Fall Oncology Nursing Series

A Complimentary NCPD-Accredited Virtual Curriculum

Prostate Cancer

Thursday, September 2, 2021
5:00 PM – 6:00 PM ET

Faculty

Mary-Ellen Taplin, MD
Kathy D Burns, RN, MSN, AGACNP-BC, OCN

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Faculty

Mary-Ellen Taplin, MD
Professor of Medicine
Harvard School of Medicine
Dana-Farber Cancer Institute
Boston, Massachusetts

Moderator
Neil Love, MD
Research To Practice
Miami, Florida

Kathy D Burns, RN, MSN, AGACNP-BC, OCN
GU Medical Oncology
City of Hope Comprehensive Cancer Center
Duarte, California

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Commercial Support

This activity is supported by educational grants from Astellas and Pfizer Inc, AstraZeneca Pharmaceuticals LP, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, and Merck.

Dr Love — Disclosures

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Dr Taplin — Disclosures

No relevant conflicts of interest to disclose

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Ms Burns — Disclosures

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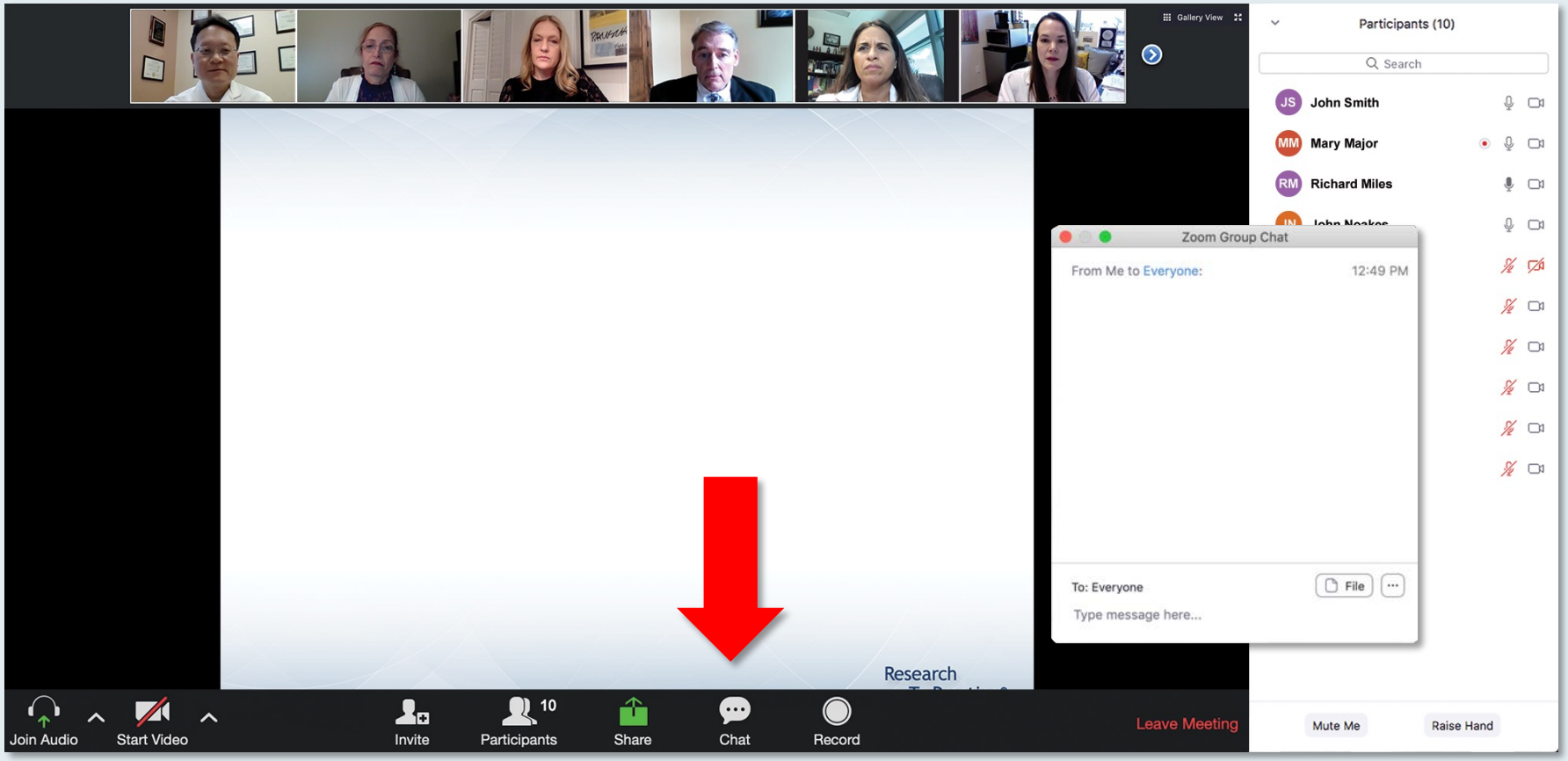

Feel free to submit questions now before the program begins and throughout the program.

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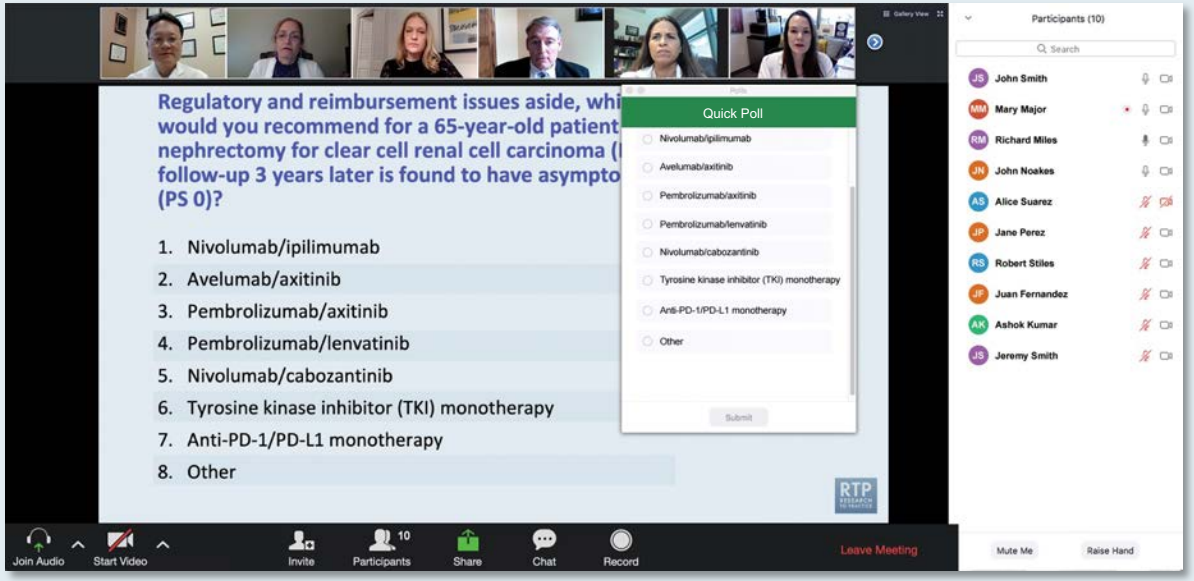
How to answer survey or poll questions



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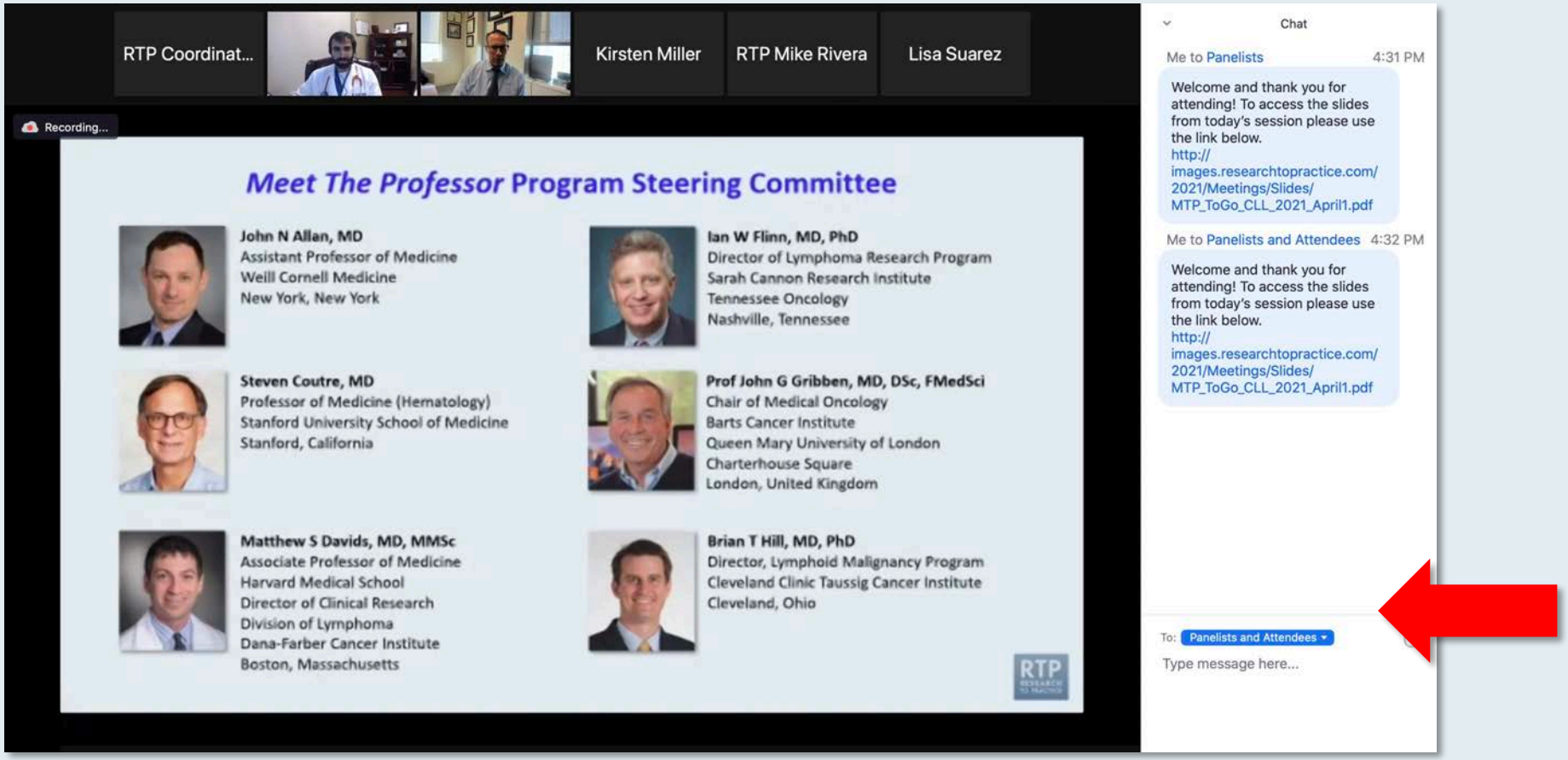
Expand chat submission box



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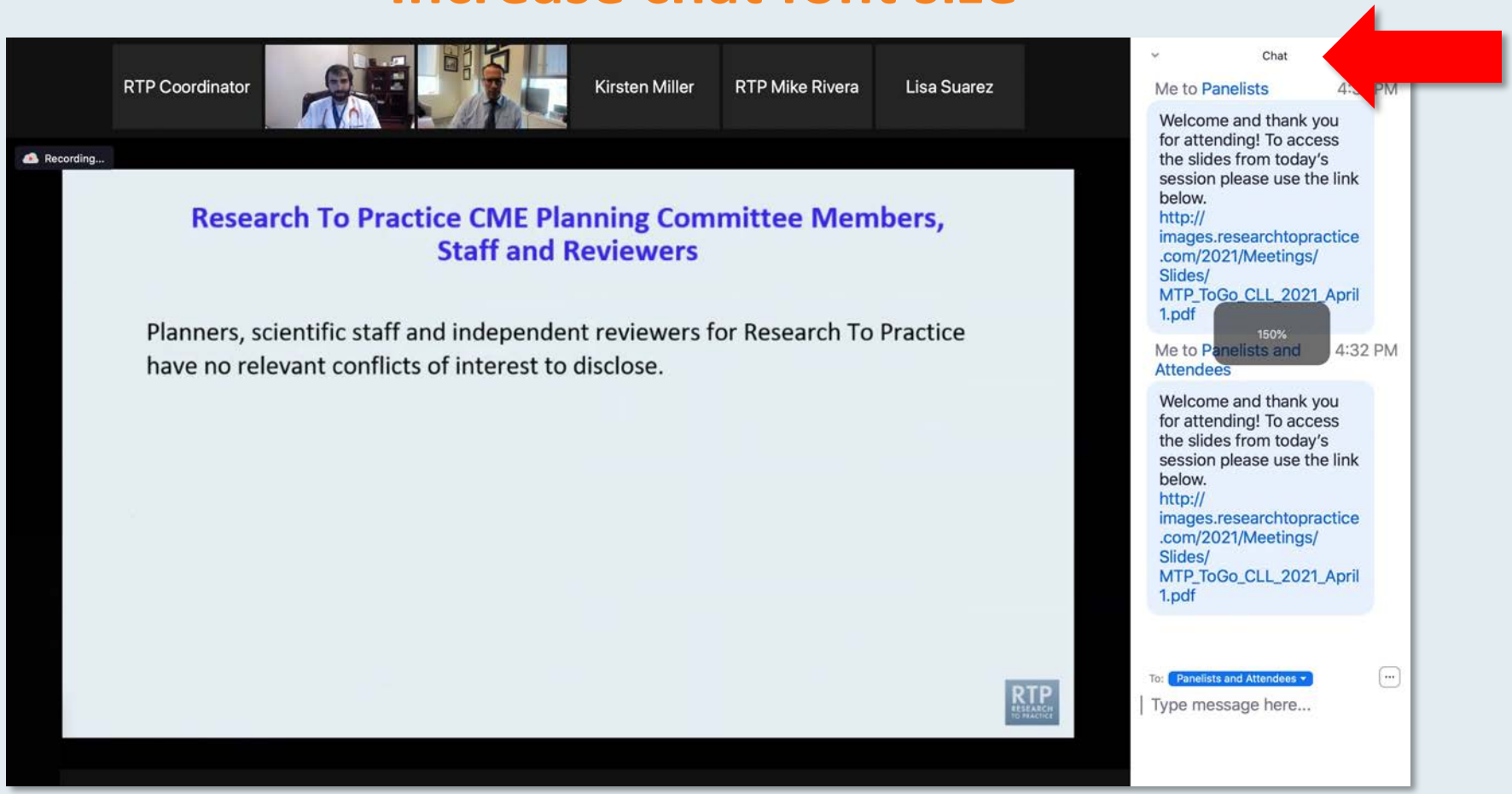
Familiarizing Yourself with the Zoom Interface

Increase chat font size



Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.

