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Metastatic Prostate Cancer Medications: What is important for the PCP?

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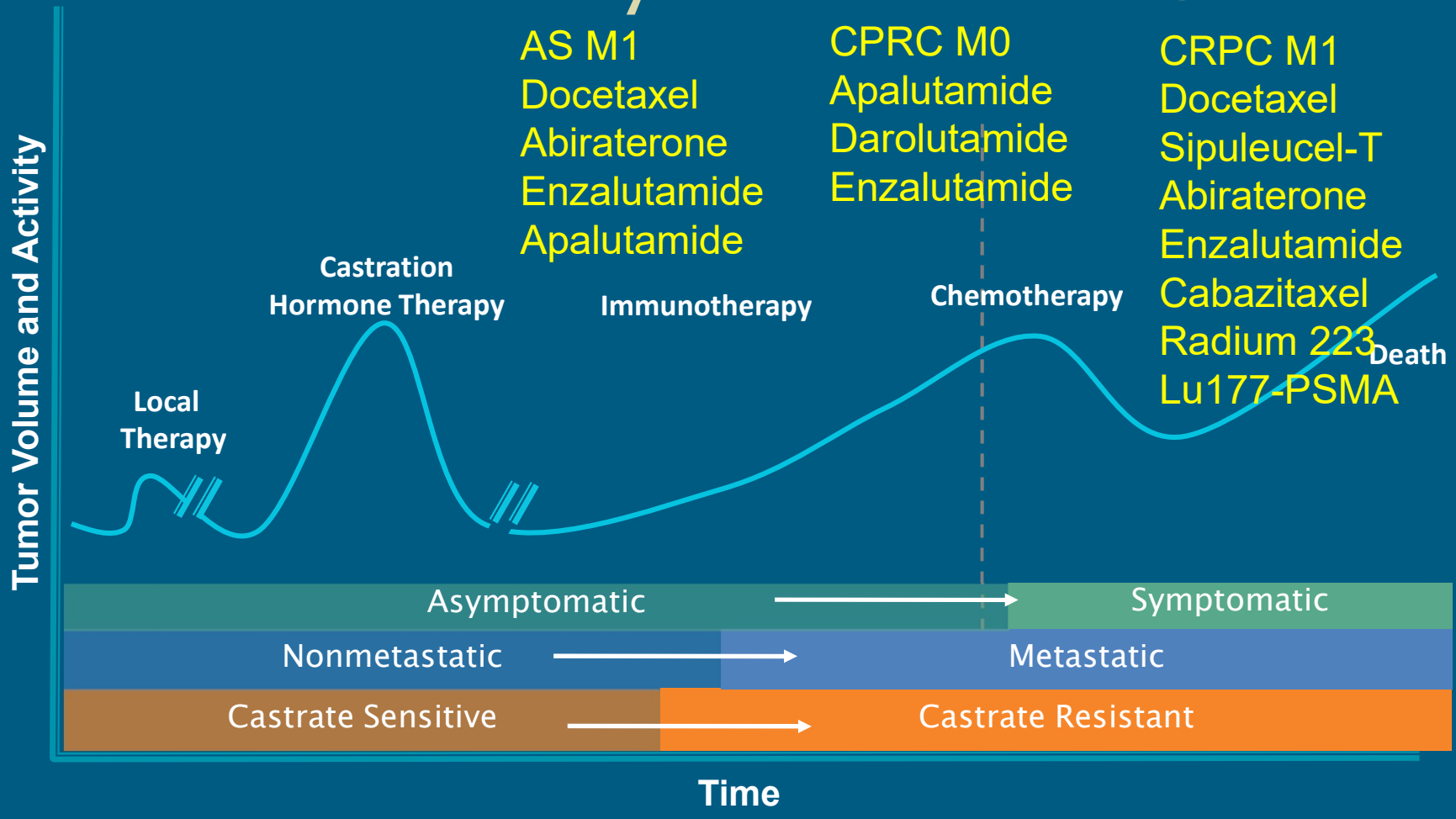
Disclosures

- Consultant
  - Ferring
  - Johnson & Johnson
- Clinical trials
  - Janssen
  - Astellas
  - Pfizer
  - Merck
  - Bayer

Objectives

- NCCN Guidelines
- Medication categories
- Side Effects
- What a PCP should look for in patients on these medications

Natural History of Prostate Cancer



Adapted from Higano CS. In: Figg WD et al. *Drug Management of Prostate Cancer*. 2010:321
Slide courtesy of R. Concepcion.

Definitions

- Androgen Sensitive
  - Suppressed Testosterone on standard ADT
  - Suppressed PSA
  - AKA Castration-Naïve, Androgen responsive, Hormone Sensitive
- Castration Resistant
  - Suppressed Testosterone on Standard ADT
  - Rising PSA
    - for most trials > 2 ng/dL

Definitions

- Metastatic status
  - Based on bone scan and CT AP imaging for all trials
  - Na-F PET-CT, Choline- PET, Flucyclovine PET, PSMA PET

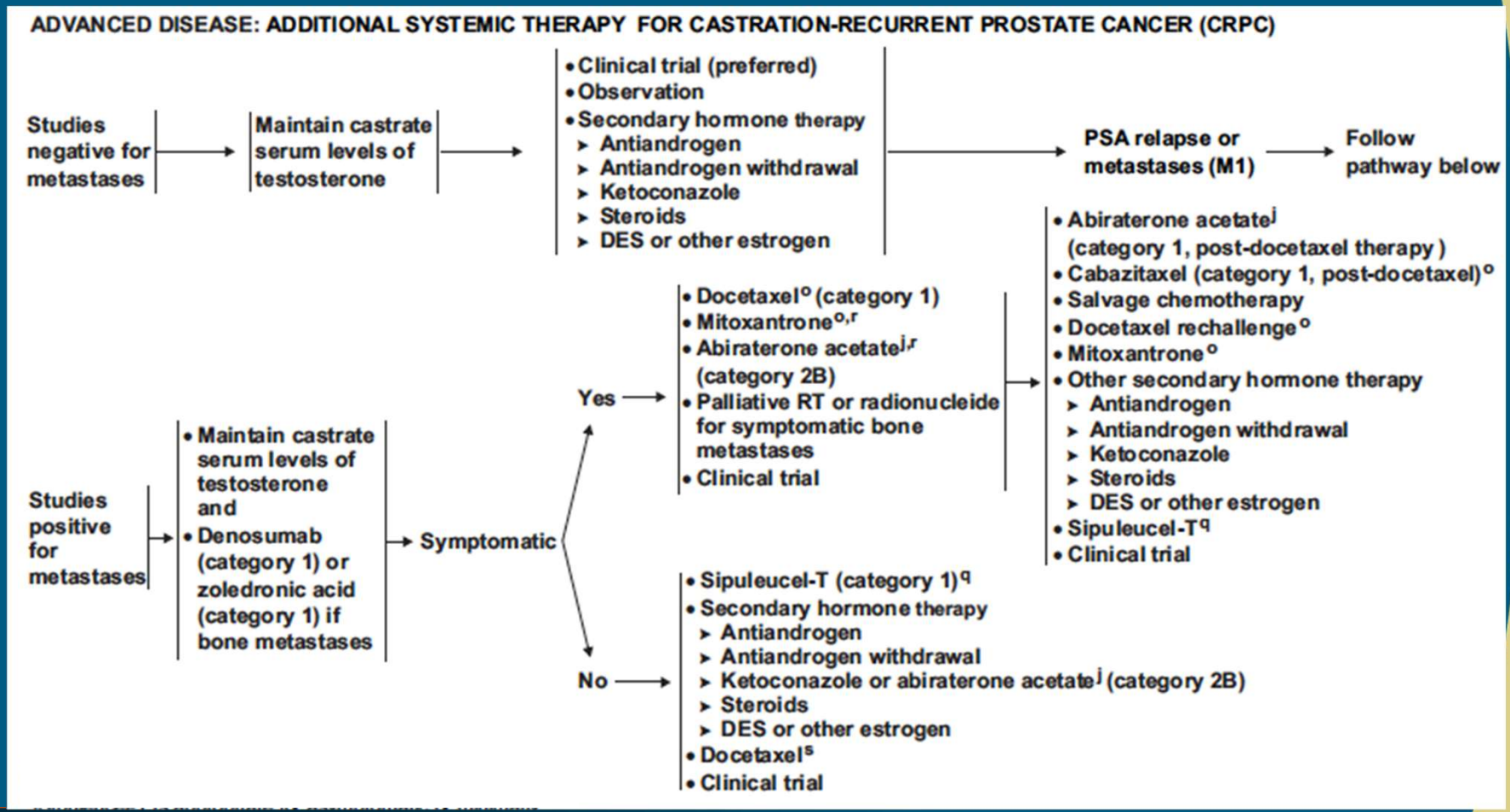
- M0
- M1
  - a non regional lymph node
  - b bone
  - c other sites (visceral mets)

Redefining Goals for the CRPC Patient

- No longer curative
  - Median survival 14–26 months without next generation agents
- Focus on quality of life
  - Multiple treatments available currently
  - Few, if any, significant side effects

Halibi et al. JCO 2014; 32:671-7

2012 NCCN Guidelines



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NCCN National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2012
Prostate Cancer

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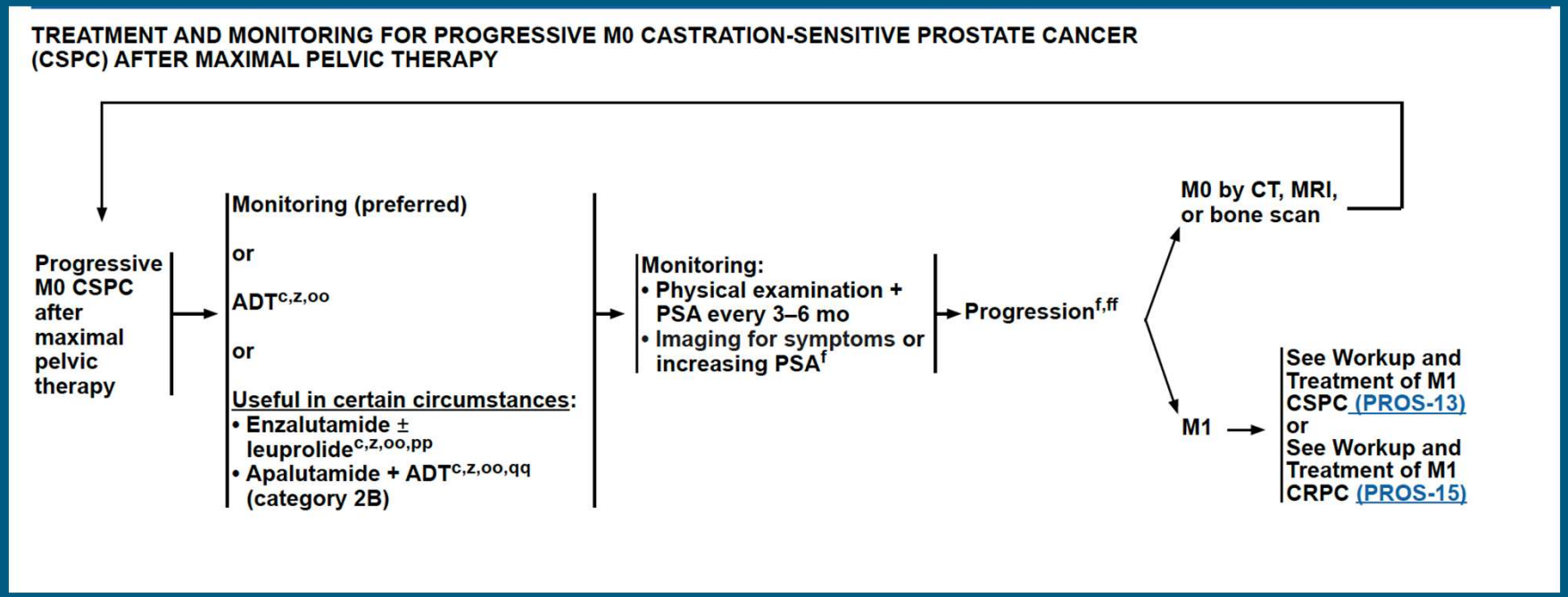
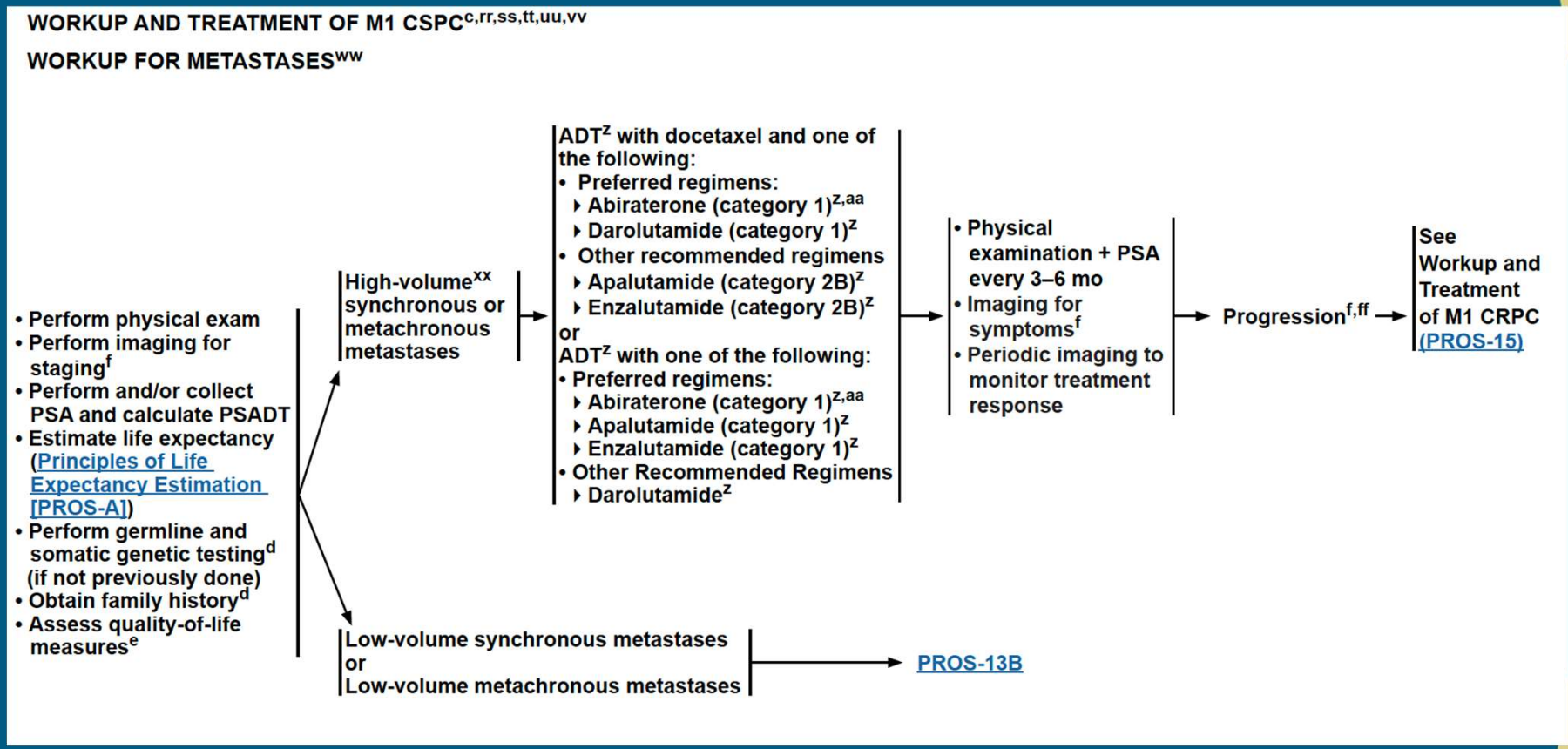
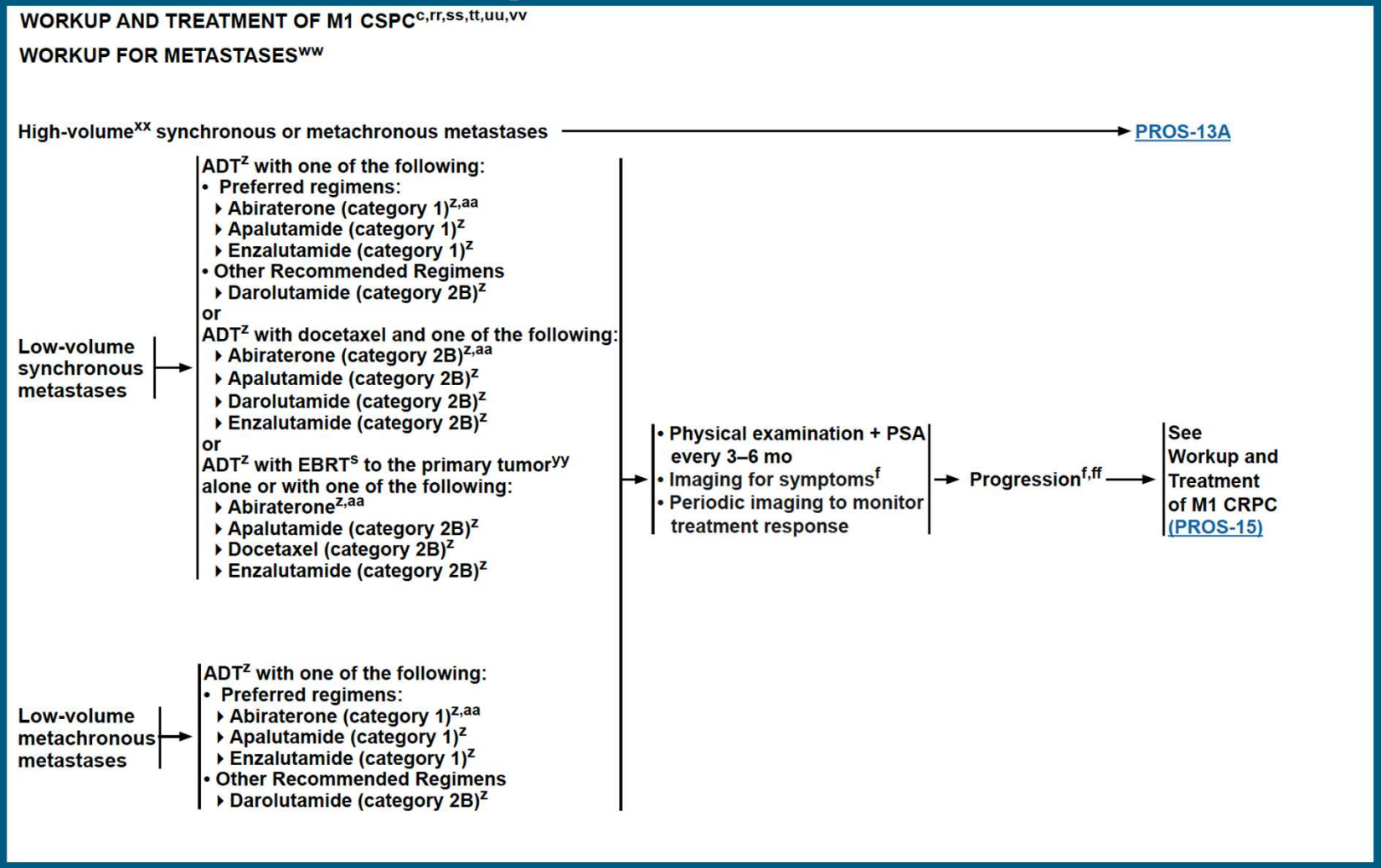
CSPC M0


