MIAMI CANCER MEETING

15th ed.

Thanks to:

- The Medical Educator Consortium
- Luis Raez, MD, Florida International University

Prostate Cancer Management:

From Early Chemical Recurrence to HRPC (excluding Immunotherapy).

Mayer Fishman, MD PhD

Member, Moffitt Cancer Center
Department of Genitourinary Oncology

Professor, University of South Florida,
Morsani College of Medicine
Department of Oncologic Sciences
Department of Internal Medicine

Mayer Fishman, MD, PhD

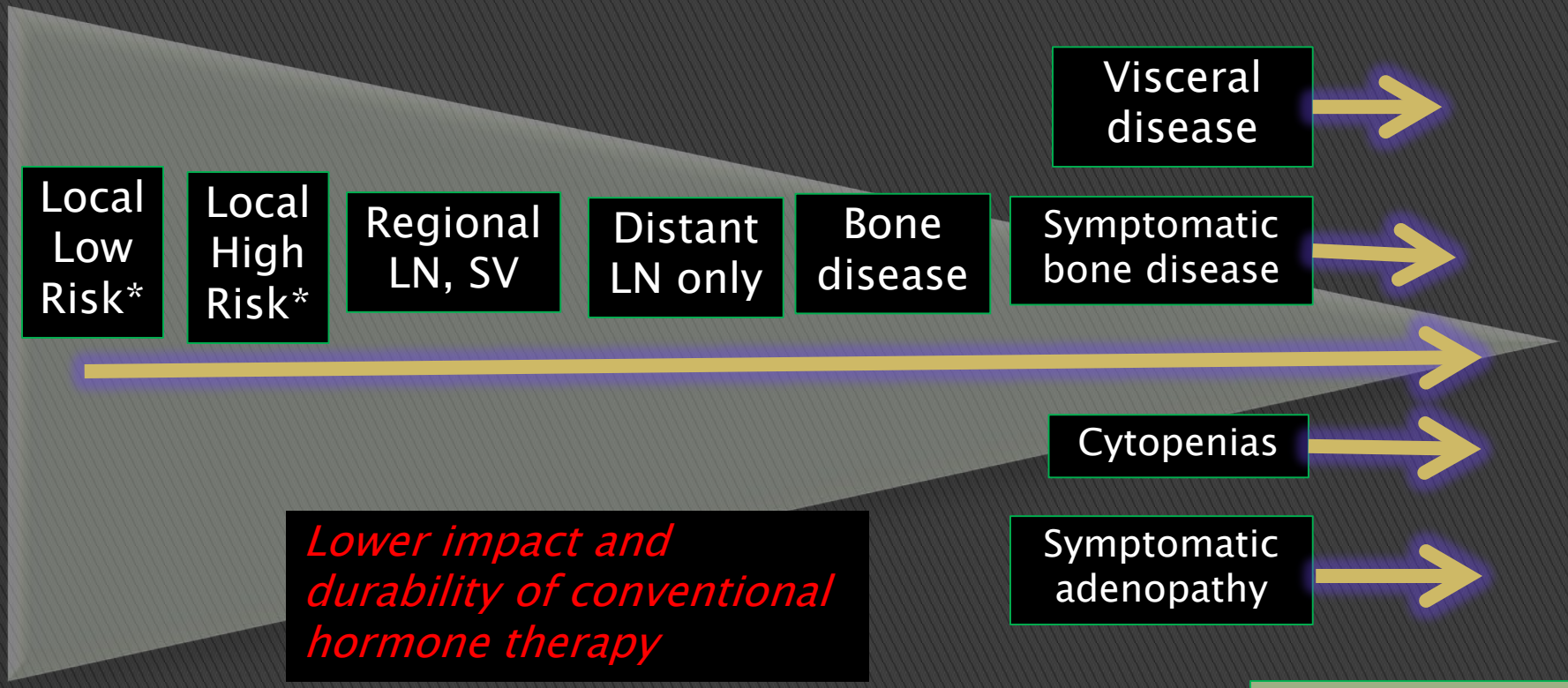
Prostate Cancer Management: From Early Chemical Recurrence to HRPC (excluding Immunotherapy)

Relevant financial relationships in the past twelve months by presenter or spouse/partner.

Speakers Bureau: Exelixis

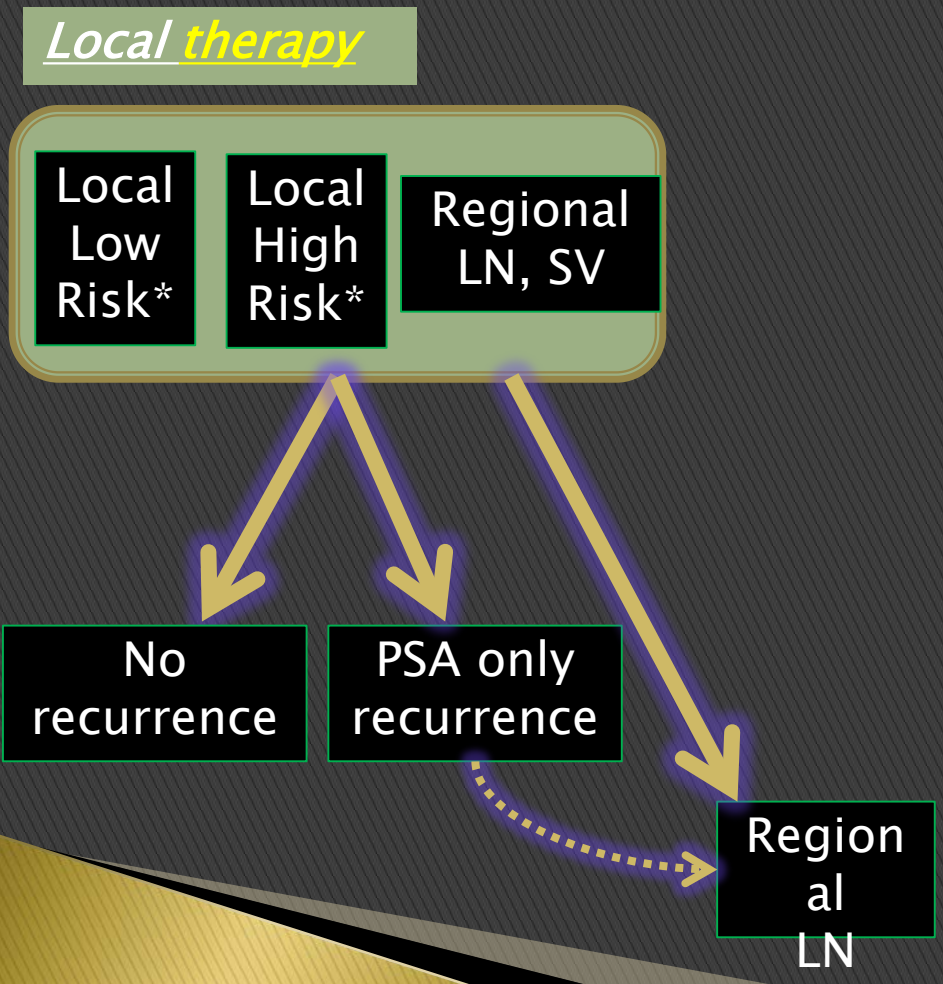
The speaker will directly disclosure the use of products for which are not labeled (e.g., off label use) or if the product is still investigational.

A conventional natural history timeline of prostate cancer

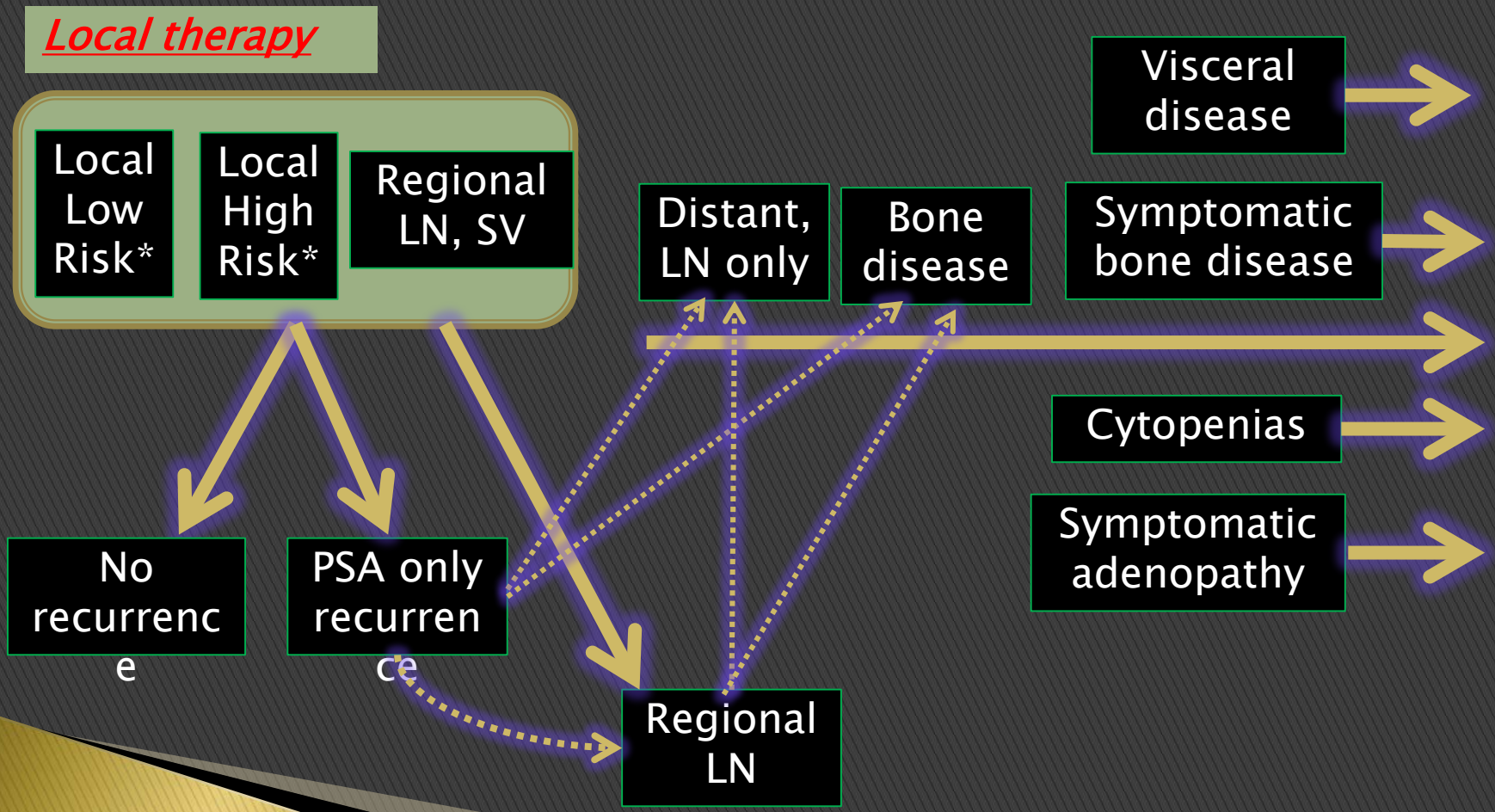


*risk:
- Gleason grade
- # cores
- Gland size
- Capsule, SV
- PSA

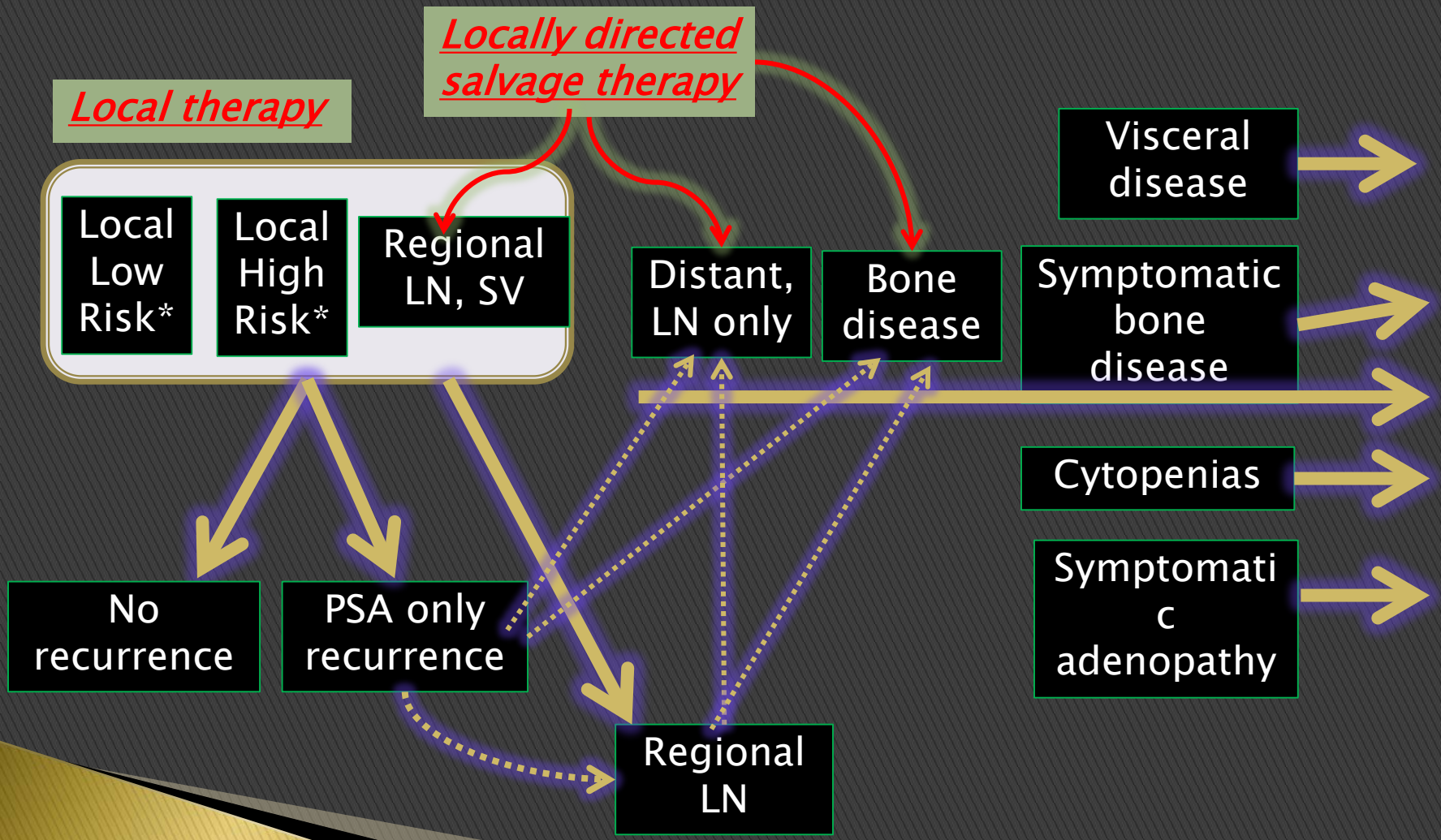
A conventional natural history timeline of treated prostate cancer



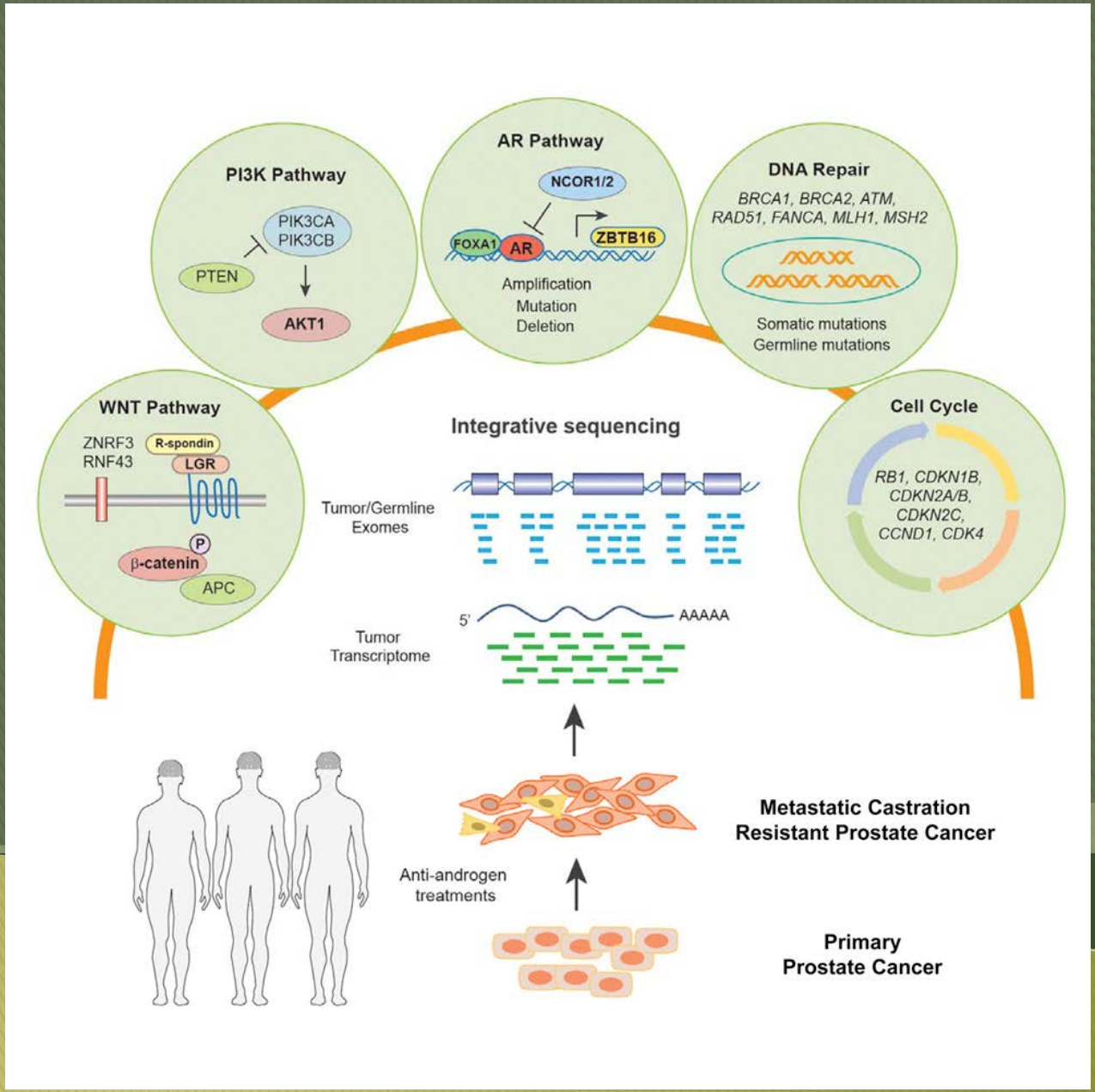
A conventional natural history timeline of treated prostate cancer



