Recent Advances and Real-World Implications in Medical Oncology: A Daylong Multitumor Educational Symposium in Partnership with the North Carolina Oncology Association and the South Carolina Oncology Society

A CME/MOC- and NCPD-Accredited Event

Saturday, February 12, 2022
8:30 AM – 4:00 PM ET

RTP
RESEARCH
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Agenda

Module 1 — Chronic Lymphocytic Leukemia and Lymphomas: *Drs Flinn and LaCasce*

Module 2 — Multiple Myeloma: *Drs Callander and Rajkumar*

Module 3 — Genitourinary Cancers: *Drs Dreicer and Heath*

Module 4 — Breast Cancer: *Drs Borges and Jhaveri*

Module 5 — Gastrointestinal Cancers: *Drs Hochster and Messersmith*

Module 6 — Lung Cancer: *Drs Govindan and Johnson*

North Carolina
ONCOLOGY ASSOCIATION

Welcome
NCOA/SCOS Members!

Contributing General Medical Oncologists

Jennifer L Dallas, MD
Novant Health Cancer Institute
Charlotte, North Carolina

Joanna Metzner-Sadurski, MD
Self Regional Healthcare Cancer Center
Greenwood, South Carolina

Justin Peter Favaro, MD, PhD
Oncology Specialists of Charlotte
Charlotte, North Carolina

William R Mitchell, MD
Southern Oncology Specialists
Charlotte, North Carolina

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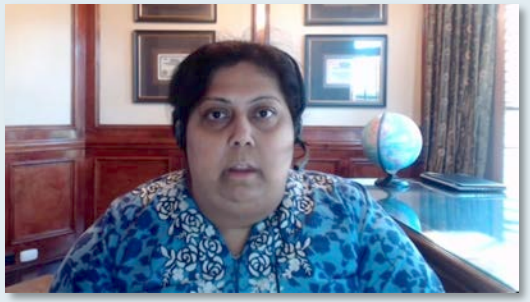
Contributing General Medical Oncologists



Niyati A Nathwani, MD
Carolina Blood and Cancer Care Associates
Charlotte, North Carolina

Nasfat Shehadeh, MD
Oncology Specialists of Charlotte, PA
Charlotte, North Carolina

Julia Saylors, MD
Charleston Oncology
North Charleston, South Carolina

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Chronic Lymphocytic Leukemia and Lymphomas Faculty

Ian W Flinn, MD, PhD
Director of Lymphoma Research Program
Sarah Cannon Research Institute
Tennessee Oncology
Nashville, Tennessee

Ann S LaCasce, MD, MMSc
Director, Dana-Farber/Mass General Brigham Fellowship in Hematology/Oncology
Associate Professor of Medicine, Harvard Medical School
Lymphoma Program
Dana-Farber Cancer Institute
Boston, Massachusetts

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Co-Moderators

MODULE 1
Justin Peter Favaro, MD, PhD
Oncology Specialists of Charlotte
Charlotte, North Carolina

MODULE 2
Suzanne R Fanning, DO
Prisma Health Cancer Institute
Greenville, South Carolina

MODULE 3
Justin Peter Favaro, MD, PhD
Oncology Specialists of Charlotte
Charlotte, North Carolina

MODULE 4
Emily Z Touloukian, DO
Coastal Cancer Center
Myrtle Beach, South Carolina

MODULE 5
Nasfat Shehadeh, MD
Oncology Specialists of Charlotte, PA
Charlotte, North Carolina

MODULE 6
Jimmy Ruiz, MD
Atrium Health Wake Forest Baptist
Comprehensive Cancer Center
Winston-Salem, North Carolina

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MODULE 1: Chronic Lymphocytic Leukemia and Lymphomas

Co-Moderator

Justin Peter Favaro, MD, PhD
Oncology Specialists of Charlotte
Charlotte, North Carolina

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Agenda

Module 1: Diffuse Large B-Cell Lymphoma (DLBCL)

Module 2: Chronic Lymphocytic Leukemia (CLL)

Module 3: Hodgkin Lymphoma

Module 4: Mantle Cell Lymphoma

Module 5: Follicular Lymphoma (FL)

Agenda

Module 1: Diffuse Large B-Cell Lymphoma (DLBCL)

Module 2: Chronic Lymphocytic Leukemia (CLL)

Module 3: Hodgkin Lymphoma

Module 4: Mantle Cell Lymphoma

Module 5: Follicular Lymphoma (FL)

N Engl J Med 2022;386(4):351-63

The NEW ENGLAND JOURNAL of MEDICINE

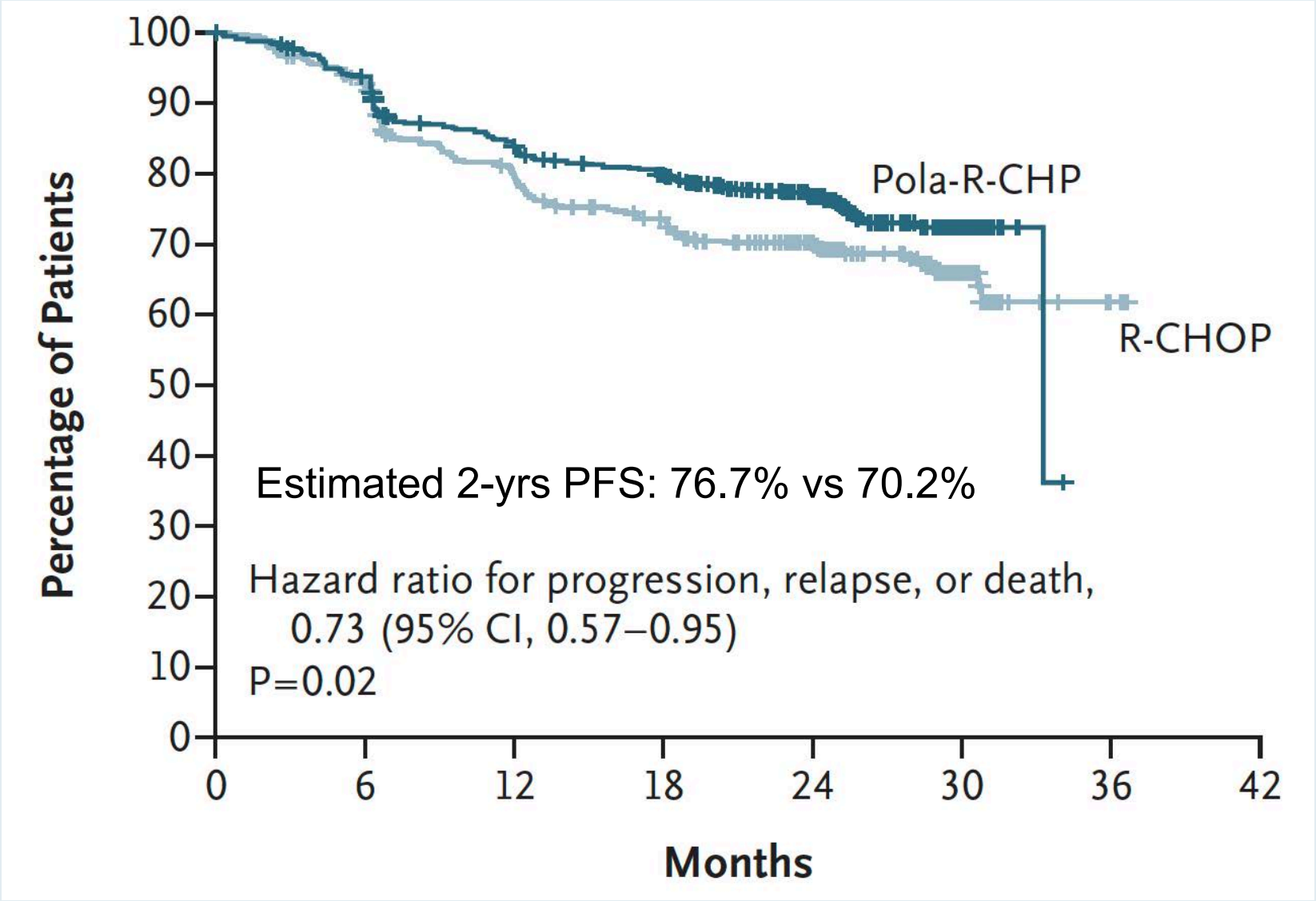
ORIGINAL ARTICLE

Polatuzumab Vedotin in Previously Untreated Diffuse Large B-Cell Lymphoma

H. Tilly, F. Morschhauser, L.H. Sehn, J.W. Friedberg, M. Trněný, J.P. Sharman, C. Herbaux, J.M. Burke, M. Matasar, S. Rai, K. Izutsu, N. Mehta-Shah, L. Oberic, A. Chauchet, W. Jurczak, Y. Song, R. Greil, L. Mykhalska, J.M. Bergua-Burgués, M.C. Cheung, A. Pinto, H.-J. Shin, G. Hapgood, E. Munhoz, P. Abrisqueta, J.-P. Gau, J. Hirata, Y. Jiang, M. Yan, C. Lee, C.R. Flowers, and G. Salles

Tilly H et al. ASH 2021;LBA-1

POLARIX: Investigator-Assessed Progression-Free Survival (Primary Endpoint)



Tilly H et al. *N Engl J Med* 2022;386(4):351-63.

original reports

Polatuzumab Vedotin in Relapsed or Refractory Diffuse Large B-Cell Lymphoma

Laurie H. Sehn, MD, MPH[1]; Alex F. Herrera, MD[2]; Christopher R. Flowers, MD, MSc[3]; Manali K. Kamdar, MD, MBBS[4]; Andrew McMillan, PhD[5]; Mark Hertzberg, MBBS, PhD[6]; Sarit Assouline, MDCM, MSc[7]; Tae Min Kim, MD[8]; Won Seog Kim, MD, PhD[9]; Muhit Ozcan, MD[10]; Jamie Hirata, PharmD[11]; Elicia Penuel, PhD[11]; Joseph N. Paulson, PhD[11]; Ji Cheng, PhD[12]; Grace Ku, MD[11]; and Matthew J. Matasar, MD[13]

J Clin Oncol 2020;38(2):155-65.

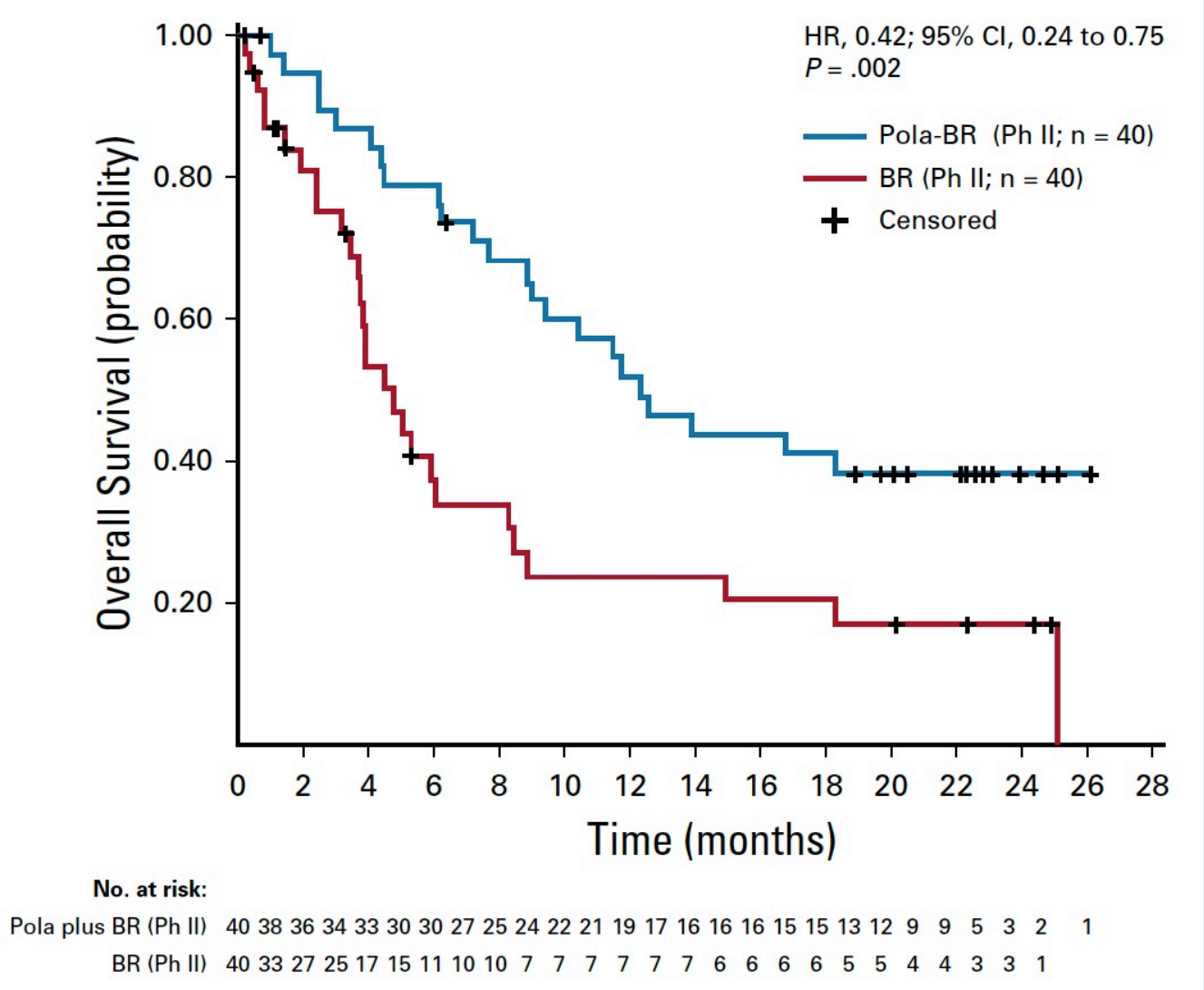
RTP RESEARCH TO PRACTICE

Polatuzumab Vedotin with Bendamustine/Rituximab (BR) for Transplant-Ineligible R/R DLBCL: End-of-Treatment Complete Response Rate

Outcome	Phase II Randomized	
	Pola-BR (n = 40)	BR (n = 40)
End of treatment		
IRC, objective response	18 (45.0)	7 (17.5)
Complete response	16 (40.0)	7 (17.5)
Partial response	2 (5.0)	0
Stable disease	6 (15.0)	1 (2.5)
Progressive disease	8 (20.0)	10 (25.0)
Missing or unevaluable†	8 (20.0)	22 (55.0)

Sehn LH et al. *J Clin Oncol* 2020;38(2):155-65.

Polatuzumab Vedotin with BR for Transplant-Ineligible R/R DLBCL: Overall Survival



Sehn LH et al. *J Clin Oncol* 2020;38(2):155-65.

ZUMA-12 Study Demonstrates 78% Complete Response Rate as Part of First-Line Treatment in Newly Diagnosed High-Risk Large B-Cell Lymphoma

December 13, 2021

"Primary results were announced from ZUMA-12, a global, multicenter, single-arm, open-label Phase 2 study evaluating axicabtagene ciloleucel as part of first-line treatment in patients with high-risk large B-cell lymphoma (LBCL). This is the first study to evaluate CAR T-cell therapy as part of first-line therapy in high-risk LBCL. The study is based on the desire to utilize potential curative treatment as quickly as possible and the hypothesis that earlier use of CAR T-cell therapy when T cells are healthier may produce better outcomes. The data were presented in an oral session during the 63rd American Society of Hematology (ASH) Annual Meeting & Exposition (Abstract #739).

After a single infusion of axicabtagene ciloleucel, 89% of evaluable patients achieved a response (ORR) (n=37 evaluable for efficacy), including 78% of patients with a complete response (CR) at a median follow-up of 15.9 months. CR rate was consistent among key subgroups. Among evaluable patients, median time to response was one month. At time of data cut-off, 73% of evaluable patients had ongoing responses. Medians for duration of response (DOR), event-free survival (EFS), and progression-free survival (PFS) were not yet reached, with 12-month estimates of 81%, 73%, and 75%, respectively, and an estimated 12-month OS rate of 91%."

https://www.gilead.com/news-and-press/press-room/press-releases/2021/12/yescarta-zuma12-study-demonstrates-78-complete-response-rate-as-part-of-firstline-treatment-in-newly-diagnosed-highrisk-large-bcell-lymphoma

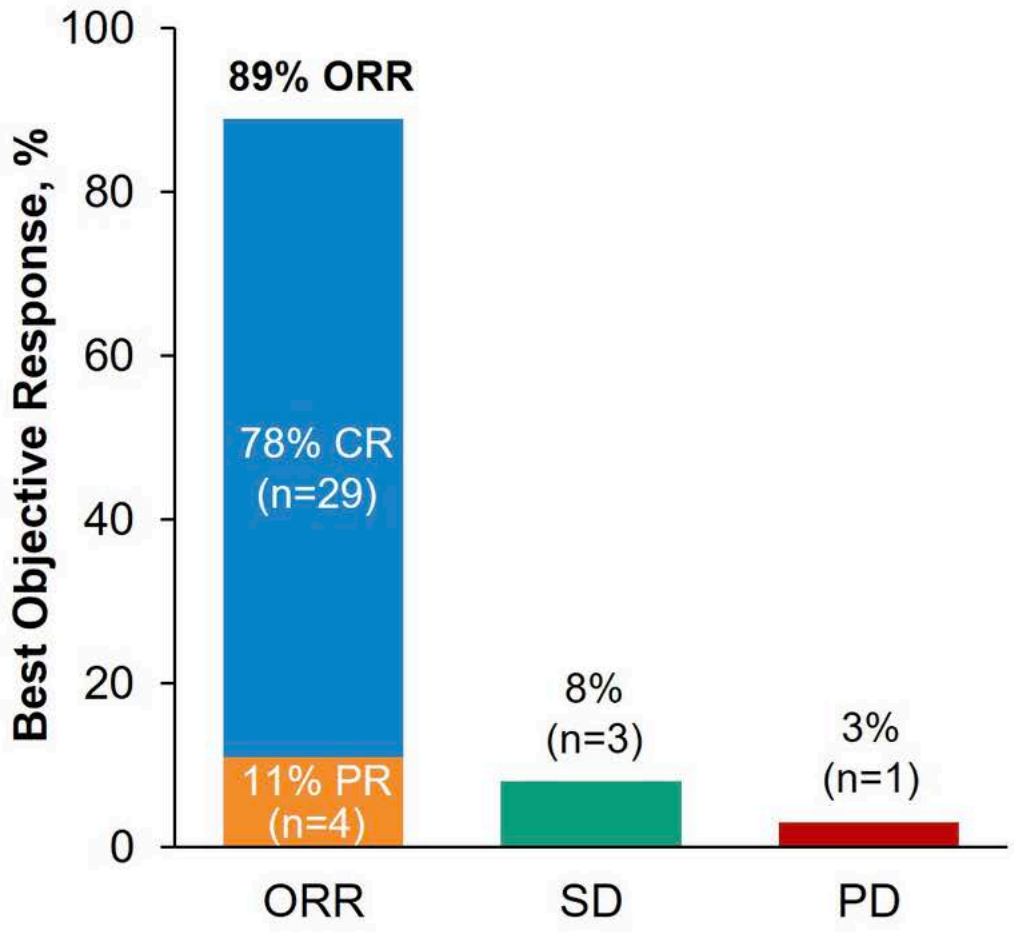
RTP RESEARCH TO PRACTICE

Primary Analysis of ZUMA-12: A Phase 2 Study of Axicabtagene Ciloleucel (Axi-Cel) as First-Line Therapy in Patients with High-Risk Large B-Cell Lymphoma (LBCL)

Neelapu SS et al.

ASH 2021;Abstract 739.

Primary Analysis of ZUMA-12: A Phase II Study of Axicabtagene Ciloleucel as First-Line Therapy for High-Risk Large B-Cell Lymphoma



	Response Evaluable (N=37)
Median follow-up (range), months	15.9 (6.0–26.7)
Patients with ≥12-month follow-up, n (%)	23 (62)
Patients with ongoing response as of data cutoff, n (%)	27 (73)
Median time to response (range), months	
Initial objective response	1.0 (0.9–6.8)
CR	1.0 (0.9–6.8)
Patients converted from PR/SD to CR, n (%)	7 (19)
PR to CR	6 (16)
SD to CR	1 (3)

Neelapu SS et al. ASH 2021;Abstract 739.

FDA Approves Lisocabtagene Maraleucel for R/R Large B-Cell Lymphoma

Press Release – February 5, 2021

"The Food and Drug Administration approved lisocabtagene maraleucel for the treatment of adult patients with relapsed or refractory (R/R) large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (including DLBCL arising from indolent lymphoma), high-grade B-cell lymphoma, primary mediastinal large B-cell lymphoma, and follicular lymphoma grade 3B.

Lisocabtagene maraleucel is a CD19-directed chimeric antigen receptor (CAR) T cell immunotherapy. It consists of autologous T cells that are genetically modified to produce a CAR protein, allowing the T cells to identify and eliminate CD19-expressing normal and malignant cells.

Efficacy was evaluated in TRANSCEND (NCT02631044), a single-arm, open label, multicenter trial that evaluated lisocabtagene maraleucel, preceded by lymphodepleting chemotherapy, in adults with R/R large B-cell lymphoma after at least two lines of therapy."

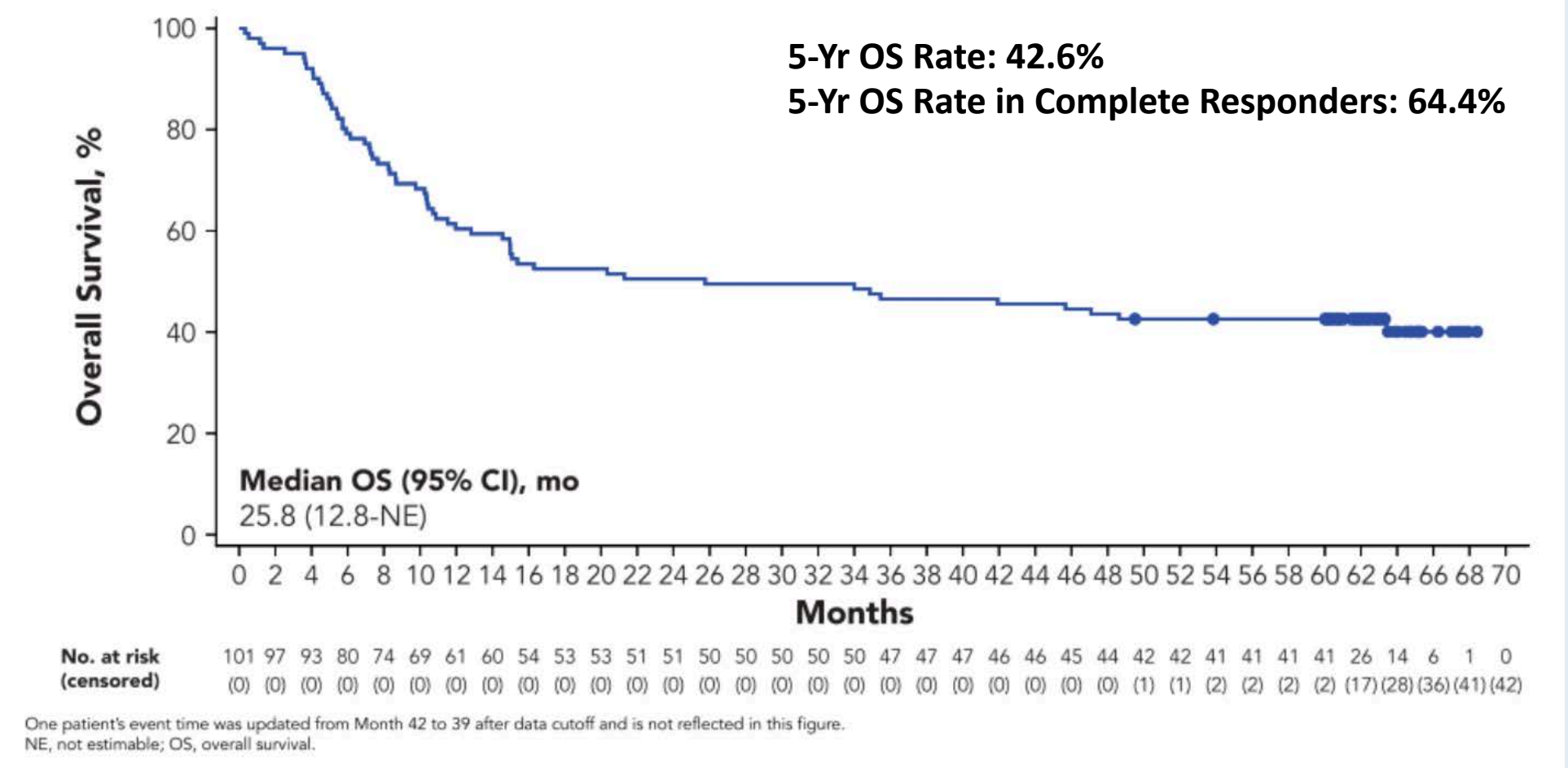
https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-lisocabtagene-maraleucel-relapsed-or-refractory-large-b-cell-lymphoma

Long-Term (4- and 5-Year) Overall Survival in ZUMA-1, the Pivotal Study of Axicabtagene Ciloleucel (Axi-Cel) in Patients with Refractory Large B-Cell Lymphoma (LBCL)

Jacobson C et al.

ASH 2021;Abstract 1764.

ZUMA-1: Five-Year Update



One patient's event time was updated from Month 42 to 39 after data cutoff and is not reflected in this figure.
NE, not estimable; OS, overall survival.

- Median time to next cancer therapy: 8.7 months
- Safety findings were similar to those in previous reports

Jacobson C et al. ASH 2021;Abstract 1764.

RTP RESEARCH TO PRACTICE

N Engl J Med 2021;[Online ahead of print].

The NEW ENGLAND JOURNAL of MEDICINE

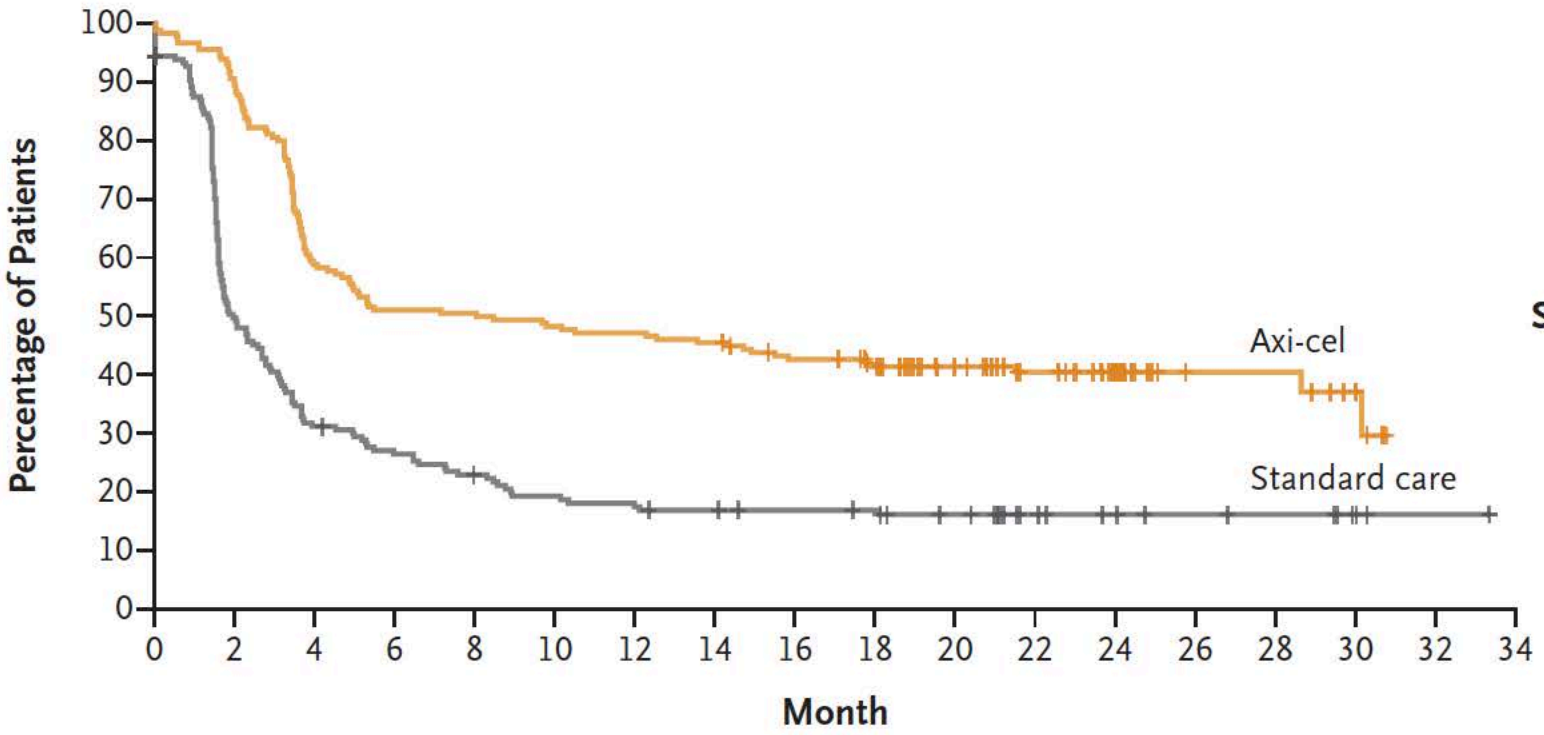
ORIGINAL ARTICLE

Axicabtagene Ciloleucel as Second-Line Therapy for Large B-Cell Lymphoma

F.L. Locke, D.B. Miklos, C.A. Jacobson, M.-A. Perales, M.-J. Kersten, O.O. Oluwole, A. Ghobadi, A.P. Rapoport, J. McGuirk, J.M. Pagel, J. Muñoz, U. Farooq, T. van Meerten, P.M. Reagan, A. Sureda, I.W. Flinn, P. Vandenberghe, K.W. Song, M. Dickinson, M.C. Minnema, P.A. Riedell, L.A. Leslie, S. Chaganti, Y. Yang, S. Filosto, J. Shah, M. Schupp, C. To, P. Cheng, L.I. Gordon, and J.R. Westin, for All ZUMA-7 Investigators and Contributing Kite Members*

Locke FL et al. ASH 2021;Abstract 2.

