A MASTER LECTURE SERIES
MEDPRO

Prostate Cancer Update
August 27, 2022

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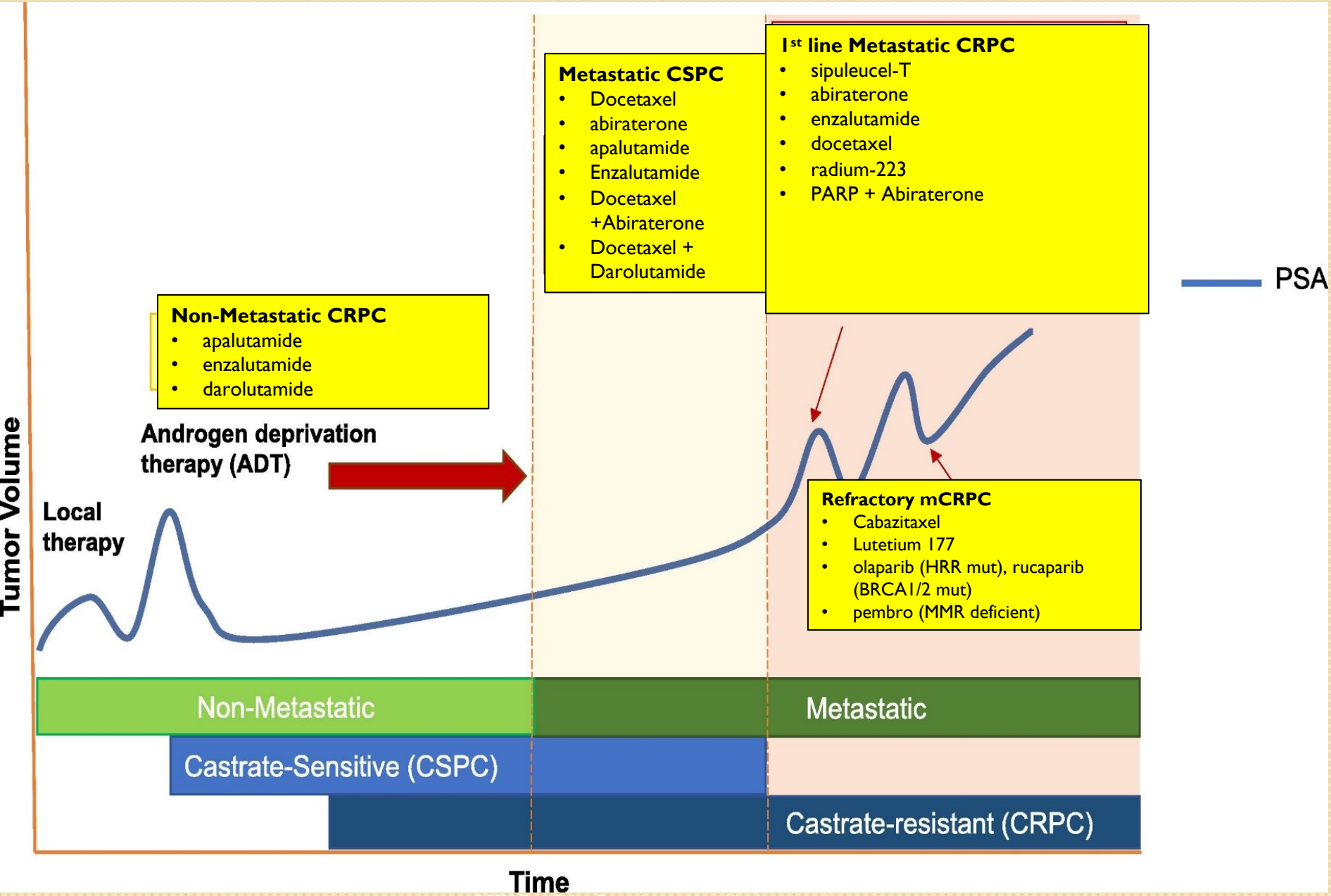
CANCER INSTITUTE

Agenda

- Metastatic castrate sensitive Prostate CA
  - CHAARTED, LATITUDE, ENZAMET, TITAN, PEACE-1, ARASENS
- Metastatic castrate resistant Prostate CA
  - PROpel, Magnitude, VISION, TheraP,

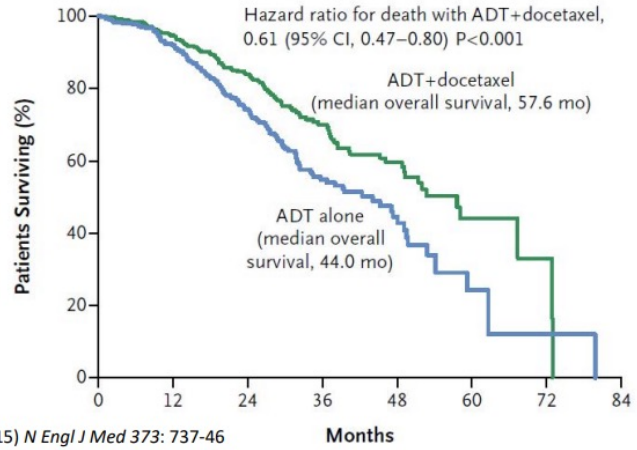
Systemic therapy of prostate cancer 2022



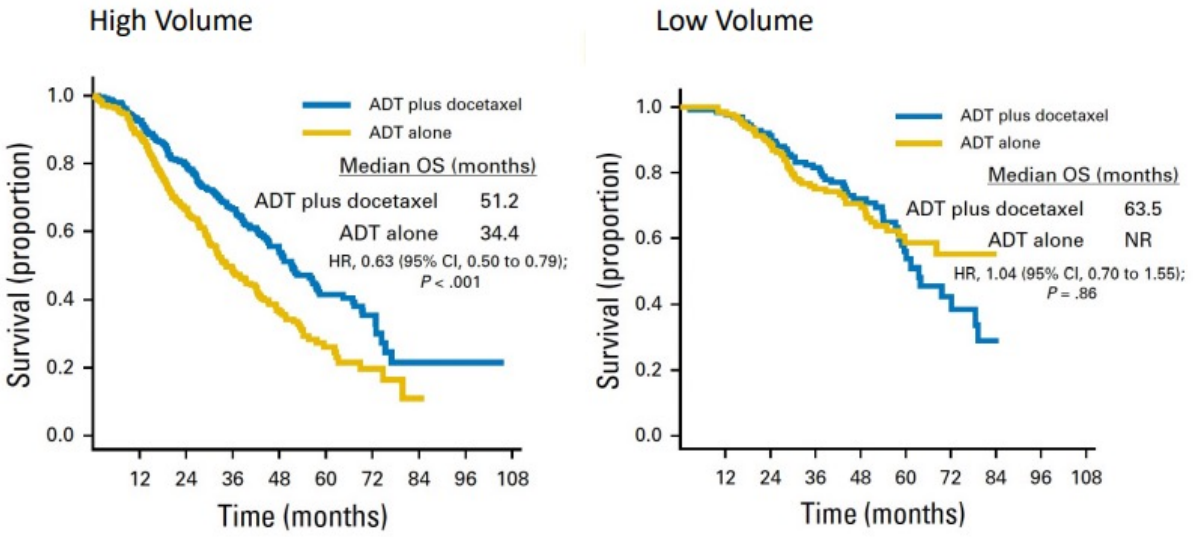
Alkhudair NA. *Saudi Pharm J.* 2019 Mar;27(3):368-372.

Metastatic Hormone Sensitive Prostate Cancer

Historical Data: CHAARTED Study



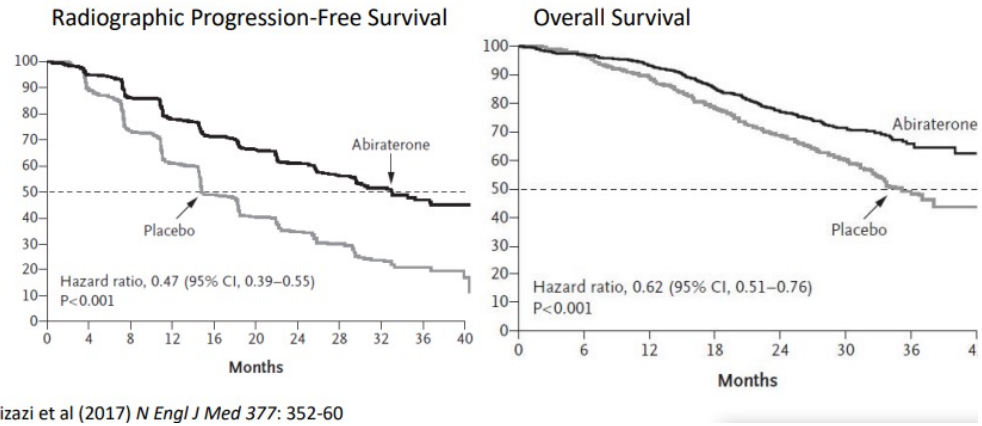
Sweeney et al (2015) *N Engl J Med 373*: 737-46



Kyriakopoulos et al (2018) *J Clin Oncol 36*: 1080-0187

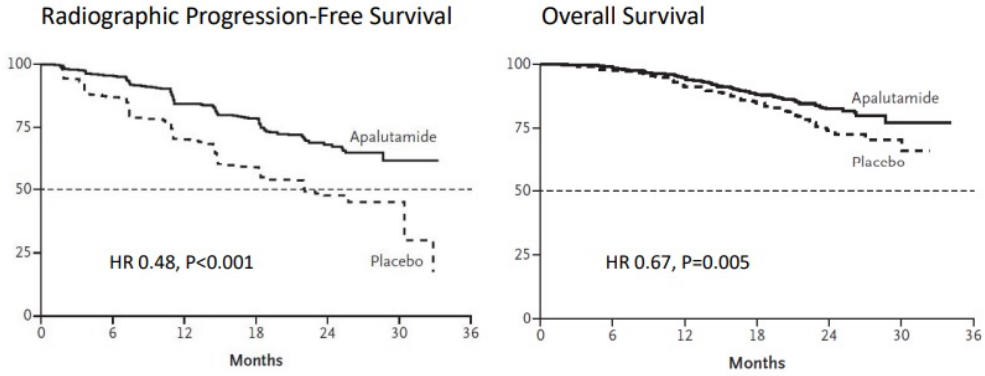
Androgen Pathway Inhibitors

LATITUDE: Abiraterone Acetate for mHSPC



Fizazi et al (2017) *N Engl J Med 377*: 352-60

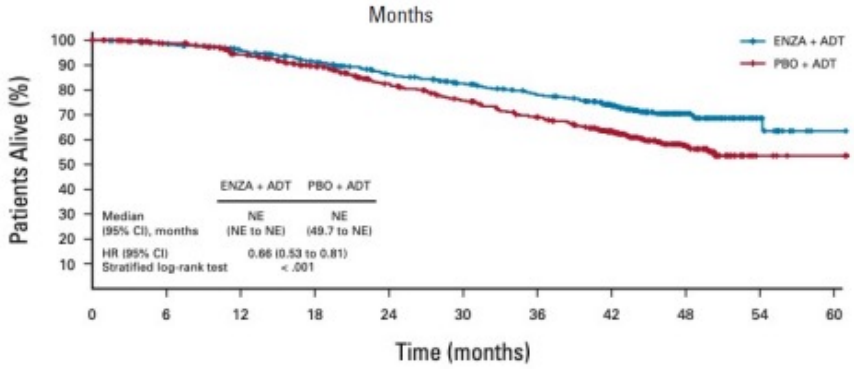
TITAN: Apalutamide for mHSPC



Chi et al (2019) *N Engl J Med 381*: 13-24

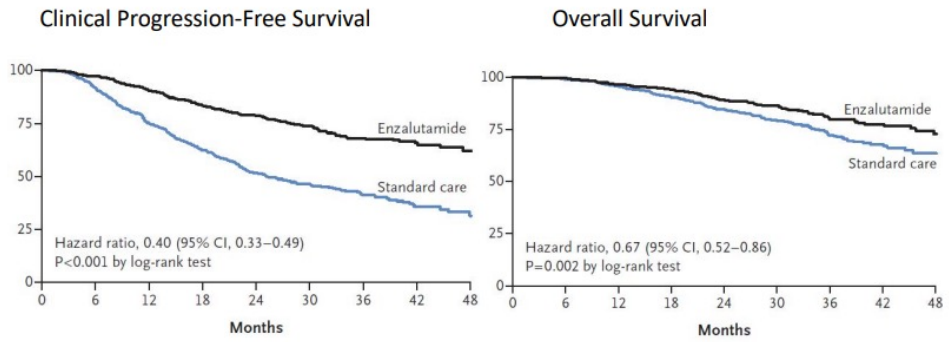
ARCHES and ENZAMET

OS



Armstrong et al (2019) *J Clin Oncol 37:* 2974-2986; Armstrong et al (2022) *J Clin Oncol* DOI: 10.1200/JCO.22.00193

