Recent Advances and Real-World Implications in Medical Oncology: A Daylong Multitumor Educational Symposium in Partnership with the American Oncology Network

A CME/MOC- and NCPD-Accredited Hybrid Event

Saturday, August 6, 2022
9:00 AM – 4:30 PM PT

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Welcome AON Members!

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Agenda

Module 1 — Breast Cancer: *Drs Burstein and O'Shaughnessy*

Module 2 — Genitourinary Cancers: *Drs Agarwal and Srinivas*

Module 3 — Multiple Myeloma: *Drs Fonseca and Patel*

Module 4 — Chronic Lymphocytic Leukemia and Lymphomas: *Drs Kahl and Moskowitz*

Module 5 — Gastrointestinal Cancers: *Drs Mehta and Philip*

Module 6 — Lung Cancer: *Drs Dagogo-Jack and Ramalingam*

Breast Cancer Faculty

Harold J Burstein, MD, PhD
Institute Physician, Dana-Farber Cancer Institute
Professor of Medicine, Harvard Medical School
Boston, Massachusetts

Joyce O'Shaughnessy, MD
Celebrating Women Chair in Breast Cancer Research
Baylor University Medical Center
Director, Breast Cancer Research Program
Texas Oncology
US Oncology
Dallas, Texas

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Co-Moderators

Breast Cancer
Stephen “Fred” Divers, MD
American Oncology Network
Hot Springs, Arkansas

CLL and Lymphomas
Jeanna L Knoble, MD
Zangmeister Cancer Center
Columbus, Ohio

Genitourinary Cancers
Michael J Castine, MD
Hematology Oncology Clinic
Baton Rouge, Louisiana

Gastrointestinal Cancers
Pavani Ellipeddi, MD
Hematology Oncology Clinic
Baton Rouge, Louisiana

Multiple Myeloma
Taral Patel, MD
Zangmeister Cancer Center
Columbus, Ohio

Lung Cancer
Ram Trehan, MD
George Washington University
Silver Spring, Maryland

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MODULE 1: Breast Cancer

Co-Moderator

Stephen “Fred” Divers, MD
American Oncology Network
Hot Springs, Arkansas

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Breast Cancer Agenda

Module 1: HER2-Positive Disease

Module 2: Use of PARP Inhibitors in Localized HER2-Negative Disease (OlympiA/Olaparib)

Module 3: Triple-Negative Disease

Module 4: ER/PR-Positive, HER2-Negative Disease

Breast Cancer Agenda

Module 1: HER2-Positive Disease

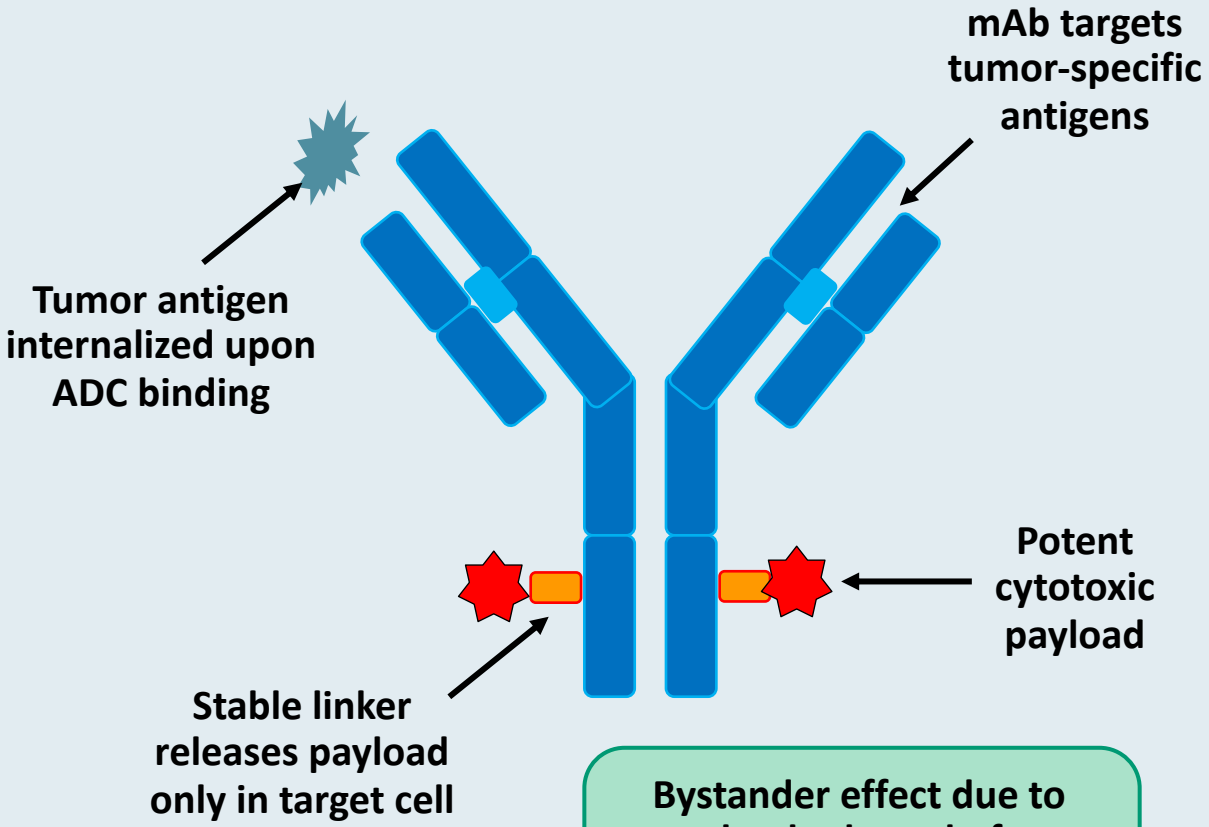
- Use of trastuzumab deruxtecan for HER2-low breast cancer: Impact of ER status, optimal sequencing, management of interstitial lung disease – DESTINY-Breast04 trial
- Sequencing of agents for patients with brain metastases – TUXEDO-1, HER2CLIMB trials
- Adjuvant and postadjuvant anti-HER2 treatment – APHINITY, ExteNET trials

Module 2: Use of PARP Inhibitors in Localized HER2-Negative Disease (OlympiA/Olaparib)

Module 3: Triple-Negative Disease

Module 4: ER/PR-Positive, HER2-Negative Disease

HER2-Targeting Antibody-Drug Conjugates (ADCs)



ADC attributes	T-DM1	T-DXd
Payload mechanism of action	Antimicrotubule	Topoisomerase I inhibitor
Drug-to-antibody ratio	~3.5:1	~8:1
Tumor-selective cleavable linker?	No	Yes
Evidence of bystander antitumor effect?	No	Yes

Schmid P et al. SABCS 2021.

Trastuzumab Deruxtecan Approved for Patients with HER2-Positive Metastatic Breast Cancer Treated with a Prior Anti-HER2-Based Regimen

Press Release: May 5, 2022

"Fam-trastuzumab deruxtecan-nxki has been approved in the US for the treatment of adult patients with unresectable or metastatic HER2-positive breast cancer who have received a prior anti-HER2-based regimen either in the metastatic setting, or in the neoadjuvant or adjuvant setting and have developed disease recurrence during or within six months of completing therapy.

The approval by the Food and Drug Administration (FDA) was based on positive results from the DESTINY-Breast03 Phase III trial that showed fam-trastuzumab deruxtecan-nxki reduced the risk of disease progression or death by 72% versus trastuzumab emtansine (T-DM1) (hazard ratio [HR] 0.28; $p<0.0001$) in patients with HER2-positive unresectable and/or metastatic breast cancer previously treated with trastuzumab and a taxane.

The approval was granted under the FDA's Real-Time Oncology Review (RTOR) program and converts the accelerated approval of fam-trastuzumab deruxtecan-nxki in later line HER2-positive metastatic breast cancer to standard approval, broadening fam-trastuzumab deruxtecan-nxki's breast cancer indication in the US to earlier lines of use in patients with HER2-positive metastatic breast cancer."

https://finance.yahoo.com/news/enhertu-fam-trastuzumab-deruxtecan-nxki-110000498.html

RTP RESEARCH TO PRACTICE

The NEW ENGLAND JOURNAL of MEDICINE

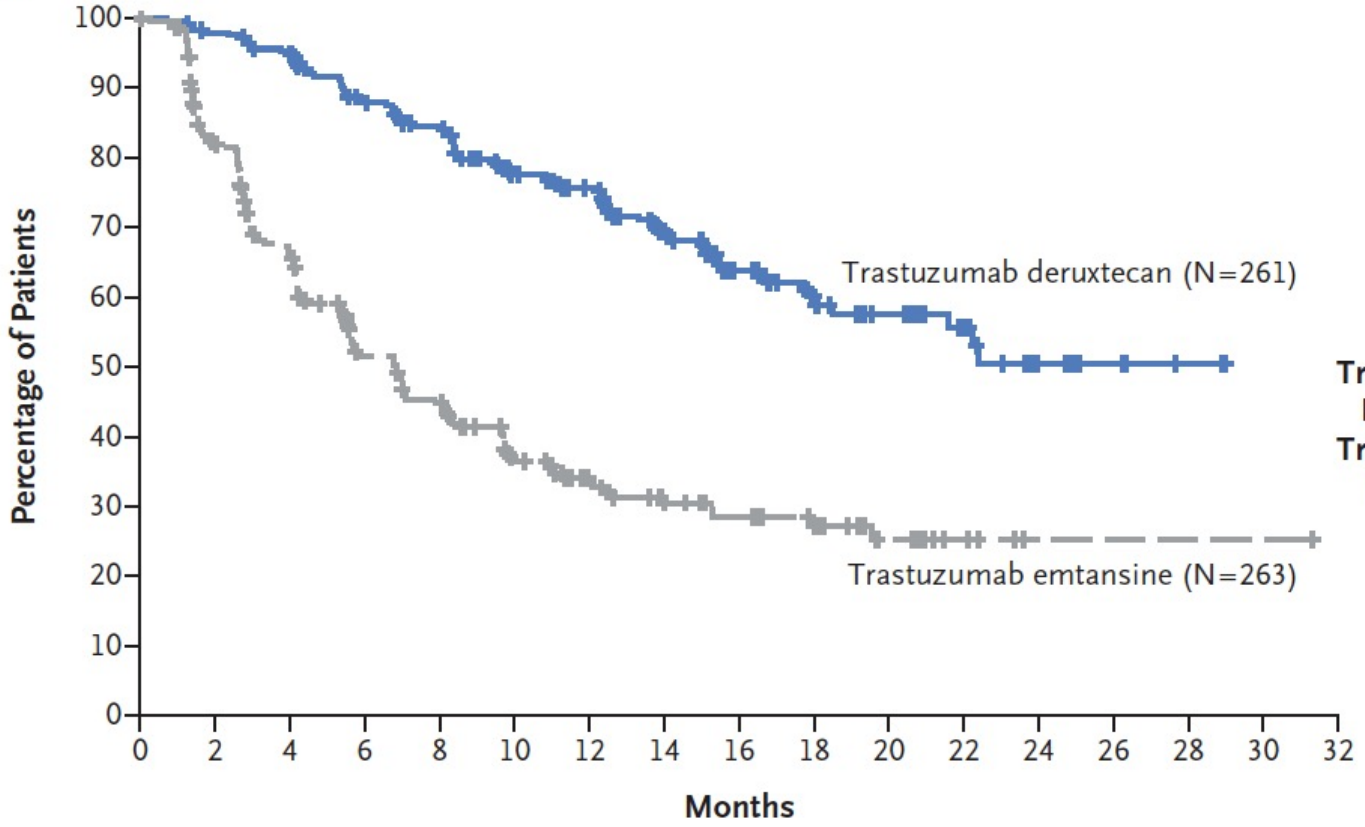
N Engl J Med 2022;386(12):1143-54.

ORIGINAL ARTICLE

Trastuzumab Deruxtecan versus Trastuzumab Emtansine for Breast Cancer

J. Cortés, S.-B. Kim, W.-P. Chung, S.-A. Im, Y.H. Park, R. Hegg, M.H. Kim, L.-M. Tseng, V. Petry, C.-F. Chung, H. Iwata, E. Hamilton, G. Curigliano, B. Xu, C.-S. Huang, J.H. Kim, J.W.Y. Chiu, J.L. Pedrini, C. Lee, Y. Liu, J. Cathcart, E. Bako, S. Verma, and S.A. Hurvitz, for the DESTINY-Breast03 Trial Investigators*

DESTINY-Breast03: Progression-Free Survival



	Median Progression-free Survival (95% CI)	12-Mo Progression-free Survival (95% CI)
	mo	%
Trastuzumab Deruxtecan	NR (18.5–NE)	75.8 (69.8–80.7)
Trastuzumab Emtansine	6.8 (5.6–8.2)	34.1 (27.7–40.5)

Hazard ratio for disease progression or death, 0.28 (95% CI, 0.22–0.37)
P<0.001

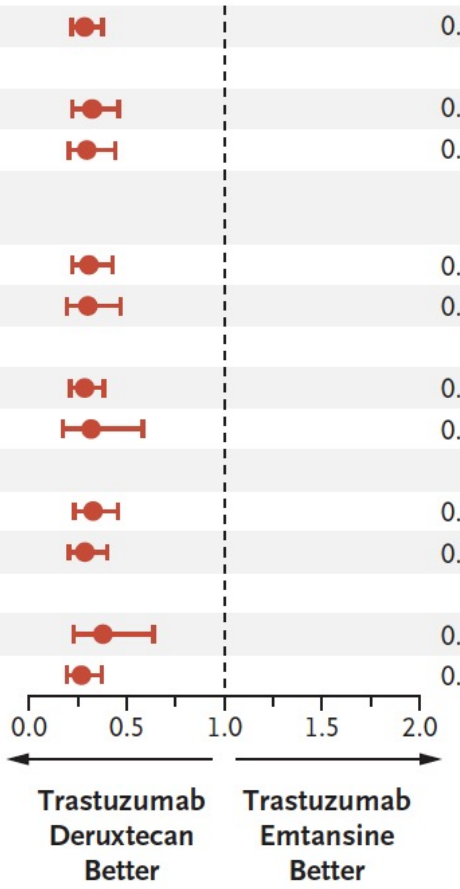
No. at Risk

Trastuzumab deruxtecan	261	250	240	214	200	168	150	112	79	53	36	25	10	5	2	
Trastuzumab emtansine	263	200	155	108	93	65	51	37	29	21	12	6	1	1	1	1	0

Cortés J et al. *N Engl J Med* 2022;386(12):1143-54.

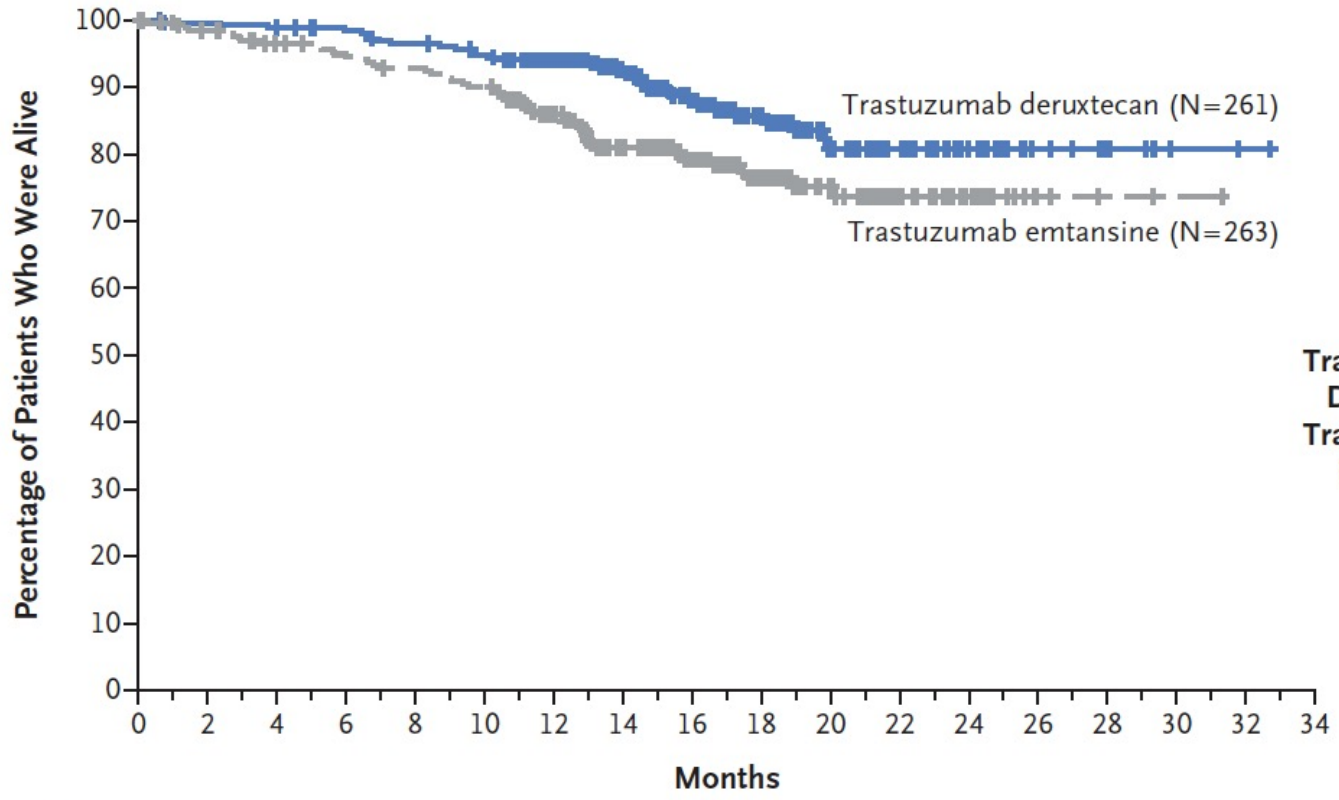
DESTINY-Breast03: Progression-Free Survival in Prespecified Subgroups

Subgroup	No. of Patients	No. of Events/No. of Patients		Median Progression-free Survival (95% CI) *mo*		Hazard Ratio for Disease Progression or Death (95% CI)
		Trastuzumab deruxtecan	Trastuzumab emtansine	Trastuzumab deruxtecan	Trastuzumab emtansine	
All patients		87/261	158/263	NE (18.5–NE)	6.8 (5.6–8.2)	0.28 (0.22–0.37)
Hormone-receptor status						
Positive	272	46/133	84/139	22.4 (17.7–NE)	6.9 (4.2–9.8)	0.32 (0.22–0.46)
Negative	248	41/126	73/122	NE (18.0–NE)	6.8 (5.4–8.3)	0.30 (0.20–0.44)
Previous pertuzumab treatment						
Yes	320	57/162	98/158	NE (18.5–NE)	6.8 (5.4–8.3)	0.30 (0.22–0.43)
No	204	30/99	60/105	NE (16.5–NE)	7.0 (4.2–9.7)	0.30 (0.19–0.47)
Visceral disease						
Yes	384	72/195	123/189	22.2 (16.5–NE)	5.7 (4.2–7.0)	0.28 (0.21–0.38)
No	140	15/66	35/74	NE (NE–NE)	11.3 (6.8–NE)	0.32 (0.17–0.58)
Lines of previous therapy						
0 or 1	258	46/132	75/126	22.4 (17.9–NE)	8.0 (5.7–9.7)	0.33 (0.23–0.48)
≥2	266	41/129	83/137	NE (16.8–NE)	5.6 (4.2–7.1)	0.28 (0.19–0.41)
Stable brain metastases						
Yes	114	31/62	31/52	15.0 (12.6–22.2)	5.7 (2.9–7.1)	0.38 (0.23–0.64)
No	410	56/199	127/211	NE (22.4–NE)	7.0 (5.5–9.7)	0.27 (0.19–0.37)



Cortés J et al. *N Engl J Med* 2022;386(12):1143-54.

DESTINY-Breast03: First Interim Analysis of Overall Survival



	Median Overall Survival (95% CI)	12-Mo Overall Survival (95% CI)
	mo	%
Trastuzumab Deruxtecan	NE (NE–NE)	94.1 (90.3–96.4)
Trastuzumab Emtansine	NE (NE–NE)	85.9 (80.9–89.7)

Hazard ratio for death, 0.55 (95% CI, 0.36–0.86)
P=0.007

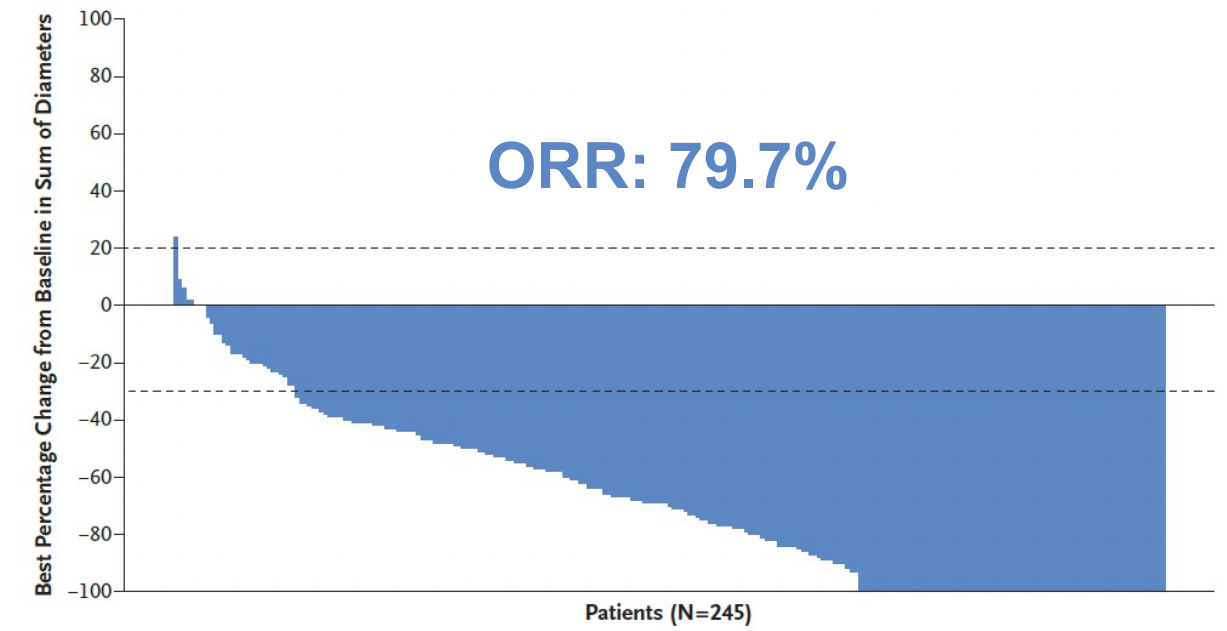
No. at Risk

Trastuzumab deruxtecan	261	256	254	249	243	237	218	180	133	86	56	42	24	11	7	6	2	2	1	0
Trastuzumab emtansine	263	253	243	236	231	224	188	151	120	75	52	32	18	5	3	3	1	1	0	

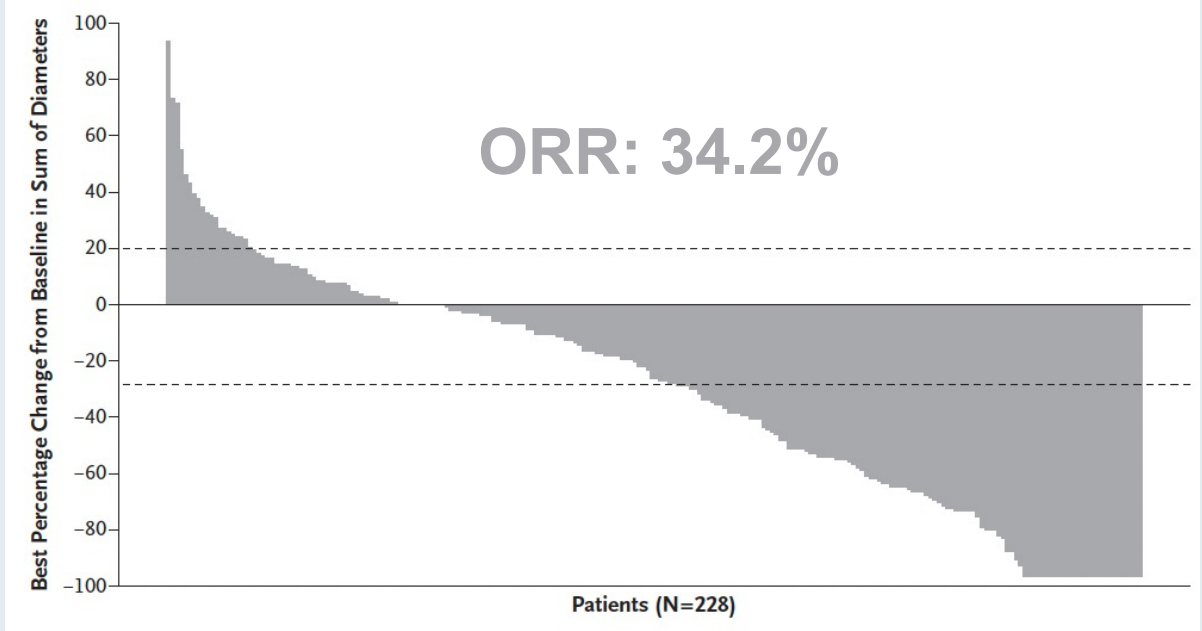
Cortés J et al. *N Engl J Med* 2022;386(12):1143-54.

DESTINY-Breast03: Antitumor Activity

Trastuzumab deruxtecan



Trastuzumab emtansine



ORR = overall response rate

Cortés J et al. *N Engl J Med* 2022;386(12):1143-54.

RTP RESEARCH TO PRACTICE

DESTINY-Breast03: Most Common Drug-Related Adverse Events and Adjudicated Drug-Related Interstitial Lung Disease or Pneumonitis

Event	Trastuzumab Deruxtecan (N=257)		Trastuzumab Emtansine (N=261)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
	number of patients (percent)			
Most common drug-related adverse events				
Blood and lymphatic system disorders				
Neutropenia*	110 (42.8)	49 (19.1)	29 (11.1)	8 (3.1)
Anemia†	78 (30.4)	15 (5.8)	37 (14.2)	11 (4.2)
Leukopenia‡	77 (30.0)	17 (6.6)	20 (7.7)	1 (0.4)
Thrombocytopenia§	64 (24.9)	18 (7.0)	135 (51.7)	65 (24.9)
Gastrointestinal disorders				
Nausea	187 (72.8)	17 (6.6)	72 (27.6)	1 (0.4)
Vomiting	113 (44.0)	4 (1.6)	15 (5.7)	1 (0.4)
Diarrhea	61 (23.7)	1 (0.4)	10 (3.8)	1 (0.4)
Constipation	58 (22.6)	0	25 (9.6)	0
General disorders				
Fatigue¶	115 (44.7)	13 (5.1)	77 (29.5)	2 (0.8)
Investigations				
Aspartate aminotransferase increased	60 (23.3)	2 (0.8)	97 (37.2)	13 (5.0)
Alanine aminotransferase increased	50 (19.5)	4 (1.6)	71 (27.2)	12 (4.6)
Metabolism and nutrition disorders				
Decreased appetite	67 (26.1)	3 (1.2)	33 (12.6)	0
Skin and subcutaneous tissue disorders				
Alopecia‖	93 (36.2)	1 (0.4)	6 (2.3)	0
Adjudicated drug-related interstitial lung disease or pneumonitis**	27 (10.5)	2 (0.8)	5 (1.9)	0

Cortés J et al. *N Engl J Med* 2022;386(12):1143-54.

RTP RESEARCH TO PRACTICE

Trastuzumab-Deruxtecan (T-DXd) in HER2-Positive Breast Cancer Patients (pts) with Active Brain Metastases: Primary Outcome Analysis from the TUXEDO-1 Trial

Bartsch R et al.

ESMO Breast 2022;Abstract 165MO.

Study Design

Primary Endpoint: ORR (CNS) by RANO-BM criteria
Secondary Endpoints:
- Clinical Benefit Rate (CR+PR+SD ≥6 months)
- Extracranial Response rate
- PFS
- OS
- Safety
- Ouality of Life

TUXEDO-1 (NCT04752059)

BM, brain metastasis; BW, body weight; CNS, central nervous system; D1, day 1; EOT, end of treatment; FU, follow up; IV, intravenous; KPS, Karnofsky performance; LVEF, left ventricular ejection fraction; q3w, once every 3 weeks; RANO, response assessment in neuro-oncology; T-DXd, trastuzumab deruxtecan.
EudraCT: 2020-000981-41.

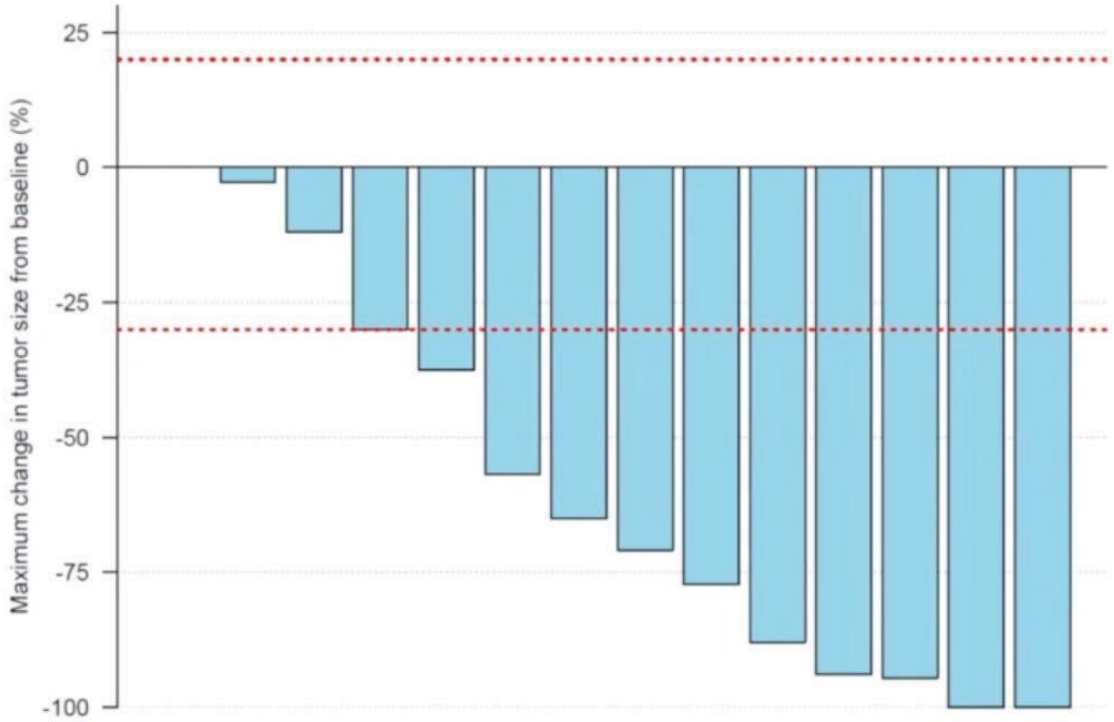
Simon Two Stage Design
- RR (CNS) >60% suggests clinically relevant activity
- RR (CNS) <26% suggests no benefit compared to previous systemic treatment options
- Stage 1: 6 pts. (at least three responses); Stage 2: 9 pts; overall 15 pts. (at least 7 responses)
- Type 1 error rate 5%; power 80%

Bartsch R et al. ESMO Breast 2022;Abstract 165MO.

TUXEDO-1: Primary Endpoint

Objective Response Rate (RANO-BM criteria)

ORR (intention-to-treat population; *n*=15): 73.3% (95% CI 48.1-89.1)

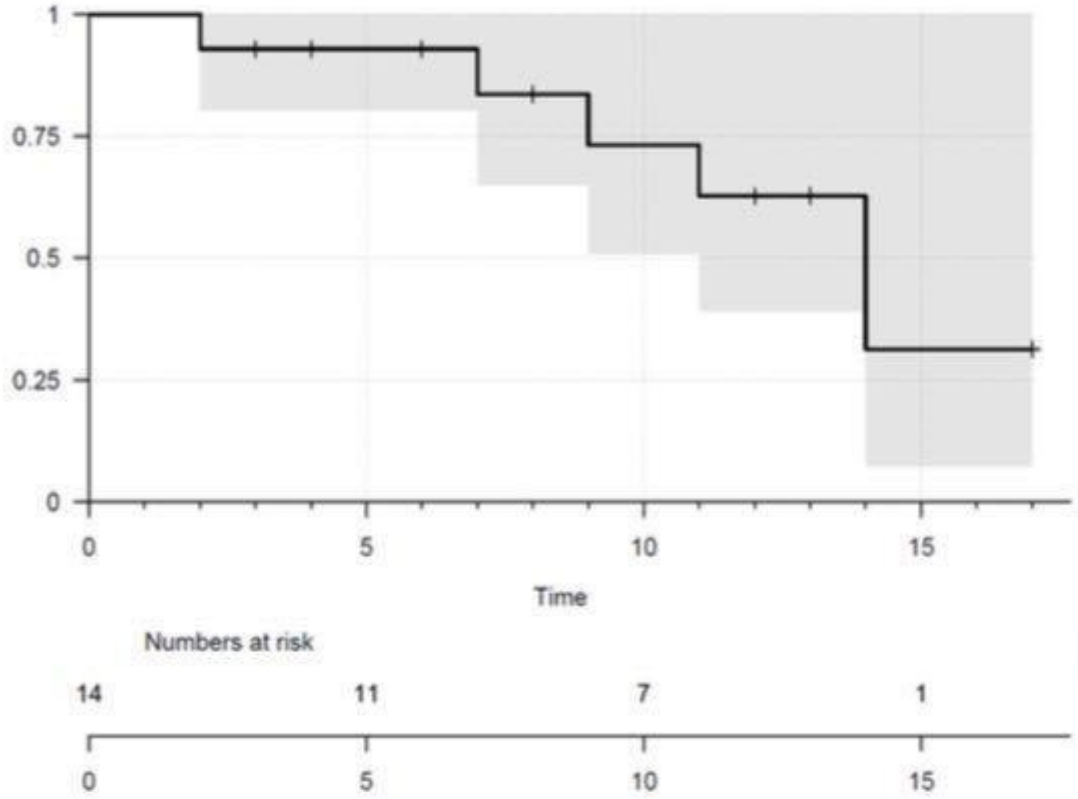


One patient with dural metastases

RR (per-protocol-population; *n*=14): 78.6%

Bartsch R et al. ESMO Breast 2022;Abstract 165MO.

TUXEDO-1: Secondary Endpoints

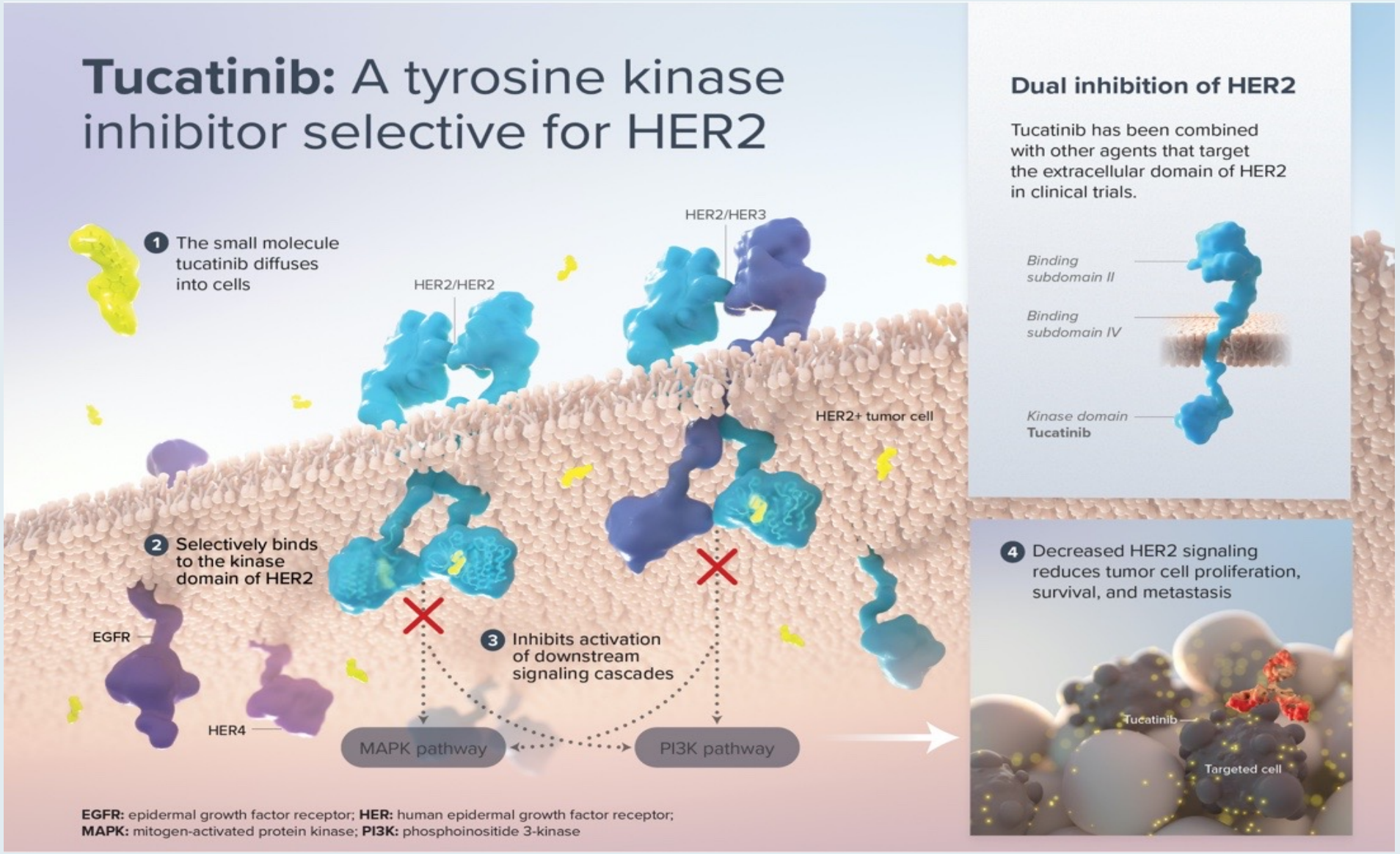


- PFS: 14 months (95% CI 11.0-n.r.)
- Median follow-up 11 months (range 3 – 17 months)

- Clinical Benefit Rate (CR+PR+SD ≥6 months): 13/15 (86.7%) in the ITT population and 13/14 (92.9%) in the PP population
- Median OS not reached
- Extracranial Response Rate:
- Pts. with extracranial metastases at baseline (*n*=13): PR 5/13 (27.8%)
- Pts with measurable extracranial disease at baseline (*n*=8): PR 5/8 (62.5%)

Bartsch R et al. ESMO Breast 2022;Abstract 165MO.

Tucatinib Mechanism of Action



www.seagen.com/science/pipeline/tucatinib

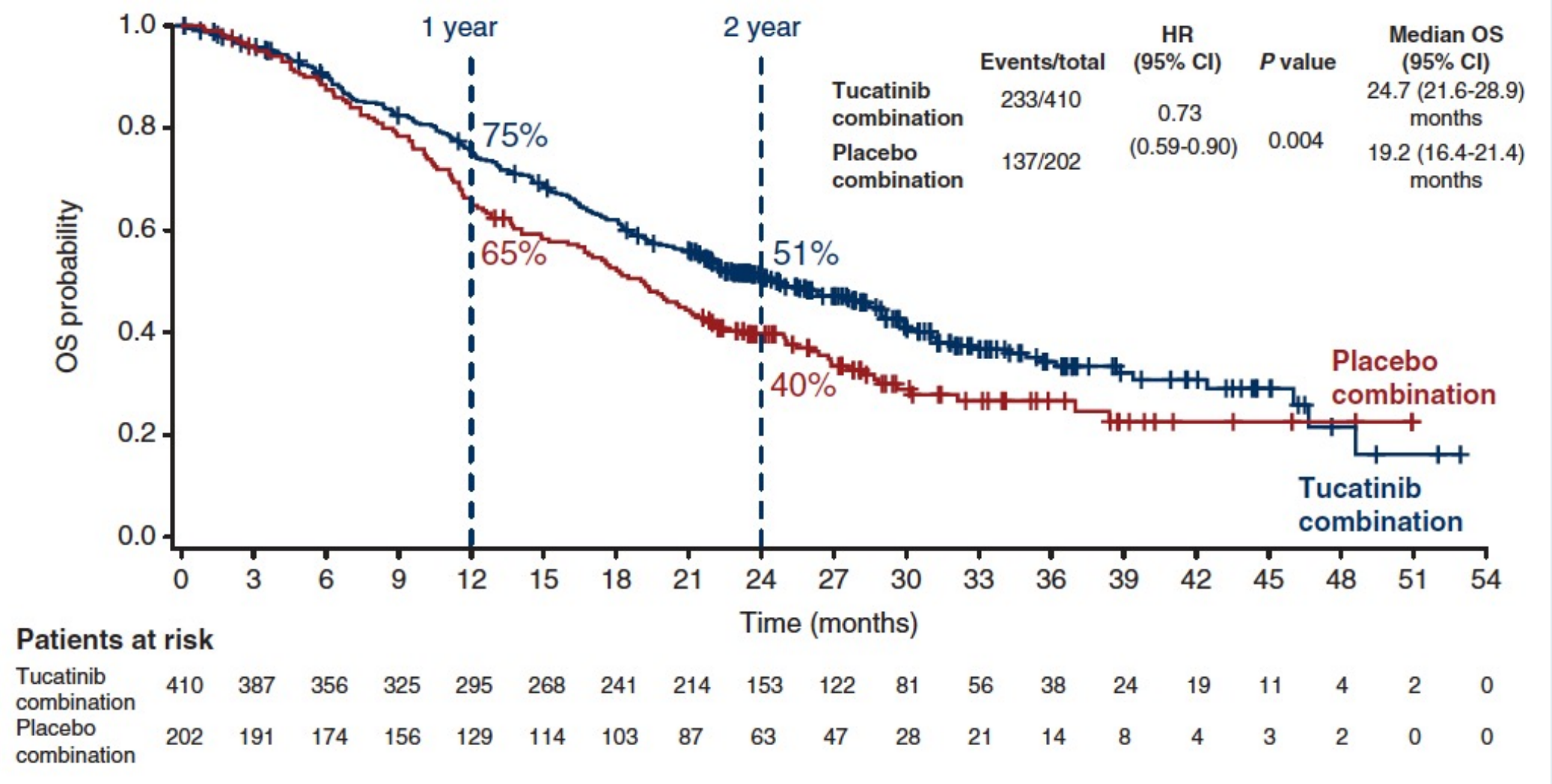
RTP RESEARCH TO PRACTICE

Tucatinib versus placebo added to trastuzumab and capecitabine for patients with pretreated HER2+ metastatic breast cancer with and without brain metastases (HER2CLIMB): final overall survival analysis

G. Curigliano[1*], V. Mueller[2], V. Borges[3], E. Hamilton[4], S. Hurvitz[5], S. Loi[6], R. Murthy[7], A. Okines[8], E. Paplomata[9†], D. Cameron[10], L. A. Carey[11], K. Gelmon[12], G. N. Hortobagyi[7], I. Krop[13], S. Loibl[14], M. Pegram[15], D. Slamon[5], J. Ramos[16], W. Feng[16] & E. Winer[13]

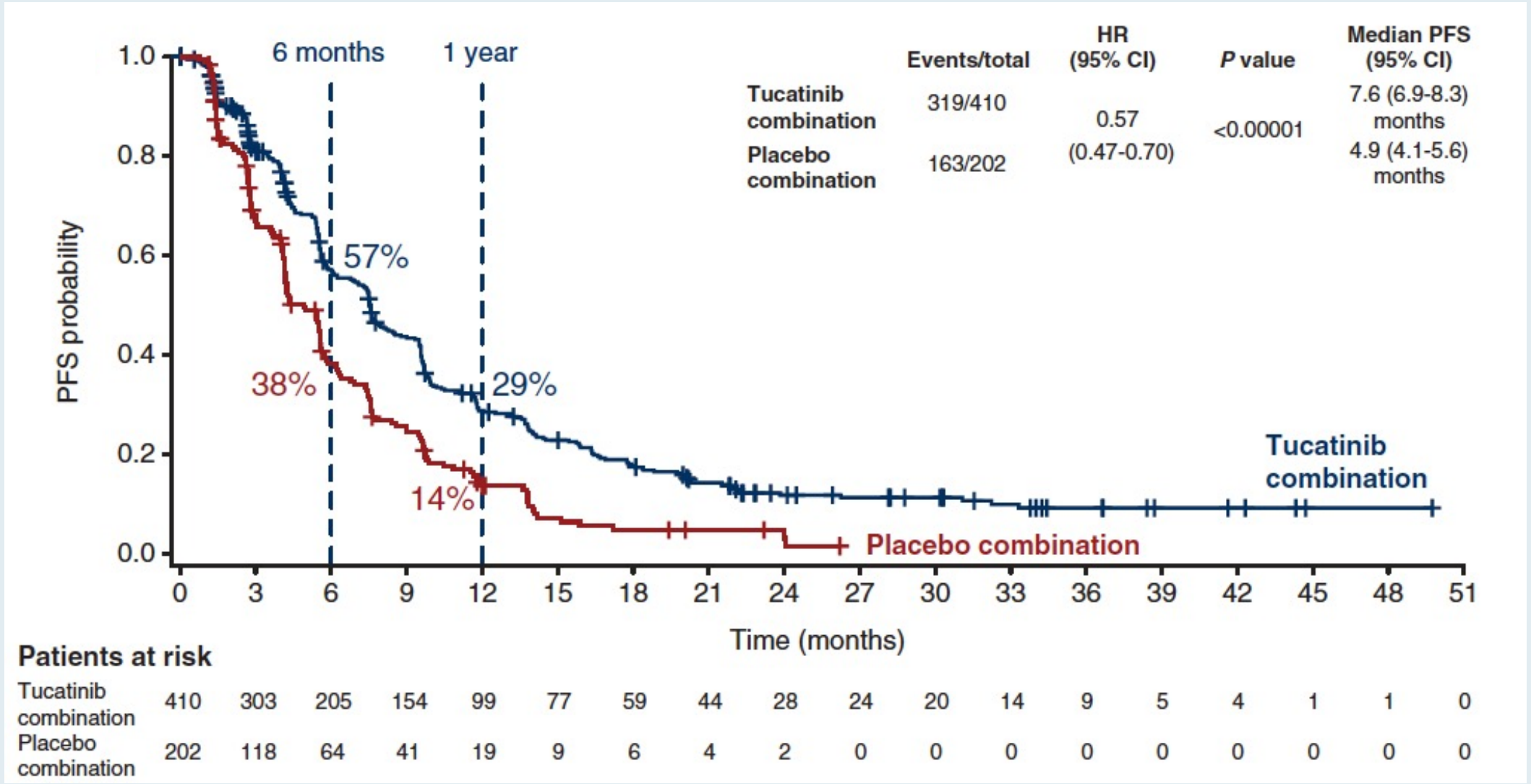
Ann Oncol 2022;33(3):321-29.

HER2CLIMB: Final Overall Survival (OS) Analysis



Curigliano G et al. *Ann Oncol* 2022;33(3):321-29.

HER2CLIMB: Progression-Free Survival (PFS)



	Events/total	HR (95% CI)	*P* value	Median PFS (95% CI)
Tucatinib combination	319/410	0.57 (0.47-0.70)	<0.00001	7.6 (6.9-8.3) months
Placebo combination	163/202			4.9 (4.1-5.6) months

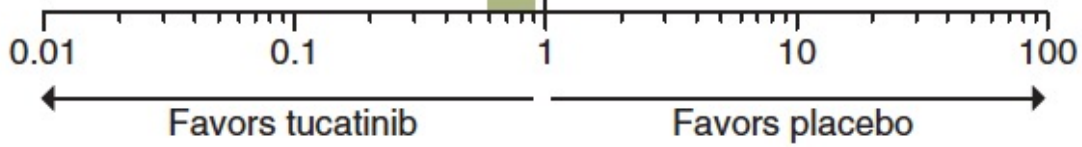
Patients at risk

Tucatinib combination	410	303	205	154	99	77	59	44	28	24	20	14	9	5	4	1	1	0
Placebo combination	202	118	64	41	19	9	6	4	2	0	0	0	0	0	0	0	0	0

Curigliano G et al. *Ann Oncol* 2022;33(3):321-29.

HER2CLIMB: Overall Survival for Patients with Baseline Brain Metastases

Subgroups	Event/*N*	HR (95% CI)
All patients	**370/612**	**0.73 (0.59-0.90)**
Age		
≥65 years	76/116	0.64 (0.38-1.06)
<65 years	294/496	0.76 (0.60-0.96)
Race		
White	268/444	0.75 (0.58-0.96)
Non-White	102/168	0.57 (0.37-0.89)
Hormone receptor status		
Positive	226/370	0.81 (0.61-1.06)
Not positive	144/242	0.61 (0.43-0.87)
Baseline brain metastases		
Yes	189/291	0.60 (0.44-0.81)
No	180/319	0.85 (0.63-1.16)
ECOG performance status		
0	155/298	0.60 (0.43-0.83)
1	215/314	0.85 (0.64-1.13)
Region		
North America	240/369	0.78 (0.60-1.02)
Rest of world	130/243	0.63 (0.44-0.91)



Curigliano G et al. ASCO 2021;Abstract 1043.

RTP RESEARCH TO PRACTICE

HER2CLIMB: Safety Outcomes

Select adverse events	Tucatinib (n = 404)		Placebo (n = 197)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Any	99.3%	55.2%	97.0%	48.7%
Diarrhea	80.9%	12.9%	53.3%	8.6%
PPE syndrome	63.4%	13.1%	52.8%	9.1%
Nausea	58.4%	3.7%	43.7%	3.0%
Fatigue	45.0%	4.7%	43.1%	4.1%
Vomiting	35.9%	3.0%	25.4%	3.6%
Stomatitis	25.5%	2.5%	14.2%	0.5%
Increased AST	21.3%	4.5%	11.2%	0.5%
Increased ALT	20.0%	5.4%	6.6%	0.5%

Murthy RK et al. SABCS 2019;Abstract GS1-01; Murthy RK et al. *N Engl J Med* 2020;382(7):597-609.

Trastuzumab Deruxtecan Granted FDA Approval for HER2-Low Breast Cancer

Press Release: August 5, 2022

"Today, the US Food and Drug Administration approved fam-trastuzumab-deruxtecan-nxki, an IV infusion for the treatment of patients with unresectable (unable to be removed) or metastatic (spread to other parts of the body) HER2-low breast cancer. This is the first approved therapy targeted to patients with the HER2-low breast cancer subtype, which is a newly defined subset of HER2-negative breast cancer.

Patients with HER2-low breast cancer are eligible for fam-trastuzumab-deruxtecan-nxki if they have received a prior chemotherapy in the metastatic setting, or their cancer returned during, or within 6 months of completing, adjuvant chemotherapy.

This approval is based on DESTINY-Breast04, a randomized, multicenter, open label clinical trial that enrolled 557 adult patients with unresectable or metastatic HER2-low breast cancer."

https://www.fda.gov/news-events/press-announcements/fda-approves-first-targeted-therapy-her2-low-breast-cancer

RTP RESEARCH TO PRACTICE

2022 ASCO ANNUAL MEETING

DESTINY-Breast04

Abstract LBA3

Trastuzumab deruxtecan (T-DXd) vs treatment of physician's choice in patients with HER2-low unresectable and/or metastatic breast cancer: Results of DESTINY-Breast04, a randomized, phase 3 study

Shanu Modi Memorial Sloan Kettering Cancer Center, Memorial Hospital, New York, NY, USA

June 5, 2022

Additional authors: William Jacot, Toshinari Yamashita, Joo Hyuk Sohn, Maria Vidal, Eriko Tokunaga, Junji Tsurutani, Naoto Ueno, Yee Soo Chae, Keun Seok Lee, Naoki Niikura, Yeon Hee Park, Xiaojia Wang, Binghe Xu, Dhiraj Gambhire, Lotus Yung, Gerold Meinhardt, Yibin Wang, Nadia Harbeck, David Cameron

On behalf of the DESTINY-Breast04 investigators

The NEW ENGLAND JOURNAL of MEDICINE

N Engl J Med 2022;387(1):9-20.

ORIGINAL ARTICLE

Trastuzumab Deruxtecan in Previously Treated HER2-Low Advanced Breast Cancer

S. Modi, W. Jacot, T. Yamashita, J. Sohn, M. Vidal, E. Tokunaga, J. Tsurutani, N.T. Ueno, A. Prat, Y.S. Chae, K.S. Lee, N. Niikura, Y.H. Park, B. Xu, X. Wang, M. Gil-Gil, W. Li, J.-Y. Pierga, S.-A. Im, H.C.F. Moore, H.S. Rugo, R. Yerushalmi, F. Zagouri, A. Gombos, S.-B. Kim, Q. Liu, T. Luo, C. Saura, P. Schmid, T. Sun, D. Gambhire, L. Yung, Y. Wang, J. Singh, P. Vitazka, G. Meinhardt, N. Harbeck, and D.A. Cameron, for the DESTINY-Breast04 Trial Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

N Engl J Med 2022;387(1):75-6.

EDITORIALS

DESTINY-Changing Results for Advanced Breast Cancer

Sara A. Hurvitz, M.D.

RTP RESEARCH TO PRACTICE

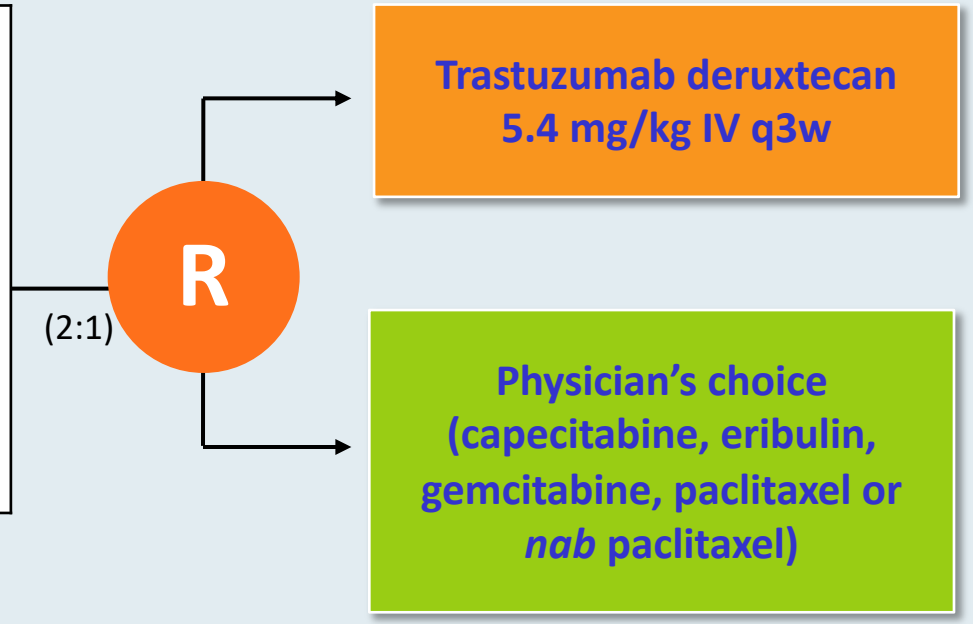
DESTINY-Breast04: Phase III Trial Schema

Target Accrual: 557

Unresectable and/or metastatic HER2-low breast cancer
(IHC 2+/ISH- or IHC 1+)

HER2 status is centrally confirmed and is based on ASCO-CAP 2018 guidelines using archival or fresh biopsy tissue samples

If archival tissue is not available, a fresh biopsy is required



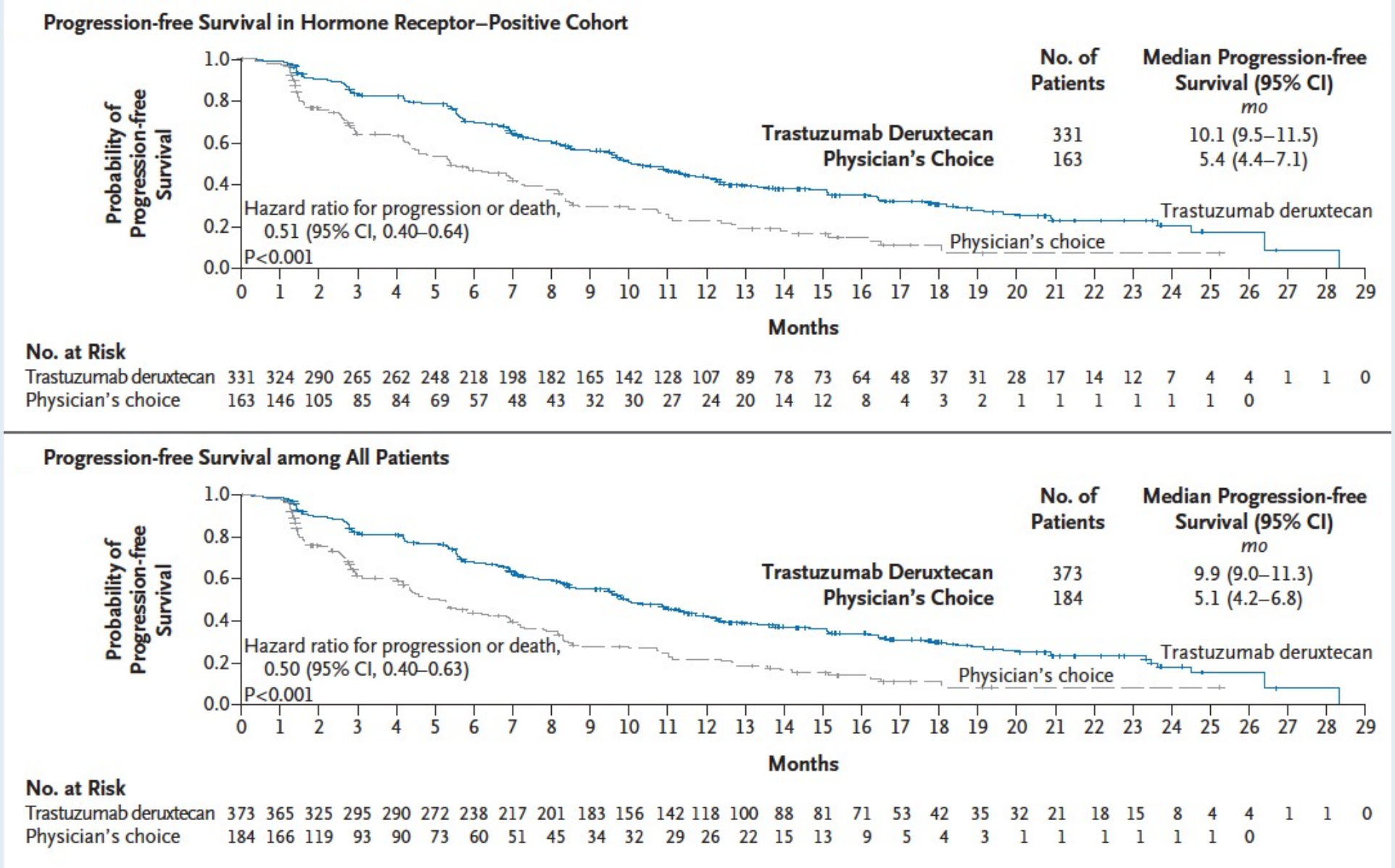
Randomization is stratified by

- HER2 IHC status (HER2 IHC 1+ vs HER2 IHC 2+/ISH-)
- Number of prior lines of chemotherapy (1 vs 2)
- HR/CDK status (HR+ with prior CDK4/6 inhibitor treatment vs HR+ without prior CDK4/6 inhibitor treatment vs HR-)

Primary endpoint: Progression-free survival per modified RECIST v1.1 by blinded independent central review

www.clinicaltrials.gov. Accessed August 2022.

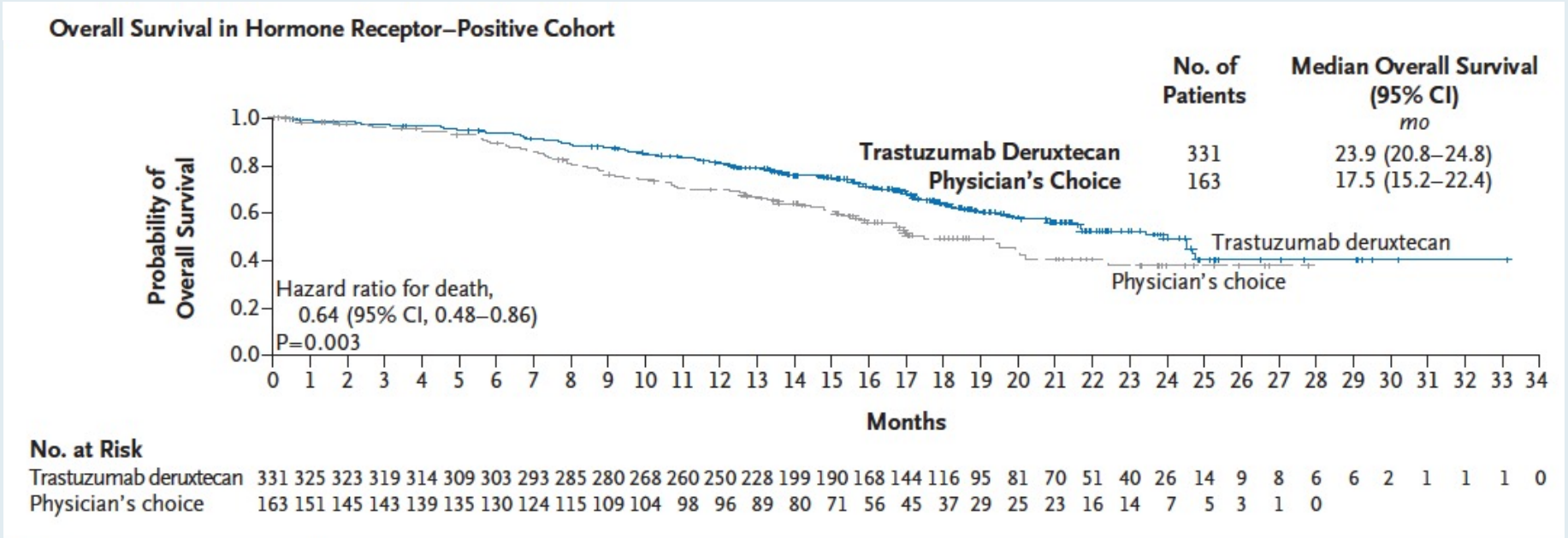
DESTINY-Breast04: Progression-Free Survival

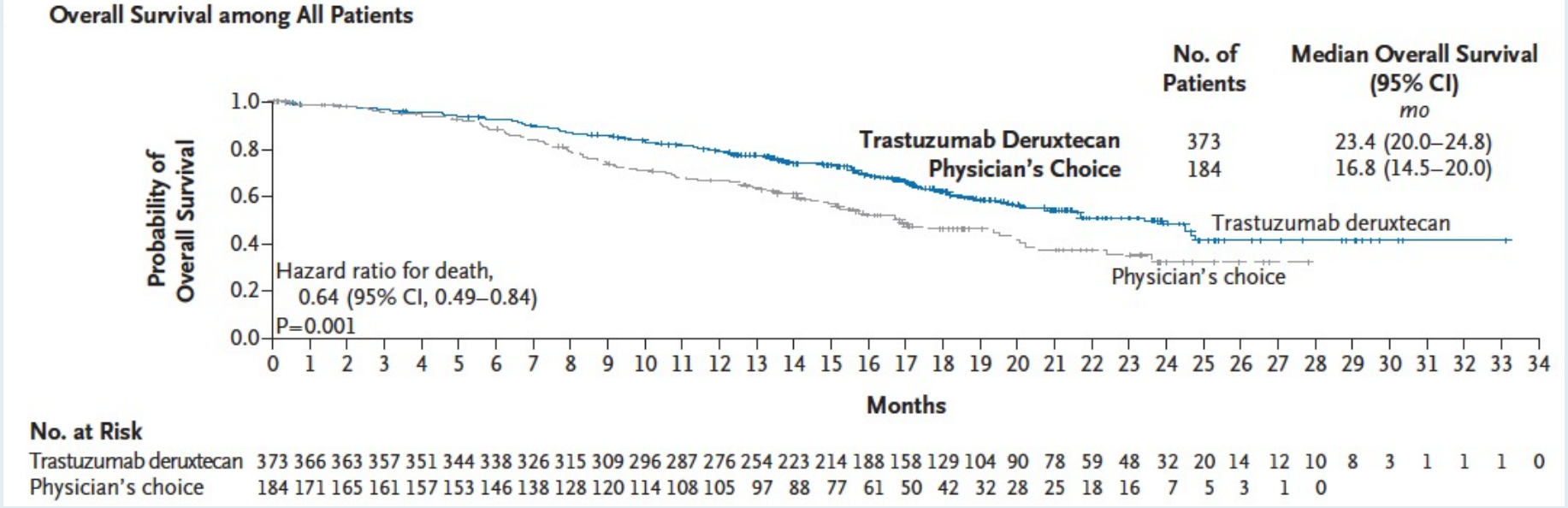


Modi S et al. *N Engl J Med* 2022;387(1):9-20; ASCO 2022;Abstract LBA3.

RTP RESEARCH TO PRACTICE

DESTINY-Breast04: Overall Survival





Modi S et al. *N Engl J Med* 2022;387(1):9-20; ASCO 2022;Abstract LBA3.

RTP RESEARCH TO PRACTICE

DESTINY-Breast04: Select Adverse Events

Event	Trastuzumab Deruxtecan (N=371)		Physician's Choice of Chemotherapy (N=172)	
	All Grades	Grade ≥3	All Grades	Grade ≥3
	number of patients (percent)			
Blood and lymphatic system disorders				
Neutropenia†	123 (33.2)	51 (13.7)	88 (51.2)	70 (40.7)
Anemia‡	123 (33.2)	30 (8.1)	39 (22.7)	8 (4.7)
Thrombocytopenia§	88 (23.7)	19 (5.1)	16 (9.3)	1 (0.6)
Leukopenia¶	86 (23.2)	24 (6.5)	54 (31.4)	33 (19.2)
Gastrointestinal disorders				
Nausea	271 (73.0)	17 (4.6)	41 (23.8)	0
Vomiting	126 (34.0)	5 (1.3)	17 (9.9)	0
Diarrhea	83 (22.4)	4 (1.1)	31 (18.0)	3 (1.7)
Constipation	79 (21.3)	0	22 (12.8)	0

Modi S et al. *N Engl J Med* 2022;387(1):9-20; ASCO 2022;Abstract LBA3.

DESTINY-Breast04: Adverse Events of Special Interest

Adjudicated as drug-related ILD/pneumonitis

n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any grade
T-DXd (n = 371)	13 (3.5)	24 (6.5)	5 (1.3)	0	3 (0.8)	45 (12.1)
TPC (n = 172)	1 (0.6)	0	0	0	0	1 (0.6)

Left ventricular dysfuctions

n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any grade
Ejection fraction decreased						
T-DXd (n = 371)	1 (0.3)	12 (3.8)	1 (0.3)	0	0	16 (4.3)
TPC (n = 172)	0	0	0	0	0	0
Cardiac failure						
T-DXd (n = 371)	0	1 (0.3)	1 (0.3)	0	0	2 (0.5)
TPC (n = 172)	0	0	0	0	0	0

ILD = interstitial lung disease; TPC = treatment of physician's choice

Modi S et al. ASCO 2022;Abstract LBA3.

DESTINY-Breast06 Phase III Trial Design

Estimated enrollment (N = 850)

- Metastatic breast cancer
- HER2-low or negative by local test IHC2+/ISH- or IHC1/ISH- or IHC0/ISH-
- HER2-low or HER2 IHC >0<1 by central lab
- HR-positive disease
- No prior chemotherapy for advanced or metastatic disease
- PD within 6 months of starting first-line therapy with ET/CDK4/6 OR PD on at least 2 prior lines of ET +/- targeted therapy

R

Trastuzumab deruxtecan

Physician's choice:

Capecitabine or paclitaxel or *nab* paclitaxel

ET = endocrine therapy

Primary endpoint: PFS in HR-positive, HER2-low population

www.clinicaltrials.gov. NCT04494425. Accessed August 2022.

ASCO rapid recommendations

Chemotherapy and Targeted Therapy for Human Epidermal Growth Factor Receptor 2–Negative Metastatic Breast Cancer That Is Either Endocrine-Pretreated or Hormone Receptor–Negative: ASCO Guideline Rapid Recommendation Update

Beverly Moy, MD, MPH[1]; R. Bryan Rumble, MSc[2]; and Lisa A. Carey, MD, ScM[3]; for the Chemotherapy and Targeted Therapy for HER2-Negative Metastatic Breast Cancer that is Either Endocrine-Pretreated or Hormone Receptor–Negative Expert Panel

ASCO Rapid Recommendations Updates highlight revisions to select ASCO guideline recommendations as a response to the emergence of new and practice-changing data. The rapid updates are supported by an evidence review and follow the guideline development processes outlined in the ASCO Guideline Methodology Manual. The goal of these articles is to disseminate updated recommendations, in a timely manner, to better inform health practitioners and the public on the best available cancer care options.

***J Clin Oncol* 2022;Aug 4;[Online ahead of print].**

ASCO Guideline Rapid Recommendation Update for HER2-Negative Metastatic Breast Cancer

Updated Recommendation

Patients with HER2 IHC 1+ or 2+ and ISH-negative metastatic breast cancer who have received at least one prior chemotherapy for metastatic disease, and if hormone receptor–positive are refractory to endocrine therapy, should be offered treatment with trastuzumab deruxtecan

- (Type: evidence based, benefits outweigh harms; Evidence quality: moderate; Strength of recommendation: strong).

Moy B et al. *J Clin Oncol* 2022;Aug 4;[Online ahead of print].

FDA-Approved Agents for Localized HER2-Positive Breast Cancer

Agent	Setting	Pivotal trial(s)	Regimens	Year approved
Trastuzumab	Adjuvant HER2-positive localized breast cancer (LBC), first line	NSABP B-31 N9831 BCIRG 006 HERA	AC-T-placebo vs AC-T-H AC-T vs AC-H vs AC-T-H AC-T vs AC-T-H vs TC-H Observation vs trastuzumab	2006
Pertuzumab	Neoadjuvant HER2-positive, LBC	NeoSphere	TD vs PTD vs PT vs PD	2013
Pertuzumab	Adjuvant HER2-positive, LBC	APHINITY	Chemotherapy plus trastuzumab plus pertuzumab vs placebo	2017
Neratinib	Extended adjuvant treatment of HER2-positive LBC	ExteNET	Placebo vs neratinib	2017
T-DM1	Adjuvant HER2-positive LBC with residual disease after neoadjuvant taxane and trastuzumab-based treatment	KATHERINE	Trastuzumab vs T-DM1	2019

AC-T = doxorubicin, cyclophosphamide and paclitaxel; AC-T-H = doxorubicin, cyclophosphamide, paclitaxel and trastuzumab; AC-H = doxorubicin, cyclophosphamide, and trastuzumab; TC-H = docetaxel, cyclophosphamide and trastuzumab; TD = trastuzumab and docetaxel; PTD = pertuzumab, trastuzumab and docetaxel; PT = trastuzumab and pertuzumab; PD = pertuzumab and docetaxel

Choong GM et al. *CA Cancer J Clin* 2020;70(5):355-74.

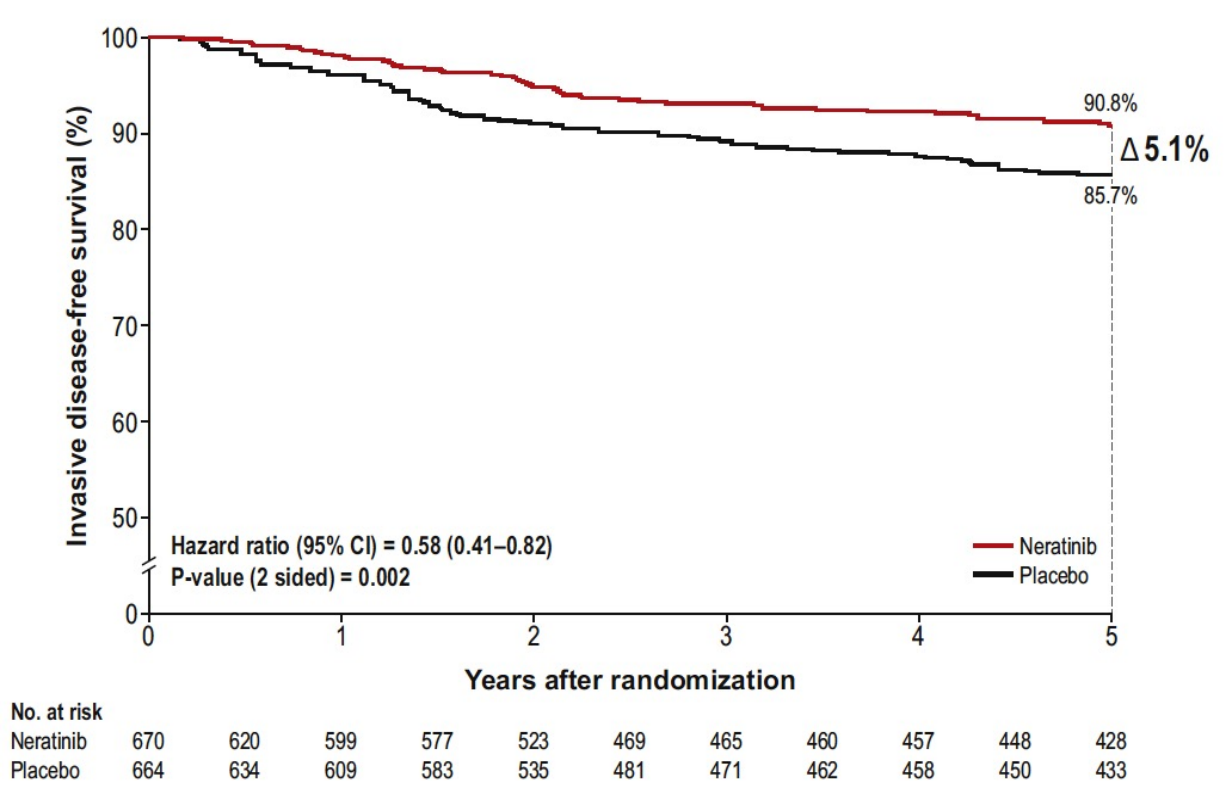
Final Efficacy Results of Neratinib in HER2-positive Hormone Receptor-positive Early-stage Breast Cancer From the Phase III ExteNET Trial

Arlene Chan,[1] Beverly Moy,[2] Janine Mansi,[3] Bent Ejlertsen,[4] Frankie Ann Holmes,[5] Stephen Chia,[6] Hiroji Iwata,[7] Michael Gnant,[8] Sibylle Loibl,[9] Carlos H. Barrios,[10] Isil Somali,[11] Snezhana Smichkoska,[12] Noelia Martinez,[13] Mirta Garcia Alonso,[14] John S. Link,[15] Ingrid A. Mayer,[16] Søren Cold,[17] Serafin Morales Murillo,[18] Francis Senecal,[19] Kenichi Inoue,[20] Manuel Ruiz-Borrego,[21] Rina Hui,[22] Neelima Denduluri,[23] Debra Patt,[24] Hope S. Rugo,[25] Stephen R.D. Johnston,[26] Richard Bryce,[27] Bo Zhang,[27] Feng Xu,[27] Alvin Wong,[27] Miguel Martin,[28] for the ExteNET Study Group

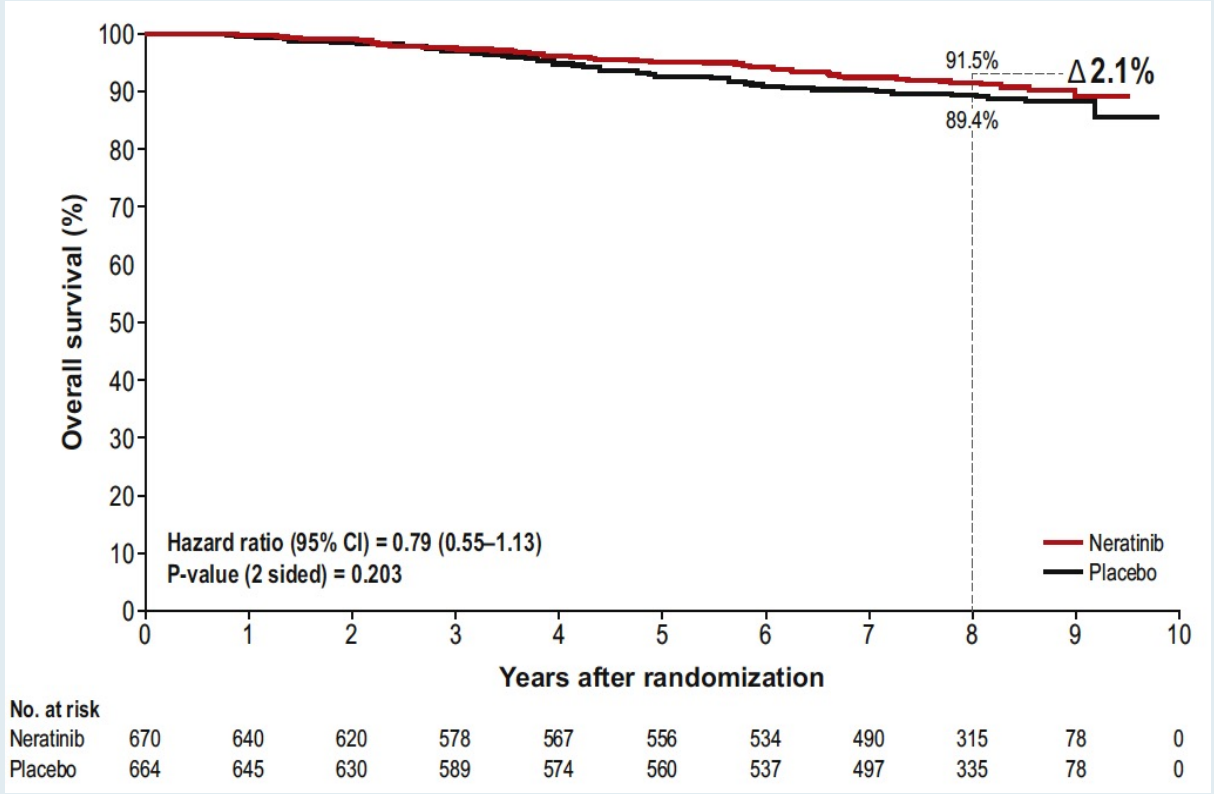
***Clin Breast Cancer* 2021;21(1):80-91.**

ExteNET: Final Analysis of Neratinib for HER2-Positive Localized Breast Cancer

Invasive disease-free survival at 5 years*



Overall survival at 8 years*



* HR-positive/≤1-year population

Chan A et al. *Clin Breast Cancer* 2021;21(1):80-91.

RTP RESEARCH TO PRACTICE

ExteNET: Cumulative Incidence of CNS Recurrences

Population or subgroup	Events, n		Cumulative incidence of CNS recurrences	
	Neratinib	Placebo	Neratinib	Placebo
Intention-to-treat population (n = 2,840)	16	23	1.3%	1.8%
HR-positive/≤1-year population (EU indication) (n = 1,334)	4	12	0.7%	2.1%
Adjuvant or neoadjuvant therapy (n = 1,334)				
Adjuvant (n = 980)	3	6	0.7%	1.5%
Neoadjuvant (n = 354)	1	6	0.7%	3.7%
pCR status (n = 354)				
No (n = 295)	1	5	0.8%	3.6%
Yes (n = 38)	0	1	0	5.0%

Chan A et al. *Clin Breast Cancer* 2021;21(1):80-91; Holmes FA et al. SABCS 2020;Abstract PD3-03.

ExteNET: Adverse Events (AEs)

Summary of AEs

	Neratinib (n = 662)	Placebo (n = 657)
Any TEAE	649 (98)	567 (86)
Grade 3 or 4 TEAE	327 (49)	76 (12)
Fatal TEAE	1 (<1)	0 (0)
Serious TEAE	45 (7)	36 (6)
Treatment-related TEAE	630 (95)	360 (55)
Serious treatment-related TEAE	19 (3)	5 (<1)
TEAE leading to		
Treatment discontinuation	178 (27)	30 (5)
Study withdrawal	11 (2)	2 (<1)
Dose reduction	203 (31)	13 (2)
Hospitalization	41 (6)	35 (5)
Dose interruption	280 (42)	75 (11)

Frequent Treatment-Emergent AEs (TEAEs)

	Neratinib (n = 662)		Placebo (n = 657)	
	Grade 1-2	Grade 3	Grade 1-2	Grade 3
Diarrhea	365 (55)	261 (39)	213 (32)	7 (1)
Nausea	280 (42)	9 (1)	135 (21)	2 (<1)
Fatigue	177 (27)	13 (2)	129 (20)	2 (<1)
Vomiting	150 (23)	24 (4)	41 (6)	2 (<1)
Abdominal pain	145 (22)	11 (2)	58 (9)	1 (<1)
Headache	119 (18)	6 (<1)	125 (19)	1 (<1)
Upper abdominal pain	90 (14)	6 (<1)	35 (5)	3 (<1)
Rash	90 (14)	3 (<1)	40 (6)	0 (0)
Decreased appetite	79 (12)	1 (<1)	13 (2)	0 (0)
Muscle spasms	81 (12)	0 (0)	21 (3)	1 (<1)

Chan A et al. *Clin Breast Cancer* 2021;21(1):80-91.

ESMO VIRTUAL PLENARY

Updated results of APHINITY at 8.4 years median follow up

A randomised multi-center, double-blind, placebo-controlled trial comparing chemotherapy plus trastuzumab plus pertuzumab versus chemotherapy plus trastuzumab plus placebo as adjuvant therapy in patients with operable HER2-positive early breast cancer

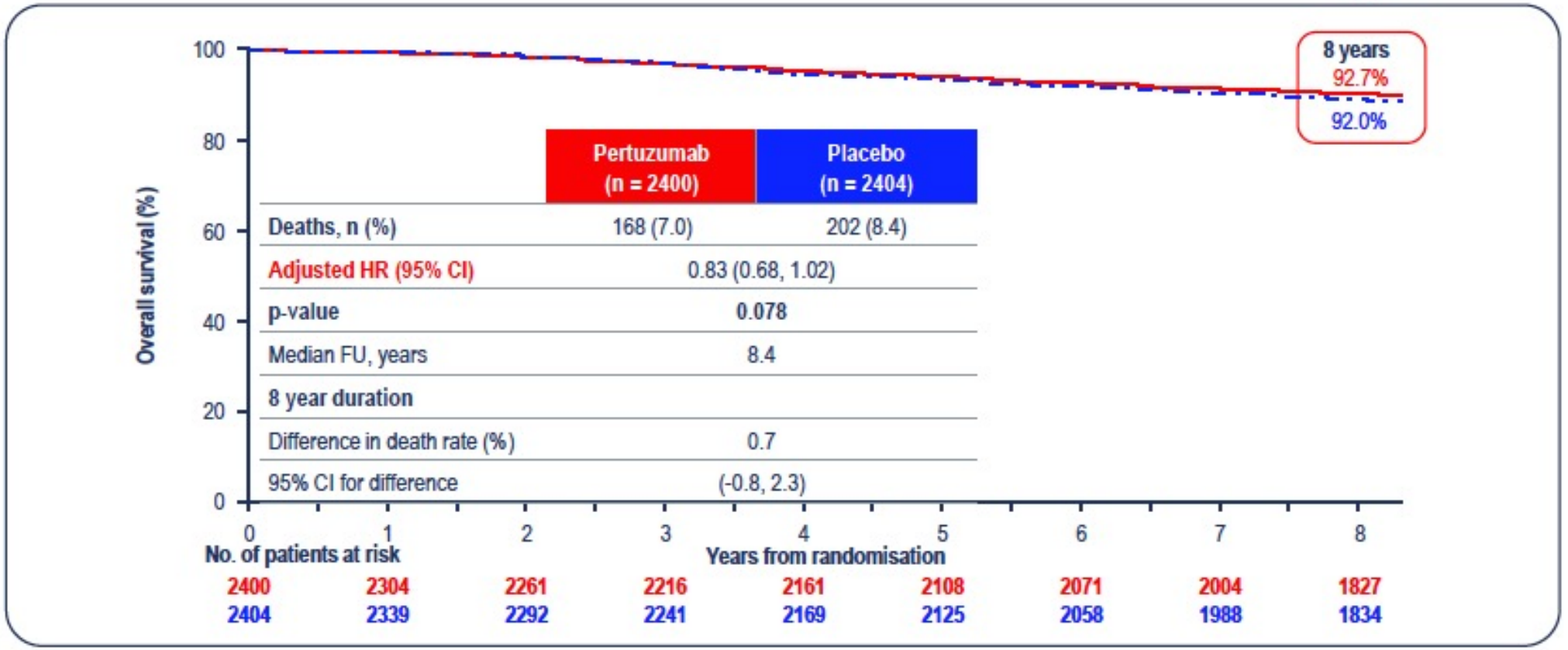
Sibylle Loibl, Jacek Jassem, Amir Sonnenblick, Damien Parlier, Eric Winer, Jonas Bergh, Richard Gelber, Eleonora Restuccia , Young-Hyuck Im, Chiun-Sheng Huang, Florence Dalenc, Isabel Calvo, Marion Procter, Carmela Caballero, Emma Clark, Henry Gomez Moreno, Judith Bliss, Giuseppe Viale, Jose Bines, Martine Piccart

On behalf of the APHINITY Steering Committee and Investigators

ESMO

July 14, 2022

APHINITY Interim Overall Survival Analysis at 8.4 years Median FU by Treatment Regimen (ITT Population)



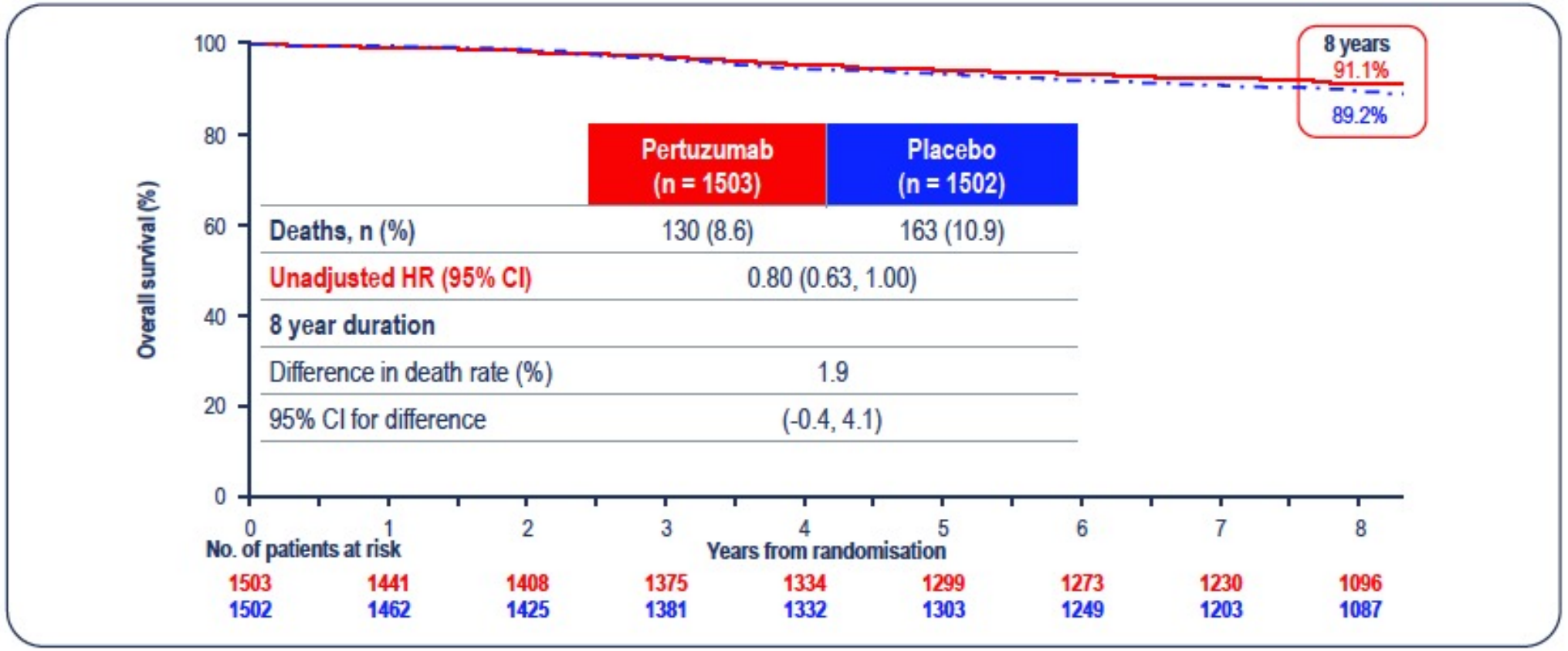
ESMO VIRTUAL PLENARY

Sibylle Loibl, MD, PhD

Loibl S et al. ESMO Virtual Plenary 2022;Abstract VP6-2022.

APHINITY Interim Overall Survival Analysis at 8.4 Years Median FU by Treatment Regimen

Node-positive Cohort



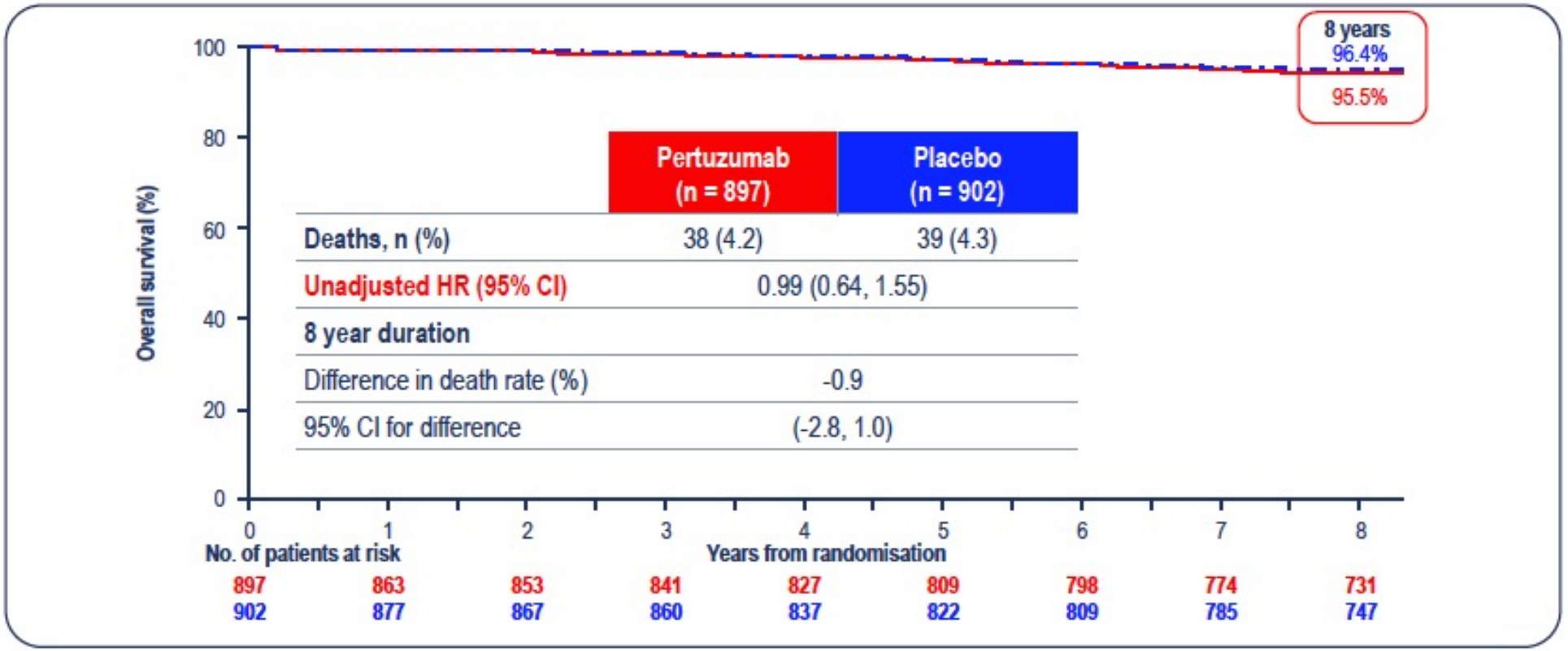
ESMO VIRTUAL PLENARY

Sibylle Loibl, MD, PhD

Loibl S et al. ESMO Virtual Plenary 2022;Abstract VP6-2022.

APHINITY Interim Overall Survival Analysis at 8.4 Years Median FU by Treatment Regimen

Node-negative Cohort



ESMO VIRTUAL PLENARY

Sibylle Loibl, MD, PhD

Loibl S et al. ESMO Virtual Plenary 2022;Abstract VP6-2022.

APHINITY Updated Descriptive Analysis
Cardiac Safety, 8.4 years Median FU

	Pertuzumab (N = 2364)	Placebo (N = 2405)
Primary cardiac event • Heart failure New York Heart Association class III or IV + LVEF drop* • Cardiac death**	19 (0.8%)	10 (0.4%)
Heart failure NYHA class class III or IV + LVEF drop*	16 (0.7%)	6 (0.2%)
Cardiac death ** **Three further patients with a primary cardiac event (cardiac death) were reported; 1 in the pertuzumab arm and 2 in the placebo arm**	3 (0.1%)	4 (0.2%)

No new cardiac safety issues emerged.

*LVEF drop = ejection fraction drop > 10% from baseline AND to below 50%;
**Identified by the Cardiac Advisory Board for the trial according to a prospective definition.

ESMO VIRTUAL PLENARY

Sibylle Loibl, MD, PhD

Loibl S et al. ESMO Virtual Plenary 2022;Abstract VP6-2022.

Breast Cancer Agenda

Module 1: HER2-Positive Disease

Module 2: Use of PARP Inhibitors in Localized HER2-Negative Disease (OlympiA/Olaparib)

- PARP inhibitors (eg, olaparib) in the adjuvant/postneoadjuvant setting for localized breast cancer; impact of ER and HER2 status, risk versus treatment benefit, germline versus somatic genomic alterations

Module 3: Triple-Negative Disease

Module 4: ER/PR-Positive, HER2-Negative Disease

J Clin Oncol 2021;39(26):2959-61.

ASCO rapid recommendations

Adjuvant PARP Inhibitors in Patients With High-Risk Early-Stage HER2-Negative Breast Cancer and Germline *BRCA* Mutations: ASCO Hereditary Breast Cancer Guideline Rapid Recommendation Update

Nadine M. Tung, MD[1]; Dana Zakalik, MD[2]; and Mark R. Somerfield, PhD[3]; for the Hereditary Breast Cancer Guideline Expert Panel

ASCO Rapid Recommendations Updates highlight revisions to select ASCO guideline recommendations as a response to the emergence of new and practice-changing data. The rapid updates are supported by an evidence review and follow the guideline development processes outlined in the ASCO Guideline Methodology Manual. The goal of these articles is to disseminate updated recommendations, in a timely manner, to better inform health practitioners and the public on the best available cancer care options.

ASCO 2021 Adjuvant PARP Inhibitor Updated Recommendations

- **For patients with localized, HER2-negative breast cancer** with high risk of recurrence and germline BRCA1 or BRCA2 pathogenic or likely pathogenic variants, 1 year of adjuvant olaparib should be offered after completion of (neo)adjuvant chemotherapy and local treatment, including radiation therapy.
- **For those who underwent surgery first**, 1 year of adjuvant olaparib should be offered for patients with triple-negative breast cancer and tumor size >2 cm or any involved axillary nodes.
- **For those with hormone receptor (HR)-positive disease**, 1 year of adjuvant olaparib should be offered to those with at least 4 involved axillary lymph nodes.
- **For patients who received neoadjuvant chemotherapy,** 1 year of adjuvant olaparib should be offered to patients with triple-negative breast cancer and any residual cancer; **for patients with HR-positive disease**, 1 year of adjuvant olaparib should be offered to patients with residual disease and a clinical stage, pathologic stage, estrogen receptor and tumor grade score ≥3.

Tung NM et al. *J Clin Oncol* 2021;39(26):2959-61.

FDA Approves Olaparib as Adjuvant Treatment for HER2-Negative High-Risk Localized Breast Cancer with a Germline BRCA Mutation Previously Treated with Neoadjuvant or Adjuvant Chemotherapy

Press Release: March 11, 2022

"Olaparib has been approved by the US Food and Drug Administration (FDA) for the adjuvant treatment of adult patients with deleterious or suspected deleterious germline *BRCA*-mutated (g*BRCA*m), human epidermal growth factor receptor 2 (HER2)-negative high-risk early breast cancer who have been treated with neoadjuvant or adjuvant chemotherapy. Patients will be selected for therapy based on an FDA-approved companion diagnostic for olaparib.

The approval was based on results from the Phase 3 OlympiA trial, including data for the trial's primary endpoint of invasive disease-free survival (IDFS), which were presented during the 2021 American Society of Clinical Oncology Annual Meeting and published in *The New England Journal of Medicine,* as well as overall survival (OS) data from a more recent interim analysis."

https://finance.yahoo.com/news/fda-approves-lynparza-olaparib-adjuvant-005100263.html

RTP RESEARCH TO PRACTICE

Abstract VP1-2022

ESMO VIRTUAL PLENARY

PRE-SPECIFIED EVENT DRIVEN ANALYSIS OF OVERALL SURVIVAL (OS) IN THE OLYMPIA PHASE III TRIAL OF ADJUVANT OLAPARIB (OL) IN GERMLINE *BRCA1/2* MUTATION (*gBRCAm*) ASSOCIATED BREAST CANCER

Andrew Nicholas James Tutt[1], Judy Garber[2], Richard D. Gelber[2], Kelly-Anne Phillips[3], Andrea Eisen[4], Oskar Thor Jóhannsson[5], Priya Rastogi[6], Karen Yongzhi Cui[7], Seock-Ah Im[8], Rinat Yerushalmi[9], Adam Matthew Brufsky[10], Maria Taboada[11], Giovanna Rossi[12], Greg Yothers[13], Christian Singer[14], Luis E. Fein[15], Niklas Loman[16], David Cameron[17], Christine Campbell[18], Charles Edward Geyer Jr[19]

[1]Breast Cancer Now Research Unit, Institute of Cancer Research, London, United Kingdom; [2]Dana Farber Cancer Institute, Boston, MA, USA; [3]Department of Medical Oncology, Peter MacCallum Cancer Center, Melbourne, Australia; [4]Odette Cancer Centre, Sunnybrook Health Sciences Centre, Toronto, Canada; [5]Landspitali – The National University Hospital of Iceland, Reykjavik, Iceland; [6]Department of Oncology, NSABP Foundation, Pittsburgh, PA, USA; [7]Global Medicine Development, AstraZeneca US, Gaithersburg, MD, USA; [8]Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea; [9]Department of Oncology, Clalit Health Services, Petah Tikva, Israel; [10]Department of Hematology-Oncology, Magee-Womens Hospital of UPMC, Pittsburgh, PA, USA; [11]AstraZeneca, Royston, United Kingdom; [12]Department of R&D, Breast International Group (BIG) – AISBL, Brussels, Belgium; [13]Department of Biostatistics, University of Pittsburgh, Pittsburgh, PA, USA;

[14]Center for Breast Health, Medical University of Vienna, Vienna, Austria; [15]Department of Oncology, Instituto de Oncología de Rosario, Rosario, Santa Fe, Argentina; [16]Skane University Hospital, Lund, Sweden; [17]Department of Oncology, Edinburgh Cancer Centre, Edinburgh, United Kingdom; [18]Frontier Science Scotland, Kincraig, United Kingdom; [19]Department of Clinical Research, Houston Methodist Cancer Center, Houston, TX, USA

RTP RESEARCH TO PRACTICE

OlympiA: Comparison of Efficacy Results at Data Cutoffs 1 and 2

	Prior IA IDFS analysis Median follow-up 2.5 years	Current IA2 OS analysis Median follow-up 3.5 years
IDFS hazard ratios (CI)	*0.58 (99.5% CI: 0.41, 0.82)*	0.63 (95% CI: 0.50, 0.78)
P value needed for significance	*0.005*	N/A
P value observed at analysis	*< 0.0001*	N/A
Difference in IDFS rate (CI)	*3 Yr. 8.8% (95% CI: 4.5, 13.0)*	3 Yr. 8.8% (95% CI: 5.0, 12.6) 4 Yr. 7.3% (95% CI: 3.0, 11.5)
DDFS hazard ratios (CI)	*0.57 (99.5% CI: 0.39, 0.83)*	0.61 (95% CI: 0.48, 0.77)
P value needed for significance	*0.005*	N/A
P value observed at analysis	*< 0.0001*	N/A
Difference in DDFS rate (CI)	*3 Yr. 7.1% (95% CI: 3.0, 11.1)*	3 Yr. 7.0% (95% CI: 3.5, 10.6) 4 Yr. 7.4% (95% CI: 3.6, 11.3)
OS hazard ratios (CI)	***0.68 (99% CI: 0.44, 1.05)***	0.68 (98.5% CI: 0.47, 0.97)
P value needed for significance	***0.010***	0.015
P value observed at analysis	***0.024***	0.009
Difference in OS rate (CI)	***3 Yr. 3.7%*** *(95% CI: 0.3, 7.1)*	3 Yr. 3.8% (95% CI: 0.9, 6.6) 4 Yr. 3.4% (95% CI: -0.1, 6.8)

IA = interim analysis; IDFS = invasive disease-free survival; DDFS = distant disease-free survival; OS = overall survival

Tutt ANJ et al. ESMO Virtual Plenary 2022;Abstract VP1-2022.