ZUMA-7: Event-Free Survival



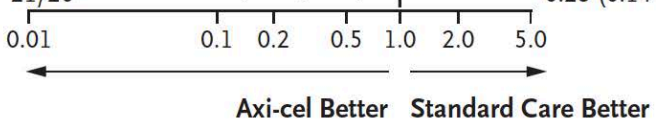
	No. of Patients	Median Event-free Survival (95% CI)
		mo
Axi-cel	180	8.3 (4.5–15.8)
Standard Care	179	2.0 (1.6–2.8)

Stratified hazard ratio for event or death, 0.40 (95% CI, 0.31–0.51)
P<0.001

Locke FL et al. *N Engl J Med* 2021;[Online ahead of print].

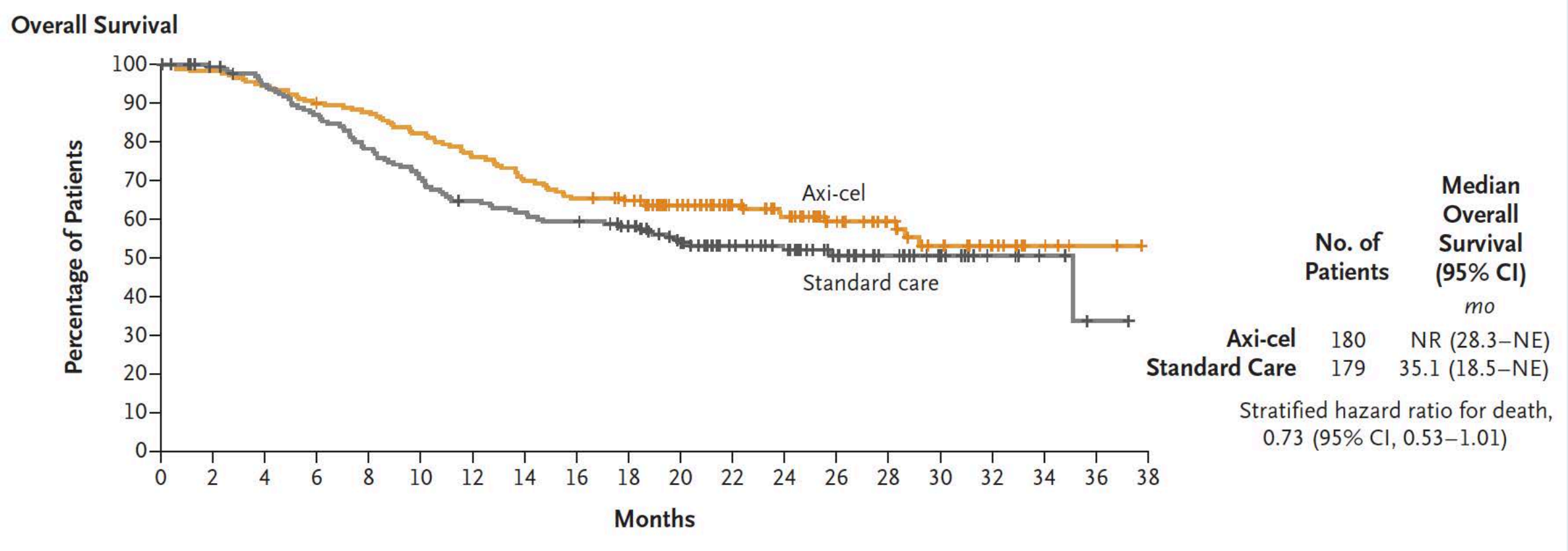
ZUMA-7: Event-Free Survival Subgroup Analysis

Subgroup	Axi-cel	Standard Care	Hazard Ratio for Event or Death (95% CI)
	no. of patients with event/total no.		
Overall	108/180	144/179	0.40 (0.31–0.51)
Age			
<65 yr	81/129	96/121	0.49 (0.36–0.67)
≥65 yr	27/51	48/58	0.28 (0.16–0.46)
Response to first-line therapy at randomization			
Primary refractory disease	85/133	106/131	0.43 (0.32–0.57)
Relapse ≤12 mo after initiation or completion of first-line therapy	23/47	38/48	0.34 (0.20–0.58)
Second-line age-adjusted IPI			
0 or 1	54/98	73/100	0.41 (0.28–0.58)
2 or 3	54/82	71/79	0.39 (0.27–0.56)
Prognostic marker according to central laboratory			
HGBL, double- or triple-hit	15/31	21/25	0.28 (0.14–0.59)
Double-expressor lymphoma	35/57	50/62	0.42 (0.27–0.67)
Molecular subgroup according to central laboratory			
Germinal center B-cell–like	64/109	80/99	0.41 (0.29–0.57)
Activated B-cell–like	11/16	9/9	0.18 (0.05–0.72)
Unclassified	8/17	12/14	—
Disease type according to investigator			
DLBCL, not otherwise specified	68/110	97/116	0.37 (0.27–0.52)
Large-cell transformation from follicular lymphoma	10/19	24/27	0.35 (0.16–0.77)
HGBL, including rearrangement of *MYC* with *BCL2* or *BCL6* or both	23/43	18/27	0.47 (0.24–0.90)
Disease type according to central laboratory			
DLBCL	79/126	95/120	0.44 (0.32–0.60)
HGBL, including rearrangement of *MYC* with *BCL2* or *BCL6* or both	15/31	21/26	0.28 (0.14–0.59)



Tilly H et al. *N Engl J Med* 2021;[Online ahead of print].

ZUMA-7: Overall Survival



Tilly H et al. *N Engl J Med* 2021;[Online ahead of print].

N Engl J Med 2021;[Online ahead of print].

The NEW ENGLAND JOURNAL of MEDICINE

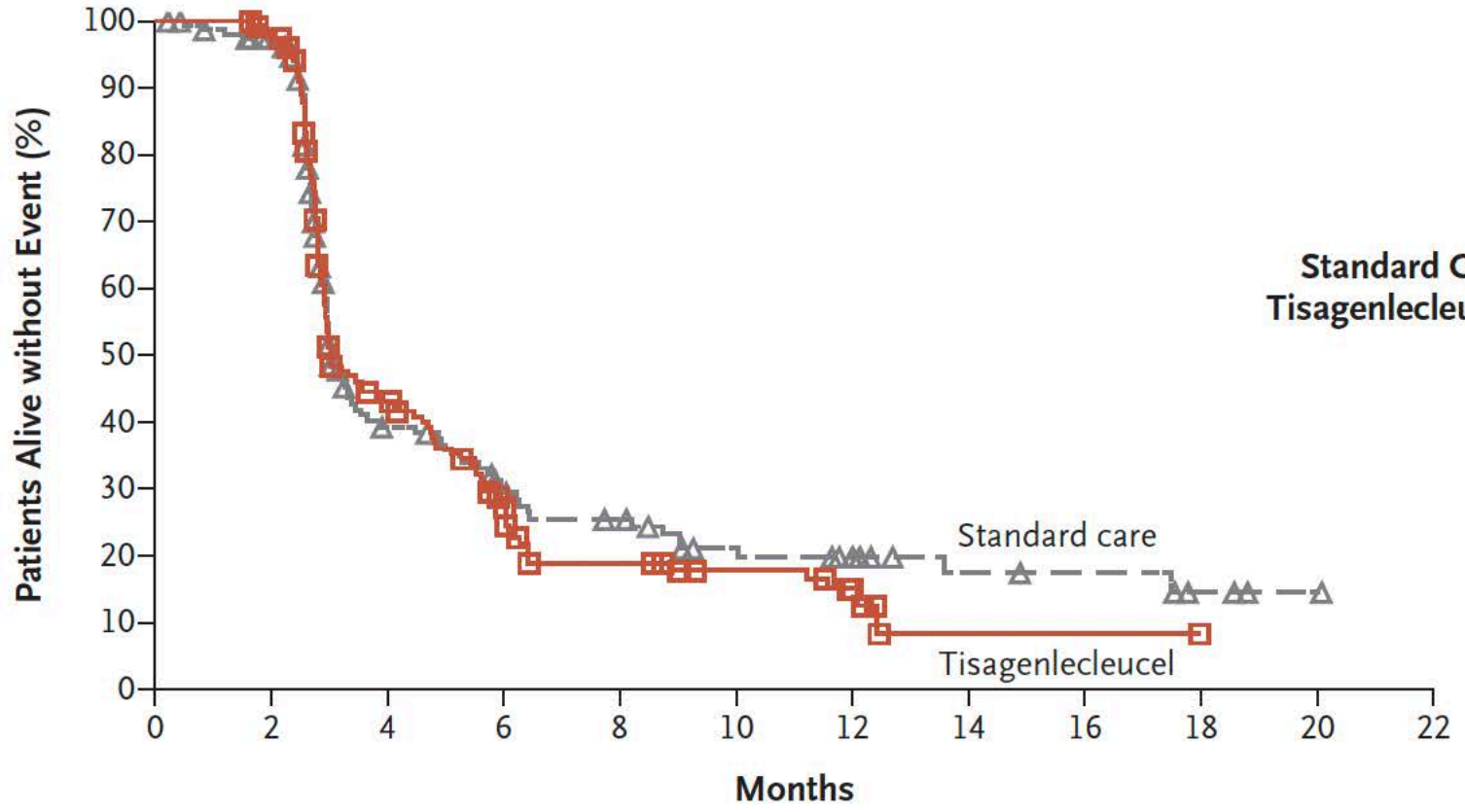
ORIGINAL ARTICLE

Second-Line Tisagenlecleucel or Standard Care in Aggressive B-Cell Lymphoma

M.R. Bishop, M. Dickinson, D. Purtill, P. Barba, A. Santoro, N. Hamad, K. Kato, A. Sureda, R. Greil, C. Thieblemont, F. Morschhauser, M. Janz, I. Flinn, W. Rabitsch, Y.-L. Kwong, M.J. Kersten, M.C. Minnema, H. Holte, E.H.L. Chan, J. Martinez-Lopez, A.M.S. Müller, R.T. Maziarz, J.P. McGuirk, E. Bachy, S. Le Gouill, M. Dreyling, H. Harigae, D. Bond, C. Andreadis, P. McSweeney, M. Kharfan-Dabaja, S. Newsome, E. Degtyarev, R. Awasthi, C. del Corral, G. Andreola, A. Masood, S.J. Schuster, U. Jäger, P. Borchmann, and J.R. Westin

Bishop MR et al. ASH 2021;Abstract LBA-6.

BELINDA: Event-Free Survival (Primary Endpoint)



	No. of Patients	No. of Events	Median Event-free Survival (95% CI)
			mo
Standard Care	160	104	3.0 (3.0–3.5)
Tisagenlecleucel	162	117	3.0 (2.9–4.2)

Hazard ratio for event or death (tisagenlecleucel vs. standard care), 1.07 (95% CI, 0.82–1.40)
P=0.61

No. at Risk

Standard care	160	148	45	31	25	17	12	7	6	3	1	0
Tisagenlecleucel	162	156	57	32	19	13	6	1	1	0	0	0

Bishop MR et al. *N Engl J Med* 2021;[Epub ahead of print].

RTP RESEARCH TO PRACTICE

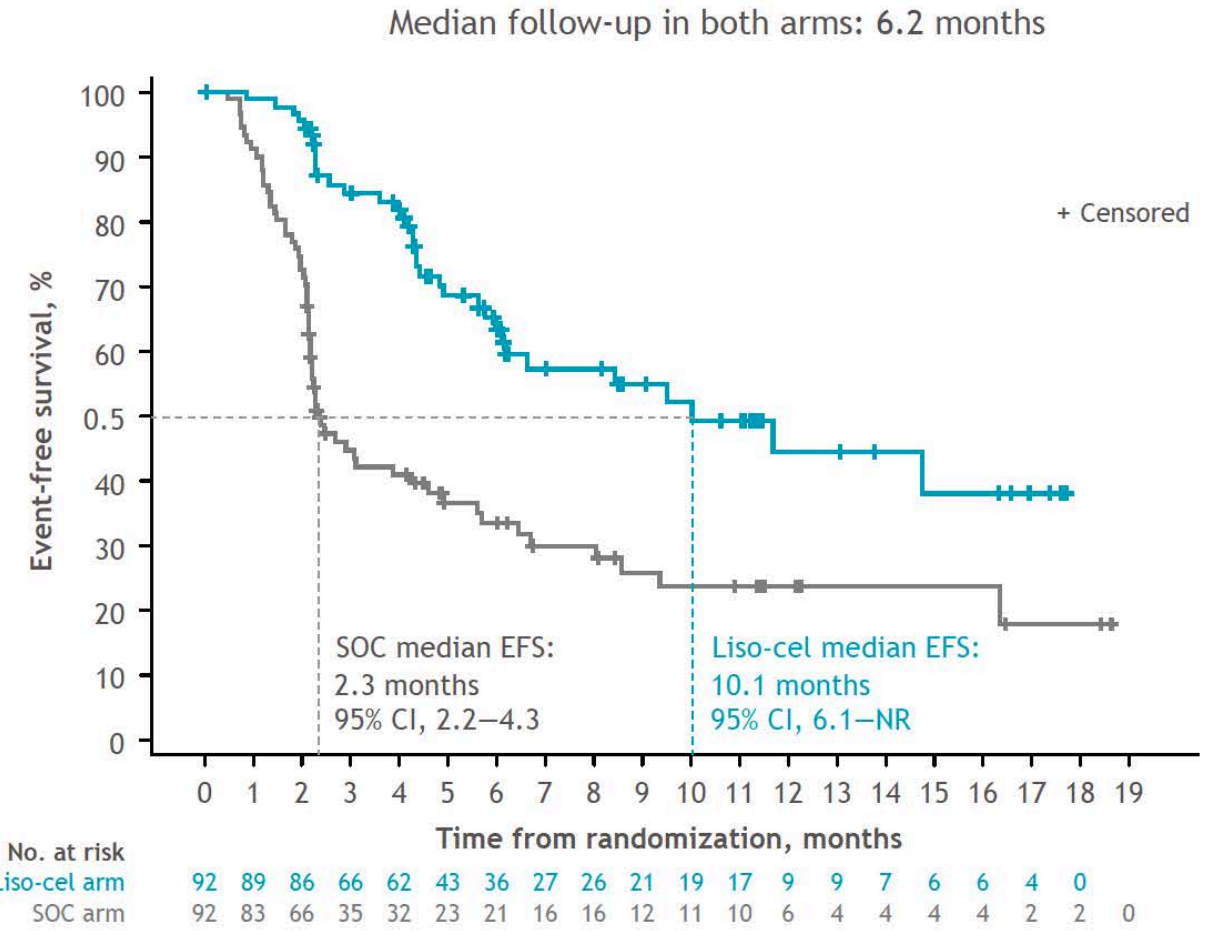
Lisocabtagene Maraleucel, a CD19-Directed Chimeric Antigen Receptor T Cell Therapy, Versus Standard of Care with Salvage Chemotherapy Followed by Autologous Stem Cell Transplantation as Second-Line Treatment in Patients with Relapsed or Refractory Large B-Cell Lymphoma: Results from the Randomized Phase 3 TRANSFORM Study

Manali Kamdar,[1] Scott R. Solomon,[2] Jon Arnason,[3] Patrick B. Johnston,[4] Bertram Glass,[5] Veronika Bachanova,[6] Sami Ibrahimi,[7] Stephan Mielke,[8] Pim Mutsaers,[9] Francisco Hernandez-Ilizaliturri,[10] Koji Izutsu,[11] Franck Morschhauser,[12] Matthew Lunning,[13] David G. Maloney,[14] Alessandro Crotta,[15] Sandrine Montheard,[15] Alessandro Previtali,[15] Lara Stepan,[16] Ken Ogasawara,[16] Timothy Mack,[16] Jeremy S. Abramson[17]

[1]University of Colorado Cancer Center, Aurora, CO, USA; [2]Northside Hospital Cancer Institute, Atlanta, GA, USA; [3]Beth Israel Deaconess Medical Center, Boston, MA, USA; [4]Mayo Clinic, Rochester, MN, USA; [5]Helios Klinikum Berlin-Buch, Berlin, Germany; [6]University of Minnesota, Minneapolis, MN, USA; [7]University of Oklahoma Stephenson Cancer Center, Oklahoma City, OK, USA; [8]Center of Allogeneic Stem Cell Transplantation and Cellular Therapy (CAST), Karolinska Institutet and University Hospital, Stockholm, Sweden; [9]Erasmus University Medical Center, Rotterdam, The Netherlands, on behalf of HOVON/LLPC; [10]Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA; [11]National Cancer Center Hospital, Tokyo, Japan; [12]Université de Lille, Centre Hospitalier Universitaire de Lille. ULR 7365, GRITA - Groupe de Recherche sur les formes Injectables et les Technologies Associées, Lille, France; [13]University of Nebraska Medical Center, Omaha, NE, USA; [14]Fred Hutchinson Cancer Research Center, Seattle, WA, USA; [15]Celgene, a Bristol-Myers Squibb Company, Boudry, Switzerland; [16]Bristol Myers Squibb, Princeton, NJ, USA; [17]Massachusetts General Hospital Cancer Center, Boston, MA, USA

ASH 2021, Presentation Number 91

TRANSFORM: Event-Free Survival per Independent Review Committee (ITT, Primary Endpoint)



	Liso-cel arm (n = 92)	SOC arm (n = 92)
Patients with events, n	35	63
Stratified HR (95% CI)	0.349 (0.229–0.530)	
	P < 0.0001	
6-month EFS rate, % (SE)	63.3 (5.77)	33.4 (5.30)
Two-sided 95% CI	52.0–74.7	23.0–43.8
12-month EFS rate, % (SE)	44.5 (7.72)	23.7 (5.28)
Two-sided 95% CI	29.4–59.6	13.4–34.1

One-sided *P* value significance threshold to reject the null hypothesis was < 0.012

Kamdar M et al. ASH 2021;Abstract 91.

FDA Grants Accelerated Approval to Loncastuximab Tesirine-lpyl for Large B-Cell Lymphoma

Press Release – April 23, 2021

"The Food and Drug Administration granted accelerated approval to loncastuximab tesirine-lpyl, a CD19-directed antibody and alkylating agent conjugate, for adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, DLBCL arising from low grade lymphoma, and high-grade B-cell lymphoma.

Approval was based on LOTIS-2 (NCT03589469), an open-label, single-arm trial in 145 adult patients with relapsed or refractory DLBCL or high-grade B-cell lymphoma after at least two prior systemic regimens. Patients received loncastuximab tesirine-lpyl 0.15 mg/kg every 3 weeks for 2 cycles, then 0.075 mg/kg every 3 weeks for subsequent cycles. Patients received treatment until progressive disease or unacceptable toxicity."

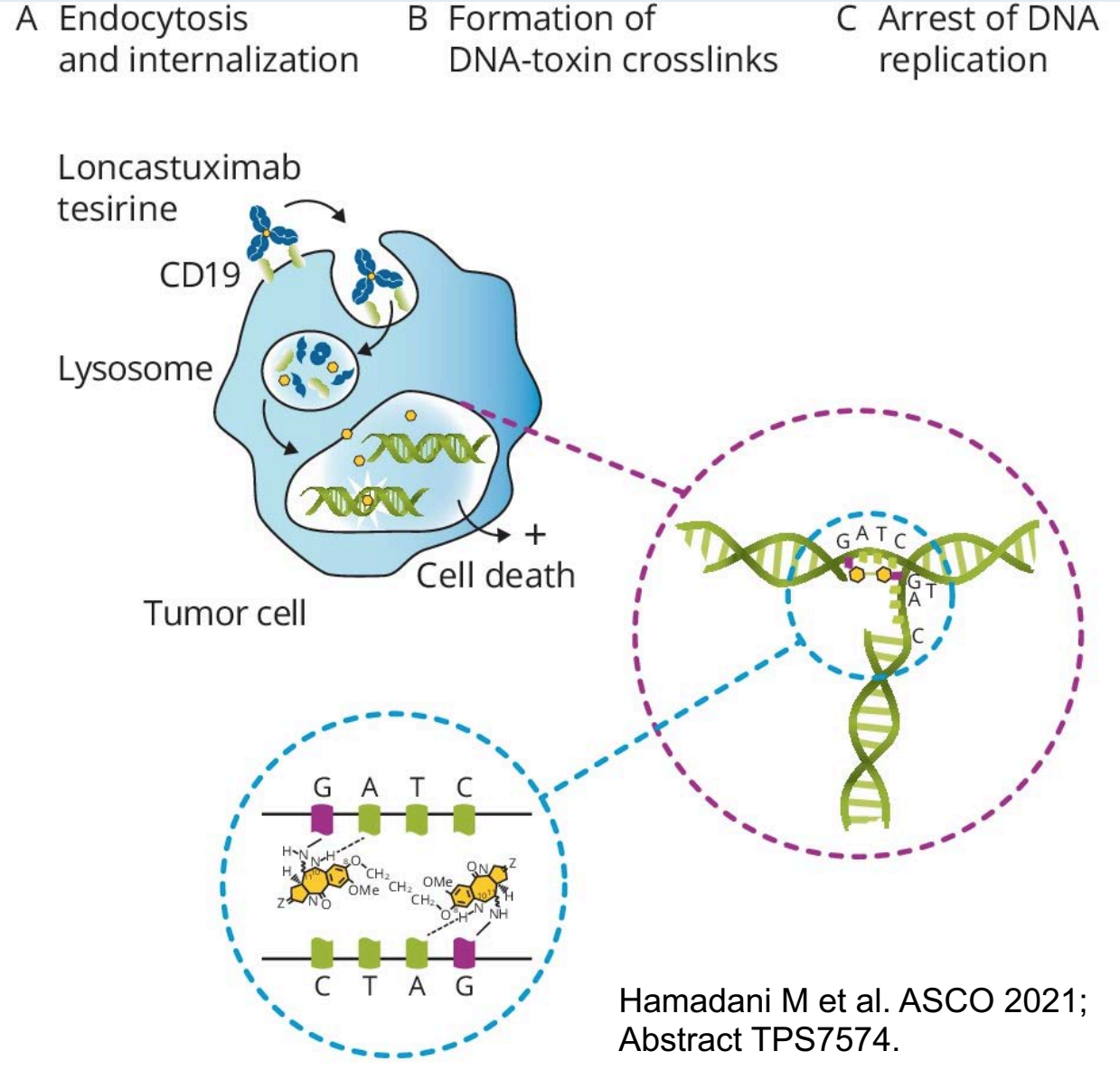
www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-loncastuximab-tesirine-lpyl-large-b-cell-lymphoma

Lancet Oncol 2021;22(6):790-800

Loncastuximab tesirine in relapsed or refractory diffuse large B-cell lymphoma (LOTIS-2): a multicentre, open-label, single-arm, phase 2 trial

Paolo F Caimi, Weiyun Ai, Juan Pablo Alderuccio, Kirit M Ardeshna, Mehdi Hamadani, Brian Hess, Brad S Kahl, John Radford, Melhem Solh, Anastasios Stathis, Pier Luigi Zinzani, Karin Havenith, Jay Feingold, Shui He, Yajuan Qin, David Ungar, Xiaoyan Zhang, Carmelo Carlo-Stella

Mechanism of Action of Loncastuximab Tesirine



Hamadani M et al. ASCO 2021; Abstract TPS7574.

LOTIS-2: Response and Survival with Loncastuximab Tesirine for R/R DLBCL

Response	As-treated population (N = 145)
Overall response rate	70/145 (48.3%)
Complete response rate	35/145 (24.1%)
Complete response	35 (24%)
Partial response	35 (24%)
Stable disease	22 (15%)
Progressive disease	30 (21%)
Not evaluable	23 (16%)
Survival	**As-treated population (N = 145)**
Median progression-free survival	4.9 months
Median overall survival	9.9 months

Caimi PF et al. *Lancet Oncol* 2021;22(6):790-800.

LOTIS-2: Common Treatment-Emergent AEs

Treatment-Emergent AEs	Grade 1-2	Grade 3-4
Anemia	16%	10%
Thrombocytopenia	15%	18%
Neutropenia	14%	26%
Leukopenia	6%	9%

Caimi PF et al. *Lancet Oncol* 2021;22(6):790-800.

RTP RESEARCH TO PRACTICE

Lancet Oncol 2020;21(7):978-88

Tafasitamab plus lenalidomide in relapsed or refractory diffuse large B-cell lymphoma (L-MIND): a multicentre, prospective, single-arm, phase 2 study

Gilles Salles, Johannes Duell*, Eva González Barca, Olivier Tournilhac, Wojciech Jurczak, Anna Marina Liberati, Zsolt Nagy, Aleš Obr, Gianluca Gaidano, Marc André, Nagesh Kalakonda, Martin Dreyling, Johannes Weirather, Maren Dirnberger-Hertweck, Sumeet Ambarkhane, Günter Fingerle-Rowson, Kami Maddocks*

L-MIND: Best Objective Response According to Independent Radiology Committee or Clinical Review Committee

	Patients treated with tafasitamab plus lenalidomide (n=80)*
Best objective response	
Complete response	34 (43%; 32–54)
Partial response	14 (18%; 10–28)
Stable disease	11 (14%; 7–23)
Progressive disease	13 (16%; 9–26)
Not evaluable†	8 (10%; 4–19)
PET-confirmed complete response	30/34 (88%; 73–97)
Objective response‡	48 (60%; 48–71)
Disease control§	59 (74%; 63–83)

Data are n (%; 95% CI) or n/N (%). *One patient received tafasitamab only. †Patients had no valid postbaseline response assessments. ‡Complete response plus partial response. §Complete response plus partial response plus stable disease.

Salles G et al. *Lancet Oncol* 2020;21(7):978-88.