ENZAMET: Enzalutamide for mHSPC



Davis et al (2019) *N Engl J Med 381*: 121-131

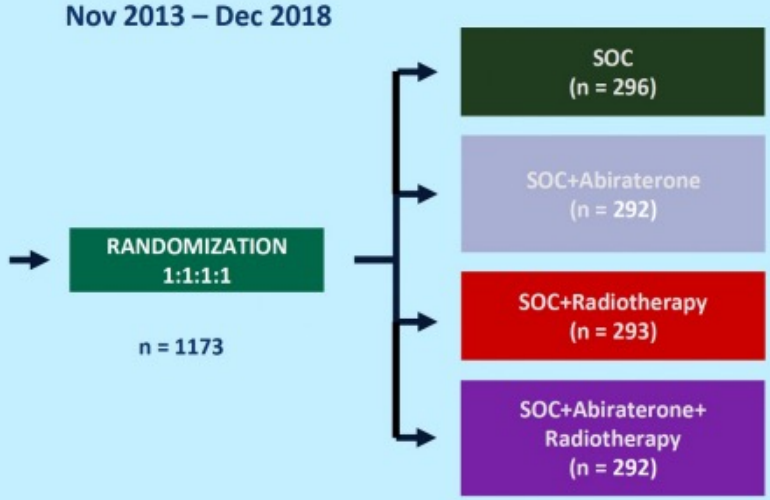
PEACE -1

Key Eligibility Criteria
De novo mCSPC
Distant metastatic disease by ≥ 1 lesion on bone scan and/or CT scan
ECOG PS 0 -2

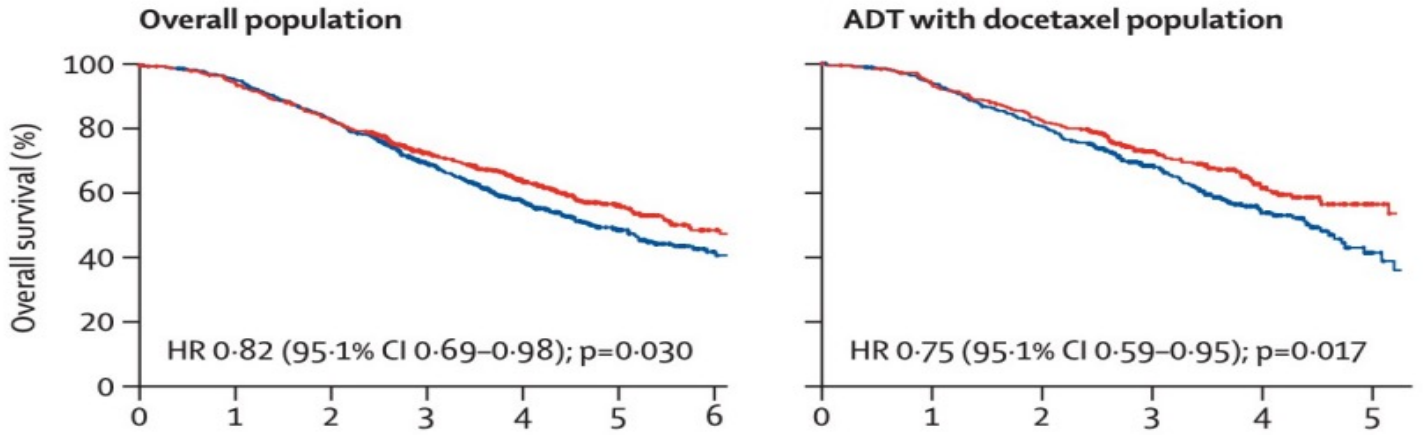
On-Study Requirement
Continuous ADT

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



Fizazi et al (2022) *Lancet* https://doi.org/10.1016/ S0140-6736(22)00367-1

August 5, 2022

FDA approves darolutamide tablets for metastatic hormone-sensitive prostate cancer

Efficacy was based on ARASENS (NCT02799602), a randomized, multicenter, double-blind, placebo-controlled clinical trial in 1306 patients with mHSPC. Patients were randomized to receive either darolutamide 600 mg orally twice daily plus docetaxel 75 mg/m^2 intravenously administered every 3 weeks for up to 6 cycles or docetaxel plus placebo. All patients received a gonadotropin-releasing hormone analog concurrently or had a bilateral orchiectomy.

ARASENS Study

ASCO Genitourinary Cancers Symposium

Overall survival with darolutamide versus placebo in combination with androgen-deprivation therapy and docetaxel for metastatic hormone-sensitive prostate cancer in the phase 3 ARASENS trial

Matthew R. Smith, MD, PhD,[1] Maha Hussain, MD,[2] Fred Saad, MD,[3] Karim Fizazi, MD, PhD,[4] Cora N. Sternberg, MD,[5] E. David Crawford, MD,[6] Evgeny Kopyltsov, MD,[7] Chandler H. Park, MD,[8] Boris Alekseev, MD,[9] Álvaro Montesa Pino, MD,[10] Dingwei Ye, MD,[11] Francis Parnis, MB, BS,[12] Felipe Melo Cruz, MD,[13] Teuvo L.J. Tammela, MD, PhD,[14] Hiroyoshi Suzuki, MD, PhD,[15] Heikki Joensuu, MD,[16] Silke Thiele, MD,[17] Rui Li, MS,[18] Iris Kuss, MD,[17] Bertrand Tombal, MD, PhD[19]

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Darolutamide and Survival in Metastatic, Hormone-Sensitive Prostate Cancer

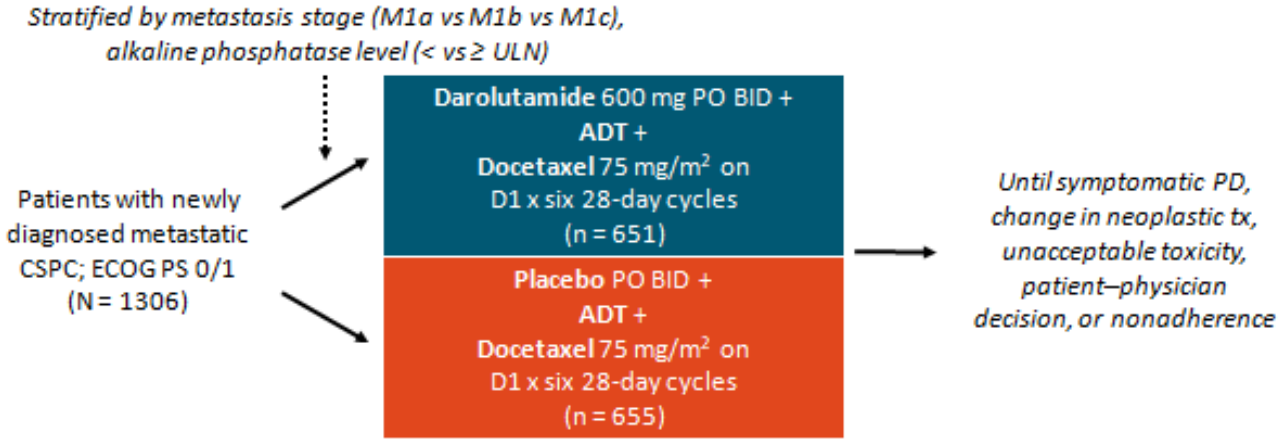
Matthew R. Smith, M.D., Ph.D., Maha Hussain, M.D., Fred Saad, M.D., Karim Fizazi, M.D., Ph.D., Cora N. Sternberg, M.D., E. David Crawford, M.D., Evgeny Kopyltsov, M.D., Chandler H. Park, M.D., Boris Alekseev, M.D., Álvaro Montesa-Pino, M.D., Dingwei Ye, M.D., Francis Parnis, M.B., B.S., Felipe Cruz, 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*

March 24, 2022
N Engl J Med 2022; 386:1132-1142
DOI: 10.1056/NEJMoa2119115

ARASENS

ARASENS: Darolutamide vs Placebo in Combination With ADT + Docetaxel in mCSPC

- International, randomized, double-blind phase III trial in 286 sites across 23 countries

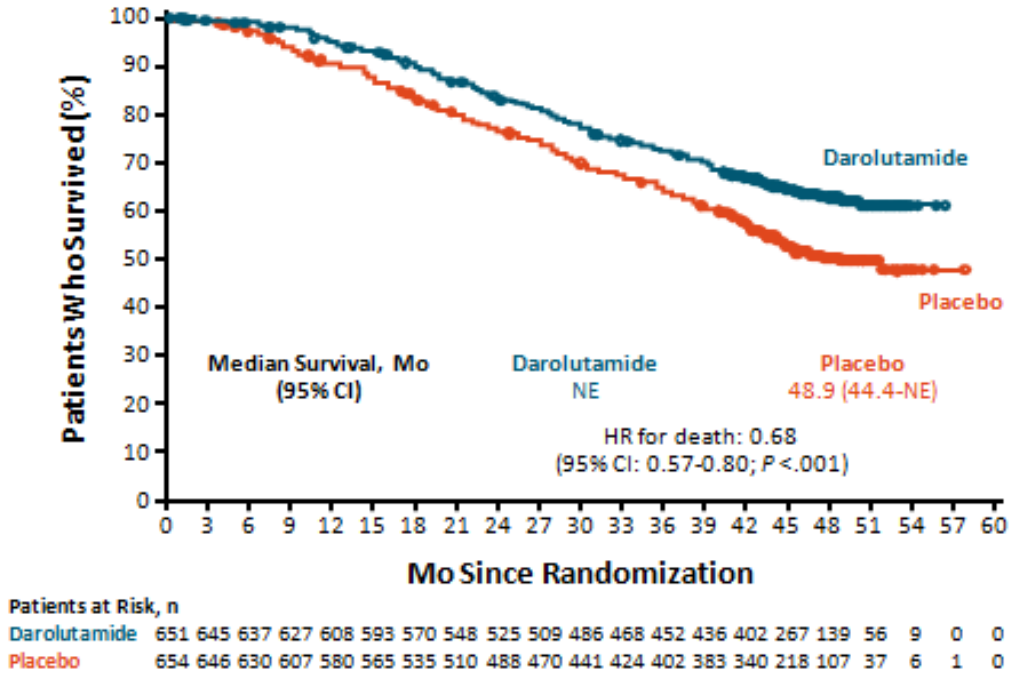


- **Primary endpoint:** OS
- **Secondary endpoints tested hierarchically in this order:** time to CRPC, time to pain progression, SSE-free survival, time to first SSE, time to initiation of subsequent anticancer therapy, time to worsening of physical symptoms, time to first opioid use, safety

Smith. NEJM. 2022;[Epub]. Smith. ASCO GU 2022. Abstr 13. NCT02799602.

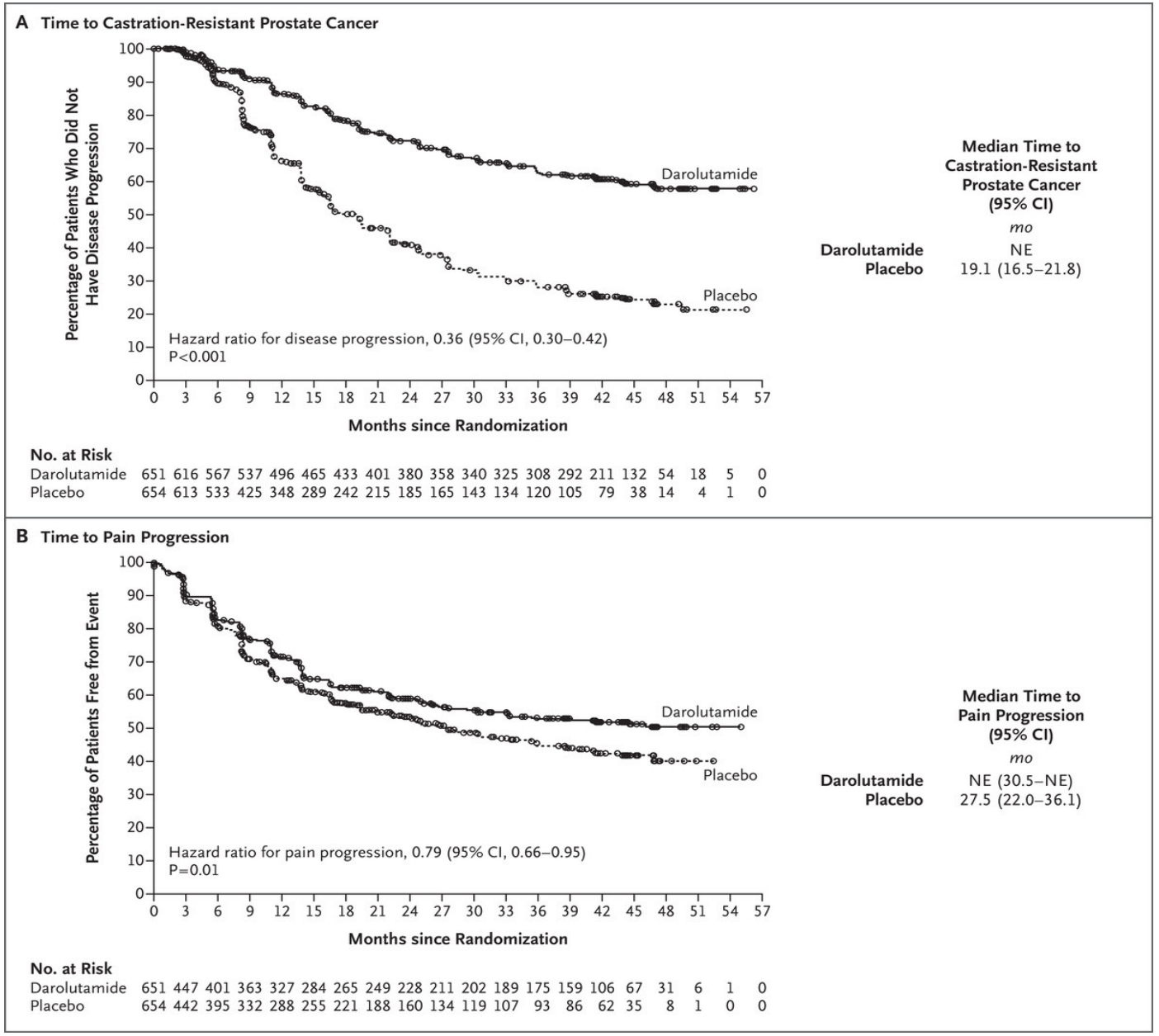
Overall Survival

ARASENS: OS (Primary Endpoint)



