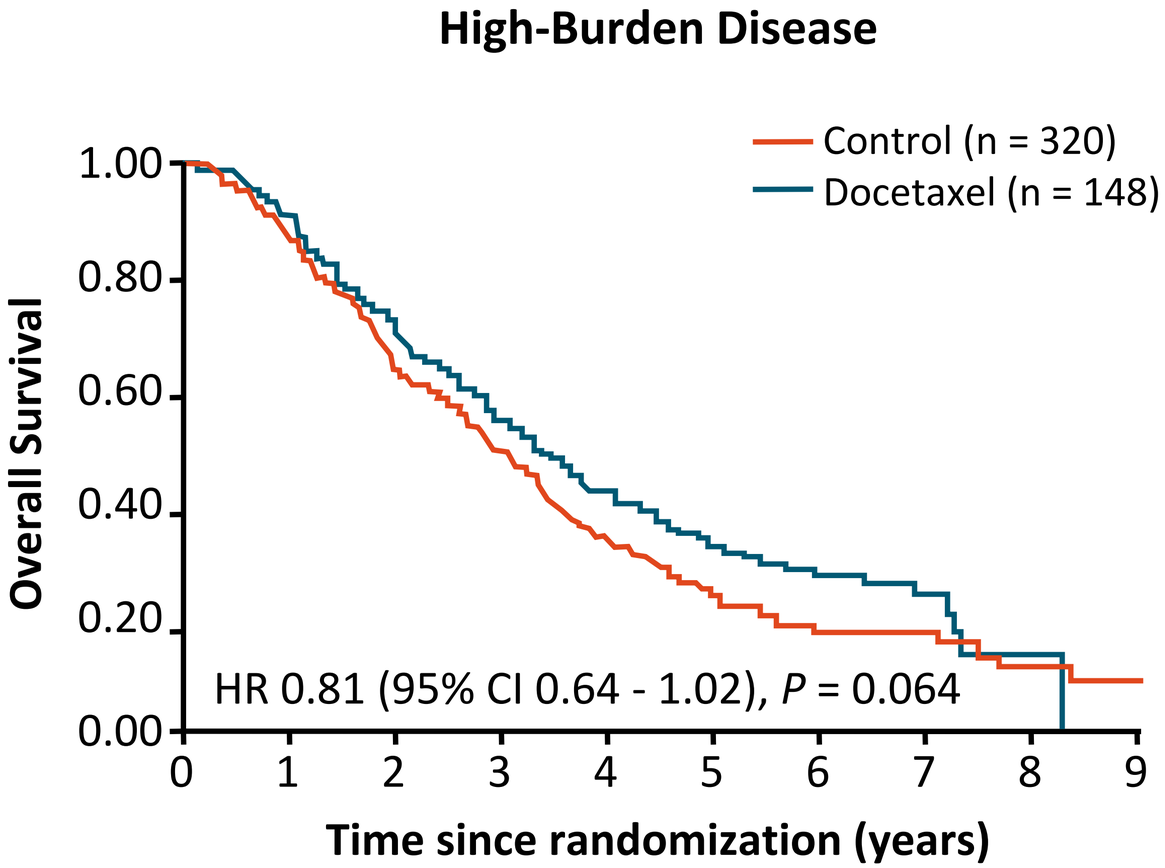
CHAARTED: High-Volume vs Low-Volume Disease

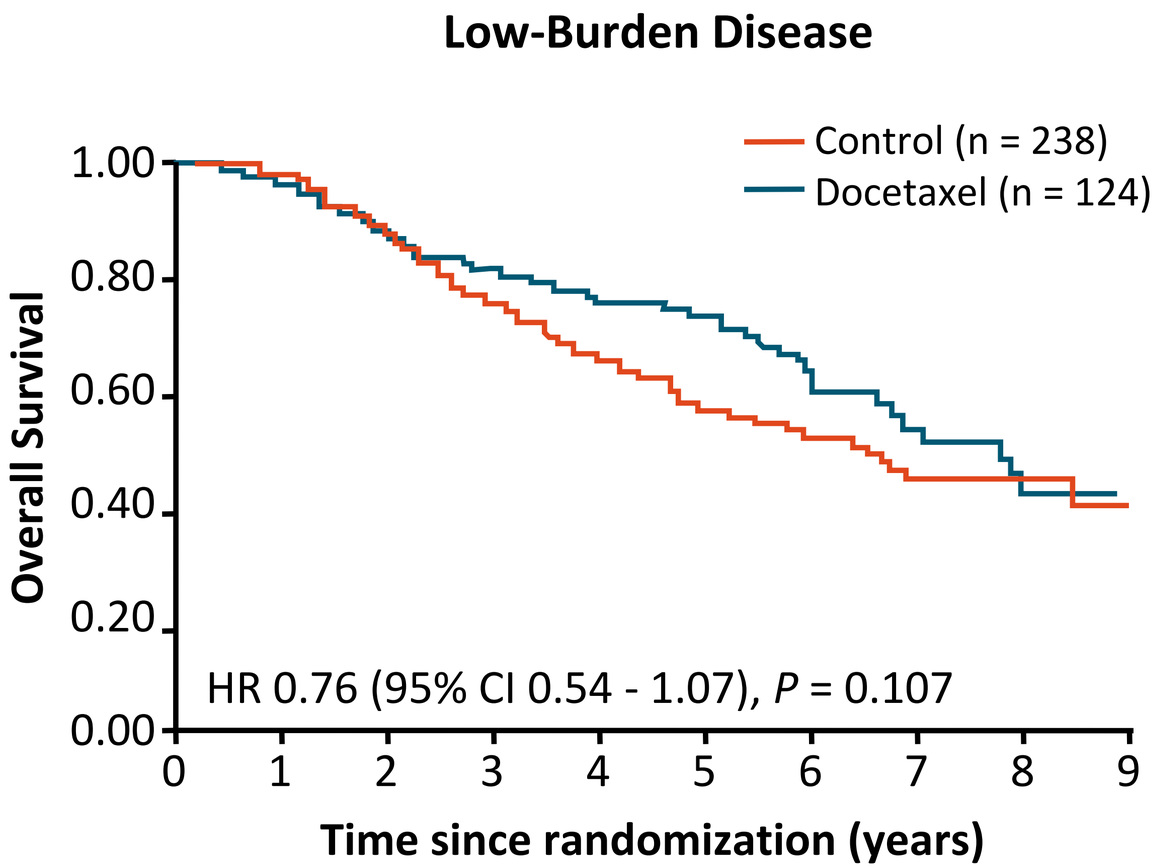
- Median follow-up of 53.7 mo in patients with metastatic hormone-sensitive prostate cancer randomized to ADT + docetaxel vs ADT alone (N = 790)



Kyriakopoulos. JCO. 2018;36:1080.

STAMPEDE: High-Volume vs Low-Volume Disease





Clarke. Ann Oncol. 2019;30:1992.

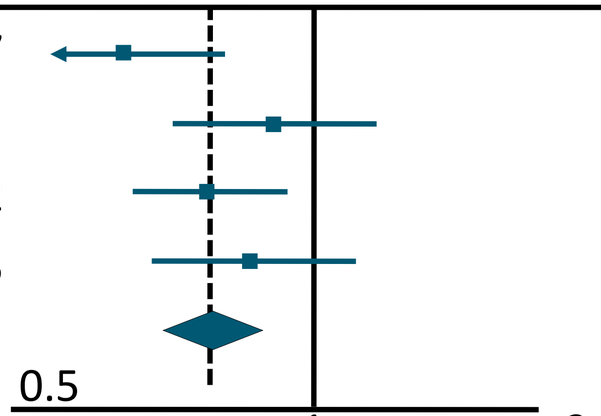
Meta-analysis of RCTs of Docetaxel in mCSPC

- Results based on 2992 men/1271 events

OS

	Control	Treatment	HR (95% CI)
CHAARTED	136/393	101/397	0.61 (0.47-0.80)
GETUG-15	NA/193	NA/192	0.90 (0.69-1.81)
STAMPEDE (SoC ± Doc)	350/724	144/362	0.76 (0.62-0.93)
STAMPEDE (SoC + ZA ± Doc)	170/366	158/365	0.85 (0.65-1.10)
Overall			0.77 (0.68-0.87)

Heterogeneity: $X^2 = 4.80$; df = 3; $P = .187$; $I^2 = 37.5\%$



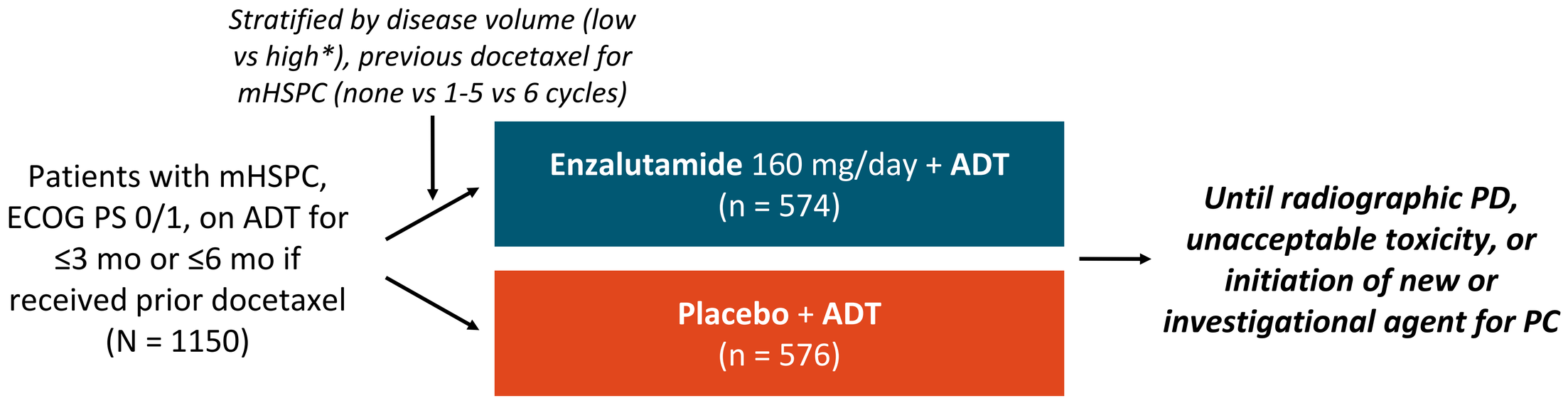
- 9% absolute improvement in survival at 4 yr

Vale. Lancet Oncol. 2016;17:243.

¿QUÉ OCURRE CON LOS ESTUDIOS CON TERAPIAS DIRIGIDAS AL RECEPTOR ANDROGÉNICO?

ARCHES: Enzalutamide + ADT vs Placebo + ADT in mHSPC

- International, double-blind, randomized phase III trial



*High disease volume defined as either visceral metastases or ≥4 bone lesions with ≥1 lesion in bony structure beyond vertebral column and pelvic bone.

- Primary endpoint: centrally assessed radiographic PFS
- Secondary endpoints: OS, ORR, time to first SSE, PSA progression, time to new antineoplastic therapy, time to castration resistance, PSA undetectable rate

Armstrong. JCO. 2019;37:2974.

ARCHES: Características basales

Characteristic	Enzalutamide Plus ADT (n = 574)	Placebo Plus ADT (n = 576)
Age (years)		
Median	70.0	70.0
Range	46-92	42-92
Age category, years		
< 65	148 (25.8)	152 (26.4)
65-74	256 (44.6)	255 (44.3)
≥ 75	170 (29.6)	169 (29.3)
ECOG performance status score on day 1		
0	448 (78.0)	443 (76.9)
1	125 (21.8)	133 (23.1)
Total Gleason score at initial diagnosis		
< 8	171 (29.8)	187 (32.5)
≥ 8	386 (67.2)	373 (64.8)
Confirmed metastases at screening[b]		
Yes	536 (93.4)	531 (92.2)
No	34 (5.9)	45 (7.8)
Unknown	4 (0.7)	0
Localization of confirmed metastases at screening[b]		
Bone only	268 (46.7)	245 (42.5)
Soft tissue only	51 (8.9)	45 (7.8)
Bone and soft tissue	217 (37.8)	241 (41.8)
Distant metastasis at initial diagnosis		
M1	402 (70.0)	365 (63.4)
M0	83 (14.5)	86 (14.9)
MX/unknown	88 (15.3)	125 (21.7)

Characteristic	Enzalutamide Plus ADT (n = 574)	Placebo Plus ADT (n = 576)
Disease volume		
High[c]	354 (61.7)	373 (64.8)
Low	220 (38.3)	203 (35.2)
Prior local therapy		
Radical prostatectomy	72 (12.5)	89 (15.5)
Radiation therapy	73 (12.7)	72 (12.5)
No. of cycles of prior docetaxel chemotherapy		
0	471 (82.1)	474 (82.3)
1-5	14 (2.4)	11 (1.9)
6	89 (15.5)	91 (15.8)
Previous use of ADT[d]		
None	39 (6.8)	61 (10.6)
≤ 3 months	414 (72.1)	394 (68.4)
> 3 months	121 (21.1)	120 (20.8)
Unknown[e]	0	1 (0.2)
Median duration of prior ADT, months (range)[f]	1.6 (0.03-55.3)	1.6 (0.03-198.8)
Previous use of antiandrogen[g]	205 (35.8)	229 (39.9)
Median PSA, ng/mL (range)[g]	5.4 (0-4,823.5)	5.1 (0-19,000.0)
Modified QLQ-PR25 urinary symptoms score, mean (SD)[h]	35.2 (25.3)	35.8 (25.4)
FACT-P total score, mean (SD)[i]	113.9 (19.8)	112.7 (19.0)
BPI-SF item 3 (worst pain), mean (SD)[j]	1.8 (2.4)	1.8 (2.3)
BPI-SF pain severity score, mean (SD)[j]	1.4 (1.8)	1.4 (1.7)

62-65 % pacientes alto volumen

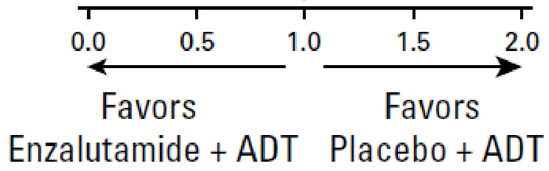
18% pacientes docetaxel previo

63-70% metastásicos de novo

Armstrong AJ, et al. J Clin Oncol. 2019;37(32):2974–2986.

ARCHES: SLPr

Subgroup	Enzalutamide + ADT No. of patients (E)	Placebo + ADT No. of patients (E)	HR (95% CI)†
All patients	574 (91)	576 (201)	0.39 (0.30 to 0.50)
Age < 65 years	148 (21)	152 (58)	0.29 (0.17 to 0.47)
Age ≥ 65 years	426 (70)	424 (143)	0.44 (0.33 to 0.58)
Geographic region – Europe	341 (55)	344 (122)	0.42 (0.31 to 0.58)
Geographic region – North America	86 (14)	77 (29)	0.30 (0.16 to 0.57)
Geographic region – rest of the world	147 (22)	155 (50)	0.40 (0.24 to 0.66)
ECOG status 0 at baseline	448 (67)	443 (146)	0.38 (0.29 to 0.51)
ECOG status 1 at baseline	125 (24)	133 (55)	0.43 (0.27 to 0.70)
Gleason score at initial diagnosis < 8	171 (21)	187 (47)	0.42 (0.25 to 0.70)
Gleason score at initial diagnosis ≥ 8	386 (65)	373 (151)	0.36 (0.27 to 0.48)
Disease localization at baseline – bone only	268 (35)	245 (82)	0.33 (0.22 to 0.49)
Disease localization at baseline – soft tissue only	51 (5)	45 (12)	0.42 (0.15 to 1.20)
Disease localization at baseline – bone and soft tissue	217 (50)	241 (104)	0.42 (0.30 to 0.60)
Baseline PSA value at or below overall median	293 (41)	305 (96)	0.38 (0.26 to 0.54)
Baseline PSA value above overall median	279 (50)	269 (104)	0.41 (0.30 to 0.58)
Low volume of disease	220 (14)	203 (47)	0.25 (0.14 to 0.46)
High volume of disease	354 (77)	373 (154)	0.43 (0.33 to 0.57)
No prior docetaxel therapy	471 (70)	474 (166)	0.37 (0.28 to 0.49)
Prior docetaxel therapy	103 (21)	102 (35)	0.52 (0.30 to 0.89)
Previous use of ADT or orchiectomy	535 (88)	515 (179)	0.41 (0.32 to 0.53)
No previous use of ADT or orchiectomy	39 (3)	61 (22)	0.19 (0.06 to 0.62)



Forest plot of rPFS for prespecified subgroups (intent-to-treat population).

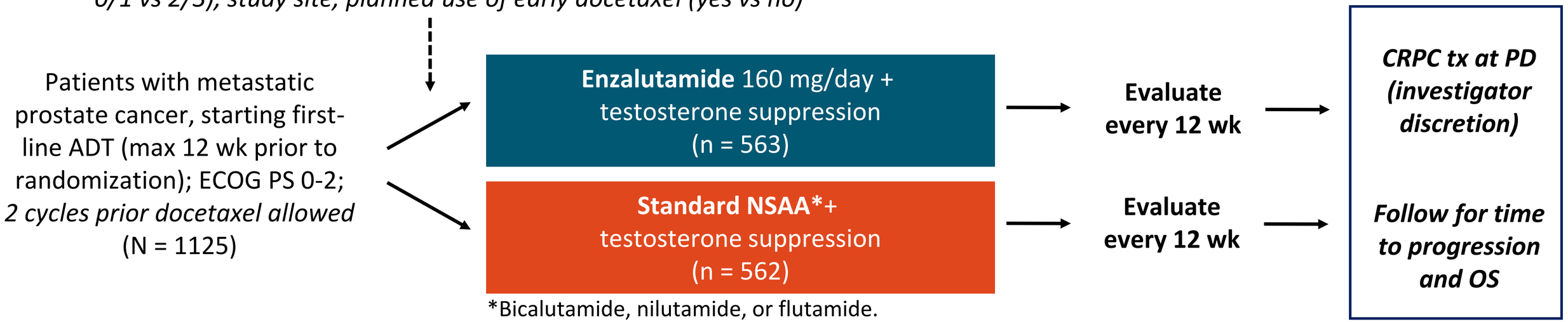
SLPr: Supervivencia Libre de Progresión Radiológica; TDA: Terapia de Deprivación Androgénica; HR: Hazard Ratio; mFU: Mediana de seguimiento.