RTP RESEARCH TO PRACTICE

Agenda

Module 1: Diffuse Large B-Cell Lymphoma (DLBCL)

Module 2: Chronic Lymphocytic Leukemia (CLL)

Module 3: Hodgkin Lymphoma

Module 4: Mantle Cell Lymphoma

Module 5: Follicular Lymphoma (FL)

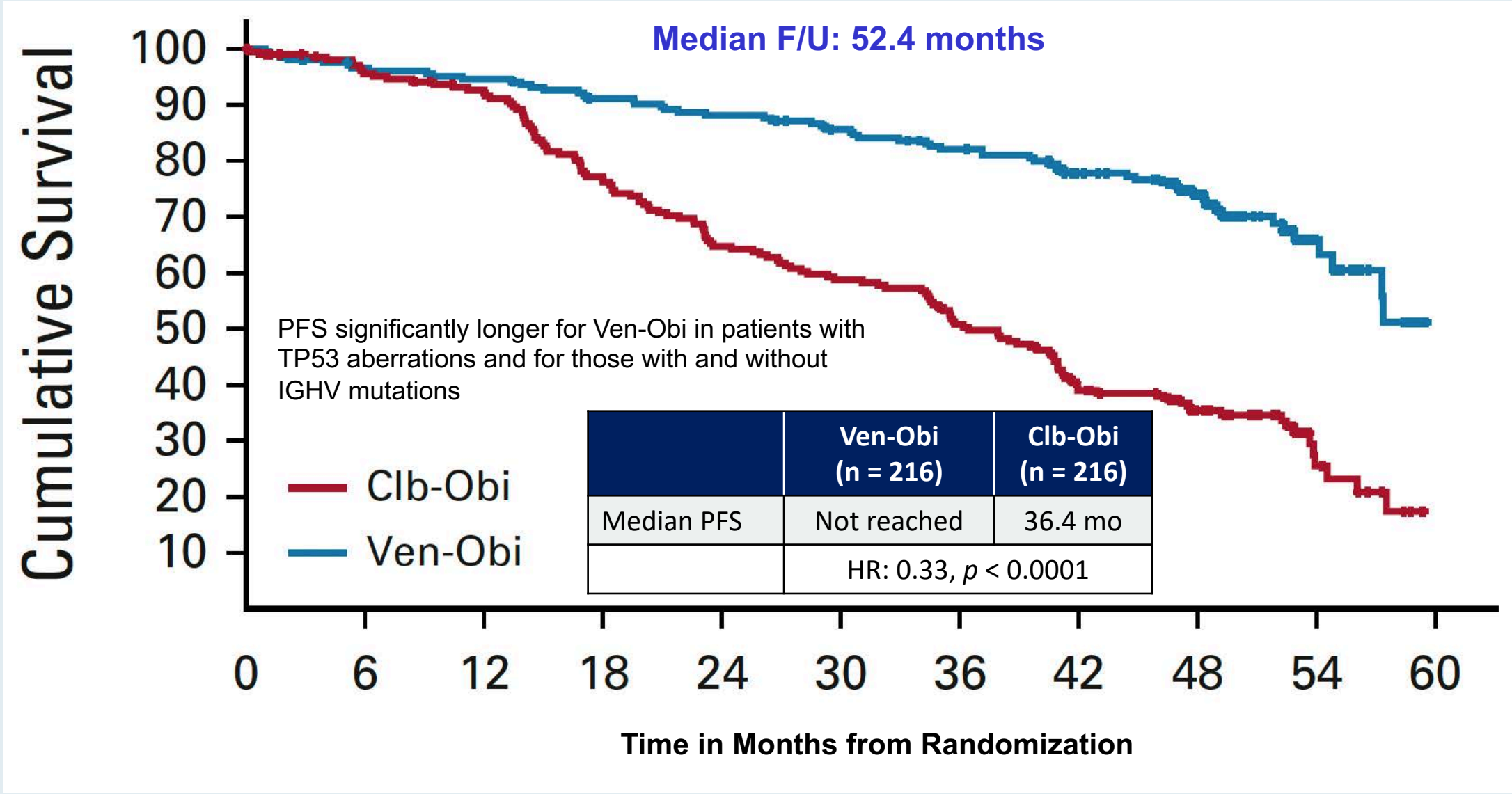
original reports

Minimal Residual Disease Dynamics after Venetoclax-Obinutuzumab Treatment: Extended Off-Treatment Follow-up From the Randomized CLL14 Study

Othman Al-Sawaf, MD[1,2,3]; Can Zhang, PhD[1]; Tong Lu, PhD[4]; Michael Z. Liao, PhD[4]; Anesh Panchal, MSc[5]; Sandra Robrecht, PhD[1]; Travers Ching, PhD[6]; Maneesh Tandon, MBChB[5]; Anna-Maria Fink, MD[1]; Eugen Tausch, MD[7]; Christof Schneider, MD[7]; Matthias Ritgen, MD[8]; Sebastian Böttcher, MD[9]; Karl-Anton Kreuzer, MD[1]; Brenda Chyla, PhD[10]; Dale Miles, PhD[4]; Clemens-Martin Wendtner, MD[11]; Barbara Eichhorst, MD[1]; Stephan Stilgenbauer, MD[7,12]; Yanwen Jiang, PhD[4]; Michael Hallek, MD[1]; and Kirsten Fischer, MD[1]

J Clin Oncol 2021;39(36):4049-60

CLL14 Update: Progression-Free Survival

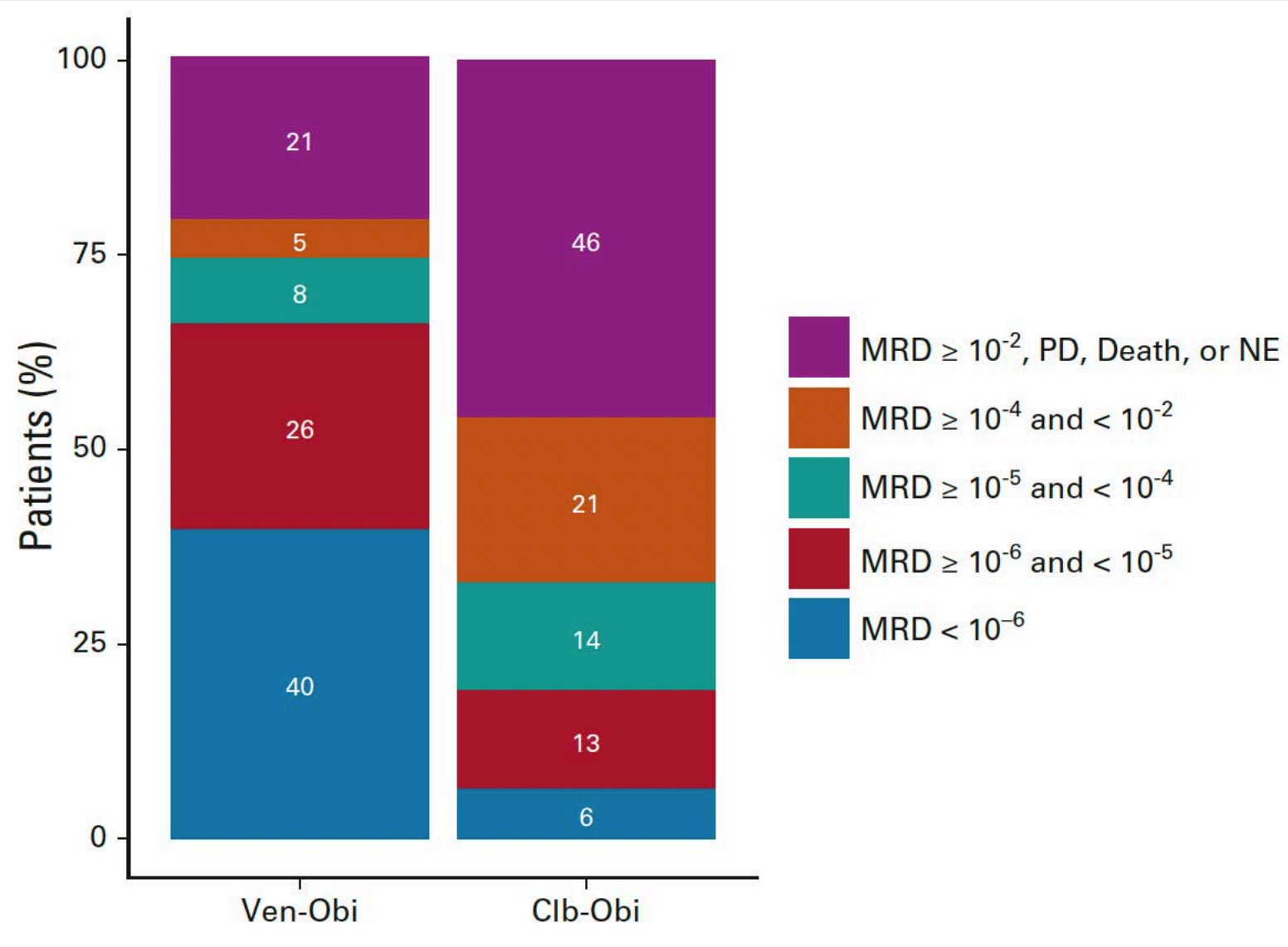


	Ven-Obi (n = 216)	Clb-Obi (n = 216)
Median PFS	Not reached	36.4 mo
	HR: 0.33, $p < 0.0001$	

Al-Sawaf O et al. *J Clin Oncol* 2021;39(36):4049-60.

RTP RESEARCH TO PRACTICE

CLL14 Update: Minimum Residual Disease (MRD) Status by Next-Generation Sequencing 2 Months After Completion of Treatment



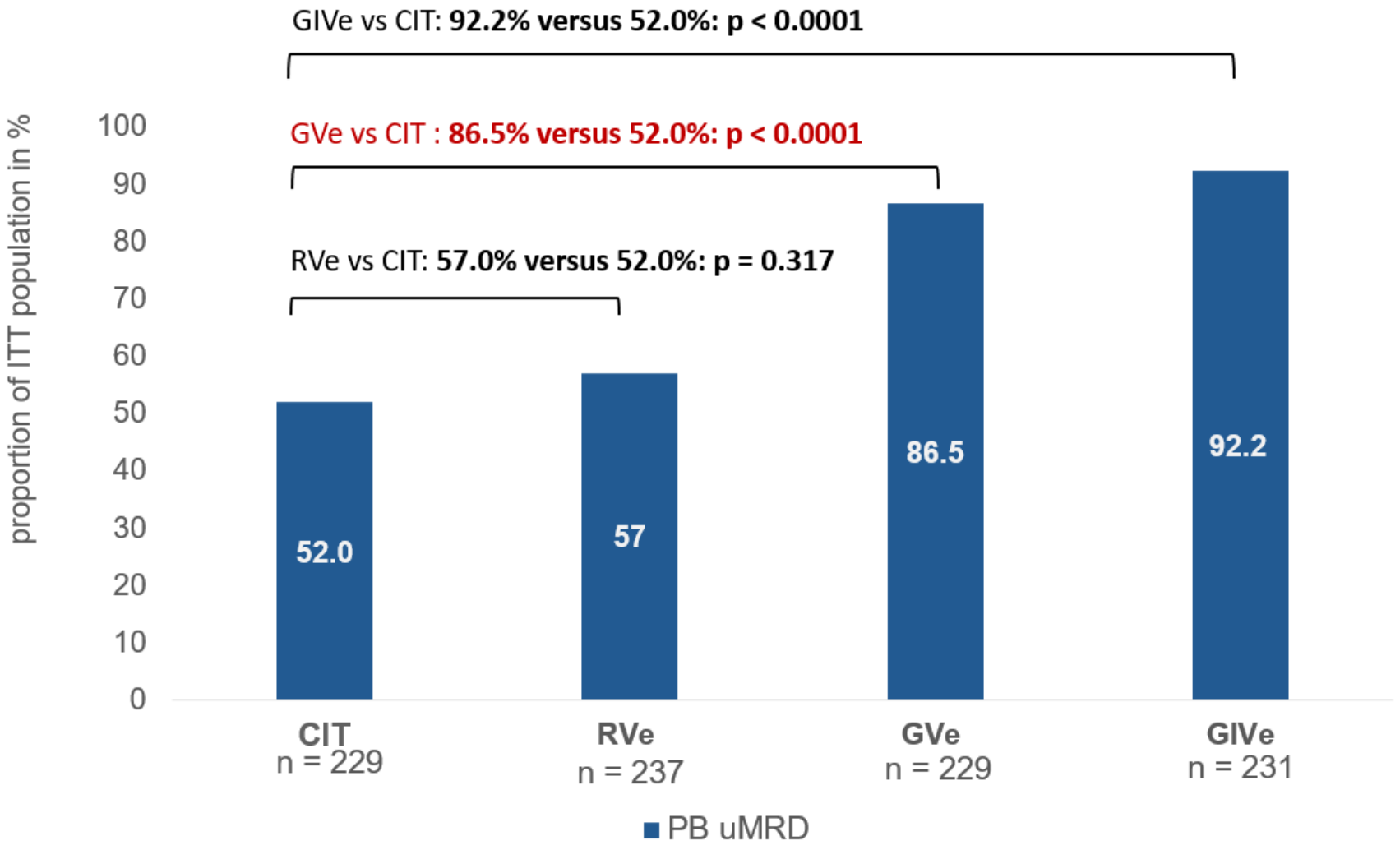
Al-Sawaf O et al. *J Clin Oncol* 2021;39(36):4049-60.

A Randomized Phase III Study of Venetoclax-Based Time-Limited Combination Treatments (RVe, GVe, GIVe) vs Standard Chemoimmunotherapy (CIT: FCR/BR) in Frontline Chronic Lymphocytic Leukemia (CLL) of Fit Patients: First Co-Primary Endpoint Analysis of the International Intergroup GAIA (CLL13) Trial

Eichhorst B et al.

ASH 2021;Abstract 71.

GAIA/CLL13 Coprimary Endpoint: Undetectable MRD (uMRD) ($<10^{-4}$) at Month 15 in Peripheral Blood by 4-Color Flow



CIT
- BR >65
- ≤FCR 65

RVe
Rituximab/venetoclax

GVe
Obinutuzumab/venetoclax

GIVe
Obinutuzumab/ibrutinib/venetoclax

Eichhorst B et al. ASH 2021;Abstract 71.

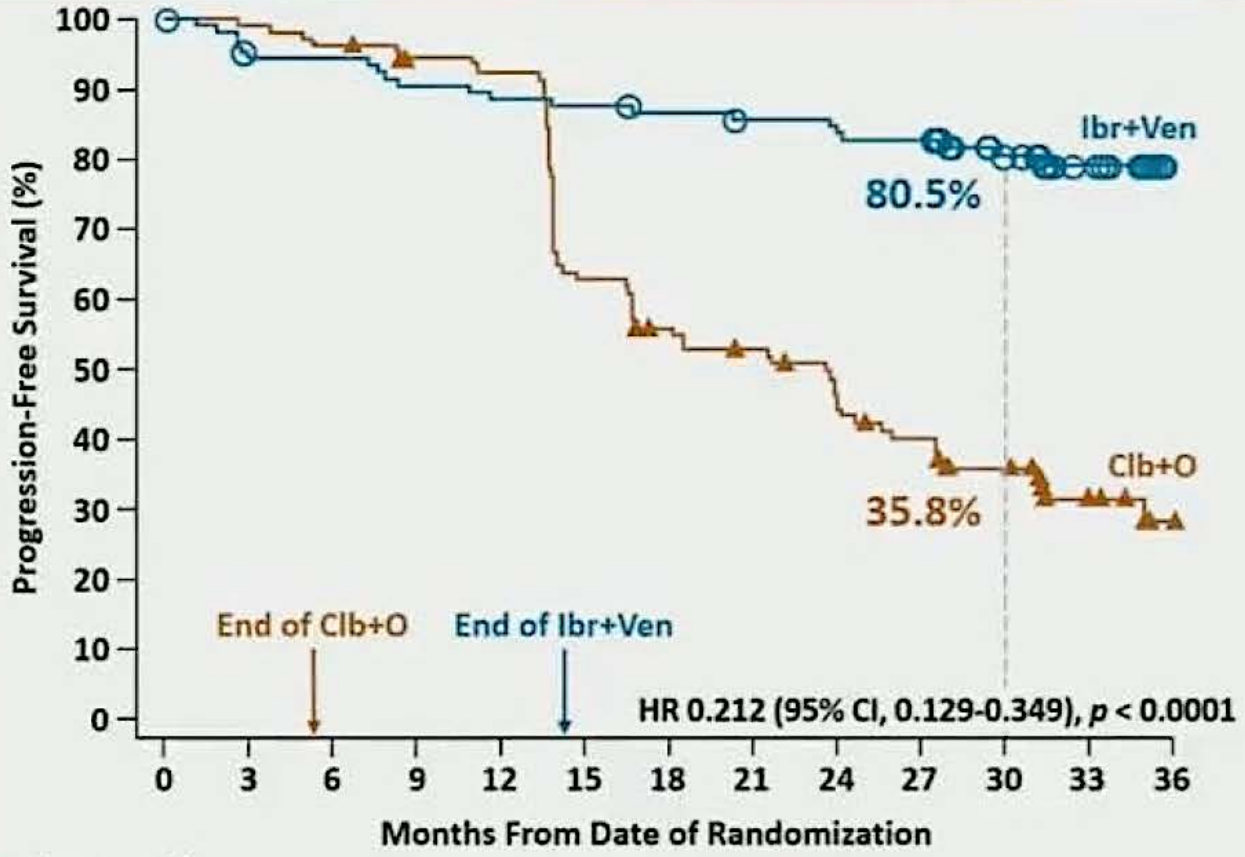
First Prospective Data on Minimal Residual Disease (MRD) Outcomes After Fixed-Duration Ibrutinib Plus Venetoclax (Ibr+Ven) Versus Chlorambucil Plus Obinutuzumab (Clb+O) for First-Line Treatment of CLL in Elderly or Unfit Patients: The GLOW Study

Talha Munir,[1] Carol Moreno,[2] Carolyn Owen,[3] George Follows,[4] Ohad Benjamini,[5] Ann Janssens,[6] Mark-David Levin,[7] Anders Osterborg,[8] Tadeusz Robak,[9] Martin Simkovic,[10] Don Stevens,[11] Sergey Voloshin,[12] Vladimir Vorobyev,[13] Munci Yagci,[14] Loic Ysebaert,[15] Qianya Qi,[16] Andrew J. Steele,[17] Natasha Schuier,[18] Kurt Baeten,[19] Donne Bennett Caces,[16] Carsten U. Niemann,[20] Arnon P. Kater[21]

[1]St James's Hospital, Leeds, UK; [2]Hospital de la Santa Creu i Sant Pau, Autonomous University of Barcelona, Spain; [3]Tom Baker Cancer Centre, Calgary, Canada; [4]Addenbrookes Hospital, Cambridge, UK; [5]Sheba Medical Center, Ramat Gan, Israel; [6]UZ Leuven Gasthuisberg, Leuven, Belgium; [7]Albert Schweitzer Hospital, Dordrecht, Netherlands; [8]Karolinska University Hospital, Stockholm, Sweden; [9]Medical University of Lodz, Copernicus Memorial Hospital, Lodz, Poland; [10]University Hospital Hradec Kralove, Hradec Kralove, Czech Republic; [11]Norton Cancer Institute, Louisville, KY, USA; [12]Russian Scientific and Research Institute of Hematology and Transfusiology, St. Petersburg, Russia; [13]S.P. Botkin Moscow City Clinical Hospital, Moscow, Russia; [14]Gazi Universitesi Tip Fakultesi, Ankara, Turkey; [15]Institut Universitaire du Cancer Toulouse Oncopole, Toulouse, France; [16]Janssen Research & Development, Raritan, NJ, USA; [17]Janssen Research & Development, Spring House, PA, USA; [18]Janssen Research & Development, Düsseldorf, Germany; [19]Janssen Research & Development, Beerse, Belgium; [20]Rigshospitalet Copenhagen University Hospital, Copenhagen, Denmark; [21]Amsterdam University Medical Centers, Cancer Center Amsterdam, University of Amsterdam, Netherlands

ASH 2021;Abstract 70.

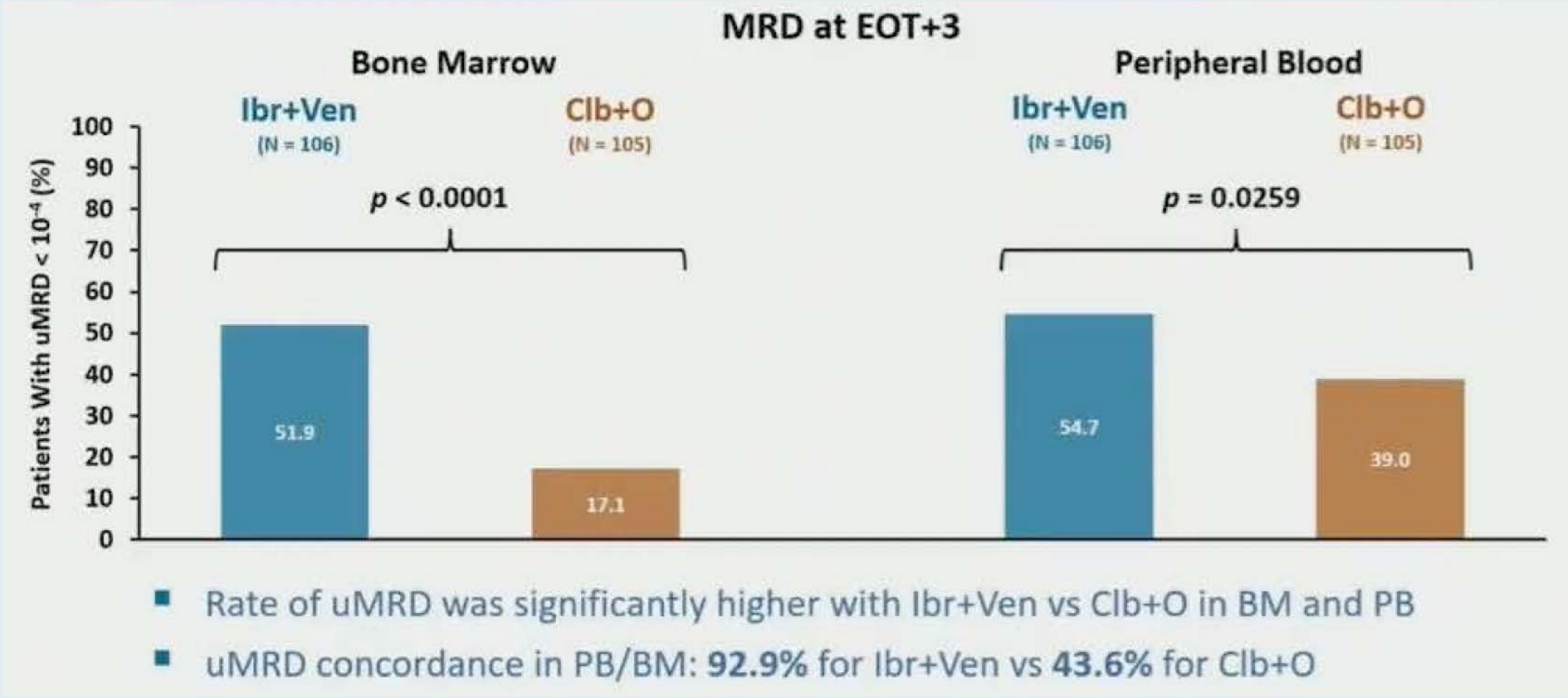
GLOW: IRC-Assessed PFS



- IRC-assessed PFS for Ibr+Ven was superior to Clb+O at primary analysis (median 27.7 months of follow-up)
  - HR 0.216 (95% CI, 0.131-0.357; $p < 0.0001$)
- **With median follow-up of 34.1 months:**
  - IRC-assessed PFS remained superior for Ibr+Ven (HR 0.212, 95% CI, 0.129-0.349; $p < 0.0001$)
  - 30-month PFS: 80.5% for Ibr+Ven vs 35.8% for Clb+O
  - Overall survival HR 0.76 (95% CI, 0.35-1.64), with 11 deaths for Ibr+Ven vs 16 for Clb+O

Munir T et al. ASH 2021;Abstract 70.

GLOW: uMRD Rate $<10^{-4}$



Munir T et al. ASH 2021;Abstract 70.

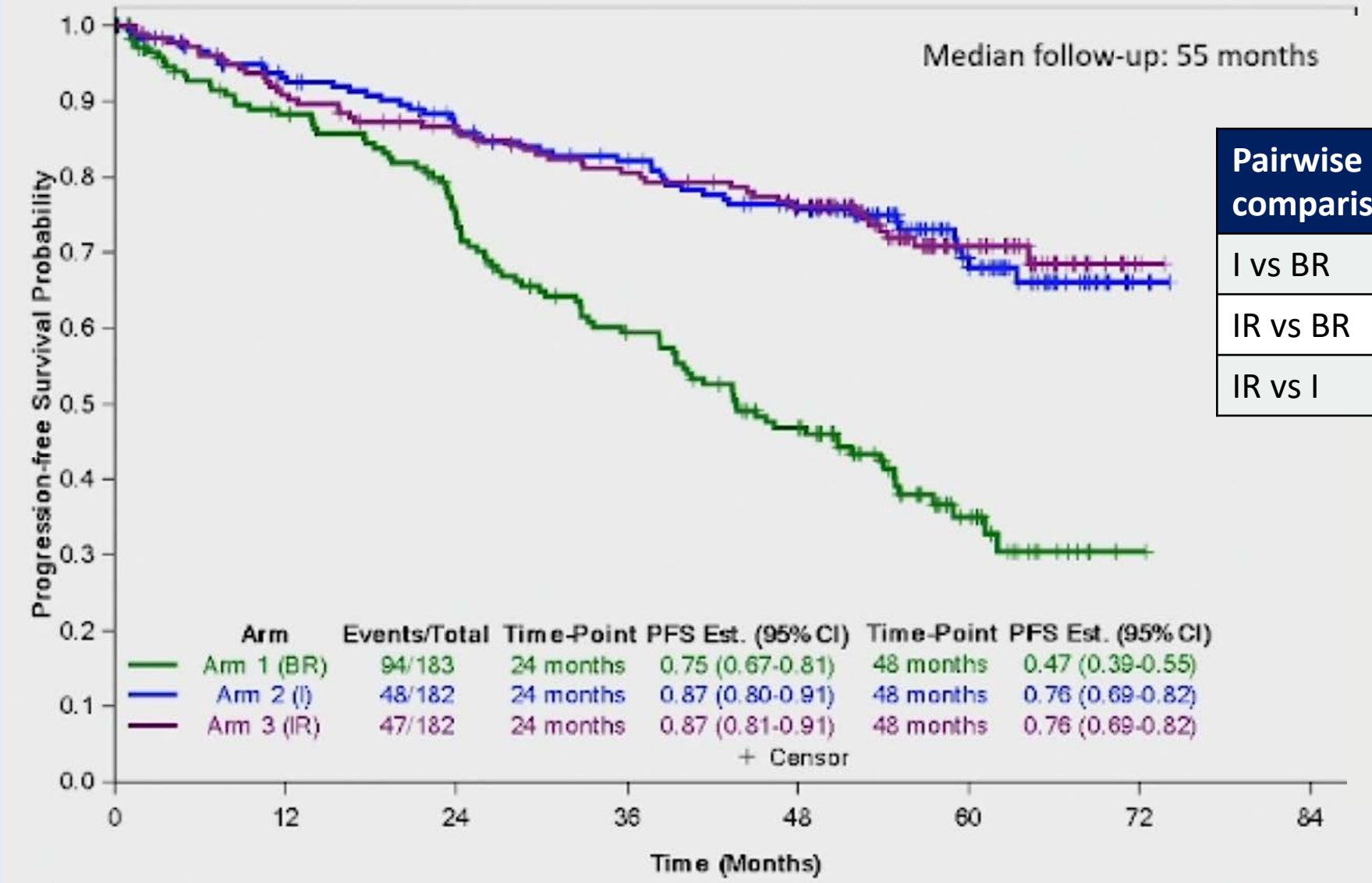
RTP RESEARCH TO PRACTICE

Long-Term Results of Alliance A041202 Show Continued Advantage of Ibrutinib-Based Regimens Compared with Bendamustine Plus Rituximab (BR) Chemoimmunotherapy

Woyach JA et al.

ASH 2021;Abstract 639.

Alliance A041202: Progression-Free Survival



Pairwise comparisons	Hazard ratio	*p*-value
I vs BR	0.36	<0.0001
IR vs BR	0.36	<0.001
IR vs I	0.99	0.96

Woyach JA et al. ASH 2021;Abstract 639.

RTP RESEARCH TO PRACTICE

CHRONIC LYMPHOCYTIC LEUKEMIA

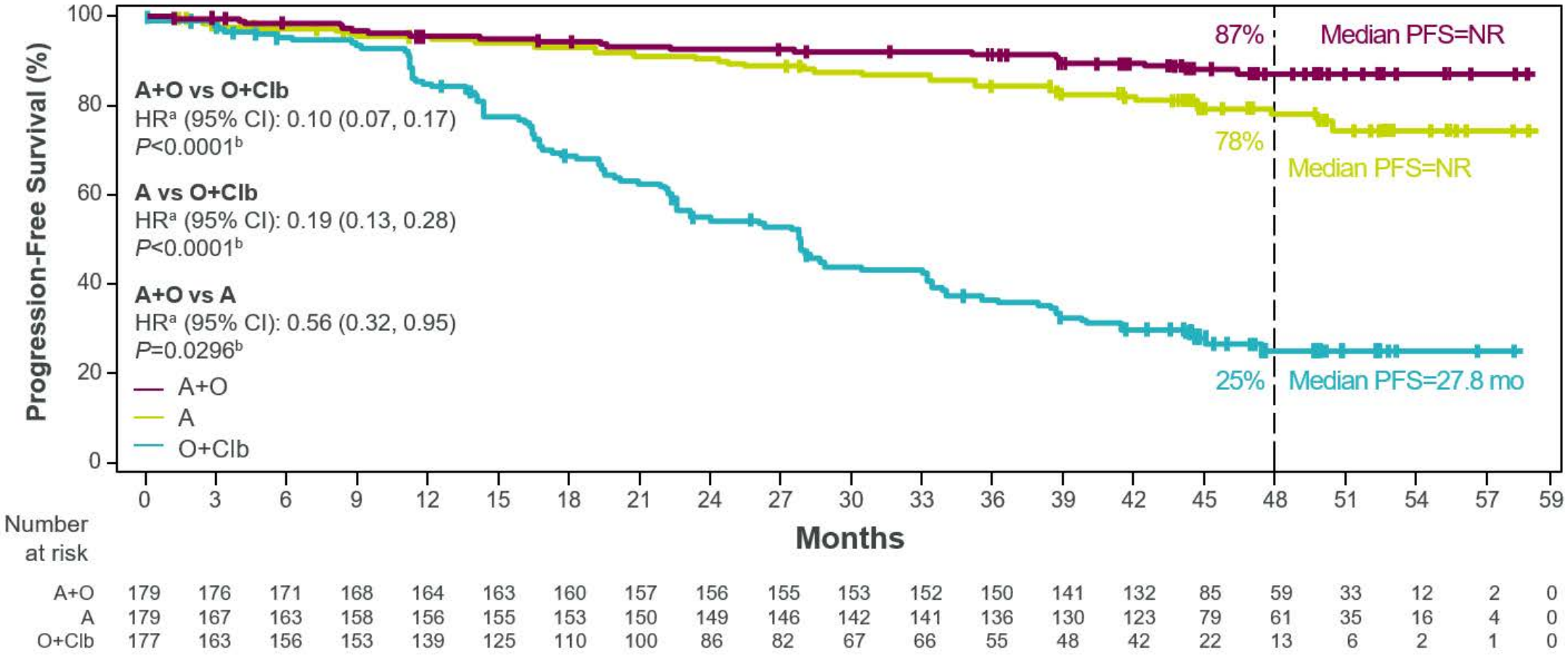
Leukemia 2022;[Online ahead of print].

