ARASENS & DAROLUTAMIDE ASCO GU 2025 UPDATES

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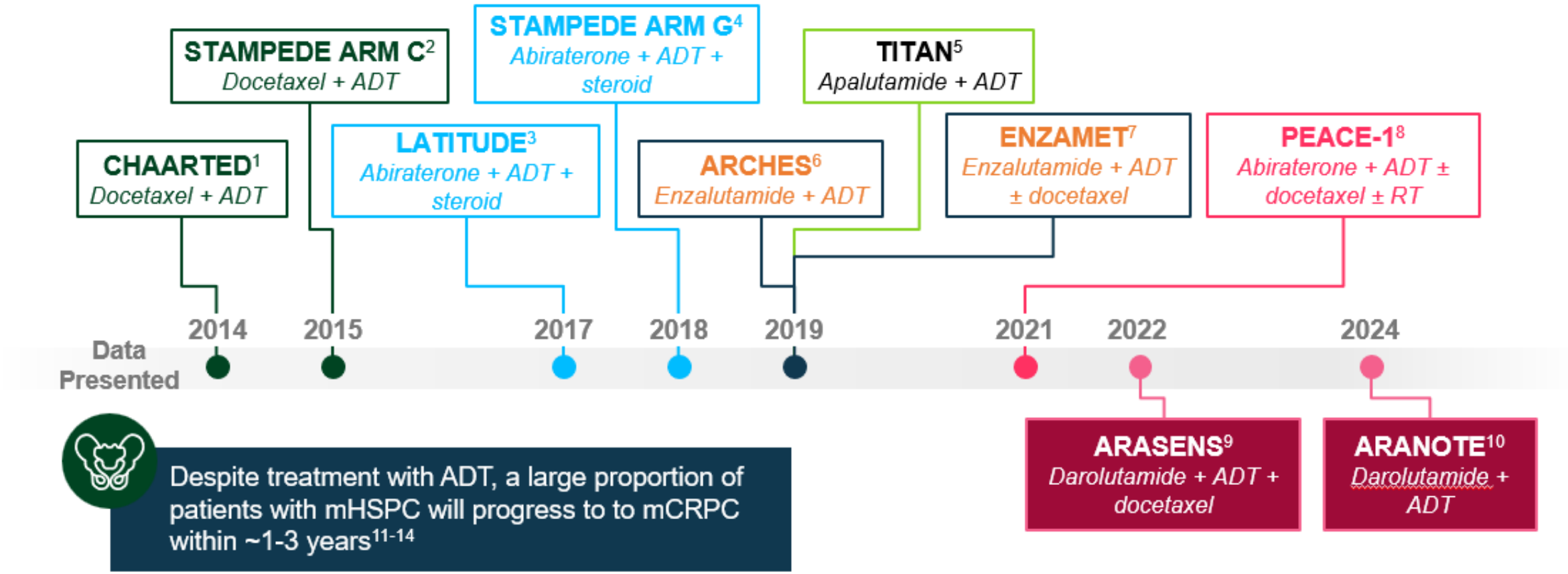
- In India approval status of available 2nd generation ARI's:
  - Darolutamide is approved for treatment of nmCRPC patients and mHSPC in combination with Docetaxel
  - Apalutamide is approved for treatment of nmCRPC and mHSPC whereas enzalutamide is approved for use in mCRPC patients

Key clinical trials in the setting of mHSPC



ADT: androgen deprivation therapy; CHAARTED: Chemohormonal Therapy Versus Androgen Ablation Randomized Trial for Extensive Disease in Prostate Cancer; ENZAMET: Enzalutamide in First Line Androgen Deprivation Therapy for Metastatic Prostate Cancer; mCRPC: metastatic castration-resistant prostate cancer; mHSPC: metastatic hormone-sensitive prostate cancer; RT: radiotherapy; STAMPEDE: Systemic Therapy in Advancing or Metastatic Prostate Cancer: Evaluation of Drug Efficacy; TITAN: Targeted Investigational Treatment Analysis of Novel Anti-androgen

1. Sweeney C et al. J Clin Oncol 2014;32(suppl; abstr LBA2). 2. James ND et al. J Clin Oncol 2015;33(suppl_15):5001. 3. Fizazi K et al. J Clin Oncol 2017;35(suppl; LBA3). 4. Hoyle A et al. Ann Oncol 2018;29(suppl_8; LBA4). 5. Chi KN et al. J Clin Oncol 2019;37(suppl_15; abstr 5006). 6. Armstrong AJ et al. J Clin Oncol 2019;37(suppl_7; abstr 687). 7. Sweeney C et al. J Clin Oncol 2019;37(suppl_18; LBA2). 8. Fizazi K et al. Ann Oncol 2021;32(suppl_5; LBA5_PR). 9. ClinicalTrials.gov identifier: NCT02799602. Available at: https://clinicaltrials.gov/ct2/show/NCT02799602 [accessed October 2024]. 10. Saad F et al. J Clin Oncol 2024:JCO2401798. 11. Sweeney C et al. N Engl J Med 2015;373(8):737-46. 12. Fizazi K et al. N Engl J Med 2017;377(4):352-60. 13. Armstrong A et al. J Clin Oncol 2019;37(32):2974-86. 14. Karantanos T et al. Oncogene 2013;32(49):5501-11.

Treatment Landscape for mHSPC

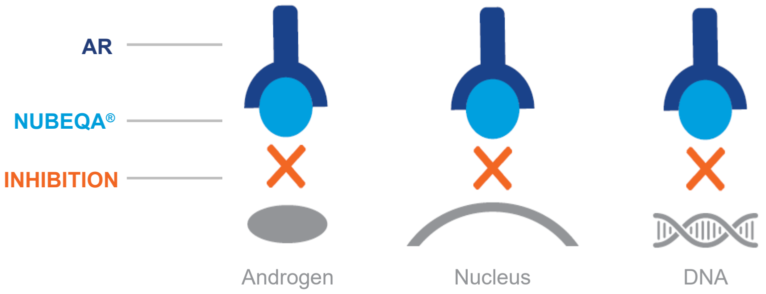
Trial[1]	Comparator Arm	Control Arm	N	HR for PFS (or Other Endpoint)	HR for OS
Docetaxel					
▪ CHAARTED[2]	ADT + Doc	ADT	513	0.58 (time to CRPC)	0.72 (0.63 HV)
▪ GETUG-15[3]	ADT + Doc	ADT	183	NA	0.78
▪ STAMPEDE Arm C[4]	ADT + Doc	ADT	148	NA	0.81
AR Pathway Inhibitors					
▪ LATITUDE[5]	ADT + ABI + Pred	ADT	955	NA	**0.62**
▪ STAMPEDE Arm G[6]	ADT + ABI + Pred	ADT	473	0.31 (FFS)	**0.54**
▪ ENZAMET[7]	ADT + ENZA (± Doc)	ADT + NSAA **(± Doc)**	588	0.45	**0.67**
▪ ARCHES[8]	ADT + ENZA*	ADT*	727	0.43 (rPFS)	**0.66**
▪ TITAN[9]	ADT + APA*	ADT*	660	0.48	**0.65**
▪ ARANOTE [10]	ADT + DARO	ADT	669	0.54	0.81
Triple Therapy					
▪ PEACE-1[11]	ADT + (DOC)+ABI	ADT (+ DOC recommended)	1173	0.50	0.72 (HV)
▪ ARASENS[12]	ADT + Doc+DARO	ADT+Doc	1305	NA	0.68

1. VanderWeele. JCO. 2019;37:2961. 2. Kyriakopoulos. JCO. 2018;36:1080. 3. Gravis. Eur Urol. 2016;70:256. 4. Clark. Ann Oncol. 2019;30:1992. 5. Fizazi. Lancet Oncol. 2019;20:686. 6. Hoyle. Eur Urol. 2019;76:719. 7. Davis. NEJM. 2019;381:121. 8. Armstrong. JCO. 2019;37:2974. 9. Chi. NEJM. 2019;381:13. 10. Saad JCO 2024 J11. Fizazi JCO 2022;. 12..

Darolutamide has a unique structure with a distinct safety profile[1-4]

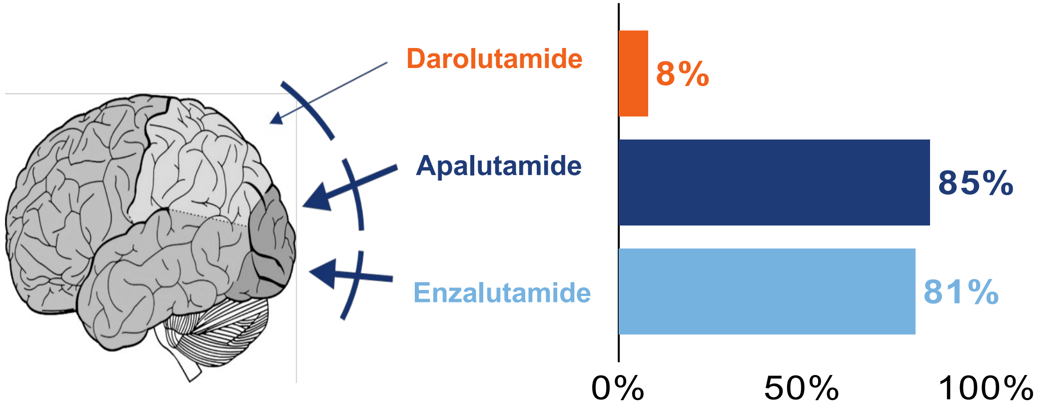
Mechanism of action

NUBEQA® inhibits the androgen receptor (AR)



* *Adapted from Moilanen 2015*

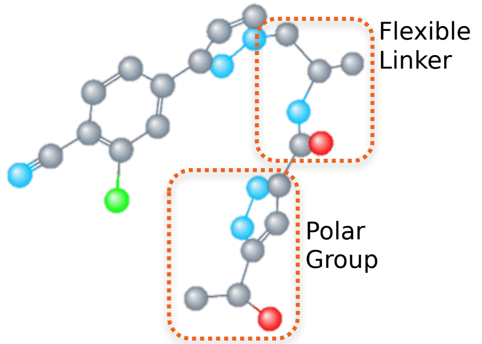
Ratio of brain/blood concentration[2]



* *Preclinical study data*

Unique molecular structure

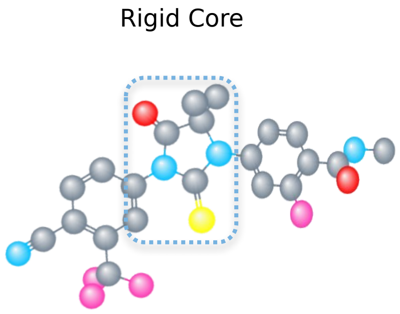
Darolutamide[3,4]



Interacts with **45** drugs

while **12** with major severity

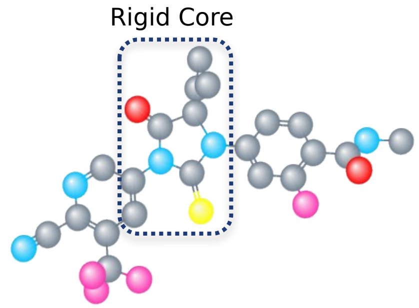
Enzalutamide[5]



Interacts with **426** drugs

whille **143** with major severity

Apalutamide[6]



Interacts with **428** drugs

While **160** with major severity

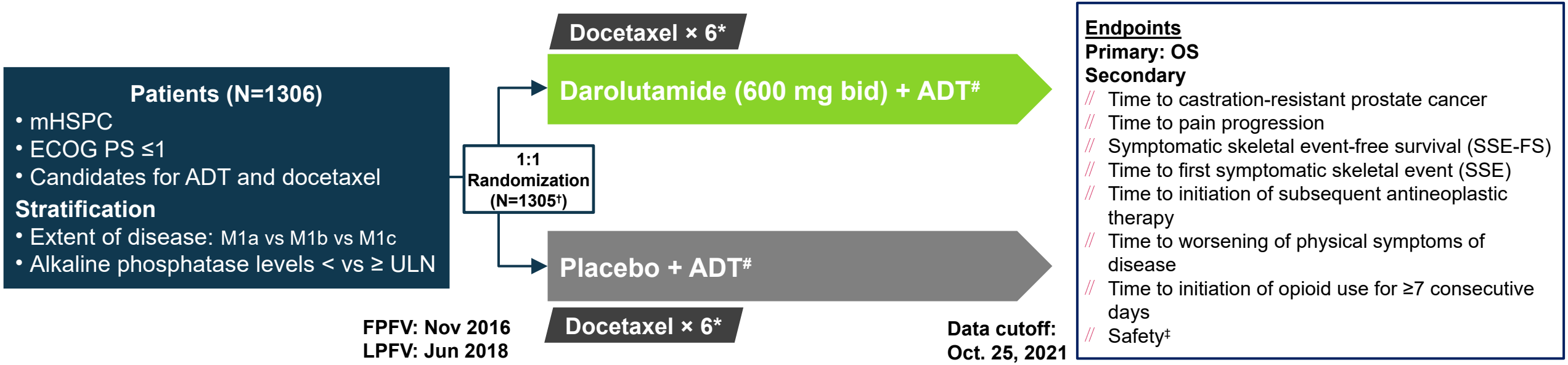
Individual information for each molecule, without comparative value.

