Seattle Cancer Care Alliance

Fred Hutch · Seattle Children's · UW Medicine

Prostate Cancer Board Review

2021

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Disclosures

- Research Funding to UW/FHCRC: Janssen, Tmunity, AstraZeneca, Zenith, Pfizer, SignalOne Bio, and Hoffmann-La Roche.

Outline

- Epidemiology/risk factors
- Evidence for screening
- Definitive local therapies
- Management of advanced disease

Epidemiology

Estimated New Cases

Prostate	248,530	26%
Lung & bronchus	119,100	12%
Colon & rectum	79,520	8%
Urinary bladder	64,280	7%
Melanoma of the skin	62,260	6%
Kidney & renal pelvis	48,780	5%
Non-Hodgkin lymphoma	45,630	5%
Oral cavity & pharynx	38,800	4%
Leukemia	35,530	4%
Pancreas	31,950	3%
All Sites	**970,250**	**100%**

Estimated Deaths

Males

Lung & bronchus	69,410	22%
Prostate	34,130	11%
Colon & rectum	28,520	9%
Pancreas	25,270	8%
Liver & intrahepatic bile duct	20,300	6%
Leukemia	13,900	4%
Esophagus	12,410	4%
Urinary bladder	12,260	4%
Non-Hodgkin lymphoma	12,170	4%
Brain & other nervous system	10,500	3%
All Sites	**319,420**	**100%**

Siegel, et al. CA Cancer J Clin. 2021

Epidemiology

- Incidence
  - 1 in 3 men will have prostate cancer
  - 1 in 8 men will know he has prostate cancer
  - 1 in 33 men will die of prostate cancer
- 2X risk if 1st degree relative
  - 4x risk if 2 or more relatives with affected age <70
- Higher risk from high fat diet
- African American men
  - Higher incidence and mortality

Siegel, et al. CA Cancer J Clin. 2021
Farkas, et al. Urology 1998; 52:444

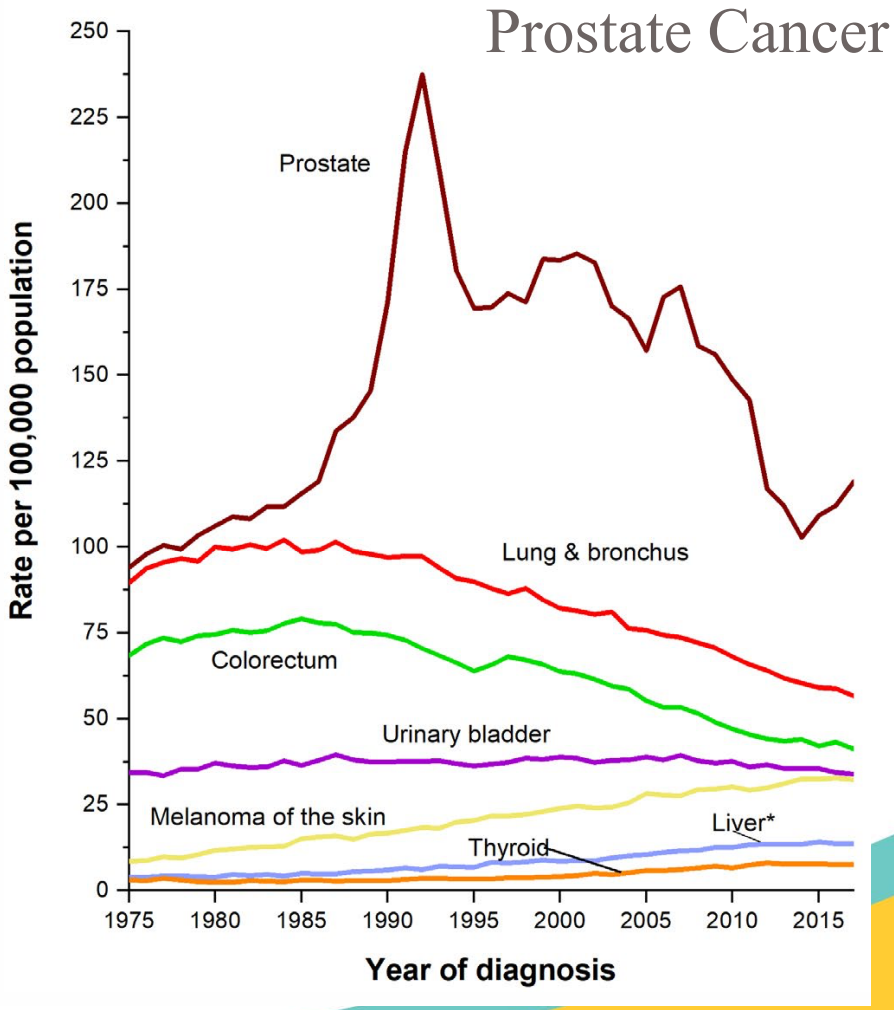
Randomized Screening Trials

- PLCO: No mortality benefit to screening
  - N >75,000; age 55-74; 7-10 yr f/u
  - ~20% more cancers detected in screened arm
  - ~90% in control group had PSA testing
- ERSPC: 20% reduction in cancer mortality
  - N > 160,000; age 55-69; 9 years f/u
  - ~70% more cancers detected in screened arm
  - NNS = 1410; NNT = 48
  - NNT = 12 in Goteborg series (f/u 14 years)

Andriole, et al. N Engl J Med. 2009 Mar 26;360(13):1310-9
Schroder, et al. N Engl J Med. 2009 Mar 26;360(13):1320-8
Shoag, et al. N Engl J Med. 2016 May 5;374(18):1795-6

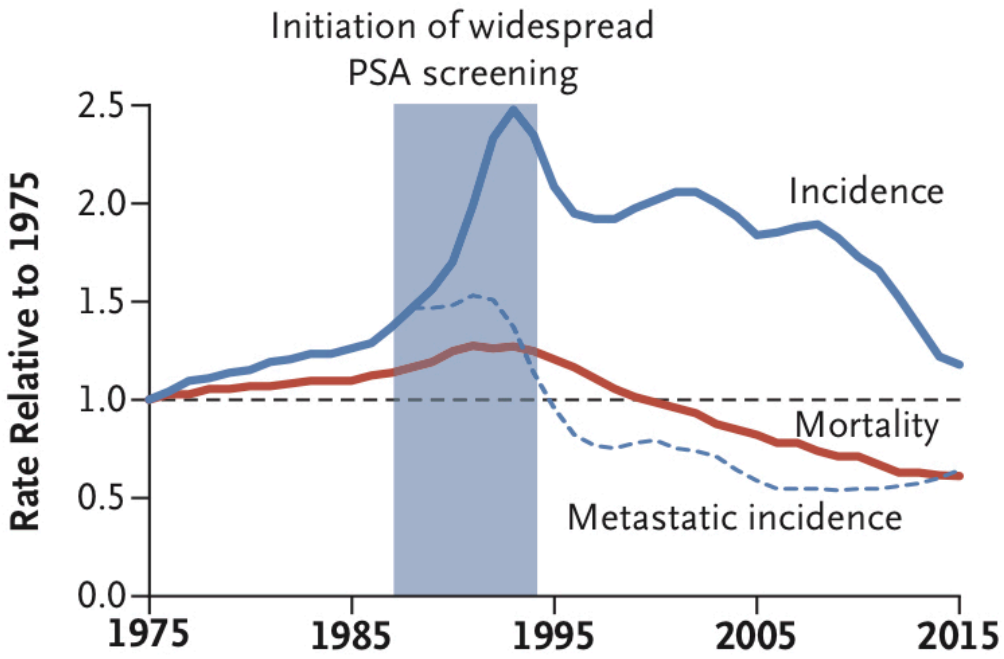
Prostate Cancer Screening: USPSTF

- 2012: No Screening
- 2018: Consider in men age 55-69
- NOTE: Did not evaluate the use of the PSA test as part of a diagnostic strategy in men with symptoms suggestive of prostate cancer



Siegel, et al. CA Cancer J Clin. 2021

What to expect in the future?



Models suggest that completely abandoning screening would increase prostate cancer deaths by 13-20% by 2025

Welch, et al. N Engl J Med 2015; 373:1685-1687
Gulati, et al. Cancer. 2014 Nov 15;120(22):3519-26
Welch, et al. NEJM 2019

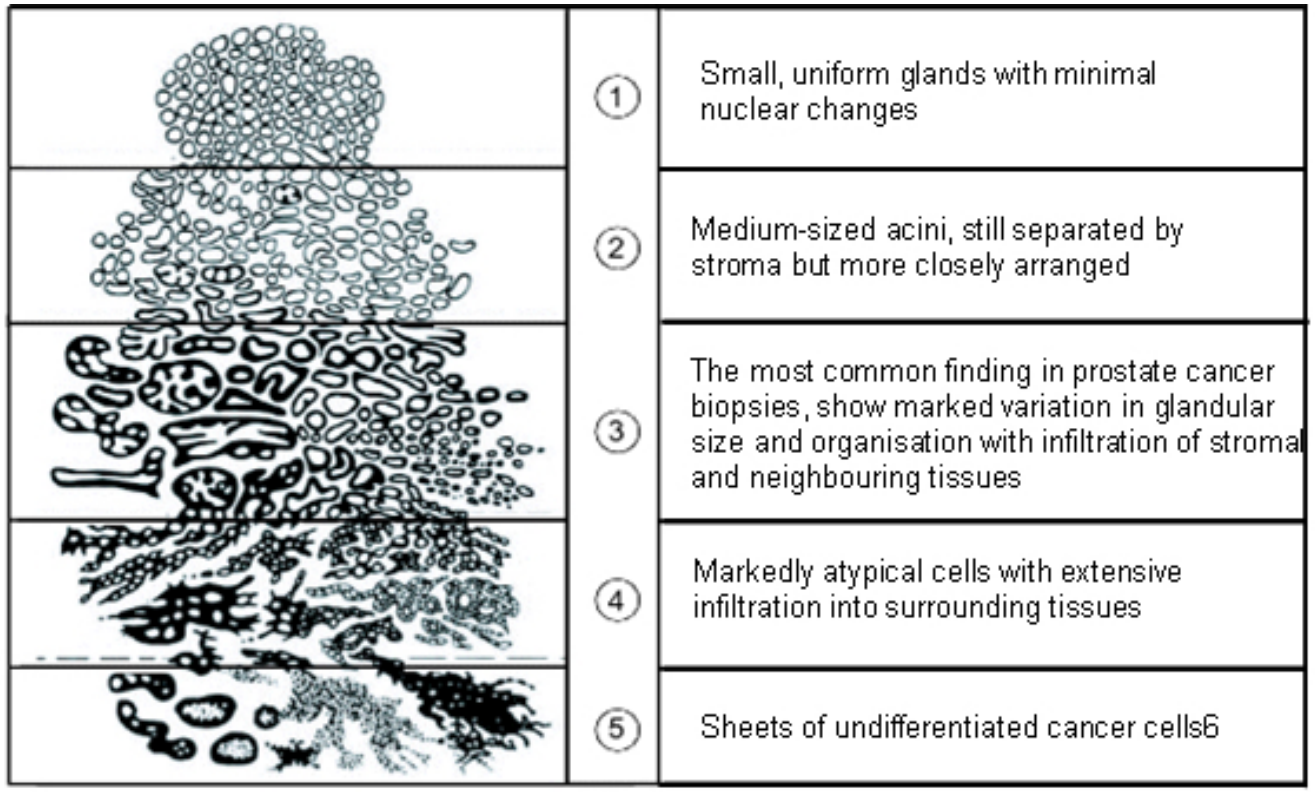
Workup

- Referral to urology for biopsy if:
  - Abnormal DRE
  - Elevated PSA
- Additional testing dependent on risk:
  - Bone scan: T1 and PSA>20, T2 and PSA>10, Gleason ≥8, T3-T4 or symptomatic
  - Pelvic CT or MRI: T3-T4, T1-T2 and >10% chance of lymph node involvement

Risk Group	Clinical Features
Very low	T1c Gleason score ≤6 PSA <10 <3 positive biopsy cores ≤50% cancer in each core PSA density <0.15
Low	T1-T2a Gleason ≤6 PSA <10
Intermediate	T2b-T2c or Gleason score 7 or PSA 10-20
High	T3a or Gleason score 8-10 or PSA >20
Very high	T3b-T4

Gleason Score

- Based on cancer architecture
  - Range from 1 (well differentiated) to 5 (poorly differentiated)
- Correlates closely with clinical behavior
  - High score is worse
- Reported as a composite score:
  - Primary + Secondary = total Gleason score



Gleason Grade Group

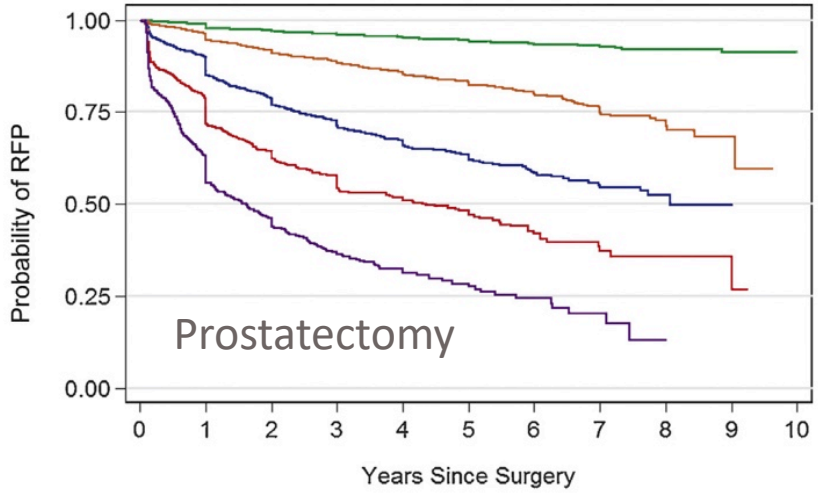
- Grade Group reporting recommended by International Society of Urological Pathology and WHO
- More accurate risk stratification than composite Gleason score

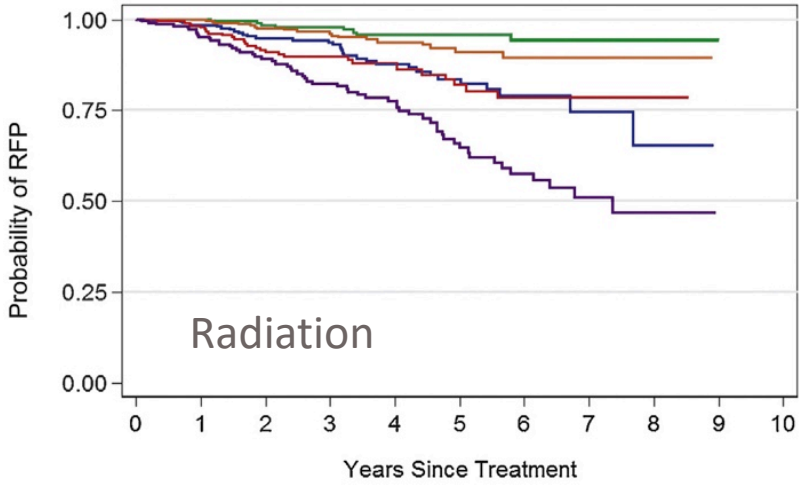
Grade Group	Gleason Pattern
Group 1	Gleason 3+3
Group 2	Gleason 3+4
Group 3	Gleason 4+3
Group 4	Gleason 4+4
Group 5	Gleason 4+5, 5+4 or 5+5

Epstein, et al. Eur Urol. 2016;69(3):428.

Gleason Grade Group

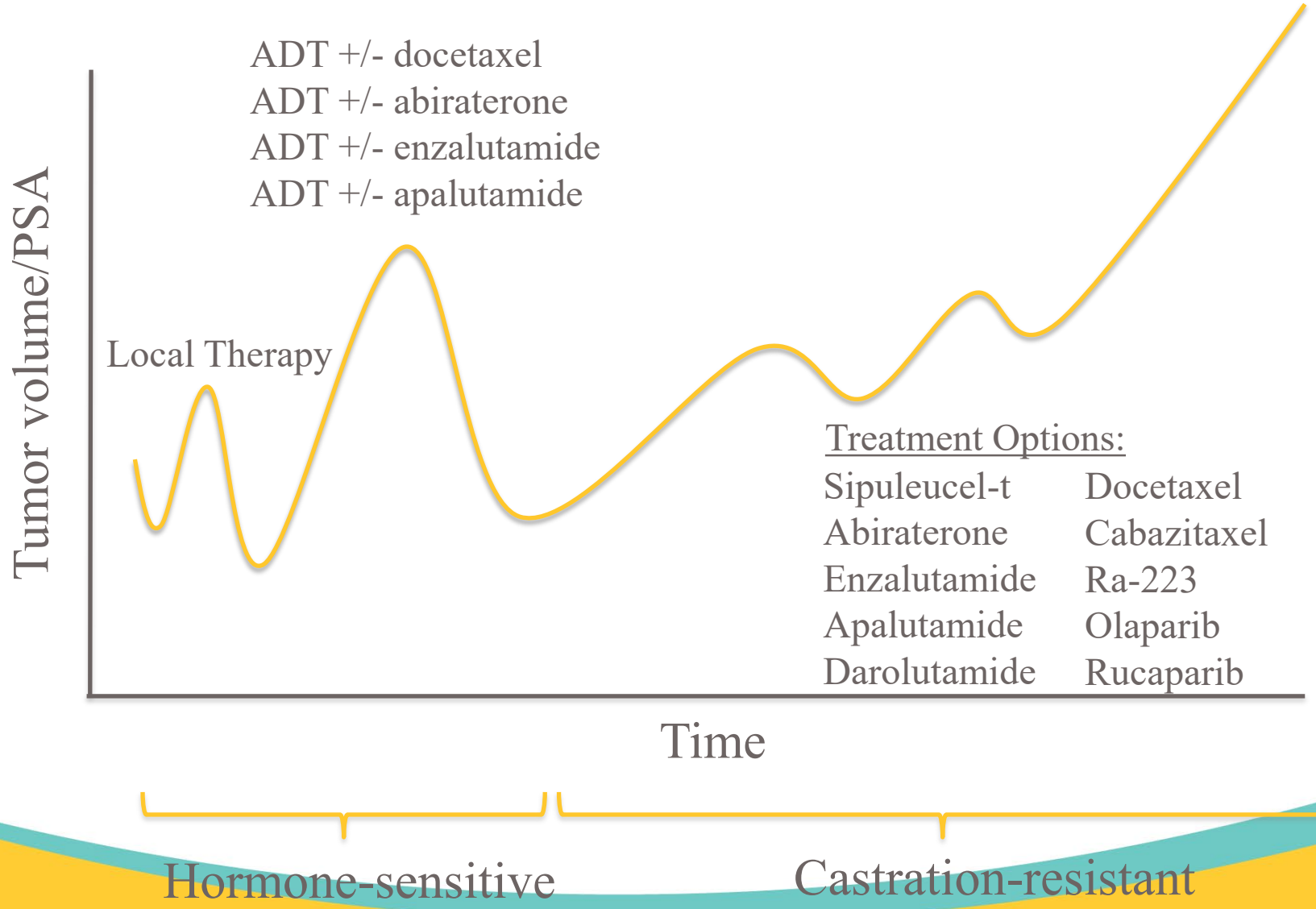
- Included patients treated with radiation (EBRT) or prostatectomy (RP) between 2005 and 2014
  - N=20,845 treated with RP
  - N=5,501 treated with EBRT
- Primary endpoint: Biochemical (i.e. PSA) recurrence



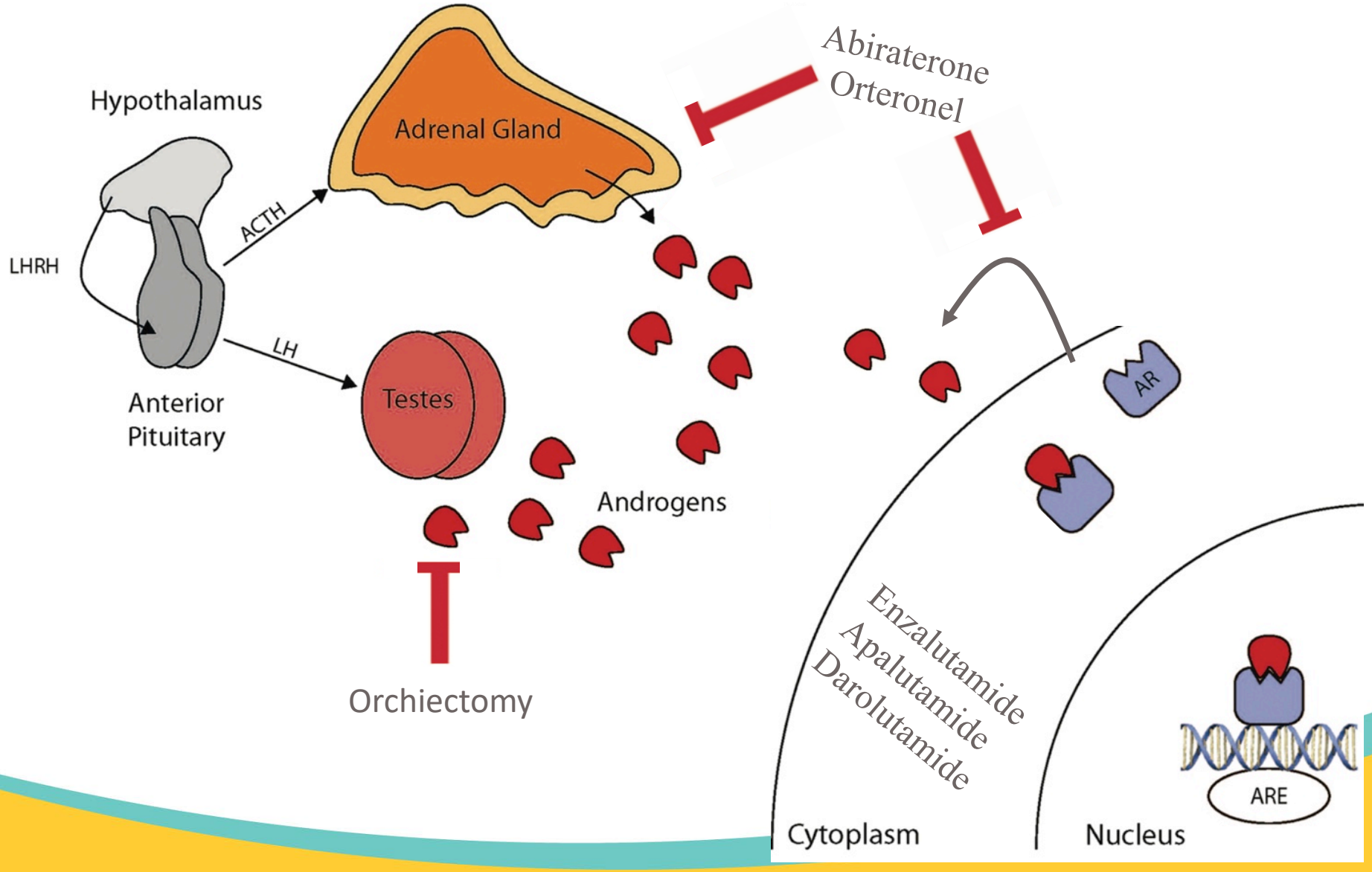


Epstein, et al. Eur Urol. 2016;69(3):428.

Prostate Cancer Disease Continuum



AR-Signaling Inhibitors



Androgen Deprivation Therapy – Side Effects

- Common: sexual (impotence and decreased libido), hot flashes, fatigue, loss of motivation, gynecomastia, weight gain
- Metabolic: diabetes, hyperlipidemia, **osteopenia**, cardiovascular disease
  - Check DEXA – if osteopenia or osteoporosis denosumab 60 mg SC q6 months reduces risk of osteoporotic fractures[1]
  - Resistance and Aerobic **Exercise** can improve muscle mass, physical function and potentially survival
  - **Vitamin D 800-1000 IU + Calcium 1000-1200 mg po qd**

1. Smith MR et al. NEJM 2009; 361:745

Prostate Cancer Prevention

	PCPT[1]	SELECT[2]
Number enrolled	18,000	35,553
Intervention	Finasteride 5 mg Placebo	Vit E (400 IU), Selenium, Both, or Neither
Results	22.9% risk PC for placebo vs 16.6% risk PC for finasteride RR 0.7 (0.64 – 0.76); p<0.0001	17% increased risk PC in Vitamin E group

1. Thompson IM et al. NEJM 2003; 349:297
2. Lippman SM et al. JAMA 2009; 301:39

Prostate Cancer Active Surveillance

- Well recognized management strategy for men with lower risk prostate cancer
- Aim to decrease overtreatment while maintaining cure rates
- ASCO/AUA/ASTRO/SUO Active Surveillance Guidelines:
  - Very low-risk : best option
  - Low-risk: preferred option
  - Favorable intermediate risk: offer to select patients; inform risk of metastases is higher

Bekelman, et al. J Clin Oncol. 2018 Nov 10;36(32):3251-3258.

Prostate Cancer Active Surveillance

Safe and effective strategy to mitigate overtreatment of lower risk prostate cancers

Center	Toronto[1,2,3]	Johns Hopkins[4,5,6,7]	UCSF[8]	UCSF (newer cohort)[9]	Canary PASS[10]
No. patients	993	1298	321	810	905
Median follow-up (mos)	77	60	43	60	28
Cancer-specific survival	98% (10-y)	99.9% (10-y)	100% (5-y)	-	-
Conversion to treatment	36.5% (10-y)	50% (10-y)	24% (3-y)	40% (5-y)	19% (28-mos)

Adapted from Prostate Cancer NCCN Guidelines v2.2020

1. Klotz, et al. J Clin Oncol. 2015 Jan 20;33(3):272-7.
2. Klotz, et al. J Clin Oncol. 2010 Jan 1;28(1):126-31.
3. Yamamoto, et al. J Urol. 2016 May;195(5):1409-1414.
4. Tosoian, et al. J Clin Oncol. 2015 Oct 20;33(30):3379-85.
5. Carter, et al. J Urol. 2007 Dec;178(6):2359-64
6. Sheridan, et al. J Urol. 2008 Mar;179(3):901-4
7. Tosoian, et al. J Clin Oncol. 2011 Jun 1;29(16):2185-90.
8. Dall'era, et al. Cancer. 2008 Jun 15;112(12):2664-70.
9. Welty, et al. J Urol. 2015 Mar;193(3):807-11.
10. Newcomb, et al. J Urol. 2016 Feb;195(2):313-20.

How to Perform Active Surveillance

Recommended Surveillance Schedule

PSA	Every 3–4 mo
DRE	Every 3–6 mo
TRUS	Every 9–12 mo*
Prostate biopsy	After 1 y then every 1–2 y or as indicated by PSA or examination trends

PSA indicates prostate-specific antigen; DRE, digital rectal examination; TRUS, transrectal ultrasonography.

* Imaging not found beneficial in some studies.

Dall'Era MA et al. Cancer 2008; 112:1650-9

ASCO Endorsement Recommendation

The AS protocol should include the following tests:

- A PSA test every 3 to 6 months
- DRE ***at least*** every year
- ***At least*** a 12-core confirmatory TRUS ***guided*** biopsy (including anterior-directed cores) within 6 to 12 months, and then serial biopsy every **2** to 5 years thereafter ***or more frequently if clinically warranted. Men with limited life expectancy may transition to watchful waiting and avoid further biopsies.***

Chen RC et al. J Clin Oncol 2016 (Feb 16)

- 25% will progress and need treatment
- 25% will select more treatment without meeting progression criteria

Dall'Era MA et al. Eur Urol 2012; 62:976-83

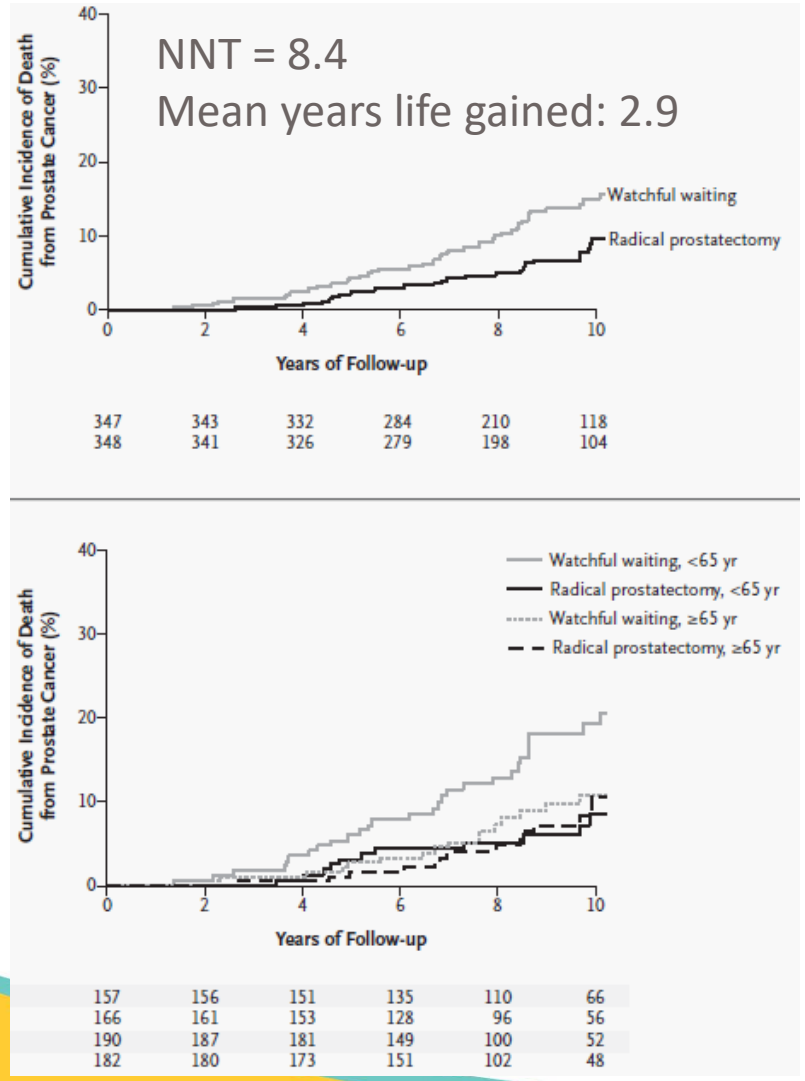
Radiation for Localized Prostate Cancer

- ADT added to radiation (EBRT) improves survival for higher risk or locally advanced patients[1]
  - 4-6 months (short course) for intermediate risk
  - Neoadjuv + concurrent + adjuvant (2-3 years LHRH) for high risk[2,3]
- Doses <70 Gy inadequate
  - Unclear whether escalation >78 Gy beneficial

1. Pilepich MV et al. JCO 1997; 15:1013 (RTOG 8531)
2. Hanks GE et al. JCO 2003; 21:3972 (RTOG 9202)
3. Bolla M et al. Lancet 2002; 360:103 (EORTC)

Radical Prostatectomy for Localized Prostate Cancer

SPCG4 Trial: Prostatectomy vs. Observation



Bill-Axelson A et al. NEJM 2005; 352:1977-84
Bill-Axelson, et al, NEJM 2018;379:2319-29.