A conventional natural history timeline of treated prostate cancer



Molecular lesions of prostate cancer

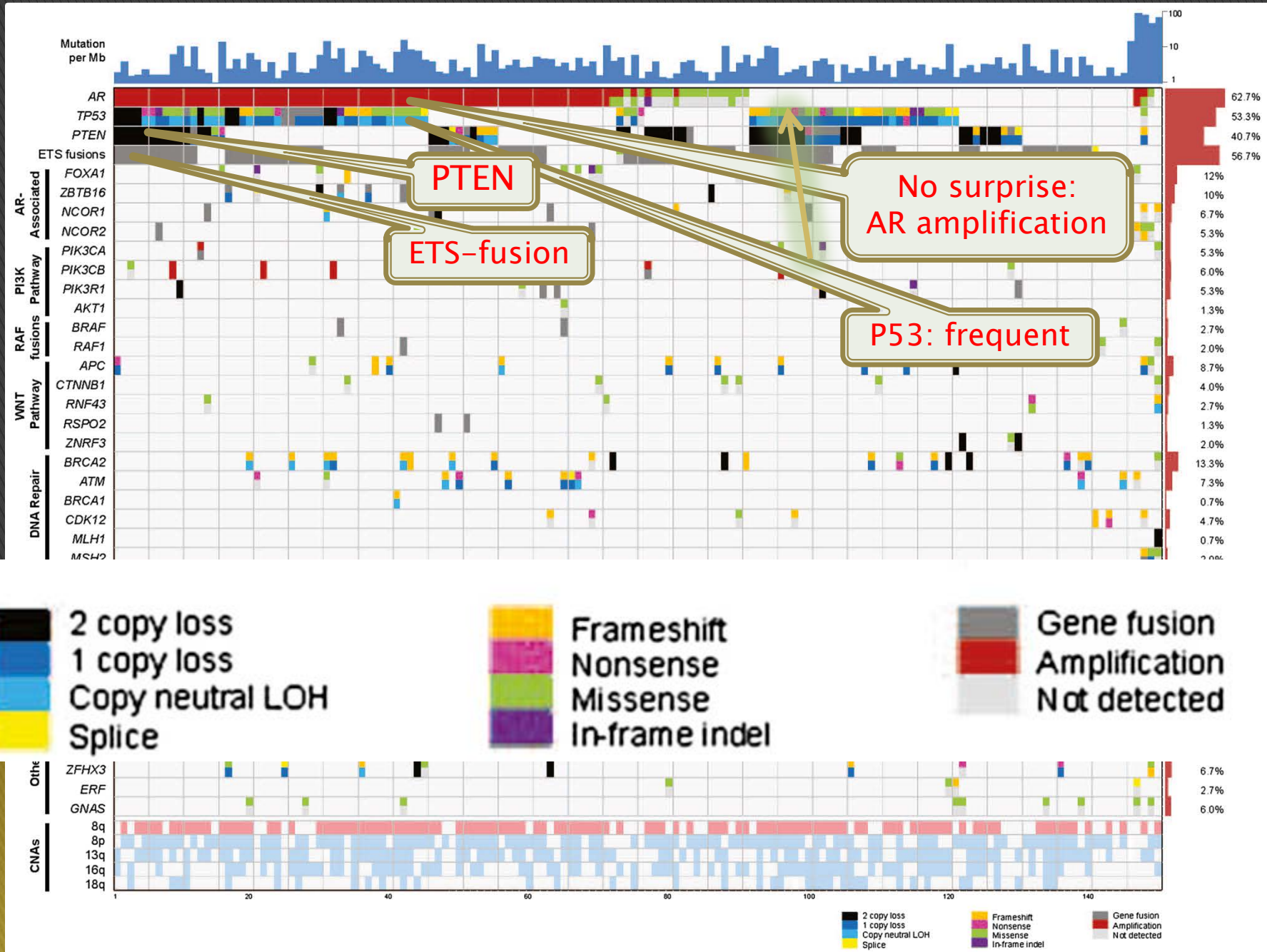


Cell

Volume 161, Issue 5, 21 May 2015, Pages 1215–1228

Integrative Clinical Genomics of Advanced Prostate Cancer

Dan Robinson and 72 more.


Mutation per Mb
100
10
1
AR
TP53
PTEN
ETS fusions
AR-Associated
FOXA1
ZBTB16
NCOR1
NCOR2
PI3K Pathway
PIK3CA
PIK3CB
PIK3R1
AKT1
RAF fusions
BRAF
RAF1
WNT Pathway
APC
CTNNB1
RNF43
RSPO2
ZNRF3
DNA Repair
BRCA2
ATM
BRCA1
CDK12
MLH1
62.7%
53.3%
40.7%
56.7%
12%
10%
6.7%
5.3%
5.3%
6.0%
5.3%
1.3%
2.7%
2.0%
8.7%
4.0%
2.7%
1.3%
2.0%
13.3%
7.3%
0.7%
4.7%
0.7%
PTEN
ETS-fusion
No surprise:
AR amplification
P53: frequent
2 copy loss
1 copy loss
Copy neutral LOH
Splice
Frameshift
Nonsense
Missense
In-frame indel
Gene fusion
Amplification
Not detected
ZFHX3
ERF
GNAS
CNAs
8q
8p
13q
16q
18q
6.7%
2.7%
6.0%
1
20
40
60
80
100
120
140

Cell
Volume 161, Issue 5, 21 May 2015, Pages 1215–1228
Integrative Clinical Genomics of Advanced Prostate Cancer
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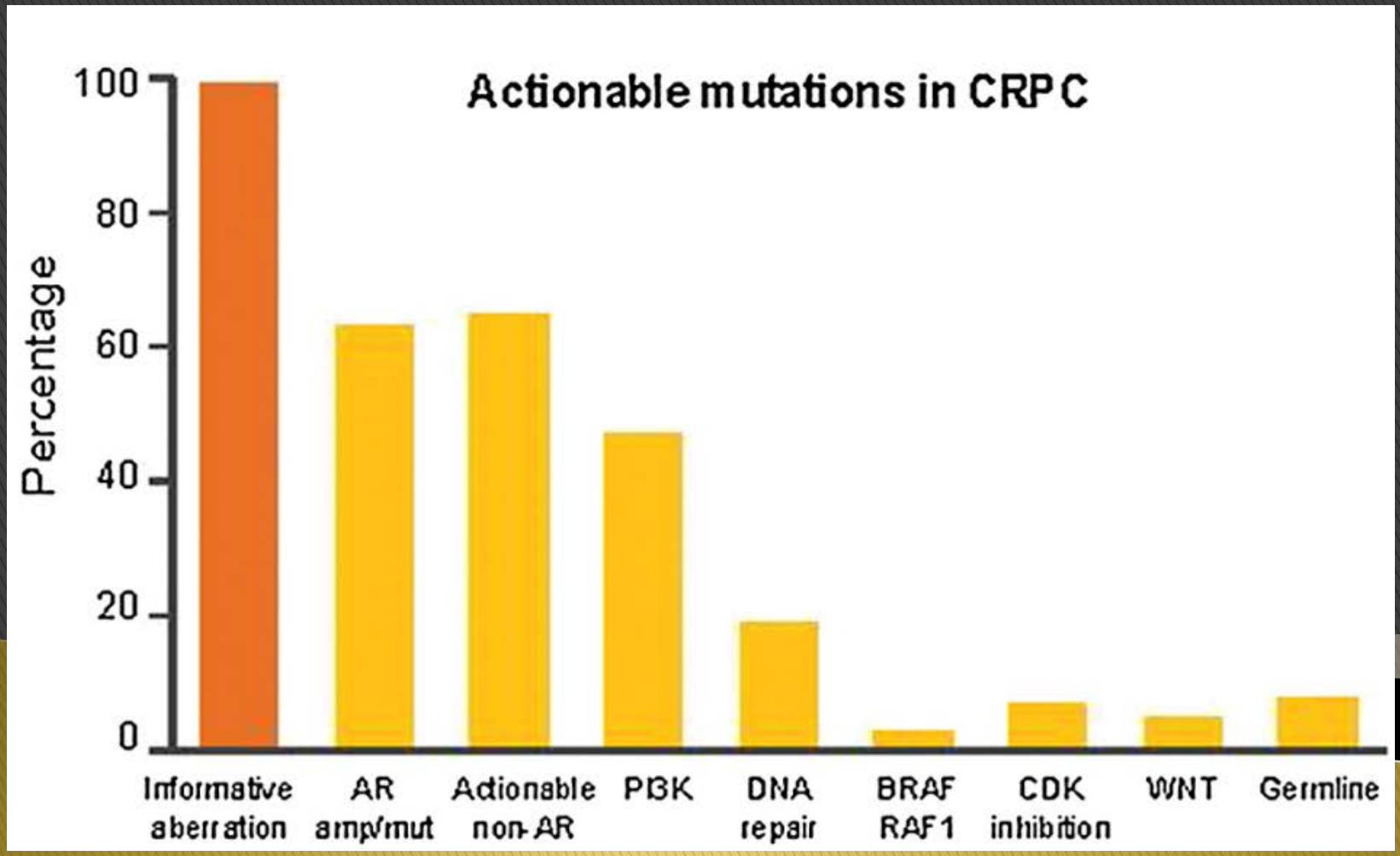
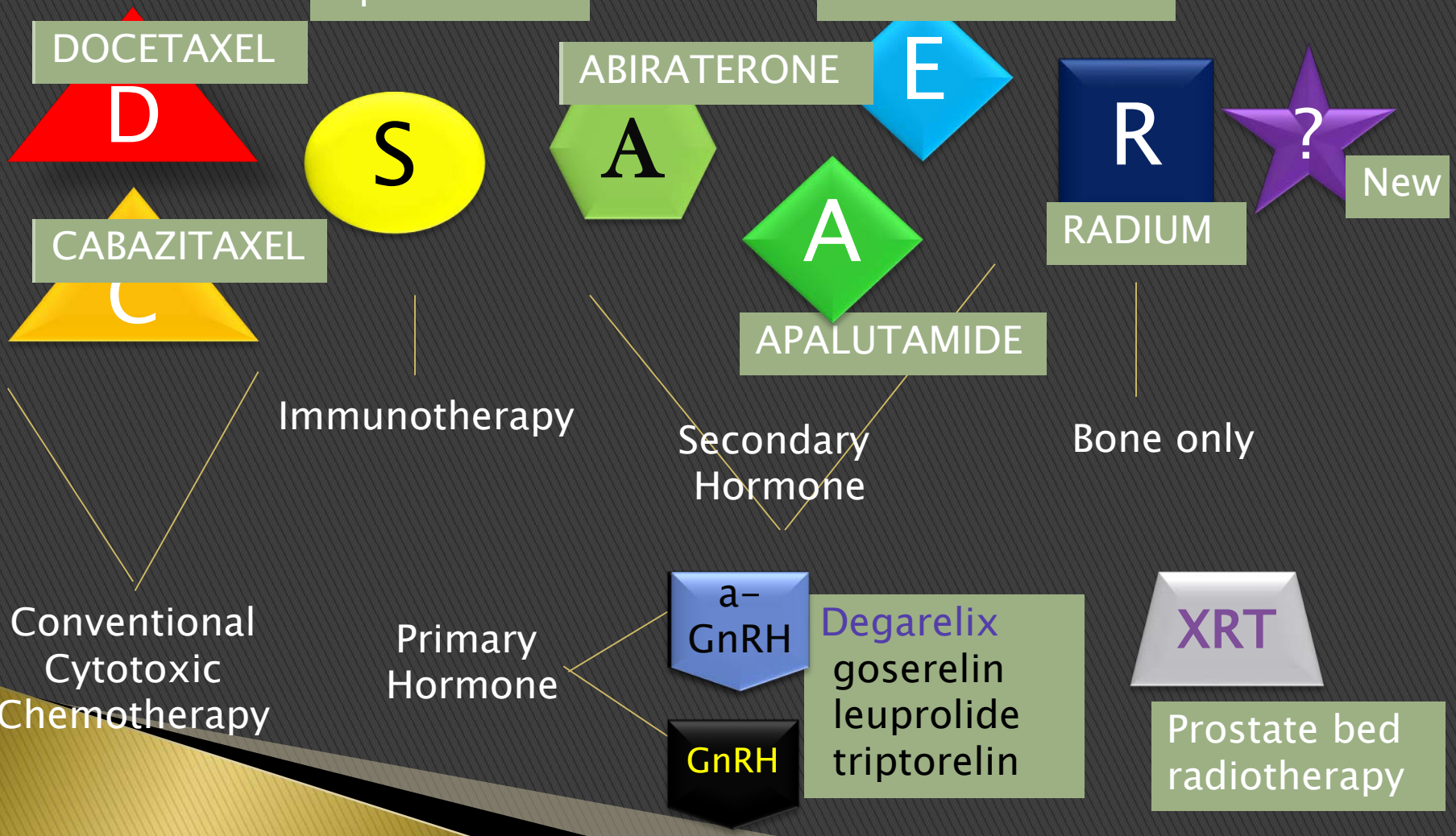


Types of (on label) therapies



VOLUME 34 · NUMBER 12 · APRIL 20, 2016

JOURNAL OF CLINICAL ONCOLOGY

SPECIAL ARTICLE

Trial Design and Objectives for Castration-Resistant Prostate Cancer: Updated Recommendations From the Prostate Cancer Clinical Trials Working Group 3

Howard I. Scher, Michael J. Morris, Walter M. Stadler, Celestia Higano, Ethan Basch, Karim Fizazi, Emmanuel S. Antonarakis, Tomasz M. Beer, Michael A. Carducci, Kim N. Chi, Paul G. Corn, Johann S. de Bono, Robert Dreicer, Daniel J. George, Elisabeth I. Heath, Maha Hussain, Wm. Kevin Kelly, Glenn Liu, Christopher Logothetis, David Nanus, Mark N. Stein, Dana E. Rathkopf, Susan F. Slovin, Charles J. Ryan, Oliver Sartor, Eric J. Small, Matthew Raymond Smith, Cora N. Sternberg, Mary-Ellen Taplin, George Wilding, Peter S. Nelson, Lawrence H. Schwartz, Susan Halabi, Philip W. Kantoff, and Andrew J. Armstrong

