

Metastatic prostate cancer Therapeutic options

Orazio Caffo



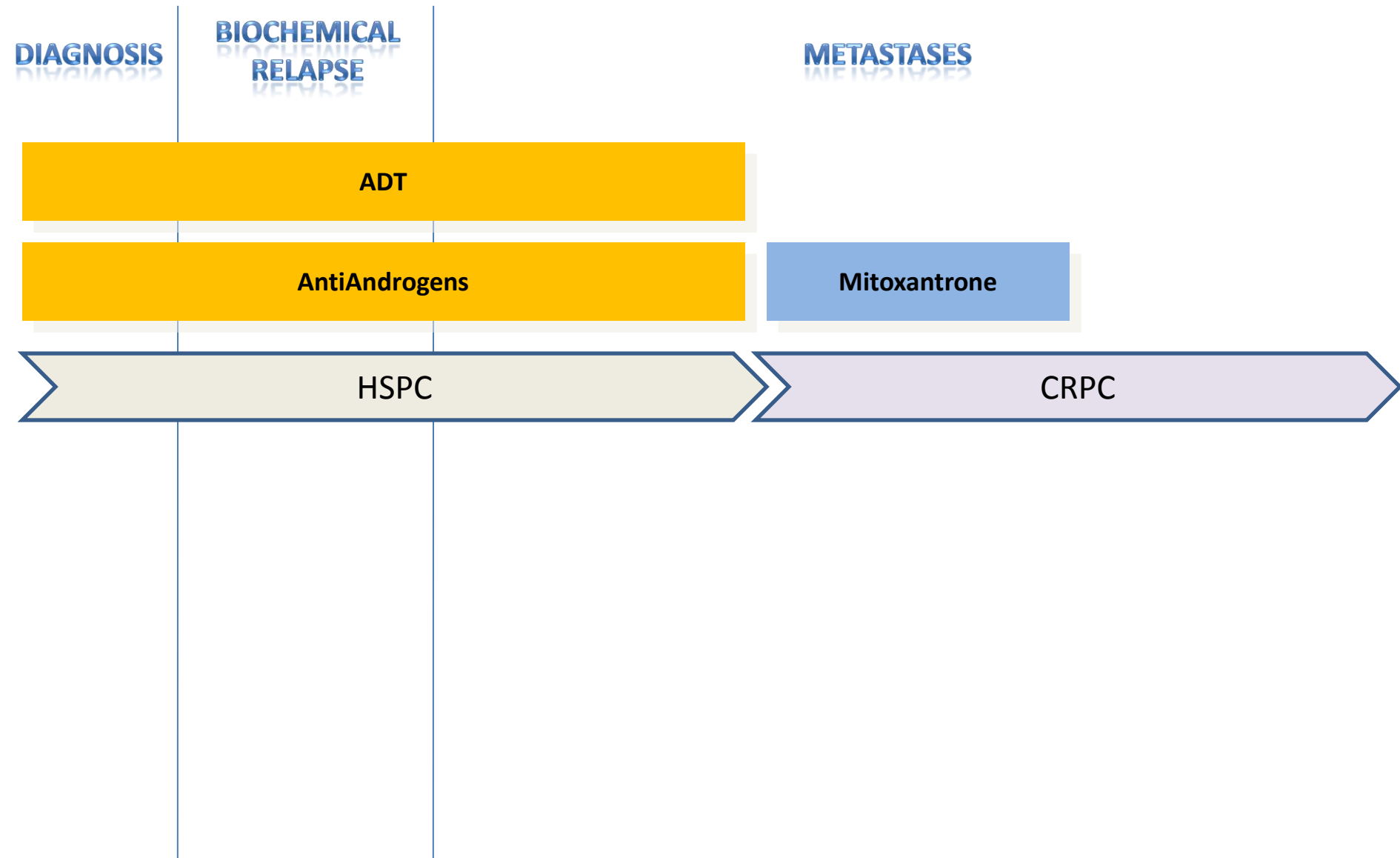
Ospedale
"Sacro Cuore - Don Calabria"

Incontri
di aggiornamento
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Oncologico

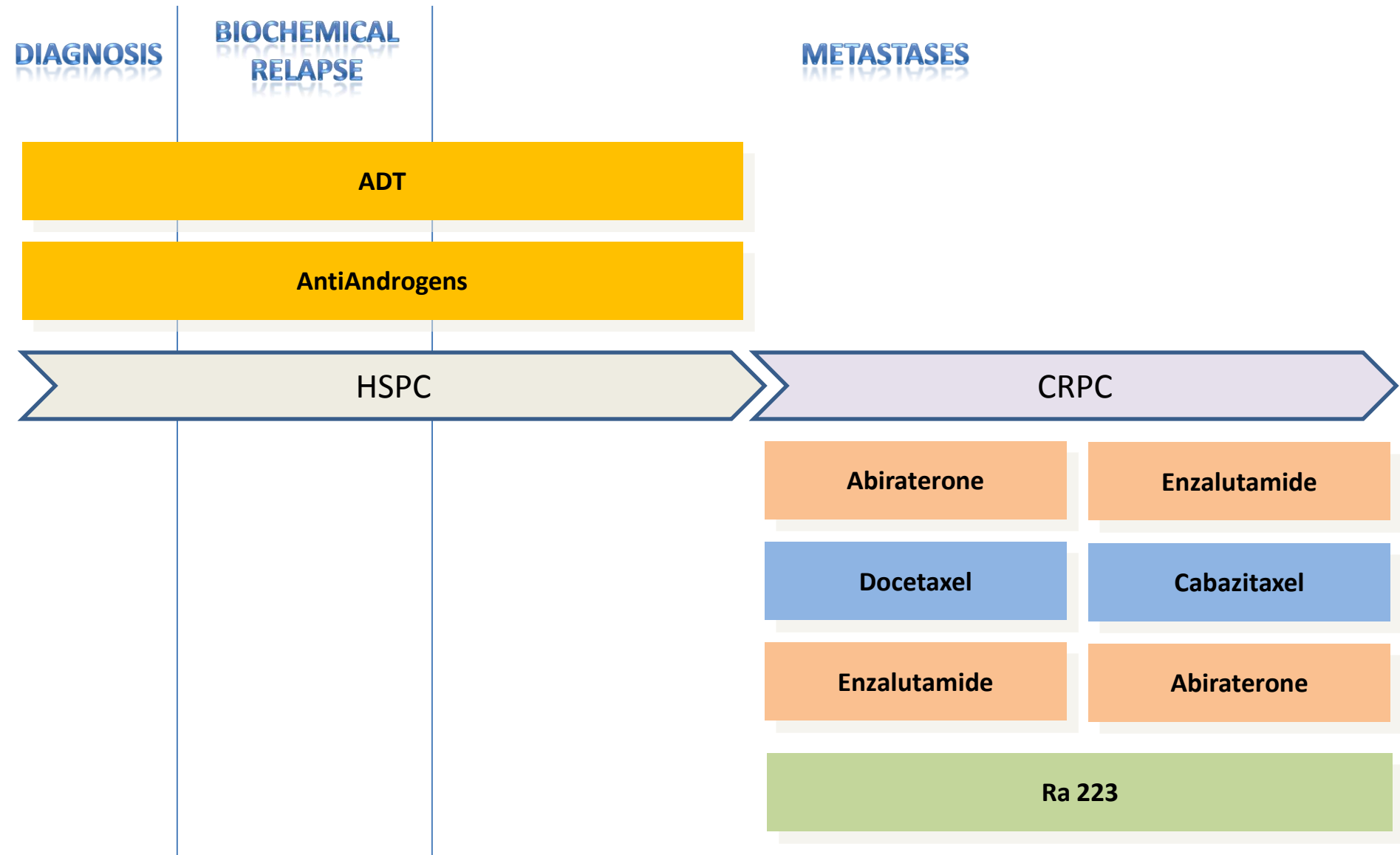


Unità Operativa
di Oncologia Medica
Ospedale di Trento

2000 landscape



2015 landscape



CRPC front line

	Arm	Median OS	HR
TAX327	DOC+PDN	19.2	0.79
	MITOX+PDN	17.8	
COU-AA-302	AA+PDN	34.7	0.81
	PLC+PDN	30.3	
PREVAIL	ENZ	32.4	0.71
	PLC	30.2	



CRPC front line

	PS2	ELDERLY	VISCERAL METS	SYMPTOMATIC
TAX327	√	√	√	√
COU-302	√	√		
PREVAIL	√	√	√	

Choice criteria

- Disease oriented
 - Visceral mets
- Patient oriented
 - Comorbidities (cardiovascular, diabetes, seizure)
- Patient preferences and feelings
- Physician preferences and feelings



CRPC second line

	Arm	Median OS	HR
TROPIC	CABA+PDN	15.1	0.70
	MITOX+PDN	12.7	
COU-AA-301	AA+PDN	15.8	0.74
	PLC+PDN	11.1	
AFFIRM	ENZ	18.4	0.63
	PLC	13.6	



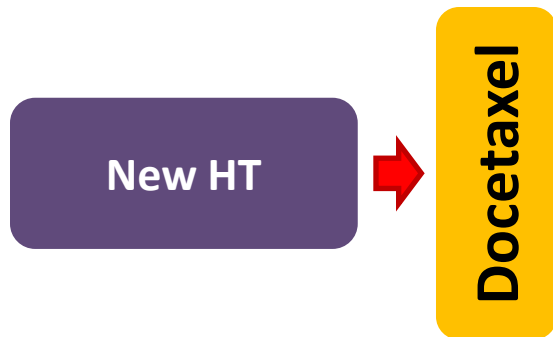
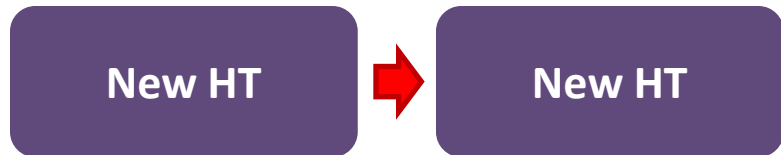
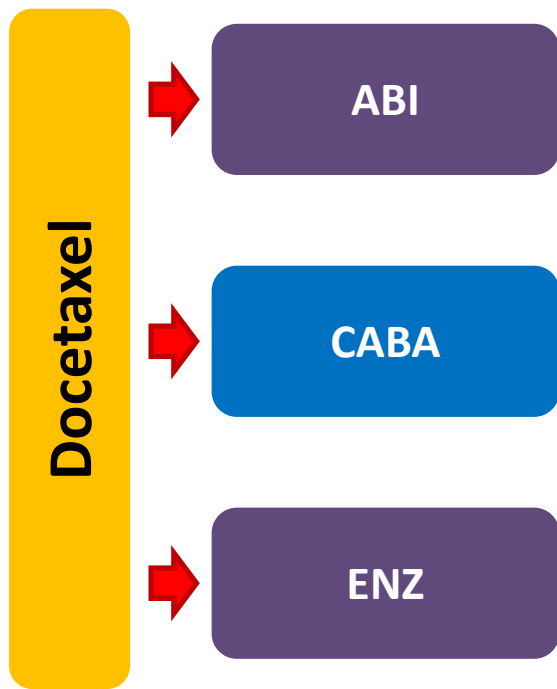
CRPC second line

	PS2	ELDERLY	VISCERAL METS	SYMPTOMATIC
TROPIC	√	√	√	√
COU-301	√	√	√	√
AFFIRM	√	√	√	√

Choice criteria?

FIRST LINE TREATMENT





- To date no clear evidence supports the superiority of one drug over another
- The only decision-making issue should be patient-oriented
 - Burden of 1st-line-related toxicity
 - Time of recovery
 - 2nd-line toxicity profile (vs comorbidities)
 - Patient's preference



Second line First line	DOCETAXEL (TAX327)	ABIRATERONE (COU-302)	ENZALUTAMIDE (AFFIRM)
DOCETAXEL		✓	✓
ABIRATERONE	?		?
ENZALUTAMIDE	?	?	



DATA FROM CLINICAL PRACTICE



ABI (1) → DOC (2)

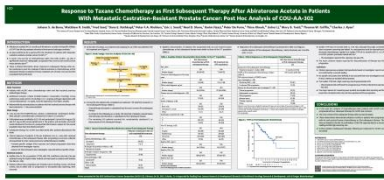
Authors	# pts	PSA RR	Treatment duration	Median PFS	Median OS
Azad	37	32	N.A.	N.A.	N.A.
Mezynski	35	26	5 mos	4.6^ mos	12.5 mos
Schweizer	24	38	N.A.	4.1^ mos 4.4 mos	N.A.
Aggarwal	23	48	4.3 mos	N.A.	12.4 mos

ABI (1) → ENZ (2)

Authors	# pts	PSA RR	Treatment duration	Median PFS	Median OS
Suzman	30	34	N.A.	4.7 mos 4.1^ mos	N.A.
Zhang	9	11	4.0 mos	3.6 mos 4.0^ mos	8.5 mos

^ biochemical PFS





Response to taxane chemotherapy as first subsequent therapy after abiraterone acetate (AA) in patients with metastatic castration-resistant prostate cancer (mCRPC): Post-hoc analysis of COU-AA-302

Figure 1. Study Design: Post Hoc Analysis of COU-AA-302

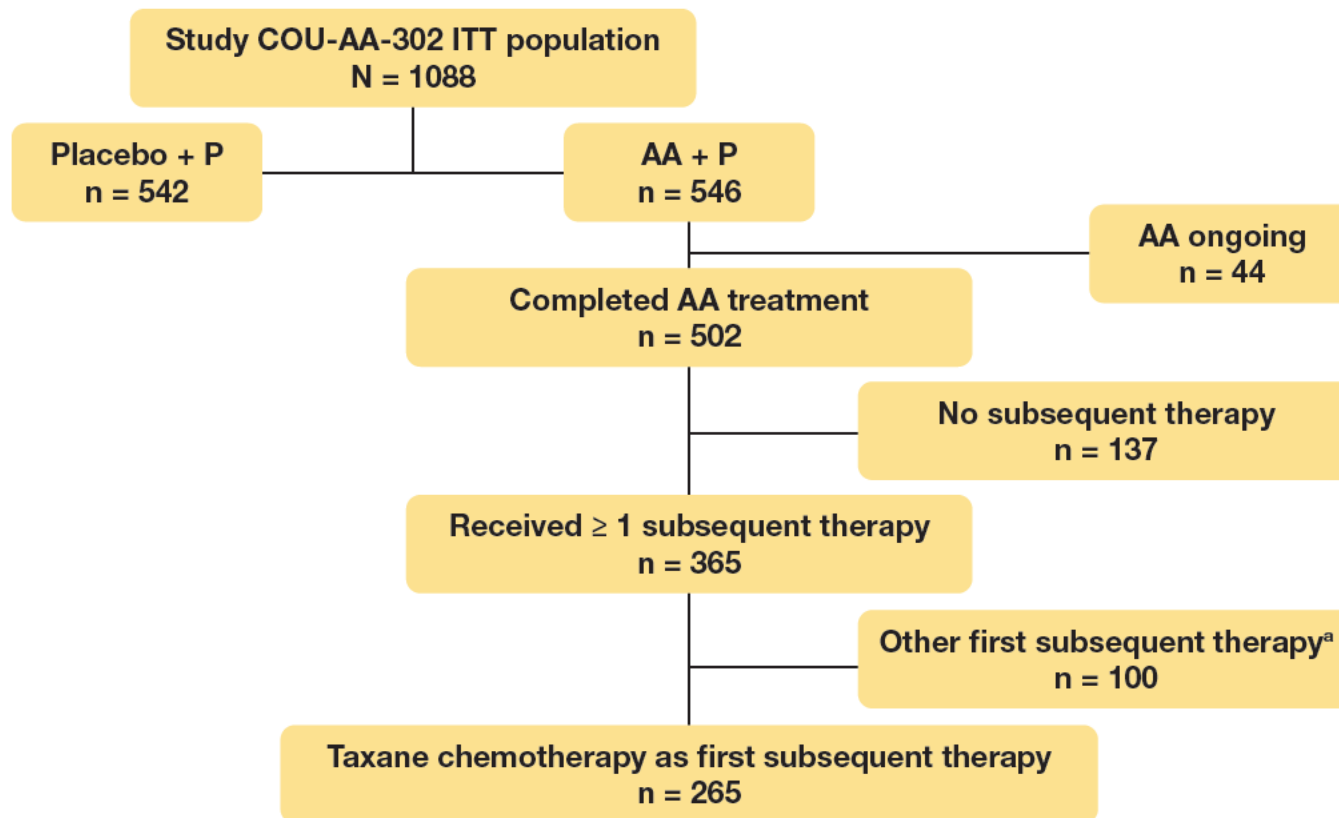


Table 3. Clinical Response on First Subsequent Chemotherapy

	AA, then taxane chemotherapy as first subsequent therapy
n	265
Exposure to first subsequent chemotherapy	
Treatment duration ^a , median (IQR)	3 months (1.0-5.0)
TTPP ^b on first subsequent chemotherapy, median (95% CI)	7.59 months (4.99, NE)
PSA response based on PCWG2 criteria (per investigator), n (%)	
PSA fall by 50% ^c , n (%)	117 (47)
Confirmed PSA progression	31 (13)

Limitations

- Clinical response was evaluated retrospectively based on investigator reports and not confirmed by a second reading.
- No specific end points were defined; it was assumed that most investigators used PCWG2 criteria as is standard clinical practice.
- The median TTPP had a high censoring rate of approximately 87%.
 - 13% of patients had confirmed PSA progression per PCWG2 criteria from reported PSA data.
- The major reasons for censoring were possibly incomplete data reporting and the proportion of patients who may not have experienced PSA progression.



ABI (2)



ENZ (3)

Authors	# pts	PSA RR	Treatment duration	Median PFS	Median OS
Bianchini	39	12.8	2.9 mos	2.8	N.R.
Schrader	35	28.6	4.9 mos	4 mos	7.1 mos
Schmid	35	10	2.8 mos	3.1° mos	7.5 mos
Badrising	61	21	14.9 wks	12 wks/17.4^ wks	31.6 wks
Thomsen	24	N.A.	4 mos	N.A.	4.8
Thomson	23	39.1	N.A.	2.8^ mos	8.5 mos
Røder	24	N.A.	N.A.	N.A.	4.8 mos
Vera-Badillo	26	27	4.4 mos	4.9	N.A.
Sandhu	23	17.3	142 days	43 days	N.A.
Scholz	66	N.A.	N.A.	N.A.	N.A.
Cheng	165	26	N.A.	2.8^ mos	12.2 mos
Stevenson	62	N.A.	50.43 wks	18.43 wks	11.43 wks
Caffo	49	20	N.A.	4 mos	8 mos
Bournakis	25	40	N.A.	N.A.	N.A.
Azad	68	22	4.1 mos	4.6 mos	10.6 mos
Zhang	19	5	3 mos	2.8 mos/3.0^ mos	9.6 mos



ENZ (2)→ ABI (3)

Authors	# pts	PSA RR	Treatment duration	Median PFS	Median OS
Noonan	30	50	13 wks	15.4 wks	50.1 wks
Loriot	38	8	3 mos	2.7 mos	7.2 mos
Caffo	12	8	N.A.	4 mos	N.A.

CABA(2)→ ABI (3)

Authors	# pts	PSA RR	Treatment duration	Median PFS	Median OS
Sonpavde	77	N.A	N.A.	10.4 mos	18.2 mos
Caffo	68	26	N.A.	5 mos	15 mos
Wissing	63	18	113 days	2.4 mos 2.7^ mos	N.A.

CABA(2)→ ENZ (3)

Authors	# pts	PSA RR	Treatment duration	Median PFS	Median OS
Caffo	21	19	N.A.	6 mos	13 mos



ABI(2)→ CABA (3)

Authors	# pts	PSA RR	Treatment duration	Median PFS	Median OS
Sonpavde	36	N.A.	N.A.	7.1 mos	11.8 mos
Al-Nakouzi	79	35	4 mos	4.4 mos	10.9 mos
Sella	24	31.5	N.A.	N.A.	8.2 mos
Caffo	94	29	N.A.	5 mos	12 mos
Albiges	38	56	N.A.	N.A.	N.A.
Wissing	69	31.8	90 days	2.6 mos 4.1^ mos	N.A.

ENZ(2)→ CABA (3)

Authors	# pts	PSA RR	Treatment duration	Median PFS	Median OS
Caffo	16	25%	N.A.	4 mos	8 mos
Pezaro	4	25	N.A.	N.A.	N.A.