- ADT does not offer benefit prior to surgery
- Robotic (minimally invasive) is an option
- Adjuvant ADT for lymph node positive[1] and other high risk patients[2] "Investigational"
- **Adjuvant XRT** for +margins or T3b status[3,4]

1. Messing EM et al. NEJM 1999; 341:1781
2. Dorff TB et al. JCO 2011;29:2040
3. Thompson IM et al. JAMA 2006; 296:2329 (S8794)
4. Bolla M et al. Lancet 2005; 366:13 (EORTC 22911)

Biochemical Recurrence (AKA M0)

- Definition: PSA >0.2 after RRP, “nadir +2” after XRT
- Natural history can be long
  - Consecutive series from 1981 to 2010
  - N=450 men with biochemical recurrence following prostatectomy
    - >50% with Gleason ≥7
    - Median baseline PSA = 8.5
  - No adjuvant therapy
  - Median metastasis free survival = 10 years

Antonarakis, et al. BJU Int. 2012 Jan;109(1):32-9.

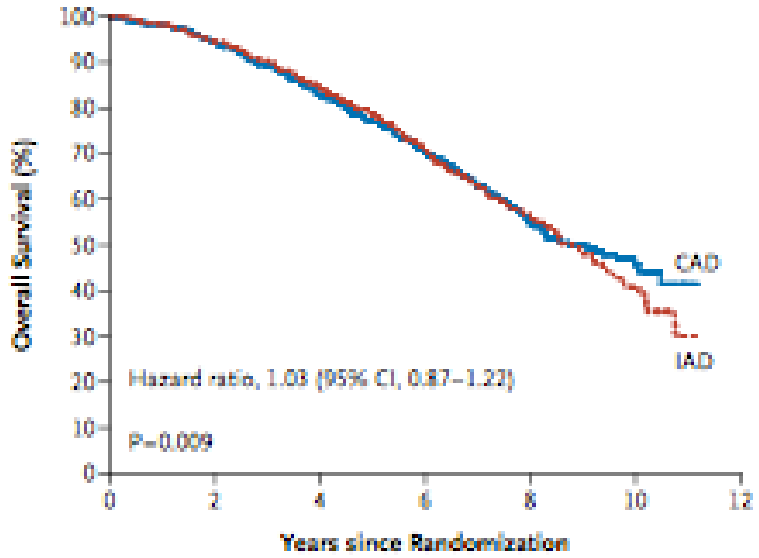
Biochemical Recurrence (AKA M0)

- ADT beneficial when giving salvage radiation for BCR
- GETUG-AFU16[1]
  - 6 months of goserelin with XRT 66 Gy or XRT alone
  - 10 year MFS: 75% (ADT+XRT) vs. 69% (XRT), P=0.0339
- RTOG 9601[2]
  - High dose bicalutamide 150 mg for 24 months with XRT 64.8 Gy or XRT alone
  - HR for OS 0.75 (2-sided p = 0.036).

1. Carrie C. et al Lancet Oncol 2019; 20: 1740–49
2. Shipley WU et al. NEJM 2017; 376:417-28

Intermittent vs. Continuous ADT

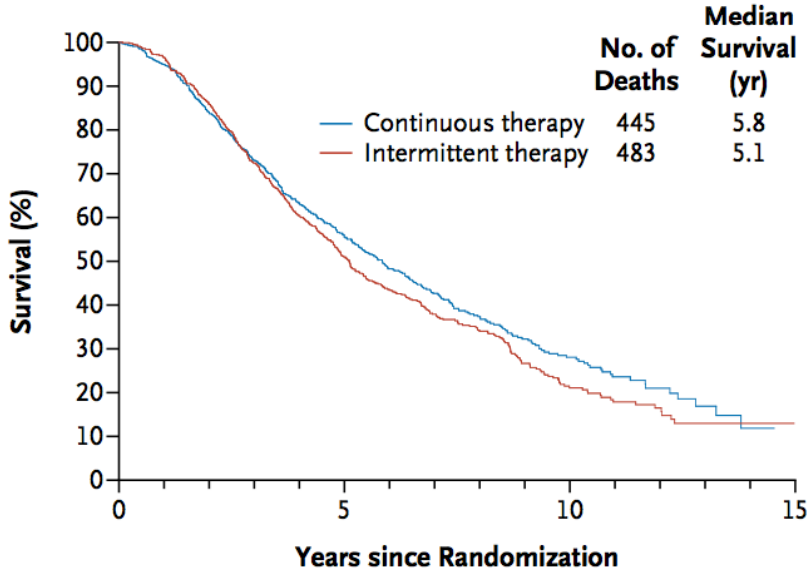
PR7 for BCR



No. at Risk							
CAD	696	652	561	319	125	35	0
IAD	690	651	571	327	140	34	0

No difference in OS

SWOG 9346 for mHSPC



No. at Risk			
Continuous therapy	765	325	64
Intermittent therapy	770	291	52

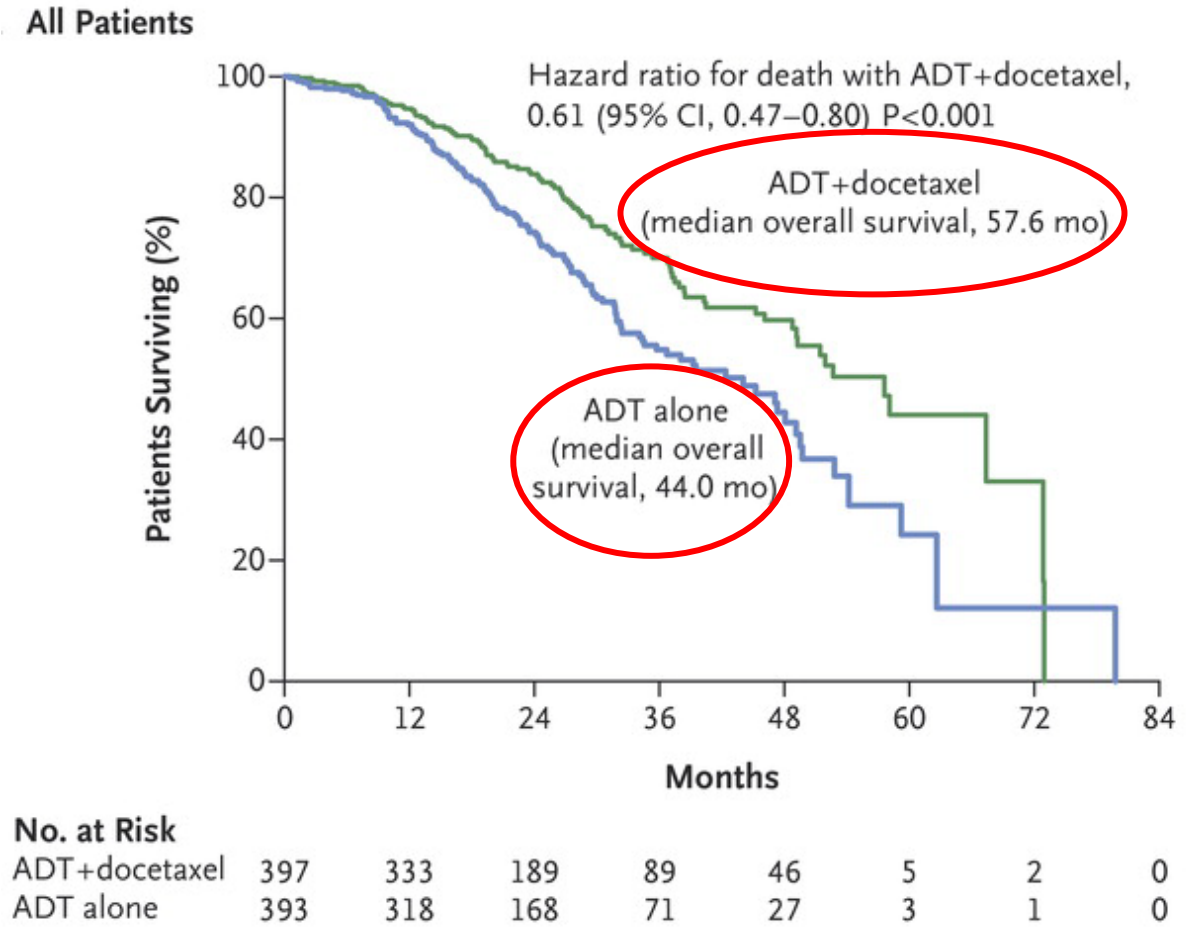
Intermittent therapy was not non-inferior to continuous ADT

Crook JM et al. N Engl J Med. 2012; 367:895-903.

Hussain M et al. N Engl J Med 2013;368:1314-25.

E3805 CHAARTED: ChemoHormonal Therapy vs. Androgen Ablation for Metastatic Prostate Cancer

- N=790 men accrued 07/28/06 - 11/21/12
- Enrollment allowed up to 16 weeks from initiation of ADT
- ADT was initiated a median of 1.1 months prior to enrollment – docetaxel was most certainly layered even later



Sweeney C et al. N Engl J Med 2015; 373:737-46.

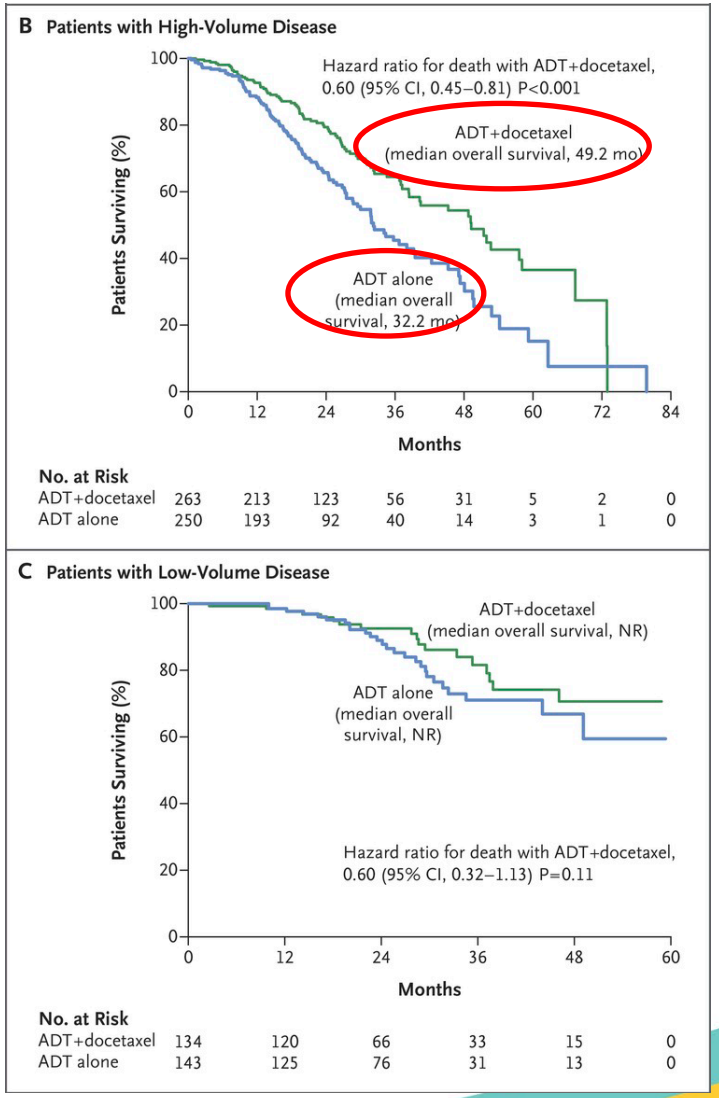
E3805 CHAARTED: ChemoHormonal Therapy vs. Androgen Ablation for Metastatic Prostate Cancer

Overall survival was 17.0 months longer in the combination group in men with high volume disease

≥4 bone lesions *and*
≥1 lesion in any bony structure beyond the spine/pelvis
OR
visceral disease

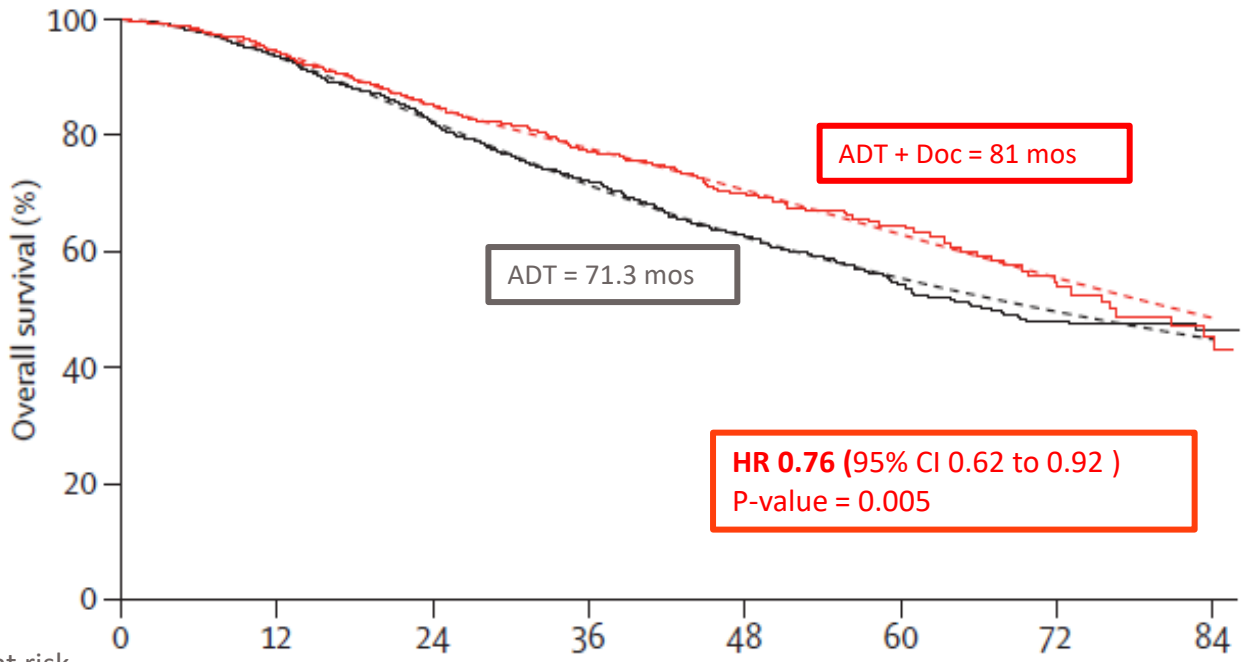
No statistically significant OS was observed between groups in those deemed to have low volume disease (p=0.11)

After a longer follow-up of 54 months, the survival benefit was experienced by only those men who had high volume disease (median 51 months vs. 34 months, HR 0.63, 95% CI 0.50-0.79), and not in those with low volume disease (median 64 months vs. not reached, HR 1.04, 95% CI 0.70-1.55)



Sweeney C et al. N Engl J Med 2015; 373:737-46.

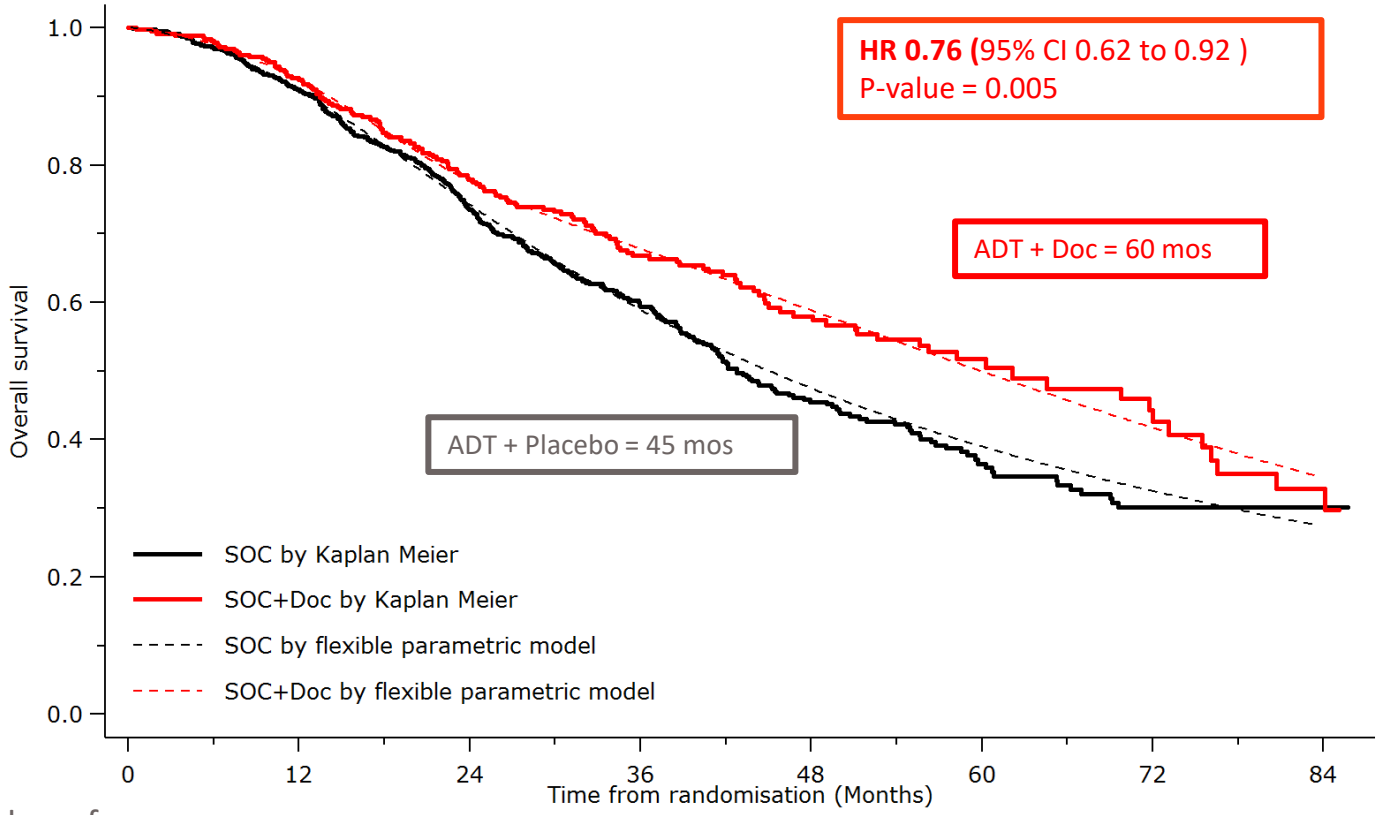
STAMPEDE Overall Survival



No effect on survival with zoledronic acid

James ND et al. Lancet 2016; 387:1163-77.

STAMPEDE Overall Survival for Metastatic Patient Population (61% of Trial Population)



Number of patients (events)

ADT	724	(65)	646	(121)	474	(78)	262	(53)	137	(21)	60	(10)	26	(0)	13
ADT + Doc	362	(27)	326	(50)	250	(30)	155	(16)	91	(8)	38	(6)	25	(5)	11

Pre-planned subset analysis in patients with metastatic disease

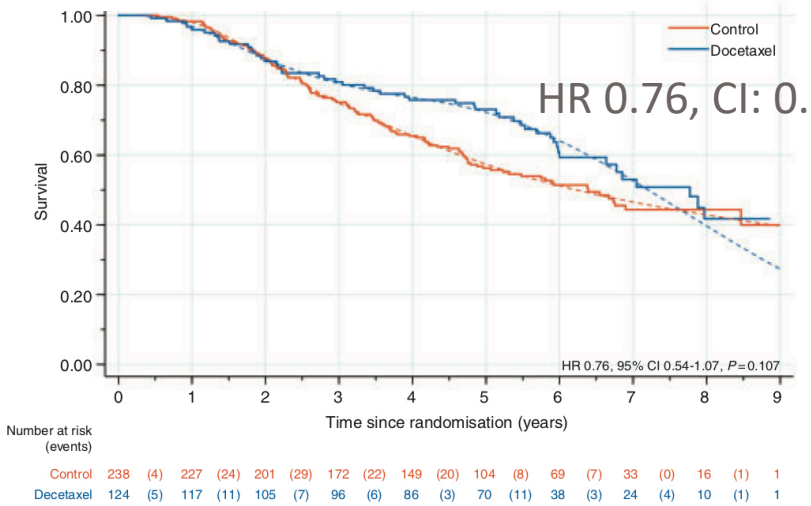
60 months vs. 45 months, HR 0.76, 95% CI 0.62-0.92; p=0.005)

James ND et al. Lancet 2016; 387:1163-77.

Treatment Effect by Metastatic Burden: Docetaxel

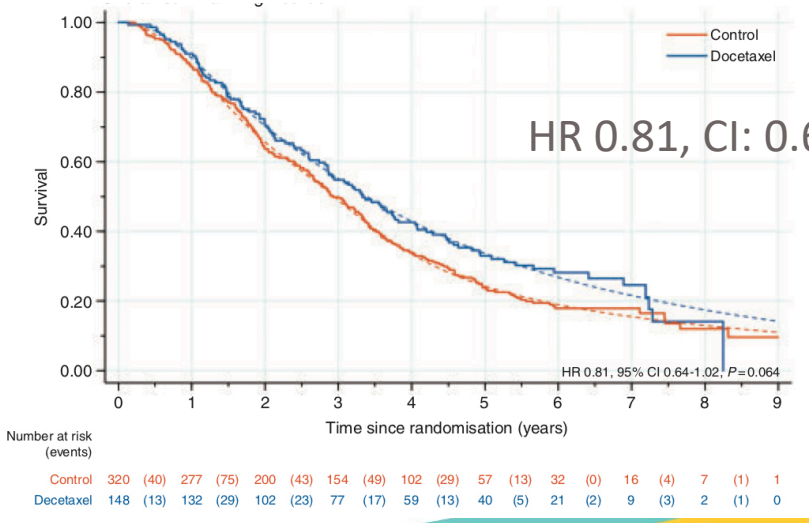
- STAMPEDE: Metastatic burden assessable in 76% of M1 patients
  - Per CHAARTED definition
- No evidence of heterogeneity of docetaxel effect between high vs low metastatic burden subgroups (interaction P = 0.827)
- Underpowered to detect OS benefit in metastatic burden subgroups → no obvious difference in survival
- Significant FFS benefit in both high and low metastatic burden patients

OS: Low metastatic burden



HR 0.76, CI: 0.54-1.07, P=0.107

OS: High metastatic burden



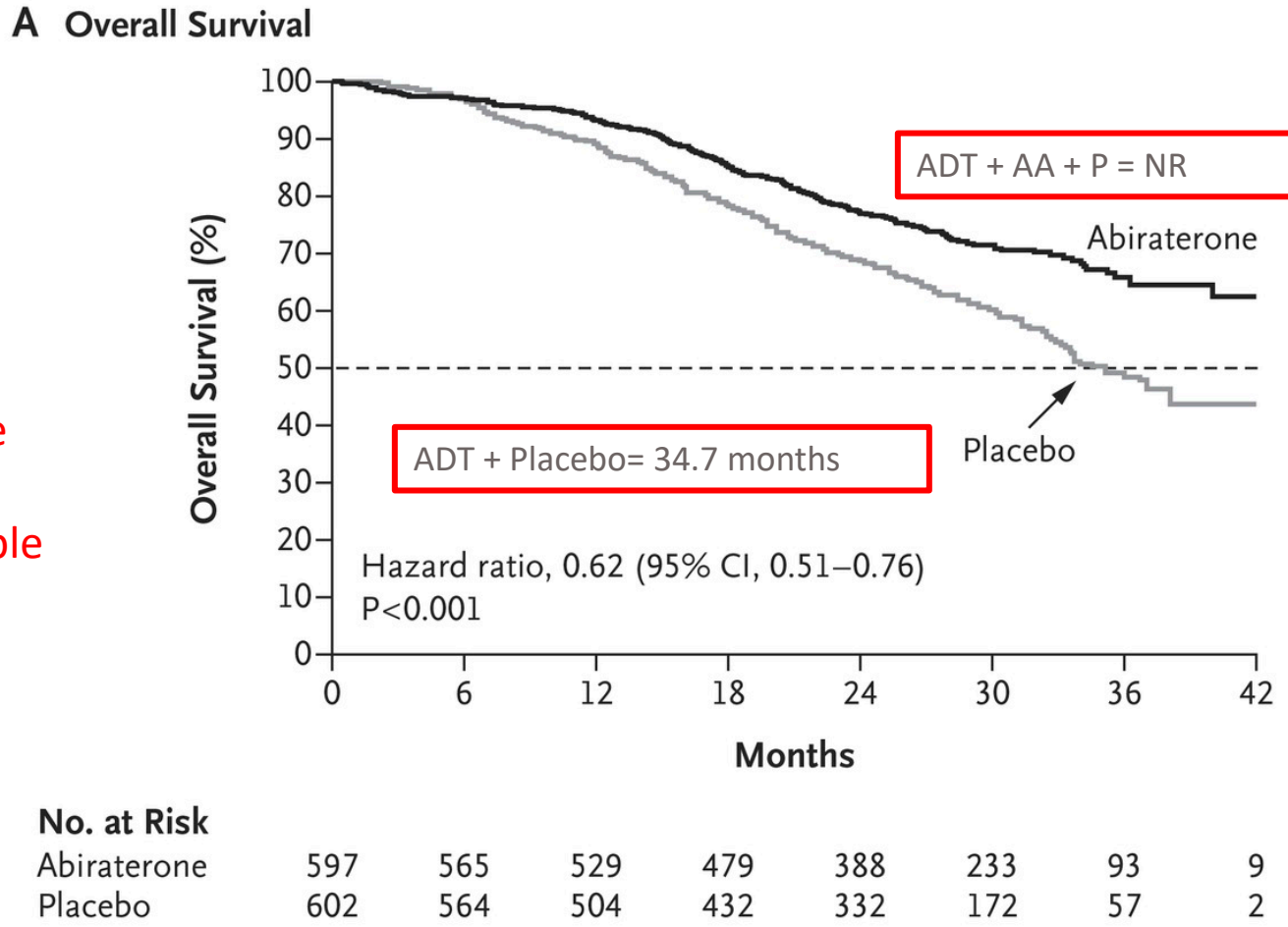
HR 0.81, CI: 0.64-1.02, P=0.064

Clarke NW, et al. Annals Oncol 2019

LATITUDE – Overall Survival with Abiraterone

High risk defined as at least of 2 of 3 criteria:

- Gleason score of 8 or more
- Presence of 3 or more lesions on bone scan
- Presence of measurable visceral lesion

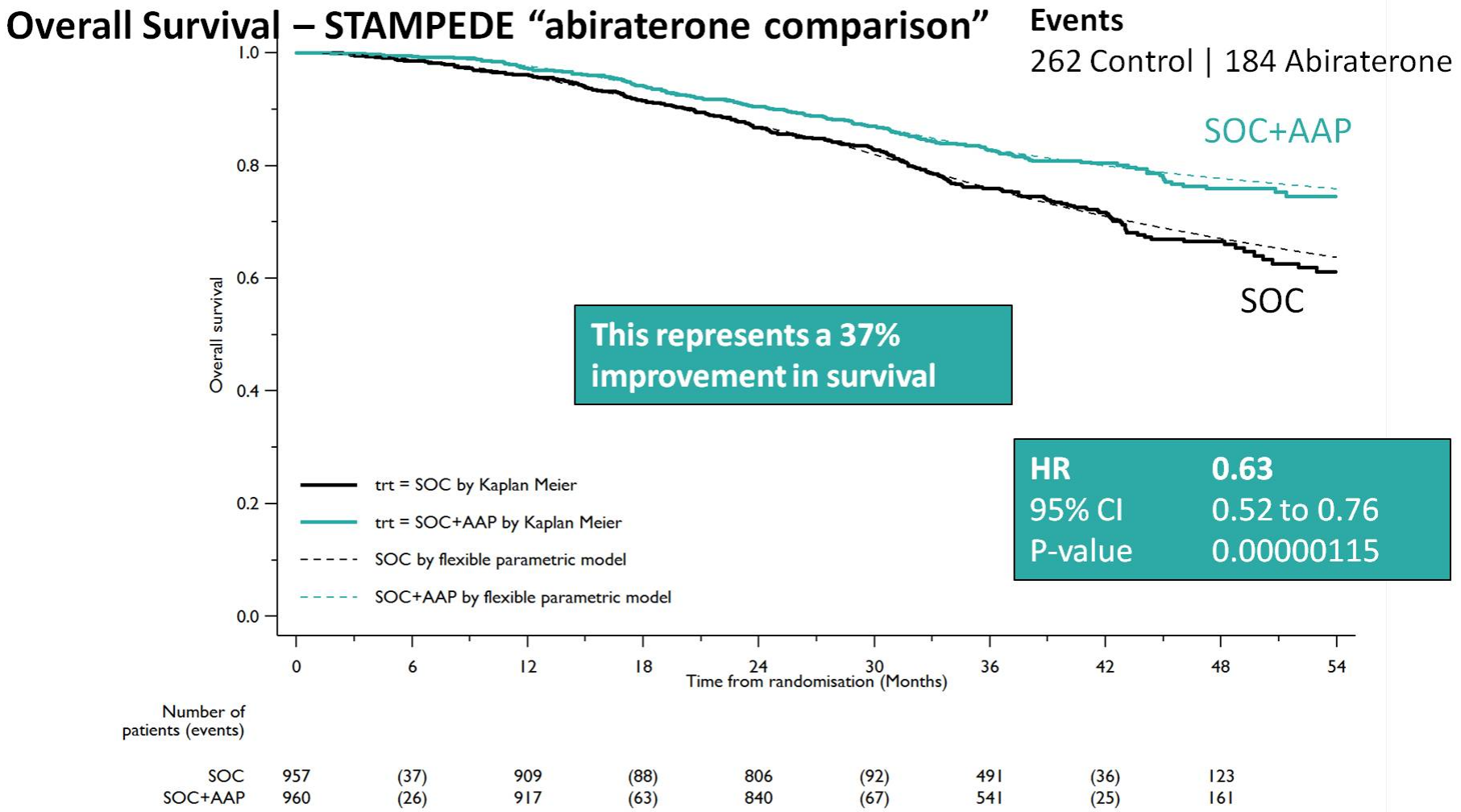


OS rate at three years:
ADT + AA + P: 66%
ADT + placebos: 49%

Median follow-up:
30.4 months

Fizazi K et al. N Engl J Med 2017; 377:352-60.

