Updates in Prostate Cancer

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Disclosure of Conflicts of Interest

Oliver Sartor, MD has the following financial relationships to disclose:

Consultant - Advanced Accelerator Applications (AAA), Astellas, AstraZeneca, Bayer, Blue Earth Diagnostics, Inc., Bavarian Nordic, Bristol Myers Squibb, Clarity Pharmaceuticals, Clovis, Constellation, Dendreon, EMD Serono, Fusion, Isotopen Technologien Meunchen, Janssen, Myovant, Myriad, Noria Therapeutics, Inc., Novartis, Noxopharm, Progenics, POINT Biopharma, Pfizer, Sanofi, Tenebio, Telix, Theragnostics

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Evolving Landscape of Treatment for Advanced Prostate Cancer Update 2022

Overview

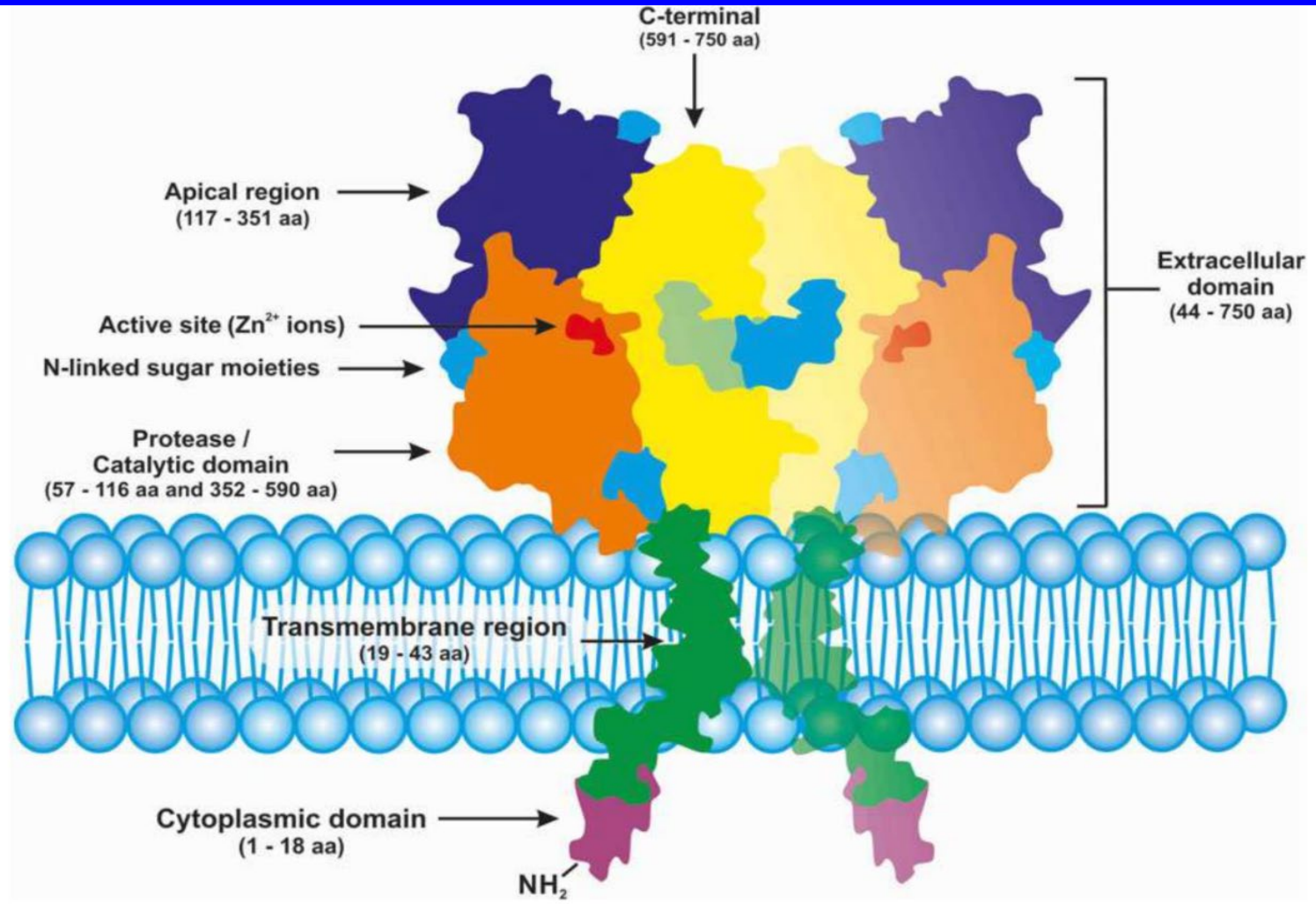
- PSMA PET scan….disrupting staging in a huge way
- Hormone sensitive prostate cancer update
- Castrate-Resistant prostate cancer uptake

PET imaging improves detection of prostate cancer

- Bone and soft tissue
  - PSMA PET (Ga^{68} or F^{18})
    - Two new FDA approvals in 2021
  - Choline PET (C^{11} or F^{18})
    - FDA approved thanks to Mayo
  - Fluciclovine (F^{18})
    - FDA approved but less sensitive than PSMA
  - FDG PET (F^{18})
    - FDA approved but not in prostate cancer
- Bone only------stromal reaction only
  - NaF (F^{18}) PET

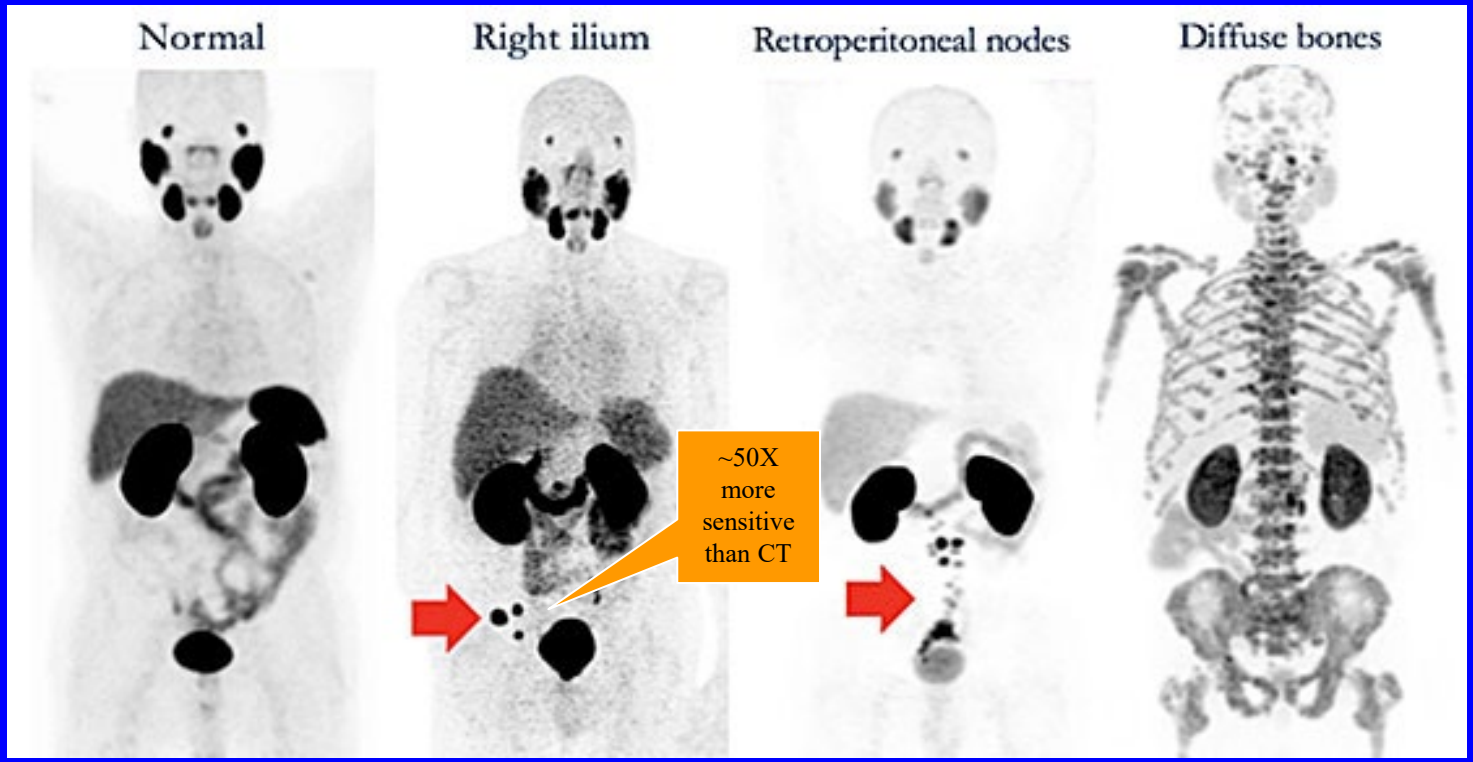
PSMA: Transmembrane Protein

O'Driscott C et al, Br J Pharm 2016



PSMA PET (molecular imaging): A disruptive force across the spectrum of prostate cancer

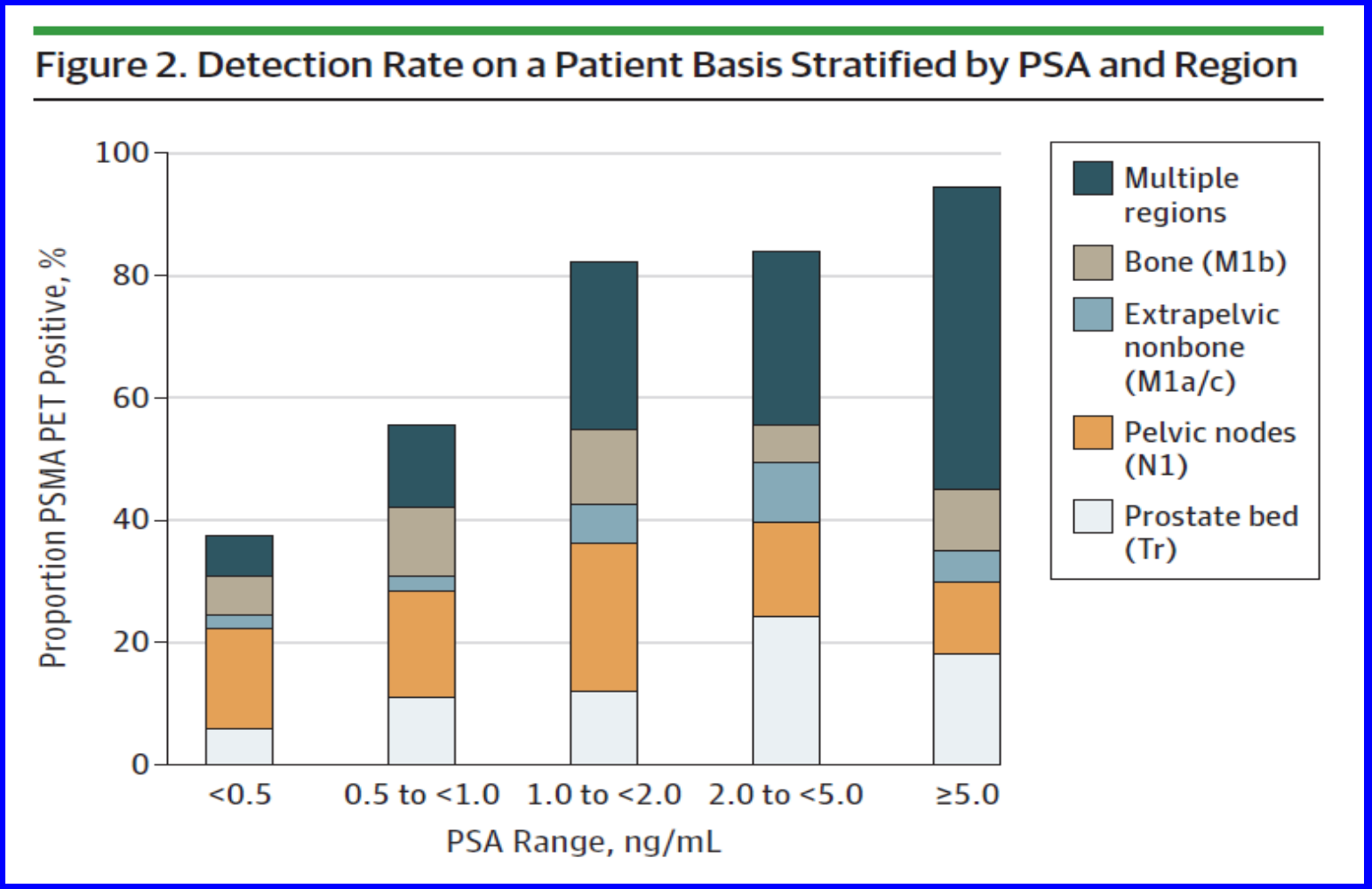
FDA approvals in "high risk" and recurrent settings



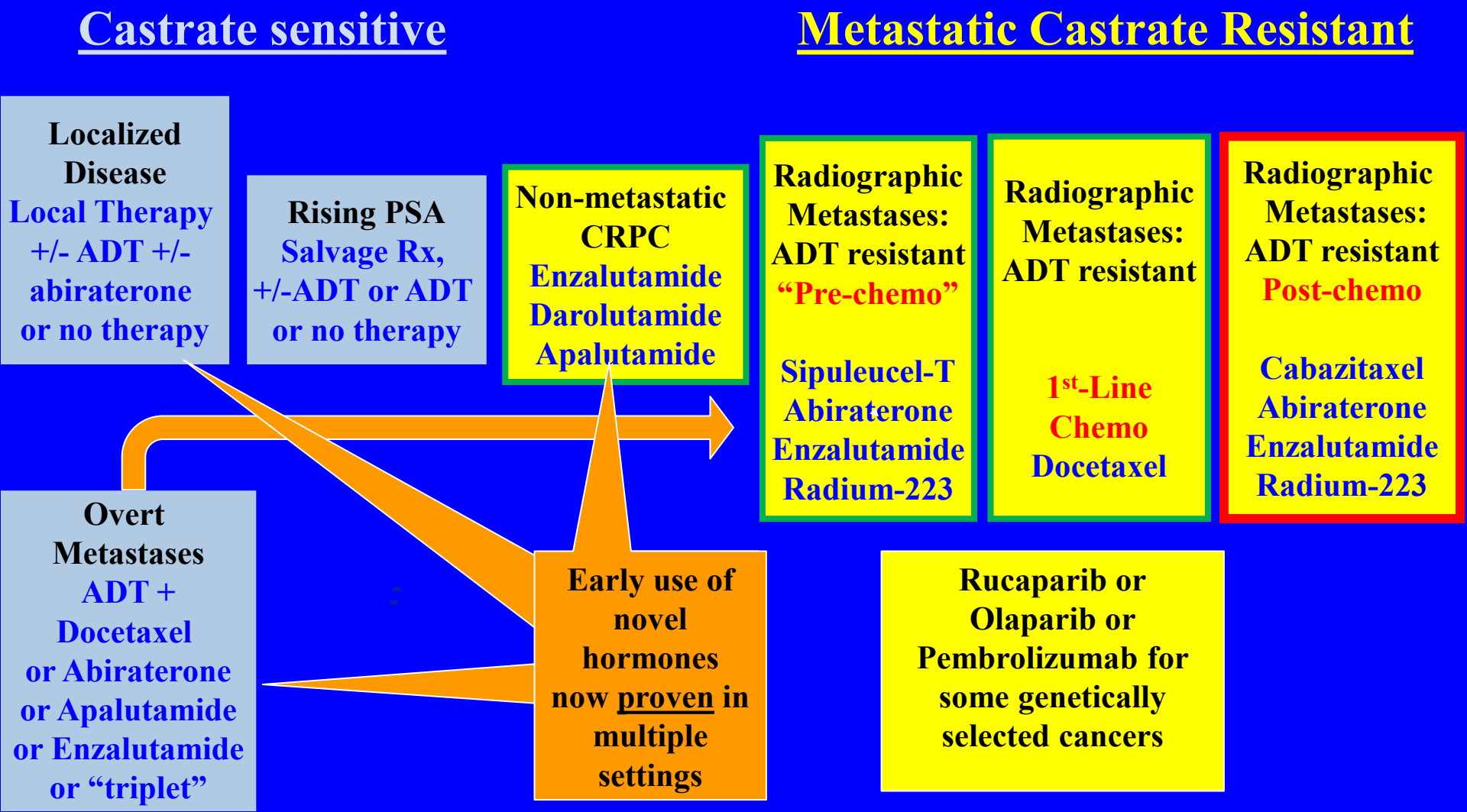
Molecular imaging is redefining staging for all manner of patients (both at diagnosis and in the recurrent setting)