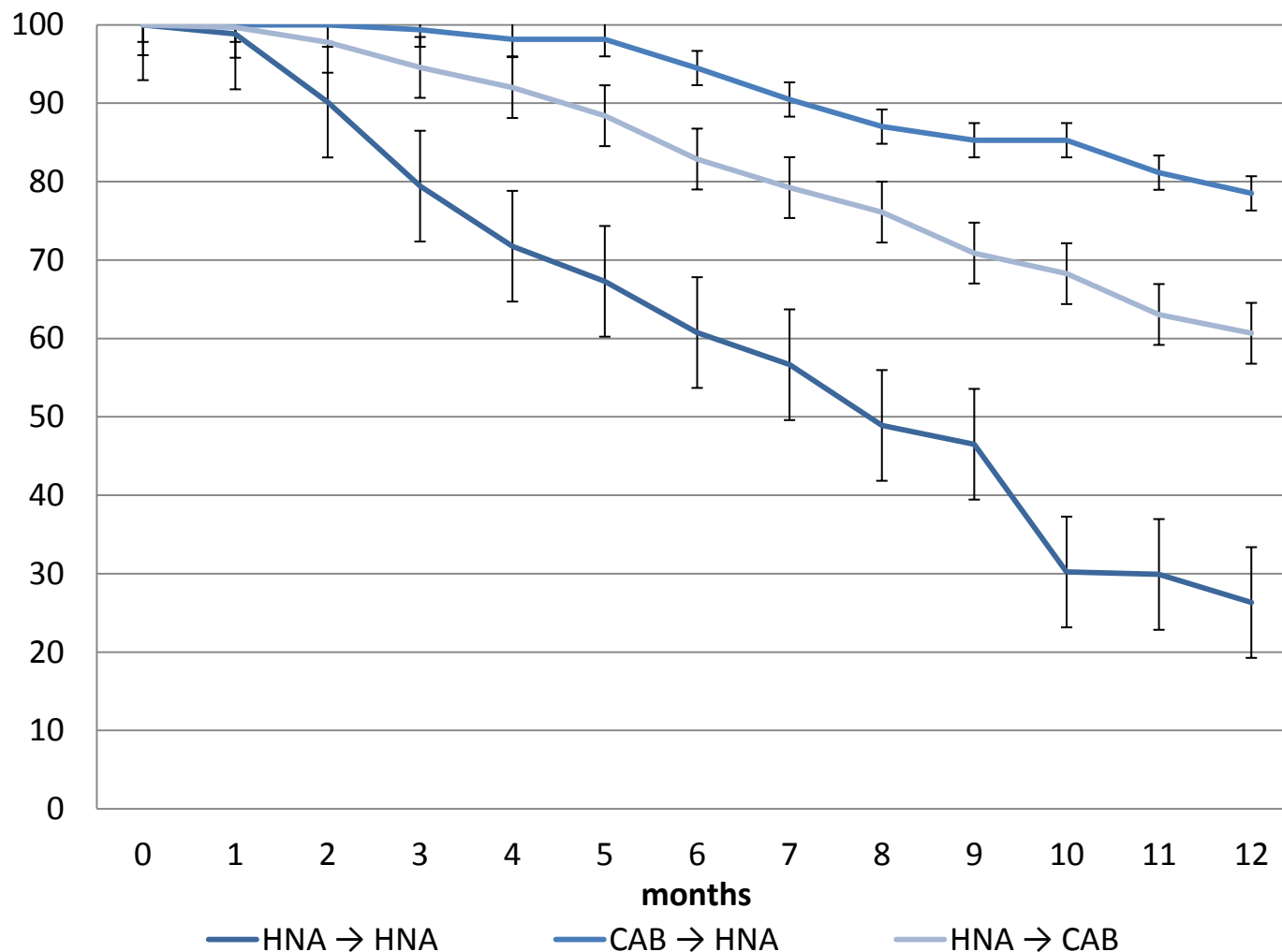


Sequence	# patients	Median OS
ABI →ENZ	744	7.5 mos
ENZ →ABI	80	8.8 mos
CABA → ABI	208	16.6 mos
CABA → ENZ	21	13 mos
ABI → CABA	340	11.3 mos
ENZ →CABA	20	8 mos



Background Metastatic CRPC is a complex disease with a poor prognosis. The standard of care for this disease is androgen deprivation therapy (ADT) plus docetaxel. However, the use of new agents (NAs) has emerged as a promising option. The aim of this study was to evaluate the sequential use of NAs after docetaxel in metastatic CRPC.	Results The sequential use of NAs after docetaxel was associated with a significant improvement in overall survival (OS) compared to the use of docetaxel alone. The median OS was 12.5 months in the sequential use group versus 10.5 months in the docetaxel alone group.
Methods This was a retrospective study of 100 patients with metastatic CRPC who received docetaxel as first-line treatment. The patients were divided into two groups: sequential use of NAs and docetaxel alone.	Conclusions The sequential use of NAs after docetaxel is a promising strategy for improving OS in metastatic CRPC.
References 1. [Reference 1] 2. [Reference 2] 3. [Reference 3] 4. [Reference 4] 5. [Reference 5] 6. [Reference 6] 7. [Reference 7] 8. [Reference 8] 9. [Reference 9] 10. [Reference 10] 11. [Reference 11] 12. [Reference 12] 13. [Reference 13] 14. [Reference 14] 15. [Reference 15] 16. [Reference 16] 17. [Reference 17] 18. [Reference 18] 19. [Reference 19] 20. [Reference 20] 21. [Reference 21] 22. [Reference 22] 23. [Reference 23] 24. [Reference 24] 25. [Reference 25] 26. [Reference 26] 27. [Reference 27] 28. [Reference 28] 29. [Reference 29] 30. [Reference 30] 31. [Reference 31] 32. [Reference 32] 33. [Reference 33] 34. [Reference 34] 35. [Reference 35] 36. [Reference 36] 37. [Reference 37] 38. [Reference 38] 39. [Reference 39] 40. [Reference 40] 41. [Reference 41] 42. [Reference 42] 43. [Reference 43] 44. [Reference 44] 45. [Reference 45] 46. [Reference 46] 47. [Reference 47] 48. [Reference 48] 49. [Reference 49] 50. [Reference 50] 51. [Reference 51] 52. [Reference 52] 53. [Reference 53] 54. [Reference 54] 55. [Reference 55] 56. [Reference 56] 57. [Reference 57] 58. [Reference 58] 59. [Reference 59] 60. [Reference 60] 61. [Reference 61] 62. [Reference 62] 63. [Reference 63] 64. [Reference 64] 65. [Reference 65] 66. [Reference 66] 67. [Reference 67] 68. [Reference 68] 69. [Reference 69] 70. [Reference 70] 71. [Reference 71] 72. [Reference 72] 73. [Reference 73] 74. [Reference 74] 75. [Reference 75] 76. [Reference 76] 77. [Reference 77] 78. [Reference 78] 79. [Reference 79] 80. [Reference 80] 81. [Reference 81] 82. [Reference 82] 83. [Reference 83] 84. [Reference 84] 85. [Reference 85] 86. [Reference 86] 87. [Reference 87] 88. [Reference 88] 89. [Reference 89] 90. [Reference 90] 91. [Reference 91] 92. [Reference 92] 93. [Reference 93] 94. [Reference 94] 95. [Reference 95] 96. [Reference 96] 97. [Reference 97] 98. [Reference 98] 99. [Reference 99] 100. [Reference 100]	References 1. [Reference 1] 2. [Reference 2] 3. [Reference 3] 4. [Reference 4] 5. [Reference 5] 6. [Reference 6] 7. [Reference 7] 8. [Reference 8] 9. [Reference 9] 10. [Reference 10] 11. [Reference 11] 12. [Reference 12] 13. [Reference 13] 14. [Reference 14] 15. [Reference 15] 16. [Reference 16] 17. [Reference 17] 18. [Reference 18] 19. [Reference 19] 20. [Reference 20] 21. [Reference 21] 22. [Reference 22] 23. [Reference 23] 24. [Reference 24] 25. [Reference 25] 26. [Reference 26] 27. [Reference 27] 28. [Reference 28] 29. [Reference 29] 30. [Reference 30] 31. [Reference 31] 32. [Reference 32] 33. [Reference 33] 34. [Reference 34] 35. [Reference 35] 36. [Reference 36] 37. [Reference 37] 38. [Reference 38] 39. [Reference 39] 40. [Reference 40] 41. [Reference 41] 42. [Reference 42] 43. [Reference 43] 44. [Reference 44] 45. [Reference 45] 46. [Reference 46] 47. [Reference 47] 48. [Reference 48] 49. [Reference 49] 50. [Reference 50] 51. [Reference 51] 52. [Reference 52] 53. [Reference 53] 54. [Reference 54] 55. [Reference 55] 56. [Reference 56] 57. [Reference 57] 58. [Reference 58] 59. [Reference 59] 60. [Reference 60] 61. [Reference 61] 62. [Reference 62] 63. [Reference 63] 64. [Reference 64] 65. [Reference 65] 66. [Reference 66] 67. [Reference 67] 68. [Reference 68] 69. [Reference 69] 70. [Reference 70] 71. [Reference 71] 72. [Reference 72] 73. [Reference 73] 74. [Reference 74] 75. [Reference 75] 76. [Reference 76] 77. [Reference 77] 78. [Reference 78] 79. [Reference 79] 80. [Reference 80] 81. [Reference 81] 82. [Reference 82] 83. [Reference 83] 84. [Reference 84] 85. [Reference 85] 86. [Reference 86] 87. [Reference 87] 88. [Reference 88] 89. [Reference 89] 90. [Reference 90] 91. [Reference 91] 92. [Reference 92] 93. [Reference 93] 94. [Reference 94] 95. [Reference 95] 96. [Reference 96] 97. [Reference 97] 98. [Reference 98] 99. [Reference 99] 100. [Reference 100]

SEQUENTIAL USE OF NEW AGENTS (NAs) AFTER DOCETAXEL (DOC) FIRST LINE IN METASTATIC CASTRATION-RESISTANT PROSTATE CANCER



SUGGESTIONS FROM AR-V7 ANALYSIS

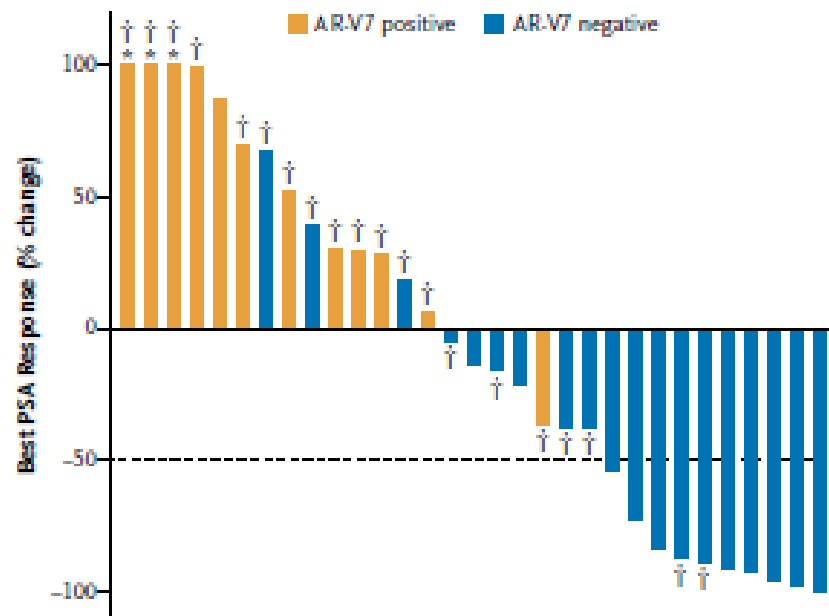


ORIGINAL ARTICLE

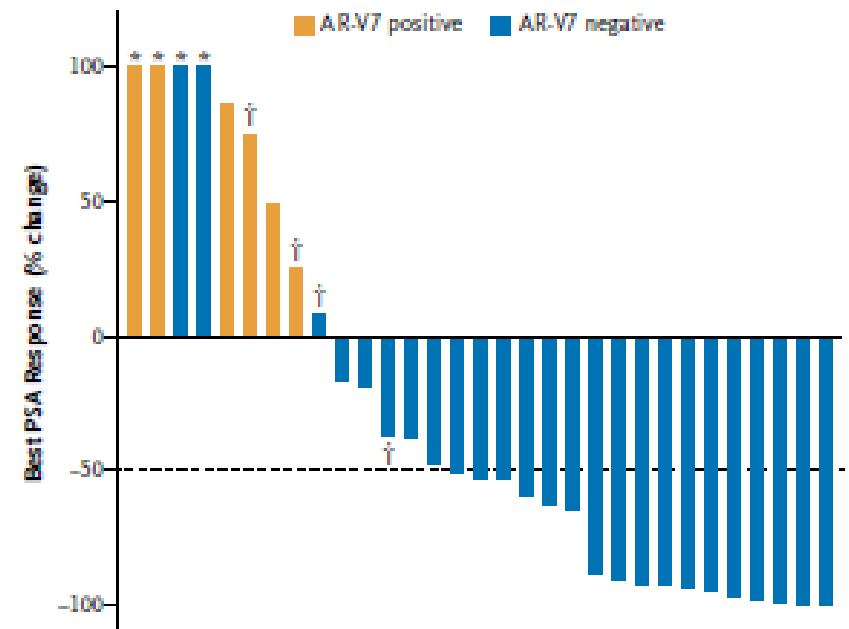
AR-V7 and Resistance to Enzalutamide and Abiraterone in Prostate Cancer

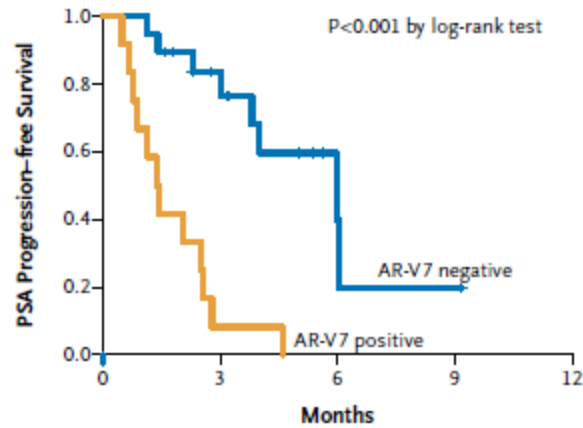
N Engl J Med 2014;371:1028-38.

A Enzalutamide-Treated Patients

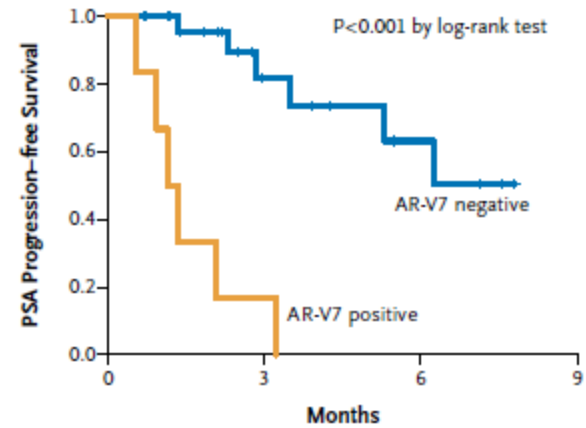


B Abiraterone-Treated Patients

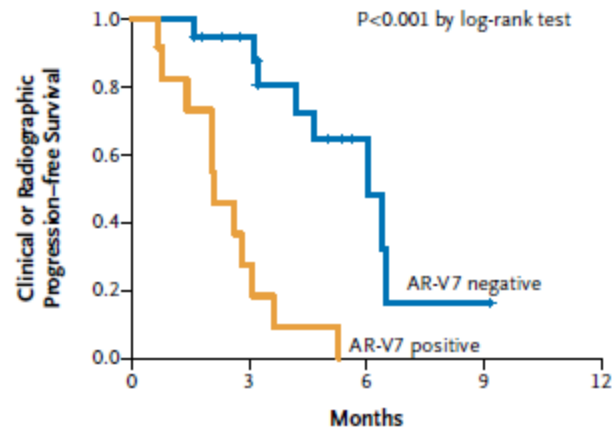


A Enzalutamide-Treated Patients**No. at Risk**

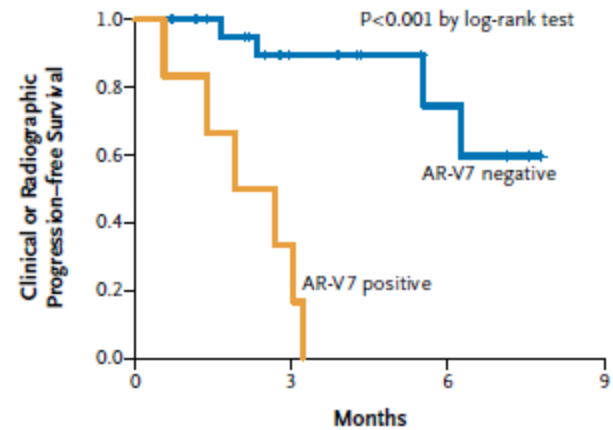
AR-V7 negative	19	12	2	1	0
AR-V7 positive	12	1	0	0	0

B Abiraterone-Treated Patients**No. at Risk**

AR-V7 negative	25	10	5	0
AR-V7 positive	6	1	0	0

C Enzalutamide-Treated Patients**No. at Risk**

AR-V7 negative	19	14	4	1	0
AR-V7 positive	12	3	0	0	0

D Abiraterone-Treated Patients**No. at Risk**

AR-V7 negative	25	11	5	0
AR-V7 positive	6	2	0	0

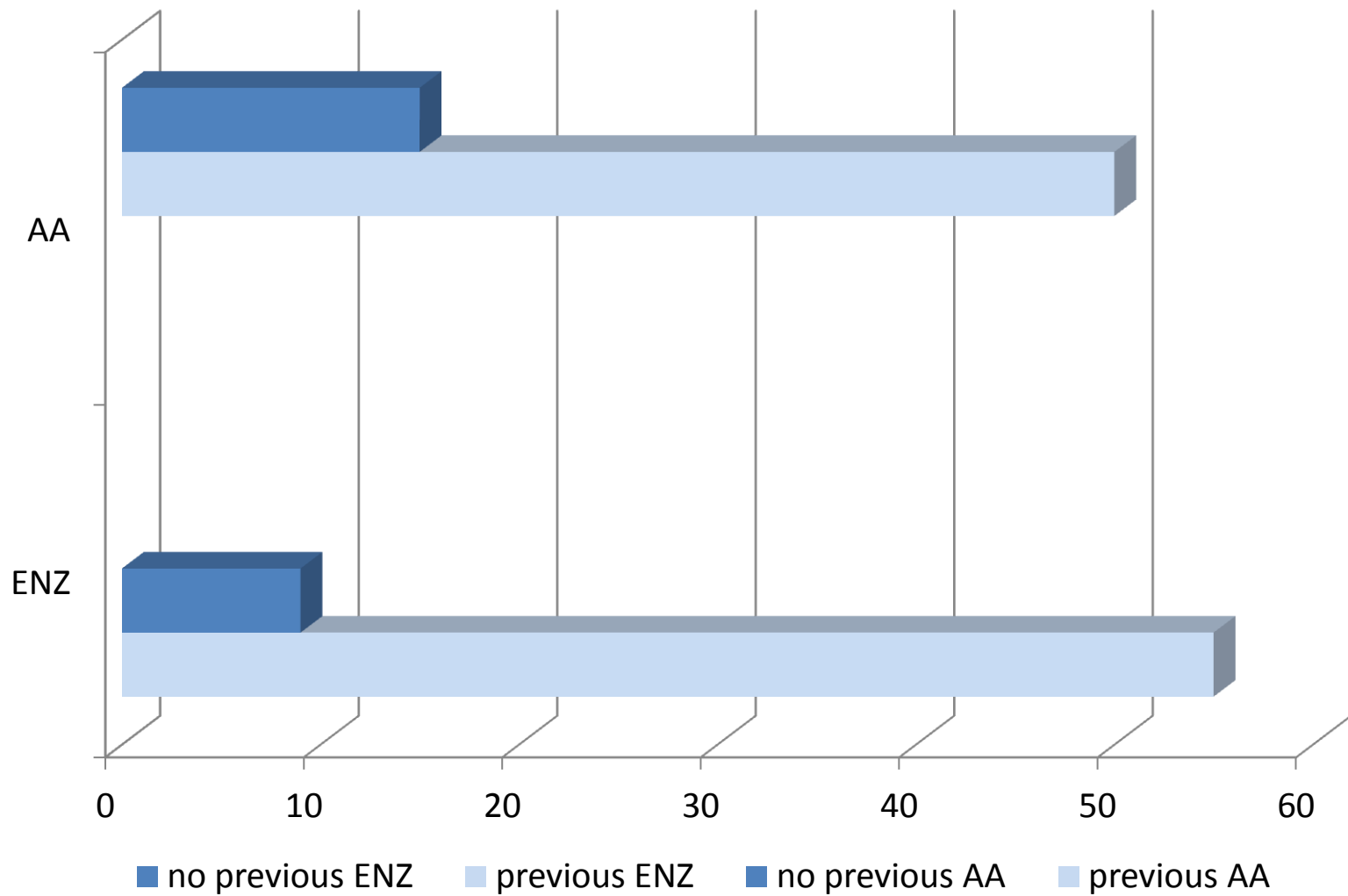


Outcomes: AR-V7 “conversions”