ONCOLOGY TODAY

WITH DR NEIL LOVE

Side Effects of Hormonal Therapy in Prostate Cancer

DR ROBERTO IACOVELLI

FONDAZIONE POLICLINICO UNIVERSITARIO A GEMELLI

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Data + Perspectives: Clinical Investigators Discuss the Current and Future Management of Acute Myeloid Leukemia and Myelodysplastic Syndromes

A Virtual CME Satellite Symposium During the Society of Hematologic Oncology 2021 Annual Meeting

Wednesday, September 8, 2021
7:30 PM – 9:00 PM Central Time

Faculty

Courtney D DiNardo, MD, MSCE
Daniel A Pollyea, MD, MS
David Sallman, MD
Eunice S Wang, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Exploring Key Issues Affecting the Care of Patients with Metastatic Colorectal Cancer with BRAF Mutations

A CME/MOC-Accredited Virtual Event

Thursday, September 9, 2021
5:00 PM – 6:00 PM ET

Faculty
Scott Kopetz, MD, PhD

Consulting Clinical Investigator
Wells A Messersmith, MD

Moderator
Neil Love, MD

RTP RESEARCH TO PRACTICE

Expert Second Opinion: Investigators Discuss Available Clinical Research in the Care of Patients with Early-Stage Non-Small Cell Lung Cancer

A Live Webinar Held as a Satellite CME/MOC Symposium During the IASLC 2021 World Conference on Lung Cancer Worldwide Virtual Event

Sunday, September 12, 2021
9:15 PM – 10:15 PM MDT / 11:15 PM – 12:15 AM ET

Faculty

Edward B Garon, MD, MS
Harvey I Pass, MD
Heather Wakelee, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

What Urologists Want To Know: Addressing Current Questions and Controversies in the Management of Bladder Cancer

A Virtual CME Satellite Symposium During the American Urological Association (AUA) 2021 Annual Meeting

Monday, September 13, 2021
11:00 AM – 12:30 PM ET / 8:00 AM – 9:30 AM PT

Faculty

Arjun Balar, MD
Ashish M Kamat, MD, MBBS
Guru Sonpavde, MD

Moderator

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RTP RESEARCH TO PRACTICE

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A Oliver Sartor, MD
Neal D Shore, MD

Additional faculty to be announced

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Meet The Professor

Optimizing the Clinical Management of Hodgkin and Non-Hodgkin Lymphomas

Thursday, September 16, 2021
5:00 PM – 6:00 PM ET

Faculty

Loretta J Nastoupil, MD

Moderator

Neil Love, MD

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Thank you for joining us!

NCPD credit information will be emailed to each participant shortly.

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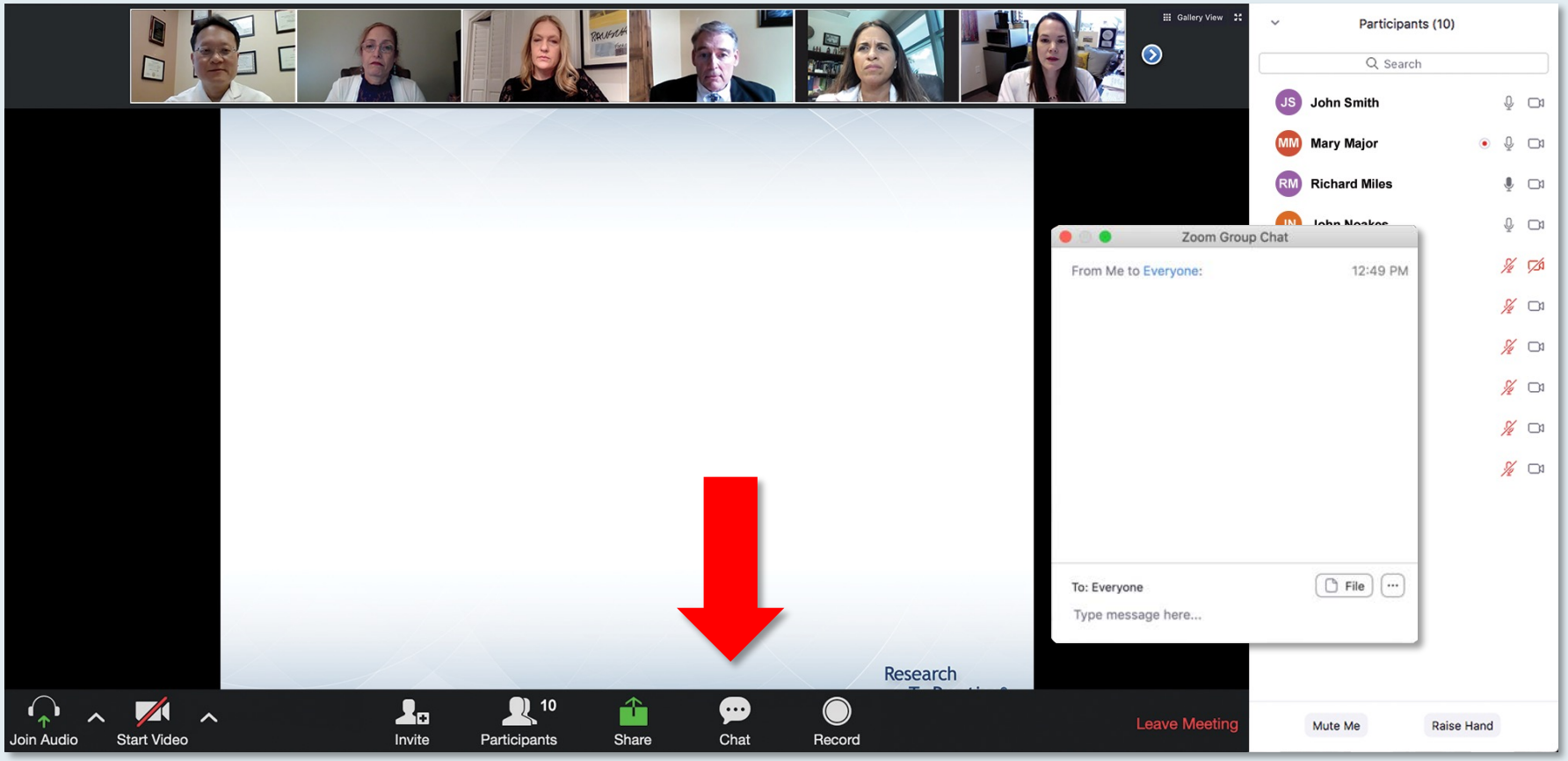

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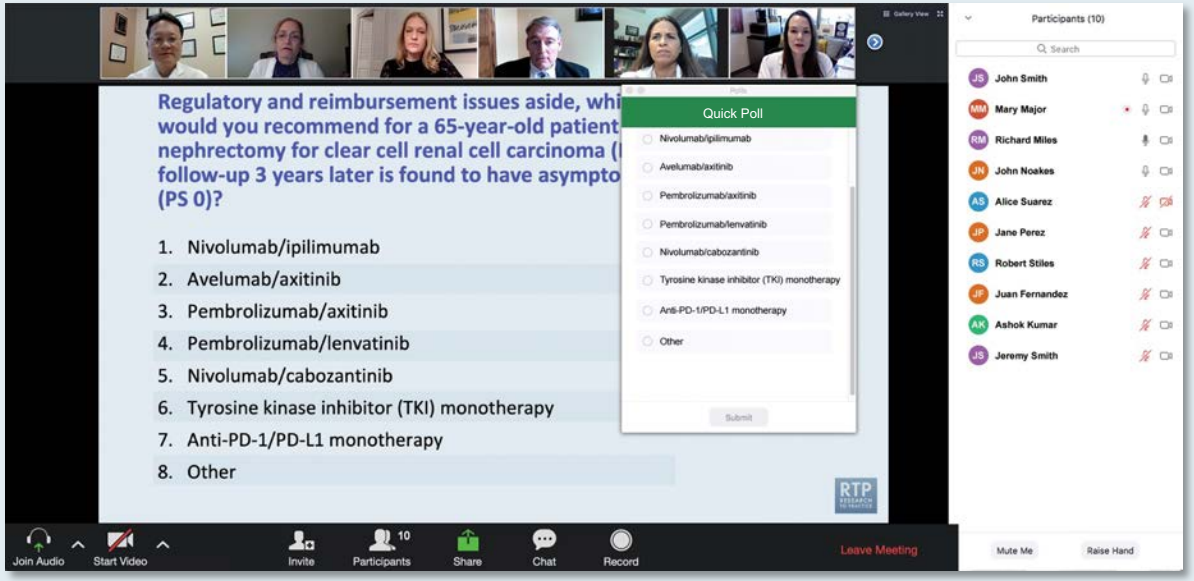

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Oncology Grand Rounds Nursing Webinar Series

April 2021

Monday	Tuesday	Wednesday	Thursday	Friday
19	20 Breast Ca 8:30 AM --- Lung Ca 5:00 PM	21 AML 12:00 PM --- CRC and GE Ca 4:45 PM	22 Prostate Ca 8:30 AM --- Lymphomas 5:00 PM	23
26	27 Multiple Myeloma 8:30 AM --- GYN 5:00 PM	28 Bladder Ca 12:00 PM	29 CLL 8:30 AM --- CAR-T 5:00 PM	30

RTP RESEARCH TO PRACTICE

13th Annual Oncology Grand Rounds

A Complimentary NCPD Live Webinar Series
Held During the 46th Annual ONS Congress

Prostate Cancer

Thursday, April 22, 2021
8:30 AM – 10:00 AM ET

Medical Oncologists

Charles J Ryan, MD
A Oliver Sartor, MD
Mary-Ellen Taplin, MD

Oncology Nurse Practitioners

Kathy D Burns, RN, MSN, AGACNP-BC, OCN
Brenda Martone, MSN, NP-BC, AOCNP
Ronald Stein, JD, MSN, NP-C, AOCNP

Moderator

Neil Love, MD

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Kathleen Burns, NP


Brenda Martone MSN NP-BC AOCNP


Ronald Stein, JD, MSN, NP-C, AOCNP

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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Research To Practice Education Platform

Oncology Nurse Practitioners

Case Presentations

- Key patient-education issues
- Biopsychosocial considerations:
  - Family/loved ones
  - The bond that heals

Clinical Investigators

Oncology Strategy

- New agents and regimens
- Predictive biomarkers
- Ongoing research and implications

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Agenda

Prologue: What are some of the unique psychosocial issues associated with the clinical care of patients with prostate cancer?

Case 1: A 70-year-old man with prostate cancer and lymph node and bone metastases

^{177}Lu-PSMA-617: Is the future now?

Case 2: A 70-year-old man with metastatic CRPC with a somatic BRCA2 mutation

Agenda

Prologue: What are some of the unique psychosocial issues associated with the clinical care of patients with prostate cancer?

Case 1: A 70-year-old man with prostate cancer and lymph node and bone metastases

- For a patient with prior localized prostate cancer with PSA-only recurrence, how do you determine when to use androgen deprivation therapy (ADT), and which treatment do you prefer?
- What are the usual side effects of ADT, and what complementary strategies are useful to ameliorate?
- For patients with M0 disease and increasing PSA, how do you determine when to bring in additional hormonal therapy, and which treatment do you prefer?
- For patients with metastatic prostate cancer, how do you determine whether to use ADT alone or in combination with chemotherapy or other endocrine agents? Which agent(s) do you prefer?
- How do you prepare patients to receive the various forms of secondary hormonal therapy (anti-androgens, abiraterone)?

Agenda

^{177}Lu-PSMA-617: Is the future now?

- What is ^{177}Lu-PSMA-617 targeted therapy? What are the risks and potential benefits of treatment?

Case 2: A 70-year-old man with metastatic CRPC with a somatic BRCA2 mutation

- How are treatments sequenced for patients with mCRPC? What are the survival outcomes with each regimen?
- When is radium-223 used? What is the tolerability profile? What benefit do patients derive from this treatment?
- Which patients with mCRPC are eligible to receive a PARP inhibitor? How is eligibility determined?
- How do PARP inhibitors work? What are the risks and potential benefits? How is a specific PARP inhibitor selected?