PSMA PET positivity (and location) as function of baseline PSA

Fendler et al. *JAMA Oncol.* 5:856-863



Standard Therapies Today: New hormonal agents are moving earlier and earlier



Hormone-Sensitive Prostate Cancer Landscape: Improvements in overall survival (1941-2021)

- Metastatic
  - ADT + docetaxel
    - CHAARTED (2015) and STAMPEDE (2015)
  - ADT + abiraterone
    - LATITUDE (2019) and STAMPEDE (2020)
  - ADT + enzalutamide
    - ENZAMET (2019) and ARCHES (2021)

Recent Updates for HSPC: New data on systemic treatments

- PEACE-1 (M1)
- ARASENS (M1)
- STAMPEDE (M0)

A phase 3 trial with a 2x2 factorial design in men with *de novo* metastatic castration-sensitive prostate cancer (mCSPC): Overall survival with abiraterone acetate plus prednisone in PEACE-1

Fizazi et al, ESMO 2021 LBA5

Key Eligibility Criteria

De novo mCSPC

Distant metastatic disease by ≥ 1 lesion on bone scan and/or CT scan

ECOG PS 0 -2

On-Study Requirement

Continuous ADT

Permitted

ADT ≤ 3 months

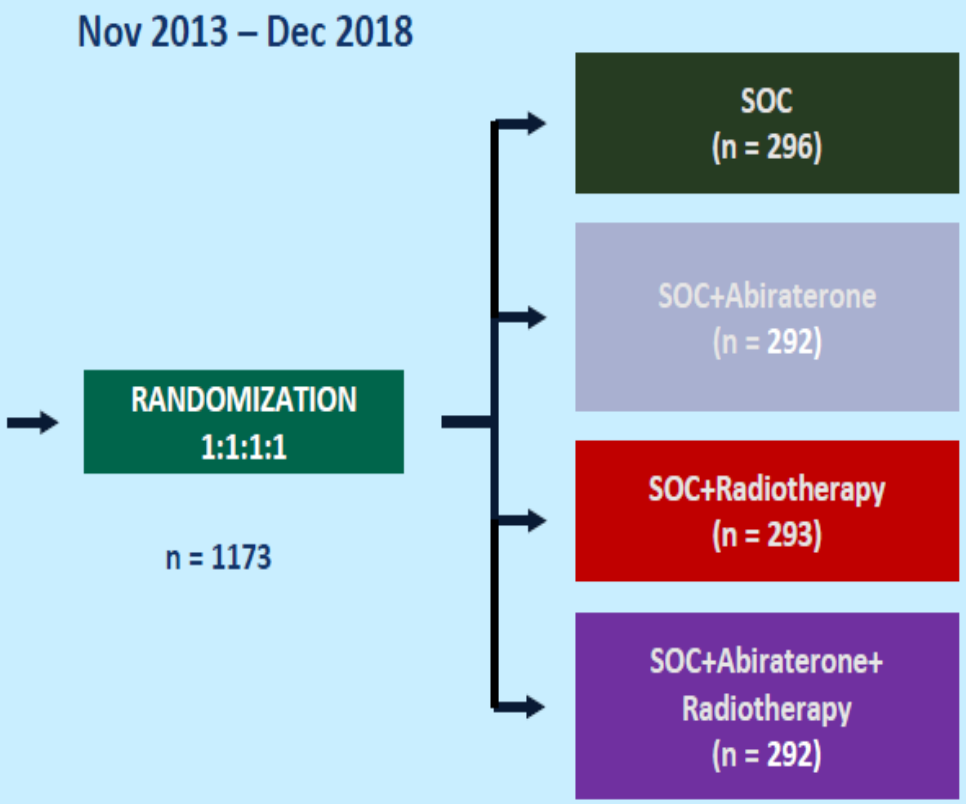
Stratification

ECOG PS (0 vs 1-2)

Metastatic sites (LN vs bone vs visceral)

Type of castration (orchidectomy vs LHRH agonist vs LHRH antagonist)

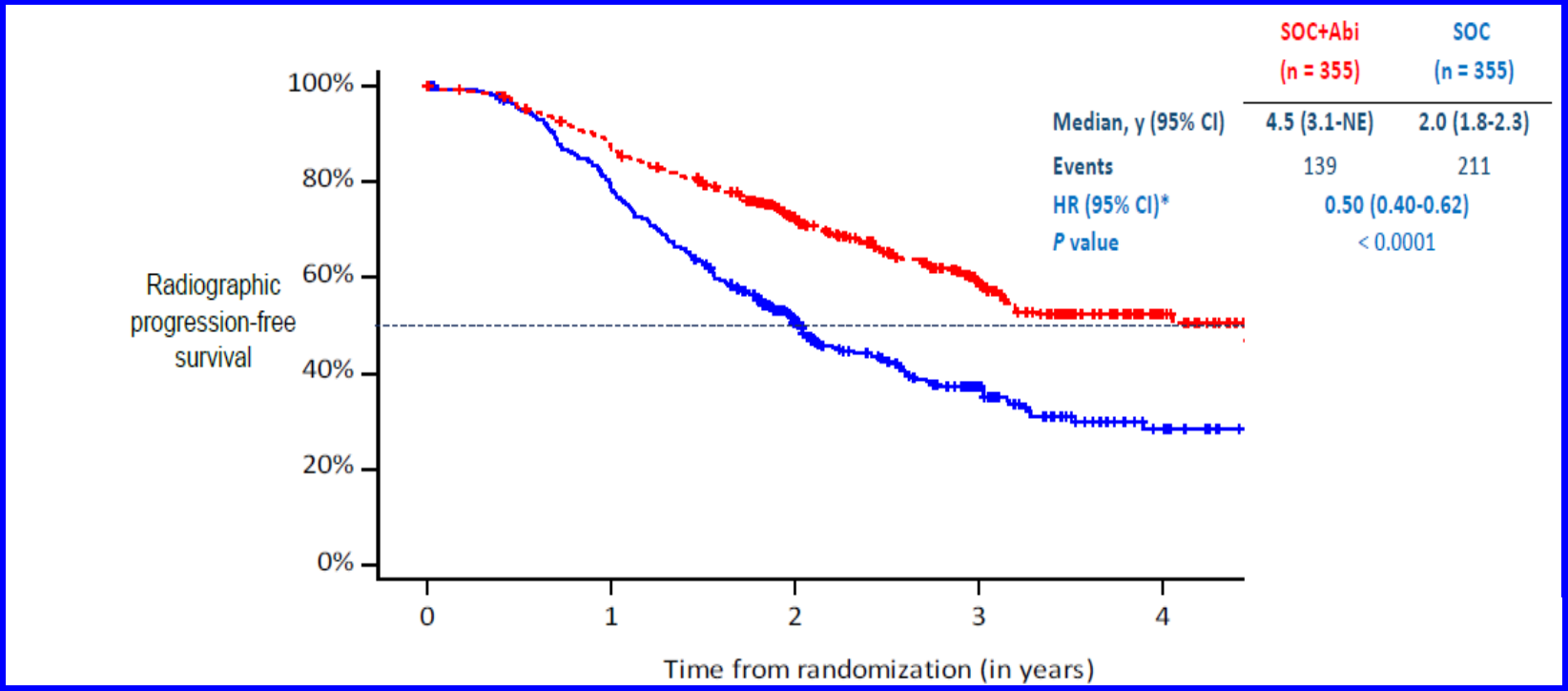
Docetaxel (yes vs no)



ECOG PS, Eastern Cooperative Oncology Group performance status

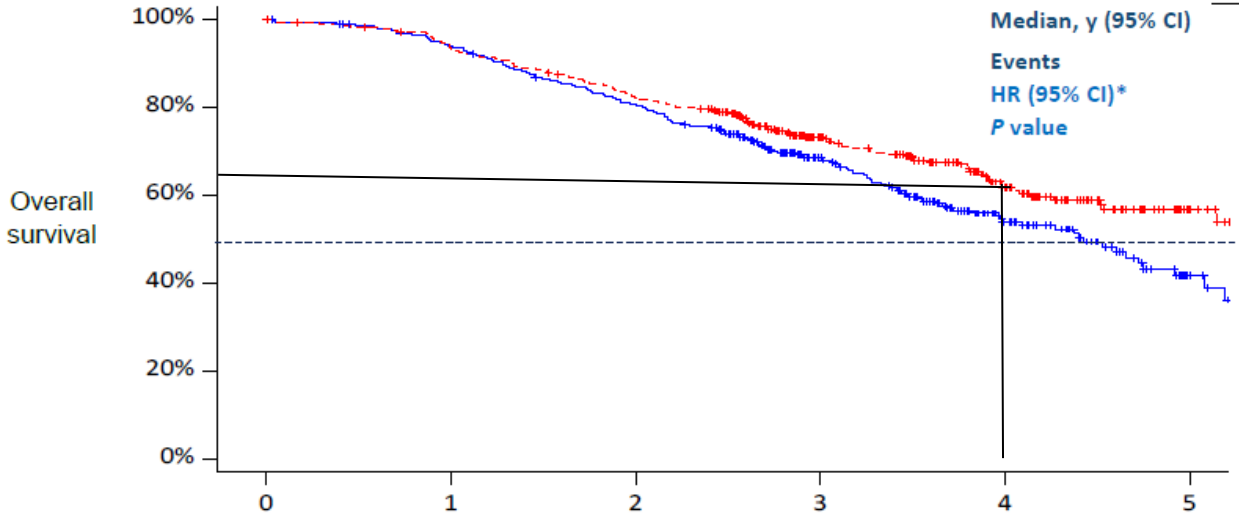
rPFS in PEACE-1

Fizazi et al, ESMO 2021 LBA5



Overall Survival in PEACE-1

Fizazi et al, ESMO 2021 LBA5



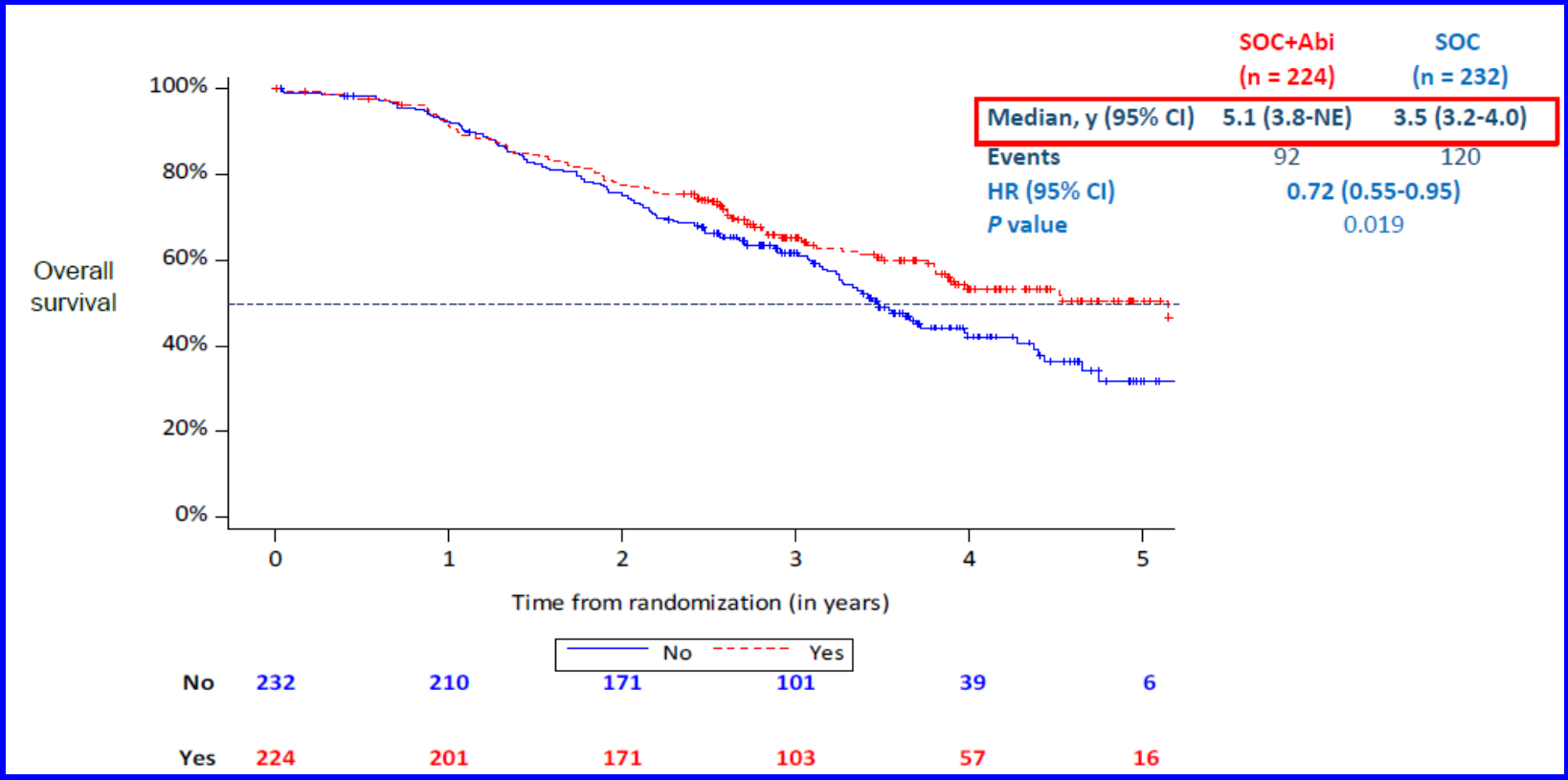
	SOC+Abi (n = 355)	SOC (n = 355)
Median, y (95% CI)	NE (4.5-NE)	4.4 (3.8-4.9)
Events	121	151
HR (95% CI)*	0.75 (0.59-0.95)	
P value	0.017	

No	355	329	281	172	78	18
Yes	355	328	287	183	98	25

*Adjusted on stratification parameters (RXT, type of castration, PS, metastatic burden)

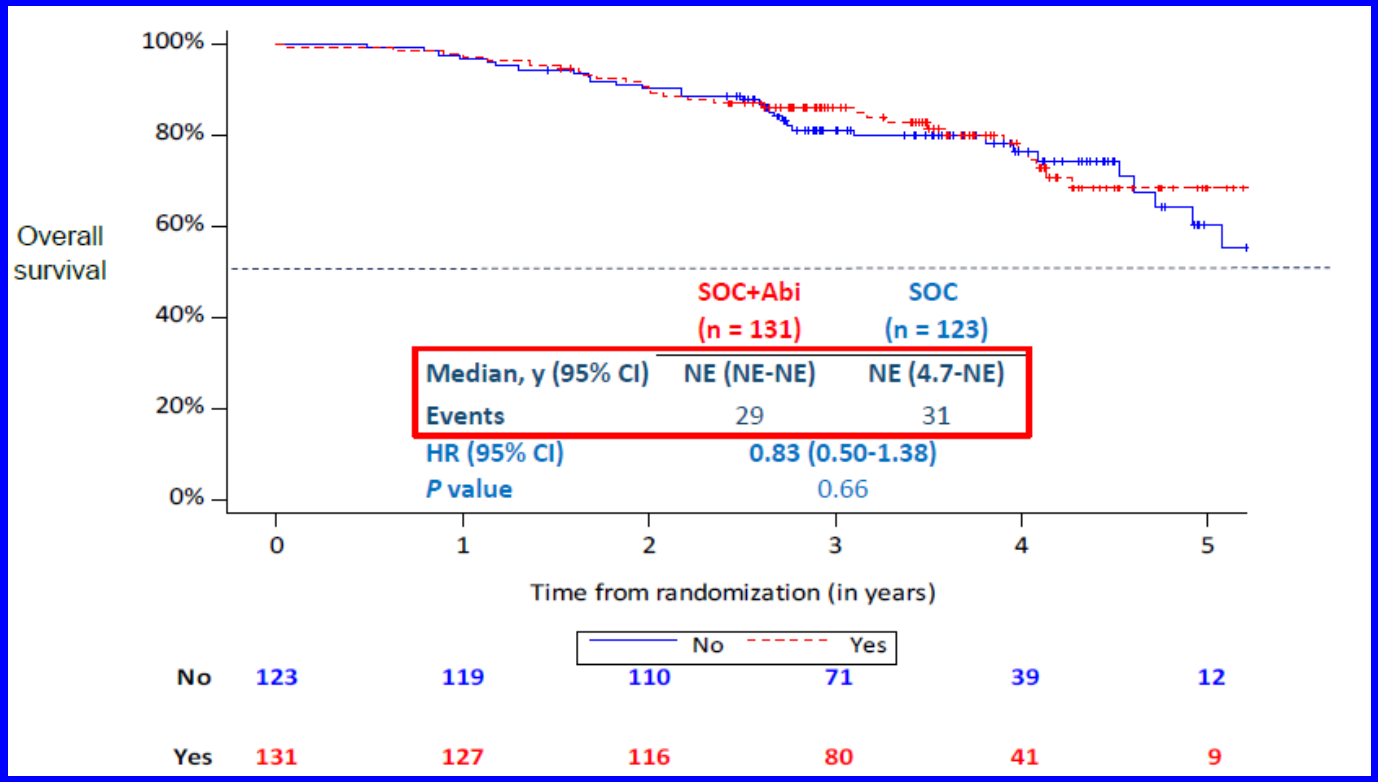
PEACE-1 survival in "high-volume" subset

