The Clinical Implications of Key Recent Data Sets in Oncology: A Daylong Multitumor Educational Symposium in Partnership with Florida Cancer Specialists

A CME/MOC- and NCPD-Accredited Event

Saturday, October 22, 2022
7:30 AM – 5:30 PM ET

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Agenda

Module 1 — Lung Cancer: *Drs Langer and Lovly*

Module 2 — Chronic Lymphocytic Leukemia and Lymphomas: *Drs LaCasce and Smith*

Module 3 — Prostate and Bladder Cancers: *Drs Morgans and Yu*

Module 4 — Renal Cell Carcinoma: *Prof Powles*

Module 5 — Multiple Myeloma: *Dr Usmani*

Module 6 — Hepatobiliary Cancers: *Prof Abou-Alfa*

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Module 7 — Breast Cancer: *Drs Goetz and Krop*

Module 8 — Endometrial Cancer: *Dr Westin*

Module 9 — Ovarian Cancer and PARP Inhibitors: *Dr O'Malley*

Module 10 — Gastrointestinal Cancers: *Drs Messersmith and Strickler*

Module 11 — Melanoma: *Prof Long*

Prostate and Bladder Cancers Faculty

Alicia K Morgans, MD, MPH
Genitourinary Medical Oncologist
Medical Director, Survivorship Program
Dana-Farber Cancer Institute
Boston, Massachusetts

Evan Y Yu, MD
Professor of Medicine
Division of Oncology, Department of Medicine
University of Washington School of Medicine
Member, Clinical Research Division
Fred Hutchinson Cancer Center
Medical Director, Clinical Research Services
Fred Hutchinson Cancer Research Consortium
Seattle, Washington

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Prostate and Bladder Cancers Agenda

Module 1: Prostate Cancer

Module 2: Urothelial Bladder Cancer

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Prostate and Bladder Cancers Agenda

Module 1: Prostate Cancer

Module 2: Urothelial Bladder Cancer

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Updates in Advanced Prostate Cancer

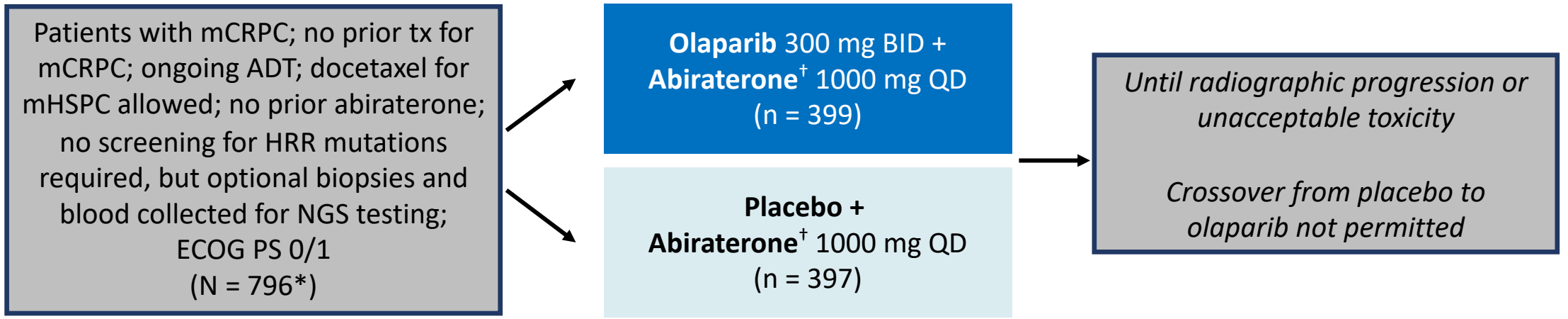
Alicia Morgans, MD, MPH
Dana-Farber Cancer Institute

Dana-Farber
Cancer Institute

PROpel: First-Line Olaparib + Abiraterone vs Placebo + Abiraterone in mCRPC

- Interim analysis of international, randomized, double-blind phase III trial (data cutoff: July 30, 2021)

Stratified by metastatic disease sites (bone only vs visceral vs other), taxane for mHSPC (yes vs no)

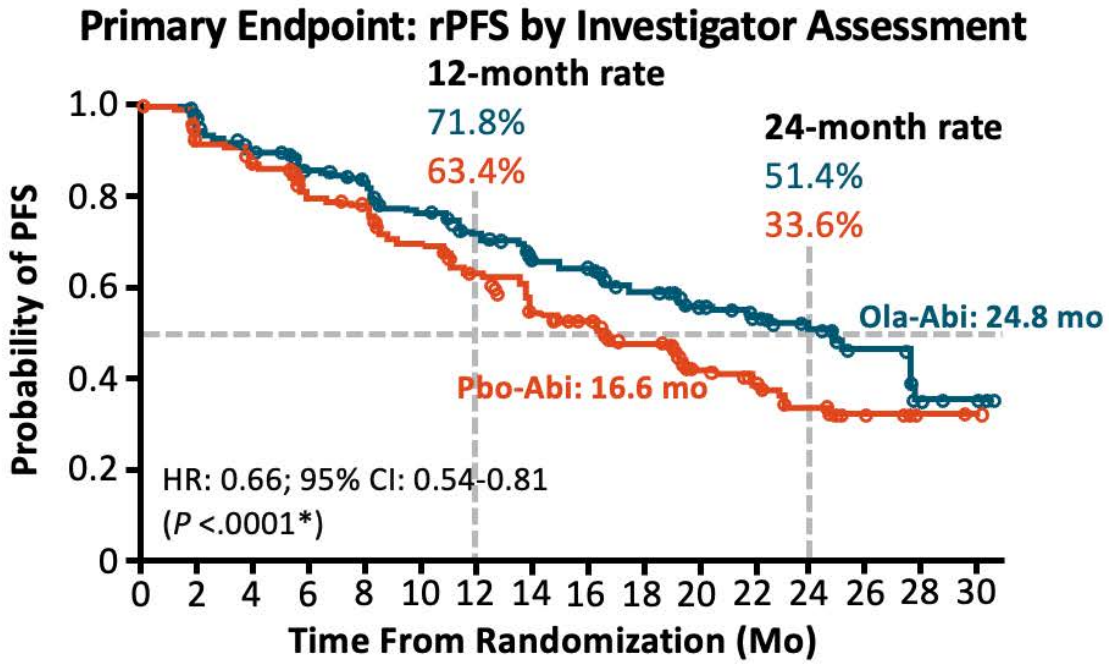


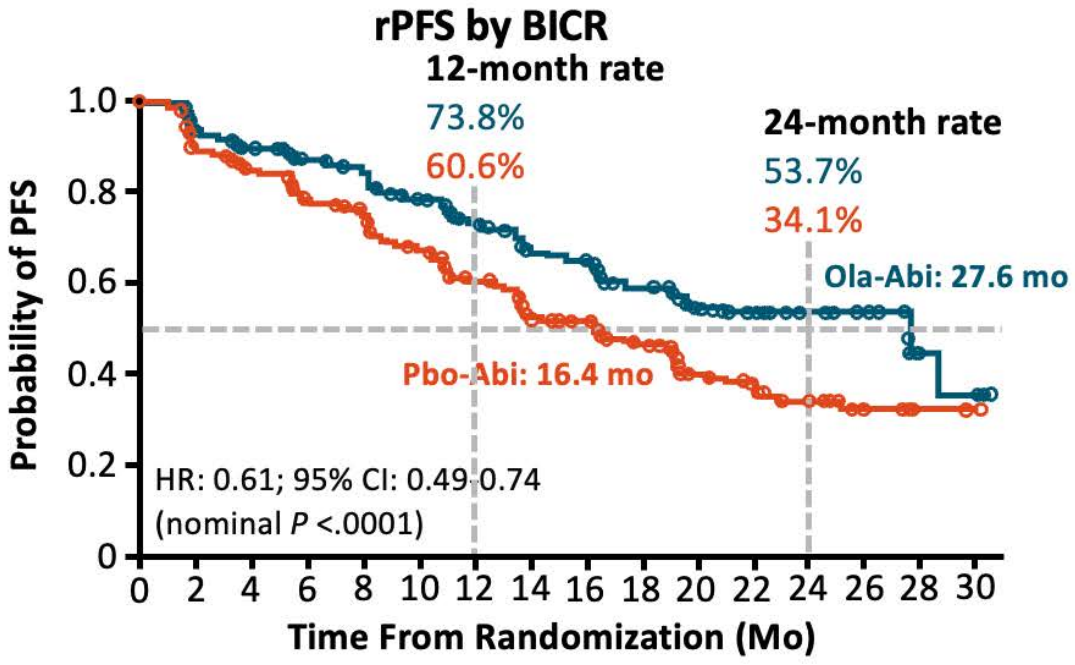
*An additional 108 patients will be randomized 1:1 in China.
†Prednisone/prednisolone (5 mg BID) given with abiraterone.

- **Primary endpoint:** rPFS by investigator
- **Key secondary endpoints:** OS, time to subsequent therapy or death, PFS2, ORR, HRRm prevalence (retrospectively assessed), HRQOL, safety

Saad F, et al. ASCO GU 2022. Abstract 11; Clarke NW, et al. ASCO 2019. Abstract TPS340; ClinicalTrials.gov ID: NCT03732820.

PROpel: Radiologic PFS





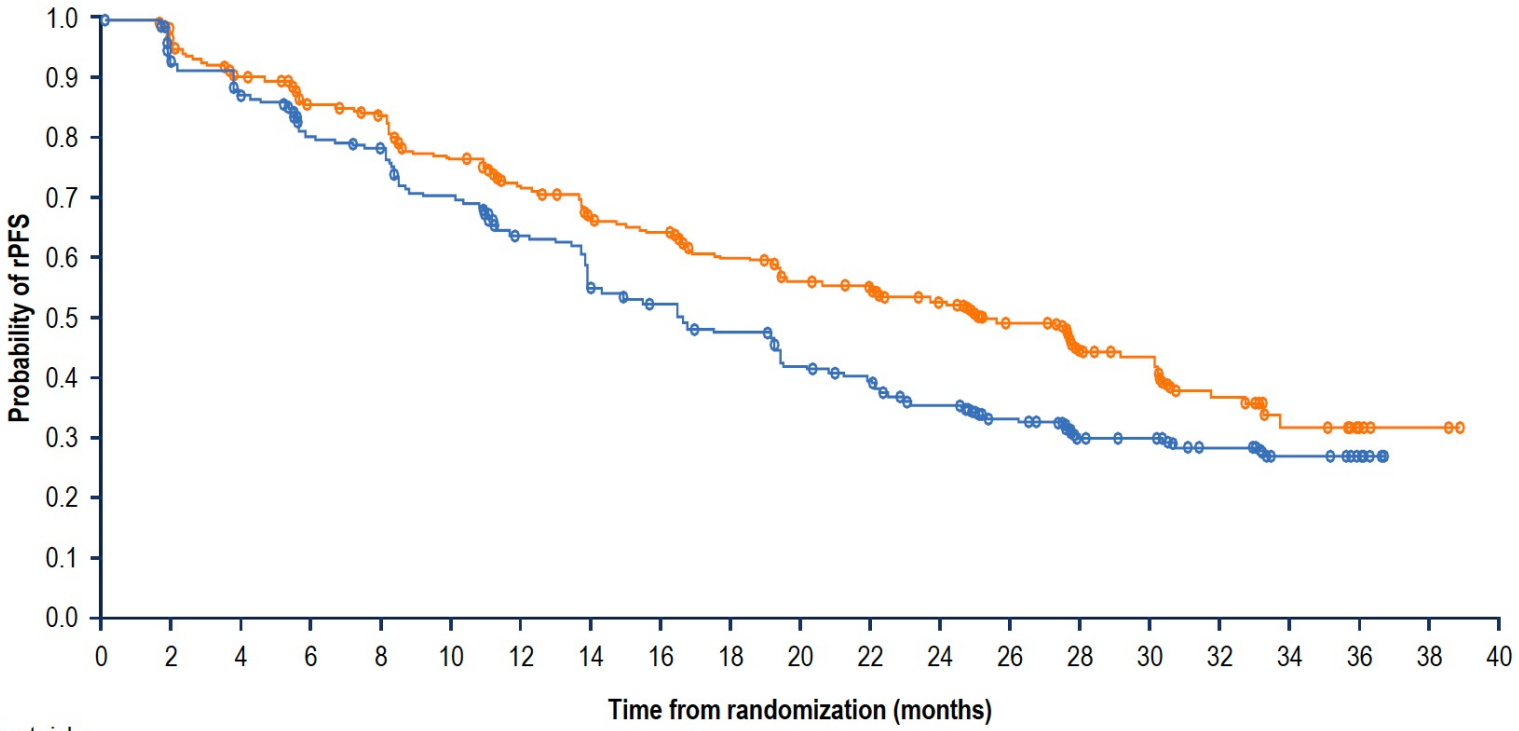
Subgroup	n	Median rPFS		HR (95% CI)
		Olaparib + Abiraterone	Placebo + Abiraterone	
HRRm	226	NR	13.9	0.50 (0.34–0.73)
Non-HRRm	552	24.1	19.0	0.76 (0.60–0.97)

Saad F, et al. ASCO GU 2022. Abstract 11.

*Prespecified 2-sided α = 0.0324.

PROpel: updated rPFS by investigator assessment in the ITT population

At DCO2, rPFS was 8.6 months greater for abiraterone + olaparib versus abiraterone + placebo



Number of patients at risk:

Abiraterone + olaparib	399	367	340	313	301	274	251	228	220	200	184	174	158	110	62	58	33	15	5	3	0
Abiraterone + placebo	397	359	338	306	297	264	232	199	187	169	145	135	117	84	51	48	30	8	3	0	0

	Abiraterone + olaparib (n=399)	Abiraterone + placebo (n=397)
Events, n (%)	199 (49.9)	258 (65.0)
Median rPFS (months)	25.0	16.4
HR (95% CI)	0.67 (0.56–0.81); *P*<0.0001*	

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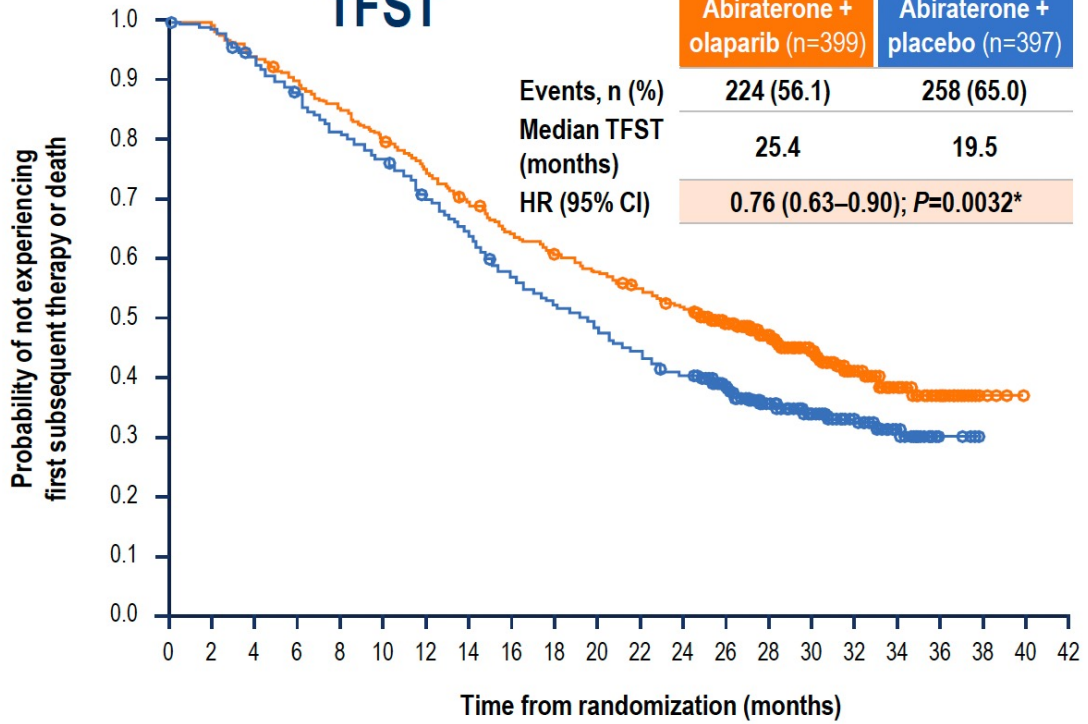
*Nominal

Median duration of follow-up for censored patients was 24.9 months (range 0.03–38.80) in the abiraterone + olaparib arm and 27.4 months (range 0.03–36.76) in the abiraterone + placebo arm

PROpel key secondary endpoints: TFST and PFS2

At DCO2, TFST and PFS2 results supported a trend towards longer-term benefit with abiraterone + olaparib

TFST

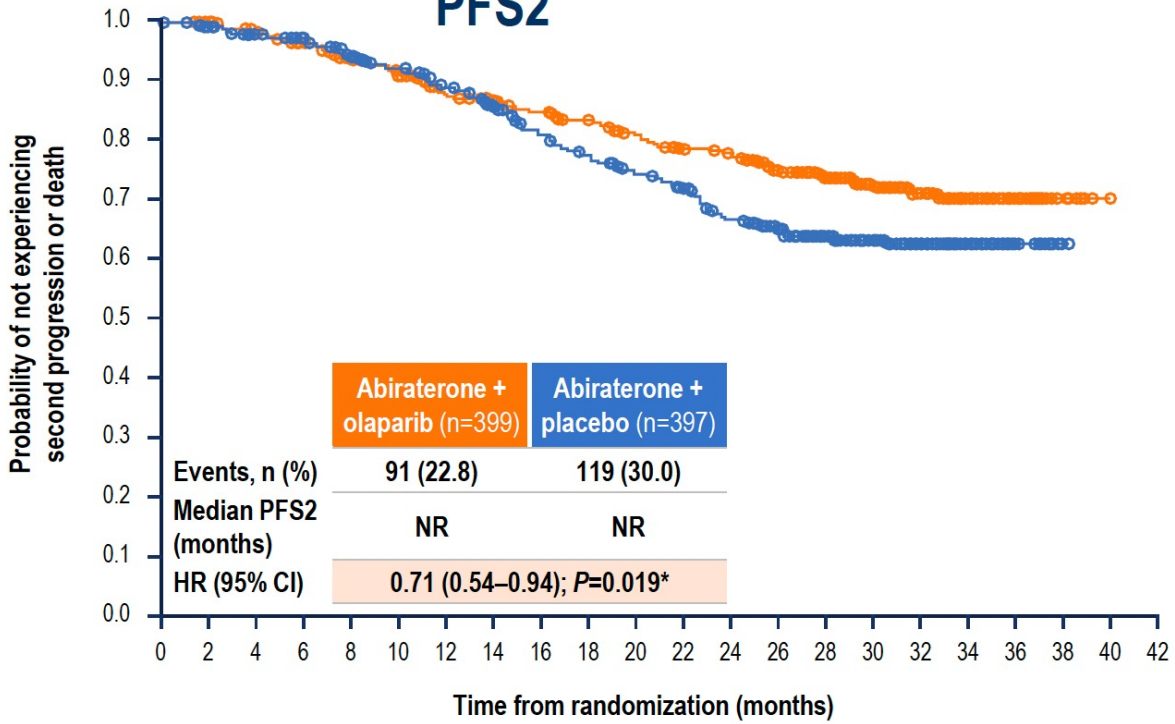


	Abiraterone + olaparib (n=399)	Abiraterone + placebo (n=397)
Events, n (%)	224 (56.1)	258 (65.0)
Median TFST (months)	25.4	19.5
HR (95% CI)	0.76 (0.63–0.90); *P*=0.0032*	

Number of patients at risk:

Abiraterone + olaparib	399	396	374	358	338	317	296	274	252	239	226	213	200	170	132	93	58	36	19	4	1	0
Abiraterone + placebo	397	391	369	345	319	303	273	250	222	203	188	171	156	129	98	66	46	26	6	0	0	0

PFS2



	Abiraterone + olaparib (n=399)	Abiraterone + placebo (n=397)
Events, n (%)	91 (22.8)	119 (30.0)
Median PFS2 (months)	NR	NR
HR (95% CI)	0.71 (0.54–0.94); *P*=0.019*	

Abiraterone + olaparib	399	385	369	349	334	311	289	276	267	259	245	234	230	196	156	113	79	47	22	5	1	0
Abiraterone + placebo	397	380	367	351	338	316	293	271	252	238	225	215	196	162	123	85	62	37	11	1	0	0

First subsequent therapies

- 157 (39.3%) patients in the abiraterone + olaparib arm and 197 (49.6%) in the abiraterone + placebo arm had subsequent therapies
- The most common first subsequent therapies were cytotoxic chemotherapy (n=221) and hormonal therapy (n=103)

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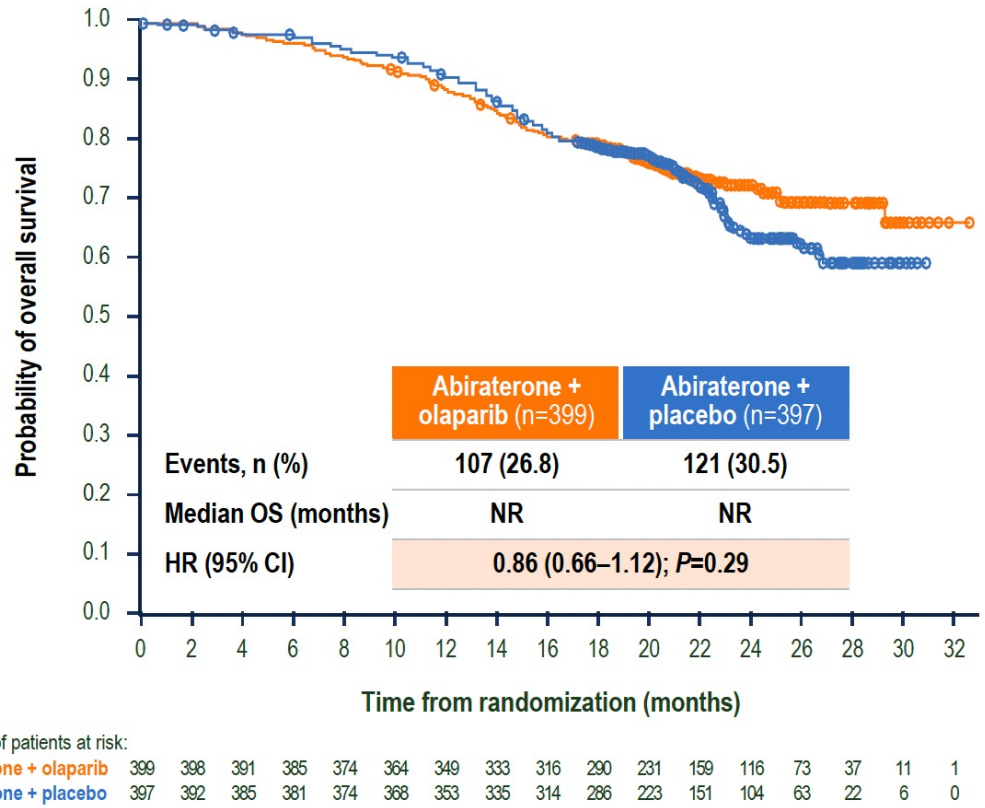
A circle indicates a censored observation
*Nominal
PSF2, time to second progression or death; TSFT, time to first subsequent therapy or death

PROpel key secondary endpoint: OS in the ITT population

At DCO2, there was a continued trend towards improved OS with abiraterone + olaparib, with KM curves showing clear separation between the arms after ~22 months before extensive censoring was observed

Primary analysis (DCO1, 28.6% maturity)

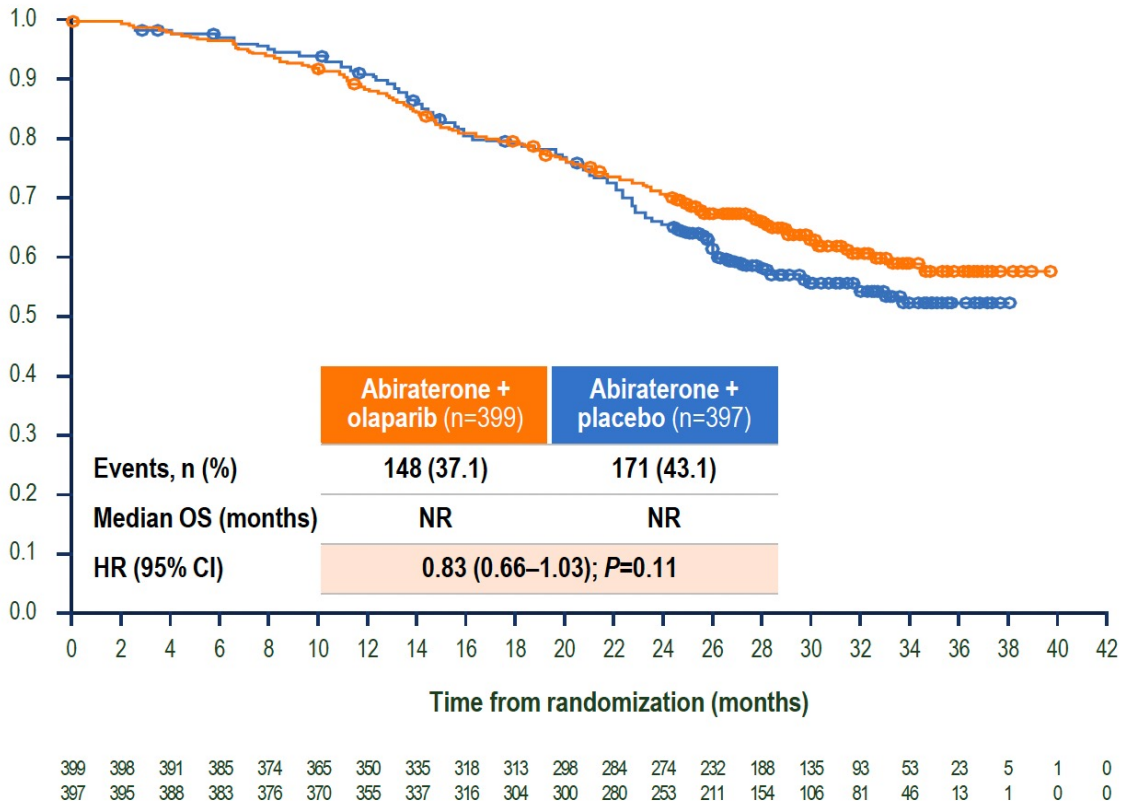


	Abiraterone + olaparib (n=399)	Abiraterone + placebo (n=397)
Events, n (%)	107 (26.8)	121 (30.5)
Median OS (months)	NR	NR
HR (95% CI)	0.86 (0.66–1.12); *P*=0.29	

Number of patients at risk:

Abiraterone + olaparib	399	398	391	385	374	364	349	333	316	290	231	159	116	73	37	11	1
Abiraterone + placebo	397	392	385	381	374	368	353	335	314	286	223	151	104	63	22	6	0

Updated results (DCO2, 40.1% maturity)



	Abiraterone + olaparib (n=399)	Abiraterone + placebo (n=397)
Events, n (%)	148 (37.1)	171 (43.1)
Median OS (months)	NR	NR
HR (95% CI)	0.83 (0.66–1.03); *P*=0.11	

Abiraterone + olaparib	399	398	391	385	374	365	350	335	318	313	298	284	274	232	188	135	93	53	23	5	1	0
Abiraterone + placebo	397	395	388	383	376	370	355	337	316	304	300	280	253	211	154	106	81	46	13	1	0	0

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A circle indicates a censored observation

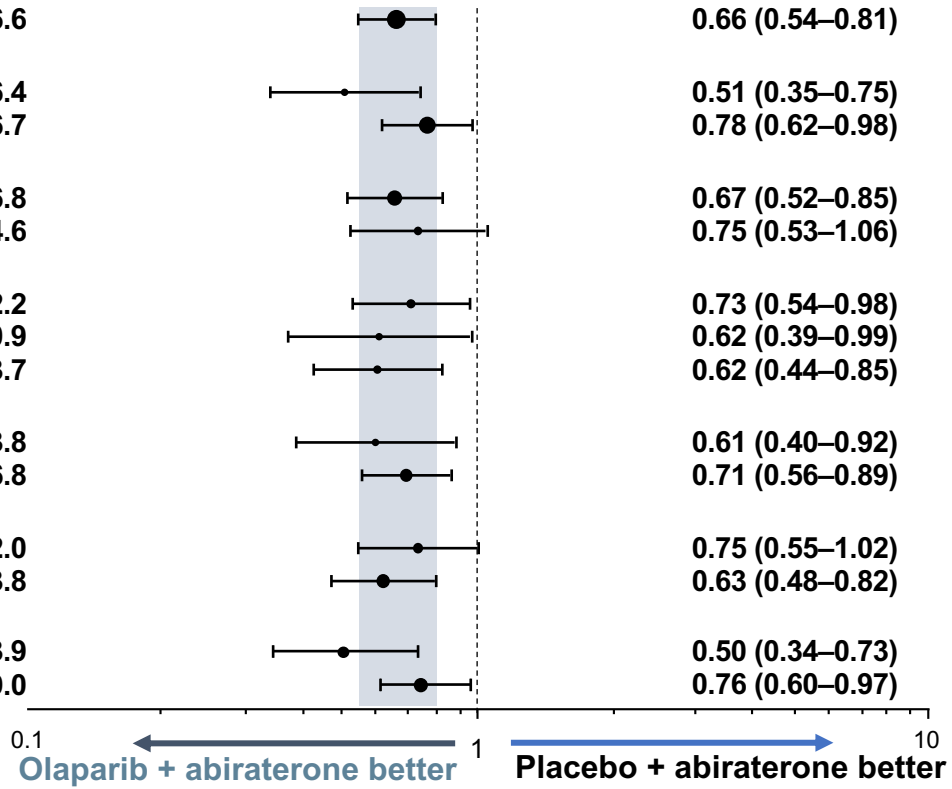
Median duration of follow-up for censored patients at DCO1 was 22.2 months (range 0.03–32.56) in the abiraterone + olaparib arm and 21.8 months (range 0.10–30.88) in the abiraterone + placebo arm.

Median duration of follow-up for censored patients at DCO2 was 30.0 months (range 0.03–40.02) in the abiraterone + olaparib arm and 29.4 months (range 2.89–38.34) in the abiraterone + placebo arm

PROpel: subgroup analysis of rPFS

rPFS benefit observed across all pre-specified subgroups

	Number of patients, n	Median rPFS, months		HR (95% CI)
All patients	796	24.8	16.6	0.66 (0.54–0.81)
Age at randomisation				
<65	227	NR	16.4	0.51 (0.35–0.75)
≥65	569	22.0	16.7	0.78 (0.62–0.98)
ECOG performance status at baseline				
0	558	24.9	16.8	0.67 (0.52–0.85)
1	236	17.5	14.6	0.75 (0.53–1.06)
Site of distant metastases				
Bone only	434	27.6	22.2	0.73 (0.54–0.98)
Visceral	105	13.7	10.9	0.62 (0.39–0.99)
Other	257	20.5	13.7	0.62 (0.44–0.85)
Docetaxel treatment at mHSPC stage				
Yes	189	27.6	13.8	0.61 (0.40–0.92)
No	607	24.8	16.8	0.71 (0.56–0.89)
Baseline PSA				
Below median baseline PSA	396	25.2	22.0	0.75 (0.55–1.02)
Above or equal to median baseline PSA	397	18.5	13.8	0.63 (0.48–0.82)
HRRm status[a]				
HRRm	226	NR	13.9	0.50 (0.34–0.73)
Non-HRRm	552	24.1	19.0	0.76 (0.60–0.97)



Global interaction test not significant at 10% level

Global interaction test not significant at 10% level. [a]The HRRm status of patients in PROpel was determined retrospectively using results from tumour tissue and plasma ctDNA HRRm tests. Patients were classified as HRRm if (one or more) HRR gene mutation was detected by either test; patients were classified as non-HRRm patients if no HRR gene mutation was detected by either test; patients were classified as unknown HRRm if no valid HRR test result from either test was achieved. 18 patients did not have a valid HRR testing result from either a tumour tissue or ctDNA test and were excluded from the subgroup analysis. This subgroup analysis is post hoc exploratory analysis.

CI, confidence interval; ctDNA, circulating tumour DNA; ECOG, Eastern Cooperative Oncology Group; HR, hazard ratio; HRR(m), homologous recombination (mutation); mHSPC, metastatic hormone sensitive prostate cancer; NR, not reached; PSA, prostate specific antigen; rPFS, radiographic progression-free survival

Saad F, et al. ASCO GU 2022. Abstract 11.

Adverse Events and HRQOL

Safety Outcome, n (%)	Olaparib + Abiraterone (n = 399)	Placebo + Abiraterone (n = 397)
Any AE	387 (97.2)	376 (94.9)
Any grade ≥3 AE	188 (47.2)	152 (38.4)
Death due to an AE	16 (4.0)	17 (4.3)
Any AE leading to		
• Dose interruption of olaparib/placebo	178 (44.7)	100 (25.3)
• Dose reduction of olaparib/placebo	80 (20.1)	22 (5.6)
• D/c of olaparib/placebo	55 (13.8)	31 (7.8)
• D/c of abiraterone	34 (8.5)	35 (8.8)

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

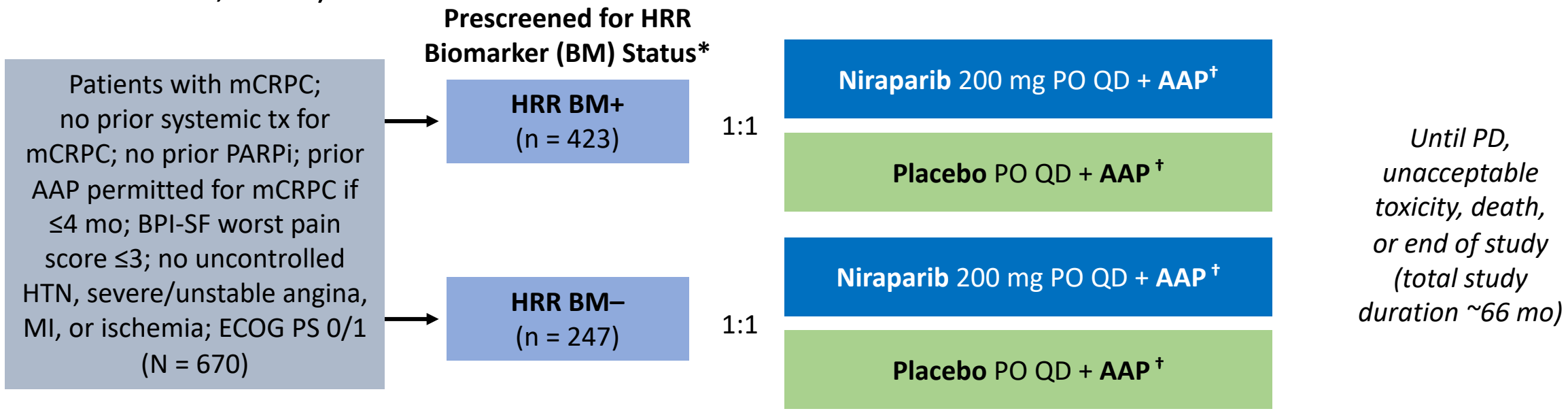
*Standardized MedDRA query (SMQ).

