Meet The Professor

Optimizing the Management of Metastatic Castration-Resistant Prostate Cancer

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

Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Exelixis Inc, Merck, Novartis Pharmaceuticals Corporation on behalf of Advanced Accelerator Applications, and Sanofi Genzyme.

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Dr Love — Disclosures

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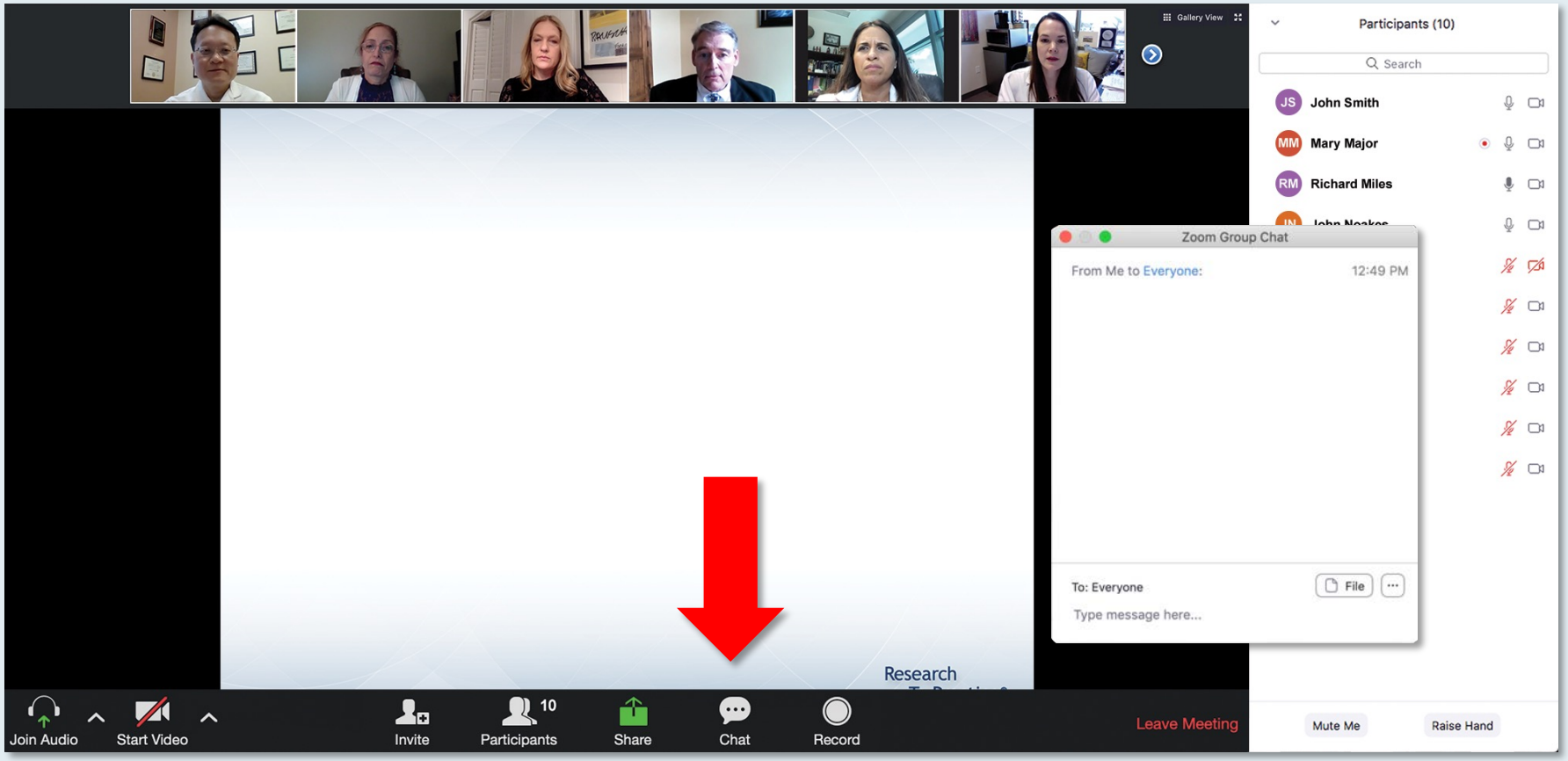

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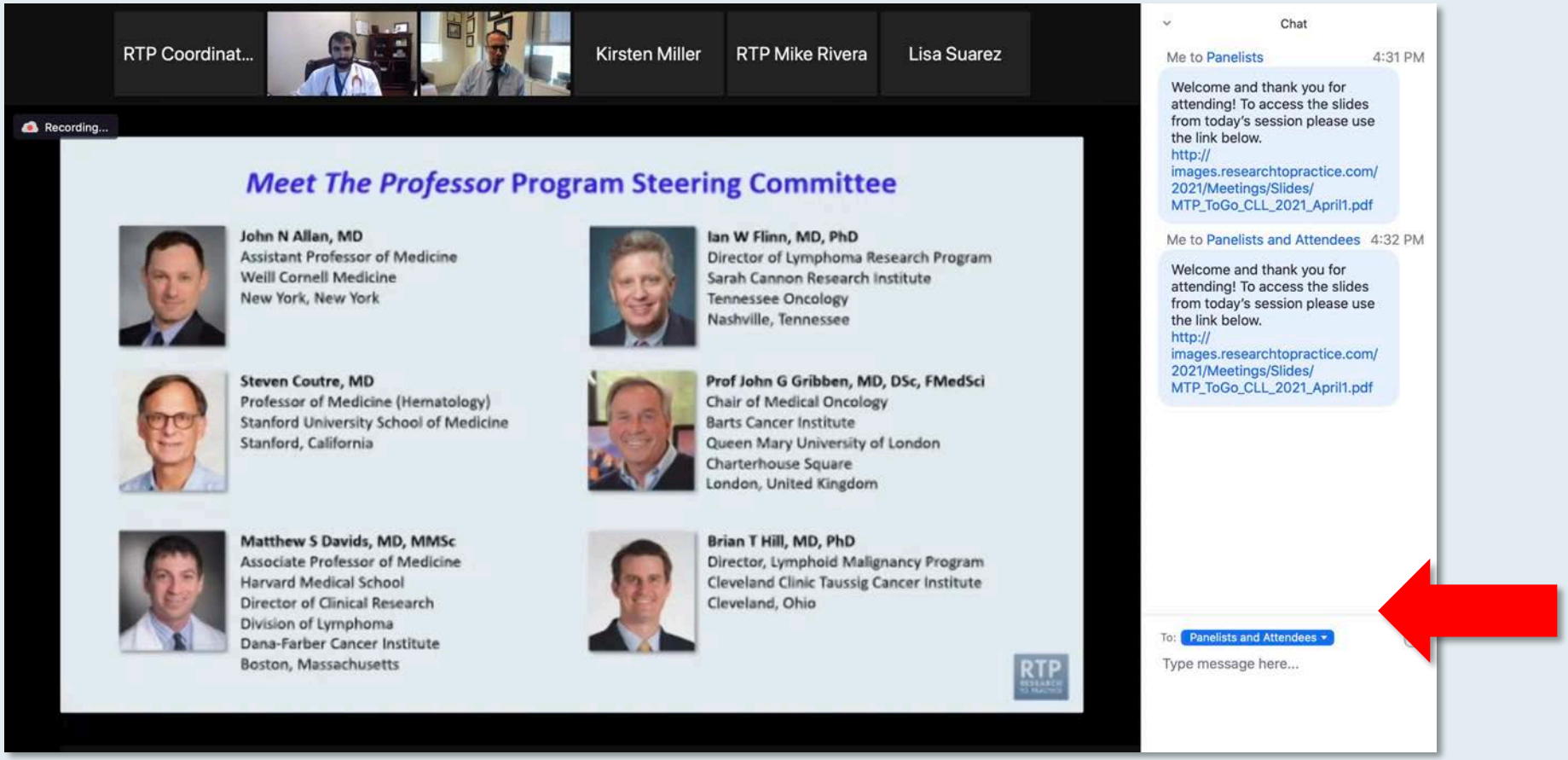
Expand chat submission box



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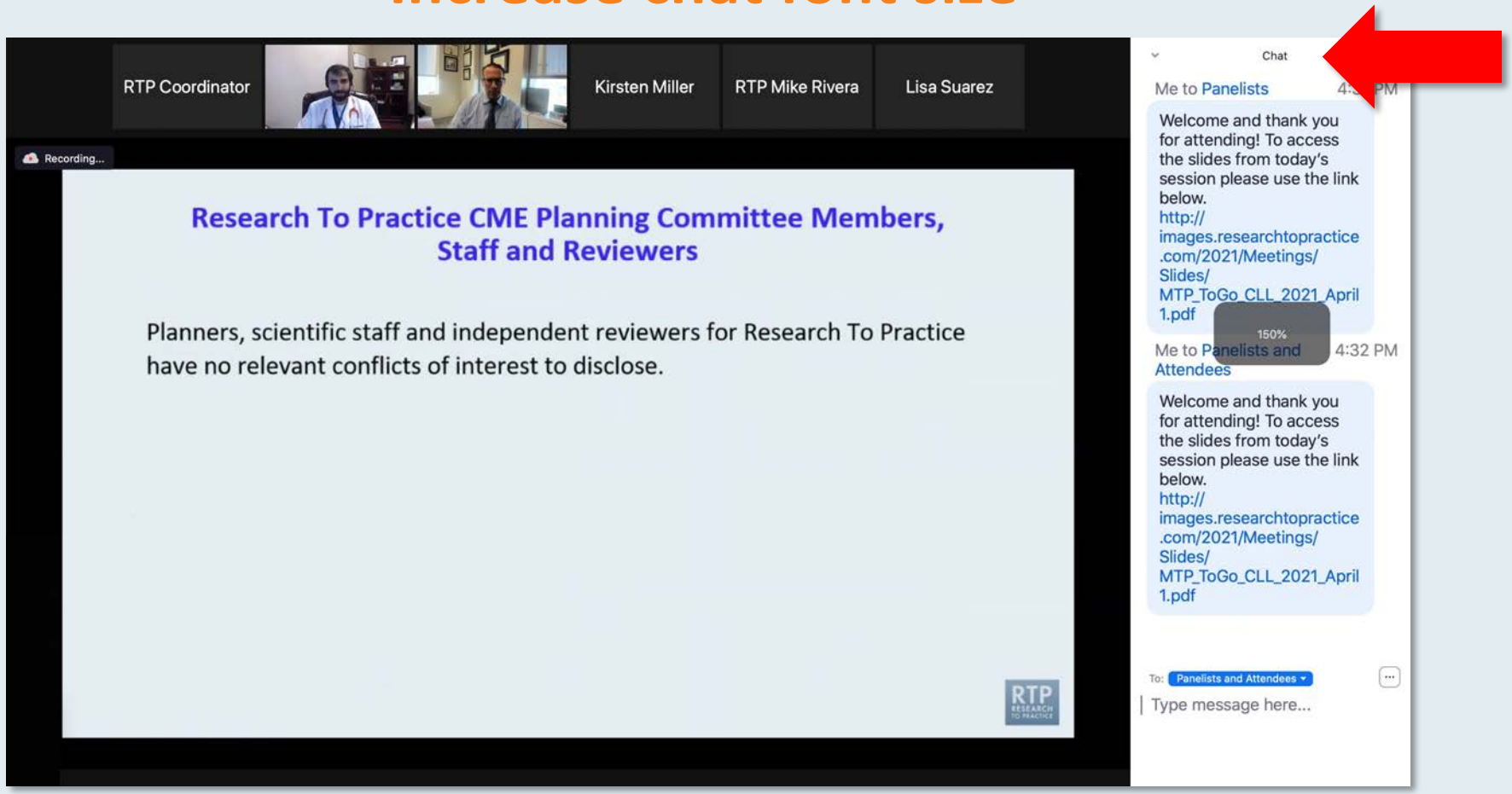

Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.

ONCOLOGY TODAY

WITH DR NEIL LOVE

Novel Agents and Strategies for the Treatment of Metastatic Castration-Resistant Prostate Cancer

DR EVAN YU

FRED HUTCHINSON CANCER RESEARCH CENTER

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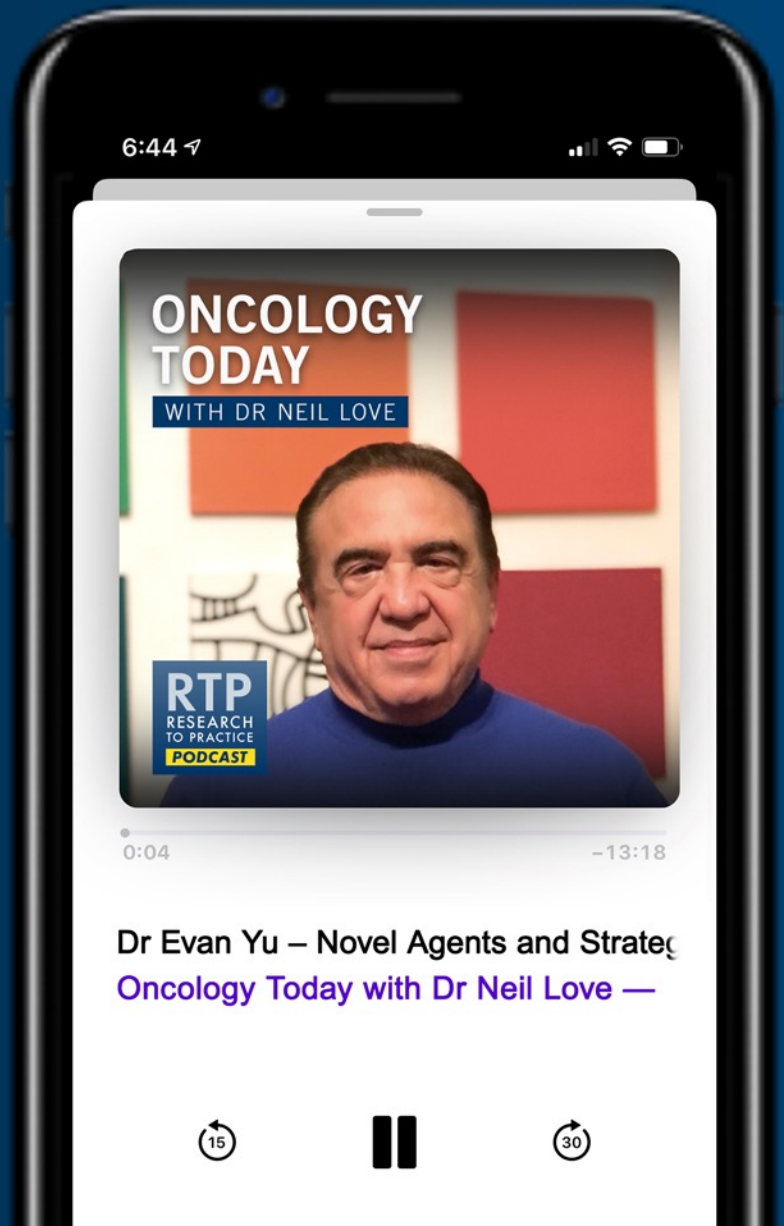

Meet The Professor

Current and Future Management of Chronic Lymphocytic Leukemia

Thursday, March 3, 2022
5:00 PM – 6:00 PM ET

Faculty

William G Wierda, MD, PhD

Moderator

Neil Love, MD

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Meet The Professor

Current and Future Role of Immunotherapy in the Management of Lung Cancer

Monday, March 7, 2022
5:00 PM – 6:00 PM ET

Faculty

Charu Aggarwal, MD

Moderator

Neil Love, MD

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Year in Review:
Kidney and Bladder Cancer

Tuesday, March 8, 2022
5:00 PM – 6:00 PM ET

Faculty

Elizabeth R Plimack, MD, MS
Thomas Powles, MBBS, MRCP, MD

Moderator

Neil Love, MD

RTP Year in Review 2022

Meet The Professor

Optimizing the Management of Acute Myeloid Leukemia

Wednesday, March 9, 2022
5:00 PM – 6:00 PM ET

Faculty

Rebecca L Olin, MD, MSCE

Moderator

Neil Love, MD

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Meet The Professor

Current and Future Management of Myelofibrosis

Thursday, March 10, 2022
5:00 PM – 6:00 PM ET

Faculty

Srdan Verstovsek, MD, PhD

Moderator

Neil Love, MD

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Meet The Professor

Current and Future Management of Chronic Lymphocytic Leukemia

Thursday, March 17, 2022
5:00 PM – 6:00 PM ET

Faculty

Peter Hillmen, MB ChB, PhD

Moderator

Neil Love, MD

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Thank you for joining us!

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

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Duke Cancer Institute Center for Prostate and Urologic Cancers
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Phoenix, Arizona

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Head of Service and Full Professor
Institut Gustave Roussy
University of Paris Saclay
Villejuif, France

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Meet The Professor Program Participating Faculty

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Medical Director, Survivorship Program
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Boston, Massachusetts

Moderator
Neil Love, MD
Research To Practice
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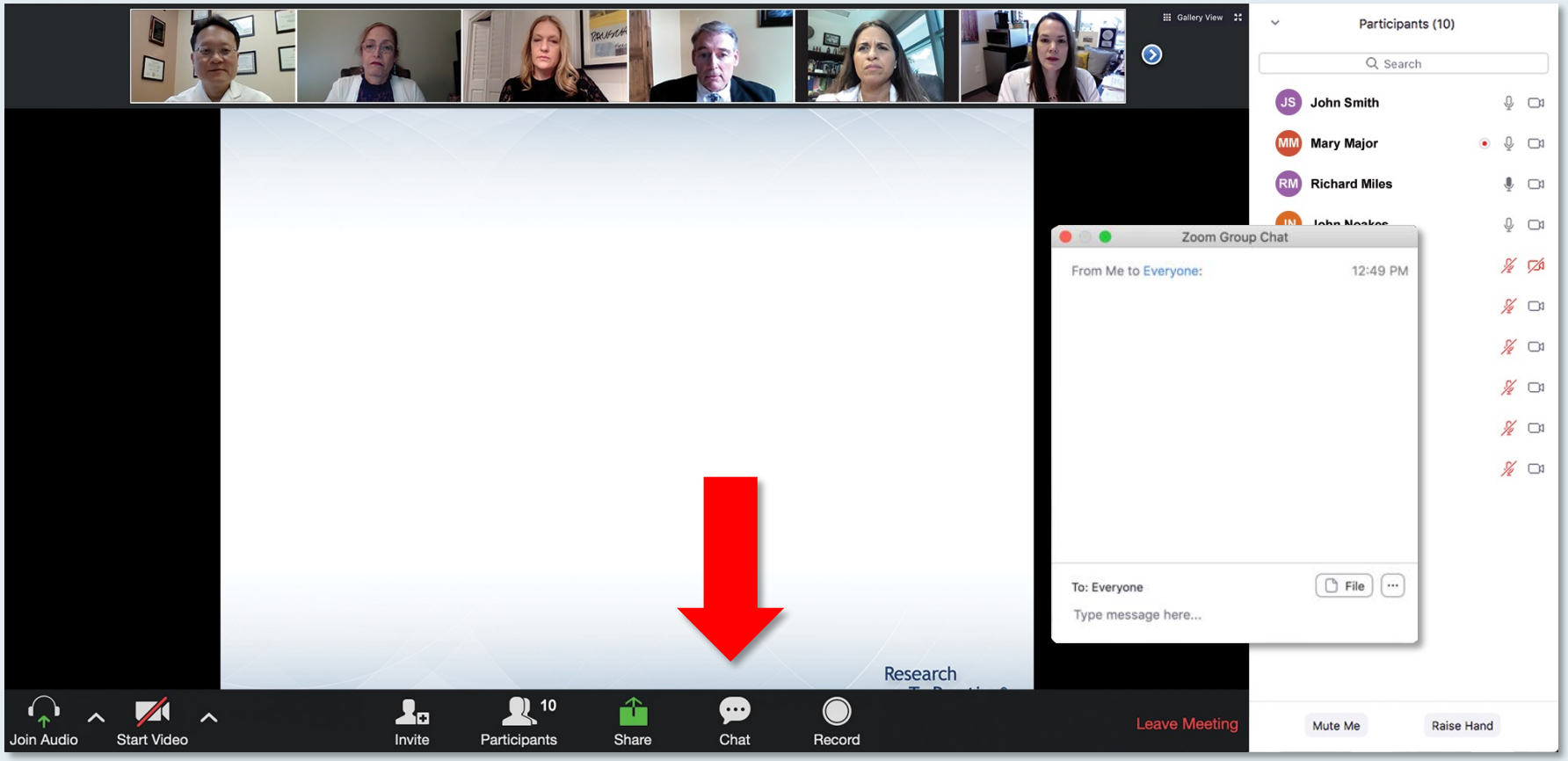

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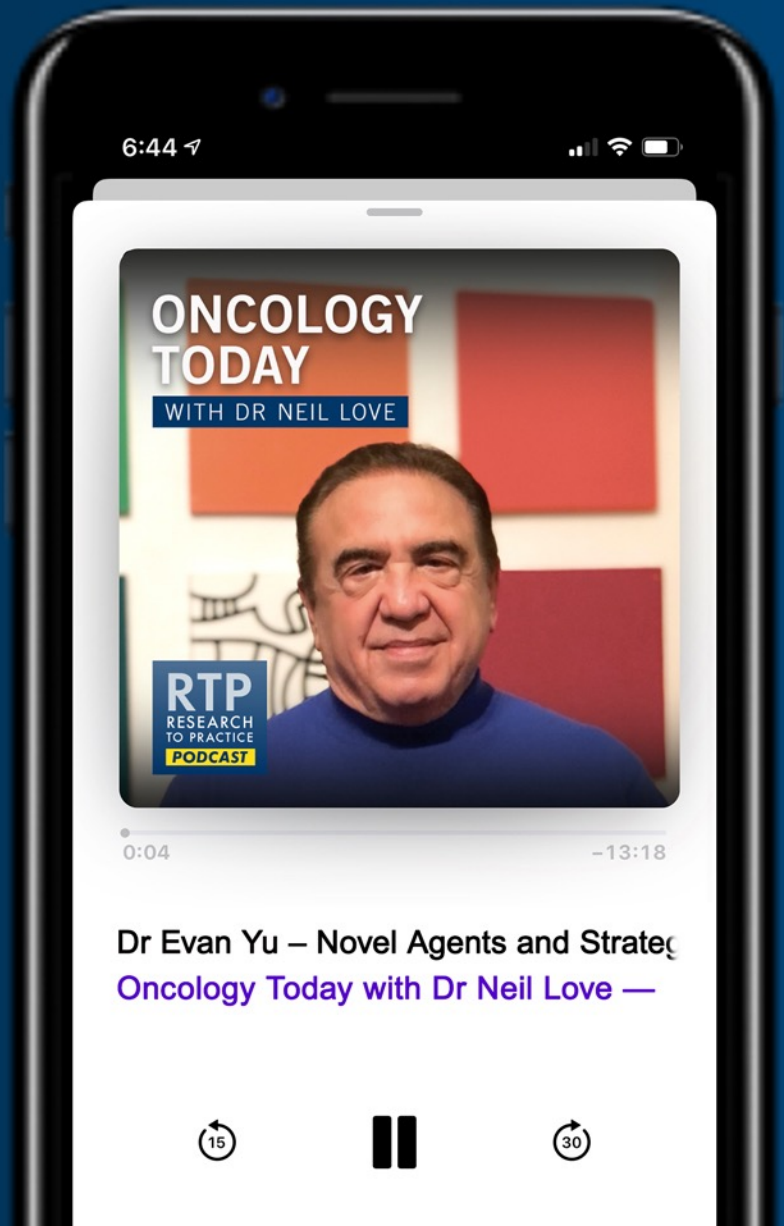

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Florida Cancer Specialists
New Port Richey, Florida

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Meet The Professor with Dr Armstrong

Introduction: Genitourinary Cancers Symposium 2022

MODULE 1: Dr Saylors — A 58-year-old man with metastatic hormone-sensitive prostate cancer, a history of breast cancer and a germline BRCA1 mutation

MODULE 2: Dr Ibrahim — A 70-year-old man with multiple prior therapies for metastatic prostate cancer, including lutetium on the VISION trial

MODULE 3: Dr Ma — An 88-year-old man with metastatic prostate cancer who received leuprolide/enzalutamide/denosumab and sipuleucel-T

MODULE 4: Dr Bachow — A 55-year-old man with metastatic adenocarcinoma of the prostate with neuroendocrine differentiation (genomic LOH high, germline PALB2 VUS)

MODULE 5: Dr Kumar — A 74-year-old man with metastatic castration-resistant prostate cancer and Lynch syndrome (BRCA VUS, MSH6 and BRAF V601E mutations)

MODULE 6: Dr Ibrahim — An 89-year-old man with mCRPC and a CHEK2 mutation

MODULE 7: Journal Club with Dr Armstrong

MODULE 8: Relevant Data Sets

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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

Genitourinary Cancers Symposium 2022;Abstract 11.

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PROPEL

- Abiraterone with olaparib or placebo in a genetically unselected population
  - Serum Collected for cfDNA on all patients
  - Tissue testing performed on ~70% of patients
- All patients submitted tissue for NGS
- Primary outcome: rPFS- data presented today
- Secondary outcome: OS- not yet mature

	Olaparib + abiraterone (n=399)	Placebo + Abiraterone (n=397)
Events, n (%)	157 (39.3%)	218 (54.9)
Median rPFS (mos)	27.6	16.4
HR (95% CI)	0.61 (0.49-0.74) P<0.0001	
HRR mut (n=226) HR (95% CI)	0.50 (0.34-0.73)	
Non-HRR mut (n=552) HR (95% CI)	0.76 (0.60-0.97)	

Courtesy of Alan H Bryce, MD

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]Kyiv City Clinical Oncology Center, 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

- Abiraterone with or without niraparib in the pre chemotherapy setting
- 765 patients
- **Tissue and Serum for genetic testing required for entry to study**
- HRR gene alteration as follows:
  - **Cohort 1: positive for HRR gene alteration**
    - **population for presented data**
  - Cohort 2: not positive for DRD
    - Halted for futility
- Primary outcome: rPFS
- Secondary outcome: **OS not yet mature**

Cohort 1: HRR mutated

	Niraparib + abiraterone (n=399)	Placebo + Abiraterone (n=397)
Number	212	211
Median rPFS (mos)	16.5	13.7
HR (95% CI)	0.73 (0.56-0.96) P=0.0217	

Courtesy of Alan H Bryce, MD

SUMMARY
PROPEL AND MAGNITUDE

- Very Different studies- meaningful cross study comparisons are not possible
- Overall survival data will be critical
  - The studies have not established that concurrent will be better than sequential
  - Prolonged treatment with a myelosuppressive drug can impact later lines of therapy
- Study populations are very different on the basis of prior treatment with 1st generation API in the first line
  - Reflected in the striking difference in rPFS on the control arms
- Method of assessing HRR status is likely to make a difference
- Review of more detailed data in the respective publications will be crucial- what treatments did patients receive for mHSPC?

Courtesy of Alan H Bryce, MD

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

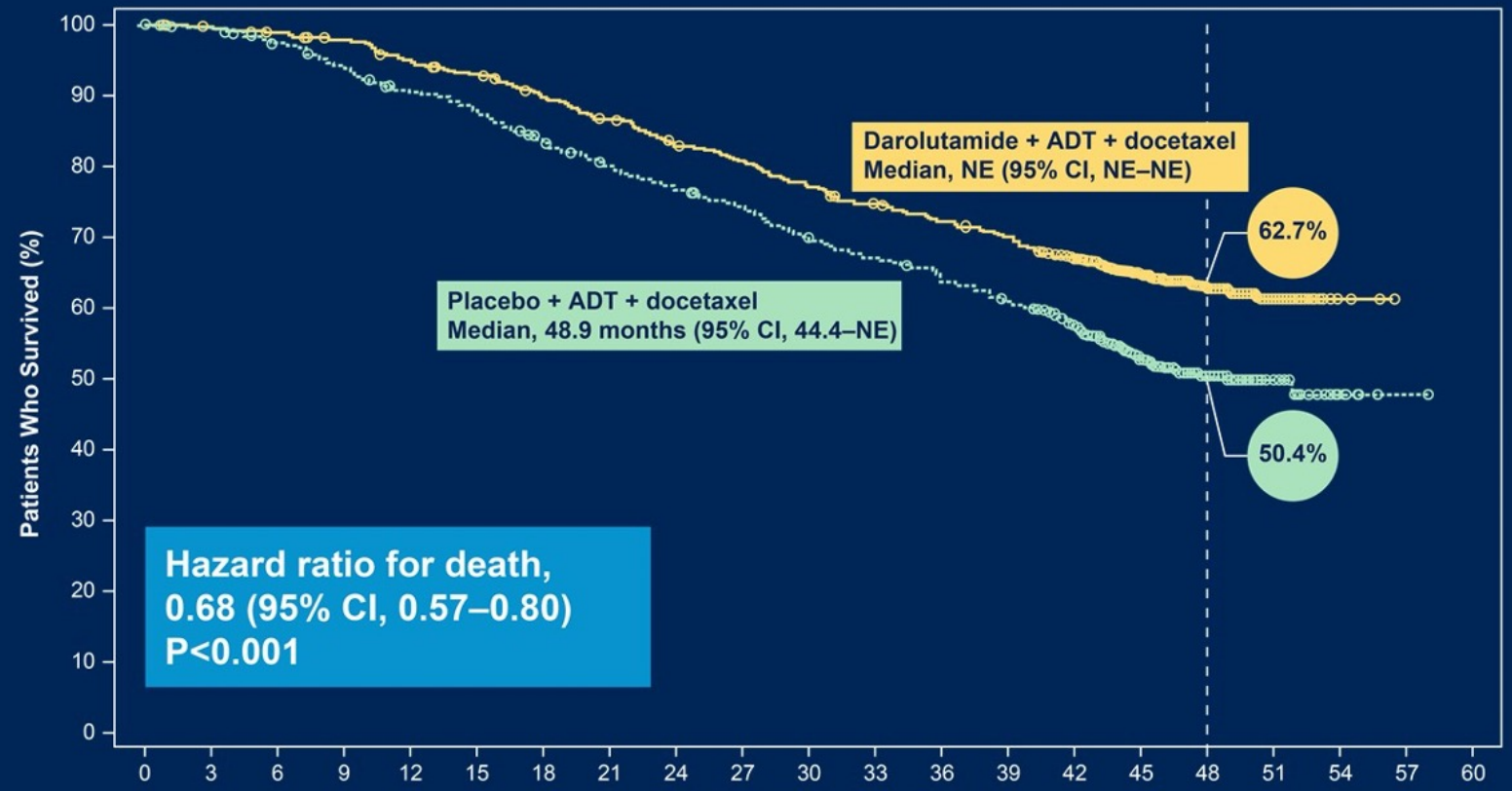
Matthew R. Smith, MD, PhD,[1] Maha Hussain, MD,[2] Fred Saad, MD,[3] Karim Fizazi, MD, PhD,[4] Cora N. Sternberg, MD,[5] E. David Crawford, MD,[6] Evgeny Kopyltsov, MD,[7] Chandler H. Park, MD,[8] Boris Alekseev, MD,[9] Álvaro Montesa Pino, MD,[10] Dingwei Ye, MD,[11] Francis Parnis, MB, BS,[12] Felipe 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

Genitourinary Cancers Symposium 2022;Abstract 13.

