Nubeqa (Darolutamide) – committed to change the treatment paradigm in prostate cancer

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Investor Webinar
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Head of Oncology, Bayer Pharmaceuticals

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Agenda

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Welcome

Oliver Maier

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2

Prepared Remarks

Christian Rommel

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3

Q&A

Cautionary statements regarding forward-looking information

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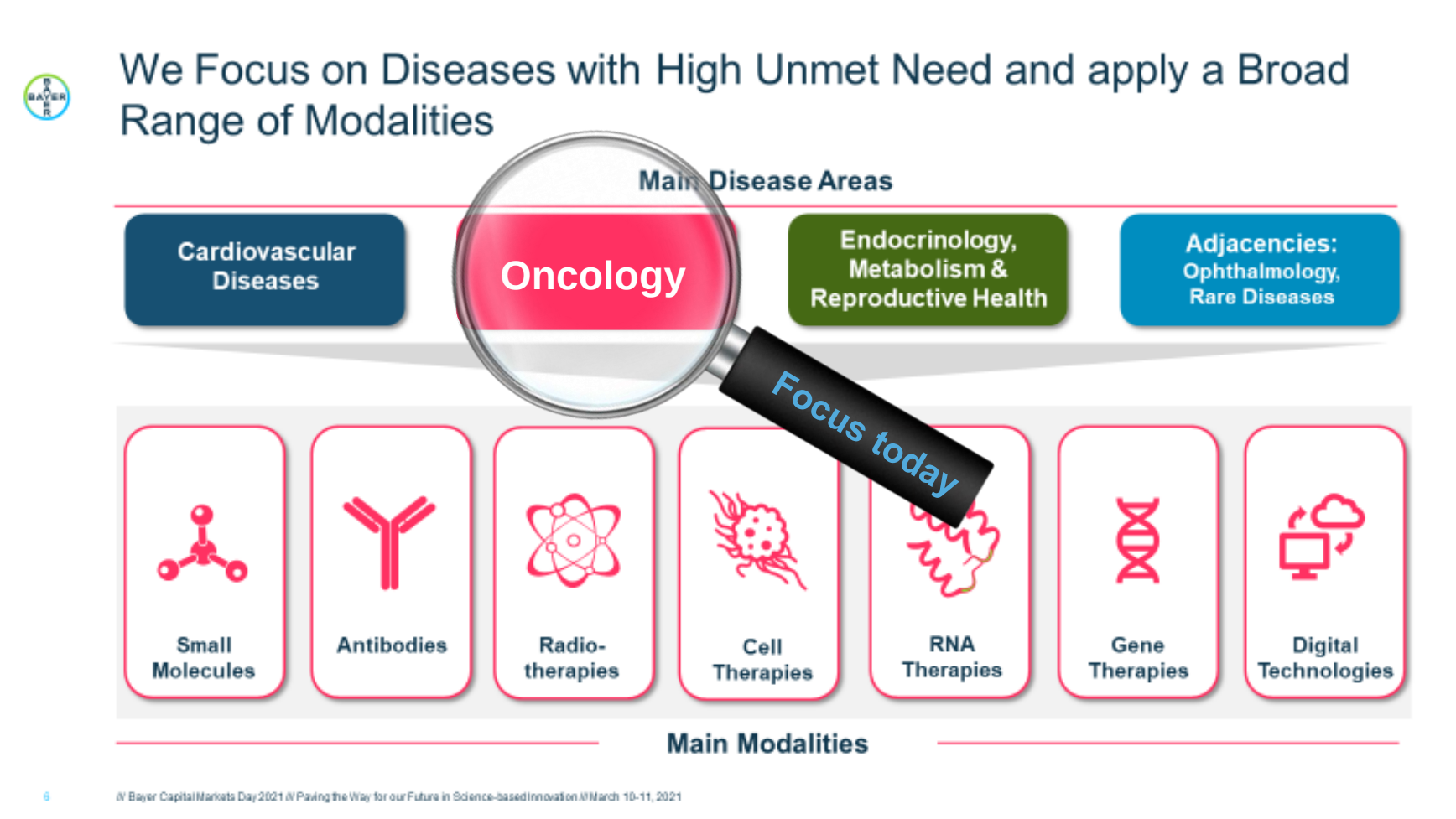
The company assumes no liability whatsoever to update these forward-looking statements or to conform them to future events or developments.

Oncology is a key focus of our Pharma growth strategy – our ambition is to be among top-10 players by 2030

Bayer Capital Markets Day March 2021:



Nubeqa is a key cornerstone to grow our Oncology franchise short-to-mid term

Launch Brands

VITRAKVI® (larotrectinib) 25-mg/100-mg CAPSULES 20-mg/mL ORAL SOLUTION

Main Inline Brands

Stivarga® (regorafenib) tablets

Xofigo® radium Ra 223 dichloride INJECTION

Aliqopa™ (copanlisib) 60 mg vial for injection

Nexavar® (sorafenib) tablets

Pipeline

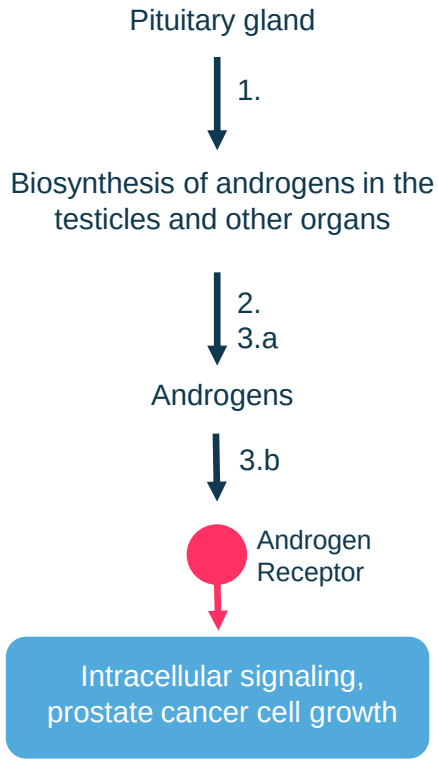
- Precision molecular oncology
- Targeted alpha therapies
- Next generation IO e.g. cell therapy

Drive short to mid-term growth

Lay foundation for future sustainable growth

Despite significant advancements in the treatment of prostate cancer patients there are still high unmet medical needs

Blocking androgen signaling



1. Chemical castration (ADT*): inhibition of hormonal signaling by the pituitary gland
2. Surgical castration (orchiectomy)
3. Anti-androgen therapy
   a. Inhibition of androgen biosynthesis
   b. Blocking of the androgen receptor (AR) with potent inhibitors (ARi)

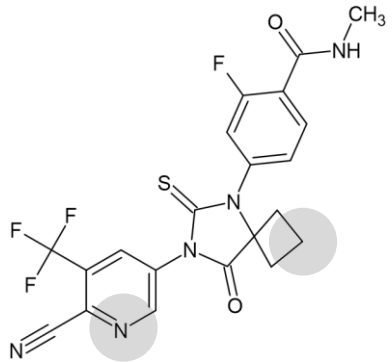
Key Unmet Needs

Prolong Survival	Extend overall survival (OS) and delaying the development of metastases
Maintain Lifestyle	Limit additional toxicity burden on often asymptomatic, fit, active men
Managing Comorbidities	Drug-drug interactions can lead to changes in the efficacy and safety of patient's ongoing medications

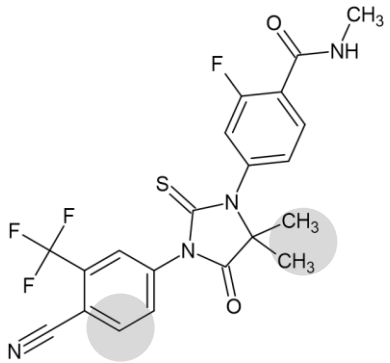
* ADT: androgen deprivation therapy

Darolutamide is an ARi with a structure that is associated with low blood-brain barrier penetration