- Incidence of new primary malignancies and pneumonitis balanced between arms
- No cases reported of MDS/AML
- HRQOL per FACT-P was comparable between arms over time

Saad F, et al. ASCO GU 2022. Abstract 11.

MAGNITUDE: First-Line Niraparib + Abiraterone Acetate and Prednisone in mCRPC

- International, randomized, double-blind phase III trial (cutoff for final rPFS analysis: October 8, 2021)

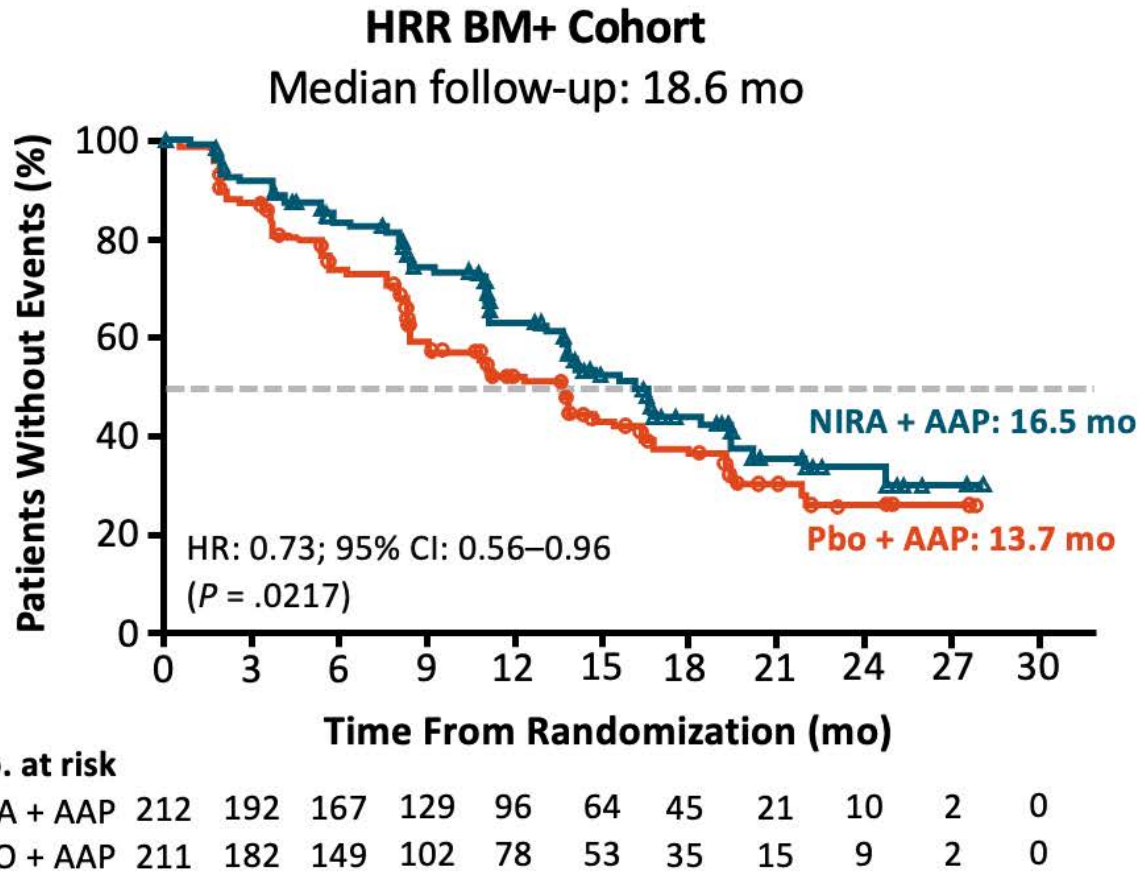


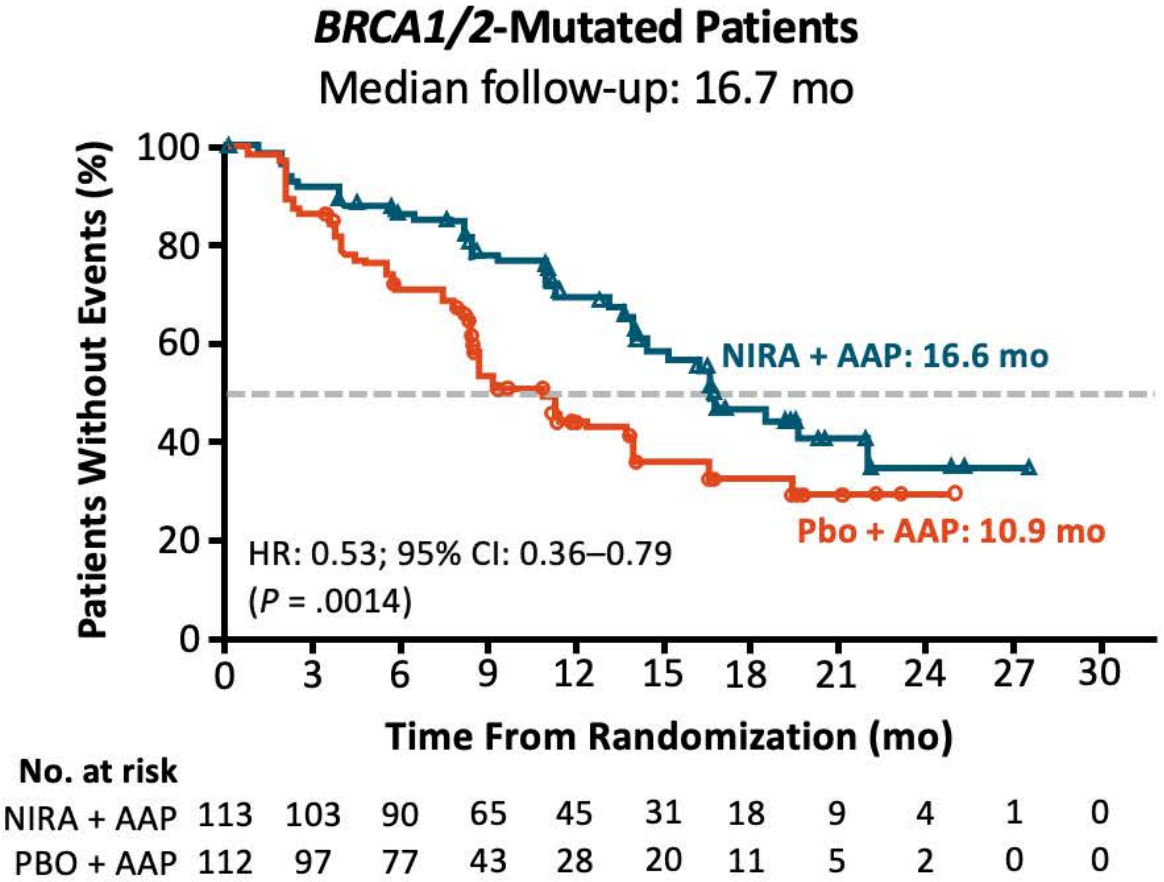
*HRR BM+ per tissue and/or plasma assays for *ATM, BRCA1, BRCA2, BRIP1, CDK12, CHEK2, FANCA, HDAC2, PALB2*;
†AAP: abiraterone acetate 1000 mg PO QD + prednisone 10 mg PO QD.

- **Primary endpoint:** radiographic PFS by central review
- **Secondary endpoints:** OS, time to symptomatic progression, time to cytotoxic chemotherapy

Chi KN, et al. ASCO GU 2022. Abstract 12; Chi KN, et al. ASCO 2020. Abstract TPS5588. ClinicalTrials.gov ID: NCT03748641.

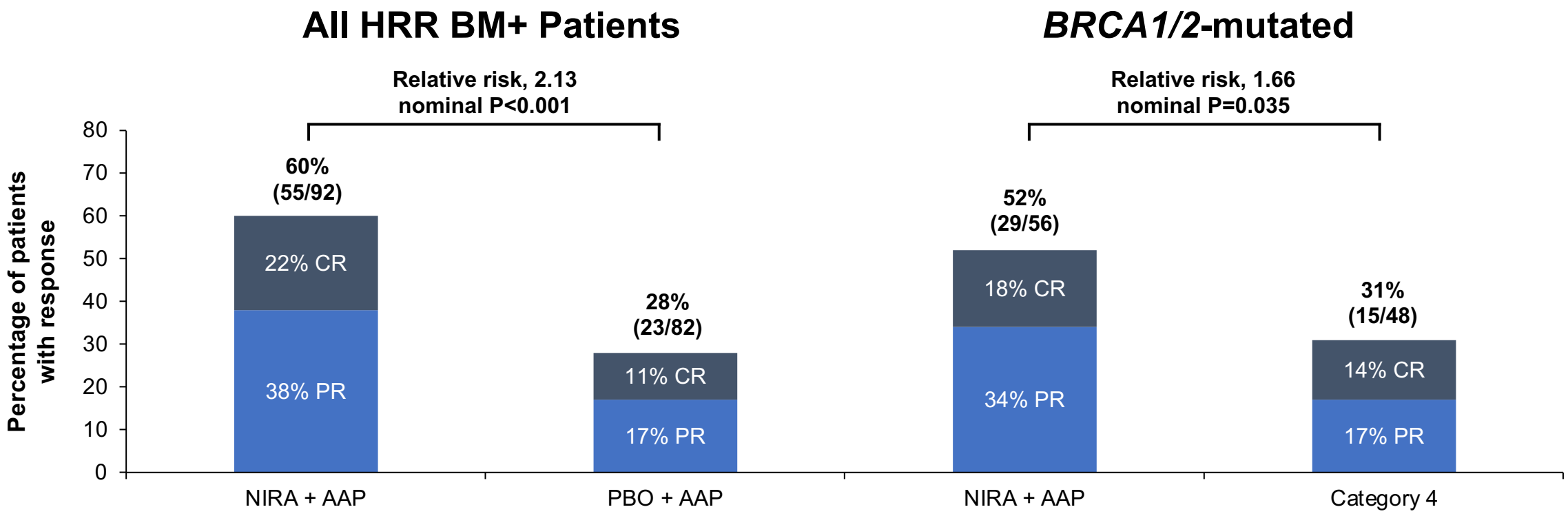
MAGNITUDE: Radiologic PFS by Central Review (primary endpoint)





Chi KN, et al. ASCO GU 2022. Abstract 12.

MAGNITUDE: NIRA + AAP Improves Overall Response Rate Consistently Across Gene Alterations



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

Note: Relative risk >1 favours niraparib and AAP treatment. Percent of responder is based on the number of subjects with measurable disease at baseline
AAP, abiraterone acetate plus prednisone; CR, complete response; HRR, homologous recombination repair, NIRA, niraparib; PBO, placebo; PR, partial response

Chi K, et al. J Clin Oncol. 2022;40 (suppl 6; abstr 12) (ASCO GU 2022 oral presentation

Treatment-Emergent AEs in HRR BM+ Cohort

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

- AEs most frequently leading to dose reduction in niraparib arm
  - Anemia: 13.2%
  - Thrombocytopenia: 2.8%
- Median relative dose intensity in niraparib arm: 99%

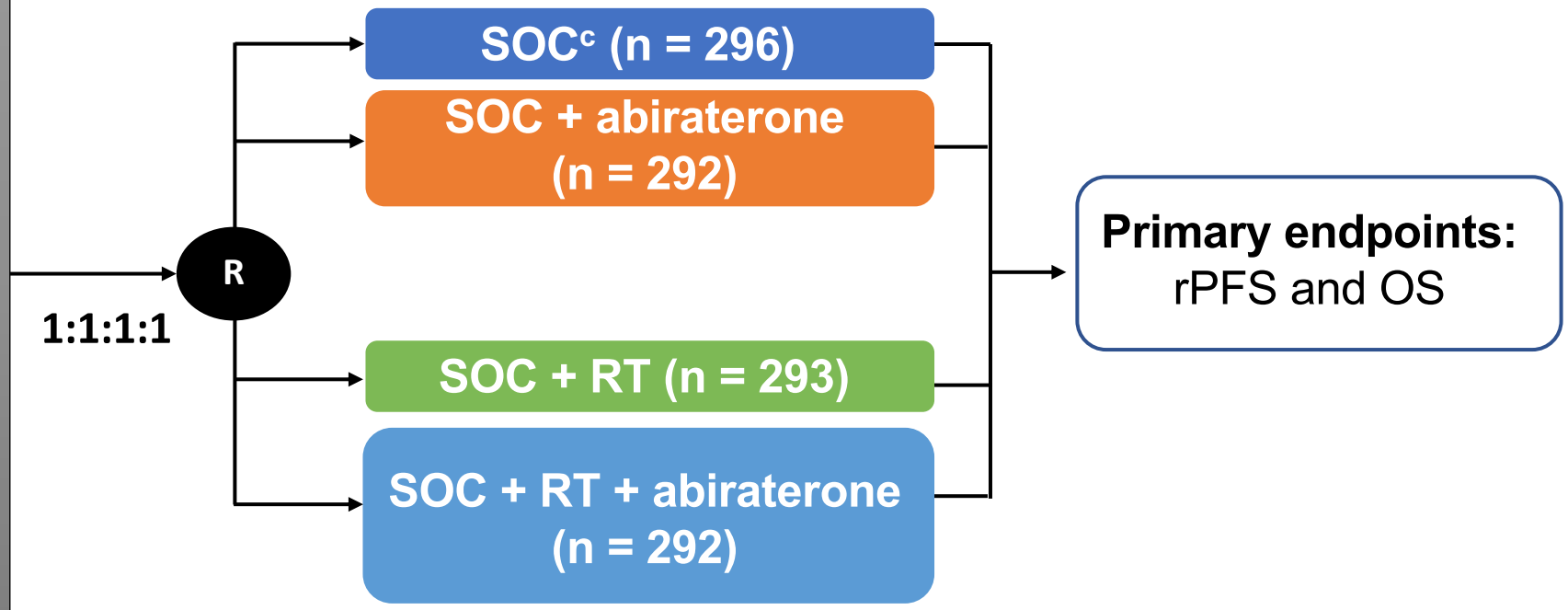
Chi KN, et al. ASCO GU 2022. Abstract 12.

mHSPC: Data on Triplet Therapy

PEACE-1: Abiraterone + Prednisone in Men With De Novo mCSPC

Key Eligibility Criteria
- De novo mCSPC
- Distant metastatic disease
- On-study requirement of continuous ADT
- ADT ≤3 months permitted

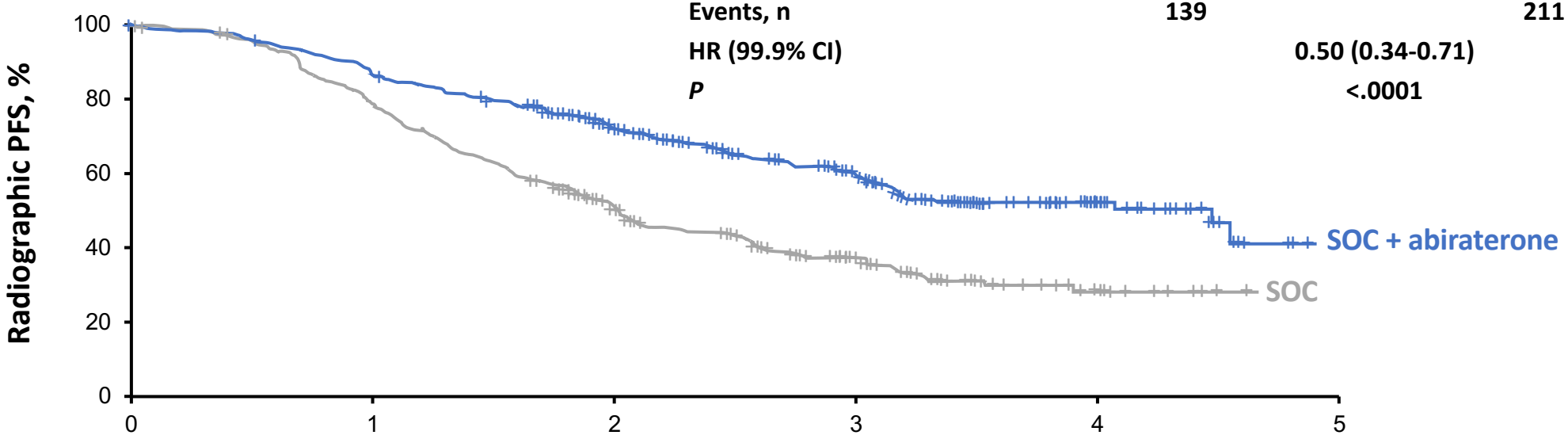
Stratification Factors
- ECOG PS 0 vs 1-2
- Site of metastases (LN vs bone vs viscera)
- Castration type (orchiectomy vs GnRH agonist vs GnRH antagonist)
- Docetaxel (yes vs no)



Fizazi K et al. *J Clin Oncol*. 2021;39(suppl 15):5000. Fizazi K. ESMO 2021. Abstract LBA5_PR.

PEACE-1: Improved rPFS With Abiraterone in the ADT + Docetaxel (+/- RT) Population

	SOC + Abiraterone (n = 355)	SOC (n = 355)
Median, y (IQR)	4.46 (1.9-NR)	2.03 (1.09-NR)
Events, n	139	211
HR (99.9% CI)	0.50 (0.34-0.71)	
P	<.0001	

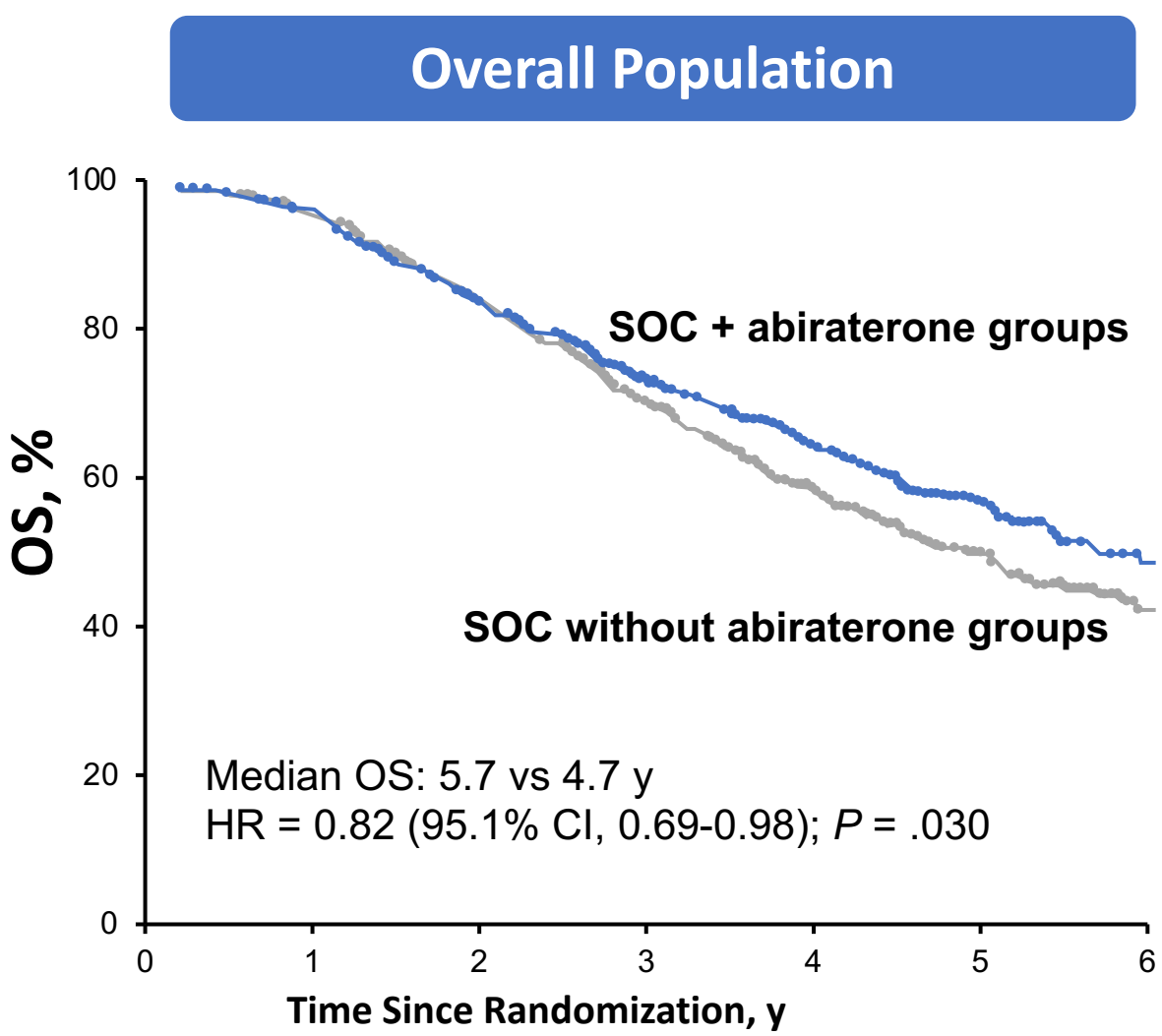


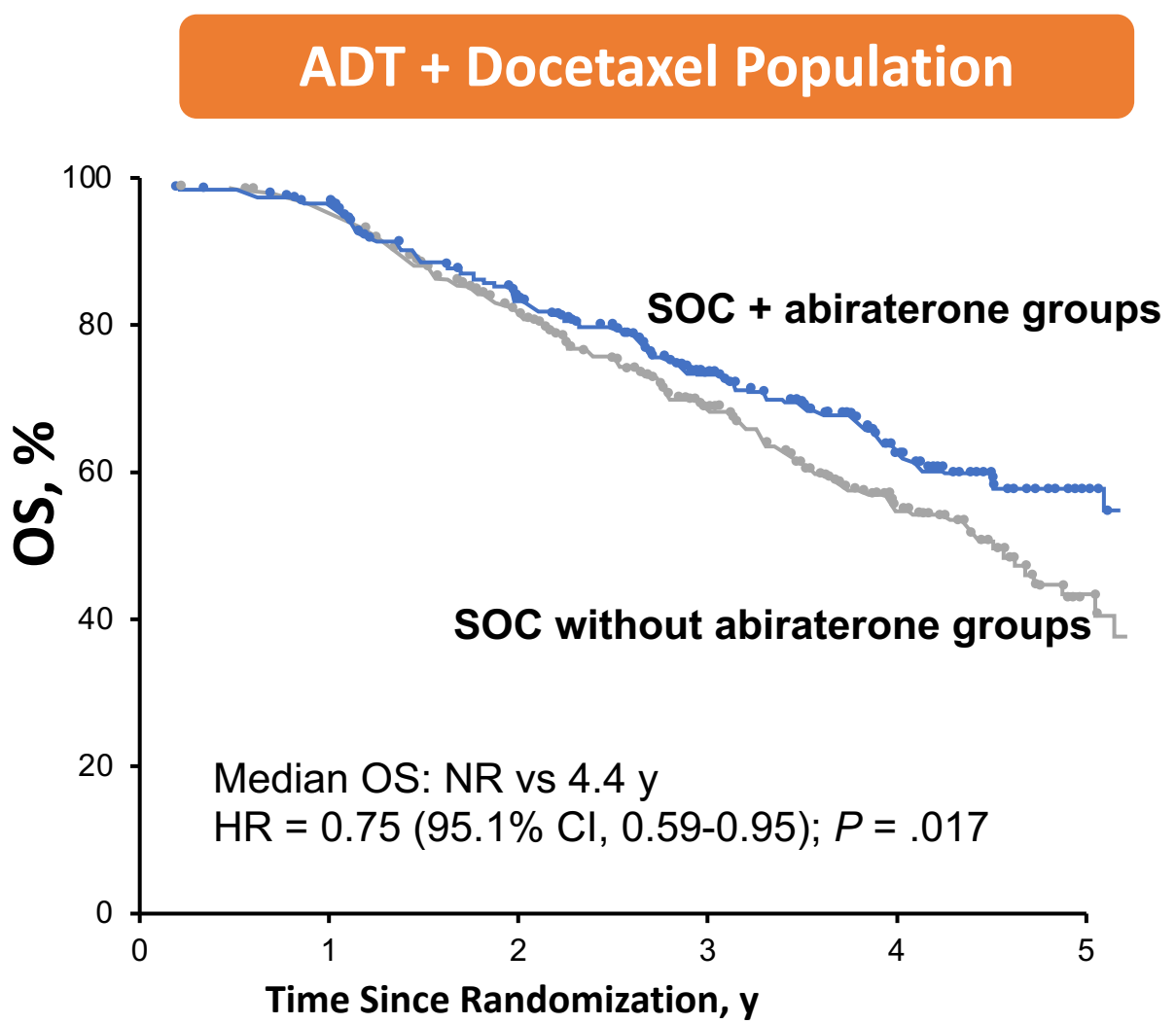
No	355	274	137	61	16	0
Yes	355	303	200	105	35	0

Adding abiraterone to ADT + docetaxel significantly improved rPFS

Fizazi K et al. *Lancet*. 2022;399:1695-1707.

Phase 3 PEACE-1: Improved OS in Men With De Novo mCSPC

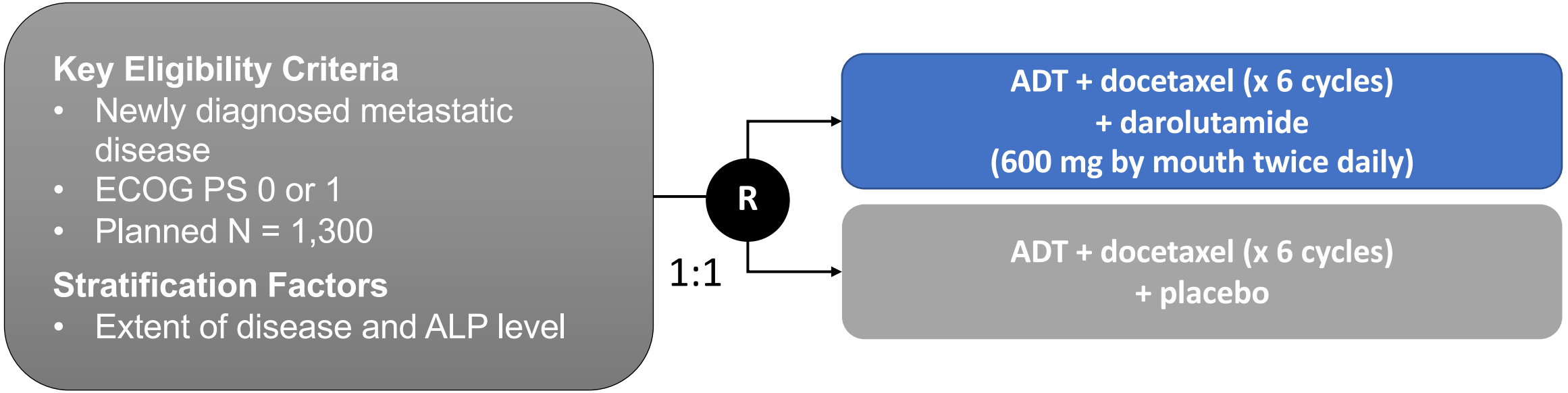




Fizazi K et al. *Lancet*. 2022;399:1695-1707.

ARASENS: Phase 3 Trial

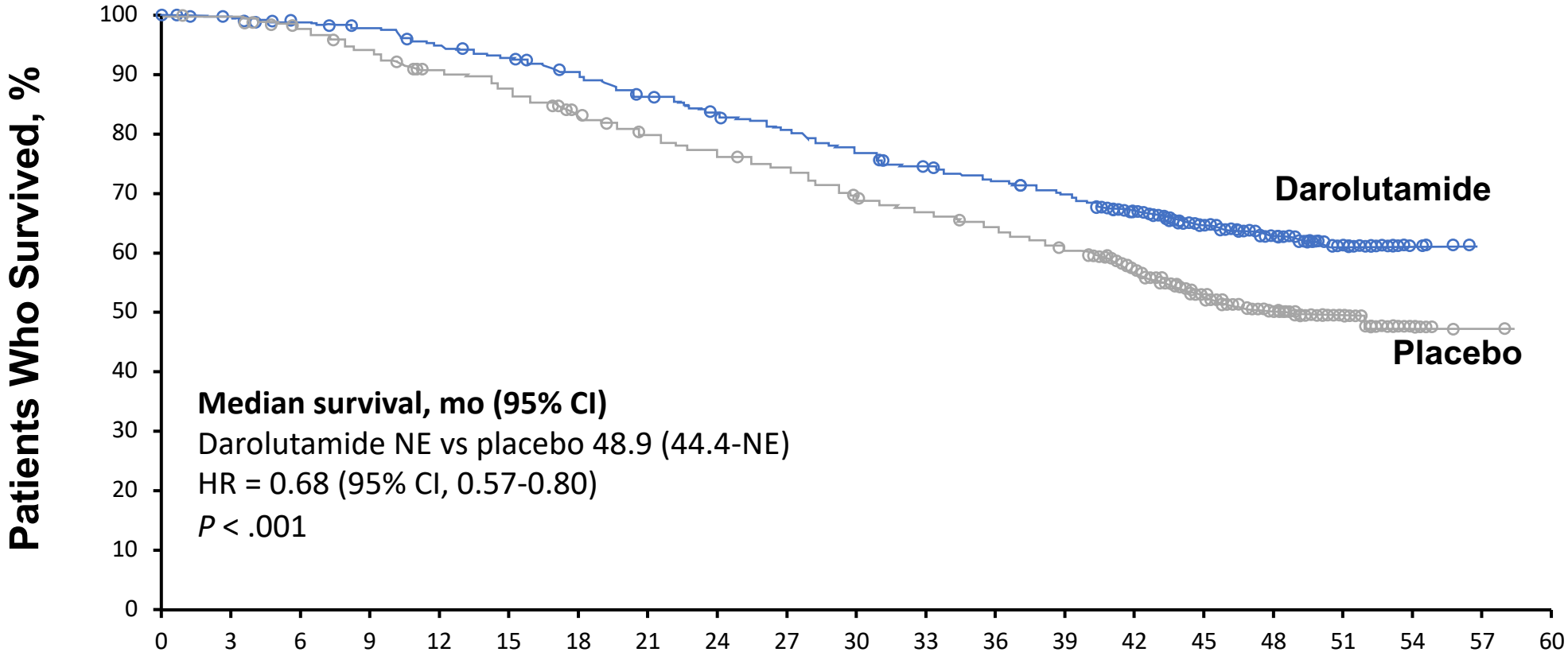
International trial conducted at >300 sites in 23 countries



- **Primary endpoint:** OS
- **Key Secondary endpoints:** time to mCRPC, time to initiation of subsequent anticancer therapy, time to SSE-free survival, time to first SSE, time to pain progression

https://clinicaltrials.gov/ct2/show/NCT02799602. Smith MR et al. ASCO GU 2022. Abstract 13. Smith MR et al. *N Engl J Med*. 2022;386:1132-1142.

ARASENS: Overall Survival

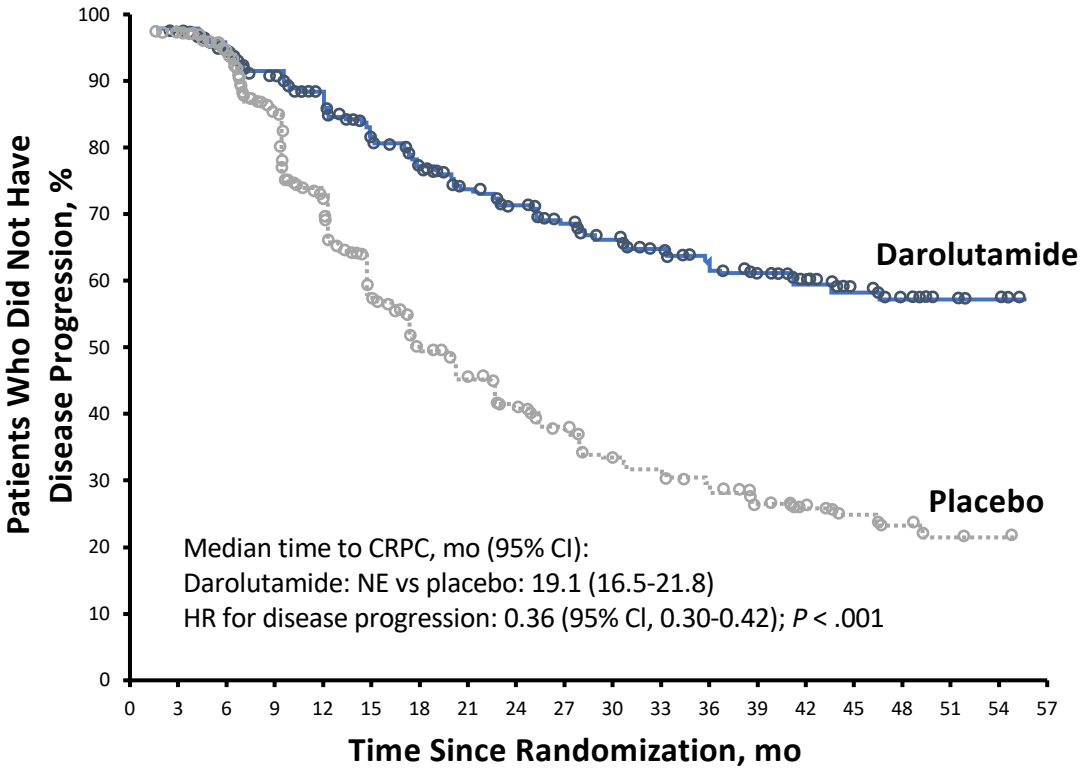


No. at Risk																				
Darolutamide	651	645	637	627	608	593	570	548	525	509	486	468	452	436	402	267	139	56	9	0	0
Placebo	654	646	630	607	580	565	535	510	488	470	441	424	402	383	340	218	107	37	6	1	0

Smith MR et al. *N Engl J Med*. 2022;386:1132-1142.

