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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TO PRACTICE

Welcome AON Members!

RTP
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TO PRACTICE

Data + Perspectives — Investigators Discuss the Current and Future Roles of Chimeric Antigen Receptor T-Cell Therapy and Bispecific Antibodies in the Care of Patients with Hematologic Cancers

Tuesday, August 9, 2022

5:00 PM – 6:30 PM ET

Faculty

Ajai Chari, MD
Ian W Flinn, MD, PhD
Nikhil C Munshi, MD
Laurie H Sehn, MD, MPH

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Meet The Professor

Optimizing the Management of Small Cell Lung Cancer

Thursday, August 11, 2022
5:00 PM – 6:00 PM ET

Faculty

Jacob Sands, MD

Moderator

Neil Love, MD

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In-Person and Zoom Audience Clinician Survey

In-person audience

- **Please complete the premeeting survey on the iPads. A link to the postmeeting survey will be sent to you after the meeting**

Zoom participants

- **Please complete the pre- and postmeeting surveys for each module**

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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 – APHINTY, ExteNET trial

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

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- 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 – APHINTY, ExteNET trial

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

Discussion Question

Regulatory and reimbursement issues aside, what next therapy would you recommend for a 60-year-old woman with hormone receptor (HR)-positive, IHC HER2 1+ metastatic breast cancer and worsening liver disease who has experienced disease progression on a CDK4/6 inhibitor/fulvestrant?

- T-DXd
- Sacituzumab govitecan
- Capecitabine
- Paclitaxel
- Alpelisib/everolimus
- Other

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Discussion Question

Regulatory and reimbursement issues aside, what next therapy would you recommend for a 60-year-old woman with HR-negative, IHC HER2 1+ BRCA wild-type metastatic breast cancer and symptomatic disease progression on first-line chemoimmunotherapy?

- T-DXd
- Sacituzumab govitecan
- Capecitabine
- Eribulin
- Other

RTP RESEARCH TO PRACTICE

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

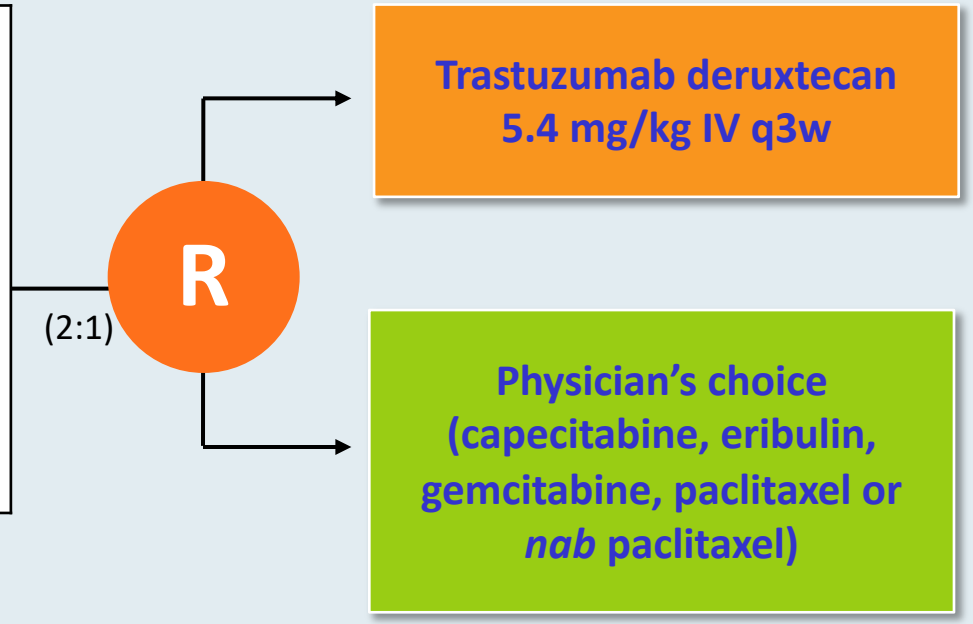
DESTINY-Breast04: Phase III Trial Schema

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



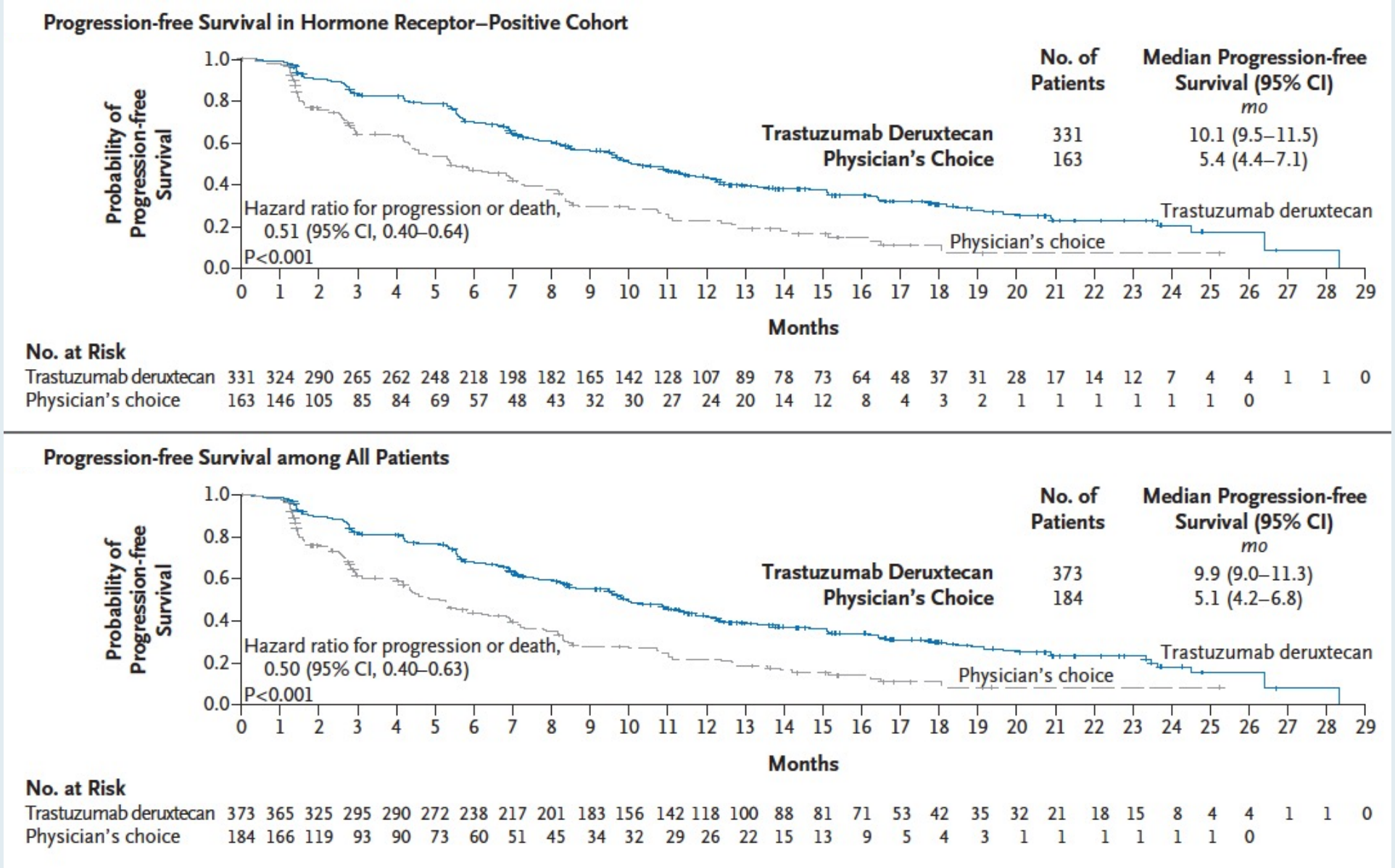
Randomization is stratified by

- 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.

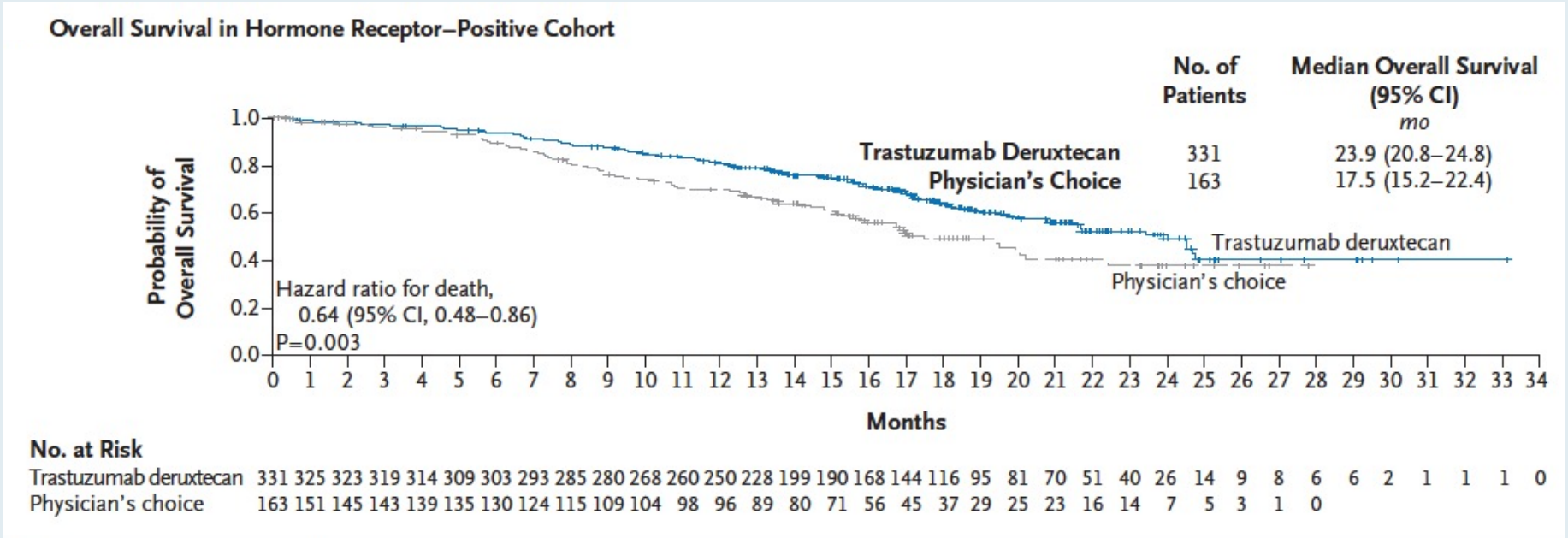
DESTINY-Breast04: Progression-Free Survival

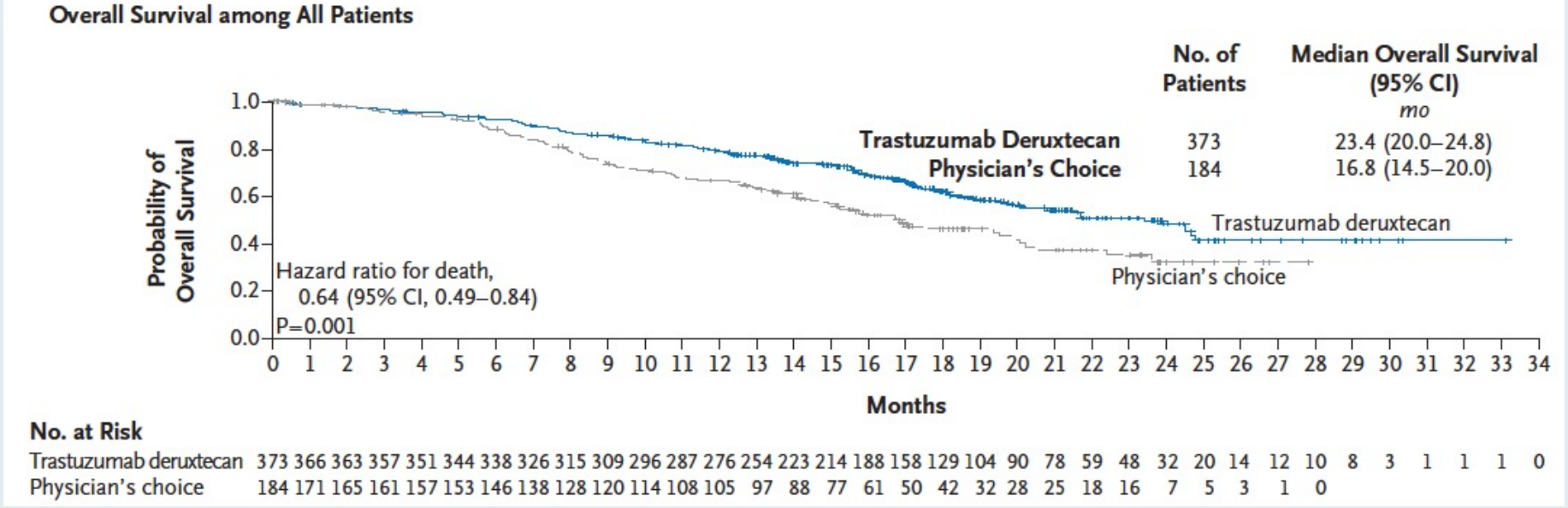


Modi S et al. *N Engl J Med* 2022;387(1):9-20; ASCO 2022;Abstract LBA3.

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.

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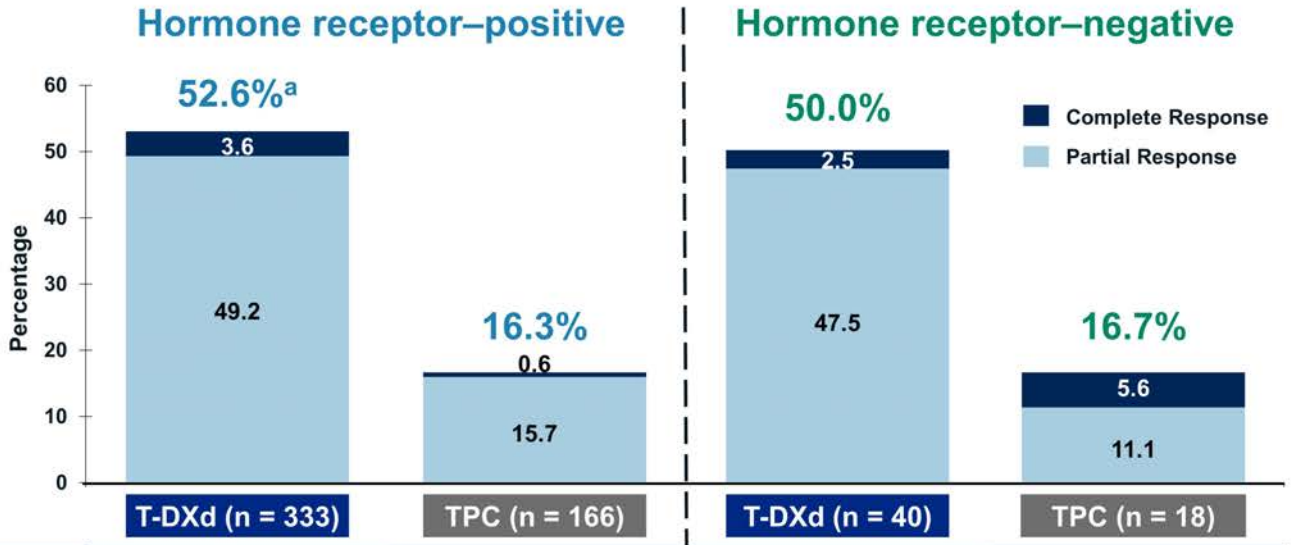
Confirmed ORR

Confirmed Objective Response Rate

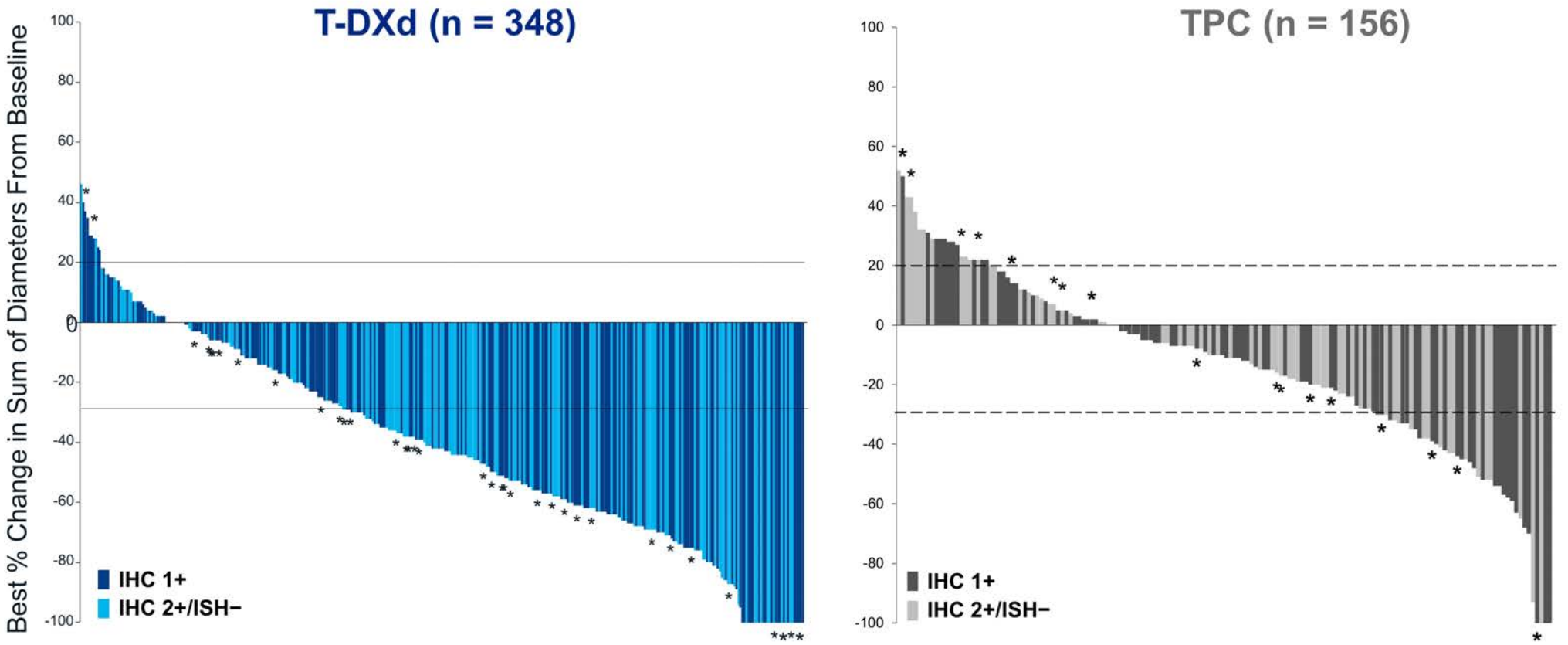


	T-DXd (n = 333)	TPC (n = 166)	T-DXd (n = 40)	TPC (n = 18)
Progressive disease, %	7.8	21.1	12.5	33.3
Not evaluable, %	4.2	12.7	7.5	5.6
Clinical benefit rate,[b] %	71.2	34.3	62.5	27.8
Duration of response, months	10.7	6.8	8.6	4.9

Hormone receptor status is based on data from the electronic data capture corrected for misstratification.
ORR, objective response rate; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.
[a]The response of 1 patient was not confirmed. [b]Clinical benefit rate is defined as the sum of complete response rate, partial response rate, and more than 6 months' stable disease rate, based on blinded independent central review.

Modi S et al. ASCO 2022;Abstract LBA3.

Best Change in Target Lesions (All Patients)



*Patients with HR− disease

Shown are the best percentage changes from baseline in the sum of the largest diameters of measurable tumors in patients for whom data from both baseline and postbaseline assessments of target lesions by independent central review were available. The upper dashed horizontal line indicates a 20% increase in tumor size in the patients who had disease progression, and the lower dashed line indicates a 30% decrease in tumor size (partial response).

HR, hormone receptor; IHC, immunohistochemistry; ISH, in situ hybridization; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.

Modi S et al. 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.

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].

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 – APHINTY, ExteNET trial

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

Discussion Question

Regulatory and reimbursement issues aside, which second-line therapy would you recommend for a patient with HR-negative, HER2-amplified breast cancer with multiple asymptomatic brain metastases?

- Tucatinib, capecitabine and trastuzumab
- T-DXd
- Neratinib and capecitabine
- Neratinib and lapatinib
- Other

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

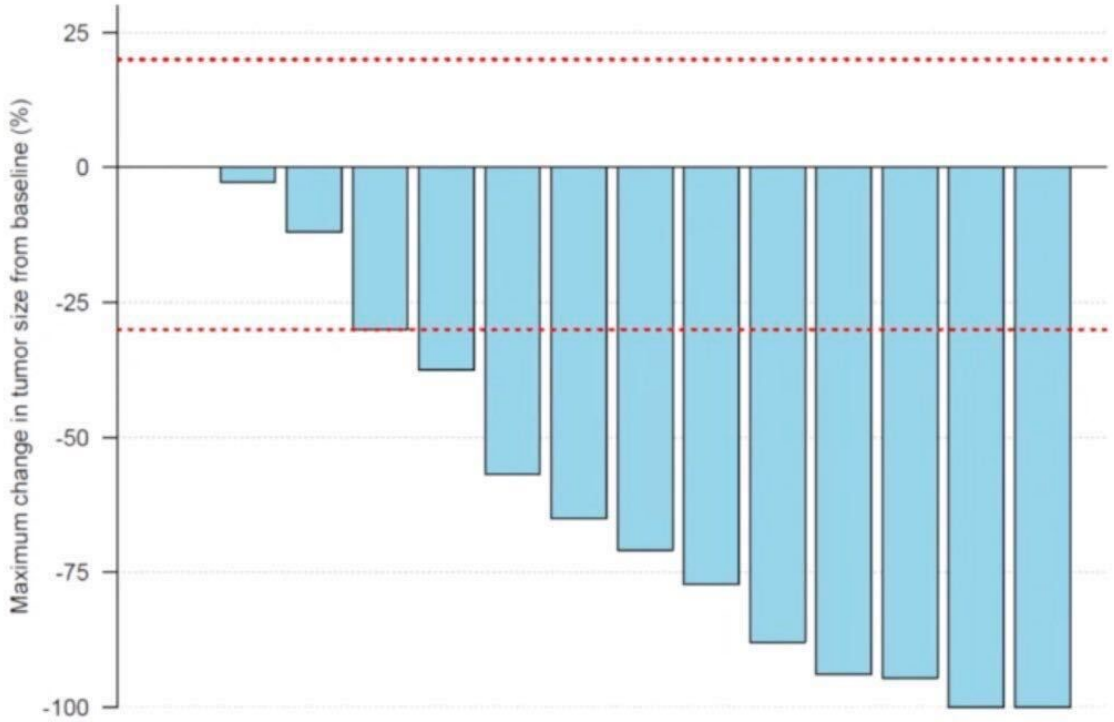
Bartsch R et al.

ESMO Breast 2022;Abstract 165MO.

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.

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.

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
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- Adjuvant and postadjuvant anti-HER2 treatment – APHINTY, ExteNET trial

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

Discussion Question

Which adjuvant HER2-directed therapy would you recommend for a 60-year-old woman with HR-positive, HER2-amplified breast cancer who receives neoadjuvant TCHP and has 2 positive nodes at the time of surgery?

- T-DM1
- T-DM1 followed by neratinib
- T-DXd
- T-DXd followed by neratinib
- Other

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: 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.

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

Discussion Question

Regulatory and reimbursement issues aside, have you attempted or would you attempt to access olaparib as part of adjuvant therapy for a patient with a germline PALB2 mutation and TNBC who had residual disease after neoadjuvant chemotherapy/immunotherapy?

I have

I haven't but would for the right patient

I haven't and would not

RTP RESEARCH TO PRACTICE

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.

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

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)
- Sequencing of therapy in metastatic disease
- New agents and strategies under investigation

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

Breast Cancer Agenda

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- New agents and strategies under investigation

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

Discussion Question

Regulatory and reimbursement issues aside, what adjuvant therapy would you recommend for a patient with a 3-cm TNBC who receives neoadjuvant chemotherapy/pembrolizumab and is found to have significant residual disease at the time of surgery?

- Pembrolizumab
- Capecitabine
- Both pembrolizumab and capecitabine
- I'm not sure

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*

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)
- Sequencing of therapy in metastatic disease
- New agents and strategies under investigation

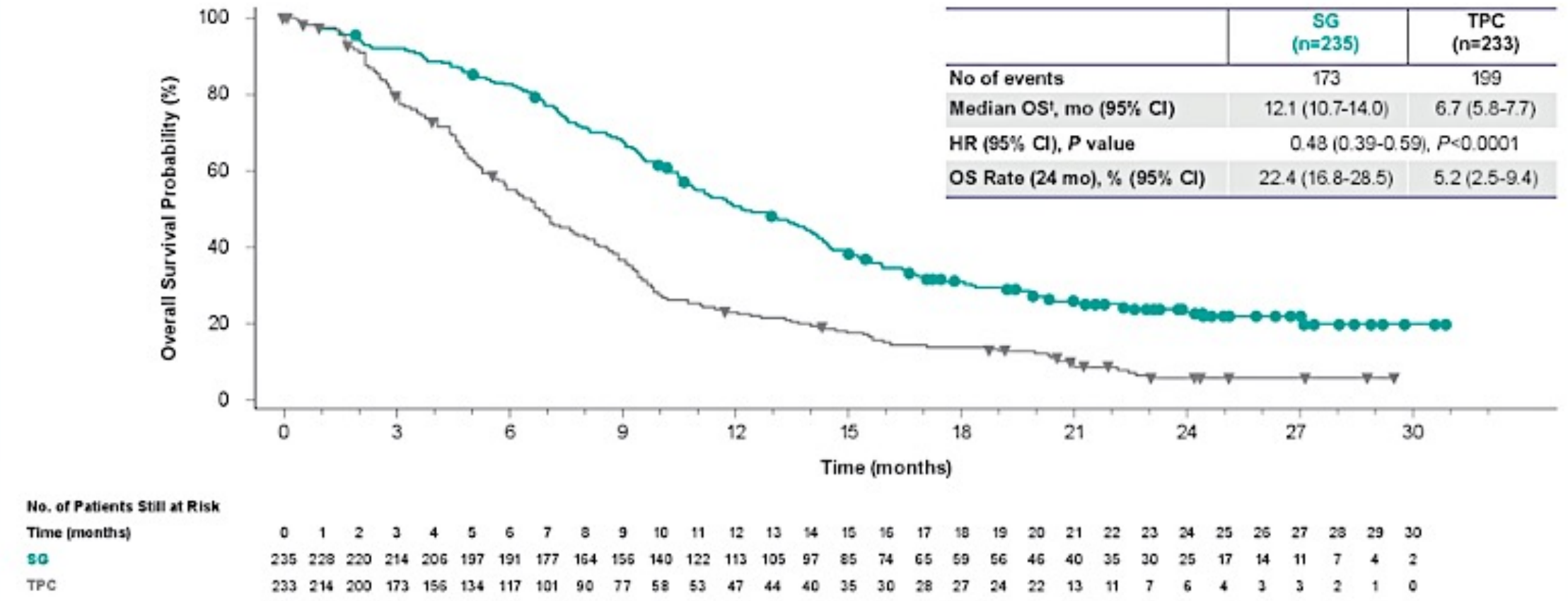
Module 4: ER/PR-Positive, HER2-Negative Disease

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: 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.