Fizazi et al. ESMO 2021 LBA5



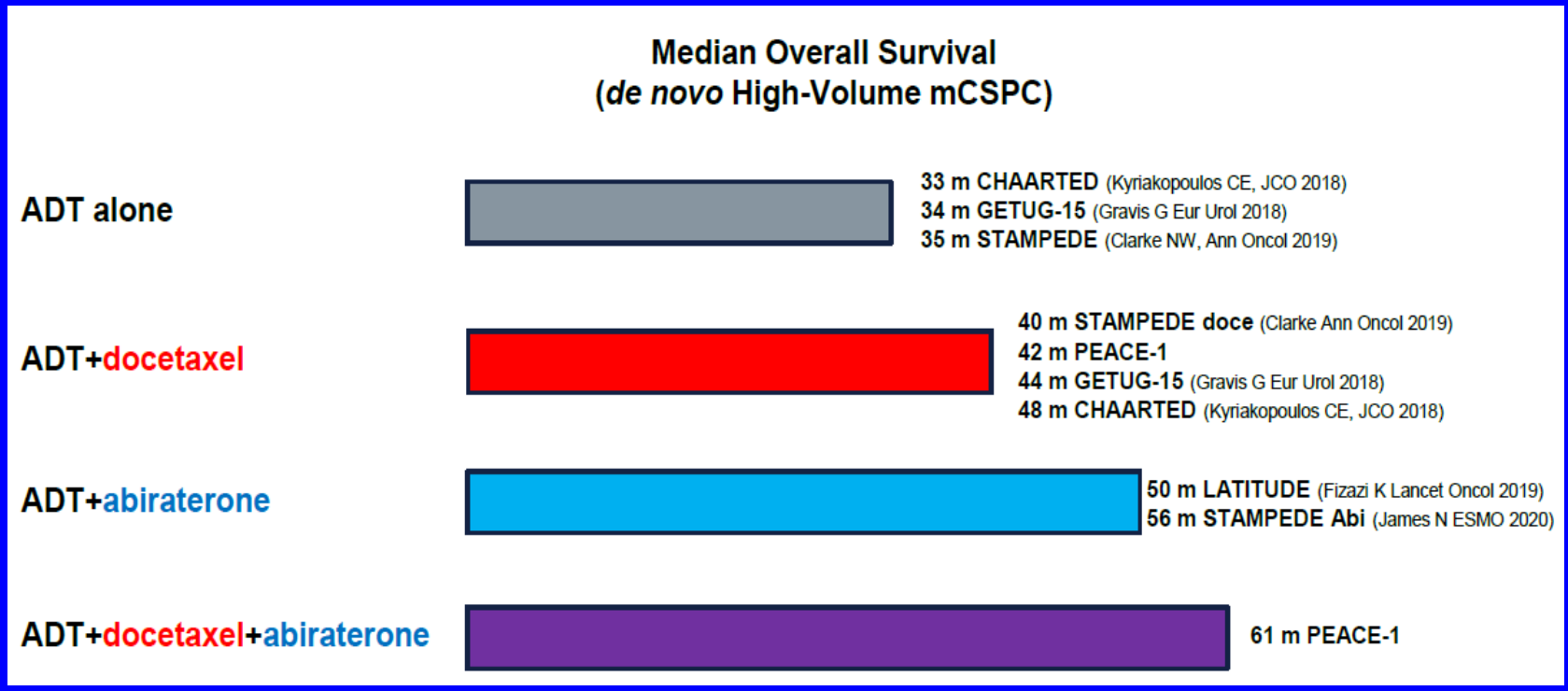
PEACE-1 survival in "low-volume" subset

Fizazi et al. ESMO 2021 LBA5

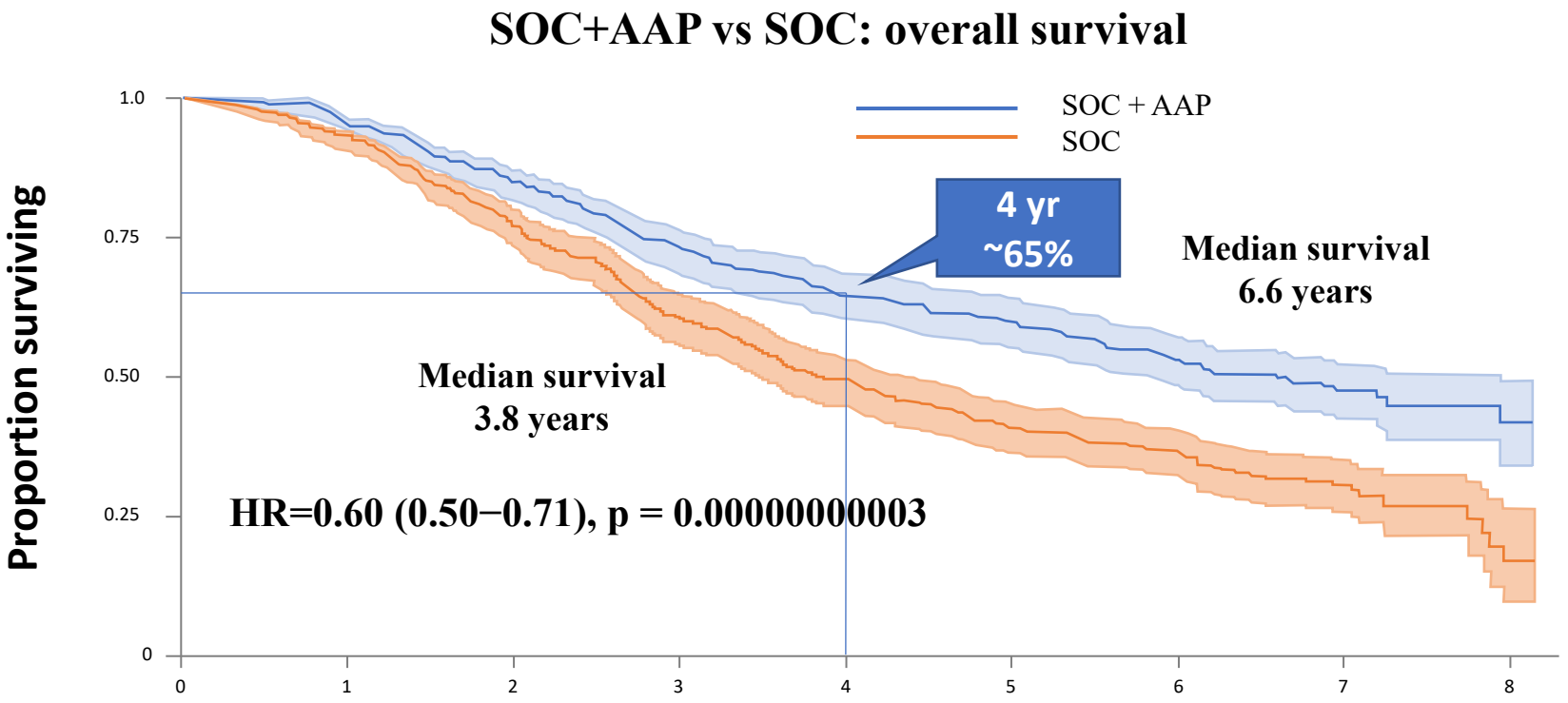


Comparisons of high-volume subset in various mHSPC trials

Fizazi et al., ESMO 2021 LBA5



STAMPEDE randomized trial: Abiraterone acetate plus prednisolone for hormone-naïve prostate cancer: long-term results from metastatic (M1) patients



Nicholas James; oral presentation number 611O, ESMO 2020

Do we accept PEACE-1 and use a triplet in high volume disease?

- Impressive results on PFS
- OS clearly trended positive in high volume
- No trials using ADT + abiraterone +/- docetaxel
- What about ARASENS new report as “positive”
- Use triplets in the young fit patient?

- NOTE: PSMAddition trial bringing ADT + novel hormone +/- PSMA-617 Lu-177 forward

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

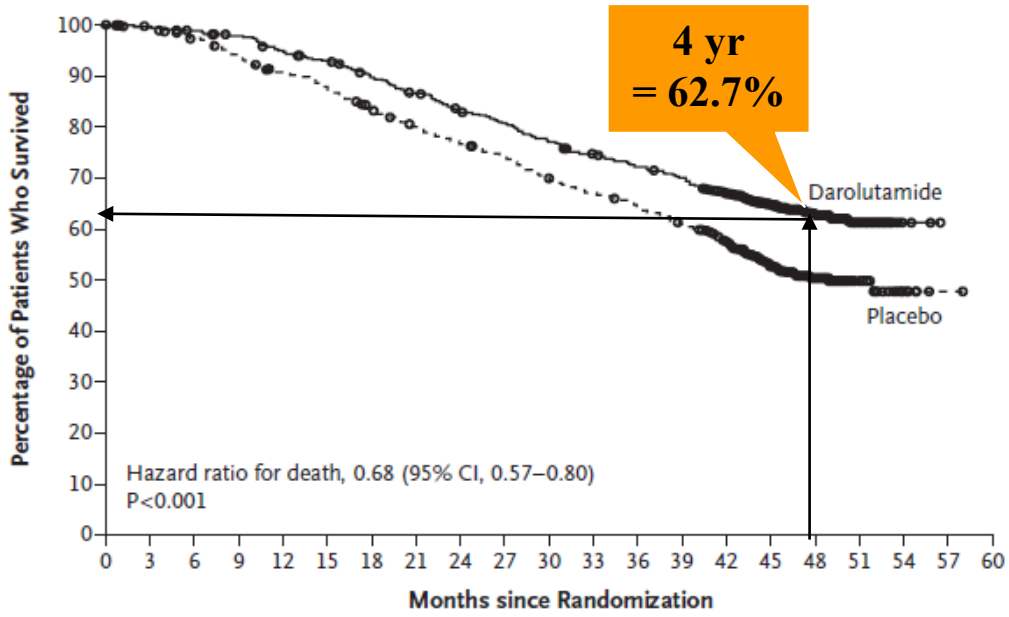
Darolutamide and Survival in Metastatic, Hormone-Sensitive Prostate Cancer

Matthew R. Smith, M.D., Ph.D., Maha Hussain, M.D., Fred Saad, M.D., Karim Fizazi, M.D., Ph.D., Cora N. Sternberg, M.D., E. David Crawford, M.D., Evgeny Kopyltsov, M.D., Chandler H. Park, M.D., Boris Alekseev, M.D., Álvaro Montesa-Pino, M.D., Dingwei Ye, M.D., Francis Parnis, M.B., B.S., Felipe Cruz, M.D., Teuvo L.J. Tammela, M.D., Ph.D., Hiroyoshi Suzuki, M.D., Ph.D., Tapio Utriainen, M.D., Cheng Fu, M.D., Motohide Uemura, M.D., Ph.D., María J. Méndez-Vidal, M.D., Benjamin L. Maughan, M.D., Pharm.D., Heikki Joensuu, M.D., Silke Thiele, M.D., Rui Li, M.S., Iris Kuss, M.D., and Bertrand Tombal, M.D., Ph.D., for the ARASENS Trial Investigators*

NEJM Feb 17, 2022

ARASENS OS (primary endpoint)

NEJM Feb 17, 2022



	Median Survival (95% CI) *mo*
Darolutamide	NE
Placebo	48.9 (44.4–NE)

No. at Risk

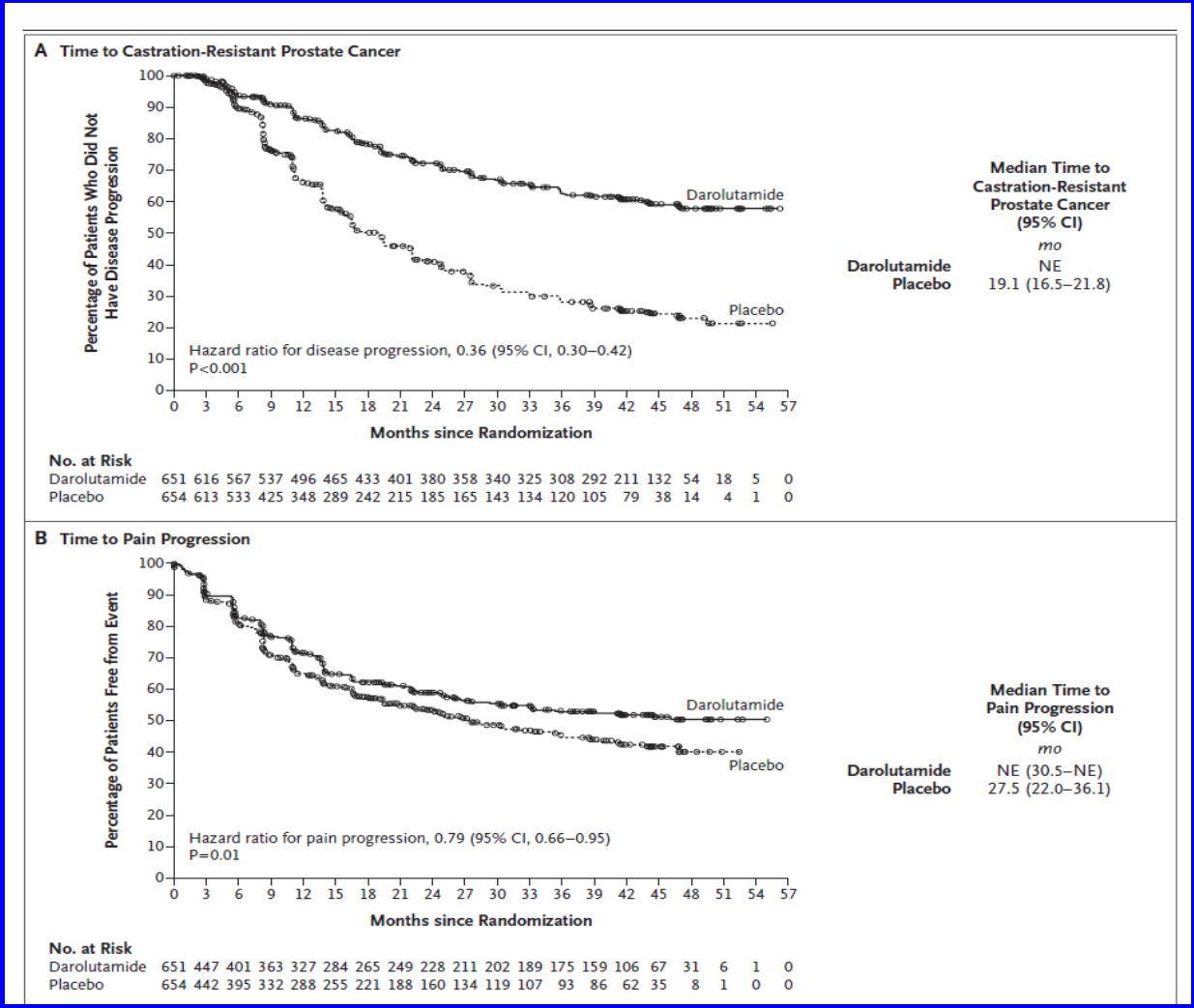
Darolutamide	651	645	637	627	608	593	570	548	525	509	486	468	452	436	402	267	139	56	9	0	0
Placebo	654	646	630	607	580	565	535	510	488	470	441	424	402	383	340	218	107	37	6	1	0

Figure 1. Overall Survival (Full Analysis Set).