Footnotes, abbreviations, and references are in the slide notes

1.Darolutamida. [Bula]. Finlândia: Bayer. Disponível em: <https://consultas.anvisa.gov.br/#/bulario/q/?nomeProduto=NUBEQA>. Acesso em: 20/01/2023; 2. Zurth et al. Higher blood–brain barrier penetration of [14c]apalutamide and [14c]enzalutamide compared to [14c]darolutamide in rats using wholebody autoradiography. Asco. 2019. Disponível em: https://ascopubs.Org/doi/10.1200/jco.2019.37.7_suppl.156. Acesso em: 23/01/2023*2. 3. Moilanen A, et al. Sci Rep. 2015;5:12007; 4. PubChem. Compound ID: 67171867. Acessado em 31 de Janeiro de 2019; 5. Pubchem. Compound ID: 15951529. Acessado em 31 de janeiro de 2019; 6. PubChem. Compound ID: 24872560. Acessado em 31 de janeiro de 2019;*

ARASENS Is a Blinded, Prospective, Pivotal Study Designed to Evaluate Efficacy and Safety of Darolutamide in Combination With ADT and Docetaxel in Patients With mHSPC

- Global, randomized, double-blind, placebo-controlled phase 3 study (NCT02799602)[1,2]



- The primary analysis was conducted after 533 deaths
- Secondary efficacy endpoints were tested hierarchically

Inclusion Criteria

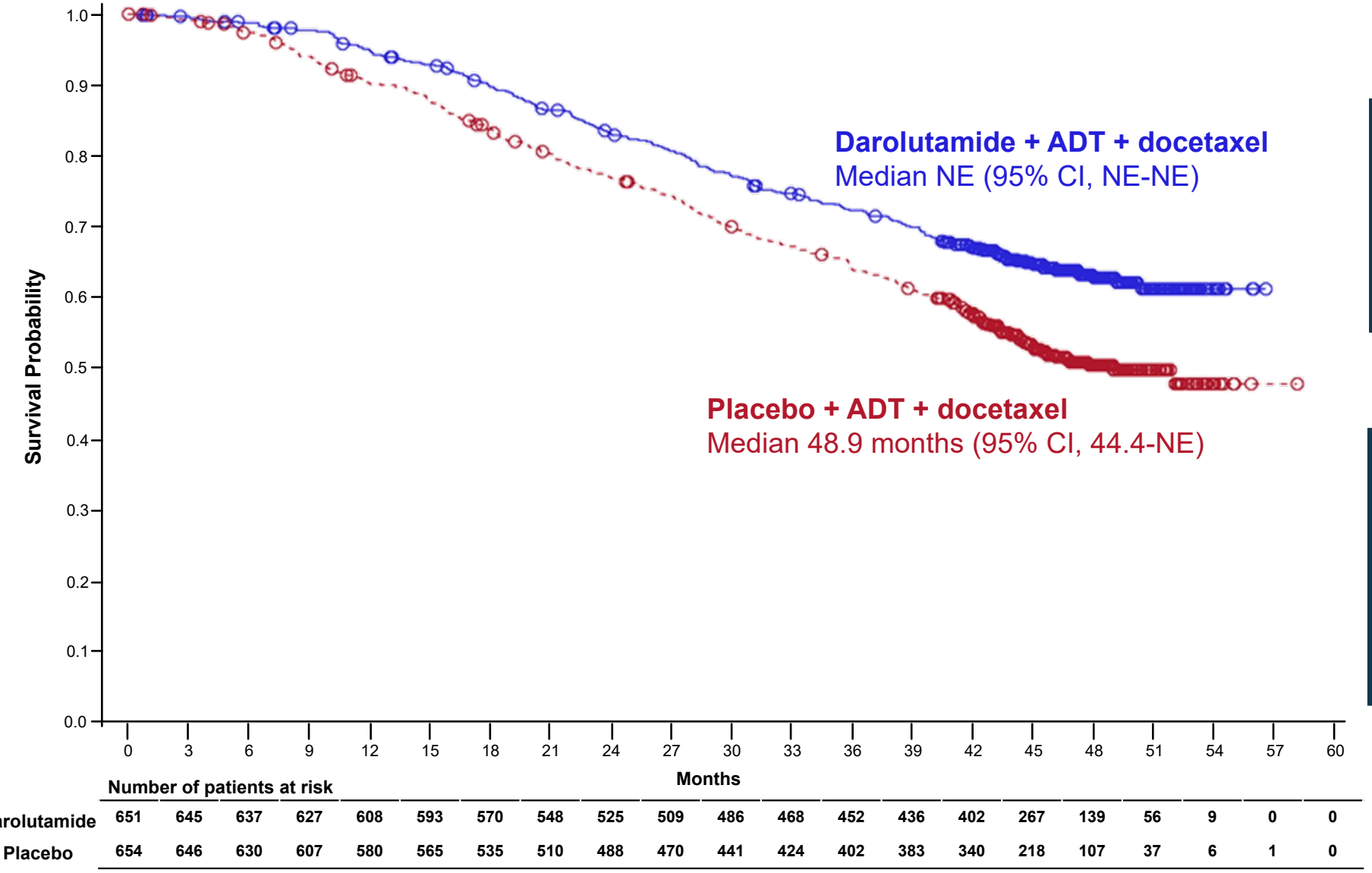
- Histologically or cytologically confirmed adenocarcinoma of prostate
- Metastatic disease
- Candidates for ADT and docetaxel
- Started ADT with or without first-generation anti-androgen, but <12 weeks before randomization
- ECOG PS: 0 or 1
- Adequate bone marrow, liver and renal function

Exclusion Criteria

- Prior treatment with
  - LHRH agonist/antagonists more than 12 weeks before randomization
  - Second-generation androgen receptor (AR) inhibitors such as enzalutamide, ARN-509, darolutamide (ODM-201), other investigational AR inhibitors
  - CYP17 enzyme inhibitor such as abiraterone acetate or oral ketoconazole as antineoplastic treatment for prostate cancer
  - Chemotherapy or immunotherapy for prostate cancer prior to randomization
- Treatment with radiotherapy/radiopharmaceuticals within 2 weeks before randomization
- Stroke, myocardial infarction, severe/unstable angina pectoris, coronary/peripheral artery bypass graft, congestive heart failure (New York Heart Association Class III or IV)
- Prior malignancy

*Starting ≤6 weeks after start of study drug at 75 mg/m² / 3 weeks, 6 cycles (in combination with prednisone/prednisolc at the discretion of the investigator).
#Investigators' choice (including orchiectomy) starting ≤12 weeks before randomization
†One enrolled patient was excluded from all analysis sets because of Good Clinical Practice violations.
‡One patient randomized to the placebo group but who received darolutamide was included in the placebo group for th full analysis set and in the darolutamide group for the safety analysis set.
1. Smith M, et al. *N Engl J Med*. 2022; DOI: 10.1056/NEJMoa2119115. 2. ClinicalTrials.gov identifier: NCT0279960. Accessed January 2022. https://clinicaltrials.gov/ct2/show/NCT02799602.

Primary Endpoint of Overall Survival Risk of Death Reduced by 32.5%



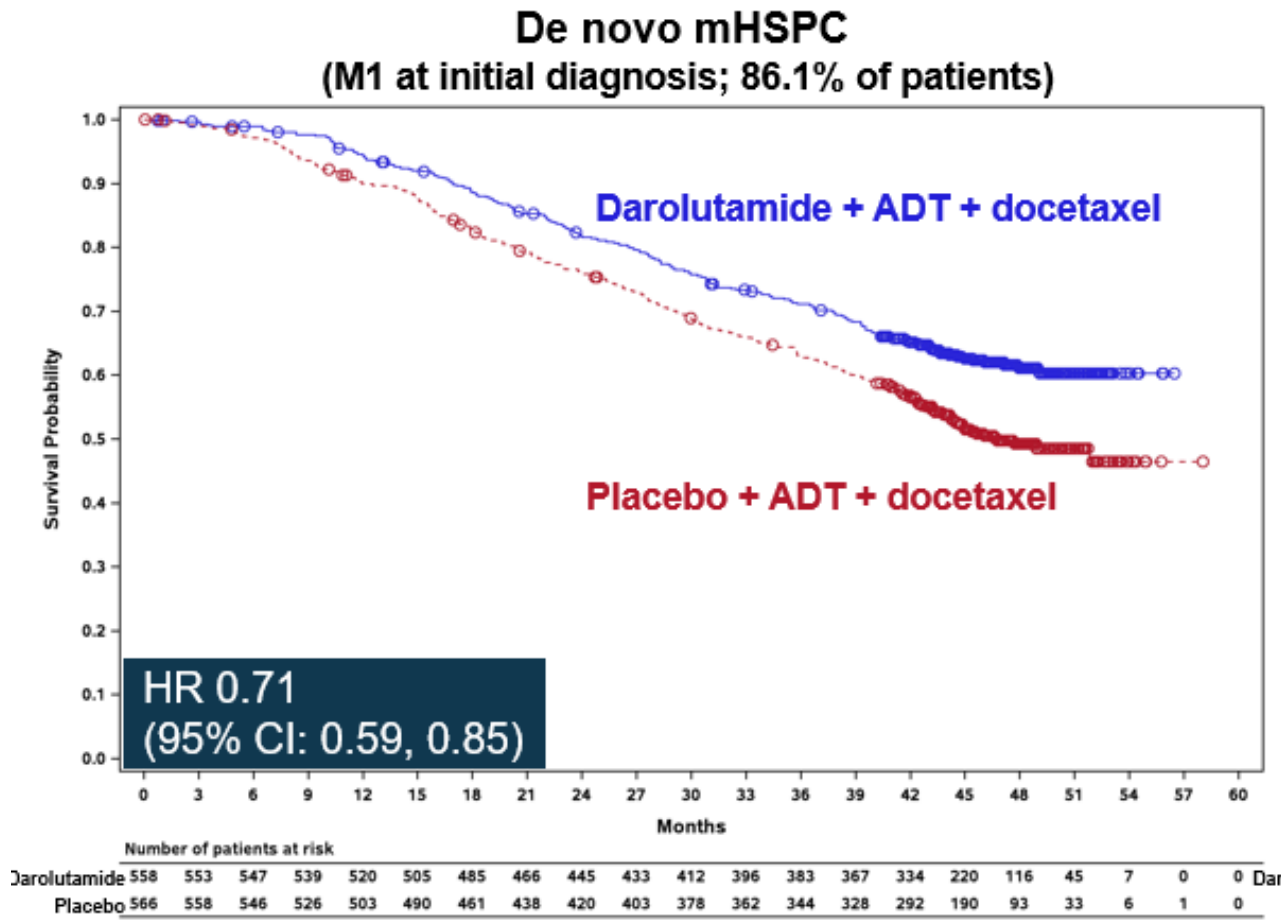
Primary endpoint

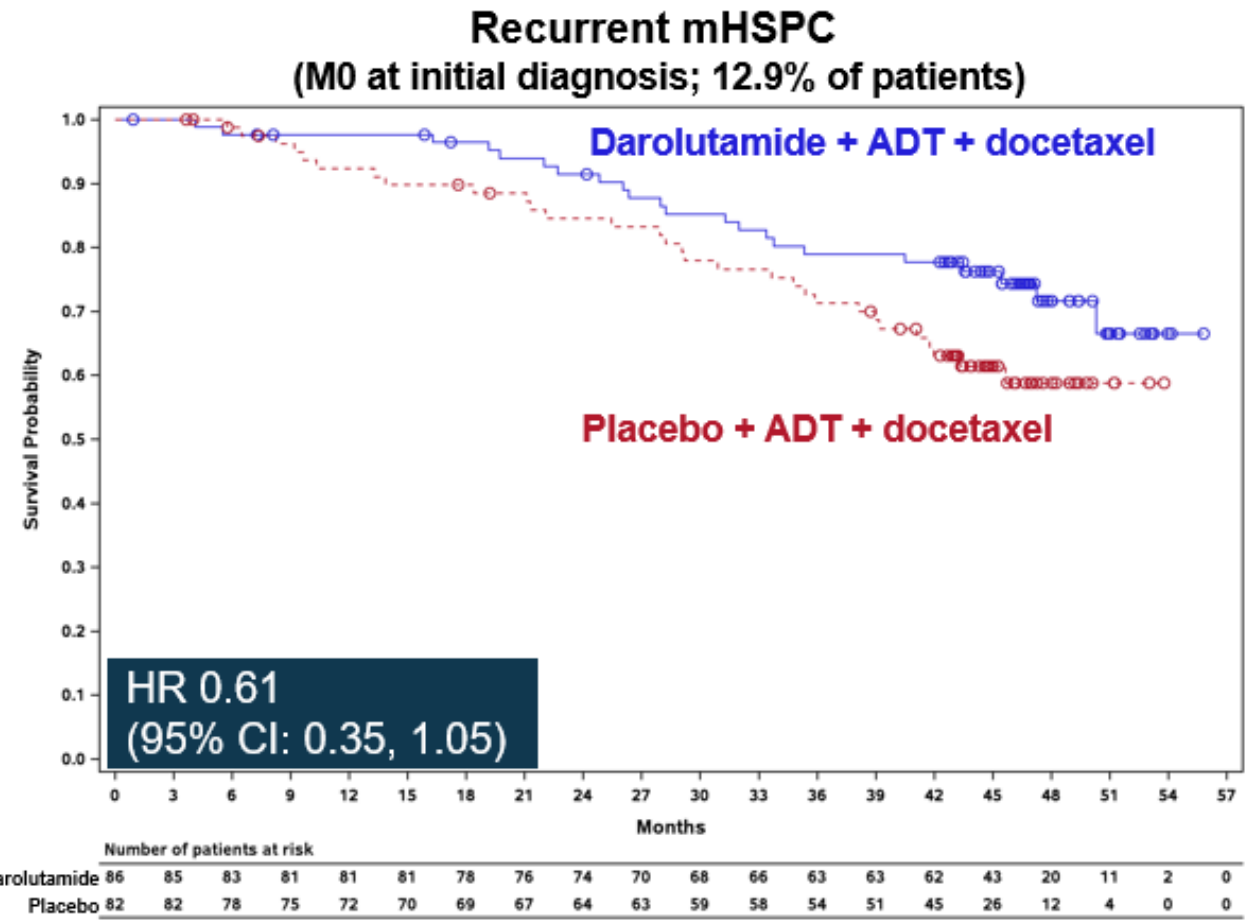
Hazard ratio for overall survival, 0.68 (95% CI, 0.57-0.80)
P<0.001

Patients' 4-year survival rate increased from **50%** with docetaxel + ADT to **63%** with the combination of darolutamide + ADT with docetaxel

Smith M, et al. *N Engl J Med*. 2022;
DOI: 10.1056/NEJMoa2119115.

Overall Survival: Consistent Benefit for De Novo and Recurrent Disease*





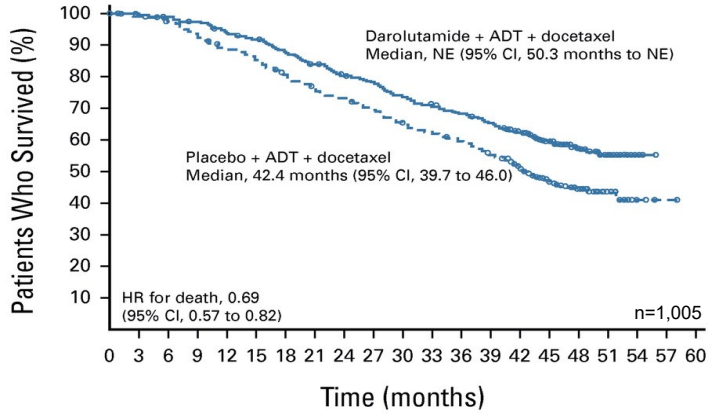
*These subgroups were not powered to demonstrate statistical superiority. 13 patients had unknown metastatic stage at initial diagnosis.

Smith M, et al. *N Engl J Med*. 2022; DOI: 10.1056/NEJMoa2119115.

