Year in Review: Clinical Investigators Provide Perspectives on the Most Relevant New Publications, Data Sets and Advances in Oncology

Prostate Cancer

Tuesday, December 1, 2020
5:00 PM – 6:00 PM ET

Faculty

Emmanuel S Antonarakis, MD
Andrew J Armstrong, MD, ScM

Moderator

Neil Love, MD

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Commercial Support

This activity is supported by educational grants from Astellas and Pfizer Inc, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Clovis Oncology, Merck, and Sanofi Genzyme.

Dr Love — Disclosures

Dr Love is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following commercial interests: AbbVie Inc, Acerta Pharma — A member of the AstraZeneca Group, Adaptive Biotechnologies Corporation, Agendia Inc, Agios Pharmaceuticals Inc, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Biodesix Inc, bioTheranostics Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Daiichi Sankyo Inc, Dendreon Pharmaceuticals Inc, Eisai Inc, EMD Serono Inc, Epizyme Inc, Exelixis Inc, Foundation Medicine, Genentech, a member of the Roche Group, Genmab, Genomic Health Inc, Gilead Sciences Inc, GlaxoSmithKline, Grail Inc, Guardant Health, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Infinity Pharmaceuticals Inc, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Lexicon Pharmaceuticals Inc, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Merrimack Pharmaceuticals Inc, Myriad Genetic Laboratories Inc, Natera Inc, Novartis, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Prometheus Laboratories Inc, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sandoz Inc, a Novartis Division, Sanofi Genzyme, Seagen Inc, Sirtex Medical Ltd, Spectrum Pharmaceuticals Inc, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro, A GSK Company, Teva Oncology, Tokai Pharmaceuticals Inc and Verastem Inc.

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Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

Dr Antonarakis — Disclosures

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Dr Armstrong — Disclosures

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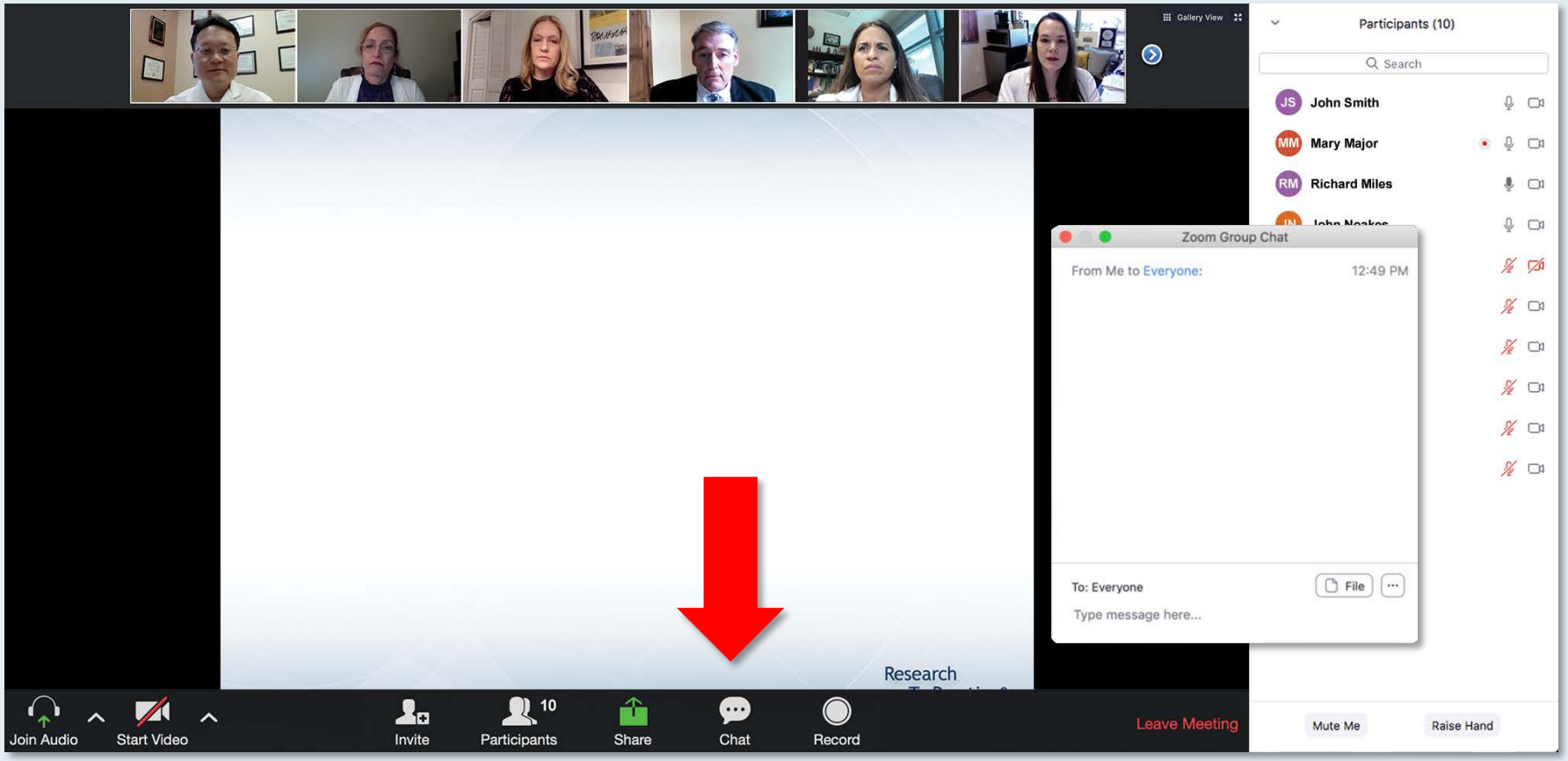
Speakers Bureau	Bayer HealthCare Pharmaceuticals, Dendreon Pharmaceuticals Inc

We Encourage Clinicians in Practice to Submit Questions



Feel free to submit questions now before the program begins and throughout the program.

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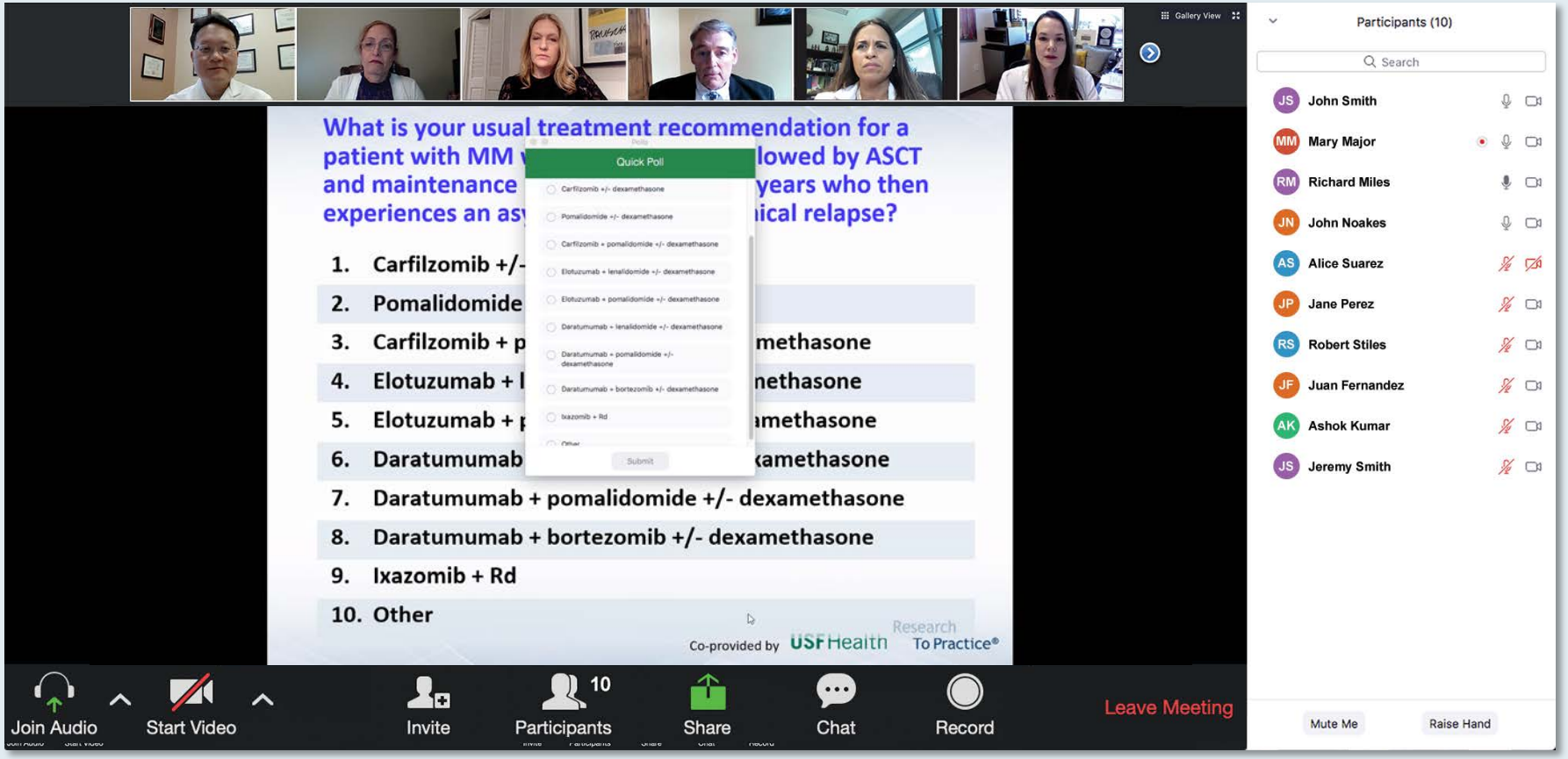
Familiarizing Yourself with the Zoom Interface

How to answer poll questions



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Results will be shown after everyone has answered.

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Upcoming Webinars

Wednesday, December 2, 2020
12:00 PM – 1:00 PM ET

Meet The Professor: Management of Lung Cancer

Faculty
Ramaswamy Govindan, MD

Moderator
Neil Love, MD

Friday, December 4, 2020

Consensus or Controversy? Investigators Discuss Clinical Practice Patterns and Available Research Data Guiding the Management of Hematologic Cancers

A 4-Part Friday Satellite Symposia Live Webinar Series Preceding the 62nd ASH Annual Meeting

Moderator
Neil Love, MD

Upcoming Webinars

Tuesday, December 8, 2020
5:00 PM – 6:00 PM ET

Year in Review: Clinical Investigators Provide Perspectives on the Most Relevant New Publications, Data Sets and Advances in Oncology
Colorectal and Gastroesophageal Cancers

Faculty
Peter C Enzinger, MD
Zev Wainberg, MD, MSc

Moderator
Neil Love, MD

Thursday, December 10, 2020
8:30 PM – 10:00 PM ET

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of HER2-Positive Breast Cancer

Faculty
Carey K Anders, MD
Erika Hamilton, MD
Sara Hurvitz, MD
Mark D Pegram, MD
Sara M Tolaney, MD, MPH

Moderator
Neil Love, MD

Upcoming Webinars

Friday, December 11, 2020
8:30 PM – 10:00 PM ET

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Triple-Negative Breast Cancer

Faculty
P Kelly Marcom, MD
Joyce O'Shaughnessy, MD
Hope S Rugo, MD
Professor Peter Schmid, MD, PhD

Moderator
Neil Love, MD

Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.

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ONCOLOGY TODAY

WITH DR NEIL LOVE

CURRENT AND FUTURE ROLE OF IMMUNE CHECKPOINT INHIBITORS AND OTHER NOVEL THERAPIES IN UROTHELIAL BLADDER CANCER

DR ASHISH KAMAT

UNIVERSITY OF TEXAS
MD ANDERSON CANCER CENTER

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YiR Prostate Cancer Faculty

Emmanuel S Antonarakis, MD
Professor of Oncology and Urology
Johns Hopkins University
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Baltimore, Maryland

Andrew J Armstrong, MD, ScM
Professor of Medicine, Surgery, Pharmacology and Cancer Biology
Director of Research
Duke Cancer Institute Center for Prostate and Urologic Cancers
Divisions of Medical Oncology and Urology
Duke University
Durham, North Carolina

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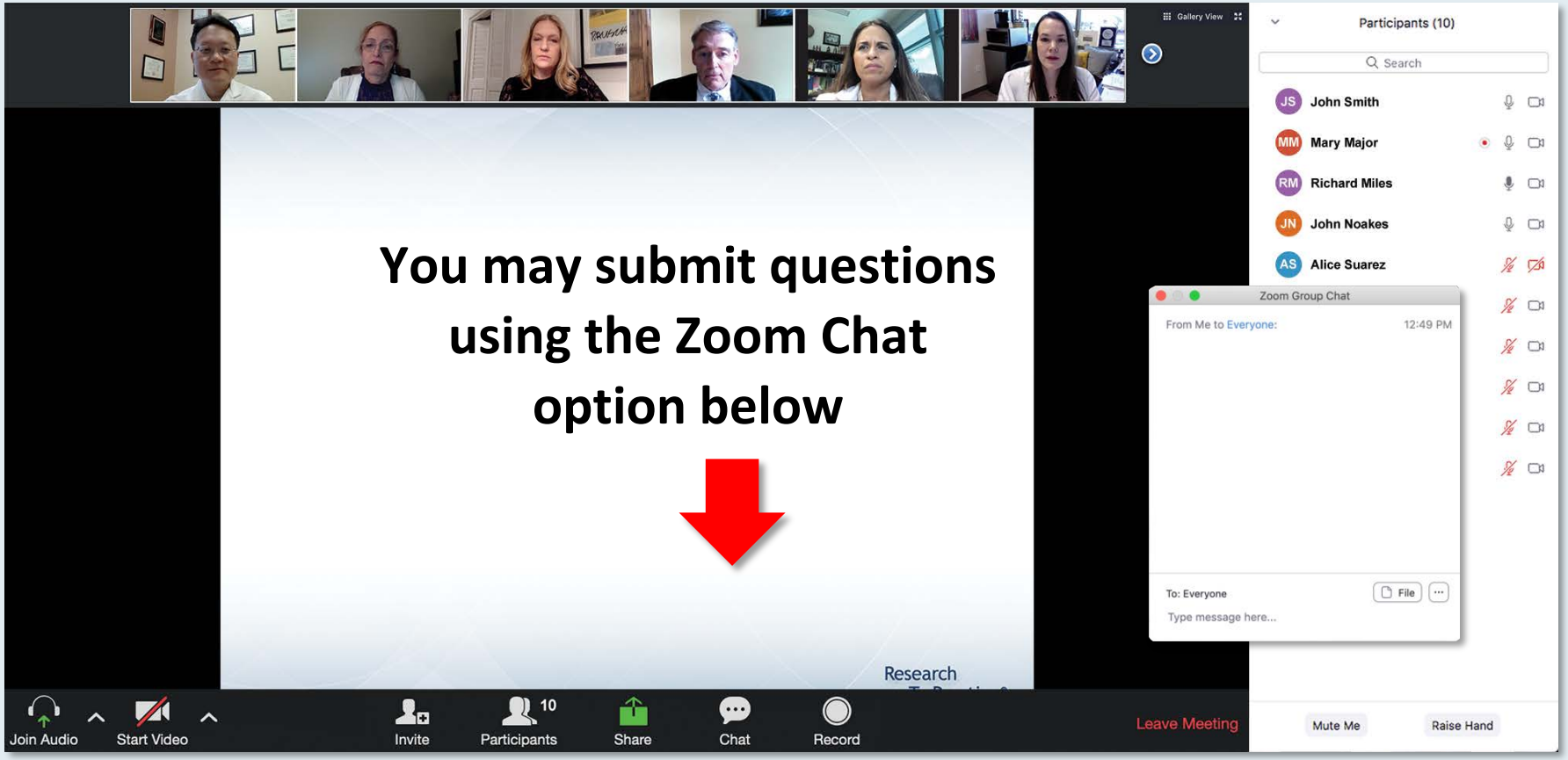
We Encourage Clinicians in Practice to Submit Questions