ARASENS Primary Endpoint*: Overall Survival

Darolutamide significantly reduced the risk of death by 32.5%



No. at Risk

Darolutamide	651	645	637	627	608	593	570	548	525	509	486	468	452	436	402	267	139	56	9	0	0
Placebo	654	646	630	607	580	565	535	510	488	470	441	424	402	383	340	218	107	37	6	1	0

*Primary analysis occurred after 533 deaths (darolutamide, 229; placebo, 304). CI, confidence interval; NE, not estimable.

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

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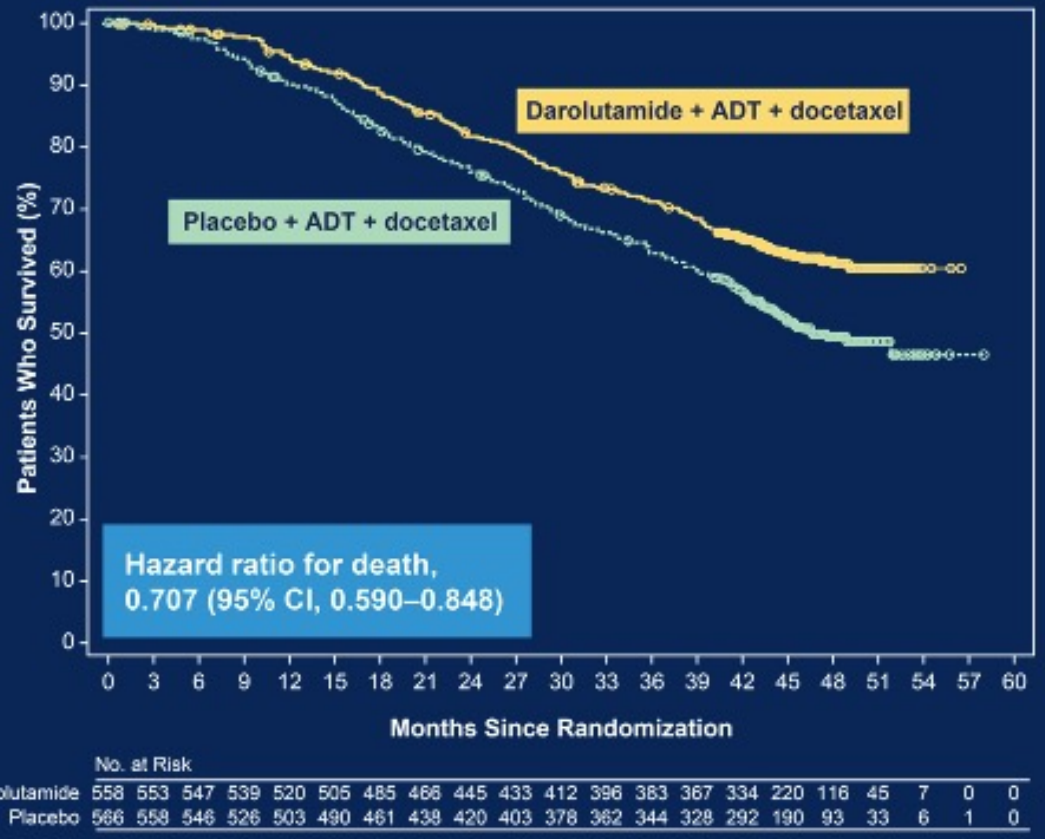
ARASENS: ADT + docetaxel +/- darolutamide
Overall Survival By Metastatic Stage at Initial Diagnosis

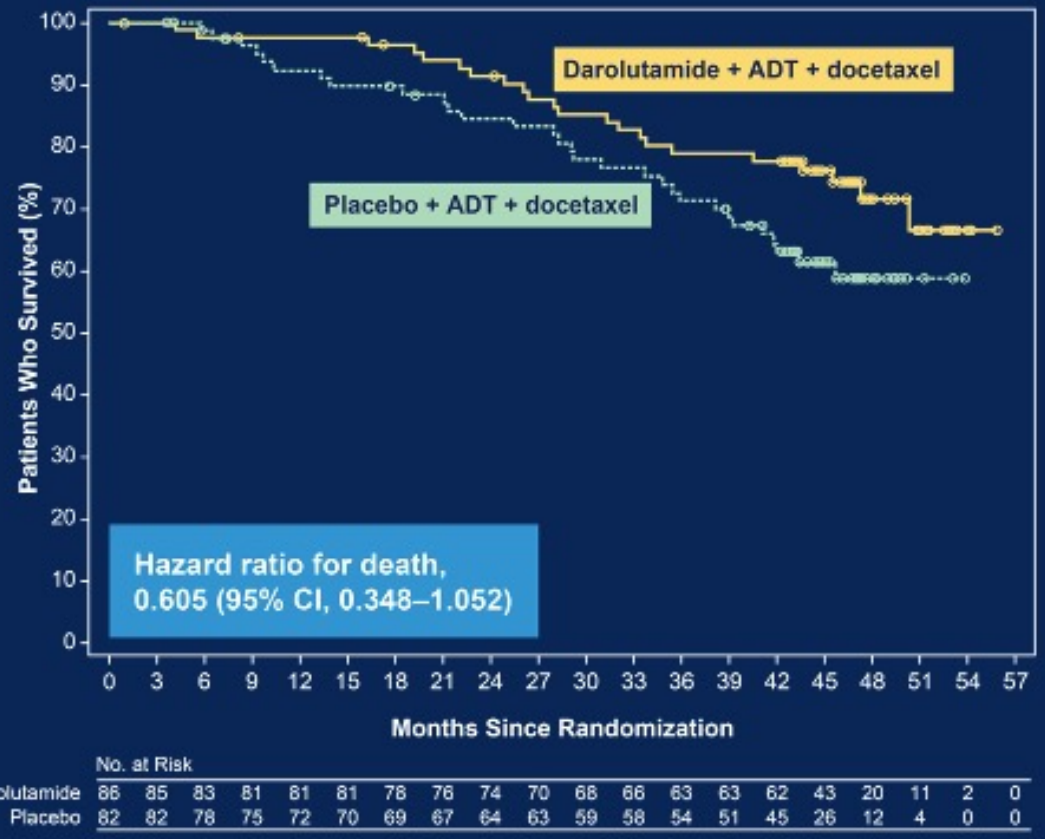
OS in Patients with M1 (*de novo*)



No. at Risk

Darolutamide	558	553	547	539	520	505	485	466	445	433	412	396	383	367	334	220	116	45	7	0	0
Placebo	566	558	546	526	503	490	461	438	420	403	378	362	344	328	292	190	93	33	6	1	0

OS in Patients with M0 (recurrent)



No. at Risk

Darolutamide	86	85	83	81	81	81	78	76	74	70	68	66	63	63	62	43	20	11	2	0
Placebo	82	82	78	75	72	70	69	67	64	63	59	58	54	51	45	26	12	4	0	0

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

RTP RESEARCH TO PRACTICE

Adverse Events of Special Interest for 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

*EAIR is the number of patients with a given AE divided by the total darolutamide/placebo treatment duration of all patients in years and expressed in 100 PY. †This category combines the following MedDRA terms: rash, maculopapular rash, drug eruption, pruritic rash, erythematous rash, macular rash, papular rash, follicular rash, pustular rash, and vesicular rash. ‡This category is a MedDRA High-Level Group Term. EAIR, exposure-adjusted incidence rate; PY, patient year.

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

ARASENS Conclusions

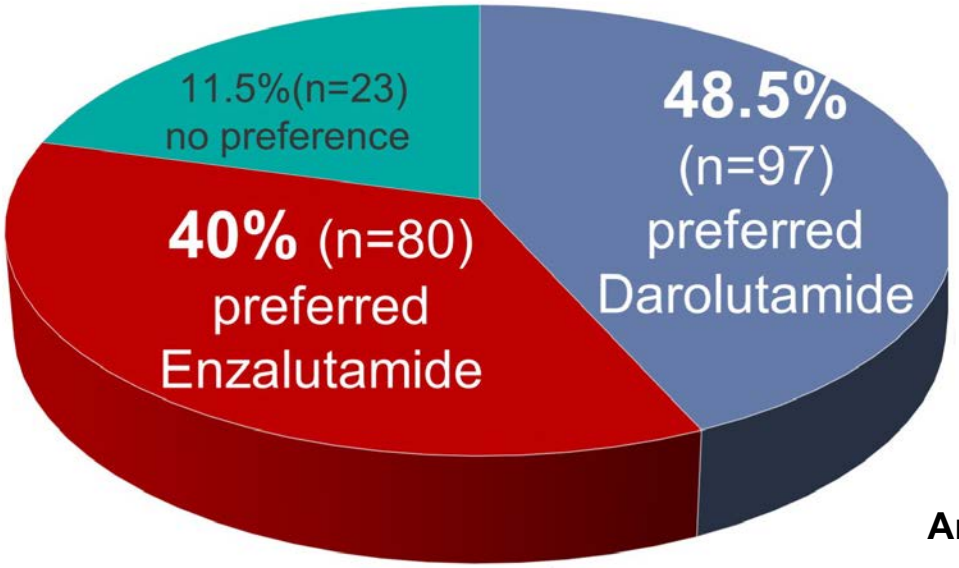
- Darolutamide in combination with ADT and docetaxel significantly improved OS compared with ADT and docetaxel in patients with mHSPC. Darolutamide reduced the risk of death by 32.5%
- Darolutamide improved OS despite a high rate of subsequent life-prolonging systemic therapy in the placebo group
- The OS benefit for darolutamide was consistent across prespecified subgroups
- Darolutamide also significantly improved key secondary endpoints, including time to castration-resistant prostate cancer, time to pain progression, time to first SSE, and time to first subsequent antineoplastic therapy
- Rates of adverse events were similar between the darolutamide and placebo groups

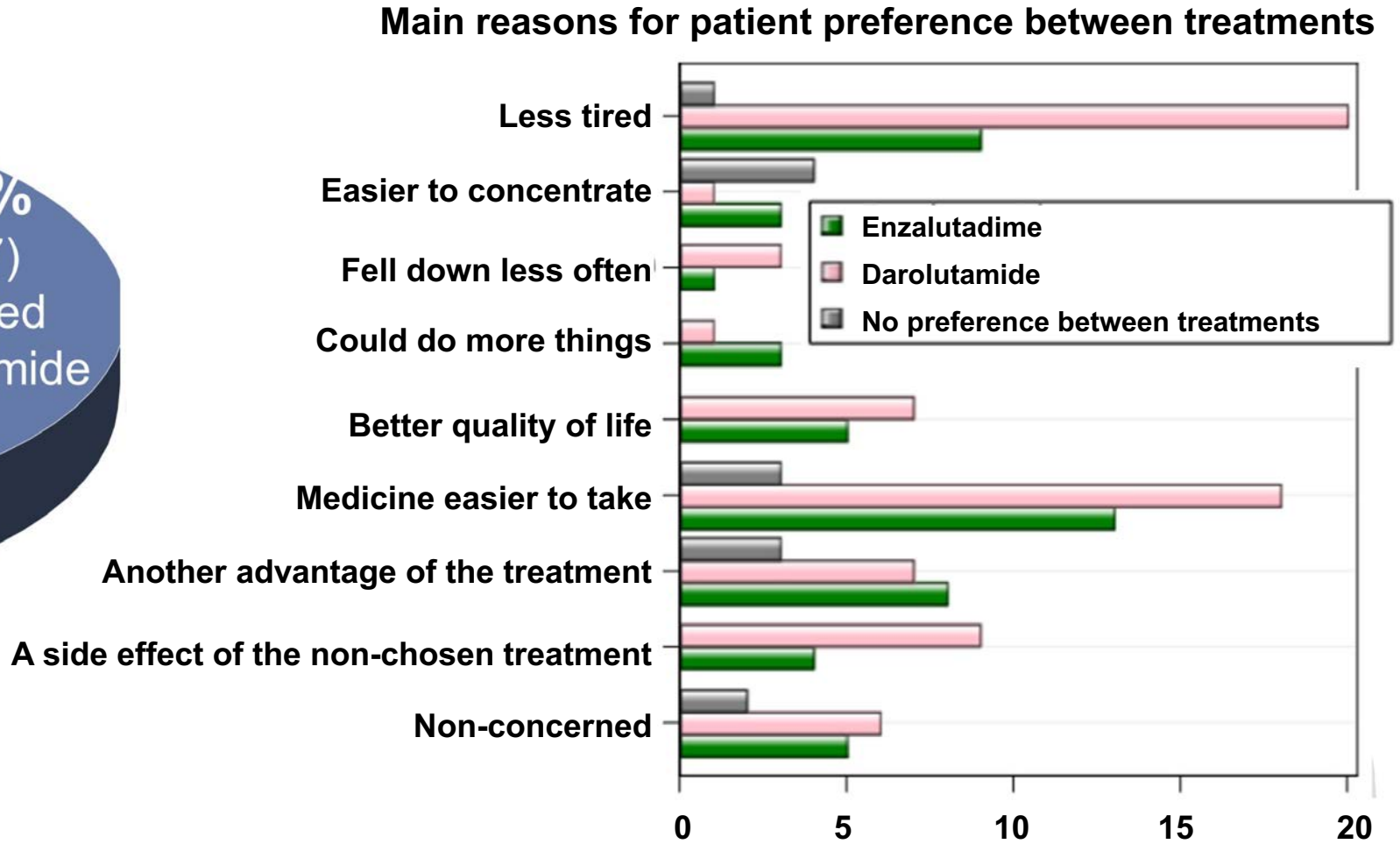
Darolutamide in combination with ADT and docetaxel should become a new standard of care for treatment of mHSPC

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

RTP RESEARCH TO PRACTICE

ODENZA: A Phase II Crossover Trial Evaluating Preference Between Darolutamide and Enzalutamide in Men with Asymptomatic or Mildly Symptomatic mCRPC





Colomba E et al. ASCO 2021;Abstract 5046.

Meet The Professor with Dr Armstrong

Introduction: Genitourinary Cancers Symposium 2022

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MODULE 7: Journal Club with Dr Armstrong

MODULE 8: Relevant Data Sets

RTP RESEARCH TO PRACTICE

Case Presentation: A 58-year-old man with metastatic hormone-sensitive prostate cancer, a history of breast cancer and a germline BRCA1 mutation

Dr Julia Saylors (North Charleston, South Carolina)

RTP
RESEARCH
TO PRACTICE

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

 Dr Armstrong	After at least 1 line of both hormonal therapy and chemotherapy	 Prof Fizazi	After 1 line of hormonal therapy
 Dr Bryce	After 1 line of hormonal therapy	 Dr Morgans	After 1 line of hormonal therapy
 Prof Chowdhury	After 1 line of hormonal therapy	 Dr Sartor	After 1 line of hormonal therapy

RTP RESEARCH TO PRACTICE

A 65-year-old man with MSS prostate cancer metastatic to the bone and a germline BRCA2 mutation who is receiving abiraterone/dexamethasone for hormone-sensitive metastatic disease develops new low-volume asymptomatic bone metastases. Which systemic treatment would you most likely recommend?

 Dr Armstrong	Sipuleucel-T followed by olaparib or docetaxel at further progression	 Prof Fizazi	Olaparib
 Dr Bryce	Olaparib	 Dr Morgans	Olaparib
 Prof Chowdhury	Olaparib	 Dr Sartor	Olaparib

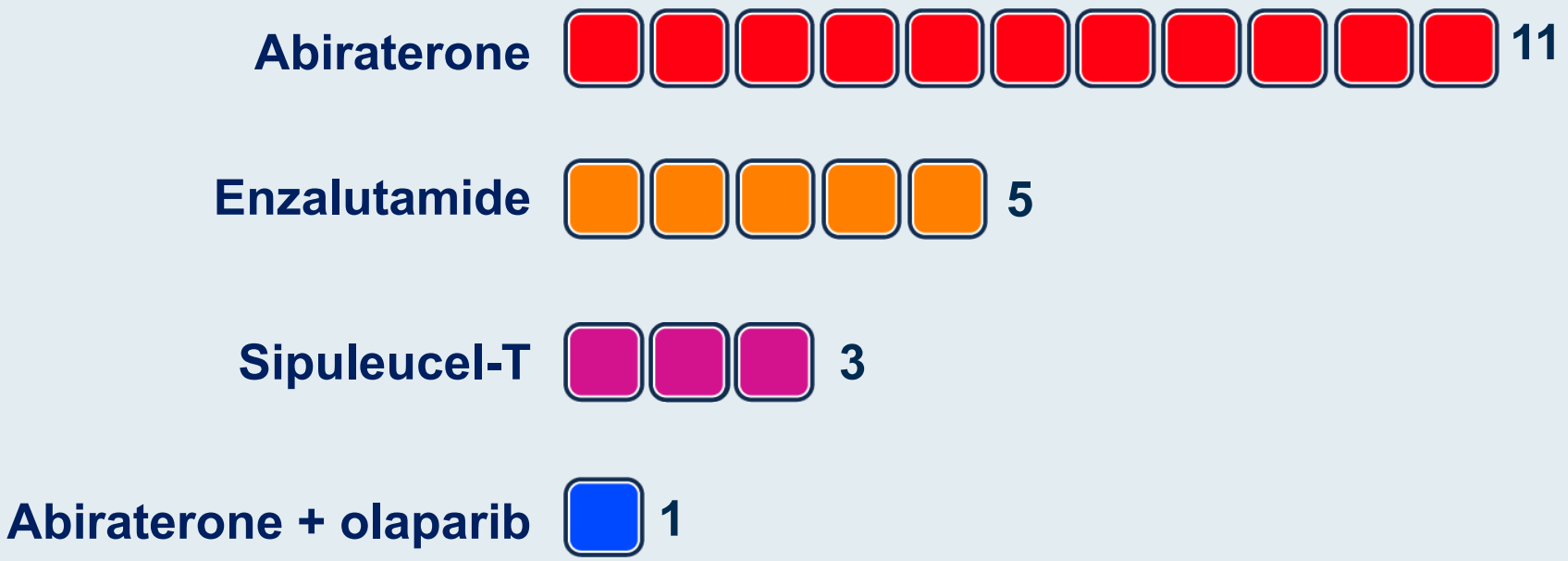
RTP RESEARCH TO PRACTICE

A 65-year-old man receiving androgen deprivation therapy (ADT) for M0 disease after radical prostatectomy (RP) is found to have asymptomatic bone metastases. Genetic testing is negative for homologous recombination repair (HRR) mutations. Regulatory and reimbursement issues aside, what systemic treatment would you most likely recommend?

1. Abiraterone
2. Enzalutamide
3. Docetaxel
4. Sipuleucel-T
5. Abiraterone + olaparib
6. Other

RTP
RESEARCH
TO PRACTICE

A 65-year-old man receiving ADT for M0 disease after RP is found to have asymptomatic bone metastases. Genetic testing is negative for homologous recombination repair (HRR) mutations. Regulatory and reimbursement issues aside, what systemic treatment would you most likely recommend?



Survey of genitourinary cancer clinical investigators

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Prostate Cancer (Part 1 of a 2-Part Series)

Thursday, February 17, 2022

7:00 PM – 9:00 PM PT

Faculty

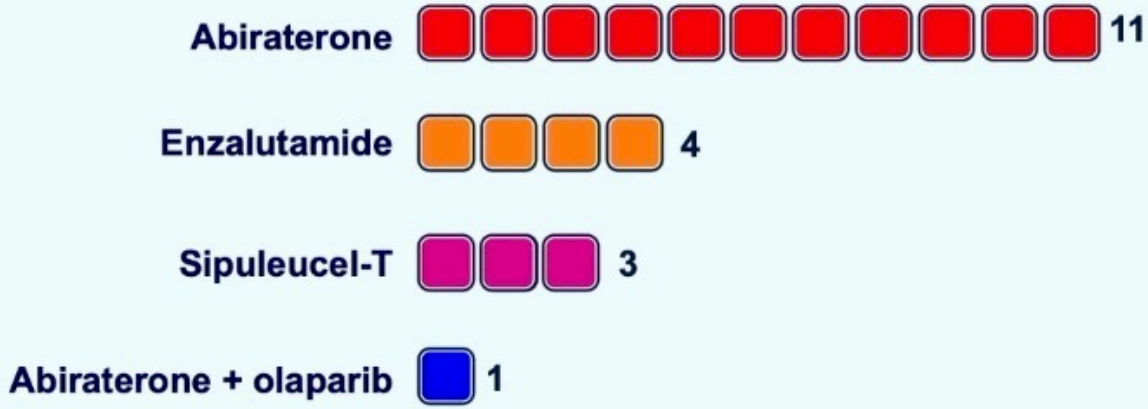
Neeraj Agarwal, MD
Himisha Beltran, MD
Fred Saad, MD
A Oliver Sartor, MD

Moderator

Alan H Bryce, MD

RTP
RESEARCH
TO PRACTICE

A 65-year-old man receiving ADT for M0 disease after RP is found to have asymptomatic bone metastases. Genetic testing is negative for homologous recombination repair (HRR) mutations. Regulatory and reimbursement issues aside, what systemic treatment would you most likely recommend?



Survey of genitourinary cancer clinical investigators

Meet The Professor with Dr Armstrong

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RTP
RESEARCH
TO PRACTICE

Case Presentation: A 70-year-old man with multiple prior therapies for metastatic prostate cancer, including lutetium on the VISION trial

Dr Sulfi Ibrahim (Richmond, Indiana)

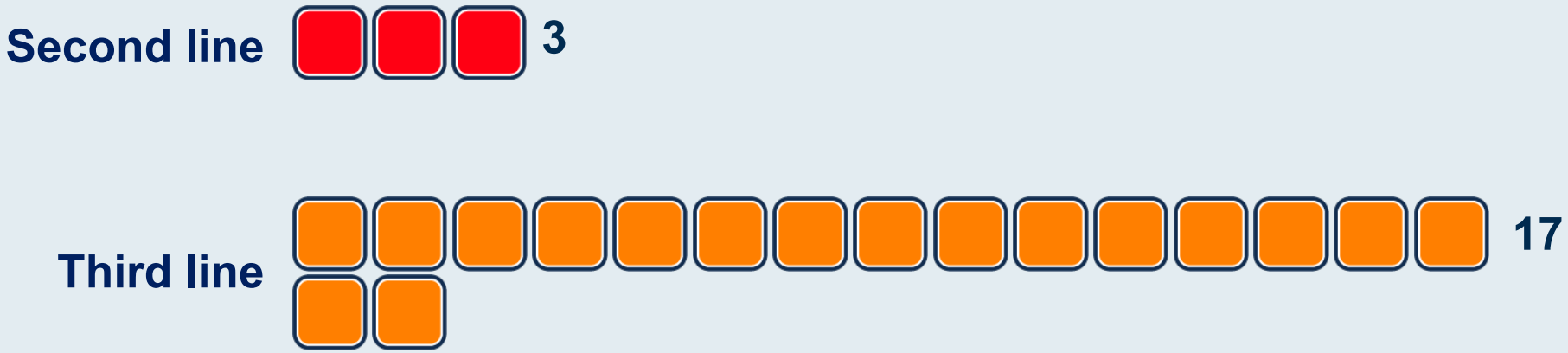
RTP
RESEARCH
TO PRACTICE

Regulatory and reimbursement issues aside, in which line of therapy would you administer 177Lu-PSMA-617 for patients with metastatic prostate cancer?

 Dr Armstrong	Third line or beyond	 Prof Fizazi	Third line
 Dr Bryce	Third line	 Dr Morgans	Third line
 Prof Chowdhury	Third line	 Dr Sartor	First line and beyond

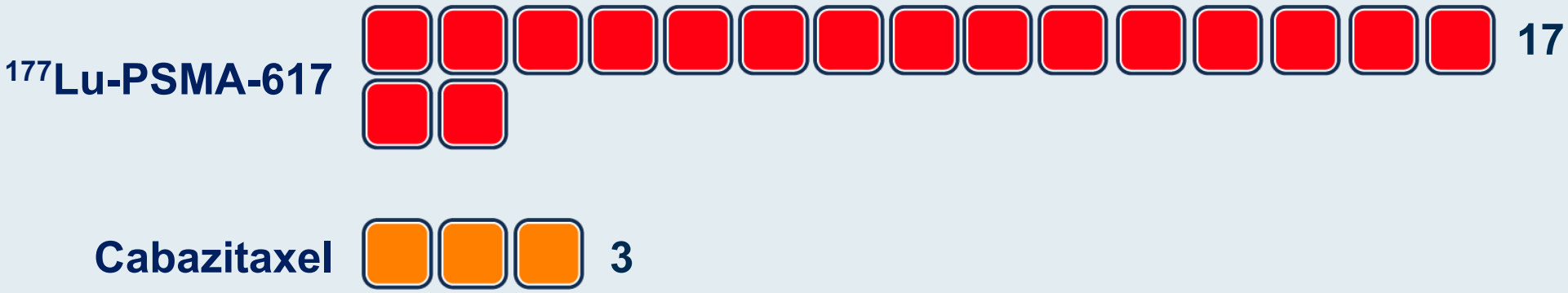
RTP RESEARCH TO PRACTICE

If ^{177}Lu-PSMA-617 were available, in what line of therapy would you like to offer it to your patients with PSMA-positive mCRPC?



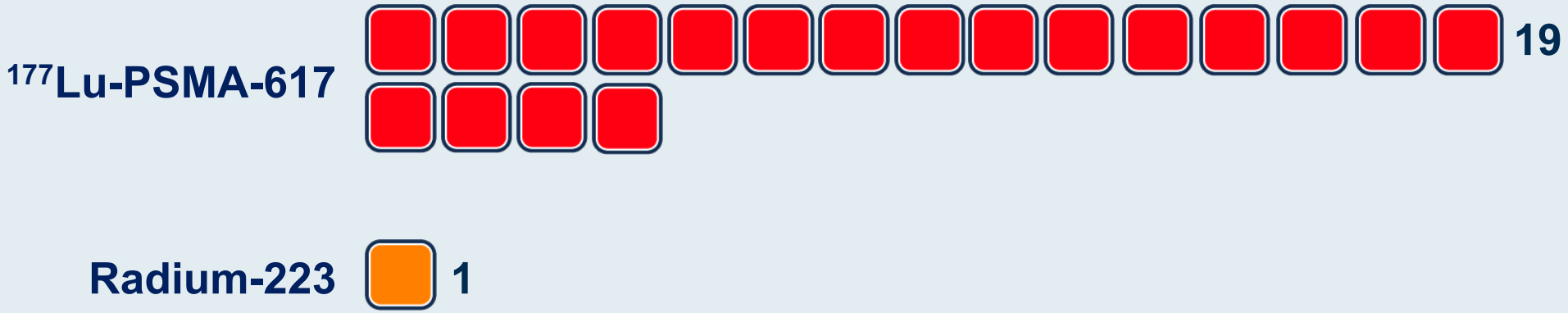
Survey of genitourinary cancer clinical investigators

If ^{177}Lu-PSMA-617 were available, which of the following would you generally recommend first for a patient with PSMA-positive mCRPC?



Survey of genitourinary cancer clinical investigators

If ^{177}Lu-PSMA-617 were available, which of the following would you generally prefer for a patient with PSMA-positive mCRPC and bone-only metastases?