Agenda

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Case Presentation – A 70-year-old man with prostate cancer and lymph node and bone metastases

- S/p primary radiation therapy 2010
- 2016: PSA recurrence (M0); initially observed and then started on ADT
- 2020: PSA progression; metastasis noted to lymph nodes and bone; started on abiraterone and then switched to apalutamide
- More recently developed Grade 3 maculopapular skin rash all over body
  - Antihistamines

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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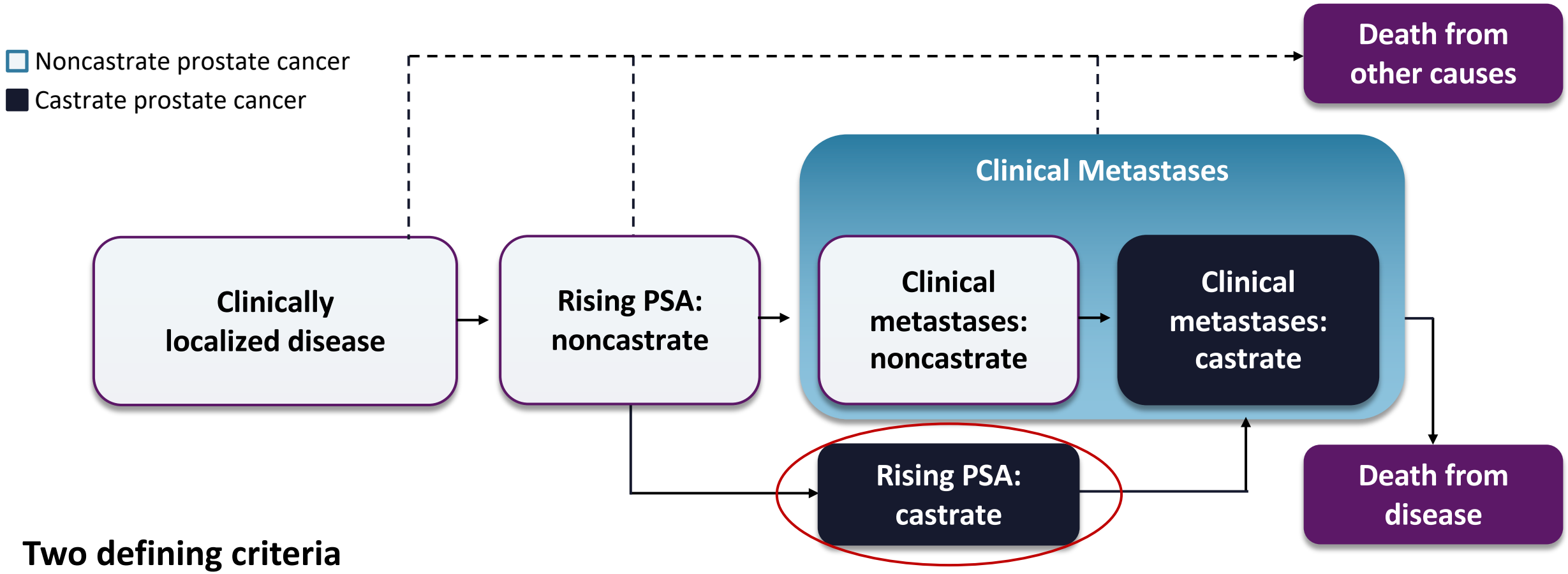
Results of a Randomized Phase II Trial of Intense Androgen Deprivation Therapy prior to Radical Prostatectomy in Men with High-Risk Localized Prostate Cancer

Rana R. McKay,* Wanling Xie, Huihui Ye,† Fiona M. Fennessy, Zhenwei Zhang, Rosina Lis,† Carla Calagua, Dana Rathkopf,‡ Vincent P. Laudone, Glenn J. Bubley, David J. Einstein,§ Peter K. Chang, Andrew A. Wagner, J. Kellogg Parsons,‖ Mark A. Preston, Kerry Kilbridge, Steven L. Chang, Atish D. Choudhury,¶ Mark M. Pomerantz, Quoc-Dien Trinh,** Adam S. Kibel†† and Mary-Ellen Taplin§§,‡‡

Journal of Urology 2021;206:80-7.

Clinical Disease States Model of Prostate Cancer[1]



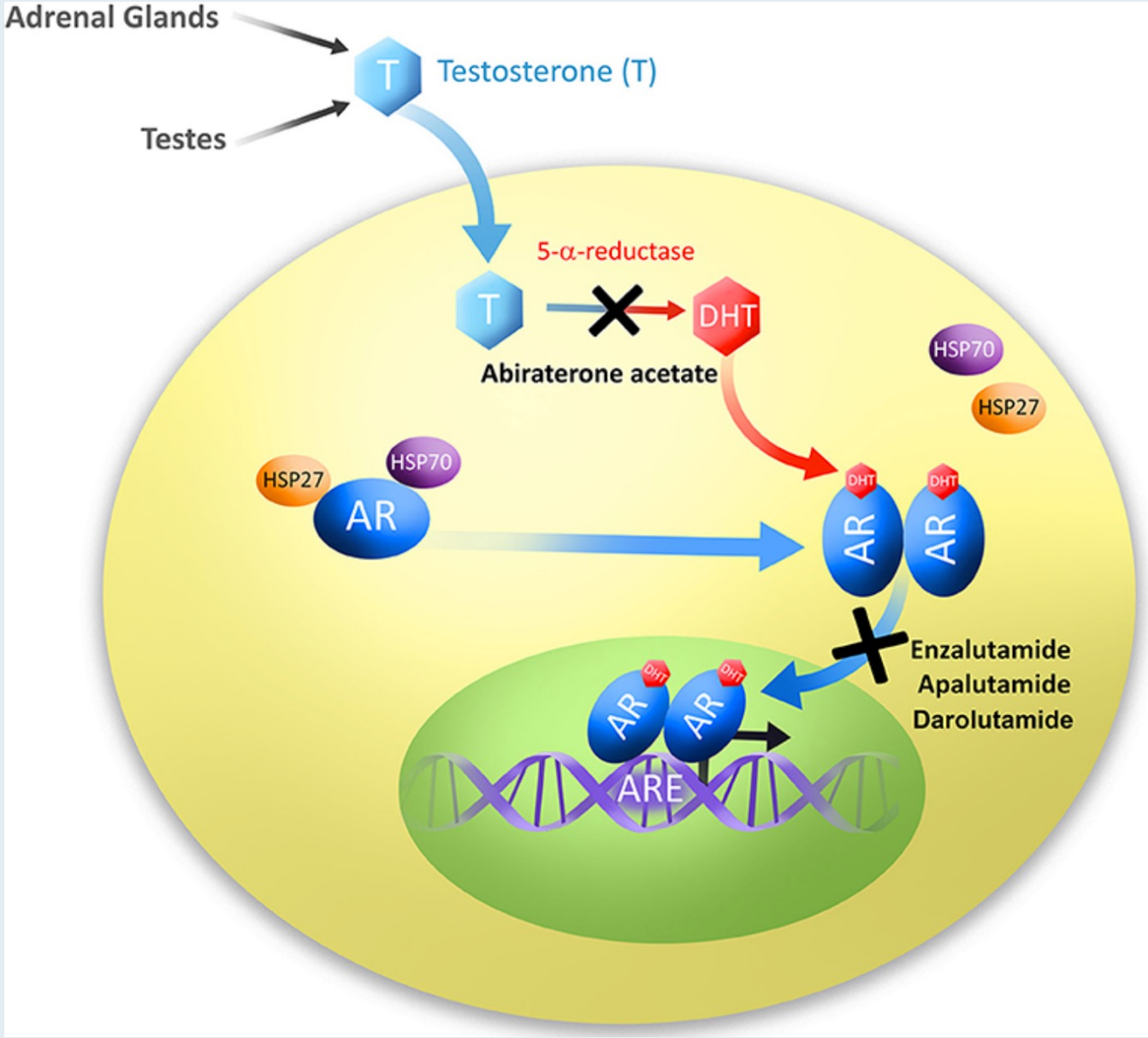
Two defining criteria

- Rising PSA in the setting of castrate testosterone levels (<50 ng/dL)
- No radiographically identifiable metastasis

1. Adapted from Scher HI et al. *J Clin Oncol.* 2008;26:1148-1159.

Courtesy of Matthew R Smith, MD, PhD

Diagram of Androgen Production and Its Targeted Inhibition



Rice MA et al. *Front Oncol* 2019; https://doi.org/10.3389/fonc.2019.00801

FDA Approves Relugolix for Advanced Prostate Cancer

Press Release: December 18, 2020

"On December 18, 2020, the U.S. Food and Drug Administration approved the first oral gonadotropin-releasing hormone (GnRH) receptor antagonist, relugolix, for adult patients with advanced prostate cancer.

Efficacy was evaluated in HERO (NCT03085095), a randomized, open label trial in men requiring at least one year of androgen deprivation therapy with either prostate cancer recurrence following radiation or surgery or newly diagnosed castration-sensitive advanced prostate cancer.

Patients (N=934) were randomized (2:1) to receive relugolix 360 mg oral loading dose on the first day, followed by daily oral doses of 120 mg, or leuprolide acetate 22.5 mg injection subcutaneously every 3 months for 48 weeks."

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-relugolix-advanced-prostate-cancer

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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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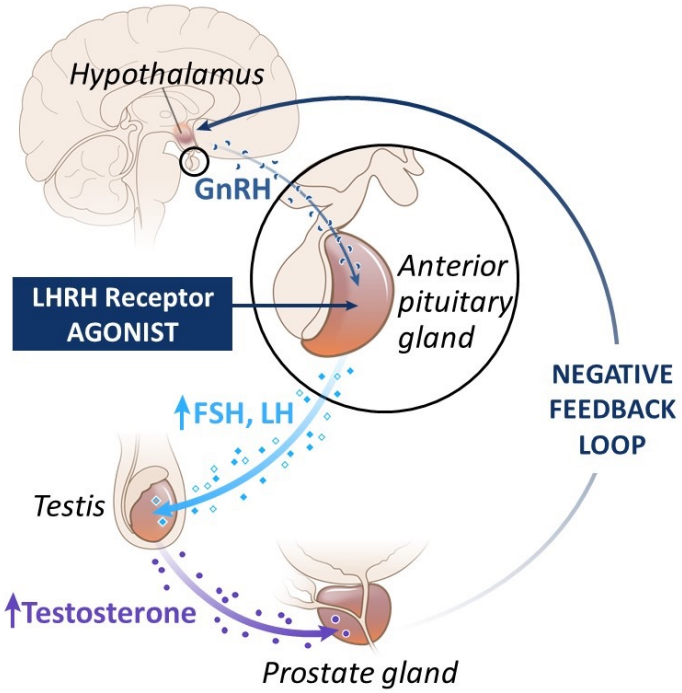
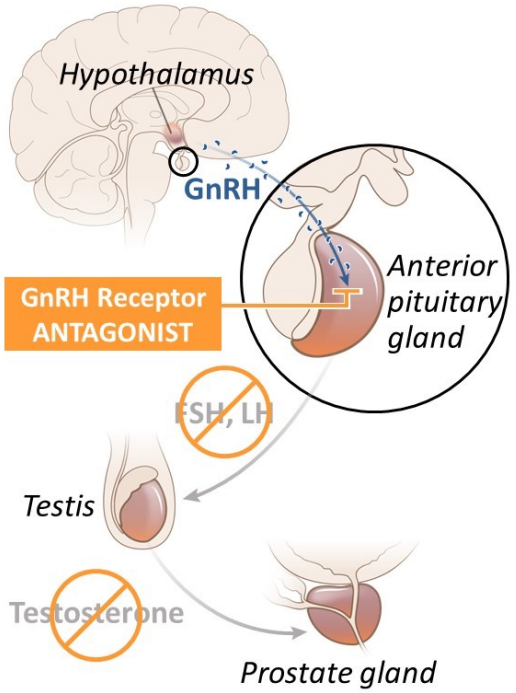
LHRH agonist vs antagonist MOA and side effect profile





PRESENTED AT: 2020 ASCO ANNUAL MEETING #ASCO20 Slides are the property of the author, permission required for reuse.

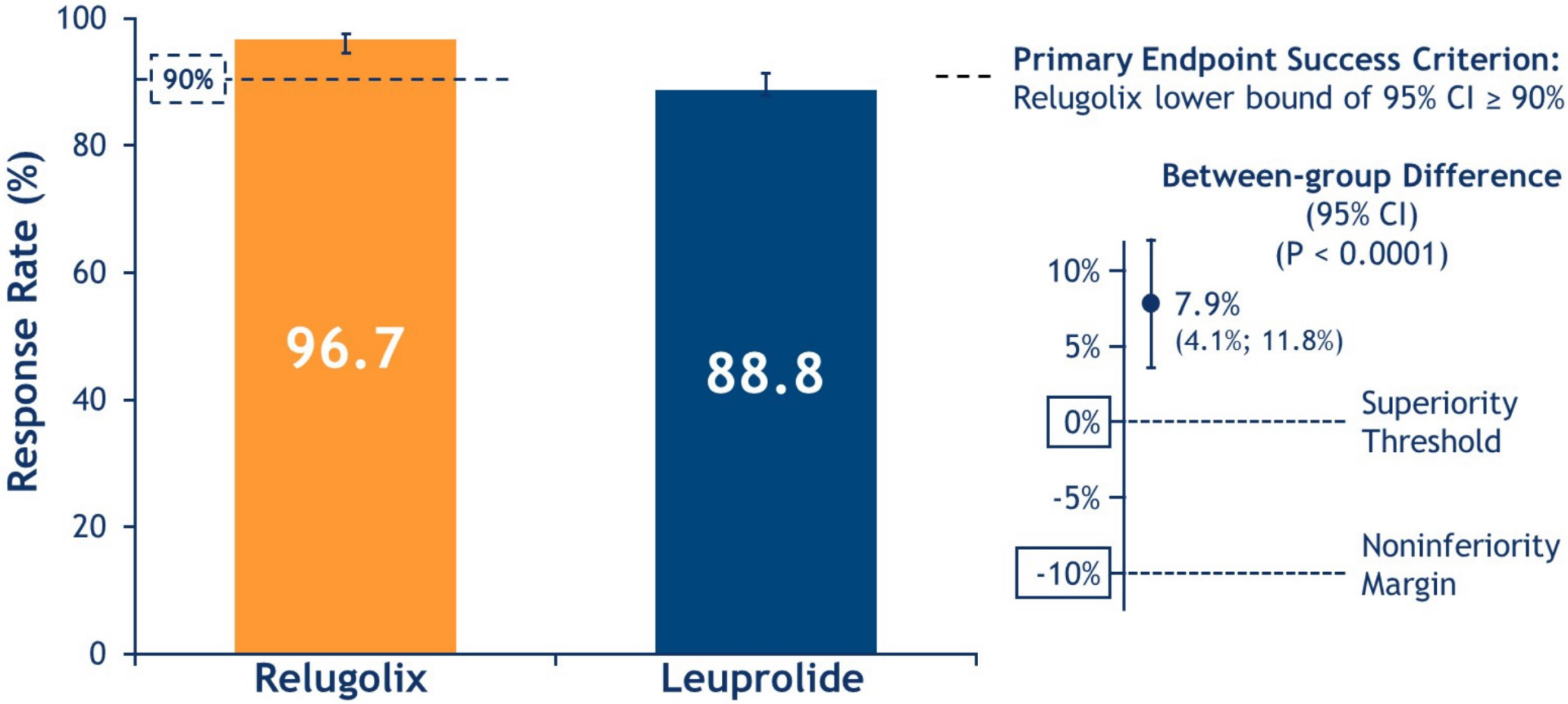
PRESENTED BY: Neal Shore, MD, FACS
Carolina Urologic Research Center, SC, USA

3

	Relugolix (N = 622)	Leuprolide (N = 308)
Hot flush	54.3%	51.6%
Fatigue	21.5%	18.5%
Constipation	12.2%	9.7%
Diarrhea*	12.2%	6.8%
Arthralgia	12.1%	9.1%
Hypertension	7.9%	11.7%

Courtesy of Tanya B Dorff, MD

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



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

Relugolix: Cardiovascular Safety

Event	Relugolix (n = 622)		Leuprolide (n = 308)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Major adverse cardiac event (MACE)*	2.9%	1.3%	6.2%	1.3%
In patients *without* prior history of MACE	2.8%	—	4.2%	—
In patients *with* prior history of MACE	3.6%	—	17.8%	—

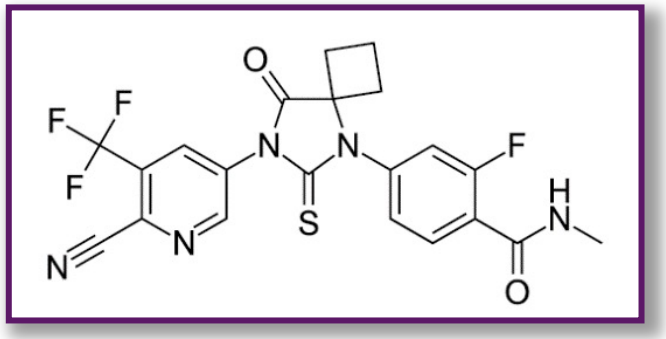
*Nonfatal myocardial infarction, nonfatal stroke and death from any cause

In the subgroup of patients with a reported medical history of MACE, the odds of having an event were 4.8 times as high with leuprolide as with relugolix.