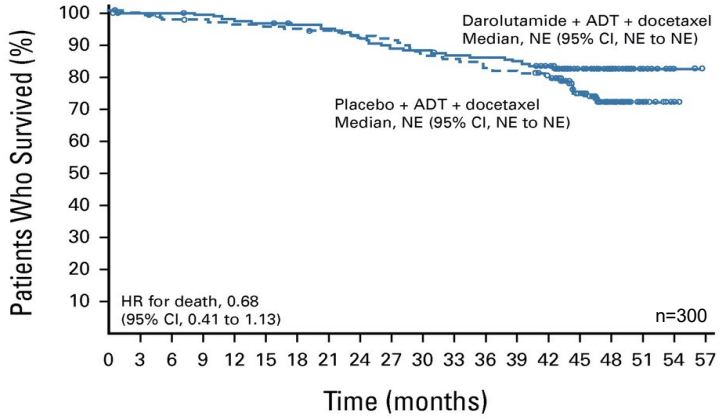
Overall survival in subgroups of patients

Primary endpoint

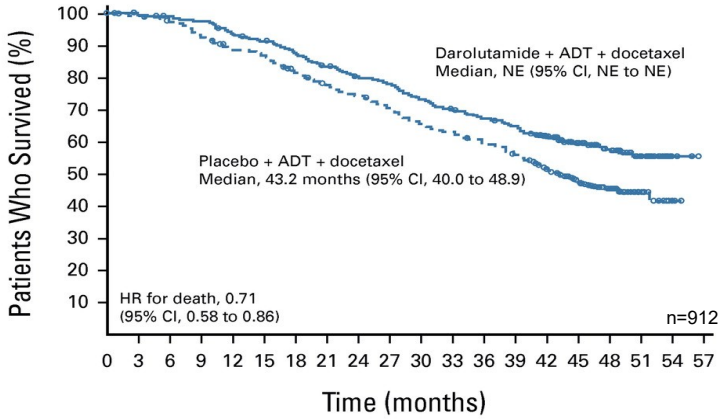
A. high-volume disease



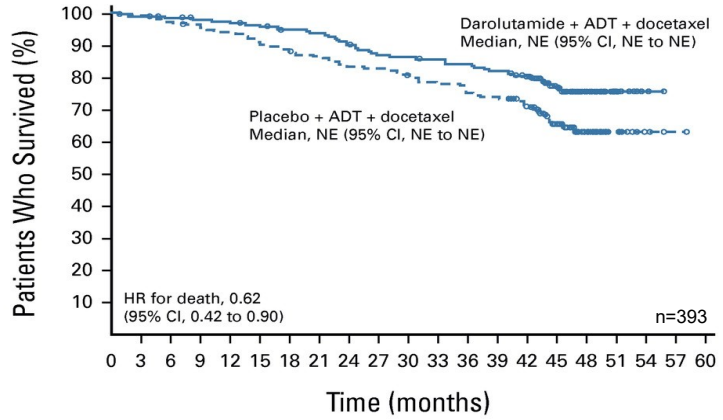
B. low-volume disease



C. high-risk disease



D. low-risk disease



High-Volume Disease: CHAARTED Criteria[1]	High-Risk Disease: LATITUDE Criteria[2]
• Visceral metastases • ≥4 bone metastases with ≥1 beyond the vertebral column/pelvis[a]	• ≥2 risk factors: ▪ Gleason score ≥8 ▪ ≥3 bone metastases[a] ▪ Visceral metastases

Low-volume and low-risk disease were defined as not meeting the respective high-volume and high-risk criteria
[a]Including those with diffusely increased skeletal metastases with superscan.

Figures taken from Hussain et al 2023[1]

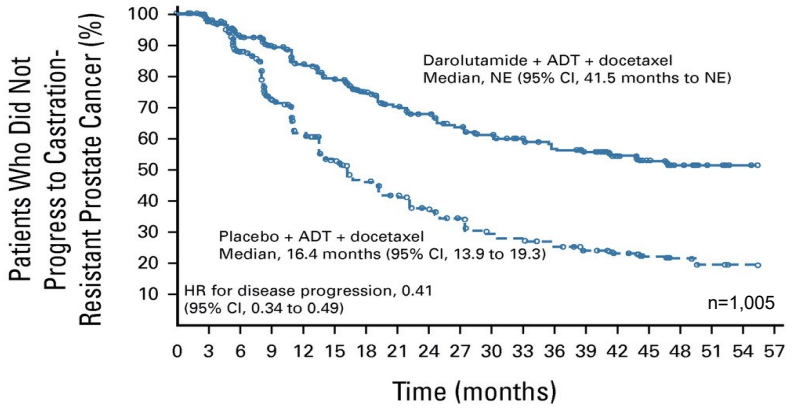
ADT: androgen deprivation therapy; CI: confidence interval; HR: hazard ratio; NE: not estimable

1. Hussain M et al. J Clin Oncol 2023;41(20):3595-607.

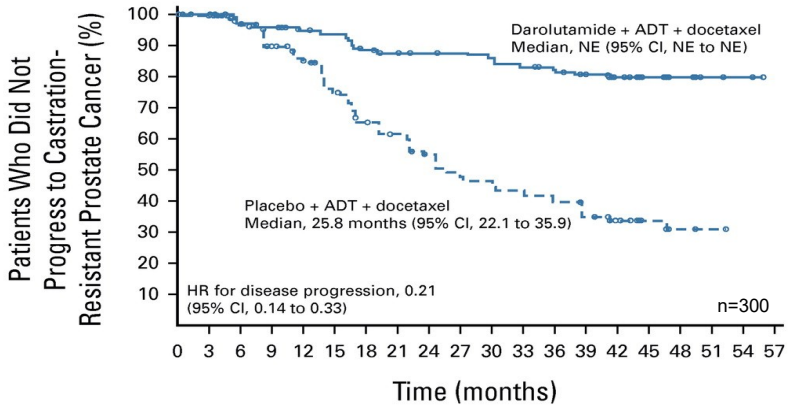
Secondary endpoint

Time to castration-resistant prostate cancer in subgroups of patients

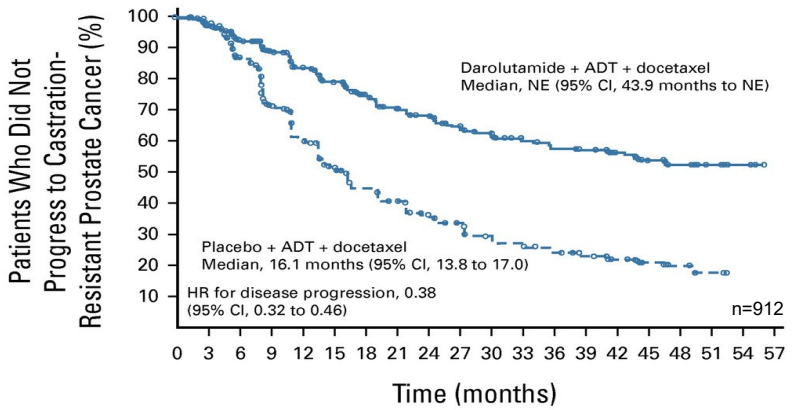
A. high-volume disease



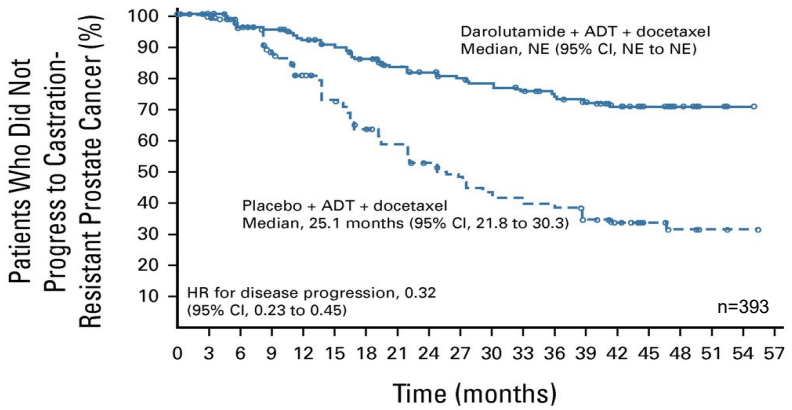
B. low-volume disease



C. high-risk disease



D. low-risk disease



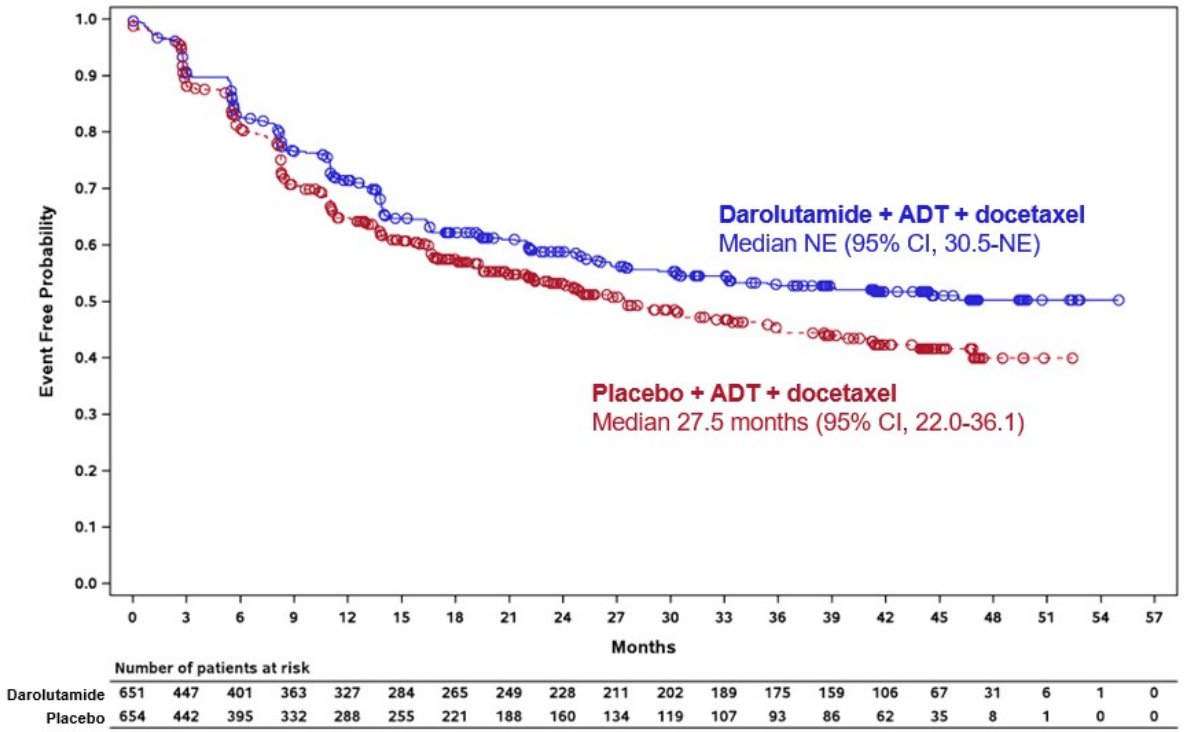
ADT: androgen deprivation therapy; CI: confidence interval; HR: hazard ratio; NE: not estimable

1. Hussain M et al. J Clin Oncol 2023;41(20):3595-607.

Figures taken from Hussain et al 2023[1]

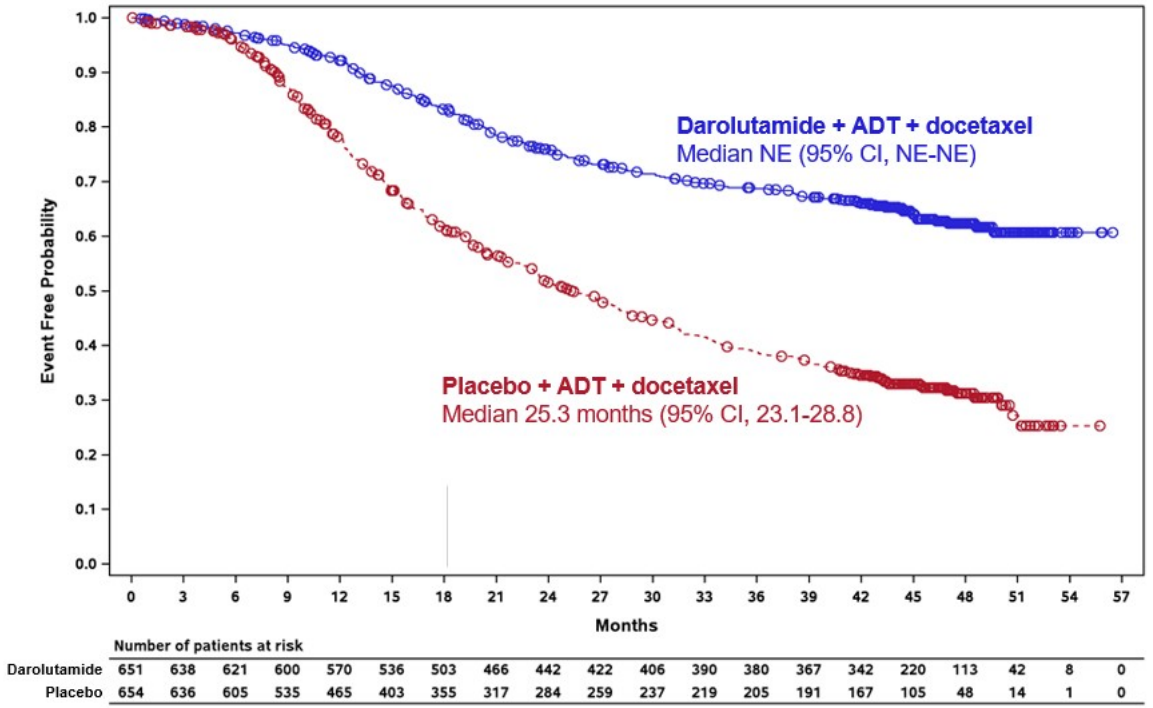
Secondary endpoint

Time to Pain Progression



Hazard ratio for time to pain progression,
0.79 (95% CI, 0.66-0.95) *P*=0.01

Time to Initiation of Subsequent Systemic Antineoplastic Therapy

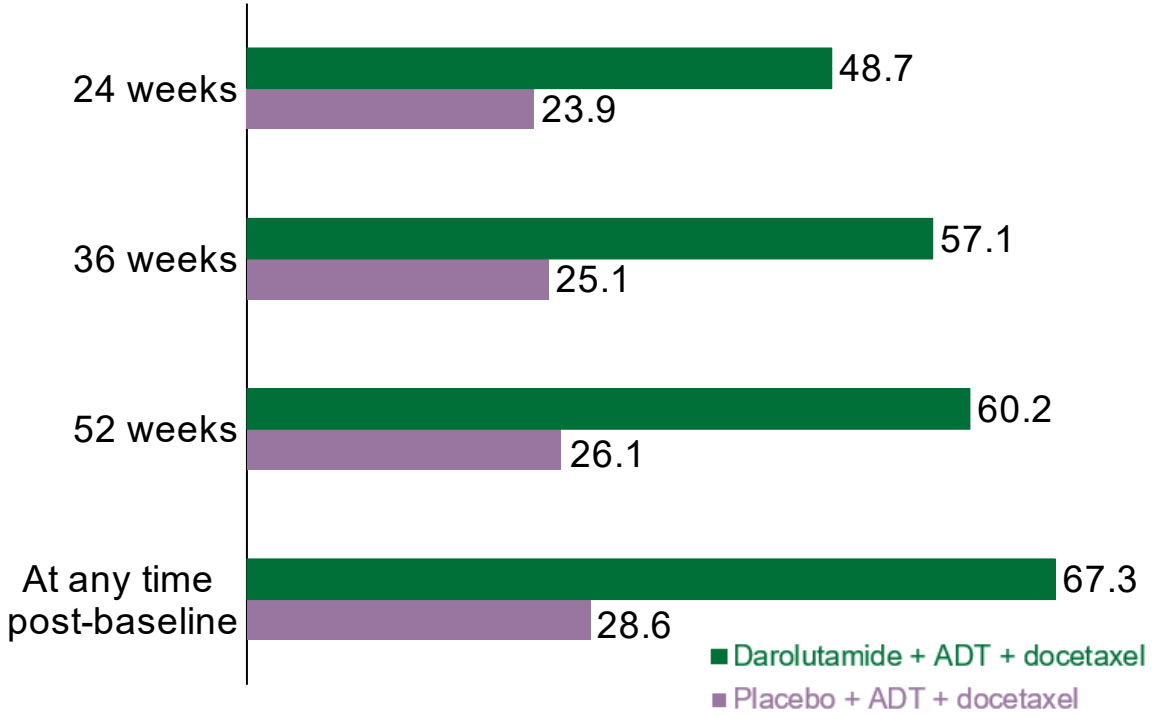


Hazard ratio for time to initiation of subsequent systemic antineoplastic therapy,
0.39 (95% CI, 0.33-0.46) *P*<0.001