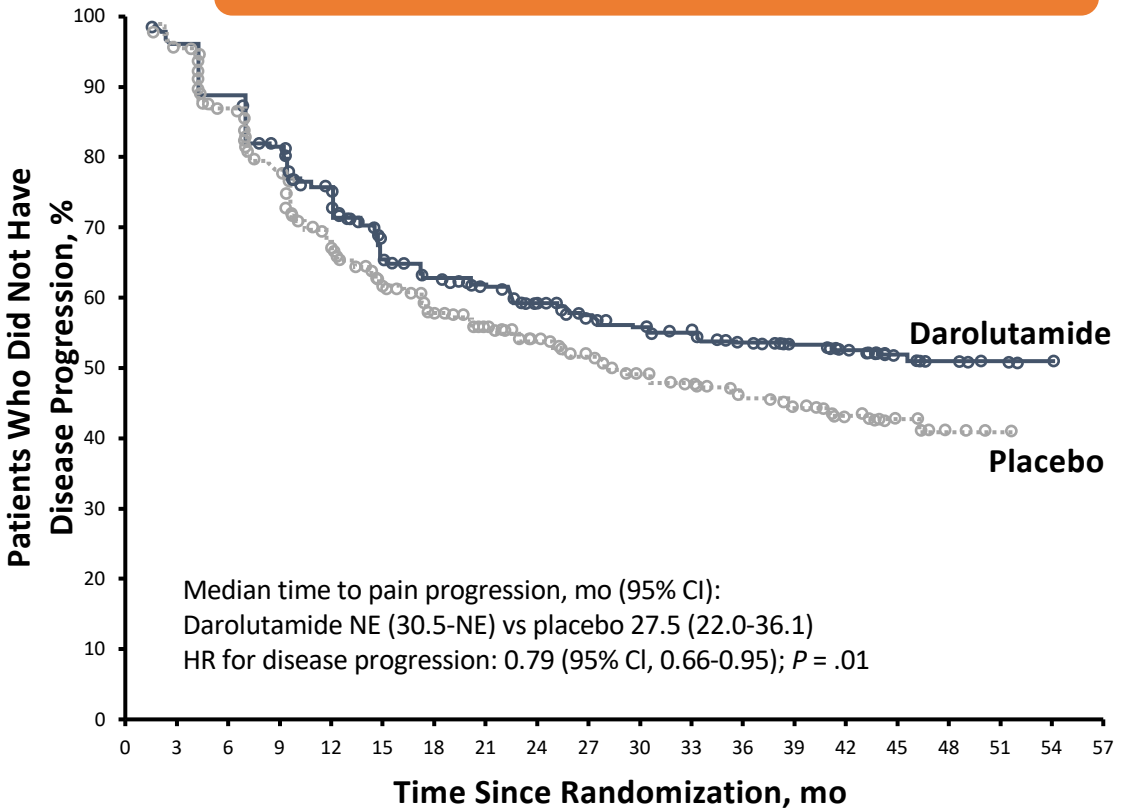
ARASENS: Key Secondary Endpoints

Time to CRPC



No. at Risk																				
Darolutamide	651	616	567	537	496	465	433	401	380	358	340	325	308	292	211	132	54	18	5	0
Placebo	654	613	533	425	348	289	242	215	185	165	143	134	120	105	79	38	14	4	1	0

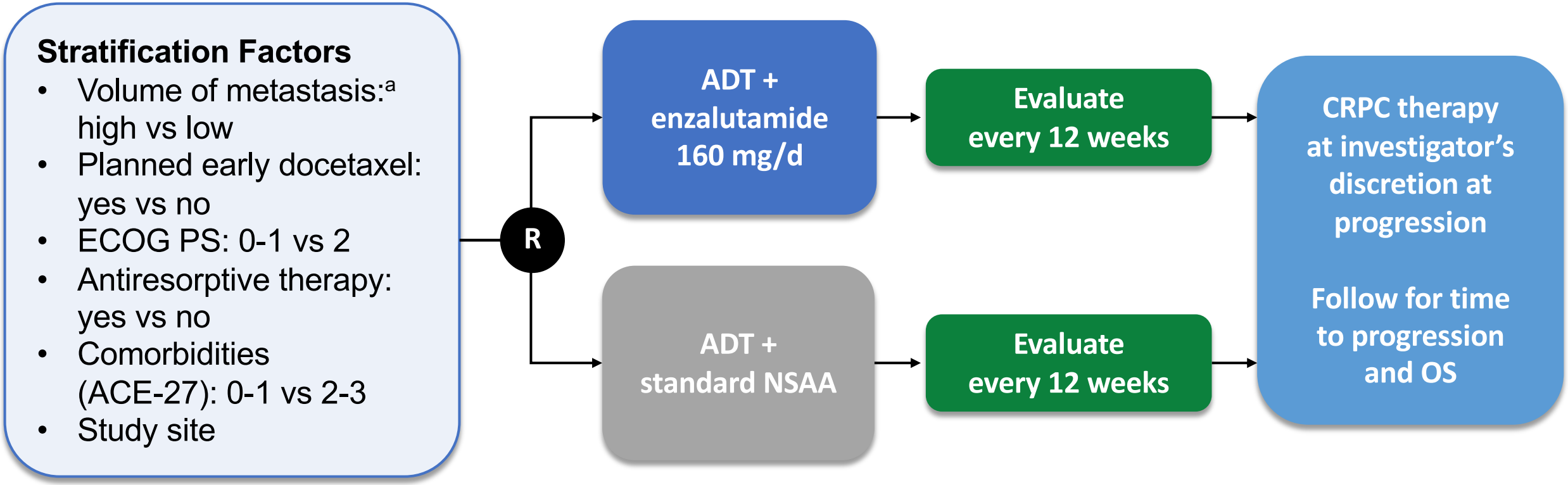
Time to Pain Progression



No. at Risk																				
Darolutamide	651	447	401	363	327	284	265	249	228	211	202	189	175	159	106	67	31	6	1	0
Placebo	654	442	395	332	288	255	221	188	160	134	119	107	93	86	62	35	8	1	0	0

Smith MR et al. *N Engl J Med.* 2022;386:1132-1142.

ENZAMET: SOC ± Enzalutamide in mHSPC



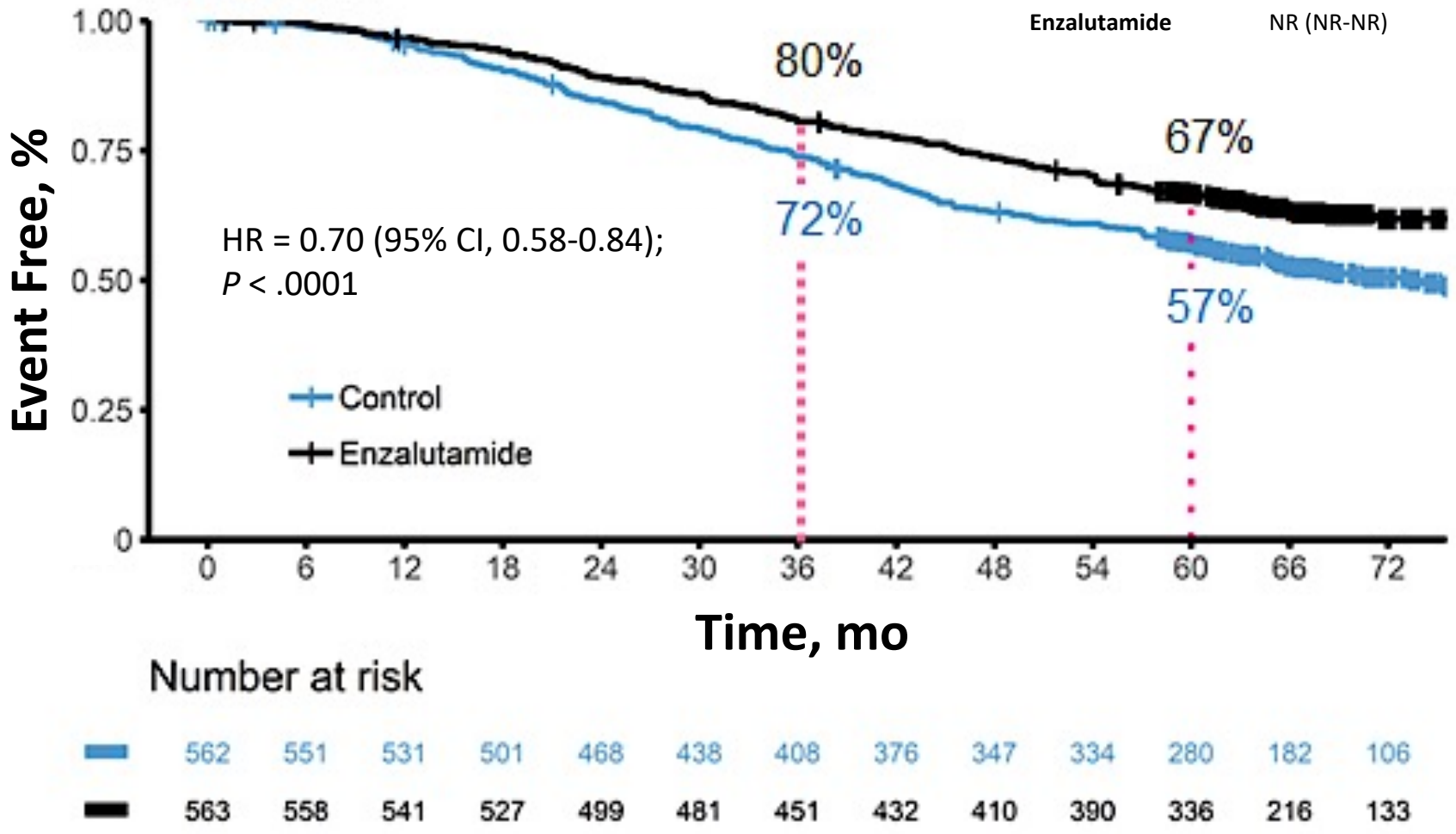
Primary endpoint: OS

- Prior to randomization, testosterone suppression up to 12 weeks and two cycles of docetaxel were allowed
- Intermittent ADT and cyproterone were not allowed
- NSAA: bicalutamide, nilutamide, flutamide

Davis ID et al. New Engl J Medicine. 2019.

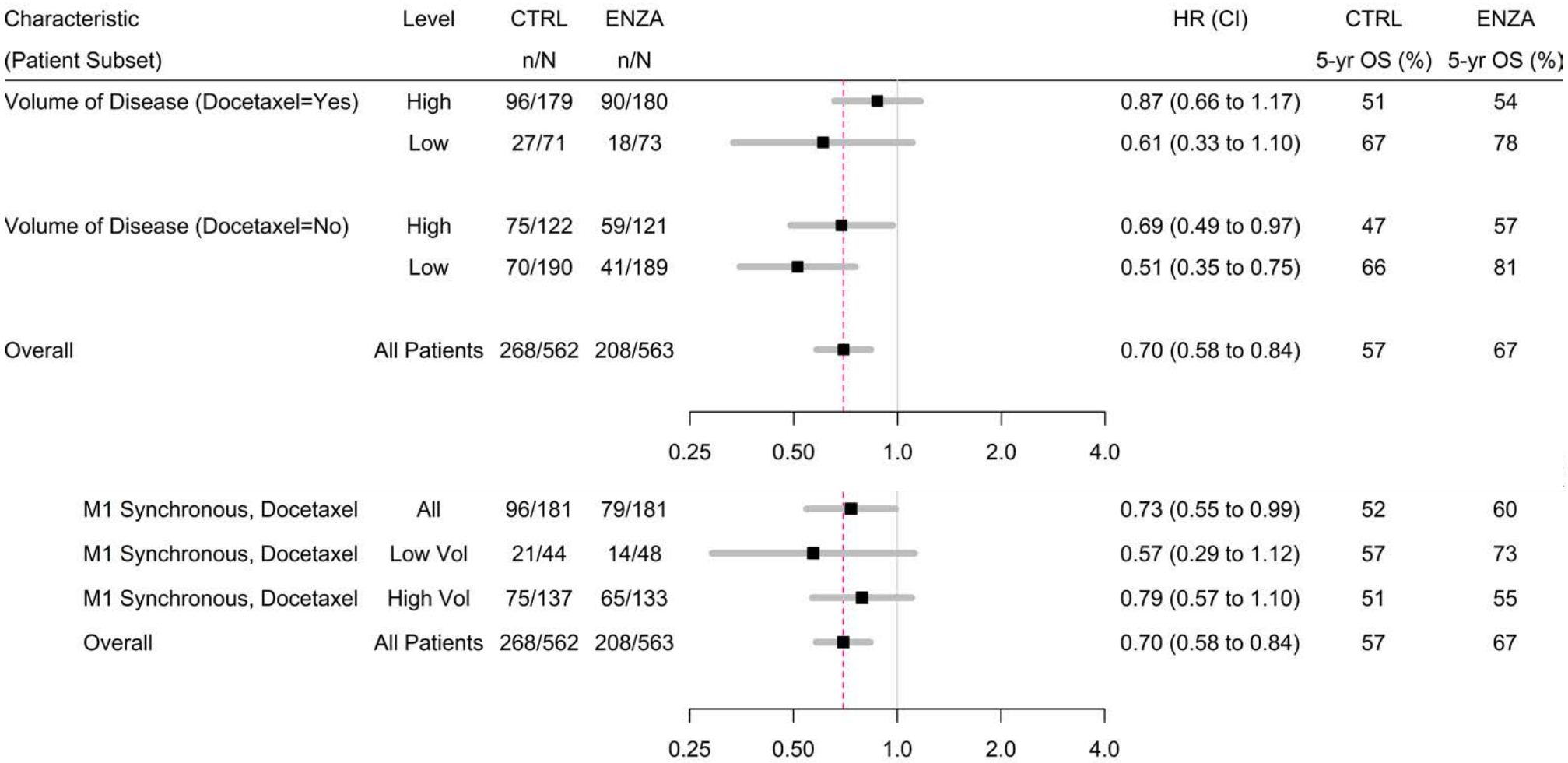
ENZAMET: OS Update

	Median OS, mo (95% CI)	5-Year Survival, %	Median Follow-Up, mo
Control (NSAA)	73.2 (64.7-NR)	57	68
Enzalutamide	NR (NR-NR)	67	



Davis ID et al. ASCO 2022, Abstract LBA5004

ENZAMET: Overall survival



Davis ID et al. ASCO 2022, Abstract LBA5004

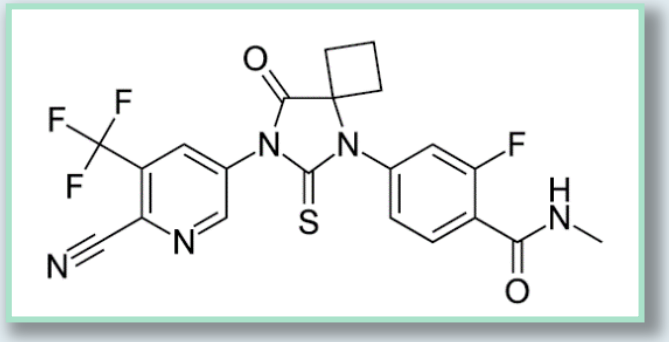
Conclusions

- PARPi combinations suggest potential synergy between PARPi and AR targeted treatment
  - Overall survival data not yet mature
  - Ongoing studies will demonstrate whether benefit is confined to patients with HRR mutations or extends to others

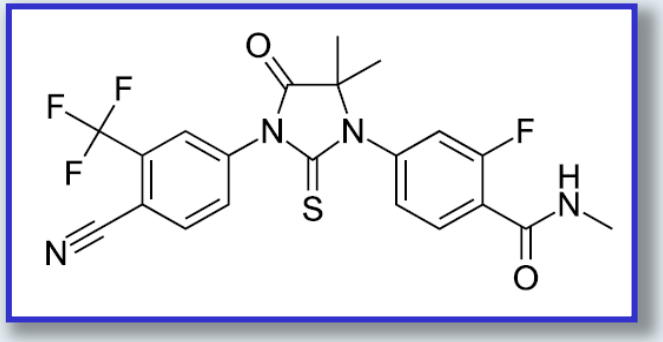
- Triplet therapy studies suggest that the addition of darolutamide or abiraterone to ADT and docetaxel is associated with improved overall survival

Next-Generation Androgen Receptor Inhibitors

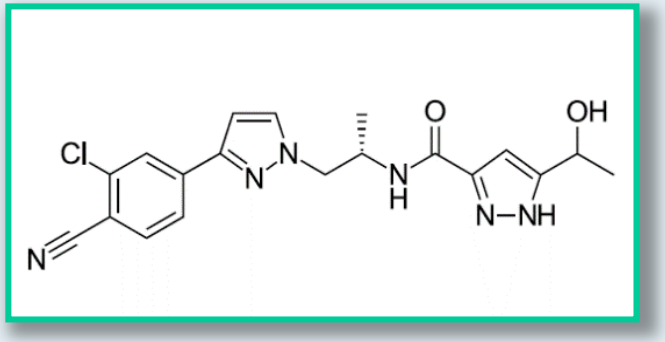
Apalutamide



Enzalutamide



Darolutamide



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

Zurth C et al. Genitourinary Cancers Symposium 2018;Abstract 345; Sandmann S et al. Genitourinary Cancers Symposium 2019;Abstract 156.

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‡*

ESMO 2022;Abstract LBA62.

First combined analysis of metastatic patients starting androgen deprivation therapy and randomised in the abiraterone acetate and prednisolone (AAP) or enzalutamide (ENZ) + AAP Phase III trials from the STAMPEDE platform protocol

Gerhardt Attard, Laura Murphy, Noel Clarke, William Cross, Silke Gillessen, Claire Amos, Chris Brawley, Rob Jones, Carmel Pezaro, Zafar Malik, Amir Montazeri, Robin Millman, Adrian Cook, Duncan Gilbert, Ruth Langley, Chris Parker, Matthew Sydes, Louise Brown, 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

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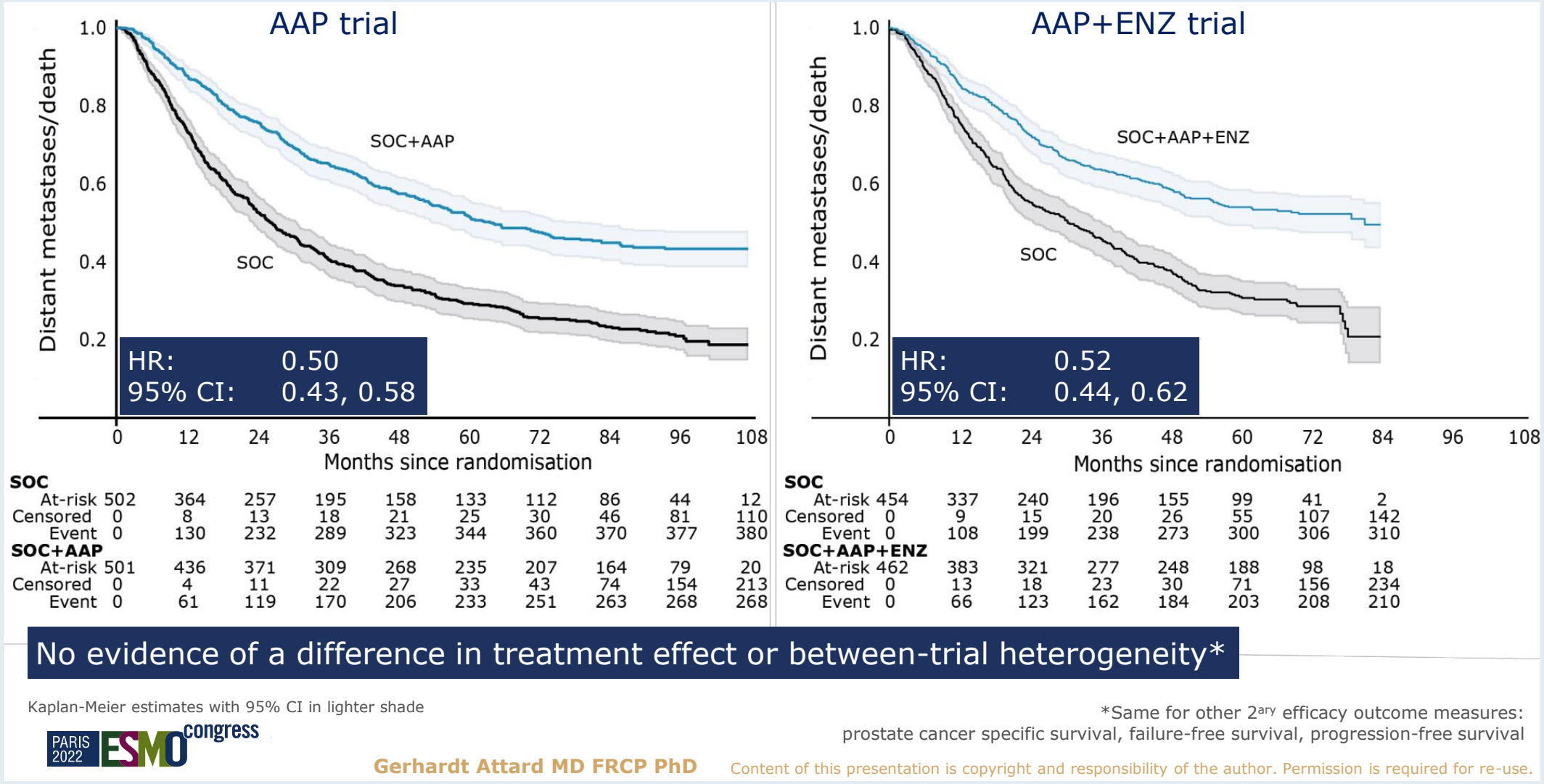
RTP RESEARCH TO PRACTICE

STAMPEDE: Metastatic Progression-Free Survival with AAP or AAP + ENZ for Metastatic Hormone-Sensitive Prostate Cancer



No evidence of a difference in treatment effect or between-trial heterogeneity*

Kaplan-Meier estimates with 95% CI in lighter shade

*Same for other 2ary efficacy outcome measures:
prostate cancer specific survival, failure-free survival, progression-free survival

PARIS 2022 ESMO congress

Gerhardt Attard MD FRCP PhD

RTP RESEARCH TO PRACTICE

Attard G et al. ESMO 2022;Abstract LBA62.

FDA Approves Darolutamide for Metastatic Hormone-Sensitive Prostate Cancer

Press Release: August 5, 2022

"The FDA approved darolutamide in combination with docetaxel chemotherapy for patients with metastatic hormone-sensitive prostate cancer (mHSPC).

The approval is based on the results of a large Phase 3 clinical trial called ARASENS. This trial compared outcomes among 1300 patients who received docetaxel + standard ADT + darolutamide vs patients who received docetaxel + standard ADT + placebo. 86% of the patients were newly diagnosed with prostate cancer that had metastasized to the bones or other organs.

Patients treated with the addition of darolutamide were 32% less likely to die during the study follow-up period compared to patients treated with docetaxel + ADT alone. These patients also had improved time to castration resistance (when the PSA increases and disease worsens, despite hormone therapy), time to pain progression, time to symptomatic skeletal related events (ie, bone fractures, needing radiation to the bones, etc), and time to next cancer therapy. Importantly, these improved outcomes of triplet therapy intensification were associated with only a modest increase in adverse events."

https://www.pcf.org/c/breaking-news-fda-approves-darolutamide-for-metastatic-hormone-sensitive-prostate-cancer/

RTP RESEARCH TO PRACTICE

ASCO Genitourinary Cancers Symposium 2022;Abstract 13.

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

N Engl J Med 2022;386(12):1132-42.

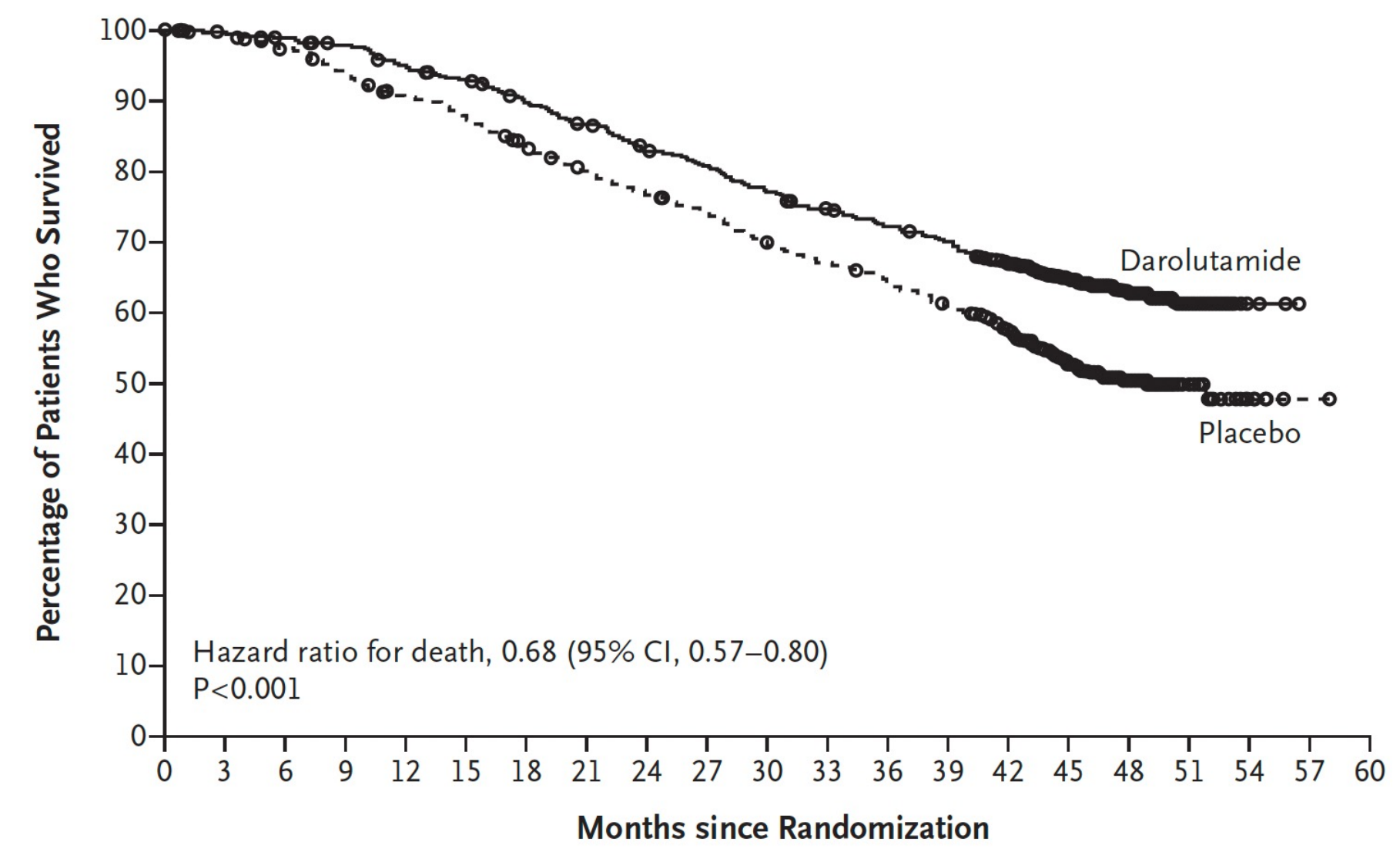
ORIGINAL ARTICLE

Darolutamide and Survival in Metastatic, Hormone-Sensitive Prostate Cancer

Matthew R. Smith, M.D., Ph.D., Maha Hussain, M.D., Fred Saad, M.D., Karim Fizazi, M.D., Ph.D., Cora N. Sternberg, M.D., E. David Crawford, M.D., Evgeny Kopyltsov, M.D., Chandler H. Park, M.D., Boris Alekseev, M.D., Álvaro Montesa-Pino, M.D., Dingwei Ye, M.D., Francis Parnis, M.B., B.S., Felipe Cruz, M.D., Teuvo L.J. Tammela, M.D., Ph.D., Hiroyoshi Suzuki, M.D., Ph.D., Tapio Utriainen, M.D., Cheng Fu, M.D., Motohide Uemura, M.D., Ph.D., María J. Méndez-Vidal, M.D., Benjamin L. Maughan, M.D., Pharm.D., Heikki Joensuu, M.D., Silke Thiele, M.D., Rui Li, M.S., Iris Kuss, M.D., and Bertrand Tombal, M.D., Ph.D., for the ARASENS Trial Investigators*

RTP RESEARCH TO PRACTICE

ARASENS: Overall Survival (Primary Endpoint)



Smith MR et al. *N Engl J Med* 2022;386(12):1132-42.

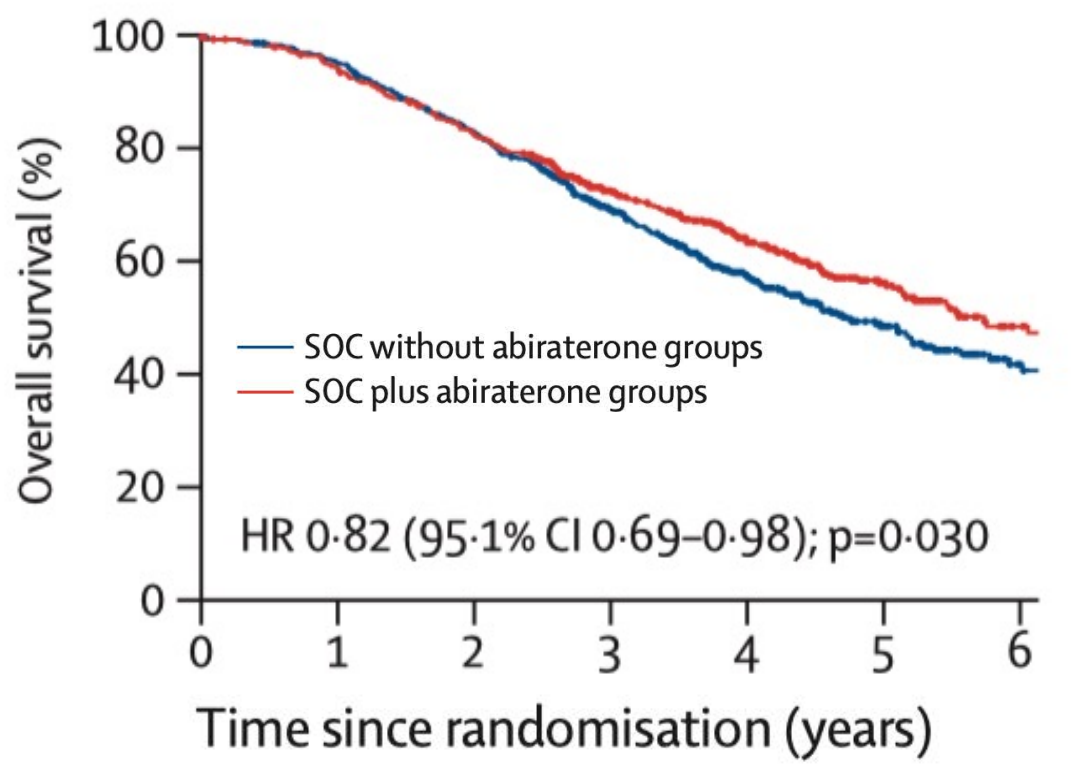
Lancet 2022 April;399(10336):1695-707.