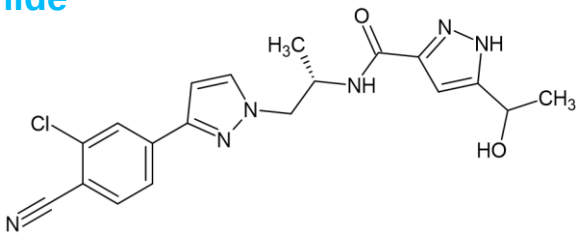
Apalutamide[3]



Enzalutamide[2]



Darolutamide[1]



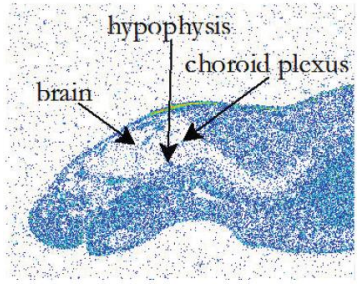
Structural difference of Darolutamide:

- more flexible structure[2-4], higher polarity
- increased hydrogen bond-forming potential

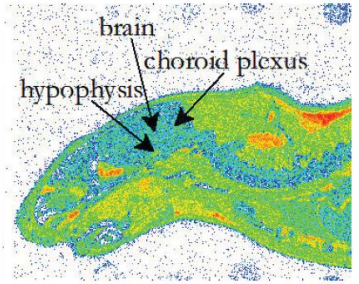
→ associated with low blood-brain barrier penetration[5]

Qualitative [^{14}C] brain distribution in rats[1]

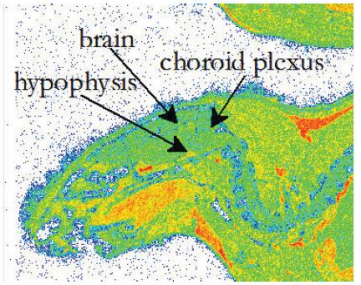
Darolutamide

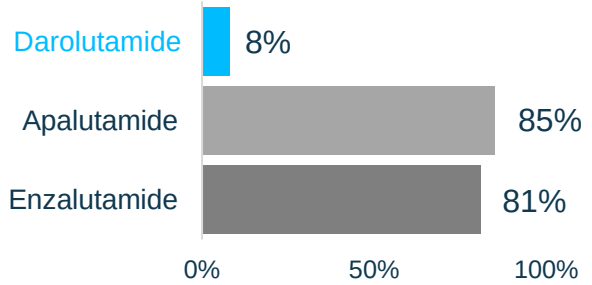


Apalutamide



Enzalutamide



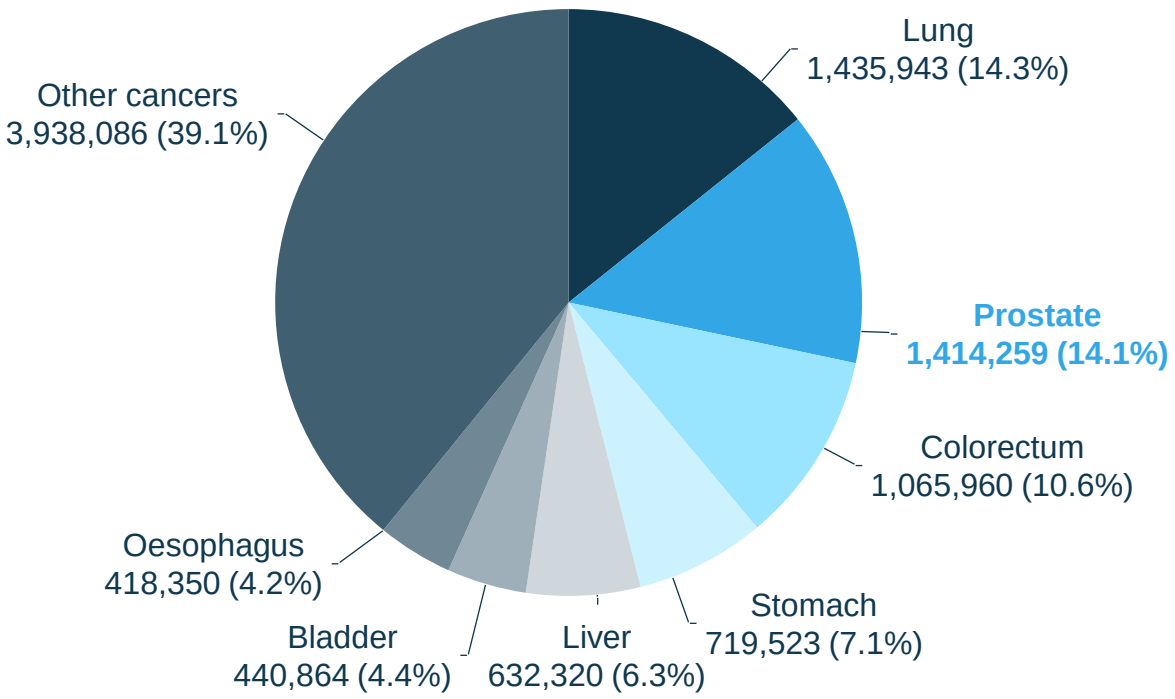


- Brain-to-blood ratios of Enzalutamide and Apalutamide were 10-fold higher than Darolutamide in preclinical models
- Concentration of Darolutamide in the brain was ~50-fold lower than Enzalutamide and 30-fold lower than Apalutamide

[1] Sandmann S, et al. ASCO Genitourinary Cancers Symposium. 2019, San Francisco. Abstract 156. [2] PubChem. Compound ID: 67171867. Accessed: January 31, 2019. [3] Pubchem. Compound ID: 15951529. Accessed: January 31, 2019. [4] PubChem. Compound ID: 24872560. Accessed: January 31, 2019. [5] Pajouhesh H, Lenz GR. NeuroRx. 2005;2(4):541-553. [6] [14C]DARO, [14C]ENZA, and [14C]APA at 8 h post-dosing in male Wistar rats based on whole-body autoradiography

Prostate cancer is at #2 of the most common cancer types in men worldwide with significant unmet medical need

Estimated number of new cases in 2020, worldwide, males, all ages

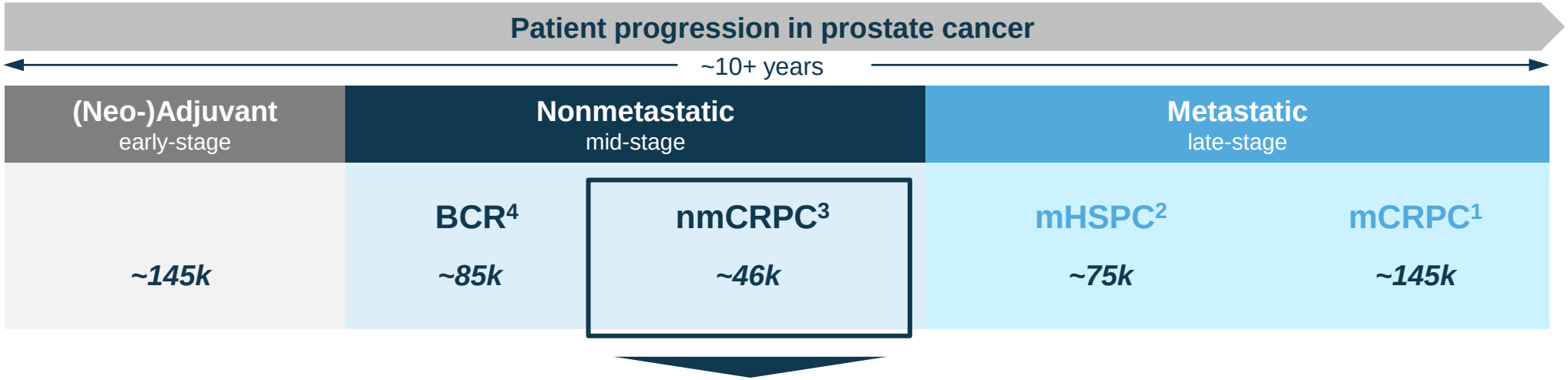


Source: International Agency for Research on Cancer, https://gco.iarc.fr/today/online-analysis-table