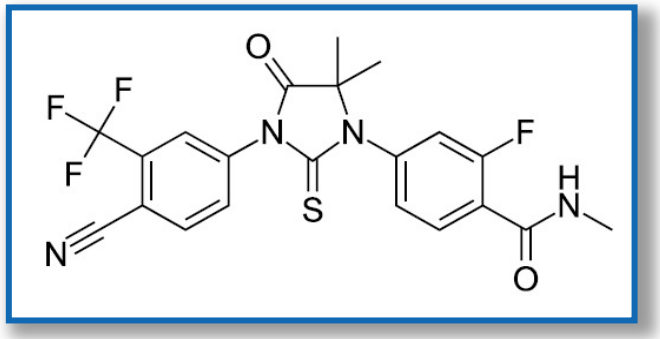
Shore ND et al. *N Engl J Med* 2020;382(23):2187-96.

Next-Generation Androgen Receptor Inhibitors[1,2]

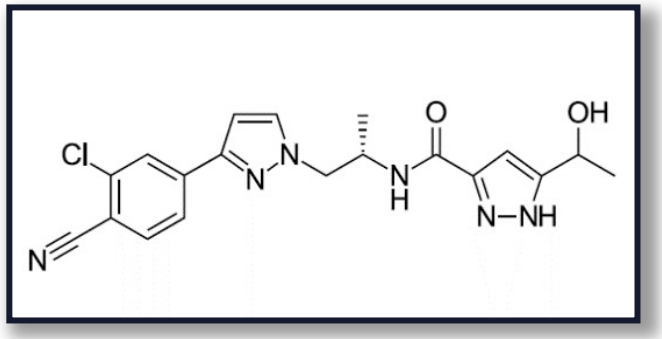
Apalutamide



Enzalutamide



Darolutamide



- Apalutamide and enzalutamide have similar structures
- Darolutamide is structurally distinct from apalutamide and enzalutamide, characterized by low blood–brain barrier penetration[1,2,] and may have improved tolerability

1. Zurth C et al. *J Clin Oncol*. 2018;36(Suppl 6):Abstract 345.
2. Sandmann S et al. American Society of Clinical Oncology 2019 Genitourinary Cancers Symposium (ASCO GU 2019). Abstract 156.

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 2021;79(1):150-58.

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* 2021;79(1):150-158.

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.

FDA-Approved Next-Generation Antiandrogens for 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

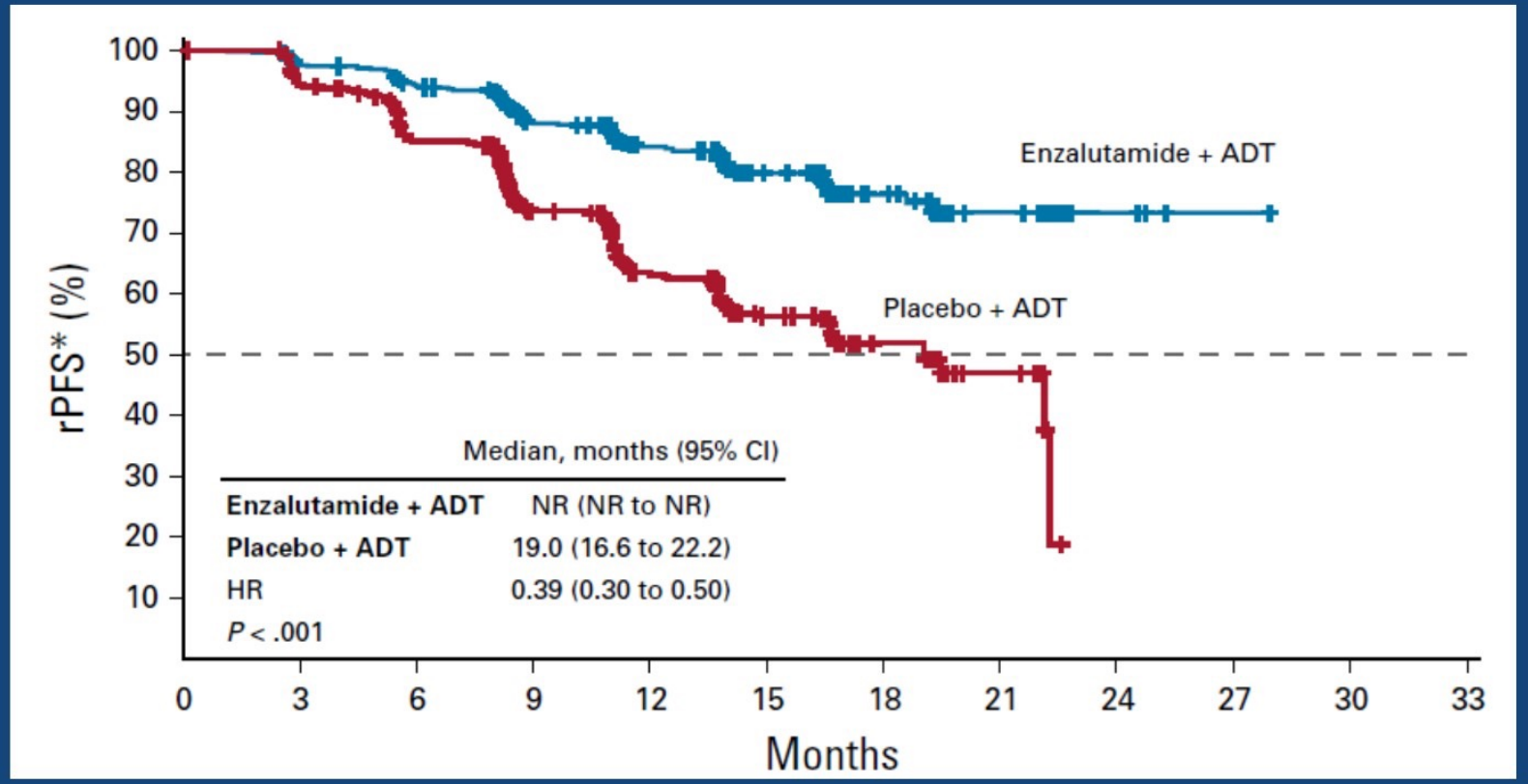
Survival Analyses for ARCHES and TITAN: ADT + Enzalutamide or Apalutamide for Metastatic Hormone-Sensitive Prostate Cancer

	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.

ARCHES: Enzalutamide for mHSPC

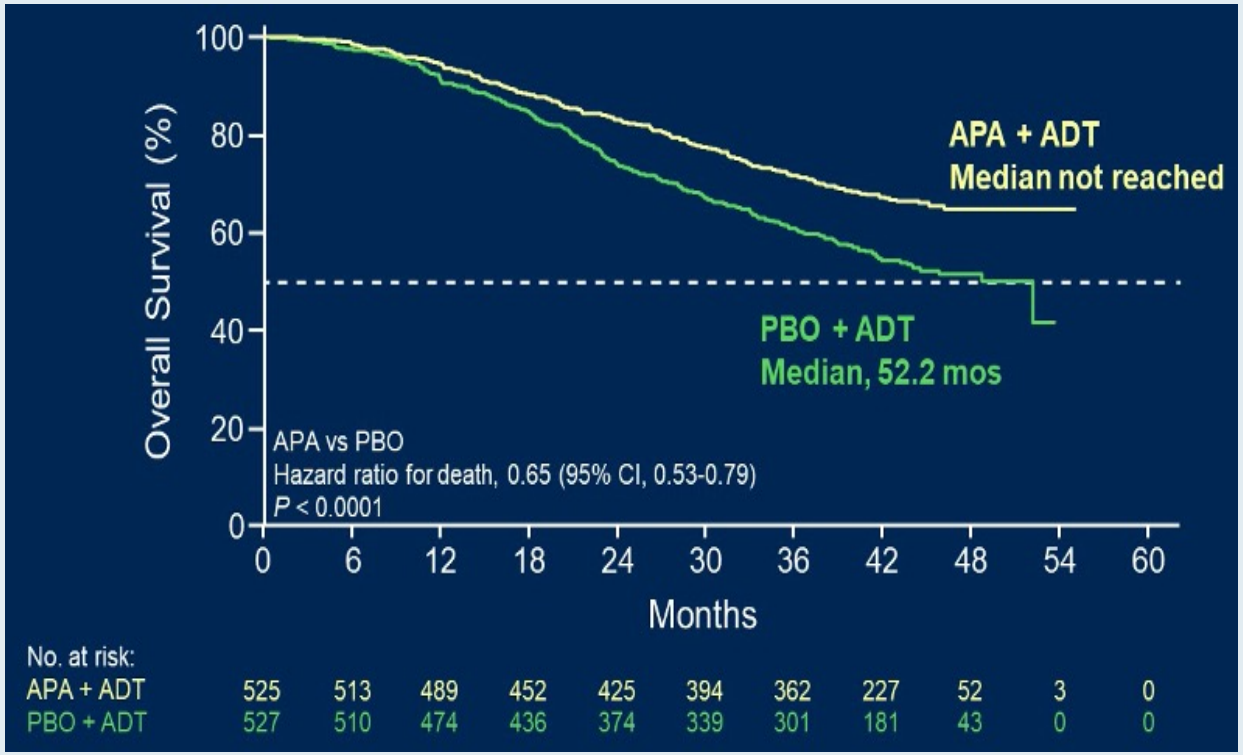


Overall Survival: HR 0.81 (95% CI 0.53, 1.25), P=0.3361 but survival data were immature with only 14.4 months median follow-up and 84 deaths

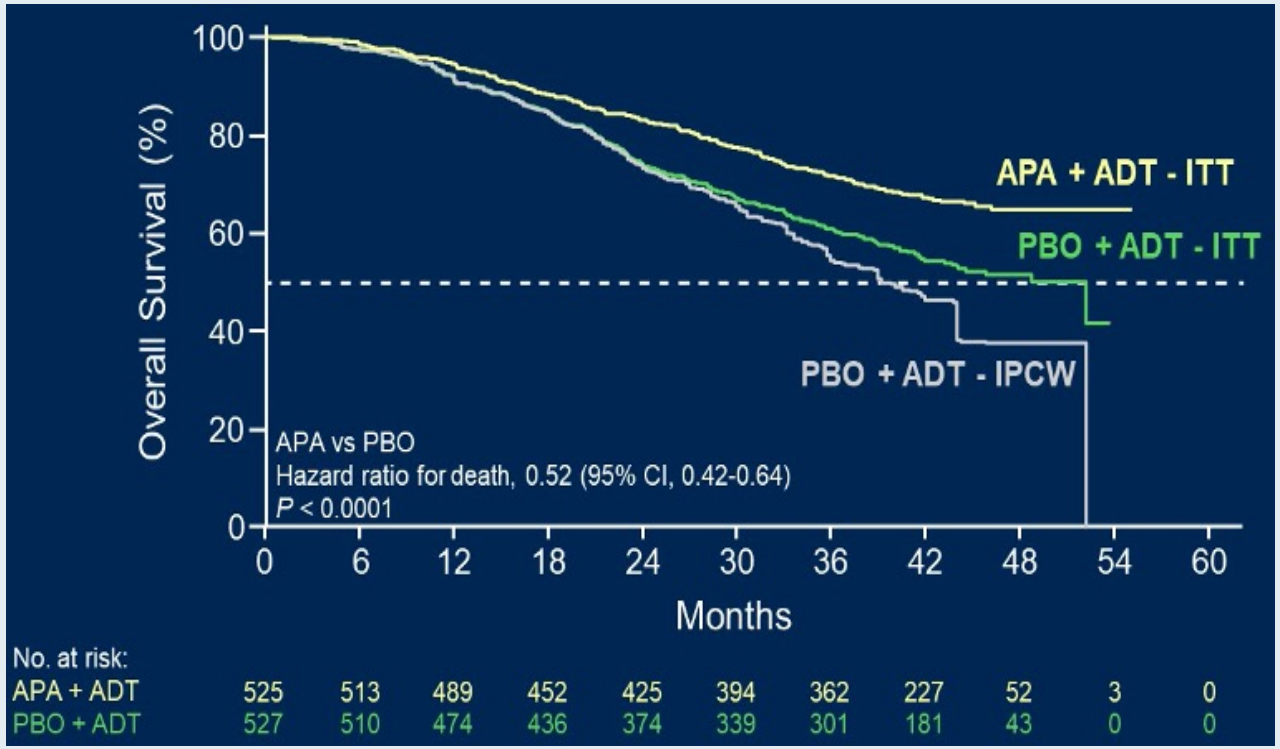
Armstrong et al (2019) *J Clin Oncol 37:* 2974-2986

TITAN – Final Analysis: Overall Survival

OS (coprimary endpoint)
Median follow-up: 44.0 months



OS with adjustment for ~40% crossover from PBO



Chi KN et al. Genitourinary Cancers Symposium 2021;Abstract 11.