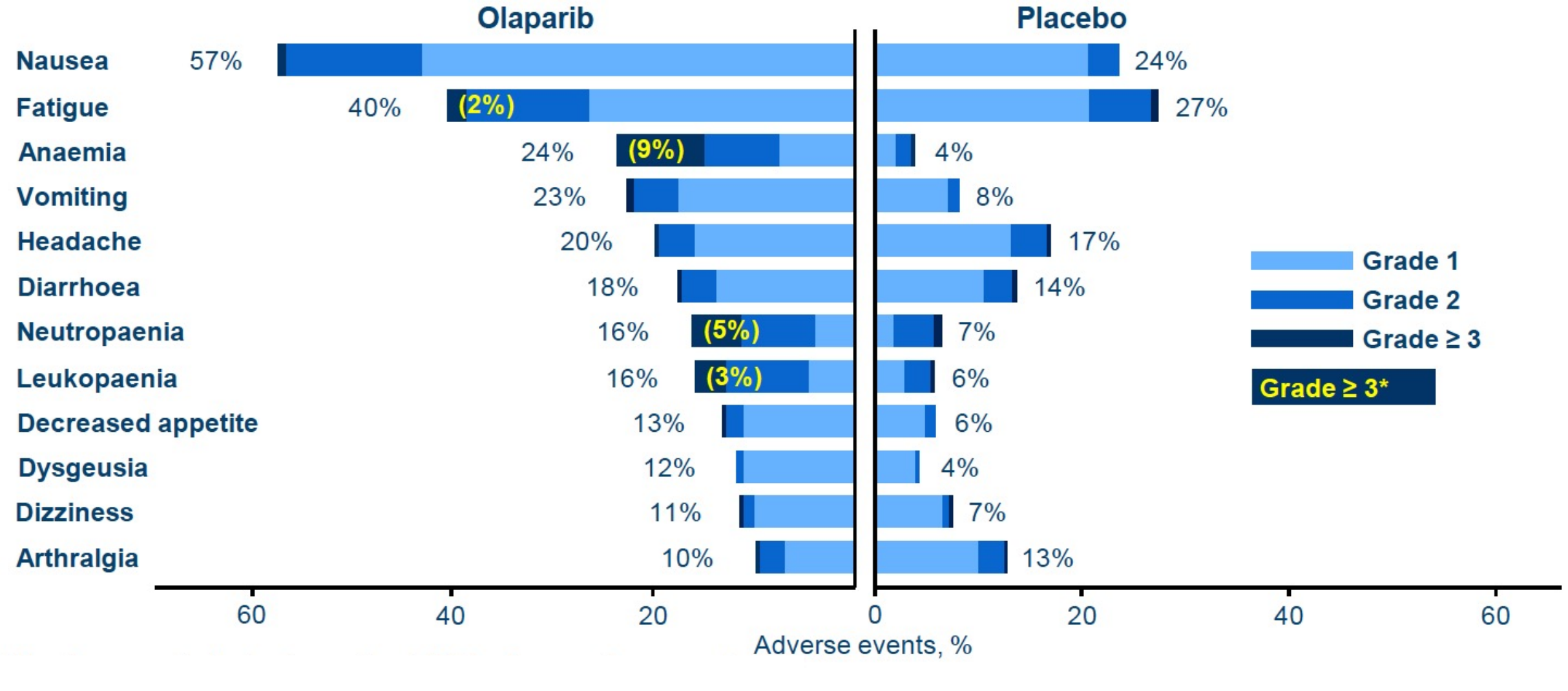
OlympiA: Adverse Event Profile Update

	Olaparib (N = 911)	Placebo (N = 904)
Any adverse event	**836 (91.8%)**	**758 (83.8%)**
Serious adverse event (SAE)	79 (8.7%)	**78 (8.6%)**
Adverse event of special interest*	**31 (3.4%)**	**51 (5.6%)**
MDS/AML	2 (0.2%)	3 (0.3%)
Pneumonitis	9 (1.0%)	**12 (1.3%)**
New primary malignancy	**21 (2.3%)**	**36 (4.0%)**
Grade ≥ 3 adverse event	**223 (24.5%)**	102 (11.3%)
Grade 4 adverse event	17 (1.9%)	4 (0.4%)
Adverse event leading to permanent discontinuation of treatment†	**98 (10.8%)**	**42 (4.6%)**
Adverse event leading to death‡	1 (0.1%)	2 (0.2%)

There have been no additional adverse events leading to death reported since IA IDFS

Tutt ANJ et al. ESMO Virtual Plenary 2022;Abstract VP1-2022.

OlympiA: Adverse Events of Any Grade ≥10%



Tutt ANJ et al. ESMO Virtual Plenary 2022;Abstract VP1-2022.

Breast Cancer Agenda

Module 1: HER2-Positive Disease

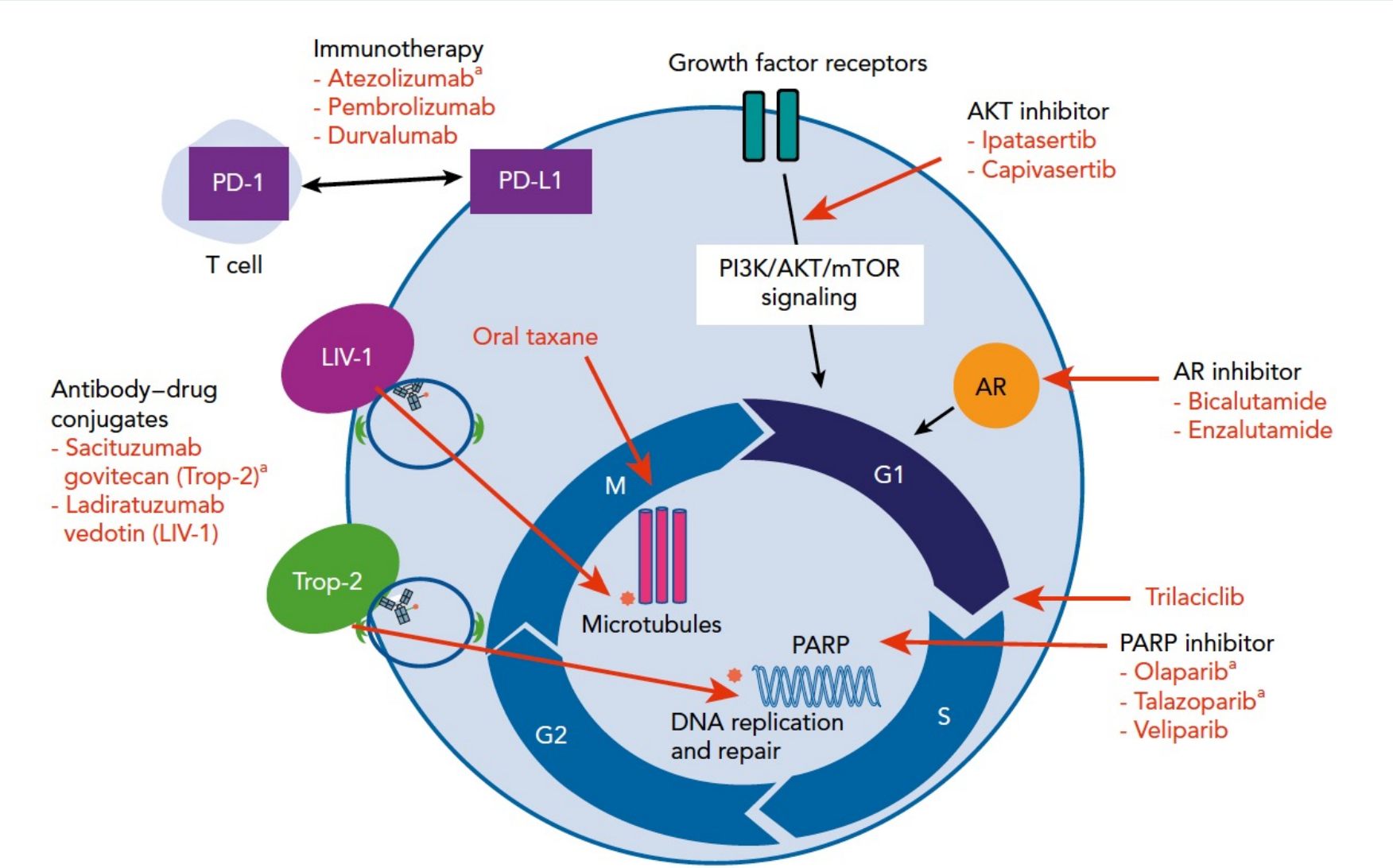
Module 2: Use of PARP Inhibitors in Localized HER2-Negative Disease (OlympiA/Olaparib)

Module 3: Triple-Negative Disease

- Management of localized disease (neoadjuvant and adjuvant IO)
- Sacituzumab govitecan in metastatic disease
- New agents and strategies under investigation

Module 4: ER/PR-Positive, HER2-Negative Disease

Novel Targets for Therapeutic Intervention in Triple-Negative Breast Cancer



Vidula N et al. *J Natl Compr Canc Netw* 2020;[Online ahead of print].

RTP RESEARCH TO PRACTICE

N Engl J Med 2022;386(6):556-67.

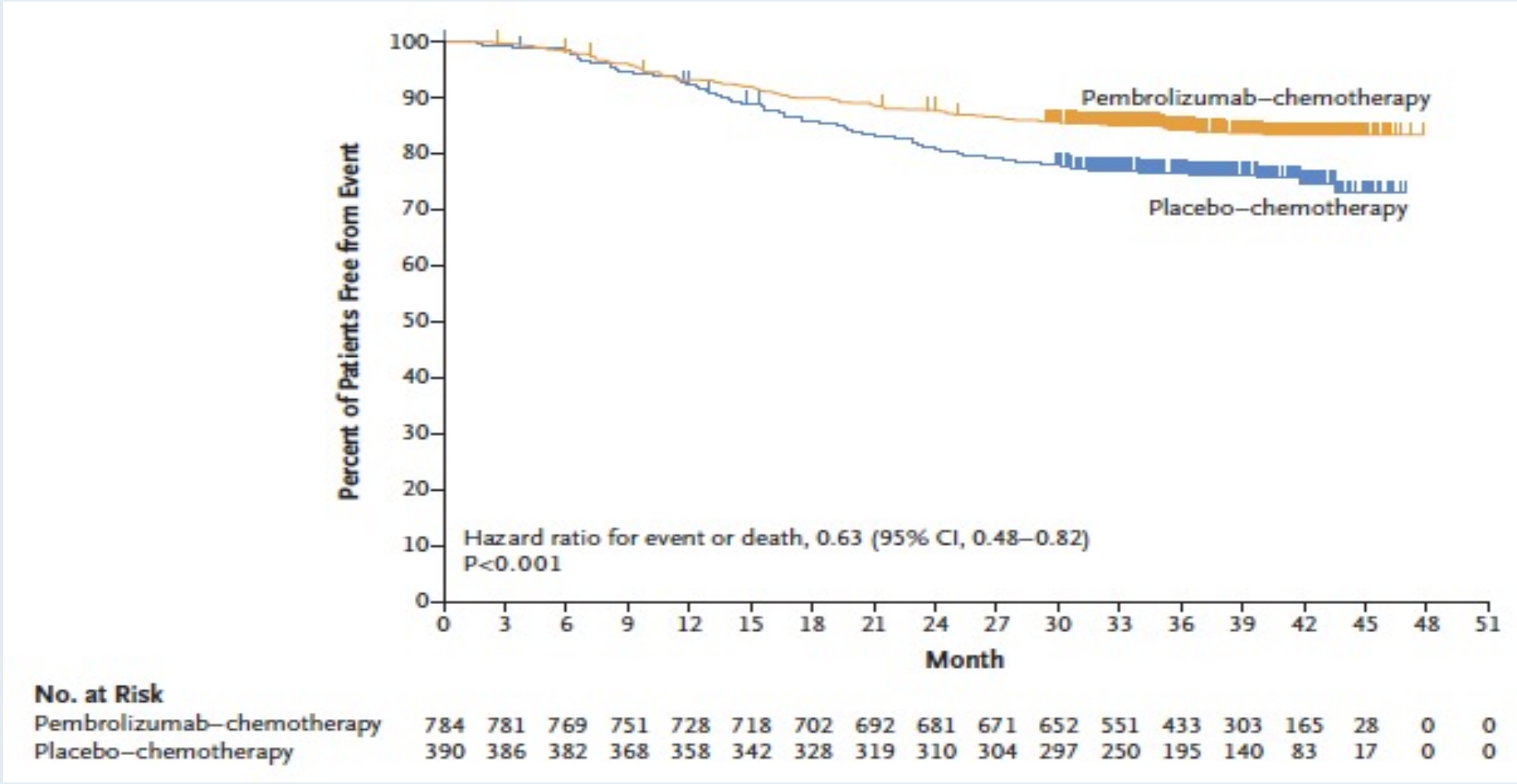
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Event-free Survival with Pembrolizumab in Early Triple-Negative Breast Cancer

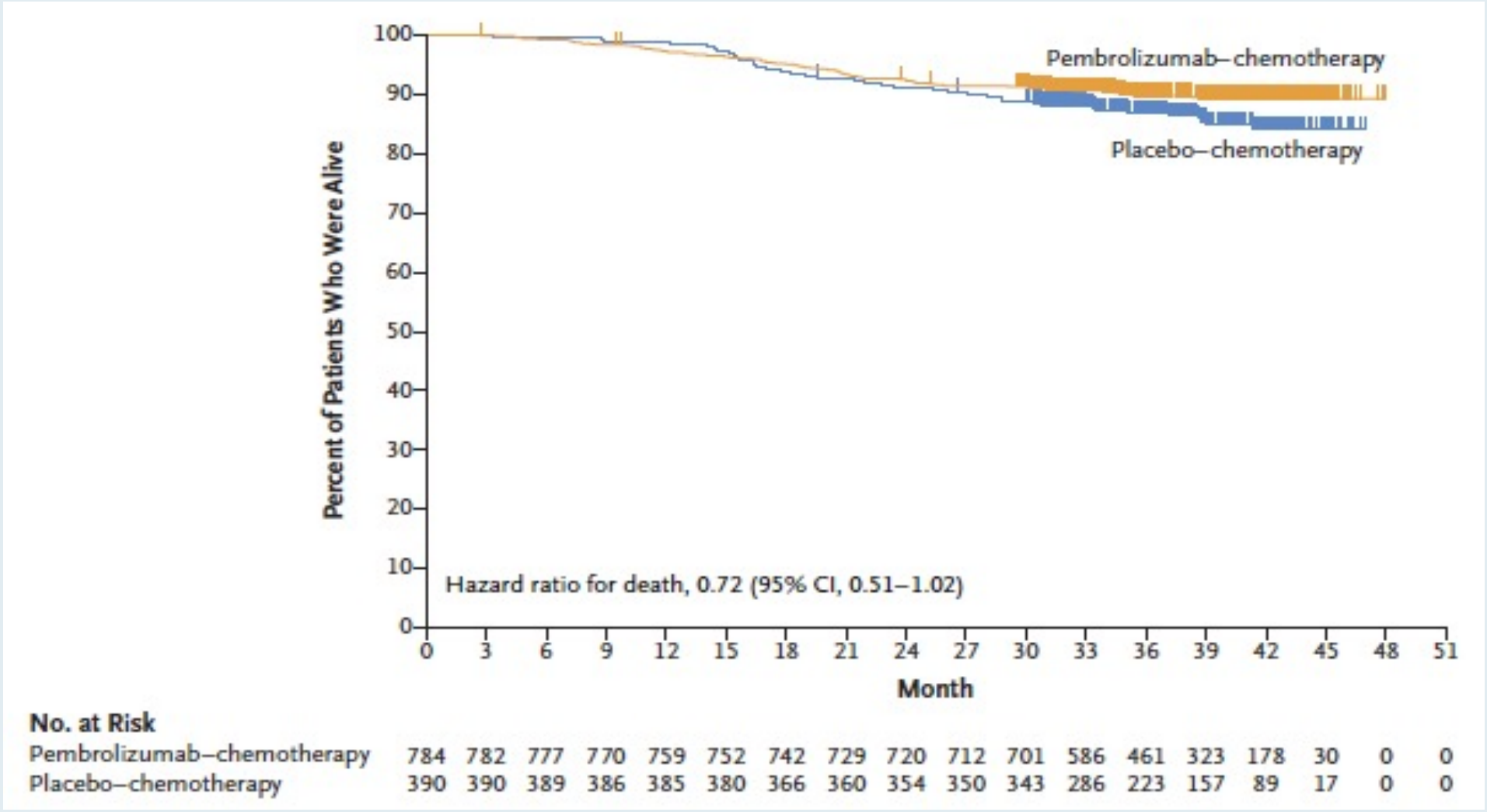
P. Schmid, J. Cortes, R. Dent, L. Pusztai, H. McArthur, S. Kümmel, J. Bergh, C. Denkert, Y.H. Park, R. Hui, N. Harbeck, M. Takahashi, M. Untch, P.A. Fasching, F. Cardoso, J. Andersen, D. Patt, M. Danso, M. Ferreira, M.-A. Mouret-Reynier, S.-A. Im, J.-H. Ahn, M. Gion, S. Baron-Hay, J.-F. Boileau, Y. Ding, K. Tryfonidis, G. Aktan, V. Karantza, and J. O'Shaughnessy, for the KEYNOTE-522 Investigators*

KEYNOTE-522: Event-Free Survival According to Treatment Group (ITT Population)



Schmid P et al. *N Engl J Med* 2022;386(6):556-67.

KEYNOTE-522: Overall Survival According to Treatment Group (ITT Population)



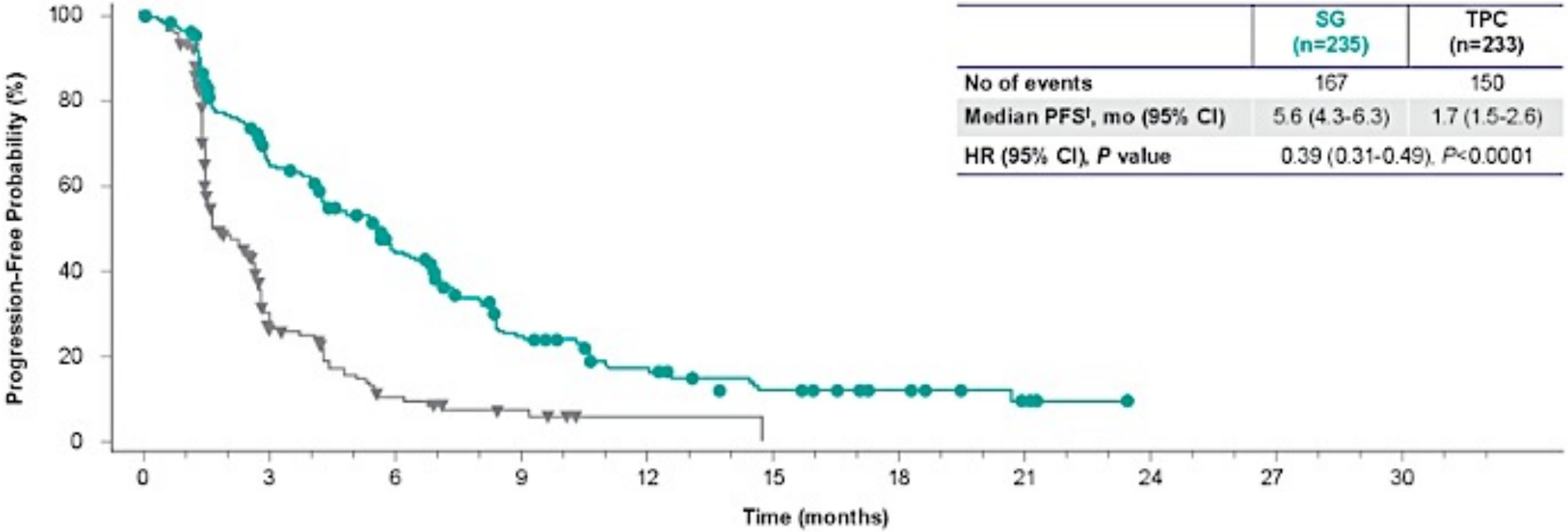
Schmid P et al. *N Engl J Med* 2022;386(6):556-67.

Sacituzumab Govitecan (SG) versus Treatment of Physician's Choice (TPC) in Patients (pts) with Previously Treated, Metastatic Triple-Negative Breast Cancer (mTNBC): Final Results from the Phase 3 ASCENT Study

Bardia A et al.

ASCO 2022;Abstract 1071.

ASCENT: Progression-Free Survival (BMNeg Population)



	SG (n=235)	TPC (n=233)
No of events	167	150
Median PFS[1], mo (95% CI)	5.6 (4.3-6.3)	1.7 (1.5-2.6)
HR (95% CI), *P* value	0.39 (0.31-0.49), *P*<0.0001	

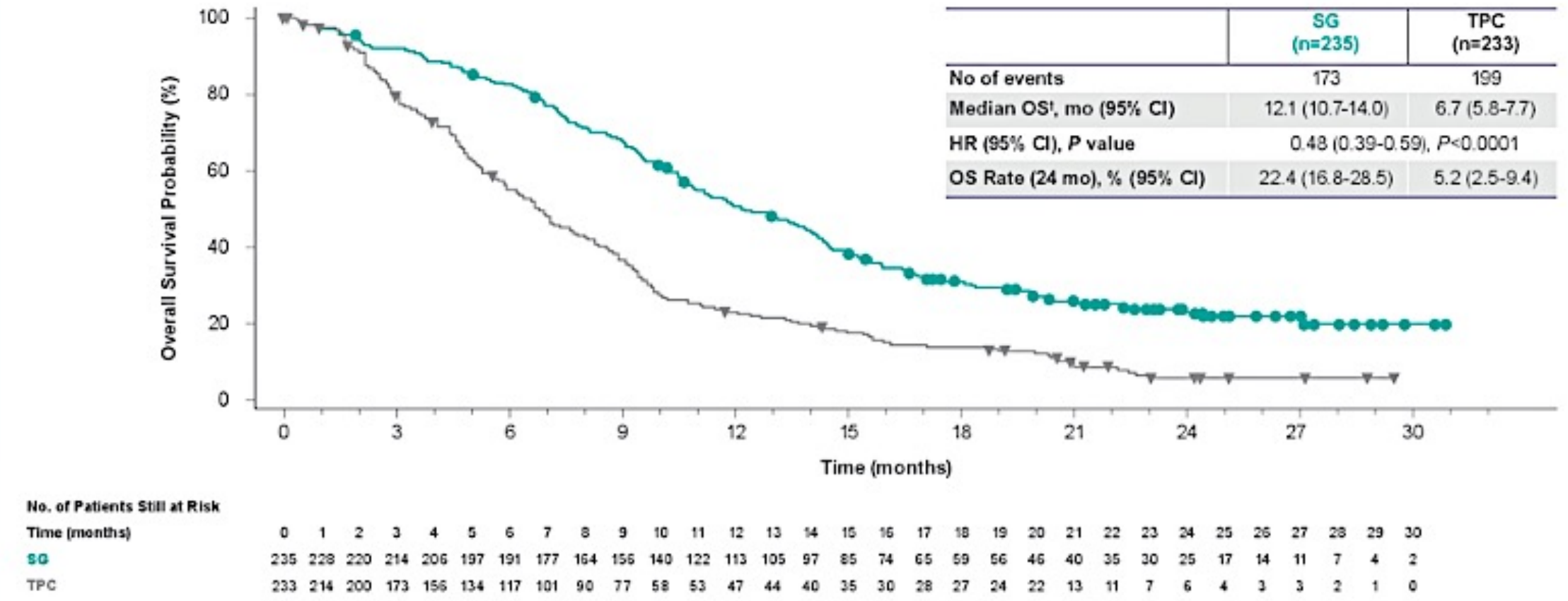
No. of Patients Still at Risk																									
Time (months)	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
SG	235	222	166	134	127	104	81	63	54	37	33	24	22	17	16	13	11	10	8	6	5	3	1	1	0
TPC	233	178	77	34	31	18	11	8	6	5	3	1	1	1	1	0	0	0	0	0	0	0	0	0	0

BMNeg = brain metastases-negative; SG = sacituzumab govitecan; TPC = treatment of physician's choice;
PFS = progression-free survival

Bardia A et al. ASCO 2022;Abstract 1071.

RTP RESEARCH TO PRACTICE

ASCENT: Overall Survival (BMNeg Population)



	SG (n=235)	TPC (n=233)
No of events	173	199
Median OS[1], mo (95% CI)	12.1 (10.7-14.0)	6.7 (5.8-7.7)
HR (95% CI), *P* value	0.48 (0.39-0.59), *P*<0.0001	
OS Rate (24 mo), % (95% CI)	22.4 (16.8-28.5)	5.2 (2.5-9.4)

No. of Patients Still at Risk

Time (months)	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
SG	235	228	220	214	206	197	191	177	164	156	140	122	113	105	97	85	74	65	59	56	46	40	35	30	25	17	14	11	7	4	2
TPC	233	214	200	173	156	134	117	101	90	77	58	53	47	44	40	35	30	28	27	24	22	13	11	7	6	4	3	3	2	1	0

BMNeg = brain metastases-negative; SG = sacituzumab govitecan; TPC = treatment of physician's choice;
OS = overall survival

Bardia A et al. ASCO 2022;Abstract 1071.

ASCENT: Selected Adverse Events

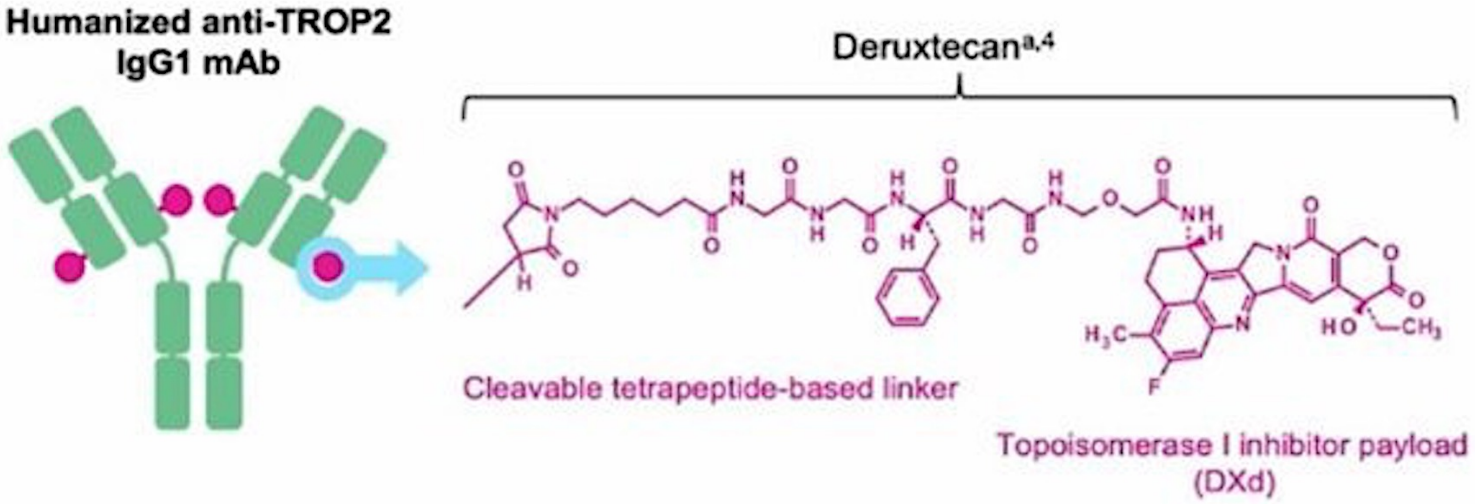
Adverse event	Patients (N = 108)		
	Any grade	Grade 3	Grade 4
Gastrointestinal disorders			
Nausea	67%	6%	0
Diarrhea	62%	8%	0
Vomiting	49%	6%	0
Blood and lymphatic system disorders			
Neutropenia	64%	26%	16%
Anemia	50%	11%	0
Abnormal values			
Decrease white blood cell counts	21%	8%	3%

Bardia A et al. *N Engl J Med* 2021;384(16):1529-41.

Datopotamab Deruxtecan (Dato-DXd) Mechanism of Action

Dato-DXd is an ADC with 3 components[1,2]:

- A humanized anti-TROP2 IgG1[3] monoclonal antibody attached to:
- A topoisomerase I inhibitor payload, an exatecan derivative, via
- A tetrapeptide-based cleavable linker



Payload mechanism of action: topoisomerase I inhibitor [b,1]
High potency of payload [b,2]
Optimized drug to antibody ratio ≈4 [b,c,1]
Payload with short systemic half-life [b,c,2]
Stable linker-payload [b,2]
Tumor-selective cleavable linker [b,2]
Bystander antitumor effect [b,2,5]

[a] Image is for illustrative purposes only; actual drug positions may vary. [b] The clinical relevance of these features is under investigation. [c] Based on animal data.

1. Okajima D, et al. AACR-NCI-EORTC 2019; [abstract C026]; 2. Nakada T, et al. *Chem Pharm Bull.* 2019;67(3):173-185; 3. Daiichi Sankyo Co. Ltd. DS-1062. Daiichi Sankyo.com. Accessed October 6, 2020. https://www.daiichisankyo.com/media_investors/investor_relations/ir_calendar/files/005438/DS-1062%20Seminar%20Slides_EN.pdf; 4. Krop I, et al. SABCS 2019; [abstract GS1-03]; 5. Ogitani Y, et al. *Cancer Sci.* 2016;107(7):1039-1046.

Krop I et al. San Antonio Breast Cancer Symposium 2021;Abstract GS1-05.

San Antonio Breast Cancer Symposium®, December 7 – 10, 2021

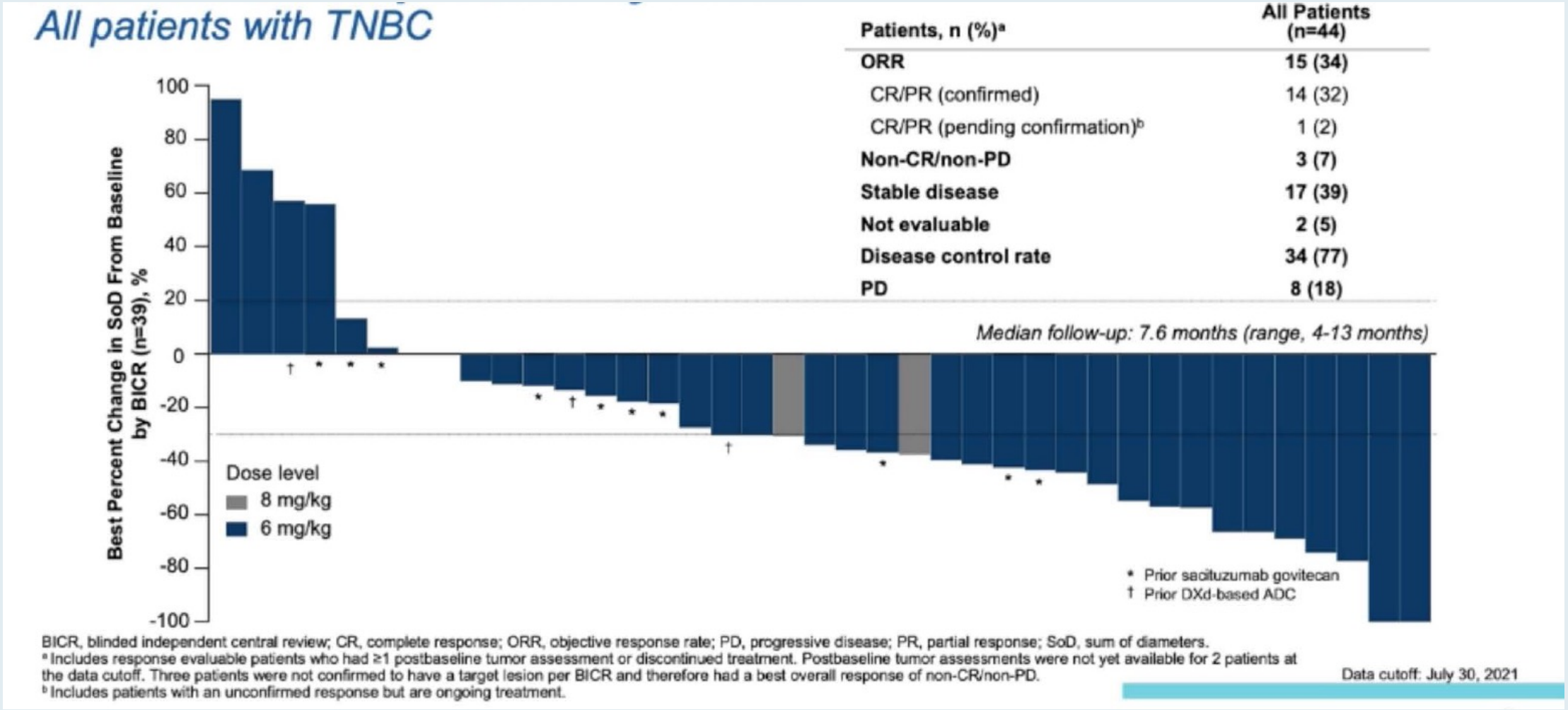
Datopotamab Deruxtecan (Dato-DXd) in Advanced/Metastatic HER2 Negative Breast Cancer: Triple Negative Breast Cancer Results from the Phase 1 TROPION-PanTumor01 Study

Ian Krop,[1] Dejan Juric,[2] Toshio Shimizu,[3] Anthony Tolcher,[4] Alexander Spira,[5] Toru Mukohara,[6] Aaron E. Lisberg,[7] Takahiro Kogawa,[8] Kyriakos P. Papadopoulos,[9] Erika Hamilton,[10] Senthil Damodaran,[11] Jonathan Greenberg,[12] Wen Gu,[12] Fumiaki Kobayashi,[13] Takahiro Jikoh,[13] Yui Kawasaki,[13] Funda Meric-Bernstam,[11] Aditya Bardia[2]

[1]Dana-Farber Cancer Institute, Boston, MA; [2]Department of Hematology/Oncology, Massachusetts General Hospital Cancer Center, Harvard Medical School, Boston, MA; [3]National Cancer Center Hospital, Tokyo, Japan; [4]NEXT Oncology, San Antonio, TX; [5]Virginia Cancer Specialists, Fairfax, VA; [6]Department of Medical Oncology, National Cancer Center Hospital East, Kashiwa, Japan; [7]UCLA Jonsson Comprehensive Cancer Center, Santa Monica, CA; [8]Advanced Medical Development Center, The Cancer Institute Hospital of JFCR, Tokyo, Japan; [9]START Center for Cancer Care San Antonio, San Antonio, TX; [10]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN; [11]The University of Texas MD Anderson Cancer Center, Houston, TX; [12]Daiichi Sankyo Inc., Basking Ridge, NJ; [13]Daiichi Sankyo Co, Ltd, Tokyo, Japan

Abstract GS1-05

TROPION-PanTumor01: Antitumor Response in Triple-Negative Breast Cancer (TNBC) Cohort



Patients, n (%)[a]	All Patients (n=44)
ORR	**15 (34)**
CR/PR (confirmed)	14 (32)
CR/PR (pending confirmation)[b]	1 (2)
Non-CR/non-PD	**3 (7)**
Stable disease	**17 (39)**
Not evaluable	**2 (5)**
Disease control rate	**34 (77)**
PD	**8 (18)**

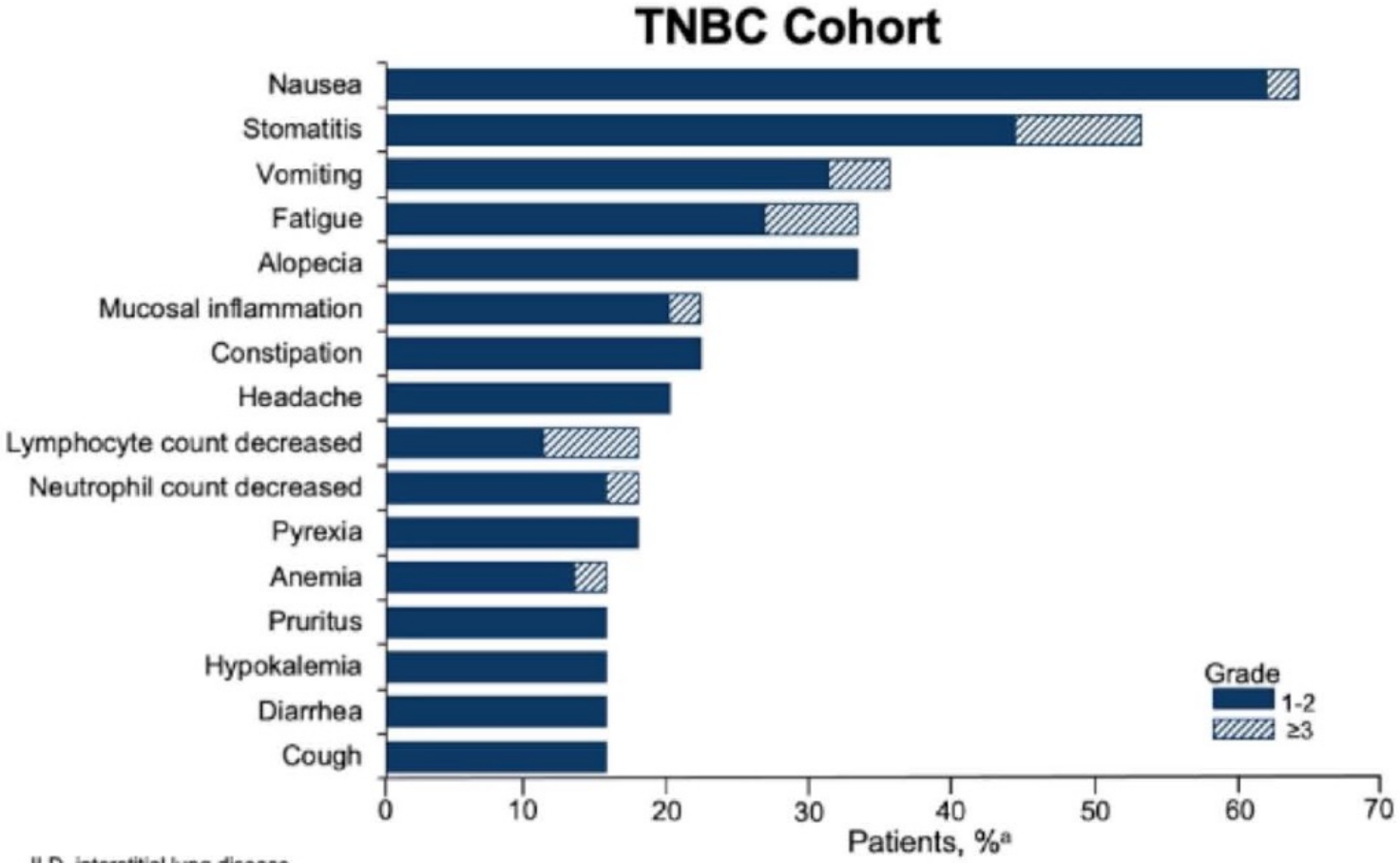
BICR, blinded independent central review; CR, complete response; ORR, objective response rate; PD, progressive disease; PR, partial response; SoD, sum of diameters.
[a] Includes response evaluable patients who had ≥1 postbaseline tumor assessment or discontinued treatment. Postbaseline tumor assessments were not yet available for 2 patients at the data cutoff. Three patients were not confirmed to have a target lesion per BICR and therefore had a best overall response of non-CR/non-PD.
[b] Includes patients with an unconfirmed response but are ongoing treatment.

Data cutoff: July 30, 2021

Krop I et al. SABCS 2021;Abstract GS1-05.

RTP RESEARCH TO PRACTICE

TROPION-PanTumor01: Treatment-Emergent Adverse Events in ≥15% of Patients in TNBC Cohort



- Most common adverse events observed were nausea and stomatitis (predominantly grade 1-2)
- Low frequency of hematologic toxicity and diarrhea
- No cases adjudicated as drug-related ILD

ILD, interstitial lung disease.
[a] n=44 patients.

Data cutoff: July 30, 2021

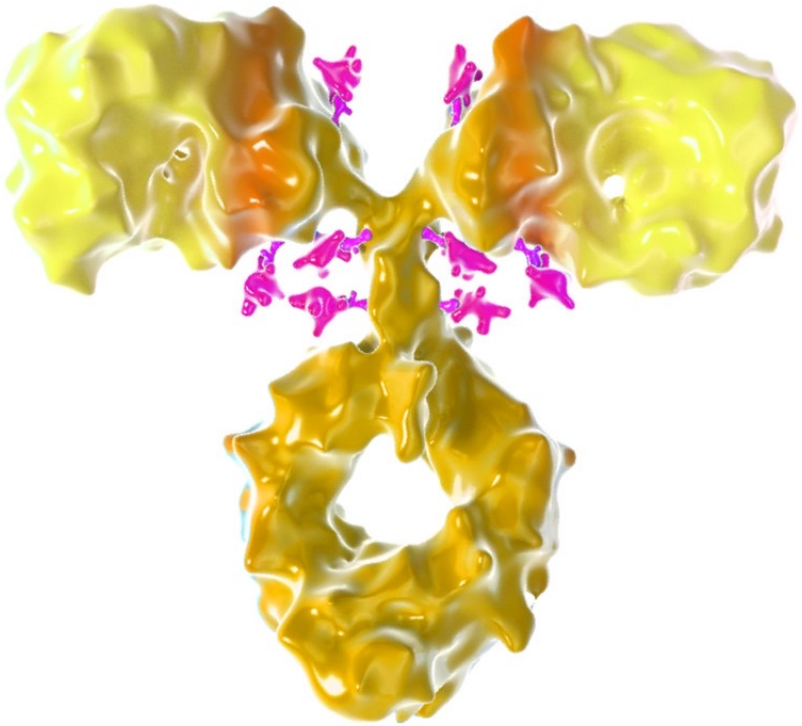
Krop I et al. SABCS 2021;Abstract GS1-05.

RTP RESEARCH TO PRACTICE

2022 ASCO® ANNUAL MEETING

Abstract 1002

Results From the Phase 1/2 Study of Patritumab Deruxtecan, a HER3-Directed Antibody-Drug Conjugate (ADC), in Patients With HER3-Expressing Metastatic Breast Cancer



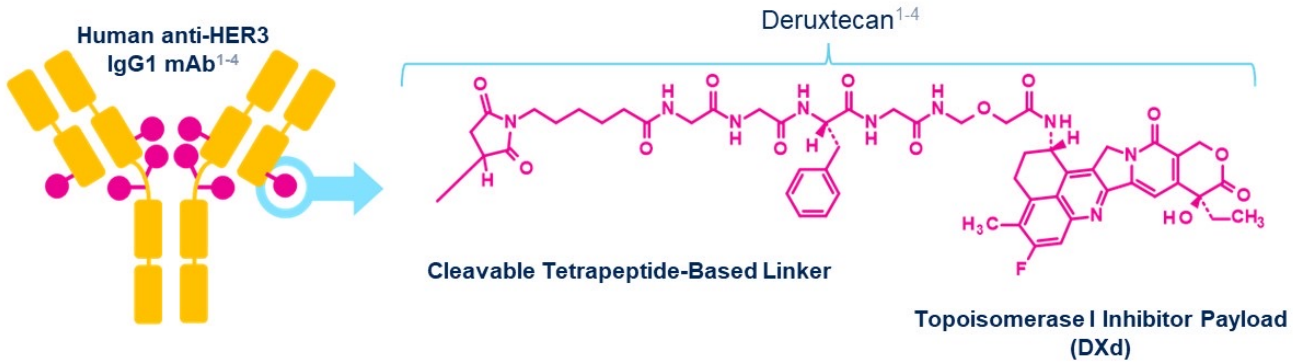
June 4, 2022

Ian E. Krop,[1] Norikazu Masuda,[2] Toru Mukohara,[3] Shunji Takahashi,[4] Takahiro Nakayama,[5] Kenichi Inoue,[6] Hiroji Iwata,[7] Tatsuya Toyama,[8] Yutaka Yamamoto,[9] Damien Hansra,[10] Masato Takahashi,[11] Akihiko Osaki,[12] Kumiko Koyama,[13] Tatsuya Inoue,[14] Takatoshi Yonekura,[13] Joseph Mostillo,[15] Shoichi Ohwada,[13] Yoshimi Tanaka,[13] David Sternberg,[15] Kan Yonemori[16]

[1] Yale Cancer Center, New Haven, CT; [2] Nagoya University Graduate School of Medicine, Nagoya, Japan; [3] National Cancer Center Hospital East, Kashiwa, Japan; [4] The Cancer Institute Hospital of Japanese Foundation for Cancer Research, Tokyo, Japan; [5] Osaka International Cancer Institute, Osaka, Japan; [6] Saitama Cancer Center, Saitama Japan; [7] Aichi Cancer Center Hospital, Nagoya, Japan; [8] Nagoya City University, Nagoya, Japan; [9] Kumamoto University Hospital, Kumamoto, Japan; [10] Piedmont Physicians Medical Oncology, Fayetteville, GA; [11] National Hospital Organization, Hokkaido Cancer Center, Sapporo, Japan; [12] Saitama Medical University International Medical Center; Hidaka, Japan; [13] Daiichi Sankyo Co., Ltd., Tokyo, Japan; [14] Daiichi Sankyo RD Novare Co., Ltd., Tokyo, Japan; [15] Daiichi Sankyo, Inc., Basking Ridge, NJ; [16] National Cancer Center Hospital, Tokyo, Japan

Patritumab Deruxtecan (HER3-DXd)

- HER3-DXd is an ADC with 3 components[1-6]:
  - A fully human anti-HER3 IgG1 mAb (patritumab), covalently linked to
  - A topoisomerase I inhibitor payload, an exatecan derivative, via
  - A tetrapeptide-based cleavable linker



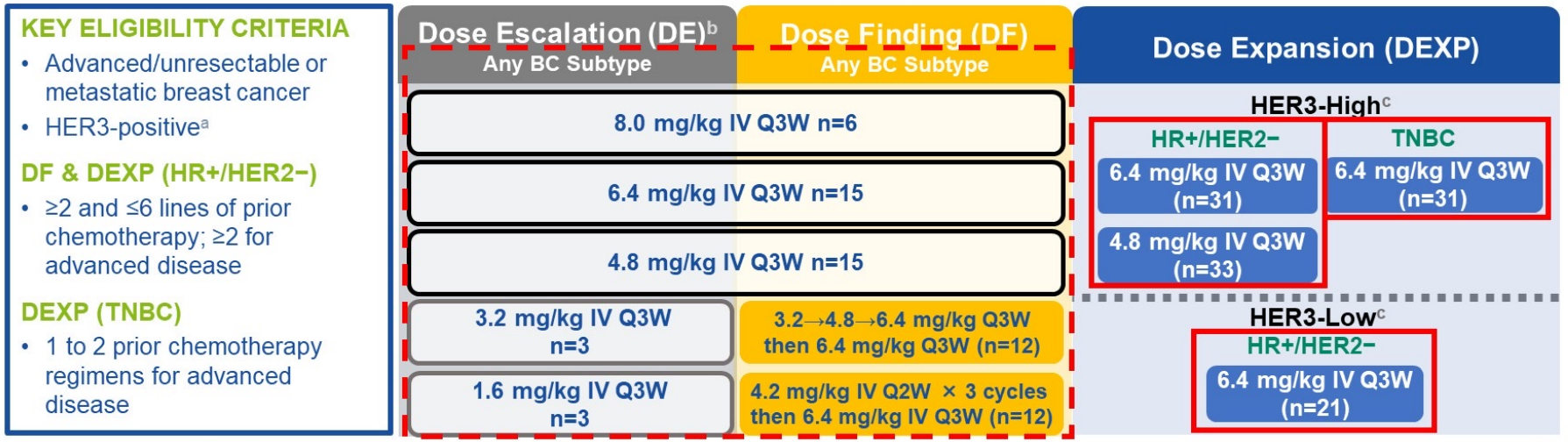
7 Key Attributes of HER3-DXd

Payload mechanism of action: topoisomerase I inhibitor [a,1-4]
High potency of payload [a,1-4]
High drug to antibody ratio ≈ 8 [a,1,2]
Payload with short systemic half-life [a,b,2,3]
Stable linker-payload [a,2-4]
Tumor-selective cleavable linker [a,1-5]
Bystander antitumor effect [a,2,6]

HER, human epidermal growth factor receptor; IgG1, immunoglobulin G1; mAb, monoclonal antibody.
[a] The clinical relevance of these features is under investigation. [b] Based on animal data.
1. Hashimoto Y, et al. *Clin Cancer Res.* 2019;25:7151-7161. 2. Nakada T, et al. *Chem Pharm Bull (Tokyo).* 2019;67(3):173-185. 3. Ogitani Y, et al. *Clin Cancer Res.* 2016;22(20):5097-5108. 4. Koganemaru S, et al. *Mol Cancer Ther.* 2019;18:2043-2050. 5. Haratani K, et al. *J Clin Invest.* 2020;130(1):374-388. 6. Ogitani Y, et al. *Cancer Sci.* 2016;107(7):1039-1046.

Krop I et al. ASCO 2022;Abstract 1002.

U31402-A-J101: Study Design



Data for all 3 phases were pooled

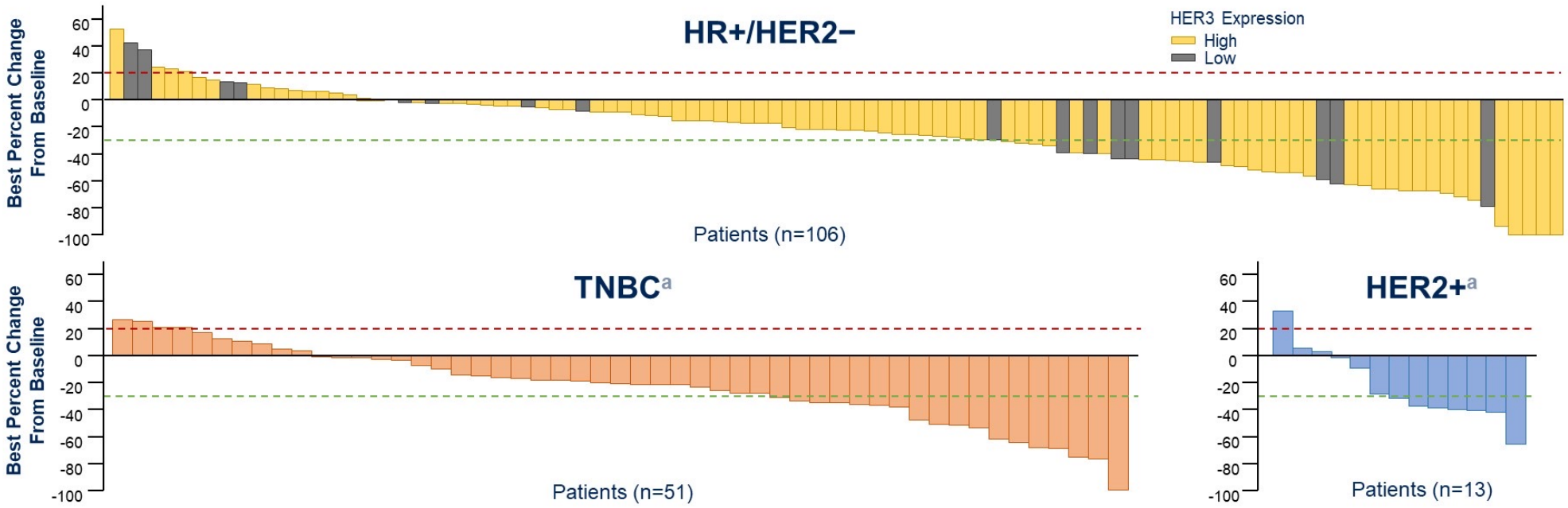
- **Efficacy** is reported by BC subtype: HR+/HER2− (n=113), TNBC (n=53), and HER2+ (n=14)
- **Safety** is reported for patients who received HER3-DXd 4.8 mg/kg (n=48), 6.4 mg/kg (n=98), and all patients (N=182[d])

DE, dose escalation; DEXP, dose expansion; DF, dose finding; EWOC, escalation with overdose control; HR, hormone receptor; IHC, immunohistochemistry; mCRM, modified continuous reassessment method; Q2W, once every 2 weeks; Q3W, once every 3 weeks; TNBC, triple-negative breast cancer.

[a] HER3 status was determined by IHC in archival tumor tissue (pre-treatment samples [<6 months prior to HER3-DXd treatment] were used for screening when archival tissue was not available); HER3-positive was defined as IHC 2+ and IHC 3+ for DE/DF cohorts and as ≥25% membrane positivity at 10x for DEXP cohorts. [b] Guided by mCRM with EWOC. [c] HER3-high was defined as ≥75% membrane positivity at 10x; HER3-low was defined as ≥25% and <75% membrane positivity at 10x. [d] Includes two patients with unknown BC subtype.

Krop I et al. ASCO 2022;Abstract 1002.

Change in Tumor Size from Baseline



HER3-DXd induced a clinically meaningful decrease in tumor size by BICR in most patients across BC subtypes.[b]

[a] Patients with TNBC and HER2+ were all HER3-high.
[b] Best percentage change from baseline in sum of diameters based on BICR for all target lesions identified is represented by patient. If any lesion measurement is missing at a post-baseline tumor assessment visit, that visit is not taken into consideration for best percent change from baseline in sum of diameters.

Krop I et al. ASCO 2022;Abstract 1002.

Pivotal Phase III Trials Supporting the FDA Approvals of Olaparib and Talazoparib for Metastatic Breast Cancer with a Germline BRCA Mutation

Trial	Eligibility	Randomization	Primary endpoint
OlympiAD[1] (n = 302)	• HER2-negative metastatic breast cancer – ER-positive and/or PR-positive or TNBC • Deleterious or suspected deleterious gBRCA mutation • Prior anthracycline and taxane • ≤2 prior chemotherapy lines in metastatic setting	• Olaparib • Physician's choice – Capecitabine – Eribulin – Vinorelbine	• PFS by blinded independent central review
EMBRACA[2] (n = 431)	• HER2-negative locally advanced or metastatic breast cancer • Germline BRCA1 or BRCA2 mutation • ≤3 prior cytotoxic chemotherapy regimens • Prior treatment with a taxane and/or anthracycline unless medically contraindicated	• Talazoparib • Physician's choice – Capecitabine – Eribulin – Gemcitabine – Vinorelbine	• PFS by blinded independent central review

TNBC = triple-negative breast cancer; gBRCA = germline BRCA; PFS = progression-free survival

[1] Robson M et al. *N Engl J Med* 2017;377(6):523-33. [2] Litton JK et al. SABCS 2017;Abstract GS6-07. www.clinicaltrials.gov. Accessed August 2019.

OlympiAD and EMBRACA: Efficacy Summary

	OlympiAD[1-3]	EMBRACA[4-6]
HR (PFS)	0.58	0.54
HR (PFS) ER/PR-positive	0.82	0.47
HR (PFS) TNBC	0.43	0.60
HR (OS)	0.84	0.76
ORR	59.9% (vs 28.8% TPC)	67.6% (vs 27.2% TPC)

TPC = treatment of physician's choice

Cross-trial comparisons are challenging in terms of determining the relative efficacy and tolerability of treatments

[1] Robson M et al. *N Engl J Med* 2017;377(6):523-33. [2] Robson M et al. *Ann Oncol* 2019;30(4):558-66. [3] Robson M et al. San Antonio Breast Cancer Symposium 2019;Abstract PD4-03. [4] Litton JK et al. *N Engl J Med* 2018;379(8):753-63. [5] Litton JK et al. San Antonio Breast Cancer Symposium 2017;Abstract GS6-07. [6] Rugo HS et al. ASCO 2018;Abstract 1069.

OlympiAD and EMBRACA: Adverse Event (AE) and Quality of Life Summary

	OlympiAD [1,2]	EMBRACA[3,4]
Serious AEs Grade ≥3	36.6% (vs 50.5% TPC)	25.5% (v. 25.4% TPC)
Anemia Grade ≥3	16.1%	39.2%
Neutropenia Grade ≥3	9.3%	20.9%
Thrombocytopenia Grade ≥3	2.4%	14.7%
MDS/AML	0	0
Nausea (any grade)	58.0%	48.6%
Alopecia (any grade)	3.4%	25.2%
Dose modification/reduction due to AE	25.4% (vs 30.8% TPC)	66% (vs 60% TPC)
Treatment discontinuation due to AE	4.9% (vs 7.7% TPC)	5.9% (vs 8.7% TPC)

Cross-trial comparisons are challenging in terms of determining the relative efficacy and tolerability of treatments

[1] Robson M et al. *N Engl J Med* 2017;377(6):523-33. [2] Robson M et al. *Ann Oncol* 2019;30(4):558-66. [3] Litton JK et al. *N Engl J Med* 2018;379(8):753-63. [4] Litton JK et al. San Antonio Breast Cancer Symposium 2017;Abstract GS6-07.

N Engl J Med 2022;387(3):217-26.

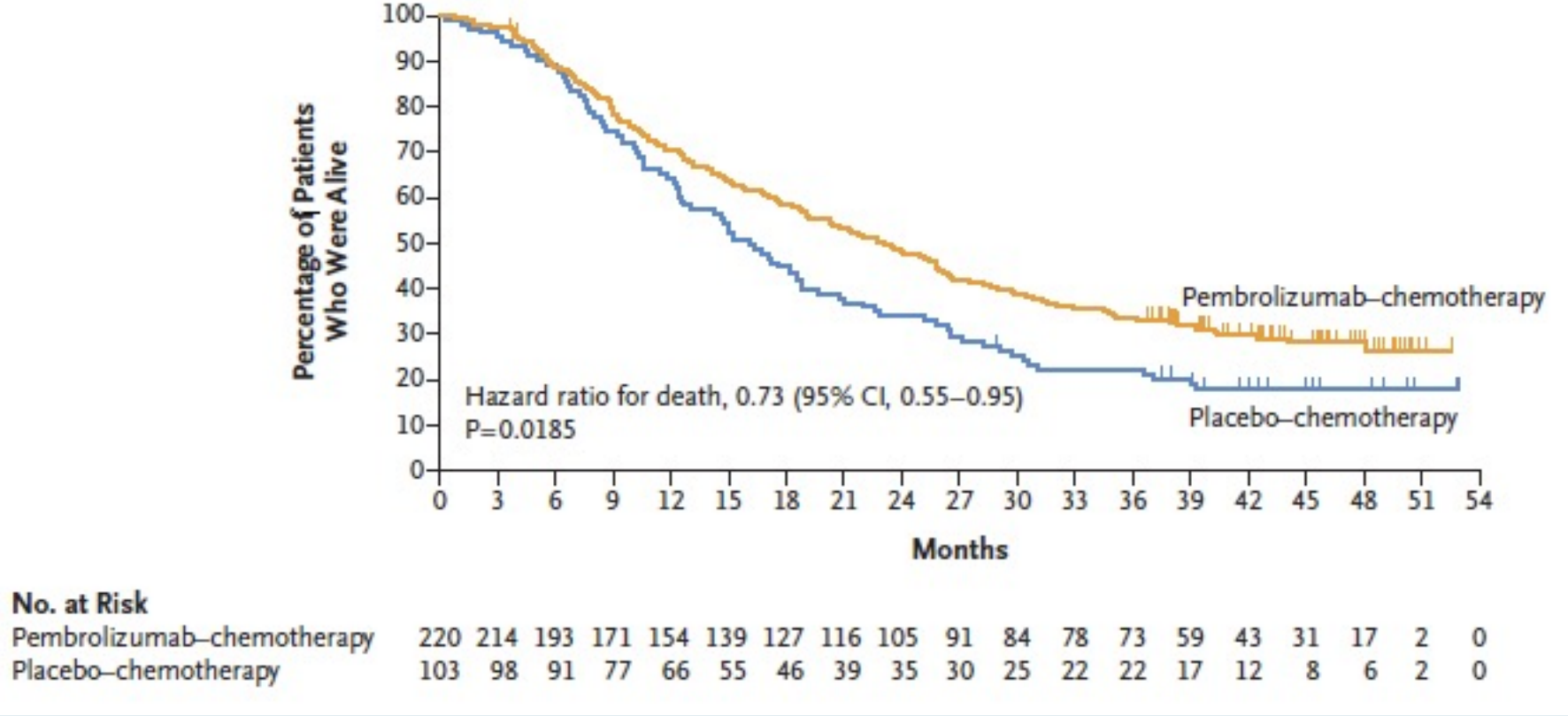
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Pembrolizumab plus Chemotherapy in Advanced Triple-Negative Breast Cancer

J. Cortes, H.S. Rugo, D.W. Cescon, S.-A. Im, M.M. Yusof, C. Gallardo, O. Lipatov, C.H. Barrios, J. Perez-Garcia, H. Iwata, N. Masuda, M. Torregroza Otero, E. Gokmen, S. Loi, Z. Guo, X. Zhou, V. Karantza, W. Pan, and P. Schmid, for the KEYNOTE-355 Investigators*

KEYNOTE-355: Overall Survival in the CPS-10 Subgroup

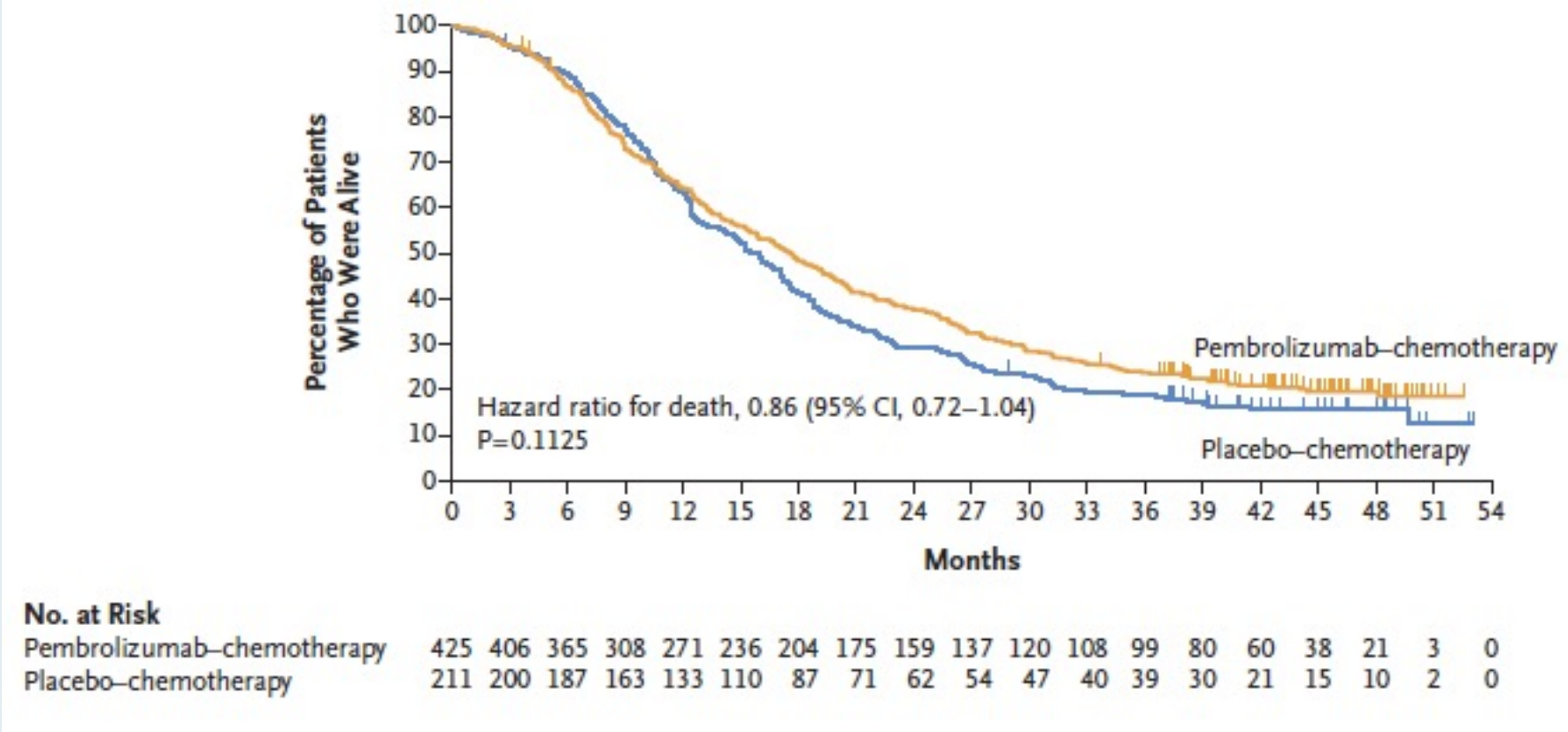


CPS-10 subgroup = patients whose tumors expressed PD-L1 with a combined positive score of ≥10

Cortes J et al. *N Engl J Med* 2022;387(3):217-26.

RTP RESEARCH TO PRACTICE

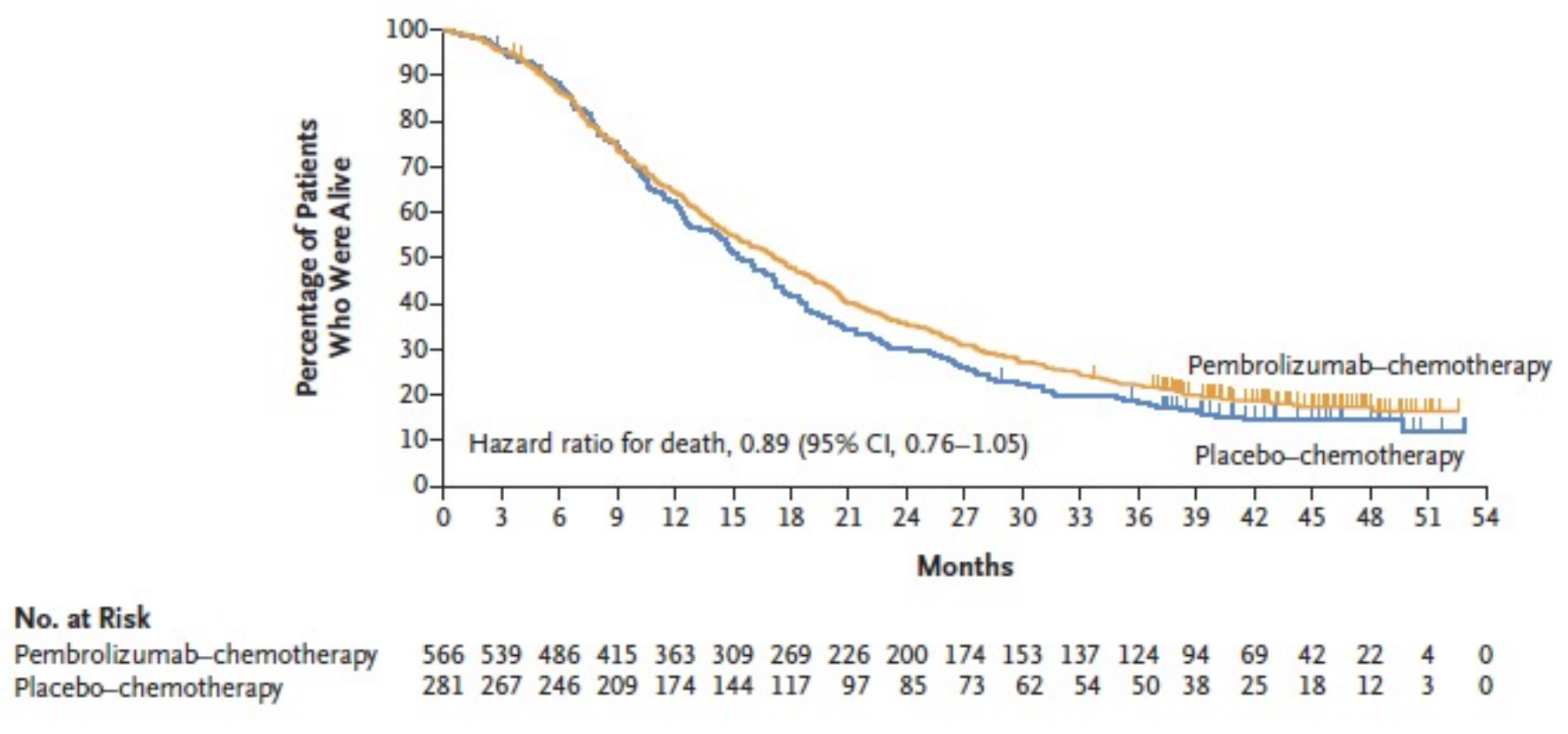
KEYNOTE-355: Overall Survival in the CPS-1 Subgroup



CPS-1 subgroup = patients whose tumors expressed PD-L1 with a combined positive score of ≥1

Cortes J et al. *N Engl J Med* 2022;387(3):217-26.

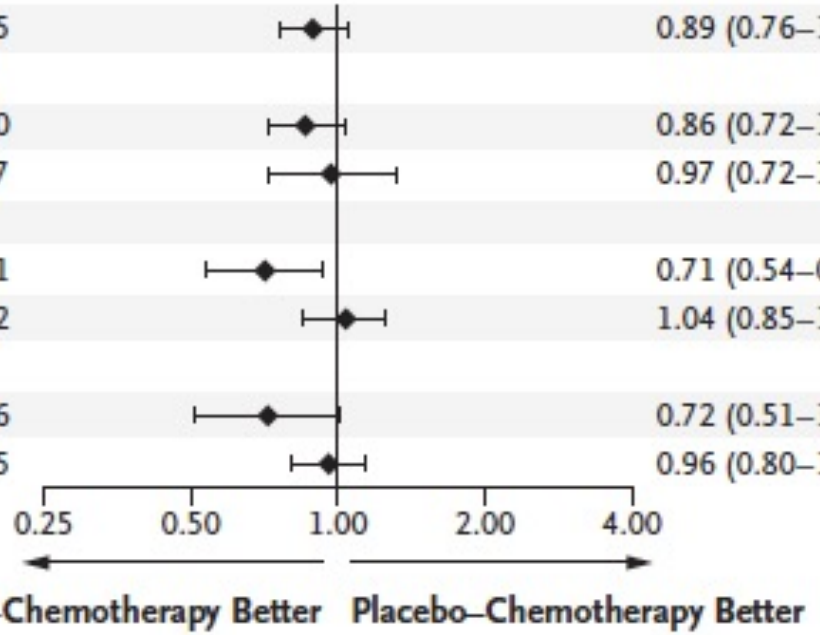
KEYNOTE-355: Overall Survival in the Intention-to-Treat Population



Cortes J et al. *N Engl J Med* 2022;387(3):217-26.

KEYNOTE-355: Overall Survival in Subgroups According to PD-L1 CPS Status at Baseline

Subgroup	No. of Patients	Median Overall Survival		Hazard Ratio for Death (95% CI)
		Pembrolizumab–chemotherapy	Placebo–chemotherapy	
		mo		
Overall	847	17.2	15.5	0.89 (0.76–1.05)
PD-L1 CPS cutoff of 1				
CPS ≥1	636	17.6	16.0	0.86 (0.72–1.04)
CPS <1	211	16.2	14.7	0.97 (0.72–1.32)
PD-L1 CPS cutoff of 10				
CPS ≥10	323	23.0	16.1	0.71 (0.54–0.93)
CPS <10	524	14.7	15.2	1.04 (0.85–1.26)
PD-L1 CPS cutoff of 20				
CPS ≥20	204	24.0	15.6	0.72 (0.51–1.01)
CPS <20	643	15.9	15.5	0.96 (0.80–1.14)



CPS = combined positive score

Cortes J et al. *N Engl J Med* 2022;387(3):217-26.

KEYNOTE-355: Adverse Events

Event	Pembrolizumab–Chemotherapy (N=562)		Placebo–Chemotherapy (N=281)	
	Any Grade	Grade 3, 4, or 5	Any Grade	Grade 3, 4, or 5
	number of patients (percent)			
Any adverse event	554 (98.6)	438 (77.9)	276 (98.2)	207 (73.7)
Adverse events that were attributed to the trial regimen†	541 (96.3)	383 (68.1)	267 (95.0)	188 (66.9)
Anemia	276 (49.1)	93 (16.5)	129 (45.9)	41 (14.6)
Neutropenia	231 (41.1)	167 (29.7)	107 (38.1)	84 (29.9)
Nausea	221 (39.3)	9 (1.6)	116 (41.3)	4 (1.4)
Alopecia	186 (33.1)	5 (0.9)	94 (33.5)	3 (1.1)
Fatigue	161 (28.6)	16 (2.8)	84 (29.9)	7 (2.5)
Neutrophil count decreased	126 (22.4)	98 (17.4)	74 (26.3)	57 (20.3)
Alanine aminotransferase increased	115 (20.5)	34 (6.0)	46 (16.4)	13 (4.6)
Immune-mediated adverse events‡	149 (26.5)	30 (5.3)	18 (6.4)	0
Hypothyroidism	89 (15.8)	2 (0.4)	9 (3.2)	0
Hyperthyroidism	24 (4.3)	1 (0.2)	3 (1.1)	0
Pneumonitis	14 (2.5)	6 (1.1)	0	0
Colitis	10 (1.8)	2 (0.4)	4 (1.4)	0
Severe skin reactions	10 (1.8)	10 (1.8)§	1 (0.4)	0

Cortes J et al. *N Engl J Med* 2022;387(3):217-26.

RTP RESEARCH TO PRACTICE

Breast Cancer Agenda

Module 1: HER2-Positive Disease

Module 2: Use of PARP Inhibitors in Localized HER2-Negative Disease (OlympiA/Olaparib)

Module 3: Triple-Negative Disease

Module 4: ER/PR-Positive, HER2-Negative Disease

- Genomic assays in node-positive disease
- Adjuvant CDK4/6 inhibitors: monarchE (abemaciclib)
- Selection of CDK4/6 inhibitors in metastatic disease (ribociclib survival); sacituzumab govitecan

ASCO special articles

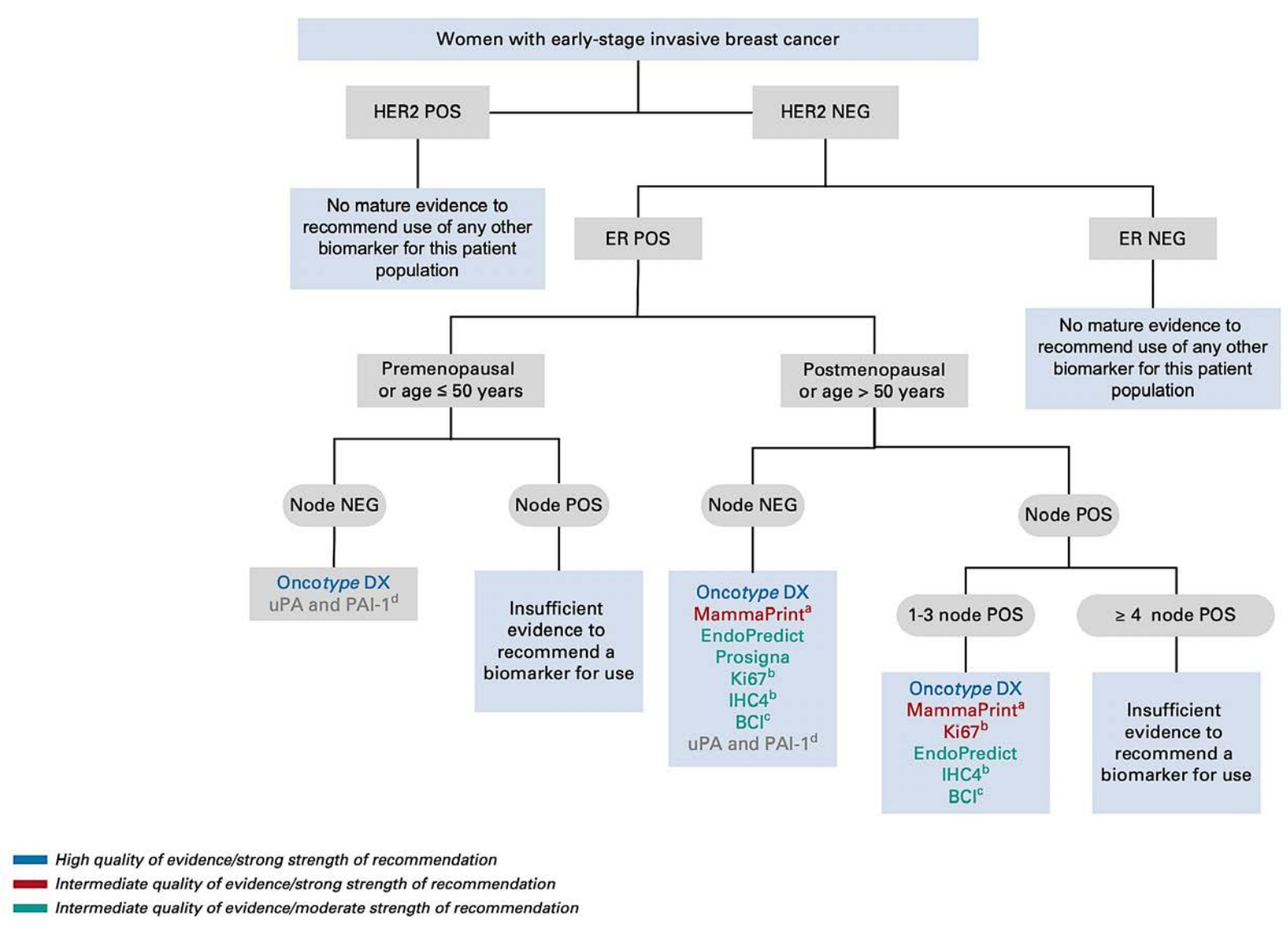
Biomarkers for Adjuvant Endocrine and Chemotherapy in Early-Stage Breast Cancer: ASCO Guideline Update

Fabrice Andre, MD[1]; Nofisat Ismaila, MD, MSc[2]; Kimberly H. Allison, PhD[3]; William E. Barlow, PhD[4]; Deborah E. Collyar, BSc[5]; Senthil Damodaran, MD, PhD[6]; N. Lynn Henry, MD, PhD[7]; Komal Jhaveri, MD[8,9]; Kevin Kalinsky, MD, MS[10]; Nicole M. Kuderer, MD[11]; Anya Litvak, MD[12]; Erica L. Mayer, MD, MPH[13]; Lajos Pusztai, MD[14]; Rachel Raab, MD[15]; Antonio C. Wolff, MD[16]; and Vered Stearns, MD[16]

J Clin Oncol 2022;40(16):1816-37.

RTP RESEARCH TO PRACTICE

Biomarkers for Adjuvant Endocrine and Chemotherapy in Localized Breast Cancer: ASCO Guideline Update



Andre F et al. *J Clin Oncol* 2022;40(16):1816-37.

RTP RESEARCH TO PRACTICE

NCCN Guidelines: Gene Expression Assays for Consideration of Adjuvant Systemic Therapy

Assay	Predictive	Prognostic	NCCN Category of Preference	NCCN Category of Evidence and Consensus
21-gene (Oncotype Dx) (for pN0)	Yes	Yes	Preferred	1
21-gene (Oncotype Dx) for pN1 (1–3 positive nodes)[c]	Yes	Yes	Postmenopausal: Preferred	1
			Premenopausal: Other	2A
70-gene (MammaPrint) for pN0 and pN1 (1–3 positive nodes)	Not determined	Yes	Other	1
50-gene (Prosigna) for pN0 and pN1 (1–3 positive nodes)	Not determined	Yes	Other	2A
12-gene (EndoPredict) for pN0 and pN1 (1–3 positive nodes)	Not determined	Yes	Other	2A
Breast Cancer Index (BCI)	Predictive of benefit of extended adjuvant endocrine therapy	Yes	Other	2A

NCCN Guidelines. Breast Cancer. Version 4.2022. Accessed August 2, 2022.

N Engl J Med 2021;385(25):2336-47.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

21-Gene Assay to Inform Chemotherapy Benefit in Node-Positive Breast Cancer

K. Kalinsky, W.E. Barlow, J.R. Gralow, F. Meric-Bernstam, K.S. Albain, D.F. Hayes, N.U. Lin, E.A. Perez, L.J. Goldstein, S.K.L. Chia, S. Dhesy-Thind, P. Rastogi, E. Alba, S. Delaloge, M. Martin, C.M. Kelly, M. Ruiz-Borrego, M. Gil-Gil, C.H. Arce-Salinas, E.G.C. Brain, E.-S. Lee, J.-Y. Pierga, B. Bermejo, M. Ramos-Vazquez, K.-H. Jung, J.-M. Ferrero, A.F. Schott, S. Shak, P. Sharma, D.L. Lew, J. Miao, D. Tripathy, L. Pusztai, and G.N. Hortobagyi

San Antonio Breast Cancer Symposium®, December 7-10, 2021

RxPONDER: A Clinical Trial Rx for Positive Node, Endocrine Responsive Breast Cancer

Updated results from a phase 3 randomized clinical trial in participants (pts) with 1-3 positive lymph nodes, hormone receptor-positive (HR+) and HER2-negative breast cancer with recurrence score of 25 or less: SWOG S1007

Kevin Kalinsky, William E Barlow, Julie R Gralow, Funda Meric-Bernstam, Kathy S Albain, Daniel F Hayes, Nancy U Lin, Edith A Perez, Lori J Goldstein, Stephen K Chia, Sukhbinder Dhesy-Thind, Priya Rastogi, Emilio Alba, Suzette Delaloge, Miguel Martin, Catherine M Kelly, Manuel Ruiz-Borrego, Miguel Gil Gil, Claudia Arce-Salinas, Etienne G.C. Brain, Eun Sook Lee, Jean-Yves Pierga, Begoña Bermejo, Manuel Ramos-Vazquez, Kyung Hae Jung, Jean-Marc Ferrero, Anne F. Schott, Steven Shak, Priyanka Sharma, Danika L. Lew, Jieling Miao, Debasish Tripathy, Lajos Pusztai, Gabriel N. Hortobagyi

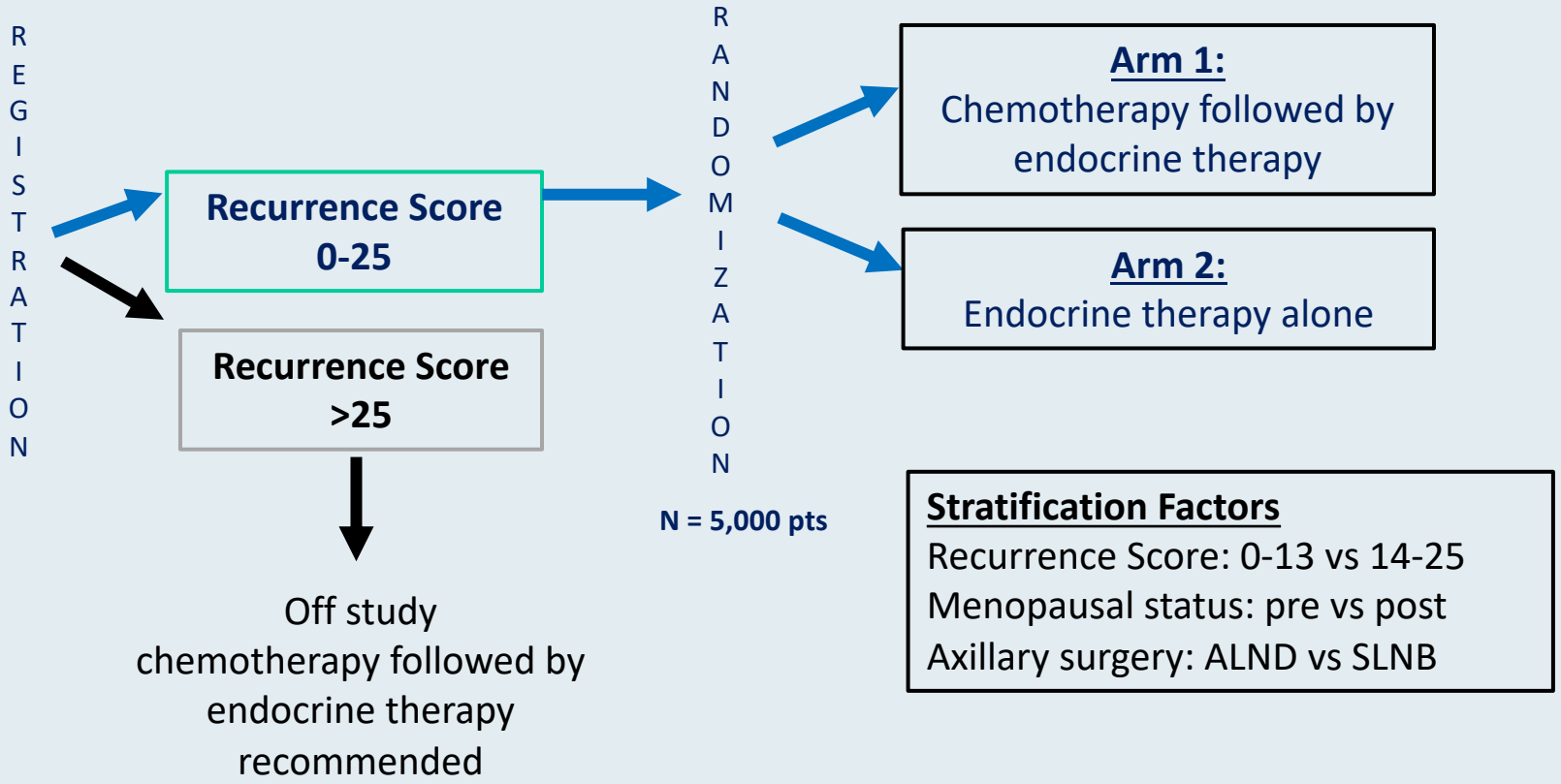
On Behalf of the RxPonder Investigators

SABCS 2021;Abstract GS2-07.

RxPONDER Trial Schema

Key Entry Criteria

- Women age ≥18
- ER and/or PR ≥1%, HER2-neg breast cancer with 1*-3 pos LN without distant metastasis
- Able to receive adjuvant taxane and/or anthracycline-based chemotherapy†
- Axillary staging by SLNB or ALND



* After randomization of 2,493 pts, the protocol was amended to exclude enrollment of pts with pN1mic as only nodal disease.

† Approved chemotherapy regimens included TC, FAC (or FEC), AC/T (or EC/T), FAC/T (or FEC/T). AC alone or CMF not allowed.

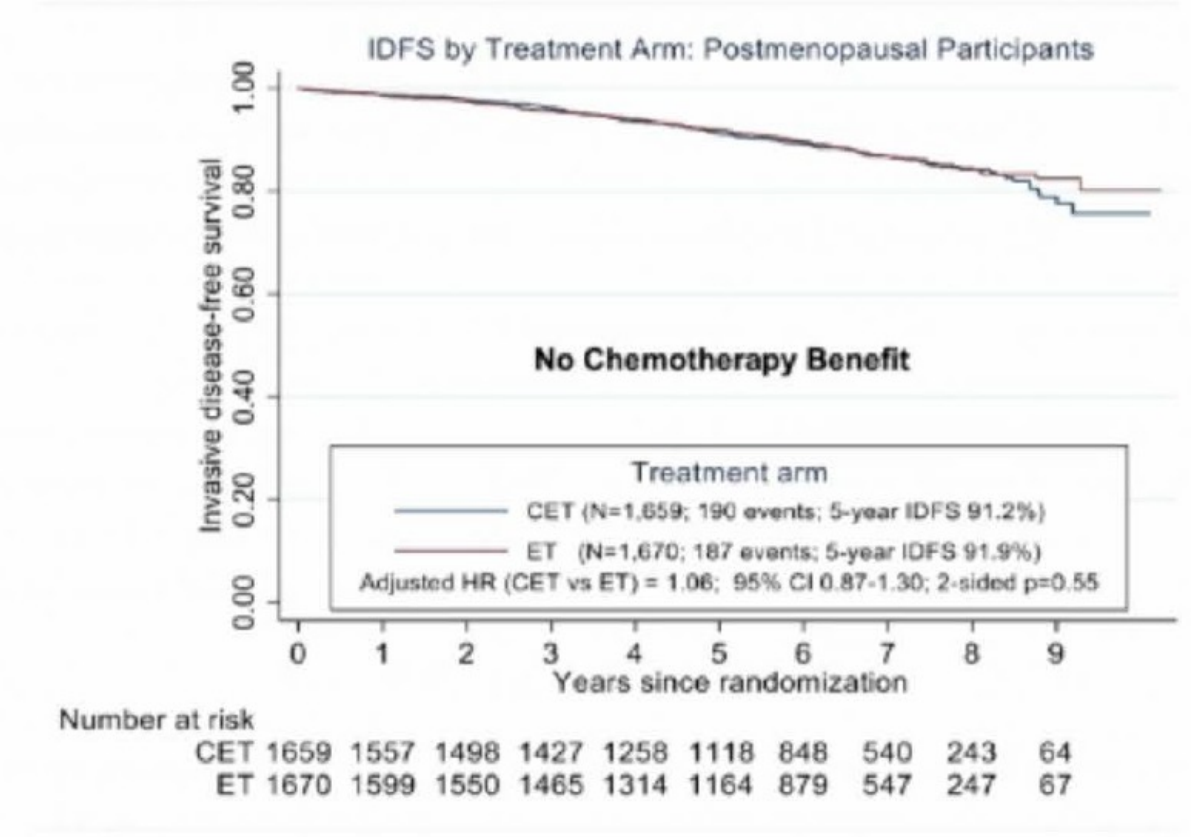
SLNB = sentinel lymph node biopsy; ALND = axillary lymph node dissection

Kalinsky K et al. SABCS 2020;Abstract GS3-00.

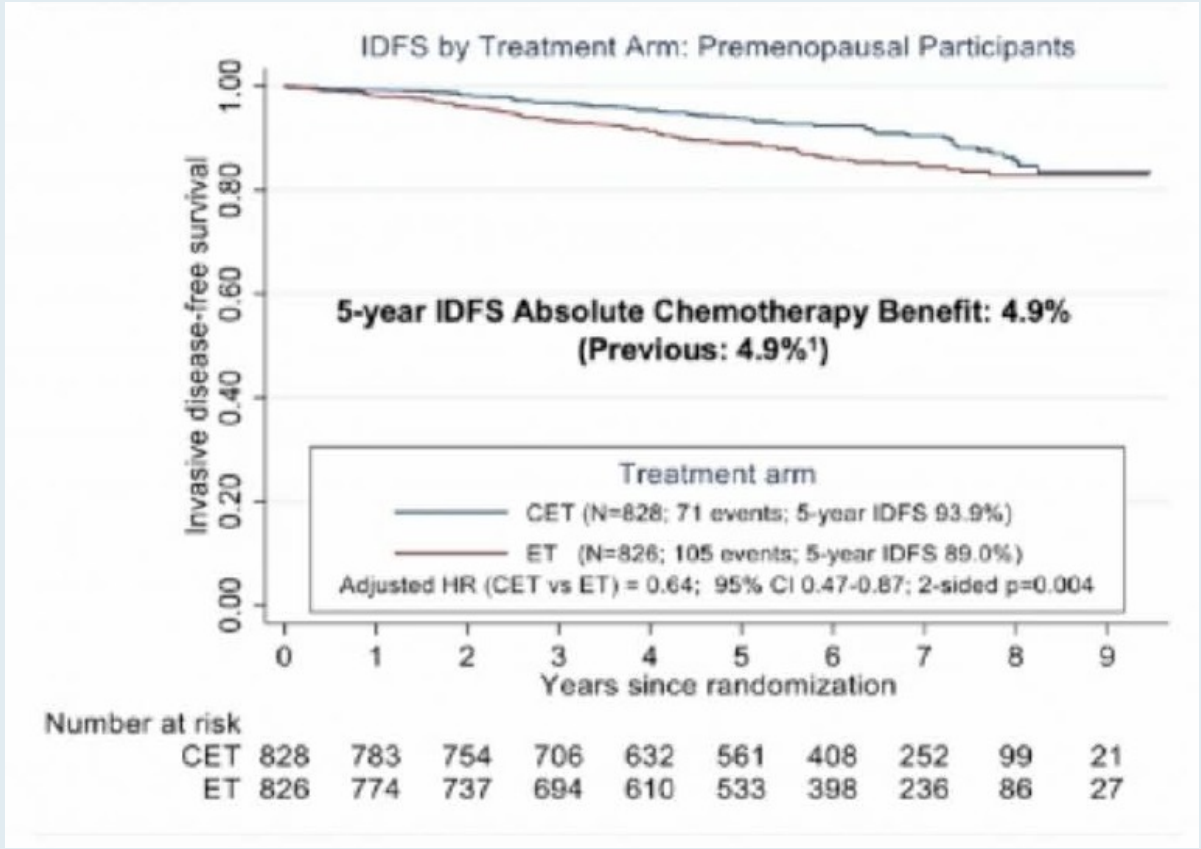
RTP RESEARCH TO PRACTICE

RxPONDER Updated Analysis: IDFS Stratified by Menopausal Status

Postmenopausal



Premenopausal



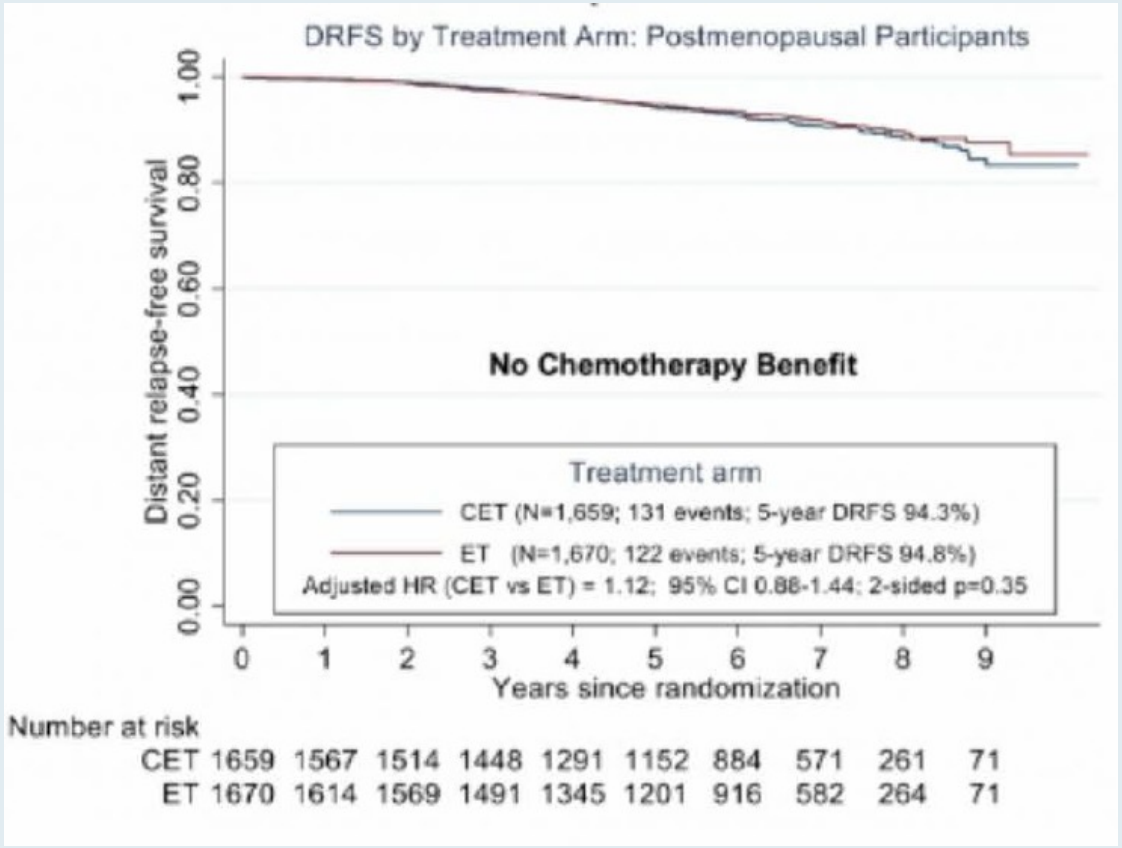
IDFS = invasive disease-free survival

Kalinsky K et al. SABCS 2021;Abstract GS2-07.

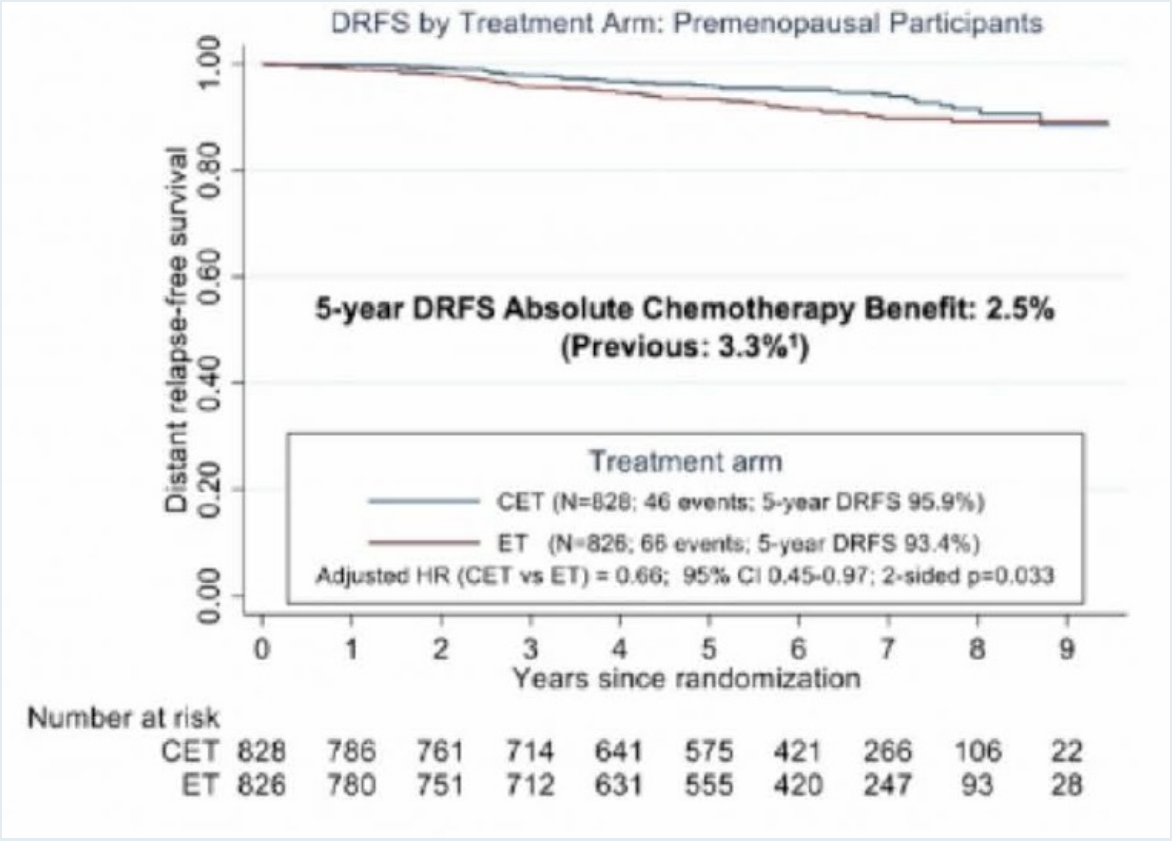
RTP RESEARCH TO PRACTICE

RxPONDER Updated Analysis: DRFS Stratified by Menopausal Status

Postmenopausal



Premenopausal



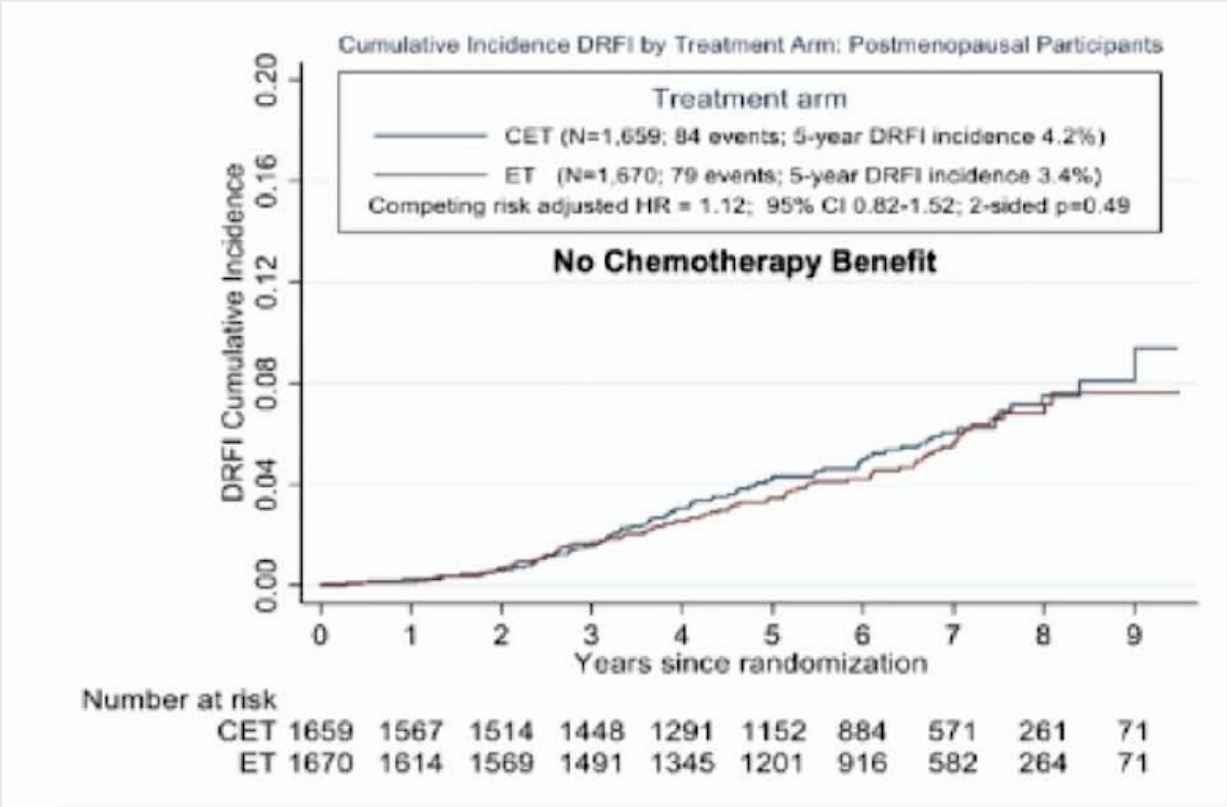
DRFS = distant recurrence-free survival

Kalinsky K et al. SABCS 2021;Abstract GS2-07.