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

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]

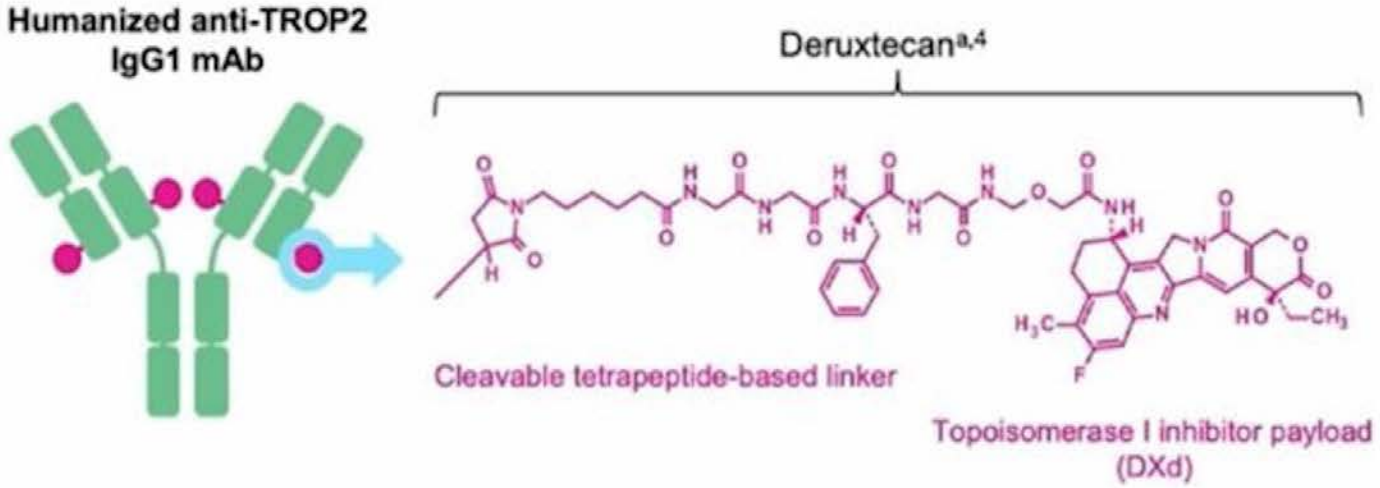
[1]Dana-Farber Cancer Institute, Boston, MA; [2]Department of Hematology/Oncology, Massachusetts General Hospital Cancer Center, Harvard Medical School, Boston, MA; [3]National Cancer Center Hospital, Tokyo, Japan; [4]NEXT Oncology, San Antonio, TX; [5]Virginia Cancer Specialists, Fairfax, VA; [6]Department 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

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



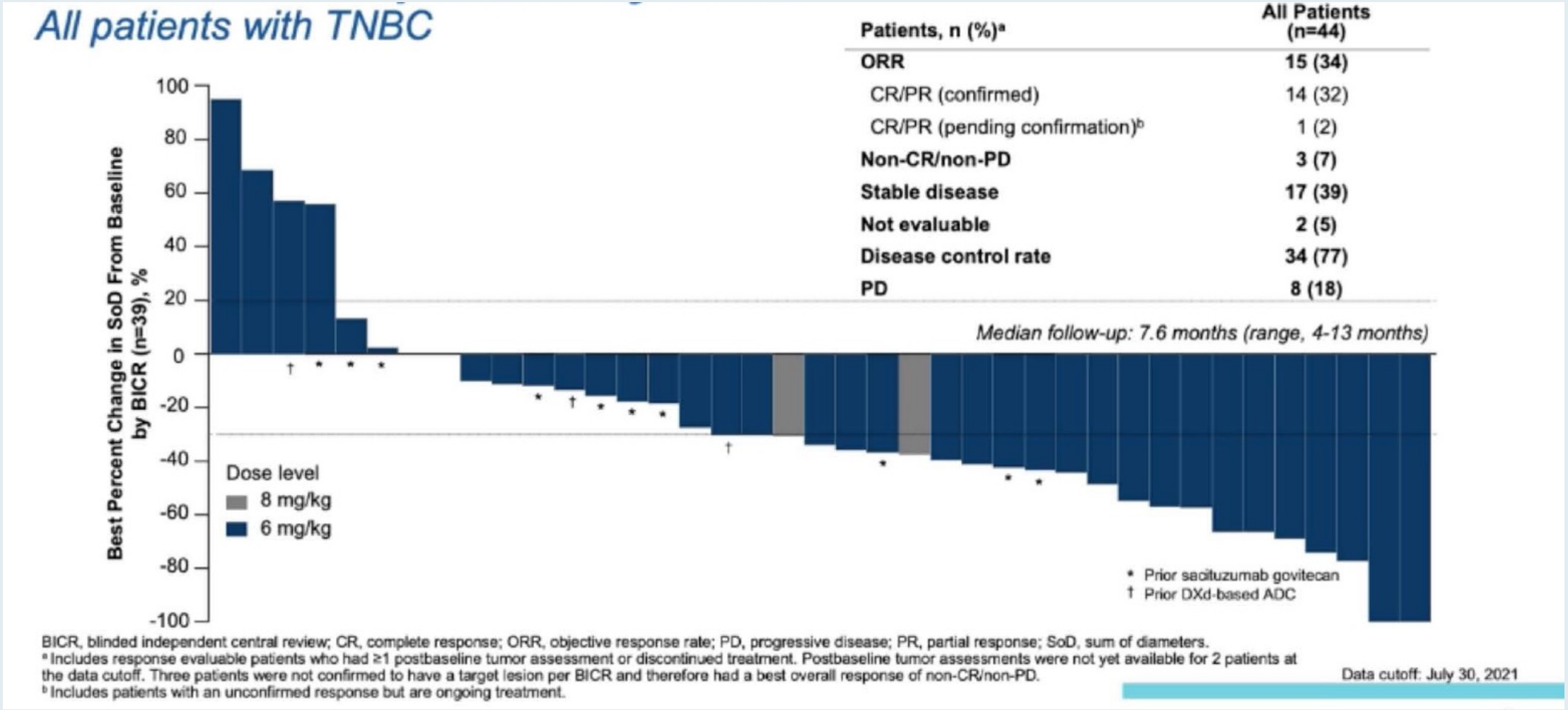
Payload mechanism of action: topoisomerase I inhibitor[b,1]
High potency of payload[b,2]
Optimized drug to antibody ratio ≈4[b,c,1]
Payload with short systemic half-life[b,c,2]
Stable linker-payload[b,2]
Tumor-selective cleavable linker[b,2]
Bystander antitumor effect[b,2,5]

[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.

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)**

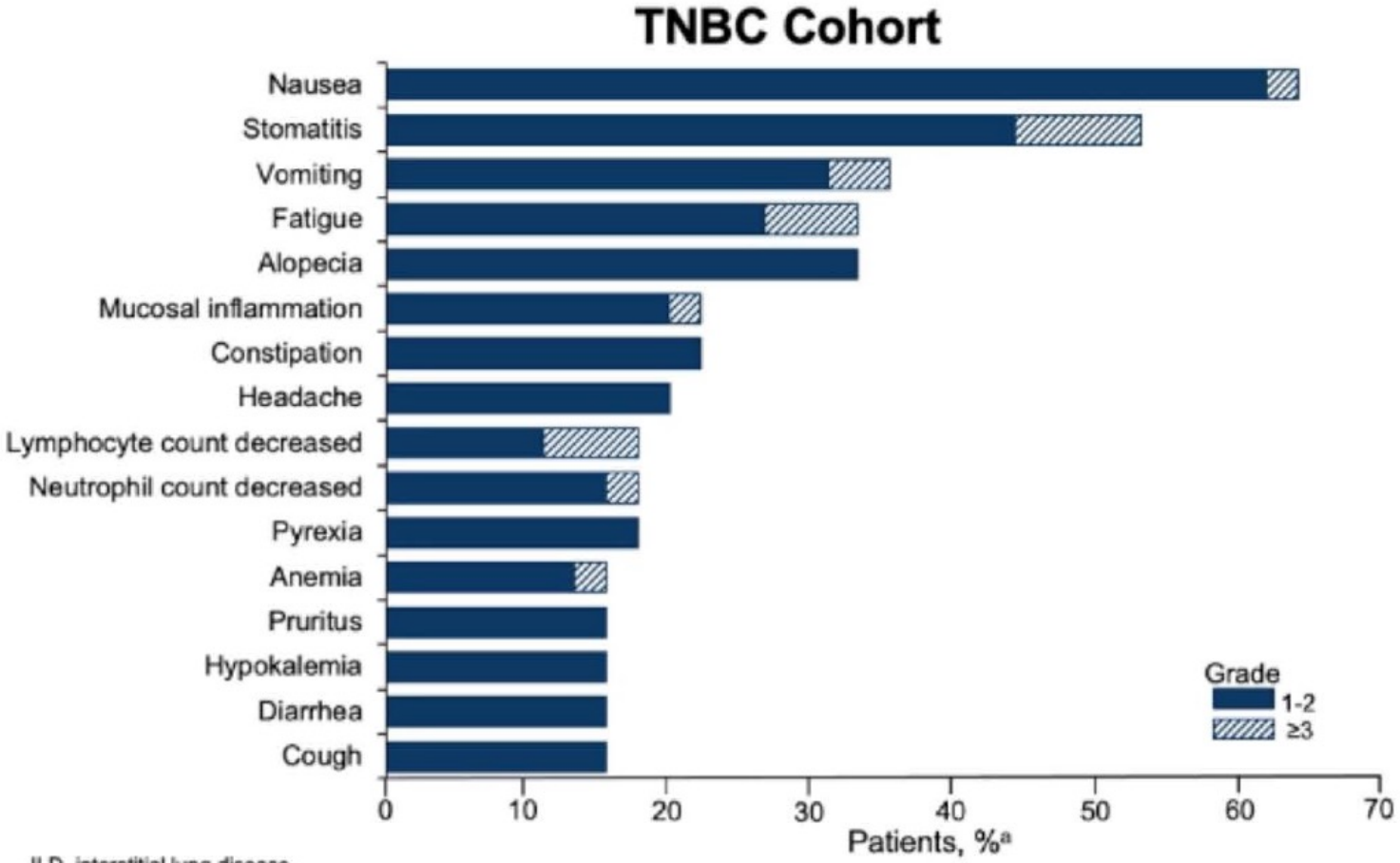
BICR, blinded independent central review; CR, complete response; ORR, objective response rate; PD, progressive disease; PR, partial response; SoD, sum of diameters.
[a] Includes response evaluable patients who had ≥1 postbaseline tumor assessment or discontinued treatment. Postbaseline tumor assessments 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

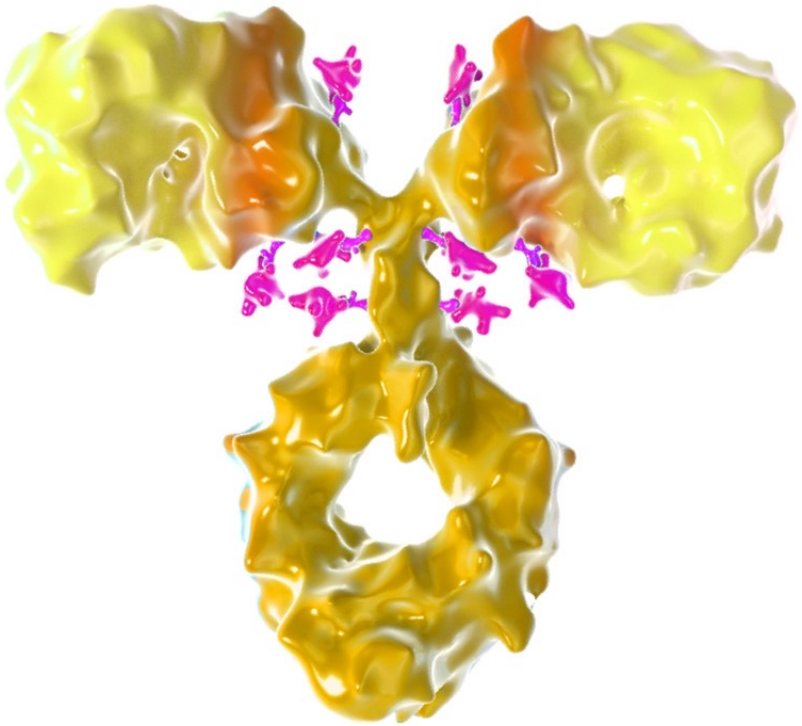
Krop I et al. SABCS 2021;Abstract GS1-05.

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



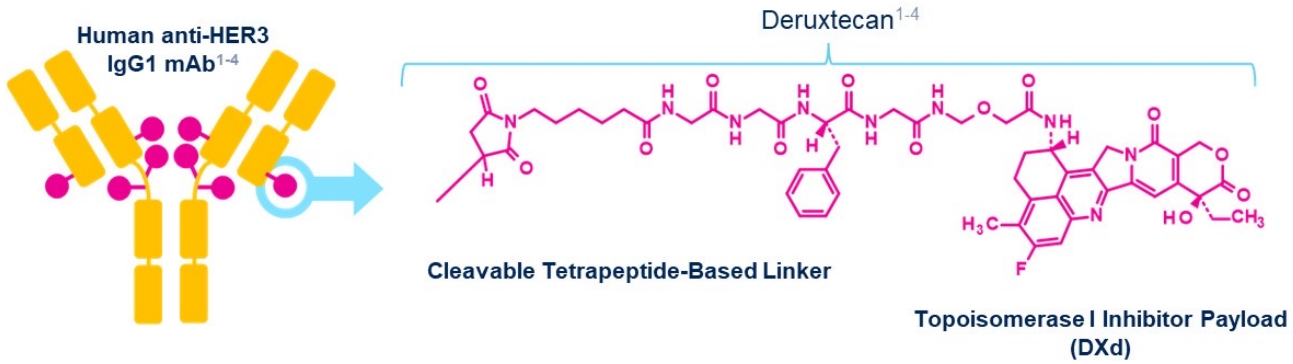
June 4, 2022

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



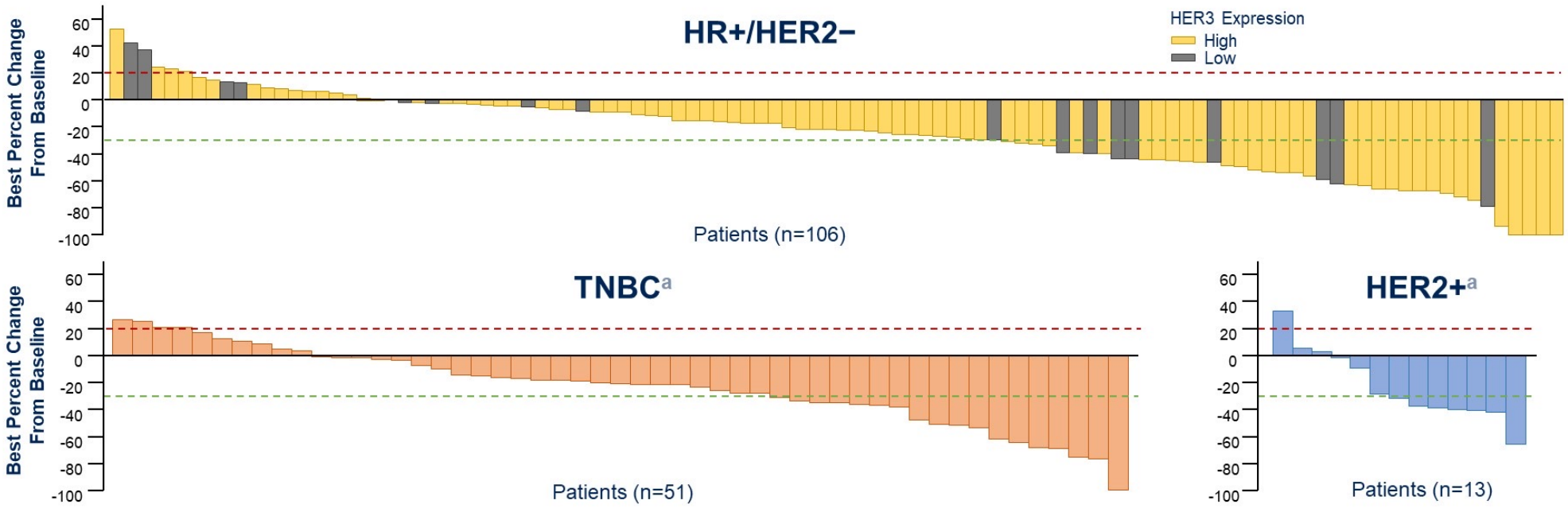
7 Key Attributes of HER3-DXd

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.

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.

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

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- Selection of CDK4/6 inhibitors in metastatic disease (ribociclib survival); sacituzumab govitecan

Discussion Question

For a 65-year-old postmenopausal woman with HR-positive, HER2-negative breast cancer with 2 positive axillary nodes and a Recurrence Score® of 24, would you recommend chemotherapy?

- Yes
- No
- I'm not sure

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

Breast Cancer Agenda

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

Discussion Question

Why do you think abemaciclib, but not palbociclib, has demonstrated positive clinical results in the adjuvant setting?

- Better antitumor activity
- Schedule of administration
- The way the trials were designed
- I’m not sure
- Other

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

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[†]

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

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- Selection of CDK4/6 inhibitors in metastatic disease (ribociclib survival); sacituzumab govitecan

Discussion Question

Which CDK4/6 inhibitor would you generally recommend in combination with endocrine therapy as first-line treatment for a postmenopausal woman with metastatic HR-positive, HER2-negative breast cancer?

- Palbociclib
- Ribociclib
- Abemaciclib
- No preference

RTP RESEARCH TO PRACTICE

The NEW ENGLAND JOURNAL of MEDICINE

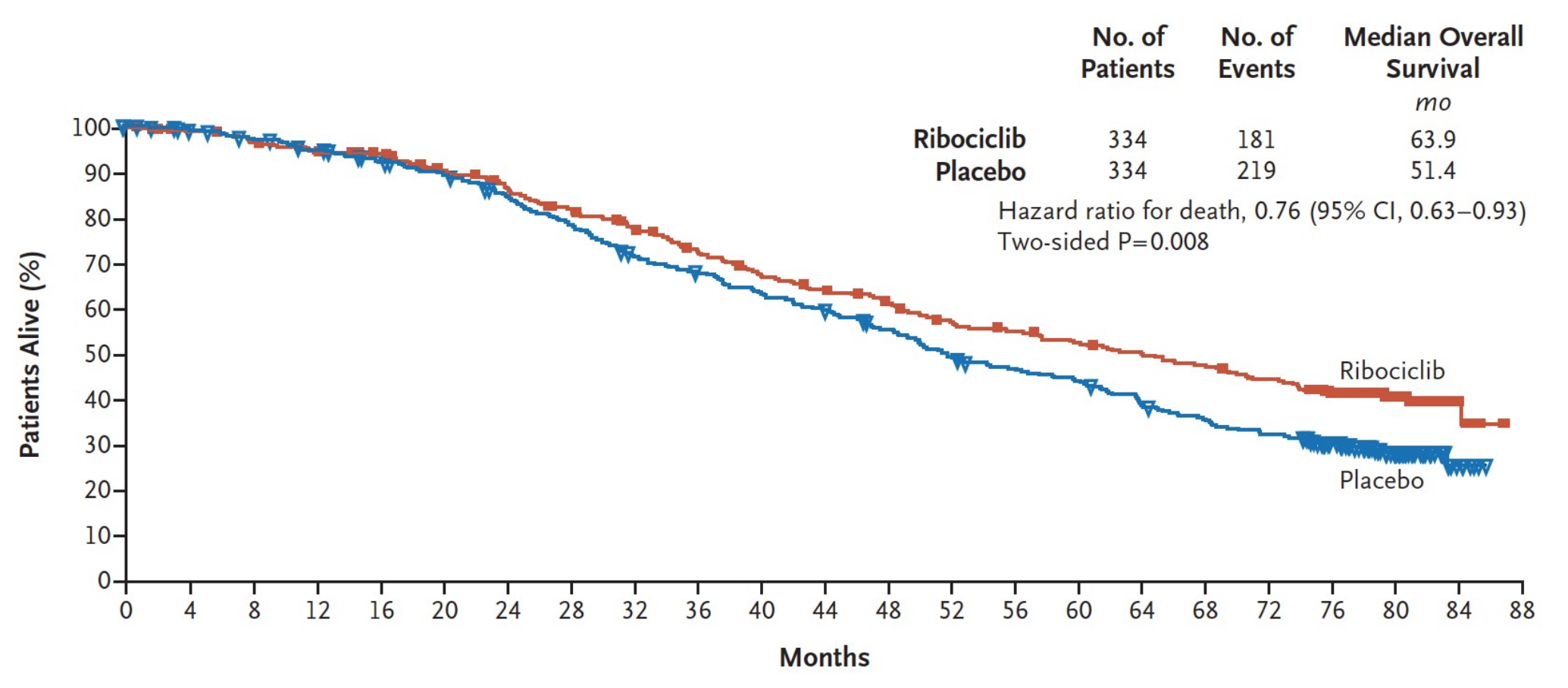
ORIGINAL ARTICLE

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.

2022 ASCO® ANNUAL MEETING

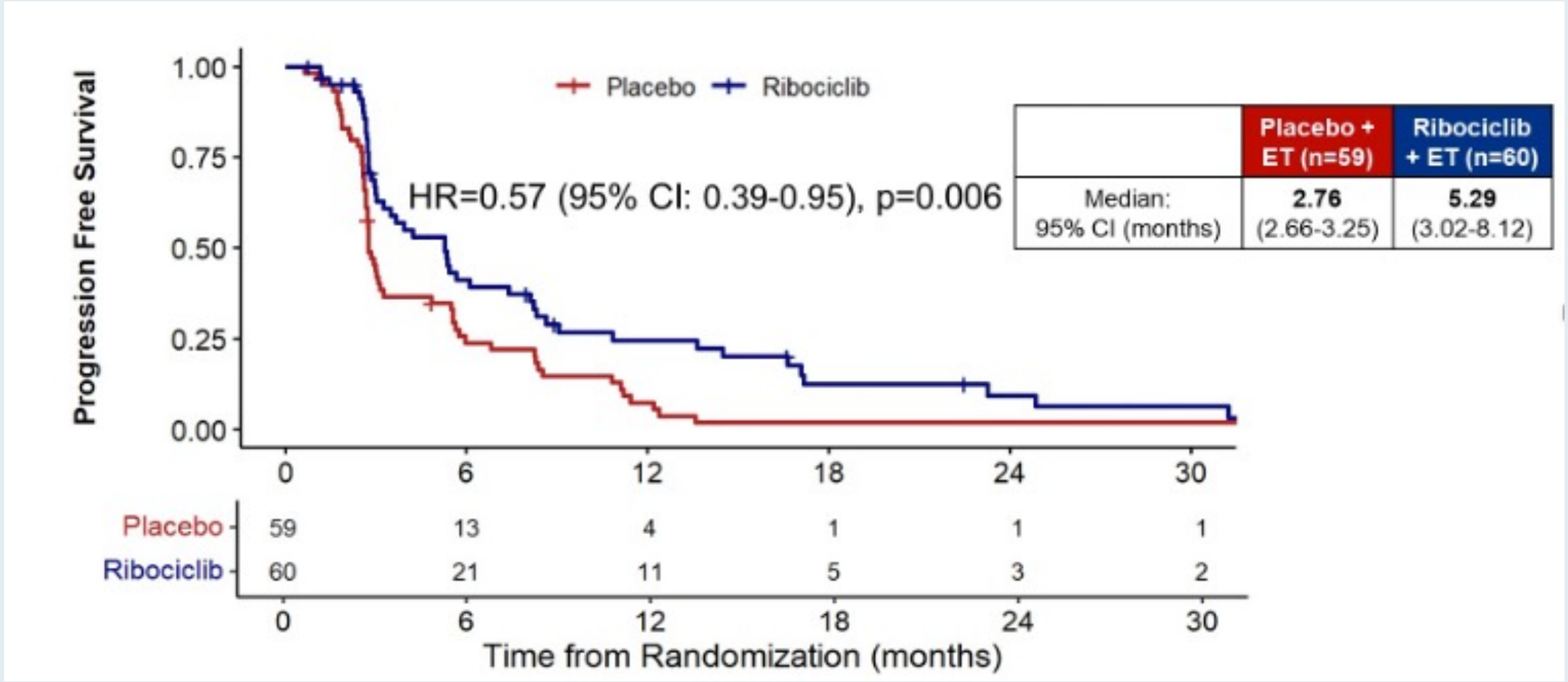
Abstract LBA1004

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.

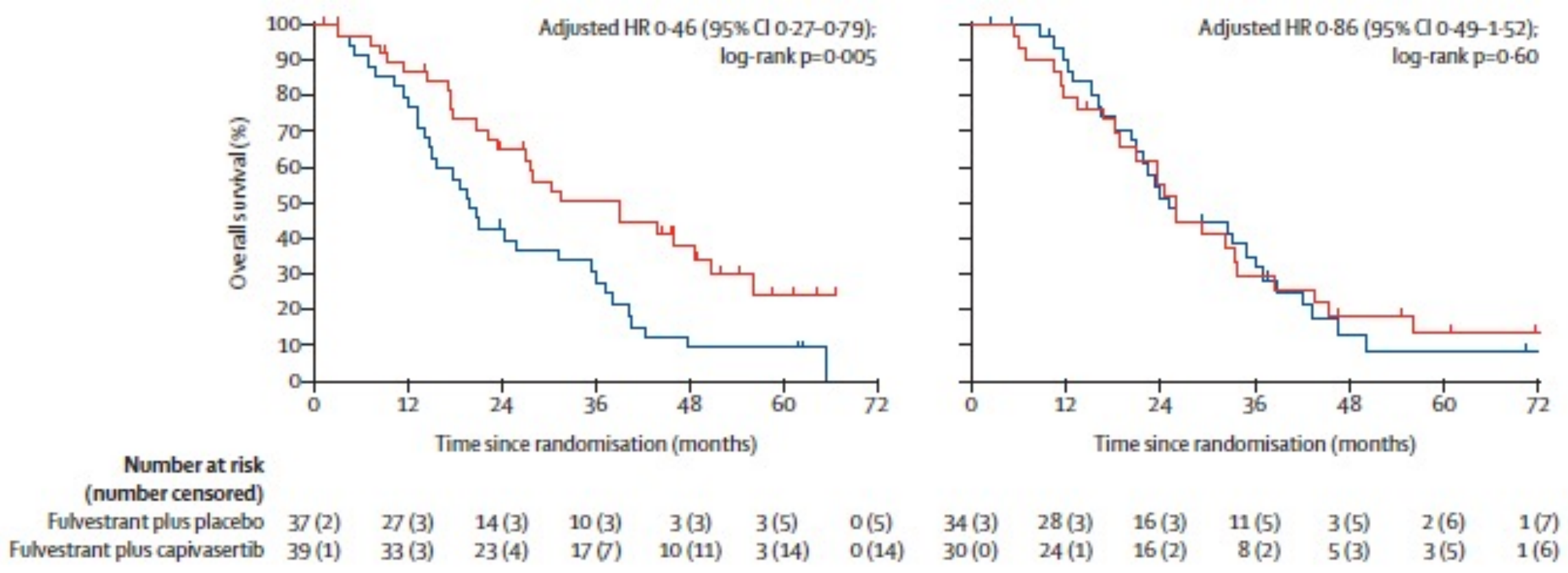
RTP RESEARCH TO PRACTICE

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



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

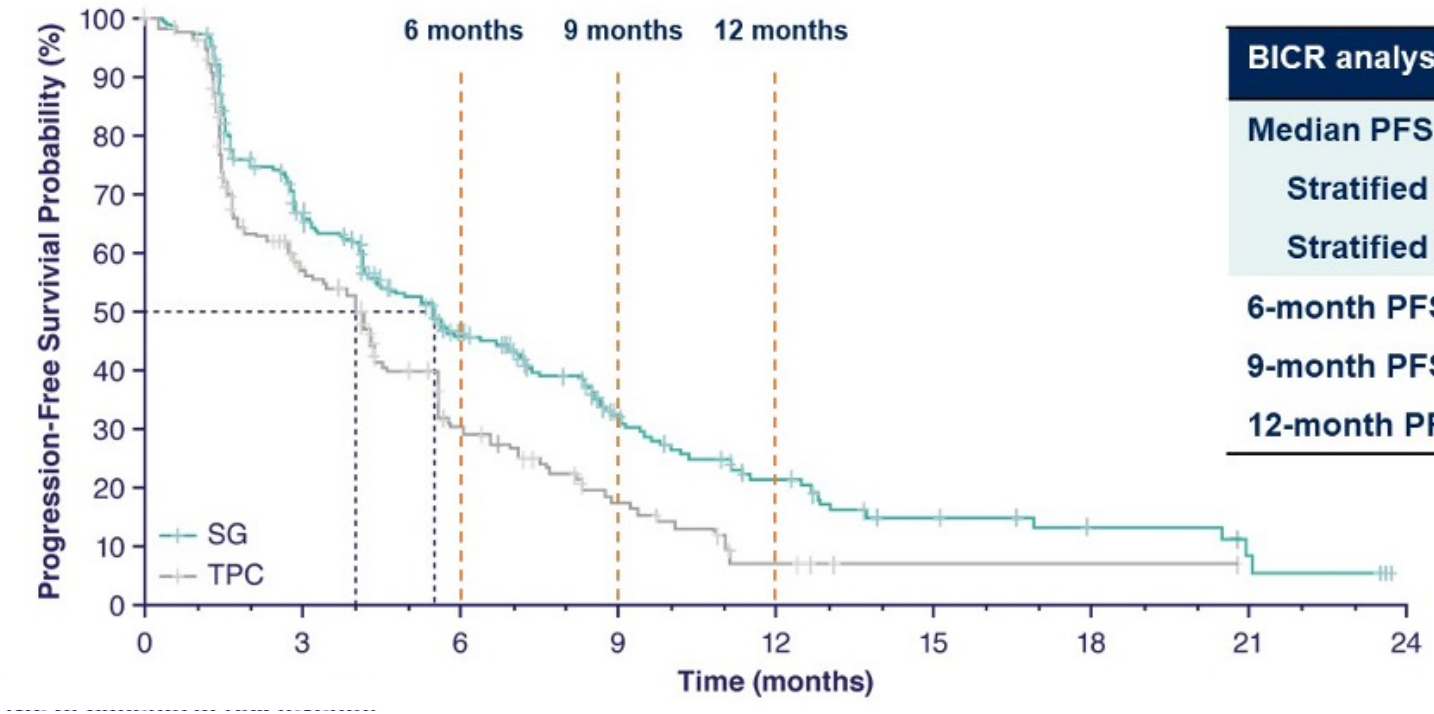
2022 ASCO® ANNUAL MEETING

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]

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.

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

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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*

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

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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 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

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
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Module 2: Urothelial Bladder Cancer

Module 3: Renal Cell Carcinoma

Discussion Question

A man with locally advanced PCA is about to receive radiation therapy and leuprolide. Regulatory and reimbursement issues aside, would you prescribe an additional agent?

- No
- Abiraterone
- Enzalutamide
- Darolutamide
- Apalutamide
- Docetaxel
- Other

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‡*

Discussion Question

A 65-year-old man receiving androgen-deprivation therapy for M0 disease after radical prostatectomy is found to have bone and liver metastases. Genetic testing is negative for HRR mutations. Regulatory and reimbursement issues aside, which systemic treatment would you most likely recommend?

- Abiraterone
- Enzalutamide
- Docetaxel
- Sipuleucel-T
- Abiraterone + olaparib
- Abiraterone + niraparib
- Darolutamide
- Apalutamide
- Other

RTP RESEARCH TO PRACTICE

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.