Characteristics of Prostate Cancer

- Usual onset: age >50 years
- Diagnostic method: PSA testing, tissue biopsy, medical imaging
- Prognosis: long-term survival in early-stage, significant higher morbidity in late-stage

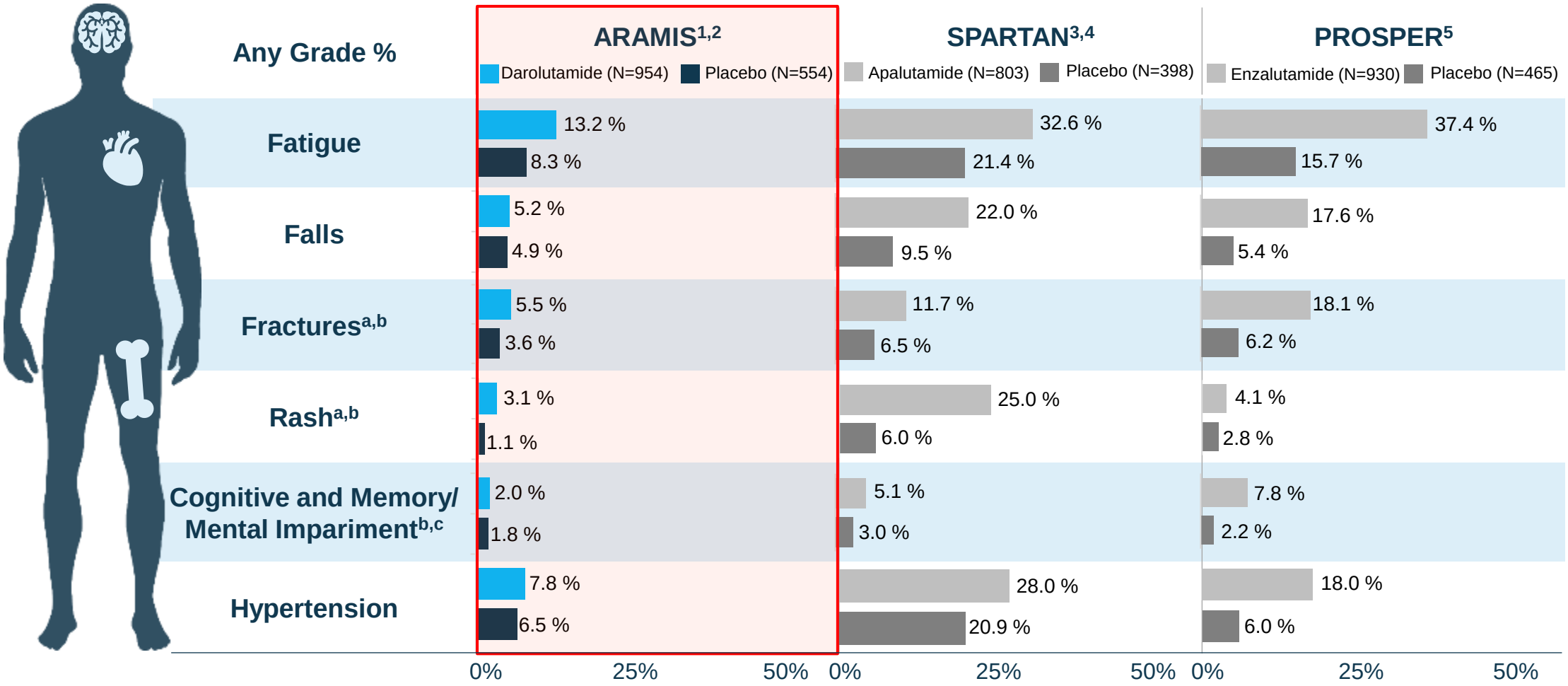
Results of ARAMIS study demonstrated already Nubeqa's strong clinical benefit for mid-stage prostate cancer patients



nmCRPC	Metastasis Free Survival (months)	Overall Survival (HR)
NUBEQA (darolutamide) *ARAMIS* 2019	**40.4** (18.4) **(22 months more than placebo)**	**0.69 (0.53-0.88)** p=0.003
Enzalutamide (PROSPER)	**36.6** (14.7) **(22 months more than placebo)**	**0.73 (0.61-0.89)** p=0.001
Apalutamide (SPARTAN)	**40.5** (16.2) **(24.3 months more than placebo)**	**0.78 (0.65-0.96)** p=0.0161

[1] Metastatic castration resistant prostate cancer [2] Metastatic hormone sensitive prostate cancer [3] Non-metastatic castration resistant prostate cancer [4] Biochemical relapse [5] G7: US, EU5, JP

On top of strong efficacy, ARAMIS also revealed Darolutamide's positive tolerability profile



[1] Fizazi K, et al. N Engl J Med. 2019;380:1235-1246 [2] Fizazi K, et al. J Clin Oncol. 2020; 38(suppl 15):5514. [3] Erleada® (apalutamide) [United States prescribing information]. Janssen Biotech, Inc.; 2019. [4] Small EJ, et al. J Clin Oncol. 2020;38(suppl 15):abstr 5516. [5] Sternberg CN, et al. N Engl J Med. 2020;382:2197-2206.

Based on its strong value proposition for patients and physicians, Nubeqa showed a successful market launch in nmCRPC

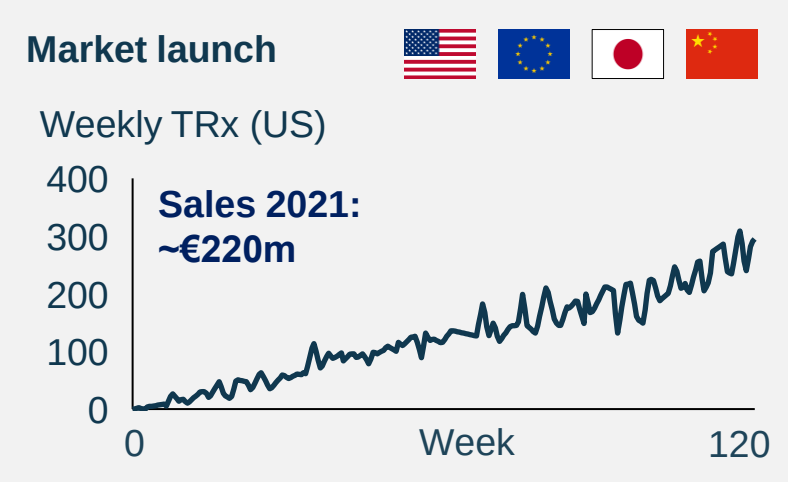
Rapid progress of global launches

- 32 commercial market launches + 24 private market / PAP launches
- Regulatory approval received in 65 countries
- 32 countries have pricing and reimbursement

External validation of differentiated profile

- Approval in China despite no local patients enrolled in the ARAMIS trial
- In Germany, NUBEQA the only 2nd generation ARi to be awarded considerable benefit in nmCRPC by IQWIG and GB-A
- Favorable customer perceptions support continued uptake in US

Strong launch performance



- Rapid adoption of managed health care lives covered in the US (92%)
- Prescriber recognition of differentiated profile, with positive repeat prescribers