Efficacy and safety in a 4-year follow-up of the ELEVATE-TN study comparing acalabrutinib with or without obinutuzumab versus obinutuzumab plus chlorambucil in treatment-naïve chronic lymphocytic leukemia

Jeff P. Sharman[1]✉, Miklos Egyed[2], Wojciech Jurczak[3], Alan Skarbnik[4], John M. Pagel[5], Ian W. Flinn[6], Manali Kamdar[7], Talha Munir[8], Renata Walewska[9], Gillian Corbett[10], Laura Maria Fogliatto[11], Yair Herishanu[12], Versha Banerji[13], Steven Coutre[14], George Follows[15], Patricia Walker[16], Karin Karlsson[17], Paolo Ghia[18], Ann Janssens[19], Florence Cymbalista[20], Jennifer A. Woyach[21], Emmanuelle Ferrant[22], William G. Wierda[23], Veerendra Munugalavadla[24], Ting Yu[24], Min Hui Wang[24] and John C. Byrd[21]

ELEVATE-TN: Investigator-Assessed PFS (Overall)

4-Year Follow-Up



Sharman JP et al. *Leukemia* 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

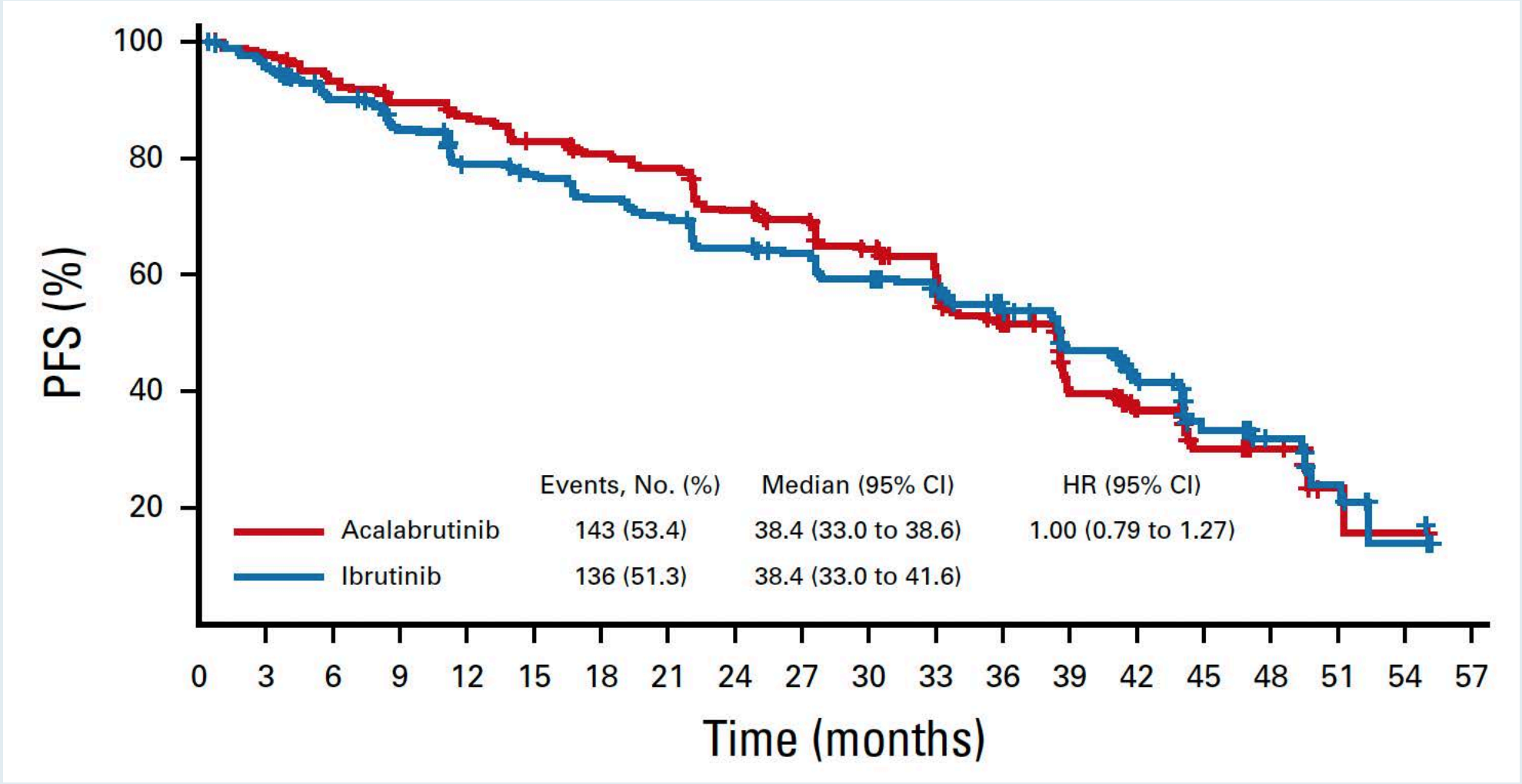
original reports

Acalabrutinib Versus Ibrutinib in Previously Treated Chronic Lymphocytic Leukemia: Results of the First Randomized Phase III Trial

John C. Byrd, MD[1]; Peter Hillmen, MD, MBChB, PhD[2]; Paolo Ghia, MD, PhD[3,4]; Arnon P. Kater, MD, PhD[5]; Asher Chanan-Khan, MD[6]; Richard R. Furman, MD[7]; Susan O'Brien, MD[8]; Mustafa Nuri Yenerel, MD[9]; Arpad Illés, MD[10]; Neil Kay, MD[11]; Jose A. Garcia-Marco, MD, PhD[12]; Anthony Mato, MD[13]; Javier Pinilla-Ibarz, MD, PhD[14]; John F. Seymour, PhD[15]; Stephane Lepretre, MD[16,17]; Stephan Stilgenbauer, MD[18]; Tadeusz Robak, PhD[19]; Wayne Rothbaum, MS[20]; Raquel Izumi, PhD[20]; Ahmed Hamdy, MD[20]; Priti Patel, MD[21]; Kara Higgins, MS[21]; Sophia Sohoni, MD[21]; and Wojciech Jurczak, MD, PhD[22]

J Clin Oncol 2021;39(31):3441-52

ELEVATE-RR: Independent Review Committee-Assessed PFS



Byrd JC et al. *J Clin Oncol* 2021;39(31):3441-52.

ELEVATE-RR: Characterization of Adverse Events with Acalabrutinib versus Ibrutinib

	Incidence, %				Exposure-Adjusted Incidence[b]				Exposure-Adjusted Time With Event[c]			
	Any grade		Grade ≥3		Any grade		Grade ≥3		Any grade		Grade ≥3	
	Acala[d]	Ibru[e]	Acala[d]	Ibru[e]	Acala[d]	Ibru[e]	Acala[d]	Ibru[e]	Acala[d]	Ibru[e]	Acala[d]	Ibru[e]
ECIs												
Cardiac events	24%	30%	9%	10%	1.2	1.9	0.4	0.5	7.1	13.0	0.4	0.2
Afib/flutter	9%	**16%***	5%	4%	0.4	0.7	0.2	0.1	1.3	3.8	0.3	0.1
HTN[f]	9%	**23%***	4%	**9%***	0.4	1.2	0.1	0.4	4.1	15.0	1.6	4.0
Bleeding events[g]	38%	**51%***	4%	5%	2.4	3.8	0.1	0.2	13.7	24.6	0.1	0.1
Major bleeding events[h]	5%[i]	5%[i]	4%	5%	0.2	0.2	0.1	0.2	0.1	0.3	0.1	0.1
Infections[k]	78%	81%	31%	30%	8.9	10.4	1.6	2.0	14.6	15.6	1.5	1.1
Selected Common AEs (preferred term)												
Diarrhea	35%	**46%***	1%	**5%***	1.9	2.8	<0.1	0.2	6.7	9.6	<0.1	0.1
Headache	**35%***	20%	**2%***	0	1.8	1.1	<0.1	0	7.8	5.4	<0.1	0
Cough	**29%***	21%	1%	<1%	1.3	1.1	<0.1	<0.1	5.6	4.9	<0.1	<0.1
Fatigue	20%	17%	**3%***	0%	0.9	0.9	0.1	0	7.4	7.0	0.6	0
Arthralgia	16%	**23%***	0	1%	0.6	1.3	0	<0.1	7.5	10.4	0	<0.1
Back pain	8%	**13%***	0	1%	0.3	0.5	0	<0.1	1.9	3.2	0	0.1
Muscle spasms	6%	**13%***	0	1%	0.2	0.7	0	<0.1	0.8	10.0	0	0.1
Dyspepsia	4%	**12%***	0	0	0.1	0.5	0	0	1.0	2.4	0	0

Seymour JF et al. ASH 2021;Abstract 3721.

New Acalabrutinib Formulation Enables Co-Administration with Proton Pump Inhibitors and Dosing in Patients Unable to Swallow Capsules (ELEVATE-PLUS)

Shringi Sharma, Xavier Pepin, Harini Burri, Lianqing Zheng, Nataliya Kuptsova-Clarkson, Anouk de Jong, Ting Yu, Holly L MacArthur, Michal Majewski, Joseph A Ware, James Mann, David Ramies, Veerendra Munugalavadla, Louise Sheridan, Helen Tomkinson

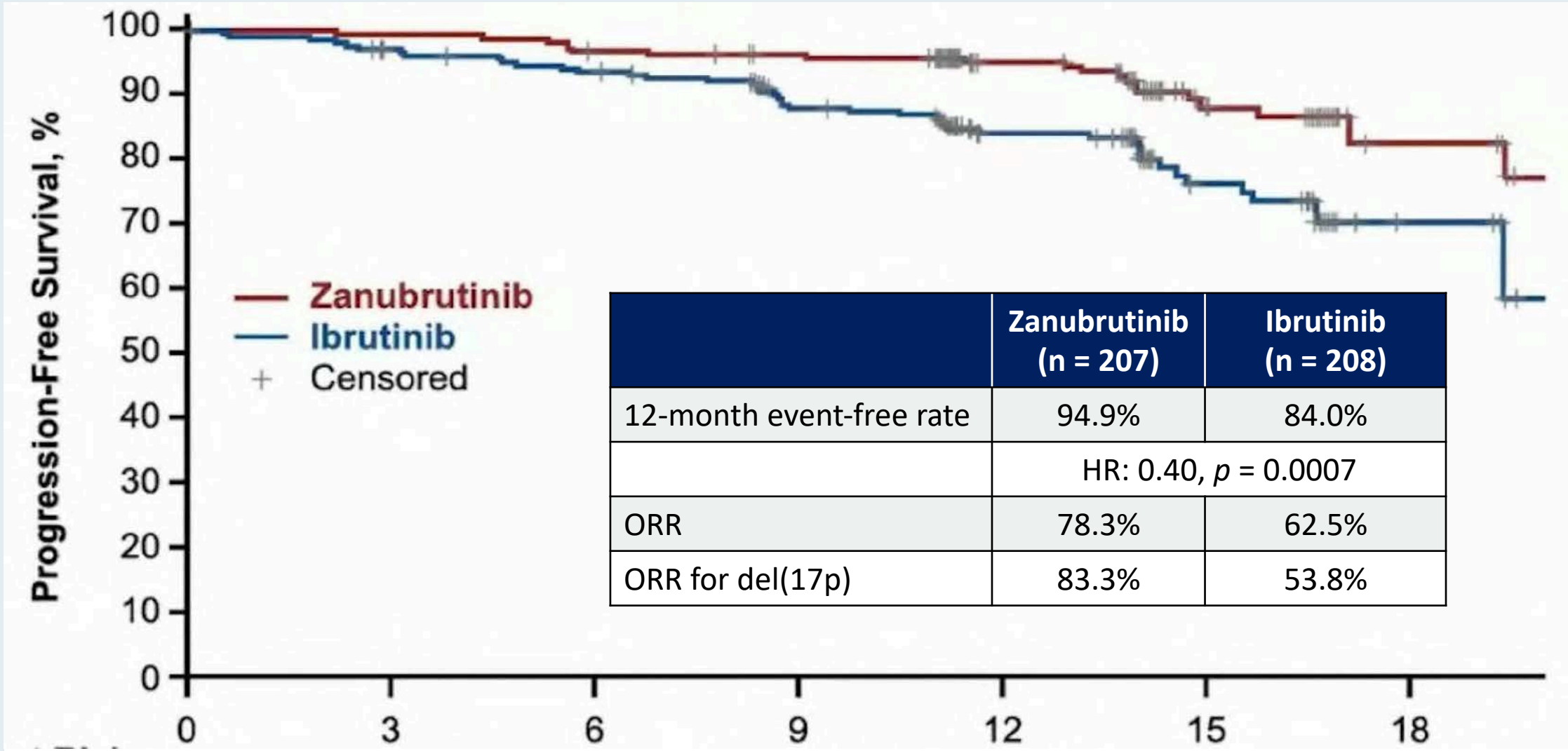
ASH 2021;Abstract 605.MOLECULAR PHARMACOLOGY AND DRUG RESISTANCE: LYMPHOID NEOPLASMS| NOVEMBER 5, 2021

First Interim Analysis of Alpine Study: Results of a Phase 3 Randomized Study of Zanubrutinib vs Ibrutinib in Patients with Relapsed/Refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

Hillmen P et al.

EHA 2021;Abstract LBA1900.

ALPINE: Response and Investigator-Assessed PFS



	Zanubrutinib (n = 207)	Ibrutinib (n = 208)
12-month event-free rate	94.9%	84.0%
	HR: 0.40, *p* = 0.0007	
ORR	78.3%	62.5%
ORR for del(17p)	83.3%	53.8%

Hillmen P et al. EHA 2021;Abstract LBA1900.

ALPINE: Adverse Events of Special Interest

Safety Analysis Population	Zanubrutinib (n=204), n (%)		Ibrutinib (n=207), n (%)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Cardiac disorders[a]	28 (13.7)	5 (2.5)	52 (25.1)	14 (6.8)
Atrial fibrillation and flutter (key 2º endpoint)	**5 (2.5)**	**2 (1.0)**	**21 (10.1)**	**4 (1.9)**
Hemorrhage	73 (35.8)	6 (2.9)	75 (36.2)	6 (2.9)
Major hemorrhage[b]	6 (2.9)	6 (2.9)	8 (3.9)	6 (2.9)
Hypertension	34 (16.7)	22 (10.8)	34 (16.4)	22 (10.6)
Infections	122 (59.8)	26 (12.7)	131 (63.3)	37 (17.9)
Neutropenia[c]	58 (28.4)	38 (18.6)	45 (21.7)	31 (15.0)
Thrombocytopenia[c]	19 (9.3)	7 (3.4)	26 (12.6)	7 (3.4)
Secondary primary malignancies	17 (8.3)	10 (4.9)	13 (6.3)	4 (1.9)
Skin cancers	7 (3.4)	3 (1.5)	10 (4.8)	2 (1.0)

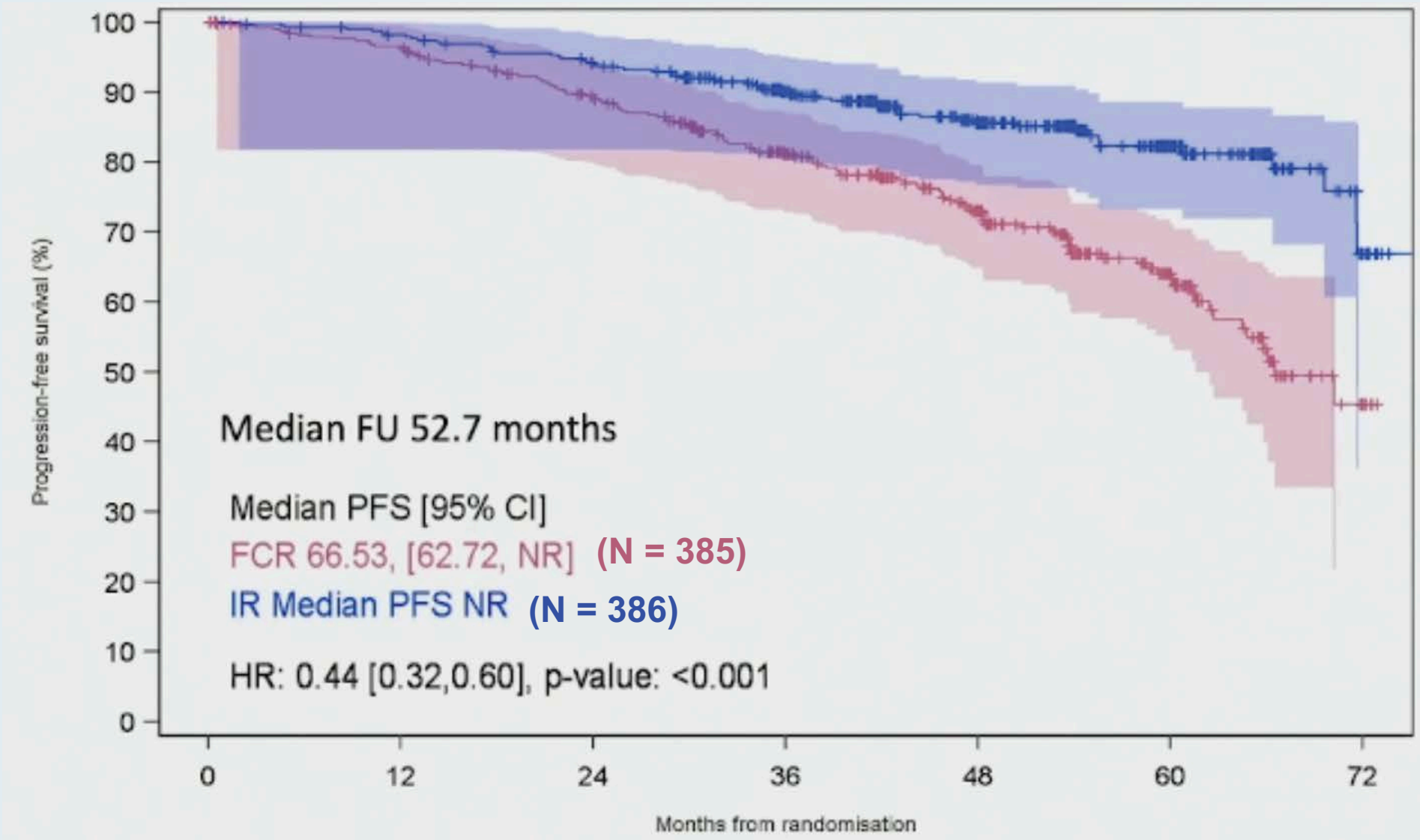
Hillmen P et al. EHA 2021;Abstract LBA1900.

Ibrutinib plus Rituximab Is Superior to FCR in Previously Untreated CLL: Results of the Phase III NCRI FLAIR Trial

Hillmen P et al.

ASH 2021;Abstract 642.

NCRI FLAIR: Progression-Free Survival



Hillmen P et al. ASH 2021;Abstract 642.

RTP RESEARCH TO PRACTICE

FDA Has Placed a Partial Clinical Hold on Some Combination Candidate Studies for Leukemia and Lymphoma

Press Release – January 27, 2022

The FDA placed partial holds on studies of the U2 combination umbralisib and ublituximab for chronic lymphocytic leukemia (CLL) and non-Hodgkin lymphoma (NHL).

The updated overall survival (OS) preliminary results from the UNITY-CLL study showed improvement. The OS hazard ratio was 1.23, and, including COVID-19-related deaths, the ratio reached 1.04.

An OS hazard ratio above 1.00 implies a risk that the investigational therapy might be causing harm.

No new patients can be enrolled in some CLL and NHL trials, but those deriving a benefit may continue with consent.

https://www.yahoo.com/now/tg-therapeutics-falls-30-ceo-173034141.html

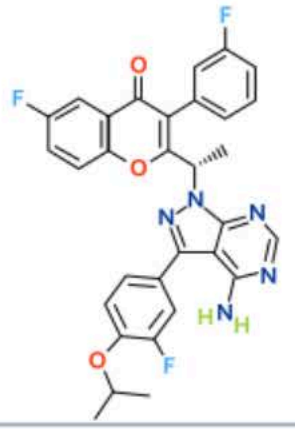
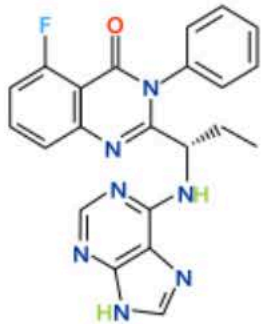
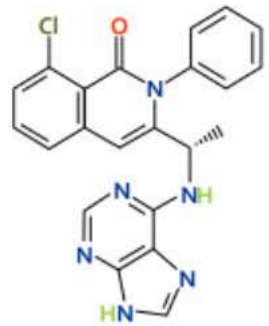
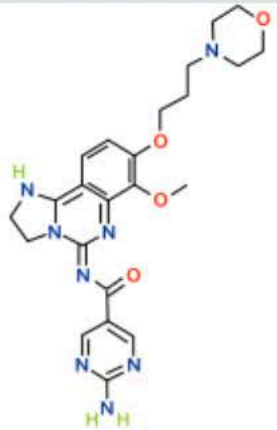
RTP RESEARCH TO PRACTICE

Efficacy and Safety of Ublituximab in Combination with Umbralisib (U2) in Patients with Chronic Lymphocytic Leukemia (CLL) By Treatment Status: A Sub-Analysis of the Phase 3 Unity-CLL Study

Jacobs R et al.

ASH 2021;Abstract 3726.

Umbralisib: A Selective Inhibitor of PI3Kδ and CK1ε

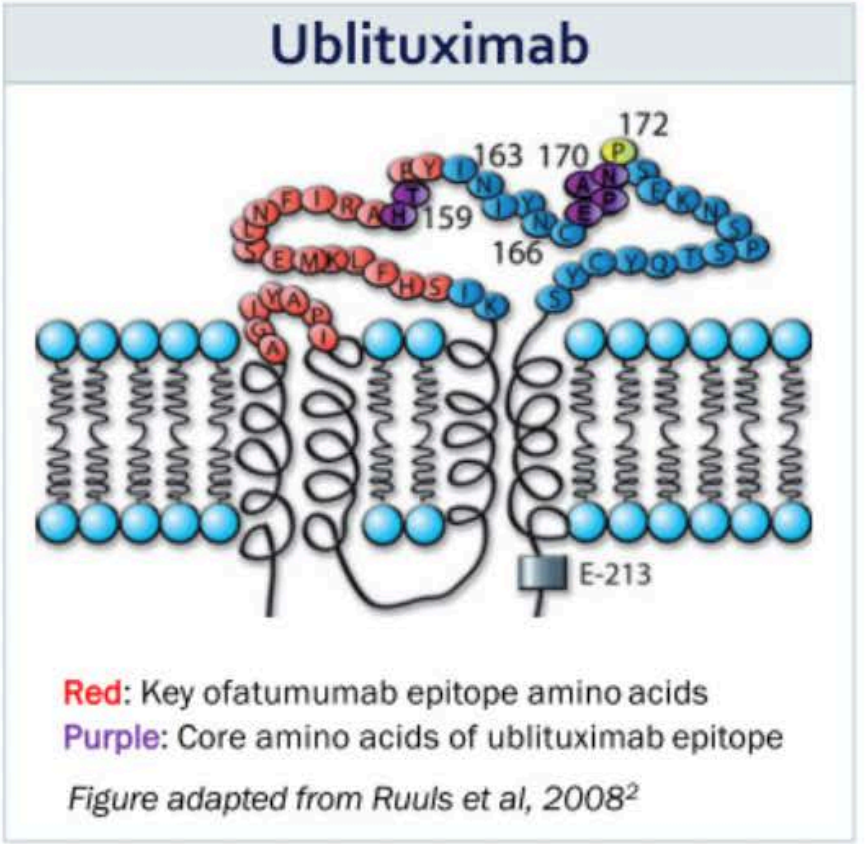
	Umbralisib[1]	Idelalisib[1]	Duvelisib[1]	Copanlisib[2]
				
Isoform	**K_d (nM)**			
PI3kα	>10000	600	40	0.04
PI3Kβ	>10000	19	0.89	1.5
PI3Kγ	1400	9.1	0.21	0.31
PI3Kδ	6.2	1.2	0.047	0.068
CK1ε	180	>30,000	>30,000	>6,000

- Umbralisib is an oral, once daily, selective inhibitor of PI3Kδ and CK1ε
- Umbralisib has >1000-fold greater selectivity for PI3Kδ compared to α and β isoforms
- Umbralisib is also **>200-fold** more selective for PI3Kδ relative to **PI3Kγ**

Jacobs R et al. ASH 2021;Abstract 3726.

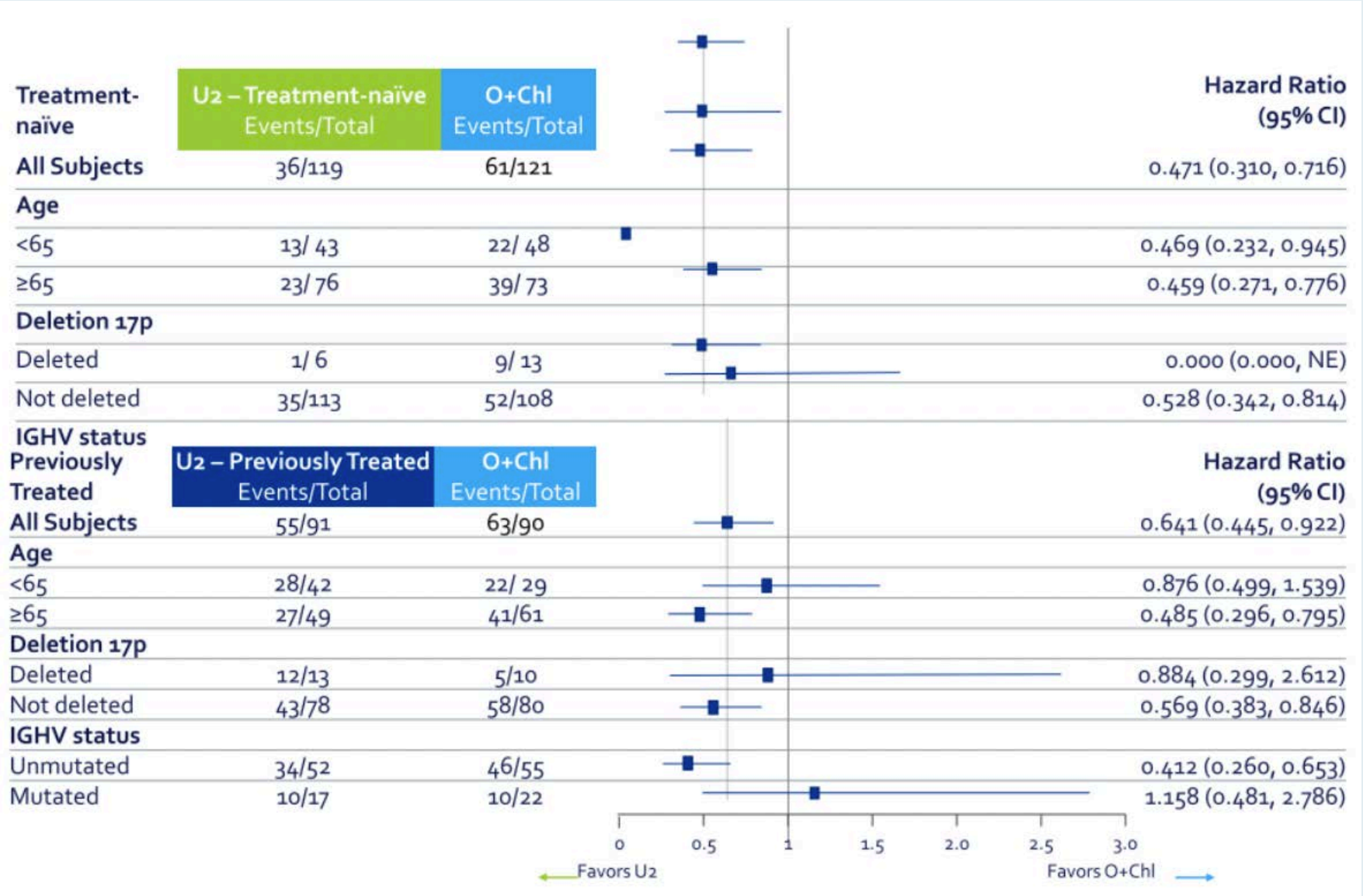
Ublituximab: A Novel Glycoengineered Anti-CD20 Monoclonal Antibody

- Ublituximab (TG-1101, UTX) is a novel, glycoengineered, Type I, anti-CD20 monoclonal antibody with several defining features:
  - Targets a unique epitope on the CD20 antigen
  - Type I maintains complement-dependent cytotoxicity (CDC)
  - Glycoengineered to enhance affinity for all variants of FcγRIIIa receptors, thereby demonstrating greater antibody-dependent cellular cytotoxicity (ADCC) activity than rituximab and ofatumumab, including in 17p deleted CLL cells[1]



Jacobs R et al. ASH 2021;Abstract 3726.

UNITY-CLL: IRC-Assessed PFS by Treatment Status



Jacobs R et al. ASH 2021;Abstract 3726.

RTP RESEARCH TO PRACTICE

UNITY-CLL: Adverse Events (AEs) of Clinical Interest

AEs, n (%)	Treatment-naïve N=116			Previously Treated N=90		
	Any	Grade ≥3	Discontinued U2[b]	Any	Grade ≥3	Discontinued U2[b]
ALT elevation	27 (23)	14 (12)	3 (3)	8 (9)	3 (3)	-
AST elevation	21 (18)	9 (8)	3 (3)	7 (8)	2 (2)	-
Rash[a]	17 (15)	4 (3)	1 (1)	9 (10)	1 (1)	1 (1)
Pneumonia	14 (12)	8 (7)	1 (1)	18 (20)	10 (11)	1 (1)
Colitis (non-infectious)[a]	8 (7)	3 (3)	-	2 (2)	1 (1)	1 (1)
Pneumonitis	4 (3)	1 (1)	2 (2)	2 (2)	-	1 (1)
Opportunistic infections[a]	3 (3)	1 (1)	1 (1)	3 (3)	1 (1)	-

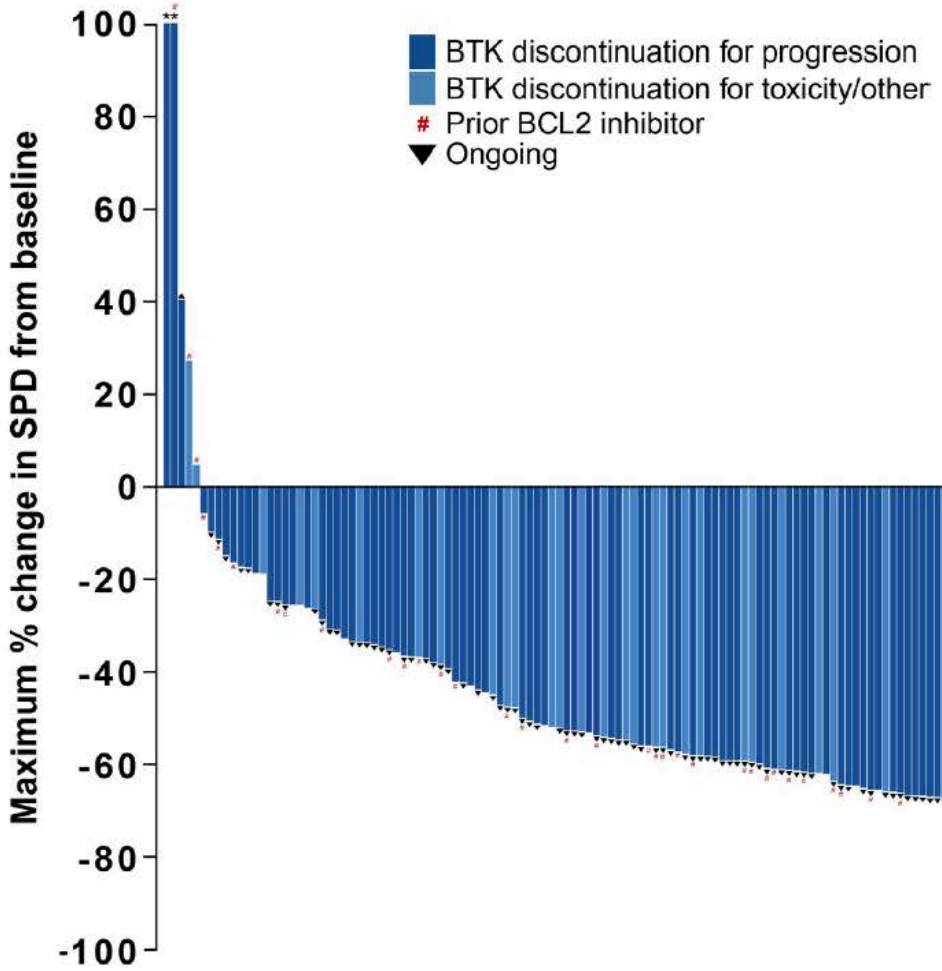
Jacobs R et al. ASH 2021;Abstract 3726.