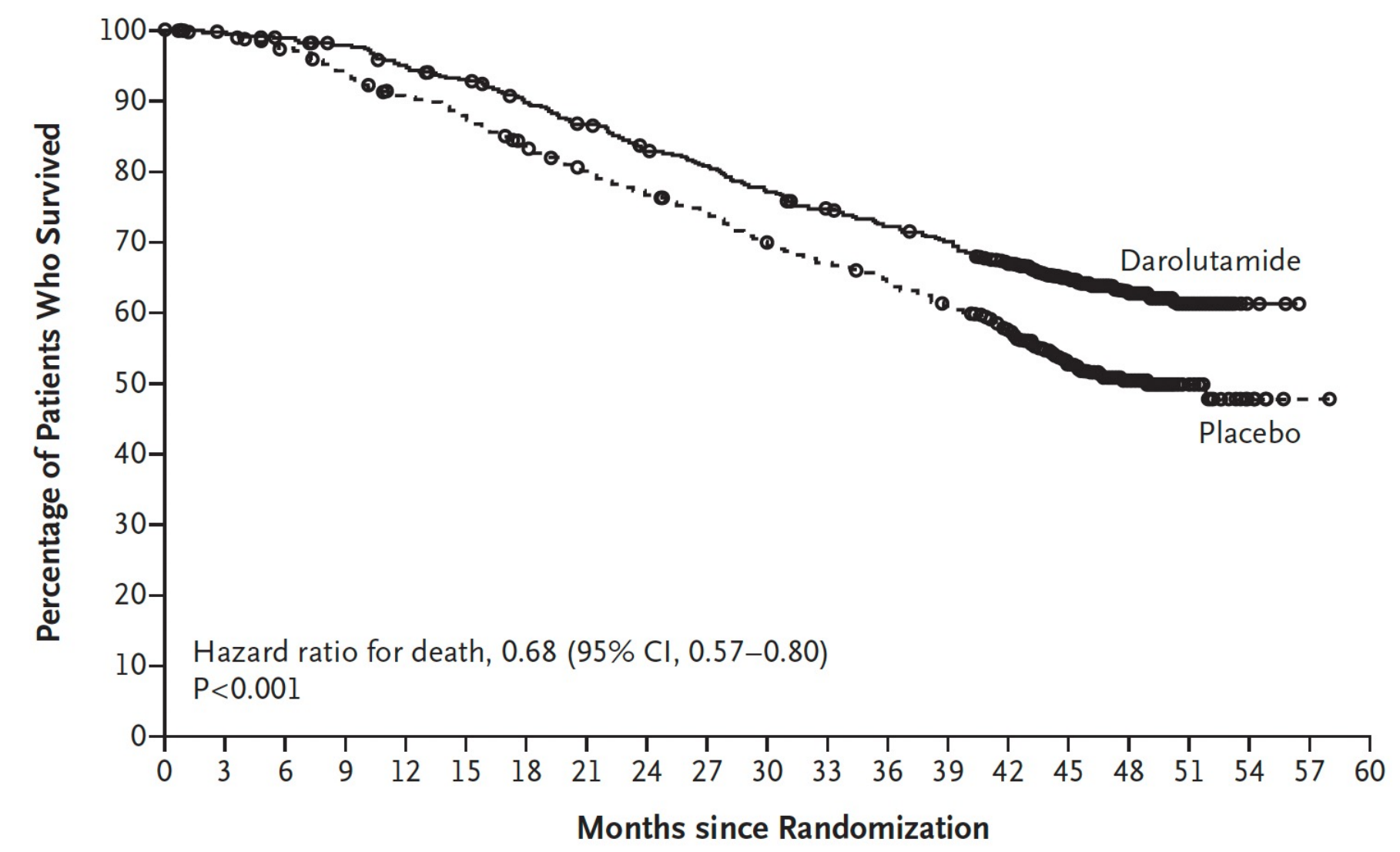
ORIGINAL ARTICLE

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*

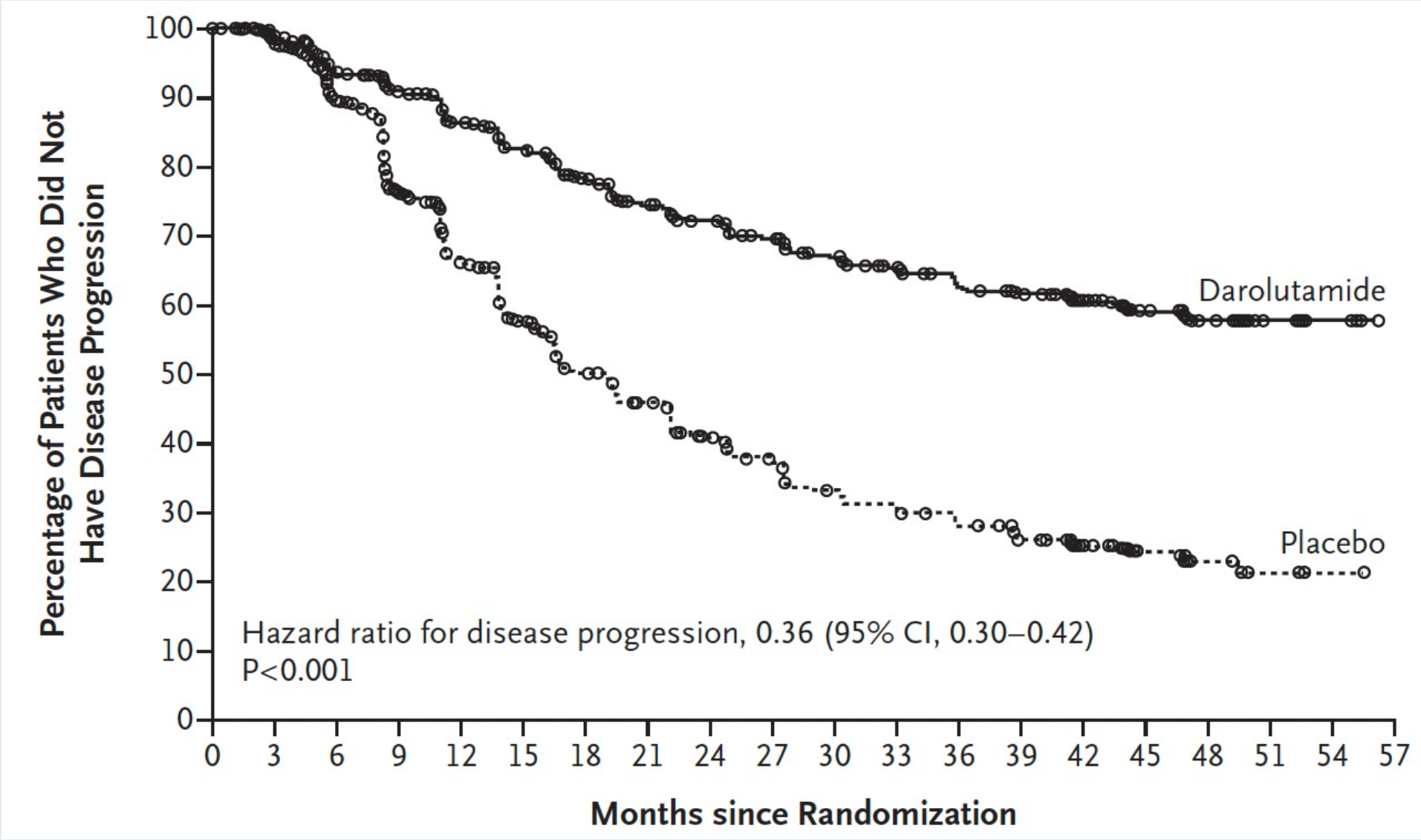
RTP RESEARCH TO PRACTICE

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.

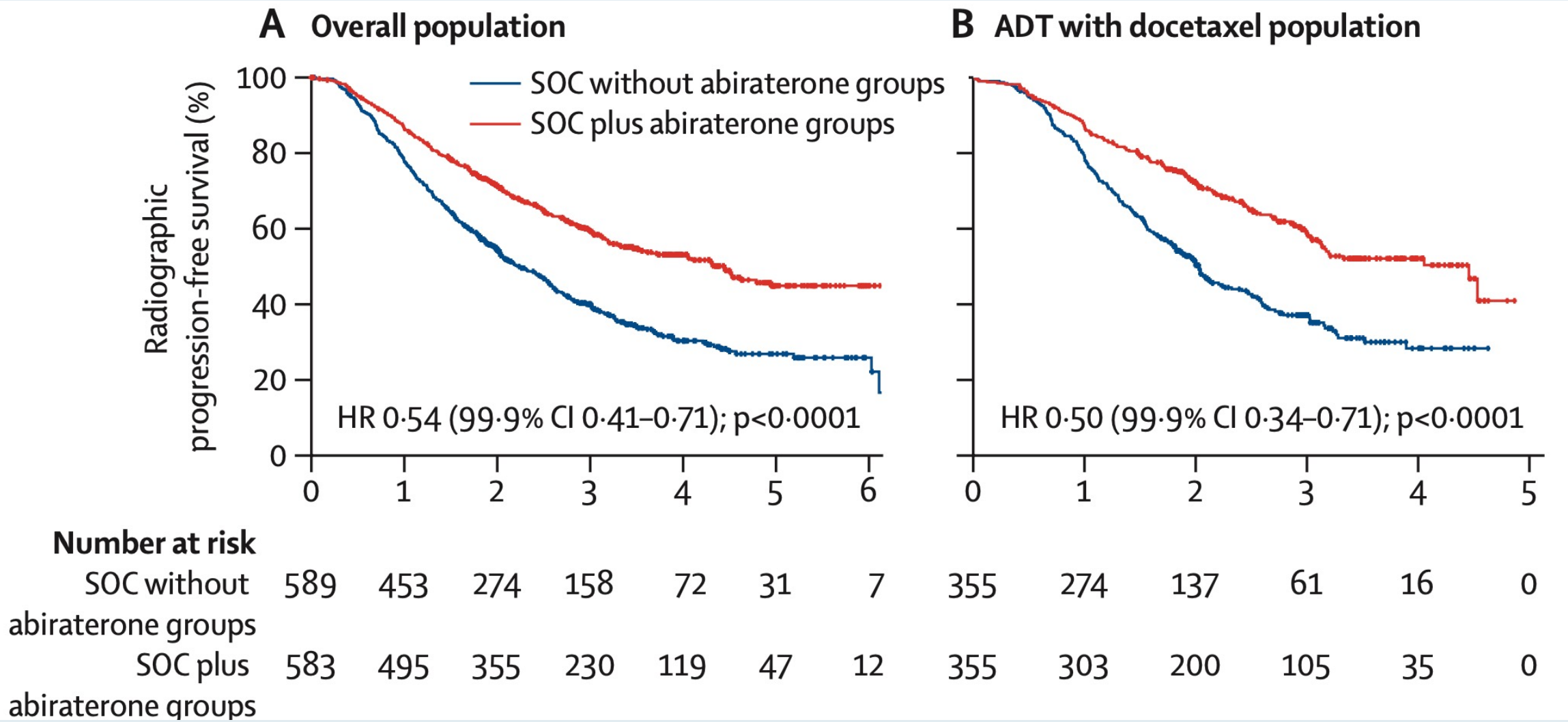
RTP RESEARCH TO PRACTICE

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.

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
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- 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

Discussion Question

Regulatory and reimbursement issues aside, which is your most likely second-line treatment for a 65-year-old man with asymptomatic low-volume disease who experiences disease progression after receiving an LHRH agonist with darolutamide and docetaxel for hormone-sensitive metastatic disease?

- Abiraterone
- Apalutamide
- Cabazitaxel
- Docetaxel and another secondary hormonal therapy
- Enzalutamide
- ^{177}Lu-PSMA-617
- Other

RTP RESEARCH TO PRACTICE

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

RTP RESEARCH TO PRACTICE

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

The NEW ENGLAND JOURNAL of MEDICINE

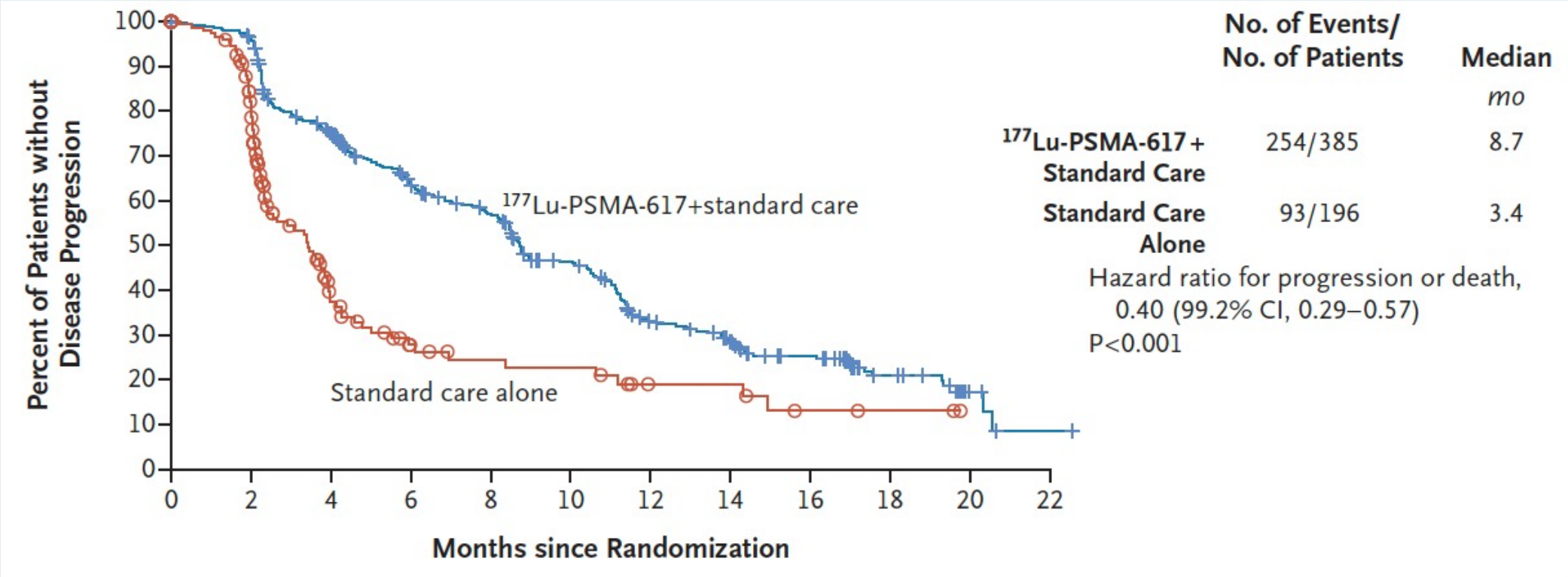
ORIGINAL ARTICLE

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.

RTP RESEARCH TO PRACTICE

VISION: Selected Adverse Events

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

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

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Genitourinary Cancers Agenda

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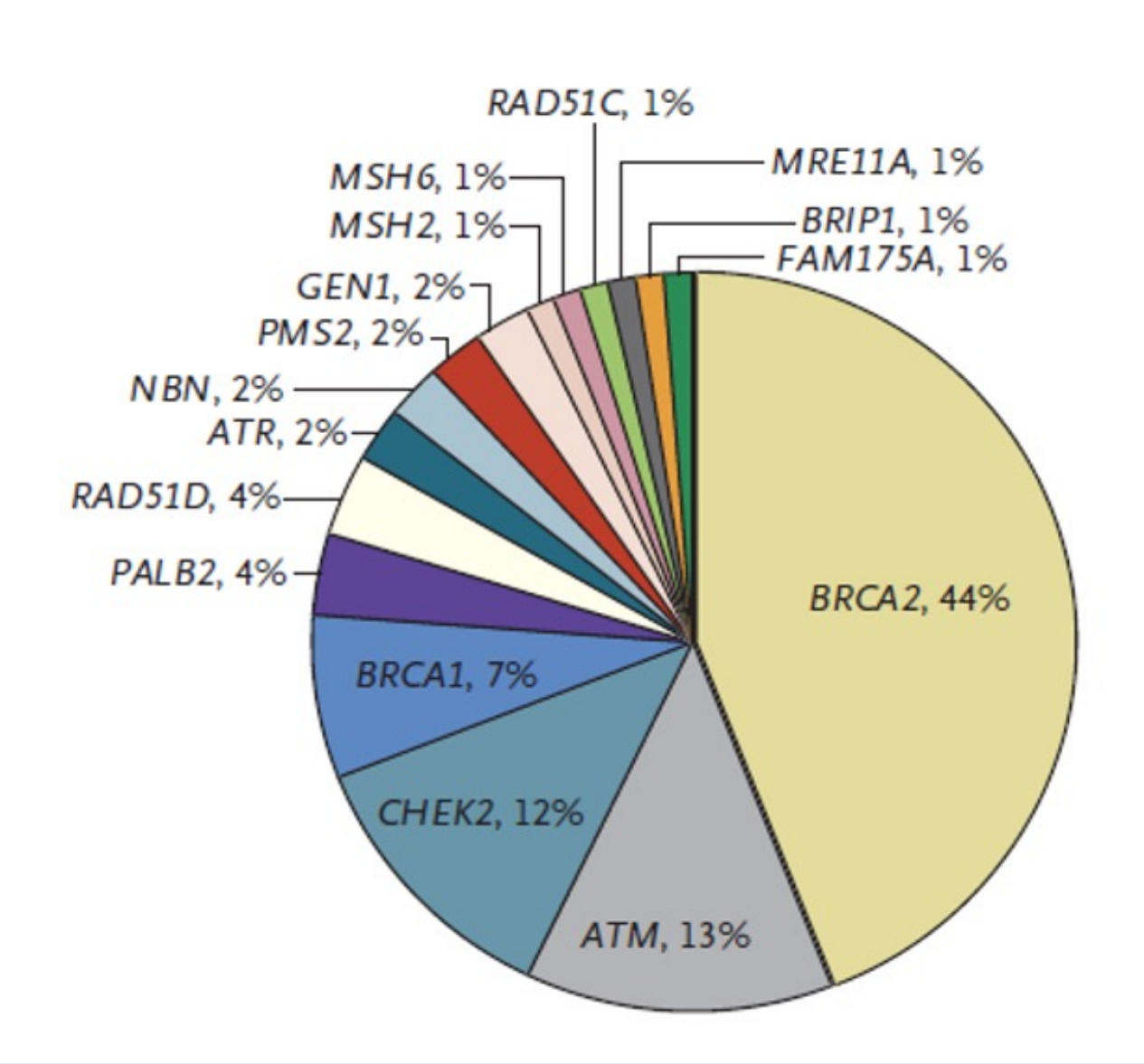
- PARP inhibitors in combination with secondary hormonal therapy for patients with mCRPC with or without HRR gene mutations

Module 2: Urothelial Bladder Cancer

Module 3: Renal Cell Carcinoma

RTP RESEARCH TO PRACTICE

Inherited DNA Repair Gene Mutations in Men with Metastatic Prostate Cancer



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

Courtesy of Matthew Smith, MD, PhD

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/

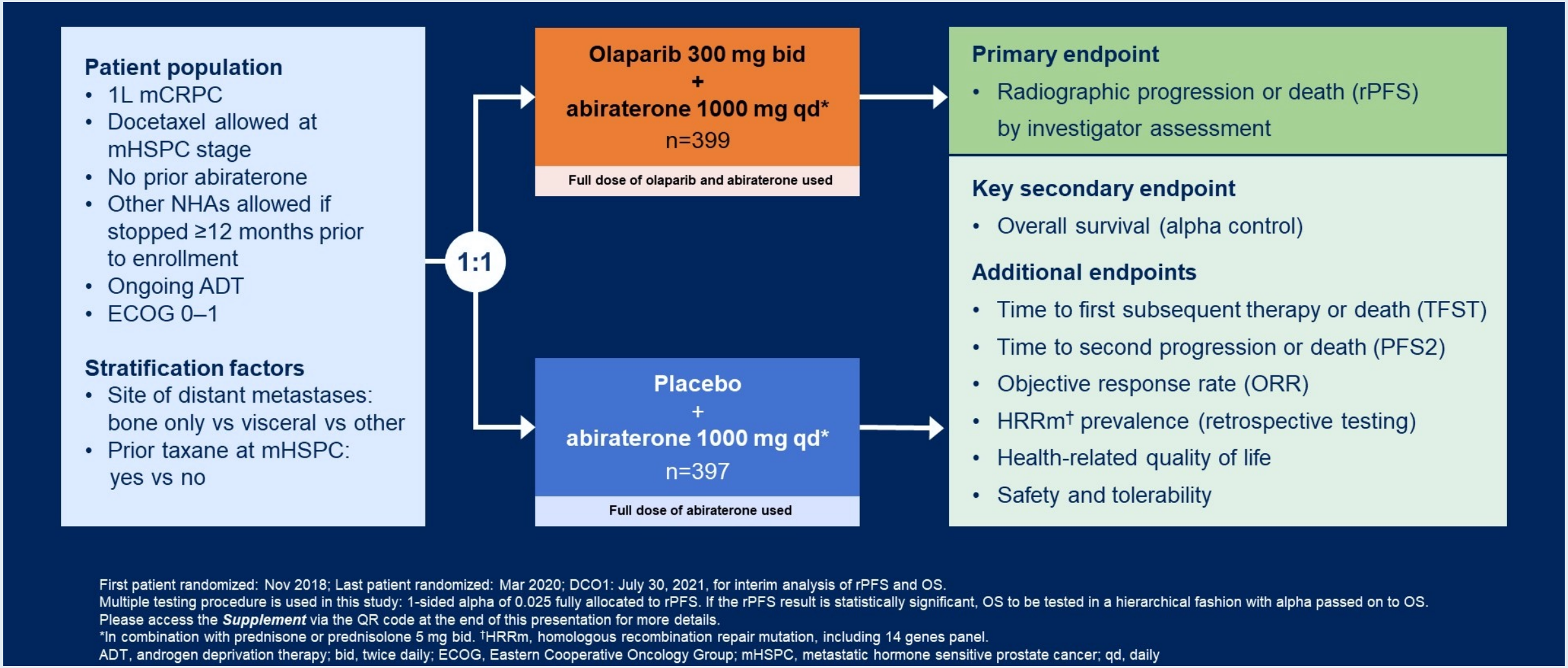
ASCO Genitourinary Cancers Symposium 2022;Abstract 11.

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

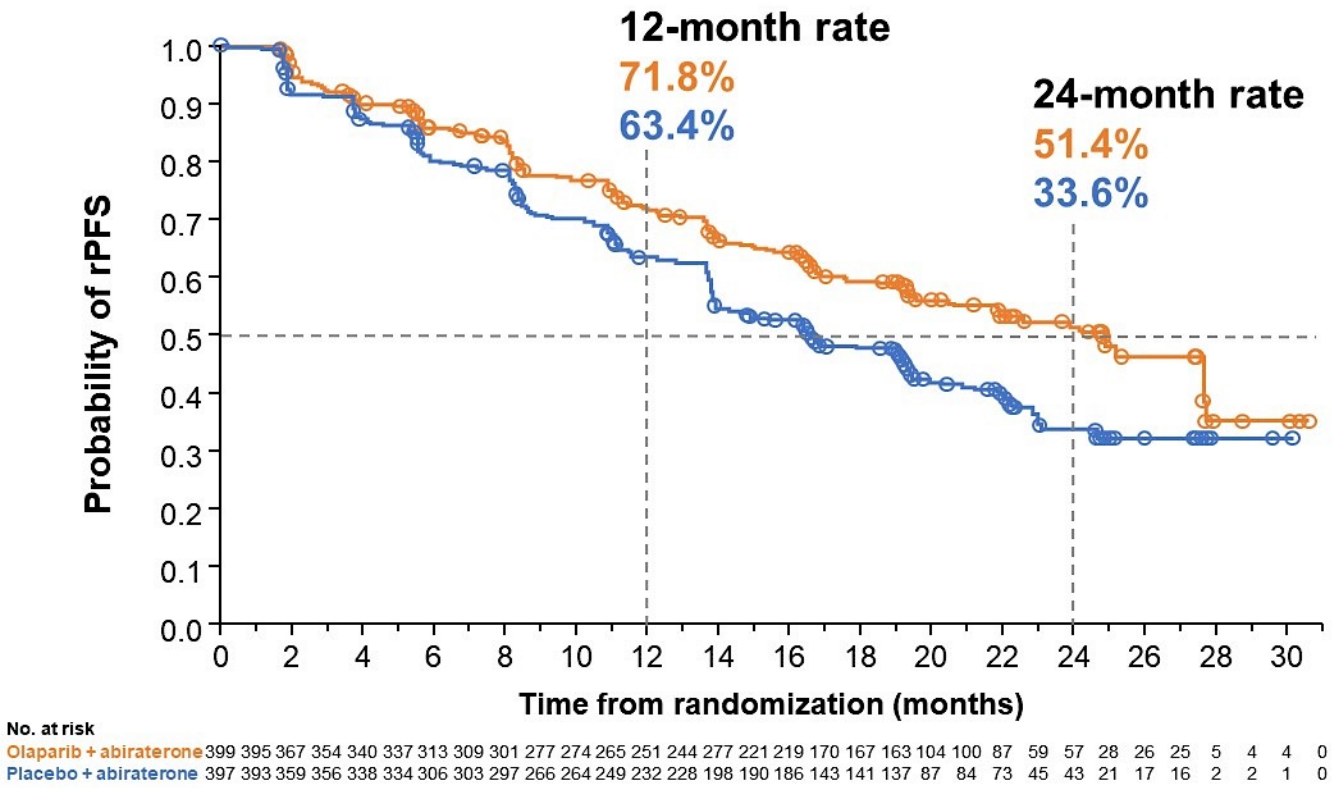


First patient randomized: Nov 2018; Last patient randomized: Mar 2020; DCO1: July 30, 2021, for interim analysis of rPFS and OS.
Multiple testing procedure is used in this study: 1-sided alpha of 0.025 fully allocated to rPFS. If the rPFS result is statistically significant, OS to be tested in a hierarchical 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*

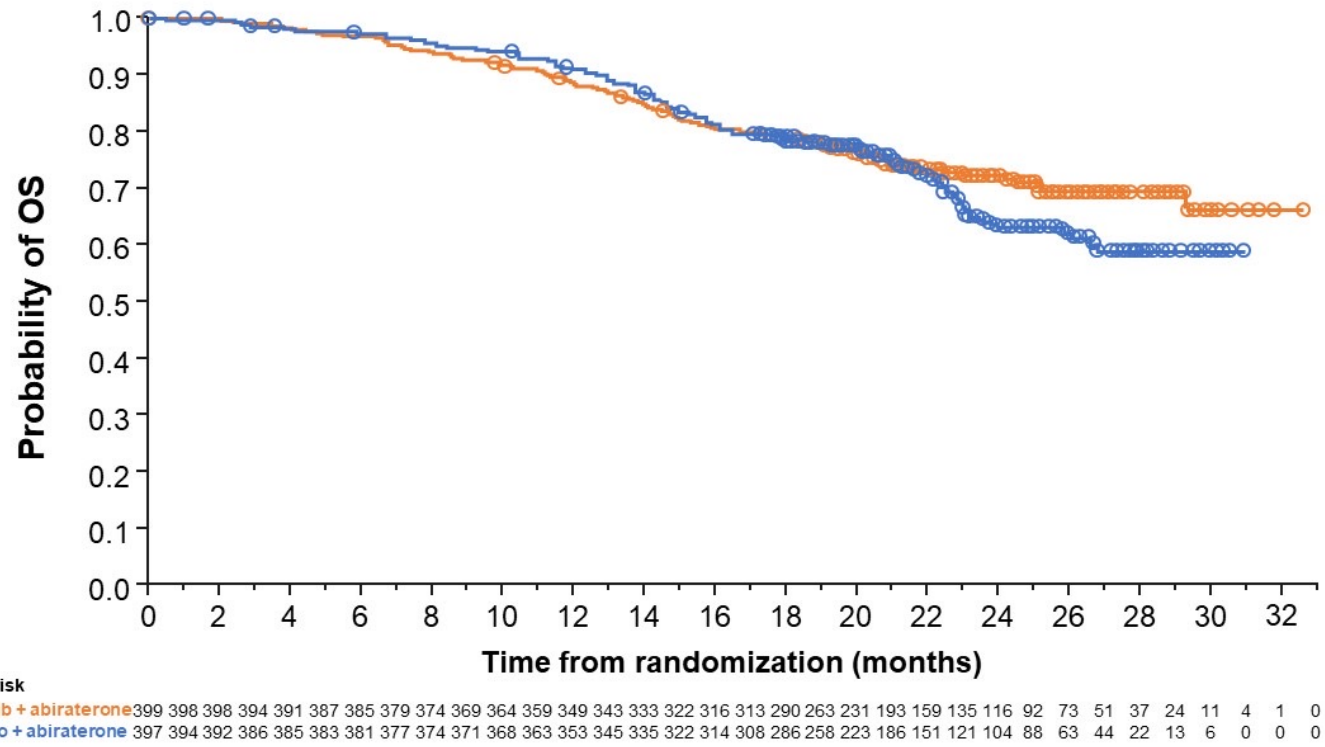
Events: 394; Maturity 49.5%
*In combination with prednisone or prednisolone
CI, confidence interval; HR, hazard ratio.

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

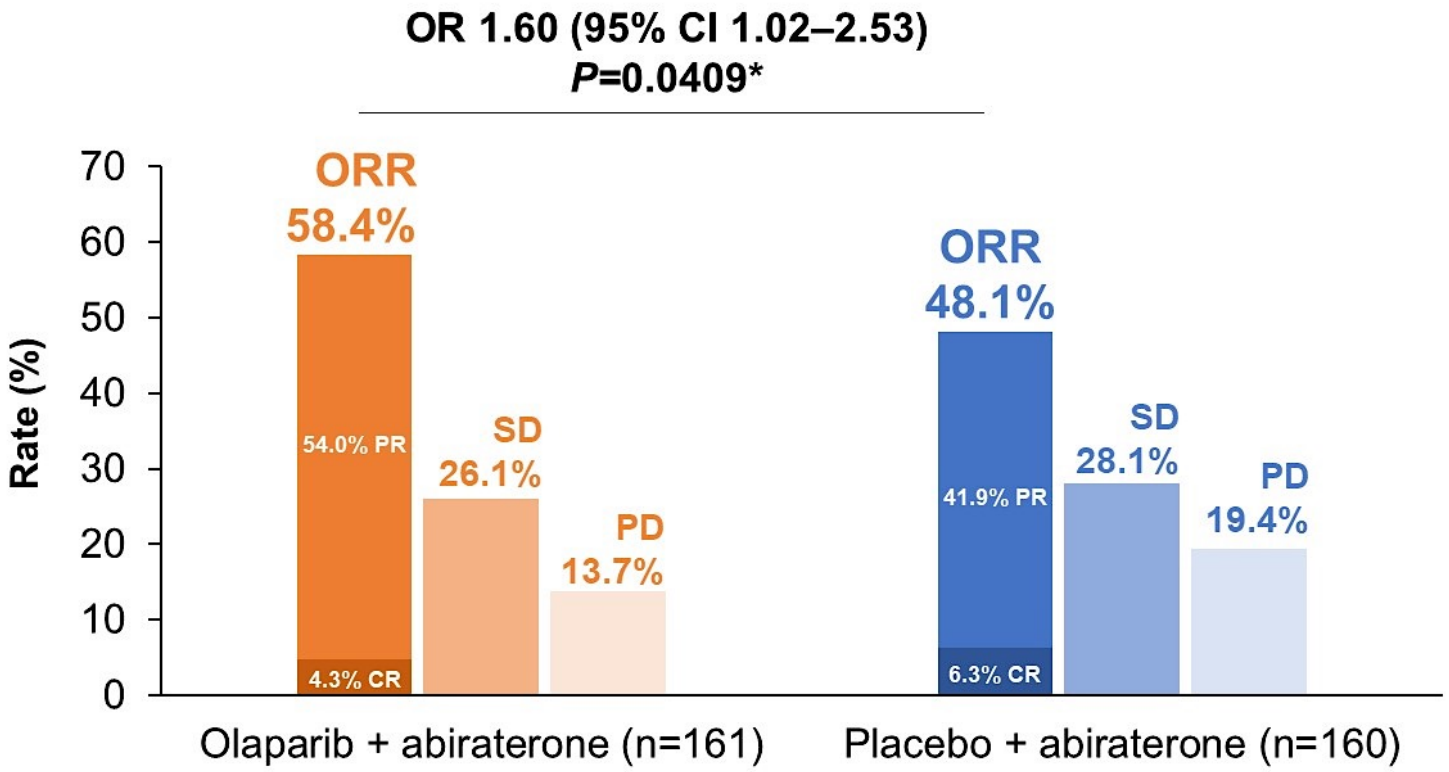
Events: 228
NR, not reached.