ARASENS Study Design

Global, randomized, double-blind, placebo-controlled phase III study (NCT02799602)

Patients (N=1306)
- mHSPC
- ECOG PS 0 or 1
- Candidates for ADT and docetaxel

Stratification
- Extent of disease: M1a vs M1b vs M1c
- ALP < vs ≥ ULN

1:1 randomization (N=1305*)

Darolutamide 600 mg twice daily + ADT + Docetaxel × 6

Placebo twice daily + ADT + Docetaxel × 6

FPFV: Nov 2016
LPFV: June 2018

Primary analysis

Data cut-off Oct 25, 2021

Endpoints

Primary: OS

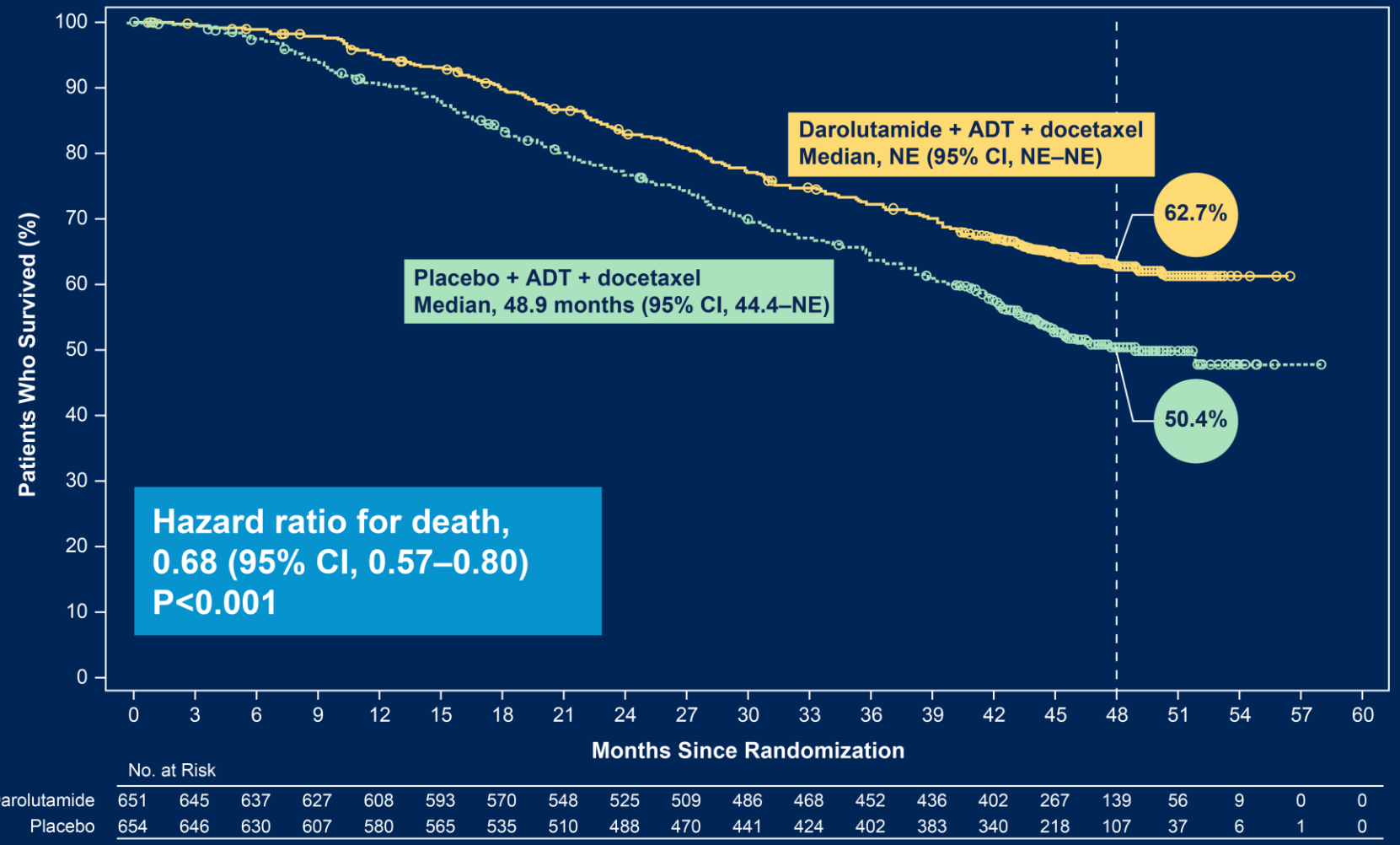
Secondary
- Time to CRPC
- Time to pain progression
- SSE-free survival
- Time to first SSE
- Time to initiation of subsequent systemic antineoplastic therapy
- Time to worsening of disease-related physical symptoms
- Time to initiation of opioid use for ≥7 consecutive days
- Safety

- The primary analysis was planned to occur after ~509 deaths
- Secondary efficacy endpoints were tested hierarchically

*One enrolled patient was excluded from all analysis sets because of Good Clinical Practice violations. ALP, alkaline phosphatase; CRPC, castration-resistant prostate cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; FPFV, first patient first visit; LPFV, last patient first visit; M1a, nonregional lymph node metastases only; M1b, bone metastases ± lymph node metastases; M1c, visceral metastases ± lymph node or bone metastases; Q3W, every 3 weeks; SSE, symptomatic skeletal event; ULN, upper limit of normal.

ARASENS Primary Endpoint*: Overall Survival

Darolutamide significantly reduced the risk of death by 32.5%



*Primary analysis occurred after 533 deaths (darolutamide, 229; placebo, 304). CI, confidence interval; NE, not estimable.