TREATMENT AND MONITORING FOR PROGRESSIVE M0 CASTRATION-SENSITIVE PROSTATE CANCER (CSPC) AFTER MAXIMAL PELVIC THERAPY
Progressive M0 CSPC after maximal pelvic therapy
Monitoring (preferred)
or
ADT[c,z,oo]
or
Useful in certain circumstances:
• Enzalutamide ± leuprolide[c,z,oo,pp]
• Apalutamide + ADT[c,z,oo,qq] (category 2B)
Monitoring:
• Physical examination + PSA every 3–6 mo
• Imaging for symptoms or increasing PSA[f]
Progression[f,ff]
M0 by CT, MRI, or bone scan
M1
See Workup and Treatment of M1 CSPC (PROS-13)
or
See Workup and Treatment of M1 CRPC (PROS-15)

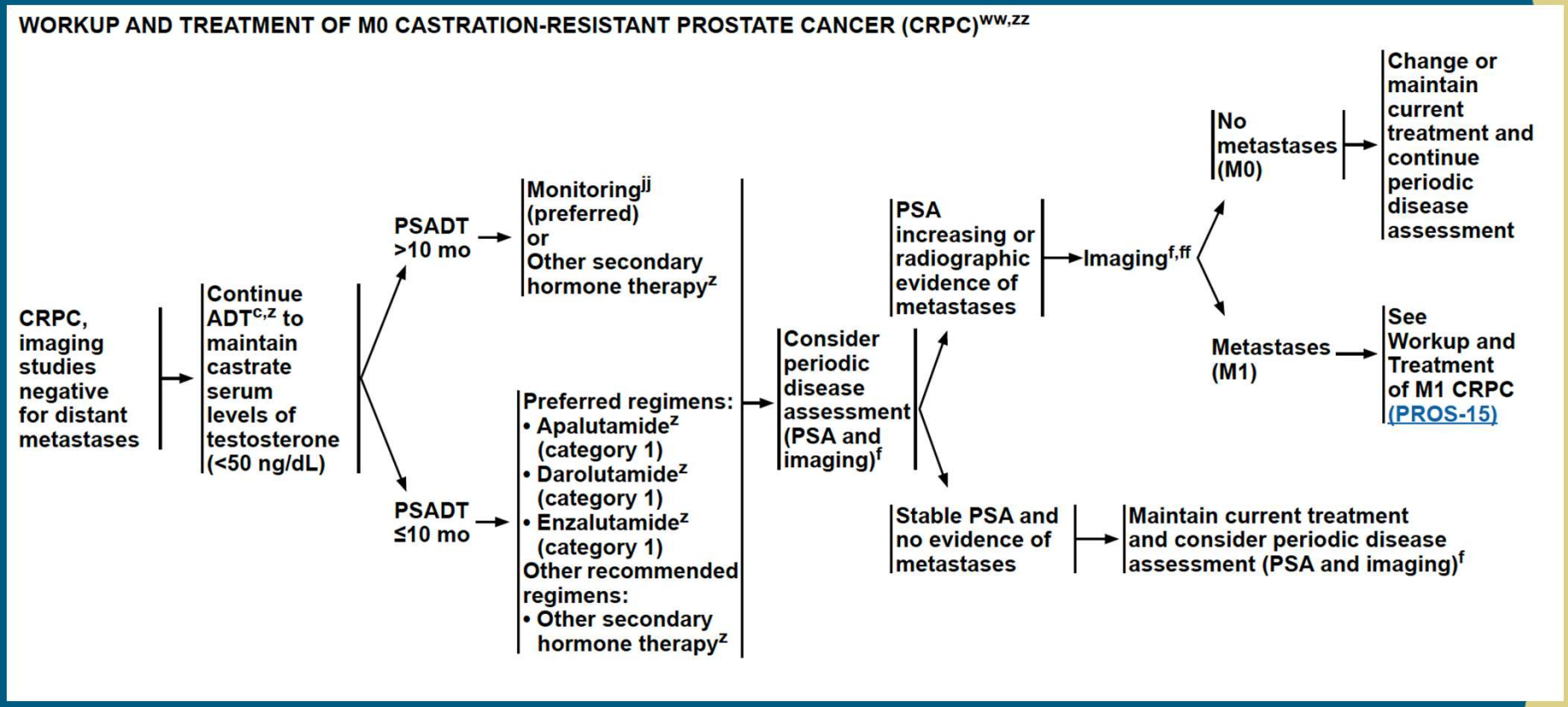
CSPC M1


WORKUP AND TREATMENT OF M1 CSPC[c,rr,ss,tt,uu,vv]
WORKUP FOR METASTASES[ww]
• Perform physical exam
• Perform imaging for staging[f]
• Perform and/or collect PSA and calculate PSADT
• Estimate life expectancy (Principles of Life Expectancy Estimation [PROS-A])
• Perform germline and somatic genetic testing[d] (if not previously done)
• Obtain family history[d]
• Assess quality-of-life measures[e]
High-volume[xx] synchronous or metachronous metastases
ADT[z] with docetaxel and one of the following:
• Preferred regimens:
▸ Abiraterone (category 1)[z,aa]
▸ Darolutamide (category 1)[z]
• Other recommended regimens
▸ Apalutamide (category 2B)[z]
▸ Enzalutamide (category 2B)[z]
or
ADT[z] with one of the following:
• Preferred regimens:
▸ Abiraterone (category 1)[z,aa]
▸ Apalutamide (category 1)[z]
▸ Enzalutamide (category 1)[z]
• Other Recommended Regimens
▸ Darolutamide[z]
• Physical examination + PSA every 3–6 mo
• Imaging for symptoms[f]
• Periodic imaging to monitor treatment response
Progression[f,ff]
See Workup and Treatment of M1 CRPC (PROS-15)
Low-volume synchronous metastases
or
Low-volume metachronous metastases
PROS-13B

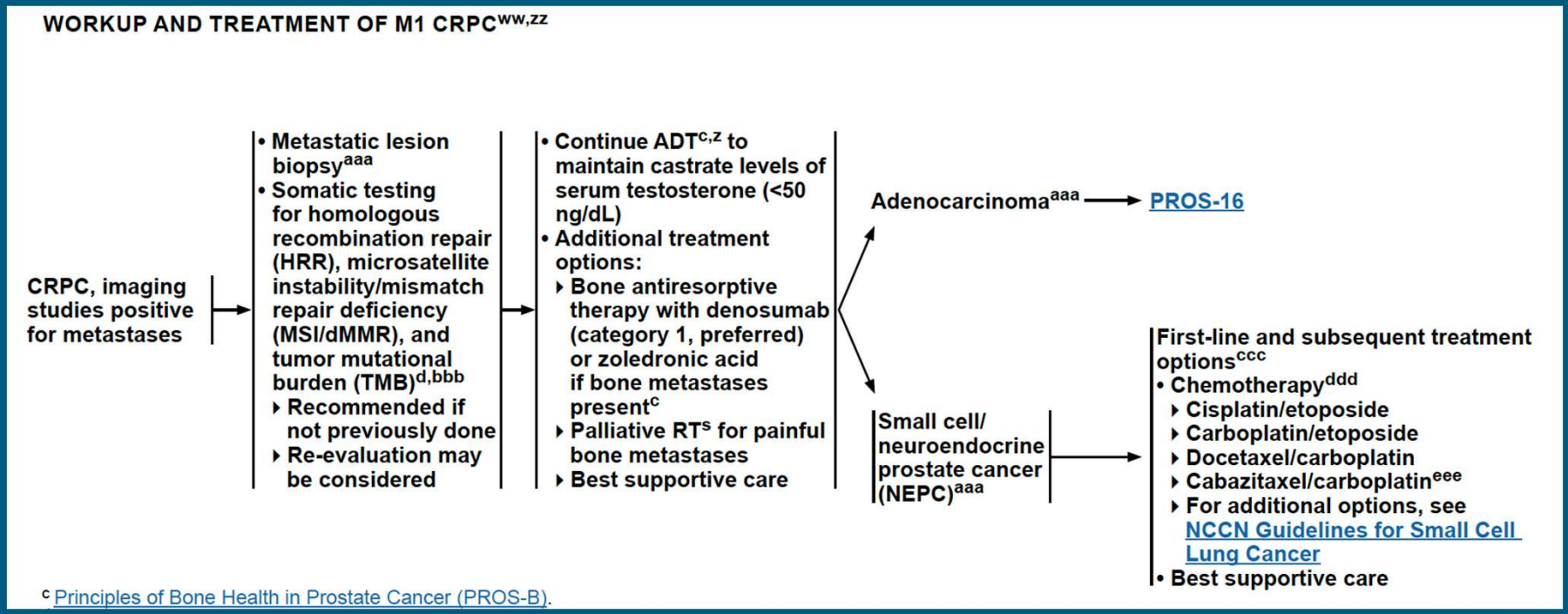
CSPC M1 (part 2)



CRPC M0


WORKUP AND TREATMENT OF M0 CASTRATION-RESISTANT PROSTATE CANCER (CRPC)ww,zz
CRPC, imaging studies negative for distant metastases
Continue ADTc,z to maintain castrate serum levels of testosterone (<50 ng/dL)
PSADT >10 mo
Monitoringjj (preferred) or Other secondary hormone therapyz
PSADT ≤10 mo
Preferred regimens:
• Apalutamidez (category 1)
• Darolutamidez (category 1)
• Enzalutamidez (category 1)
Other recommended regimens:
• Other secondary hormone therapyz
Consider periodic disease assessment (PSA and imaging)f
PSA increasing or radiographic evidence of metastases
Imagingf,ff
No metastases (M0)
Change or maintain current treatment and continue periodic disease assessment
Metastases (M1)
See Workup and Treatment of M1 CRPC (PROS-15)
Stable PSA and no evidence of metastases
Maintain current treatment and consider periodic disease assessment (PSA and imaging)f

CRPC M1


WORKUP AND TREATMENT OF M1 CRPC[ww,zz]
CRPC, imaging studies positive for metastases
• Metastatic lesion biopsy[aaa]
• Somatic testing for homologous recombination repair (HRR), microsatellite instability/mismatch repair deficiency (MSI/dMMR), and tumor mutational burden (TMB)[d,bbb]
▸ Recommended if not previously done
▸ Re-evaluation may be considered
• Continue ADT[c,z] to maintain castrate levels of serum testosterone (<50 ng/dL)
• Additional treatment options:
▸ Bone antiresorptive therapy with denosumab (category 1, preferred) or zoledronic acid if bone metastases present[c]
▸ Palliative RT[s] for painful bone metastases
▸ Best supportive care
Adenocarcinoma[aaa]
PROS-16
Small cell/ neuroendocrine prostate cancer (NEPC)[aaa]
First-line and subsequent treatment options[ccc]
• Chemotherapy[ddd]
▸ Cisplatin/etoposide
▸ Carboplatin/etoposide
▸ Docetaxel/carboplatin
▸ Cabazitaxel/carboplatin[eee]
▸ For additional options, see NCCN Guidelines for Small Cell Lung Cancer
• Best supportive care
[c] Principles of Bone Health in Prostate Cancer (PROS-B).