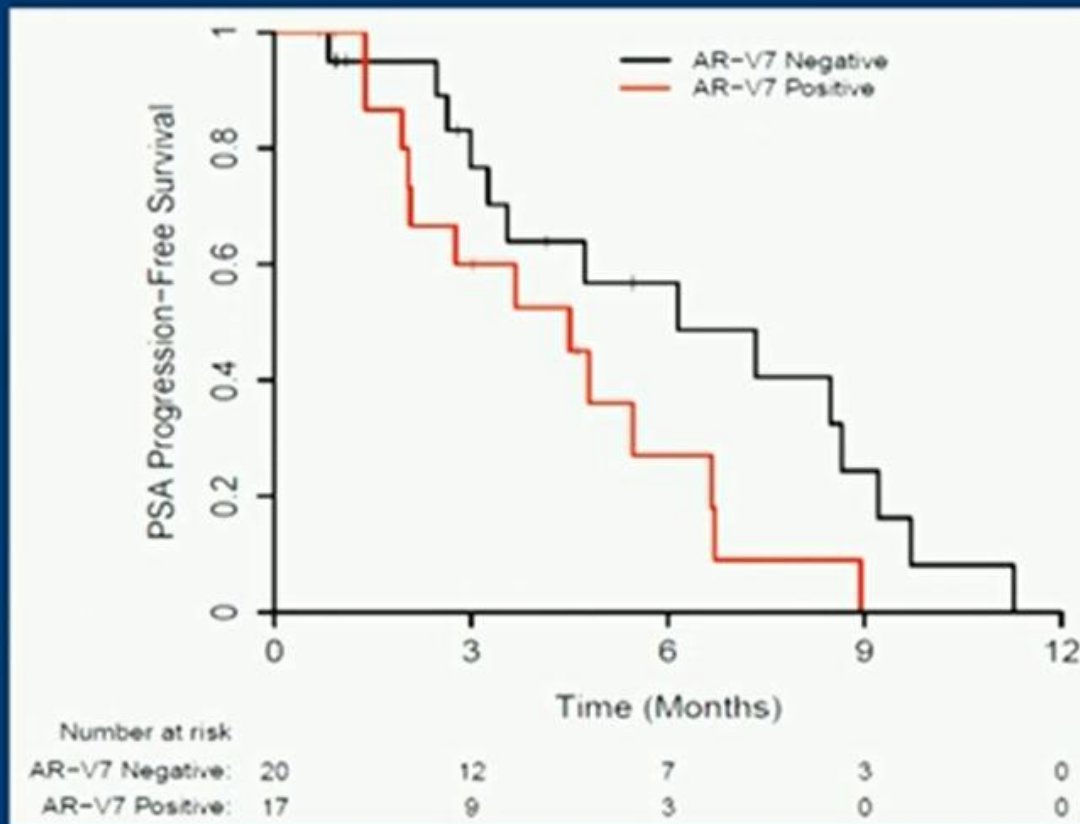


Outcome	AR-V7[-] → AR-V7[-] (n=36)	AR-V7[-] → AR-V7[+] (n=6)	AR-V7[+] → AR-V7[+] (n=16)
PSA Response	68% (95%CI, 52 – 81%)	17% (95%CI, 4 – 58%)	0% (95%CI, 0 – 19%)
PSA Progression-Free Survival	6.1 months (95%CI, 5.9 mo – NR)	3.0 months (95%CI, 2.3 mo – NR)	1.4 months (95%CI, 0.9 – 2.6 mo)
Progression-Free Survival	6.5 months (95%CI, 6.1 mo – NR)	3.2 months (95%CI, 3.1 mo – NR)	2.1 months (95%CI, 1.9 – 3.1 mo)





PSA Progression-Free Survival

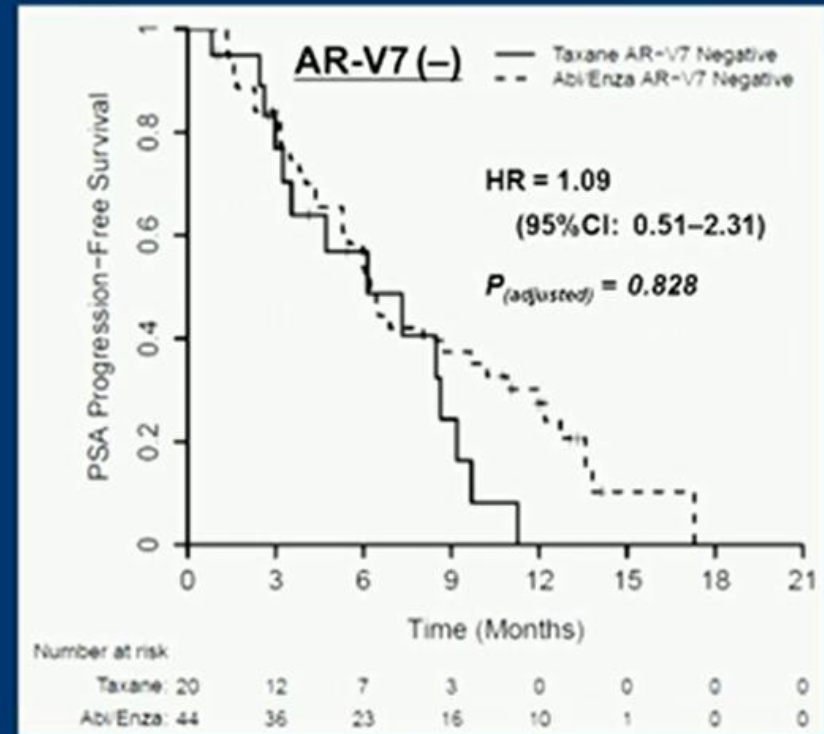
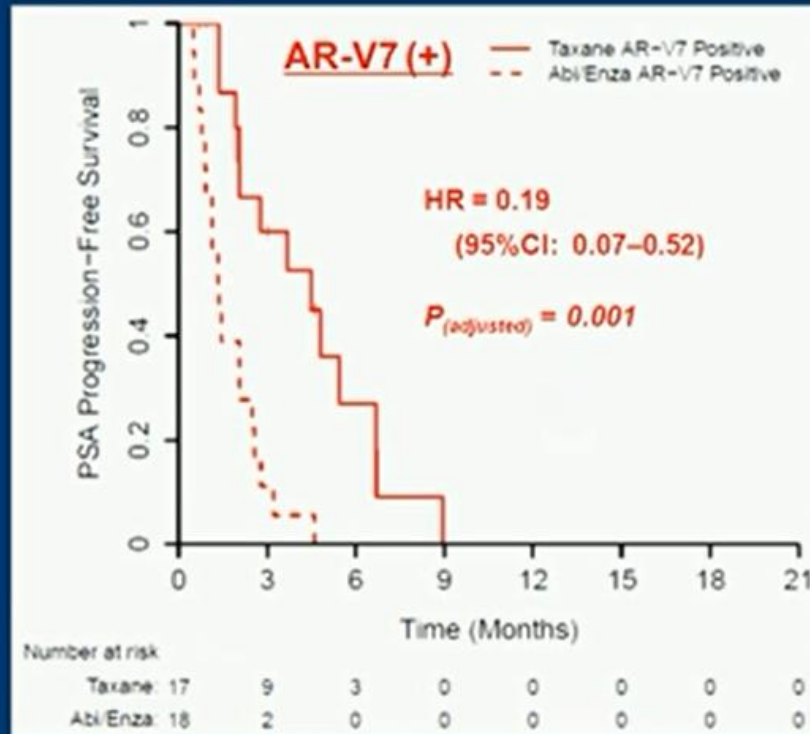


HR = 1.72
(95%CI: 0.59–5.01)

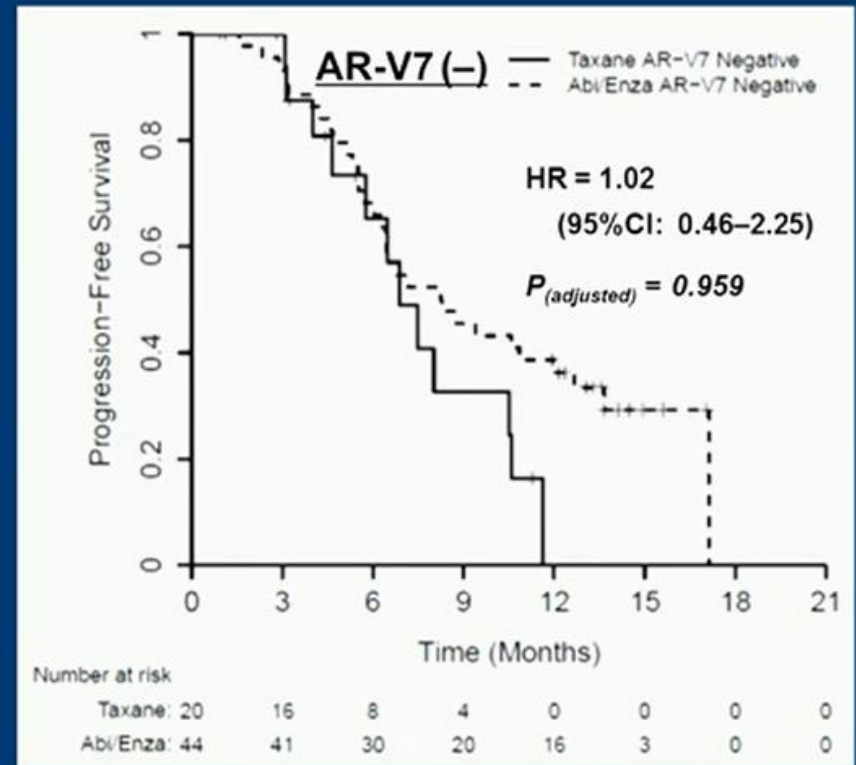
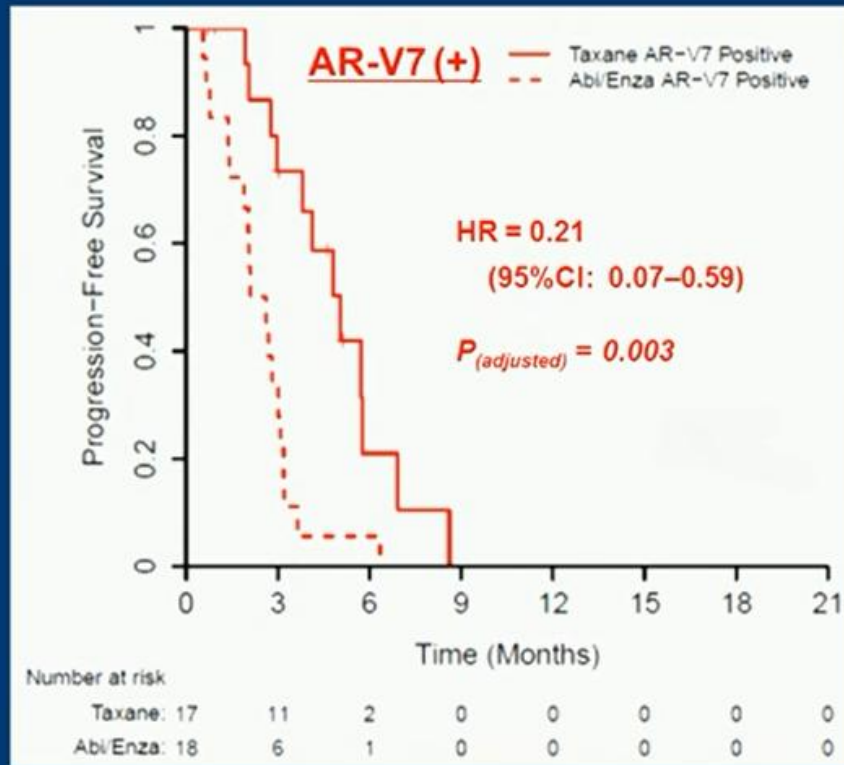
$P_{(adjusted)} = 0.324$



PSA-PFS: Taxane-treated vs Abi/Enza-treated

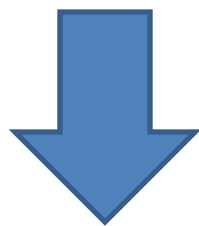


PFS: Taxane-treated vs Abi/Enza-treated pts



No cross resistance between taxanes and HNA

- Converging suggestions from both patients series and experimental data on AR-V7
 - Cumulative feelings from small retrospective series
 - Retrospectively collected data from COU-302
 - AR-V7 analysis from 62 (AA-ENZ) and 37 pts (TAX)



PROOF OF CONCEPT





Available at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejancer.com



Cross-resistance between taxanes and new hormonal agents abiraterone and enzalutamide may affect drug sequence choices in metastatic castration-resistant prostate cancer

R.J. van Soest^{a,*}, M.E. van Royen^b, E.S. de Morrée^a, J.M. Moll^a, W. Teubel^a,
E.A.C. Wiemer^c, R.H.J. Mathijssen^c, R. de Wit^c, W.M. van Weerden^a

MULTIPLE MECHANISMS OF RESISTANCE





Available at www.sciencedirect.com

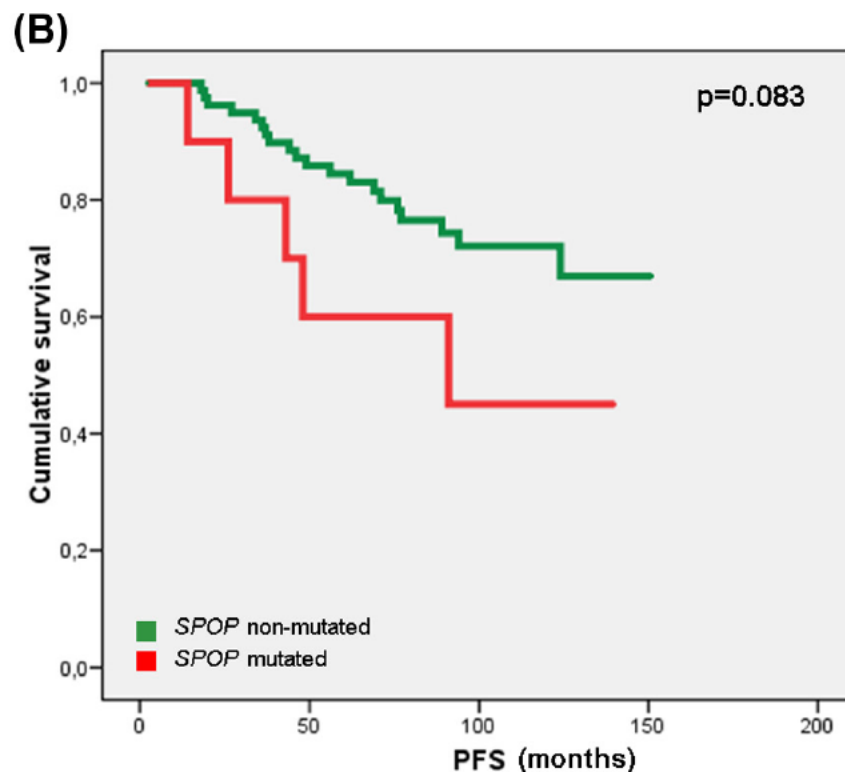
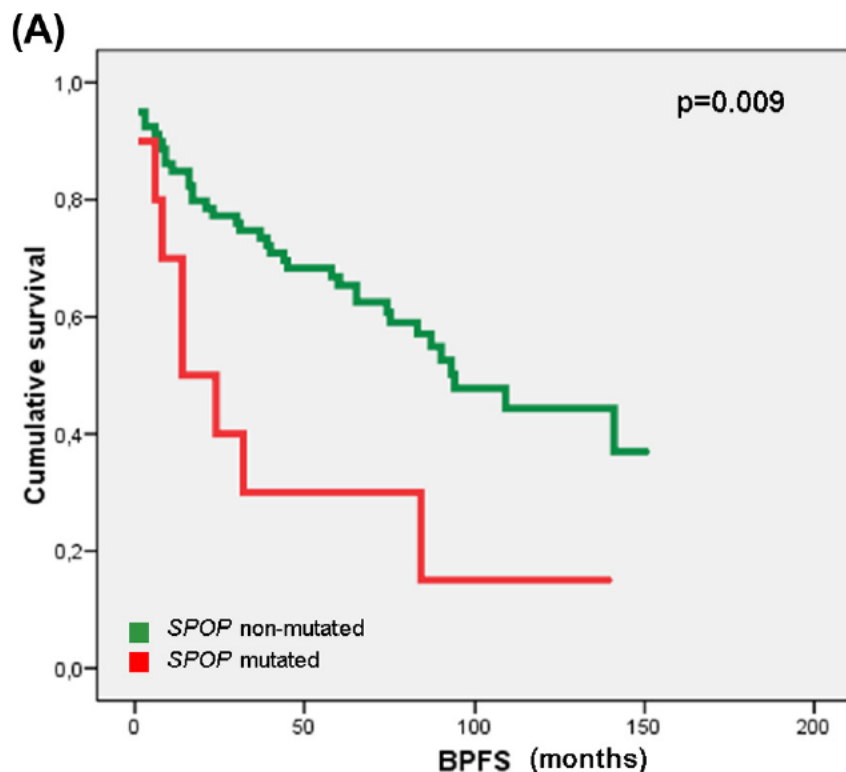
ScienceDirect

journal homepage: www.ejancer.com



Original Research

Clinico-pathological significance of the molecular alterations of the *SPOP* gene in prostate cancer



CRPC front line

Choice criteria

- Disease oriented
 - Visceral mets
- Patient oriented
 - Comorbidities (cardiovascular, diabetes, seizure)
- Patient preferences and feelings
- Physician preferences and feelings