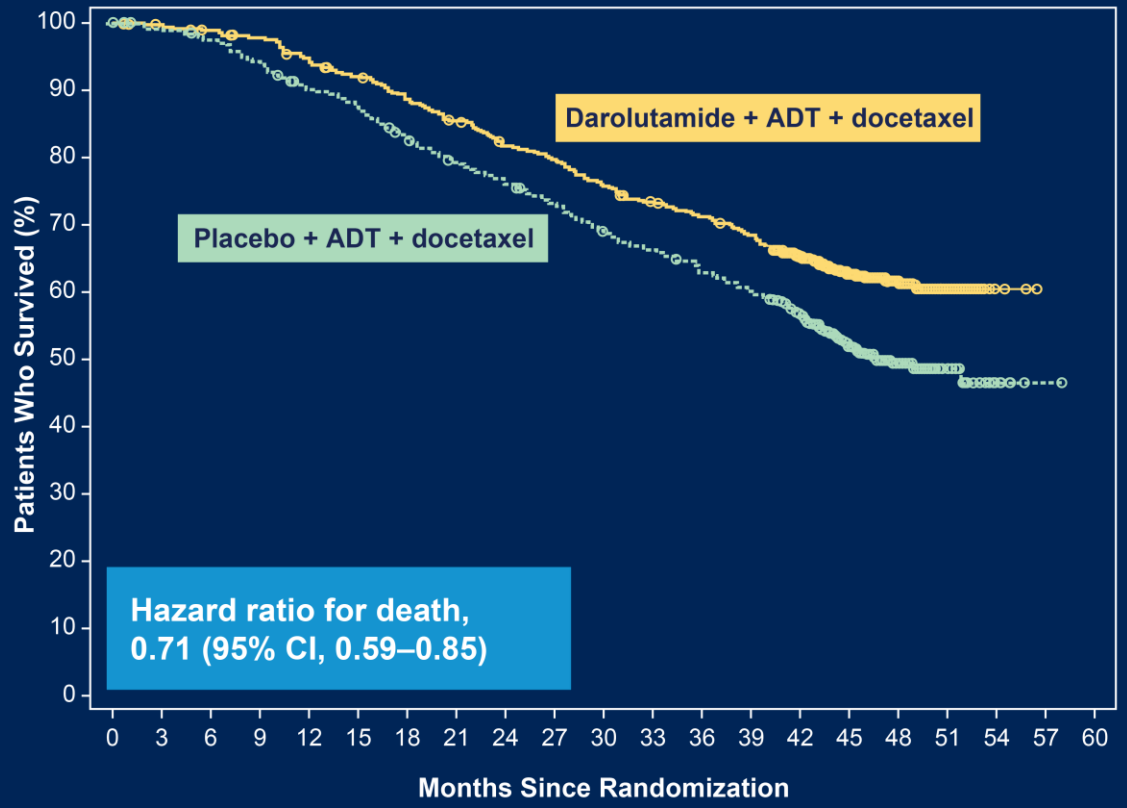
Subsequent Life-Prolonging Therapies

Subsequent life-prolonging therapy	Darolutamide + ADT + docetaxel (n=315*)	Placebo + ADT + docetaxel (n=495*)
No. (%) of patients with subsequent life-prolonging therapy	179 (56.8)	374 (75.6)†
Abiraterone acetate	112 (35.6)	232 (46.9)
Enzalutamide	48 (15.2)	136 (27.5)
Cabazitaxel	57 (18.1)	89 (18.0)
Docetaxel	46 (14.6)	89 (18.0)
Radium-223	19 (6.0)	34 (6.9)
Sipuleucel-T	4 (1.3)	10 (2.0)
Lutetium-177 PSMA	2 (0.6)	7 (1.4)
Apalutamide	2 (0.6)	2 (0.4)

*The denominators are the number of patients who entered follow-up. Patients could receive more than one subsequent life-prolonging therapy.
†66% of patients in the placebo group received subsequent life-prolonging therapy with an AR pathway inhibitor.

Overall Survival By Metastatic Stage at Initial Diagnosis

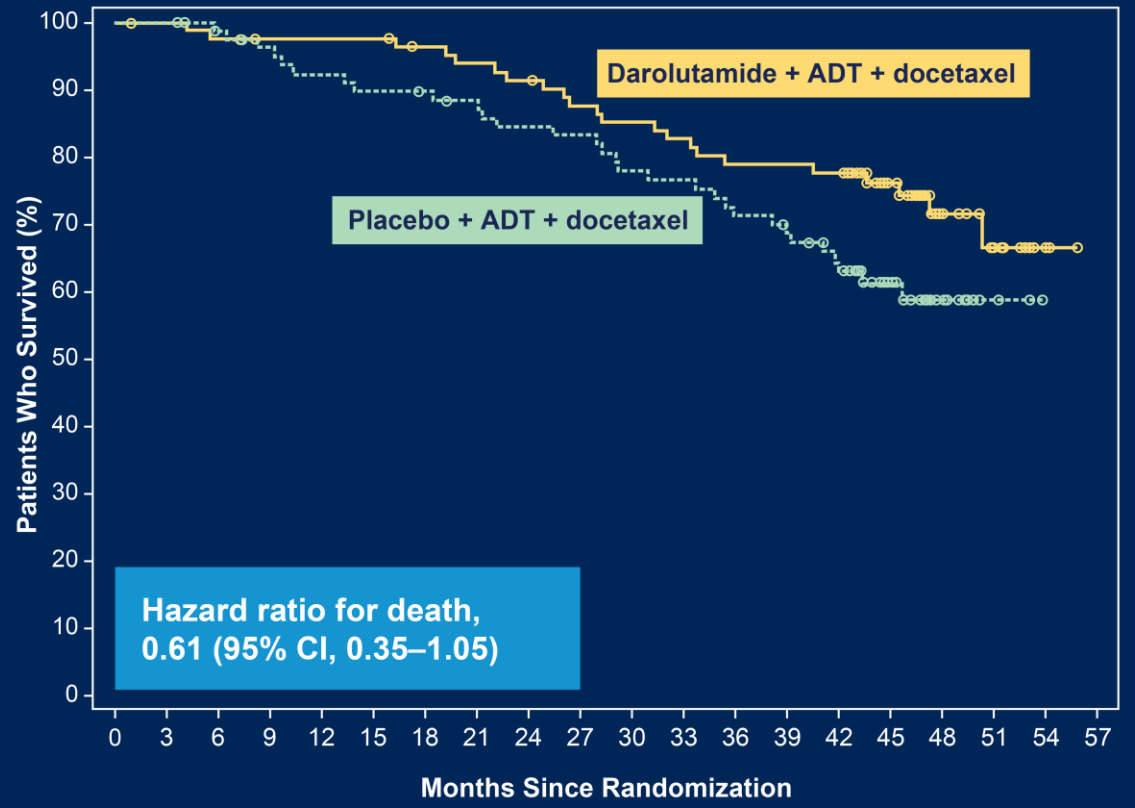
De novo metastatic disease



No. at Risk

Darolutamide	558	553	547	539	520	505	485	466	445	433	412	396	383	367	334	220	116	45	7	0	0
Placebo	566	558	546	526	503	490	461	438	420	403	378	362	344	328	292	190	93	33	6	1	0

Recurrent metastatic disease

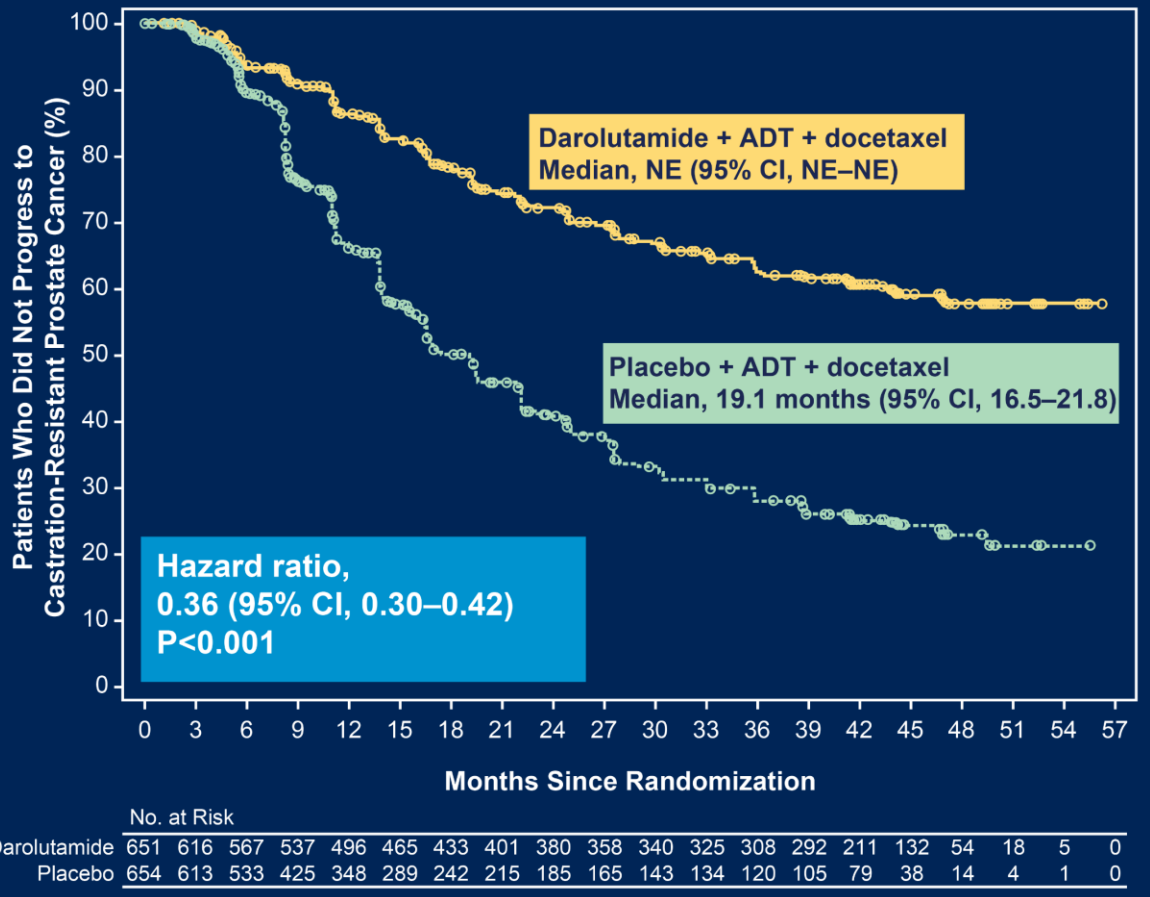


No. at Risk

Darolutamide	86	85	83	81	81	81	78	76	74	70	68	66	63	63	62	43	20	11	2	0
Placebo	82	82	78	75	72	70	69	67	64	63	59	58	54	51	45	26	12	4	0	0