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



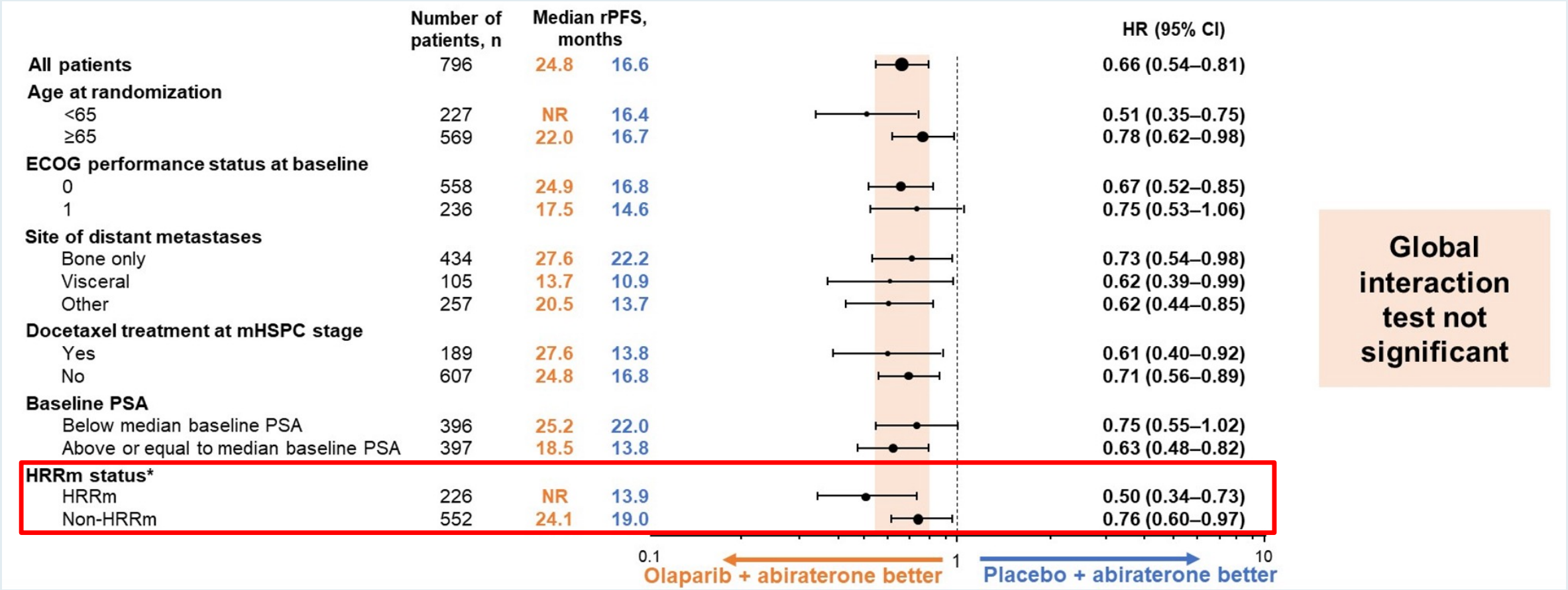
321/796 patients (40.3%) had measurable disease by RECIST v1.1 criteria at baseline

*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.

ASCO Genitourinary Cancers Symposium 2022;Abstract 12.

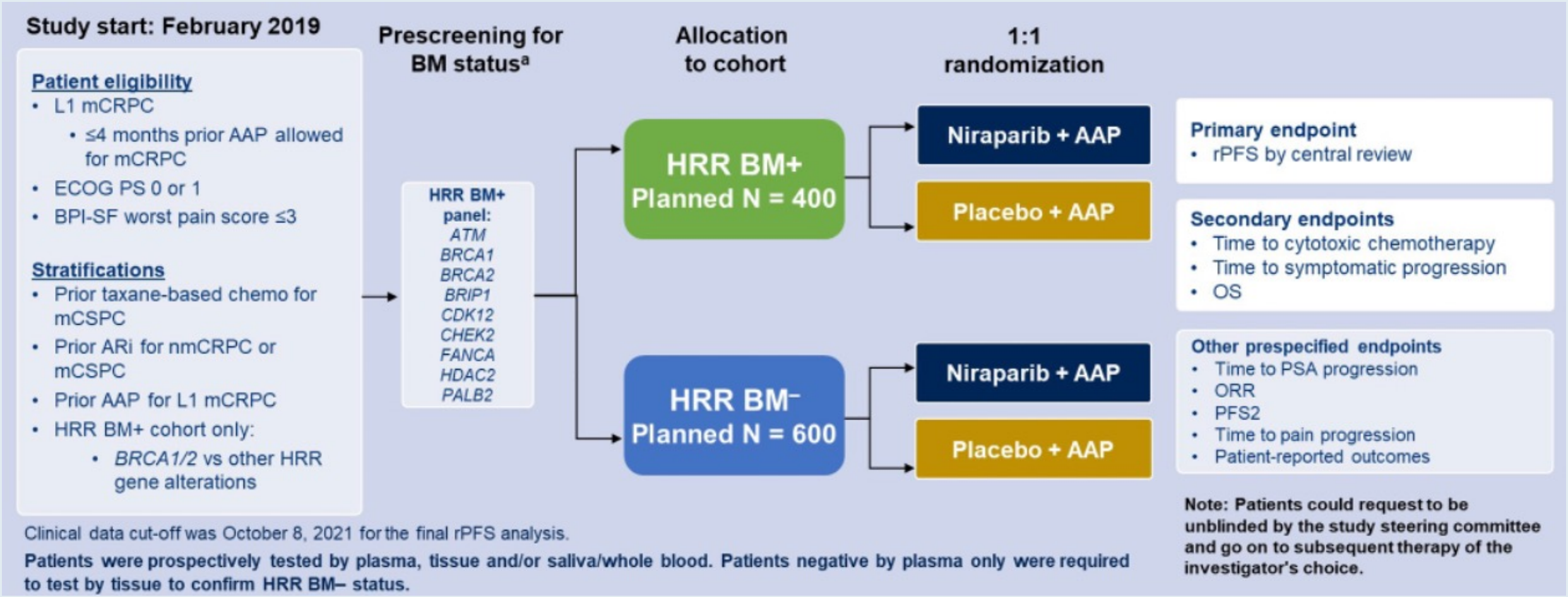
Phase 3 MAGNITUDE study: First results of niraparib (NIRA) with abiraterone acetate and prednisone (AAP) as first-line therapy in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC) with and without homologous recombination repair (HRR) gene alterations

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-

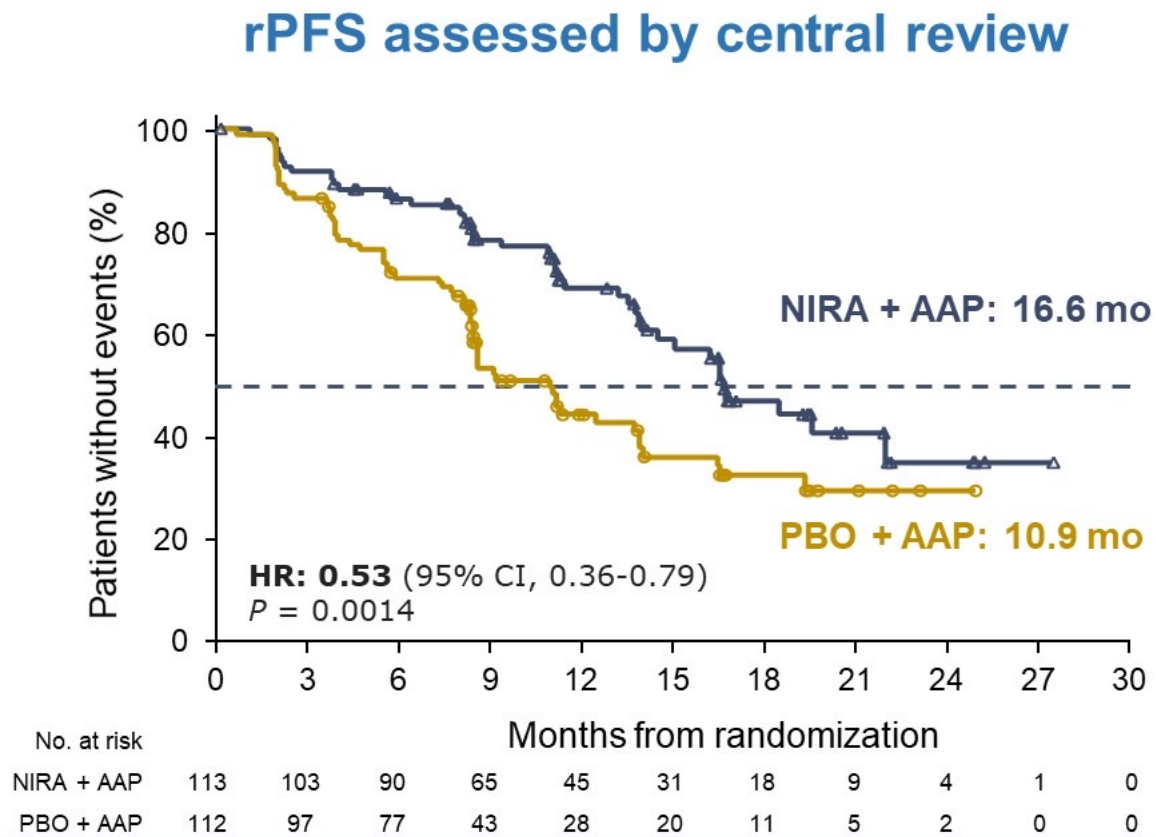


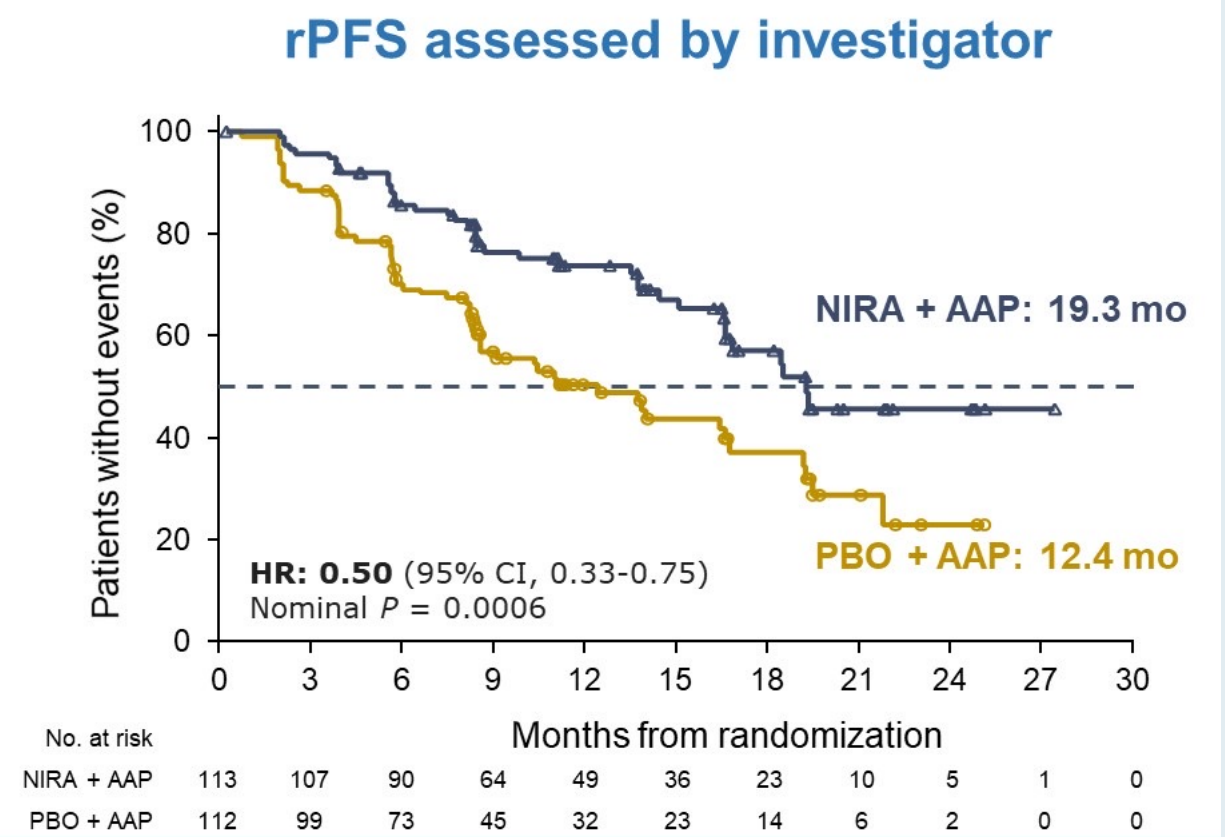
HRR = homologous recombination repair; BM = biomarker; mCRPC = metastatic castration-resistant prostate cancer; mCSPC = metastatic castration-sensitive prostate cancer; nmCRPC = nonmetastatic castration-resistant prostate cancer; AAP = abiraterone acetate and prednisone; rPFS = radiographic progression-free 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

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
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- Selection of patients to receive erdafitinib; prevention and management of toxicity

Module 3: Renal Cell Carcinoma

Genitourinary Cancers Agenda

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Module 3: Renal Cell Carcinoma

Discussion Question

Would you generally recommend pembrolizumab to a young, cystectomy-eligible patient with BCG-unresponsive non-muscle-invasive urothelial bladder cancer who refused cystectomy?

- Yes
- Yes, for select patients
- No
- I'm not sure

RTP RESEARCH TO PRACTICE

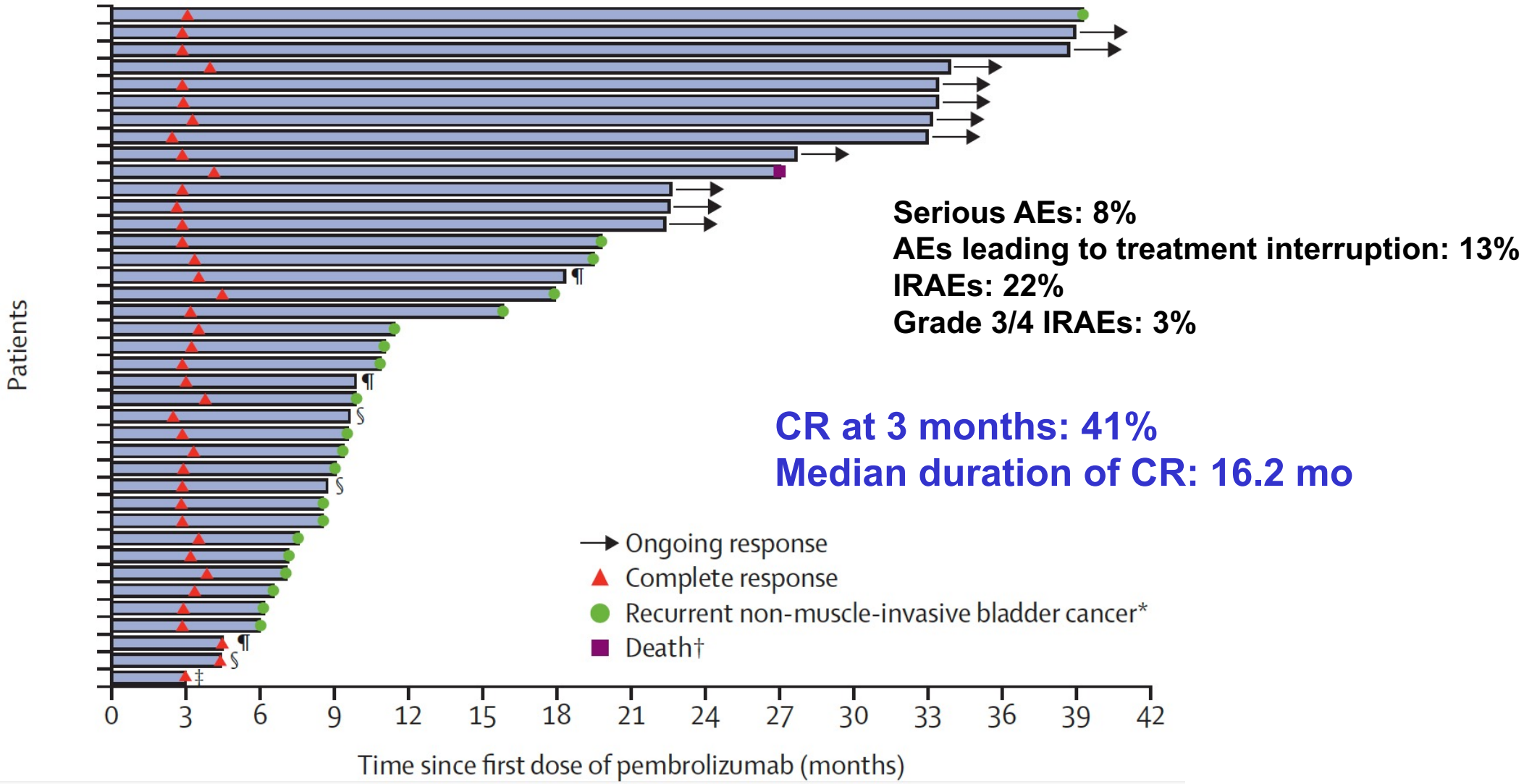
Pembrolizumab monotherapy for the treatment of high-risk non-muscle-invasive bladder cancer unresponsive to BCG (KEYNOTE-057): an open-label, single-arm, multicentre, phase 2 study

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.

ELSEVIER

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

UROLOGIC ONCOLOGY

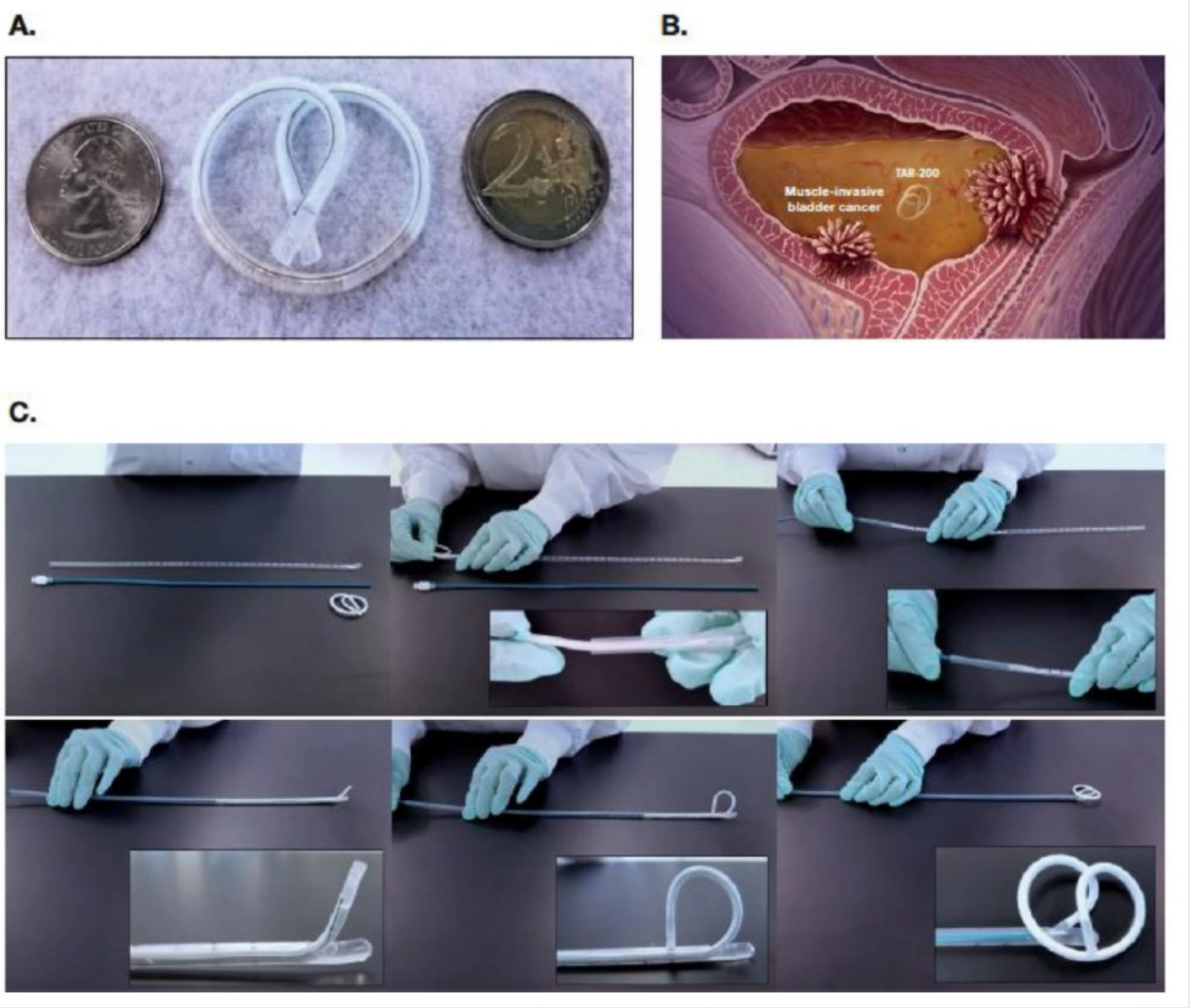
Clinical-Bladder cancer

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.

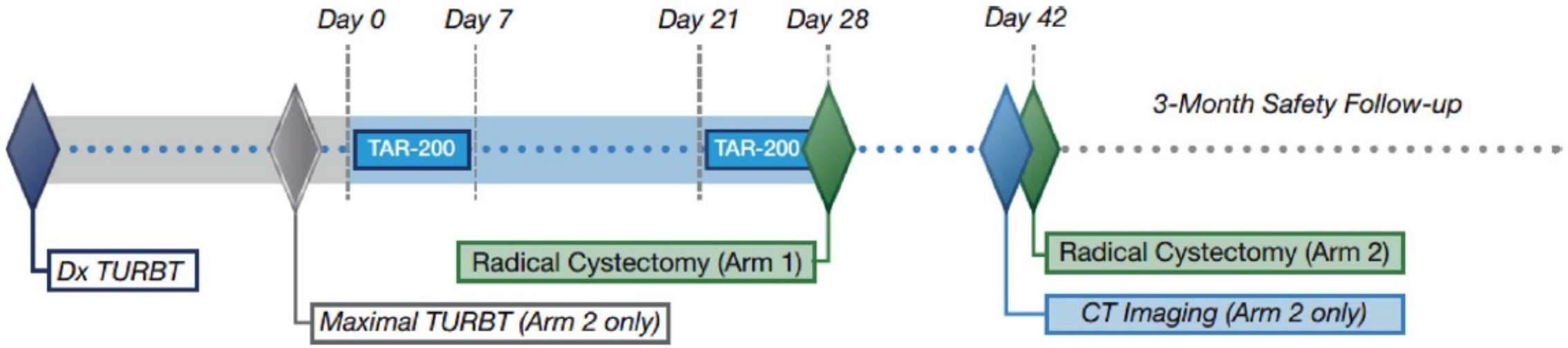
TAR-200

- 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].

Genitourinary Cancers Agenda

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Module 3: Renal Cell Carcinoma

RTP RESEARCH TO PRACTICE

Discussion Question

Use of which of the following agents requires tumor biomarker positivity?

- Enfortumab vedotin
- Sacituzumab govitecan
- Neither
- Both
- I’m not sure

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

Press Release: July 26, 2022

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

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

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

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

RTP RESEARCH TO PRACTICE

2022 ASCO® ANNUAL MEETING

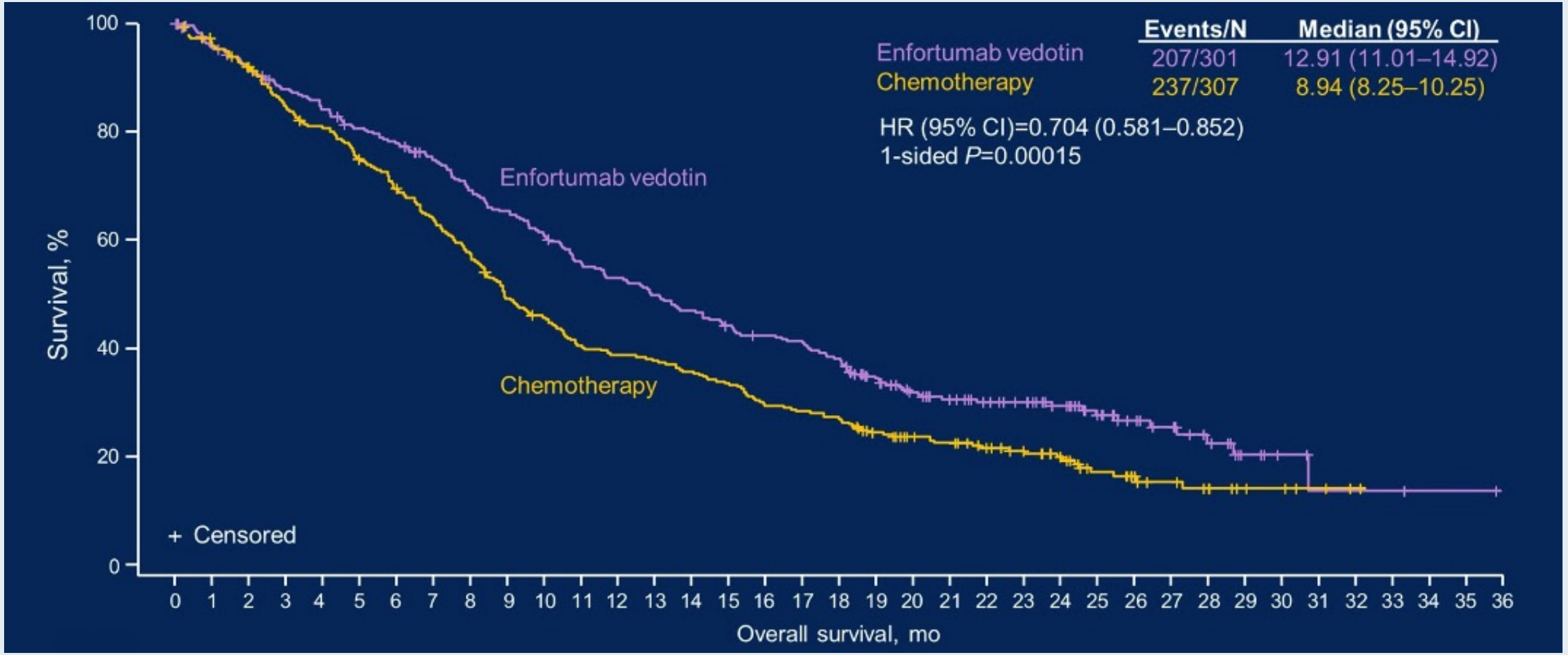
Abstract 4516

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

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

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

EV-301: Overall Survival



Rosenberg JE et al. ASCO 2022;Abstract 4516.

RTP RESEARCH TO PRACTICE

ASCO Genitourinary Cancers Symposium 2022;Abstract 434.

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

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

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

Abstract # 434
ClinicalTrials.gov Number: NCT03547973.