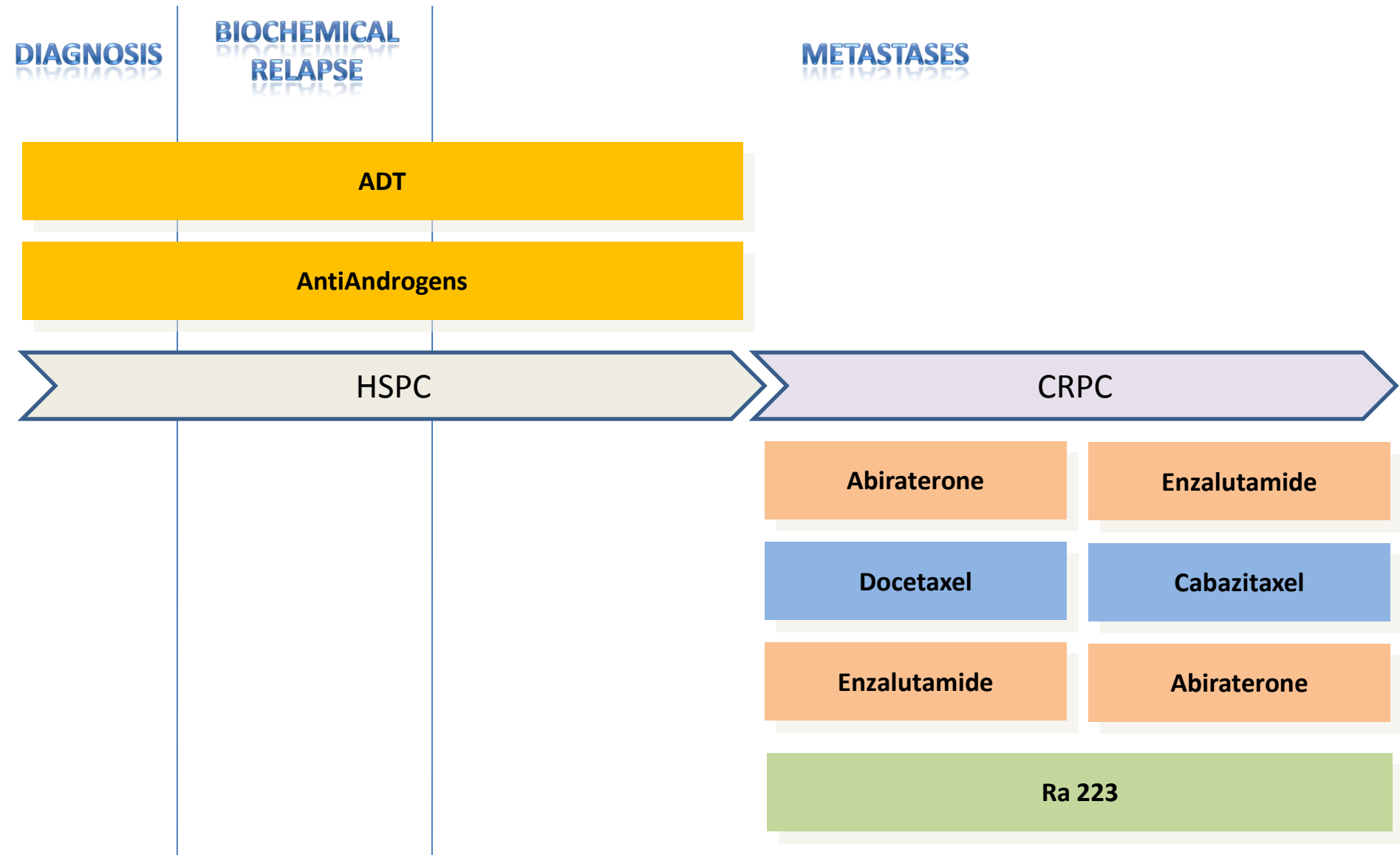


CRPC second line

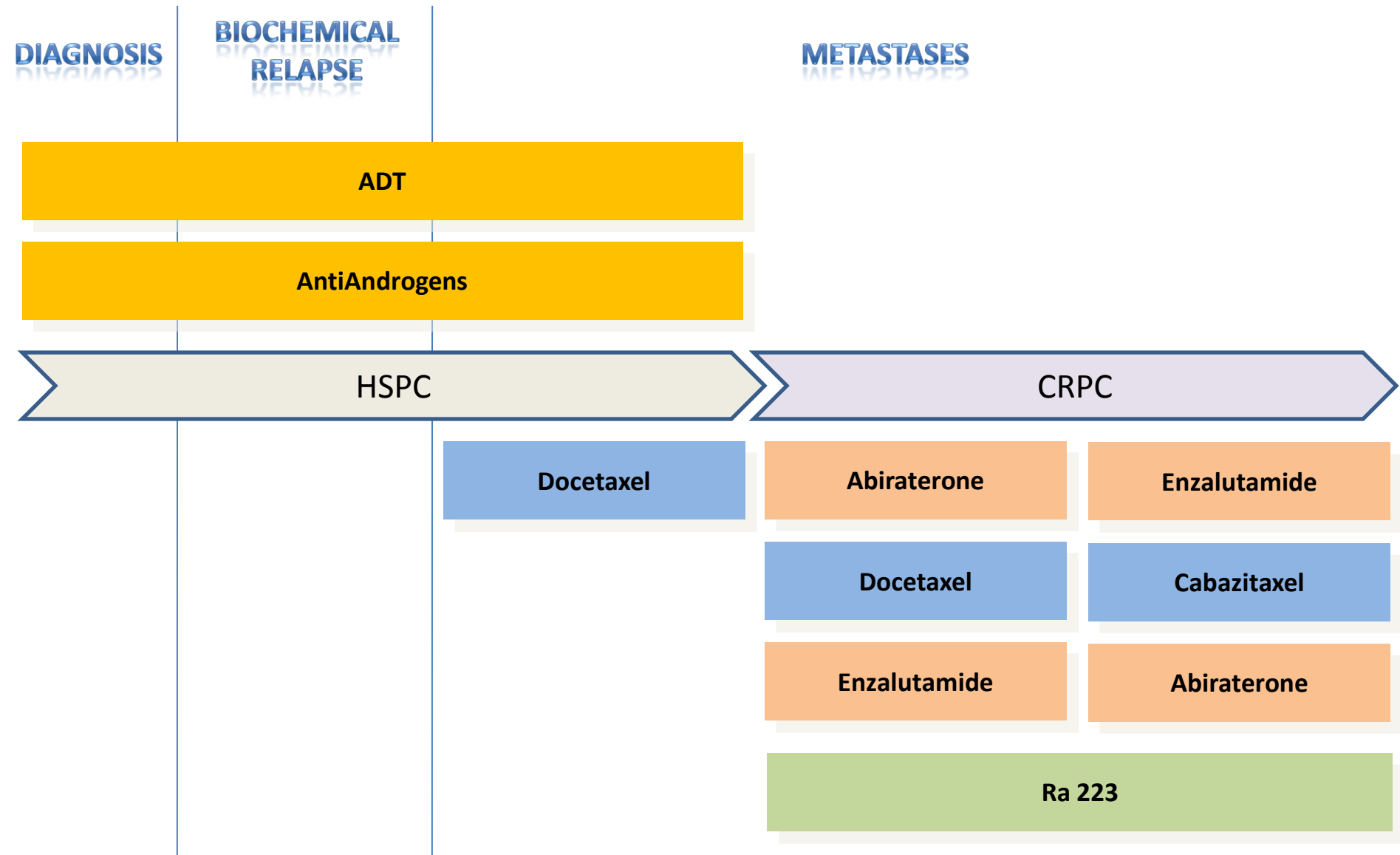
- After DOC
 - The only decision-making issue should be patient-oriented
 - Burden of 1st-line-related toxicity
 - Time of recovery
 - 2nd-line toxicity profile (vs comorbidities)
 - Patient preference
- After ABI or ENZ
 - No robust data are currently available supporting changed (or unchanged) activity of DOC, ABI, ENZ



2015 landscape



2015 landscape



E3805

CHAARTED: ChemoHormonal Therapy versus Androgen Ablation Randomized Trial for Extensive Disease in Prostate Cancer

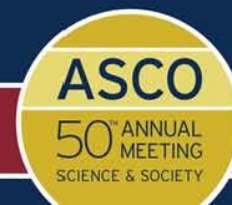
Presenting Author: Christopher Sweeney

Yu-Hui Chen, Michael Carducci, Glenn Liu, Mario Eisenberger, Yu-Ning Wong, Noah Hahn, Manish Kohli, Robert Dreicer, Nicholas Vogelzang, Joel Picus, Daniel Shevrin, Maha Hussain, Jorge Garcia, Robert DiPaola



ECOG-ACRIN
cancer research group
Reshaping the future of patient care

PRESENTED AT:



E3805 / CHAARTED Treatment

STRATIFICATION

Extent of Mets

-High vs Low

Age

≥70 vs < 70yo

ECOG PS

- 0-1 vs 2

CAB> 30 days

-Yes vs No

SRE Prevention

-Yes vs No

Prior Adjuvant ADT

≤12 vs > 12 months

R
A
N
D
O
M
I
Z
E

ARM A:

ADT + docetaxel
75mg/m² every 21
days for maximum
6 cycles

Evaluate
every 3 weeks
while
receiving
docetaxel and
at week 24
then every 12
weeks

ARM B:

ADT (androgen
deprivation therapy
alone)

Evaluate
every 12
weeks

Follow for time
to progression
and overall
survival

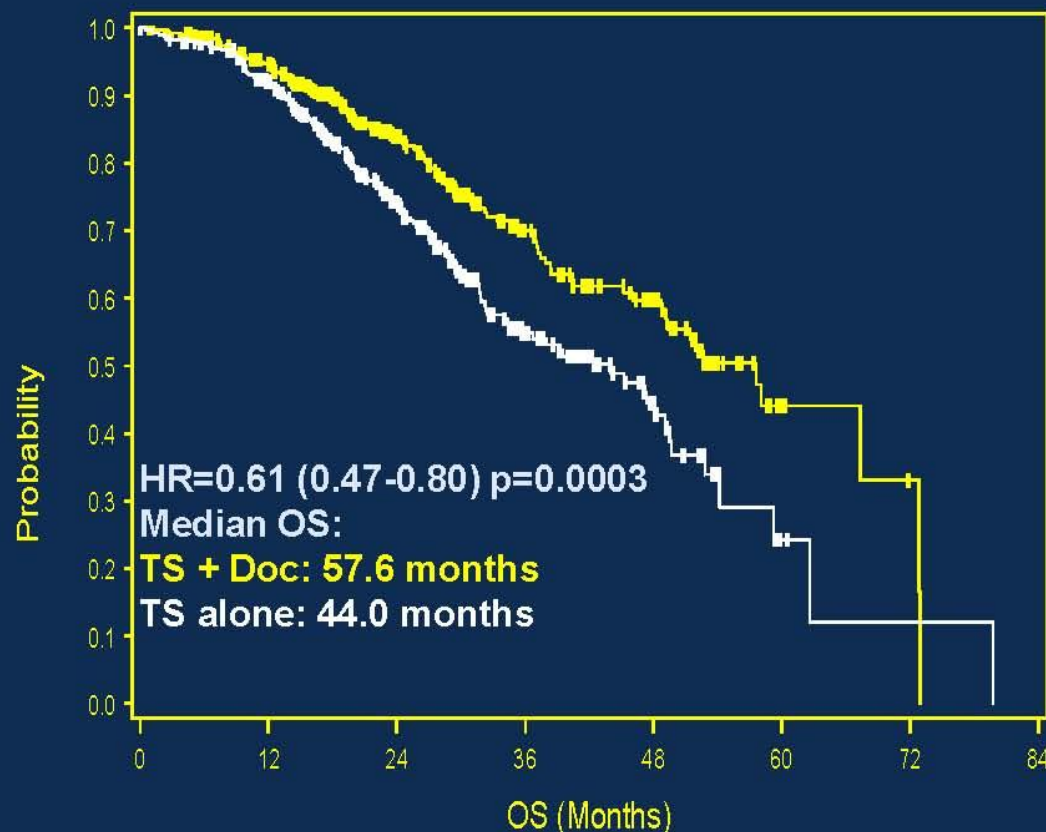
Chemotherapy
at investigator's
discretion at
progression

- ADT allowed up to 120 days prior to randomization
- Intermittent ADT dosing was not allowed
- Standard dexamethasone premedication but no daily prednisone



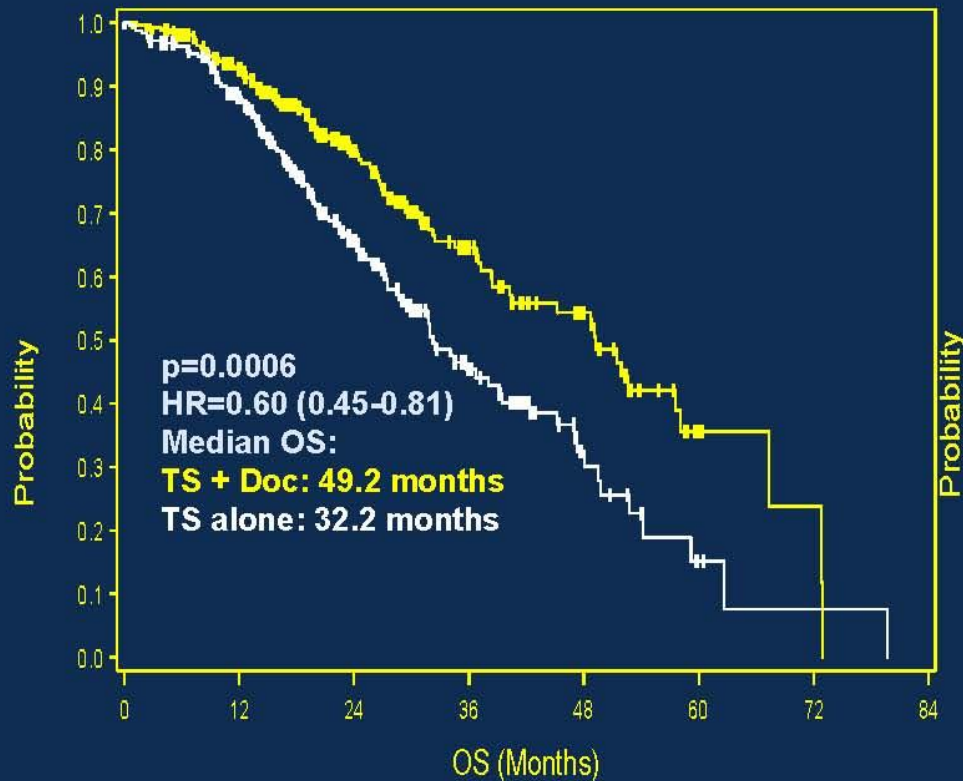
Primary endpoint: Overall survival

- 790 men accrued 7/28/06 to 11/21/2012
 - Planned interim analysis at 53% information, Oct 2013 met pre-specified criteria for significance and release of data
 - Jan 16, 2014 median follow-up of 29 months
 - 136 deaths TS alone vs. 101 deaths TS+Docetaxel

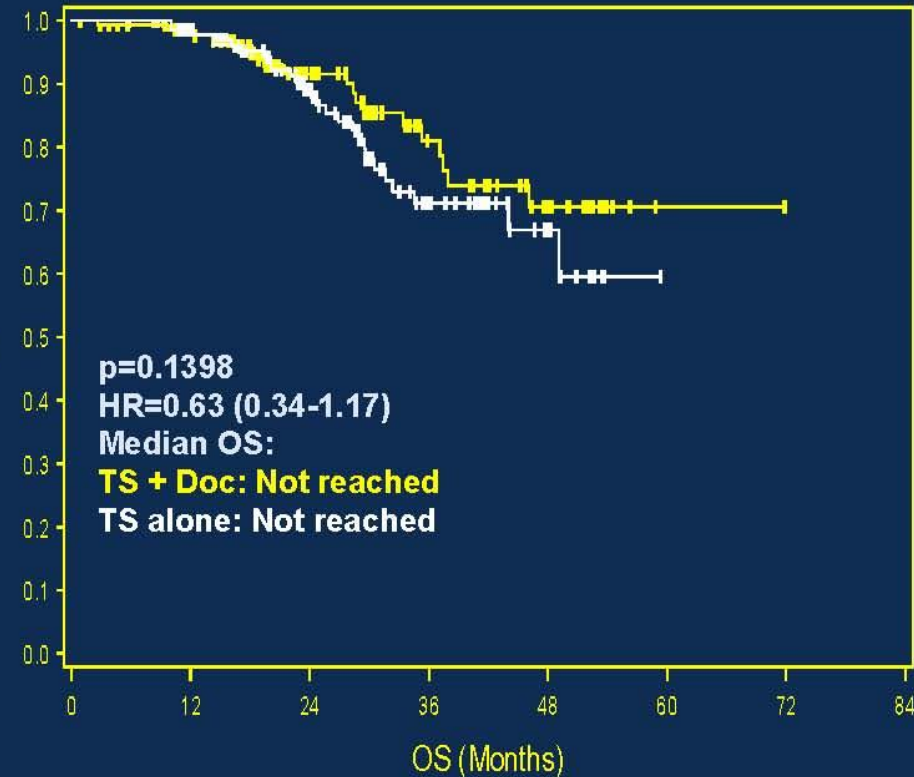


OS by extent of metastatic disease at start of ADT

High volume



Low volume

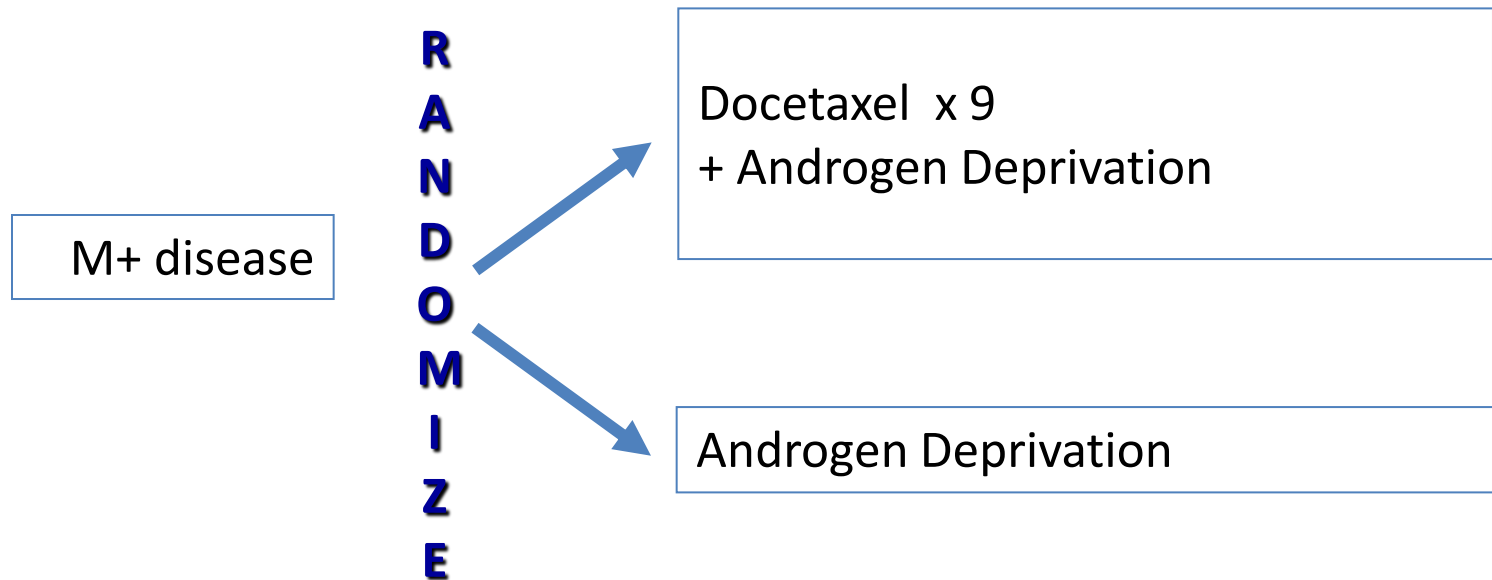


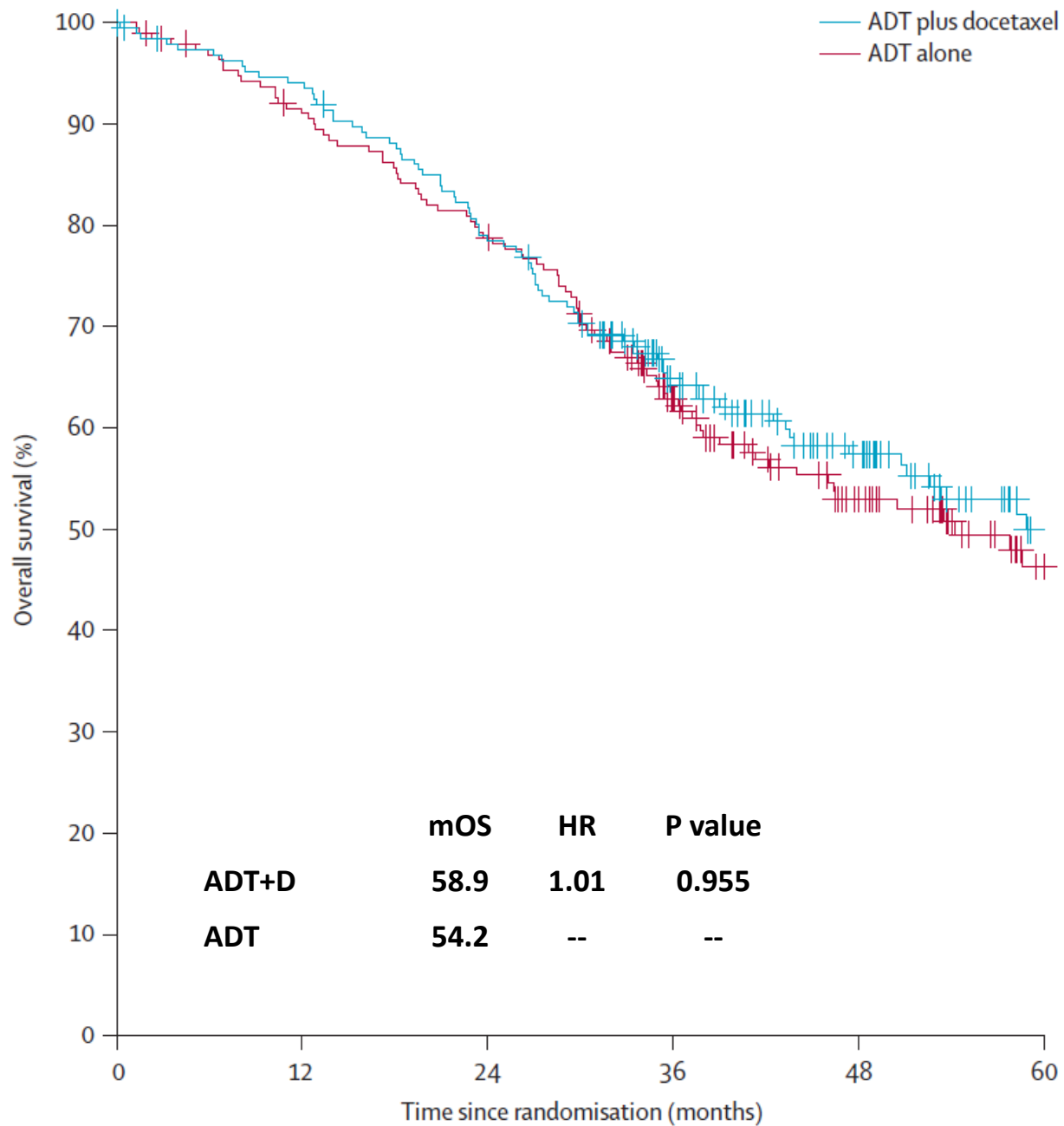
In patients with **high volume metastatic disease**, testosterone suppression plus early **docetaxel improves median overall survival by 17 months** - increased from 32.2 months to 49.2 months.