- Addition of darolutamide to ADT + docetaxel significantly reduced risk of death by 32.5% vs placebo (*P* <.001)
  - 75.6% of patients in placebo arm received subsequent life-prolonging systemic tx
- OS benefit observed across most subgroups
  - HR (95%) for those stratified by metastatic stage at initial dx: M1, 0.707 (0.590-0.848); M0, 0.605 (0.348-1.052)

Smith. NEJM. March 2023


A Time to Castration-Resistant Prostate Cancer
Percentage of Patients Who Did Not Have Disease Progression
Darolutamide
Placebo
Hazard ratio for disease progression, 0.36 (95% CI, 0.30–0.42)
P<0.001
Months since Randomization
No. at Risk
Darolutamide 651 616 567 537 496 465 433 401 380 358 340 325 308 292 211 132 54 18 5 0
Placebo 654 613 533 425 348 289 242 215 185 165 143 134 120 105 79 38 14 4 1 0
Median Time to Castration-Resistant Prostate Cancer (95% CI)
mo
Darolutamide NE
Placebo 19.1 (16.5–21.8)
B Time to Pain Progression
Percentage of Patients Free from Event
Darolutamide
Placebo
Hazard ratio for pain progression, 0.79 (95% CI, 0.66–0.95)
P=0.01
Months since Randomization
No. at Risk
Darolutamide 651 447 401 363 327 284 265 249 228 211 202 189 175 159 106 67 31 6 1 0
Placebo 654 442 395 332 288 255 221 188 160 134 119 107 93 86 62 35 8 1 0 0
Median Time to Pain Progression (95% CI)
mo
Darolutamide NE (30.5–NE)
Placebo 27.5 (22.0–36.1)

Adverse Events

Selected Grade 3/4 AE, n (%)	Darolutamide + ADT + Docetaxel (n = 652)	Placebo + ADT + Docetaxel (n = 650)
Neutropenia	220 (33.7)	222 (34.2)
Febrile neutropenia	51 (7.8)	48 (7.4)
Hypertension	42 (6.4)	21 (3.2)
Anemia	31 (4.8)	33 (5.1)
Pneumonia	21 (3.2)	20 (3.1)
Hyperglycemia	18 (2.8)	24 (3.7)
Increased ALT	18 (2.8)	11 (1.7)
Increased AST	17 (2.6)	7 (1.1)
Increased weight	14 (2.1)	8 (1.2)
UTI	13 (2.0)	12 (1.8)

Safety Outcome, n (%)	Darolutamide + ADT + Docetaxel (n = 652)	Placebo + ADT + Docetaxel (n = 650)
Any AE	649 (99.5)	643 (98.9)
Serious AE	292 (44.8)	275 (42.3)
AE leading to permanent d/c of trial agent		
▪ Darolutamide or placebo	88 (13.5)	69 (10.6)
▪ Docetaxel	52 (8.0)	67 (10.3)

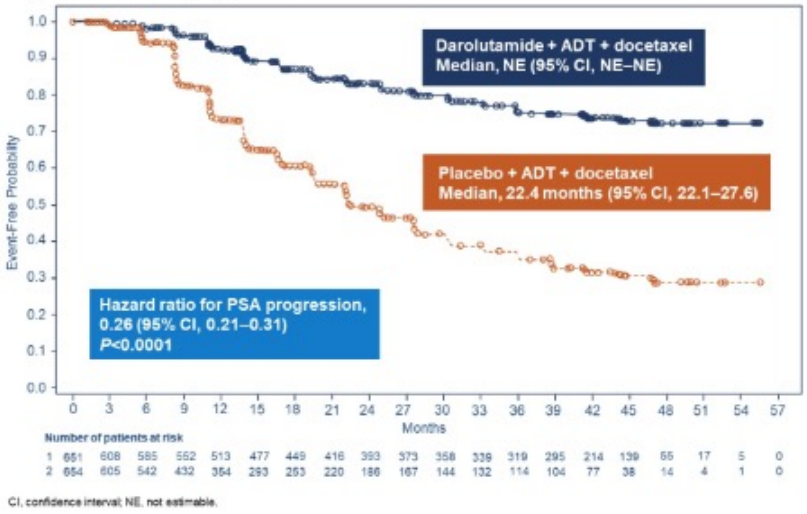
Smith. NEJM. March 2023

ARASENS Update ASCO 2022

RESULTS (cont'd)

- Darolutamide significantly prolonged time to PSA progression versus placebo (HR 0.26; 95% CI 0.21–0.31; *P* <0.0001) (**Figure 1**)

Figure 1. Time to PSA progression



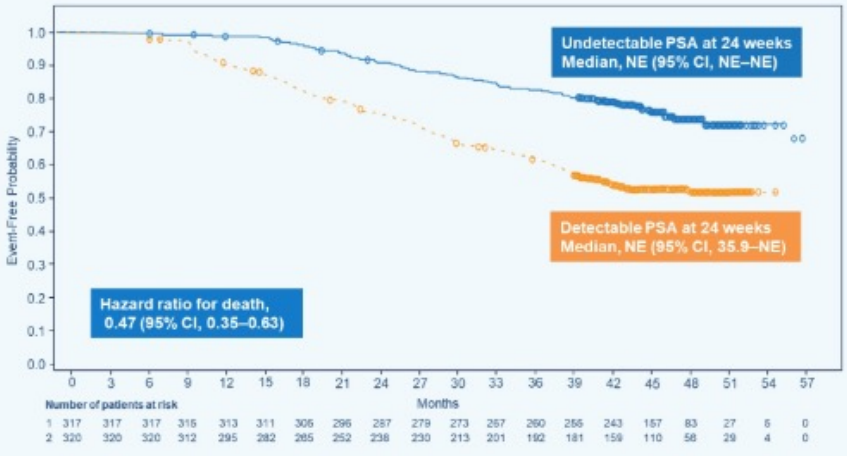
CI, confidence interval; NE, not estimable.

- Incidences of adverse events (AEs) were generally similar in patients achieving and not achieving undetectable PSA and by treatment groups, with a higher rate of drug discontinuations due to AEs among patients who did not achieve undetectable PSA at any time (**Table 2**)

Overall survival was improved for patients who achieved undetectable PSA

- Among darolutamide-treated patients, achievement of undetectable PSA at 24 and 36 weeks was associated with improved OS; risk reductions of death were 53% and 63%, respectively, by stratified Cox regression

Darolutamide + ADT + docetaxel



Saad et al. ASCO 2022 J Clin Oncol 40, 2022 (suppl 16; abstr 5078)

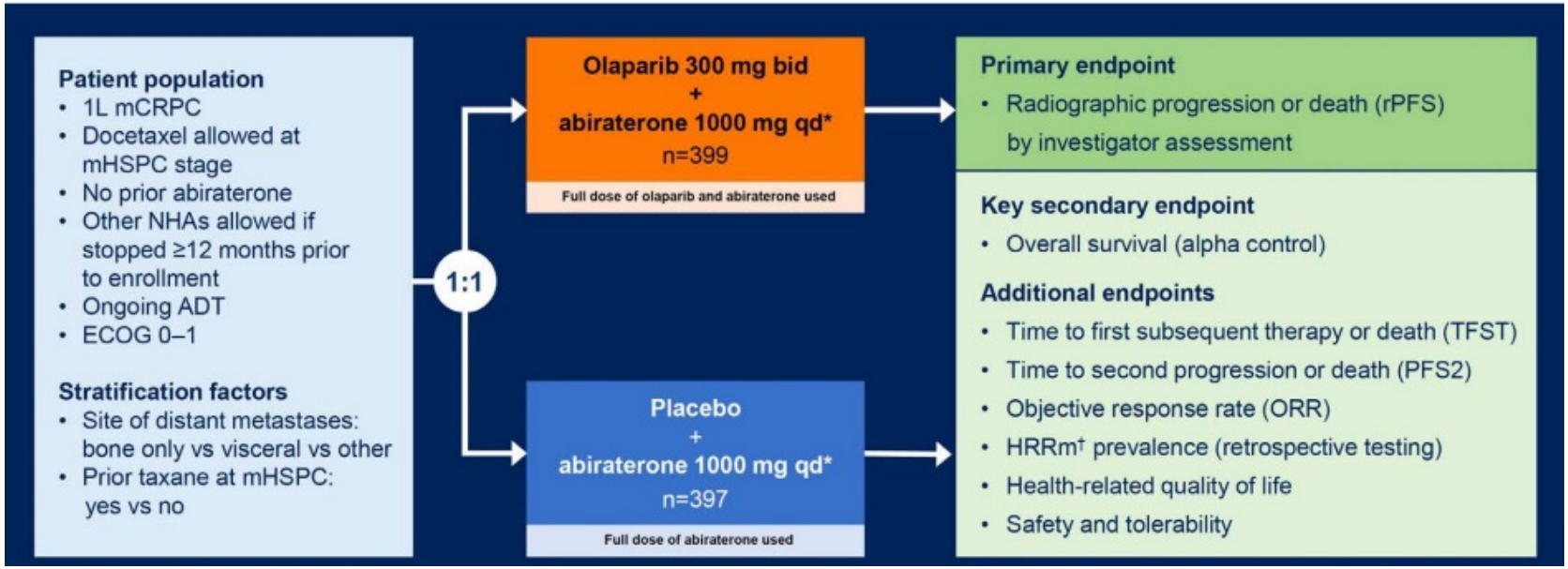
ARASENS Conclusion

- Darolutamide, Docetaxel, and ADT significantly increased OS vs placebo + ADT + docetaxel in patients with metastatic castrate sensitive prostate cancer
- Median OS: NE vs 48.9 mo (HR: 0.68; 95% CI: 0.57-0.80; *P* <.001)
- Adverse events comparable between arms,
- Every patient with metastatic hormone sensitive prostate adenocarcinoma should receive androgen pathway inhibitor with ADT at a bare minimum.
- Consider Darolutamide, Docetaxel, and ADT as new standard of care for mHSPC

Metastatic Castrate Resistant Prostate Cancer

PROpel Study

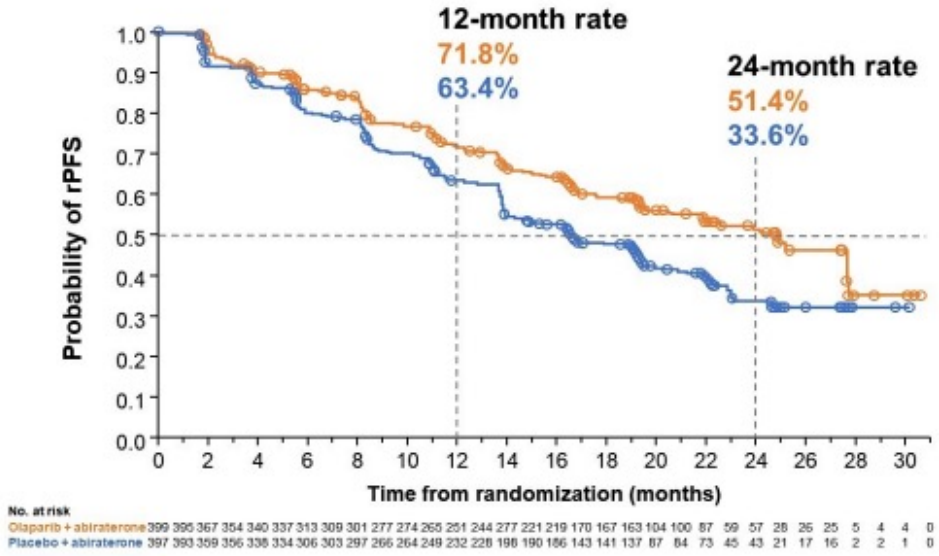
PROpel Study



Saad F et al. Genitourinary Cancers Symposium 2022;Abstract 11.