STAMPEDE – Overall Survival with Abiraterone



James ND et al. N Engl J Med 2017; 377:338-53.

STAMPEDE – Direct Non-randomized Comparison of Docetaxel with Abiraterone

- N=566
- 60% metastatic
- No difference in OS, MFS, cancer-specific survival, or skeletal related events
- PFS (driven by PSA) favored abiraterone

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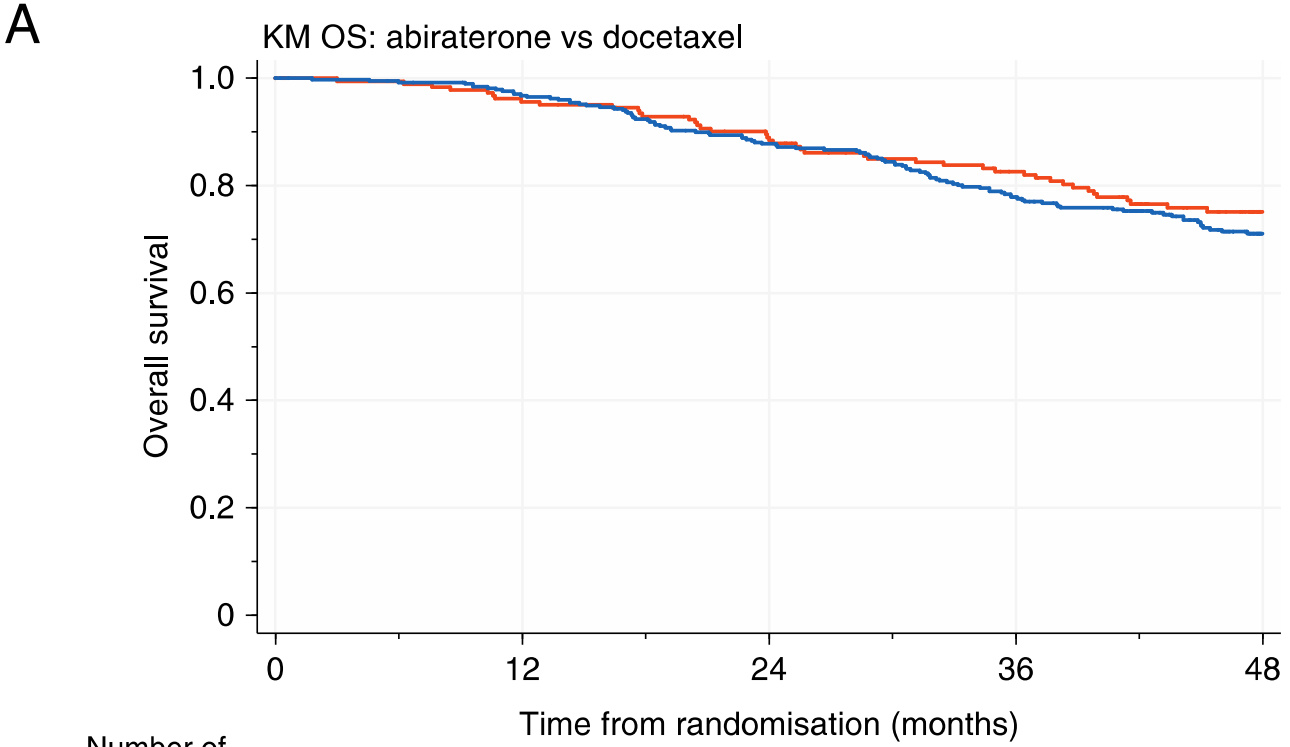
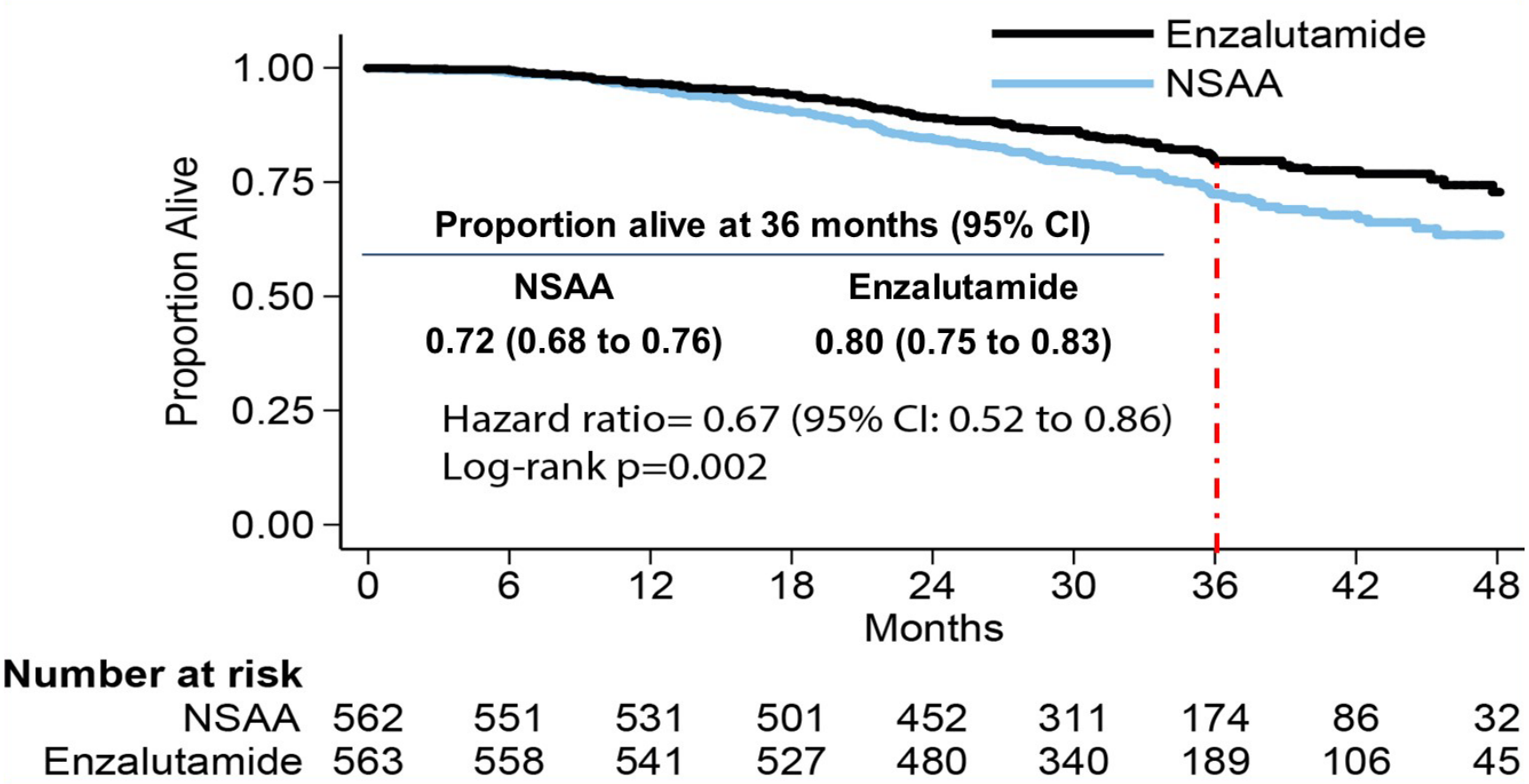


Number of patients (events)																								
SOC+DocP	189	(1)	183	(7)	175	(5)	168	(7)	158	(7)	146	(4)	139	(10)	112	(2)	74							
SOC+AAP	377	(3)	371	(9)	358	(16)	339	(17)	320	(12)	307	(24)	278	(9)	240	(12)	161							

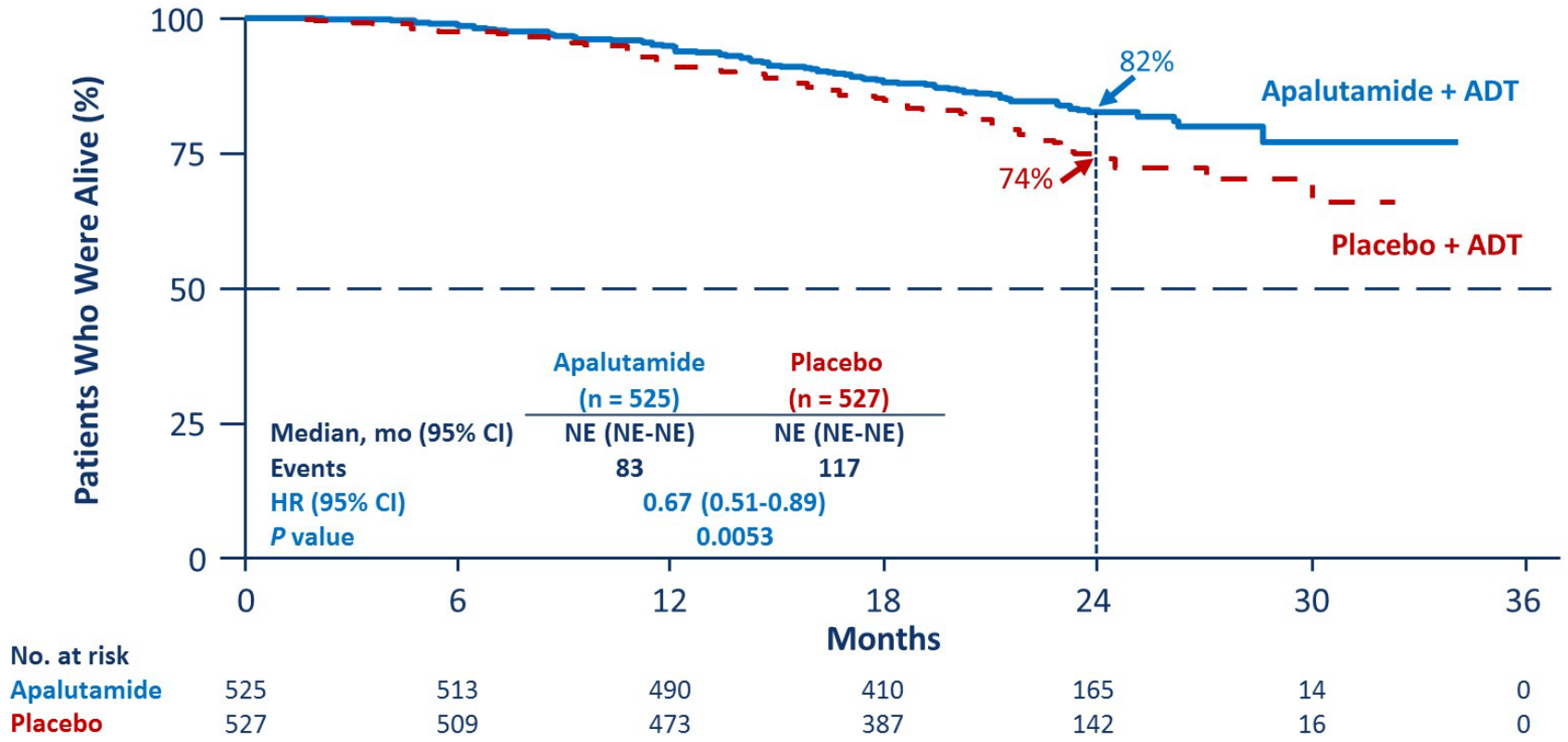
Sydes M et al. Ann Oncol 2018; 29(5):1235–48.

ENZAMET Primary Endpoint: Overall Survival



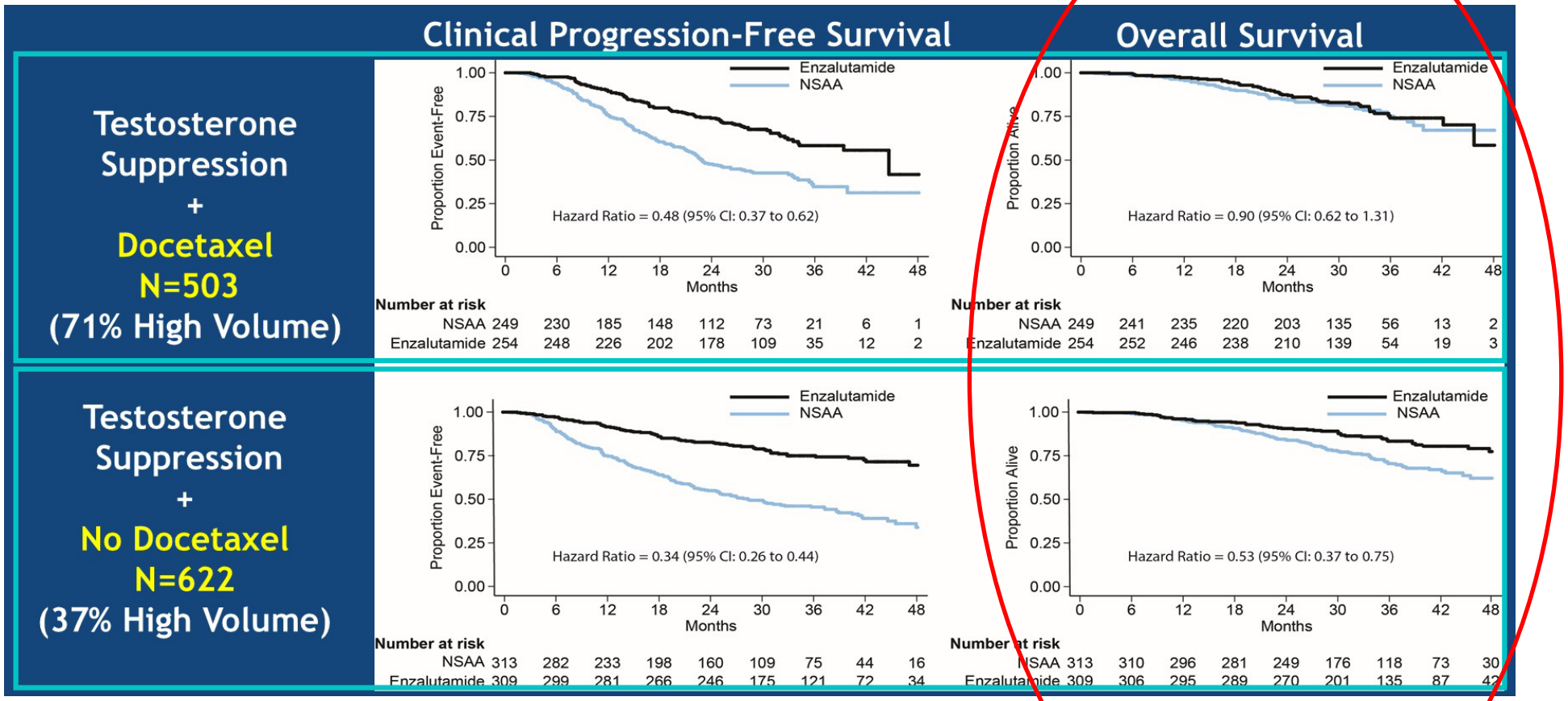
Davis ID et al. N Engl J Med. Epub June 2, 2019.

TITAN: Apalutamide in mHSPC



11% of patients received prior docetaxel

ENZAMET Concurrent Docetaxel Data

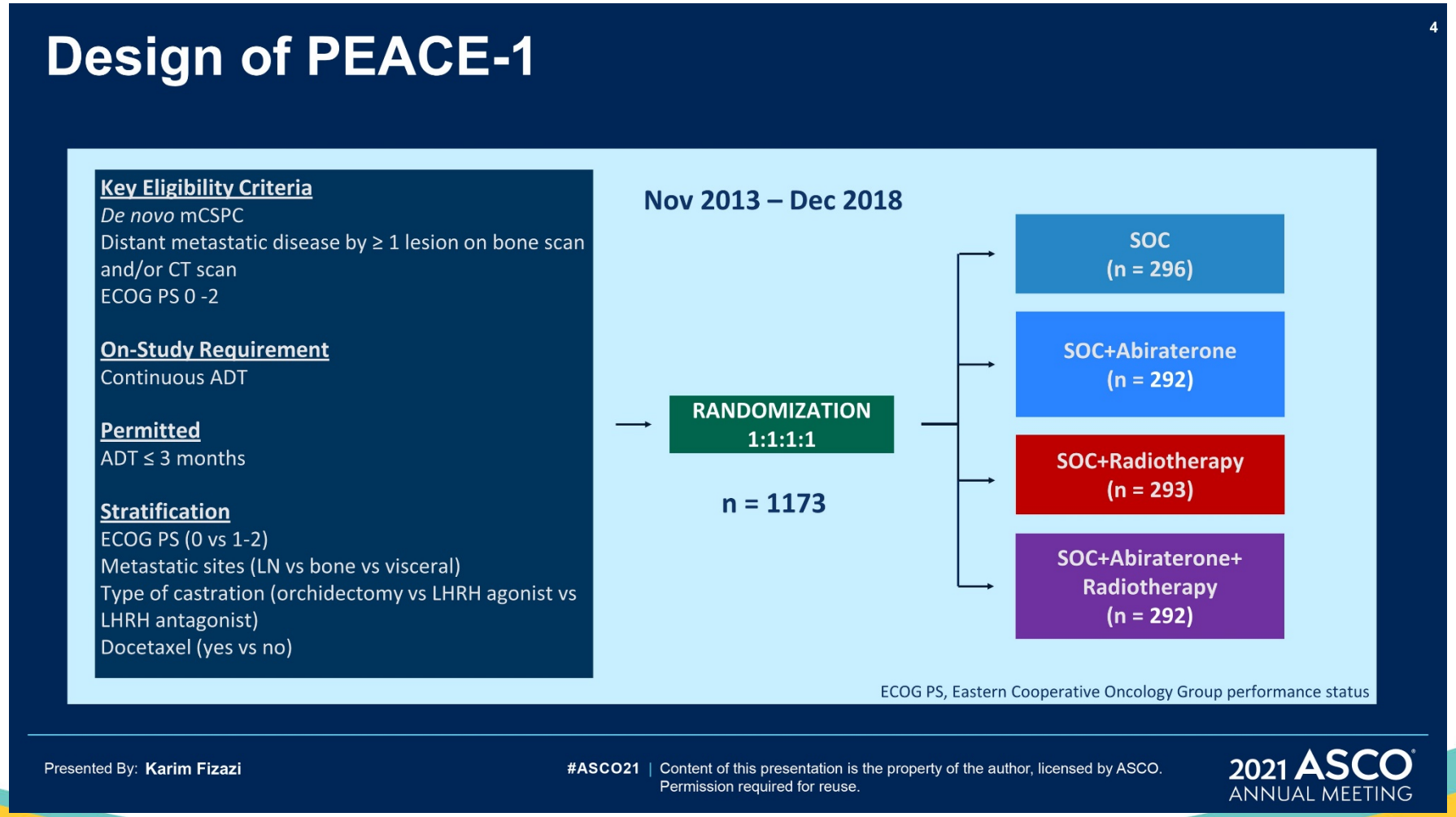


Triple therapy with ADT + Docetaxel + Enzalutamide had more adverse events

- Sensory neuropathy 9 vs. 3%
- Nail discoloration 10 vs. 5%
- Grade 1-2 watery eyes 20 vs. 6%
- Grade 2 fatigue 20 vs. 14%

Davis ID et al. N Engl J Med. Epub June 2, 2019.

PEACE1 Study: Docetaxel vs. Docetaxel followed by abiraterone



PEACE1 Study: Docetaxel vs. Docetaxel followed by abiraterone

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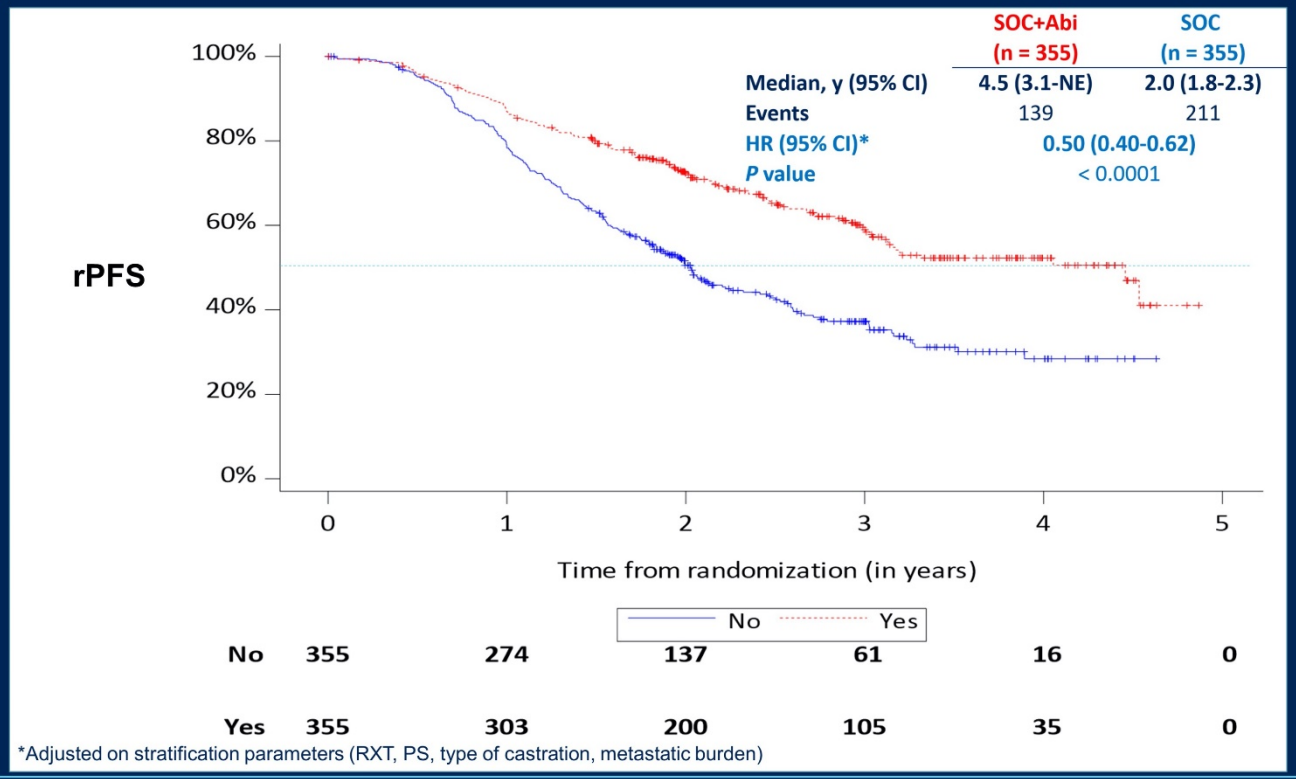
Radiographic Progression-Free Survival (rPFS)
ADT+Docetaxel population: SOC=ADT+Docetaxel (+/- RXT)



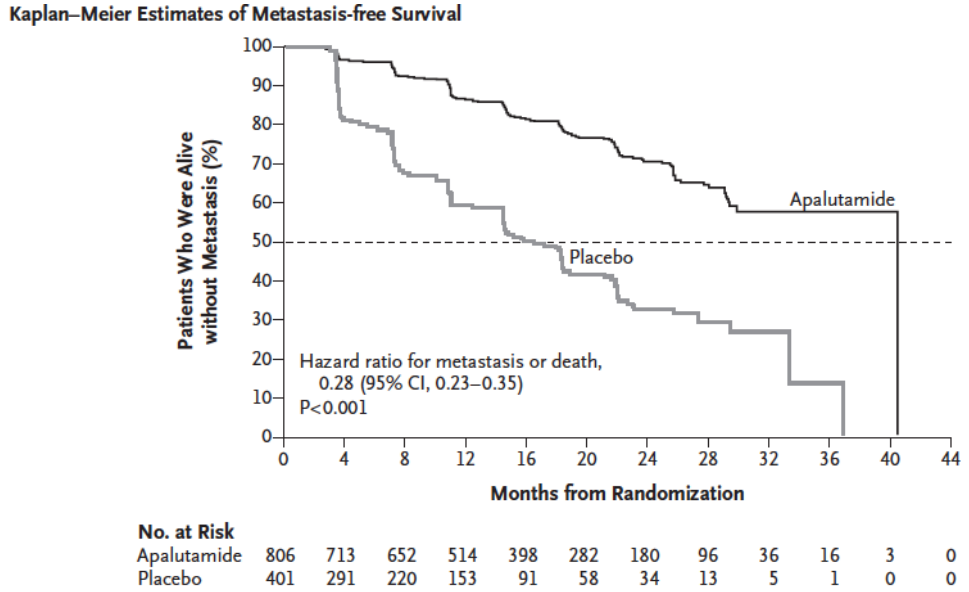
Presented By: **Karim Fizazi**

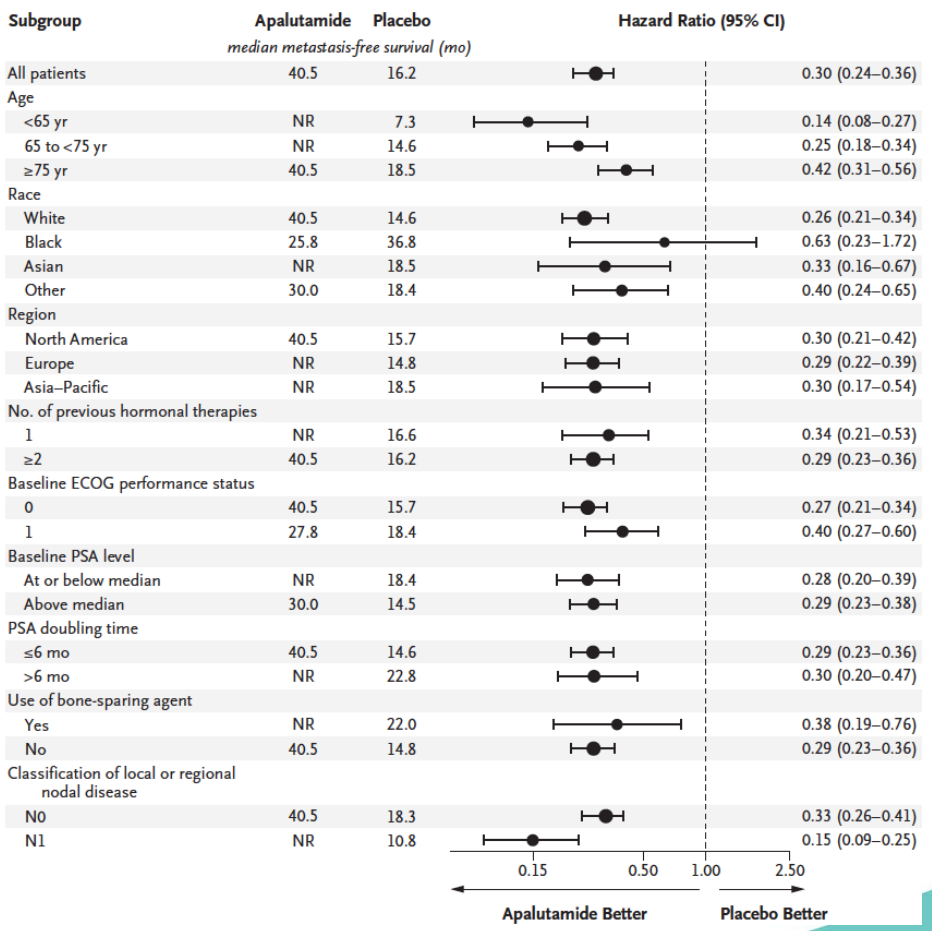
2021 ASCO ANNUAL MEETING

What should we do with mHSPC after all this?