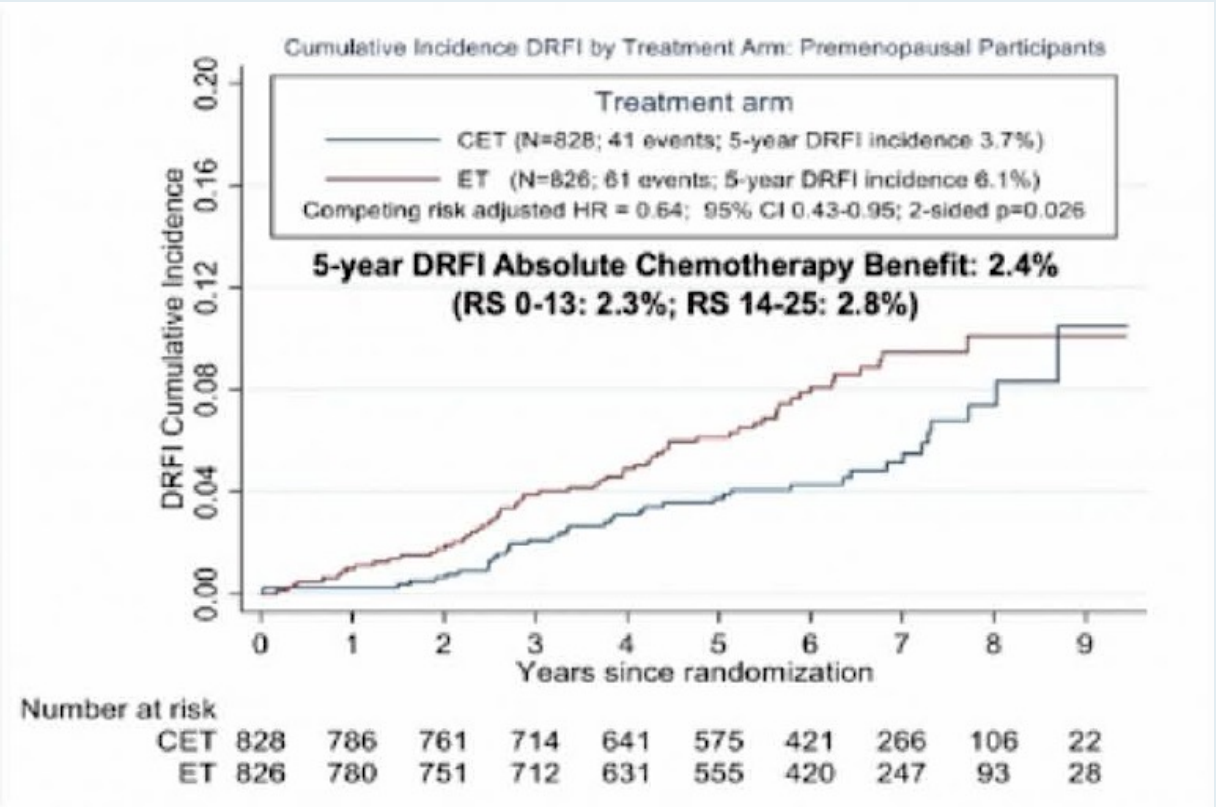
RTP RESEARCH TO PRACTICE

RxPONDER New Analysis: DRFI Stratified by Menopausal Status

Postmenopausal



Premenopausal



Time from randomization assignment to date of first invasive recurrence (distant) or death from breast cancer

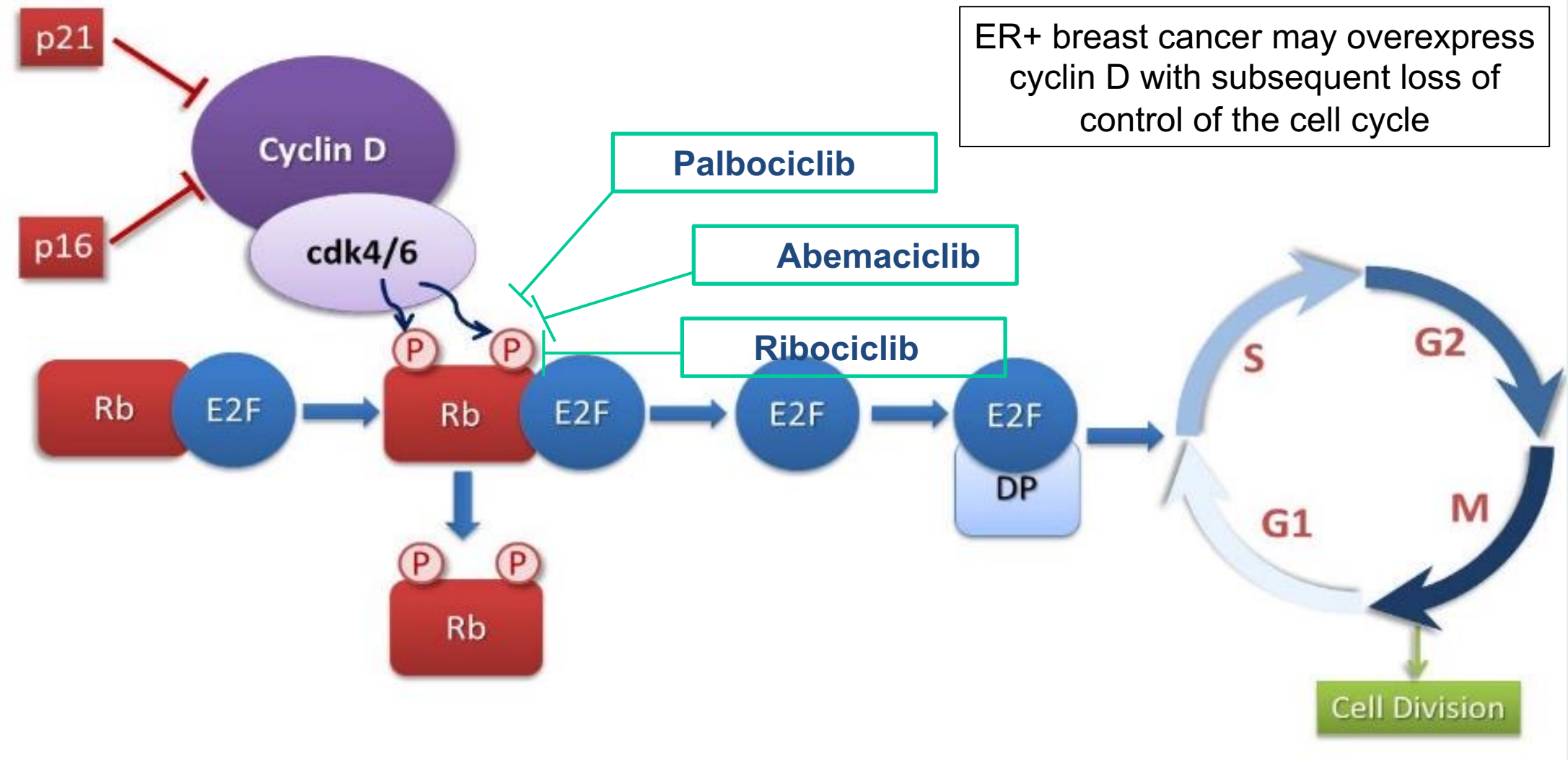
In multivariate analysis, higher RS (continuous) and larger tumor size remained independently prognostic in both treatment arms

DRFI = distant recurrence-free interval

Kalinsky K et al. SABCS 2021;Abstract GS2-07.

RTP RESEARCH TO PRACTICE

CDK4/6 Regulates Cell Cycle Progression



Adapted from Finn RS et al. *Breast Cancer Res* 2016;18:17.

Key Trials Exploring CDK4/6 Inhibitors for Localized Breast Cancer

	MonarchE	PALLAS	PENELOPE-B
Number of patients	5,637	5,761	1,250
Eligibility	≥ N2 or N1 with at least one of the following: grade 3, tumor size ≥ 5 cm, or Ki-67 ≥ 20%.	Anatomic stage II/III	Lack of pCR after NACT CPS-EG score ≥3 or ≥2 with ypN+
Study treatment	Abemaciclib-continuous (twice daily) Duration: 2 years	Palbociclib (once a day)-3 weeks on/1 week off Duration: 2 years	Palbociclib (once a day)-3 weeks on/1 week off Duration: 1 year
Timing of initiation of CDK4/6i in relation to ET	Within 12 weeks of beginning adjuvant ET	Within 6 months of beginning adjuvant ET	NA
Discontinuation rate	27.7%	42.0%	19.5%
Median follow-up time	19.1 months	31.0 months[1]	42.8 months
iDFS	92.2% (Abemaciclib + ET) vs. 88.7% (ET alone) at 2 years Ki67 ≥20% group-91.6% vs. 87.1%	84.2% (Palbociclib + ET) vs. 84.5% (ET alone)[1]	2 years: 88.3% (Palbociclib + ET) vs. 84% (ET alone) 3 years: 81.2% vs. 77.7% 4 years: 73.5% vs. 72.4%
DRFS	93.8% vs. 90.8%	89.3% vs. 90.7%	–

https://dailynews.ascopubs.org/do/10.1200/ADN.21.200483/full/; [1]Gnant M et al. SABCS 2021;Abstract GS1-07.

RTP RESEARCH TO PRACTICE

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Ann Oncol 2021;32(12):1571-81.

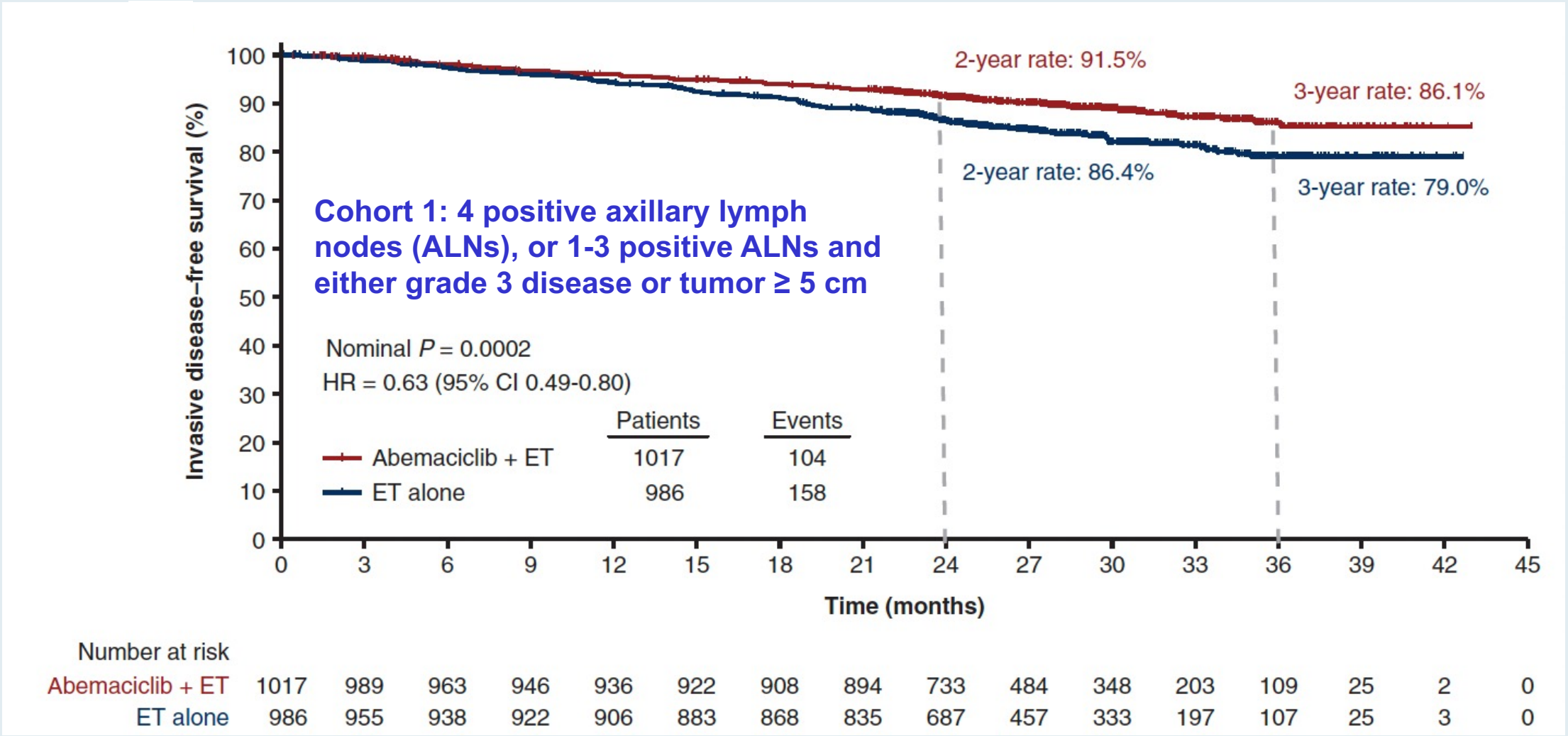
ANNALS OF ONCOLOGY driving innovation in oncology

ORIGINAL ARTICLE

Adjuvant abemaciclib combined with endocrine therapy for high-risk early breast cancer: updated efficacy and Ki-67 analysis from the monarchE study

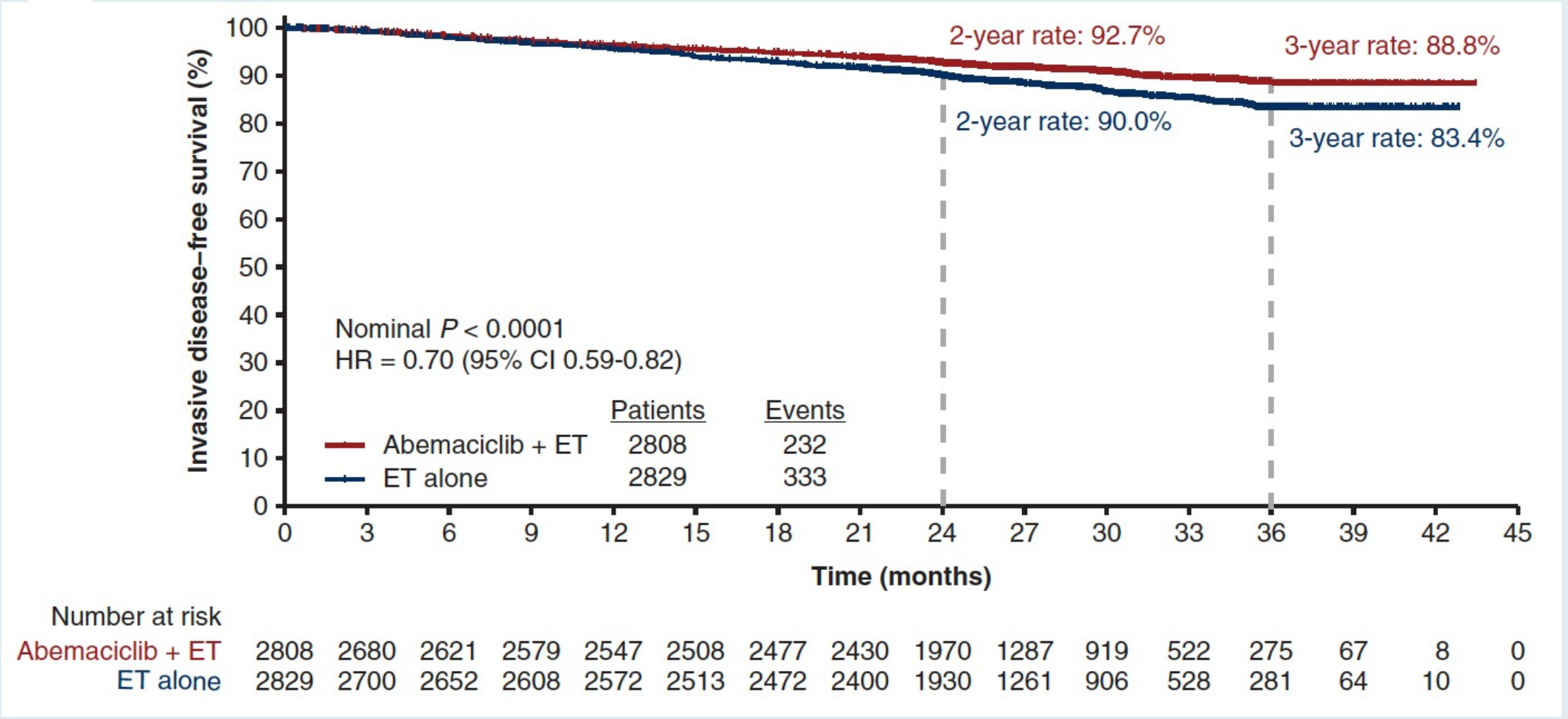
N. Harbeck[1*†], P. Rastogi[2†], M. Martin[3], S. M. Tolaney[4], Z. M. Shao[5], P. A. Fasching[6], C. S. Huang[7], G. G. Jaliffe[8], A. Tryakin[9], M. P. Goetz[10], H. S. Rugo[11], E. Senkus[12], L. Testa[13], M. Andersson[14], K. Tamura[15], L. Del Mastro[16,17], G. G. Steger[18], H. Kreipe[19], R. Hegg[20], J. Sohn[21], V. Guarneri[22,23], J. Cortés[24,25], E. Hamilton[26], V. André[27], R. Wei[27], S. Barriga[27], S. Sherwood[27], T. Forrester[27], M. Munoz[27], A. Shahir[27], B. San Antonio[27], S. C. Nabinger[27], M. Toi[28], S. R. D. Johnston[29‡] & J. O'Shaughnessy[30‡], On behalf of the monarchE Committee Members

monarchE: Invasive Disease-Free Survival in Cohort 1, Ki67-High Population with Adjuvant Abemaciclib



Harbeck N et al. *Ann Oncol* 2021;32(12):1571-81.

monarchE: Invasive Disease-Free Survival in the Intent-to-Treat (ITT) Population with Adjuvant Abemaciclib



Harbeck N et al. *Ann Oncol* 2021;32(12):1571-81.

monarchE: Select Adverse Events (AEs)

	Abemaciclib + ET (n = 2,791)			ET Alone (n = 2,800)		
≥ 10% in Either Arm	Any Grade	Grade 3	Grade 4	Any Grade	Grade 3	Grade 4
Any adverse event	2,731 (97.9)	1,200 (43.0)	70 (2.5)	2,410 (86.1)	335 (12.0)	19 (0.7)
Diarrhea	2,294 (82.2)	212 (7.6)	0	199 (7.1)	3 (0.1)	0
Neutropenia	1,246 (44.6)	501 (18.0)	18 (0.6)	141 (5.0)	16 (0.6)	3 (0.1)
Fatigue	1,073 (38.4)	78 (2.8)	0	433 (15.5)	4 (0.1)	0
Leukopenia	1,027 (36.8)	301 (10.8)	4 (0.1)	171 (6.1)	10 (0.4)	0
Abdominal pain	948 (34.0)	37 (1.3)	0	227 (8.1)	9 (0.3)	0
Nausea	779 (27.9)	13 (0.5)	0	223 (8.0)	1 (0.0)	0
Anemia	638 (22.9)	47 (1.7)	1 (0.0)	90 (3.2)	9 (0.3)	1 (0.0)
Arthralgia	571 (20.5)	6 (0.2)	0	876 (31.3)	18 (0.6)	0
Hot flush	393 (14.1)	3 (0.1)	0	587 (21.0)	8 (0.3)	0
Lymphopenia	372 (13.3)	140 (5.0)	2 (0.1)	94 (3.4)	13 (0.5)	0
Thrombocytopenia	341 (12.2)	25 (0.9)	6 (0.2)	40 (1.4)	1 (0.0)	2 (0.1)

- Abemaciclib dose adjustments due to AEs: 68.1% (56.9% dose omissions and 41.2% dose reductions)
- Abemaciclib discontinuation due to AEs: 16.6%
- Discontinuation of ET due to AEs in the control arm: 0.8%

Johnston SRD et al. *J Clin Oncol* 2020;38(34):3987-98.

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

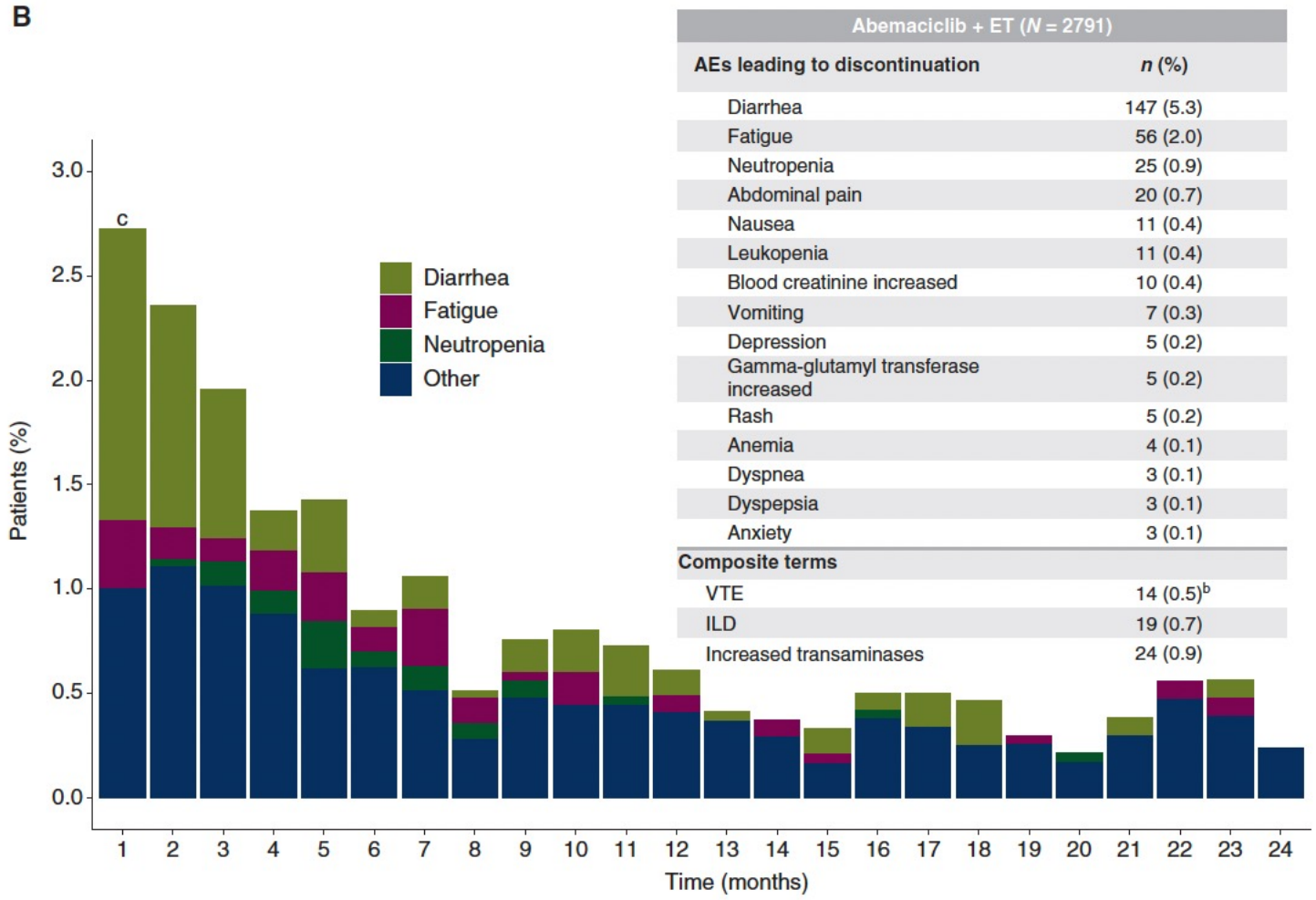
Ann Oncol 2022;33(6):616-27.

ORIGINAL ARTICLE

Adjuvant abemaciclib combined with endocrine therapy for high-risk early breast cancer: safety and patient-reported outcomes from the monarchE study

H. S. Rugo[1*], J. O'Shaughnessy[2], F. Boyle[3,4], M. Toi[5], R. Broom[6], I. Blancas[7,8], M. Gumus[9], T. Yamashita[10], Y.-H. Im[11], P. Rastogi[12], F. Zagouri[13], C. Song[14], M. Campone[15], B. San Antonio[16], A. Shahir[16], M. Hulstijn[16], J. Brown[16], A. Zimmermann[16], R. Wei[16], S. R. D. Johnston[17], M. Reinisch[18] & S. M. Tolaney[19], on behalf of the monarchE Committee Members[†]

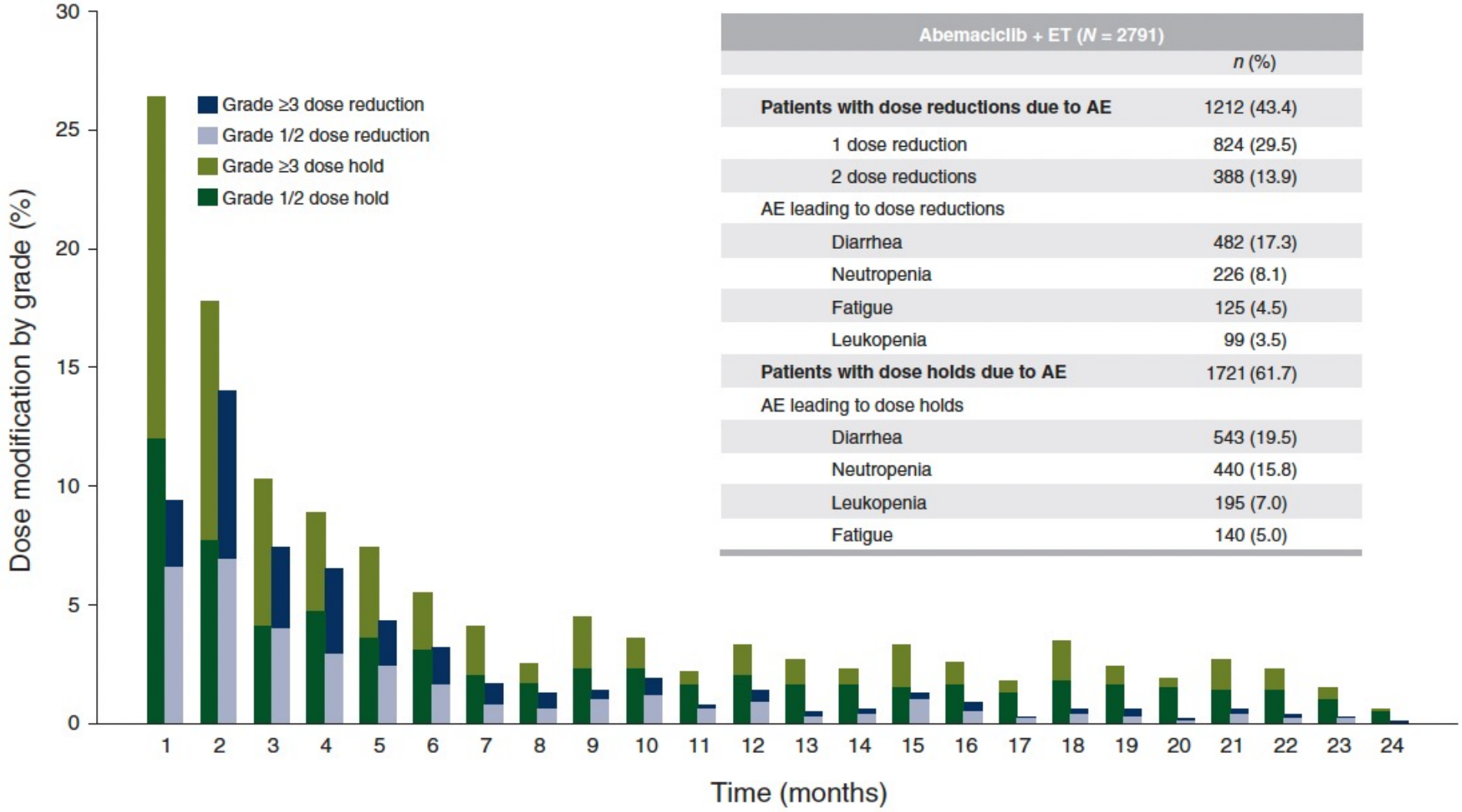
monarchE: Discontinuations in the Abemaciclib Arm Due to Adverse Events



Abemaciclib + ET (*N* = 2791)	
AEs leading to discontinuation	***n*** **(%)**
Diarrhea	147 (5.3)
Fatigue	56 (2.0)
Neutropenia	25 (0.9)
Abdominal pain	20 (0.7)
Nausea	11 (0.4)
Leukopenia	11 (0.4)
Blood creatinine increased	10 (0.4)
Vomiting	7 (0.3)
Depression	5 (0.2)
Gamma-glutamyl transferase increased	5 (0.2)
Rash	5 (0.2)
Anemia	4 (0.1)
Dyspnea	3 (0.1)
Dyspepsia	3 (0.1)
Anxiety	3 (0.1)
Composite terms	
VTE	14 (0.5)[b]
ILD	19 (0.7)
Increased transaminases	24 (0.9)

Rugo HS et al. *Ann Oncol* 2022;33(6):616-27.

monarchE: Abemaciclib Dose Modifications



Abemaciclib + ET (*N* = 2791)	*n* (%)
Patients with dose reductions due to AE	1212 (43.4)
1 dose reduction	824 (29.5)
2 dose reductions	388 (13.9)
AE leading to dose reductions	
Diarrhea	482 (17.3)
Neutropenia	226 (8.1)
Fatigue	125 (4.5)
Leukopenia	99 (3.5)
Patients with dose holds due to AE	1721 (61.7)
AE leading to dose holds	
Diarrhea	543 (19.5)
Neutropenia	440 (15.8)
Leukopenia	195 (7.0)
Fatigue	140 (5.0)

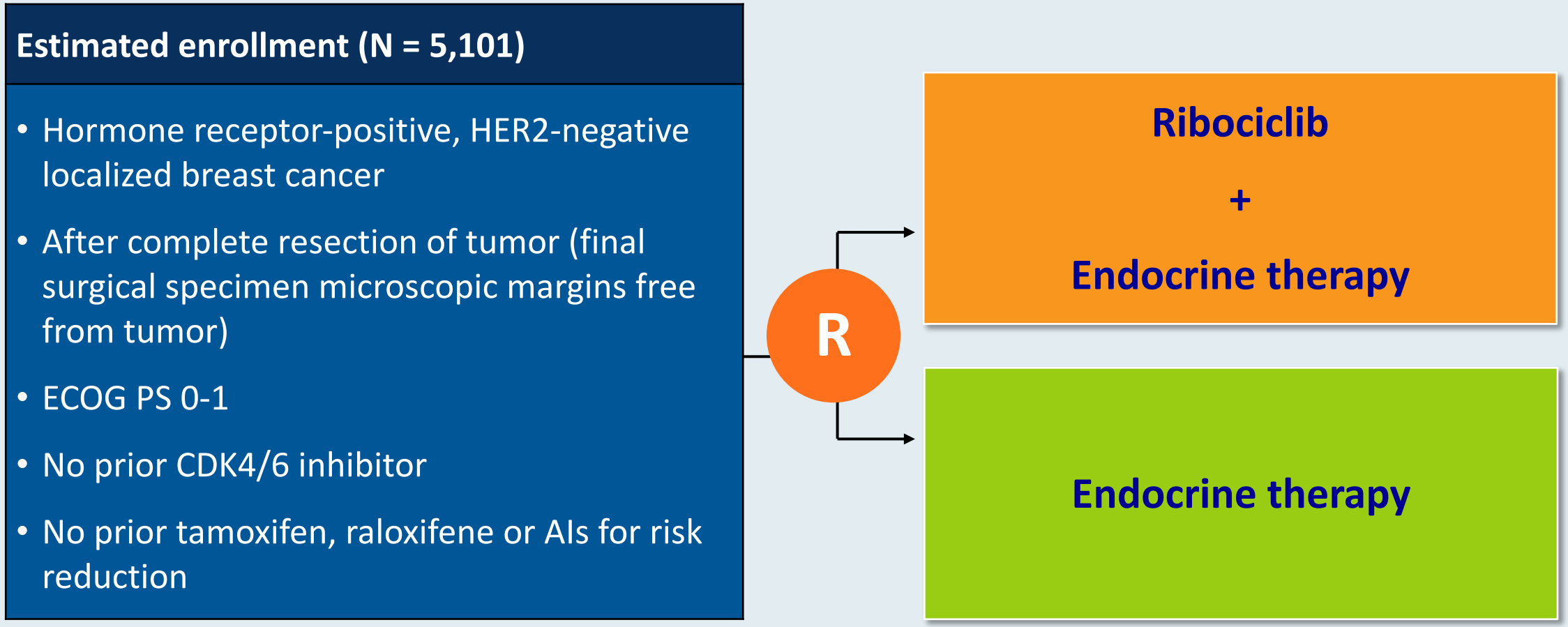
Rugo HS et al. *Ann Oncol* 2022;33(6):616-27.

ASCO Rapid Recommendation Update for Abemaciclib for HR-Positive, HER2-Negative, Node-Positive Localized Breast Cancer

- Abemaciclib with endocrine therapy (ET; tamoxifen or an aromatase inhibitor) is FDA approved for adjuvant treatment of HR-positive, HER2-negative, node-positive localized breast cancer with high risk of recurrence **and a Ki-67 score ≥20%**.
- Based on analyses reported by Harbeck and colleagues, the panel recommends that abemaciclib for 2 years with ET for 5 years or longer may be offered to the broader intent-to-treat population of patients with resected HR-positive, HER2-negative, node-positive localized breast cancer at high risk of recurrence, defined as having >4 positive axillary lymph nodes **or** as having 1 to 3 positive axillary lymph nodes and 1 or more of the following features: histologic Grade III, tumor size >5 cm **or Ki-67 index >20%**.
- Despite similar hazard ratios in favor of abemaciclib regardless of Ki-67 status, relatively few low Ki-67 tumors were reported in monarchE. When discussing treatment options with patients, the potential benefits (improved IDFS) should be weighed against the potential harms (treatment toxicity, financial cost).

Harbeck N et al. *Ann Oncol* 2021;32(12):1571-81.
https://www.asco.org/practice-patients/guidelines/breast-cancer#/11081

NATALEE: Ongoing Adjuvant Phase III Trial Design



Primary endpoint: Invasive disease-free survival

Secondary endpoints include recurrence-free survival, overall survival and quality of life

www.clinicaltrials.gov. NCT03701334. Accessed August 2022.

Randomized Trials of Endocrine Therapy with and without CDK4/6 Inhibition

Line	Trial	Schema	PFS HR compared to endocrine alone	OS HR compared to endocrine alone
First line	PALOMA-1	Letrozole ± palbociclib	0.49	0.897
	PALOMA-2	Letrozole ± palbociclib	0.58	NR
	MONALEESA-2	Letrozole ± ribociclib	0.56	0.76
	MONALEESA-3	Fulvestrant ± ribociclib	0.55	0.72
	MONALEESA-7 (premenopausal)	Goserelin + AI or tamoxifen ± ribociclib	0.55	0.71
	MONARCH 3	Letrozole or anastrozole ± abemaciclib	0.54	NR
Second line	PALOMA-3	Fulvestrant ± palbociclib	0.46	0.75
	MONARCH 2	Fulvestrant ± abemaciclib	0.55	0.757

Finn RS et al. *Breast Cancer Res Treat* 2020; Finn RS et al. *NEJM* 2016; Hortobagyi GN et al. *Ann Oncol* 2019, *N Engl J Med* 2022; Slamon DJ et al. *Ann Oncol* 2021; Im SA et al. *NEJM* 2019; Goetz MP et al. *JCO* 2017; Loibl S et al. *Oncologist* 2017; Sledge GW Jr et al. *JAMA Oncol* 2020.

The NEW ENGLAND JOURNAL of MEDICINE

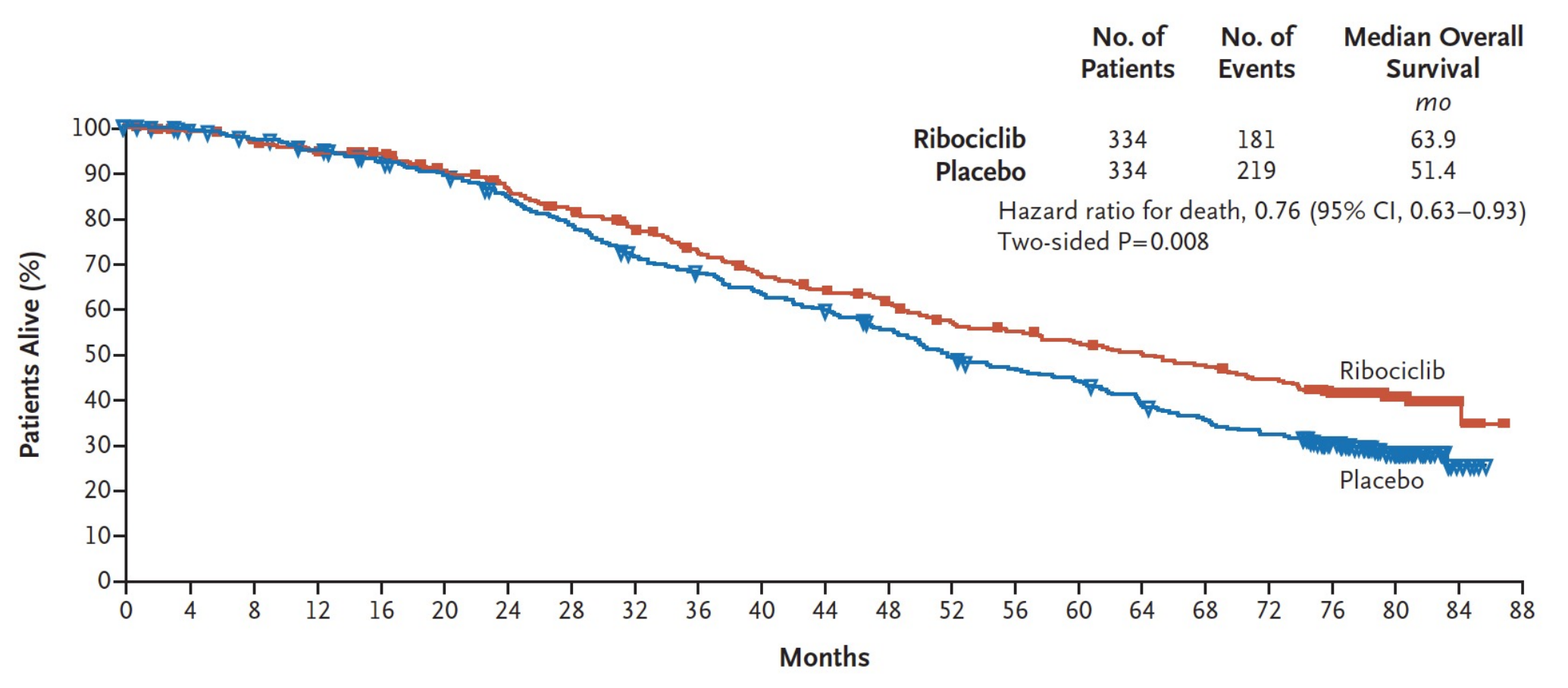
ORIGINAL ARTICLE

Overall Survival with Ribociclib plus Letrozole in Advanced Breast Cancer

Gabriel N. Hortobagyi, M.D., Salomon M. Stemmer, M.D., Howard A. Burris, M.D., Yoon-Sim Yap, M.D., Gabe S. Sonke, M.D., Ph.D., Lowell Hart, M.D., Mario Campone, M.D., Ph.D., Katarina Petrakova, M.D., Ph.D., Eric P. Winer, M.D., Wolfgang Janni, M.D., Ph.D., Pierfranco Conte, M.D., Ph.D., David A. Cameron, M.D., Fabrice André, M.D., Ph.D., Carlos L. Arteaga, M.D., Juan P. Zarate, M.D., Arunava Chakravartty, Ph.D., Tetiana Taran, M.D., Fabienne Le Gac, Ph.D., Pharm.D., Paolo Serra, M.Sc., and Joyce O'Shaughnessy, M.D.

N Engl J Med 2022;386(10):942-50.

MONALEESA-2: Overall Survival (OS)



- The OS benefit with ribociclib observed in an exploratory subgroup analysis was consistent with the results in the overall population.

Hortobagyi GN et al. *N Engl J Med* 2022;386(10):942-50.

MONALEESA-2: The OS Benefit Increased Over Time

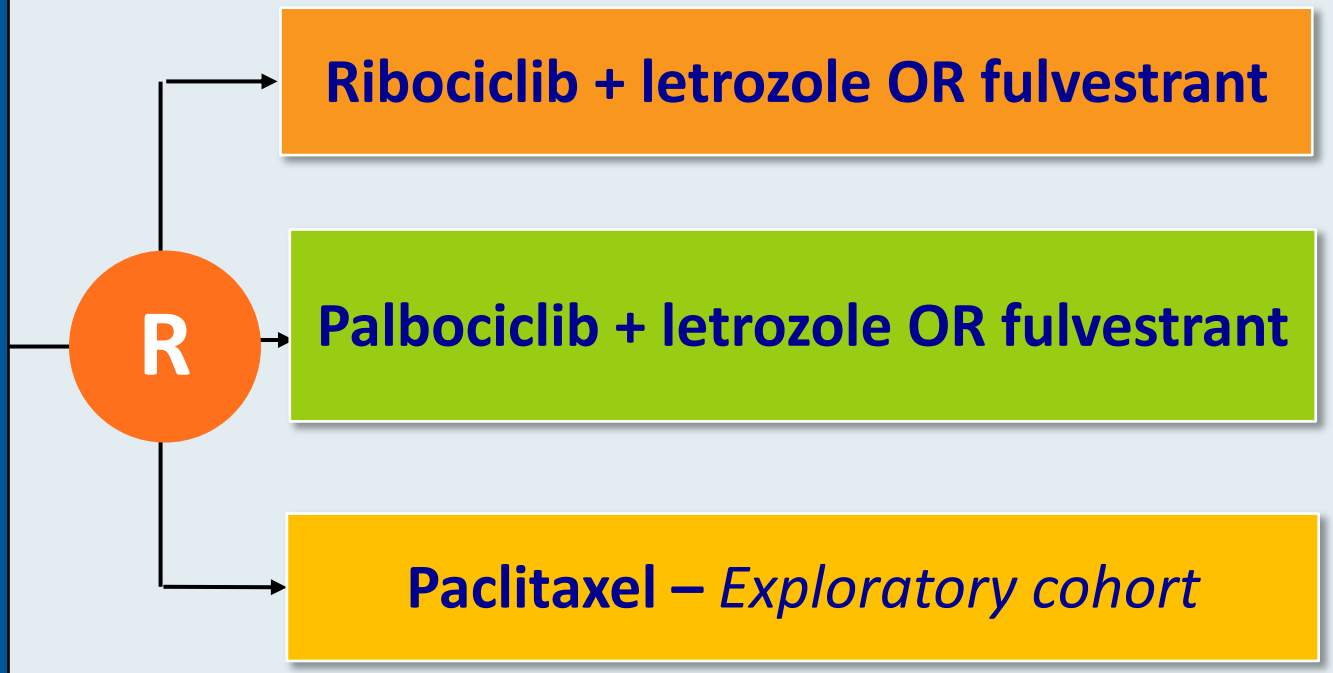
KM-estimated OS rate	Ribociclib + letrozole (n = 334)	Placebo + letrozole (n = 334)	Δ in OS
At 48 months	60.9%	55.2%	5.7%
At 60 months	52.3%	43.9%	8.4%
At 72 months	44.2%	32.0%	12.2%

Hortobagyi GN et al. *N Engl J Med* 2022;386(10):942-50.

HARMONIA: Ongoing Phase III Trial Comparing Palbociclib to Ribociclib

Estimated enrollment (N = 456)

- Hormone receptor-positive, HER2-negative and HER2-enriched advanced breast cancer
- HER2-E or basal-like subtype as per central PAM50 analysis
- ECOG PS 0-1
- No prior CDK4/6 inhibitor
- No prior chemotherapy for advanced disease



Primary endpoint: Progression-free survival (PFS) by RECIST 1.1

Secondary endpoints include PFS2, overall survival, overall response

www.clinicaltrials.gov. NCT05207709. Accessed August 2022.

RTP RESEARCH TO PRACTICE

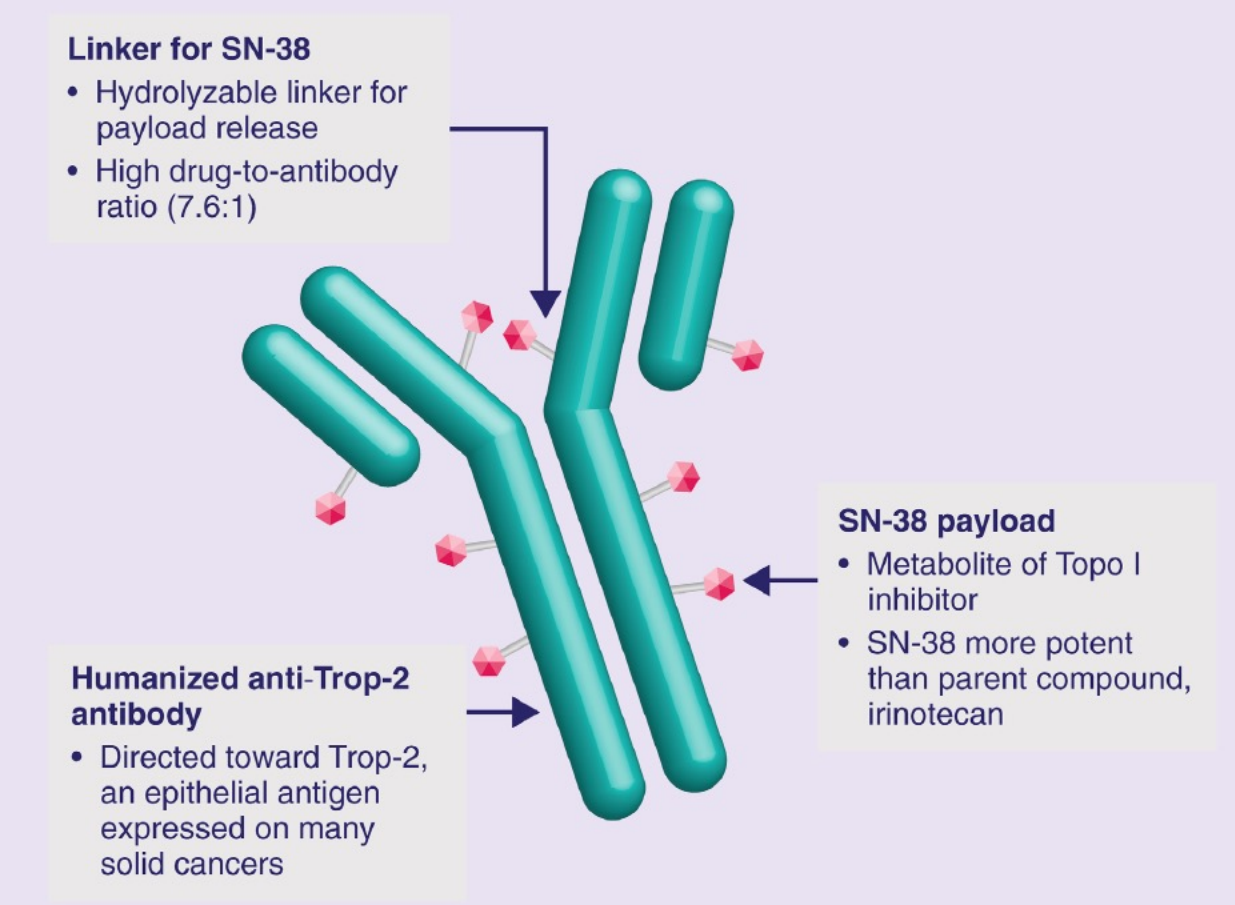
2022 ASCO® ANNUAL MEETING

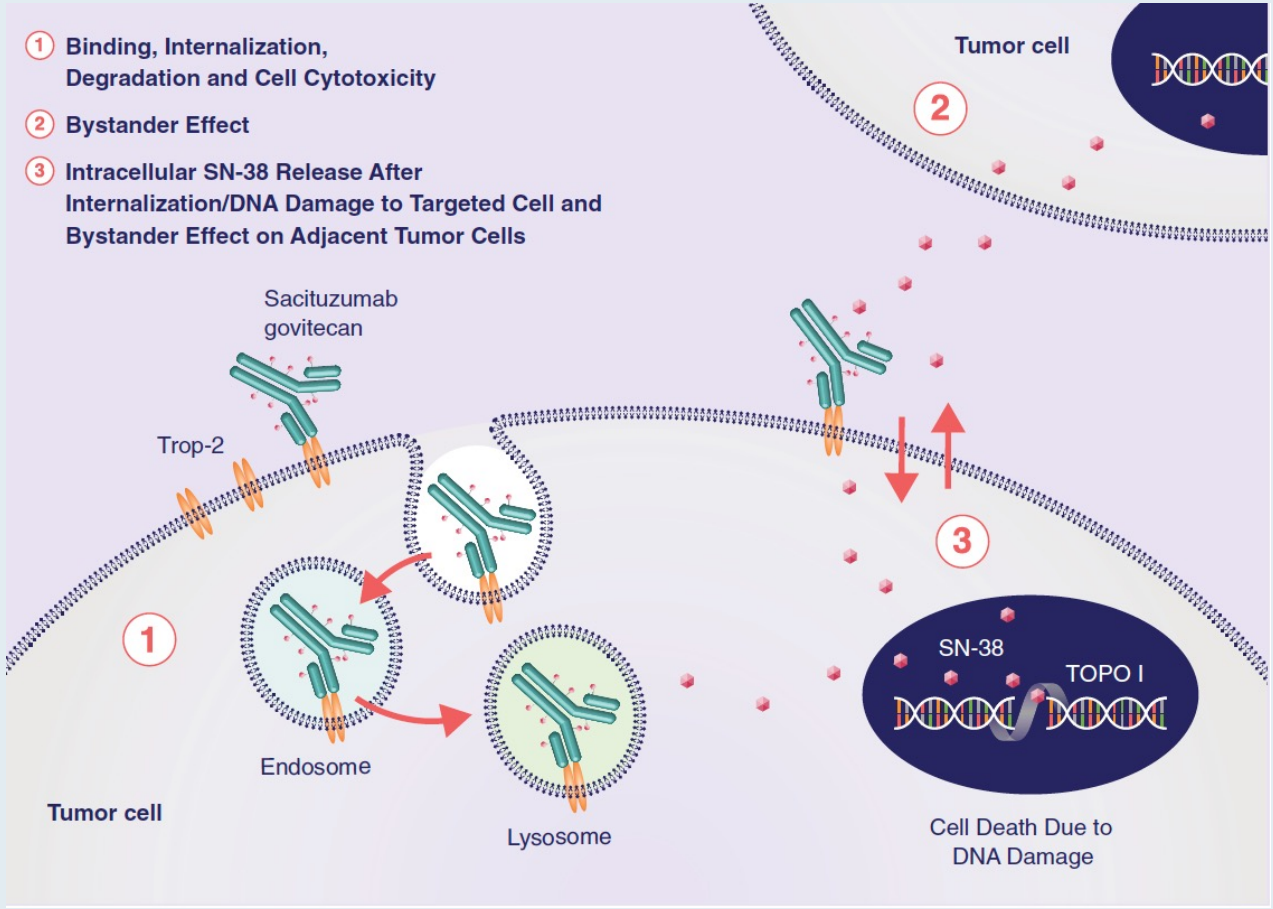
LBA1001

Primary Results From TROPiCS-02: A Randomized Phase 3 Study of Sacituzumab Govitecan Vs Treatment of Physician's Choice in Patients With Hormone Receptor-Positive/HER2-Negative Advanced Breast Cancer

Hope S. Rugo,[1] Aditya Bardia,[2] Frederik Marmé,[3] Javier Cortes,[4] Peter Schmid,[5] Delphine Loirat,[6] Olivier Trédan,[7] Eva Ciruelos,[8] Florence Dalenc,[9] Patricia Gómez Pardo,[10] Komal L. Jhaveri,[11] Rosemary Delaney,[12] Olivia Fu,[12] Lanjia Lin,[12] Wendy Verret,[12] Sara M. Tolaney[13]

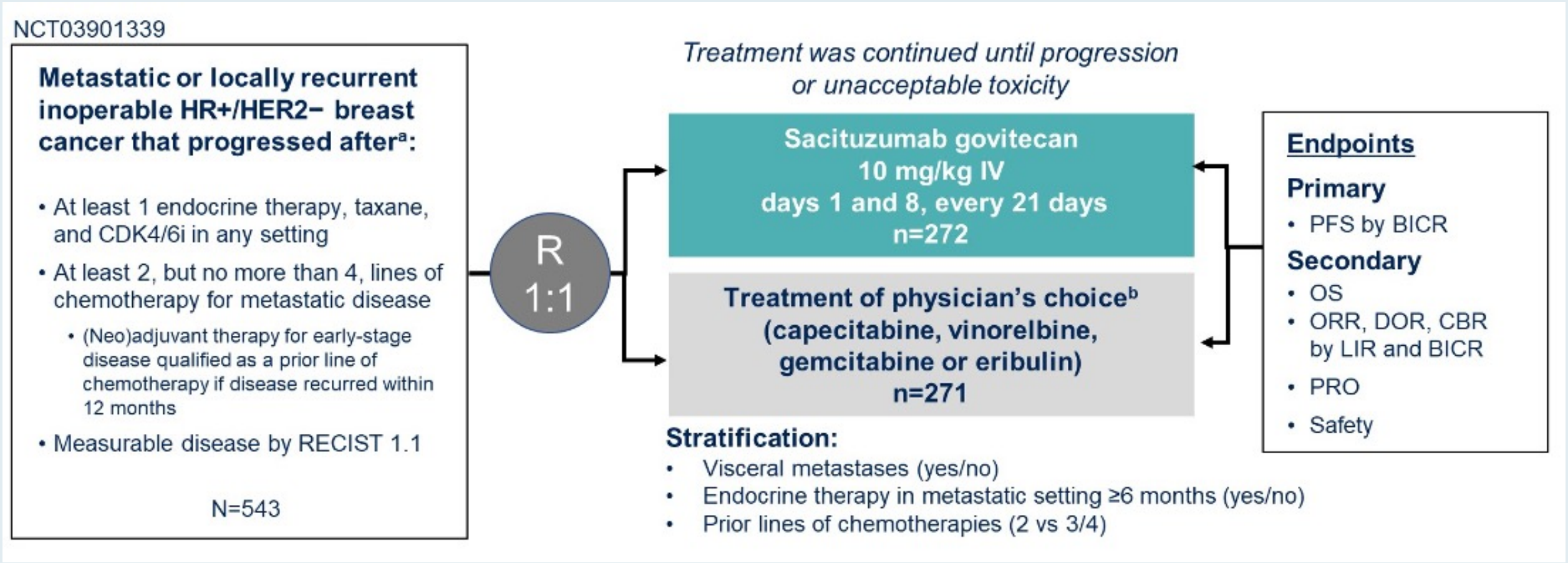
Sacituzumab Govitecan: A First-in-Class TROP-2-Directed Antibody-Drug Conjugate





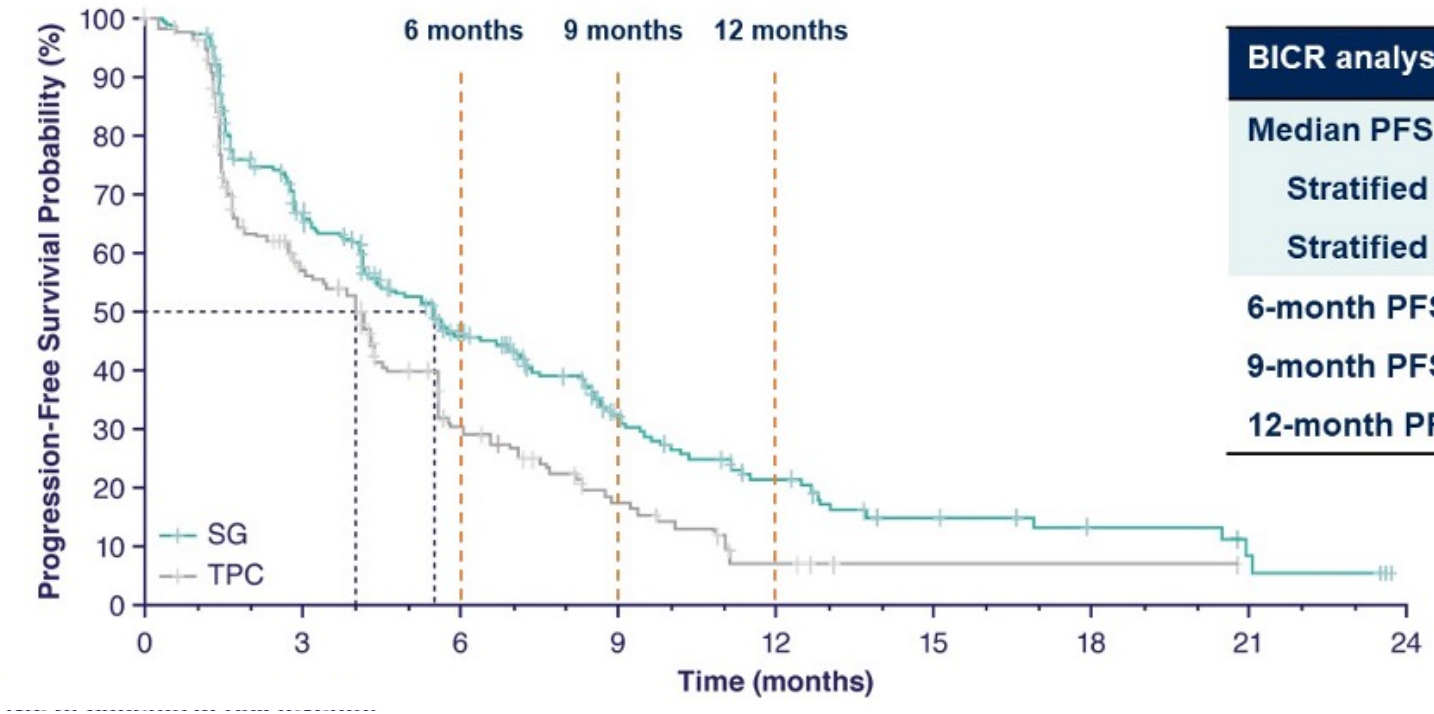
Rugo HS et al. *Future Oncol* 2020;16(12):705-15.

TROPiCS-02: Phase III Trial Design



Rugo HS et al. ASCO 2022;Abstract LBA1001.

TROPiCS-02: Progression-Free Survival (Primary Endpoint)



BICR analysis	SG (n=272)	TPC (n=271)
Median PFS, mo (95% CI)	5.5 (4.2–7.0)	4.0 (3.1–4.4)
Stratified HR (95% CI)	**0.66** (0.53–0.83)	
Stratified Log Rank *P* value	0.0003	
6-month PFS rate, % (95% CI)	46.1 (39.4–52.6)	30.3 (23.6–37.3)
9-month PFS rate, % (95% CI)	32.5 (25.9–39.2)	17.3 (11.5–24.2)
12-month PFS rate, % (95% CI)	21.3 (15.2–28.1)	7.1 (2.8–13.9)

SG demonstrated a statistically significant improvement in PFS vs TPC with a 34% reduction in the risk of disease progression/death; a higher proportion of patients were alive and progression-free at all landmark timepoints

BICR = blinded independent central review; SG = sacituzumab govitecan; TPC = treatment of physician's choice; PFS = progression-free survival

Rugo HS et al. ASCO 2022;Abstract LBA1001.

TROPiCS-02: Key Adverse Events

TRAEs, n (%)		SG (n=268)		TPC (n=249)	
		All grade	Grade ≥3	All grade	Grade ≥3
Hematologic	**Neutropenia[b]**	188 (70)	**136 (51)**	134 (54)	**94 (38)**
	Anemia[c]	91 (34)	17 (6)	62 (25)	8 (3)
	Leukopenia[d]	37 (14)	23 (9)	23 (9)	13 (5)
	Lymphopenia[e]	31 (12)	10 (4)	25 (10)	8 (3)
	Febrile neutropenia	**14 (5)**	**14 (5)**	**11 (4)**	**11 (4)**
Gastrointestinal	**Diarrhea**	152 (57)	**25 (9)**	41 (16)	**3 (1)**
	Nausea	148 (55)	3 (1)	77 (31)	7 (3)
	Vomiting	50 (19)	1 (<1)	30 (12)	4 (2)
	Constipation	49 (18)	0	36 (14)	0
	Abdominal pain	34 (13)	2 (1)	17 (7)	0
Other	Alopecia	123 (46)	0	41 (16)	0
	Fatigue	100 (37)	15 (6)	73 (29)	6 (2)
	Asthenia	53 (20)	5 (2)	37 (15)	2 (1)
	Decreased appetite	41 (15)	1 (<1)	34 (14)	1 (<1)
	Neuropathy[f]	23 (9)	3 (1)	38 (15)	6 (2)

- **There were no events of interstitial lung disease in the SG arm (vs 1% in the TPC arm) and no TRAEs of cardiac failure or left ventricular dysfunction in either arm**

TRAEs = treatment-related adverse events; SG = sacituzumab govitecan; TPC = treatment of physician's choice

Rugo HS et al. ASCO 2022;Abstract LBA1001.

2022 ASCO® ANNUAL MEETING

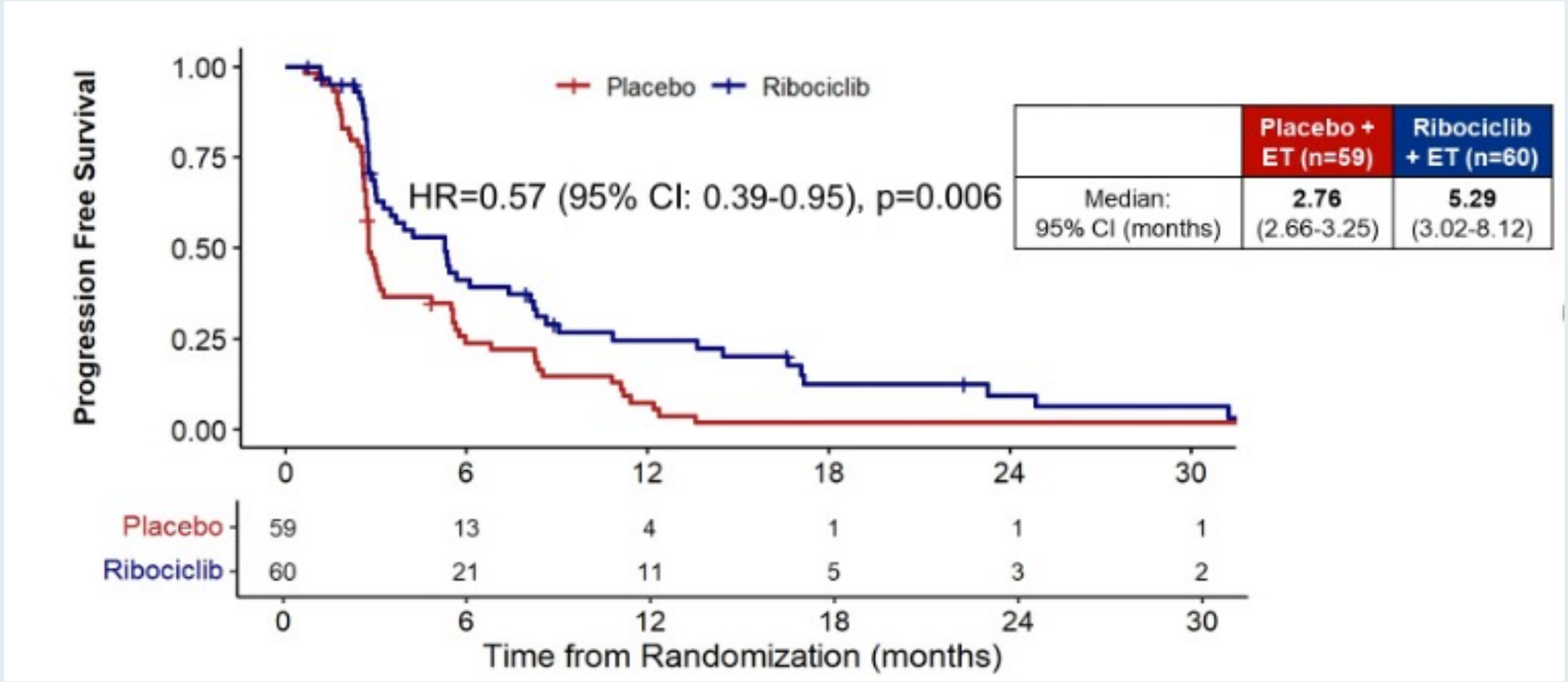
Abstract LBA1004

A randomized phase II trial of fulvestrant or exemestane with or without ribociclib after progression on anti-estrogen therapy plus cyclin-dependent kinase 4/6 inhibition in patients with unresectable or metastatic hormone receptor positive, HER2 negative breast cancer: MAINTAIN Trial

Kevin Kalinsky, Melissa K Accordino, Cody Chiuzan, Prabhjot Mundi, Meghna S Trivedi, Yelena Novik, Amy Tiersten, Amelia Zelnak, George Raptis, Lea Baer, Sun Y Oh, Erica Stringer-Reasor, Sonya Reid, Eleni Andreopoulou, William Gradishar, Kari B Wisinski, Anne O'Dea, Ruth O'Regan, Katherine D Crew, Dawn L Hershman

PRESENTED BY:
Kevin Kalinsky, MD, MS

MAINTAIN: Progression-Free Survival (Primary Endpoint)



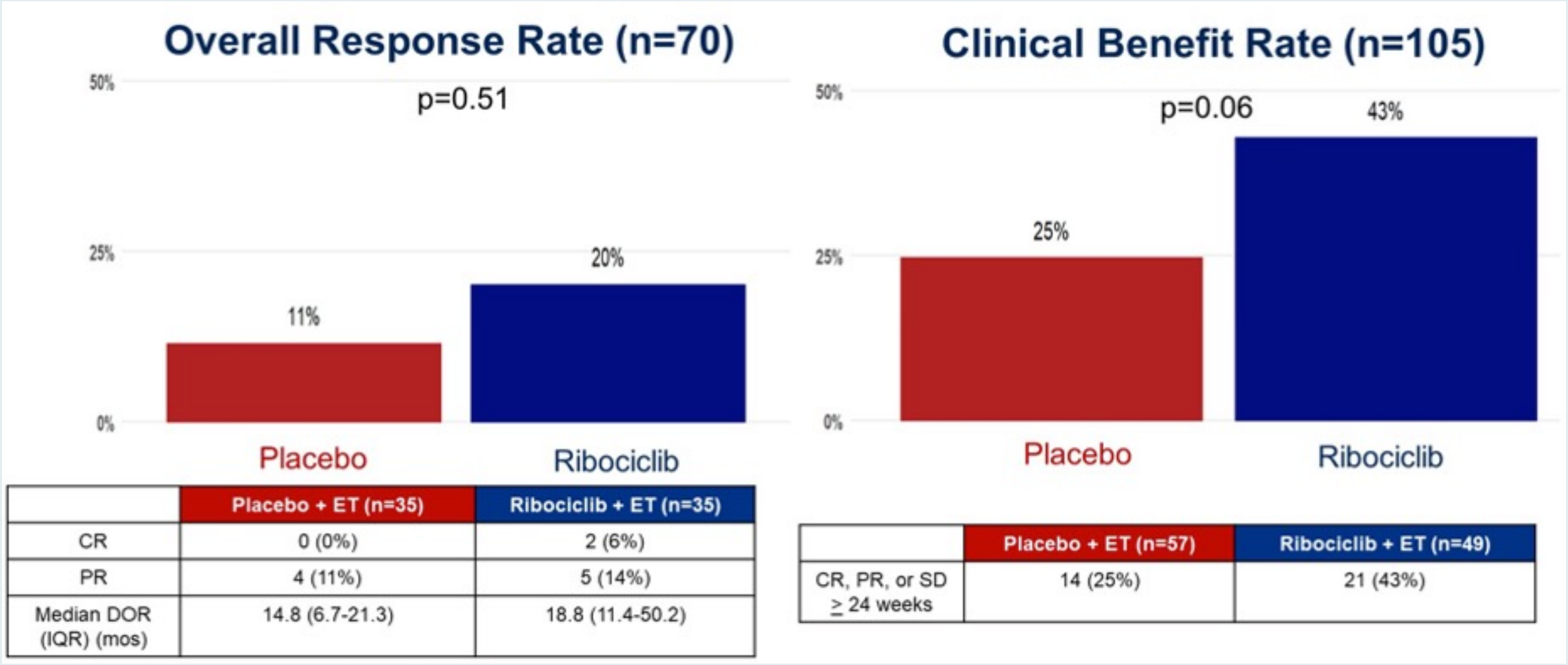
	Placebo + ET (n=59)	Ribociclib + ET (n=60)
Median: 95% CI (months)	**2.76** (2.66-3.25)	**5.29** (3.02-8.12)

ET = endocrine therapy

Kalinsky K et al. ASCO 2022;Abstract LBA1004.

RTP RESEARCH TO PRACTICE

MAINTAIN: Response



	Placebo + ET (n=35)	Ribociclib + ET (n=35)
CR	0 (0%)	2 (6%)
PR	4 (11%)	5 (14%)
Median DOR (IQR) (mos)	14.8 (6.7-21.3)	18.8 (11.4-50.2)

	Placebo + ET (n=57)	Ribociclib + ET (n=49)
CR, PR, or SD ≥ 24 weeks	14 (25%)	21 (43%)

ET = endocrine therapy; CR = complete response; PR = partial response; SD = stable disease; DOR = duration of response

Kalinsky K et al. ASCO 2022;Abstract LBA1004.

RTP RESEARCH TO PRACTICE

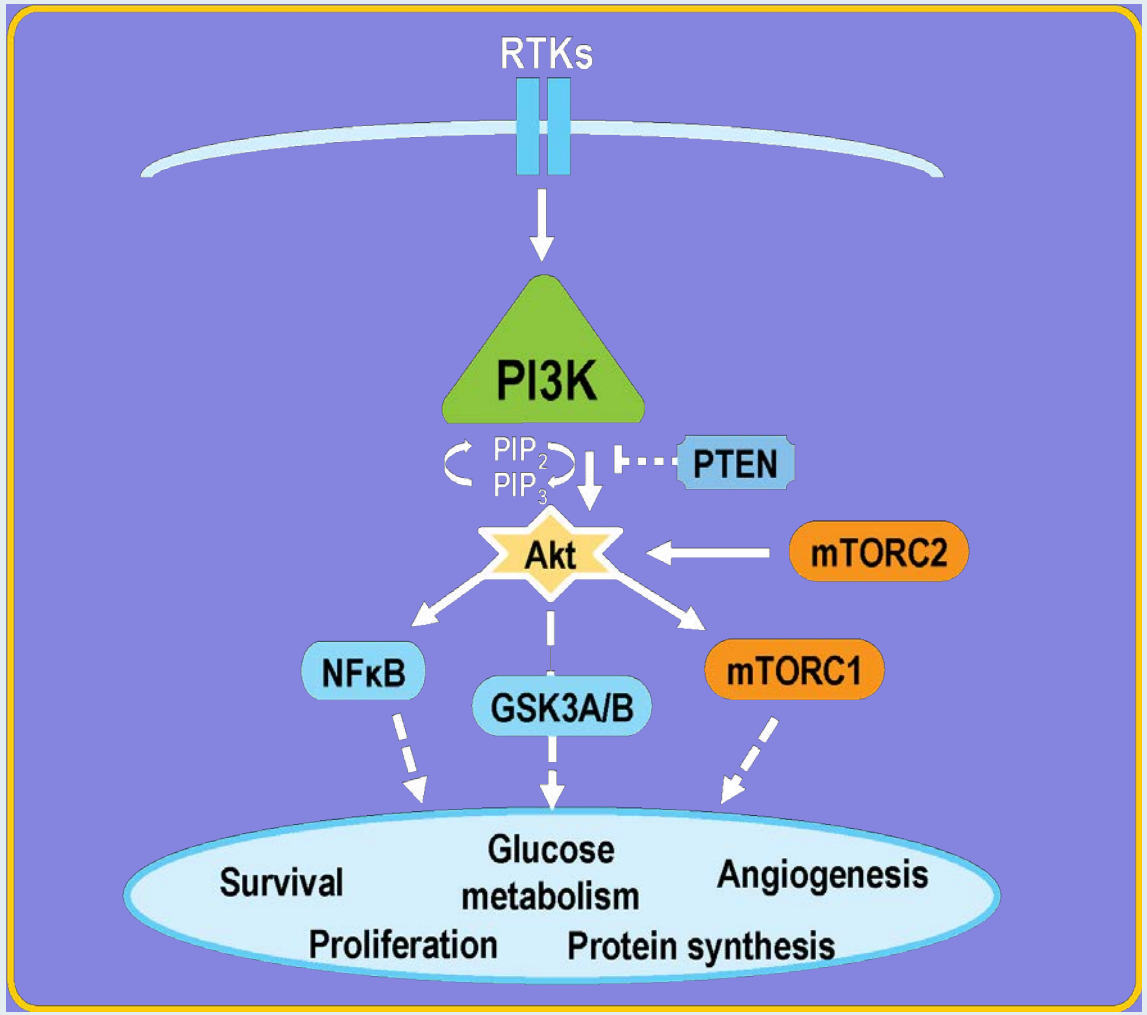
MAINTAIN: Treatment-Related Adverse Events

	Placebo + ET (n=59)			Ribociclib + ET (n=60)		
	All Grades	Grade 3	Grade 4	All Grades	Grade 3	Grade 4
Hematologic						
Neutropenia*	9 (15%)	0 (0%)	1 (2%)	43 (72%)	23 (38%)	1 (2%)
Anemia	13 (22%)	1 (2%)	0 (0%)	14 (23%)	1 (2%)	0 (0%)
Thrombocytopenia	3 (5%)	0 (0%)	0 (0%)	15 (25%)	0 (0%)	0 (0%)
Non-Hematologic						
ALT increased	12 (20%)	1 (2%)	0 (0%)	10 (17%)	0 (0%)	0 (0%)
AST increased	17 (29%)	4 (7%)	0 (0%)	15 (25%)	1 (2%)	0 (0%)
Vomiting	3 (5%)	0 (0%)	0 (0%)	9 (15%)	0 (0%)	0 (0%)
Fatigue	19 (32%)	0 (0%)	0 (0%)	20 (33%)	1 (2%)	0 (0%)
Headache	6 (10%)	0 (0%)	0 (0%)	5 (8%)	0 (0%)	0 (0%)
Diarrhea	6 (10%)	0 (0%)	0 (0%)	9 (15%)	0 (0%)	0 (0%)
Pneumonitis	0 (0%)	0 (0%)	0 (0%)	2 (3%)	1 (2%)	0 (0%)
Infection	3 (5%)	0 (0%)	0 (0%)	6 (10%)	3 (5%)	0 (0%)

ET = endocrine therapy

Kalinsky K et al. ASCO 2022;Abstract LBA1004.

PI3K Inhibitors: Mechanism of Action



- PI3K is involved in the activation of Akt.
- Hyperactivation of the PI3K pathway is implicated in malignant transformation, cancer progression and endocrine therapy resistance.
- PIK3CA encodes the alpha isoform of the PI3K catalytic subunit.
- Around 40% of patients with HR-positive, HER2-negative breast cancer present with an activating PIK3CA tumor mutation.
- Alpelisib is a specific inhibitor of the PI3K alpha isoform.

André F et al. ESMO 2018;Abstract LBA3_PR.

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

ORIGINAL ARTICLE

Alpelisib plus fulvestrant for *PIK3CA*-mutated, hormone receptor-positive, human epidermal growth factor receptor-2—negative advanced breast cancer: final overall survival results from SOLAR-1

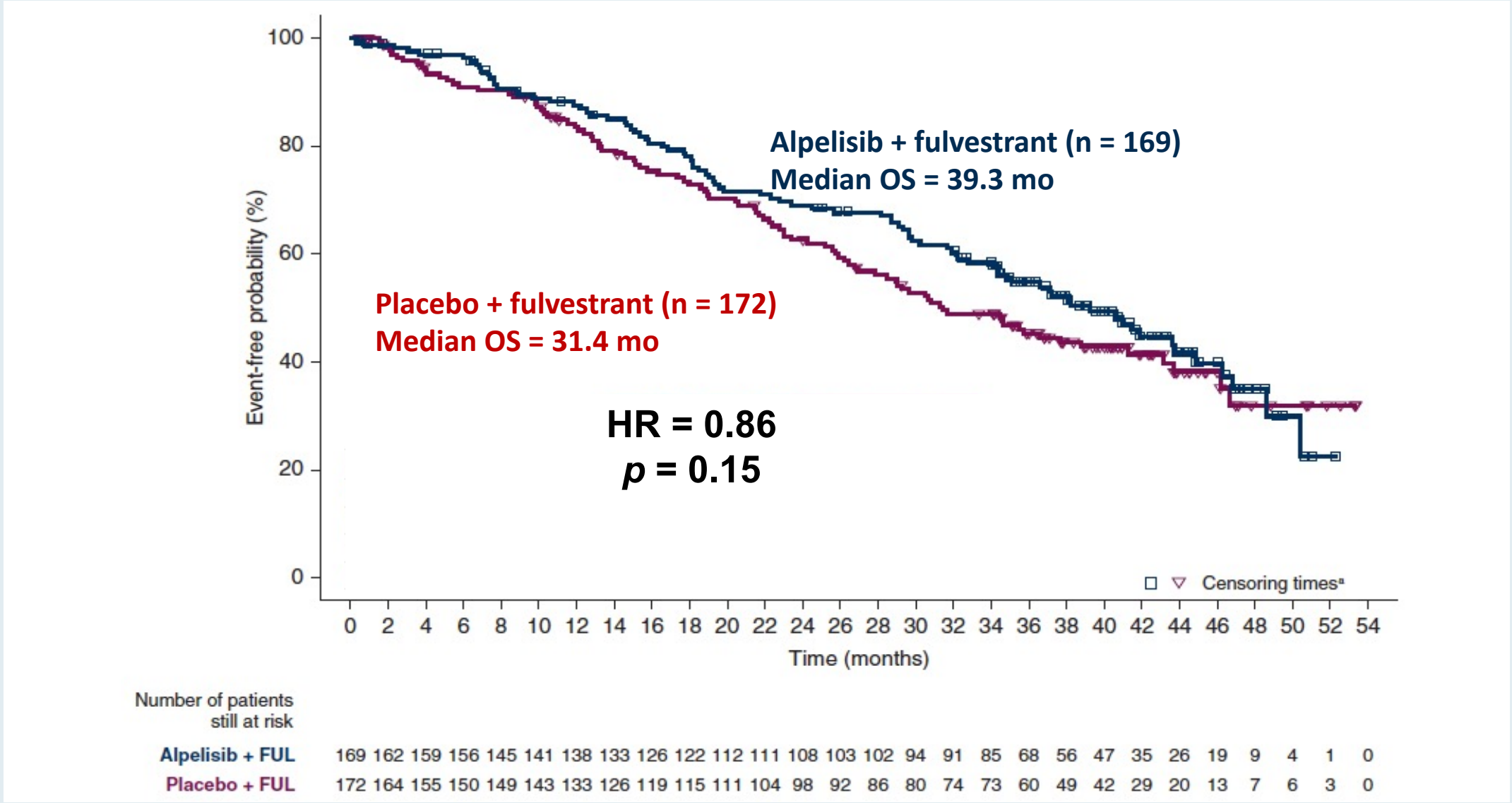
F. André[1*], E. M. Ciruelos[2], D. Juric[3], S. Loibl[4], M. Campone[5], I. A. Mayer[6], G. Rubovszky[7], T. Yamashita[8], B. Kaufman[9], Y.-S. Lu[10], K. Inoue[11], Z. Pápai[12], M. Takahashi[13], F. Ghaznawi[14], D. Mills[15], M. Kaper[14], M. Miller[14], P. F. Conte[16], H. Iwata[17] & H. S. Rugo[18]

[1]Department of Medical Oncology, Institut Gustave Roussy, Villejuif and Paris Saclay University, Orsay, France; [2]Medical Oncology, Hospital Universitario 12 de Octubre, Madrid, Spain; [3]Department of Medicine, Massachusetts General Hospital Cancer Center, Boston, USA; [4]Department of Medicine and Research, German Breast Group, GBG Forschungs GmbH, Neu-Isenburg, Germany; [5]Medical Oncology, Institut de Cancerologie de l'Ouest, Saint-Herblain, Nantes Cedex, France; [6]Hematology/Oncology, Vanderbilt University, Nashville, USA; [7]Department of Medical Oncology and Clinical Pharmacology, National Institute of Oncology, Budapest, Hungary; [8]Department of Breast and Endocrine Surgery, Kanagawa Cancer Center, Yokohama, Japan; [9]Medical Oncology, Tel Aviv University, Sheba Medical Centre, Tel Hashomer, Israel; [10]Medical Oncology, National Taiwan University Hospital, Taipei, Taiwan; [11]Breast Surgery, Saitama Cancer Center, Saitama, Japan; [12]Medical Oncology, Hungarian Defence Forces Medical Centre, Budapest, Hungary; [13]Breast Surgery, NHO Hokkaido Cancer Center, Sapporo, Japan; [14]Novartis Pharmaceuticals Corporation, East Hanover, USA; [15]Novartis Pharma AG, Basel, Switzerland; [16]Medical Oncology, Universita di Padova and Oncologia Medica 2, Istituto Oncologico Veneto IRCCS, Padua, Italy; [17]Breast Oncology, Aichi Cancer Center Hospital, Aichi, Japan; [18]Breast Department, UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, USA

Available online 25 November 2020

***Ann Oncol* 2021;32(2):208-17.**

SOLAR-1: Overall Survival (OS) for Patients with Advanced Breast Cancer with a PIK3CA Mutation



André F et al. *Ann Oncol* 2021;32(2):208-17.

RTP RESEARCH TO PRACTICE

SOLAR-1: Select Adverse Events in Overall Patient Population

Adverse Event	Alpelisib–Fulvestrant Group (N = 284)			Placebo–Fulvestrant Group (N = 287)		
	Any Grade	Grade 3	Grade 4	Any Grade	Grade 3	Grade 4
	number of patients (percent)					
Any adverse event	282 (99.3)	183 (64.4)	33 (11.6)	264 (92.0)	87 (30.3)	15 (5.2)
Hyperglycemia	181 (63.7)	93 (32.7)	11 (3.9)	28 (9.8)	1 (0.3)	1 (0.3)
Diarrhea	164 (57.7)	19 (6.7)	0	45 (15.7)	1 (0.3)	0
Nausea	127 (44.7)	7 (2.5)	0	64 (22.3)	1 (0.3)	0
Decreased appetite	101 (35.6)	2 (0.7)	0	30 (10.5)	1 (0.3)	0
Rash	101 (35.6)	28 (9.9)	0	17 (5.9)	1 (0.3)	0

André F et al. *N Engl J Med* 2019;380(20):1929-40.

Lancet Oncol 2021;22(4):489-98.

Alpelisib plus fulvestrant in *PIK3CA*-mutated, hormone receptor-positive advanced breast cancer after a CDK4/6 inhibitor (BYLieve): one cohort of a phase 2, multicentre, open-label, non-comparative study

Hope S Rugo, Florence Lerebours, Eva Ciruelos, Pamela Drullinsky, Manuel Ruiz-Borrego, Patrick Neven, Yeon Hee Park, Aleix Prat, Thomas Bachelot, Dejan Juric, Nicholas Turner, Nickolas Sophos, Juan Pablo Zarate, Christina Arce, Yu-Ming Shen, Stuart Turner, Hemanth Kanakamedala, Wei-Chun Hsu, Stephen Chia

BYLieve: A Phase II, Open-Label, 3-Cohort, Noncomparative Trial (NCT03056755)

Goal: In the post-CDKi setting, assess the efficacy and safety of alpelisib + endocrine therapy (ET; fulvestrant or letrozole) for HR-positive, HER2-negative advanced breast cancer (ABC) with a PIK3CA mutation

Men or pre/postmenopausal[a] women with HR+, HER2– ABC with a PIK3CA mutation

- Last line of prior therapy: CDKi + ET, systemic chemotherapy or ET
- ECOG PS ≤2
- Measurable disease (per RECIST v1.1) or ≥1 predominantly lytic bone lesion

Patients who received CDKi + AI as immediate prior treatment (N = 112)[b] (Cohort A)

Alpelisib 300 mg oral QD + fulvestrant 500 mg[c]

Patients who received CDKi + fulvestrant as immediate prior treatment (N = 112) (Cohort B)

Alpelisib 300 mg oral QD + letrozole 2.5 mg[d]

Patients who experienced disease progression on/after AI and received chemotherapy or ET as immediate prior treatment (N = 112) (Cohort C)

Alpelisib 300 mg oral QD + fulvestrant 500 mg[c]

Treatment crossover between cohorts is not permitted

Primary endpoint

- Proportion of patients alive without PD at 6 months (RECIST v1.1) in each cohort
- **Secondary endpoints include**

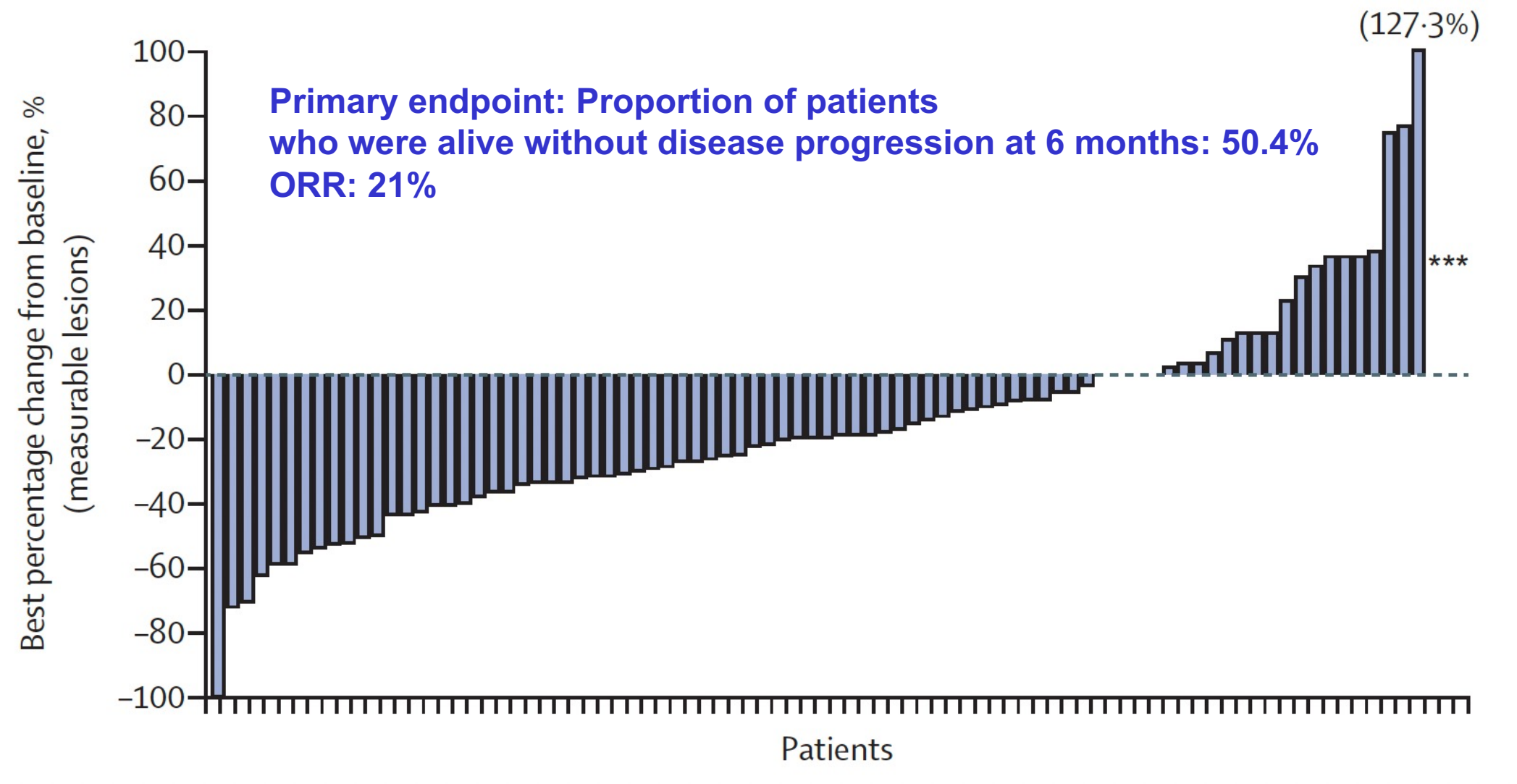
(assessed in each cohort)

- PFS
- PFS2
- ORR, CBR, DOR
- OS
- Safety

[a]Men in the letrozole cohort and premenopausal women also received goserelin 3.6 mg SC every 28 days or leuprolide 7.5 mg IM every 28 days for adequate gonadal suppression. [b]Enrollment in each cohort continued until at least 112 patients with a centrally confirmed PIK3CA mutation was reached.
[c]IM on D1 and D15 of Cycle 1 and D1 for all other cycles thereafter. [d]Oral QD.

Cohort A: Rugo HS et al. *Lancet Oncol* 2021;22(4):489-98.

BYLieve Efficacy Outcomes



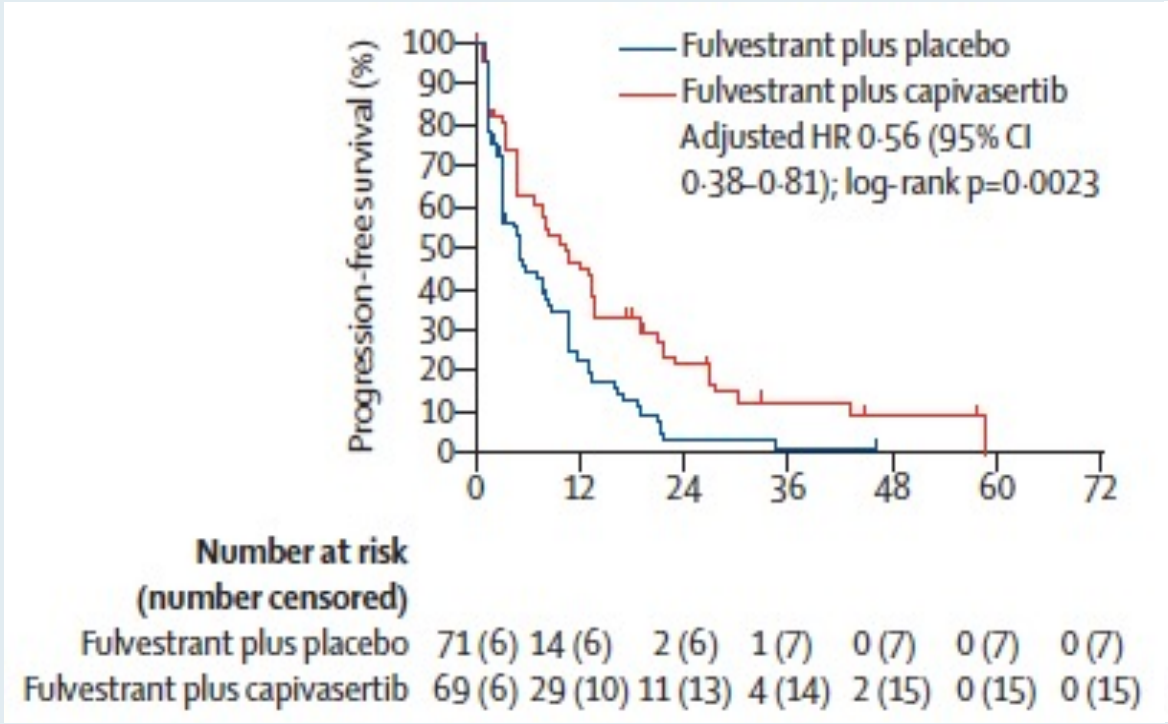
Rugo HS et al. *Lancet Oncol* 2021;22(4):489-98.

Lancet Oncol 2022;23(7):851-64.

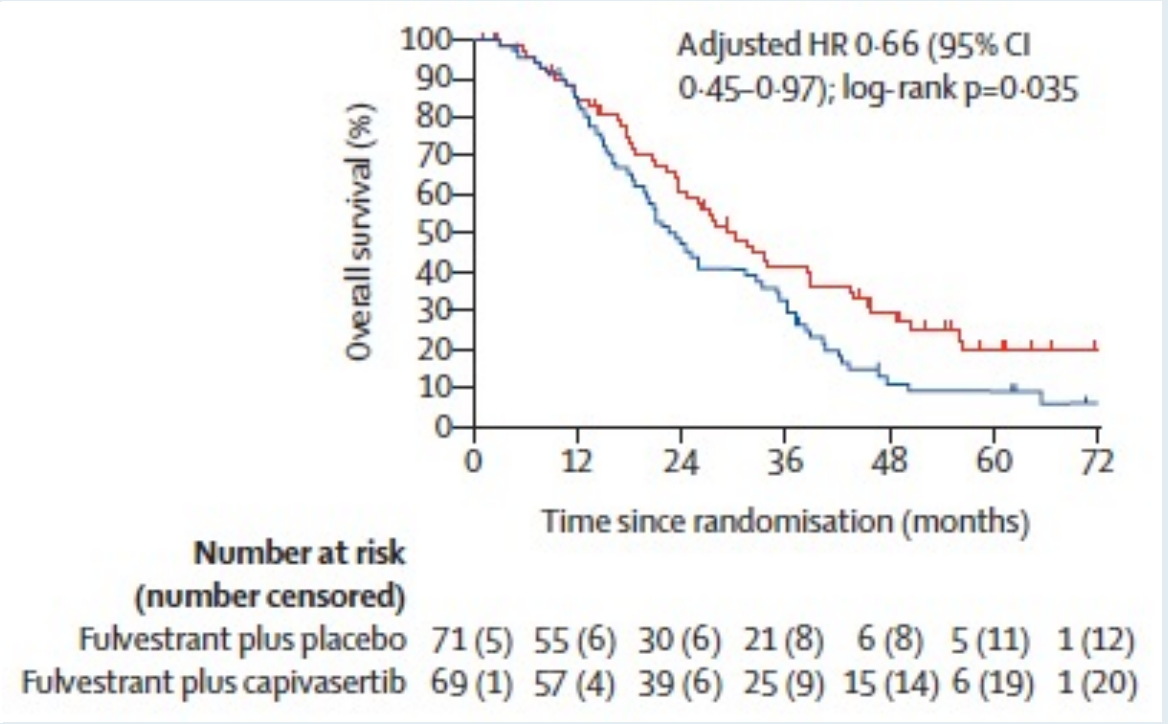
Fulvestrant plus capivasertib versus placebo after relapse or progression on an aromatase inhibitor in metastatic, oestrogen receptor-positive, HER2-negative breast cancer (FAKTION): overall survival, updated progression-free survival, and expanded biomarker analysis from a randomised, phase 2 trial

Sacha J Howell*, Angela Casbard*, Margherita Carucci, Kate Ingarfield, Rachel Butler, Sian Morgan, Magdalena Meissner, Catherine Bale, Pavel Bezecny, Sarah Moon, Chris Twelves, Ramachandran Venkitaraman, Simon Waters, Elza C de Bruin, Gaia Schiavon, Andrew Foxley, Robert H Jones

FAKTION: Progression-Free Survival and Overall Survival in the ITT Population



Number at risk (number censored)							
Fulvestrant plus placebo	71 (6)	14 (6)	2 (6)	1 (7)	0 (7)	0 (7)	0 (7)
Fulvestrant plus capivasertib	69 (6)	29 (10)	11 (13)	4 (14)	2 (15)	0 (15)	0 (15)

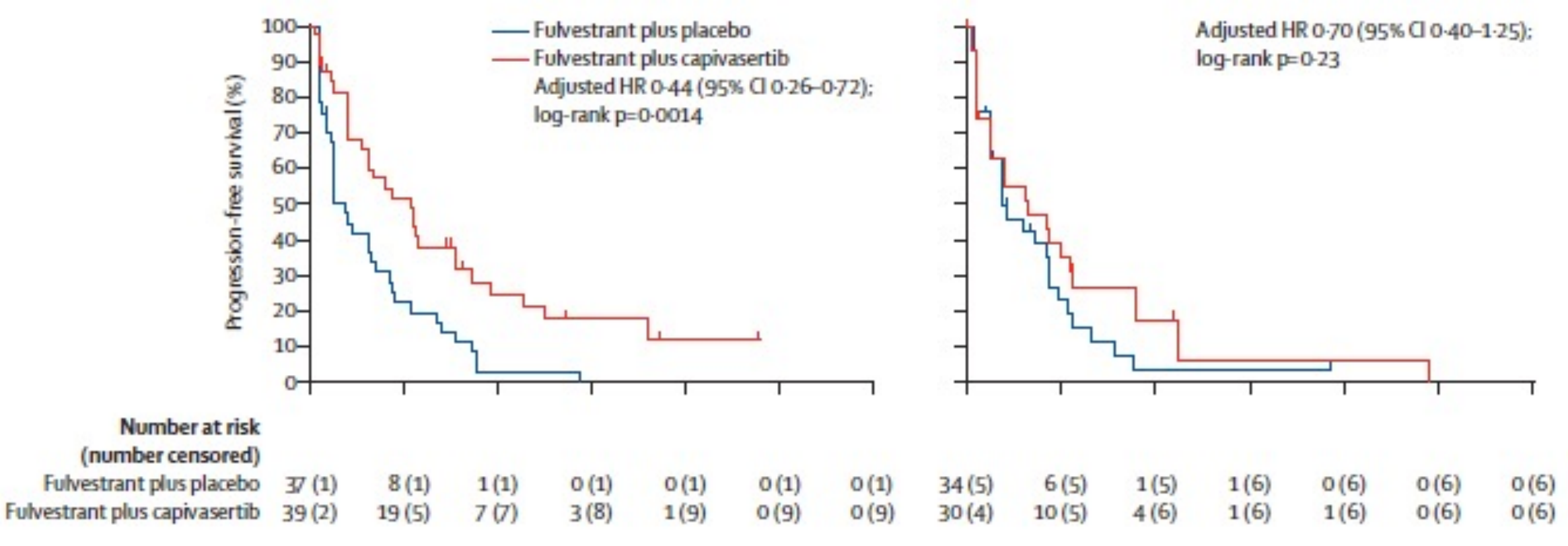


Number at risk (number censored)							
Fulvestrant plus placebo	71 (5)	55 (6)	30 (6)	21 (8)	6 (8)	5 (11)	1 (12)
Fulvestrant plus capivasertib	69 (1)	57 (4)	39 (6)	25 (9)	15 (14)	6 (19)	1 (20)

Howell SJ et al. *Lancet Oncol* 2022;23(7):851-64.

RTP RESEARCH TO PRACTICE

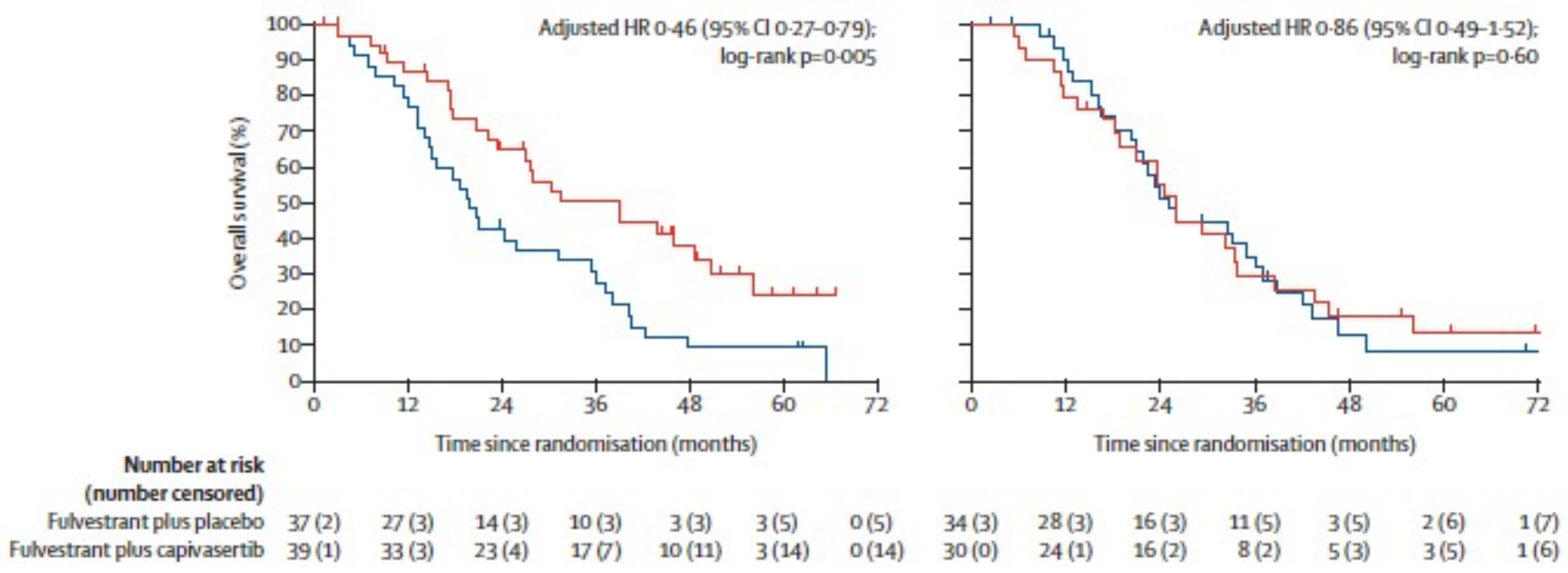
FAKTION: PFS in Expanded PI3K/AKT/PTEN Pathway-Altered and Nonaltered Subgroups



Howell SJ et al. *Lancet Oncol* 2022;23(7):851-64.