Armstrong AJ, et al. J Clin Oncol. 2019;37(32):2974–2986.

ENZAMET: Enzalutamide + ADT vs NSAA + ADT in mHSPC

- Randomized, open-label, multicenter phase III clinical trial

Stratified by volume of metastases (high vs low), antiresorptive therapy (yes vs no), ECOG PS (0/1 vs 2), comorbidities (ACE-27: 0/1 vs 2/3), study site, planned use of early docetaxel (yes vs no)



*Bicalutamide, nilutamide, or flutamide.

- Primary endpoint: OS
- Secondary endpoints: PSA PFS (including clinical progression if occurring first), clinical PFS, AEs, HRQoL

Davis. NEJM. 2019;381:121.

ENZAMET: Baseline Characteristics

Characteristic	Enzalutamide (n = 563)	NSAA (n = 562)
Median age, yrs (IQR)	69.2 (63.2-74.5)	69.0 (63.6-74.5)
Australian, n (%)	324 (58)	321 (57)
ECOG PS 0/1/2, %	72/27/1	72/27/1
Planned early docetaxel*, n (%)	254 (45)	249 (44)
Disease volume, n (%) ▪ High ▪ Low	 291 (52) 272 (48)	 297 (53) 265 (47)
ACE-27 score 0/1, n (%)	422 (75)	419 (75)
Treatment for prostate cancer, n (%)		
▪ Planned treatment for SRE	55 (10)	58 (10)
▪ Prior local prostatectomy or radiotherapy	238 (42)	235 (42)
▪ Prior adjuvant ADT	58 (10)	40 (7)
▪ Prior docetaxel	95 (17)	83 (15)

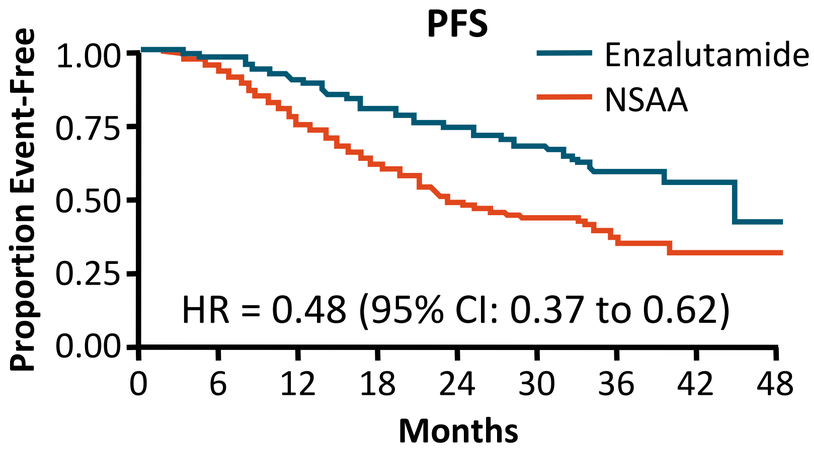
*Early docetaxel: 61% of high volume, 27% of low volume

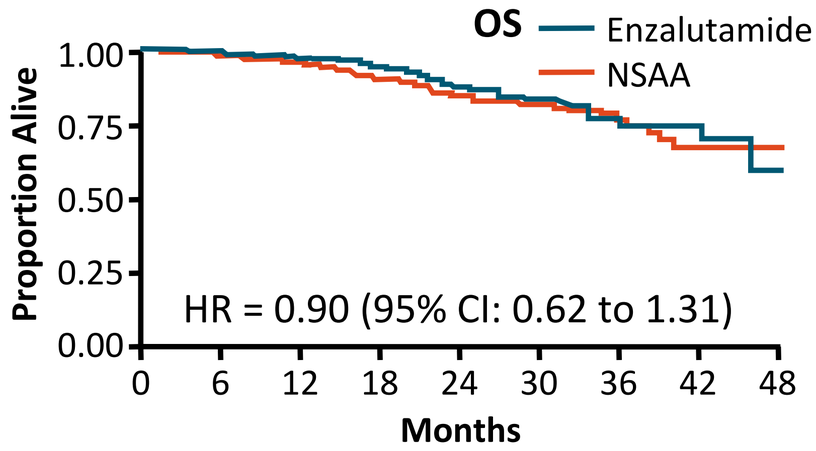
(26% concurrent , 17% prior)

Sweeney. ASCO 2019. Abstr LBA2. Davis. NEJM. 2019;[Epub].

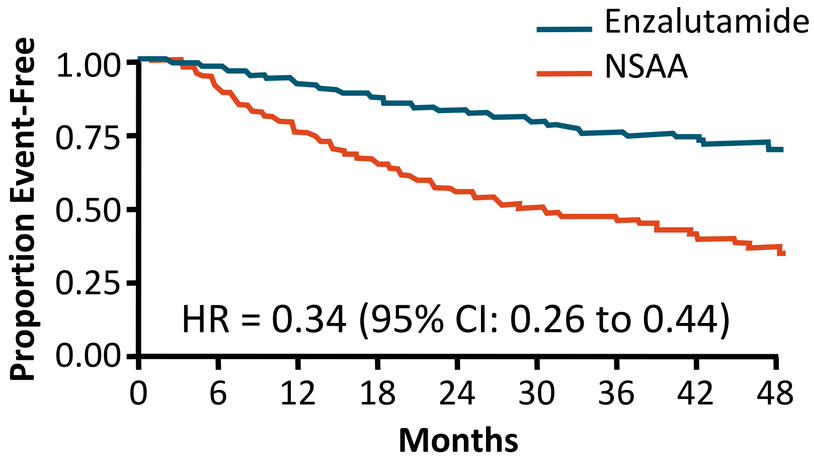
ENZAMET: PFS and OS With Concurrent Docetaxel (45%)

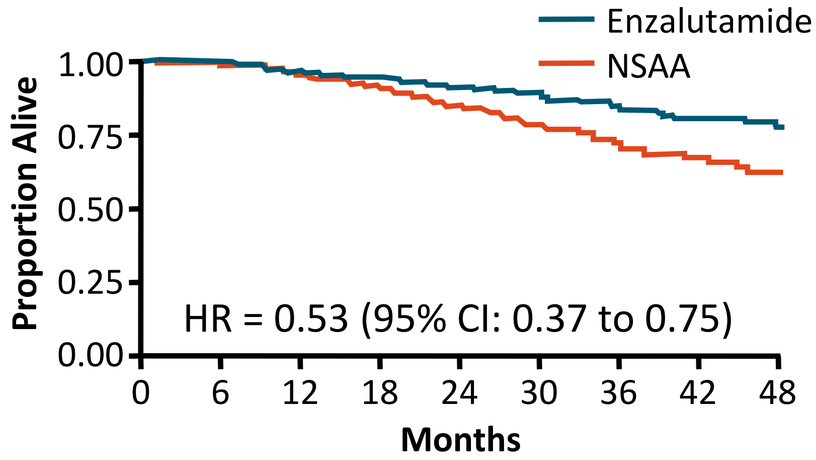
Testosterone Suppression + Docetaxel (n = 503; 71% high volume)





Testosterone Suppression + No Docetaxel (n = 622; 37% high volume)

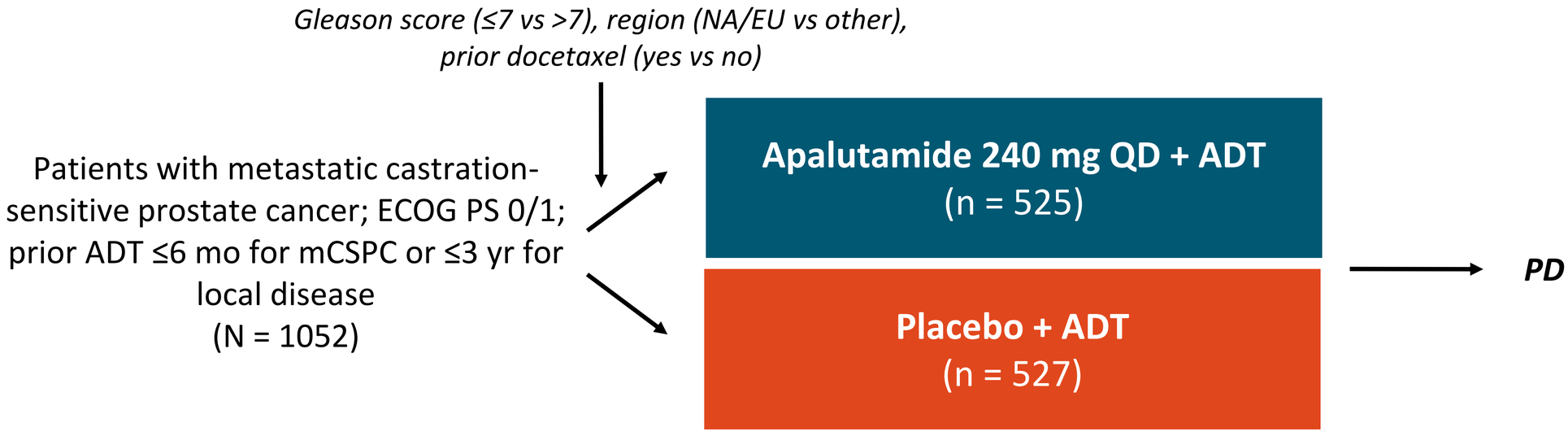




Davis. NEJM. 2019;381:121.

TITAN: Apalutamide + ADT vs Placebo + ADT in mHSPC

- International, randomized, double-blind, placebo-controlled phase III trial

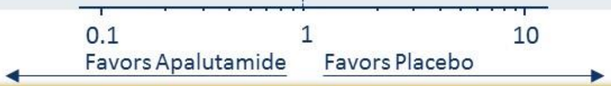


- Primary endpoints: OS, radiographic PFS
- Secondary endpoints: time to pain progression, time to SRE, time to chronic opioid use, time to cytotoxic chemotherapy
- Exploratory endpoints including time to PSA progression, PFS2

Chi. NEJM. 2019;381:13.

TITAN rPFS Benefit Consistent Across Subgroups

Variable		Hazard Ratio (95% CI)	Events (n/n) Apalutamide + ADT	Events (n/n) Placebo + ADT
All patients		0.49 (0.40-0.61)	134/525	231/527
Baseline ECOG PS	0	0.52 (0.39-0.68)	79/328	142/348
	1	0.42 (0.30-0.59)	55/197	89/178
Geographic region	EU/NA	0.43 (0.28-0.66)	32/173	67/173
	Other	0.51 (0.40-0.65)	102/352	164/354
Bone metastasis only at baseline	YES	0.38 (0.27-0.54)	49/289	102/269
	NO	0.60 (0.46-0.80)	85/236	129/258
Visceral disease and bone metastasis at baseline	YES	0.71 (0.43-1.18)	25/56	38/72
	NO	0.46 (0.37-0.59)	109/469	193/455
Prior docetaxel use	YES	0.47 (0.22-1.01)	10/58	19/55
	NO	0.49 (0.39-0.62)	124/467	212/472
Age, yr	< 65	0.45 (0.31-0.66)	40/149	85/182
	65-74	0.47 (0.34-0.64)	61/243	105/232
	≥ 75	0.65 (0.41-1.03)	33/133	41/113
Disease volume	High	0.53 (0.41-0.67)	109/325	173/335
	Low	0.36 (0.22-0.57)	25/200	58/192
Metastasis stage at initial diagnosis	M0	0.41 (0.22-0.78)	17/85	23/59
	M1	0.49 (0.39-0.63)	108/411	196/441



TITAN: OS by Subgroups (11% recibieron docetaxel previo)

Variable		HR (95% CI)	Events, n/N: Apalutamide + ADT	Events, n/N: Placebo + ADT
All patients		0.68 (0.51-0.90)	83/525	117/527
Baseline ECOG PS	0	0.71 (0.47-1.05)	41/328	60/348
	1	0.59 (0.40-0.89)	42/197	57/178
Geographic region	EU/NA	0.71 (0.40-1.25)	21/173	29/173
	Other	0.66 (0.48-0.91)	62/352	88/354
Bone metastasis only at baseline	Yes	0.47 (0.30-0.75)	28/289	53/269
	No	0.88 (0.61-1.26)	55/236	64/258
Visceral disease and bone metastasis at baseline	Yes	0.99 (0.55-1.77)	20/56	25/72
	No	0.63 (0.46-0.87)	63/469	92/455
Prior docetaxel use	**Yes**	1.27 (0.52-3.09)	11/58	9/55
	No	0.63 (0.47-0.85)	72/467	108/472
Age, yrs.	< 65	0.56 (0.33-0.94)	21/149	43/182
	65-74	0.73 (0.48-1.10)	42/243	51/232
	≥ 75	0.74 (0.41-1.35)	20/133	23/113
Disease volume	High	0.68 (0.50-0.92)	79/325	97/335
	Low	0.67 (0.34-1.32)	14/200	20/192
Metastasis stage at initial diagnosis	M0	0.40 (0.15-1.03)	7/85	11/59
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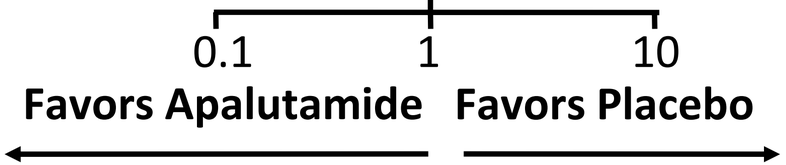

Chi. ASCO 2019. Abstr 5006. Chi. NEJM. 2019;[Epub].

RESUMEN: TTO SECUENCIAL.

- Los ensayos fundamentales de fase III ARCHES, ENZAMET y TITAN se diseñaron para evaluar el impacto de la adición de ENZA o APA a la ADT para el tratamiento de primera línea del mHSPC.
- En estos ensayos hubo pacientes que recibieron triple terapia secuencial o (concurrente en el caso del ENZAMET), ya que se permitió el tratamiento previo con DOCE antes de la aleatorización a ARPI o placebo.
- Sin embargo, ninguno de estos análisis secundarios de terapia triple mostró una mejora en la SG, probablemente debido al bajo número de pacientes dentro de estos subgrupos.

https://www.esmoopen.com/article/S2059-7029(23)00416-7/fulltext

TRIPLETES: CONCURRENTE

TABLE 1. BASELINE CHARACTERISTICS OF THE INCLUDED TRIALS

Study	Treatment arms		Total participants	Median age (years)	Volume of disease (%)		Metastatic Presentation (%)		Docetaxel
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ARASENS 2022	Darolutamide + Docetaxel + ADT	Docetaxel + ADT	1305	Rx: 67; Control: 67	77	23	86	13	Yes (Concurrent 100%)

https://www.urotoday.com/conference-highlights/asco-gu-2023/asco-gu-2023-prostate-cancer.html

Phase III ARASENS Trial: Darolutamide in mCSPC

- Global, randomized, double-blind, placebo-controlled phase III trial

Stratified by metastasis stage (M1a vs M1b vs M1c), alkaline phosphatase level (< vs ≥ ULN)

Patients with newly diagnosed mCSPC who are candidates for ADT and docetaxel; no previous ADT ≥12 wk before randomization; no ARPIs, CT, or IO for PC; ECOG PS 0/1 (N = 1306)

Darolutamide 600 mg PO BID + **ADT** + **Docetaxel** 75 mg/m^2 on D1 x six 21-day cycles* (n = 651)

Placebo PO BID + **ADT** + **Docetaxel** 75 mg/m^2 on D1 x six 21-day cycles* (n = 655)

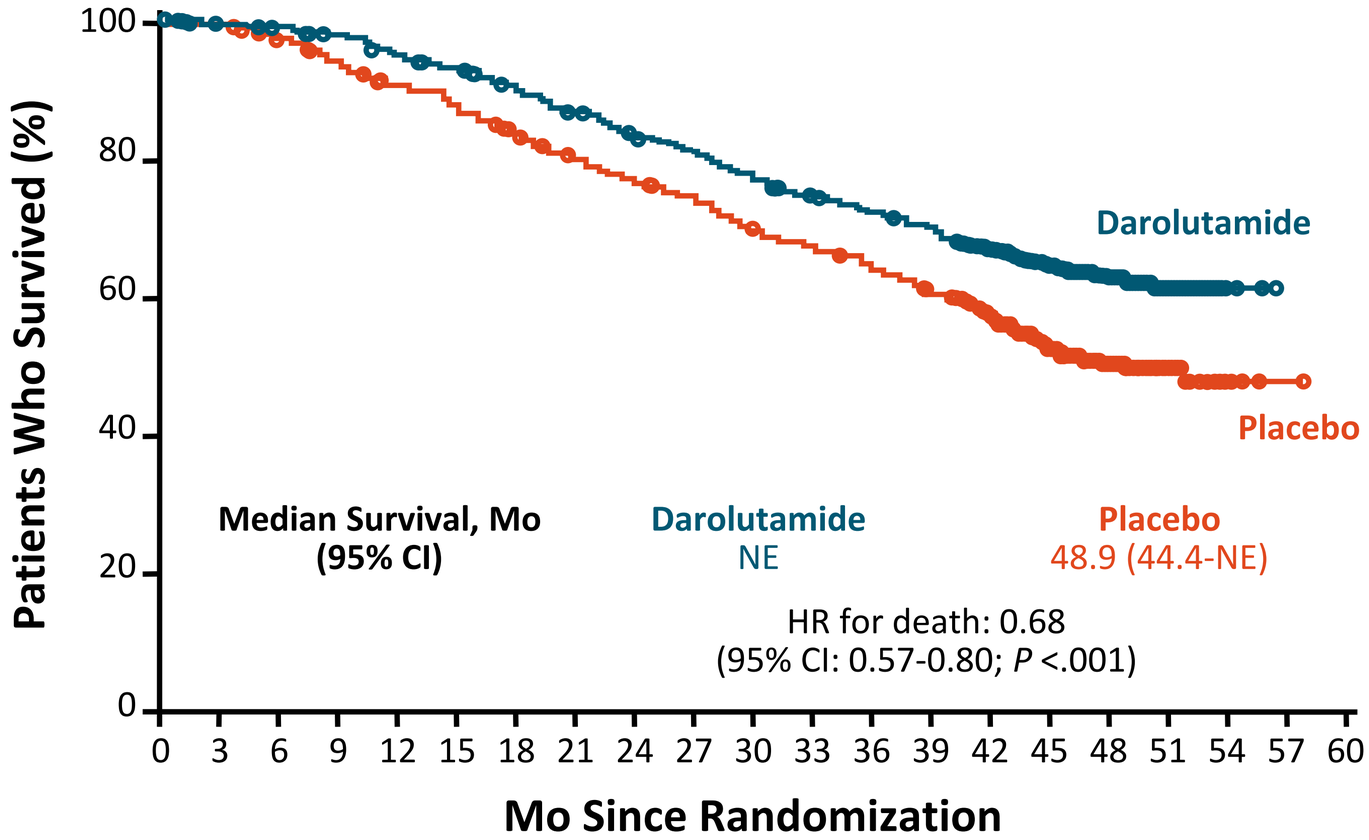
Until symptomatic PD, change in neoplastic tx, unacceptable toxicity, patient/physician decision, or nonadherence

*With prednisone or prednisolone at investigator's discretion. Recommended premedication with oral dexamethasone 8 mg at 12 hr, 3 hr, and 1 hr before docetaxel infusion.