- My preference is to use a novel hormonal agent (NHA) in low volume patients
- Consider NHA or docetaxel for high volume metastatic disease delineating between the two by:
  - Patient comorbidities
  - Side effect profiles
  - Duration of therapy
  - Financial toxicity
- Insufficient data to justify giving an NHA (i.e. abiraterone or enzalutamide) after docetaxel

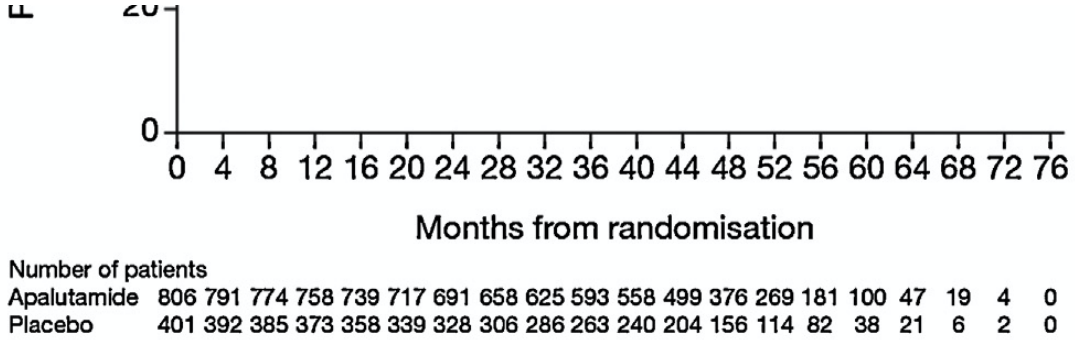
SPARTAN: Apalutamide Improves Metastasis-free Survival for Patients with M0 CRPC





Smith MR et al. N Engl J Med 2018; 378:1408-18.

SPARTAN: Apalutamide Improves Overall Survival for Patients with M0 CRPC



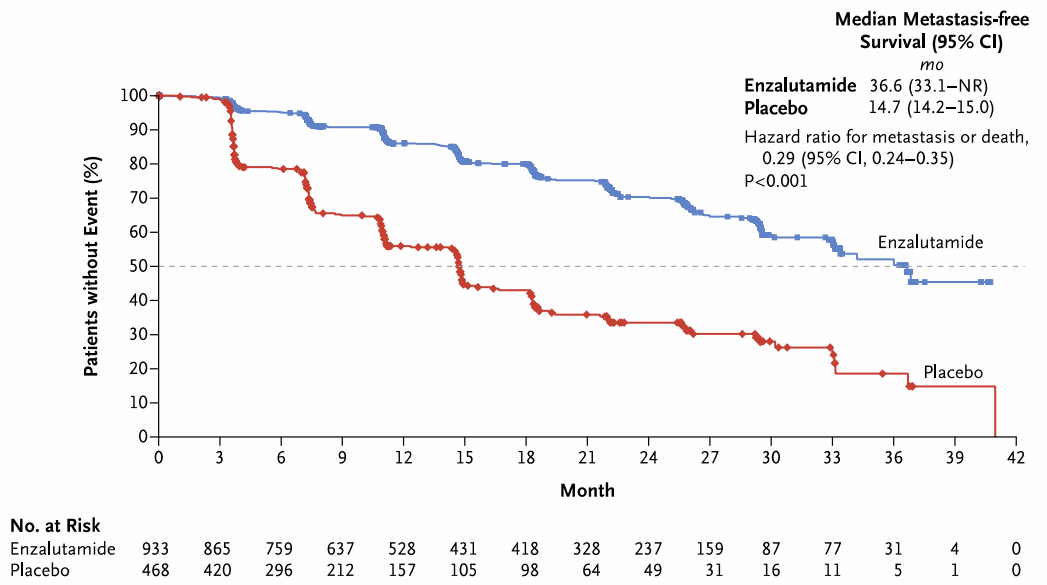
C

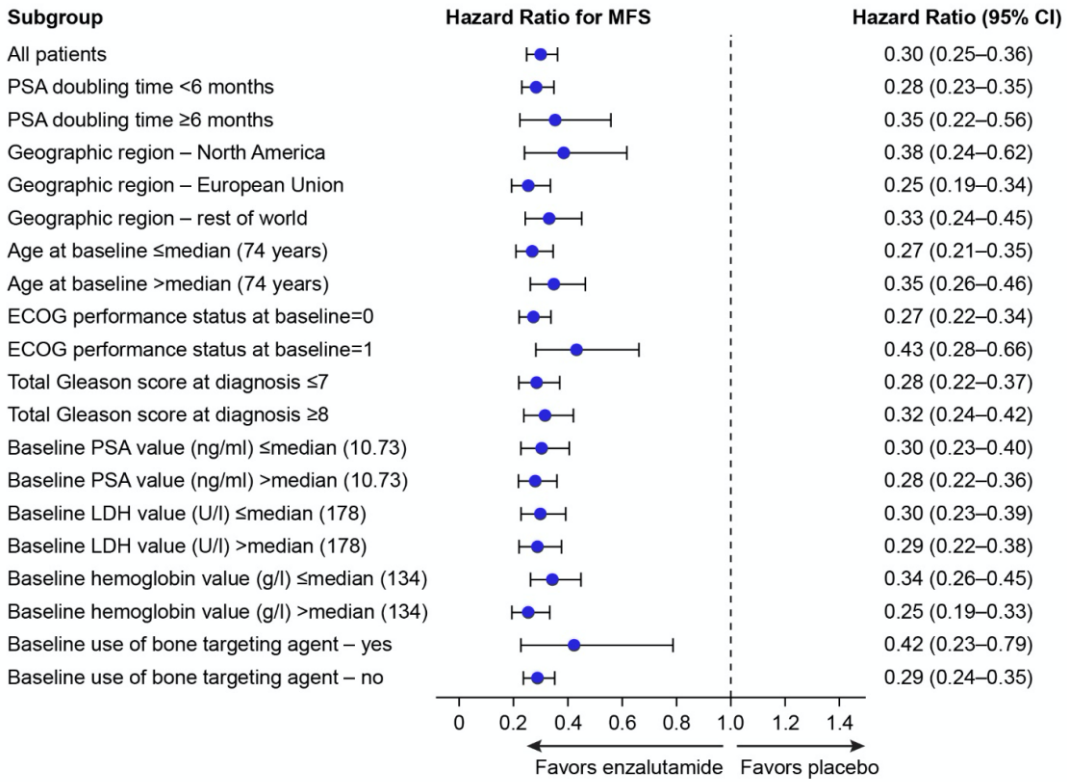
Subgroup	Median overall survival (mo) Apalutamide	Placebo	Haz
All patients	73.9	59.9	
Age			
<65 yr	NR	NR	
≥65 yr	61.5	58.7	
Race			
White	73.9	57.7	
Black	65.1	NR	
Asian	NR	NR	
Others	66.1	NR	

Median follow up: 52 months
Overall survival: HR = 0.78 [95%CI: 0.64-0.96], P=0.016
Median OS: 73.9 mos vs. 59.9 mos

Smith MR et al. Eur Urol. 2021 Jan;79(1):150-158

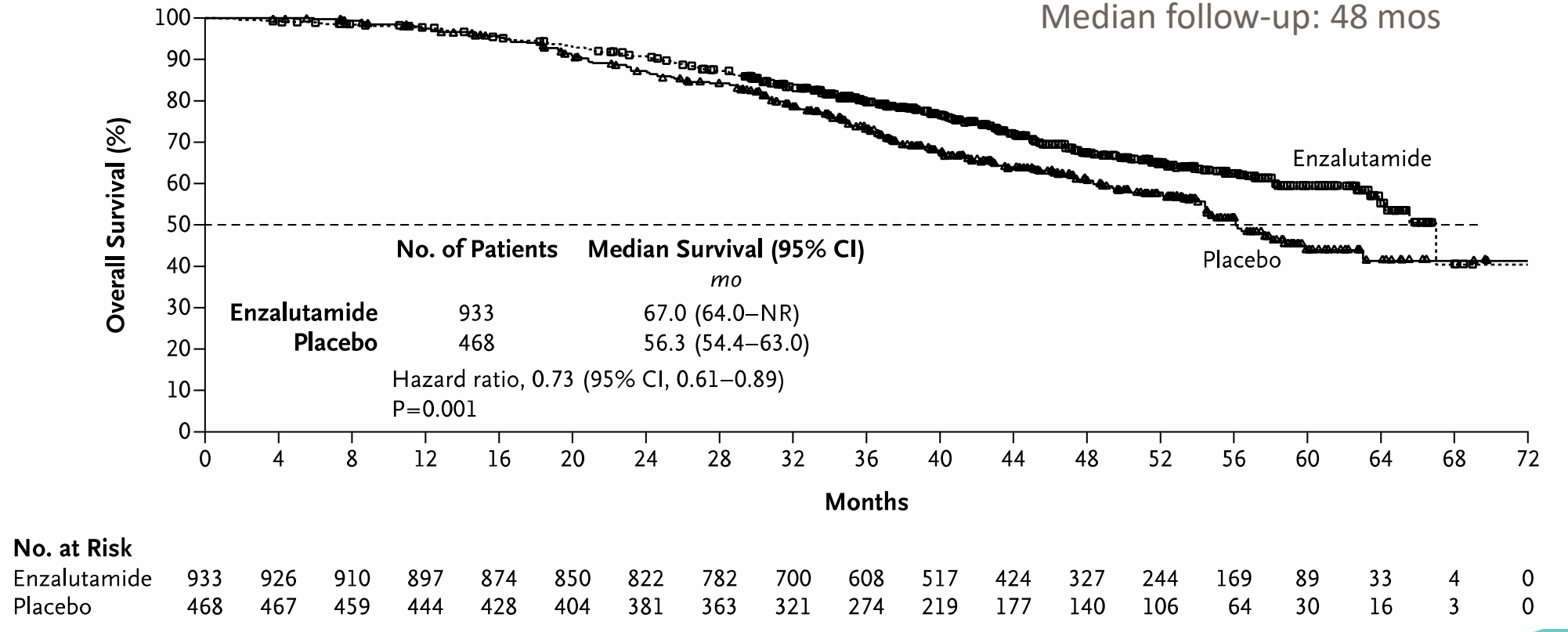
PROSPER: Enzalutamide Improves Metastasis-free Survival for Patients with M0 CRPC





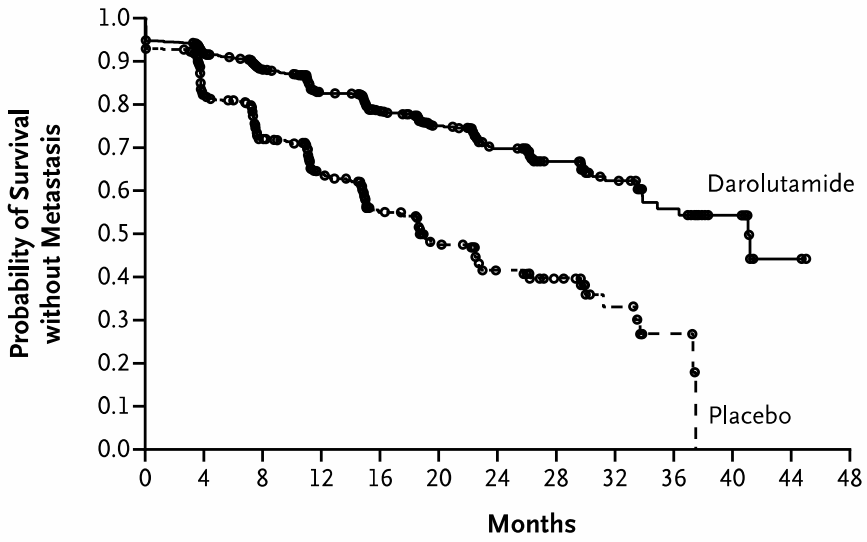
Hussain M et al. **N Engl J Med 2018;378:2465-74.**

PROSPER: Enzalutamide Improves Overall Survival for Patients with M0 CRPC



Sternberg, et al. **N Engl J Med 2020;382:2197-206.**

ARAMIS: Darolutamide Improves Metastasis Free Survival for Patients with M0 CRPC

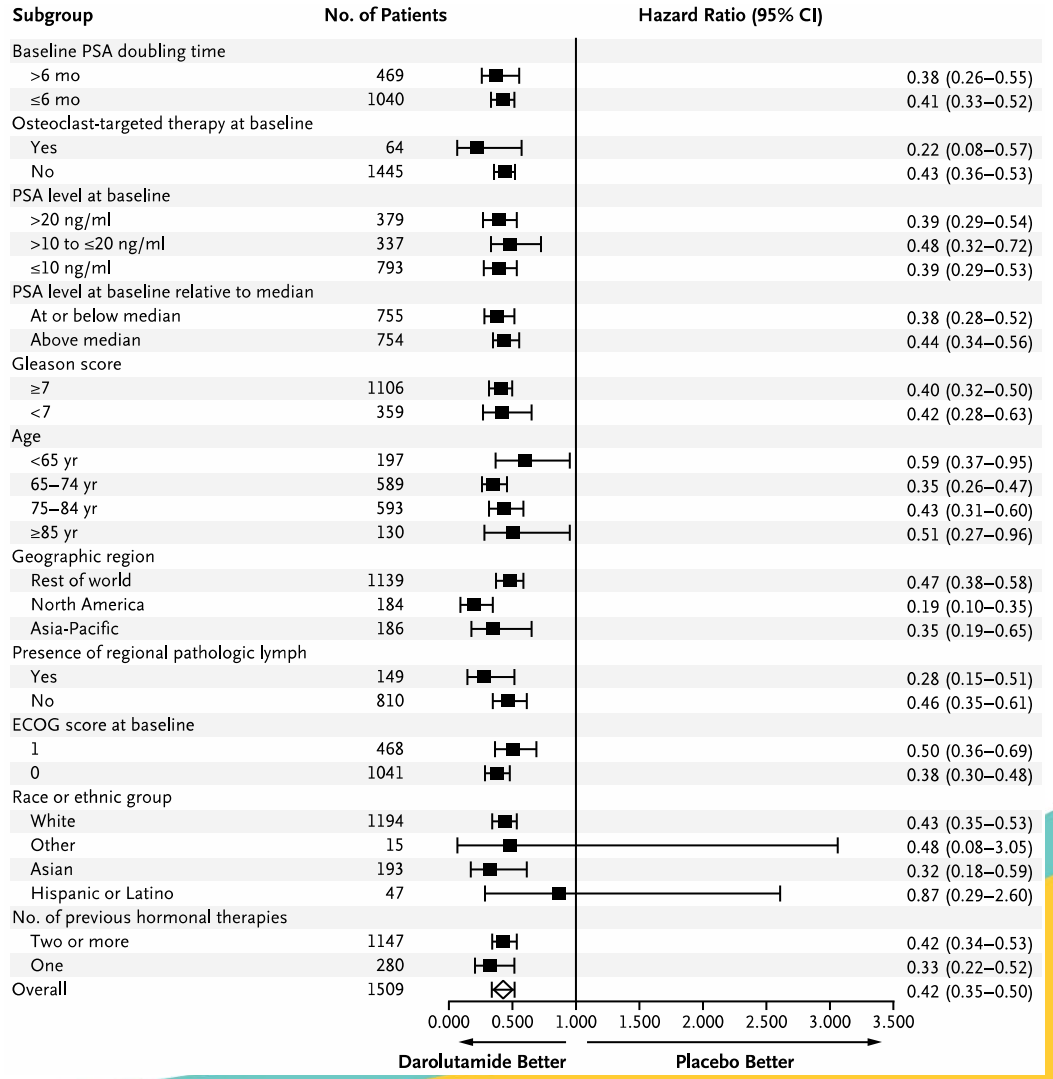


No. at Risk

Darolutamide	955	817	675	506	377	262	189	116	68	37	18	2	0
Placebo	554	368	275	180	117	75	50	29	12	4	0	0	0

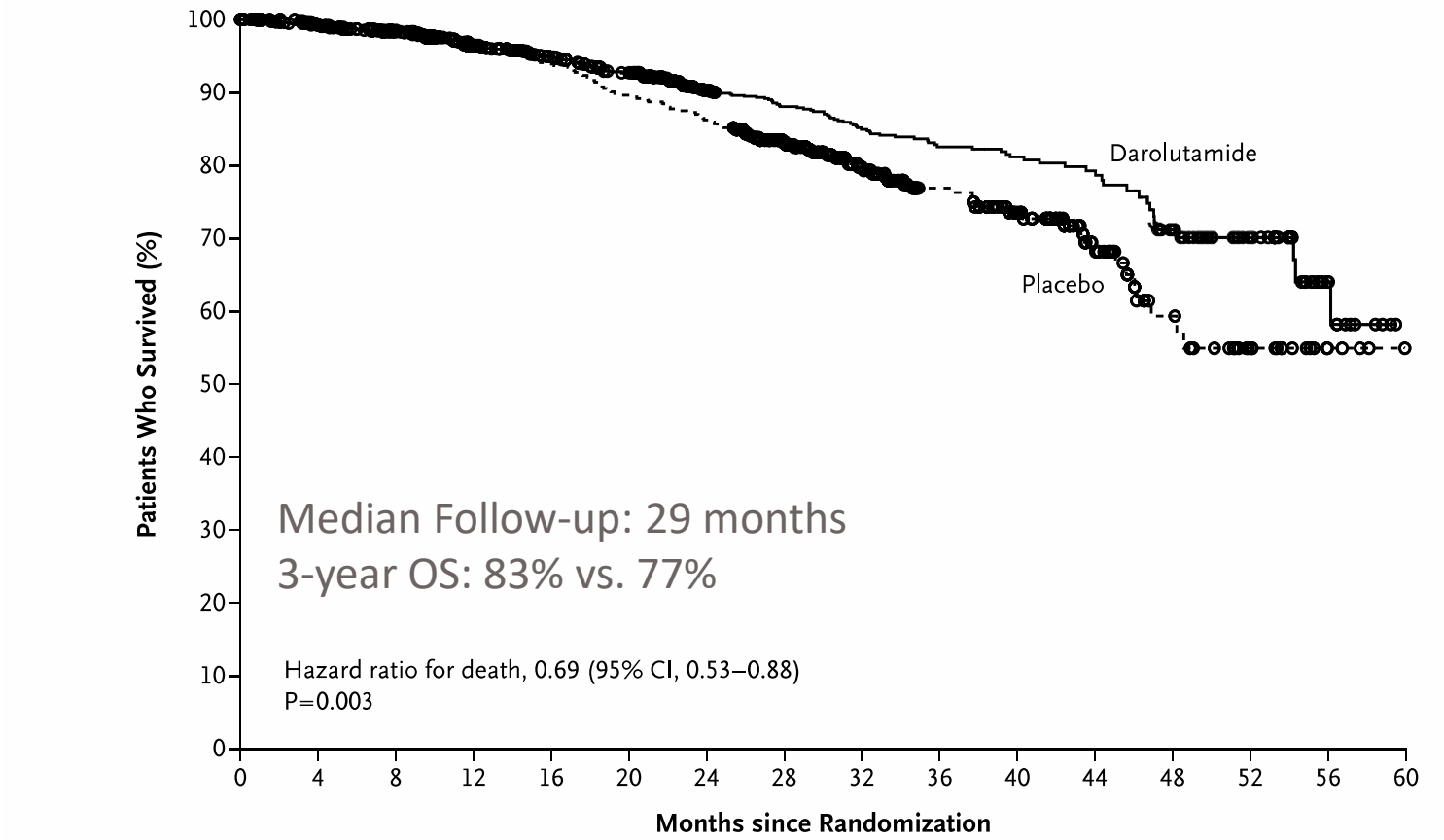
	Median Metastasis-free Survival (95% CI) *mo*
Darolutamide	40.4 (34.3–NR)
Placebo	18.4 (15.5–22.3)

Hazard ratio, 0.41 (95% CI, 0.34–0.50)
P<0.001



Fizazi, et al N Engl J Med 2019;380:1235-46.

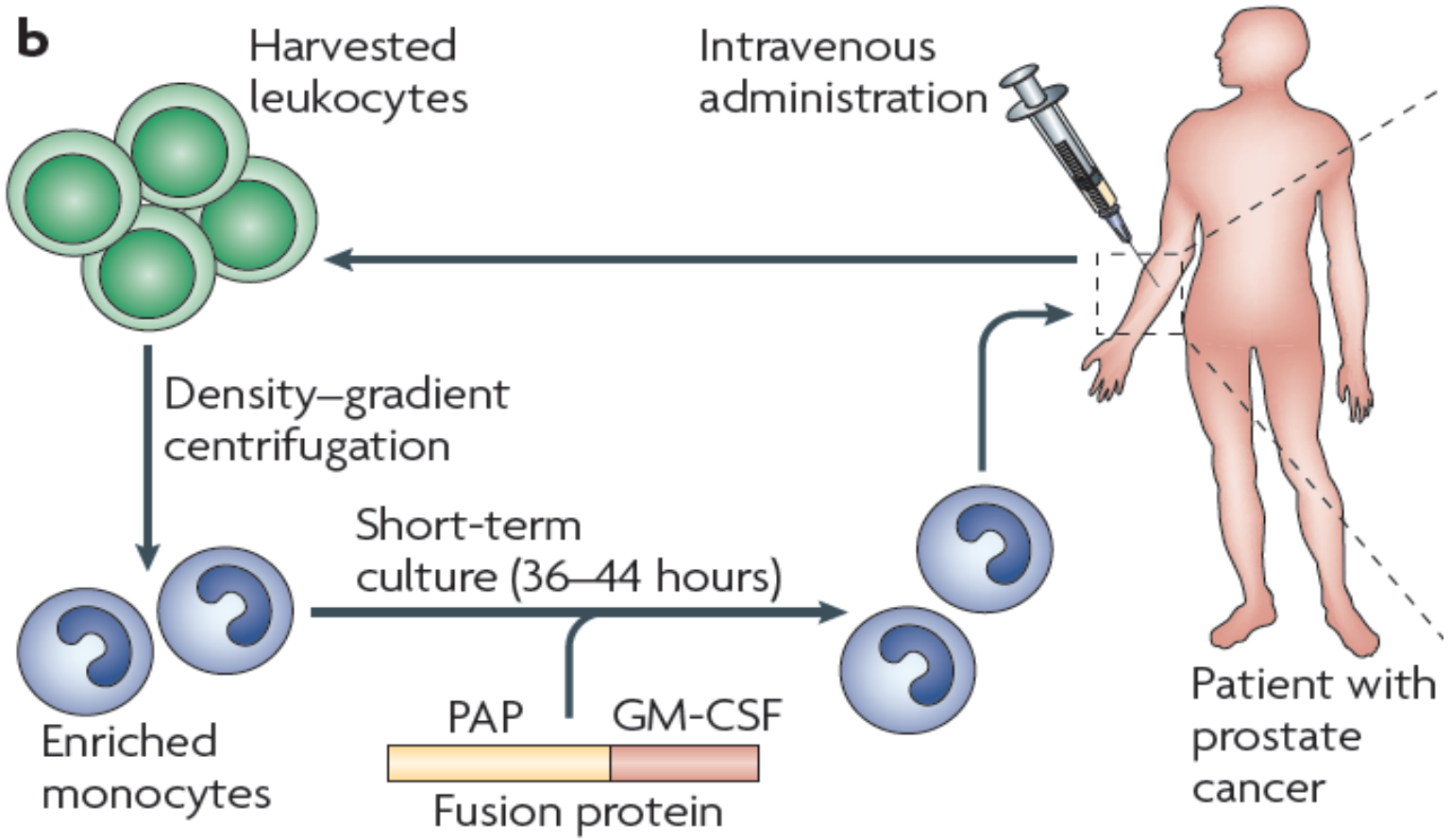
ARAMIS: Darolutamide Improves Overall Survival for Patients with M0 CRPC



No. at Risk																
Darolutamide	955	932	908	863	816	771	680	549	425	293	214	129	69	37	12	0
Placebo	554	530	497	460	432	394	333	261	182	130	93	54	28	16	4	0

Fizazi, et al. **N Engl J Med 2020;383:1040-9**

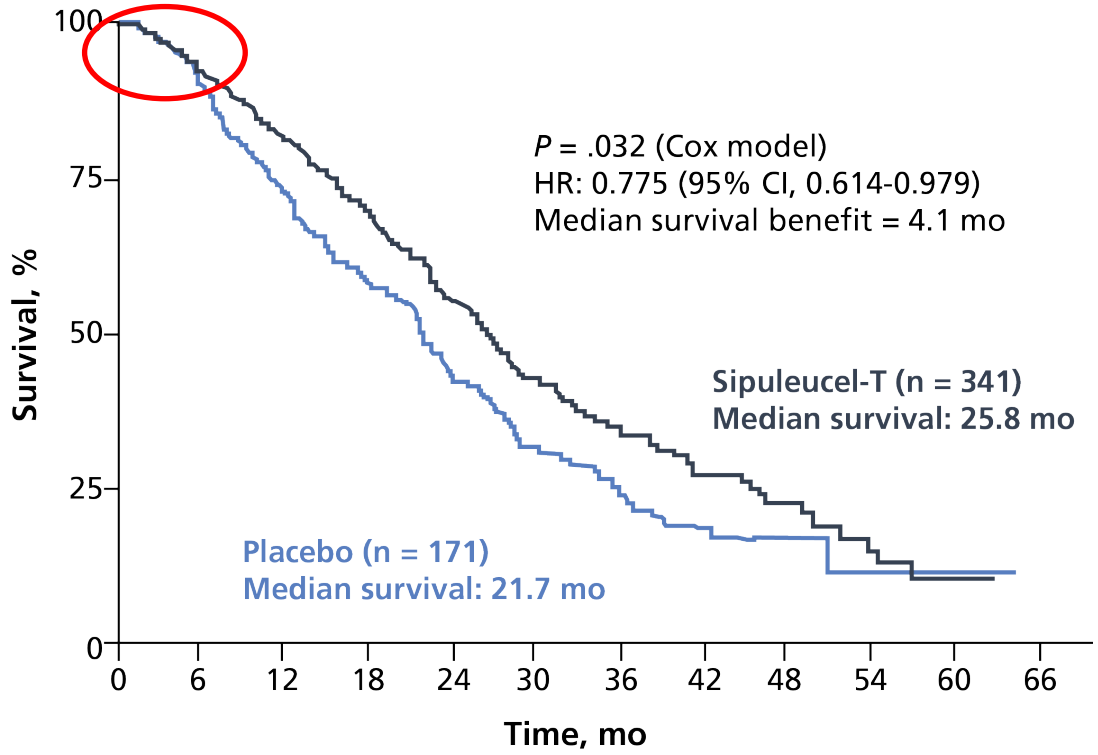
Activated Cellular Immunotherapy (Sipuleucel-T)



Drake et al. Curr Opin Urol 2010

Sipuleucel-T

- Must have asymptomatic metastatic castration-resistant prostate cancer
- Short window of opportunity
  - Survival curves don't split until the 6-month time point → should have reasonably indolent disease
- Typically, do not see objective responses
  - Only 1-3% with a significant PSA decline
- No improvement in PFS



Kantoff PW et al. *N Engl J Med.* 2010; 363:411-22.

Potential Sipuleucel-T Side Effects

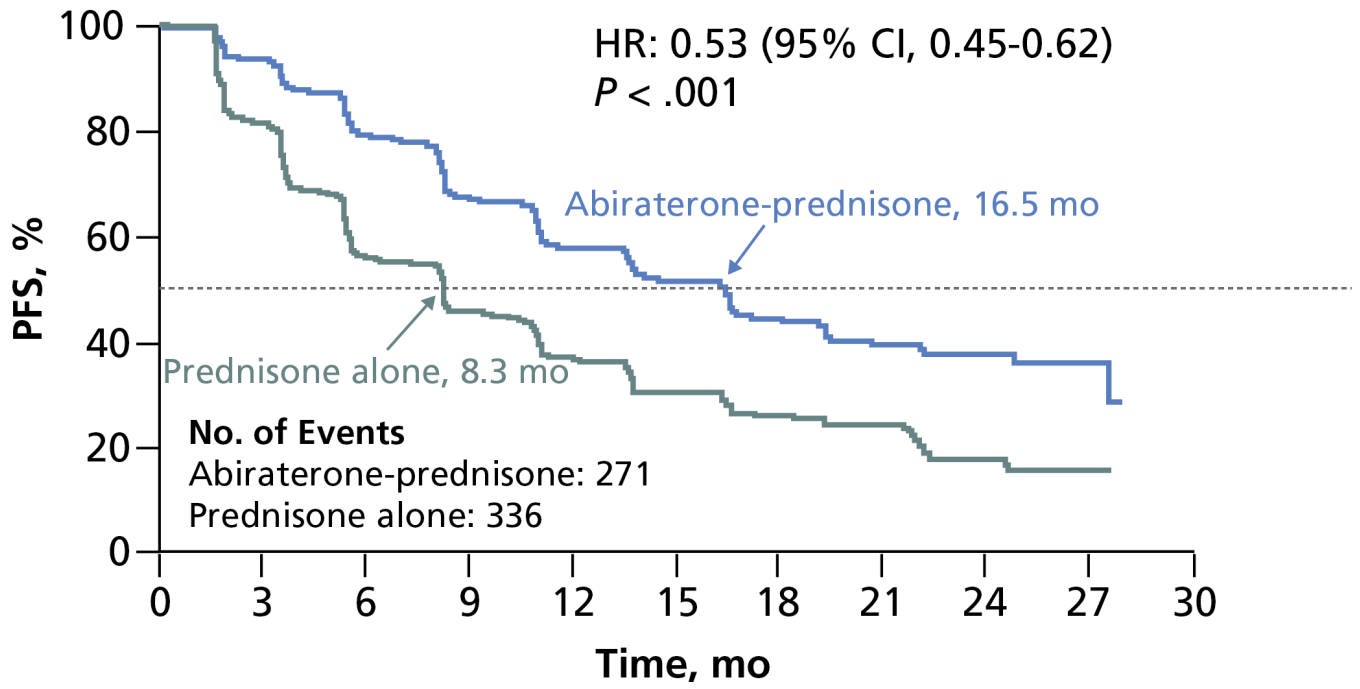
- Most common adverse events within 1 day of sipuleucel-T infusion:
  - chills (51.2%)
  - fever (22.5%)
  - fatigue (16.0%)
  - nausea (14.2%)
  - headache (10.7%)
- Events generally occurred within 1 day after infusion and resolved within 1-2 days

Table 2. Adverse Events.*

Event	Sipuleucel-T (N=338)		Placebo (N=168)	
	All Grades	Grade 3–5	All Grades	Grade 3–5
	number (percent)			
Any	334 (98.8)	107 (31.7)	162 (96.4)	59 (35.1)
Chills†	183 (54.1)	4 (1.2)	21 (12.5)	0
Fatigue	132 (39.1)	4 (1.2)	64 (38.1)	3 (1.8)
Back pain	116 (34.3)	12 (3.6)	61 (36.3)	8 (4.8)
Pyrexia†	99 (29.3)	1 (0.3)	23 (13.7)	3 (1.8)
Nausea	95 (28.1)	2 (0.6)	35 (20.8)	0
Arthralgia	70 (20.7)	7 (2.1)	40 (23.8)	5 (3.0)
Citrate toxicity‡	68 (20.1)	0	34 (20.2)	0
Vomiting	60 (17.8)	0	20 (11.9)	0
Headache†	54 (16.0)	1 (0.3)	8 (4.8)	0
Anemia	50 (14.8)	5 (1.5)	21 (12.5)	7 (4.2)
Limb pain	49 (14.5)	4 (1.2)	25 (14.9)	1 (0.6)
Dizziness	49 (14.5)	0	16 (9.5)	0
Paresthesia‡	45 (13.3)	0	26 (15.5)	0
Constipation	45 (13.3)	0	24 (14.3)	2 (1.2)
Musculoskeletal pain	44 (13.0)	3 (0.9)	20 (11.9)	3 (1.8)
Pain§	44 (13.0)	6 (1.8)	12 (7.1)	2 (1.2)
Paresthesia (oral)‡	41 (12.1)	0	21 (12.5)	0
Asthenia	37 (10.9)	6 (1.8)	13 (7.7)	2 (1.2)
Diarrhea	36 (10.7)	1 (0.3)	17 (10.1)	3 (1.8)
Musculoskeletal chest pain	33 (9.8)	2 (0.6)	19 (11.3)	2 (1.2)
Myalgia†	33 (9.8)	2 (0.6)	8 (4.8)	0
Influenza-like illness†	33 (9.8)	0	6 (3.6)	0
Bone pain	32 (9.5)	3 (0.9)	18 (10.7)	2 (1.2)
Hypertension†	25 (7.4)	2 (0.6)	5 (3.0)	0
Anorexia	24 (7.1)	1 (0.3)	27 (16.1)	3 (1.8)
Weight loss	20 (5.9)	2 (0.6)	18 (10.7)	1 (0.6)
Hyperhidrosis†	18 (5.3)	0	1 (0.6)	0
Groin pain†	17 (5.0)	0	4 (2.4)	0
Anxiety	13 (3.8)	0	14 (8.3)	0
Flank pain	9 (2.7)	0	10 (6.0)	0
Contusion	9 (2.7)	0	9 (5.4)	0
Depression	8 (2.4)	1 (0.3)	11 (6.5)	0

Kantoff PW et al. *N Engl J Med.* 2010; 363:411-22.