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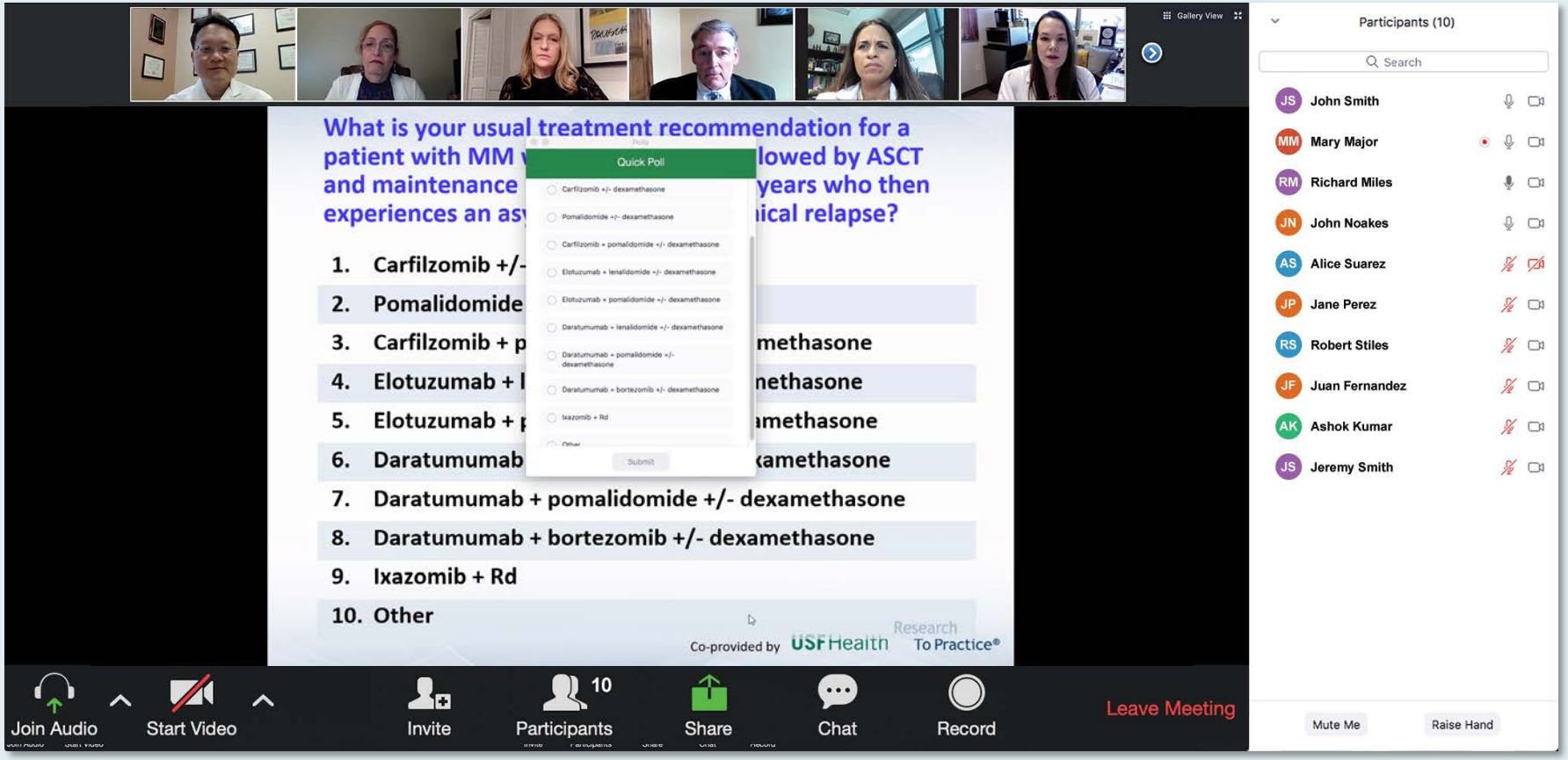

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Friday, December 4, 2020

Multiple Myeloma
8:30 AM – 10:00 AM Pacific Time
(11:30 AM – 1:00 PM ET)

Chronic Lymphocytic Leukemia
12:00 PM – 1:30 PM Pacific Time
(3:00 PM – 4:30 PM ET)

Acute Myeloid Leukemia
3:00 PM – 4:30 PM Pacific Time
(6:00 PM – 7:30 PM ET)

Hodgkin and Non-Hodgkin Lymphoma
7:00 PM – 8:30 PM Pacific Time
(10:00 PM – 11:30 PM ET)

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Key Prostate Cancer Clinical Algorithms: What We've Learned This Year – Part 1

In the treatment algorithm, when should the following generally be recommended?

- Post-prostatectomy radiation therapy – *Dr Armstrong*
- Oral GnRH receptor antagonist relugolix – *Dr Antonarakis*
- Androgen deprivation therapy (ADT) for PSA-only relapse after local therapy (M0) – *Dr Armstrong*
- Adding an antiandrogen agent to ADT in castration-resistant M0 disease – *Drs Antonarakis and Armstrong*
- Utilizing prostate-directed local therapy for metastatic hormone-sensitive prostate cancer (mHSPC) – *Dr Antonarakis*
- Adding an antiandrogen, abiraterone or docetaxel to ADT for mHSPC – *Drs Armstrong and Antonarakis*

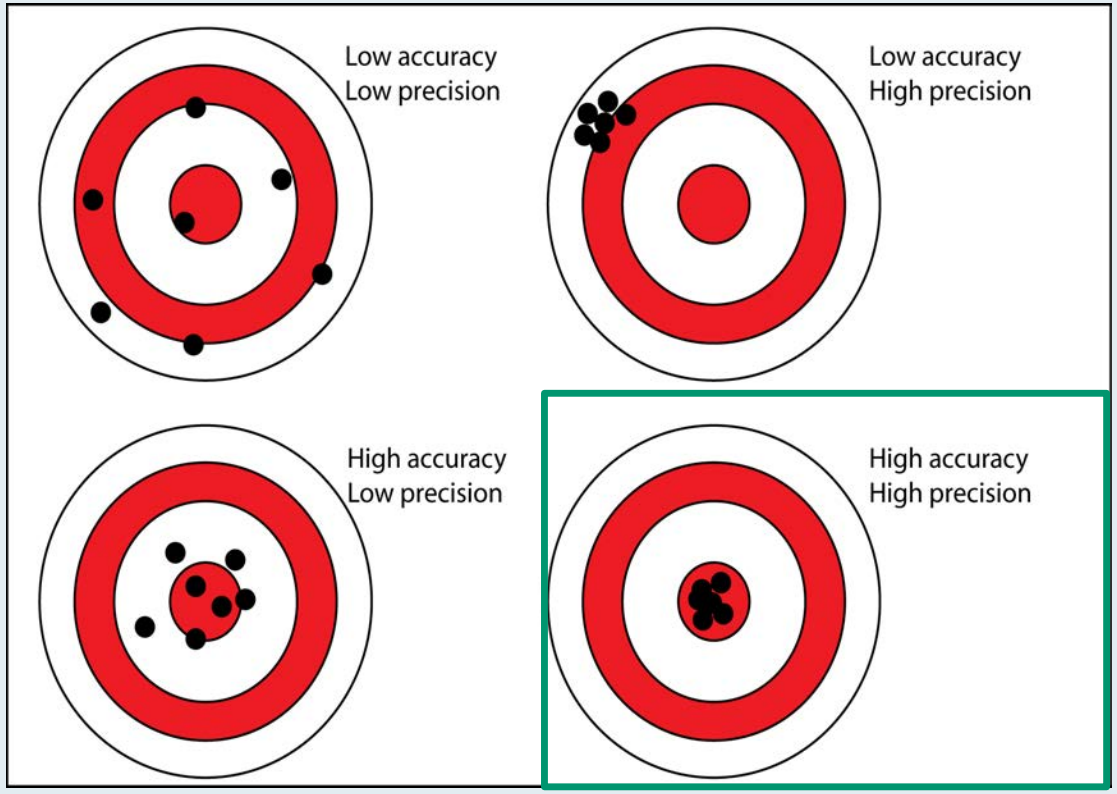
Key Prostate Cancer Clinical Algorithms: What We've Learned This Year – Part 2

In the treatment algorithm, when should the following generally be recommended?

- Endocrine treatment versus chemotherapy after first-line endocrine therapy for metastatic castration-resistant prostate cancer (mCRPC) – *Drs Antonarakis and Armstrong*
- Radium-223 in mCRPC – *Dr Armstrong*
- PARP inhibitors in mCRPC; recommended genomic evaluation – *Drs Antonarakis and Armstrong*
- PSMA-targeted treatment and imaging – *Drs Armstrong and Antonarakis*
- TMPRSS2 and COVID-19 – *Dr Antonarakis*

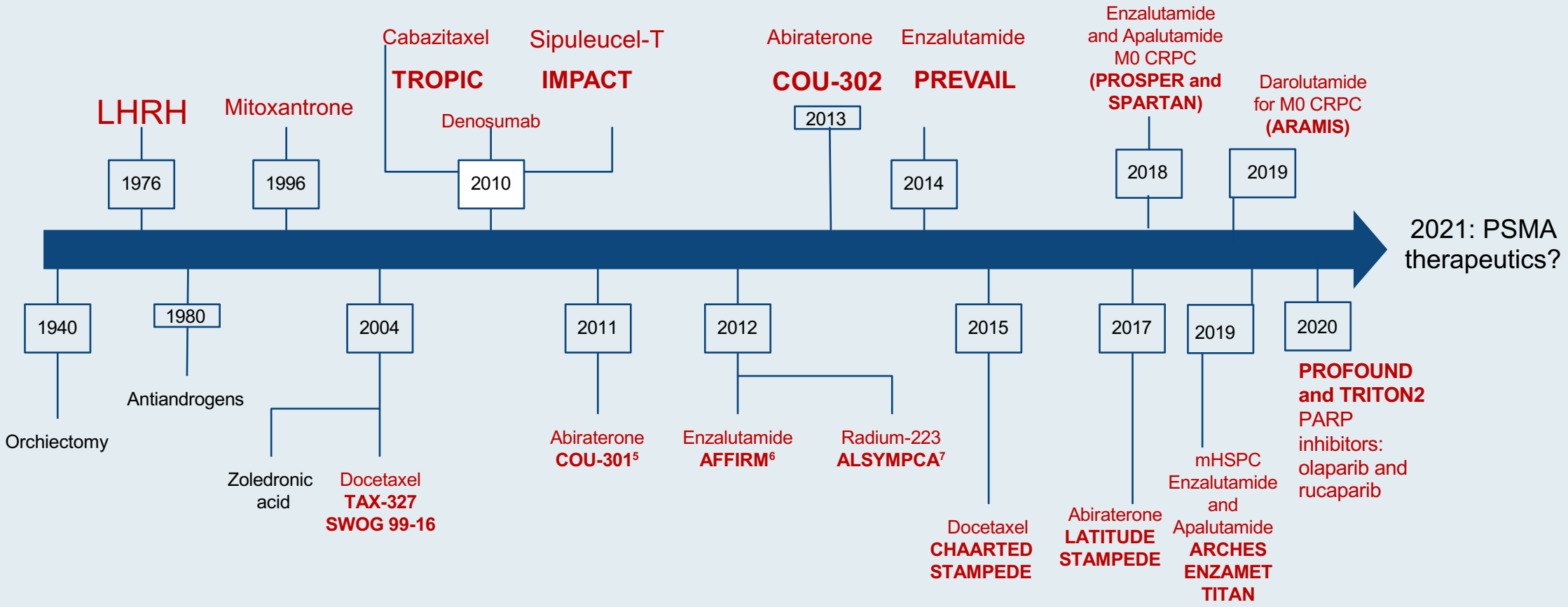
Four Key Advances in 2019-20 in Advanced Prostate Cancer

1. Improved survival in nmCRPC with new AR therapies
2. Improved survival in mHSPC with new AR therapies
3. Cabazitaxel solidified as 3rd line therapy in mCRPC: the CARD trial
4. Precision medicine comes in mCRPC: homologous repair and PARP inhibition



Courtesy of Andrew J Armstrong, MD, ScM

Treatment Evolution in Metastatic Prostate Cancer



1. Tannock IF, et al. N Engl J Med. 2004;351:1502-12. 2. Petrylak D, et al. N Engl J Med. 2004;351:1513-20. 3. de Bono J, et al. Lancet. 2010;376:1147-54. 4. Kantoff PW, et al. N Engl J Med. 2010;363:411-22. 5. de Bono JS, et al. N Engl J Med. 2011;364:1995-2005. 6. Scher HI, et al. N Engl J Med. 2012;367:1187-97. 7. Parker C, et al. N Engl J Med. 2013;369:213-23. 8. Ryan CJ, et al. N Engl J Med. 2013;368:138-48. 9. Beer TM, et al. N Engl J Med. 2014;371:424-33. 10. Sweeney CJ, et al. N Engl J Med. 2015;373:737-46. 11. James ND, et al. Lancet. 2016;387:1163-77. 12. Fizazi K, et al. N Engl J Med. 2017;377:352-60. 13. James ND, et al. N Engl J Med. 2017;377:338-51.

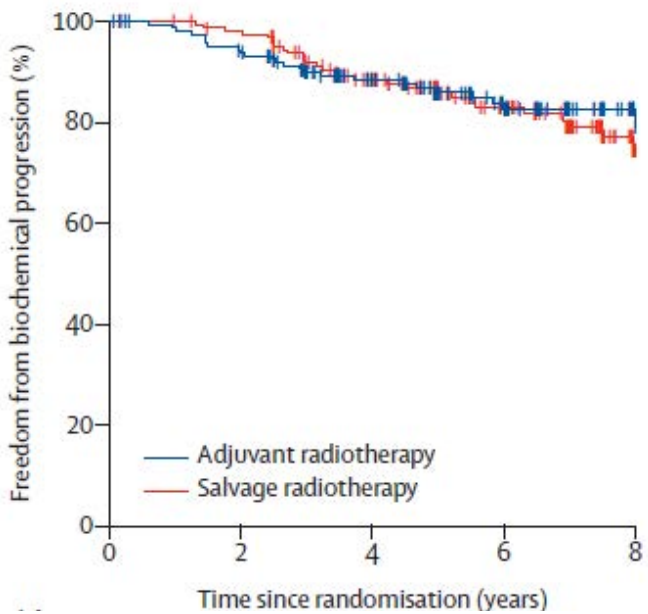
Courtesy of Andrew J Armstrong, MD, ScM

Module 1

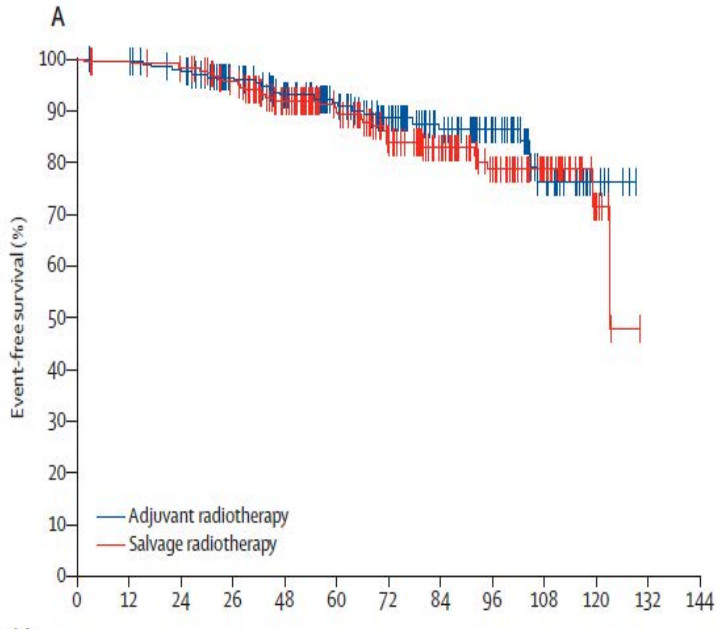
In the treatment algorithm, when should post-prostatectomy radiation therapy generally be recommended?