Key Secondary Endpoints

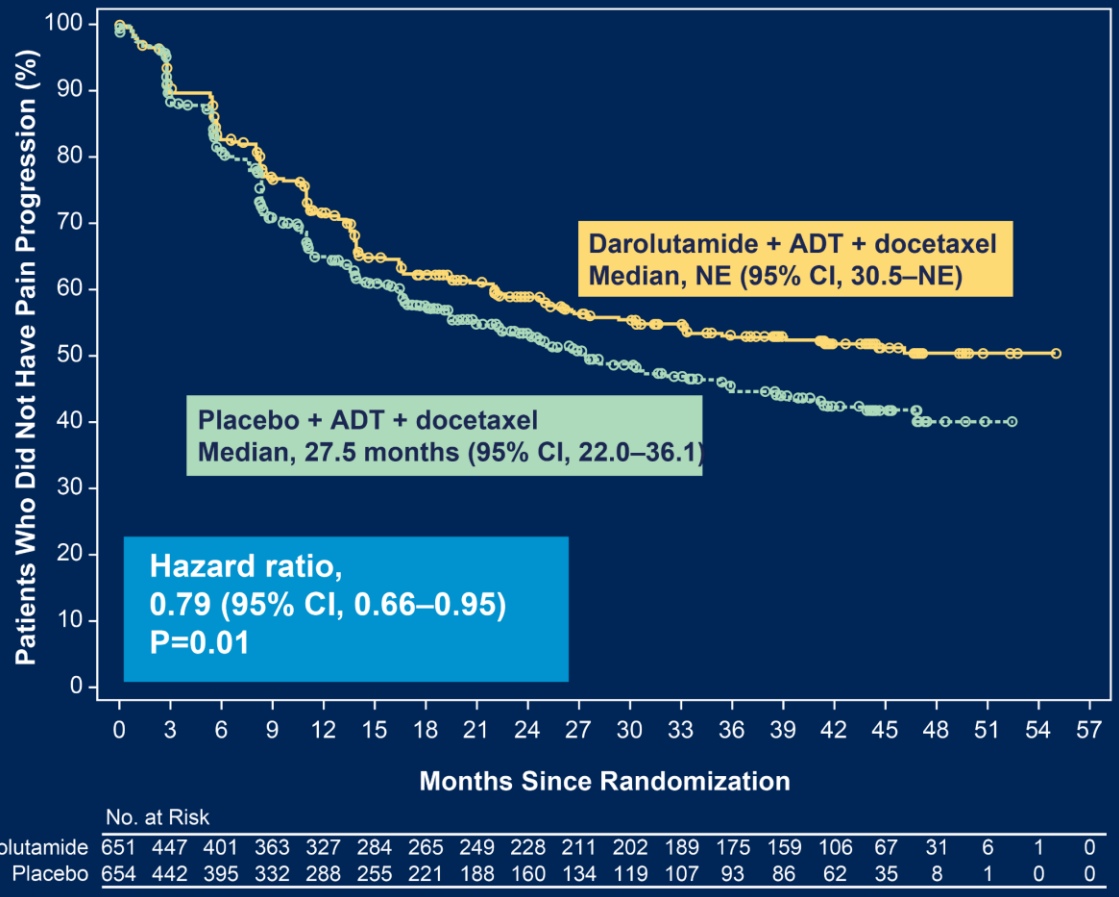
Time to CRPC



No. at Risk

Darolutamide	651	616	567	537	496	465	433	401	380	358	340	325	308	292	211	132	54	18	5	0
Placebo	654	613	533	425	348	289	242	215	185	165	143	134	120	105	79	38	14	4	1	0

Time to pain progression*



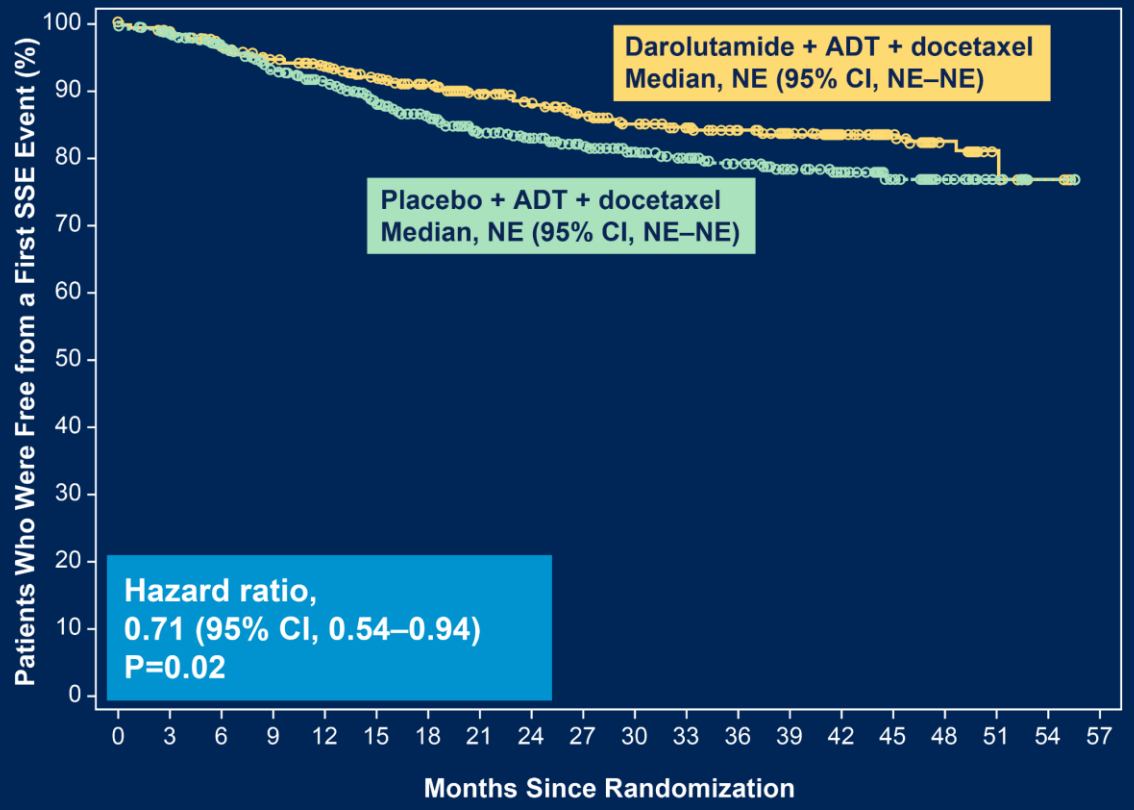
No. at Risk

Darolutamide	651	447	401	363	327	284	265	249	228	211	202	189	175	159	106	67	31	6	1	0
Placebo	654	442	395	332	288	255	221	188	160	134	119	107	93	86	62	35	8	1	0	0

*Pain progression was defined by change in the Brief Pain Inventory–Short Form questionnaire worst pain score or initiation of opioid therapy for ≥7 days.