Androgen-deprivation therapy alone or with docetaxel in non-castrate metastatic prostate cancer (GETUG-AFU 15): a randomised, open-label, phase 3 trial

Lancet Oncol 2013; 14: 149–58





...



CHAARTED VS GETUG15

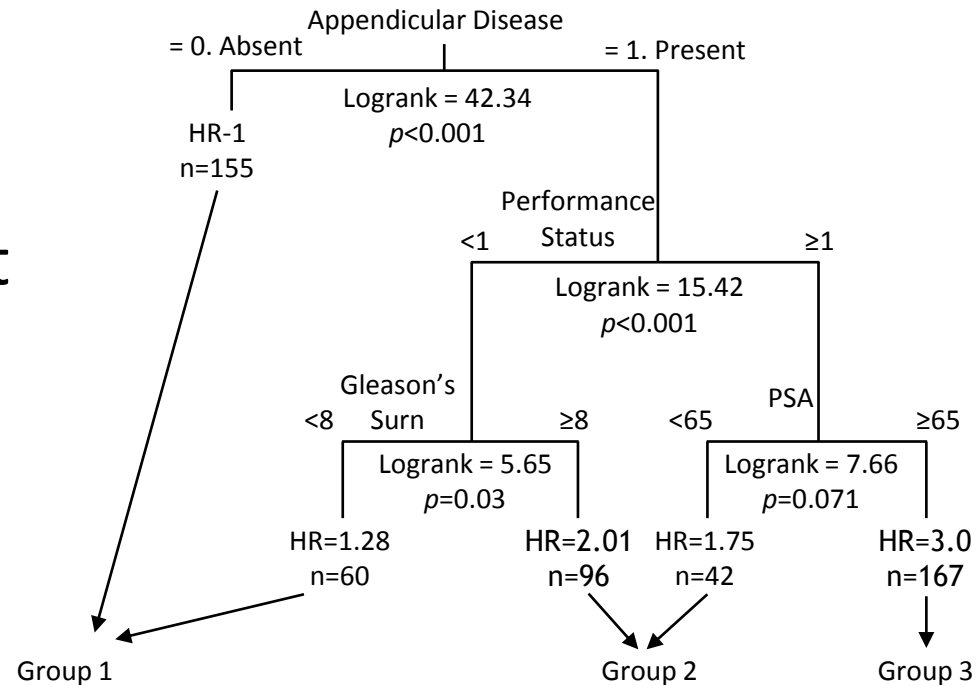
	CHAARTED	GETUG 15
Recruitment period	2006-2012	2004-2008
Patients	790	385
Median age	64 yrs	64 yrs
Metastases at presentation	73%	71%
High risk group rate	66%	22%



CHAARTED VS GETUG15

High risk definition

- High volume
 - Visceral mets and/or
 - ≥ 4 bone mets (at least 1 beyond pelvis and vertebral column)

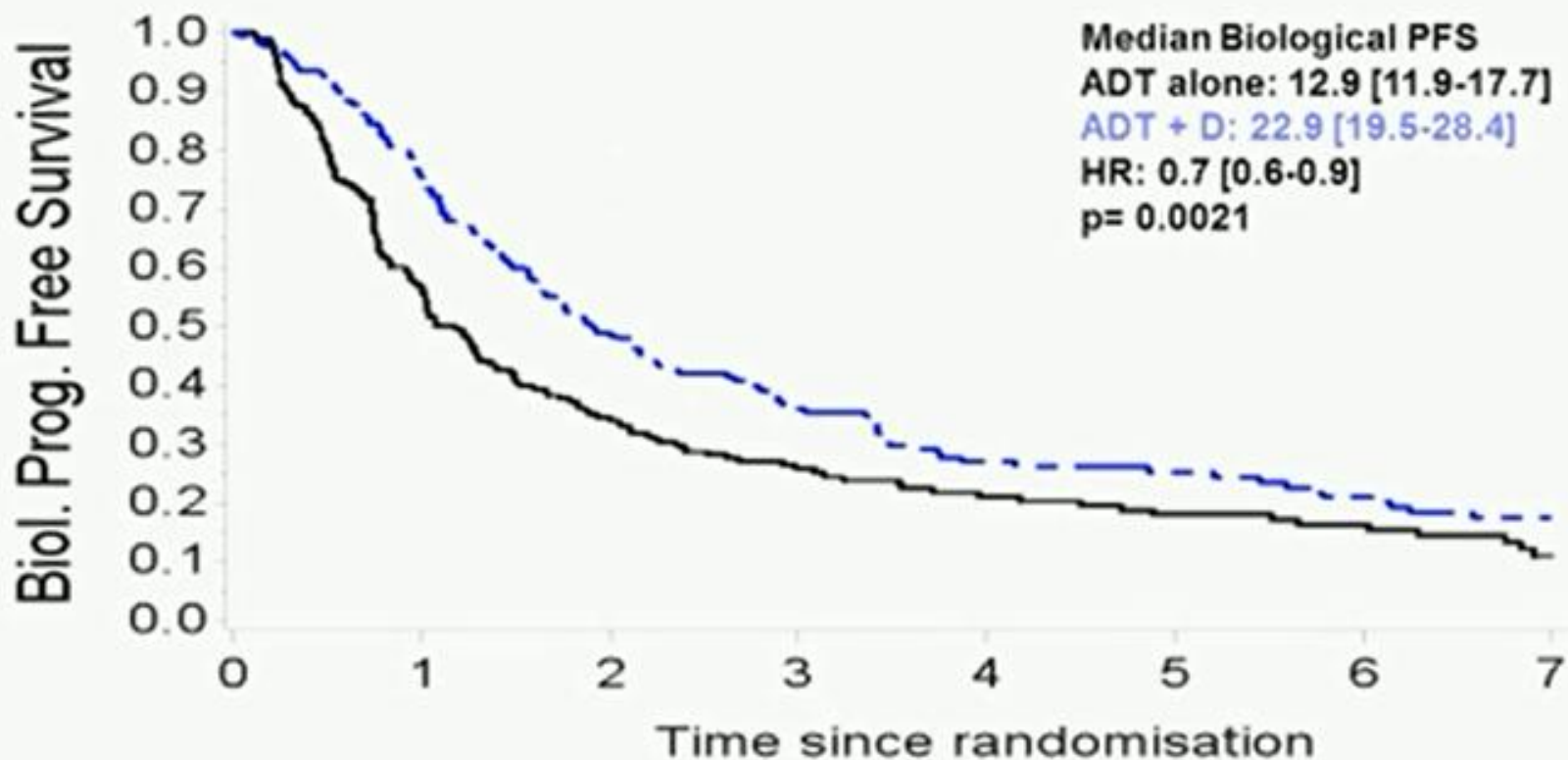


GETUG 15 Update (at 2015 ASCO GU)

- Updated analysis for OS
 - 50 mos → 82.9 mos
- CHAARTED volume definition applied to GETUG pts



Biological PFS



ADT
ADT +D

193
192

105
141

64
92

42
56

28
36

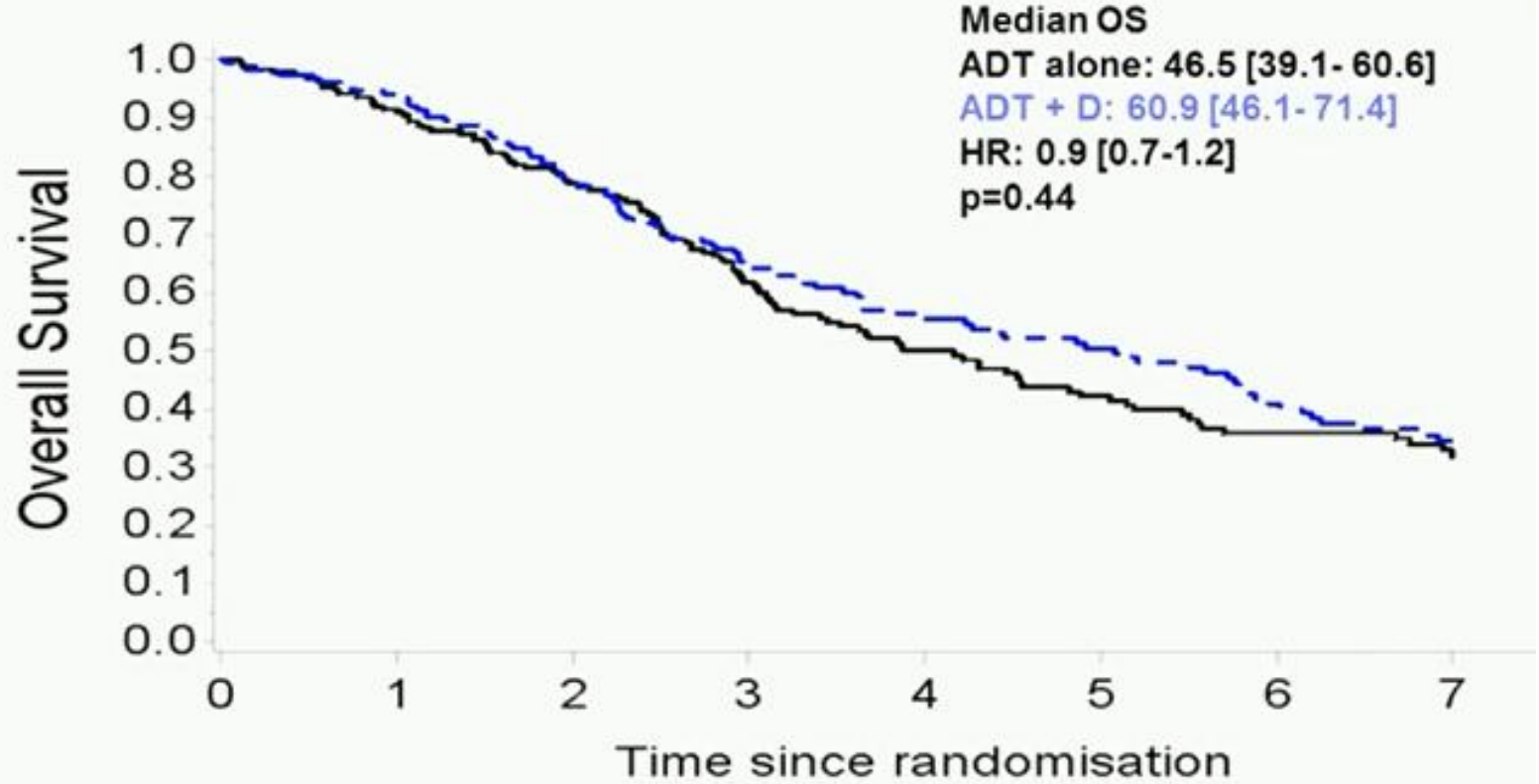
23
29

18
24

7
13



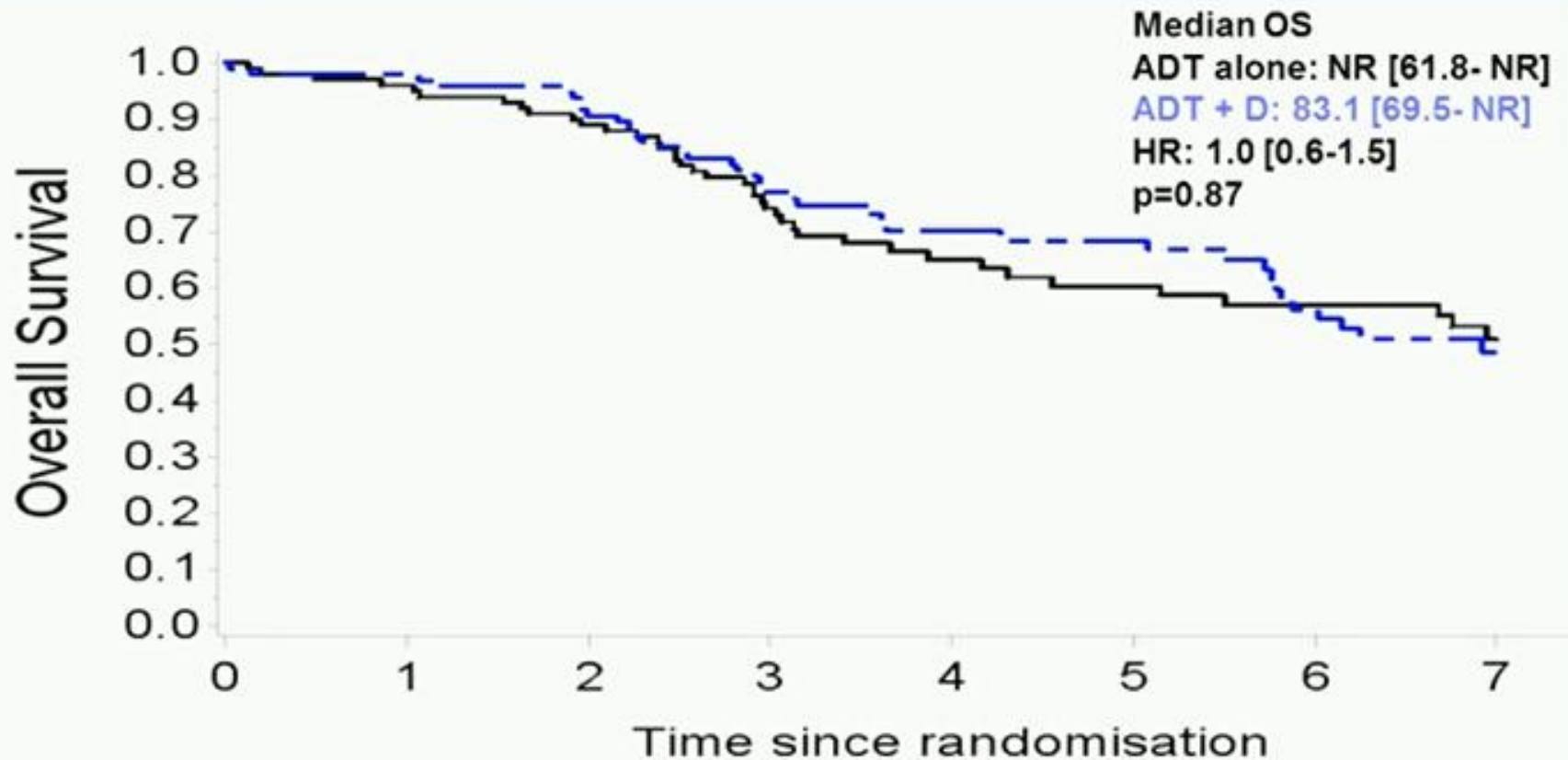
OS



ADT	193	171	148	105	66	53	43	29
ADT +D	192	175	145	100	70	58	47	27



OS: low volume



ADT
ADT + D

102
100

95
94

88
86

65
62

43
45

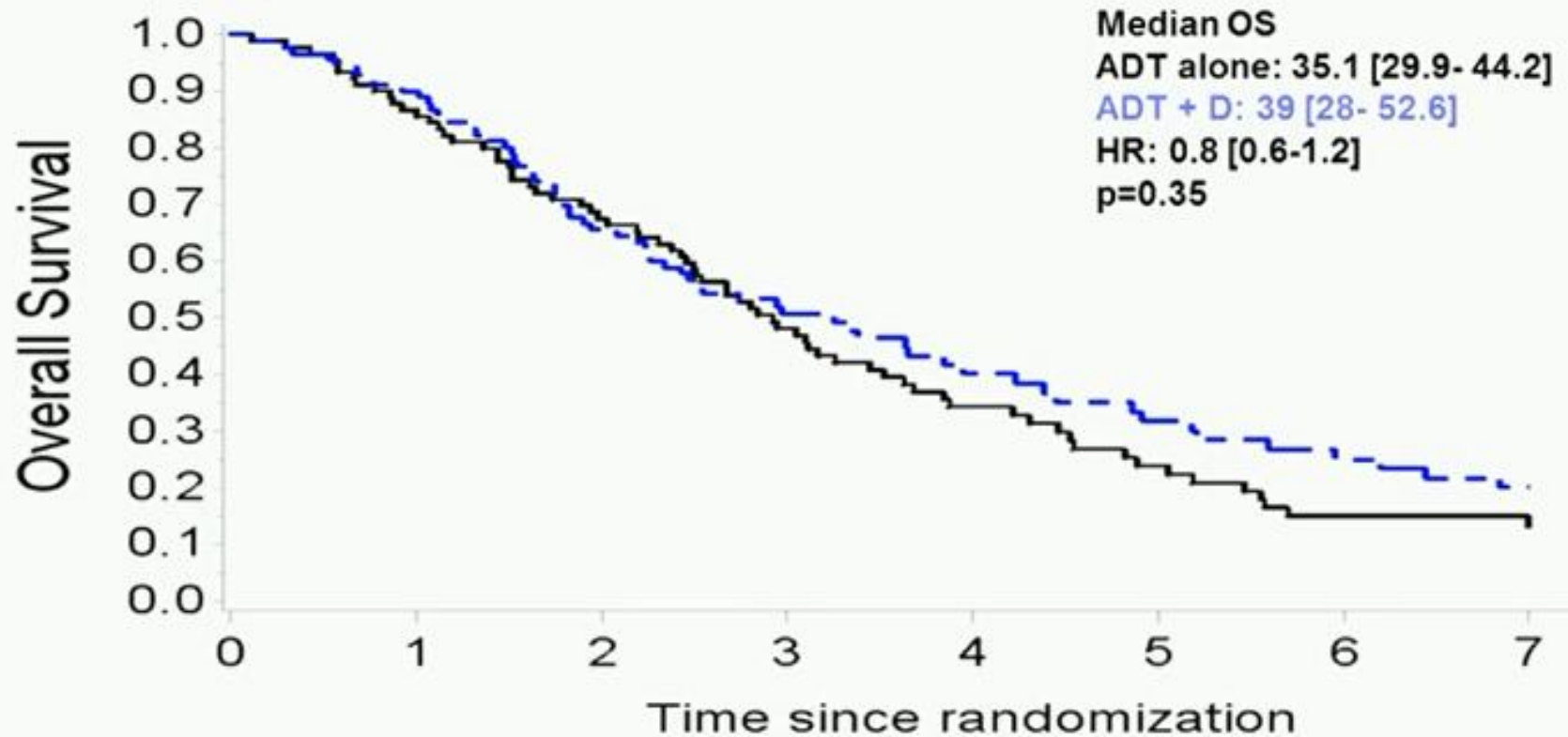
37
39

33
32

21
18



OS high volume



ADT
ADT +D

91
92

76
81

60
59

40
38

23
25

16
19

10
15

8
9



CHAARTED VS GETUG15

	CHAARTED	GETUG 15
High volume rate	66%	48%
Follow-up	29 mos	82.9 mos
Improved PSA/clinical PFS	21 mos vs 15 mos HR 0.56	23 mos vs 13 mos HR 0.70
OS ADT+D vs ADT	57 mos vs 44 mos HR 0.61	61 mos vs 46 mos HR 0.44
OS ADT+D vs ADT (high volume)	49 mos vs 32 mos HR 0.60	39 mos vs 35 mos HR 0.80



CHAARTED VS GETUG15

Sample size (statistical design)

790 pts

- 33% improvement in mOS
 - 33 → 44 mos (high volume)
 - 67 → 89 mos (low volume)
- Power 80%
- 1-sided α 0.025

385 pts

- 15 % improvement in 36-mo survival rate
 - 50% → 65%
- Power 80%
- 2-sided α 0.05