PROpel study

34% risk reduction of progression or death with olaparib + abiraterone



	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

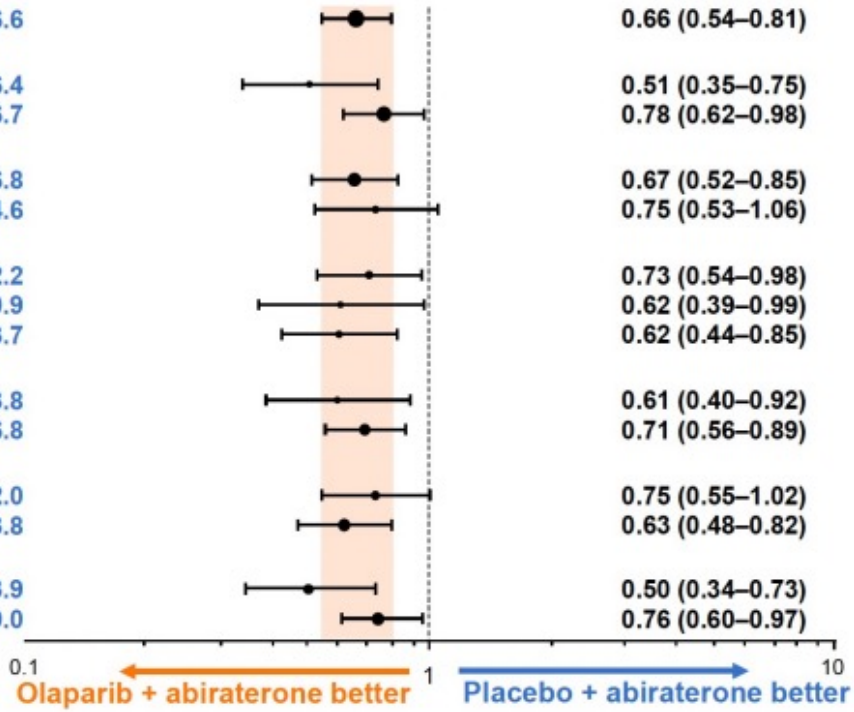
Median rPFS improvement of 8.2 months favors olaparib + abiraterone*

Events: 394; Maturity 49.5%
*In combination with prednisone or prednisolone
CI, confidence interval; HR, hazard ratio.

Saad F et al. Genitourinary Cancers Symposium 2022;Abstract 11.

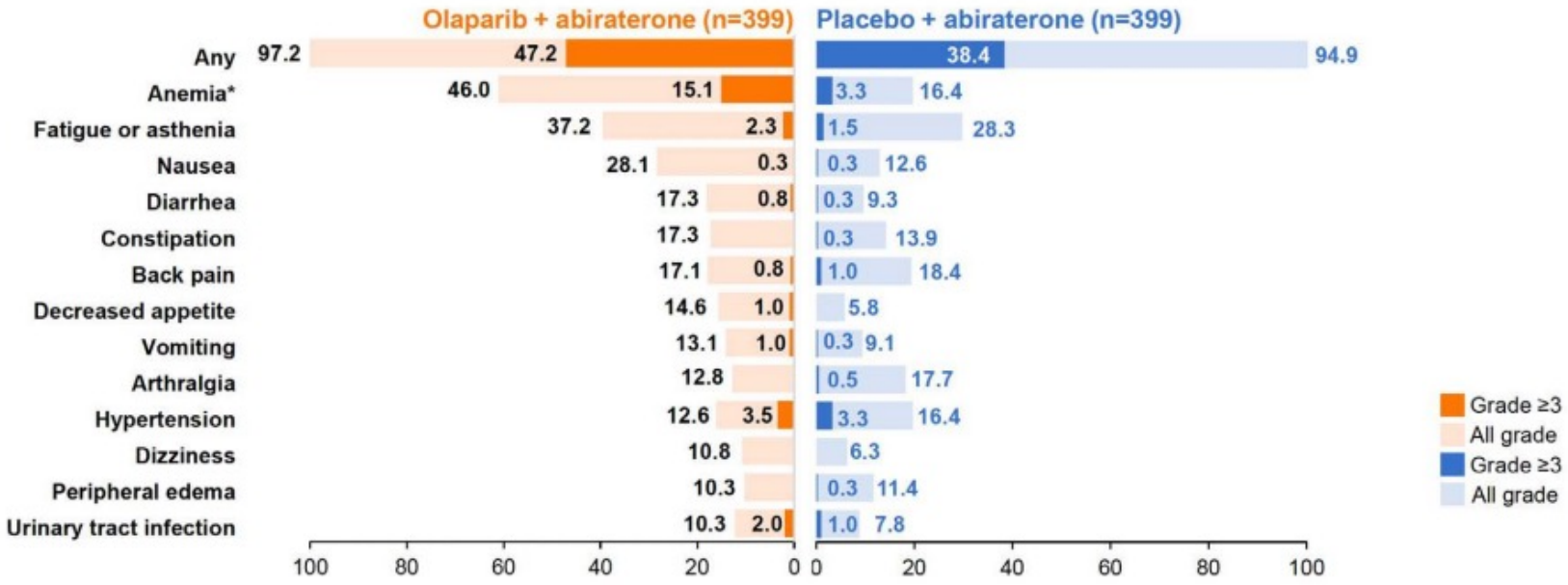
PROpel Study

	Number of patients, n	Median rPFS, months		HR (95% CI)
All patients	796	24.8	16.6	0.66 (0.54–0.81)
Age at randomization				
<65	227	NR	16.4	0.51 (0.35–0.75)
≥65	569	22.0	16.7	0.78 (0.62–0.98)
ECOG performance status at baseline				
0	558	24.9	16.8	0.67 (0.52–0.85)
1	236	17.5	14.6	0.75 (0.53–1.06)
Site of distant metastases				
Bone only	434	27.6	22.2	0.73 (0.54–0.98)
Visceral	105	13.7	10.9	0.62 (0.39–0.99)
Other	257	20.5	13.7	0.62 (0.44–0.85)
Docetaxel treatment at mHSPC stage				
Yes	189	27.6	13.8	0.61 (0.40–0.92)
No	607	24.8	16.8	0.71 (0.56–0.89)
Baseline PSA				
Below median baseline PSA	396	25.2	22.0	0.75 (0.55–1.02)
Above or equal to median baseline PSA	397	18.5	13.8	0.63 (0.48–0.82)
HRRm status*				
HRRm	226	NR	13.9	0.50 (0.34–0.73)
Non-HRRm	552	24.1	19.0	0.76 (0.60–0.97)



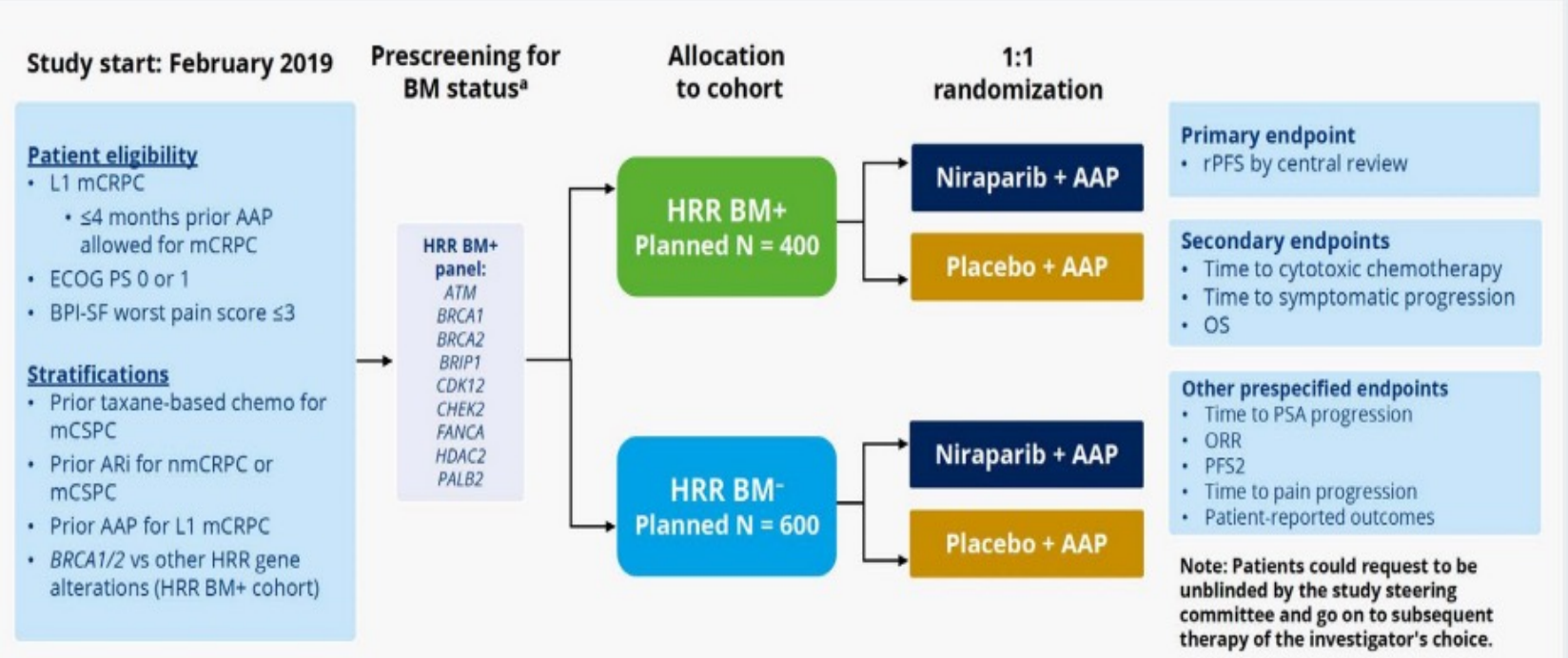
Saad F et al. Genitourinary Cancers Symposium 2022;Abstract 11.

PROpel Study



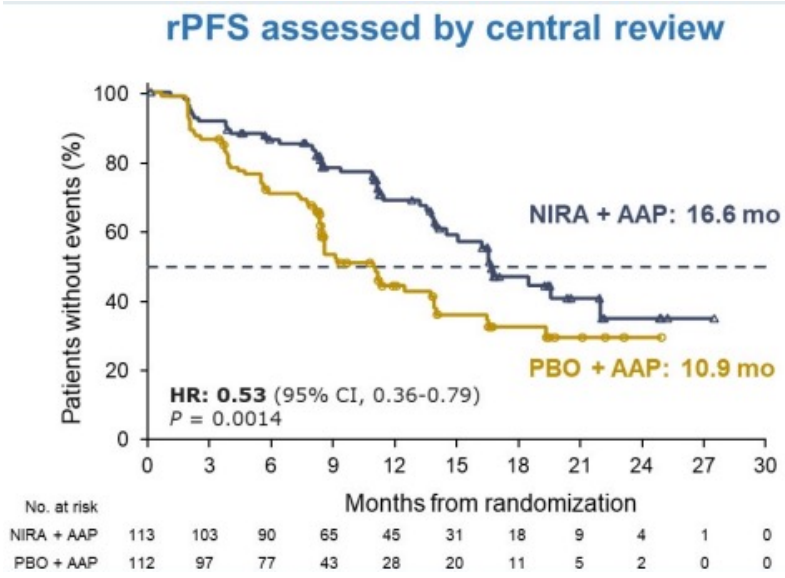
Saad F et al. Genitourinary Cancers Symposium 2022;Abstract 11.

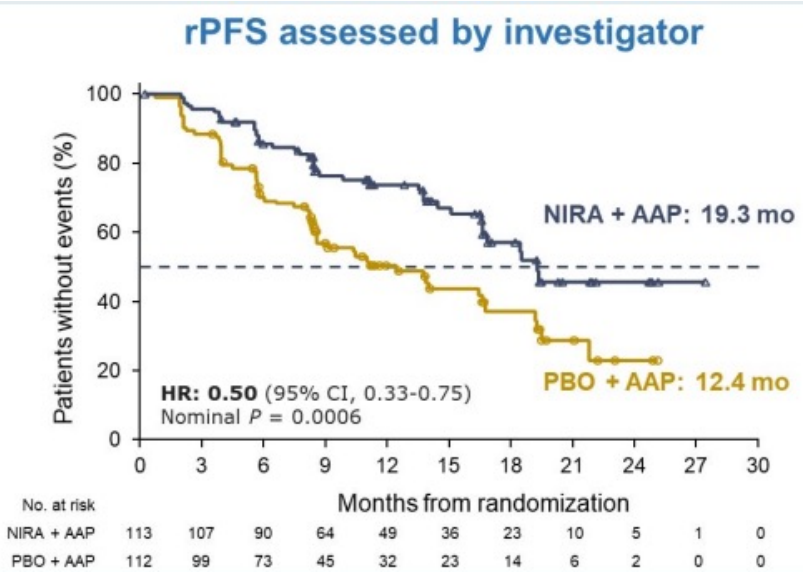
Magnitude Study



Chi et al Journal of Clinical Oncology 40, no. 6_suppl (February 20, 2022) 12-12.