Key Secondary Endpoints

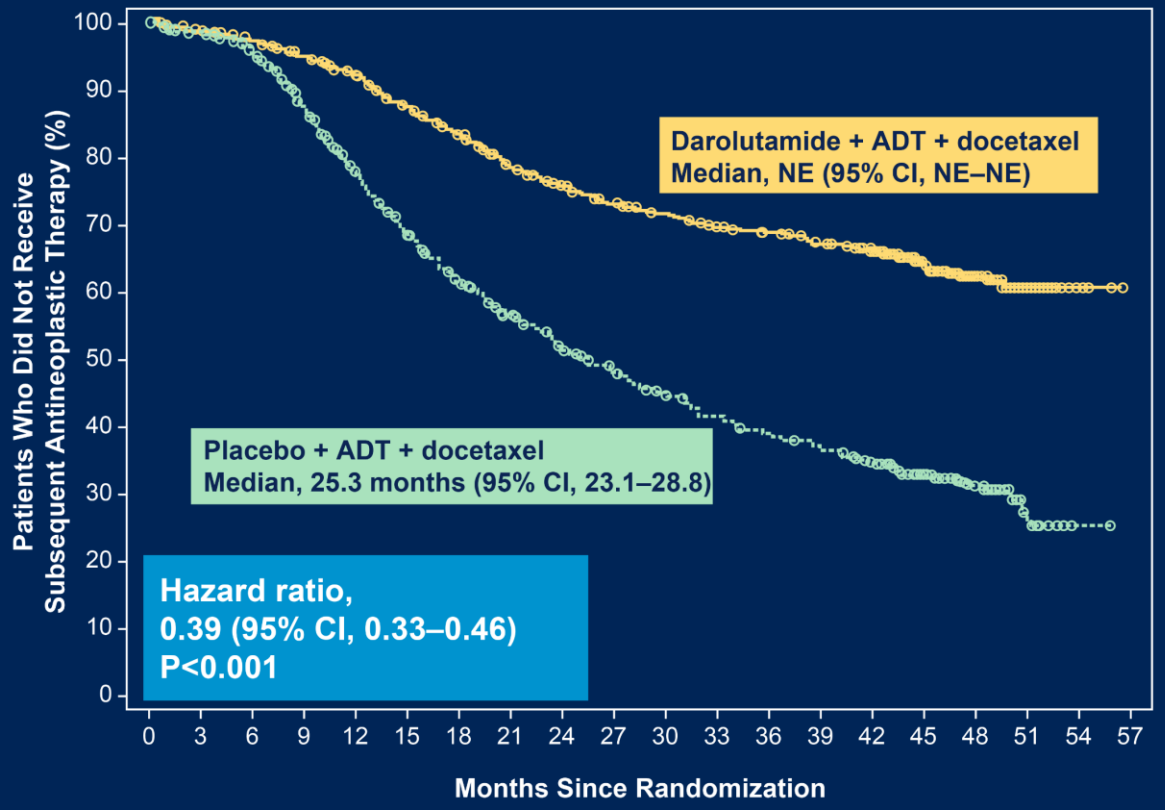
Time to first SSE



No. at Risk

Darolutamide	651	620	595	570	546	518	486	457	431	407	388	372	353	327	239	155	61	20	5	0
Placebo	654	618	582	535	494	439	399	349	309	268	238	219	202	183	134	72	28	7	1	0

Time to first subsequent antineoplastic therapy



No. at Risk

Darolutamide	651	638	621	600	570	536	503	466	442	422	406	390	380	367	342	220	113	42	8	0
Placebo	654	636	605	535	465	403	355	317	284	259	237	219	205	191	167	105	48	14	1	0

ARASENS: Treatment-Emergent Adverse Events

TEAE, n (%)	Darolutamide + ADT + docetaxel (n=652*)	Placebo + ADT + docetaxel (n=650*)
Any	649 (99.5)	643 (98.9)
Worst grade		
Grade 1	28 (4.3)	35 (5.4)
Grade 2	162 (24.8)	169 (26.0)
Grade 3	248 (38.0)	232 (35.7)
Grade 4	183 (28.1)	181 (27.8)
Grade 5	27 (4.1)	26 (4.0)
Serious	292 (44.8)	275 (42.3)
Leading to permanent discontinuation of:		
Darolutamide/placebo	88 (13.5)	69 (10.6)
Docetaxel	52 (8.0)	67 (10.3)

Median treatment duration was 41.0 months for darolutamide-treated patients and 16.7 months for placebo-treated patients.
*Three randomized patients (all in the placebo group) were never treated and were excluded from the safety analysis set. One patient randomized to placebo but who received darolutamide was included in the darolutamide group for the safety analysis set.
TEAE, treatment-emergent adverse event.

Grade 3–4 Adverse Events

Grade 3–4 AEs in ≥2% of darolutamide-treated patients, n (%)	Darolutamide + ADT + docetaxel (n=652)	Placebo + ADT + docetaxel (n=650)
Any AE	431 (66.1)	413 (63.5)
Neutropenia*	220 (33.7)	222 (34.2)
Febrile neutropenia	51 (7.8)	48 (7.4)
Hypertension	42 (6.4)	21 (3.2)
Anemia	31 (4.8)	33 (5.1)
Pneumonia	21 (3.2)	20 (3.1)
Hyperglycemia	18 (2.8)	24 (3.7)
Increased alanine aminotransferase	18 (2.8)	11 (1.7)
Increased aspartate aminotransferase	17 (2.6)	7 (1.1)
Increased weight	14 (2.1)	8 (1.2)
Urinary tract infection	13 (2.0)	12 (1.8)

*Neutropenia includes the preferred terms leukopenia, neutropenia, neutrophil count decreased, and white blood cell count decreased.

Adverse Events of Special Interest for AR Pathway Inhibitors

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

*EAIR is the number of patients with a given AE divided by the total darolutamide/placebo treatment duration of all patients in years and expressed in 100 PY. †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. EAIR, exposure-adjusted incidence rate; PY, patient year.

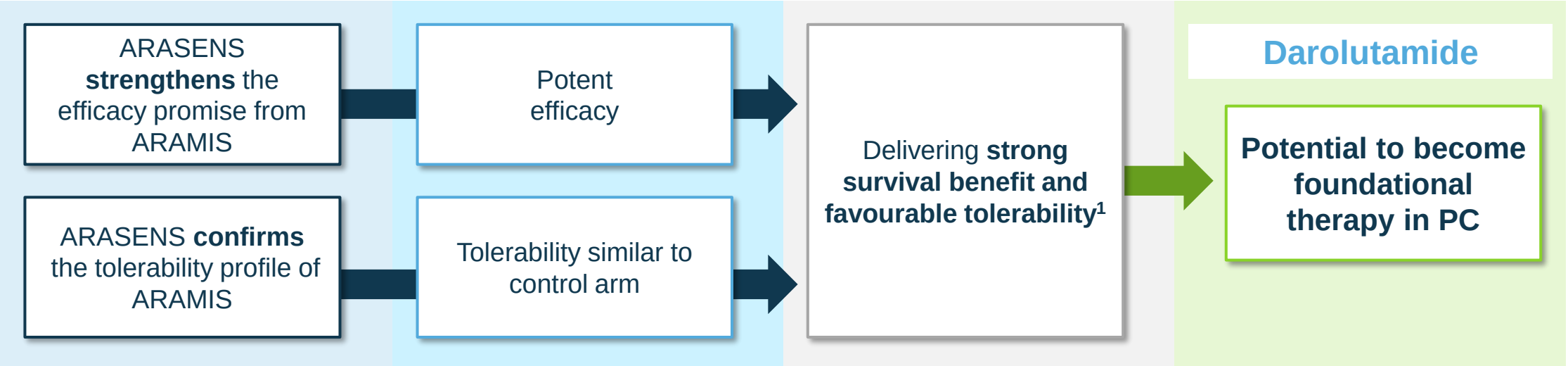
ARASENS Conclusions

- Darolutamide in combination with ADT and docetaxel significantly improved OS compared with ADT and docetaxel in patients with mHSPC. Darolutamide reduced the risk of death by 32.5%
- Darolutamide improved OS despite a high rate of subsequent life-prolonging systemic therapy in the placebo group
- The OS benefit for darolutamide was consistent across prespecified subgroups
- Darolutamide also significantly improved key secondary endpoints, including time to castration-resistant prostate cancer, time to pain progression, time to first SSE, and time to first subsequent antineoplastic therapy
- Rates of adverse events were similar between the darolutamide and placebo groups