Discussant: Dr Armstrong

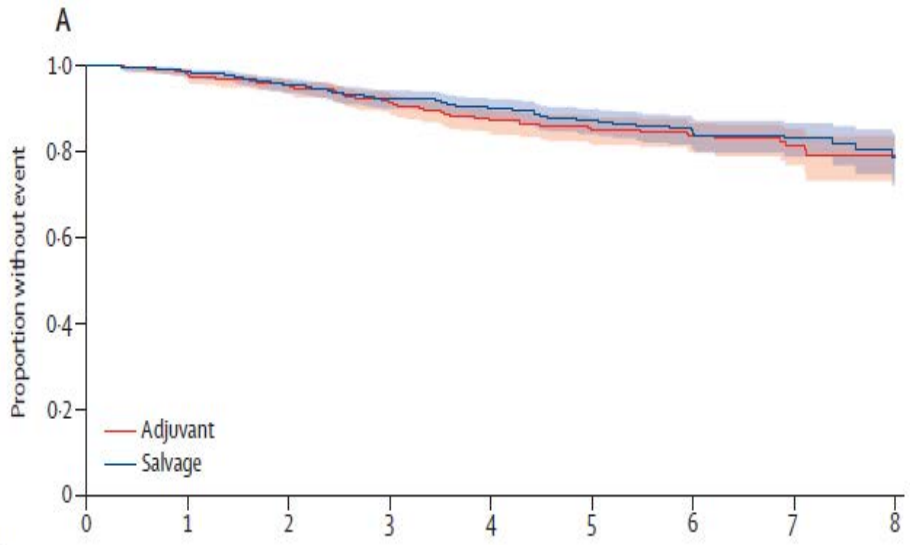
3 Trials, Same Result: Evidence-Based Medicine!



TROG 08: Kneebone et al Lancet Oncol 2020



GETUG-AFU 17: Sargos P et al Lancet Oncol 2020



RADICALS: Parker CS et al Lancet Oncol 2020

Implications for men: avoidance of the side effects of radiation in many situations without compromising cure, such as erectile dysfunction and bowel/bladder risks

Courtesy of Andrew J Armstrong, MD, ScM

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Module 2

In the treatment algorithm, when should the oral GnRH receptor antagonist relugolix be recommended if it were available?

Discussant: Dr Antonarakis

HERO Phase III Trial: Results Comparing Relugolix, an Oral GnRH Receptor Antagonist, versus Leuprolide Acetate for Advanced Prostate Cancer[1]

Oral Relugolix for Androgen-Deprivation Therapy in Advanced Prostate Cancer[2]

[1] Shore N et al.
ASCO 2020;Abstract 5602.

[2] Shore ND et al.
N Engl J Med 2020;382(23):2187-96.

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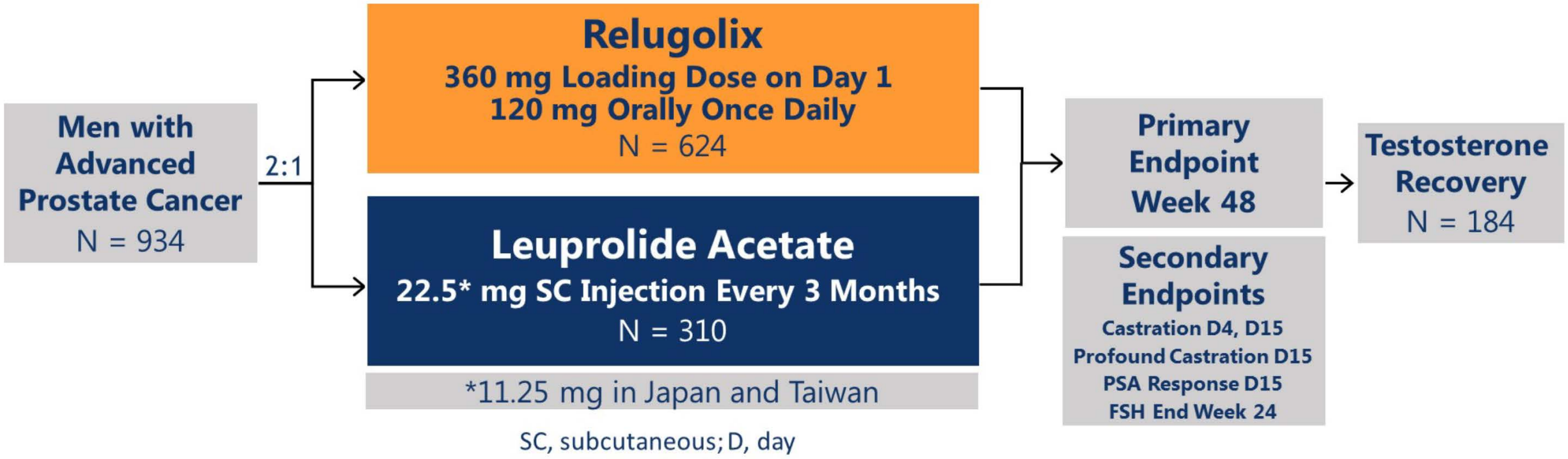
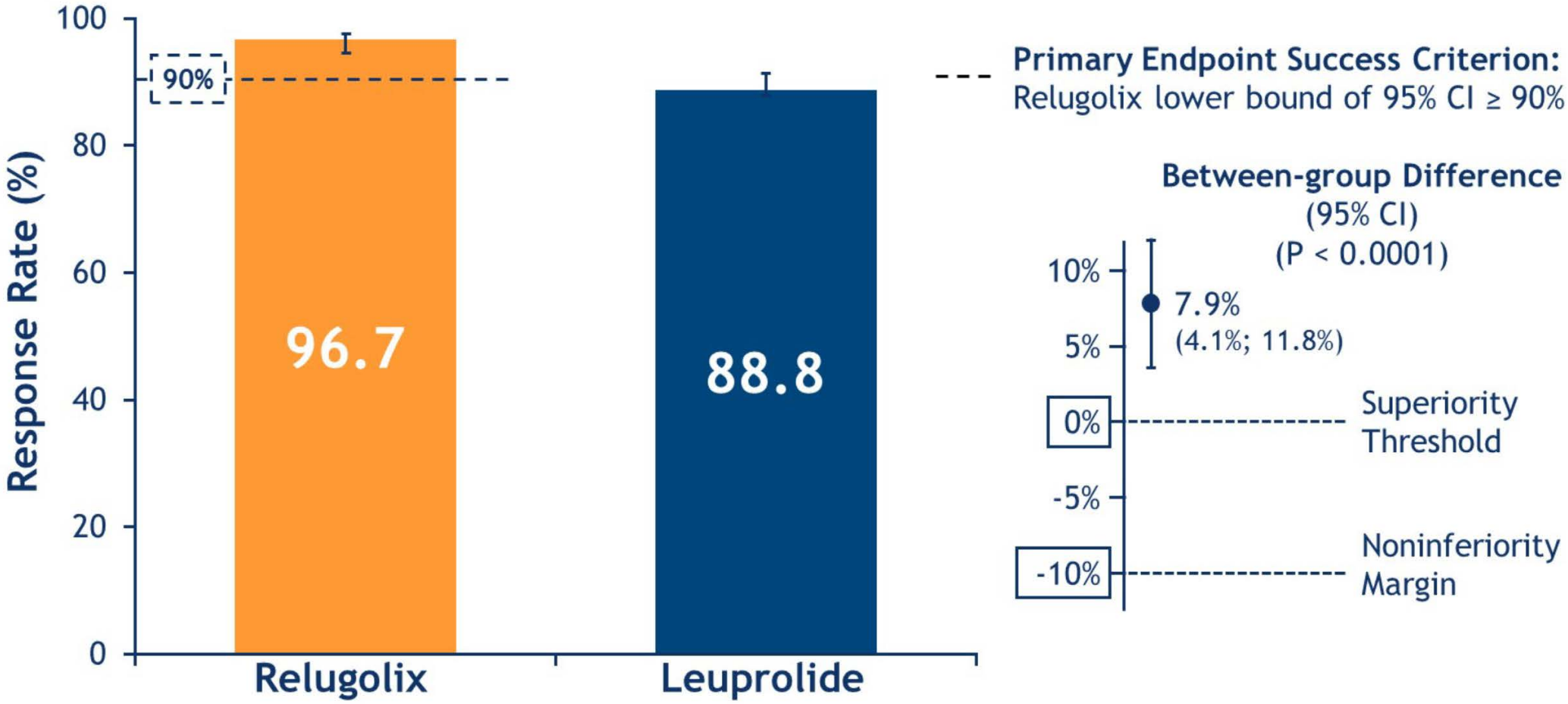
HERO: Ongoing Phase III Trial of Relugolix versus Leuprolide Acetate for Advanced HSPC



Shore N et al. ASCO 2020;Abstract 5602; Shore ND et al. *N Engl J Med* 2020;382(23):2187-96.

HERO: Primary Endpoint – Sustained Castration
Key Secondary Endpoint – Noninferiority to Leuprolide



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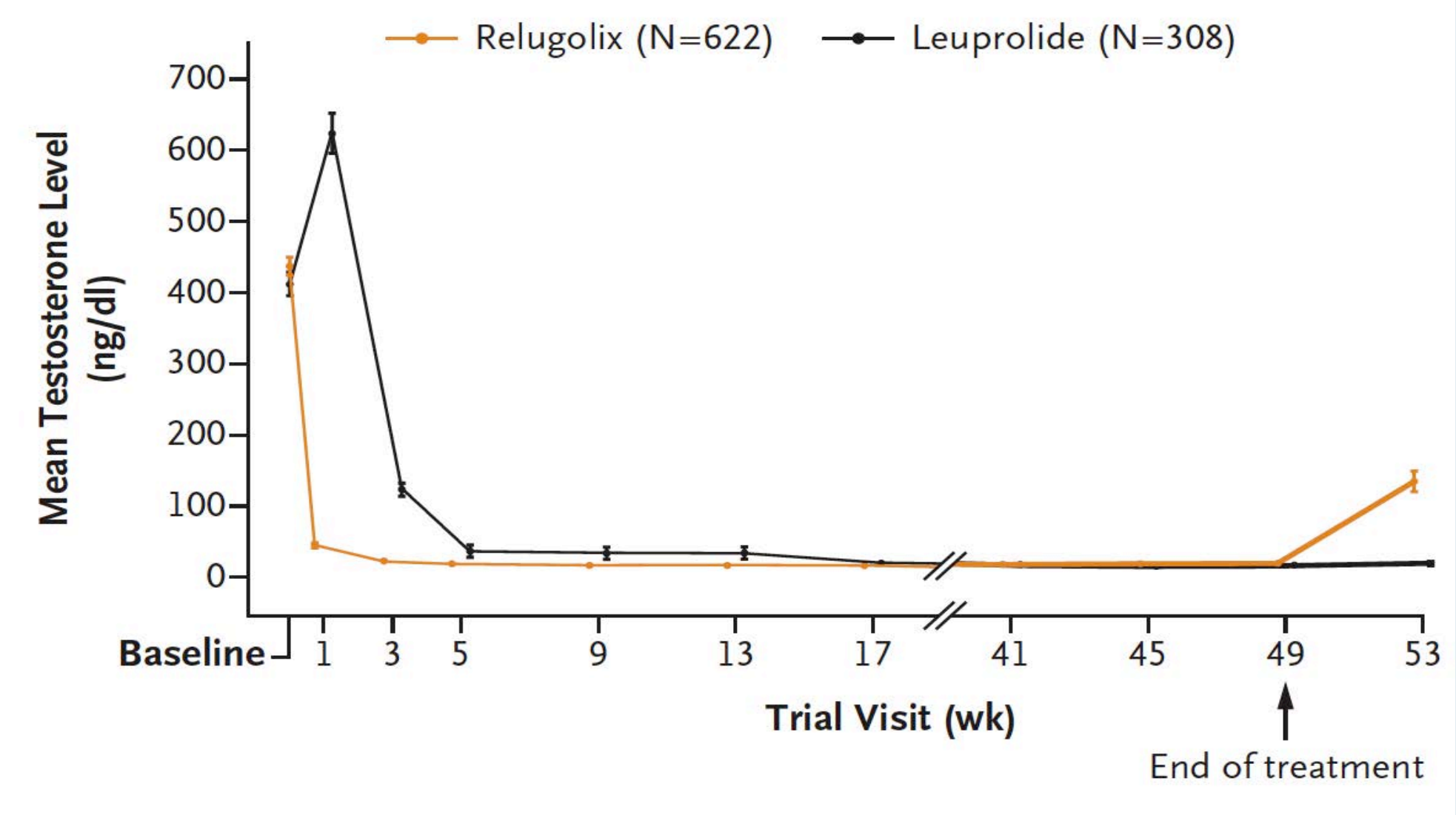
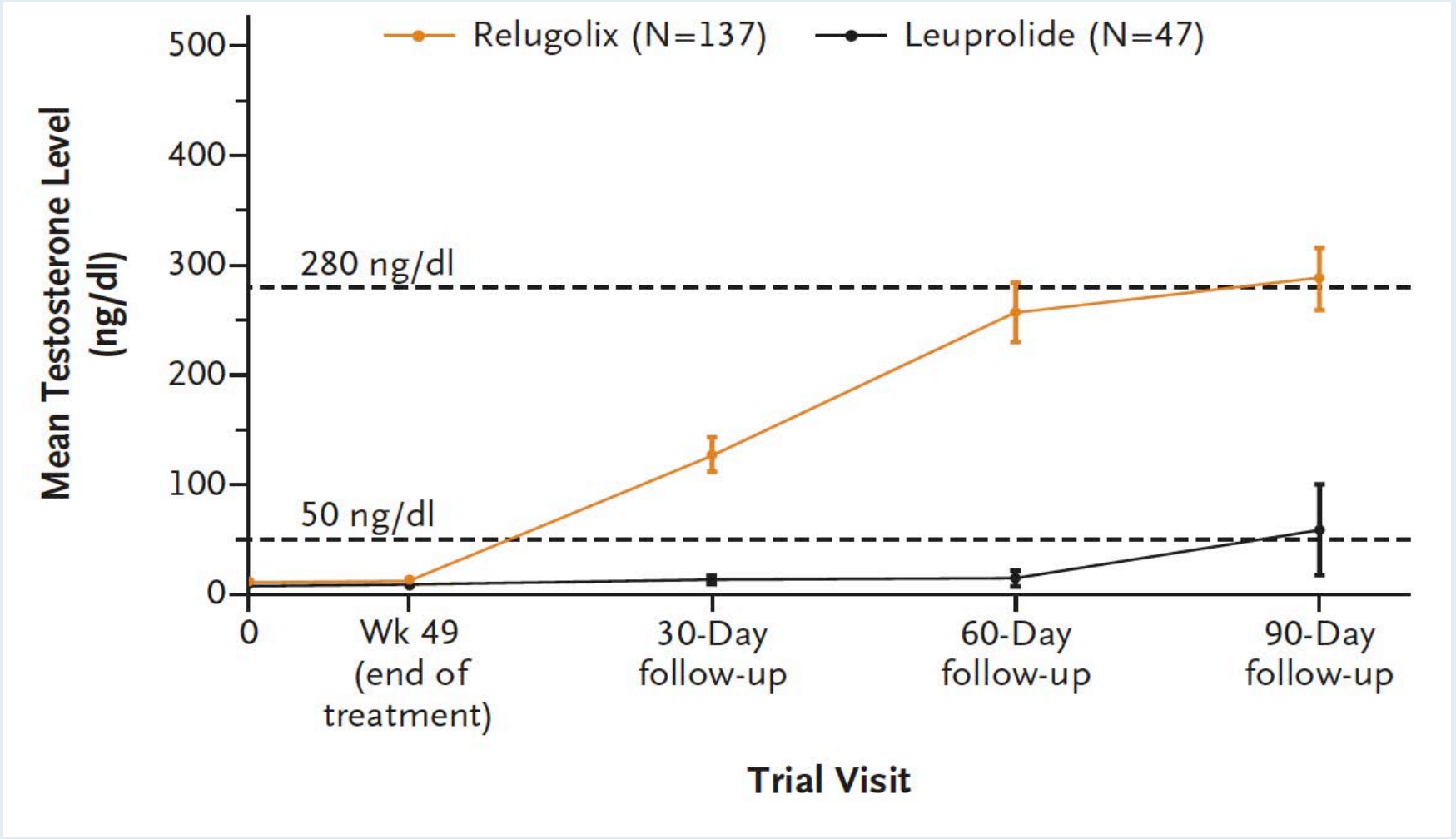
HERO: Mean Testosterone Level among All Patients



Shore ND et al. *N Engl J Med* 2020;382(23):2187-96.