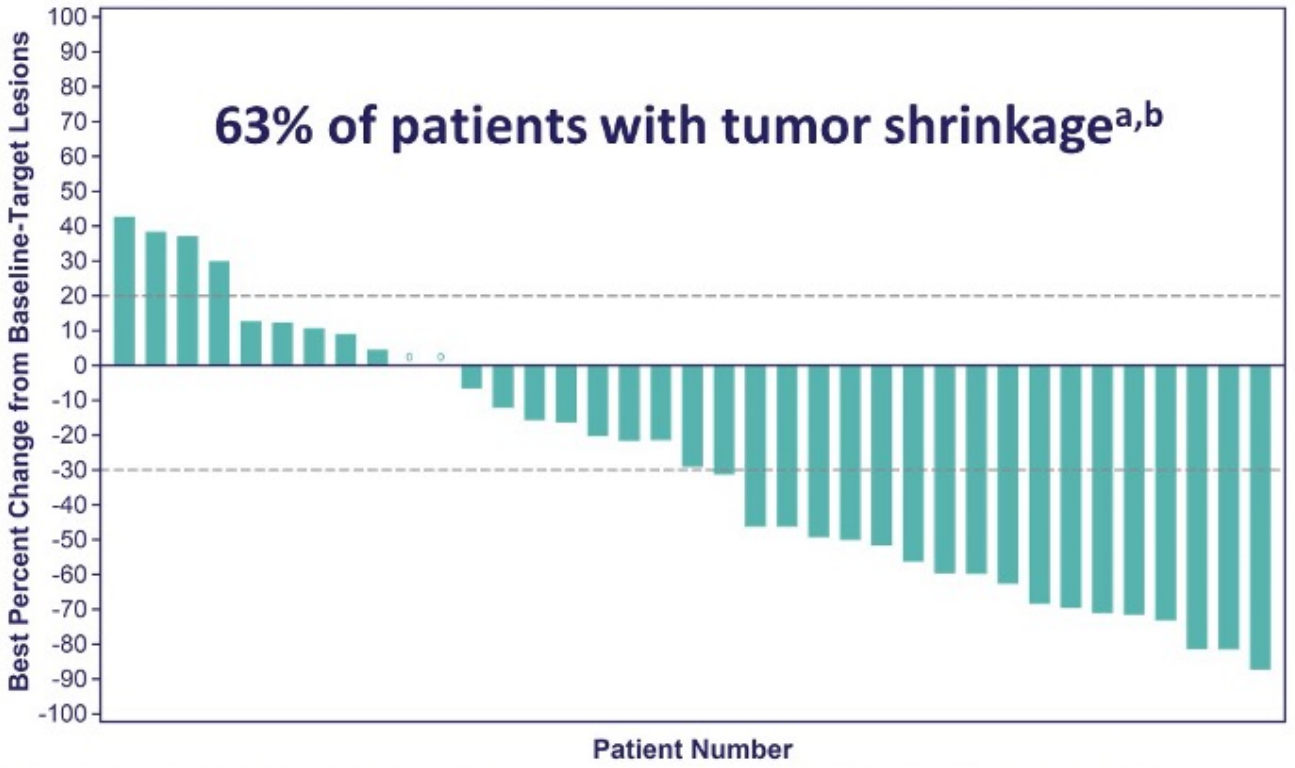
@PGrivasMDPhD

TROPHY U-01

RTP RESEARCH TO PRACTICE

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

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



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

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

RTP RESEARCH TO PRACTICE

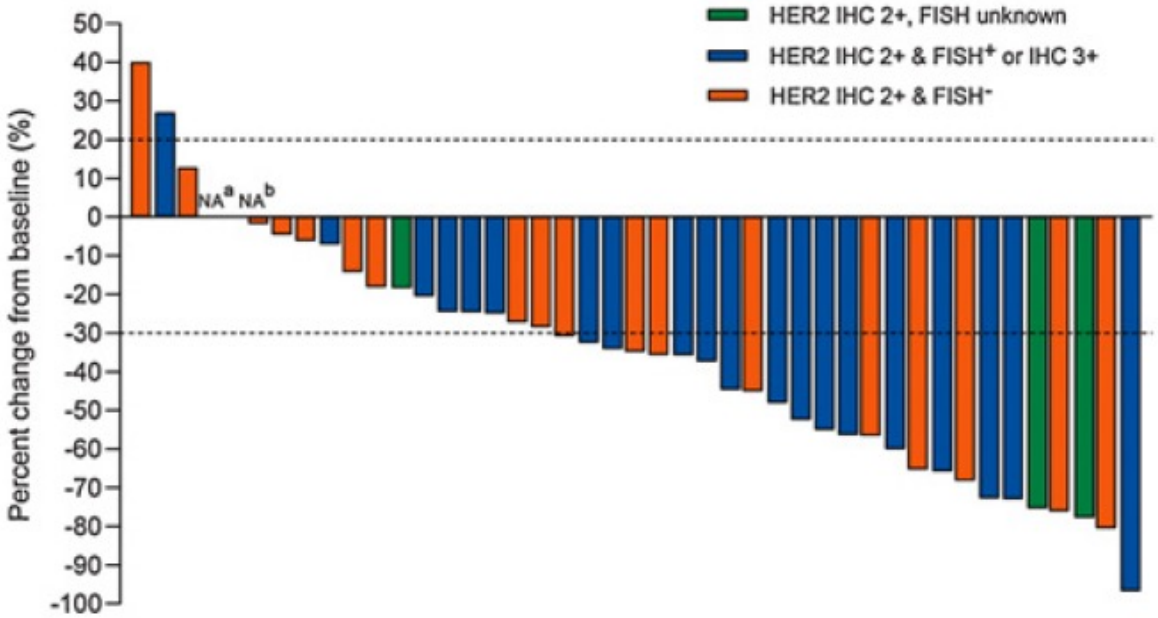
CLINICAL CANCER RESEARCH | CLINICAL TRIALS: TARGETED THERAPY

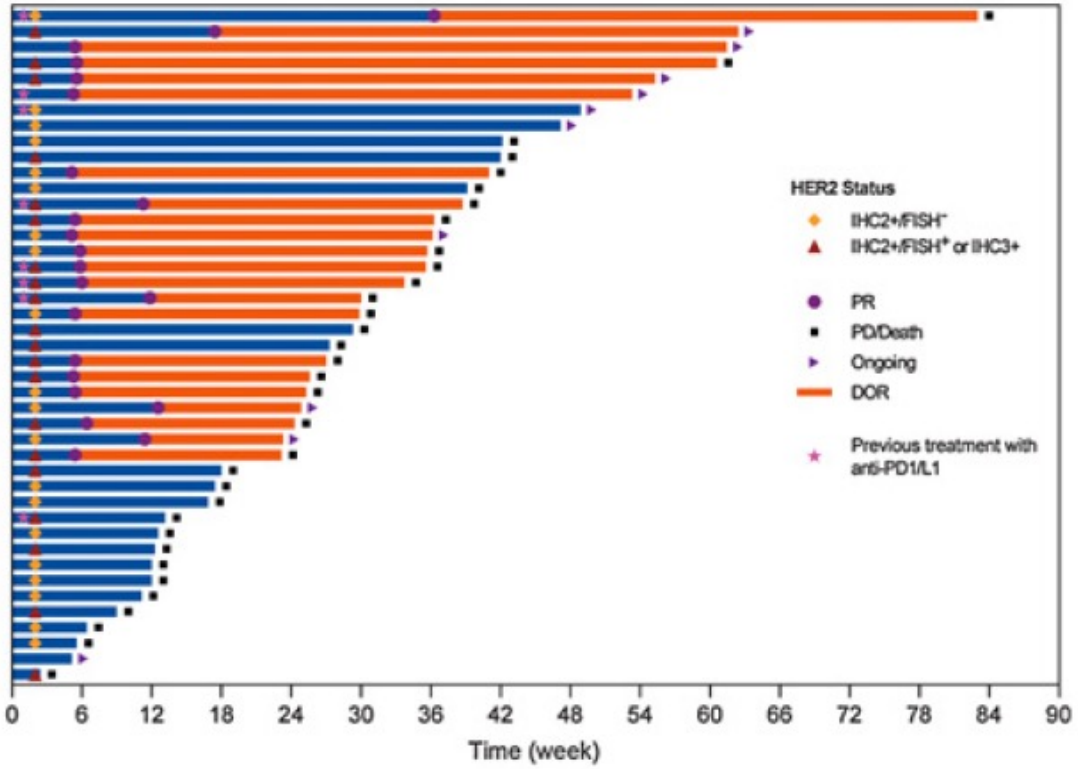
Open-label, Multicenter, Phase II Study of RC48-ADC, a HER2-Targeting Antibody–Drug Conjugate, in Patients with Locally Advanced or Metastatic Urothelial Carcinoma AC

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

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

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





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

RTP RESEARCH TO PRACTICE

Genitourinary Cancers Agenda

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Module 3: Renal Cell Carcinoma

RTP RESEARCH TO PRACTICE

Discussion Question

Which of the following is a side effect of erdafitinib?

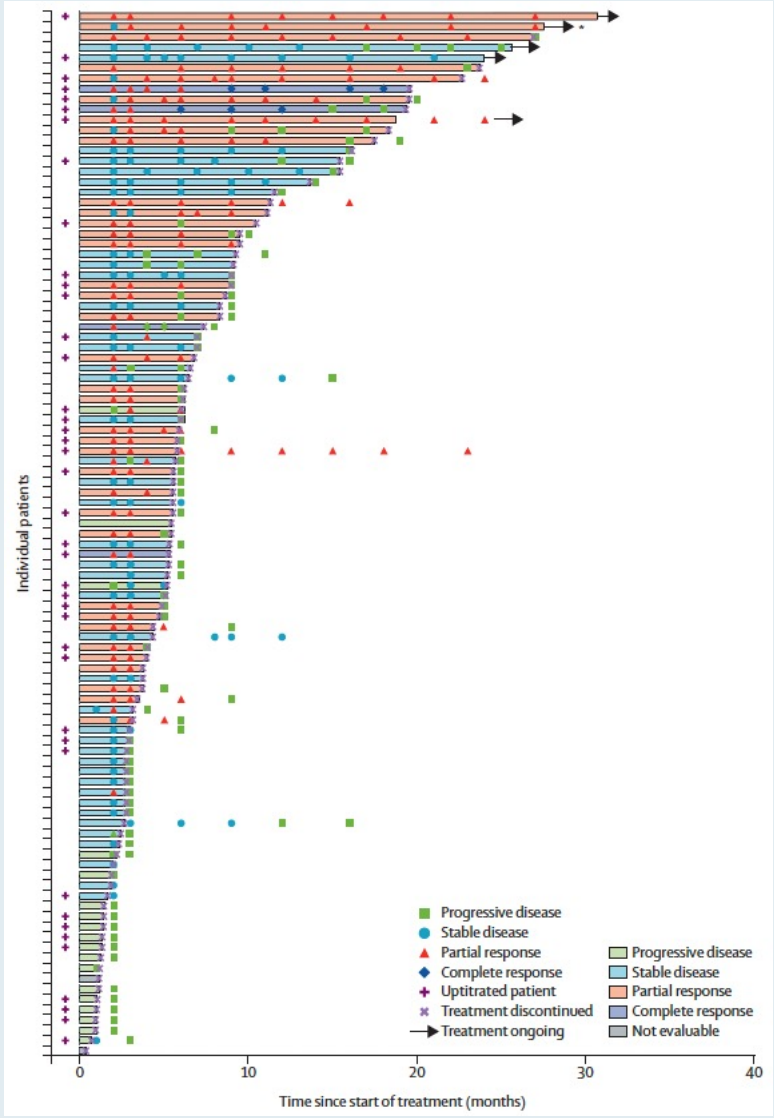
- LFT abnormalities
- Hyperphosphatemia
- Pneumonitis
- Hand-foot syndrome
- I’m not sure

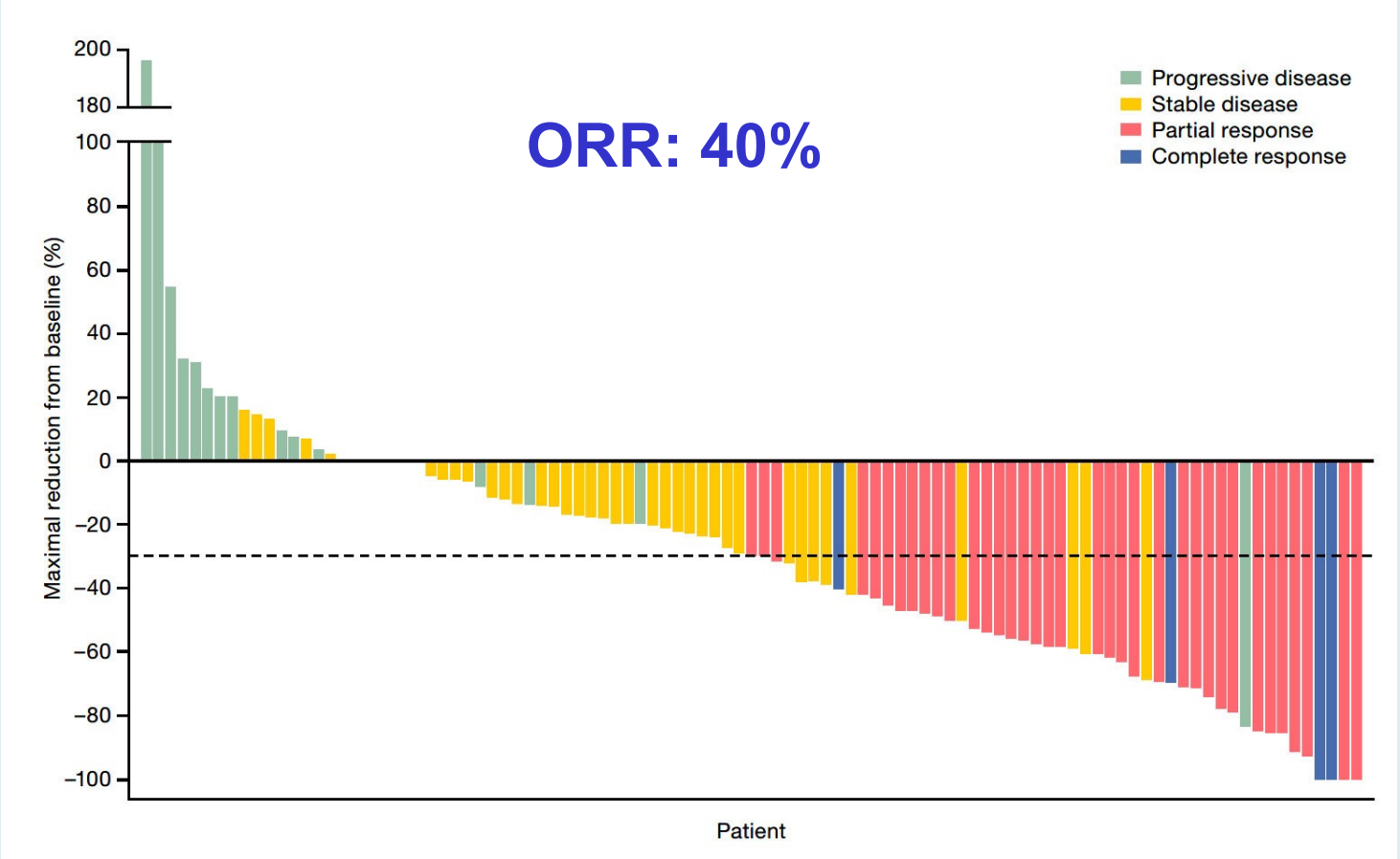
Lancet Oncol 2022;23(2):248-58.

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

Genitourinary Cancers Agenda

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- 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

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Discussion Question

What is known about the efficacy of adjuvant ipilimumab/ nivolumab for renal cell carcinoma?

- Improved PFS
- No impact on PFS
- I’m not sure
- It has not been studied

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

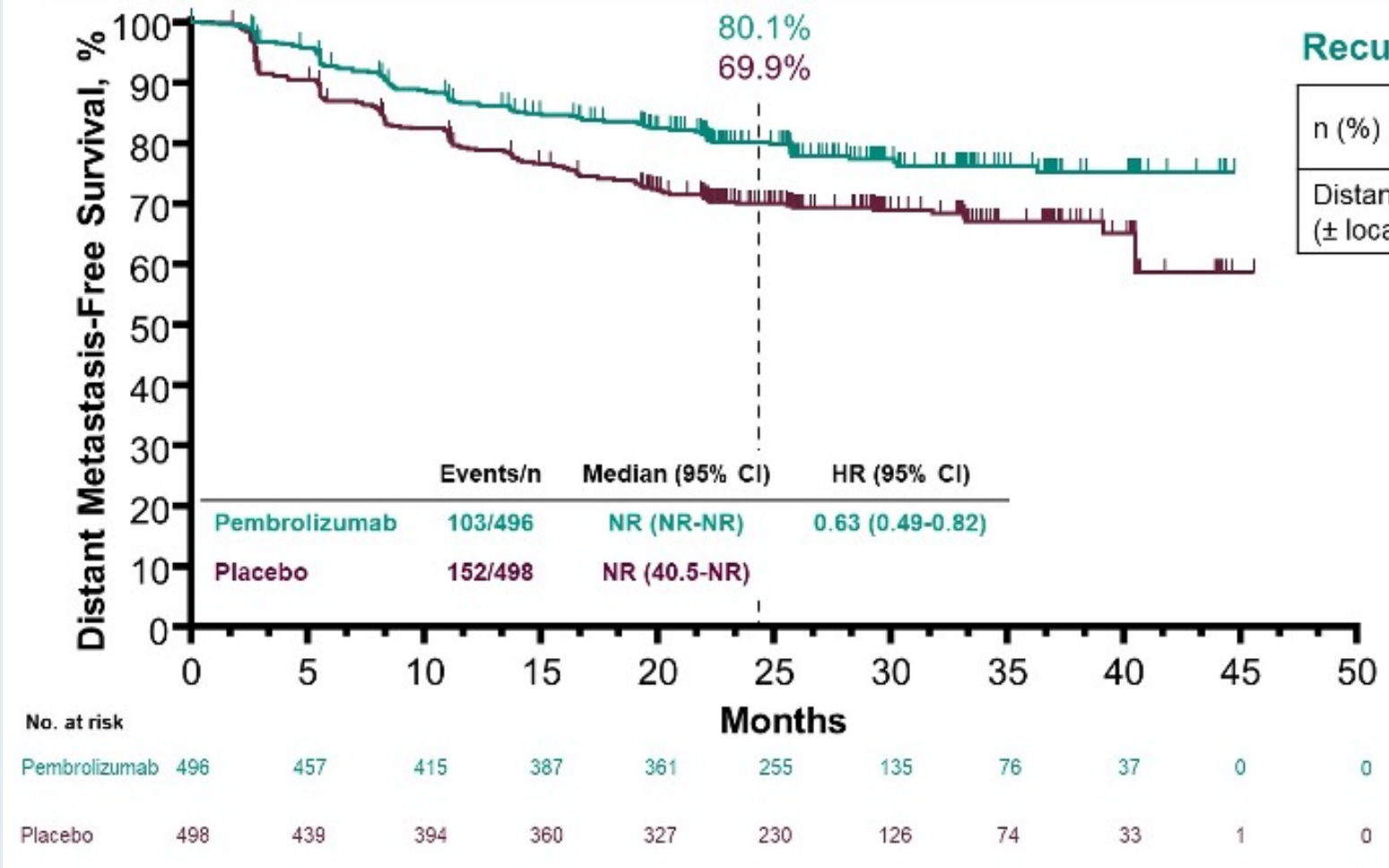
Adjuvant pembrolizumab for postnephrectomy renal cell carcinoma: Expanded efficacy analyses from KEYNOTE-564

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.

Genitourinary Cancers Agenda

Module 1: Prostate Cancer

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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

Discussion Question

In general, what is your preferred first-line therapy for a symptomatic patient with metastatic renal cell carcinoma and high tumor burden?

- Pembrolizumab/lenvatinib
- Ipilimumab/nivolumab
- Pembrolizumab/axitinib
- Nivolumab/cabozantinib
- Avelumab/axitinib
- Other

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.**

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.

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

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

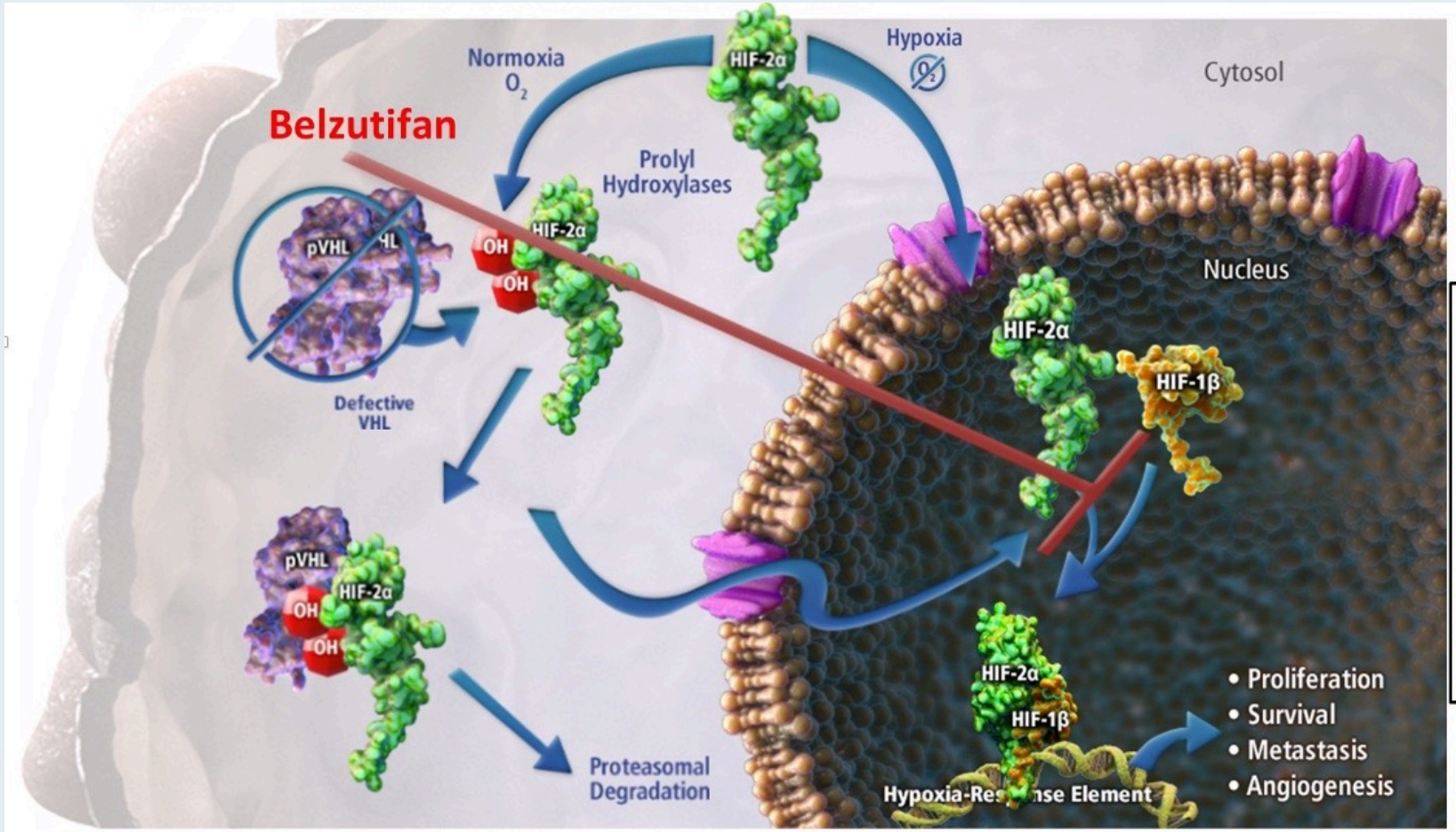
Discussion Question

A Phase II clinical trial is currently evaluating belzutifan in combination with pembrolizumab and lenvatinib for which of the following cancer types?

- Endometrial cancer
- Urothelial bladder cancer
- GI Cancers
- Lung cancer
- I’m not sure

RTP RESEARCH TO PRACTICE

Von Hippel Lindau Tumor Suppressor (pVHL) Deficiency Results in HIF-2-alpha Activation



- 90% of patients with sporadic ccRCC have defective pVHL function[1]
- Loss of pVHL function results in constitutive activation of HIF-2α[2]
- Belzutifan is a potent, selective, small molecule HIF-2α inhibitor

1. Linehan WM, Rickets CJ. *Nat Rev Urol.* 2019;16:539-552. 2. Couvé S et al. *Cancer Res.* 2014;74:6554-6564.

Bauer TD et al. GU Cancers Symposium 2021;Abstract 273.

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

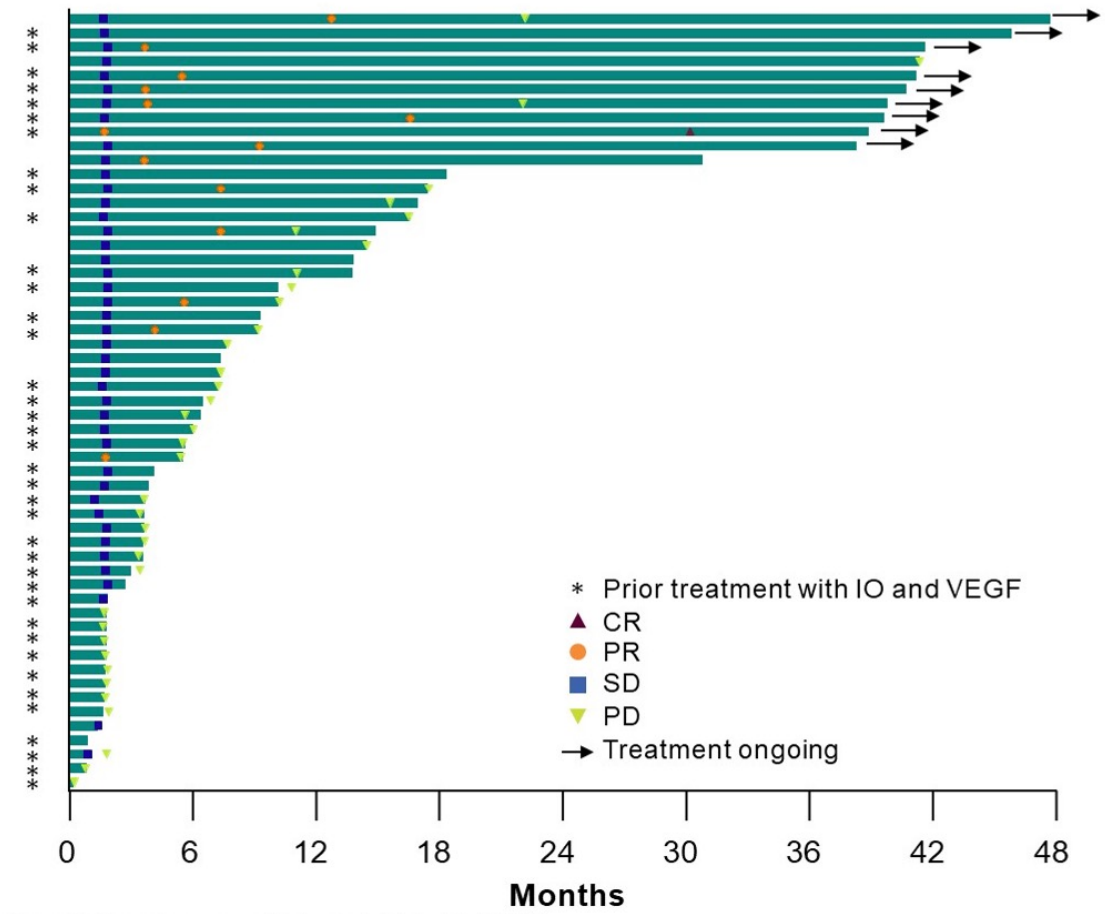
E. Jonasch[1]; T. M. Bauer[2]; K. P. Papadopoulos[3]; E. R. Plimack[4]; J. R. Merchan[5]; D. F. McDermott[6]; M. D. Michaelson[7]; L. J. Appleman[8]; A. Roy[9]; R. F. Perini[9]; Y. Liu[9]; T. K. Choueiri[10]

[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

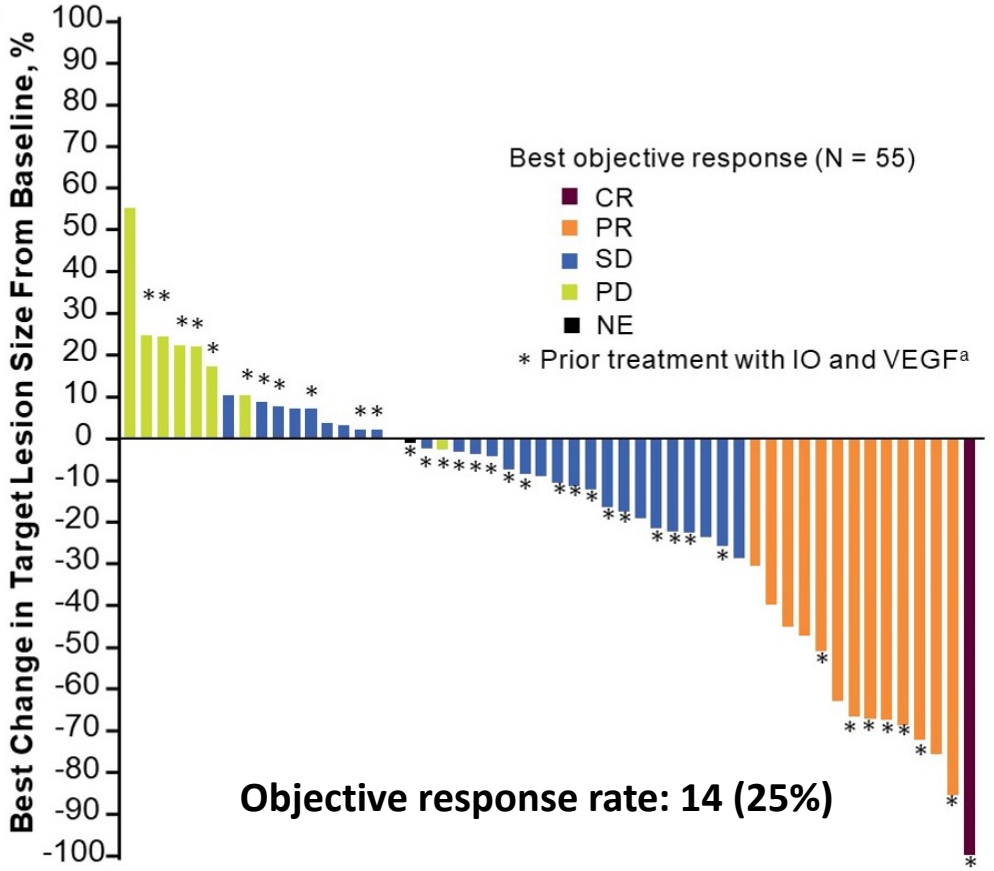
ASCO 2022;Abstract 4509.

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

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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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
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 3: Multiple Myeloma

Co-Moderator

Taral Patel, MD
Zangmeister Cancer Center
Columbus, Ohio

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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

Multiple Myeloma Agenda

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

- Current role of stem cell transplant
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Module 2: Management of Relapsed/Refractory MM

Module 3: Other Novel Agents and Strategies

Discussion Question

Regulatory and reimbursement issues aside, what would be your preferred induction treatment for a younger transplant-eligible patient with standard-risk multiple myeloma (MM)?

- RVd
- D-RVd (daratumumab with RVd)
- KRd
- D-KRd
- Other

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.