Survey of genitourinary cancer clinical investigators

N Engl J Med 2021;385:1091-103

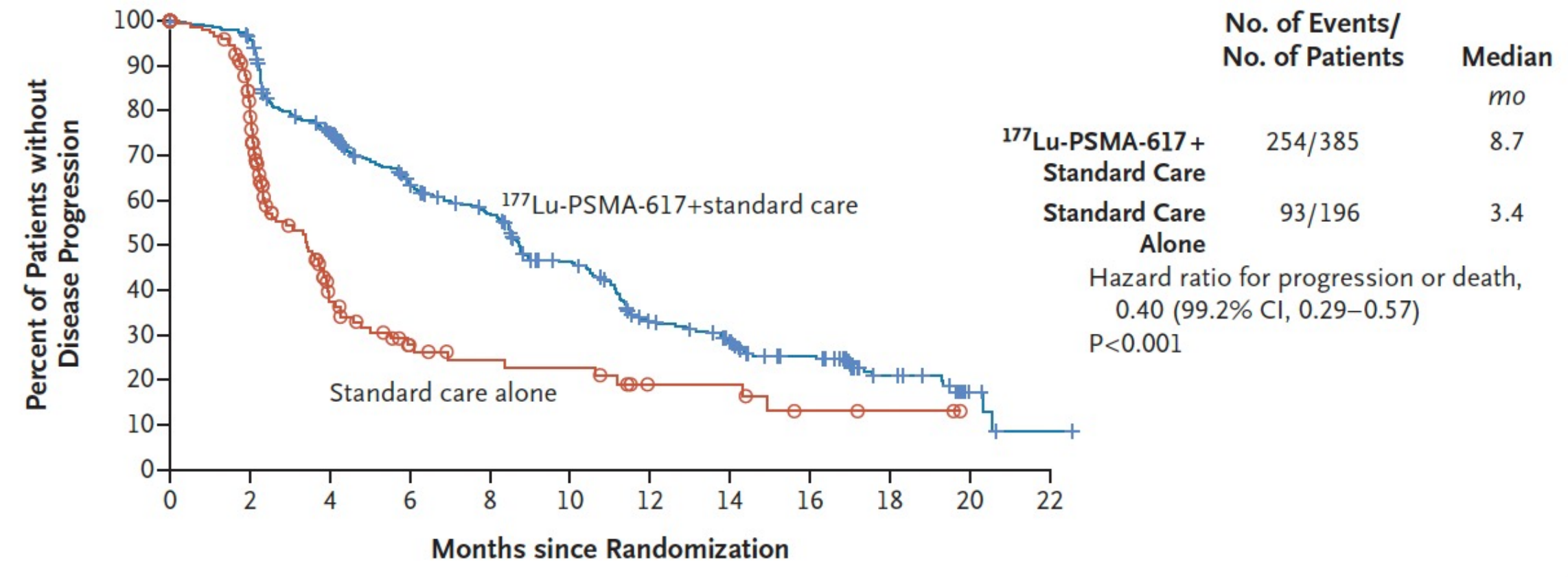
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

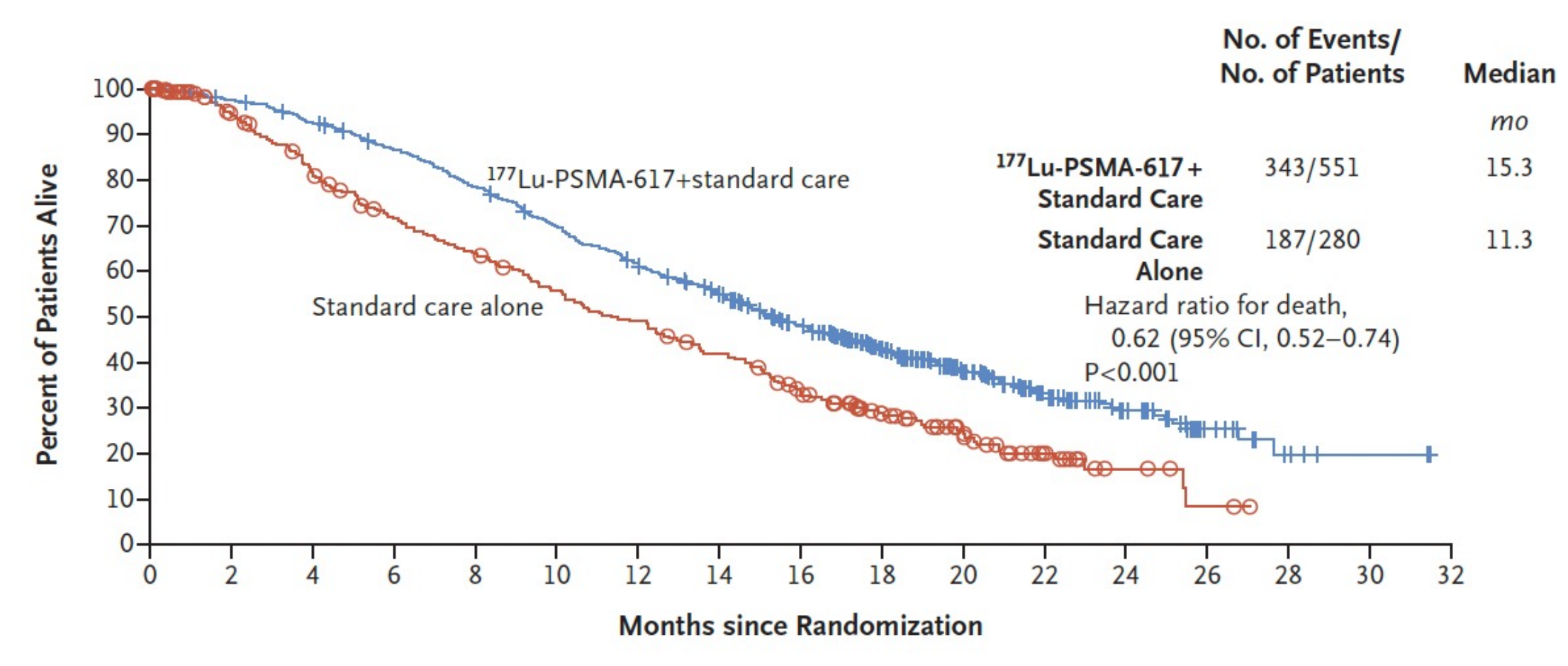
O. Sartor, J. de Bono, K.N. Chi, K. Fizazi, K. Herrmann, K. Rahbar, S.T. Tagawa, L.T. Nordquist, N. Vaishampayan, G. El-Haddad, C.H. Park, T.M. Beer, A. Armour, W.J. Pérez-Contreras, M. DeSilvio, E. Kpamegan, G. Gericke, R.A. Messmann, M.J. Morris, and B.J. Krause, for the VISION Investigators*

VISION: Imaging-Based Progression-Free Survival



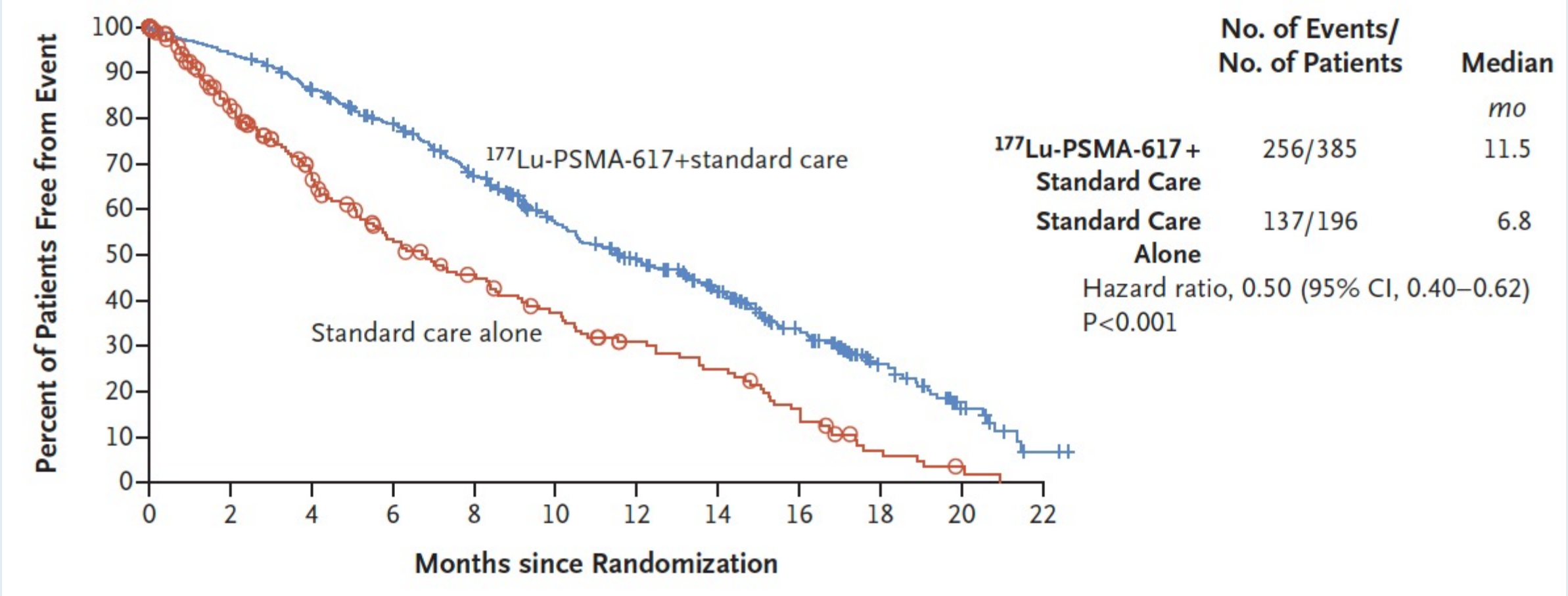
Sartor O et al. *N Engl J Med* 2021;385:1091-103.

VISION: Overall Survival



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

VISION: Time to First Symptomatic Skeletal Event



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

RTP RESEARCH TO PRACTICE

177Lu-PSMA-617 (LuPSMA) versus Cabazitaxel in Metastatic Castration-Resistant Prostate Cancer (mCRPC) Progressing After Docetaxel: Updated Results Including Progression-Free Survival (PFS) and Patient-Reported Outcomes (PROs) (TheraP ANZUP 1603)[1]

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

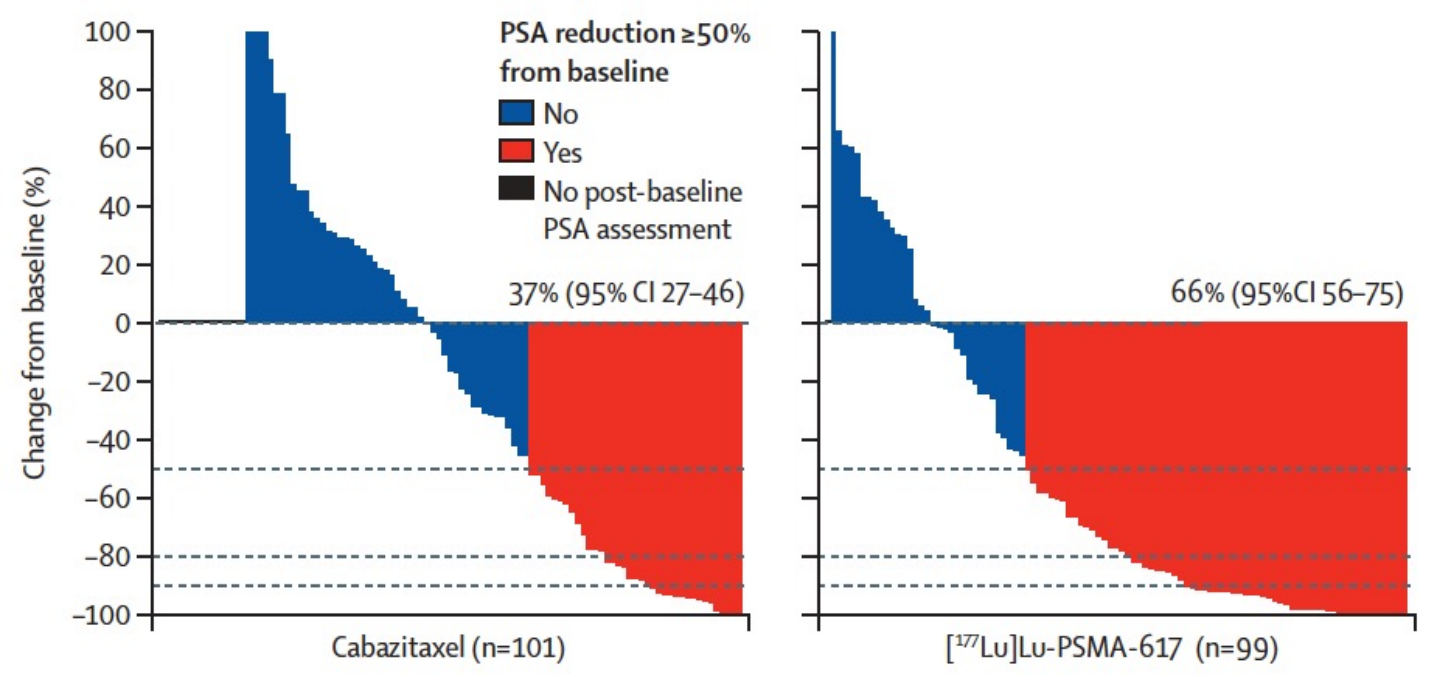
Michael S Hofman, Louise Emmett, Shahneen Sandhu, Amir Iravani, Anthony M Joshua, Jeffrey C Goh, David A Pattison, Thean Hsiang Tan, Ian D Kirkwood, Siobhan Ng, Roslyn J Francis, Craig Gedye, Natalie K Rutherford, Andrew Weickhardt , Andrew M Scott, Sze-Ting Lee, Edmond M Kwan, Arun A Azad, Shakher Ramdave, 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†*

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

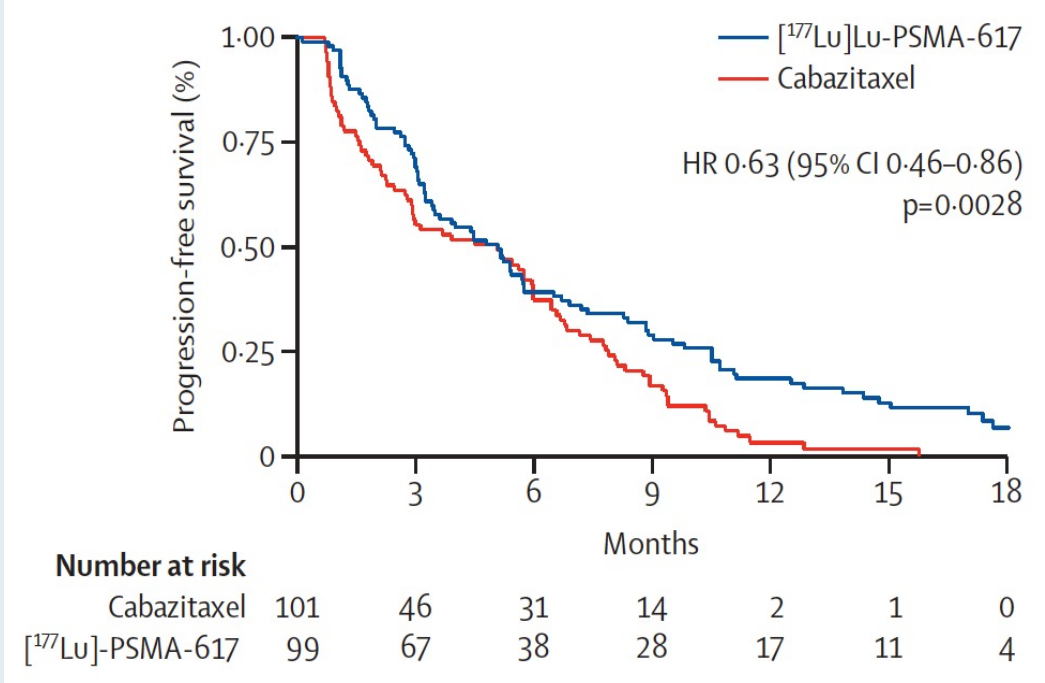
RTP RESEARCH TO PRACTICE

TheraP ANZUP 1603: PSA Response and PFS

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.

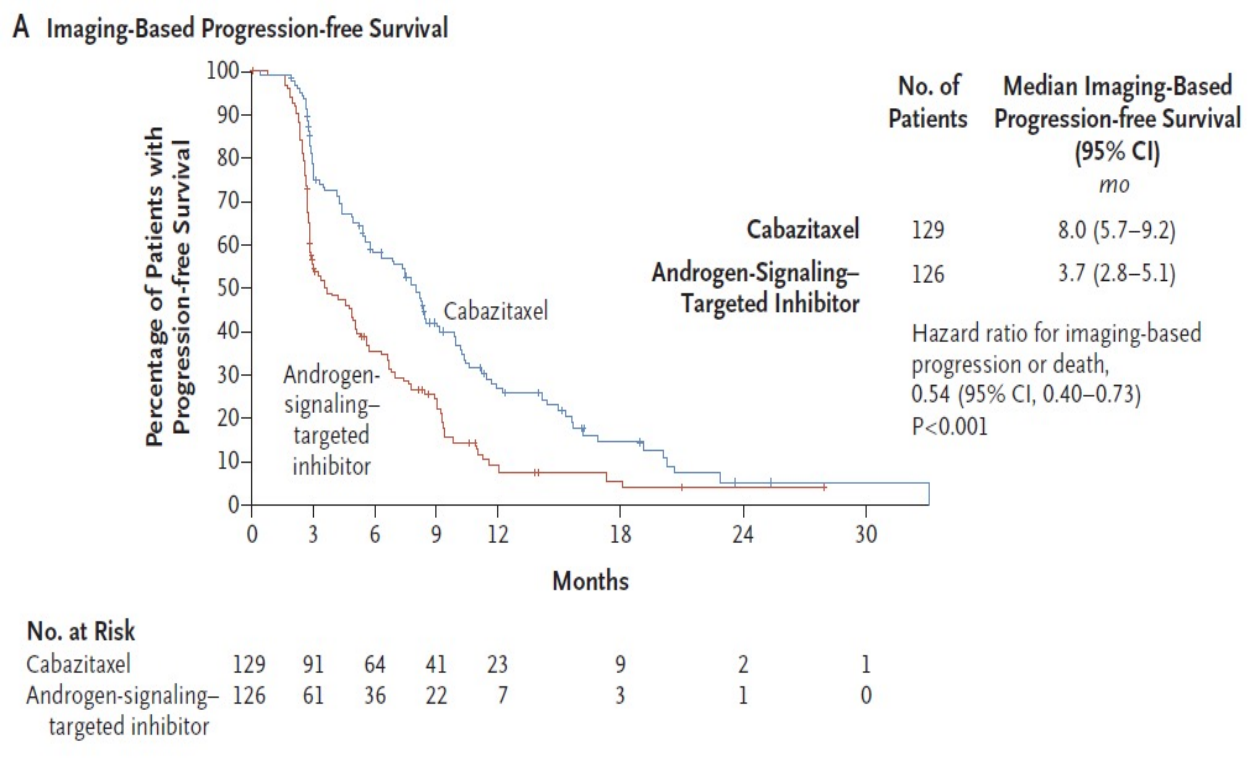
TheraP ANZUP 1603: Adverse Events

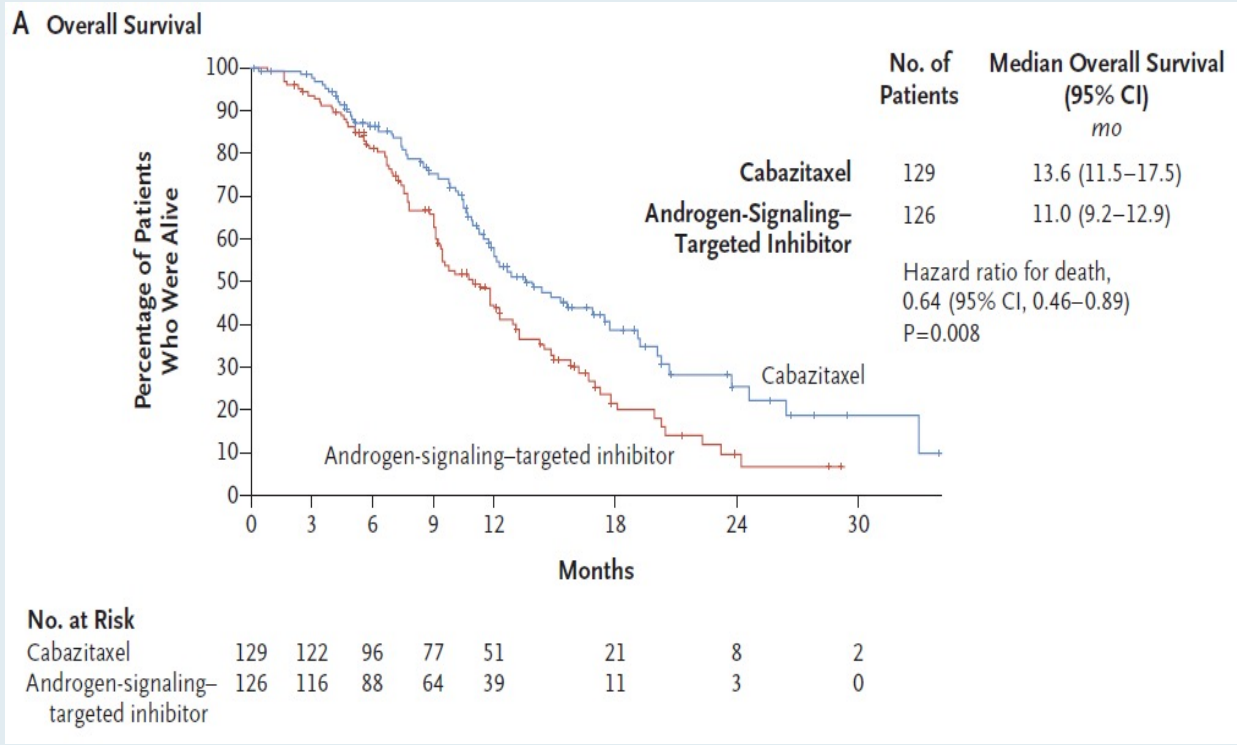
	[^{177}Lu]Lu-PSMA-617 (n=98)		Cabazitaxel (n=85)	
	Grade 1–2	Grade 3–4	Grade 1–2	Grade 3–4
Fatigue	69 (70%)	5 (5%)	61 (72%)	3 (4%)
Pain*	60 (61%)	11 (11%)	52 (61%)	4 (5%)
Dry mouth	59 (60%)	0	18 (21%)	0
Diarrhoea	18 (18%)	1 (1%)	44 (52%)	4 (5%)
Nausea	39 (40%)	1 (1%)	29 (34%)	0
Thrombocytopenia	18 (18%)	11 (11%)	4 (5%)	0
Dry eyes	29 (30%)	0	3 (4%)	0
Anaemia	19 (19%)	8 (8%)	11 (13%)	7 (8%)
Neuropathy†	10 (10%)	0	22 (26%)	1 (1%)
Dysgeusia	12 (12%)	0	23 (27%)	0
Haematuria	3 (3%)	1 (1%)	12 (14%)	5 (6%)
Neutropenia‡	7 (7%)	4 (4%)	4 (5%)	11 (13%)
Insomnia	9 (9%)	0	12 (14%)	1 (1%)
Vomiting	12 (12%)	1 (1%)	10 (12%)	2 (2%)
Dizziness	4 (4%)	0	11 (13%)	0
Leukopenia	10 (10%)	1 (1%)	5 (6%)	1 (1%)
Any adverse event	53 (54%)	32 (33%)	34 (40%)	45 (53%)

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

RTP RESEARCH TO PRACTICE

CARD: Imaging-Based PFS and OS with Cabazitaxel versus Abiraterone or Enzalutamide for mCRPC





de Wit R. et al. *NEJM* 2019;381:2506-18.

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Armstrong

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MODULE 8: Relevant Data Sets

RTP
RESEARCH
TO PRACTICE

Case Presentation: An 88-year-old man with metastatic prostate cancer who received leuprolide/enzalutamide/ denosumab and sipuleucel-T

Dr Yanjun Ma (Murfreesboro, Tennessee)

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RTP RESEARCH TO PRACTICE

Case Presentation: A 55-year-old man with metastatic adenocarcinoma of the prostate with neuroendocrine differentiation (genomic LOH high, germline PALB2 VUS)

Dr Spencer Bachow (Boca Raton, Florida)

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RESEARCH
TO PRACTICE

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RTP RESEARCH TO PRACTICE

Case Presentation: A 74-year-old man with mCRPC and Lynch syndrome (BRCA VUS, MSH6 and BRAF V601E mutations)

Dr KS Kumar (New Port Richey, Florida)

RTP RESEARCH TO PRACTICE

Immune Checkpoint Inhibitors in mCRPC

Therapy	Disease State	Disease Response
Pembrolizumab monotherapy[a]	Post-chemotherapy	ORR 9% PSA RR 14%
Pembrolizumab + enzalutamide[b]	Pre-chemotherapy progressing on enzalutamide	ORR 12% PSA RR 14%
Atezolizumab + enzalutamide[c]	Pre- and post-chemotherapy, s/p abiraterone	ORR 14% PSA RR 26%
Atezolizumab + cabozantinib[d]	Pre-chemotherapy s/p enzalutamide or abiraterone	ORR 34% PSA RR 29%

[a]JCO 2020: 38(5) 395-405. [b]Presented at the 2021 ASCO Annual Meeting – Virtual; June 4-8, 2021. [c]Sweeney C. AACR 2020. IMbassador250. [d]Agarwal ASCO 2020. COSMIC-021

2021 ESMO congress

Abstract LBA24

Cabozantinib in combination with atezolizumab in patients with metastatic castration-resistant prostate cancer (mCRPC): results of expanded cohort 6 of the COSMIC-021 Study

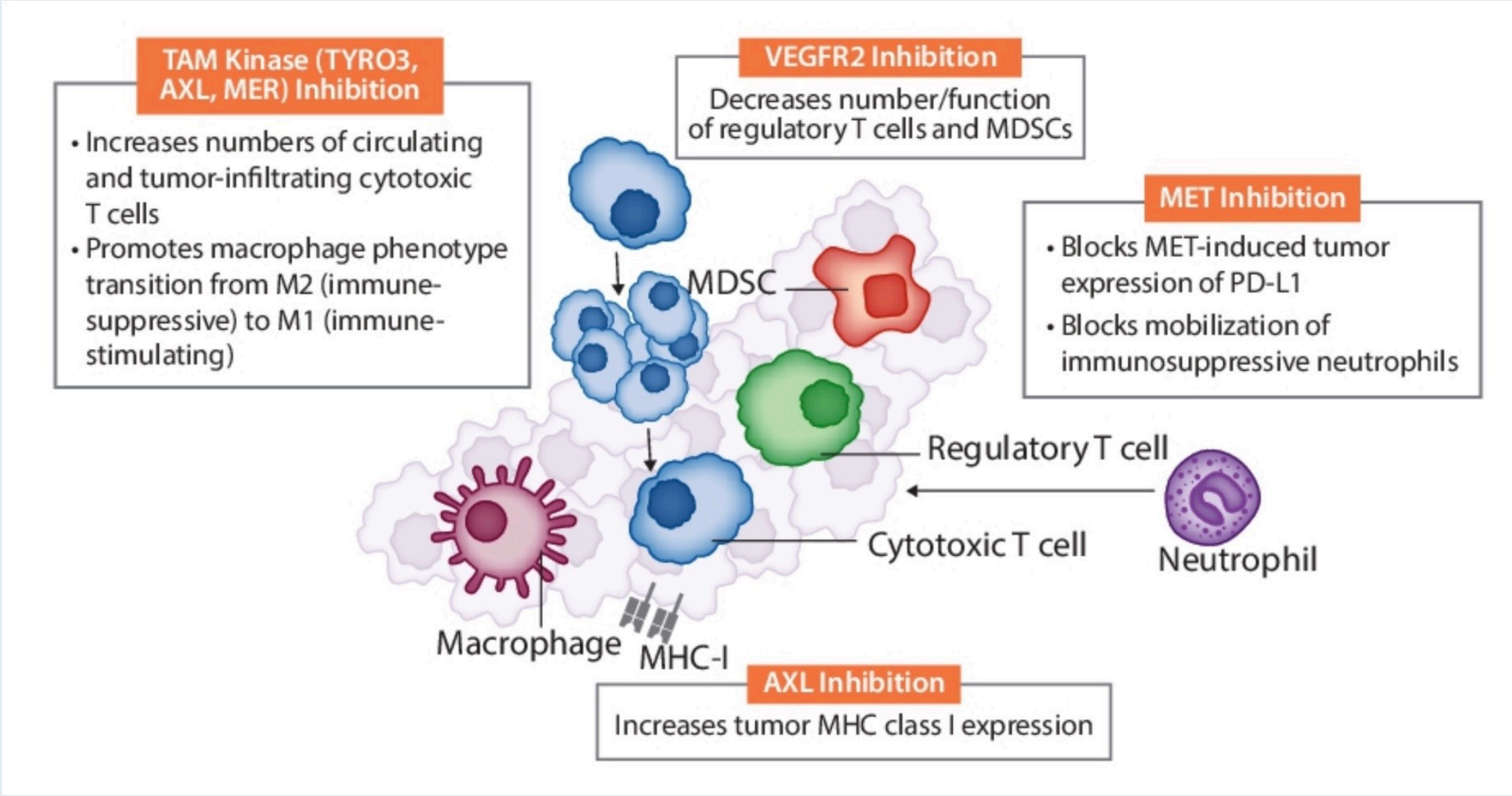
Neeraj Agarwal,[1] Bradley McGregor,[2] Benjamin L. Maughan,[1] Tanya B. Dorff,[3] William Kelly,[4] Bruno Fang,[5] Rana R. McKay,[6] Parminder Singh,[7] Lance Pagliaro,[8] Robert Dreicer,[9] Sandy Srinivas,[10] Yohann Loriot,[11] Ulka Vaishampayan,[12] Sanjay Goel,[13] Dominic Curran,[14] Ashok Panneerselvam,[14] Li-Fen Liu,[14] Toni K. Choueiri,[2*] Sumanta Pal[3*]

[1]Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA; [2]Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA; [3]City of Hope Comprehensive Cancer Center, Duarte, CA, USA; [4]Sidney Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA, USA; [5]Regional Cancer Care Associates, East Brunswick, NJ, USA; [6]University of California San Diego, San Diego, CA, USA; [7]Department of Oncology, Mayo Clinic, Scottsdale, AZ, USA; [8]Department of Oncology, Mayo Clinic, Rochester, MN, USA; [9]University of Virginia Cancer Center, Charlottesville, VA, USA; [10]Division of Medical Oncology, Stanford University Medical Center, Stanford, CA, USA; [11]Department of Cancer Medicine, Gustave Roussy Institute, INSERM 981, University Paris-Saclay, Villejuif, France; [12]Karmanos Cancer Center, Wayne State University, Detroit, MI, USA (Current affiliation: Division of Hematology/Oncology, University of Michigan, Ann Arbor, MI, USA); [13]Department of Medical Oncology, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY, USA; [14]Exelixis, Inc., Alameda, CA, USA

*Co-senior authors

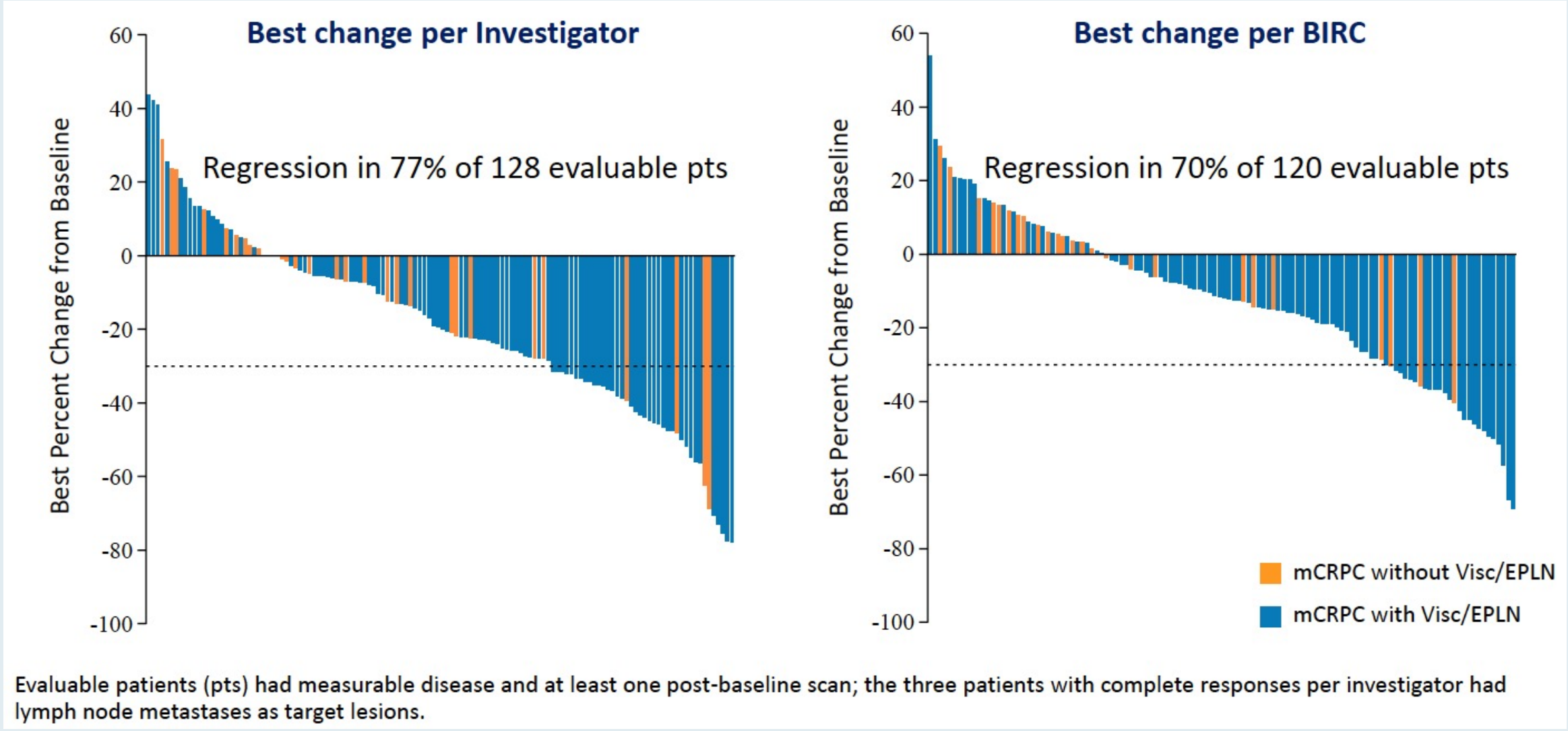
RTP RESEARCH TO PRACTICE

Cabozantinib Targets Pathways Associated with Tumor Immune Suppression



Agarwal N et al. ASCO 2020;Abstract 5564.