HERO: Mean Testosterone Level in Subgroup Followed for Testosterone Recovery



Shore ND et al. *N Engl J Med* 2020;382(23):2187-96.

HERO: Cardiovascular Adverse Events

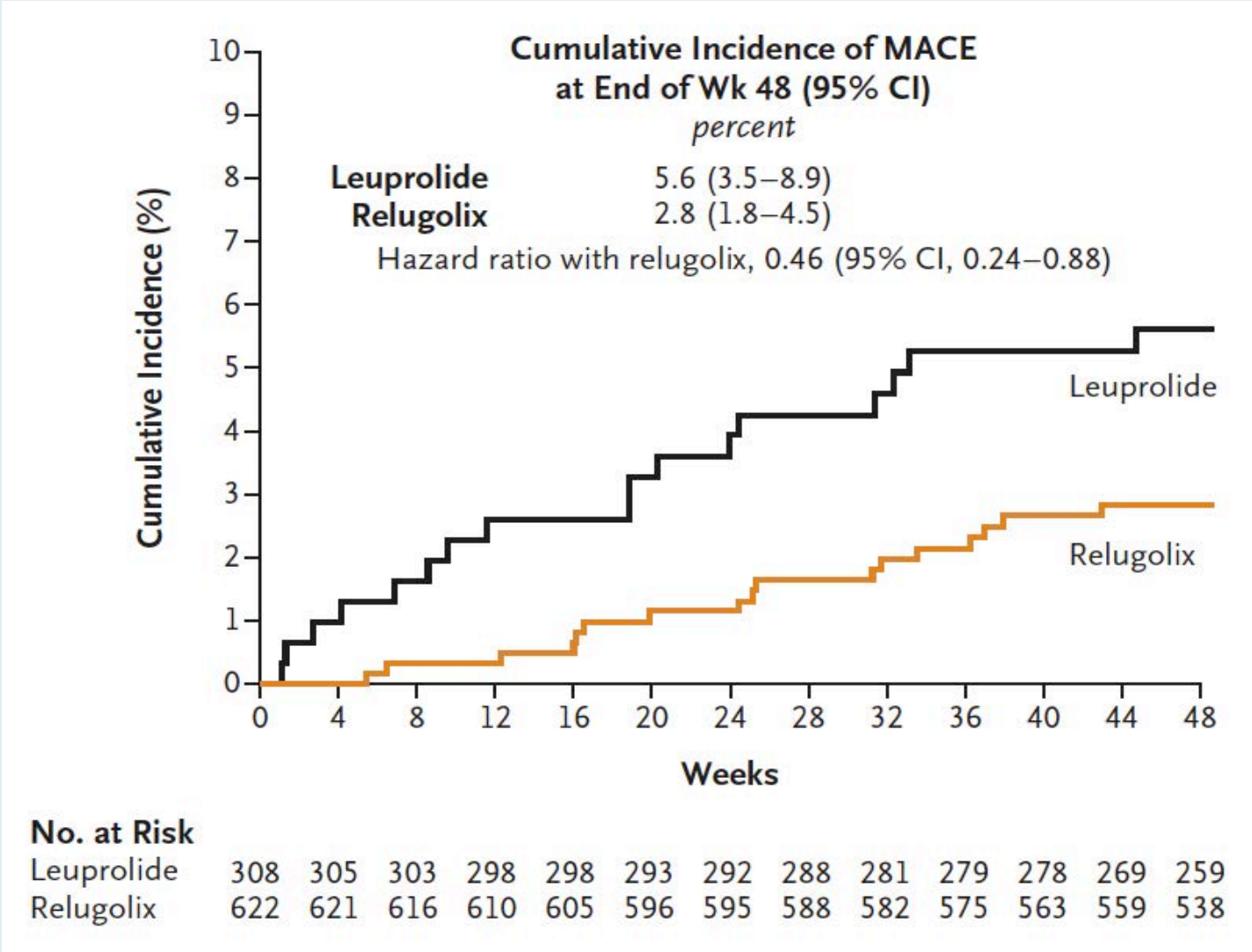
	Relugolix (N = 622)	Leuprolide (N = 308)
Adverse Cardiovascular Events	3.9%	7.1%
Major Adverse Cardiovascular Events (MACE)	2.9%	6.2%
Ischemic Heart Disease	2.4%	1.6%

History of MACE	Yes		No	
N (%)	Relugolix 84 (13.5%)	Leuprolide 45 (14.6%)	Relugolix 538 (86.5%)	Leuprolide 263 (85.4%)
MACE	3.6%	17.8%	2.8%	4.2%
Odds Ratio Leuprolide vs Relugolix (95% confidence interval)	5.8 (1.5, 23.3)		1.5 (0.7, 3.4)	

MACE = non-fatal myocardial infarction + non-fatal stroke + all-cause mortality

Shore N et al. ASCO 2020;Abstract 5602.

HERO: Cumulative Incidence of Major Adverse Cardiovascular Events (MACE)



Shore ND et al. *N Engl J Med* 2020;382(23):2187-96.

Module 3

In the treatment algorithm, when should ADT for PSA-only relapse (M0) after local therapy be recommended?

Discussant: Dr Armstrong

What PSA doubling time will generally lead you to initiate ADT for hormone-naïve M0 prostate cancer?

a. Less than 4 months
b. Less than 6 months
c. Less than 10 months
d. Less than 12 months
e. Less than 18 months
f. Less than 24 months
g. I don’t generally use PSA doubling time as the critical decision factor

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Module 4

In the treatment algorithm, when should an antiandrogen agent be added to ADT for castration-resistant M0 prostate cancer? (Selection of agent)

Discussants: Drs Antonarakis and Armstrong

In general, which is your preferred antiandrogen agent to add to ADT for patients with castration-resistant M0 prostate cancer?

a. I don’t have a preferred antiandrogen agent in this setting
b. Enzalutamide
c. Darolutamide
d. Apalutamide

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Recent FDA Approvals of Next-Generation Antiandrogens in Nonmetastatic Castration-Resistant Prostate Cancer

Agent	Approval date	Pivotal study
Darolutamide	July 30, 2020	ARAMIS
Enzalutamide	July 12, 2018	PROSPER
Apalutamide	February 14, 2018	SPARTAN

https://www.fda.gov/drugs/resources-information-approved-drugs/

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The NEW ENGLAND JOURNAL of MEDICINE

N Engl J Med 2020;383:1040-9.

ORIGINAL ARTICLE

Nonmetastatic, Castration-Resistant Prostate Cancer and Survival with Darolutamide

K. Fizazi, N. Shore, T.L. Tammela, A. Ulys, E. Vjaters, S. Polyakov, M. Jievaltas, M. Luz, B. Alekseev, I. Kuss, M.-A. Le Berre, O. Petrenciuc, A. Snapir, T. Sarapohja, and M.R. Smith, for the ARAMIS Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

N Engl J Med 2020;382(23):2197-206.

ORIGINAL ARTICLE

Enzalutamide and Survival in Nonmetastatic, Castration-Resistant Prostate Cancer

Cora N. Sternberg, M.D., Karim Fizazi, M.D., Ph.D., Fred Saad, M.D., Neal D. Shore, M.D., Ugo De Giorgi, M.D., Ph.D., David F. Penson, M.D., M.P.H., Ubirajara Ferreira, M.D., Ph.D., Eleni Efstathiou, M.D., Ph.D., Katarzyna Madziarska, M.D., Ph.D., Michael P. Kolinsky, M.D., Daniel I. G. Cubero, M.D., Ph.D., Bettina Noerby, M.D., Fabian Zohren, M.D., Ph.D., Xun Lin, Ph.D., Katharina Modelska, M.D., Ph.D., Jennifer Sugg, M.S., Joyce Steinberg, M.D., and Maha Hussain, M.D., for the PROSPER Investigators*

European Association of Urology

Eur J Cancer 2020;[Online ahead of print].

Prostate Cancer

Apalutamide and Overall Survival in Prostate Cancer

Matthew R. Smith[a,], Fred Saad[b], Simon Chowdhury[c], Stéphane Oudard[d], Boris A. Hadaschik[e], Julie N. Graff[f], David Olmos[g], Paul N. Mainwaring[h], Ji Youl Lee[i], Hiroji Uemura[j], Peter De Porre[k], Andressa A. Smith[l], Sabine D. Brookman-May[m,n], Susan Li[l], Ke Zhang[o], Brendan Rooney[p], Angela Lopez-Gitlitz[m], Eric J. Small[q]*

Overall Survival: Darolutamide, Enzalutamide, Apalutamide

	ARAMIS[1]	PROSPER[2]	SPARTAN[3]
Antiandrogen	Darolutamide	Enzalutamide	Apalutamide
Median follow-up	49 mo	47 mo	52 mo
Median OS	Not estimated	57 vs 56 mo	74 vs 60 mo
OS hazard ratio	0.69 (p = 0.003)	0.73 (p = 0.001)	0.78 (p = 0.0161)

[1] Fizazi K et al; ARAMIS Investigators. *N Engl J Med* 2020;383:1040-9.
[2] Sternberg CN et al; PROSPER Investigators. *N Engl J Med* 2020;382(23):2197-206.
[3] Smith MR et al; SPARTAN Investigators. *Eur Urol* 2020;[Online ahead of print].

Comparison of Toxicities: Darolutamide, Enzalutamide, Apalutamide

Toxicity	ARAMIS		PROSPER		SPARTAN	
	Darolutamide	Placebo	Enzalutamide	Placebo	Apalutamide	Placebo
Fatigue/asthenia	16%	11%	33%	14%	30%	21%
Falling	4%	5%	11%	4%	16%	9%
Dizziness	5%	4%	10%	4%	9%	6%
Mental impairment	1%	2%	5%	2%	5%	3%

Sternberg CN et al; PROSPER Investigators. *N Engl J Med* 2020;382(23):2197-206.
Fizazi K et al; ARAMIS Investigators. *N Engl J Med* 2020;383:1040-9.
Small EJ et al; SPARTAN Investigators. ASCO 2020;Abstract 5516.

Module 5

In the treatment algorithm, when do you use prostate-directed local therapy for mHSPC?

Discussant: Dr Antonarakis

Module 6

In the treatment algorithm, when do you add an antiandrogen agent, abiraterone or docetaxel to ADT for mHSPC? (Selection of agent)

Discussants: Drs Antonarakis and Armstrong

What is your most likely treatment approach for a 75-year-old man presenting de novo with prostate cancer with multiple symptomatic bone metastases and 2 lung metastases?

a. ADT alone
b. ADT and enzalutamide
c. ADT and apalutamide
d. ADT and abiraterone
e. ADT and docetaxel
f. ADT with docetaxel and endocrine treatment

Recent FDA Approvals of Next-Generation Antiandrogens in Metastatic Hormone-Sensitive Prostate Cancer

Agent	Approval date	Pivotal study
Enzalutamide	December 16, 2019	ARCHES
Apalutamide	September 17, 2019	TITAN

https://www.fda.gov/drugs/resources-information-approved-drugs/

original report

ARCHES: A Randomized, Phase III Study of Androgen Deprivation Therapy With Enzalutamide or Placebo in Men With Metastatic Hormone-Sensitive Prostate Cancer

Andrew J. Armstrong, MD, ScM[1]; Russell Z. Szmulewitz, MD[2]; Daniel P. Petrylak, MD[3]; Jeffrey Holzbeierlein, MD[4]; Arnauld Villers, MD[5]; Arun Azad, MBBS, PhD[6]; Antonio Alcaraz, MD, PhD[7]; Boris Alekseev, MD[8]; Taro Iguchi, MD, PhD[9]; Neal D. Shore, MD[10]; Brad Rosbrook, MS[11]; Jennifer Sugg, MS[12]; Benoit Baron, MS[13]; Lucy Chen, MD[12]; and Arnulf Stenzl, MD[14]

J Clin Oncol 2019;37(32):2974-86.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 4, 2019 VOL. 381 NO. 1

Apalutamide for Metastatic, Castration-Sensitive Prostate Cancer

Kim N. Chi, M.D., Neeraj Agarwal, M.D., Anders Bjartell, M.D., Byung Ha Chung, M.D., Andrea J. Pereira de Santana Gomes, M.D., Robert Given, M.D., Álvaro Juárez Soto, M.D., Axel S. Merseburger, M.D., Mustafa Özgüroğlu, M.D., Hirotsugu Uemura, M.D., Dingwei Ye, M.D., Kris Deprince, M.D., Vahid Naini, Pharm.D., Jinhui Li, Ph.D., Shinta Cheng, M.D., Margaret K. Yu, M.D., Ke Zhang, Ph.D., Julie S. Larsen, Pharm.D., Sharon McCarthy, B.Pharm., and Simon Chowdhury, M.D., for the TITAN Investigators*

N Engl J Med 2019;381(1):13-24.

RTP RESEARCH TO PRACTICE

Survival Analyses for ARCHES and TITAN: ADT + Enzalutamide or Apalutamide in Metastatic HSPC

	ARCHES (N = 1,150)		TITAN (N = 1,052)	
Characteristics	• 2/3rd high volume • 17% prior docetaxel • 25% prior RP/XRT		• 2/3rd high volume • 10% prior docetaxel • 17% prior RP/XRT	
	ADT + enzalutamide (n = 574)	**ADT (n = 576)**	**ADT + apalutamide (n = 955)**	**ADT (n = 554)**
Radiographic PFS	NR	19.0 mo	NR	22.1 mo
	HR (overall): 0.39 • HR (prior docetaxel): 0.52 • HR (high volume): 0.43 • HR (low volume): 0.25		**HR (overall): 0.48** • HR (prior docetaxel): 0.47 • HR (high volume): 0.53 • HR (low volume): 0.36	
Overall survival	NR	NR	NR	NR
	HR: 0.81 (immature)		**HR (overall): 0.67** • HR (prior docetaxel): 1.27 • HR (high volume): 0.68 • HR (low volume): 0.67	

NR = not reached

Armstrong AJ et al. *J Clin Oncol* 2019;37(32):2974-86. Chi KN et al. *N Engl J Med* 2019;381(1):13-24.