RTP RESEARCH TO PRACTICE

A PHASE 3 TRIAL WITH A 2X2 FACTORIAL DESIGN OF ABIRATERONE ACETATE PLUS PREDNISONE AND/OR LOCAL RADIOTHERAPY IN MEN WITH *DE NOVO* METASTATIC CASTRATION-SENSITIVE PROSTATE CANCER (mCSPC): FIRST RESULTS OF PEACE-1

Karim Fizazi, MD, PhD

Institut Gustave Roussy, France

June 8, 2021

Karim Fizazi, Xavier Maldonado, Stéphanie Foulon, Guilhem Roubaud, Ray McDermott, Aude Fléchon, Bertrand Tombal, Stéphane Supiot, Dominik Berthold, Philippe Ronchin, Gabriel Kacsó, Gwenaëlle Gravis, Fabio Calabro, Jean-François Berdah, Ali Hasbini, Marlon Silva, Antoine Thiery-Vuillemin, Isabelle Rieger, Marie-Laure Tanguy, Alberto Bossi

ASCO 2021;Abstract 5000.

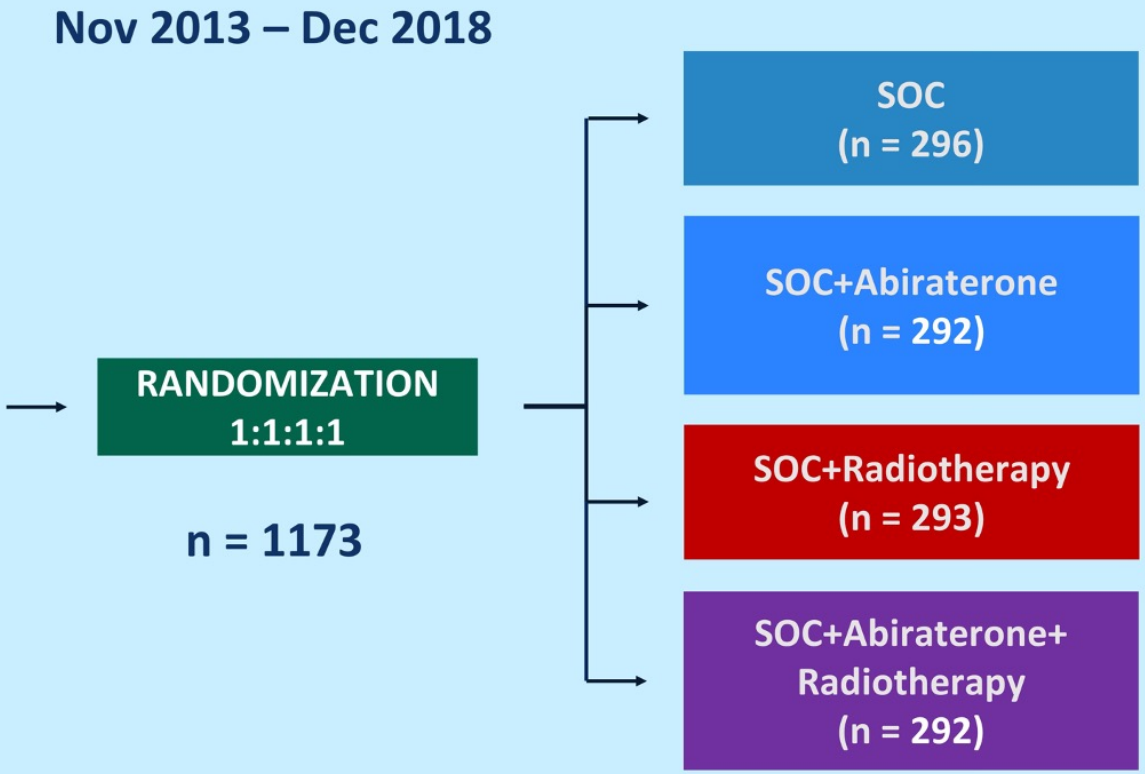
Design of PEACE-1

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

On-Study Requirement
Continuous ADT

Permitted
ADT ≤ 3 months

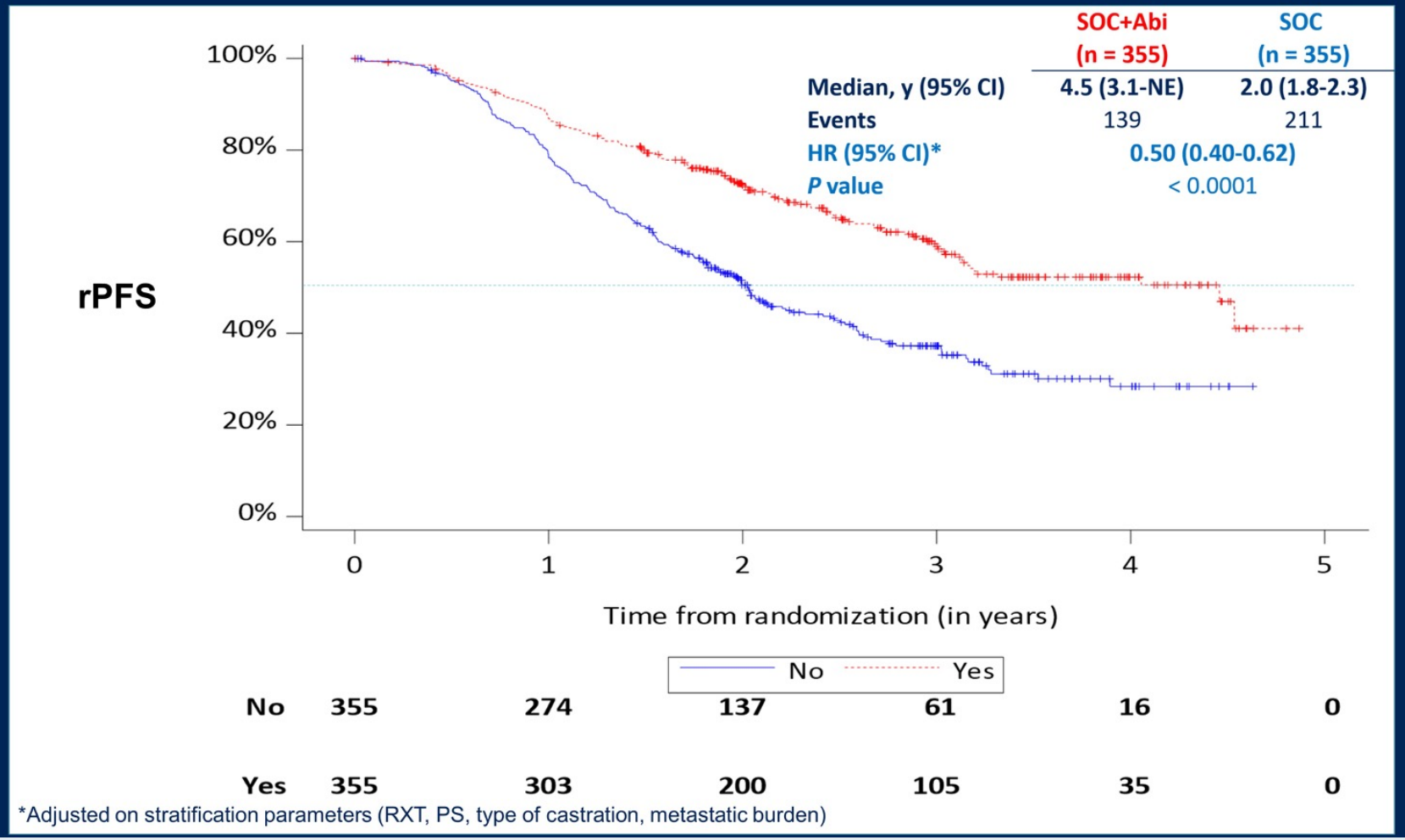
Stratification
ECOG PS (0 vs 1-2)
Metastatic sites (LN vs bone vs visceral)
Type of castration (orchidectomy vs LHRH agonist vs LHRH antagonist)
Docetaxel (yes vs no)



ECOG PS, Eastern Cooperative Oncology Group performance status

Fizazi K et al. ASCO 2021;Abstract 5000.

Radiographic Progression-Free Survival (rPFS)
ADT+Docetaxel population: SOC=ADT+Docetaxel (+/- RXT)



Fizazi K et al. ASCO 2021;Abstract 5000.

Agenda

^{177}Lu-PSMA-617: Is the future now?

- What is ^{177}Lu-PSMA-617 targeted therapy? What are the risks and potential benefits of treatment?

Case 2: A 70-year-old man with metastatic CRPC with a somatic BRCA2 mutation

- How are treatments sequenced for patients with mCRPC? What are the survival outcomes with each regimen?
- When is radium-223 used? What is the tolerability profile? What benefit do patients derive from this treatment?
- Which patients with mCRPC are eligible to receive a PARP inhibitor? How is eligibility determined?
- How do PARP inhibitors work? What are the risks and potential benefits? How is a specific PARP inhibitor selected?

2021 ASCO ANNUAL MEETING

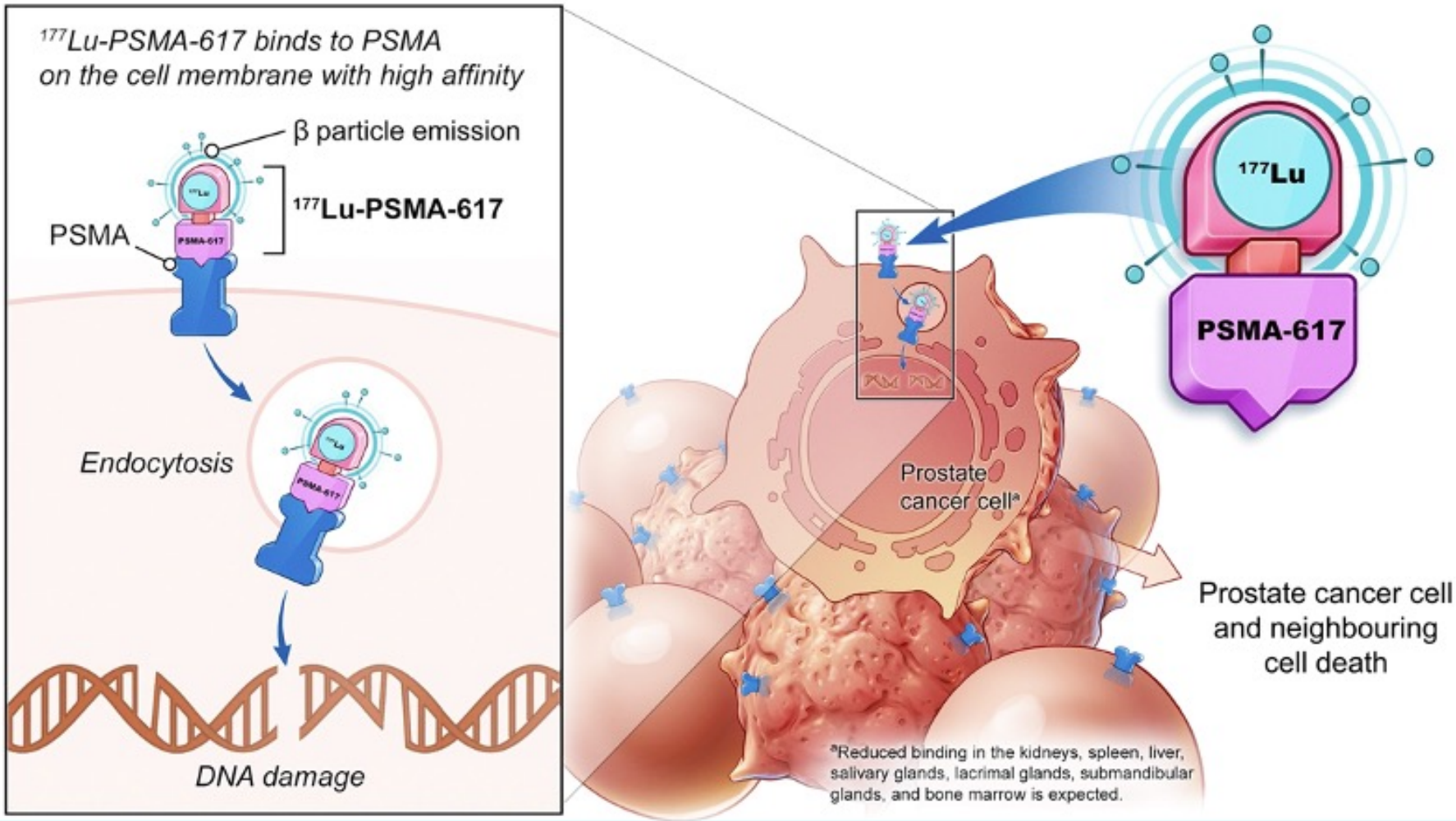
Phase 3 study of ^{177}Lu-PSMA-617 in patients with metastatic castration-resistant prostate cancer (VISION)

MJ Morris, J de Bono, KN Chi, K Fizazi, K Herrmann, K Rahbar, ST Tagawa, LT Nordquist, N Vaishampayan, G El-Haddad, CH Park, TM Beer, WJ Perez-Contreras, M DeSilvio, E Kpamegan, G Gericke, RA Messmann, BJ Krause, AO Sartor, VISION Investigators

Mary-Ellen Taplin, MD
Dana-Farber Cancer Institute
Boston, MA

June 6, 2021

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



Morris MJ et al. ASCO 2021;Abstract LBA4.