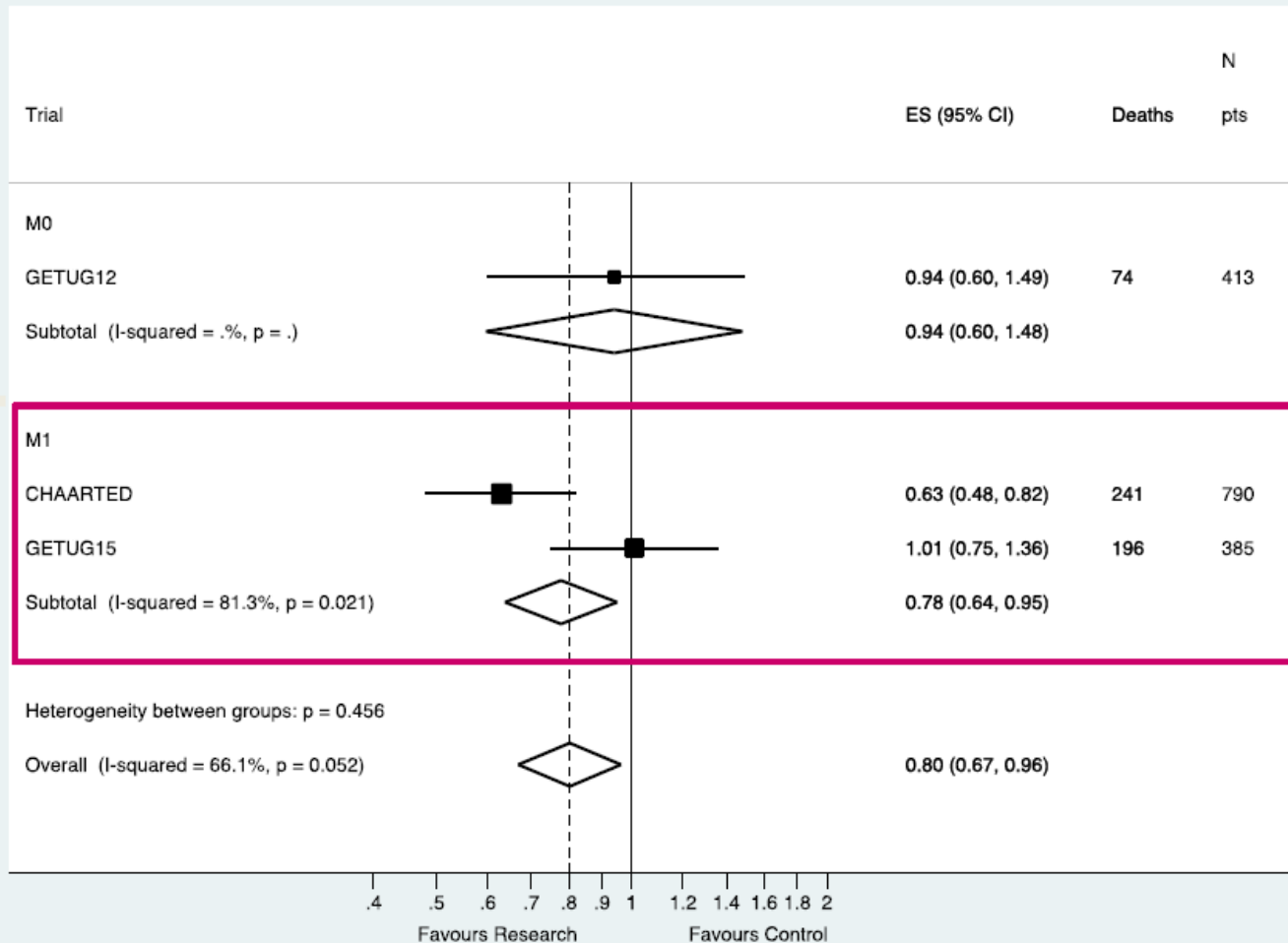
514 PTS (HV)

183 PTS (HV)



Meta-analysis of trials: Matt Sydes MRC

Docetaxel effect: published data and by metastases



CHAARTED VS GETUG15

Post-progression treatments

	Experimental arm		Control arm	
	GETUG15	CHAARTED	GETUG15	CHAARTED
Docetaxel	45%	12%	80%	33%
Abiraterone /Enzalutamide	15%*	23%	15%*	20%

* Enrolled in clinical trials vs placebo



- Is chemo the new standard for HSPC pts?
 - YES (for a quote of pts...waiting more accurate selection criteria)
- Are the presented data enough?
 - NO (we are still waiting the full paper)
(further data from other trials)



STAMPEDE trial

Newly diagnosed high risk patients T3/4 N0 M0 with:

- At least two of: PSA ≥ 40 ng/ml or Gleason sum score 8-10
- And intention to treat with radical radiotherapy (unless there is a contra-indication; exemption must be sought in advance of consent, after discussion with MRC CTU)

Newly diagnosed metastatic or nodal disease

- Stage T_{any} N+ M0 **or** T_{any} N_{any} M+

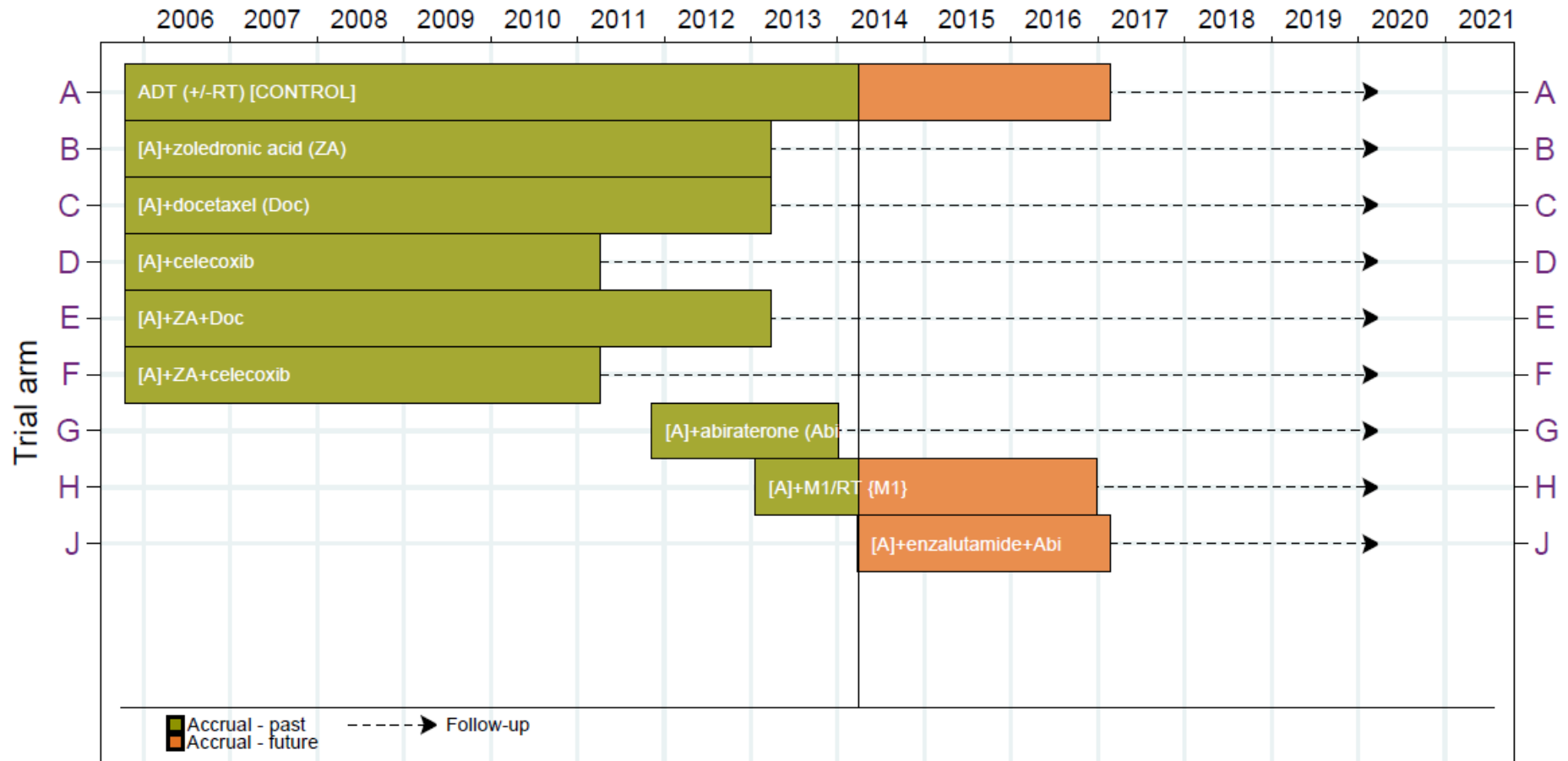
Previously treated relapsing patients with either

- PSA ≥ 4 ng/ml and rising with doubling time < 6 months
- PSA ≥ 20 ng/ml
- N+
- M+

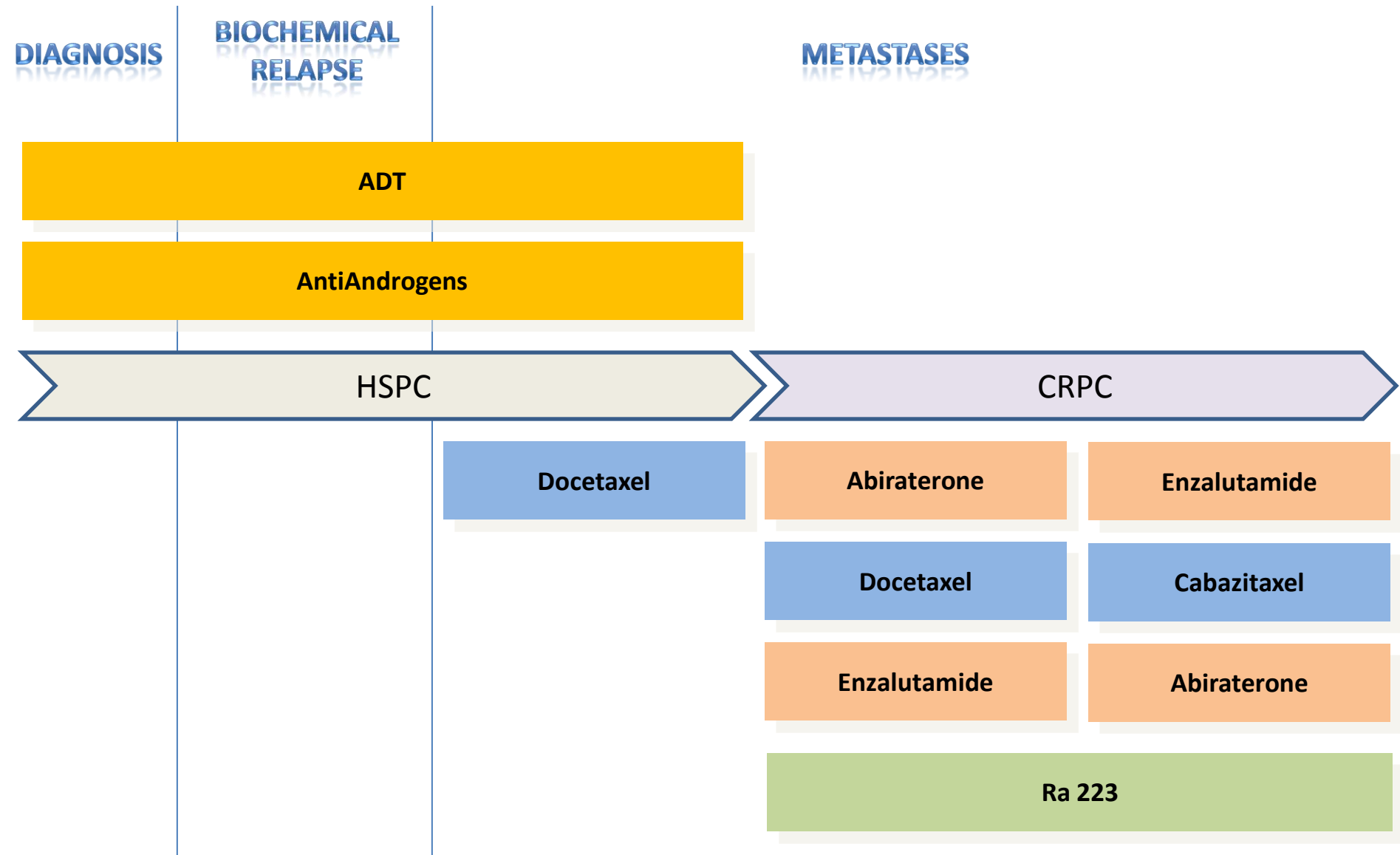


STAMPEDE

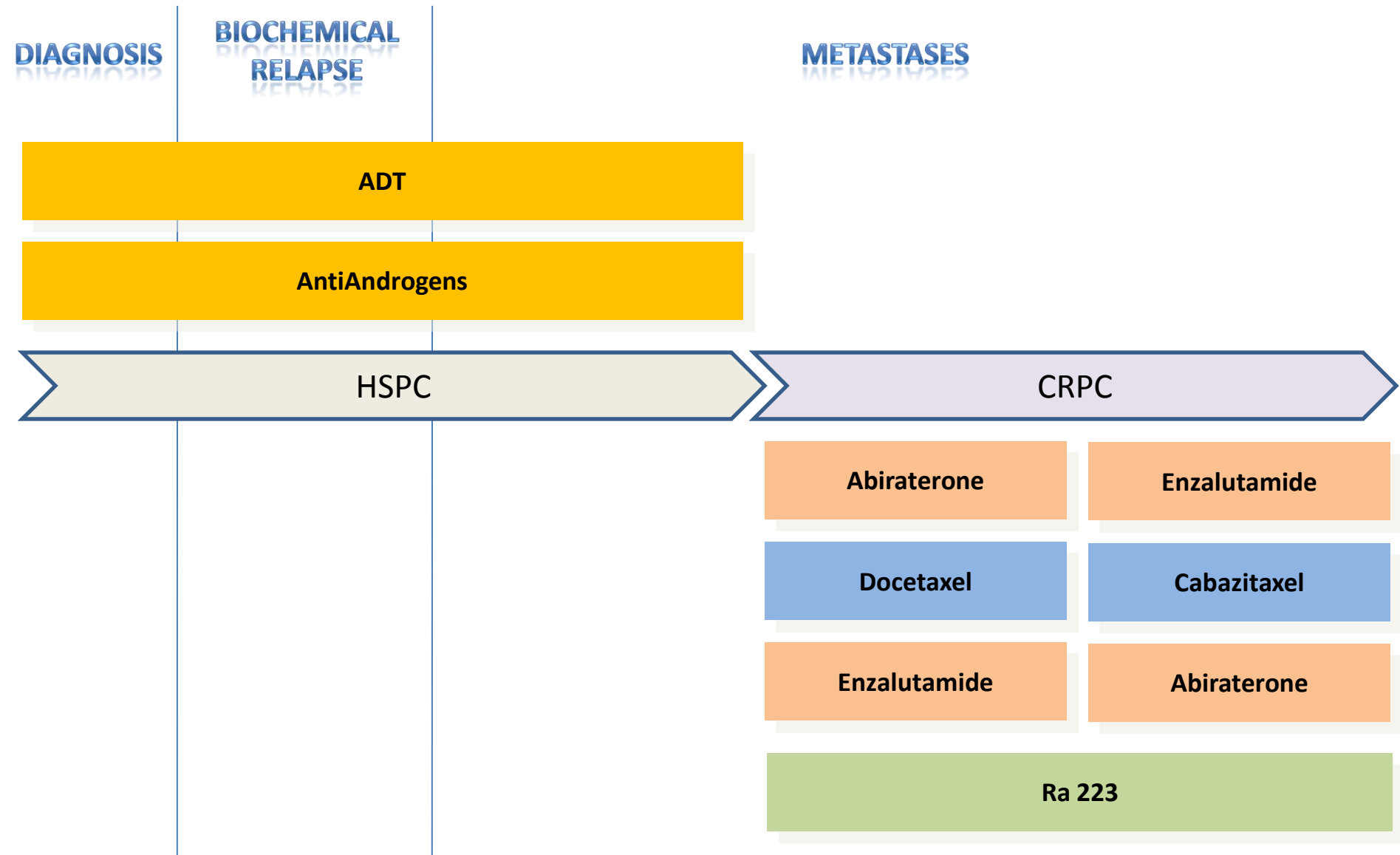
Systemic Therapy in Advancing or Metastatic Prostate cancer: Evaluation of Drug Efficacy



2015 landscape



Landscape around the corner



BUT
ROI



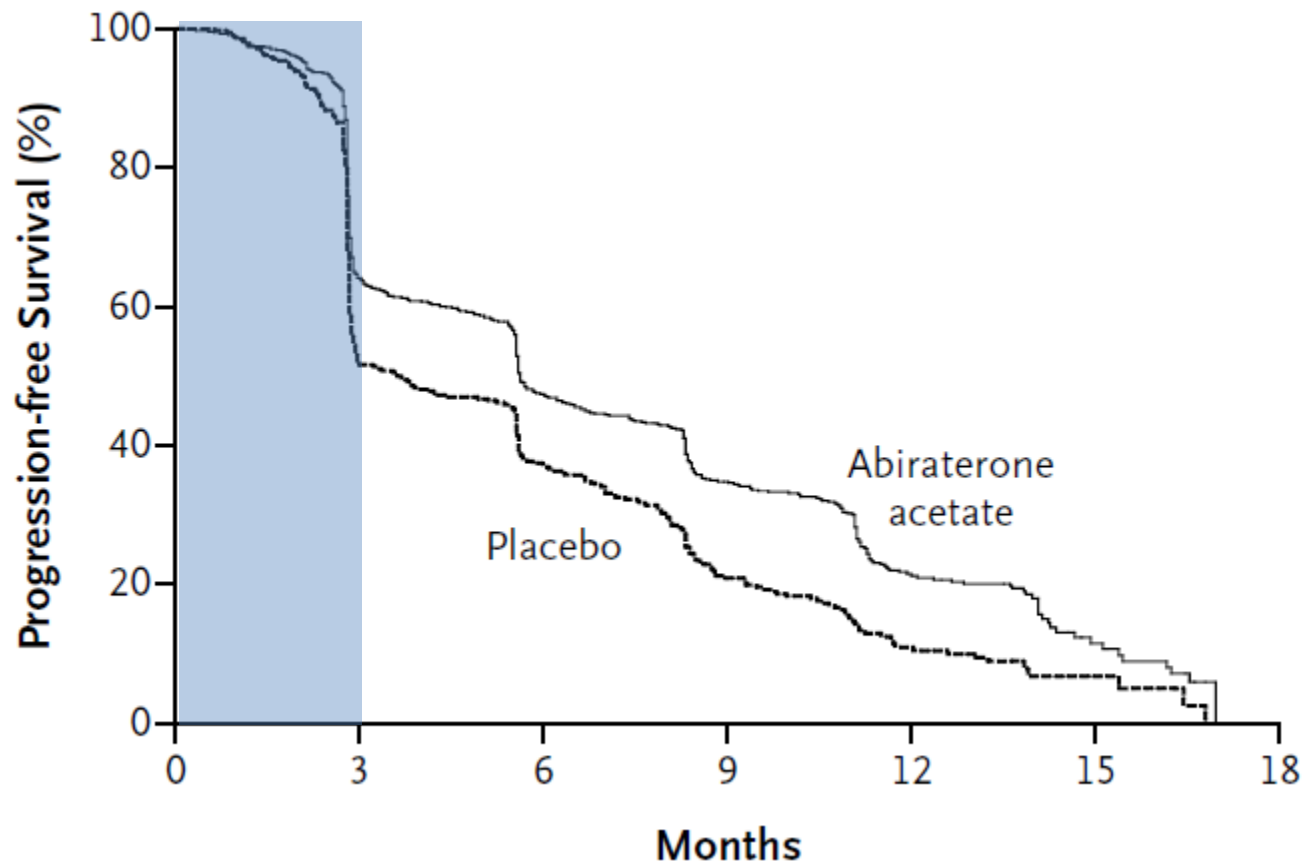
The NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