Kaplan–Meier estimates of overall survival are shown. For the analysis of overall survival, data were censored as of the last known date the patients were alive. One patient who was randomly assigned to the placebo group but received darolutamide was included in the placebo group in the full analysis set. CI denotes confidence interval, and NE not estimable.

ARASENS: time to CRPC and time to pain progression

NEJM Feb 17, 2022



ARASENS: TEAE time adjusted events

Table S5. Treatment-Emergent Adverse Events of Any Grade that Occurred in ≥10% of Patients in Either Group, with Exposure-Adjusted Incidence Rates (Safety Analysis Set)

Adverse Event*	Darolutamide + ADT + Docetaxel (N = 652†)		Placebo + ADT + Docetaxel (N = 650†)	
	No. of patients (%)	*EAIR/ 100 PY‡*	*No. of patients (%)*	*EAIR/ 100 PY‡*
Alopecia	264 (40.5)	15.3	264 (40.6)	22.0
Neutropenia§	256 (39.3)	NA¶	252 (38.8)	NA¶
Fatigue	216 (33.1)	12.5	214 (32.9)	17.8
Anemia	181 (27.8)	10.5	163 (25.1)	13.6
Arthralgia	178 (27.3)	10.3	174 (26.8)	14.5
Peripheral edema	173 (26.5)	10.0	169 (26.0)	14.1
Diarrhea	167 (25.6)	9.6	156 (24.0)	13.0
Constipation	147 (22.5)	8.5	130 (20.0)	10.8
Hot flush	124 (19.0)	7.2	122 (18.8)	10.2
Back pain	123 (18.9)	7.1	123 (18.9)	10.2
Decreased appetite	121 (18.6)	7.0	85 (13.1)	7.1
Increased weight	116 (17.8)	6.7	102 (15.7)	8.5
Nausea	115 (17.6)	6.6	133 (20.5)	11.1
Increased alanine aminotransferase	102 (15.6)	5.9	84 (12.9)	7.0
Pain in extremity	98 (15.0)	5.7	78 (12.0)	6.5
Increased aspartate aminotransferase	91 (14.0)	5.3	68 (10.5)	5.7

ARASENS summary

- In mHSPC, OS clearly better for ADT + docetaxel + darolutamide compared to ADT + docetaxel
- Very well tolerated as a whole
- Very similar to PEACE-1 data with abiraterone
- What does docetaxel add?

Abiraterone acetate and prednisolone with or without enzalutamide for high-risk non-metastatic prostate cancer: a meta-analysis of primary results from two randomised controlled phase 3 trials of the STAMPEDE platform protocol

Gerhardt Attard, Laura Murphy, Noel W Clarke, William Cross, Robert J Jones, Christopher C Parker, Silke Gillessen, Adrian Cook, Chris Brawley, Claire L Amos, Nafisah Atako, Cheryl Pugh, Michelle Buckner, Simon Chowdhury, Zafar Malik, J Martin Russell, Clare Gilson, Hannah Rush, Jo Bowen, Anna Lydon, Ian Pedley, Joe M O'Sullivan, Alison Birtle, Joanna Gale, Narayanan Srihari, Carys Thomas, Jacob Tanguay, John Wagstaff, Prantik Das, Emma Gray, Mymoona Alzoueb, Omi Parikh, Angus Robinson, Isabel Syndikus, James Wylie, Anjali Zarkar, George Thalmann, Johann S de Bono, David P Dearnaley, Malcolm D Mason*, Duncan Gilbert, Ruth E Langley, Robin Millman, David Matheson, Matthew R Sydes†, Louise C Brown†, Mahesh K B Parmar†, Nicholas D James†, on behalf of the Systemic Therapy in Advancing or Metastatic Prostate cancer: Evaluation of Drug Efficacy (STAMPEDE) investigators‡*

Lancet 2022; 399: 447–60

STAMPEDE M0 Eligibility

Attard et al. ESMO 2021 LBA4

Patient population

M0
No evidence of metastases on bone and CT scan of pelvis, abdo, chest
(pre-defined stratification criterion)

Newly-diagnosed
Any of:
- Node-Positive
- ≥2 of: Stage T3 or T4
  PSA≥40ng/ml
  Gleason 8, 9 or 10

Relapsing after previous RP or RT
Any of:
- Node-positive
- PSA≥4ng/ml, rising & doubling time <6m
- PSA≥20ng/ml

All patients
Written informed consent
Fit for all protocol treatment
Fit for follow-up

Full criteria: www.stampedetrial.org

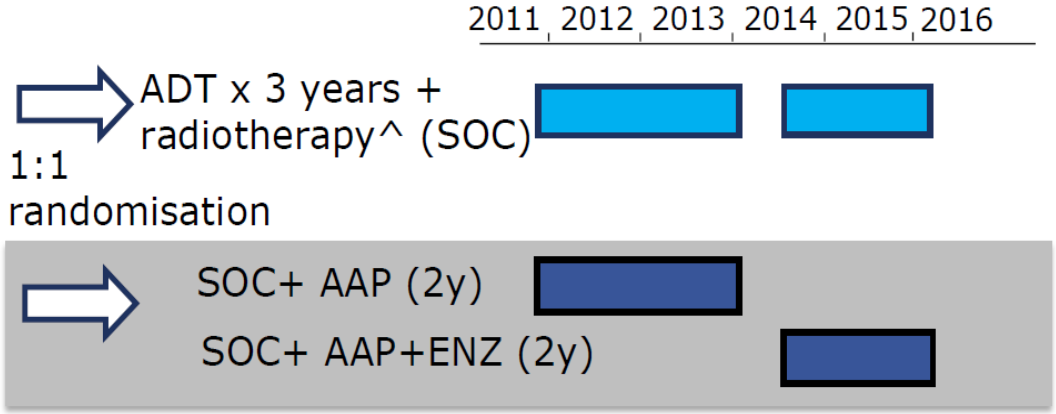
- In truth 97% of patients were de novo…….

Two trials combined into one after data indicated no differences in the two experimental arms

XRT per standard of care + 3 years ADT vs

XRT per standard of care + 2 years of abiraterone or

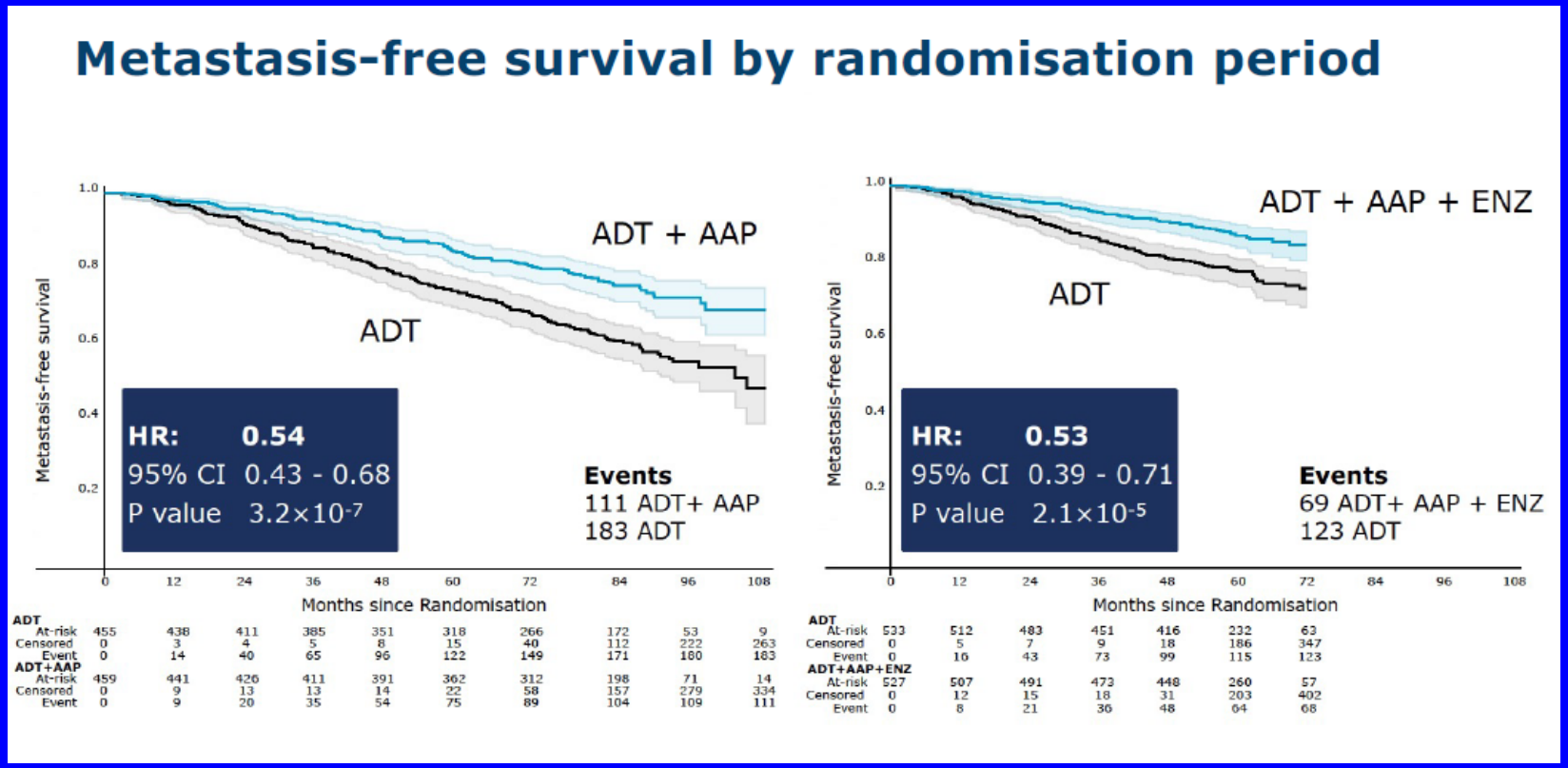
XRT per standard of care + 2 years of abiraterone + enzalutamide



- **N=1974**
- No overlapping controls
- Same protocol & eligibility criteria
- 2 years AAP+/-ENZ
- Report from mCRPC (after accrual completed)[1]

Two trials combined into one after data indicated no differences in the two experimental arms

Attard et al. ESMO 2021 LBA4

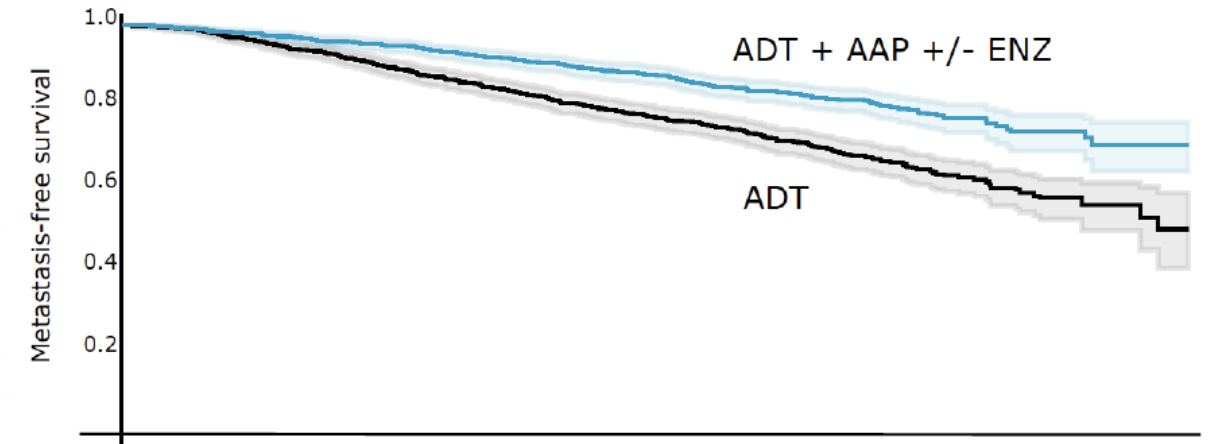


Interaction HR: 1.02, 95% CI: 0.70 – 1.50, P=0.908

STAMPEDE: MFS was primary endpoint

Attard et al. ESMO 2021 LBA4

Metastasis-free survival



ADT										
At-risk	988	950	894	836	767	550	329	172	53	9
Censored	0	8	11	14	26	201	387	522	632	673
Event	0	30	83	138	195	237	272	294	303	306
ADT+AAP+/-ENZ										
At-risk	986	948	917	884	839	622	369	198	71	14
Censored	0	21	28	31	45	225	460	615	737	792
Event	0	17	41	71	102	139	157	173	178	180

Events
180 ADT+ AAP +/- ENZ
306 ADT

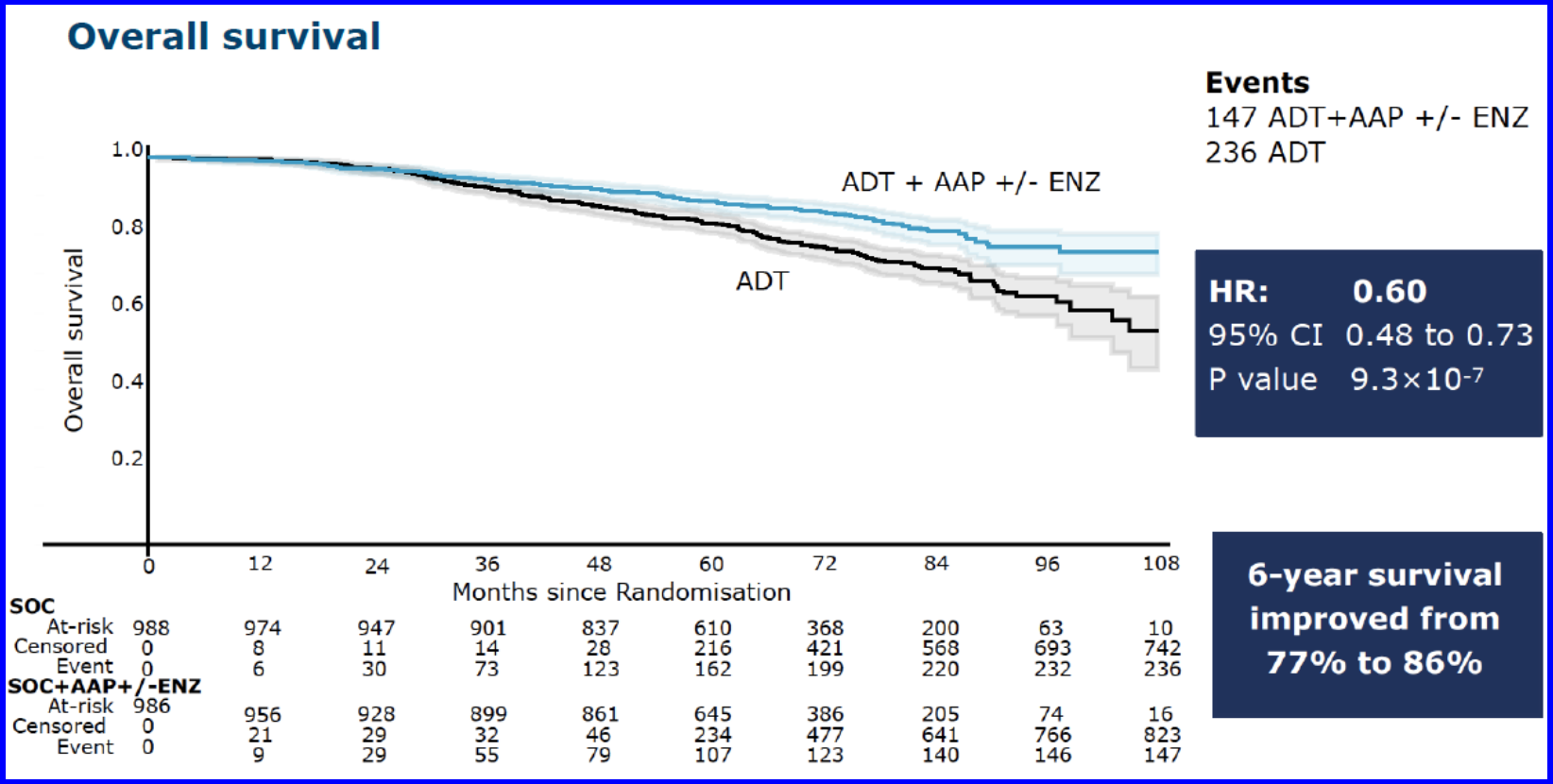
HR:	**0.53**
95% CI:	0.44-0.64
P value	2.9×10^{-11}