Abiraterone plus prednisone added to androgen deprivation therapy and docetaxel in de novo metastatic castration-sensitive prostate cancer (PEACE-1): a multicentre, open-label, randomised, phase 3 study with a 2 × 2 factorial design

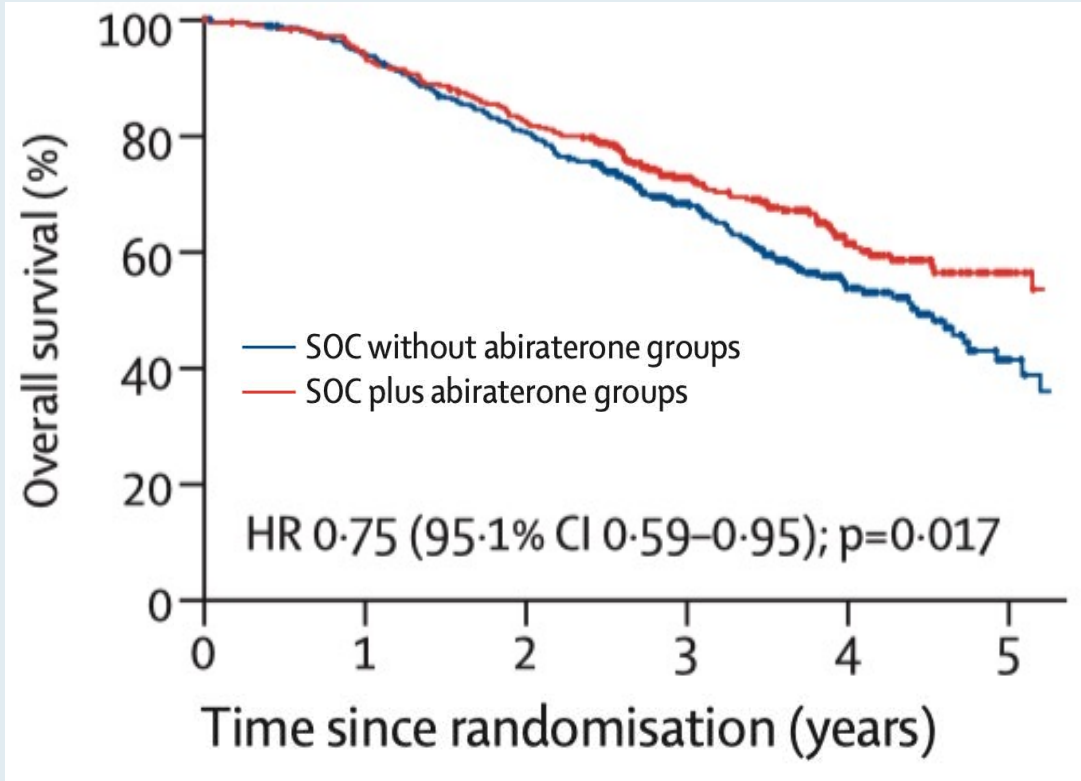
*Karim Fizazi, Stéphanie Foulon, Joan Carles, Guilhem Roubaud, Ray McDermott, Aude Fléchon, Bertrand Tombal, Stéphane Supiot, Dominik Berthold, Philippe Ronchin, Gabriel Kacso, Gwenaëlle Gravis, Fabio Calabro, Jean-François Berdah, Ali Hasbini, Marlon Silva, Antoine Thiery-Vuillemin, Igor Latorzeff, Loïc Mourey, Brigitte Laguerre, Sophie Abadie-Lacourtoisie, Etienne Martin, Claude El Kouri, Anne Escande, Alvar Rosello, Nicolas Magne, Friederike Schlurmann, Frank Priou, Marie-Eve Chand-Fouche, Salvador Villà Freixa, Muhammad Jamaluddin, Isabelle Rieger, Alberto Bossi, on behalf of the PEACE-1 investigators**

PEACE-1: Overall Survival

Overall Population



ADT + Docetaxel Population

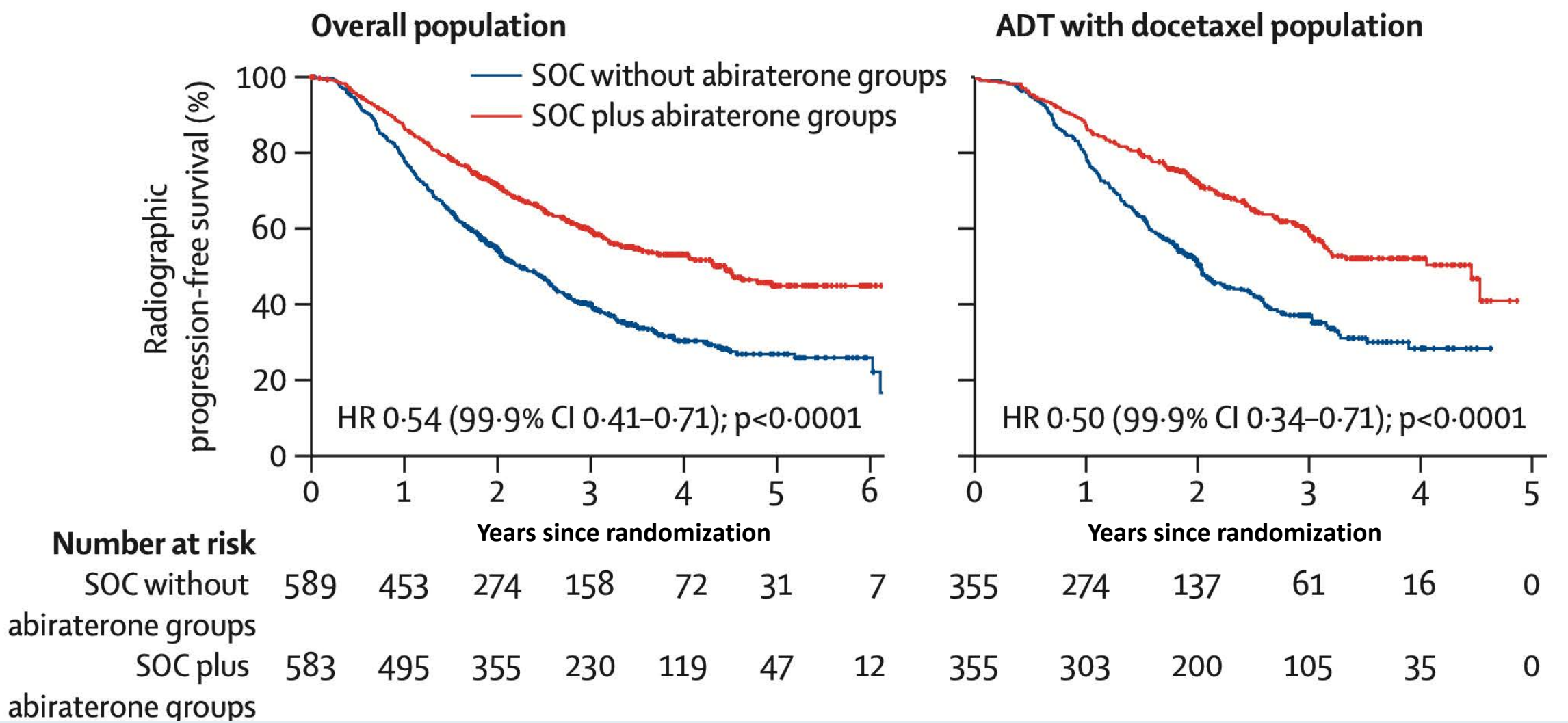


ADT = androgen deprivation therapy; SOC = standard of care

Fizazi K et al. *Lancet* 2022;399(10336):1695-707.

RTP RESEARCH TO PRACTICE

PEACE-1: Radiographic Progression-Free Survival



ADT = androgen deprivation therapy; SOC = standard of care

Fizazi K et al. *Lancet* 2022;399(10336):1695-707.

RTP RESEARCH TO PRACTICE

Comparison of Toxicities: Darolutamide, Enzalutamide and Apalutamide for Nonmetastatic Hormone-Resistant Prostate Cancer

Toxicity	ARAMIS trial		PROSPER trial		SPARTAN trial	
	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(11):1040-9.
Small EJ et al; SPARTAN Investigators. ASCO 2020;Abstract 5516.

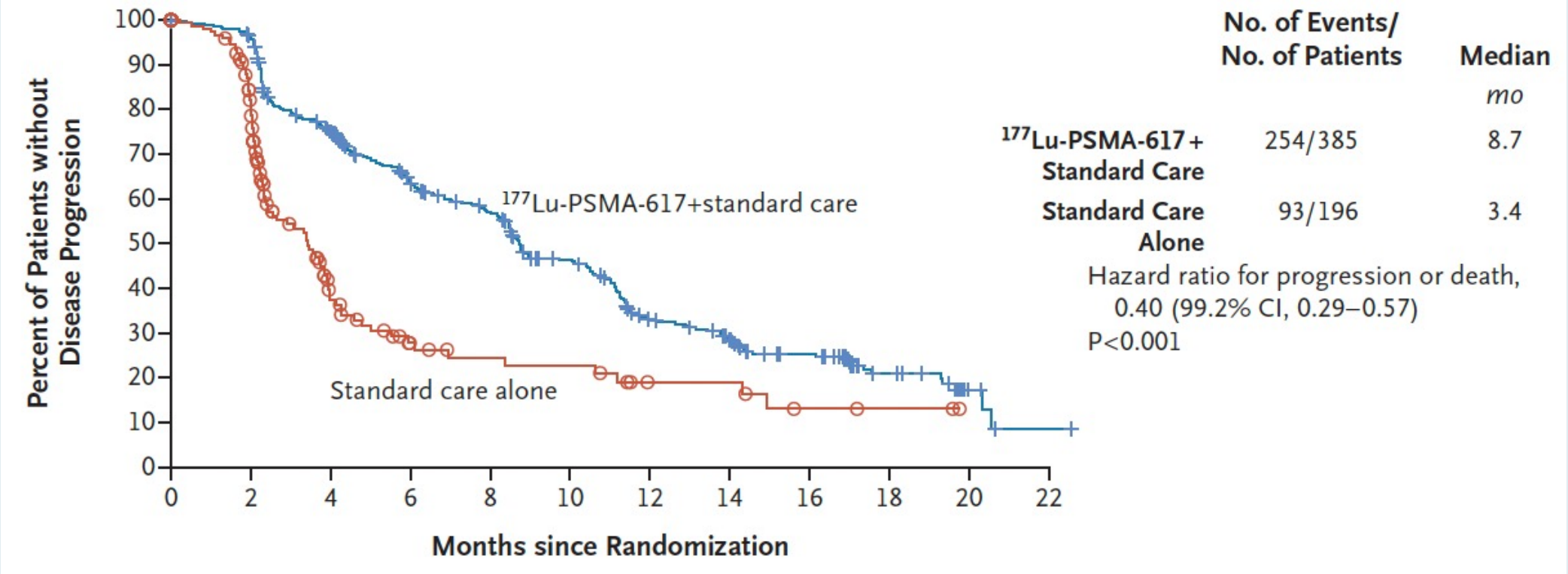
N Engl J Med 2021;385(12):1091-103.
The NEW ENGLAND JOURNAL of MEDICINE

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 by Independent Central Review

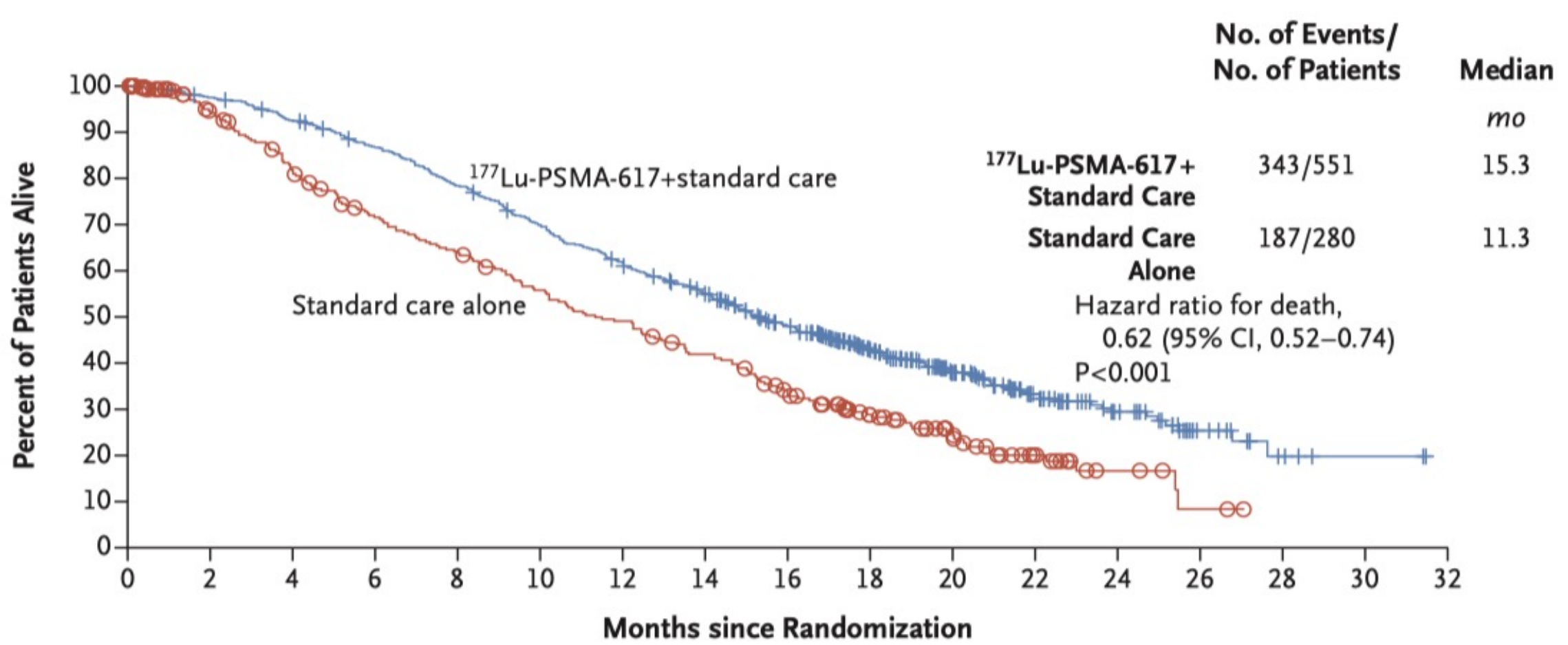


- Median overall survival (^{177}Lu-PSMA-617 vs standard therapy): 15.3 months vs 11.3 months (HR 0.62, $p < 0.001$)
- Median time to first symptomatic skeletal event (^{177}Lu-PSMA-617 vs standard therapy): 11.5 months vs 6.8 months (HR 0.50, $p < 0.001$)

Sartor O et al. *N Engl J Med* 2021;385(12):1091-103.

RTP RESEARCH TO PRACTICE

VISION: Overall Survival



Sartor O et al. *N Engl J Med* 2021;385(12):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)
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(12):1091-103.

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

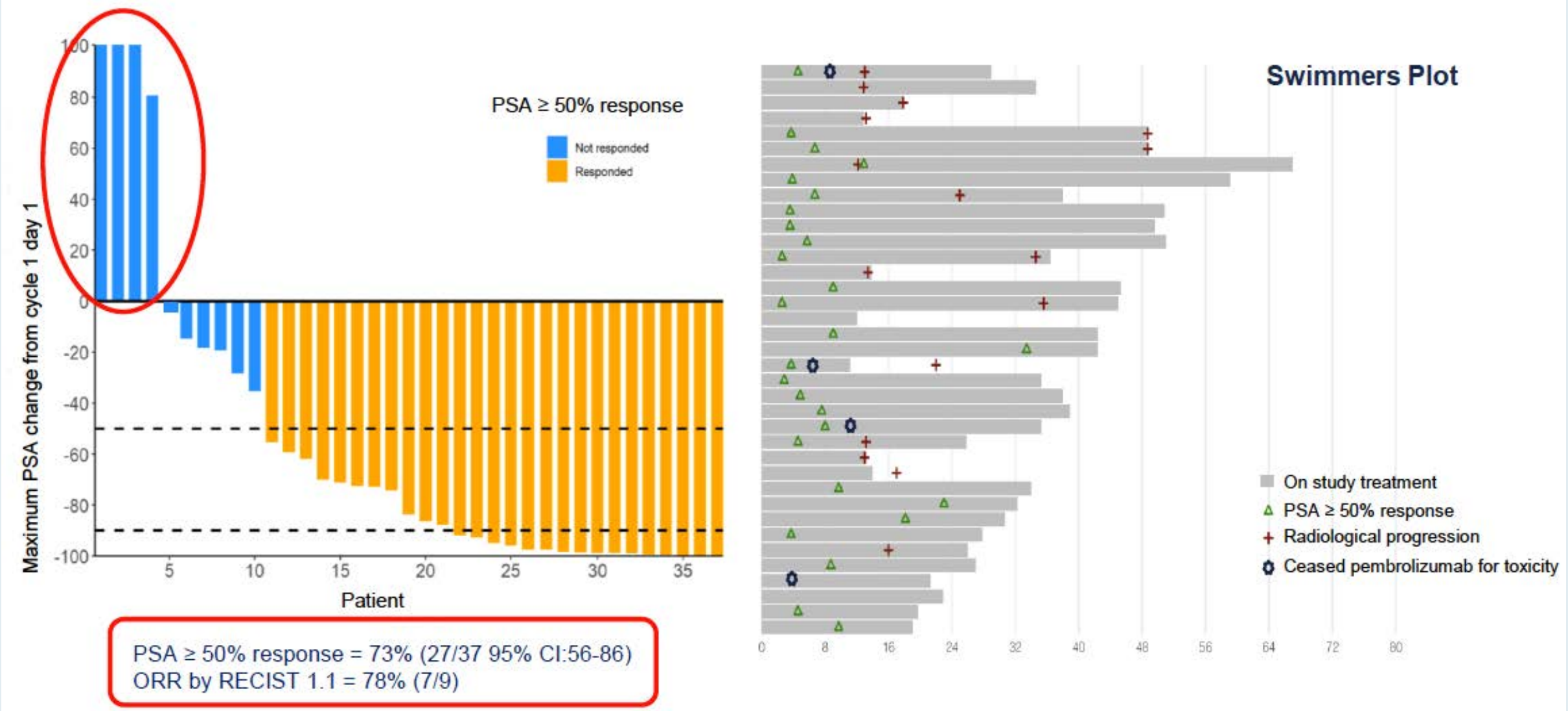
Shahneen Sandhu, Anthony M. Joshua, Louise Emmett, Lavinia Spain, Lisa G. Horvath, Megan Crumbaker, Arsha Anton, Roslyn Wallace, Anupama Pasam, Mathias Bressel, Erin Cassidy, Patricia Banks, Aravind Ravi Kumar, Ramin Alipour, Tim Akhurst, Grace Kong, Ian D. Davis, Scott Williams, Rod Hicks, Michael S.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

Abstract 577O

2021 ESMO congress

Presented by: Shahneen Sandhu

PRINCE: PSA Response Rate



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

TRITON3 Meets Primary Endpoint for Patients with mCRPC with BRCA or ATM Mutations

Press Release: October 3, 2022

"[The manufacturer] today announced positive top-line data from the Phase 3, open-label, multicenter, randomized TRITON3 trial demonstrating that rucaparib monotherapy treatment achieved the primary endpoint of significantly improved radiographic progression-free survival (rPFS) by independent radiology review (IRR) compared with the control group, which consisted of physician's choice of docetaxel, abiraterone acetate, or enzalutamide.

Benefit was observed in both primary efficacy analyses of patients with chemotherapy-naïve metastatic castration-resistant prostate cancer (mCRPC): first, those who had mutations in BRCA, as well as all patients randomized in the trial, inclusive of mutations in BRCA or ATM (the overall intent-to-treat population (ITT)). The safety profile of rucaparib observed in the TRITON3 study was consistent with rucaparib labelling."

https://www.businesswire.com/news/home/20221003005303/en

RTP RESEARCH TO PRACTICE

Phase III TALAPRO-2 Trial Meets Primary Endpoint for Patients with mCRPC with or without HRR Gene Mutations

Press Release: October 4, 2022

"[The manufacturer] today announced positive topline results from the Phase 3 TALAPRO-2 study of talazoparib, an oral poly ADP-ribose polymerase (PARP) inhibitor, in combination with enzalutamide compared to placebo plus enzalutamide in men with metastatic castration-resistant prostate cancer (mCRPC), with or without homologous recombination repair (HRR) gene mutations. The study met its primary endpoint with a statistically significant and clinically meaningful improvement in radiographic progression-free survival (rPFS) compared with placebo plus enzalutamide. The results of the primary endpoint exceeded the pre-specified hazard ratio of 0.696.

Results showed a trend toward improved overall survival, a key secondary endpoint, at the time of the analysis, but these data are not yet mature. Benefits were also observed in other secondary endpoints, including investigator assessed rPFS, prostate specific antigen (PSA) response, time to PSA progression, and overall response rate. Other secondary endpoints are being analyzed. At the time of topline analysis, the safety of talazoparib plus enzalutamide were generally consistent with the known safety profile of each medicine."

https://www.pfizer.com/news/press-release/press-release-detail/pfizer-announces-positive-topline-results-phase-3-talapro-2

ORIGINAL ARTICLE

NEJM Evidence 2022;1(9).

Abiraterone and Olaparib for Metastatic Castration-Resistant Prostate Cancer

Noel W. Clarke, M.B.B.S., Ch.M., F.R.C.S.,[1] Andrew J. Armstrong, Sc.M., M.D.,[2] Antoine Thiery-Vuillemin, M.D., Ph.D.,[3] Mototsugu Oya, M.D.,[4] Neal Shore, M.D.,[5] Eugenia Loredo, M.D.,[6] Giuseppe Procopio, M.D.,[7] Juliana de Menezes, M.D.,[8] Gustavo Girotto, M.D.,[9] Cagatay Arslan, M.D.,[10] Niven Mehra, M.D., Ph.D.,[11] Francis Parnis, F.R.A.C.P.,[12] Emma Brown, M.D.,[13] Friederike Schlürmann, M.D.,[14] Jae Y. Joung, M.D., Ph.D.,[15] Mikio Sugimoto, M.D., Ph.D.,[16] Juan A. Virizuela, M.D., Ph.D.,[17] Urban Emmenegger, M.D.,[18] Jiri Navratil, M.D.,[19] Gary L. Buchschacher, Jr., M.D., Ph.D.,[20] Christian Poehlein, M.D.,[21] Elizabeth A. Harrington, Ph.D.,[22] Chintu Desai, Ph.D.,[23] Jinyu Kang, M.D.,[24] Fred Saad, M.D., F.R.C.S.,[25] for the PROpel Investigators*

Abstract 1357O

PARIS 2022 ESMO congress

Biomarker analysis and updated results from the Phase III PROpel trial of abiraterone and olaparib vs abiraterone and placebo as first-line therapy for patients with metastatic castration-resistant prostate cancer

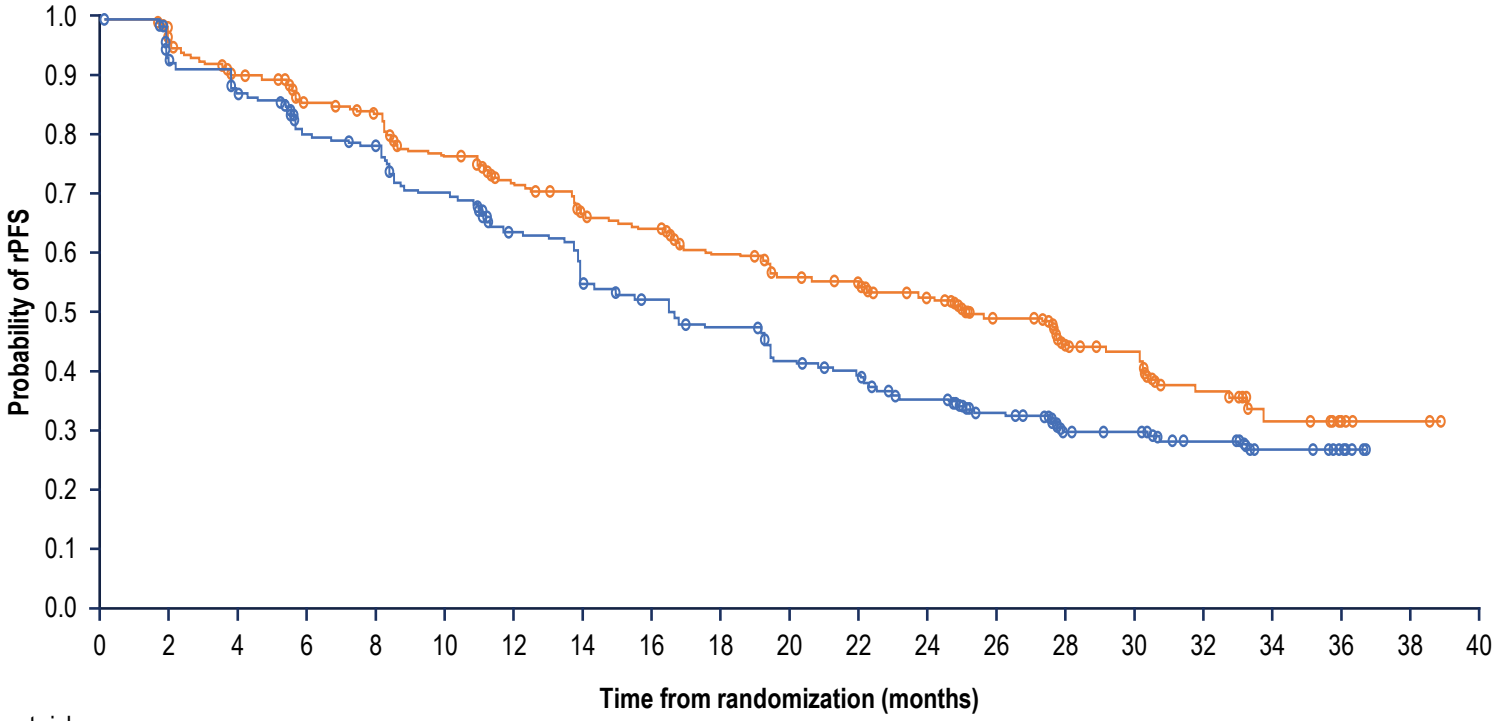
Fred Saad,[1] Andrew J. Armstrong,[2] Antoine Thiery-Vuillemin,[3] Mototsugu Oya,[4] Neal Shore,[5] Giuseppe Procopio,[6] Cagatay Arslan,[7] Niven Mehra,[8] Francis Parnis,[9] Emma Brown,[10] Friederike Schlürmann,[11] Jae Young Joung,[12] Mikio Sugimoto,[13] Oliver Sartor,[14] Yuzhen Liu,[15] Christian Poehlein,[16] Chintu Desai,[17] Paula Michelle del Rosario,[17] Noel Clarke[18]

[1]Centre Hospitalier de l'Université de Montréal/CRCHUM, Université de Montreal, Montreal, Canada; [2]Duke Cancer Institute Center for Prostate and Urologic Cancer, Duke University, Durham, NC, USA; [3]CHRU Besançon Hôpital J.Minjoz, Besançon, France; [4]Keio University School of Medicine, Tokyo, Japan; [5]Carolina Urologic Research Center, Myrtle Beach, SC, USA; [6]Istituto Nazionale Tumori Milano, Milan, Italy; [7]Izmir Economy University Medical Park Hospital, Karsiyaka, Turkey; [8]Radboud Universitair Medisch Centrum, Nijmegen, Netherlands; [9]Ashford Cancer Centre Research, Kurralta Park, SA, Australia; [10]University Hospital Southampton, Southampton, UK; [11]Centre Hospitalier de Cornouaille, Quimper, France; [12]National Cancer Center, Goyang-si, South Korea; [13]Kagawa University Hospital, Kagawa, Japan; [14]Tulane Cancer Center, New Orleans, LA, USA; [15]Precision Medicine, Oncology R&D, AstraZeneca, Cambridge, UK; [16]Merck & Co., Inc., Rahway, NJ, USA; [17]Global Medicines Development, Oncology R&D, AstraZeneca, Cambridge, UK; [18]The Christie and Salford Royal NHS Foundation Trusts, Manchester, UK

Presentation number: 1357O
ClinicalTrials.gov identifier: NCT03732820
This study was supported by AstraZeneca and Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA who are codeveloping olaparib.

RTP RESEARCH TO PRACTICE

PROpel: Updated Radiographic Progression-Free Survival (rPFS) in the ITT Population by Investigator Assessment



Number of patients at risk:

Abiraterone + olaparib	399	367	340	313	301	274	251	228	220	200	184	174	158	110	62	58	33	15	5	3	0
Abiraterone + placebo	397	359	338	306	297	264	232	199	187	169	145	135	117	84	51	48	30	8	3	0	0

	Abiraterone + olaparib (n=399)	Abiraterone + placebo (n=397)
Events, n (%)	199 (49.9)	258 (65.0)
Median rPFS (months)	25.0	16.4
HR (95% CI)	0.67 (0.56–0.81); *P*<0.0001*	

Saad F et al. ESMO 2022;Abstract 1357O.

ASCO® Genitourinary Cancers Symposium

2022;Abstract 12.

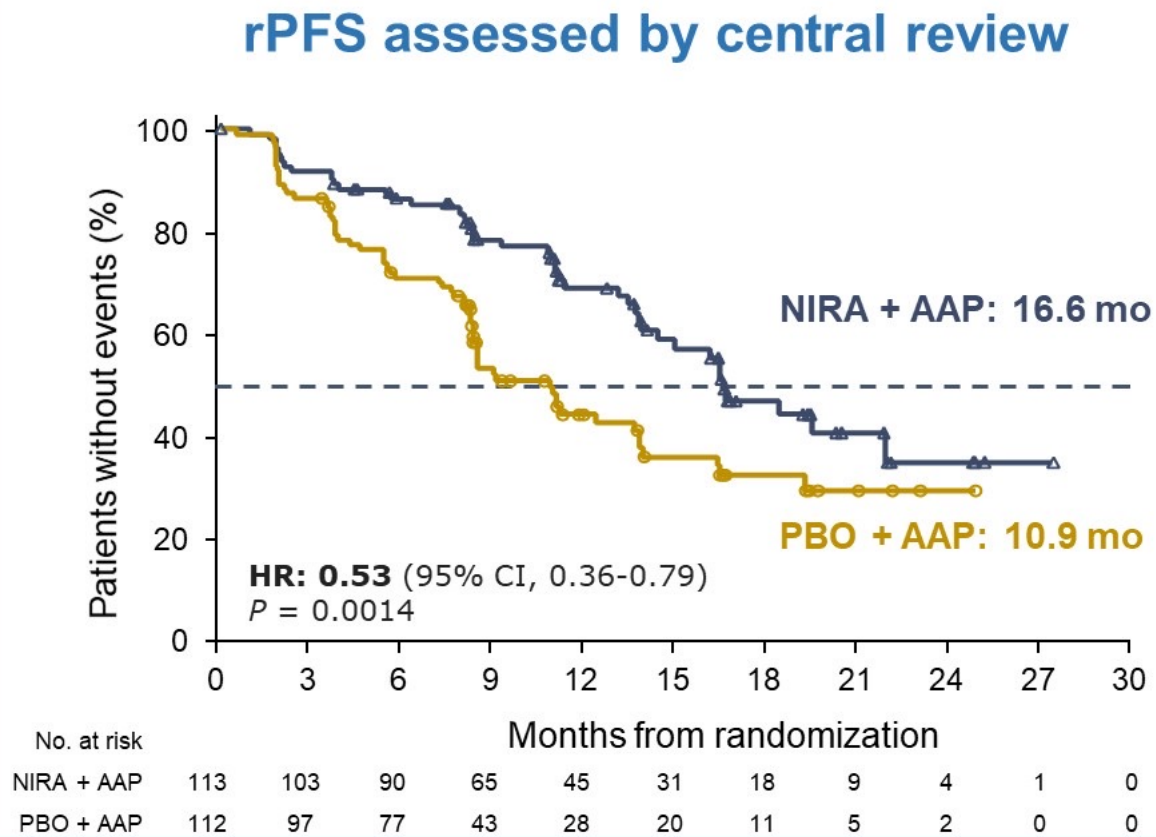
Phase 3 MAGNITUDE study: First results of niraparib (NIRA) with abiraterone acetate and prednisone (AAP) as first-line therapy in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC) with and without homologous recombination repair (HRR) gene alterations

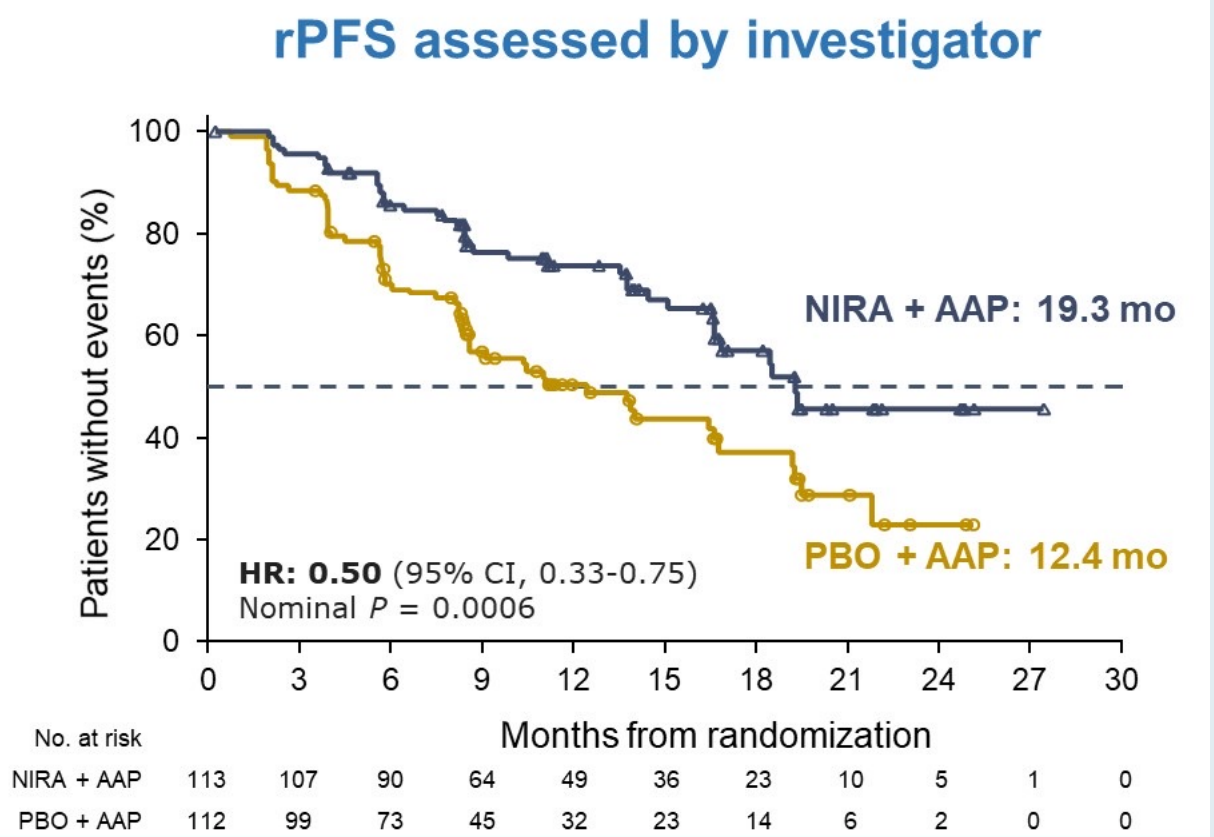
Kim N. Chi,[1] Dana E. Rathkopf,[2] Matthew R. Smith,[3] Eleni Efstathiou,[4] Gerhardt Attard,[5] David Olmos,[6] Ji Youl Lee,[7] Eric J. Small,[8] Andrea J. Pereira de Santana Gomes,[9] Guilhem Roubaud,[10] Marniza Saad,[11] Bogdan Zurawski,[12] Valerii Sakalo,[13] Gary E. Mason,[14] Adam del Corral,[15] 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