COSMIC-021: Best Change from Baseline in Sum of Target Lesions

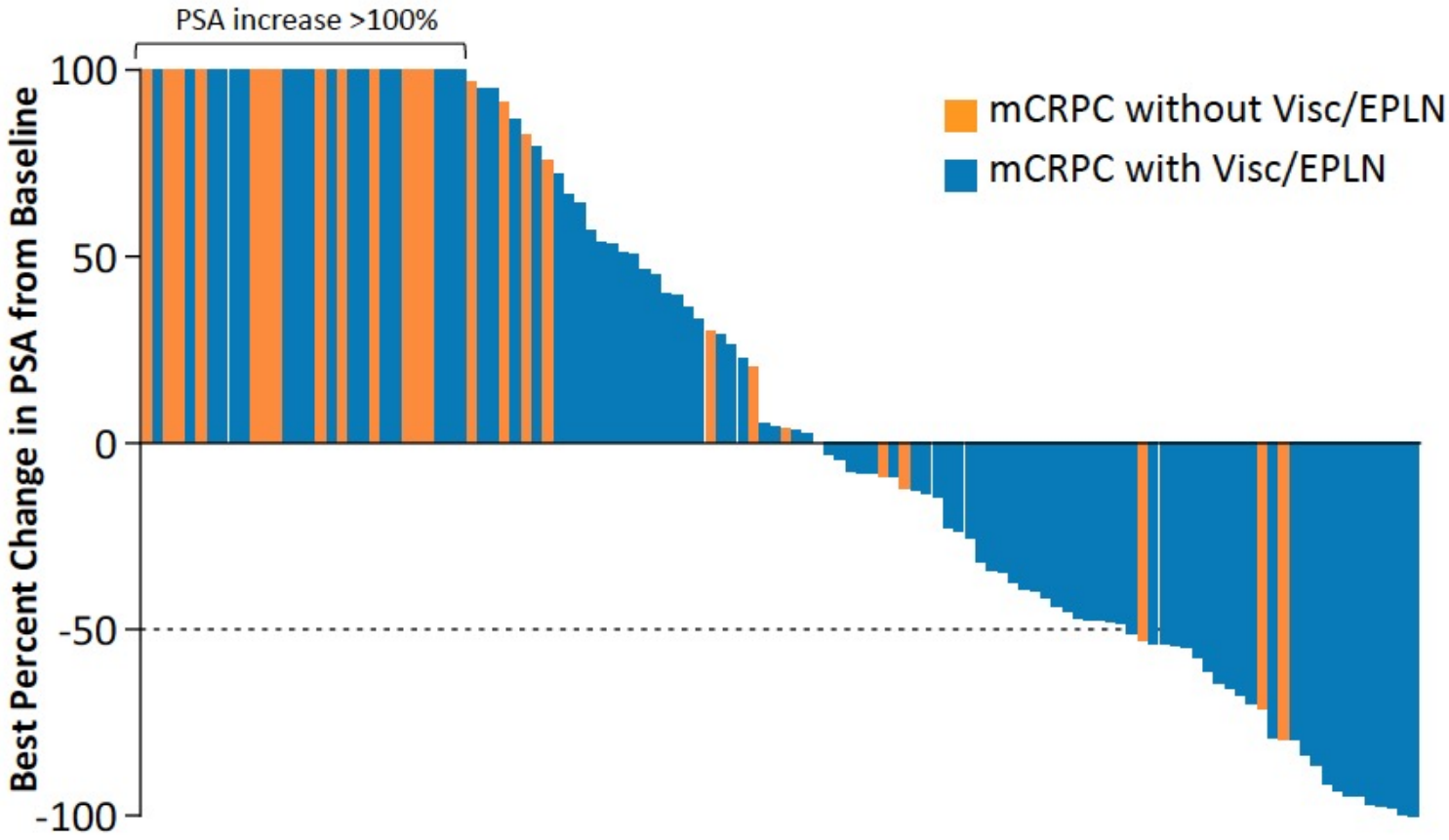


Evaluable patients (pts) had measurable disease and at least one post-baseline scan; the three patients with complete responses per investigator had lymph node metastases as target lesions.

Agarwal et al. ESMO 2021;Abstract LBA24.

RTP RESEARCH TO PRACTICE

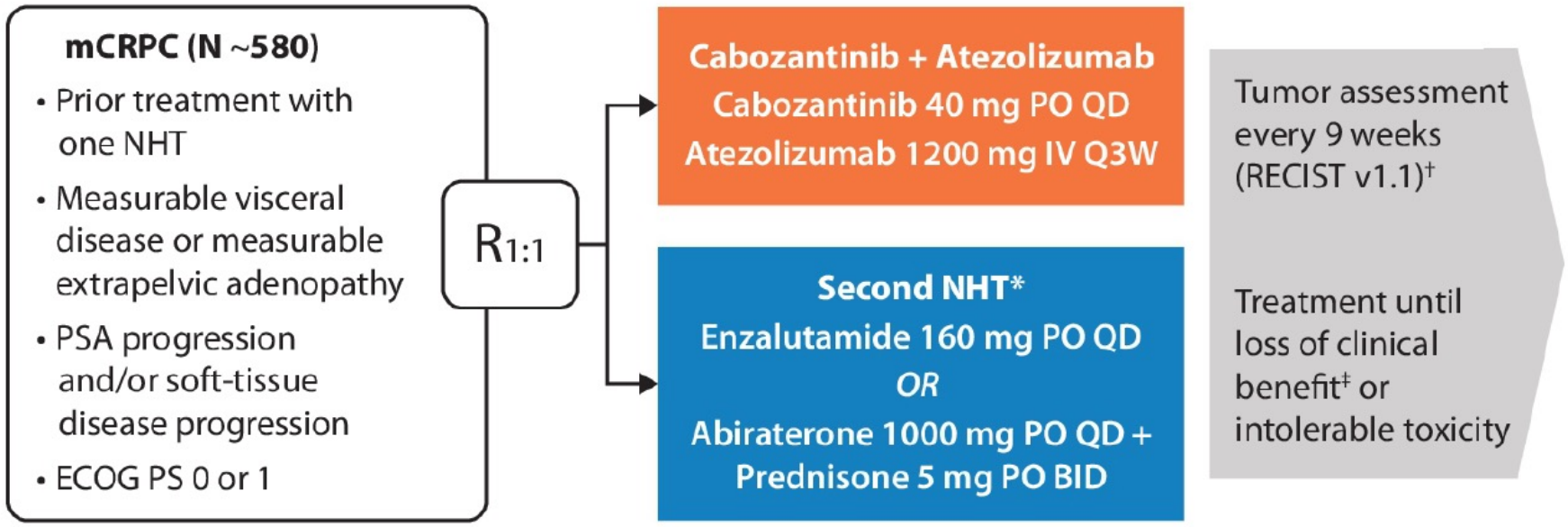
COSMIC-021: Best Change in PSA from Baseline



- In 118 patients with post-baseline assessments, 55 (47%) had a decrease in PSA, and 27 (23%) had a decrease ≥50%
- In 92 patients with Visc/EPLN, 50 (54%) had a decrease in PSA, and 24 (26%) had a decrease ≥50%

Agarwal et al. ESMO 2021;Abstract LBA24.

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)

Primary Endpoints:

- PFS per RECIST v1.1 by BIRC
- OS

Secondary Endpoint:

- ORR per RECIST v1.1 by BIRC

*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

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

RTP RESEARCH TO PRACTICE

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MODULE 7: Journal Club with Dr Armstrong

MODULE 8: Relevant Data Sets

RTP RESEARCH TO PRACTICE

Case Presentation: An 89-year-old man with mCRPC and a CHEK2 mutation

Dr Sulfi Ibrahim (Richmond, Indiana)

Meet The Professor with Dr Armstrong

Introduction: Genitourinary Cancers Symposium 2022

MODULE 1: Dr Saylors — A 58-year-old man with metastatic hormone-sensitive prostate cancer, a history of breast cancer and a germline BRCA1 mutation

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RTP
RESEARCH
TO PRACTICE

Exposure-Adjusted Safety Analyses of the VISION Phase 3 Trial of ^{177}Lu-PSMA-617 in Patients with Metastatic Castration-Resistant Prostate Cancer

Chi KN et al.

Genitourinary Cancers Symposium 2022;Abstract 85.

DNA Damaging Therapies in Patients (pts) with Prostate Cancer (PC) and Pathogenic Alterations in Homologous Recombination Repair (HRR) Genes

Graham L et al.

Genitourinary Cancers Symposium 2022;Abstract 129.

Clin Adv Hematol Oncol 2021;19(11):694-7.

Prostate Cancer

PROSTATE CANCER IN FOCUS

Current Developments in the Management of Prostate Cancer

Section Editor: Andrew J. Armstrong, MD

The Role of AR-V7 Testing in the Management of Metastatic CRPC

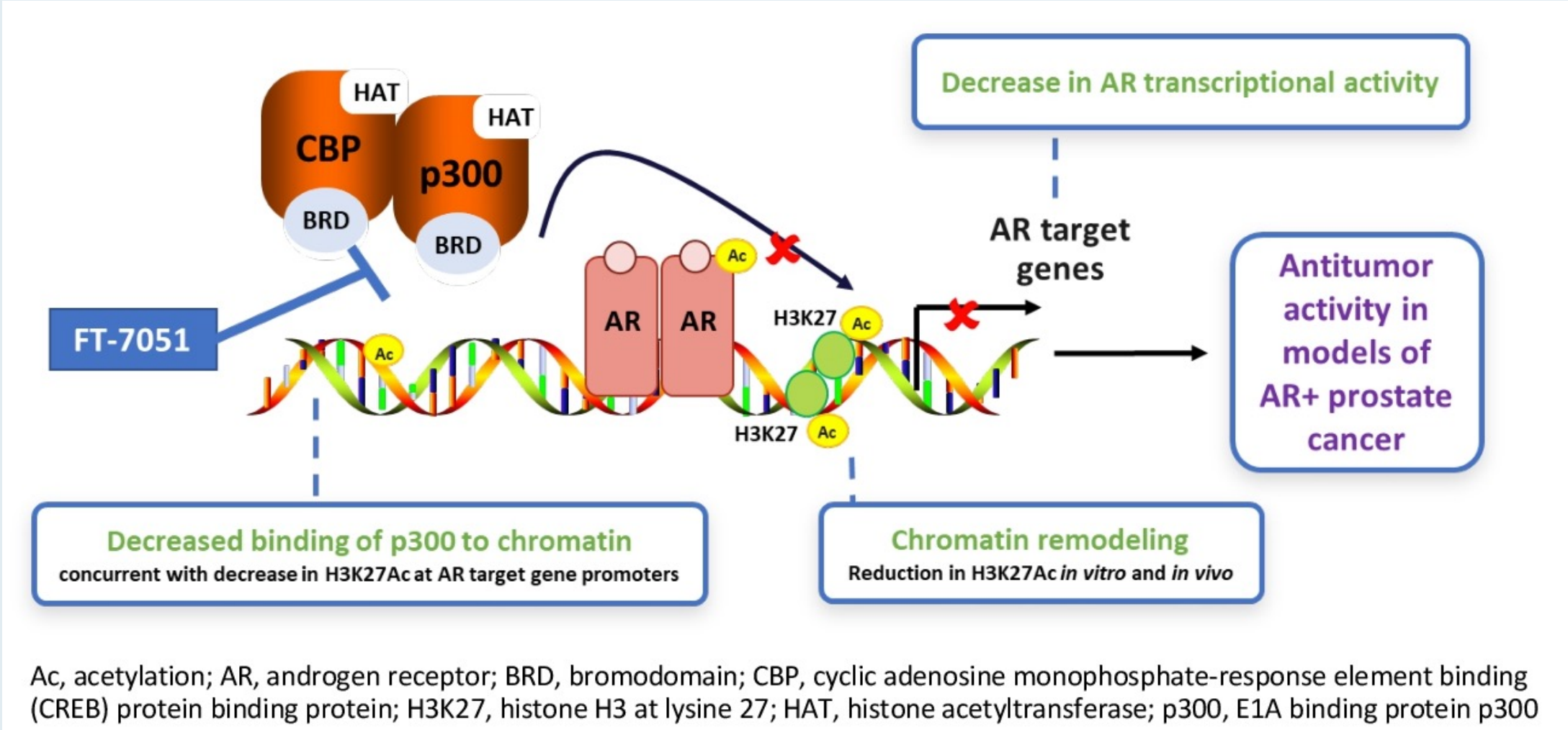
Andrew J. Armstrong, MD
Professor of Medicine
Duke University Medical Center
Durham, North Carolina

The Courage Study: A First-in-Human Phase 1 Study of the CBP/p300 Inhibitor FT-7051 in Men with Metastatic Castration-Resistant Prostate Cancer

Armstrong AJ et al.

ASCO 2021;Abstract TPS5085.

FT-7051 Mechanism of Action



Ac, acetylation; AR, androgen receptor; BRD, bromodomain; CBP, cyclic adenosine monophosphate-response element binding (CREB) protein binding protein; H3K27, histone H3 at lysine 27; HAT, histone acetyltransferase; p300, E1A binding protein p300

Armstrong AJ et al. ASCO 2021;Abstract TPS5085.

Efficacy of the PD-L1 Inhibitor Avelumab in Neuroendocrine or Aggressive Variant Prostate Cancer: Results from a Phase II, Single-Arm Study

Brown LC et al.

Genitourinary Cancers Symposium 2021;Abstract 89.

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY

Genitourinary Cancers Symposium

CheckMate 9KD arm B final analysis: efficacy and safety of nivolumab plus docetaxel for chemotherapy-naïve metastatic castration-resistant prostate cancer

Karim Fizazi,[1] Pablo González Mella,[2] Daniel Castellano,[3] Jose N. Minatta,[4] Arash Rezazadeh Kalebasty,[5] David Shaffer,[6] Juan Carlos Vázquez Limón,[7] Héctor Manuel Sánchez López,[8] Andrew J. Armstrong,[9] Lisa Horvath,[10] Carlos Dzik,[11] Neha P. Amin,[12] Jia Li,[12] Keziban Unsal-Kacmaz,[12] Margitta Retz,[13] Fred Saad,[14] Daniel P. Petrylak,[15] Russell K. Pachynski[16]

[1]Gustave Roussy, University Paris Saclay, Villejuif, France; [2]Fundación Arturo López Pérez, Santiago, Chile; [3]Hospital Universitario 12 de Octubre, Madrid, Spain; [4]Hospital Italiano de Buenos Aires, Buenos Aires, Argentina; [5]Norton Cancer Institute, Louisville, KY; [6]New York Oncology Hematology, Albany, NY; [7]Instituto Jalisciense de Cancerología, Guadalajara, Mexico; [8]Hospital Regional de Alta Especialidad del Bajío, Guanajuato, Mexico; [9]Duke Cancer Institute Center for Prostate and Urologic Cancers, Duke University, Durham, NC; [10]Chris O'Brien Lifehouse, Camperdown, NSW, Australia; [11]Instituto de Cancer do Estado de São Paulo, São Paulo, Brazil; [12]Bristol Myers Squibb, Princeton, NJ; [13]Rechts der Isar Medical Center, Technical University Munich, Munich, Germany; [14]Centre Hospitalier de l'Université de Montréal/CHUM, Montreal, QC, Canada; [15]Smilow Cancer Center, Yale School of Medicine, New Haven, CT; [16]Washington University School of Medicine, St. Louis, MO

2021, Abstract Number 12

Clin Cancer Res 2021;27(17):4746-56.

CLINICAL CANCER RESEARCH | CLINICAL TRIALS: IMMUNOTHERAPY

A Phase Ib Study of Atezolizumab with Radium-223 Dichloride in Men with Metastatic Castration-Resistant Prostate Cancer

Lawrence Fong[1], Michael J. Morris[2], Oliver Sartor[3], Celestia S. Higano[4], Lance Pagliaro[5], Ajjai Alva[6], Leonard J. Appleman[7], Winston Tan[8], Ulka Vaishampayan[9], Raphaelle Porcu[10], Darren Tayama[11], Edward E. Kadel III[11], Kobe C. Yuen[11], Asim Datye[10], Andrew J. Armstrong[12], and Daniel P. Petrylak[13]

CLINICAL CANCER RESEARCH | TRANSLATIONAL CANCER MECHANISMS AND THERAPY

A Randomized Controlled Trial of a 6-Month Low-Carbohydrate Intervention on Disease Progression in Men with Recurrent Prostate Cancer: Carbohydrate and Prostate Study 2 (CAPS2)

Stephen J. Freedland[1,4], Jenifer Allen[2], Aubrey Jarman[1], Taofik Oyekunle[3], Andrew J. Armstrong[3], Judd W. Moul[3], Howard M. Sandler[1], Edwin Posadas[1], Dana Levin[1], Emily Wiggins[4], Lauren E. Howard[4,5], Yuan Wu[5], and Pao-Hwa Lin[5]

Clin Cancer Res 2021;27(6):1823

Mol Cancer Res. 2021 June ; 19(6): 1040–1050. doi:10.1158/1541-7786.MCR-20-0975.

Circulating tumor cell genomic evolution and hormone therapy outcomes in men with metastatic castration-resistant prostate cancer (mCRPC)

Santosh Gupta[1,2,6], Susan Halabi[1,3], Gabor Kemeny[1], Monika Anand[1], Paraskevi Giannakakou[5], David M. Nanus[5], Daniel J. George[1,4], Simon G. Gregory[1,2], Andrew J. Armstrong[1,4,*]

Published in final edited form as:
Clin Cancer Res. 2021 June 01; 27(11): 2961–2963. doi:10.1158/1078-0432.CCR-21-0531.

Liquid Biopsy: It's the Bloody Truth!

Nathan M. Hawkey, MD MBA,
Duke University, Division of Hematology and Medical Oncology

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

Comment on Tukachinsky H et al. Genomic analysis of circulating tumor DNA in patients with advanced prostate cancer identifies targetable BRCA alterations and AR resistance mechanisms. *Clin Cancer Res* 2021;27(11):3094-105.

ORIGINAL RESEARCH

Cancer Medicine Open Access WILEY

Cancer Med 2021;10(7):2341-9.

Combination antiangiogenic tyrosine kinase inhibition and anti-PD1 immunotherapy in metastatic renal cell carcinoma: A retrospective analysis of safety, tolerance, and clinical outcomes

Andrew L. Laccetti[1] | Benjamin Garmezy[2] | Lianchun Xiao[3] | Minas Economides[4] | Aradhana Venkatesan[5] | Jianjun Gao[3] | Eric Jonasch[3] | Paul Corn[2] | Amado Zurita-Saavedra[2] | Landon C. Brown[6] | Chester Kao[6] | Emily N. Kinsey[6] | Rajan T. Gupta[7,8] | Michael R. Harrison[6,7] | Andrew J. Armstrong[6,7] | Daniel J. George[6,7] | Nizar Tannir[3] | Pavlos Msaouel[3] | Amishi Shah[3] | Tian Zhang[6,7] | Matthew T. Campbell[3]

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Development and Validation of Circulating Tumor Cell … Enumeration as a Prognostic Biomarker in Men with Metastatic Castration-Resistant Prostate Cancer

Scher HI et al.

Genitourinary Cancers Symposium 2021;Abstract 157.

original reports

Prospective Evaluation of Clinical Outcomes Using a Multiplex Liquid Biopsy Targeting Diverse Resistance Mechanisms in Metastatic Prostate Cancer

Jamie M. Sperger, PhD[1]; Hamid Emamekhoo, MD[1]; Rana R. McKay, MD[2]; Charlotte N. Stahlfeld, BS[1]; Anupama Singh, PhD[1]; Xinyi E. Chen, BS[3]; Lucia Kwak, MS[4]; Cole S. Gilsdorf, BS[1]; Serena K. Wolfe, BS[1]; Xiao X. Wei, MD[4]; Rebecca Silver, BS[4]; Zhenwei Zhang, MD, PhD[4]; Michael J. Morris, MD[5]; Glenn Bubley, MD[6]; Felix Y. Feng, MD[7,8,9]; Howard I. Scher, MD[5]; Dana Rathkopf, MD[5]; Scott M. Dehm, PhD[10]; Toni K. Choueiri, MD[4]; Susan Halabi, PhD[11,12]; Andrew J. Armstrong, MD[11]; Alexander W. Wyatt, PhD[3]; Mary-Ellen Taplin, MD[4]; Shuang G. Zhao, MD[1,13,14]; and Joshua M. Lang, MD[1,15]

J Clin Oncol 2021;39(26):2926-37.

Zhang *et al. Biomarker Research* (2021) 9:14
https://doi.org/10.1186/s40364-021-00267-y

Biomarker Research

RAPID COMMUNICATION Open Access

Expression of immune checkpoints on circulating tumor cells in men with metastatic prostate cancer

Tian Zhang[1,2*], Anika Agarwal[1], R. Garland Almquist[1], Daniella Runyambo[1], Sally Park[1], Elizabeth Bronson[2], Rengasamy Boominathan[3], Chandra Rao[3], Monika Anand[2], Taofik Oyekunle[4], Patrick Healy[4], Megan A. McNamara[1,2], Kathryn Ware[1,2], Jason A. Somarelli[1,2], Daniel J. George[1,2] and Andrew J. Armstrong[1,2,5]

Meet The Professor with Dr Armstrong

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RTP RESEARCH TO PRACTICE

Abiraterone acetate plus prednisolone with or without enzalutamide added to androgen deprivation therapy compared to ADT alone for men with high-risk nonmetastatic prostate cancer: primary combined analysis from two comparisons in the STAMPEDE platform protocol

Gerhardt Attard, Louise Brown, Noel Clarke, Laura Murphy, William Cross, Rob Jones, Silke Gillessen, J.Martin Russell, Adrian Cook, Jo Bowen, Anna Lydon, Ian Pedley, Omi Parikh, Simon Chowdhury, Zafar Malik, David Matheson, Chris Parker, Matthew Sydes, Mahesh Parmar, Nicholas James **on behalf of the STAMPEDE investigators***

Conducted by Medical Research Council Trials Unit at University College London, U.K.

ClinicalTrials.gov number, NCT00268476 & Current Controlled Trials number, ISRCTN78818544

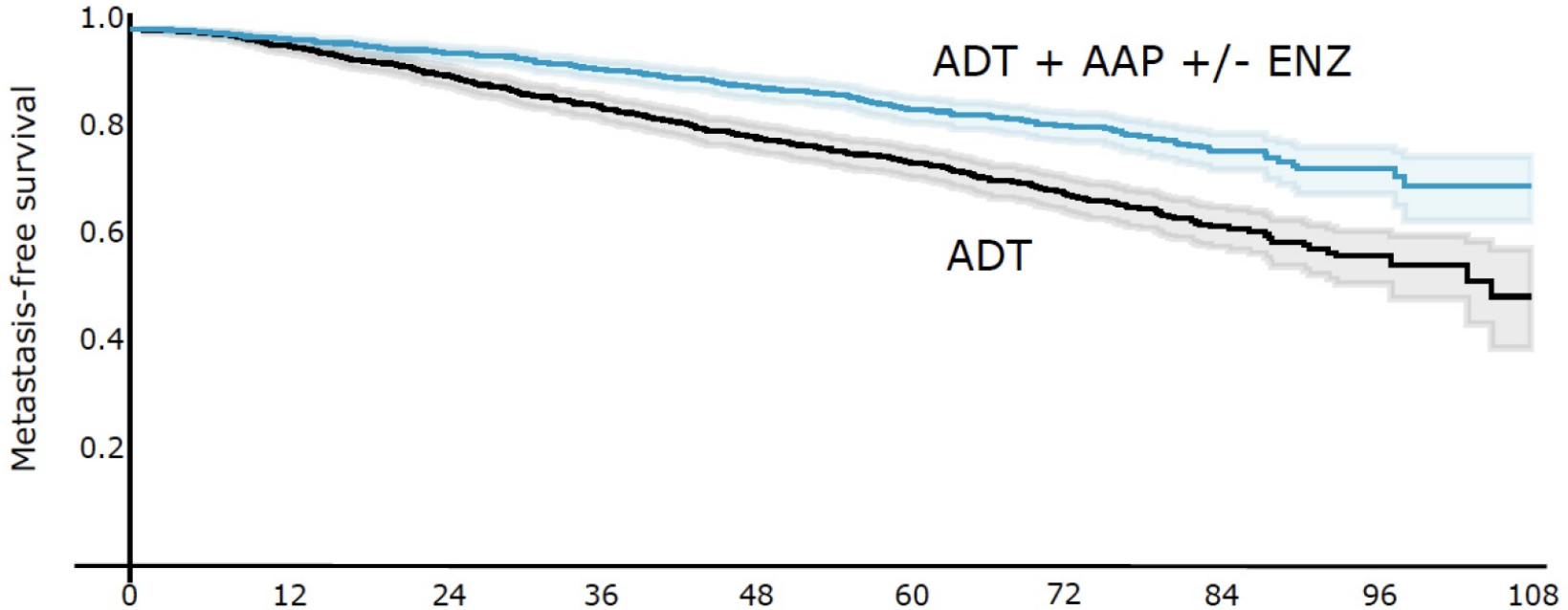
*113 U.K. and Swiss sites: list of investigators and collaborators at www.stampedetrial.org

www.stampedetrial.org

2021 ESMO congress

ESMO 2021;Abstract LBA4_PR.

