What I Tell My Patients:
New Treatments and Clinical Trial Options

An NCPD Hybrid Symposium Series
Held During the 47th Annual ONS Congress

Prostate Cancer

Thursday, April 28, 2022
6:00 AM – 7:30 AM PT

Faculty

Kathy D Burns, RN, MSN, AGACNP-BC, OCN
Robert Dreicer, MD, MS
Sandy Srinivas, MD
Ronald Stein, JD, MSN, NP-C, AOCNP

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Faculty

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

Ronald Stein, JD, MSN, NP-C, AOCNP
Clinical Instructor of Medicine
USC Norris Comprehensive Cancer Center
Los Angeles, California

Robert Dreicer, MD, MS
Section Head, Medical Oncology
Deputy Director, University of Virginia Comprehensive Cancer Center
Associate Director for Clinical Research
Professor of Medicine and Urology
University of Virginia School of Medicine
Charlottesville, Virginia

Moderator
Neil Love, MD
Research To Practice
Miami, Florida

Sandy Srinivas, MD
Professor of Oncology
Clinical Research Leader, GU Oncology
Stanford University
Stanford, California

RTP
RESEARCH
TO PRACTICE

Ms Burns — Disclosures

Advisory Committee	EMD Serono Inc, Pfizer Inc
Speakers Bureau	Astellas, Aveo Pharmaceuticals, Exelixis Inc, Myovant Sciences, Pfizer Inc

Dr Dreicer — Disclosures

Advisory Committee	Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, Bristol-Myers Squibb Company, EMD Serono Inc, Exelixis Inc, Gilead Sciences Inc, Hinova Pharmaceuticals Inc, Infinity Pharmaceuticals Inc, Janssen Biotech Inc, Merck, Myovant Sciences, Pfizer Inc, Propella Therapeutics Inc, Seagen Inc, Tavanta Therapeutics, Veru Inc
Consulting Agreements	Astellas, Pfizer Inc
Contracted Research	Arvinas, Exelixis Inc, Seagen Inc

Dr Srinivas — Disclosures

Advisory Committee	Bayer HealthCare Pharmaceuticals, Janssen Biotech Inc, Merck, Novartis
Contracted Research	Bayer HealthCare Pharmaceuticals, Merck, Novartis
Data and Safety Monitoring Board/Committee	Pfizer Inc

Mr Stein — Disclosures

No relevant conflicts of interest to disclose

RTP
RESEARCH
TO PRACTICE

Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, and Novartis Pharmaceuticals Corporation on behalf of Advanced Accelerator Applications.

Research To Practice CME Planning Committee Members, Staff and Reviewers

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

RTP
RESEARCH
TO PRACTICE

Clinicians in the Meeting Room

Networked iPads are available.

Review Program Slides: Tap the Program Slides button to review speaker presentations and other program content.

Answer Survey Questions: Complete the premeeting survey before the meeting. Survey results will be presented and discussed throughout the meeting.

Ask a Question: Tap Ask a Question to submit a challenging case or question for discussion. We will aim to address as many questions as possible during the program.

Complete Your Evaluation: Tap the CME Evaluation button to complete your evaluation electronically to receive credit for your participation.

For assistance, please raise your hand. Devices will be collected at the conclusion of the activity.

RTP RESEARCH TO PRACTICE

Clinicians Attending via Zoom

Review Program Slides: A link to the program slides will be posted in the chat room at the start of the program.

Answer Survey Questions: Complete the premeeting survey before the meeting. Survey results will be presented and discussed throughout the meeting.

Ask a Question: Submit a challenging case or question for discussion using the Zoom chat room.

Get CME Credit: A CME credit link will be provided in the chat room at the conclusion of the program.

RTP
RESEARCH
TO PRACTICE

About the Enduring Program

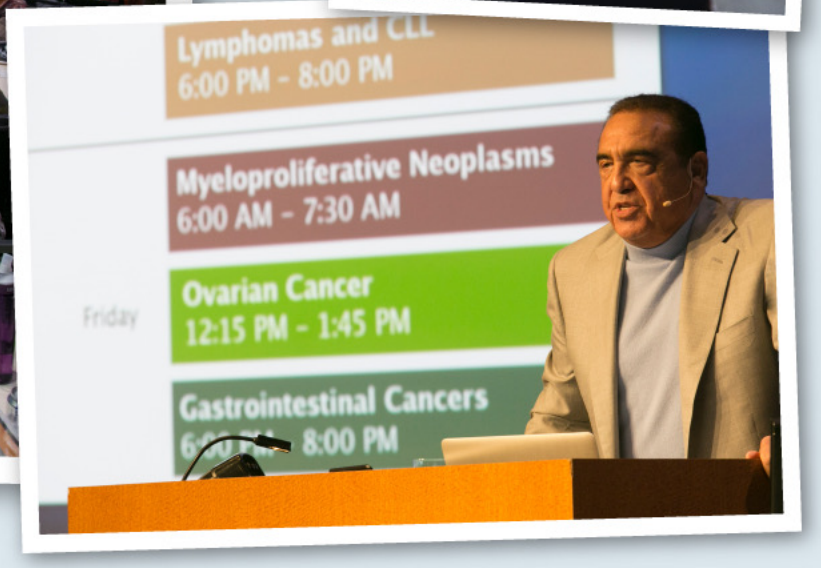
- The live meeting is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based video/PowerPoint program.
  An email will be sent to all attendees when the activity is available.
- To learn more about our education programs, visit our website, **www.ResearchToPractice.com**

RTP
RESEARCH
TO PRACTICE

Oncology Grand Rounds

2009-2022

75 Symposia 311 Faculty




COACHELLA
COACHELLA VALLEY MUSIC AND ARTS FESTIVAL


YouTube Originals
COACHELLA
20 YEARS IN THE DESERT
A YOUTUBE ORIGINAL DOCUMENTARY
STREAMING FREE
APRIL 10

"What I Tell My Patients"
14th Annual RTP-ONS NCPD Symposium Series
ONS Congress, Anaheim, California — April 27 - May 1, 2022

Thursday April 28	**Prostate Cancer** 6:00 AM – 7:30 AM PT (9:00 AM – 10:30 AM ET)
	Ovarian Cancer 12:15 PM – 1:45 PM PT (3:15 PM – 4:45 PM ET)
	Non–Small Cell Lung Cancer 6:00 PM – 8:00 PM PT (9:00 PM – 11:00 PM ET)
	Hepatobiliary Cancers 8:20 PM – 9:20 PM PT (11:20 PM – 12:20 AM ET)
Friday April 29	**Small Cell Lung Cancer** 6:00 AM – 7:30 AM PT (9:00 AM – 10:30 AM ET)
	Chronic Lymphocytic Leukemia 12:15 PM – 1:45 PM PT (3:15 PM – 4:45 PM ET)
	Breast Cancer 6:00 PM – 8:00 PM PT (9:00 PM – 11:00 PM ET)
	Acute Myeloid Leukemia and Myelodysplastic Syndromes 8:20 PM – 9:20 PM PT (11:20 PM – 12:20 AM ET)
Saturday April 30	**Cervical and Endometrial Cancer** 6:00 AM – 7:30 AM PT (9:00 AM – 10:30 AM ET)
	Bladder Cancer 12:15 PM – 1:45 PM PT (3:15 PM – 4:45 PM ET)

RTP RESEARCH TO PRACTICE

What I Tell My Patients: Expert Insights into Patient Education on New Treatments and Clinical Trial Participation

An NCPD Hybrid Symposium Series Held During the 47th Annual ONS Congress

Prostate Cancer

Thursday, April 28, 2022
6:00 AM – 7:30 AM PT (9:00 AM – 10:30 AM ET)

Faculty
Kathy D Burns, RN, MSN, AGACNP-BC, OCN
Robert Dreicer, MD, MS
Sandy Srinivas, MD
Ronald Stein, JD, MSN, NP-C, AOCNP

Non-Small Cell Lung Cancer

Thursday, April 28, 2022
6:00 PM – 8:00 PM PT (9:00 PM – 11:00 PM ET)

Faculty
Edward B Garon, MD, MS
Kelly EH Goodwin, MSN, RN, ANP-BC
Tara Plues, APRN, MSN
Anne S Tsao, MD, MBA

Ovarian Cancer

Thursday, April 28, 2022
12:15 PM – 1:45 PM PT (3:15 PM – 4:45 PM ET)

Faculty
Jennifer Filipi, MSN, NP
Kathleen N Moore, MD, MS
Krishnansu S Tewari, MD
Deborah Wright, MSN, APRN, AGCNS-BC

Hepatobiliary Cancers

Thursday, April 28, 2022
8:20 PM – 9:20 PM PT (11:20 PM – 12:20 AM ET)

Faculty
Richard S Finn, MD
Amanda K Wagner, APRN-CNP, AOCNP

What I Tell My Patients: Expert Insights into Patient Education on New Treatments and Clinical Trial Participation

An NCPD Hybrid Symposium Series Held During the 47th Annual ONS Congress

Small Cell Lung Cancer

Friday, April 29, 2022
6:00 AM – 7:30 AM PT (9:00 AM – 10:30 AM ET)

Faculty
Marianne J Davies, DNP, MSN, RN, APRN
Matthew Gubens, MD, MS
Lowell L Hart, MD
Chaely J Medley, MSN, AGNP

Breast Cancer

Friday, April 29, 2022
6:00 PM – 8:00 PM PT (9:00 PM – 11:00 PM ET)

Faculty
Jamie Carroll, APRN, MSN, CNP
Sara A Hurvitz, MD
Kelly Leonard, MSN, FNP-BC
Hope S Rugo, MD

Chronic Lymphocytic Leukemia

Friday, April 29, 2022
12:15 PM – 1:45 PM PT (3:15 PM – 4:45 PM ET)

Faculty
Lesley Camille Ballance, MSN, FNP-BC
Amy Goodrich, CRNP
Anthony R Mato, MD, MSCE
Susan O'Brien, MD

Acute Myeloid Leukemia and Myelodysplastic Syndromes

Friday, April 29, 2022
8:20 PM – 9:20 PM PT (11:20 PM – 12:20 AM ET)

Faculty
Ilene Galinsky, NP
Eunice S Wang, MD

What I Tell My Patients: Expert Insights into Patient Education on New Treatments and Clinical Trial Participation

An NCPD Hybrid Symposium Series Held During the 47th Annual ONS Congress

Cervical and Endometrial Cancer

Saturday, April 30, 2022
6:00 AM – 7:30 AM PT (9:00 AM – 10:30 AM ET)

Faculty
Paula J Anastasia, MN, RN, AOCN
Robert L Coleman, MD
David M O'Malley, MD
Jaclyn Shaver, MS, APRN, CNP, WHNP

Bladder Cancer

Saturday, April 30, 2022
12:15 PM – 1:45 PM PT (3:15 PM – 4:45 PM ET)

Faculty
Monica Averia, MSN, AOCNP, NP-C
Shilpa Gupta, MD
Brenda Martone, MSN, NP-BC, AOCNP
Sumanta Kumar Pal, MD

Join Us After ONS for Our Series Continuation

What I Tell My Patients —
A 2-Part NCPD Webinar Series

Hodgkin and Non-Hodgkin Lymphomas

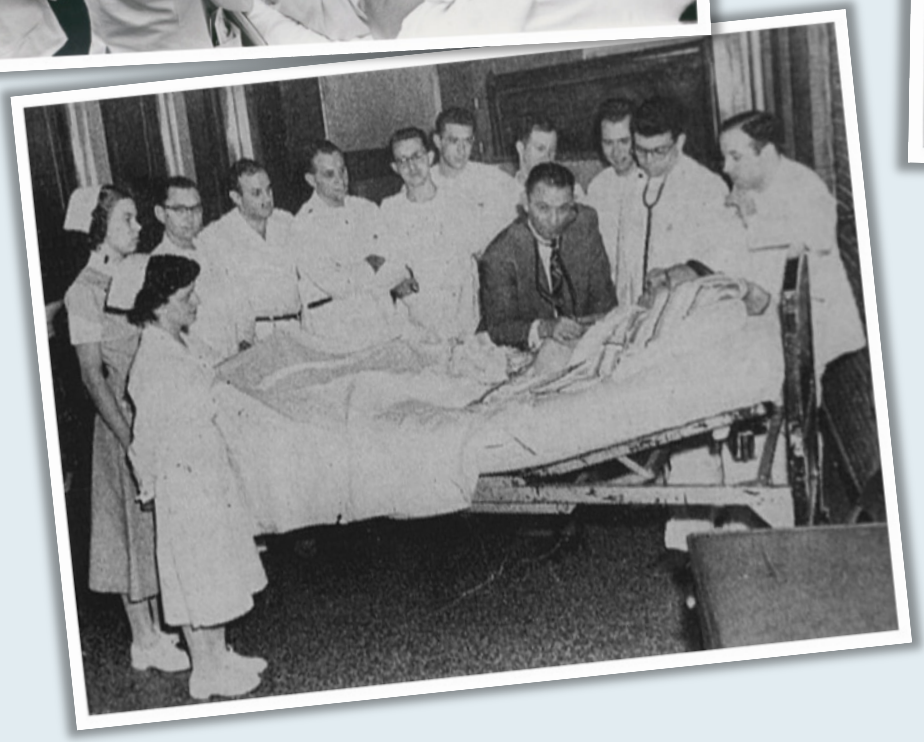
Date and time to be announced

Gastroesophageal Cancers

Wednesday, May 18, 2022

5:00 PM – 6:00 PM ET

RTP
RESEARCH
TO PRACTICE



RTP
RESEARCH
TO PRACTICE

RTP
RESEARCH
TO PRACTICE

The Core Oncology Triad
Developing an Individualized Oncology Strategy

RTP RESEARCH TO PRACTICE

Oncology Grand Rounds
2022 ONS Congress
Anaheim, California

Symposia Themes

Personalized oncology: Implementing an individualized oncologic strategy

- Tumor factors (eg, biomarkers, numeracy)
- Biopsychosocial factors (eg, adherence, available family support, comorbidities, mood)

Novel agents and treatment strategies

- The new-agents revolution (beginning of the end?)

The bond that heals (both ways)

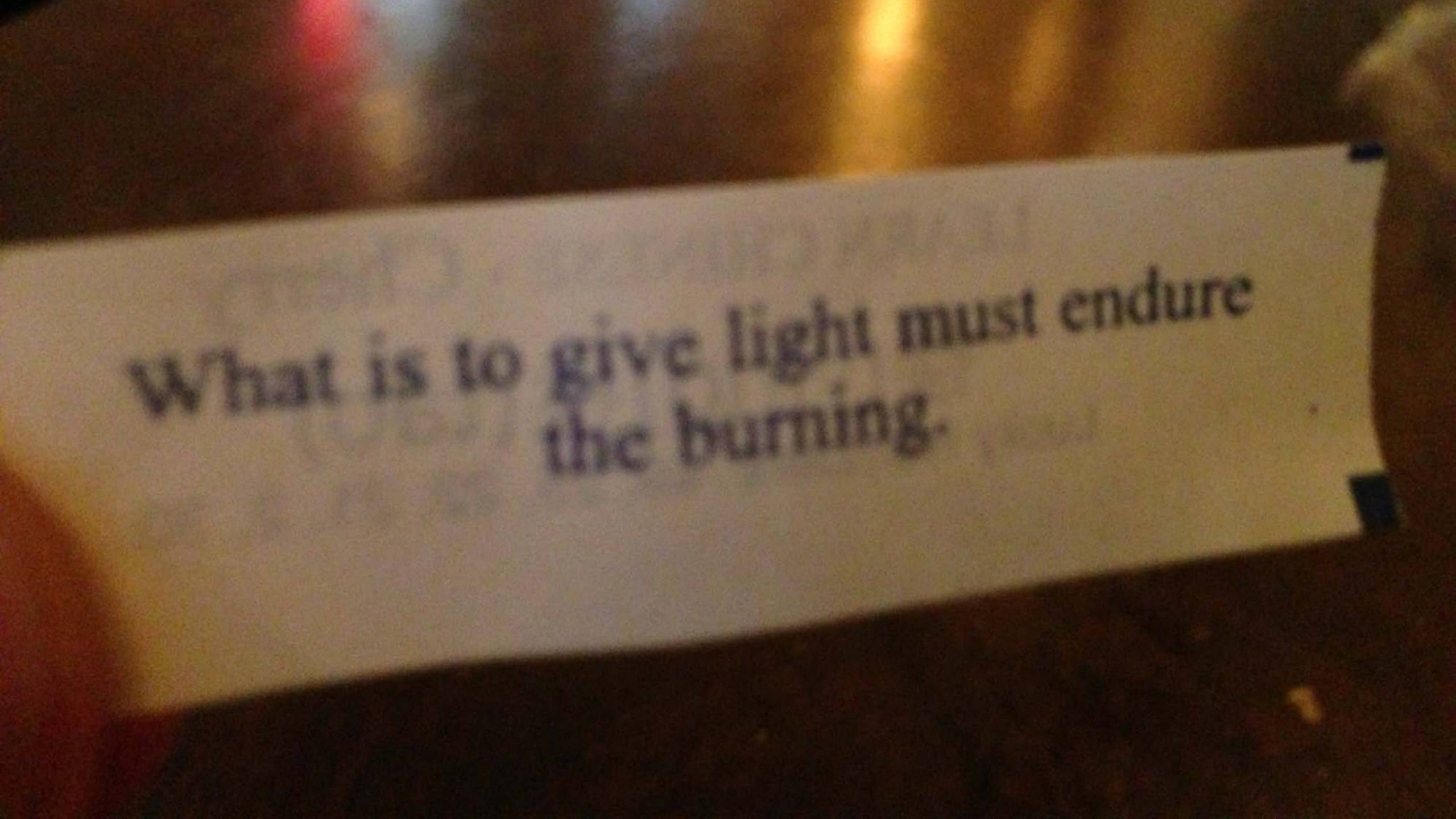
RTP RESEARCH TO PRACTICE

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?

How long have you been in the field of oncology?

1. <1 year
2. 1-5 years
3. 6-10 years
4. 11-15 years
5. 16-20 years
6. 21-40 years
7. >40 years


What is to give light must endure
the burning.

Faculty

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

Ronald Stein, JD, MSN, NP-C, AOCNP
Clinical Instructor of Medicine
USC Norris Comprehensive Cancer Center
Los Angeles, California

Robert Dreicer, MD, MS
Section Head, Medical Oncology
Deputy Director, University of Virginia Comprehensive Cancer Center
Associate Director for Clinical Research
Professor of Medicine and Urology
University of Virginia School of Medicine
Charlottesville, Virginia

Moderator
Neil Love, MD
Research To Practice
Miami, Florida

Sandy Srinivas, MD
Professor of Oncology
Clinical Research Leader, GU Oncology
Stanford University
Stanford, California

RTP
RESEARCH
TO PRACTICE

What I Tell My Patients:
New Treatments and Clinical Trial Options

An NCPD Hybrid Symposium Series
Held During the 47th Annual ONS Congress

Prostate Cancer

Thursday, April 28, 2022
6:00 AM – 7:30 AM PT

Faculty

Kathy D Burns, RN, MSN, AGACNP-BC, OCN
Robert Dreicer, MD, MS
Sandy Srinivas, MD
Ronald Stein, JD, MSN, NP-C, AOCNP

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Agenda

Module 1 – PSA-Only Recurrence (M0 Disease)

Module 2 – Metastatic Hormone-Sensitive Prostate Cancer

Module 3 – Metastatic Castration-Resistant Prostate Cancer (BRCA Wild Type)

Module 4 – Metastatic Castration-Resistant Prostate Cancer (BRCA Mutant)

Agenda

Module 1 – PSA-Only Recurrence (M0 Disease)

Module 2 – Metastatic Hormone-Sensitive Prostate Cancer

Module 3 – Metastatic Castration-Resistant Prostate Cancer (BRCA Wild Type)

Module 4 – Metastatic Castration-Resistant Prostate Cancer (BRCA Mutant)

SELF-ASSESSMENT QUIZ

Available options for androgen deprivation therapy are intramuscular and intravenous only.

1. Agree
2. Disagree
3. I don’t know

RTP
RESEARCH
TO PRACTICE

SELF-ASSESSMENT QUIZ

Men with detectable PSA levels after radical prostatectomy almost always die of metastatic disease.

1. Agree
2. Disagree
3. I don’t know

RTP
RESEARCH
TO PRACTICE

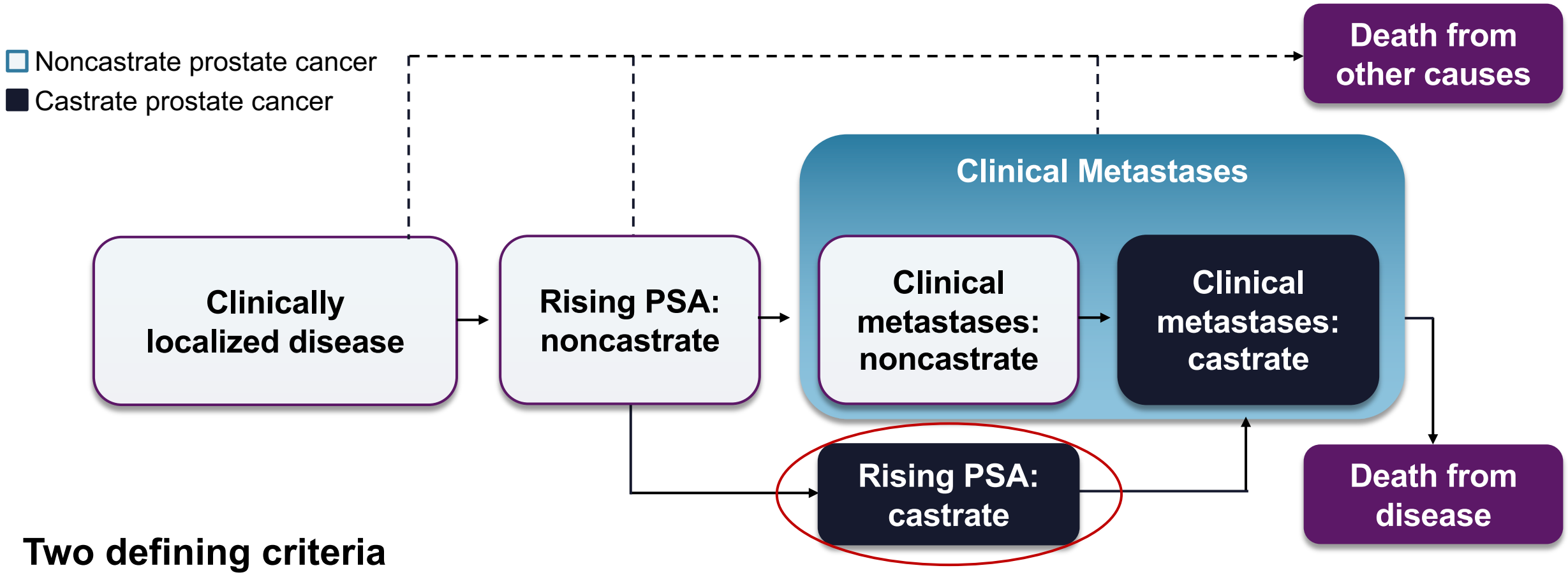
SELF-ASSESSMENT QUIZ

There is no discernible difference between the side-effect profiles of enzalutamide, darolutamide and apalutamide.