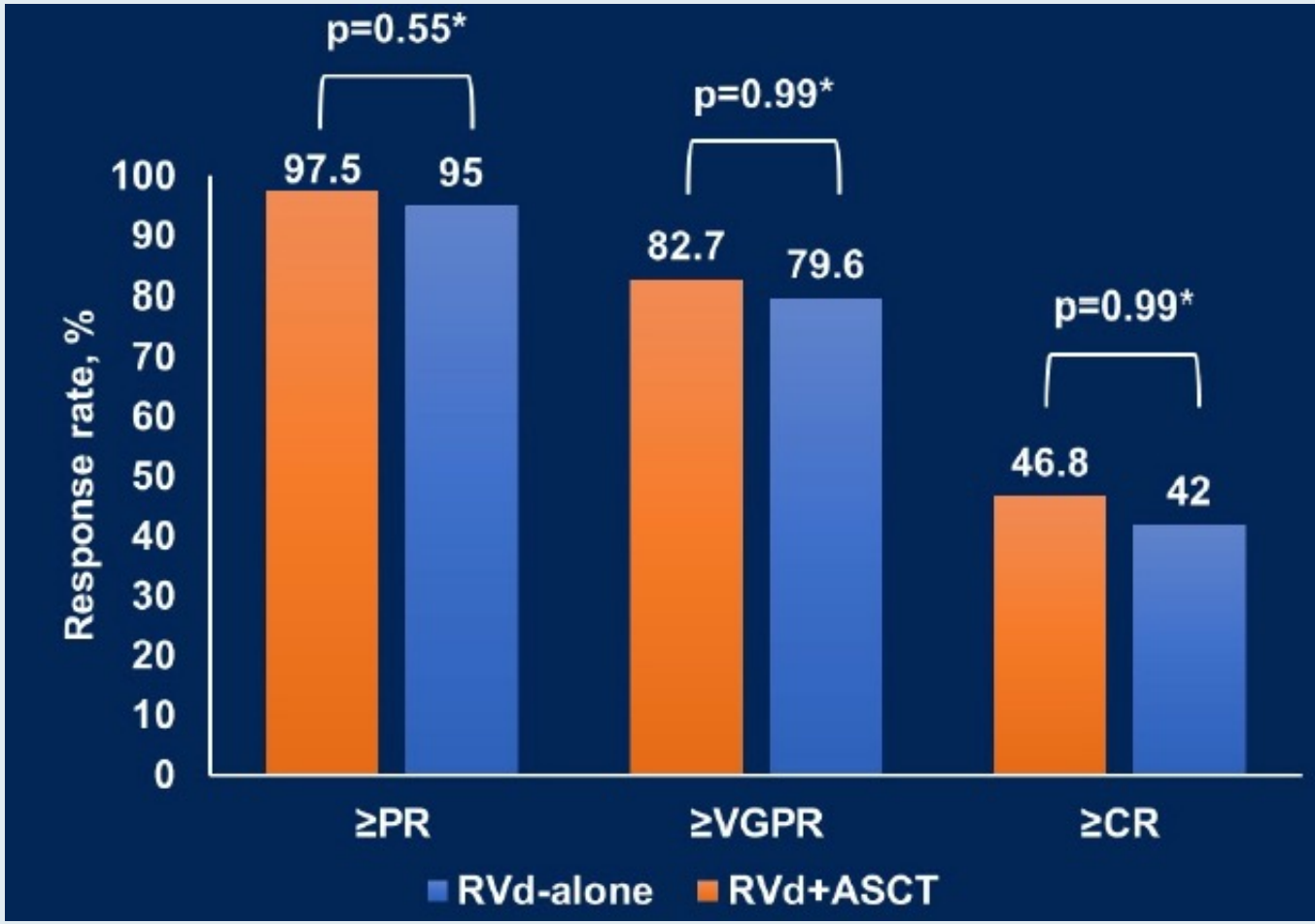
ORIGINAL ARTICLE

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

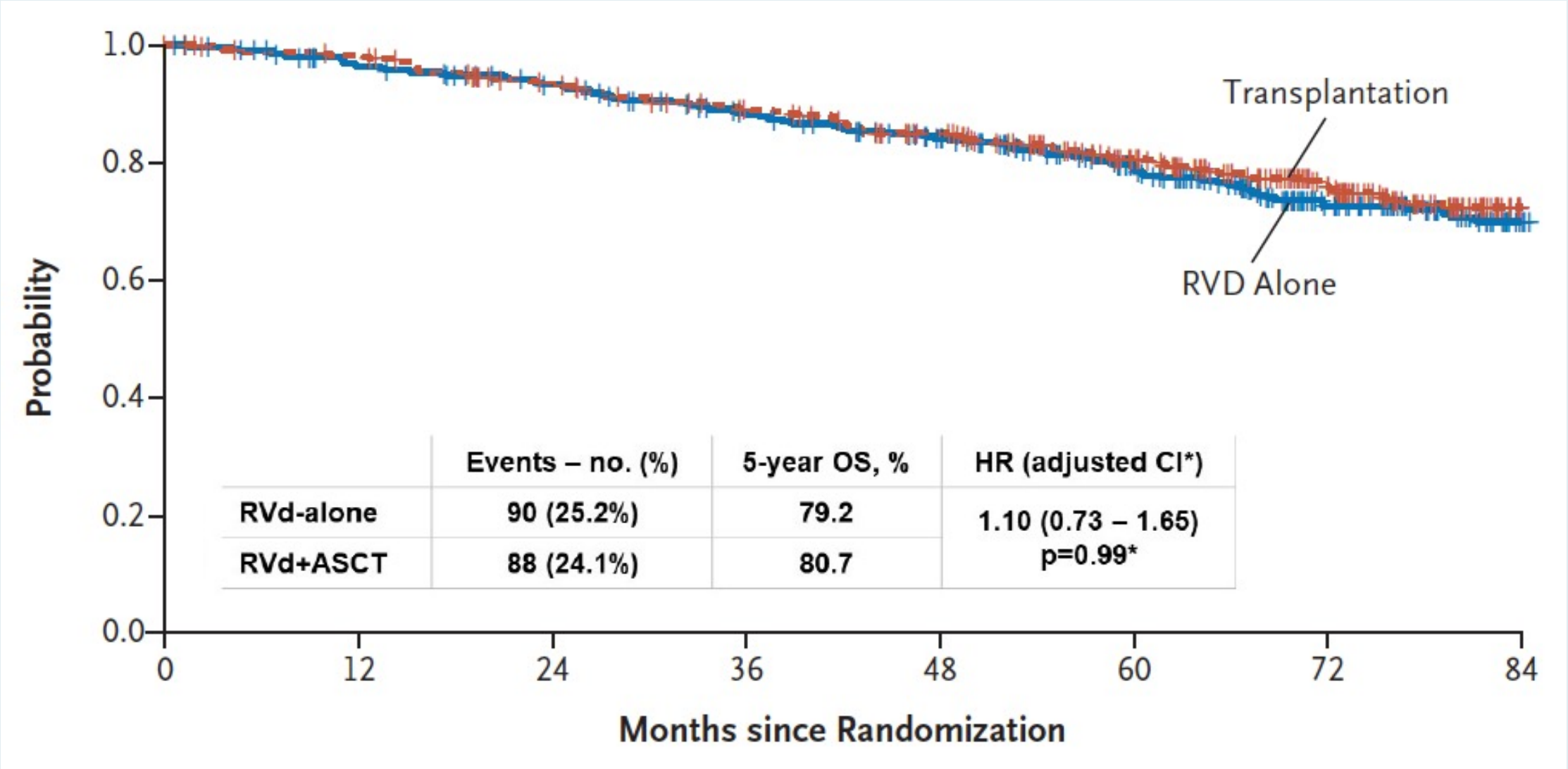
DETERMINATION: Best Response to Treatment and Duration of Response



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.

Multiple Myeloma Agenda

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

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Module 2: Management of Relapsed/Refractory MM

Module 3: Other Novel Agents and Strategies

2022 ASCO® ANNUAL MEETING

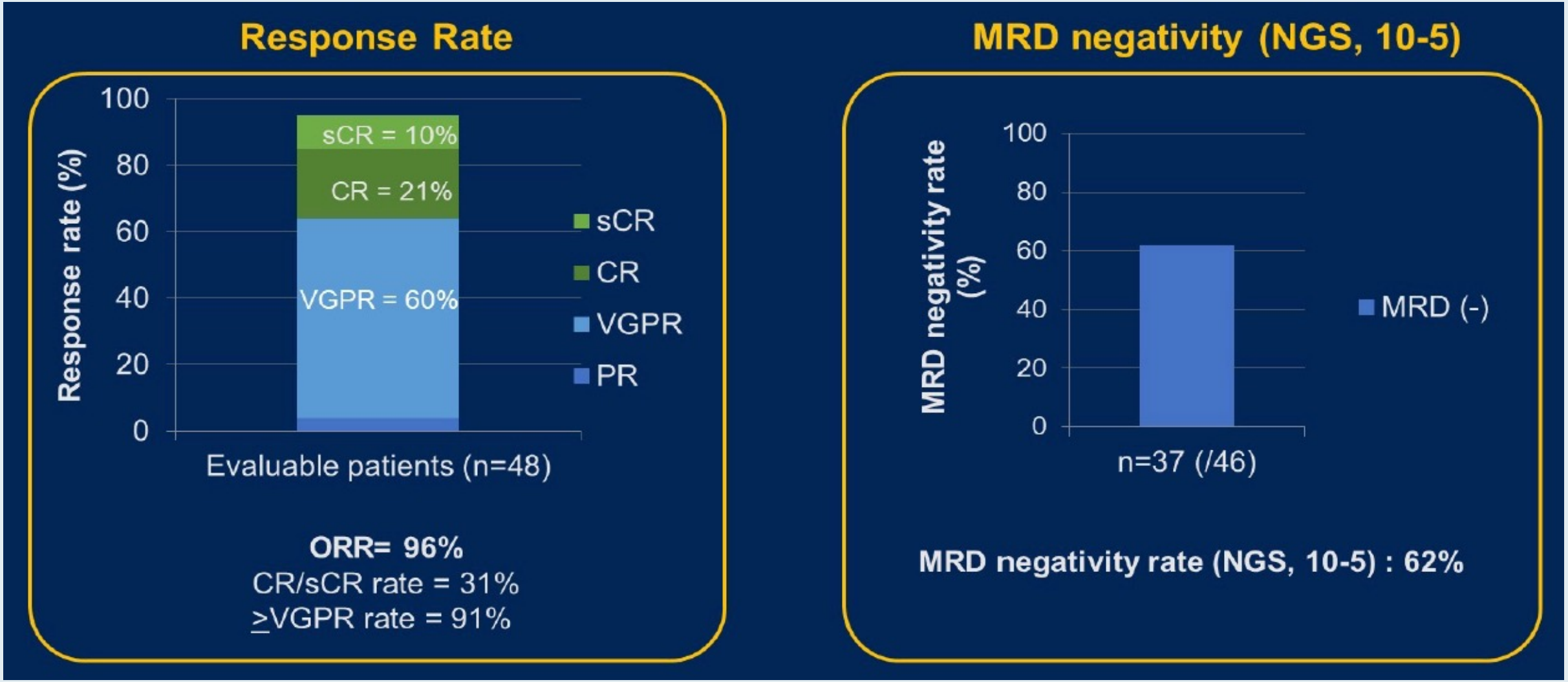
Abstract 8002

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: 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

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

Discussion Question

In general, would you offer lenalidomide maintenance therapy to a patient who is MRD-negative after induction and autologous transplant?

- Yes
- Yes, for select patients
- No
- I’m not sure

RTP RESEARCH TO PRACTICE

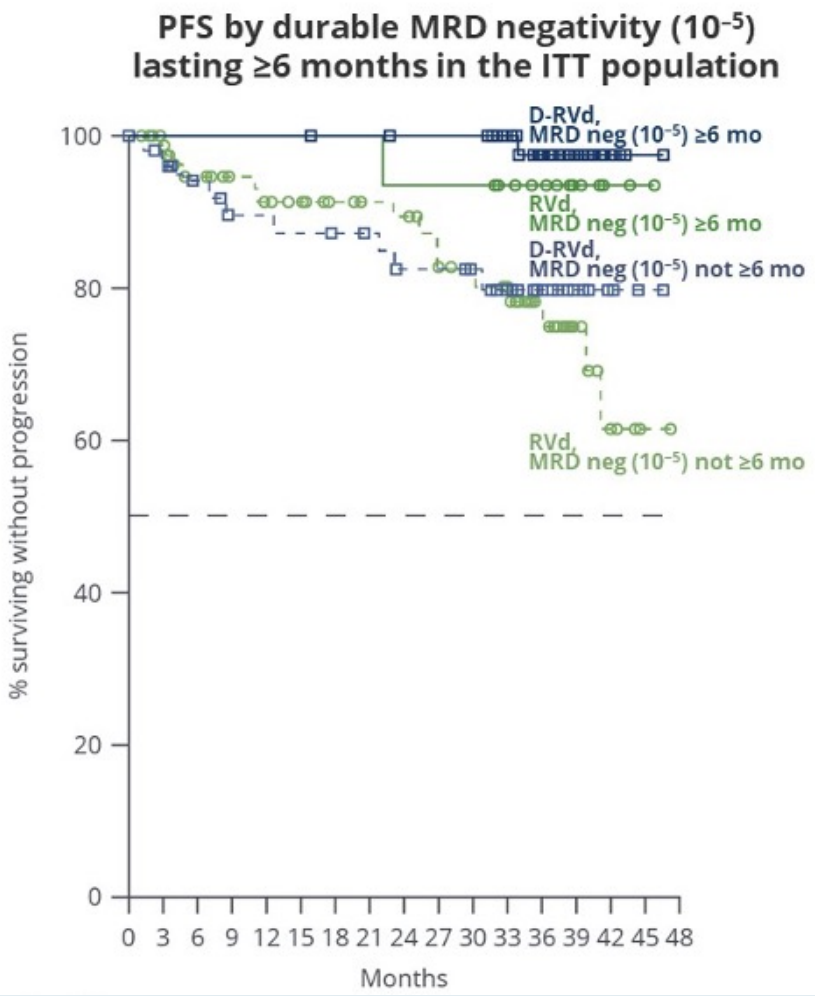
Daratumumab (DARA) plus Lenalidomide, Bortezomib, and Dexamethasone (RVd) in Patients (Pts) with Transplant-Eligible Newly Diagnosed Multiple Myeloma (NDMM): Updated Analysis of Griffin After 24 Months of Maintenance[1]

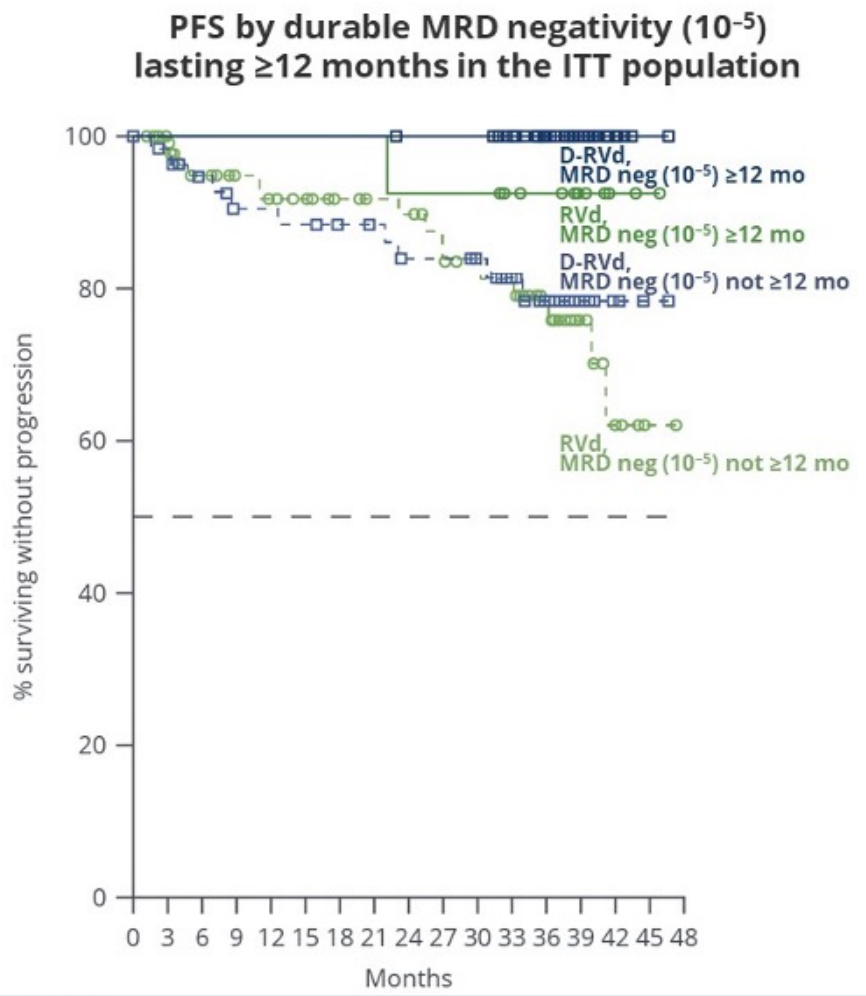
Daratumumab (DARA) + Lenalidomide, Bortezomib, and Dexamethasone (RVd) in Transplant-Eligible Newly Diagnosed Multiple Myeloma (NDMM): A Post Hoc Analysis of Sustained Minimal Residual Disease (MRD) Negativity from GRIFFIN[2]

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

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

GRIFFIN: PFS by Sustained MRD Negativity





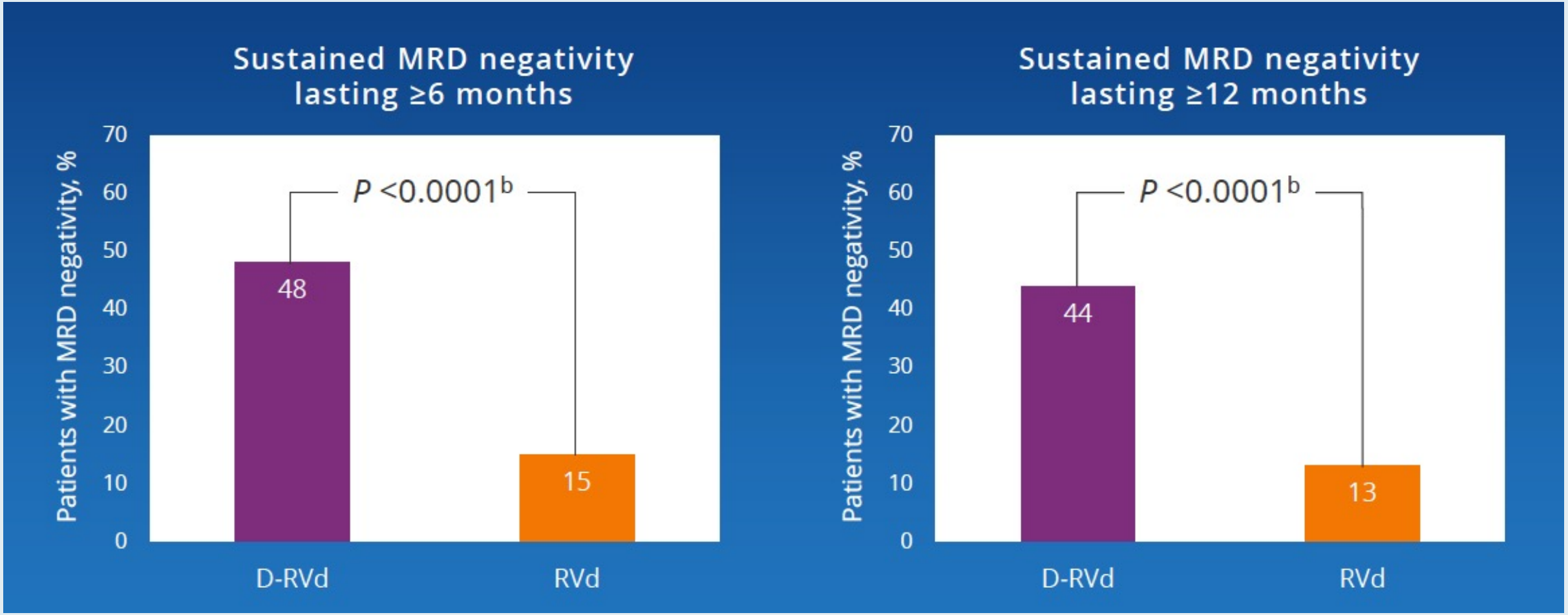
- PFS was better in the D-RVd group versus the RVd group among patients who achieved durable MRD negativity at the 10^{-5} threshold
- PFS was better for patients who reached durable MRD negativity ≥6 or ≥12 months versus those who did not reach durable MRD negativity

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: 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

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

Multiple Myeloma Agenda

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

- Current role of stem cell transplant
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- Use of maintenance therapy after transplant; clinical role of MRD
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Module 2: Management of Relapsed/Refractory MM

Module 3: Other Novel Agents and Strategies

Discussion Question

In general, what is your preferred induction regimen for an 80-year-old patient with MM who is transplant ineligible with normal renal function and no high-risk features?

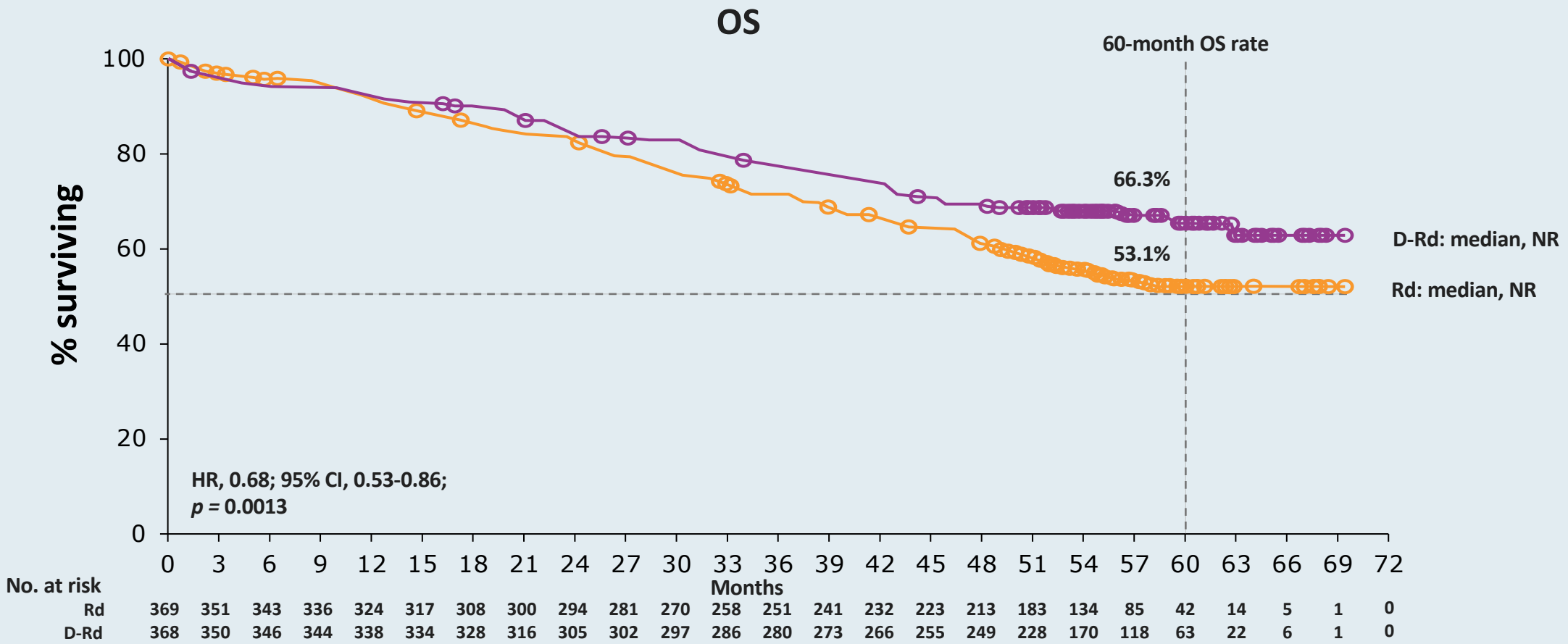
- Rd
- RVd or RVd lite
- KRd
- MPV/daratumumab
- Rd/daratumumab
- VTd
- MPV, MPR or MPT
- Other

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: 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

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

Multiple Myeloma Agenda

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- Bispecific antibodies (teclistamab, talquetamab): Similarities and differences in MOA; efficacy, toxicity, future clinical role

Module 3: Other Novel Agents and Strategies

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

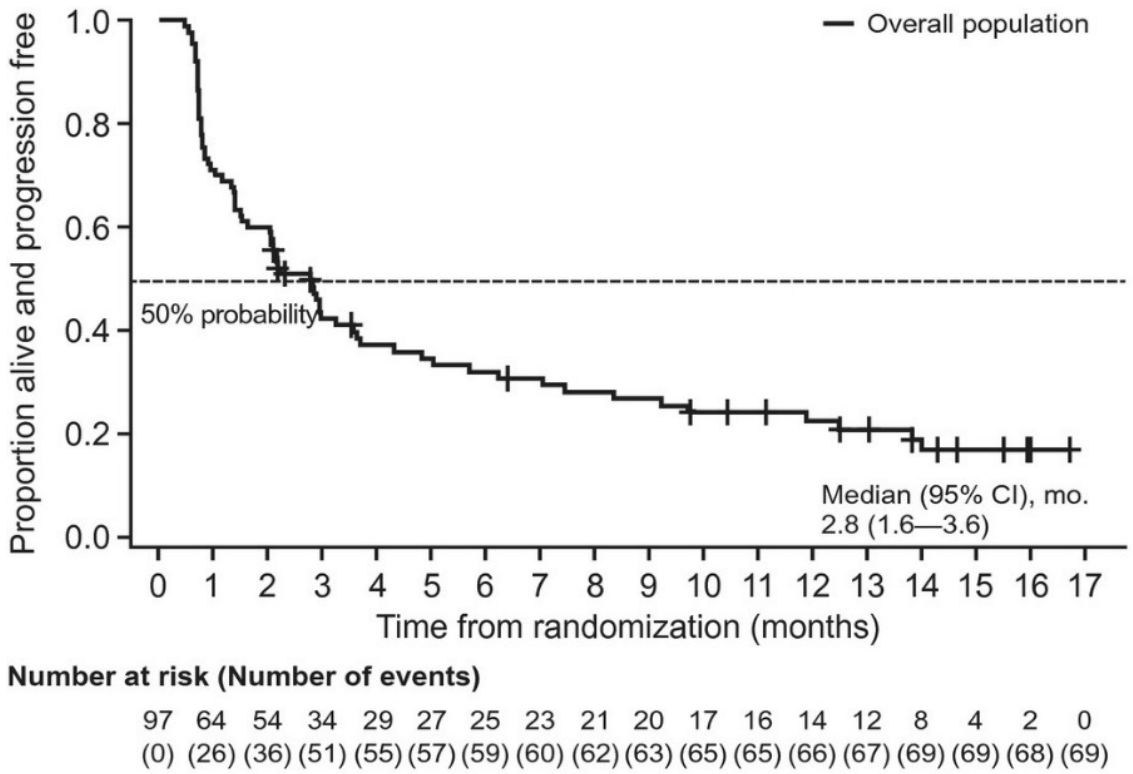
Sagar Lonial, MD [1]; Hans C. Lee, MD[2]; Ashraf Badros, MD [3]; Suzanne Trudel, MD[4]; Ajay K. Nooka, MD [1]; Ajai Chari, MD [5]; Al-Ola Abdallah, MD[6]; Natalie Callander, MD[7]; Douglas Sborov, MD[8]; Attaya Suvannasankha, MD[9]; Katja Weisel, MD[10]; Peter M. Voorhees, MD[11]; Lynsey Womersley, MSc[12]; 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.