Darolutamide in combination with ADT and docetaxel should become a new standard of care for treatment of mHSPC

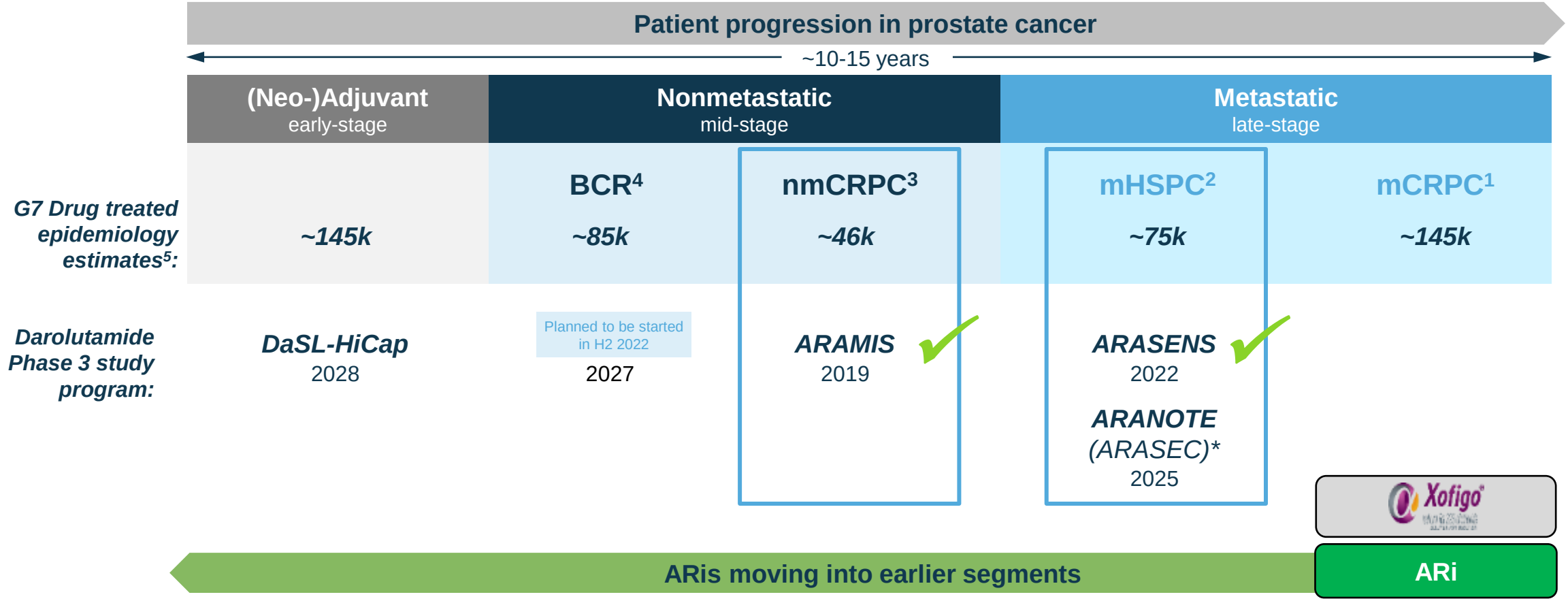
ARASENS strengthens Darolutamide's clinical profile – strong survival benefit with favourable tolerability

	Efficacy		Tolerability
	Primary endpoint	Selected secondary endpoints	
ARAMIS nmCRPC	**Metastasis free survival** prolongation by 22.0 months, 59% risk reduction (HR=0.41, p<0.001)	**Overall survival** 31% risk reduction (HR=0.69, p=0.003) **Time to pain progression** prolongation by 14.9 months, 35% risk reduction (HR=0.65, p<0.001)	favourable tolerability profile
ARASENS mHSPC	**Overall survival** 32.5% risk reduction (HR=0.675, p<0.0001)	**Time to castration resistant PC** 64% risk reduction (HR=0.357, p<0.0001	



[1] compared to control arm [2] Androgen receptor inhibitor

We are committed to make Darolutamide available to a broad spectrum of prostate cancer patients



[1] Metastatic castration resistant prostate cancer [2] Metastatic hormone sensitive prostate cancer [3] Non-metastatic castration resistant prostate cancer [4] Biochemical relapse [5] G7: US, EU5, JP
** Not label generating; supports ARANOTE submission*

Darolutamide with the chance to become a foundational drug in prostate cancer – peak sales potential lifted to >€3bn

Efficacy

- Highly efficacious ARi
- First to show more than 30% risk reduction of death in nmCRPC and mHSPC

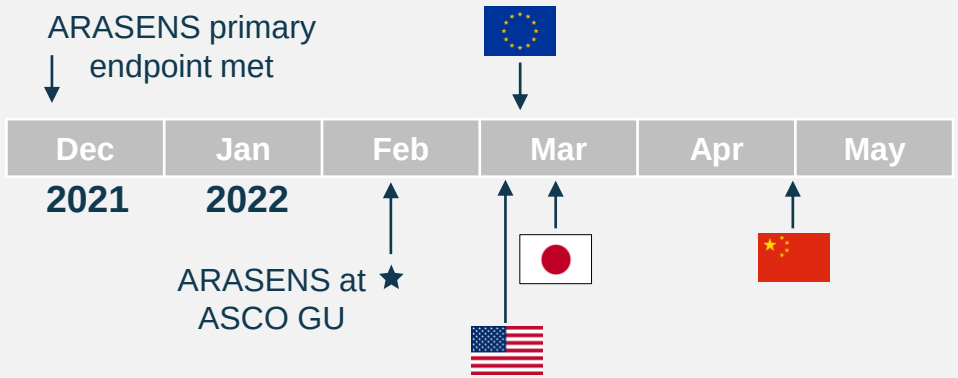
Safety

- Well tolerated safety profile
- Limited potential for drug-interactions
- Early data indicate limited blood-brain barrier penetration

Lifecycle Management

- Become agent of choice across prostate cancer indications
- Combination opportunities

Planned submissions for mHSPC label extension



Potential Nubeqa peak sales

We have significantly advanced Bayer's Oncology franchise over the last 5 years

Oncology planned to be a key growth pillar for Bayer Pharma

Growth in product portfolio

- Doubled number of marketed products from 3 to 6
- >75 commercialization approvals across multiple indications
- Broader tumor focus

Innovation

- 3 FDA breakthrough designations
- 15 ongoing registrational studies
- Entry in newer platforms such as radio pharmaceuticals, precision oncology, next generation IO e. g. cell therapy

New Launches

- NUBEQA expected to be key driver for Bayer's growth in Oncology
- VITRAKVI first ever tumor agnostic approval in both pediatrics and adults

Questions & Answers

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