PCWG3

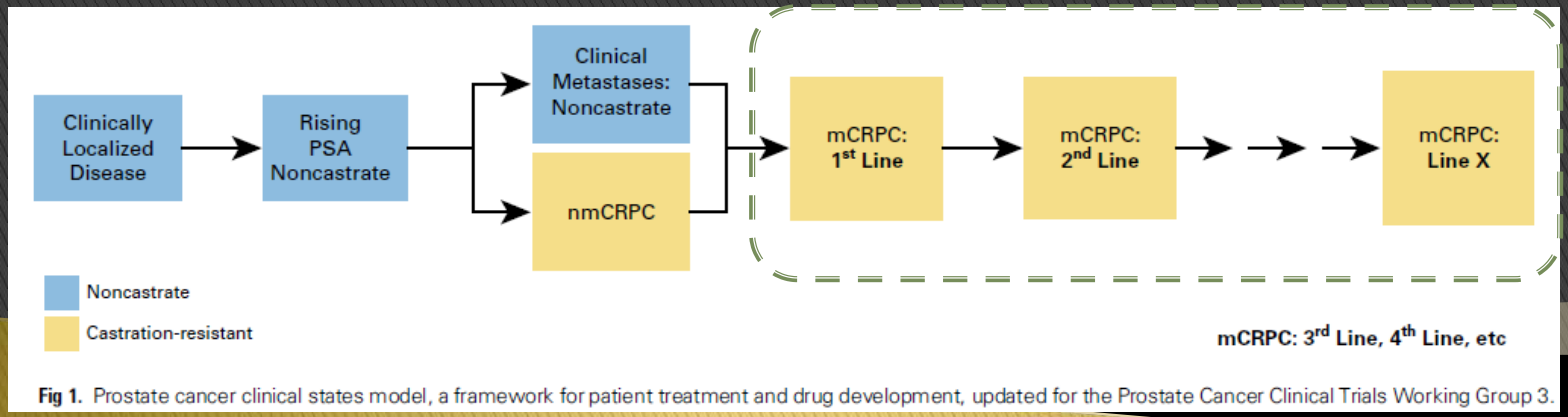
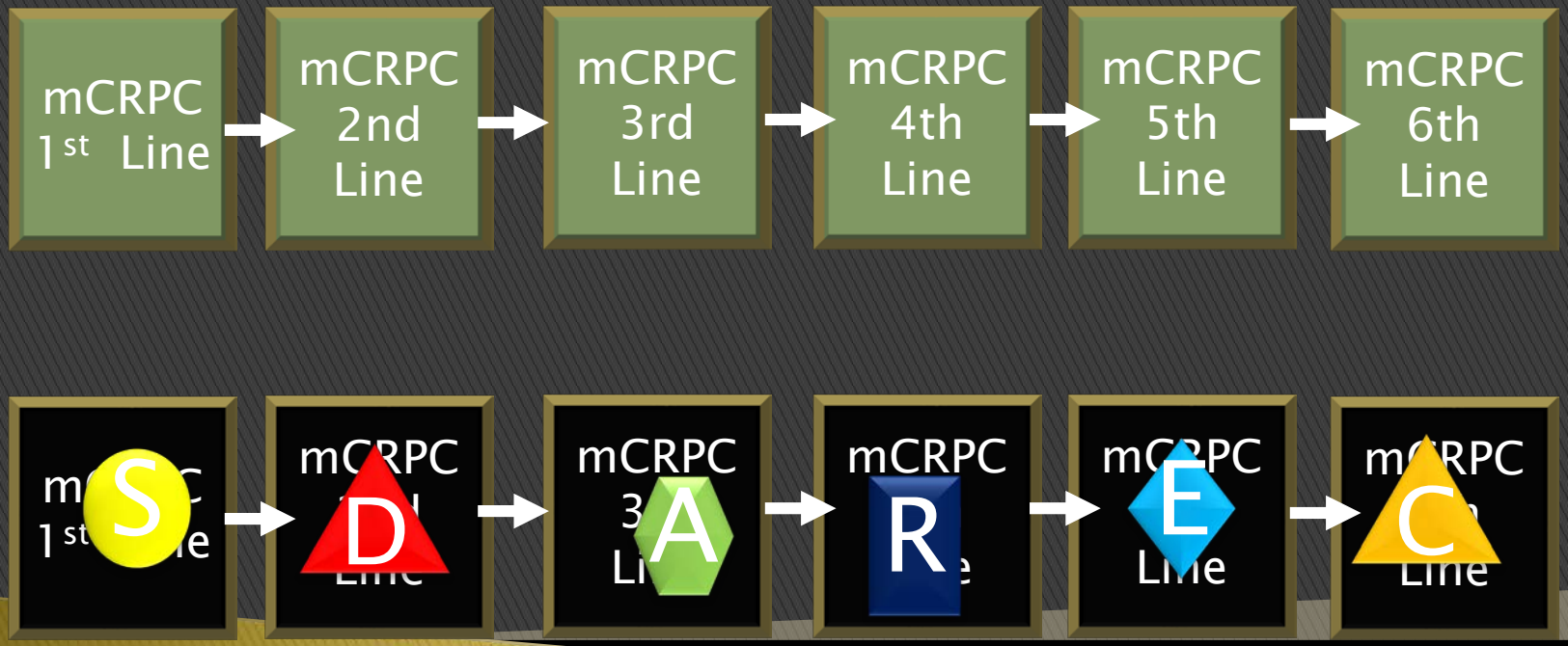


Fig 1. Prostate cancer clinical states model, a framework for patient treatment and drug development, updated for the Prostate Cancer Clinical Trials Working Group 3.

CLINICAL STATES MODEL

Sequencing: Not so simple



Also -- there is no reason to think there is only one best sequence, or that the same sequence is best for everyone

Real life is not as predictable as the diagrams.

91 d

Therapeutic opportunities of the androgen axis

- Whole-body hormone changes
- Systemic *vs* intratumoral testosterone
- Intracellular testosterone and Androgen Receptor, and intranuclear Androgen receptor

Blocking androgen signaling: Hormonal vs molecular perspectives

Conventional hormonal axis:
GnRH: Hypothalamus –pituitary

FSH: pituitary FSH secretion
LH: pituitary LH secretion

T: Circulating testosterone

17-beta hydroxylase
ketoconazole
abiraterone

AR/dihydroxytestosterone binding

Leuprolide
Goserelin
Degarelix

ADH
Oxytocin

ACTH
GH
PRL
TSH
FSH
LH

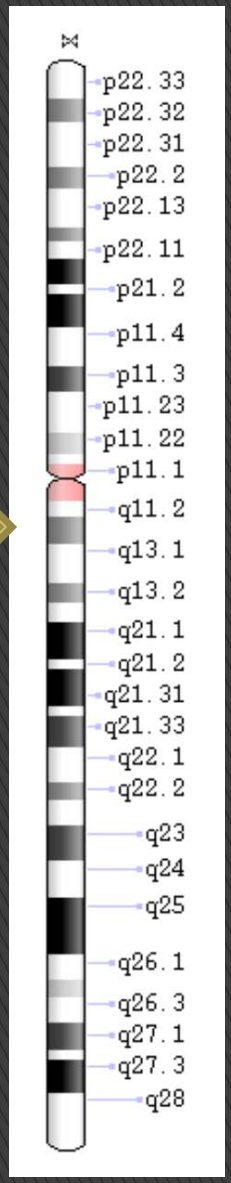
ADRENAL

Prostate

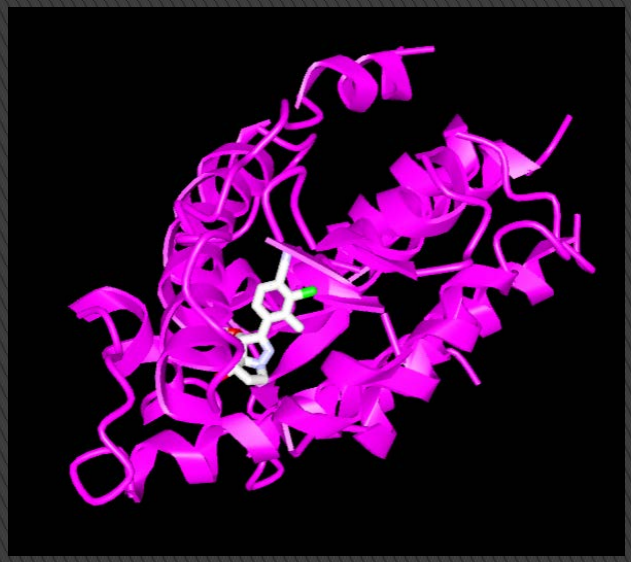
T

Testes

CANCER



Splice variants of AR



Androgen Receptor AR:

- single copy
- X chromosome
- allelic for CAG repeats (poly-Q)
- 920 a.a.
- 9 exons

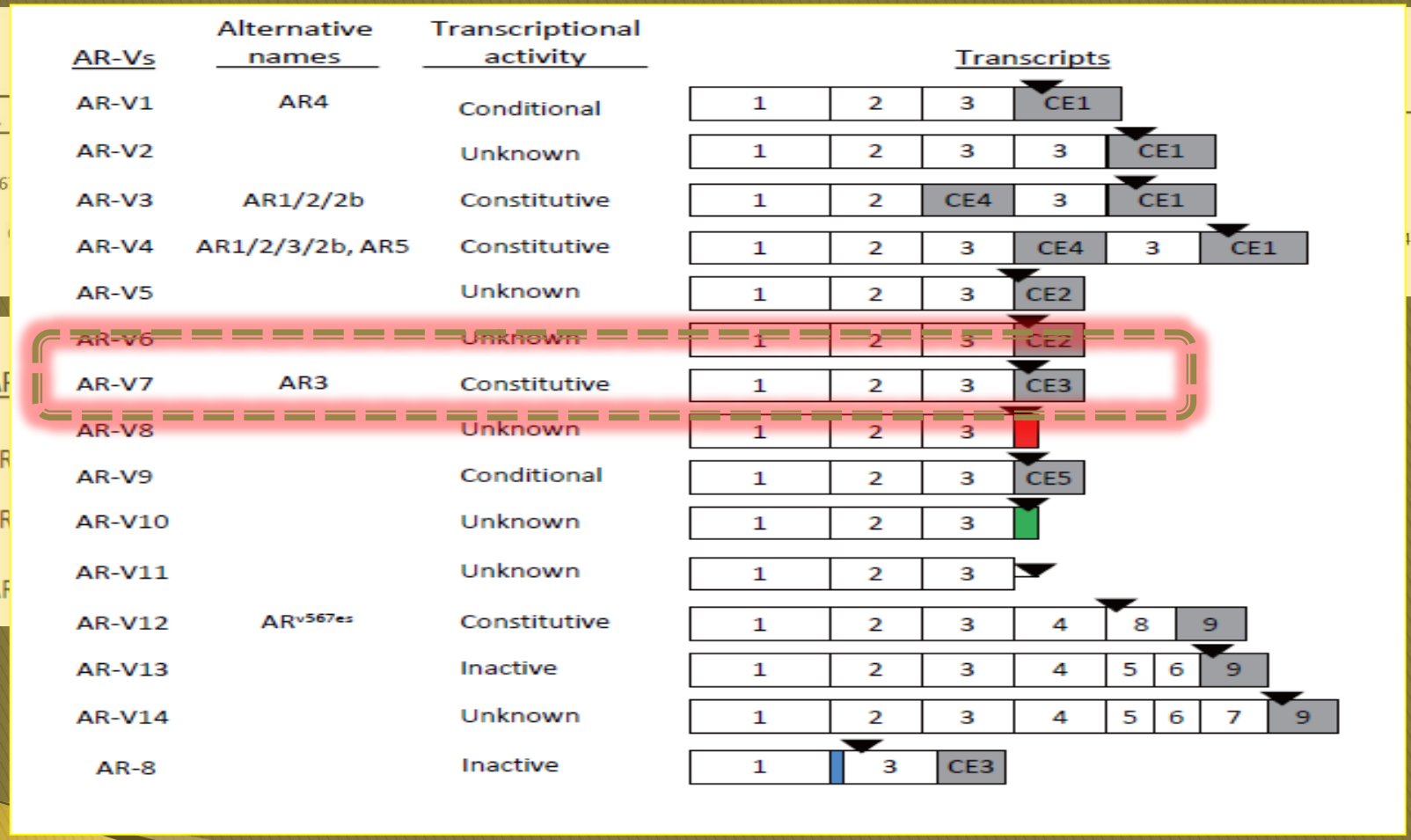
  >>> **Splice variants** <<<

Cn3d:
http://www.ncbi.nlm.nih.gov/Structure/icn3d/full.html?complexity=3&buidx=1&showseq=1&mmdbid=130049

Ref: https://ghr.nlm.nih.gov/chromosome/X

Ref: Decoding the androgen receptor splice variants
Changxue Lu, Jun Luo. Transl Androl Urol. 2013 Sep; 2(3): 178–186.
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4209743/figure/f1/

- 9 exons
- 5 additional cryptic exons (CE) within introns



Intrinsically resistant splice variant (ARv7)

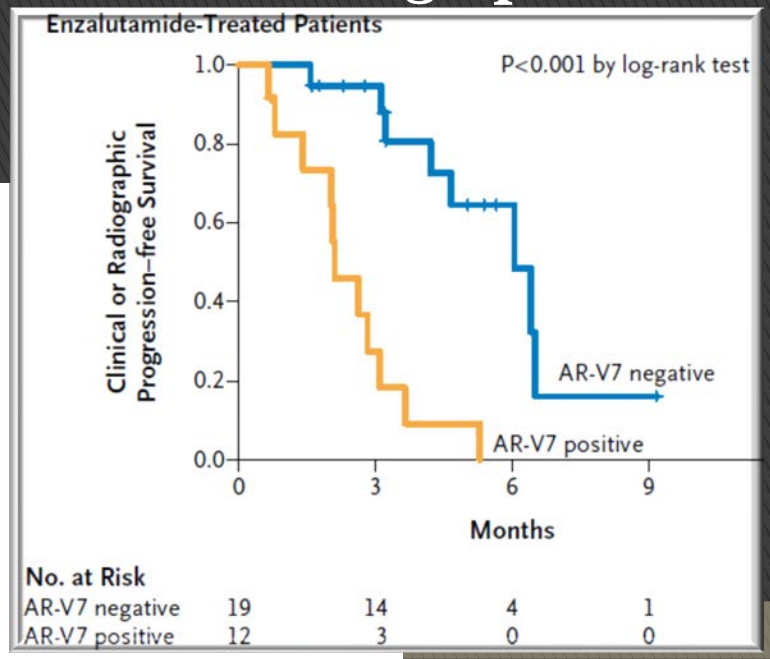
The NEW ENGLAND JOURNAL of MEDICINE

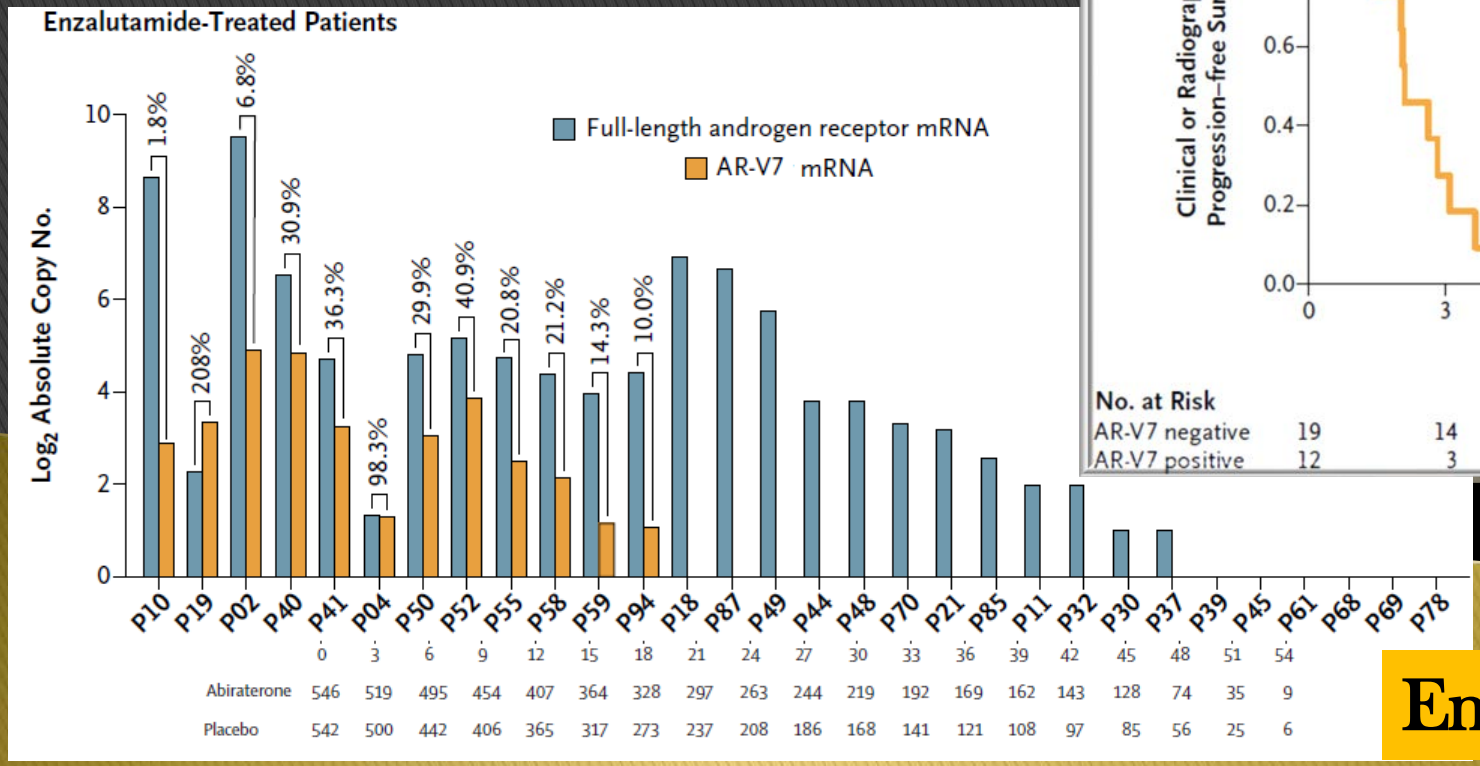
AR-V7 and Resistance to Enzalutamide and Abiraterone in Prostate Cancer

Emmanuel S. Antonarakis, M.D., Changxue Lu, Ph.D., Hao Wang, Ph.D., Brandon Luber, Sc.M., Mary Nakazawa, M.H.S., Jeffrey C. Roeser, B.S., Yan Chen, Ph.D., Tabrez A. Mohammad, Ph.D., Yidong Chen, Ph.D., Helen L. Fedor, B.S., Tamara L. Lotan, M.D., Qizhi Zheng, M.D., Angelo M. De Marzo, M.D., Ph.D., John T. Isaacs, Ph.D., William B. Isaacs, Ph.D., Rosa Nadal, M.D., Channing J. Paller, M.D., Samuel R. Denmeade, M.D., Michael A. Carducci, M.D., Mario A. Eisenberger, M.D., and Jun Luo, Ph.D.