COU-AA-302 Radiographic Progression-free Survival

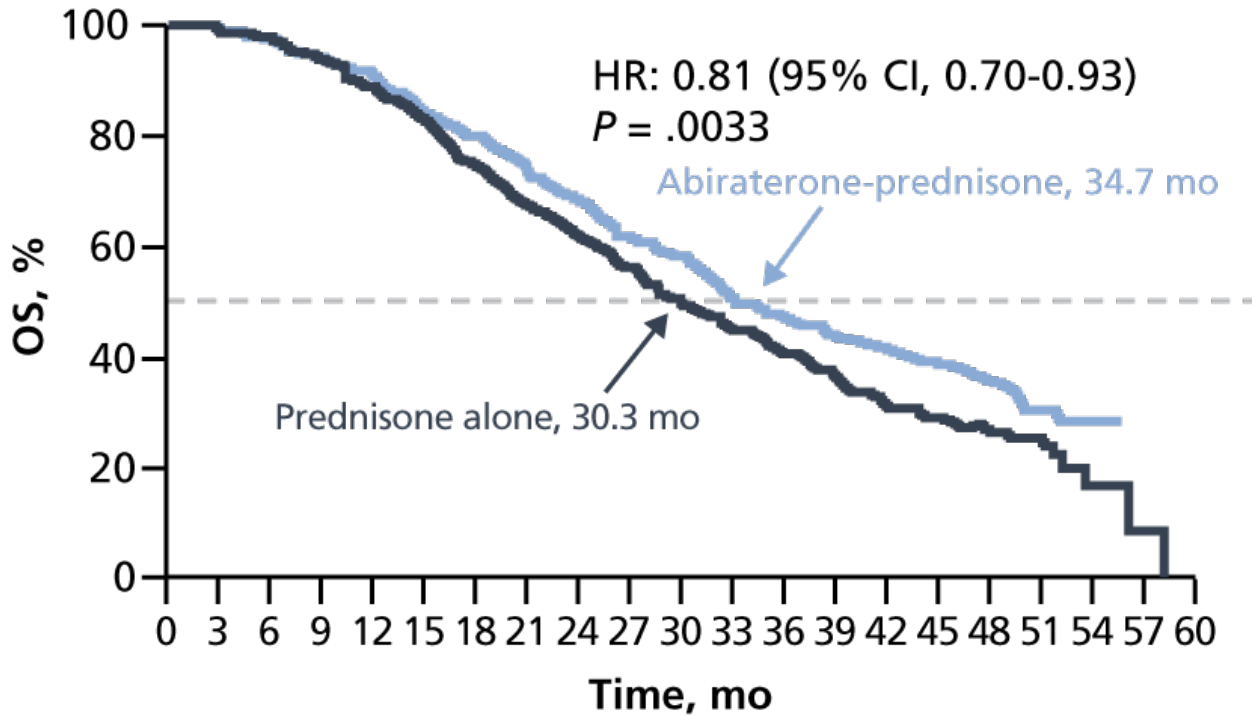


No. at Risk											
Abiraterone-prednisone	546	485	389	311	240	195	155	85	38	9	0
Prednisone alone	542	406	244	177	133	100	80	37	14	1	0

OS: overall survival; PFS: progression-free survival.

Ryan CJ et al. *N Engl J Med.* 2013;368:138-148.
Ryan CJ, Smith MR, Fizazi K, Miller K. 39th ESMO 2014. Abstract 7530

COU-AA-302 Overall Survival



No. at Risk

Abiraterone-prednisone	546	538	525	504	483	453	422	394	359	330	296	273	235	218	202	189	118	59	15	0	0
Prednisone alone	542	534	509	493	466	438	401	363	322	292	261	227	201	176	148	132	84	42	10	1	0

OS: overall survival; PFS: progression-free survival.

Ryan CJ et al. *N Engl J Med.* 2013;368:138-148.

Ryan CJ, Smith MR, Fizazi K, Miller K. European Society for Medical Oncology 2014 Congress (ESMO 2014). Abstract 7530.

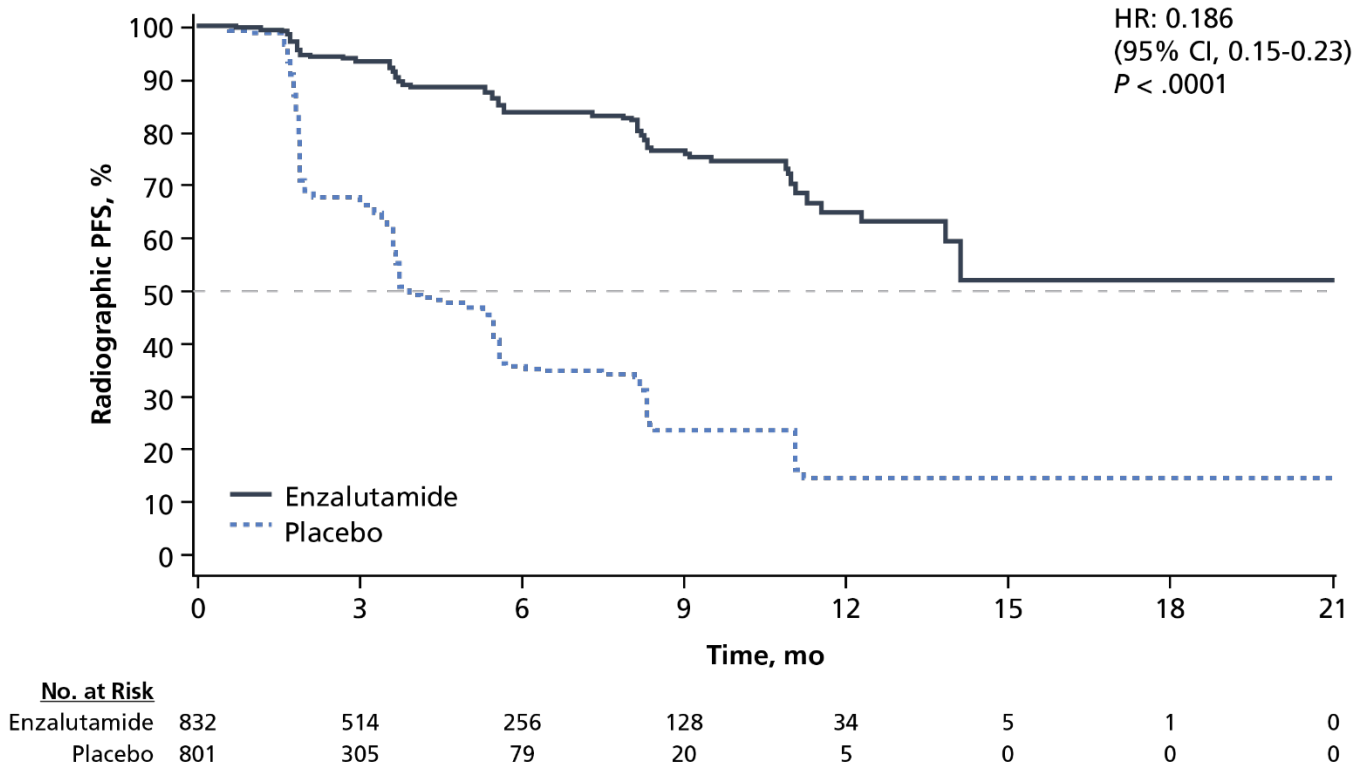
Safety Data from Cou-AA-302

	AA + P (n = 542) %		Placebo + P (n = 540) %	
	All Grades	Grades 3/4	All Grades	Grades 3/4
Fatigue	39	2	34	2
Fluid retention	28	0.7	24	1.7
Hypokalemia	17	2	13	2
Hypertension	22	4	13	3
Cardiac disorders	19	6	16	3
Atrial fibrillation	4	1.3	5	0.9
ALT increased	12	5.4	5	0.8
AST increased	11	3.0	5	0.9

Most ALT and AST increases occurred during the first 3 months of treatment

Ryan CJ et al. *N Engl J Med.* 2013; 368:138-48.

PREVAIL Radiographic Progression-free Survival

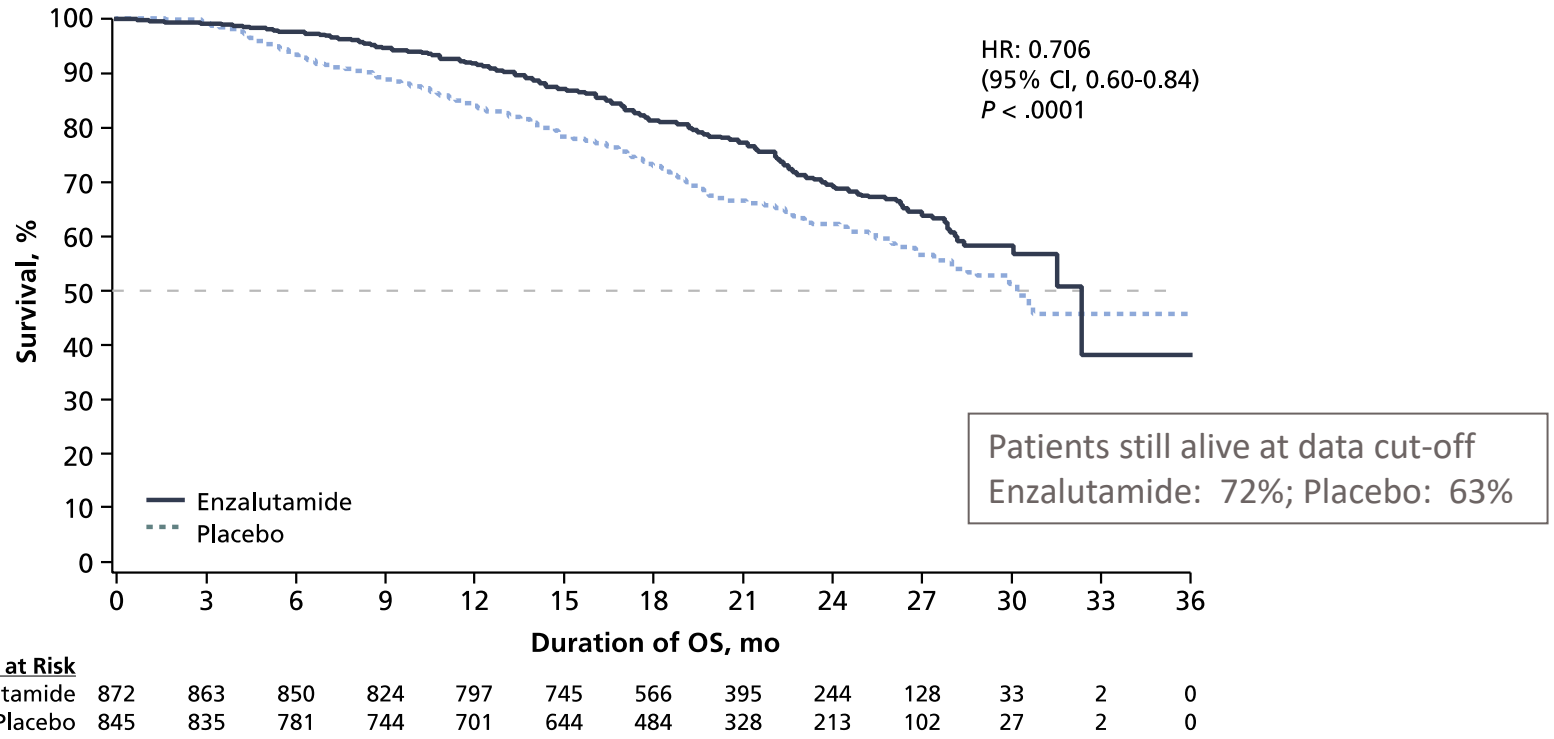


	Estimated Median Radiographic PFS, mo (95% CI)
Enzalutamide	NYR (13.8-NYR)
Placebo	3.9 (3.7-5.4)

NYR: not yet reached.

Beer TM et al. *J Clin Oncol*. 2014;32(suppl 4):Abstract LBA1^.

PREVAIL Overall Survival



Patients still alive at data cut-off
Enzalutamide: 72%; Placebo: 63%

	Estimated Median OS, mo (95% CI)
Enzalutamide	32.4 (30.1-NYR)
Placebo	30.2 (28.0-NYR)

Beer TM et al. *J Clin Oncol*. 2014;32(suppl 4):Abstract LBA1^.

PREVAIL: Most Common Enzalutamide Side Effects

	All Grades, %		Grade ≥ 3 Events, %	
	Enzalutamide (n = 871)	Placebo (n = 844)	Enzalutamide (n = 871)	Placebo (n = 844)
Fatigue	35.6%	25.8%	1.8%	1.9%
Back pain	27.0%	22.2%	2.5%	3.0%
Constipation	22.2%	17.2%	0.5%	0.4%
Arthralgia	20.3%	16.0%	1.4%	1.1%
Decreased appetite	18.1%	16.1%	0.2%	0.7%
Hot flush	18.0%	7.7%	0.1%	0%
Diarrhea	16.3%	14.1%	0.2%	0.4%
Hypertension	13.4%	4.1%	6.8%	2.3%
Asthenia	13.0%	7.9%	1.3%	0.9%
Fall	11.6%	5.3%	1.4%	0.7%
Weight loss	11.5%	8.4%	0.6%	0.2%
Edema peripheral	10.6%	8.2%	0.2%	0.4%
Headache	10.4%	7.0%	0.2%	0.4%

* *At least 10% on enzalutamide and ≥ 2% more than placeb*

Beer TM, et al. *N Engl J Med.* 2014 Jul 31;371(5):424-33.

PREVAIL: Key Enzalutamide Side Effects

	All Grades, %		Grade ≥ 3 Events, %	
	Enzalutamide (n = 871)	Placebo (n = 844)	Enzalutamide (n = 871)	Placebo (n = 844)
Hypertension	13.4%	4.1%	6.8%	2.3%
Any cardiac adverse event	10.1%	7.8%	2.8%	2.1%
ALT increased	0.9%	0.6%	0.2%	0.1%
Seizure	0.1%*	0.1%#	0.1%*	0

** This seizure (n = 1) occurred after the data cutoff date*

 # Seizure in placebo arm was classified as grade 2

ALT = alanine aminotransferase

Beer TM, et al. *N Engl J Med.* 2014 Jul 31;371(5):424-33.

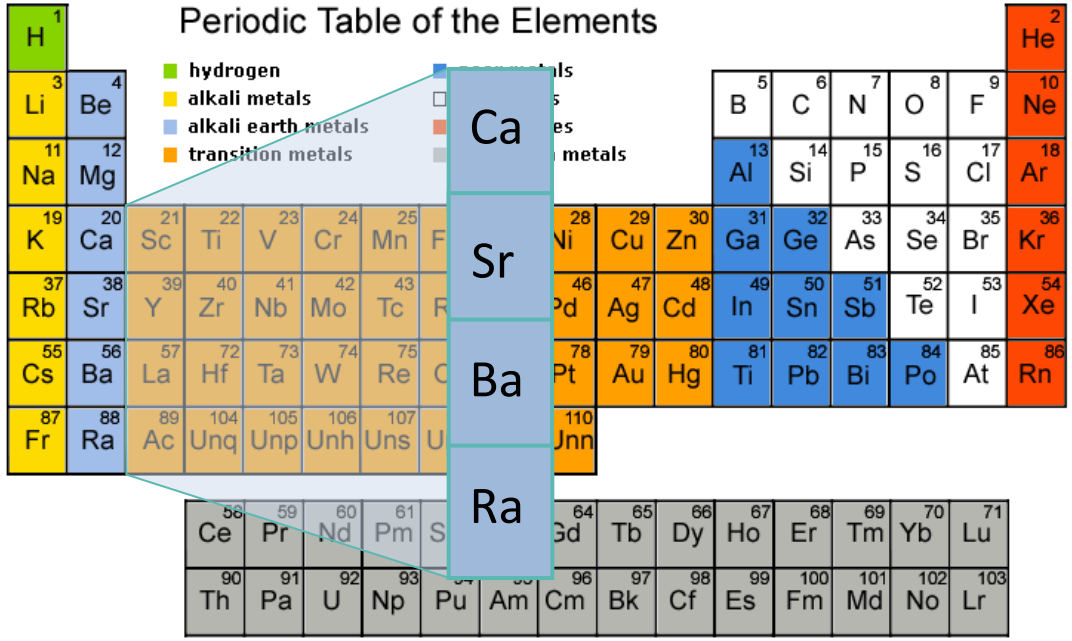
High Rates of Cross-Resistance between Abiraterone and Enzalutamide

	Prior Docetaxel	N	PSA Decline ≥30%, %	PSA Decline ≥50%, %	Median TTP, mo	Median PFS, mo
Abiraterone after enzalutamide						
Noonan[1]	Y	27	11	4	NR	3.5
Loriot[2]	Y	38	18	8	NR	2.7
Enzalutamide after abiraterone						
Schrader[3]	Y	35	37	29	4.0[a]	–
Bianchini[4]	Y	39	41	13	2.2	2.8
Badrising[5]	Y	61	46	21	4.0	2.8
Cheng[6]	Y	122	39	26	–	–
Azad[7]	Y	68	–	22	4.6	–
Cheng[6]	N	28	40	36	–	–
Azad[7]	N	47	–	26	6.6	–

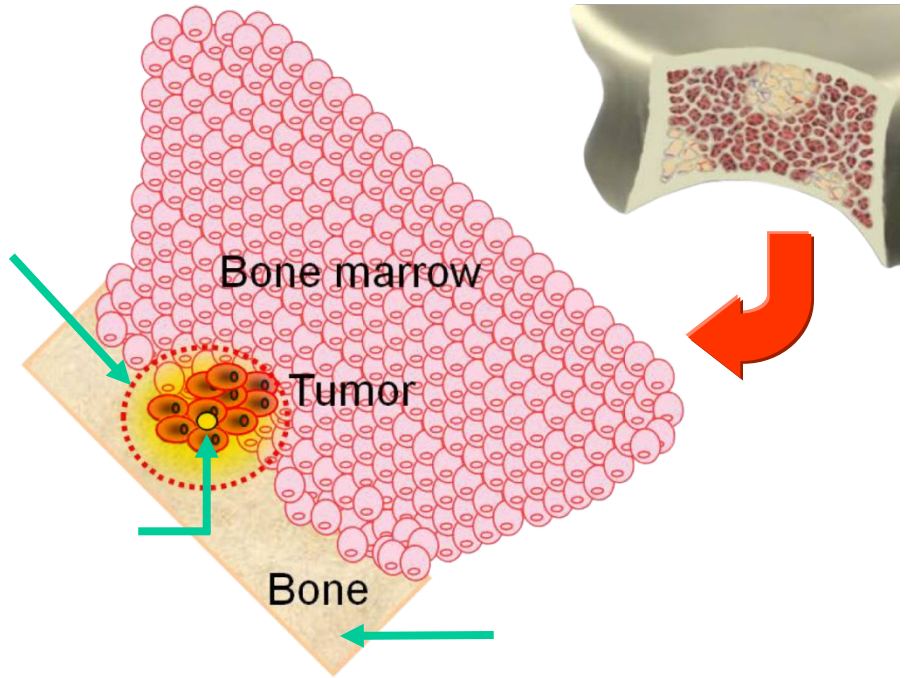
1. Noonan KL et al. *Ann Oncol*. 2013;24:1802-1807. 2. Loriot Y et al. *Ann Oncol*. 2013;24:1807-1812. 3. Schrader AJ et al. *Eur Urol*. 2014;65:30-36. 4. Bianchini D et al. *Eur J Cancer*. 2014;50:78-84. 5. Badrising S et al. *Cancer*. 2014;12:968-975. 6. Cheng HH et al. *J Clin Oncol*. 2014;32(Suppl 4):Abstract 18. 7. Azad AA et al. *Eur Urol*. 2015;67:23-29.

Radium-223 Mechanism of Action

- Radium-223 acts as a calcium mimic
- Naturally targets new bone growth in and around bone metastases
- Radium-223 is excreted by the small intestine



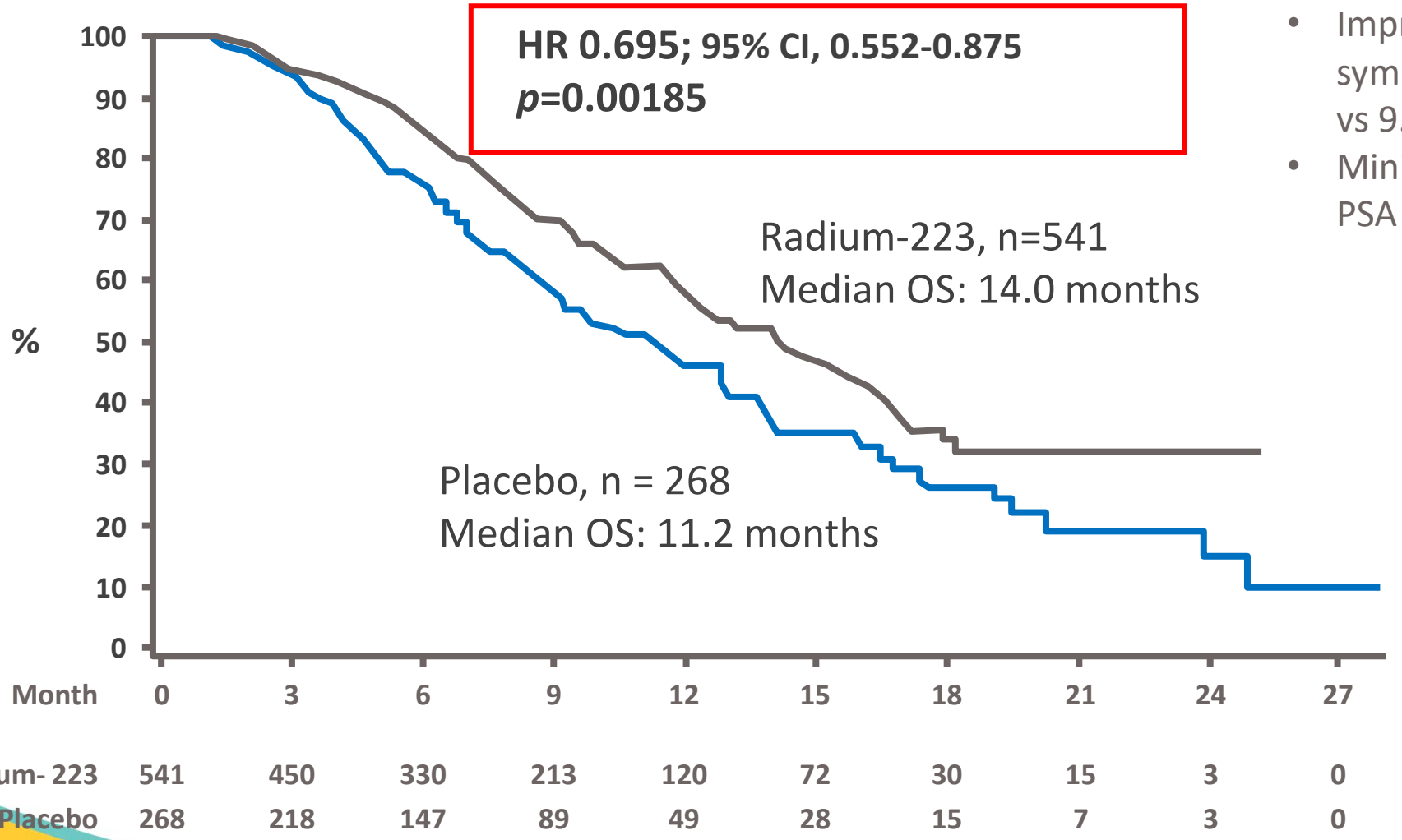
Radium-223 Mechanism of Action



- **Alpha-particles induce double-strand DNA breaks** in adjacent tumour cells[1]
- Short penetration of alpha emitters (2-10 cell diameters) = **highly localized tumour cell killing** and minimal damage to surrounding normal tissue

Perez et al. *Principles and Practice of Radiation Oncology.* 5th ed. Lippincott Williams & Wilkins; 2007:103.

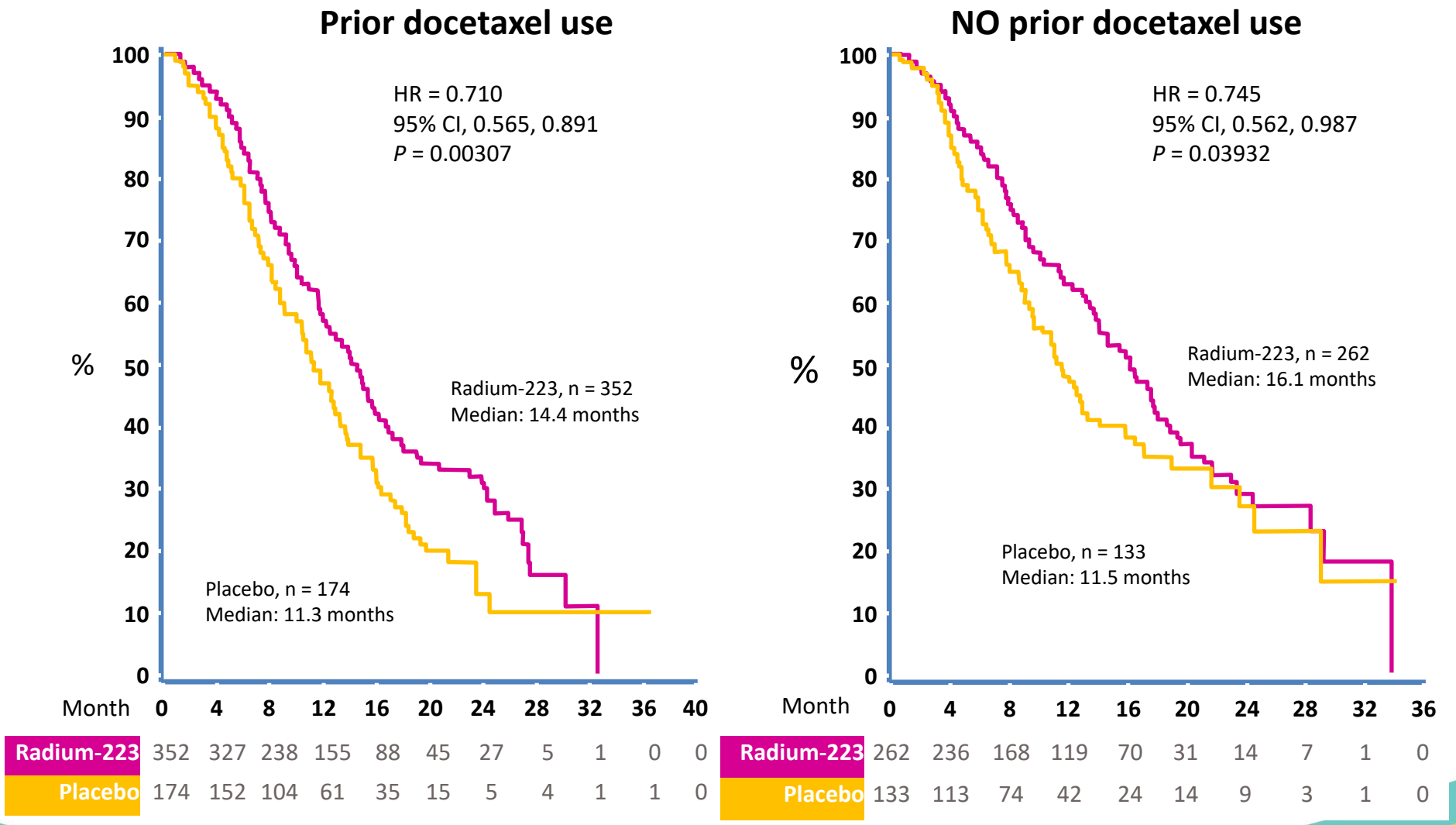
ALSYMPCA Trial Overall Survival Results



- Improvement in time to first symptomatic SRE → Median 15.6 mos vs 9.8 mos, P<0.001
- Minimal effect on PSA → 16% had PSA decline ≥30%

Parker C et al. *N Engl J Med* 2013;369:213-23.