- **Primary endpoint:** OS
- **Secondary endpoints tested hierarchically in this order:** time to CRPC, time to pain progression, SSE-free survival, time to first SSE, time to initiation of subsequent anticancer therapy, time to worsening of physical symptoms, time to first opioid use for ≥7 consecutive days, safety

Smith. NEJM. 2022;386:1132.

ARASENS: OS (Primary Endpoint)



Patients at Risk, n

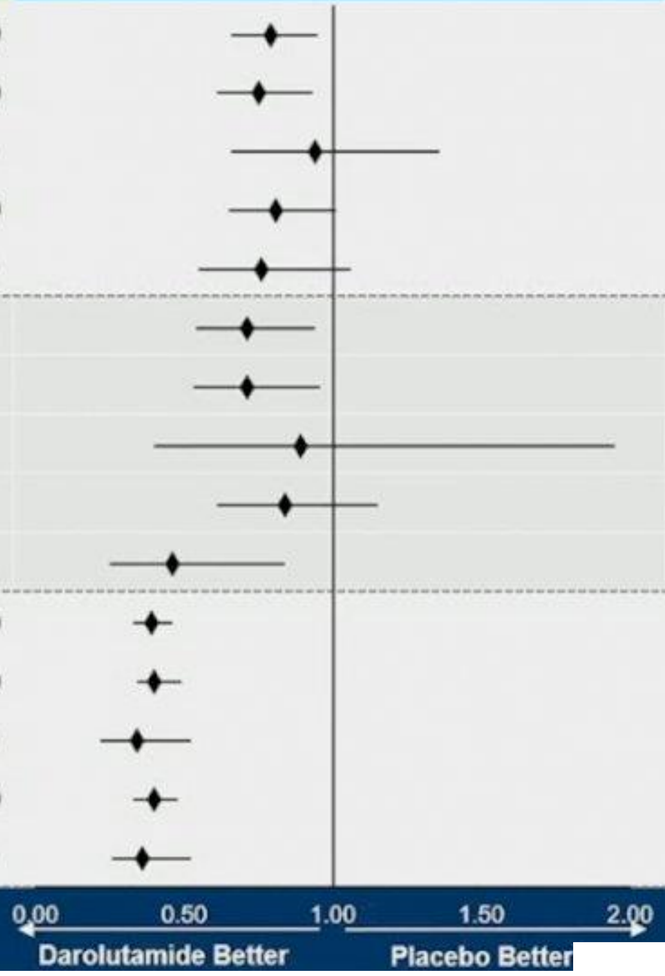
Darolutamide	651	645	637	627	608	593	570	548	525	509	486	468	452	436	402	267	139	56	9	0	0
Placebo	654	646	630	607	580	565	535	510	488	470	441	424	402	383	340	218	107	37	6	1	0

- Addition of darolutamide to ADT + docetaxel significantly reduced risk of death by 32.5% vs placebo (*P* <.001)
  - 75.6% of patients on placebo arm received subsequent life-prolonging systemic tx
- OS benefit observed across most subgroups
  - HR (95%) for those stratified by metastatic stage at initial dx: M1, 0.707 (0.590-0.848); M0, 0.605 (0.348-1.052)

Smith. NEJM. 2022;386:1132.

Secondary endpoints

Secondary endpoint	Patient subgroups	Number of events/ Number of patients		Median (95% CI), months		HR (95% CI)[a]
		DARO	PBO	DARO	PBO	
Time to pain progression	All patients[b]	222/651	248/654	NE (30.5–NE)	27.5 (22.0–36.1)	0.79 (0.66–0.95)
	High volume	161/497	192/508	NE (26.7–NE)	24.4 (16.8–33.3)	0.75 (0.61–0.93)
	Low volume	61/154	56/146	46.1 (25.0–NE)	39.5 (24.6–NE)	0.94 (0.66–1.36)
	High risk	155/452	173/460	35.4 (25.0–NE)	25.0 (18.2–35.9)	0.81 (0.65–1.01)
	Low risk	67/199	75/194	NE (39.2–NE)	28.8 (19.3–NE)	0.76 (0.55–1.06)
Time to first symptomatic skeletal event	All patients[b]	95/651	108/654	NE (NE–NE)	NE (NE–NE)	0.71 (0.54–0.94)
	High volume	82/497	96/508	NE (NE–NE)	NE (NE–NE)	0.71 (0.53–0.96)
	Low volume	13/154	12/146	NE (NE–NE)	NE (NE–NE)	0.89 (0.40–1.95)
	High risk	78/452	79/460	NE (NE–NE)	NE (NE–NE)	0.84 (0.61–1.15)
	Low risk	17/199	29/194	NE (51.2–NE)	NE (NE–NE)	0.46 (0.25–0.84)
Time to initiation of subsequent systemic antineoplastic therapy	All patients[b]	219/651	395/654	NE (NE–NE)	25.3 (23.1–28.8)	0.39 (0.33–0.46)
	High volume	187/497	324/508	NE (49.6–NE)	22.7 (19.6–25.1)	0.40 (0.34–0.49)
	Low volume	32/154	71/146	NE (NE–NE)	42.5 (34.0–NE)	0.34 (0.22–0.52)
	High risk	173/452	299/460	NE (49.6–NE)	21.3 (19.2–24.0)	0.40 (0.33–0.48)
	Low risk	46/199	96/194	NE (NE–NE)	39.0 (31.8–NE)	0.36 (0.26–0.52)



[a]Based on unstratified Cox regression model.
[b]Includes all randomized patients according to planned treatment.

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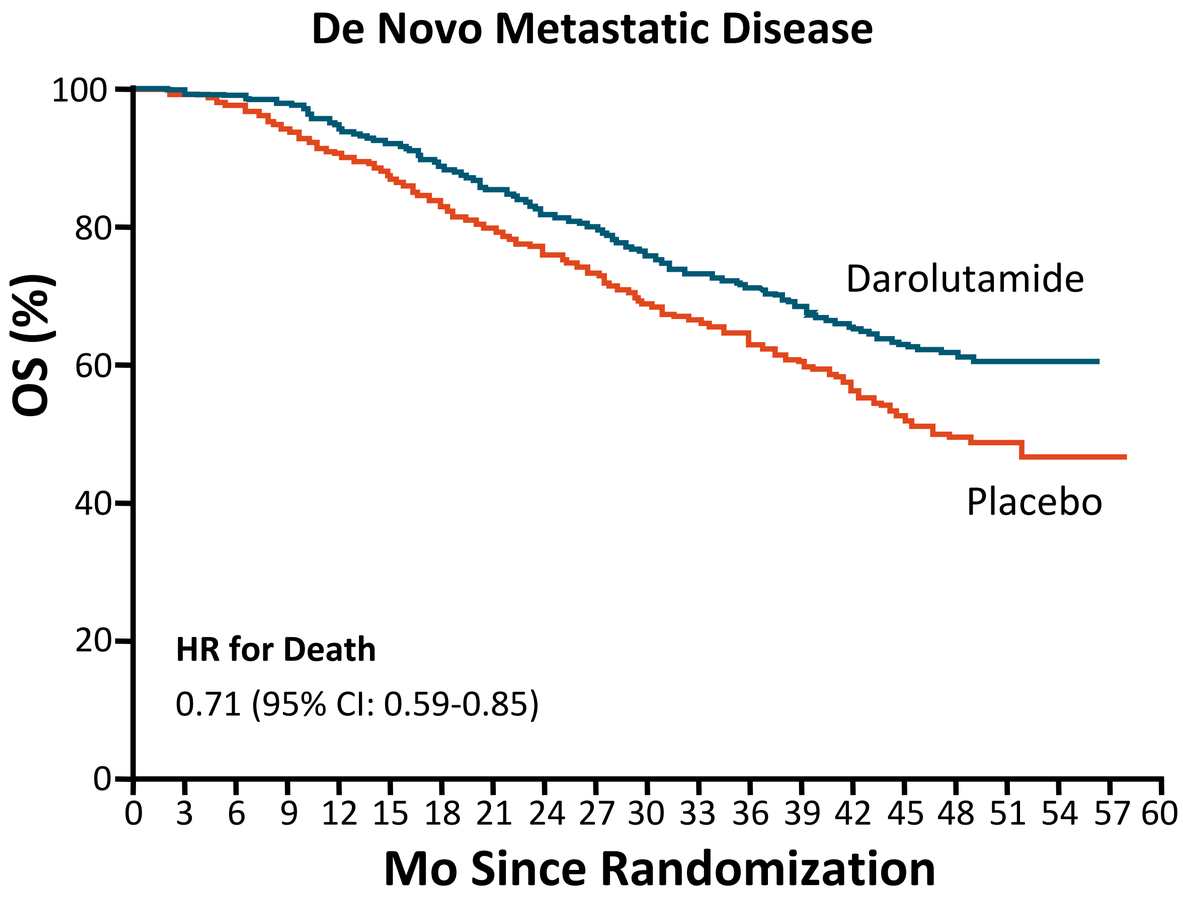
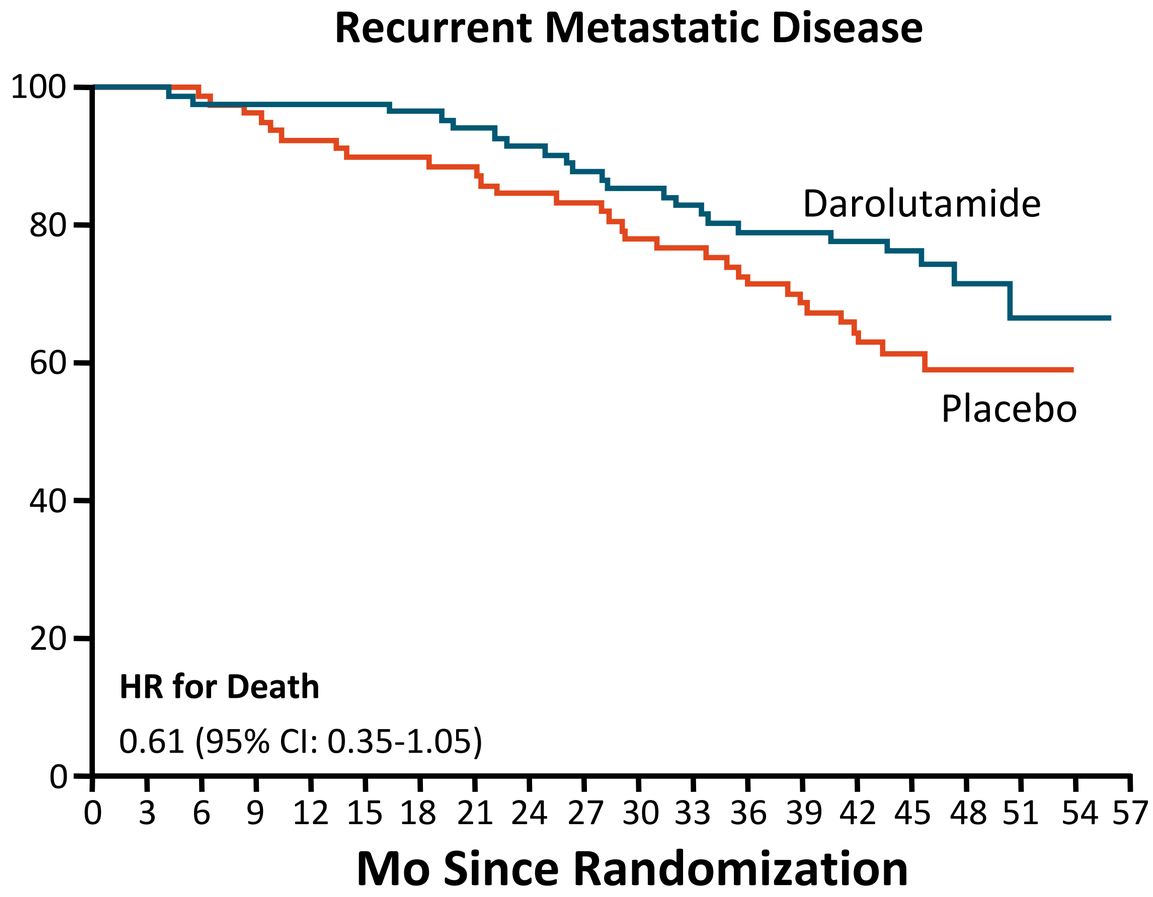
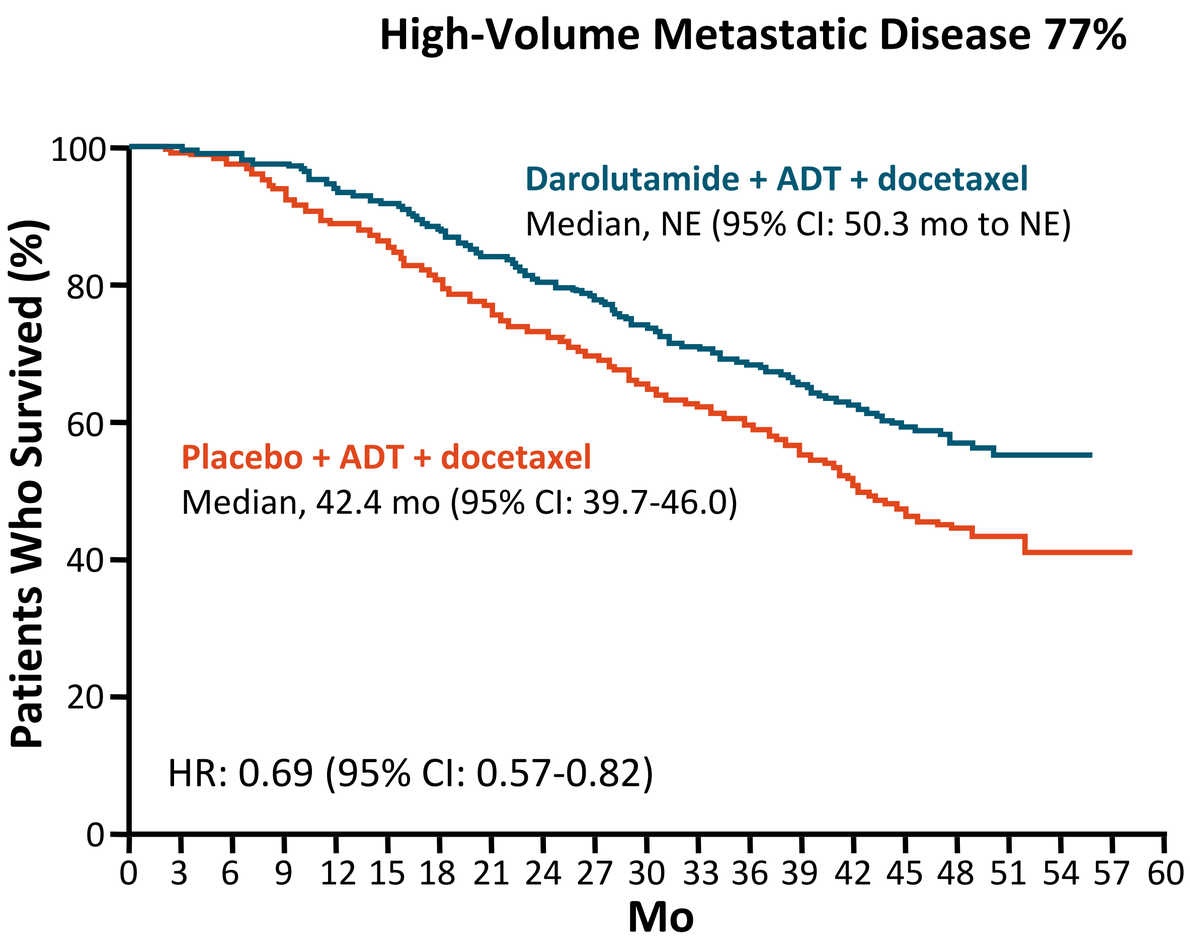
ARASENS: Overall Survival by Metastatic Stage at Diagnosis