6-year MFS improved from 69% to 82%

Kaplan-Meier estimates with 95% CI in lighter shade

STAMPEDE: Overall Survival

Attard et al. ESMO 2021 LBA4



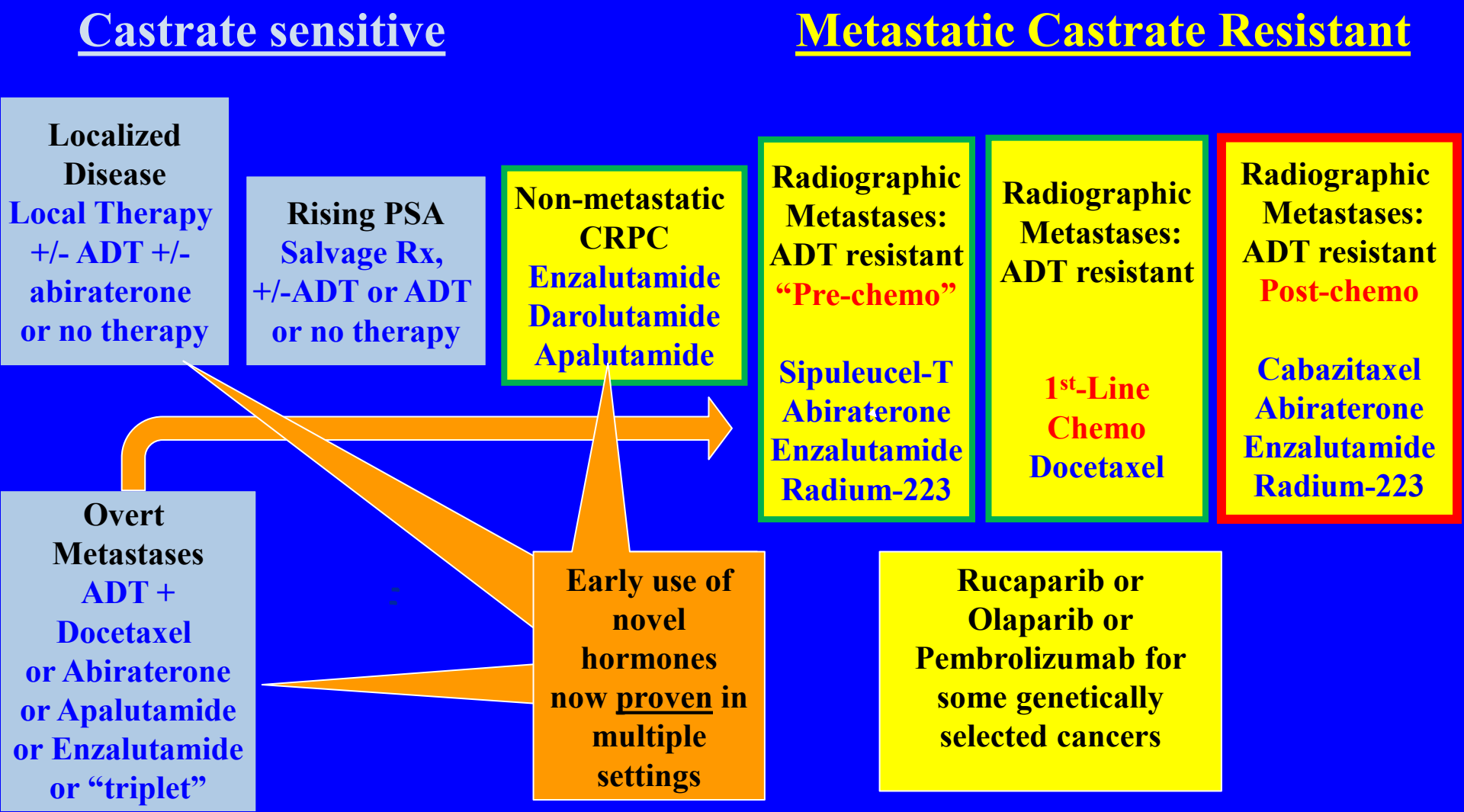
Stampede M0 Summary

- Clearly positive trial in the “super” high risk non-metastatic subset
- Another clear demonstration that earlier use of abiraterone improves outcomes and implications follow
- Lack of PSMA imaging somewhat problematic in today’s world where many of these patients would have had metastatic lesions by PSMA PET

What is next for mHSPC?

- **PSMAddition:** An International Prospective Open-label, Randomized, Phase III Study Comparing 177Lu-PSMA-617 in Combination With Soc, Versus SoC Alone, in mHSPC
- **Keynote 991:** Efficacy and Safety of Pembrolizumab (MK-3475) Plus Enzalutamide Plus Androgen Deprivation Therapy (ADT) Versus Placebo Plus Enzalutamide Plus ADT in Participants With Metastatic Hormone-Sensitive Prostate Cancer (mHSPC)
- **CAPItello-281:** Capivasertib + Abiraterone as Treatment for Patients With mHSPC and PTEN Deficiency
- **TALAPRO-3:** Study of Talazoparib With Enzalutamide in Men With DDR Gene Mutated mHSPC
- **STAMPEDE:** Evaluating the role of metformin (ARM K) and the role transdermal estrogen in place of ADT (ARM L)

Standard Therapies Today: Now concentrate on CRPC



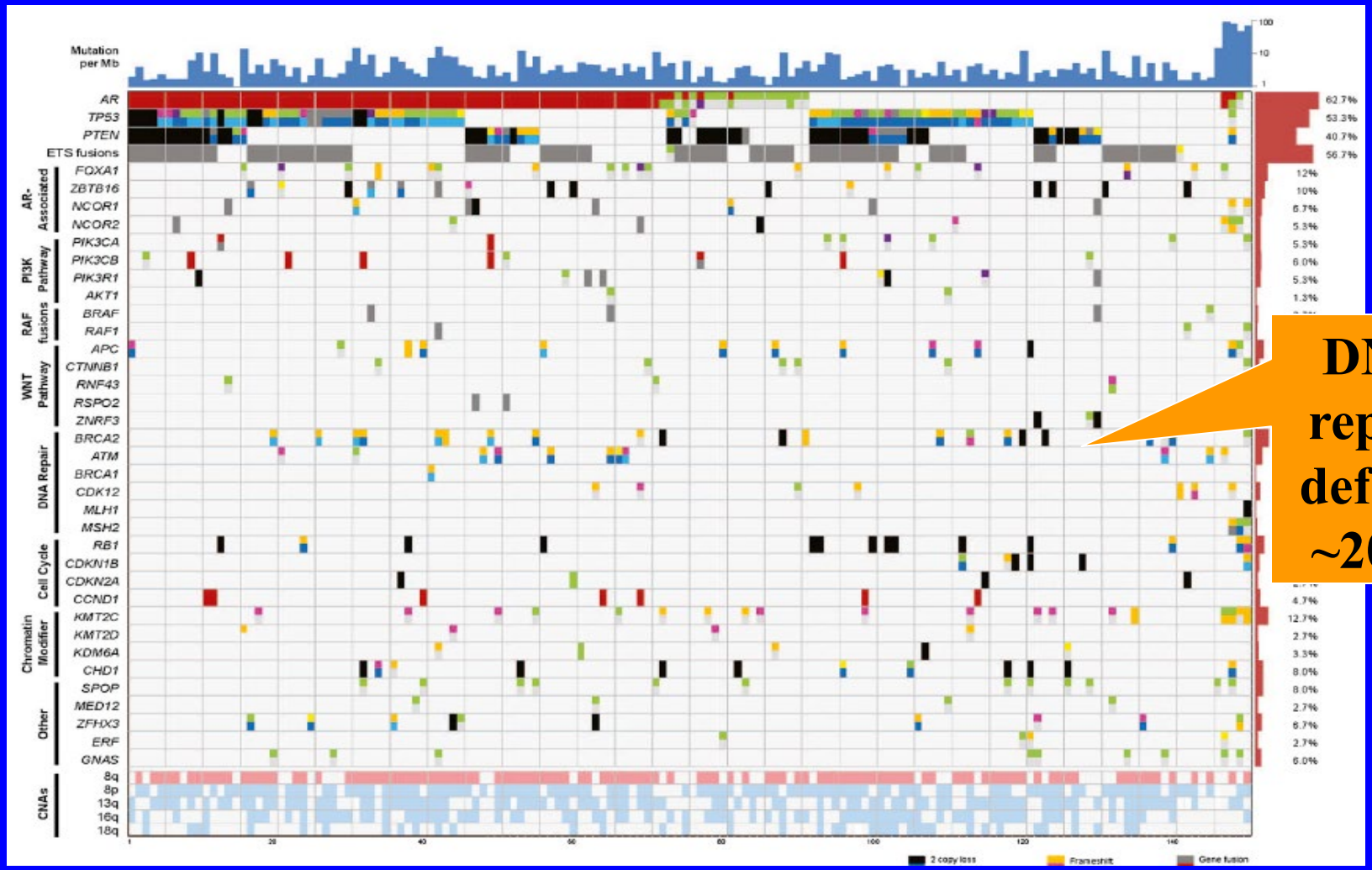
TRIAL	FRONT LINE mCRPC	HR	Survival (months)
TAX 327	Docetaxel/prednisone vs mitoxantrone/prednisone	0.79	19.2 vs 16.3* (2.9 months)
IMPACT	Sipuleucel-T vs Control	0.78	25.8 vs 21.7 (4.1 months
COU-AA-302	Abiraterone/prednisone vs Placebo/prednisone	0.79	35.3 vs. 31.1* (4.2 months)
PREVAIL	Enzalutamide vs Placebo	0.71	35.3 vs. 31.3* (4.0 months)
	POST-DOCETAXEL mCRPC		
TROPIC	Cabazitaxel/prednisone vs mitoxantrone/prednisone	0.70	15.1 vs 12.7 (2.4 months)
COU-AA- 301	Abiraterone/prednisone vs Placebo/prednisone	0.74	15.8 vs 11.2* (4.6 months)
AFFIRM	Enzalutamide vs Placebo	0.63	18.4 vs 13.6 (4.8 months)
	FRONT LINE and POST-DOCETAXEL mCRPC		
ALSYMPCA	Standard of care +/- radium-223	0.70	14.9 vs 11.3* (3.6 months)
	POST-ABI OR -ENZA OR POST-ABI OR -ENZA AND -DOCETAXEL (HRR SUBSET)		
PROfound	Olaparib vs abi/enza second line	0.69	19.1 vs 14.7** (4.4 months)
	Third Line (POST-ABI or -ENZA and POST-DOCETAXEL		
CARD	Cabazitaxel vs abi/enza second line	0.64	13.6 vs 11.0 (2.6 months)
VISION	Standard of care +/- PSMA-617 Lu-177	0.62	15.3 vs 11.3 (4.0 months)

* Mature analysis **BRCA1/BRCA2/ATM subset

Biomarkers Used in FDA Approved Targeted Therapy Today

- Homologous recombination repair genes
  - *BRCA2, BRCA1, PALB2, RAD54L*, etc.
    - via PARP inhibitors olaparib and rucaparib
- Mismatch repair genes
  - *MSH2, MSH6, MLH1, PMS2* (mismatch repair)
    - via anti-PD1 pembrolizumab

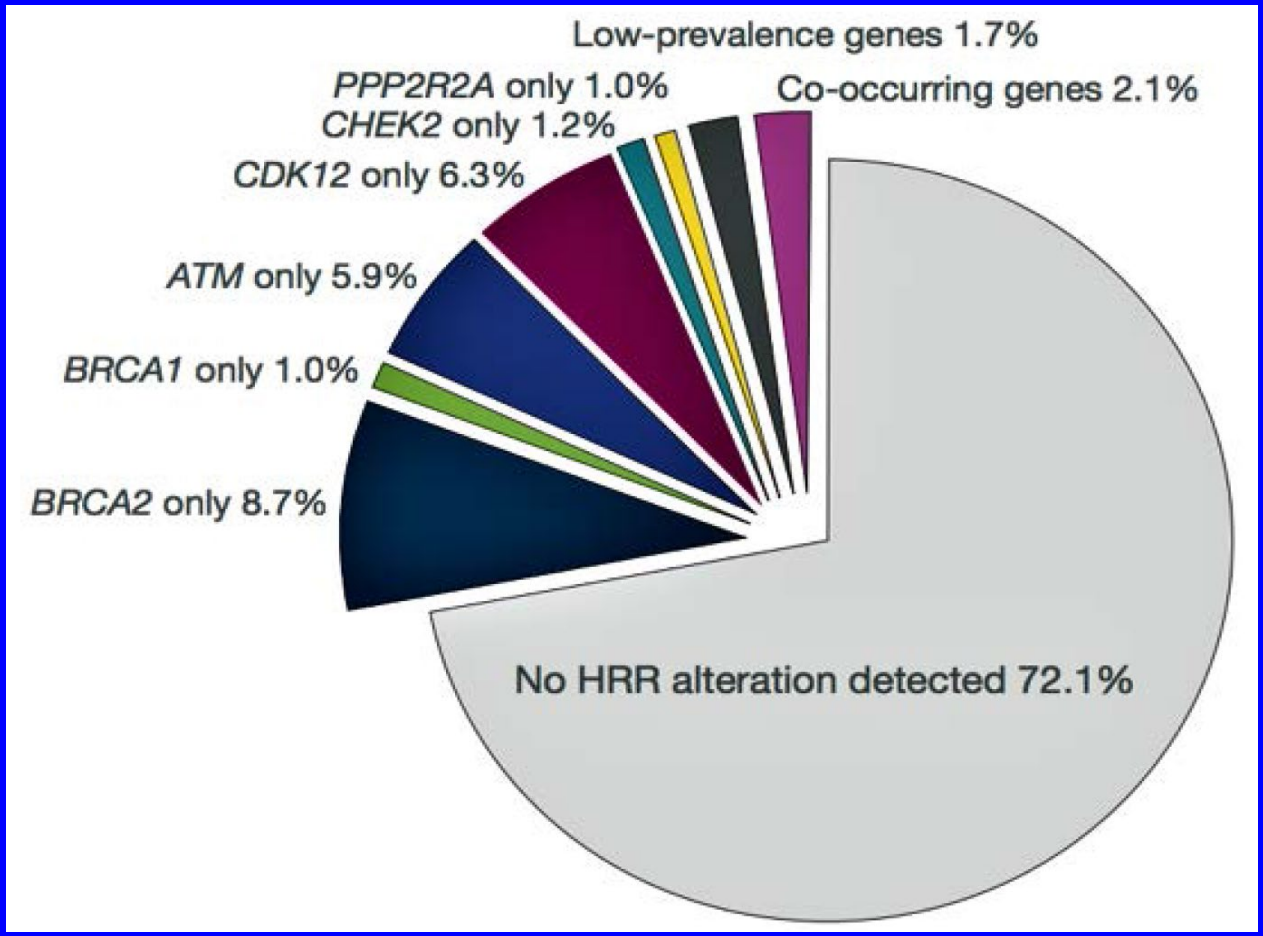
Challenges: mCRPC is a heterogeneous group of diseases



Robinson et al. Cell 161:1215, 2015

PROfound data: 4047 pts tested, 31% had Quality Issues with NGS assays, 28% had DNA repair defects

De Bono et al. ESMO 2019, #5118



Improved Survival: Phase III Olaparib Trial (PROfound) in Prostate Cancer

Sept 20, 2020

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Survival with Olaparib in Metastatic Castration-Resistant Prostate Cancer

M. Hussain, J. Mateo, K. Fizazi, F. Saad, N. Shore, S. Sandhu, K.N. Chi, O. Sartor, N. Agarwal, D. Olmos, A. Thiery-Vuillemin, P. Twardowski, G. Roubaud, M. Özgüroğlu, J. Kang, J. Burgents, C. Gresty, C. Corcoran, C.A. Adelman, and J. de Bono, for the PROfound Trial Investigators*

FDA PARP approvals

- Rucaparib accelerated approval (May 15, 2020)
  - Deleterious germline or somatic *BRCA1/2* mutations after both chemotherapy and novel hormones