1. Agree
2. Disagree
3. I don’t know

RTP
RESEARCH
TO PRACTICE

Clinical Disease States Model of Prostate Cancer[1]

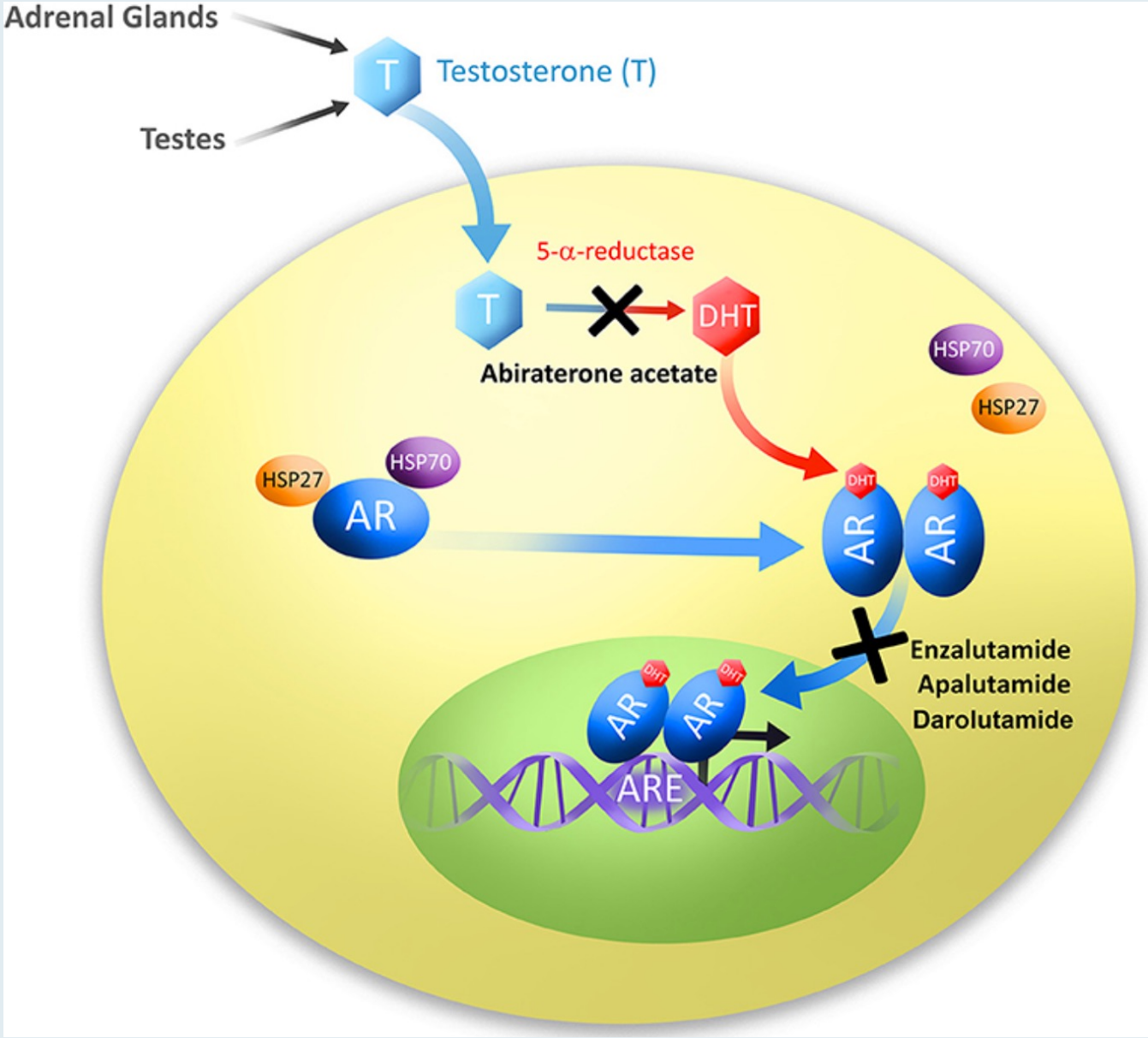


Two defining criteria

- 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.

Androgen Production and Its Targeted Inhibition

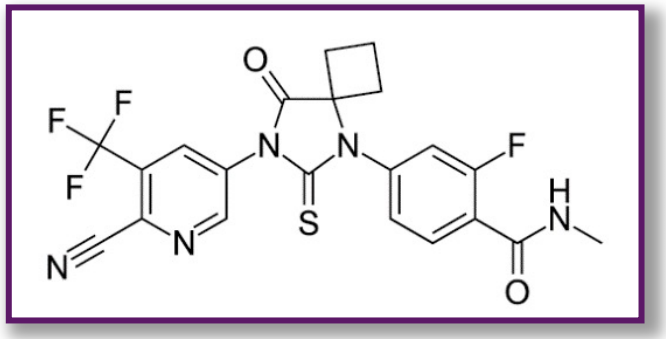


Rice MA et al. *Front Oncol* 2019; https://doi.org/10.3389/fonc.2019.00801

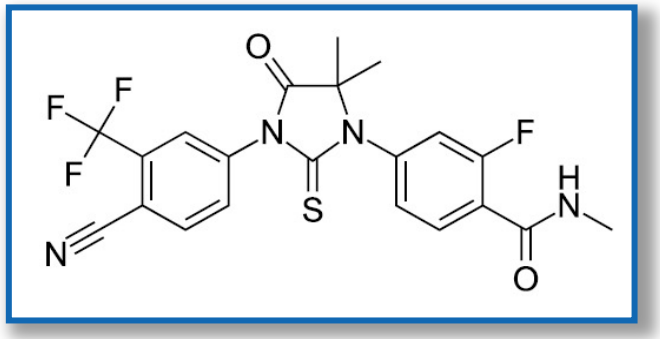
RTP RESEARCH TO PRACTICE

Next-Generation Androgen Receptor Inhibitors[1,2]

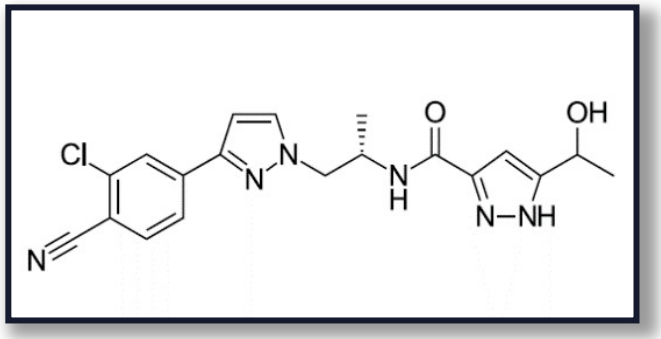
Apalutamide



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 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]*

RTP RESEARCH TO PRACTICE

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.

Lancet 2022;399(10323):447-60.

Abiraterone acetate and prednisolone with or without enzalutamide for high-risk non-metastatic prostate cancer: a meta-analysis of primary results from two randomised controlled phase 3 trials of the STAMPEDE platform protocol

Gerhardt Attard, Laura Murphy, Noel W Clarke, William Cross, Robert J Jones, Christopher C Parker, Silke Gillessen, Adrian Cook, Chris Brawley, Claire L Amos, Nafisah Atako, Cheryl Pugh, Michelle Buckner, Simon Chowdhury, Zafar Malik, J Martin Russell, Clare Gilson, Hannah Rush, Jo Bowen, Anna Lydon, Ian Pedley, Joe M O'Sullivan, Alison Birtle, Joanna Gale, Narayanan Srihari, Carys Thomas, Jacob Tanguay, John Wagstaff, Prantik Das, Emma Gray, Mymoona Alzoueb, Omi Parikh, Angus Robinson, Isabel Syndikus, James Wylie, Anjali Zarkar, George Thalmann, Johann S de Bono, David P Dearnaley, Malcolm D Mason*, Duncan Gilbert, Ruth E Langley, Robin Millman, David Matheson, Matthew R Sydes†, Louise C Brown†, Mahesh K B Parmar†, Nicholas D James†, on behalf of the Systemic Therapy in Advancing or Metastatic Prostate cancer: Evaluation of Drug Efficacy (STAMPEDE) investigators‡*

Balancing the benefits/risks of treatment

- Improved survival
- Delayed progression
- Psychological benefits of receiving treatment

Benefits

Shared decision making: goals of patient

- Expense: COST $$$$... ↓ QOL
- ED and ↓ libido
- Hot flashes
- Changes in mood/ ↓cognition
- ↓ strength/ muscle mass
- Osteoporosis
- Anemia, fatigue
- Metabolic syndrome
- Cardiac risk, DM

Risks

Courtesy of Victoria Sinibaldi, RN, MS, CS, CANP, BC

Questions — Robert Dreicer, MD, MS

PSA-only recurrence (M0 disease)

- **What therapies are used to treat prostate cancer in this setting, and how is treatment selected?**

Commentary — Robert Dreicer, MD, MS

PSA-only recurrence (M0 disease)

- **Baseline data: pathology, primary therapy, time to relapse**
  - **Did the patient need definitive therapy in the first place?**
- **Salvage therapy potential vs s/p maximal local therapy**
- **Conventional vs next generation imaging**
- **Early vs later ADT and its implications**
  - **PSA psychotherapy**

Questions — Kathy D Burns, RN, MSN, AGACNP-BC, OCN

PSA-only recurrence (M0 disease)

- **What are some of the clinical issues that arise for patients in this situation?**
- **What are the key discussion points prior to starting treatment in terms of expected benefits and treatment toxicities?**
- **What are some of the psychosocial issues that arise in this situation?**

RTP
RESEARCH
TO PRACTICE

PSA-only recurrence (M0 disease)

What are some of the clinical issues that arise for patients in this situation?

- **Starting Androgen Deprivation Therapy: variety of medications: injectable versus orals.**
  - **Financial toxicity:**
    - **Pills/relugolix: insurance coverage/patient assistance, education around specialty pharmacies, adherence to taking medication.**
    - **Injections:**
      - **LHRH agonist: Leuprolide, goserelin, triptorelin**
      - **LHRH antagonist degarelix**

Commentary — Kathy D Burns, RN, MSN, AGACNP-BC, OCN

Side effects – managing expectations.

It's important to touch on all of them and give written materials or a reliable website.

- Reduced or absent sexual desire
- Erectile dysfunction (impotence)
- Shrinkage of testicles and penis
- Hot flashes, which may get better or go away with time
- Breast tenderness and growth of breast tissue (gynecomastia)
- Osteoporosis (bone thinning), which can lead to broken bones
- Anemia (low red blood cell counts)
- Decreased mental sharpness/mental fogginess
- Loss of muscle mass
- Weight gain
- Fatigue
- Increased cholesterol levels
- Depression/mood swings

RTP
RESEARCH
TO PRACTICE

Commentary — Kathy D Burns, RN, MSN, AGACNP-BC, OCN

Please provide examples of key discussion points prior to starting treatment in terms of expected benefits and treatment toxicities.

- **Temporary vs long term or permanent?**
- **Are there medications that can help with these side effects?**
- **The importance of maintaining or starting a healthy diet and exercise regimen.**

Please cite brief instructive examples of actual clinical experiences with patients in your practice.

- **A couple in their early 80s was in clinic talking about next steps.**

RTP
RESEARCH
TO PRACTICE

Commentary — Kathy D Burns, RN, MSN, AGACNP-BC, OCN

What are some of the psychosocial issues that arise in this situation?

- Men and their perception of manhood. Feeling like they are out of control: mood swings, more emotionally labile, hot flashes can expose their cancer treatment to others.
- Family caregivers: partners may be severely affected

Agenda

Module 1 – PSA-Only Recurrence (M0 Disease)

Module 2 – Metastatic Hormone-Sensitive Prostate Cancer

Module 3 – Metastatic Castration-Resistant Prostate Cancer (BRCA Wild Type)

Module 4 – Metastatic Castration-Resistant Prostate Cancer (BRCA Mutant)

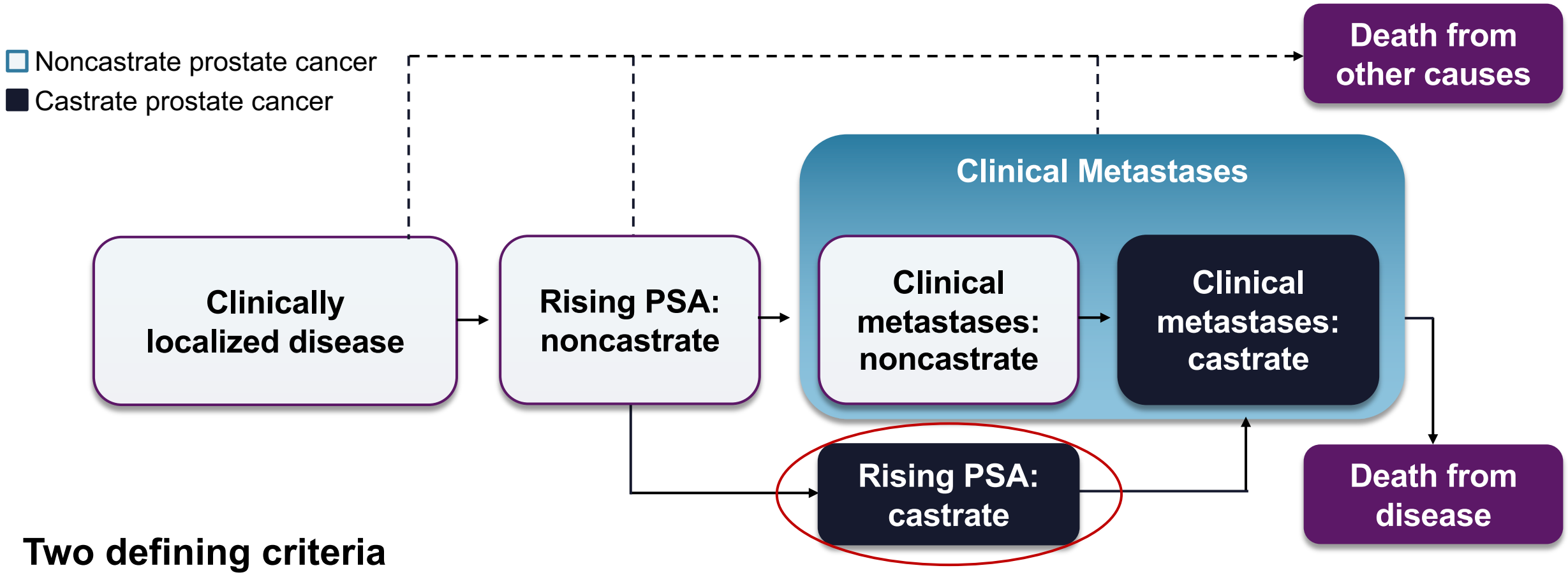
SELF-ASSESSMENT QUIZ

The standard treatment for men who present with metastatic prostate cancer is androgen deprivation therapy.

1. Agree
2. Disagree
3. I don’t know

RTP
RESEARCH
TO PRACTICE

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.

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.

Clinical Decision-Making Hormone-Sensitive Metastatic Disease

- Patient factors
  - Performance status
  - Co-morbidities, i.e. pre-existing peripheral neuropathy
  - I hate taking pills doc etc.
- Disease factor
  - Extent of disease, volume of disease, presence/absence of visceral i.e. liver metastases
  - Non AR biology, i.e. poor psa expresser, significant neuroendocrine features
- Economic factors
  - Non viable co-pay or oral agents

Courtesy of Robert Dreicer, MD, MS

ASCO Genitourinary Cancers Symposium

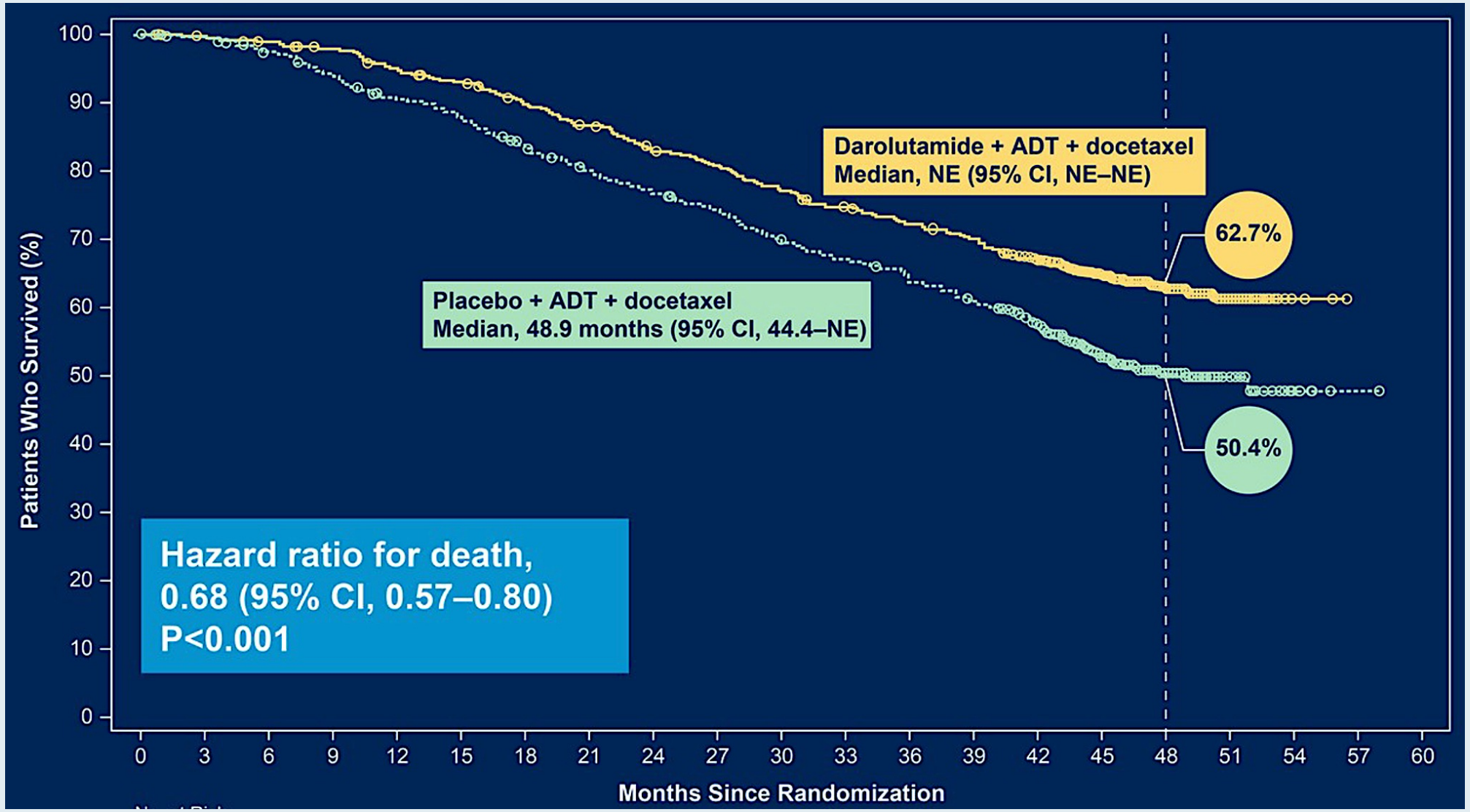
Overall survival with darolutamide versus placebo in combination with androgen-deprivation therapy and docetaxel for metastatic hormone-sensitive prostate cancer in the phase 3 ARASENS trial

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

[1]Massachusetts General Hospital Cancer Center, Boston, MA; [2]Northwestern University, Feinberg School of Medicine, Chicago, IL; [3]University of Montreal Hospital Center, Montreal, Quebec, Canada; [4]Institut Gustave Roussy, University of Paris-Saclay, Villejuif, France; [5]Englander Institute for Precision Medicine, Weill Cornell Department of Medicine, Meyer Cancer Center, New York-Presbyterian Hospital, New York, NY; [6]UC San Diego School of Medicine, San Diego, CA; [7]Clinical Oncological Dispensary of Omsk Region, Omsk, Russian Federation; [8]Norton Cancer Institute, Louisville, KY; [9]P. Hertsen Moscow Oncology Research Institute, Moscow, Russian Federation; [10]UGC Intercentros de Oncología Médica, Hospitales Universitarios Regional y Virgen Victoria, IBIMA, Málaga, Spain; [11]Fudan University Shanghai Cancer Center, Xuhui District, Shanghai, China; [12]Ashford Cancer Centre Research, Kurralta Park, SA, Australia; [13]Núcleo de Pesquisa e Ensino da Rede São Camilo, São Paulo, Brazil; [14]Tampere University Hospital, Tampere, Finland; [15]Toho University Sakura Medical Center, Chiba, Japan; [16]Orion Corporation Orion Pharma, Espoo, Finland; [17]Bayer AG, Berlin, Germany; [18]Bayer HealthCare Pharmaceuticals Inc., Whippany, NJ, USA; [19]Division of Urology, IREC, Cliniques Universitaires Saint Luc, UCLouvain, Brussels, Belgium

ASCO GU 2022; Abstract 13.

ARASENS: Primary Endpoint — Overall Survival



Smith MR et al. Genitourinary Cancers Symposium 2022;Abstract 13.

RTP RESEARCH TO PRACTICE

ARASENS: Grade 3-4 Adverse Events

Grade 3–4 AEs in ≥2% of darolutamide-treated patients, n (%)	Darolutamide + ADT + docetaxel (n=652)	Placebo + ADT + docetaxel (n=650)
Any AE	431 (66.1)	413 (63.5)
Neutropenia*	220 (33.7)	222 (34.2)
Febrile neutropenia	51 (7.8)	48 (7.4)
Hypertension	42 (6.4)	21 (3.2)
Anemia	31 (4.8)	33 (5.1)
Pneumonia	21 (3.2)	20 (3.1)
Hyperglycemia	18 (2.8)	24 (3.7)
Increased alanine aminotransferase	18 (2.8)	11 (1.7)
Increased aspartate aminotransferase	17 (2.6)	7 (1.1)
Increased weight	14 (2.1)	8 (1.2)
Urinary tract infection	13 (2.0)	12 (1.8)

Smith MR et al. Genitourinary Cancers Symposium 2022;Abstract 13.

ARASENS: Adverse Events of Special Interest with Androgen Receptor (AR) Pathway Inhibitors

AEs associated with AR pathway inhibitor therapy	Darolutamide + ADT + docetaxel (n=652)		Placebo + ADT + docetaxel (n=650)	
	Patients, n (%)	EAIR/100 PY*	Patients, n (%)	EAIR/100 PY*
Fatigue	216 (33.1)	12.5	214 (32.9)	17.8
Bone fracture	49 (7.5)	2.8	33 (5.1)	2.7
Falls	43 (6.6)	2.5	30 (4.6)	2.5
Rash†	108 (16.6)	6.2	88 (13.5)	7.3
Diabetes mellitus and hyperglycemia‡	99 (15.2)	5.7	93 (14.3)	7.7
Weight decreased	22 (3.4)	1.3	35 (5.4)	2.9
Vasodilatation and flushing	133 (20.4)	7.7	141 (21.7)	11.7
Breast disorders/gynecomastia‡	21 (3.2)	1.2	10 (1.5)	0.8
Hypertension‡	89 (13.7)	5.1	60 (9.2)	5.0
Cardiac disorder‡	71 (10.9)	4.1	76 (11.7)	6.3
Cerebral ischemia	8 (1.2)	0.5	8 (1.2)	0.7
Mental impairment disorder‡	23 (3.5)	1.3	15 (2.3)	1.2
Depressed mood disorder‡	21 (3.2)	1.2	24 (3.7)	2.0
Seizure	4 (0.6)	0.2	1 (0.2)	0.1

Smith MR et al. Genitourinary Cancers Symposium 2022;Abstract 13.