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

Eligible patients

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

2:1

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

Protocol-permitted SOC alone

Treatment → Follow-up → Final analysis

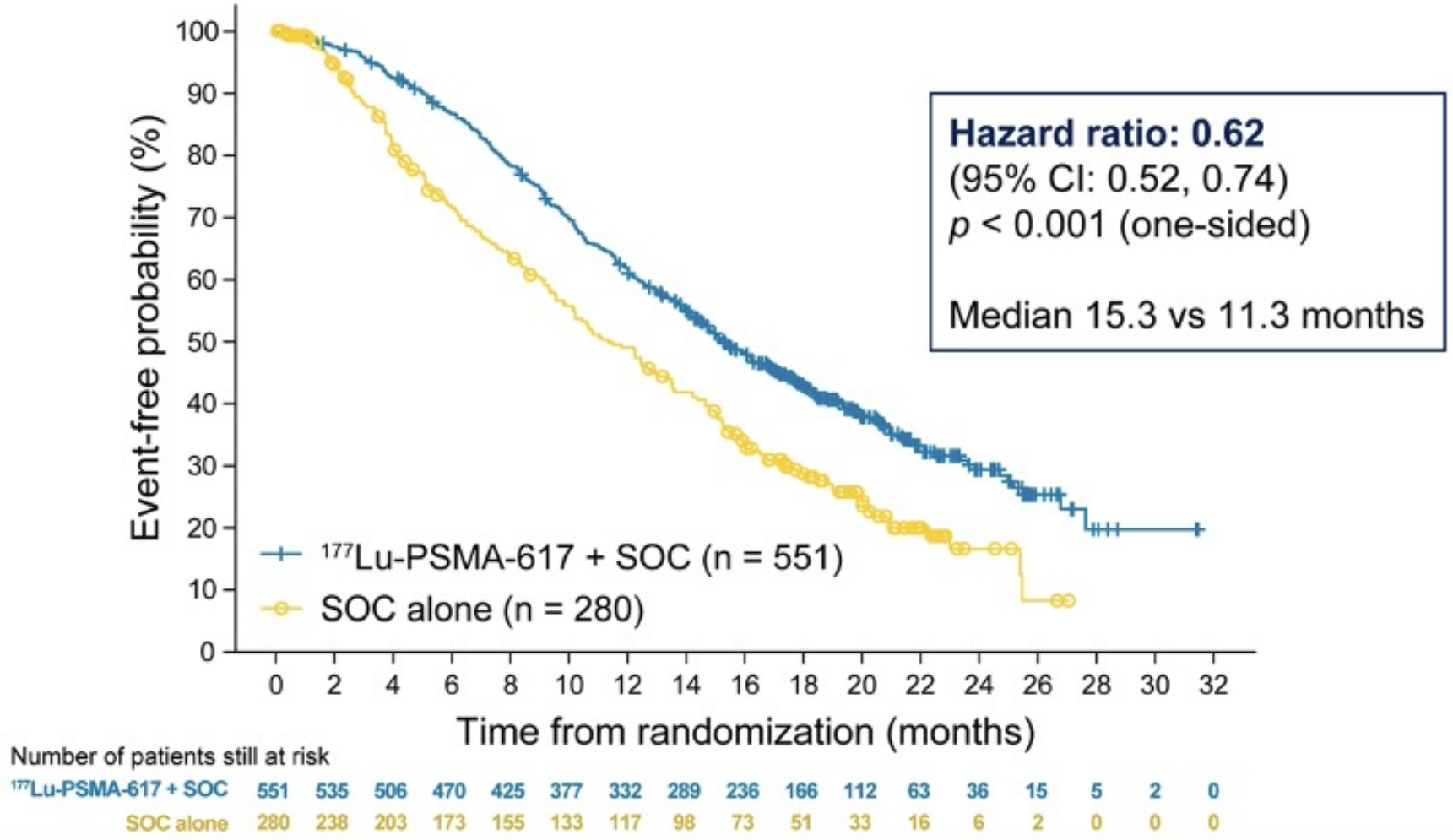
- Randomization stratified by
  - ECOG status (0–1 or 2)
  - LDH (high or low)
  - Liver metastases (yes or no)
  - Androgen receptor pathway inhibitors in SOC (yes or no)
- CT/MRI/bone scans
  - Every 8 weeks (treatment)
  - Every 12 weeks (follow-up)
  - Blinded independent central review

Morris MJ et al. ASCO 2021;Abstract LBA4.

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

Primary analysis

All randomized patients (N = 831)



Morris MJ et al. ASCO 2021;Abstract LBA4.

RTP RESEARCH TO PRACTICE

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

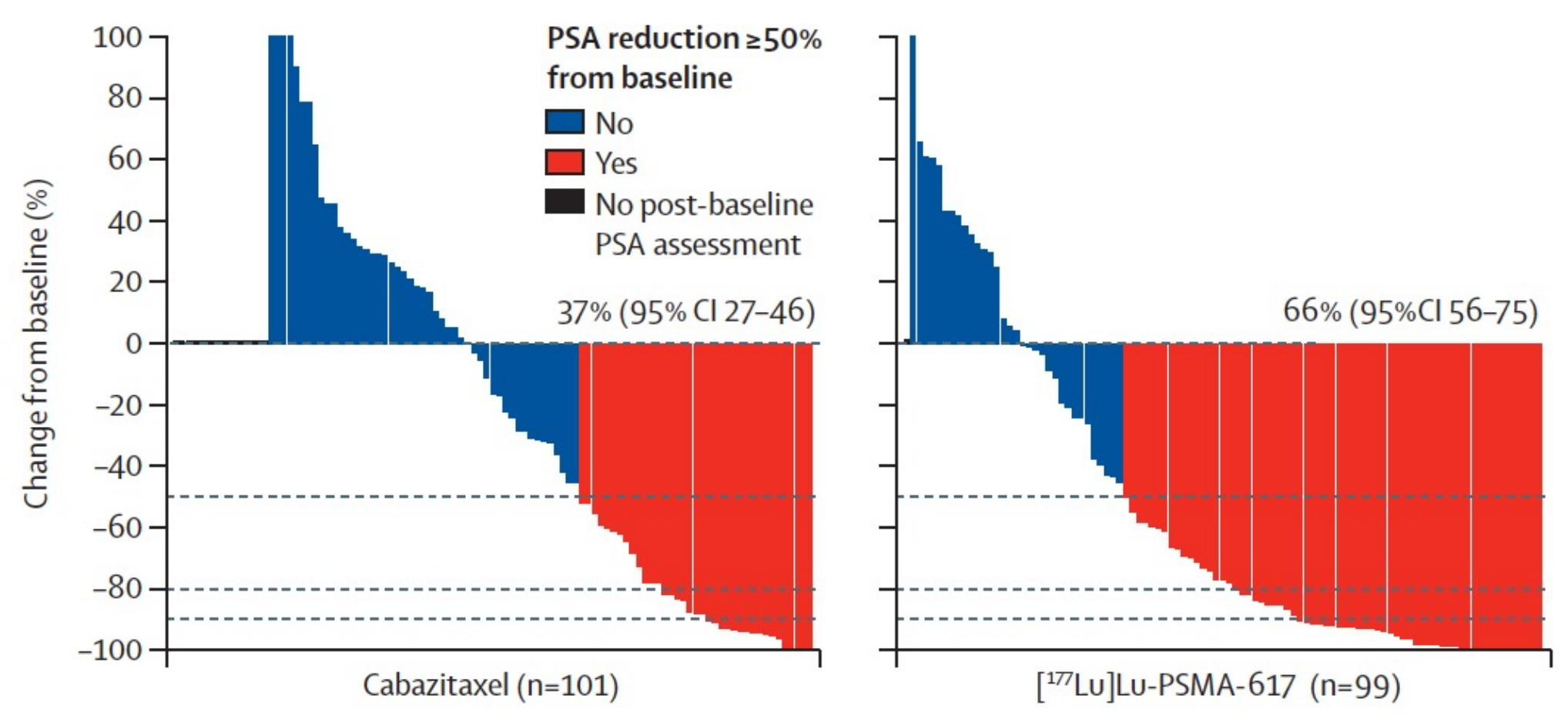
Patients, n (%)	All grades		Grade 3–5	
	^{177}Lu-PSMA-617 + SOC (n = 529)	SOC alone (n = 205)	^{177}Lu-PSMA-617 + SOC (n = 529)	SOC alone (n = 205)
Fatigue	260 (49.1)	60 (29.3)	37 (7.0)	5 (2.4)
Bone marrow suppression	251 (47.4)	36 (17.6)	124 (23.4)	14 (6.8)
Leukopenia	66 (12.5)	4 (2.0)	13 (2.5)	1 (0.5)
Lymphopenia	75 (14.2)	8 (3.9)	41 (7.8)	1 (0.5)
Anemia	168 (31.8)	27 (13.2)	68 (12.9)	10 (4.9)
Thrombocytopenia	91 (17.2)	9 (4.4)	42 (7.9)	2 (1.0)
Dry mouth	208 (39.3)	2 (1.0)	0 (0.0)	0 (0.0)
Nausea and vomiting	208 (39.3)	35 (17.1)	8 (1.5)	1 (0.5)
Renal effects	46 (8.7)	12 (5.9)	18 (3.4)	6 (2.9)
Second primary malignancies	11 (2.1)	2 (1.0)	4 (0.8)	1 (0.5)
Intracranial hemorrhage	7 (1.3)	3 (1.5)	5 (0.9)	2 (1.0)

Lancet 2021;397:797-804.

[^{177}Lu]Lu-PSMA-617 versus cabazitaxel in patients with metastatic castration-resistant prostate cancer (TheraP): a randomised, open-label, phase 2 trial

Michael S Hofman, Louise Emmett, Shahneen Sandhu, Amir Iravani, Anthony M Joshua, Jeffrey C Goh, David A Pattison, Thean Hsiang Tan, Ian D Kirkwood, Siobhan Ng, Roslyn J Francis, Craig Gedye, Natalie K Rutherford, Andrew Weickhardt , Andrew M Scott, Sze-Ting Lee, Edmond M Kwan, Arun A Azad, Shakher Ramdave, Andrew D Redfern, William Macdonald, Alex Guminski, Edward Hsiao, Wei Chua, Peter Lin, Alison Y Zhang, Margaret M McJannett, Martin R Stockler, John A Violet, Scott G Williams, Andrew J Martin, Ian D Davis, for the TheraP Trial Investigators and the Australian and New Zealand Urogenital and Prostate Cancer Trials Group†*

TheraP: Primary Endpoint — PSA Response ≥50%



Hofman MS et al. *Lancet* 2021;397(10276):797-804.

RTP RESEARCH TO PRACTICE

Agenda

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Case Presentation – A 70-year-old man with metastatic CRPC with a somatic BRCA2 mutation

- S/p prostatectomy followed by leuprolide for Gleason 9 prostate cancer
- Biochemical recurrence necessitated salvage radiation followed by enzalutamide
- 2020: Abiraterone for second recurrence and radiographic progression seen within 2 months
- Radium-223 x 4 cycles → rising PSA
- Rucaparib initiated
  - Weight loss, nausea, anorexia, drop in hemoglobin from 15-12 g/dL

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

RTP
RESEARCH
TO PRACTICE

Case 2 – A 70-year-old man with metastatic CRPC with a somatic BRCA2 mutation

- How are treatments sequenced for patients with mCRPC? What are the survival outcomes with each regimen?
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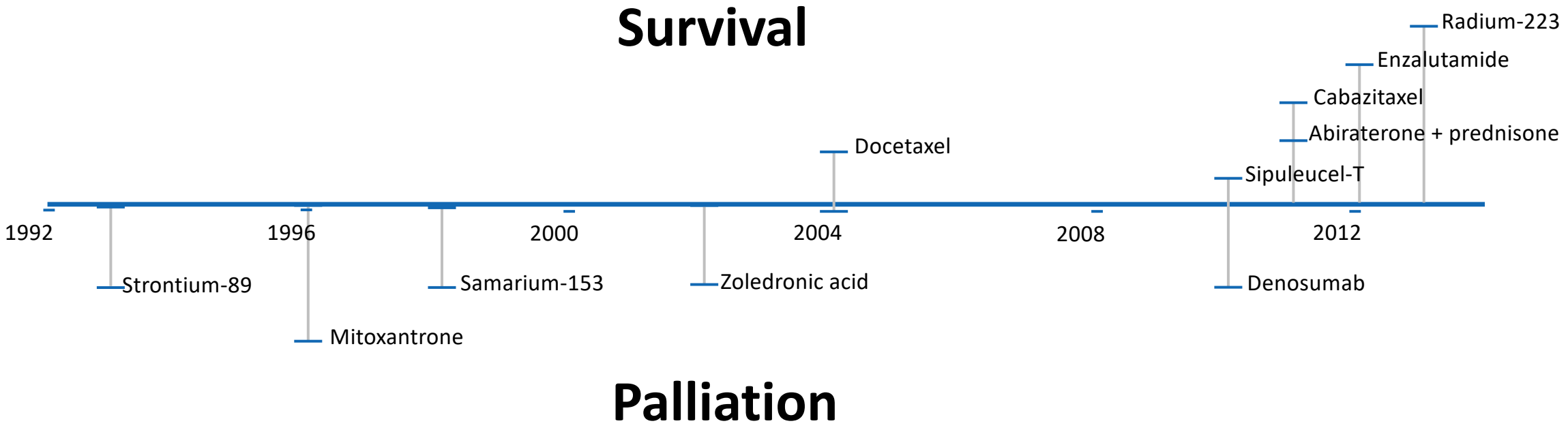
Timeline of FDA Approvals in Metastatic Castration-Resistant Prostate Cancer



Metastatic disease was defined by conventional imaging (eg, bone scan, CT scans)

Courtesy of Matthew R Smith, MD, PhD

Management of Metastatic Castration-Resistant Prostate Cancer (mCRPC)