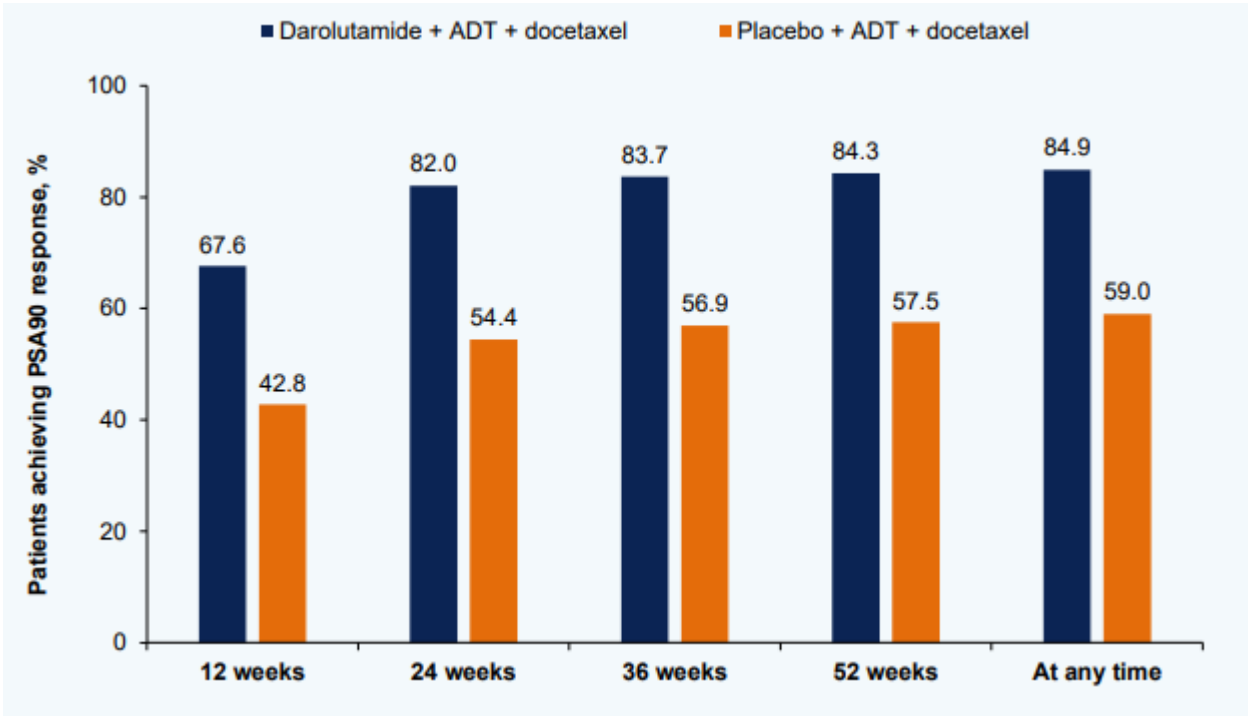
Smith M, et al. *N Engl J Med*. 2022;
DOI: 10.1056/NEJMoa2119115.

Darolutamide + ADT With Docetaxel Induced a Robust PSA Response in Patients With mHSPC

Patients Achieving Undetectable PSA (%)[a]



PSA 90 responses over time



More than twice the number of patients treated with darolutamide + ADT with docetaxel achieved undetectable PSA at any time after baseline than those treated with ADT + docetaxel

[a]Post hoc landmark analyses using Kaplan-Meier estimates. Undetectable PSA was defined as PSA <0.2 ng/mL.

Saad F, et al. Presented at American Society of Clinical Oncology; June 3-7, 2022; Chicago, IL, USA. Abstract 5078; Saad F, et al. Presented at AUA, April 28-May 1, 2023

After Adjusting for Exposure, the Rates of Adverse Events of Special Interest Were Similar Between Treatment Arms

AEs associated with AR pathway inhibitor therapy	Darolutamide + ADT + Docetaxel N=652		Placebo + ADT + Docetaxel N=650	
	Patients, n (%)	**EAIR/100 PY**	**Patients, n (%)**	**EAIR/100 PY**
Fatigue	216 (33.1)	12.5	214 (32.9)	17.8
Bone fracture	49 (7.5)	2.8	33 (5.1)	2.7
Falls	43 (6.6)	2.5	30 (4.6)	2.5
Rash*	108 (16.6)	6.2	88 (13.5)	7.3
Diabetes mellitus and hyperglycemia†	99 (15.2)	5.7	93 (14.3)	7.7
Weight decreased	22 (3.4)	1.3	35 (5.4)	2.9
Vasodilatation and flushing	133 (20.4)	7.7	141 (21.7)	11.7
Breast disorders/gynecomastia†	21 (3.2)	1.2	10 (1.5)	0.8
Hypertension†	89 (13.7)	5.1	60 (9.2)	5.0
Cardiac disorder†	71 (10.9)	4.1	76 (11.7)	6.3
Cerebral ischemia	8 (1.2)	0.5	8 (1.2)	0.7
Mental impairment disorder†	23 (3.5)	1.3	15 (2.3)	1.2
Depressed mood disorder†	21 (3.2)	1.2	24 (3.7)	2.0
Seizure	4 (0.6)	0.2	1 (0.2)	0.1

*This category combines the following MedDRA terms: rash, maculopapular rash, drug eruption, pruritic rash, erythematous rash, macular rash, papular rash, follicular rash, pustular rash, and vesicular rash.
†This category is a MedDRA High-Level Group Term.
Smith M, et al. *N Engl J Med*. 2022; DOI: 10.1056/NEJMoa2119115.

Common Comorbidities in Prostate Cancer

// Most patients with prostate cancer have comorbidities that require concomitant treatment[1,2]

Hypertension[1-4]

Diabetes mellitus[2-4]

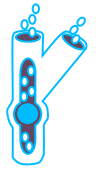
Cardiovascular problems[1,2]

Urologic complications[3,4]

Depression[4]

Sexual dysfunction[3]

Osteoarthritis/arthralgia[2]



Hypercholesterolemia[1,2,4]

1. Jefferson M, et al. *Ethn Dis*. 2020;30(suppl 1):185-192. 2. Shore N, et al. *Target Oncol*. 2019;14:527-539. 3. Appukkuttan S, et al. *J Clin Oncol*. 2020;38(29_suppl):149-149. 4. Spratt DE, et al. *Prostate Cancer Prostatic Dis*. 2021;24(3):647-661.

Potential ARPI Drug-Drug Interactions With Common Comedications for Patients With Prostate Cancer

Common Comedications in Prostate Cancer[1-3]

Depression	nefazodone
Cardiovascular	rivaroxaban
Hypertension	verapamil
Dyslipidemia	atorvastatin
Dyslipidemia	rosuvastatin
Diabetes mellitus	repaglinide
Sexual dysfunction	sildenafil

Potential DDIs for Common ARPIs[4]

Abiraterone	Apalutamide	Enzalutamide	Darolutamide
No action	Monitor	Monitor	
	Avoid	Consider modifying	
	Consider modifying	Consider modifying	No action
Monitor	Monitor		Monitor
Monitor	Monitor		Consider modifying
Monitor	Monitor	Monitor	Monitor
	Monitor	Monitor	

Shaded boxes represent potential DDIs.

Interaction Severity

- None
- Minor
- Moderate
- Major

Potential Interaction

Darolutamide may simplify treatment management, with a low potential for DDIs that may result in additional monitoring or changes to patients' comedications[a]

This slide is not meant to be a comparison between ARPIs.
[a]NUBEQA is currently approved for the treatment of mHSPC in combination with ADT and docetaxel, and for the treatment nmCRPC in combination with ADT.Please refer to local regulatory guidance and prescribing information on use of these drugs in specific populations.
ARPI, androgen receptor pathway inhibitor; DDI, drug-drug interaction.

What do patients want?

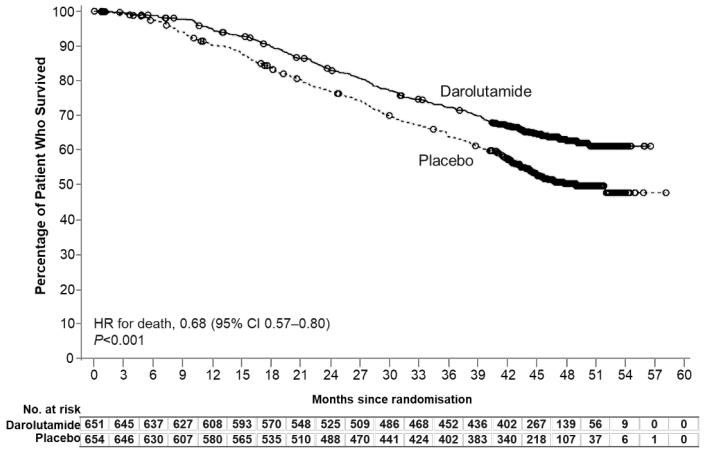
Live longer

Reduced risk of death: 32.5%[1]

Median OS: NR (darolutamide) vs 48.9 months (placebo)

4-year survival: 63% (darolutamide) vs 50% (placebo)

ARASENS: overall survival[1]



Good quality of life

Most AEs occurred during docetaxel treatment, the overall incidences of AEs were similar in the groups[2]

Rash[2]

// 17.3% (darolutamide) vs 13.7% (placebo)

Hypertension[2]

// 13.8% (darolutamide) vs 9.7% (placebo)

Rate of discontinuation[3]

// 13.7% (darolutamide) vs 10.6% (placebo)

Management of mHSPC in Practice

Several questions are unanswered, BUT….

According to the guidelines, ADT alone in M1 disease is generally not recommended for a fit and eligible patient

“Volume” is an aspect for consideration of treatment of prostate

Both high and low volume have similar benefits with treatment intensification

ADT, androgen deprivation therapy; EAU, European Association of Urology; mHSPC, metastatic hormone-sensitive prostate cancer.

Mottet N, et al. EAU - EANM - ESTRO - ESUR - ISUP - SIOG guidelines on prostate cancer. Published 2023. Accessed May 2023. https://d56bochluxqnz.cloudfront.net/documents/full-guideline/EAU-EANM-ESTRO-ESUR-ISUP-SIOG-Guidelines-on-Prostate-Cancer-2023_2023-03-27-131655_pdvy.pdf

Darolutamide Sets a New Standard For Patients With mHSPC

Darolutamide is a potent ARi with robust efficacy and favorable tolerability in patients with mHSPC[1]

Darolutamide has a low risk of clinically relevant DDIs, which may lower the burden of managing comorbidities[2]

Darolutamide requires minimal patient monitoring [2]

Footnotes, abbreviations, and references are in the slide notes.
1. Smith M, et al. *N Engl J Med*. 2022;386(12):1132-1142. 2. Nubeqa. Prescribing information. Bayer HealthCare Pharmaceuticals Inc.; 2022.

Age-related efficacy and safety of darolutamide plus androgen-deprivation therapy and docetaxel in patients with metastatic hormone-sensitive prostate cancer: A subgroup analysis of ARASENS

Joan Carles, Bertrand Tombal, Maha Hussain, Fred Saad, Karim Fizazi, Alvaro Montesa Pino, Maria José Méndez-Vidal, Alejo Rodriguez-Vida, Daniel Castellano, Patrick Adorjan, Cristina Moretones, Manjari Dissanayake, Matthew Smith

ASCO GU 2025, Abstract 143

Age-related efficacy and safety of darolutamide plus androgen-deprivation therapy (ADT) and docetaxel in patients with metastatic hormone-sensitive prostate cancer: A subgroup analysis of ARASENS [Joan Carles, Abstract 143]

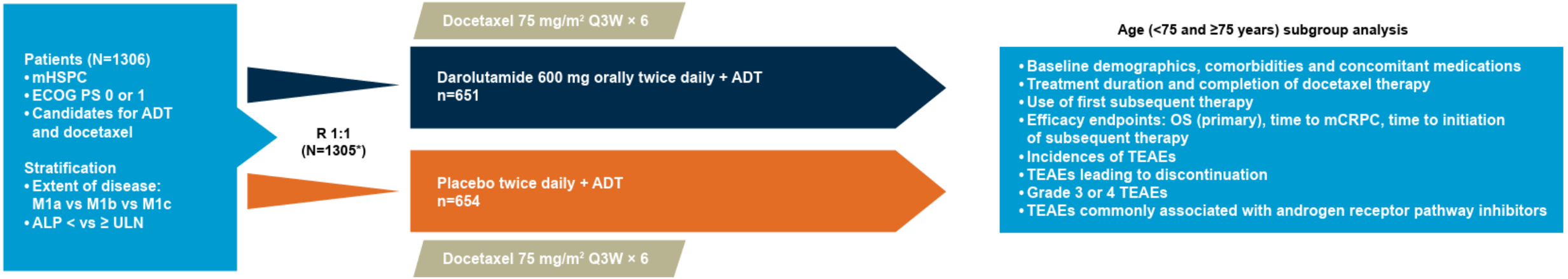
INTRODUCTION

- Older men have a higher incidence of prostate cancer, and 20% of cases are diagnosed in men aged >75 years[1]
- This study reports post hoc efficacy and safety of darolutamide + ADT + docetaxel by age subgroup (<75 and ≥75 years) in ARASENS

METHODS

- ARASENS was a global, randomized, double-blind, placebo-controlled phase 3 study (NCT02799602)

Study design



*One enrolled patient was excluded from all analysis sets because of Good Clinical Practice violations.

1. Graham LS, et al. *Am Soc Clin Oncol Educ Book.* 2023;43:e390396.

ADT, androgen-deprivation therapy; ALP, alkaline phosphatase; ECOG PS, Eastern Cooperative Oncology Group performance status; mCRPC, metastatic castration-resistant prostate cancer; mHPSC, metastatic hormone-sensitive prostate cancer; M1a, nonregional lymph node metastases only; M1b, bone metastases ± lymph node metastases; M1c, visceral metastases ± lymph node or bone metastases; OS, overall survival; Q3W, every 3 weeks; R, randomization; TEAE, treatment-emergent adverse event; ULN, upper limit of normal.