PEACE-1: Study Design

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

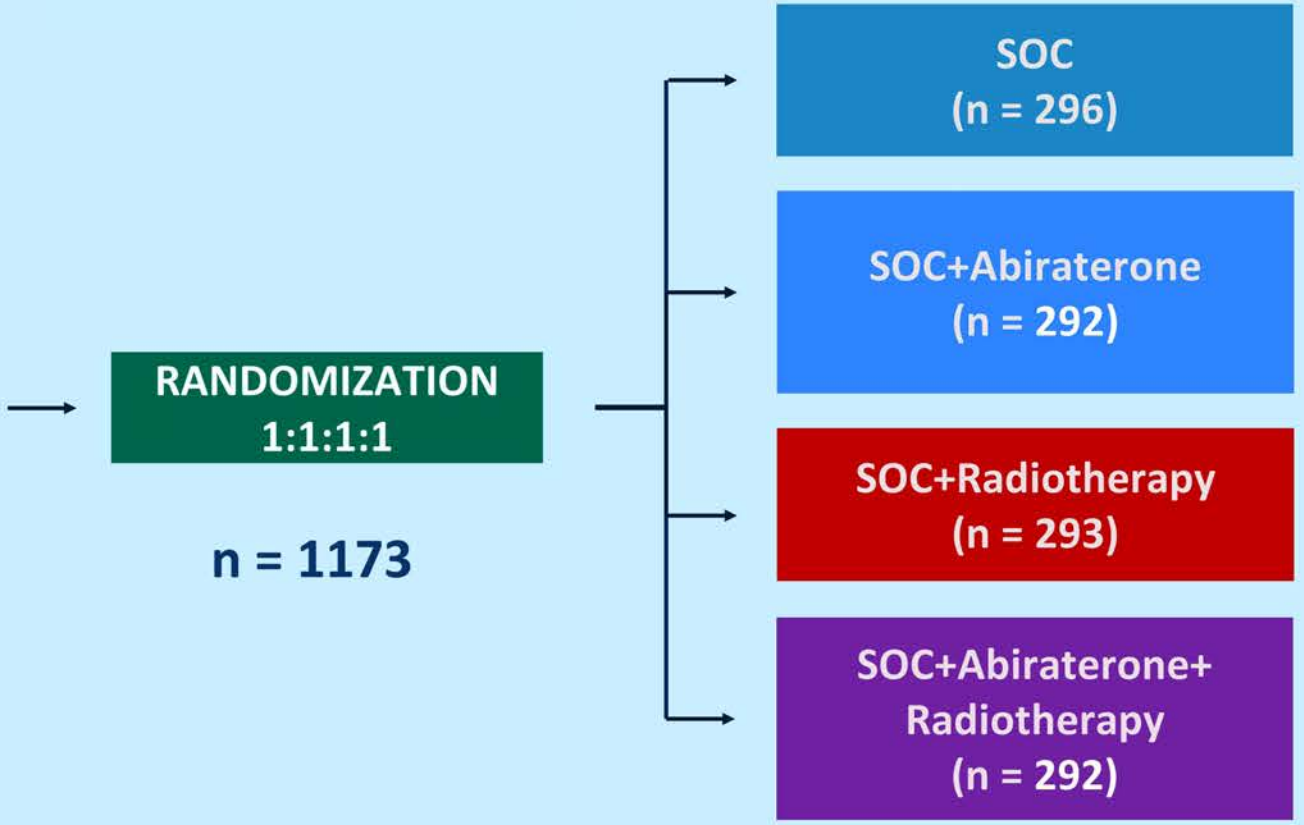
Stratification

ECOG PS (0 vs 1-2)

Metastatic sites (LN vs bone vs visceral)

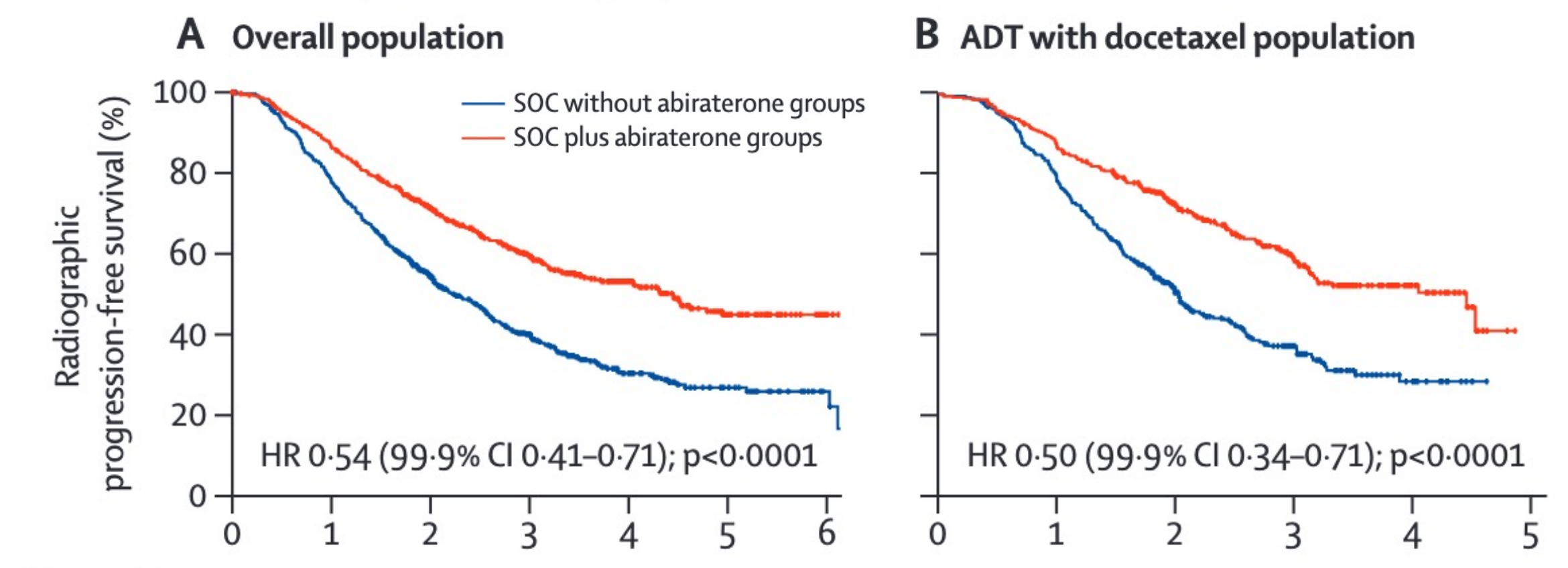
Type of castration (orchidectomy vs LHRH agonist vs LHRH antagonist)

Docetaxel (yes vs no)



Fizazi K et al. ASCO 2021;Abstract 5000.

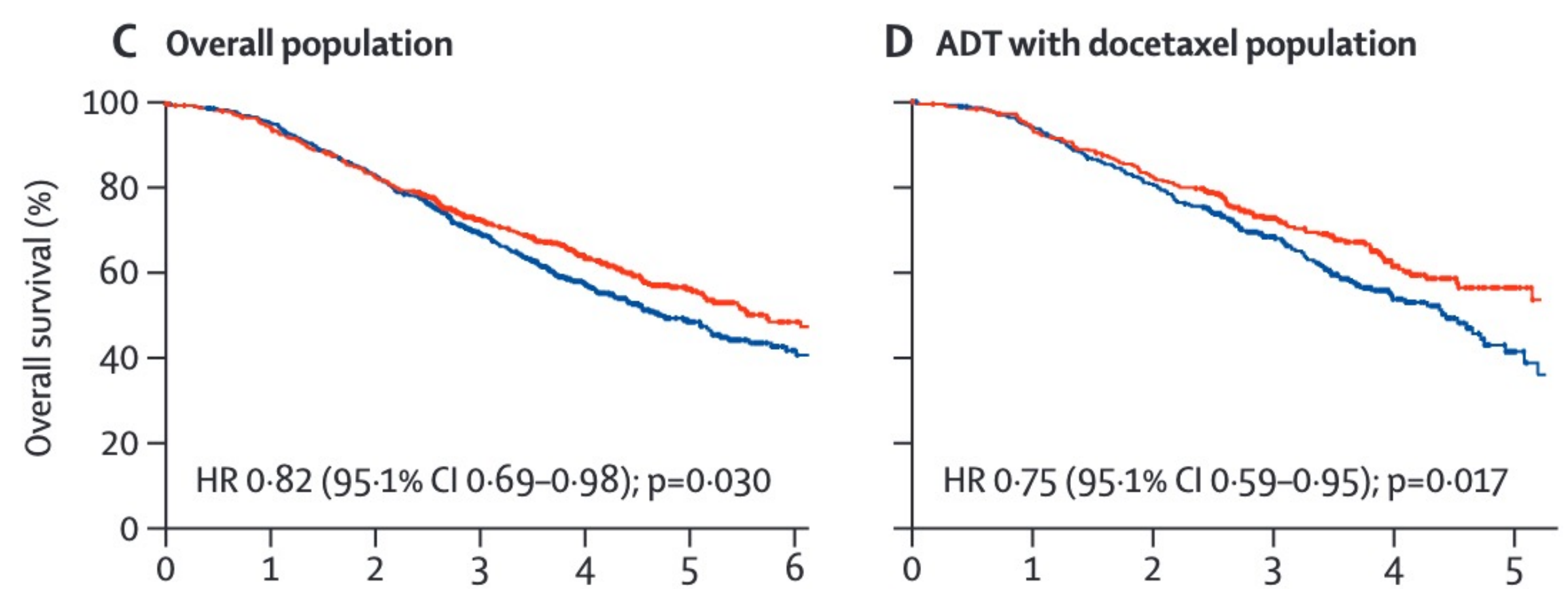
PEACE-1: Radiographic Progression-Free Survival



Fizazi K et al. *Lancet* 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

PEACE-1: Overall Survival



Fizazi K et al. *Lancet* 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

Questions — Sandy Srinivas, MD

Metastatic hormone-sensitive prostate cancer

- **What therapies are used to treat prostate cancer in this setting, and how is treatment selected?**

Commentary — Sandy Srinivas, MD

Metastatic hormone-sensitive prostate cancer

- **ADT is the backbone for the treatment of mHSPC**
- **Adding either docetaxel or abiraterone improved OS by 30%**
- **Benefit of docetaxel clear in high volume vs low volume disease**
- **Debate over docetaxel vs abiraterone: multiple choices; efficacy the same**
- **ARI: apalutamide/enzalutamide superior to ADT alone**
- **Triple Rx: PEACE-1: ADT + Docetaxel + Abiraterone > ADT + Docetaxel**
- **ARASENS: ADT + Docetaxel + Darolutamide > ADT + Docetaxel**
- **Selection of Rx: High volume vs low volume; de novo vs metachronous; chemo fitness; frailty; comorbidities; # HTN meds; cardiac health; support @home**

RTP
RESEARCH
TO PRACTICE

Commentary — Sandy Srinivas, MD

mHSPC trials

Trial name	Experimental arm	Comparator arm	rPFS	OS
CHAARTED[1]	Docetaxel	ADT	32 vs 19 mo	HR: 0.72; 57.6 vs 47.2 mo
STAMPEDE-C[2]	Docetaxel	ADT	44 vs 34.8 mo, HR: 0.61	HR: 0.81; 81 vs 71 mo
LATITUDE[3]	Abiraterone	ADT	NR	HR: 0.66; 53.3 vs 36.5 mo
STAMPEDE-G[4]	Abiraterone	ADT	NR	HR: 0.6; 6.6 vs 3.8 y
ARCHES[5]	Enzalutamide	ADT	HR: 0.39 NR vs 19	HR: 0.66; NR vs NR
ENZAMET[6]	Enzalutamide	ADT + NSAA with docetaxel	HR: 0.34 HR: 0.48	HR: 0.53 HR: 90
TITAN[7]	Apalutamide	ADT	HR: 0.48	HR: 0.67; NR vs 52.2
PEACE-1[8]	Abiraterone	ADT + docetaxel	4.5 vs 2 y HR: 0.50	HR: 0.75
ARASENS[9]	Darolutamide	ADT + docetaxel	NR	HR: 0.68; NR vs 48.9 mo

1. Sweeney C *NEJM* 2015; 2. James ND *Eur Urol* 2015; 3. Fizazi K *Lancet Oncol* 2019; 4. Clark N *Ann Oncol* 2019; 5. Armstrong A *J Clin Oncol* 2019; 6. Davis *NEJM* 2019; 7. Chi KN *NEJM* 2019; 8. Fizazi *Lancet* 2022; 9. Smith MR *NEJM* 2022

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

Metastatic hormone-sensitive prostate cancer

- **What are some of the clinical issues that arise for patients in this situation?**
- **What are key discussion points prior to starting treatment in terms of expected benefits and treatment toxicities?**
- **What are some of the psychosocial issues that arise in this situation?**

RTP
RESEARCH
TO PRACTICE

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

Metastatic hormone-sensitive prostate cancer

Associated clinical issues:

-pain
-swelling/lymphedema to lower extremities/scrotum
-fatigue
-GU problems
-unintentional weight loss
-cough/dyspnea/effusion (eg, lung mets)
-anemia

Key discussion points prior to treatment:

-stage IV prostate CA is treatable but not curable
-treatment will be life-long and change based on response
-potential ADT side effects, including decreased libido, erectile dysfunction, fatigue, weight gain, insulin resistance and osteopenia/osteoporosis
-potential chemo side effects including pancytopenia, alopecia, neuropathy, n/v/d, fever
-importance of exercise
-regular PSA testing and lab monitoring; scans in the event of PSA increase

RTP RESEARCH TO PRACTICE

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

Instructive examples:

-sending pt to ER for fever

-chemotherapy education

-hospital admission for misc reasons (neutropenic fever, AKI)

-discussions about sexuality/ED

-seizures (seen with enzalutamide)

Psychological issues:

-sexuality and intimacy

-meaning of stage IV disease

-potential genetic and family implications

-depression and anxiety

-employment issues/disability

-weight gain

-guilt

-economic stress, eg, treatment affordability

RTP RESEARCH TO PRACTICE

Agenda

Module 1 – PSA-Only Recurrence (M0 Disease)

Module 2 – Metastatic Hormone-Sensitive Prostate Cancer

Module 3 – Metastatic Castration-Resistant Prostate Cancer (BRCA Wild Type)

Module 4 – Metastatic Castration-Resistant Prostate Cancer (BRCA Mutant)

SELF-ASSESSMENT QUIZ

Radium-223 is a therapy for patients with prostate cancer and...

1. Bone metastases
2. Visceral metastases
3. Brain metastases
4. All of the above
5. I don’t know

RTP
RESEARCH
TO PRACTICE

SELF-ASSESSMENT QUIZ

^{117}Lu-PSMA-617 is a newly approved treatment for prostate cancer that is administered by a…

1. Medical oncologist
2. Radiation oncologist
3. Nuclear medicine specialist
4. Either 2 or 3
5. I don’t know

RTP RESEARCH TO PRACTICE

SELF-ASSESSMENT QUIZ

Which of the following is a potential side effect of ^{177}Lu-PSMA-617?

1. Alopecia
2. Dry mouth
3. Gastrointestinal toxicity
4. All of the above
5. I don’t know

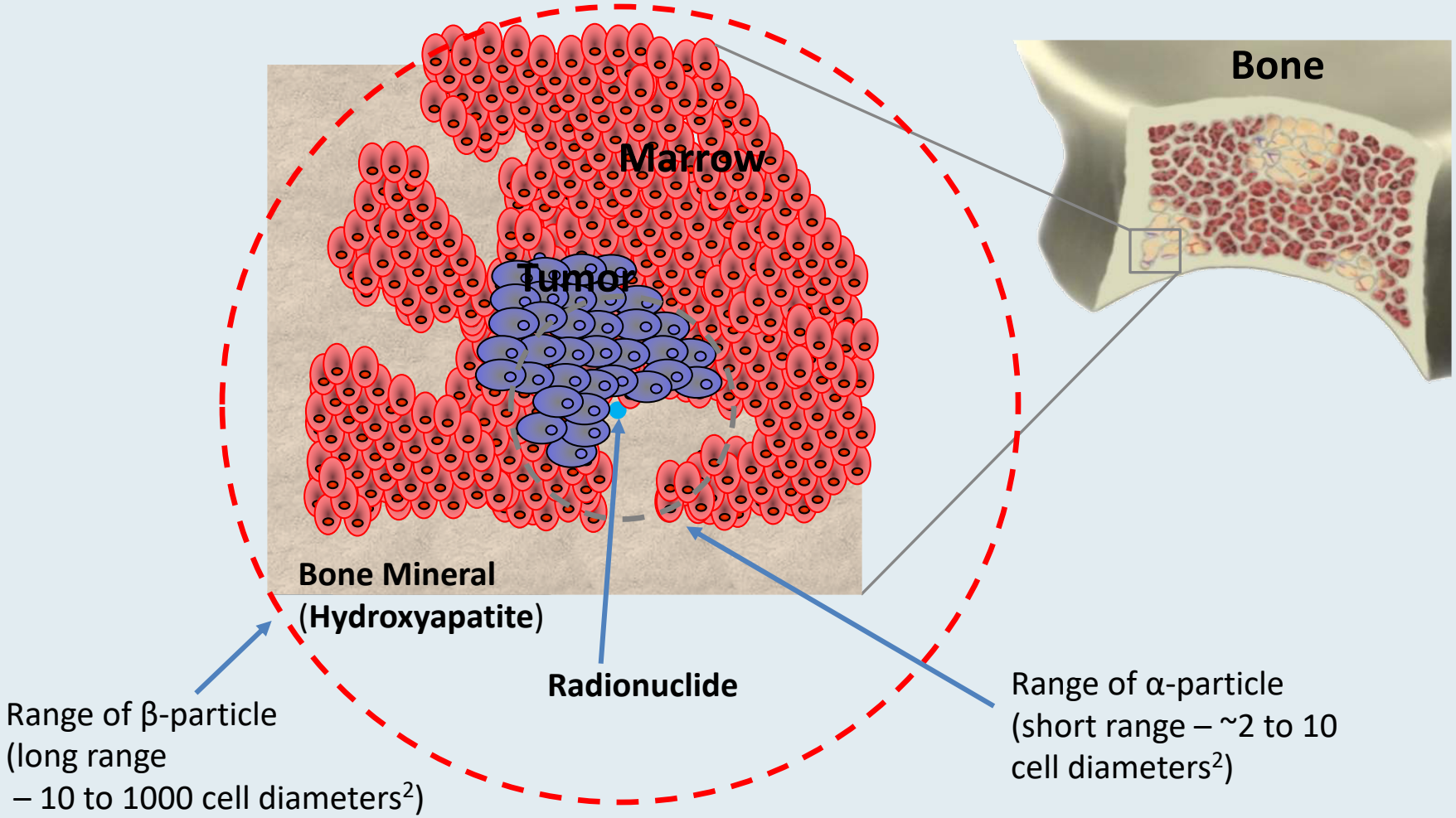
RTP
RESEARCH
TO PRACTICE

Management of Metastatic Castration-Resistant Prostate Cancer

- Enzalutamide
- Abiraterone/prednisone
- Radium-223
- Sipuleucel-T
- Chemotherapy (cabazitaxel, docetaxel)
- ^{177}Lu-PSMA-617
- PARP inhibitors

Range of an α-emitting Radiopharmaceutical Compared to a β-emitter

Short range of α-particles could reduce bone marrow exposure[1]



References: 1. Henriksen G, et al. *Cancer Res*. 2002;62:3120–3125. **2.** Brechbiel MW. *Dalton Trans*. 2007;43:4918-4928.

RTP RESEARCH TO PRACTICE

Nursing implications: Radium-223

- Fatigue
- GI: Nausea, Vomiting, Diarrhea
- Peripheral edema
- Pancytopenia: Anemia, Lymphopenia, leukopenia, thrombocytopenia, neutropenia
- Black tarry stools
- CP, Chills, Cough
- Erythema at the injection site

Courtesy of Victoria Sinibaldi, RN, MS, CS, CANP, BC

FDA Approves ^{177}Lu-PSMA-617 for mCRPC

Press Release: March 23, 2022

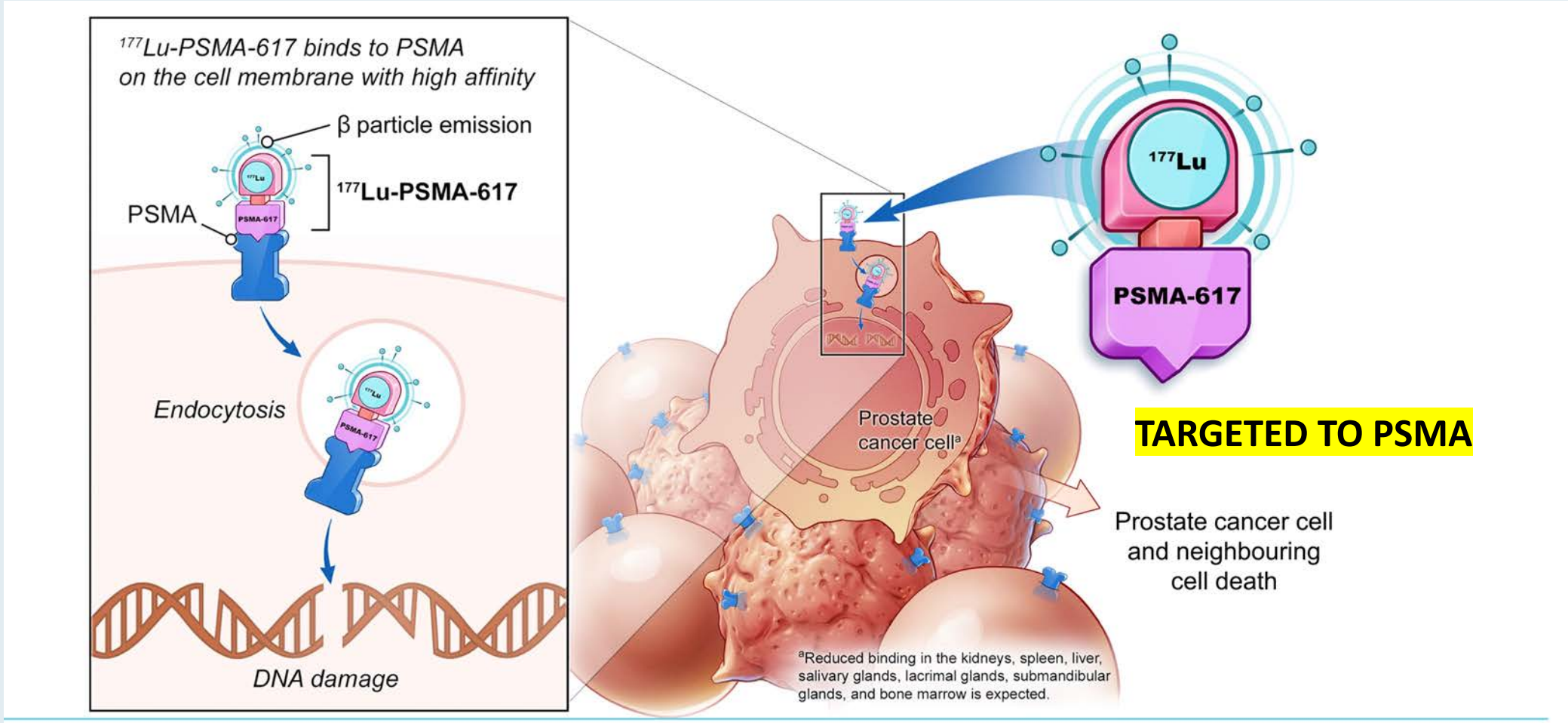
On March 23, 2022, the Food and Drug Administration approved the radioligand therapy ^{177}Lu-PSMA-617 for the treatment of prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) in adult patients who have received treatment with androgen receptor pathway inhibition and taxane-based chemotherapy.

On the same day, the FDA approved gallium Ga 68 gozetotide, a radioactive diagnostic agent for positron emission tomography (PET) of PSMA-positive lesions, including selection of patients with metastatic prostate cancer for whom ^{177}Lu-PSMA-617 PSMA-directed therapy is indicated. Gallium Ga 68 gozetotide is the first radioactive diagnostic agent approved for patient selection for a radioligand therapeutic agent.

Efficacy was evaluated in the Phase III VISION trial, which demonstrated a statistically significant improvement in the primary endpoints OS and radiographic progression-free survival. Hazard ratio (HR) for OS was 0.62 (95% CI: 0.52-0.74; $p < 0.001$) for the comparison of ^{177}Lu-PSMA-617 with best standard care (BSoC) to BSoC. Median OS was 15.3 months (95% CI: 14.2-16.9) on the ^{177}Lu-PSMA-617 with BSoC arm and 11.3 months (95% CI: 9.8, 13.5) on the BSoC arm.

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-pluvicto-metastatic-castration-resistant-prostate-cancer

^{177}Lu-PSMA-617: Mechanism of Action



Morris MJ et al. ASCO 2021;Abstract LBA4.