Metastasis-Free Survival with the Addition of Abiraterone Acetate and Prednisolone with or without Enzalutamide to ADT for High-Risk M0 Prostate Cancer



ADT										
At-risk	988	950	894	836	767	550	329	172	53	9
Censored	0	8	11	14	26	201	387	522	632	673
Event	0	30	83	138	195	237	272	294	303	306
ADT+AAP+/-ENZ										
At-risk	986	948	917	884	839	622	369	198	71	14
Censored	0	21	28	31	45	225	460	615	737	792
Event	0	17	41	71	102	139	157	173	178	180

Events
180 ADT+ AAP +/- ENZ
306 ADT

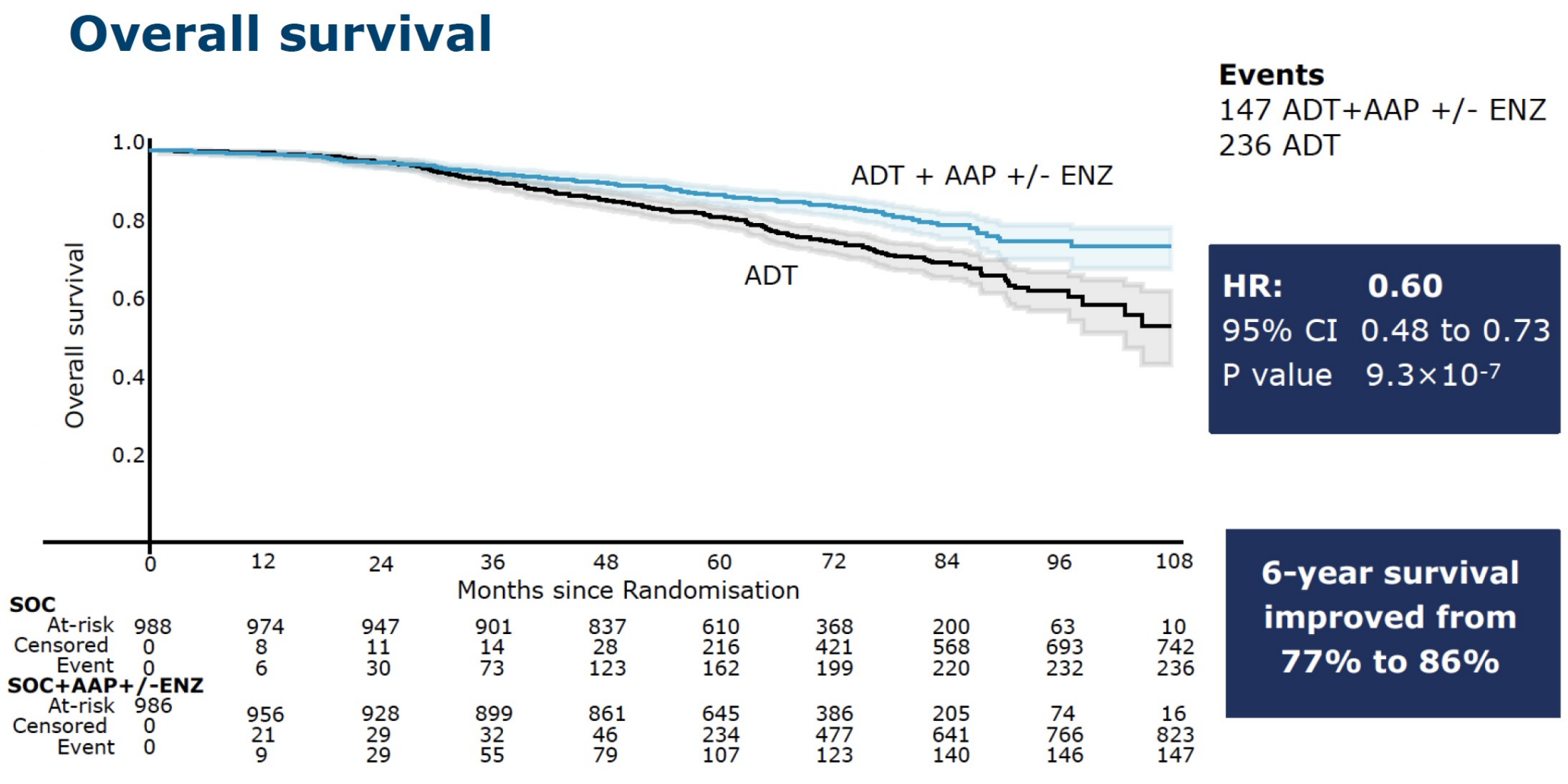
HR:	**0.53**
95% CI:	0.44-0.64
P value	2.9×10^{-11}

6-year MFS improved from 69% to 82%

Attard G et al. ESMO 2021;Abstract LBA4_PR.

RTP RESEARCH TO PRACTICE

Overall Survival with the Addition of Abiraterone Acetate and Prednisolone with or without Enzalutamide to ADT for High-Risk M0 Prostate Cancer



Attard G et al. ESMO 2021;Abstract LBA4_PR.

A phase 3 trial with a 2x2 factorial design in men with *de novo* metastatic castration-sensitive prostate cancer (mCSPC): Overall survival with abiraterone acetate plus prednisone in PEACE-1

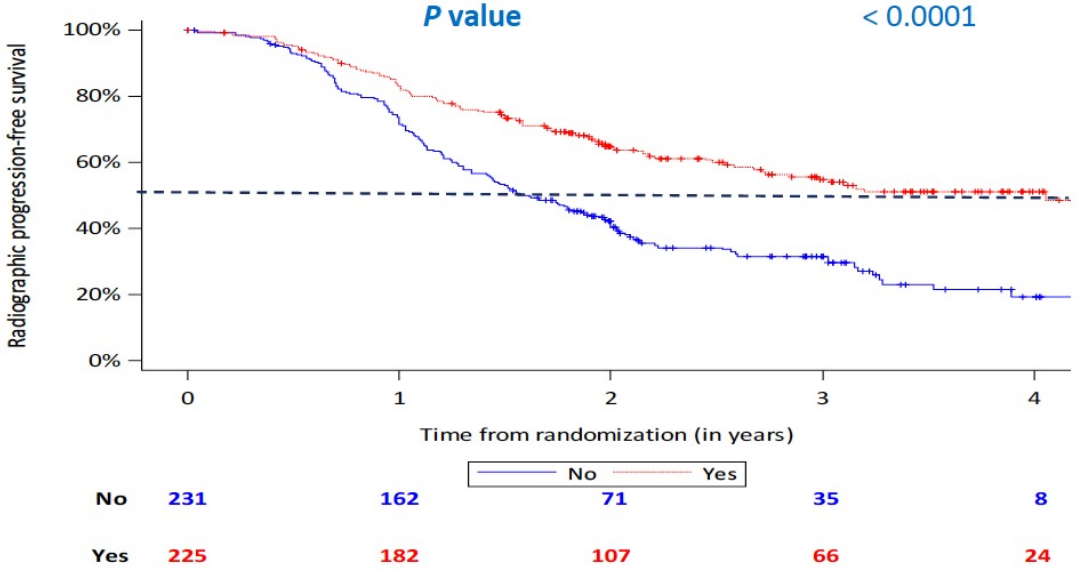
Karim Fizazi, Joan Carles, Stéphanie Foulon, Guilhem Roubaud, Ray McDermott, Aude Fléchon, Bertrand Tombal, Stéphane Supiot, Dominik Berthold, Philippe Ronchin, Gabriel Kacsó, Gwenaëlle Gravis, Fabio Calabro, Jean-François Berdah, Ali Hasbini, Marlon Silva, Antoine Thiery-Vuillemin, Igor Latorzeff, Isabelle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

ESMO 2021;Abstract LBA5

PEACE-1: Radiographic PFS (rPFS) by Metastatic Burden

« High Volume »

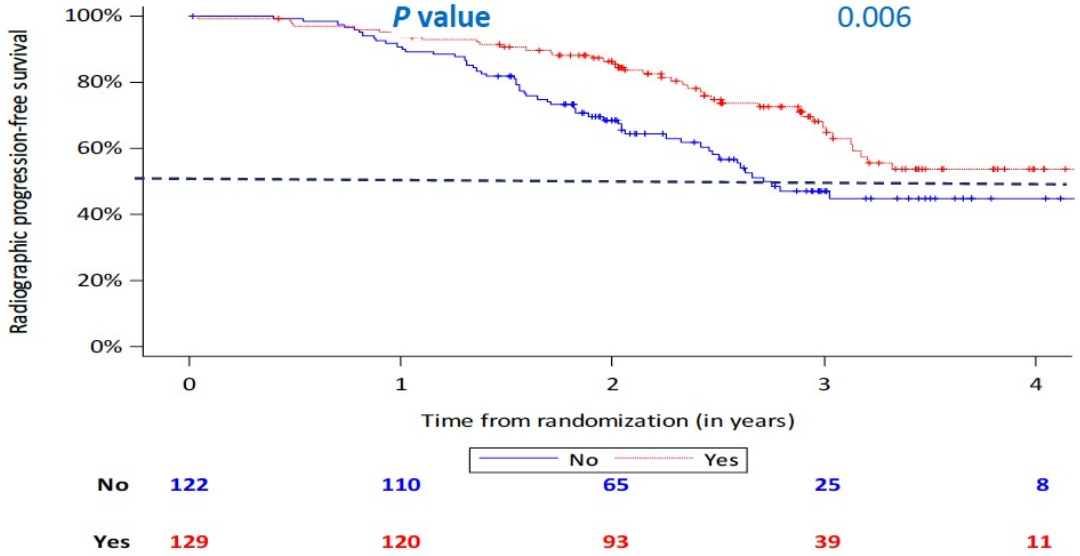
	SOC+Abi (n = 225)	SOC (n = 231)
Median, y (95% CI)	4.1 (2.7-NE)	1.6 (1.4-2.0)
Events	97	156
HR (95% CI)*	0.47 (0.36-0.60)	
P value	< 0.0001	



No	231	162	71	35	8
Yes	225	182	107	66	24

« Low Volume »

	SOC+Abi (n = 129)	SOC (n = 122)
Median, y (95% CI)	NE (3.1-NE)	2.7 (2.5-NE)
Events	41	55
HR (95% CI)*	0.58 (0.39-0.87)	
P value	0.006	



No	122	110	65	25	8
Yes	129	120	93	39	11

*Adjusted on stratification parameters (RXT, PS, type of castration, metastatic burden)

2021 ESMO congress

Karim Fizazi

Fizazi K et al. ESMO 2021;Abstract LBA5.

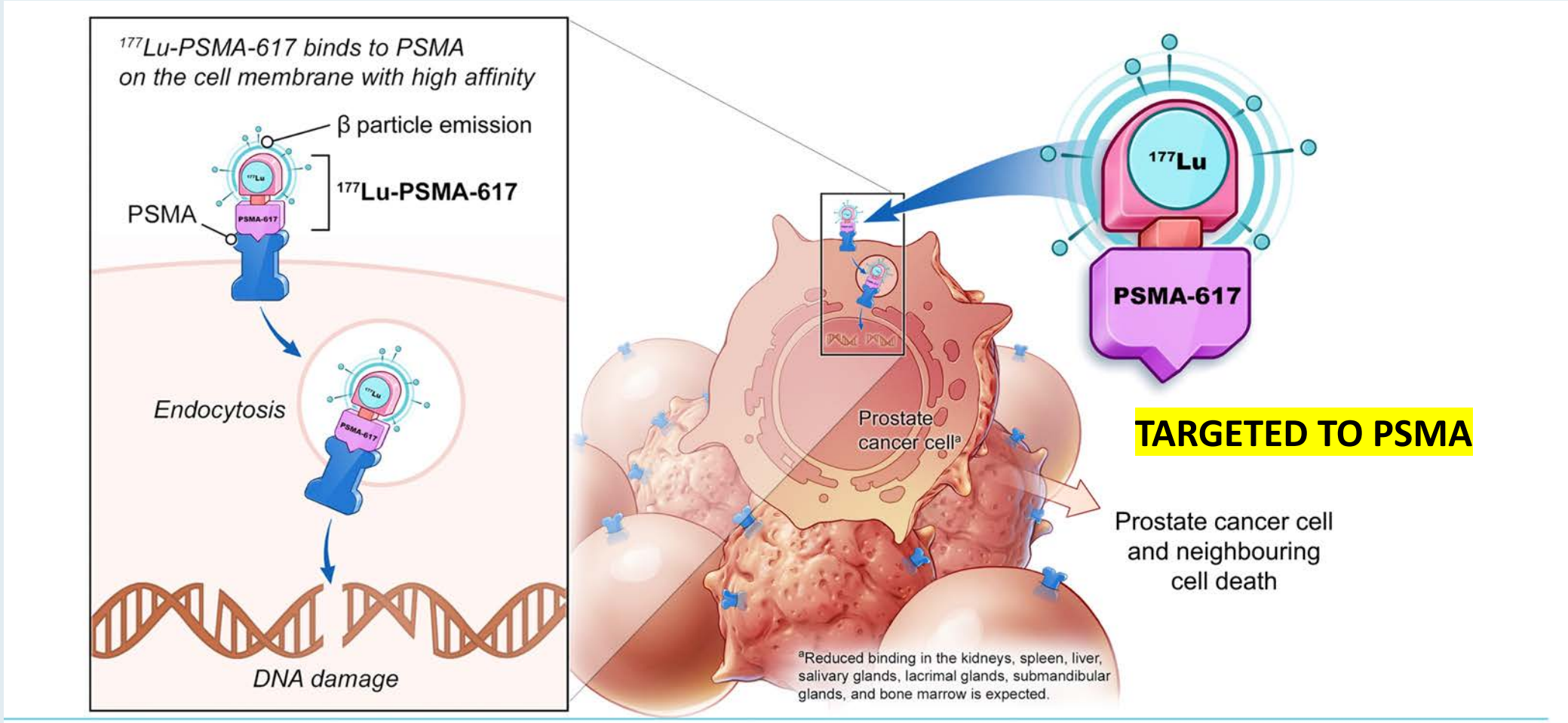
RTP RESEARCH TO PRACTICE

PEACE-1: Grade 3-5 Adverse Events (ADT + Docetaxel Safety Population)

Toxicity, n (%)	SOC (+/- RXT) + Abiraterone (n=346)	SOC (+/- RXT) (n=350)
Neutropenia	34 (10)	32 (9)
Febrile neutropenia	18 (5)	19 (5)
Liver	20 (6)	2 (1)
Hypertension	76 (22)	45 (13)
Hypokalemia	11 (3)	1 (0)
Cardiac	6 (2)	5 (1)
Fatigue	10 (3)	15 (4)
Gastro-intestinal	14 (4)	18 (5)
Grade 5	7 (2)	3 (1)

Fizazi K et al. ESMO 2021;Abstract LBA5.

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



Morris MJ et al. ASCO 2021;Abstract LBA4.

RTP RESEARCH TO PRACTICE

N Engl J Med 2021;385:1091-103

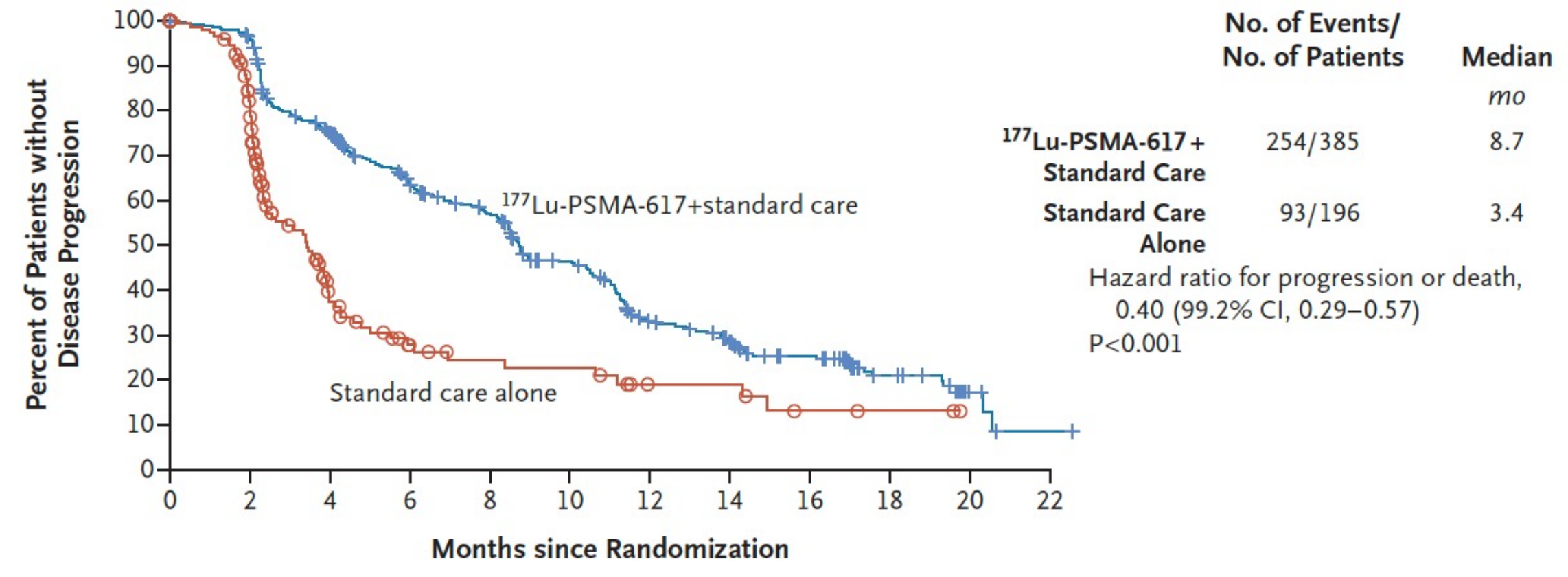
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

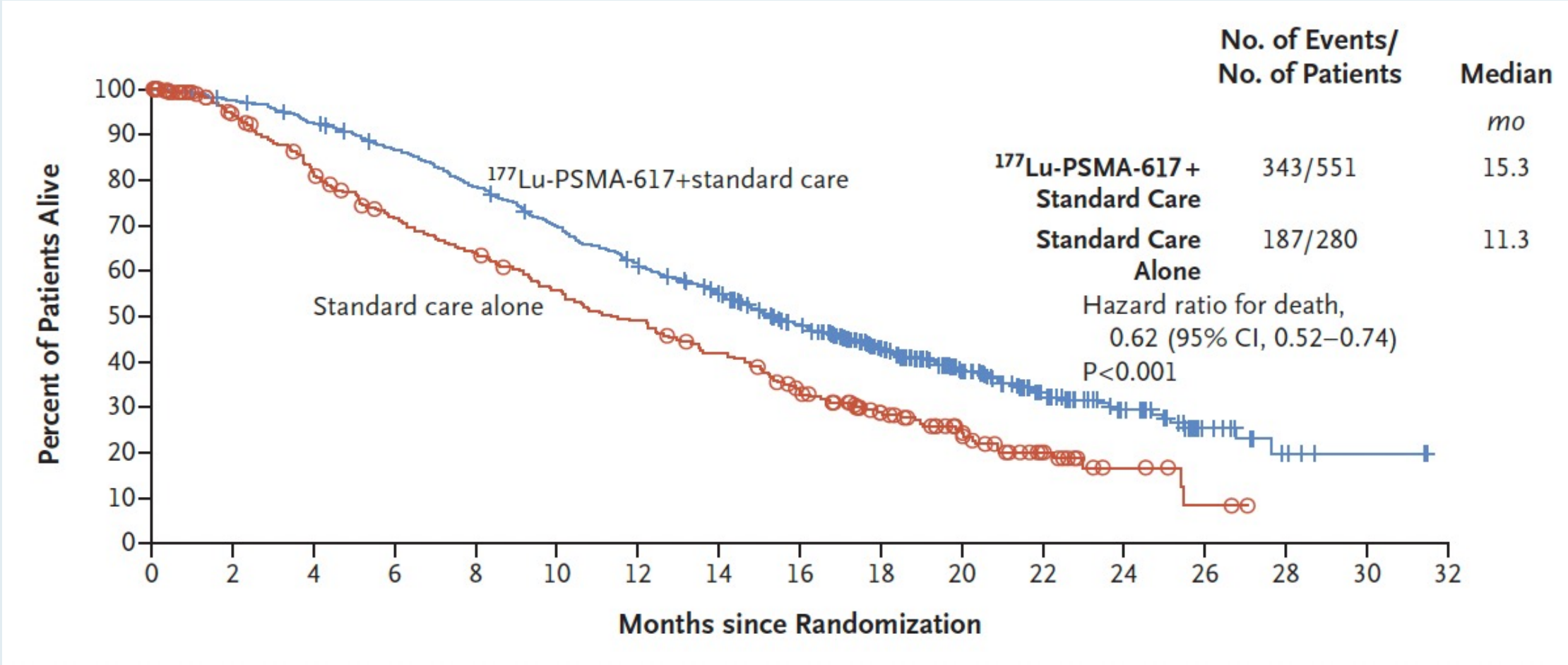
O. Sartor, J. de Bono, K.N. Chi, K. Fizazi, K. Herrmann, K. Rahbar, S.T. Tagawa, L.T. Nordquist, N. Vaishampayan, G. El-Haddad, C.H. Park, T.M. Beer, A. Armour, W.J. Pérez-Contreras, M. DeSilvio, E. Kpamegan, G. Gericke, R.A. Messmann, M.J. Morris, and B.J. Krause, for the VISION Investigators*

VISION: Imaging-Based Progression-Free Survival



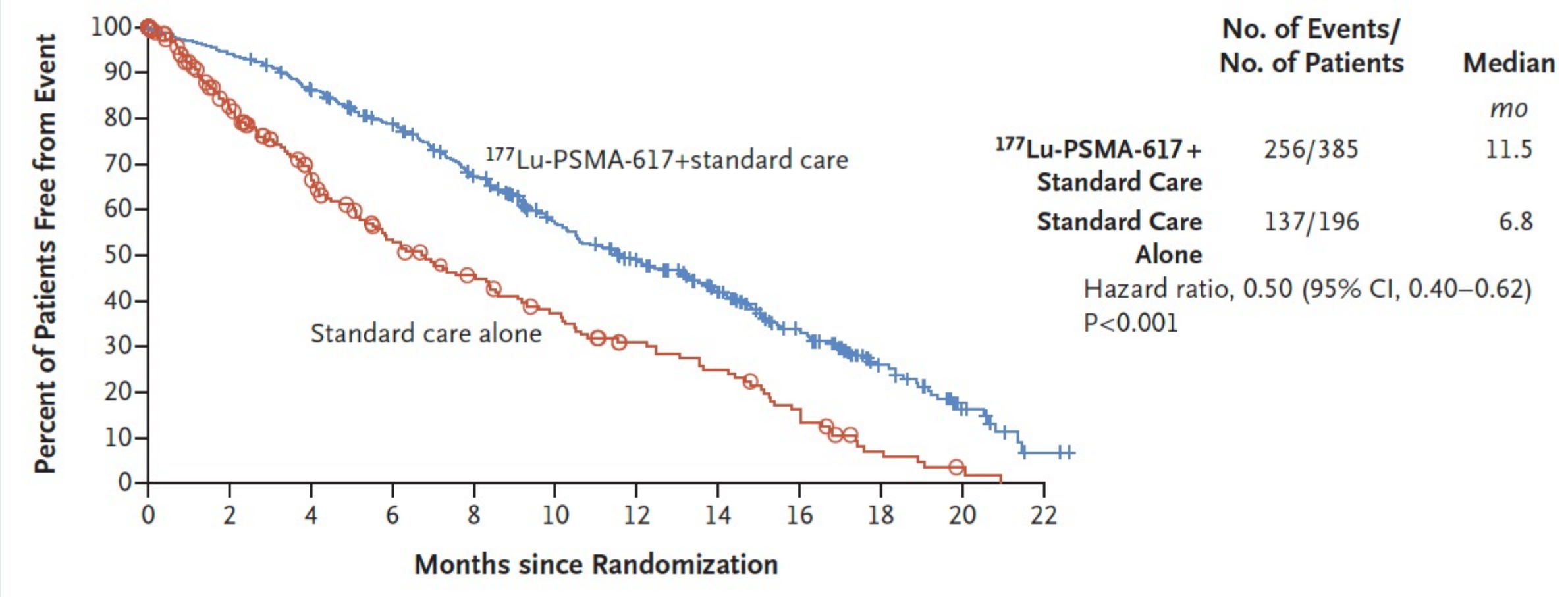
Sartor O et al. *N Engl J Med* 2021;385:1091-103.

VISION: Overall Survival



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

VISION: Time to First Symptomatic Skeletal Event



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

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)
Fatigue	228 (43.1)	31 (5.9)	47 (22.9)	3 (1.5)
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

177Lu-PSMA-617 (LuPSMA) versus Cabazitaxel in Metastatic Castration-Resistant Prostate Cancer (mCRPC) Progressing After Docetaxel: Updated Results Including Progression-Free Survival (PFS) and Patient-Reported Outcomes (PROs) (TheraP ANZUP 1603)[1]

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

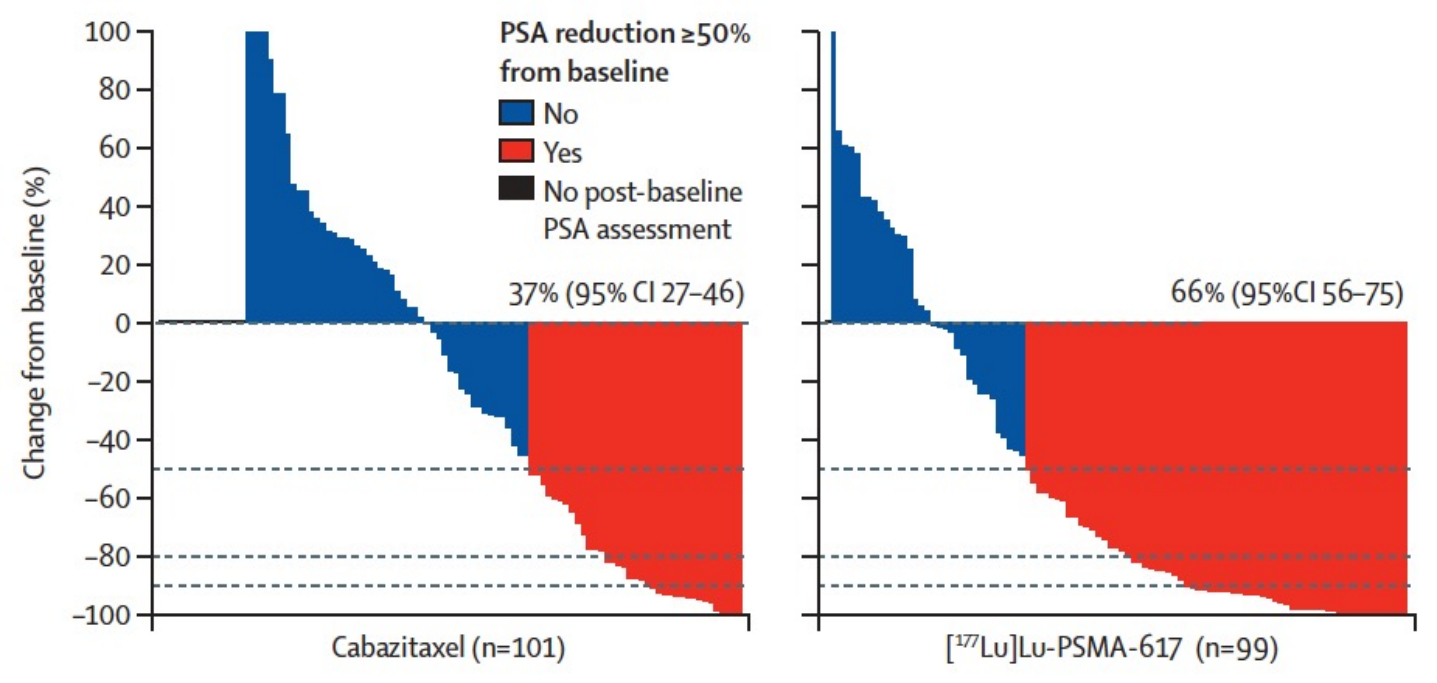
Michael S Hofman, Louise Emmett, Shahneen Sandhu, Amir Iravani, Anthony M Joshua, Jeffrey C Goh, David A Pattison, Thean Hsiang Tan, Ian D Kirkwood, Siobhan Ng, Roslyn J Francis, Craig Gedye, Natalie K Rutherford, Andrew Weickhardt , Andrew M Scott, Sze-Ting Lee, Edmond M Kwan, Arun A Azad, Shakher Ramdave, 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†*

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

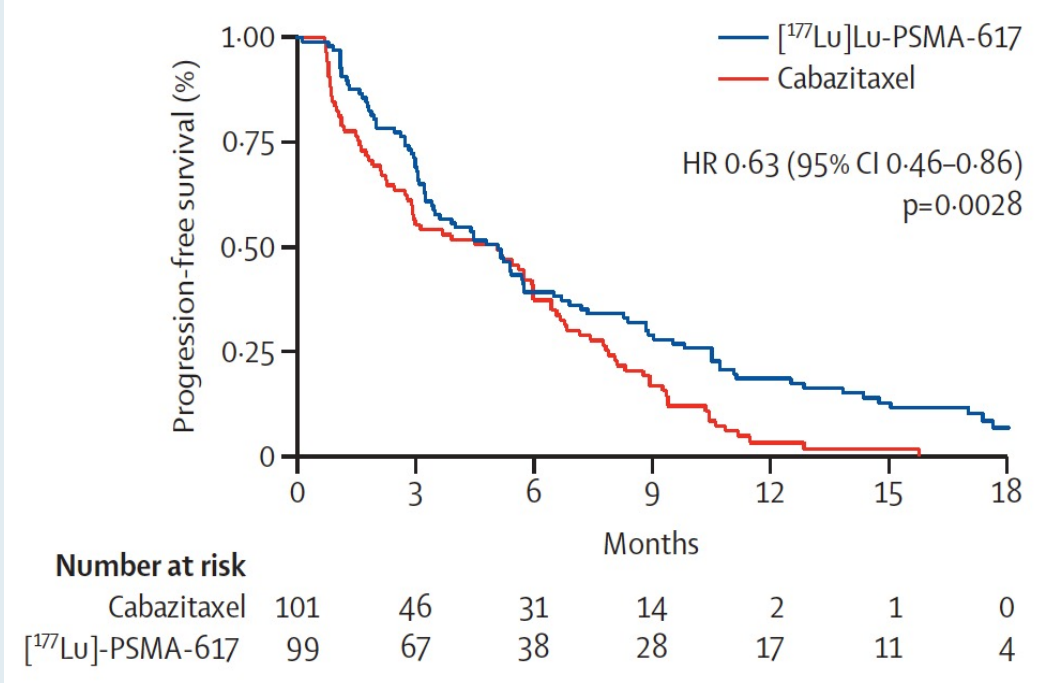
RTP RESEARCH TO PRACTICE

TheraP ANZUP 1603: PSA Response and PFS

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.