Age-related efficacy and safety of darolutamide plus androgen-deprivation therapy (ADT) and docetaxel in patients with metastatic hormone-sensitive prostate cancer: A subgroup analysis of ARASENS [Joan Carles, Abstract 143]

PATIENTS AND TREATMENT

- The ages of the 1305 patients analyzed in ARASENS ranged from 41 to 89 years, with 1086 patients aged <75 years (83%; darolutamide n=546; placebo, n=540) and 219 patients aged ≥75 years (17%; darolutamide n=105; placebo n=114)
- Baseline demographics and disease characteristics were generally similar in the darolutamide and placebo groups by age subgroup

Baseline demographics and disease characteristics by age subgroup

Characteristic at baseline	Age <75 years		Age ≥75 years		All patients	
	Darolutamide (n=546)	Placebo (n=540)	Darolutamide (n=105)	Placebo (n=114)	Darolutamide (n=651)	Placebo (n=654)
Age, median (range), years	65 (41–74)	67 (42–86)	67 (41–89)	67 (42–86)	67 (41–89)	67 (42–86)
ECOG PS, n (%)						
0	391 (71.6)	462 (70.6)	466 (71.6)	462 (70.6)	466 (71.6)	462 (70.6)
1	155 (28.4)	190 (29.1)	185 (28.4)	190 (29.1)	185 (28.4)	190 (29.1)
Metastatic stage at screening, n (%)						
M1a, nonregional LN only	22 (4.0)	16 (2.4)	23 (3.5)	16 (2.4)	23 (3.5)	16 (2.4)
M1b, bone ± LN	435 (79.7)	520 (79.5)	517 (79.4)	520 (79.5)	517 (79.4)	520 (79.5)
M1c, visceral ± LN or bone	89 (16.3)	118 (18.0)	111 (17.1)	118 (18.0)	111 (17.1)	118 (18.0)
Metastatic stage at initial diagnosis, n (%)						
De novo	469 (85.9)	566 (86.5)	558 (85.7)	566 (86.5)	558 (85.7)	566 (86.5)
Recurrent	70 (12.8)	82 (12.5)	86 (13.2)	82 (12.5)	86 (13.2)	82 (12.5)
PSA, median (range), ng/mL	31.1 (0–9219.0)	24.2 (0–11,947.0)	30.3 (0–9219.0)	24.2 (0–11,947.0)	30.3 (0–9219.0)	24.2 (0–11,947.0)
ALP, median (range), U/L	148.0 (40–4793)	140.0 (36–7680)	148.0 (40–4885)	140.0 (36–7680)	148.0 (40–4885)	140.0 (36–7680)
ALP <ULN, n (%)	245 (44.9)	291 (44.5)	290 (44.5)	291 (44.5)	290 (44.5)	291 (44.5)
ALP ≥ULN, n (%)	301 (55.1)	363 (55.5)	361 (55.5)	363 (55.5)	361 (55.5)	363 (55.5)

ADT, androgen-deprivation therapy; ALP, alkaline phosphatase; ECOG PS, Eastern Cooperative Oncology Group performance status; LN, lymph node; M1a, nonregional lymph node metastases only; M1b, bone metastases ± lymph node metastases; M1c, visceral metastases ± lymph node or bone metastases; PSA, prostate-specific antigen; ULN, upper limit of normal.

Age-related efficacy and safety of darolutamide plus androgen-deprivation therapy (ADT) and docetaxel in patients with metastatic hormone-sensitive prostate cancer: A subgroup analysis of ARASENS [Joan Carles, Abstract 143]

PATIENTS AND TREATMENT (CONT'D)

- The most common ongoing comorbidities (started prior to, but ongoing at the start of study treatment) by system organ class (SOC) in patients aged <75 years and ≥75 years were vascular (55%, 67%), musculoskeletal/connective tissue (42%, 42%), and metabolism/nutrition (35%, 43%) disorders
- The most common ongoing comorbid conditions (>10%) were generally more frequent in patients aged ≥75 years versus those aged <75 years
- The median number of concomitant medications was higher for older patients overall but when the time period was limited to after 9 months from randomization (i.e., after the period of docetaxel use when comedications might have been required to manage associated toxicity), the number of concomitant medications was similar in the two age subgroups

Most common ongoing comorbidities and number of concomitant medications by age subgroup

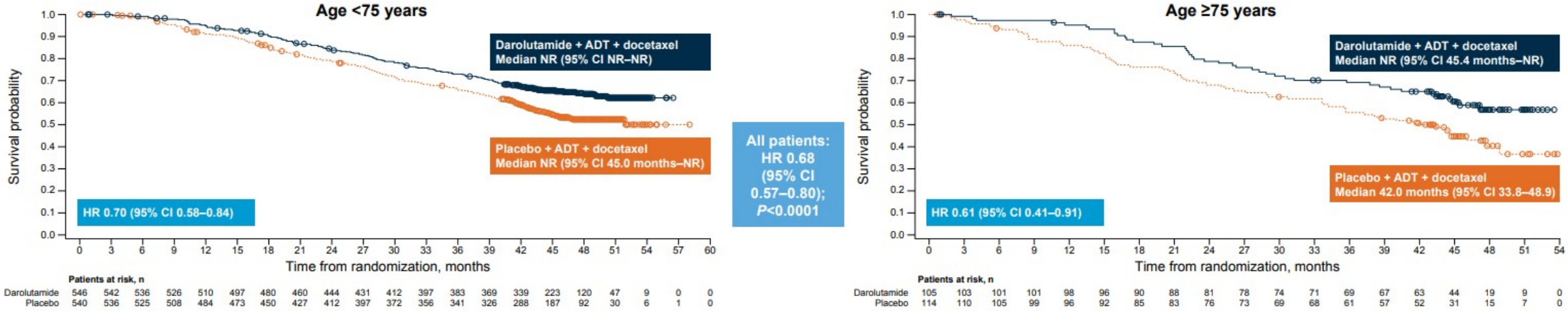
Comorbidities and concomitant medications	Age <75 years		Age ≥75 years		All patients	
	Darolutamide (n=546)	Placebo (n=540)	Darolutamide (n=105)	Placebo (n=114)	Darolutamide (n=651)	Placebo (n=654)
Ongoing comorbidities* by preferred term (>10% in any subgroup), n (%)						
Hypertension	268 (49.1)	252 (46.7)	64 (61.0)	69 (60.5)	332 (51.0)	321 (49.1)
Benign prostatic hyperplasia	98 (17.9)	82 (15.2)	17 (16.2)	33 (28.9)	115 (17.7)	115 (17.6)
Back pain	77 (14.1)	76 (14.1)	9 (8.6)	18 (15.8)	86 (13.2)	94 (14.4)
Constipation	53 (9.7)	44 (8.1)	17 (16.2)	10 (8.8)	70 (10.8)	54 (8.3)
Diabetes mellitus	54 (9.9)	44 (8.1)	7 (6.7)	18 (15.8)	61 (9.4)	62 (9.5)
Hyperlipidemia	43 (7.9)	47 (8.7)	13 (12.4)	16 (14.0)	56 (8.6)	63 (9.6)
Bone pain	48 (8.8)	44 (8.1)	5 (4.8)	15 (13.2)	53 (8.1)	59 (9.0)
Anemia	34 (6.2)	40 (7.4)	13 (12.4)	19 (16.7)	47 (7.2)	59 (9.0)
No. of concomitant medications, median (IQR)	26.5 (20.0–35.0)	25.5 (19.0–32.0)	29.0 (20.0–36.0)	28.0 (22.0–37.0)	27.0 (20.0–35.0)	26.0 (19.0–33.0)
No. of concomitant medications after 9 months from randomization, median (IQR)	8.0 (3.0–16.0)	8.0 (3.0–15.0)	9.0 (5.0–18.0)	8.0 (4.0–17.0)	8.0 (4.0–17.0)	8.0 (3.0–15.0)

*Ongoing comorbid conditions are defined as those starting before randomization and ongoing after randomization.
ADT, androgen deprivation therapy; IQR, interquartile range; SOC, system organ class.

Age-related efficacy and safety of darolutamide plus androgen-deprivation therapy (ADT) and docetaxel in patients with metastatic hormone-sensitive prostate cancer: A subgroup analysis of ARASENS [Joan Carles, Abstract 143]

- **EFFICACY**
  - Efficacy benefits with darolutamide versus placebo, in terms of improved OS and delayed time to mCRPC and time to initiation of subsequent antineoplastic therapy, were similar in the two age subgroups, and consistent with the overall population

Overall survival



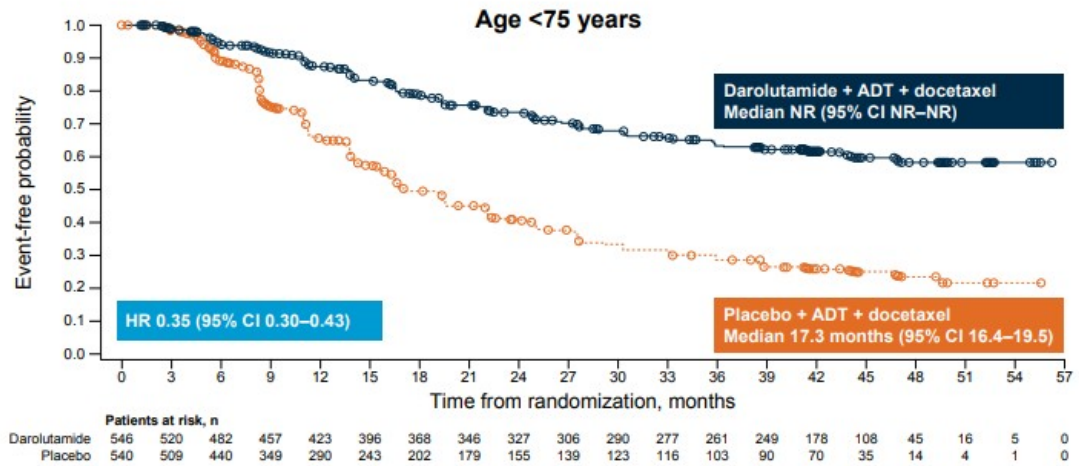
ADT, androgen deprivation therapy; CI, confidence interval; HR, hazard ratio; mCRPC, metastatic castration-resistant prostate cancer; NR, not reached; OS, overall survival.

Age-related efficacy and safety of darolutamide plus androgen-deprivation therapy (ADT) and docetaxel in patients with metastatic hormone-sensitive prostate cancer: A subgroup analysis of ARASENS [Joan Carles, Abstract 143]

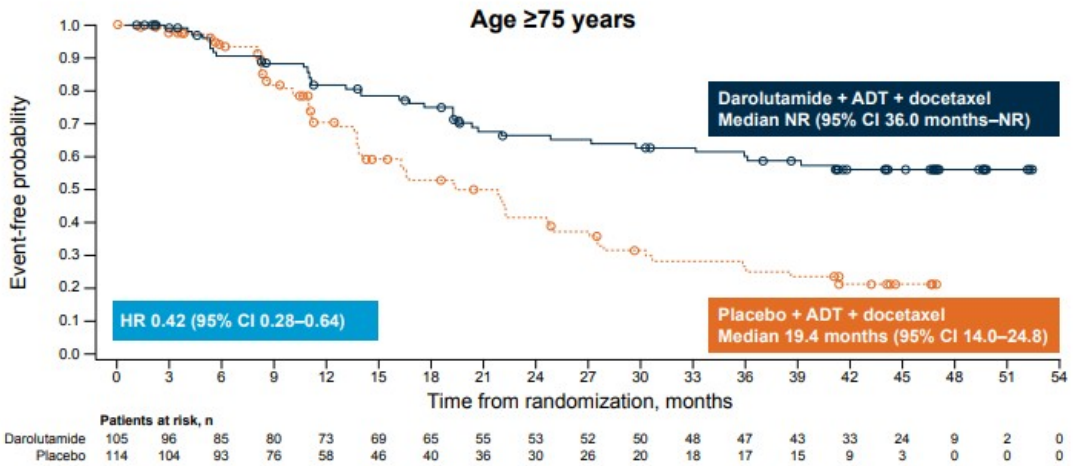
Bayer-sponsored study

EFFICACY (CONT'D)

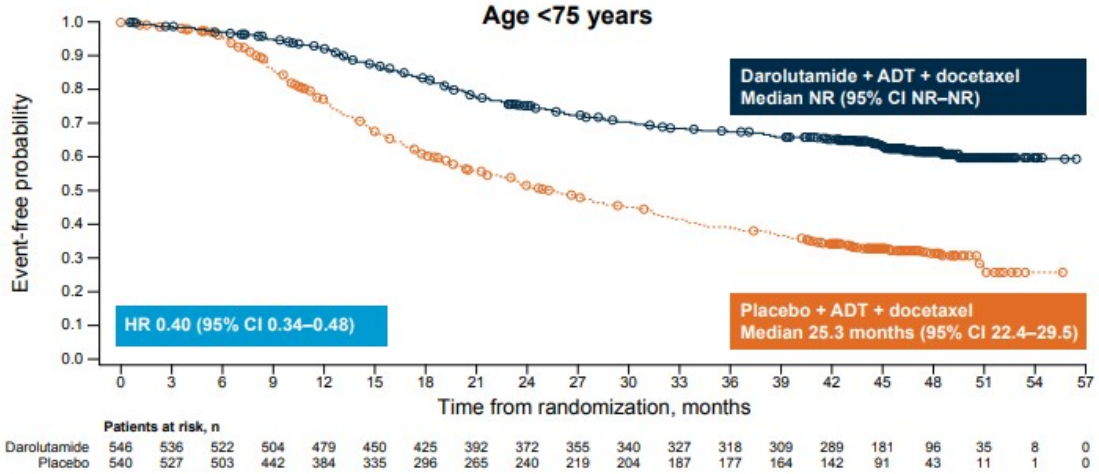
Time to mCRPC



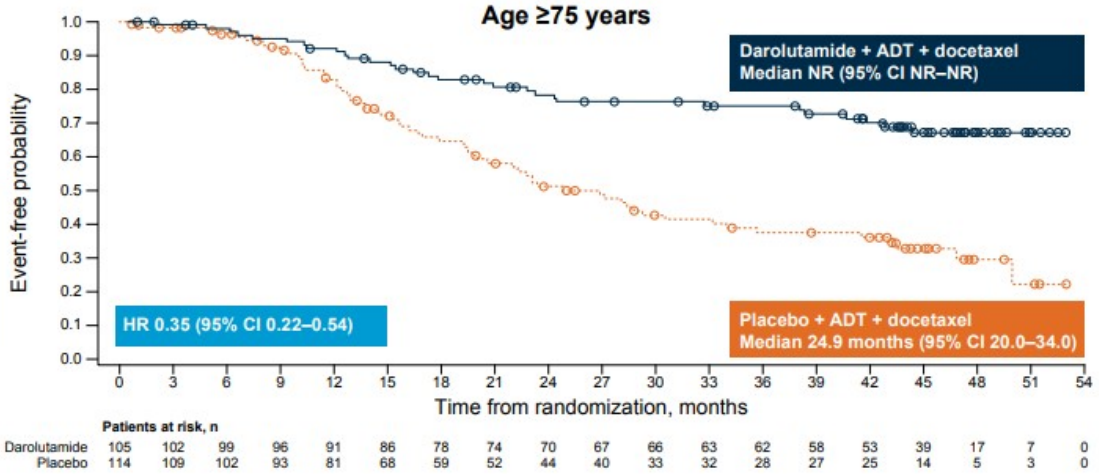
All patients: HR 0.36 (95% CI 0.30–0.42); *P*<0.001



Time to initiation of subsequent systemic antineoplastic therapy



All patients: HR 0.39 (95% CI 0.33–0.46); *P*<0.001



ADT, androgen deprivation therapy; CI, confidence interval; HR, hazard ratio; mCRPC, metastatic castration-resistant prostate cancer; NR, not reached.