CRPC M1: Progressing

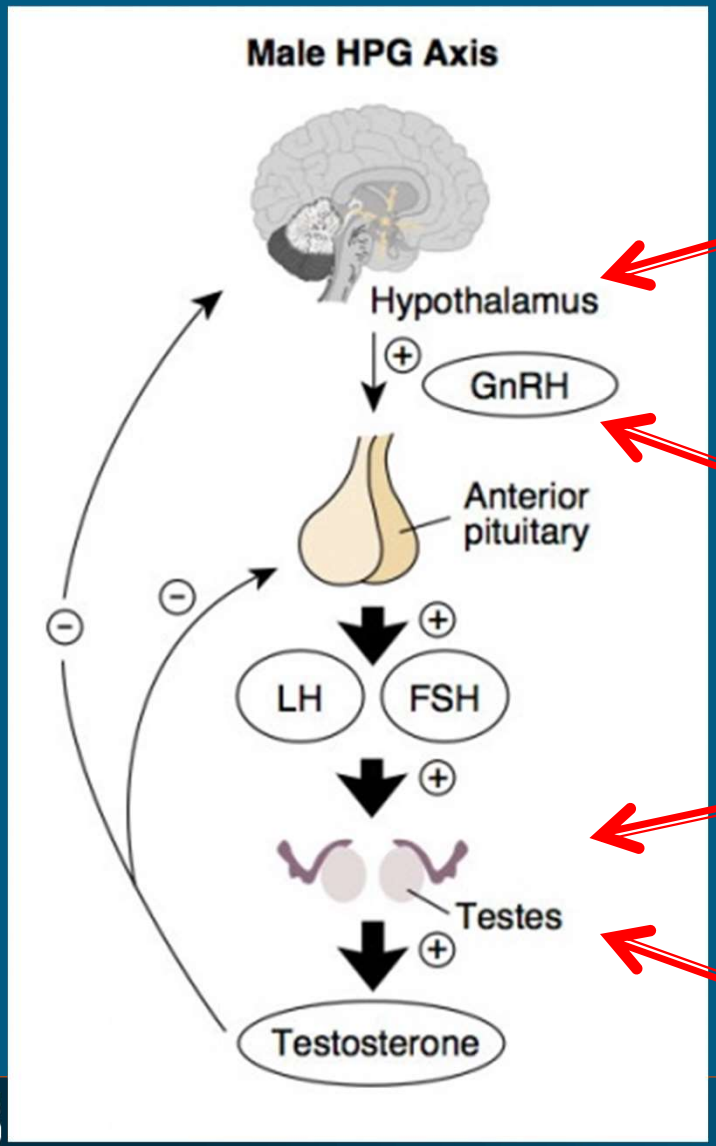
SYSTEMIC THERAPY FOR M1 CRPC: ADENOCARCINOMA[f,fff,ggg,hhh,iii]

No prior docetaxel/no prior novel hormone therapy[jjj]	Progression on prior novel hormone therapy/no prior docetaxel[jjj]
• Preferred regimens ▸ Abiraterone[z,kkk] (category 1 if no visceral metastases) ▸ Docetaxel[ddd] (category 1) ▸ Enzalutamide[z] (category 1) • Useful in certain circumstances ▸ Niraparib/abiraterone[z,lll,mmm] for *BRCA* mutation (category 1) ▸ Olaparib/abiraterone[z,kkk,lll] for *BRCA* mutation (category 1) ▸ Pembrolizumab for MSI-high (MSI-H)/dMMR[ddd] (category 2B) ▸ Radium-223[s,nnn] for symptomatic bone metastases (category 1) ▸ Sipuleucel-T[ddd,ooo] (category 1) ▸ Talazoparib/enzalutamide for HRR mutation[z,lll] (category 1) • Other recommended regimens ▸ Other secondary hormone therapy[z]	• Preferred regimens ▸ Docetaxel (category 1)[ddd] ▸ Olaparib for *BRCA* mutation[lll] (category 1) ▸ Rucaparib for *BRCA* mutation[lll] (category 1) • Useful in certain circumstances ▸ Cabazitaxel/carboplatin[ddd] ▸ Niraparib/abiraterone[z,lll,mmm] for *BRCA* mutation (category 2B) ▸ Olaparib for HRR mutation other than *BRCA1/2*[lll] ▸ Pembrolizumab for MSI-H/dMMR or TMB ≥10 mut/Mb[ddd] (category 2B) ▸ Radium-223[s,nnn] for symptomatic bone metastases (category 1) ▸ Sipuleucel-T[ddd,ooo] ▸ Talazoparib/enzalutamide for HRR mutation[z,lll] (category 2B) • Other recommended regimens ▸ Other secondary hormone therapy[z]
Progression on prior docetaxel/no prior novel hormone therapy[jjj]	**Progression on prior docetaxel and a novel hormone therapy[jjj]**
• Preferred regimens ▸ Abiraterone[z,kkk] (category 1) ▸ Cabazitaxel[ddd] ▸ Enzalutamide[z] (category 1) • Useful in certain circumstances ▸ Cabazitaxel/carboplatin[ddd] ▸ Mitoxantrone for palliation in symptomatic patients who cannot tolerate other therapies[ddd] ▸ Niraparib/abiraterone[z, lll,mmm] for *BRCA* mutation ▸ Olaparib/abiraterone[z,kkk,lll] for *BRCA* mutation ▸ Pembrolizumab for MSI-H/dMMR[ddd] (category 2B) ▸ Radium-223[s,nnn] for symptomatic bone metastases (category 1) ▸ Sipuleucel-T[ddd,ooo] ▸ Talazoparib/enzalutamide for HRR mutation[z,lll] • Other recommended regimens ▸ Other secondary hormone therapy[z]	• Preferred regimens ▸ Cabazitaxel[ddd] (category 1) ▸ Docetaxel rechallenge[ddd] • Useful in certain circumstances ▸ Cabazitaxel/carboplatin[ddd] ▸ Lutetium Lu 177 vipivotide tetraxetan (Lu-177–PSMA-617) for PSMA-positive metastases[ppp] (category 1) ▸ Mitoxantrone for palliation in symptomatic patients who cannot tolerate other therapies[ddd] ▸ Olaparib for HRR mutation[lll] (category 1 for *BRCA* mutation) ▸ Pembrolizumab for MSI-H/dMMR, or TMB ≥10 mut/Mb[ddd] ▸ Radium-223[s,nnn] for symptomatic bone metastases (category 1) ▸ Rucaparib for *BRCA* mutation[lll] • Other recommended regimens ▸ Other secondary hormone therapy[z]

Quite the advancement, but…

- The basics of treatment are relatively the same
  - Limit Testosterone
- Consequently, the side effects are relatively the same across therapies
  - Certainly some exceptions…

Hypothalamic Pituitary Testis

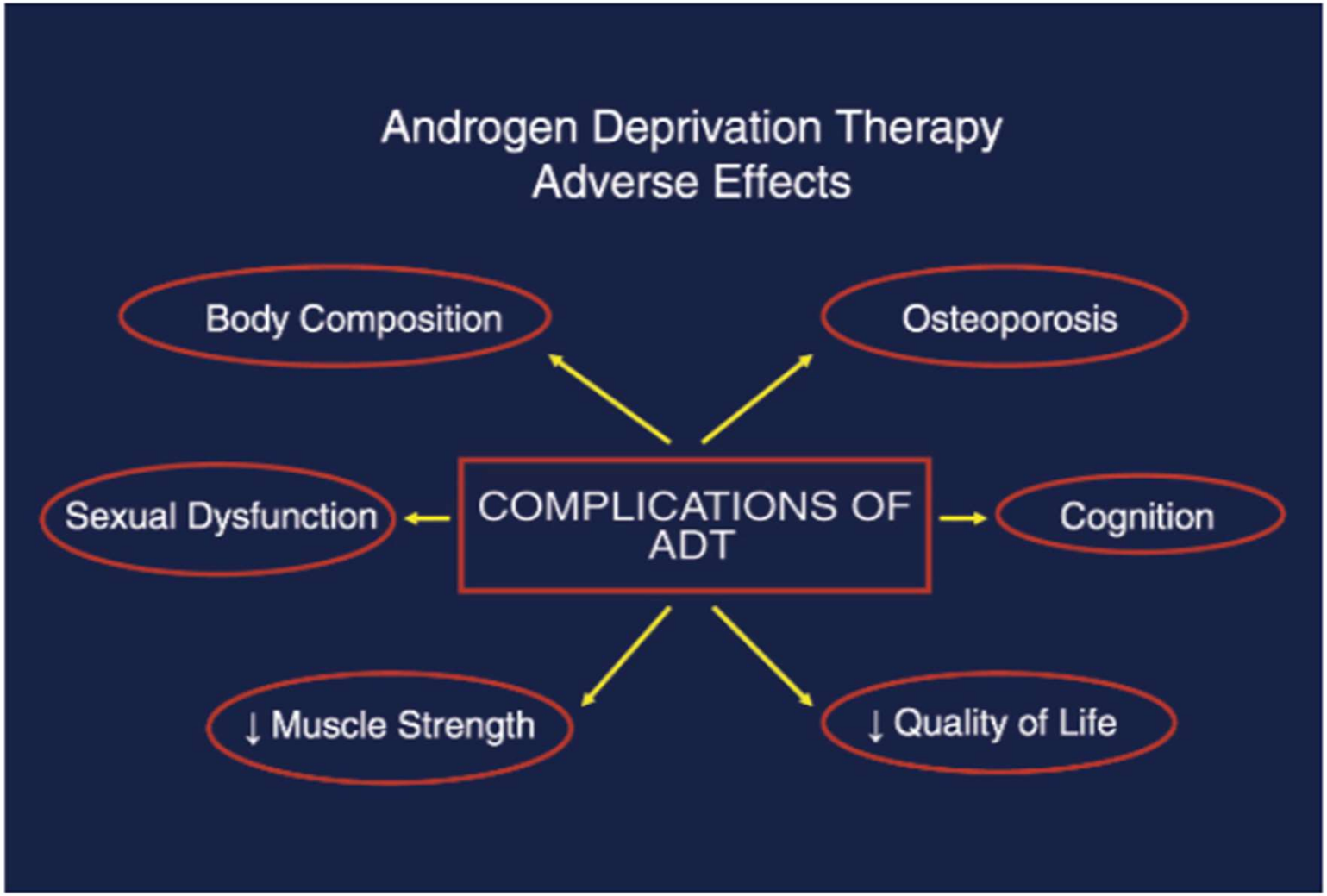


(+) LHRH agonist (leuprolide)

(-) LHRH antagonist (degarelix, relugolix)

(-) Antiandrogens (bicalutamide)

Orchiectomy



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J Androl 2008;29:534–539

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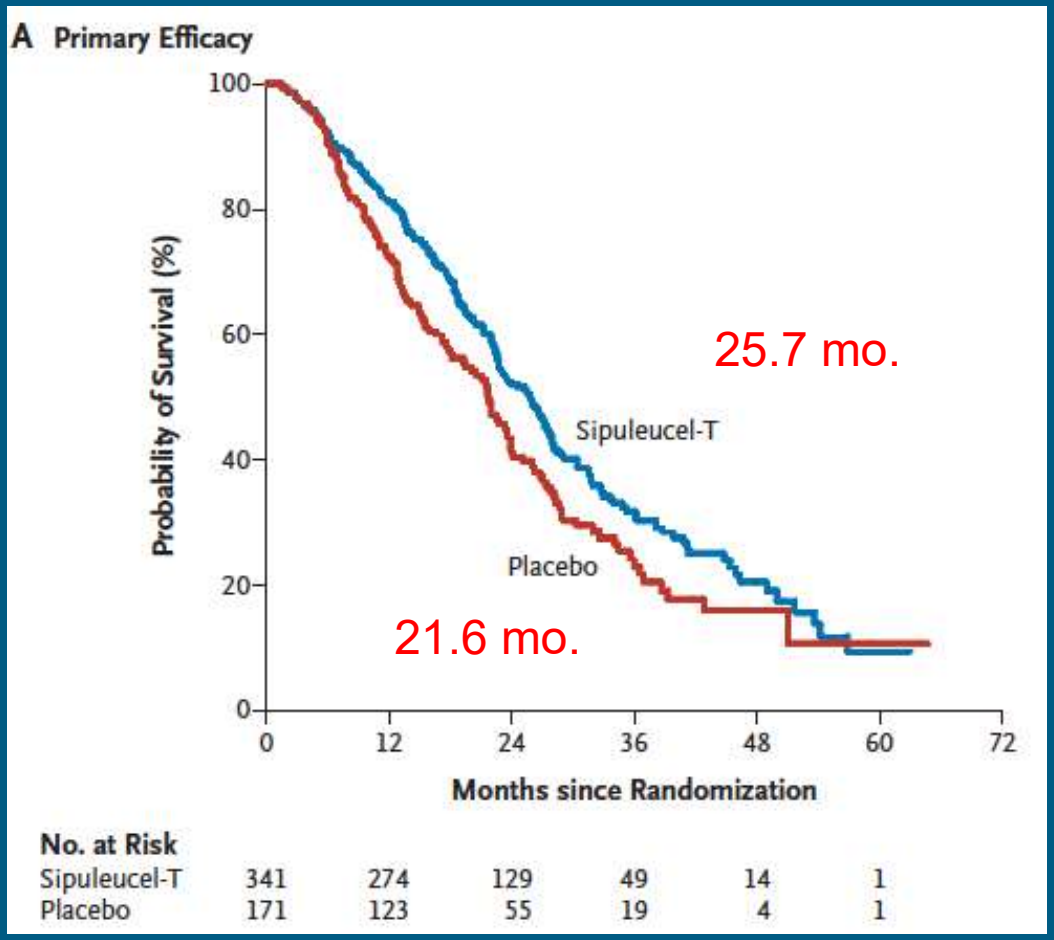
Medication Categories

- Immunotherapy
  - Sipuleucel-T
- Androgen Synthesis Inhibitor
  - Abiraterone + prednisone
- Androgen Receptor Inhibitors
  - Enzalutamide
  - Apalutamide
  - Darolutamide
- Radiopharmaceutical
  - Radium-223
  - Lutetium-177
- Immuno-oncologic
  - Pembrolizumab
- PARP inhibitors
  - Olaparib
  - Rucaparib

Immunotherapy

- Sipuleucel-T (Provenge)
  - 1st autologous immunotherapy that demonstrated an improved OS in M1 CaP
- Autologous peripheral blood mononuclear cells with APCs
  - Combined ex-vivo with recombinant fusion protein
  - Prostate antigen, PAP, GM-CSF

Sipuleucel-T Immunotherapy for Castration-Resistant Prostate Cancer



IMPACT

4.1 mo. OS

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NEJM 2010; 363:411-22

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Adverse Events

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- Grade 1 or 2
  - 65.2%
  - Chills, fever, headache, flu-like illness, myalgia
- Grade 3
  - Chills 4 patients
  - Fatigue 3 patients
  - Back pain/HTN/Hypokalemia/Muscle weakness 2 patients each
- Grade 4
  - IV associated bacteremia 1 patient

Primary issues seen- Sipuleucel-T

- Requires going to Red Cross for leukapheresis
  - Vein access can be problematic
  - Can require PICC lines (apheresis catheters)
    - PICC line DVTs have occurred
- Anti-inflammatory utilization

Abiraterone (Zytiga)