N Engl J Med 2021;385:1091-103

The NEW ENGLAND JOURNAL of MEDICINE

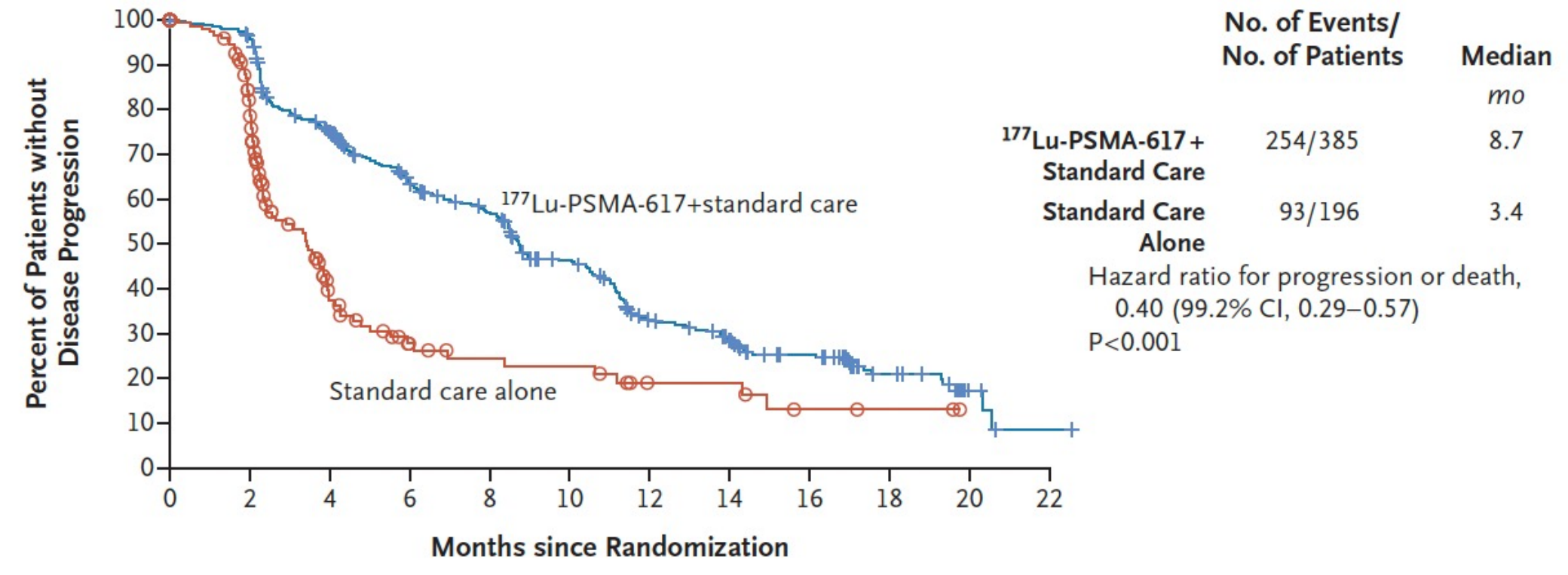
ORIGINAL ARTICLE

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

O. Sartor, J. de Bono, K.N. Chi, K. Fizazi, K. Herrmann, K. Rahbar, S.T. Tagawa, L.T. Nordquist, N. Vaishampayan, G. El-Haddad, C.H. Park, T.M. Beer, A. Armour, W.J. Pérez-Contreras, M. DeSilvio, E. Kpamegan, G. Gericke, R.A. Messmann, M.J. Morris, and B.J. Krause, for the VISION Investigators*

VISION: Efficacy Summary

Imaging–based progression-free survival



- Median OS (^{177}Lu-PSMA-617 vs standard therapy): 15.3 mo vs 11.3 mo (HR 0.62, $p < 0.001$)
- Time to first symptomatic skeletal event (^{177}Lu-PSMA-617 vs standard therapy): 11.5 mo vs 6.8 mo (HR 0.50, $p < 0.001$)

Sartor O et al. *N Engl J Med* 2021;385:1091-103.

RTP RESEARCH TO PRACTICE

VISION: Selected Adverse Events

Event	^{177}Lu-PSMA-617 plus Standard Care (N = 529)		Standard Care Alone (N = 205)	
	All Grades	Grade ≥3	All Grades	Grade ≥3
	number of patients (percent)			
Any adverse event	519 (98.1)	279 (52.7)	170 (82.9)	78 (38.0)
Adverse event that occurred in >12% of patients				
Fatigue	228 (43.1)	31 (5.9)	47 (22.9)	3 (1.5)
Dry mouth	205 (38.8)	0	1 (0.5)	0
Thrombocytopenia	91 (17.2)	42 (7.9)	9 (4.4)	2 (1.0)
Lymphopenia	75 (14.2)	41 (7.8)	8 (3.9)	1 (0.5)
Leukopenia	66 (12.5)	13 (2.5)	4 (2.0)	1 (0.5)
Adverse event that led to reduction in ^{177}Lu-PSMA-617 dose	30 (5.7)	10 (1.9)	NA	NA
Adverse event that led to interruption of ^{177}Lu-PSMA-617†	85 (16.1)	42 (7.9)	NA	NA
Adverse event that led to discontinuation of ^{177}Lu-PSMA-617†	63 (11.9)	37 (7.0)	NA	NA
Adverse event that led to death‡	19 (3.6)	19 (3.6)	6 (2.9)	6 (2.9)

Sartor O et al. *N Engl J Med* 2021;385:1091-103.

RTP RESEARCH TO PRACTICE

Questions — Robert Dreicer, MD, MS

Metastatic castration-resistant prostate cancer (BRCA wild type)

- **What therapies are used to treat prostate cancer in this setting, and how is treatment selected?**

Commentary — Robert Dreicer, MD, MS

Metastatic castration-resistant prostate cancer (BRCA wild type)

- **mCRPC biochemically defined vs overt radiographic/symptomatic progression**
- **Disease related symptoms?**
- **Status and implications of prior therapies (cSMPC and mCRPC)**
- **Educating the patient, it's a journey not a race to the next treatment**

Questions — Kathy D Burns, RN, MSN, AGACNP-BC, OCN

Metastatic castration-resistant prostate cancer (BRCA wild type)

- **What are some of the clinical issues that arise for patients in this situation?**
- **What are key discussion points prior to starting treatment in terms of expected benefits and treatment toxicities?**
- **What are some of the psychosocial issues that arise in these situations?**

RTP
RESEARCH
TO PRACTICE

Commentary — Kathy D Burns, RN, MSN, AGACNP-BC, OCN

Metastatic castration-resistant prostate cancer (BRCA wild type)

What are some of the clinical issues that arise for patients in this situation?

- **Financial toxicity/navigating insurance coverage**
- **Ability to work/socialize related to fatigue**
- **Pain**
- **Mobility/exercise**
- **Bone strength**

RTP RESEARCH TO PRACTICE

Commentary — Kathy D Burns, RN, MSN, AGACNP-BC, OCN

Please provide examples of key discussion points prior to starting treatment in terms of expected benefits and treatment toxicities.

- **Quality of life**
- **Dealing with stress related to scans and PSA**
- **Dealing with side effects of treatment**
- **Body image related to chemotherapy/long-term ADT**

Please cite brief instructive examples of actual clinical experiences with patients in your practice.

- **Men in our prostate support group – conversations between men**
- **Strategies for symptom mgmnt: empowering men to have control over symptoms**

RTP
RESEARCH
TO PRACTICE

Commentary — Kathy D Burns, RN, MSN, AGACNP-BC, OCN

What are some of the psychosocial issues that arise in these situations?

- **Men considering refusing or discontinuing treatment**
- **Low testosterone can mean lack of motivation for healthy behaviors**

RTP
RESEARCH
TO PRACTICE

Agenda

Module 1 – PSA-Only Recurrence (M0 Disease)

Module 2 – Metastatic Hormone-Sensitive Prostate Cancer

Module 3 – Metastatic Castration-Resistant Prostate Cancer (BRCA Wild Type)

Module 4 – Metastatic Castration-Resistant Prostate Cancer (BRCA Mutant)

RTP
RESEARCH
TO PRACTICE

SELF-ASSESSMENT QUIZ

All patients with metastatic castration-resistant prostate cancer should undergo germline DNA repair mutation testing regardless of family history.

1. Agree
2. Disagree
3. I don’t know

RTP RESEARCH TO PRACTICE

SELF-ASSESSMENT QUIZ

The most common DNA repair mutation in prostate cancer is...

1. BRCA1
2. BRCA2
3. ATM
4. CHEK2
5. I don’t know

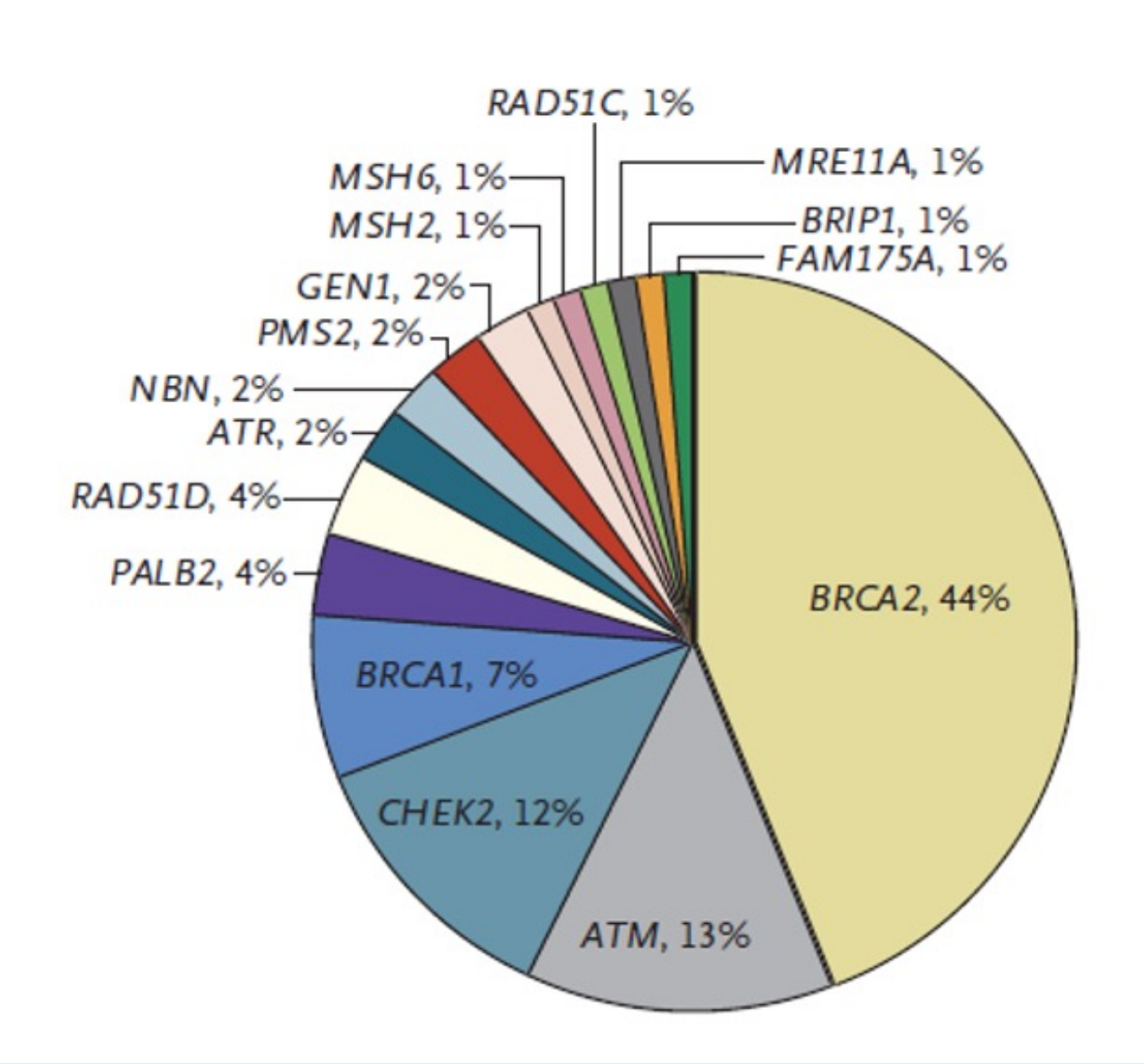
RTP RESEARCH TO PRACTICE

SELF-ASSESSMENT QUIZ

Patients who are receiving PARP inhibitors frequently experience which of the following side effects?

1. Gastrointestinal toxicity
2. Cytopenias
3. Both 1 and 2
4. Neither 1 nor 2
5. I don’t know

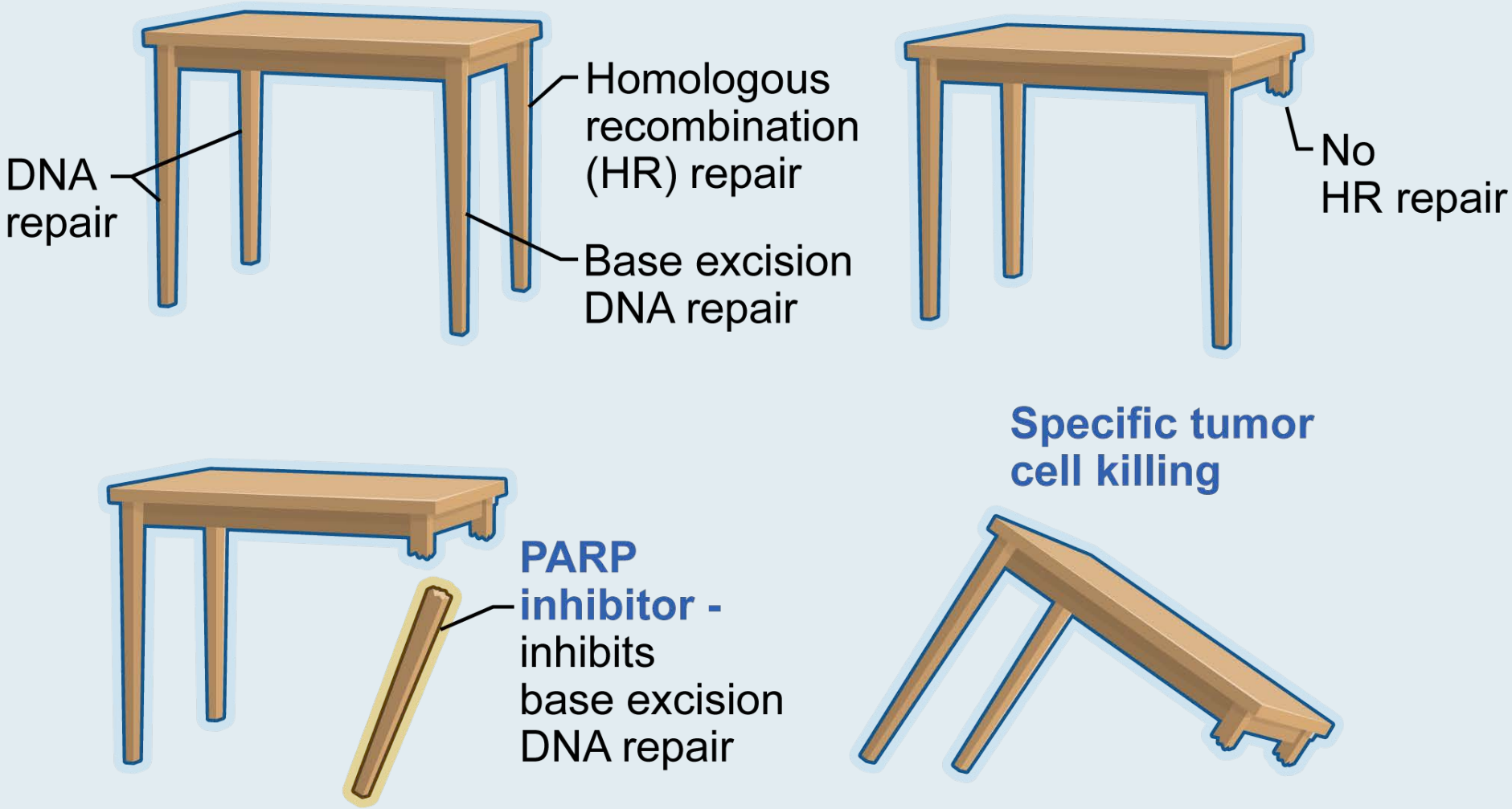
Inherited DNA Repair Gene Mutations in Men with Metastatic Prostate Cancer



- Multicenter study of 692 men
- Deleterious mutations were found in 82 men (11.8%) in 16 genes
- Observed rate exceeded that associated with localized prostate cancer (4.6%) and general population without cancer (2.7%)

Courtesy of Matthew Smith, MD, PhD

Mechanism of Cell Death from Synthetic Lethality Induced by PARP Inhibition



Courtesy of Jenny C Chang, MD

ASCO® Genitourinary Cancers Symposium

PROpel: phase III trial of olaparib and abiraterone versus placebo and abiraterone as first-line therapy for patients with metastatic castration-resistant prostate cancer

Fred Saad, Andrew J. Armstrong, Antoine Thiery-Vuillemin, Mototsugu Oya, Eugenia Loredo, Giuseppe Procopio, Juliana de Menezes, Gustavo Girotto, Cagatay Arslan, Niven Mehra, Francis Parnis, Emma Brown, Friederike Schlürmann, Jae Young Joung, Mikio Sugimoto, Christian Poehlein, Elizabeth A. Harrington, Chintu Desai, Jinyu Kang, and Noel Clarke

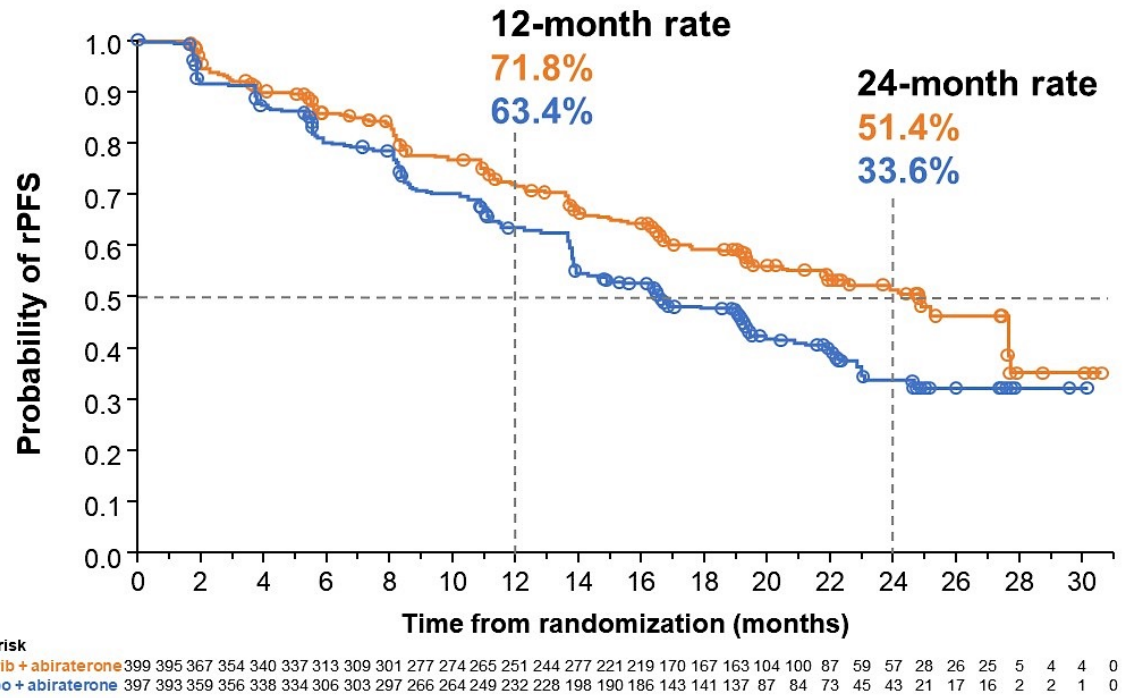
ClinicalTrials.gov identifier: NCT03732820.

Genitourinary Cancers Symposium 2022;Abstract 11.

PROpel: Olaparib and Abiraterone versus Placebo and Abiraterone as First-Line Therapy for mCRPC

Primary Endpoint: Investigator-Assessed Radiographic Progression-Free Survival (rPFS)

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



	Olaparib + abiraterone (n=399)	Placebo + abiraterone (n=397)
Events, n (%)	168 (42.1)	226 (56.9)
Median rPFS (months)	24.8	16.6
HR (95% CI)	0.66 (0.54–0.81); *P*<0.0001	

Pre-specified 2-sided alpha: 0.0324

Median rPFS improvement of 8.2 months favors olaparib + abiraterone*

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

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

ASCO® Genitourinary Cancers Symposium

Phase 3 MAGNITUDE study: First results of niraparib (NIRA) with abiraterone acetate and prednisone (AAP) as first-line therapy in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC) with and without homologous recombination repair (HRR) gene alterations

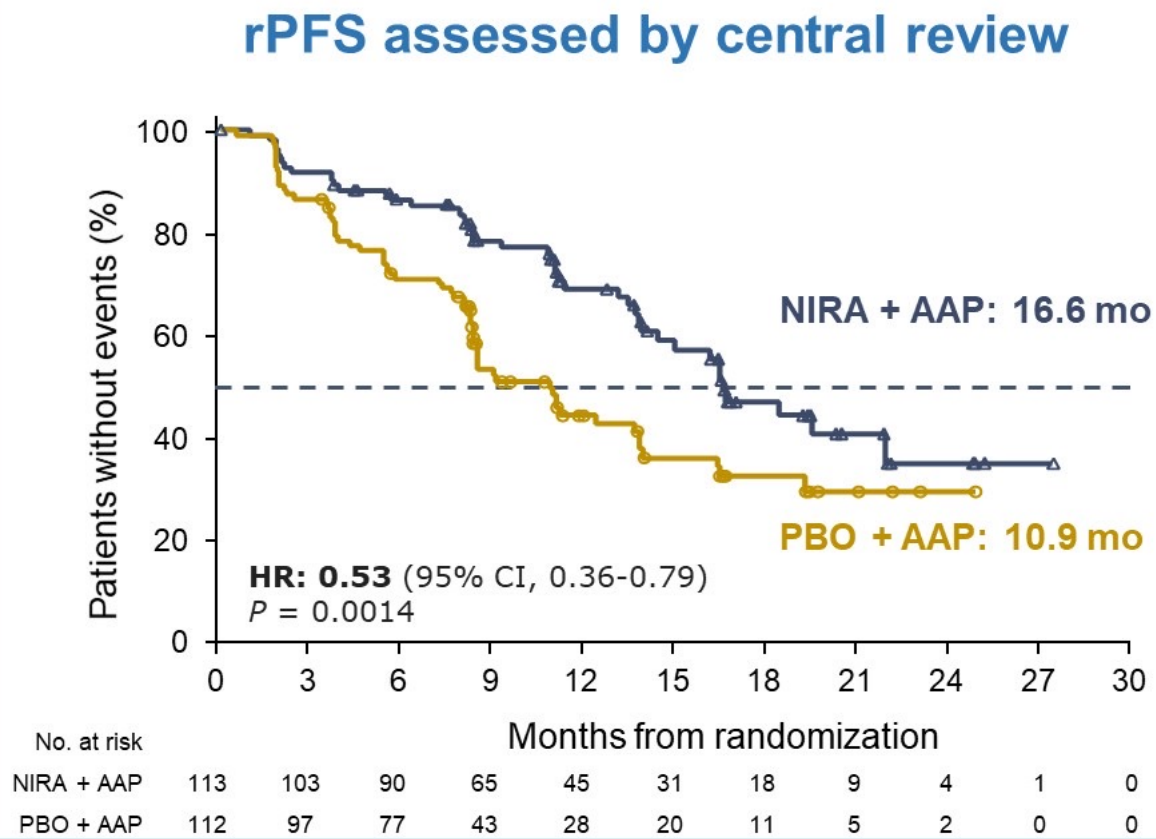
Kim N. Chi,[1] Dana E. Rathkopf,[2] Matthew R. Smith,[3] Eleni Efstathiou,[4] Gerhardt Attard,[5] David Olmos,[6] Ji Youl Lee,[7] Eric J. Small,[8] Andrea J. Pereira de Santana Gomes,[9] Guilhem Roubaud,[10] Marniza Saad,[11] Bogdan Zurawski,[12] Valerii Sakalo,[13] Gary E. Mason,[14] Adam del Corral,[15] George Wang,[14] Daphne Wu,[16] Brooke Diorio,[17] Angela Lopez-Gitlitz,[16] Shahneen Sandhu[18]