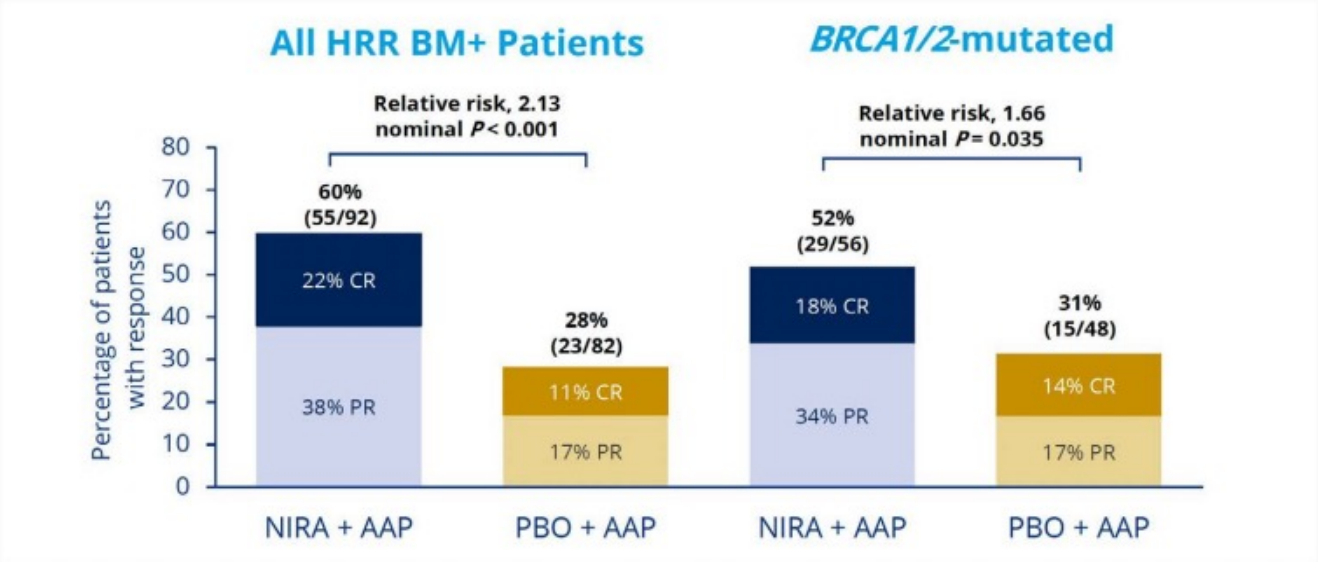
Magnitude study





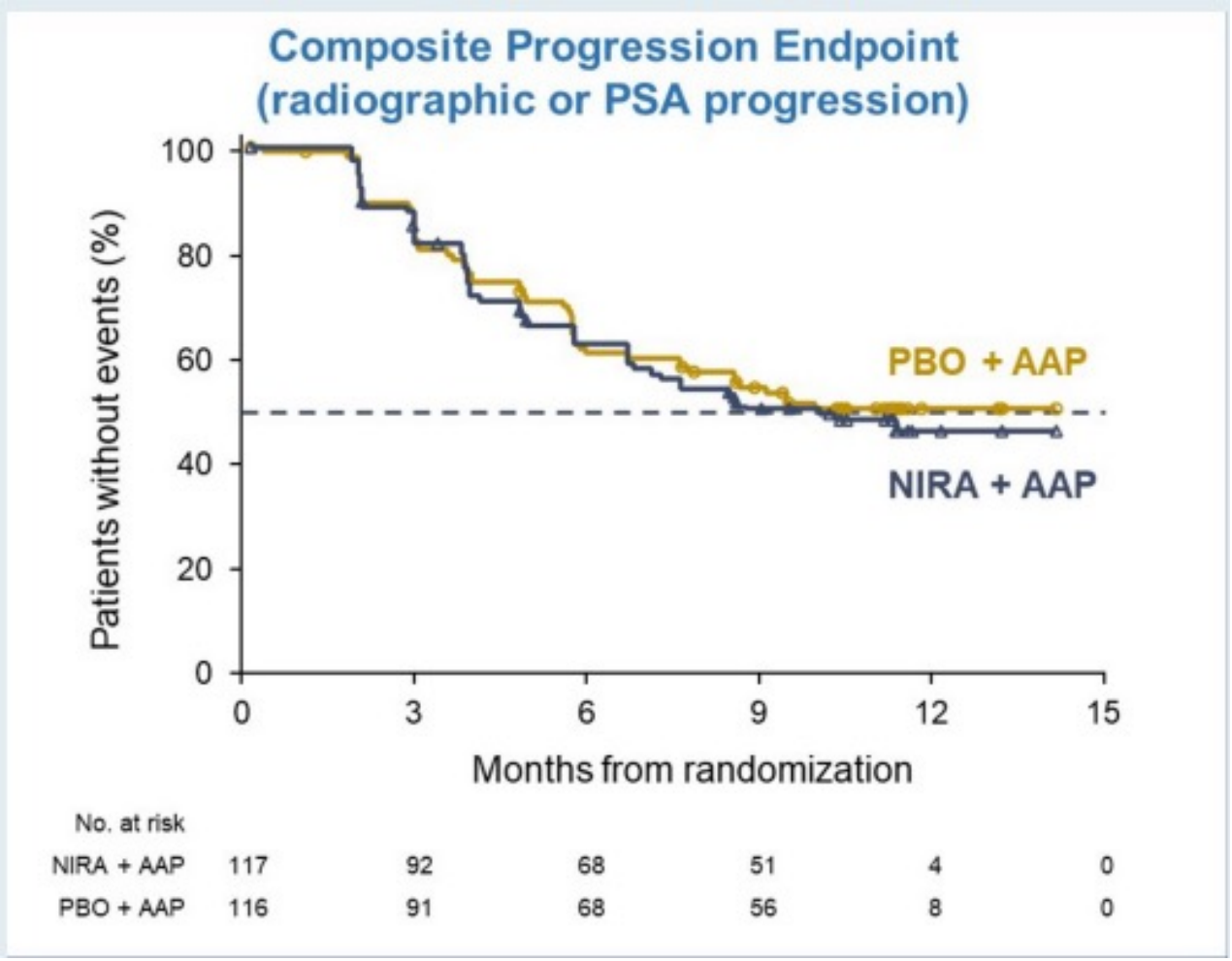
Chi et al Journal of Clinical Oncology *40, no. 6_suppl (February 20, 2022) 12-12.*

Magnitude Study



Chi et al Journal of Clinical Oncology 40, no. 6_suppl (February 20, 2022) 12-12.

MAGNITUDE study (HRR-)



Chi et al Journal of Clinical Oncology *40, no. 6_suppl (February 20, 2022) 12-12.*

PARP + Abiraterone Take Home

- **PROpel**
  - rPFS benefit for olaparib + Abi/Pred vs placebo + Abi/Pred in overall population
  - (24.8 vs 16.6 mo; HR: 0.66; *P* <.0001)
  - Patients were not stratified by HRR status
- **MAGNITUDE Study**
  - rPFS benefit for niraparib + Abi/Pred vs placebo + Abi/Pred
  - Patients with HRR alterations (16.5 vs 13.7 mo; HR: 0.53; *P* = .0014)
  - No benefit in HRRmut -ve cohort

My practice

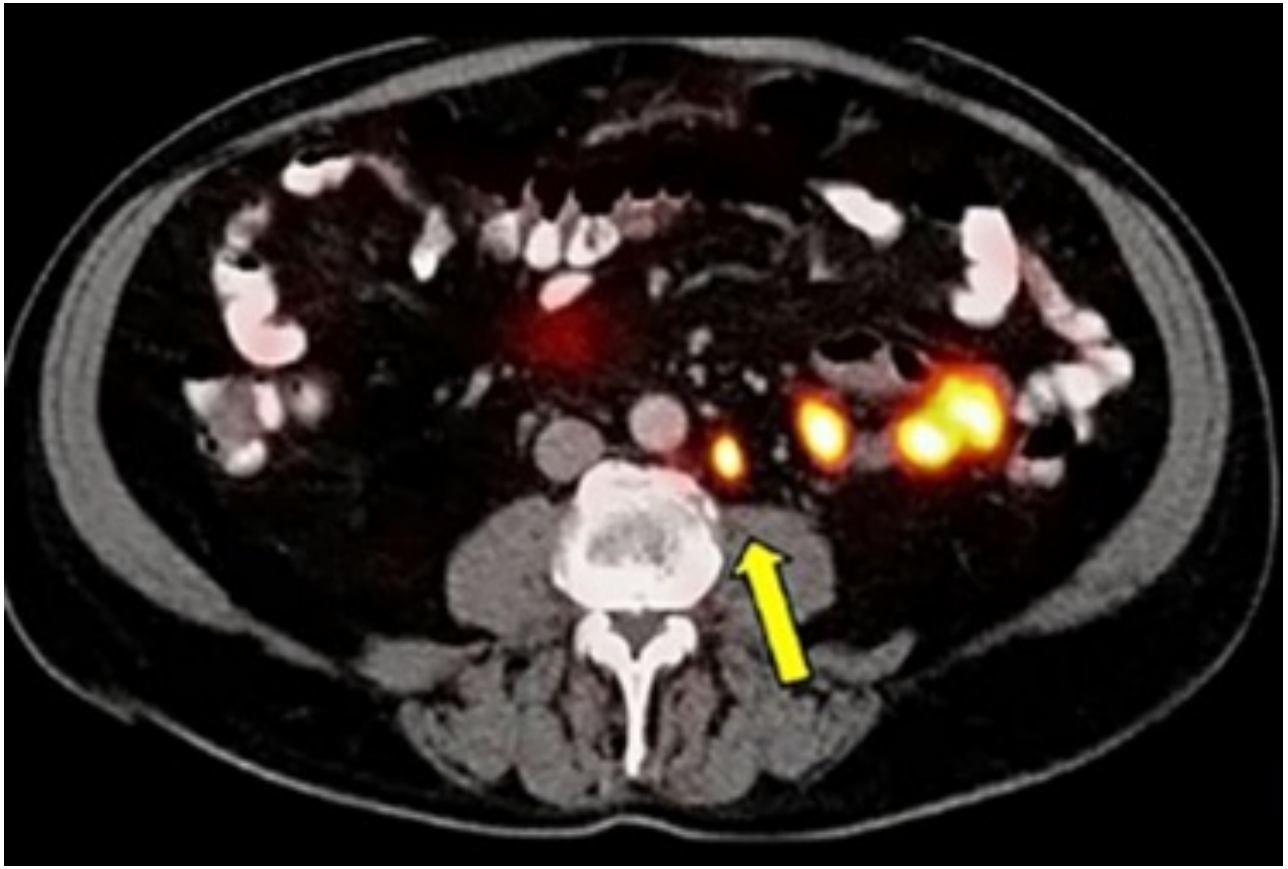
- I would consider PARP + Abiraterone + ADT for patients with metastatic castrate resistant prostate cancer with BRCA2 mutation
- Will await follow up studies with Enzalutamide + Rucaparib (CASPAR trial) since there appears to be discordance with MAGNITUDE and PROpel for unselected patients

SYSTEMIC THERAPY FOR M1 CRPC: ADENOCARCINOMA[ddd,ggg,hhh]

No prior docetaxel/no prior novel hormone therapy[iii]	Prior novel hormone therapy/No prior docetaxel[iii,ooo]
• Preferred regimens ▸ Abiraterone[t,jjj] (category 1[kkk]) ▸ Docetaxel[yy,lll] (category 1) ▸ Enzalutamide[t] (category 1) • Useful in certain circumstances ▸ Radium-223[nnn] for symptomatic bone metastases (category 1) ▸ Sipuleucel-T[yy,mmm] (category 1) • Other recommended regimens ▸ Other secondary hormone therapy[t]	• Preferred regimens ▸ Docetaxel (category 1)[yy] ▸ Sipuleucel-T[yy,mmm] • Useful in certain circumstances ▸ Cabazitaxel/carboplatin[yy,fff] ▸ Olaparib for HRRm (category 1)[ppp] ▸ Pembrolizumab for MSI-H, dMMR, or TMB ≥10 mut/Mb[yy] ▸ Radium-223[nnn] for symptomatic bone metastases (category 1) ▸ Rucaparib for BRCAm[qqq] • Other recommended regimens ▸ Abiraterone[t,jjj] ▸ Abiraterone + dexamethasone[jjj,rrr] ▸ Enzalutamide[t] ▸ Other secondary hormone therapy[t]
Prior docetaxel/no prior novel hormone therapy[iii]	**Prior docetaxel and prior novel hormone therapy[iii,ooo]**
• Preferred regimens ▸ Abiraterone[t,jjj] (category 1) ▸ Cabazitaxel[yy] ▸ Enzalutamide[t] (category 1) • Useful in certain circumstances ▸ Cabazitaxel/carboplatin[yy,fff] ▸ Mitoxantrone for palliation in symptomatic patients who cannot tolerate other therapies[yy] ▸ Pembrolizumab for MSI-H, dMMR, or TMB ≥10 mut/Mb[yy] ▸ Radium-223[nnn] for symptomatic bone metastases (category 1) • Other recommended regimens ▸ Sipuleucel-T[yy,mmm] ▸ Other secondary hormone therapy[t]	• Useful in certain cicumstances ▸ Lutetium Lu 177 vipivotide tetraxetan (Lu-177–PSMA-617) for PSMA-positive metastases (category 1)[sss] (The following systemic therapies are category 2B if visceral metastases are present) • Preferred regimens ▸ Cabazitaxel[yy] (category 1[kkk]) ▸ Docetaxel rechallenge[yy] • Useful in certain circumstances ▸ Cabazitaxel/carboplatin[yy,fff] ▸ Mitoxantrone for palliation in symptomatic patients who cannot tolerate other therapies[yy] ▸ Olaparib for HRRm (category 1[kkk])[ppp] ▸ Pembrolizumab for MSI-H, dMMR, or TMB ≥10 mut/Mb[yy] ▸ Radium-223[nnn] for symptomatic bone metastases (category 1[kkk]) ▸ Rucaparib for BRCAm[qqq] • Other recommended regimens ▸ Abiraterone[t,jjj] ▸ Enzalutamide[t] ▸ Other secondary hormone therapy[t]

See Footnotes for Systemic Therapy M1 CRPC (PROS-15A).