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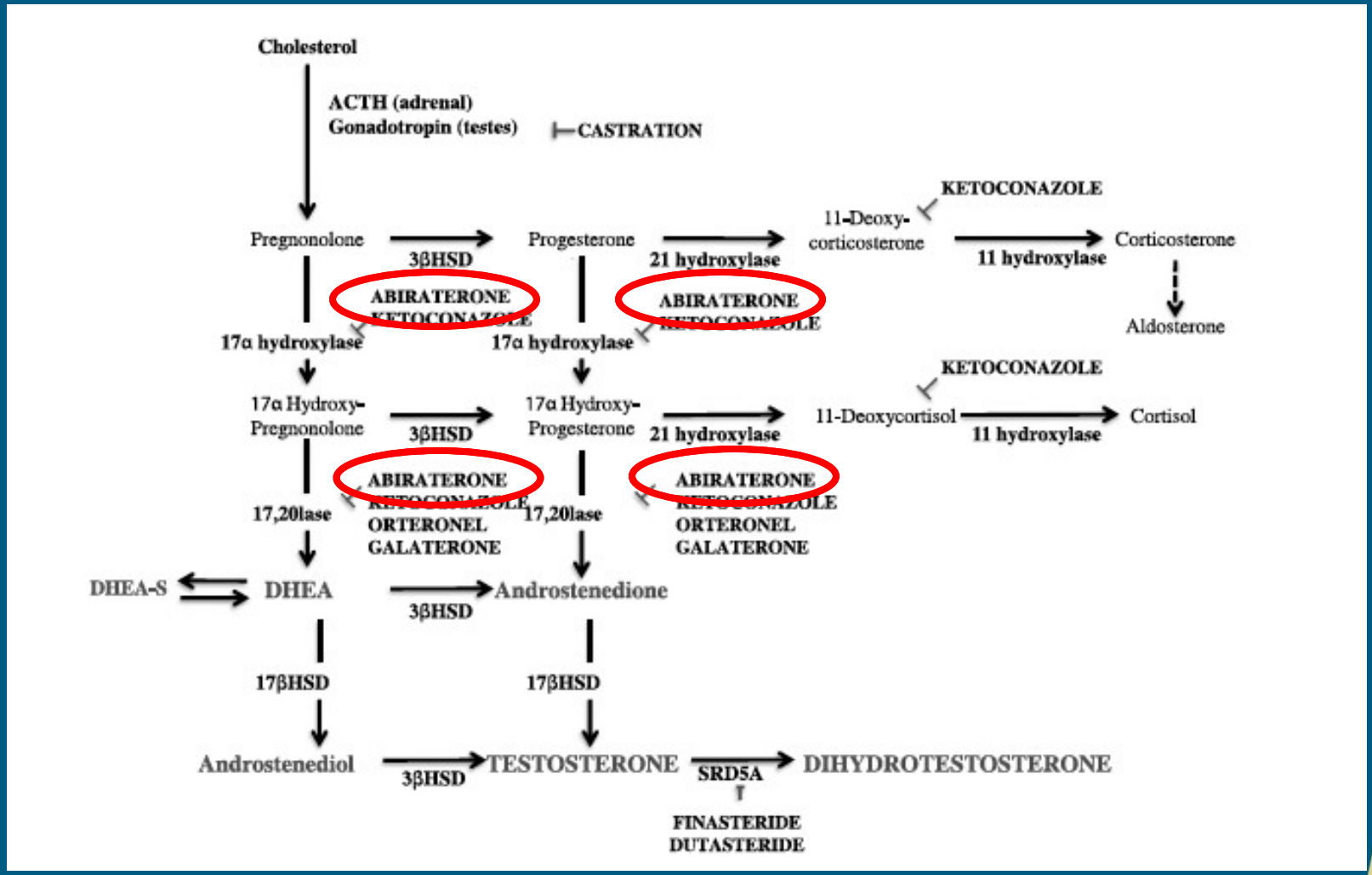
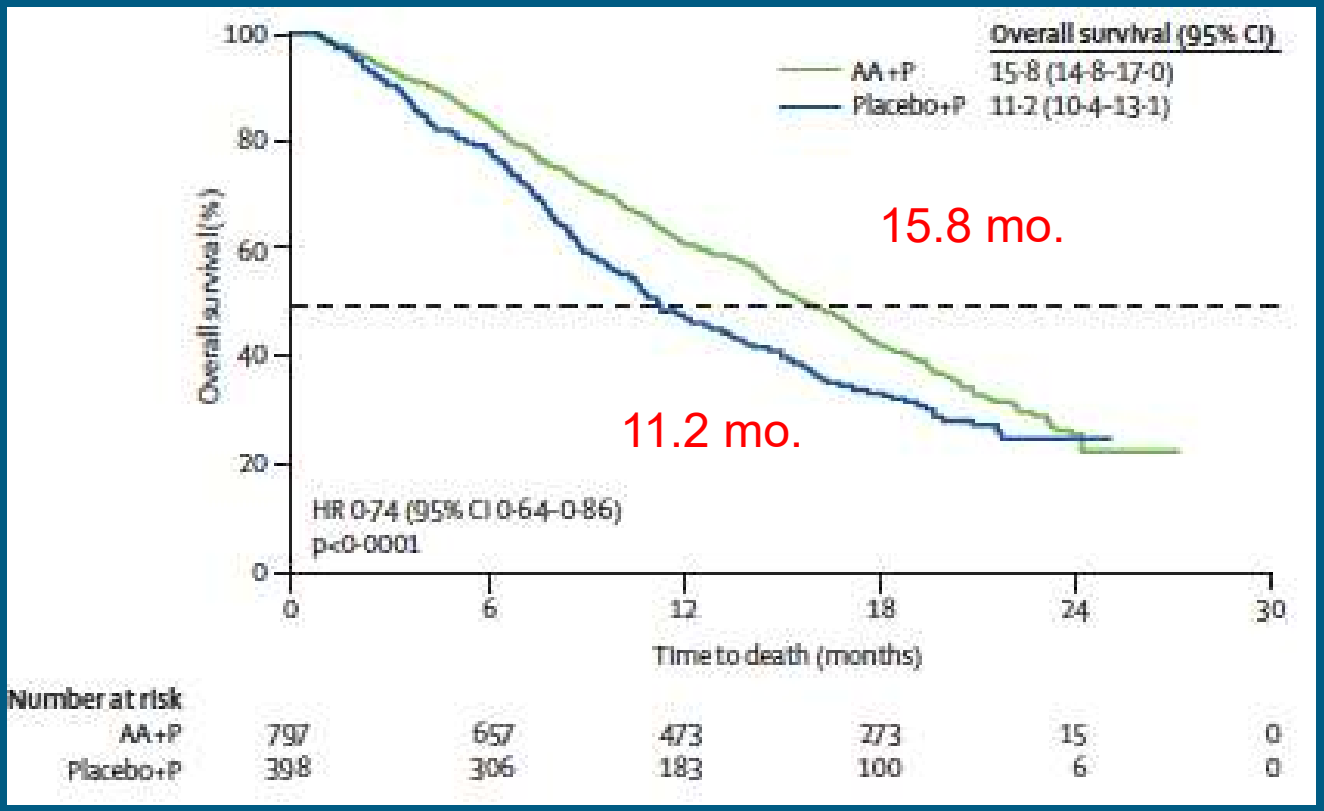


Abiraterone acetate for treatment of metastatic castration-resistant prostate cancer: final overall survival analysis of the COU-AA-301 randomised, double-blind, placebo-controlled phase 3 study



4.6 mo. OS

Adverse Events

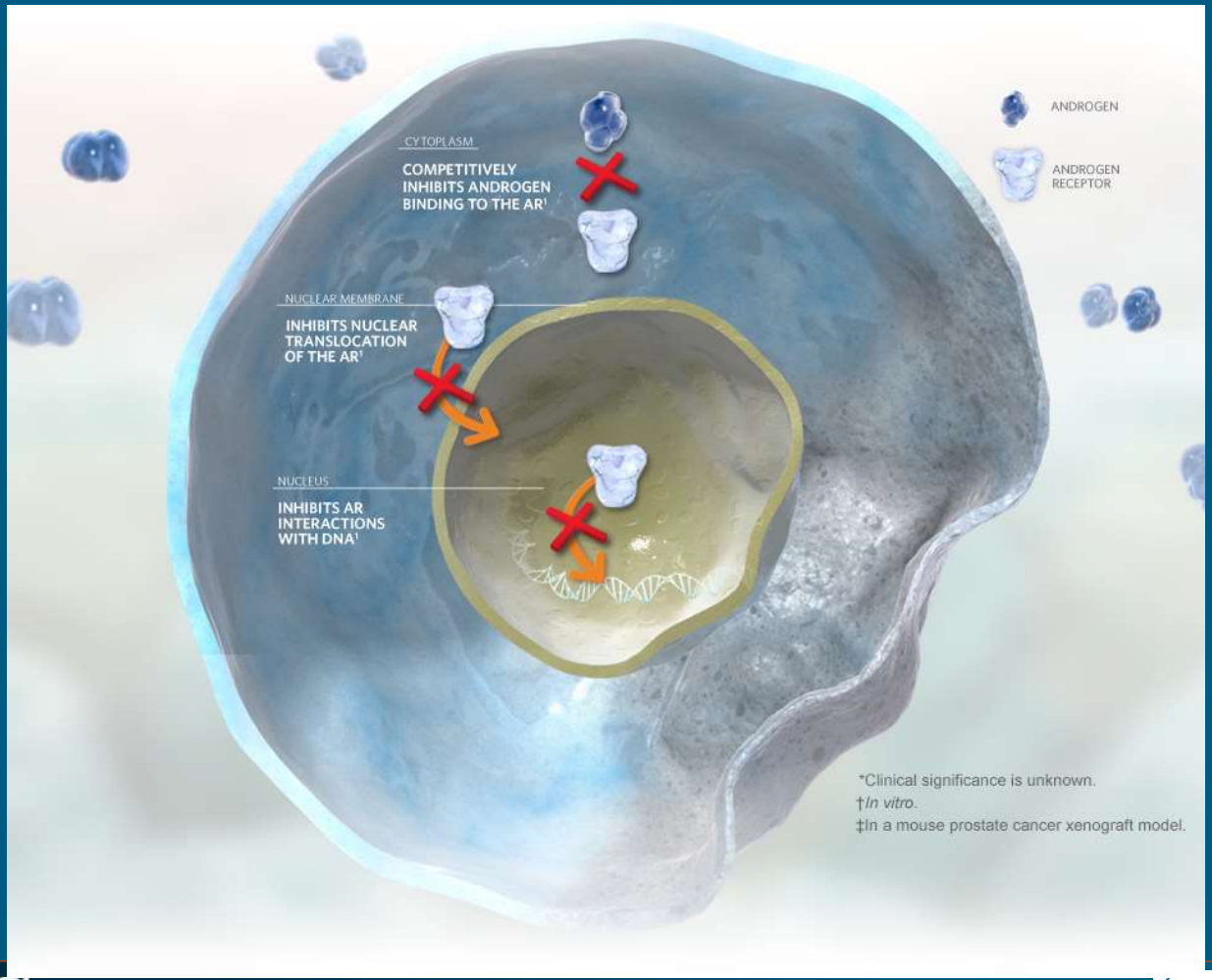
- Similar number of Grade 3 and 4 events between groups
- Mineralocorticoid related events more common in abiraterone population
  - Fluid retention 33% v. 24%
  - Hypokalemia 18% v. 9%

Lancet Oncol 2012; 13:983-92

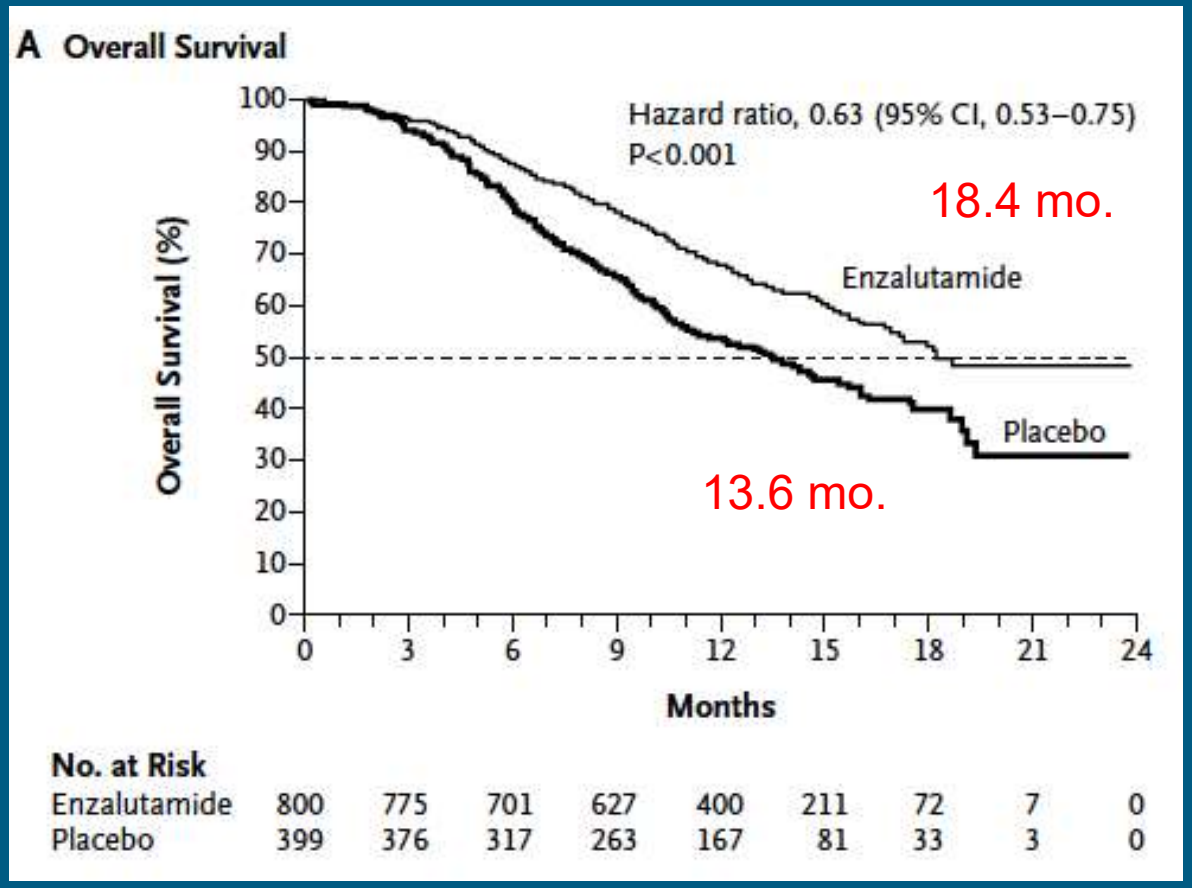
Primary Issues seen- Abiraterone

- Lower extremity edema
- Transaminase elevation
  - Dose reduce
- Compliance issues
  - Patients forgetting to take prednisone as directed
  - Not keeping with the lab schedule for monitoring

Enzalutamide (MDV-3100/Xtandi)