Age-related efficacy and safety of darolutamide plus androgen-deprivation therapy (ADT) and docetaxel in patients with metastatic hormone-sensitive prostate cancer: A subgroup analysis of ARASENS [Joan Carles, Abstract 143]

- **FIRST SUBSEQUENT THERAPY**
  - Among patients who entered follow-up, a higher percentage in the placebo group received subsequent life-prolonging systemic therapy compared with the darolutamide group in the overall population, and this was consistent in both age groups
    - Abiraterone was the most frequently used subsequent therapy in both age groups, consistent with the overall population
    - Use of chemotherapy (docetaxel or cabazitaxel) as first subsequent therapy was less frequent in older versus younger patients

Use of first subsequent therapies by age subgroup

	Age <75 years		Age ≥75 years		All patients	
	Darolutamide (n=546)	Placebo (n=540)	Darolutamide (n=105)	Placebo (n=114)	Darolutamide (n=651)	Placebo (n=654)
Patients who entered active or long-term follow-up, n (%)*	265/546 (48.5)	413/540 (76.5)	50/105 (47.6)	82/114 (71.9)	315/651 (48.4)	495/654 (75.7)
Patients with first subsequent life-prolonging systemic antineoplastic therapy, n (%)†	152/265 (57.4)	314/413 (76.0)	27/50 (54.0)	60/82 (73.2)	179/315 (56.8)	374/495 (75.6)
Abiraterone	70/152 (46.1)	159/314 (50.6)	13/27 (48.1)	34/60 (56.7)	83/179 (46.4)	193/374 (51.6)
Enzalutamide	24/152 (15.8)	83/314 (26.4)	5/27 (18.5)	14/60 (23.3)	29 /179 (16.2)	97/374 (25.9)
Cabazitaxel	23/152 (15.1)	25/314 (8.0)	3/27 (11.1)	1/60 (1.7)	26/179 (14.5)	26/374 (7.0)
Docetaxel	23/152 (15.1)	37/314 (11.8)	3/27 (11.1)	8/60 (13.3)	26/179 (14.5)	45/374 (12.0)
Abiraterone or enzalutamide	94/152 (61.8)	242/314 (77.1)	18/27 (66.7)	48/60 (80.0)	112/179 (62.6)	290/374 (77.5)
Cabazitaxel or docetaxel	46/152 (30.3)	62/314 (19.7)	6/27 (22.2)	9/60 (15.0)	52/179 (29.1)	71/374 (19.0)

*Plus one patient who did not enter follow-up but received subsequent therapy. †Subsequent life-prolonging systemic antineoplastic therapies for prostate cancer include abiraterone, apalutamide, enzalutamide, docetaxel, cabazitaxel, radium-223, sipuleucel-T, and/or lutetium-177; 28 patients overall (darolutamide n=15, placebo n=13; aged <75 years subgroup n=22, aged ≥75 years subgroup n=6) received radium-223, sipuleucel-T, lutetium-177, and/or apalutamide as their first subsequent therapy.
Patients may have received more than one therapy as their first subsequent therapy.
ADT, androgen deprivation therapy.

Age-related efficacy and safety of darolutamide plus androgen-deprivation therapy (ADT) and docetaxel in patients with metastatic hormone-sensitive prostate cancer: A subgroup analysis of ARASENS [Joan Carles, Abstract 143]

- **SAFETY**
  - The incidence, type, and severity of TEAEs were generally similar between darolutamide and placebo, with slightly higher frequencies in patients aged ≥75 years, consistent with more comorbidities in this subgroup
    - In both age subgroups, the proportion of patients who discontinued darolutamide or placebo due to TEAEs was low

TEAEs by age subgroup

Treatment-emergent adverse events, n (%)	Age <75 years		Age ≥75 years		All patients	
	Darolutamide (n=546)	Placebo (n=537)	Darolutamide (n=106)	Placebo (n=113)	Darolutamide (n=652*)	Placebo (n=650*)
Any TEAE	544 (99.6)	531 (98.9)	105 (99.1)	112 (99.1)	649 (99.5)	643 (98.9)
Grade 3 or 4 TEAEs	353 (64.7)	334 (62.2)	78 (73.6)	79 (69.9)	431 (66.1)	413 (63.5)
Most common (≥5% in overall population)						
Neutropenia†	178 (32.6)	176 (32.8)	42 (39.6)	46 (40.7)	220 (33.7)	222 (34.2)
Febrile neutropenia	36 (6.6)	37 (6.9)	15 (14.2)	11 (9.7)	51 (7.8)	48 (7.4)
Hypertension	32 (5.9)‡	15 (2.8)	10 (9.4)	6 (5.3)	42 (6.4)‡	21 (3.2)
Anemia	24 (4.4)	21 (3.9)	7 (6.6)	12 (10.6)	31 (4.8)	33 (5.1)
Serious TEAEs	234 (42.9)	214 (39.9)	58 (54.7)	61 (54.0)	292 (44.8)	275 (42.3)
TEAEs leading to discontinuation of						
Darolutamide or placebo	72 (13.2)	49 (9.1)	16 (15.1)	20 (17.7)	88 (13.5)	69 (10.6)
Docetaxel	39 (7.1)	44 (8.2)	13 (12.3)	23 (20.4)	52 (8.0)	67 (10.3)

*Safety analysis set: three patients underwent randomization and never received study treatment; all three patients were in the placebo group. One patient assigned to the placebo group received darolutamide and is included in the darolutamide group of the safety analysis set. †Grouped term (includes leukopenia, neutropenia, decreased neutrophil count, and decreased white-cell count). ‡In addition to the grade 3/4 events, one patient had a grade 5 event of hypertension.ADT, androgen deprivation therapy; MedDRA, Medical Dictionary for Regulatory Activities; TEAE, treatment-emergent adverse event.

Age-related efficacy and safety of darolutamide plus androgen-deprivation therapy (ADT) and docetaxel in patients with metastatic hormone-sensitive prostate cancer: A subgroup analysis of ARASENS [Joan Carles, Abstract 143]

SAFETY (CONT'D)

- Incidences of the most common grade 3/4 TEAEs, including neutropenia and anemia, were slightly higher in the older age subgroup and occurred most frequently during overlapping docetaxel treatment
- TEAEs commonly associated with AR pathway inhibitors occurred at similar incidences between treatment groups in both age subgroups

TEAEs commonly associated with androgen receptor pathway inhibition by age subgroup

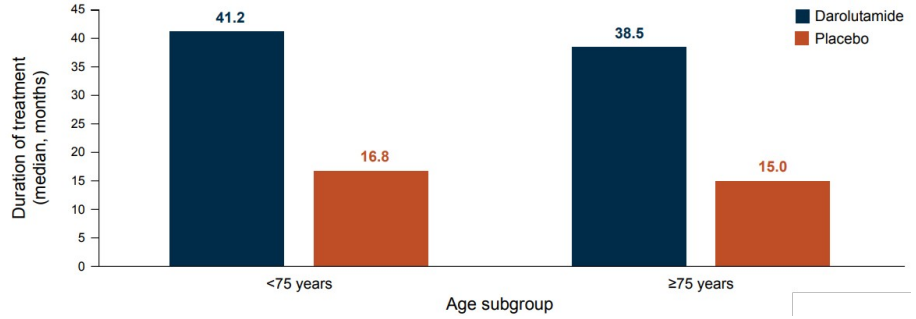
Adverse events	Age <75 years				Age ≥75 years				All patients			
	Darolutamide (n=546)		Placebo (n=537)		Darolutamide (n=106)		Placebo (n=113)		Darolutamide (n=652*)		Placebo (n=650*)	
	n (%)	EAIR	n (%)	EAIR	n (%)	EAIR	n (%)	EAIR	n (%)	EAIR	n (%)	EAIR
Fatigue	181 (33.2)	12.4	173 (32.2)	17.2	35 (33.0)	12.9	41 (36.3)	21.0	216 (33.1)	12.5	214 (32.9)	17.8
Rash†	95 (17.4)	6.5	70 (13.0)	7.0	13 (12.3)	4.8	18 (15.9)	9.2	108 (16.6)	6.2	88 (13.5)	7.3
Hypertension‡	75 (13.7)	5.1	50 (9.3)	5.0	14 (13.2)	5.1	10 (8.8)	5.1	89 (13.7)	5.1	60 (9.2)	5.0
Bone fracture§	40 (7.3)	2.7	31 (5.8)	3.1	9 (8.5)	3.3	2 (1.8)	1.0	49 (7.5)	2.8	33 (5.1)	2.7
Fall	31 (5.7)	2.1	20 (3.7)	2.0	12 (11.3)	4.4	10 (8.8)	5.1	43 (6.6)	2.5	30 (4.6)	2.5
Mental impairment disorders‡	17 (3.1)	1.2	10 (1.9)	1.0	6 (5.7)	2.2	5 (4.4)	2.6	23 (3.5)	1.3	15 (2.3)	1.2

*Safety analysis set: three patients underwent randomization and never received study treatment; all three patients were in the placebo group. One patient assigned to the placebo group received darolutamide and is included in the darolutamide group of the safety analysis set. †Includes MedDRA terms: rash, maculopapular rash, drug eruption, pruritic rash, erythematous rash, macular rash, popular rash, follicular rash, pustular rash, and vesicular rash. ‡MedDRA High-Level Group Term. §Excludes pathological fractures.

DURATION OF TREATMENT

- Duration of treatment was consistently longer with darolutamide vs placebo (Figure 5)
- Most patients completed 6 cycles of docetaxel:
  - <75 years: darolutamide 89%, placebo 88%
  - ≥75 years: darolutamide 80%, placebo 76%

Median duration of treatment



ADT, androgen deprivation therapy; AR, androgen receptor; EAIR, exposure-adjusted incidence rate (defined as the number of patients with a given event divided by the total darolutamide/placebo treatment duration of all patients in years; expressed as 100 patient years [PY]); MedDRA, Medical Dictionary for Regulatory Activities; TEAE, treatment-emergent adverse event.

Age-related efficacy and safety of darolutamide plus androgen-deprivation therapy (ADT) and docetaxel in patients with metastatic hormone-sensitive prostate cancer: A subgroup analysis of ARASENS [Joan Carles, Abstract 143]

Conclusion:

- Patients with mHSPC benefited from darolutamide + ADT + docetaxel irrespective of age (<75 years and ≥75 years), with improvements in OS, time to mCRPC, and time to initiation of subsequent therapy compared with placebo + ADT + docetaxel, consistent with the overall population
- Darolutamide was well tolerated in both age subgroups, with most patients (≥80%) able to receive the full 6 cycles of docetaxel and with similar incidences of TEAEs compared with placebo, including TEAEs commonly associated with ARIs
- The results support the use of darolutamide in combination with ADT and docetaxel in all patients with mHSPC, regardless of age

ADT, androgen deprivation therapy; ARI, androgen receptor inhibitor; mCRPC, metastatic castration-resistant prostate cancer; mHSPC, metastatic hormone-sensitive prostate cancer; OS, overall survival; TEAE, treatment-emergent adverse event.

Concomitant granulocyte colony stimulating factor use in maintaining an efficacious dose and safe delivery of docetaxel in combination with darolutamide in patients with metastatic hormone-sensitive prostate cancer: ARASENS, a phase 3 study

Michael Ong, Hiroyoshi Suzuki, Matthew Smith, Bertrand Tombal, Maha Hussain, Fred Saad, Karim Fizazi, Frank Verholen, Ha Pham, Shankar Srinivasan, Aly-Khan A. Lalani

ASCO GU 2025, Abstract 152

Concomitant granulocyte colony stimulating factor use in maintaining an efficacious dose and safe delivery of docetaxel in combination with darolutamide in patients with metastatic hormone-sensitive prostate cancer: ARASENS, a phase 3 study [Michael Ong, Abstract 152]

- **INTRODUCTION**
  - Both ARASENS and PEACE-1 used granulocyte colony stimulating factor (G-CSF) to mitigate the risk of neutropenic complications, but the role and frequency of primary versus secondary G-CSF prophylaxis is debated
- **OBJECTIVE**
  - We report the impact of docetaxel dose intensity and G-CSF use on the safety and efficacy of the ARASENS triplet regimen
- **METHODS**
  - Patients were randomized to receive darolutamide 600 mg orally twice daily or placebo, with ADT + docetaxel
  - Baseline characteristics, G-CSF use, safety, overall survival (OS), and time to prostate-specific antigen (PSA) progression at week 24 (for consistency with prior studies) were analyzed according to docetaxel relative dose intensity (RDI; ≤85% vs >85%), defined as the ratio of docetaxel dose received vs protocol-defined full planned dose (75 mg/m^2 × 6 cycles)
  - In total, 1305 patients were available for analysis in ARASENS; of these, 1279 received docetaxel therapy and 1273 had docetaxel RDI data
- **PATIENT BASELINE CHARACTERISTICS**
  - Aside from geographic difference, patient demographics and baseline disease characteristics were mostly consistent between the docetaxel RDI ≤85% and >85% subgroups in both darolutamide and placebo treatment groups

Patient disease characteristics

Demographics and baseline characteristics		Darolutamide		Placebo		Overall ARASENS population*	
		DOC RDI ≤85% (n=69)	DOC RDI >85% (n=568)	DOC RDI ≤85% (n=74)	DOC RDI >85% (n=562)	Darolutamide (n=651)	Placebo (n=654)
Gleason score at initial diagnosis, n (%)	<8	8 (11.6)	114 (20.1)	12 (16.2)	102 (18.1)	122 (18.7)	118 (18.0)
	≥8	59 (85.5)	433 (76.2)	61 (82.4)	442 (78.6)	505 (77.6)	516 (78.9)
	Missing	2 (2.9)	21 (3.7)	1 (1.4)	18 (3.2)	24 (3.7)	20 (3.1)
ECOG PS, n (%)†	0	54 (78.3)	400 (70.4)	58 (78.4)	394 (70.1)	466 (71.6)	462 (70.6)
	1	15 (21.7)	168 (29.6)	16 (21.6)	166 (29.5)	185 (28.4)	190 (29.1)
Median PSA concentration, ng/mL (range)		16.4 (0.2–2648.8)	31.4 (0.0–9219)	30.3 (0.0–2430)	22.7 (0.0–11,947)	30.3 (0.0–9219)	24.2 (0.0–11,947)
Median ALP, U/L (range)		150 (46–1975)	148 (40–4793)	135 (47–3573)	141 (36–4854)	148 (40–4885)	140 (36–7680)
ALP category, n (%)	<ULN	32 (46.4)	253 (44.5)	35 (47.3)	247 (44.0)	290 (44.5)	291 (44.5)
	≥ULN	37 (53.6)	315 (55.5)	39 (52.7)	315 (56.0)	361 (55.5)	363 (55.5)
De novo/ recurrent disease, n (%)	*de novo*	57 (82.6)	487 (85.7)	65 (87.8)	485 (86.3)	558 (85.7)	566 (86.5)
	Recurrent	11 (15.9)	75 (13.2)	9 (12.2)	72 (12.8)	86 (13.2)	82 (12.5)
	Missing	1 (1.4)	6 (1.1)	0	5 (0.9)	7 (1.1)	6 (0.9)