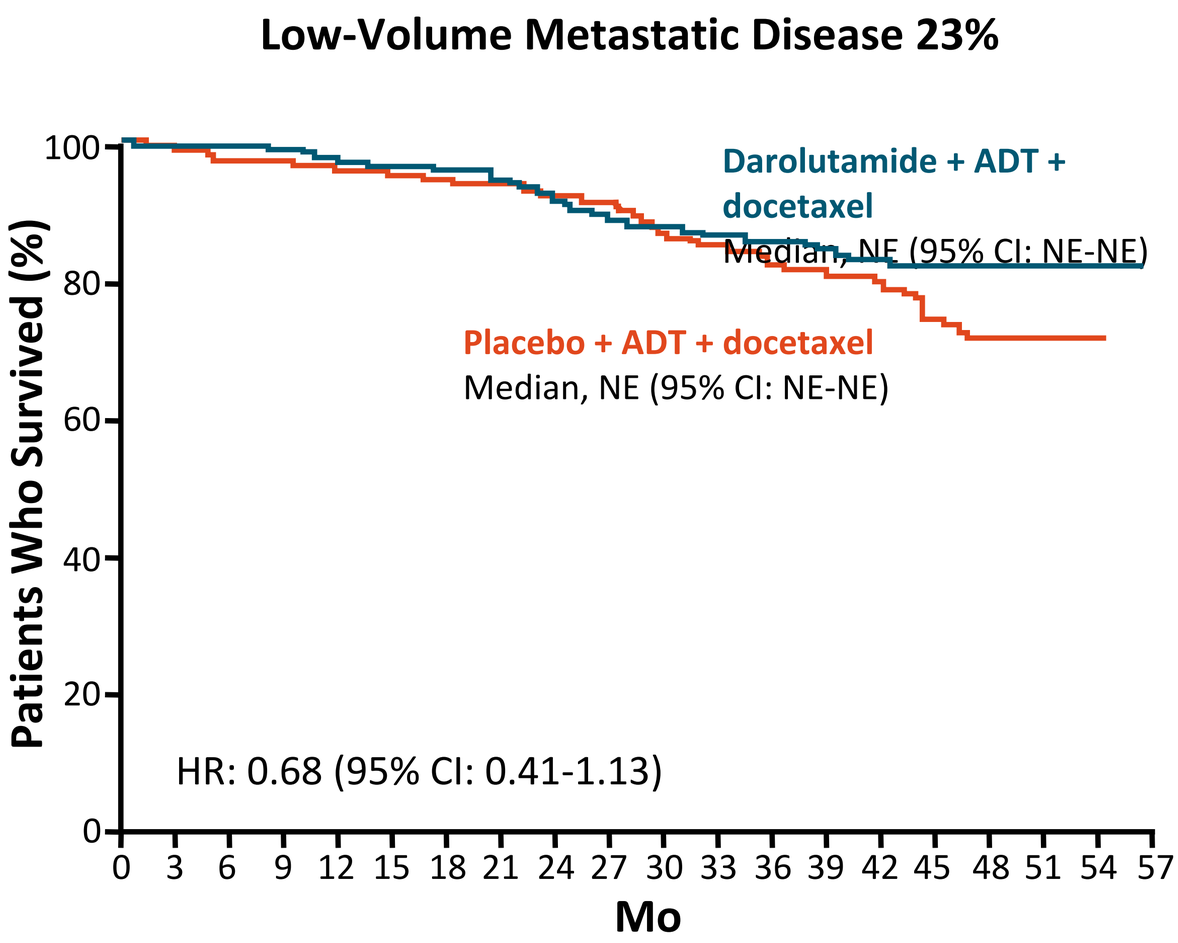




Smith. NEJM. 2022;386:1132.

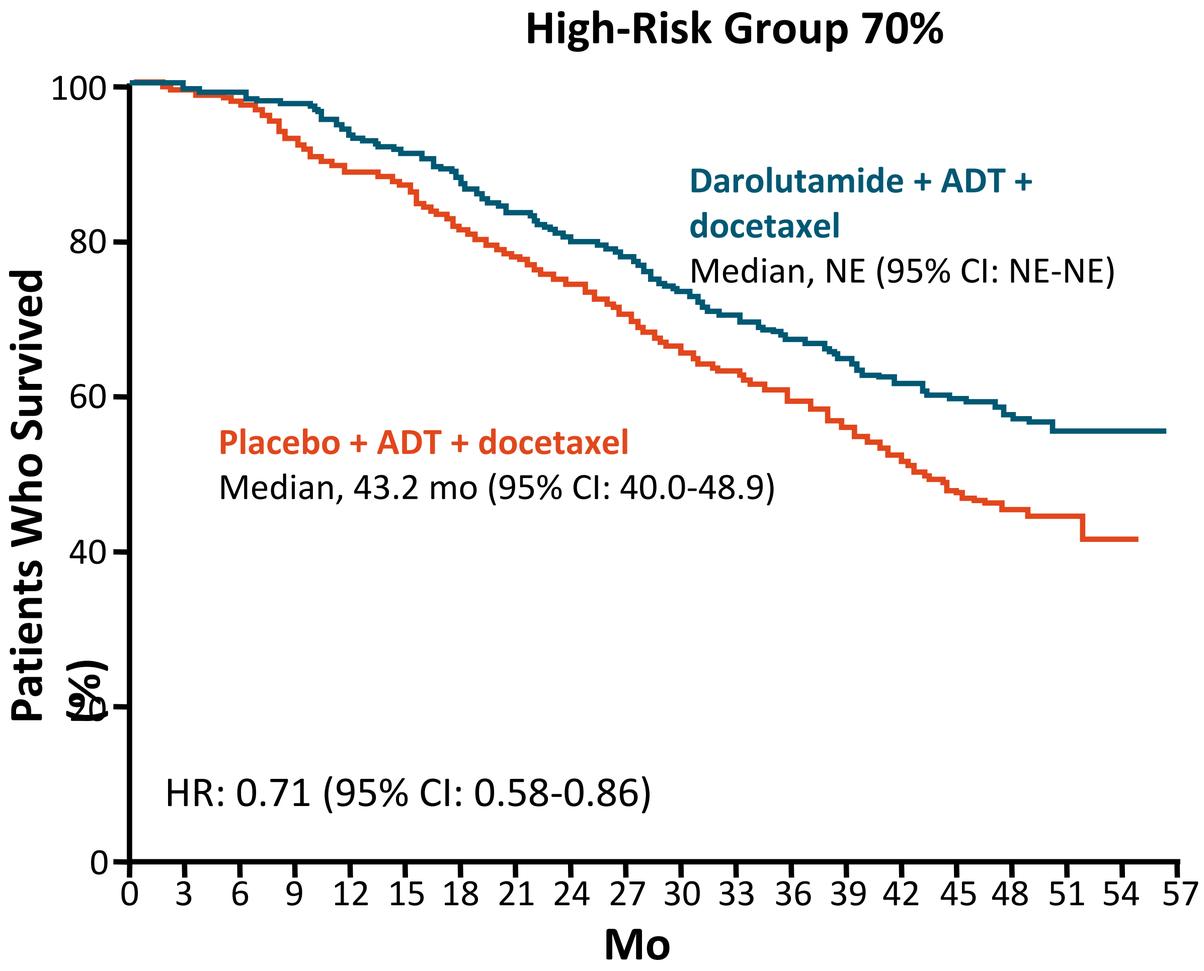
ARASENS: Overall Survival by Disease Volume

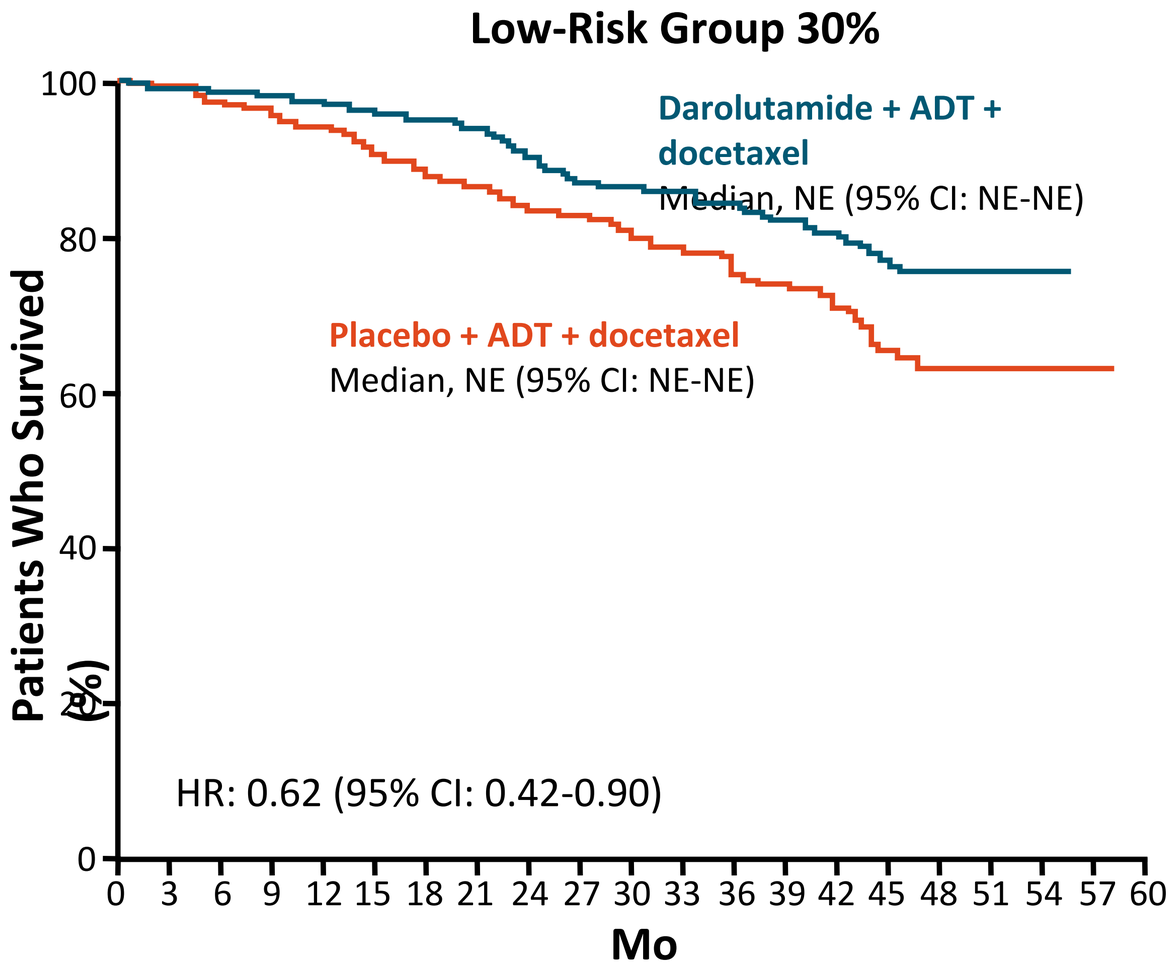




Hussain. JCO. 2023;[Epub].

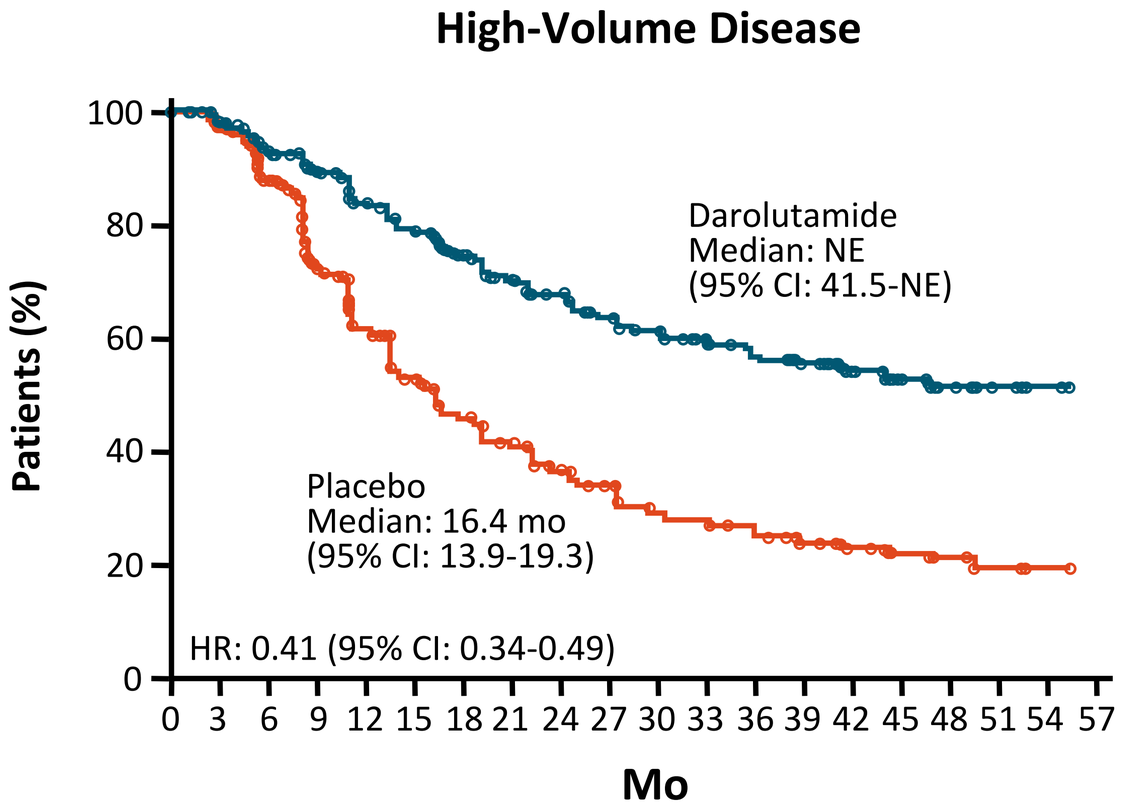
ARASENS: Overall Survival by Risk Group

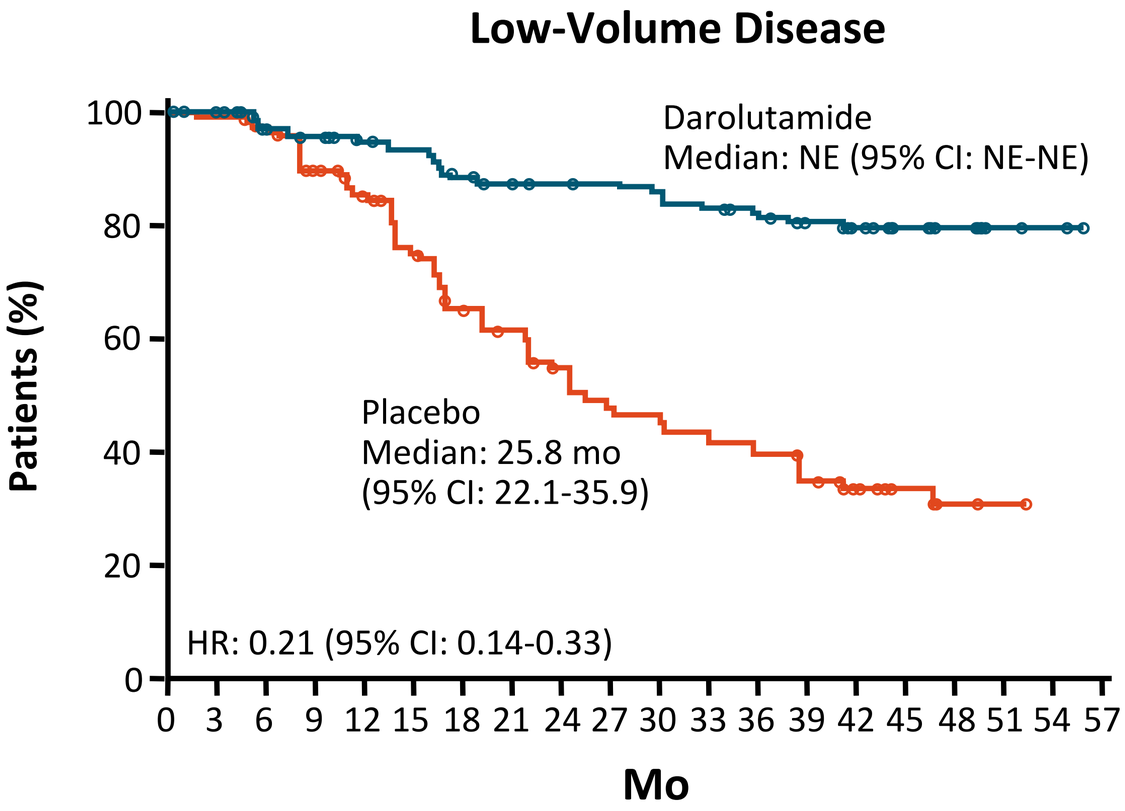




Hussain. JCO. 2023;[Epub].