PSMA PET



March 23, 2022

FDA Approves 177Lu-PSMA-617 for Pretreated PSMA+ Metastatic Castration-Resistant Prostate Cancer

Phase III study of lutetium-177-PSMA-617 in patients with metastatic castration-resistant prostate cancer (VISION).

Michael J. Morris, Johann S. De Bono, Kim N. Chi, Karim Fizazi, Ken Herrmann, Kambiz Rahbar, Scott T. Tagawa, Luke T. Nordquist, Nitin Vaishampayan, Ghassan El-Haddad, Chandler H. Park, Tomasz M. Beer, Wendy J Pérez-Contreras, Michelle Desilvio, Euloge E. Kpamegan, Germo Gericke, Richard Adam Messmann, Bernd J. Krause, A. Oliver Sartor, on behalf of the VISION Trial Investigators

VISION Study

ORIGINAL ARTICLE

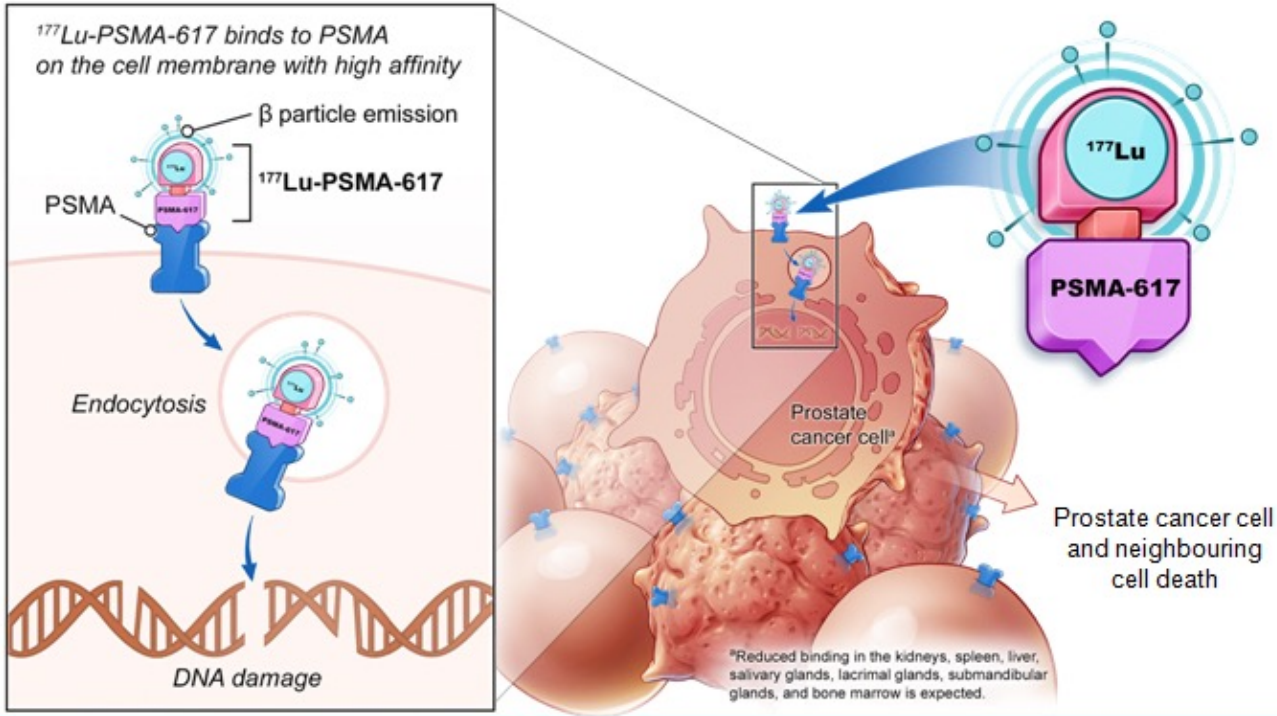
Lutetium-177–PSMA-617 for Metastatic Castration-Resistant Prostate Cancer

Oliver Sartor, M.D., Johann de Bono, M.B., Ch.B., Ph.D., Kim N. Chi, M.D., Karim Fizazi, M.D., Ph.D., Ken Herrmann, M.D., Kambiz Rahbar, M.D., Scott T. Tagawa, M.D., Luke T. Nordquist, M.D., Nitin Vaishampayan, M.D., Ghassan El-Haddad, M.D., Chandler H. Park, M.D., Tomasz M. Beer, M.D., et al., for the VISION Investigators*

September 16, 2021
N Engl J Med 2021; 385:1091-1103
DOI: 10.1056/NEJMoa2107322
Chinese Translation 中文翻译

Mechanism of Action

^{177}Lu-PSMA-617 targeted radioligand therapy



VISION Study

Open-label study of protocol-permitted standard of care ± ^{177}Lu-PSMA-617 in adults with PSMA-positive mCRPC

Eligible patients

- Previous treatment with <u>both</u>
  - ≥ 1 androgen receptor pathway inhibitor
  - 1 or 2 taxane regimens
- Protocol-permitted standard of care (SOC) planned before randomization
  - Excluding chemotherapy immunotherapy, radium-223, investigational drugs
- ECOG performance status 0–2
- Life expectancy > 6 months
- PSMA-positive mCRPC on PET/CT with ^{68}Ga-PSMA-11

2:1

Protocol-permitted SOC + ^{177}Lu-PSMA-617
7.4 GBq (200 mCi) every 6 weeks
4 cycles, increasable to 6

Protocol-permitted SOC alone

Treatment → Follow-up → Final analysis

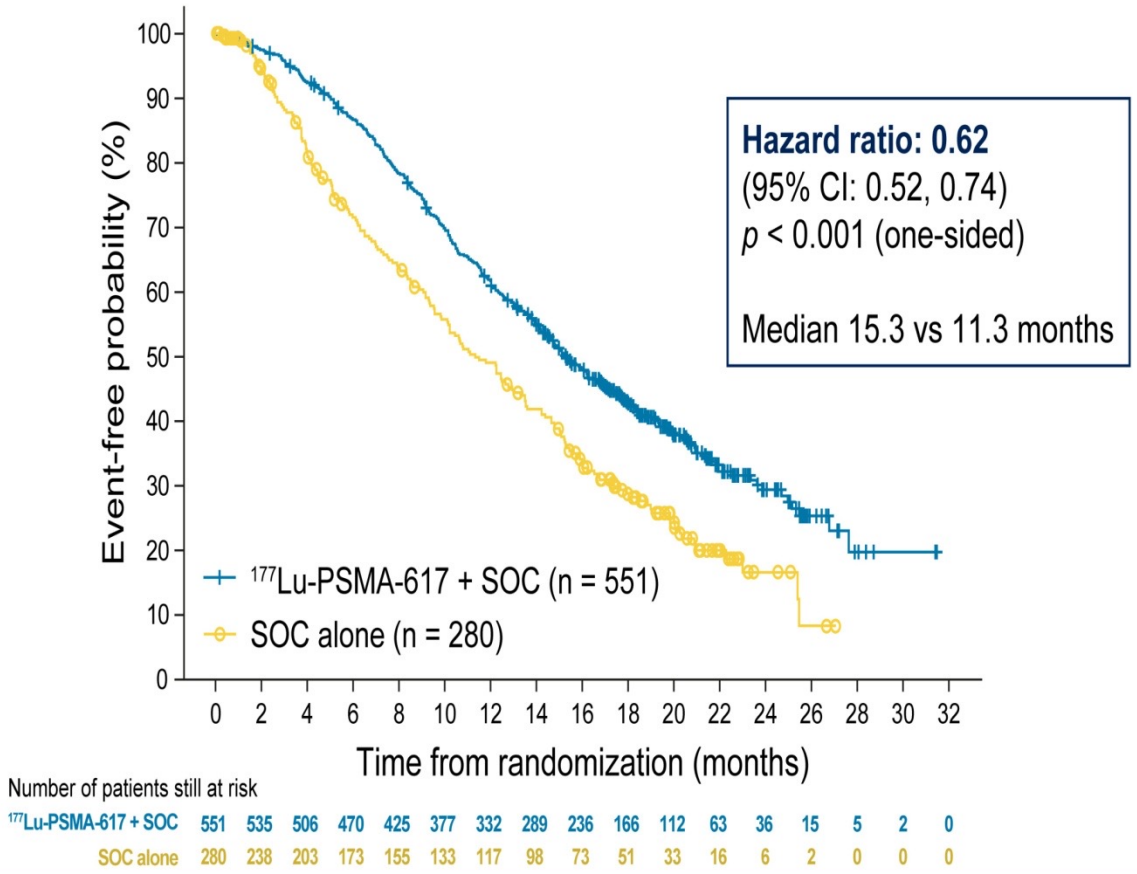
- Randomization stratified by
  - ECOG status (0–1 or 2)
  - LDH (high or low)
  - Liver metastases (yes or no)
  - Androgen receptor pathway inhibitors in SOC (yes or no)

- CT/MRI/bone scans
  - Every 8 weeks (treatment)
  - Every 12 weeks (follow-up)
  - Blinded independent central review

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

Primary analysis

All randomized patients
(N = 831)

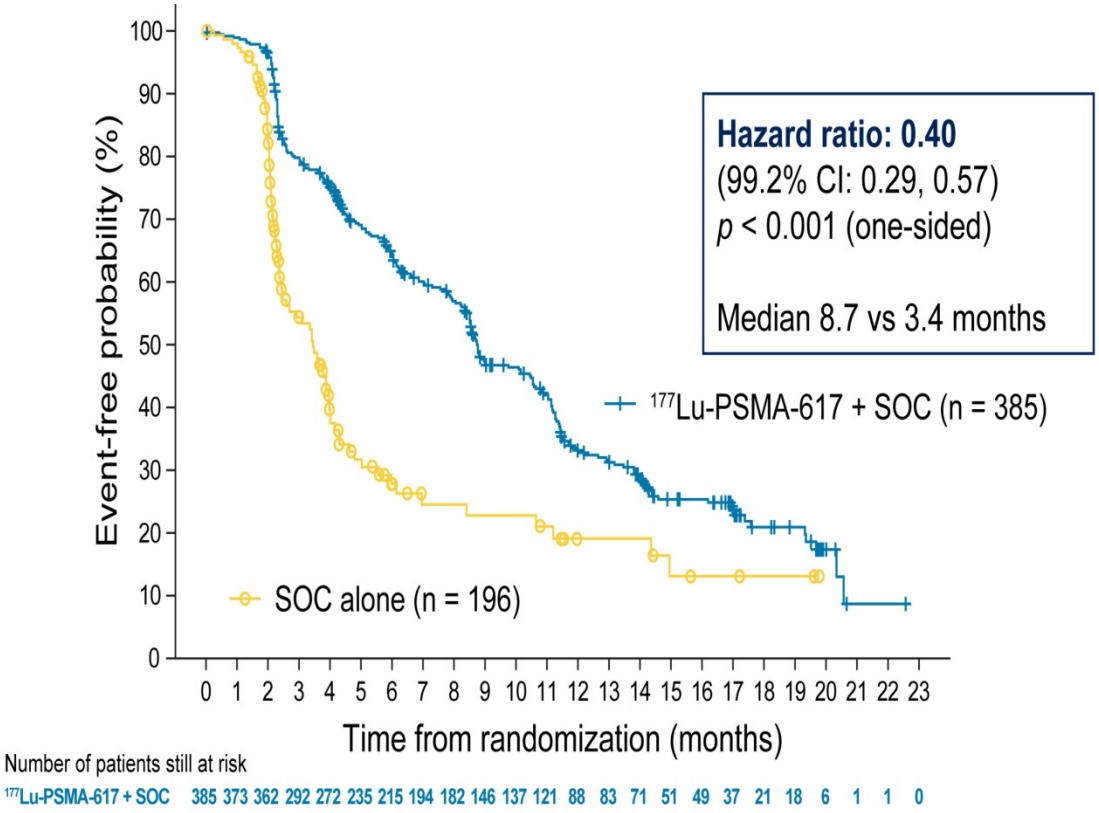


Morris MJ, ASCO 2021

Primary endpoints: ^{177}Lu-PSMA-617 improved rPFS

Primary analysis

rPFS analysis set (n = 581)