MAGNITUDE: BRCA1/2 Mutations

NIRA + AAP Significantly Reduced the Risk of Disease Progression or Death by 47%



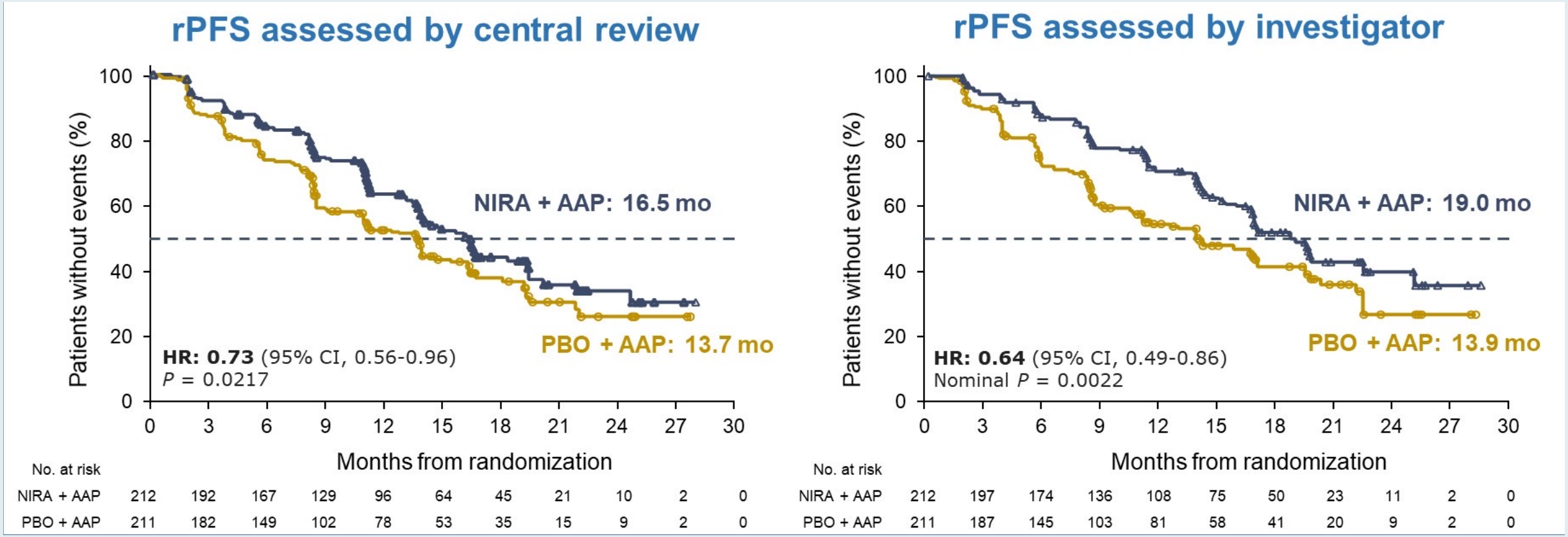


NIRA = niraparib; AAP = abiraterone acetate and prednisone; rPFS = radiographic progression-free survival; PBO = placebo

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

MAGNITUDE: All HRR Biomarker-Positive

NIRA + AAP Significantly Reduced the Risk of Disease Progression or Death by 27%



HRR = homologous recombination repair; NIRA = niraparib; AAP = abiraterone acetate and prednisone; rPFS = radiographic progression-free survival; PBO = placebo

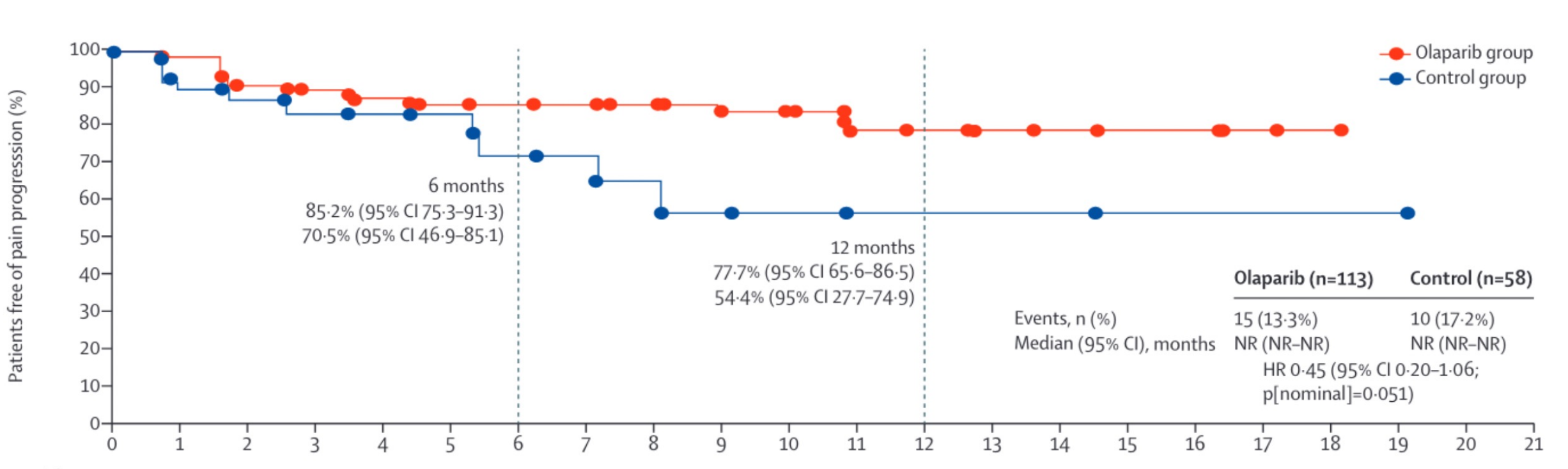
Chi KN et al. Genitourinary Cancers Symposium 2022;Abstract 12.

Lancet Oncol 2022 March;23:393-405.

Pain and health-related quality of life with olaparib versus physician's choice of next-generation hormonal drug in patients with metastatic castration-resistant prostate cancer with homologous recombination repair gene alterations (PROfound): an open-label, randomised, phase 3 trial

Antoine Thiery-Vuillemin, Johann de Bono, Maha Hussain, Guilhem Roubaud, Giuseppe Procopio, Neal Shore, Karim Fizazi, Gabriel dos Anjos, Gwenaelle Gravis, Jae Young Joung, Nobuaki Matsubara, Daniel Castellano, Arnold Degboe, Chris Gresty, Jinyu Kang, Allison Allen, Christian Poehlein, Fred Saad

PROfound: Time to Pain Progression in Patients without Opiate Use at Baseline



Thiery-Vuillemin A et al. *Lancet Oncol* 2022;23:393-405.

Prostate and Bladder Cancers Agenda

Module 1: Prostate Cancer

Module 2: Urothelial Bladder Cancer

RTP
RESEARCH
TO PRACTICE

Optimal Integration of Antibody Drug Conjugates and Targeted Treatment in Metastatic Urothelial Bladder Cancer

Evan Y. Yu, M.D

Florida Cancer Specialists Retreat
Orlando, FL

October 22, 2022

BLC2001: Phase 2 Trial of Erdafitinib[1]

- Fifteen percent of patients with MIBC have *FGFR* alterations[2]

Patients

- Unresectable Ia/mUC with prespecified *FGFR3/2* alterations
- ECOG PS 0-2
- History of disease progression during or after ≥1 line of prior systemic chemotherapy, or within 12 months after receiving (neo)adjuvant chemotherapy in the metastatic setting (chemo-refractory patients)
- Were cisplatin ineligible (for impaired renal function or peripheral neuropathy)
- Chemotherapy naïve

Screening for *FGFR* fusions/mutations

Randomized 1:1

Regimen 1

Erdafitinib 10 mg/d
7 days on/7 days off
Locally advanced UC

Regimen 2

Erdafitinib 6 mg/d

Regimen 3

Erdafitinib 8 mg/d with potential for uptitration to 9 mg/d

(n=99)

Primary endpoint

- Confirmed ORR

Secondary endpoints

- PFS, DOR, OS, safety, predictive biomarker evaluation, and PK

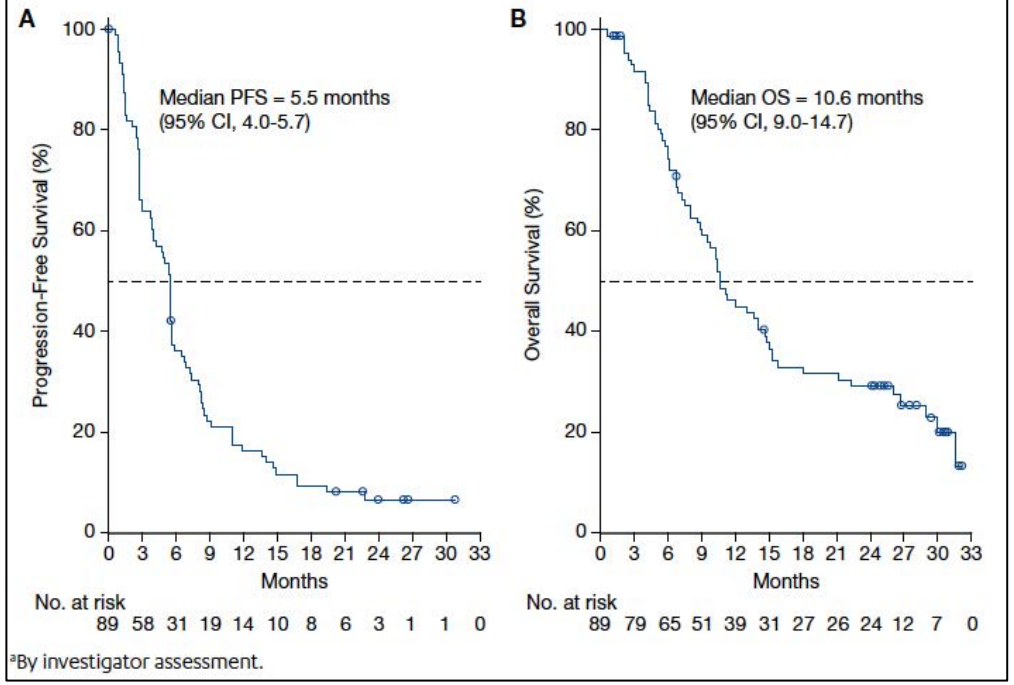
***FGFR* Alterations (n=99)**	
FGFR2 or *FGFR3* fusion, No. (%)	25 (25)
FGFR3 mutation, No. (%)	74 (75)
FGFR2/3 fusions and mutations	0

1. Loriot Y, et al. *N Engl J Med.* 2019;381(4):338-348.
2. Helsten T, et al. *Clin Cancer Res.* 2016;22(1):259-267.

BLC2001: Efficacy

	All Patients (N=99)	*FGFR3* Mutation (n=74)	*FGFR2/3* Fusion (n=25)
ORR, n (%) (95% CI)	40 (**40**) (31-50)	36 (**49**) (37-60)	4 (**16**) (2-30)

Figure 3. A) PFS[a] and B) OS in Patients Who Had Prior Chemotherapy



[a]By investigator assessment.

- **Confirmed response rate 40% (3% CR; 37% PR)**
- **Among 22 pts with prior ICI, confirmed response rate 59%**

Table 2. Efficacy Outcomes by Subgroup

	n	Median DoR[a], mo	n[b]	Median PFS[a], mo	Median OS, mo
FGFR alteration					
FGFRm+f-	33	6.0	70	5.6	12.0
FGFRm-f+	4	6.2	25	2.8	10.3
FGFRm+f+	3	5.6	6	6.9	15.0
Primary tumor location					
Upper tract	11	6.7	25	4.2	10.3
Lower tract	29	6.0	76	5.6	13.8
Presence of visceral metastases					
Yes	30	6.0	78	5.5	10.3
No	10	5.3	23	5.8	14.1
Prior systemic therapy					
None	4	10.9	10	9.8	18.1
1 line	17	6.0	48	5.5	11.3
2 lines	10	6.1	28	5.5	8.0
3 lines	7	4.4	11	5.7	11.2
> 3 lines	2	4.8	4	3.4	12.4
Use of prior chemotherapy					
Yes	35	5.6	89	5.5	10.6
No	5	14.3	12	14.9	20.8
Use of prior IO					
Prior IO	14	6.5	24	5.7	10.9
No prior IO	26	5.6	77	5.5	12.0

[a]By investigator assessment. [b]For PFS and OS.

1. Loriot Y, et al. *N Engl J Med.* 2019;381(4):338-348.

2. Necchi A, et al. ESMO 2020. Presentation 750P.

BLC2001: Safety

Grade ≥3 AEs Occurring in ≥5% of Patients, No. (%)	(N=99)
Stomatitis	10 (10)
Hyponatremia	11 (11)
Asthenia	7 (7)
Nail dystrophy	6 (6)
Hand-foot syndrome	5 (5)
Urinary tract infection	5 (5)

Final Analysis (n=101)

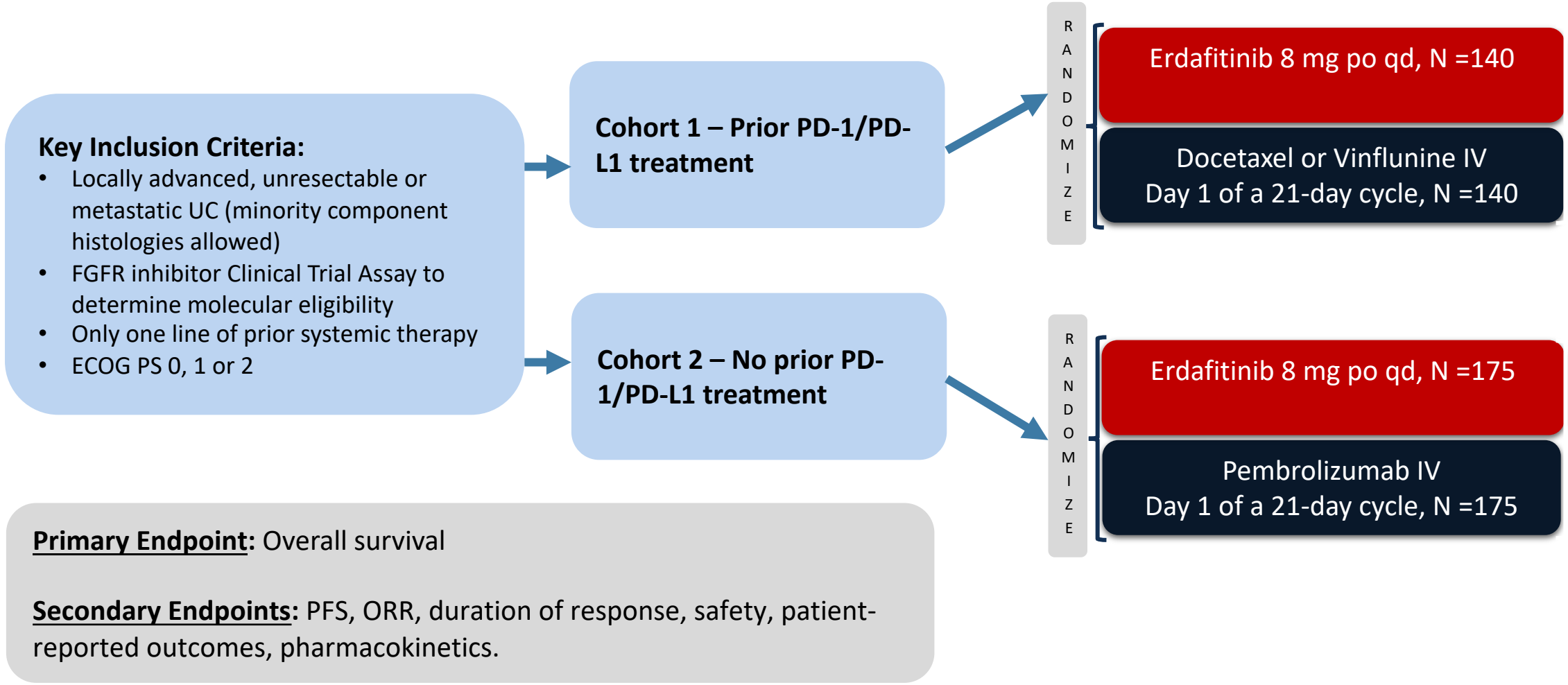
TEAE of Interest	Overall Incidence n (%)
Hyperphosphatemia[a]	**79 (78%)**
Stomatitis	**60 (59%)**
Nail disorders	**60 (59%)**
Skin disorders	**55 (55%)**
Central serous retinopathy	**27 (27%)**

1. Loriot Y, et al. *N Engl J Med.* 2019;381(4):338-348.

2. Necchi A, et al. ESMO 2020. Presentation 750P.

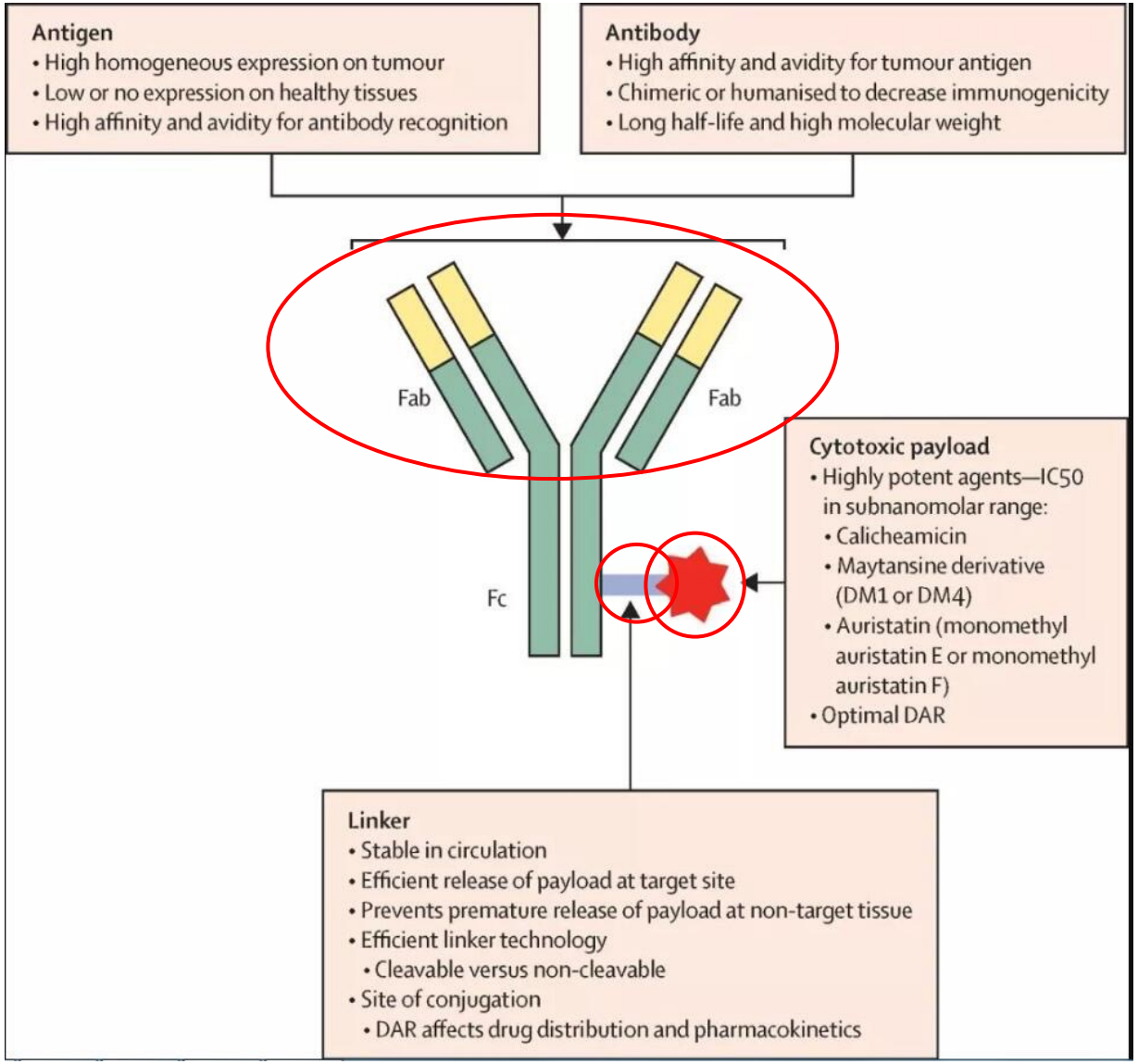
3. Siefker-Radtke *Lancet Oncol*. 2022;23(2):248-258.

Randomized Phase 3 Erdafitinib THOR Trial Schema



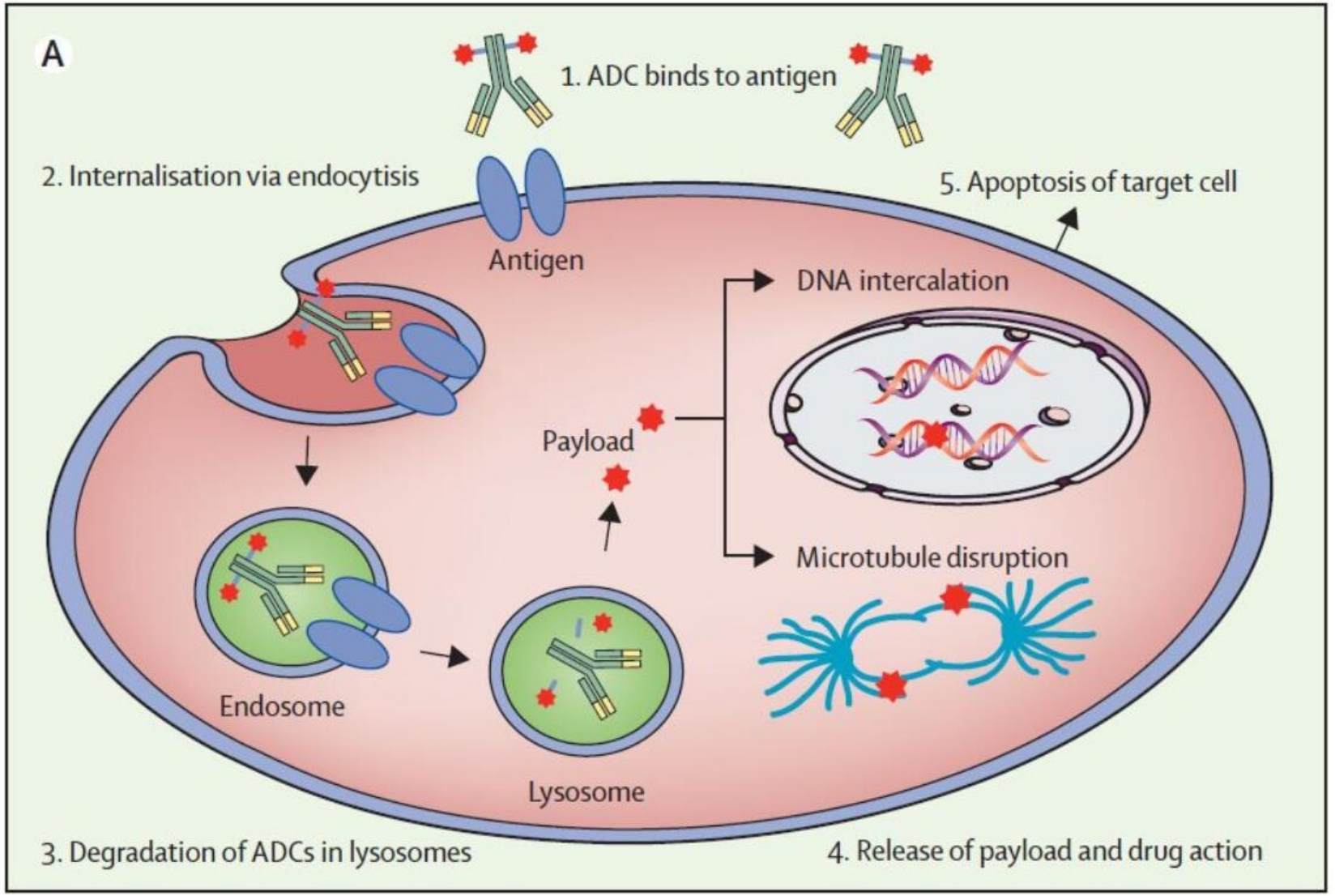
https://clinicaltrials.gov/ct2/show/NCT03390504

General Design Elements for an Antibody Drug Conjugate (ADC)



Chau CH, et al. Lancet 2019; 394:793-804

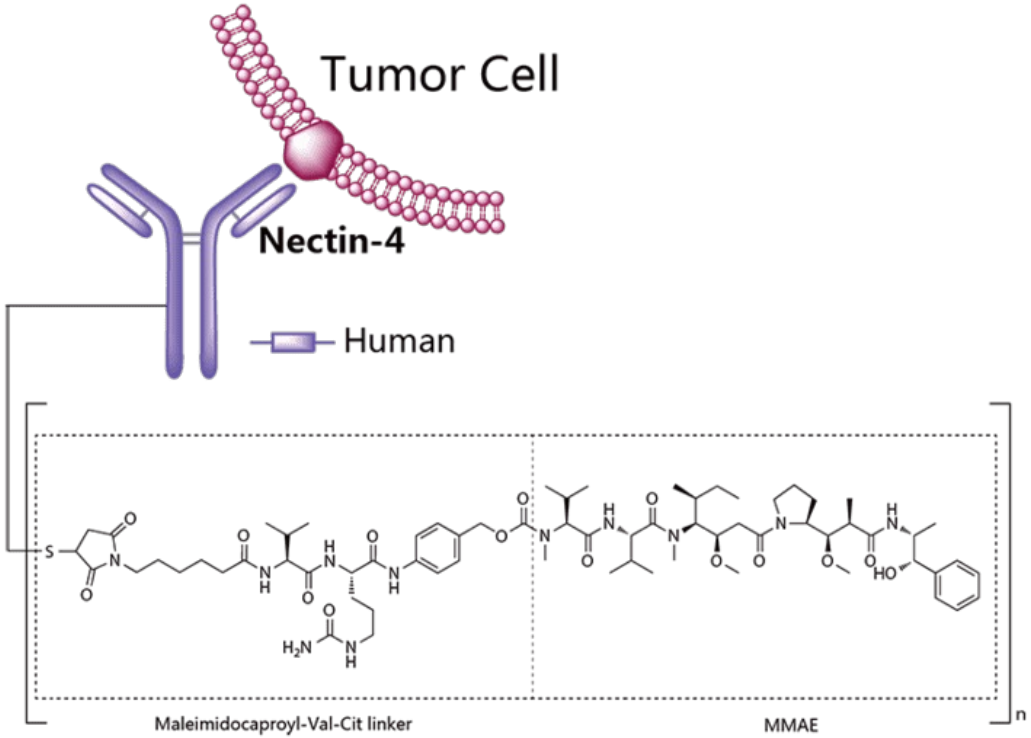
ADC Mechanism of Action



Chau CH, et al. Lancet 2019; 394:793-804

Nectin-4 and ASG-22E (Enfortumab Vedotin)

- Nectin-4 is a transmembrane protein that regulates cell-cell adhesions and mechanisms that underlie contact inhibition of cell movement and proliferation[1]
- Moderate to strong IHC staining was observed in 60% of bladder tumor specimens, whereas normal tissue had very limited staining[2]
  - Clinical data have shown very high H-scores in Enfortumab Vedotin trials
- Initial preclinical work with ASG-22E (eventually enfortumab vedotin) showed inhibition of growth in human breast, bladder, pancreatic and lung cancer xenografts, but breast and bladder showed dramatic tumor regression[2]



1. Takai Y, et al. Nat Rev Mol Cell Biol 2008; 9:603-15
2. Challita-Eid PM, et al. Cancer Res 2016; 76:3003-13

EV-301 Randomized Phase 3 Data

Key Inclusion Criteria:

- Locally advanced, unresectable or metastatic UC (squamous differentiation and mixed histologies allowed)
- Progression or relapse after PD-1/PD-L1 therapy
- Receipt of prior platinum chemotherapy (if perioperative receipt must have progressed within 12 months)
- ECOG PS 0 or 1

→ **1:1** RANDOMIZE

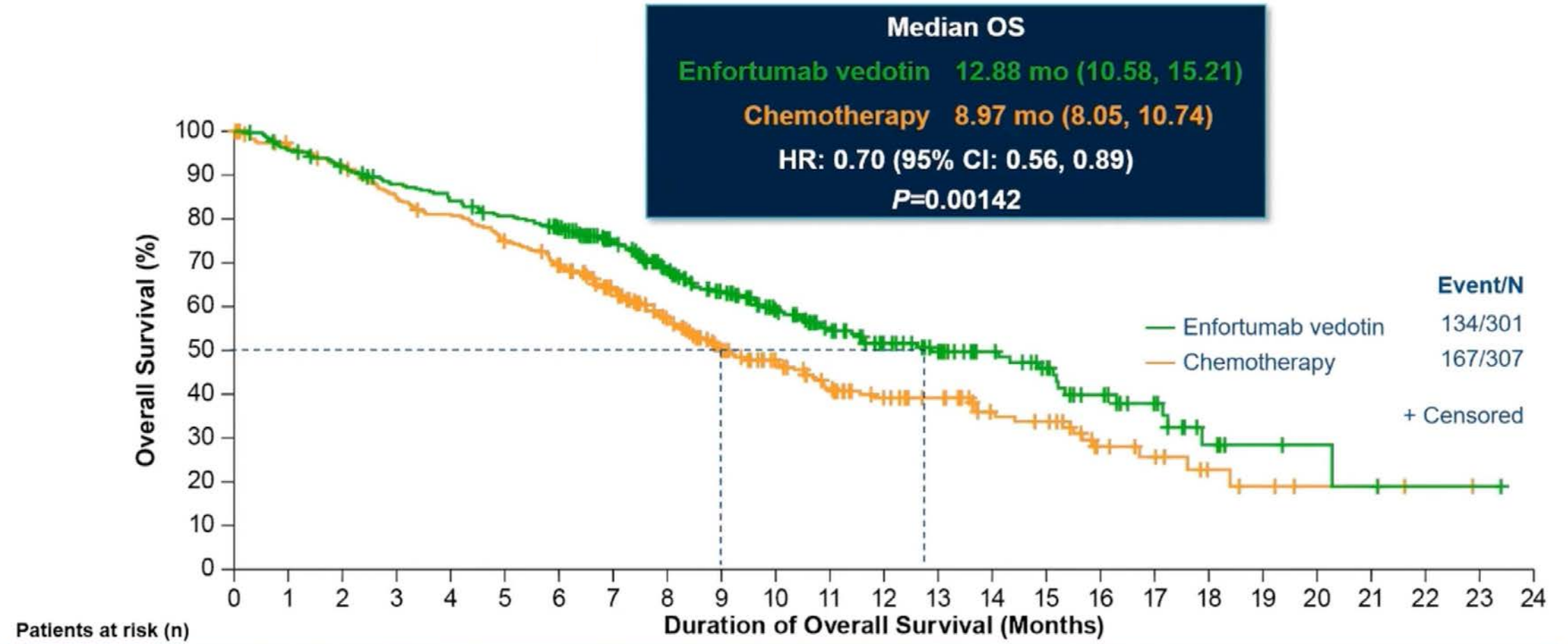
- Enfortumab vedotin 1.25 mg/kg IV on day 1, 8 and 15 of each 28 day cycle, N =301
- Docetaxel, Vinflunine, or Paclitaxel IV Day 1 of a 21-day cycle, N =307

Disease progression or other withdrawal criteria met

Primary Endpoint: Overall survival

Secondary Endpoints: PFS, ORR, disease control rate, duration of response, safety, patient-reported outcomes.

EV-301 Overall Survival



Evaluated in the intent-to-treat population.
Abbreviations: CI, confidence interval; HR, hazard ratio; OS, overall survival.

Data cut-off: July 15, 2020

Powles T, et al. N Engl J Med 2021; Epub February 12, 2021.

EV-301 Treatment Related Adverse Events

	Enfortumab Vedotin (N=296)		Chemotherapy (N=291)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any AE	278 (94%)	152 (51%)	267 (92%)	145 (50%)
Alopecia	134 (45%)	0	106 (36%)	0
Peripheral sensory neuropathy[a]	100 (34%)	9 (3%)	62 (21%)	6 (2%)
Pruritus	95 (32%)	4 (1%)	13 (4%)	0
Fatigue	92 (31%)	19 (6%)	66 (23%)	13 (4%)
Decreased appetite	91 (31%)	9 (3%)	68 (23%)	5 (2%)
Diarrhea	72 (24%)	10 (3%)	48 (16%)	5 (2%)
Dysgeusia	72 (24%)	0	21 (7%)	0
Nausea	67 (23%)	3 (1%)	63 (22%)	4 (1%)
Maculopapular rash	48 (16%)	22 (7%)	5 (2%)	0
Anemia	34 (11%)	8 (3%)	59 (20%)	22 (8%)
Decreased neutrophil count	30 (10%)	18 (6%)	49 (17%)	39 (13%)
Neutropenia	20 (7%)	14 (5%)	24 (8%)	18 (6%)
Decreased white cell count	16 (5%)	4 (1%)	31 (11%)	20 (7%)
Febrile neutropenia	2 (<1%)	2 (<1%)	16 (5%)	16 (5%)

[a] A total of 113 patients (55 in the EV group and 58 in the chemotherapy group) had preexisting peripheral neuropathy.