Pirtobrutinib, a Next Generation, Highly Selective, Non-Covalent BTK Inhibitor in Previously Treated CLL/SLL: Updated Results from the Phase 1/2 BRUIN Study

Mato AR et al.

ASH 2021;Abstract 391.

BRUIN: Pirtobrutinib Efficacy in Patients with BTK-Pretreated CLL or Small Lymphocytic Lymphoma (SLL)



Efficacy evaluable BTK pre-treated CLL/SLL Patients[a]	n = 252
Overall Response Rate, % (95% CI)[b]	**68 (62 – 74)**
Best response	
CR, n (%)	2 (1)
PR, n (%)	137 (54)
PR-L, n (%)	32 (13)
SD, n (%)	62 (25)

Mato AR et al. ASH 2021;Abstract 391.

RTP RESEARCH TO PRACTICE

BRUIN: Pirtobrutinib Safety Profile

	All doses and patients (n=618)						
	Treatment-emergent AEs, (≥15%), %					Treatment-related AEs, %	
Adverse Event	Grade 1	Grade 2	Grade 3	Grade 4	Any Grade	Grades 3/4	Any Grade
Fatigue	13%	8%	1%	-	23%	1%	9%
Diarrhea	15%	4%	<1%	<1%	19%	<1%	8%
Neutropenia[a]	1%	2%	8%	6%	18%	8%	10%
Contusion	15%	2%	-	-	17%	-	12%
AEs of special interest[b]							
Bruising[c]	20%	2%	-	-	22%	-	15%
Rash[d]	9%	2%	<1%	-	11%	<1%	5%
Arthralgia	8%	3%	<1%	-	11%	-	3%
Hemorrhage[e]	5%	2%	1%[g]	-	8%	<1%	2%
Hypertension	1%	4%	2%	-	7%	<1%	2%
Atrial fibrillation/flutter[f]	-	1%	<1%	<1%	2%[h]	-	<1%

No DLTs reported and MTD not reached
96% of patients received ≥1 pirtobrutinib dose at or above RP2D of 200 mg daily
1% (n=6) of patients permanently discontinued due to treatment-related AEs

Mato AR et al. ASH 2021;Abstract 391.

Nature 2022;[Online ahead of print].

Article

Decade-long leukaemia remissions with persistence of CD4$^+$ CAR T cells

https://doi.org/10.1038/s41586-021-04390-6

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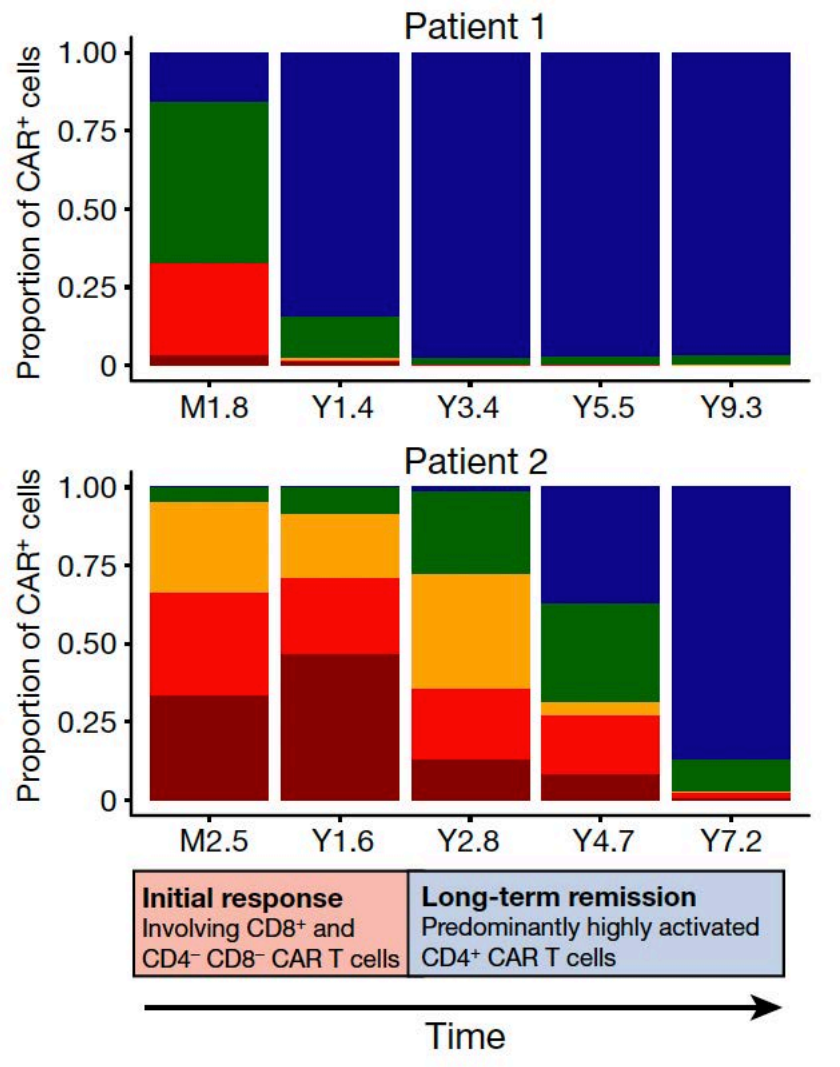
Published online: 02 February 2022

J. Joseph Melenhorst[1,2,3,4,5,15,16]✉, Gregory M. Chen[6,15], Meng Wang[1,2,3,14], David L. Porter[3,7,15], Changya Chen[8,9], McKensie A. Collins[1,2,3,10], Peng Gao[8,9], Shovik Bandyopadhyay[10], Hongxing Sun[1,2,3], Ziran Zhao[1,2,3], Stefan Lundh[1,2,3], Iulian Pruteanu-Malinici[11], Christopher L. Nobles[12], Sayantan Maji[1,2,3], Noelle V. Frey[3], Saar I. Gill[3], Lifeng Tian[1,3], Irina Kulikovskaya[1,2,3], Minnal Gupta[1,2,3], David E. Ambrose[1,2,3], Megan M. Davis[1,2,3], Joseph A. Fraietta[1,2,3,12], Jennifer L. Brogdon[11], Regina M. Young[1,2,3], Anne Chew[1,2,3], Bruce L. Levine[1,2,3], Donald L. Siegel[1,2,13], Cécile Alanio[4,5,14], E. John Wherry[4,5,14], Frederic D. Bushman[12], Simon F. Lacey[1,2,3], Kai Tan[2,4,6,9,10,16]✉ & Carl H. June[1,2,3,4,5,16]✉

Analysis of CD3+ CAR+ T Cells Using CyTOF Across Multiple Time Points



"Here we studied long-lasting CD19-redirected chimeric antigen receptor (CAR) T cells in two patients with chronic lymphocytic leukaemia who achieved a complete remission in 2010. CAR T cells remained detectable more than ten years after infusion, with sustained remission in both patients. Notably, a highly activated CD4+ population emerged in both patients, dominating the CAR T cell population at the later time points… …Our identification and characterization of these unexpected CAR T cell populations provide novel insight into the CAR T cell characteristics associated with anti-cancer response and long-term remission in leukaemia."

Melenhorst JJ et al. *Nature* 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

American Society of Hematology
2021 L Street NW, Suite 900,
Washington, DC 20036
Phone: 202-776-0544 | Fax 202-776-0545
editorial@hematology.org

Blood 2021;[Online ahead of print].

Phase 1 TRANSCEND CLL 004 study of lisocabtagene maraleucel in patients with relapsed/refractory CLL or SLL

Tracking no: BLD-2021-011895R2

Tanya Siddiqi (City of Hope Medical Center, United States) Jacob Soumerai (Massachusetts General Hospital Cancer Center, United States) Kathleen Dorritie (UPMC, United States) Deborah Stephens (University of Utah, United States) Peter Riedell (University of Chicago, United States) Jon Arnason (BIDMC, United States) Thomas Kipps (University of California-San Diego School of Medicine, United States) Heidi Gillenwater (Bristol Myers Squibb, United States) Lucy Gong (Bristol Myers Squibb, United States) Lin Yang (Bristol Myers Squibb, United States) Ken Ogasawara (Bristol Myers Squibb, United States) Jerill Thorpe (Bristol Myers Squibb, United States) William Wierda (University of Texas M.D. Anderson Cancer Center, United States)

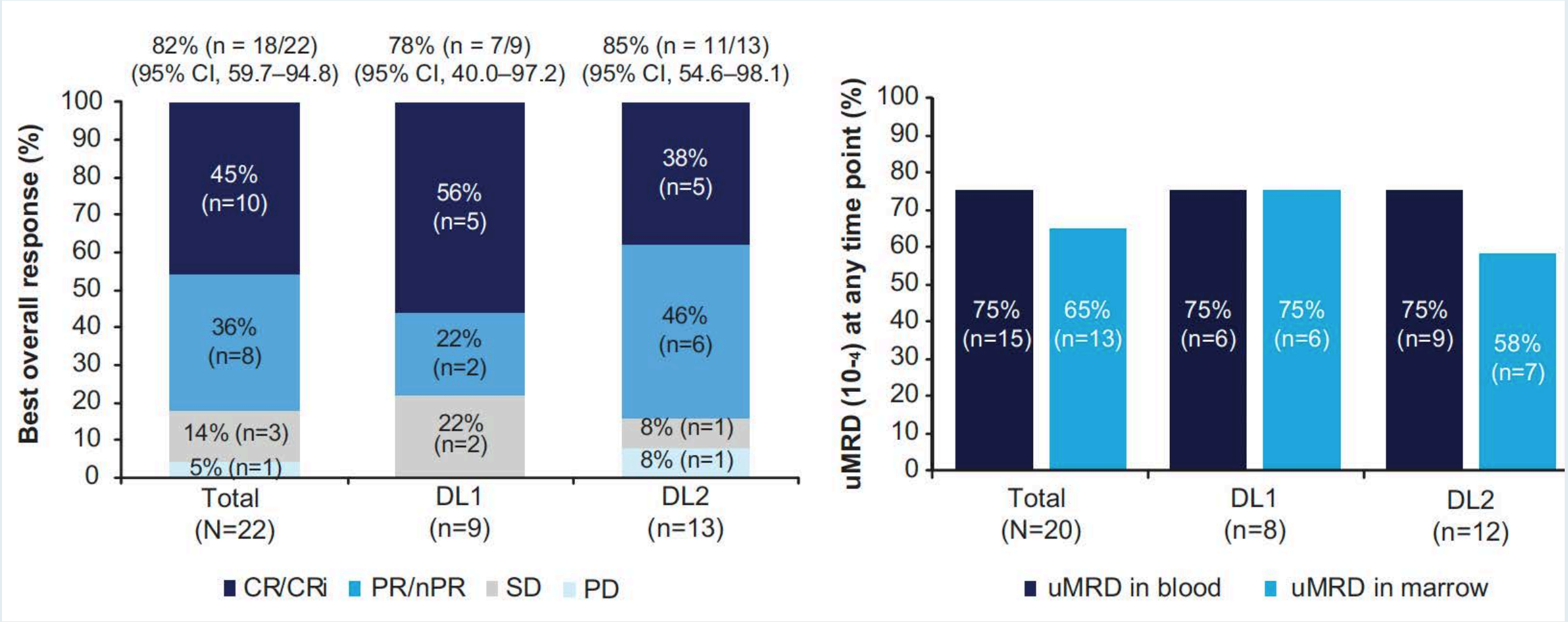
TRANSCEND CLL 004: Rates of Cytokine Release Syndrome (CRS), Neurologic Events (NE) and Rehospitalization After Liso-cel Infusion

	All patients (N = 23)	Dose level 1 50×10^6 (n = 9)	Dose level 2 100×10^6 (n = 14)
CRS any grade	17 (74%)	7 (78%)	10 (71%)
CRS Grade ≥3	2 (9%)	0	2 (14%)
NE any grade	9 (39%)	2 (22%)	7 (50%)
NE Grade ≥3	5 (21%)	2 (22%)	2 (14%)
Reasons for patient rehospitalization			
Adverse events	11 (48%)	3 (33%)	8 (57%)
CRS and/or NE	5 (22%)	1 (11%)	4 (29%)
CRS and NE	2 (9%)	0	2 (14%)
NE only	3 (13%)	1 (11%)	2 (14%)

Siddiqi T et al. *Blood* 2021;[Online ahead of print].

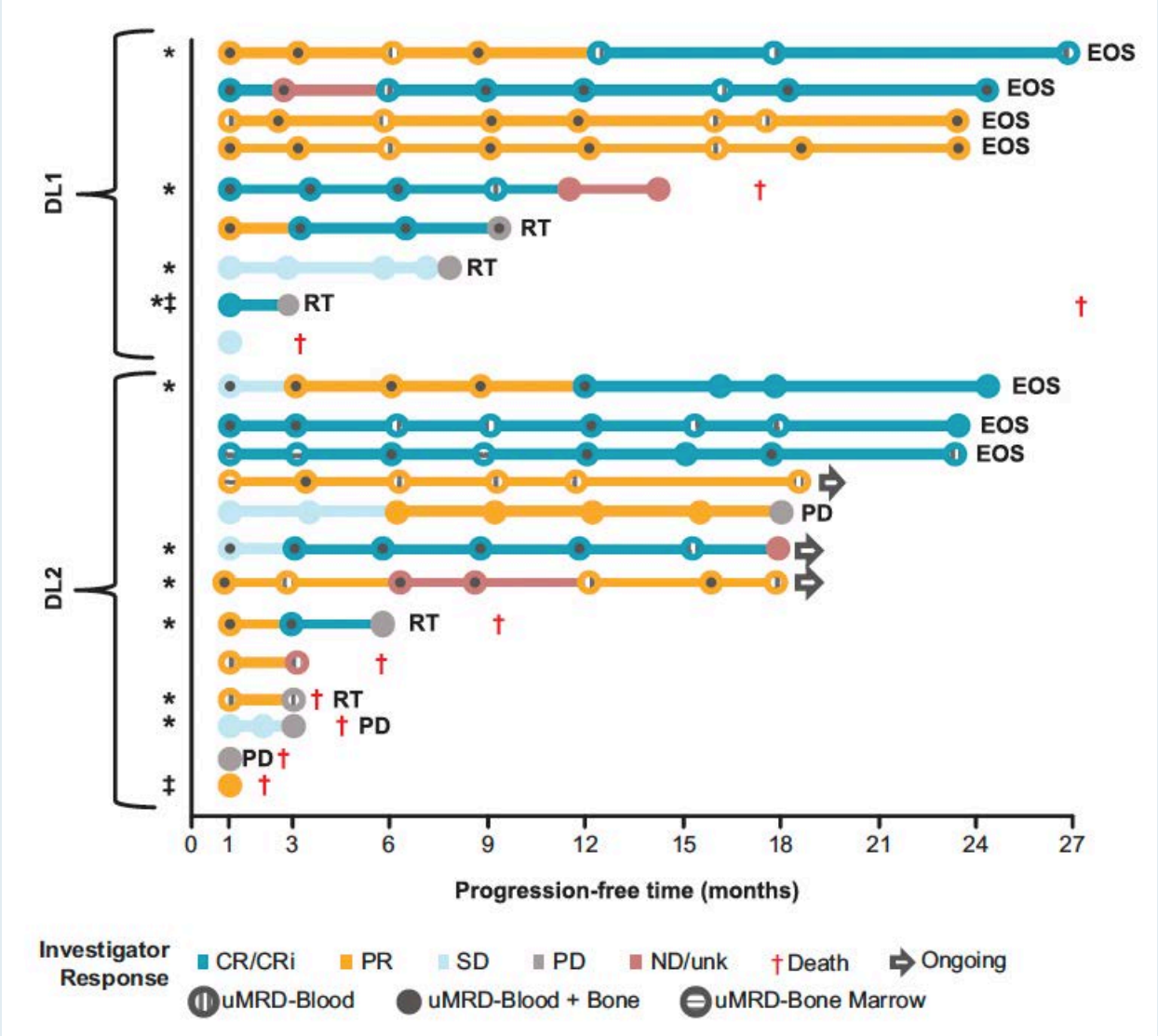
RTP RESEARCH TO PRACTICE

TRANSCEND CLL 004: Response and uMRD (10^{-4}) Rates



Siddiqi T et al. *Blood* 2021;[Online ahead of print].

TRANSCEND CLL 004: Swim Lane Plot, Duration of Response and PFS



Siddiqi T et al. *Blood* 2021;[Online ahead of print].

Agenda

Module 1: Diffuse Large B-Cell Lymphoma (DLBCL)

Module 2: Chronic Lymphocytic Leukemia (CLL)

Module 3: Hodgkin Lymphoma

Module 4: Mantle Cell Lymphoma

Module 5: Follicular Lymphoma (FL)

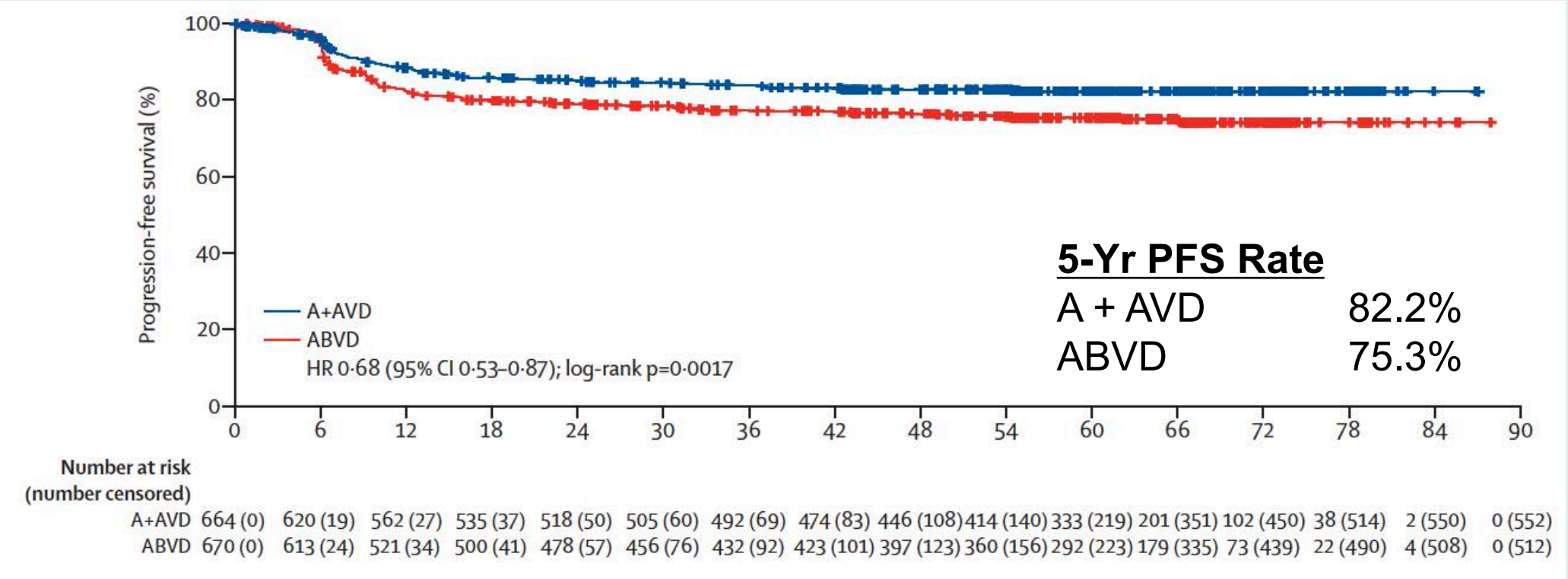
Lancet Haematol 2021;8(6):e410-21

Articles

Brentuximab vedotin with chemotherapy for stage III or IV classical Hodgkin lymphoma (ECHELON-1): 5-year update of an international, open-label, randomised, phase 3 trial

David J Straus, Monika Długosz-Danecka, Joseph M Connors, Sergey Alekseev, Árpád Illés, Marco Picardi, Ewa Lech-Maranda, Tatyana Feldman, Piotr Smolewski, Kerry J Savage, Nancy L Bartlett, Jan Walewski, Radhakrishnan Ramchandren, Pier Luigi Zinzani, Martin Hutchings, Javier Munoz, Hun Ju Lee, Won Seog Kim, Ranjana Advani, Stephen M Ansell, Anas Younes, Andrea Gallamini, Rachael Liu, Meredith Little, Keenan Fenton, Michelle Fanale, John Radford

ECHELON-1: Five-Year Update



- Five-year PFS was higher with brentuximab vedotin with doxorubicin, vinblastine and dacarbazine (A + AVD) than with doxorubicin, bleomycin, vinblastine and dacarbazine (ABVD) for both PET-2-negative and PET-2-positive patients.
- Peripheral neuropathy continued to improve or resolve over time with both A + AVD and ABVD; more patients had ongoing peripheral neuropathy in the A + AVD group than in the ABVD group (19% vs 9%).

Straus DJ et al. *Lancet Haematol* 2021;8(6):e410-21.

RTP RESEARCH TO PRACTICE

Brentuximab Vedotin Combination Significantly Improves Overall Survival in Newly Diagnosed Patients with Advanced Hodgkin Lymphoma

Press Release – February 3, 2022

"The phase 3 ECHELON-1 clinical trial demonstrated a statistically significant improvement in overall survival (OS) (p=0.009) in patients with advanced classical Hodgkin lymphoma (cHL) following treatment with brentuximab vedotin in combination with chemotherapy. With approximately six years median follow up, patients receiving brentuximab vedotin plus doxorubicin, vinblastine, and dacarbazine (A+AVD) in the frontline setting had a 41 percent reduction in the risk of death (HR 0.59; [95% CI: 0.396 to 0.879]) compared with patients receiving doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD). The safety profile of brentuximab vedotin was consistent with previous studies and no new safety signals were observed."

https://investor.seagen.com/press-releases/news-details/2022/ADCETRIS-Combination-Significantly-Improves-Overall-Survival-in-Newly-Diagnosed-Patients-with-Advanced-Hodgkin-Lymphoma/default.aspx

RTP RESEARCH TO PRACTICE

original reports

Brentuximab Vedotin Combined With Chemotherapy in Patients With Newly Diagnosed Early-Stage, Unfavorable-Risk Hodgkin Lymphoma

Anita Kumar, MD[1]; Carla Casulo, MD[2]; Ranjana H. Advani, MD[3]; Elizabeth Budde, MD[4]; Paul M. Barr, MD[2]; Connie L. Batlevi, MD, PhD[1]; Philip Caron, MD[1]; Louis S. Constine, MD[2]; Savita V. Dandapani, MD[4]; Esther Drill, MD[1]; Pamela Drullinsky, MD[1]; Jonathan W. Friedberg, MD[2]; Clare Grieve, BA[1]; Audrey Hamilton, MD[1]; Paul A. Hamlin, MD[1]; Richard T. Hoppe, MD[3]; Steven M. Horwitz, MD[1]; Ashlee Joseph, BA[1]; Niloufer Khan, MD[1]; Leana Laraque, BA[1]; Matthew J. Matasar, MD[1]; Alison J. Moskowitz, MD[1]; Ariela Noy, MD[1]; Maria Lia Palomba, MD[1]; Heiko Schöder, MD[1]; David J. Straus, MD[1]; Shreya Vemuri, BA[1]; Joanna Yang, MD[5]; Anas Younes, MD[6]; Andrew D. Zelenetz, MD, PhD[1]; Joachim Yahalom, MD[1]; and Craig H. Moskowitz, MD[7]

J Clin Oncol 2021;[Online ahead of print].

Multicenter Pilot Study of Brentuximab Vedotin (BV) and AVD with or without Consolidative Radiation Therapy for Early-Stage, Unfavorable-Risk Hodgkin Lymphoma

- Patients who achieved a negative end-of-therapy (EOT) PET-4 scan after 4 cycles of BV + AVD were studied with de-escalating radiation dose and field.

Clinical endpoint	Cohort 1 30-Gy ISRT (n = 29)	Cohort 2 20-Gy ISRT (n = 29)	Cohort 3 30-Gy CVRT (n = 29)	Cohort 4 No radiation (n = 29)	All patients (n = 114)
EOT CR rate	27 (93%)	29 (100%)	27 (93%)	28 (97%)	111 (96%)
2-year PFS rate	93.1%	96.6%	89.7%	96.6%	94%

"BV + AVD x four cycles is a highly active and well-tolerated treatment program for ES, unfavorable-risk Hodgkin lymphoma, including bulky disease. The efficacy of BV + AVD supports the safe reduction or elimination of consolidative radiation among PET-4–negative patients."

Kumar A et al. *J Clin Oncol* 2021;[Online ahead of print].

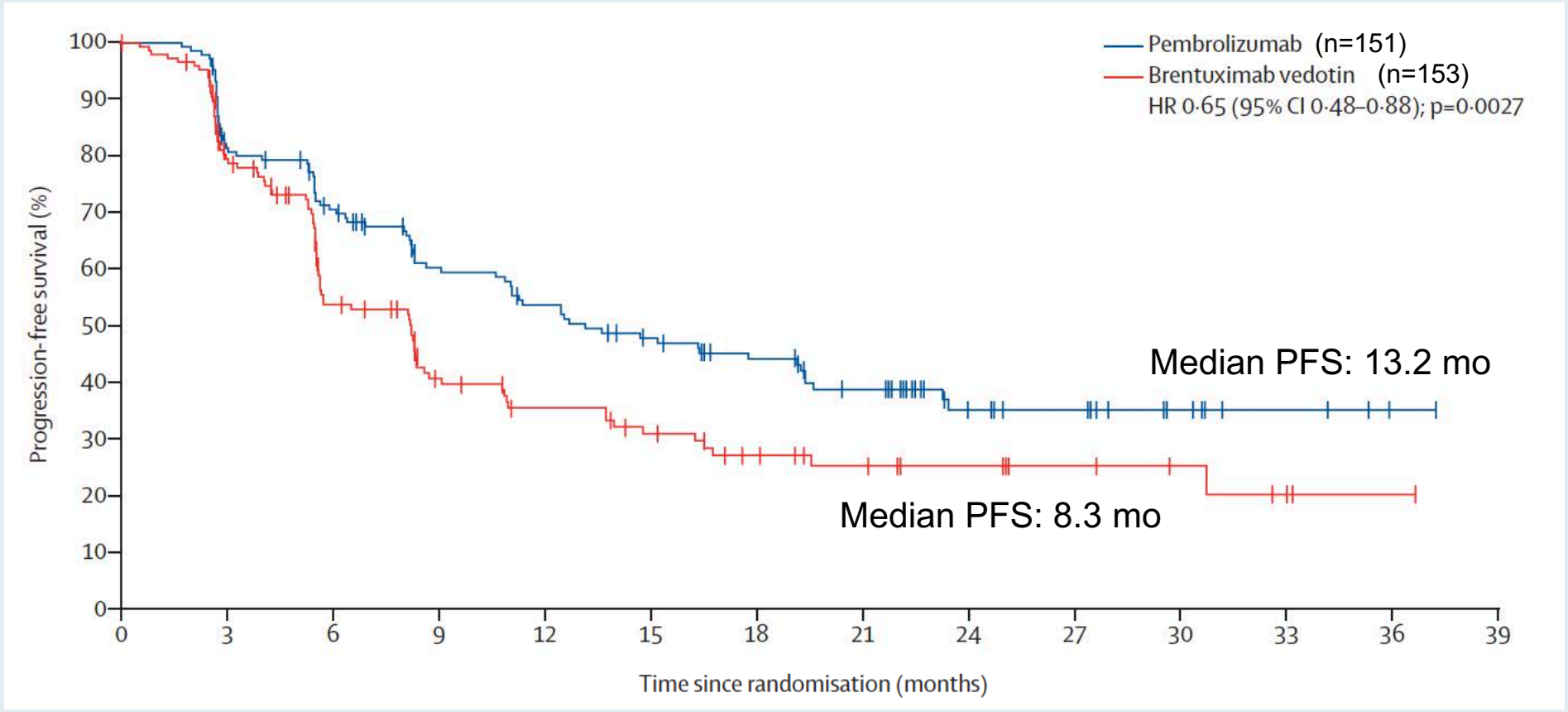
Articles

Lancet Oncol 2021;22(4):512-24.

Pembrolizumab versus brentuximab vedotin in relapsed or refractory classical Hodgkin lymphoma (KEYNOTE-204): an interim analysis of a multicentre, randomised, open-label, phase 3 study

*John Kuruvilla, Radhakrishnan Ramchandren, Armando Santoro, Ewa Paszkiewicz-Kozik, Robin Gasiorowski, Nathalie A Johnson, Laura Maria Fogliatto, Iara Goncalves, Jose S R de Oliveira, Valeria Buccheri, Guilherme F Perini, Neta Goldschmidt, Iryna Kriachok, Michael Dickinson, Mieczyslaw Komarnicki, Andrew McDonald, Muhit Ozcan, Naohiro Sekiguchi, Ying Zhu, Akash Nahar, Patricia Marinello, Pier Luigi Zinzani, on behalf of the KEYNOTE-204 investigators**

KEYNOTE-204: Interim Analysis



- The most common Grade 3-5 treatment-related AEs (TRAEs) in the pembrolizumab and brentuximab vedotin study arms included pneumonitis (4% vs 1%), neutropenia (2% vs 7%) and peripheral neuropathy (1% vs 3%).
- Serious TRAEs occurred in 16% of patients receiving pembrolizumab and 11% of patients receiving brentuximab vedotin.