RTP RESEARCH TO PRACTICE

FAKTION: OS in Expanded PI3K/AKT/PTEN Pathway-Altered and Nonaltered Subgroups



Howell SJ et al. *Lancet Oncol* 2022;23(7):851-64.

Thank you for joining us!

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

Recent Advances and Real-World Implications in Medical Oncology: A Daylong Multitumor Educational Symposium in Partnership with the American Oncology Network

A CME/MOC- and NCPD-Accredited Hybrid Event

Saturday, August 6, 2022
9:00 AM – 4:30 PM PT

RTP
RESEARCH
TO PRACTICE

Agenda

Module 1 — Breast Cancer: *Drs Burstein and O'Shaughnessy*

Module 2 — Genitourinary Cancers: *Drs Agarwal and Srinivas*

Module 3 — Multiple Myeloma: *Drs Fonseca and Patel*

Module 4 — Chronic Lymphocytic Leukemia and Lymphomas: *Drs Kahl and Moskowitz*

Module 5 — Gastrointestinal Cancers: *Drs Mehta and Philip*

Module 6 — Lung Cancer: *Drs Dagogo-Jack and Ramalingam*

RTP RESEARCH TO PRACTICE

Genitourinary Cancers Faculty

Neeraj Agarwal, MD
Professor of Medicine
Senior Director for Clinical Research Innovation
Huntsman Cancer Institute Presidential
Endowed Chair of Cancer Research
Director
Center of Investigational Therapeutics
Director
Genitourinary Oncology Program
Huntsman Cancer Institute
University of Utah (NCI-CCC)
Salt Lake City, Utah

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

RTP
RESEARCH
TO PRACTICE

Co-Moderators

Breast Cancer
Stephen “Fred” Divers, MD
American Oncology Network
Hot Springs, Arkansas

CLL and Lymphomas
Jeanna L Knoble, MD
Zangmeister Cancer Center
Columbus, Ohio

Genitourinary Cancers
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Gastrointestinal Cancers
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Multiple Myeloma
Taral Patel, MD
Zangmeister Cancer Center
Columbus, Ohio

Lung Cancer
Ram Trehan, MD
George Washington University
Silver Spring, Maryland

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MODULE 2: Genitourinary Cancers

Co-Moderator

Michael J Castine, MD
Hematology Oncology Clinic
Baton Rouge, Louisiana

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Genitourinary Cancers Agenda

Module 1: Prostate Cancer

Module 2: Urothelial Bladder Cancer

Module 3: Renal Cell Carcinoma

Genitourinary Cancers Agenda

Module 1: Prostate Cancer

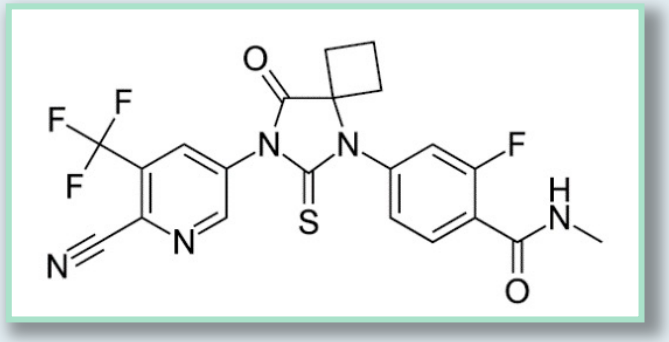
- Optimal use of hormonal therapy/chemotherapy in patients with locally-advanced, PSA-only relapse (M0); Castration-sensitive metastatic prostate cancer (mHSPC); choice of ADT
- Selection of patients and clinical management of ^{177}Lu-PSMA-617 in the treatment of metastatic CRPC (mCRPC)
- PARP inhibitors in combination with secondary hormonal therapy for patients with mCRPC with or without HRR gene mutations

Module 2: Urothelial Bladder Cancer

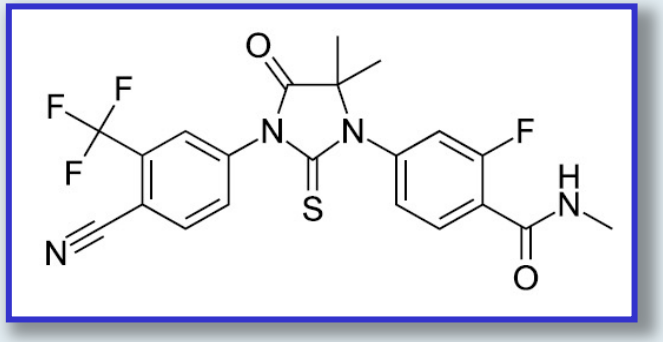
Module 3: Renal Cell Carcinoma

Next-Generation Androgen Receptor Inhibitors

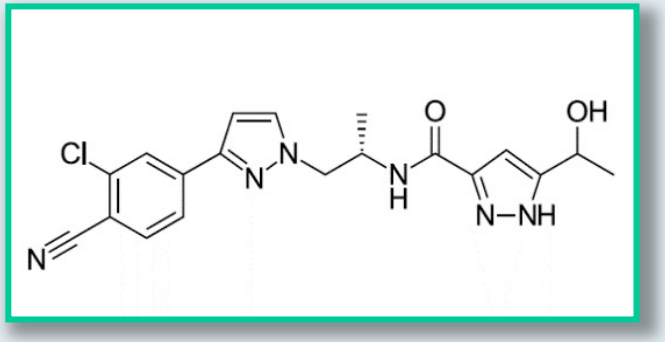
Apalutamide



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.

FDA Approves Darolutamide for Nonmetastatic Castration-Resistant Prostate Cancer

Press Release: July 30, 2022

"The US Food and Drug Administration (FDA) today approved darolutamide, an androgen receptor inhibitor (ARi), for the treatment of patients with non-metastatic castration-resistant prostate cancer (nmCRPC). The FDA approval is based on the Phase III ARAMIS trial evaluating darolutamide plus androgen deprivation therapy (ADT), which demonstrated a highly significant improvement in the primary efficacy endpoint of metastasis-free survival (MFS), with a median of 40.4 months versus 18.4 months for placebo plus ADT ($p < 0.0001$). MFS is defined as the time from randomization to the time of first evidence of blinded independent central review (BICR)-confirmed distant metastasis or death from any cause within 33 weeks after the last evaluable scan, whichever occurred first. Darolutamide was approved under the FDA's Priority Review designation, which is reserved for medicines that may provide significant improvements in the safety or effectiveness of the treatment for serious conditions."

https://www.prnewswire.com/news-releases/fda-approves-bayers-nubeqa-darolutamide-a-new-treatment-for-men-with-non-metastatic-castration-resistant-prostate-cancer-300893680.html

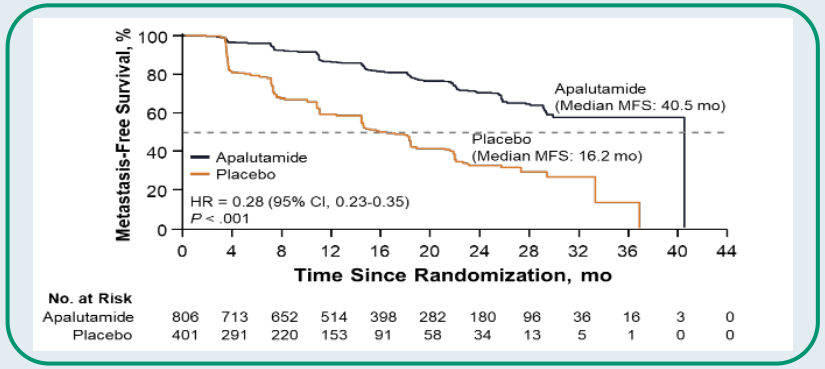
FDA Approvals of Next-Generation Antiandrogens for Nonmetastatic Castration-Resistant Prostate Cancer (CRPC)

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

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

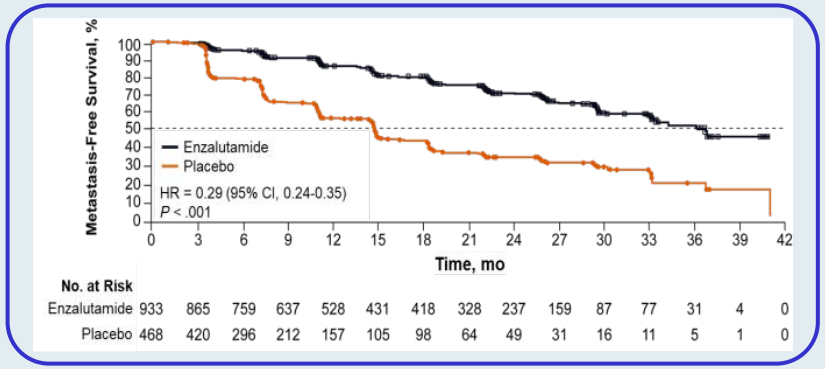
Primary Endpoint: Metastasis-Free Survival (MFS) in Nonmetastatic CRPC

SPARTAN[1] Apalutamide (APA)



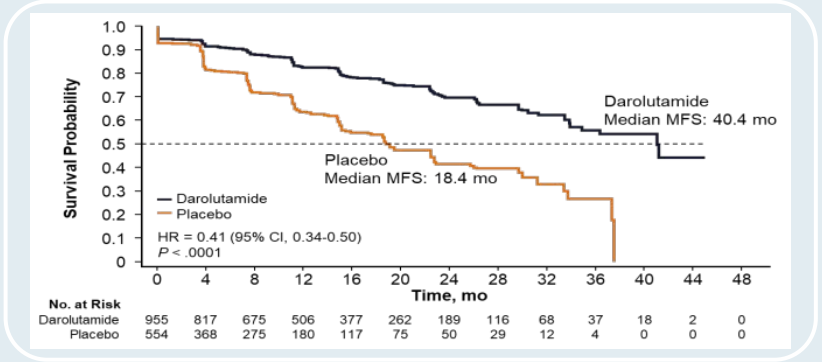
- 72% reduction in distant progression or death
- Median MFS: APA 40.5 vs placebo (PBO) 16.2 months
- 24-month MFS benefit

PROSPER[2] Enzalutamide (ENZA)



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

ARAMIS[3] Darolutamide (DARO)



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

1. Smith MR et al. *NEJM* 2018;378(15):1408-18. 2. Hussain M et al. *NEJM* 2018;378(26):2465-74. 3. Fizazi K et al. *NEJM* 2019;380(13):1235-46.

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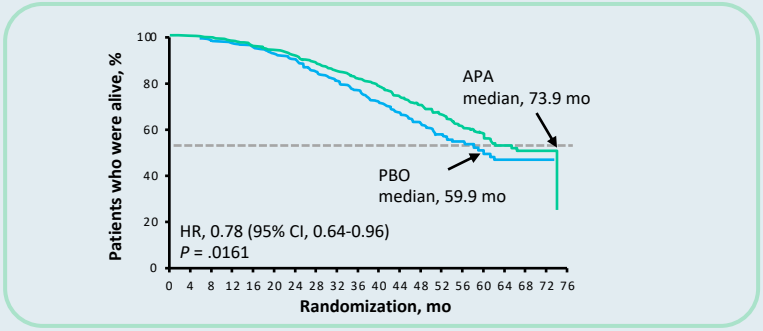
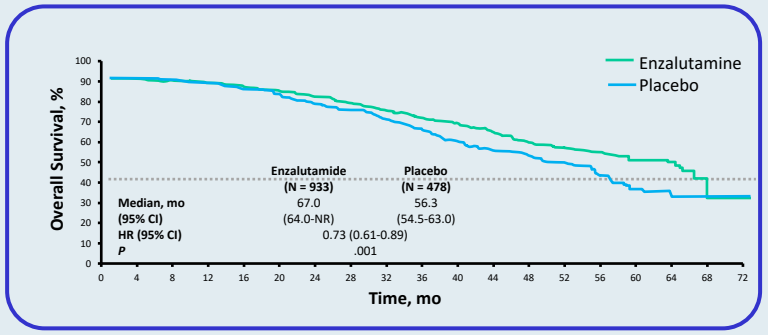
Secondary Endpoint: Overall Survival (OS) in Nonmetastatic CRPC

SPARTAN1[1] Apalutamide



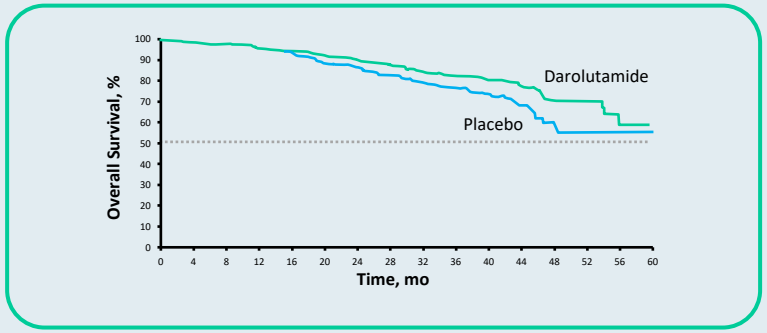
- 22% reduction in risk of death
- Median follow-up of 52.0 months
- Median OS was significantly longer for apalutamide vs placebo
  - 73.9 months vs 59.9 months
  - **HR = 0.78 (95% CI 0.64-0.96); *p* = 0.016**

PROSPER[2] Enzalutamide



- 27% reduction in risk of death
- Median follow-up of 48 months
- Median OS was significantly longer for enzalutamide vs placebo
  - 67.0 months vs 56.3 months
  - **HR = 0.73 (95% CI 0.61-0.89); *p* = 0.001**

ARAMIS[3] Darolutamide



- 31% reduction in risk of death
- Median follow-up of 29.0 months
- Median OS was significantly longer for darolutamide vs placebo
  - **HR = 0.69 (95% CI, 0.53-0.88); *p* = 0.003**

1. Smith MR et al. *Eur Urol* 2020;79(1):150-8. 2. Sternberg CN et al. *NEJM* 2020;382(23):2197-206. 3. Fizazi K et al. *NEJM* 2020;383(11):1040-9.

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

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

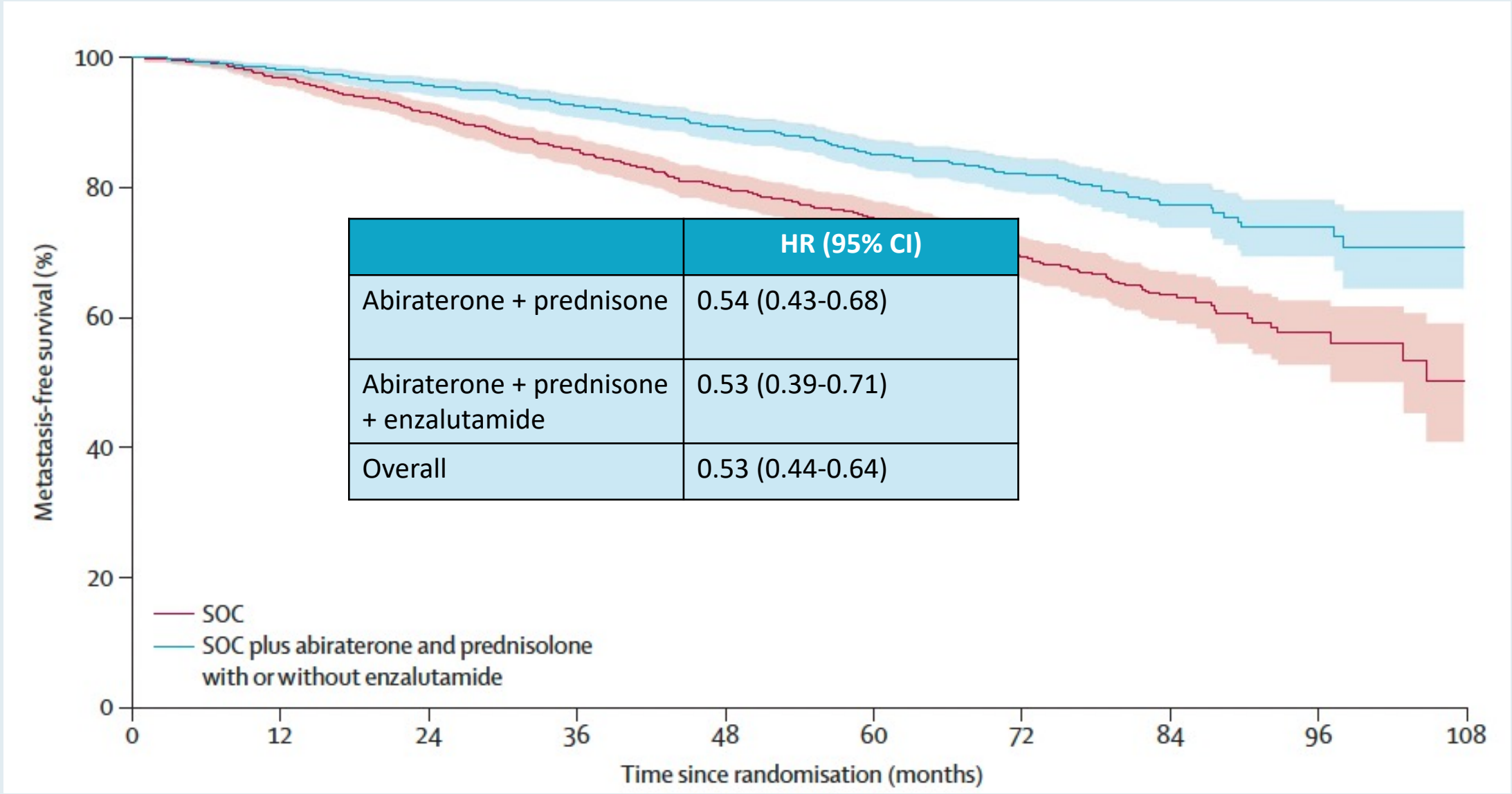
Sternberg CN et al; PROSPER Investigators. *N Engl J Med* 2020;382(23):2197-206.
Fizazi K et al; ARAMIS Investigators. *N Engl J Med* 2020;383(11):1040-9.
Small EJ et al; SPARTAN Investigators. ASCO 2020;Abstract 5516.

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‡*

STAMPEDE Platform Protocol Meta-Analysis: Metastasis-Free Survival



	HR (95% CI)
Abiraterone + prednisone	0.54 (0.43-0.68)
Abiraterone + prednisone + enzalutamide	0.53 (0.39-0.71)
Overall	0.53 (0.44-0.64)

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

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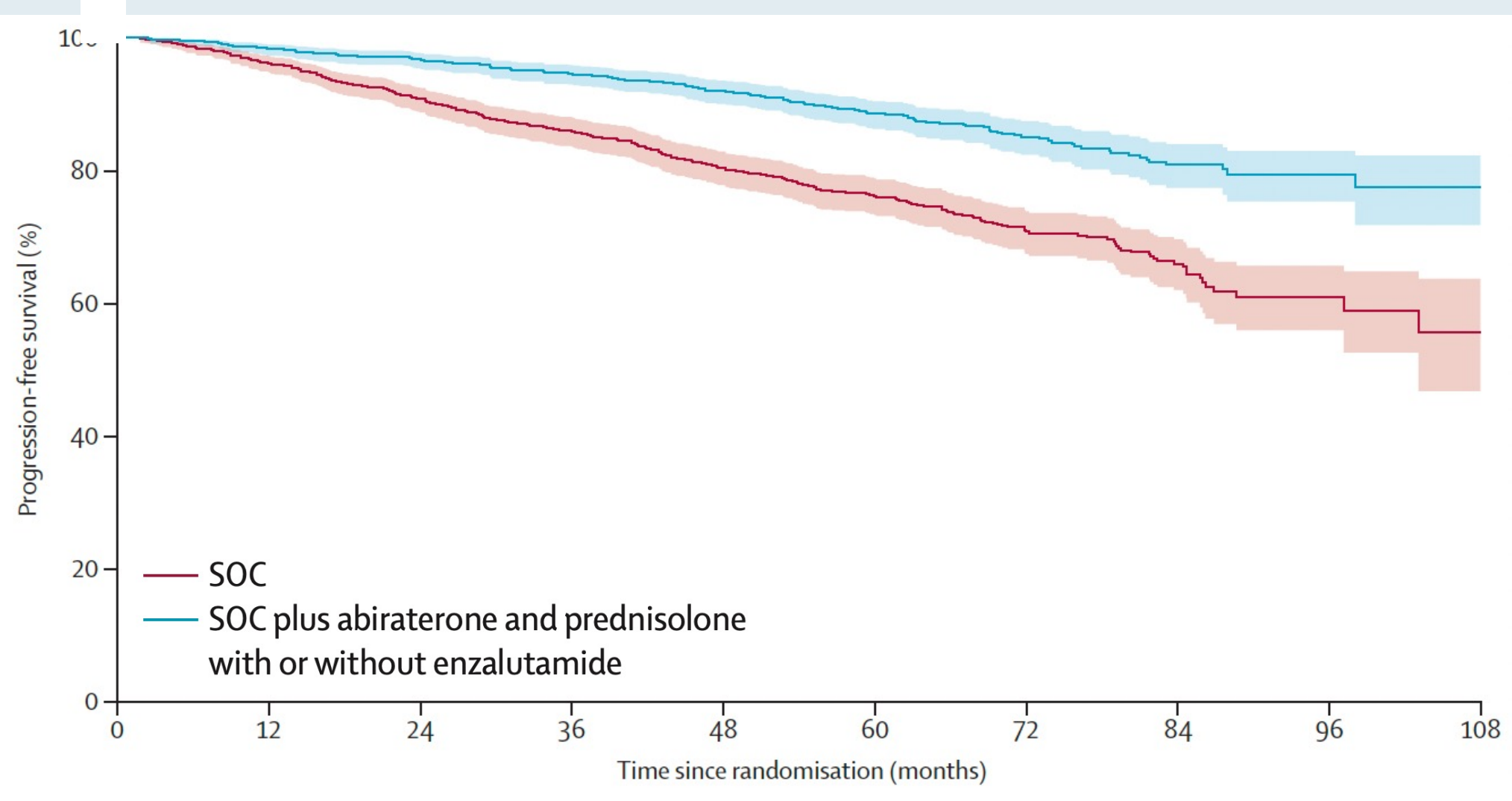
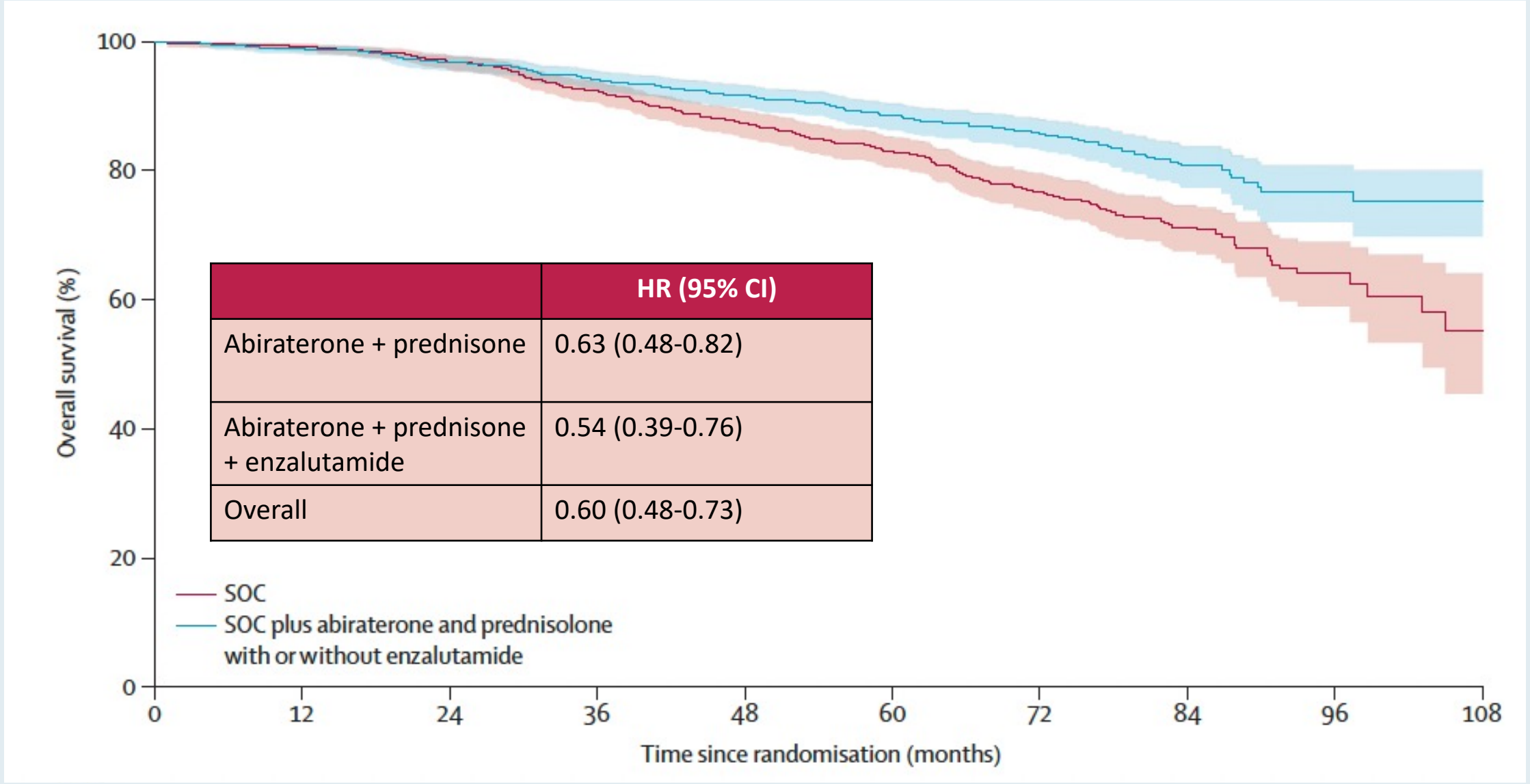
STAMPEDE Platform Protocol Meta-Analysis: Progression-Free Survival



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

RTP RESEARCH TO PRACTICE

STAMPEDE Platform Protocol Meta-Analysis: Overall Survival



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

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

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STAMPEDE Platform Protocol Meta-Analysis: Select Adverse Events

	Control group in the abiraterone trial (n=455)			Control group in the abiraterone and enzalutamide trial (n=533)			Combination therapy in the abiraterone trial (n=451)			Combination therapy in the abiraterone and enzalutamide trial (n=513)		
	Grade 1–2	Grade 3	Grade 4	Grade 1–2	Grade 3	Grade 4	Grade 1–2	Grade 3	Grade 4	Grade 1–2	Grade 3	Grade 4
Erectile dysfunction	211 (46%)	48 (11%)	0	237 (44%)	55 (10%)	0	209 (46%)	41 (9%)	0	243 (47%)	71 (14%)	0
Hypertension	65 (14%)	6 (1%)	0	74 (14%)	8 (2%)	0	108 (24%)	23 (5%)	0	189 (37%)	73 (14%)	0
ALT increased	51 (11%)	0	0	72 (14%)	4 (1%)	0	82 (18%)	23 (5%)	2 (<1%)	145 (28%)	59 (12%)	5 (1%)
Fatigue	279 (61%)	4 (1%)	NM	371 (70%)	12 (2%)	NM	299 (66%)	10 (2%)	NM	411 (80%)	49 (10%)	NM
AST increased	14 (3%)	1 (<1%)	0	17 (3%)	0	0	33 (7%)	2 (<1%)	0	61 (12%)	17 (3%)	2 (<1%)
Insomnia	126 (28%)	1 (<1%)	NM	162 (30%)	1 (<1%)	NM	133 (29%)	8 (2%)	NM	200 (39%)	7 (1%)	NM
Hypokalemia	4 (1%)	1 (<1%)	0	9 (2%)	1 (<1%)	0	50 (11%)	4 (1%)	1 (<1%)	56 (11%)	6 (1%)	0
Anaemia	142 (31%)	3 (1%)	2 (<1%)	211 (40%)	2 (<1%)	0	185 (41%)	1 (<1%)	1 (<1%)	225 (44%)	2 (<1%)	0
Dizziness	53 (12%)	0	NM	70 (13%)	1 (<1%)	NM	72 (16%)	1 (<1%)	NM	126 (25%)	4 (1%)	NM
Constipation	104 (23%)	3 (1%)	0	149 (28%)	0	0	128 (28%)	1 (<1%)	0	181 (35%)	1 (<1%)	0
Cough	72 (16%)	0	0	107 (20%)	0	0	103 (23%)	5 (1%)	0	103 (20%)	0	0
Nausea	43 (9%)	1 (<1%)	NM	67 (13%)	0	NM	60 (13%)	0	NM	130 (25%)	3 (1%)	NM

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

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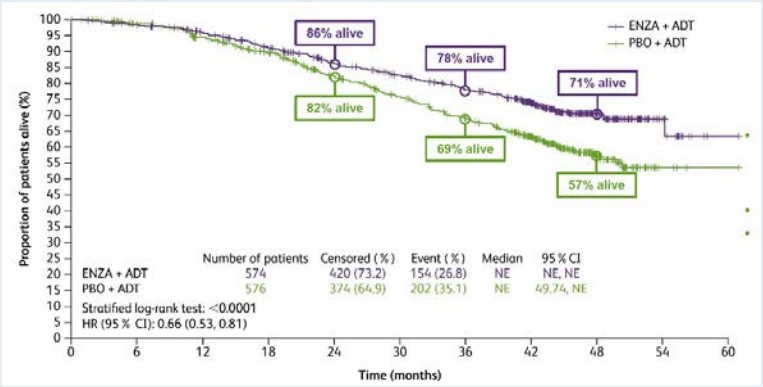
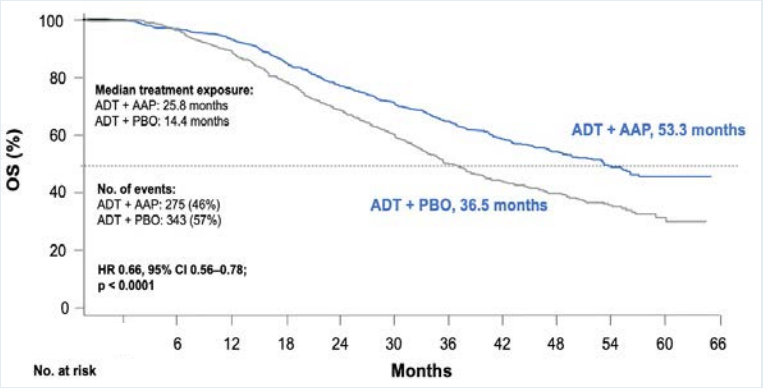
Final Overall Survival (OS) Analyses: Enzalutamide, Abiraterone and Apalutamide for Metastatic Hormone-Sensitive Prostate Cancer

ARCHES[1] Enzalutamide + androgen deprivation therapy (ADT)



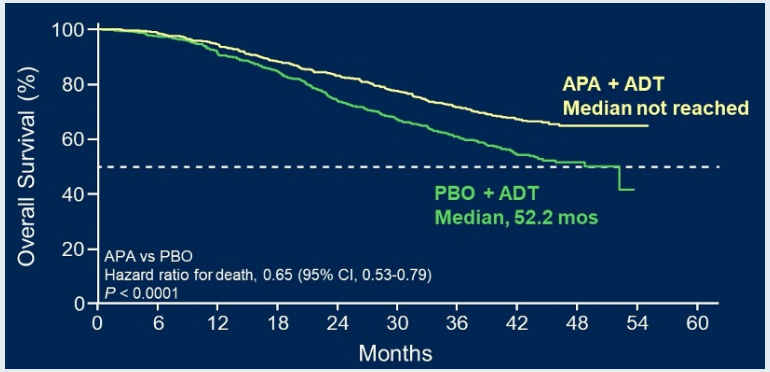
- 34% reduction in risk of death
- Median follow-up of 44.6 months
- Median OS was significantly longer for enzalutamide + ADT vs placebo + ADT
  - **40.2 months vs 13.8 months**
  - **HR = 0.66; *p* < 0.0001**

LATITUDE[2] Abiraterone + ADT



- 34% reduction in risk of death
- Median follow-up of 51.8 months
- Median OS was significantly longer for abiraterone + ADT vs placebo + ADT
  - 53.3 months vs 36.5 months
  - **HR = 0.66; *p* < 0.0001**

TITAN[3] Apalutatmide + ADT



- 35% reduction in risk of death
- Median follow-up of 44.0 months
- Median OS was significantly longer for apalutamide + ADT vs placebo + ADT
  - Not reached vs 52.2 months
  - **HR = 0.65; *p* < 0.0001**

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

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

Press Release: March 23, 2022

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

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

Efficacy was evaluated in the phase 3 VISION trial which demonstrated a statistically significant improvement in the primary endpoints OS and rPFS. Hazard ratio (HR) for OS was 0.62 (95% CI: 0.52, 0.74; $p<0.001$) for the comparison of ^{177}Lu-PSMA-617 plus BSoC versus BSoC. Median OS was 15.3 months (95% CI: 14.2, 16.9) in the ^{177}Lu-PSMA-617 plus BSoC arm and 11.3 months (95% CI: 9.8, 13.5) in the BSoC arm, respectively."

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

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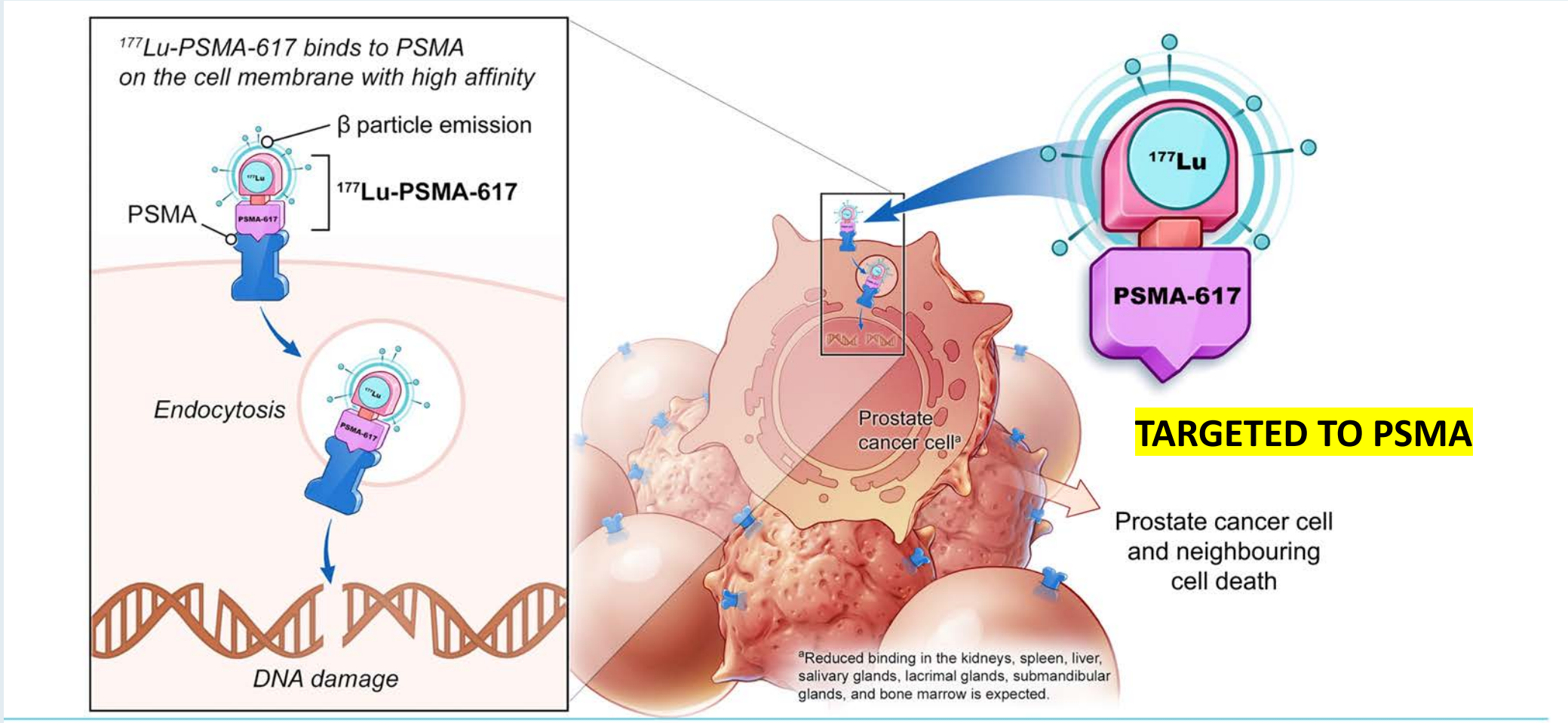
^{177}Lu-PSMA-617: Mechanism of Action



Morris MJ et al. ASCO 2021;Abstract LBA4.

N Engl J Med 2021;385(12):1091-103.

The NEW ENGLAND JOURNAL of MEDICINE

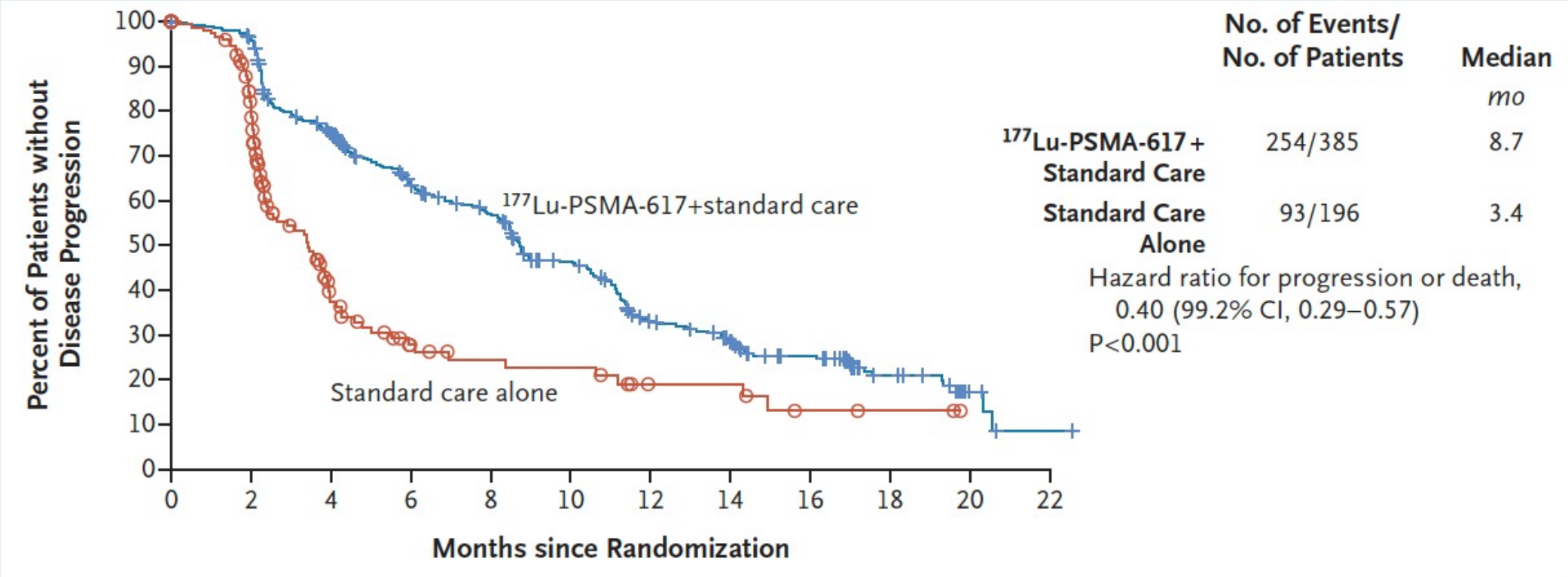
ORIGINAL ARTICLE

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: Efficacy Summary

Imaging-based progression-free survival



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

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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.

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)

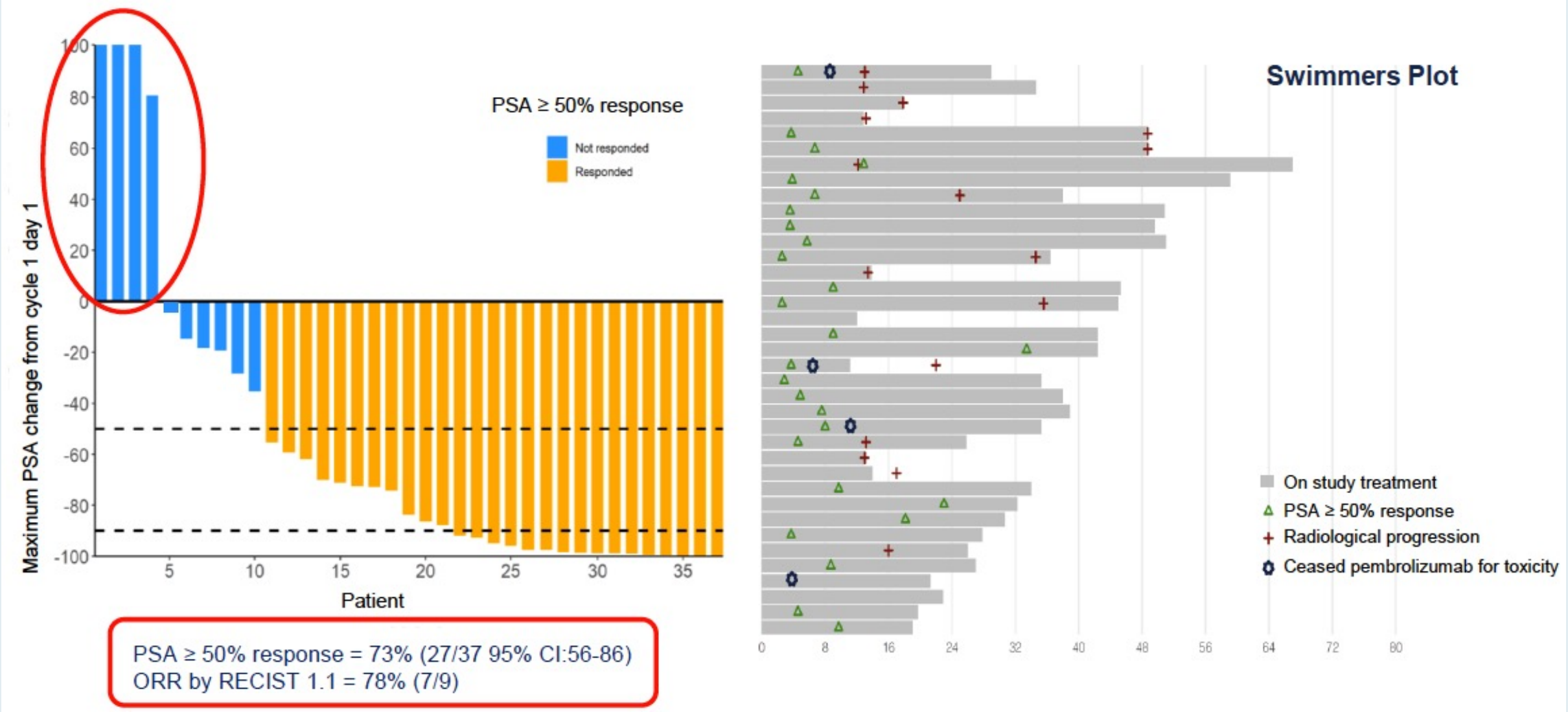
Shahneen Sandhu, Anthony M. Joshua, Louise Emmett, Lavinia Spain, Lisa G. Horvath, Megan Crumbaker, Arsha Anton, Roslyn Wallace, Anupama Pasam, Mathias Bressel, Erin Cassidy, Patricia Banks, Aravind Ravi Kumar, Ramin Alipour, Tim Akhurst, Grace Kong, Ian D. Davis, Scott Williams, Rod Hicks, Michael S.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

Abstract 577O

2021 ESMO congress

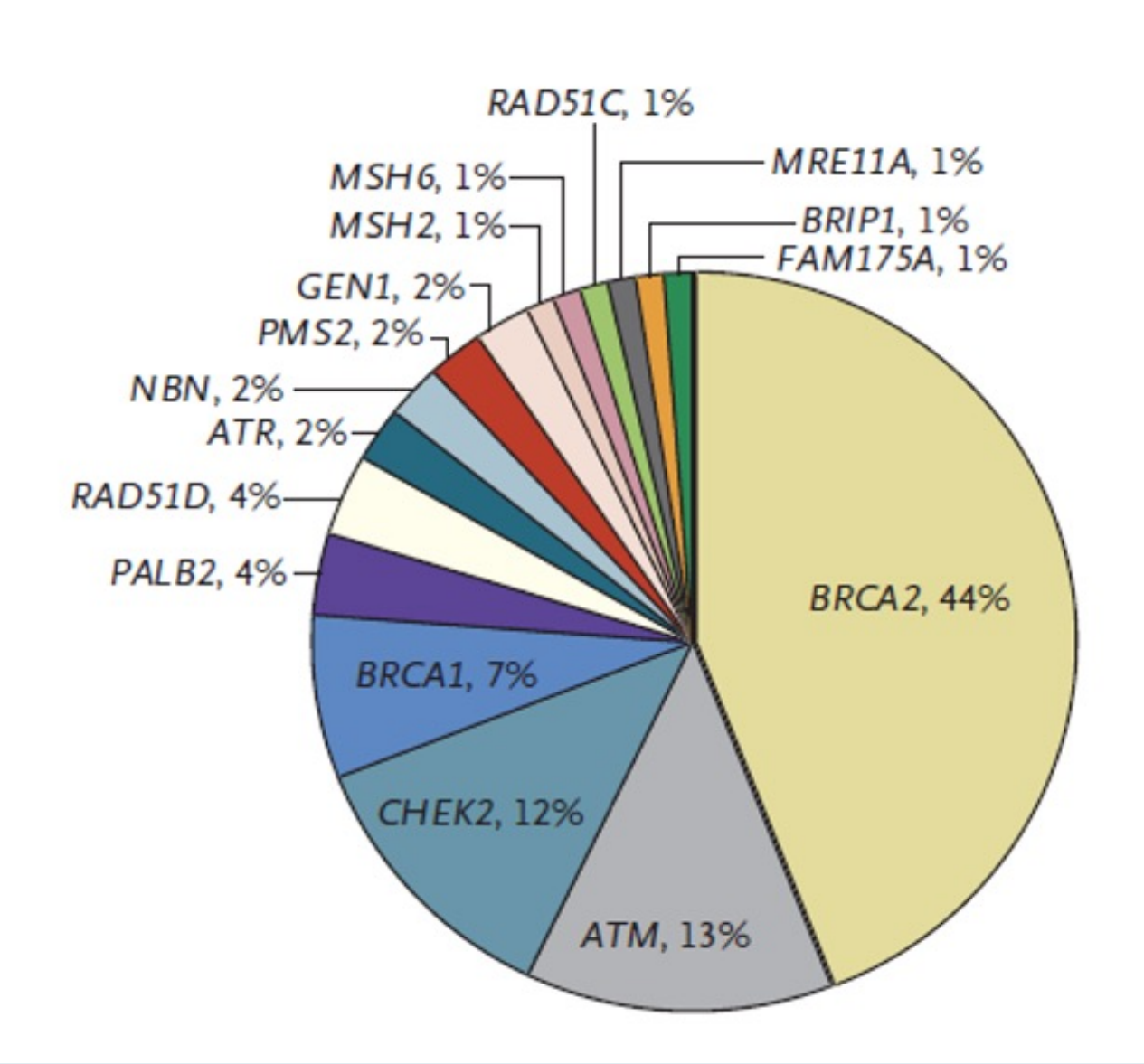
Presented by: Shahneen Sandhu

PRINCE: PSA Response Rate (Primary Endpoint)



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

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

Recent FDA Approvals of PARP Inhibitors for Metastatic Castration-Resistant Prostate Cancer

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/

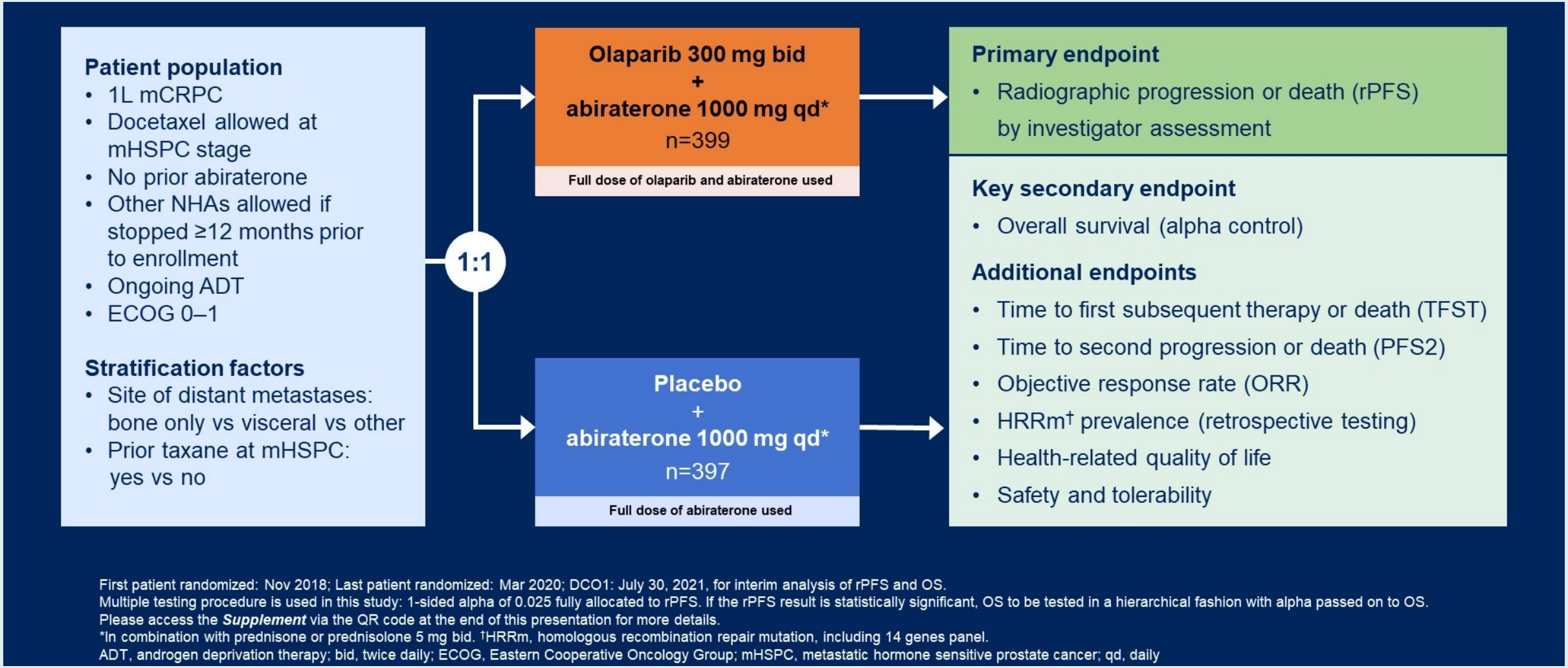
ASCO Genitourinary Cancers Symposium 2022;Abstract 11.

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

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

ClinicalTrials.gov identifier: NCT03732820.

PROpel: Study Design

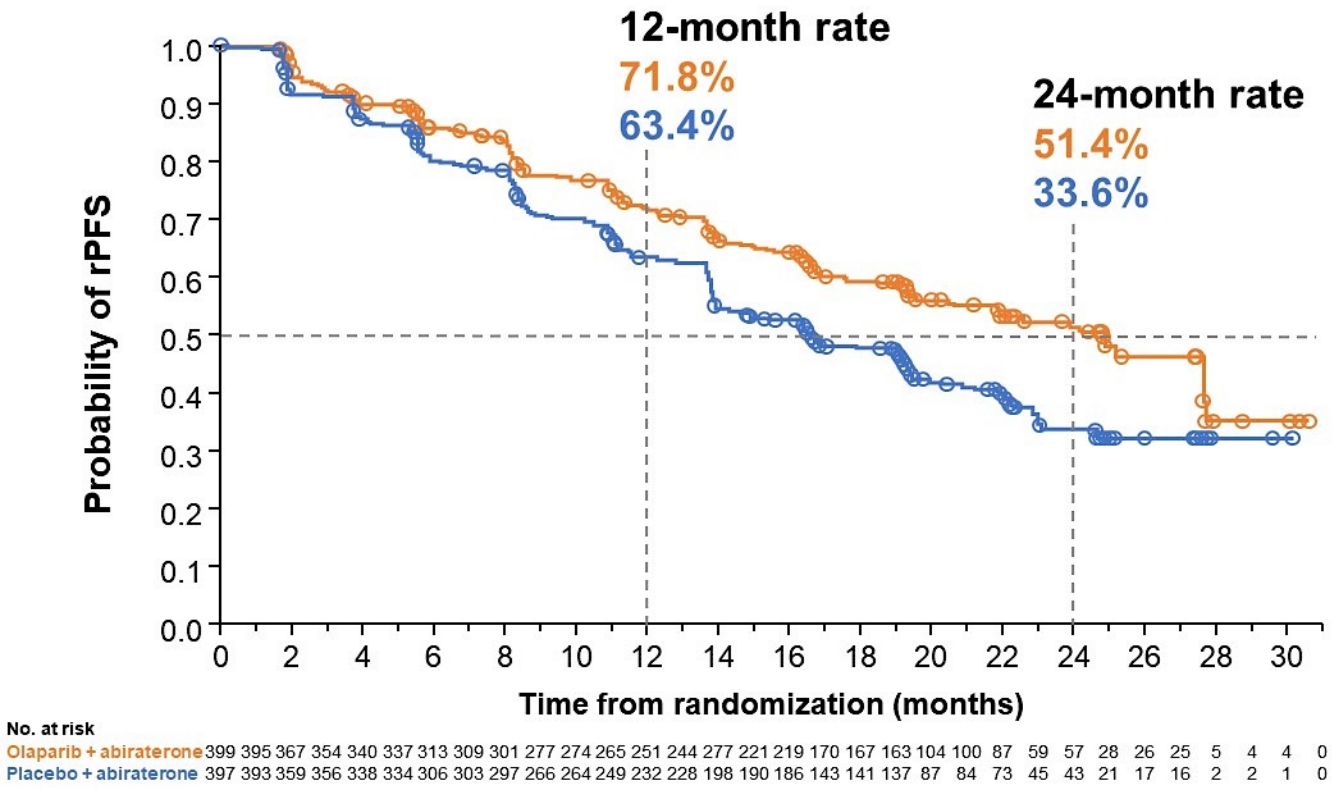


First patient randomized: Nov 2018; Last patient randomized: Mar 2020; DCO1: July 30, 2021, for interim analysis of rPFS and OS.
Multiple testing procedure is used in this study: 1-sided alpha of 0.025 fully allocated to rPFS. If the rPFS result is statistically significant, OS to be tested in a hierarchical fashion with alpha passed on to OS.
Please access the ***Supplement*** via the QR code at the end of this presentation for more details.
*In combination with prednisone or prednisolone 5 mg bid. †HRRm, homologous recombination repair mutation, including 14 genes panel.
ADT, androgen deprivation therapy; bid, twice daily; ECOG, Eastern Cooperative Oncology Group; mHSPC, metastatic hormone sensitive prostate cancer; qd, daily

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

PROpel Primary Endpoint: Investigator-Assessed rPFS

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



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

Pre-specified 2-sided alpha: 0.0324

Median rPFS improvement of 8.2 months favors olaparib + abiraterone*

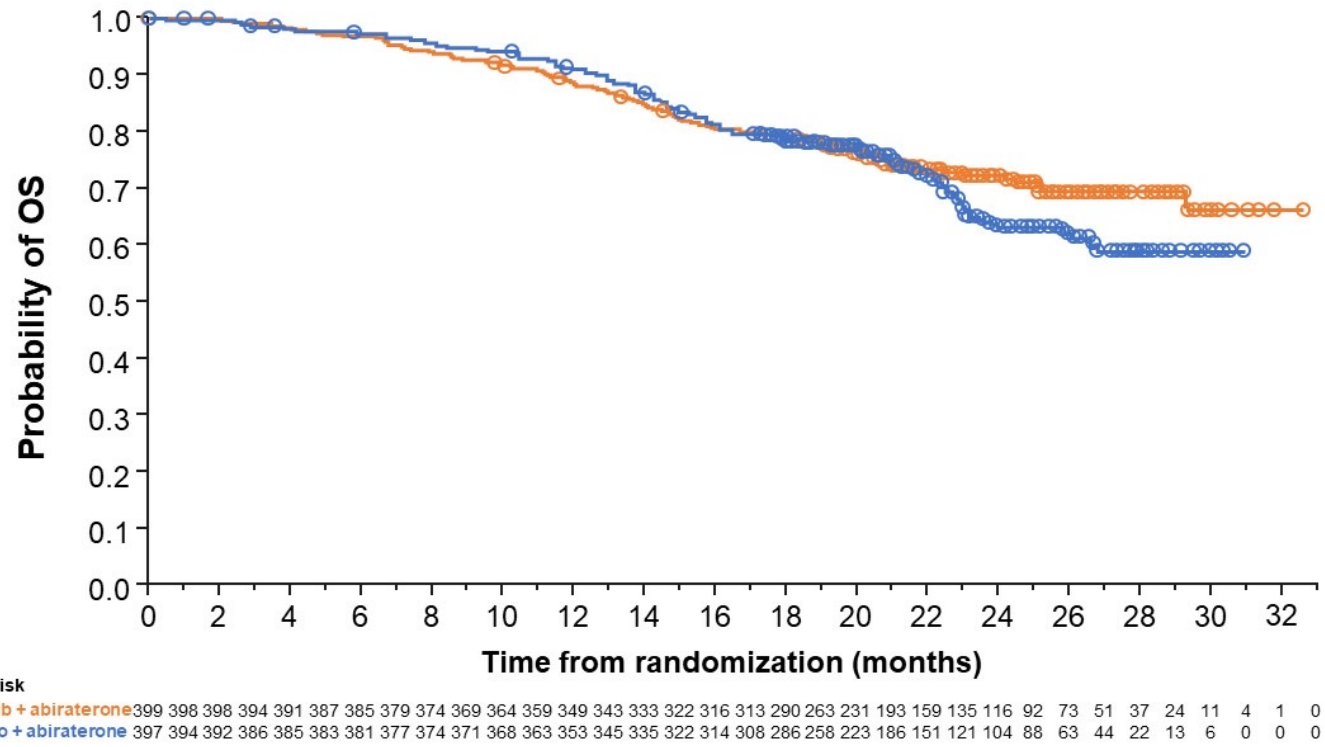
Events: 394; Maturity 49.5%
*In combination with prednisone or prednisolone
CI, confidence interval; HR, hazard ratio.

rPFS = radiographic progression-free survival

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

PROpel: Overall Survival (OS)

28.6% maturity; trend towards improved OS with olaparib + abiraterone



	Olaparib + abiraterone (n=399)	Placebo + abiraterone (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	

Pre-specified 2-sided alpha: 0.001

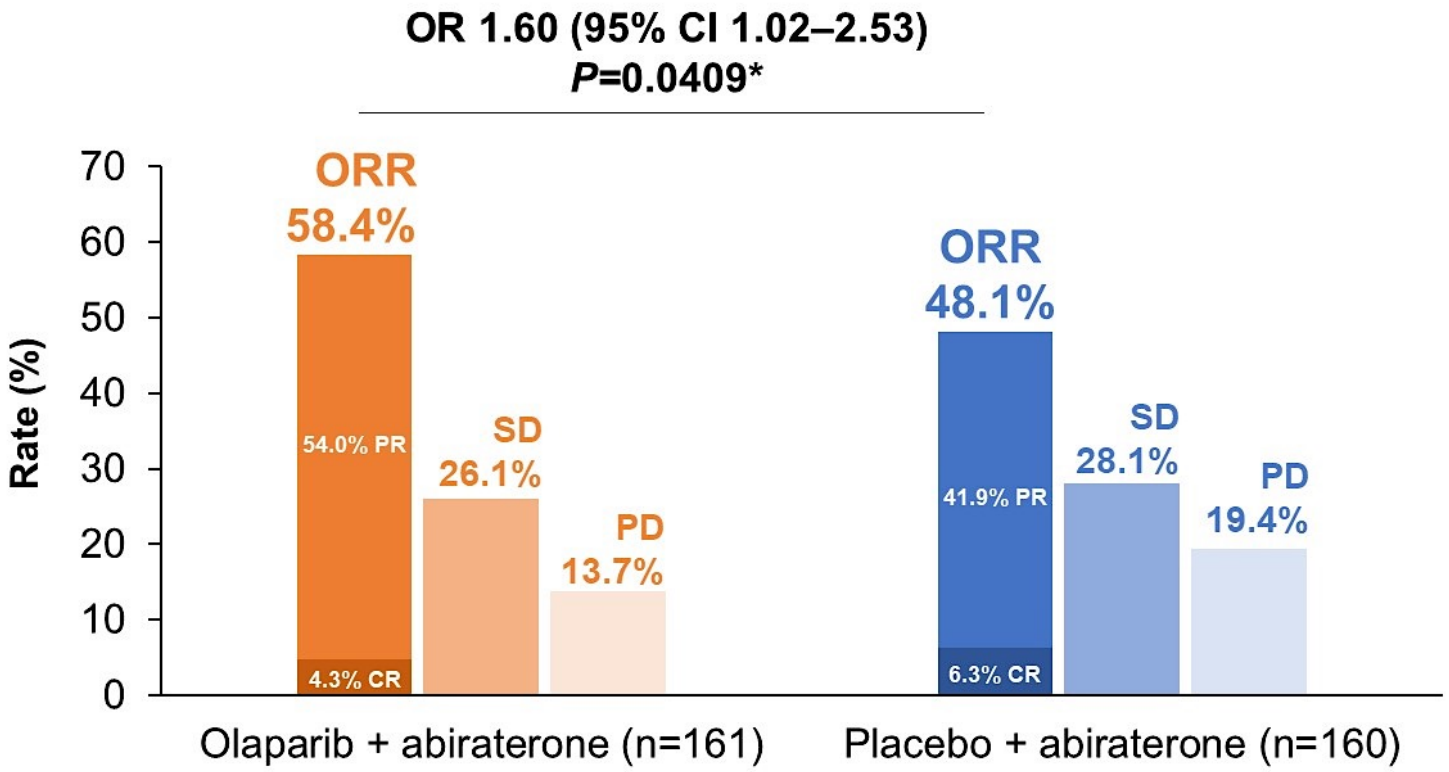
Events: 228
NR, not reached.

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

RTP RESEARCH TO PRACTICE

PROpel: ORR for Patients with Measurable Disease

10% improvement in ORR with olaparib + abiraterone



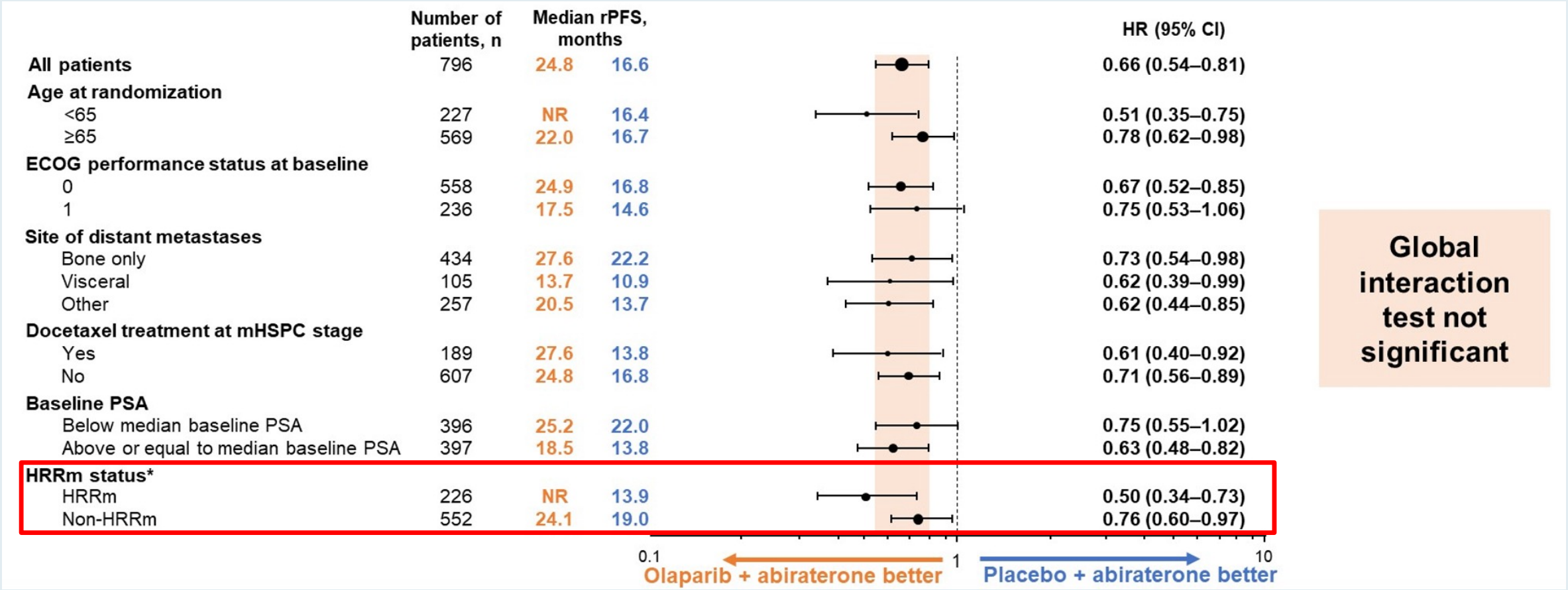
321/796 patients (40.3%) had measurable disease by RECIST v1.1 criteria at baseline

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

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

RTP RESEARCH TO PRACTICE

PROpel: Subgroup Analysis of rPFS



Global interaction test not significant

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

PROpel: Cardiac and Thromboembolic Adverse Events

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

CT, computerized tomography; SMQ, Standardised MedDRA Query.

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

ASCO Genitourinary Cancers Symposium 2022;Abstract 12.

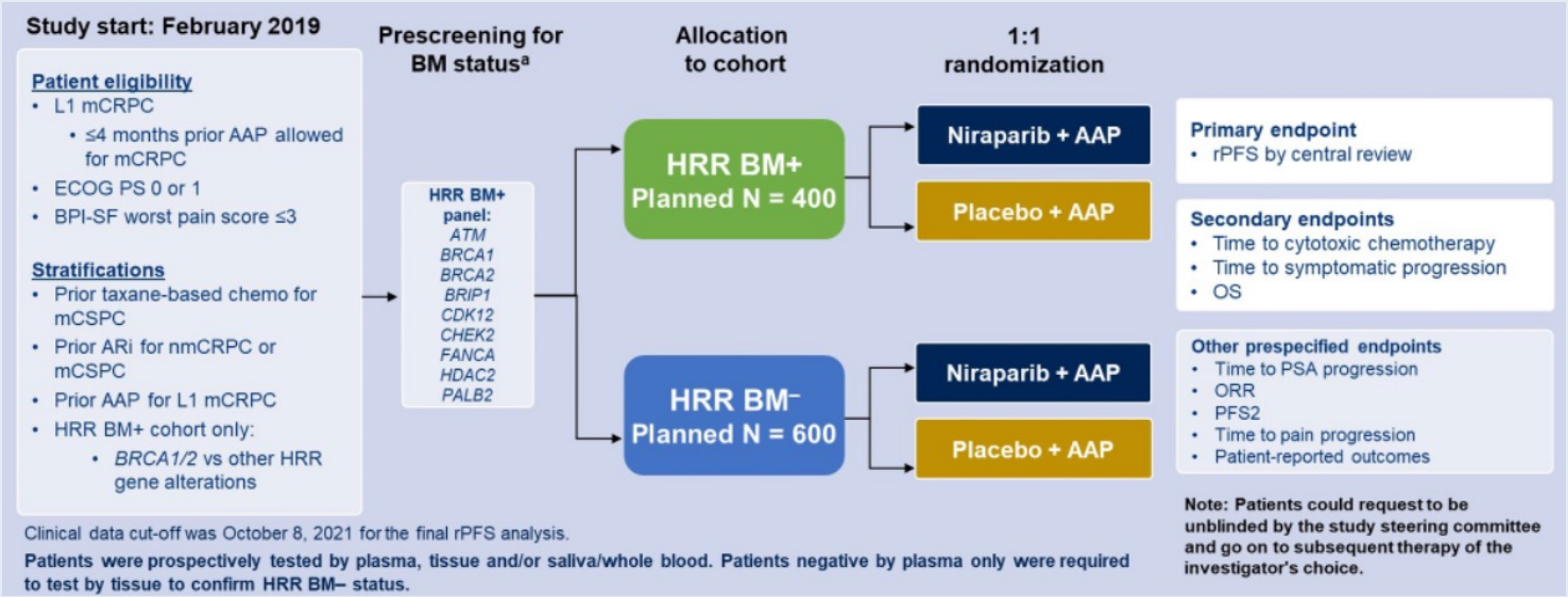
Phase 3 MAGNITUDE study: First results of niraparib (NIRA) with abiraterone acetate and prednisone (AAP) as first-line therapy in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC) with and without homologous recombination repair (HRR) gene alterations

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: Randomized, Double-Blind, Placebo-Controlled Study

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

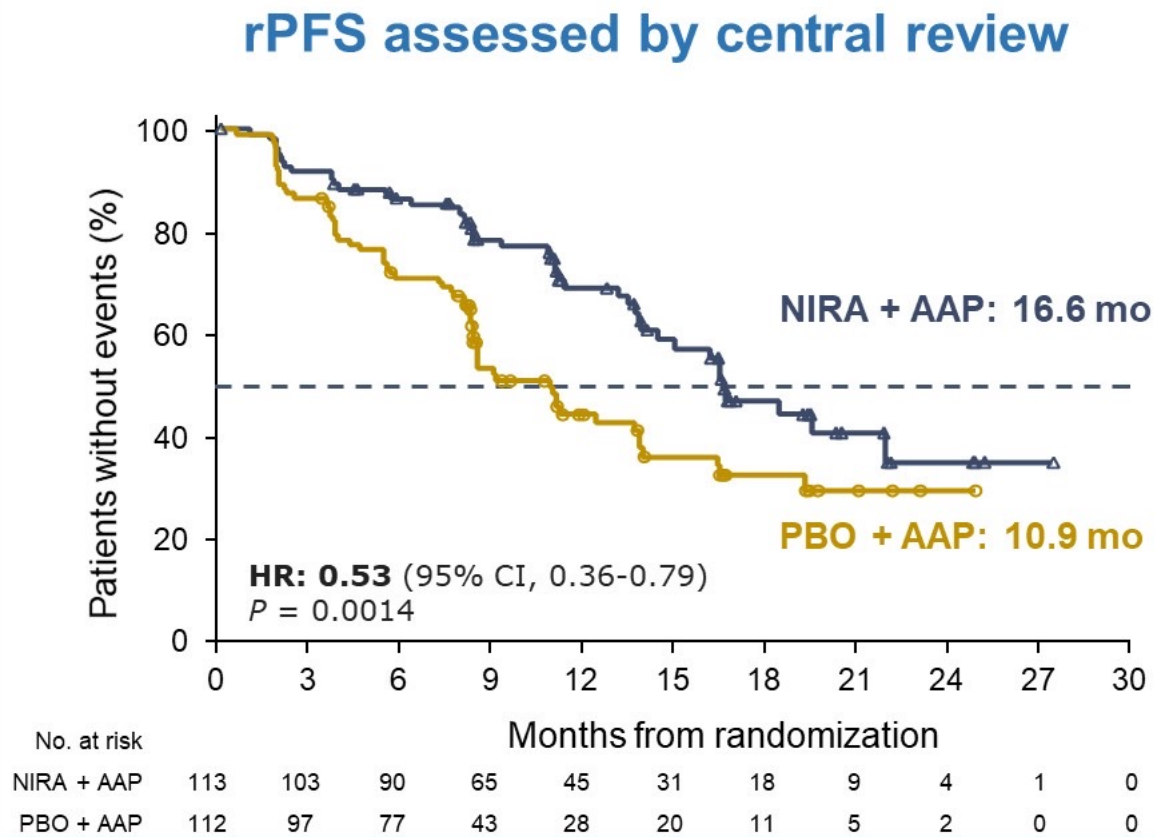


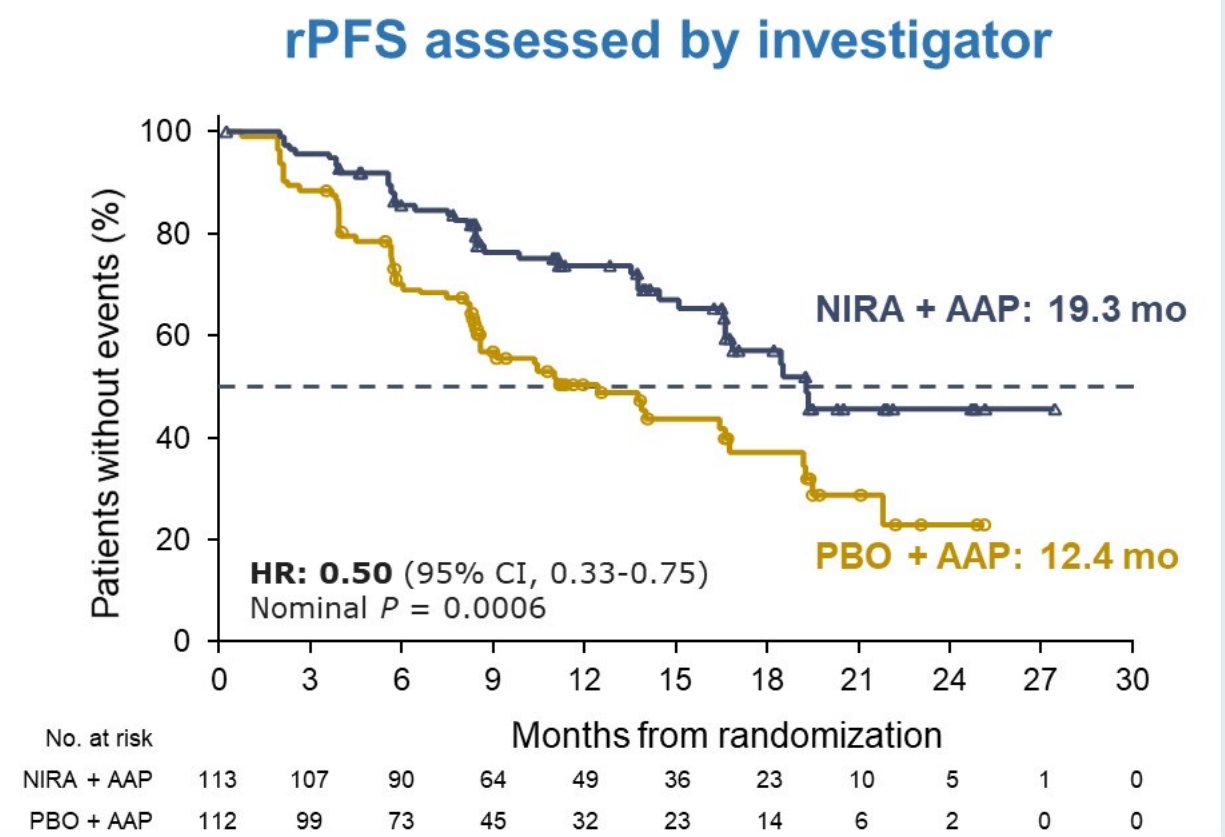
HRR = homologous recombination repair; BM = biomarker; mCRPC = metastatic castration-resistant prostate cancer; mCSPC = metastatic castration-sensitive prostate cancer; nmCRPC = nonmetastatic castration-resistant prostate cancer; AAP = abiraterone acetate and prednisone; rPFS = radiographic progression-free survival; OS = overall survival; PSA = prostate-specific antigen; ORR = objective response rate

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

MAGNITUDE: BRCA1/2 Mutations — Primary Endpoint

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





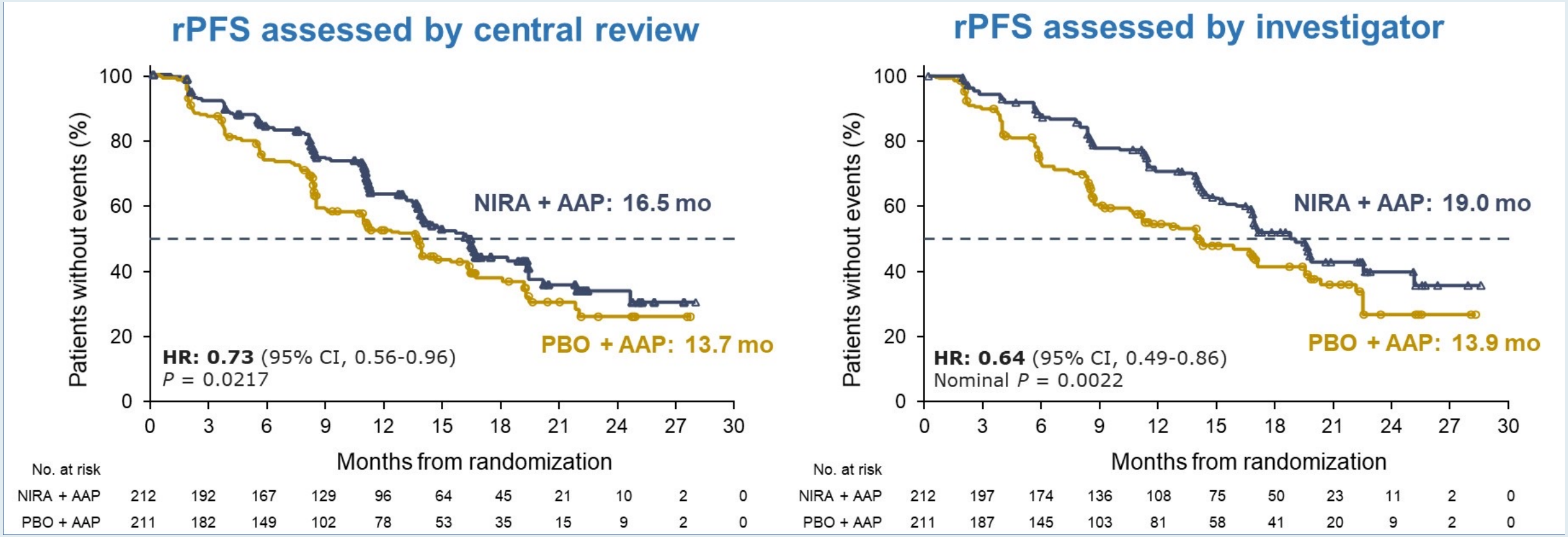
NIRA = niraparib; AAP = abiraterone acetate and prednisone; rPFS = radiographic progression-free survival; PBO = placebo

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

RTP RESEARCH TO PRACTICE

MAGNITUDE: All HRR Biomarker-Positive — Primary Endpoint

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

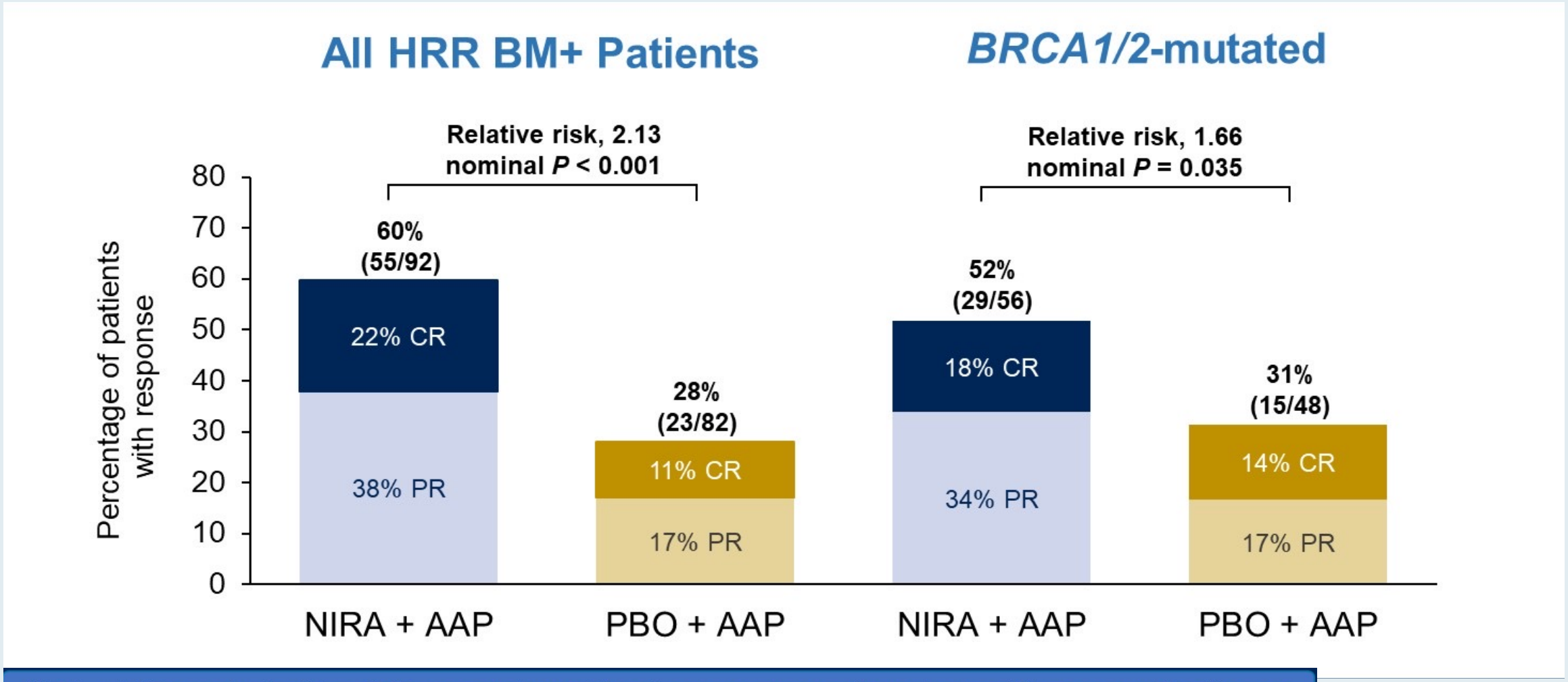


HRR = homologous recombination repair; NIRA = niraparib; AAP = abiraterone acetate and prednisone; rPFS = radiographic progression-free survival; PBO = placebo

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

RTP RESEARCH TO PRACTICE

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



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

NIRA = niraparib; AAP = abiraterone acetate and prednisone; HRR = homologous recombination repair; BM = biomarker; CR = complete response; PR = partial response; PBO = placebo

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

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 (i.e., 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.

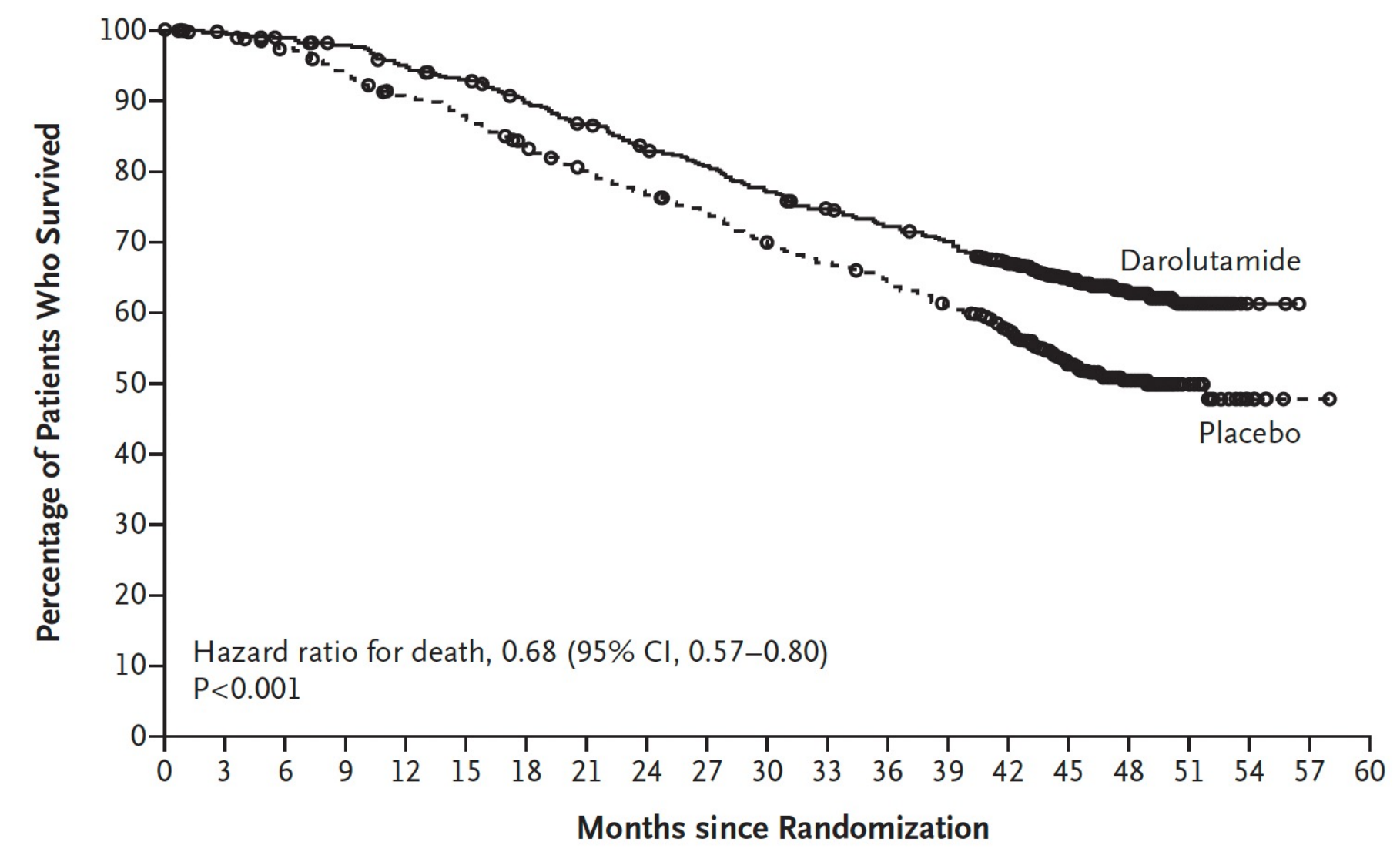
ORIGINAL ARTICLE

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*

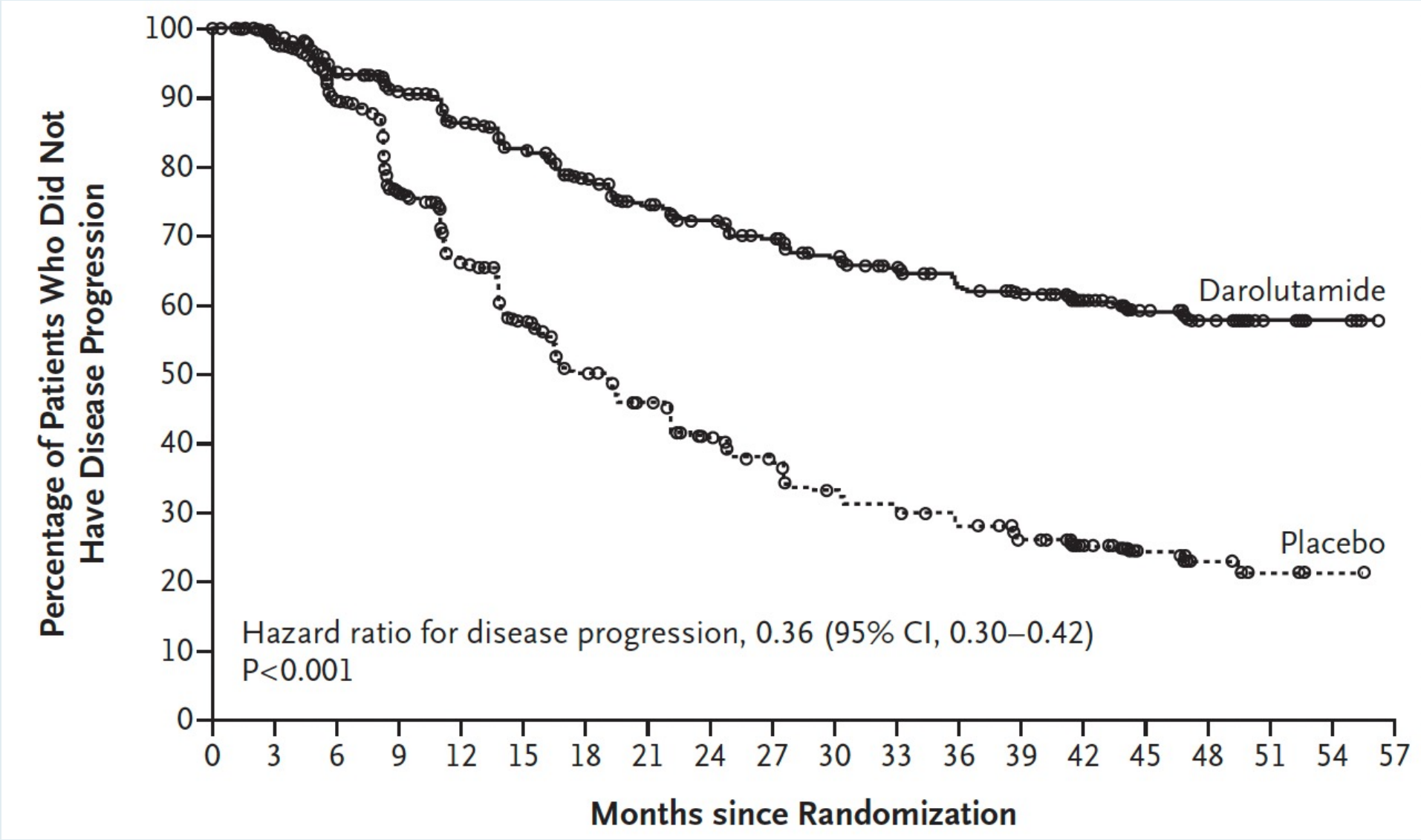
RTP RESEARCH TO PRACTICE

ARASENS: Overall Survival (Primary Endpoint)



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

ARASENS: Progression-Free Survival



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

RTP RESEARCH TO PRACTICE

ARASENS: Adverse Events

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.

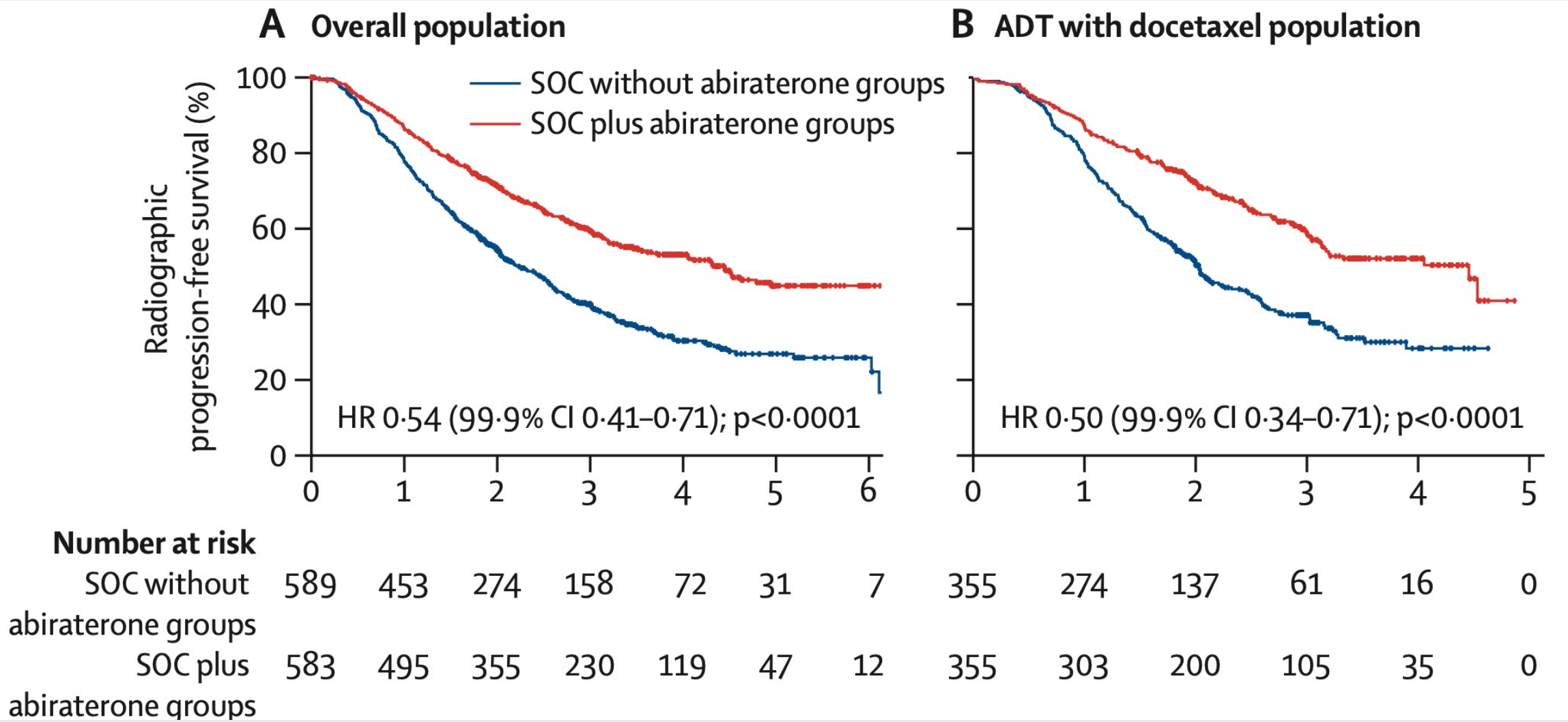
Smith MR et al. Genitourinary Cancers Symposium 2022;Abstract 13.

Lancet 2022;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: Radiographic Progression-Free Survival (rPFS)



ADT = androgen deprivation therapy

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

PEACE-1: Grade 3-5 Adverse Events (Androgen Deprivation Therapy with 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.

Immune Checkpoint Inhibitors for Metastatic Castration-Resistant Prostate Cancer

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

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

RTP RESEARCH TO PRACTICE

Genitourinary Cancers Agenda

Module 1: Prostate Cancer

Module 2: Urothelial Bladder Cancer

- Selection of patients with non-muscle-invasive urothelial bladder cancer for IO (pembrolizumab) therapy; use of adjuvant IO after cystectomy for muscle-invasive disease; intravesicle drug delivery system TAR-200
- Optimal integration of ADC's (enfortumab vedotin, sacituzumab) into the treatment algorithm for patients with metastatic UBC; disitamab vedotin for HER2-overexpressing disease
- Selection of patients to receive erdafitinib; prevention and management of toxicity

Module 3: Renal Cell Carcinoma

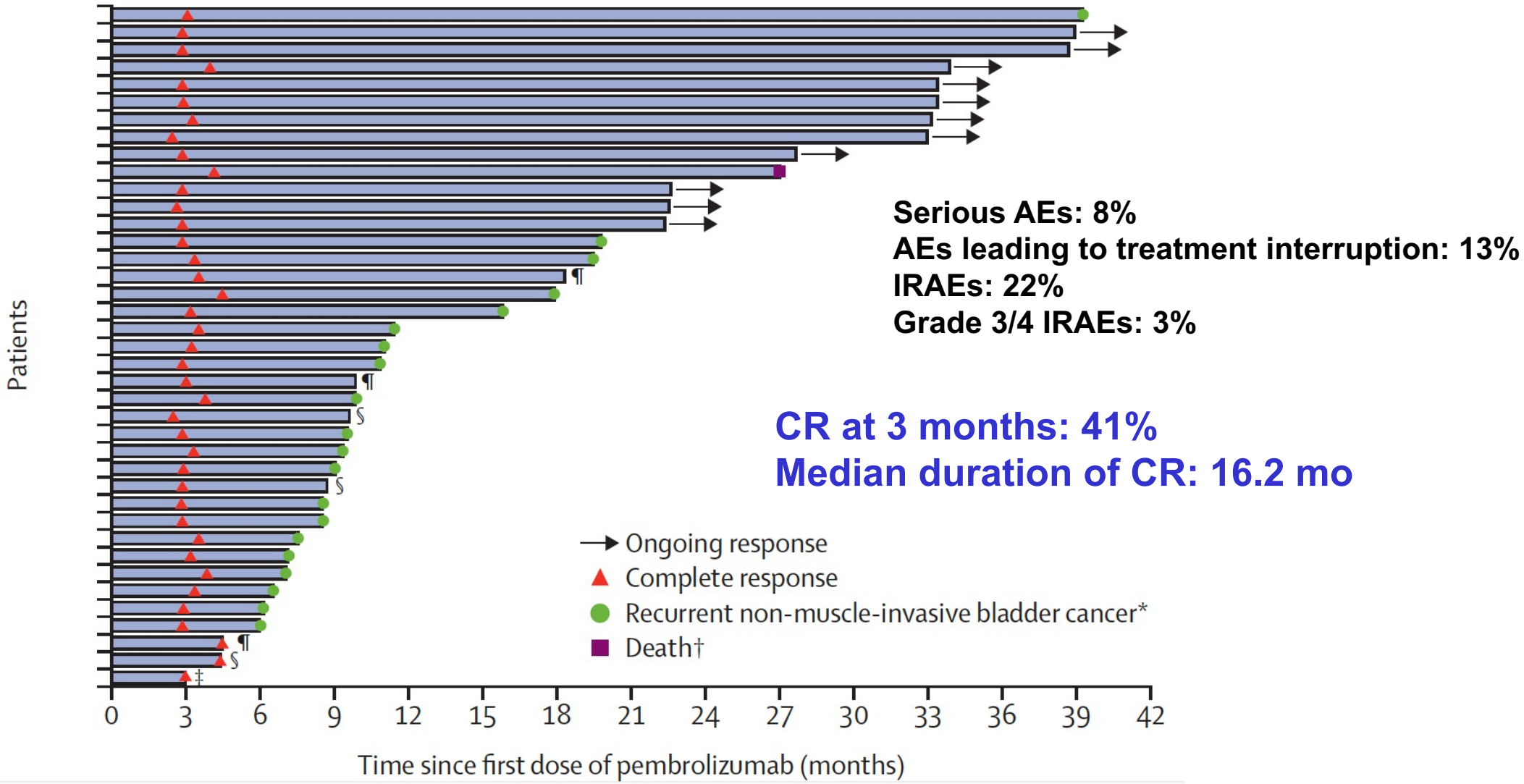
Pembrolizumab monotherapy for the treatment of high-risk non-muscle-invasive bladder cancer unresponsive to BCG (KEYNOTE-057): an open-label, single-arm, multicentre, phase 2 study

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;22(7):919-30.**

RTP RESEARCH TO PRACTICE

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



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

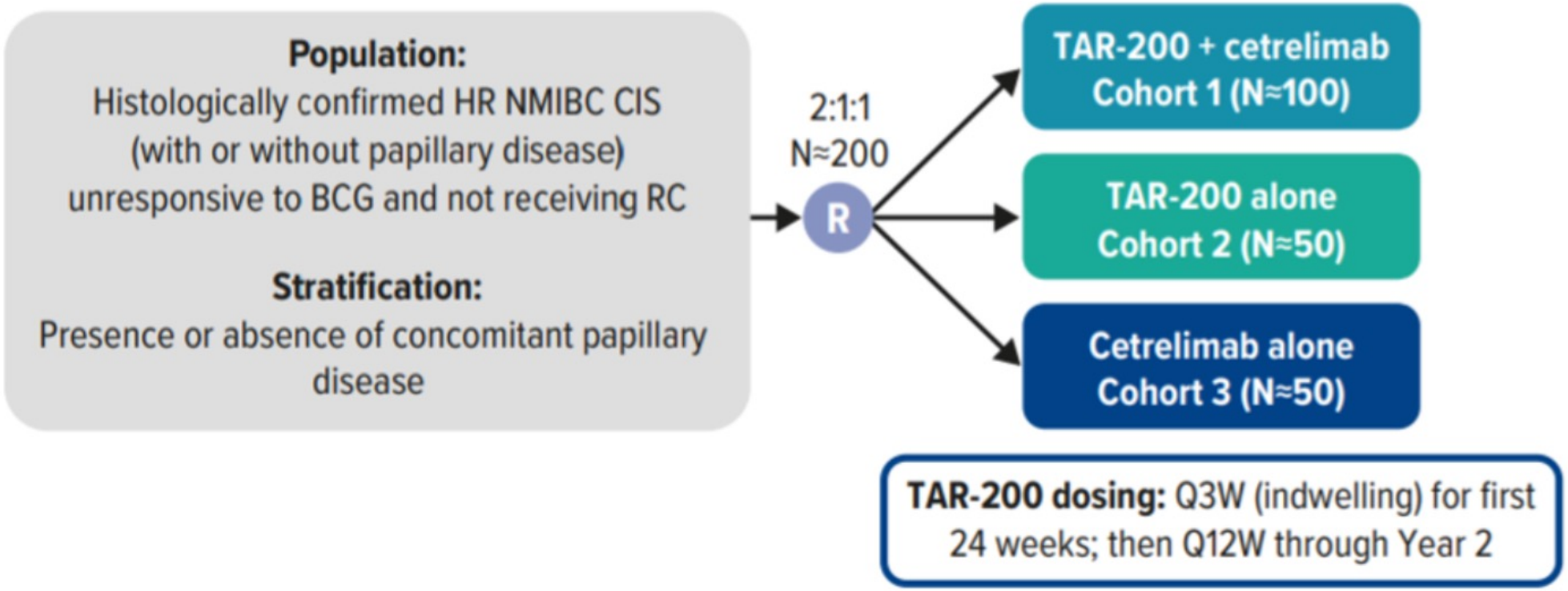
CR at 3 months: 41%
Median duration of CR: 16.2 mo

AEs = adverse events; IRAEs = immune-related AEs; CR = complete response

Balar AV et al. *Lancet Oncol* 2021;22(7):919-30.