N Engl J Med 2014; 371:1028-1038 | September 11, 2014 |

Radiographic PFS





Enzalutamide

The NEW ENGLAND JOURNAL of MEDICINE

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

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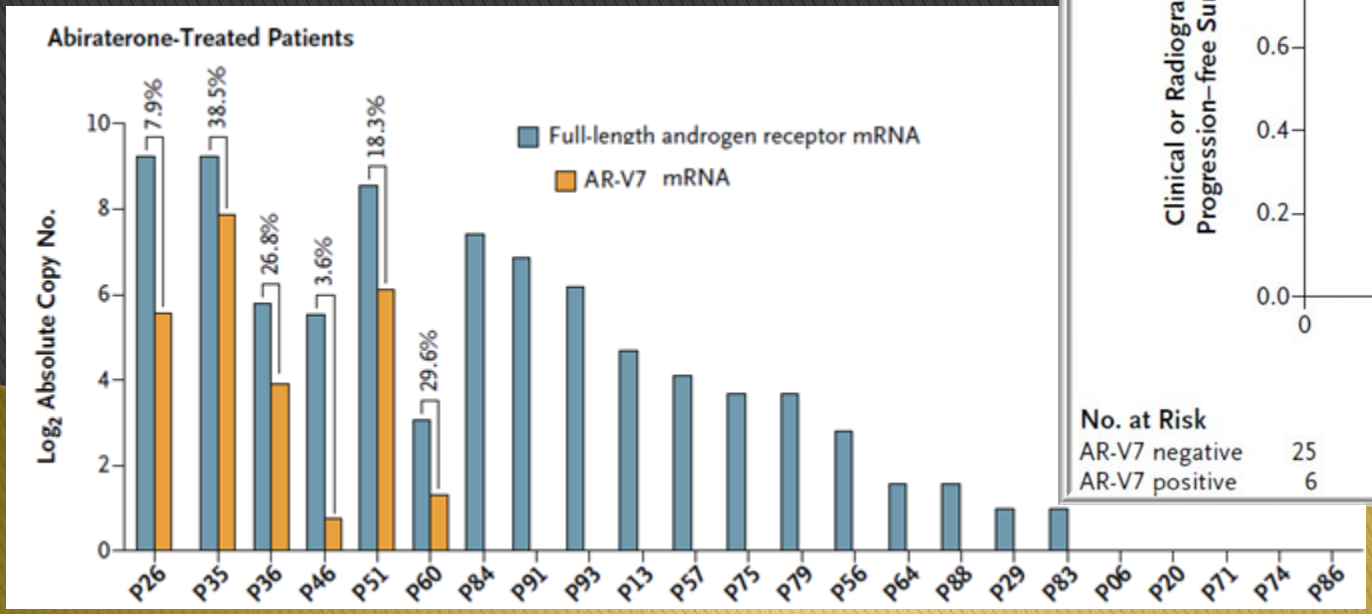
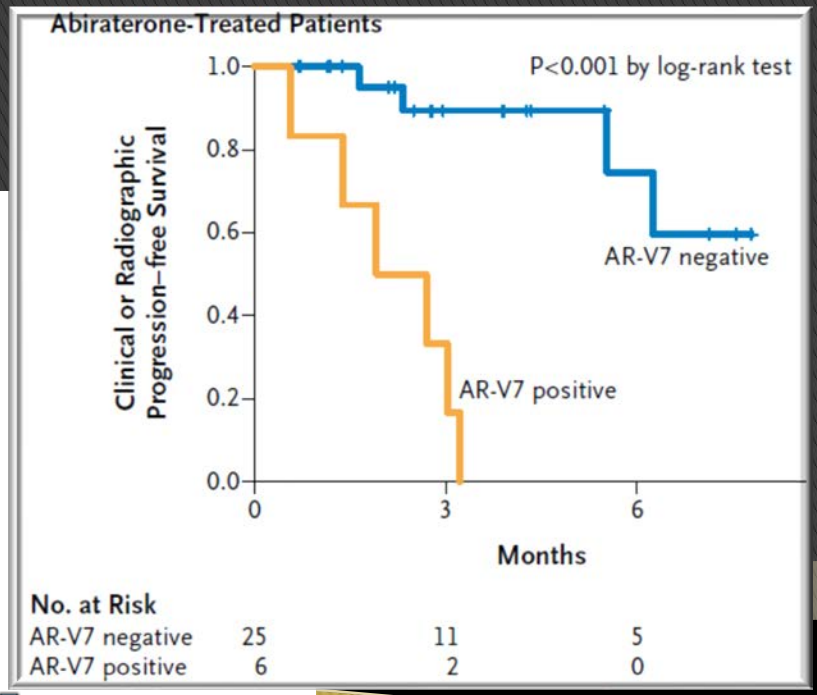
N Engl J Med 2014; 371:1028-1038 | September 11, 2014 |

Abiraterone

Radiographic PFS





Early chemical recurrence: The rising PSA

Local therapy

Local Low Risk

Local High Risk

Regional LN, SV

No recurrence

PSA only recurrence

Risk stratification

Late, slow, low, no prior XRT:
Consider for salvage bed XRT

Late, slow:
Observe vs hormone therapy
Comorbid assessment

Not slow: GnRH therapy

Comorbidity

Long doubling time: (?)

Doubling time < 10 months:
SPARTAN (apalutamide)
PROSPER (enzalutamide)

SPARTAN:
Introducing apalutamide

April 12, 2018
N Engl J Med 2018; 378:1408-1418

Apalutamide Treatment and Metastasis-free Survival in Prostate Cancer

Matthew R. Smith, M.D., Ph.D., Fred Saad, M.D., Simon Chowdhury, M.B., B.S., Ph.D., Stéphane Oudard, M.D., Ph.D., Boris A. Hadaschik, M.D., Julie N. Graff, M.D., David Olmos, M.D., Ph.D., Paul N. Mainwaring, M.B., B.S., M.D., Ji Youl Lee, M.D., Hiroji Uemura, M.D., Ph.D., Angela Lopez-Gitlitz, M.D., Géralyn C. Trudel, Ph.D., et al., for the SPARTAN Investigators*

Age ~74

7.9 y since dx

DT < 10 mo
71% < 6 mo

XRT: 77%
GnRH: 97%
Bica: 73%

R

806 → 240 mg apalutamide= 8 x30 mg/d

401 → placebo

Check bone scan & CT scans every 16 weeks

primary → Metastasis free survival HR = 0.28

Secondary & exploratory → None unmet Next slide

Apalutamide Treatment and Metastasis-free Survival in Prostate Cancer

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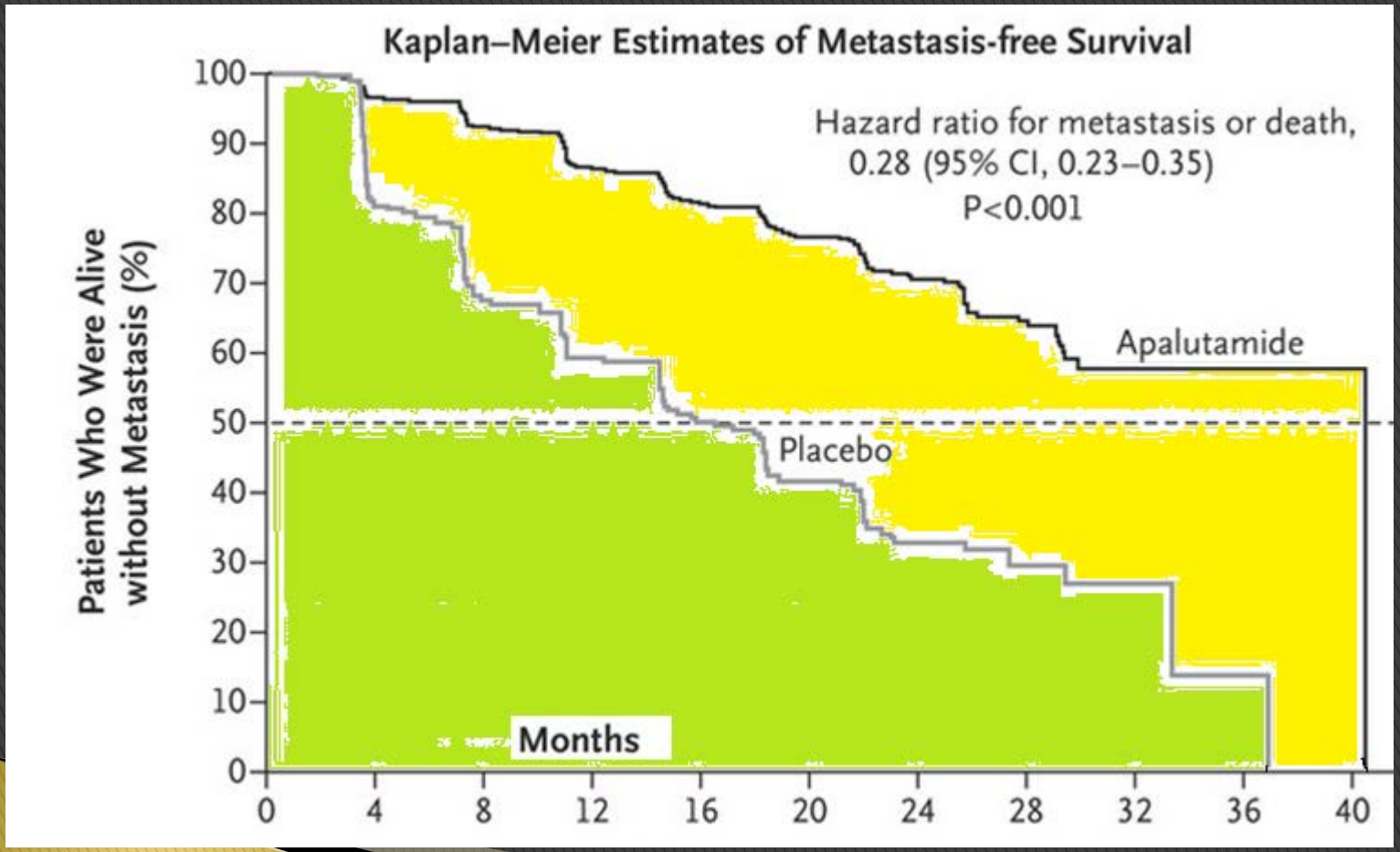

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All secondary and exploratory endpoints met

	Apalutamide	Placebo	Hazard Ratio (95% CI)	P
Secondary end points (mo)†				
Median time to metastasis	40.5	16.6	0.27 (0.22–0.34)	<0.001
Median progression-free survival	40.5	14.7	0.29 (0.24–0.36)	<0.001
Median time to symptomatic progression	NR	NR	0.45 (0.32–0.63)	<0.001
Median overall survival	NR	39.0	0.70 (0.47–1.04)	0.07
Median time to the initiation of cytotoxic chemotherapy	NR	NR	0.44 (0.29–0.66)	
Exploratory end points				
Median second-progression–free survival (mo)	NR	39.0	0.49 (0.36–0.66)	
Median time to PSA progression (mo)	NR	3.7	0.06 (0.05–0.08)	
Patients with a PSA response (%)	89.7	2.2	40 (21–77)‡	
Patient-reported outcomes§				
Change in total FACT-P score from baseline to 29 months¶	−0.99±0.9	−3.29±1.9		
Change in total EQ VAS score from baseline to 29 months‖	1.44±0.8	0.26±1.7		

PROSPER:
Early enzalutamide

C Sternberg
EAU 10/2017

Median age 74

Median PSA: 11

DT < 10 mo
75% < 6 mo

prostatectomy: 54%

R

933

Enzalutamide 4x40 = 160 mg

primary

Metastasis free survival
HR = 0.29

468

placebo

Secondary & exploratory

Time to next treatment: HR = .21
Time to PSA progression HR = .07

>50% PSA decrease: 76 vs 2.4%
>90% PSA decrease: 56 vs 0.4 %
Undetectable PSA: 9.6 vs 0 %

OS first eval (NS; not mature)
HR = 0.80, P=.15

Enzalutamide at various points of PC treatment:

- PROSPER: Rising PSA, M0, <10 mo DT
- AFFIRM: CRPC after chemotherapy
- PREVAIL: CRPC, before chemotherapy
- STRIVE (phase II), CRPC, before chemotherapy

What is the best time to use enzalutamide?

Apalutamide >> placebo
vs
Enzalutamide >> placebo

No obvious difference
What to do with PSA-DT > 10 months?

The NEW ENGLAND JOURNAL of MEDICINE

SEPTEMBER 27, 2012 VOL. 367 NO. 13

Increased Survival with Enzalutamide in Prostate Cancer after Chemotherapy

Howard I. Scher, M.D., Karim Fizazi, M.D., Ph.D., Fred Saad, M.D., Mary-Ellen Taplin, M.D., Cora N. Sternberg, M.D., Kurt Miller, M.D., Ronald de Wit, M.D., Peter Mulders, M.D., Ph.D., Kim N. Chi, M.D., Neal D. Shore, M.D., Andrew J. Armstrong, M.D., Thomas W. Flaig, M.D., Aude Fléchon, M.D., Ph.D., Paul Mainwaring, M.D., Mark Fleming, M.D., John D. Hainsworth, M.D., Mohammad Hirmand, M.D., Bryan Selby, M.S., Lynn Seely, M.D., and Johann S. de Bono, M.B., Ch.B., Ph.D., for the AFFIRM Investigators*

AFFIRM

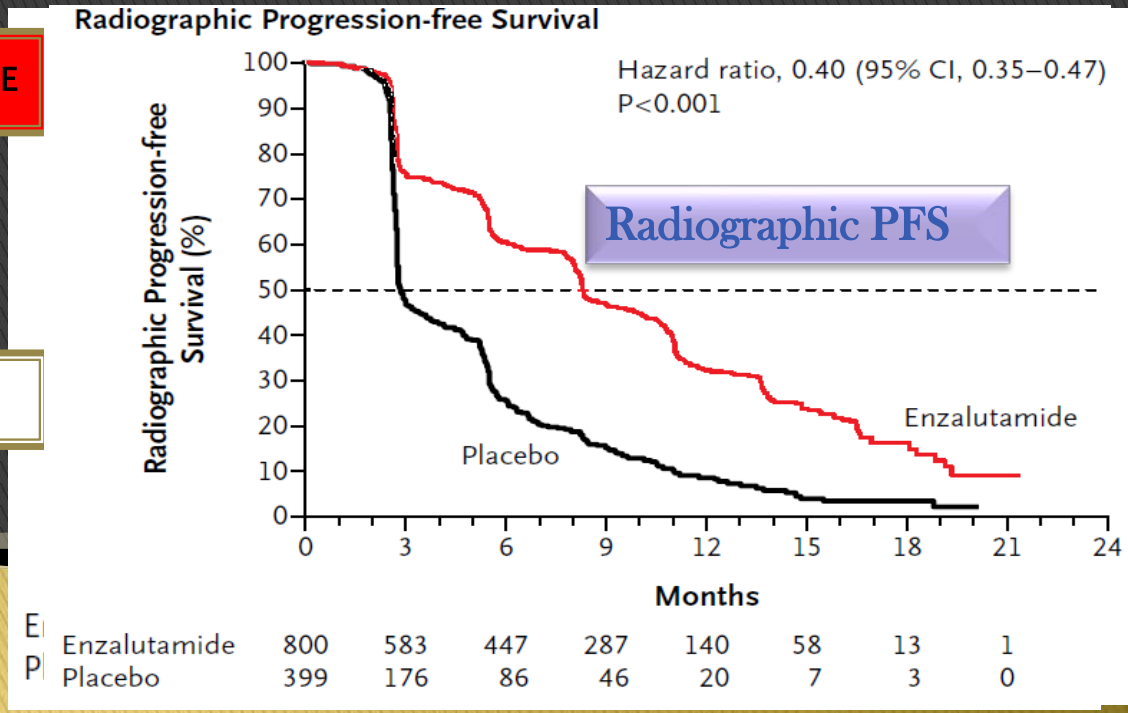
mCRPC

After chemotherapy

R

800 → ENZALUTAMIDE

399 → Placebo



"The study was stopped after a planned interim analysis."