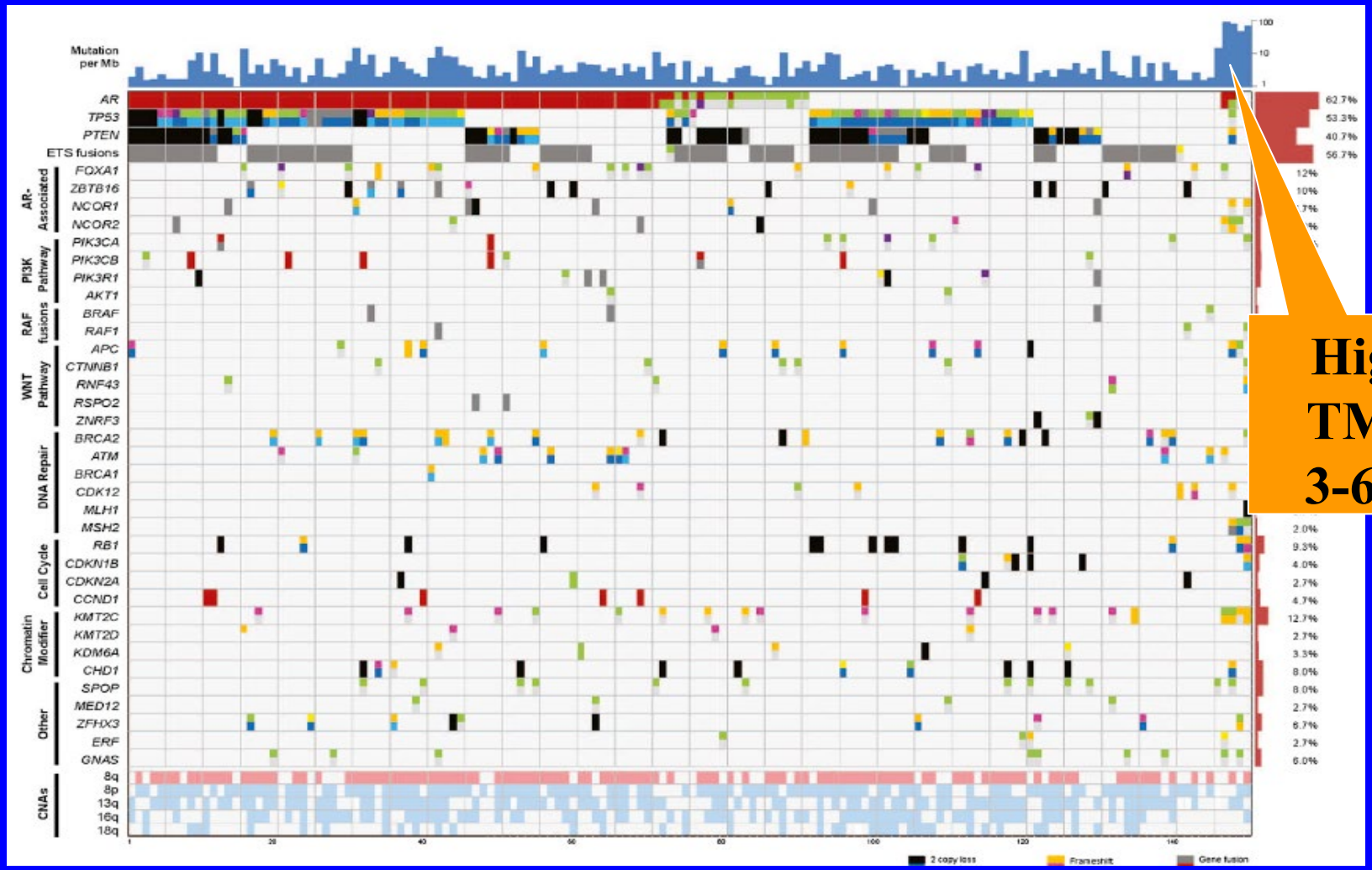
- Olaparib approval (May 19, 2020)
  - Deleterious germline *BRCA1/2* or deleterious somatic homologous recombination repair (HRR) gene mutated metastatic castration resistant prostate cancer (mCRPC) after novel hormones
  - *ATM, BRCA1/2, BARD, BRIP, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D,*

FDA approvals for assessment of circulating tumor DNA (ctDNA)

- ctDNA accessible in most everyone whereas tissue based assays can be problematic in prostate cancer

- FoundationOne® Liquid CDx companion diagnostic to identify eligible patients with specific mutations
  - Rucaparib for BRCA1/2 mutations (Aug 26, 2020)
  - Olaparib for BRCA1/2 or ATM mutations (Nov 9, 2020)

Challenges: mCRPC is a heterogeneous group of diseases



Robinson et al. Cell 161:1215, 2015

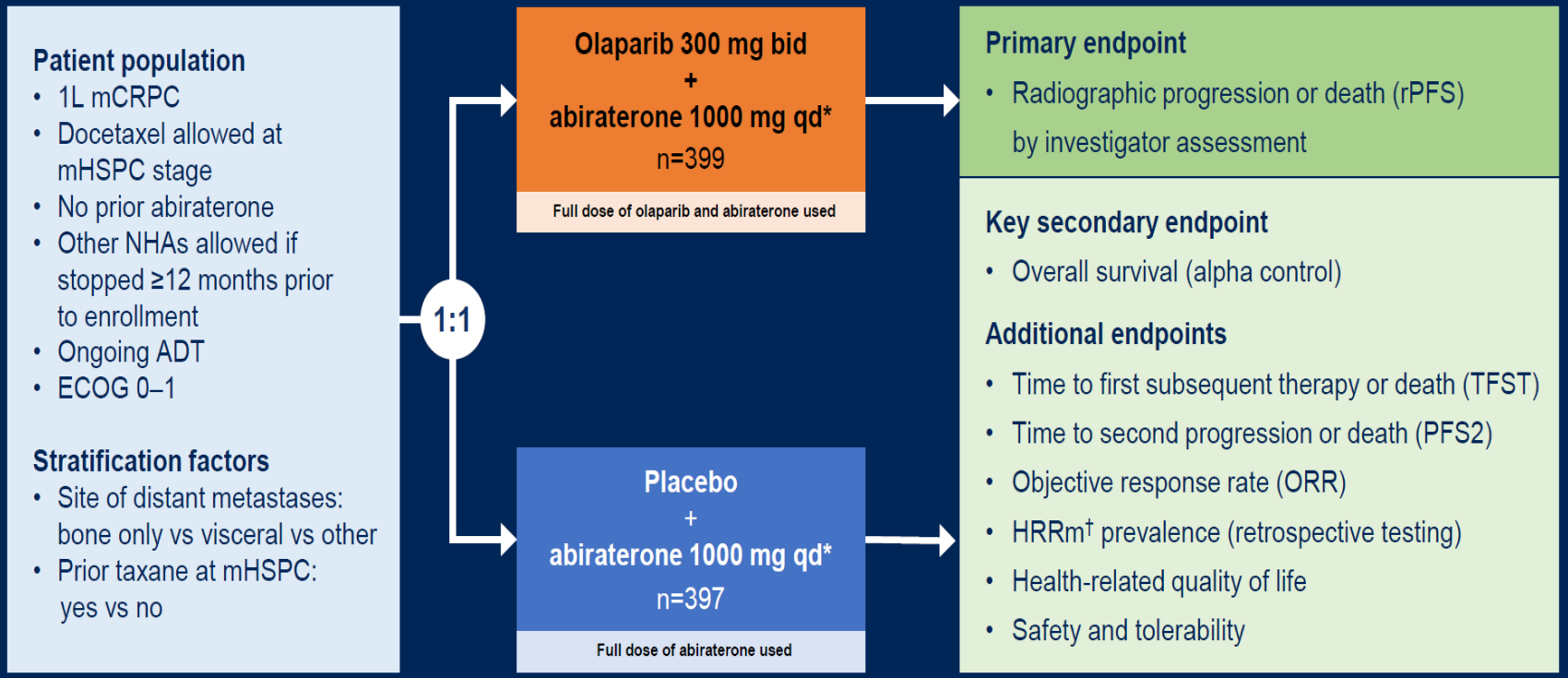
Pembrolizumab FDA approved for tumors that are MSI high or high tumor mutational burden (>10 per Mb) or mismatch repair deficient

"Solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options"

Are there particular therapeutic combinations that deserve to be used as standard of care in CRPC?

No…. But some combinations deserve scrutiny

PROpel: a global randomized double-blind phase III trial

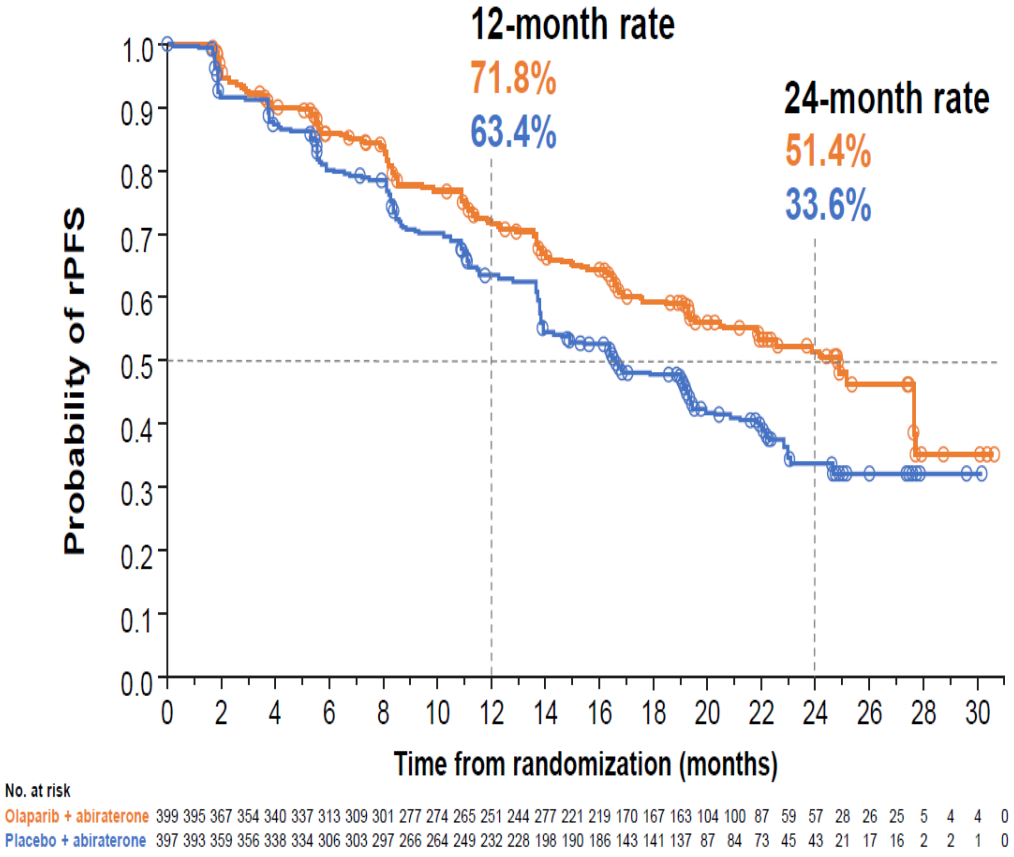


HRR mutations were determined retrospectively

Saad et al. ASCO GU 2022

PROpel primary endpoint rPFS

Saad et al. ASCO GU 2022



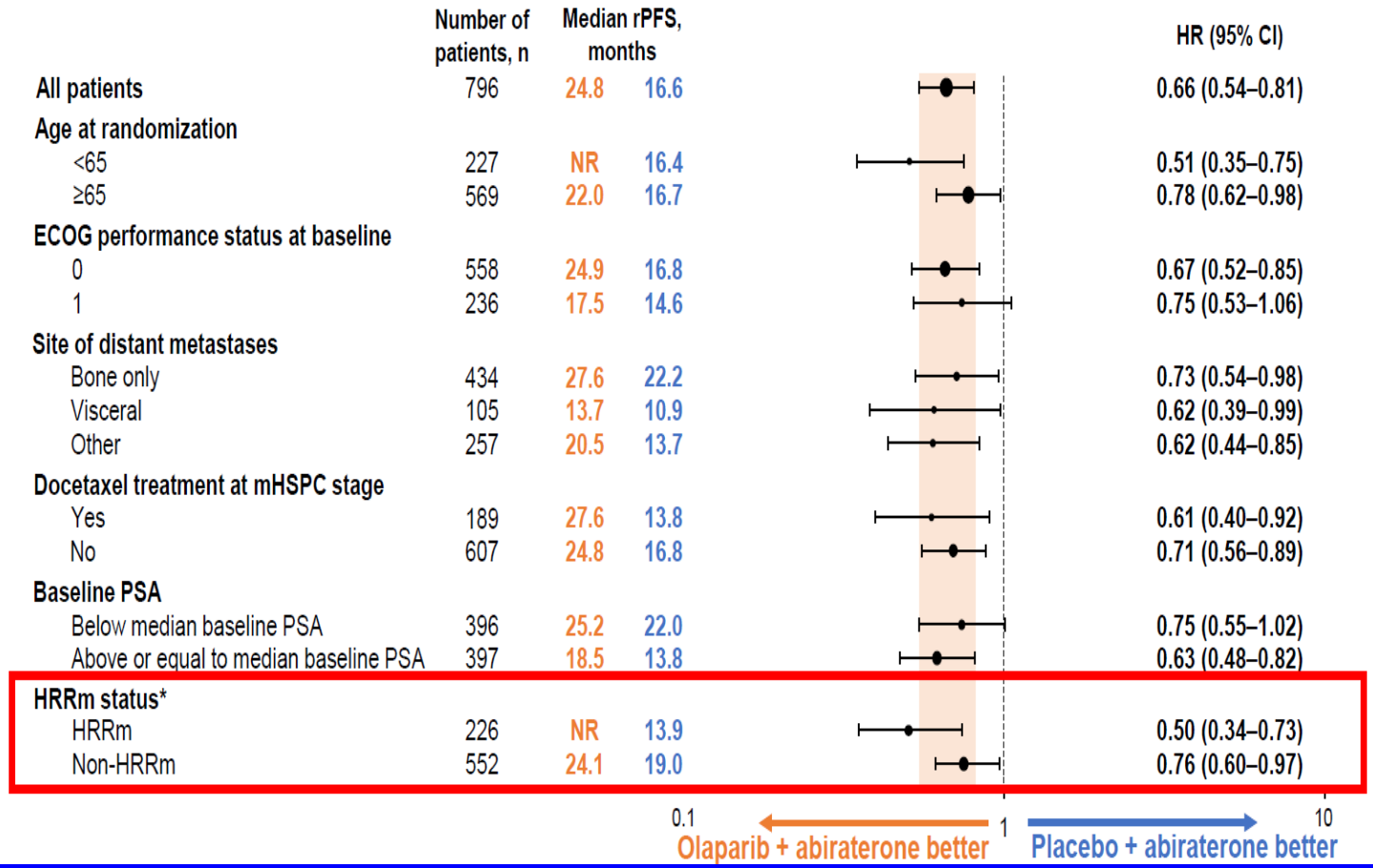
	Olaparib + abiraterone (n=399)	Placebo + abiraterone (n=397)
Events, n (%)	168 (42.1)	226 (56.9)
Median rPFS (months)	24.8	16.6
HR (95% CI)	0.66 (0.54–0.81); *P*<0.0001	