Morris MJ, ASCO 2021

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

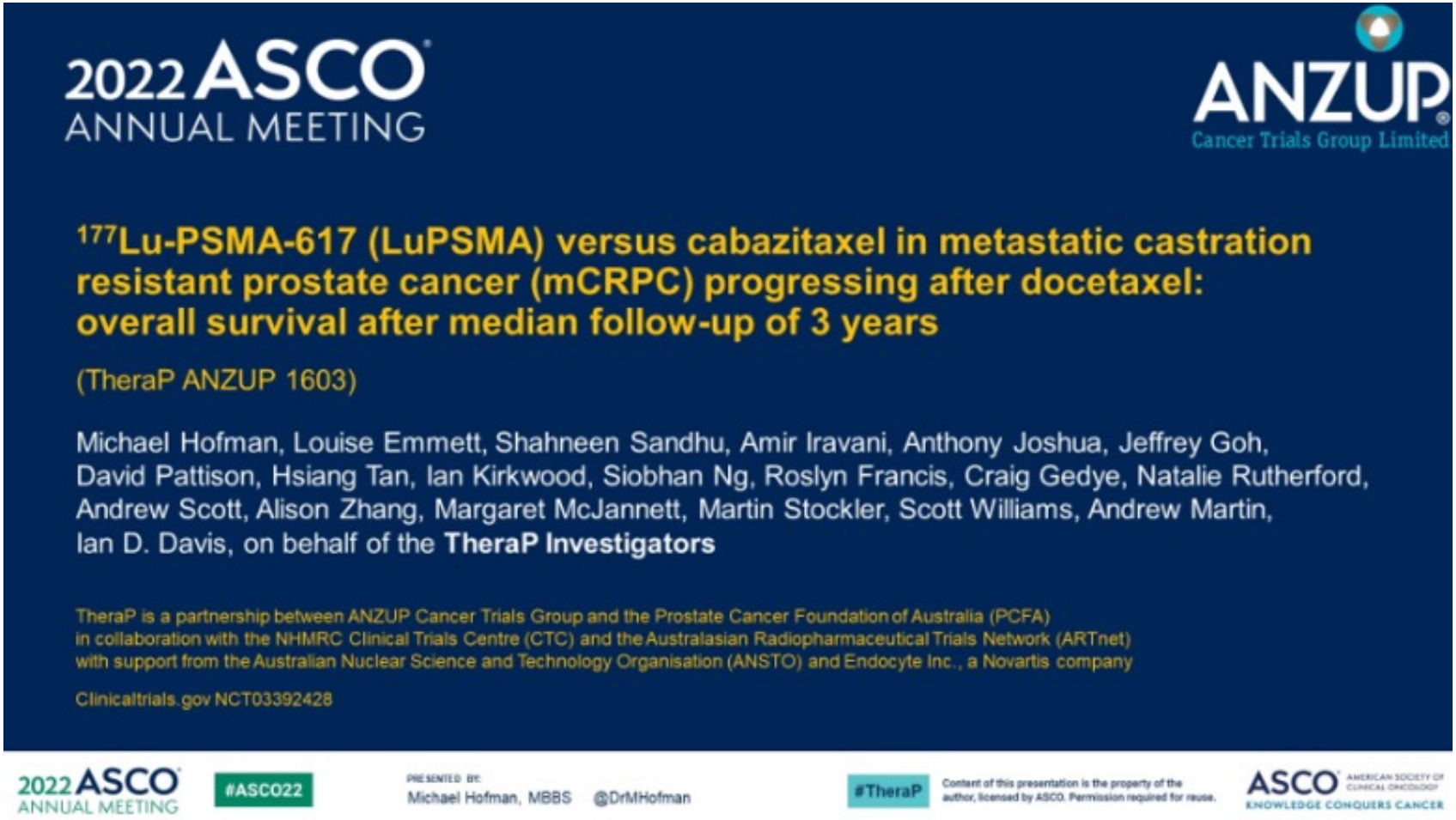
Patients, n (%)	All grades		Grade 3–5	
	^{177}Lu-PSMA-617 + SOC (n = 529)	SOC alone (n = 205)	^{177}Lu-PSMA-617 + SOC (n = 529)	SOC alone (n = 205)
Fatigue	260 (49.1)	60 (29.3)	37 (7.0)	5 (2.4)
Bone marrow suppression	251 (47.4)	36 (17.6)	124 (23.4)	14 (6.8)
Leukopenia	66 (12.5)	4 (2.0)	13 (2.5)	1 (0.5)
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 MJ, ASCO 2021

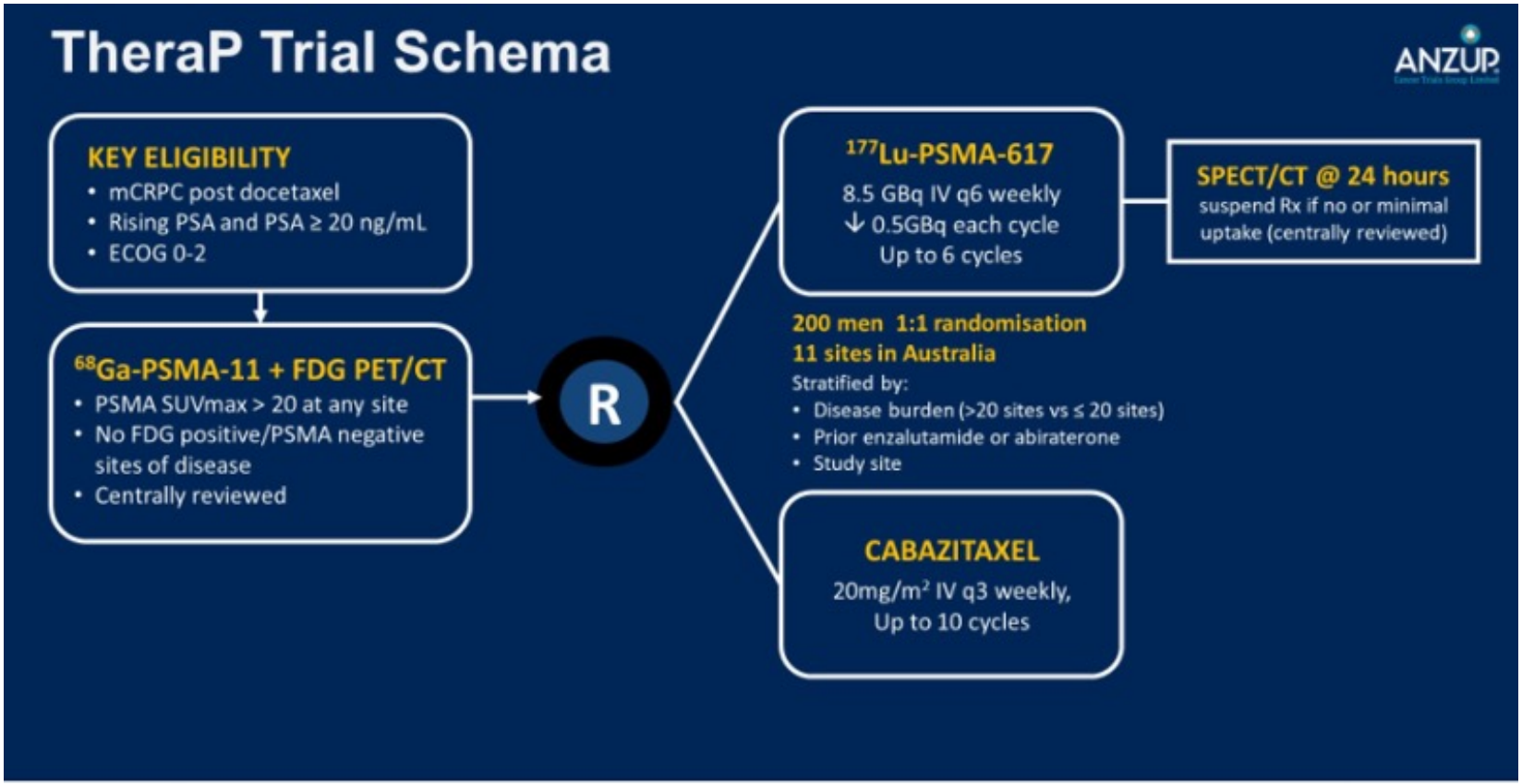
VISION study

- ^{177}Lu-PSMA-617 significantly prolonged vs standard care
- Imaging-based progression-free survival (median, 8.7 vs. 3.4 months; hazard ratio for progression or death, 0.40;)
- Overall survival (median, 15.3 vs. 11.3 months; hazard ratio for death, 0.62;)
- Next Question: ^{177}Lu-PSMA-617 vs Cabizitaxel.