TheraP ANZUP 1603: Adverse Events

	[^{177}Lu]Lu-PSMA-617 (n=98)		Cabazitaxel (n=85)	
	Grade 1–2	Grade 3–4	Grade 1–2	Grade 3–4
Fatigue	69 (70%)	5 (5%)	61 (72%)	3 (4%)
Pain*	60 (61%)	11 (11%)	52 (61%)	4 (5%)
Dry mouth	59 (60%)	0	18 (21%)	0
Diarrhoea	18 (18%)	1 (1%)	44 (52%)	4 (5%)
Nausea	39 (40%)	1 (1%)	29 (34%)	0
Thrombocytopenia	18 (18%)	11 (11%)	4 (5%)	0
Dry eyes	29 (30%)	0	3 (4%)	0
Anaemia	19 (19%)	8 (8%)	11 (13%)	7 (8%)
Neuropathy†	10 (10%)	0	22 (26%)	1 (1%)
Dysgeusia	12 (12%)	0	23 (27%)	0
Haematuria	3 (3%)	1 (1%)	12 (14%)	5 (6%)
Neutropenia‡	7 (7%)	4 (4%)	4 (5%)	11 (13%)
Insomnia	9 (9%)	0	12 (14%)	1 (1%)
Vomiting	12 (12%)	1 (1%)	10 (12%)	2 (2%)
Dizziness	4 (4%)	0	11 (13%)	0
Leukopenia	10 (10%)	1 (1%)	5 (6%)	1 (1%)
Any adverse event	53 (54%)	32 (33%)	34 (40%)	45 (53%)

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: Interim Analysis of the Phase Ib Study of ^{177}Lu-PSMA-617 in Combination with Pembrolizumab for Metastatic Castration Resistant Prostate Cancer (mCRPC)

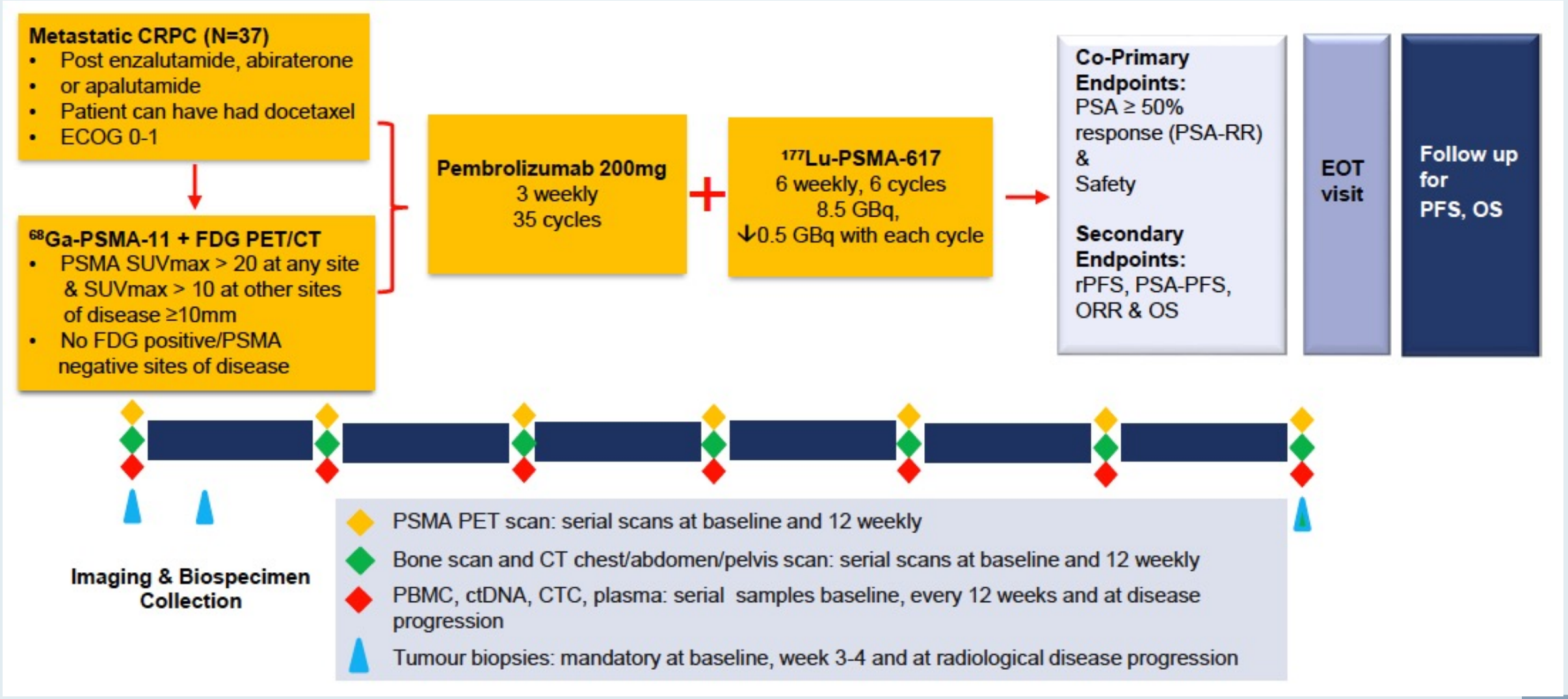
Shahneen Sandhu, Anthony M. Joshua, Louise Emmett, Lavinia Spain, Lisa G. Horvath, Megan Crumbaker, Arsha Anton, Roslyn Wallace, Anupama Pasam, Mathias Bressel, Erin Cassidy, Patricia Banks, Aravind Ravi Kumar, Ramin Alipour, Tim Akhurst, Grace Kong, Ian D. Davis, Scott Williams, Rod Hicks, Michael S. Hofman

Abstract 577O

2021 ESMO congress

Presented by: Shahneen Sandhu

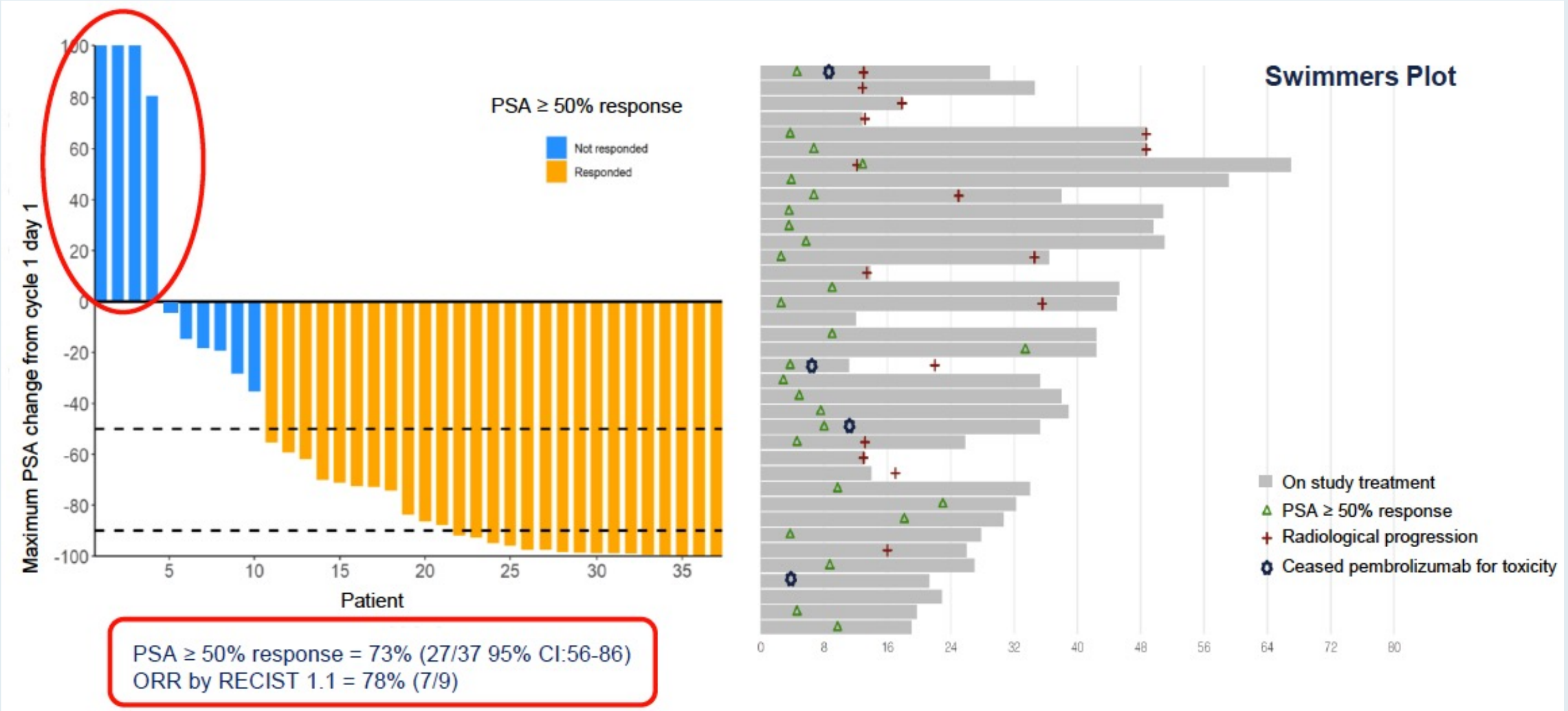
PSMA-Lutetium Radionuclide Therapy and ImmuNotherapy for Prostate CancEr (PRINCE) Trial Schema



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

RTP RESEARCH TO PRACTICE

PRINCE: PSA Response Rate (Primary Endpoint)



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

RTP RESEARCH TO PRACTICE

PRINCE: Treatment-Related Adverse Events

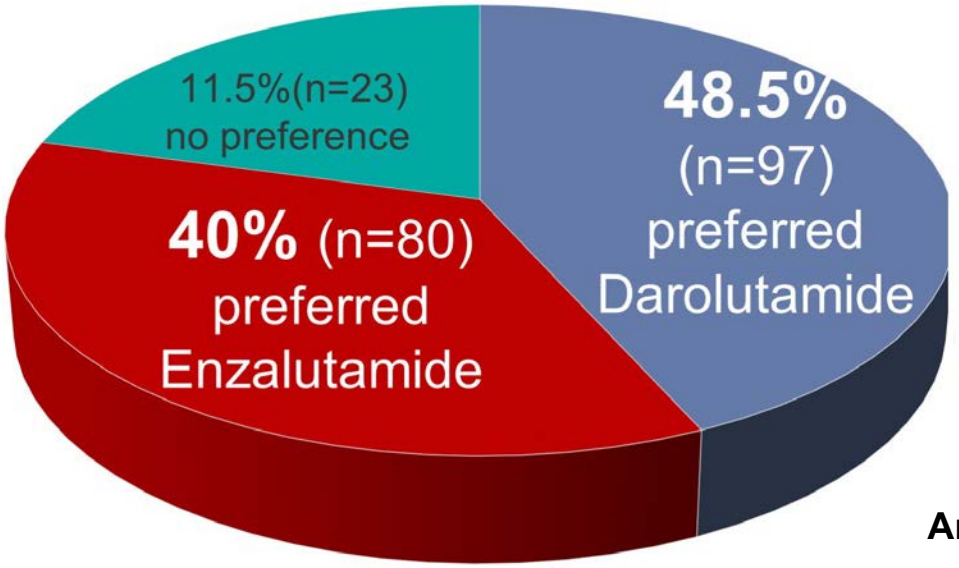
TRAE term	Grade 1 (%)	Grade 2 (%)	Grade 3 (%)	N=37 (%)
Xerostomia	21 (57%)	7 (19%)	-	28 (76%)
Fatigue	11 (29 %)	3 (8%)	2 (5%)	16 (43%)
Rash	5 (14%)	4 (11%)		9 (25%)
Nausea	8 (21%)	1 (3%)	-	9 (24%)
Pruritis	6 (16%)	1 (3%)	-	7 (19%)
Anorexia	3 (8%)	3 (8%)	-	6 (16%)
Thrombocytopenia	4 (11%)	1(3%)	-	5 (14%)
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%)

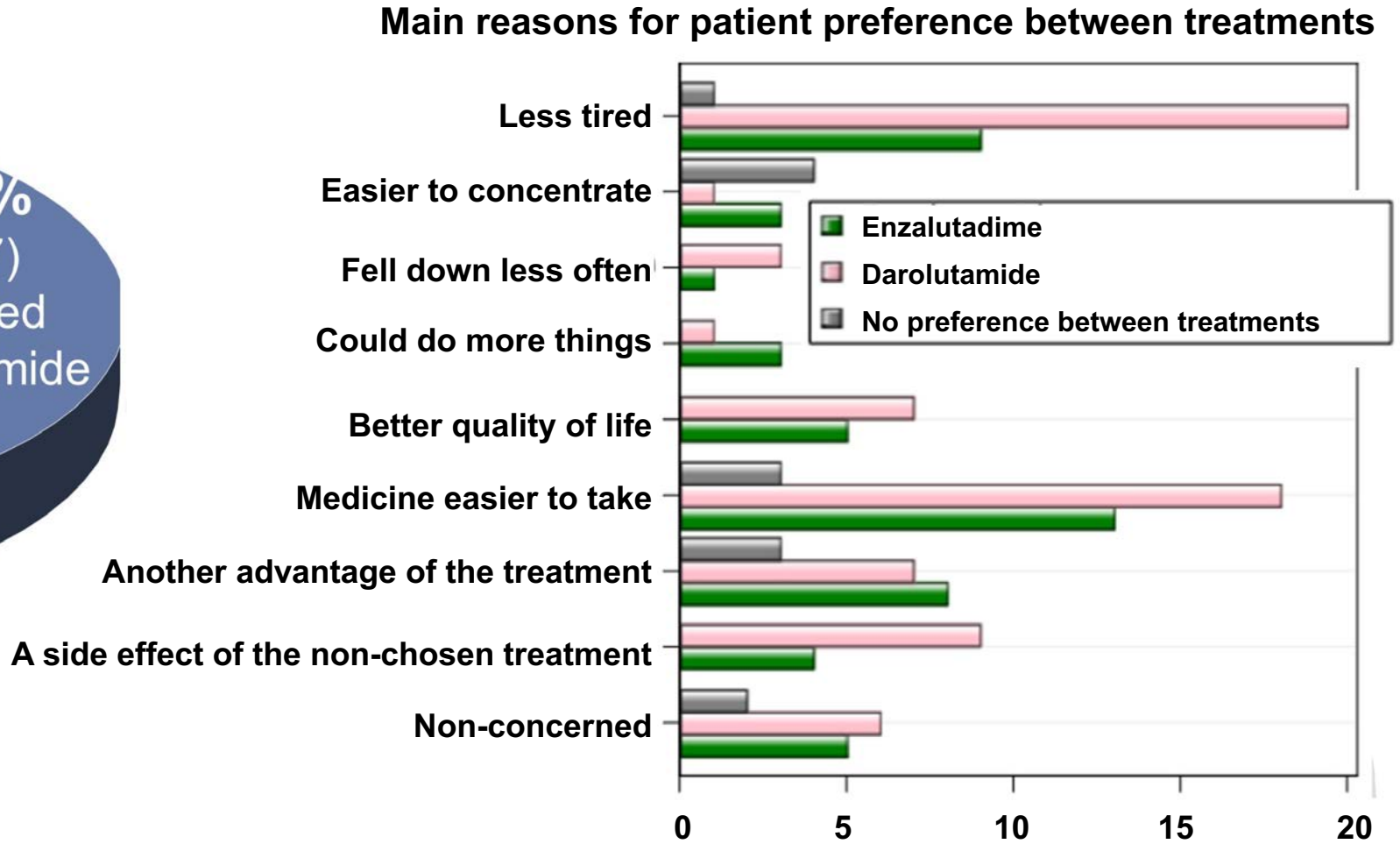
Pembrolizumab cycles: Median (range)	8 (1 - 22)
^{177}Lu-PSMA-617 cycles: Median (range)	4 (2 - 6)
Discontinuation for toxicity:	
Pembrolizumab, n (%)	4 (11%)
^{177}Lu-PSMA-617, n (%)	0 (0%)

- 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

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

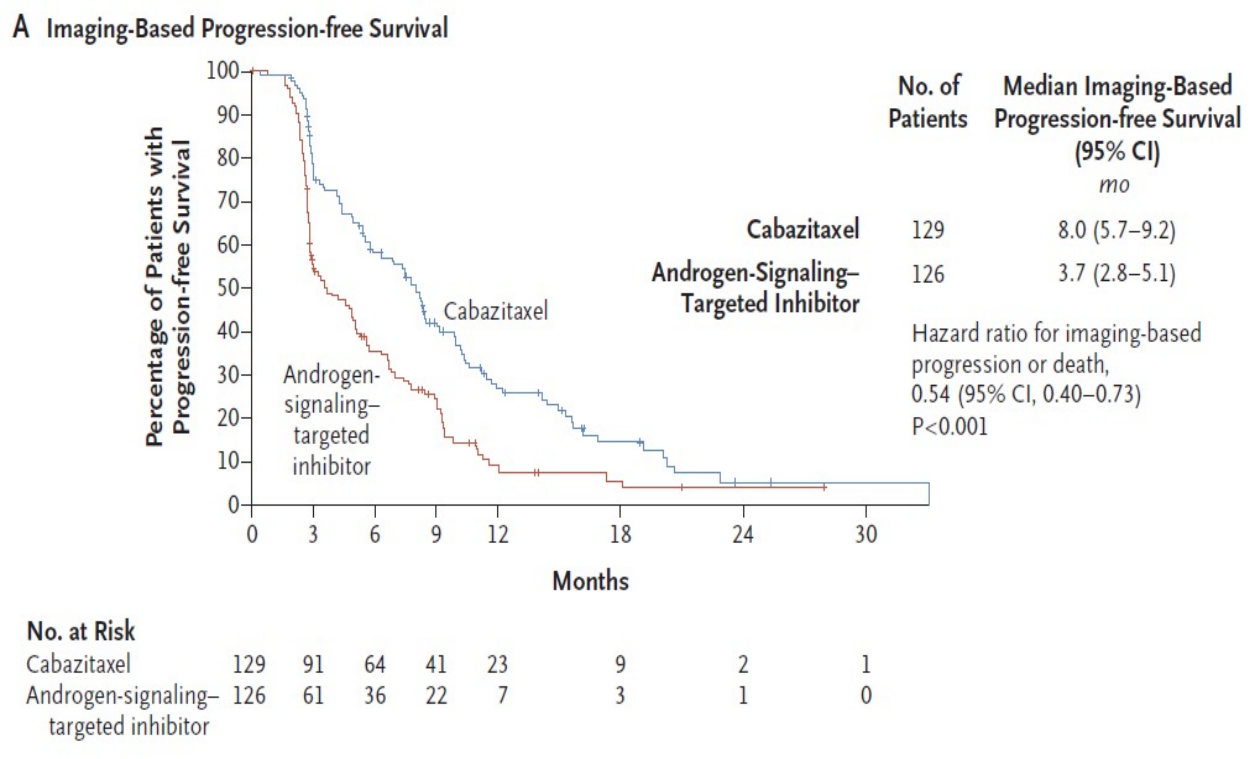
ODENZA: A Phase II Crossover Trial Evaluating Preference Between Darolutamide and Enzalutamide in Men with Asymptomatic or Mildly Symptomatic mCRPC

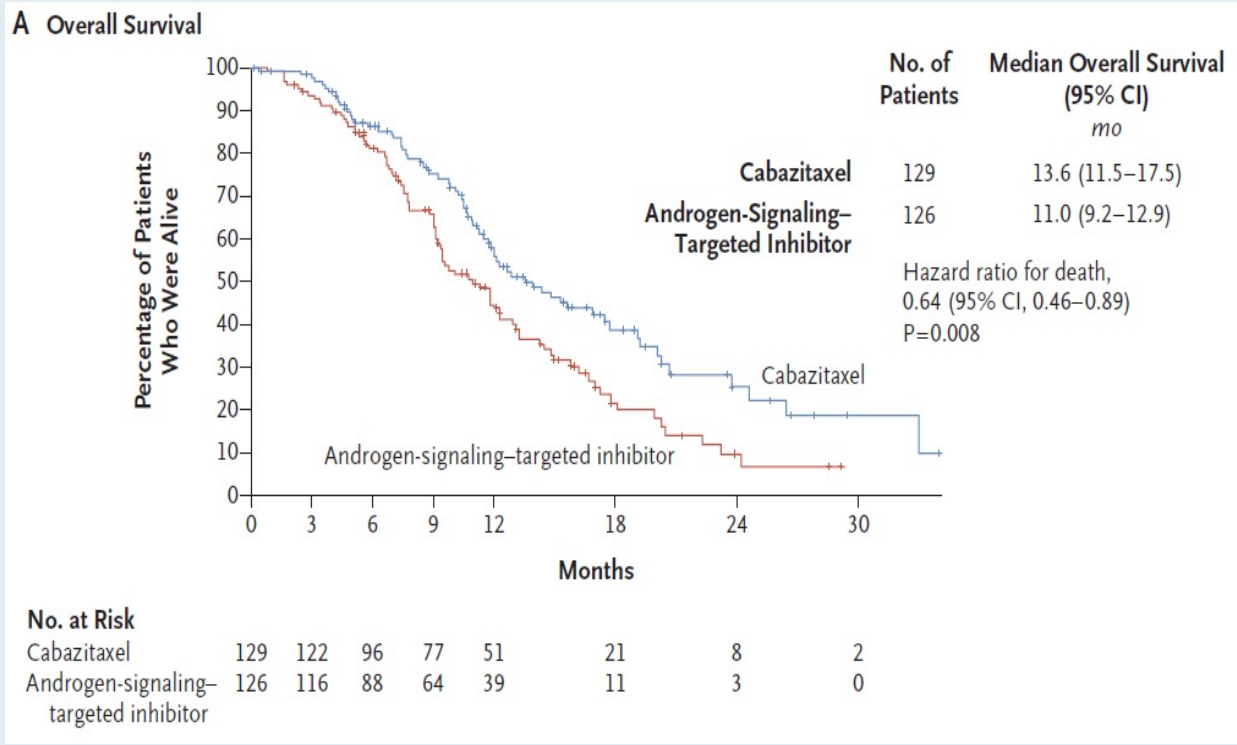




Colomba E et al. ASCO 2021;Abstract 5046.

CARD: Imaging-Based PFS and OS with Cabazitaxel versus Abiraterone or Enzalutamide for mCRPC





de Wit R. et al. *NEJM* 2019;381:2506-18.

RTP RESEARCH TO PRACTICE

CARD: Select Adverse Events

Table 2. Adverse Events (Safety Population).

Event	Cabazitaxel (N = 126)		Androgen-Signaling–Targeted Inhibitor (N = 124)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any adverse event — no. (%)	124 (98.4)	—	117 (94.4)	—
Any grade ≥3 adverse event — no. (%)	—	71 (56.3)	—	65 (52.4)
Any serious adverse event — no. (%)	49 (38.9)	—	48 (38.7)	—
Any adverse event leading to permanent discontinuation of treatment — no. (%)	25 (19.8)	—	11 (8.9)	—
Any adverse event leading to death — no. (%)*	7 (5.6)	—	14 (11.3)	—
Common adverse events — no. (%)†				
Asthenia or fatigue	67 (53.2)	5 (4.0)	45 (36.3)	3 (2.4)
Diarrhea	50 (39.7)	4 (3.2)	8 (6.5)	0
Infection	40 (31.7)	10 (7.9)	25 (20.2)	9 (7.3)
Musculoskeletal pain or discomfort‡	34 (27.0)	2 (1.6)	49 (39.5)	7 (5.6)
Nausea or vomiting	33 (26.2)	0	29 (23.4)	2 (1.6)
Peripheral neuropathy	25 (19.8)	4 (3.2)	4 (3.2)	0
Constipation	19 (15.1)	0	13 (10.5)	0
Hematuria	19 (15.1)	1 (0.8)	7 (5.6)	2 (1.6)
Laboratory abnormalities — no./total no. (%)††				
Anemia	124/125 (99.2)	10/125 (8.0)	118/124 (95.2)	6/124 (4.8)
Leukopenia	93/125 (74.4)	40/125 (32.0)	39/124 (31.5)	2/124 (1.6)
Neutropenia	81/123 (65.9)	55/123 (44.7)	8/124 (6.5)	4/124 (3.2)
Thrombocytopenia	51/125 (40.8)	4/125 (3.2)	20/124 (16.1)	2/124 (1.6)
Aspartate aminotransferase increased	27/124 (21.8)	4/124 (3.2)	35/124 (28.2)	0/124
Alanine aminotransferase increased	24/124 (19.4)	1/124 (0.8)	11/124 (8.9)	0/124
Hypokalemia	15/125 (12.0)	1/125 (0.8)	19/124 (15.3)	1/124 (0.8)

de Wit R et al. *NEJM* 2019;381:2506-18.

ORIGINAL RESEARCH

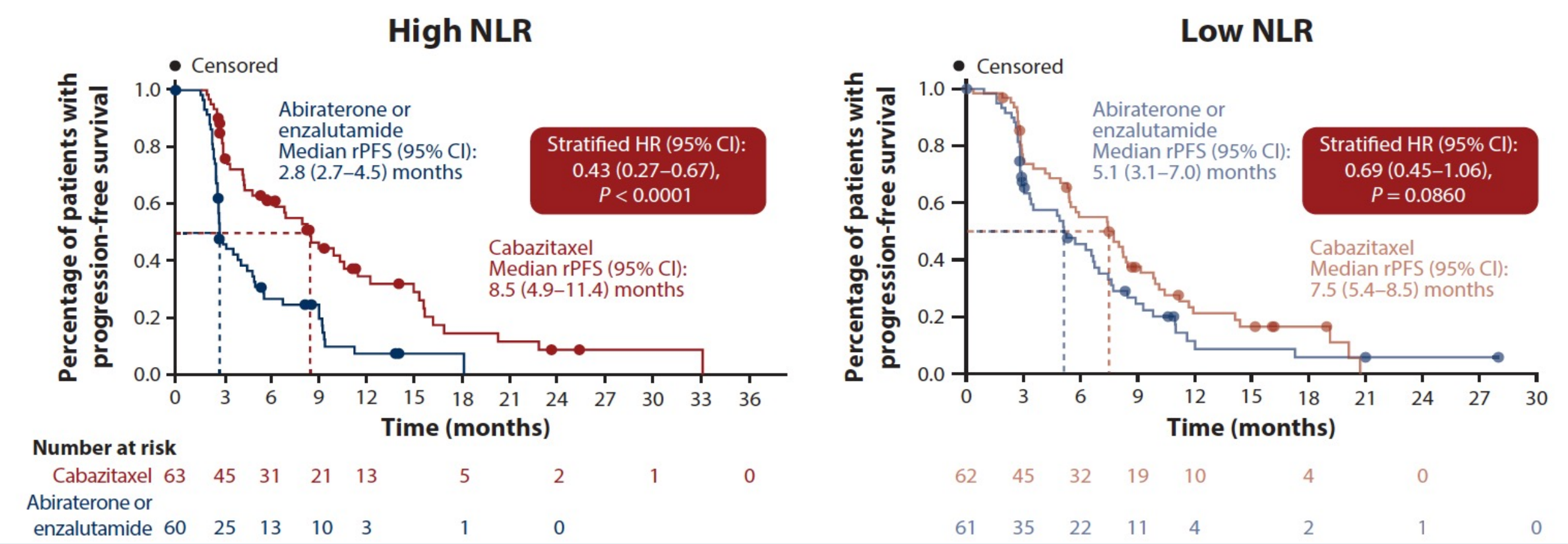
Baseline neutrophil-to-lymphocyte ratio as a predictive and prognostic biomarker in patients with metastatic castration-resistant prostate cancer treated with cabazitaxel versus abiraterone or enzalutamide in the CARD study

R. de Wit[1*], C. Wülfing[2], D. Castellano[3], G. Kramer[4], J.-C. Eymard[5], C. N. Sternberg[6], K. Fizazi[7,8], B. Tombal[9], A. Bamias[10], J. Carles[11], R. Iacovelli[12,13], B. Melichar[14], Á. Sverrisdóttir[15], C. Theodore[16], S. Feyerabend[17], C. Helissey[18], M. C. Foster[19], A. Ozatilgan[19], C. Geffriaud-Ricouard[20] & J. de Bono[21,22]

ESMO Open 2021;[Online ahead of print].