Increased Survival with Enzalutamide in Prostate Cancer after Chemotherapy



AFFIRM

4.8 mon OS

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NEJM 2012; 367:1187-97

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Adverse Events

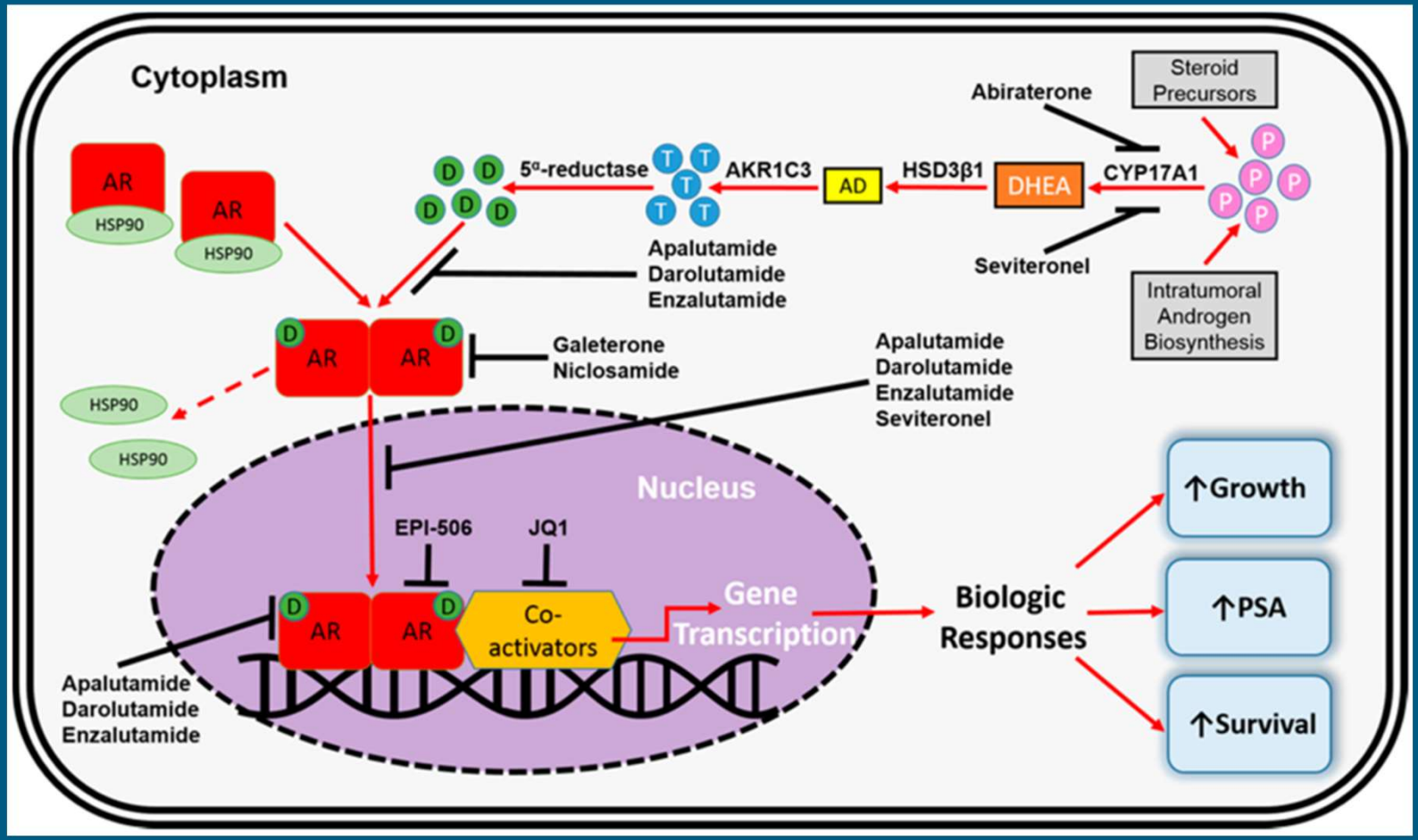
Table 3. Adverse Events, According to Grade.

Adverse Event	Enzalutamide (N=800)		Placebo (N=399)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
	number of patients (percent)			
≥1 Adverse event	785 (98)	362 (45)	390 (98)	212 (53)
Any serious adverse event	268 (34)	227 (28)	154 (39)	134 (34)
Discontinuation owing to adverse event	61 (8)	37 (5)	39 (10)	28 (7)
Adverse event leading to death	23 (3)	23 (3)	14 (4)	14 (4)
Frequent adverse events more common with enzalutamide*				
Fatigue	269 (34)	50 (6)	116 (29)	29 (7)
Diarrhea	171 (21)	9 (1)	70 (18)	1 (<1)
Hot flash	162 (20)	0	41 (10)	0
Musculoskeletal pain	109 (14)	8 (1)	40 (10)	1 (<1)
Headache	93 (12)	6 (<1)	22 (6)	0
Clinically significant adverse events				
Cardiac disorder				
Any	49 (6)	7 (1)	30 (8)	8 (2)
Myocardial infarction	2 (<1)	2 (<1)	2 (<1)	2 (<1)
Abnormality on liver-function testing†	8 (1)	3 (<1)	6 (2)	3 (<1)
Seizure	5 (<1)	5 (<1)	0	0

Primary Issues seen- Enzalutamide

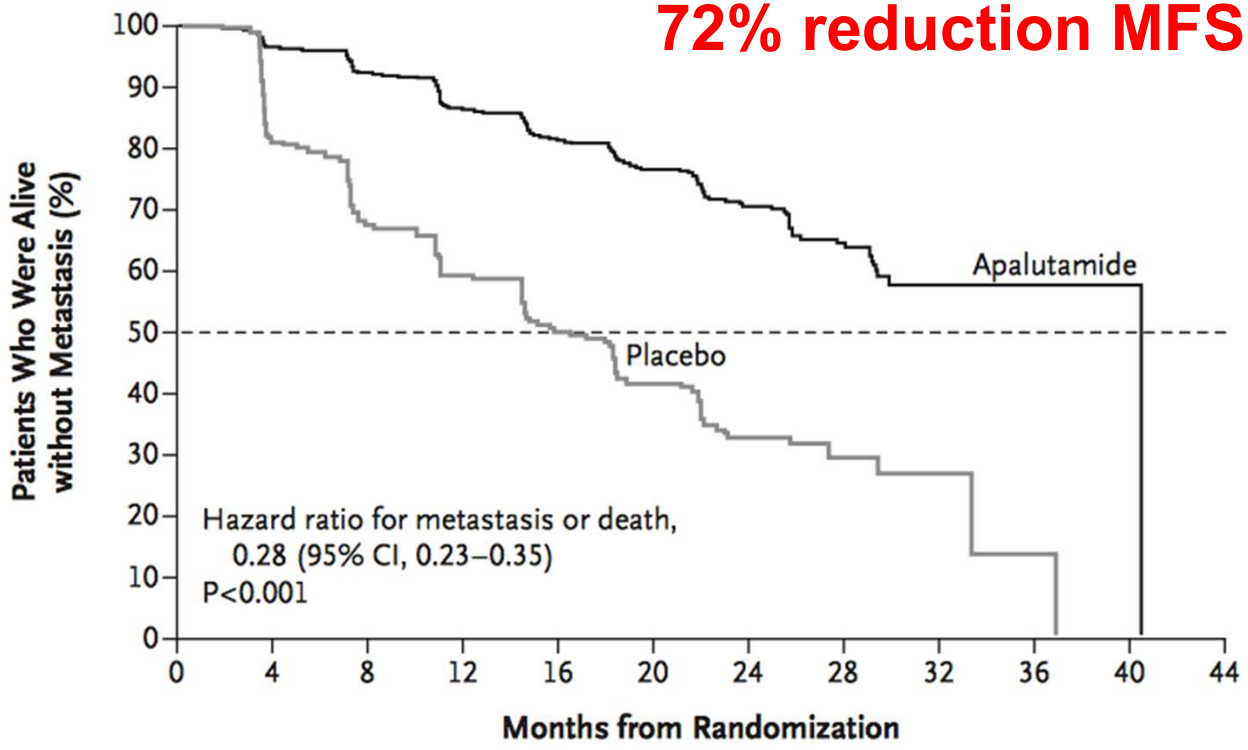
- Hypertension
- Cardiovascular issues
  - Close monitoring in terms of CV health
- Fatigue
  - Encouraging daily activity
- Unusual neurologic symptoms
  - Posterior reversible encephalopathy syndrome (PRES)

Apalutamide (ARN509/Erleada)



A Kaplan–Meier Estimates of Metastasis-free Survival

72% reduction MFS



No. at Risk

Apalutamide	806	713	652	514	398	282	180	96	36	16	3	0
Placebo	401	291	220	153	91	58	34	13	5	1	0	0

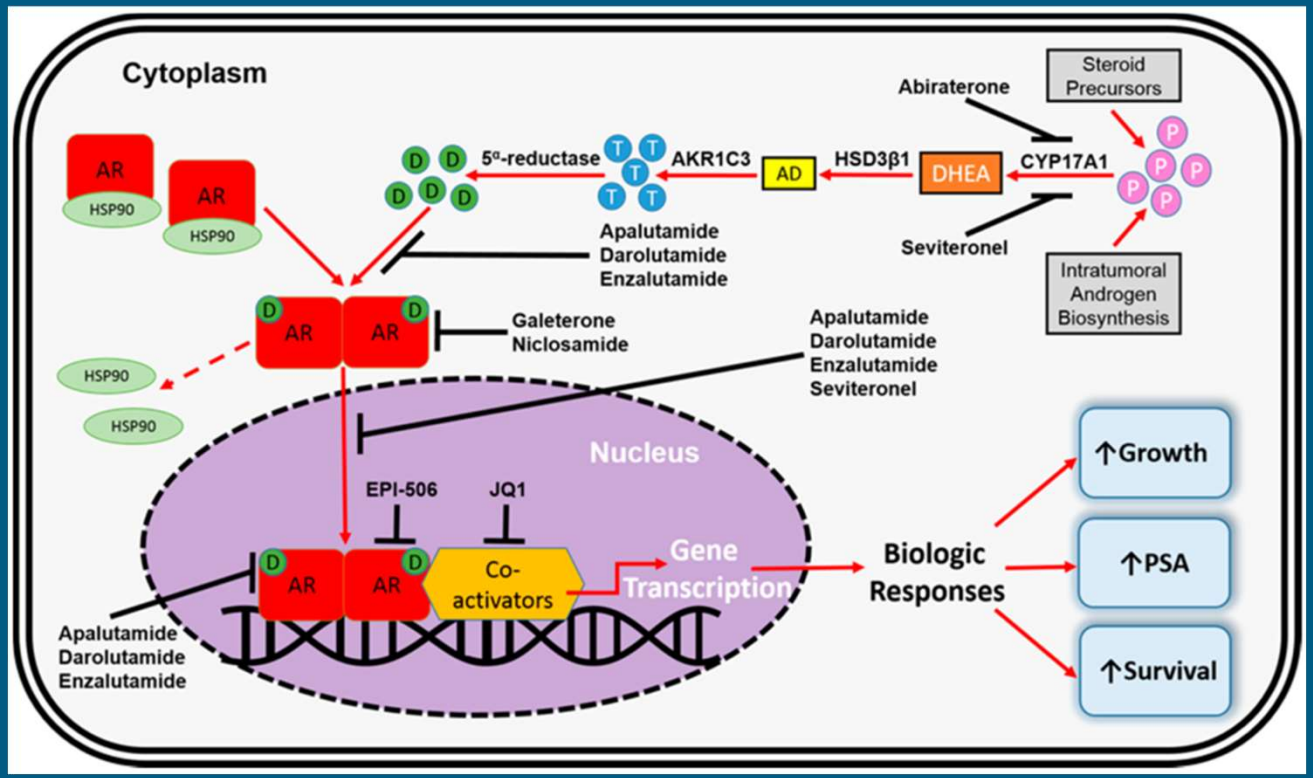
Adverse Event*	Apalutamide (N=803)		Placebo (N=398)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
	no. of patients (%)			
Any adverse event	775 (96.5)	362 (45.1)	371 (93.2)	136 (34.2)
Serious adverse event	199 (24.8)	—	92 (23.1)	—
Adverse event leading to discontinuation of the trial regimen	85 (10.6)	—	28 (7.0)	—
Adverse event associated with death	10 (1.2)	—	1 (0.3)	—
Adverse events that occurred in ≥15% of patients in either group†				
Fatigue‡	244 (30.4)	7 (0.9)	84 (21.1)	1 (0.3)
Hypertension	199 (24.8)	115 (14.3)	79 (19.8)	47 (11.8)
Rash‡	191 (23.8)	42 (5.2)	22 (5.5)	1 (0.3)
Diarrhea	163 (20.3)	8 (1.0)	60 (15.1)	2 (0.5)
Nausea	145 (18.1)	0	63 (15.8)	0
Weight loss	129 (16.1)	9 (1.1)	25 (6.3)	1 (0.3)
Arthralgia	128 (15.9)	0	30 (7.5)	0
Falls‡	125 (15.6)	14 (1.7)	36 (9.0)	3 (0.8)

Adverse Event*	Apalutamide (N=803)		Placebo (N=398)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
	no. of patients (%)			
Other adverse events of interest				
Fracture‡	94 (11.7)	22 (2.7)	26 (6.5)	3 (0.8)
Dizziness	75 (9.3)	5 (0.6)	25 (6.3)	0
Hypothyroidism‡	65 (8.1)	0	8 (2.0)	0
Mental-impairment disorder§	41 (5.1)	0	12 (3.0)	0
Seizure‡	2 (0.2)	0	0	0

Primary Issues seen- Apalutamide

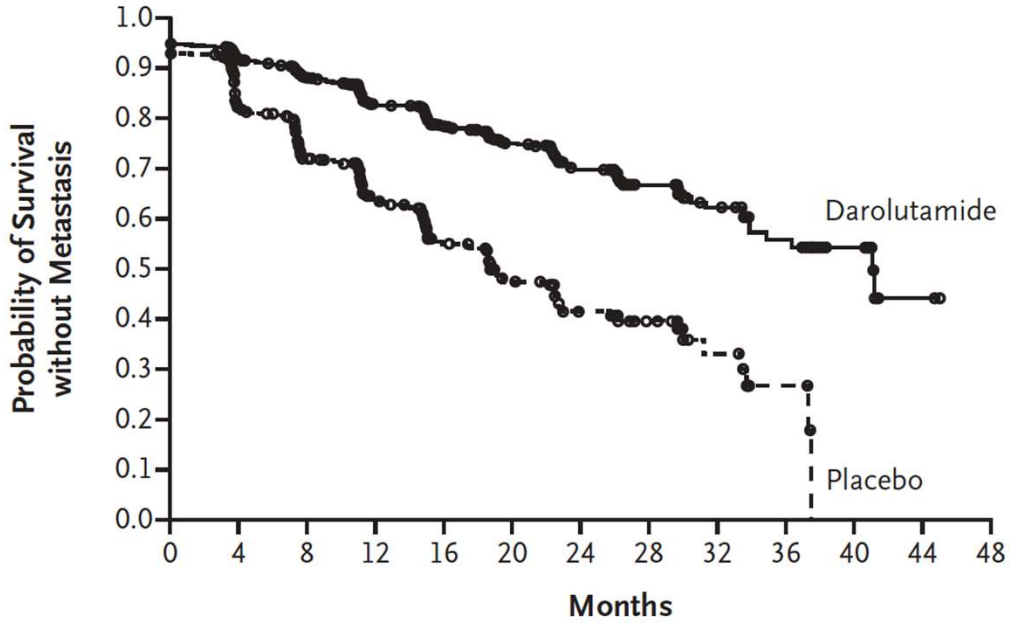
- Rash
- Thyroid disorders
  - Normally check TSH 3 months after start