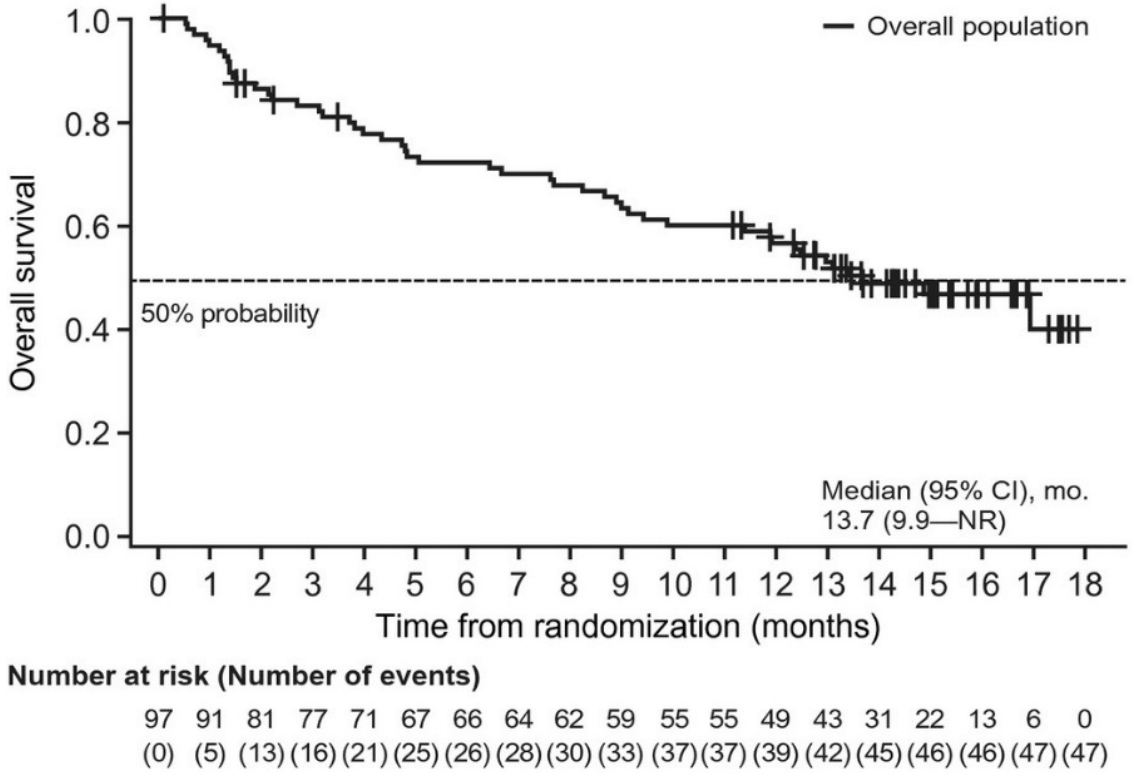
RTP RESEARCH TO PRACTICE

DREAMM-2: Longitudinal Outcomes

Progression-Free Survival



Overall Survival

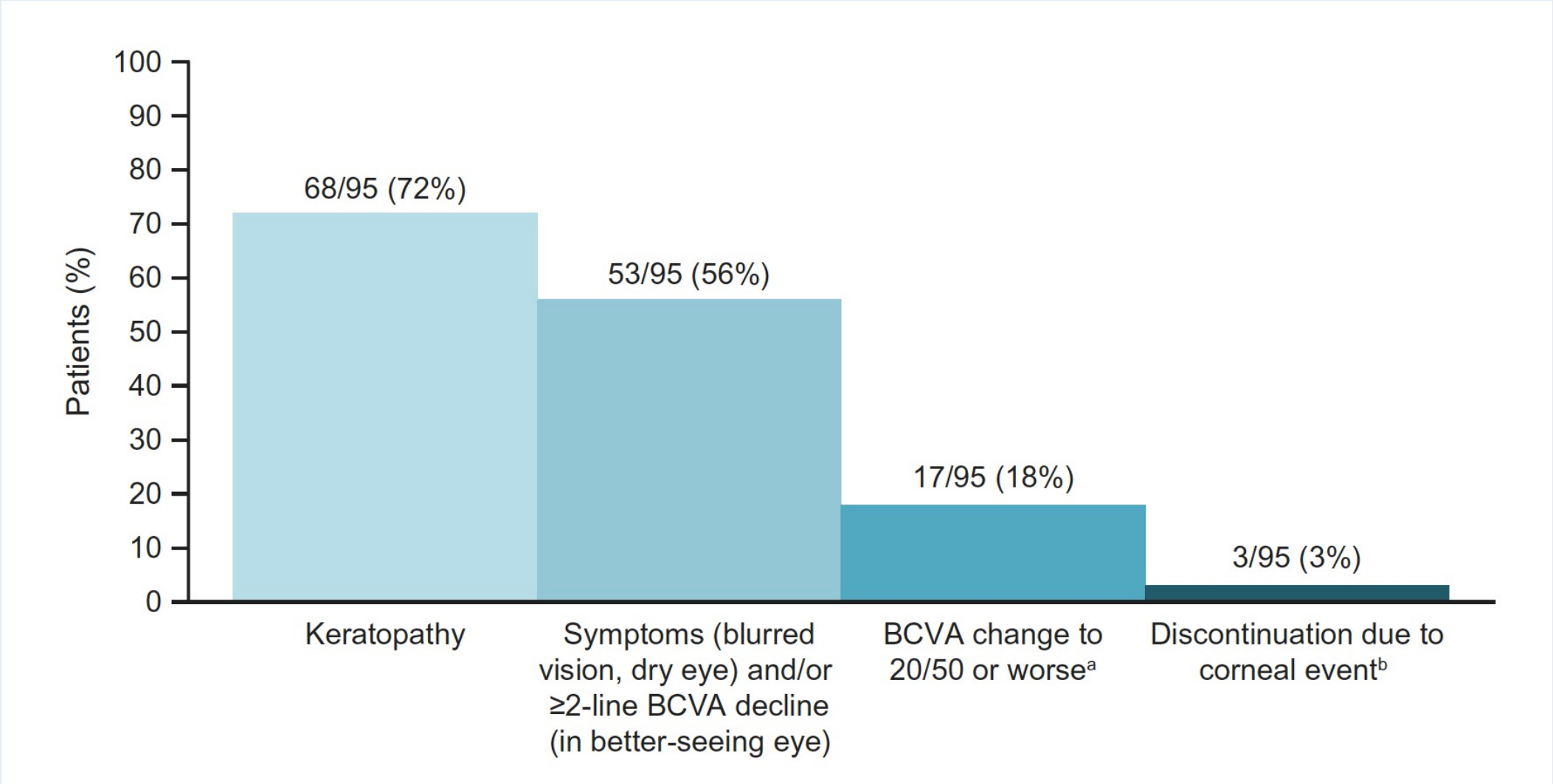


Expected median OS in triple-class refractory myeloma: 8.6 months

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

Multiple Myeloma Agenda

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

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- Bispecific antibodies (teclistamab, talquetamab): Similarities and differences in MOA; efficacy, toxicity, future clinical role

Module 3: Other Novel Agents and Strategies

Discussion Question

Based on your knowledge of available data and personal clinical experience, how would you compare the efficacy of idecabtagene vicleucel to that of ciltacabtagene autoleucel for patients with relapsed/refractory MM?

- Ide-cel is more efficacious
- Cilta-cel is more efficacious
- Efficacy is similar with both agents
- I'm not sure

Discussion Question

Based on your knowledge of available data and personal clinical experience, how would you compare the tolerability of ciltacabtagene autoleucel to that of idecabtagene vicleucel for patients with relapsed/refractory MM?

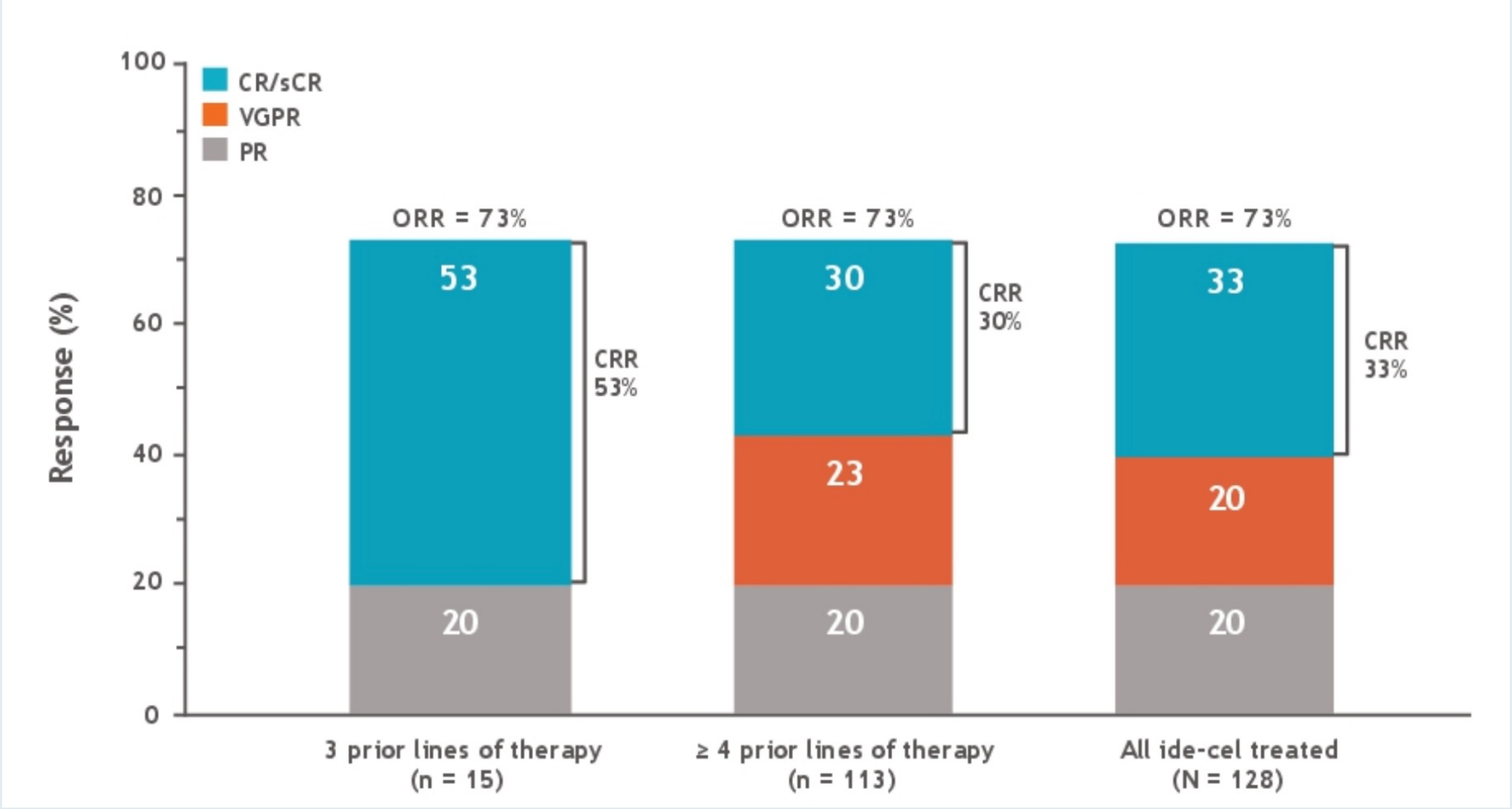
- Ciltacabtagene autoleucel is more tolerable
- Idecabtagene vicleucel is more tolerable
- Tolerability is similar with both agents
- I’m not sure

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.

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=

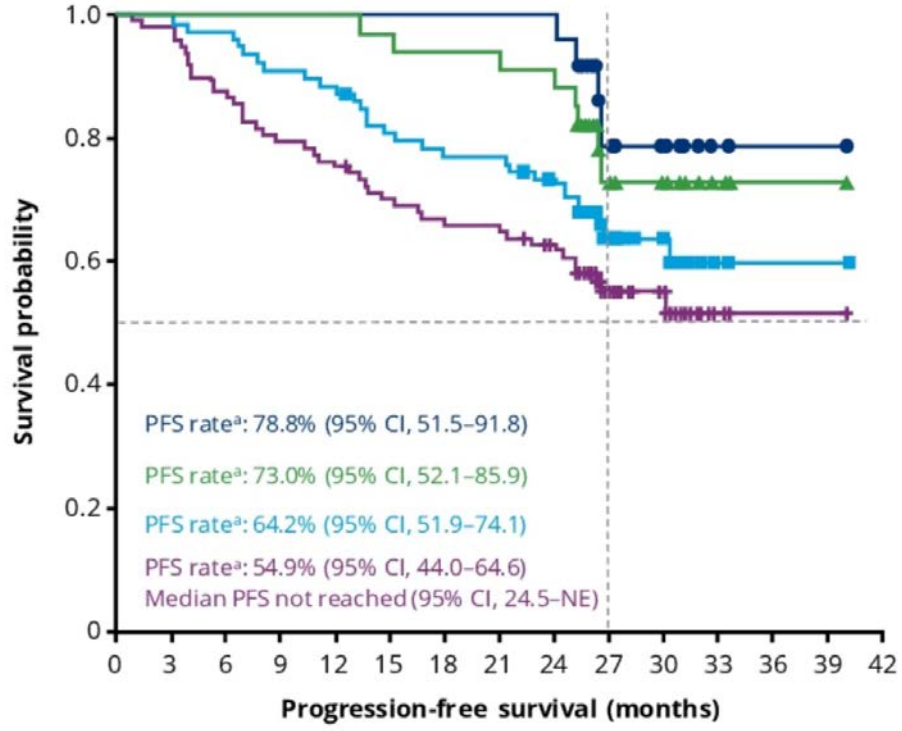
Phase 1b/2 Study of Ciltacabtagene Autoleucel, a BCMA-Directed CAR-T Cell Therapy, in Patients with Relapsed/Refractory Multiple Myeloma (CARTITUDE-1): 2 Years Post LPI

Usmani SZ et al.

ASCO 2022;Abstract 8028.

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

PFS

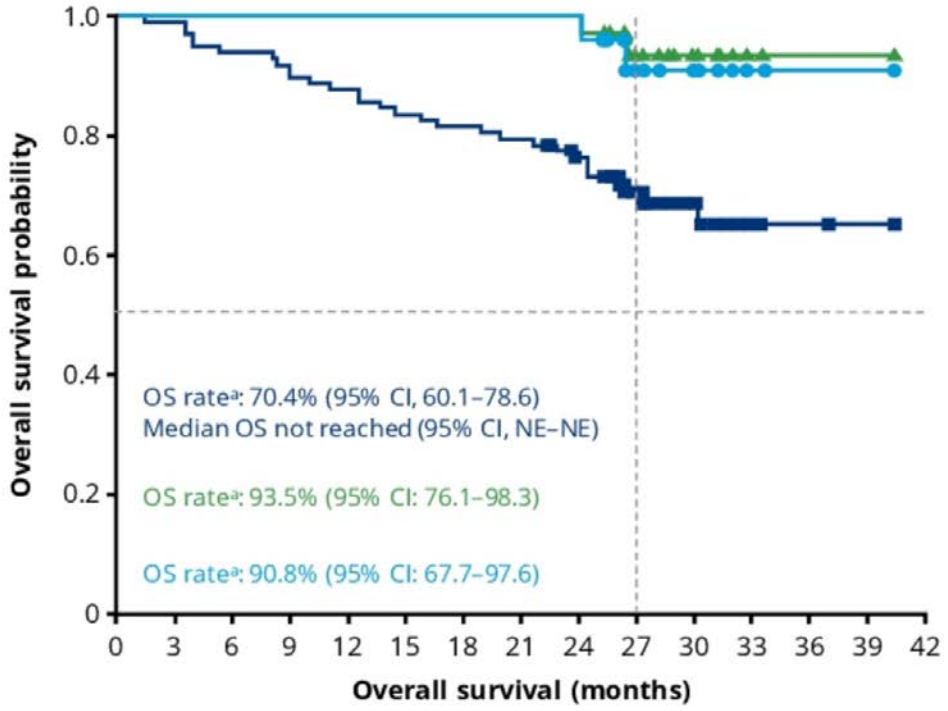


Patients at risk

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.

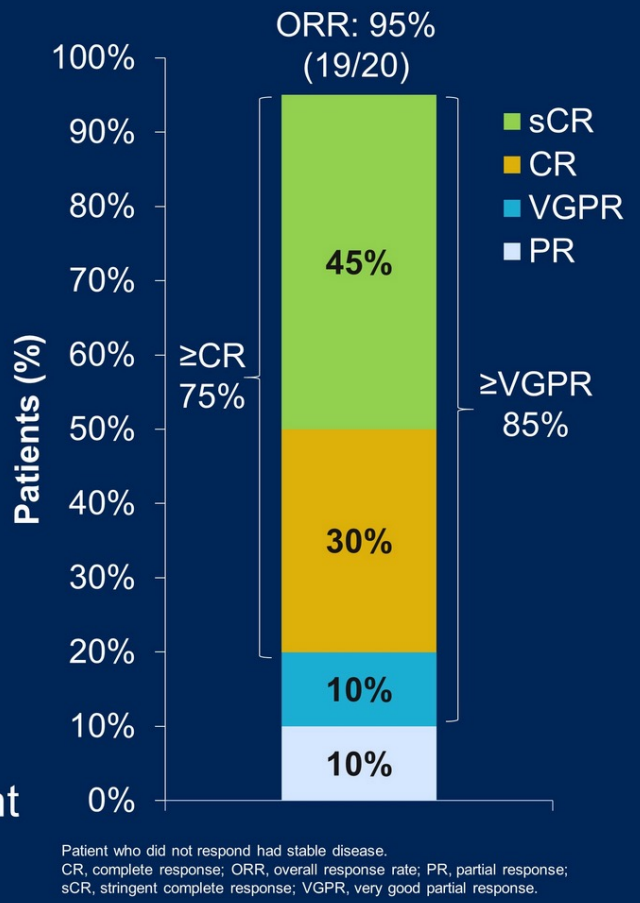
CARTITUDE-2: Ciltacabtagene Autoleucel After 1 to 3 Prior Lines of Therapy

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.

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

Discussion Question

In general, would you use another BCMA-directed therapy prior to a patient receiving CAR T-cell therapy?

- Yes
- No
- I'm not sure

Discussion Question

The first dose of teclistamab and of talquetamab require inpatient administration.

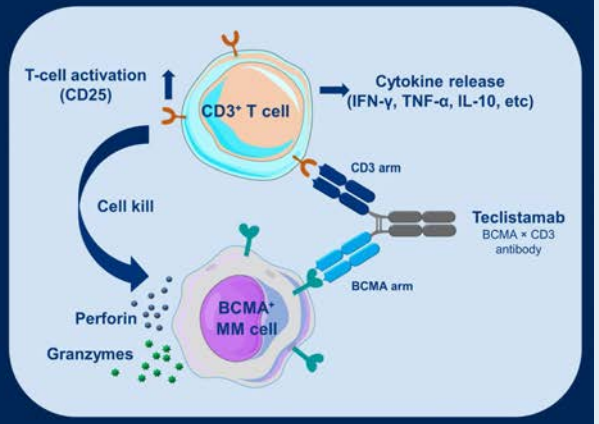
- Agree
- Disagree
- I’m not sure

Bispecific Antibodies for R/R MM

TECLISTAMAB

BCMA × CD3 Bispecific Antibody

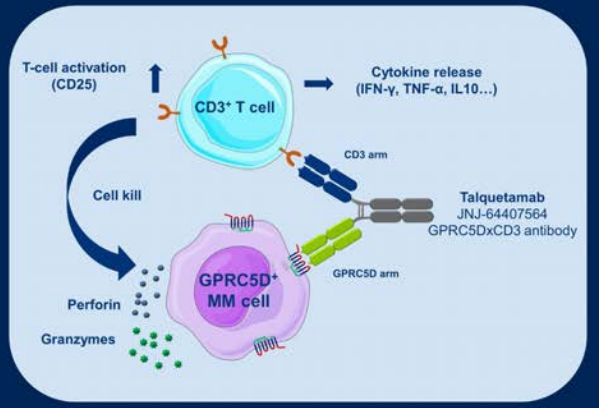
- Standard treatments and newly approved therapies for RRMM have limitations[1-3]
- Agents with new MOAs, including BCMA-targeted immunotherapies, offer considerable promise for RRMM
- Teclistamab (JNJ-64007957) is an off-the-shelf, full-size, BCMA × CD3, T-cell redirecting, bispecific antibody
- In 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

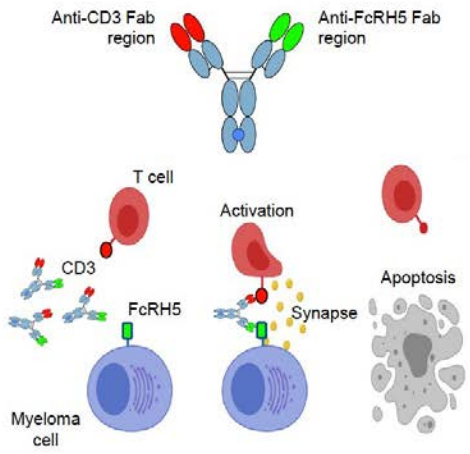
GPRC5D × CD3 Bispecific Antibody

- 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

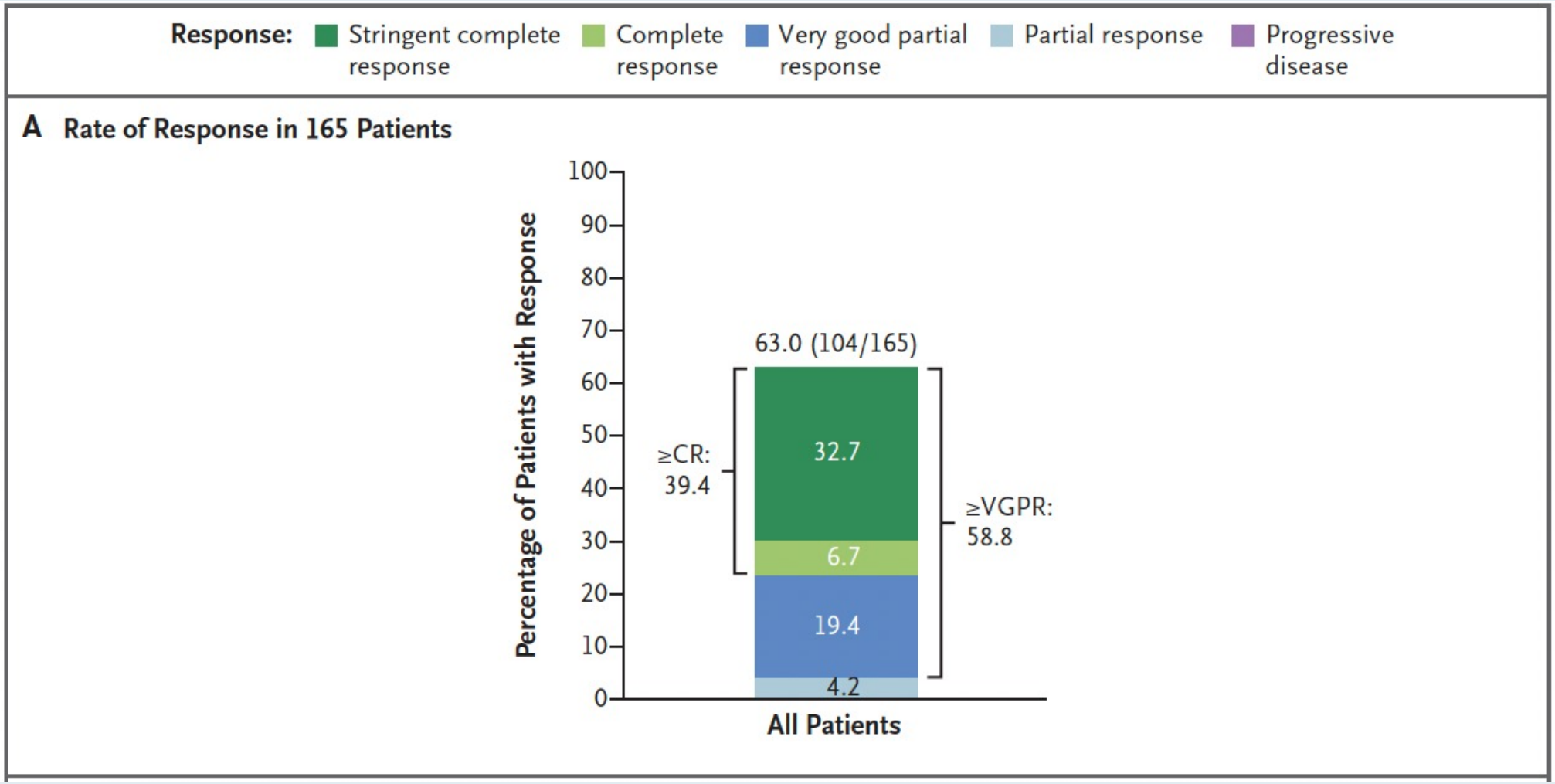
ORIGINAL ARTICLE

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

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

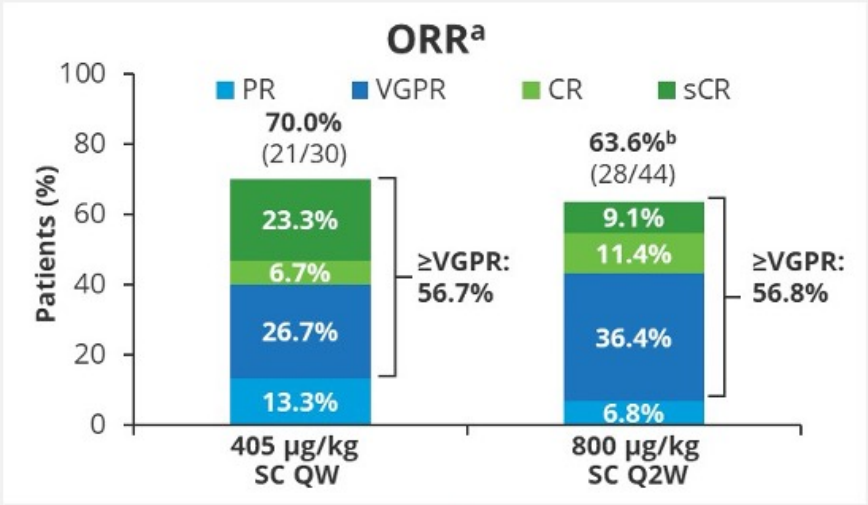
RTP RESEARCH TO PRACTICE

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

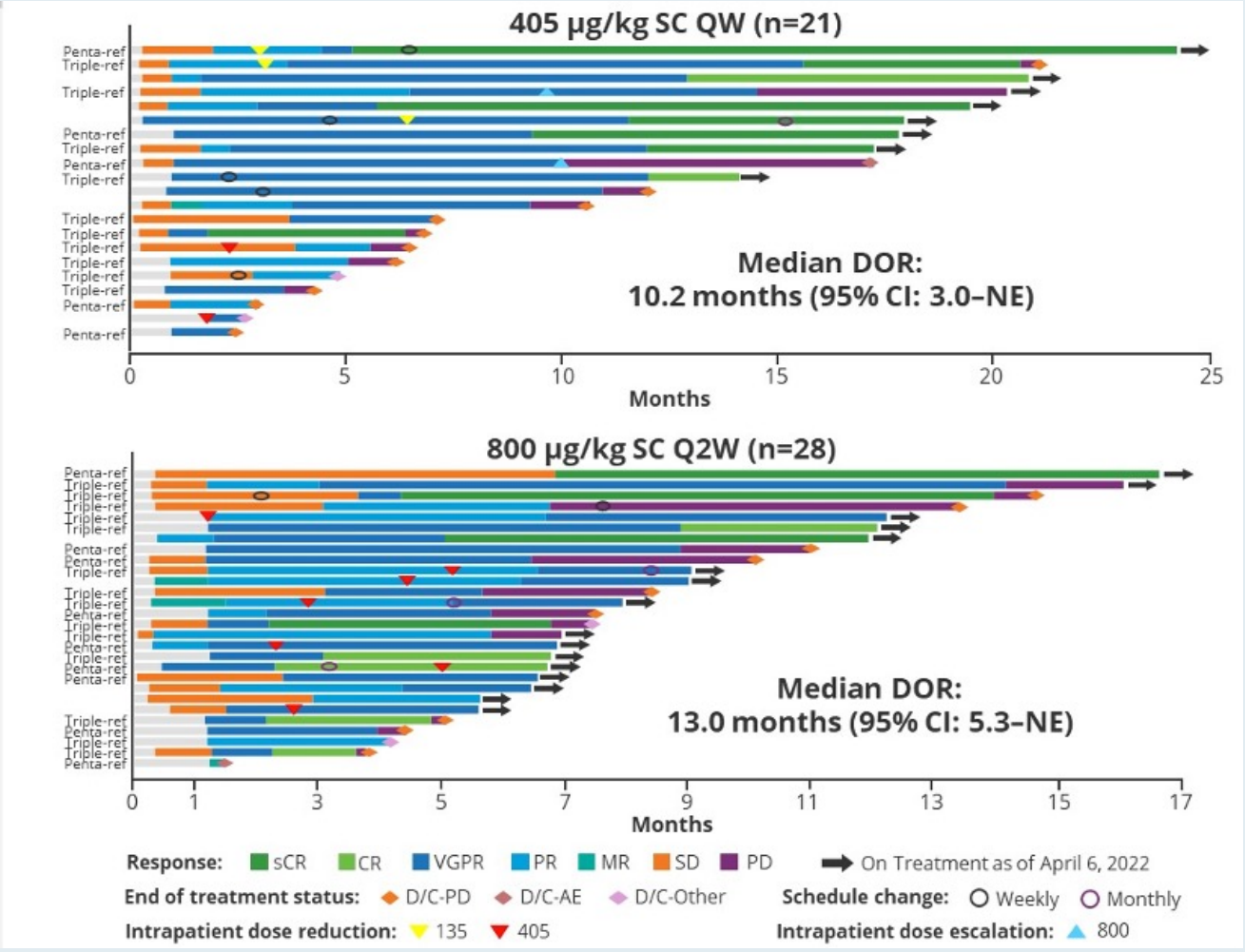
Monique C Minnema[1], Amrita Krishnan[2], Jesus G. Berdeja[3], Albert Oriol[4], Niels WCJ van de Donk[5], Paula Rodríguez-Otero[6], Daniel Morillo[7], María-Victoria Mateos[8], Luciano J. Costa[9], Jo Caers[10], Deeksha Vishwamitra[11], Joanne Ma[11], Shiyi Yang[11], Brandi W Hilder[11], Jaszianne Tolbert[11],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

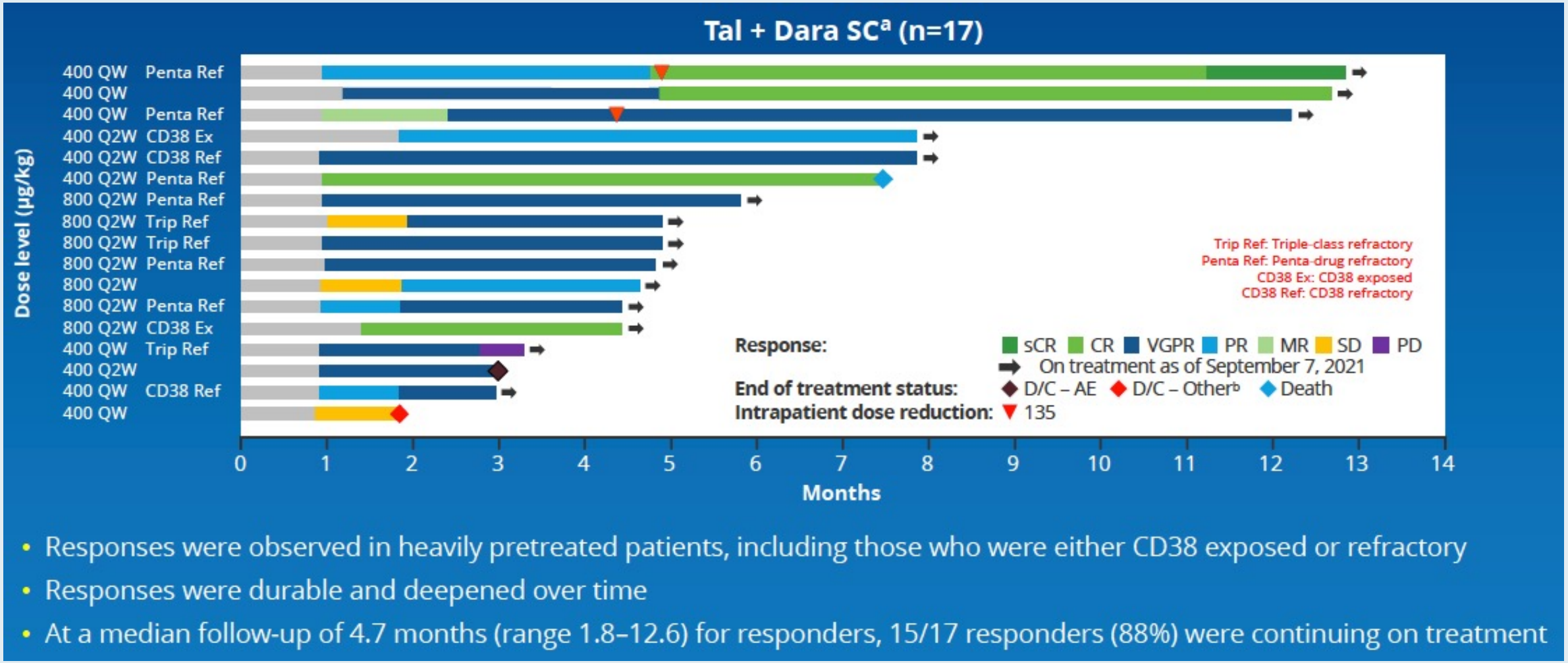
RTP RESEARCH TO PRACTICE

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]

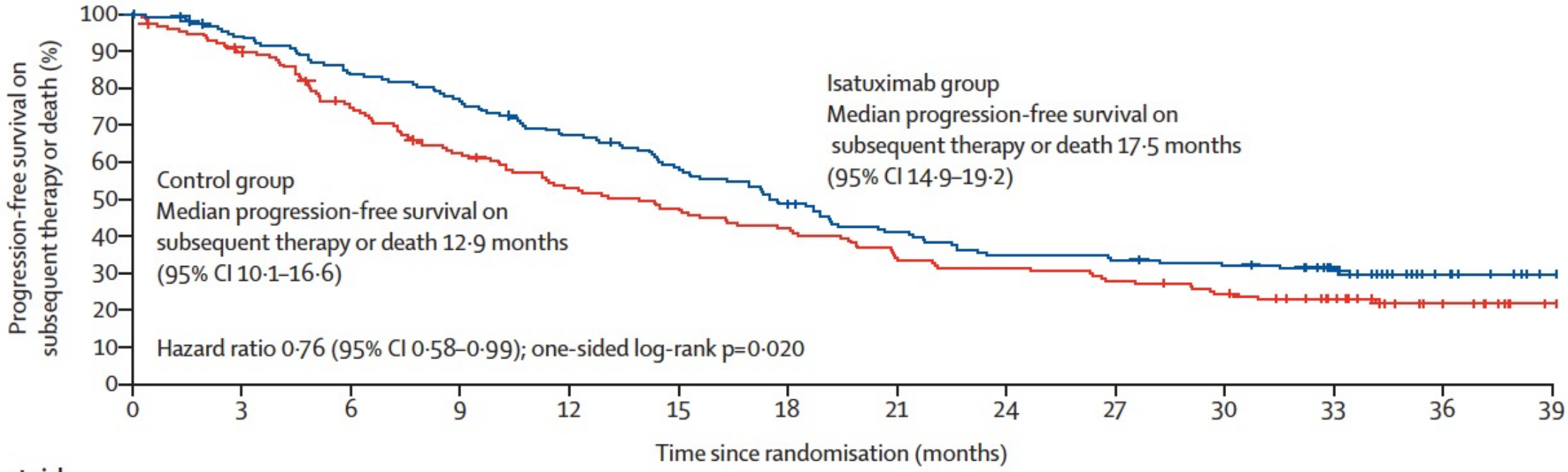
TRIMM-2: Duration of Response



- 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.