ARASENS: Time to CRPC by Disease Volume





Patients at Risk, n

Darolutamide	497	469	428	401	365	337	313	284	266	246	231	220	205	195	147	89	38	13	2	0
Placebo	508	474	408	312	247	202	169	149	128	115	95	89	79	70	52	26	11	3	1	0

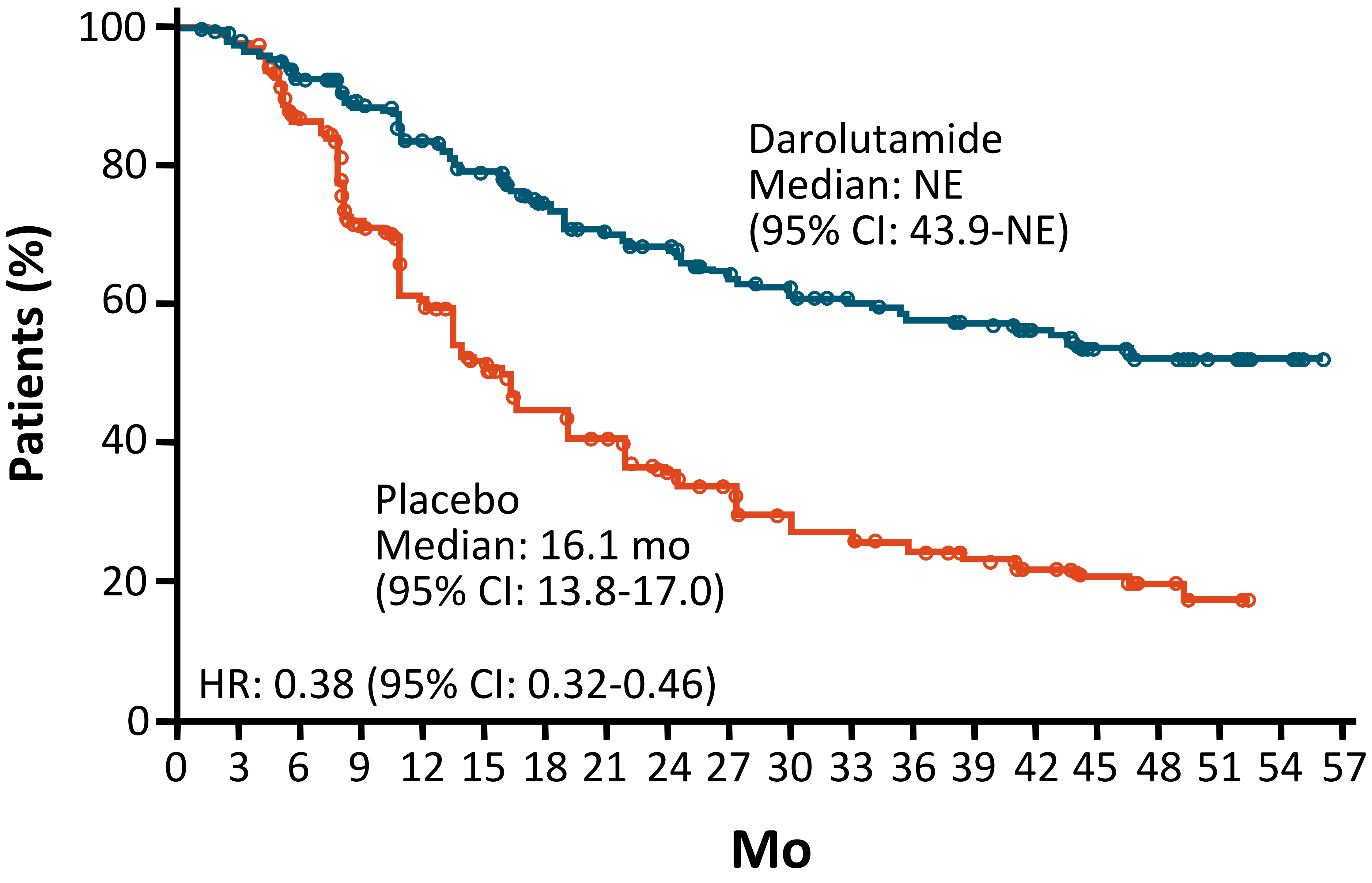
Patients at Risk, n

Darolutamide	154	147	139	136	131	128	120	117	114	112	109	105	103	97	64	43	16	5	3	0
Placebo	146	139	125	113	101	87	73	66	57	50	48	45	41	35	27	12	3	1	0	0

Hussain. JCO. 2023;[Epub]. Hussain. ASCO GU 2023. Abstr 15.

ARASENS: Time to CRPC by Disease Risk

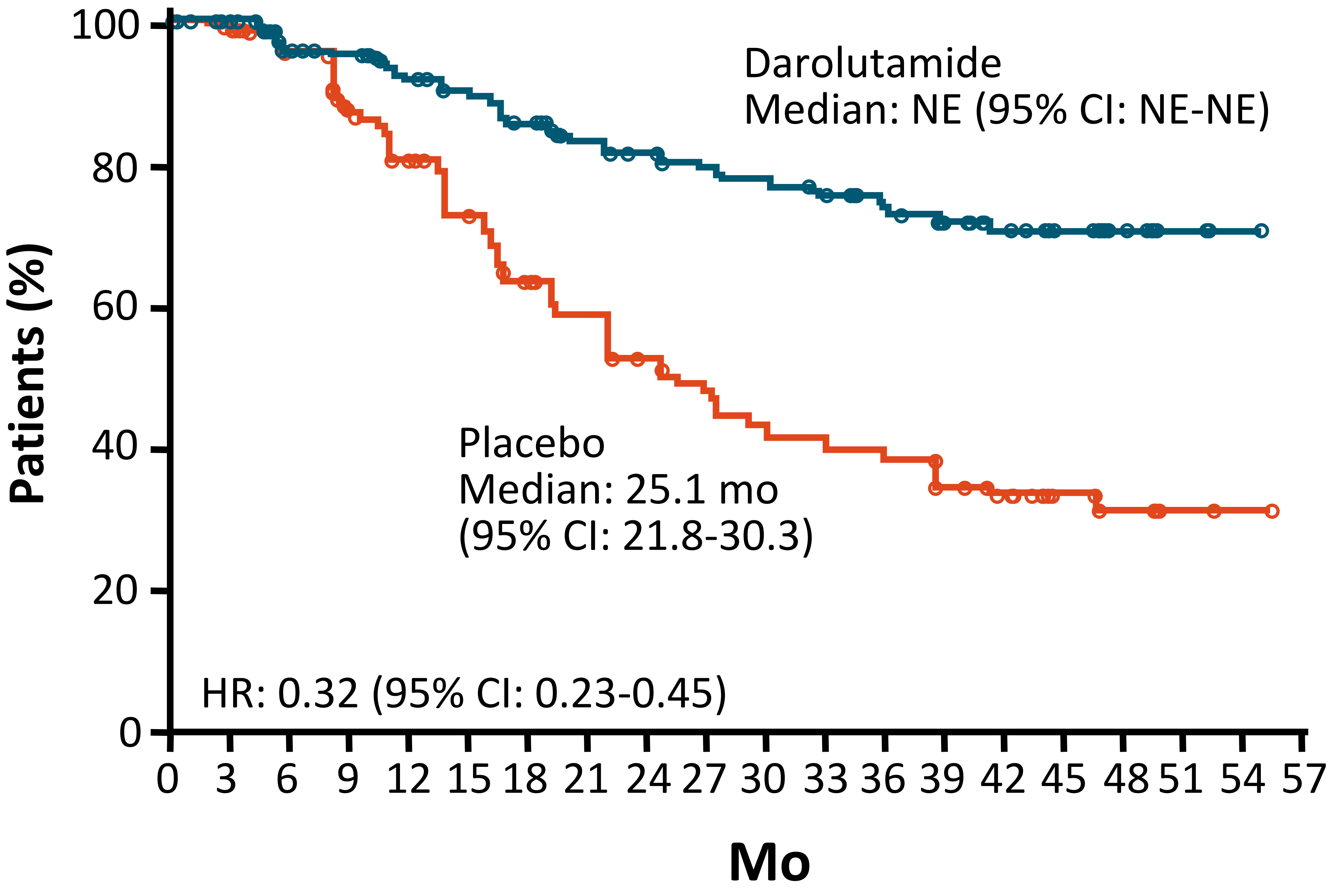
High-Risk Disease



Patients at Risk, n

Darolutamide	452	427	391	363	331	306	284	261	246	229	215	205	192	182	137	85	39	12	3	0
Placebo	460	429	367	283	223	179	147	130	111	98	83	77	67	59	46	22	9	2	0	0

Low-Risk Disease



Patients at Risk, n

Darolutamide	199	189	176	174	165	159	149	140	134	129	125	120	116	110	74	47	15	6	2	0
Placebo	194	184	166	142	125	110	95	85	74	67	60	57	53	46	33	16	5	2	1	0

Hussain. JCO. 2023;[Epub]. Hussain. ASCO GU 2023. Abstr 15.

CONCLUSIONES ARASENS

- En el ensayo ARASENS, 1306 pacientes con mHSPC (86% de los cuales tenían enfermedad metastásica sincrónica *de novo*).

- Redujo el riesgo de muerte en un 32 % (HR 0,68) a pesar de que una alta proporción de pacientes en el grupo de SoC recibieron tratamiento posterior con ARPI tras la progresión a mCRPC (76 %).

  - OS HR in high-volume disease: 0.69 (0.68 in low-volume disease)
  - OS HR in high-risk disease: 0.71 (0.62 in low-risk disease)

- Otros endopoints, como el tiempo transcurrido hasta el mCRPC, la progresión del dolor y los eventos relacionados con el esqueleto, también favorecieron al triplete.

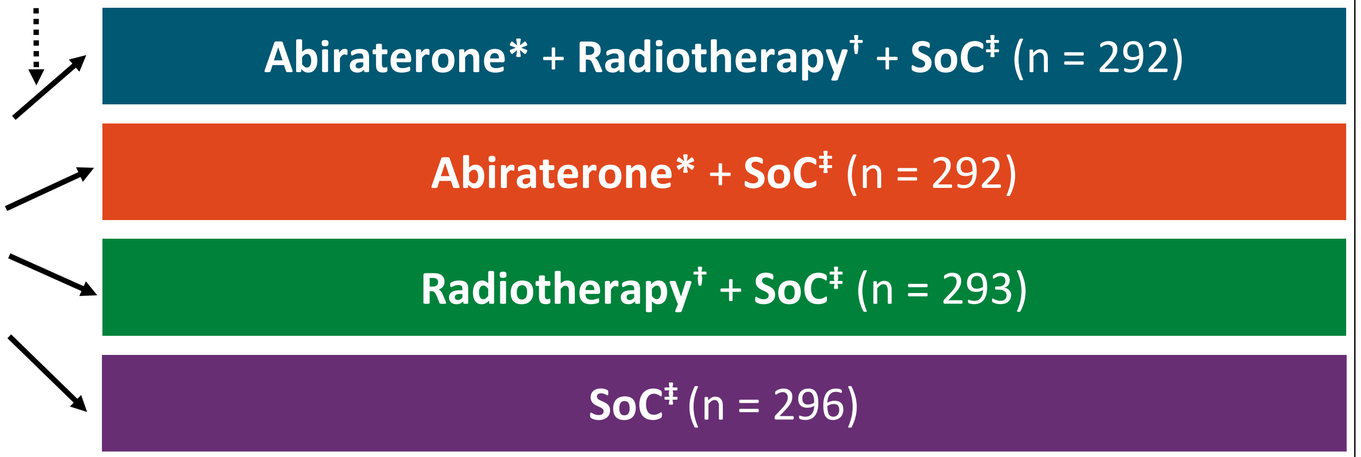
- SG similar para mHSPC
  - sincrónico (HR 0,71; IC 95 % 0,59-0,85)
  - metacrónico (HR 0,61; IC 95 % 0,35-1,05)

PEACE-1: Study Design

- Multicenter, randomized, open-label phase III trial[1,2]

Stratified by ECOG PS (0 vs 1/2), metastatic site (LN vs bone vs visceral), type of castration (surgical vs LHRH agonist), docetaxel (yes vs no)

Patients with de novo mCSPC; distant mets by ≥1 lesion on bone scan and/or CT scan; ECOG PS 0-2; continuous on-study ADT; ADT for ≤3 mo before enrollment permitted (N = 1173)



Upon reaching CRPC, treatment can include abiraterone if previously received in this trial

*Abiraterone 1000 mg/day + prednisone 5 mg BID until PD or intolerance, concomitant to docetaxel.
†74 Gy in 37 fractions after completion of docetaxel. ‡Continuous ADT ± docetaxel 75 mg/m^2 Q3W x 6 cycles.

- **Coprimary endpoints:** rPFS and OS with 2x2 factorial design and hierarchical testing[1]
- **Key secondary endpoints:** castration resistance–free survival, time to next SRE, PSA response rate, time to pain progression, QoL, safety[1]

1. Fizazi. ASCO 2021. Abstr 5000. 2. Fizazi. ESMO 2021. Abstr LBA5.

PEACE-1: Baseline Characteristics (61% de docetaxel)

Characteristic	Abiraterone + SoC (± RT)(n = 583)	SoC +-/ RT (n = 589)
Median age, yr (IQR)	67 (61-72)	66 (59-72)
ECOG PS 0, %	71	70
Gleason score >7 at diagnosis, %	75	77
Median time from diagnosis, mo (IQR)	2.3 (1.6-3.2)	2.3 (1.5-3.1)
Metastatic sites, % ▪ Lymph node only ▪ Bone without visceral ▪ Visceral	 8 81 11	 9 81 11
Disease burden, % ▪ Low ▪ High	 43 57	 43 57
Median baseline PSA, ng/mL (IQR)	14.2 (3.2-62.1)	11.4 (3.1-55.3)
Docetaxel, % ▪ Yes ▪ No	 61 39	 60 40

Fizazi. ASCO 2021. Abstr 5000.

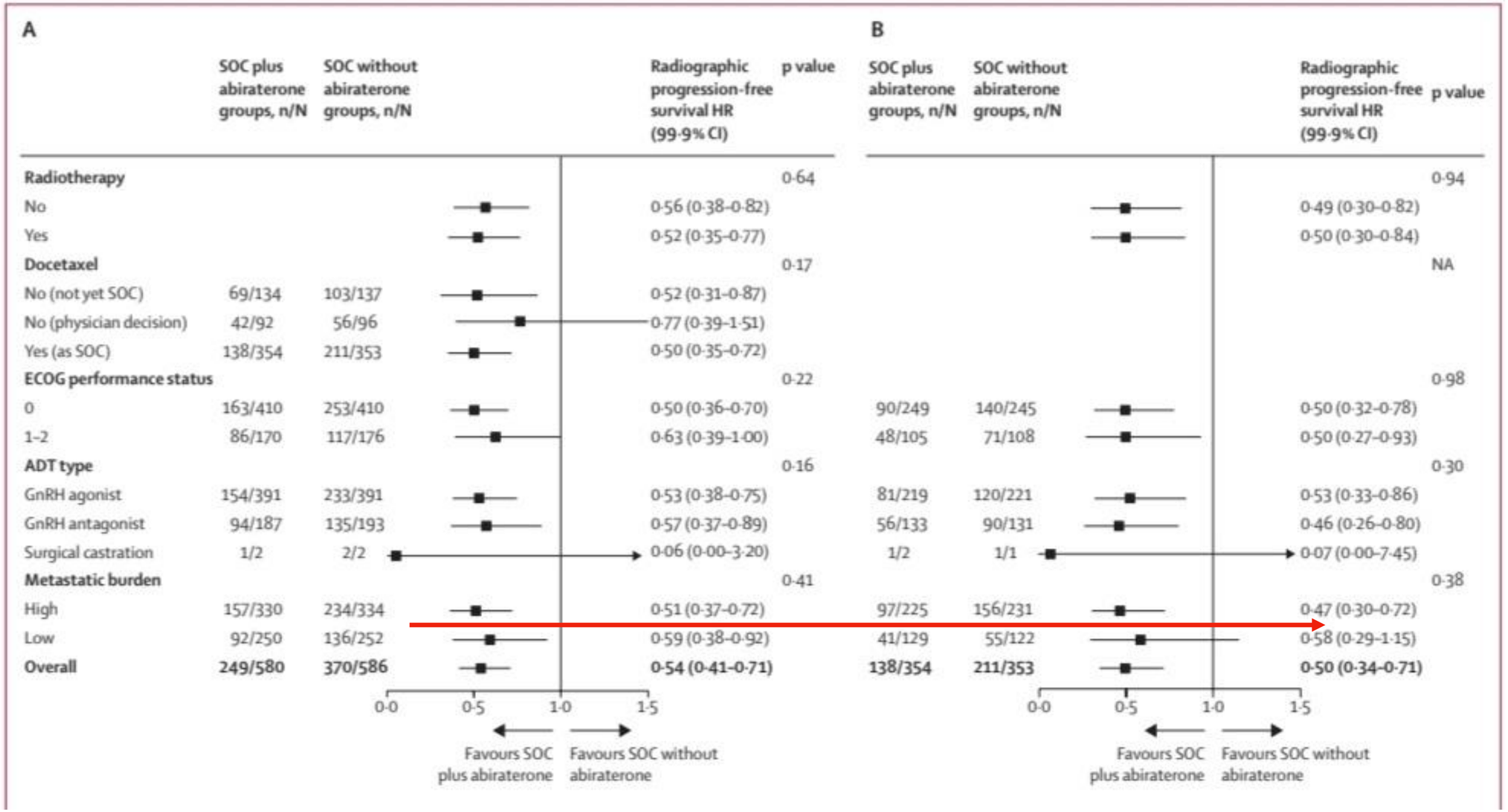
PEACE-1: Radiologic PFS (Coprimary Endpoint)

Outcome	Abiraterone + SoC (± Radiotherapy)	SoC (± Radiotherapy)
rPFS* in overall population	(n = 583)	(n = 589)
▪ Median rPFS, yr (95% CI)	4.5 (3.5-NE)	2.2 (2.0-2.6)
▪ Events	252	371
▪ HR (95% CI)	0.54 (0.46-0.64); P <.0001	
rPFS in ADT + docetaxel population	(n = 355)	(n = 355)
▪ Median rPFS, yr (95% CI)	4.5 (3.1-NE)	2.0 (1.8-2.3)
▪ Events	139	211
▪ HR (95% CI)	0.50 (0.40-0.62); P <.0001	

*rPFS benefit with abiraterone observed across subgroups including patients who had radiotherapy and those with high metastatic burden. No interaction detected between effect of radiotherapy and abiraterone on rPFS (*P* = .64), allowing for arms to be pooled for analysis

Fizazi. ASCO 2021. Abstr 5000.