ALSYMPCA Overall Survival Stratified by Prior Docetaxel Use



Parker GU ASCO 2013

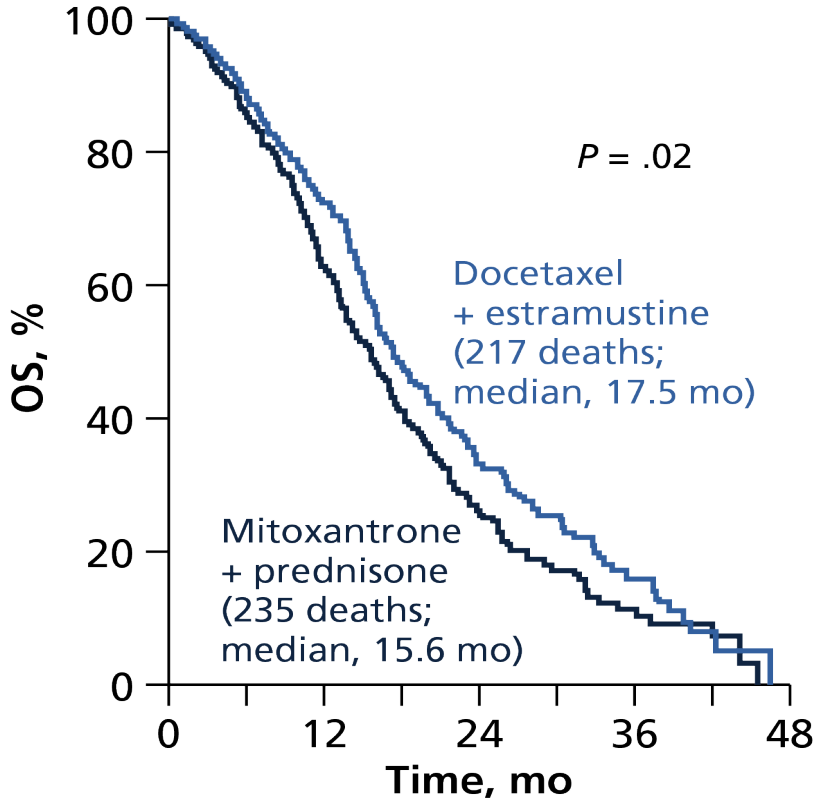
ALSYMPCA: Adverse Events of Interest

	All Grades		Grades 3 or 4	
	Radium-223 (n=509) n (%)	Placebo (n=253) n (%)	Radium-223 (n=509) n (%)	Placebo (n=253) n (%)
Haematologic				
Anemia	136 (27)	69 (27)	54 (11)	29 (12)
Neutropenia	20 (4)	2 (1)	9 (2)	2 (1)
Thrombocytopenia	42 (8)	14 (6)	22 (4)	4 (2)
Non-Haematologic				
Bone pain	217 (43)	147 (58)	89 (18)	59 (23)
Diarrhea	112 (22)	34 (13)	6 (1)	3 (1)
Nausea	174 (34)	80 (32)	8 (2)	4 (2)
Vomiting	88 (17)	32 (13)	10 (2)	6 (2)
Constipation	89 (18)	46 (18)	6 (1)	2 (1)

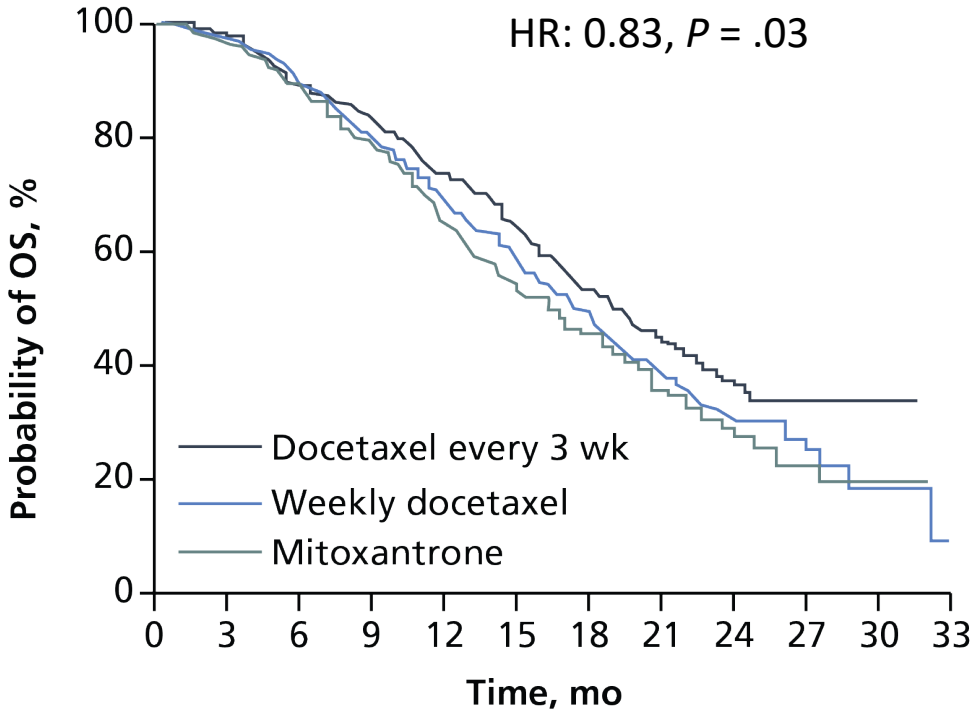
Parker C et al. *N Engl J Med* 2013;369:213-23.

Docetaxel – First Drug to Improve OS in mCRPC

SWOG 99-16[1]



TAX-327[2]



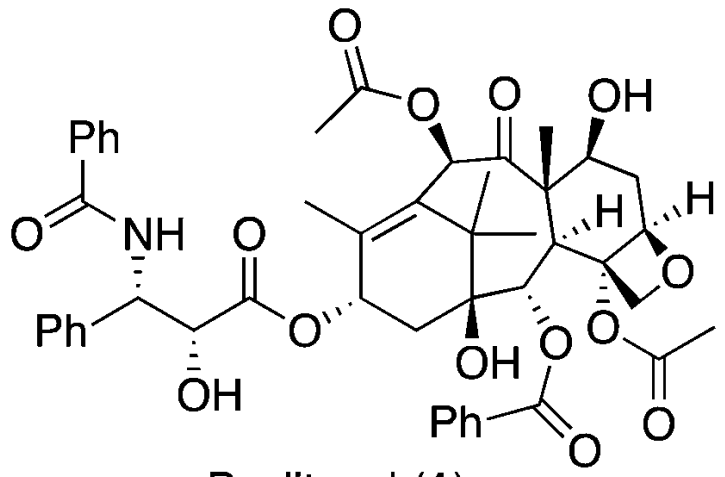
1. Petrylak DP et al. *N Engl J Med.* 2004;351:1513-1520.
2. Tannock IF et al. *N Engl J Med*. 2004;351:1502-1512.

TAX 327: Docetaxel Adverse Events

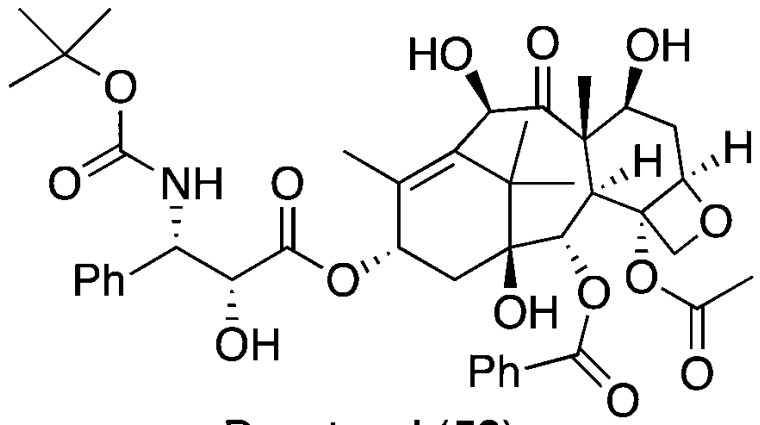
Table 4. Adverse Events of Any Grade, or of Grade 3 or 4, That Occurred or Worsened during Treatment.

Adverse Event	Docetaxel Every 3 Wk (N=332)	Weekly Docetaxel (N=330)	Mitoxantrone Every 3 Wk (N=335)
		percent	
Grade 3 or 4 anemia	5	5	2
Grade 3 or 4 thrombocytopenia	1	0	1
Grade 3 or 4 neutropenia	32*	2†	22
Febrile neutropenia	3	0	2
Impaired LVEF‡	10†	8†	22
Major decrease	1†	2*	7
Fatigue	53†	49†	35
Grade 3 or 4	5	5	5
Alopecia	65†	50†	13
Nausea, vomiting, or both	42	41	38
Diarrhea	32†	34†	10
Nail changes	30†	37†	7
Sensory neuropathy	30†	24†	7
Anorexia	17	21*	14
Change in taste	18†	24†	7
Stomatitis	20†	17†	8
Myalgia	14	14	13
Dyspnea	15*	14*	9
Tearing	10†	21†	1
Peripheral edema	19†	12†	1
Epistaxis	6	17†	2
≥1 Serious adverse event	26	29	20
Treatment-related death	0.3	0.3	1

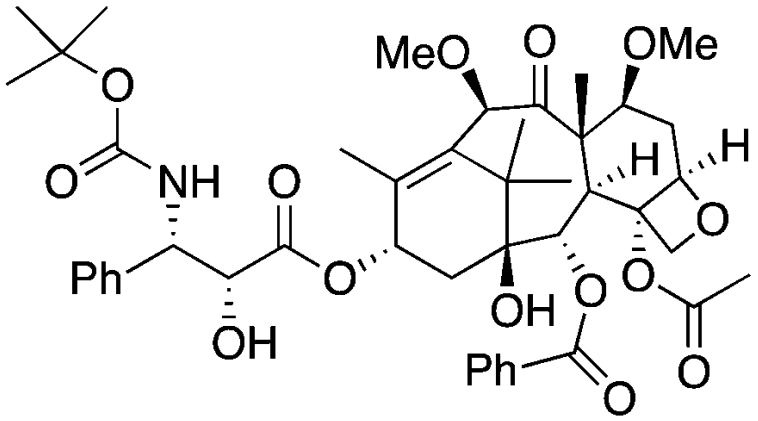
Cabazitaxel vs. Docetaxel Biochemical Structure



Paclitaxel (**1**)

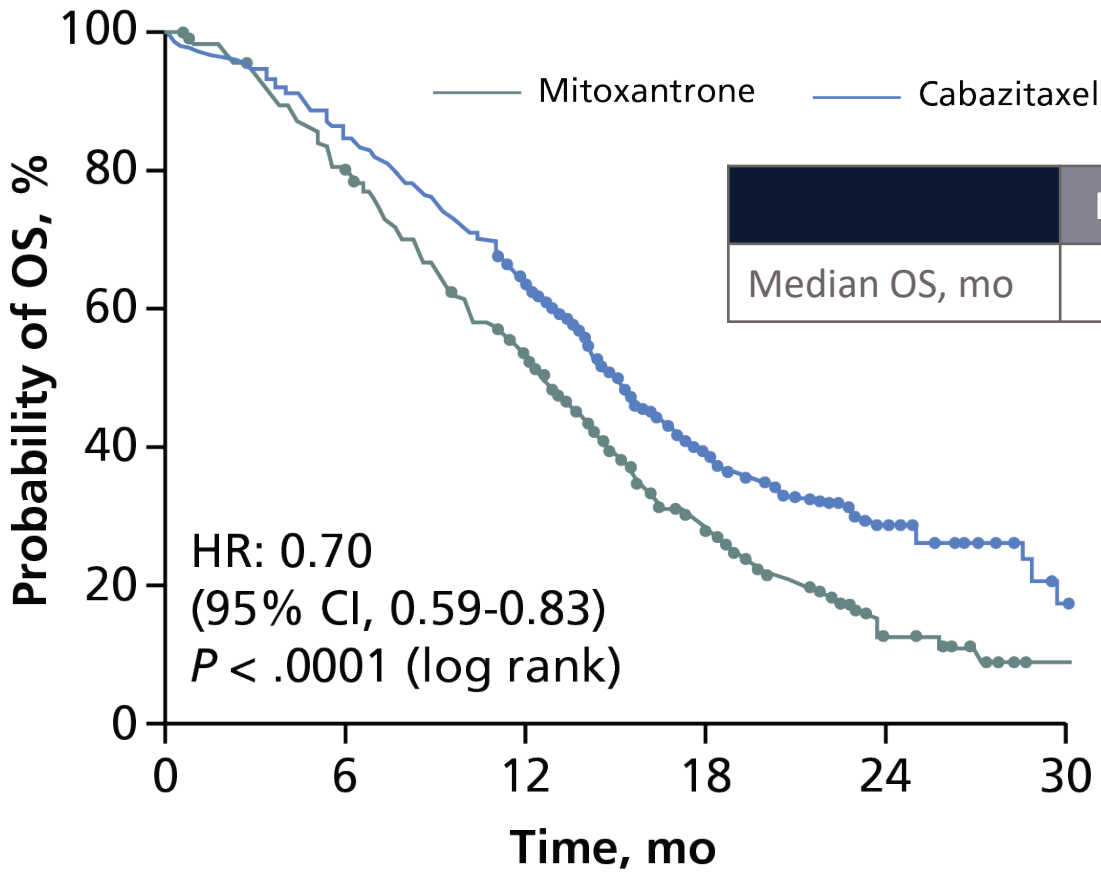


Docetaxel (**58**)



Cabazitaxel (**59**)

TROPIC Trial Overall Survival



	Mitoxantrone	Cabazitaxel
Median OS, mo	12.7	15.1

No. at Risk

Mitoxantrone	377	300	188	67	11	1
Cabazitaxel	378	321	231	90	28	4

De Bono J et al. *Lancet.* 2010; 376:1147-1154.

TROPIC: Most Frequent Grade ≥3 Treatment-emergent AEs

	MP (n = 371)		CBZP (n = 371)	
	All grades, %	Grade ≥3, %	All grades, %	Grade ≥3, %
Any adverse event	88.4	39.4	95.7	57.4
Febrile neutropenia	1.3	1.3	7.5	7.5
Diarrhea	10.5	0.3	46.6	6.2
Fatigue	27.5	3	36.7	4.9
Asthenia	12.4	2.4	20.5	4.6
Back pain	12.1	3	16.2	3.8
Nausea	22.9	0.3	34.2	1.9
Vomiting	10.2	0	22.6	1.9
Hematuria	3.8	0.5	16.7	1.9
Abdominal pain	3.5	0	11.6	1.9

[a]Sorted by decreasing frequency of events grade ≥ 3 in the CBZP arm.

CBZP: cabazitaxel; MP: mitoxantrone.

De Bono J et al. *Lancet.* 2010;376:1147-1154.

TROPIC: Hematologic AEs and Deaths

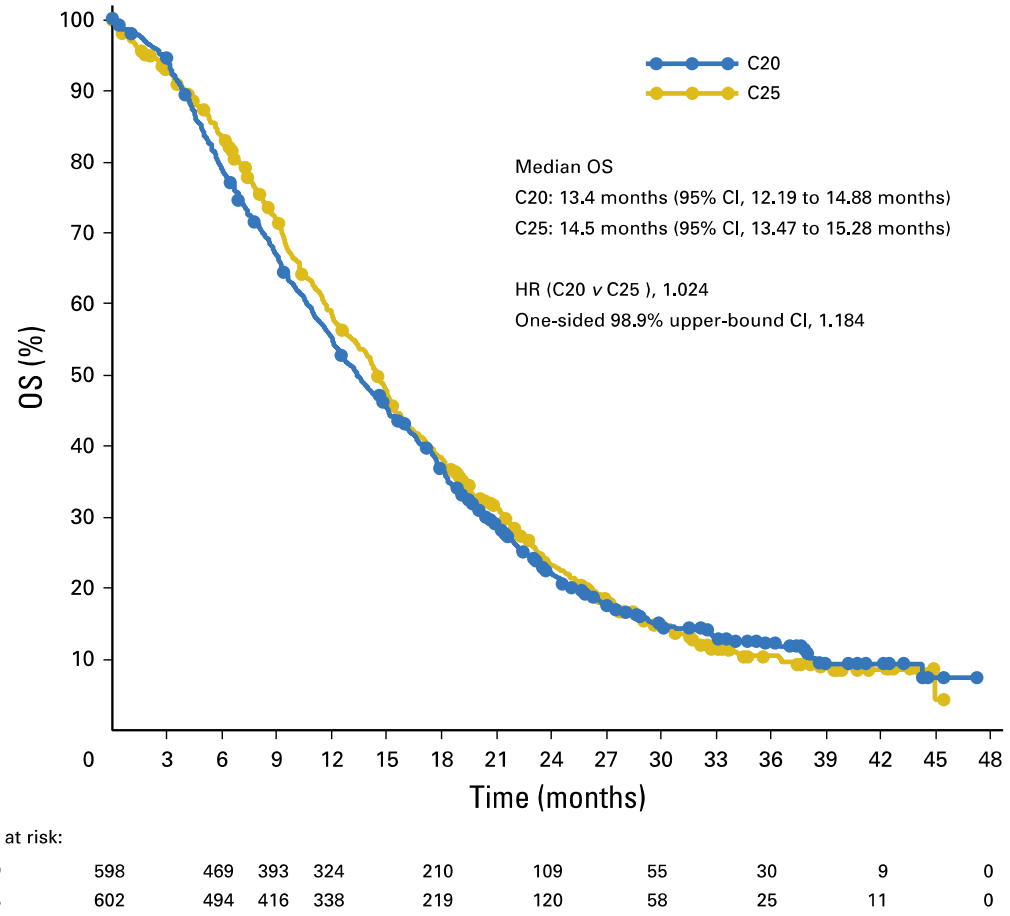
Hematologic AE, %	MP (n = 371)		CBZP (n = 371)	
	All grades	Grade ≥3	All grades	Grade ≥3
Anemia	81.4	4.9	97.3	10.5
Leukopenia	92.5	42.3	95.7	68.2
Neutropenia[a]	87.6	58.0	93.5	81.7
Thrombocytopenia	43.1	1.6	47.4	4.0

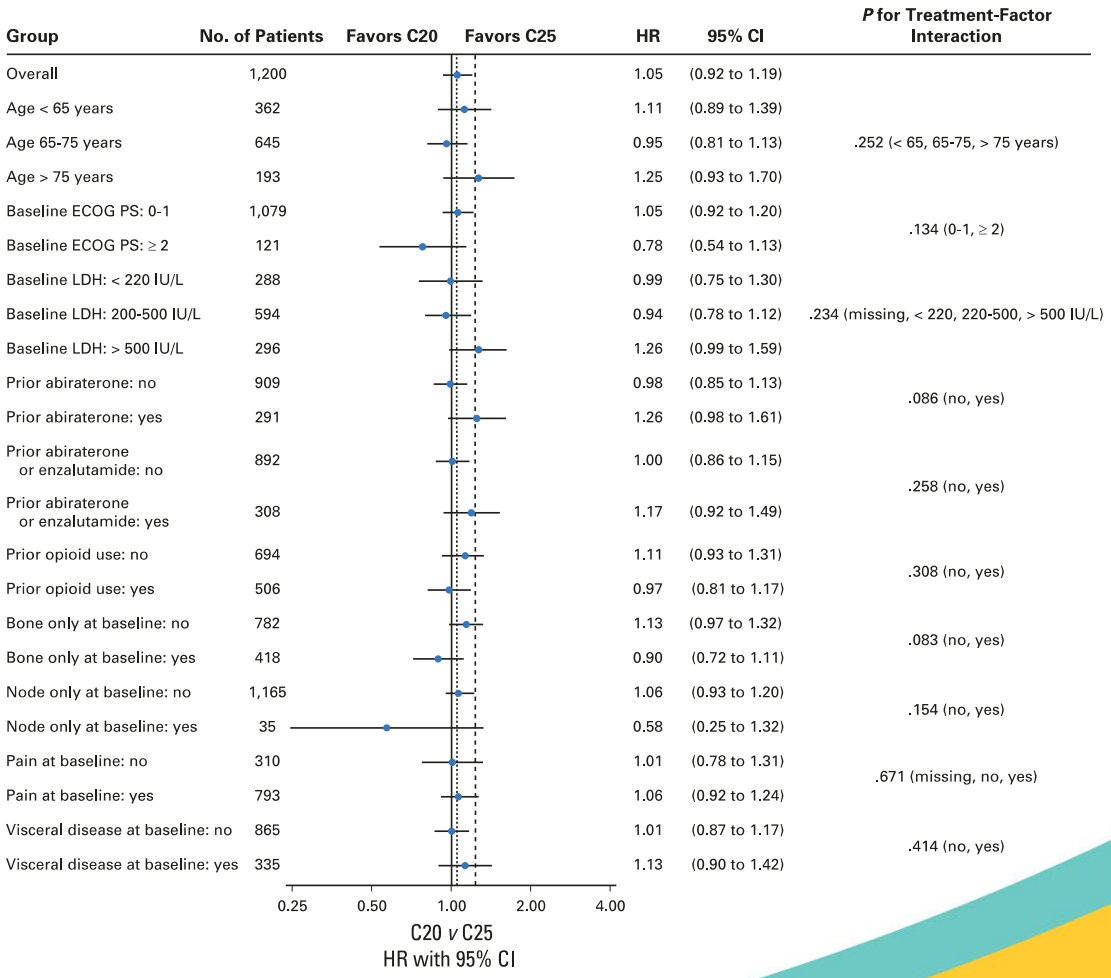
Other Safety, n (%)	MP (n = 371)	CBZP (n = 371)
Total deaths during study	304 (81.9%)	270 (72.8%)
Due to progression	264 (71.2%)	218 (58.8%)
Due to AE	7 (1.9%)	18 (4.9%)
Due to AE (N America, n = 235)	1 (0.3%)	1 (0.3%)
Due to AE (Europe, n = 402)	6 (1.6%)	10 (2.7%)
Due to other reasons	15 (4.0%)	12 (3.2%)
Cause unknown (>3 mo following last dose)	11 (3.0%)	20 (5.4%)

[a] Prophylactic use of G-CSF was permitted except for cycle 1 of treatment at the discretion of the investigator.

De Bono J et al. *Lancet.* 2010;376:1147-1154.

The PROSELICA Study - OS





Eisenberger, et al. J Clin Oncol 35:3198-3206

The PROSELICA Study – Adverse Events

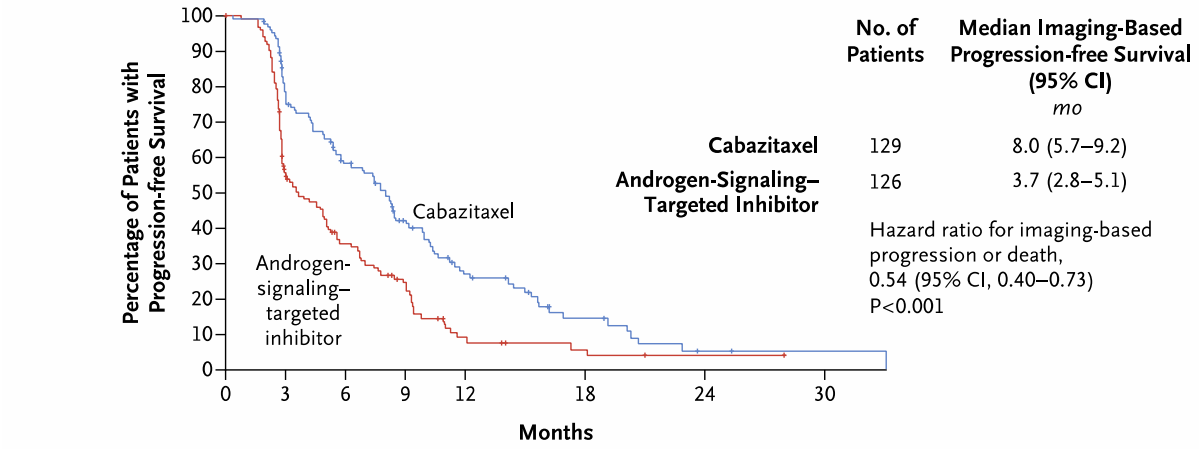
PROSELICA: Treatment-Emergent Adverse Events

Patients, n (%)	CBZ 20 + PRED N = 580	CBZ 25 + PRED N = 595
Any Grade TEAE	529 (91.2)	559 (93.9)
Grade 3–4 TEAE	230 (39.7)	324 (54.5)
Serious TEAE	177 (30.5)	257 (43.2)
TEAE leading to permanent treatment discontinuation	95 (16.4)	116 (19.5)
Most frequent Grade 3–4 TEAEs reported in ≥ 5% pts, n (%)		
Febrile neutropenia	12 (2.1)	55 (9.2)
Hematuria	11 (1.9)	25 (4.2)
Diarrhea	8 (1.4)	24 (4.0)
Fatigue	15 (2.6)	22 (3.7)
Urinary tract infection	10 (1.7)	13 (2.2)
Bone pain	10 (1.7)	13 (2.2)
Asthenia	11 (1.9)	12 (2.0)
Vomiting	7 (1.2)	8 (1.3)
Nausea	4 (0.7)	7 (1.2)

DeBono JS, et al. Presented at: ASCO Annual Meeting; June 3-7, 2016; Chicago, Illinois: abstract 5008.