Kuruvilla J et al. *Lancet Oncol* 2021;22(4):512-24.

RTP RESEARCH TO PRACTICE

Agenda

Module 1: Diffuse Large B-Cell Lymphoma (DLBCL)

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Module 3: Hodgkin Lymphoma

Module 4: Mantle Cell Lymphoma

Module 5: Follicular Lymphoma (FL)

FDA Approves Brexucabtagene Autoleucel for Relapsed or Refractory Mantle Cell Lymphoma

Press Release – July 24, 2020

"The Food and Drug Administration granted accelerated approval to brexucabtagene autoleucel, a CD19-directed genetically modified autologous T cell immunotherapy, for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL).

Approval was based on ZUMA-2 (NCT02601313), an open-label, multicenter, single-arm trial of 74 patients with relapsed or refractory MCL who had previously received anthracycline- or bendamustine-containing chemotherapy, an anti-CD20 antibody, and a Bruton tyrosine kinase inhibitor. Patients received a single infusion of brexucabtagene autoleucel following completion of lymphodepleting chemotherapy. The primary efficacy outcome measure was objective response rate (ORR) per Lugano [2014] criteria as assessed by an independent review committee."

www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-brexucabtagene-autoleucel-relapsed-or-refractory-mantle-cell-lymphoma

N Engl J Med 2020;382(14):1331-42

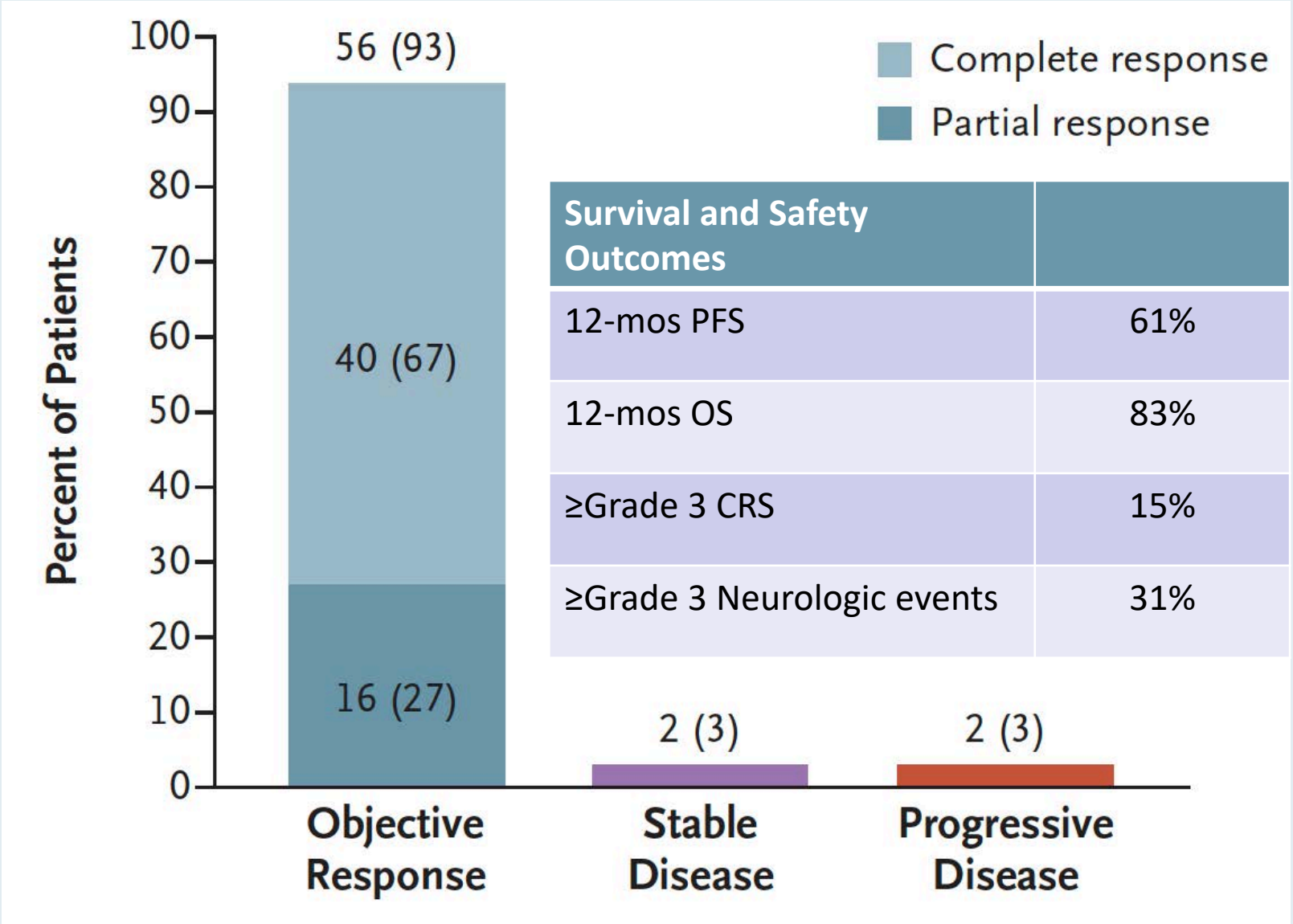
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

KTE-X19 CAR T-Cell Therapy in Relapsed or Refractory Mantle-Cell Lymphoma

M. Wang, J. Munoz, A. Goy, F.L. Locke, C.A. Jacobson, B.T. Hill, J.M. Timmerman, H. Holmes, S. Jaglowski, I.W. Flinn, P.A. McSweeney, D.B. Miklos, J.M. Pagel, M.-J. Kersten, N. Milpied, H. Fung, M.S. Topp, R. Houot, A. Beitinjaneh, W. Peng, L. Zheng, J.M. Rossi, R.K. Jain, A.V. Rao, and P.M. Reagan

ZUMA-2: Response Rates, Survival and Select Safety Outcomes with Brexucabtagene Autoleucel for Mantle Cell Lymphoma



Survival and Safety Outcomes	
12-mos PFS	61%
12-mos OS	83%
≥Grade 3 CRS	15%
≥Grade 3 Neurologic events	31%

Wang M et al. *N Engl J Med* 2020;382(14):1331-42.

Agenda

Module 1: Diffuse Large B-Cell Lymphoma (DLBCL)

Module 2: Chronic Lymphocytic Leukemia (CLL)

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Module 4: Mantle Cell Lymphoma

Module 5: Follicular Lymphoma (FL)

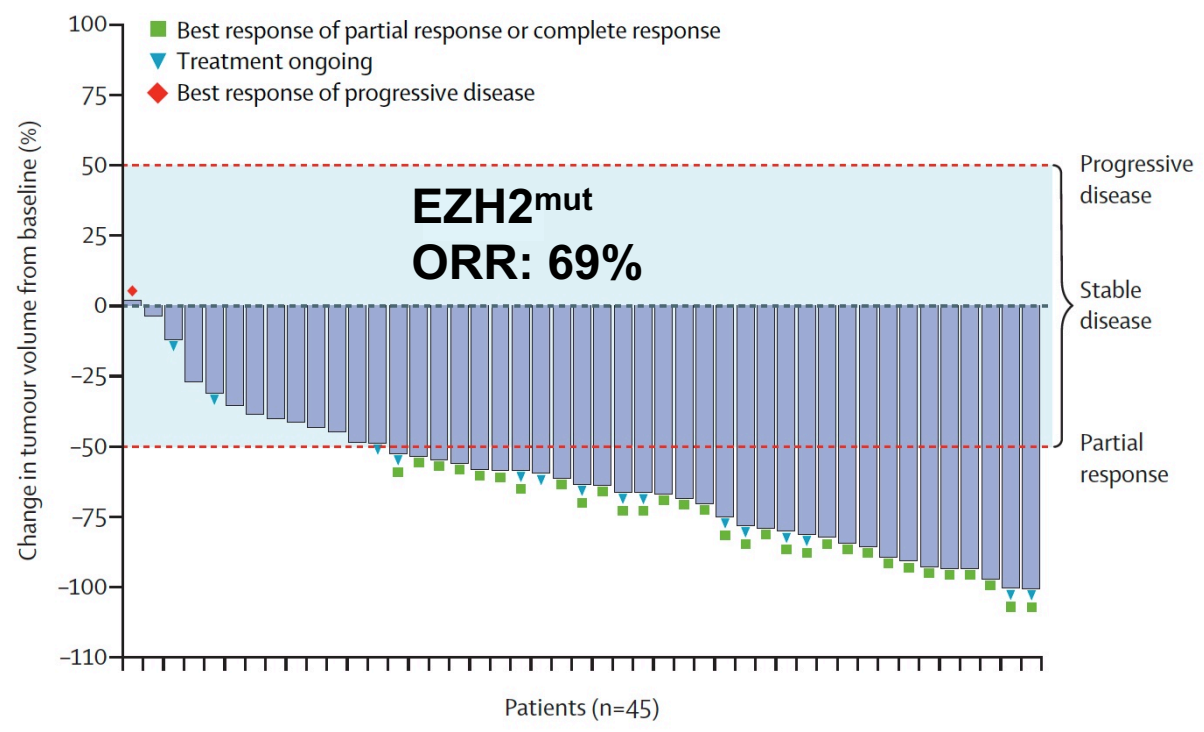
RTP RESEARCH TO PRACTICE

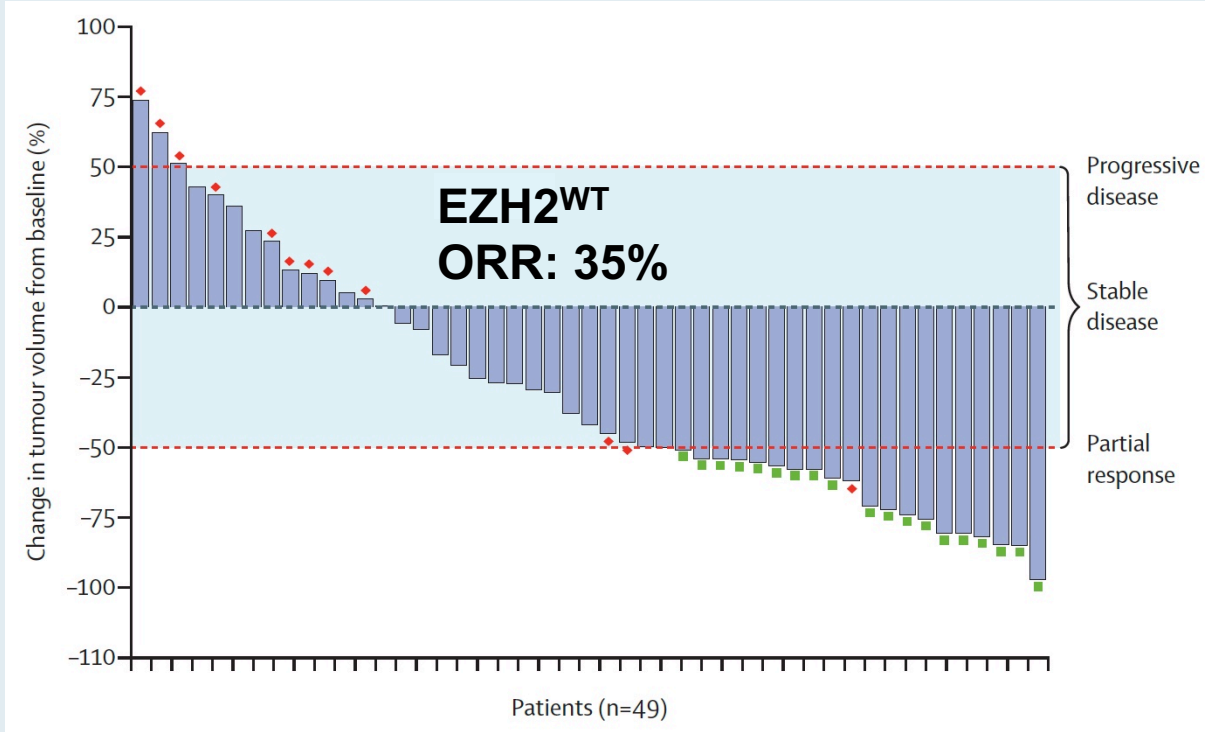
Lancet Oncol 2020;21(11):1433-42

Tazemetostat for patients with relapsed or refractory follicular lymphoma: an open-label, single-arm, multicentre, phase 2 trial

Franck Morschhauser, Hervé Tilly, Aristeidis Chaidos, Pamela McKay, Tycel Phillips, Sarit Assouline, Connie Lee Batlevi, Phillip Campbell, Vincent Ribrag, Gandhi Laurent Damaj, Michael Dickinson, Wojciech Jurczak, Maciej Kazmierczak, Stephen Opat, John Radford, Anna Schmitt, Jay Yang, Jennifer Whalen, Shefali Agarwal, Deyaa Adib, Gilles Salles

Response to Tazemetostat in Patients with R/R FL and an EZH2 Mutation or EZH2 Wild-Type Tumors





Morschhauser F et al. *Lancet Oncol* 2020;21(11):1433-42.

RTP RESEARCH TO PRACTICE

Approved PI3K Inhibitors for FL: Indication and Dosing

	Idelalisib[1]	Copanlisib[2]	Duvelisib[3]	Umbralisib[4]
Mechanism of action	Selective PI3Kδ inhibitor	Dual inhibitor of PI3Kδ,α	Dual inhibitor of PI3Kδ,γ	Dual inhibitor of PI3Kδ and casein kinase CK1ε
Indication	Relapsed FL after at least 2 prior systemic therapies	Relapsed FL after at least 2 prior systemic therapies	R/R FL after at least 2 prior systemic therapies	R/R FL after at least 3 prior systemic therapies
Dosing	150 mg orally, twice daily	60 mg as a 1-hour IV infusion weekly (3 weeks on, 1 week off)	25 mg orally, twice daily	800 mg orally, once daily

[1] Gopal AK et al. *N Engl J Med* 2014;370(11):1008-18; Idelalisib package insert, January 2018.
[2] Dreyling M et al. *J Clin Oncol* 2017;35(35):3898-905; Copanlisib package insert, September 2017.
[3] Flinn IW et al. *J Clin Oncol* 2019;[Epub ahead of print]; Zinzani PL et al. EHA 2017;Abstract S777; Duvelisib package insert, September 2018. [4] Umbralisib package insert, February 2021.

Duvelisib Indication in R/R FL Withdrawn

Press Release – December 6, 2021

"A United States indication for duvelisib in previously treated relapsed/refractory follicular lymphoma has been voluntarily withdrawn by developer Secura Bio following an assessment of the drug and subsequent consultation with the FDA.

Secura Bio has voluntarily withdrawn an indication for duvelisib in the United States for the treatment of patients with relapsed/refractory follicular lymphoma who have undergone treatment with 2 prior therapies after assessing the drug and holding discussion with the FDA, according to a press release from the company.

These measures highlighted that the cost, logistics, and timing of the post-marketing requirements were no longer merited. Duvelisib will continue to be developed for patients with T-cell lymphoma. In September 2018, duvelisib received accelerated approval by the FDA, but a confirmatory trial was required before it was given full approval. The decision to withdraw the indication does not affect other approved indications.

The initial approval was based on findings from the phase 3 DUO trial (NCT02004522) and the phase 2 DYNAMO trial (NCT01882803)."

https://www.cancernetwork.com/view/duvelisib-indication-in-relapsed-refractory-follicular-lymphoma-withdrawn-in-u-s-market

Idelalisib for Relapsed FL and SLL Voluntarily Withdrawn

Press Release – January 18, 2022

"Without confirmed clinical benefit in follicular lymphoma and small lymphocytic leukemia, idelalisib's indications for these malignancies were withdrawn from the United States market.

The developer of idelalisib, Gilead, has announced the withdrawal of 2 indications for the agent from the United States (US), according to a press release. Idealisib will no longer be available for the treatment of relapsed follicular B-cell non-Hodgkin lymphoma (FL) and relapsed small lymphocytic leukemia (SLL).

FDA accelerated approval was previously granted to idelalisib for the treatment of both malignancies based on results from a phase 2 clinical trial of patients with indolent Hodgkin lymphoma.

Although these data from the DELTA study were promising, continued FDA approval of idelalisib for the treatment of relapsed FL and SLL was contingent upon a positive confirmatory study, and this was not achieved. Withdrawal of idelalisib from the US market for relapsed FL and SLL does not impact other idelalisib indications."

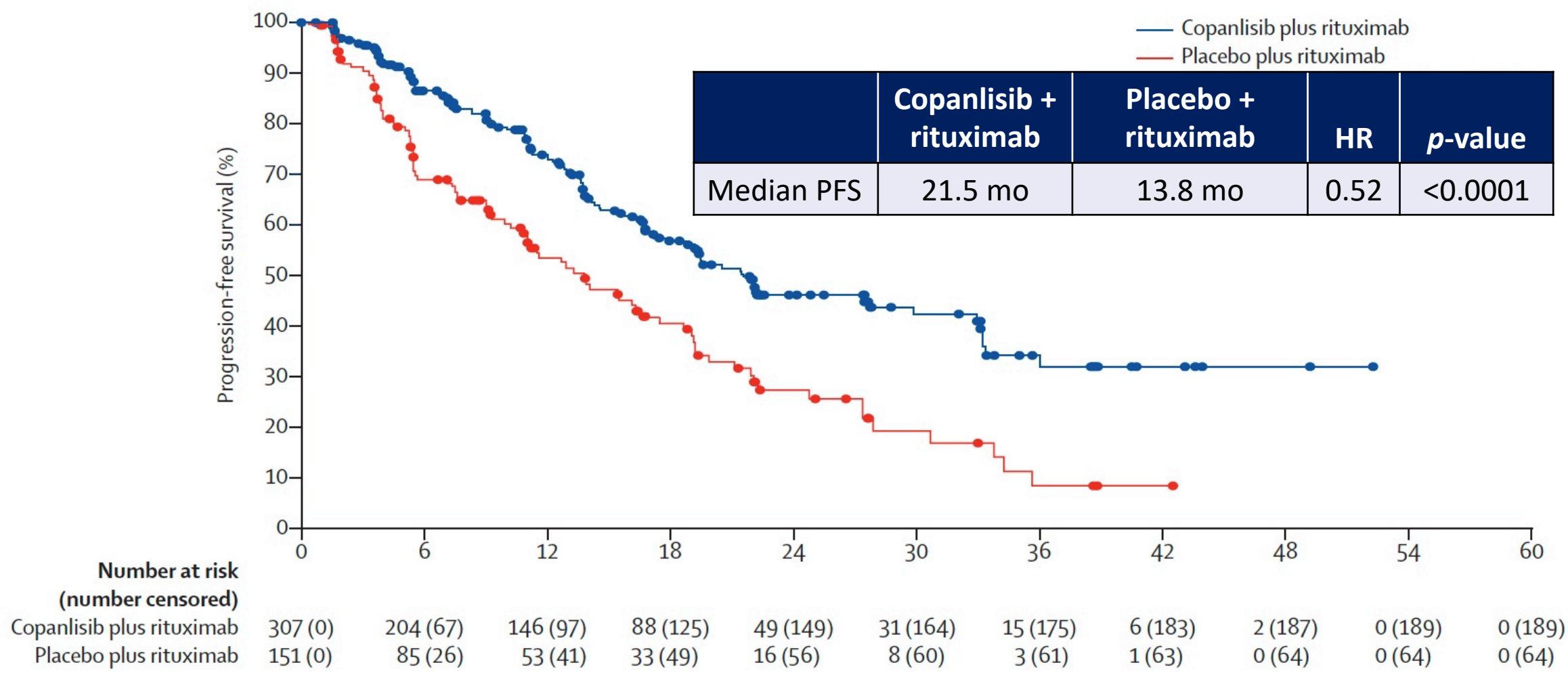
https://www.targetedonc.com/view/idelalisib-for-relapsed-fl-and-sll-voluntarily-withdrawn-from-us-market

Lancet Oncol 2021;22(5):678-89

Copanlisib plus rituximab versus placebo plus rituximab in patients with relapsed indolent non-Hodgkin lymphoma (CHRONOS-3): a double-blind, randomised, placebo-controlled, phase 3 trial

Matthew J Matasar, Marcelo Capra, Muhit Özcan, Fangfang Lv, Wei Li, Eduardo Yañez, Katya Sapunarova, Tongyu Lin, Jie Jin, Wojciech Jurczak, Aryan Hamed, Ming-Chung Wang, Ross Baker, Igor Bondarenko, Qingyuan Zhang, Jifeng Feng, Klaus Geissler, Mihaela Lazaroiu, Guray Saydam, Árpád Szomor, Krimo Bouabdallah, Rinat Galiulin, Toshiki Uchida, Lidia Mongay Soler, Anjun Cao, Florian Hiemeyer, Aruna Mehra, Barrett H Childs, Yuankai Shi, Pier Luigi Zinzani

CHRONOS-3: PFS in Relapsed/Refractory (R/R) Indolent Non-Hodgkin Lymphoma (NHL)



	Copanlisib + rituximab	Placebo + rituximab	HR	*p*-value
Median PFS	21.5 mo	13.8 mo	0.52	<0.0001

Matasar MJ et al. *Lancet Oncol* 2021;22(5):678-89.

FDA Grants Accelerated Approval to Umbralisib for Marginal Zone Lymphoma and Follicular Lymphoma

Press Release – February 5, 2021

"On February 5, 2021, the Food and Drug Administration granted accelerated approval to umbralisib, a kinase inhibitor including PI3K-delta and casein kinase CK1-epsilon, for the following indications:

- Adult patients with relapsed or refractory marginal zone lymphoma (MZL) who have received at least one prior anti-CD20-based regimen;
- Adult patients with relapsed or refractory follicular lymphoma (FL) who have received at least three prior lines of systemic therapy.

Approval was based on two single-arm cohorts of an open-label, multi-center, multi-cohort trial, UTX-TGR-205 (NCT02793583), in 69 patients with MZL who received at least one prior therapy, including an anti-CD20 containing regimen, and in 117 patients with FL after at least 2 prior systemic therapies. Patients received umbralisib 800 mg orally once daily until disease progression or unacceptable toxicity.

Efficacy was based on overall response rate (ORR) and duration of response (DOR) using modified 2007 International Working Group criteria assessed by an independent review committee."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-umbralisib-marginal-zone-lymphoma-and-follicular-lymphoma

RTP RESEARCH TO PRACTICE

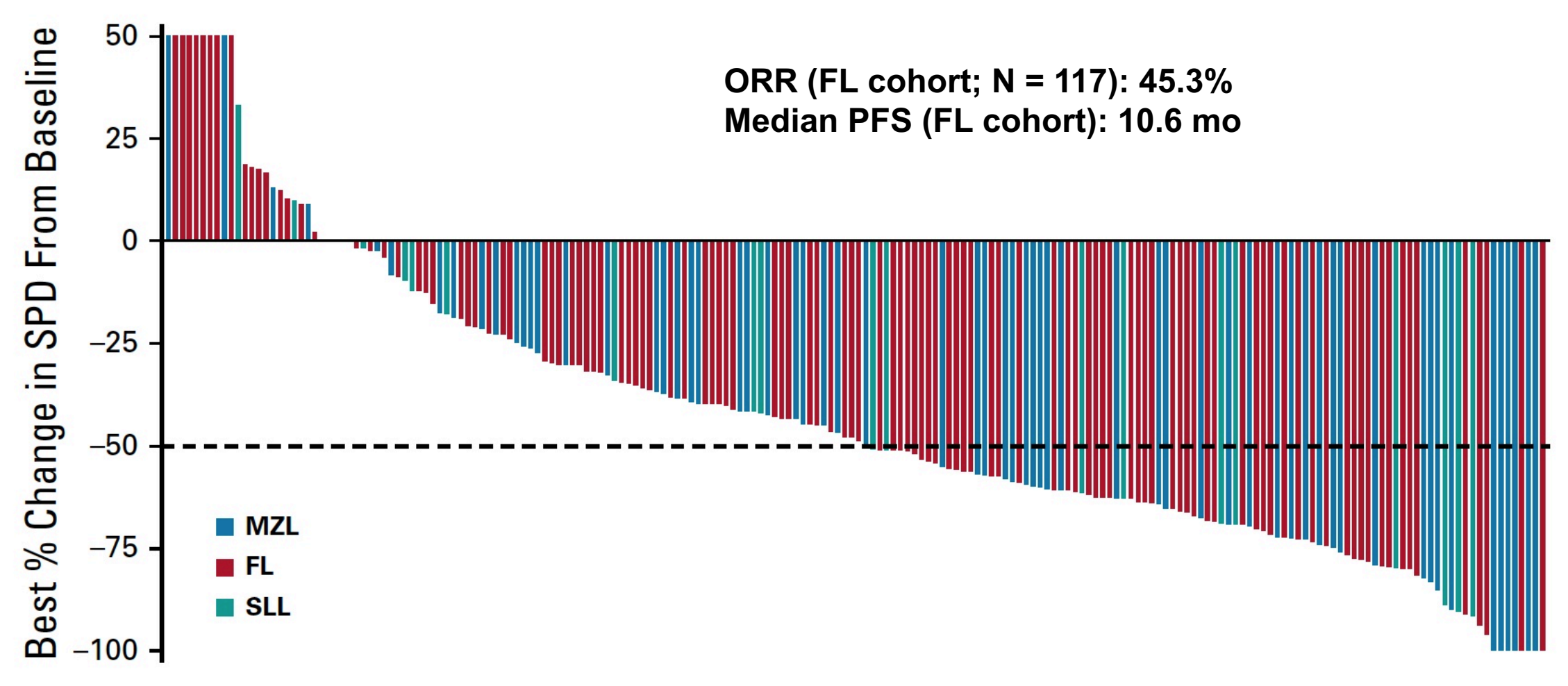
rapid communications

Umbralisib, a Dual PI3Kδ/CK1ε Inhibitor in Patients With Relapsed or Refractory Indolent Lymphoma

Nathan H. Fowler, MD[1]; Felipe Samaniego, MD[1]; Wojciech Jurczak, MD, PhD[2]; Nilanjan Ghosh, MD, PhD[3]; Enrico Derenzini, MD[4,5]; James A. Reeves, MD[6]; Wanda Knopińska-Posłuszny, MD[7]; Chan Y. Cheah, DMSc[8]; Tycel Phillips, MD[9]; Ewa Lech-Maranda, MD, PhD[10]; Bruce D. Cheson, MD[11]; Paolo F. Caimi, MD[12]; Sebastian Grosicki, MD, PhD[13]; Lori A. Leslie, MD[14]; Julio C. Chavez, MD[15]; Gustavo Fonseca, MD[16]; Sunil Babu, MD[17]; Daniel J. Hodson, MD[18]; Spencer H. Shao, MD[19]; John M. Burke, MD[20]; Jeff P. Sharman, MD[21]; Jennie Y. Law, MD[22]; John M. Pagel, MD, PhD[23]; Hari P. Miskin, MSc[24]; Peter Sportelli, BS[24]; Owen A. O'Connor, MD, PhD[24,25]; Michael S. Weiss, JD[24]; and Pier Luigi Zinzani, MD, PhD[26,27]

J Clin Oncol 2021;39(15):1609-18

Umbralisib for Heavily Pretreated R/R Indolent NHL



Fowler NH et al. *J Clin Oncol* 2021;39(15):1609-18.

RTP RESEARCH TO PRACTICE

FDA Grants Accelerated Approval to Axicabtagene Ciloleucel for Relapsed or Refractory Follicular Lymphoma

Press Release – March 5, 2021

"The Food and Drug Administration granted accelerated approval to axicabtagene ciloleucel for adult patients with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy.

Approval in FL was based on a single-arm, open-label, multicenter trial (ZUMA-5; NCT03105336) that evaluated axicabtagene ciloleucel, a CD19-directed chimeric antigen receptor (CAR) T cell therapy, in adult patients with relapsed or refractory FL after two or more lines of systemic therapy, including the combination of an anti-CD20 monoclonal antibody and an alkylating agent. Following lymphodepleting chemotherapy, axicabtagene ciloleucel was administered as a single intravenous infusion.