PEACE-1: rPFS

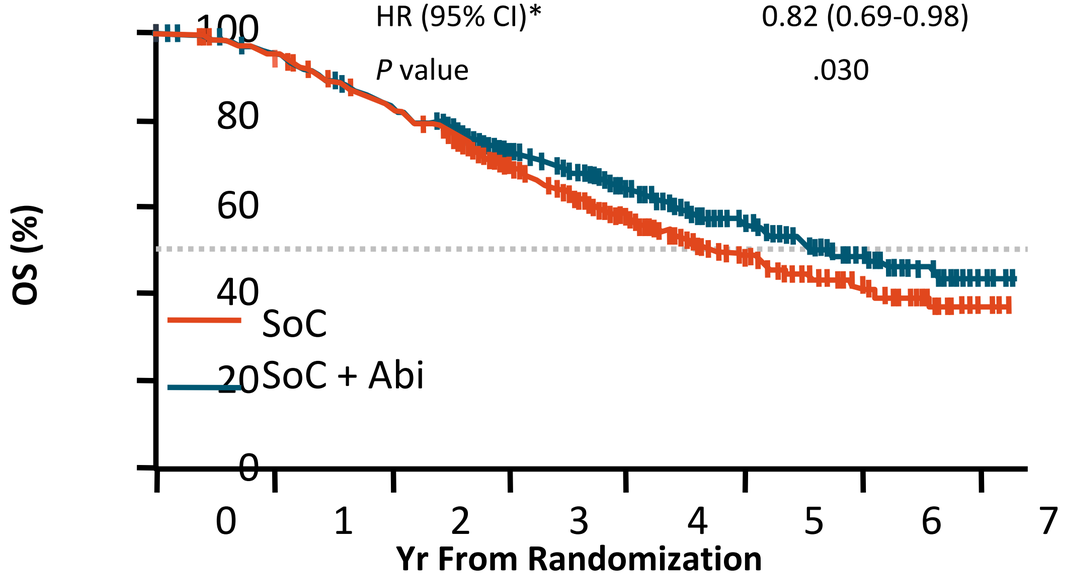


Fizazi. Lancet. 2022;399:1695.

PEACE-1: OS With Addition of Abiraterone to SoC in De Novo mCSPC

Overall Population (de novo mHSPC)

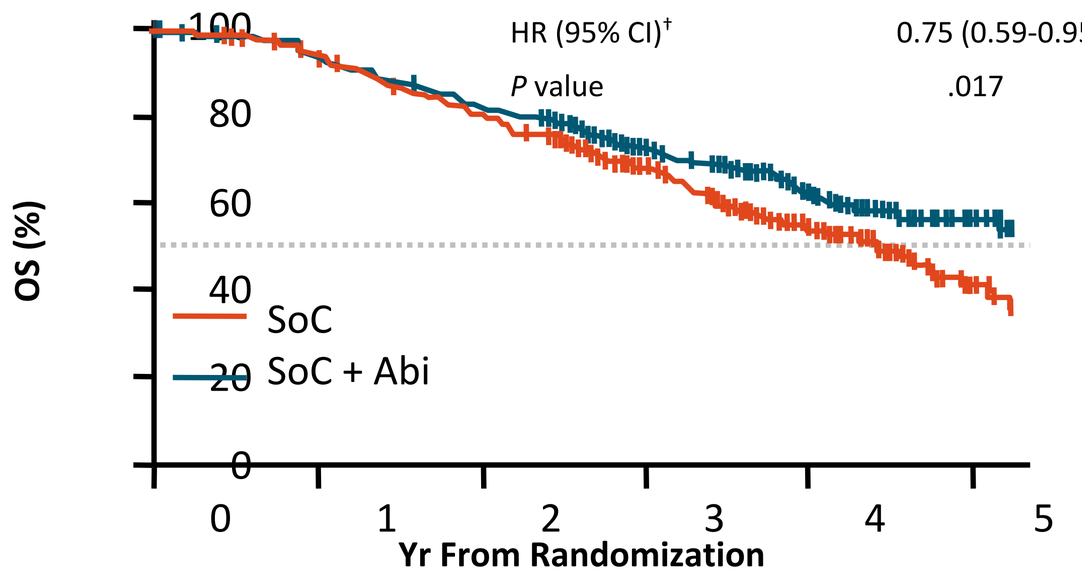
	SoC + Abi (n = 583)	SoC (n = 589)
Median, yr (95% CI)	5.7 (5.1-NE)	4.7 (4.3-5.3)
Events	228	268
HR (95% CI)*	0.82 (0.69-0.98)	
P value	.030	



SoC	589	556	480	334	207	101	37	4
SoC + Abi	583	541	470	340	230	111	47	6

OS With Abiraterone in ADT + Docetaxel Population (± Radiotherapy)

	SoC + Abi (n = 355)	SoC (n = 355)
Median, yr (95% CI)	NE (4.5-NE)	4.4 (3.8-4.9)
Events	121	151
HR (95% CI)†	0.75 (0.59-0.95)	
P value	.017	



SoC	355	329	281	172	78	18
SoC + Abi	355	328	287	183	98	25

*Adjusted on stratification parameters (RT, PS, type of castration, metastatic burden, docetaxel).
†Adjusted on stratification parameters (RT, PS, type of castration, metastatic burden)

Fizazi. ESMO 2021. Abstr LBA5.

PEACE-1: OS

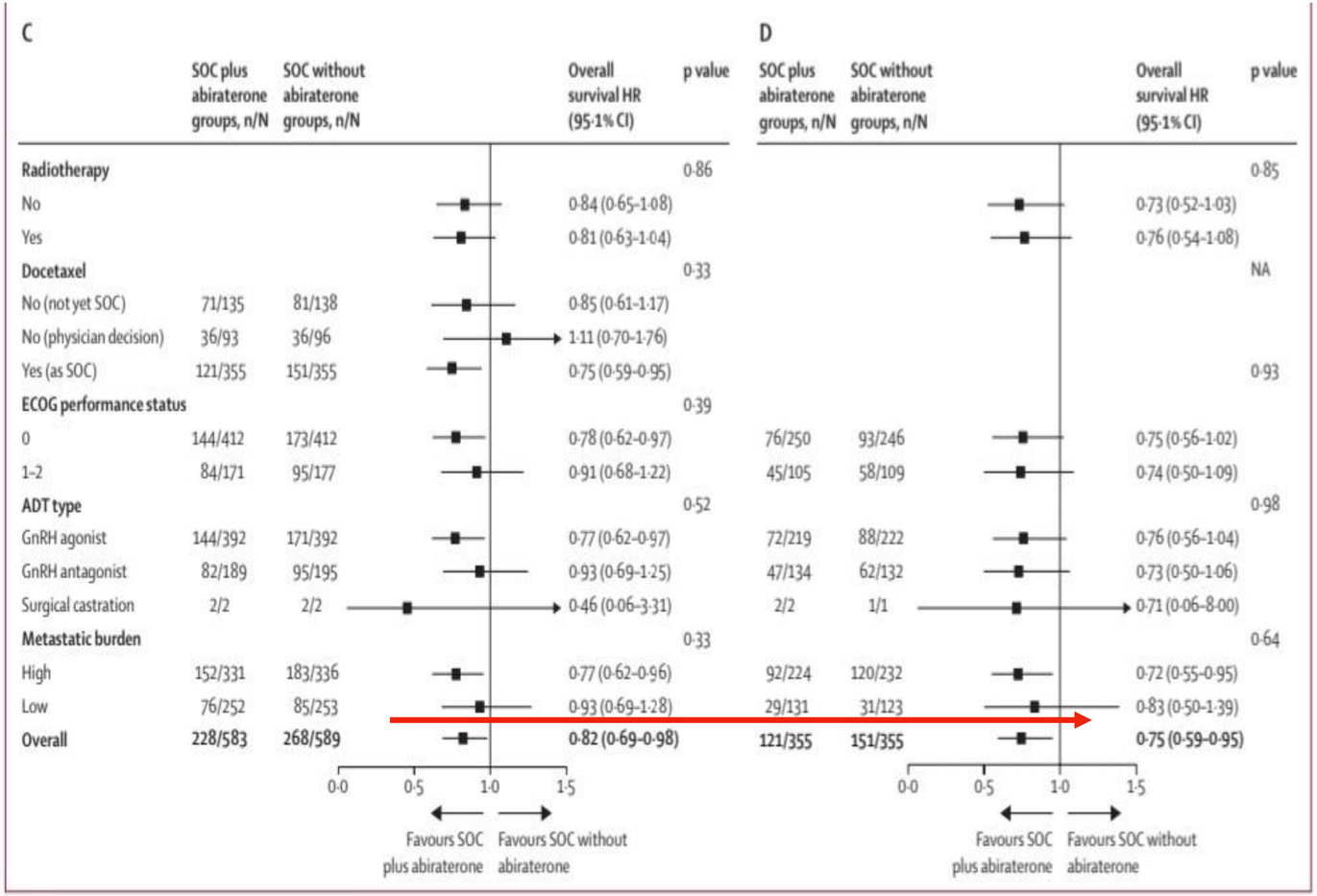


***Figure 3*: HRs for radiographic progression-free survival and overall survival by predefined stratification factors in the overall population and ADT with docetaxel population**

(A) Radiographic progression-free survival in the overall population. (B) Radiographic progression-free survival in the ADT with docetaxel population. (C) Overall survival in the overall population. (D) Overall survival in the ADT with docetaxel population. n/N represents events/patients. The number of events per patients in the radiotherapy subgroup analysis is not presented as the efficacy of radiotherapy is still under investigation. HRs are plotted on a linear scale. At time of the radiographic progression-free survival analysis, metastatic burden data were not available for six patients who were excluded from the Cox model. Overall survival analysis by predefined stratification factors was conducted in the intention-to-treat population. ADT=androgen deprivation therapy. ECOG=Eastern Cooperative Oncology Group. GnRH=gonadotropin releasing hormone. HR=hazard ratio. NA=not applicable. SOC=standard of care (with or without radiotherapy).

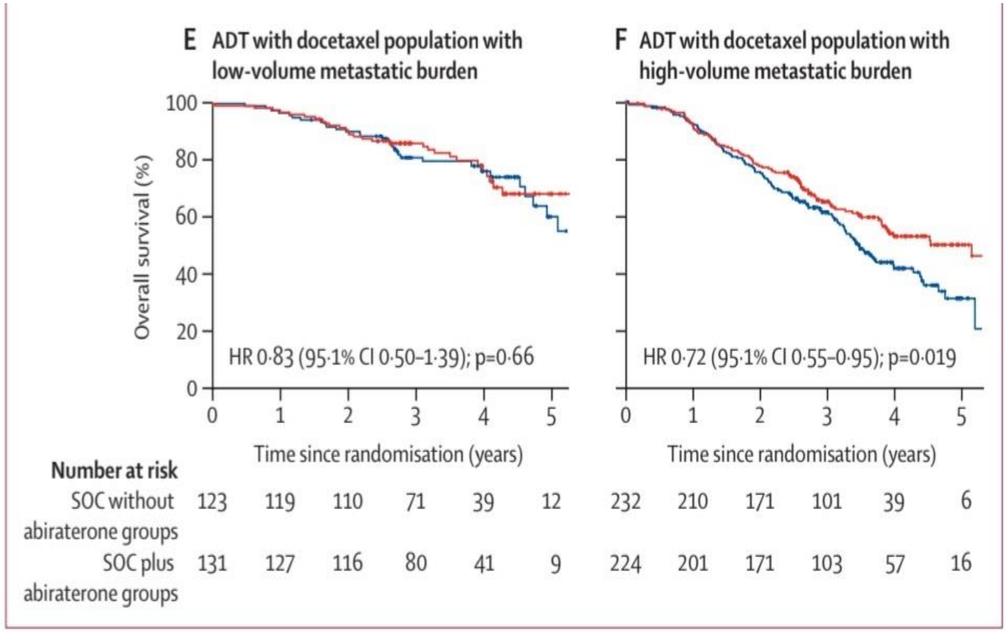


***Figure 2*: Kaplan-Meier estimates of radiographic progression-free survival and overall survival in the overall population and ADT with docetaxel population**

Time-to-event curves are presented for radiographic progression-free survival (A) and overall survival (C) in the overall population, radiographic progression-free survival (B) and overall survival (D) in the ADT with docetaxel population, and overall survival in the ADT with docetaxel population in patients with low-volume metastatic burden (E) and high-volume metastatic burden (F). SOC in the overall population was ADT with or without docetaxel. SOC in the ADT with docetaxel population was ADT with docetaxel. ADT=androgen deprivation therapy. SOC=standard of care (with or without radiotherapy).

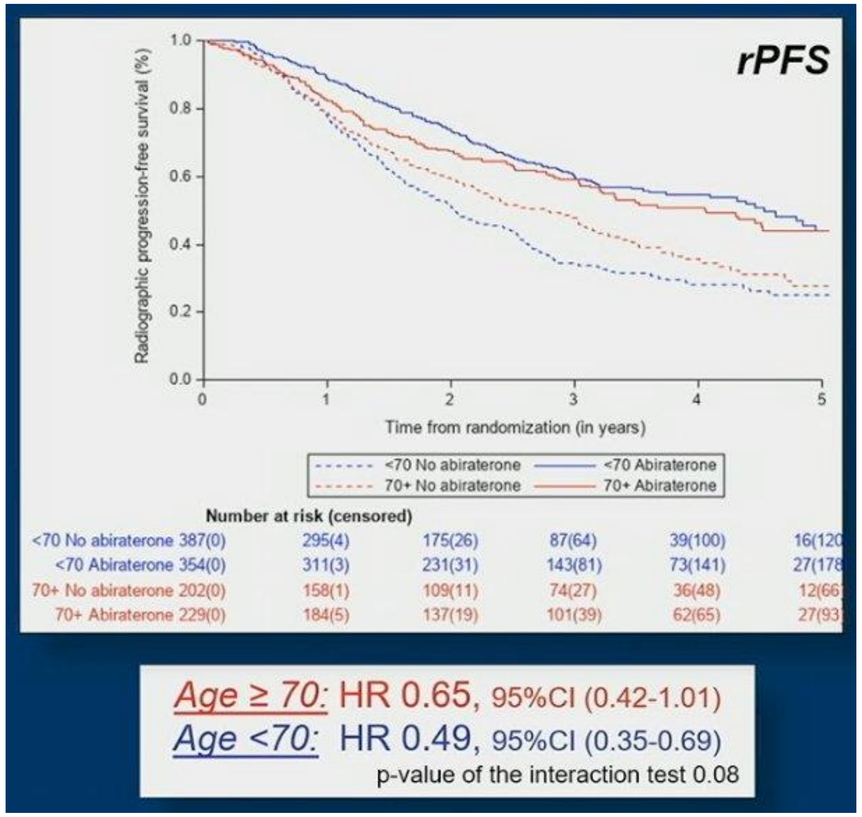
Fizazi. Lancet. 2022;399:1695.

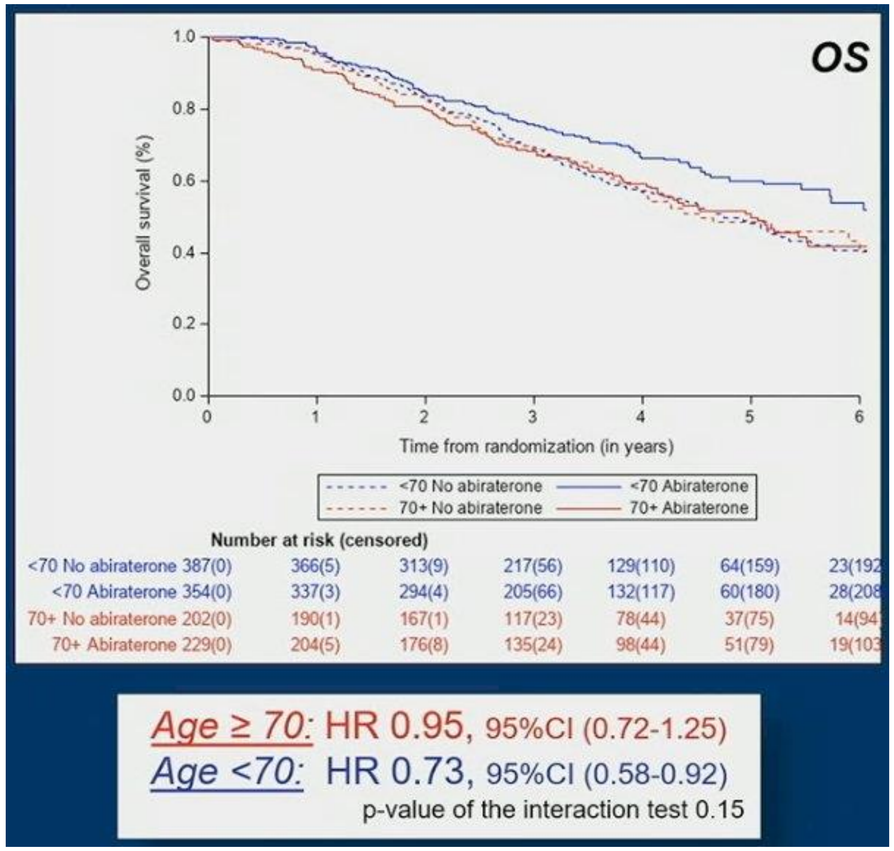
PEACE-1: CRPC-Free Survival

Outcome	Abiraterone + SoC (± Radiotherapy)	SoC (± Radiotherapy)
CRPC-free survival in overall population	(n = 583)	(n = 589)
▪ Median CRPC-free survival, yr (95% CI)	3.8 (3.1-4.5)	1.5 (1.4-1.6)
▪ Events	276	453
▪ HR (95% CI)	0.40 (0.35-0.47); P <.0001	
CRPC-free survival in ADT + docetaxel population	(n = 355)	(n = 355)
▪ Median CRPC-free survival, yr (95% CI)	3.2 (3.0-4.5)	1.4 (1.3-1.6)
▪ Events	156	268
▪ HR (95% CI)	0.38 (0.31-0.47); P <.0001	

Fizazi. ASCO 2021. Abstr 5000.