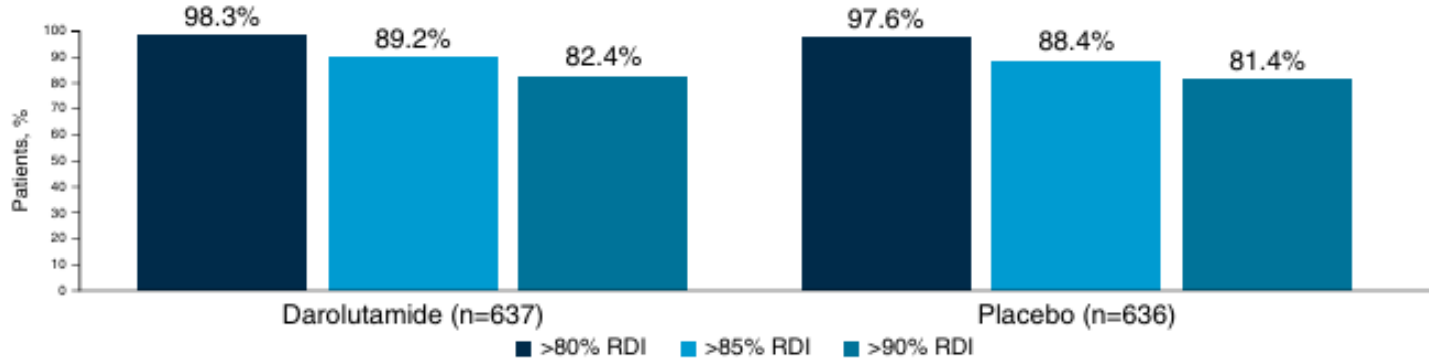
*One patient who was randomized to placebo but received darolutamide was included in the placebo group for baseline characteristics and efficacy analyses and in the darolutamide group for safety analyses. †Percentages in the placebo DOC RDI >85% and overall population placebo treatment groups do not total 100% due to missing ECOG PS data for two patients.
ADT, androgen deprivation therapy; ALP, alkaline phosphatase; DOC, docetaxel; ECOG PS, Eastern Cooperative Oncology Group performance status; G-CSF, granulocyte colony stimulating factor; OS, overall survival; PSA, prostate-specific antigen; RDI, relative dose intensity; ULN, upper limit of normal.

Concomitant granulocyte colony stimulating factor use in maintaining an efficacious dose and safe delivery of docetaxel in combination with darolutamide in patients with metastatic hormone-sensitive prostate cancer: ARASENS, a phase 3 study [Michael Ong, Abstract 152]

RDI IN PATIENTS RECEIVING DAROLUTAMIDE OR PLACEBO

- In both darolutamide and placebo treatment groups, >97% of patients received an efficacious dose of docetaxel (RDI >80%) and over 88% received RDI >85%, indicating that darolutamide does not have an impact on received docetaxel dose intensity

Proportion of patients receiving docetaxel >80%, >85%, and >90% RDI



G-CSF USE AND DOCETAXEL DOSE MODIFICATION

- Overall, 800/1279 (63%) patients required docetaxel dose modification, and 556/1279 (43%) patients required G-CSF, mainly for secondary prophylaxis (>98%)
  - 376/800 (47%) of patients with docetaxel dose modification received G-CSF
- The addition of darolutamide did not increase G-CSF use or docetaxel dose modification

Proportion of patients treated with docetaxel who received G-CSF

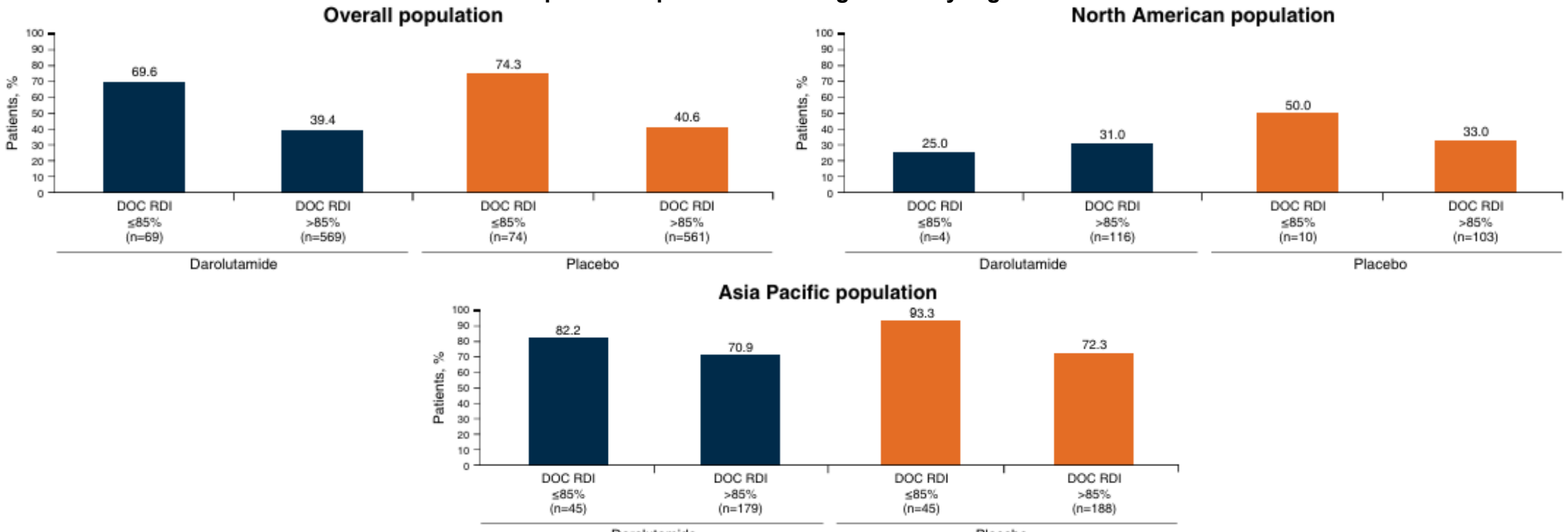
G-CSF use, n (%)	DOC dose modification subgroup		Overall population	
	Darolutamide N=391	Placebo N=409	Darolutamide N=642	Placebo N=637
With concomitant G-CSF	186 (47.6%)	190 (46.5%)	272 (42.4%)	284 (44.6%)
Primary G-CSF prophylaxis	2 (0.5)	2 (0.5)	3 (0.5)	2 (0.3)
Secondary G-CSF prophylaxis	184 (47.1%)	188 (46.0%)	269 (41.9%)	282 (43.3%)
Without concomitant G-CSF	205 (52.4%)	219 (53.5%)	370 (57.6%)	353 (55.4%)

DOC, docetaxel; G-CSF, granulocyte colony stimulating factor; RDI, relative dose intensity.

Concomitant granulocyte colony stimulating factor use in maintaining an efficacious dose and safe delivery of docetaxel in combination with darolutamide in patients with metastatic hormone-sensitive prostate cancer: ARASENS, a phase 3 study [Michael Ong, Abstract 152]

- **G-CSF USE BY REGION**
  - Overall and in the Asia Pacific region, a higher rate of G-CSF use was observed for patients with lower vs higher RDI (≤85% vs >85%)
  - G-CSF use was highest in the Asia Pacific patient population compared with the North American and overall populations
    - G-CSF was primarily used for secondary prophylaxis, independent of region

Proportion of patients receiving G-CSF by region*,†



*G-CSF use as primary prophylaxis: overall population – da[illegible] group [illegible], DOC RDI >85% 0.2%; Asia Pacific region – darolutamide DOC RDI ≤85% 0, >85% 1.1%; placebo DOC RDI ≤85% 2.2%, DOC RDI >85% 0.5%. G-CSF was not used for primary prophylaxis in any patients in the North American region.

†G-CSF as secondary prophylaxis: overall population – darolutamide group DOC RDI ≤85% 69.6%, DOC RDI >85% 38.8%; placebo group DOC RDI ≤85% 73.0%, DOC RDI >85% 40.5%; North American region – darolutamide group DOC RDI ≤85% 25.0%, DOC RDI >85% 31.0%, placebo group DOC RDI ≤85% 50.0%, DOC RDI >85% 33.0%; Asia Pacific region – darolutamide group DOC RDI ≤85% 82.2%, DOC RDI >85% 69.8%; placebo group DOC RDI ≤85% 91.1%, DOC RDI >85% 71.8%.

DOC, docetaxel; G-CSF, granulocyte colony stimulating factor; RDI, relative dose intensity.

Concomitant granulocyte colony stimulating factor use in maintaining an efficacious dose and safe delivery of docetaxel in combination with darolutamide in patients with metastatic hormone-sensitive prostate cancer: ARASENS, a phase 3 study [Michael Ong, Abstract 152]

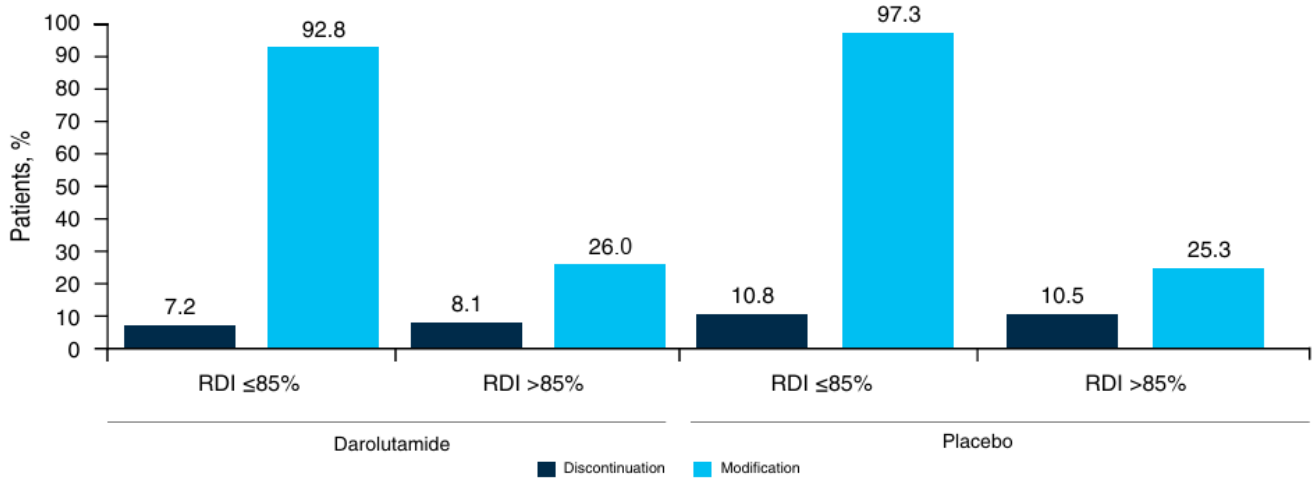
- **OVERALL SURVIVAL AND TIME TO PSA PROGRESSION BY DOCETAXEL RDI SUBGROUP**
  - OS was similar in both treatment groups in patients who achieved docetaxel RDI ≤85% or >85% at week 24:
    - Darolutamide group: Median OS was not reached (NR) for both ≤85% vs >85% docetaxel RDI subgroups (hazard ratio [HR] 1.41, 95% confidence interval [CI]: 0.88–2.26)
    - Placebo group: Median OS was NR vs 45.8 months for the ≤85% vs >85% docetaxel RDI subgroups, respectively (HR 1.17, 95% CI: 0.80–1.71)
  - Time to PSA progression (TTPSA) was also similar between the subgroups with docetaxel RDI ≤85% or >85% at week 24 in both treatment groups:
    - Darolutamide group: Median TTPSA was NR for both ≤85% vs >85% docetaxel RDI subgroups (HR 1.28, 95% CI: 0.71–2.33)
    - Placebo group: Median TTPSA was 21.7 vs 19.0 months for the ≤85% vs >85% docetaxel RDI subgroups, respectively (HR 1.18, 95% CI: 0.81–1.73)

CI, confidence interval; HR, hazard ratio; NR, not reached; OS, overall survival; PSA, prostate-specific antigen; RDI, relative dose intensity; TTPSA, time to PSA progression.

Concomitant granulocyte colony stimulating factor use in maintaining an efficacious dose and safe delivery of docetaxel in combination with darolutamide in patients with metastatic hormone-sensitive prostate cancer: ARASENS, a phase 3 study [Michael Ong, Abstract 152]

- **SAFETY**
  - TEAEs leading to docetaxel dose modification were higher with docetaxel RDI ≤85% vs RDI >85%
  - Incidences of grade ≥3 TEAEs, including neutropenia and febrile neutropenia, were higher for patients with RDI ≤85% vs RDI >85%
  - Almost all instances (87/97, 91.3%) of febrile neutropenia were grade 3
  - Rates of docetaxel discontinuation were low in all groups, indicating that appropriate use of G-CSF allows effective docetaxel administration and that darolutamide does not impact docetaxel tolerability

TEAEs leading to docetaxel discontinuation and dose modification*,†



*Modifications include interruption/delay and reductions.
†Discontinuation of docetaxel due to AE was calculated where action taken was checked as 'drug withdrawn'.

Rates of grade 3/4 febrile neutropenia and neutropenia

Grade 3/4 events, n (%)	Darolutamide		Placebo	
	DOC RDI ≤85% n=69	DOC RDI >85% n=569	DOC RDI ≤85% n=74	DOC RDI >85% n=561
Febrile neutropenia	18 (21.6)	32 (5.6)	13 (17.6)	34 (6.1)
Neutropenia‡	46 (66.7)	169 (29.7)	52 (70.3)	167 (29.8)

‡Grouped: neutrophil count decreased, white blood cell count decreased, neutropenia, and leukopenia.