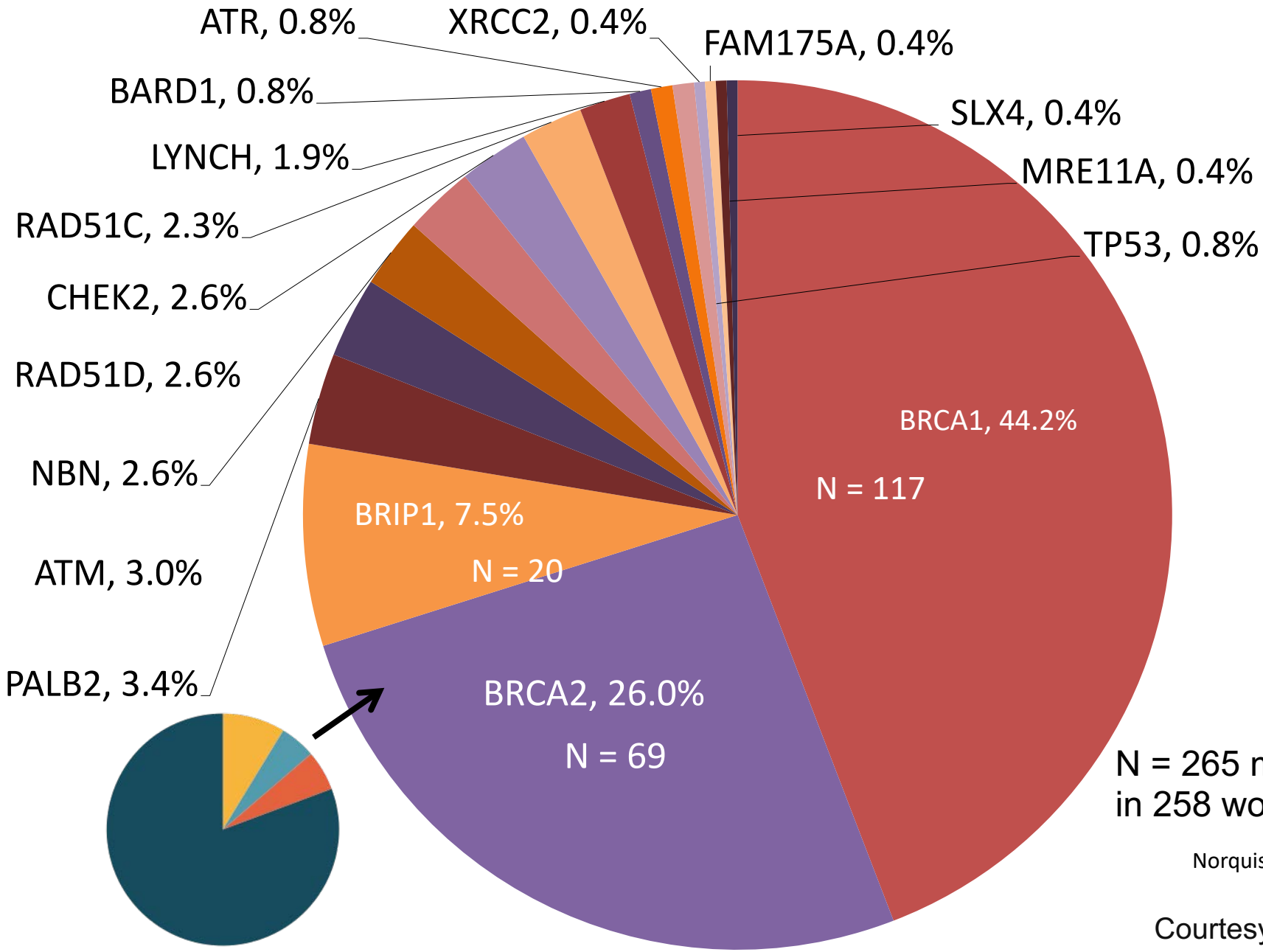
- Enzalutamide
- Abiraterone/prednisone
- Radium-223
- Sipuleucel-T
- Cabazitaxel
- Docetaxel
- PARP inhibitors

Practical Considerations and Challenges for Germline Genetic Testing in Patients With Prostate Cancer: Recommendations From the Germline Genetics Working Group of the PCCTC

Brittany M. Szymaniak, PhD[1]; Lauren A. Facchini, MS[2]; Veda N. Giri, MD[3]; Emmanuel S. Antonarakis, MD[4]; Tomasz M. Beer, MD[5]; Maria I. Carlo, MD[6]; Daniel C. Danila, MD[6]; Mallika Dhawan, MD[7]; Daniel George, MD[8]; Julie N. Graff, MD[9]; Shilpa Gupta, MD[10]; Elisabeth Heath, MD[11]; Celestia S. Higano, MD[12]; Glenn Liu, MD[13]; Ana M. Molina, MD[14]; Channing J. Paller, MD[4]; Akash Patnaik, MD, PhD, MMSc[15]; Daniel P. Petrylak, MD[16]; Zachery Reichert, MD, PhD[17]; Matthew B. Rettig, MD[18]; Charles J. Ryan, MD[10]; Mary-Ellen Taplin, MD[19]; Jake Vinson, BSc[20]; Young E. Whang, MD, PhD[21]; Alicia K. Morgans, MD, MPH[22]; Heather H. Cheng, MD, PhD[12]; and Rana R. McKay, MD[23]

JCO Oncology Practice 2020;16:811-2

Summary of Germline Cancer-Associated Mutations: GOG 218 and GOG 262

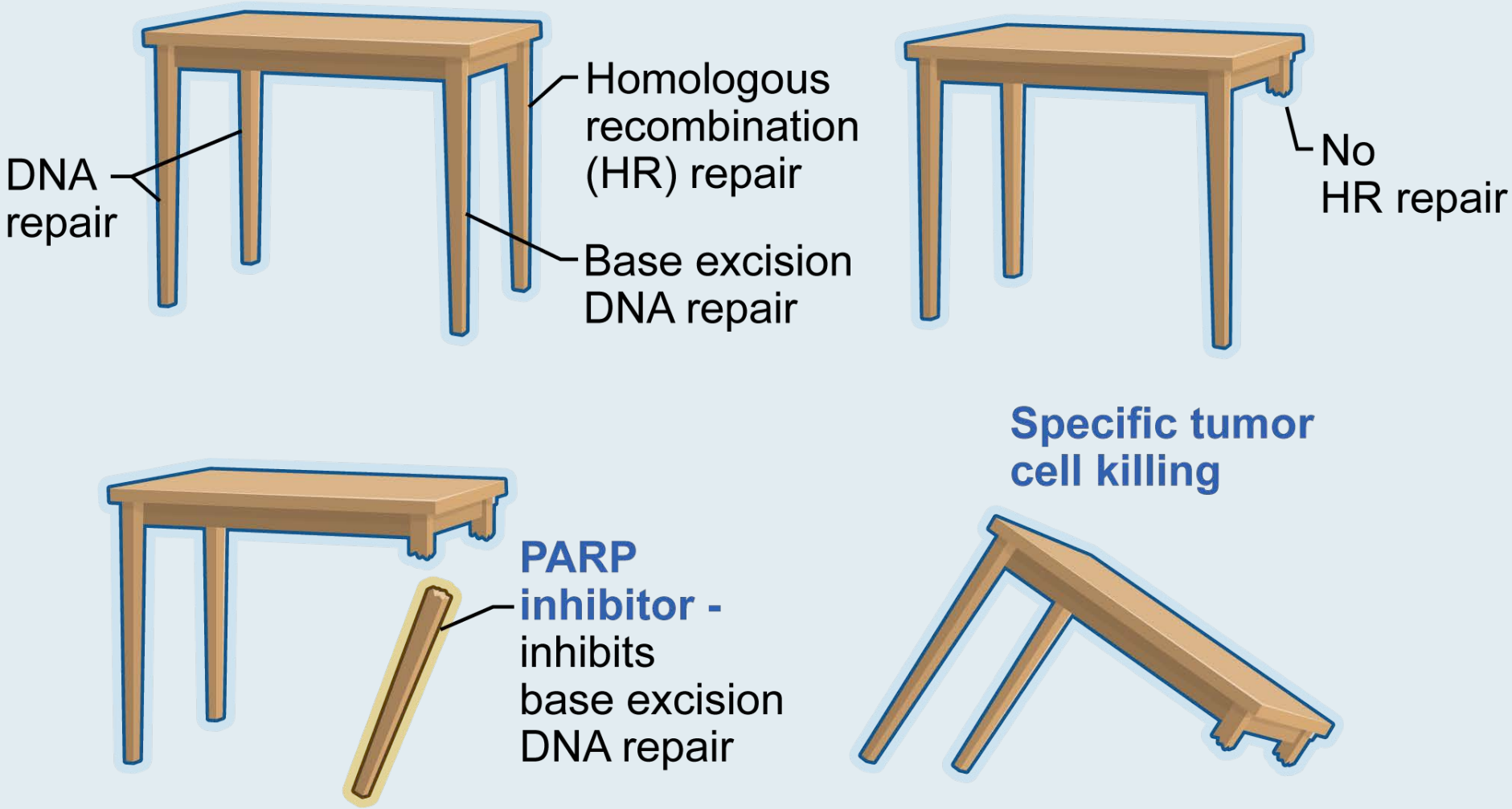


N = 265 mutations
in 258 women

Norquist, et al. JAMA Oncol. 2016;2:482-490.

Courtesy of Michael J Birrer, MD, PhD

Mechanism of Cell Death from Synthetic Lethality Induced by PARP Inhibition



Courtesy of Jenny C Chang, MD

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/

RTP RESEARCH TO PRACTICE

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

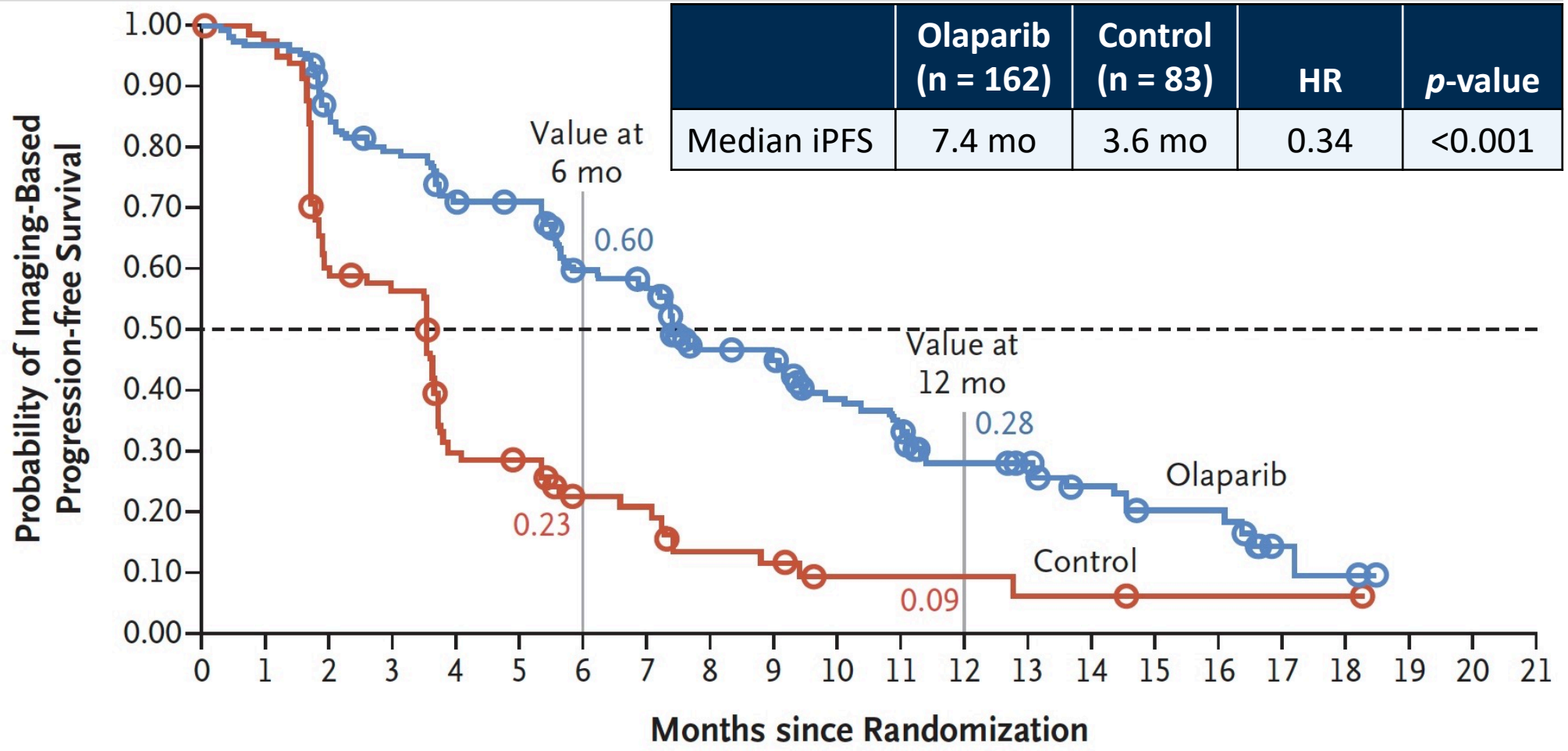
Olaparib for Metastatic Castration-Resistant Prostate Cancer

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(22):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. *N Engl J Med* 2020;382(22):2091-102.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

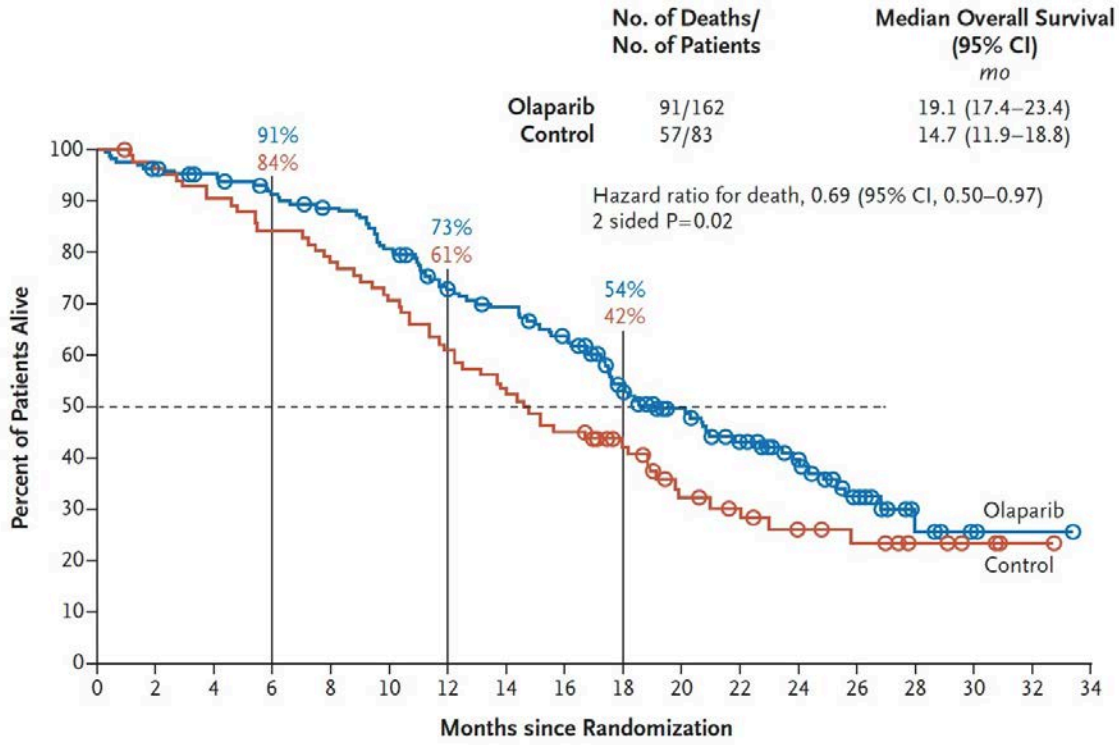
Survival with Olaparib in Metastatic Castration-Resistant Prostate Cancer