Darolutamide



Metastatic Free Survival

A Kaplan–Meier Analysis of Metastasis-free Survival



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

59% reduction

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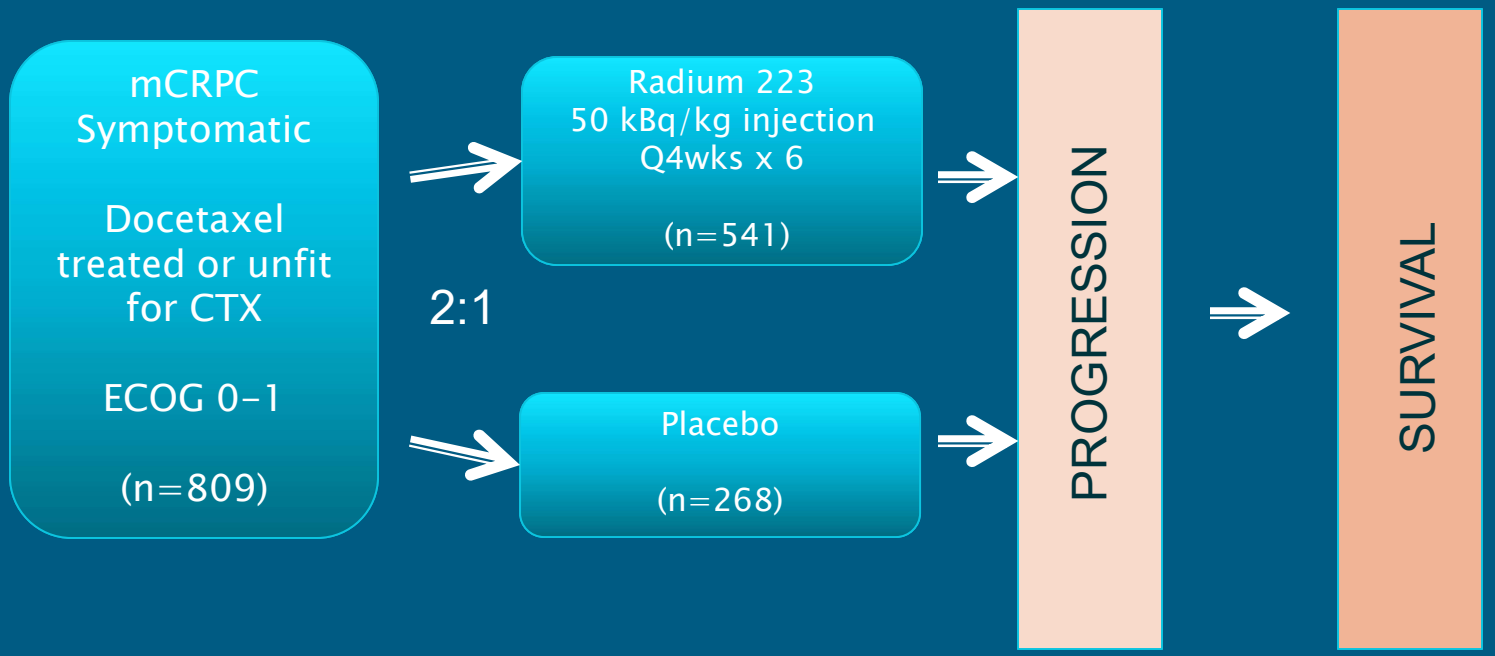
Adverse Events of Concern

Adverse Event*	Darolutamide (N=954)		Placebo (N=554)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
	number of patients (percent)			
Adverse events of interest				
Fatigue or asthenic conditions†	151 (15.8)	6 (0.6)	63 (11.4)	6 (1.1)
Bone fracture‡	40 (4.2)	9 (0.9)	20 (3.6)	5 (0.9)
Falls, including accident§	40 (4.2)	8 (0.8)	26 (4.7)	4 (0.7)
Seizure, any event	2 (0.2)	0	1 (0.2)	0
Rash¶	28 (2.9)	1 (0.1)	5 (0.9)	0
Weight decrease, any event	34 (3.6)	0	12 (2.2)	0
Dizziness, including vertigo	43 (4.5)	2 (0.2)	22 (4.0)	1 (0.2)
Cognitive disorder	4 (0.4)	0	1 (0.2)	0
Memory impairment	5 (0.5)	0	7 (1.3)	0
Change in mental status	0	0	1 (0.2)	0
Hypothyroidism	2 (0.2)	0	0	0
Cerebral ischemia‖	13 (1.4)	7 (0.7)	8 (1.4)	4 (0.7)
Coronary-artery disorder**	31 (3.2)	16 (1.7)	14 (2.5)	2 (0.4)
Heart failure††	18 (1.9)	5 (0.5)	5 (0.9)	0

Primary Issues seen- Darolutamide

- Hypertension
  - Less common than other ARi
- Thyroid disorders
  - Less common than other ARi
- Fatigue
  - Similar amounts

ALSYMPCA – Radium-223



Primary Endpoint: Overall Survival
Secondary Endpoint: Time to first SRE
Measures of progression (PSA, Alk Phos)

Lancet 2011; 377: 813-22

ALSYMPCA – Radium-223

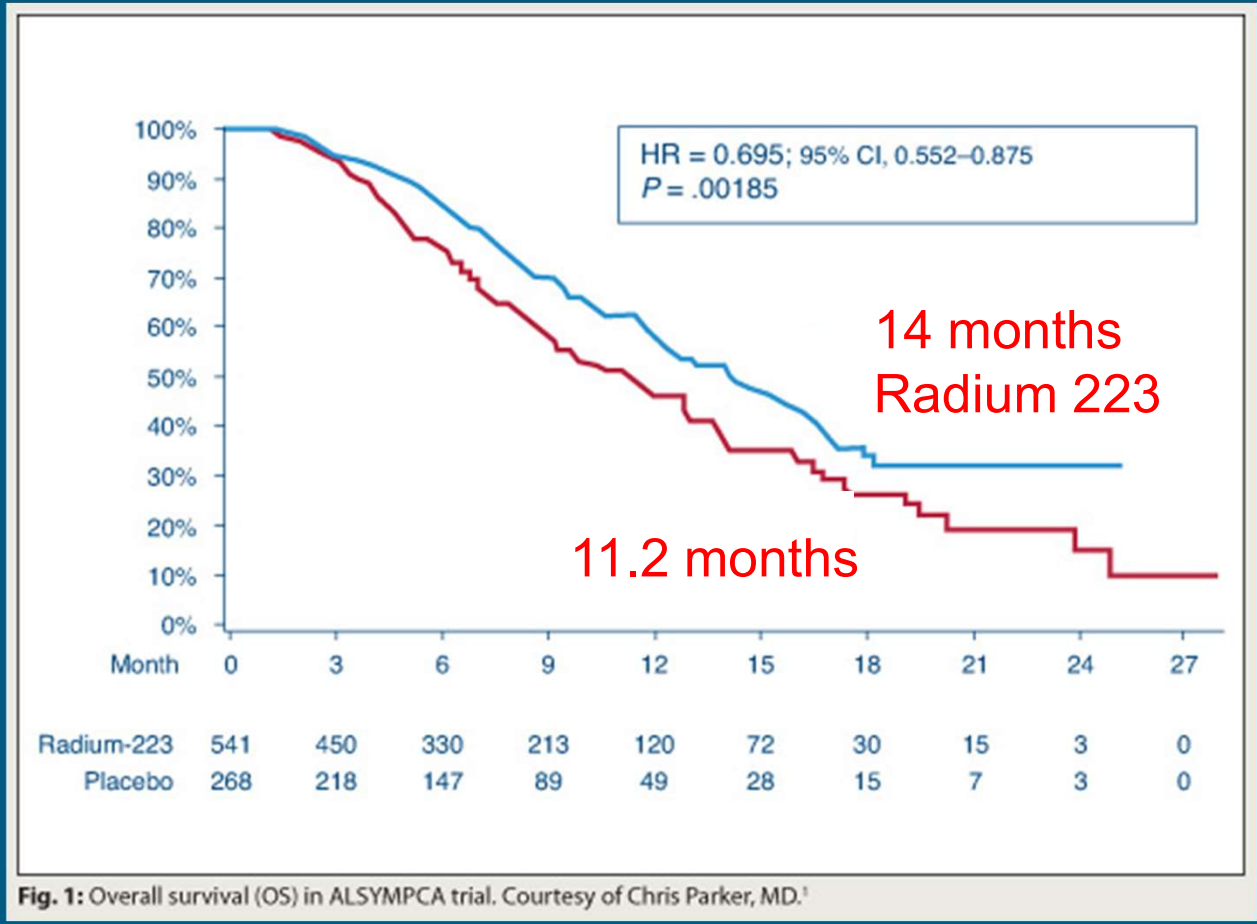


Fig. 1: Overall survival (OS) in ALSYMPCA trial. Courtesy of Chris Parker, MD.[1]

2.8 mo. OS

Side Effects

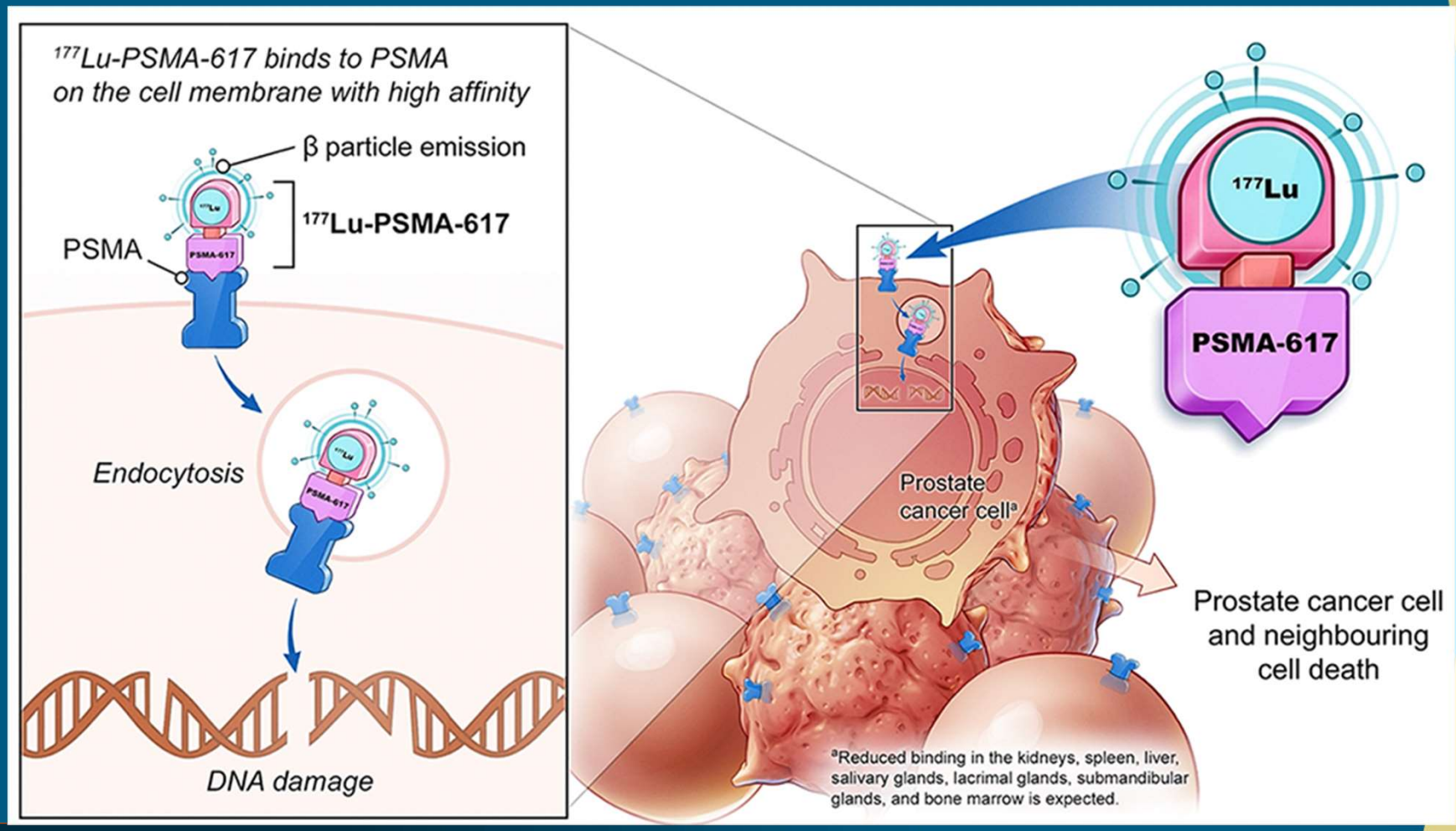
- Fewer AE in Radium 223 group v Placebo
  - 88% v 94%
  - This effect held for serious AE (Grade 3 and 4)
    - 51% v 59%

- Specific to Radium 223
  - G3/4 neutropenia 2% v 1%
  - G3/4 thrombocytopenia 4% v 2%
  - Diarrhea/Vomiting

Primary Issues seen-Radium223

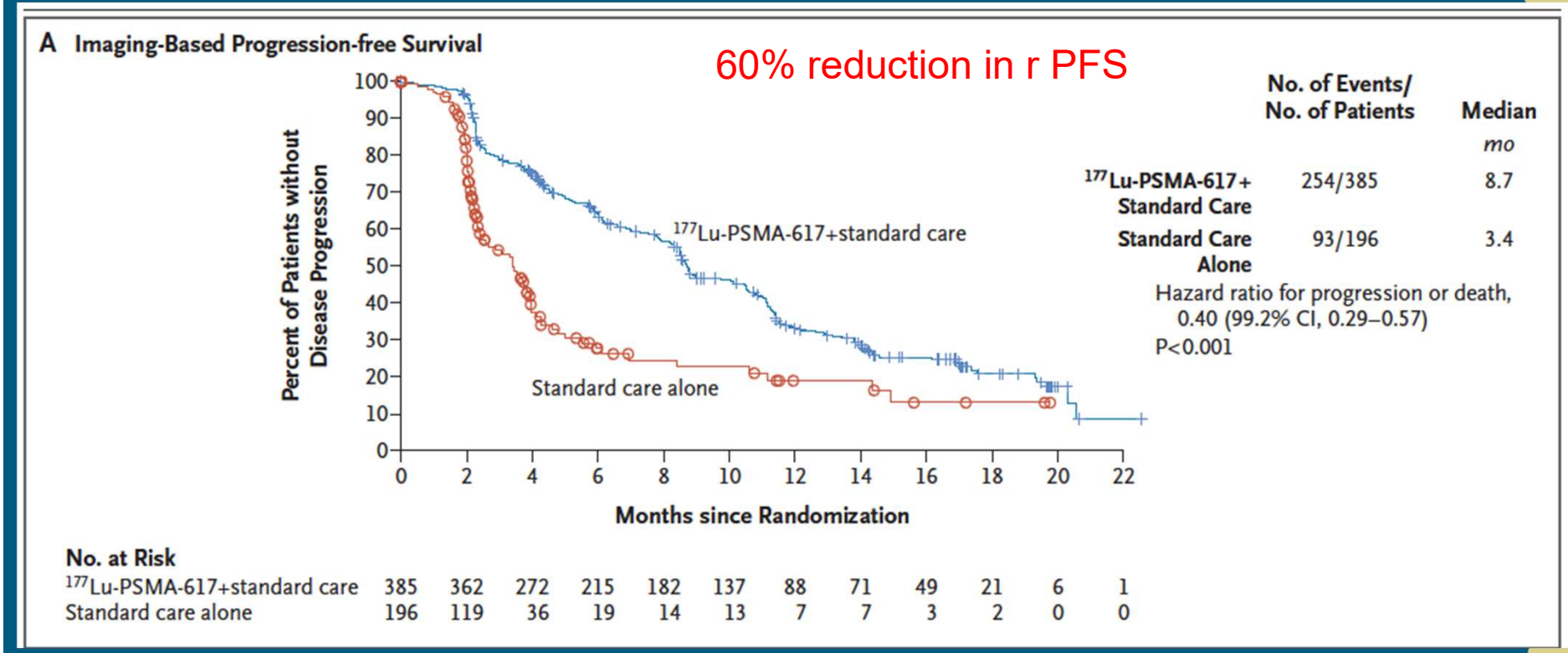
- Vascular access issues
  - Peripheral IV placement with each infusion
- Close monitoring of CBC
  - Thrombocytopenia
  - Anemia