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

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Discussion Question

Venetoclax is efficacious in patients with MM and which of the following biomarkers?

- t(11;14)
- Bcl-2 overexpression
- Efficacy is similar for both
- I'm not sure

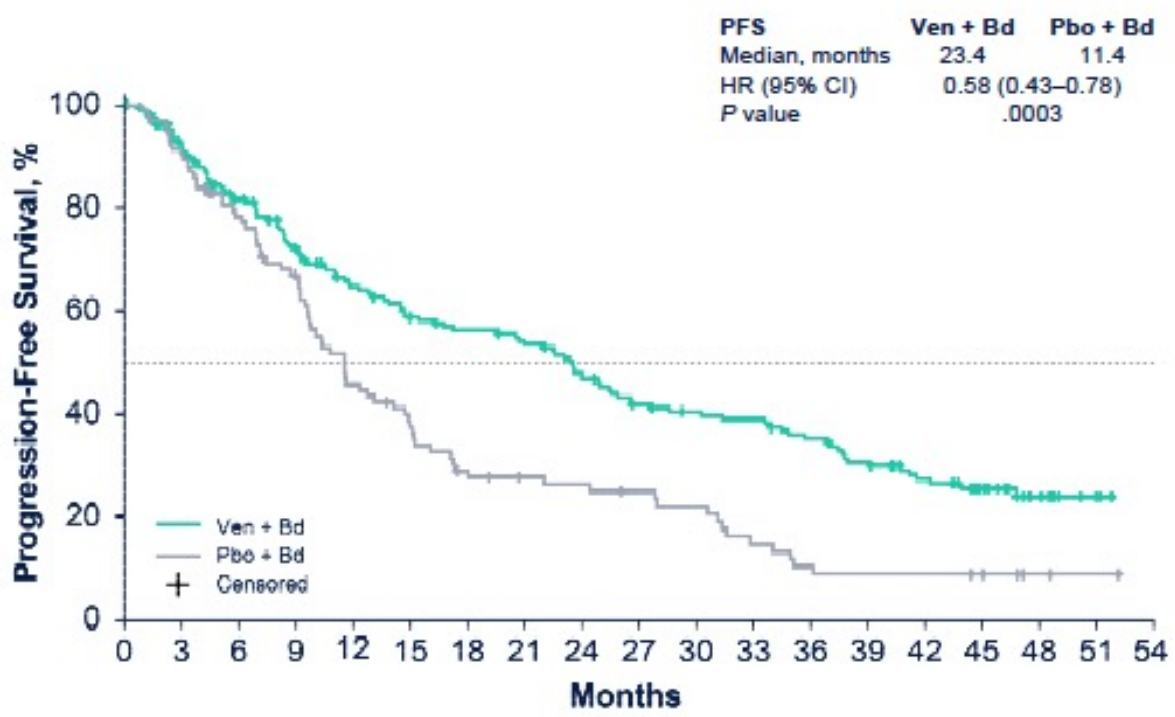
ASH 2021;Abstract 84

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

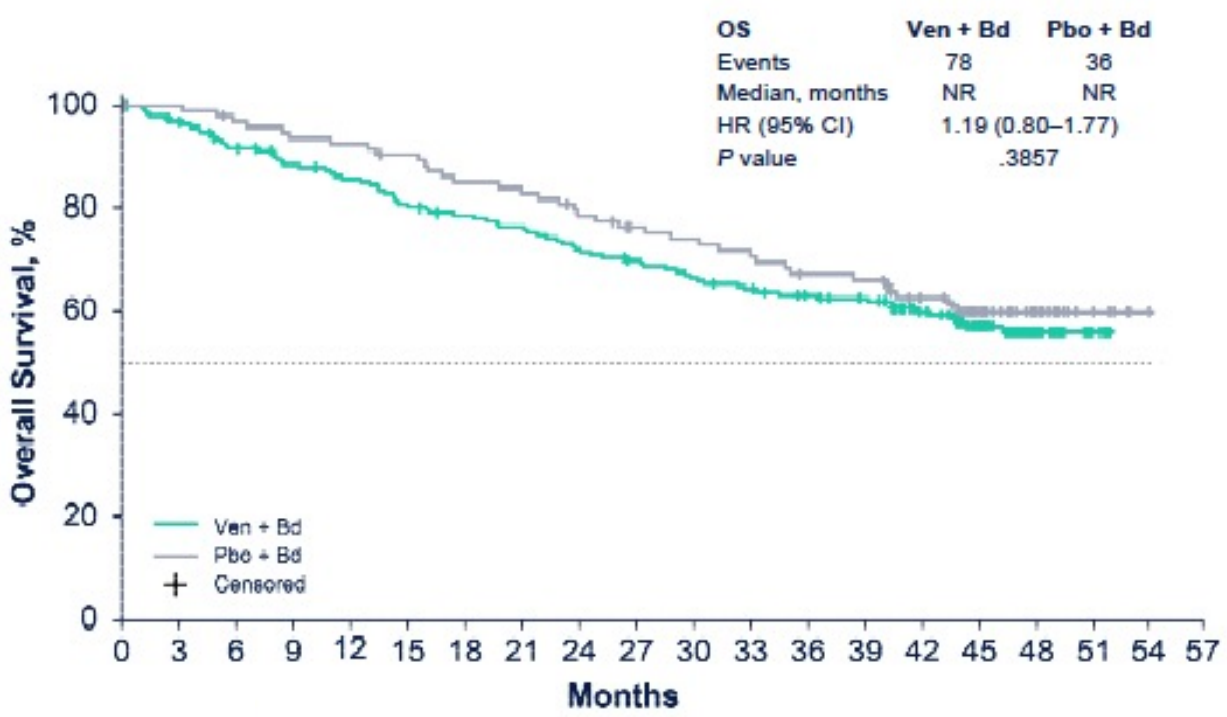
Shaji K. Kumar,[1] Simon J. Harrison,[2] Michele Cavo,[3] Javier de la Rubia,[4] Rakesh Popat,[5] Cristina Gasparetto,[6] Vania Hungria,[7] Hans Salwender,[8] Kenshi Suzuki,[9] Inho Kim,[10] Maika Onishi,[11] Grace Ku,[11] Rajvineeth Pothacamury,[12] Vasudha Sehgal,[12] Abdullah Masud,[12] Jeremy A.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

BELLINI: Updated Survival Results

Investigator-Assessed PFS in All Patients



OS in All Patients

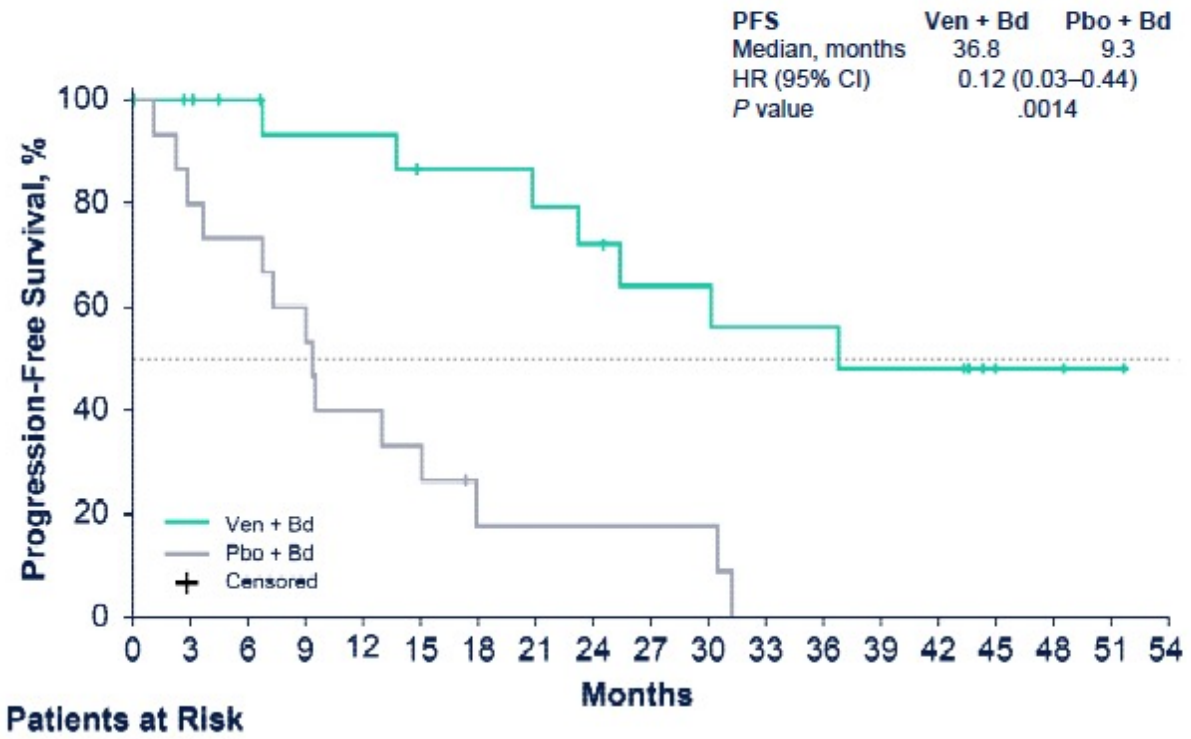


Kumar SK et al. ASH 2021;Abstract 84.

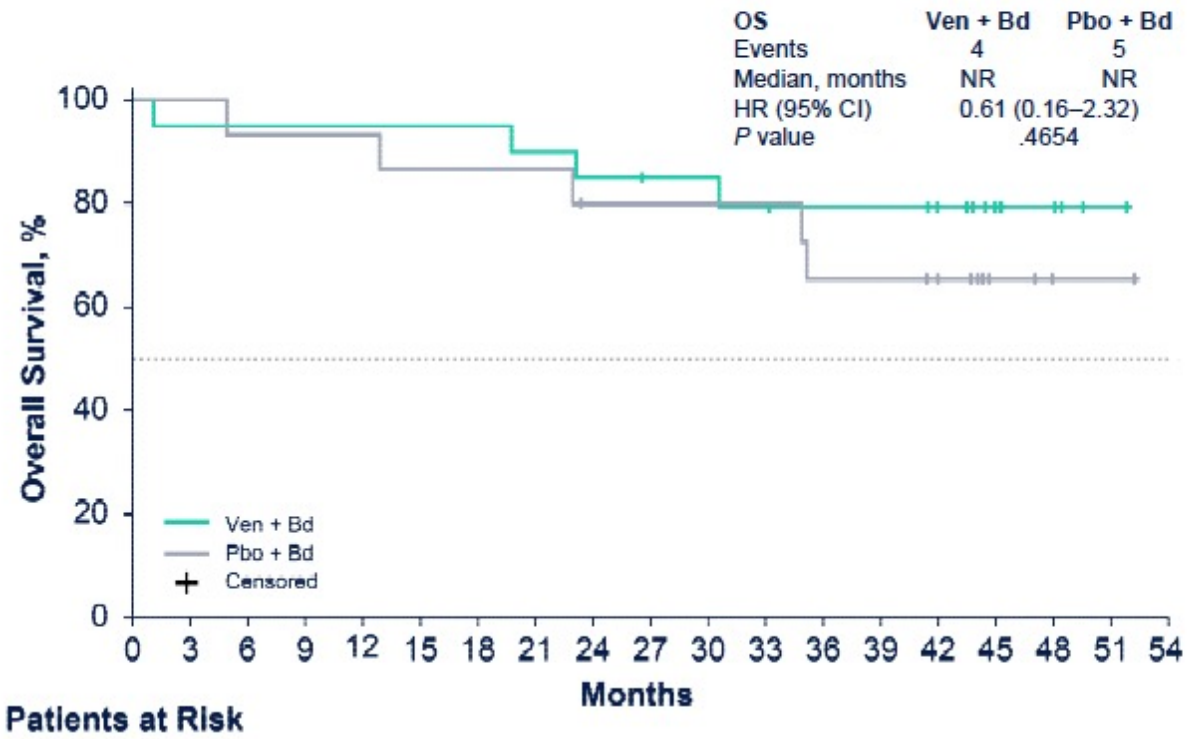
RTP RESEARCH TO PRACTICE

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

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



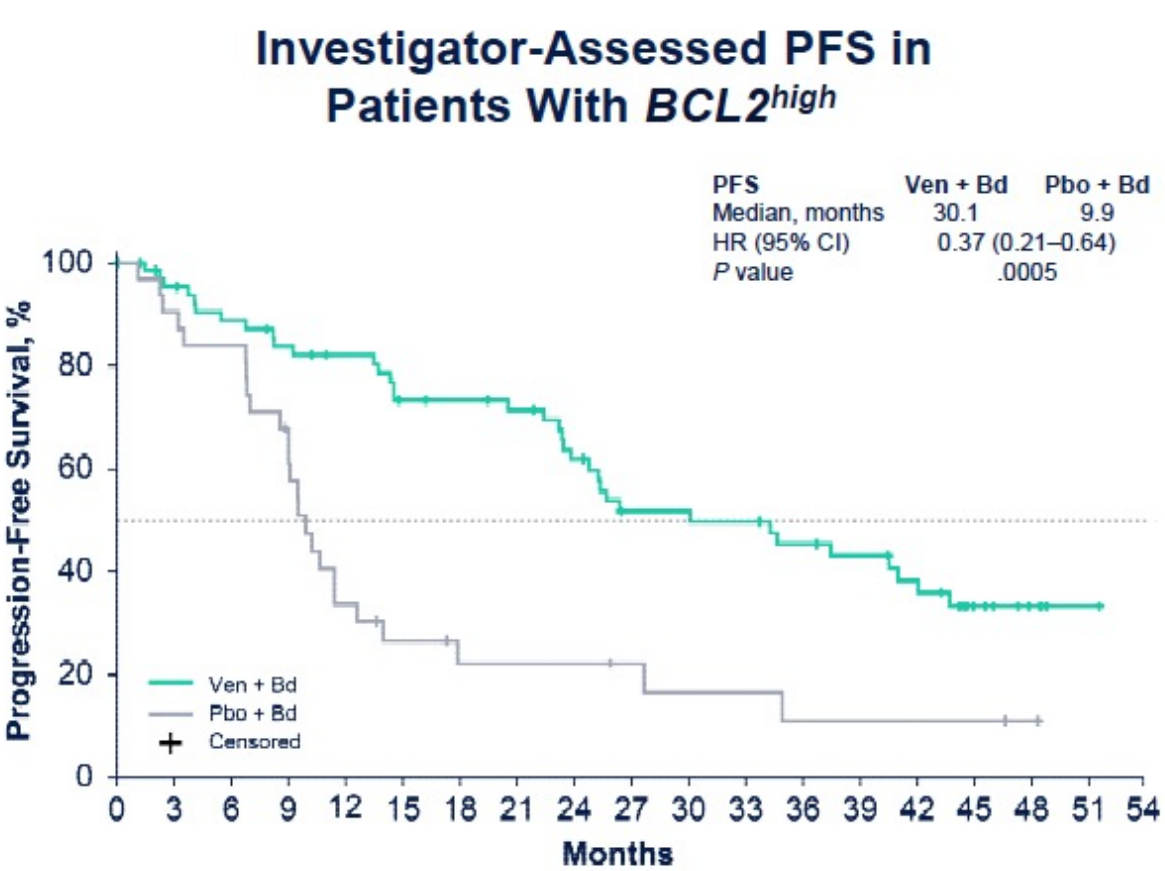
OS in Patients With t(11;14)

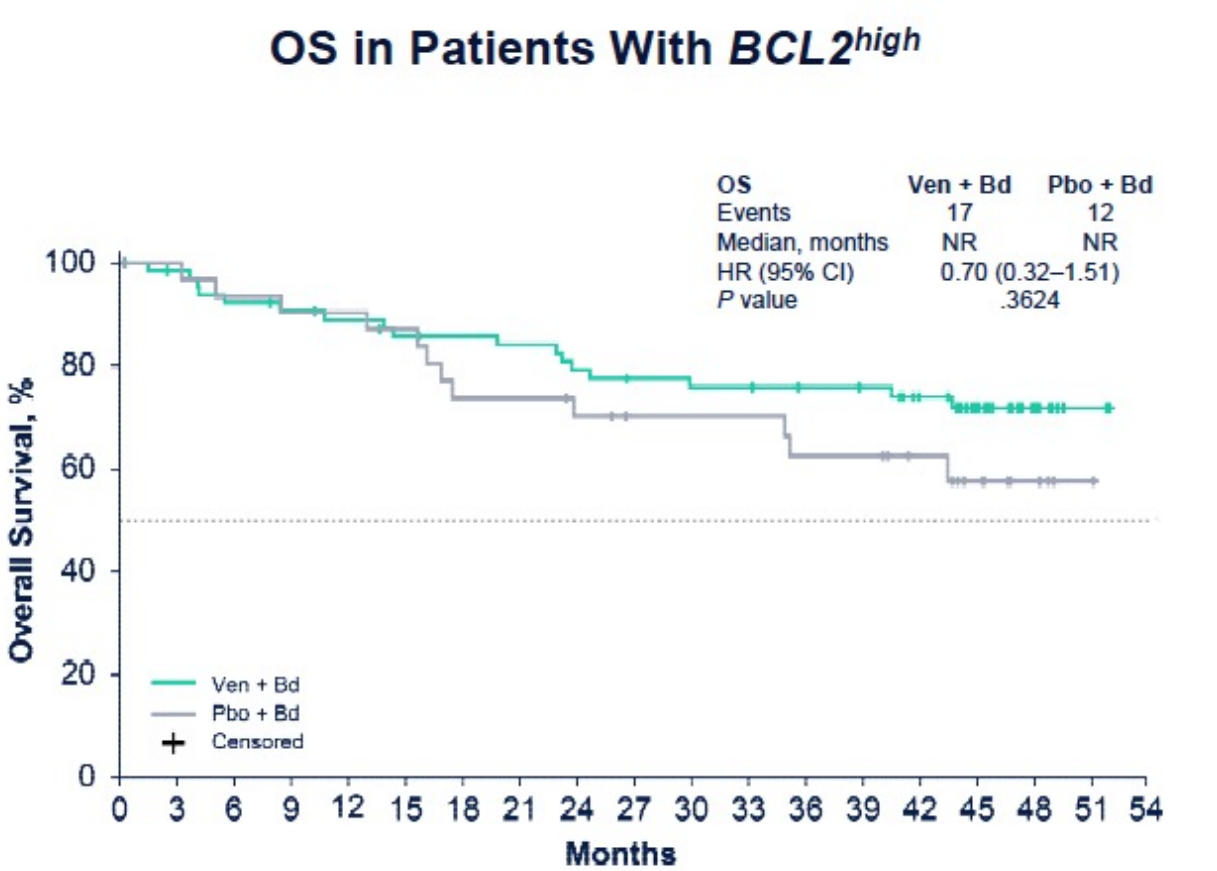


Kumar SK et al. ASH 2021;Abstract 84.

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

Multiple Myeloma Agenda

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Discussion Question

In general, how would you prefer to use selinexor in the treatment of relapsed/refractory MM?

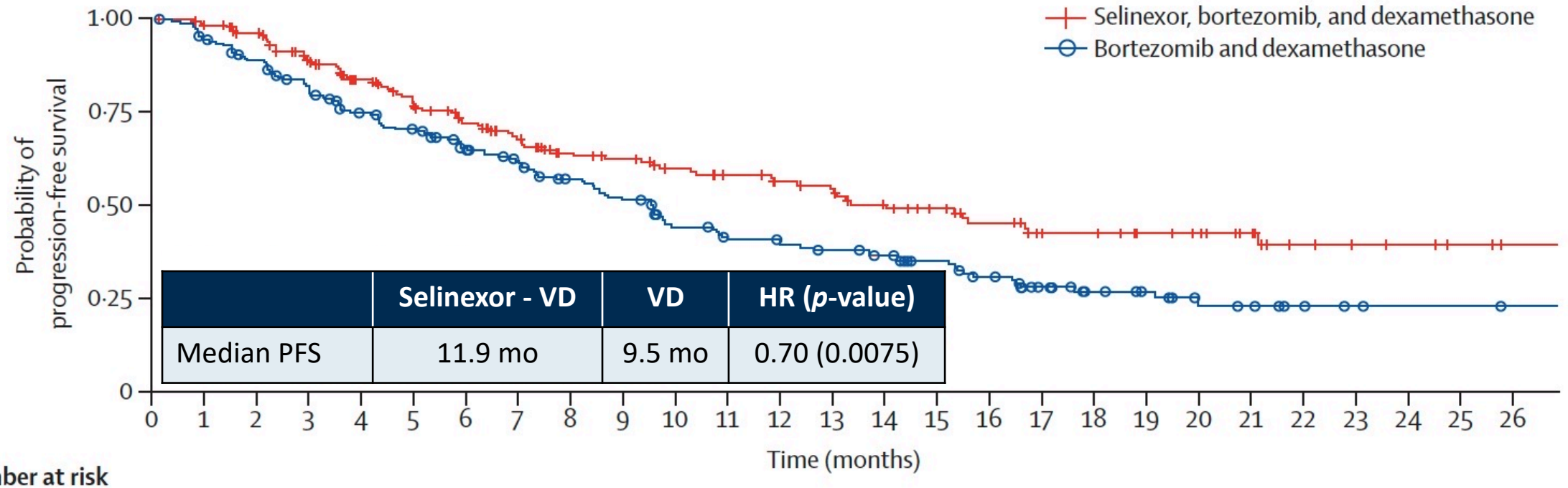
- Twice a week in combination with dexamethasone
- Once a week in combination with dexamethasone
- Once a week in combination with bortezomib and dexamethasone
- I do not use selinexor
- Other

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.

Multiple Myeloma Agenda

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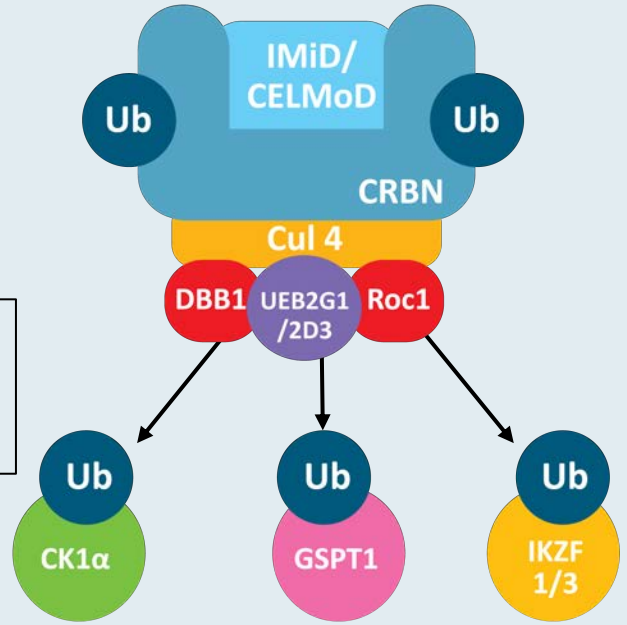
- Available data and ongoing trials evaluating venetoclax for patients with t(11;14) MM or Bcl-2 overexpression
- Sequencing of agents (eg, selinexor, isatuximab) alone or in combination for patients with relapsed/refractory MM
- Mechanism of action and potential clinical role of the CELMoDs (cereblon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

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.

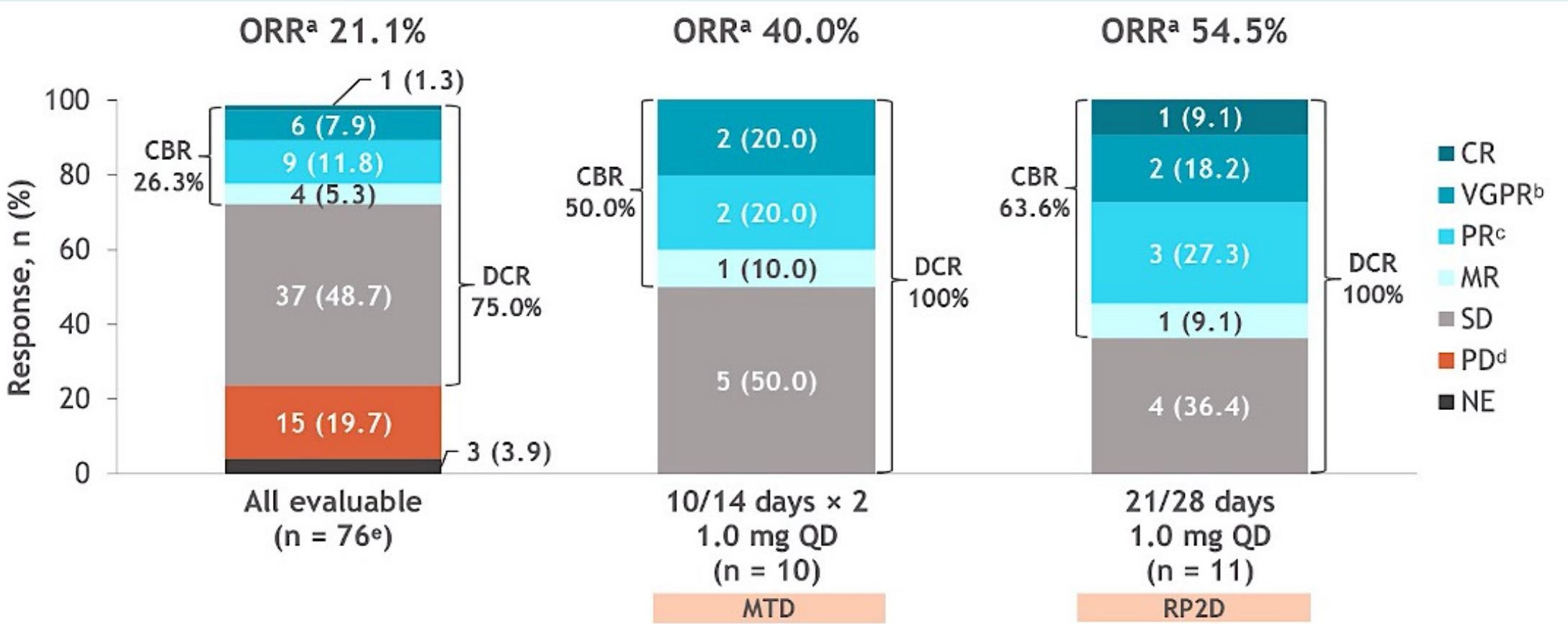
Lonial S et al. ASH 2021;Abstract 162.

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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