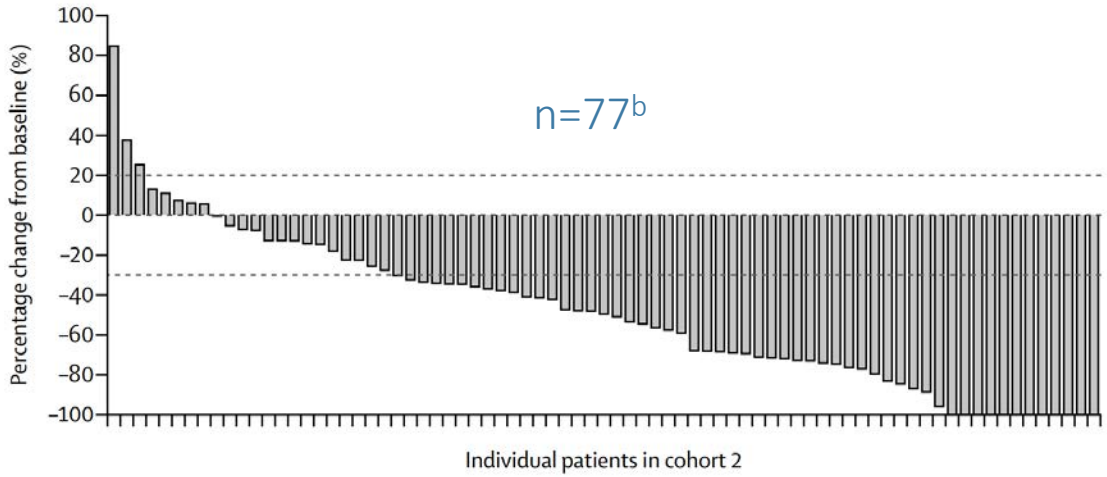
Powles T, et al. *N Engl J Med.* 2021;384(12):1125-1135.

EV-201 Cohort 2 Supports FDA Approval for Cisplatin-Ineligible Patients

Confirmed Best Overall Response per BICR

	Cohort 2 (n=89)
Objective response rate	46 (52%)
95% CI	41-62
Best overall response	
Complete response	18 (20%)
Partial response	28 (31%)
Stable disease	27 (30%)
Progressive disease	8 (9%)
Not evaluable[a]	8 (9%)

Change in Target Lesions From Baseline



Median duration of treatment: 6 months

[a] Includes 5 patients who did not have a response assessment postbaseline, 2 patients whose postbaseline assessment did not meet the minimum interval requirement for stable disease, and 1 patient whose response cannot be assessed due to incomplete anatomy.

[b] Data are not available for 12 patients due to no response assessment of response postbaseline (n=5), incomplete assessment of target lesions postbaseline (n=1), or no measurable disease at baseline per BICR (n=6).

Yu EY, et al. *Lancet Oncol.* 2021;22(6):872-882.

EV-103: Phase 1b/2 Trial of Enfortumab + Pembrolizumab

Patients With 1L Cisplatin-Ineligible la/mUC (N=45)

Dose escalation	Dose expansion cohort A
EV + Pembro (n=5)	EV + Pembro (n=40)

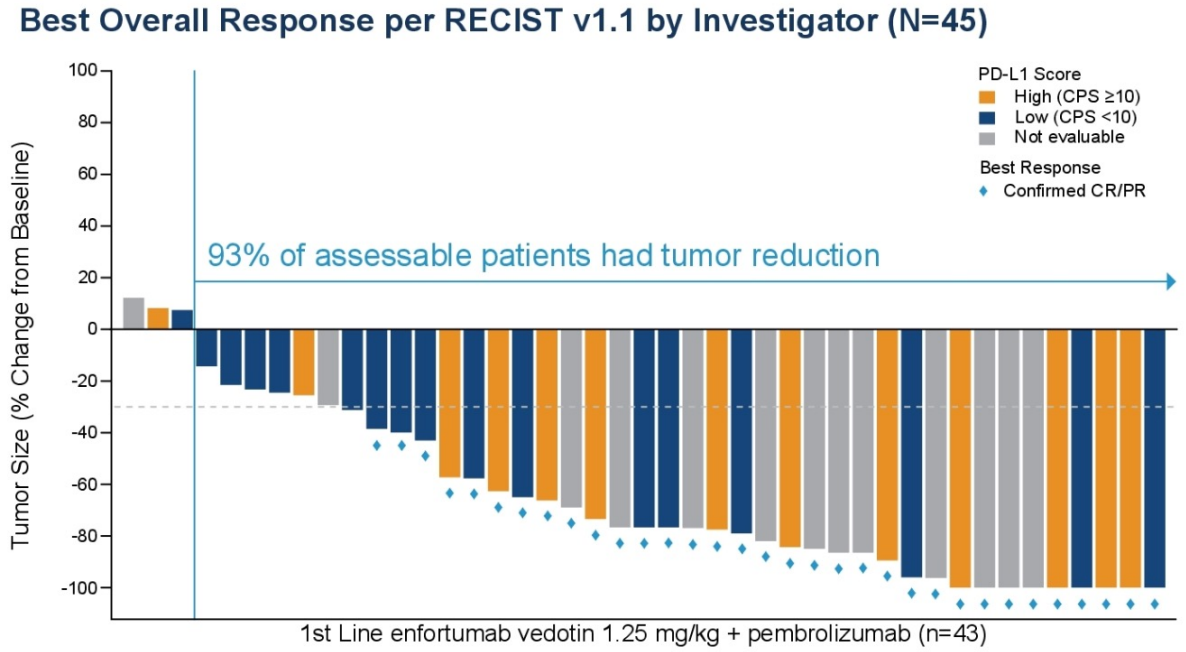
EV 1.25 mg/kg days 1 and 8 of a 3-week cycle
+
Pembrolizumab 200 mg on day 1 of a 3-week cycle

- 84% of patients had visceral disease and 31% had liver metastasis
- 31% of patients had PD-L1 CPS ≥10

Confirmed ORR 95% CI	**73%** (33/45) (58.1, 85.4)
Complete response	16% (7/45)
Partial response	58% (26/45)

- 57% confirmed ORR in patients with liver metastases

Maximum Target Lesion Reduction From Baseline by PD-L1 Status



Friedlander TW, et al. ASCO 2021. Abstract 4528.

EV-103 Cohort K: Phase 1b/2 Trial

Cohort K

- Unresectable la/mUC
- Cisplatin ineligible
- No prior treatment for la/mUC

N=149

R
1:1

n=76
EV 1.25 mg/kg days 1 and 8 of a 3-week cycle
+
Pembrolizumab 200 mg on day 1 of a 3-week cycle

n=73
EV 1.25 mg/kg days 1 and 8 of a 3-week cycle

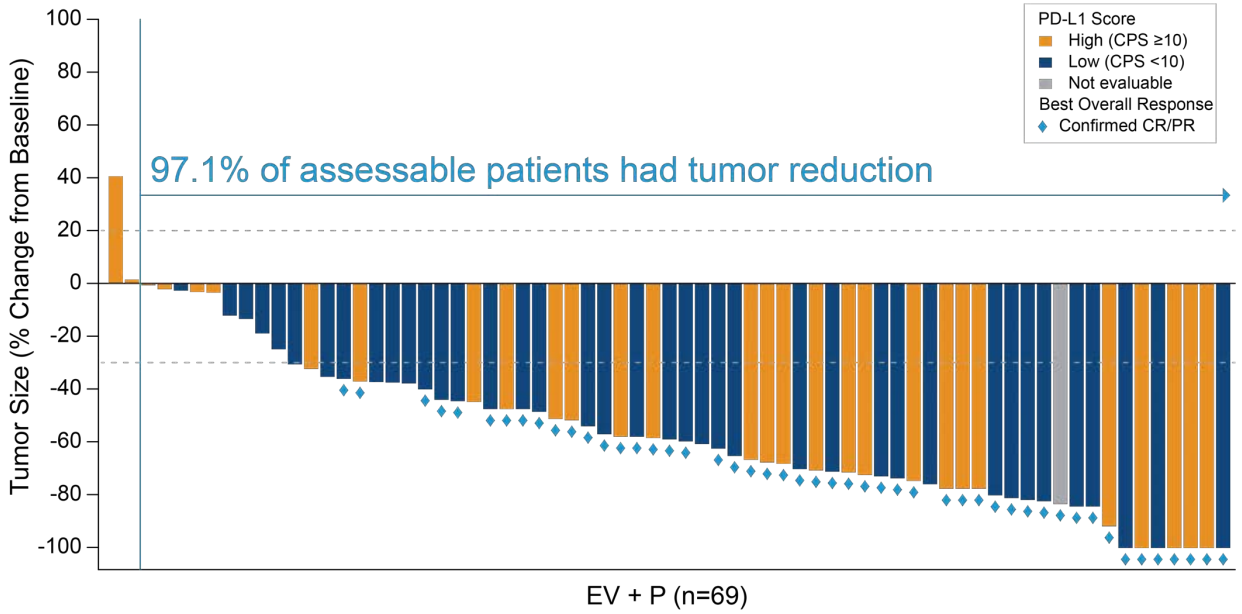
Primary Endpoint

- ORR per BICR

Secondary Endpoints

- ORR per investigator assessment
- DOR
- Disease control rate
- PFS
- OS
- Safety

	EV+P (N=76)	EV Mono (N=73)
Confirmed ORR, n (%) (95% CI)	49 (64.5) (52.7, 75.1)	33 (45.2) (33.5, 57.3)
Best overall response, n (%)		
Complete Response	8 (10.5)	3 (4.1)
Partial Response	41 (53.9)	30 (41.1)
Stable Disease	17 (22.4)	25 (34.2)
Progressive Disease	6 (7.9)	7 (9.6)
Not Evaluable	3 (3.9)	5 (6.8)
No Assessment	1 (1.3)	3 (4.1)
Median time to objective response (range), mos	2.07 (1.1, 6.6)	2.07 (1.9, 15.4)
Median number of treatment cycles (range)	11.0 (1, 29)	8.0 (1, 33)



Data cutoff: 10Jun2022
BICR: Blinded Independent Central Review; cORR: Confirmed Objective Response Rate; NR: Not Reached

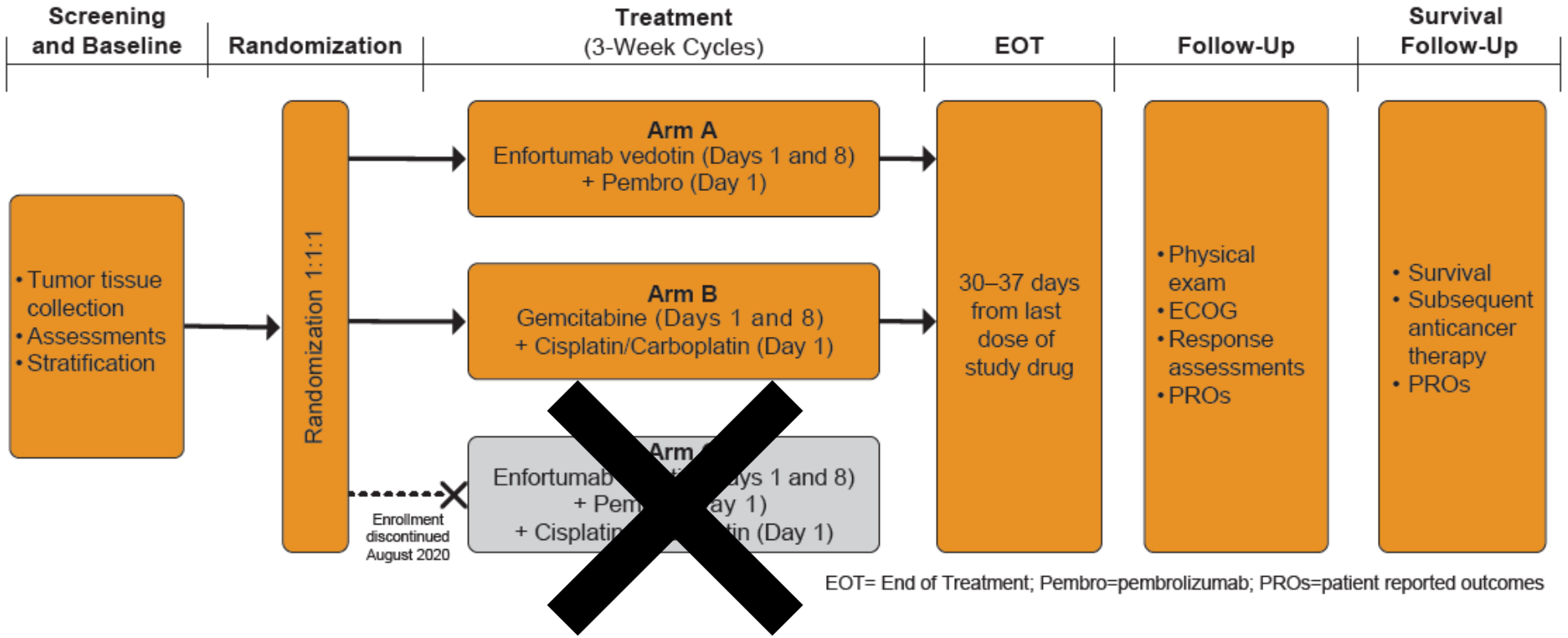
BICR: Blinded Independent Central Review; CPS: Combined Positive Score; CR: Complete Response; PD-L1: Programmed Death-Ligand 1 PR: Partial Response

Rosenberg JE, et al. ESMO 2022. Abstract 2895/LBA73.

EV-302 Randomized Phase 3 Trial Schema

Eligibility

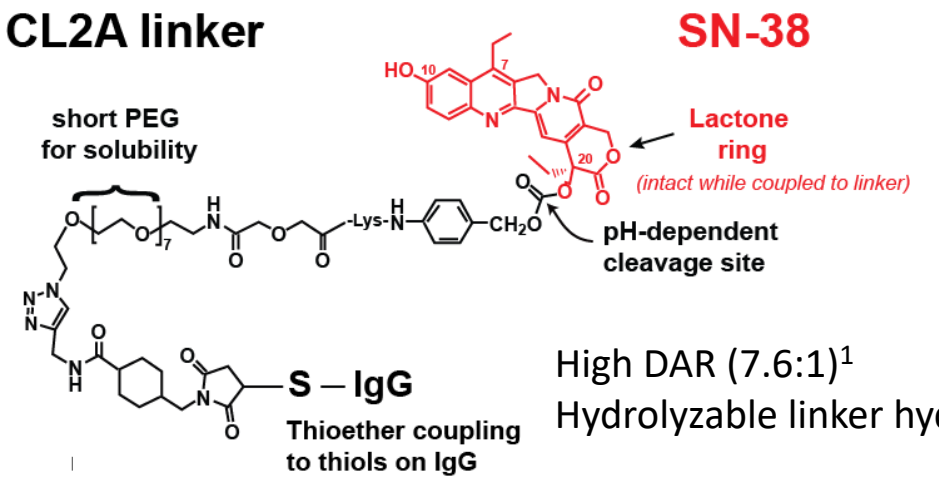
- Locally advanced or metastatic urothelial carcinoma
- 1st line systemic therapy
- Platinum-eligible



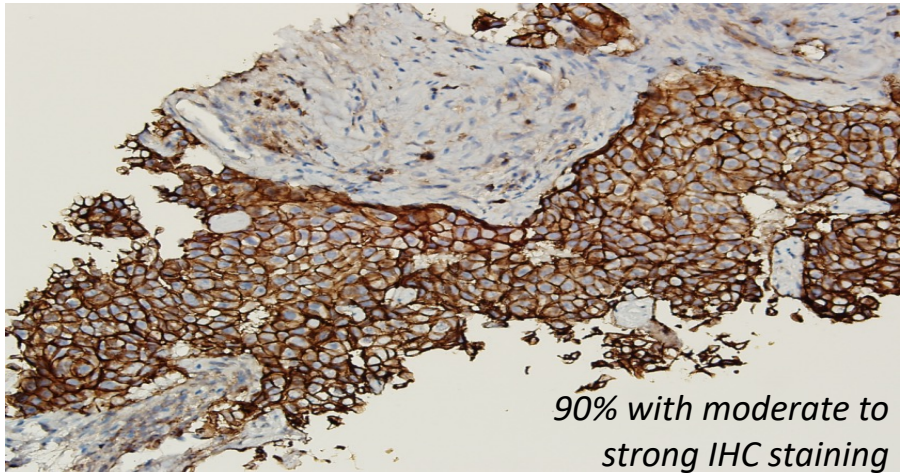
- Stratification Factors for Randomization: cisplatin eligibility (eligible/ineligible), liver metastases (present/absent), PD-L1 expression (high/low)
- Follow-up until disease progression, death, consent withdrawal, or study closure

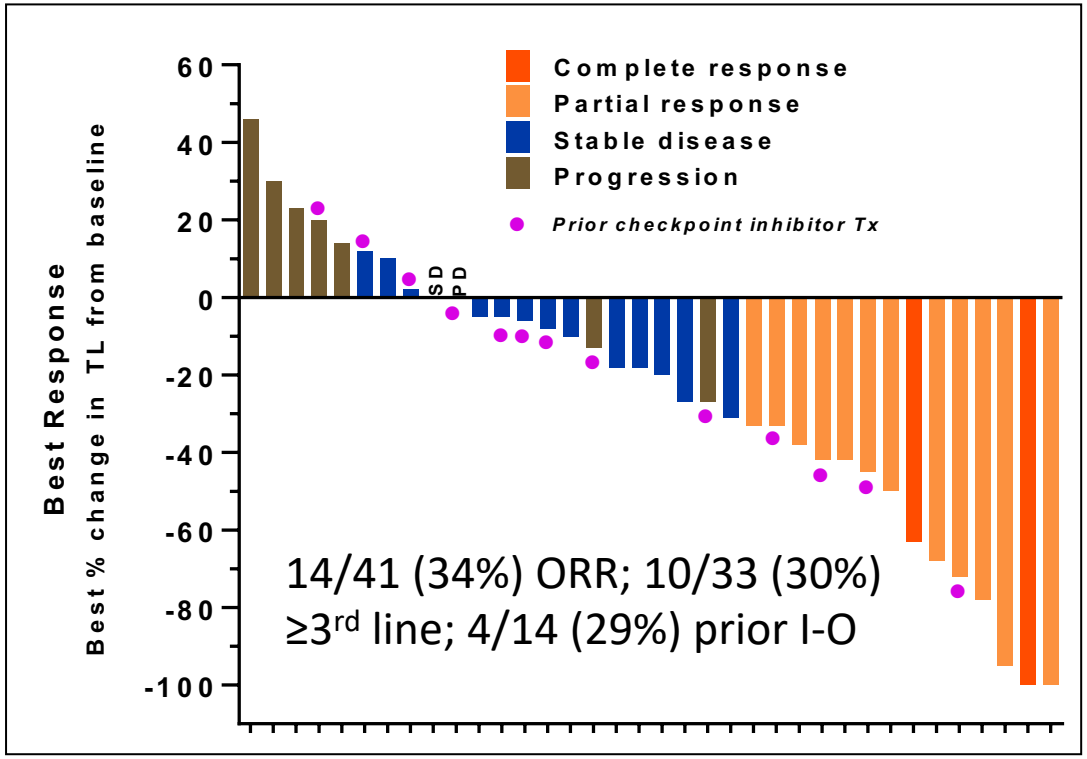
Primary Endpoints: PFS, OS
Secondary Endpoints: ORR, DOR, DCR, QOL, PRO, Safety

Sacituzumab govitecan



High DAR (7.6:1)[1]
Hydrolyzable linker hydrolysis[2]





- Final 14/45 (31%) ORR
- Median PFS 7.3 months
- Median OS 18.9 months

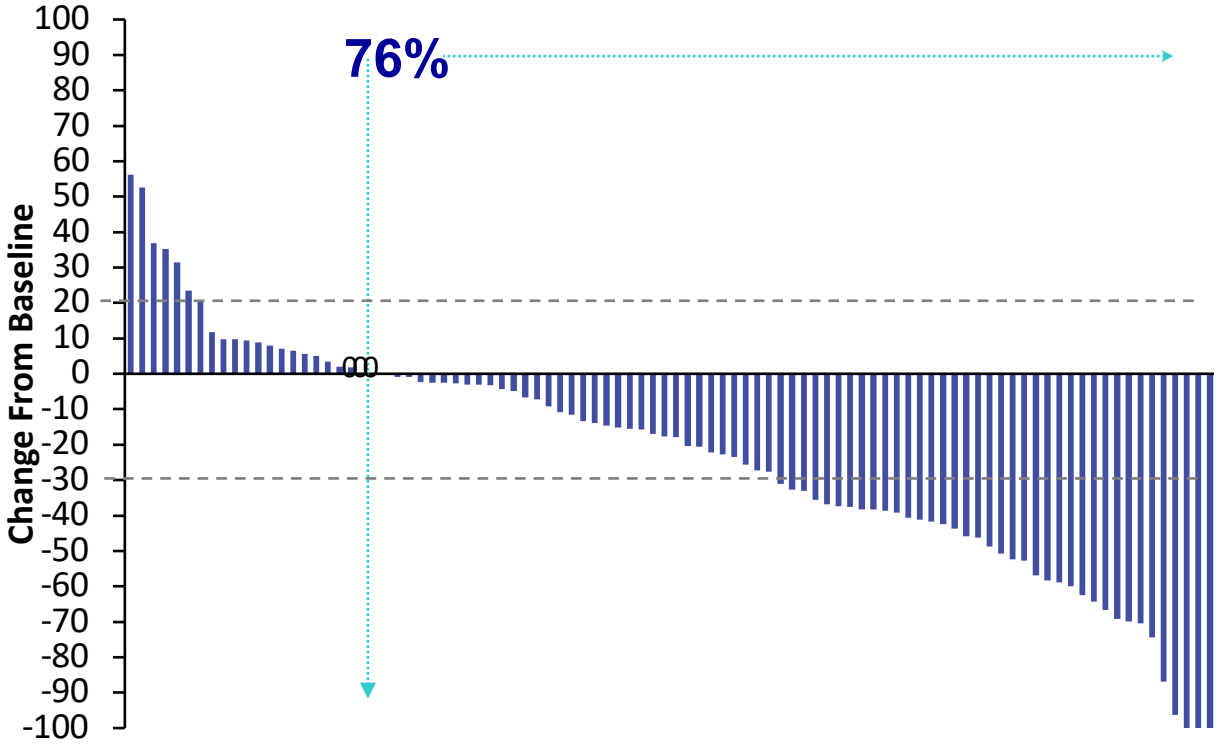
1. Cardillo TM, et al. Bioconjug Chem 2015; 26:919-31
2. Govindan SV, et al. Mol Cancer Ther 2013; 12:968-78

Tagawa S, et al. Ann Oncol (2017) 28 (suppl_5):v295-v329
Tagawa S, et al. J Clin Oncol 37, no. 7_suppl (March 1, 2019) 354-354

TROPHY-U-01 Cohort 1 (Prior Platinum and CPI) Response and Reduction in Tumor Size

Endpoint	Cohort 1 (N=113)
ORR, n (%) [95% CI]	**31 (27) [19, 37]**
CR, n (%)	6 (5)
PR, n (%)	25 (22)
Median duration of response, mos [95% CI] (Range)	**5.9** [4.70, 8.60] (1.4–11.7)
Median time to onset of response, mos (Range)	1.6 (1.2–5.5)

[a]Assessments were per Blinded Independent Review Assessment, RECIST 1.1.
CI, confidence interval; CR, complete response; ORR, objective response rate; PR, partial response; TTR, time to response.



[a]71/94 patients with at least one post-baseline target lesion measurement and accepted for central review. Fourteen patients had no post-treatment imaging, 1 patient lacked measurable lesions by central review, and 4 patients had poor image quality.

Loriot Y, et al. Annal Oncol (2020) 31 (suppl_4):S1142-S1215; LBA24

TROPHY-U-01 Cohort 1 Treatment-Related Adverse Events ≥20% any grade or ≥5% Grade ≥3 (n=113)

Category	Event	All Grades (%)	Grade 3 (%)	Grade 4 (%)
Hematologic[a]	**Neutropenia**	**46**	**22**	**12**
	Leukopenia	26	12	5
	Anemia	34	14	0
	Lymphopenia	12	5	2
	Febrile neutropenia	**10**	**7**	**3**
Gastrointestinal	**Diarrhea[b]**	**65**	**9**	**1**
	Nausea	**58**	**4**	**0**
	Vomiting	28	1	0
General disorders & administrative site conditions	**Fatigue**	**50**	**4**	**0**
Skin & subcutaneous tissue	**Alopecia**	**47**	**0**	**0**
Metabolism & nutrition	Decreased appetite	36	3	0
Infections & infestations	Urinary tract infection	8	6	0

Median treatment cycles: 6 (range: 1–22); worst grade CTCAE reported

- 7 (6%) pts discontinued due to TRAEs
  - 3 discontinued due to neutropenia or its complications
- 30% GCSF usage
- One treatment-related death (sepsis due to febrile neutropenia)

Loriot Y, et al. Annal Oncol (2020) 31 (suppl_4):S1142-S1215; LBA24

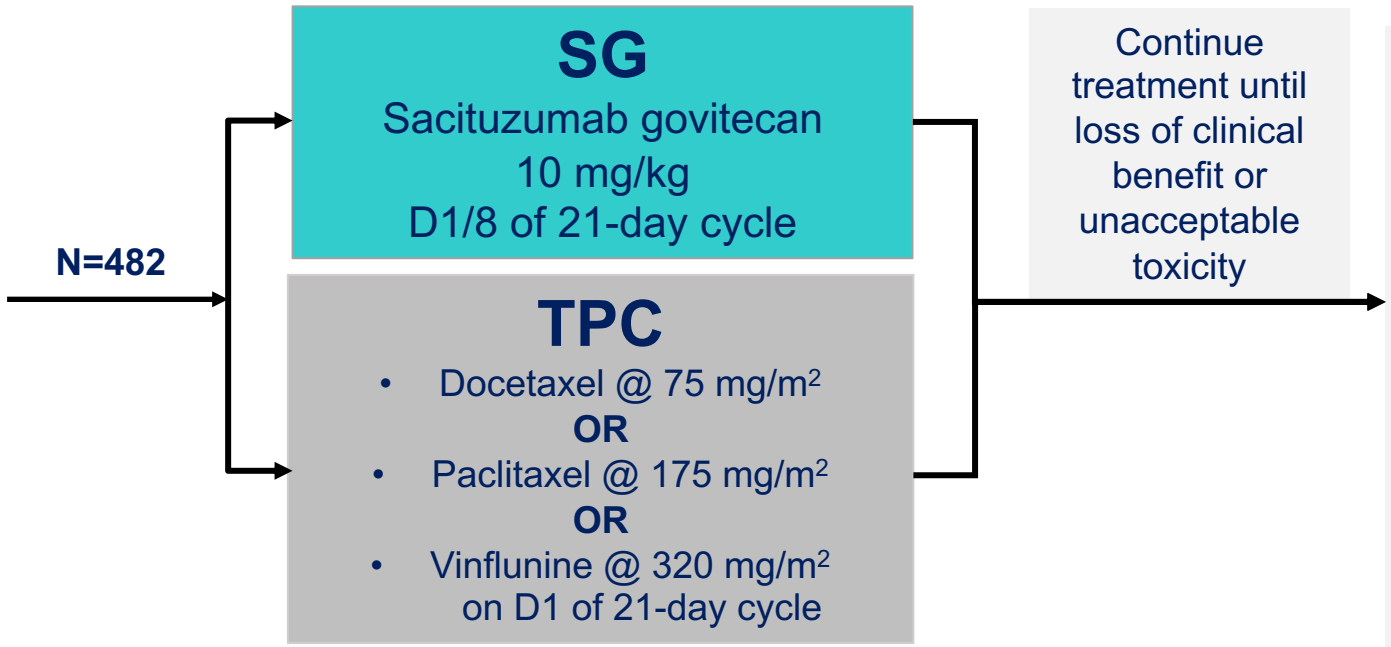
TROPiCS-04 Study Design

Study Population

- Locally advanced unresectable or mUC
- Upper/lower tract tumors
- Mixed histologic types are allowed if urothelial is predominant
- Progression after platinum-based **and** anti–PD-1/PD-L1 therapy

OR

- Platinum in neo/adj setting if progression within 12 months and subsequent CPI



Endpoint (EP)

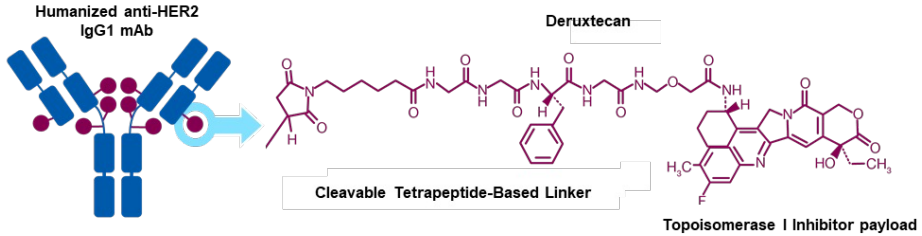
Primary EP:

- OS

Secondary EPs:

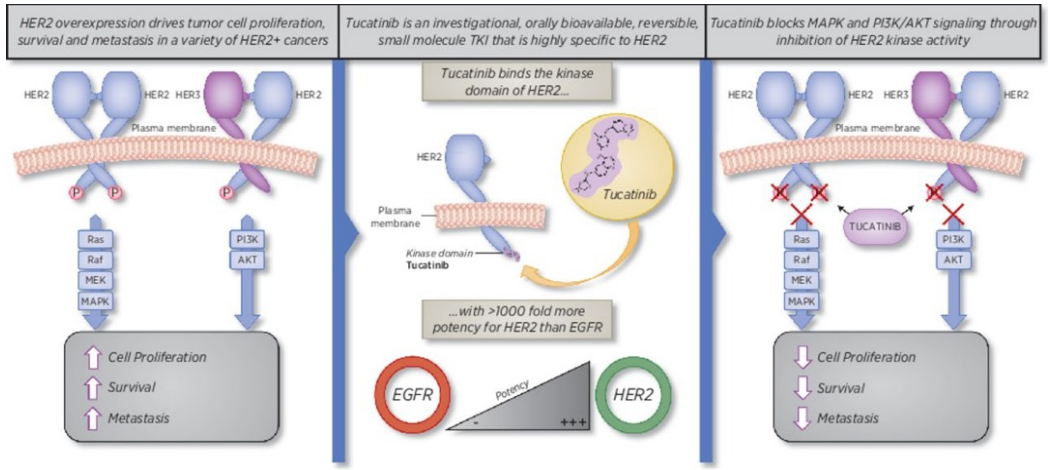
- PFS by PI assessment using RECIST 1.1
- ORR, DOR, and CBR by PI assessment using RECIST 1.1
- EORTC QLQ C30 score and EuroQOL EQ-5D-5L QOL score

HER2 as a Bladder Cancer Target



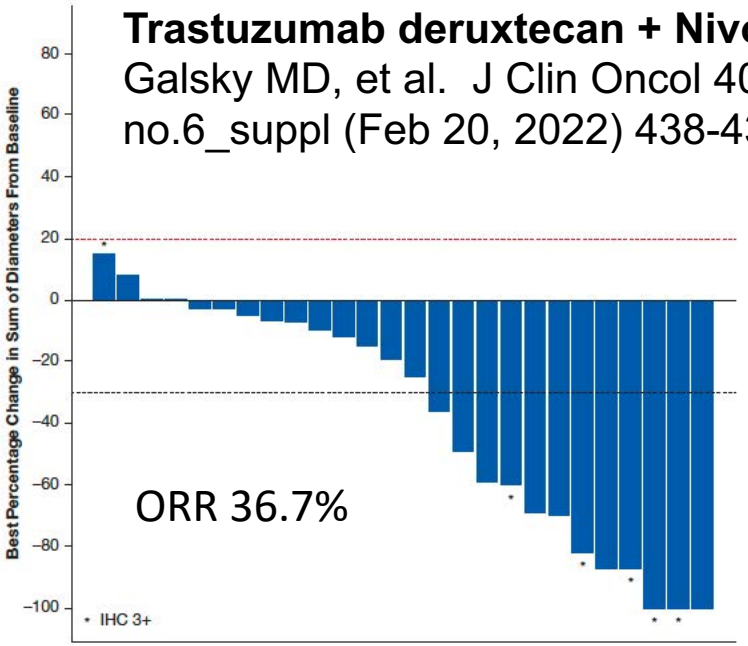
Conjugation chemistry
The tetrapeptide-based cleavable linker is connected to the humanized anti-HER2 IgG1 monoclonal antibody, with the same amino acid sequence as trastuzumab

Tucatinib basket trial with enough responses to go on to Stage 2 of design.



Tucatinib is an investigational agent and its efficacy and safety have not been established

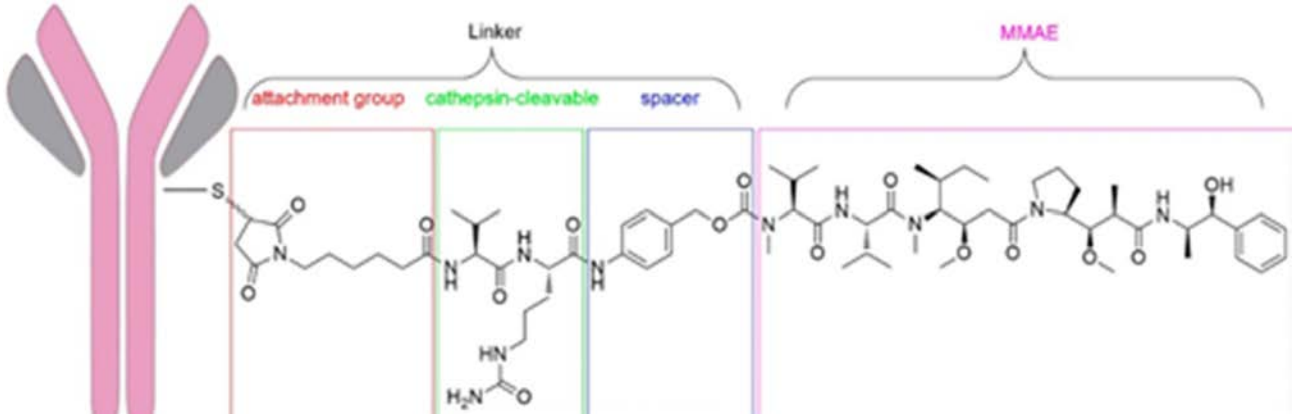
Trastuzumab deruxtecan + Nivolumab
Galsky MD, et al. J Clin Oncol 40, no.6_suppl (Feb 20, 2022) 438-438.