^{177}Lutetium-PSMA-617



GU ASCO 2021; Morris et al

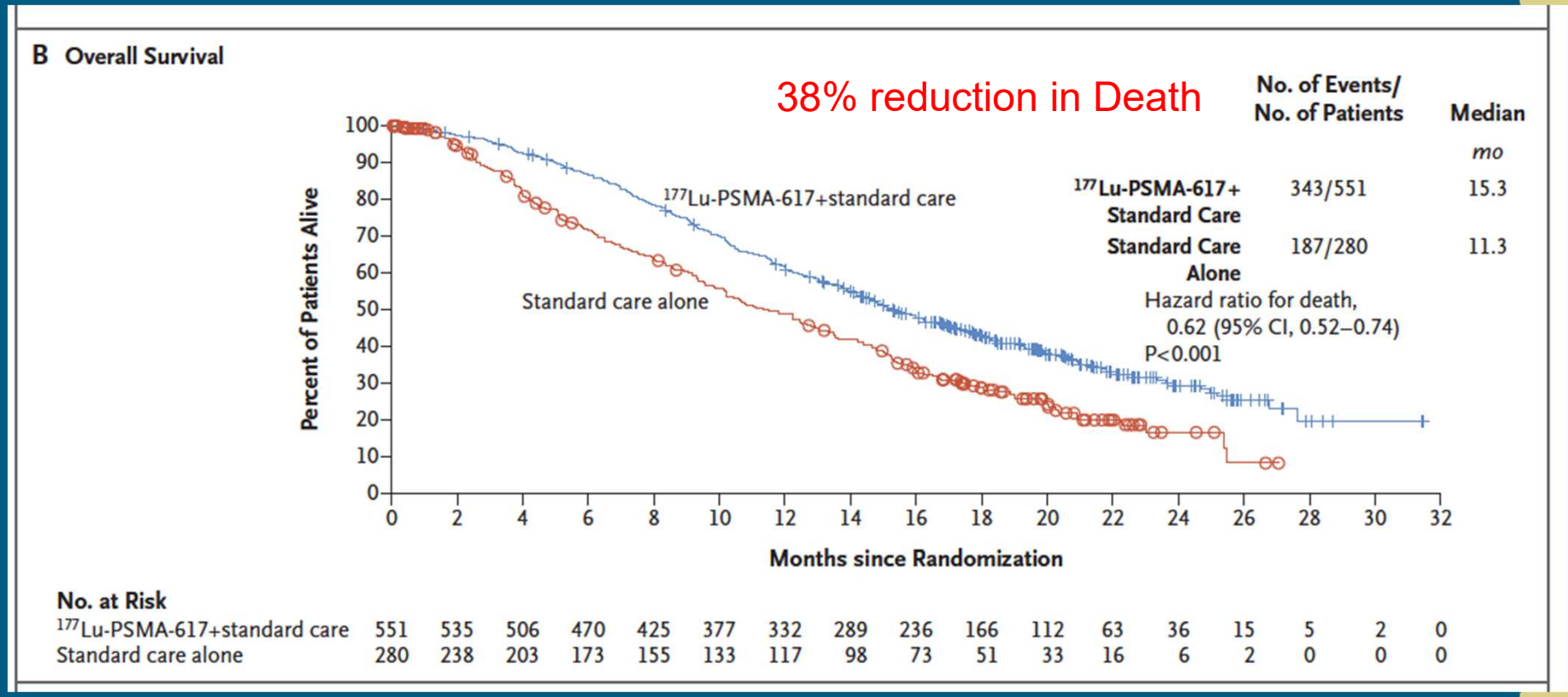
Radiographic PFS



EVMS Eastern Virginia Medical School

Urology of Virginia

Overall Survival



EVMS Eastern Virginia Medical School

Urology of Virginia

Adverse Events

Table 2. Adverse Events.*

Event	^{177}Lu-PSMA-617 plus Standard Care (N=529)		Standard Care Alone (N=205)	
	All Grades	Grade ≥3	All Grades	Grade ≥3
	number of patients (percent)			
Any adverse event	519 (98.1)	279 (52.7)	170 (82.9)	78 (38.0)
Adverse event that occurred in >12% of patients				
Fatigue	228 (43.1)	31 (5.9)	47 (22.9)	3 (1.5)
Dry mouth	205 (38.8)	0	1 (0.5)	0
Nausea	187 (35.3)	7 (1.3)	34 (16.6)	1 (0.5)
Anemia	168 (31.8)	68 (12.9)	27 (13.2)	10 (4.9)
Back pain	124 (23.4)	17 (3.2)	30 (14.6)	7 (3.4)
Arthralgia	118 (22.3)	6 (1.1)	26 (12.7)	1 (0.5)
Decreased appetite	112 (21.2)	10 (1.9)	30 (14.6)	1 (0.5)
Constipation	107 (20.2)	6 (1.1)	23 (11.2)	1 (0.5)
Diarrhea	100 (18.9)	4 (0.8)	6 (2.9)	1 (0.5)
Vomiting	100 (18.9)	5 (0.9)	13 (6.3)	1 (0.5)
Thrombocytopenia	91 (17.2)	42 (7.9)	9 (4.4)	2 (1.0)
Lymphopenia	75 (14.2)	41 (7.8)	8 (3.9)	1 (0.5)
Leukopenia	66 (12.5)	13 (2.5)	4 (2.0)	1 (0.5)
Adverse event that led to reduction in ^{177}Lu-PSMA-617 dose	30 (5.7)	10 (1.9)	NA	NA
Adverse event that led to interruption of ^{177}Lu-PSMA-617†	85 (16.1)	42 (7.9)	NA	NA
Adverse event that led to discontinuation of ^{177}Lu-PSMA-617†	63 (11.9)	37 (7.0)	NA	NA
Adverse event that led to death‡	19 (3.6)	19 (3.6)	6 (2.9)	6 (2.9)

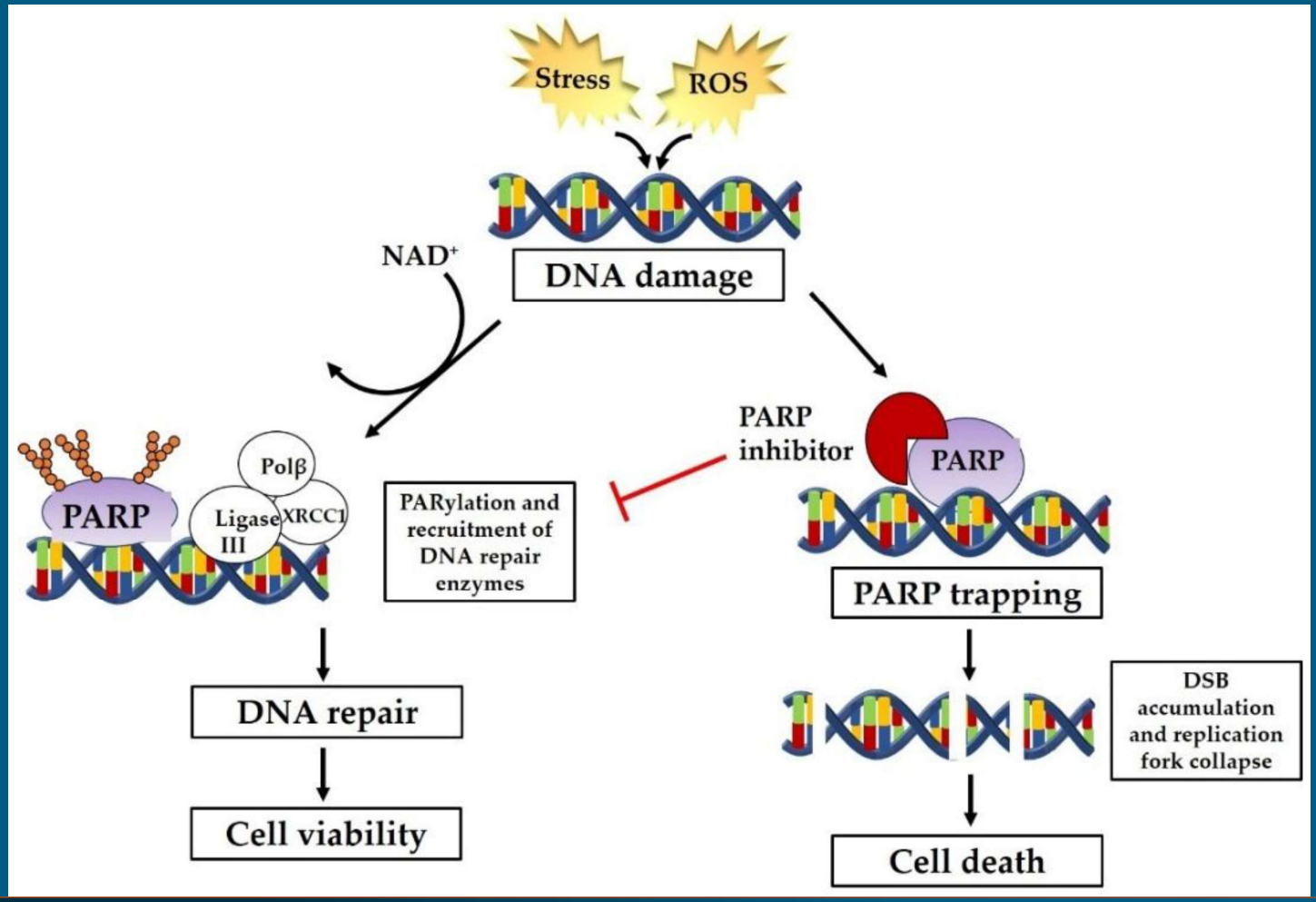
Primary Issues seen- Lu 177

- Grade >=3 AE are seen in 50% of patients
- Anemia
  - Requiring transfusion >10%
- Fatigue
  - Not as significant as with other medications
  - Most are G1-2

Genetic Testing

- PARP inhibitors
  - BRCA1/2, ATM, CHEK
- PD-1 inhibitors
  - MSI- high

Olaparib (Lynparza)



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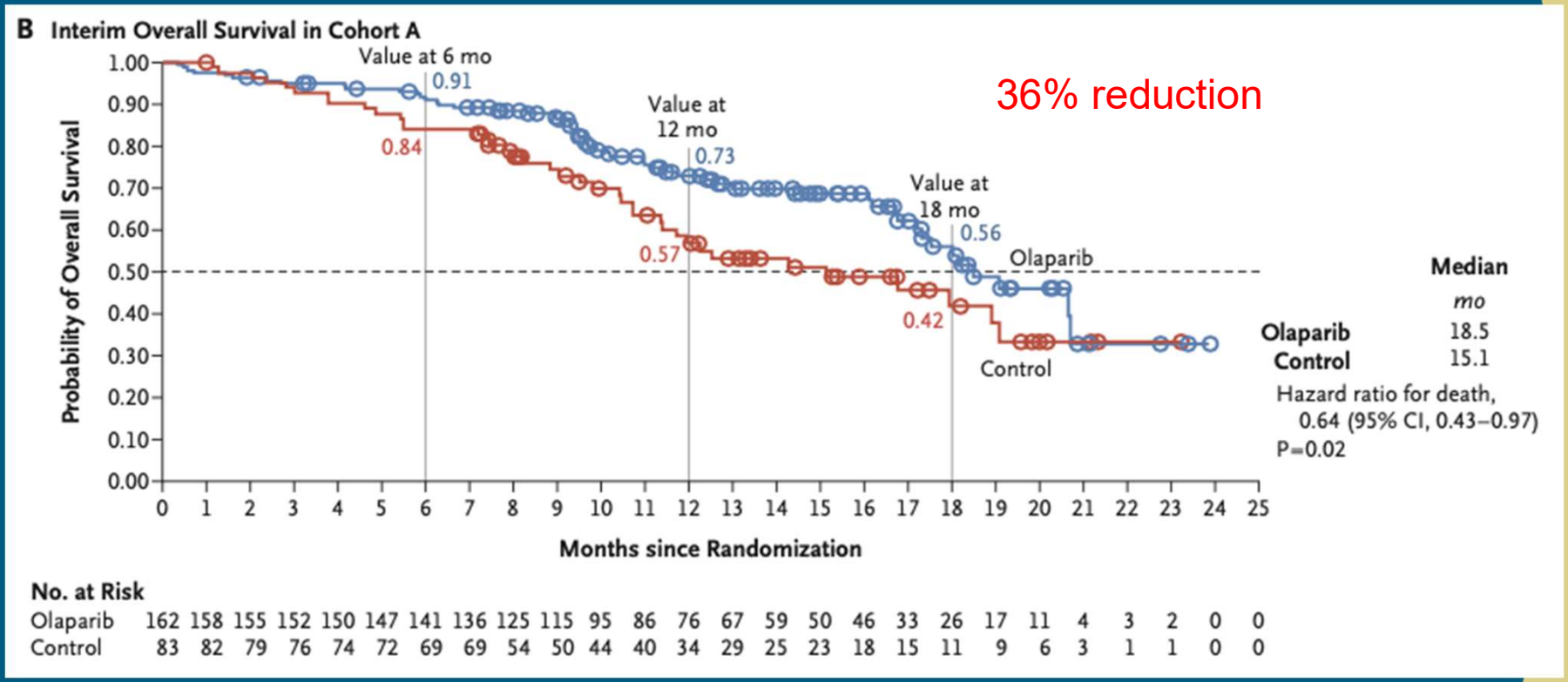
Olaparib – OS


B Interim Overall Survival in Cohort A
Probability of Overall Survival
1.00
0.90
0.80
0.70
0.60
0.50
0.40
0.30
0.20
0.10
0.00
Value at 6 mo
0.91
0.84
Value at 12 mo
0.73
0.57
Value at 18 mo
0.56
0.42
Olaparib
Control
36% reduction
Median
mo
Olaparib 18.5
Control 15.1
Hazard ratio for death, 0.64 (95% CI, 0.43–0.97)
P=0.02
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25
Months since Randomization
No. at Risk
Olaparib 162 158 155 152 150 147 141 136 125 115 95 86 76 67 59 50 46 33 26 17 11 4 3 2 0 0
Control 83 82 79 76 74 72 69 69 54 50 44 40 34 29 25 23 18 15 11 9 6 3 1 1 0 0

Adverse Events

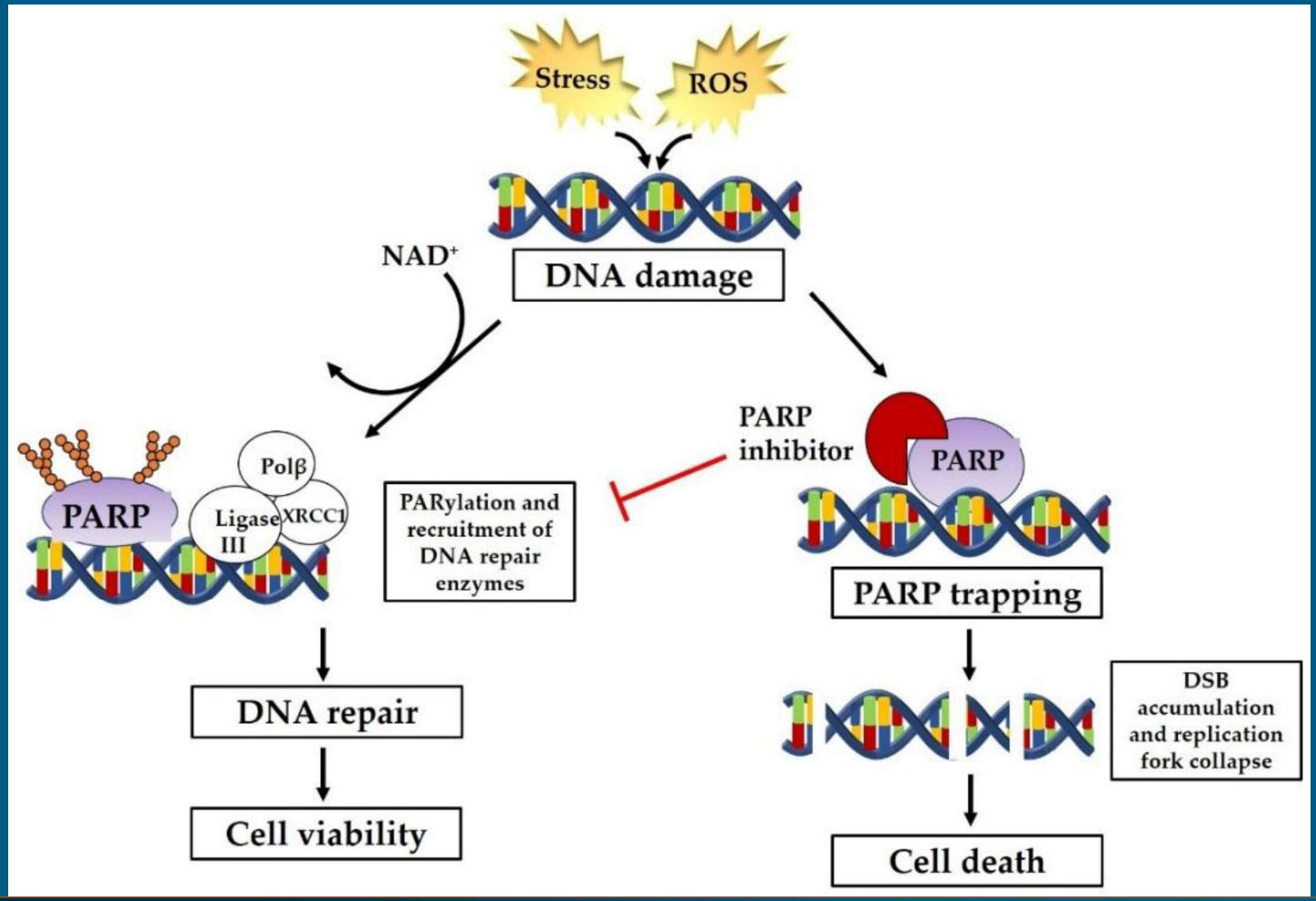
Table 2. Adverse Events in the Overall Population (Cohorts A and B).*