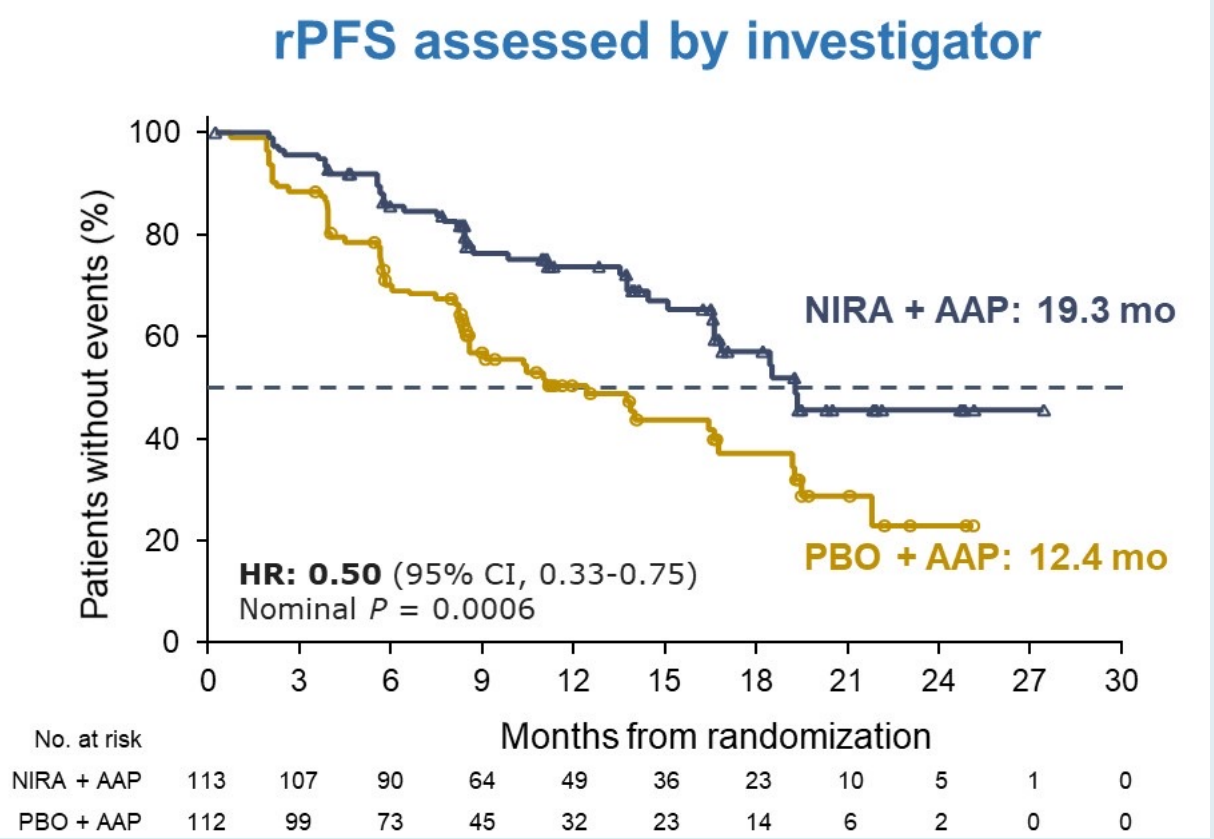
[1]University of British Columbia, BC Cancer – Vancouver Center, Vancouver, BC, Canada; [2]Memorial Sloan Kettering Cancer Center and Weill Cornell Medicine, New York, NY, USA; [3]Massachusetts General Hospital Cancer Center and Harvard Medical School, Boston, MA, USA; [4]Houston Methodist Cancer Center, Houston, TX, USA; [5]University College London, London, UK; [6]Department of Medical Oncology, Hospital Universitario 12 de Octubre, Instituto de Investigación Sanitaria Hospital 12 de Octubre (imas12), Madrid, Spain; [7]Department of Urology Cancer Center, Seoul St. Mary's Hospital, The Catholic University of Korea, Seoul, South Korea; [8]Helen Diller Family Comprehensive Cancer Center, University of California San Francisco, San Francisco, CA, USA; [9]Liga Norte Riograndense Contra o Câncer, Natal, Brazil; [10]Department of Medical Oncology, Institut Bergonié, Bordeaux, France; [11]Department of Clinical Oncology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia; [12]Department of Outpatient Chemotherapy, Professor Franciszek Lukaszczyk Oncology Center, Bydgoszcz, Poland; [13]Institute of Urology named after Academician OF Vozianov of NAMS of Ukraine, Kyiv, Ukraine; [14]Janssen Research & Development, Spring House, PA, USA; [15]Janssen Research & Development, Bridgewater, NJ, USA; [16]Janssen Research & Development, Los Angeles, CA, USA; [17]Janssen Research & Development, Titusville, NJ, USA; [18]Peter MacCallum Cancer Center and the University of Melbourne, Melbourne, Australia

Genitourinary Cancers Symposium 2022;Abstract 12.

MAGNITUDE: BRCA1/2 Mutations — Primary Endpoint

Niraparib with Abiraterone Acetate Significantly Reduced the Risk of Disease Progression or Death by 47% in mCRPC





Chi KN et al. Genitourinary Cancers Symposium 2022;Abstract 12.

Questions — Sandy Srinivas, MD

Metastatic castration-resistant prostate cancer (BRCA mutant)

- **What therapies are used to treat prostate cancer in this setting, and how is treatment selected?**

RTP
RESEARCH
TO PRACTICE

Commentary — Sandy Srinivas, MD

Metastatic castration-resistant prostate cancer (BRCA mutant)

- **Timing/Sequence in mCRPC**
- **Also when testing was done**
- **Olaparib approved pre-docetaxel: PROfound study: rPFS in cohort A: 7.4 vs 3.6 mos; OS- 19.1 vs 14.7**
- **Rucaparib approved post NHT and docetaxel: TRITON2: ORR of 40%**

Recent data:

- **MAGNITUDE: Niraparib + Abiraterone vs Placebo + Abiraterone**
- **HRRm+: Niraparib + Abiraterone improved rPFS:0.53; 16.6 vs 10.9 mos; HRRm-: Neg**
- **PROpel: Olaparib + Abiraterone vs Placebo + Abiraterone**
- **rPFS: 24.8 vs 16.6 mos; HR-0.54; HRRm+: HR-0.5; HRRm-: HR- 0.76**

RTP RESEARCH TO PRACTICE

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

Metastatic castration-resistant prostate cancer (BRCA mutant)

- **What are some of the clinical issues that arise for patients in this situation?**
- **What are key discussion points prior to starting treatment in terms of expected benefits and treatment toxicities?**
- **What are some of the psychosocial issues that arise in these situations?**

RTP
RESEARCH
TO PRACTICE

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

Metastatic castration-resistant prostate cancer (BRCA mutant)

Associated clinical issues:

-pain

-swelling/lymphedema to lower extremities/scrotum

-cough/dyspnea/effusion (eg, lung mets)

-unintentional weight loss

-anemia

-GU problems

Key Discussion Points Prior to Treatment:

-stage IV prostate CA is treatable but not curable

-treatment will be life-long and will change based on response

-potential ADT side effects, including decreased libido, erectile dysfunction, fatigue, weight gain, insulin resistance and osteopenia/osteoporosis

-potential PARP inhibitor side effects, including pancytopenia, thrombosis, fatigue, cough, dyspnea, pneumonitis, n/v/d, abd pain, decreased appetite, MDS (rare)

-regular PSA monitoring, imaging if PSA progression, regular lab testing with PARP inhibitors

-importance of exercise

RTP RESEARCH TO PRACTICE

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

Instructive examples:

-sending pt to ER for neutropenic fever

-pt education – PARP inhibitors

-nutritional counseling on PARP inhibitors

-skin manifestations and photosensitivity (referral to Derm)

-potential need for blood transfusion on PARP inhibitors

-regular interval blood draws on PARP inhibitors

-antiemetics/antidiarrheals

Psychological issues:

-sexuality and intimacy

-meaning of stage IV disease

-potential genetic and family implications

-depression and anxiety

-employment issues/disability

-weight gain

-guilt

-economic stress, eg, treatment affordability

RTP RESEARCH TO PRACTICE

Appendix of Key Data Sets

Prostate Cancer

- Prostate cancer is still a major health problem in the US.
- Approximately 191,930 new cases; approximately 33,330 deaths are expected to occur in 2020.
- With these large numbers, it is more likely that nurses will be seeing these patients in their practice.
- It becomes imperative that nurses keep abreast of current patient issues, current treatments, their associated side effects, and nursing interventions that can help to mitigate problems and ensure quality care.
- Treatment depends on diagnosis (stage and grade of the tumor), co-morbidies, prior therapies, performance status and patient's desires in terms of goals of treatment and QOL.
- Patient-centered strategies to optimize symptom management and improve patient adherence to therapies and outcomes are of paramount importance.

Courtesy of Victoria Sinibaldi, RN, MS, CS, CANP, BC

Definition of nmCRPC

- Patients with rising PSA despite ongoing ADT and no detectable metastases by conventional imaging (bone scan and CT or MRI)
- Most patients with nmCRPC are presumed to have occult metastatic disease not detected by conventional imaging

Courtesy of Matthew R Smith, MD, PhD

Context

- Men with nmCRPC are at significant risk for metastatic disease and prostate cancer–specific death[1]
- Metastases are a major cause of morbidity and mortality[2,3]
- Prevention of metastases represents an important unmet medical need

1. Smith MR et al. *J Clin Oncol*. 2013;31:3800-3806. 2. Scher HI et al. *PLoS One*. 2015;10;e0139440. 3. Gartrell BA et al. *Nat Rev Clin Oncol*. 2014;11:335-345.

Considerations

- Side effects of ADT in young men related to muscle loss, fatigue and sexual health impact quality of life.
- Prioritize access to adequate support for management of sexual health and mental health.
- Ongoing discussion regarding rationale for treatment and how it’s related to long term survival.

Courtesy of Kara M Olivier, NP, APRN-BC

Oral Anti Androgens Approved For M0 Prostate Cancer – How do you choose?

- Enzalutamide
  - Cautious with patients with a history of falls and seizure
- Apalutamide
  - Risk of rash
- Darolutamide
  - Mild fatigue

*For all patients monitor CBC/diff, comprehensive metabolic panel and PSA.

Courtesy of Kara M Olivier, NP, APRN-BC

Nursing implications: oral agents

- Nurses need to be aware that there needs to be a shift in management from provider to patient
- Nurses need to become familiar with the oral agents and develop educational strategies to ensure patient understanding of medication, dosing and administration, potential side effects, symptom management, self care measures, proactive follow-up.
- Stress the import' of need to keep scheduled visits and contact the health care provider when side effects develop. If side effects are not reported, necessary adjustments will not be made and serious consequences can occur and have impact on their life and further therapy.

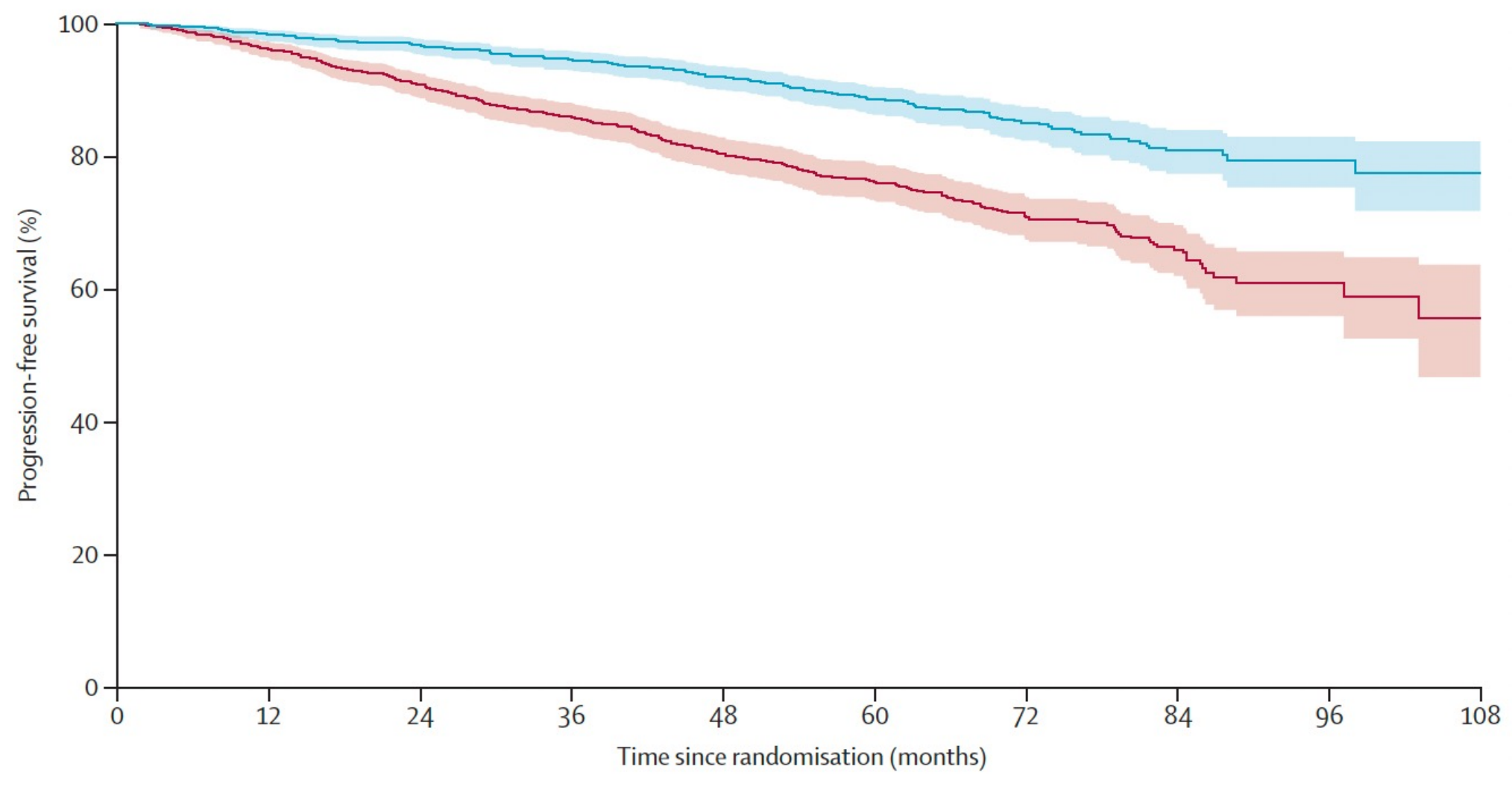
Courtesy of Victoria Sinibaldi, RN, MS, CS, CANP, BC

Nursing implications: oral agents (cont.')

- Nurses need to be aware of factors that affect patient compliance and reporting
- Patients are often reluctant to notify the provider because they fear that their therapy may be interrupted or dose lowered
  - Most side effects resolve with brief interruption of therapy
  - Any necessary dose reduction is simply to customize a dose that the individual needs
  - A dose reduction does not necessarily decrease the efficacy of the treatment
- Communication, education, organization, and trusting relationship are key!!

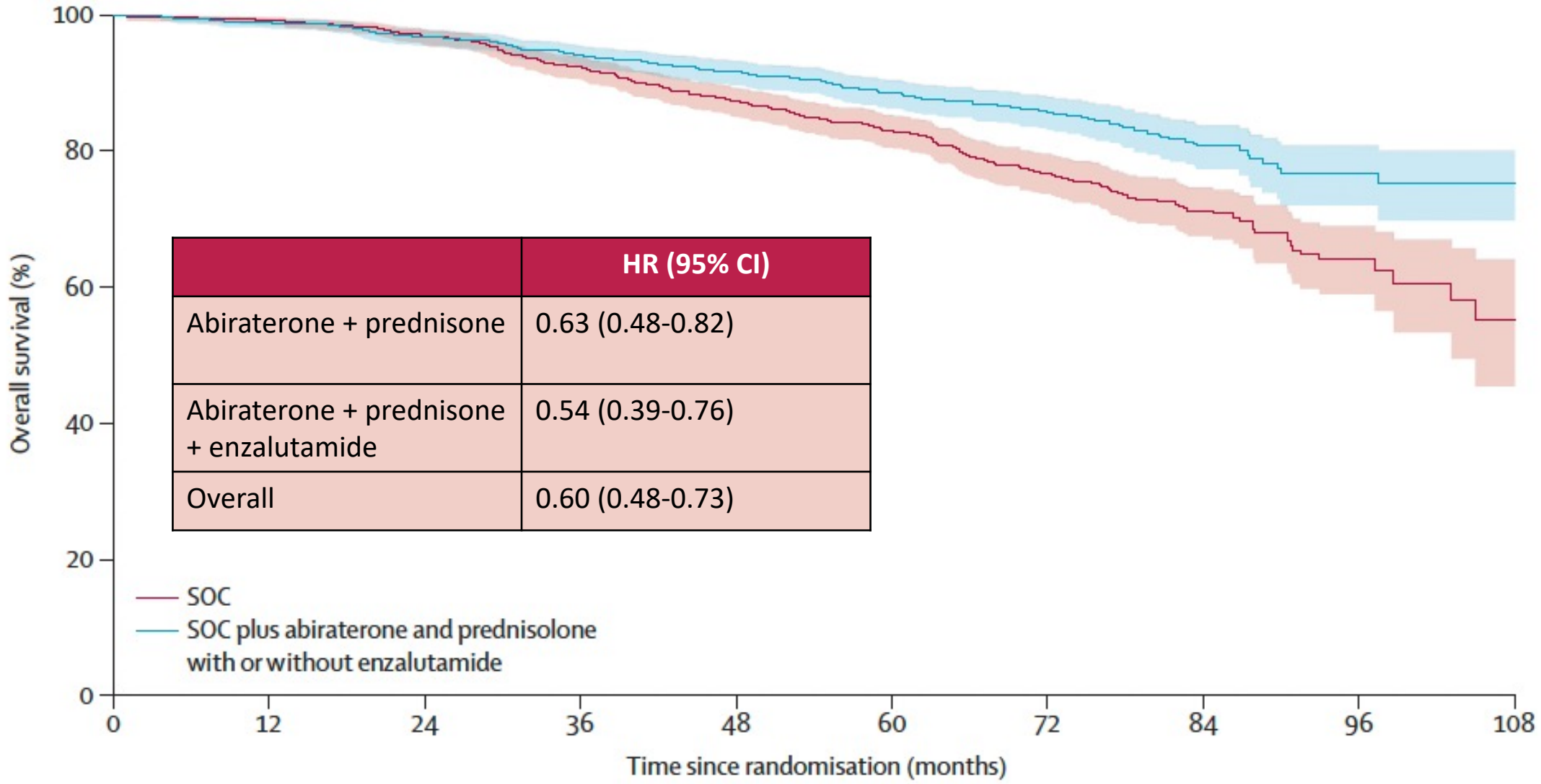
Courtesy of Victoria Sinibaldi, RN, MS, CS, CANP, BC

STAMPEDE: Progression-Free Survival



Attard G et al. *Lancet* 2022;399(10323):447-60.

STAMPEDE: Overall Survival



	HR (95% CI)
Abiraterone + prednisone	0.63 (0.48-0.82)
Abiraterone + prednisone + enzalutamide	0.54 (0.39-0.76)
Overall	0.60 (0.48-0.73)

Attard G et al. *Lancet* 2022;399(10323):447-60.

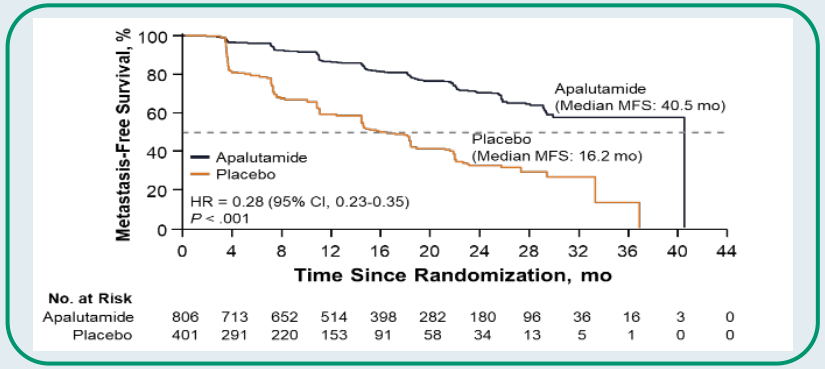
FDA Approvals of Next-Generation Antiandrogens for Nonmetastatic Castration-Resistant Prostate Cancer (CRPC)

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/

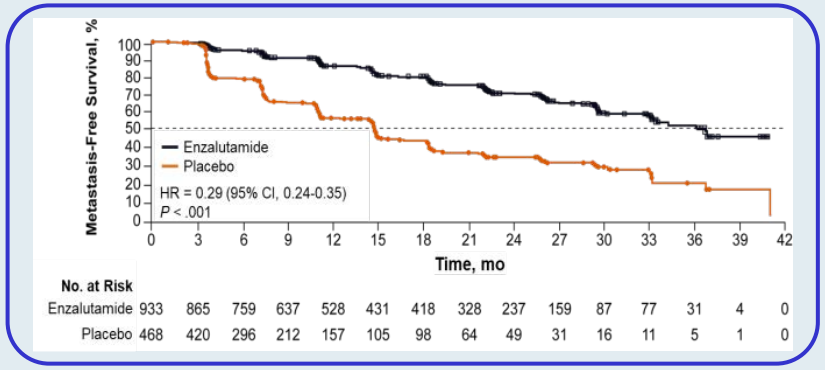
Primary Endpoint: Metastasis-Free Survival (MFS) in Nonmetastatic CRPC

SPARTAN[1]
Apalutamide



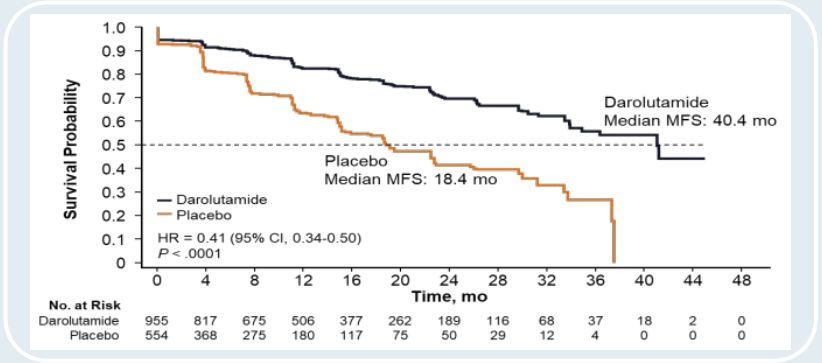
- 72% reduction of distant progression or death
- Median MFS: APA 40.5 vs PBO 16.2 months
- 24-month MFS benefit

PROSPER[2]
Enzalutamide



- 71% reduction of distant progression or death
- Median MFS: ENZA 36.6 vs PBO 14.7 months
- 22-month MFS benefit

ARAMIS[3]
Darolutamide



- 59% reduction of distant progression or death
- Median MFS: DARO 40.4 vs PBO 18.4 months
- 22-month MFS benefit

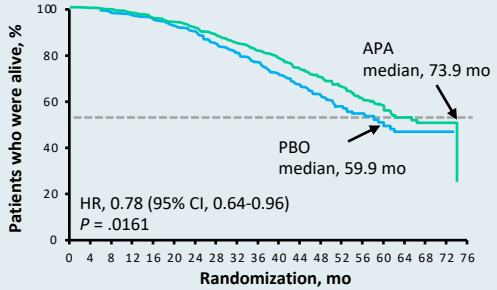
PBO = placebo

1. Smith MR et al. *NEJM* 2018;378:1408-18. 2. Hussain M et al. *NEJM* 2018;378:2465-74. 3. Fizazi K et al. *NEJM* 2019;380:1235-46.

RTP RESEARCH TO PRACTICE

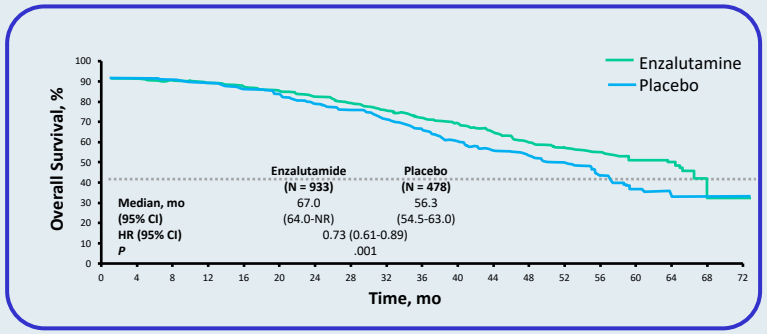
Secondary Endpoint: Overall Survival (OS) in Nonmetastatic CRPC

SPARTAN1[1]
Apalutamide



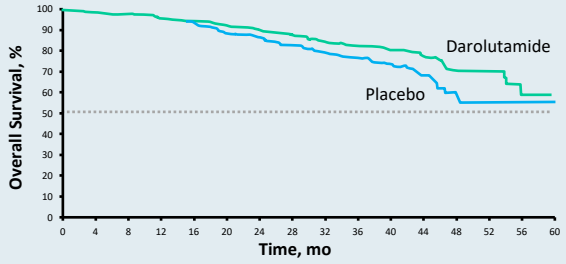
- 22% reduction in risk of death
- Median OS
  - 73.9 mo vs 59.9 mo
  - **HR = 0.78; *p* = 0.016**

PROSPER[2]
Enzalutamide



- 27% reduction in risk of death
- Median OS
  - 67.0 mo vs 56.3 mo
  - **HR = 0.73; *p* = 0.001**

ARAMIS[3]
Darolutamide



- 31% reduction in risk of death
- Median OS
  - **HR = 0.69; *p* = 0.003**

1. Smith MR et al. *Eur Urol* 2020;79:150-8. 2. Sternberg CN et al. *NEJM* 2020;382:2197-206. 3. Fizazi K et al. *NEJM* 2020;383:1040-9.