ASCO GU 2023: Efficacy and Safety of Abiraterone Acetate plus Prednisone and ADT +/- Docetaxel in Older Patients (≥70 Years), with De Novo mCSPC, Compared to Younger Patients (70 Years): The PEACE-1 Trial





- En la población general, los hombres mayores obtienen un beneficio menor, tanto en términos de SLPr como de SG, al agregar AAP al SoC en comparación con los hombres más jóvenes.
- Probable menor beneficio debido a mayor toxicidad que conduce a una interrupción más frecuente y temprana .
- > 70 años fit para ADT + docetaxel, el beneficio de agregar AAP+ al SoC fue comparable al de los hombres más jóvenes.
- >70 años considerados para terapia triple deben de ser seleccionados. (G8 +/- evaluación geriátrica, comorbilidades, polifarmacia)

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CONCLUSIONES PEACE 1

- El triplete redujo en un 25% el riesgo de muerte (HR) 0,75 con una mediana de SG de 4,4 años para los pacientes que recibieron ADT + DOCE (±XRT).
- Beneficio de AAP a ADT + DOCE **Alto Volumen** (HR 0,72)→ ganancia de 1,6 años en la mediana de SG (3,5 frente a 5,1 años).
- El tiempo de transición a mCRPC más largo con el triplete, a pesar de que el 81% de los pacientes tratados con ADT + DOCE recibieron posteriormente ADT + ARPI para mCRPC.
- 61% de pacientes que reciben docetaxel.
- No se incluyeron pacientes con enfermedad de metacrónica.
- En >70 años para triplete deben de ser seleccionados. (G8 +/- evaluación geriátrica, comorbilidades, polifarmacia)

https://www.esmoopen.com/article/S2059-7029(23)00416-7/fulltext

TRIPLETE..¿CÚANDO INTENSIFICAR?

ASCO 2023: The Role of Volume of Disease for Treatment Selection in Patients with mCSPC: A Living Meta-Analysis

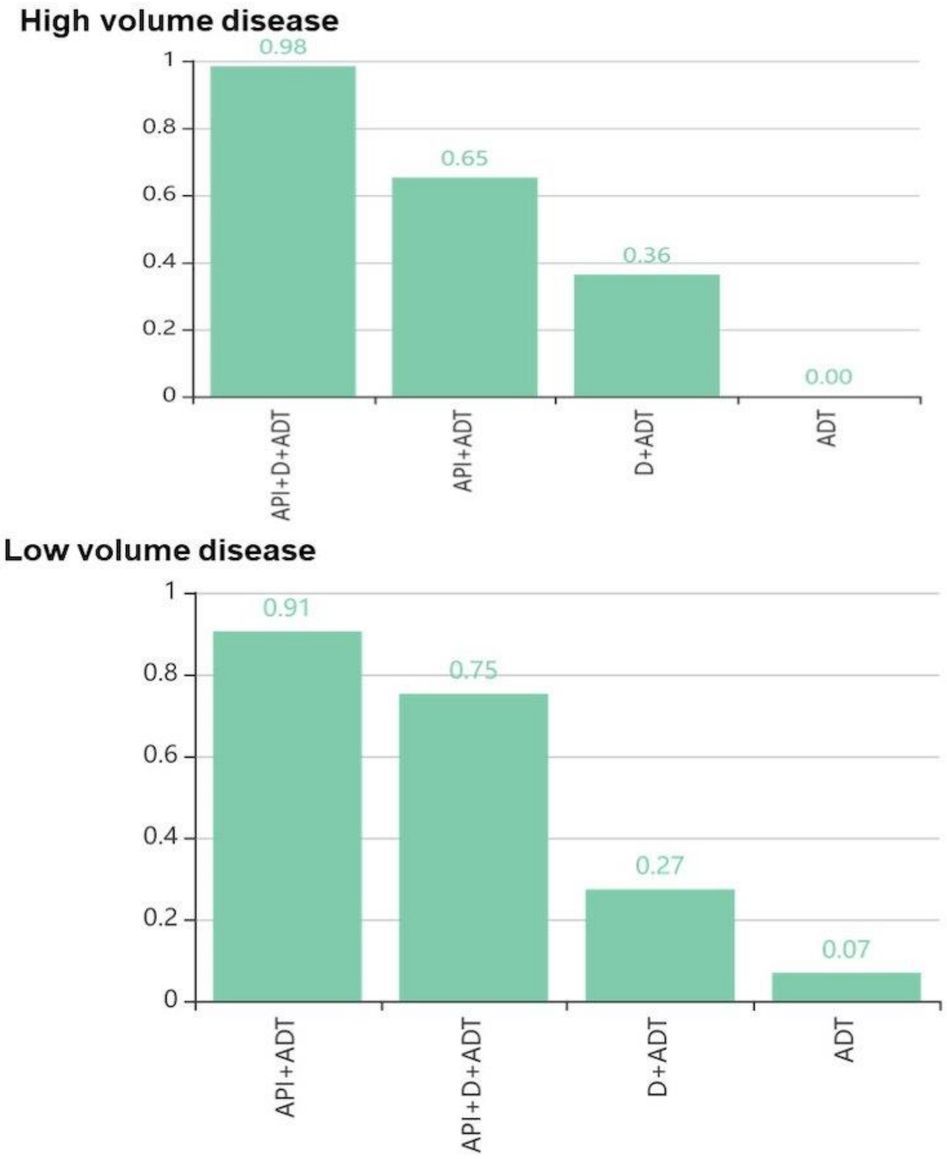
TABLE 2. OVERALL SURVIVAL WITH TRIPLET THERAPY BY VOLUME OF DISEASE

Trial	Triplet therapy	D+ADT	HR (95% CI)
High Volume			
ARASENS	203/497	268/508	0.69 (0.57-0.82)
PEACE-1	92/224	120/232	0.72 (0.55-0.95)
ENZAMET	90/180	96/179	0.87 (0.66-1.17)
Low Volume			
ARASENS	26/154	36/146	0.68 (0.41-1.13)
PEACE-1	29/131	31/123	0.83 (0.50-1.39)
ENZAMET	18/73	27/71	0.61 (0.33-1.1)

El metanálisis por pares incluyó un total de 3 ensayos aleatorios (ARASENS, PEACE-1, ENZAMET) con 2518 pacientes (volumen alto: [3] 1820; volumen bajo: 698)

https://www.urotoday.com/conference-highlights/asco-gu-2023/asco-gu-2023-prostate-cancer.html

ASCO 2023: The Role of Volume of Disease for Treatment Selection in Patients with mCSPC: A Living Meta-Analysis



•El metanaálisis en red que incluye 10 ensayos clínicos y más de 11,500 pacientes actualizado al 13 de febrero de 2023 mostró que en mCSPC de gran volumen, el triplete se convierte en la opción más eficaz y que mejora la SG en comparación con la terapia doble con ARPIs (HR : 0,83)

En mCSPC de bajo volumen, la terapia doble con ARPIs es el más eficaz, seguida del triplete. No hubo diferencias significativas HR 1,12.

-EL triplete mejoró la SG en comparación con el doblete de docetaxel en la enfermedad de alto volumen (HR: 0,73)
-En pacientes con enfermedad de bajo volumen, se observaron (20%) y (28%) muertes respectivamente.
- El triplete aumenta SG frente al doblete de docetaxel en bajo volumen (HR: 0,71)

https://www.urotoday.com/conference-highlights/asco-gu-2023/asco-gu-2023-prostate-cancer.html

CONSIDERACIONES A TENER EN CUENTA PARA EL USO DE QUIMIOTERAPIA…

FACTORES DE RIESGO ASOCIADOS A LA QT

*** Fragilidad y edad avanzada**

- Neutropenia febril (grado 3-5 en el 6-15% de los pacientes).

- Fatiga (grado 3-5 en el 6-7% de los pacientes). Suspenden hasta en un 30% de los pacientes.

-STAMPEDE, los pacientes ≥65 a con docetaxel >reacciones de hipersensibilidad, neutropenia, anemia, retención de líquidos, disnea y cambios en las uñas.

-En pacientes ≥75 : >10% incidencia de neutropenia, anemia, diarrea, disnea e infección del tracto respiratorio superior

*** Trastornos hematológicos**

- Neutropenia es el EA más frecuente.

- La trombocitopenia g 3-4 es poco frecuente (1% en el estudio CHAARTED). 2ª a mielosupresión (p. ej.,SMD) o autoinmune, docetaxel puede estar contraindicado.

Si asociada a una carga tumoral ósea elevada, el uso de docetaxel podría mejorar los recuentos de plaquetas.

*** Neuropatía**

-Relevante inducido por docetaxel. En los estudios CHAARTED o GETUG-AFU1521, a pesar de la presencia de neuropatía previa de grado ≥2 como criterio de exclusión, se notificó neuropatía de grado ≥3 en el 1-2% de los pacientes.

1. A. Borque-Fernando, M.A. Calleja-Hernández, J.M. Cózar-Olmo et al : A multidisciplinary consensus statement on the optimal pharmacological treatment for metastatic hormone-sensitive prostate cancer. Actas urológicas españolas.www.elsevier.es/actasuro https://doi.org/10.1016/j.acuroe.2022.12.004

FACTORES DE RIESGOS ASOCIADOS AL TIPO DE ARSI

- Interacciones del ARSi con el tto médico habitual del paciente.
- Enfermedad cardiovascular
- Hepatotoxicidad
- Osteoporosis
- Toxicidad cutánea. Por ej Apalutamida

- **¡ESCALAS DE VALORACIÓN GERIÁTRICA**!

Conclusión TRIPLETES/ DOBLETES

- La supervivencia en mHSPC sincrónico de *novo* supera una mediana de >5 años al agregar un ARPI a ADT + DOCE según los datos del PEACE-1 y ARASENS.

- La enfermedad metacrónica NO se incluyó en el estudio PEACE-1 y suponía el 14% en el ARASENS.

- El **metacrónico *l***que recaen con un volumen bajo después de una terapia local (mSG 92,4 meses) **tienen un mejor pronóstico en comparación con los pacientes con mHSPC *de novo* (**mSG 43,2 meses)

- En bajo volumen, no se no hay un claro beneficio según el PEACE-1, mientras que sí se objetiva en el ARASENS (ASCO-GU23)

https://www.esmoopen.com/article/S2059-7029(23)00416-7/fulltext

Conclusión
TRIPLETES/DOBLETES

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ESMO OPEN SCIENCE FOR OPTIMAL CANCER CARE

PRO AND CON DISCUSSIONS

Systemic treatment of metastatic hormone-sensitive prostate cancer—upfront triplet versus doublet combination therapy

- Jóvenes con mHSPC sincrónico el triplete inicial ha definido un beneficio de supervivencia y en >70 fit.
- Si un triplete no es factible ADT + ARPIs puede ser una opción eficaz, segura y manejable.
- Decisión sobre una u otra opción debe tomarse en función:
  - Volumen de la enfermedad, el momento de la metástasis, el estado funcional y las preferencias del paciente, comorbilidades y el impacto en la calidad de vida.
  - En cuanto a la carga de enfermedad, los pacientes de alto volumen se pueden beneficiar de ambas opciones y con volumen bajo de enfermedad de ARPIs.
- Los perfiles de toxicidad en ambos estudios fase III mostraron un aumento de HTA grado ≥3 y elevación de las enzimas hepáticas con la adición de ARPIs + la toxicidad hematológica de DOCE (~10% superior).

https://www.esmoopen.com/article/S2059-7029(23)00416-7/fulltext

TAKE HOME…

- **Testar somático/germinal desde el escenario de hormonosensible** sería ideal antes de iniciar un tratamiento.

-Individualizar cada paciente en el comité multidisciplinar

Buen PS + alto volumen + joven +sincrónico : Doce + ARSI

** Mal PS/ bajo volumen/comorbilidades NO FIT para Doce /añoso/metacrónico: ARSI+ TDA **

- **Elegir bien la estrategia de tto:** estudiar mutaciones al debut , perfil del paciente, factores de riesgo propios del tumor, comorbilidades y preferencias del paciente.

Guías al respecto…

National Comprehensive Cancer Network®

NCCN Guidelines Version 4.2023 Prostate Cancer

PRINCIPLES OF NON-HORMONAL SYSTE

Non-Hormonal Systemic Therapy for M1 Castration-Sensitive Prostate Cancer

- **Patients with high-volume castration-sensitive metastatic prostate cancer who are fit for chemotherapy should be considered for ADT plus docetaxel and either abiraterone or darolutamide based on phase 3 studies:**
  - **ADT plus docetaxel and abiraterone improved overall survival and rPFS in the open-label PEACE-1 study. A modest increase in toxicity was seen.**
  - **ADT plus docetaxel and darolutamide improved overall survival in the ARASENS trial. Adverse events were similar between arms.**
  - **The use of myeloid growth factors should follow the NCCN Guidelines for Hematopoietic Growth Factors, based on risk of neutropenic fever.**

****The panel therefore does not include docetaxel with ADT as an option for patients with metastatic castration-sensitive prostate cancer. Rather, patients with high-volume castration-sensitive metastatic prostate cancer who are fit for chemotherapy should be considered for triplet therapy****

https://www.esmoprostatecancer.
Nccn.Prostate cancer V4. 2023.

Table 1. ESMO-MCBS table for therapies/indications in prostate cancer

Therapy	Disease setting	Trial	Control	Absolute survival gain	HR (95% CI)	QoL/toxicity	ESMO-MCBS score[a]
mHSPC							
Abiraterone—prednisone—ADT	Newly diagnosed high-risk mHSPC in patients in combination with ADT	STAMPEDE[9,10] Phase II/III NCT00268476	Placebo—ADT Median OS: 46 months	OS gain: 33 months	OS: 0.60 (0.50-0.71)	QoL data pending	4[b] (Form 2a)
Abiraterone—prednisone—ADT	Newly diagnosed high-risk mHSPC in patients in combination with ADT	LATITUDE[11-13] Phase III NCT01715285	Placebo—ADT Median OS: 36.5 months Median PFS: 14.8 months	OS gain: 16.8 months PFS gain: 18.2 months	OS: 0.66 (0.56-0.78) PFS: 0.47 (0.39-0.55)	QoL was not a secondary endpoint	4[b] (Form 2a)
Abiraterone—ADT ± docetaxel ± RT[c] Overall population	*De novo* mHSPC	PEACE-1[3] Phase III NCT01957436	ADT ± docetaxel ± RT Median rPFS: 2.2 years Median OS: 4.7 years	rPFS gain: 2.3 years OS gain: 1 year	rPFS: 0.54 (0.41-0.71)[d] OS: 0.82 (0.69-0.98)	QoL data pending	4[b] (Form 2a)
Abiraterone—ADT—docetaxel ± RT[c] ADT with docetaxel population	*De novo* mHSPC	PEACE-1[3] Phase III NCT01957436	ADT—docetaxel ± RT Median rPFS: 2.0 years Median OS: 4.4 years	rPFS gain: 2.5 years OS gain: 1.5 years[e]	rPFS: 0.50 (0.34-0.71)[d] OS: 0.75 (0.59-0.95)	QoL data pending	4[b] (Form 2a)
Apalutamide—ADT	mHSPC in combination with ADT	TITAN[14-16] Phase III NCT02489318	Placebo—ADT Median PFS: 22.1 months Median OS: 52.2 months	PFS gain: 23.9 months[f] OS gain: 28.1 months[g]	PFS: 0.48 (0.39-0.60) OS: 0.65 (0.53-0.79)	No QoL benefit Ischaemic heart disease 4.4% versus 1.5%	4[b] (Form 2a)
Darolutamide—docetaxel—ADT	For adult men with mHSPC	ARASENS[4] Phase III NCT02799602	Docetaxel—ADT Median OS: 48.9 months	OS gain: 23.0 months[h]	OS: 0.68 (0.57-0.80)	QoL was not a prespecified endpoint	4[b] (Form 2a)
Docetaxel—ADT[i] Metastatic and high-risk locally advanced	In combination with ADT, with or without prednisone or prednisolone, for the treatment of patients with mHSPC	STAMPEDE[17] Phase II/III NCT00268476	ADT Median OS: 71.0 months	OS gain: 10.0 months	OS: 0.78 (0.66-0.93)	QoL data pending	4 (Form 2a)
Docetaxel—ADT[i]	In combination with ADT, with or without prednisone or prednisolone, for the treatment of patients with mHSPC	CHAARTED[18-20] Phase III NCT00309985	ADT ITT median OS: 47.2 months	ITT OS gain: 10.4 months	OS: 0.72 (0.59-0.89)	QoL benefits were lower than the described threshold for significance	4 (Form 2a)
Docetaxel—ADT[i]	In combination with ADT, with or without prednisone or prednisolone, for the treatment of patients with mHSPC	GETUG-15[21] Phase III NCT00104715	ADT Median OS: 54.2 months	OS gain: 4.7 months	OS: 1.01 (0.75-1.36)	No QoL benefit	No evaluable benefit (Form 2a)
Enzalutamide—ADT First-line treatment	Adult men with mHSPC in combination with ADT	ENZAMET[22,23] Phase III NCT02446405	ADT Median PFS: 24.0 months[j] 3-year OS: 72%	PFS gain: 36.0 months[k] 3-year OS gain: 8%	PFS: 0.40 (0.33-0.49) OS: 0.67 (0.52-0.86) interim OS ($P = 0.002$; <0.003 threshold for interim analysis)	Improved QoL	4[b] (Form 2b)[l]
Enzalutamide—ADT	Adult men with mHSPC in combination with ADT	ARCHES[24-26] Phase III NCT02677896	Placebo—ADT Median PFS: 38.9 months 4-year OS: 57%	PFS gain: 10.9 months 4-year OS gain: 14%	PFS: 0.63 (0.52-0.76) OS: 0.66 (0.53-0.81)	No QoL benefit	3[b] (Form 2b)