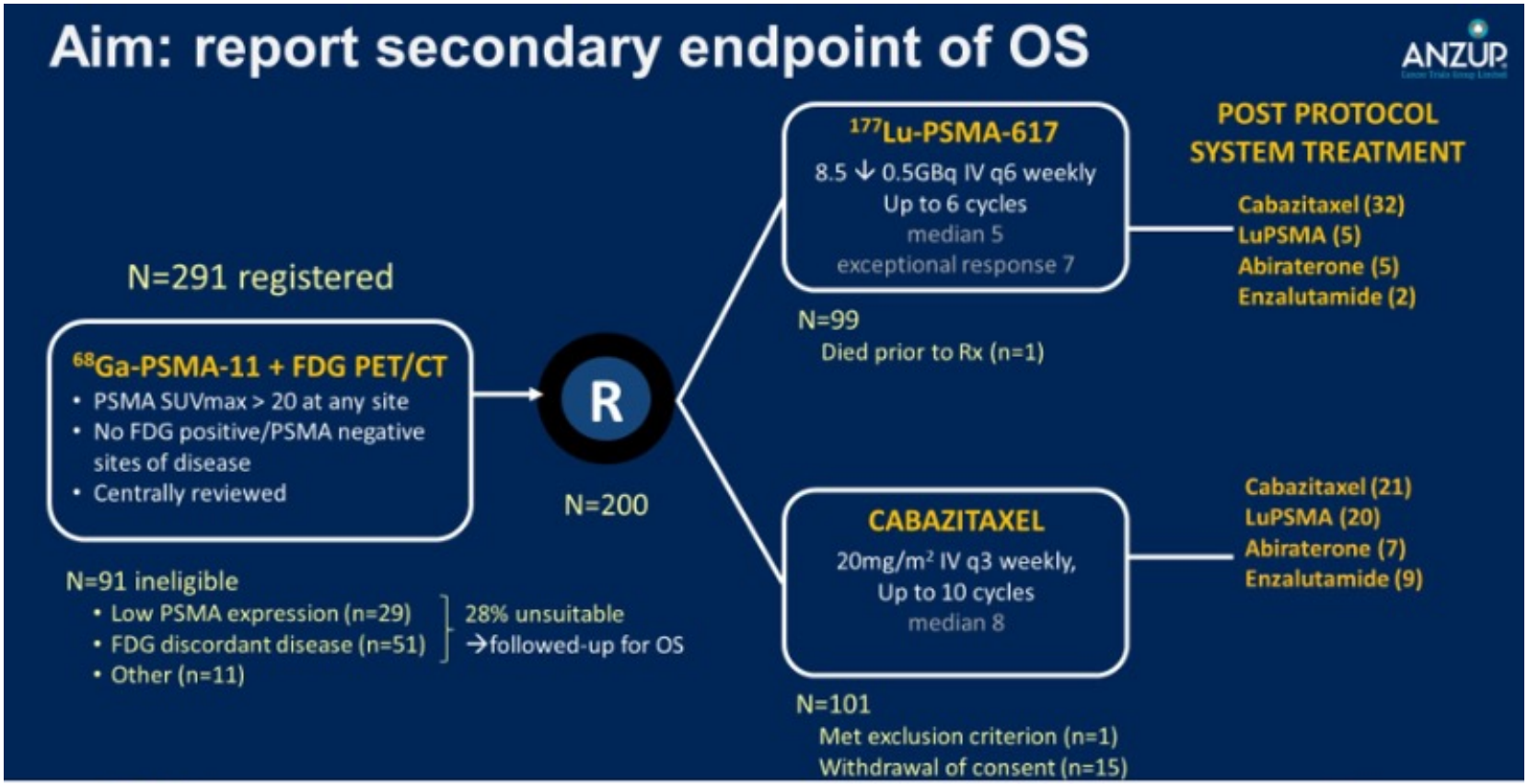
ASCO 2022 TheraP



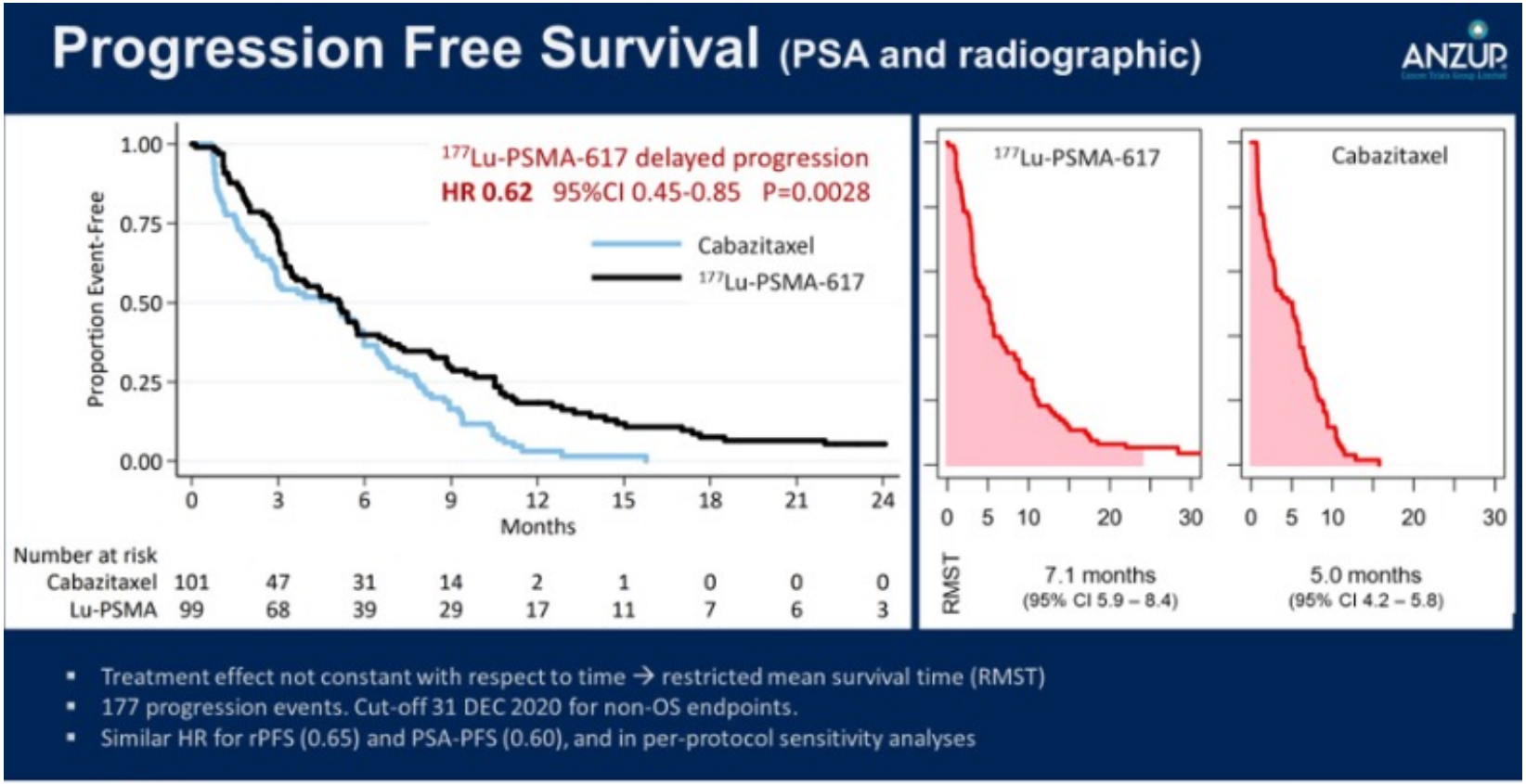
TheraP Trial Study Design



TheraP Study Design



TheraP


Progression Free Survival (PSA and radiographic)
ANZUP
Proportion Event-Free
1.00
0.75
0.50
0.25
0.00
177Lu-PSMA-617 delayed progression
HR 0.62 95%CI 0.45-0.85 P=0.0028
Cabazitaxel
177Lu-PSMA-617
0 3 6 9 12 15 18 21 24
Months
Number at risk
Cabazitaxel 101 47 31 14 2 1 0 0 0
Lu-PSMA 99 68 39 29 17 11 7 6 3
177Lu-PSMA-617
Cabazitaxel
0 5 10 20 30
RMST
7.1 months
(95% CI 5.9 – 8.4)
5.0 months
(95% CI 4.2 – 5.8)
Treatment effect not constant with respect to time → restricted mean survival time (RMST)
177 progression events. Cut-off 31 DEC 2020 for non-OS endpoints.
Similar HR for rPFS (0.65) and PSA-PFS (0.60), and in per-protocol sensitivity analyses
2022 ASCO ANNUAL MEETING
#ASCO22
PRESENTED BY:
Michael Hofman, MBBS @DrMHofman
#TheraP
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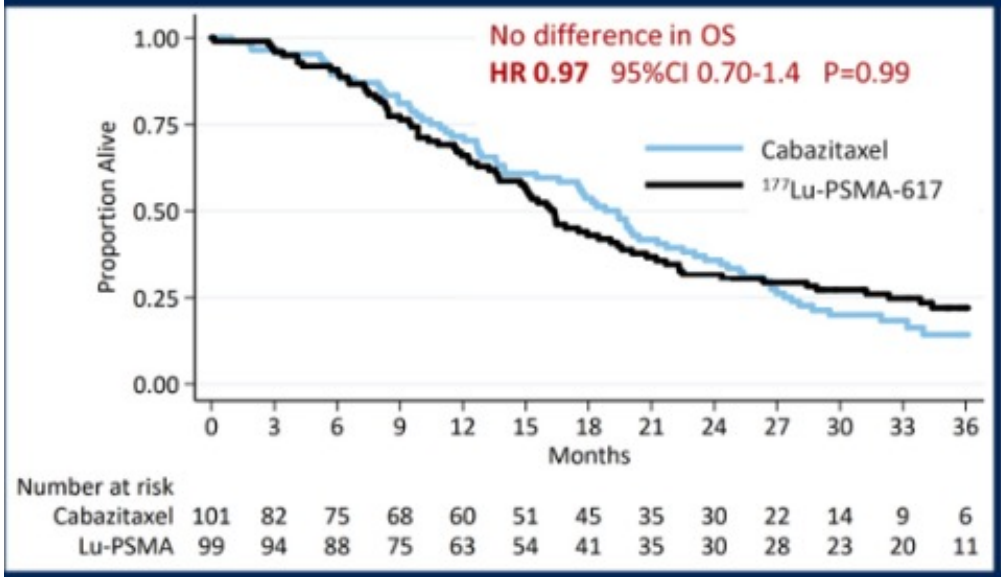
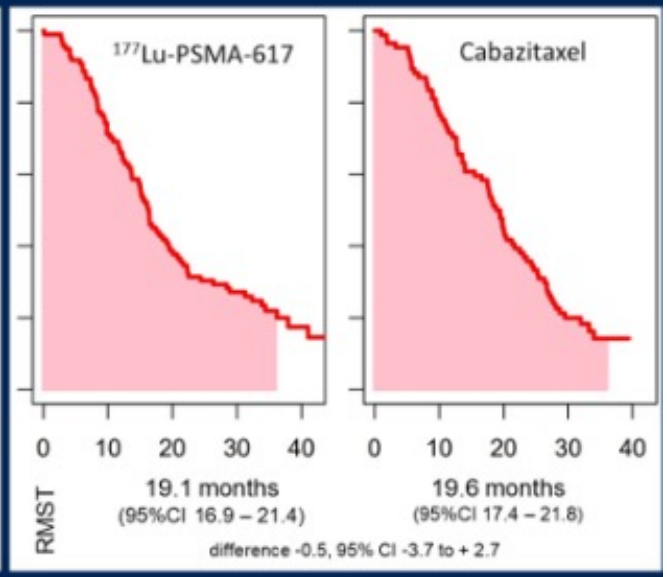
ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY
KNOWLEDGE CONQUERS CANCER
6

TheraP

Overall survival (ITT)

ANZUP

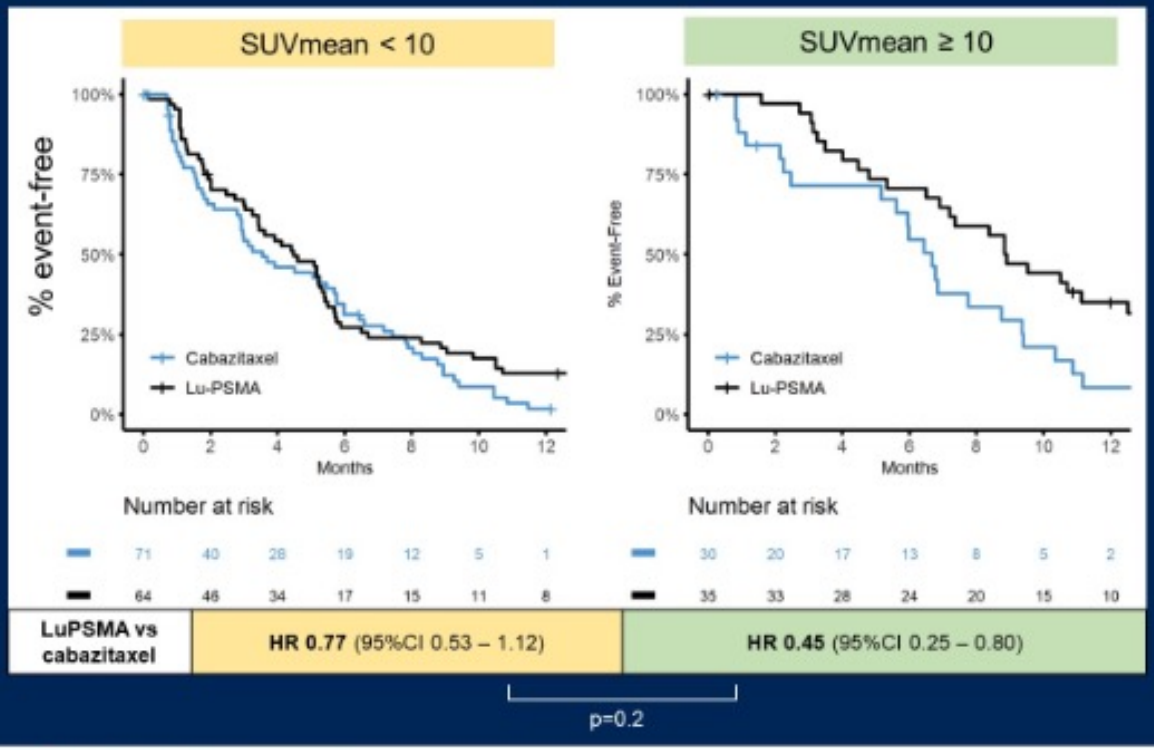




- Cut-off 31 DEC 2021 for OS
- At 36 months follow-up, death reported in 147/200; 70/101 assigned cabazitaxel vs. 77/99 assigned LuPSMA
- Per-protocol analysis: no difference in OS
- No additional safety signals with longer follow-up.

ASCO 2022: TheraP Study

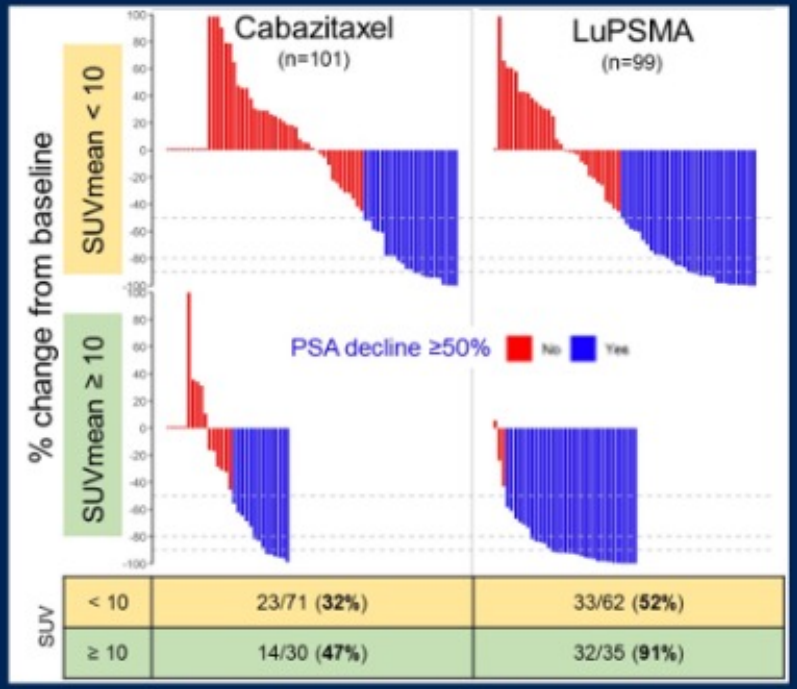
PSMA intensity *vs.* PSA PFS



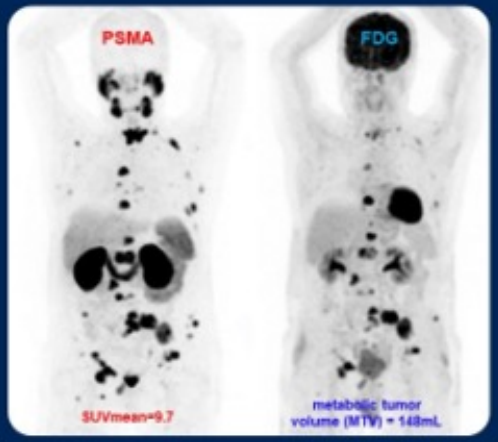
PRESENTED BY: Michael Hofman @DrMHofman

ASCO 2022: TheraP Study

Discussion: PSMA as predictive biomarker[1] (PSA50-RR)[11]



SUV	Cabazitaxel (n=101)	LuPSMA (n=99)
< 10	23/71 (**32%**)	33/62 (**52%**)
≥ 10	14/30 (**47%**)	32/35 (**91%**)



Odds of PSA50-RR to LuPSMA *vs* cabazitaxel

	OR (95% CI)	
PSMA SUVmean < 10	2.2 (1.1 – 4.5)	P=0.03
PSMA SUVmean ≥ 10	12.2 (3.4 - 59)	

[1]Buteau J et al, ASCO GU 2022. doi:10.1200/JCO.2022.40.6_suppl.010

Further analysis to be performed including OS

My practice

- Third line after Docetaxel, novel pathway inhibitors
  - Every patient should have a somatic and germline mutational studies to look for HRR deficiencies
- Patients with BRCA2 mutations, I would favor Olaparib and Rucaparib
- Patients without mutations, I would consider Lutetium 177 vs Cabizitaxel based on PSMA PET avid disease ie SUV greater than 10
- Enrolling in our CAR-T cell and BiTE therapy for metastatic castrate resistant prostate cancer

Norton Cancer Institute

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