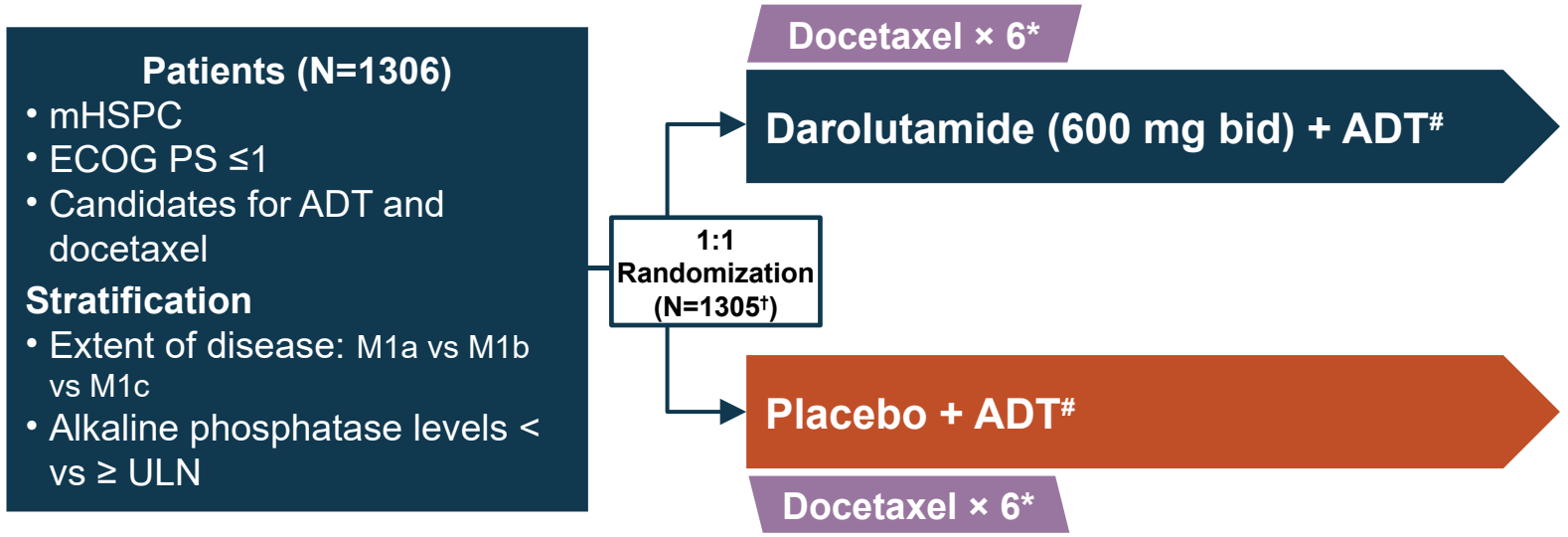
AE, adverse event; DOC, docetaxel; G-CSF, granulocyte colony stimulating factor; RDI, relative dose intensity; TEAE, treatment-emergent adverse event.

THANK YOU

Overall Survival With Darolutamide vs Placebo in Combination With Androgen-Deprivation Therapy (ADT) and Docetaxel: A Sensitivity Analysis From ARASENS Accounting for Subsequent Therapy

Shore ND, et al. Poster presented at: ASCO Genitourinary Symposium; San Francisco, USA. January 25-27, 2024. Abstract #166

This Post Hoc Sensitivity Analysis of ARASENS Evaluated The Impact of Subsequent Therapy on OS to Verify the Robustness of the Primary Analysis



Primary endpoint: OS

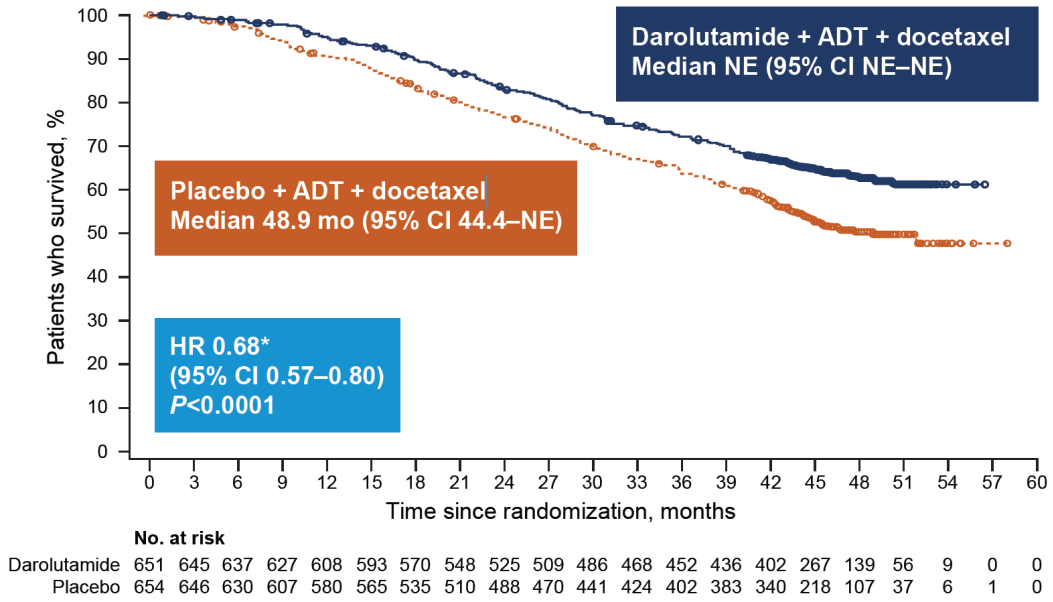
Post hoc sensitivity analysis: In addition to death, initiation of subsequent systemic antineoplastic therapy was counted as an event in censored patients who entered follow-up and were still alive at the end of follow-up

*Starting ≤6 weeks after start of study drug at 75 mg/m^2 / 3 weeks, 6 cycles (in combination with prednisone/prednisolone at the discretion of the investigator).
#Investigators' choice (including orchiectomy) starting ≤12 weeks before randomization
†One enrolled patient was excluded from all analysis sets because of Good Clinical Practice violations.
ADT, androgen deprivation therapy; bid, twice a day; ECOG PS, Eastern Cooperative Oncology Group performance status; mHSPC, metastatic hormone-sensitive prostate cancer; OS, overall survival; ULN, upper limit of normal.
Shore ND, et al. Poster presented at: ASCO Genitourinary Symposium; San Francisco, USA. January 25-27, 2024. Abstract #166.

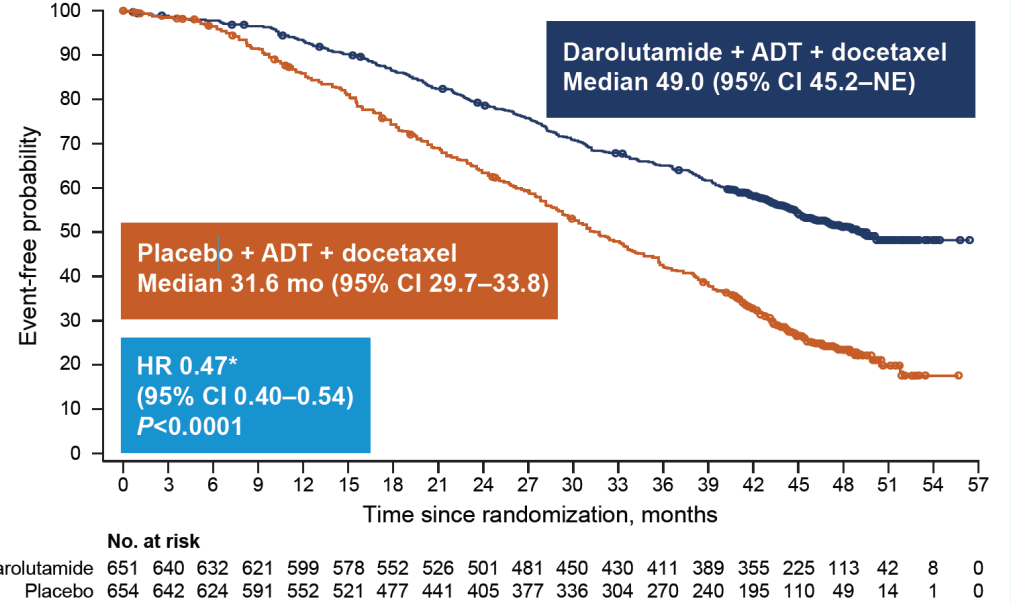
The Post Hoc Sensitivity Analysis Was Consistent With and Supportive of the Primary OS Analysis

- In the primary OS analysis, the darolutamide combination significantly improved OS by reducing the risk of death by 32.5% (HR 0.68) compared with ADT + docetaxel[1]
  - The primary analysis was performed after 533 patients had died (darolutamide n=229/651, 35%; placebo n=304/654, 46%)
- In the post hoc sensitivity analysis, 776 patients (darolutamide n=300/651, 46%; placebo n=476/654, 73%) were counted as having an event[2]

Primary OS analysis[1]



Post hoc sensitivity analysis counting use of subsequent therapy as an event in censored patients[2]



Footnotes, abbreviations, and references are in the slide notes.

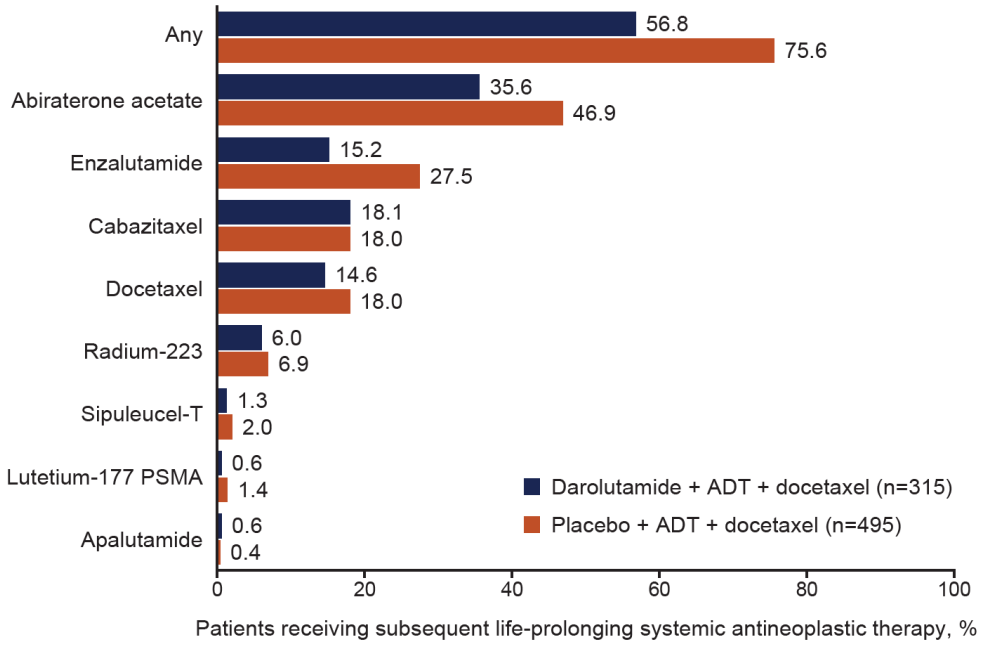
More Patients in the Placebo Group Received Subsequent Life-Prolonging Therapies Compared With the Darolutamide Group[1,2]

// The darolutamide combination with docetaxel significantly prolonged time to first subsequent antineoplastic therapy compared with placebo + ADT with docetaxel: HR 0.39, 95% CI 0.33-0.46; *P*<0.001

Subsequent therapy

Subsequent therapy	Darolutamide group n/N (%)	Placebo group n/N (%)
Patients receiving ongoing study treatment at the data cutoff date (Oct 25, 2021)	299/651 (46%)	125/654 (19%)
Patients entering follow-up and eligible for subsequent therapy*	315/651 (48%)	495/654 (76%)
Patients receiving subsequent systemic antineoplastic therapy	219/651 (34%)	395/654 (60%)

Subsequent life-prolonging systemic antineoplastic therapies in patients who entered follow-up*,†



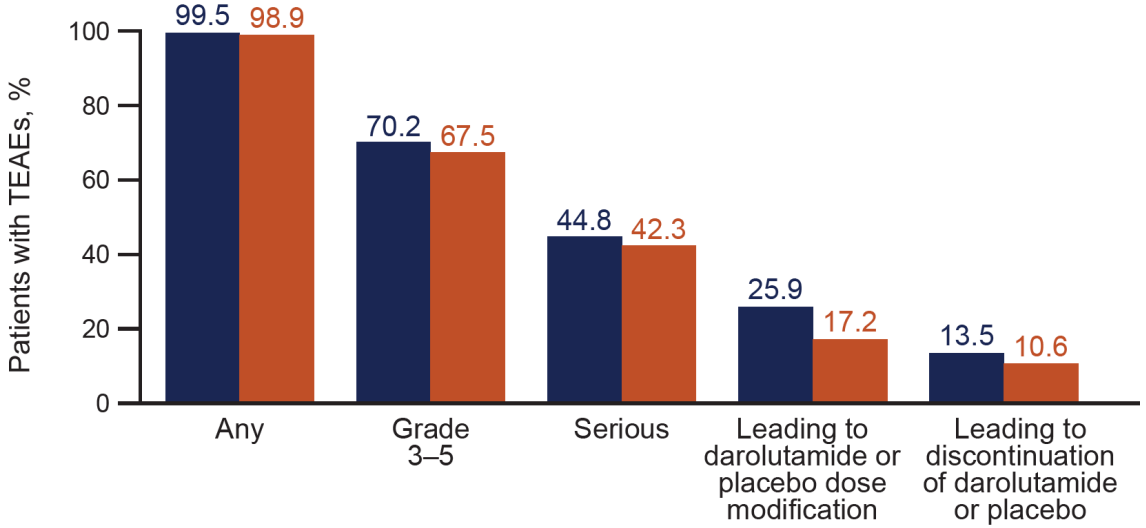
The OS benefit of darolutamide was achieved despite a higher proportion of patients receiving subsequent life-prolonging therapies in the placebo group vs the darolutamide group[1]

Footnotes, abbreviations, and references are in the slide notes.

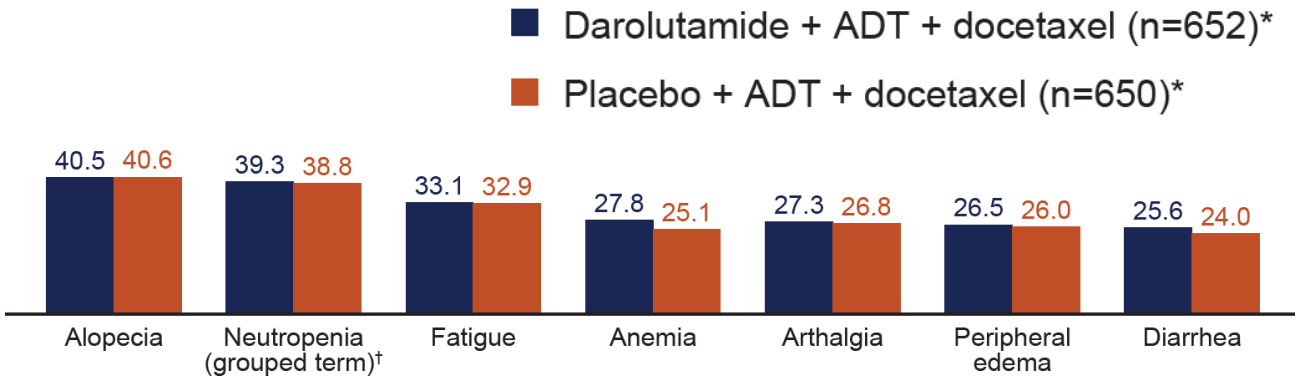
Incidences of TEAEs Were Similar Between Darolutamide and Placebo Groups[1,2]

- At the data cutoff date for the primary analysis, the median treatment duration was longer in the darolutamide group (41.0 months) than in the placebo group (16.7 months)
- Similarly, the cumulative incidences of most TEAEs commonly associated with ARis were low and similar between groups[1,2]

Overview of TEAEs



Most frequently reported TEAEs (≥25% of patients in either group)



Discontinuation of darolutamide or placebo due to TEAEs were similar between treatment groups (13.5% in the darolutamide group vs 10.6% of patients in the placebo group)

Footnotes, abbreviations, and references are in the slide notes.