Abiraterone Acetate plus Prednisolone for Hormone-Naïve Prostate Cancer (PCa): Long-Term Results from Metastatic (M1) Patients in the STAMPEDE Randomised Trial (NCT00268476)

James N et al.

ESMO 2020;Abstract 611O.

STAMPEDE — SOC + AAP vs SOC: Overall Survival

HR	0.60
95%CI	0.50 to 0.71
P-value	0.0000000003

Median survival (years)

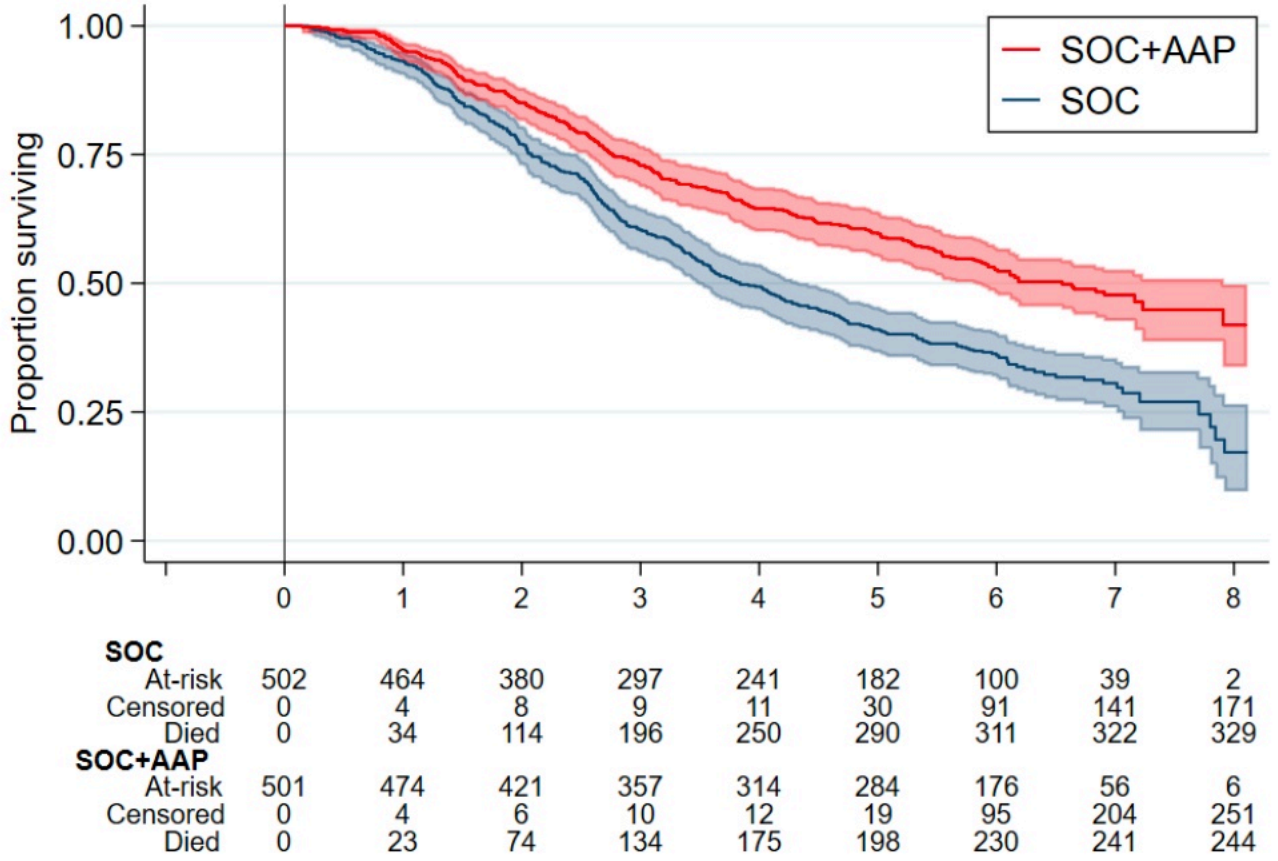
SOC=3.8 SOC+AAP=6.6

Events

SOC=329 SOC+AAP=244

2017 (M1 only)

HR	0.61
95%CI	0.49 to 0.75



James N et al. ESMO 2020;Abstract 611O.

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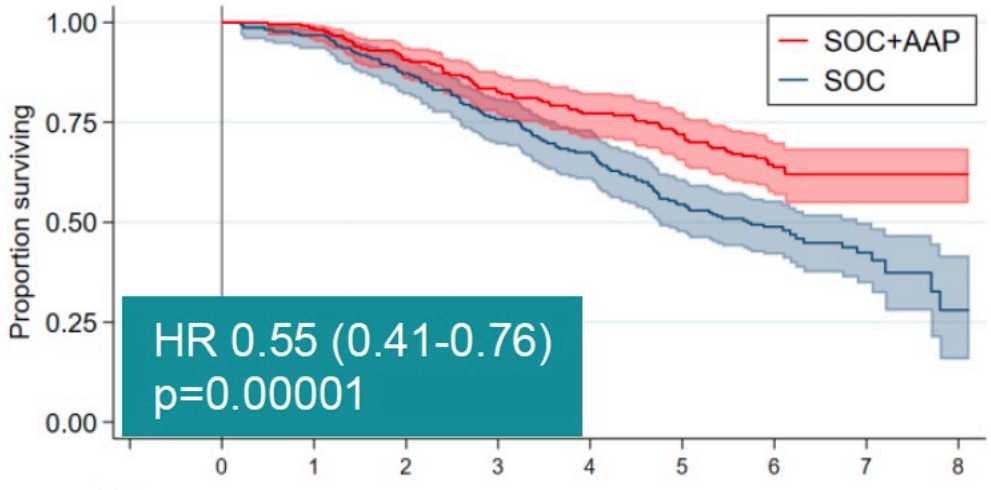
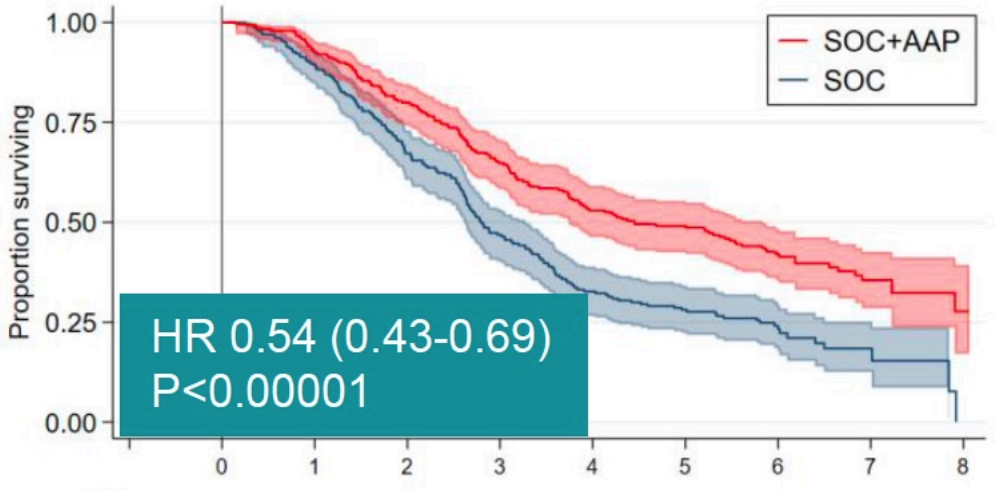
STAMPEDE: Overall Survival by Risk Group (LATITUDE)

Low risk



HR 0.66 (0.44-0.98)
p=0.041

High risk



HR 0.54 (0.41-0.70)
P<0.001

James N et al. ESMO 2020;Abstract 611O.

RTP RESEARCH TO PRACTICE

Module 7

In the treatment algorithm, how do you generally approach the selection of endocrine treatment versus chemotherapy after first-line endocrine therapy for mCRPC?

Discussants: Drs Antonarakis and Armstrong

A 75-year-old man presents with prostate cancer (BRCA wild type) metastatic to the bone and receives ADT + docetaxel with disease progression 1 year later. He responds to enzalutamide for 9 months, then has symptomatic progression in the bone along with new lung lesions. What is your most likely treatment?

a. Abiraterone
b. Apalutamide
c. Docetaxel
d. Cabazitaxel
e. Other

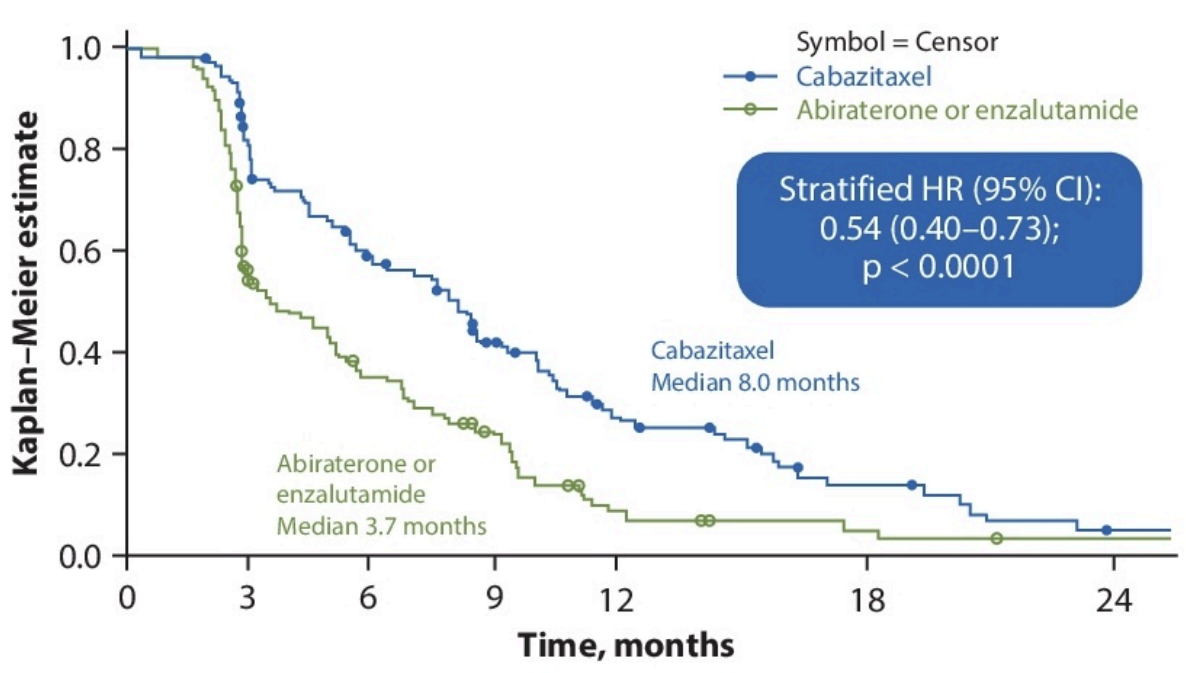
CARD: Overall Survival Analysis of Patients with Metastatic Castration-Resistant Prostate Cancer Receiving Cabazitaxel vs Abiraterone or Enzalutamide

Tombal B et al.

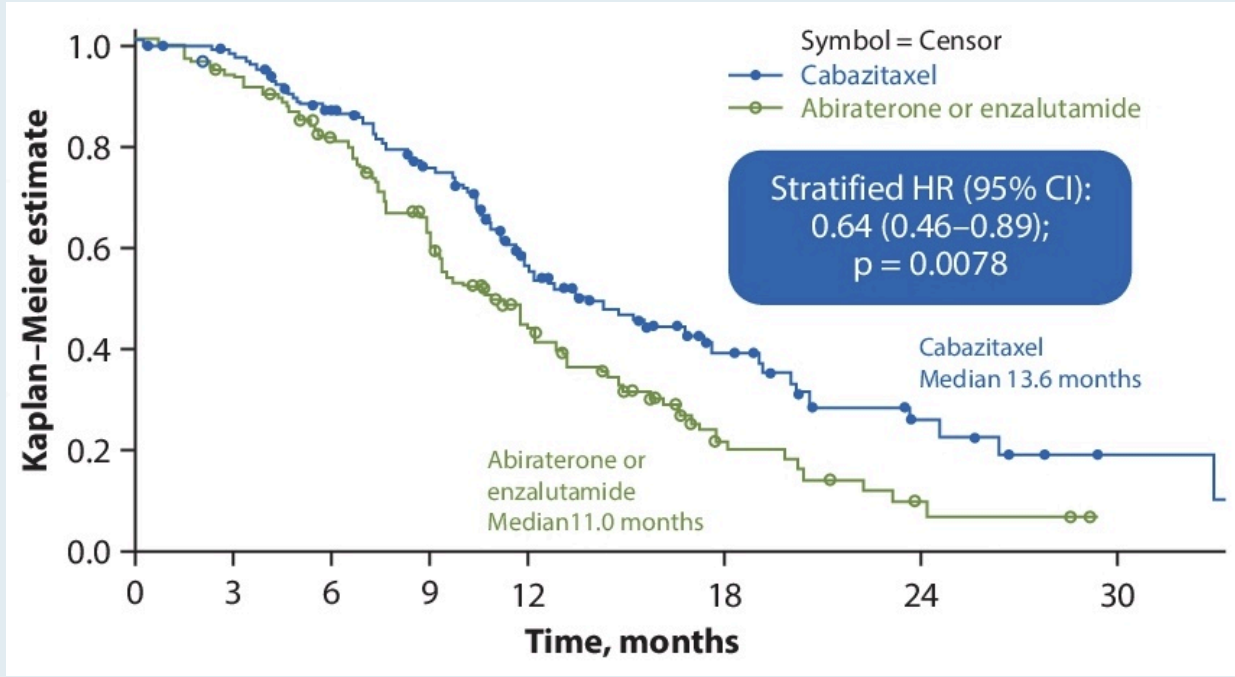
ASCO 2020;Abstract 5569.

CARD Study of Cabazitaxel: Survival Analyses

rPFS (primary endpoint)



OS (key secondary endpoint)



Tombal B et al. ASCO 2020;Abstract 5569.

RTP RESEARCH TO PRACTICE

Module 8

In the treatment algorithm, how do you generally approach the use of radium-223 for mCRPC?