Cohort 3 IHC 3+/2+ (n = 30) (part 2: T-DXd 5.4 mg/kg and nivolumab 360 mg) Best (minimum) percentage change					
n	Mean	SD	Median	Min	Max
26	−37.8	38.52	−22.0	−100	15

*In cohort 3, 4 patients did not have best percentage change available, of whom 2 were IHC 3+.
The line at 20% indicates progressive disease, and the line at −30% indicates a partial response.

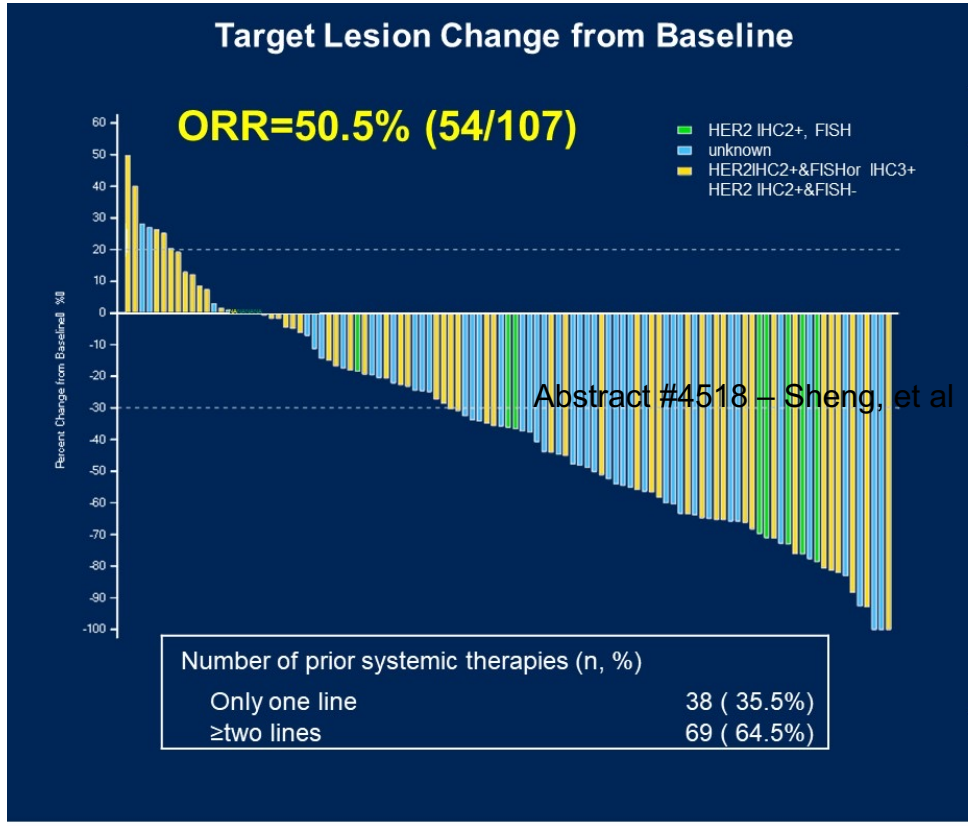
Disitamab vedotin



Hertuzumab

Disitamab Vedotin (RC48) at ASCO 2022

Activity in HER2 2-3+



Abstract #4518 – Sheng, et al

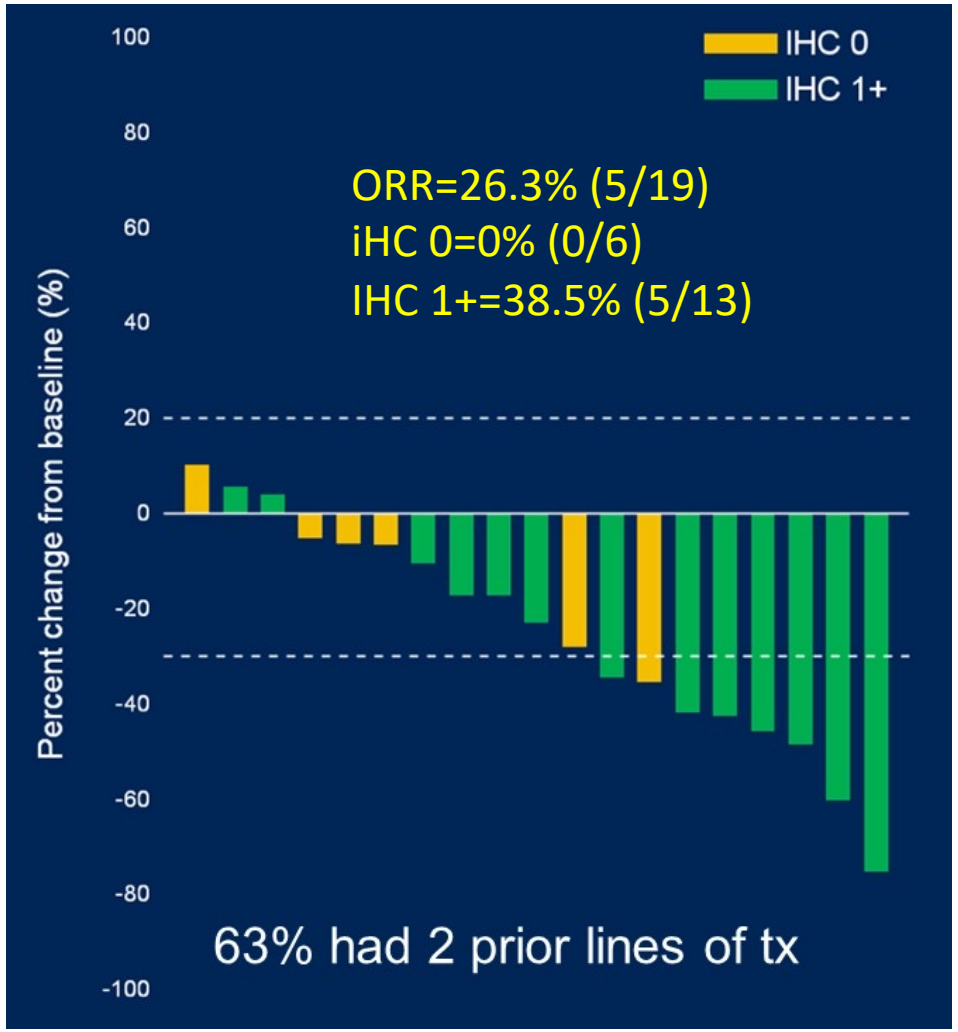
ORR

IHC2+FISH+ or IHC3+ (n=45) = 62.2%

IHC2+FISH- (n=53) = 39.6%

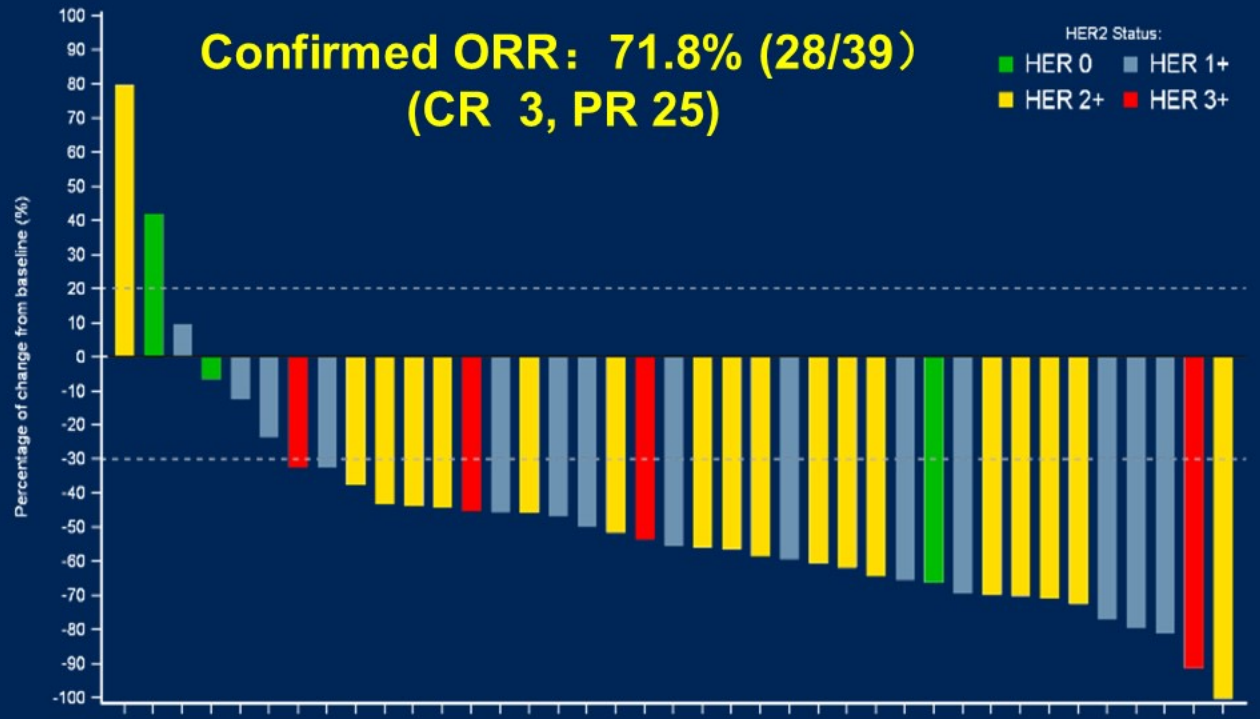
Sheng X, et al. J Clin Oncol 40, no. 16_suppl (June 1, 2022) 4518-4518.

Activity in HER2 1+

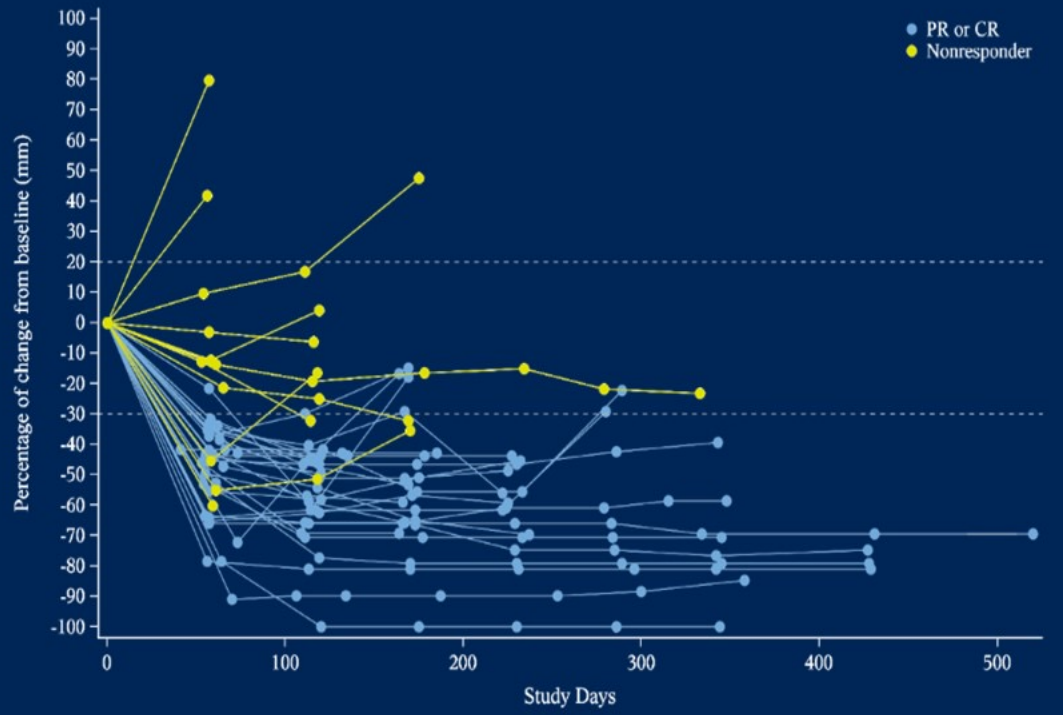


Xu H, et al. J Clin Oncol 40, no. 16_suppl (June 1, 2022) 4519-4519.

Disitamab Vedotin + Toripalimab at ASCO 2022

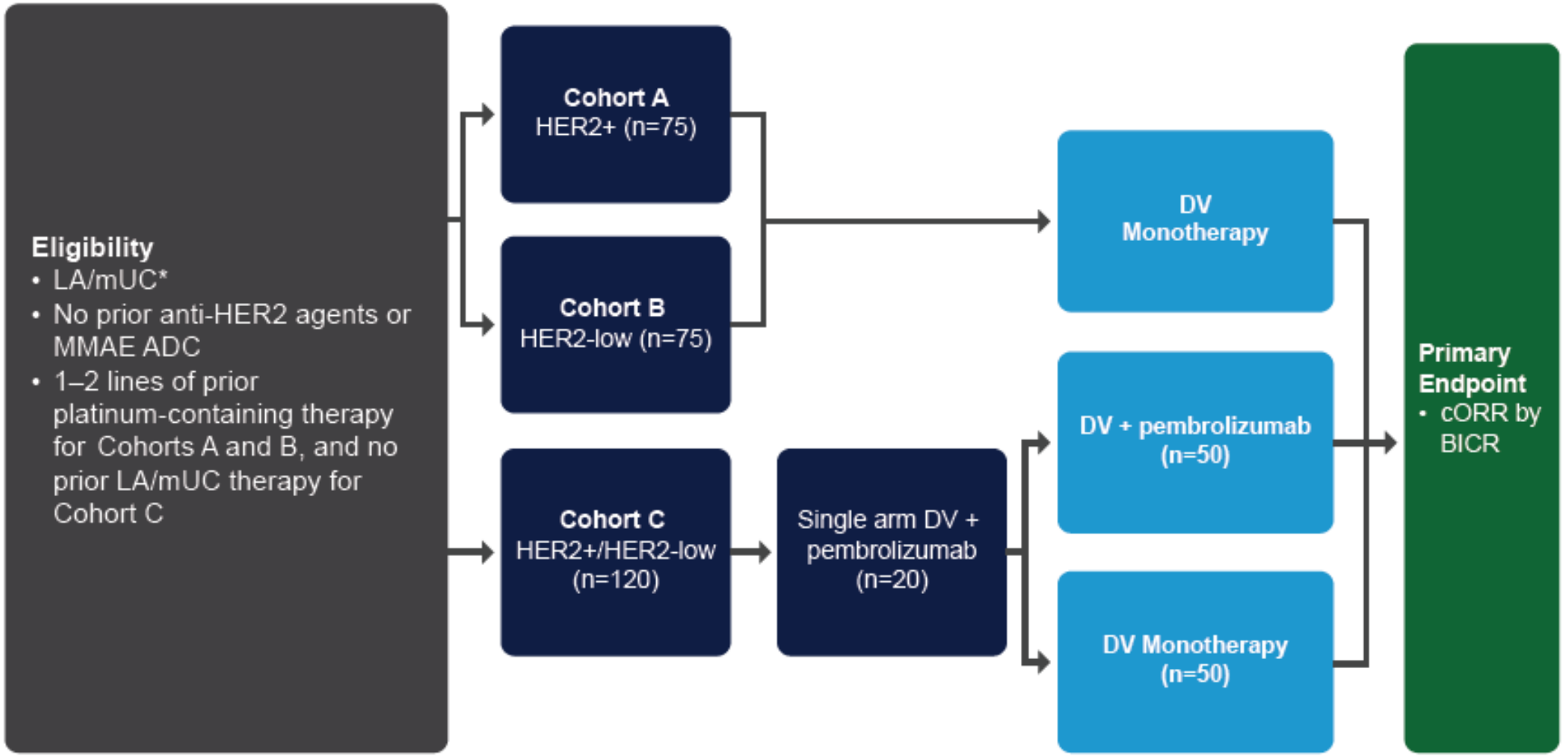


Prior systemic treatment (n,%)	
0 Line	25 (60.98%)
≥1 Lines	16 (39.02%)



Sheng X, et al. J Clin Oncol 40, no. 16_suppl (June 1, 2022) 4520-4520.

Disitamab Phase 2 Trial Schema



ADC: antibody-drug conjugate; **BICR:** blinded independent central review; **cORR:** confirmed objective response rate; **DV: disitamab vedotin; HER2: human epidermal growth factor receptor 2; LA/mUC:** locally advanced unresectable or metastatic urothelial carcinoma; **MMAE:** monomethyl auristatin E

*Histologically-confirmed, including UC originating from the renal pelvis, ureters, bladder, or urethra

Take Home Points

- Fibroblast growth factor 2/3 alterations are the only biomarker proven target with an FDA approved therapy in Erdafitinib
- Antibody drug conjugates offer an exciting technology that recently has shown clinical efficacy in many cancers, including bladder cancer
- Enfortumab vedotin is FDA approved for metastatic urothelial carcinoma patients who have received prior platinum chemotherapy and immune-oncology antibody therapy and now offers an overall survival benefit
- Enfortumab vedotin is also FDA approved in the cisplatin-ineligible disease state post therapy, as this is a significant unmet need
- Enfortumab vedotin has promise in combination with pembrolizumab for first-line metastatic disease with unprecedented ORR
- Other promising ADCs for bladder cancer include Sacituzumab govitecan (has FDA accelerated approval), trastuzumab deruxtecan and disitamab vedotin
- Her2 is being revisited as a promising drug target for patients with urothelial bladder cancer

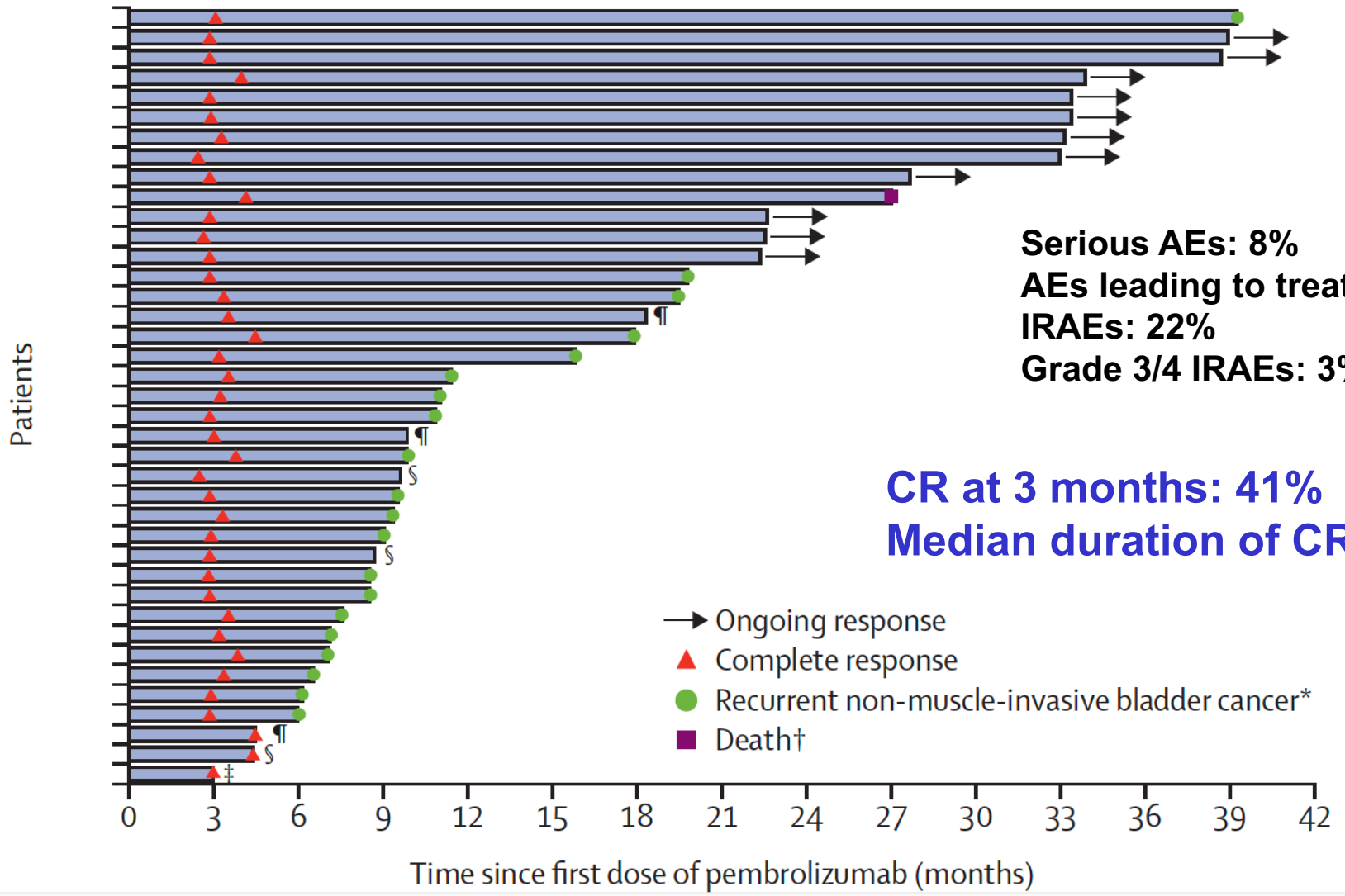
Pembrolizumab monotherapy for the treatment of high-risk non-muscle-invasive bladder cancer unresponsive to BCG (KEYNOTE-057): an open-label, single-arm, multicentre, phase 2 study

Arjun V Balar, Ashish M Kamat, Girish S Kulkarni, Edward M Uchio, Joost L Boormans, Mathieu Roumiguié, Laurence E M Krieger, Eric A Singer, Dean F Bajorin, Petros Grivas, Ho Kyung Seo, Hiroyuki Nishiyama, Badrinath R Konety, Haojie Li, Kijoeng Nam, Ekta Kapadia, Tara Frenkl, Ronald de Wit

***Lancet Oncol* 2021 July;22:919-30.**

RTP RESEARCH TO PRACTICE

KEYNOTE-057: Response, Duration of Response and Summary of Adverse Events (AEs)



Serious AEs: 8%
AEs leading to treatment interruption: 13%
IRAEs: 22%
Grade 3/4 IRAEs: 3%

CR at 3 months: 41%
Median duration of CR: 16.2 mo

Balar AV et al. *Lancet Oncol* 2021;22:919-30.

IRAEs = immune-related adverse events

RTP RESEARCH TO PRACTICE

The NEW ENGLAND JOURNAL of MEDICINE

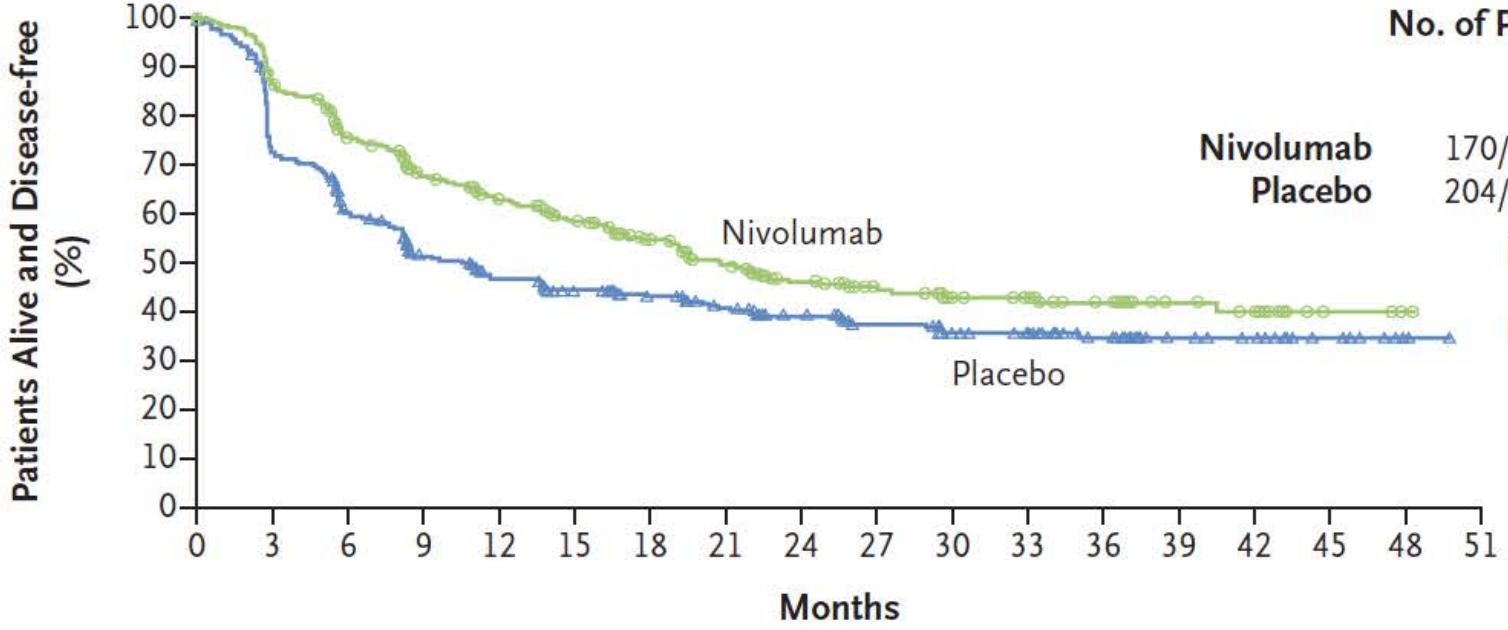
ORIGINAL ARTICLE

Adjuvant Nivolumab versus Placebo in Muscle-Invasive Urothelial Carcinoma

D.F. Bajorin, J.A. Witjes, J.E. Gschwend, M. Schenker, B.P. Valderrama, Y. Tomita, A. Bamias, T. Lebret, S.F. Shariat, S.H. Park, D. Ye, M. Agerbaek, D. Enting, R. McDermott, P. Gajate, A. Peer, M.I. Milowsky, A. Nosov, J. Neif Antonio, Jr., K. Tupikowski, L. Toms, B.S. Fischer, A. Qureshi, S. Collette, K. Unsal-Kacmaz, E. Broughton, D. Zardavas, H.B. Koon, and M.D. Galsky

***N Engl J Med* 2021 June 3;384:2102-14.**

CheckMate 274: Disease-Free Survival in the ITT Population



	No. of Events/ No. of Patients	Disease-free Survival at 6 Mo (95% CI)	Disease-free Survival at 12 Mo (95% CI)
		%	
Nivolumab	170/353	74.9 (69.9–79.2)	62.8 (57.3–67.8)
Placebo	204/356	60.3 (54.9–65.3)	46.6 (41.1–51.9)

Hazard ratio for disease recurrence or death, 0.70 (98.22% CI, 0.55–0.90)
P<0.001

Bajorin DF et al. *N Engl J Med* 2021;384:2102-14.

Analysis of Disease-Free Survival in CheckMate 274 by PD-L1 Combined Positive Score and Tumor Proportion Score

Galsky MD et al.

Genitourinary Cancers Symposium 2022;Abstract 491.

CheckMate 274: Disease-Free Survival (DFS) Outcomes by PD-L1 Combined Positive Score (CPS) and Tumor Cells (TC)

	Treatment	Median DFS (95% CI), months	DFS probability at 6 months (95% CI), %	DFS probability at 12 months (95% CI), %	HR (95% CI) for disease recurrence or death
CPS ≥ 1	NIVO n = 281	24.6 (19.2-NE)	76.7 (71.2-81.3)	66.5 (60.5-71.8)	0.62 (0.49-0.78)
	PBO n = 276	9.4 (8.2-15.2)	59.9 (53.7-65.5)	45.9 (39.7-51.8)	
CPS < 1	NIVO n = 34	6.4 (5.1-12.6)	52.2 (34.2-67.4)	36.1 (20.1-52.3)	1.22 (0.67-2.20)
	PBO n = 38	8.4 (5.4-13.8)	59.5 (42.1-73.3)	37.3 (22.0-52.6)	
TC ≥ 1%	NIVO n = 124	NR (24.6-NE)	74.7 (65.8-81.6)	68.6 (59.4-76.2)	0.50 (0.35-0.71)
	PBO n = 125	8.4 (5.6-17.9)	55.6 (46.2-64.1)	44.8 (35.6-53.6)	
TC < 1%	NIVO n = 191	16.5 (13.4-20.8)	73.7 (66.7-79.4)	59.7 (52.2-66.4)	0.80 (0.61-1.04)
	PBO n = 189	9.6 (8.2-13.9)	62.5 (55.1-69.1)	44.8 (37.5-51.9)	
TC < 1% and CPS ≥ 1	NIVO n = 157	19.2 (15.6-33.4)	78.4 (70.9-84.1)	64.8 (56.6-71.9)	0.73 (0.54-0.99)
	PBO n = 152	10.1 (8.2-19.4)	63.5 (55.2-70.7)	46.4 (38.2-54.2)	

Galsky MD et al. Genitourinary Cancers Symposium 2022;Abstract 491.

Key Ongoing Phase III Trials of Anti-PD-1/PD-L1 Antibodies for Non-Muscle-Invasive Bladder Cancer

Protocol	n	Randomization
ALBAN (NCT03799835)	516	• Atezolizumab + BCG • BCG
POTOMAC (NCT03528694)	1,018	• Durvalumab + BCG • BCG
KEYNOTE-676 (NCT03711032)	1,405	• Pembrolizumab + BCG • BCG
CheckMate 7G8 (NCT04149574)	13	• Nivolumab + BCG • BCG

BCG = Bacillus Calmette-Guérin

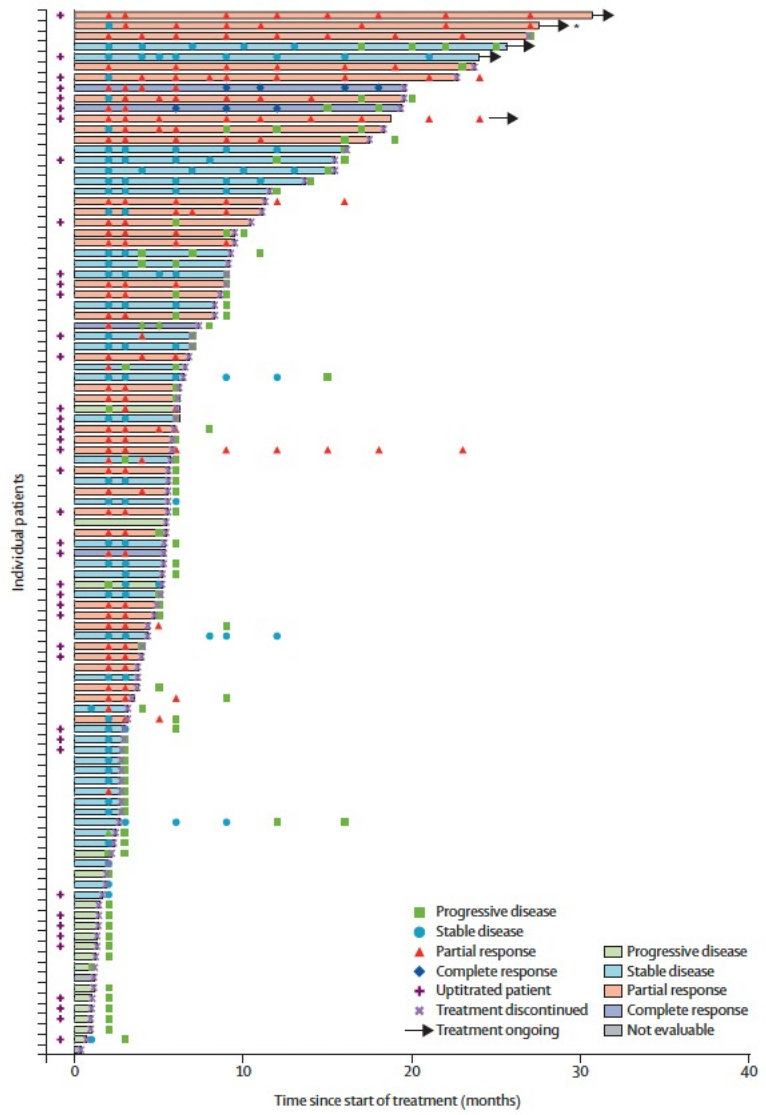
www.clinicaltrials.gov. Accessed October 2022.