Enzalutamide in Metastatic Prostate Cancer before Chemotherapy

T.M. Beer, A.J. Armstrong, D.E. Rathkopf, Y. Loriot, C.N. Sternberg, C.S. Higano, P. Iversen, S. Bhattacharya, J. Carles, S. Chowdhury, I.D. Davis, J.S. de Bono, C.P. Evans, K. Fizazi, A.M. Joshua, C.-S. Kim, G. Kimura, P. Mainwaring, H. Mansbach, K. Miller, S.B. Noonberg, F. Perabo, D. Phung, F. Saad, H.I. Scher, M.-E. Taplin, P.M. Venner, and B. Tombal, for the PREVAIL Investigators*

N ENGL J MED 371;5 NEJM.ORG JULY 31, 2014

PREVAIL

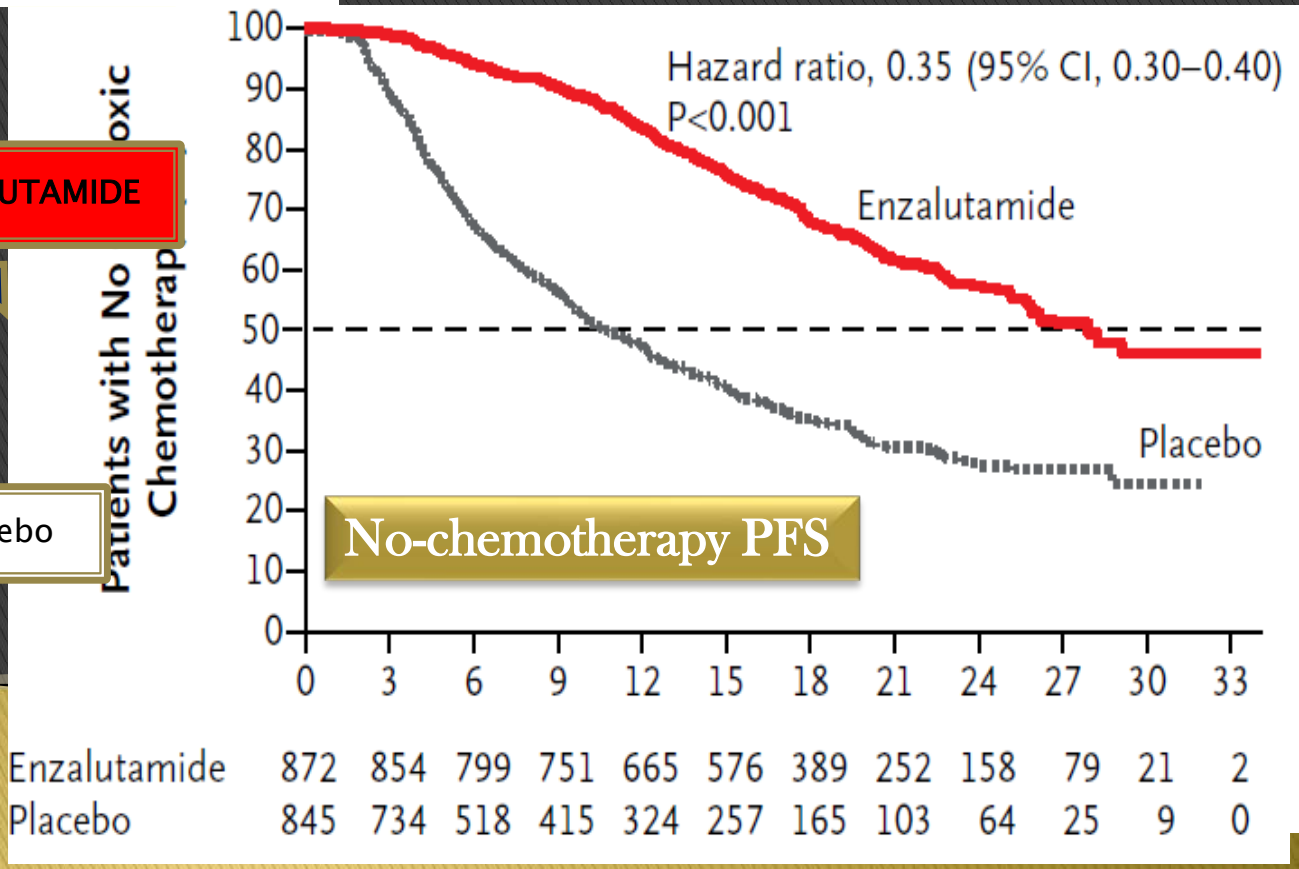
mCRPC

No prior chemotherapy

R

ENZALUTAMIDE 872

Placebo 845



VOLUME 34 · NUMBER 18 · JUNE 20, 2016

JOURNAL OF CLINICAL ONCOLOGY

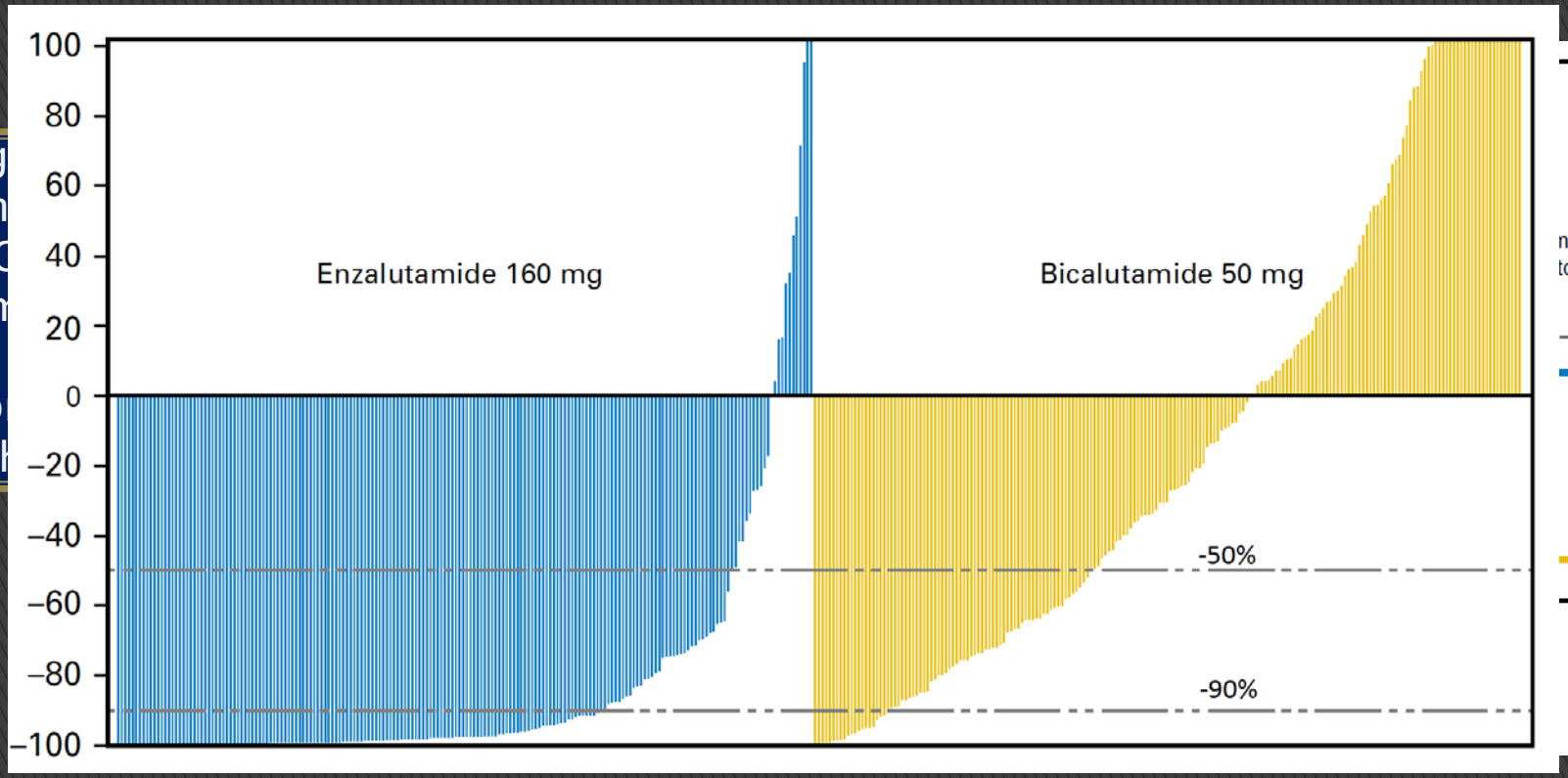
Enzalutamide Versus Bicalutamide in Castration-Resistant Prostate Cancer: The STRIVE Trial

David F. Penson, Andrew J. Armstrong, Raoul Concepcion, Neeraj Agarwal, Carl Olsson, Lawrence Karsh, Curtis Dunshee, Fong Wang, Kenneth Wu, Andrew Krivoshik, De Phung, and Celestia S. Higano

STRIVE

Rising
257: m
139: C
(nm

No p
chemoth



nonths
to NR)

27
5
1

Abiraterone
Late, earlier, very early? And at what dose?

COUGAR 301: After chemotherapy
COUGAR 302: CRPC, before chemotherapy
STAMPEDE: At initial hormone therapy of metastatic disease
LATITUDE: At initial hormone therapy of metastatic disease

(phase II) Food effect 250 + food vs 1000/fasting

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

Lancet Oncol 2012; 13: 983–92

Karim Fizazi, Howard I Scher, Arturo Molina, Christopher J Logothetis, Kim N Chi, Robert J Jones, John N Staffurth, Scott North, Nicholas J Vogelzang, Fred Saad, Paul Mainwaring, Stephen Harland, Oscar B Goodman Jr, Cora N Sternberg, Jin Hui Li, Thian Kheoh, Christopher M Haqq, Johann S de Bono, for the COU-AA-301 Investigators*

COUGAR 301

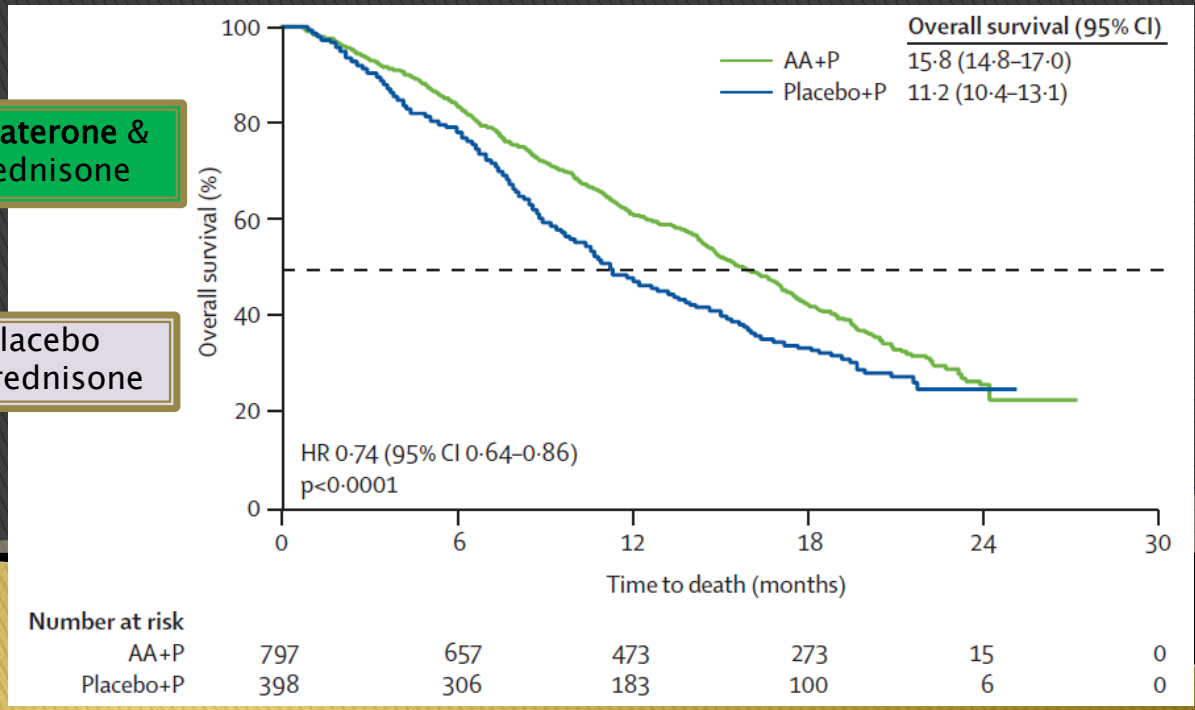
mCRPC

After chemotherapy

R

797 → abiraterone & prednisone

398 → Placebo & prednisone



Abiraterone acetate plus prednisone versus placebo plus prednisone in chemotherapy-naive men with metastatic castration-resistant prostate cancer (COU-AA-302): final overall survival analysis of a randomised, double-blind, placebo-controlled phase 3 study

Lancet Oncol 2015; 16: 152–60

*Charles J Ryan, Matthew R Smith, Karim Fizazi, Fred Saad, Peter F A Mulders, Cora N Sternberg, Kurt Miller, Christopher J Logothetis, Neal D Shore, Eric J Small, Joan Carles, Thomas W Flaig, Mary-Ellen Taplin, Celestia S Higano, Paul de Souza, Johann S de Bono, Thomas W Griffin, Peter De Porre, Margaret K Yu, Youn C Park, Jinhui Li, Thian Kheoh, Vahid Naini, Arturo Molina, Dana E Rathkopf, for the COU-AA-302 Investigators**

COUGAR 302

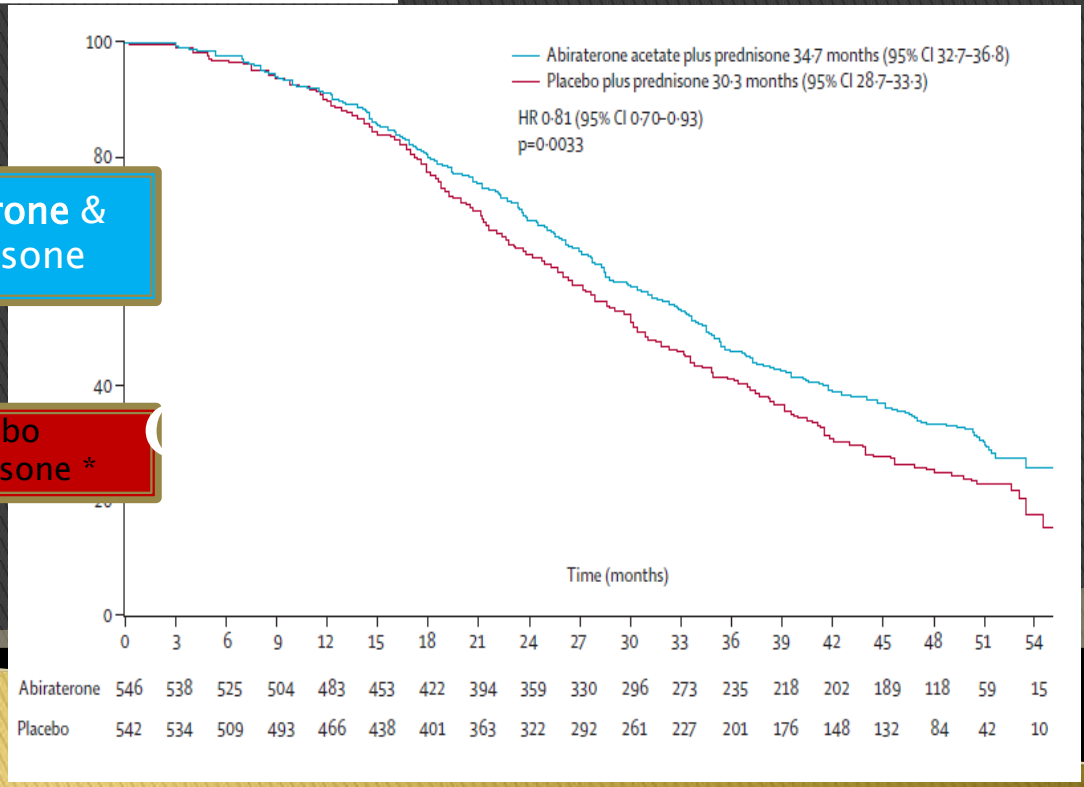
mCRPC

No prior chemotherapy

R

546 → abiraterone & prednisone

542 → Placebo & prednisone *



*44% received abiraterone after

Other subsequent therapy

67% abiraterone

80% placebo group

Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer

Karim Fizazi, M.D., Ph.D., NamPhuong Tran, M.D., Luis Fein, M.D., Nobuaki Matsubara, M.D., Alfredo Rodriguez-Antolin, M.D., Ph.D., Boris Y. Alekseev, M.D., Mustafa Özgüroğlu, M.D., Dingwei Ye, M.D., Susan Feyerabend, M.D., Andrew Protheroe, M.D., Ph.D., Peter De Porre, M.D., Thian Kheoh, Ph.D., et al., for the LATITUDE Investigators*

July 27, 2017
N Engl J Med 2017; 377:352-360

LATITUDE

US

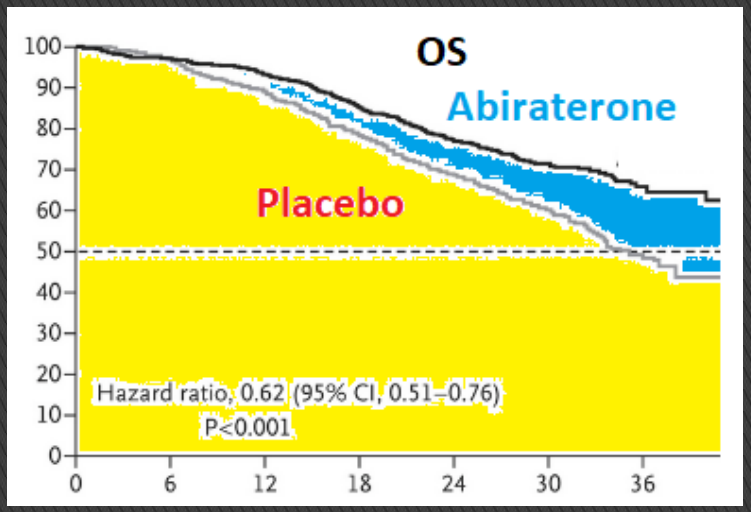
No prior hormone therapy for metastatic disease