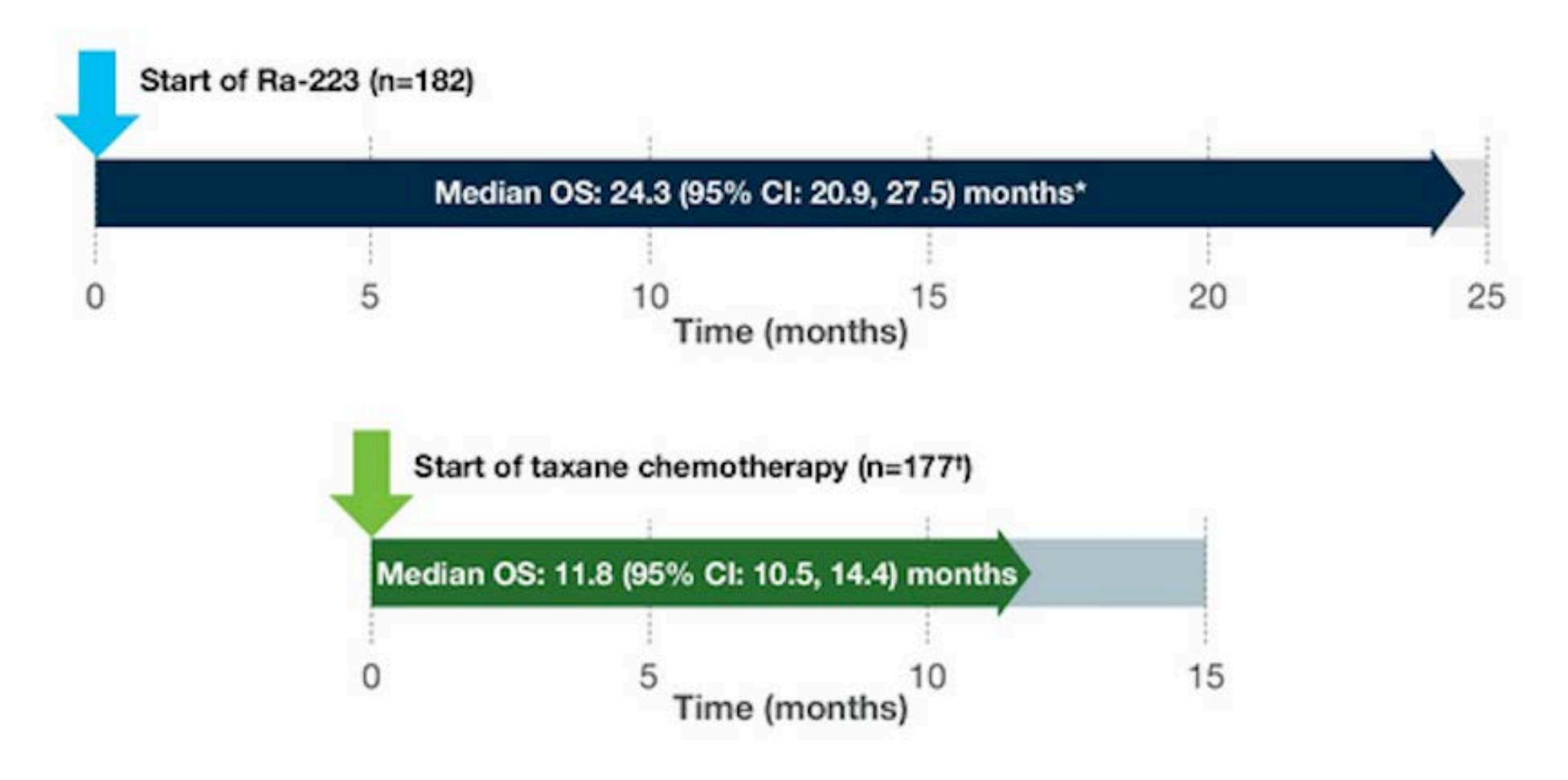
Discussant: Dr Armstrong

Safety and Overall Survival in Patients with mCRPC Treated with Radium-223 plus Subsequent Taxane Therapy: Second Interim Analysis of REASSURE

Higano CS et al.

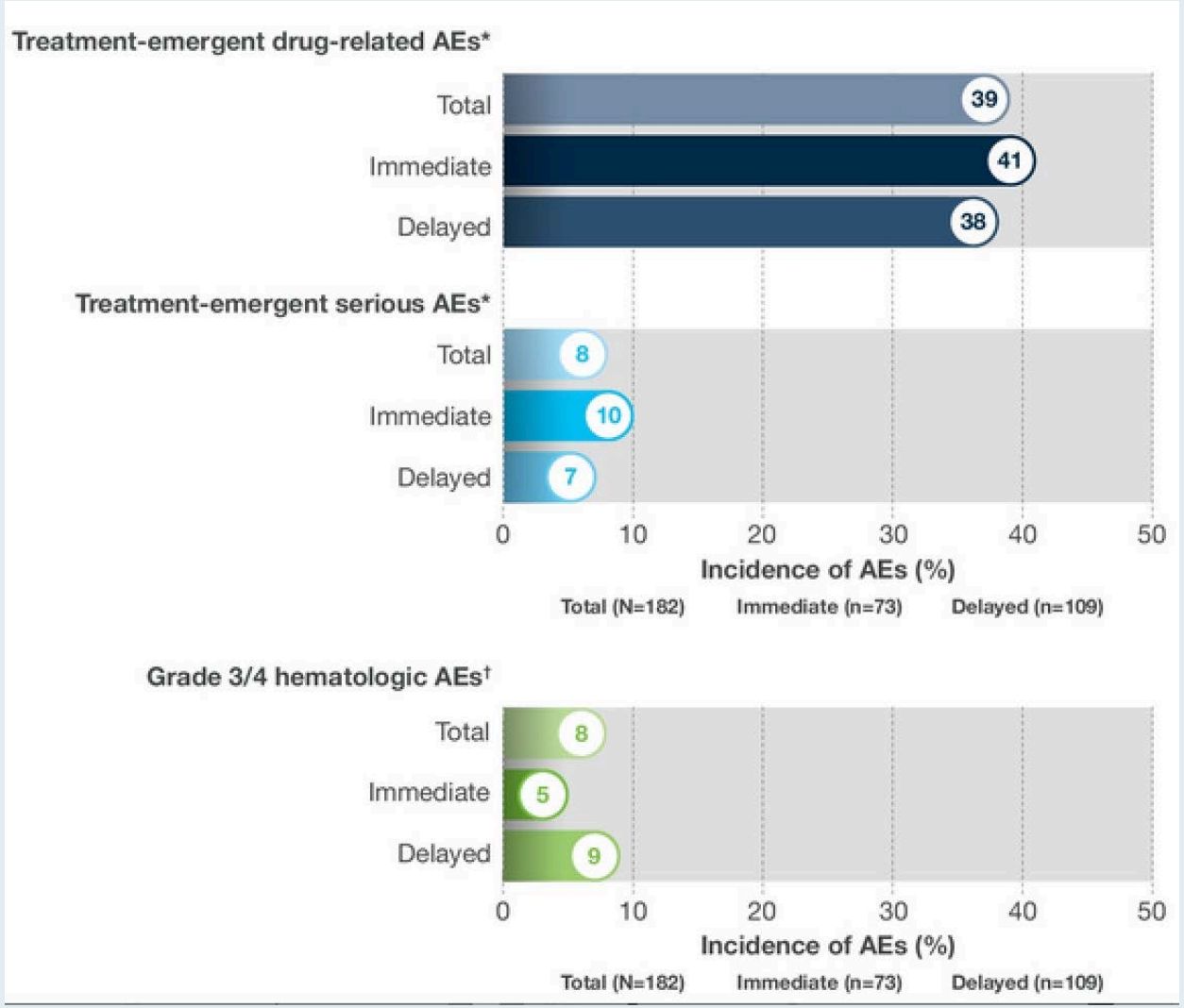
ASCO 2020;Abstract 5542.

REASSURE: Overall Survival



Higano CS et al. ASCO 2020;Abstract 5542.

REASSURE: Incidence of Treatment-Emergent Adverse Events with Radium-223 and Grade 3/4 Hematologic AEs During Subsequent Chemotherapy



Higano CS et al. ASCO 2020;Abstract 5542.

RTP RESEARCH TO PRACTICE

Conclusions: REASSURE

- Clinical Implications:
  - ❑ Radium-223 can be administered safely either before or after docetaxel
  - ❑ If docetaxel is given *after* radium-223, myelosuppression remains minimal
  - ❑ Remember to co-administer with denosumab (fragility fracture risk)
- Future Directions:
  - ❑ What combinations will be synergistic (and safe) with radium-223?
    - radium-223 + enzalutamide (PEACE III)
    - radium-223 + sipuleucel-T
    - radium-223 + PARP/ATR inhibitors
  - ❑ We still need biomarkers (clinical, genomic) of radium-223 sensitivity

Courtesy of Emmanuel S Antonarakis, MD

Module 9

In the treatment algorithm, how do you generally approach the use of PARP inhibitors for mCRPC?

Discussants: Drs Antonarakis and Armstrong

At what point, if any, do you generally recommend a PARP inhibitor to a patient with metastatic prostate cancer and a germline BRCA mutation?

a. As part of first-line treatment, alone or as maintenance therapy
b. After 1 line of hormonal therapy
c. After 1 line of chemotherapy
d. After at least 1 line of both hormonal therapy and chemotherapy
e. Other
f. I generally would not administer a PARP inhibitor

Recent FDA Approvals of PARP Inhibitors for mCRPC

PARP inhibitor	Approval date	Pivotal study
Olaparib	May 19, 2020	PROfound
Rucaparib	May 15, 2020	TRITON2

https://www.fda.gov/drugs/resources-information-approved-drugs/

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

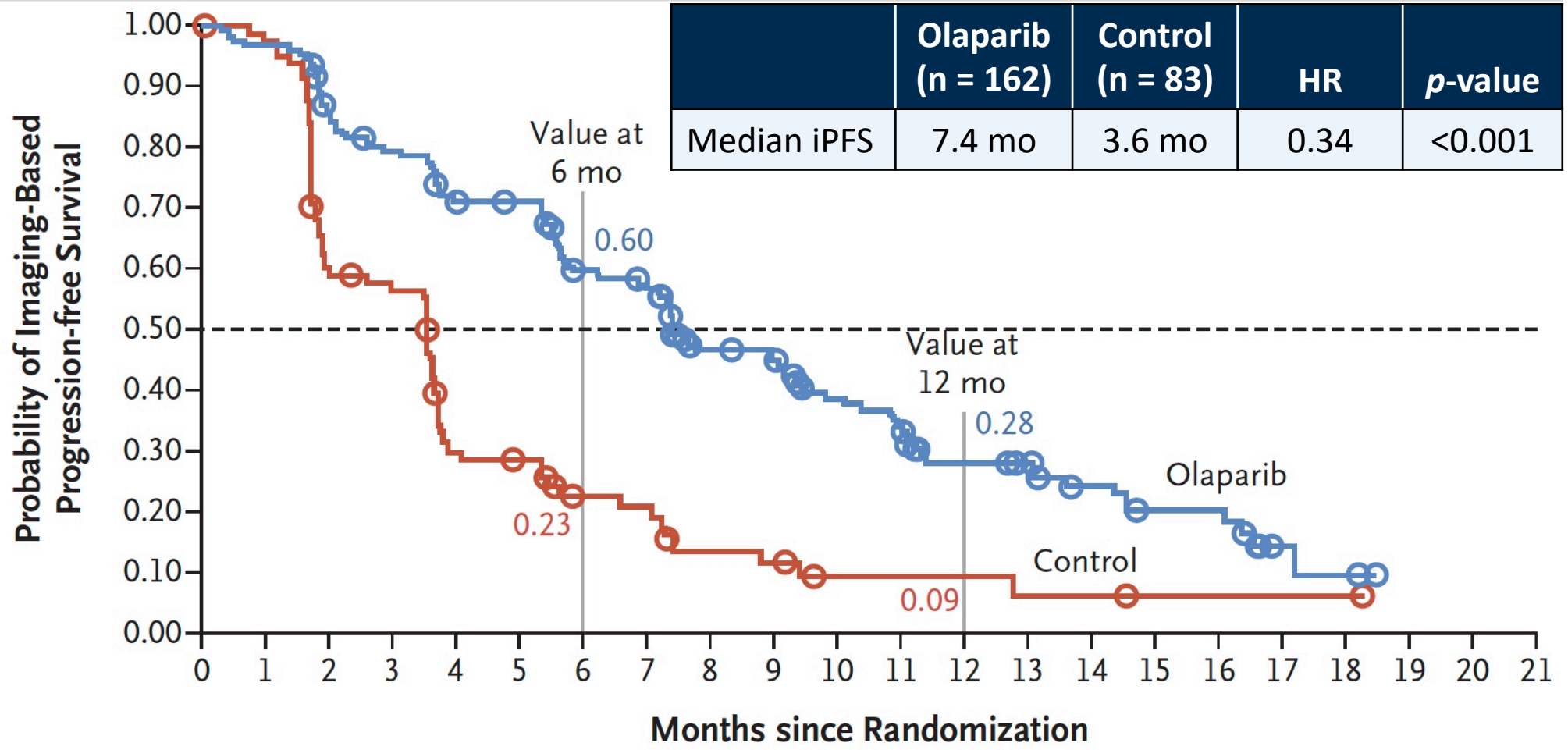
Olaparib for Metastatic Castration-Resistant Prostate Cancer

J. de Bono, J. Mateo, K. Fizazi, F. Saad, N. Shore, S. Sandhu, K.N. Chi, O. Sartor, N. Agarwal, D. Olmos, A. Thiery-Vuillemin, P. Twardowski, N. Mehra, C. Goessl, J. Kang, J. Burgents, W. Wu, A. Kohlmann, C.A. Adelman, and M. Hussain

***N Engl J Med* 2020;382:2091-102.**

PROfound Primary Endpoint: Imaging-Based PFS with Olaparib for Patients with mCRPC Who Had at Least 1 Alteration in BRCA1, BRCA2 or ATM (Cohort A)

	Olaparib (n = 162)	Control (n = 83)	HR	*p*-value
Median iPFS	7.4 mo	3.6 mo	0.34	<0.001



de Bono J et al; PROfound investigators. *N Engl J Med* 2020;382(22):2091-102.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

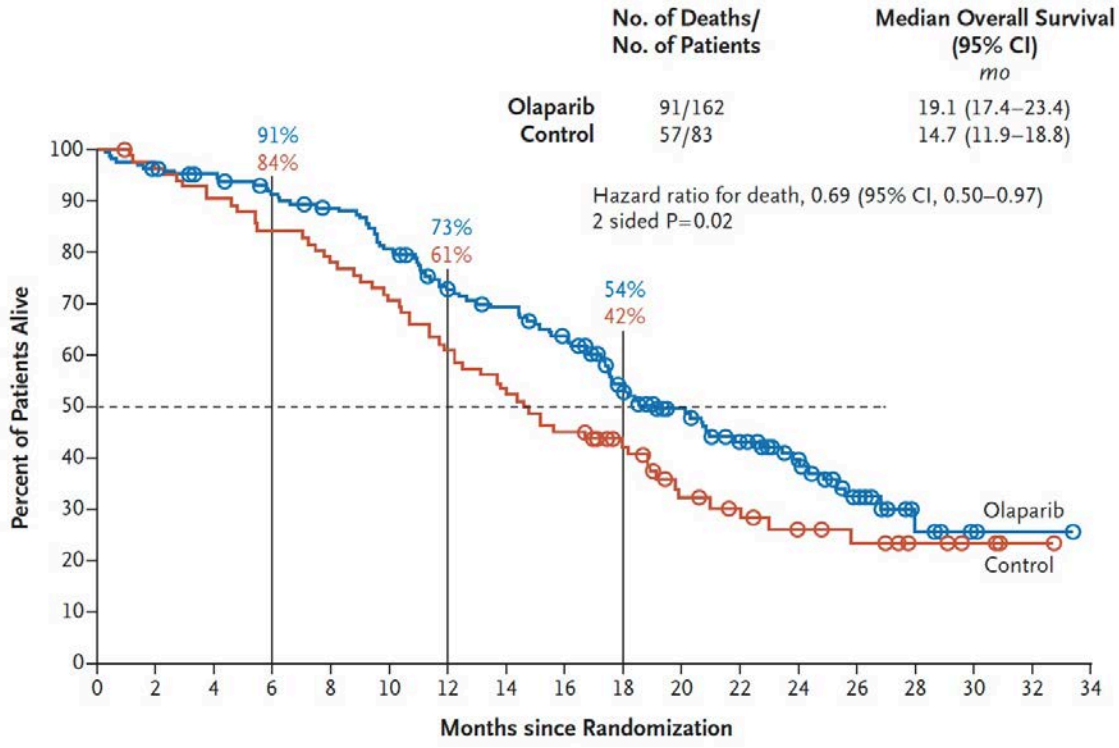
Survival with Olaparib in Metastatic Castration-Resistant Prostate Cancer