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*

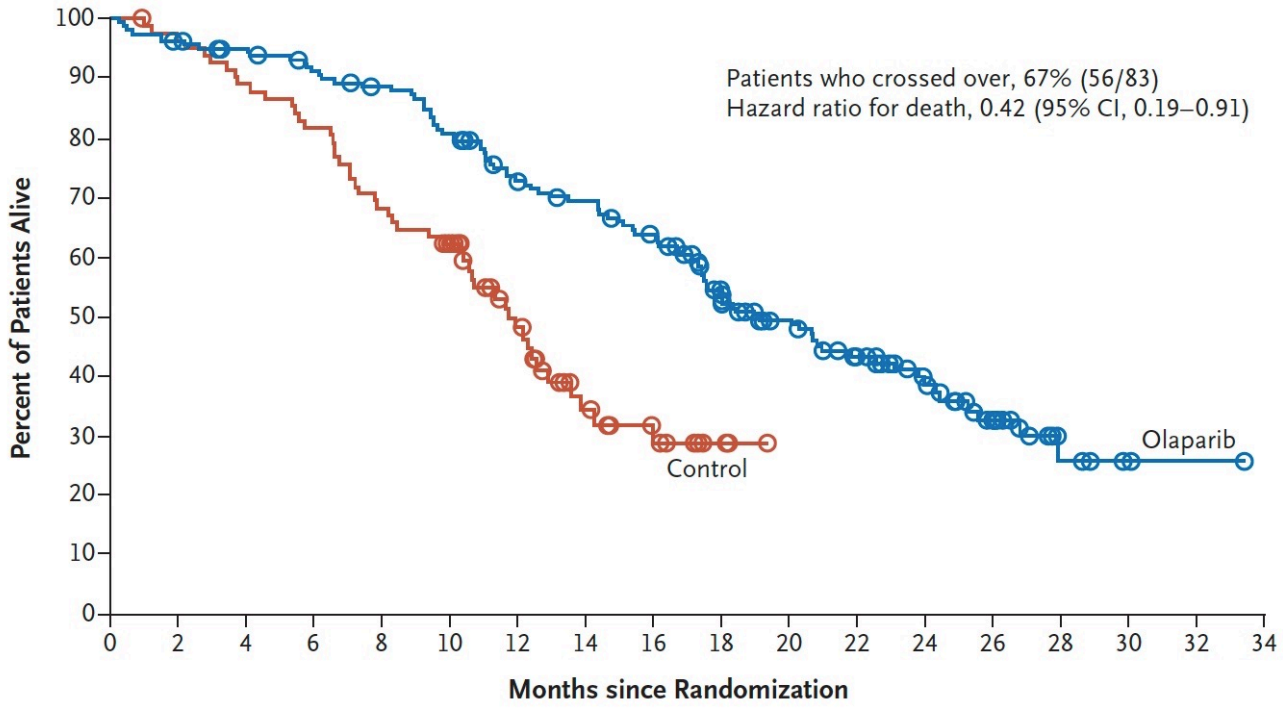
N Engl J Med 2020;383(24):2345-57.

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;383(24):2345-57. De Bono J et al. ESMO 2020;Abstract 610O.

rapid communications

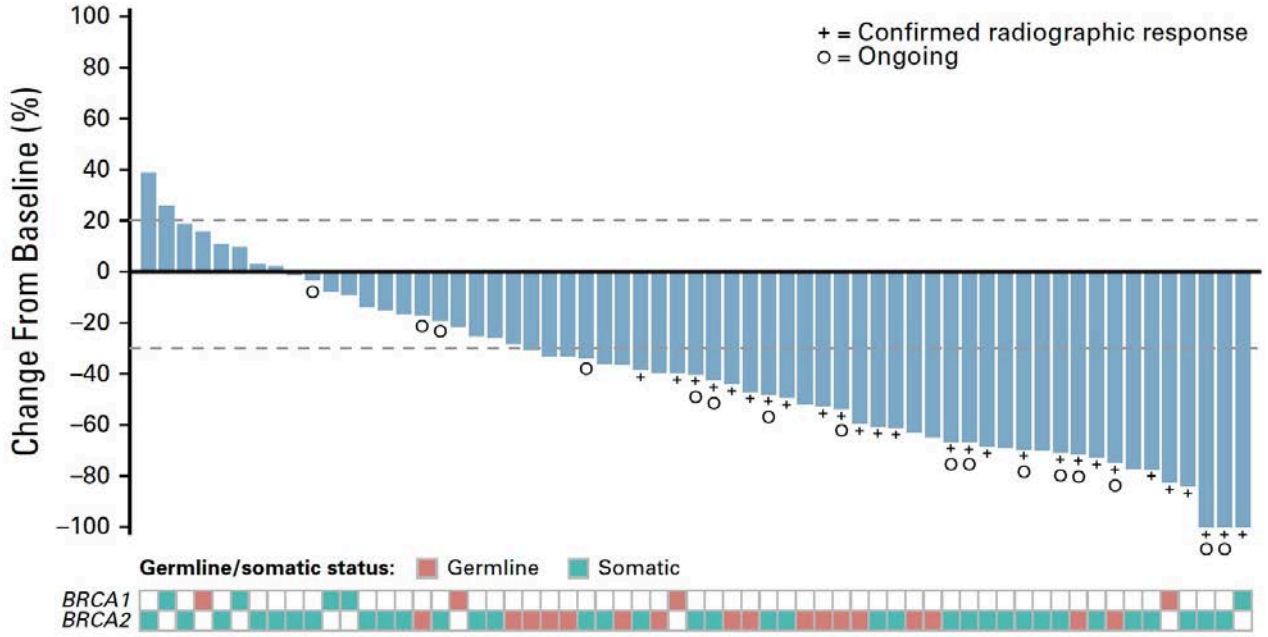
Rucaparib in Men With Metastatic Castration-Resistant Prostate Cancer Harboring a *BRCA1* or *BRCA2* Gene Alteration

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

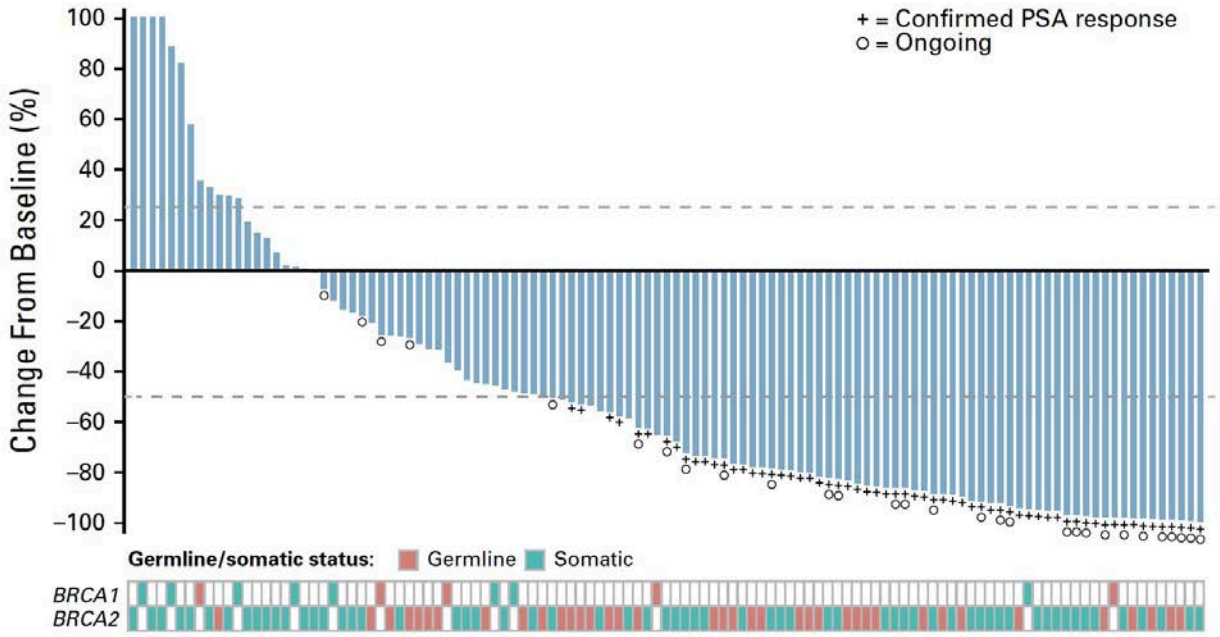
J Clin Oncol 2020;38(32):3763-72.

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, on behalf of the TRITON2 investigators. *J Clin Oncol* 2020;38(32):3763-72.

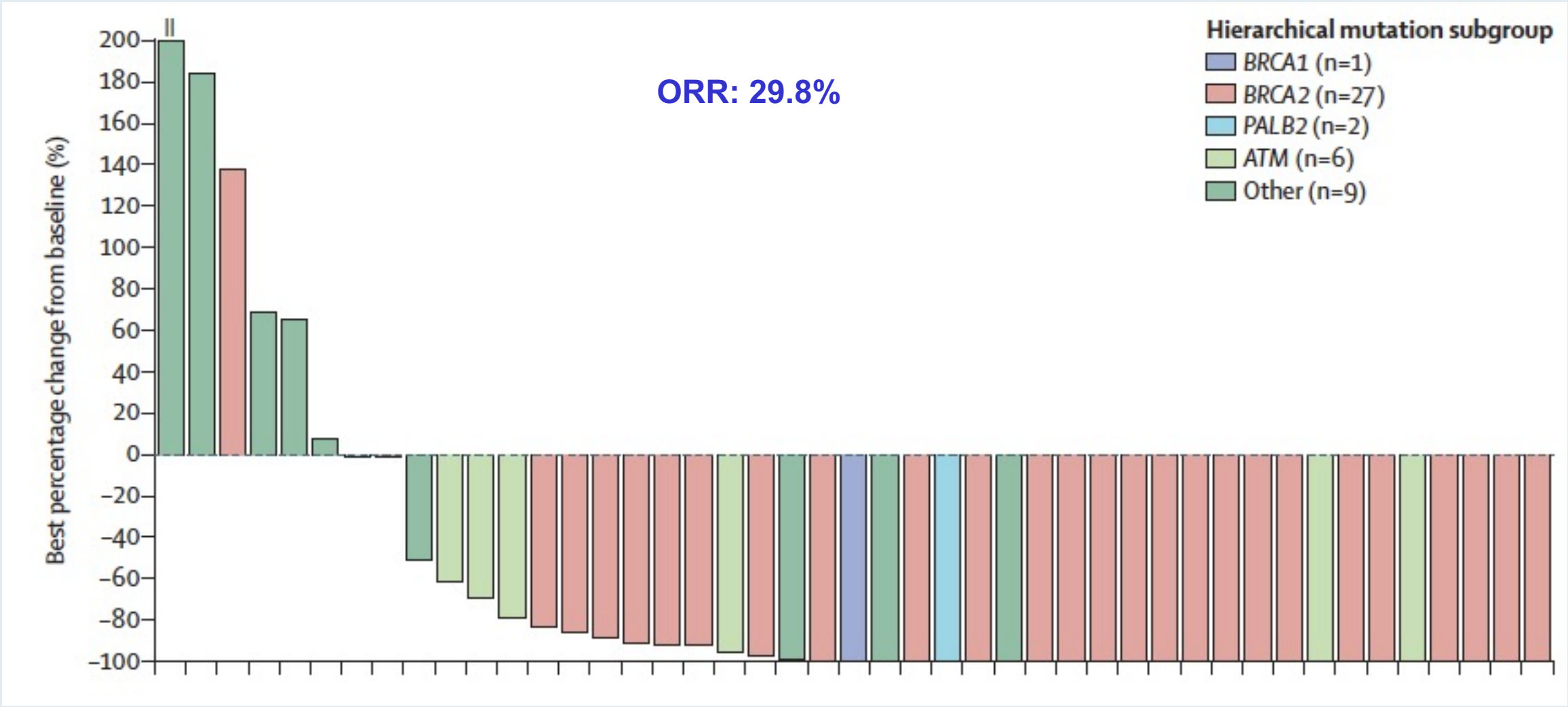
RTP RESEARCH TO PRACTICE

Talazoparib monotherapy in metastatic castration-resistant prostate cancer with DNA repair alterations (TALAPRO-1): an open-label, phase 2 trial

Johann S de Bono, Niven Mehra, Giorgio V Scagliotti, Elena Castro, Tanya Dorff, Adam Stirling, Arnulf Stenzl, Mark T Fleming, Celestia S Higano, Fred Saad, Consuelo Buttigliero, Inge M van Oort, A Douglas Laird, Marielena Mata, Hsiang-Chun Chen, Cynthia G Healy, Akos Czibere, Karim Fizazi

***Lancet Oncol* 2021;[Online ahead of print].**

TALAPRO-1: Best Change from Baseline in Circulating Tumor Cell Count with Talazoparib



de Bono JS et al. *Lancet Oncol* 2021;[Online ahead of print].

RTP RESEARCH TO PRACTICE

Data + Perspectives: Clinical Investigators Discuss the Current and Future Management of Acute Myeloid Leukemia and Myelodysplastic Syndromes

A Virtual CME Satellite Symposium During the Society of Hematologic Oncology 2021 Annual Meeting

Wednesday, September 8, 2021
7:30 PM – 9:00 PM Central Time

Faculty

Courtney D DiNardo, MD, MSCE
Daniel A Pollyea, MD, MS
David Sallman, MD
Eunice S Wang, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Thank you for joining us!

NCPD credit information will be emailed to each participant shortly.

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