Comparison of Toxicities: Darolutamide, Enzalutamide or Apalutamide for Nonmetastatic CRPC

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 Approves Relugolix for Advanced Prostate Cancer

Press Release: December 18, 2020

"On December 18, 2020, the US 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

RTP RESEARCH TO PRACTICE

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

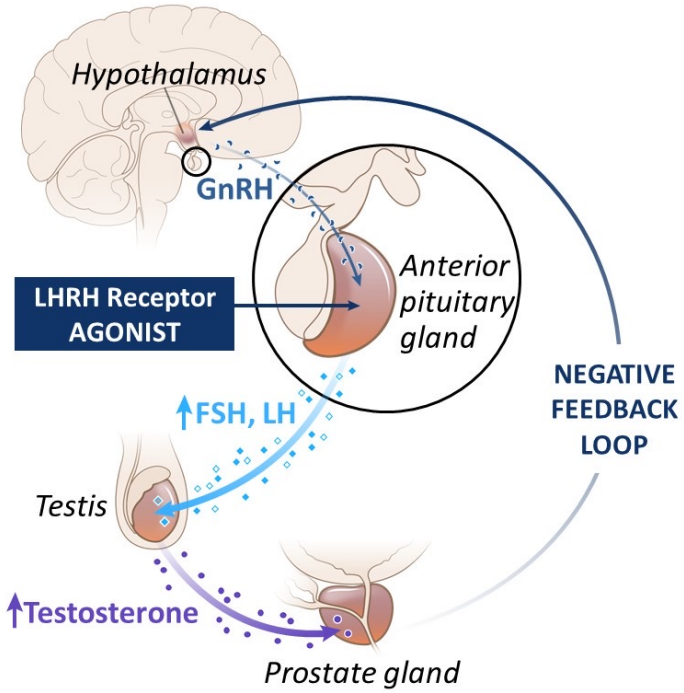
Oral Relugolix for Androgen-Deprivation Therapy in Advanced Prostate Cancer[2]

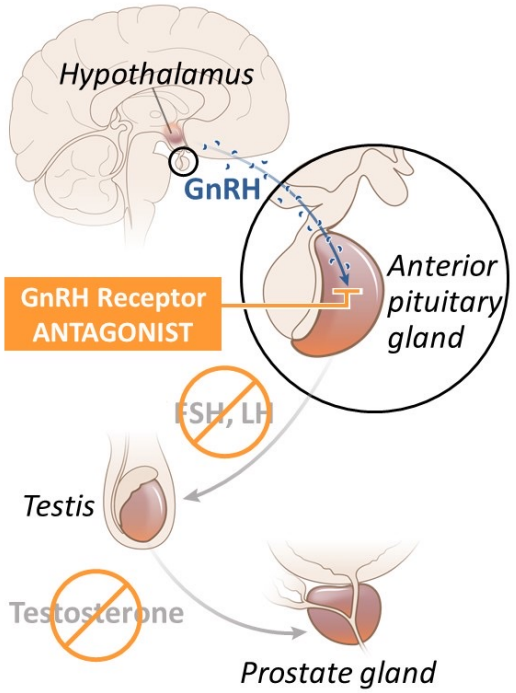
[1] Shore N et al.
ASCO 2020;Abstract 5602.

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

RTP RESEARCH TO PRACTICE

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.

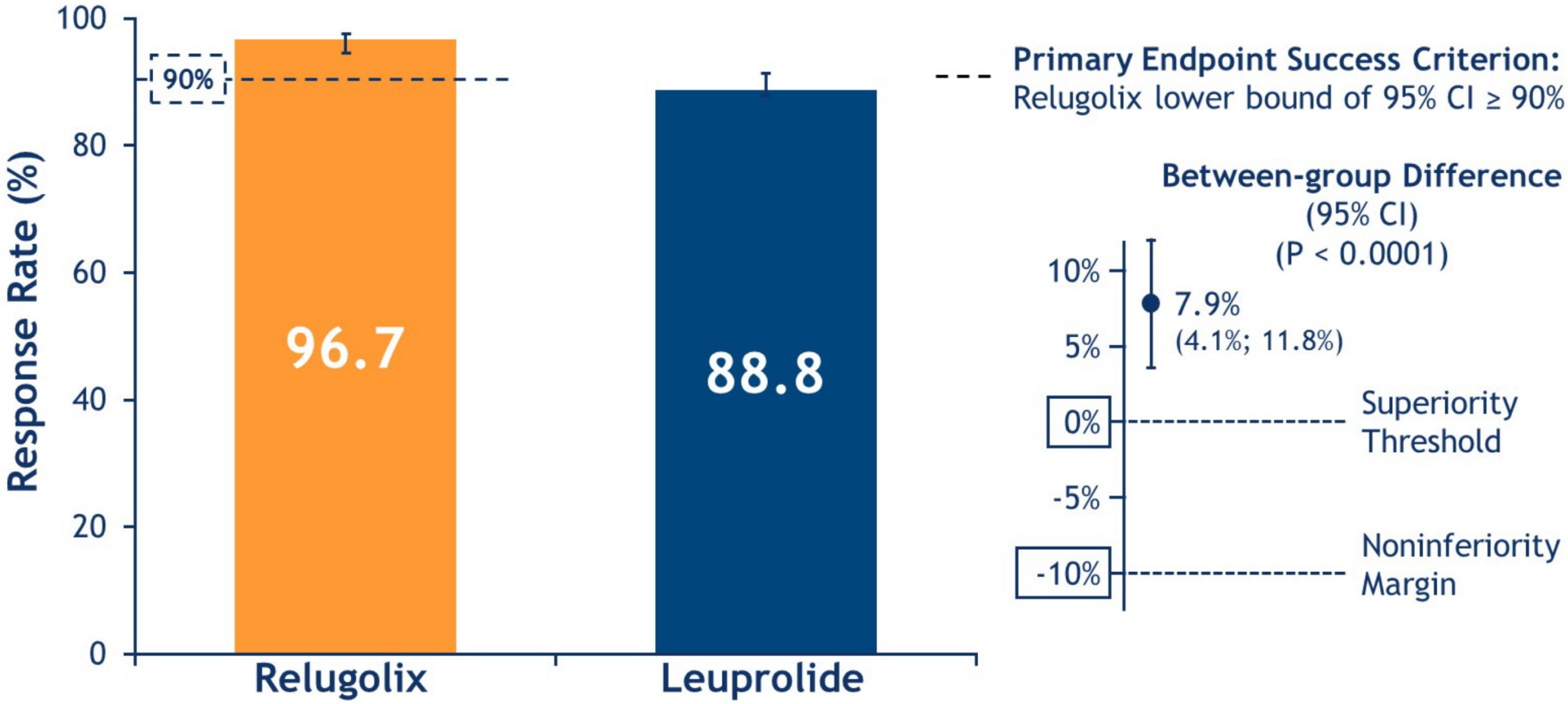
PRESENTED BY: Neal Shore, MD, FACS
Carolina Urologic Research Center, SC, USA

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

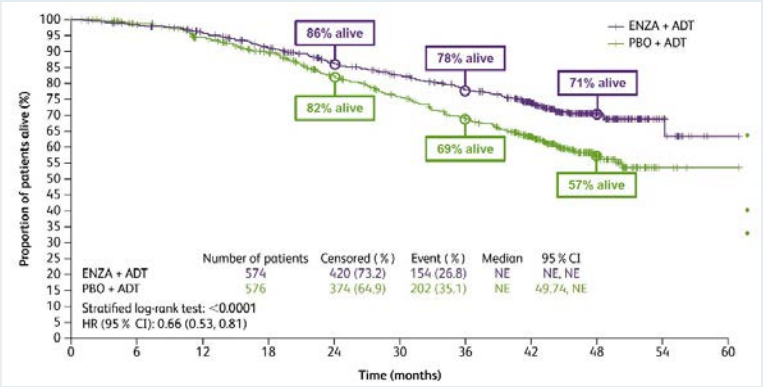
HERO: Primary Endpoint – Sustained Castration
Key Secondary Endpoint – Noninferiority to Leuprolide



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

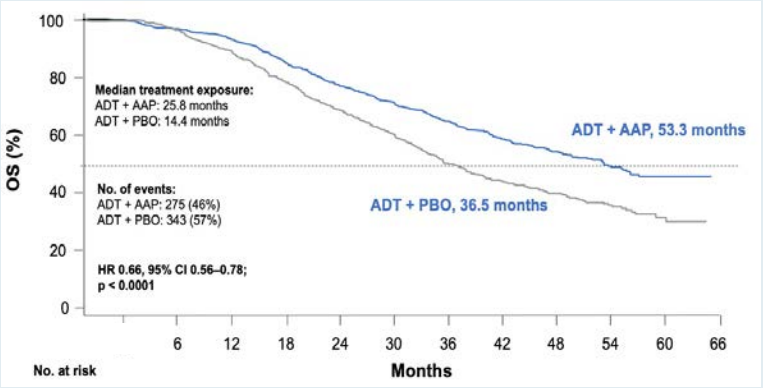
Final OS Analyses: Enzalutamide, Abiraterone and Apalutamide for mHSPC

ARCHES[1]
Enzalutamide + ADT



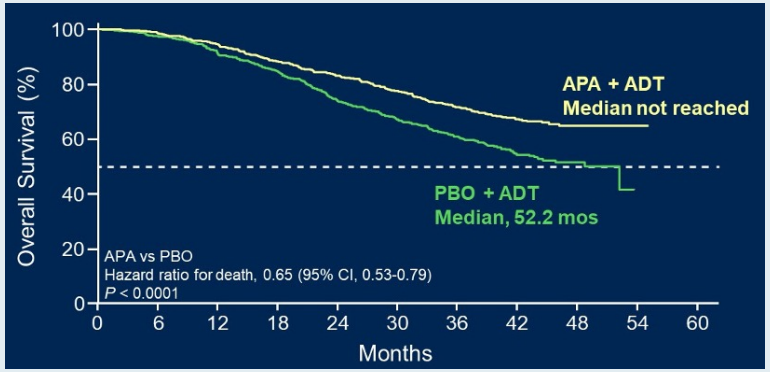
- 34% reduction in risk of death
- Median OS
  - **40.2 mo vs 13.8 mo**
  - **HR = 0.66; *p* < 0.0001**

LATITUDE[2]
Abiraterone + ADT



- 34% reduction in risk of death
- Median OS
  - 53.3 mo vs 36.5 mo
  - **HR = 0.66; *p* < 0.0001**

TITAN[3]
Apalutamide + ADT



- 35% reduction in risk of death
- Median OS
  - Not reached vs 52.2 mo
  - **HR = 0.65; *p* < 0.0001**

1. Armstrong AJ et al. ESMO 2021;Abstract LBA25. 2. Fizazi K et al. GU Cancers Symposium 2019;Abstract 141. 3. Chi KN et al. GU Cancers Symposium 2021;Abstract 11.

RTP RESEARCH TO PRACTICE

Selected FDA Approved Drugs in Advanced Prostate Cancer

- Sipuleucel-T
  - autologous cellular immunotherapy designed to stimulate a patient's own immune system against prostate cancer, MOA unknown
  - Minimal toxicity, apharesis required
- Radium-223
  - Radiopharmaceutical, alpha particle
  - GI toxicity, typically mild, important to remind patients re: lack of PSA activity
  - Administered by nuclear medicine or radiation oncology physicians
  - Important to monitor patients monthly as NO activity against non bone metastatic sites
- PSMA (prostate specific membrane antigen) targeted therapies
  - In combination with a number of molecules: Lutetium, radioactive iodine, T cell targeting combinations

Courtesy of Robert Dreicer, MD, MS

Nursing implications: Radium-223

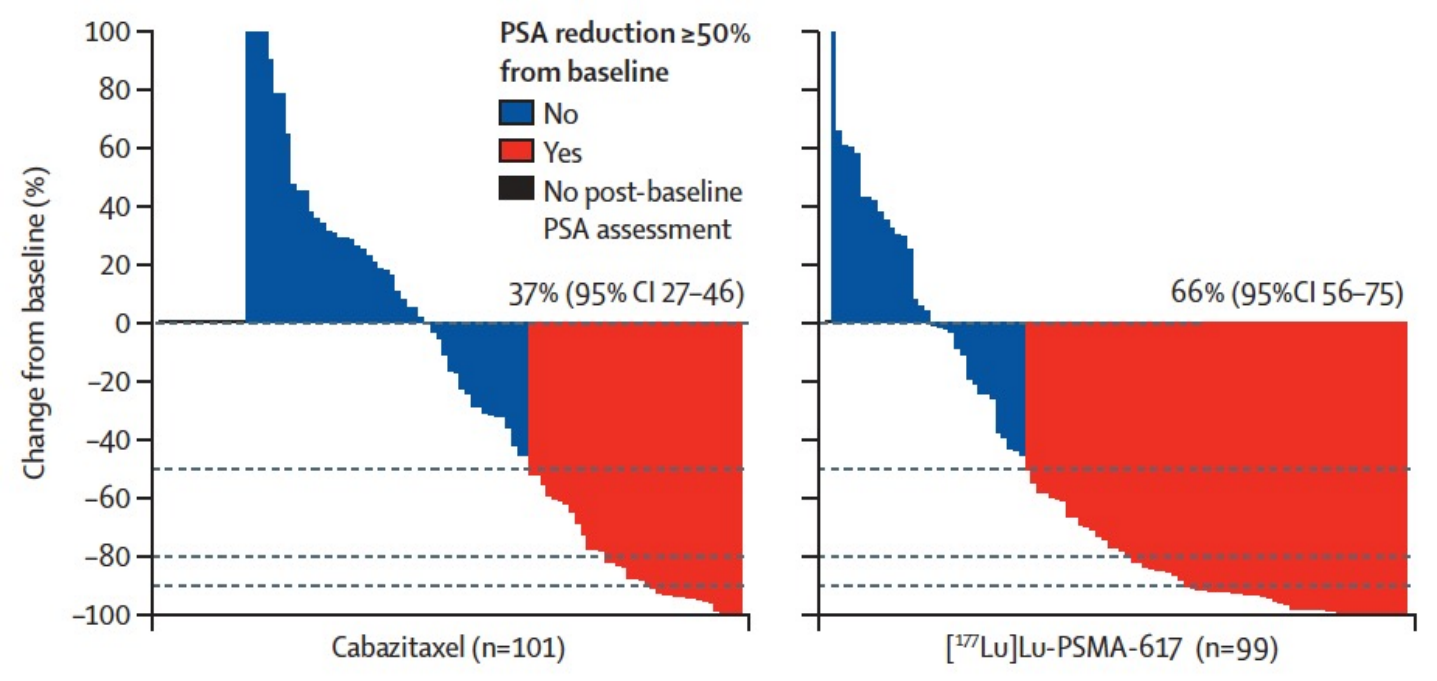
- Rad-223 is safe and effective and targets tumor cells in the bone.
- Rad-223 -form of liquid radiation, administered IV, given every 4 weeks x6.
- Explain characteristics of RAD-223- has a short range that does limit damage to healthy cells.
- Data using this modality have shown improvement in QOL with improvement in pain, improved OS (by 3.6 months), delay in SSEs.
- Patients often focus on PSA. Point out that a decline in PSA is not an expected result of Rad-223; Patient benefits have been observed in the absence of a decreasing PSA.

Courtesy of Victoria Sinibaldi, RN, MS, CS, CANP, BC

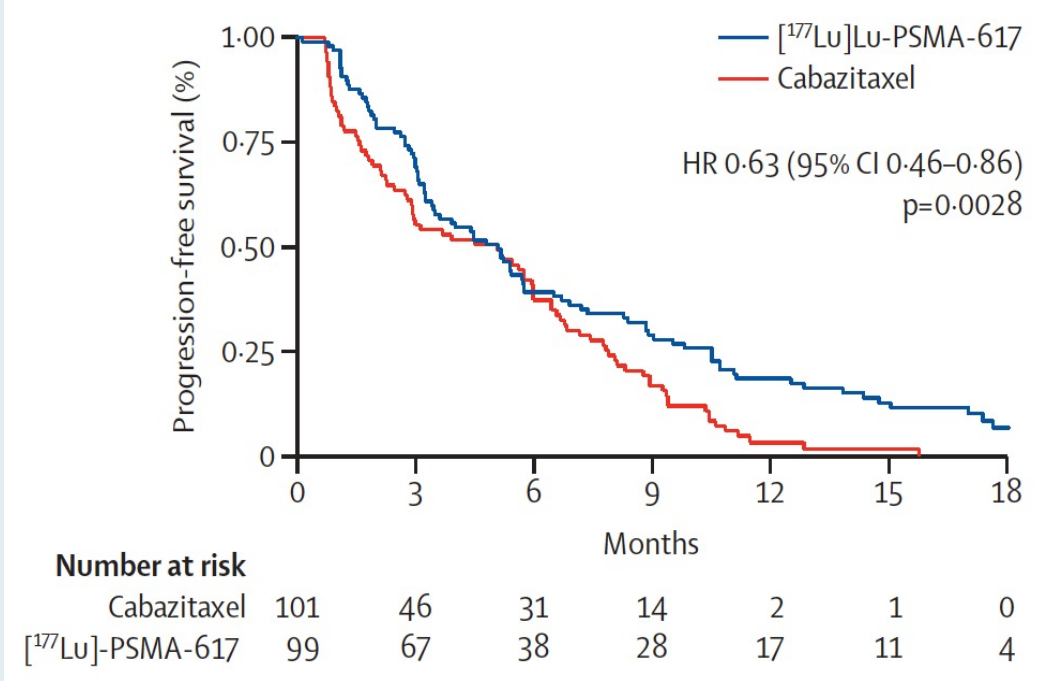
TheraP ANZUP 1603: ^{177}Lu-PSMA-617 versus Cabazitaxel for mCRPC

PSA Response and Progression-Free Survival

PSA response



Radiographic or PSA progression-free survival

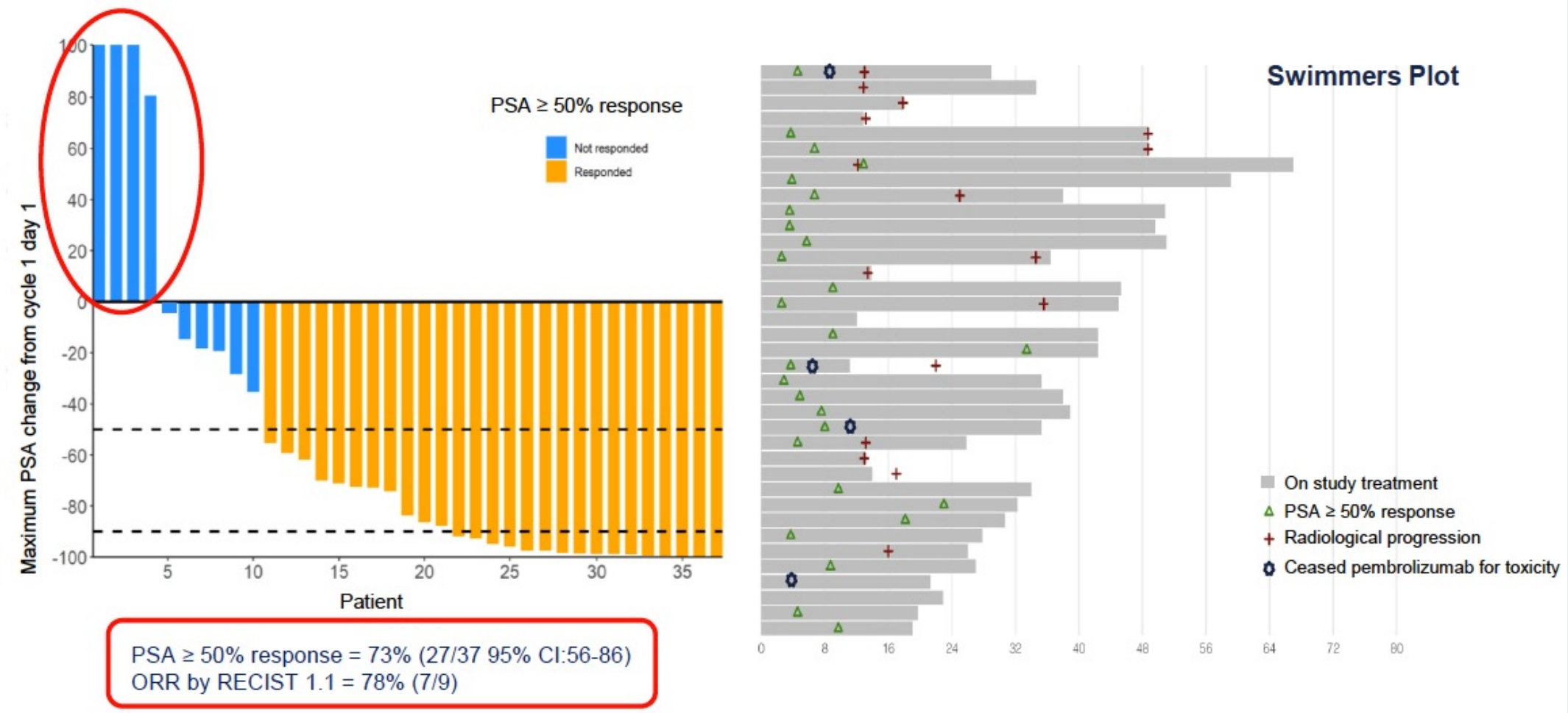


Hofman MS et al. Genitourinary Cancers Symposium 2021;Abstract 6;
Hofman MS et al. *Lancet* 2021;397(10276):797-804.

RTP RESEARCH TO PRACTICE

PRINCE: ^{177}Lu-PSMA-617 Combined with Pembrolizumab for mCRPC

PSA Response Rate (Primary Endpoint)



Sandhu S et al. ESMO 2021;Abstract 577O.

PRINCE: Treatment-Related Adverse Events (TRAEs)

TRAE term	Grade 1 (%)	Grade 2 (%)	Grade 3 (%)	N=37 (%)
Xerostomia	21 (57%)	7 (19%)	-	28 (76%)
Fatigue	11 (29 %)	3 (8%)	2 (5%)	16 (43%)
Rash	5 (14%)	4 (11%)		9 (25%)
Nausea	8 (21%)	1 (3%)	-	9 (24%)
Pruritis	6 (16%)	1 (3%)	-	7 (19%)
Anorexia	3 (8%)	3 (8%)	-	6 (16%)
Thrombocytopenia	4 (11%)	1(3%)	-	5 (14%)
Bone pain (flare)	4 (11%)	-	-	4 (11%)
Aspartate aminotransferase elevation	2 (5%)	2 (5%)	-	4 (11%)
Dry eye	3 (8%)	-	-	3 (8%)
Dysgeusia	2 (5%)	1 (3%)	-	3 (8%)
Weight loss	2 (5%)	1 (3%)		3 (8%)
Anemia	-	2 (5%)	1(3%)	3 (8%)
Alanine aminotransferase elevation	2 (5%)	1(3%)	-	3 (8%)
Amylase elevation	1 (3%)	1 (3%)	1 (3%)	3 (8%)
Arthralgia	3 (8%)	-	-	3 (8%)
Neutropenia	1 (3%)	-	-	1 (3%)

- Treatment related adverse events (TRAEs) in by worst grade affecting > 5% and all hematological toxicity
- There were no grade 4 TRAEs or treatment related deaths

Pembrolizumab cycles: Median (range)	8 (1 - 22)
^{177}Lu-PSMA-617 cycles: Median (range)	4 (2 - 6)
Discontinuation for toxicity:	
Pembrolizumab, n (%)	4 (11%)
^{177}Lu-PSMA-617, n (%)	0 (0%)

Sandhu S et al. ESMO 2021;Abstract 577O.