Pre-specified 2-sided alpha: 0.0324

Median rPFS improvement of 8.2 months favors olaparib + abiraterone*

PROpel primary endpoint rPFS

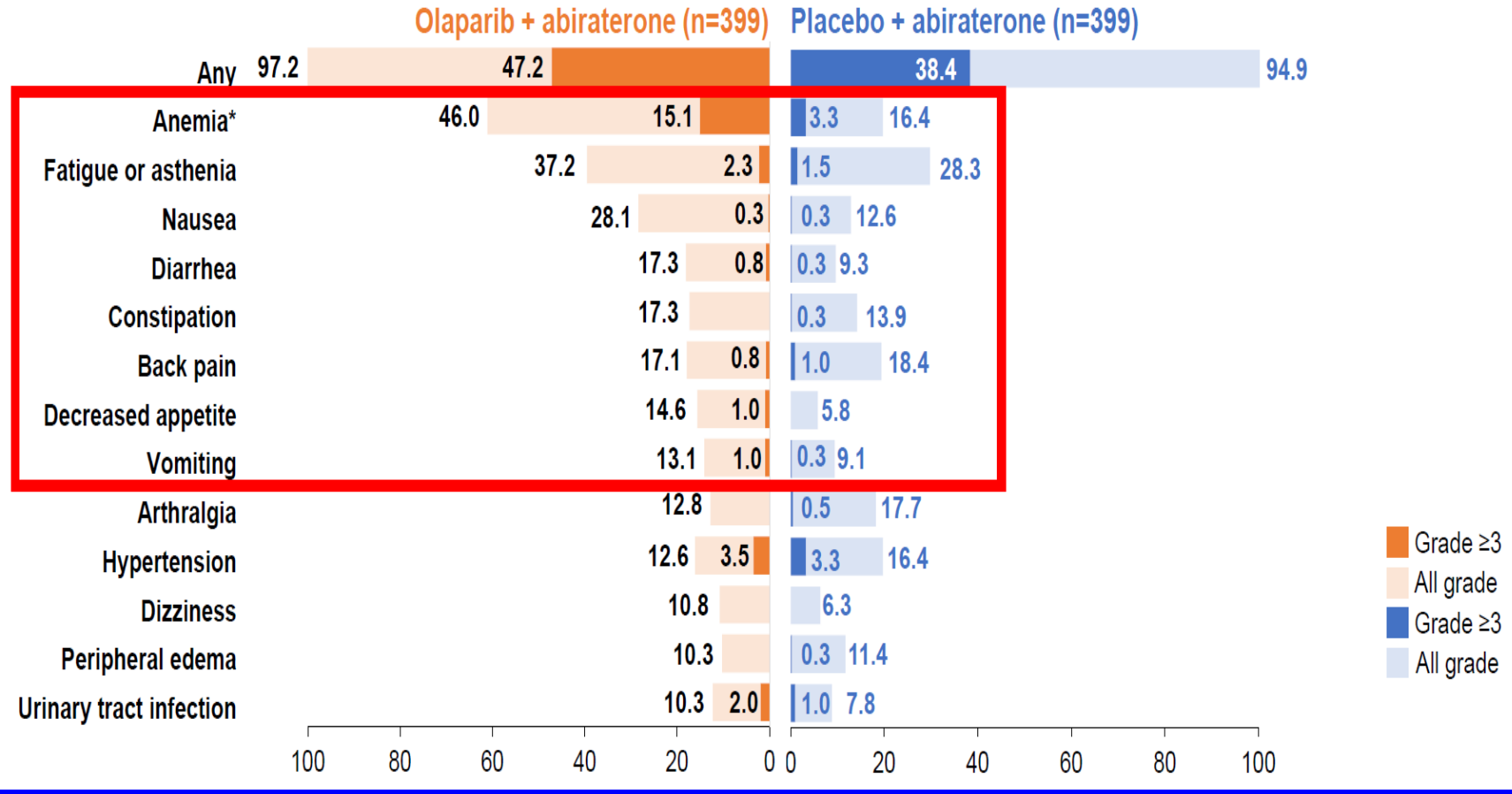
Saad et al. ASCO GU 2022



Global interaction test not significant at 10% level

AE profile PROpel

Saad et al. ASCO GU 2022

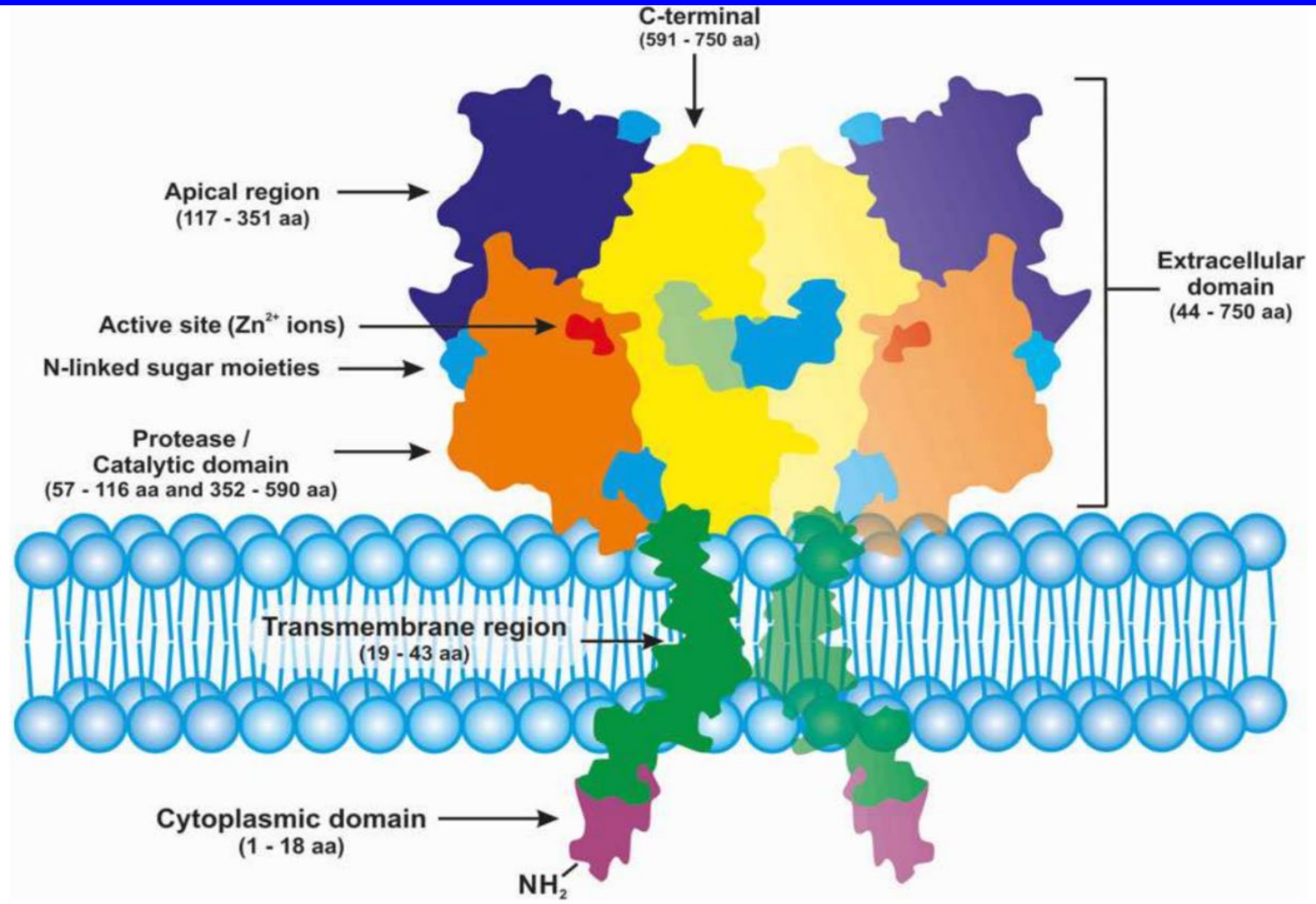


PROpel Summary

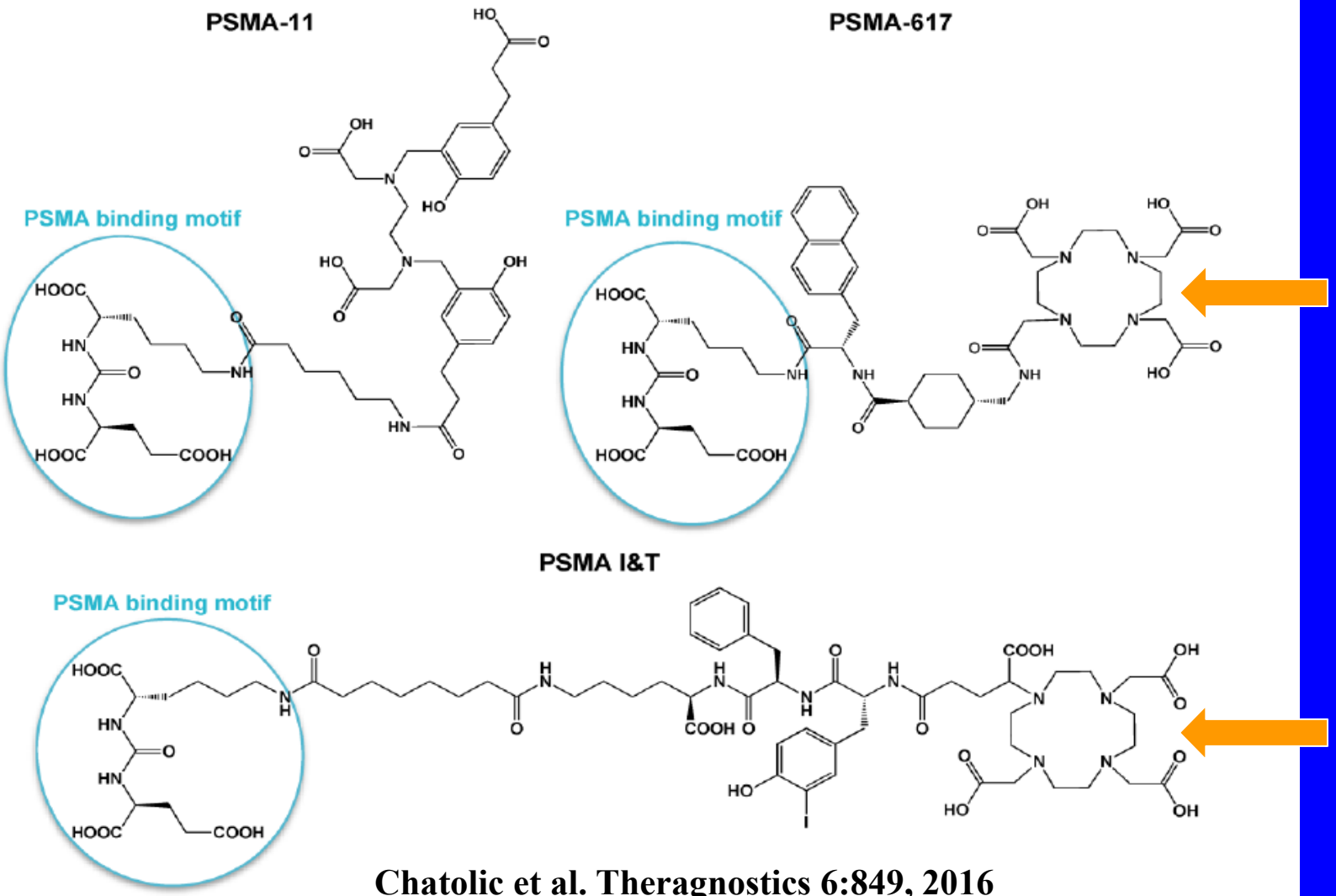
- In front line mCRPC, overall rPFS for olaparib + abiraterone better than abiraterone
- HRR mutants have HR for rPFS of 0.50
- Non-HRR mutant subset has HR for rPFS of 0.76
- OS data are immature

PSMA Targeted Therapies

Image from O'Driscott C et al, Br J Pharm 2016



PSMA binding molecules can be linked to therapeutic agents such as ^{177}Lu or ^{225}Ac



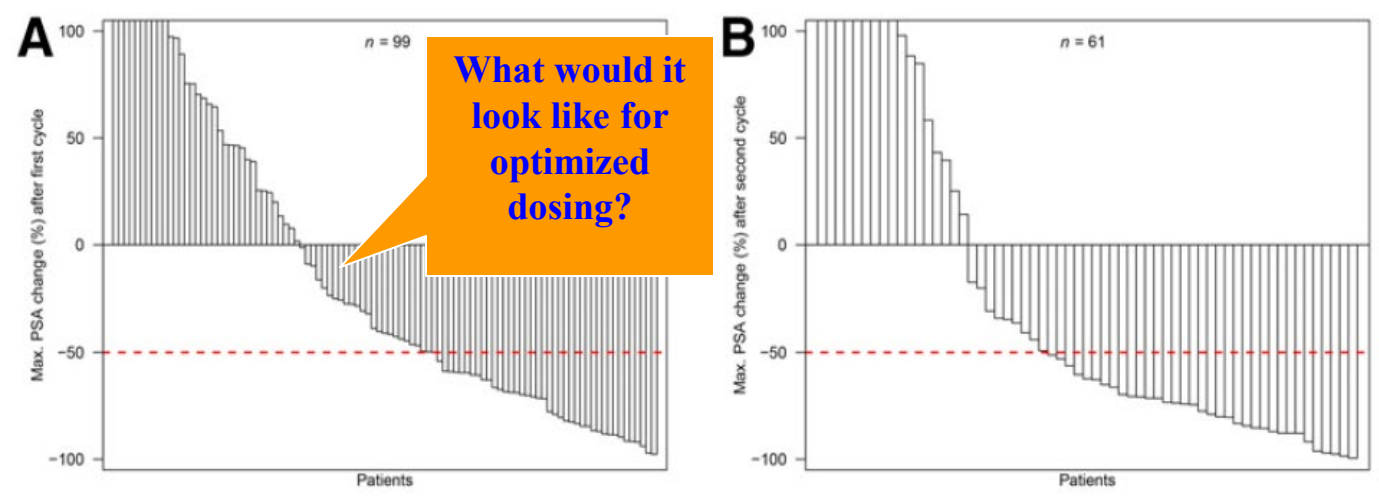
Chatolic et al. Theragnostics 6:849, 2016

German Multicenter Study Investigating ^{177}Lu-PSMA-617 Radioligand Therapy in Advanced Prostate Cancer Patients

Kambiz Rahbar*[1], Hojjat Ahmadzadehfar*[2], Clemens Kratochwil[3], Uwe Haberkorn[3], Michael Schäfers[1], Markus Essler[2], Richard P. Baum[4], Harshad R. Kulkarni[4], Matthias Schmidt[5], Alexander Drzezga[5], Peter Bartenstein[6], Andreas Pfestroff[7], Markus Luster[7], Ulf Lützen[8], Marlies Marx[8], Vikas Prasad[9], Winfried Brenner[9], Alexander Heinzel[10], Felix M. Mottaghy[10], Juri Ruf[11], Philipp Tobias Meyer[11], Martin Heuschkel[12], Maria Eveslage[13], Martin Bögemann[14], Wolfgang Peter Fendler†[6], and Bernd Joachim Krause†[12,15]

J Nucl Med 2017; 58:85–90

Optimal dose and schedule not established



First cycle best response

Best response overall

Rahbar K, et al. *J Nucl Med.* 2017;58:85-90.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Lutetium-177–PSMA-617 for Metastatic Castration-Resistant Prostate Cancer

O. Sartor, J. de Bono, K.N. Chi, K. Fizazi, K. Herrmann, K. Rahbar, S.T. Tagawa, L.T. Nordquist, N. Vaishampayan, G. El-Haddad, C.H. Park, T.M. Beer, A. Armour, W.J. Pérez-Contreras, M. DeSilvio, E. Kpamegan, G. Gericke, R.A. Messmann, M.J. Morris, and B.J. Krause, for the VISION Investigators*

June 23, 2021

VISION: ^{177}Lu PSMA-617 Pivotal Phase III

Patient Population

mCRPC
- at least 1 prior novel hormone
- at least 1 prior taxane
- PSMA PET+ but no FDG PET

Stratification Factors
- LDH (above/below 260)
- Liver mets (Y/N)
- PS (0-1 vs 2)
- NAAD as BSC (Y/N)

2:1 Randomization

- Best standard of care
- ^{177}Lu-PSMA-617
  7.4 GBq q6 wks x6

- Best standard of care

N=831

Alternative 1° endpoint:
rPFS or OS

VISION: ^{177}Lu-PSMA-617 pivotal Phase III trial

Patient Selection[1]

1179 patients assessed for eligibility → **1003** patients received ^{68}Ga-PSMA-11 PET/CT → 869/1003 patients (**~87%**) met PSMA criteria

Pre-specified criteria for PSMA positivity

- ≥ PSMA-positive lesion anywhere in the body
- PSMA PET imaging ligand uptake ≥ liver
- No size criteria for PSMA-positive lesions

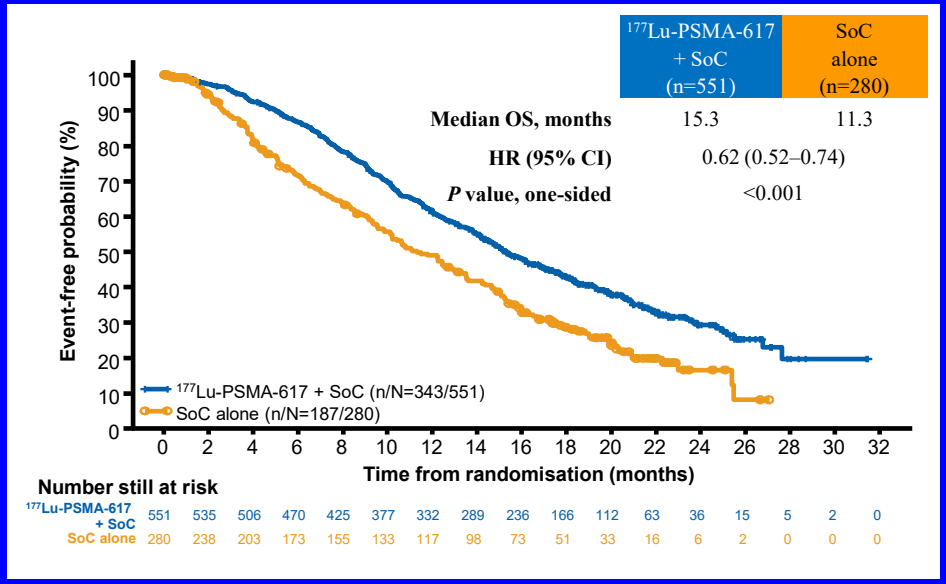
CT, computed tomography; PET, positron emission tomography; PSMA, prostate-specific membrane antigen.