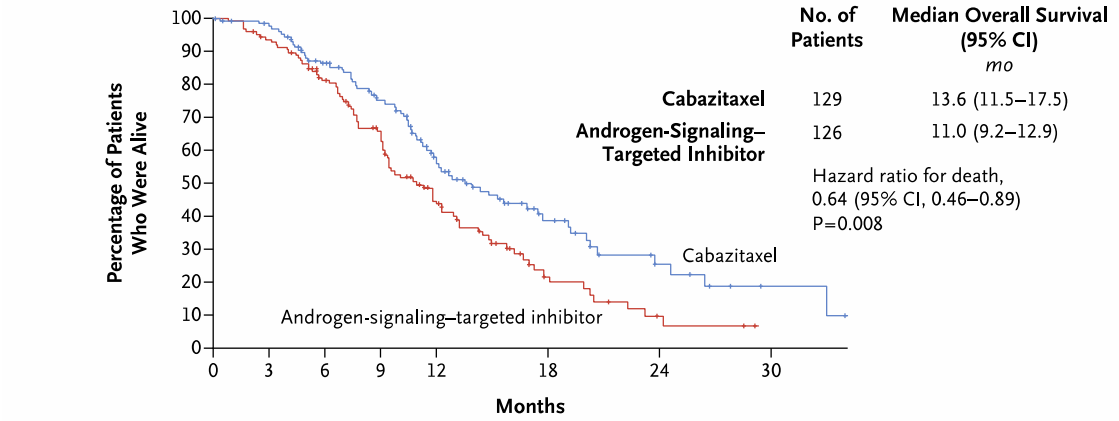
CARD: Cabazitaxel vs. Abiraterone or Enzalutamide in CRPC

- Required to have received ≥3 cycles of docetaxel
- Previously progressed on an NHA
- ~50% of patients progressed on NHA within 6 months of starting



No. at Risk

Cabazitaxel	129	91	64	41	23	9	2	1
Androgen-signaling–targeted inhibitor	126	61	36	22	7	3	1	0

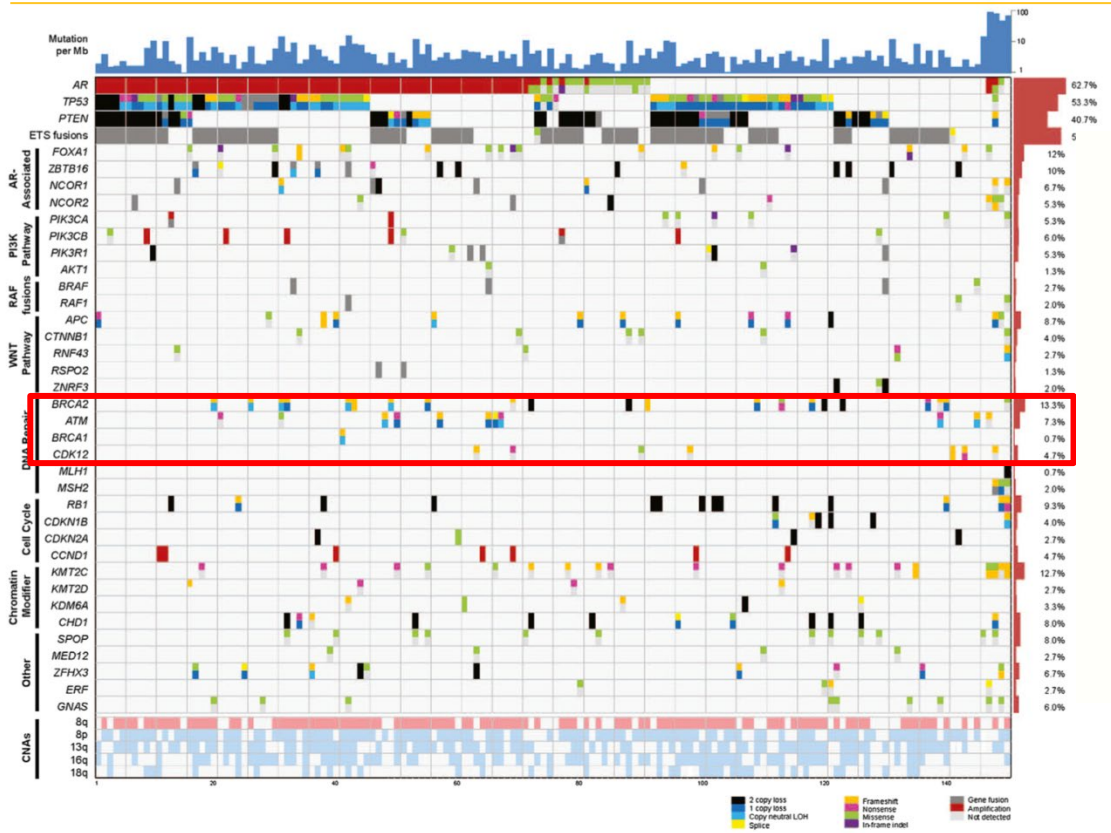


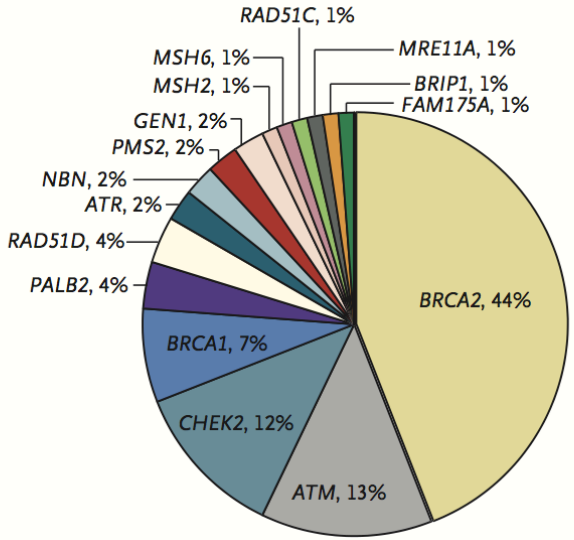
No. at Risk

Cabazitaxel	129	122	96	77	51	21	8	2
Androgen-signaling–targeted inhibitor	126	116	88	64	39	11	3	0

de Wit, et al. n engl j med 381;26

DNA Repair Gene Alterations are Common in Metastatic Prostate Cancer





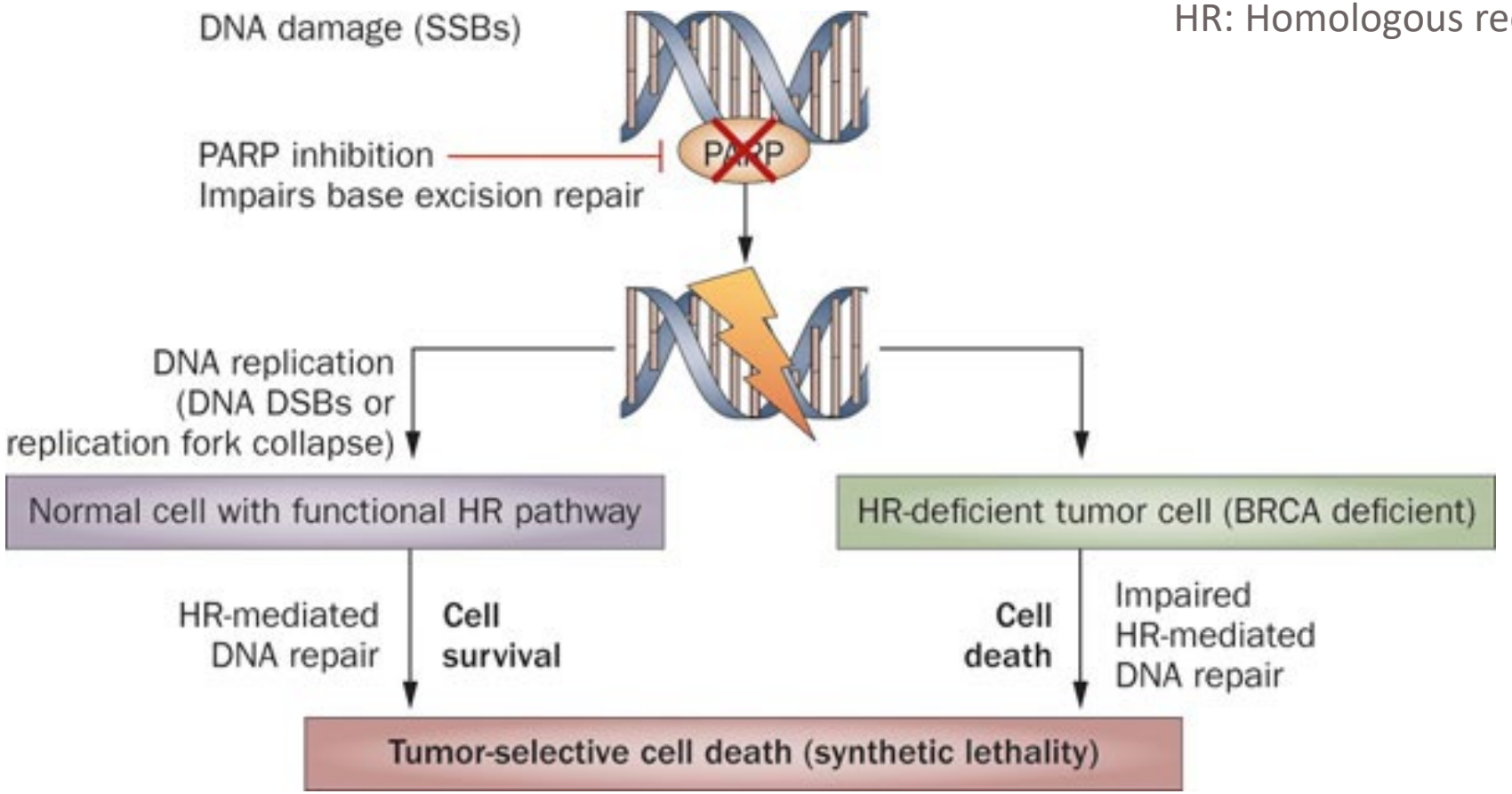
- 23% of metastatic castration-resistant prostate cancers harbor DNA repair alterations
- The frequency of DNA repair alterations increases with disease progression

- 11.8% of men with metastatic prostate cancer have a germline alteration in 16 DNA damage repair genes
- Age and family history did not affect mutation frequency

Robinson D et al. *Cell* 2015; 161:1215-28.

Pritchard CC et al. *N Engl J Med.* July 6,2016.

Synthetic Lethality: How to Selectively Stop *HR Deficient* Cancers



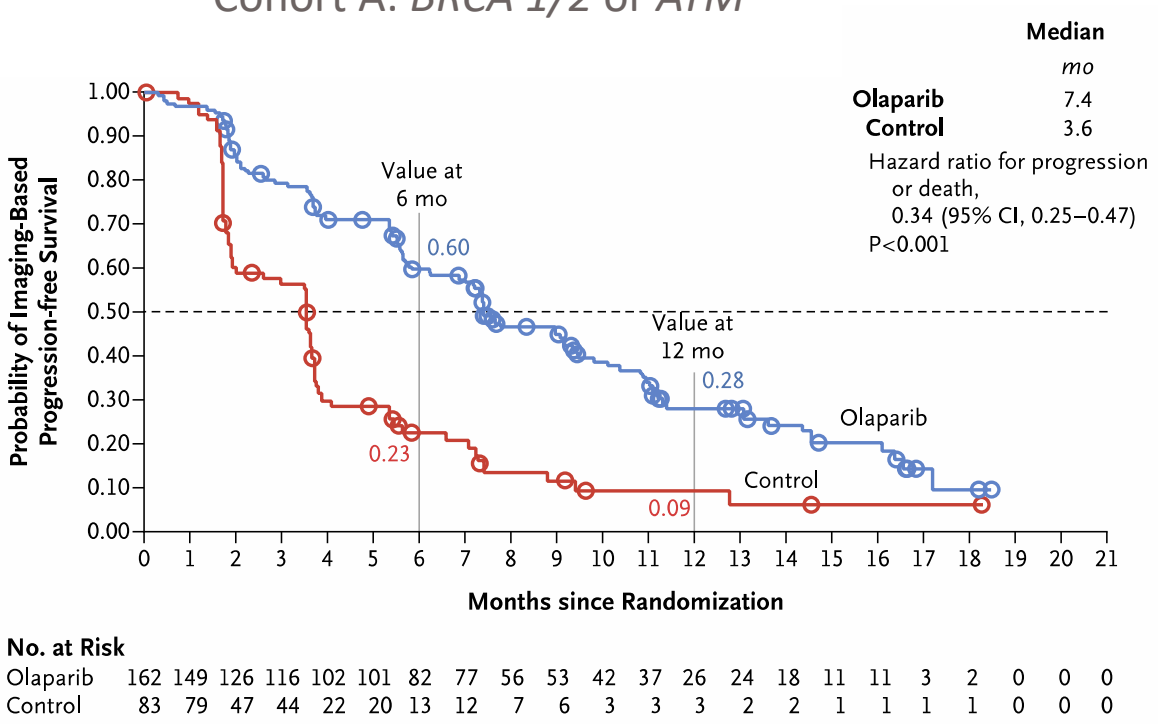
HR: Homologous recombination repair

Banerjee, S. *et al.* (2010) *Nat. Rev. Clin. Oncol.*

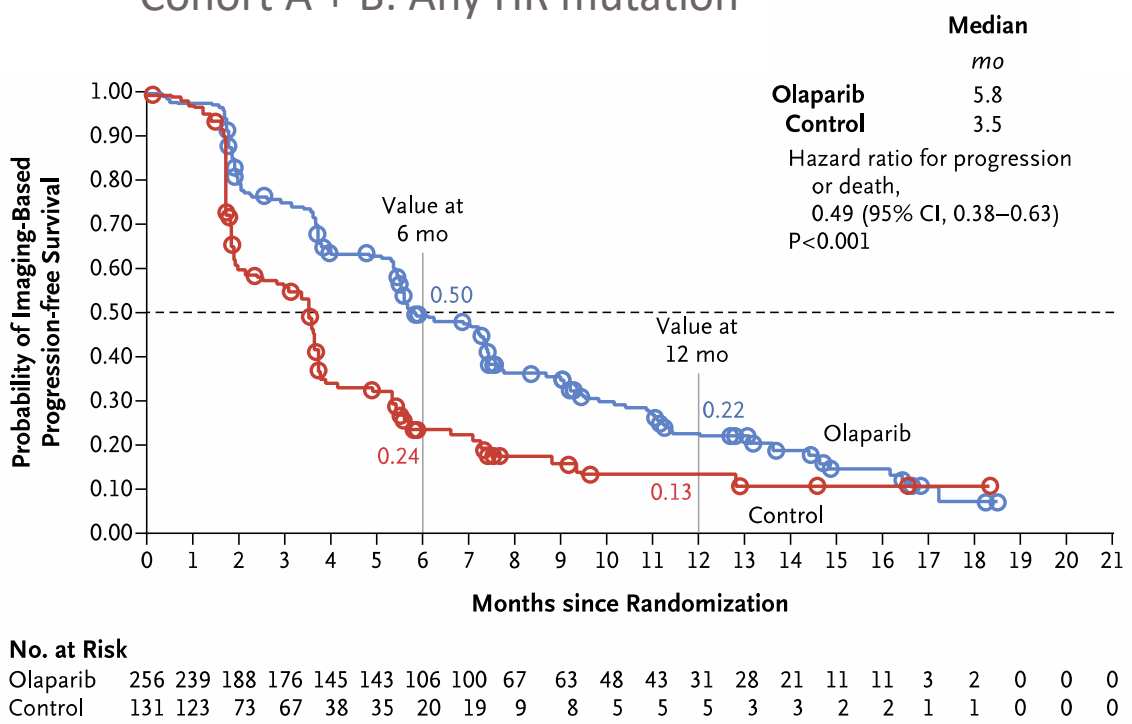
PROFound: Olaparib vs. abiraterone or enzalutamide

Radiographic PFS

Cohort A: *BRCA 1/2* or *ATM*



Cohort A + B: Any HR mutation

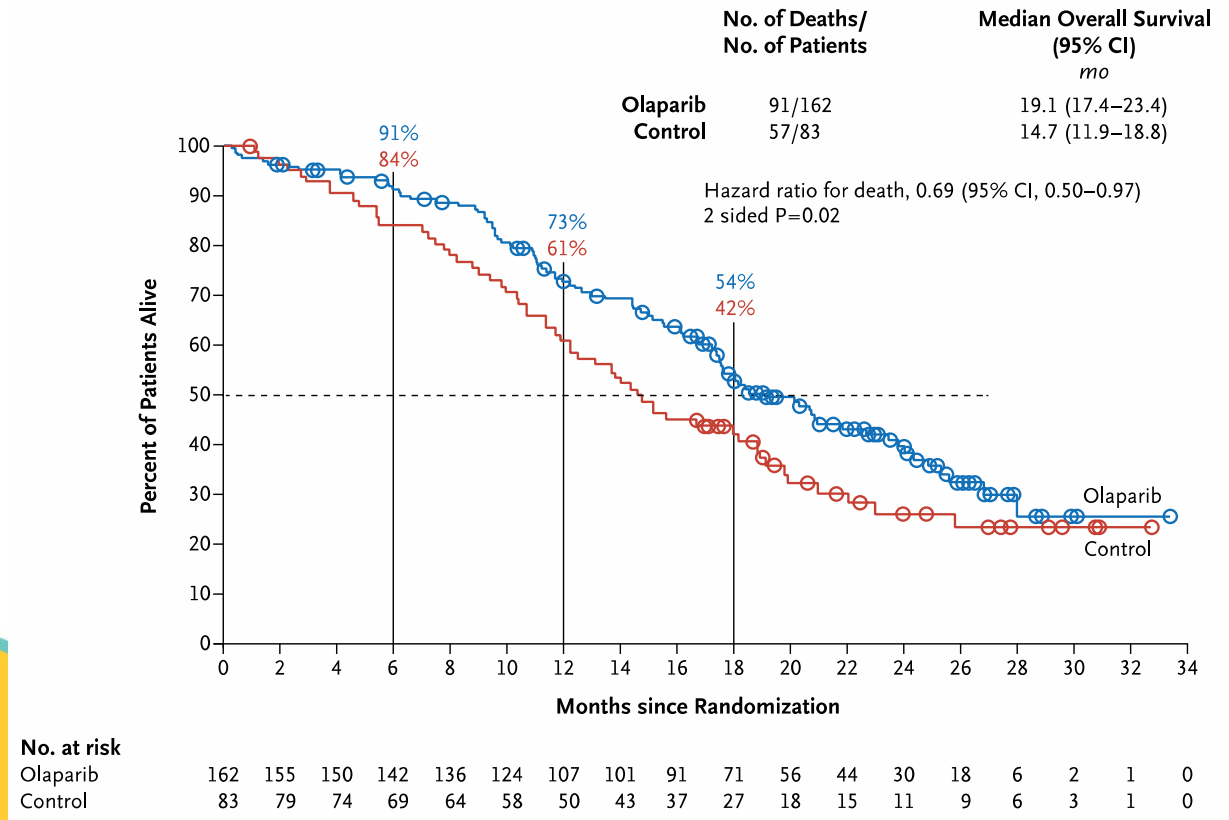


de Bono, et al. **N Engl J Med 2020;382:2091-102.**

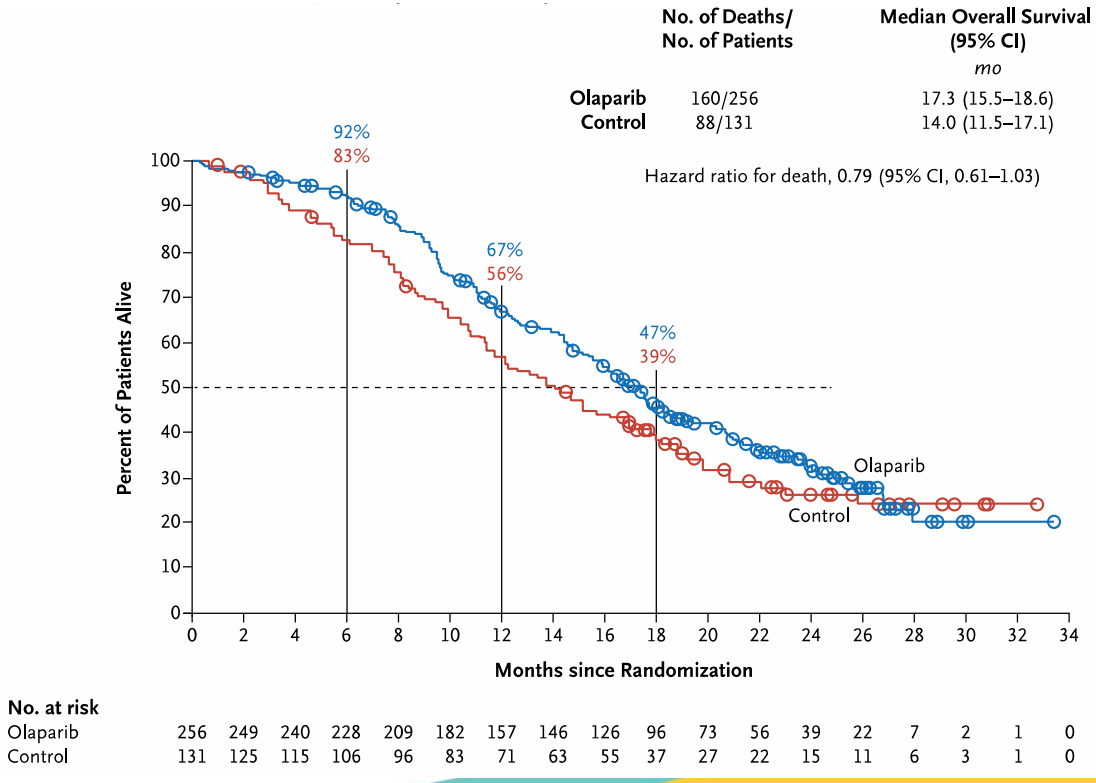
PROFound: Olaparib vs. abiraterone or enzalutamide

Overall survival

Cohort A: *BRCA 1/2* or *ATM*



Cohort A + B: Any HR mutation



Hussain, et al. N Engl J Med 2020;383:2345-57.

PROFound: Olaparib vs. abiraterone or enzalutamide

- 1 cases of AML 54 days after stopping olaparib
- 1 case of pneumonitis on olaparib arm

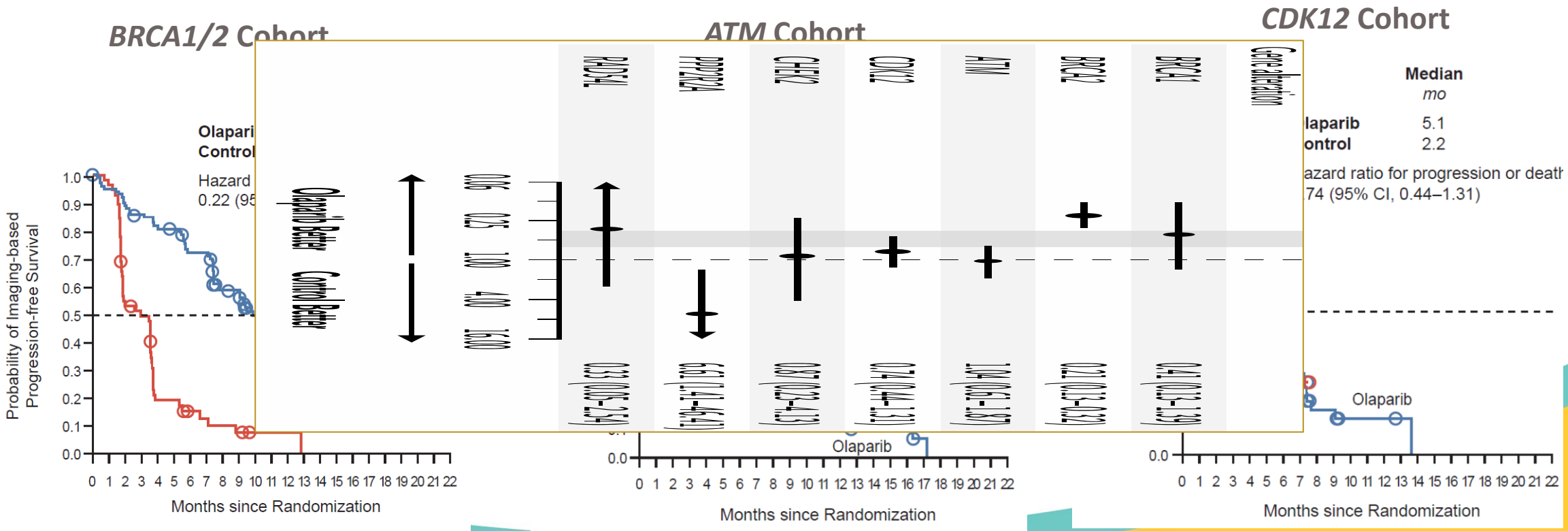
Table 2. Adverse Events in the Overall Population (Cohorts A and B).*

Event	Olaparib (N = 256)		Control (N = 130)	
	All Grades	Grade ≥3	All Grades	Grade ≥3
	number (percent)			
Adverse event				
Any	244 (95)	130 (51)	114 (88)	49 (38)
Anemia†	119 (46)	55 (21)	20 (15)	7 (5)
Nausea	106 (41)	3 (1)	25 (19)	0
Fatigue or asthenia	105 (41)	7 (3)	42 (32)	7 (5)
Decreased appetite	77 (30)	3 (1)	23 (18)	1 (<1)
Diarrhea	54 (21)	2 (<1)	9 (7)	0
Vomiting	47 (18)	6 (2)	16 (12)	1 (<1)
Constipation	45 (18)	0	19 (15)	0
Back pain	35 (14)	2 (<1)	15 (12)	2 (2)
Peripheral edema	32 (12)	0	10 (8)	0
Cough	28 (11)	0	3 (2)	0
Dyspnea	26 (10)	6 (2)	4 (3)	0
Arthralgia	24 (9)	1 (<1)	14 (11)	0
Urinary tract infection	18 (7)	4 (2)	15 (12)	5 (4)
Interruption of intervention due to adverse event	115 (45)	NA	24 (18)	NA
Dose reduction due to adverse event	57 (22)	NA	5 (4)	NA
Discontinuation of intervention due to adverse event	46 (18)	NA	11 (8)	NA
Death due to adverse event	10 (4)	NA	5 (4)	NA

de Bono, et al. N Engl J Med 2020;382:2091-102.
Hussain, et al. N Engl J Med 2020;383:2345-57.

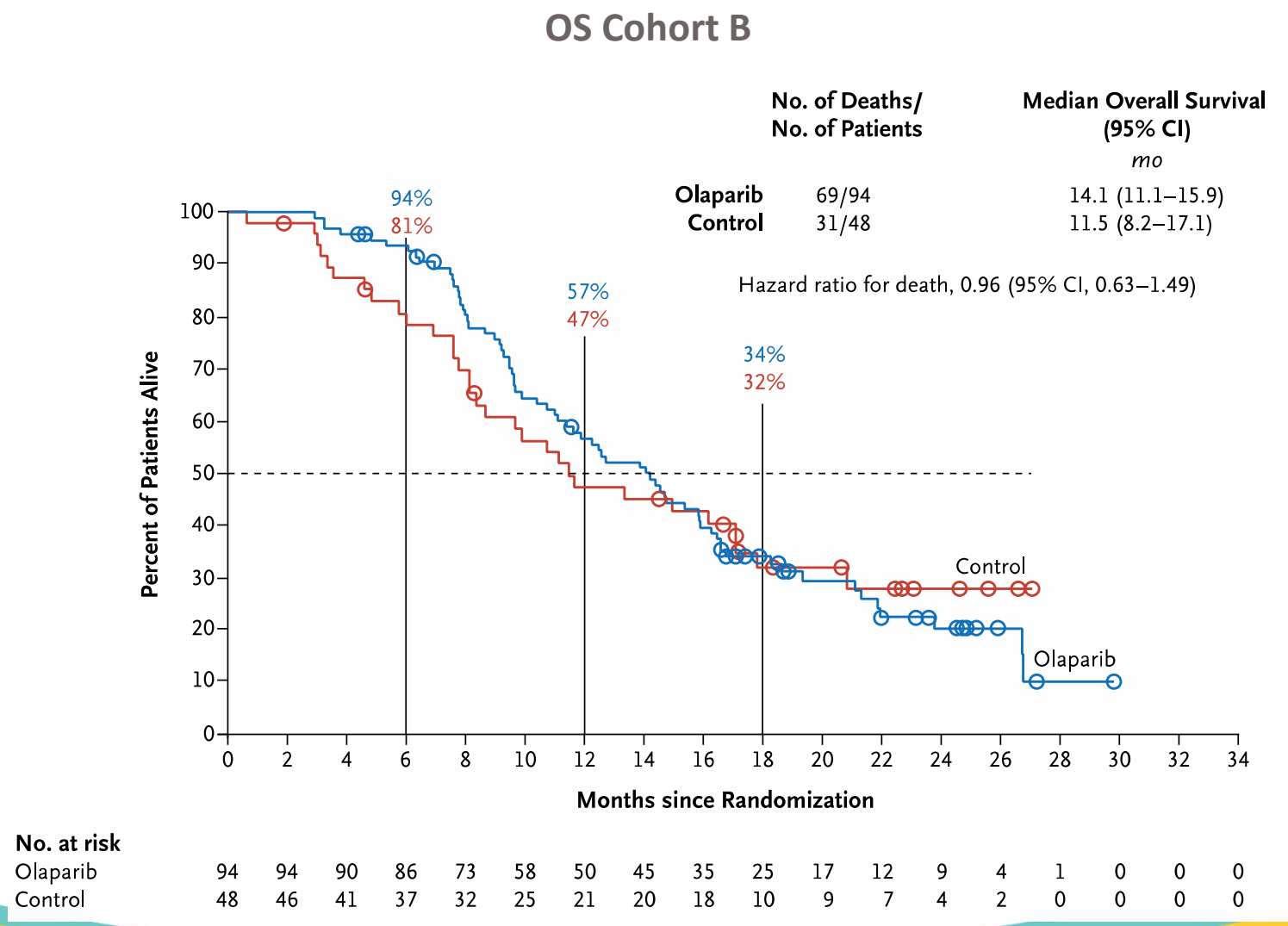
Dissecting the PROfound data

- >80% of cases had a mutation in *BRCA2* (33%), *CDK12* (23%), *ATM* (22%) and *BRCA1* (3%)



de Bono, et al. **N Engl J Med 2020;382:2091-102.**

Dissecting the PROfound data



Hussain, et al. N Engl J Med 2020;383:2345-57.

TRITON-2: Phase 2 Rucaparib Trial

Characteristic	By HRR Gene With Alteration				
	BRCA1/2 (n = 57)	*ATM* (n = 21)	*CDK12* (n = 9)	*CHEK2* (n = 5)	Other (n = 13)
ORR, n (%)[a]	25 (43.9)	2 (9.5)	0	0	5 (38.5)
Complete response, n (%)	3 (5.3)	0	0	0	1 (7.7)[b]
Partial response, n (%)	22 (38.6)	2 (9.5)	0	0	4 (30.8)[c]
Stable disease, n (%)	26 (45.6)	10 (47.6)	5 (55.6)	3 (60.0)	6 (46.2)
Progressive disease, n (%)	5 (8.8)	8 (38.1)	3 (33.3)	2 (40.0)	1 (7.7)
Not evaluable, n (%)	1 (1.8)	1 (4.8)	1 (11.1)	0	1 (7.7)
Confirmed PSA response rate (all evaluable patients)	51/98 (52%)	2/57 (3.5%)	1/14 (7.1)	1/7 (14.3)	5/14 (35.7%)

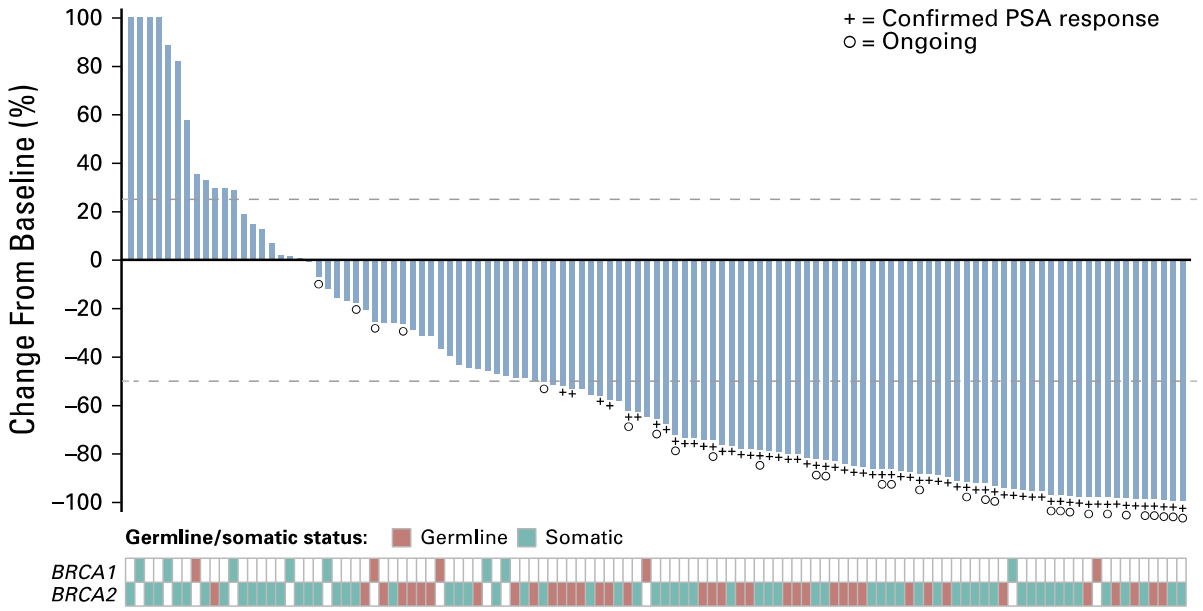
- **43.9% confirmed objective responses were reported in 57 patients with *BRCA1/2* mutation**
- **52.0% confirmed PSA response in 98 PSA-evaluable patients with *BRCA1/2* mutation**

[a] Per modified RECIST/PCWG3 criteria. [b] One patient had *FANCA* alteration. [c] Two patients had a *PALB2* alteration; 1 patient each had a *BRIP1* or *RAD51B* alteration.