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

MDS/AML developed

pneumonitis

Rucaparib (Rubraca)



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Rucaparib– ORR

A

TABLE 2. Rate of Response to Rucaparib Treatment

Response	Investigator-Evaluable Population (n = 65)	IRR-Evaluable Population (n = 62)
Confirmed ORR, No. (%; 95% CI)[a]	33 (50.8; 38.1 to 63.4)	27 (43.5; 31.0 to 56.7)
Complete response	4 (6.2)	7 (11.3)
Partial response	29 (44.6)	20 (32.3)
Stable disease	25 (38.5)	28 (45.2)
Progressive disease	6 (9.2)	6 (9.7)
Not evaluable	1 (1.5)	1 (1.6)

	Overall Efficacy Population (n = 115)
Confirmed PSA response rate, No. (5; 95% CI)	63 (54.8; 45.2 to 64.1)

Adverse Events

TABLE 3. Most Commonly Reported TEAEs (N = 115)

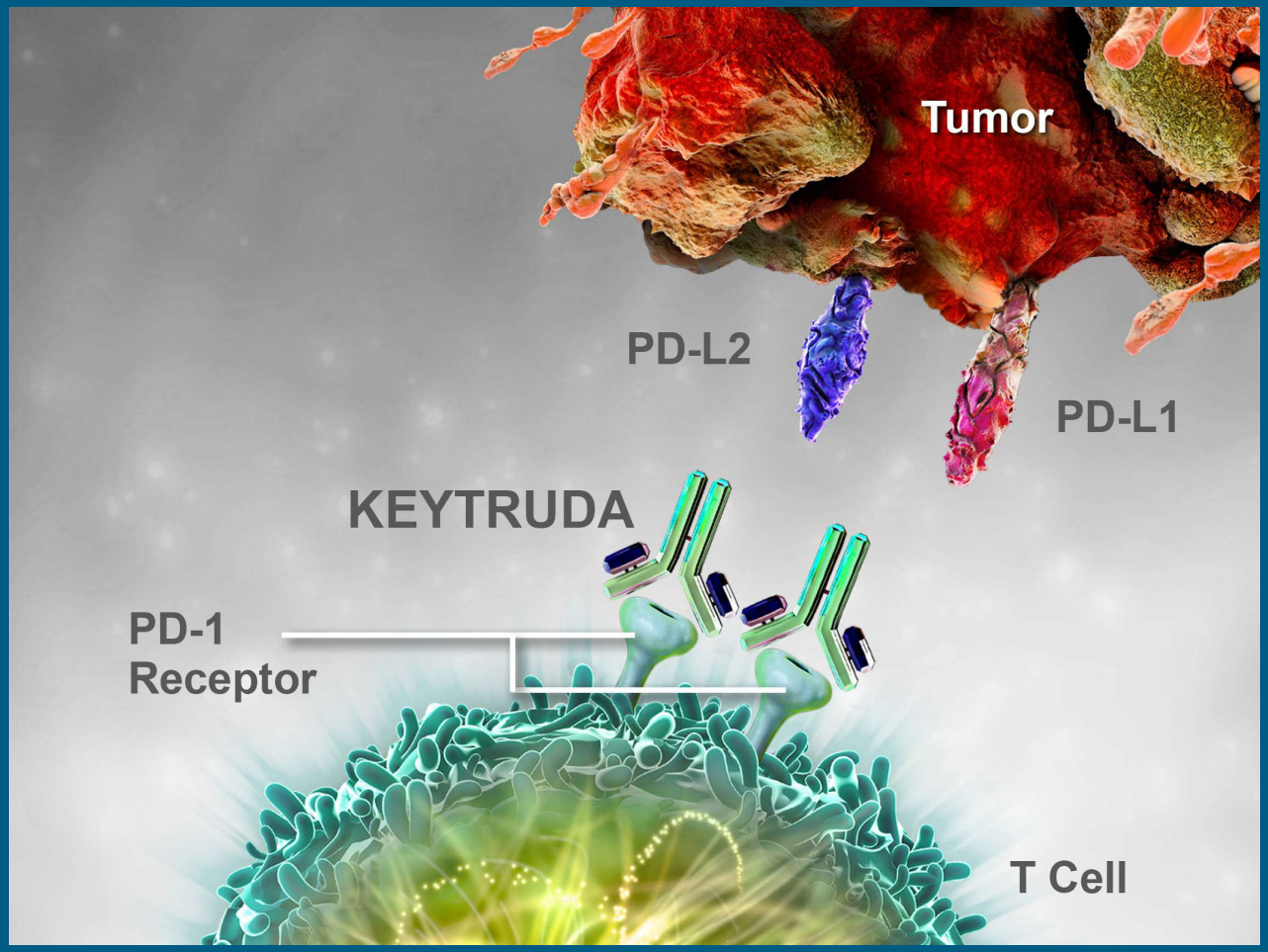
Individual TEAE (preferred terms) Occurring in ≥ 15% of Patients	Any Grade	Grade ≥ 3
Asthenia/fatigue	71 (61.7)	10 (8.7)
Nausea	60 (52.2)	3 (2.6)
Anemia/decreased hemoglobin	50 (43.5)	29 (25.2)
ALT/AST increased	38 (33.0)	6 (5.2)
Decreased appetite	32 (27.8)	2 (1.7)
Constipation	31 (27.0)	1 (0.9)
Thrombocytopenia/decreased platelets	29 (25.2)	11 (9.6)
Vomiting	25 (21.7)	1 (0.9)
Diarrhea	23 (20.0)	0
Dizziness	21 (18.3)	0
Blood creatinine increased	18 (15.7)	1 (0.9)

MDS/AML developed in 20 of 1146 patients (1.7%)

Primary Issues seen-PARPi

- Close monitoring of CBC
  - Thrombocytopenia
  - Anemia
- High index of suspicion for AML/MDS

Pembrolizumab (Keytruda)



PD1 inhibitor

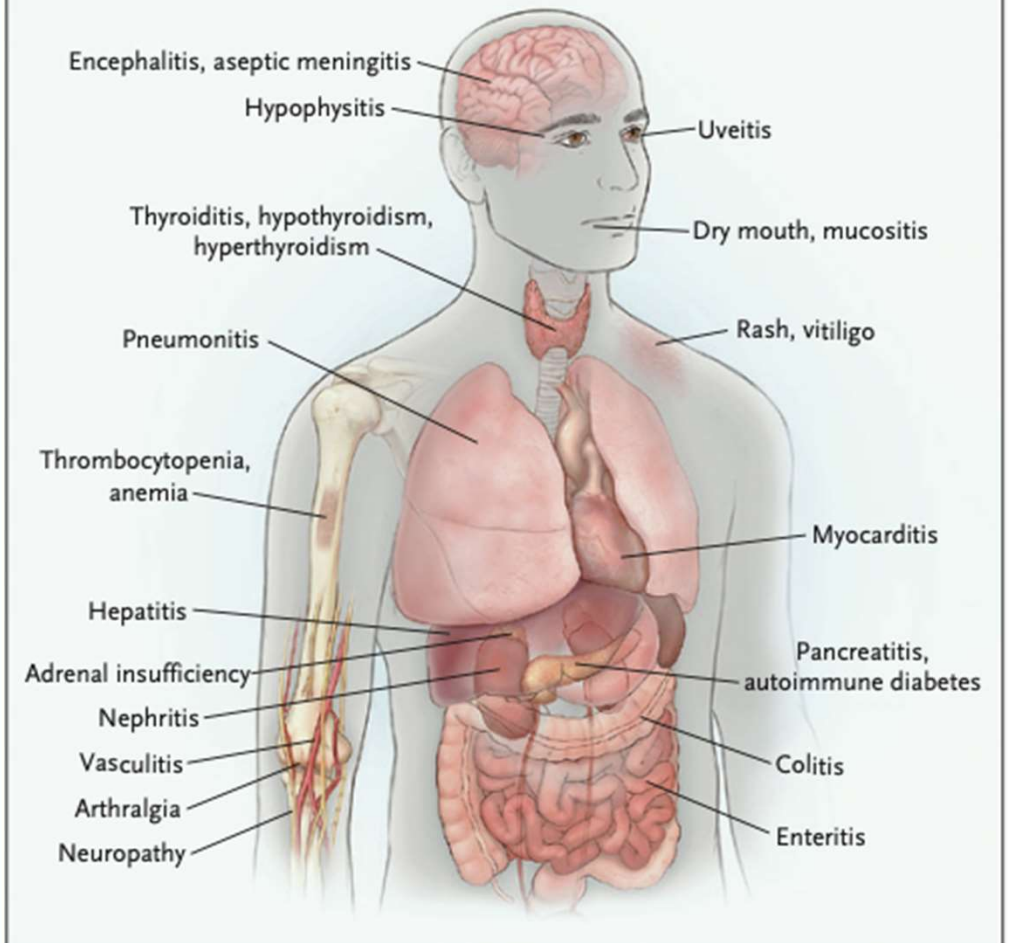


Figure 1. Organs Affected by Immune Checkpoint Blockade.

Immune checkpoint blockade can result in inflammation of any organ. Shown are the most common immune-related adverse events that clinicians encounter in patients treated with immune checkpoint blockade.

Adverse Reaction	KEYTRUDA (N=2,799)			
	All Grades % (n)	Grade 3 %	Grade 4 %	Grade 5 %
Pneumonitis	3.4 (94)	0.9	0.3	0.1
Pneumonitis in NSCLC (N=790)	8.2 (65)	3.2[a]		–
Pneumonitis in HNSCC (monotherapy) (N=300)	6.0 (18)	1.3	–	0.3
Pneumonitis in HNSCC (combination with platinum and FU) (N=276)	5.4 (15)	1.1	–	0.4
Colitis	1.7 (48)	1.1	<0.1	–
Hepatitis	0.7 (19)	0.4	<0.1	–
Adrenal Insufficiency	0.8 (22)	0.3	<0.1	–
Hypophysitis	0.6 (17)	0.3	<0.1	–
Hyperthyroidism	3.4 (96)	0.1	–	–
Hypothyroidism	8.5 (237)	0.1	–	–
Hypothyroidism in HNSCC (monotherapy and combination with platinum and FU) (N=1,185)	16 (188)	0.3	–	–
Nephritis	0.3 (9)	0.1	<0.1	–

Summary

Key Points

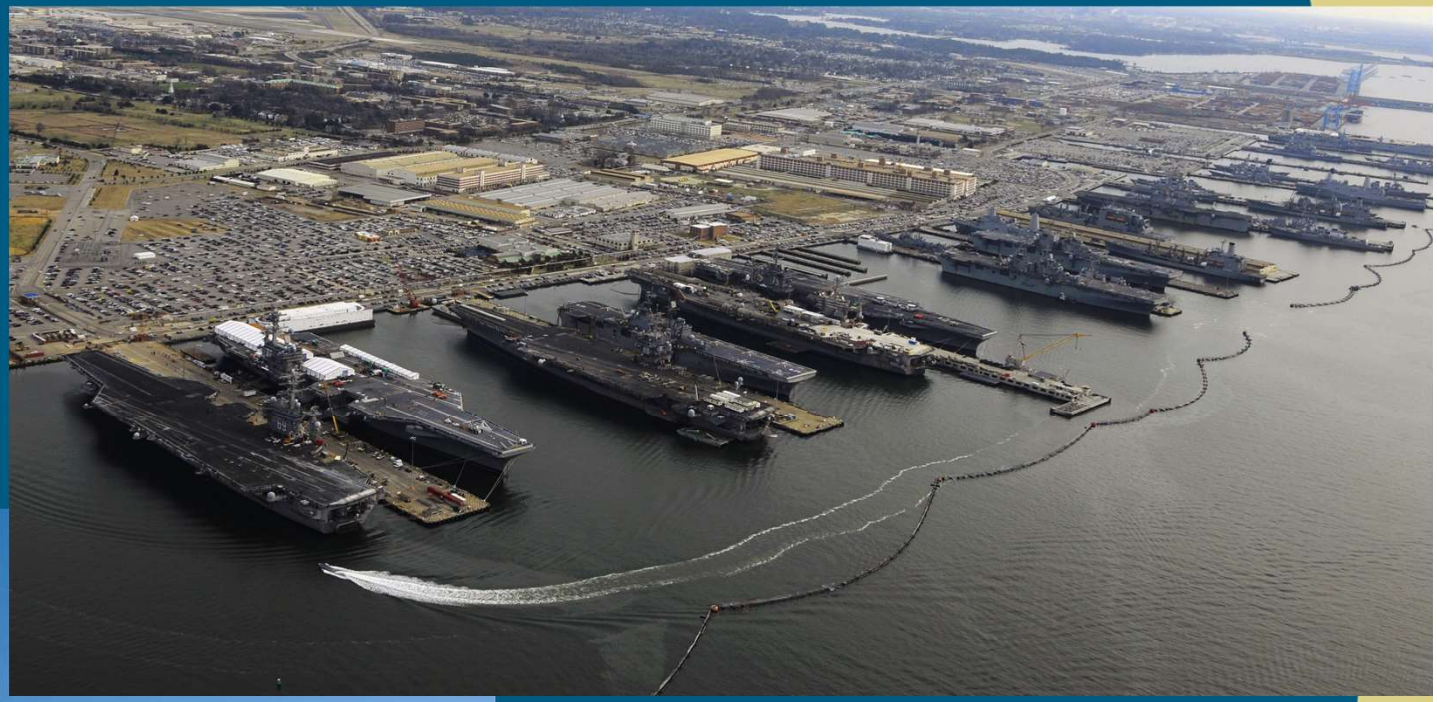
- Many new medications are coming out with various different MOA, but most have few side effects with survival advantages

- Goals of care during this stage are reset to quality of life and maintenance of activity. Though OS may be minimally different, the ability to prolong QOL is quite significant.

"I stopped taking the medicine because I prefer the original disease to the side effects."

Thank you

Teaching. Discovering. Caring.™



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