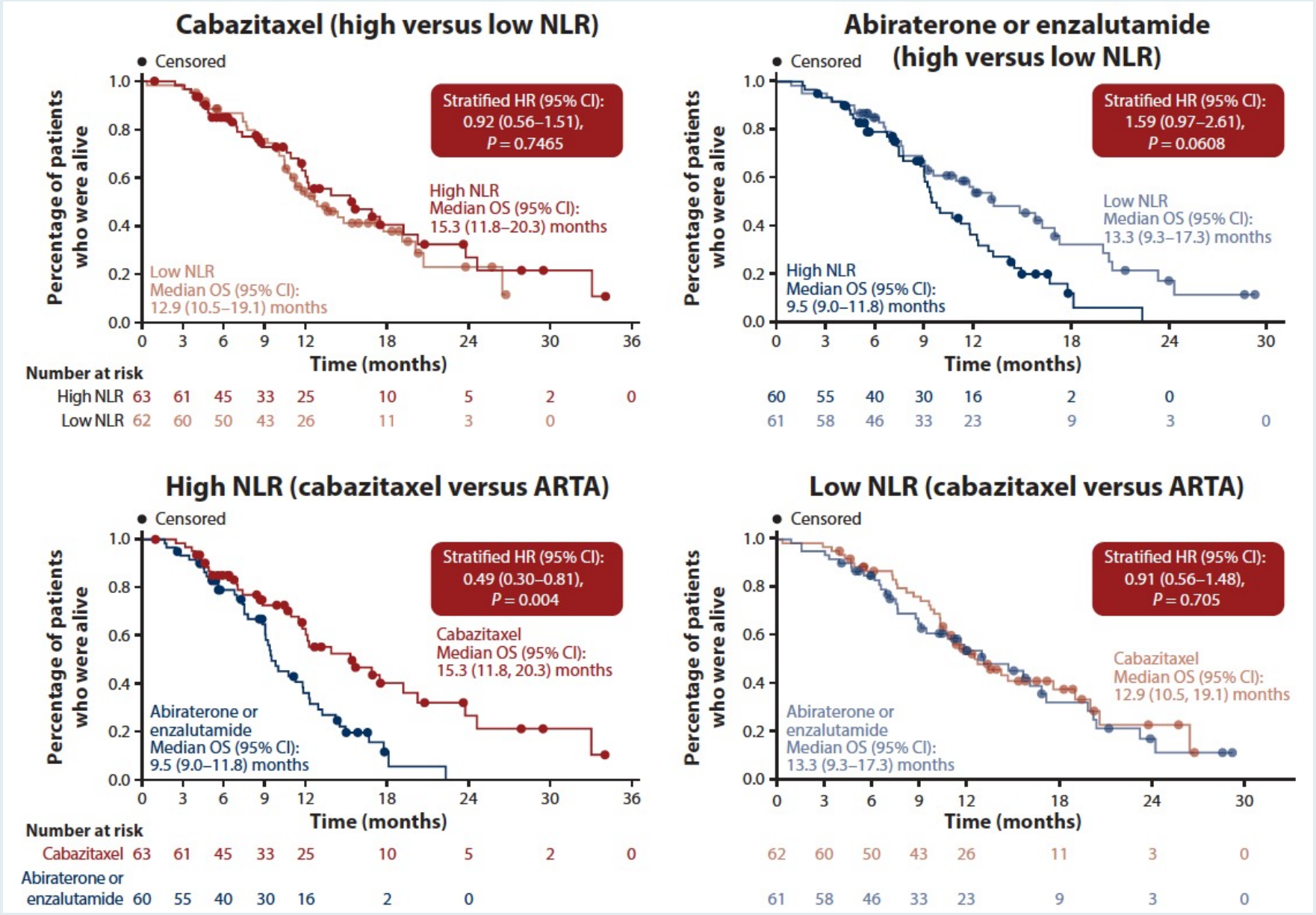
RTP RESEARCH TO PRACTICE

CARD: rPFS by Baseline Neutrophil-to-Lymphocyte Ratio (NLR)



de Wit R et al. *ESMO Open* 2021;[Online ahead of print].

CARD: OS by Baseline NLR



de Wit R et al. *ESMO Open* 2021;[Online ahead of print].

RTP RESEARCH TO PRACTICE

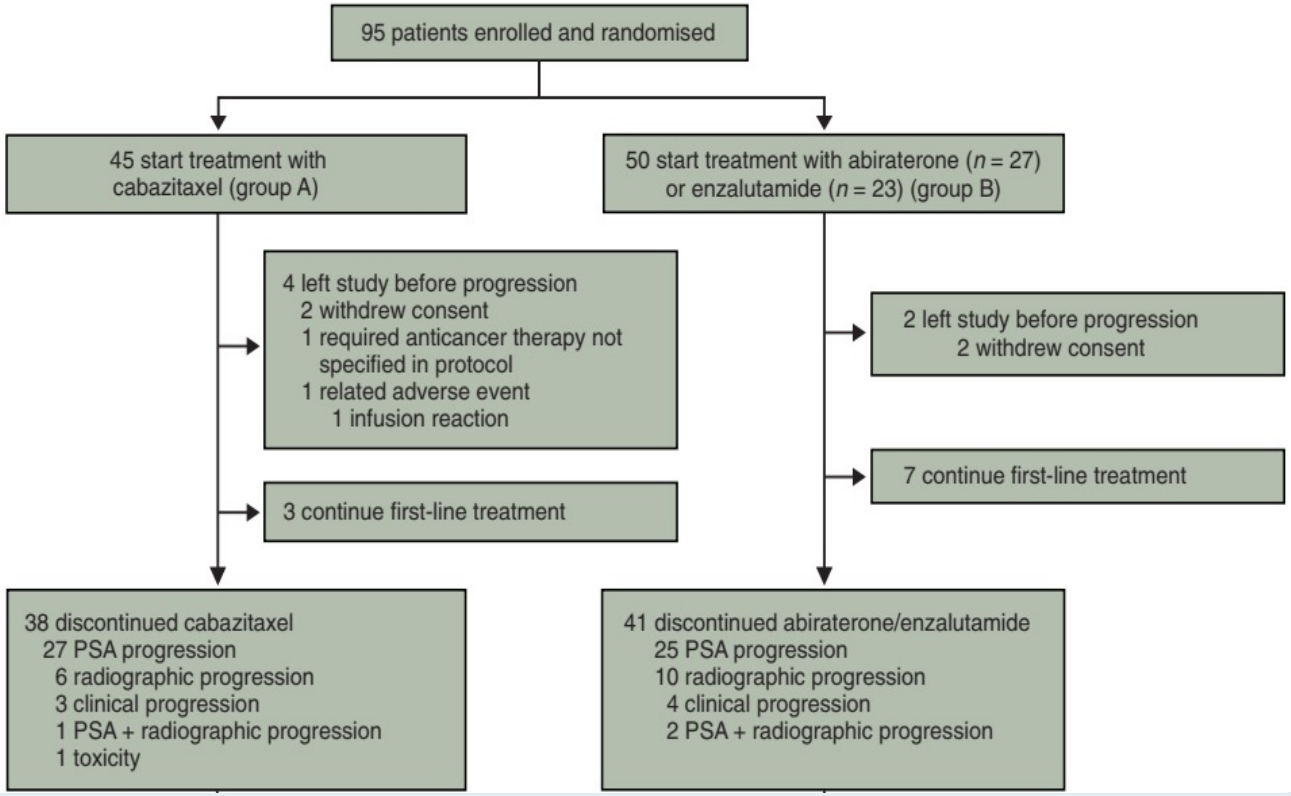
The Canadian Trial (Phase II OZM-054 Trial)

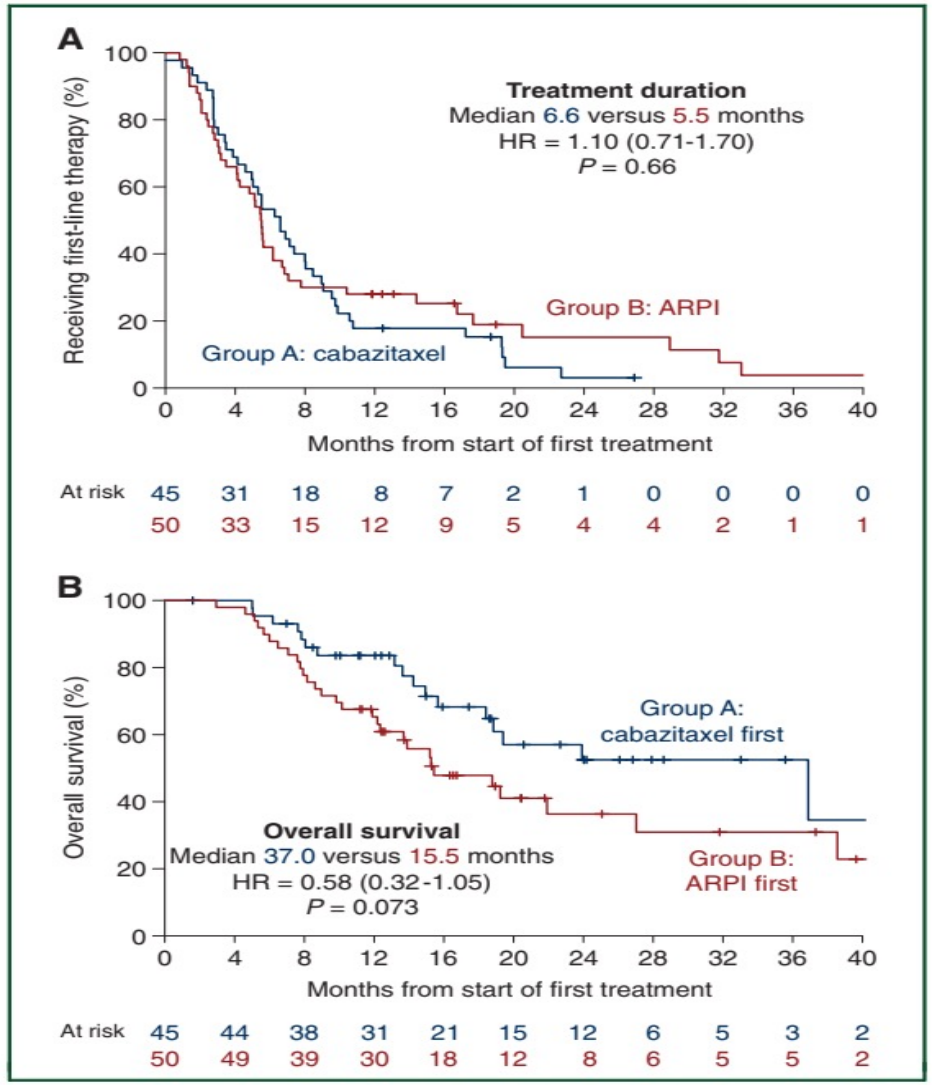
Poor prognosis:

liver mets,

CRPC <12 months,

or >3 of 6 (LDH, ECOG, visceral, albumin, ALP, <36 mo from Dx)





Annala M et al. *Ann Oncol* 2021;32:896-905.

Immune Checkpoint Inhibitors in mCRPC

Therapy	Disease State	Disease Response
Pembrolizumab monotherapy[a]	Post-chemotherapy	ORR 9% PSA RR 14%
Pembrolizumab + enzalutamide[b]	Pre-chemotherapy progressing on enzalutamide	ORR 12% PSA RR 14%
Atezolizumab + enzalutamide[c]	Pre- and post-chemotherapy, s/p abiraterone	ORR 14% PSA RR 26%
Atezolizumab + cabozantinib[d]	Pre-chemotherapy s/p enzalutamide or abiraterone	ORR 34% PSA RR 29%

[a]JCO 2020: 38(5) 395-405. [b]Presented at the 2021 ASCO Annual Meeting – Virtual; June 4-8, 2021. [c]Sweeney C. AACR 2020. IMbassador250. [d]Agarwal ASCO 2020. COSMIC-021

2021 ESMO congress

Abstract LBA24

Cabozantinib in combination with atezolizumab in patients with metastatic castration-resistant prostate cancer (mCRPC): results of expanded cohort 6 of the COSMIC-021 Study

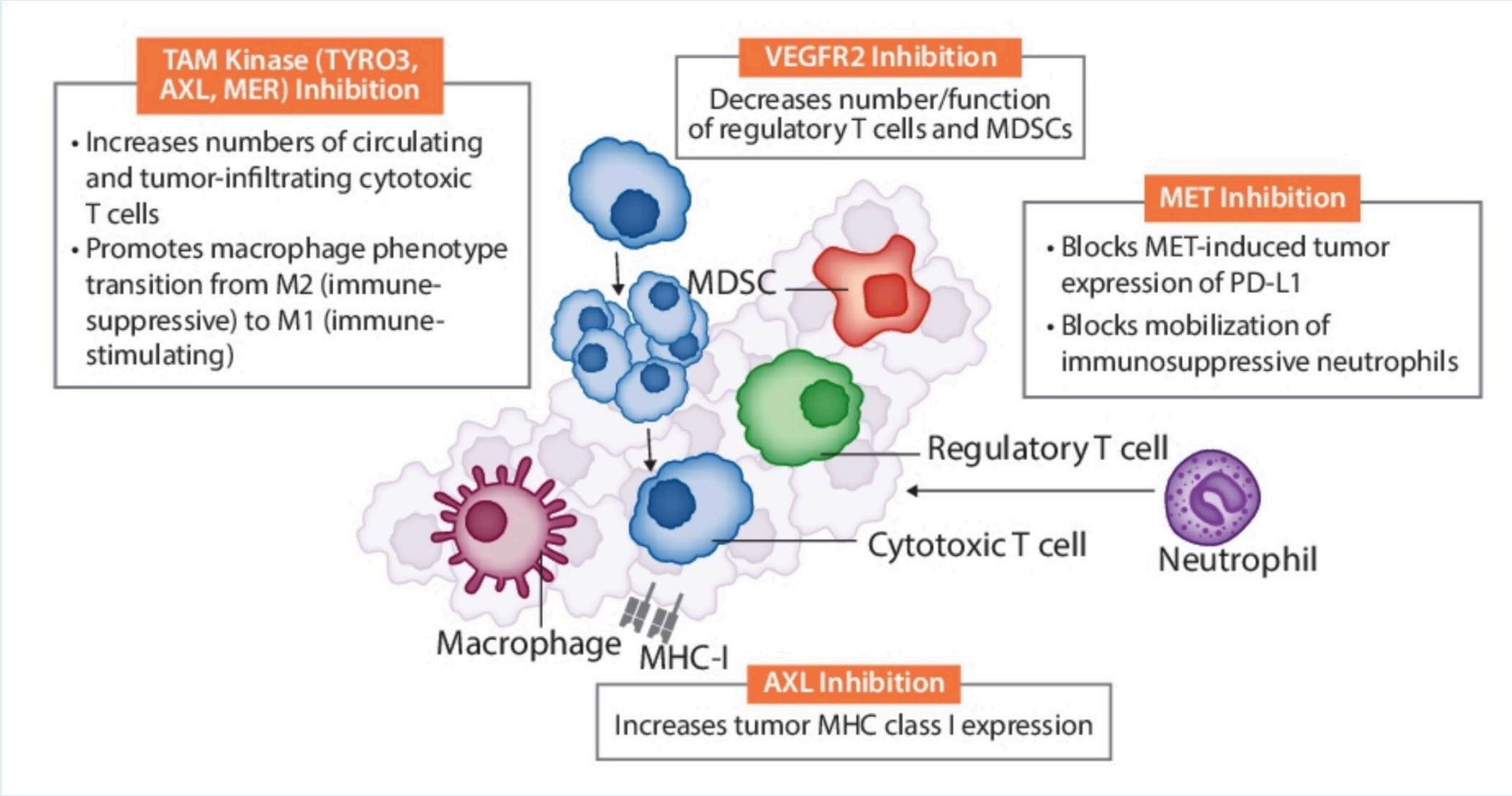
Neeraj Agarwal,[1] Bradley McGregor,[2] Benjamin L. Maughan,[1] Tanya B. Dorff,[3] William Kelly,[4] Bruno Fang,[5] Rana R. McKay,[6] Parminder Singh,[7] Lance Pagliaro,[8] Robert Dreicer,[9] Sandy Srinivas,[10] Yohann Loriot,[11] Ulka Vaishampayan,[12] Sanjay Goel,[13] Dominic Curran,[14] Ashok Panneerselvam,[14] Li-Fen Liu,[14] Toni K. Choueiri,[2*] Sumanta Pal[3*]

[1]Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA; [2]Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA; [3]City of Hope Comprehensive Cancer Center, Duarte, CA, USA; [4]Sidney Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA, USA; [5]Regional Cancer Care Associates, East Brunswick, NJ, USA; [6]University of California San Diego, San Diego, CA, USA; [7]Department of Oncology, Mayo Clinic, Scottsdale, AZ, USA; [8]Department of Oncology, Mayo Clinic, Rochester, MN, USA; [9]University of Virginia Cancer Center, Charlottesville, VA, USA; [10]Division of Medical Oncology, Stanford University Medical Center, Stanford, CA, USA; [11]Department of Cancer Medicine, Gustave Roussy Institute, INSERM 981, University Paris-Saclay, Villejuif, France; [12]Karmanos Cancer Center, Wayne State University, Detroit, MI, USA (Current affiliation: Division of Hematology/Oncology, University of Michigan, Ann Arbor, MI, USA); [13]Department of Medical Oncology, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY, USA; [14]Exelixis, Inc., Alameda, CA, USA

*Co-senior authors

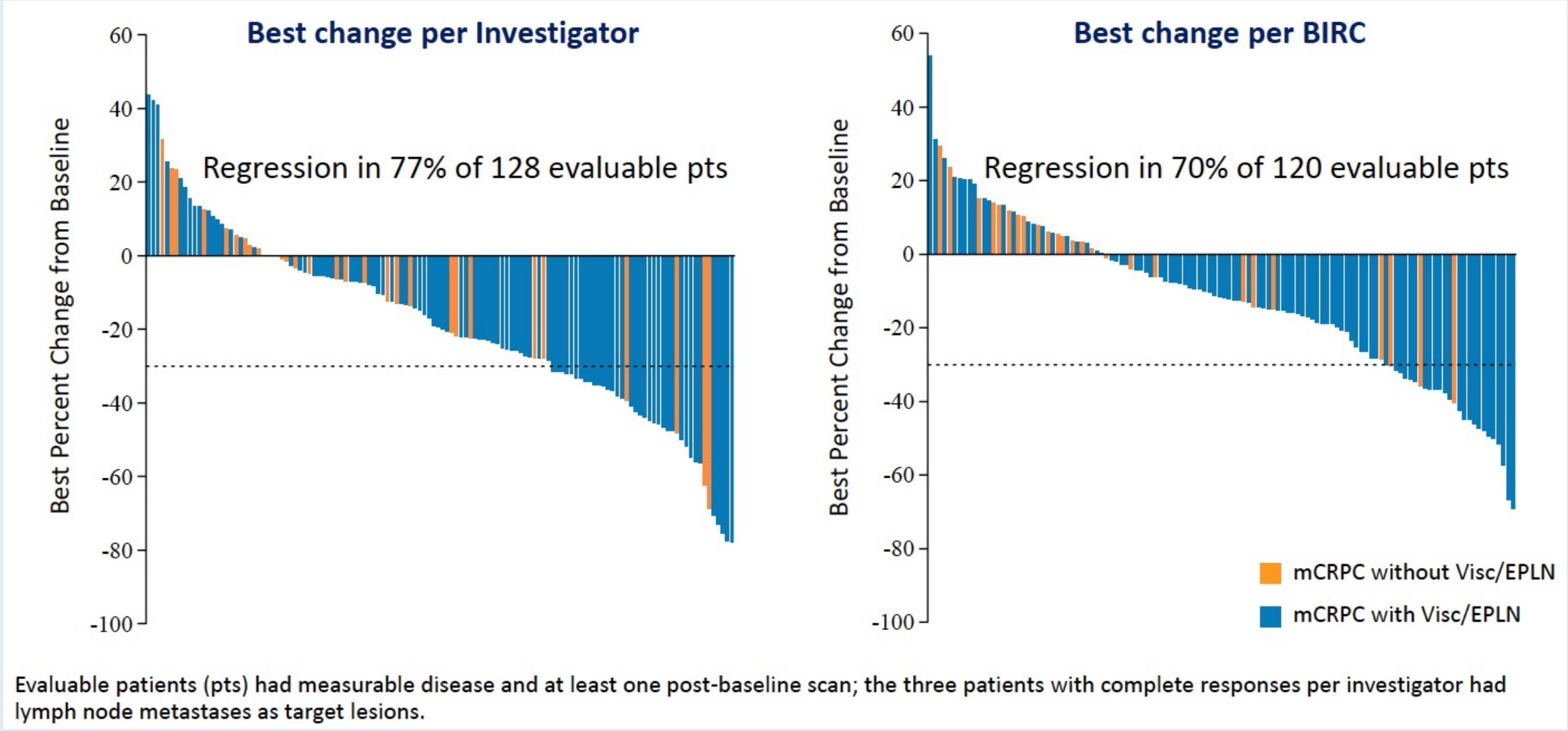
RTP RESEARCH TO PRACTICE

Cabozantinib Targets Pathways Associated with Tumor Immune Suppression



Agarwal N et al. ASCO 2020;Abstract 5564.

COSMIC-021: Best Change from Baseline in Sum of Target Lesions

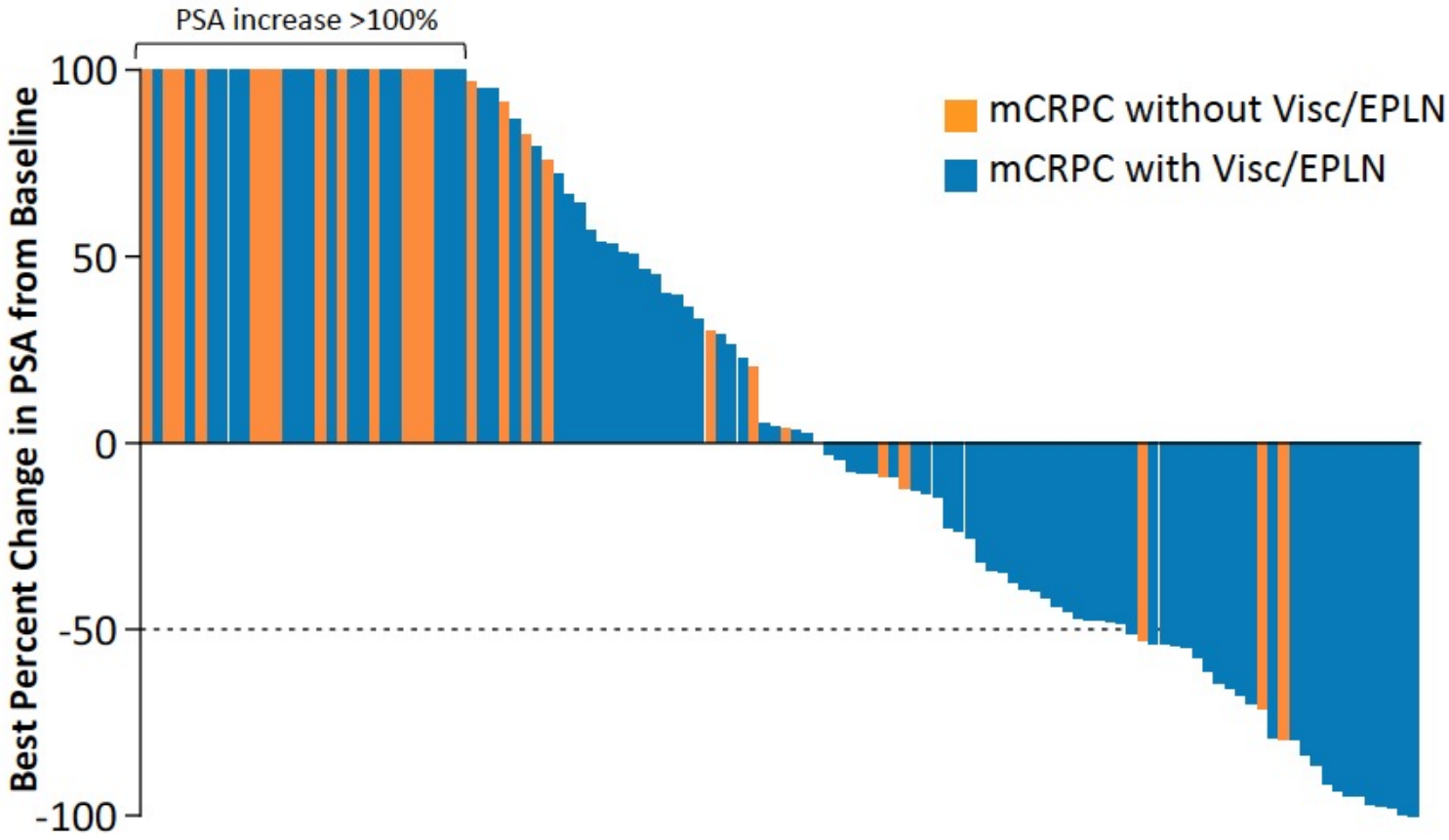


Evaluable patients (pts) had measurable disease and at least one post-baseline scan; the three patients with complete responses per investigator had lymph node metastases as target lesions.

Agarwal et al. ESMO 2021;Abstract LBA24.

RTP RESEARCH TO PRACTICE

COSMIC-021: Best Change in PSA from Baseline



- In 118 patients with post-baseline assessments, 55 (47%) had a decrease in PSA, and 27 (23%) had a decrease ≥50%
- In 92 patients with Visc/EPLN, 50 (54%) had a decrease in PSA, and 24 (26%) had a decrease ≥50%

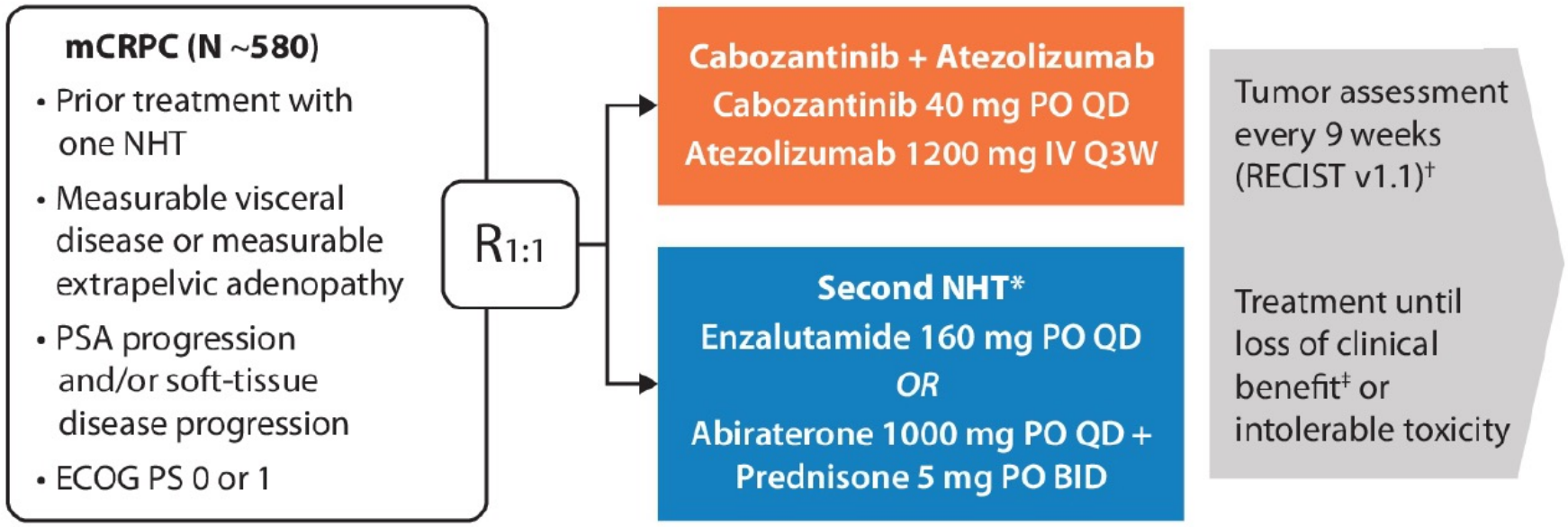
Agarwal et al. ESMO 2021;Abstract LBA24.

COSMIC-021: Select Treatment-Related Adverse Events

	mCRPC (N=132)	
	Any Grade	Grade 3/4
Any AE, %	95	55
Diarrhea	55	6.8
Fatigue	43	6.8
Nausea	42	0.8
Decreased appetite	34	1.5
Dysgeusia	27	0
Palmar-plantar erythrodysesthesia	25	2.3
Vomiting	23	1.5
Weight decreased	23	1.5
Aspartate aminotransferase increased	20	3.0
Stomatitis	16	0.8
Hypertension	14	6.8
Alanine aminotransferase increased	14	3
Dysphonia	13	0
Hypothyroidism	12	0
Pulmonary embolism	11	8.3

Agarwal et al. ESMO 2021;Abstract LBA24.

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)

Primary Endpoints:

- PFS per RECIST v1.1 by BIRC
- OS

Secondary Endpoint:

- ORR per RECIST v1.1 by BIRC

*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

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

RTP RESEARCH TO PRACTICE

First Results from a Randomized Phase II Study of Cabazitaxel (CBZ) versus an Androgen Receptor Targeted Agent (ARTA) in Patients with Poor-Prognosis Castration-Resistant Prostate Cancer (mCRPC)

van der Zande K et al.
ASCO 2021;Abstract 5059.