SunRISe-1: Ongoing Phase IIb Trial of TAR-200 Alone, Cetrelimab Alone, or the Combination for BCG-Unresponsive, High-Risk Non-Muscle-Invasive Bladder Cancer

Clinical Trial Identifier: NCT04640623



Primary Endpoint: Overall clinical response rate

HR NMIBC CIS = high-risk non-muscle-invasive bladder cancer with carcinoma in situ; BCG = bacillus Calmette-Guérin; RC = radical cystectomy

Van der Heijden SB et al. ESMO 2021;Abstract 719TiP.

RTP RESEARCH TO PRACTICE

ELSEVIER

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

UROLOGIC ONCOLOGY

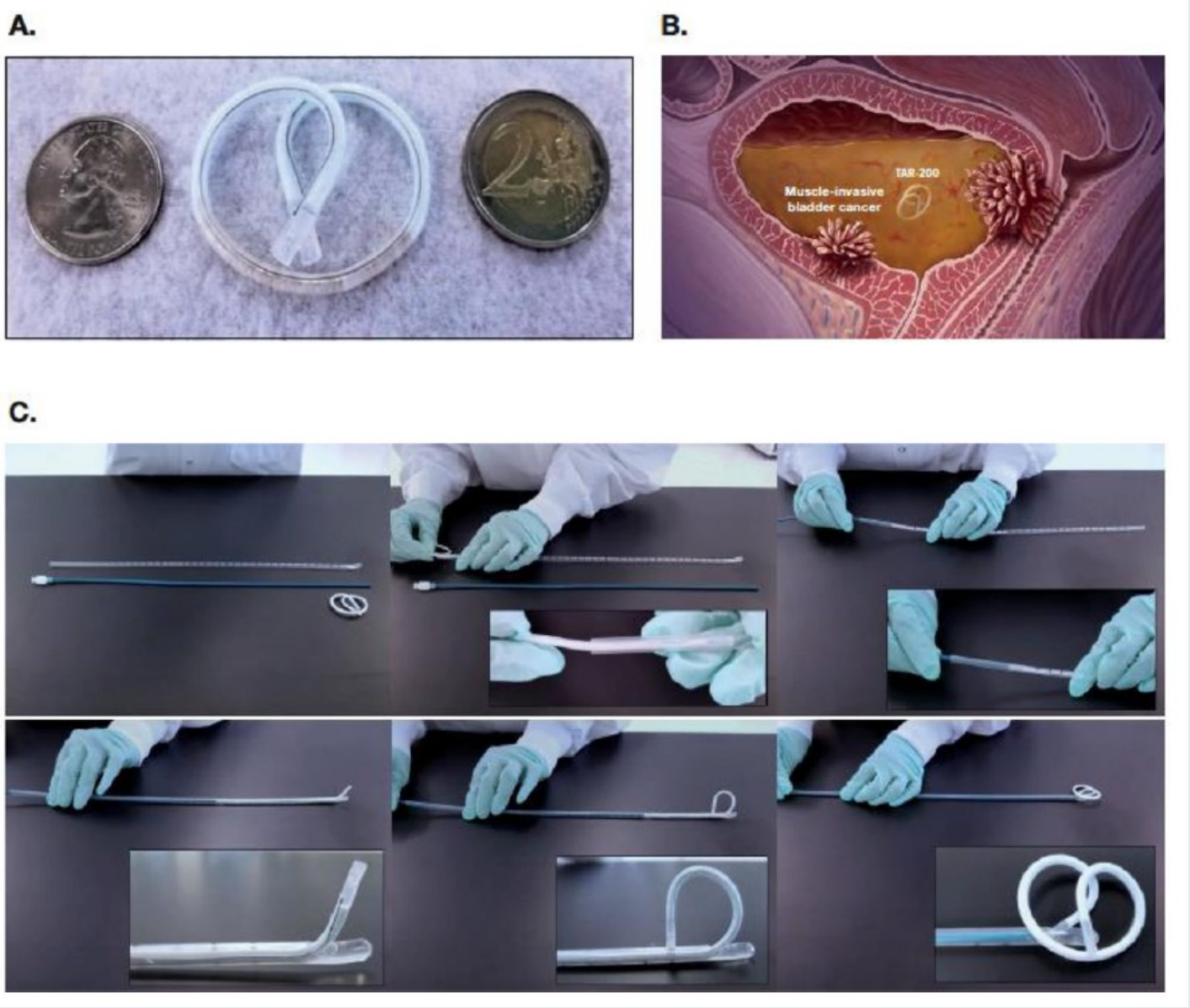
Clinical-Bladder cancer

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;[Online ahead of print].**

Components of TAR-200



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

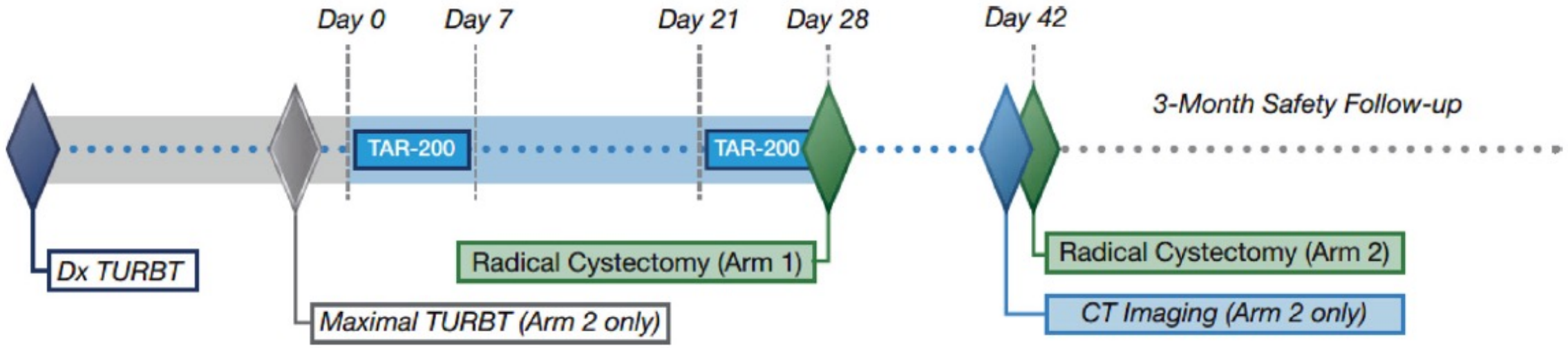
TAR-200

- 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;[Online ahead of print].

RTP RESEARCH TO PRACTICE

TAR-200-101: Study Design and Outcomes

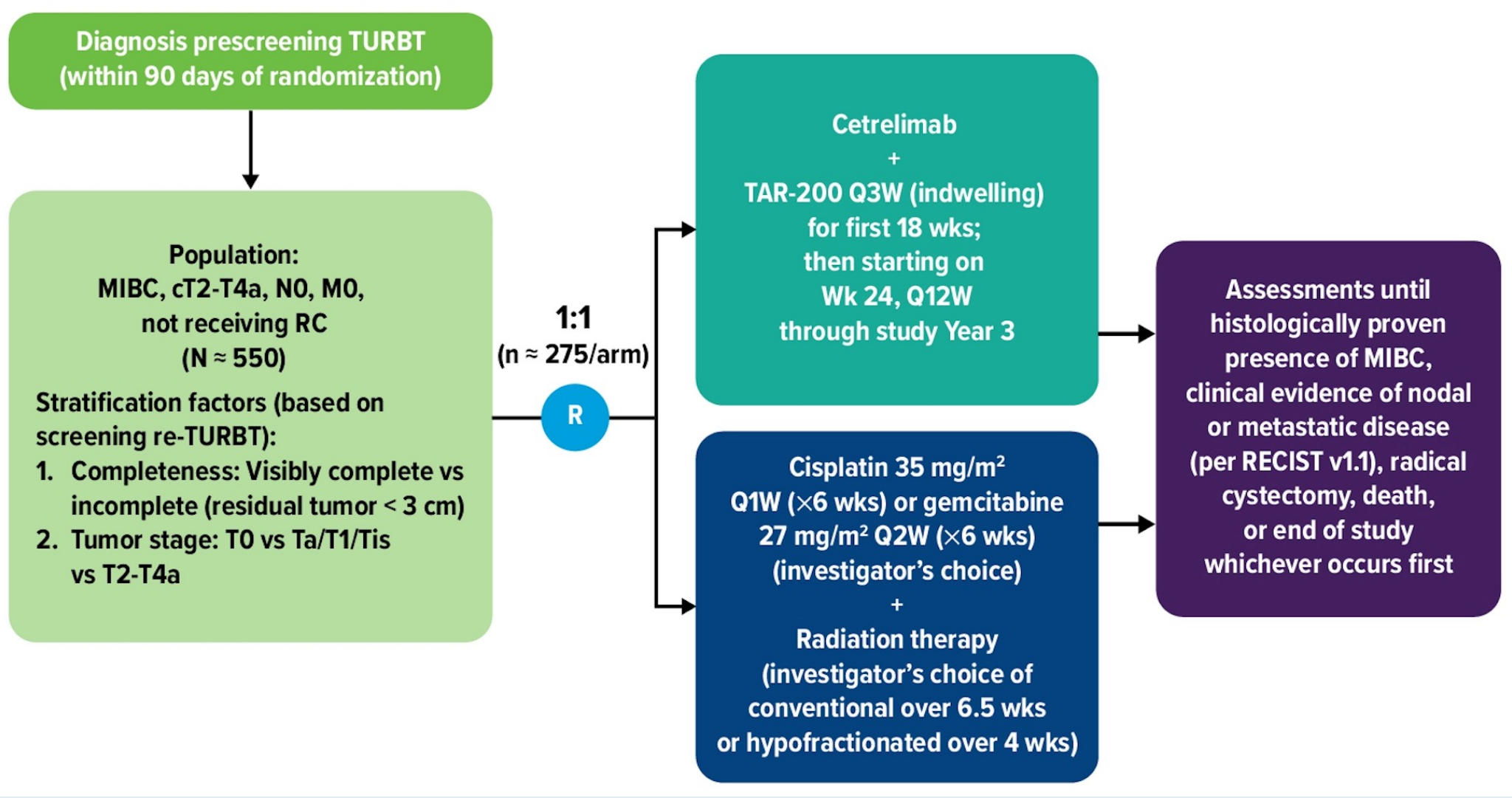


Response	Arm 1 (>3 cm)	Arm 2 (max TURBT)
Underwent pathology at RC, *n/N* (%)	10/11 (90.9)	10/12 (83.3)
Pathologic response, *n/N* (%)	4/10 (40.0)	6/10 (60.0)
Complete response, *n/N* (%)	1/10 (10.0)	3/10 (30.0)
Partial response, *n/N* (%)	3/10 (30.0)	3/10 (30.0)

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

Daneshmand S et al. *Urol Oncol* 2022;[Online ahead of print].

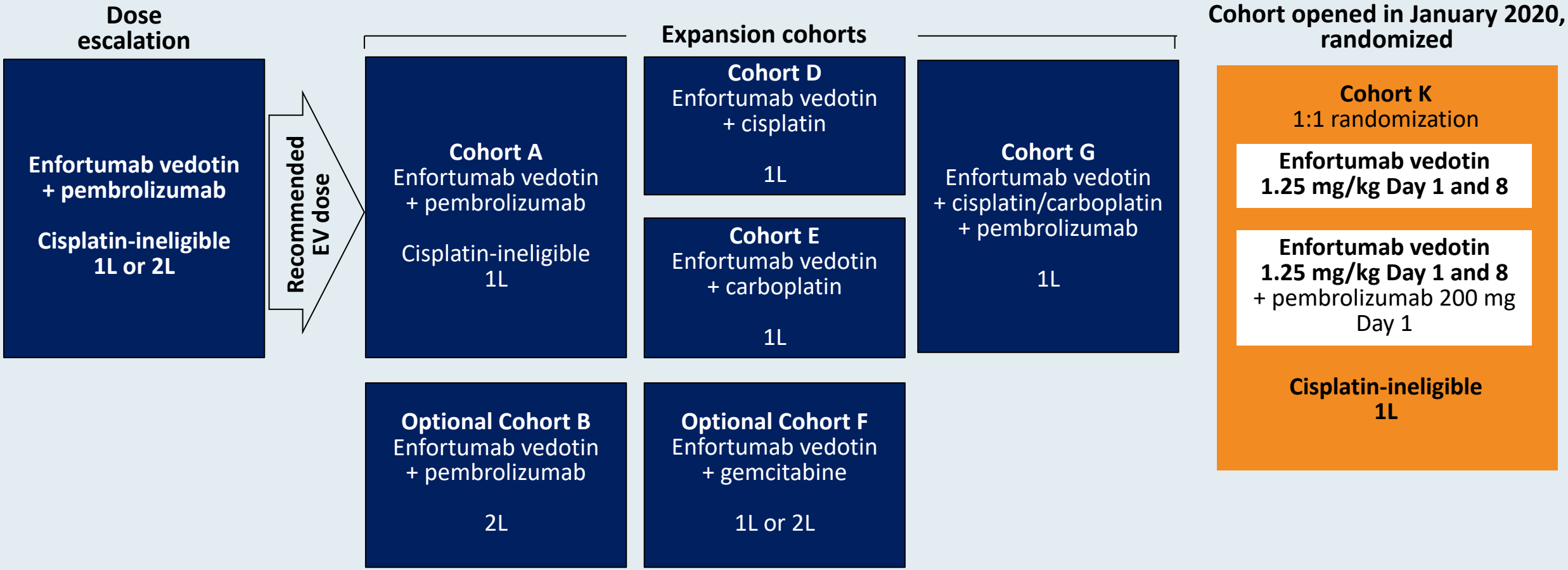
SunRISe-2: TAR-200 in Combination with Cetrelimab versus Concurrent Chemoradiation Therapy for MIBC



MIBC = muscle-invasive bladder cancer; RC = radical cystectomy

Williams SB et al. ASCO 2021;Abstract TPS4586.

EV-103: Study Design and Cohorts



Rosenberg JE et al. ASCO 2020;Abstract 5044.

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/

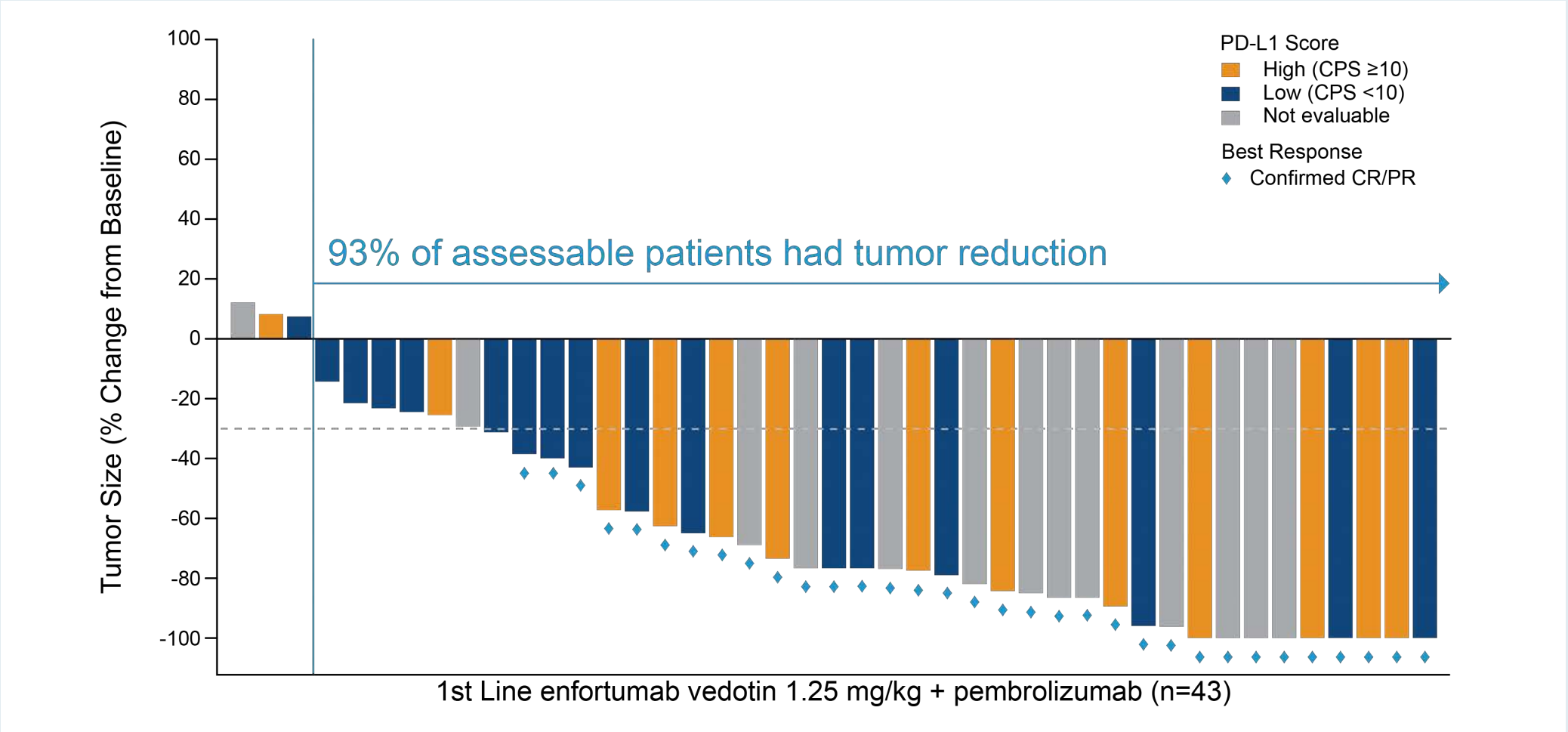
RTP RESEARCH TO PRACTICE

Study EV-103: Update on Durability Results and Long Term Outcome of Enfortumab Vedotin + Pembrolizumab in First Line Locally Advanced or Metastatic Urothelial Carcinoma (la/mUC)

Friedlander TW et al.

ASCO 2021;Abstract 4528.

EV-103 Cohort A: Enfortumab Vedotin with Pembrolizumab as First-Line Therapy for Locally Advanced or Metastatic Urothelial Carcinoma



Friedlander TW et al. ASCO 2021;Abstract 4528.

RTP RESEARCH TO PRACTICE

2022 ASCO® ANNUAL MEETING

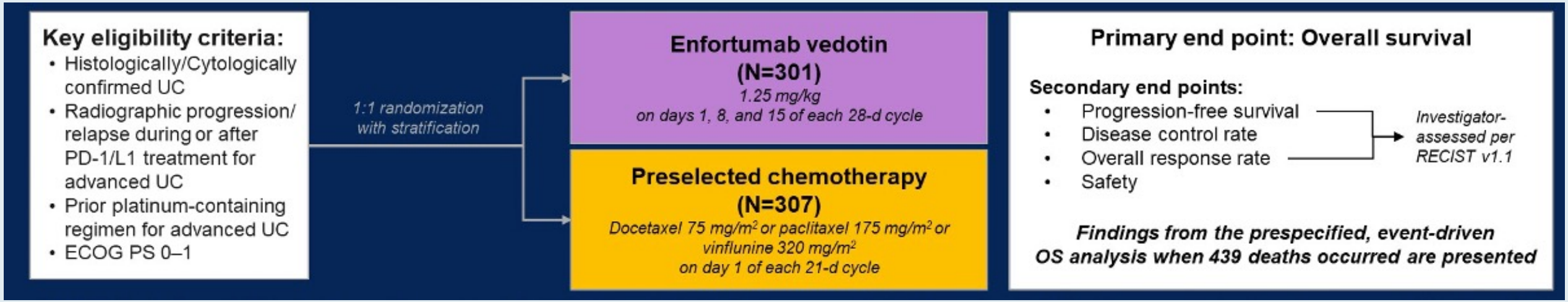
Abstract 4516

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

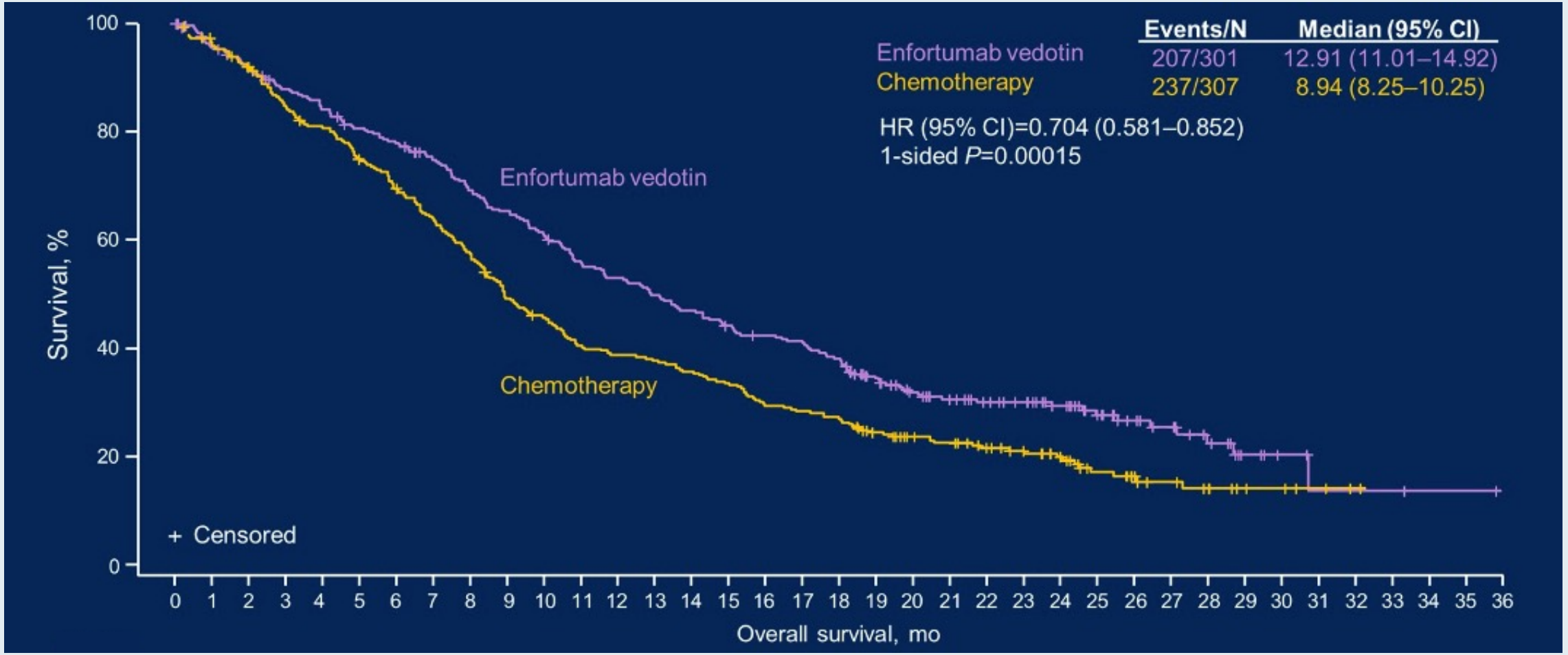
EV-301 Study Design



UC = urothelial cancer; OS = overall survival

Rosenberg JE et al. ASCO 2022;Abstract 4516.

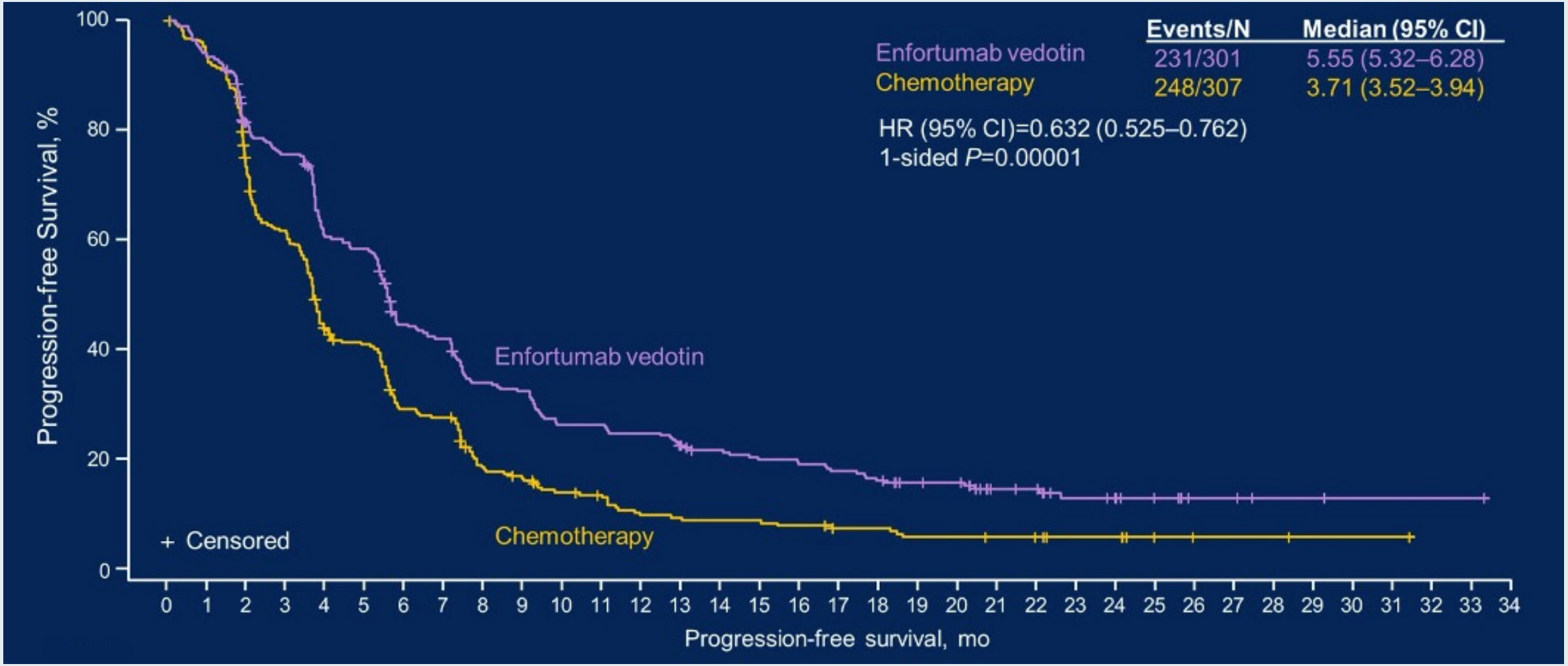
EV-301: Overall Survival



Rosenberg JE et al. ASCO 2022;Abstract 4516.

RTP RESEARCH TO PRACTICE

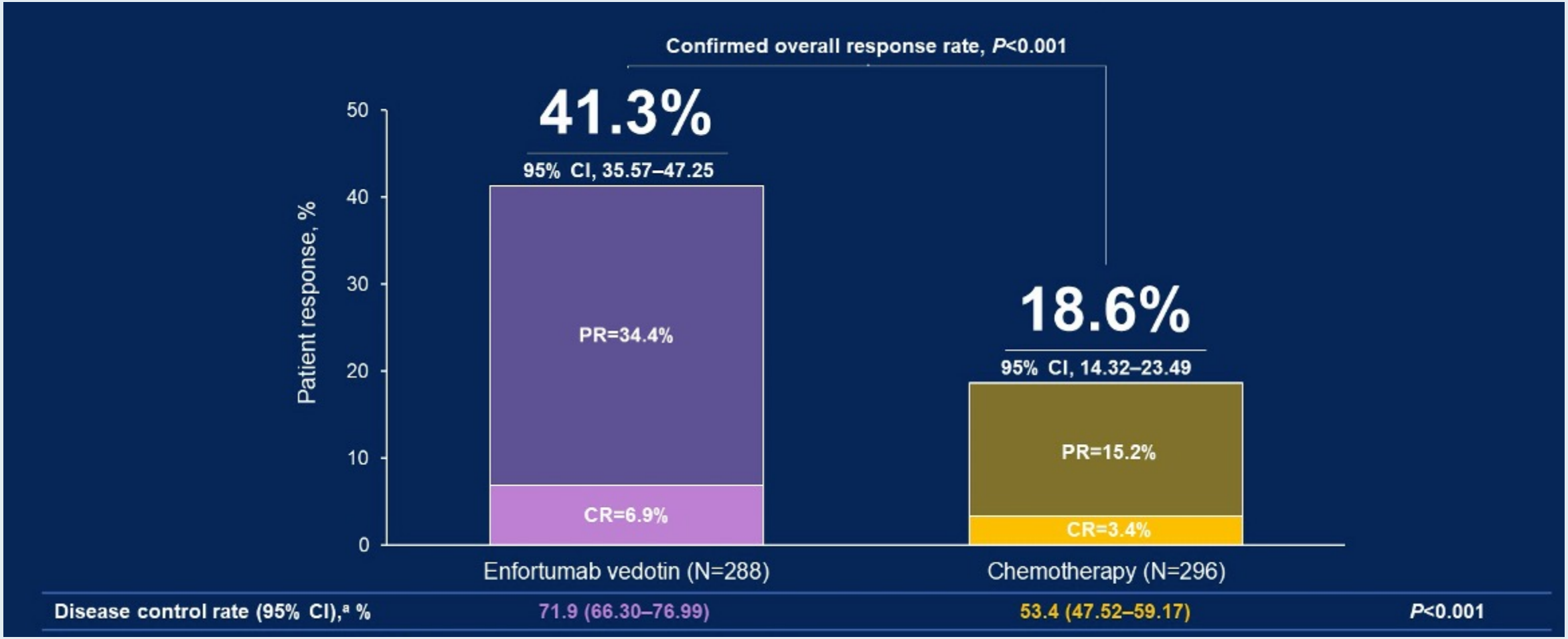
EV-301: Progression-Free Survival



Rosenberg JE et al. ASCO 2022;Abstract 4516.

RTP RESEARCH TO PRACTICE

EV-301: Investigator-Assessed Clinical Response



Rosenberg JE et al. ASCO 2022;Abstract 4516.

EV-301: Adverse Events of Special Interest (Safety Population)

Treatment-related adverse event, n (%)	Enfortumab vedotin (N=296)						Chemotherapy (N=291)					
	Any	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Rash	133 (44.9)	41 (13.9)	48 (16.2)	43 (14.5)	1 (0.3)	NR	28 (9.6)	21 (7.2)	6 (2.1)	1 (0.3)	0	NR
Severe cutaneous adverse reaction	60 (20.3)	20 (6.8)	25 (8.4)	14 (4.7)	1 (0.3)	NR	22 (7.6)	12 (4.1)	8 (2.7)	2 (0.7)	0	NR
Peripheral neuropathy	142 (48.0)	36 (12.2)	84 (28.4)	22 (7.4)	NR	NR	92 (31.6)	43 (14.8)	41 (14.1)	8 (2.7)	NR	NR
Peripheral neuropathy sensory events	135 (45.6)	35 (11.8)	82 (27.7)	18 (6.1)	NR	NR	89 (30.6)	42 (14.4)	39 (13.4)	8 (2.7)	NR	NR
Peripheral neuropathy motor events	23 (7.8)	6 (2.0)	11 (3.7)	6 (2.0)	NR	NR	7 (2.4)	5 (1.7)	2 (0.7)	0	NR	NR
Dry eye	48 (16.2)	34 (11.5)	12 (4.1)	2 (0.7)	NR	NR	9 (3.1)	6 (2.1)	2 (0.7)	1 (0.3)	NR	NR
Blurred vision	13 (4.4)	11 (3.7)	2 (0.7)	0	NR	NR	6 (2.1)	5 (1.7)	0	1 (0.3)	NR	NR
Corneal disorders	2 (0.7)	2 (0.7)	NR	NR	NR	NR	0	0	NR	NR	NR	NR
Infusion-related reaction	27 (9.1)	12 (4.1)	11 (3.7)	4 (1.4)	NR	NR	14 (4.8)	7 (2.4)	7(2.4)	0	NR	NR
Systemic infusion-related reaction event	24 (8.1)	11 (3.7)	9 (3.0)	4 (1.4)	NR	NR	9 (3.1)	4 (1.4)	5 (1.7)	0	NR	NR
Local infusion-related reaction event	4 (1.4)	2 (0.7)	2 (0.7)	0	NR	NR	7 (2.4)	5 (1.7)	2 (0.7)	0	NR	NR
Infusion-site reaction	2 (0.7)	0	2 (0.7)	0	NR	NR	5 (1.7)	4 (1.4)	1 (0.3)	0	NR	NR
Extravasation-site reaction	4 (1.4)	2 (0.7)	2 (0.7)	0	NR	NR	4 (1.4)	2 (0.7)	2 (0.7)	0	NR	NR
Hyperglycemia	20 (6.8)	3 (1.0)	4 (1.4)	12 (4.1)	0	1 (0.3)	1 (0.3)	0	1 (0.3)	0	0	0

Rosenberg JE et al. ASCO 2022;Abstract 4516.

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

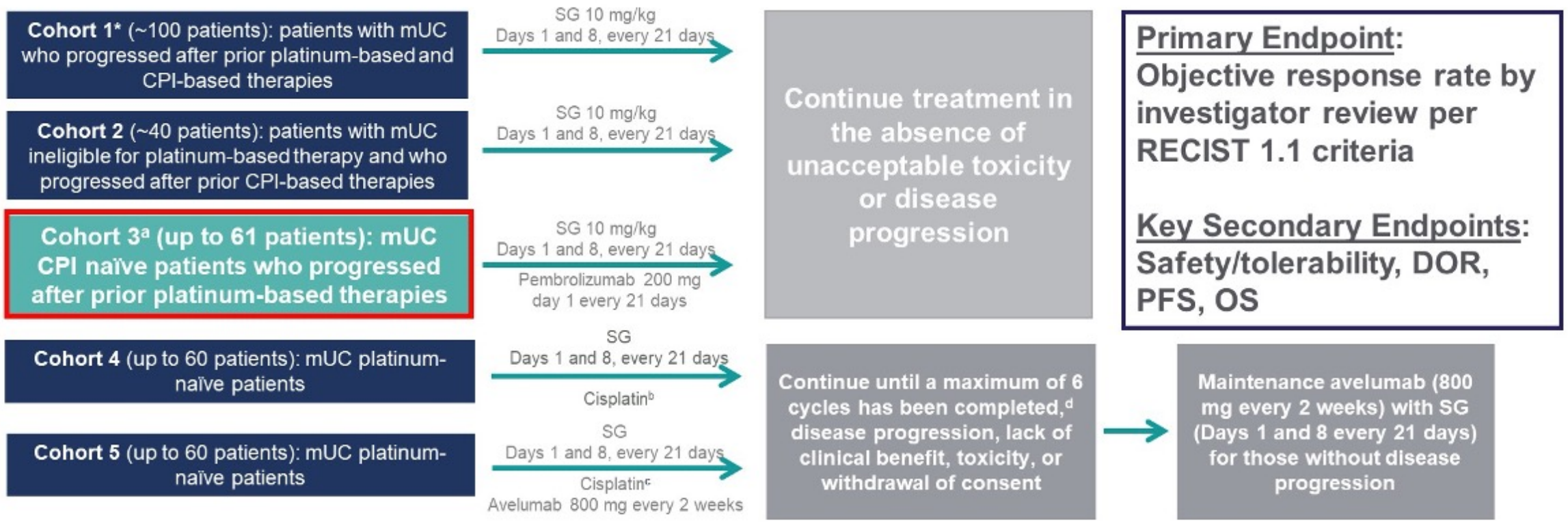
Abstract # 434
ClinicalTrials.gov Number: NCT03547973.

@PGrivasMDPhD

TROPHY U-01

RTP RESEARCH TO PRACTICE

TROPHY U-01 Multicohort-Phase Trial in Metastatic Urothelial Carcinoma (mUC)



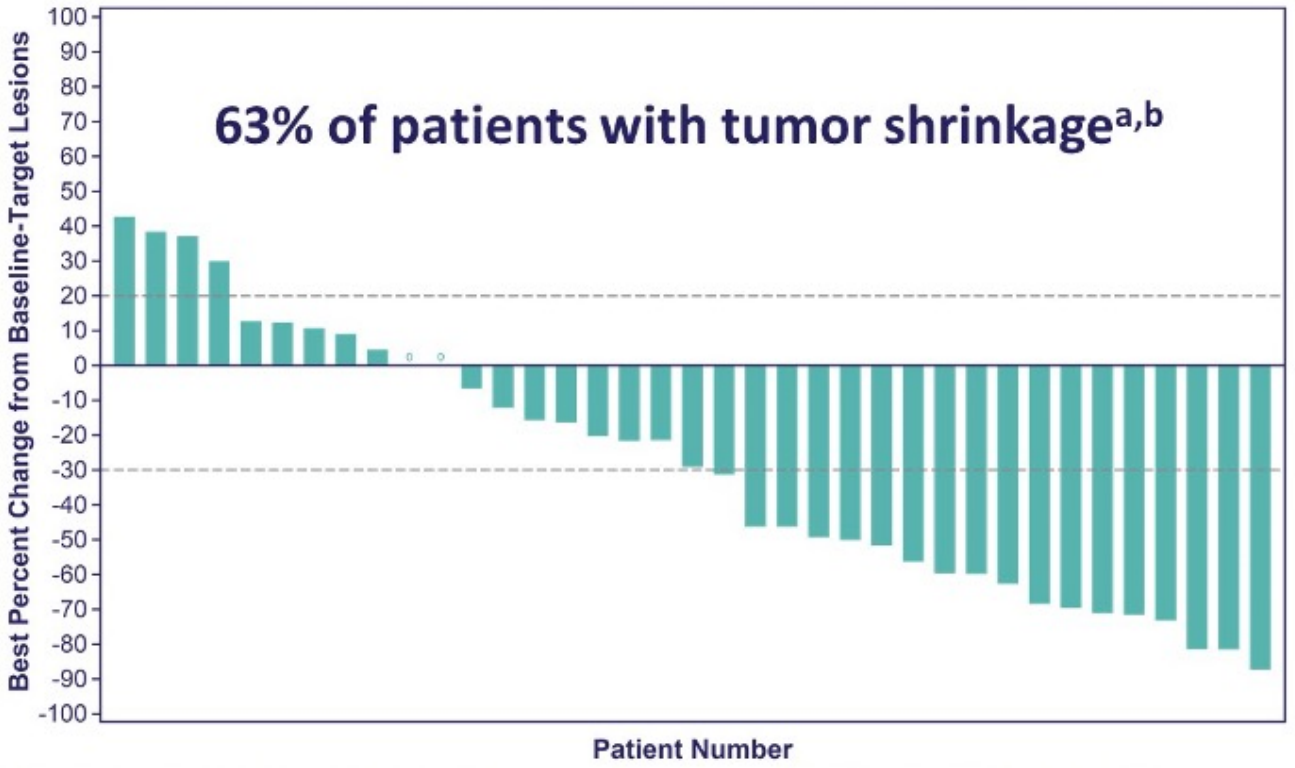
Key Inclusion Criteria: Age ≥18 years, ECOG of 0/1, creatinine clearance (CrCl) ≥30 mL/min,[b,c] adequate hepatic function
Key Exclusion Criteria: Immunodeficiency, active Hepatitis B or C, active secondary malignancy, or active brain metastases

*Accelerated FDA approval for treatment of patients with locally advanced or mUC who previously received platinum-containing chemotherapy and PD-1/L1 inhibitor[1]

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

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

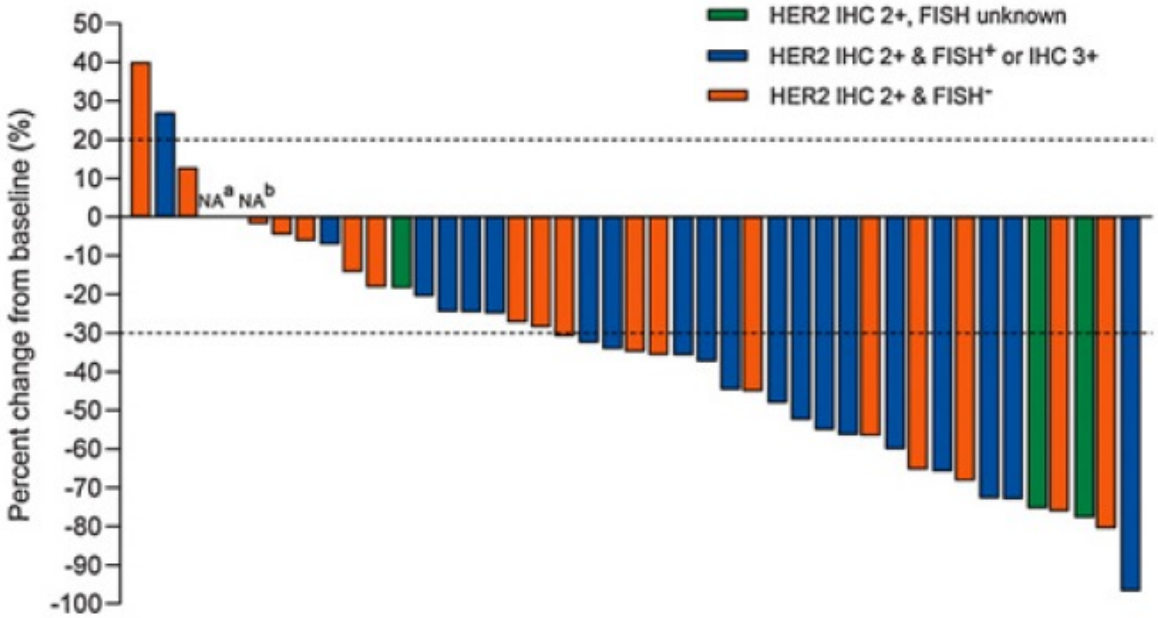
CLINICAL CANCER RESEARCH | CLINICAL TRIALS: TARGETED THERAPY

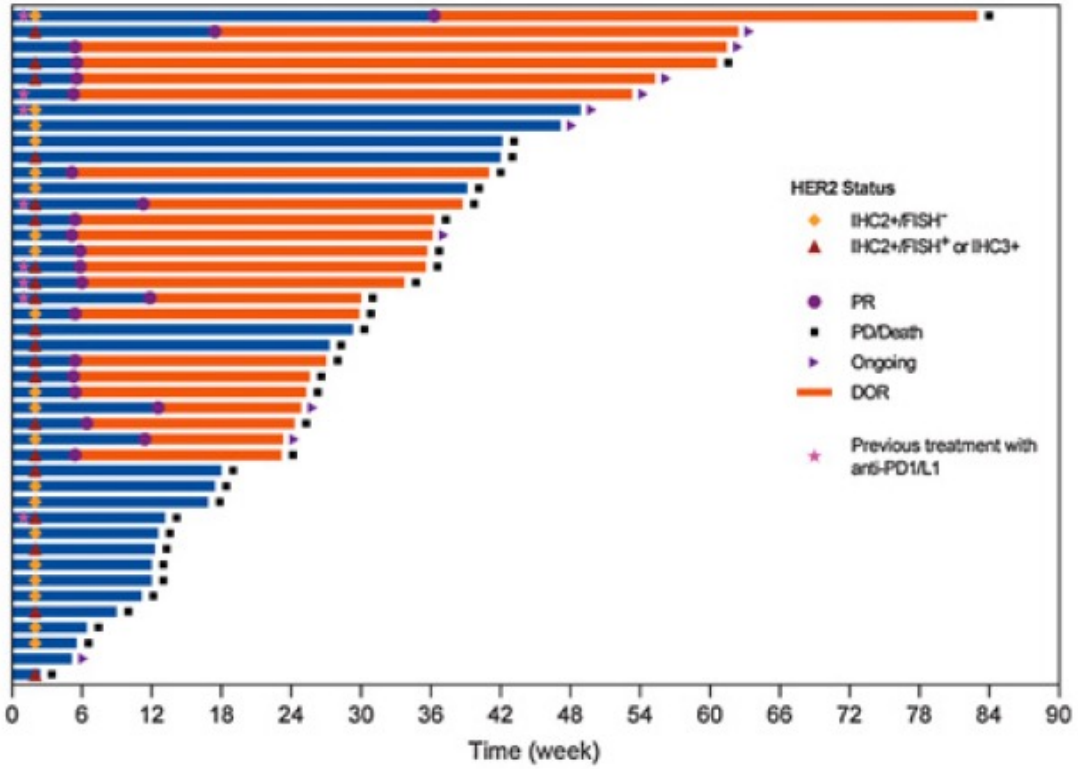
Open-label, Multicenter, Phase II Study of RC48-ADC, a HER2-Targeting Antibody–Drug Conjugate, in Patients with Locally Advanced or Metastatic Urothelial Carcinoma AC

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



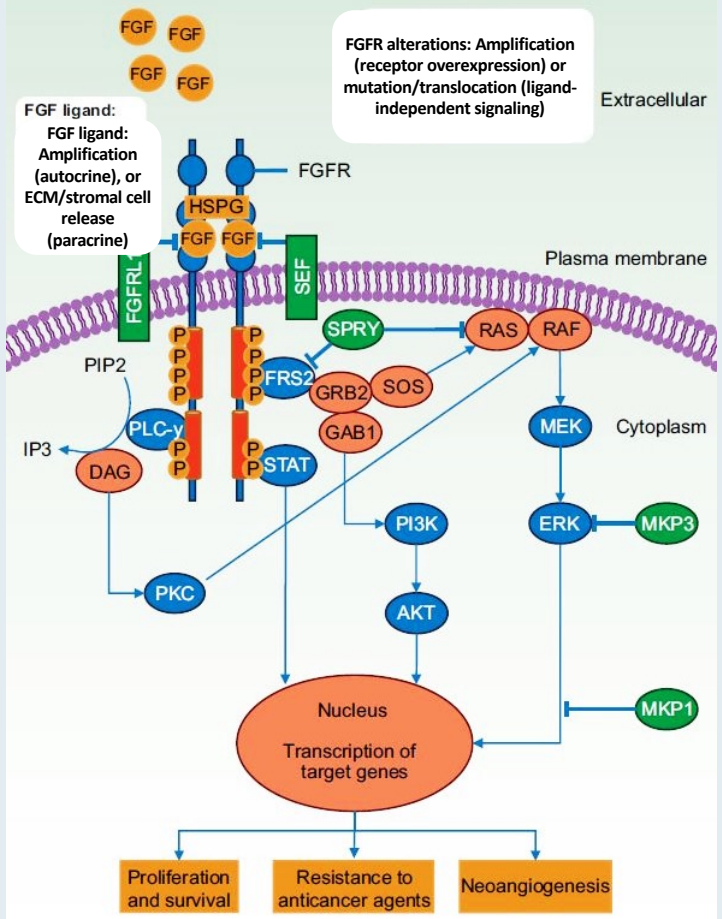


Sheng X et al. *Clin Cancer Res* 2021;27(1):43-51.

RTP RESEARCH TO PRACTICE

Rationale for Targeting FGFR in Urothelial Carcinoma (UC)[1,2]

FGFR Signaling Pathway[3]



- *FGFR* is altered in 15%-20% of advanced UC[4]
  - Mutated *FGFR3* is present in 37% of upper-tract UC[5]

Cancer Type	Frequency of FGFR Alterations[1]
Metastatic UC	15%-20%
NMIBC	40%-70%
Cholangiocarcinoma	14%-22%
NSCLC	4%
HCC (FGF19 amp by FISH)	21%
Glioblastoma	23%
Breast cancer	3%-5%
Ovarian cancer	7%
Head and neck cancer	9%-17%

NMIBC = non-muscle-invasive bladder cancer; NSCLC = non-small cell lung cancer; HCC = hepatocellular carcinoma

1. The Cancer Genome Atlas (TCGA) genomic alteration database: https://tcga-data.nci.nih.gov/docs/publications/tcga/. Accessed February 6, 2020.
2. Genomics Evidence Neoplasia Information Exchange (GENIE) genomic alteration database: https://www.aacr.org/Research/Research/pages/aacr-project-genie.aspx. Accessed February 6, 2020. 3. Touat M et al. *Clin Cancer Res* 2015;21(12):2684-94. 4. Rodriguez-Vida A et al. *J Hematol Oncol* 2015;8:119. 5. Li Q et al. *Curr Urol Rep* 2016;17(2):12.

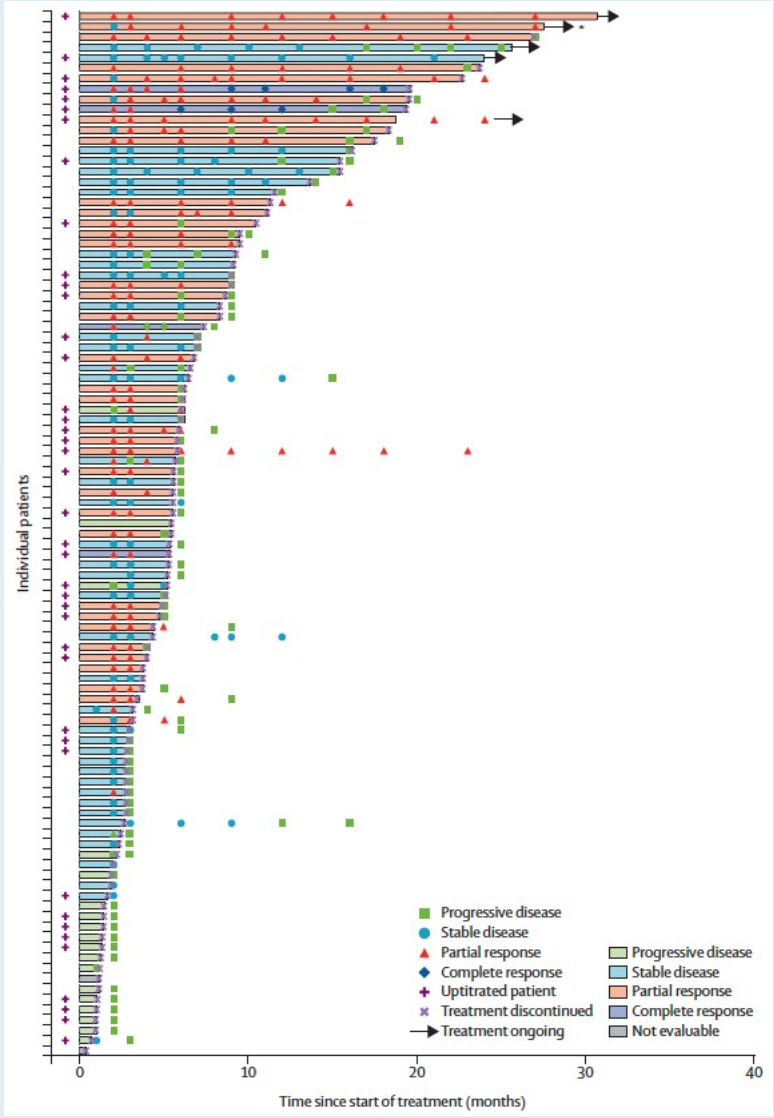
Content Courtesy of Arjun Balar, MD

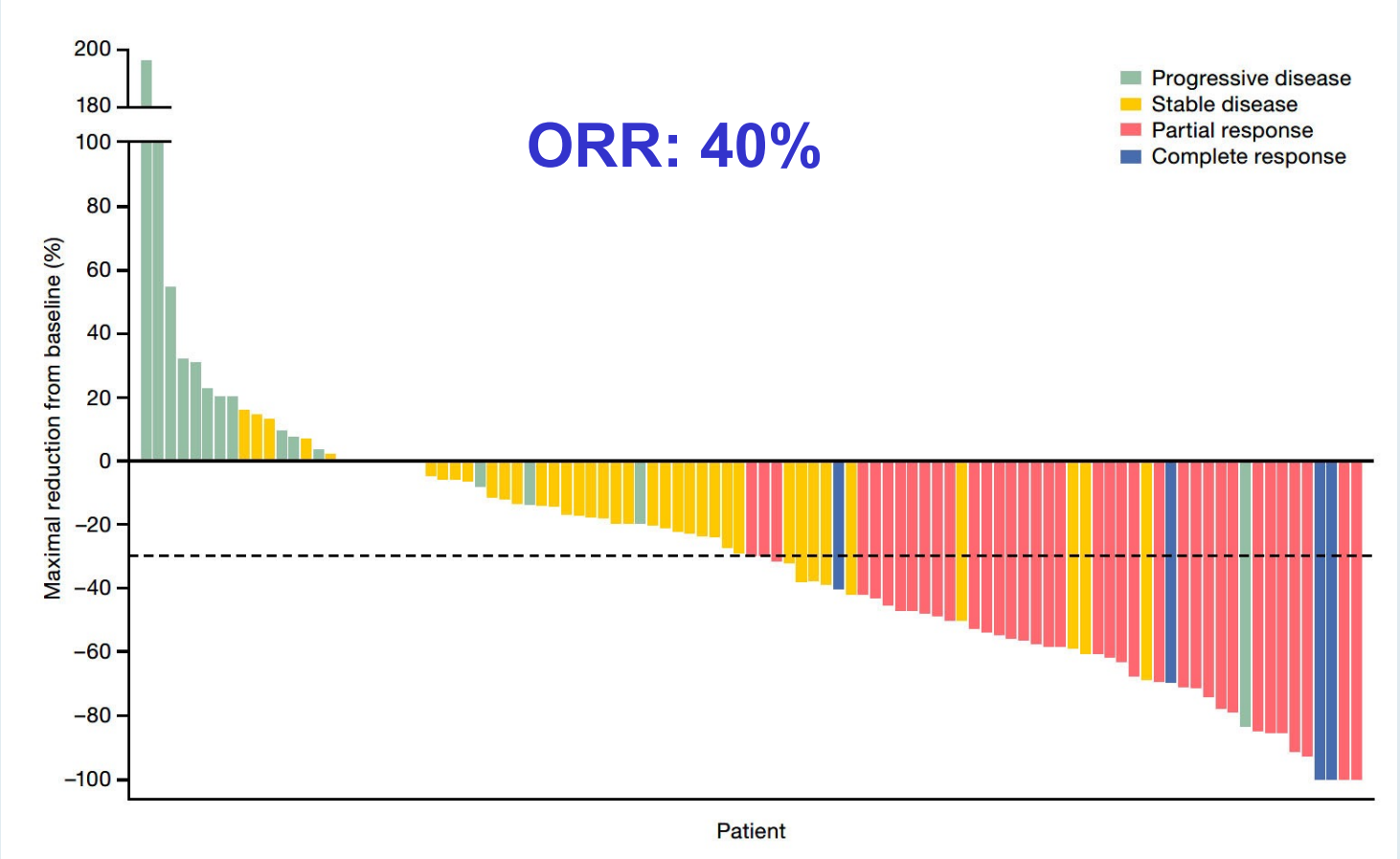
Lancet Oncol 2022;23(2):248-58.

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

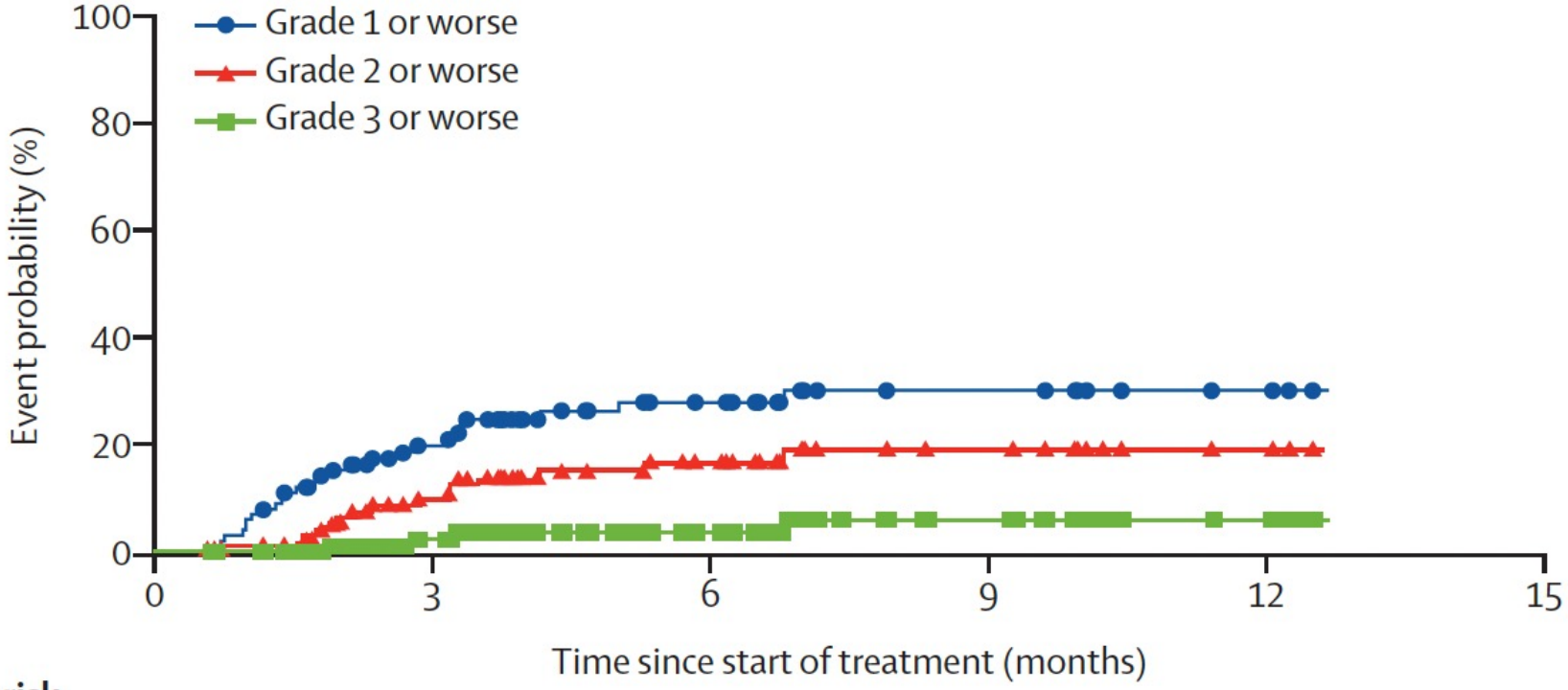




Siefker-Radtke A et al. *Lancet Oncol* 2022;23(2):248-58.

RTP RESEARCH TO PRACTICE

BLC2001: Post Hoc Analysis of the Cumulative Incidence of First-Onset Central Serous Retinopathy Events by Grade



Number at risk (number censored)						
Grade 1 or worse	101 (0)	67 (15)	41 (35)	26 (49)	19 (56)	..
Grade 2 or worse	101 (0)	74 (18)	47 (49)	29 (57)	19 (67)	..
Grade 3 or worse	101 (0)	80 (19)	53 (45)	30 (67)	20 (77)	..

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

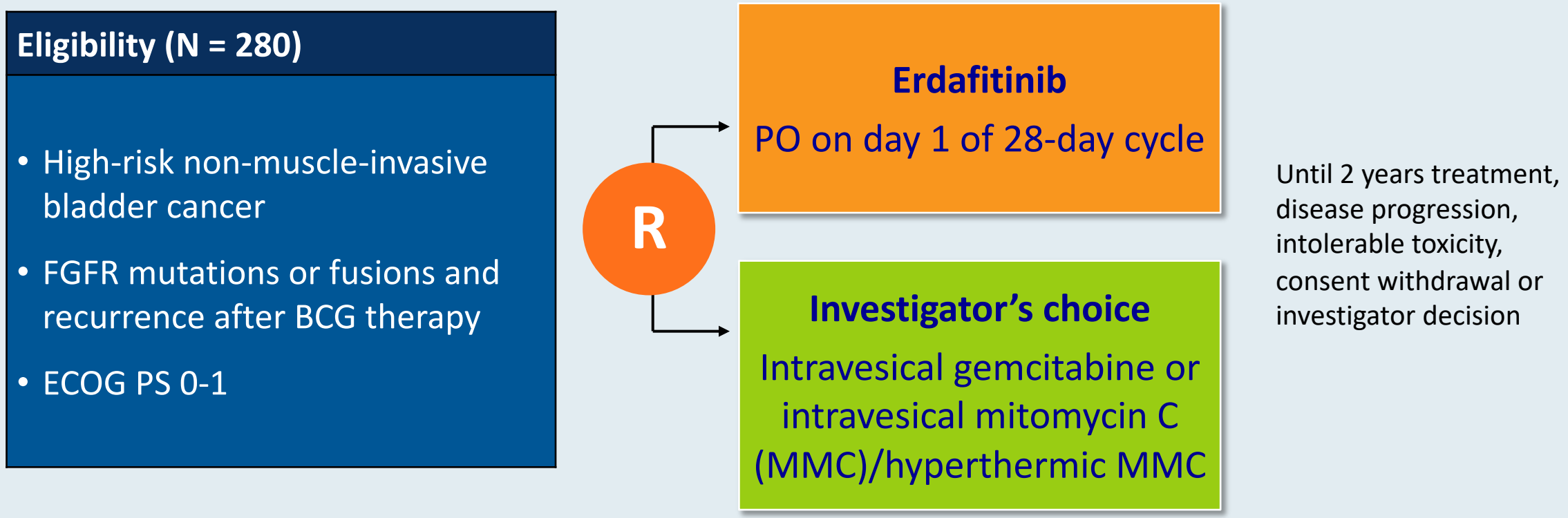
RTP RESEARCH TO PRACTICE

BLC2001: Select Treatment-Emergent Adverse Events

	Grade 1–2	Grade 3	Grade 4	Grade 5*
All treatment-emergent adverse events	29 (29%)	58 (57%)	6 (6%)	8 (8%)
Hyperphosphataemia†	77 (76%)	2 (2%)	0	0
Stomatitis	46 (21%)	14 (14%)	0	0
Diarrhoea	51 (50%)	4 (4%)	0	0
Dry mouth	45 (45%)	1 (1%)	0	0
Decreased appetite	40 (40%)	1 (1%)	0	0
Dysgeusia	39 (39%)	2 (2%)	0	0
Alopecia	34 (34%)	0	0	0
Dry skin	34 (34%)	0	0	0
Fatigue	31 (31%)	2 (2%)	0	0
Constipation	28 (28%)	1 (1%)	0	0
Dry eye	27 (27%)	1 (1%)	0	0
Palmar-plantar erythrodysaesthesia syndrome	20 (20%)	5 (5%)	0	0

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

Phase II Study of Erdafitinib versus Investigator's Choice of Intravesical Chemotherapy for Patients with Recurrence of High-Risk Non-Muscle-Invasive Bladder Cancer After Bacillus Calmette-Guérin (BCG) Therapy



Primary endpoint: Relapse-free survival (RFS)

Secondary endpoints: Time to progression/disease worsening, disease-specific survival, overall survival, RFS2, safety

www.clinicaltrials.gov. NCT04172675. Accessed May 2022.

ASCO Genitourinary Cancers Symposium

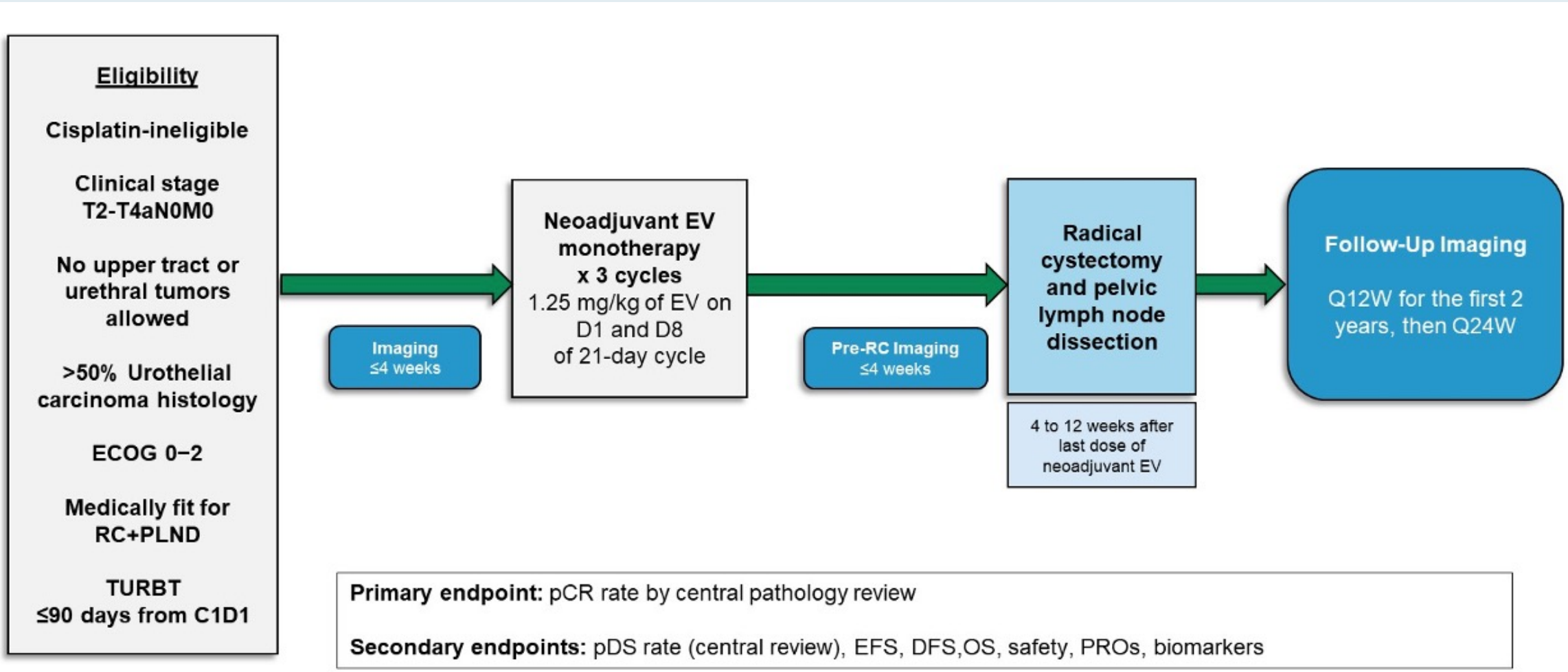
Abstract 435

Study EV-103 Cohort H: Antitumor activity of neoadjuvant treatment with enfortumab vedotin monotherapy in patients with muscle invasive bladder cancer (MIBC) who are cisplatin-ineligible

Daniel P. Petrylak, Yale University, New Haven, CT; Thomas W. Flaig, University of Colorado Comprehensive Cancer Center, Aurora, CO; Nataliya Mar, UC Irvine, Irvine, CA; Theodore S. Gourdin, Hollings Cancer Center, Medical University of South Carolina, Charleston, SC; Sandy Srinivas, Stanford University Medical Center, Palo Alto, CA; Jonathan E. Rosenberg, Memorial Sloan Kettering Cancer Center, New York, NY; Maria Guseva, Astellas Pharma Inc., Northbrook, IL; Yao Yu, Seagen Inc., Bothell, WA; Sujata Narayanan, Seagen Inc., Bothell, WA; Christopher J. Hoimes, Duke University, Duke Cancer Institute, Durham, NC

Dr. Daniel P. Petrylak, Speaker

EV-103 Cohort H Study Schema



EV = enfortumab vedotin; RC = radical cystectomy; PLND = pelvic lymph node dissection; pCR = pathologic complete response; pDS = pathologic downstaging; EFS = event-free survival; DFS = disease-free survival; OS = overall survival; PROs = patient-reported outcomes

Petrylak DP et al. Genitourinary Cancers Symposium 2022;Abstract 435.

EV-103 Cohort H: Pathologic Complete Response

Pathological Response	Central Pathology Results (N=22) n (%) [95% Confidence Interval]
Pathological Complete Response Rate (defined as absence of any viable tumor tissue: ypT0 and N0)	**8 (36.4%)** [17.2–59.3]
Pathological Downstaging Rate (defined as presence of ypT0, ypTis, ypTa, ypT1, and N0)	**11 (50.0%)** [28.2–71.8]

Petrylak DP et al. Genitourinary Cancers Symposium 2022;Abstract 435.

The NEW ENGLAND JOURNAL of MEDICINE

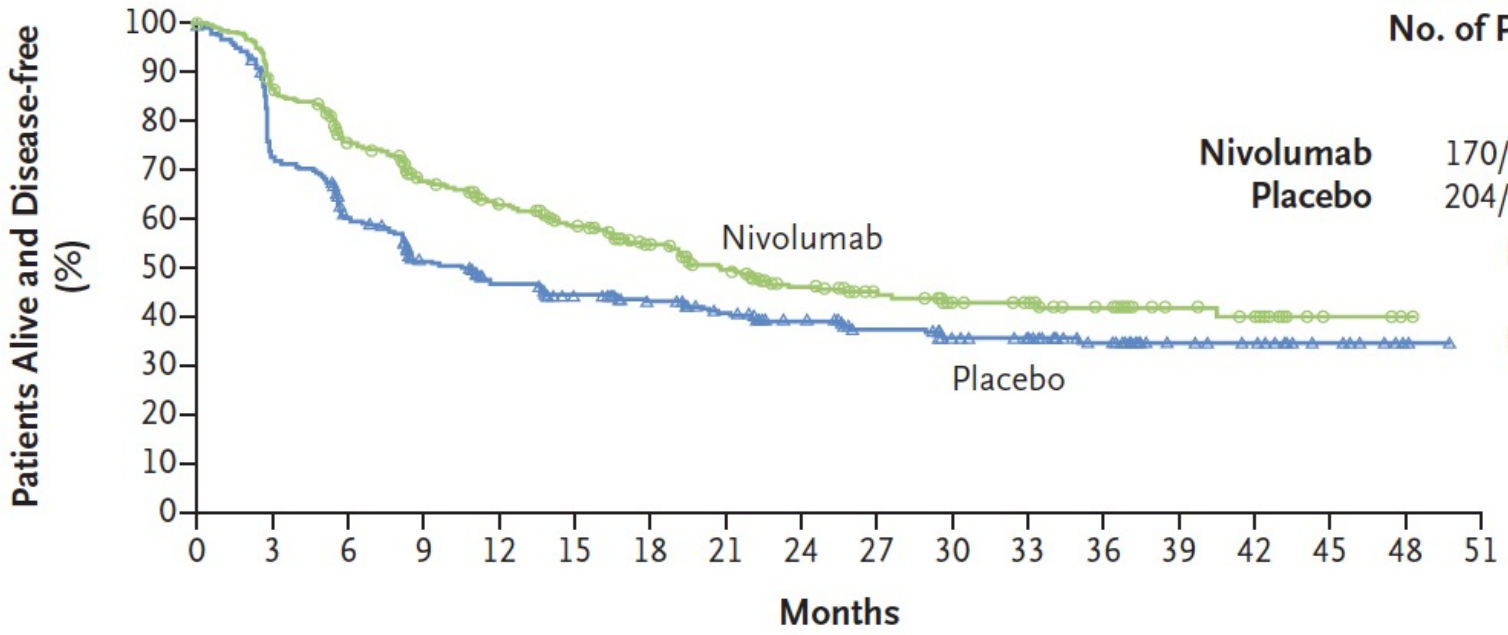
ORIGINAL ARTICLE

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;384(22):2102-14.

CheckMate 274: Disease-Free Survival in the ITT Population



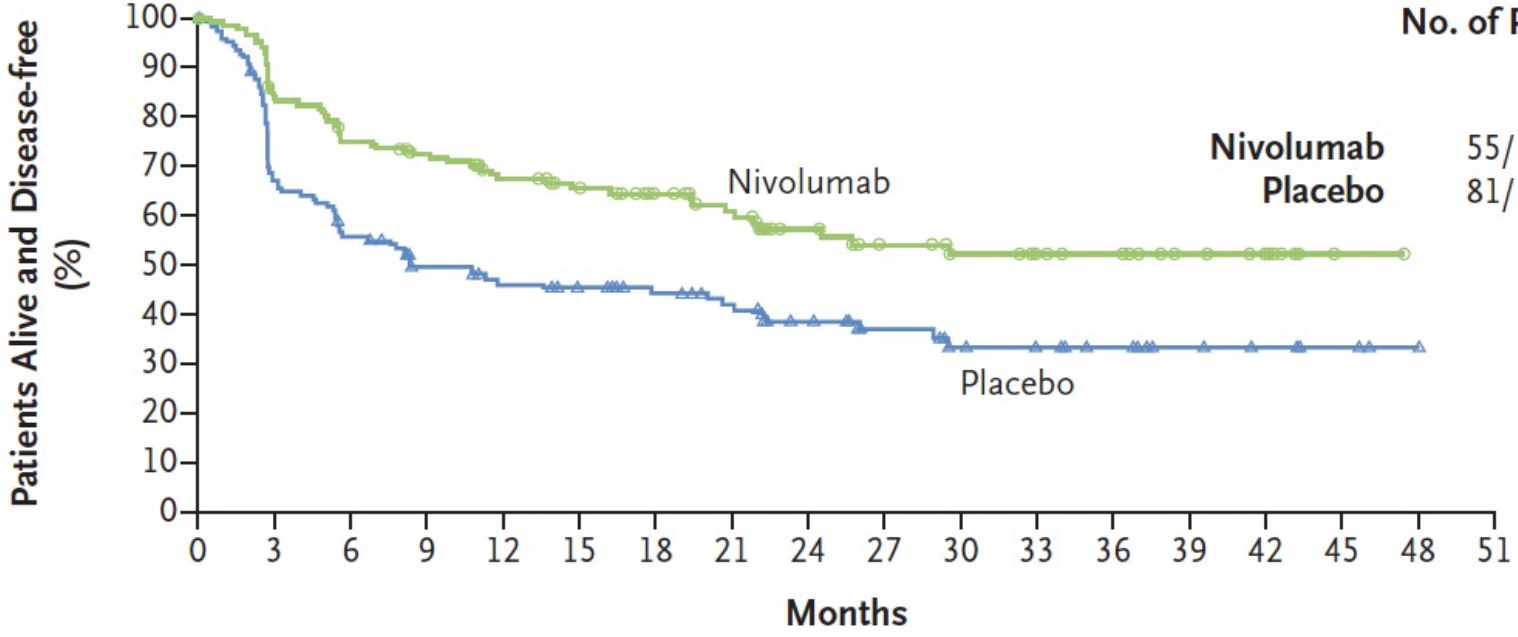
	No. of Events/ No. of Patients	Disease-free Survival at 6 Mo (95% CI)	Disease-free Survival at 12 Mo (95% CI)
		%	
Nivolumab	170/353	74.9 (69.9–79.2)	62.8 (57.3–67.8)
Placebo	204/356	60.3 (54.9–65.3)	46.6 (41.1–51.9)

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(22):2102-14.

RTP RESEARCH TO PRACTICE

CheckMate 274: Disease-Free Survival in the PD-L1 ≥1% Population



	No. of Events/ No. of Patients	Disease-free Survival at 6 Mo (95% CI)	Disease-free Survival at 12 Mo (95% CI)
		%	
Nivolumab	55/140	74.5 (66.2–81.1)	67.2 (58.4–74.5)
Placebo	81/142	55.7 (46.8–63.6)	45.9 (37.1–54.2)

Hazard ratio for disease recurrence or death, 0.55 (98.72% CI, 0.35–0.85)
P<0.001

Bajorin DF et al. *N Engl J Med* 2021;384(22):2102-14.

RTP RESEARCH TO PRACTICE

Genitourinary Cancers Agenda

Module 1: Prostate Cancer

Module 2: Urothelial Bladder Cancer

Module 3: Renal Cell Carcinoma

- Selection of patients with high-risk renal cell carcinoma (RCC) to receive pembrolizumab in the adjuvant setting
- Optimal first-line therapy for patients with metastatic RCC
- Current and future role of belzutifan in RCC

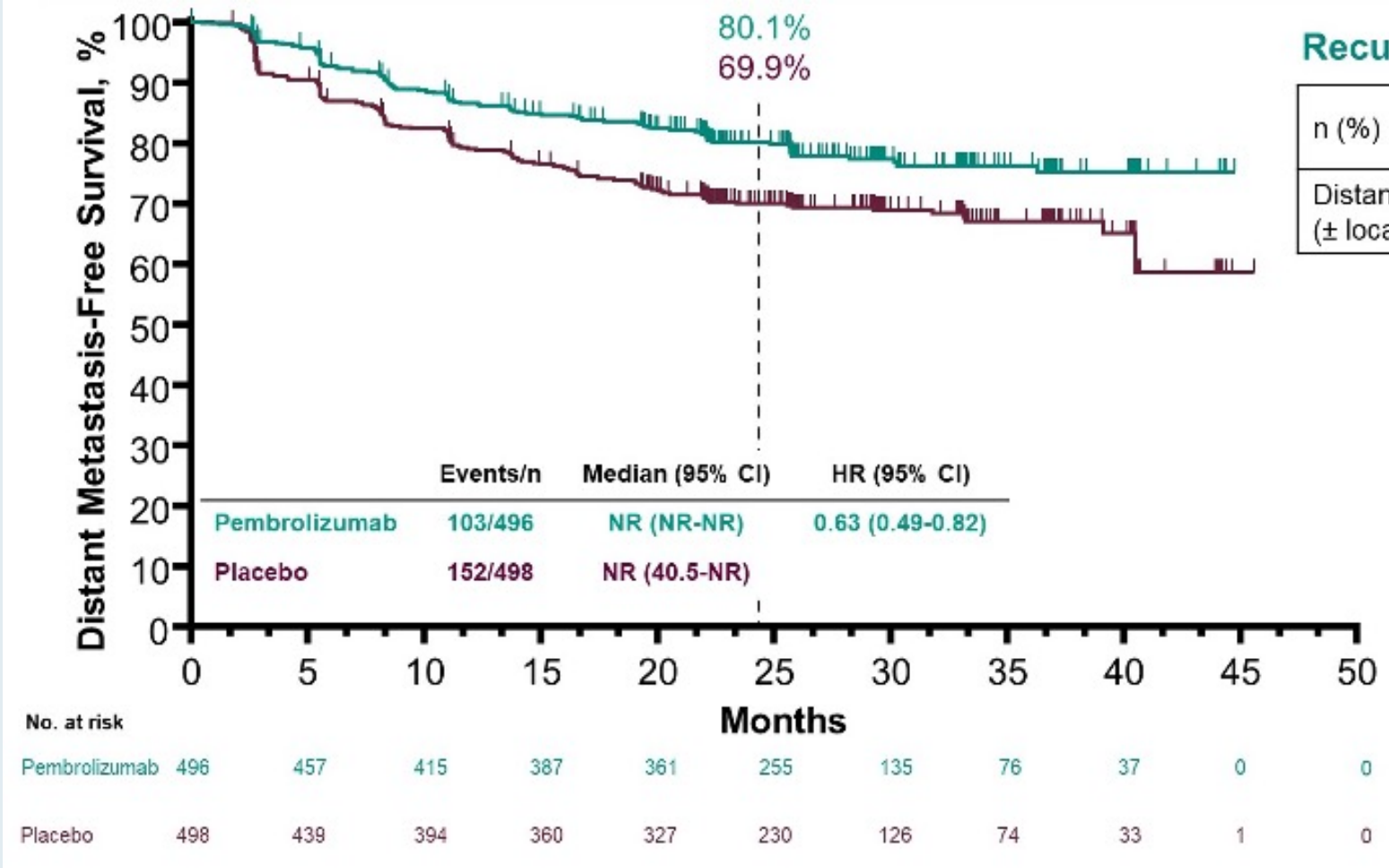
Adjuvant pembrolizumab for postnephrectomy renal cell carcinoma: Expanded efficacy analyses from KEYNOTE-564

T. K. Choueiri[1]; P. Tomczak[2]; S. H. Park[3]; B. Venugopal[4]; T. Ferguson[5]; S. N. Symeonides[6]; J. Hajek[7]; Y.-H. Chang[8]; J.-L. Lee[9]; N. Sarwar[10]; A. Thiery-Vuillemin[11]; M. Gross-Goupil[12]; M. Mahave[13]; N. B. Haas[14]; P. Sawrycki[15]; H. Gurney[16]; L. Xu[17]; K. Imai[17]; J. Burgents[17]; T. Powles[18]

[1]Dana-Farber Cancer Institute and Harvard Medical School, Boston, MA, USA; [2]Poznan University of Medical Sciences, Poznan, Poland; [3]Sungkyunkwan University, Samsung Medical Center, Seoul, South Korea; [4]Beatson West of Scotland Cancer Centre and University of Glasgow, Glasgow, United Kingdom; [5]Fiona Stanley Hospital, Perth, WA, Australia; [6]Edinburgh Cancer Centre and University of Edinburgh, Edinburgh, United Kingdom; [7]Fakultni Nemocnice Ostrava, Ostrava, Czech Republic; [8]Taipei Veterans General Hospital, Taipei, Taiwan; [9]Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea; [10]Imperial College Healthcare NHS Trust, London, United Kingdom; [11]University Hospital Jean Minjoz, Besançon, France; [12]University Hospital of Bordeaux, Bordeaux, France; [13]Fundacion Arturo Lopez Perez FALP, Santiago, Chile; [14]Abramson Cancer Center, Penn Medicine, Philadelphia, PA, USA; [15]Provincial Hospital in Torun, Torun, Poland; [16]Macquarie University, Sydney, NSW, Australia; [17]Merck & Co., Inc., Rahway, NJ, USA; [18]Barts Health NHS Trust and the Royal Free NHS Foundation Trust, Barts Cancer Institute, and Queen Mary University of London, London, United Kingdom

ASCO 2022;Abstract 4512

KEYNOTE-564: Pembrolizumab as Adjuvant Therapy for Patients with Renal Cell Carcinoma (RCC) – Disease-Free Survival



Recurrence events

n (%)	Pembrolizumab n = 496	Placebo n = 498
Distant (± local)	95 (19.2)	140 (28.1)

Choueiri TK et al. ASCO 2022;Abstract 4512.

Checkpoint Inhibitor Combinations Approved as First-Line Treatment for RCC Prior to 2021

	CheckMate 214[a]	KEYNOTE-426[b]	JAVELIN Renal 101[c]
Randomization	Nivolumab/ipilimumab vs sunitinib	Pembrolizumab/axitinib vs sunitinib	Avelumab/axitinib vs sunitinib
N	550 vs 546	432 vs 429	442 vs 444
Median OS	Not reached vs 38.4 mo (HR 0.69)	Not reached vs 35.7 mo (HR 0.68)	Not estimable vs not estimable (HR 0.80)
Median PFS	12.7 mo vs 12.3 mo (HR 0.89)	15.4 mo vs 11.1 mo (HR 0.71)	13.3 mo vs 8.0 mo (HR 0.69)

[a] Albiges L et al. *ESMO Open* 2020;5(6):e001079. [b] Powles T et al. *Lancet Oncol* 2020;21:1563-73.
[c] Choueiri TK et al. *Ann Oncol* 2020;31(8):1030-9.

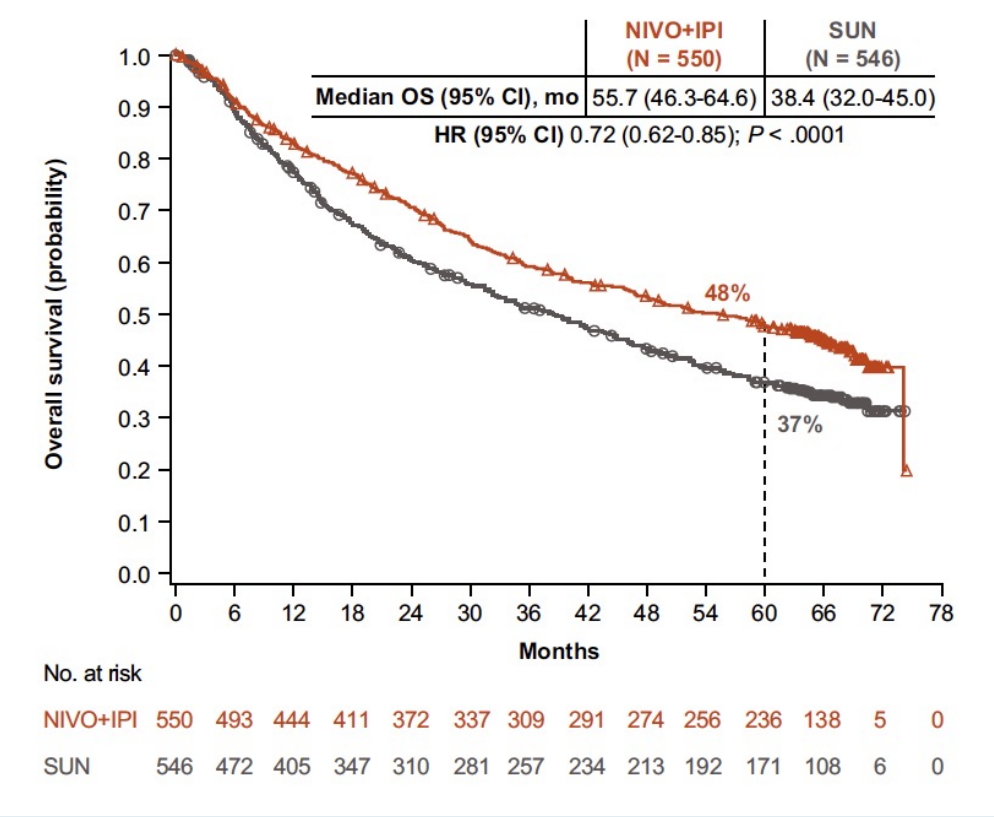
Original Article

Conditional survival and long-term efficacy with nivolumab plus ipilimumab versus sunitinib in patients with advanced renal cell carcinoma

Robert J. Motzer, MD [1]; David F. McDermott, MD[2]; Bernard Escudier, MD[3]; Mauricio Burotto, MD[4]; Toni K. Choueiri, MD [5]; Hans J. Hammers, MD, PhD[6]; Philippe Barthélémy, MD, PhD[7]; Elizabeth R. Plimack, MD[8]; Camillo Porta, MD[9]; Saby George, MD[10]; Thomas Powles, MD[11]; Frede Donskov, MD, PhD[12]; Howard Gurney, MD[13]; Christian K. Kollmannsberger, MD[14]; Marc-Oliver Grimm, MD[15]; Carlos Barrios, MD[16]; Yoshihiko Tomita, MD, PhD[17]; Daniel Castellano, MD[18]; Viktor Grünwald, MD, PhD[19]; Brian I. Rini, MD[20]; M. Brent McHenry, PhD[21]; Chung-Wei Lee, MD, PhD[22]; Jennifer McCarthy, MA[23]; Flavia Ejzykowicz, PhD[24]; and Nizar M. Tannir, MD[25]

***Cancer* 2022;128(11):2085-97.**

CheckMate 214: Efficacy Summary for Intent-to-Treat Patients (Median Follow-Up 67.7 Months)



- Progression-free survival (median, 12.3 vs 12.3 months; hazard ratio, 0.86), and objective response (39.3% vs 32.4%) benefits were maintained with nivolumab and ipilimumab versus sunitinib, respectively, in intent-to-treat patients

Motzer RJ et al. *Cancer* 2022;128(11):2085-97.

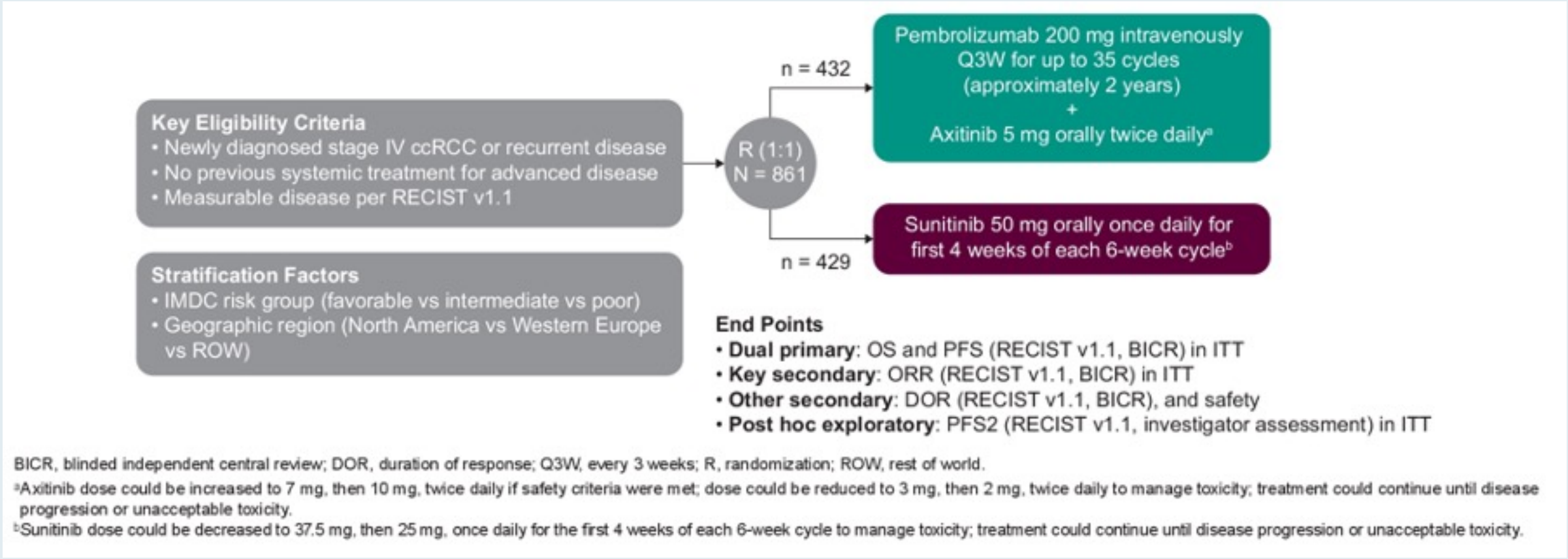
RTP RESEARCH TO PRACTICE

Pembrolizumab (pembro) plus Axitinib (axi) versus Sunitinib as First-Line therapy for Advanced Clear Cell Renal Cell Carcinoma (ccRCC): Analysis of Progression After First Subsequent Therapy in KEYNOTE-426

Powles T et al.

ASCO 2022;Abstract 4513.

KEYNOTE-426: Trial Schema



BICR, blinded independent central review; DOR, duration of response; Q3W, every 3 weeks; R, randomization; ROW, rest of world.

[a]Axitinib dose could be increased to 7 mg, then 10 mg, twice daily if safety criteria were met; dose could be reduced to 3 mg, then 2 mg, twice daily to manage toxicity; treatment could continue until disease progression or unacceptable toxicity.

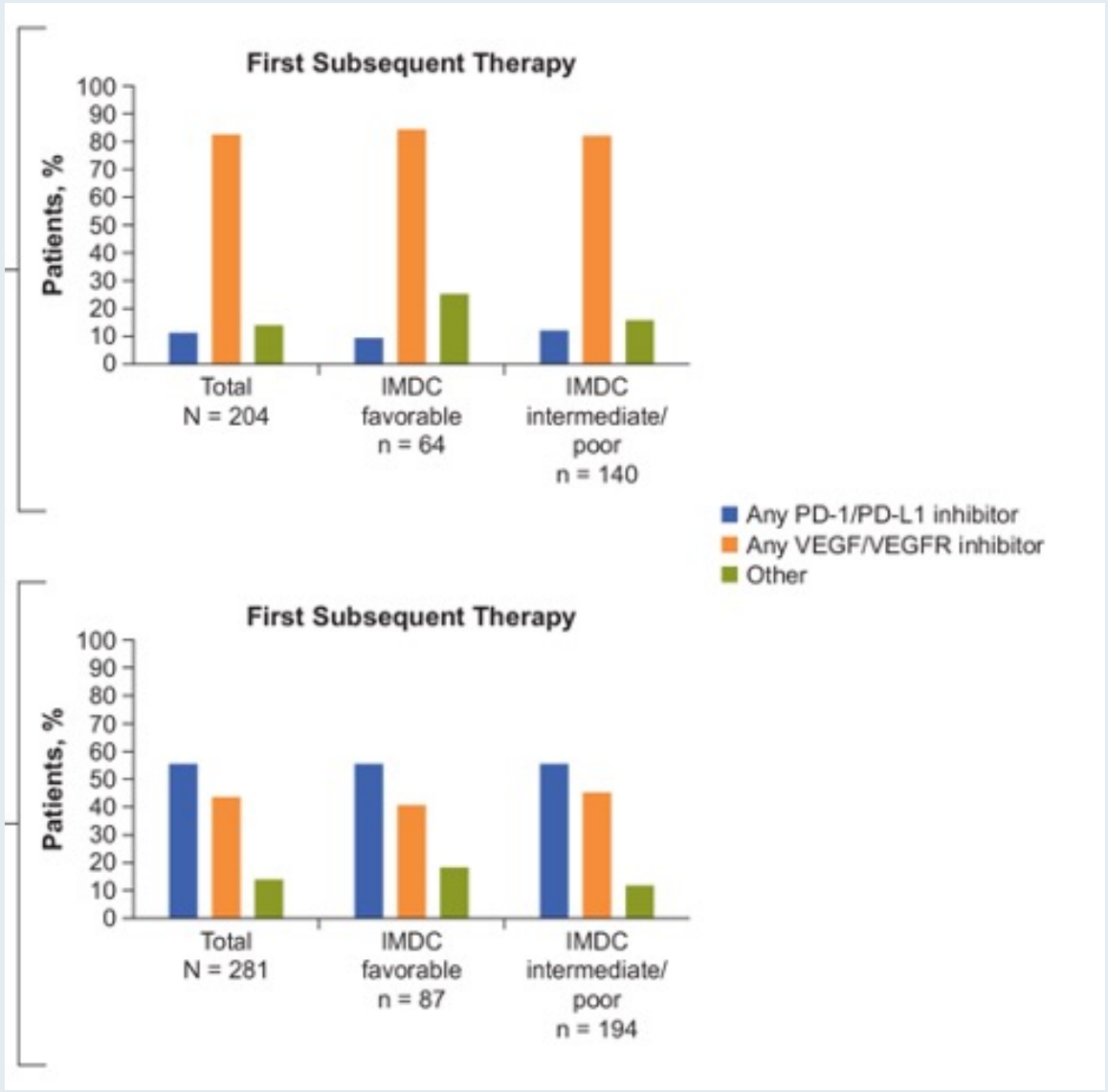
[b]Sunitinib dose could be decreased to 37.5 mg, then 25 mg, once daily for the first 4 weeks of each 6-week cycle to manage toxicity; treatment could continue until disease progression or unacceptable toxicity.

Powles T et al. ASCO 2022;Abstract 4513.

KEYNOTE-426: First Subsequent Anticancer Therapy

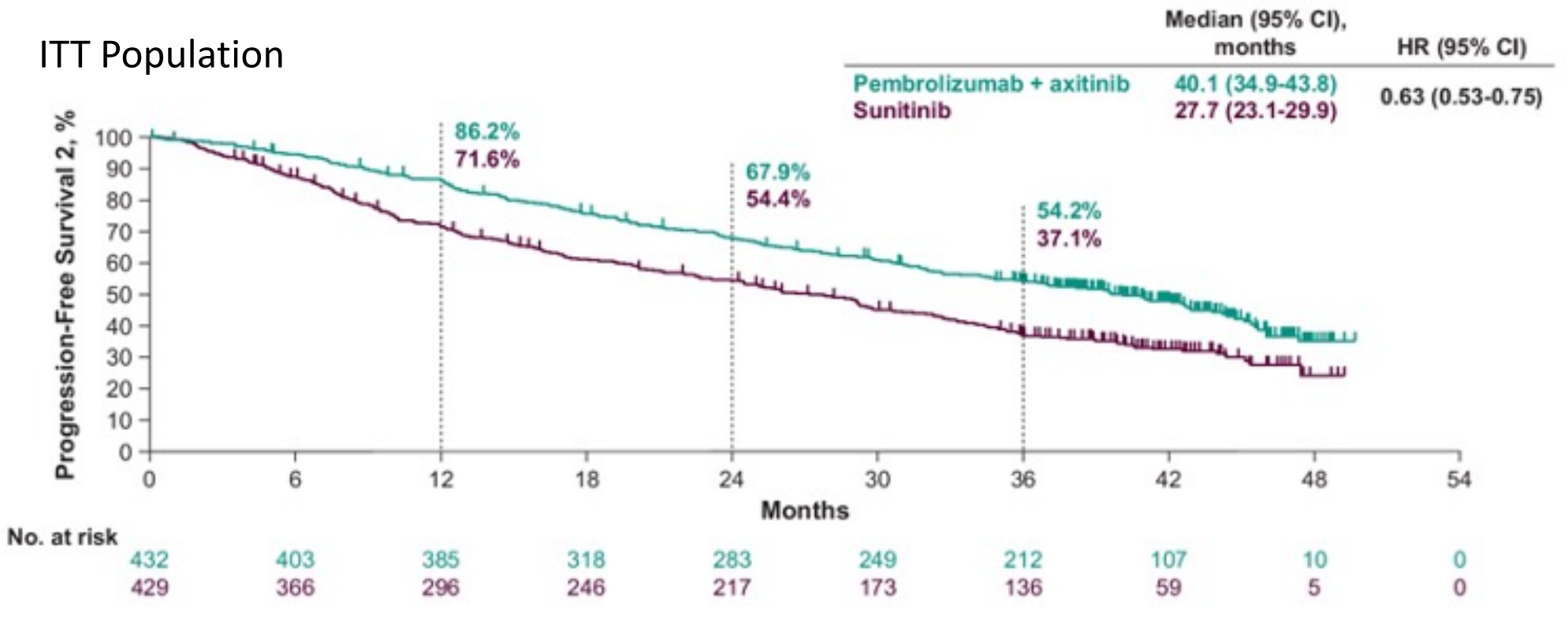
Pembrolizumab + axitinib study arm

Sunitinib study arm



Powles T et al. ASCO 2022;Abstract 4513.

KEYNOTE-426: PFS2 Summary



- Second progression-free survival (PFS2) was longer for patients in the pembrolizumab + axitinib group than for those in the sunitinib group, regardless of IMDC risk

Powles T et al. ASCO 2022;Abstract 4513.