1. Sartor O, et al. N Engl J Med. 2021; doi: 10.1056/NEJMoa2107322. Online ahead of print.

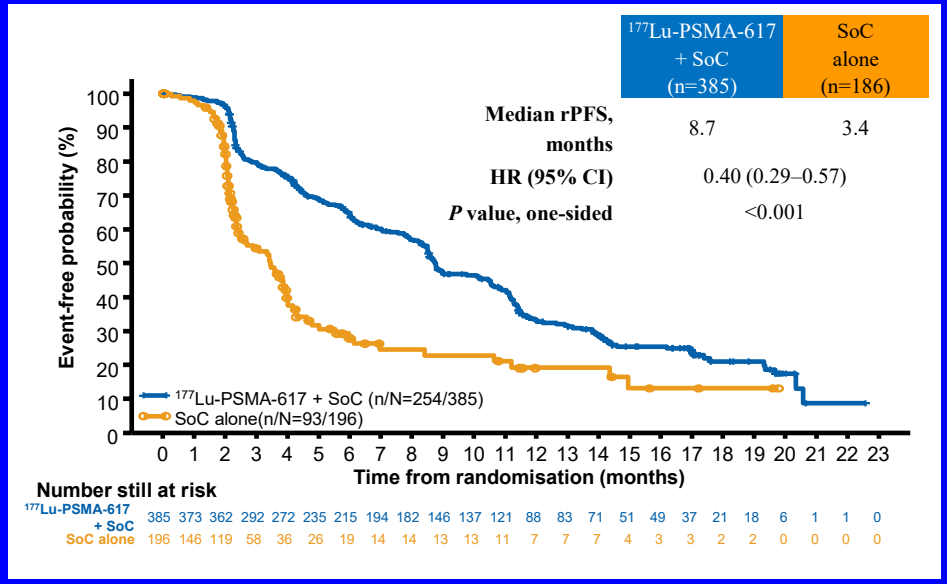
VISION: ^{177}Lu-PSMA-617 pivotal Phase III trial

VISION met both primary endpoints of OS and rPFS[1]

OS: 38% risk reduction for death[1]



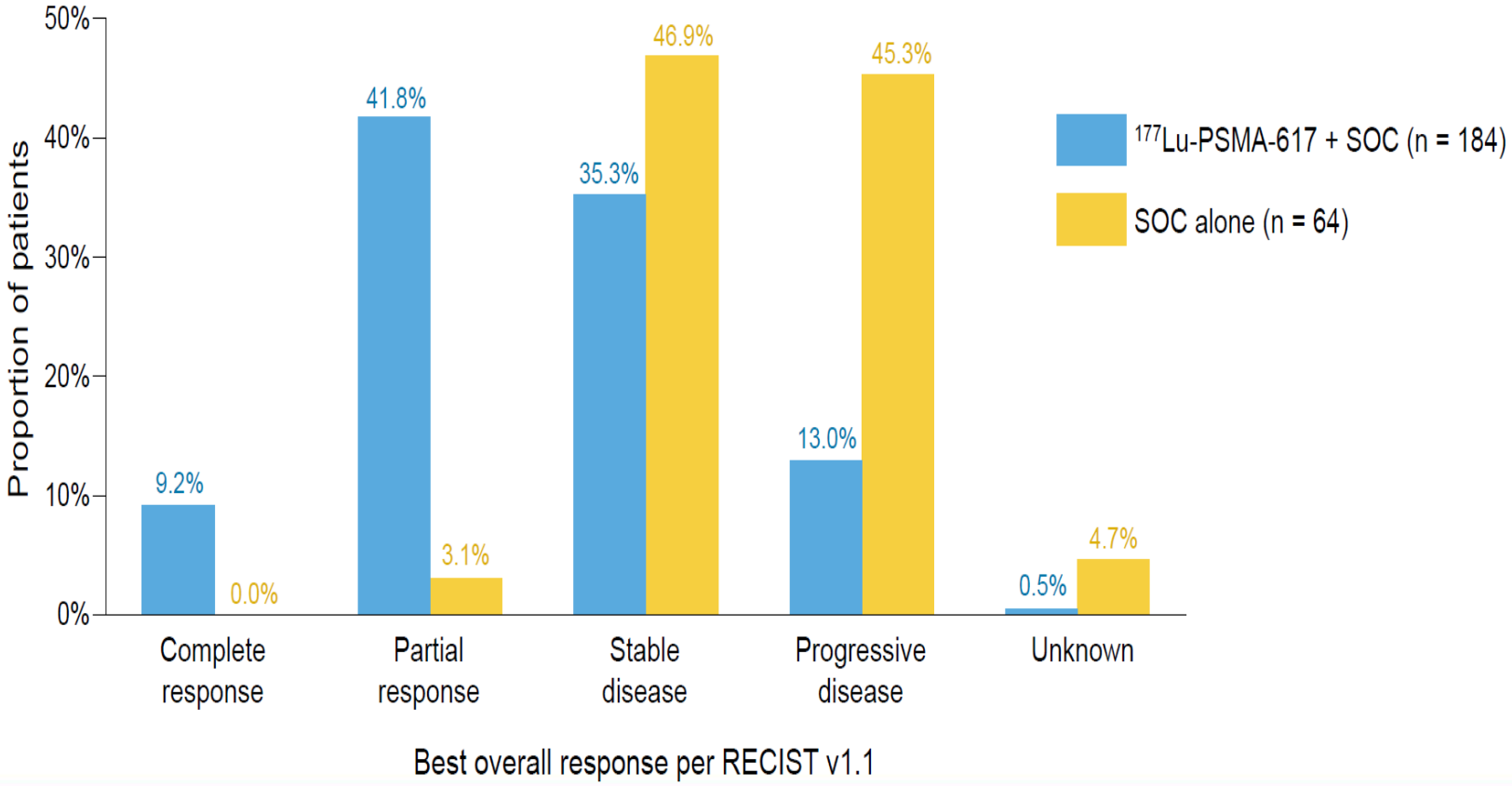
rPFS: 60% risk reduction for progression/death[1]



CI, confidence interval; HR, hazard ratio; OS, overall survival; PSMA, prostate-specific membrane antigen; rPFS, radiographic progression-free survival; SoC, standard of care.

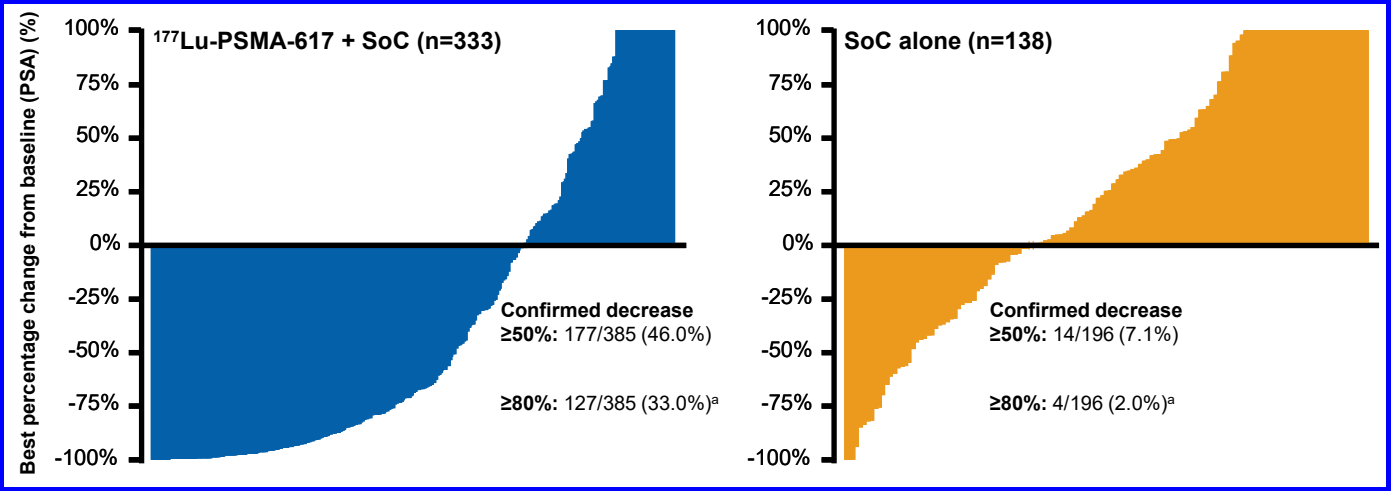
1. Sartor O, et al. N Engl J Med. 2021; doi: 10.1056/NEJMoa2107322. Online ahead of print.

Secondary endpoint: RECIST v1.1 responses favored the ^{177}Lu-PSMA-617 arm in patients with measurable disease



VISION: ^{177}Lu-PSMA-617 pivotal Phase III trial

PSA response



Objective Response

(per RECIST v1.1, patients with measurable disease)

	^{177}Lu-PSMA-617 + SoC	SoC alone
CR	9.2%	0.0%
PR	41.8%	3.1%

Sartor O, et al. N Engl J Med. 2021; doi: 10.1056/NEJMoa2107322. Online ahead of print.

VISION: ^{177}Lu-PSMA-617 pivotal Phase III trial

TEAEs occurring in ≥5% of patients[b], n (%)	Safety Set (N=734)[a]			
	All Grades		Grade 3–5[c]	
	^{177}Lu-PSMA-617 + SoC (n=529)	SoC alone (n=205)	^{177}Lu-PSMA-617 + SoC (n=529)	SoC alone (n=205)
Fatigue	228 (43.1)	47 (22.9)	31 (5.9)	3 (1.5)
Dry mouth	205 (38.8)	1 (0.5)	0	0
Nausea	187 (35.3)	34 (16.6)	7 (1.3)	1 (0.5)
Anaemia	168 (31.8)	27 (13.2)	68 (12.9)	10 (4.9)
Back pain	124 (23.4)	30 (14.6)	17 (3.2)	7 (3.4)
Arthralgia	118 (22.3)	26 (12.7)	6 (1.1)	1 (0.5)
Decreased appetite	112 (21.2)	30 (14.6)	10 (1.9)	1 (0.5)
Constipation	107 (20.2)	23 (11.2)	6 (1.1)	1 (0.5)
Diarrhea	100 (18.9)	6 (2.9)	4 (0.8)	1 (0.5)
Vomiting	100 (18.9)	13 (6.3)	5 (0.9)	1 (0.5)
Thrombocytopaenia	91 (17.2)	9 (4.4)	42 (7.9)	2 (1.0)
Lymphopaenia	75 (14.2)	8 (3.9)	41 (7.8)	1 (0.5)
Leukopaenia	66 (12.5)	4 (2.0)	13 (2.5)	1 (0.5)

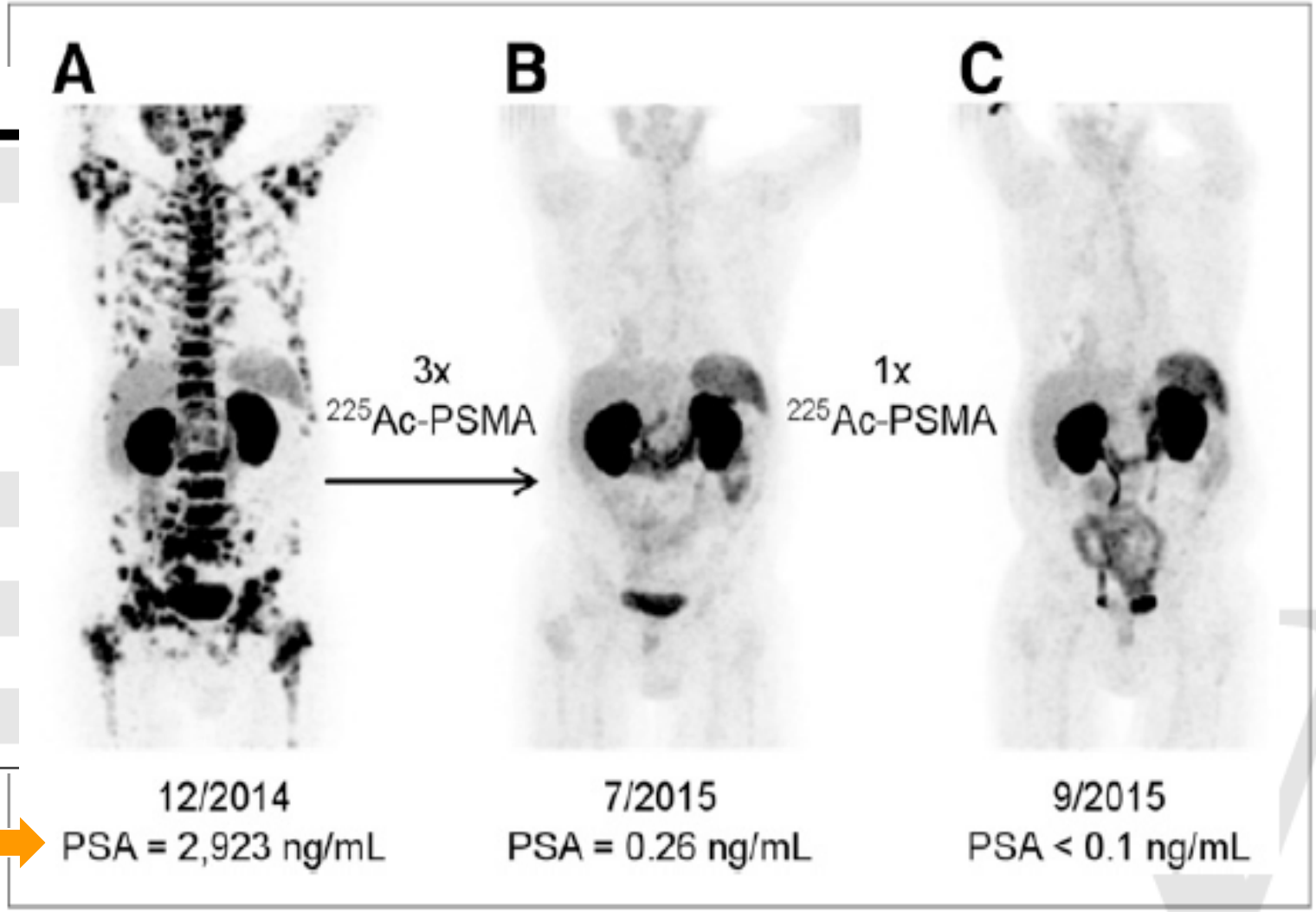
New trials will bring PSMA Lu-177 in the pre-chemo and upfront mHSPC space

Are Alpha-Particles Better than Betas?

Radio-conjugates: PSMA targeted alpha emitters (Actinium-225) as 9th line treatment

Kratochwil et a. J Nuc Med 57: 1-4, 2016

Patient A
Leuprorelin
Zoledronate
Docetaxel (50 cycles)
Carmustine/epirubicin in hyperthermia
Abiraterone
Enzalutamide
^{223}Ra (6 cycles)
Abiraterone reexposition
Estramustine



Advanced Prostate Cancer Summary

- As stated several times, new hormones are going earlier and earlier
- Triplets with ADT + novel hormone + docetaxel may gain some traction
- Precision therapy is gaining use in the CRPC setting
- PSMA Lu-177 is effective and moving up
- More work to do…..Always!!!!