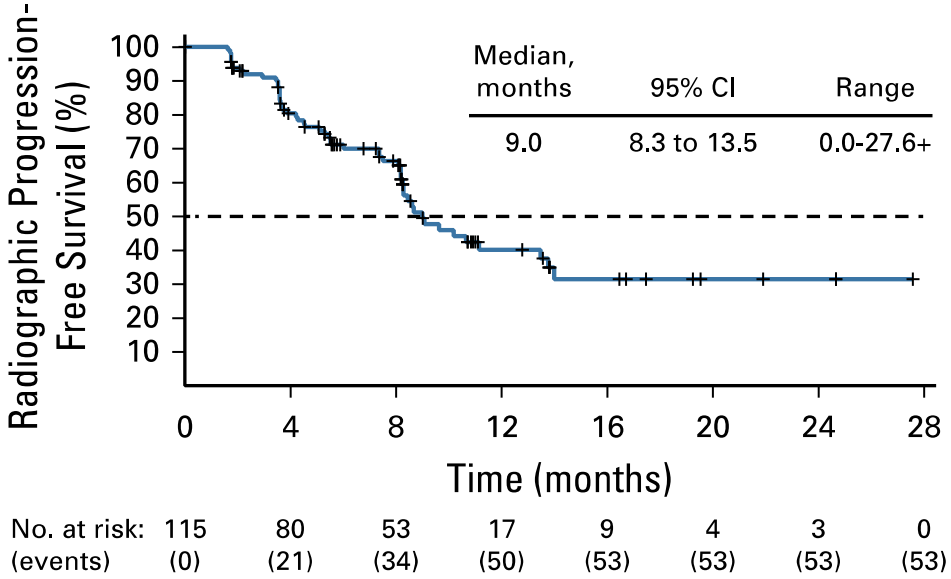
1. Abida W et al. ESMO 2019. Abstract 846PD.

TRITON-2: Phase 2 Rucaparib Trial

PSA Responses in *BRCA1/2* Population

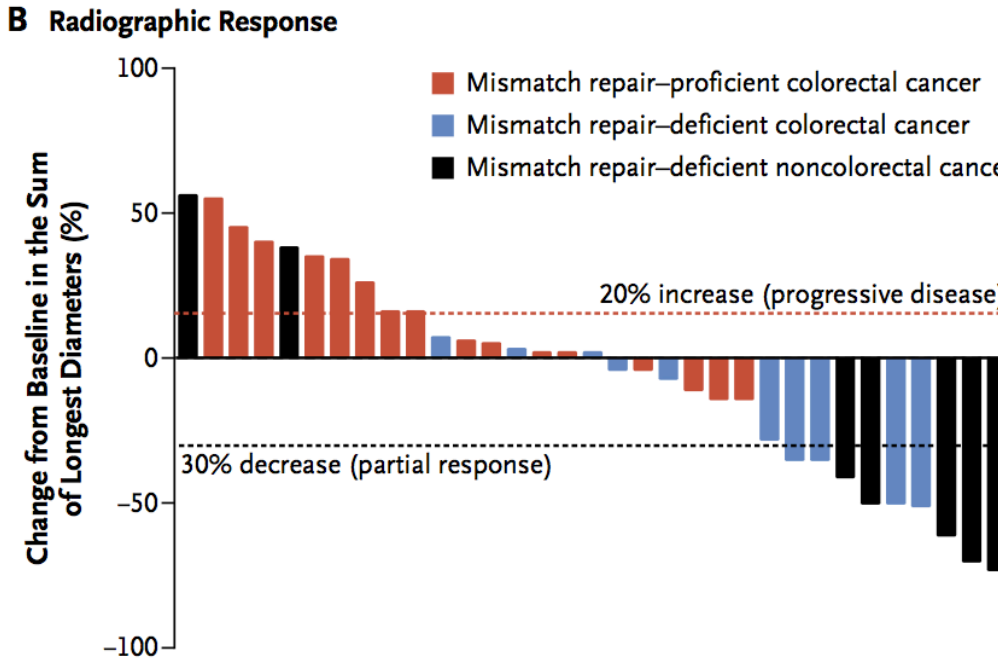


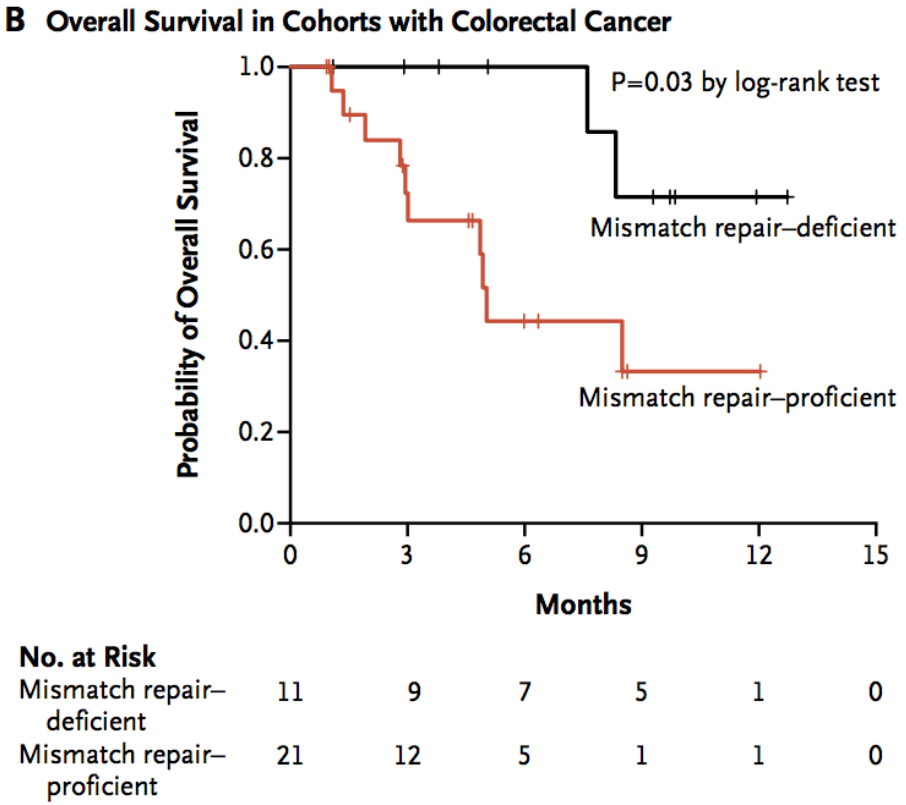
rPFS in *BRCA1/2* Population



Abida, et al. J Clin Oncol 38:3763-3772.

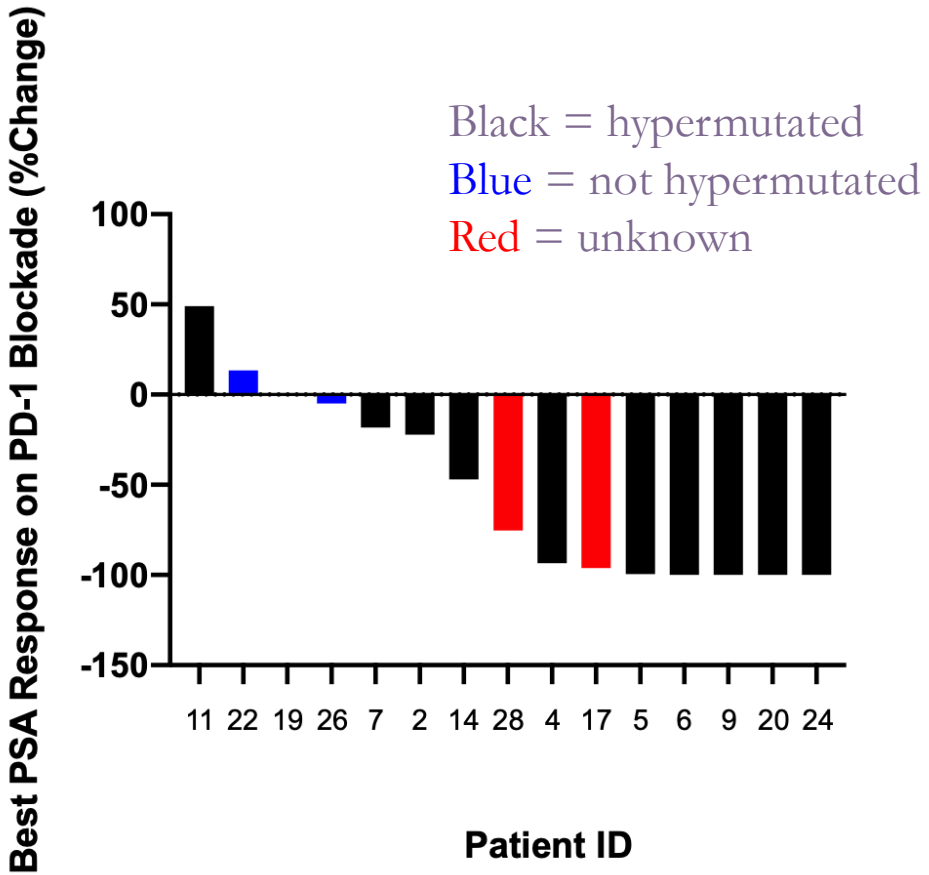
Pembrolizumab in MMR Deficient Cancers

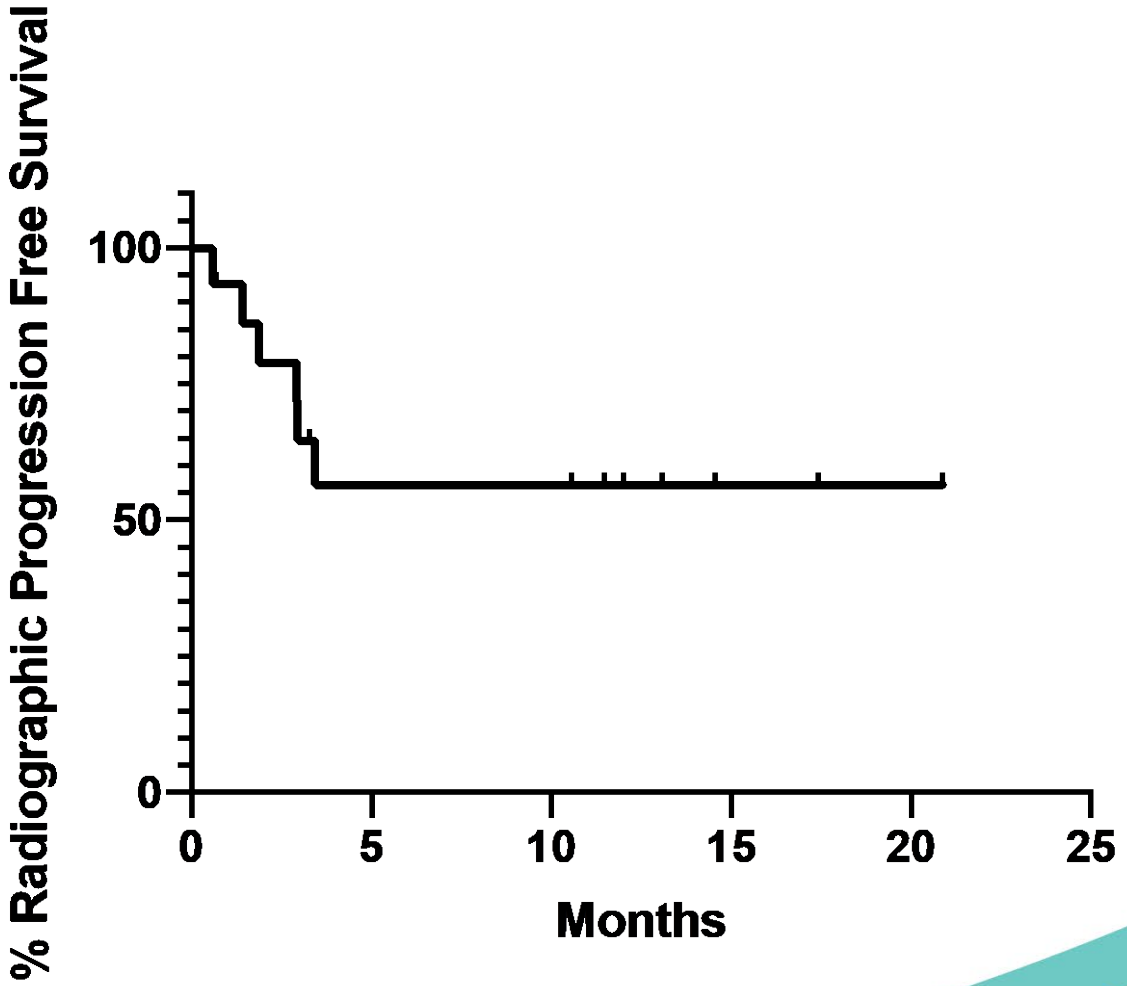




Le DT et al. *N Engl J Med.* 2015; 372:2509-2520.

Anti-PD1 Therapy in Prostate Cancer Patients



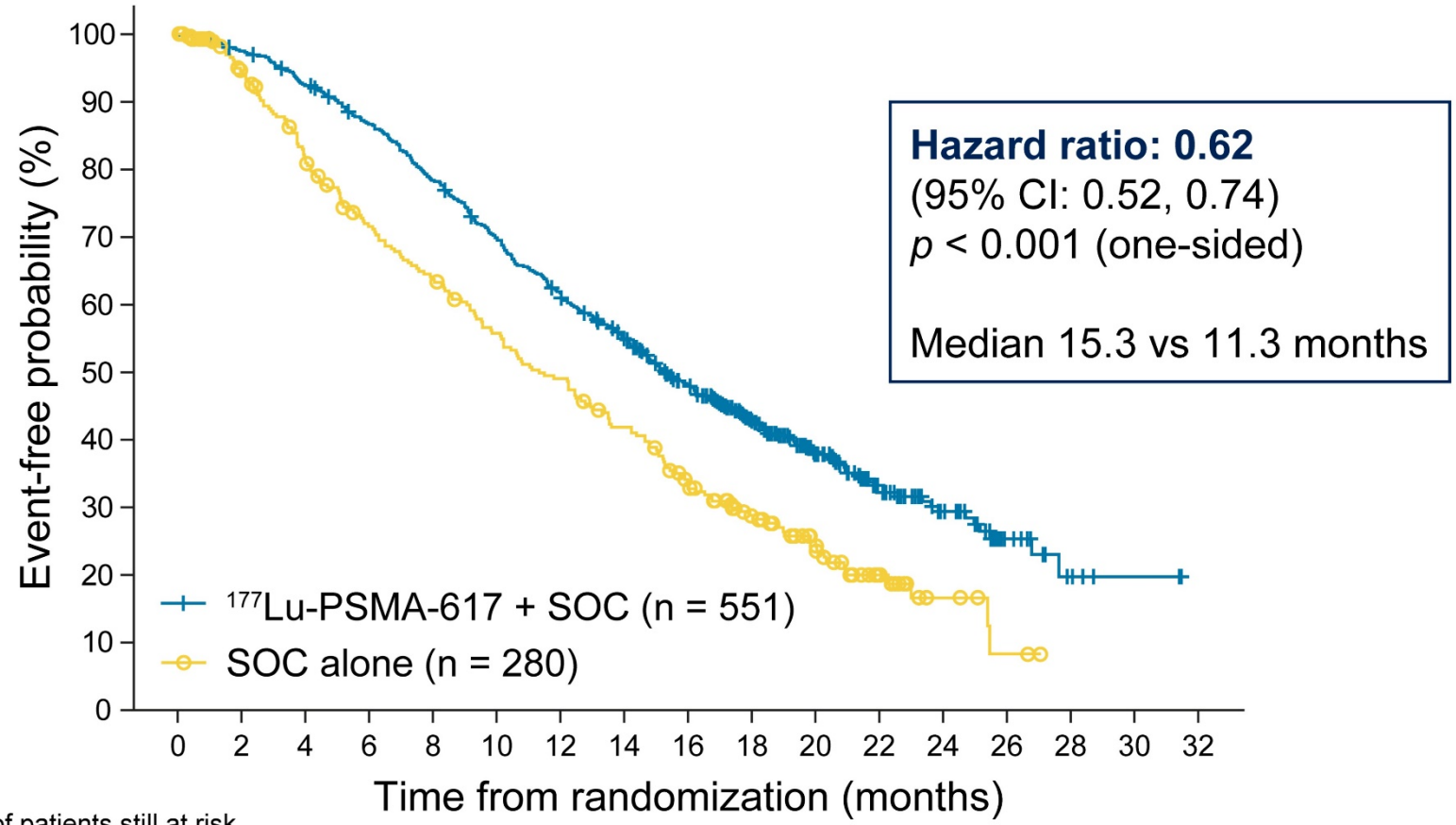


Graham et al. PlosOne, 2020

Primary endpoints: ^{177}Lu-PSMA-617 prolonged OS

Primary analysis

All randomized patients
(N = 831)



Number of patients still at risk

^{177}Lu-PSMA-617 + SOC	551	535	506	470	425	377	332	289	236	166	112	63	36	15	5	2	0
SOC alone	280	238	203	173	155	133	117	98	73	51	33	16	6	2	0	0	0

Morris, et al. J Clin Oncol 39, 2021 (suppl 15; abstr LBA4)

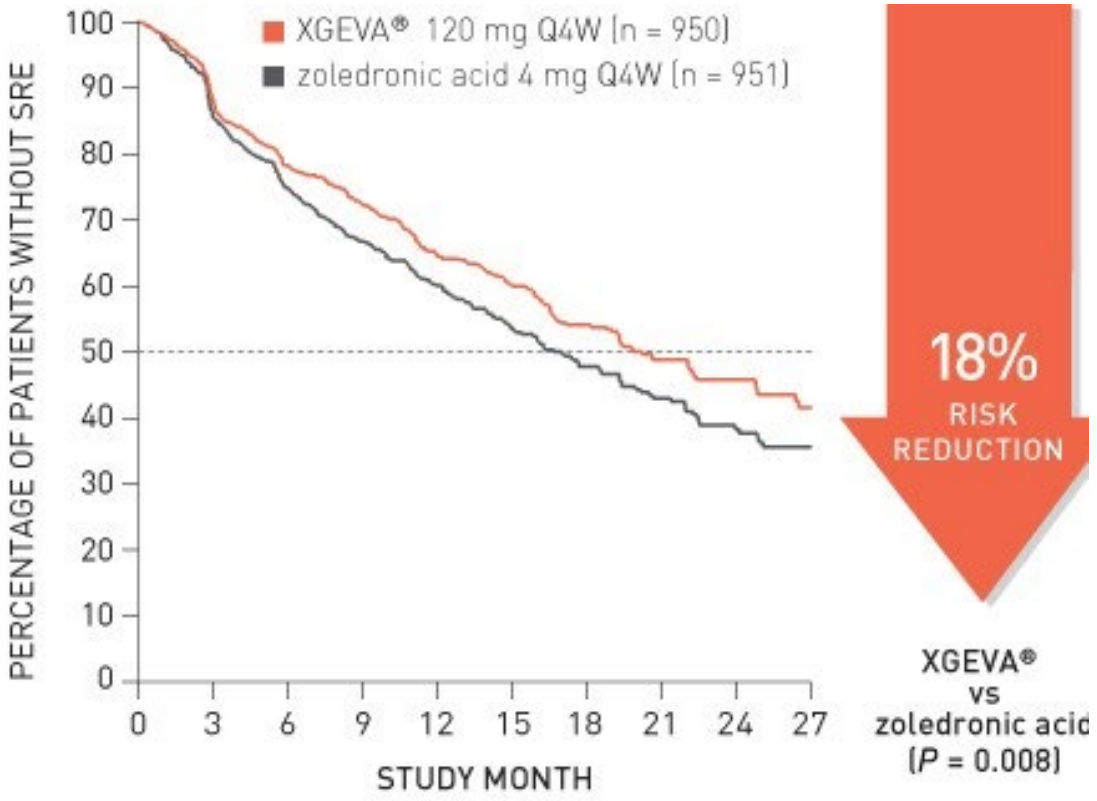
Treatment-emergent adverse events grouped as topics of interest: no unexpected or concerning safety signals

Patients, n (%)	All grades		Grade 3–5	
	^{177}Lu-PSMA-617 + SOC (n = 529)	SOC alone (n = 205)	^{177}Lu-PSMA-617 + SOC (n = 529)	SOC alone (n = 205)
Fatigue	260 (49.1)	60 (29.3)	37 (7.0)	5 (2.4)
Bone marrow suppression	251 (47.4)	36 (17.6)	124 (23.4)	14 (6.8)
Leukopenia	66 (12.5)	4 (2.0)	13 (2.5)	1 (0.5)
Lymphopenia	75 (14.2)	8 (3.9)	41 (7.8)	1 (0.5)
Anemia	168 (31.8)	27 (13.2)	68 (12.9)	10 (4.9)
Thrombocytopenia	91 (17.2)	9 (4.4)	42 (7.9)	2 (1.0)
Dry mouth	208 (39.3)	2 (1.0)	0 (0.0)	0 (0.0)
Nausea and vomiting	208 (39.3)	35 (17.1)	8 (1.5)	1 (0.5)
Renal effects	46 (8.7)	12 (5.9)	18 (3.4)	6 (2.9)
Second primary malignancies	11 (2.1)	2 (1.0)	4 (0.8)	1 (0.5)
Intracranial hemorrhage	7 (1.3)	3 (1.5)	5 (0.9)	2 (1.0)

Morris, et al. J Clin Oncol 39, 2021 (suppl 15; abstr LBA4)

Prevention of Skeletal-Related Events (SRE)

- Zolendronic acid associated with 11% reduction in risk of SRE compared to placebo[1]
- Denosumab superior to zolendronica acid
- Zoledronic acid does not add either survival or SRE benefit for patients with mHSPC[2,3]
- Because of cost and potential side effects, reserve bone-protective therapy for mCRPC
  - Zoledronic acid: renal dysfunction, ONJ
  - Denosumab: ONJ, hypocalcemia



Fizazi et al, Lancet 2011; 377:813-22.

1. Saad F, et al. J Natl Cancer Inst. 2002;94:1458-1468.
2. James ND et al. Lancet 2016; 387:1163-77.
3. Smith MR et al. J Clin Oncol 2014; 32:1143-50.

PEACE 3: Enzalutamide +/- Ra-223

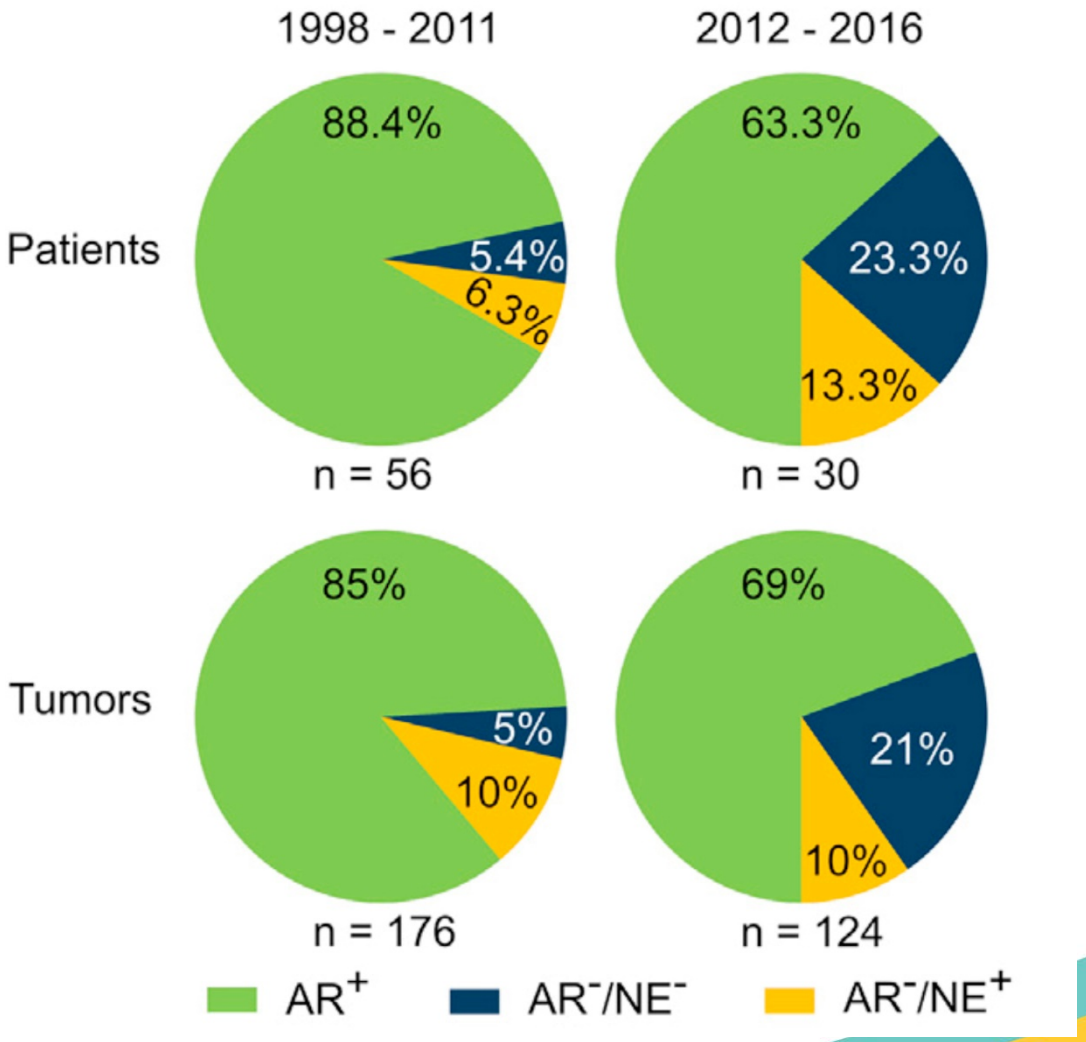
Bone fractures and cumulative incidence - safety population

Time point	Without BPA		With BPA	
	Enza+Rad (N=35)	Enza (N=32)	Enza+Rad (N=87)	Enza (N=97)
	Cum Incidence (95% CI)	Cum Incidence (95% CI)	Cum Incidence (95% CI)	Cum Incidence (95% CI)
9 months	25.7 (12.6-41.0)	9.4 (2.3-22.5)	2.7 (0.5-8.5)	1.3 (0.1-6.1)
12 months	**37.1 (21.3-53.0)**	**15.6 (5.6-30.3)**	**2.7 (0.5-8.5)**	**2.6 (0.5-8.3)**
15 months	42.9 (26.1-58.6)	21.9 (9.5-37.5)	4.3 (1.1-10.9)	2.6 (0.5-8.3)
18 months	**45.9 (28.6-61.6)**	**21.9 (9.5-37.5)**	**4.3 (1.1-10.9)**	**2.6 (0.5-8.3)**
21 months	52.0 (33.8-67.5)	21.9 (9.5-37.5)	4.3 (1.1-10.9)	2.6 (0.5-8.3)

Gillessen, et al. ASCO Annual Meeting 2021. J Clin Oncol 39, 2021 (suppl 15; abstr 5002)

AR-Null PC Incidence

- Increasing incidence of AR-null prostate cancers since approval of NHA
- Incidence of SCPC was 17% in SU2C West Coast Dream Team dataset (N=202)
- >5000 men die from small cell PC each year
- Manage per small cell lung cancer paradigm: platinum-doublet therapy



Bluemn, et al. Cancer Cell. 2017 Oct 9;32(4):474-489

Aggarwal, et al. JCO. 2018 Aug 20;36(24):2492-2503

Key Take Home Points for the Boards Exam

- There are no approved therapies for prostate cancer prevention
- Active surveillance should be recommended for most low-risk localized prostate cancer patients
- Local intervention is appropriate for higher-risk prostate cancer patient in good health
  - ADT offers survival benefit over external beam radiation alone
- Know the side effects of ADT
- Docetaxel, abiraterone, enzalutamide and apalutamide added to ADT offers survival benefit for new mHSPC
- Apalutamide, darolutamide and enzalutamide offer MFS and OS benefit for M0 CRPC
- Know the mechanisms of action, appropriate disease states and side effects of agents proven to prolong survival for mCRPC
  - Sipuleucel-T, abiraterone, enzalutamide, radium-223, docetaxel, cabazitaxel, olaparib, rucaparib
- Be aware of neuroendocrine/small cell prostate cancer and utilization of platinum chemotherapy in this setting
- Pembrolizumab is appropriate for MSI high prostate cancer
- DNA repair alterations occur in ~23% of men with mCRPC (~12% are germline with genetic counseling implications)

Seattle Cancer Care Alliance

Fred Hutch · Seattle Children's · UW Medicine

Thank You!

schweize@uw.edu