2022 ASCO® ANNUAL MEETING

Abstract 4559

Avelumab first-line maintenance for advanced urothelial carcinoma: long-term outcomes from JAVELIN Bladder 100 in subgroups defined by response to first-line chemotherapy

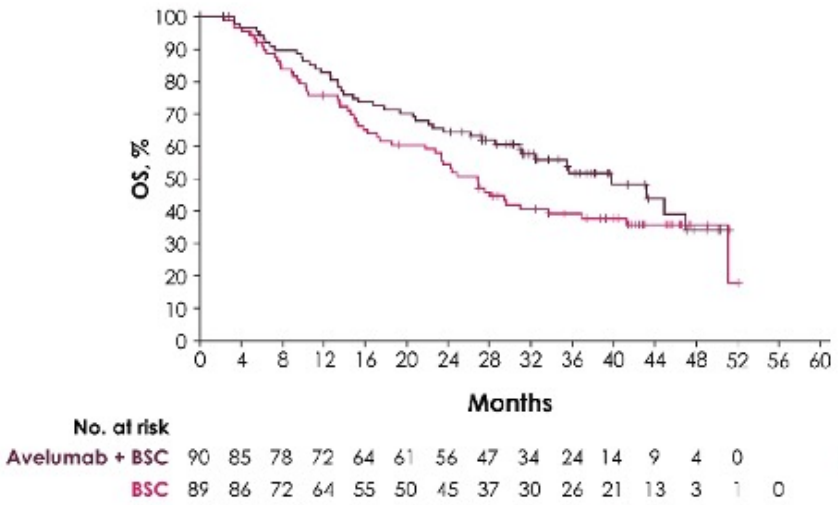
B. P. Valderrama,[1] T. Powles,[2] S. S. Sridhar,[3] C. Caserta,[4] Y. Loriot,[5] S. Gupta,[6] J. Bellmunt,[7] C. N. Sternberg,[8] J. Wang,[9] N. Costa,[10] R. J. Laliberte,[9] A. di Pietro,[11] S. H. Park,[12] P. Grivas[13]

[1]Department of Medical Oncology, Hospital Universitario Virgen del Rocío, Seville, Spain; [2]Barts Cancer Institute, Experimental Cancer Medicine Centre, Queen Mary University of London, St Bartholomew's Hospital, London, UK; [3]Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada; [4]Medical Oncology Unit, Azienda Ospedaliera S. Maria, Terni, Italy; [5]Gustave Roussy, INSERMU981, Université Paris-Saclay, Villejuif, France; [6]Department of Hematology and Medical Oncology, Cleveland Clinic, Cleveland, OH, USA; [7]Department of Medical Oncology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA; [8]Englander Institute for Precision Medicine, Weill Cornell Medicine, Hematology/Oncology, New York, NY, USA; [9]Pfizer, Cambridge, MA, USA; [10]Pfizer, Porto Salvo, Portugal; [11]Pfizer srl, Milano, Italy; [12]Sungkyunkwan University Samsung Medical Center, Seoul, Korea; [13]University of Washington, Fred Hutchinson Cancer Research Center, Seattle Cancer Care Alliance, Seattle, WA, USA

PRESENTED BY:
Srikala S. Sridhar, MD

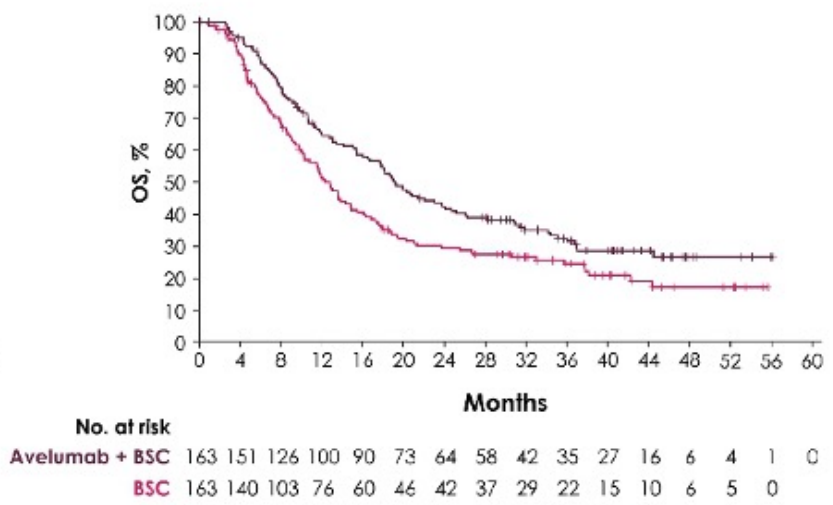
JAVELIN Bladder 100: Overall Survival by Best Response to First-Line Chemotherapy

Complete response



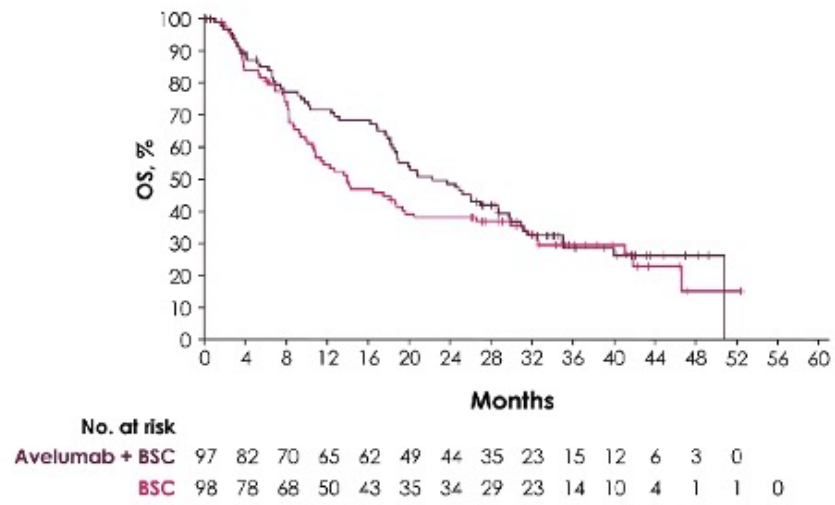
	Avelumab + BSC (n = 90)	BSC alone (n = 89)
mOS	39.8 mo	26.8 mo
Hazard ratio	0.72	

Partial response



	Avelumab + BSC (n = 163)	BSC alone (n = 163)
mOS	19.2 mo	12.8 mo
Hazard ratio	0.70	

Stable disease



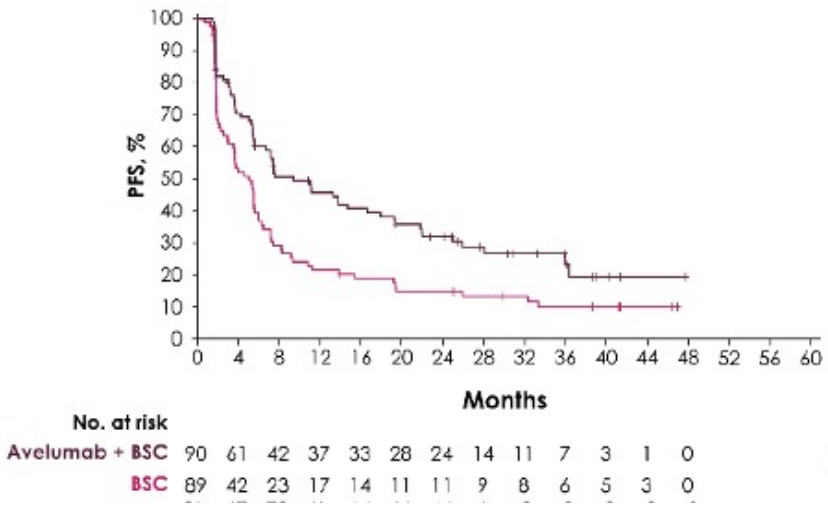
	Avelumab + BSC (n = 97)	BSC alone (n = 98)
mOS	19.2 mo	12.8 mo
Hazard ratio	0.70	

BSC = best supportive care; mOS = median overall survival

Valderrama BP et al. ASCO 2022;Abstract 4559.

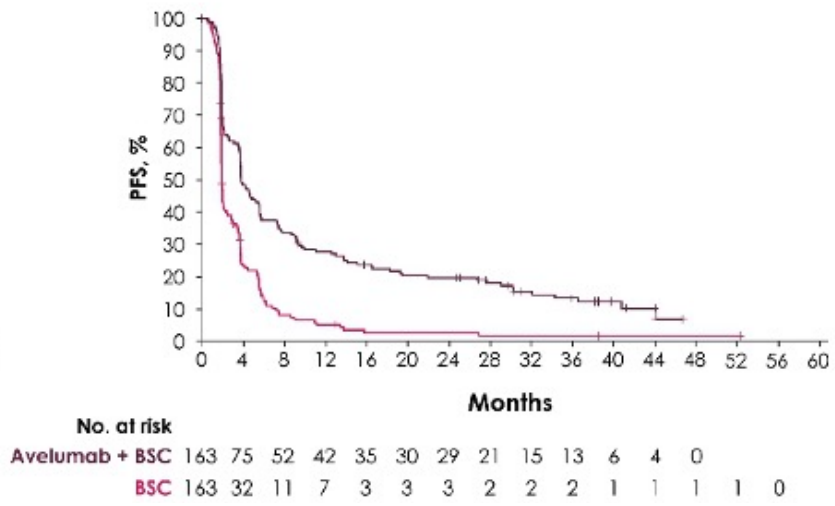
JAVELIN Bladder 100: Investigator-Assessed PFS by Best Response to First-Line Chemotherapy

Complete response



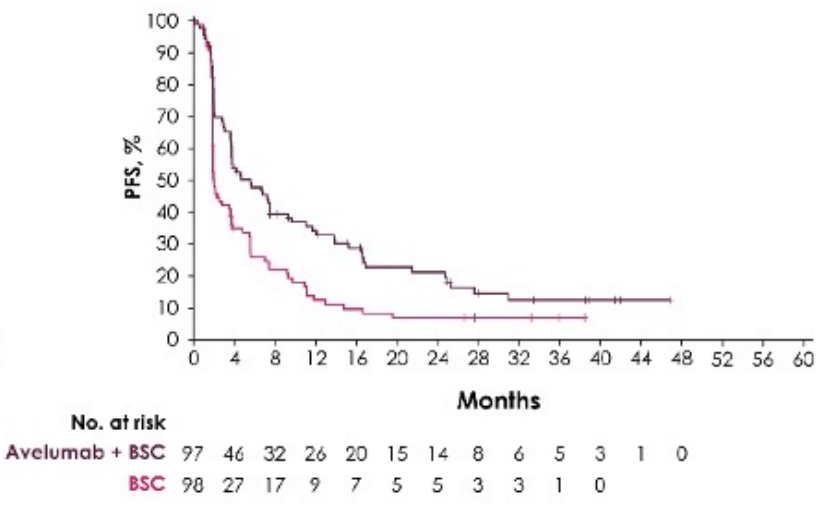
	Avelumab + BSC (n = 90)	BSC alone (n = 89)
mOS	9.5 mo	5.1 mo
Hazard ratio	0.58	

Partial response



	Avelumab + BSC (n = 163)	BSC alone (n = 163)
mOS	3.8 mo	1.9 mo
Hazard ratio	0.47	

Stable disease



	Avelumab + BSC (n = 97)	BSC alone (n = 98)
mOS	5.6 mo	2.0mo
Hazard ratio	0.59	

Valderrama BP et al. ASCO 2022;Abstract 4559.

RTP RESEARCH TO PRACTICE

original reports

Prospective Cardiovascular Surveillance of Immune Checkpoint Inhibitor–Based Combination Therapy in Patients With Advanced Renal Cell Cancer: Data From the Phase III JAVELIN Renal 101 Trial

Brian I. Rini, MD[1]; Javid J. Moslehi, MD[2,3]; Marc Bonaca, MD, MPH[4]; Manuela Schmidinger, MD[5]; Laurence Albiges, MD, PhD[6]; Toni K. Choueiri, MD[7]; Robert J. Motzer, MD[8]; Michael B. Atkins, MD[9]; John Haanen, MD, PhD[10]; Mariangela Mariani, PhD[11]; Jing Wang, PhD[12]; Subramanian Hariharan, MD[13]; and James Larkin, MD, PhD[14]

J Clin Oncol 2022;[Online ahead of print].

JAVELIN Renal 101: Relative Risk of Major Adverse Cardiovascular Event (MACE) by Baseline Serum Cardiac Biomarker Levels

Cardiac serum biomarker	Avelumab + axitinib (n = 434)		Sunitinib (n = 439)	
	MACE/no MACE	RR of MACE	MACE/no MACE	RR of MACE
Troponin-T				
High	6/29	3.31	2/39	0.89
Not high	7/128		9/156	

RR = relative risk

- Other CV baseline risk factors and serum cardiac biomarkers were not significantly predictive for MACE, although a trend toward an association with dyslipidemia was seen in the combination arm
- No clinical value of on-treatment routine monitoring of LVEF in relation to MACE was observed

Rini BI et al. *J Clin Oncol* 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

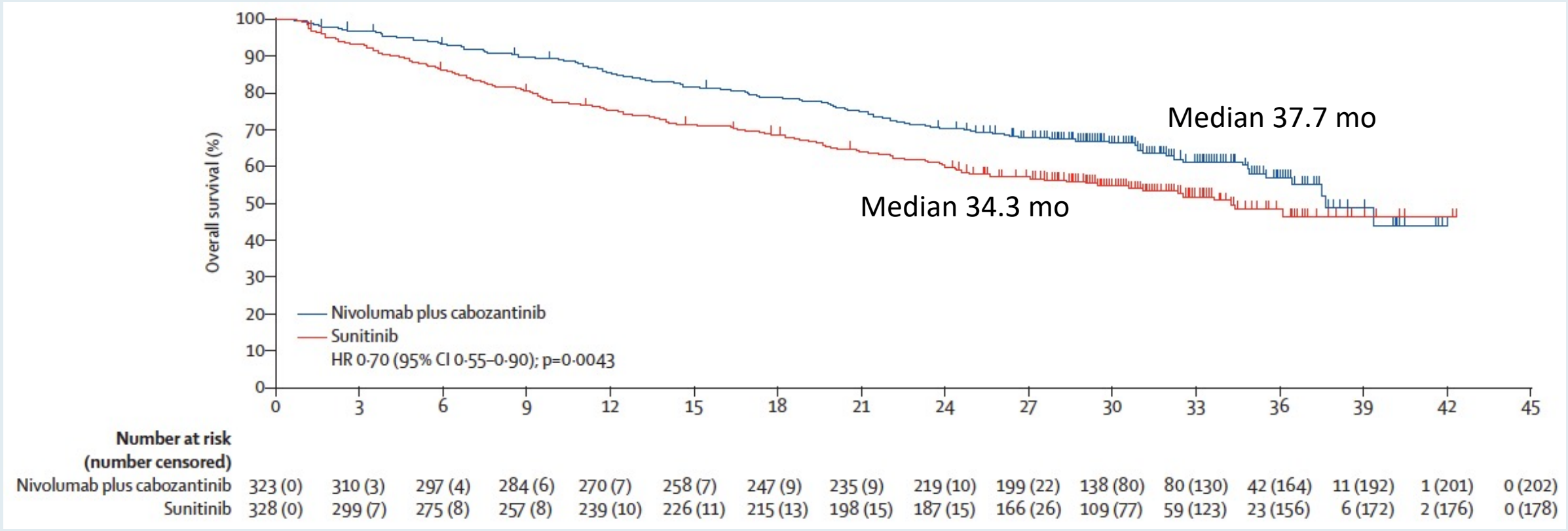
Lancet Oncol 2022;23(7):888-98.

Articles

Nivolumab plus cabozantinib versus sunitinib in first-line treatment for advanced renal cell carcinoma (CheckMate 9ER): long-term follow-up results from an open-label, randomised, phase 3 trial

Robert J Motzer, Thomas Powles, Mauricio Burotto, Bernard Escudier, Maria T Bourlon, Amishi Y Shah, Cristina Suárez, Alketa Hamzaj, Camillo Porta, Christopher M Hocking, Elizabeth R Kessler, Howard Gurney, Yoshihiko Tomita, Jens Bedke, Joshua Zhang, Burcin Simsek, Christian Scheffold, Andrea B Apolo, Toni K Choueiri

CheckMate 9ER: Overall Survival (Median Follow-Up 32.9 Months)

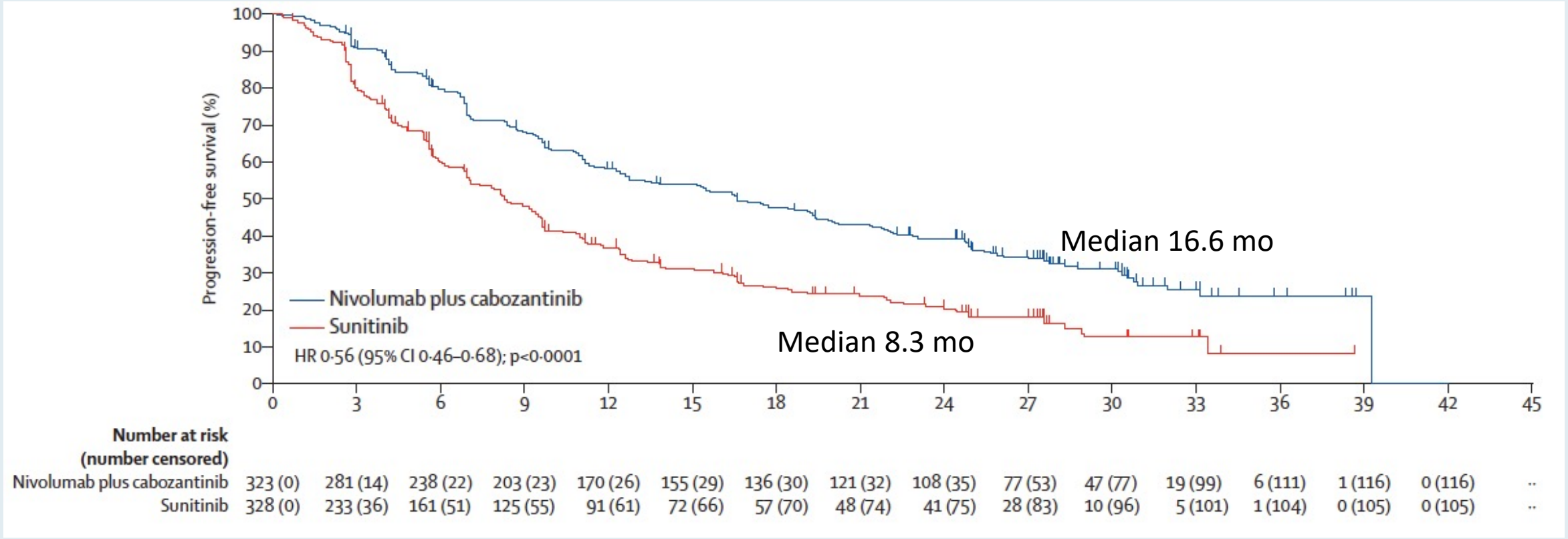


Number at risk (number censored)															
Nivolumab plus cabozantinib	323 (0)	310 (3)	297 (4)	284 (6)	270 (7)	258 (7)	247 (9)	235 (9)	219 (10)	199 (22)	138 (80)	80 (130)	42 (164)	11 (192)	1 (201)	0 (202)
Sunitinib	328 (0)	299 (7)	275 (8)	257 (8)	239 (10)	226 (11)	215 (13)	198 (15)	187 (15)	166 (26)	109 (77)	59 (123)	23 (156)	6 (172)	2 (176)	0 (178)

Motzer RJ et al. *Lancet Oncol* 2022;23(7):888-98.

RTP RESEARCH TO PRACTICE

CheckMate 9ER: Progression-Free Survival (Median Follow-Up 32.9 Months)



Number at risk (number censored)															
Nivolumab plus cabozantinib	323 (0)	281 (14)	238 (22)	203 (23)	170 (26)	155 (29)	136 (30)	121 (32)	108 (35)	77 (53)	47 (77)	19 (99)	6 (111)	1 (116)	0 (116)	..
Sunitinib	328 (0)	233 (36)	161 (51)	125 (55)	91 (61)	72 (66)	57 (70)	48 (74)	41 (75)	28 (83)	10 (96)	5 (101)	1 (104)	0 (105)	0 (105)	..

Motzer RJ et al. *Lancet Oncol* 2022;23(7):888-98.

RTP RESEARCH TO PRACTICE

CheckMate 9ER: Response Summary (Median Follow-Up 32.9 Months)

	Nivolumab plus cabozantinib group (n=323)	Sunitinib group (n=328)
Confirmed objective response (n [%; 95% CI])	180 (56%; 50–61)	93 (28%; 24–34)
Confirmed best overall response		
Complete response	40 (12%)	17 (5%)
Partial response	140 (43%)	76 (23%)
Stable disease	105 (33%)	134 (41%)
Progressive disease	20 (6%)	45 (14%)
Unable to determine	18 (6%)	55 (17%)
Not reported	0	1 (<1%)
Median time to response (IQR), months	2·8 (2·8–4·2)	4·2 (2·8–7·1)
Median duration of response (95% CI), months	23·1 (20·2–27·9)	15·1 (9·9–20·5)

Motzer RJ et al. *Lancet Oncol* 2022;23(7):888-98.

Research

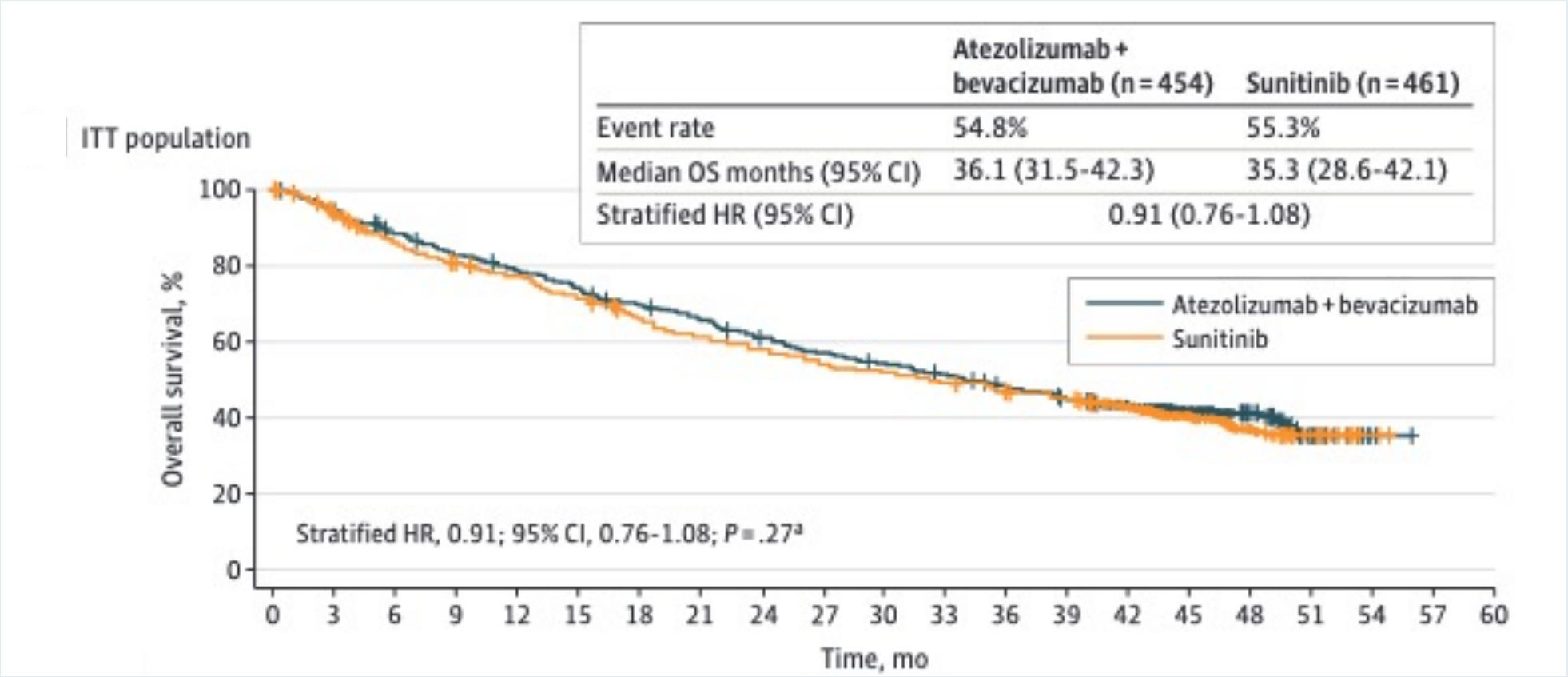
JAMA Oncology | Brief Report

Final Overall Survival and Molecular Analysis in IMmotion151, a Phase 3 Trial Comparing Atezolizumab Plus Bevacizumab vs Sunitinib in Patients With Previously Untreated Metastatic Renal Cell Carcinoma

Robert J. Motzer, MD; Thomas Powles, MD; Michael B. Atkins, MD; Bernard Escudier, MD; David F. McDermott, MD; Boris Y. Alekseev, MD; Jae-Lyun Lee, MD, PhD; Cristina Suarez, MD; Daniil Stroyakovskiy, MD; Ugo De Giorgi, MD, PhD; Frede Donskov, MD; Begoña Mellado, MD, PhD; Romain Banchereau, PhD; Habib Hamidi, PhD; Omara Khan, MSc; Veronica Craine, MS; Mahrukh Huseni, MS; Nick Flinn, PhD; Sarita Dubey, MD; Brian I. Rini, MD

JAMA Oncol 2022;8(2):275-80.

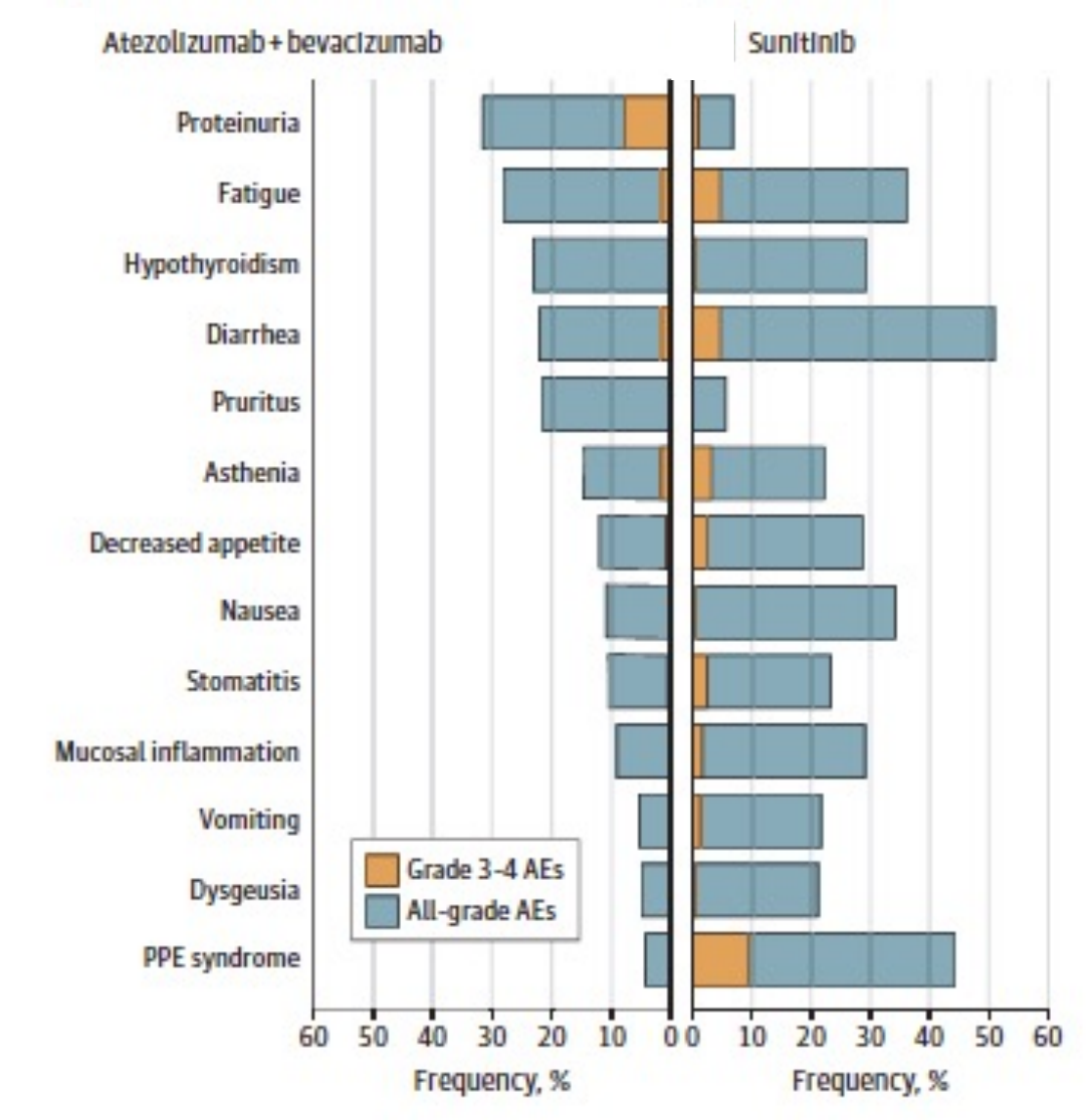
IMmotion151: Final Analysis of Overall Survival (OS) in Previously Untreated Metastatic RCC



- For the PD-L1+ population, median OS was 38.7 months for the atezolizumab and bevacizumab arm and 31.6 months for the sunitinib arm (HR, 0.85)

Motzer RJ et al. *JAMA Oncol* 2022;8(2):275-80.

IMmotion151: Treatment-Related Adverse Events



Motzer RJ et al. *JAMA Oncol* 2022;8(2):275-80.

Phase 1 LITESPARK-001 (MK-6482-001) study of belzutifan in advanced solid tumors: Update of the clear cell renal cell carcinoma cohort with more than 3 years of total follow-up

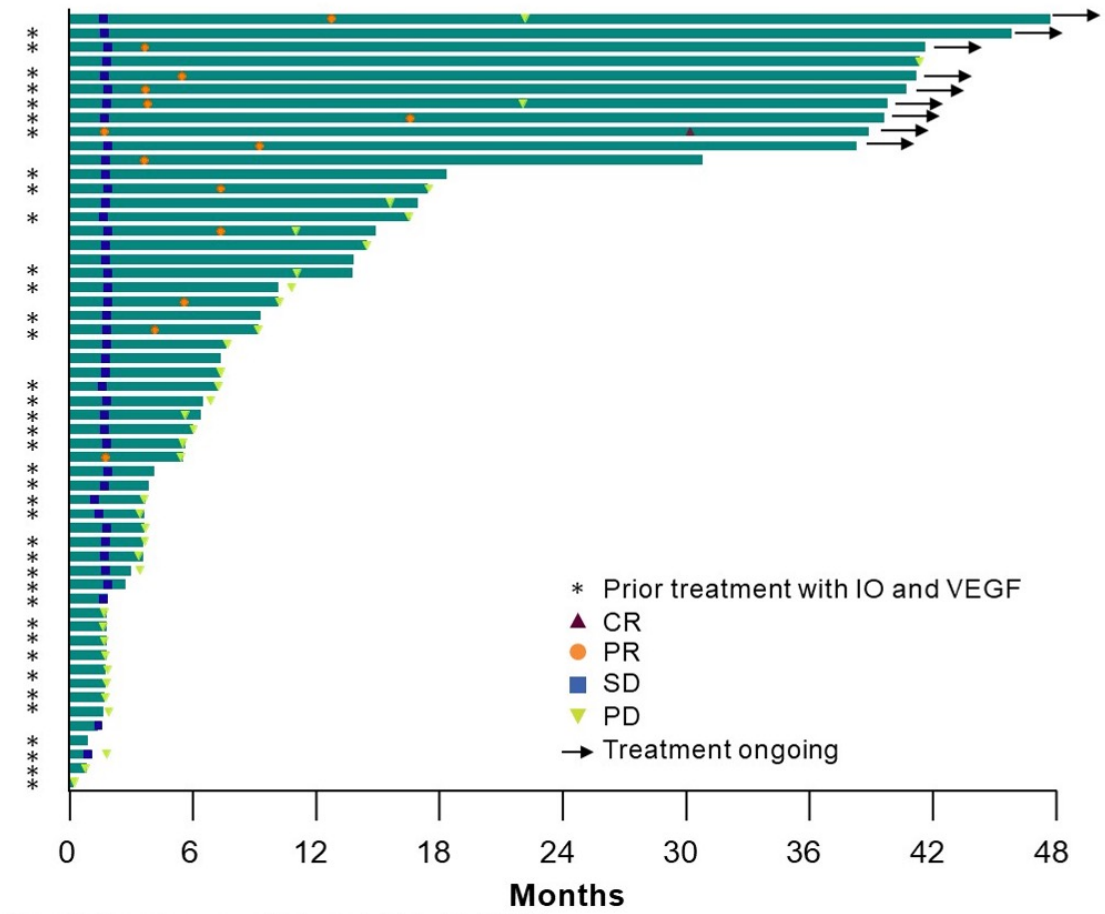
E. Jonasch[1]; T. M. Bauer[2]; K. P. Papadopoulos[3]; E. R. Plimack[4]; J. R. Merchan[5]; D. F. McDermott[6]; M. D. Michaelson[7]; L. J. Appleman[8]; A. Roy[9]; R. F. Perini[9]; Y. Liu[9]; T. K. Choueiri[10]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Sarah Cannon Research Institute and Tennessee Oncology, Nashville, TN, USA; [3]South Texas Accelerated Research Therapeutics (START), San Antonio, TX, USA; [4]Fox Chase Cancer Center, Philadelphia, PA, USA; [5]University of Miami Health System, Miami, FL, USA; [6]Beth Israel Deaconess Medical Center, Boston, MA, USA; [7]Massachusetts General Hospital, Boston, MA, USA; [8]University of Pittsburgh Medical Center, Pittsburgh, PA; [9]Merck & Co., Inc., Rahway, NJ, USA; [10]Dana-Farber Cancer Institute, Boston, MA, USA

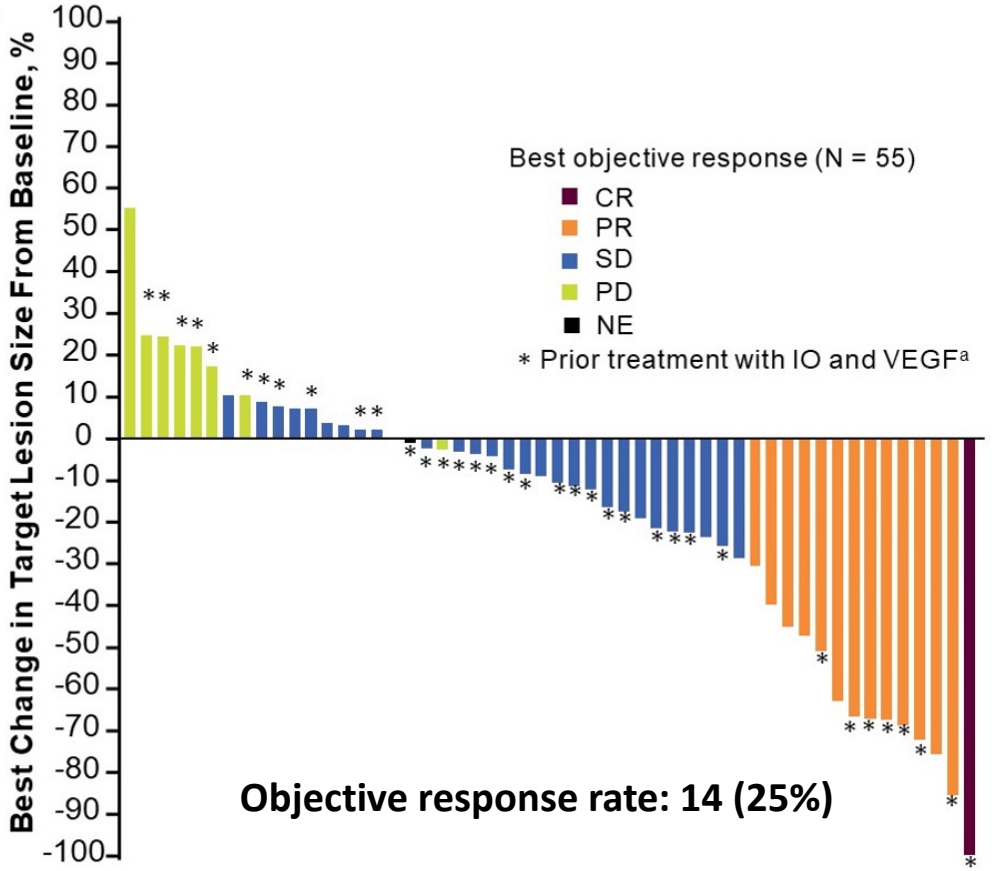
ASCO 2022;Abstract 4509.

LITESPARK-001: Updated Efficacy with Belzutifan in the Clear Cell RCC Cohort

Duration of Treatment



Best Response



Objective response rate: 14 (25%)

[a]In combination or in sequence. Database cutoff date: July 15, 2021.

Jonasch E et al. ASCO 2022;Abstract 4509.

RTP RESEARCH TO PRACTICE

LITESPARK-001: Updated Safety with Belzutifan in the Clear Cell RCC (ccRCC) Cohort

Treatment-related adverse events occurring in ≥10% of patients and associated grade 3 events in the ccRCC cohort

	ccRCC cohort N = 55	
	Any grade	**Grade 3[a,b]**
Any	53 (96)	22 (40)
Anemia	41 (75)	13 (24)
Fatigue	31 (56)	1 (2)
Hypoxia	12 (22)	7 (13)
Dyspnea	12 (22)	2 (4)
Peripheral edema	9 (16)	0 (0)
Nausea	8 (15)	1 (2)
Increased alanine aminotransferase	6 (11)	1 (2)

Values are n (%).
[a]No treatment-related grade 4 or 5 events occurred.
[b]Grade 3 decreased platelet count, hypertension, and hypophosphatemia occurred in 1 patient each.
Database cutoff date: July 15, 2021.

Jonasch E et al. ASCO 2022;Abstract 4509.

2022 ASCO® ANNUAL MEETING

SWOG CANCER RESEARCH NETWORK | NCI National Clinical Trials Network, a National Cancer Institute program | NCI Community Oncology Research Program, A program of the National Cancer Institute of the National Institutes of Health

SWOG S0931 – EVEREST
EVErolimus for Renal cancer Ensuing Surgical Therapy, a phase III study*

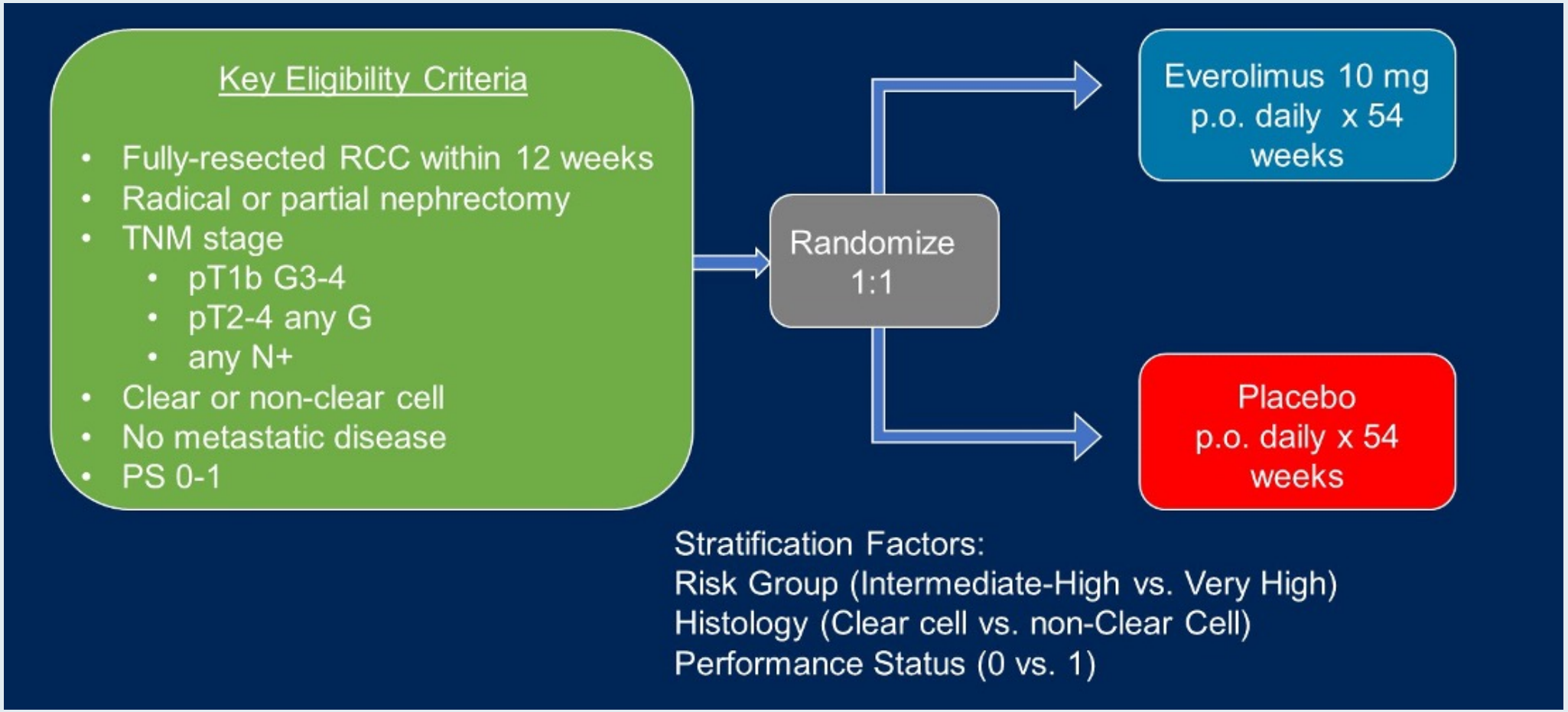
Christopher W. Ryan, Catherine Tangen, Elisabeth I. Heath, Mark N. Stein, Maxwell Meng, Ajjai Shivaram Alva, Sumanta K. Pal, Igor Puzanov, Joseph I Clark, Toni K. Choueiri, Neeraj Agarwal, Robert Uzzo, Naomi B. Haas, Timothy W. Synold, Melissa Plets, Ulka N. Vaishampayan, Brian M. Shuch, Nicholas J. Vogelzang, Ian M Thompson Jr., Primo "Lucky" N. Lara Jr

*NCT01120249

Abstract LBA4500

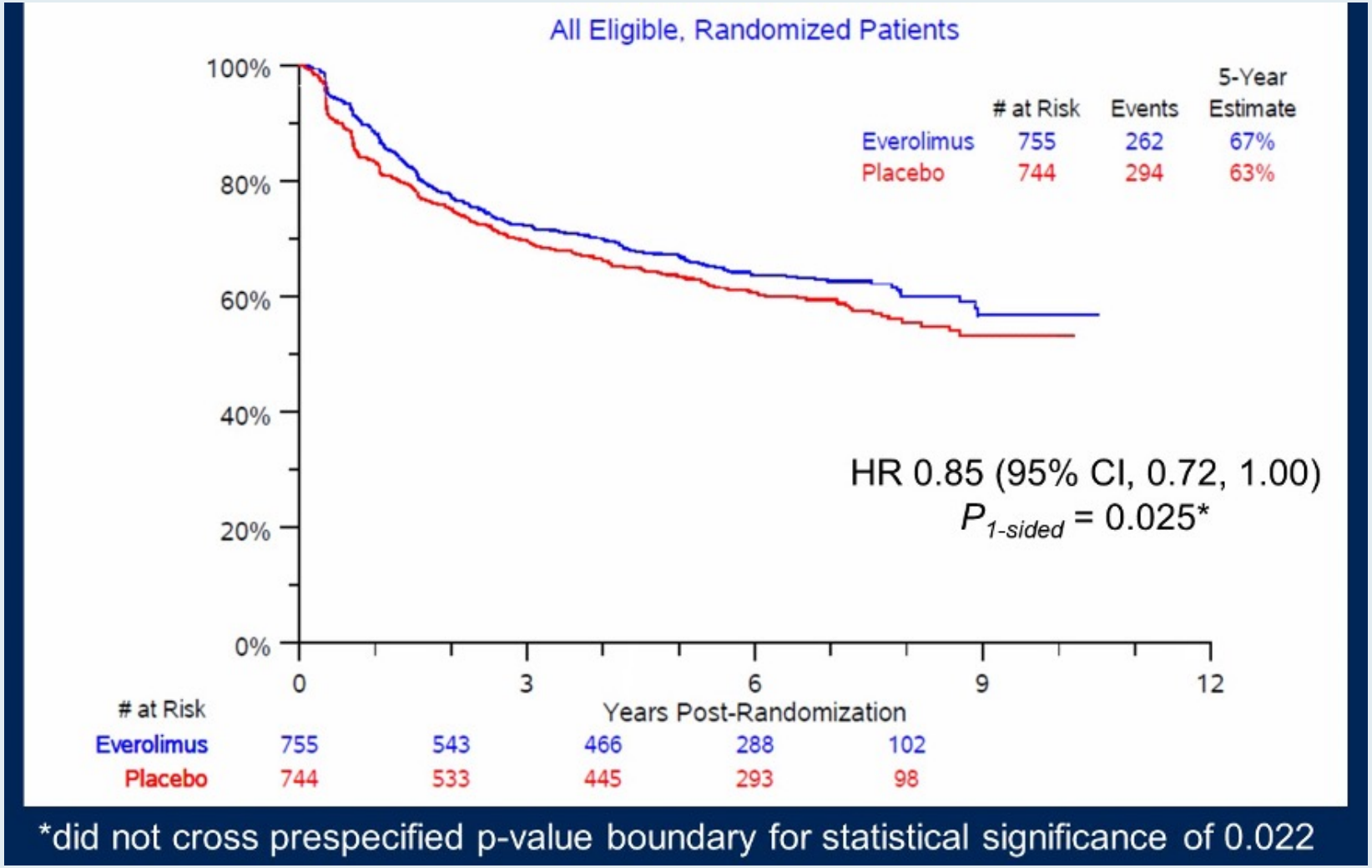
RTP RESEARCH TO PRACTICE

SWOG-S0391 (EVEREST): Phase III Trial of Adjuvant Everolimus for RCC



Ryan CW et al. ASCO 2022;Abstract LBA4500.

SWOG-S0391 (EVEREST) Primary Endpoint: Recurrence-Free Survival



Ryan CW et al. ASCO 2022;Abstract LBA4500.

Update on the CheckMate 914 Trial Evaluating Nivolumab with Ipilimumab as Adjuvant Treatment for Localized Renal Cell Carcinoma

Press Release: July 29, 2022

"Part A of the Phase 3 CheckMate-914 trial, evaluating nivolumab plus ipilimumab as an adjuvant treatment for patients with localized renal cell carcinoma (RCC) who have undergone full or partial removal of the kidney and who are at moderate or high risk of relapse, ***did not meet*** the primary endpoint of disease-free survival (DFS) as assessed by Blinded Independent Central Review (BICR). The safety profile was consistent with previously reported studies of the nivolumab plus ipilimumab combination in solid tumors."

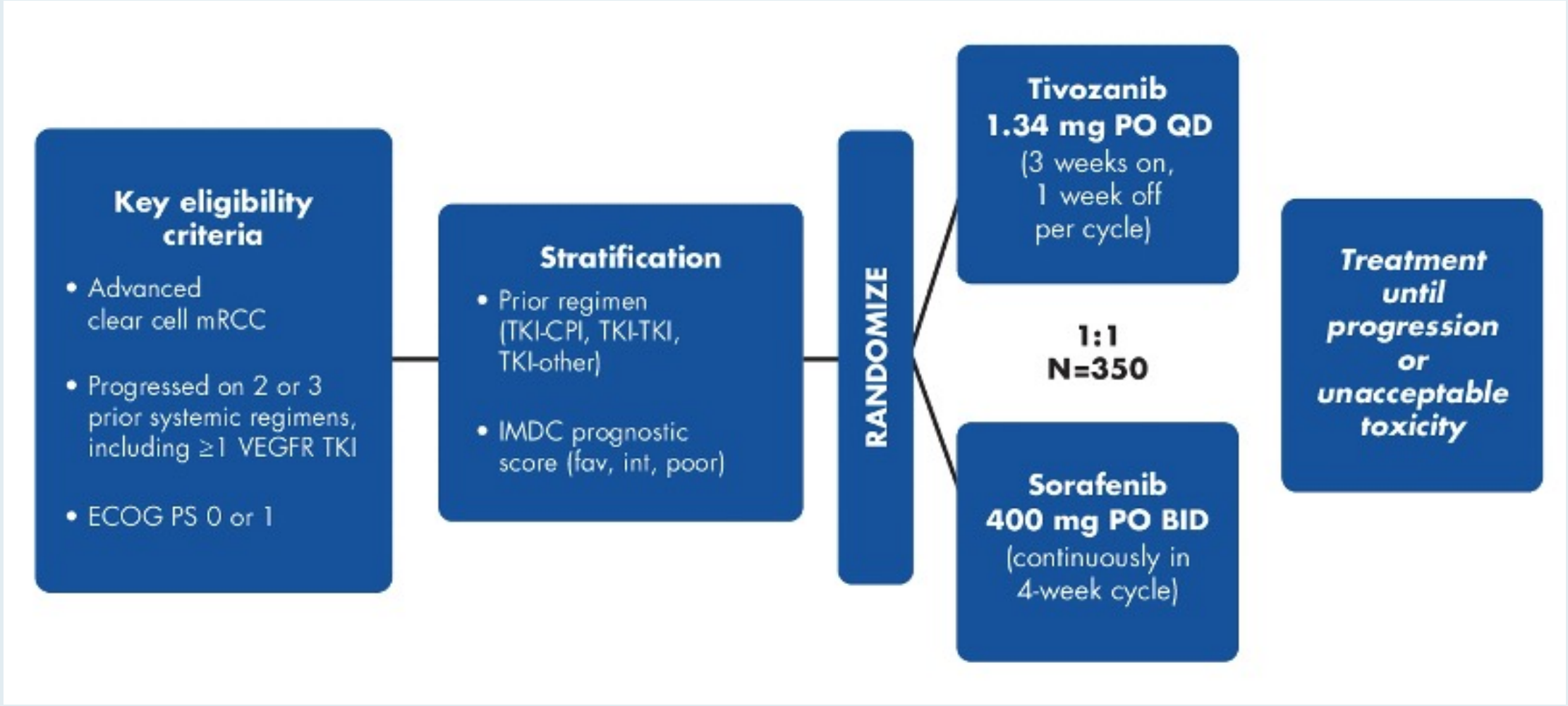
https://news.bms.com/news/details/2022/Bristol-Myers-Squibb-Provides-Update-on-CheckMate--914-Trial-Evaluating-Opdivo-nivolumab-Plus-Yervoy-ipilimumab-as-Adjuvant-Treatment-of-Localized-Renal-Cell-Carcinoma/default.aspx

Long-Term PFS From TIVO-3: Tivozanib (TIVO) versus Sorafenib (SOR) in Relapsed/Refractory (R/R) Advanced RCC

Atkins MB et al.

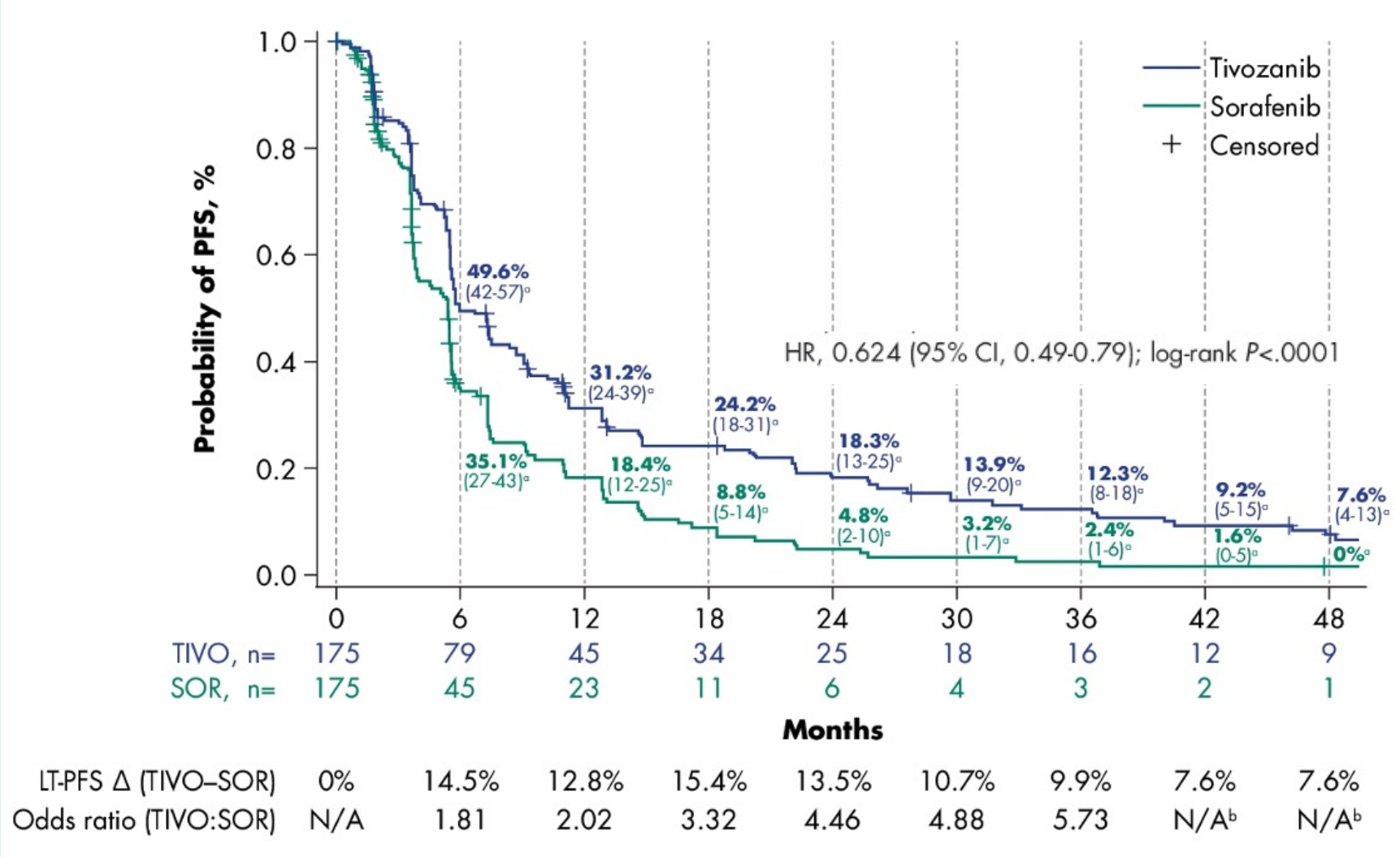
2022 Genitourinary Cancers Symposium;Abstract 362.

TIVO-3: Phase III Trial Design



Atkins MB et al. Genitourinary Cancers Symposium 2022;Abstract 362.

TIVO-3: Landmark Analysis Long-Term PFS (LT-PFS)



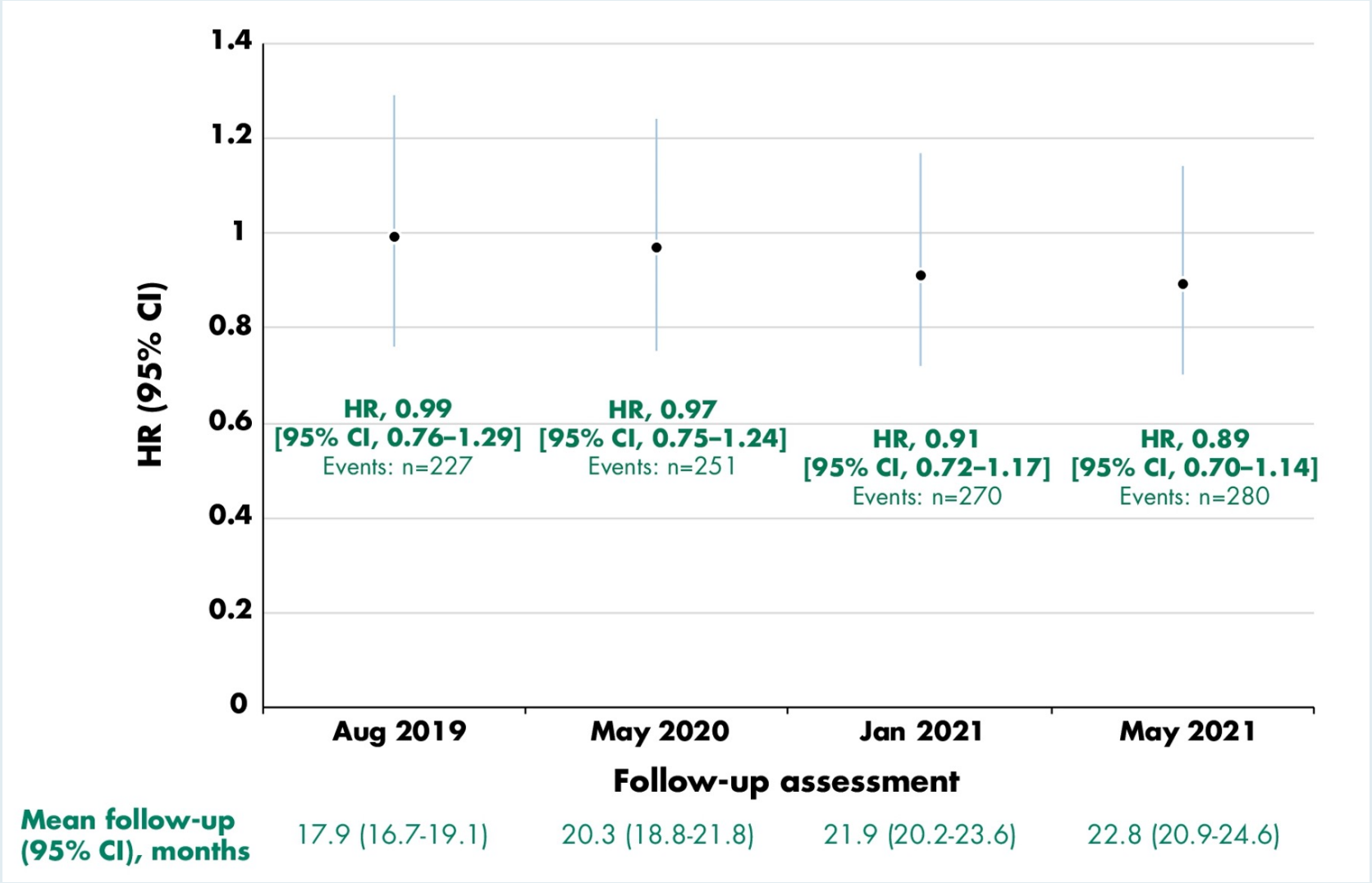
Atkins MB et al. Genitourinary Cancers Symposium 2022;Abstract 362.

Maturation of Overall Survival (OS) in TIVO-3 with Long-Term Follow-Up

Rini BI et al.

ASCO 2022;Abstract 4557.

TIVO-3: Serial Overall Survival with Extended Follow-Up (22.8 Months)



Rini BI et al. ASCO 2022;Abstract 4557.

TIVO-3: Unconditioned (ITT Population) and Landmark PFS-Conditioned Overall Survival with Extended Follow-Up

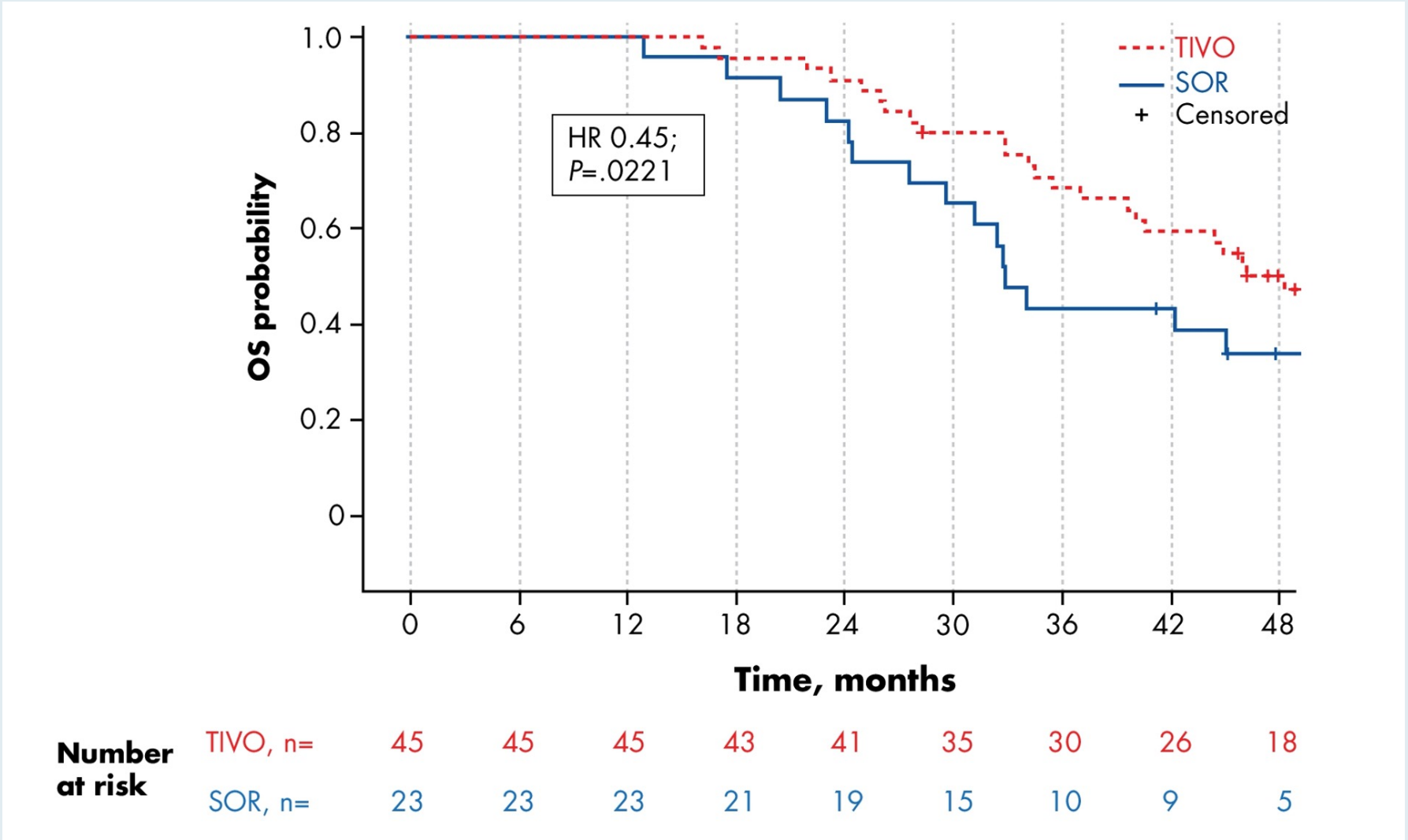
Population	Group	At risk, n	Events	Median OS (95% CI), months	HR (95% CI)	Stratified log-rank *P* value
Unconditioned (ITT population)	TIVO	175	138	16.4 (13.4-21.9)	0.89 (0.70-1.14)	0.3533
	SOR	175	142	19.1 (14.9-24.2)		
Conditioned on PFS ≥12 months	TIVO	45	25	48.3 (32.8-NR)	**0.45 (0.22-0.91)**	**0.0221**
	SOR	23	17	32.8 (27.6-50.0)		
Conditioned on PFS ≥18 months	TIVO	34	8	54.3 (44.9-NR)	0.46 (0.15-1.39)	0.1617
	SOR	11	5	50.0 (32.4-NR)		

NR, not reached.

PFS = progression-free survival

Rini BI et al. ASCO 2022;Abstract 4557.

TIVO-3: Conditional Overall Survival (OS) in Patients with 12-Month Progression-Free Survival



Rini BI et al. ASCO 2022;Abstract 4557.

2022 ASCO® ANNUAL MEETING

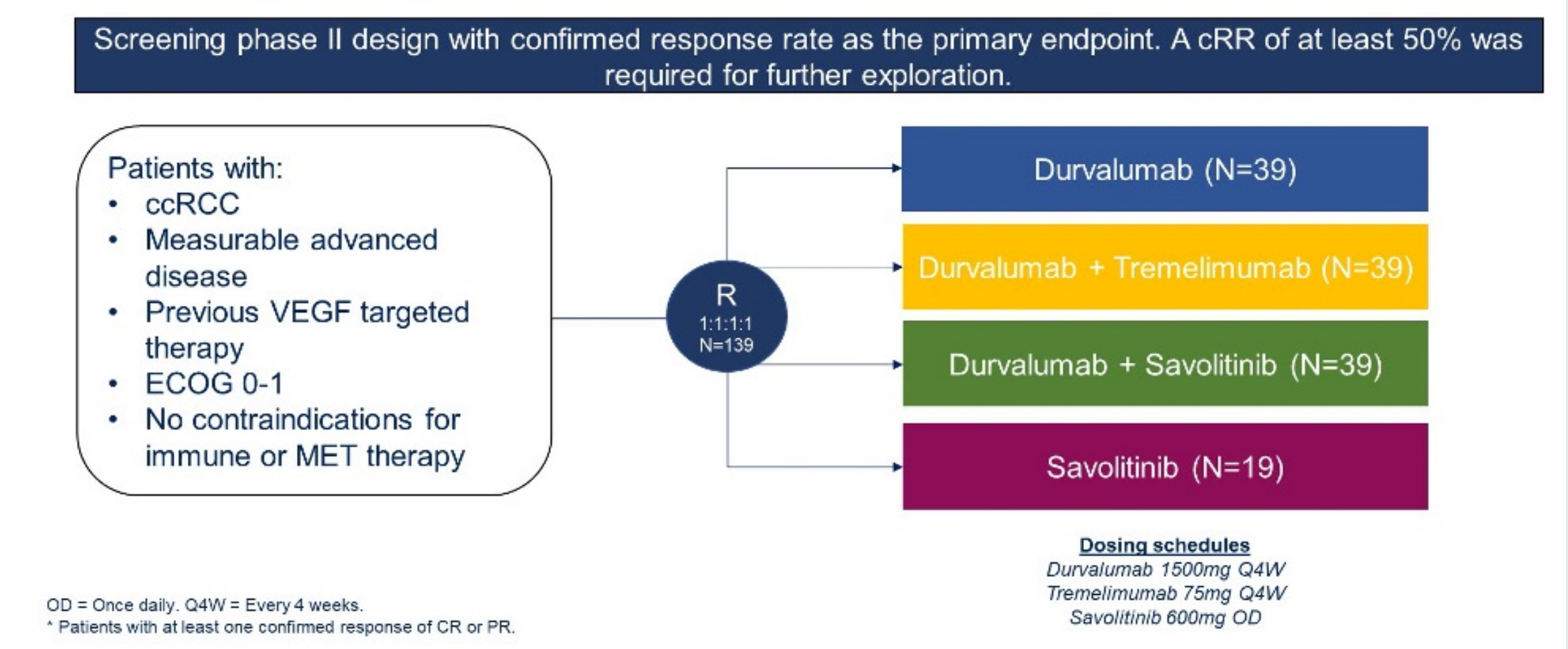
CALYPSO: A three-arm randomised phase II study of Durvalumab alone or with Savolitinib or Tremelimumab in previously treated advanced clear cell renal cancer

Thomas Powles[1], Maria Jose Mendez-Vidal[2], Alejo Rodriguez-Vida[3], Begoña Pérez-Valderrama[4], Emilio Esteban[5], Fiona Thistlethwaite[6], Poulam Patel[7], Urbano Anido[8], Gopalakrishnan Srinivasan[9], Abdel Hamid[10], James Larkin[11], Christy Ralph[12], Stefan N. Symeonides[13], Javier Puente[14], Ryan Hartmaier[15], Aleksandra Markovets[16], Aaron Prendergast[1], Kelly Mousa[1], Cristina Suarez[17]

Abstract LBA4503

RTP RESEARCH TO PRACTICE

CALYPSO: A Phase II Trial of Durvalumab Alone or with Savolitinib or Tremelimumab for Previously Treated Advanced Clear Cell RCC (ccRCC)



Powles T et al. ASCO 2022;Abstract LBA4503.

RTP RESEARCH TO PRACTICE

CALYPSO: Summary

- All four regimens appeared safe and tolerable.
- Savolitinib alone or in combination with durvalumab did not meet predefined activity levels.This also appeared to be the case in MET driven tumors.
- The addition of tremelimumab to durvalumab did not clearly improve efficacy.
- Data exploring other immune and DNA biomarker was hampered by small numbers, although no clear signals were seen.

Powles T et al. ASCO 2022;Abstract LBA4503.

Thank you for joining us!

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

We are taking a short break!

The program will resume at 11:25 AM PT (2:25 PM ET)

Up Next…

Drs Rafael Fonseca and Krina Patel
discuss the management of multiple myeloma

RTP
RESEARCH
TO PRACTICE

Recent Advances and Real-World Implications in Medical Oncology: A Daylong Multitumor Educational Symposium in Partnership with the American Oncology Network

A CME/MOC- and NCPD-Accredited Hybrid Event

Saturday, August 6, 2022
9:00 AM – 4:30 PM PT

RTP
RESEARCH
TO PRACTICE

Agenda

Module 1 — Breast Cancer: *Drs Burstein and O'Shaughnessy*

Module 2 — Genitourinary Cancers: *Drs Agarwal and Srinivas*

Module 3 — Multiple Myeloma: *Drs Fonseca and Patel*

Module 4 — Chronic Lymphocytic Leukemia and Lymphomas: *Drs Kahl and Moskowitz*

Module 5 — Gastrointestinal Cancers: *Drs Mehta and Philip*

Module 6 — Lung Cancer: *Drs Dagogo-Jack and Ramalingam*

Multiple Myeloma Faculty

Rafael Fonseca, MD
Chief Innovation Officer
Getz Family Professor of Cancer
Distinguished Mayo Investigator
Mayo Clinic in Arizona
Phoenix, Arizona

Krina Patel, MD, MSc
Associate Professor
Department of Lymphoma/Myeloma
The University of Texas
MD Anderson Cancer Center
Houston, Texas

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TO PRACTICE

Co-Moderators

Breast Cancer
Stephen “Fred” Divers, MD
American Oncology Network
Hot Springs, Arkansas

CLL and Lymphomas
Jeanna L Knoble, MD
Zangmeister Cancer Center
Columbus, Ohio

Genitourinary Cancers
Michael J Castine, MD
Hematology Oncology Clinic
Baton Rouge, Louisiana

Gastrointestinal Cancers
Pavani Ellipeddi, MD
Hematology Oncology Clinic
Baton Rouge, Louisiana

Multiple Myeloma
Taral Patel, MD
Zangmeister Cancer Center
Columbus, Ohio

Lung Cancer
Ram Trehan, MD
George Washington University
Silver Spring, Maryland

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TO PRACTICE

MODULE 3: Multiple Myeloma

Co-Moderator

Taral Patel, MD
Zangmeister Cancer Center
Columbus, Ohio

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RESEARCH
TO PRACTICE

Multiple Myeloma Agenda

Module 1: Up-Front Treatment of Multiple Myeloma (MM)

- Current role of stem cell transplant
- Quadruplet regimens
- Use of maintenance therapy after transplant; clinical role of MRD
- Treatment of MM in transplant-ineligible patients

Module 2: Management of Relapsed/Refractory MM

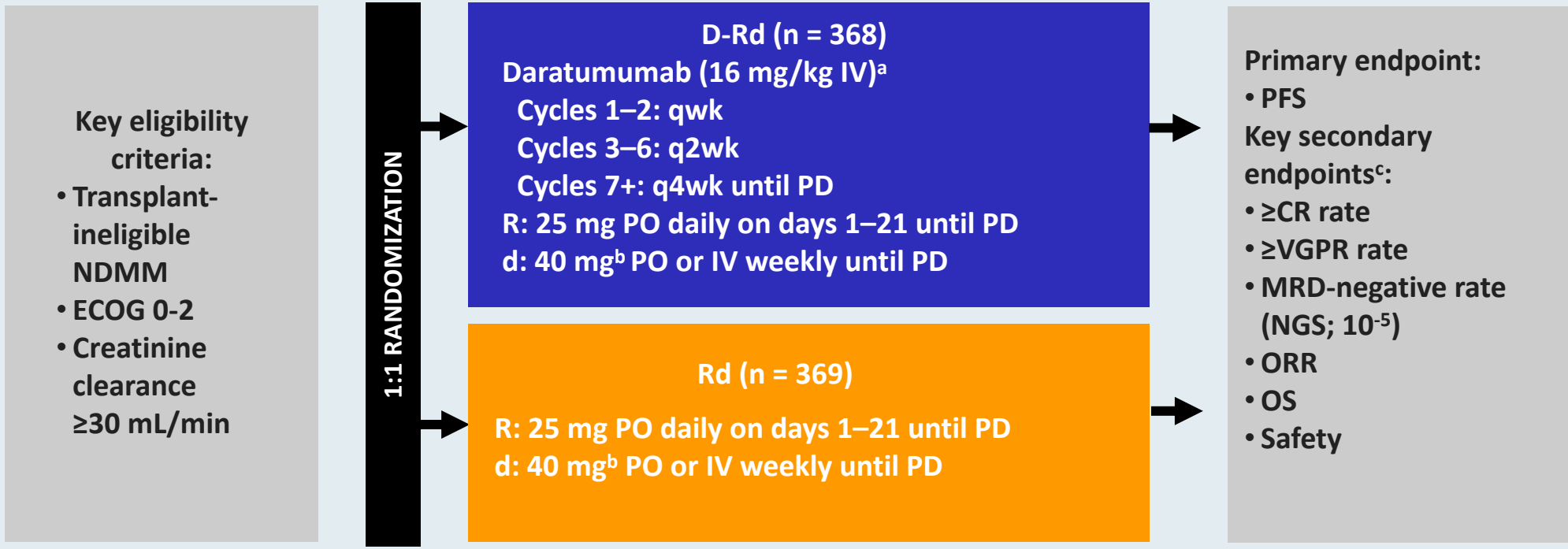
Module 3: Other Novel Agents and Strategies

Daratumumab, lenalidomide, and dexamethasone versus lenalidomide and dexamethasone alone in newly diagnosed multiple myeloma (MAIA): overall survival results from a randomised, open-label, phase 3 trial

Thierry Facon, Shaji K Kumar, Torben Plesner, Robert Z Orlowski, Philippe Moreau, Nizar Bahlis, Supratik Basu, Hareth Nahi, Cyrille Hulin, Hang Quach, Hartmut Goldschmidt, Michael O'Dwyer, Aurore Perrot, Christopher P Venner, Katja Weisel, Joseph R Mace, Noopur Raje, Mourad Tiab, Margaret Macro, Laurent Frenzel, Xavier Leleu, Tahamtan Ahmadi, Jianping Wang, Rian Van Rampelbergh, Clarissa M Uhlar, Brenda Tromp, Maria Delioukina, Jessica Vermeulen, Saad Z Usmani

***Lancet Oncol* 2021;22(11):1582-96.**

MAIA: Phase III Trial Design



Stratification factors:
- **ISS (I vs II vs III)**
- **Region (NA vs other)**
- **Age (<75 vs ≥75 years)**

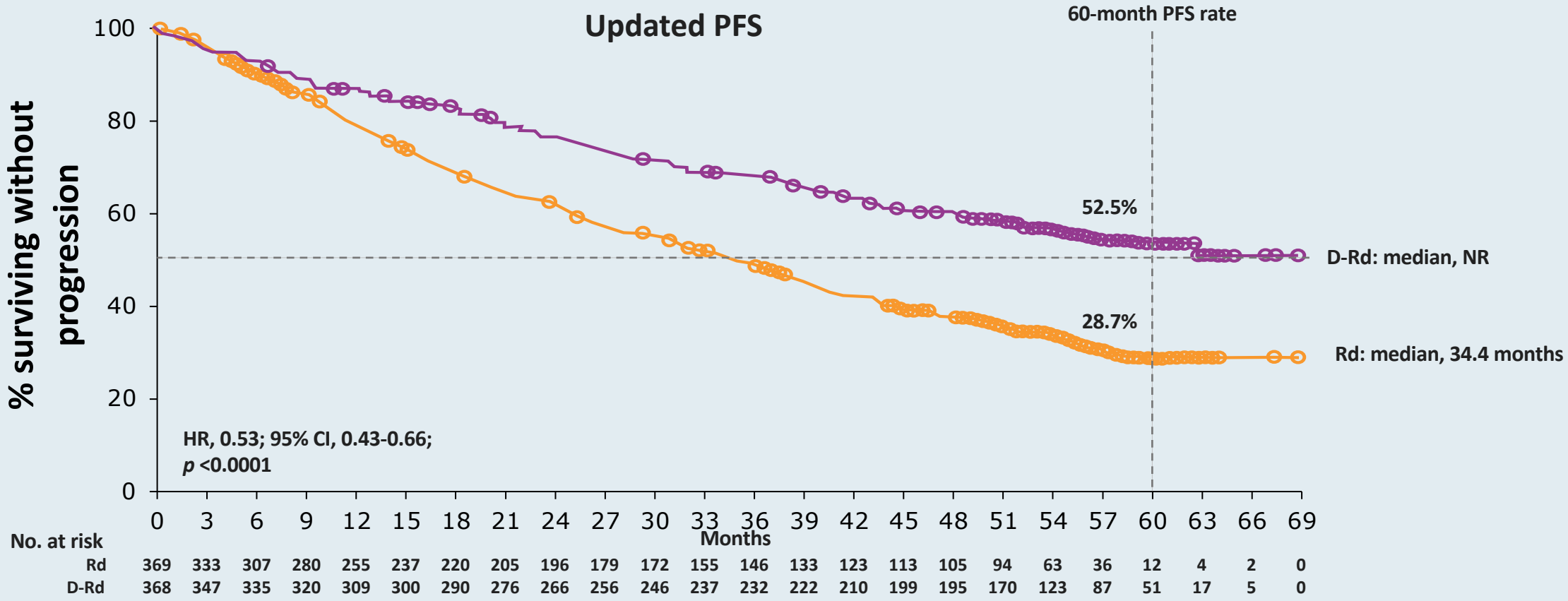
Cycle: 28 days

[a] On days when daratumumab was administered, dexamethasone was administered to patients in the D-Rd arm and served as the treatment dose of steroid for that day, as well as the required preinfusion medication.
[b] For patients older than 75 years or with BMI <18.5, dexamethasone was administered at a dose of 20 mg weekly.
[c] Efficacy endpoints were sequentially tested in the order shown.

NDMM = newly diagnosed multiple myeloma; D-Rd = daratumumab with lenalidomide and dexamethasone; PD = disease progression; PFS = progression-free survival; CR = complete response; VGPR = very good partial response; MRD = minimal residual disease; OS = overall survival

Facon T et al. *Lancet Oncol* 2021;22(11):1582-96; EHA 2021;Abstract LB1901.

MAIA: Progression-Free Survival
New 60-Month Data

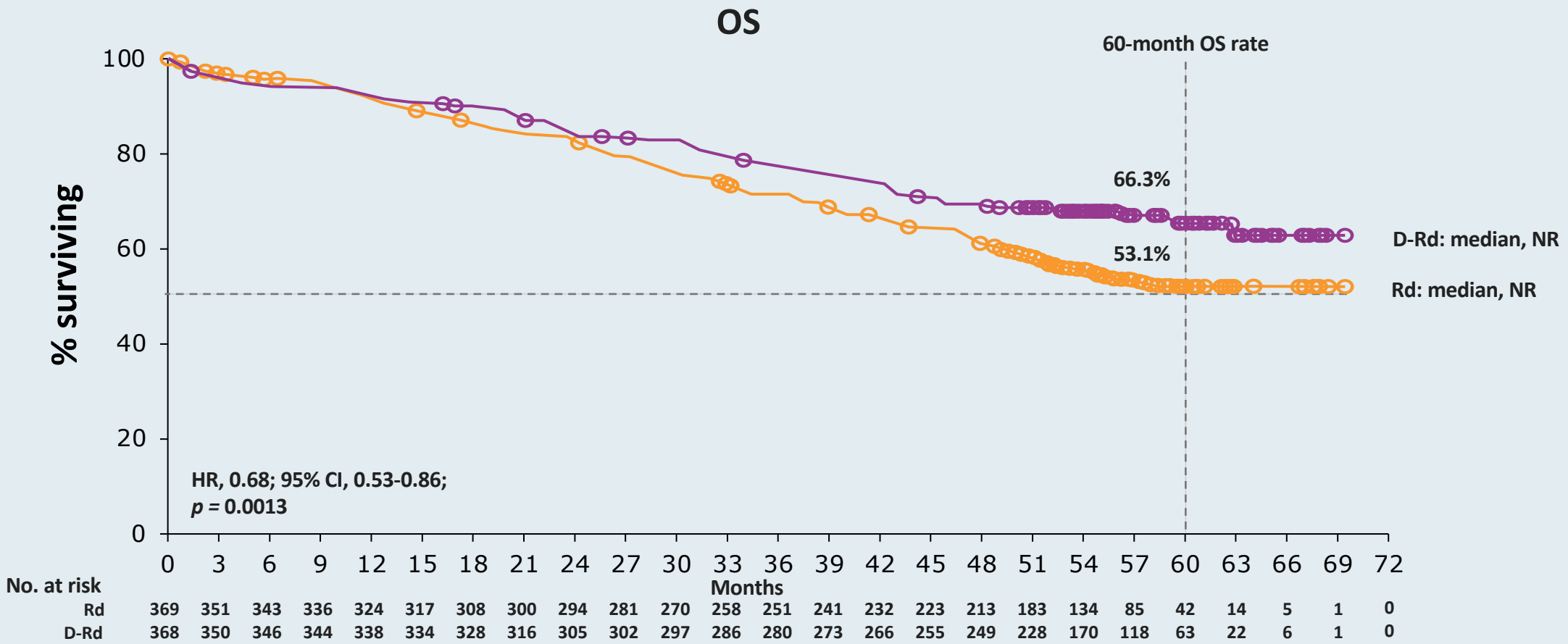


- D-Rd continued to demonstrate a significant PFS benefit, with median PFS not reached with D-Rd
  - These data provide a new PFS benchmark for patients with NDMM who are transplant ineligible

NR = not reached; HR = hazard ratio

Facon T et al. *Lancet Oncol* 2021;22(11):1582-96; EHA 2021;Abstract LB1901.

MAIA: Overall Survival

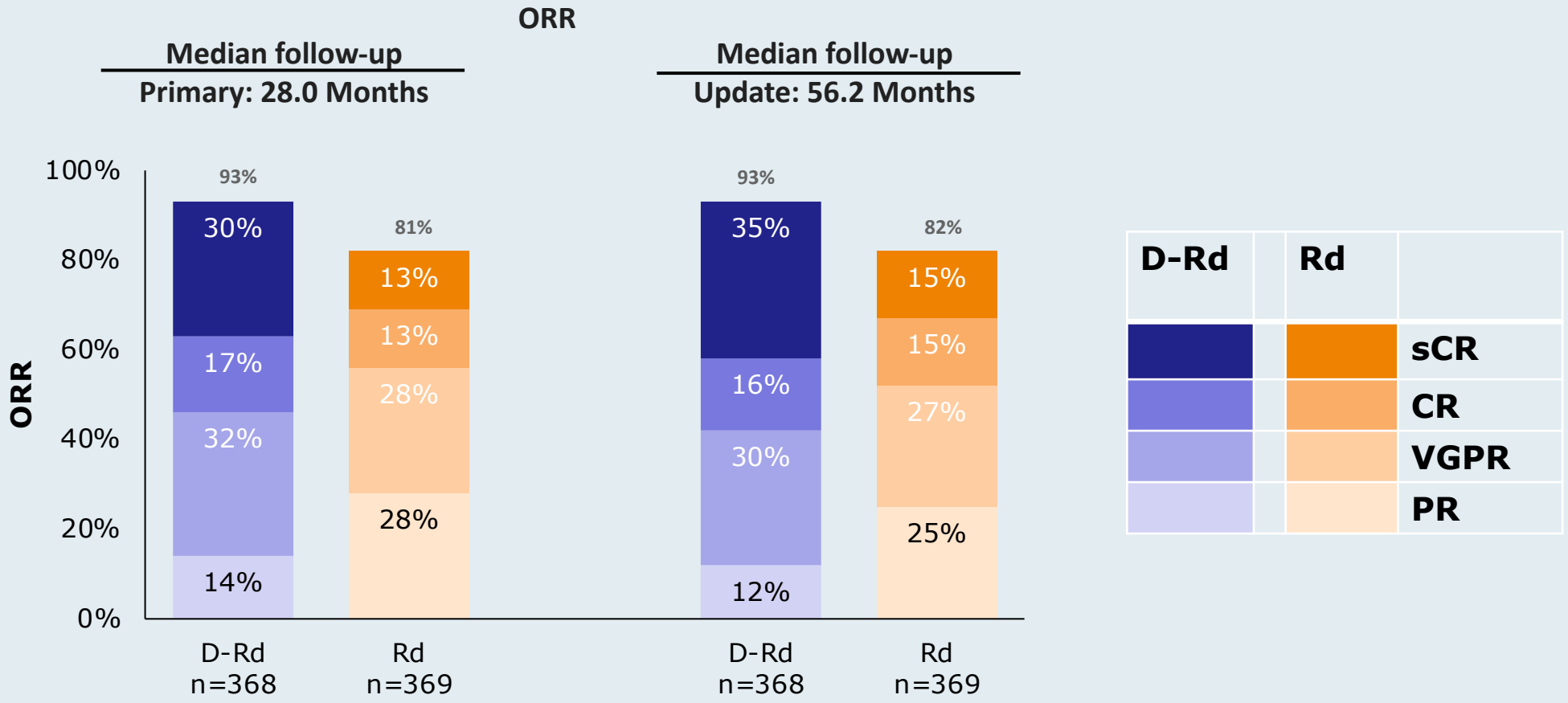


D-Rd demonstrated a significant benefit in OS, with a 32% reduction in the risk of death, for patients with NDMM who are transplant ineligible

Facon T et al. *Lancet Oncol* 2021;22(11):1582-96; EHA 2021;Abstract LB1901.

RTP RESEARCH TO PRACTICE

MAIA: Updated Overall Response Rate (ITT Population)



- D-Rd induced deeper responses with significantly higher rates of ≥CR and ≥VGPR, compared with Rd
  - With >28 months of additional follow-up, responses deepened with continued DARA therapy

sCR = stringent complete response; VGPR = very good partial response

Falcon T et al. *N Engl J Med* 2019:380(22):2104-15; EHA 2021;Abstract LB1901.

2022 ASCO® ANNUAL MEETING

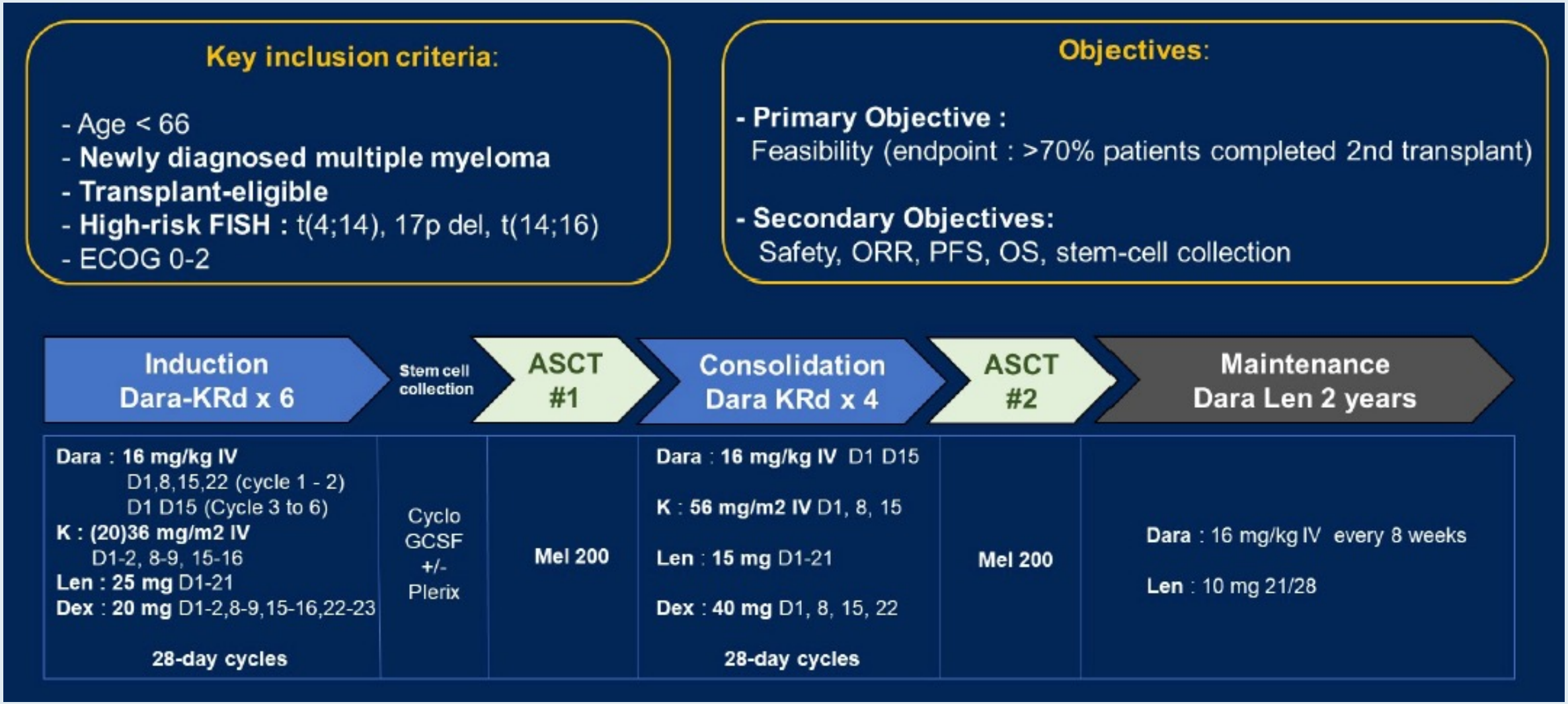
Abstract 8002

Daratumumab Carfilzomib Lenalidomide and Dexamethasone as induction therapy in high-risk transplant eligible newly diagnosed myeloma patients: results of the phase 2 study IFM 2018-04

Cyrille Touzeau[1], Aurore Perrot[2], Cyrille Hulin[3], Salomon Manier[4], Margaret Macro[5], Marie-Lorraine Chretien[6], Lionel Karlin[7], Martine Escoffre[8], Caroline Jacquet[9], Mourad Tiab[10], Xavier Leleu[11], Lucie Planche[12], Hervé Avet-Loiseau[2], Philippe Moreau[1]

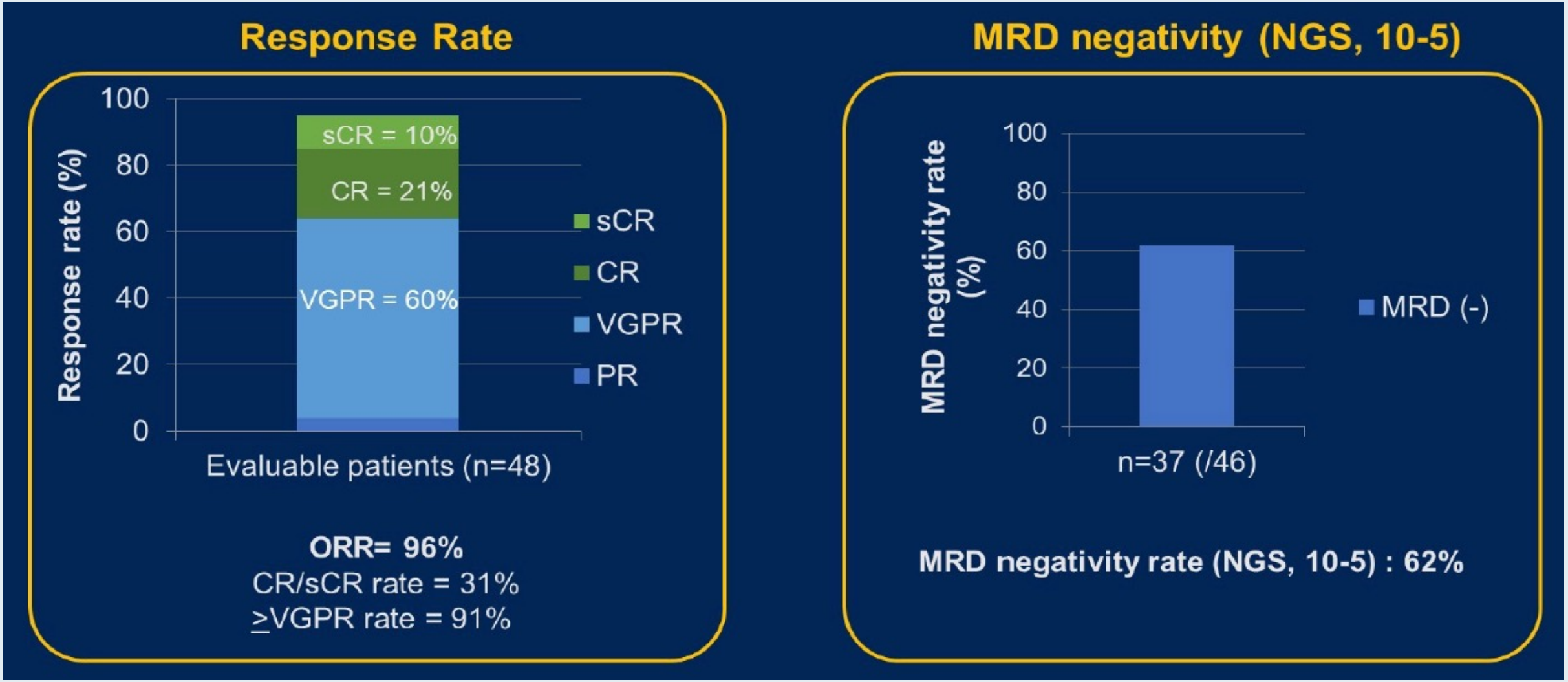
RTP RESEARCH TO PRACTICE

IFM 2018-04: Phase II Study Design



Touzeau C et al. ASCO 2022;Abstract 8002.

IFM 2018-04: Response Rates and MRD with Dara-KRd Induction



MRD = minimal residual disease; NGS = next-generation sequencing; ORR = overall response rate; sCR = stringent complete response; VGPR = very good partial response

Touzeau C et al. ASCO 2022;Abstract 8002.

RTP RESEARCH TO PRACTICE

IFM 2018-04: Safety of Dara-KRd Induction

Hematologic treatment related AE:

	Any grade N (%)	Grade 3/4 N (%)
Neutropenia	22 (44%)	20 (40%)
Anemia	14 (28%)	7 (14%)
Thrombocytopenia	13 (26%)	4 (8%)

AE leading to treatment discontinuation (n=2)
- COVID-19 infection (n=1)
- tumor lysis syndrome (n=1)

Grade 3/4 infection (n=3)
- COVID 19 infection (n=1)
- CMV infection (n=1)
- Pseudomonas aeruginosa bacteremia (n=1)

Most common non hematologic treatment related AE:

	Any grade N (%)	Grade 3/4 N (%)
GI disorders	23 (46%)	2(4%)
Infection	20 (40%)	3 (6%)
Skin rash	8 (16%)	0
Deep-vein thrombosis	7 (14%)	3 (6%)
Peripheral neuropathy	6 (12%)	0
Hepatic cytolysis	4 (8%)	2 (4%)
Renal failure	3 (6%)	3 (6%)
Cardiac event	1 (2%)	0

Touzeau C et al. ASCO 2022;Abstract 8002.

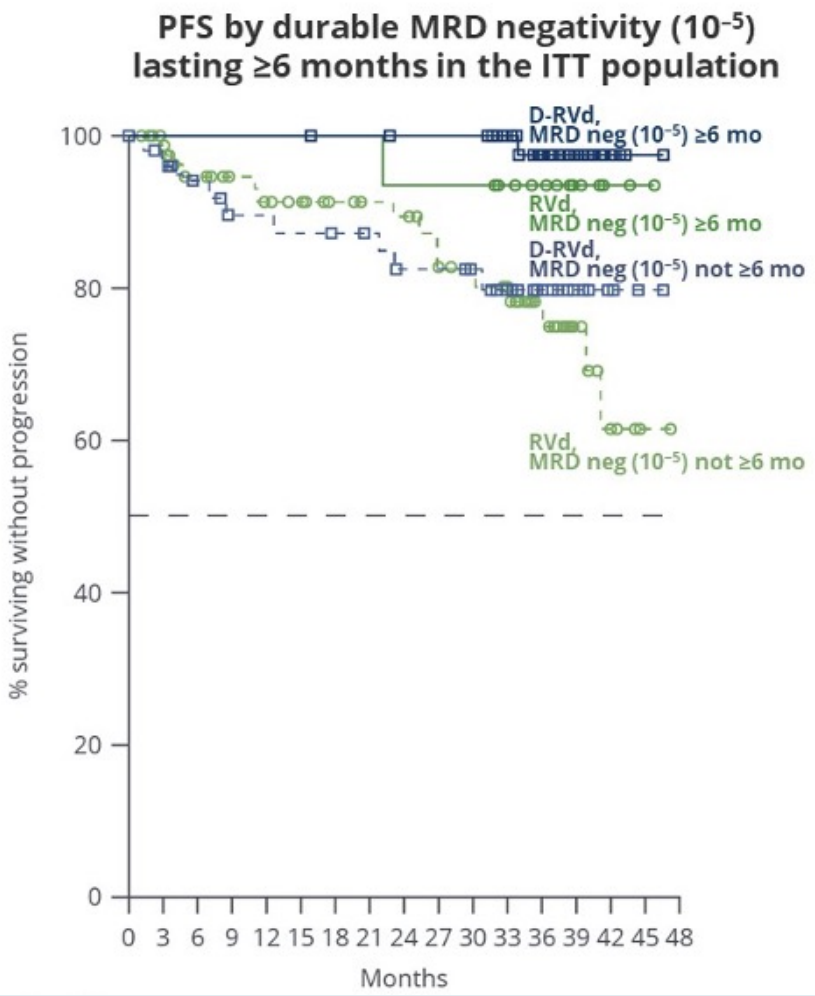
Daratumumab (DARA) plus Lenalidomide, Bortezomib, and Dexamethasone (RVd) in Patients (Pts) with Transplant-Eligible Newly Diagnosed Multiple Myeloma (NDMM): Updated Analysis of Griffin After 24 Months of Maintenance[1]

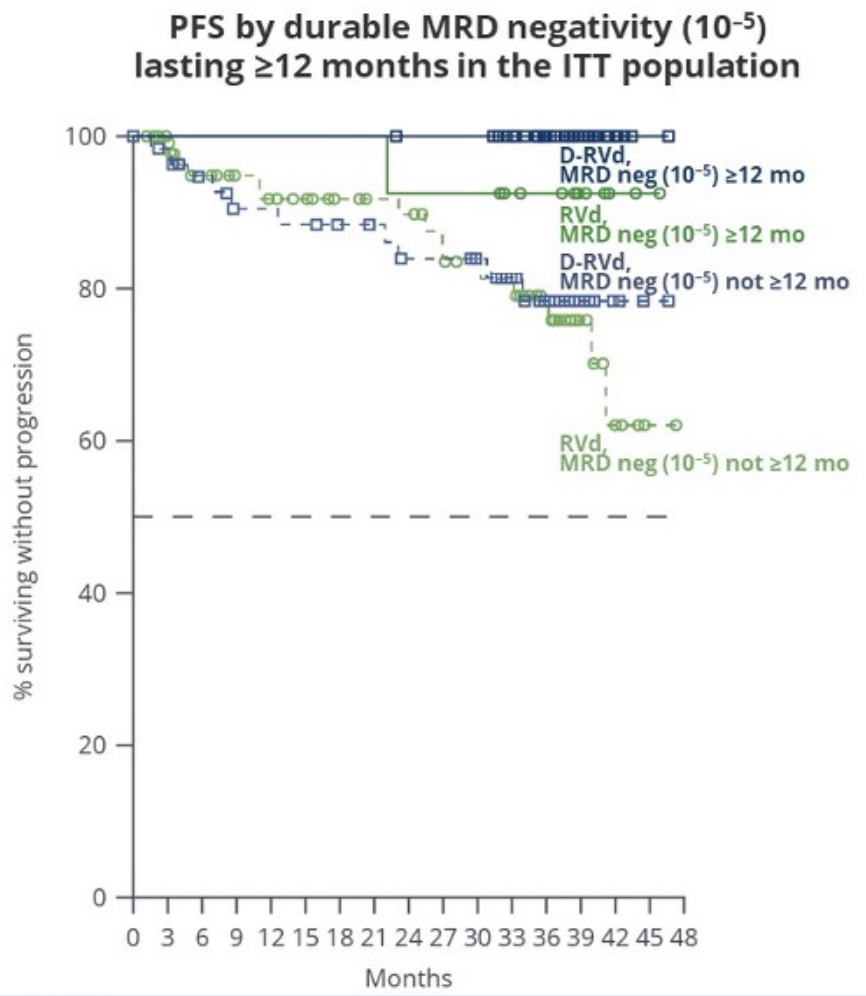
Daratumumab (DARA) + Lenalidomide, Bortezomib, and Dexamethasone (RVd) in Transplant-Eligible Newly Diagnosed Multiple Myeloma (NDMM): A Post Hoc Analysis of Sustained Minimal Residual Disease (MRD) Negativity from GRIFFIN[2]

[1] Laubach JP et al. ASH 2021;Abstract 79.

[2] Rodriguez C et al. ASCO 2022;Abstract 8011.

GRIFFIN: PFS by Sustained MRD Negativity





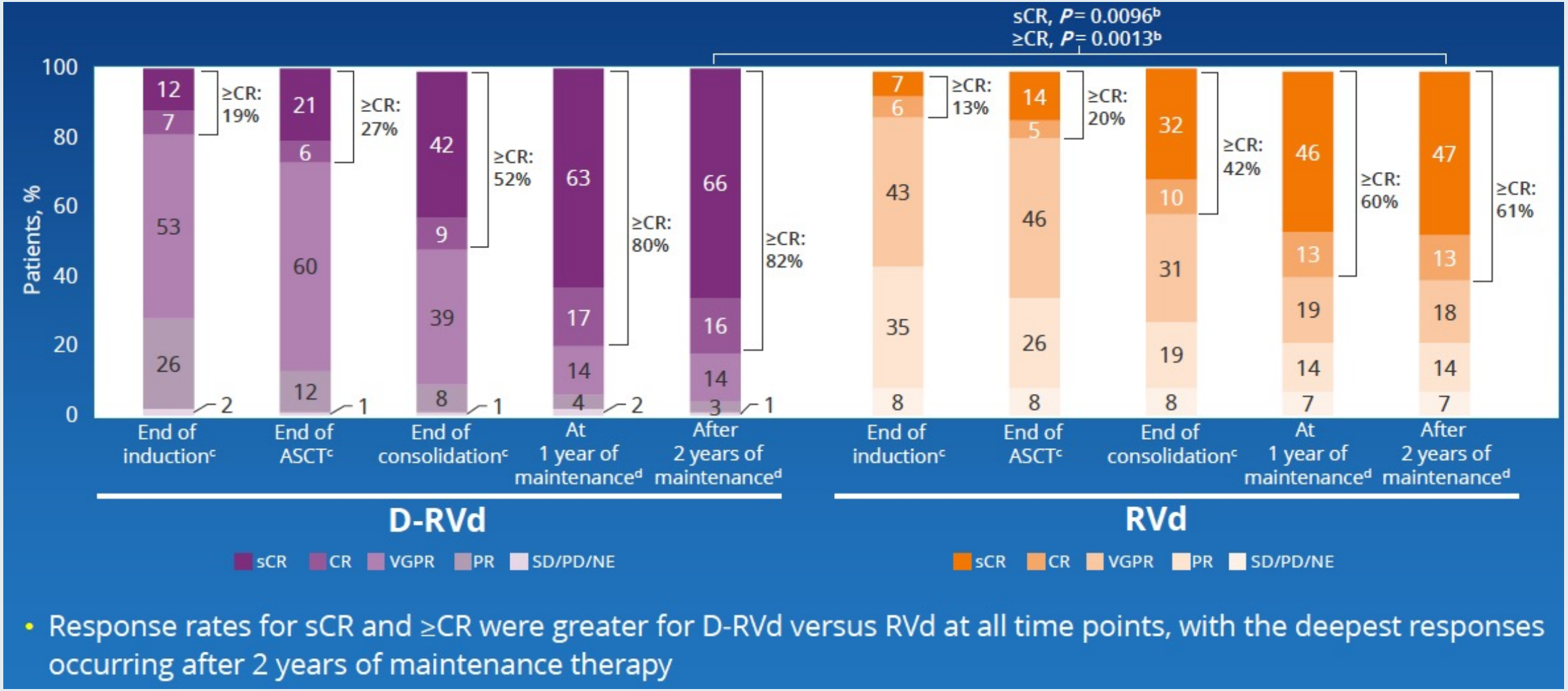
- PFS was better in the D-RVd group versus the RVd group among patients who achieved durable MRD negativity at the 10^{-5} threshold
- PFS was better for patients who reached durable MRD negativity ≥6 or ≥12 months versus those who did not reach durable MRD negativity

PFS = progression-free survival; MRD = minimum residual disease; ITT = intent to treat; D-RVd = daratumumab with lenalidomide, bortezomib and dexamethasone

Rodriguez C et al. ASCO 2022;Abstract 8011.