Continued

LANDSCAPE AND TREATMENT mHSPC

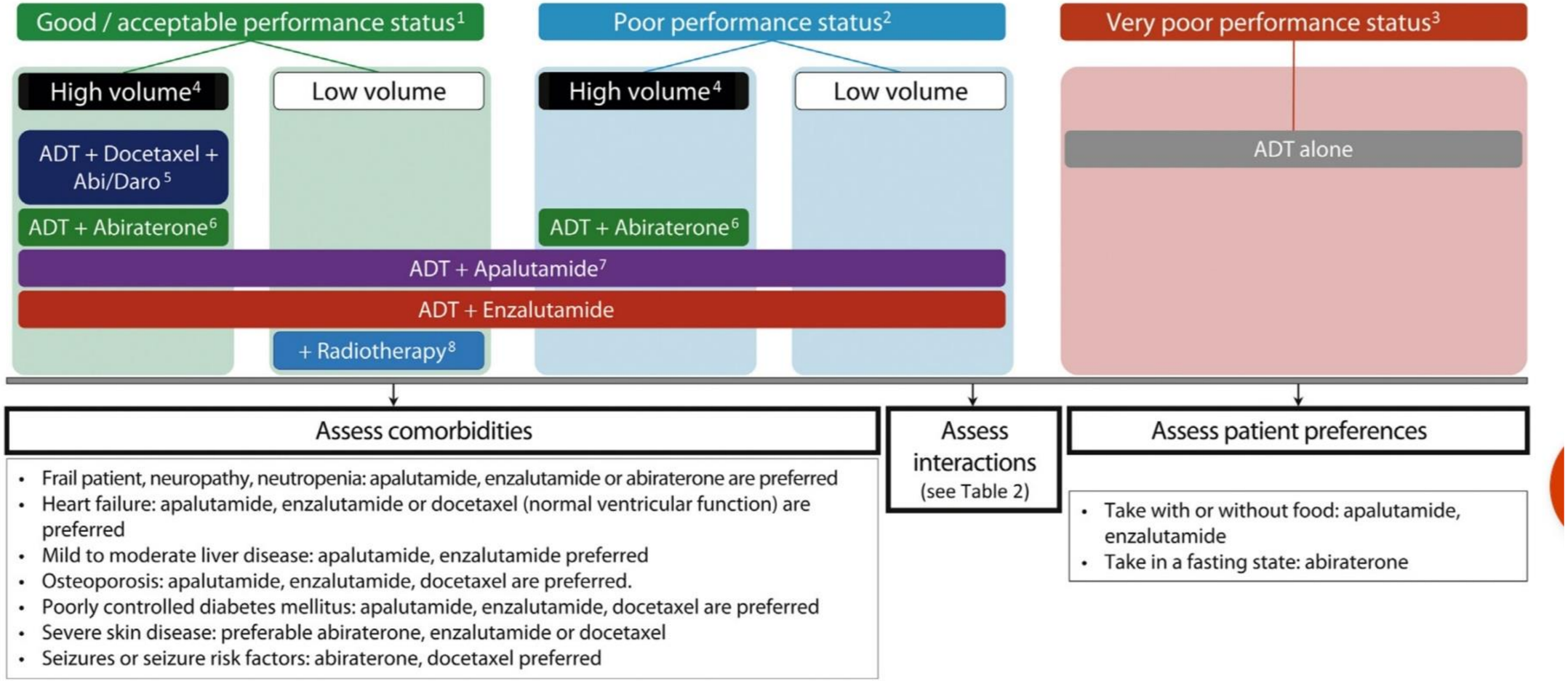


Figure 1 Algorithm with recommendations for the additional treatment to ADT in mHSPC.
mSCPH: metastatic hormone-sensitive prostate cancer; ADT: androgen deprivation therapy; Abi: Abiraterone; Daro: Darolutamide; Twelve: Docetaxel.

1. A. Borque-Fernando, M.A. Calleja-Hernández, J.M. Cózar-Olmo et al : A multidisciplinary consensus statement on the optimal pharmacological treatment for metastatic hormone-sensitive prostate cancer. Actas urológicas españolas.www.elsevier.es/actasuro https://doi.org/10.1016/j.acuroe.2022.12.004

Select Ongoing Randomized Phase III Trials in mHSPC

Trial	Regimens	Population
KEYNOTE-991(NCT04191096)	ADT + enzalutamide ± pembrolizumab	mHSPC, no prior AR inhibitor (planned N = 1232)
CAPItello-281(NCT04493853)	ADT + abiraterone acetate ± capivasertib	De novo mHSPC, PTEN deficiency (planned N = 1000)
TALAPRO-3(NCT04821622)	Enzalutamide ± talazoparib	mHSPC, DDR mutation(planned N = 550)
AMPLITUDE (NCT04497844)	Abiraterone + prednisone ± niraparib	mHSPC, HRR gene alteration (planned N = 788)

Genomic Alterations Can Occur in Germline or Somatically, Can Be Identified by Clinical NGS Testing

Germline

BRIP1
NBN
PALB2
PMS2
MITF
RECQL4
n = 1
(<1%)

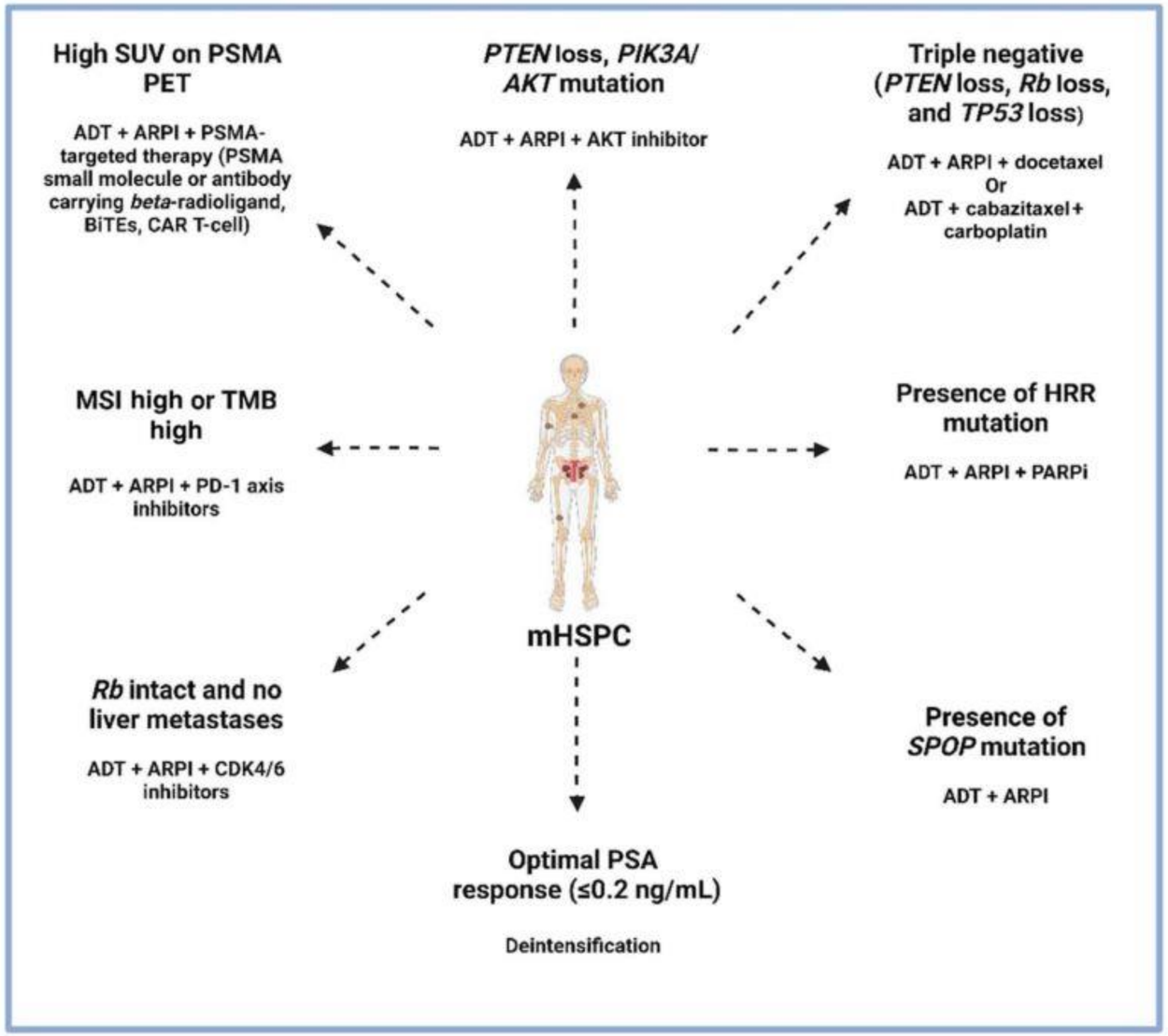
AT
n =

CHE
n = 9
(4%)

BRCA1
n = 2
(1%)

FH
n = 3
(1%)

FIG 2. Potential precision therapy approaches in mHSPC. ADT, androgen deprivation therapy; ARPI, androgen receptor pathway inhibitor; BiTEs, bispecific T-cell engager; CAR T cell, chimeric antigen receptor T cell; CDK4/6, cyclin D Kinase 4/6; HRR, homologous recombination repair; mHSPC, metastatic hormone-sensitive prostate cancer; MSI, microsatellite instability; PARPi, poly (ADP-ribose) polymerase inhibitor; PD-1, programmed cell death protein 1; PSA, prostate-specific antigen; PSMA, prostate-specific membrane antigen; TMB, tumor mutational burden.



es (n = 221)

***RCA2*,**
(2: 27%

rmline (8.6%)
matic only (7.7%)

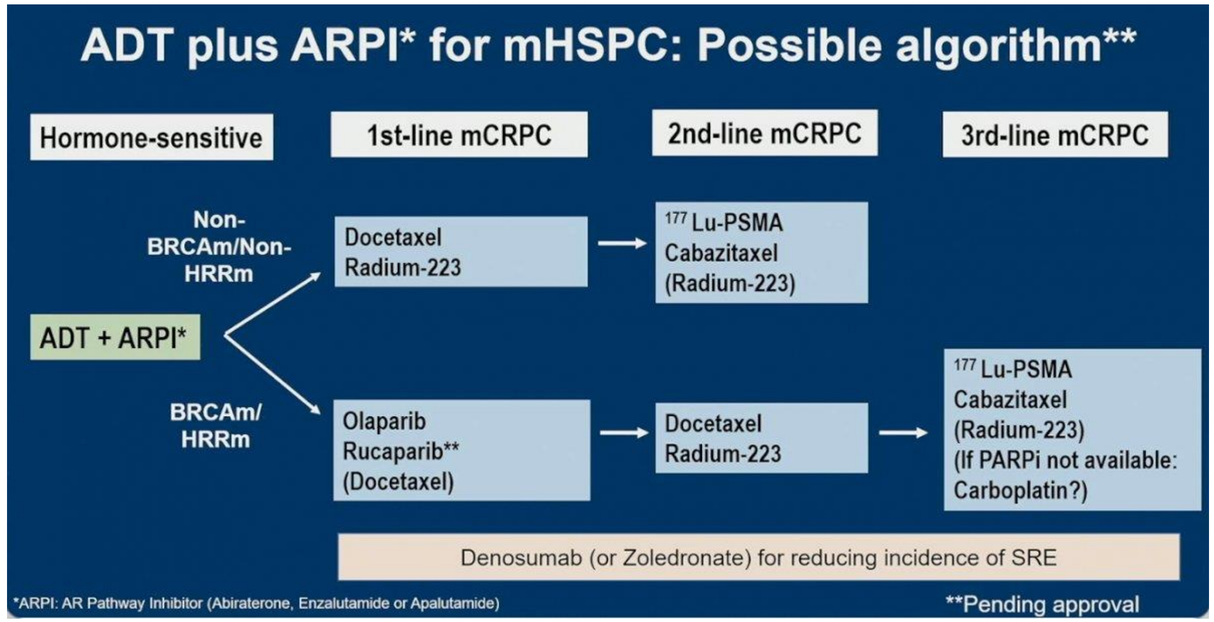
rmline (0.9%)
matic only (0.9%)

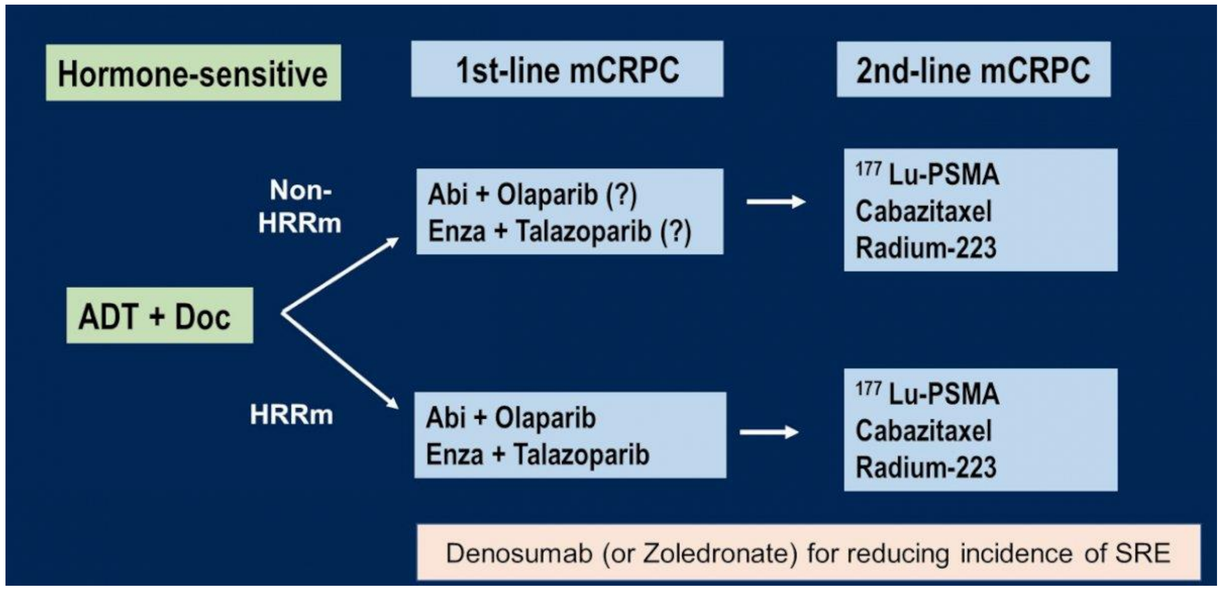
nline (2.3%)
iatic only (4.5%)

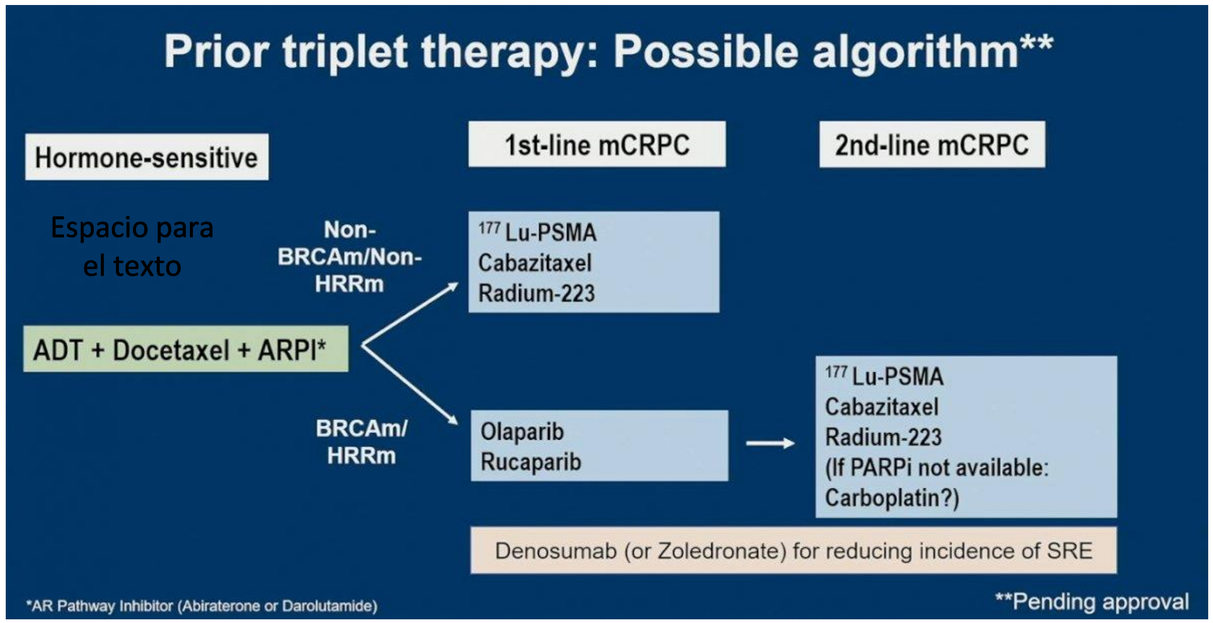
rmline (4.1%)
matic only (0.9%)

Abida. JCO Precis Onco

POSIBILIDADES A DÍA DE HOY DE SECUENCIACIÓN…







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¡MUCHAS GRACIAS!