The main efficacy measures were objective response rate (ORR) and duration of response (DOR) as determined by an independent review committee."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-axicabtagene-ciloleucel-relapsed-or-refractory-follicular-lymphoma

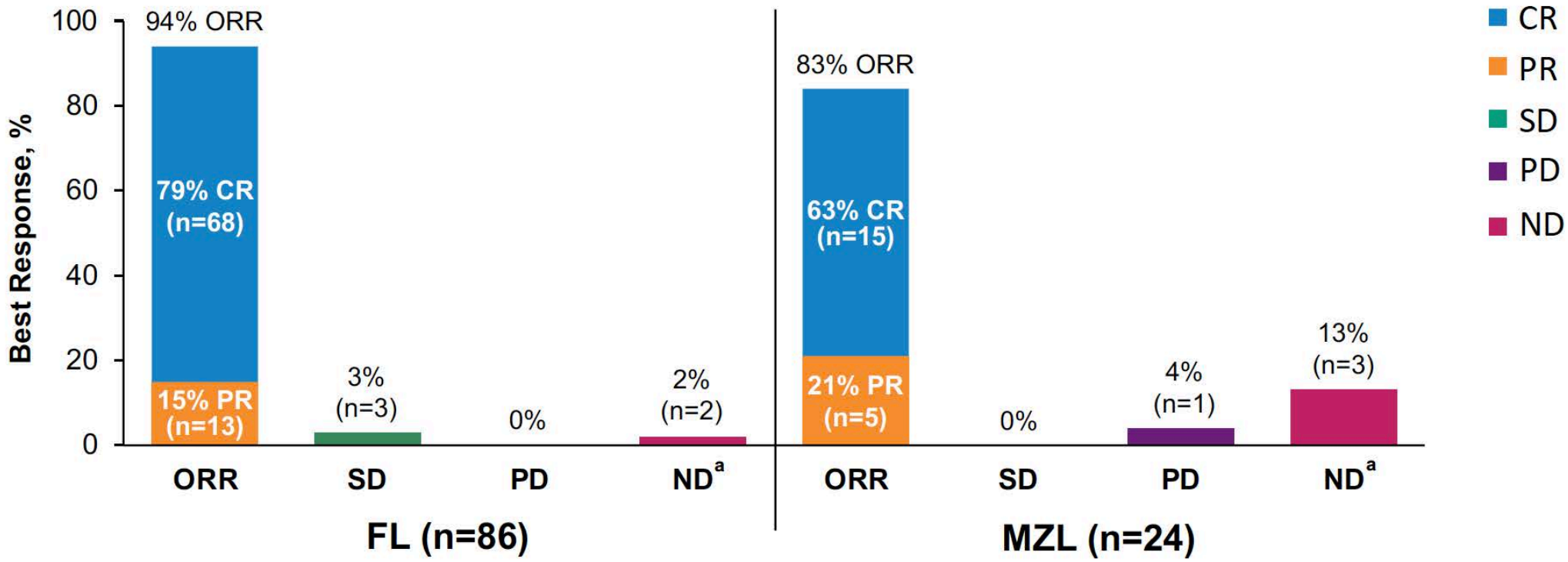
Long-Term Follow-Up Analysis of ZUMA-5: A Phase 2 Study of Axicabtagene Ciloleucel (Axi-Cel) in Patients With Relapsed/Refractory Indolent Non-Hodgkin Lymphoma

Sattva S. Neelapu, MD[1]*; Julio C. Chavez, MD[2]*; Alison R. Sehgal, MD[3]; Narendranath Epperla, MD, MS[4]; Matthew Ulrickson, MD[5]; Emmanuel Bachy, MD, PhD[6]; Pashna N. Munshi, MD[7]; Carla Casulo, MD[8]; David G. Maloney, MD, PhD[9]; Sven de Vos, MD, PhD[10]; Ran Reshef, MD[11]; Lori A. Leslie, MD[12]; Olalekan O. Oluwole, MD, MPH, MBBS[13]; Ibrahim Yakoub-Agha, MD, PhD[14]; Rashmi Khanal, MD[15]; Joseph Rosenblatt, MD[16]; Marika Sherman, MSHS[17]; Jinghui Dong, PhD[17]; Alessandro Giovanetti, BSc[17]; Yin Yang, MD, PhD[17]; Christine Lui, MS[17]; Zahid Bashir, MBBS; MS[17]; A. Scott Jung, MD[17]; and Caron A. Jacobson, MD[18]

[1]The University of Texas MD Anderson Cancer Center, Houston, Texas, USA; [2]University of South Florida H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA; [3]UPMC Hillman Cancer Center, Pittsburgh, PA, USA; [4]The Ohio State University Comprehensive Cancer Center, Columbus, OH, USA; [5]Banner MD Anderson Cancer Center, Gilbert, AZ, USA; [6]Centre Hospitalier Lyon Sud, Pierre-Bénite, France; [7]Georgetown Lombardi Comprehensive Cancer Center, Washington, DC, USA; [8]University of Rochester Medical Center - James P. Wilmot Cancer Center, Rochester, NY, USA; [9]Fred Hutchinson Cancer Research Center, Seattle, WA, USA; [10]Ronald Reagan University of California Los Angeles Medical Center, Santa Monica, CA, USA; [11]Columbia University Herbert Irving Comprehensive Cancer Center, New York City, NY, USA; [12]John Theurer Cancer Center, Hackensack, NJ, USA; [13]Vanderbilt University Medical Center, Nashville, TN, USA; [14]CHU de Lille, Univ Lille, INSERM U1286, Infinite, 59000 Lille, France; [15]Fox Chase Cancer Center, Philadelphia, PA, USA [16]University of Miami Sylvester Comprehensive Cancer Center, Miami, FL, USA; [17]Kite, a Gilead Company, Santa Monica, CA, USA; and [18]Dana-Farber Cancer Institute, Boston, MA, USA
**Equal contributors*

ASH 2021;Abstract 93.

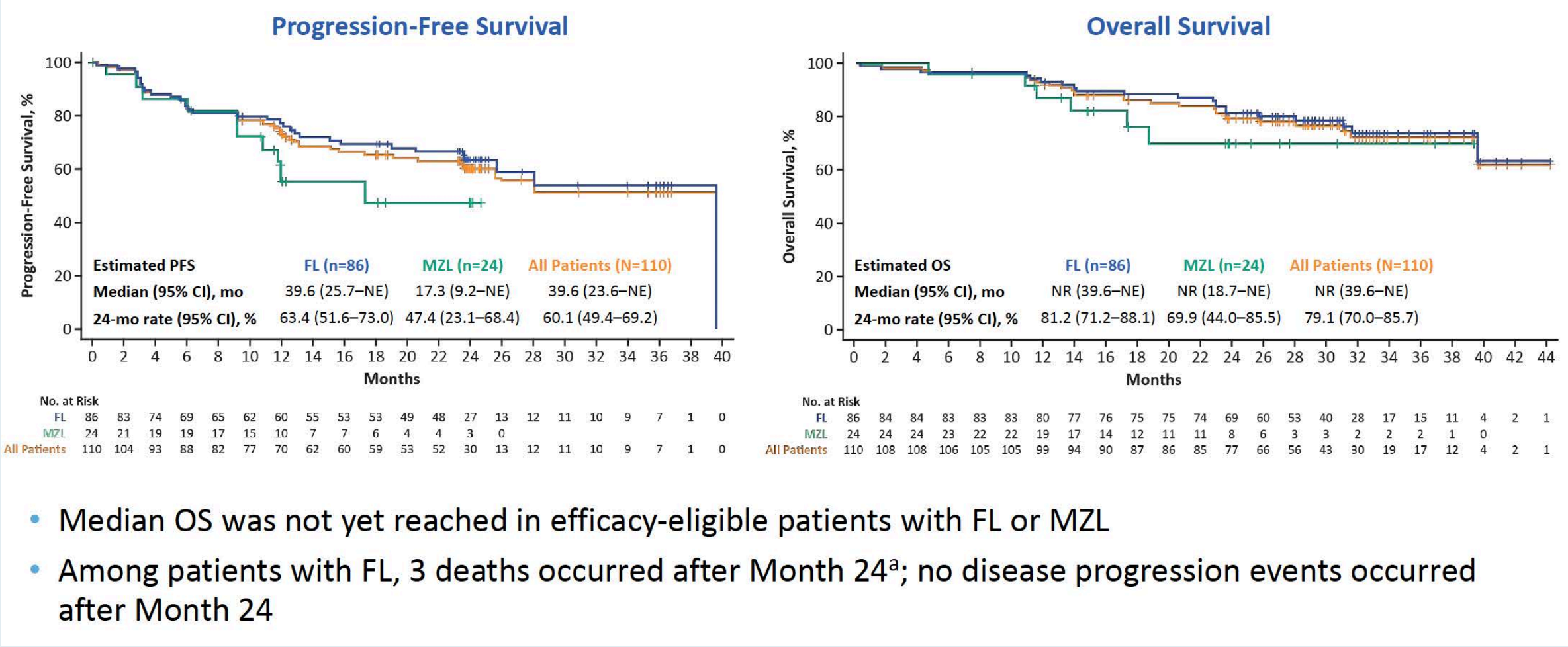
ZUMA-5: Overall Response Rate (ORR) by Central Review



- Among efficacy-eligible patients with iNHL (n=110), the ORR was 92% (95% CI, 85–96), with a 75% CR rate
- Among all treated patients with iNHL (n=149), the ORR was 92% (95% CI, 86–96), with a 77% CR rate

Neelapu SS et al. ASH 2021;Abstract 93.

ZUMA-5: PFS and Overall Survival



- Median OS was not yet reached in efficacy-eligible patients with FL or MZL
- Among patients with FL, 3 deaths occurred after Month 24[a]; no disease progression events occurred after Month 24

Neelapu SS et al. ASH 2021;Abstract 93.

ZUMA-5: AEs with First Occurrence After Primary Analysis Data Cutoff

AE, n (%)	Follicular Lymphoma (N=124)		Marginal Zone Lymphoma (N=25)		All Patients (N=149)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any AE	27 (22)	14 (11)	11 (44)	6 (24)	38 (26)	20 (13)
Serious AE	11 (9)	11 (9)	4 (16)	4 (16)	15 (10)	15 (10)
Cytopenia	8 (6)	4 (3)	3 (12)	3 (12)	11 (7)	7 (5)
Infection	18 (15)	7 (6)	7 (28)	4 (16)	25 (17)	11 (7)
CRS	0 (0)	0 (0)	2 (8)	0 (0)	2 (1)	0 (0)
Neurologic event	0 (0)	0 (0)	2 (8)	0 (0)	2 (1)	0 (0)
Hypogammaglobulinemia	2 (2)	0 (0)	2 (8)	0 (0)	4 (3)	0 (0)
Tumor lysis syndrome	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

- Grade 5 AEs occurred in 6 patients after the data cutoff of the primary analysis[b]
  - Grade 5 infectious AEs occurred in 5 patients: 1 COVID-19 (FL, Day 717, unrelated), 1 COVID-19 pneumonia (FL, Day 780, related to axi-cel), 1 PML[c] (FL, Day 697, related to axi-cel and CC) and 2 sepsis (FL, Day 1204; MZL, Day 139; both unrelated)
  - Acute bilineal leukemia occurred in 1 patient (FL, Day 623, CC related)

[a] Includes all AEs that occurred after the primary analysis data cutoff date (March 12, 2020) and by the data cutoff date of the current analysis (March 31, 2021). [b] No Grade 5 AEs were due to progressive disease.
[c] The Grade 5 PML event occurred after axi-cel retreatment.

Neelapu SS et al. ASH 2021;Abstract 93.

Efficacy of Tisagenlecleucel in Adult Patients with High-Risk Relapsed/Refractory Follicular Lymphoma: Subgroup Analysis of the Phase II ELARA Study

Catherine Thieblemont,[1] Michael Dickinson,[2] Joaquin Martinez-Lopez,[3] Arne Kolstad,[4] Jason P. Butler,[5] Monalisa Ghosh,[6] Leslie L. Popplewell,[7] Julio C. Chavez,[8] Emmanuel Bachy,[9] Koji Kato,[10] Hideo Harigae,[11] Marie José Kersten,[12] Charalambos Andreadis,[13] Peter A. Riedell,[14] P. Joy Ho,[15] José Antonio Pérez-Simón,[16] Andy I. Chen,[17] Loretta J. Nastoupil,[18] Bastian von Tresckow,[19] Andrés José María Ferreri,[20] Takanori Teshima,[21] Piers EM Patten,[22] Joseph P. McGuirk,[23] Andreas Petzer,[24] Fritz Offner,[25] Andreas Viardot,[26] Pier Luigi Zinzani,[27] Ram Malladi,[28] Aiesha Zia,[29] Chiara Lobetti Bodoni,[29] Aisha Masood,[30] Stephen J. Schuster,[31] Nathan H. Fowler,[32] Martin H. Dreyling,[33]

[1]Department of Hemato-Oncology, Saint Louis Hospital, Paris, France; [2]Department of Clinical Haematology, Peter MacCallum Cancer Centre and The Royal Melbourne Hospital, Melbourne, Australia; [3]Centro de Investigación Biomédica en Red Cáncer (CIBERONC), Hospital Universitario 12 de Octubre, Complutense University, CNIO, Madrid, Spain; [4]Oslo University Hospital Radiumhospitalet, Oslo, Norway; [5]Royal Brisbane and Women's Hospital, Brisbane, Australia; [6]Michigan Medicine University of Michigan, Ann Arbor, MI, USA; [7]Department of Hematology/HCT, City of Hope National Medical Centre, Duarte, CA, USA; [8]Division of Malignant Hematology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA; [9]Hospices Civils de Lyon and Université Claude Bernard, Pierre-Bénite, France; [10]Kyushu University Hospital, Fukuoka, Japan; [11]Tohoku University Hospital, Sendai, Japan; [12]Amsterdam UMC, Department of Hematology, Amsterdam UMC, University of Amsterdam, Amsterdam, Netherlands; [13]Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco, San Francisco, CA, USA; [14]The University of Chicago Medical Center, Chicago, IL, USA; [15]Royal Prince Alfred Hospital and Department of Medicine, The University of Sydney, Sydney, Australia; [16]Department of Hematology, Hospital Universitario Virgen del Rocio, Instituto de Biomedicina de Sevilla (IBIS)/CSIC/Universidad de Sevilla, Spain, Sevilla, Spain; [17]Oregon Health and Science University, Portland, OR, USA; [18]Department of Lymphoma and Myeloma, The University of Texas, MD Anderson Cancer Center, Houston, TX, USA; [19]University of Cologne, Cologne, Germany; [20]Lymphoma Unit, Department of Onco-Haematology, IRCCS San Raffaele Scientific Institute, Milano, Italy; [21]Department of Hematology, Hokkaido University Hospital, Sapporo, Japan; [22]Department of Haematological Medicine, King's College Hospital, London, UK; [23]Division of Hematologic Malignancies & Cellular Therapeutics, University of Kansas Medical Center, Kansas City, KS, USA; [24]Internal Medicine I, Ordensklinikum Linz GmbH Elisabethinen, Linz, Austria; [25]University Hospital Ghent, Gent, Belgium; [26]Department of Internal Medicine III, University Hospital of Ulm, Ulm, Germany; [27]Institute of Hematology "L. e A. Seràgnoli", University of Bologna, Bologna, Italy; [28]Cambridge University Hospitals NHS Foundation Trust, Cambridge, CA, UK; [29]Novartis Pharma AG, Basel, Switzerland; [30]Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; [31]Lymphoma Program, Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA, USA; [32]Lymphoma and Myeloma, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [33]Klinikum Der Universität München-Grosshadern, Medizinische Klinik und Poliklinik III, München, Germany

Thieblemont C et al. ASH 2021;Abstract 131.

ELARA: Efficacy Analysis with Extended Follow-Up

- As of March 29, 2021, 97 patients received tisagenlecleucel and 94 were evaluable for efficacy
- CR rates are consistent and durable for the interim, primary analyses, and this extended follow-up analysis
- Complete response correlated with durability and prolonged PFS
  - **Among patients who achieved CR, 12-month PFS was 85.5% (95% CI, 74-92) and estimated DOR rate at 9 months was 86.5% (95% CI, 75-93)**

Efficacy Results of Extended Follow-up Analysis

Endpoint	% (95% CI)
ORR[a]	**86.2** (77.5-92.4)
CRR[a]	**69.1** (58.8-78.3)
12-mo PFS	**67.0** (56.0-75.8)
9-mo DOR	**76.0** (64.6-84.2)

[a]ORR and CRR were comparable with the primary efficacy analysis (ORR 86.2% and CRR 66.0%).

Thieblemont C et al. ASH 2021;Abstract 131.

Thank you for joining us!

CME and MOC 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 North Carolina Oncology Association and the South Carolina Oncology Society

A CME/MOC- and NCPD-Accredited Event

Saturday, February 12, 2022
8:30 AM – 4:00 PM ET

RTP
RESEARCH
TO PRACTICE

Agenda

Module 1 — Chronic Lymphocytic Leukemia and Lymphomas: *Drs Flinn and LaCasce*

Module 2 — Multiple Myeloma: *Drs Callander and Rajkumar*

Module 3 — Genitourinary Cancers: *Drs Dreicer and Heath*

Module 4 — Breast Cancer: *Drs Borges and Jhaveri*

Module 5 — Gastrointestinal Cancers: *Drs Hochster and Messersmith*

Module 6 — Lung Cancer: *Drs Govindan and Johnson*

Multiple Myeloma Faculty

Natalie S Callander, MD
Professor of Medicine
Director, Myeloma Clinical Program
Interim Director, Bone Marrow Transplant Program
University of Wisconsin Carbone Cancer Center
Madison, Wisconsin

S Vincent Rajkumar, MD
Edward W and Betty Knight Scripps
Professor of Medicine
Mayo Clinic
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MODULE 2: Multiple Myeloma

Co-Moderator

Suzanne R Fanning, DO
Director, Blood and Marrow Transplant Program
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TO PRACTICE

Contributing General Medical Oncologists

Jennifer L Dallas, MD
Novant Health Cancer Institute
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Joanna Metzner-Sadurski, MD
Self Regional Healthcare Cancer Center
Greenwood, South Carolina

Justin Peter Favaro, MD, PhD
Oncology Specialists of Charlotte
Charlotte, North Carolina

William R Mitchell, MD
Southern Oncology Specialists
Charlotte, North Carolina

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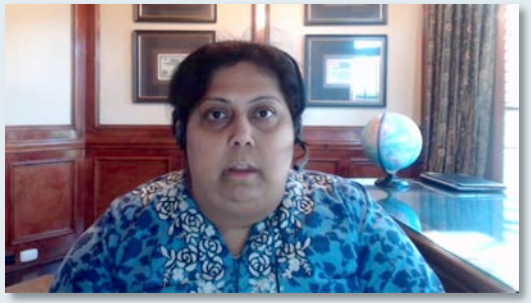
Contributing General Medical Oncologists



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RTP RESEARCH TO PRACTICE

Agenda

Module 1: Treatment of MM in Transplant-Ineligible Patients

Module 2: Treatment of MM in Transplant-Eligible Patients

Module 3: Management of Relapsed/Refractory MM

Module 4: BCMA CAR T-Cell Therapy

Module 5: Other Novel Agents and Strategies

Agenda

Module 1: Treatment of MM in Transplant-Ineligible Patients

Module 2: Treatment of MM in Transplant-Eligible Patients

Module 3: Management of Relapsed/Refractory MM

Module 4: BCMA CAR T-Cell Therapy

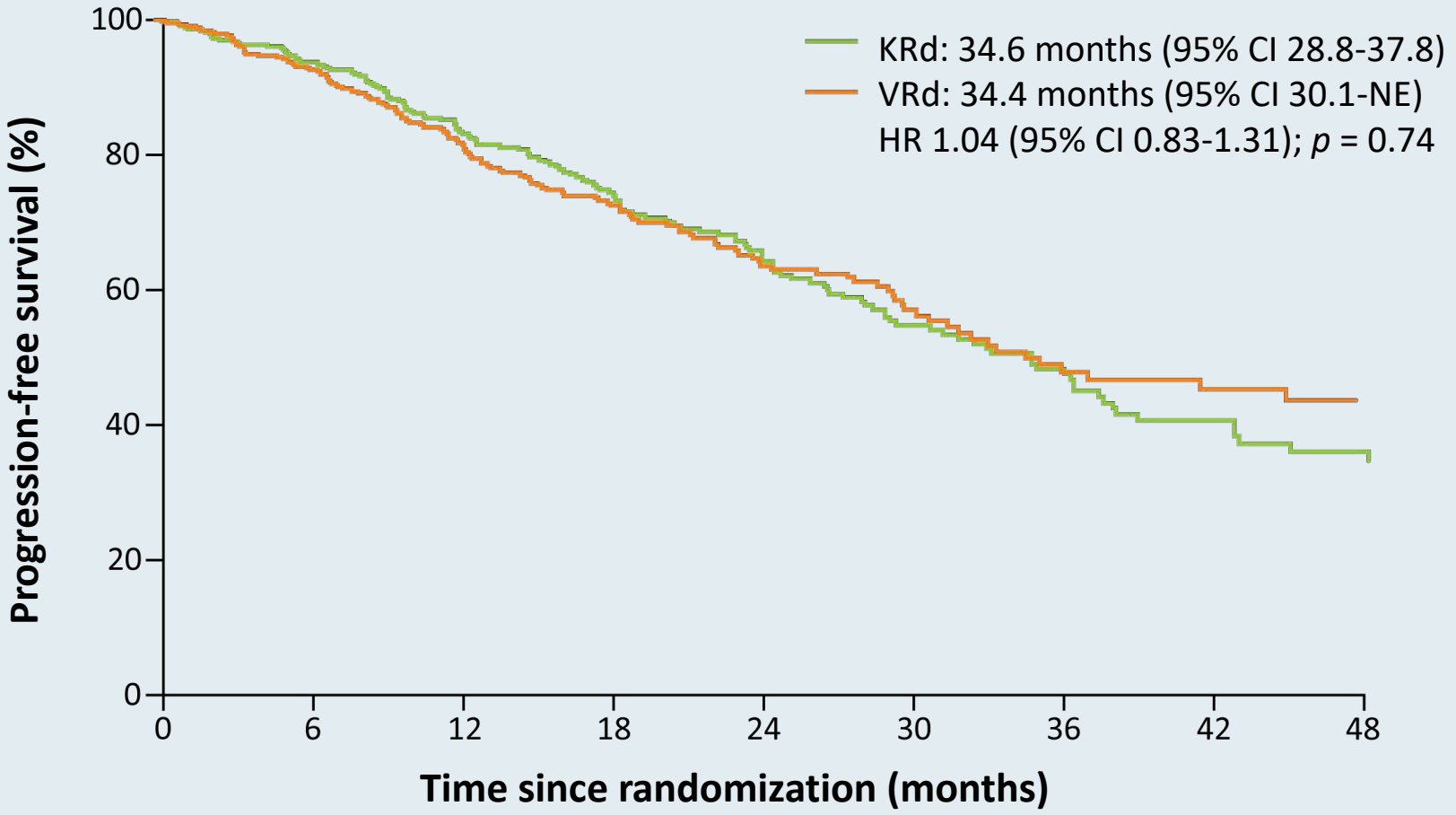
Module 5: Other Novel Agents and Strategies

Carfilzomib or bortezomib in combination with lenalidomide and dexamethasone for patients with newly diagnosed multiple myeloma without intention for immediate autologous stem-cell transplantation (ENDURANCE): a multicentre, open-label, phase 3, randomised, controlled trial

Shaji K Kumar, Susanna J Jacobus, Adam D Cohen, Matthias Weiss, Natalie Callander, Avina K Singh, Terri L Parker, Alexander Menter, Xuezhong Yang, Benjamin Parsons, Pankaj Kumar, Prashant Kapoor, Aaron Rosenberg, Jeffrey A Zonder, Edward Faber Jr, Sagar Lonial, Kenneth C Anderson, Paul G Richardson, Robert Z Orlowski, Lynne I Wagner, S Vincent Rajkumar

***Lancet Oncol* 2020;21(10):1317-30**

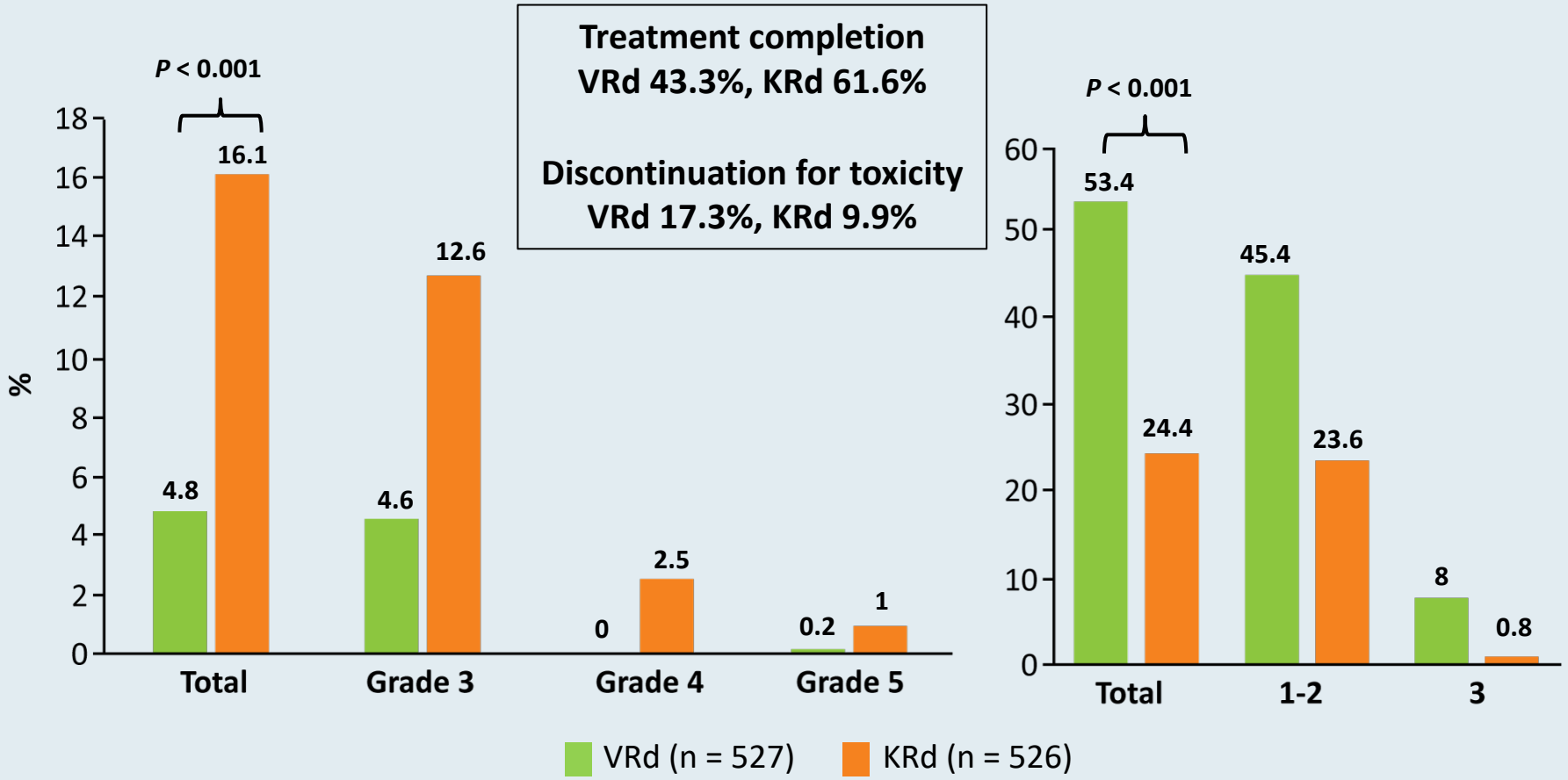
ENDURANCE (E1A11): Primary Progression-Free Survival Endpoint (Second Interim Analysis)



- Median overall survival has not been reached in either group at median follow-up of 24 months; patients will continue on long-term follow-up for overall survival

Kumar SK et al. *Lancet Oncol* 2020;21(10):1317-30.

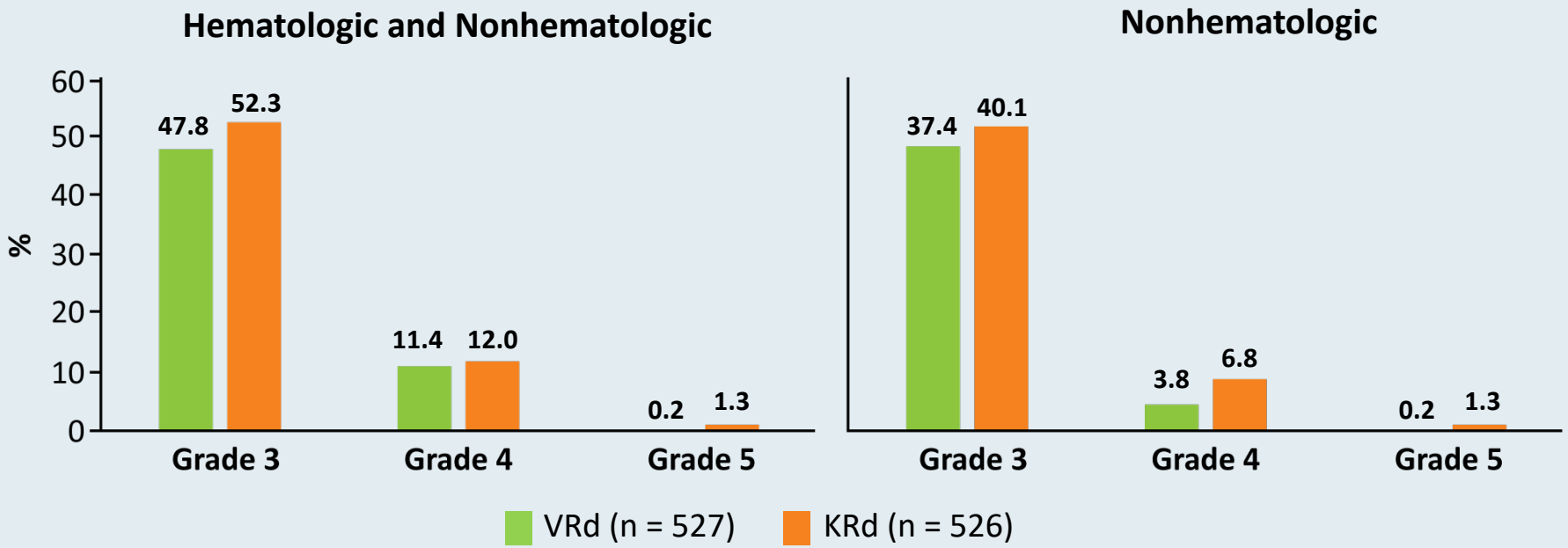
ENDURANCE (E1A11): Treatment-Emergent Adverse Events of Interest



* Grades 1-2 not required reporting

Berdeja JG. ASCO 2020 Discussant.