MAY 26, 2011

VOL. 364 NO. 21

Abiraterone and Increased Survival in Metastatic Prostate Cancer



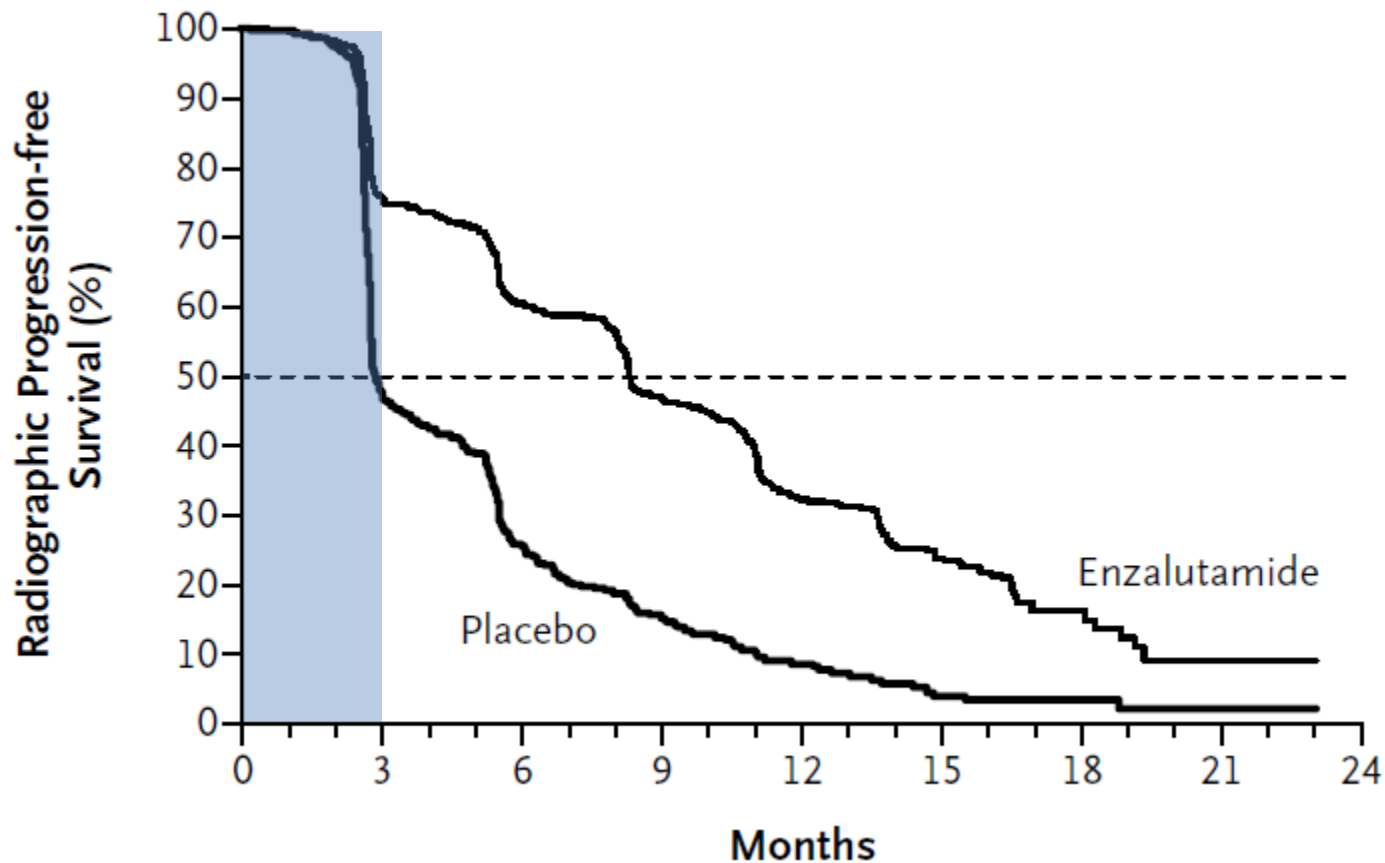
The NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

SEPTEMBER 27, 2012

VOL. 367 NO. 13

Increased Survival with Enzalutamide in Prostate Cancer after Chemotherapy



STRATEGIES FOR OVERCOMING RESISTANCE



ARMOR 3

Progressive M1 disease on ADT
Detectable AR-V7 from CTCs

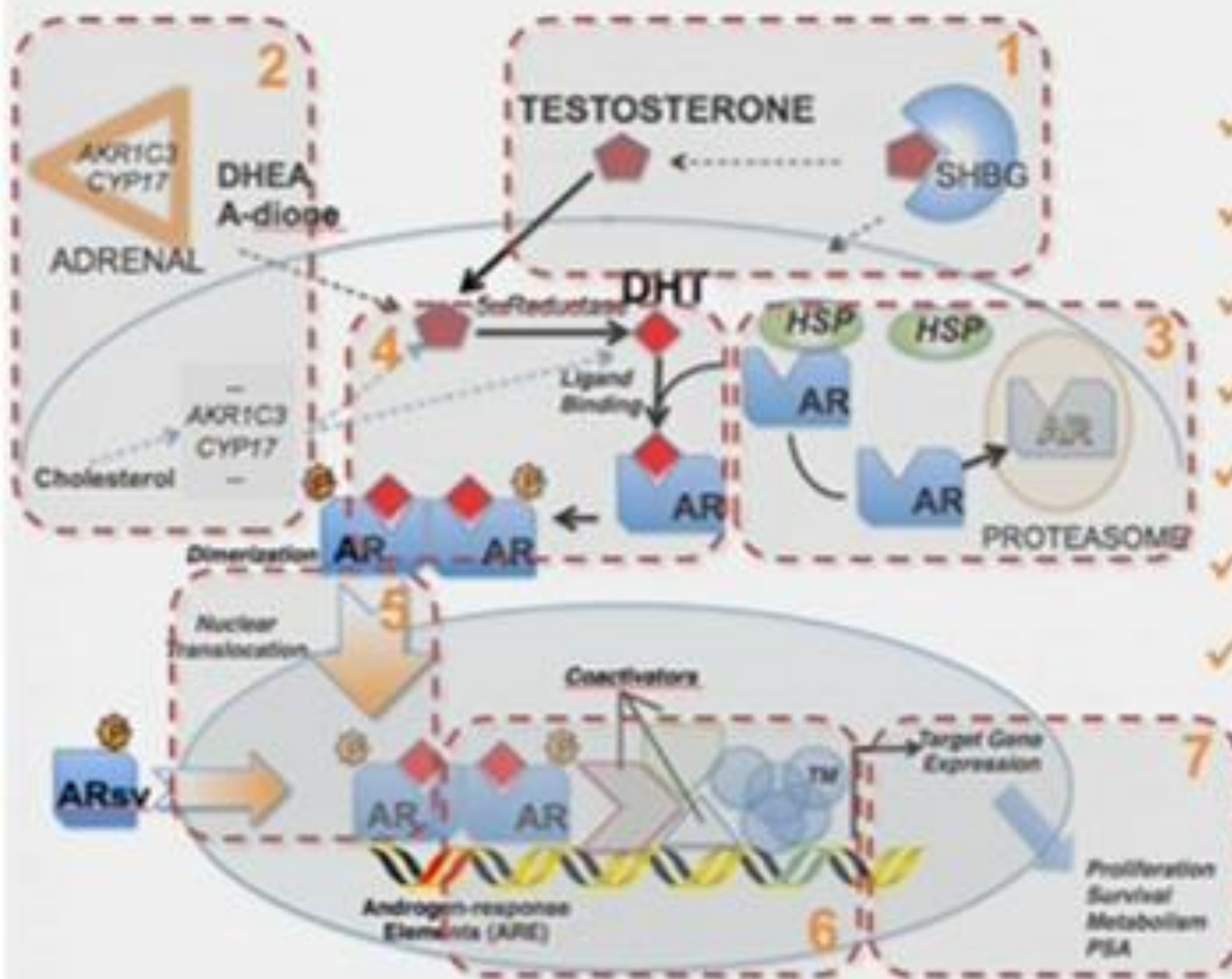
Randomize
N=148

Galeterone
2550 mg/day

Enzalutamide
160 mg/day



ZONES OF VULNERABILITY and ATTACK



- ✓ Gonadal synthesis
- ✓ Adrenal/Intracrine
- ✓ Degradation/HSP
- ✓ Competitive (LBD)
- ✓ Translocation
- ✓ DNA/CoActivator
- ✓ Target effectors



Abiraterone

PharmaTimes
digital

News Magazine JobSearch Competitions Events/Meeting

WORLD NEWS | FREE NEWS HEADLINES | FREE RSS FEED

Where am I? > Article

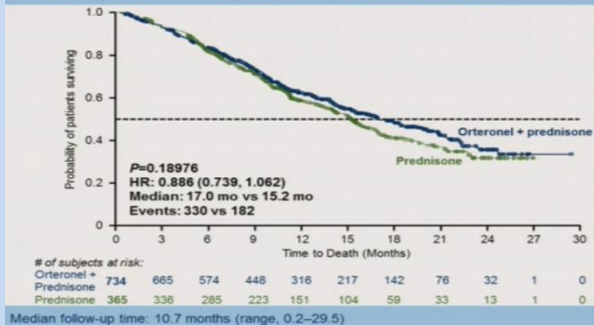
Enzalutamide
ARN-509
EZN-4176

Azacitidine

Temsirolimus
Everolimus

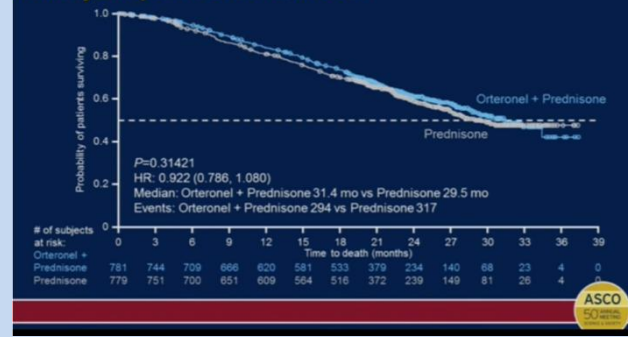
Dasatinib
Saracatinib

Primary Endpoint: Overall Survival



ELM-PC5

Primary Endpoint: Overall Survival



ELM-PC4

FAILED

nabixin
binostat
rinostat
939

vacizumab
nitinib
ibercept

Cixutumumab
Figitumumab

OGX-011

Oblimersen
AT-101

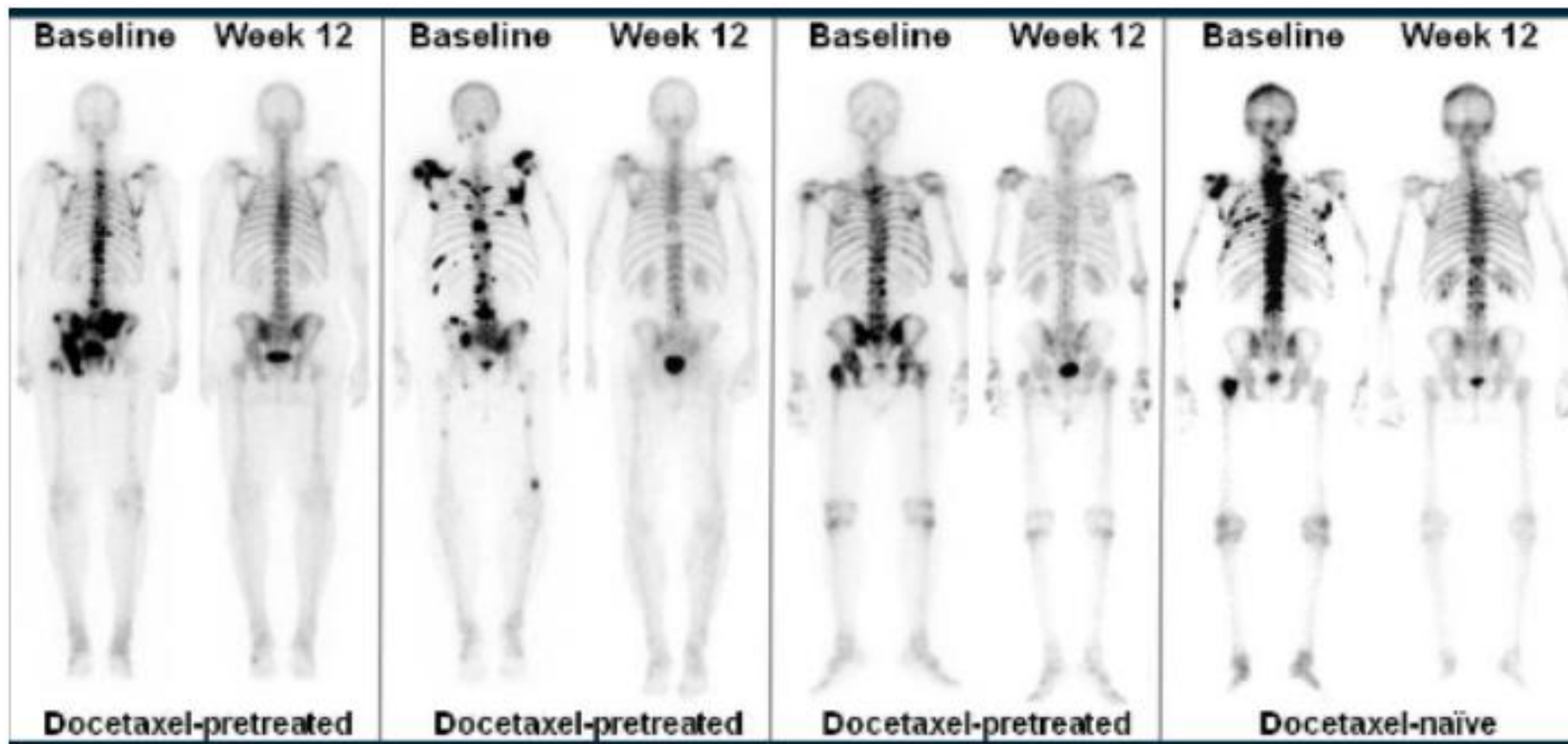
Cabozantinib

Angiogenesis



Bone Scan Effects

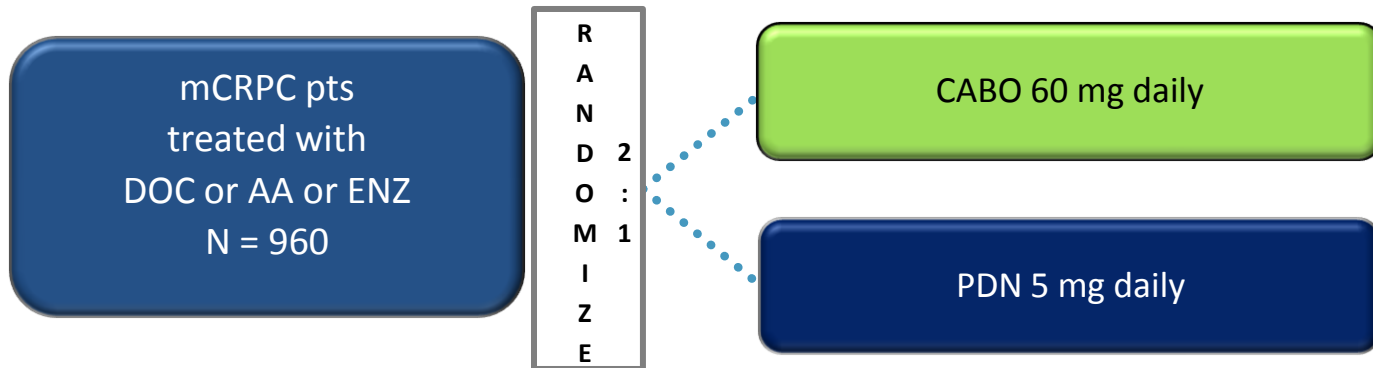
Representative Images



Each patient achieved partial response and pain improvement.

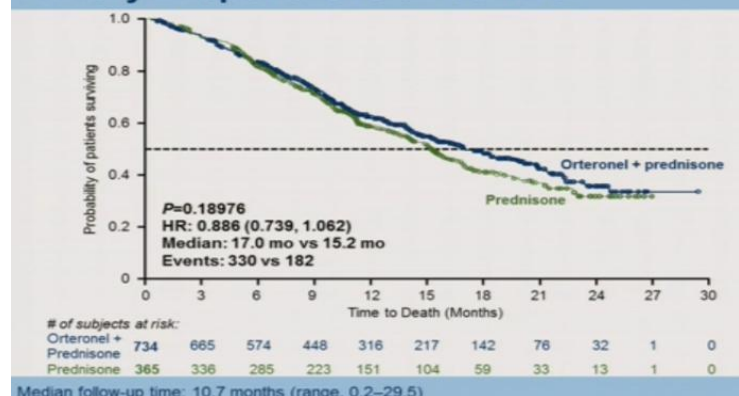


COMET-1 Trial



Primary endpoint OS:
25% reduction in the risk of death





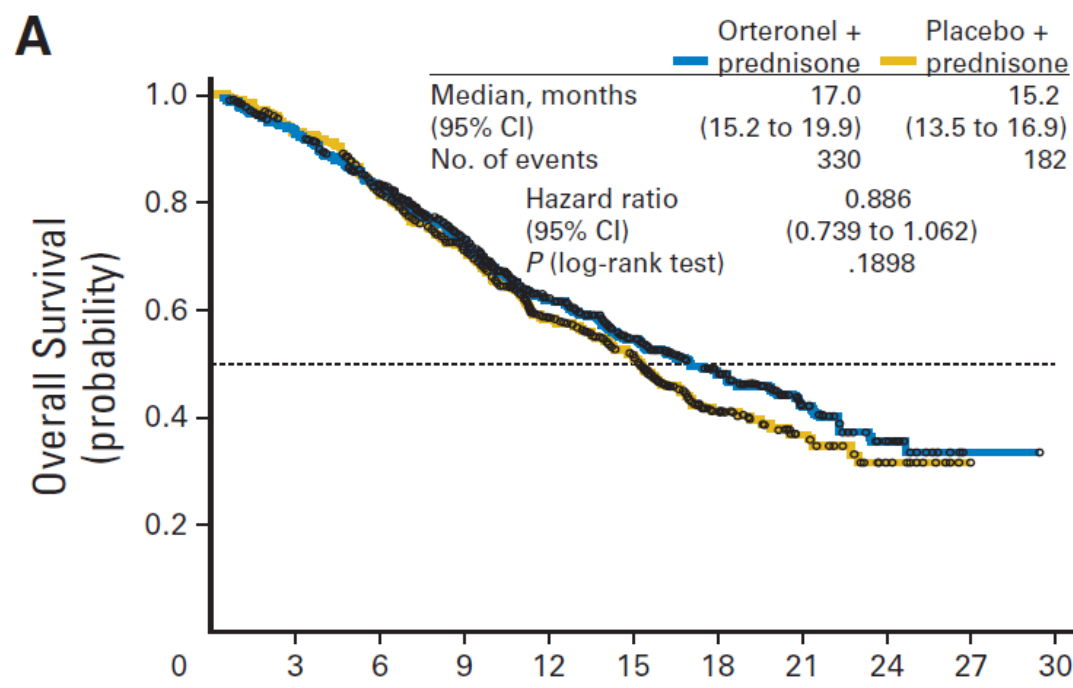
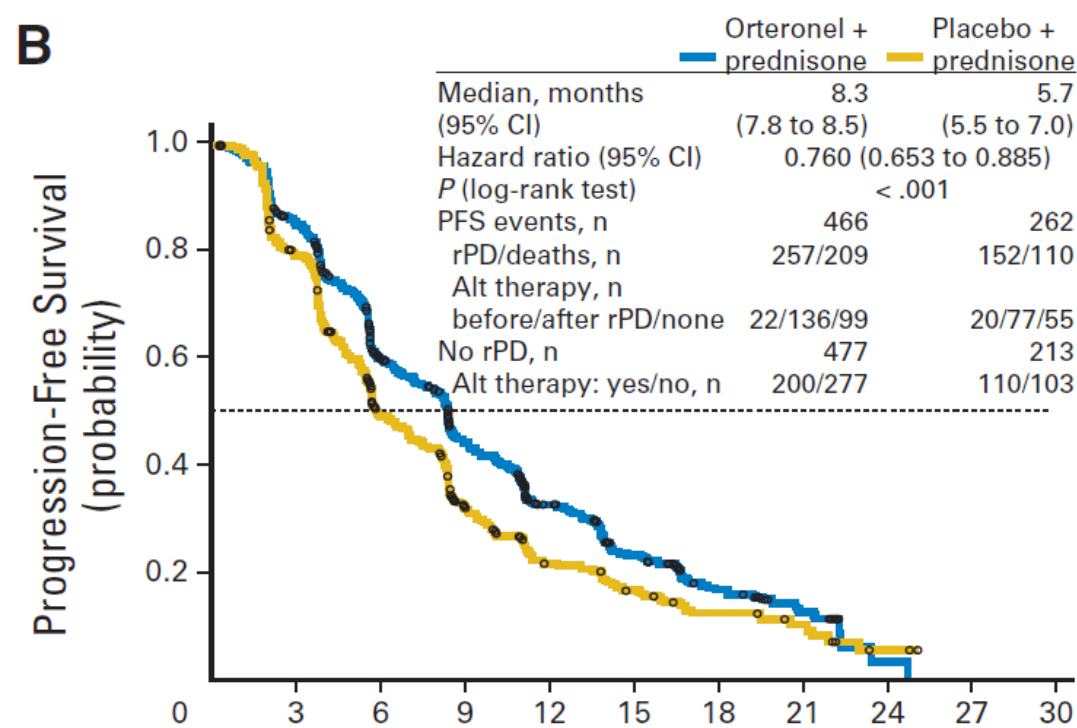
Published Ahead of Print on January 26, 2015 as 10.1200/JCO.2014.56.5119
The latest version is at <http://jco.ascopubs.org/cgi/doi/10.1200/JCO.2014.56.5119>