RTP RESEARCH TO PRACTICE

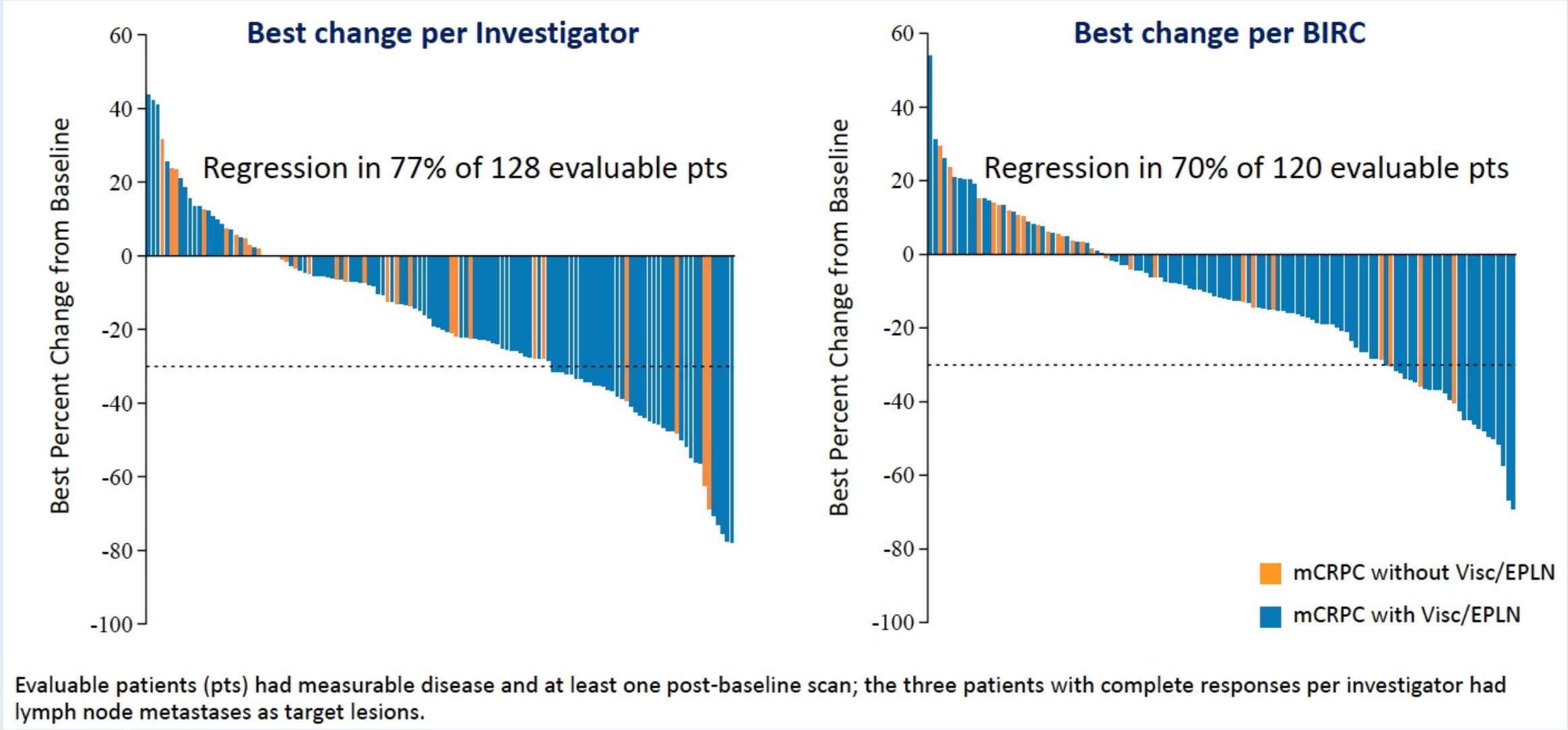
Immune Checkpoint Inhibitors in mCRPC

Therapy	Disease state	Disease response
Pembrolizumab monotherapy[a]	Postchemotherapy	ORR 9% PSA RR 14%
Pembrolizumab + enzalutamide[b]	Prechemotherapy, progressing on enzalutamide	ORR 12% PSA RR 14%
Atezolizumab + enzalutamide[c]	Pre- and postchemotherapy, s/p abiraterone	ORR 14% PSA RR 26%
Atezolizumab + cabozantinib[d]	Prechemotherapy, s/p enzalutamide or abiraterone	ORR 34% PSA RR 29%

[a] Antonarakis ES et al. *JCO* 2020:38(5):395-405. [b] Presented at the 2021 ASCO Annual Meeting – Virtual. [c] Sweeney C. AACR 2020; IMbassador250. [d] Agarwal ASCO 2020; COSMIC-021.

COSMIC-021: Cabozantinib/Atezolizumab for mCRPC

Best Change from Baseline in Sum of Target Lesions



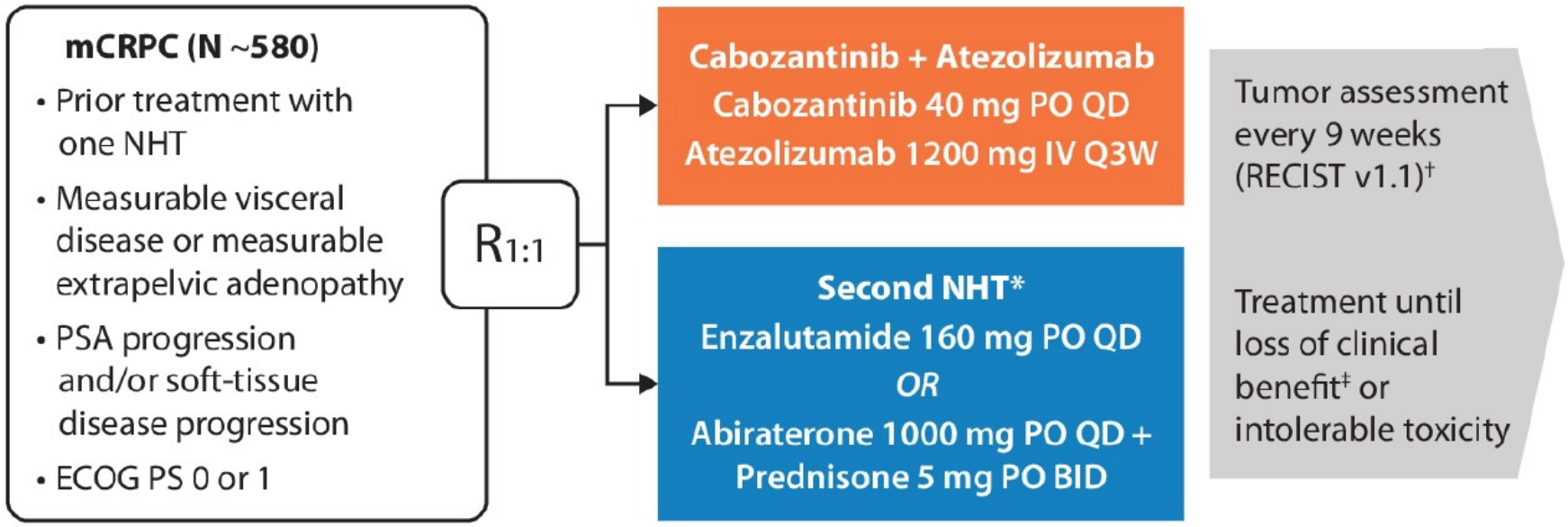
Evaluable patients (pts) had measurable disease and at least one post-baseline scan; the three patients with complete responses per investigator had lymph node metastases as target lesions.

BIRC = blinded independent review committee; EPLN = extrapelvic lymph nodes

Agarwal et al. ESMO 2021;Abstract LBA24.

RTP RESEARCH TO PRACTICE

CONTACT-02: Phase III Trial Schema



Stratification

- Liver metastasis (yes, no)
- Prior docetaxel treatment for mCSPC (yes, no)
- Disease stage for which the first NHT was given (mCSPC, M0 CRPC, mCRPC)

*Second NHT must differ from previous NHT taken
†Tumor assessment (RECIST v1.1) every 9 weeks for the first 28 weeks then every 12 weeks thereafter
‡Patients may be treated beyond progression if there is a clinical benefit in the opinion of the investigator

Primary Endpoints

- PFS per RECIST v1.1 by BIRC
- OS

Secondary Endpoint

- ORR per RECIST v1.1 by BIRC

NHT = novel hormone therapy

Agarwal N et al. Genitourinary Cancers Symposium 2021;Abstract TPS190.

PARP Inhibitors for mCRPC

- Poly(ADP-ribose) polymerase (PARP) inhibitors
  - Directed at targeting cancers with defective DNA-damage repair
  - Prostate cancer, most common defects in BRCA 1, BRCA 2 and ATM genes
  - Side effects include progressive anemia, fatigue, GI side effects indigestion, nausea/vomiting, diarrhea, headaches

Courtesy of Robert Dreicer, MD, MS

Recent FDA Approvals of PARP Inhibitors for mCRPC

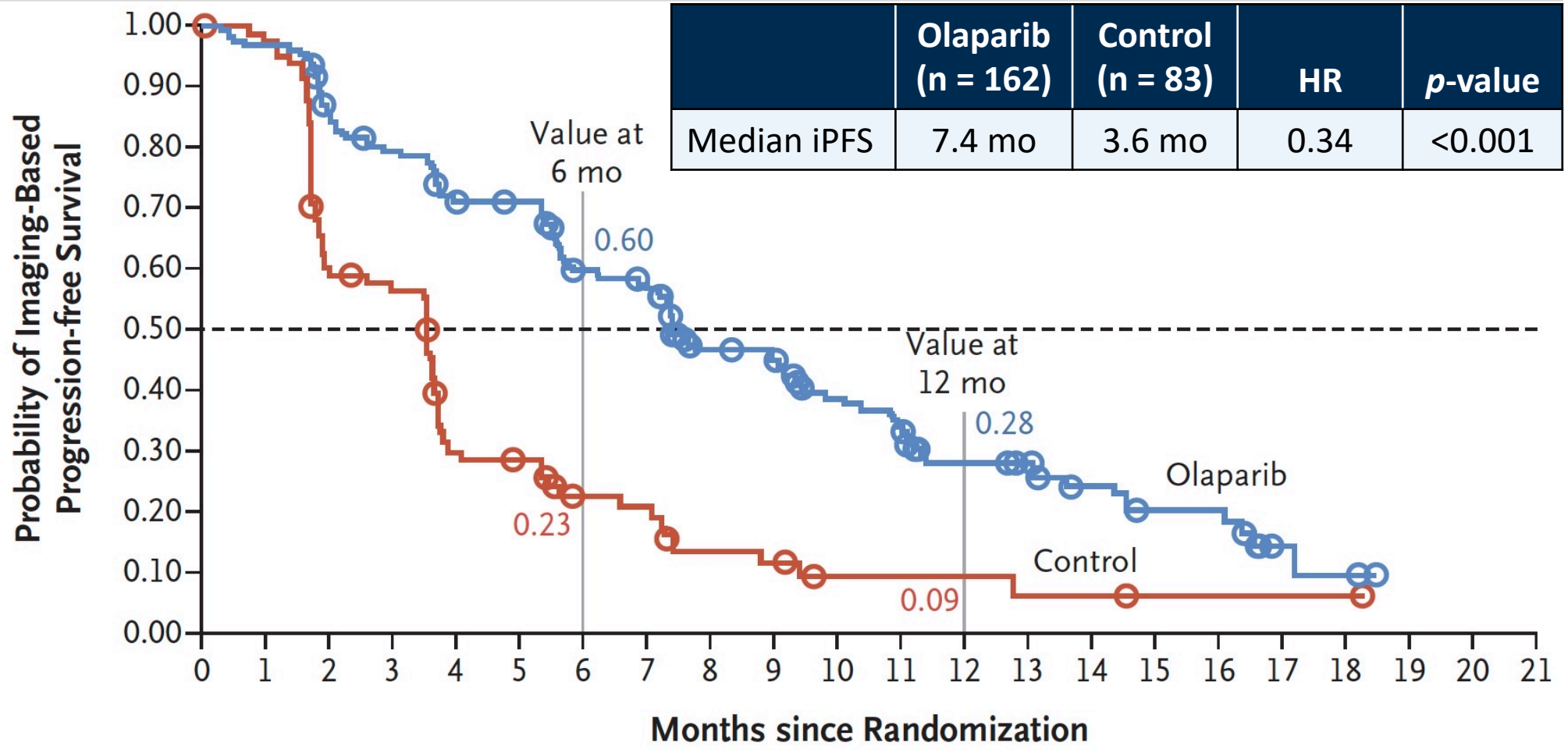
PARP inhibitor	Approval date	Pivotal study
Olaparib	May 19, 2020	PROfound
Rucaparib	May 15, 2020	TRITON2

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

RTP RESEARCH TO PRACTICE

PROfound Primary Endpoint: Imaging-Based PFS with Olaparib for Patients with mCRPC and 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

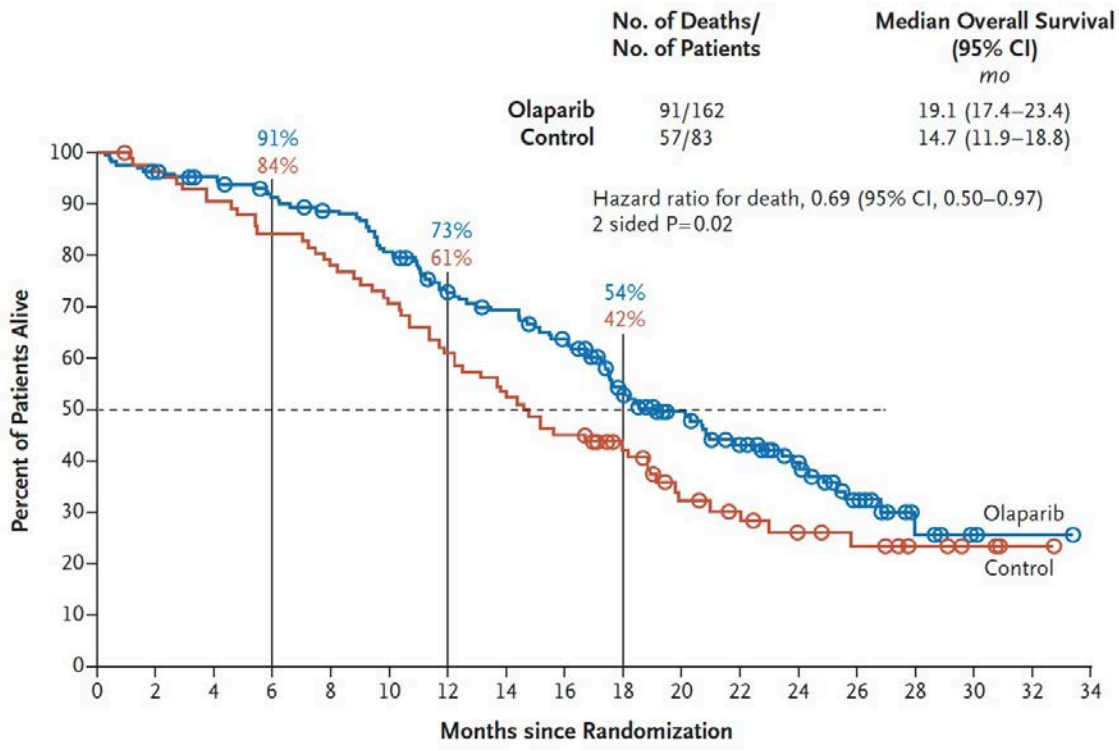


de Bono J et al; PROfound investigators. *N Engl J Med* 2020;382(22):2091-102.

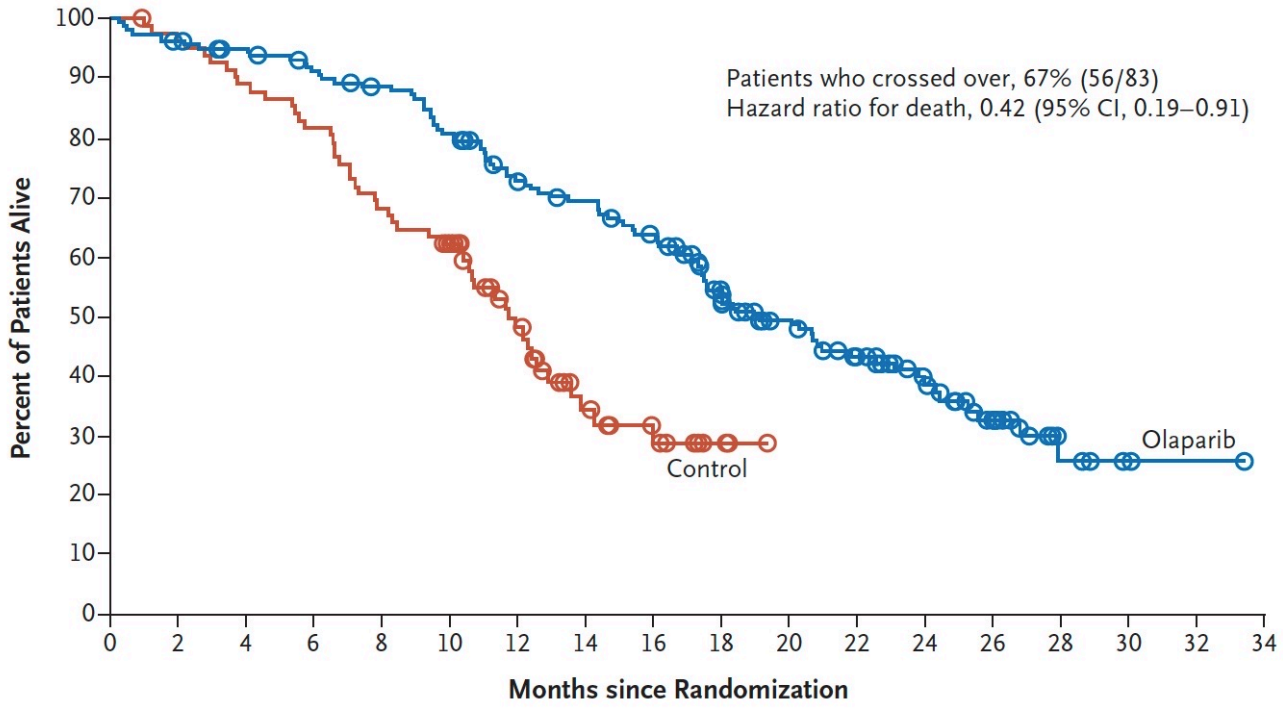
RTP RESEARCH TO PRACTICE

PROfound: OS with Olaparib for Patients with mCRPC and at Least 1 Alteration in BRCA1, BRCA2 or ATM (Cohort A)

Overall survival



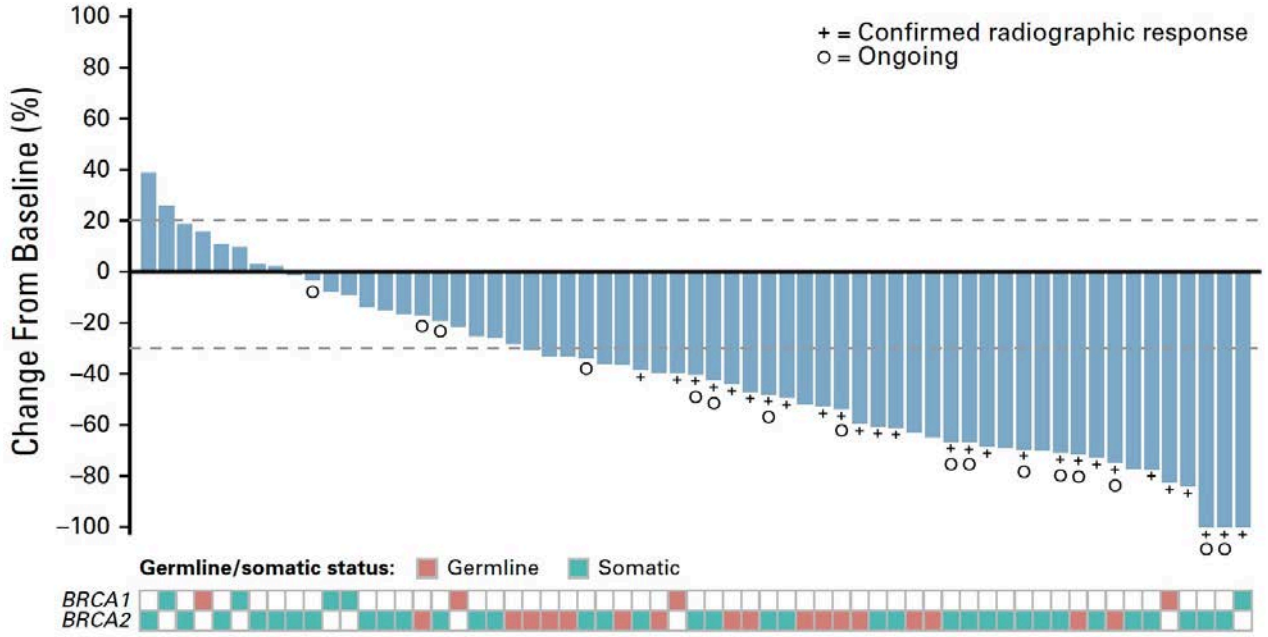
Crossover-adjusted overall survival



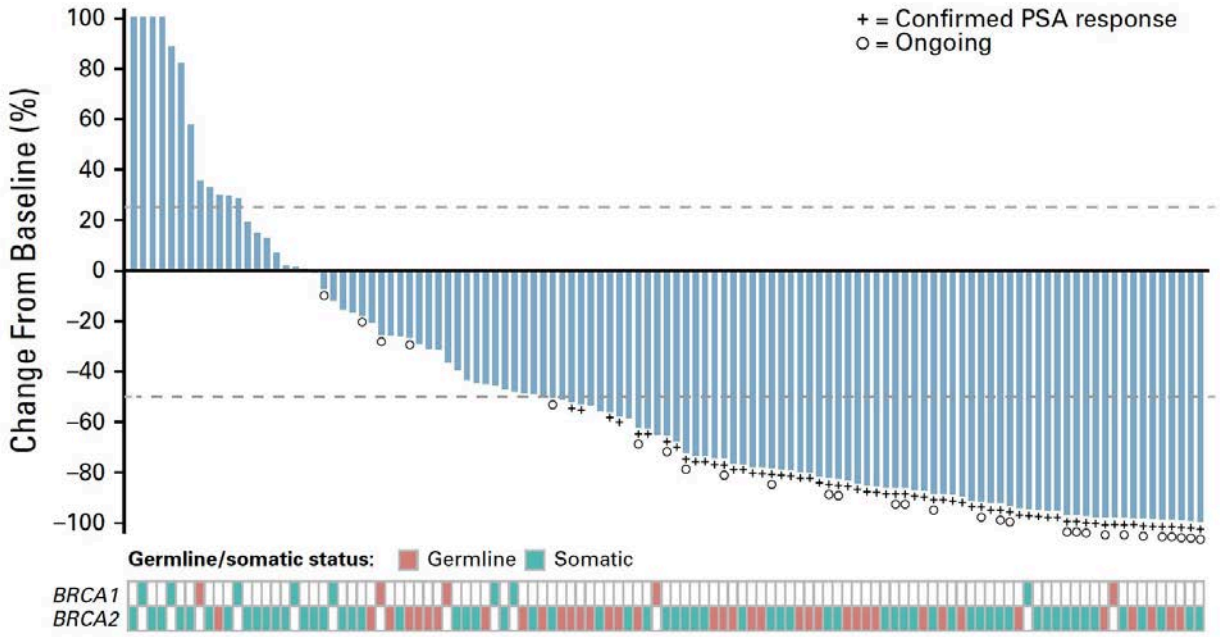
Hussain M et al; PROfound investigators. *N Engl J Med* 2020;383(24):2345-57.