The Dutch Trial (Phase II OSTRICh Trial)

Inclusion criteria
- mCRPC
- ECOG PS0-2
- Testosterone <50 ng/dL
- Adequate bone marrow and liver functions
- Prior docetaxel
- Previous ARTA was allowed
- Progressive disease
- Features of poor prognostic disease (≥1):
  - Liver metastasis
  - Castration resistant <12m
  - Progressive <6m after docetaxel

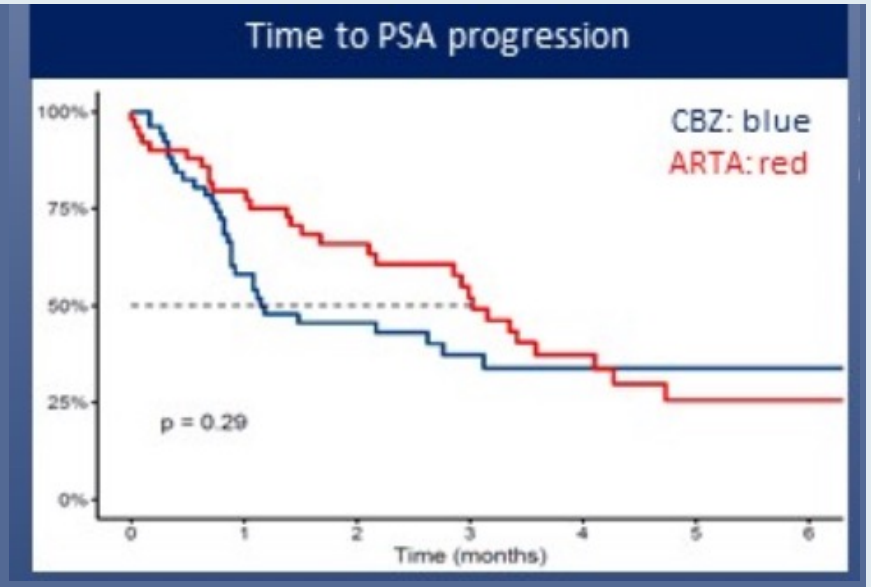
R

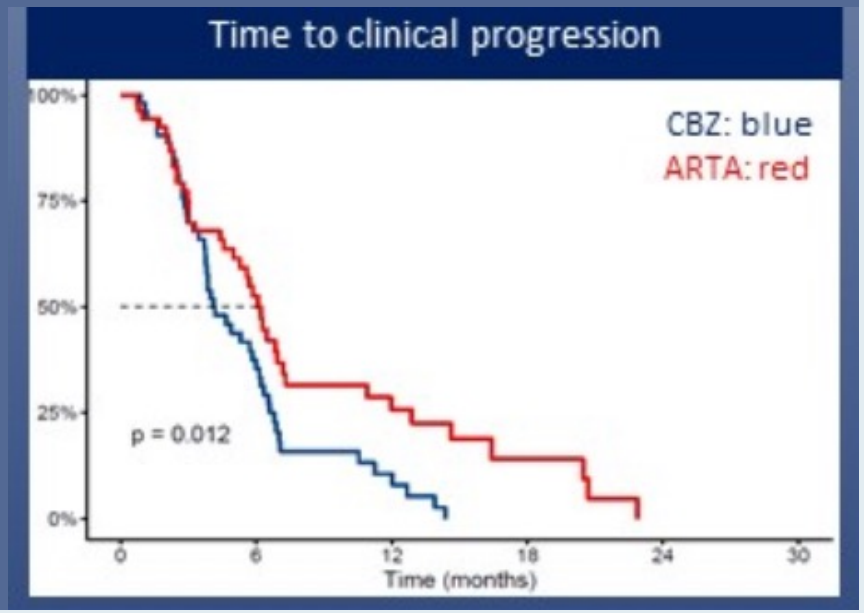
Cabazitaxel

Abiraterone/P OR enzalutamide

12 weeks CBR

Follow-up for secondary endpoints

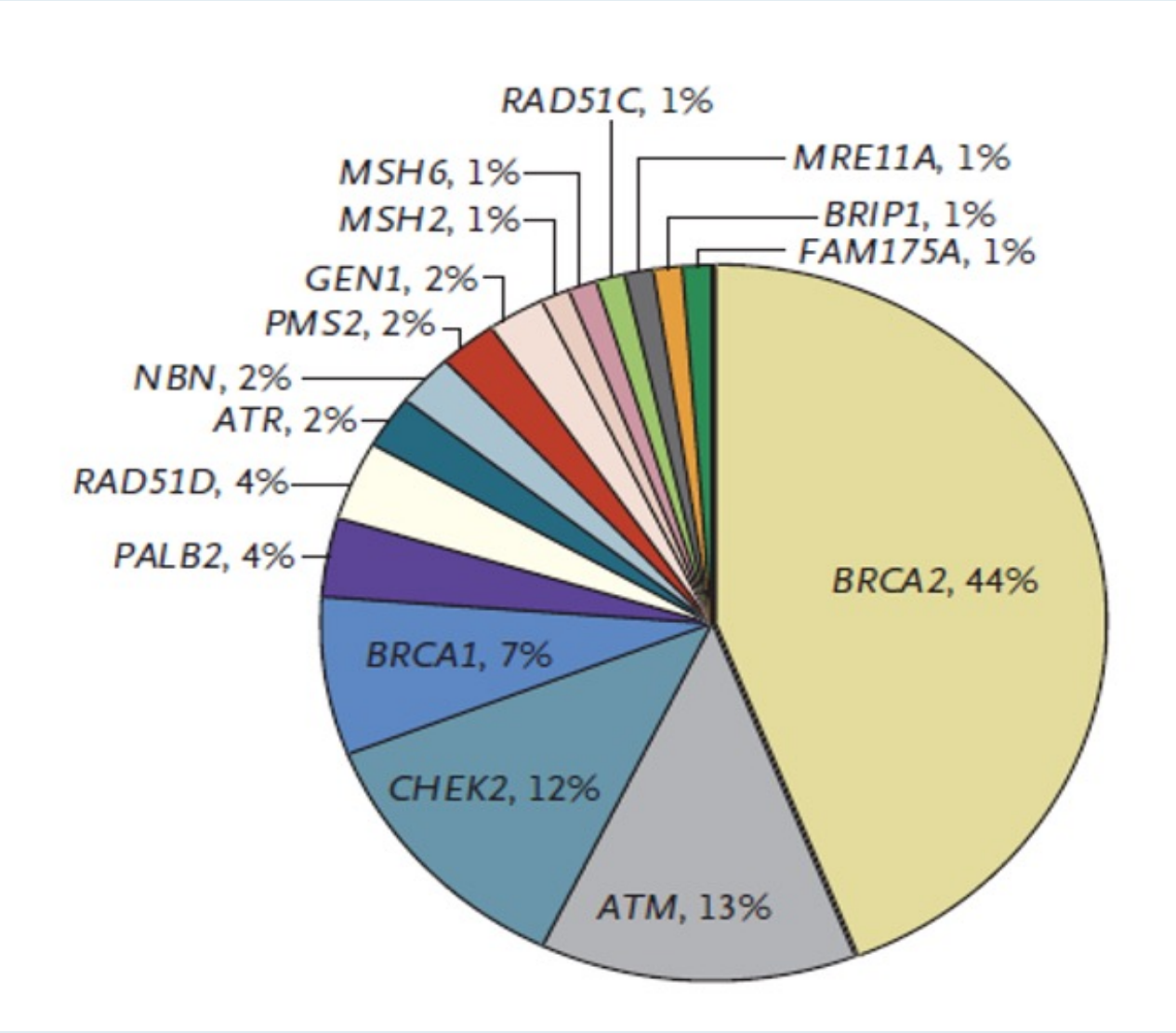




van der Zande K et al. *ASCO* 2021;Abstract 5059.

RTP RESEARCH TO PRACTICE

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.

RTP RESEARCH TO PRACTICE

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

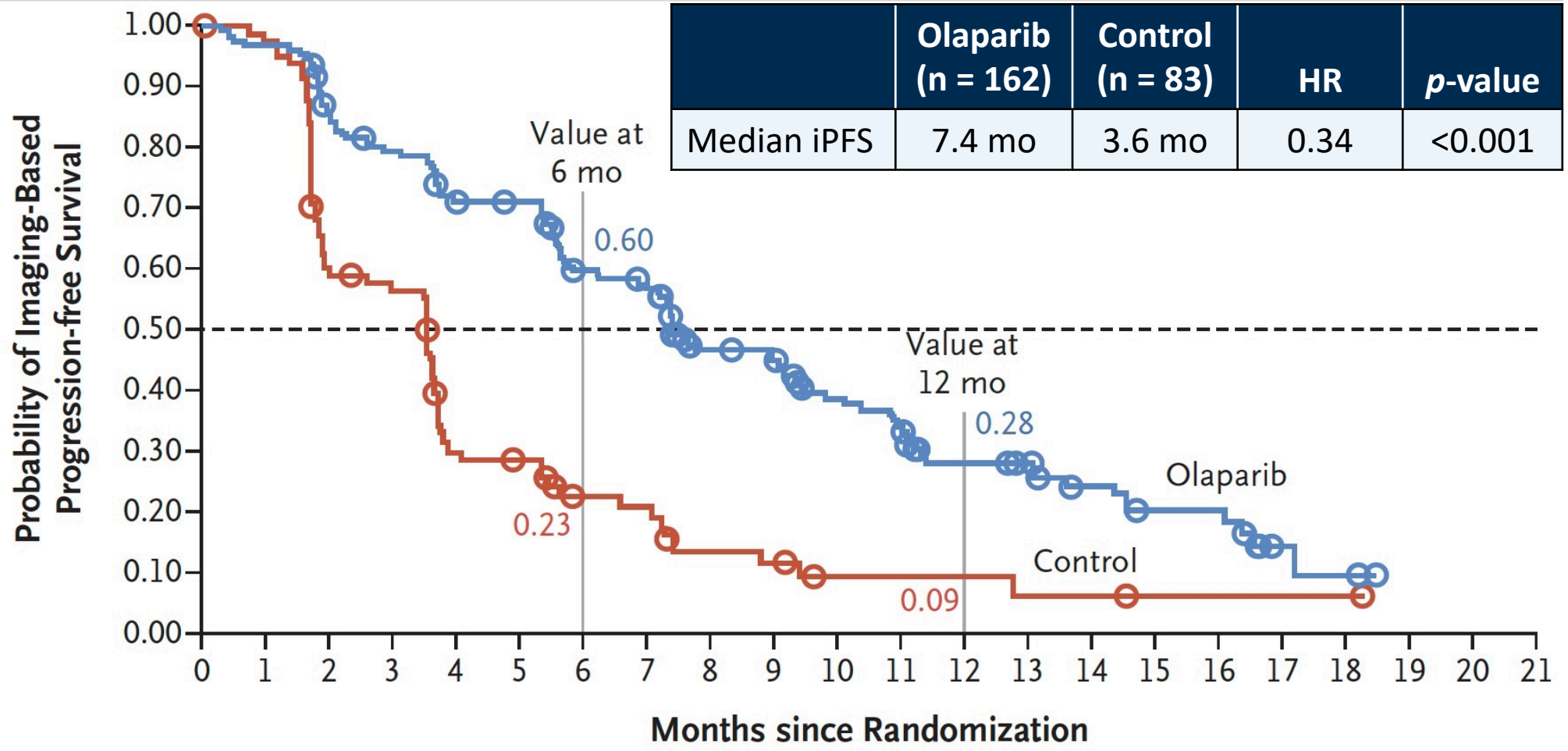
Olaparib for Metastatic Castration-Resistant Prostate Cancer

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;382:2091-102**

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

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

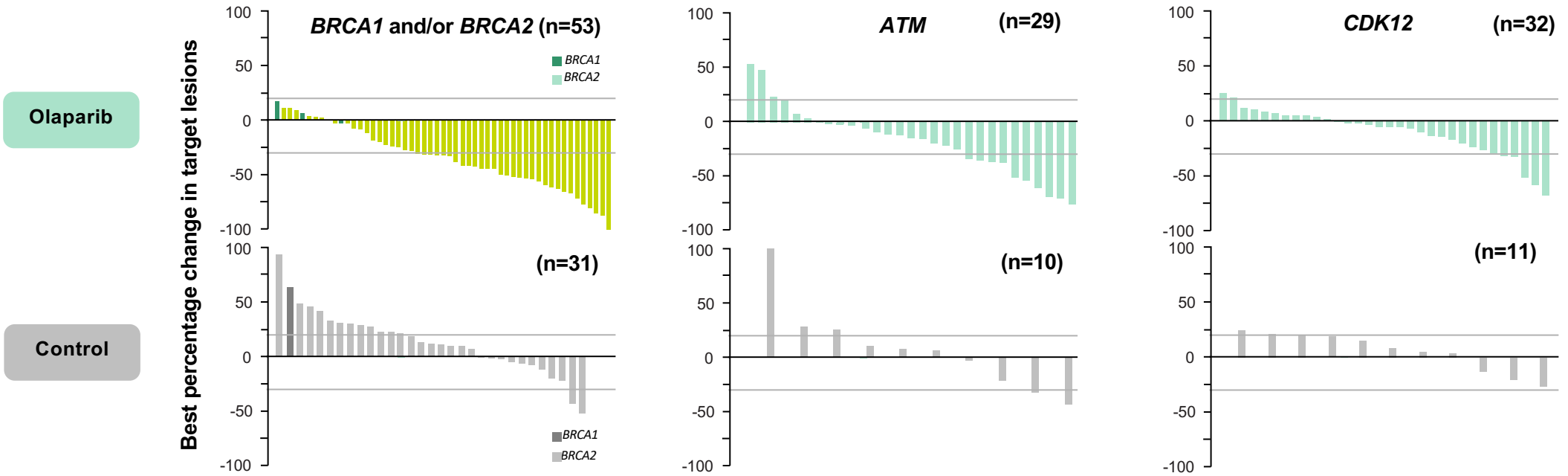


de Bono J et al; PROfound investigators. *N Engl J Med* 2020;382(22):2091-102.

RTP RESEARCH TO PRACTICE

Olaparib Antitumor Activity in PROfound

		Cohort A		Cohorts A+B		*BRCA1* and/or *BRCA2*		*ATM*		*CDK12*	
		Olaparib (N=162)	Control (N=83)	Olaparib (N=256)	Control (N=131)	Olaparib (N=102)	Control (N=58)	Olaparib (N=62)	Control (N=24)	Olaparib (N=61)	Control (N=28)
rPFS	Median, months	7.4	3.6	5.8	3.5	9.8	3.0	5.4	4.7	5.1	2.2
	HR (95% CI)	0.34 (0.25–0.47)		0.49 (0.38–0.63)		0.22 (0.15–0.32)		1.04 (0.61–1.87)		0.74 (0.44–1.31)	
OS	Median OS, months	19.1	14.7	17.3	14.0	20.1	14.4	18.0	15.6	14.1	11.5
	HR (95% CI)	0.69 (0.50–0.97)		0.79 (0.61–1.03)		0.63 (0.42–0.95)		0.93 (0.53–1.75)		0.97 (0.57–1.71)	
ORR	Evaluable patients, n	84	43	138	67	57	33	30	10	34	12
	ORR, %	33.3	2.3	21.7	4.5	43.9	0	10.0	10.0	5.9	0
PSA	Evaluable patients, n	153	77	243	123	94	54	61	22	58	27
	Confirmed response, %	43.1	7.8	30.0	9.8	61.7	0	13.1	22.7	5.2	3.7
CTC	Evaluable patients, n	52	22	78	32	29	17	25	3	14	5
	Conversion, %	55.8	22.7	52.6	21.9	69.0	23.5	40.0	33.3	50.0	40.0



de Bono et al. NEJM 2020

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

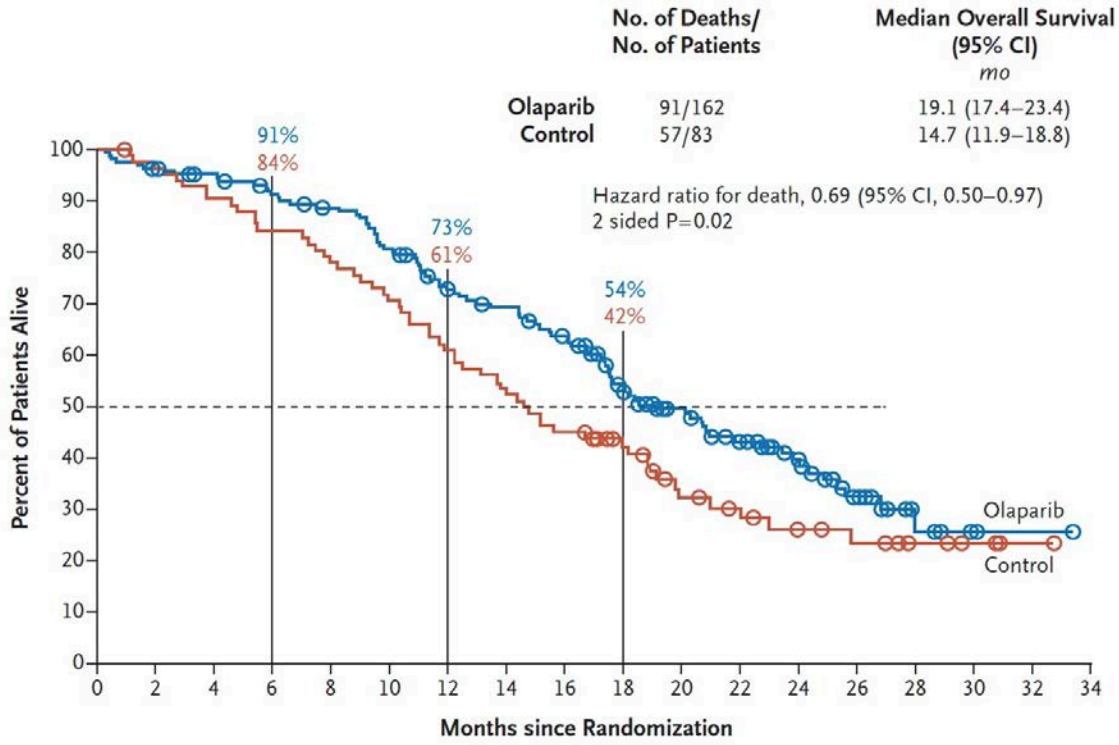
Survival with Olaparib in Metastatic Castration-Resistant Prostate Cancer

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*

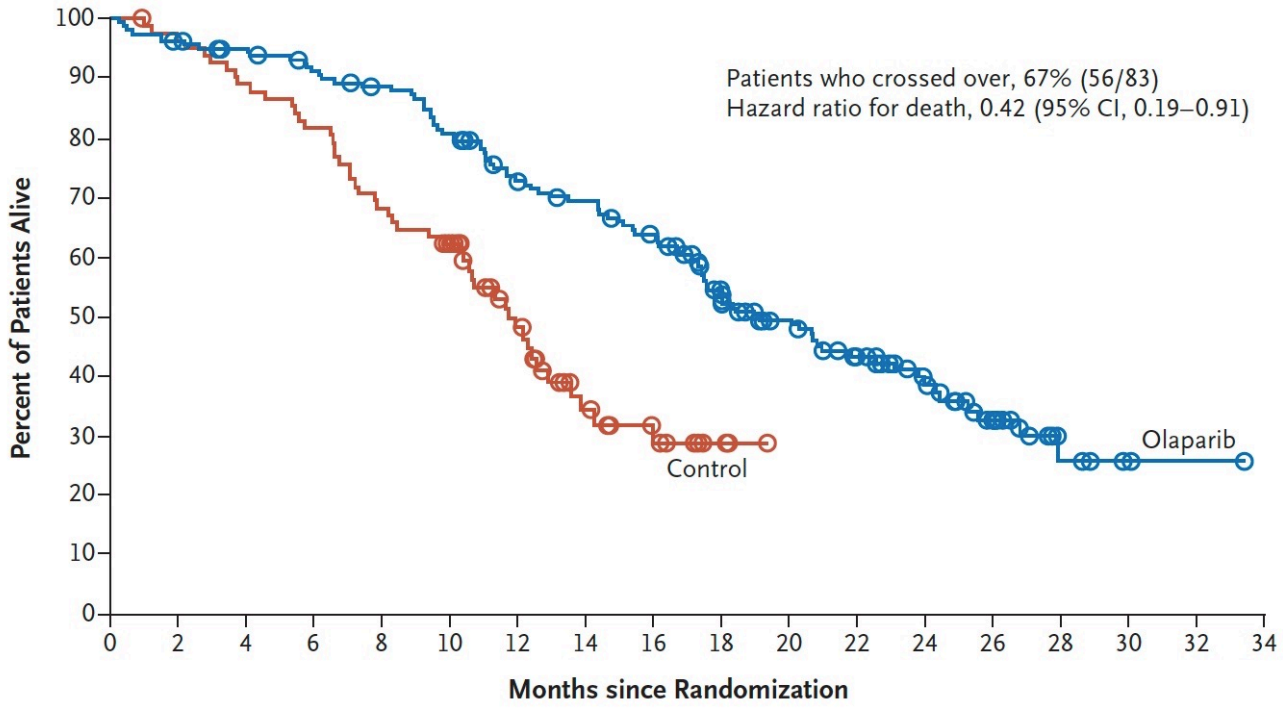
***N Engl J Med* 2020;383(24):2345-57.**

PROfound: OS with Olaparib in 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.

rapid communications

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

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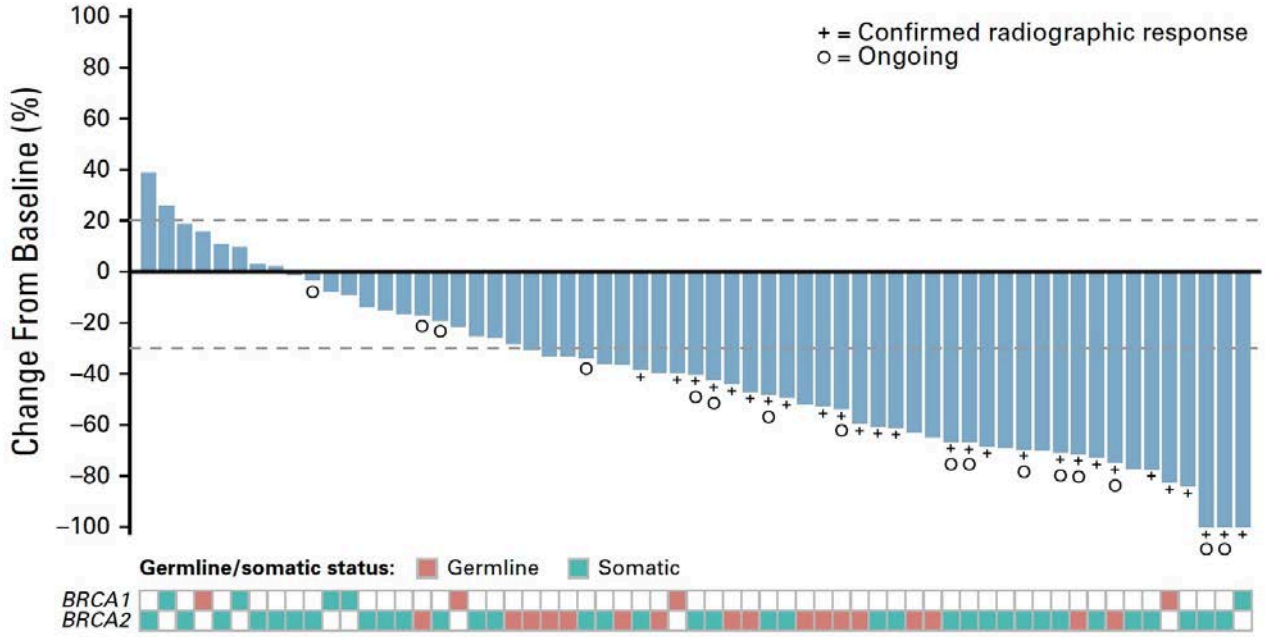
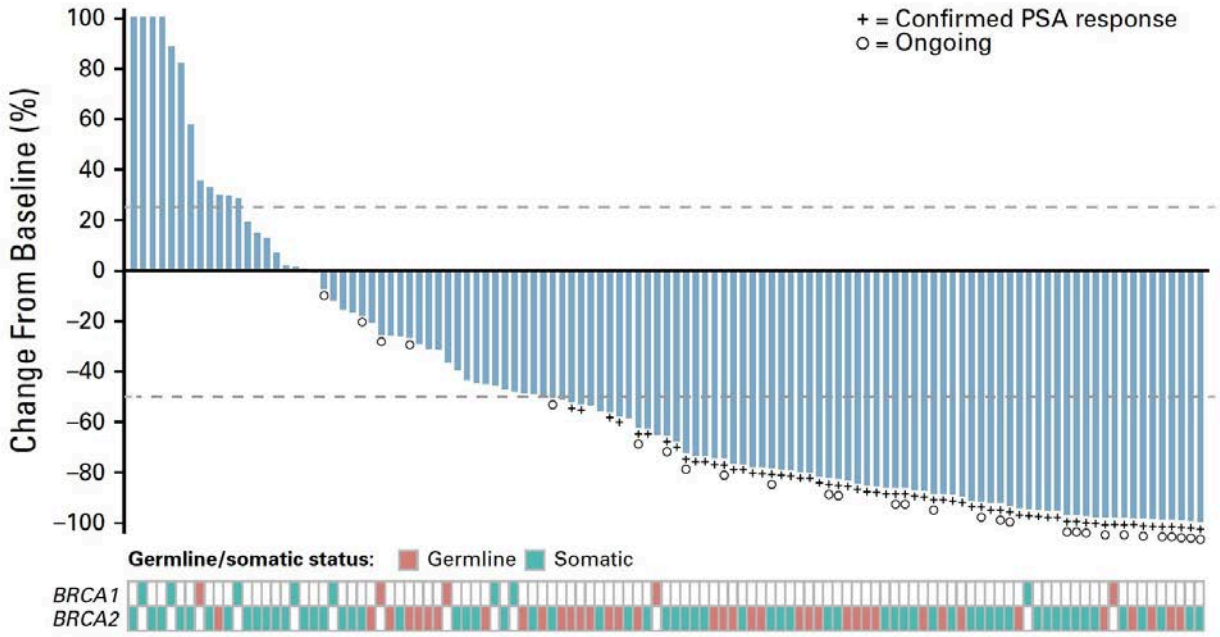
J Clin Oncol 2020;38(22):3763-72.

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

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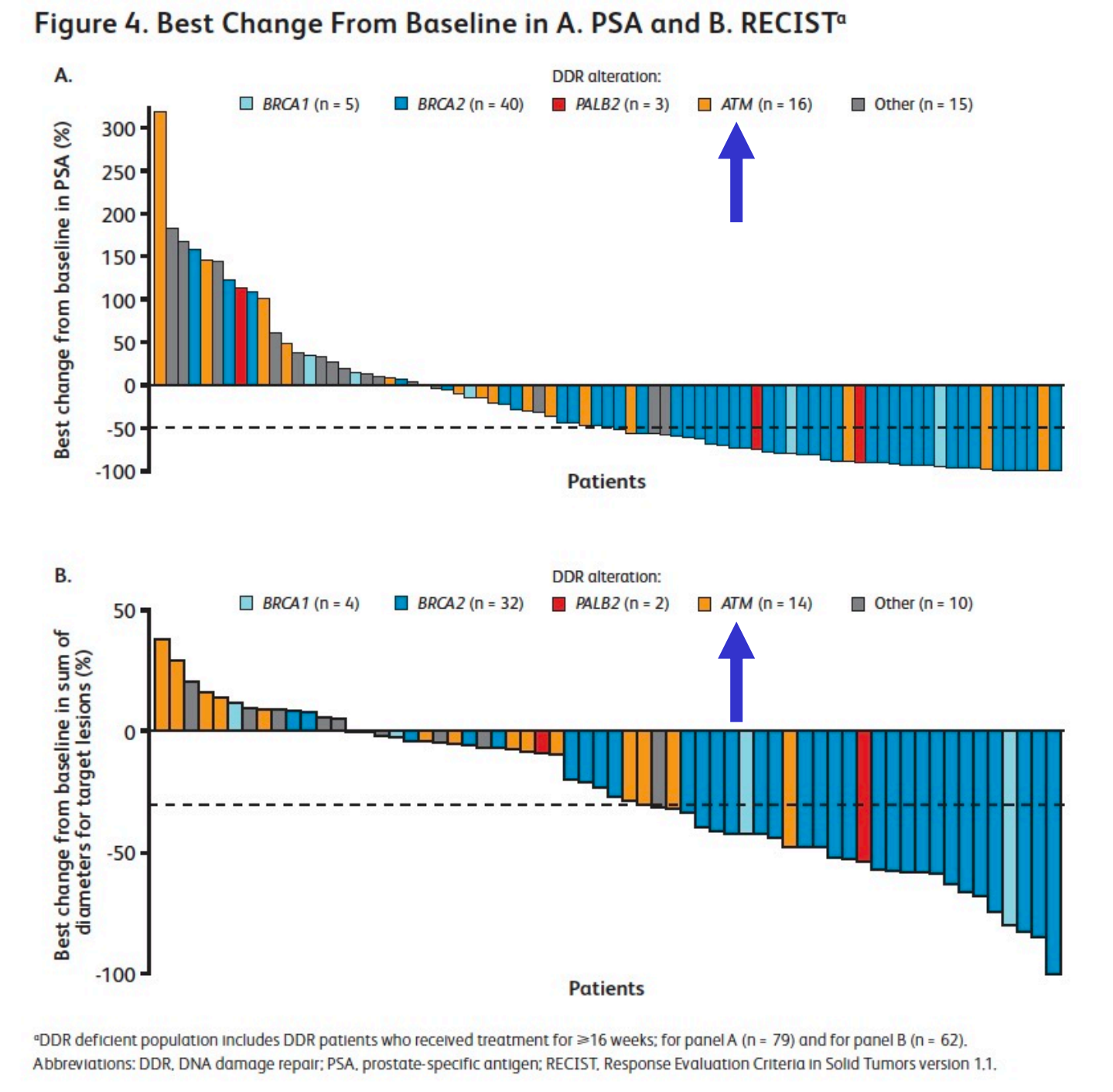
Talazoparib in mCRPC (TALAPRO-1)

BRCA in blue
ATM loss in orange
PALB2 in red



de Bono JS et al. *Lancet Oncol* 2021;22(9):1250-64.

RTP RESEARCH TO PRACTICE

Meet The Professor

Current and Future Management of Chronic Lymphocytic Leukemia

Thursday, March 3, 2022
5:00 PM – 6:00 PM ET

Faculty

William G Wierda, MD, PhD

Moderator

Neil Love, MD

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Thank you for joining us!

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

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