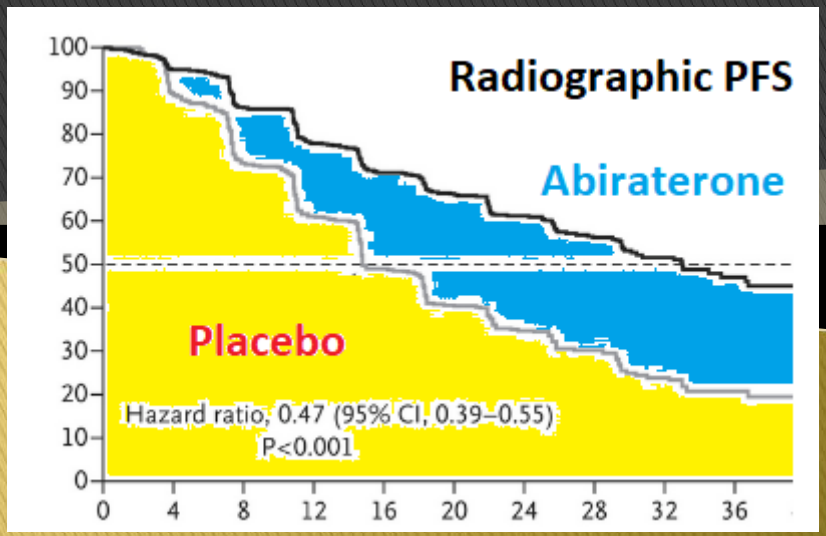
Start GnRH

R

597 → + abiraterone & prednisone

602 → + Placebo & placebo





Abiraterone for Prostate Cancer Not Previously Treated with Hormone Therapy

Nicholas D. James, Ph.D., Johann S. de Bono, Ph.D., Melissa R. Spears, M.Sc., Noel W. Clarke, Ch.M., Malcolm D. Mason, F.R.C.R., David P. Dearnaley, F.R.C.R., Alastair W.S. Ritchie, M.D., Claire L. Amos, Ph.D., Clare Gilson, M.R.C.P., Rob J. Jones, M.B., Ch.B., David Matheson, Ph.D., Robin Millman, et al., for the STAMPEDE Investigators*

July 27, 2017
N Engl J Med 2017; 377:338-351

STAMPEDE

EUROPE

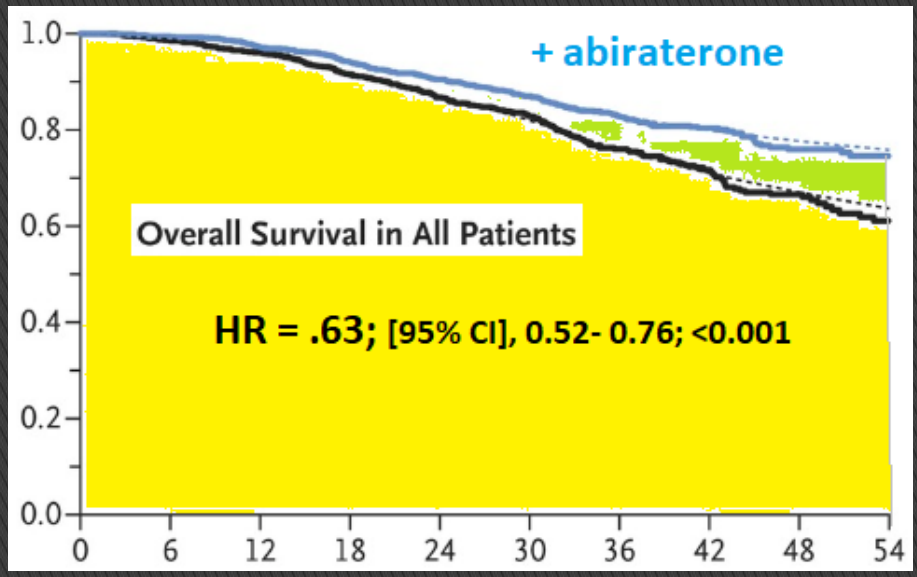
No prior hormone therapy for metastatic disease

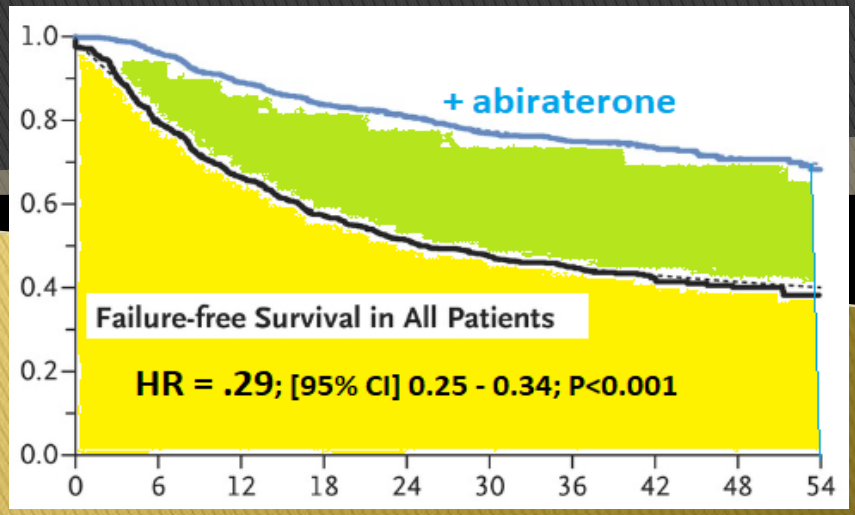
Start GnRH

R

960 → + abiraterone & prednisone

957 → + Placebo & placebo



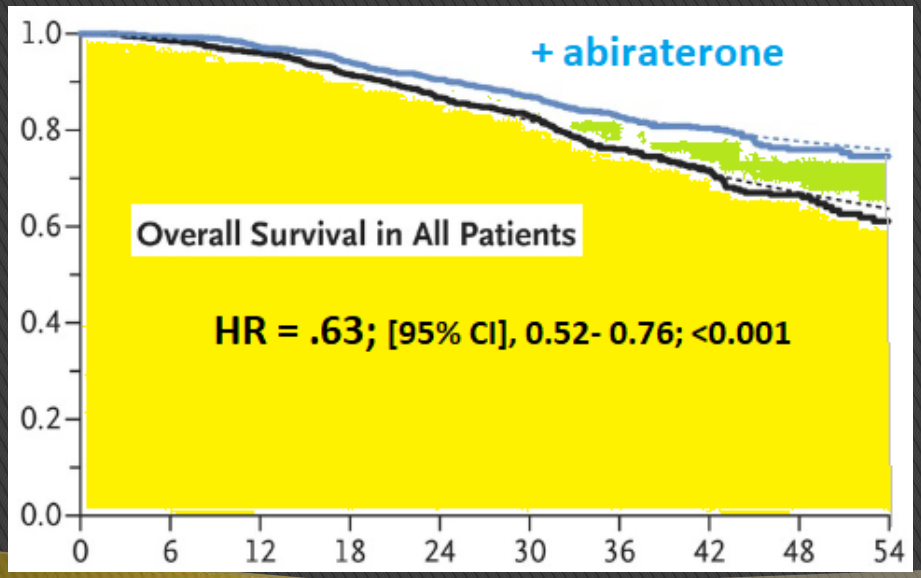


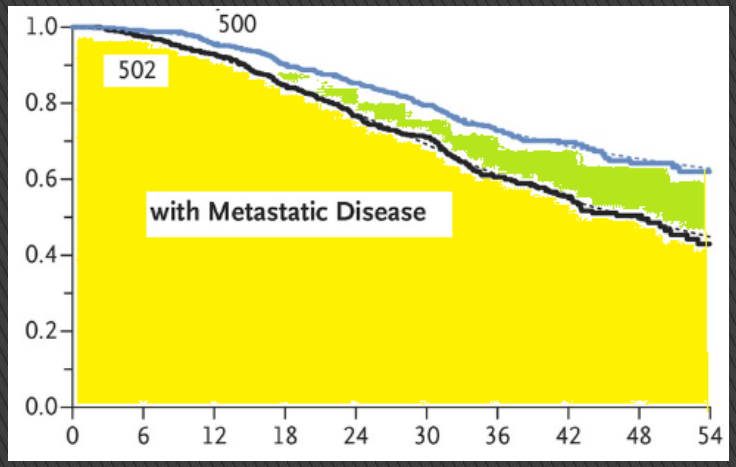
Abiraterone for Prostate Cancer Not Previously Treated with Hormone Therapy

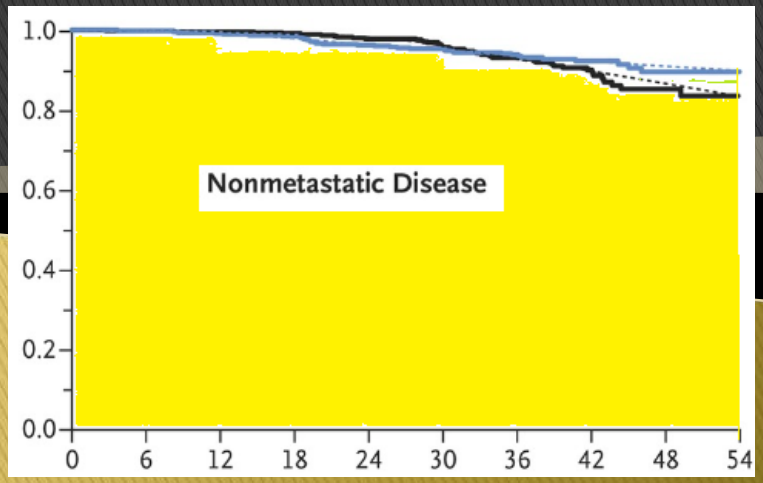
Nicholas D. James, Ph.D., Johann S. de Bono, Ph.D., Melissa R. Spears, M.Sc., Noel W. Clarke, Ch.M., Malcolm D. Mason, F.R.C.R., David P. Dearnaley, F.R.C.R., Alastair W.S. Ritchie, M.D., Claire L. Amos, Ph.D., Clare Gilson, M.R.C.P., Rob J. Jones, M.B., Ch.B., David Matheson, Ph.D., Robin Millman, et al., for the STAMPEDE Investigators*

July 27, 2017
N Engl J Med 2017; 377:338-351

STAMPEDE







*OS difference are driven by the **HIGHER RISK** subset of patients*

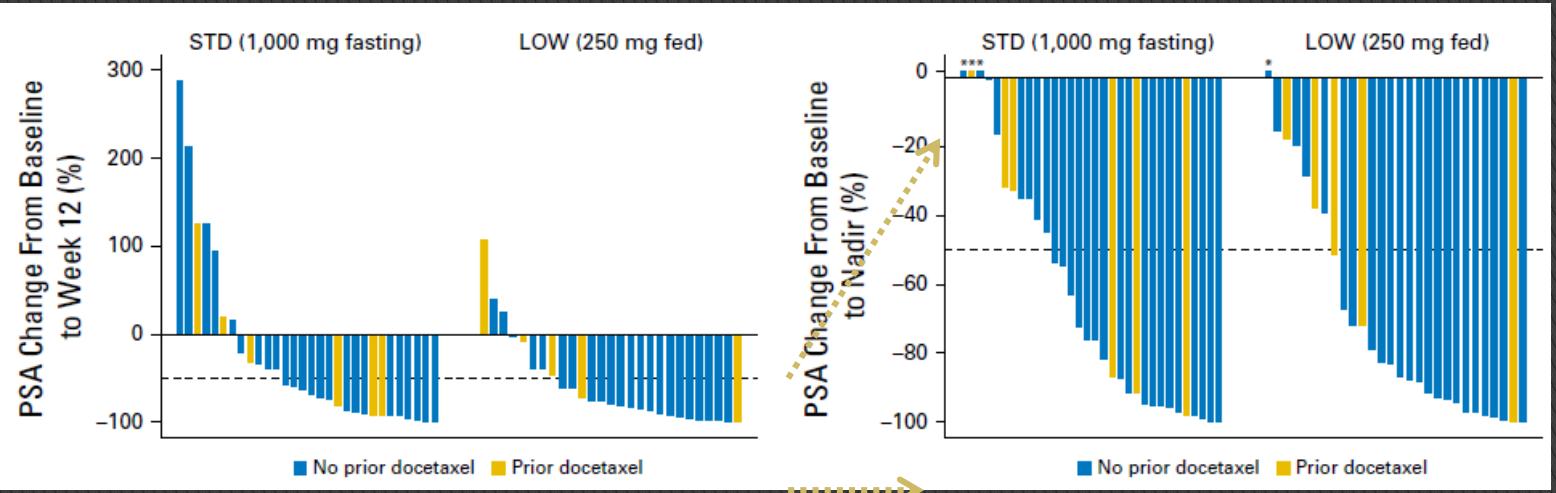
JOURNAL OF CLINICAL ONCOLOGY

Prospective International Randomized Phase II Study of Low-Dose Abiraterone With Food Versus Standard Dose Abiraterone In Castration-Resistant Prostate Cancer

Russell Z. Szmulewitz, Cody J. Peer, Abiola Ibraheem, Elia Martinez, Mark F. Kozloff, Bradley Carthon, R. Donald Harvey, Paul Fishkin, Wei Peng Yong, Edmund Chiong, Chadi Nabhan, Theodore Karrison, William D. Figg, Walter M. Stadler, and Mark J. Ratain

Small lowfat meal *vs* 750 mg abiraterone

4/7/18



CRPC

N= 72

Phase II

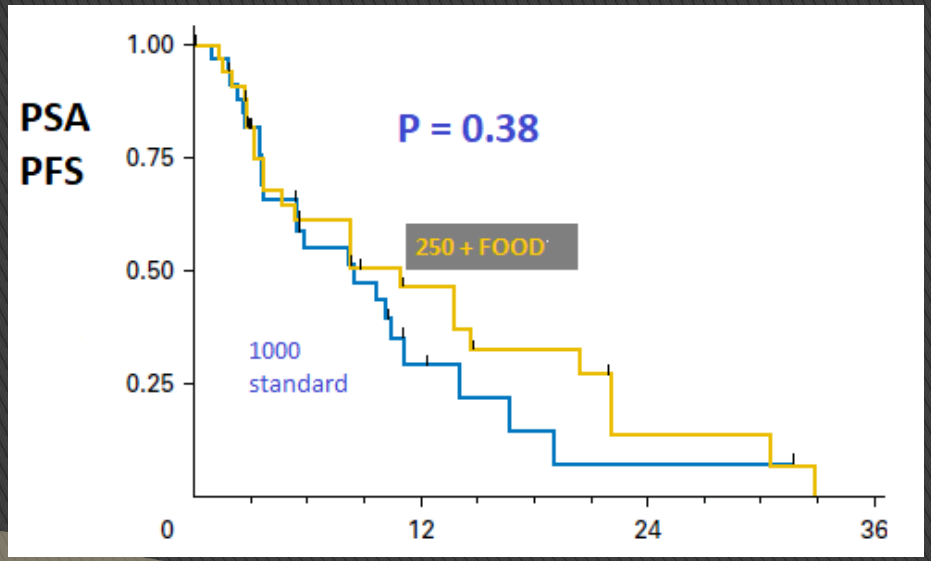
R

1000 (unfed)

36

36

250 + Food



Taxanes:

Every possible timing

CHAARTED

FIRSTANA

Some negative taxane combinations phase III trials:

- Vitamin D receptor: Docetaxel with or without calcitriol
- VEGF: Docetaxel with or without bevacizumab
- VEGF: Docetaxel with or without ziv-aflibercept
- SRC: Docetaxel with or without dasatinib
- Vaccine: Docetaxel with or without GVAX

Chemohormonal Therapy in Metastatic Hormone-Sensitive Prostate Cancer

Christopher J. Sweeney, M.B., B.S., Yu-Hui Chen, M.S., M.P.H., Michael Carducci, M.D., Glenn Liu, M.D., David F. Jarrard, M.D., Mario Eisenberger, M.D., Yu-Ning Wong, M.D., M.S.C.E., Noah Hahn, M.D., Manish Kohli, M.D., Matthew M. Cooney, M.D., Robert Dreicer, M.D., Nicholas J. Vogelzang, M.D., et al.