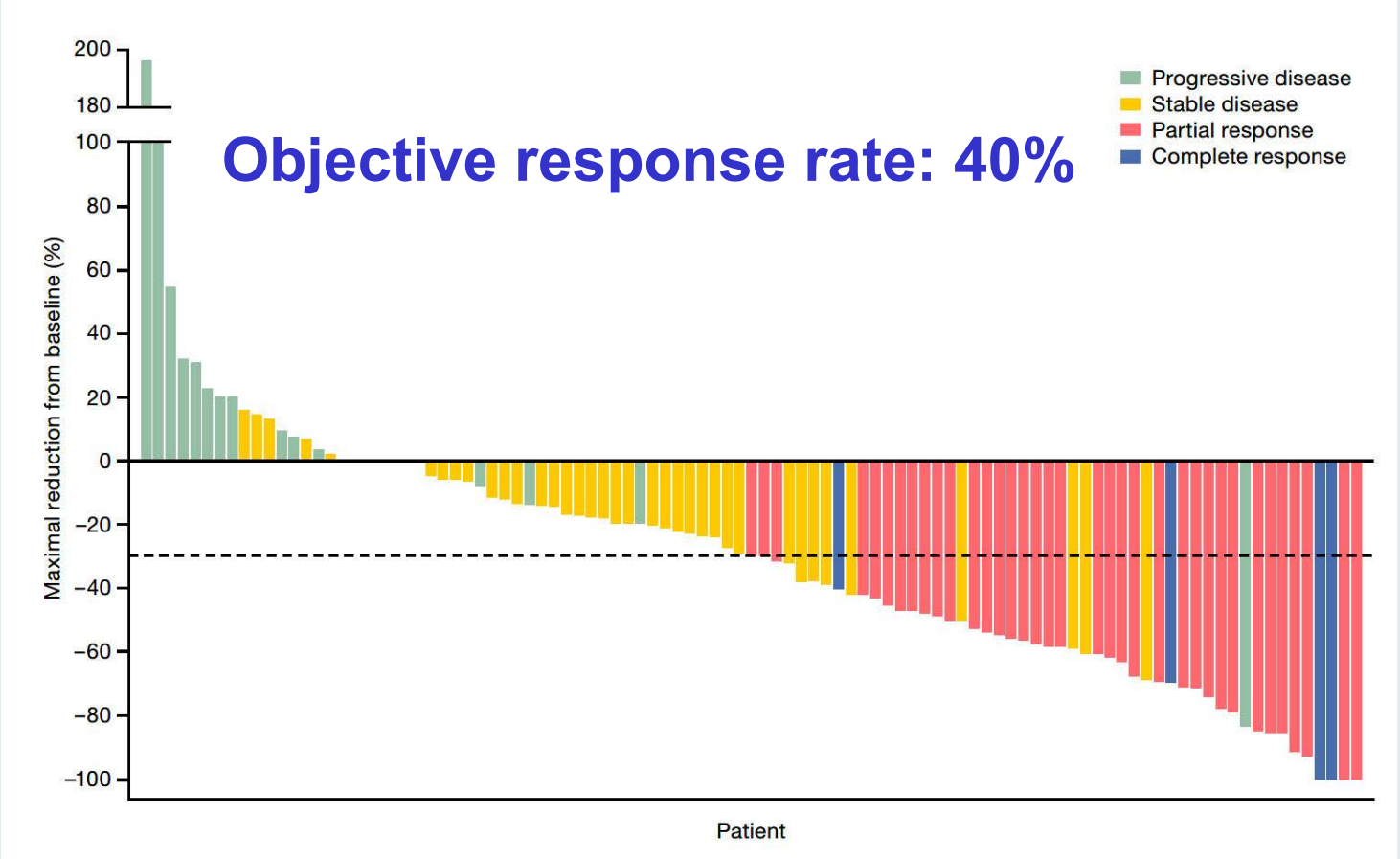
Lancet Oncol 2022;23(2):248-58.

Efficacy and safety of erdafitinib in patients with locally advanced or metastatic urothelial carcinoma: long-term follow-up of a phase 2 study

*Arlene O Siefker-Radtke, Andrea Necchi, Se Hoon Park, Jesús García-Donas, Robert A Huddart, Earle F Burgess, Mark T Fleming, Arash Rezazadeh Kalebasty, Begoña Mellado, Sergei Varlamov, Monika Joshi, Ignacio Duran, Scott T Tagawa, Yousef Zakharia, Sydney Akapame, Ademi E Santiago-Walker, Manish Monga, Anne O'Hagan, Yohann Loriot, on behalf of the BLC2001 Study Group**

BLC2001: Responses in Patients Receiving the Selected 8 mg/Day Erdafitinib UpT Regimen*





* 8 mg of oral erdafitinib once daily continuously in 28-day cycles, with provision for pharmacodynamically guided up-titration to 9 mg/d

Siefker-Radtke AO et al. *Lancet Oncol* 2022;23(2):248-58.

RTP RESEARCH TO PRACTICE

ELSEVIER

Urologic Oncology: Seminars and Original Investigations 000 (2022) 1–9

UROLOGIC ONCOLOGY

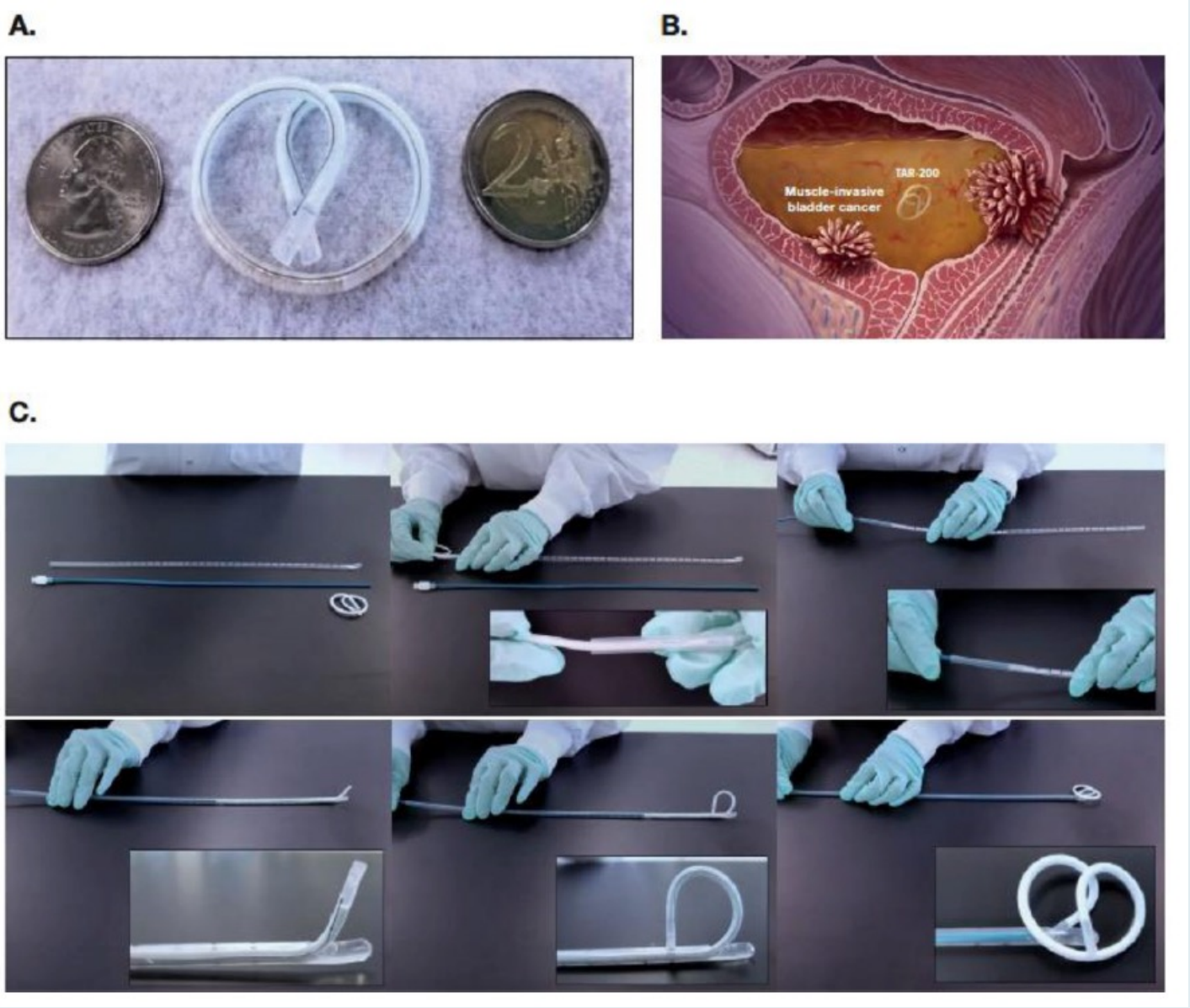
Clinical-Bladder cancer

The safety, tolerability, and efficacy of a neoadjuvant gemcitabine intravesical drug delivery system (TAR-200) in muscle-invasive bladder cancer patients: a phase I trial

Siamak Daneshmand, M.D.[a,*], Iris S.G. Brummelhuis, M.D.[b], Kamal S. Pohar, M.D.[c], Gary D. Steinberg, M.D.[d], Manju Aron, M.D.[e], Christopher J. Cutie, M.D.[f], Kirk A. Keegan, M.D.[f], John C. Maffeo, M.S.H.S.[f], Donald L. Reynolds, Ph.D.[f], Bradley Raybold, M.S.[g], Albert Chau, M.Sc.[h], J. Alfred Witjes, M.D., Ph.D.[b]

Urol Oncol **2022;40(7):344.e1-9.**

Components of TAR-200



TAR-200, a gemcitabine-releasing intravesical system, is formed into a pretzel-like configuration within the bladder.

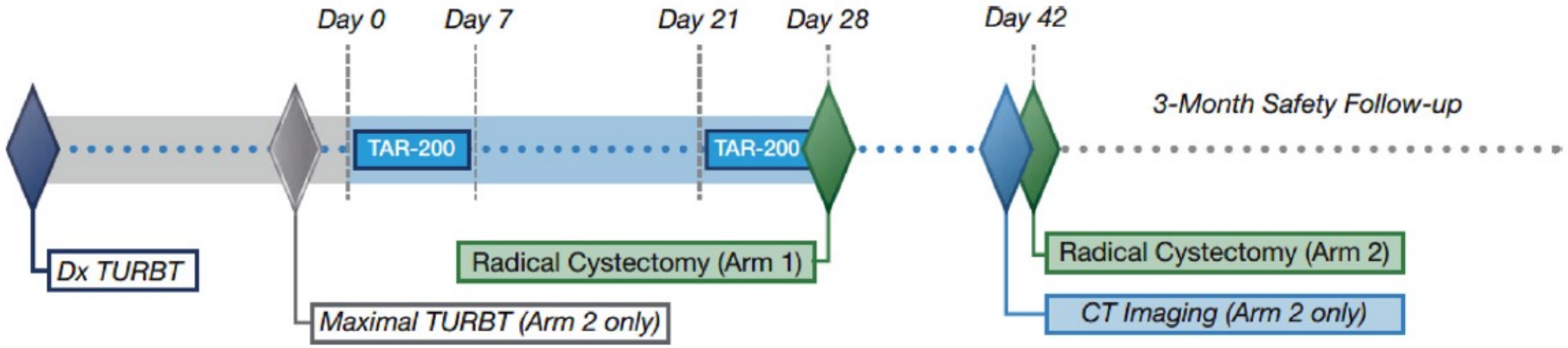
TAR-200

- Consists of a small, flexible silicone tube filled with gemcitabine (A)
- Is designed to release drug directly inside the bladder over the indwelling period (B)
- Is inserted using a TARIS urinary placement catheter (C)

Daneshmand S et al. *Urol Oncol* 2022;40(7):344.e1-9.

RTP RESEARCH TO PRACTICE

TAR-200-101: Study Design and Outcomes



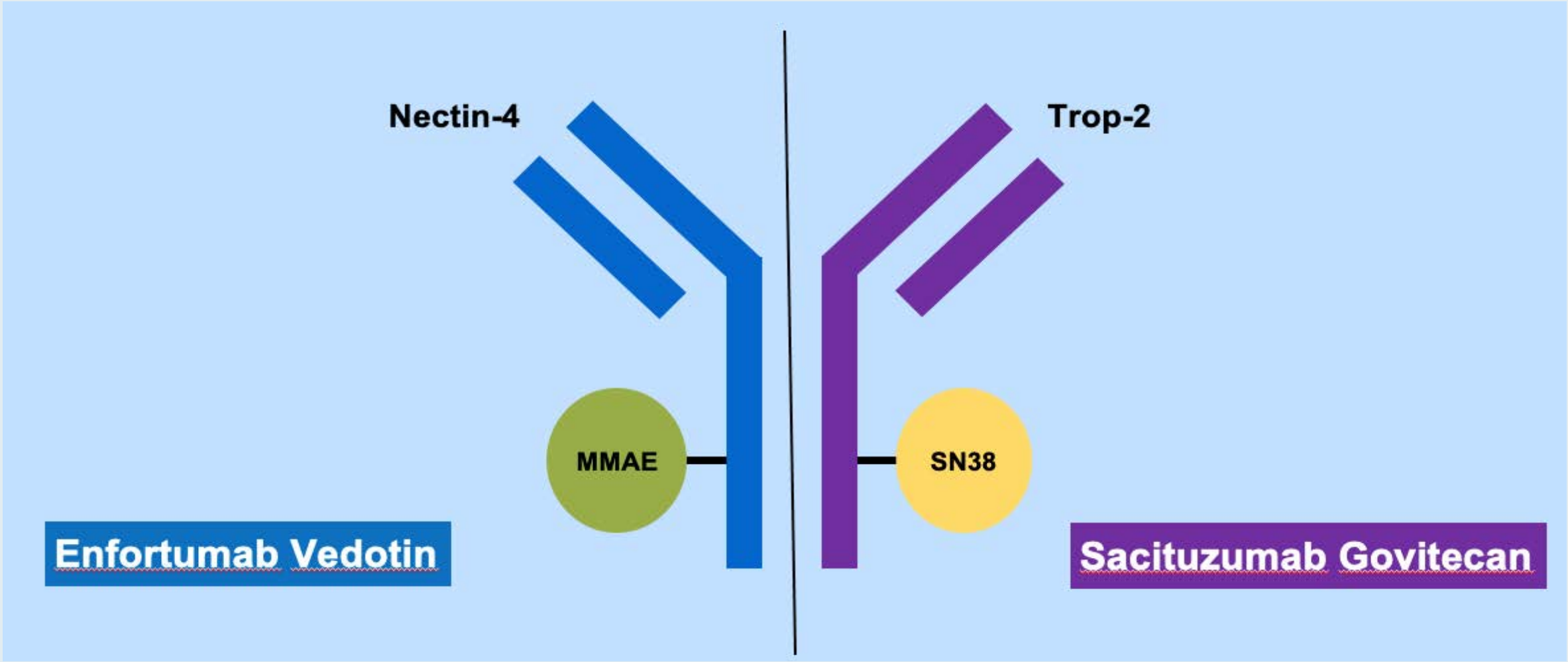
Response	Arm 1 (>3 cm)	Arm 2 (max TURBT)
Underwent pathology at RC, *n/N* (%)	10/11 (90.9)	10/12 (83.3)
Pathologic response, *n/N* (%)	4/10 (40.0)	6/10 (60.0)
Complete response, *n/N* (%)	1/10 (10.0)	3/10 (30.0)
Partial response, *n/N* (%)	3/10 (30.0)	3/10 (30.0)

Treatment-emergent adverse event, *n* (%)	TAR-200 related[a]	Procedure related[b]
Pollakiuria	3 (13)	2 (9)
Urinary incontinence	2 (9)	2 (9)
Micturation urgency	2 (9)	0
Urinary tract infection	1 (4)	2 (9)
Gross hematuria	0	1 (4)
Hematoma[c]	0	0

RC = radical cystectomy

Daneshmand S et al. *Urol Oncol* 2022;40(7):344.e1-9.

Antibody-Drug Conjugates in the Treatment of Urothelial Bladder Cancer



Courtesy of Matthew Galsky, MD

Positive Topline Results Announced from EV-103 Cohort K Evaluating Enfortumab Vedotin Alone or in Combination with Pembrolizumab as First-Line Therapy for Cisplatin-Ineligible Advanced UBC

Press Release: July 26, 2022

Positive topline results were announced from the Phase Ib/II EV-103 clinical trial (KEYNOTE-869) cohort K evaluating enfortumab vedotin-ejfv in combination with pembrolizumab as first-line treatment for patients with unresectable locally advanced or metastatic urothelial cancer (la/mUC) who are not eligible to receive cisplatin-based chemotherapy.

For patients who received enfortumab vedotin and pembrolizumab, results demonstrated a 64.5% confirmed objective response rate (ORR) per blinded independent central review (BICR), the primary endpoint of cohort K. The median duration of response (DOR) per BICR was not reached… Overall, the results are generally consistent with previously reported efficacy and safety results of the EV-103 dose-escalation cohort and expansion cohort A. Additional cohort K results will be reported at an upcoming scientific congress.

EV-103 cohort K is a randomized cohort investigating enfortumab vedotin alone or in combination with pembrolizumab as first-line treatment for patients with unresectable la/mUC who are not eligible to receive cisplatin-based chemotherapy. Secondary endpoints include ORR per investigator assessment; DOR, disease control rate and progression-free survival per BICR and investigator assessment; overall survival; and assessment of safety.

https://www.businesswire.com/news/home/20220726005377/en/

RTP RESEARCH TO PRACTICE

2022 ASCO® ANNUAL MEETING

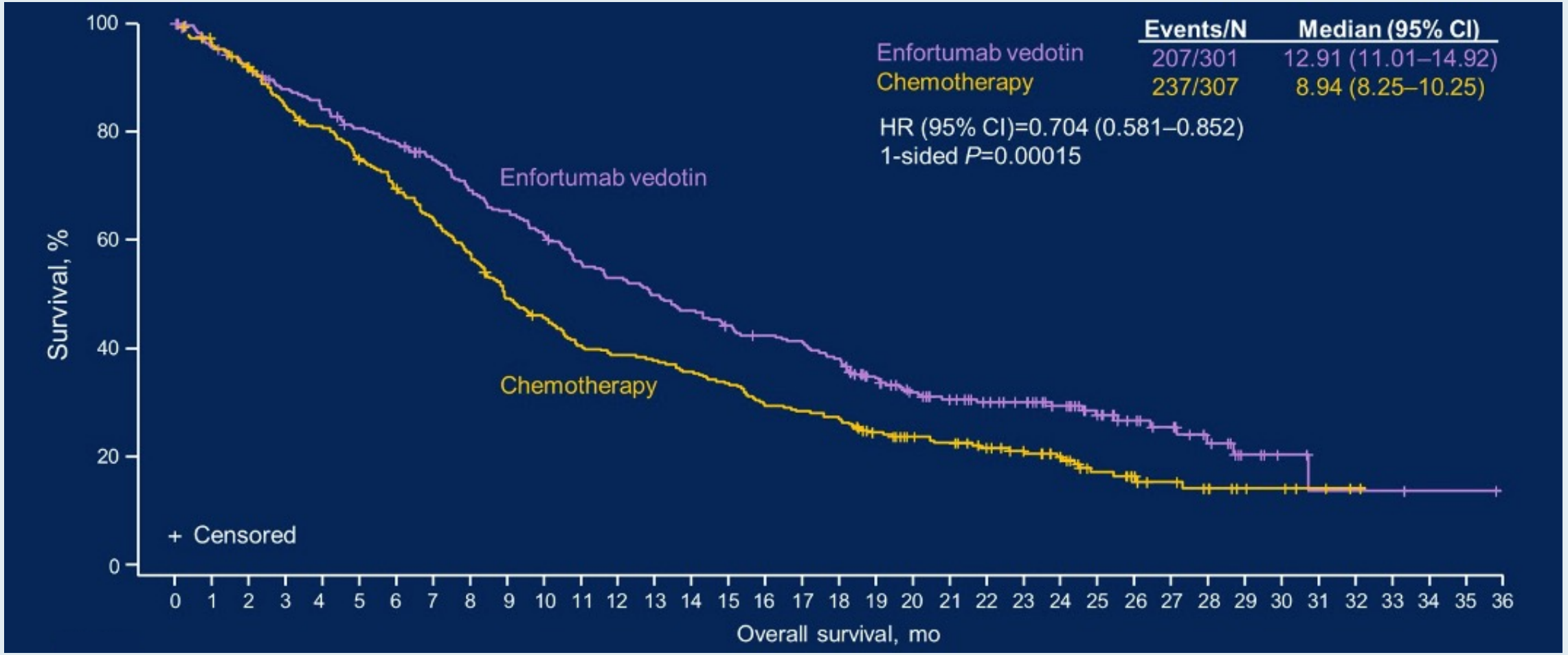
Abstract 4516

Long-Term Outcomes in EV-301: 24-Month Findings From the Phase 3 Trial of Enfortumab Vedotin vs Chemotherapy in Patients With Previously Treated Advanced Urothelial Carcinoma

Jonathan E. Rosenberg, MD[1]; Thomas Powles, MD[2]; Guru P. Sonpavde, MD[3]; Yohann Loriot, MD, PhD[4]; Ignacio Duran, MD, PhD[5]; Jae-Lyun Lee, MD, PhD[6]; Nobuaki Matsubara, MD[7]; Christof Vulsteke, MD, PhD[8]; Daniel Castellano, MD[9]; Ronac Mamtani, MD[10]; Chunzhang Wu, PhD[11]; Maria Matsangou, MD[11]; Mary Campbell, MD[12]; Daniel P. Petrylak, MD[13]

[1]Department of Medicine, Division of Solid Tumor Oncology, Genitourinary Oncology Service, Memorial Sloan Kettering Cancer Center, New York, NY; [2]Barts Cancer Institute, CRUK Experimental Cancer Medicine Centre, London, UK; [3]Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA; [4]Gustave Roussy, Université Paris-Saclay, Villejuif, France; [5]Hospital Universitario Marques de Valdecilla, IDIVAL, Cantabria, Spain; [6]Asan Medical Center and University of Ulsan College of Medicine, Seoul, South Korea; [7]National Cancer Center Hospital East, Chiba, Japan; [8]Center for Oncological Research (CORE), University of Antwerp, Integrated Cancer Center Ghent, Ghent, Belgium; [9]Hospital Universitario 12 de Octubre, Madrid, Spain; [10]Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA; [11]Astellas Pharma, Inc., Northbrook, IL; [12]Seagen Inc., Bothell, WA; [13]Yale Cancer Center, New Haven, CT

EV-301: Overall Survival



Rosenberg JE et al. ASCO 2022;Abstract 4516.

RTP RESEARCH TO PRACTICE

ASCO Genitourinary Cancers Symposium 2022;Abstract 434.

TROPHY-U-01 Cohort 3: Sacituzumab Govitecan (SG) in Combination With Pembrolizumab (Pembro) in Patients (pts) With Metastatic Urothelial Cancer (mUC) Who Progressed After Platinum (PLT)-Based Regimens

Petros Grivas,[1] Damien Pouessel,[2] Chandler H. Park,[3] Philippe Barthelemy,[4] Manojkumar Bupathi,[5] Daniel P. Petrylak,[6] Neeraj Agarwal,[7] Aude Fléchon,[8] Chethan Ramamurthy,[9] Nancy B. Davis,[10] Alejandro Recio-Boiles,[11] Scott T. Tagawa,[12] Cora N. Sternberg,[12] Astha Bhatia,[13] Cabilia Pichardo,[13] Trishna Goswami,[13] and Yohann Loriot[14]

[1]University of Washington, Seattle Cancer Care Alliance, Fred Hutchinson Cancer Research Center, Seattle, WA, USA; [2]Department of Medical Oncology & Clinical Research Unit, Institut Claudius Regaud/Institut Universitaire du Cancer de Toulouse (IUCT-Oncopôle), Toulouse, France; [3]Norton Cancer Institute, Louisville, KY, USA; [4]Institut de Cancérologie Strasbourg Europe, Strasbourg, France; [5]Rocky Mountain Cancer Centers, Littleton, CO, USA; [6]Yale School of Medicine, New Haven, CT, USA; [7]Huntsman Cancer Institute, Salt Lake City, UT, USA; [8]Centre Léon Bérard, Lyon, France; [9]University of Texas Health Science Center at San Antonio, San Antonio, TX, USA; [10]Vanderbilt-Ingram Cancer Center, Nashville, TN, USA; [11]University of Arizona Cancer Center, Tucson, AZ, USA; [12]Weill Cornell Medical College of Cornell University, New York, NY, USA; [13]Gilead Sciences, Inc, Morris Plains, NJ, USA; and [14]Institut de Cancérologie Gustave Roussy, Université Paris-Saclay, Villejuif, France

Abstract # 434
ClinicalTrials.gov Number: NCT03547973.

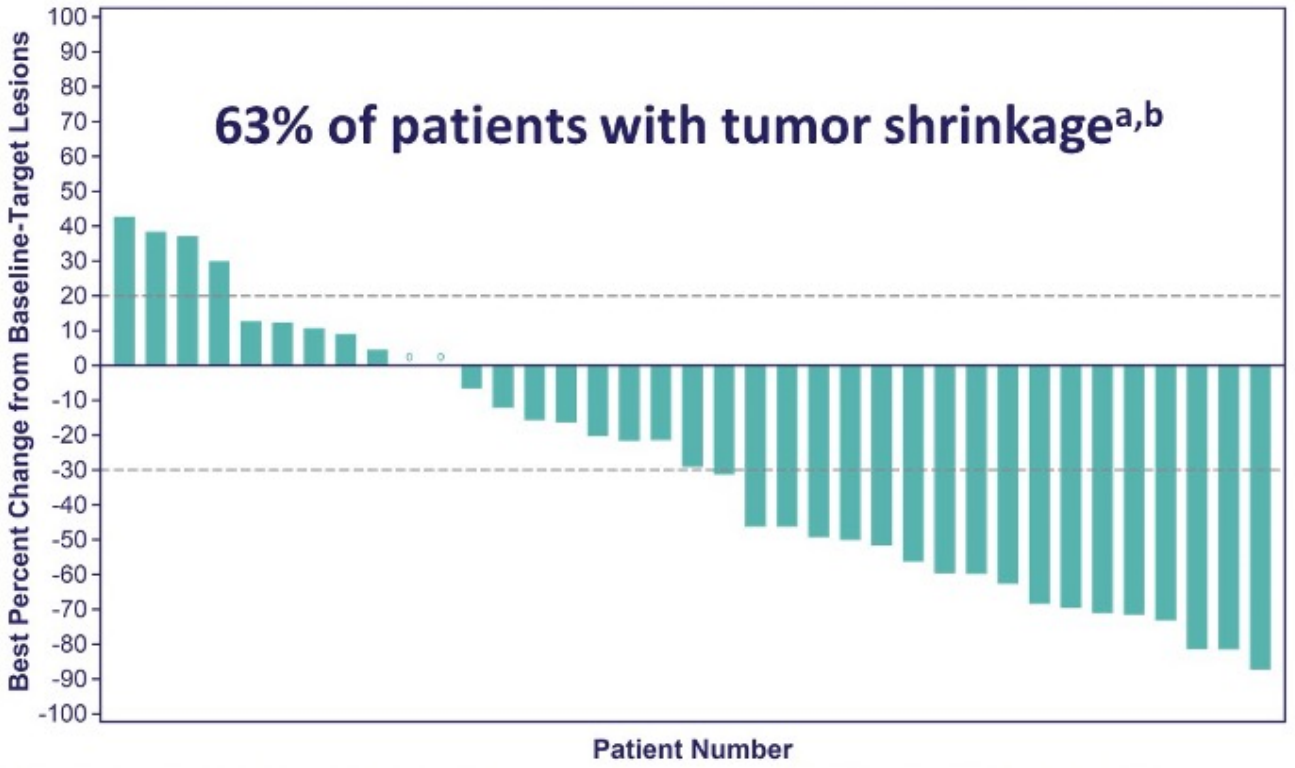
@PGrivasMDPhD

TROPHY U-01

RTP RESEARCH TO PRACTICE

TROPHY U-01: Overall Response and Best Change from Baseline in Tumor Size

- Median follow-up: 5.8 months (data cutoff date: 2021-09-24)
- Median time to response: 2 months (1.3–2.8; n=14)
- Median DOR not yet reached: N/A (2.80-N/A)
- Median PFS (95% CI), 5.5 months (1.7–NR); median OS, not reached



	Cohort 3[a] (N=41)
Objective response rate (CR + PR), n (%) [95%CI]	14 (34) [20.1-50.6]
Objective response rate (CR + PR), evaluable patients, n (%)	14 (38)
Best overall response, n (%)	
CR	1 (2)
PR	13 (32)
SD	11 (27)
SD ≥ 6 months	*4 (10)*
PD	12 (29)
Not assessed	4 (10)
Clinical Benefit Rate (CR + PR + SD), n (%) [95%CI]	25 (61) [44.5-75.8]

Grivas P et al. Genitourinary Cancers Symposium 2022;Abstract 434.

RTP RESEARCH TO PRACTICE

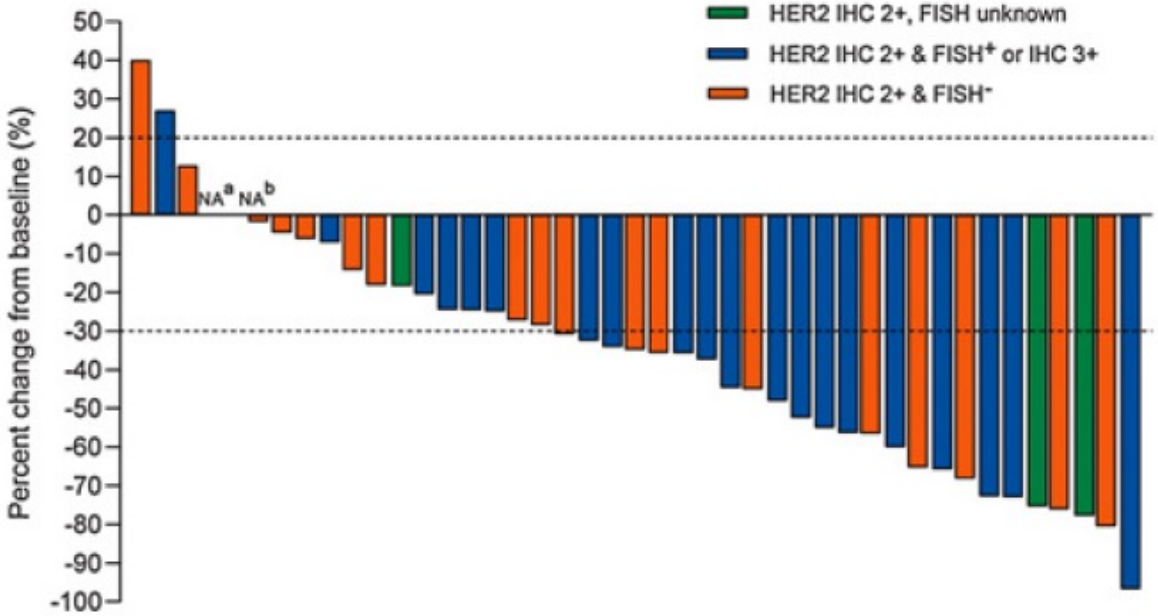
CLINICAL CANCER RESEARCH | CLINICAL TRIALS: TARGETED THERAPY

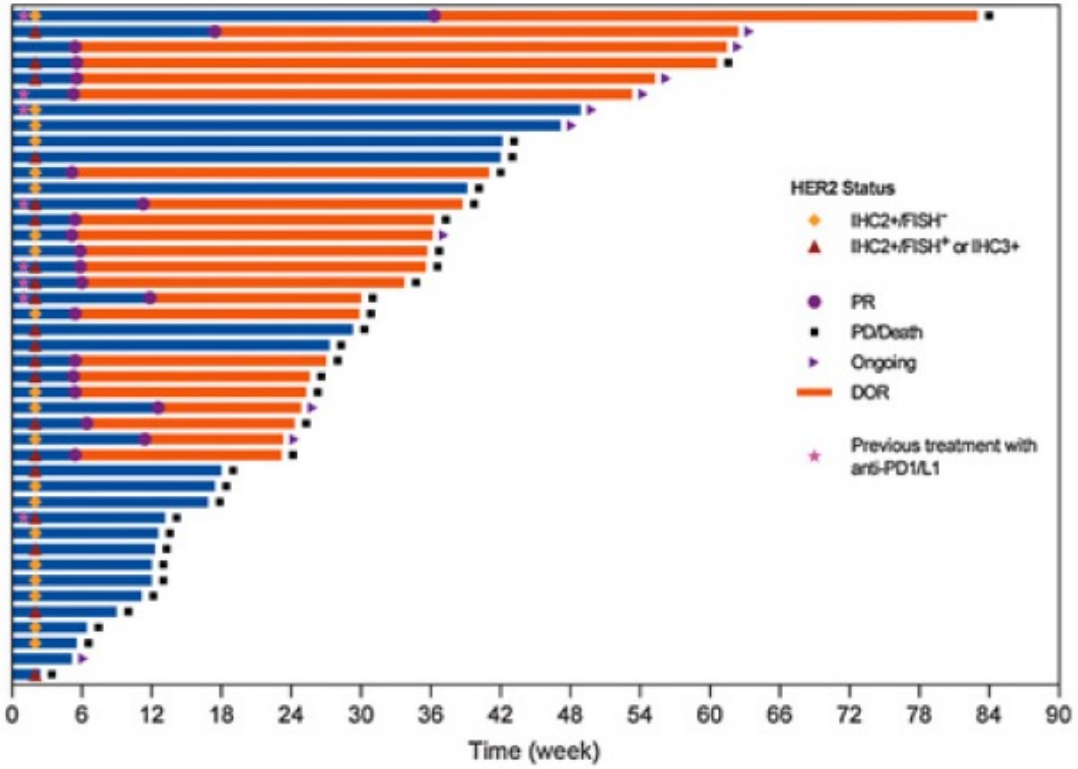
Open-label, Multicenter, Phase II Study of RC48-ADC, a HER2-Targeting Antibody–Drug Conjugate, in Patients with Locally Advanced or Metastatic Urothelial Carcinoma AC

Xinan Sheng[1], Xieqiao Yan[1], Lin Wang[2], Yanxia Shi[3], Xin Yao[4], Hong Luo[5], Benkang Shi[6], Jiyan Liu[7], Zhisong He[8], Guohua Yu[9], Jianming Ying[10], Weiqing Han[11], Changlu Hu[12], Yun Ling[10], Zhihong Chi[1], Chuanliang Cui[1], Lu Si[1], Jianmin Fang[13,14], Aiping Zhou[2], and Jun Guo[1]

Clin Cancer Res 2021;27(1):43-51.

Phase II Study of Disitamab Vedotin (RC48) for HER2-Positive Locally Advanced or Metastatic Urothelial Carcinoma





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Thank you for joining us!

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

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