RTP RESEARCH TO PRACTICE

GRIFFIN: Updated Analysis After 24 Months of Maintenance Therapy

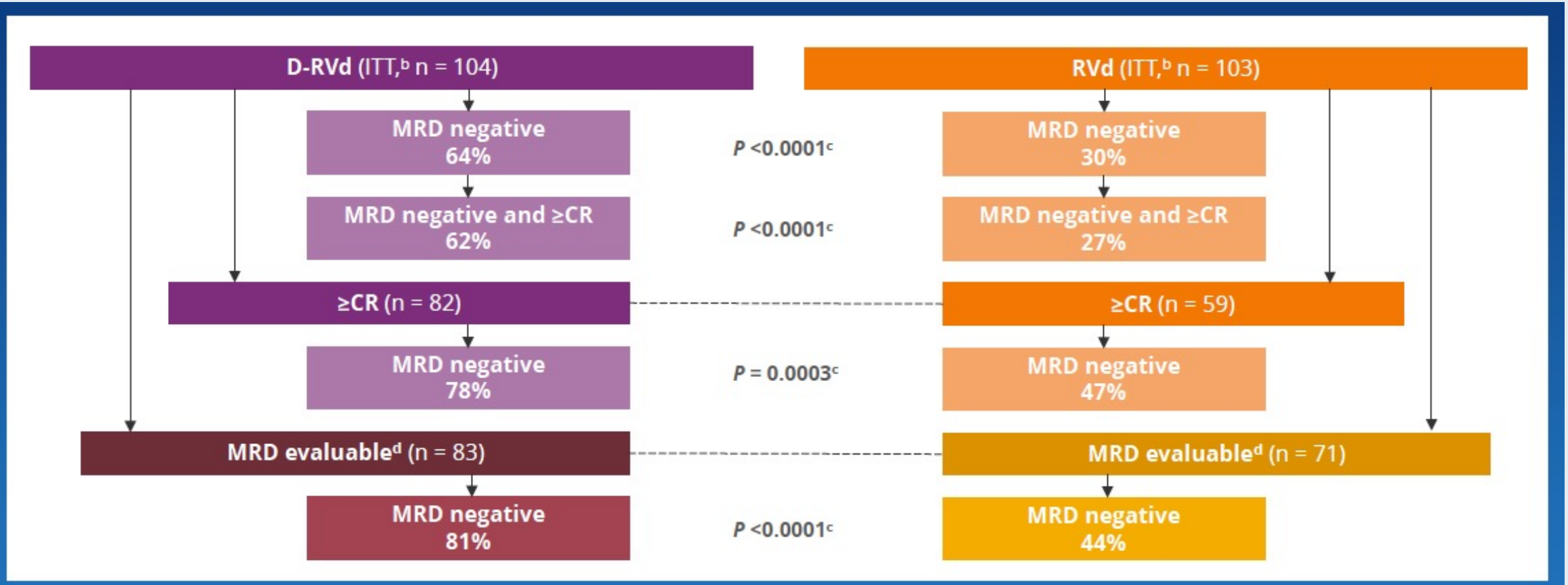


- Response rates for sCR and ≥CR were greater for D-RVd versus RVd at all time points, with the deepest responses occurring after 2 years of maintenance therapy

Laubach JP et al. ASH 2021;Abstract 79.

RTP RESEARCH TO PRACTICE

GRIFFIN: MRD Negativity (10^{-5}) After 2 Years of Maintenance Therapy

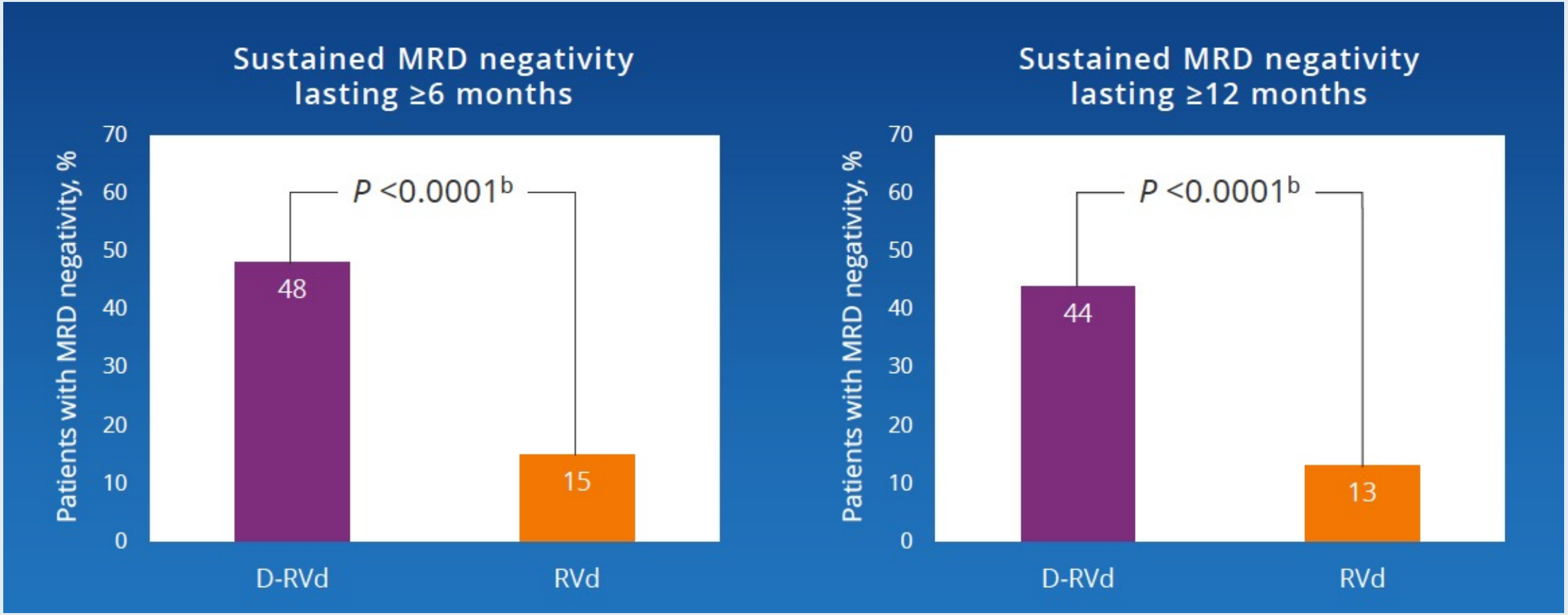


- Similarly, MRD-negativity (10^{-6}) rates favored D-RVd versus RVd in the ITT population (36% vs 15%, respectively; *P* = 0.0007), as well as among patients who achieved ≥CR (43% vs 22%; *P* = 0.0121)

MRD = minimal residual disease

Laubach JP et al. ASH 2021;Abstract 79.

GRIFFIN: D-RVd Improved Rates of Durable MRD Negativity (10^{-5}) Lasting ≥6 Months or ≥12 Months versus RVd



Laubach JP et al. ASH 2021;Abstract 79.

RTP RESEARCH TO PRACTICE

GRIFFIN: Infections and SPMs with First Onset During Maintenance Therapy (Cycles 7+)

Patients with ≥1 infections in maintenance, n (%)	D-RVd (DR maintenance, n = 89)		RVd (R maintenance, n = 71)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Overall infections in maintenance	32 (36)	16 (18)	23 (32)	15 (21)
Most common (≥5%) infections[a]				
Upper respiratory tract infection	47 (53)	2 (2)	29 (41)	2 (3)
Pneumonia	14 (16)	6 (7)	11 (15)	9 (13)
Urinary tract infection	10 (11)	0	2 (3)	0
Sinusitis	9 (10)	0	7 (10)	0
Influenza	9 (10)	0	5 (7)	0
Nasopharyngitis	9 (10)	0	2 (3)	0
Bronchitis	7 (8)	1 (1)	5 (7)	1 (1)
Cellulitis	7 (8)	1 (1)	2 (3)	1 (1)

Patients with ≥1 SPM in maintenance, n (%)	D-RVd (DR maintenance, n = 89)	RVd (R maintenance, n = 71)
Total number of patients with SPMs in maintenance	4 (4)	3 (4)
Squamous cell carcinoma of skin	3 (3)	0
Basal cell carcinoma	2 (2)	0
Nasal cavity cancer	1 (1)	0
Squamous cell carcinoma	1 (1)	0
Breast cancer	1 (1)	0
Malignant melanoma in situ	0	1 (1)
Nodular melanoma	0	1 (1)
Uterine cancer	0	1 (1)

- Similar rates of any grade and grade 3/4 infections occurred for the D-RVd and RVd groups

SPM = second primary malignancy

Laubach JP et al. ASH 2021;Abstract 79.

RTP RESEARCH TO PRACTICE

2022 ASCO ANNUAL MEETING

Abstract LBA4

RVd ± ASCT and Lenalidomide Maintenance to Progression for NDMM

The Phase 3 DETERMINATION Trial

Paul G. Richardson, MD, RJ Corman Professor of Medicine, Harvard Medical School
Clinical Program Leader, Director of Clinical Research,
Jerome Lipper Multiple Myeloma Center, Dana-Farber Cancer Institute, Boston, MA

The NEW ENGLAND JOURNAL of MEDICINE

N Engl J Med 2022 Jul 14;387(2):132-47.

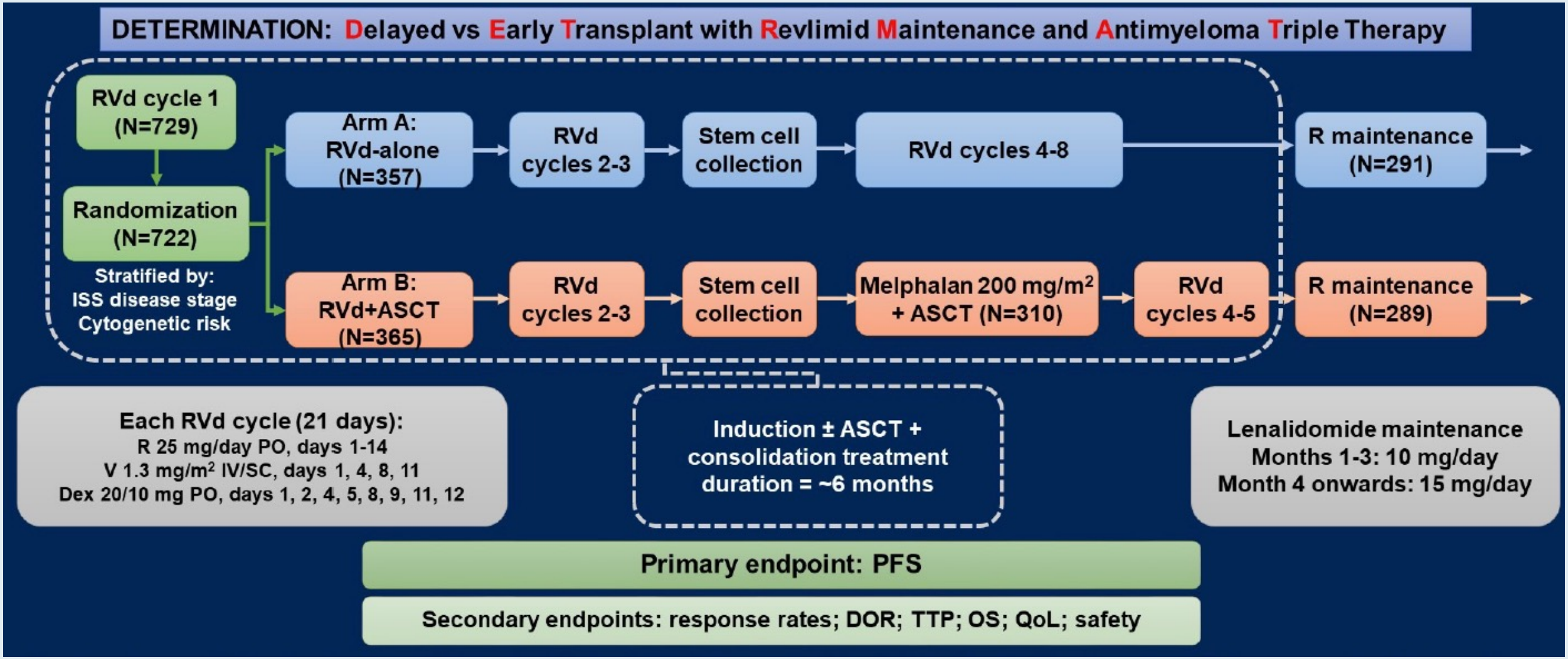
ORIGINAL ARTICLE

Triplet Therapy, Transplantation, and Maintenance until Progression in Myeloma

P.G. Richardson, S.J. Jacobus, E.A. Weller, H. Hassoun, S. Lonial, N.S. Raje, E. Medvedova, P.L. McCarthy, E.N. Libby, P.M. Voorhees, R.Z. Orlowski, L.D. Anderson, Jr., J.A. Zonder, C.P. Milner, C. Gasparetto, M.E. Agha, A.M. Khan, D.D. Hurd, K. Gowin, R.T. Kamble, S. Jagannath, N. Nathwani, M. Alsina, R.F. Cornell, H. Hashmi, E.L. Campagnaro, A.C. Andreescu, T. Gentile, M. Liedtke, K.N. Godby, A.D. Cohen, T.H. Openshaw, M.C. Pasquini, S.A. Giralt, J.L. Kaufman, A.J. Yee, E. Scott, P. Torka, A. Foley, M. Fulciniti, K. Hebert, M.K. Samur, K. Masone, M.E. Maglio, A.A. Zeytoonjian, O. Nadeem, R.L. Schlossman, J.P. Laubach, C. Paba-Prada, I.M. Ghobrial, A. Perrot, P. Moreau, H. Avet-Loiseau, M. Attal, K.C. Anderson, and N.C. Munshi, for the DETERMINATION Investigators*

RTP RESEARCH TO PRACTICE

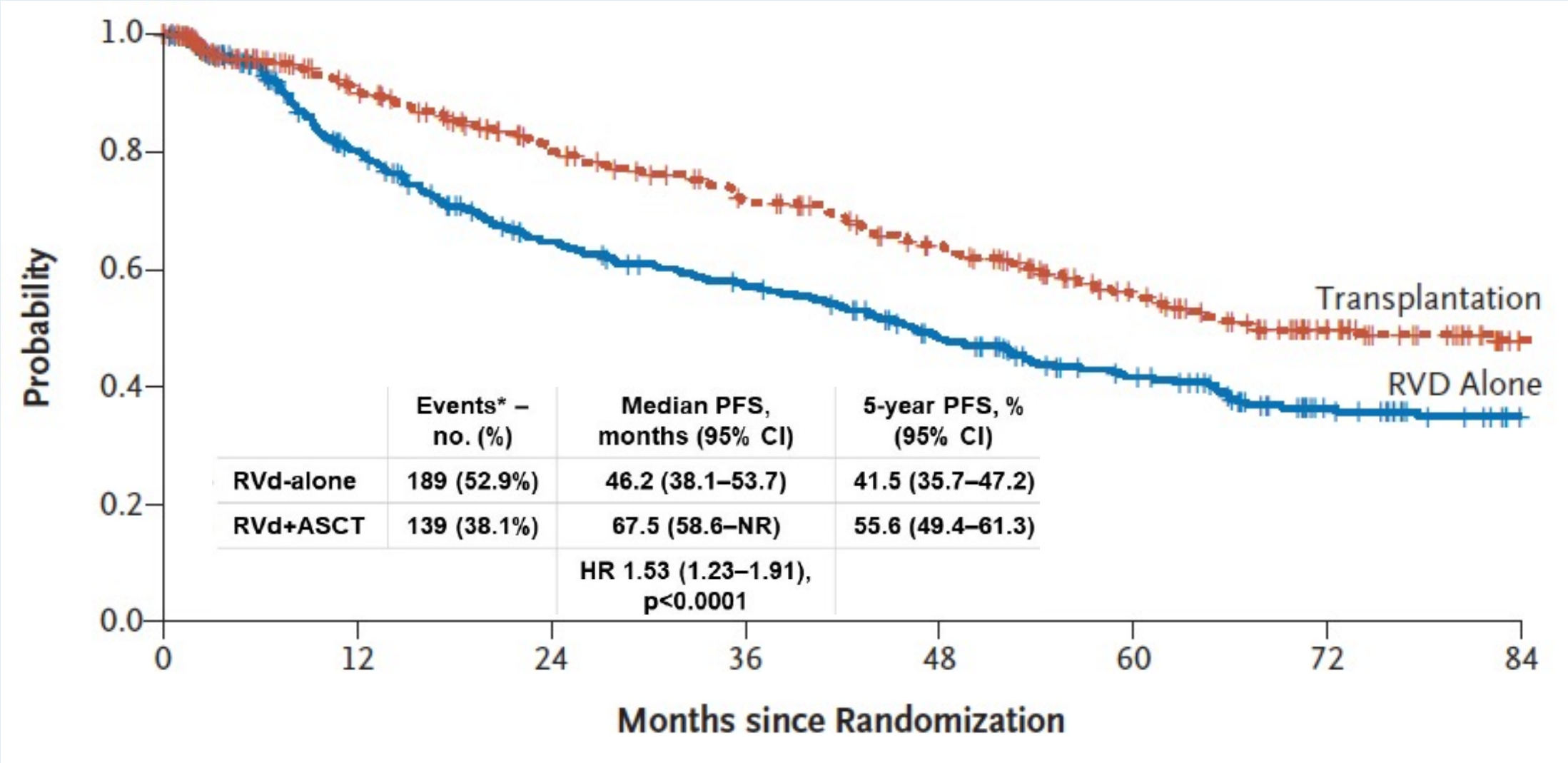
DETERMINATION: Phase III Study Design and Patient Disposition



RVd = lenalidomide, bortezomib, and dexamethasone; ASCT = autologous stem cell transplant

Richardson PG et al. *N Engl J Med* 2022;387(2):132-47; ASCO 2022;Abstract LBA4.

DETERMINATION: Progression-Free Survival (Primary Endpoint)

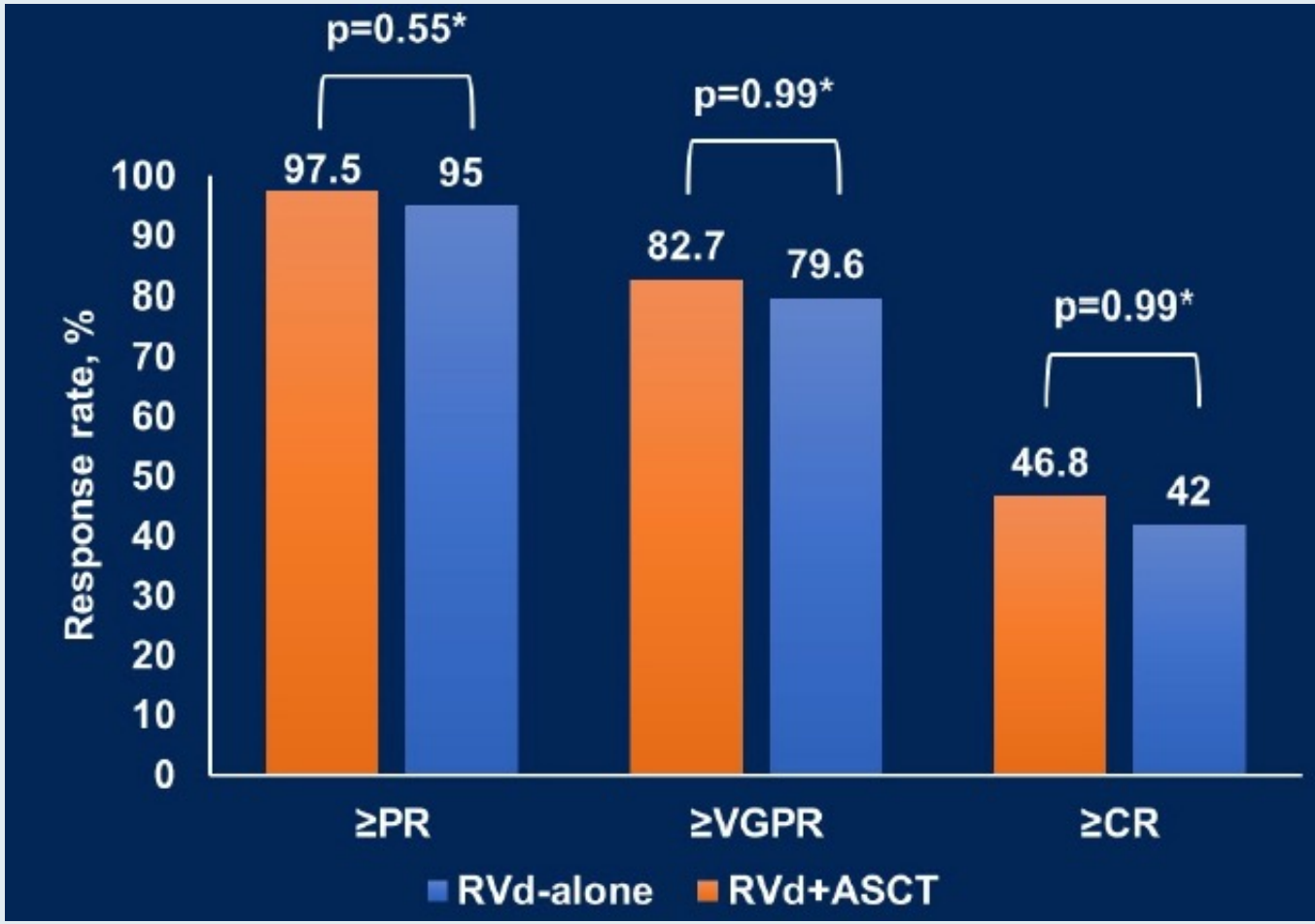


	Events* – no. (%)	Median PFS, months (95% CI)	5-year PFS, % (95% CI)
RVd-alone	189 (52.9%)	46.2 (38.1–53.7)	41.5 (35.7–47.2)
RVd+ASCT	139 (38.1%)	67.5 (58.6–NR)	55.6 (49.4–61.3)
		HR 1.53 (1.23–1.91), p<0.0001	

Richardson PG et al. *N Engl J Med* 2022;387(2):132-47; ASCO 2022;Abstract LBA4.

RTP RESEARCH TO PRACTICE

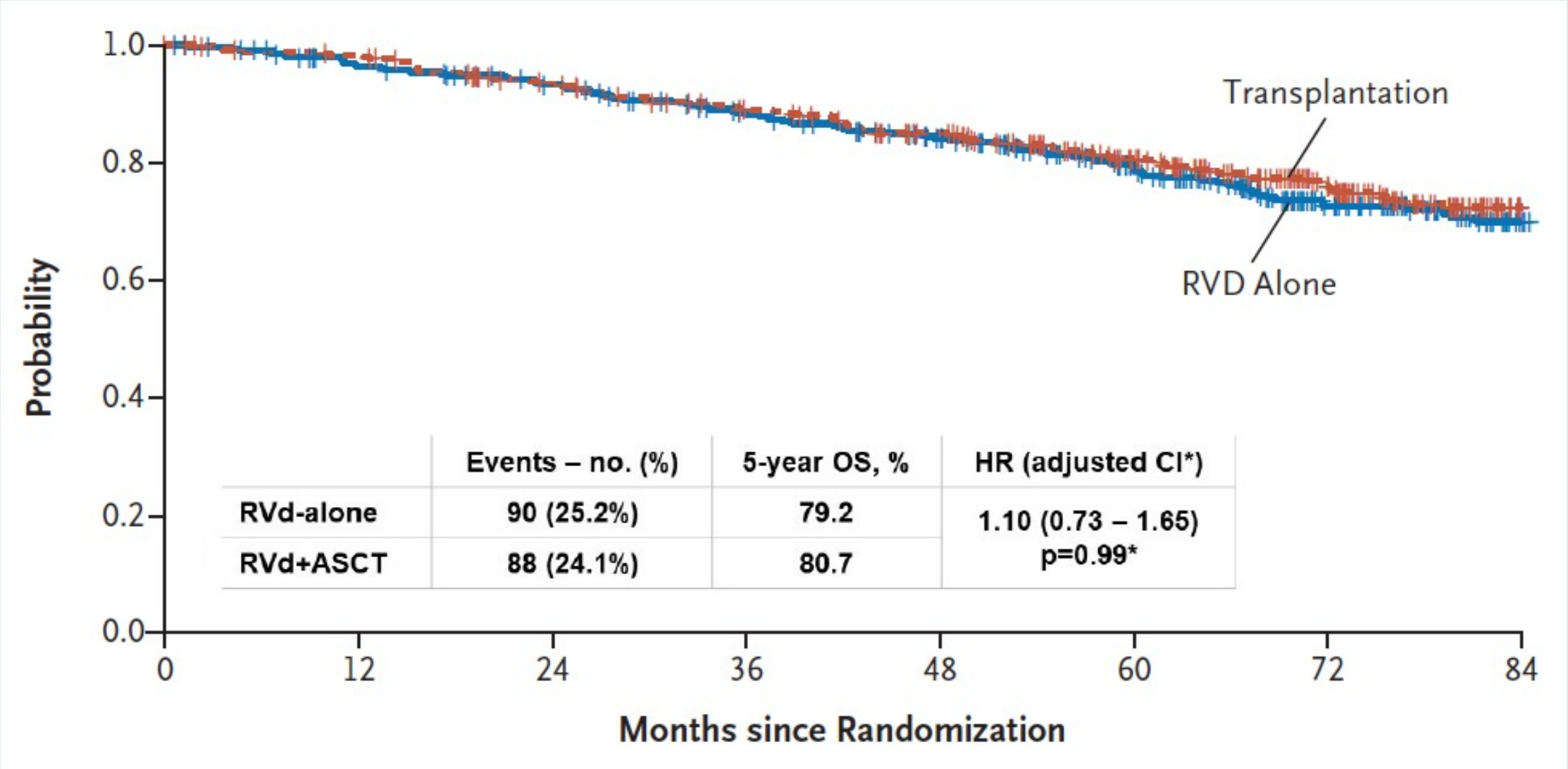
DETERMINATION: Best Response to Treatment and Duration of Response



Duration of response	RVd-alone	RVd+ASCT
Median duration of ≥PR, months	38.9	56.4
	HR 1.45 (Adjusted CI* 1.09–1.93), p=0.003*	
5-year duration of ≥CR, %	52.9	60.6
	HR 1.35 (Adjusted CI* 0.83–2.22), p=0.698*	

Richardson PG et al. *N Engl J Med* 2022;387(2):132-47; ASCO 2022;Abstract LBA4.

DETERMINATION: Overall Survival (Key Secondary Endpoint)



	Events – no. (%)	5-year OS, %	HR (adjusted CI*)
RVd-alone	90 (25.2%)	79.2	1.10 (0.73 – 1.65) p=0.99*
RVd+ASCT	88 (24.1%)	80.7	

Richardson PG et al. *N Engl J Med* 2022;387(2):132-47; ASCO 2022;Abstract LBA4.

DETERMINATION: Grade ≥3 Treatment-Related Adverse Events (AEs)

AE, %	RVd-alone (N=357)	RVd+ASCT (N=365)
Any	78.2	94.2
Any hematologic	60.5	89.9
Any grade 5 (fatal) AE	0.3	1.6 *
Neutropenia	42.6	86.3
Thrombocytopenia	19.9	82.7
Leukopenia	19.6	39.7
Anemia	18.2	29.6
Lymphopenia	9.0	10.1
Febrile neutropenia	4.2	9.0
Diarrhea	3.9	4.9
Nausea	0.6	6.6
Mucositis oral	0	5.2
Fatigue	2.8	6.0
Fever	2.0	5.2
Pneumonia	5.0	9.0
Hypophosphatemia	9.5	8.2
Neuropathy	5.6	7.1

- Rates of all grade ≥3 and of hematologic grade ≥3 treatment-related AEs during all treatment significantly higher with RVd + ASCT (both p<0.001)
  - Rates hematologic grade ≥3 treatment-related AEs during maintenance: 26.1% vs 41.9%
- Related SAEs:
  - Prior to maintenance: 40.3% vs 47.1%
  - During maintenance: 11.3% vs 16.6%

Richardson PG et al. *N Engl J Med* 2022;387(2):132-47; ASCO 2022;Abstract LBA4.

2022 ASCO ANNUAL MEETING

THE UNIVERSITY OF CHICAGO

Polish Myeloma Consortium

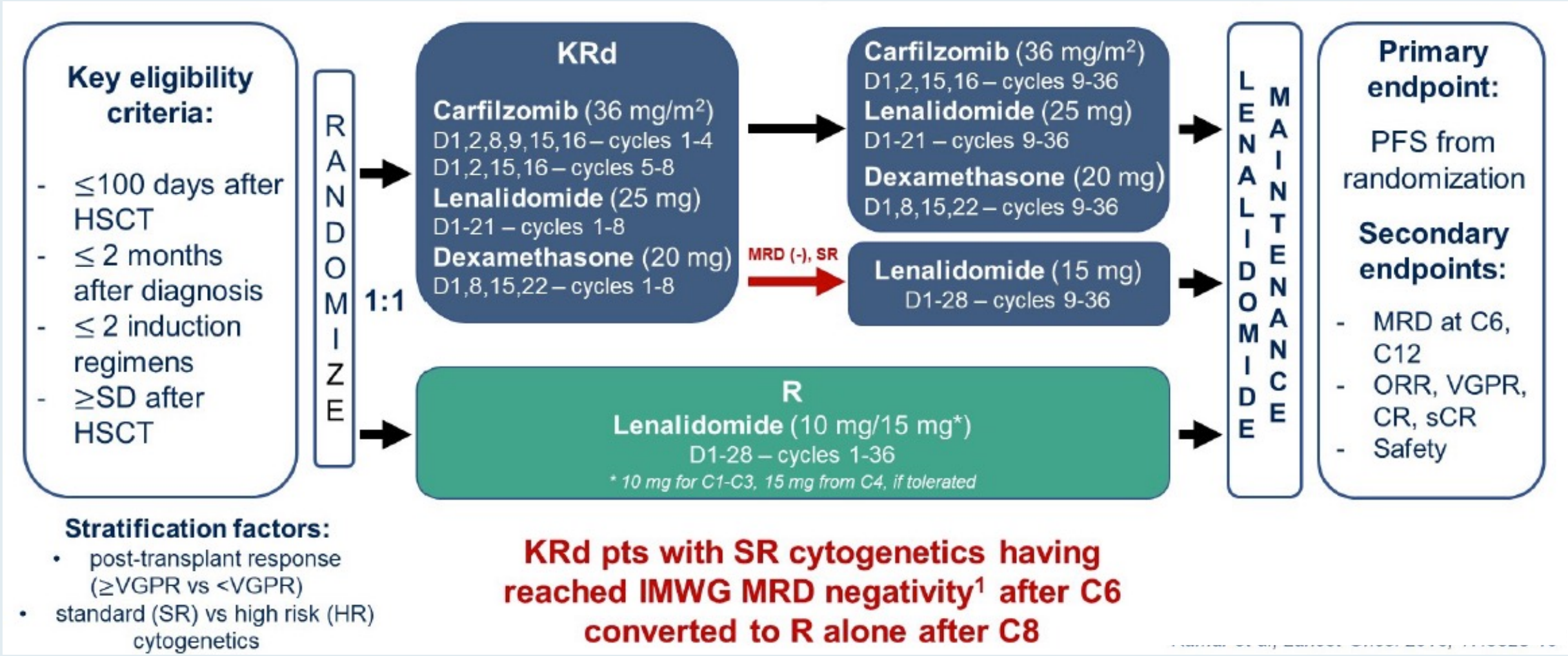
Abstract 8001

ATLAS: A Phase 3 Randomized Trial of Carfilzomib, Lenalidomide, and Dexamethasone Versus Lenalidomide Alone After Stem-cell Transplant for Multiple Myeloma

Dominik Dytfeld, Tomasz Wrobel, Krzysztof Jamroziak, Tadeusz Kubicki, Pawel Robak, Jaroslaw Czyz, Agata Tyczyńska, Agnieszka Druzd-Sitek, Krzysztof Giannopoulos, Adam Nowicki, Anna Łojko-Dankowska, Magdalena Matuszak, Lidia Gil, Bartosz Puła, Justyna Rybka, Lidia Usnarska-Zubkiewicz, Olga Czabak, Andrew T Stefka, Benjamin A Derman, Andrzej J Jakubowiak

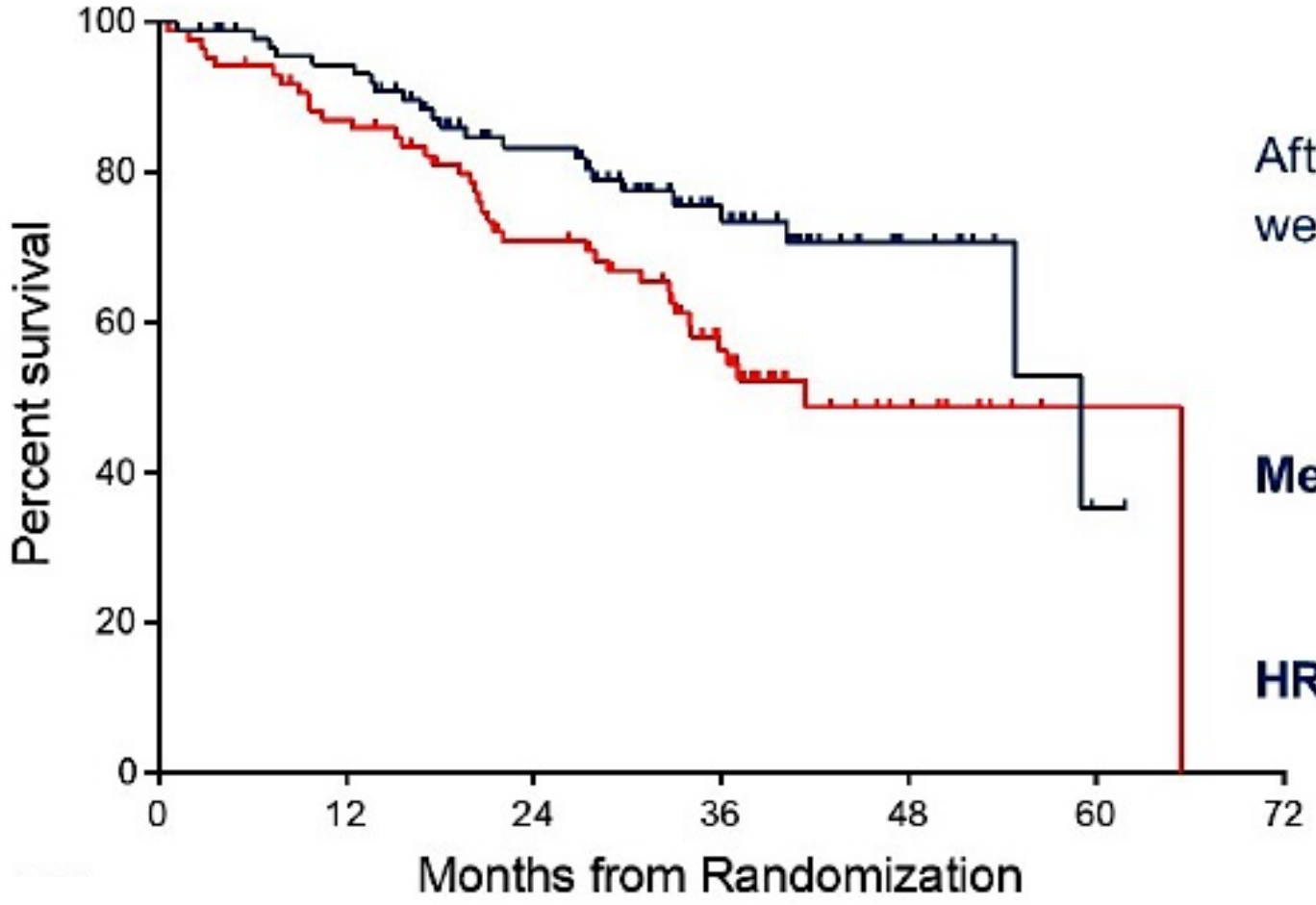
RTP RESEARCH TO PRACTICE

ATLAS: Phase III Study Design



Dytfeld D et al. ASCO 2022;Abstract 8001.

ATLAS Primary Endpoint: Progression-Free Survival (PFS)



After median follow-up of 33.8 months there were **61 PFS events:**

- **23 in the KRd arm**
- **38 in the R arm**

Median PFS:

KRd 59.0 months (95% CI 52.5-NR)

R 41.1 months (95% CI 33.4-65.4)

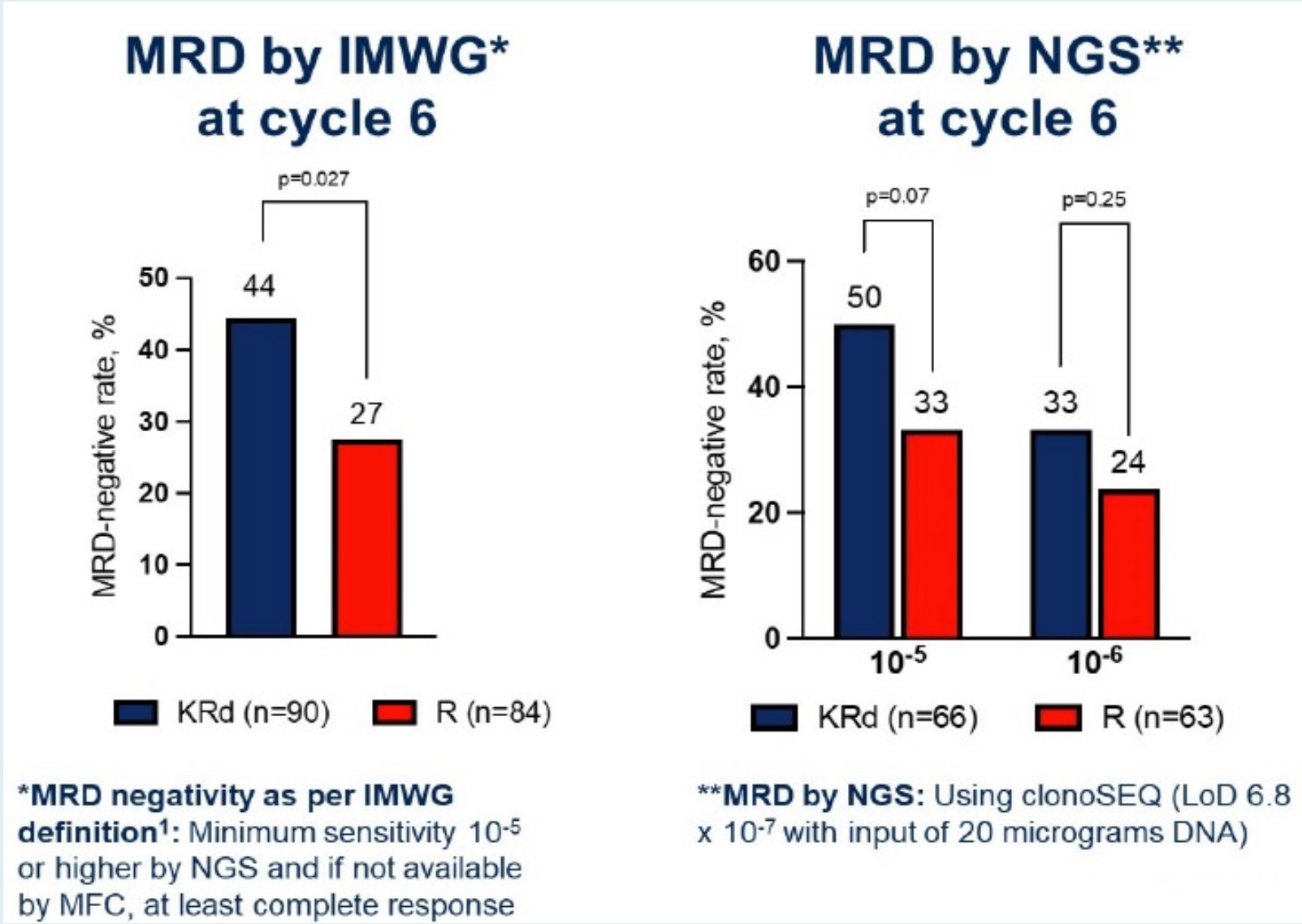
HR 0.56 (95% CI 0.34-0.93); **p=0.026**

KRd = carfilzomib, lenalidomide and dexamethasone; R = lenalidomide alone

Dytfeld D et al. ASCO 2022;Abstract 8001.

RTP RESEARCH TO PRACTICE

ATLAS: Minimal Residual Disease (MRD)



KRd = carfilzomib, lenalidomide and dexamethasone; R = lenalidomide alone

Dytfeld D et al. ASCO 2022;Abstract 8001.

RTP RESEARCH TO PRACTICE

ATLAS: Adverse Events

Adverse Events (Grade 3+), n (%)	KRd n=92	R n=86
Hematological Toxicities		
Neutropenia	44 (48)	51 (59)
Febrile Neutropenia	4 (4)	5 (6)
Thrombocytopenia	12 (13)	6 (7)
Lymphopenia	7 (8)	2 (2)
Anemia	4 (4)	0 (0)
Toxicities of Particular Interest		
Cardiovascular	4 (4)	5 (6)
Infection	14 (15)	5 (6)
Secondary malignancy	2 (2)	2 (2)
Treatment-related death	1 (1)	0 (0)
Other Toxicities (>1% of Pts)		
Elevated liver enzymes	5 (5)	0 (0)
Diarrhea	1 (1)	2 (2)
Neurological	1 (1)	2 (2)
Rash	1 (1)	2 (2)
Dental	1 (1)	1 (1)
Flu-like symptoms	1 (1)	1 (1)
Hyperglycemia	2 (2)	0 (0)
Hypokalemia	1 (1)	1 (1)
Cataract	1 (1)	1 (1)

KRd = carfilzomib, lenalidomide and dexamethasone; R = lenalidomide alone

Dytfeld D et al. ASCO 2022;Abstract 8001.

original reports

Ixazomib as Postinduction Maintenance for Patients With Newly Diagnosed Multiple Myeloma Not Undergoing Autologous Stem Cell Transplantation: The Phase III TOURMALINE-MM4 Trial

Meletios A. Dimopoulos, MD[1]; Ivan Špička, MD[2]; Hang Quach, MD[3]; Albert Oriol, MD[4]; Roman Hájek, MD[5]; Mamta Garg, MD[6]; Meral Beksac, MD[7]; Sara Bringhen, MD[8]; Eirini Katodritou, MD[9]; Wee-Joo Chng, MD[10]; Xavier Leleu, MD[11]; Shinsuke Iida, MD[12]; María-Victoria Mateos, MD[13]; Gareth Morgan, MD[14]; Alexander Vorog, MD[15]; Richard Labotka, MD[15]; Bingxia Wang, PhD[15]; Antonio Palumbo, MD[15]; and Sagar Lonial, MD[16]; on behalf of the TOURMALINE-MM4 study group

J Clin Oncol 2020;38(34):4030-41.

UNIVERSITÄTS KLINIKUM HEIDELBERG

Addition of Isatuximab to Lenalidomide, Bortezomib and Dexamethasone as Induction Therapy for Newly-Diagnosed, Transplant-Eligible Multiple Myeloma: The Phase III GMMG-HD7 Trial

Hartmut Goldschmidt[1,2], Elias K. Mai[1], Eva Nievergall[1], Roland Fenk[3], Uta Bertsch[1,2], Diana Tichy[4], Britta Besemer[5], Jan Dürig[6], Roland Schroers[7], Ivana von Metzler[8], Mathias Hänel[9], Christoph Mann[10], Anne Marie Asemissen[11], Bernhard Heilmeier[12], Stefanie Huhn[1], Katharina Kriegsmann[1], Niels Weinhold[1], Steffen Luntz[13], Tobias A. W. Holderried[14], Karolin Trautmann-Grill[15], Deniz Gezer[16], Maika Klaiber-Hakimi[17], Martin Müller[18], Cyrus Khandanpour[19], Wolfgang Knauf[20], Markus Munder[21], Thomas Geer[22], Hendrik Riesenberg[23], Jörg Thomalla[24], Martin Hoffmann[25], Marc-Steffen Raab[1], Hans J. Salwender[26], Katja C. Weisel[11] for the German-speaking Myeloma Multicenter Group (GMMG)

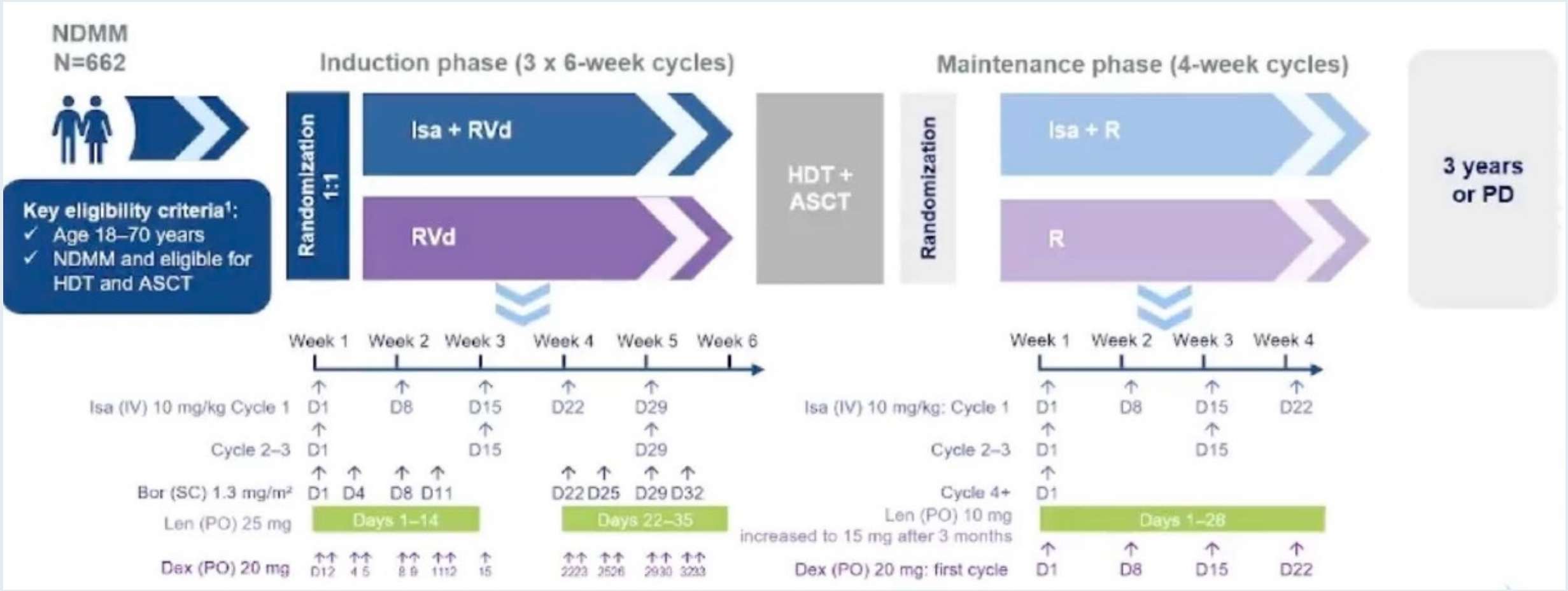
[1]Department of Internal Medicine V, University Hospital Heidelberg, Heidelberg, Germany; [2]National Center for Tumor Diseases Heidelberg, Heidelberg, Germany; [3]Department of Hematology, Oncology and Clinical Immunology, University Hospital Düsseldorf, Düsseldorf, Germany; [4]Division of Biostatistics, German Cancer Research Center (DKFZ) Heidelberg, Heidelberg, Germany; [5]Department of Internal Medicine II, University Hospital Tübingen, Tübingen, Germany; [6]Department for Hematology and Stem Cell Transplantation, University Hospital Essen, Essen, Germany; [7]Medical Clinic, University Hospital Bochum, Bochum, Germany; [8]Department of Medicine, Hematology/Oncology, University Hospital Frankfurt, Goethe University, Frankfurt am Main, Germany; [9]Department of Internal Medicine III, Clinic Chemnitz, Chemnitz, Germany; [10]Department for Hematology, Oncology and Immunology, University Hospital Gießen and Marburg, Marburg, Germany; [11]Department of Oncology, Hematology and BMT, University Medical Center Hamburg-Eppendorf, Hamburg, Germany; [12]Clinic for Oncology and Hematology, Hospital Barmherzige Brueder Regensburg, Regensburg, Germany; [13]Coordination Centre for Clinical Trails (KKS) Heidelberg, Heidelberg, Germany; [14]Department of Oncology, Hematology, Immuno-Oncology and Rheumatology, University Hospital Bonn, Bonn, Germany; [15]Department of Internal Medicine I, University Hospital Dresden, Dresden, Germany; [16]Department of Hematology, Oncology, Hemostaseology, and Stem Cell Transplantation, Faculty of Medicine, RWTH Aachen University, Aachen, Germany; [17]Clinic for Hematology, Oncology and Palliative Care, Marien Hospital Düsseldorf, Düsseldorf, Germany; [18]Clinic for Hematology, Oncology and Immunology, Klinikum Siloah Hannover, Hannover, Germany; [19]Medical Clinic A, University Hospital Münster, Münster, Germany; [20]Center for Hematology and Oncology Bethanien, Frankfurt am Main, Germany; [21]Department of Internal Medicine III, University Hospital Mainz, Mainz, Germany; [22]Department of Internal Medicine III, Diakoneo Clinic Schwäbisch-Hall, Schwäbisch-Hall, Germany; [23]Hematology/Oncology Center, Bielefeld, Germany; [24]Hematology / Oncology Center, Koblenz, Germany; [25]Medical Clinic A, Clinic Ludwigshafen, Ludwigshafen, Germany; [26]Asklepios Tumorzentrum Hamburg, AK Altona and AK St. Georg, Hamburg, Germany

ASH 2021; Final Abstract Code: 463

UK HD

RTP RESEARCH TO PRACTICE

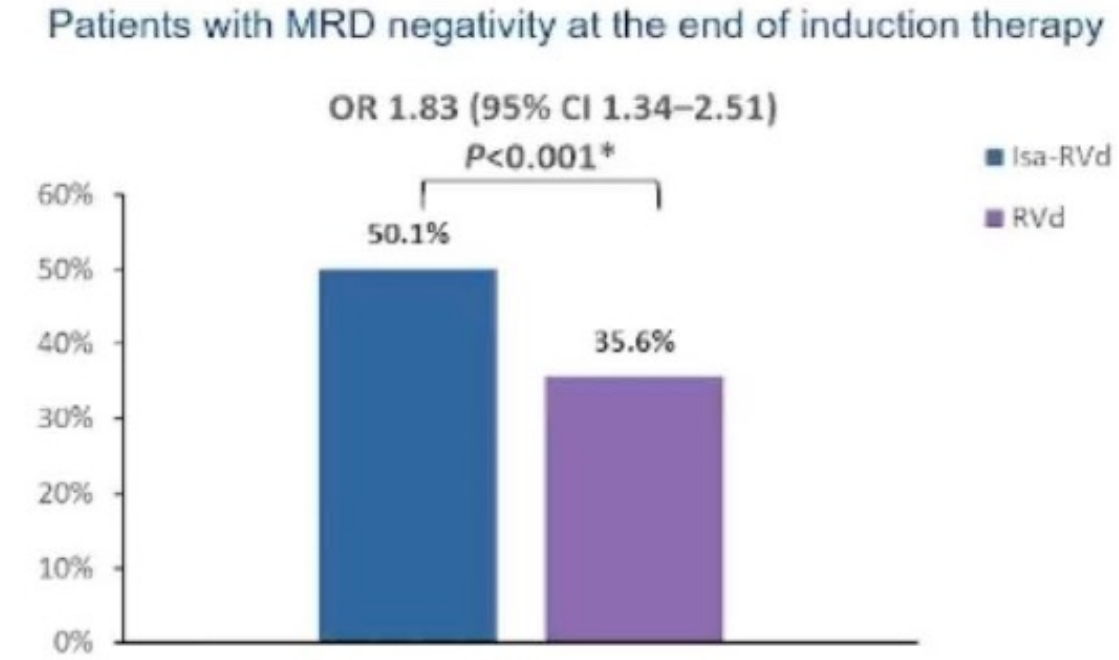
GMMG-HD7 Phase III Trial Design



Goldschmidt H et al. ASH 2021;Abstract 463.

RTP RESEARCH TO PRACTICE

GMMG-HD7: MRD Negativity at End of Induction Therapy



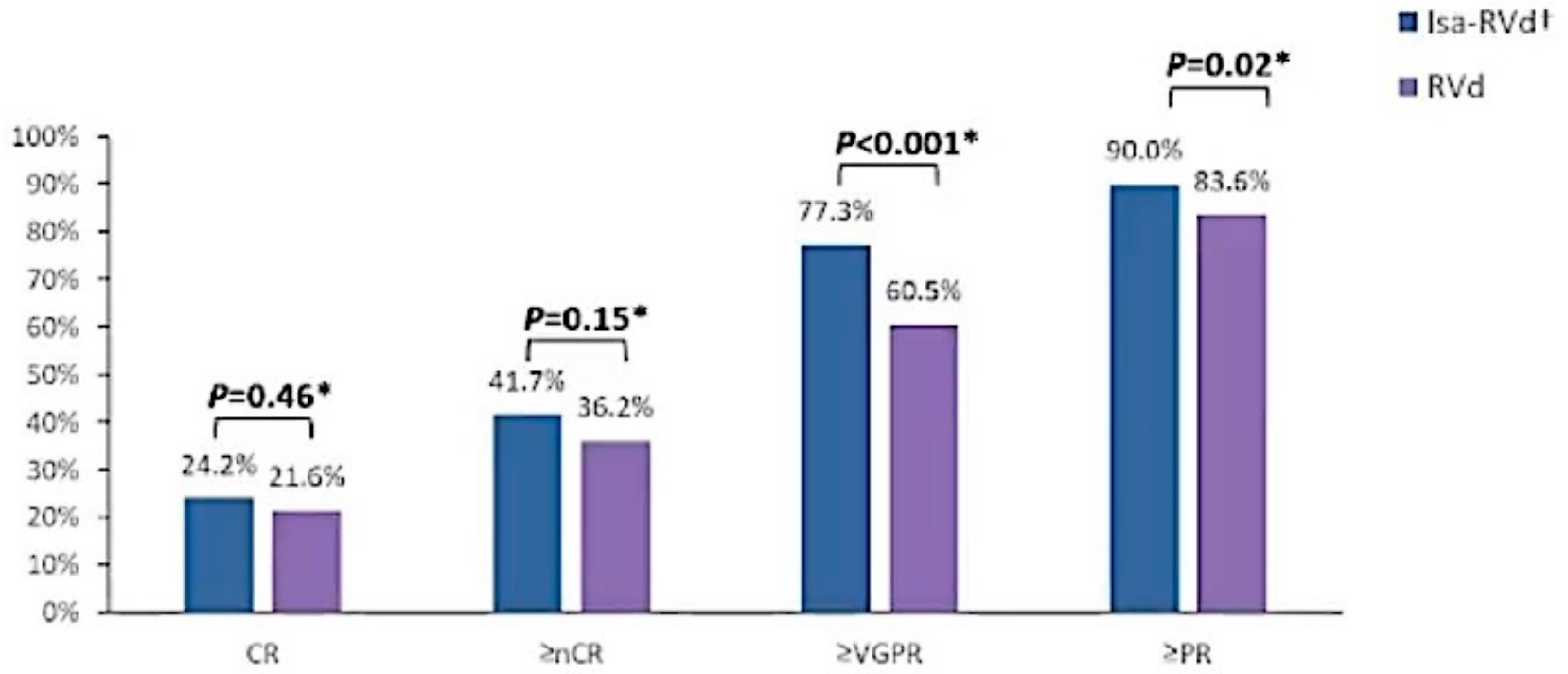
Low number of not assessable/missing† MRD status: Isa-RVd (10.6%) and RVd (15.2%)

Isa-RVd is the first regimen to demonstrate a rapid and statistically significant benefit from treatment by reaching a MRD negativity of 50.1% at the end of induction and to show superiority vs. RVd in a Phase 3 trial

Goldschmidt H et al. ASH 2021;Abstract 463.

RTP RESEARCH TO PRACTICE

GMMG-HD7: Response Rates After Induction Therapy



Although the rates of CR after induction therapy did not differ between the Isa-RVd and RVd arms, there was a significant increase in ≥VGPR rates and ORR with Isa-RVd

Goldschmidt H et al. ASH 2021;Abstract 463.

RTP RESEARCH TO PRACTICE

GMMG-HD7: Safety Profile

AEs CTCAE grade ≥3, n (%)	Isa-RVd (n=330)	RVd (n=328)
Any AE	210 (63.6)	201 (61.3)
Any serious AE (any grade)	115 (34.8)	119 (36.3)
Deaths	4 (1.2)	8 (2.4)
Investigations* (SOC)	79 (23.9)	77 (23.5)
Blood and lymphatic system disorders (SOC)	85 (25.8)	55 (16.8)
Infections and infestations (SOC)	43 (13.0)	34 (10.4)
Nervous system disorders (SOC)	28 (8.5)	33 (10.1)
Gastrointestinal disorders (SOC)	27 (8.2)	31 (9.5)
Metabolism and nutrition disorders (SOC)	12 (3.6)	26 (7.9)

AEs CTCAE grade ≥3, n (%)	Isa-RVd (n=330)	RVd (n=328)
Specific hematologic AE (PT)		
Leukocytopenia/Neutropenia†	87 (26.4)	30 (9.1)
Lymphopenia	48 (14.5)	65 (19.8)
Anemia	13 (3.9)	20 (6.1)
Thrombocytopenia	21 (6.4)	15 (4.6)
Specific non-hematologic AE (PT)		
Peripheral neuropathy	25 (7.6)	22 (6.7)
Thromboembolic events	5 (1.5)	9 (2.7)
Infusion-related reactions‡	4 (1.2)	NA

A comparable number of patients discontinued induction therapy due to AEs in the Isa-RVd arm vs. RVd arm

AE = adverse event

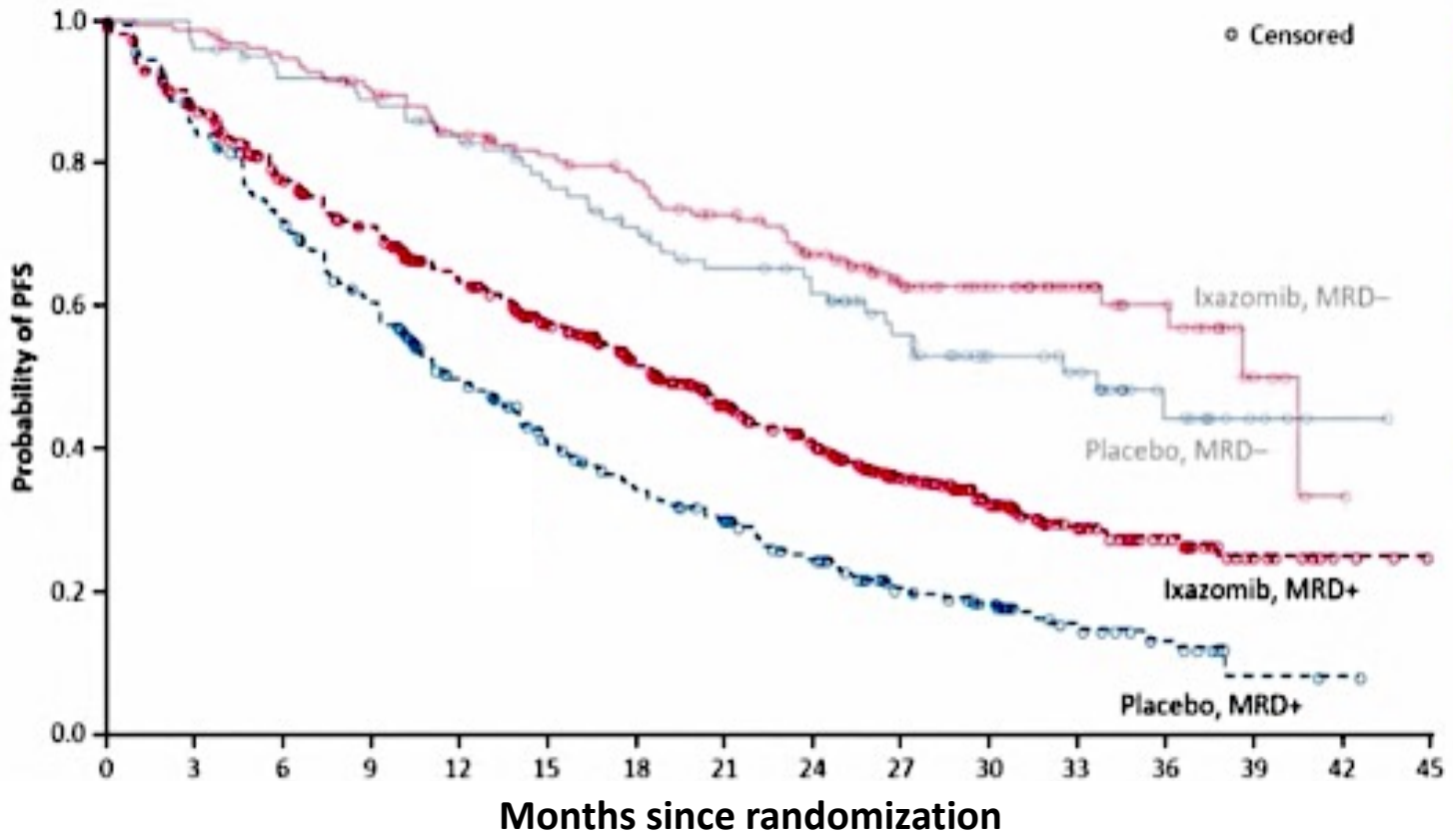
Goldschmidt H et al. ASH 2021;Abstract 463.

Measurable Residual Disease (MRD) Evaluation During Ixazomib (Ixa) Maintenance in Newly Diagnosed Multiple Myeloma (NDMM): A Large Analysis of 1280 Patients (Pts) Enrolled in TOURMALINE-MM3 and -MM4

Paiva B et al.

ESMO 2021;Abstract S184.

Pooled Analysis of TOURMALINE-MM3 and MM4: PFS for Patients with MRD at Screening



MRD+ patients	n	Events	24-month PFS, %	Median PFS, months
Ixazomib	606	351	40.7	18.8
Placebo	412	298	24.3	11.6
HR 0.651, 95% CI 0.554–0.764, p<0.001				

- There was no significant difference in PFS between ixazomib and placebo among patients who were MRD– at screening

Paiva B et al. ESMO 2021;Abstract S184.

RTP RESEARCH TO PRACTICE

Pooled Analysis of TOURMALINE-MM3 and MM4 Conclusions

This large dataset demonstrated that the prognostic value of MRD status at the start of maintenance can be enhanced by measuring MRD kinetics during treatment

Our results support the achievement and sustainability of MRD negativity as a treatment endpoint in the maintenance setting

We demonstrated poor outcomes in patients converting from MRD– to MRD+ status and those who had persistent MRD+ status, underscoring the value of serial MRD assessments to anticipate relapse and guide treatment decisions

Accordingly, ixazomib showed significant PFS benefit versus placebo in patients who were MRD+ at screening and in patients with persistent MRD+ status, highlighting the value of maintenance treatment with ixazomib in NDMM patients with MRD+ status

Paiva B et al. EHA 2021;Abstract S184.

Multiple Myeloma Agenda

Module 1: Up-Front Treatment of Multiple Myeloma (MM)

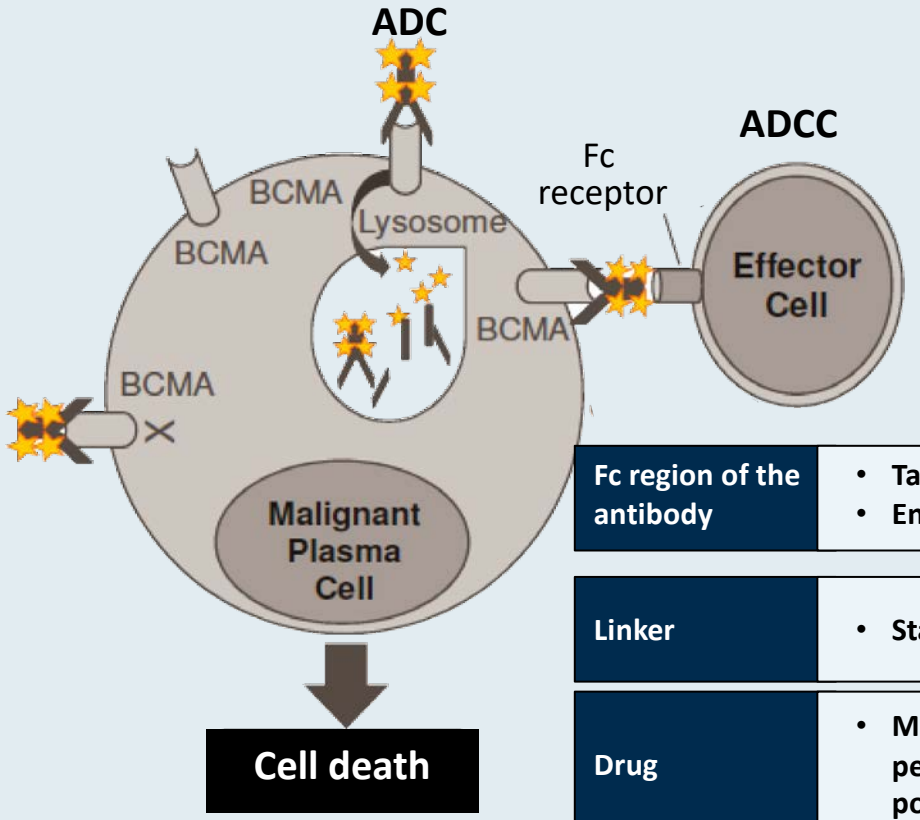
Module 2: Management of Relapsed/Refractory MM

- Belantamab mafodotin: Mechanism of action (MOA), sequencing for younger and older patients, toxicity
- CAR T-cell therapy: Idecabtegene vicleucel, ciltacabtagene autoleucel — Similarities and differences in efficacy and toxicity
- Bispecific antibodies (teclistamab, talquetamab): Similarities and differences in MOA; efficacy, toxicity, future clinical role

Module 3: Other Novel Agents and Strategies

Belantamab Mafodotin: Anti-BCMA Antibody-Drug Conjugate

- B-cell maturation factor (BCMA) expression is restricted to B cells at later stages of differentiation and is required for survival of plasma cells
- BCMA is broadly expressed at variable levels on malignant plasma cells
- Belantamab mafodotin is a humanized, afucosylated IgG1 anti-BCMA antibody conjugated to microtubule disrupting agent MMAF via a stable, protease-resistant maleimidocaproyl linker



Fc region of the antibody	• **Target specific** • **Enhanced ADCC**
Linker	• **Stable in circulation**
Drug	• **MMAF (non cell permeable, highly potent auristatin)**

Mechanisms of action:
- ADC mechanism
- ADCC mechanism
- Immunogenic cell death
- BCMA receptor signaling inhibition

Tai YT et al. *Blood* 2014;123(20):3128-38.

RTP RESEARCH TO PRACTICE

Longer Term Outcomes With Single-Agent Belantamab Mafodotin in Patients With Relapsed or Refractory Multiple Myeloma: 13-Month Follow-Up From the Pivotal DREAMM-2 Study

Sagar Lonial, MD [1]; Hans C. Lee, MD[2]; Ashraf Badros, MD [3]; Suzanne Trudel, MD[4]; Ajay K. Nooka, MD [1]; Ajai Chari, MD [5]; Al-Ola Abdallah, MD[6]; Natalie Callander, MD[7]; Douglas Sborov, MD[8]; Attaya Suvannasankha, MD[9]; Katja Weisel, MD[10]; Peter M. Voorhees, MD[11]; Lynsey Womersley, MSc[12]; January Baron, MS[13]; Trisha Piontek, BSN[13]; Eric Lewis, MD[14]; Joanna Opalinska, MD[13]; Ira Gupta, MD[13]; and Adam D. Cohen, MD[15]

Cancer 2021;127(22):4198-212.

RTP RESEARCH TO PRACTICE

DREAMM-2: Single-Agent Belantamab Mafodotin Efficacy Outcomes

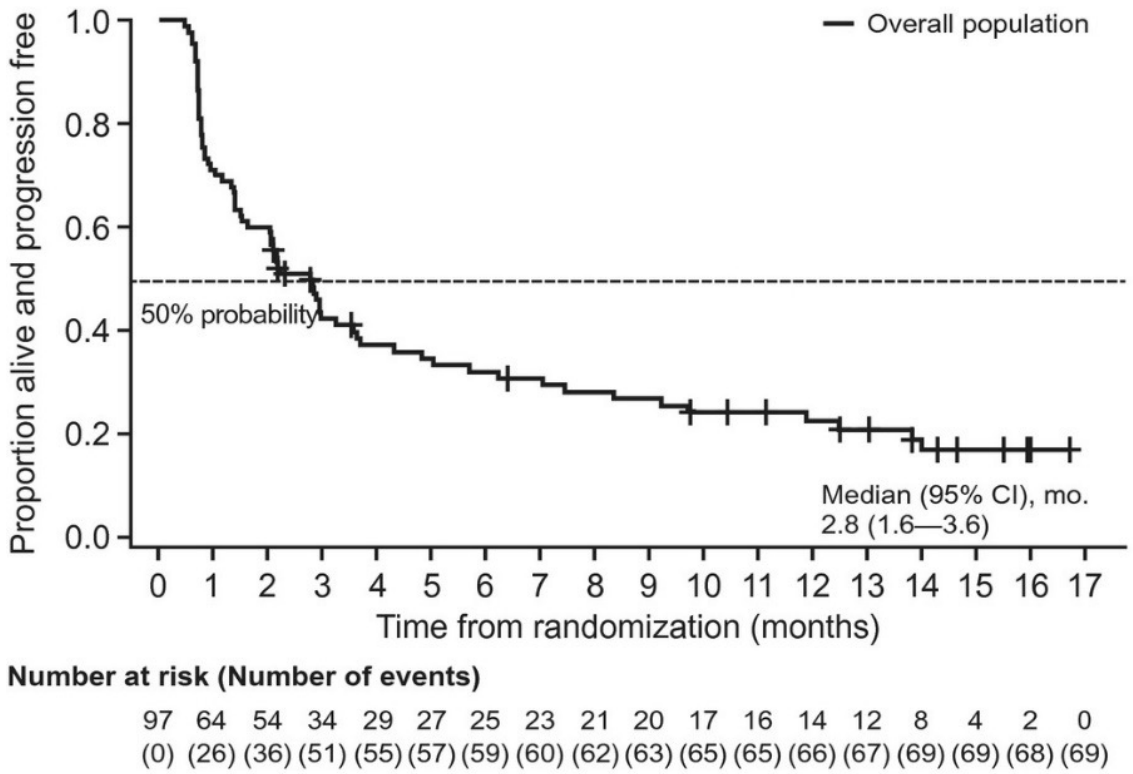
	Patients with 3-6 prior therapies (n = 47)	Patients with ≥7 prior therapies (n = 50)
ORR, % (97.5% CI)	32 (21.7-43.6)	30 (16.5-46.6)
Median DoR (95% CI estimates), months	11.0 (4.2-NR)	13.1 (4.0-NR)
Probability of DoR ≥6 months, % (95% CI estimates)	63 (31-83)	73 (44-89)
Median PFS (95% CI estimates), months	2.8 (1.6-3.6)	2.2 (1.2-3.6)
Probability of PFS at 6 months, % (95% CI estimates)	35 (20-50)	30 (17-43)

ORR = overall response rate; CI = confidence interval; DoR = duration of response; NR = not reached; PFS = progression-free survival

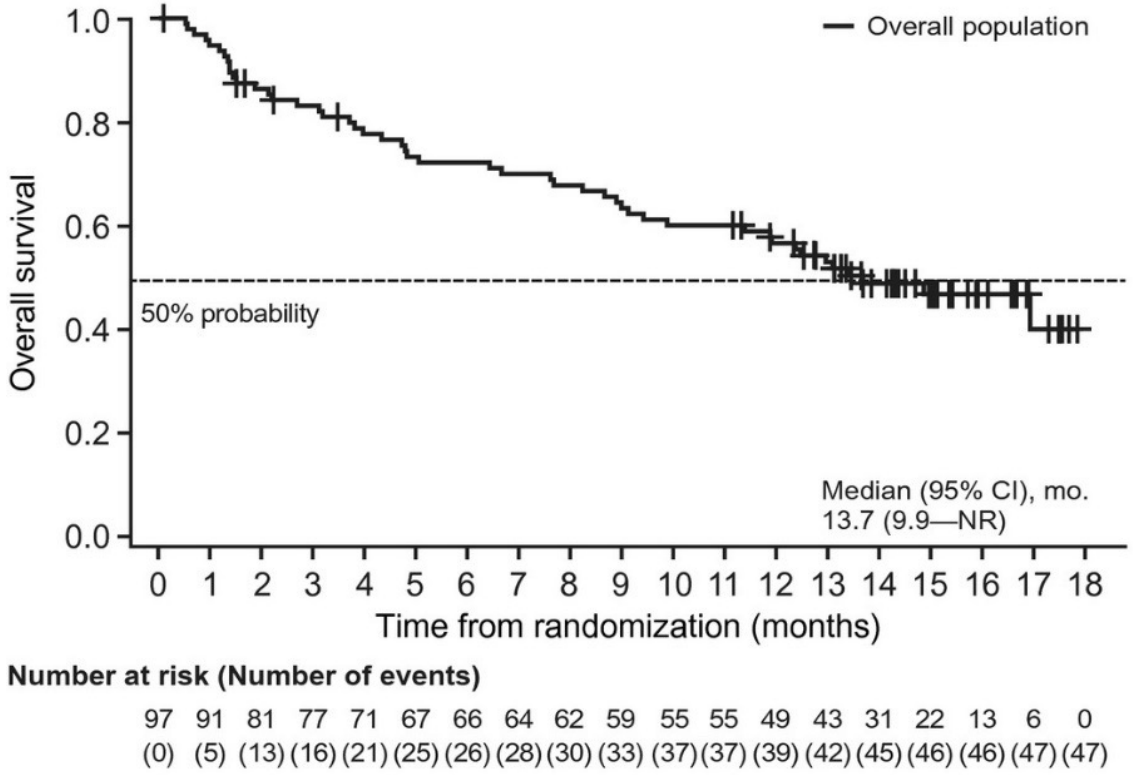
Lonial S et al. *Cancer* 2021;127(22):4198-212; ASH 2020;Abstract 1417.

DREAMM-2: Longitudinal Outcomes

Progression-Free Survival



Overall Survival

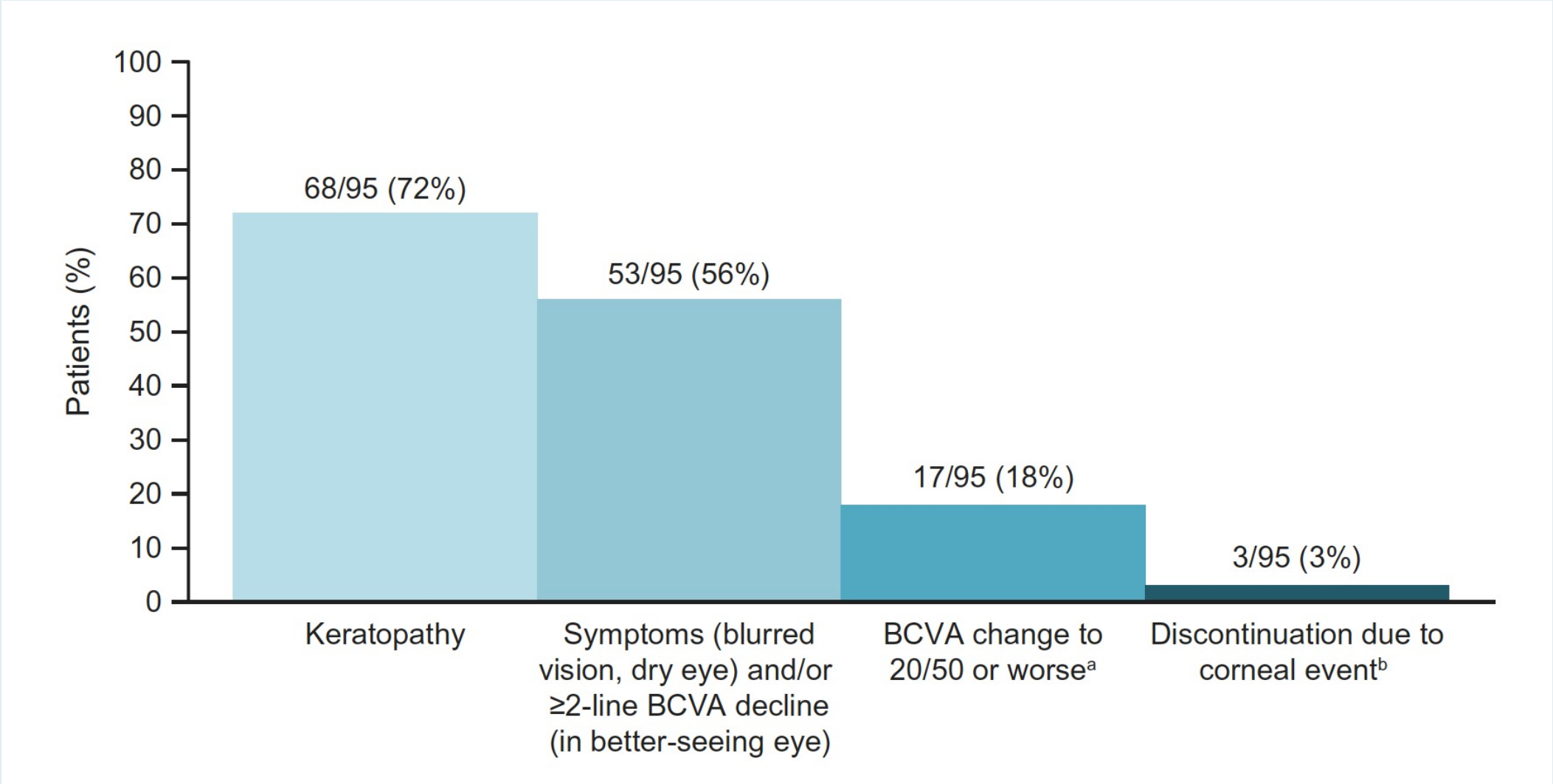


Expected median OS in triple-class refractory myeloma: 8.6 months

Lonial S et al. *Cancer* 2021;127(22):4198-212.

RTP RESEARCH TO PRACTICE

DREAMM-2: Frequency of Corneal and Vision-Related Events



BCVA = best corrected visual acuity

Lonial S et al. *Cancer* 2021;127(22):4198-212.

RTP RESEARCH TO PRACTICE

Corneal Events: Mitigation Strategy

- Corticosteroid eye drops are not beneficial for prophylaxis or treatment
- Lubricating eye drops ≥4 times per day are recommended throughout duration of the treatment period
- Contact lens use is not advised during treatment period
- Eye examination with BCVA assessment and slit lamp examination with fluorescein staining is recommended prior to each planned dose
- Dose delays and dose reductions should be utlized per recommendations

Lonial S et al. *Blood Cancer J* 2021;11:103.

RTP RESEARCH TO PRACTICE

Belantamab Mafodotin Dose Modifications for Corneal Toxicity

Eye Findings per KVA Scale		Recommended Dose Modifications
Grade 1	Corneal Exam Finding(s)	Continue treatment at the current dose
	• Mild superficial keratopathy	
	Change in BCVA	
	• Decline from baseline of 1 line on the Snellen Visual Acuity	
Grade 2	Corneal Exam Finding(s)	Withhold treatment until improvement in both corneal examination findings and changes in BCVA to Grade 1 or better and resume at same dose
	• Moderate superficial keratopathy	
	Change in BCVA	
	• Decline from baseline of 2 or 3 lines (and Snellen Visual Acuity not worse than 20/200)	
Grade 3	Corneal Exam Finding(s)	Withhold treatment until improvement in both corneal examination findings and changes in BCVA to Grade 1 or better and resume at a reduced dose
	• Severe superficial keratopathy	
	Change in BCVA	
	• Decline from baseline by more than 3 lines (and Snellen Visual Acuity not worse than 20/200)	
Grade 4	Corneal Exam Finding(s)	Consider treatment discontinuation for a Grade 4 event. Based on a benefit:risk assessment, if continuing treatment with belantamab mafodotin is being considered, treatment may be resumed at a reduced dose after the event has improved to Grade 1 or better
	• Corneal epithelial defect	
	Change in BCVA	
	• Snellen Visual Acuity worse than 20/200	

- Mild keratopathy: Nonconfluent microcyst-like epithelial changes (MECs), ≥80% involving the cornea periphery
- Moderate keratopathy: Semiconfluent MECs, ≥80% in the paracentral cornea
- Severe keratopathy: Confluent MECs, ≥80% in the corneal center

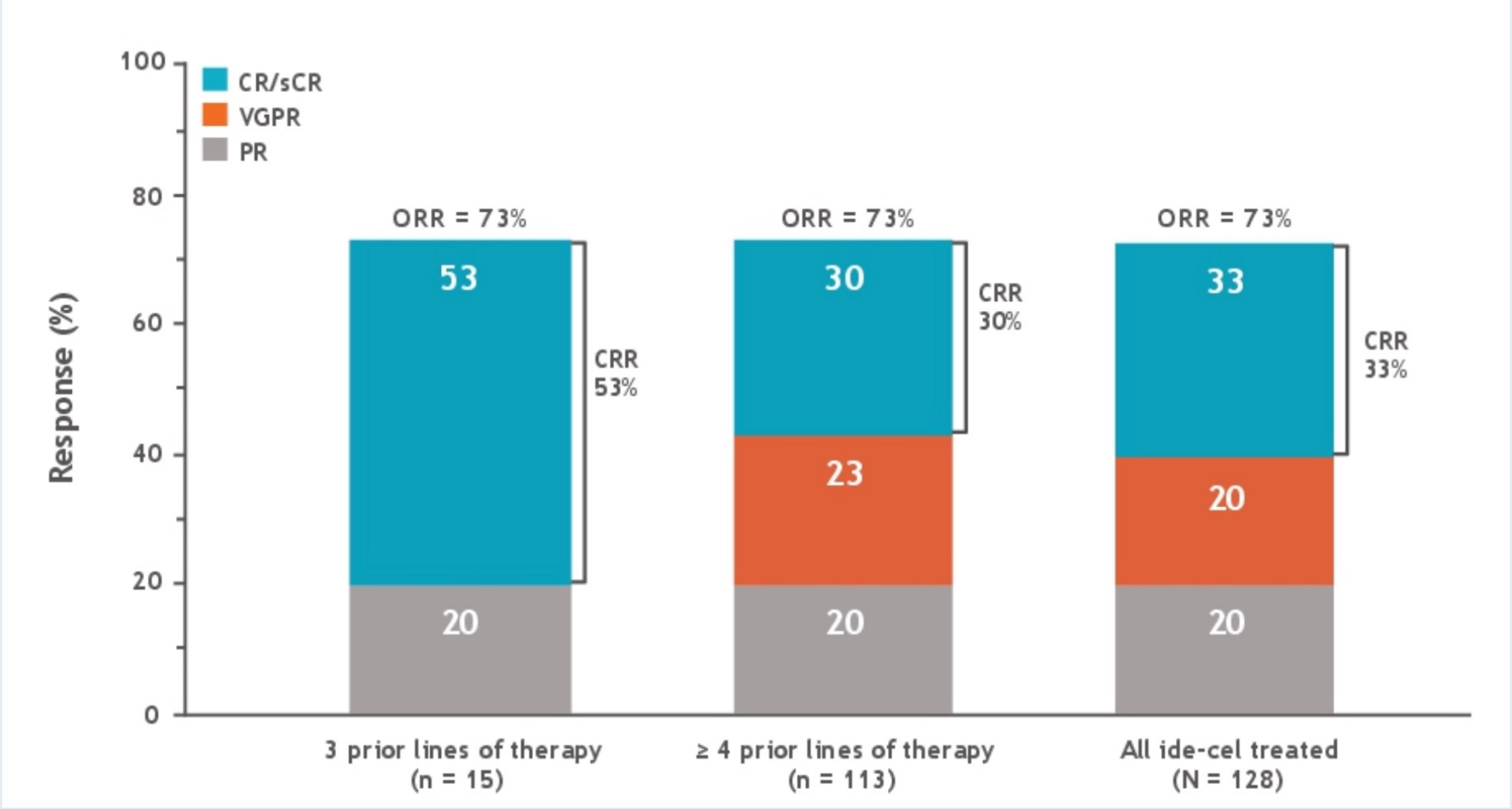
Farooq, AV et al. *Ophthalmol Ther* 2020;9:889-911; Lonial, S et al. *Blood Cancer J* 2021;11:103.

Idecabtagene Vicleucel (Ide-Cel, bb2121), a BCMA CAR T Cell Therapy, in Relapsed and Refractory Multiple Myeloma: Updated KarMMa Results

Anderson LD et al.

ASCO 2021;Abstract 8016.

KarMMa: Best Overall Response



Anderson LD et al. ASCO 2021;Abstract 8016.

KarMMa: Incidence of Cytokine Release Syndrome (CRS) and Neurotoxicity

	Prior line of therapy		All ide-cel treated (N = 128)
	3 (n = 15)	≥ 4 (n = 113)	
≥ 1 CRS event, n (%)	13 (87)	94 (83)	107 (84)
Max. grade (Lee criteria), n (%)[a]			
1/2	12 (80)	88 (78)	100 (78)
3	1 (7)	4 (4)	5 (4)
4	0	1 (< 1)	1 (< 1)
5	0	1 (< 1)	1 (< 1)
Median onset (range), d	1 (1-2)	1 (1-12)	1 (1-12)
Median duration (range), d	4 (1-63)	6 (2-28)	5 (1-63)
≥1 NT event, n (%)	2 (13)	21 (19)	23 (18)
Max. grade (CTCAE), n (%)[b]			
1	1 (7)	10 (9)	11 (9)
2	0	7 (6)	7 (5)
3	1 (7)	4 (4)	5 (4)[c]
Median onset (range), d	3 (1-5)	2 (1-10)	2 (1-10)
Median duration (range), d	3 (2-5)	3 (1-26)	3 (1-26)

Anderson LD et al. ASCO 2021;Abstract 8016.

FDA Approves Cilta-Cel for Relapsed/Refractory MM

Press Release: February 28, 2022

The FDA has approved the use of ciltacabtagene autoleucel for the treatment of relapsed/refractory MM after 4 or more lines of therapy, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody.

The approval was based on findings from the Phase Ib/II CARTITUDE-1 trial (NCT03548207), in which one-time treatment with cilta-cel resulted in an overall response rate of 98% (95% CI, 92.7%-99.7%). Investigators also reported a stringent complete response rate of 78% (95% CI, 68.8%-86.1%). The median duration of response was 21.8 months after a median follow-up of 18 months.

The CARTITUDE trial enrolled 97 patients, with a median turnaround time for cilta-cel therapy of 29 days. Patients had received a median of 6.0 lines of prior therapy. Of the 97 patients, 87.6% (n = 85) were triple-class refractory and 42.3% (n = 41) were penta-drug refractory. Nearly all patients (99%; n = 96) were refractory to their last line of therapy.

www.cancernetwork.com/view/fda-approves-cilta-cel-for-relapsed-refractory-multiple-myeloma?utm_source=sfmc&utm_medium=email&utm_campaign=3.01.22_CN_Breaking_A&eKey=cmthZGVybWFuQHJlc2VhcmNodG9wcmFjdGljZS5jb20=

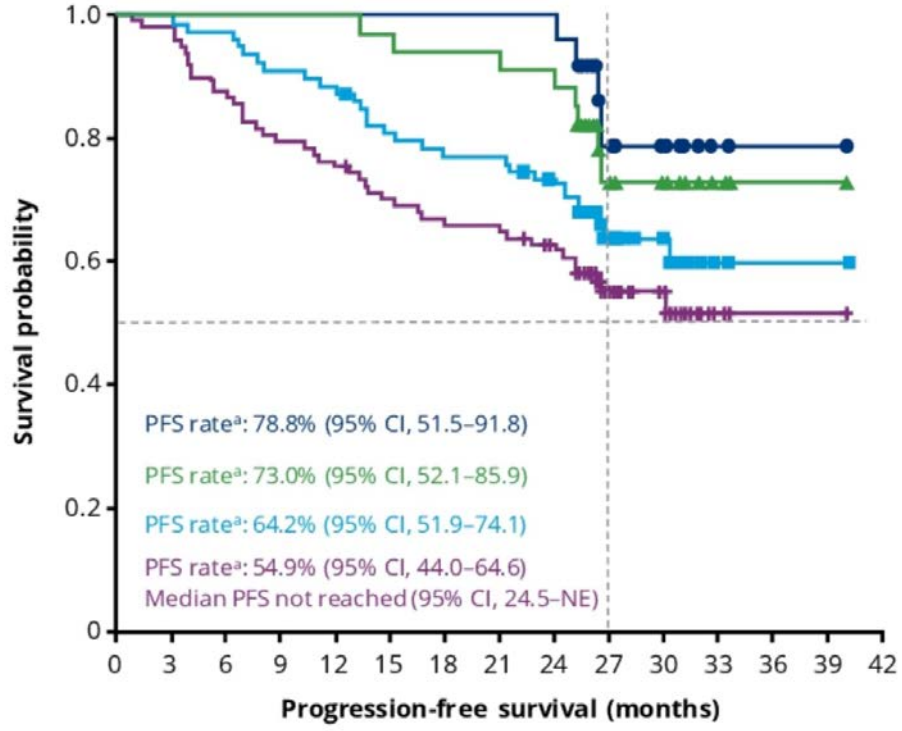
Phase 1b/2 Study of Ciltacabtagene Autoleucel, a BCMA-Directed CAR-T Cell Therapy, in Patients with Relapsed/Refractory Multiple Myeloma (CARTITUDE-1): 2 Years Post LPI

Usmani SZ et al.

ASCO 2022;Abstract 8028.

CARTITUDE-1: PFS and OS at 27.7 Months Follow-Up by MRD Status

PFS

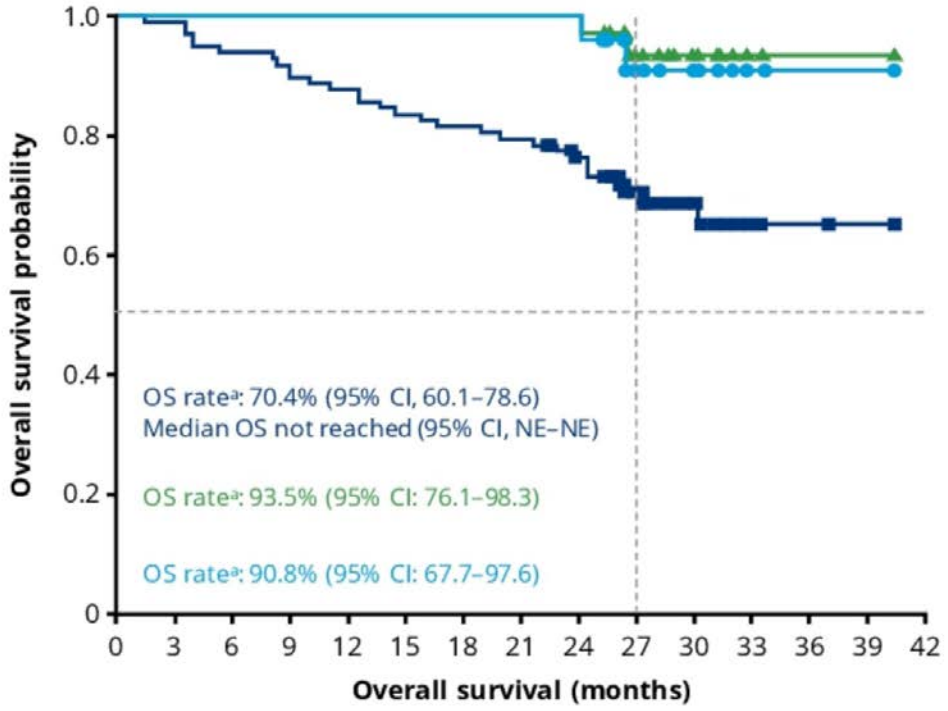


Patients at risk

MRD negative ≥12 months	24	24	24	24	24	24	24	24	24	11	8	2	1	1	0
MRD negative ≥6 months	34	34	34	34	34	33	32	32	31	13	10	3	1	1	0
sCR patients	80	80	78	73	71	64	62	61	55	27	17	3	1	1	0
All patients	97	95	85	77	74	67	64	63	57	27	17	3	1	1	0

MRD negative ≥12 months
MRD negative ≥6 months
sCR patients
All patients

OS



Patients at risk

All patients	97	96	91	88	85	81	79	77	71	42	22	6	2	1	0
Sustained (≥6 mos) MRD neg	34	34	34	34	34	34	34	34	34	18	11	3	1	1	0
Sustained (≥12 mos) MRD neg	24	24	24	24	24	24	24	24	24	13	9	2	1	1	0

All patients
Sustained (≥6 mos) MRD neg patients
Sustained (≥12 mos) MRD neg patients

Usmani SZ et al. ASCO 2022;Abstract 8028.

RTP RESEARCH TO PRACTICE

CARTITUDE-2: Efficacy and Safety of Ciltacabtagene Autoleucel (Cilta-Cel), a BCMA-Directed CAR T-Cell Therapy, in Patients with Progressive Multiple Myeloma (MM) After One to Three Prior Lines of Therapy

Agha ME et al.

ASCO 2021;Abstract 8013.

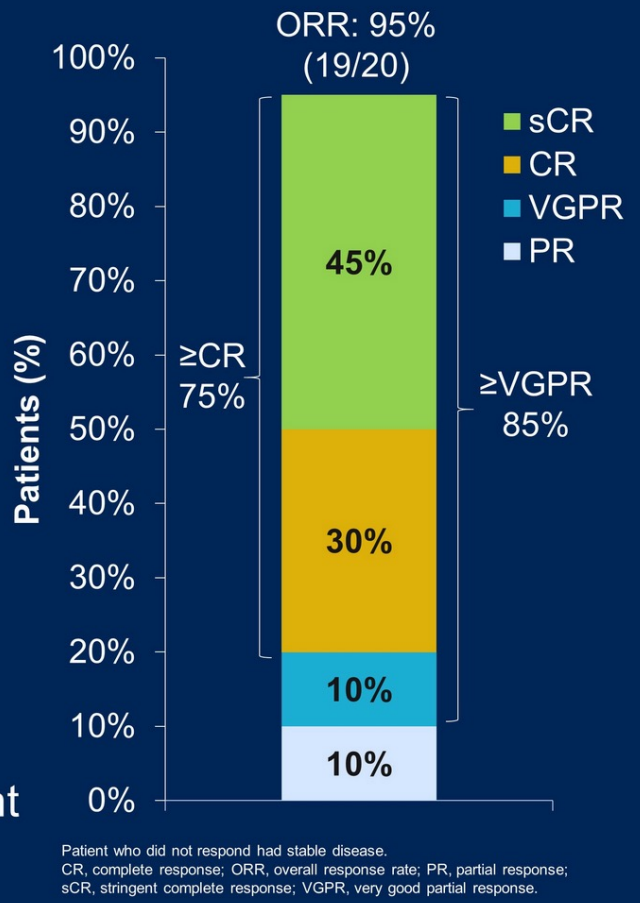
CARTITUDE-2: Ciltacabtagene Autoleucel After 1 to 3 Prior Lines of Therapy

Efficacy

- Median time to first response: 1.0 month
- Median time to best response: 1.9 months
- Median duration of response: not reached
- All patients (n=4) with MRD-evaluable samples at the 10^{-5} threshold were MRD negative at data cut-off

Safety

- Cilta-cel safety profile was manageable, including in the patient treated in an outpatient setting
- No movement and neurocognitive treatment-emergent AEs were observed in patients of Cohort A



Patient who did not respond had stable disease.
CR, complete response; ORR, overall response rate; PR, partial response; sCR, stringent complete response; VGPR, very good partial response.

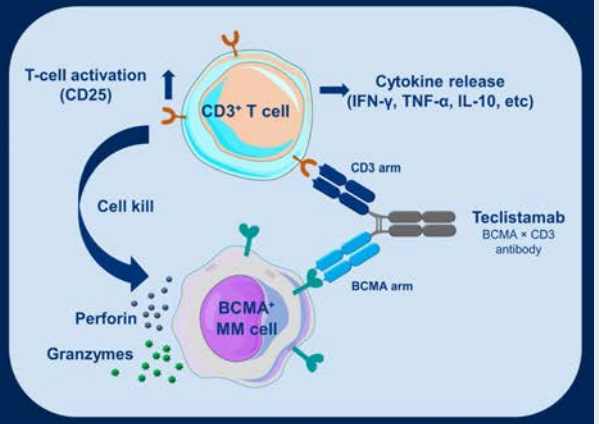
Agha M et al. ASCO 2021;Abstract 8013.

Bispecific Antibodies for R/R MM

TECLISTAMAB

BCMA × CD3 Bispecific Antibody

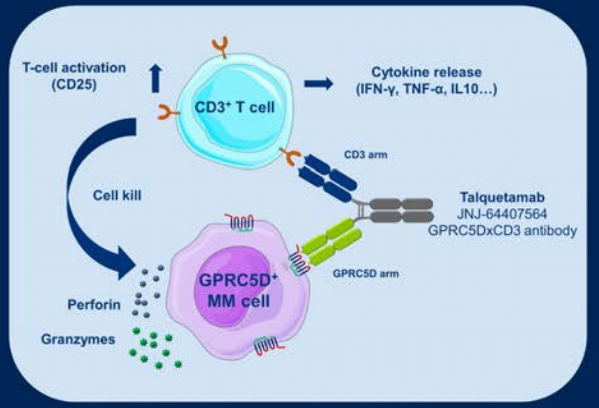
- Standard treatments and newly approved therapies for RRMM have limitations[1-3]
- Agents with new MOAs, including BCMA-targeted immunotherapies, offer considerable promise for RRMM
- Teclistamab (JNJ-64007957) is an off-the-shelf, full-size, BCMA × CD3, T-cell redirecting, bispecific antibody
- In the phase 1, first-in-human study in patients with RRMM (MajesTEC-1; NCT03145181), teclistamab was administered IV or SC in different dosing cohorts[4]
  - The RP2D was identified as a QW SC dose of teclistamab 1500 µg/kg with step-up doses of 60 µg/kg and 300 µg/kg
  - We present updated RP2D results with additional patients and longer follow-up



TALQUETAMAB

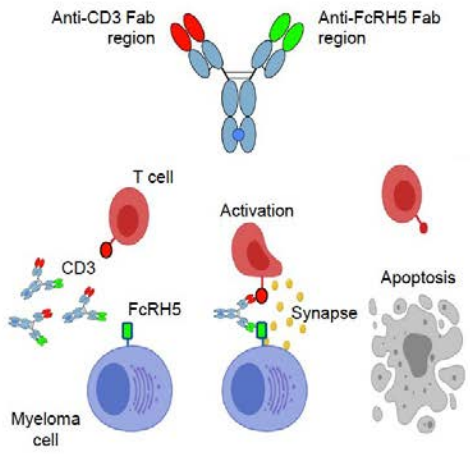
GPRC5D × CD3 Bispecific Antibody

- GPRC5D is a highly expressed receptor in MM, with limited expression in healthy human tissue[1-2]
- Talquetamab is a first-in-class antibody that binds to CD3 and GPRC5D to redirect T cells to kill MM cells[2-3]
- In the ongoing, phase 1, first-in-human study of talquetamab in patients with RRMM, the RP2D was identified as a QW SC dose of 400 µg/kg[a] (MonumenTAL-1; NCT03399799)[4]
- Here we present updated results of safety and efficacy of talquetamab at the RP2D, with additional patients and longer follow-up



Cevostamab: FcRH5xCD3 bispecific antibody

- Fc receptor-homolog 5 (FcRH5)
  - Expressed on myeloma cells with near 100% prevalence[1]
  - Expression on myeloma and plasma cells > normal B cells[1]
- Cevostamab
  - Humanized IgG-based T-cell-engaging bispecific antibody[1]
  - Targets FcRH5 on myeloma cells and CD3 on T cells[1]
- Ongoing Phase I dose-escalation and expansion trial (NCT03275103) is evaluating the safety and activity of cevostamab monotherapy in patients with RRMM[2]



Krishnan AY et al. ASCO 2021;Abstract 8007;
Berdeja JG et al. ASCO 2021;Abstract 8008;
Cohen AD et al. ASH 2020;Abstract 292.