August 20, 2015
N Engl J Med 2015; 373:737-746

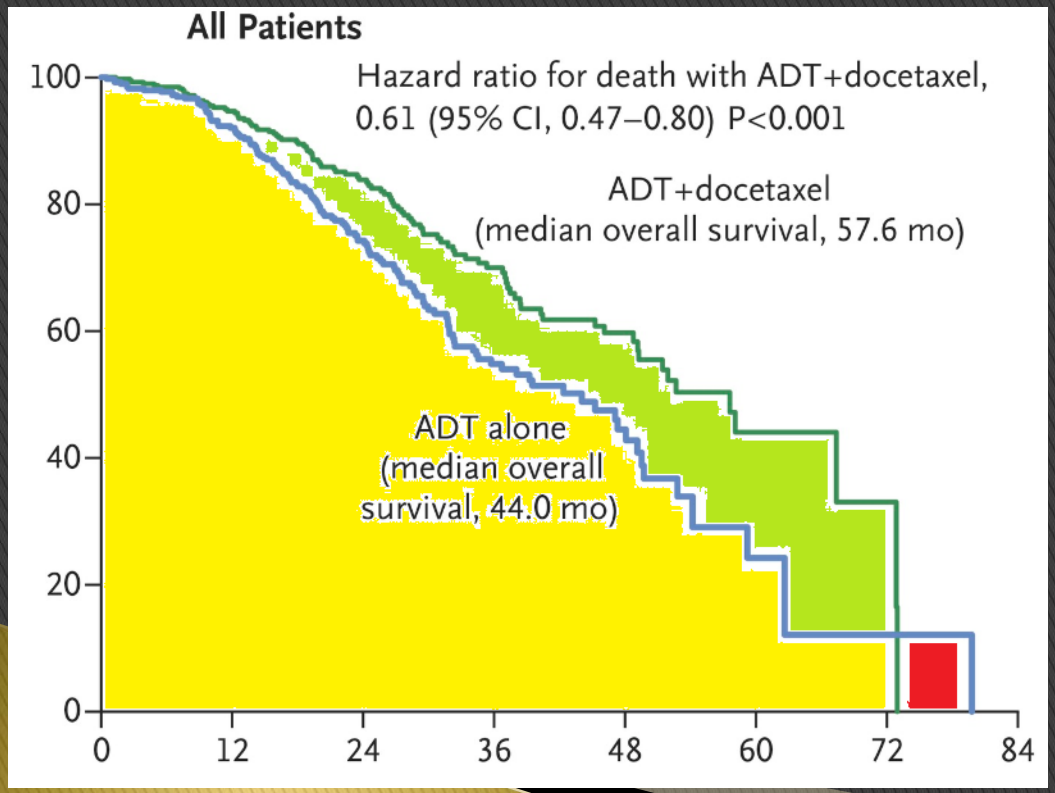
CHAARTED

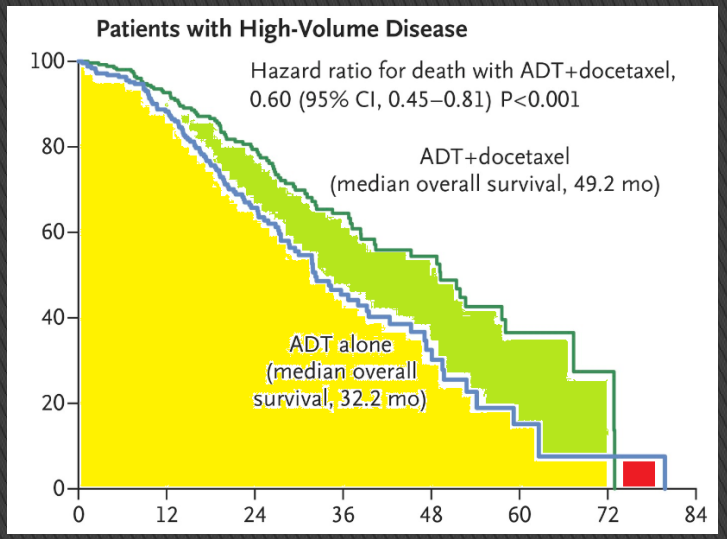
HSPC, m

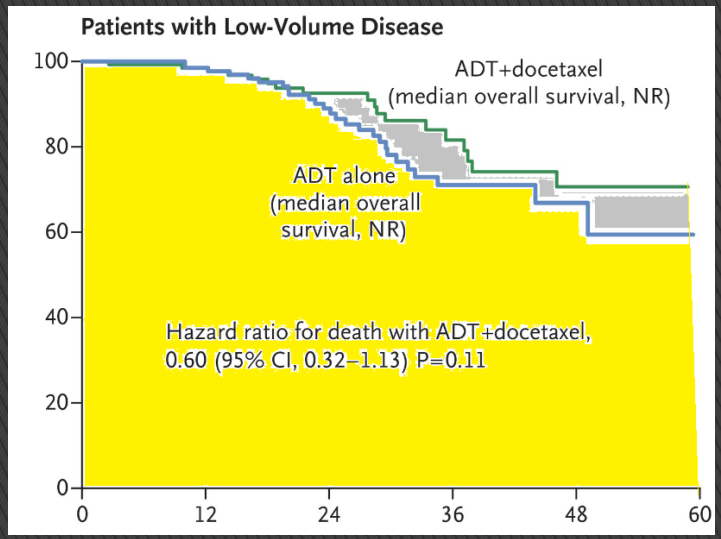
397 → Docetaxel x6 + GnRH

R

393 → Monotherapy GnRH







OS difference are driven by the HIGHER RISK subset of patients

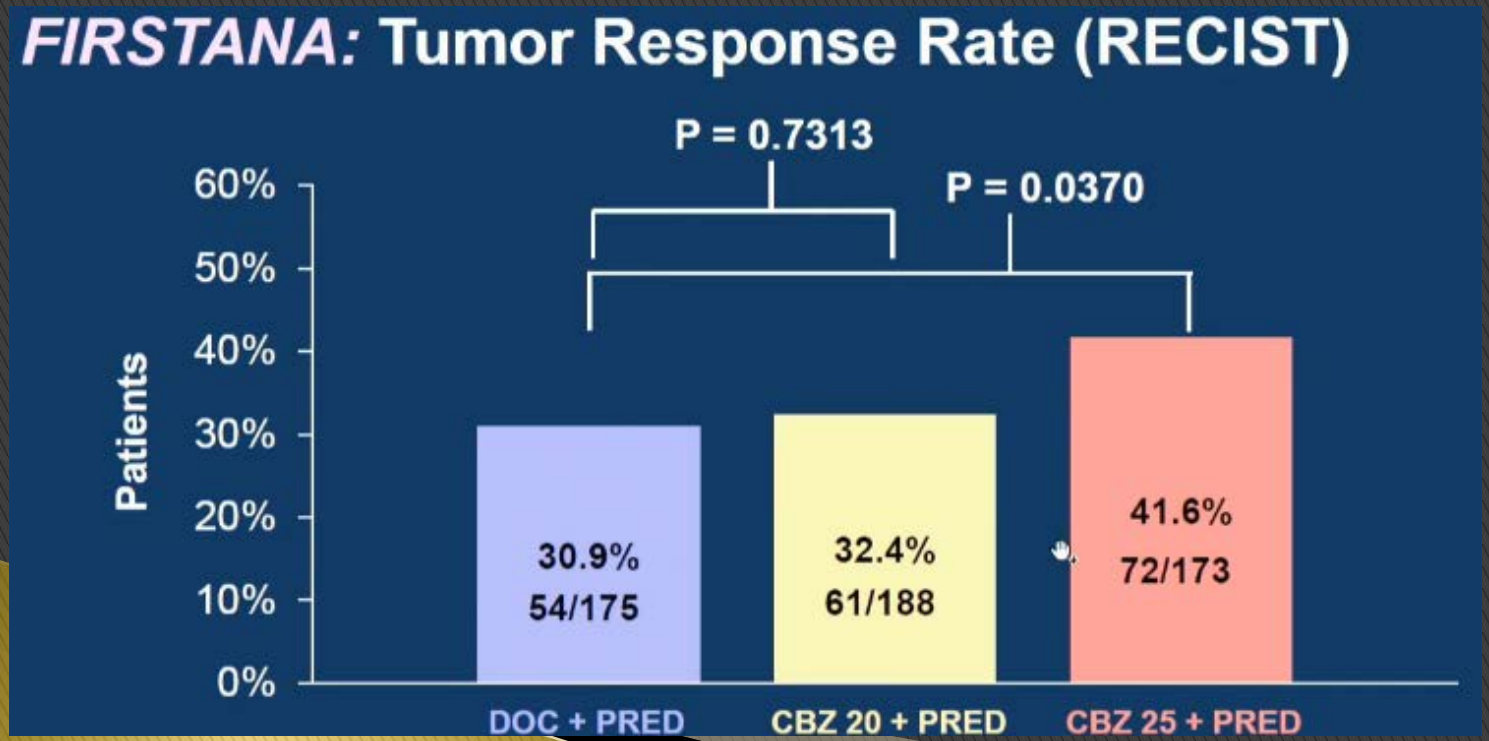
FIRSTANA

Cabazitaxel Versus Docetaxel As First-Line Therapy for Patients With Metastatic Castration-Resistant Prostate Cancer: A Randomized Phase III Trial—FIRSTANA

Stéphane Oudard, Karim Fizazi, Lisa Sengeløv, Gedske Daugaard, Fred Saad, Steinbjørn Hansen, Marie Hjälm-Eriksson, Jacek Jassem, Antoine Thiery-Vuillemin, Orazio Caffo, Daniel Castellano, Paul N. Mainwaring, John Bernard, Liji Shen, Mustapha Chadjaa, and Oliver Sartor

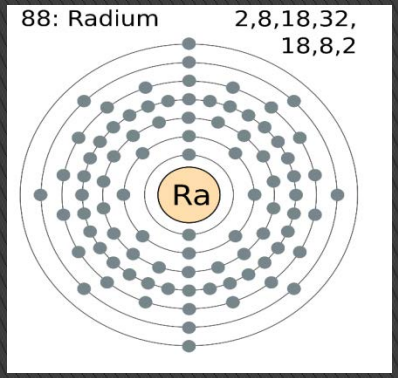
- Docetaxel 75
- Cabazitaxel 25
- Cabazitaxel 20

C20 v D75, HR =1.01 (95% CI, 0.85 1.20)
C25 v D75, HR =0.97 (95% CI, 0.82 -1.16)



Radium

Another non-AR approach



ALSYMPCA

- OS
- Time-to-event

The NEW ENGLAND JOURNAL of MEDICINE

JULY 18, 2013 VOL. 369 NO. 3

Alpha Emitter Radium-223 and Survival in Metastatic Prostate Cance

C. Parker, S. Nilsson, D. Heinrich, S.I. Helle, J.M. O'Sullivan, S.D. Fossà, A. Chodac
A. Widmark, D.C. Johannessen, P. Hoskin, D. Bottomley, N.D. James, A. Solberg,
S. Boehmer, M. Dall'Oglio, L. Franzén, R. Coleman, N.J. Vogelzang, C.G. O'
J. Garcia-Vargas, M. Shan, Ø.S. Bruland, and O. Sartor, for the ALSY

mCRPC

(Excludes:
LN> 3 cm
Visceral mets
Cord compression)

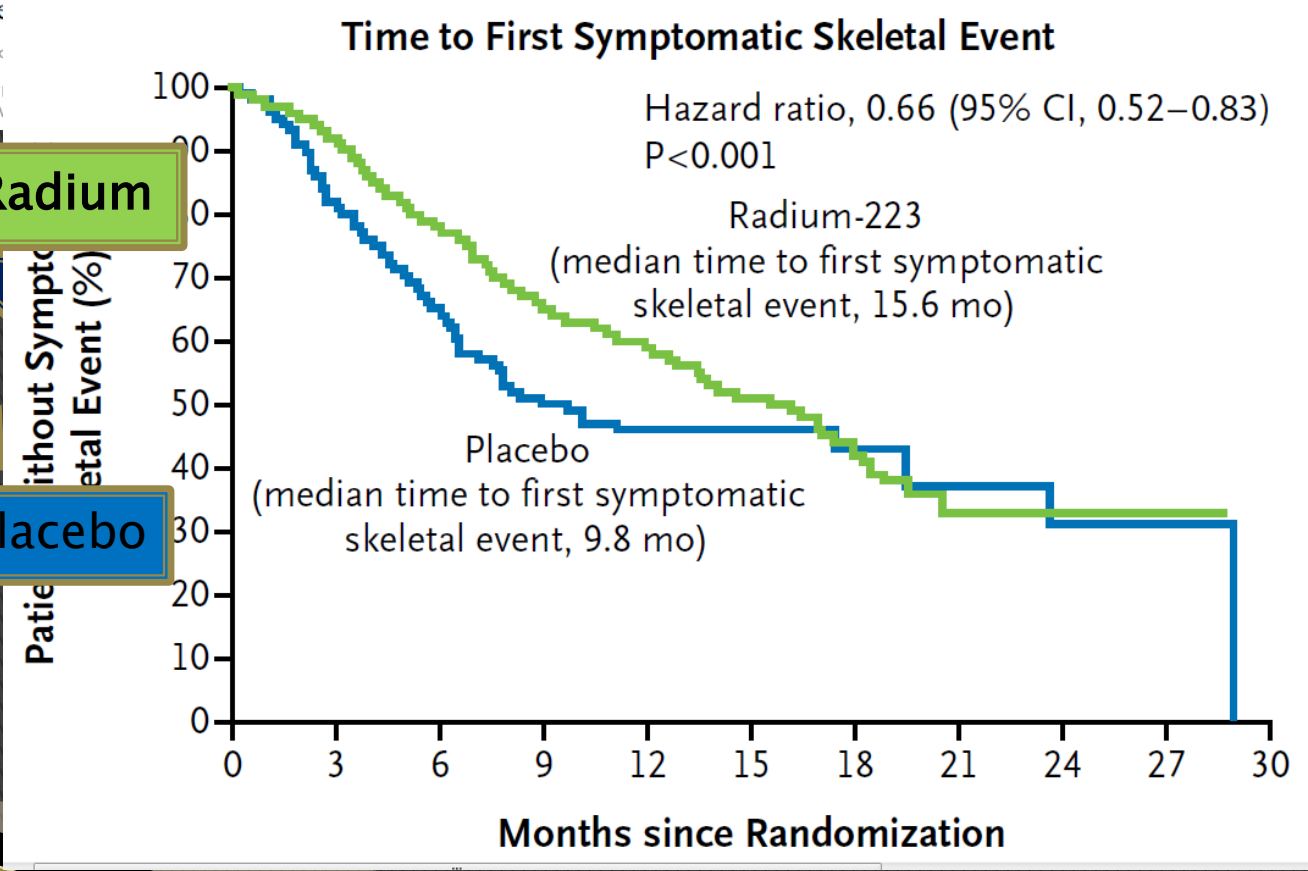
R

614

307

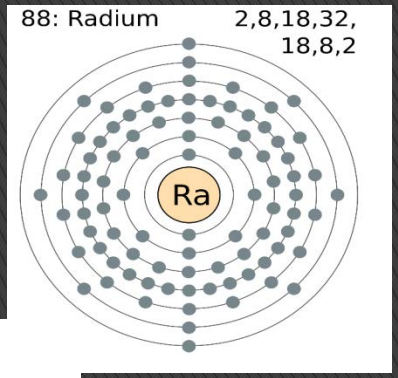
Radium

Placebo



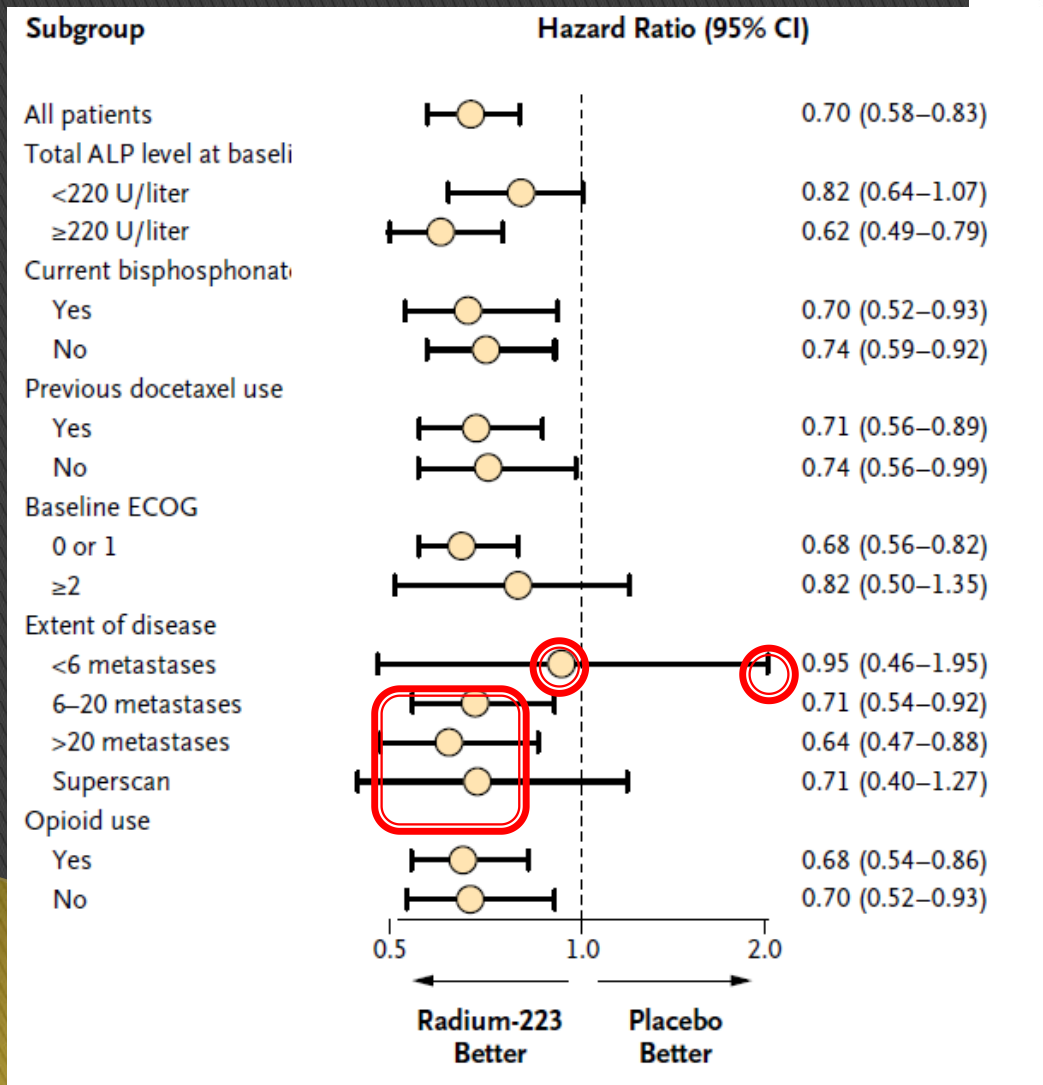
Radium

Another non-AR approach



ALSYMPCA

- OS
- Time-to-event



*OS difference are driven by the **HIGHER RISK** subset of patients*

A look forward to PARP-i opportunity:

Trials with DNA-mismatch repair phenotype as a gatekeeper

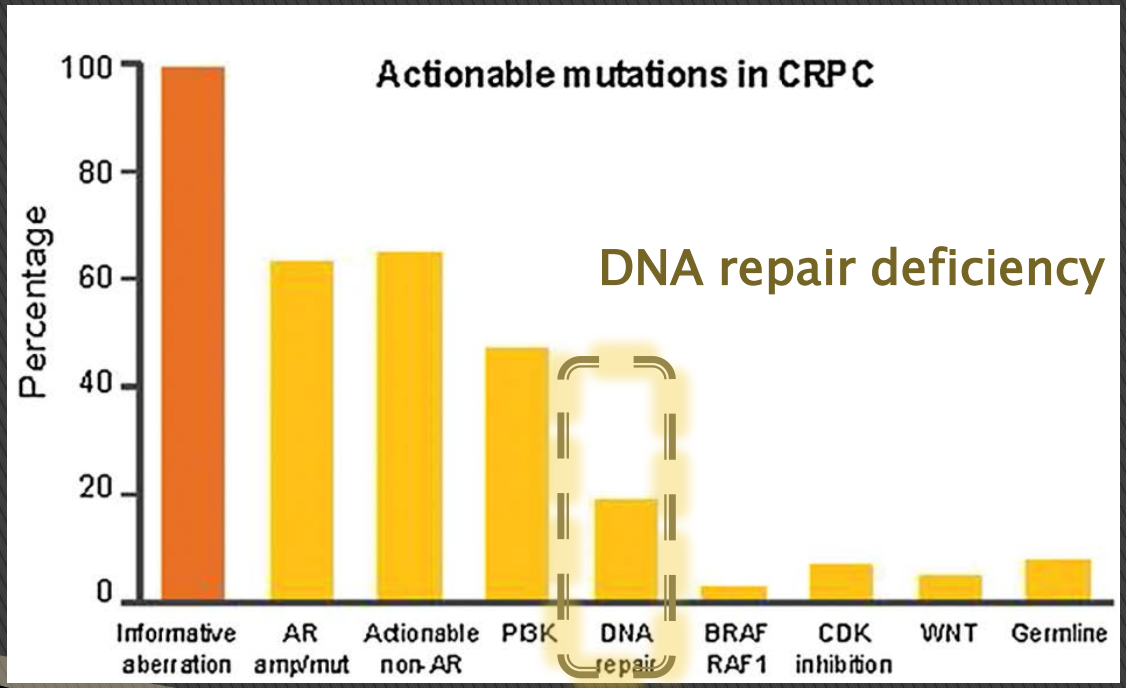
- About ¼ CRPC should be eligible
- This limits accrual rates
- All are off-label

Cell

Volume 161, Issue 5, 21 May 2015, Pages 1215–1228

Integrative Clinical Genomics of Advanced Prostate Cancer

Dan Robinson and 72 more.



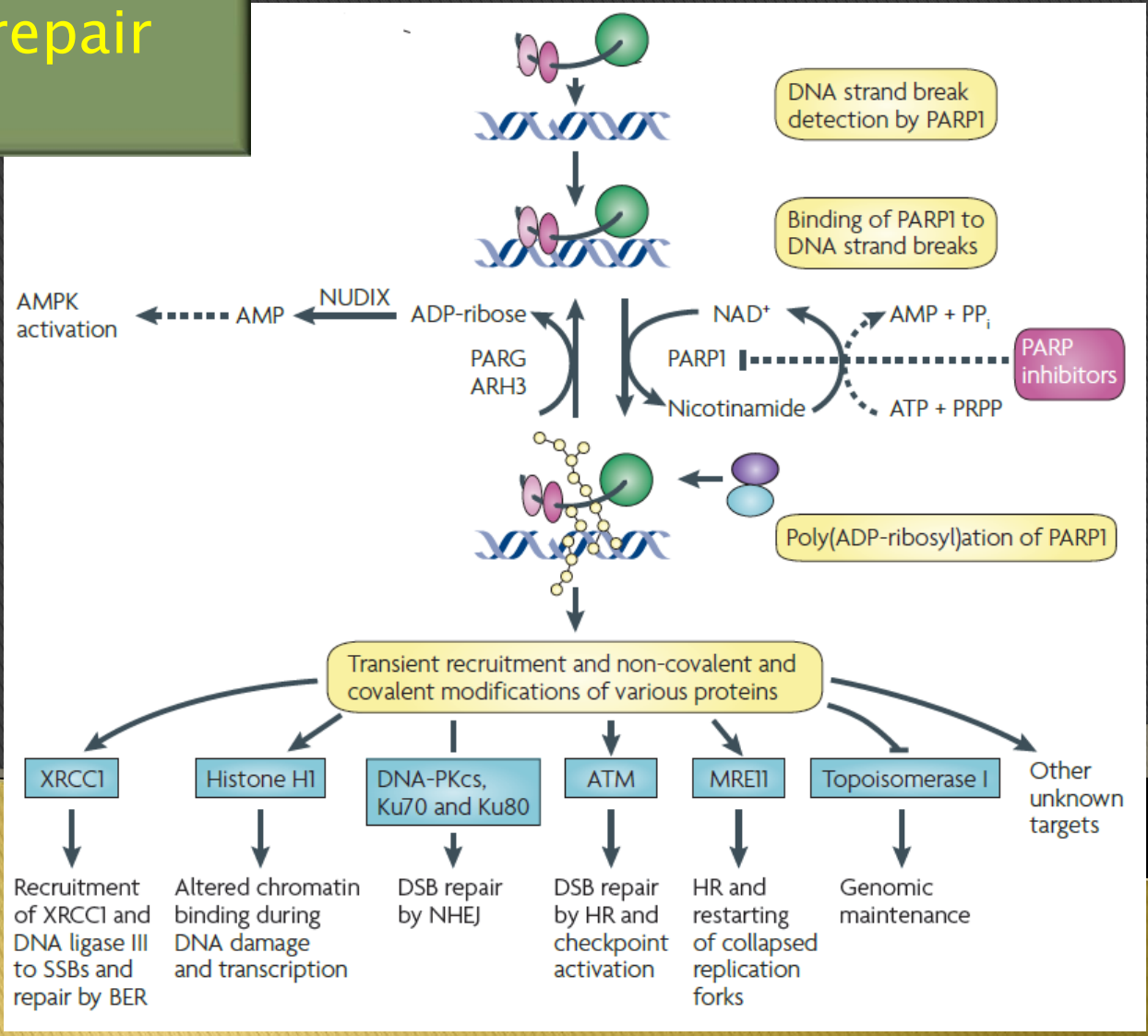
NATURE REVIEWS | CANCER

ouleau M, Patel A, Hendzel MJ, Kaufmann SH, Poirier GG. PARP inhibition: PARP1 and beyond. *Nat Rev Cancer.* 2010 Apr;10(4):293–301.

The PARP proteins are part of the DNA repair complexes

Olaparib
Rucaparib
Niraparib

…par… PARP
… ib
inhibitor



NEJM

OCTOBER 29, 2015 VOL. 373 NO. 18

DNA-Repair Defects and Olaparib in Metastatic Prostate Cancer

J. Mateo, S. Carreira, S. Sandhu, S. Miranda, H. Mossop, R. Perez-Lopez, D. Nava Rodrigues, D. Robinson, A. Omlin, N. Tunariu, G. Boysen, N. Porta, P. Flohr, A. Gillman, I. Figueiredo, C. Paulding, G. Seed, S. Jain, C. Ralph, A. Protheroe, S. Hussain, R. Jones, T. Elliott, U. McGovern, D. Bianchini, J. Goodall, Z. Zafeiriou, C.T. Williamson, R. Ferraldeschi, R. Riisnaes, B. Ebbs, G. Fowler, D. Roda, W. Yuan, Y.-M. Wu, X. Cao, R. Brough, H. Pemberton, R. A'Hern, A. Swain, L.P. Kunju, R. Eeles, G. Attard, C.J. Lord, A. Ashworth, M.A. Rubin, K.E. Knudsen, F.Y. Feng, A.M. Chinnaiyan, E. Hall, and J.S. de Bono

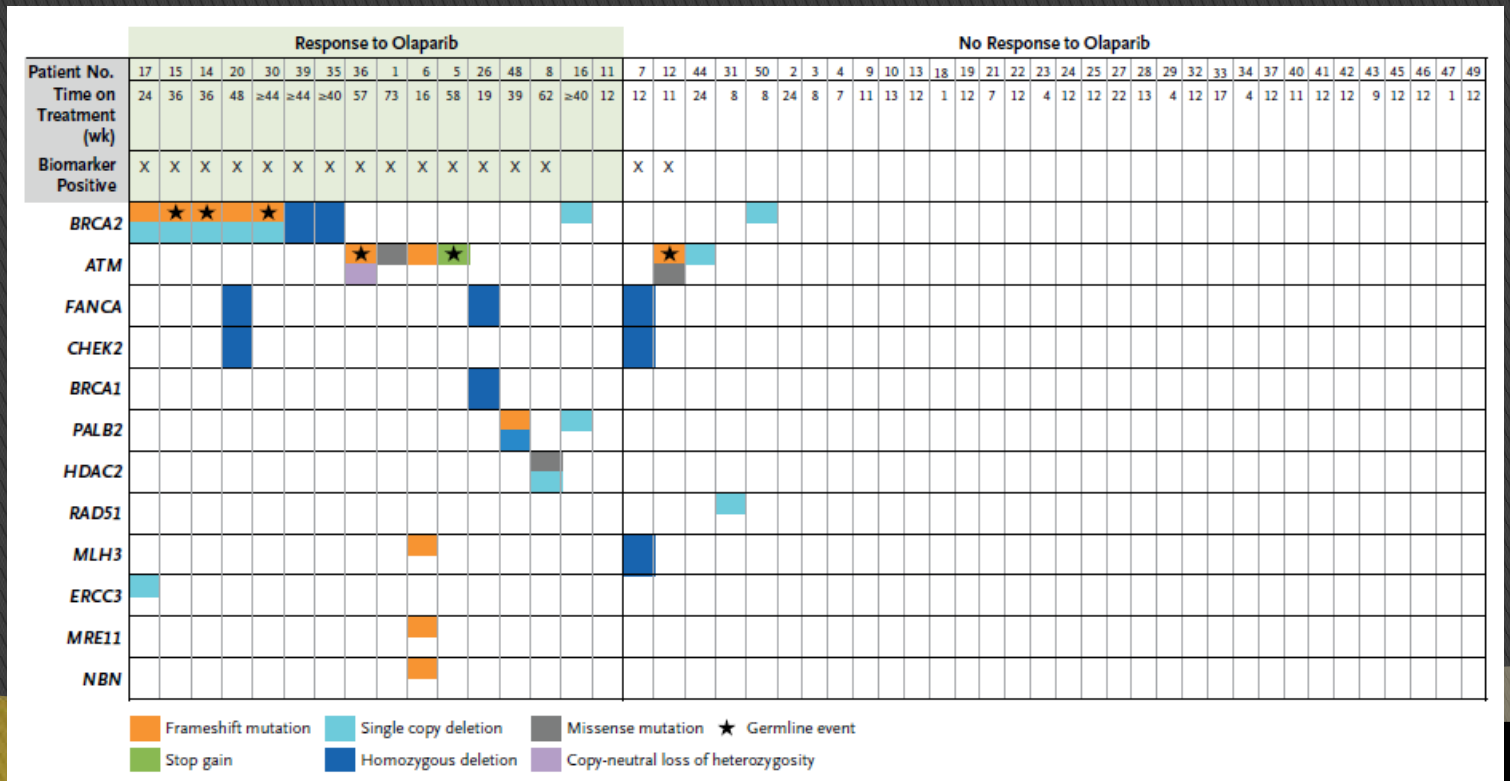


Figure 1. Genomic Aberrations in DNA Repair in Patients with Metastatic, Castration-Resistant Prostate Cancer.

Data are shown for the 49 patients who could be evaluated for a response. Mutations and deletions in DNA-repair genes were identified through next-generation sequencing studies. Green shading indicates patients who were classified as having a response to olaparib in the clinical trial. Patients were considered to be biomarker-positive if homozygous deletions, deleterious mutations, or both were detected in DNA-repair genes (but not single copy deletions without events detected in the second allele). A star indicates that a particular genomic event was detected in germline DNA. Archival tumor samples were used for the sequencing studies in Patients 13, 18, 21, 40, 41, and 49 because the biopsy samples obtained during the trial were negative for tumor content.

NEJM

OCTOBER 29, 2015 VOL. 373 NO. 18

DNA-Repair Defects and Olaparib in Metastatic Prostate Cancer

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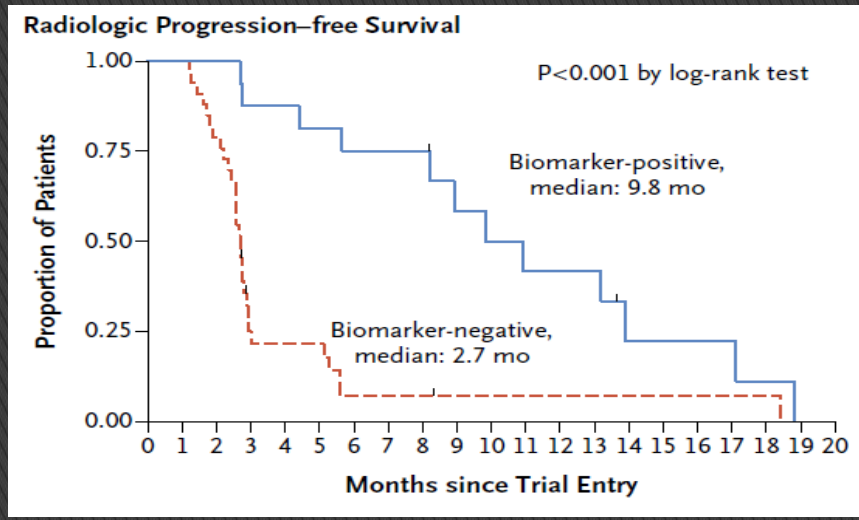

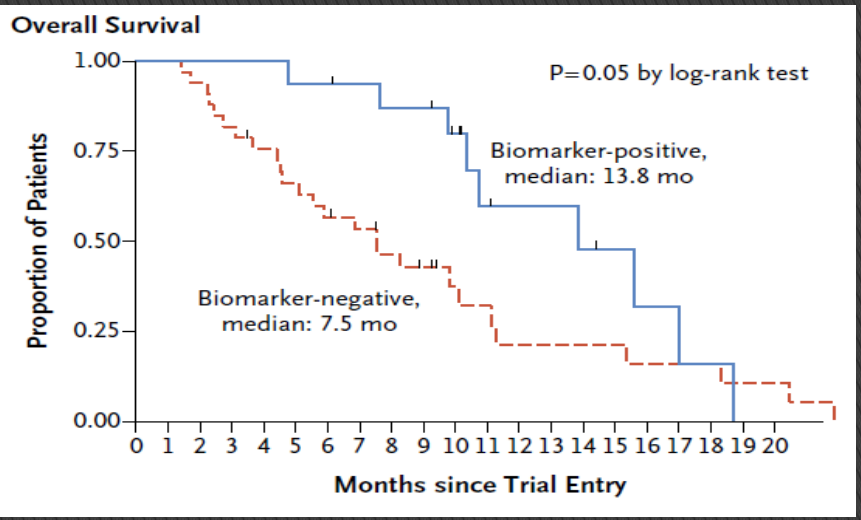

PARP directed prostate cancer trial examples:

- Olaparib vs enzalutamide vs abiraterone
- Olaparib before prostatatectomy
- Olaparib, abiraterone or both
- Olaparib with pembrolizumab

- Niraparib plus antiandrogen
- Niraparib with radium

- Rucaparib with cediranib
- Nivolumab + one of: rucaparib, docetaxel, enzalutamide

Conclusions (1/3)

Sequencing strategies to ponder

All oral first; put off parenteral drugs

Taxanes first – save lower intensity treatment for older age

Hormone therapy / non hormone therapy / hormone therapy alternation

Hormone therapy salvage of hormone therapy only for slow progressors

Radium – as soon as bone-only pattern is seen

Provenge – as early as possible (metastasis, no pain, low PSA)
Provenge – in coordination with antiandrogen initiation

Adaptive schedules: Alternate treatment and hiatus, to delay

Best timing is not obvious

What benefit for slower rising PSA?

- Hormone therapies beyond conventional GnRH: Active, but little empiric sequencing or crossover experience.
- apalutamide
- enzalutamide
- abiraterone
- Adapative vs continuous scheduling strategies
- Taxanes – early, late, in-between?
- Radium – be alert for optimal selection

Conclusions (3/3)

Other treatments and evaluations:

- Immune therapies sipuleucel-T and beyond
- Flucyclovine (Axumin) imaging to identify oligometastatic cases for radiation therapy
- Early concurrent hormone therapy for prostate bed salvage radiation therapy
- SINE inhibitor KPT-8602 trials

Thank you very much, & questions.