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*

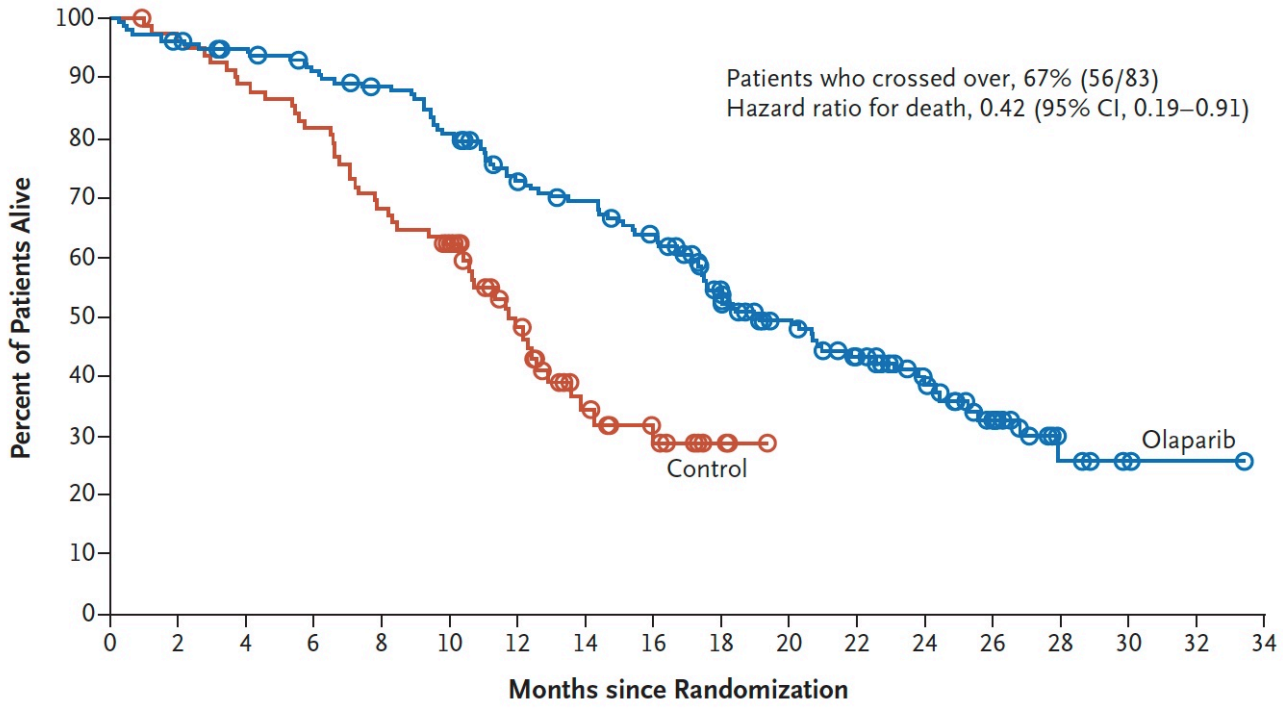
***N Engl J Med* 2020;[Online ahead of print].**

PROfound: Overall Survival with Olaparib for Patients with mCRPC Who Had at Least 1 Alteration in BRCA1, BRCA2 or ATM (Cohort A)

Overall survival



Cross-over adjusted overall survival



Hussain M et al; PROfound investigators. *N Engl J Med* 2020 Sept 20;[Online ahead of print]. De Bono J et al. ESMO 2020;Abstract 610O.

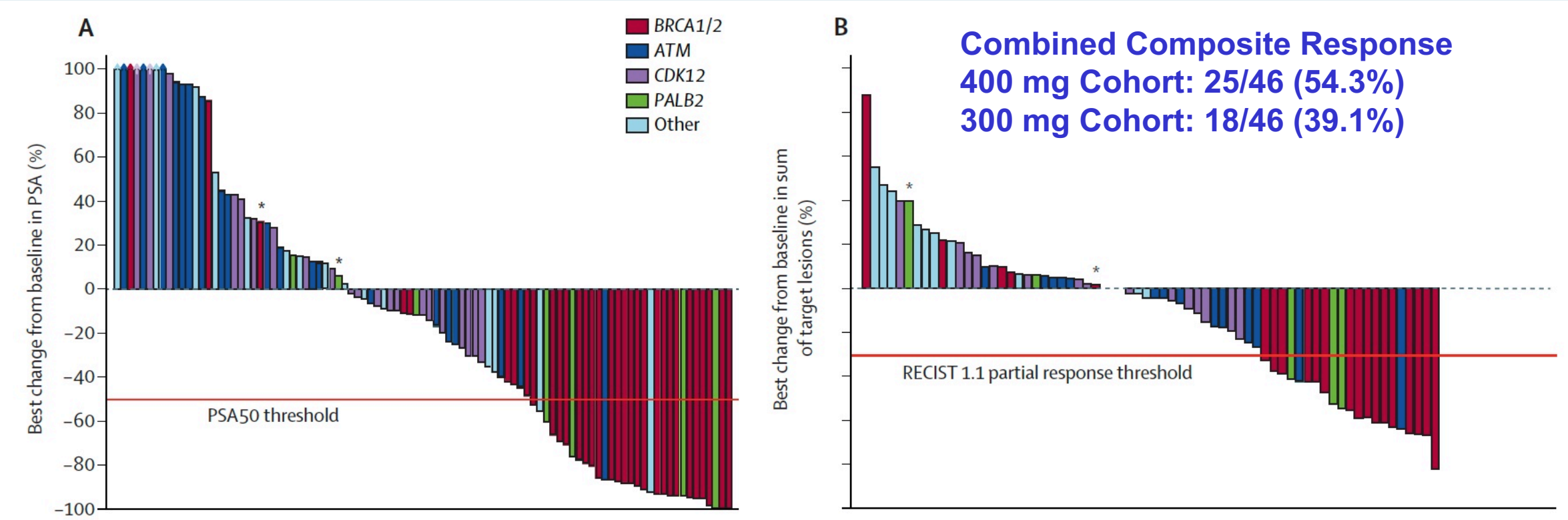
RTP RESEARCH TO PRACTICE

Lancet Oncol 2020;21:162-74.

Olaparib in patients with metastatic castration-resistant prostate cancer with DNA repair gene aberrations (TOPARP-B): a multicentre, open-label, randomised, phase 2 trial

Joaquin Mateo, Nuria Porta*, Diletta Bianchini, Ursula McGovern, Tony Elliott, Robert Jones, Isabel Syndikus, Christy Ralph, Suneil Jain, Mohini Varughese, Omi Parikh, Simon Crabb, Angus Robinson, Duncan McLaren, Alison Birtle, Jacob Tanguay, Susana Miranda, Ines Figueiredo, George Seed, Claudia Bertan, Penny Flohr, Berni Ebbs, Pasquale Rescigno, Gemma Fowler, Ana Ferreira, Ruth Riisnaes, Rita Pereira, Andra Curcean, Robert Chandler, Matthew Clarke, Bora Gurel, Mateus Crespo, Daniel Nava Rodrigues, Shahneen Sandhu, Aude Espinasse, Peter Chatfield, Nina Tunariu, Wei Yuan, Emma Hall†, Suzanne Carreira†, Johann S de Bono†*

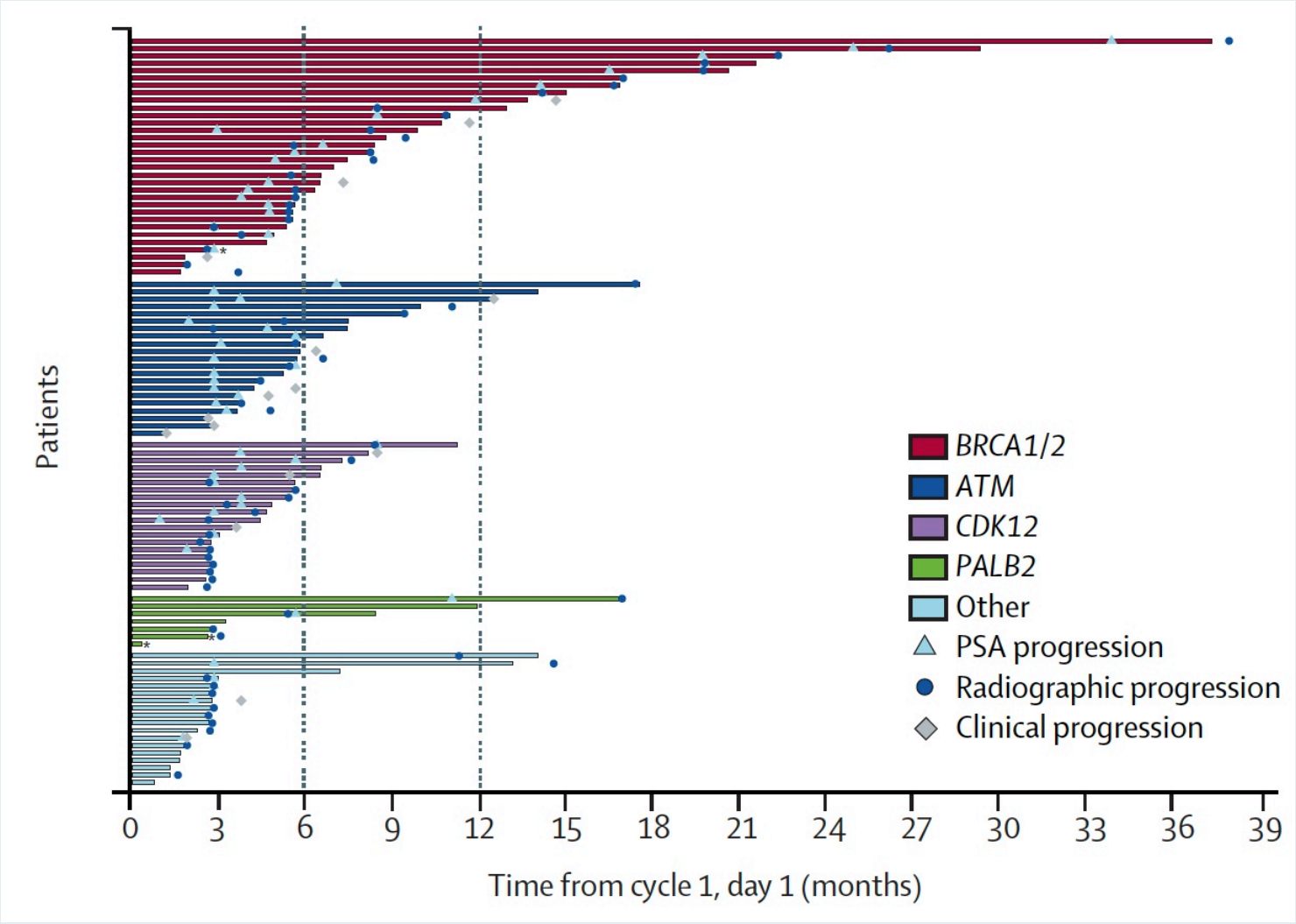
TOPARP-B: Antitumour Activity by Gene Aberration Subgroup (ITT Population, Pooled 300 mg and 400 mg Cohorts)



Mateo J et al. *Lancet Oncol* 2020;21:162-74.

RTP RESEARCH TO PRACTICE

TOPARP-B: Duration of Response by Gene Aberration Subgroup (ITT Population, Pooled 300 mg and 400 mg Cohorts)



Mateo J et al. *Lancet Oncol* 2020;21:162-74.

rapid communications

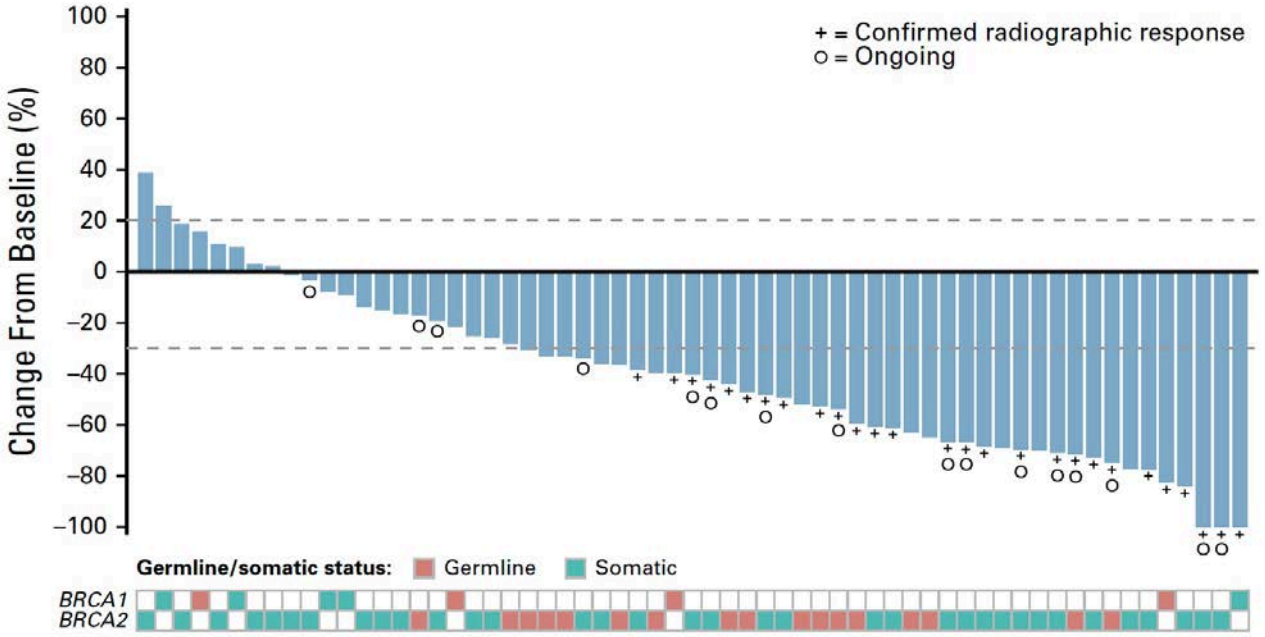
Rucaparib in Men With Metastatic Castration-Resistant Prostate Cancer Harboring a *BRCA1* or *BRCA2* Gene Alteration

Wassim Abida, MD, PhD[1]; Akash Patnaik, MD, PhD, MMSc[2]; David Campbell, MBBS[3]; Jeremy Shapiro, MBBS[4]; Alan H. Bryce, MD[5]; Ray McDermott, MD, PhD, MBA[6]; Brieuc Sautois, MD, PhD[7]; Nicholas J. Vogelzang, MD[8]; Richard M. Bambury, MD[9]; Eric Voog, MD[10]; Jingsong Zhang, MD, PhD[11]; Josep M. Piulats, MD[12]; Charles J. Ryan, MD[13]; Axel S. Merseburger, PhD[14]; Gedske Daugaard, DMSc[15]; Axel Heidenreich, MD[16]; Karim Fizazi, MD, PhD[17]; Celestia S. Higano, MD[18]; Laurence E. Krieger, MBChB[19]; Cora N. Sternberg, MD[20]; Simon P. Watkins, PhD[21]; Darrin Despain, MStat[22]; Andrew D. Simmons, PhD[23]; Andrea Loehr, PhD[23]; Melanie Dowson, BA[24]; Tony Golsorkhi, MD[25]; and Simon Chowdhury, MD, PhD[26,27]; on behalf of the TRITON2 investigators