RTP RESEARCH TO PRACTICE

ASCO 2022;Abstract 8007.

Teclistamab, a B-Cell Maturation Antigen (BCMA) x CD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma (RRMM): Updated Efficacy and Safety Results From MajesTEC-1

Ajay K Nooka (anooka@emory.edu)[1], Philippe Moreau[2], Saad Z Usmani[3], Alfred L Garfall[4], Niels WCJ van de Donk[5], Jesús San-Miguel[6], Albert Oriol[7], Ajai Chari[8], Lionel Karlin[9], Maria-Victoria Mateos[10], Rakesh Popat[11], Joaquín Martínez-López[12], Surbhi Sidana[13], Danielle Trancucci[14], Raluca Verona[15], Suzette Girgis[15], Clarissa Uhlar[15], Tara Stephenson[15], Arnob Banerjee[15], Amrita Krishnan[16]

N Engl J Med 2022;[Online ahead of print].

The NEW ENGLAND JOURNAL of MEDICINE

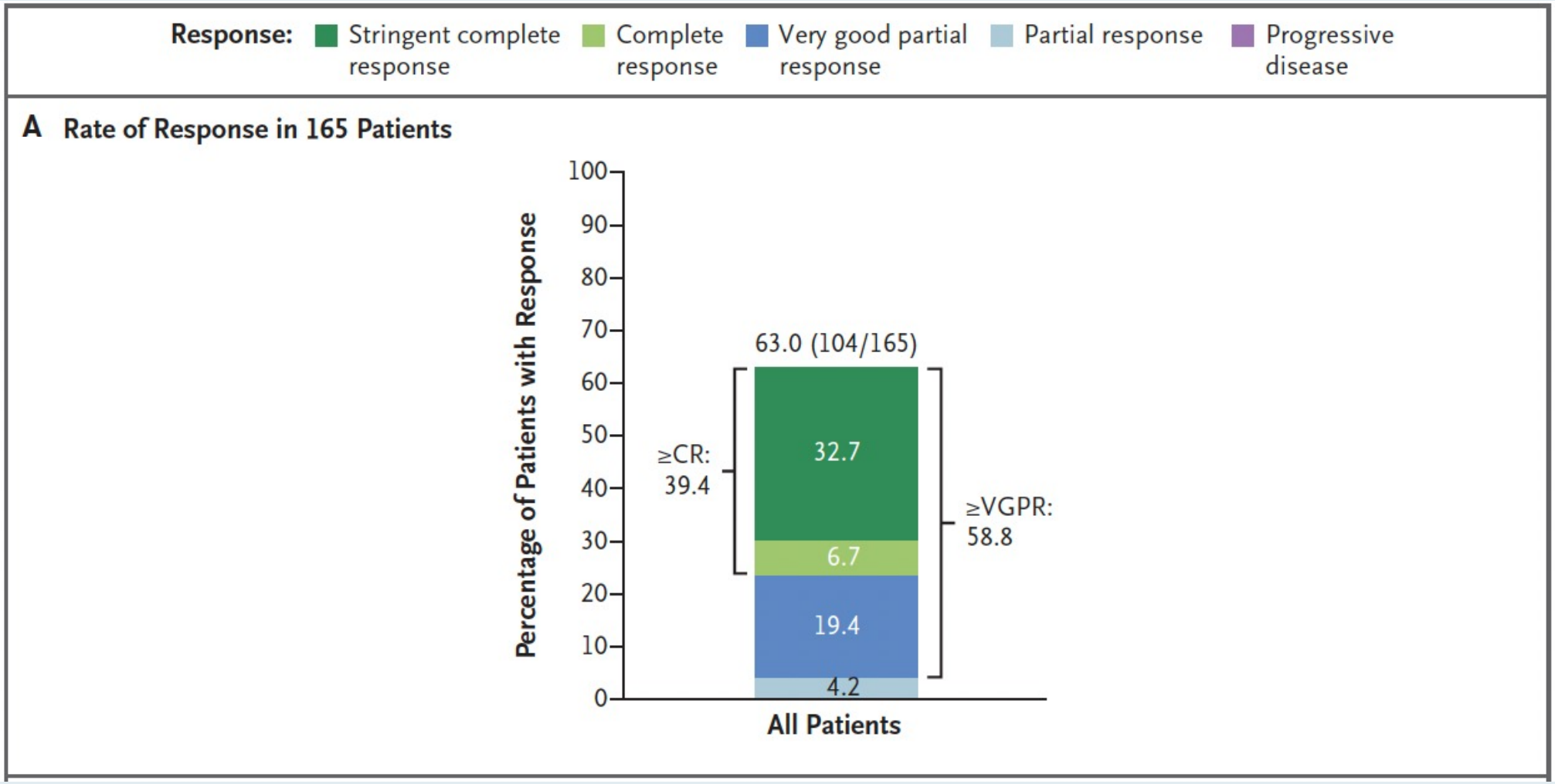
ORIGINAL ARTICLE

Teclistamab in Relapsed or Refractory Multiple Myeloma

P. Moreau, A.L. Garfall, N.W.C.J. van de Donk, H. Nahi, J.F. San-Miguel, A. Oriol, A.K. Nooka, T. Martin, L. Rosinol, A. Chari, L. Karlin, L. Benboubker, M.-V. Mateos, N. Bahlis, R. Popat, B. Besemer, J. Martínez-López, S. Sidana, M. Delforge, L. Pei, D. Trancucci, R. Verona, S. Girgis, S.X.W. Lin, Y. Olyslager, M. Jaffe, C. Uhlar, T. Stephenson, R. Van Rampelbergh, A. Banerjee, J.D. Goldberg, R. Kobos, A. Krishnan, and S.Z. Usmani

RTP RESEARCH TO PRACTICE

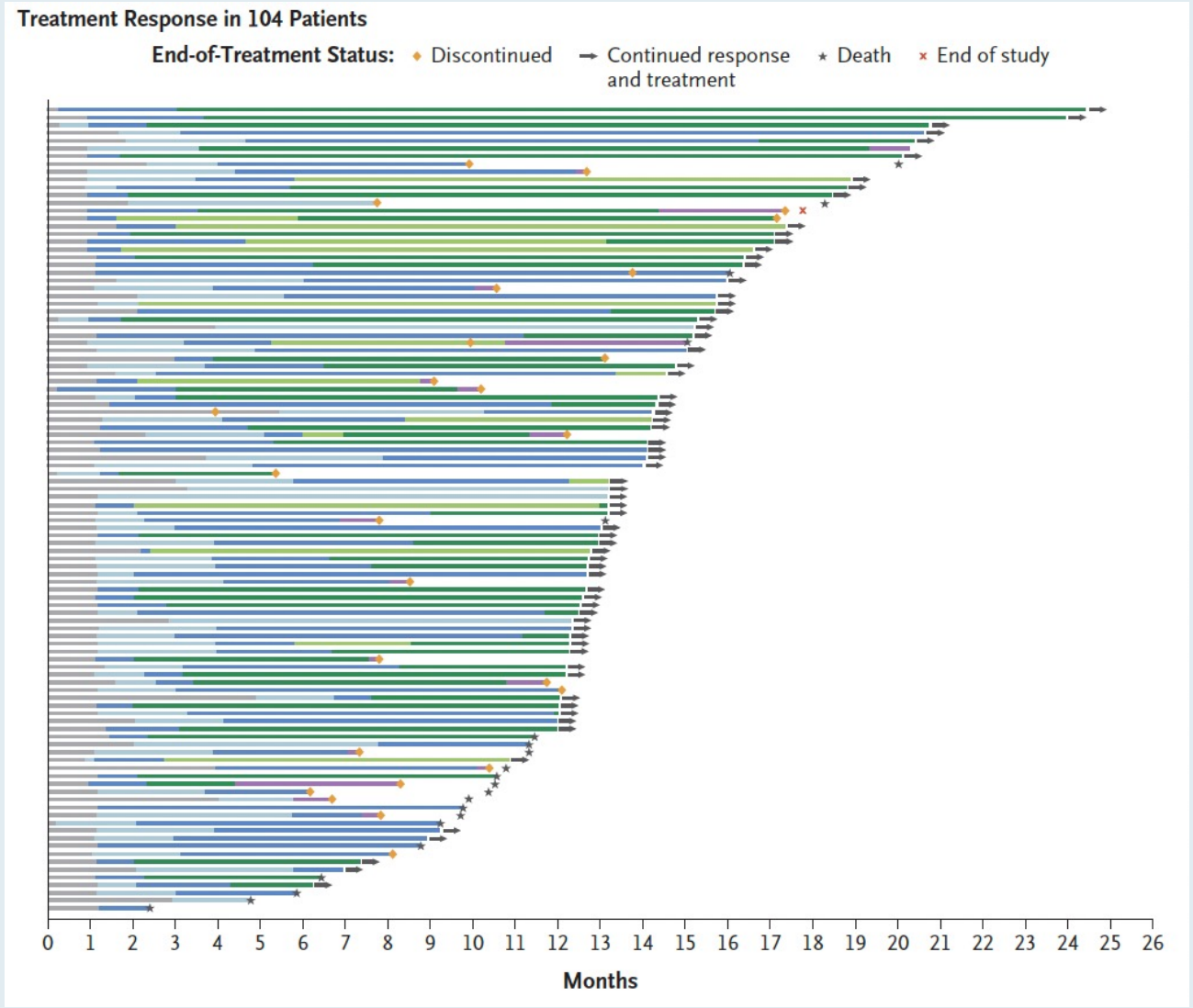
MajesTEC-1: Response to Teclistamab in Patients with R/R MM



Moreau P et al. *N Engl J Med* 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

MajesTEC-1: Response to Teclistamab Over Time in the 104 Patients Who Had a Partial Response or Better



Moreau P et al. *N Engl J Med* 2022;[Online ahead of print].

MajesTEC-1: Overall Safety Profile

AEs ≥20%, n (%)	Any Grade	Grade 3/4
Hematologic		
Neutropenia	**117 (70.9)**	**106 (64.2)**
Anemia	**86 (52.1)**	**61 (37.0)**
Thrombocytopenia	**66 (40.0)**	**35 (21.2)**
Lymphopenia	**57 (34.5)**	**54 (32.7)**
Nonhematologic		
CRS	**119 (72.1)**	**1 (0.6)**
Diarrhea	**47 (28.5)**	**6 (3.6)**
Fatigue	**46 (27.9)**	**4 (2.4)**
Nausea	**45 (27.3)**	**1 (0.6)**
Pyrexia	**45 (27.3)**	**1 (0.6)**
Injection site erythema	**43 (26.1)**	**0 (0)**
Headache	**39 (23.6)**	**1 (0.6)**
Arthralgia	**36 (21.8)**	**1 (0.6)**
Constipation	**34 (20.6)**	**0 (0)**
Cough	**33 (20.0)**	**0 (0)**

Teclistamab was well tolerated; discontinuations and dose reductions were infrequent

- 2 patients (1.2%) discontinued due to AEs (grade 3 adenoviral pneumonia; grade 4 PML)
- 1 patient had dose reduction at cycle 21
- The most common AEs were CRS and cytopenias
- Infections occurred in 126 (76.4%) patients (grade 3/4: 44.8%)
- 123 patients (74.5%) had evidence of hypogammaglobulinemia[a]
- There were 19 deaths due to AEs, including 12 COVID-19 deaths
  - 5 deaths due to teclistamab-related AEs:
    - COVID-19 (n=2)
    - Pneumonia (n=1)
    - Hepatic failure (n=1)
    - PML (n=1)

Moreau P et al. *N Engl J Med* 2022;[Online ahead of print]; Nooka AK et al. ASCO 2022;Abstract 8007.

FDA Grants Breakthrough Therapy Designation to Talquetamab for Relapsed/Refractory Multiple Myeloma

Press Release: July 1, 2022

“Talquetamab was granted breakthrough therapy designation by the FDA for the treatment of patients with relapsed/refractory multiple myeloma who were treated with a minimum of 4 previous lines of therapy, including a proteasome inhibitor, an immunomodulatory drug, and an anti-CD38 antibody.

The designation is supported by findings from the phase 1/2 MonumenTAL-1 trial (NCT03399799; NCT04634552), which assessed the agent in patients with relapsed/refractory disease. Data from the study, which were presented at the 2022 American Society of Clinical Oncology Annual Meeting, indicated that patients who were treated with 405 µg/kg of talquetamab (n = 30) experienced an overall response rate (ORR) of 70.0%, including a very good partial response (VGPR) rate or better of 56.7%. Additionally, the ORR among patients treated at the 800 µg/kg dose was 63.6%, including a VGPR or better of 56.8%. Moreover, the stringent complete response (CR) rates were 23.3% and 9.1%, CR rates were 6.7% and 11.4%, the VGPR rates were 26.7% and 36.4%, and PR rates were 13.3% and 6.8% in each respective arm.

Talquetamab is an off-the-shelf T-cell–redirecting bispecific antibody that targets GPRC5D on myeloma cells and CD3 on T cells.”

https://www.cancernetwork.com/view/fda-grants-breakthrough-therapy-designation-to-talquentamab-for-relapsed-refractory-multiple-myeloma

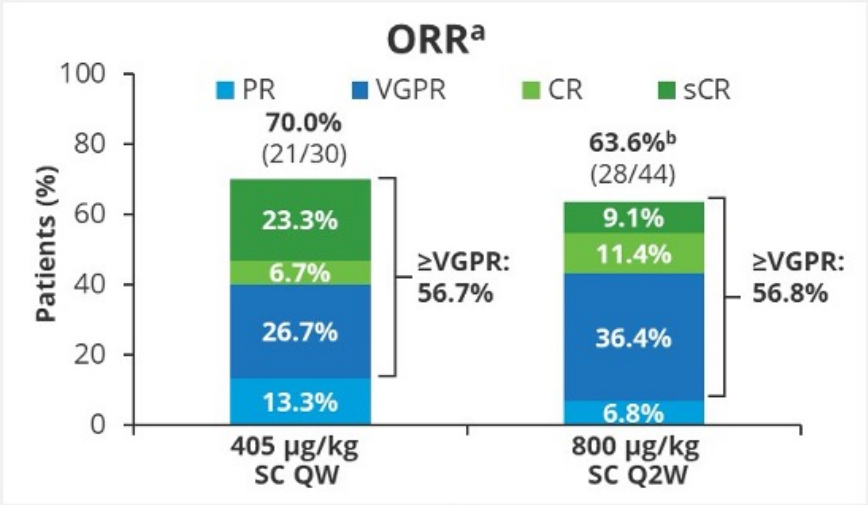
RTP RESEARCH TO PRACTICE

Efficacy and Safety of Talquetamab, a G Protein-Coupled Receptor Family C Group 5 Member D x CD3 Bispecific Antibody, in Patients With Relapsed/ Refractory Multiple Myeloma: Updated Results From MonumenTAL-1

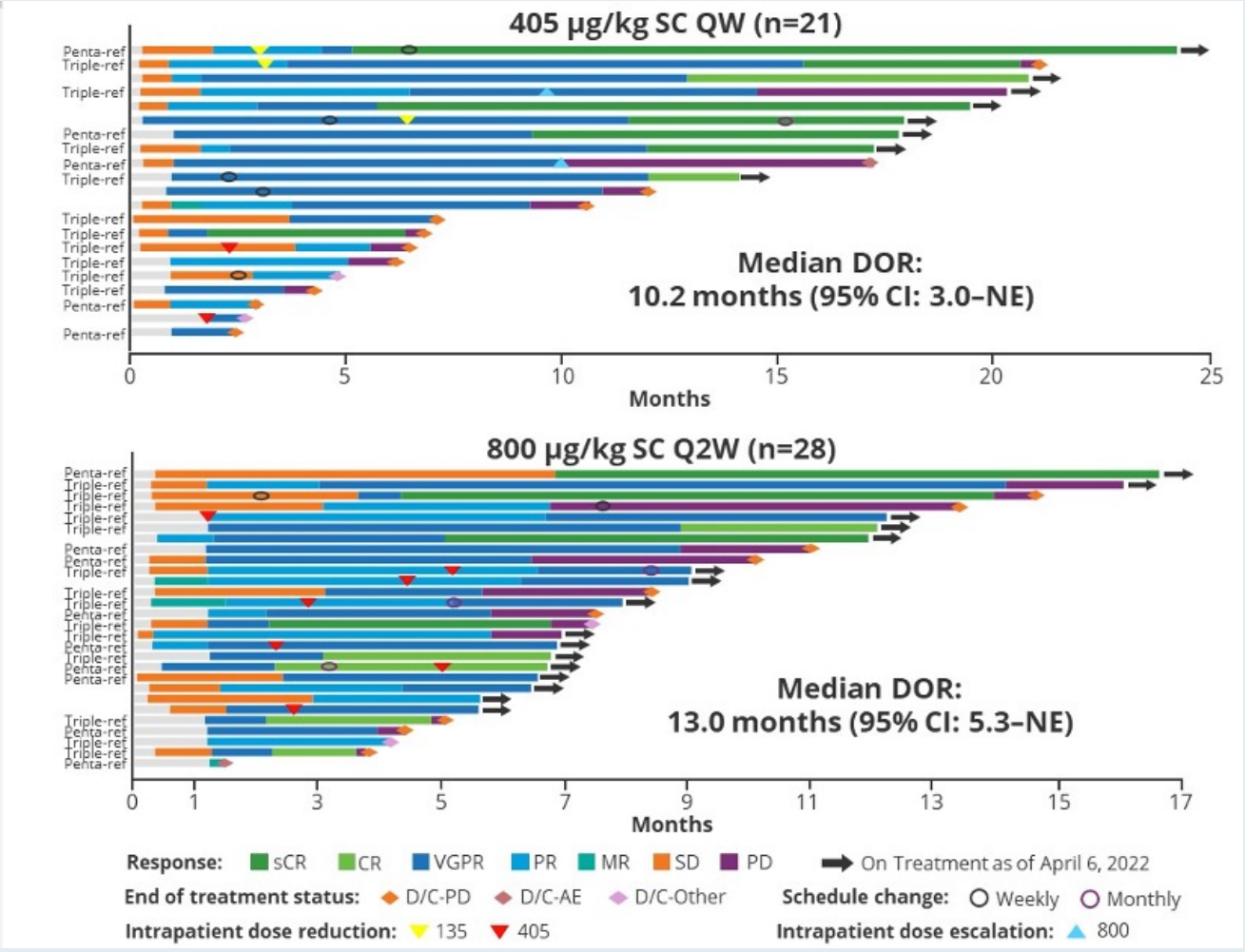
Monique C Minnema[1], Amrita Krishnan[2], Jesus G. Berdeja[3], Albert Oriol[4], Niels WCJ van de Donk[5], Paula Rodríguez-Otero[6], Daniel Morillo[7], María-Victoria Mateos[8], Luciano J. Costa[9], Jo Caers[10], Deeksha Vishwamitra[11], Joanne Ma[11], Shiyi Yang[11], Brandi W Hilder[11], Jaszianne Tolbert[11], Jenna D Goldberg[12], Ajai Chari[13]

ASCO 2022;Abstract 8015.

MonumenTAL-1: Duration of Response with Talquetamab for R/R MM



Response	405 µg/kg SC QW[c] n=30	800 µg/kg SC Q2W[c] n=44
Median follow-up (months), median (range)	13.2 (1.1–24.0)	7.7 (0.7–16.0)
ORR[a], n (%)	21 (70.0)	28 (63.6)
Triple-class–refractory patients, n/N (%)	15/23 (65.2)	23/34 (67.6)
Penta-drug–refractory patients, n/N (%)	5/6 (83.3)	9/12 (75.0)
Median time to first confirmed response (months), median (range)	0.9 (0.2–3.8)	1.2 (0.3–6.8)



Minnema MC et al. ASCO 2022;Abstract 8015.

RTP RESEARCH TO PRACTICE

MonumenTAL-1: Adverse Events with Talquetamab

AEs (≥20% of total SC population), n (%)	405 µg/kg SC QW[a] n=30		800 µg/kg SC Q2W[a] n=44	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Hematologic				
Neutropenia	20 (66.7)	18 (60.0)	18 (40.9)	15 (34.1)
Anemia	17 (56.7)	9 (30.0)	21 (47.7)	12 (27.3)
Lymphopenia	12 (40.0)	12 (40.0)	18 (40.9)	18 (40.9)
Leukopenia	12 (40.0)	9 (30.0)	10 (22.7)	8 (18.2)
Thrombocytopenia	11 (36.7)	7 (23.3)	10 (22.7)	5 (11.4)
Nonhematologic				
CRS	23 (76.7)	1 (3.3)	35 (79.5)	0
Skin-related AEs[b]	20 (66.7)	0	32 (72.7)	1 (2.3)
Dysgeusia	19 (63.3)	N/A	25 (56.8)	N/A
Nail-related AEs[c]	18 (60.0)	0	15 (34.1)	0
Rash-related AEs[d]	14 (46.7)	1 (3.3)	13 (29.5)	7 (15.9)
Dysphagia	12 (40.0)	0	12 (27.3)	0
Pyrexia	11 (36.7)	0	10 (22.7)	0
Fatigue	10 (33.3)	1 (3.3)	12 (27.3)	0
Dry mouth	9 (30.0)	0	25 (56.8)	0
Weight decreased	9 (30.0)	0	19 (43.2)	1 (2.3)
Nausea	9 (30.0)	0	9 (20.5)	0
Diarrhea	9 (30.0)	0	8 (18.2)	0
ALT increased	6 (20.0)	1 (3.3)	14 (31.8)	3 (6.8)
Decreased appetite	7 (23.3)	1 (3.3)	11 (25.0)	1 (2.3)
Headache	7 (23.3)	0	11 (25.0)	0
AST increased	3 (10.0)	0	14 (31.8)	3 (6.8)

- Overall, the most common adverse events (AEs) were CRS, skin-related events, and dysgeusia
- Cytopenias were mostly confined to step-up and cycle 1–2 doses and generally resolved within 1 week
- Infections occurred in 46.7% of patients at 405 µg/kg QW and 38.6% at 800 µg/kg Q2W (grade 3/4: 6.7%/9.1%)
- CRS events were mostly grade 1/2 and were largely confined to the step-up doses and first full dose Dysgeusia was managed with supportive care, and at times with dose adjustments
- No patients died due to drug-related AEs

Minnema MC et al. ASCO 2022;Abstract 8015.

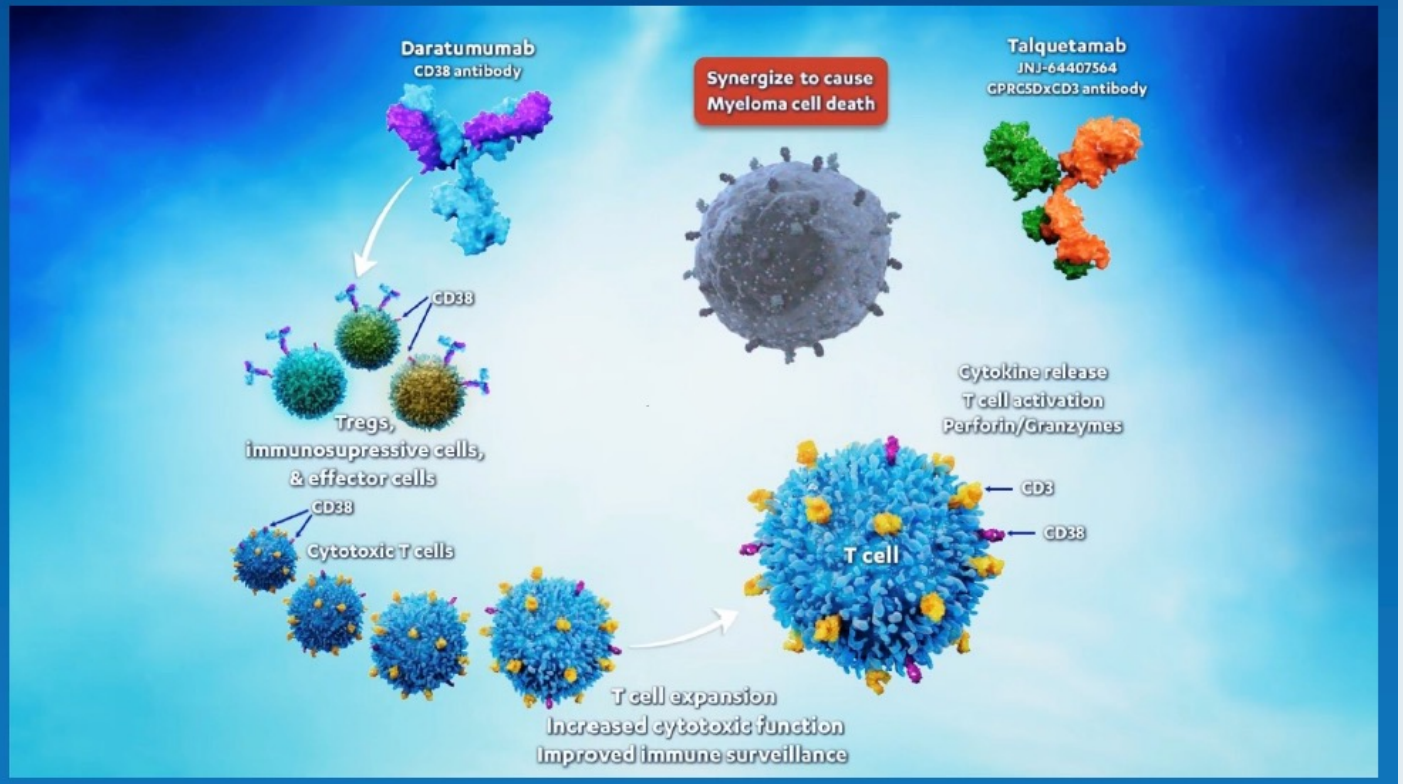
ASH 2021;Abstract 161

Phase 1b Results for Subcutaneous Talquetamab Plus Daratumumab in Patients With Relapsed/Refractory Multiple Myeloma

Ajai Chari[1*], Parameswaran Hari[2], Nizar Bahlis[3], Maria-Victoria Mateos[4], Niels WCJ van de Donk[5], Bhagirathbhai Dholaria[6], Alfred L Garfall[7], Hartmut Goldschmidt[8], K Martin Kortüm[9], Amrita Krishnan[10], Thomas Martin[11], Daniel Morillo[12], Albert Oriol[13], Donna Reece[14], Cesar Rodriguez[15], Paula Rodríguez-Otero[16], Jesús F San-Miguel[16], Saad Z Usmani[17], Raluca Verona[18], Shun Xin Wang Lin[18], Thomas J Prior[18], Mark Wade[18], Brendan Weiss[18], Jenna D Goldberg[19], Elham Askari[12]

Rationale for Combining Talquetamab and Daratumumab

- Daratumumab (dara) is a human IgG1κ mAb targeting CD38 with a direct on-tumor and immunomodulatory mechanism of action[1]
  - Dara monotherapy leads to T cell expansion and enhanced T cell cytotoxic potential[2]
  - Talquetamab (tal; JNJ-64407564) is a novel, first-in-class antibody that binds to GPRC5D and CD3 receptors, mediating T cell recruitment, activation, and subsequent lysis of GPRC5D+ MM cells[3]
- The combination of tal and dara has the potential to yield synergistic clinical efficacy
  - Preclinical studies showed the addition of dara enhanced tal-mediated lysis of MM cells[4]



Chari A et al. ASH 2021;Abstract 161.

RTP RESEARCH TO PRACTICE

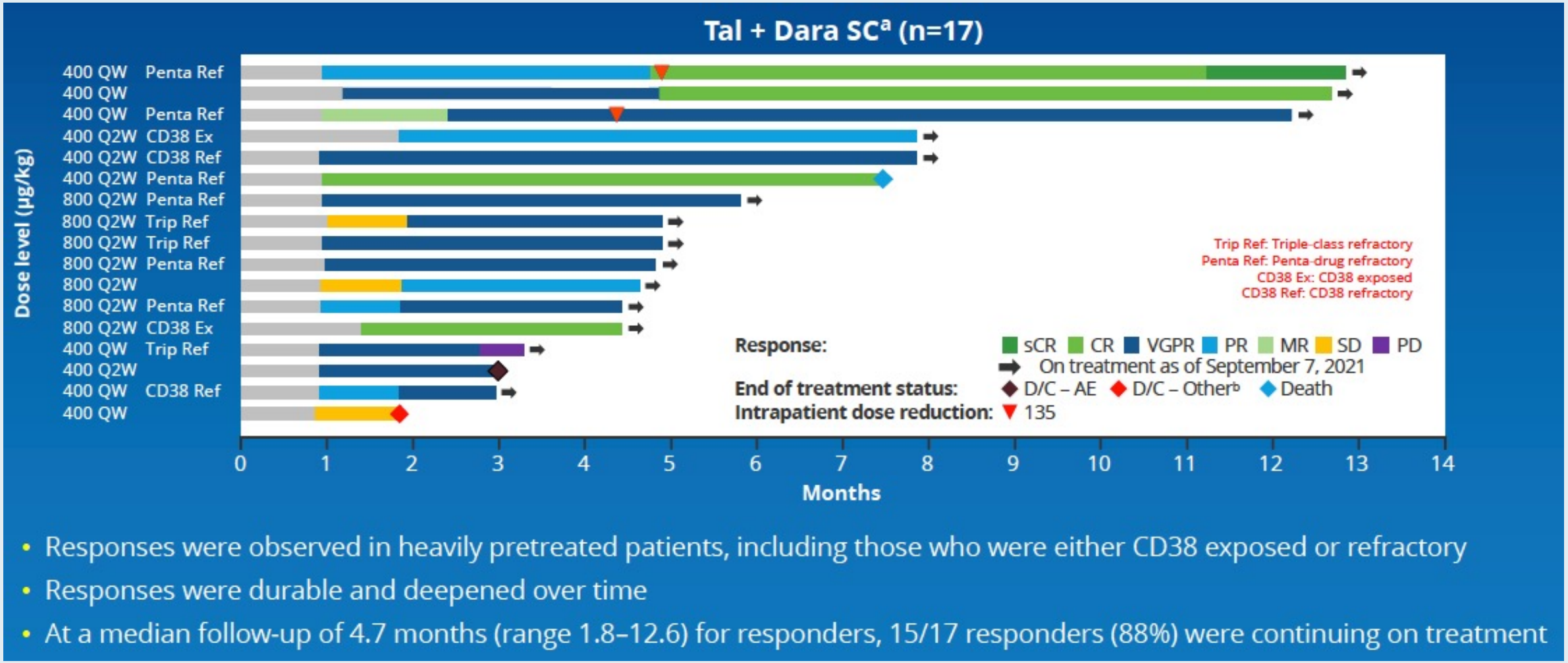
TRIMM-2: Overall Response

Response Categories	Evaluable patients[a], n (%)		
	Dara 1800 mg SC: Cycle 1-2: QW, Cycles 3-6: Q2W; Cycles 7+: monthly		
	Tal 400 µg/kg SC Q2W (n=5)	Tal 400 µg/kg SC QW (n=7)	Tal 800 µg/kg SC Q2W (n=9)
ORR[b]	**4 (80.0)**	**6 (85.7)**	**7 (77.8)**
sCR/CR	1 (20.0)	2 (28.6)	1 (11.1)
VGPR	2 (40.0)	3 (42.9)	5 (55.6)
PR	1 (20.0)	1 (14.3)	1 (11.1)
MR	0 (0)	0 (0)	0 (0)
SD	0 (0)	1 (14.3)	2 (22.2)
PD	1 (20.0)	0 (0)	0 (0)

- Median follow-up was 4.2 months
- Median time to first confirmed response: 1.0 month (range: 0.9–2.4)
- ORR across all dose levels was improved compared to RP2Ds for tal monotherapy

Chari A et al. ASH 2021;Abstract 161.

TRIMM-2: Duration of Response



- Responses were observed in heavily pretreated patients, including those who were either CD38 exposed or refractory
- Responses were durable and deepened over time
- At a median follow-up of 4.7 months (range 1.8–12.6) for responders, 15/17 responders (88%) were continuing on treatment

Chari A et al. ASH 2021;Abstract 161.

TRIMM-2: Hematologic Safety Profile

Tal + Dara SC[a] (n=29)		
AE (≥20%), n (%)	Any Grade	Grade 3/4
Hematologic		
Neutropenia	12 (41.4)	9 (31.0)
Thrombocytopenia	10 (34.5)	6 (20.7)
Anemia	9 (31.0)	6 (20.7)
Lymphopenia	8 (27.6)	8 (27.6)

Tal + dara was tolerable with no new AEs observed compared to single agents

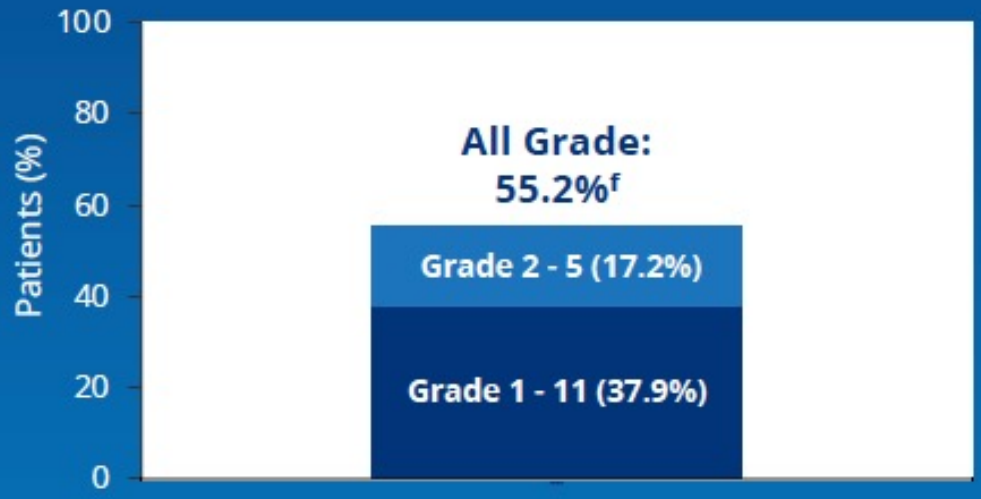
- The majority of AEs were grade 1 or 2
- No overlapping toxicities were observed
- 1 patient (3.4%) discontinued due to an AE
- Cytopenias were mostly confined to step-up and cycle 1/2 doses
  - Cytopenias resolved in the majority of patients
  - Neutropenias generally resolved within 1 week and were limited to cycles 1/2

Chari A et al. ASH 2021;Abstract 161.

TRIMM-2: Cytokine Release Syndrome (CRS)

Parameter	Tal + Dara SC[a] n=29
Patients with CRS, n (%)	16 (55.2)
Time to onset (days)[b], median (range)	2 (1–4)
Duration (days), median (range)	2 (1–6)
Patients who received supportive measures[c], n (%)	15 (51.7)
Tocilizumab[d]	10 (34.5)
Steroids	1 (3.4)
Oxygen	0

Maximum CRS Grade[e]



- **No grade 3/4 CRS events were observed**
  - All but 1 event of CRS occurred with step-up doses
- **CRS resolved in all patients, with no d/c due to CRS**
  - Only 1 patient received 2 doses of tocilizumab for a single CRS event[g]

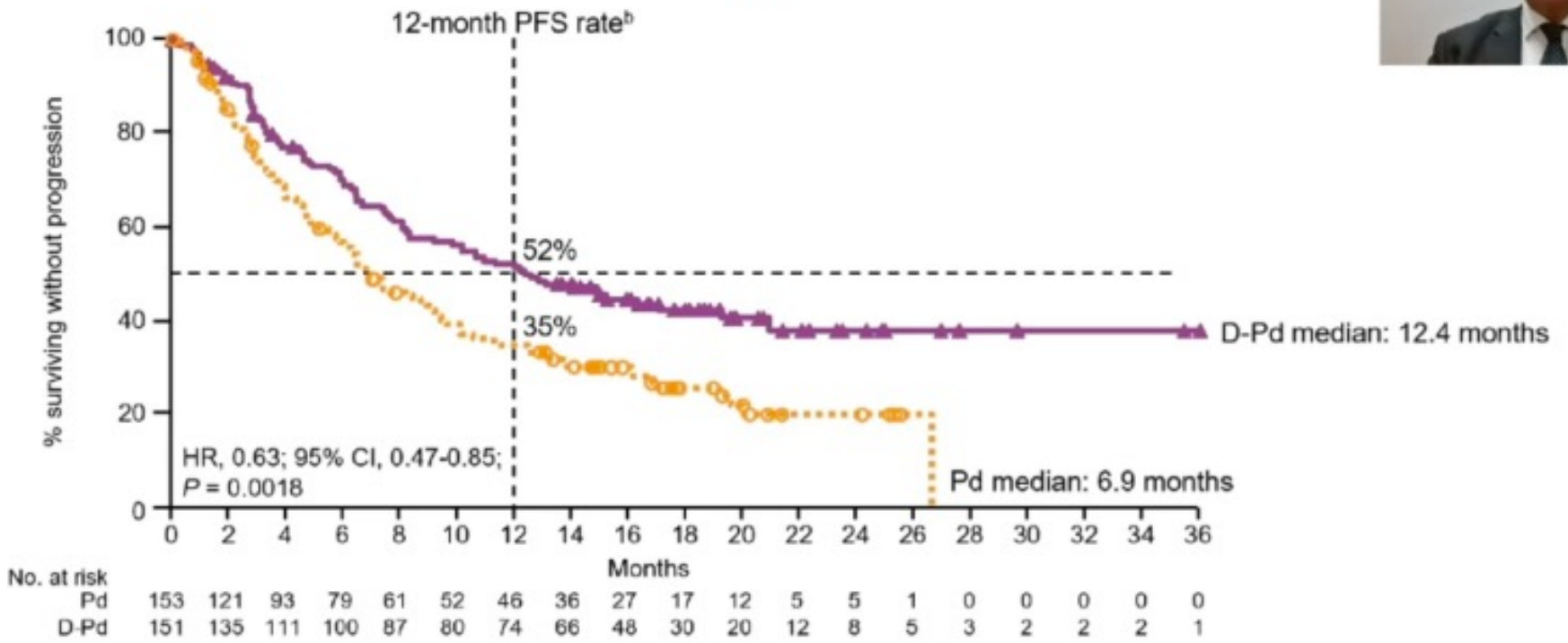
Chari A et al. ASH 2021;Abstract 161.

Apollo: Phase 3 Randomized Study of Subcutaneous Daratumumab plus Pomalidomide and Dexamethasone (D-Pd) versus Pomalidomide and Dexamethasone (Pd) Alone in Patients (Pts) with Relapsed/Refractory Multiple Myeloma (RRMM)

Dimopoulos MA et al.

ASH 2020;Abstract 412.

PFS at a Median Follow-up of 16.9 Months[a]



- Median PFS among patients refractory to lenalidomide was 9.9 months for D-Pd and 6.5 months for Pd

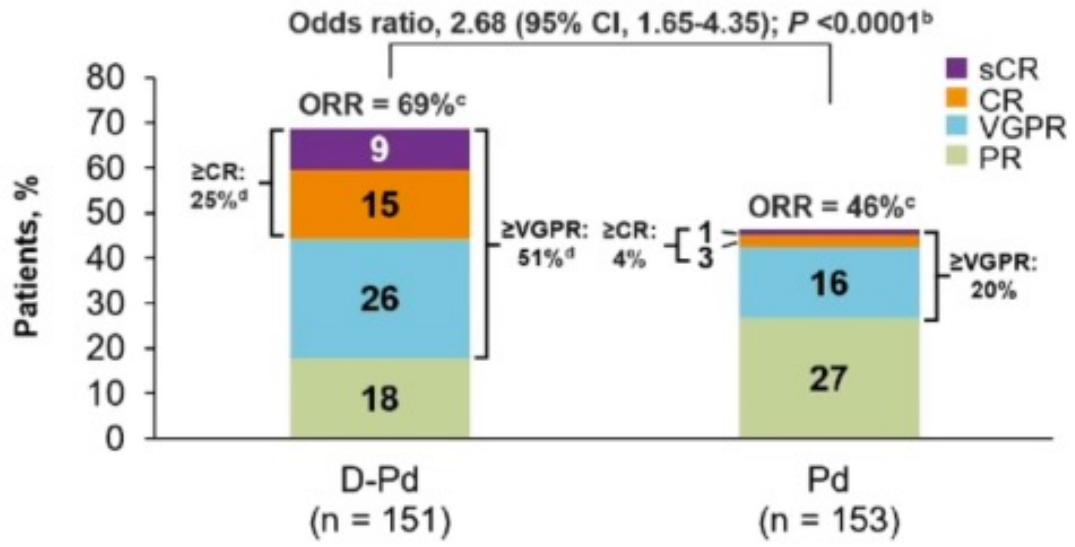
Addition of DARA SC to Pd improved PFS, with a 37% reduction in the risk of progression or death

HR, hazard ratio; CI, confidence interval. [a]Intent-to-treat population. [b]Kaplan–Meier estimate.

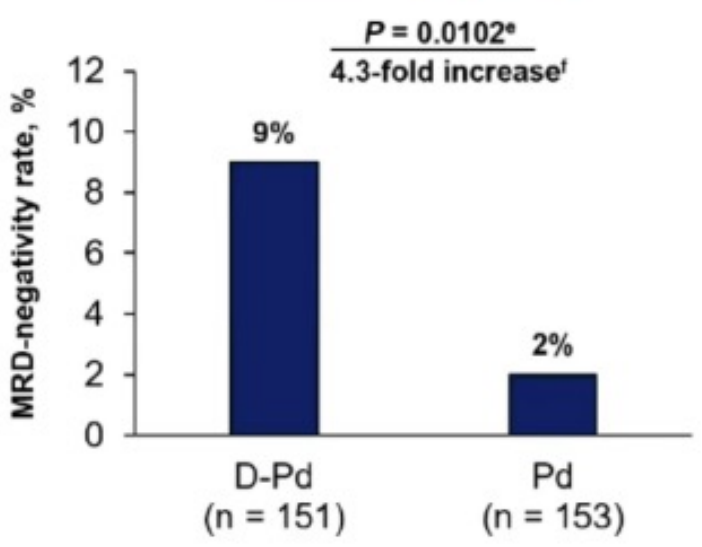
Dimopoulos MA et al. ASH 2020;Abstract 412.

Depth of Response[a]

Hematologic response



MRD negativity



ORR, ≥VGPR rate, ≥CR rate, and MRD-negativity rate were significantly higher with D-Pd versus Pd

PR, partial response; IMWG, International Myeloma Working Group; ITT, intent-to-treat. [a]Responses were assessed by computer algorithm in accordance with IMWG recommendations and included patients in the ITT population. [b]*P* value was calculated from the 2-sided Cochran–Mantel–Haenszel chi-square test, stratified for ISS stage (I, II, III) and number of lines of prior therapy (1, 2-3, ≥4). [c]Values may not add to total due to rounding. [d]*P* <0.0001. [e]*P* value (2-sided) was calculated using the Fisher's exact test. [f]Non-rounded values are 8.6% and 2.0%.

Dimopoulos MA et al. ASH 2020;Abstract 412.

2022 ASCO® ANNUAL MEETING

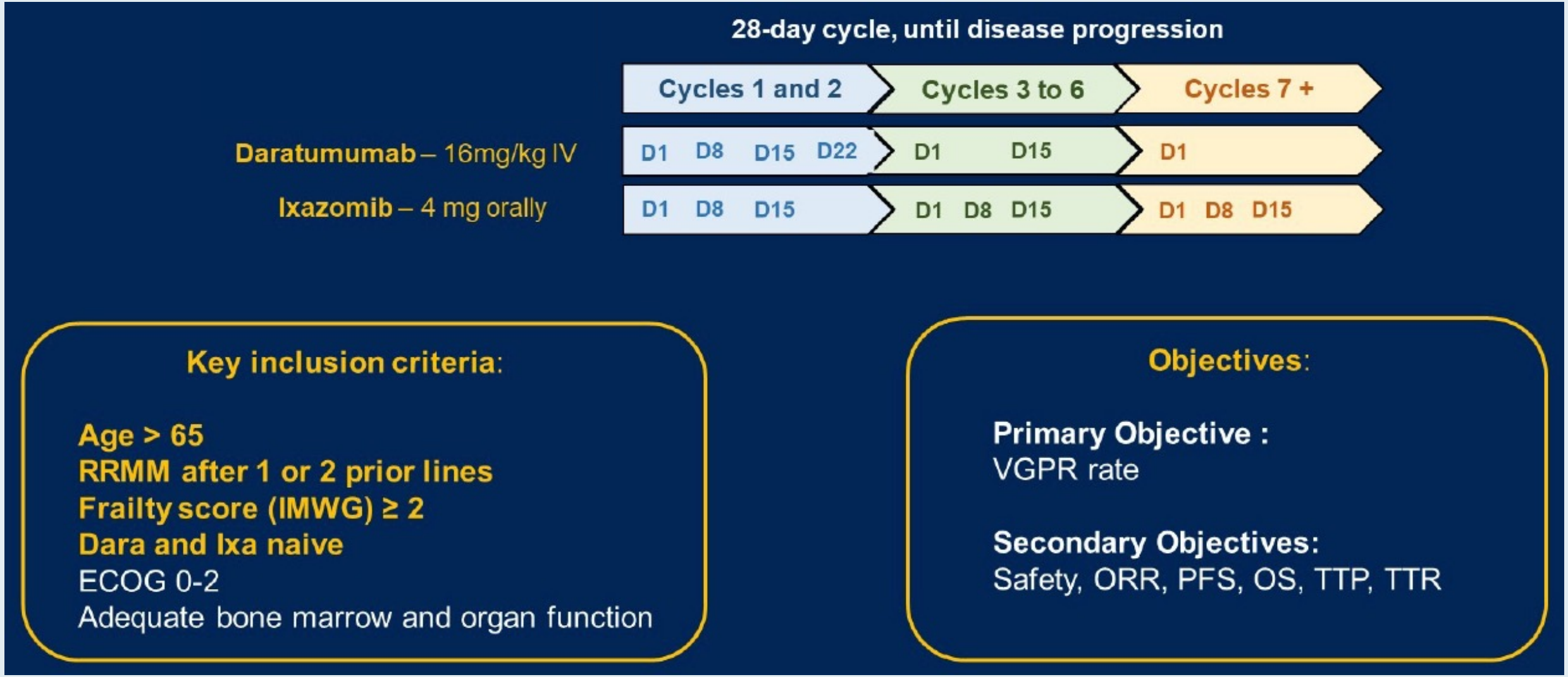
Abstract 8000

Ixazomib and Daratumumab without Dexamethasone (I-Dara) in elderly frail relapsed / refractory multiple myeloma (RRMM) patients. A multicenter phase 2 study (IFM 2018-02) of the intergroupe francophone du myelome (IFM).

Margaret Macro[1], Jean-Jacques Parienti[2], Clara Mariette[3], Salomon Manier[4], Sabine Brechignac[5], Laure Vincent[6], Benjamin Hebraud[7], Olivier Decaux[8], Samantha Schulman[9], Caroline Lenoir[10], Pascal Godmer[11], Agathe Farge[1], Laure Peyro Saint Paul[12], **Cyrille Touzeau**[13], Xavier Leleu[14]

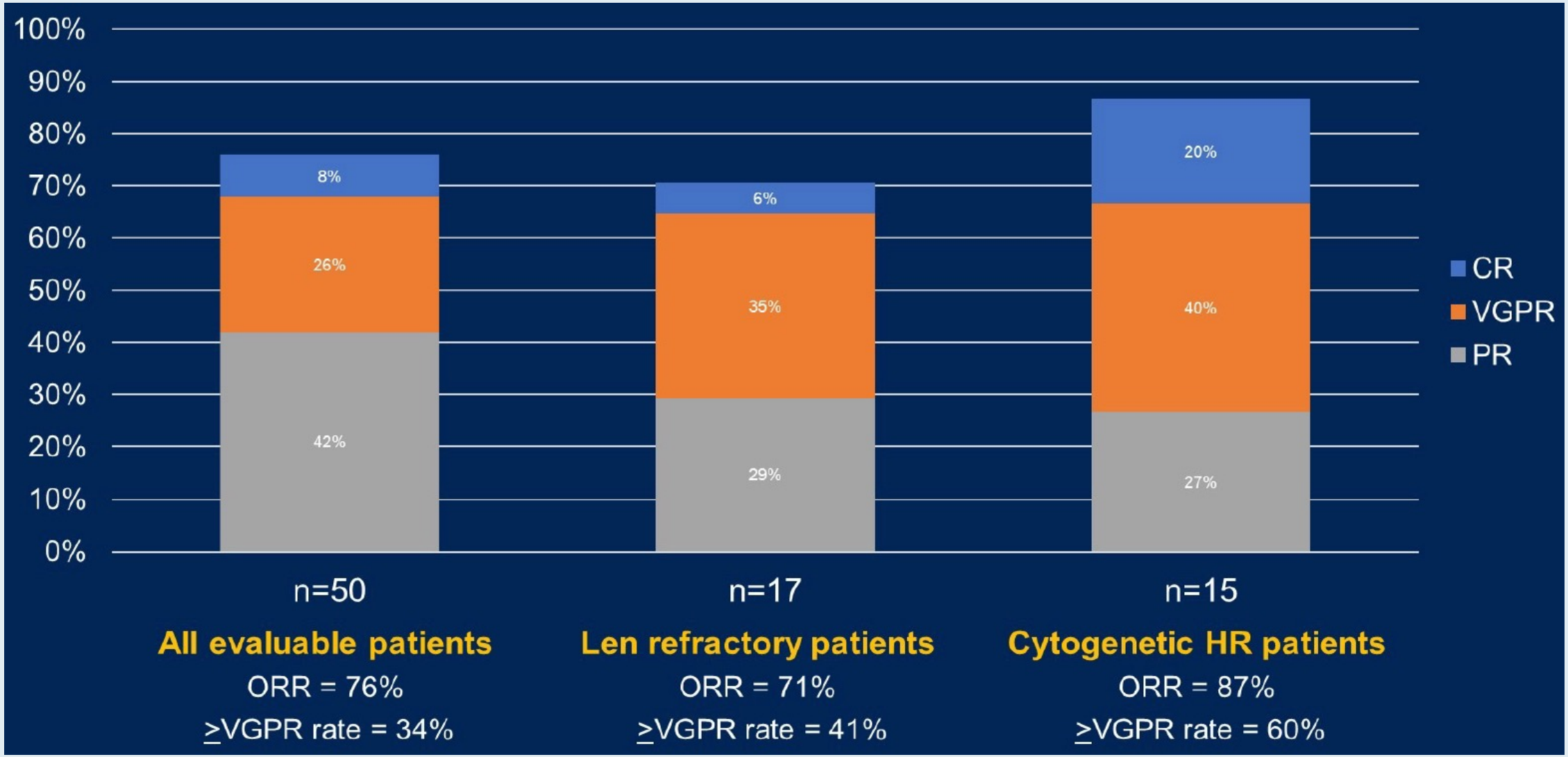
RTP RESEARCH TO PRACTICE

IFM 2018-02: Phase II Study Design



Macro M et al. ASCO 2022;Abstract 8000.

IFM 2018-02: Response Rates with I-Dara in Elderly, Frail Patients



Macro M et al. ASCO 2022;Abstract 8000.

RTP RESEARCH TO PRACTICE

IFM 2018-02: Safety of I-Dara in Elderly, Frail Patients

Deaths : n (%)	9 (16)
Treatment related	2 (4)
Disease progression	4 (7)
Infection	3 (5)
At least 1 Grade ≥3 Adverse Ev	**31 (56)**
Thrombocytopenia	9 (16)
Other cytopenias	4 (7)
Infection	8 (14)
Hypertension	3 (5)
G.I. disorder	3 (5)
Infusion Related Reaction	2 (4)

➡ **2 treatment-related deaths:**

- Daratumumab related bronchospasm (n=1)
- Ixazomib overdose (n=1)

Most Common AE (≥10 %)	N (all grades)	N (Grade ≥ 3)
Diarrhea	20 (36)	2 (4)
Daratumumab IRR	18 (32)	2 (4)
Asthenia	18 (32)	0
Nausea/vomiting	15 (27)	1 (2)
Constipation	13 (23)	0
Thrombocytopenia	13 (23)	9 (16)

Macro M et al. ASCO 2022;Abstract 8000.

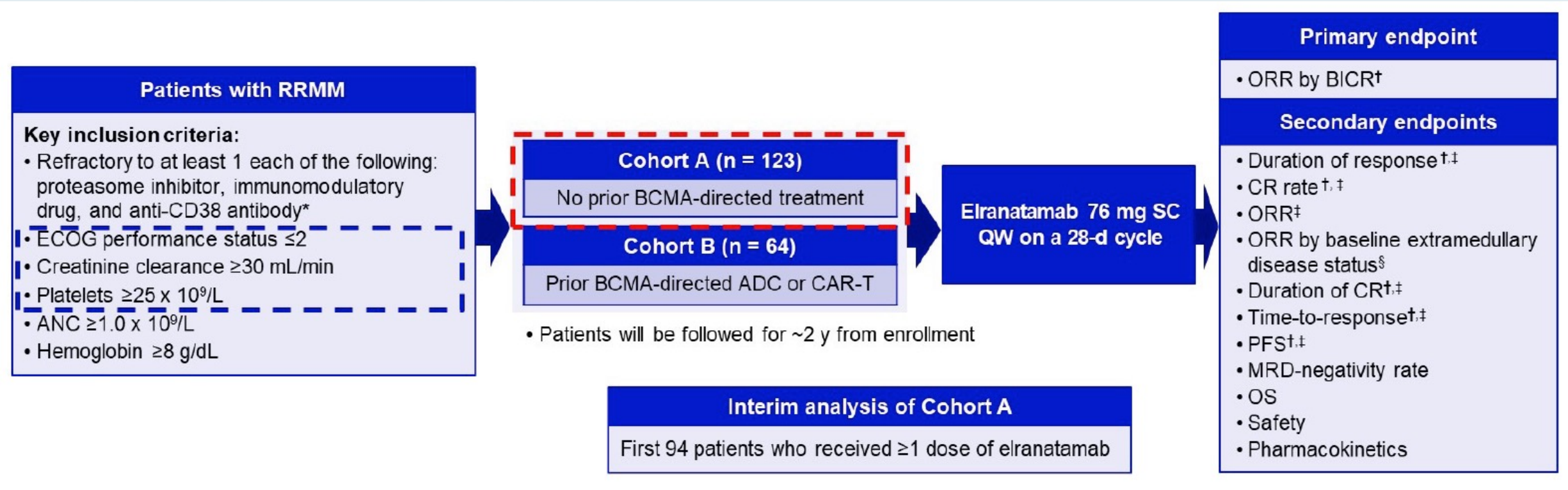
RTP RESEARCH TO PRACTICE

Initial Safety Results for MagnetisMM-3: A Phase 2 Trial of Elranatamab, a B-Cell Maturation Antigen (BCMA)-CD3 Bispecific Antibody, in Patients (pts) with Relapsed/Refractory (R/R) Multiple Myeloma (MM)

Lesokhin AM et al.

ASCO 2022;Abstract 8006.

MagnetisMM-3: Phase II Trial Design



Lesokhin AM et al. ASCO 2022;Abstract 8006.

MagnetisMM-3: Author Conclusions

- Results suggest that 76 mg QW elranatamab is efficacious and has a manageable safety profile in patients with triple-class refractory MM
  - Study enrolled a diverse population of very advanced MM patients reflective of a real-world myeloma population, with a high proportion of triple- and penta-refractory disease and unfavorable prognostic factors
- The 2-step-up priming regimen successfully mitigated the rate and severity of CRS, and the CRS profile was predictable, with the majority of events confined to the first 2 doses (88.4%) and first 3 doses (98.6%)
  - CRS (58.9%) and ICANS (2.2%) were limited to grade 1/2, with no grade ≥3 events
- Most common grade 3/4 TEAEs were hematologic, with non-hematologic TEAEs predominately low grade (grade 1/2)
- High response rate (ORR, 60.6%) was observed early, with a clinical benefit observed across subgroups
  - At the data cut-off, 89.5% of objective responders were still ongoing without confirmed progression or death
- These results support expansion of the MagnetisMM program to evaluate elranatamab alone and in combination with other drugs for the treatment of patients with MM
  - Phase 3 MagnetisMM-5 trial in patients with RRMM (NCT05020236)
  - Phase 3 MagnetisMM-7 trial in patients with newly diagnosed MM post-transplant maintenance (NCT05317416)

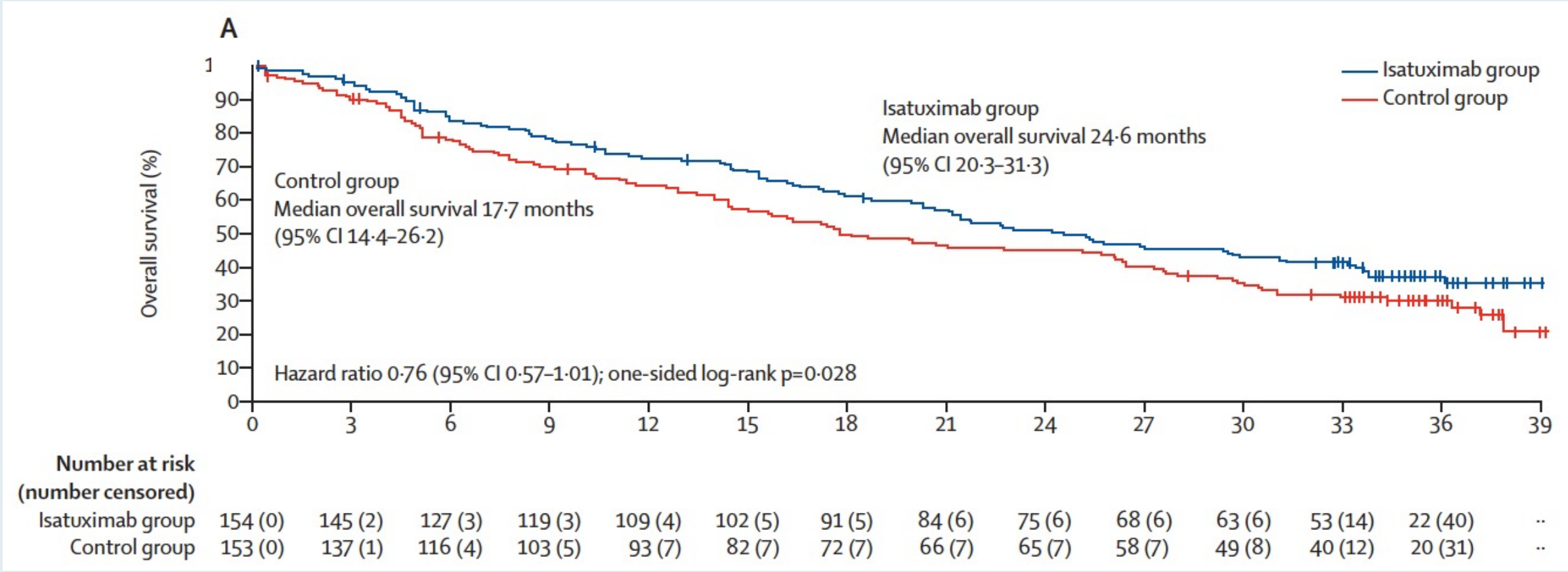
Lesokhin AM et al. ASCO 2022;Abstract 8006.

Isatuximab plus pomalidomide and low-dose dexamethasone versus pomalidomide and low-dose dexamethasone in patients with relapsed and refractory multiple myeloma (ICARIA-MM): follow-up analysis of a randomised, phase 3 study

Paul G Richardson, Aurore Perrot, Jesus San-Miguel, Meral Beksac, Ivan Spicka, Xavier Leleu, Fredrik Schjesvold, Philippe Moreau, Meletios A Dimopoulos, Jeffrey Shang-Yi Huang, Jiri Minarik, Michele Cavo, H Miles Prince, Laure Malinge, Franck Dubin, Helgi van de Velde, Kenneth C Anderson

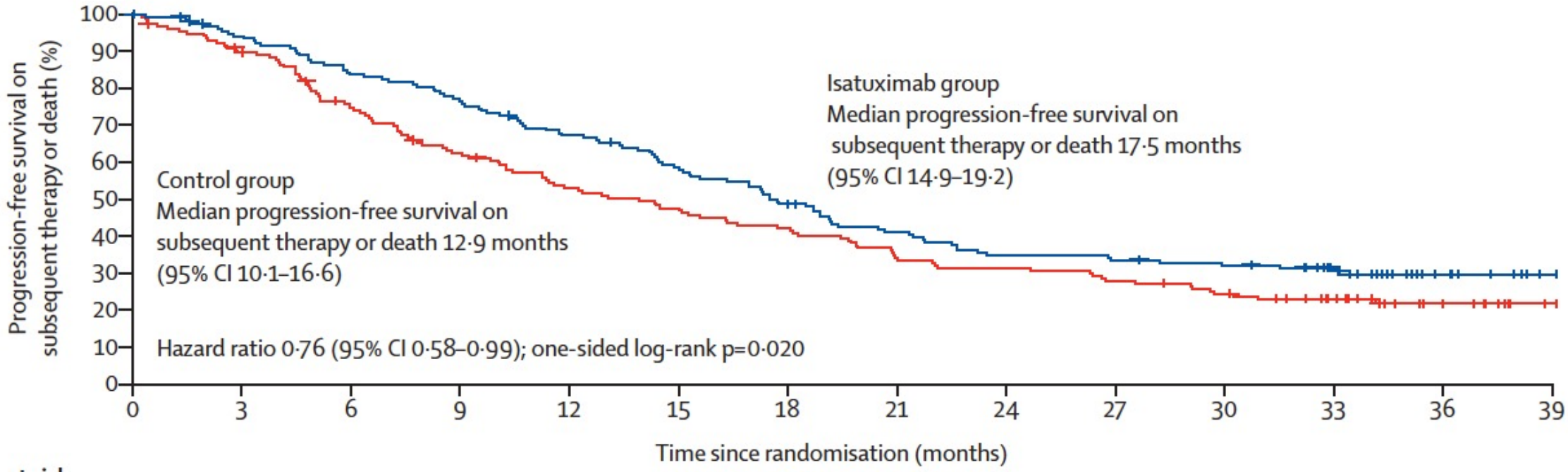
Lancet Oncol 2022; 23: 416–27

ICARIA-MM: Overall Survival



Richardson PD et al. *Lancet Oncol* 2022;23(3):416-27.

ICARIA-MM: Median PFS on Subsequent Therapy or Death



Number at risk (number censored)													
Isatuximab group	154 (0)	141 (4)	125 (4)	114 (4)	99 (5)	85 (6)	70 (6)	57 (8)	48 (8)	46 (8)	43 (9)	32 (18)	13 (36)	..
Control group	153 (0)	135 (2)	109 (5)	90 (6)	75 (7)	66 (7)	59 (7)	46 (7)	43 (7)	38 (7)	32 (8)	23 (15)	11 (26)	..

Richardson PD et al. *Lancet Oncol* 2022;23(3):416-27.

Multiple Myeloma Agenda

Module 1: Up-Front Treatment of Multiple Myeloma (MM)

Module 2: Management of Relapsed/Refractory MM

Module 3: Other Novel Agents and Strategies

- Available data and ongoing trials evaluating venetoclax for patients with t(11;14) MM or Bcl-2 overexpression
- Sequencing of agents (eg, selinexor, isatuximab) alone or in combination for patients with relapsed/refractory MM
- Mechanism of action and potential clinical role of the CELMoDs (cereblon E3 ligase inhibitors) iberdomide and CC-92480

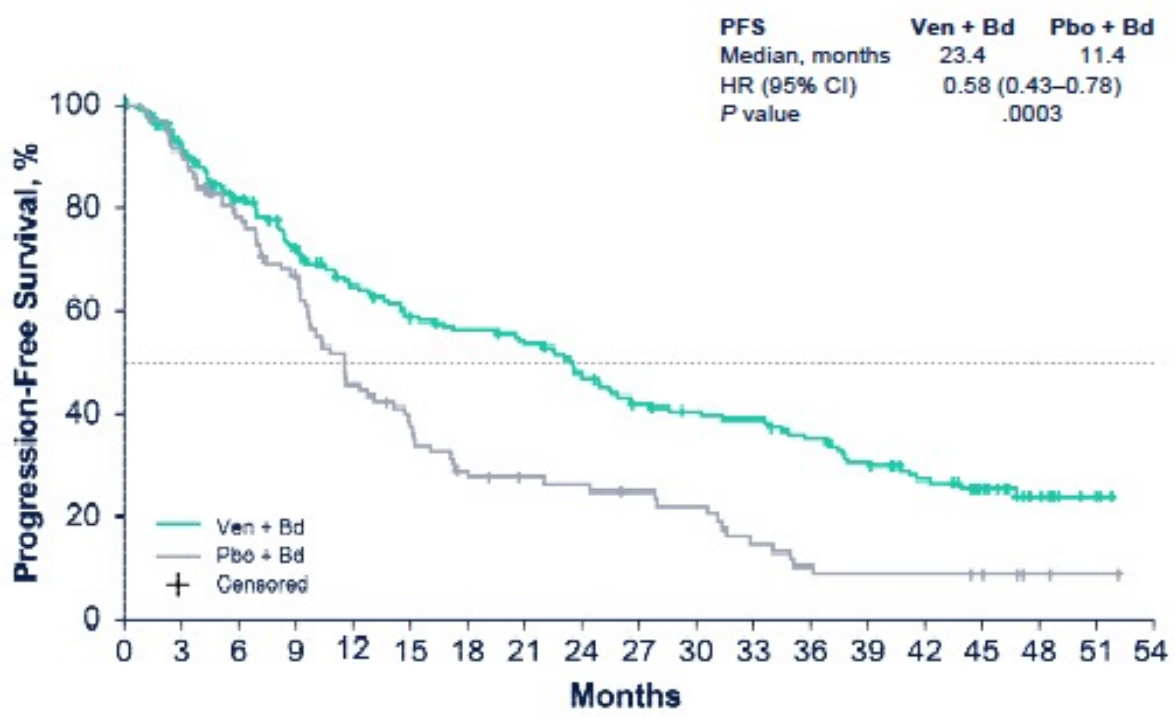
ASH 2021;Abstract 84

Final Overall Survival Results from BELLINI, a Phase 3 Study of Venetoclax or Placebo in Combination With Bortezomib and Dexamethasone in Relapsed/Refractory Multiple Myeloma

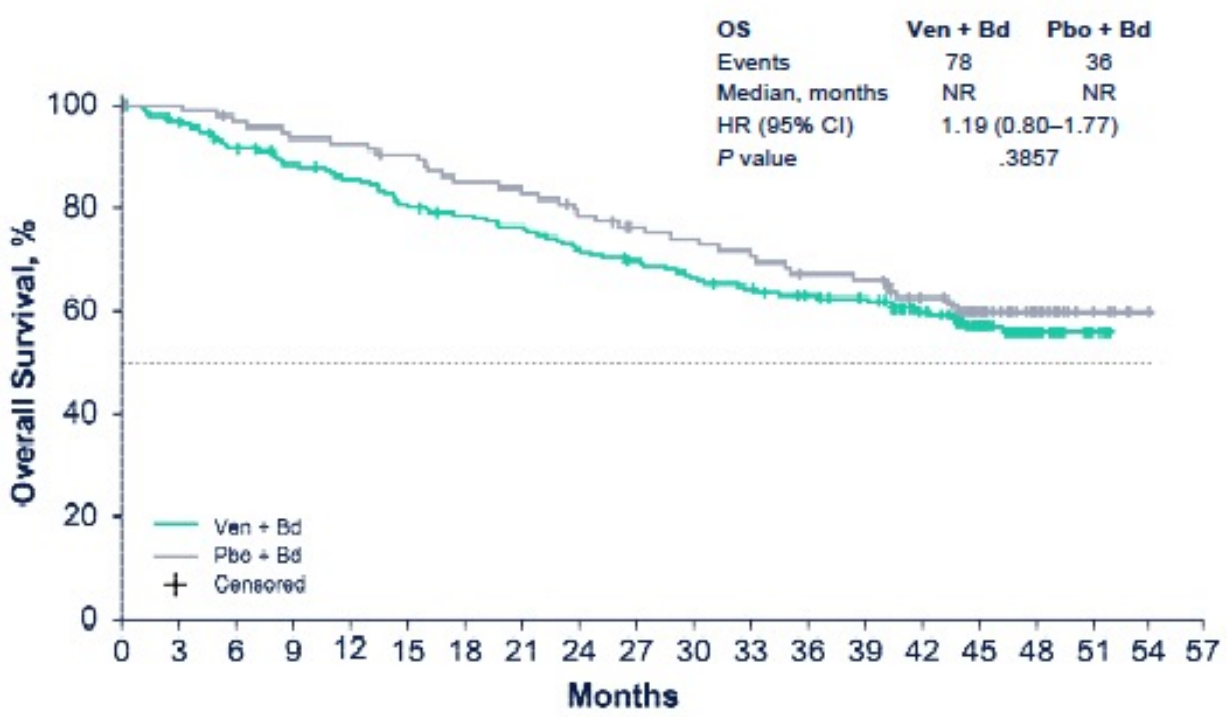
Shaji K. Kumar,[1] Simon J. Harrison,[2] Michele Cavo,[3] Javier de la Rubia,[4] Rakesh Popat,[5] Cristina Gasparetto,[6] Vania Hungria,[7] Hans Salwender,[8] Kenshi Suzuki,[9] Inho Kim,[10] Maika Onishi,[11] Grace Ku,[11] Rajvineeth Pothacamury,[12] Vasudha Sehgal,[12] Abdullah Masud,[12] Jeremy A. Ross,[12] Edyta Dobkowska,[13] and Philippe Moreau[14]

BELLINI: Updated Survival Results

Investigator-Assessed PFS in All Patients



OS in All Patients

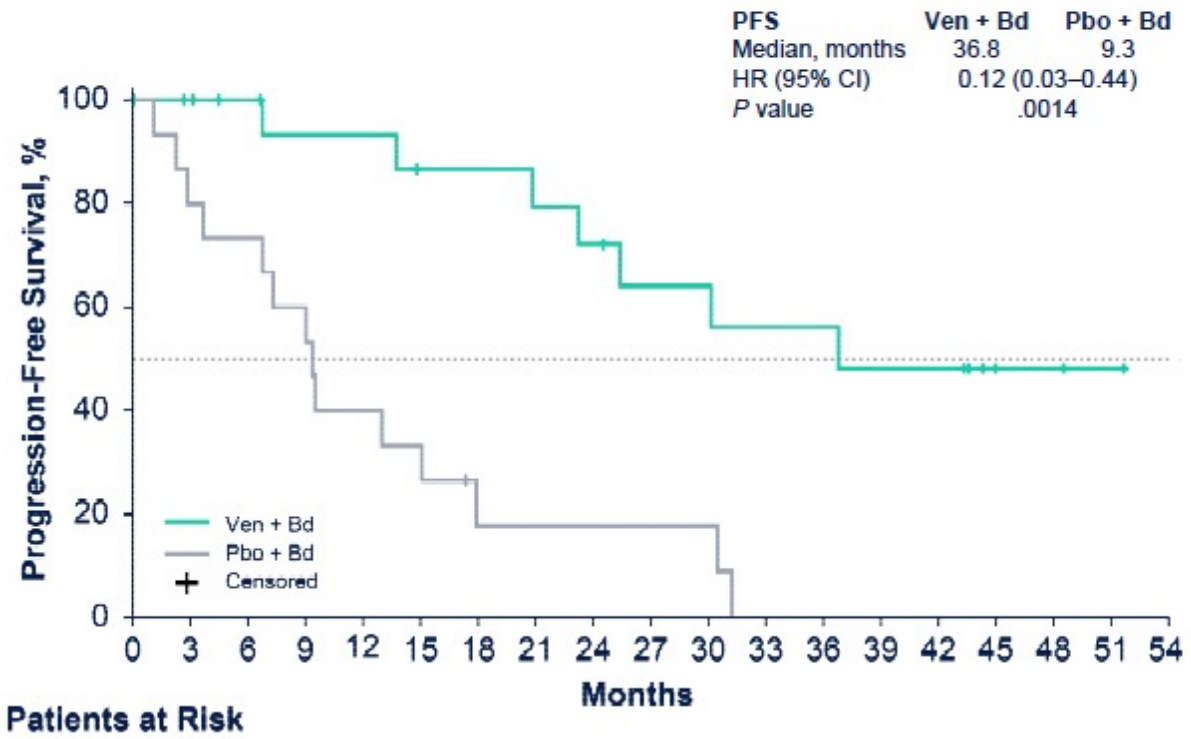


Kumar SK et al. ASH 2021;Abstract 84.

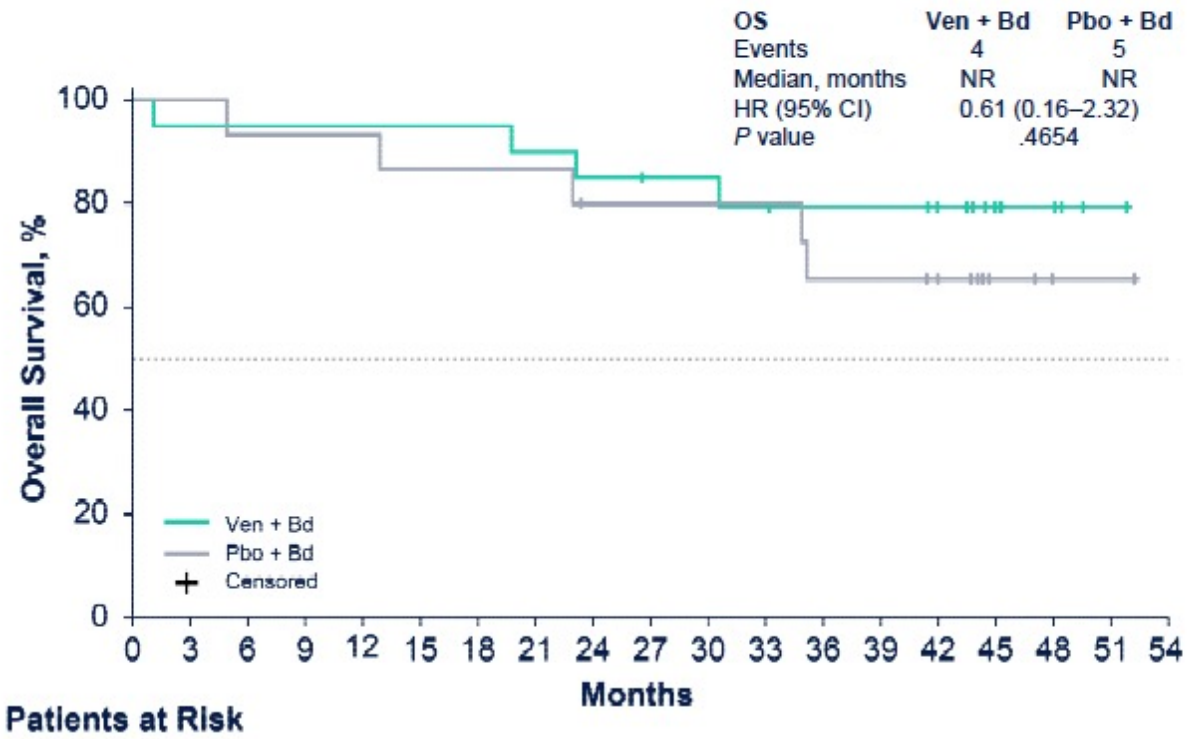
RTP RESEARCH TO PRACTICE

BELLINI: Updated Survival Results for Patients with t(11;14)

Investigator-Assessed PFS in Patients With t(11;14)



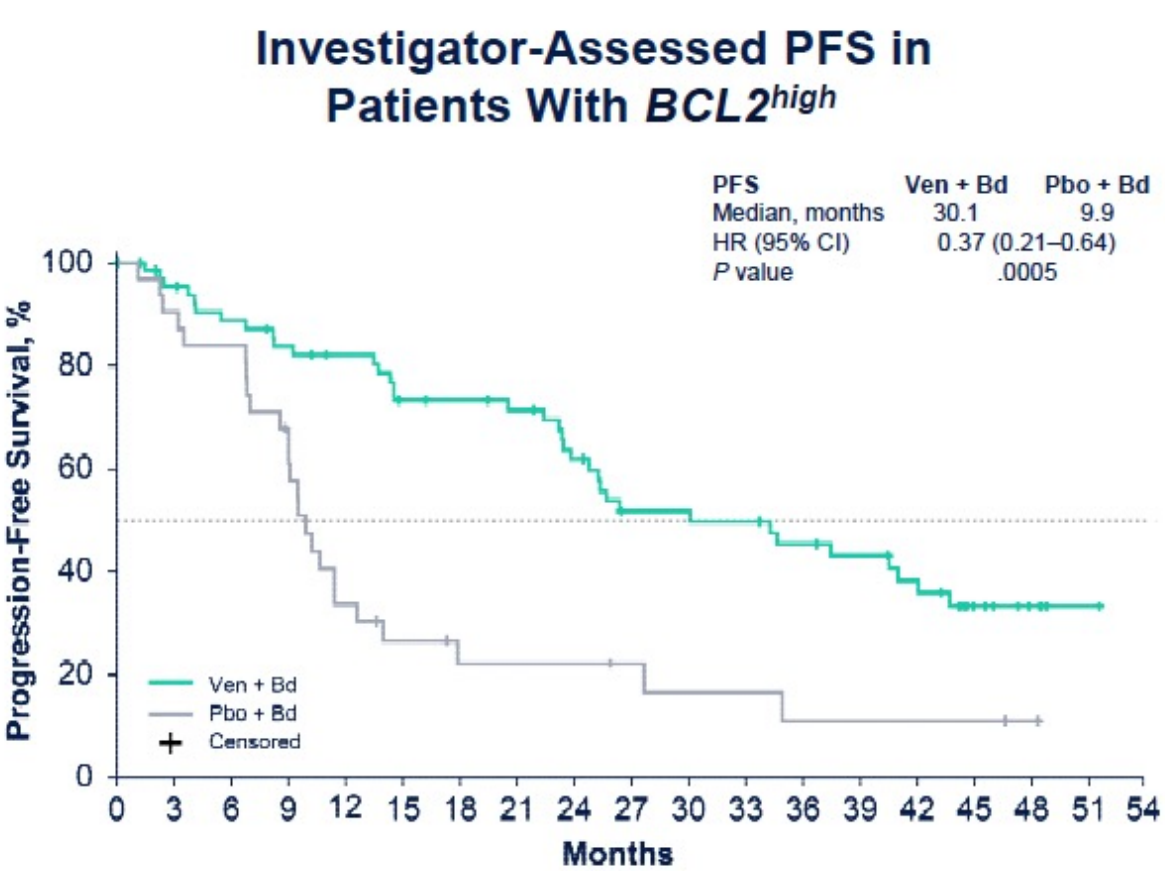
OS in Patients With t(11;14)

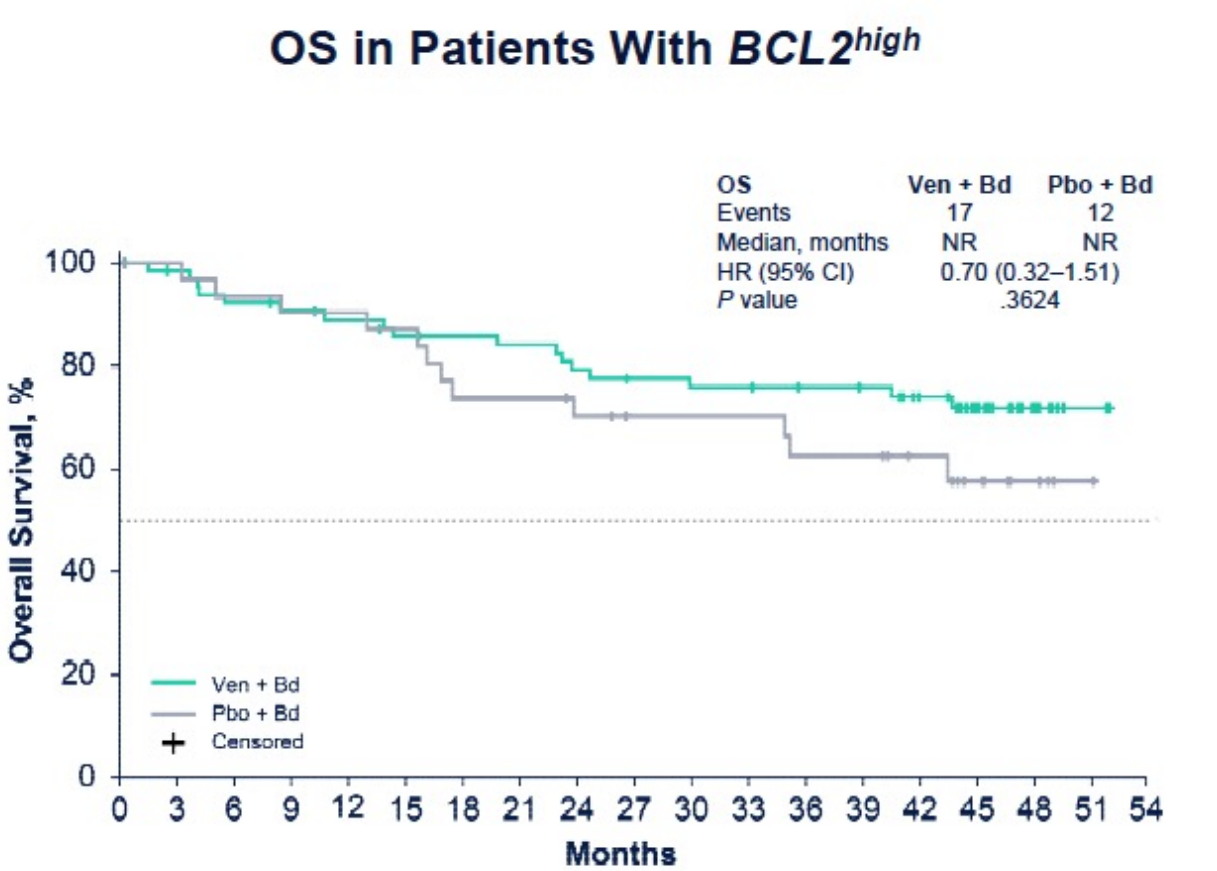


Kumar SK et al. ASH 2021;Abstract 84.

RTP RESEARCH TO PRACTICE

BELLINI: Updated Survival Results for Patients with High Bcl-2 Expression

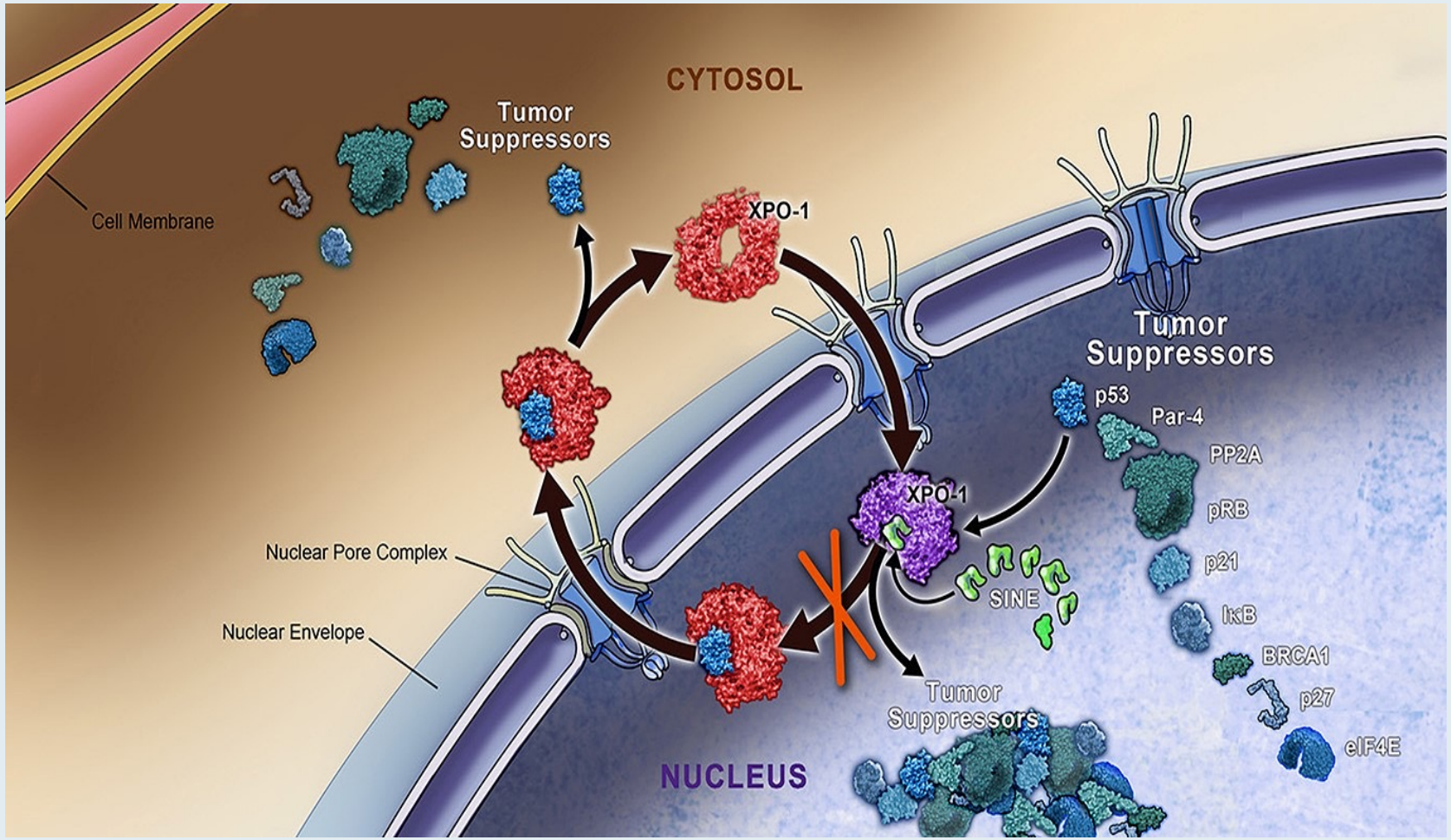




Kumar SK et al. ASH 2021;Abstract 84.

RTP RESEARCH TO PRACTICE

Selinexor Mechanism of Action



- Exportin 1 (XPO1) is the major nuclear export protein for tumor suppressor proteins (TSPs), the glucocorticoid receptor (GR) and eIF4E-bound oncoprotein mRNAs (c-myc, Bcl-2, Bcl-xL and cyclins)
- XPO1 is overexpressed in MM and its levels often correlate with poor prognosis
- Selinexor is a first-in-class XPO1 inhibitor that induces nuclear retention and activation of TSPs and the GR in the presence of steroids and suppresses oncoprotein expression

Bahlis N et al. EHA 2016;Abstract P277.

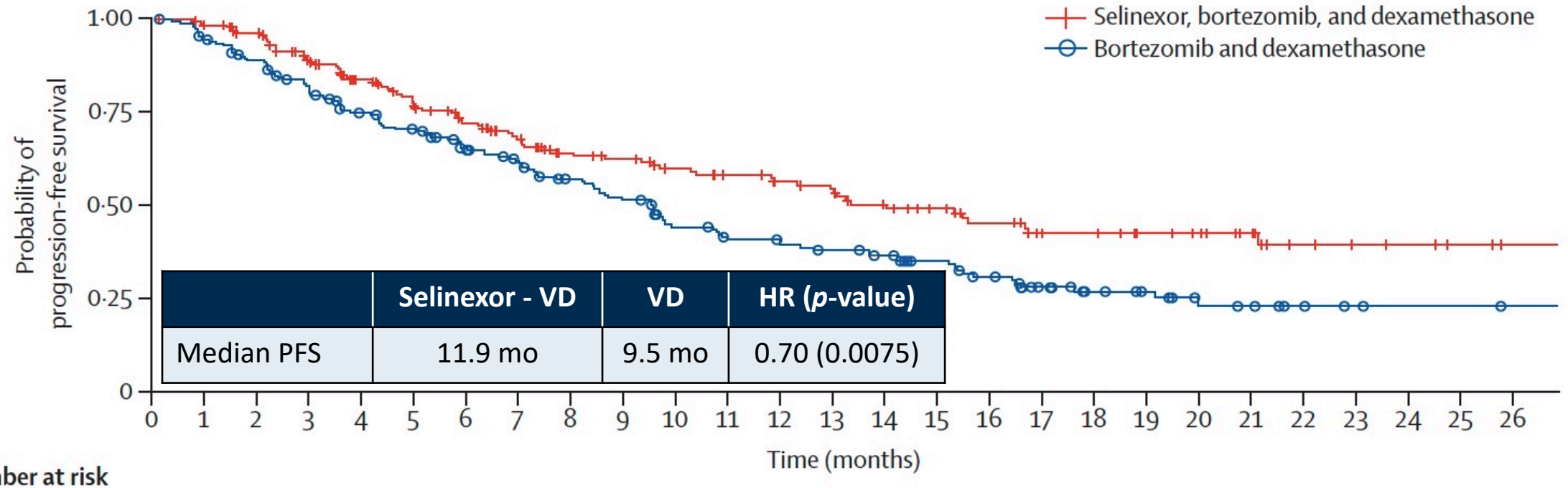
RTP RESEARCH TO PRACTICE

Lancet 2020;396:1563-73

Once-per-week selinexor, bortezomib, and dexamethasone versus twice-per-week bortezomib and dexamethasone in patients with multiple myeloma (BOSTON): a randomised, open-label, phase 3 trial

Sebastian Grosicki, Maryana Simonova, Ivan Spicka, Ludek Pour, Iryrna Kriachok, Maria Gavriatopoulou, Halyna Pylypenko, Holger W Auner, Xavier Leleu, Vadim Doronin, Ganna Usenko, Nizar J Bahlis, Roman Hajek, Reuben Benjamin, Tuphan K Dolai, Dinesh K Sinha, Christopher P Venner, Mamta Garg, Mercedes Gironella, Artur Jurczyszyn, Pawel Robak, Monica Galli, Craig Wallington-Beddoe, Atanas Radinoff, Galina Salogub, Don A Stevens, Supratik Basu, Anna M Liberati, Hang Quach, Vesselina S Goranova-Marinova, Jelena Bila, Eirini Katodritou, Hanna Oliynyk, Sybiryna Korenkova, Jeevan Kumar, Sundar Jagannath, Phillipe Moreau, Moshe Levy, Darrell White, Moshe E Gatt, Thierry Facon, Maria V Mateos, Michele Cavo, Donna Reece, Larry D Anderson Jr, Jean-Richard Saint-Martin, Jacqueline Jeha, Anita A Joshi, Yi Chai, Lingling Li, Vishnuvardhan Peddagali, Melina Arazy, Jatin Shah, Sharon Shacham, Michael G Kauffman, Meletios A Dimopoulos, Paul G Richardson, Sosana Delimpasi**

BOSTON: Progression-Free Survival (ITT Population)



	Selinexor - VD	VD	HR (*p*-value)
Median PFS	11.9 mo	9.5 mo	0.70 (0.0075)

Number at risk (number censored)

Selinexor, bortezomib, and dexamethasone	195 (0)	187 (5)	175 (12)	152 (21)	135 (31)	117 (37)	106 (42)	89 (50)	79 (57)	76 (59)	69 (63)	64 (66)	57 (71)	51 (73)	45 (76)	41 (80)	35 (83)	27 (89)	26 (90)	22 (94)	19 (97)	14 (102)	9 (106)	7 (108)	6 (109)	4 (111)	2 (113)
Bortezomib and dexamethasone	207 (0)	187 (8)	175 (10)	152 (15)	138 (20)	127 (22)	111 (29)	100 (32)	90 (37)	81 (37)	66 (41)	59 (43)	56 (44)	53 (45)	49 (47)	42 (52)	35 (55)	26 (60)	20 (65)	16 (69)	10 (73)	8 (75)	5 (78)	4 (79)	3 (80)	3 (80)	2 (81)

Grosicki S et al. *Lancet* 2020;396(10262):1563-73.

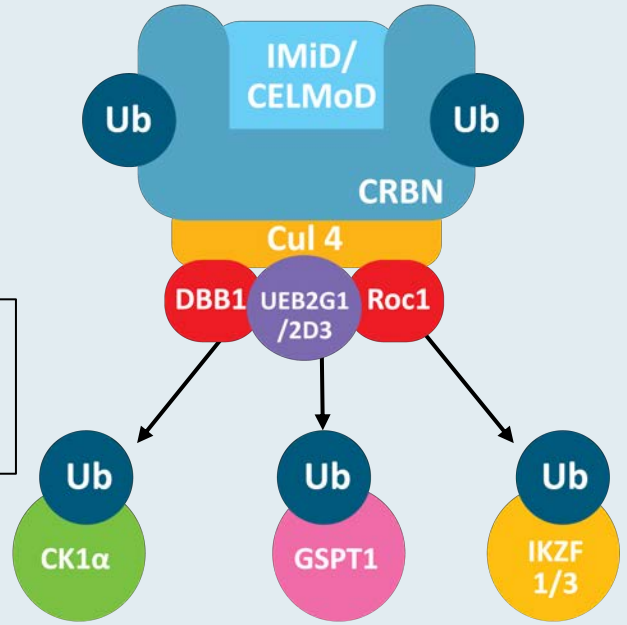
BOSTON: Select Adverse Events

Adverse event	Selinexor + Bort/dex (n = 195)		Bort/dex (n = 204)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Thrombocytopenia	60%	39%	27%	17%
Fatigue	42%	13%	18%	1%
Anemia	36%	16%	23%	10%
Peripheral neuropathy	32%	5%	47%	9%
Neutropenia	15%	9%	6%	3%

Grosicki S et al. *Lancet* 2020;396(10262):1563-73.

CC-92480/Dexamethasone Combined with Bortezomib or Daratumumab or Carfilzomib

IMiD®	Indication
Thalidomide	Erythema Nodosum Erythema Leprosum Multiple Myeloma
Lenalidomide	Mantle Cell Lymphoma Multiple Myeloma Myelodysplastic Syndrome (5q-)
Pomalidomide	Multiple Myeloma Kaposi Sarcoma



Clinical trials	CELMoDs®
Multiple Myeloma Diffuse Large B-Cell Lymphoma CNS Lymphoma Glioblastoma Hepatocellular Carcinoma Chronic Lymphocytic Leukemia	CC-122
Multiple Myeloma Systemic Lupus Erythematosus	CC-220
Acute Myeloid Leukemia	CC-90009
Multiple Myeloma	CC-92480 Indisulam
Acute Myeloid Leukemia? (in vitro)	CC-885

Abbreviation: CK1a: casein kinase 1a;
CELMods: Cereblon E3 Ligase Modulation Drugs;
CRL4: cullin-4 RING E3 ligase;
CRBN: Cereblon; CNS: Central Nervous System;
CUL4: Cullin-4; DDB1: DNA damage-binding protein 1;
GSPT1: G1 To S Phase Transition 1;
IKZF1: Ikaros zinc-finger protein 1;
IKZF3: Aiolos zonc-finger protein 3;
IMiDs: Immunomodulatory Drugs;
MDS: Myelodysplastic Syndrome;
Roc1: Ring finger protein;
UB: Ubiquitination
UBE2G1/2D3: Ubiquitin-conjugating enzymes

Holstein et al, Next-Generation Drugs. Targeting the Cereblon Ubiquitin Ligase. JCO 2018.
Lu G et al eLife 2018
Gandhi AK et al Br Haem 2014
Krönke J et al Science 2014
Hansen JD et al J Med Chem 2020
Uehara T et al Nat Chem Biol 2017

McCarthy P. ASCO 2020 Discussant

RTP RESEARCH TO PRACTICE

Iberdomide (IBER) in Combination with Dexamethasone (DEX) in Patients (pts) with Relapsed/Refractory Multiple Myeloma (RRMM): Results from the Dose-Expansion Phase of the CC-220-MM-001 Trial

Lonial S et al.

ASH 2021;Abstract 162.

CC-220-MM-001: Responses with IBER + DEX for R/R MM

	IBER + DEX (N = 107)	IBER + DEX post anti-BCMA therapy (N = 24)
Response, n (%)		
ORR[a]	28 (26.2)	6 (25.0)
sCR	1 (0.9)	0
CR	0	1 (4.2)
VGPR	8 (7.5)	1 (4.2)
PR	19 (17.8)	4 (16.7)
MR	11 (10.3)	4 (16.7)
SD	46 (43.0)	8 (33.3)
PD	15 (14.0)	4 (16.7)
NE	7 (6.5)	2 (8.3)
Median DoR (95% CI), months	7.0 (4.5–11.3)	NA

[a]Defined as PR or better

BCMA, B-cell maturation antigen; CI, confidence interval; CR, complete response; DEX, dexamethasone; DoR, duration of response; IBER, iberdomide; MR, minimal response; NA not available; NE, not evaluable; ORR, overall response rate; PD, progressive disease; PR, partial response; sCR, stringent complete response; SD, stable disease; VGPR, very good partial response.

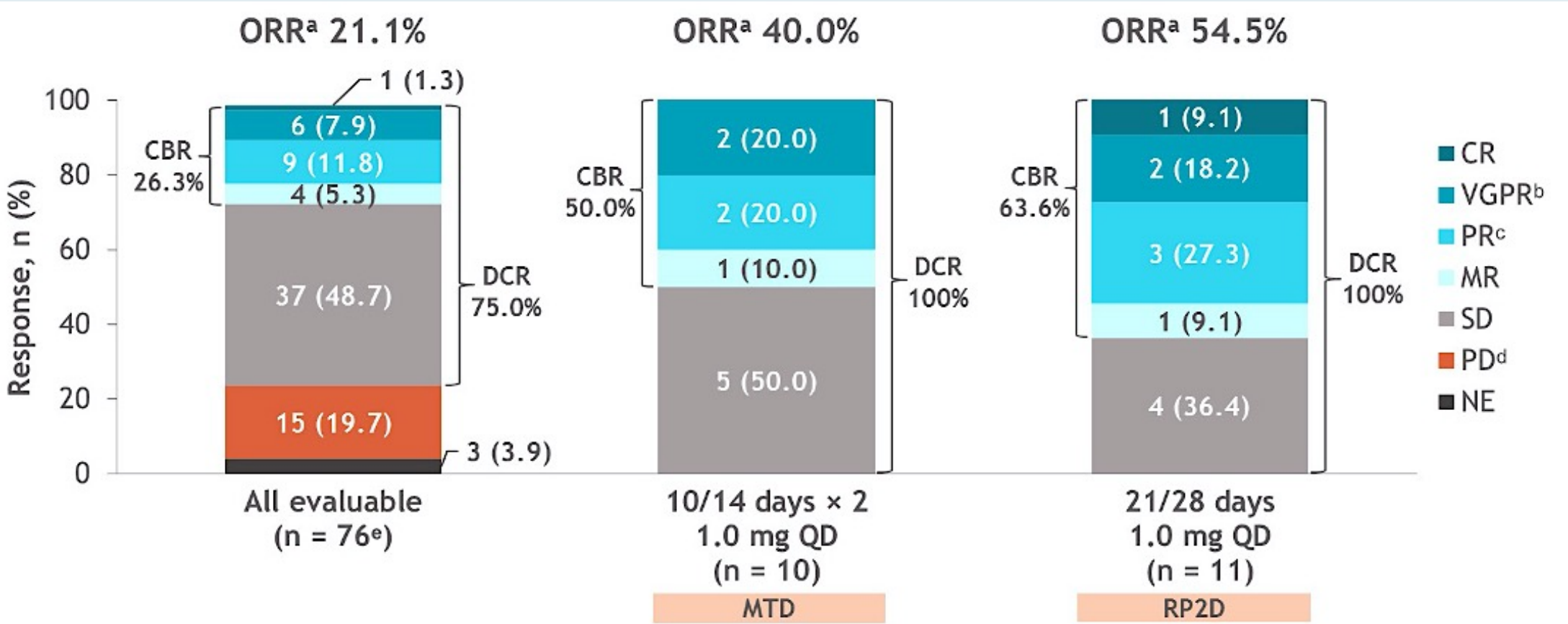
Lonial S et al. ASH 2021;Abstract 162.

First-in-Human Phase I Study of the Novel CELMoD Agent CC-92480 Combined with Dexamethasone (DEX) in Patients (pts) with Relapsed/Refractory Multiple Myeloma (RRMM)

Richardson PG et al.

ASCO 2020;Abstract 8500.

CC-92480 with Dexamethasone: Response



- At the RP2D 1.0 mg QD 21/28 days, 7 out of 11 patients were triple-class-refractory[f]
  - 1 patient had CR, 1 VGPR, 2 PR, and 1 MR

MTD = maximum tolerated dose; RP2D = recommended Phase II dose

Richardson PG et al. ASCO 2020;Abstract 8500.

Thank you for joining us!

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

We are taking a short break!

The program will resume at 1:05 PM PT (4:05 PM ET)

Up Next…

Drs Brad Kahl and Craig Moskowitz discuss the management of chronic lymphocytic leukemia and lymphomas

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