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%

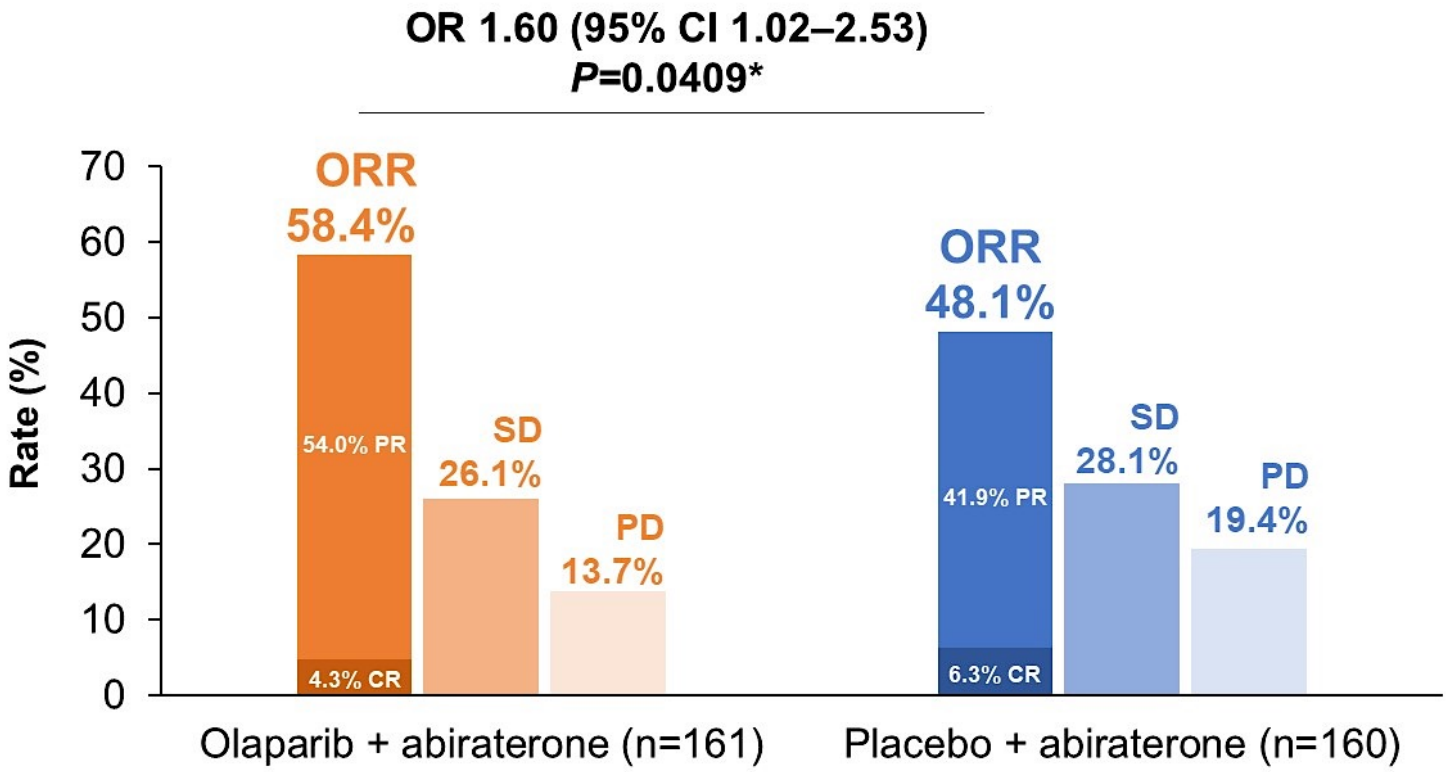


ORR = objective response rate

Abida W et al. TRITON2 investigators. *J Clin Oncol* 2020;38(32):3763-72.

PROpel: ORR for Patients with Measurable Disease

10% improvement in ORR with olaparib + abiraterone



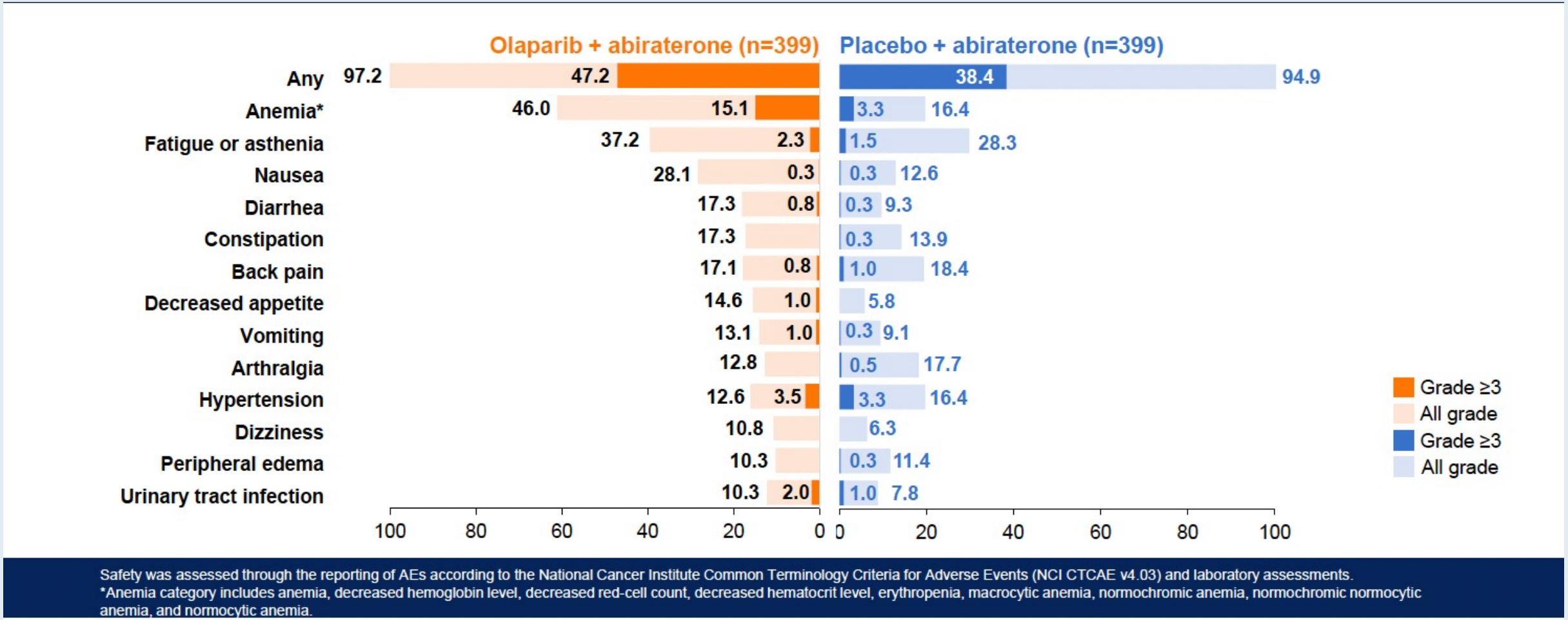
321/796 patients (40.3%) had measurable disease by RECIST v1.1 criteria at baseline

*Nominal.
CR, complete response; OR, odds ratio; ORR, overall response rate; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.

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

RTP RESEARCH TO PRACTICE

PROpel: Most Common Adverse Events



Safety was assessed through the reporting of AEs according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE v4.03) and laboratory assessments.
*Anemia category includes anemia, decreased hemoglobin level, decreased red-cell count, decreased hematocrit level, erythropenia, macrocytic anemia, normochromic anemia, normochromic normocytic anemia, and normocytic anemia.

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

RTP RESEARCH TO PRACTICE

PROpel: Cardiac and Thromboembolic Adverse Events

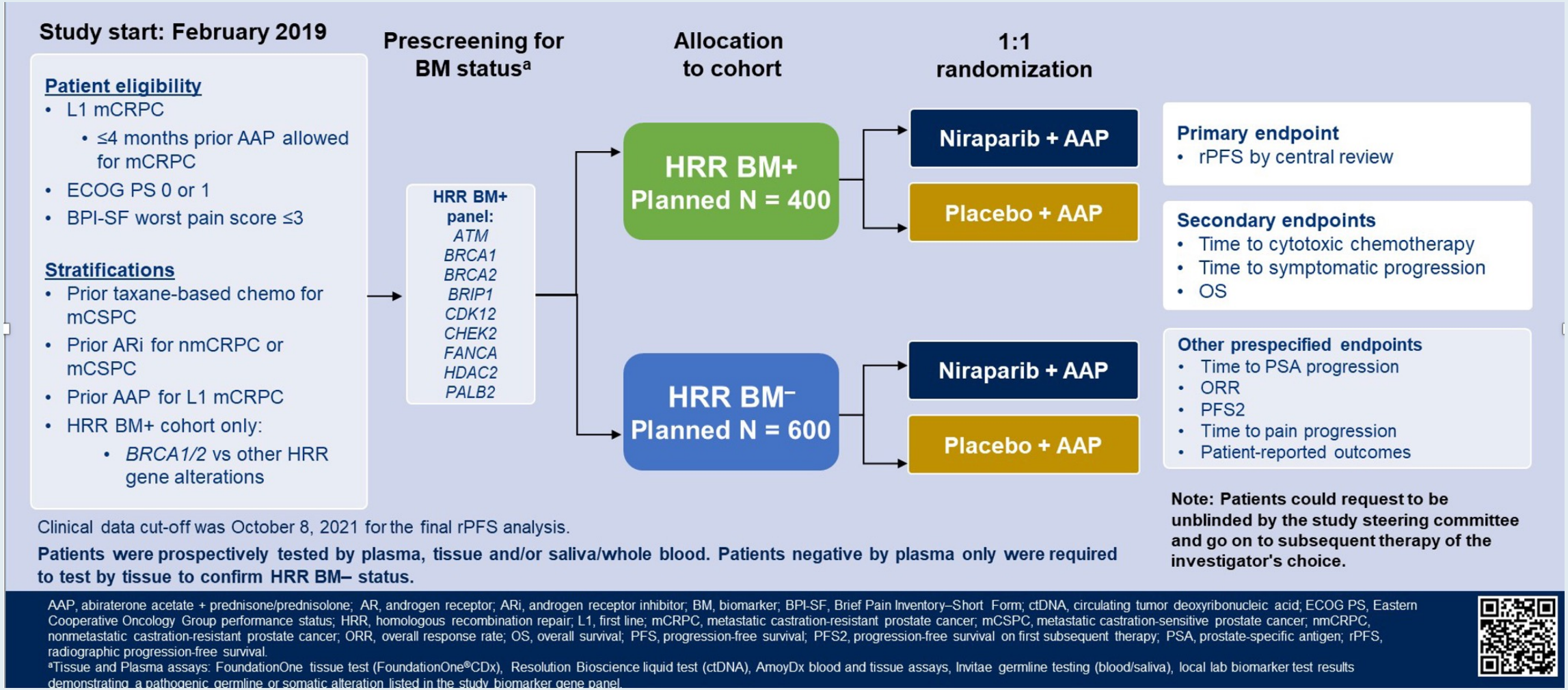
n (%)	Olaparib + abiraterone (n=399)	Placebo + abiraterone (n=397)
Cardiac failure SMQ	6 (1.5)	5 (1.3)
Embolic and thrombotic events, arterial SMQ	8 (2.0)	10 (2.5)
Embolic and thrombotic events, venous SMQ	29 (7.3)	13 (3.3)
Pulmonary embolism	26 (6.5)	7 (1.8)

CT, computerized tomography; SMQ, Standardised MedDRA Query.

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

MAGNITUDE: Randomized, Double-Blind, Placebo-Controlled Study

Prospectively Selected Biomarker (BM) Cohorts Designed to Test HRR BM+ and HRR BM-



Clinical data cut-off was October 8, 2021 for the final rPFS analysis.

Patients were prospectively tested by plasma, tissue and/or saliva/whole blood. Patients negative by plasma only were required to test by tissue to confirm HRR BM– status.

AAP, abiraterone acetate + prednisone/prednisolone; AR, androgen receptor; ARi, androgen receptor inhibitor; BM, biomarker; BPI-SF, Brief Pain Inventory–Short Form; ctDNA, circulating tumor deoxyribonucleic acid; ECOG PS, Eastern Cooperative Oncology Group performance status; HRR, homologous recombination repair; L1, first line; mCRPC, metastatic castration-resistant prostate cancer; mCSPC, metastatic castration-sensitive prostate cancer; nmCRPC, nonmetastatic castration-resistant prostate cancer; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PFS2, progression-free survival on first subsequent therapy; PSA, prostate-specific antigen; rPFS, radiographic progression-free survival.

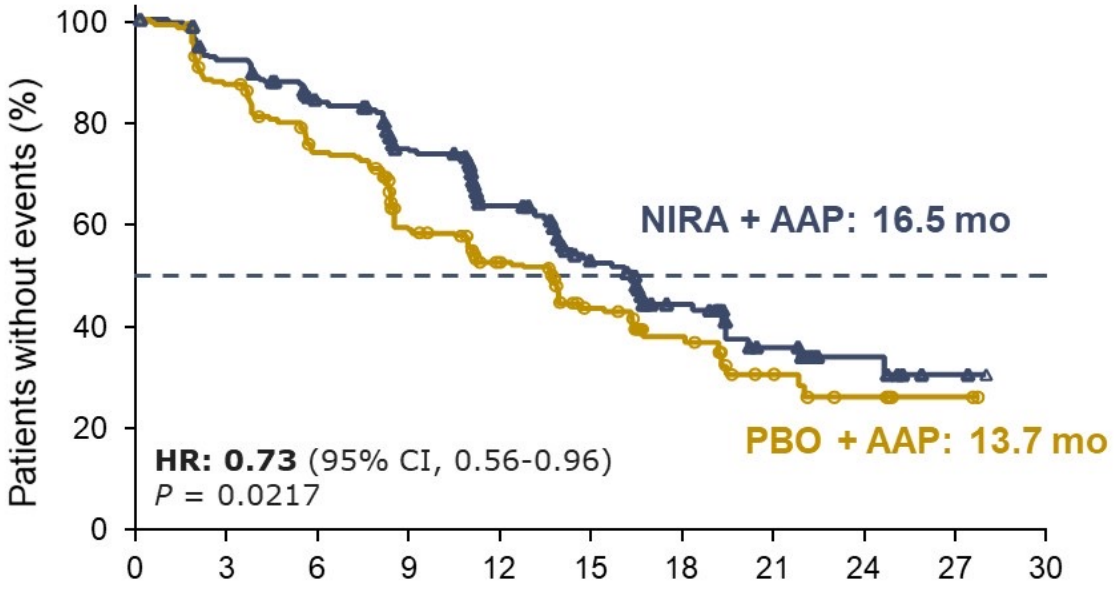
[a]Tissue and Plasma assays: FoundationOne tissue test (FoundationOne®CDx), Resolution Bioscience liquid test (ctDNA), AmoyDx blood and tissue assays, Invitae germline testing (blood/saliva), local lab biomarker test results demonstrating a pathogenic germline or somatic alteration listed in the study biomarker gene panel.

Chi KN et al. Genitourinary Cancers Symposium 2022;Abstract 12.

MAGNITUDE: All HRR Biomarker-Positive — Primary Endpoint

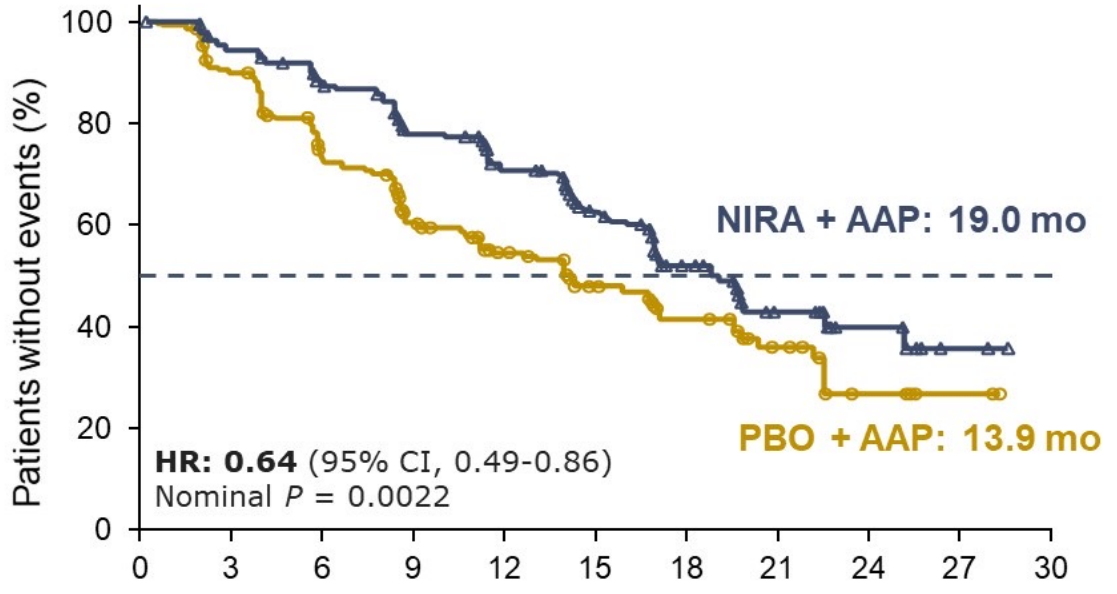
Niraparib with Abiraterone Acetate Significantly Reduced the Risk of Disease Progression or Death by 27%

rPFS assessed by central review



No. at risk											
NIRA + AAP	212	192	167	129	96	64	45	21	10	2	0
PBO + AAP	211	182	149	102	78	53	35	15	9	2	0

rPFS assessed by investigator

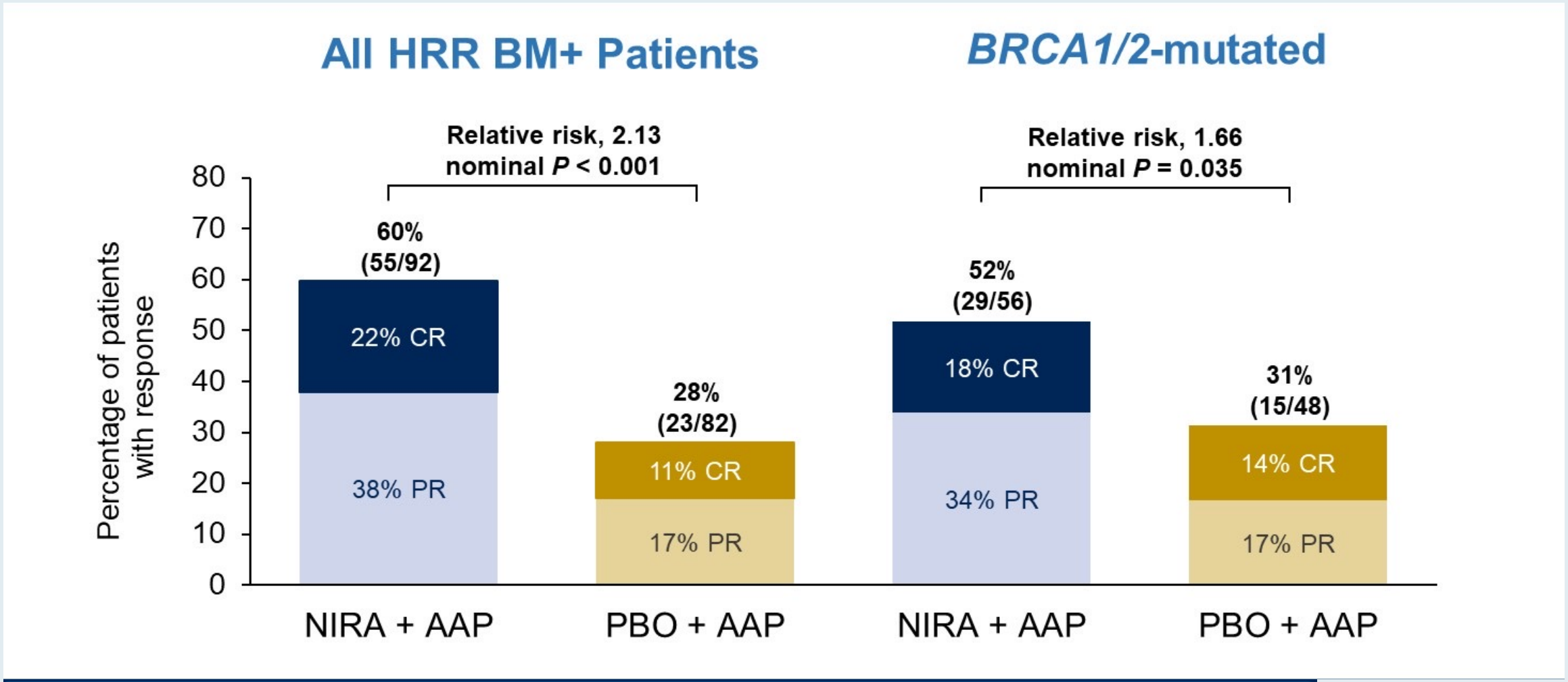


No. at risk											
NIRA + AAP	212	197	174	136	108	75	50	23	11	2	0
PBO + AAP	211	187	145	103	81	58	41	20	9	2	0

Chi KN et al. Genitourinary Cancers Symposium 2022;Abstract 12.

RTP RESEARCH TO PRACTICE

MAGNITUDE: Niraparib with Abiraterone Acetate Improves Overall Response Rate Consistently Across Gene Alterations



NIRA + AAP nearly doubles ORR rate and provides deeper response in patients with measurable disease

Chi KN et al. Genitourinary Cancers Symposium 2022;Abstract 12.

RTP RESEARCH TO PRACTICE

MAGNITUDE: HRR Biomarker-Positive — Summary of Treatment-Emergent Adverse Events (TEAEs)

Overall summary, n (%)	NIRA + AAP n = 212	PBO + AAP n = 211
All TEAEs	210 (99.1)	199 (94.3)
Drug related	162 (76.4)	116 (55.0)
Grade 3/4 TEAEs	142 (67.0)	98 (46.4)
SAEs	76 (35.8)	52 (24.6)
Drug related[a]	24 (11.3)	6 (2.8)
Dose reduction due to an AE	42 (19.8)	7 (3.3)
Discontinuation of niraparib or placebo due to AE	23 (10.8)	10 (4.7)
All deaths within 30 days of last dose	19 (9.0)	19 (9.0)
Death due to prostate cancer	8 (3.8)	12 (5.7)
AE	11 (5.2)	7 (3.3)

- The most common AEs leading to dose reduction in the niraparib group were anemia (13.2%) and thrombocytopenia (2.8%), consistent with established safety profile for NIRA
- Median relative dose intensity was 99% in the NIRA + AAP group

SAEs = serious adverse events

Chi KN et al. Genitourinary Cancers Symposium 2022;Abstract 12.

MAGNITUDE: HRR Biomarker-Positive — Common TEAEs

Treatment-emergent adverse events occurring at >20% in the NIRA arm or otherwise of clinical interest, n (%)		NIRA + AAP, n = 212		PBO + AAP, n = 211	
		All grades	Grade ≥3	All grades	Grade ≥3
Hematologic	Anemia	98 (46.2)	63 (29.7)	43 (20.4)	16 (7.6)
	Thrombocytopenia	45 (21.2)	14 (6.6)	18 (8.5)	5 (2.4)
	Neutropenia	29 (13.7)	14 (6.6)	12 (5.7)	3 (1.4)
	Acute myeloid leukemia/ Myelodysplastic syndrome	0	0	1 (0.5)	1 (0.5)
Cardiovascular	Hypertension	67 (31.6)	33 (15.6)	47 (22.3)	30 (14.2)
	Arrhythmia	27 (12.7)	6 (2.8)[a]	12 (5.7)	3 (1.4)
	Cardiac failure	4 (1.9)	3 (1.4)[a]	4 (1.9)	1 (0.5)
	Ischemic heart disease	4 (1.9)	4 (1.9)	8 (3.8)	6 (2.8)[b]
General disorders	Fatigue	56 (26.4)	7 (3.3)	35 (16.6)	9 (4.3)
Gastrointestinal	Constipation	65 (30.7)	–	29 (13.7)	–
	Nausea	50 (23.6)	1 (0.5)	29 (13.7)	0
Hepatotoxicity		25 (11.8)	4 (1.9)	26 (12.3)	10 (4.7)
Cerebrovascular disorders		6 (2.8)	2 (0.9)	2 (0.9)	1 (0.5)[a]

Chi KN et al. Genitourinary Cancers Symposium 2022;Abstract 12.

What I Tell My Patients:
New Treatments and Clinical Trial Options

An NCPD Hybrid Symposium Series
Held During the 47th Annual ONS Congress

Ovarian Cancer

Thursday, April 28, 2022
12:15 PM – 1:45 PM PT

Faculty

Jennifer Filipi, MSN, NP
Kathleen N Moore, MD, MS
Krishnansu S Tewari, MD
Deborah Wright, MSN, APRN, AGCNS-BC

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Thank you for joining us!

In-person attendees: Please fill out your Educational Assessment and NCPD Credit Form.

Online attendees: NCPD credit information will be emailed to each participant within 3 business days.

RTP
RESEARCH
TO PRACTICE