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

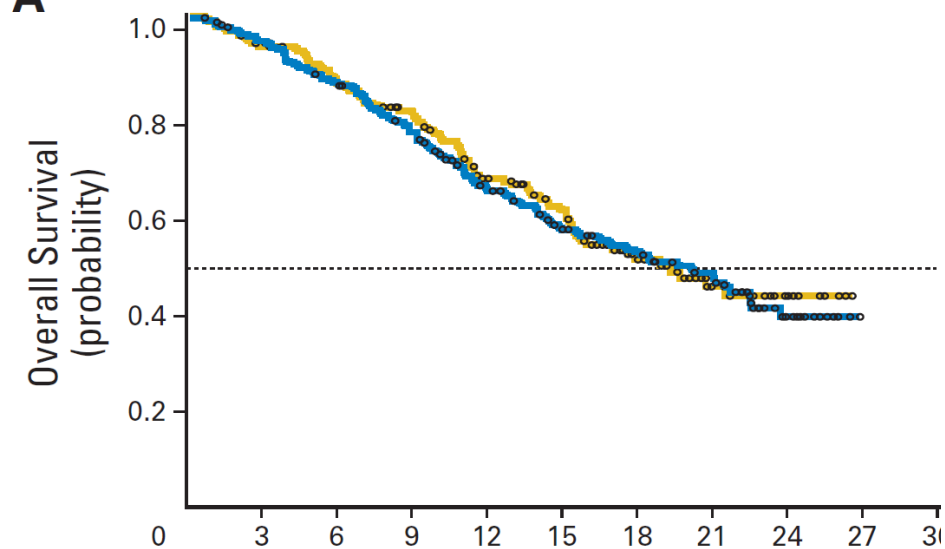
Phase III, Randomized, Double-Blind, Multicenter Trial Comparing Orteronel (TAK-700) Plus Prednisone With Placebo Plus Prednisone in Patients With Metastatic Castration-Resistant Prostate Cancer That Has Progressed During or After Docetaxel-Based Therapy: ELM-PC 5





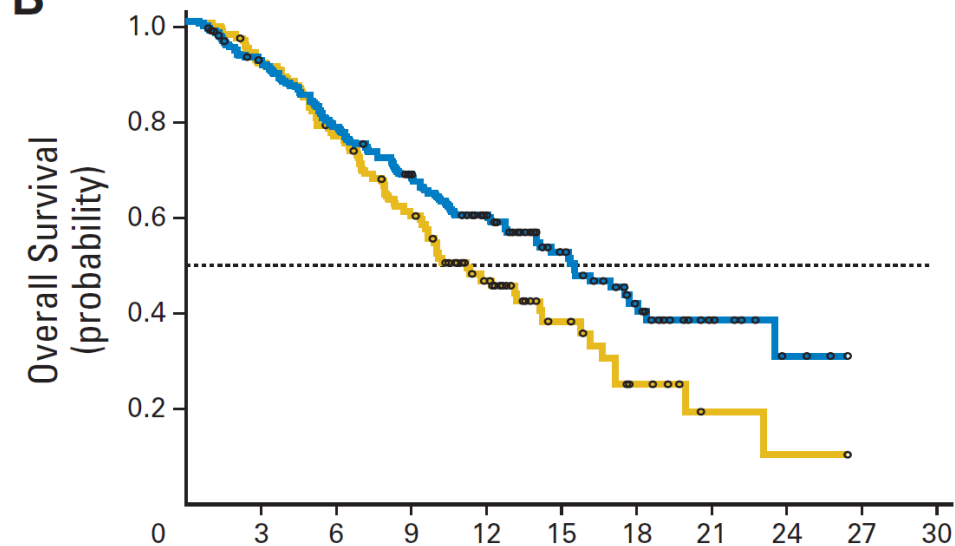
NEU/NNA

A



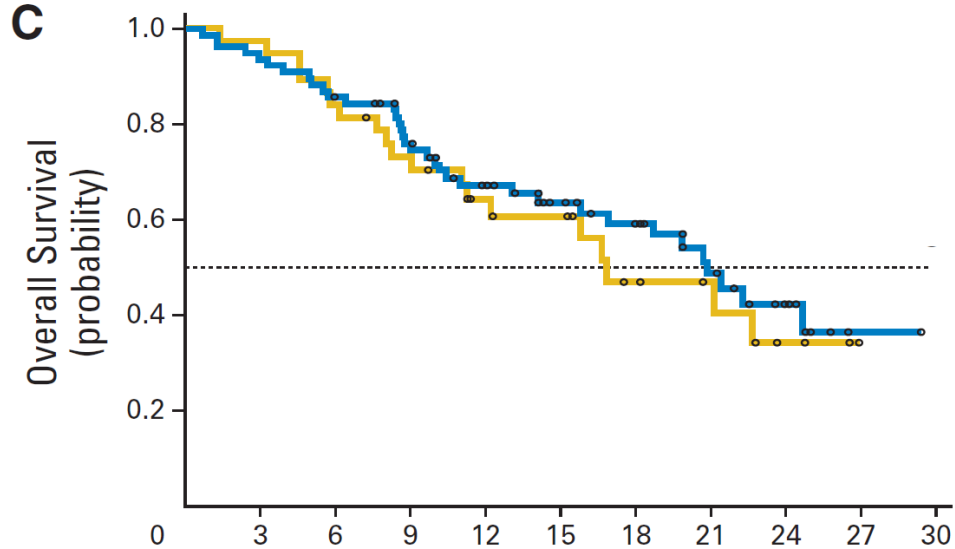
EU

B

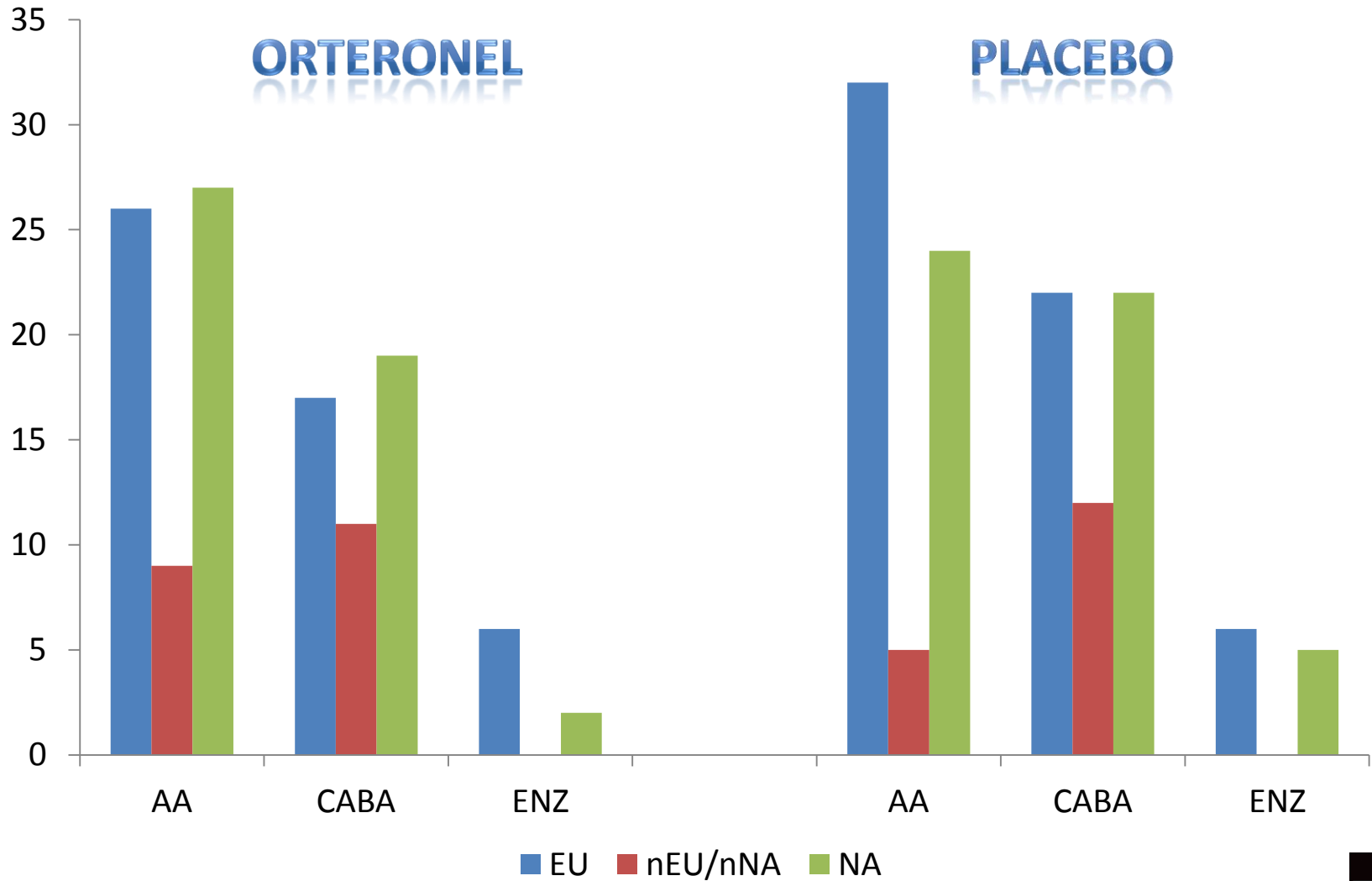


NA

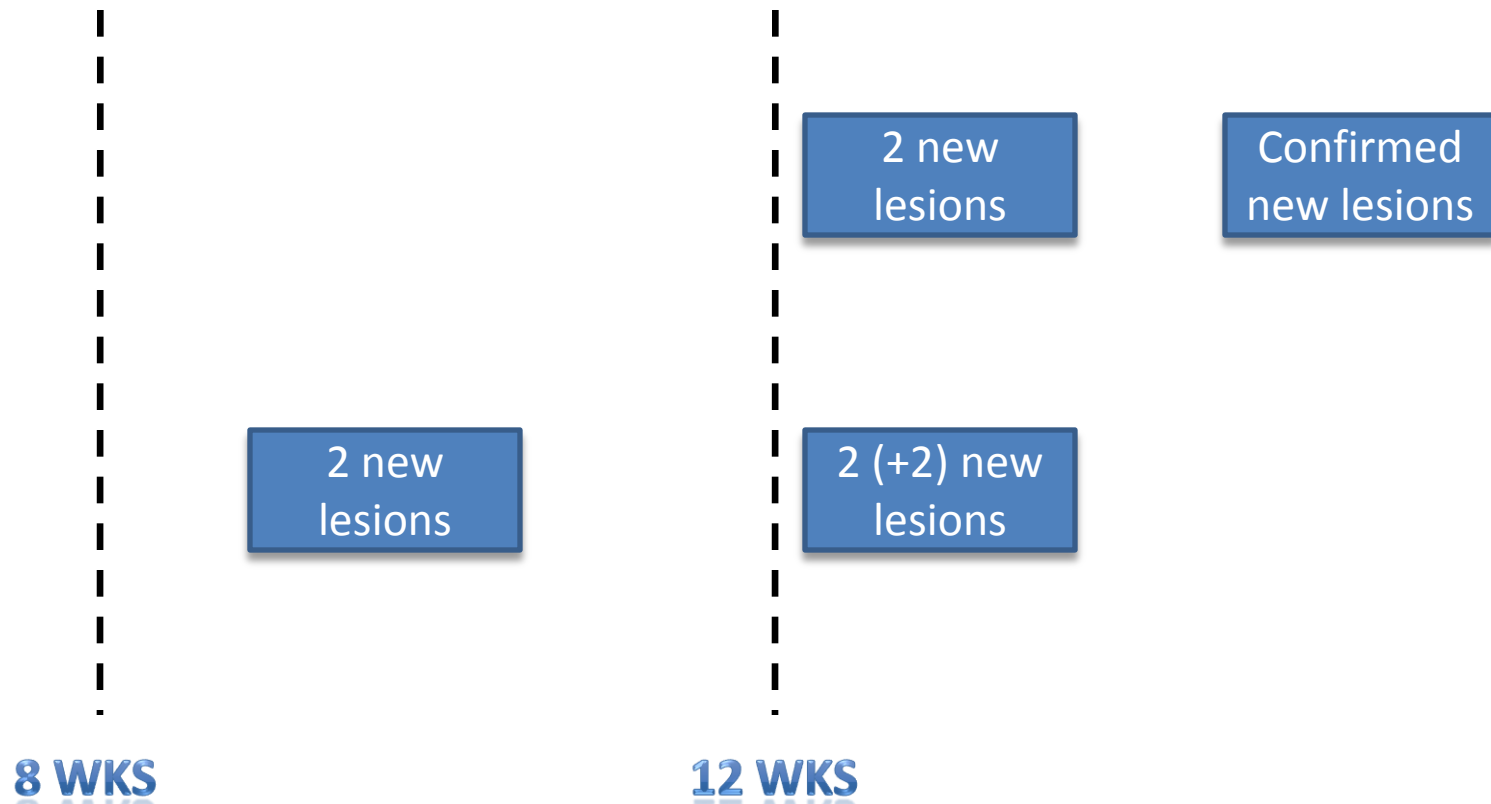
C

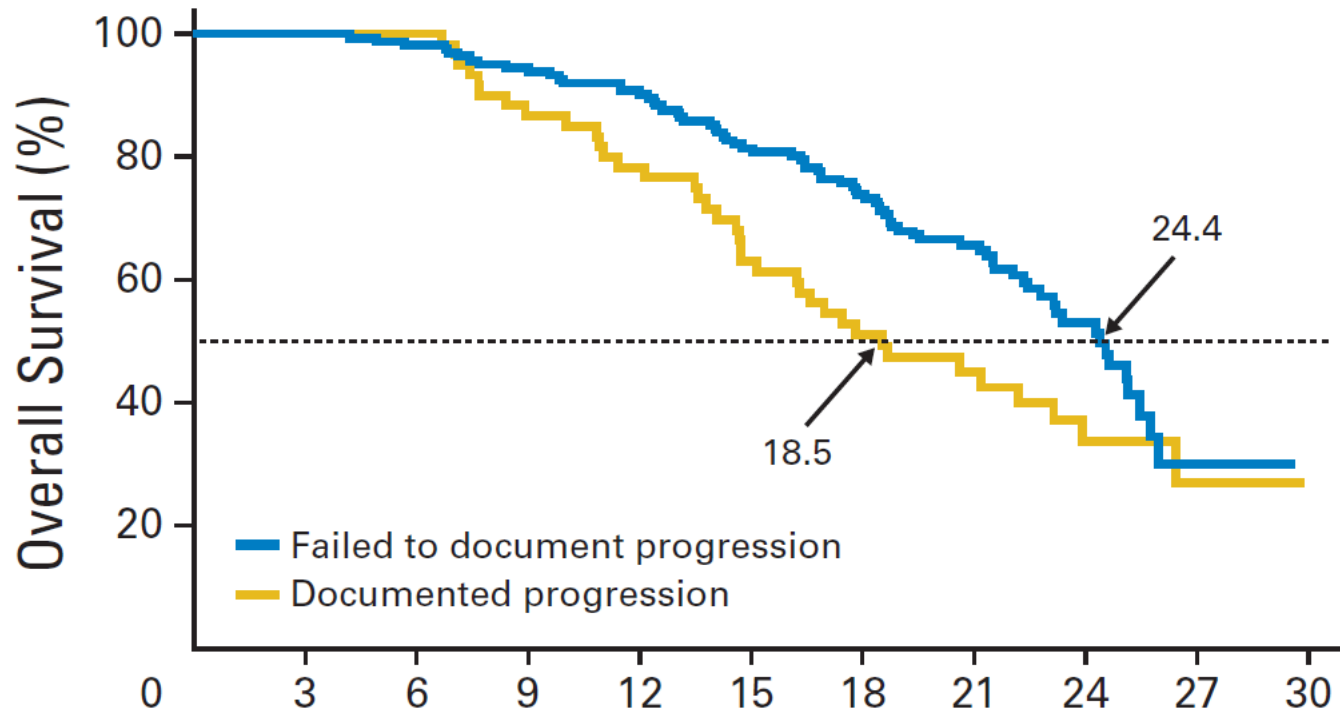


Post progression therapies

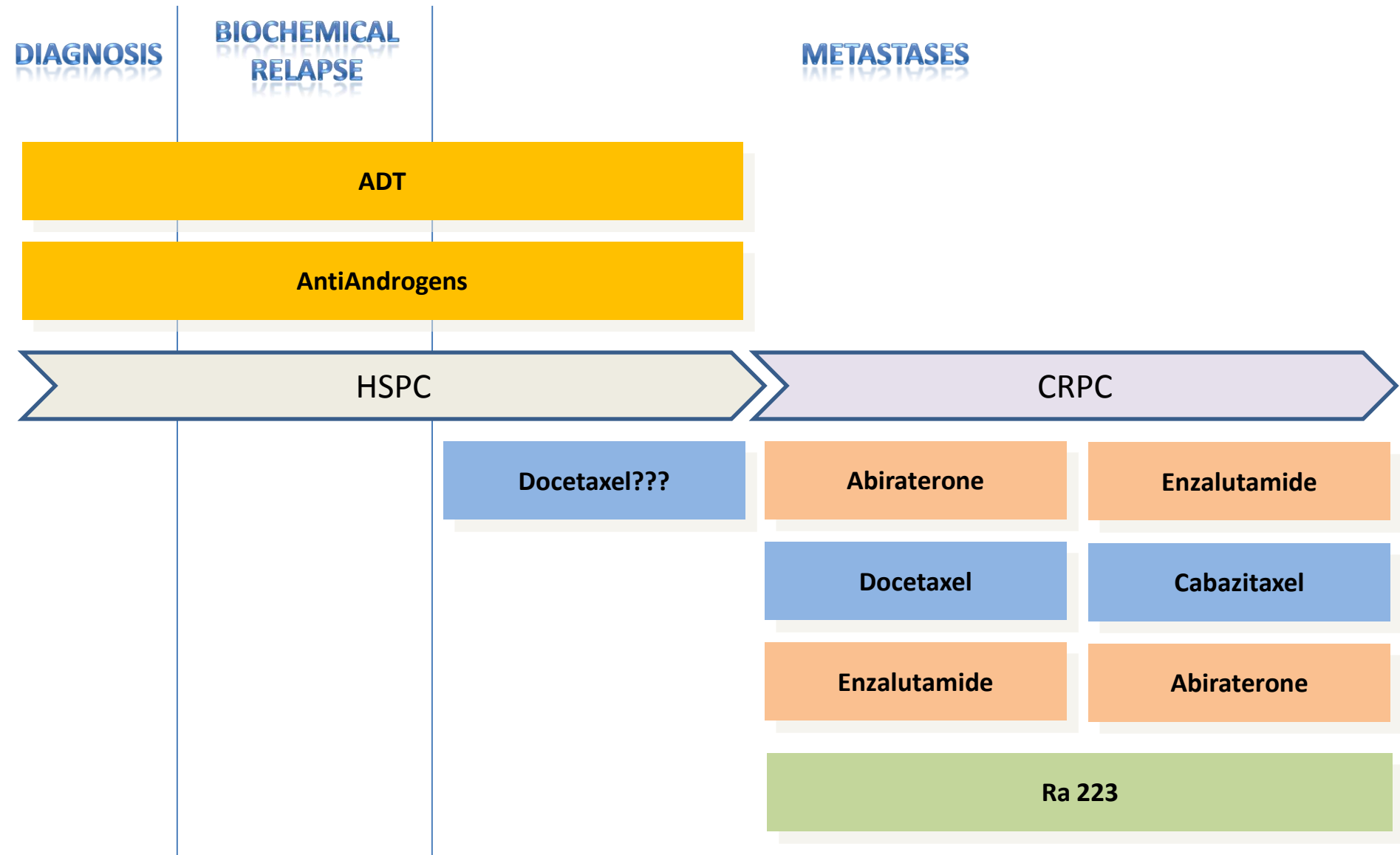


Radiographic Progression-Free Survival As a Response Biomarker in Metastatic Castration-Resistant Prostate Cancer: COU-AA-302 Results





2015 landscape



THANK YOU