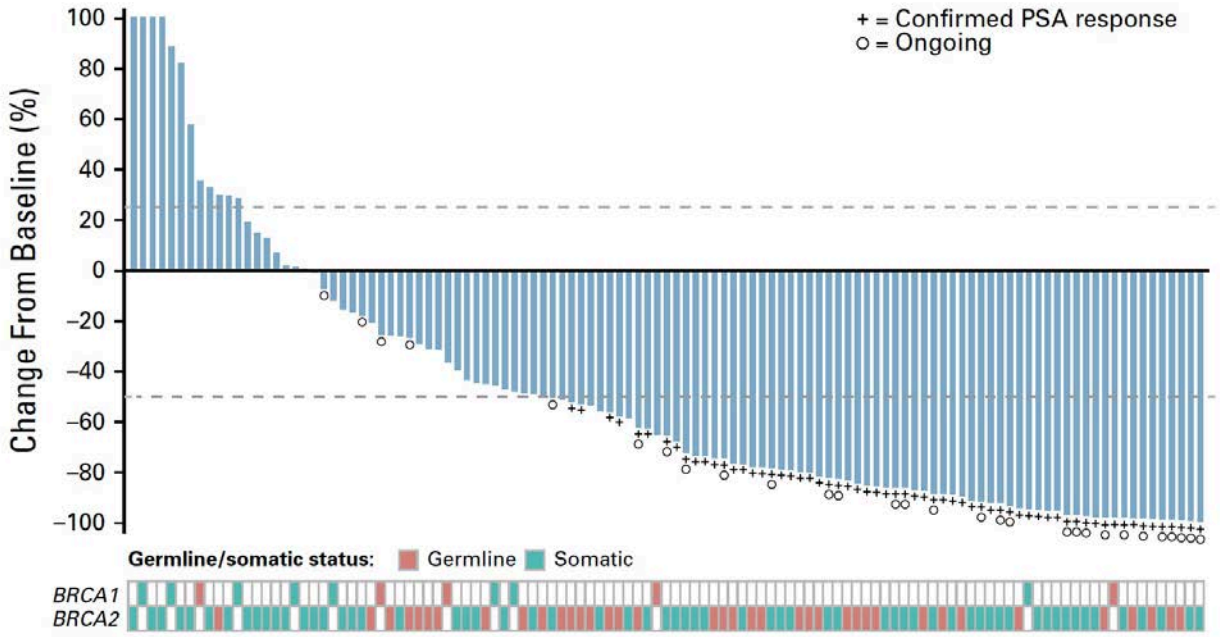
J Clin Oncol 2020;[Online ahead of print].

TRITON2: Response to Rucaparib in Patients with mCRPC Harboring a BRCA1 or BRCA2 Gene Alteration

ORR per independent radiology review: 43.5%



Confirmed PSA response rate: 54.8%



Abida W et al. TRITON2 investigators. *J Clin Oncol* 2020;[Online ahead of print].

RTP RESEARCH TO PRACTICE

Conclusions: TRITON2

- Clinical Implications:
  - ❑ Rucaparib has robust activity in mCRPC pts with *BRCA1/2* mutations
  - ❑ TRITON2 led to accelerated FDA approval of rucaparib in prostate cancer
  - ❑ Side effects: myelosuppression, fatigue, anorexia, rash, teratogenic
- Future Directions:
  - ❑ Initial FDA approval is contingent upon positive Phase III TRITON3 trial
  - ❑ Unlikely to get approved for non-*BRCA* and non-*ATM* mutations
  - ❑ CASPAR trial: rucaparib + enzalutamide for first-line mCRPC
  - ❑ CheckMate 9KD: rucaparib + nivolumab in second-line mCRPC

Courtesy of Emmanuel S Antonarakis, MD

Module 10

What is known about PSMA-targeted treatment and imaging in prostate cancer?

Discussants: Drs Armstrong and Antonarakis

FDA Approves First PSMA-Targeted PET Imaging Drug for Men with Prostate Cancer

Press Release: December 1, 2020

"The U.S. Food and Drug Administration approved Gallium 68 PSMA-11 (Ga 68 PSMA-11) – the first drug for positron emission tomography (PET) imaging of prostate-specific membrane antigen (PSMA) positive lesions in men with prostate cancer.

Ga 68 PSMA-11 is indicated for patients with suspected prostate cancer metastasis (when cancer cells spread from the place where they first formed to another part of the body) who are potentially curable by surgery or radiation therapy. Ga 68 PSMA-11 is also indicated for patients with suspected prostate cancer recurrence based on elevated serum prostate-specific antigen (PSA) levels. Ga 68 PSMA-11 is a radioactive diagnostic agent that is administered in the form of an intravenous injection.

Once administered via injection, Ga 68 PSMA-11 binds to PSMA, which is an important pharmacologic target for prostate cancer imaging because prostate cancer cells usually contain elevated levels of the antigen. As a radioactive drug that emits positrons, Ga 68 PSMA-11 can be imaged by PET to indicate the presence of PSMA-positive prostate cancer lesions in the tissues of the body."

https://www.fda.gov/news-events/press-announcements/fda-approves-first-psma-targeted-pet-imaging-drug-men-prostate-cancer#:~:text=Today%2C%20the%20U.S.%20Food%20and,in%20men%20with%20prostate%20cancer

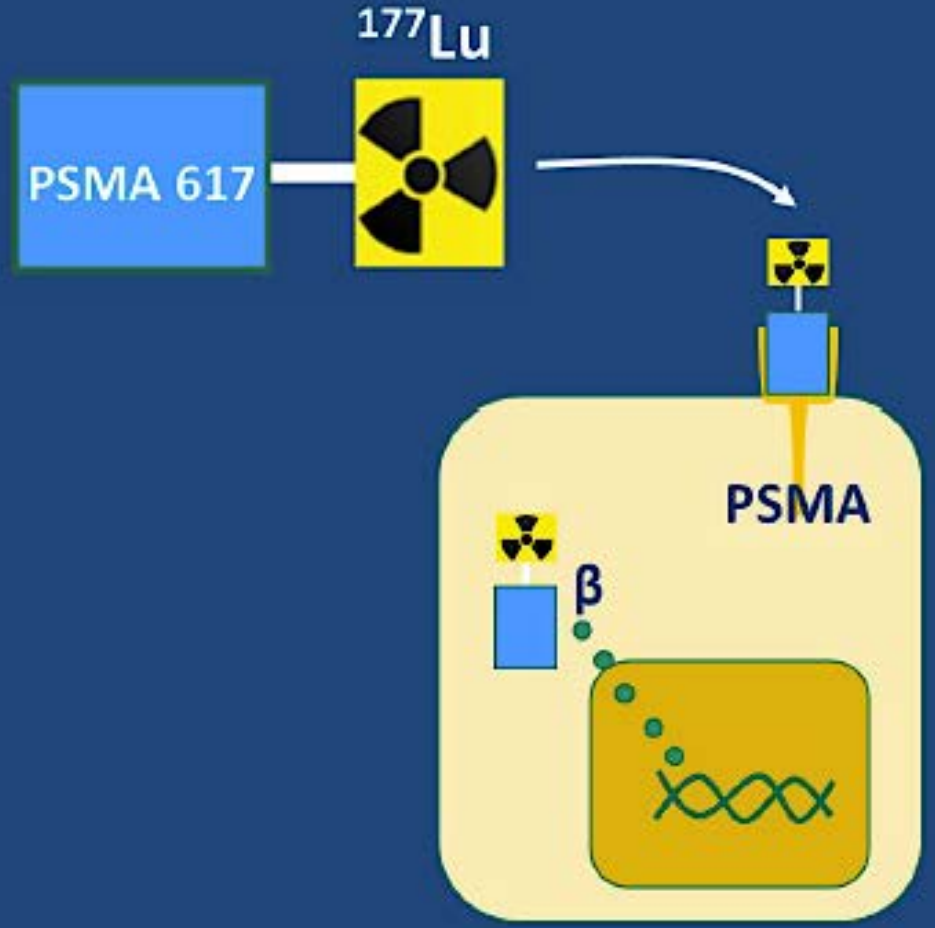
RTP RESEARCH TO PRACTICE

TheraP: A Randomised Phase II Trial of ^{177}Lu-PSMA-617 (LuPSMA) Theranostic versus Cabazitaxel in Metastatic Castration Resistant Prostate Cancer (mCRPC) Progressing After Docetaxel: Initial Results (ANZUP Protocol 1603)

Hoffman S et al.

ASCO 2020;Abstract 5500.

^{177}Lu-PSMA-617 is a small molecule RLT targeting PSMA



Hoffman S et al. ASCO 2020;Abstract 5500.

TheraP: ^{177}Lu-PSMA-617 Theranostic versus Cabazitaxel

KEY ELIGIBILITY

- mCRPC post docetaxel suitable for cabazitaxel
- Progressive disease with rising PSA and PSA ≥ 20 ng/mL
- Adequate renal, haematologic and liver function
- ECOG performance status 0-2

↓

^{68}Ga-PSMA + ^{18}F-FDG PET/CT

- PSMA SUVmax > 20 at any site
- Measurable sites SUVmax > 10
- No FDG positive/PSMA negative sites of disease
- Centrally reviewed

R

^{177}Lu-PSMA-617

8.5 GBq IV q6 weekly
↓ 0.5GBq each cycle
Up to 6 cycles

→ **SPECT/CT @ 24 hours**

suspend Rx if exceptional response; recommence upon progression

200 men 1:1 randomisation
11 sites in Australia

Stratified by:

- Disease burden (>20 sites vs ≤ 20 sites)
- Prior enzalutamide or abiraterone
- Study site

CABAZITAXEL

20mg/m^2 IV q3 weekly,
Up to 10 cycles

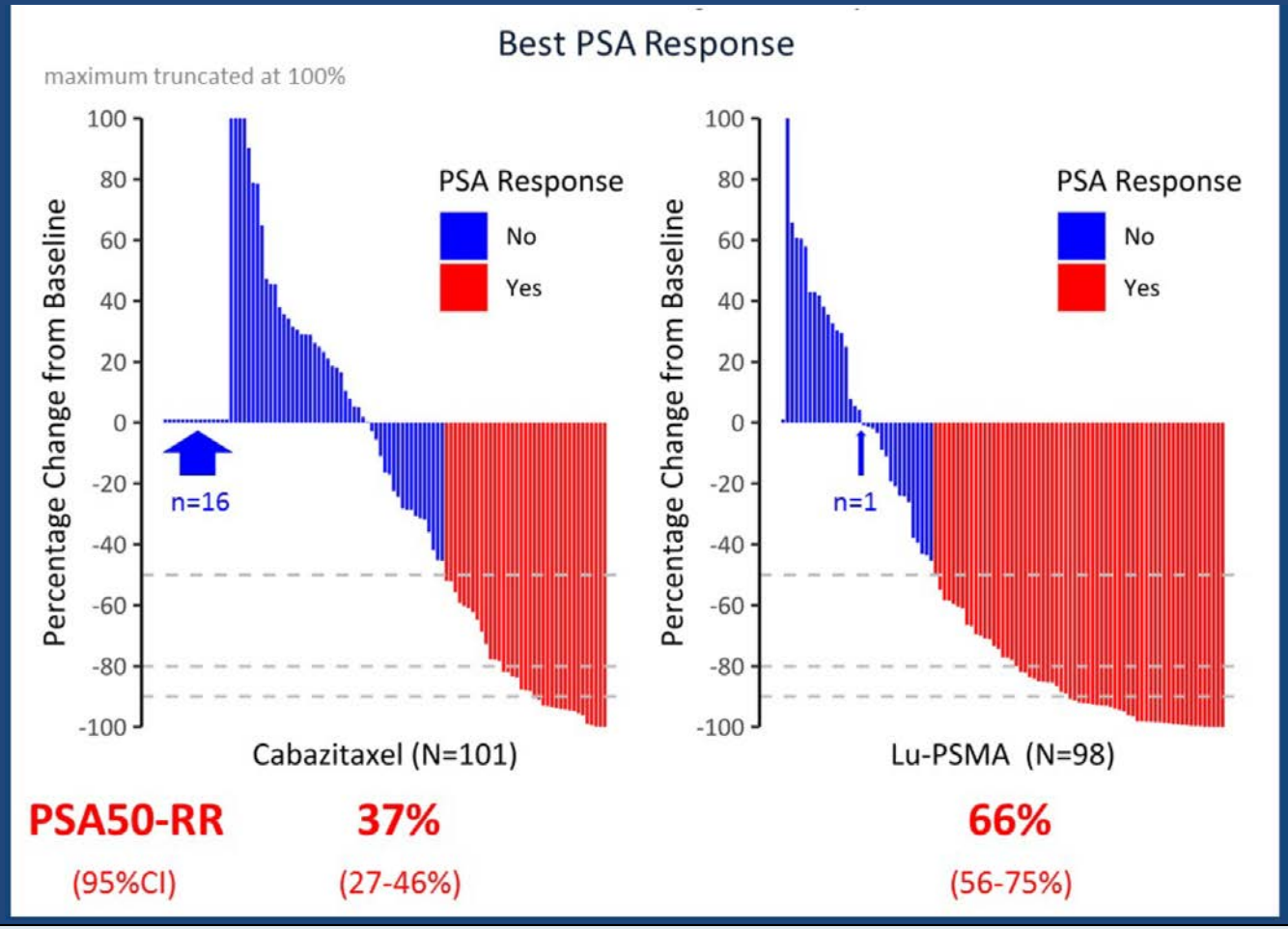
80% power to detect a true absolute difference of 20% in the PSA response rate (from 40% to 60%), with a 2-sided type 1 error of 5% and allowance of 3% for missing data.

Hoffman S et al. ASCO 2020;Abstract 5500.

RTP RESEARCH TO PRACTICE

TheraP: Primary Endpoint — PSA Response ≥50% (PSA50-RR)

Primary endpoint: PSA ≥50% response (PSA50-RR)



Lu-PSMA: 29% absolute (95% CI 16%-42%, p<0.0001) greater PSA50-RR compared to cabazitaxel

For sensitivity analysis per-protocol, the difference was 23% (95% CI 9%-37%; p=0.0016)

Hoffman S et al. ASCO 2020;Abstract 5500.

RTP RESEARCH TO PRACTICE

Module 11

What is known about TMPRSS2 and COVID-19?

Discussant: Dr Antonarakis

Compared to women, men…

a. Are more likely to contract COVID-19

b. Are more likely to contract COVID-19 and develop complications

c. Are not more likely to contract COVID-19 but are more likely to develop complications if they do contract COVID-19

d. There are currently not enough data

e. I don’t know

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RESEARCH
TO PRACTICE

IN FOCUS

TMPRSS2 and COVID-19: Serendipity or Opportunity for Intervention?

Konrad H. Stopsack[1], Lorelei A. Mucci[2], Emmanuel S. Antonarakis[3], Peter S. Nelson[4], and Philip W. Kantoff[1]

Summary: *TMPRSS2* is both the most frequently altered gene in primary prostate cancer and a critical factor enabling cellular infection by coronaviruses, including SARS-CoV-2. The modulation of its expression by sex steroids could contribute to the male predominance of severe infections, and given that *TMPRSS2* has no known indispensable functions, and inhibitors are available, it is an appealing target for prevention or treatment of respiratory viral infections.

Cancer Discov 2020;10(6):779-82.

Meet The Professor
Management of Lung Cancer

Wednesday, December 2, 2020
12:00 PM – 1:00 PM ET

Faculty

Ramaswamy Govindan, MD

Moderator

Neil Love, MD

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Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.

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