ENDURANCE (E1A11): Treatment-Related Adverse Events



Step 1 treated patients	VRd (n = 527)	KRd (n = 526)		
Rates	N (%)	N (%)	Diff KRd-VRd	Chi-sq *p*-value
Grade 3-5	313 (59.4)	345 (65.6)	6.2	0.038
(95% CI)	(55.1-63.6)	(61.3-69.6)		
Grade 4-5	61 (11.6)	70 (13.3)	1.7	0.394
(95% CI)	(9.0-14.6)	(10.5-16.5)		

Step 1 treated patients	VRd (n = 527)	KRd (n = 526)		
Rates	N (%)	N (%)	Diff KRd-VRd	Chi-sq *p*-value
Grade 3-5	254 (48.3)	254 (48.3)	6.9	0.024
(95% CI)	(37.1- 45.7)	(44.0-52.6)		
Grade 4-5	21 (4.0)	43 (8.2)	4.2	0.004
(95% CI)	(2.5-6.1)	(6.0-10.9)		

Grade 3 hematologic adverse events were not required reporting

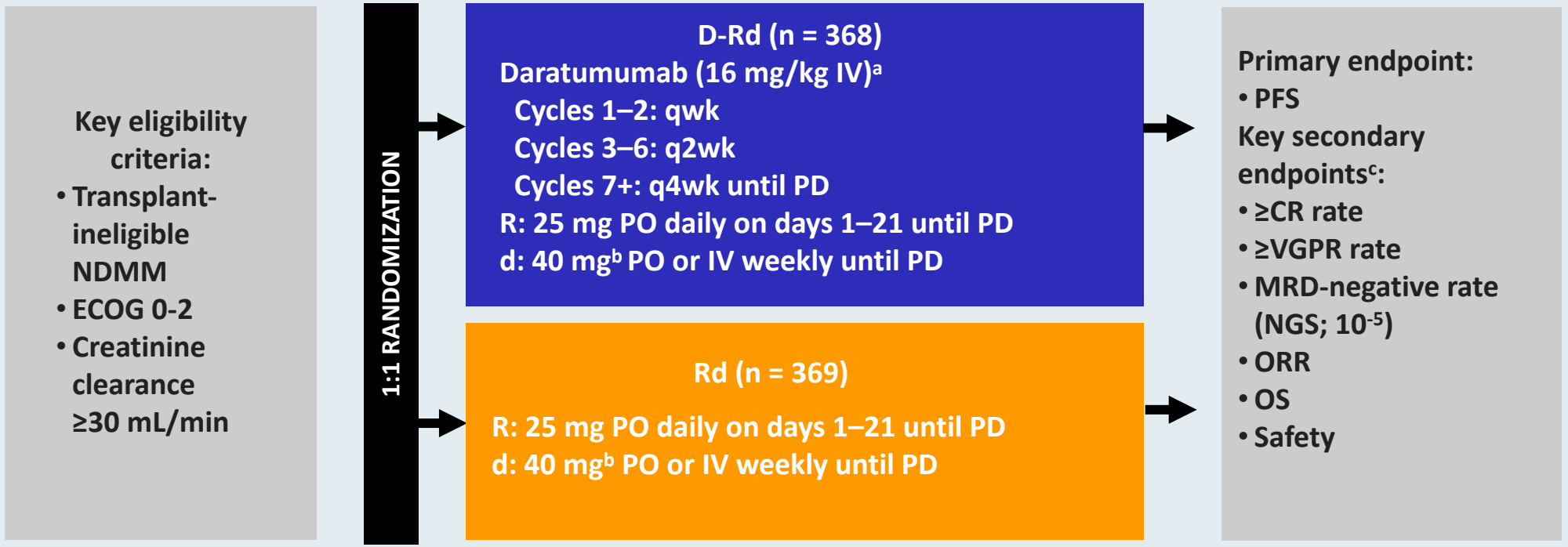
Kumar S et al. ASCO 2020;Abstract LBA3.

Overall Survival Results with Daratumumab, Lenalidomide and Dexamethasone versus Lenalidomide and Dexamethasone in Transplant-Ineligible Newly Diagnosed Multiple Myeloma (NDMM): Phase 3 MAIA Study

Facon T et al.

EHA 2021;Abstract LB1901.

MAIA: Phase III Trial Design



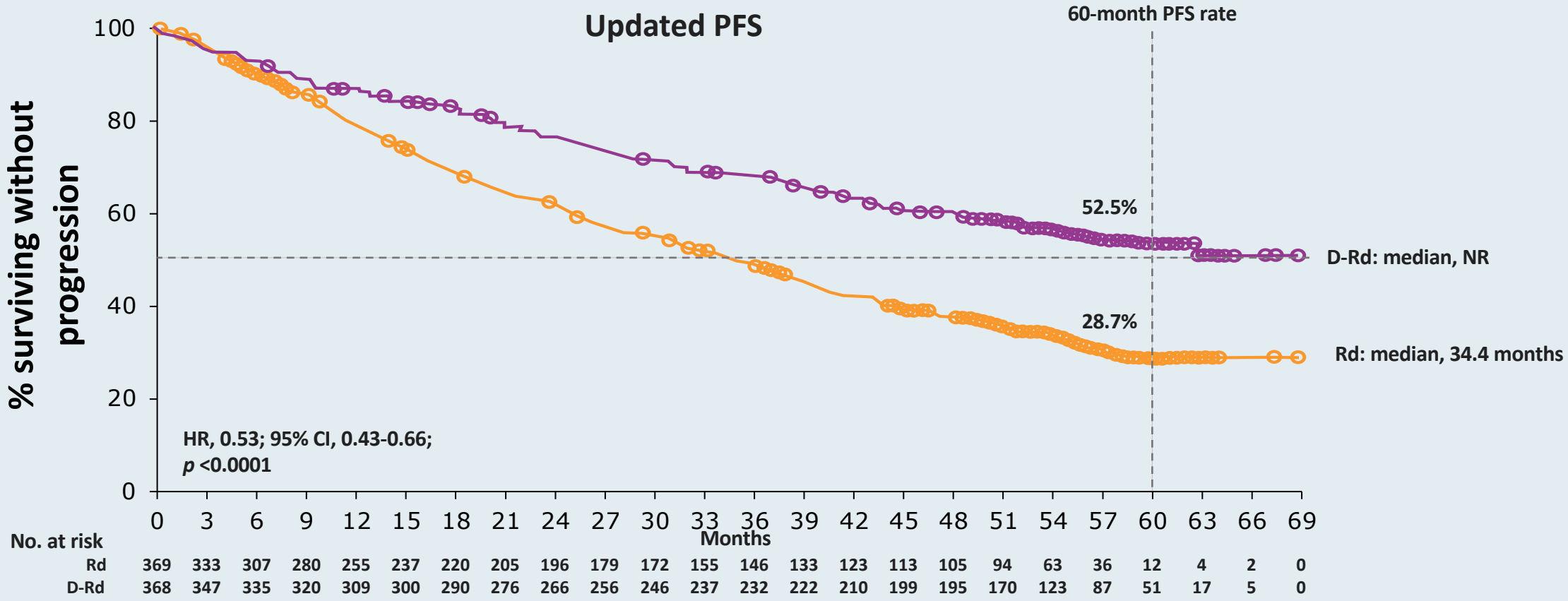
Stratification factors:
- **ISS (I vs II vs III)**
- **Region (NA vs other)**
- **Age (<75 vs ≥75 years)**

Cycle: 28 days

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

Facon T et al. EHA 2021;Abstract LB1901.

MAIA: Progression-Free Survival
New 60-Month Data



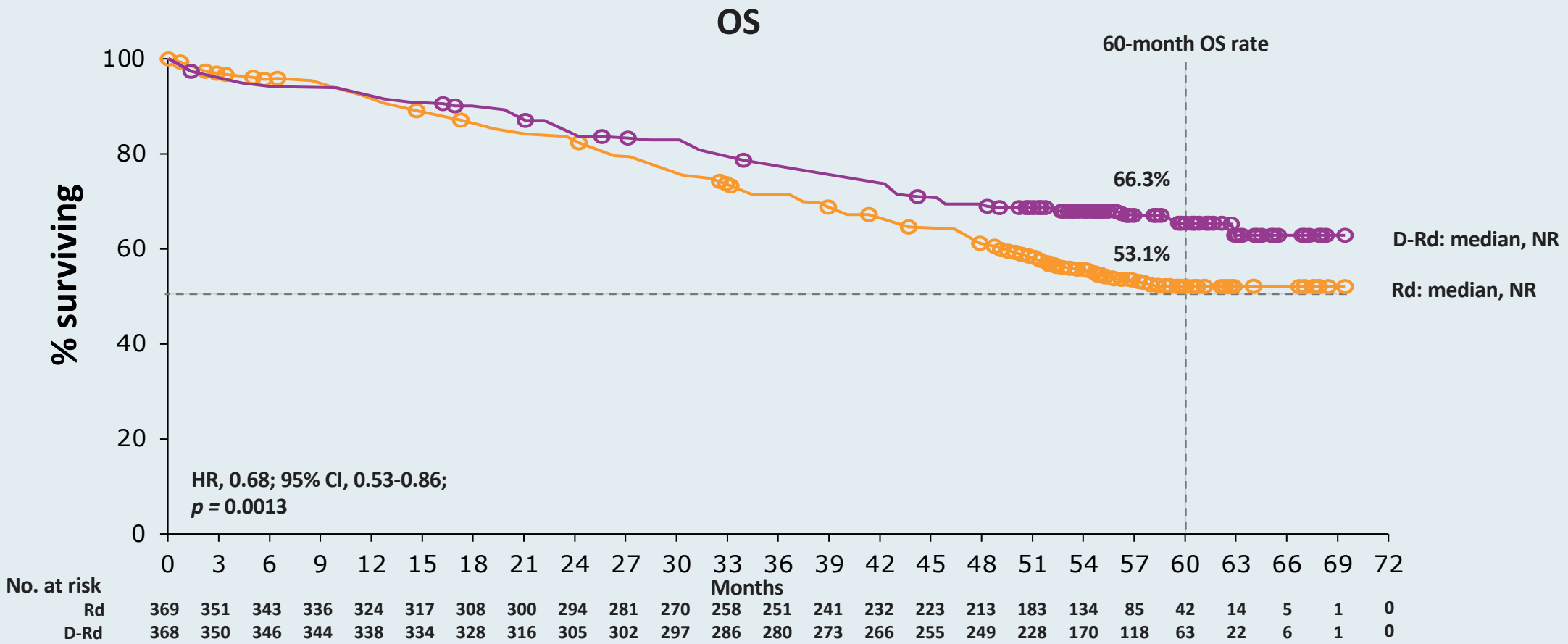
- D-Rd continued to demonstrate a significant PFS benefit, with median PFS not reached with D-Rd
  - These data provide a new PFS benchmark for patients with NDMM who are transplant ineligible

NR = not reached; HR = hazard ratio

Facon T et al. EHA 2021;Abstract LB1901.

RTP RESEARCH TO PRACTICE

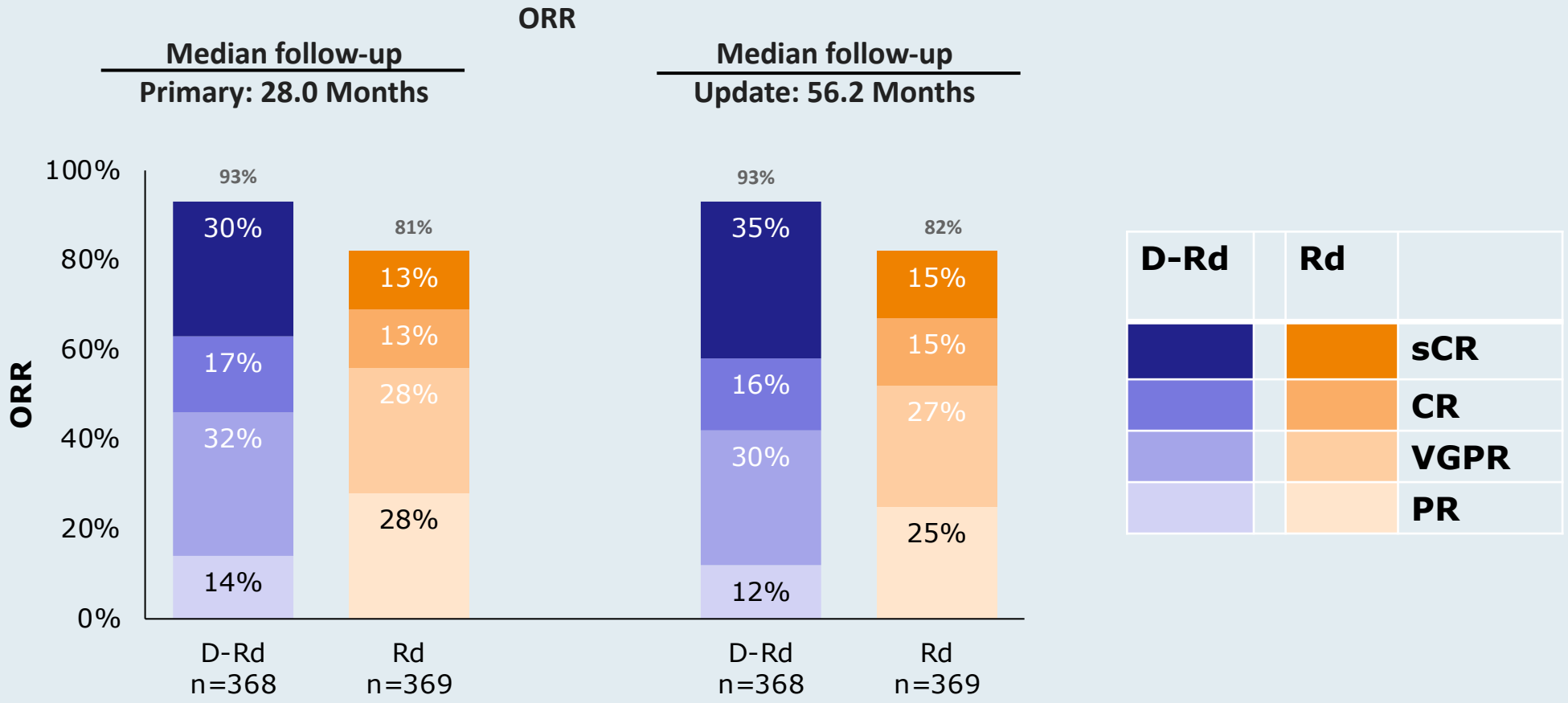
MAIA: Overall Survival



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. EHA 2021;Abstract LB1901.

MAIA: Updated Overall Response Rate (ITT Population)



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

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

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

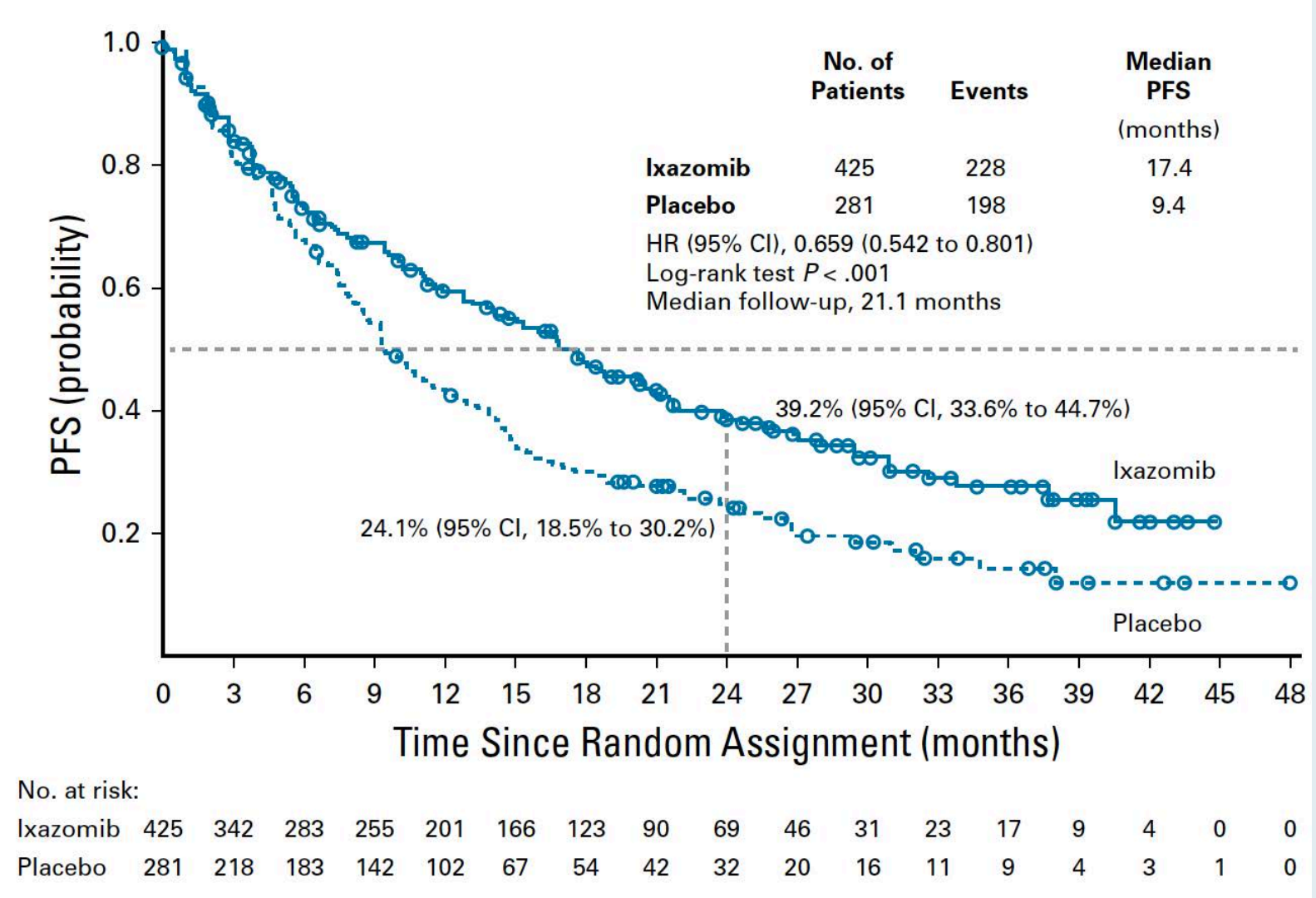
original reports

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

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

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

TOURMALINE-MM4 Primary Endpoint: Progression-Free Survival



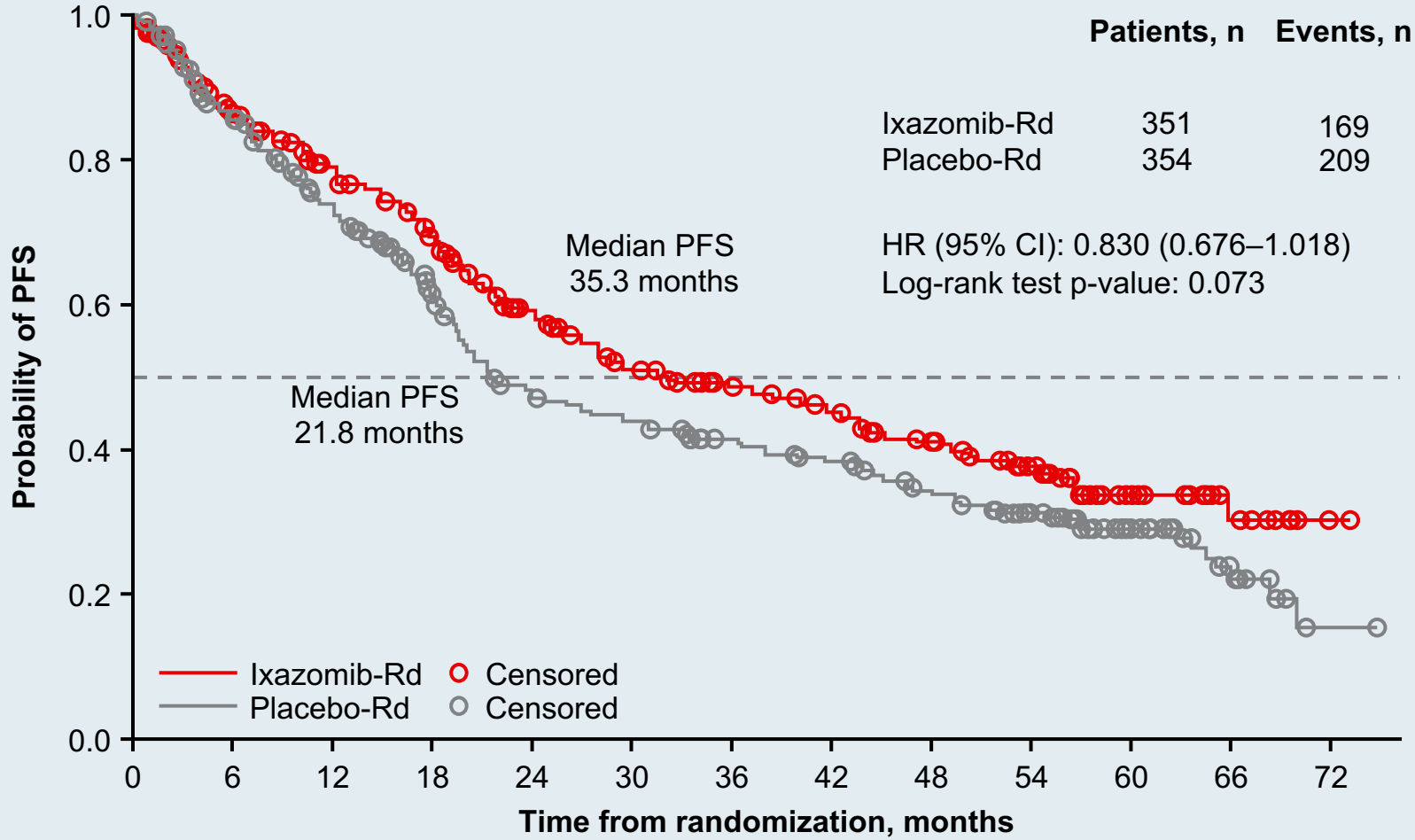
Dimopoulos MA et al. *J Clin Oncol* 2020;38(34):4030-41.

The Phase 3 TOURMALINE-MM2 Trial: Oral Ixazomib, Lenalidomide, and Dexamethasone (IRd) vs Placebo-Rd for Transplant-Ineligible Patients with Newly Diagnosed Multiple Myeloma (NDMM)

Facon T et al.

ASH 2020;Abstract 551.

TOURMALINE-MM2: Progression-Free Survival



Patients at risk, n													
Ixazomib-Rd	351	261	220	187	147	120	107	96	81	64	28	10	1
Placebo-Rd	354	273	225	174	132	121	106	98	82	63	35	16	1

Facon T et al. ASH 2020;Abstract 551.

Agenda

Module 1: Treatment of MM in Transplant-Ineligible Patients

Module 2: Treatment of MM in Transplant-Eligible Patients

Module 3: Management of Relapsed/Refractory MM

Module 4: BCMA CAR T-Cell Therapy

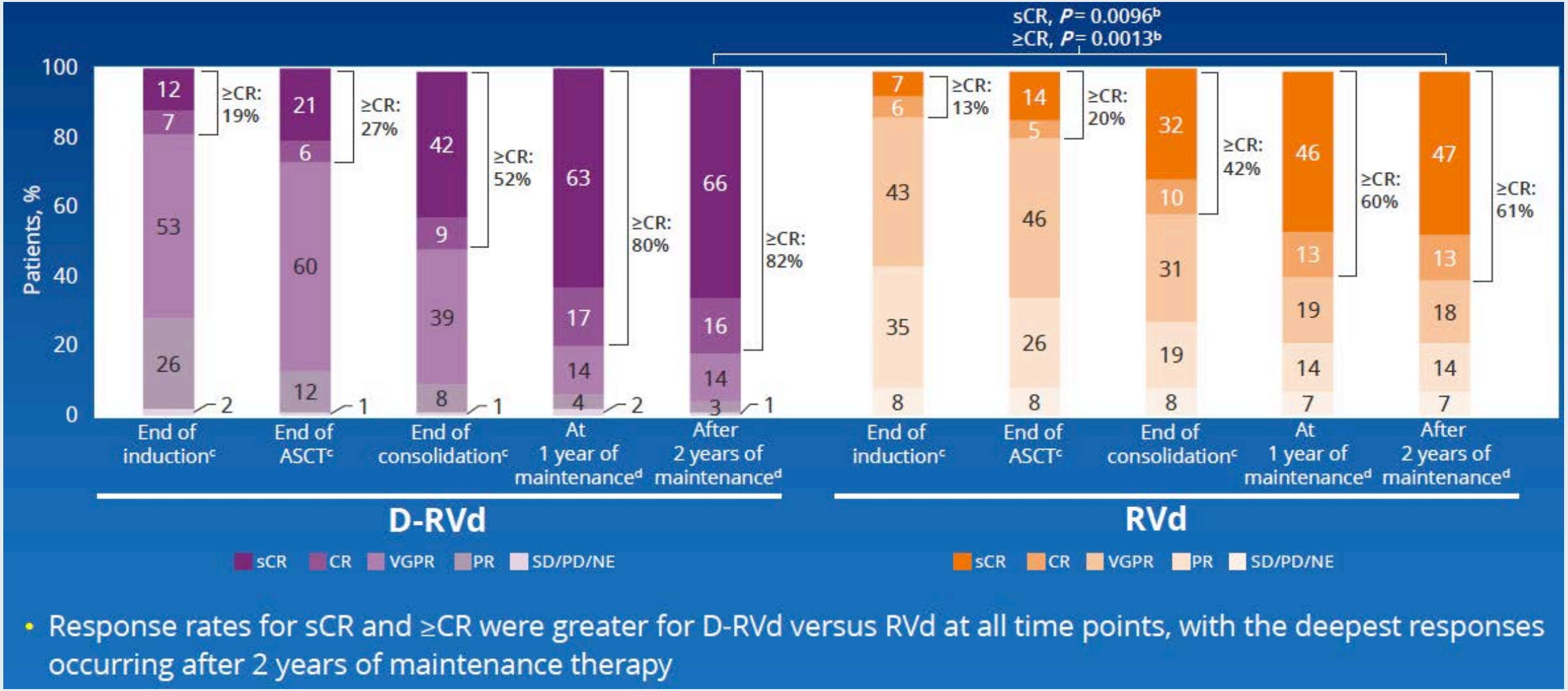
Module 5: Other Novel Agents and Strategies

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

Laubach JP et al.

ASH 2021;Abstract 79.

GRIFFIN: Updated Analysis After 24 Months of Maintenance Therapy

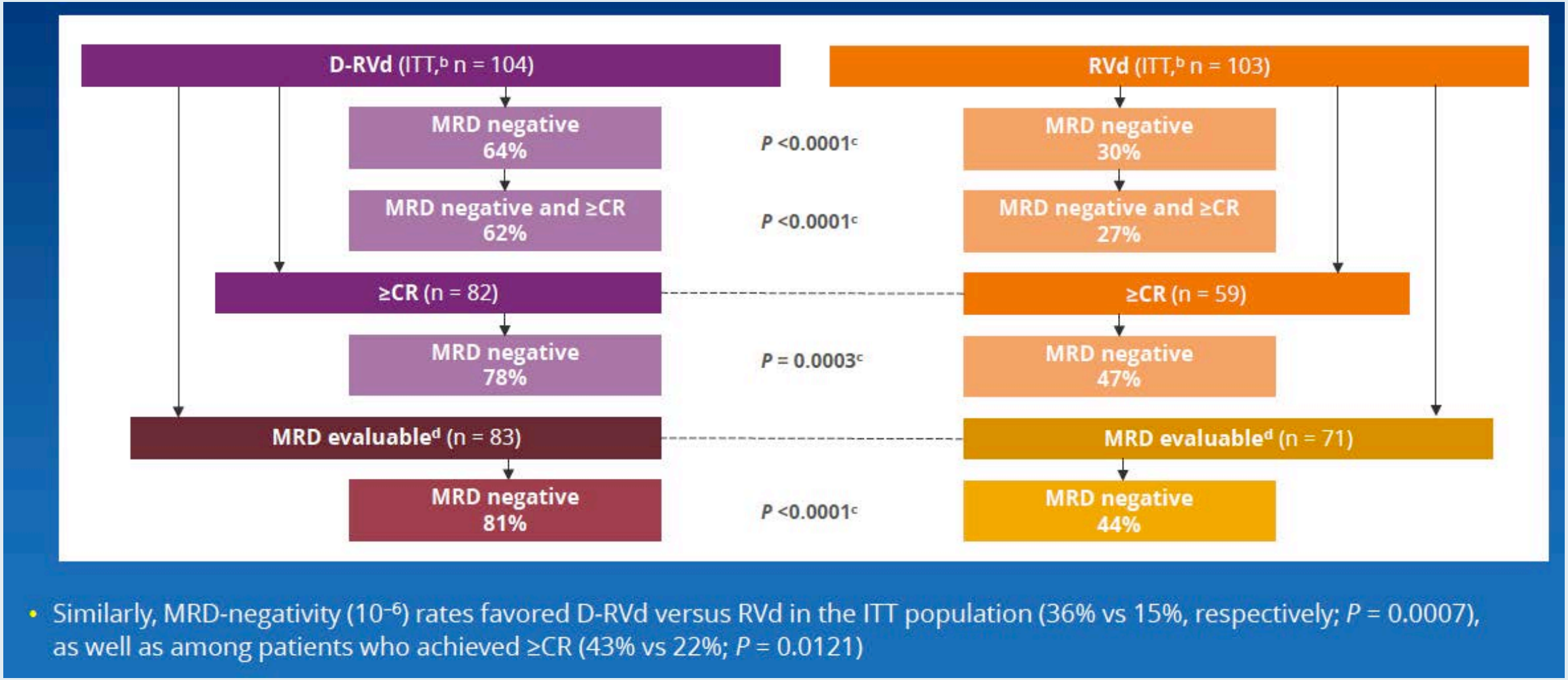


- Response rates for sCR and ≥CR were greater for D-RVd versus RVd at all time points, with the deepest responses occurring after 2 years of maintenance therapy

Laubach JP et al. ASH 2021;Abstract 79.

RTP RESEARCH TO PRACTICE

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

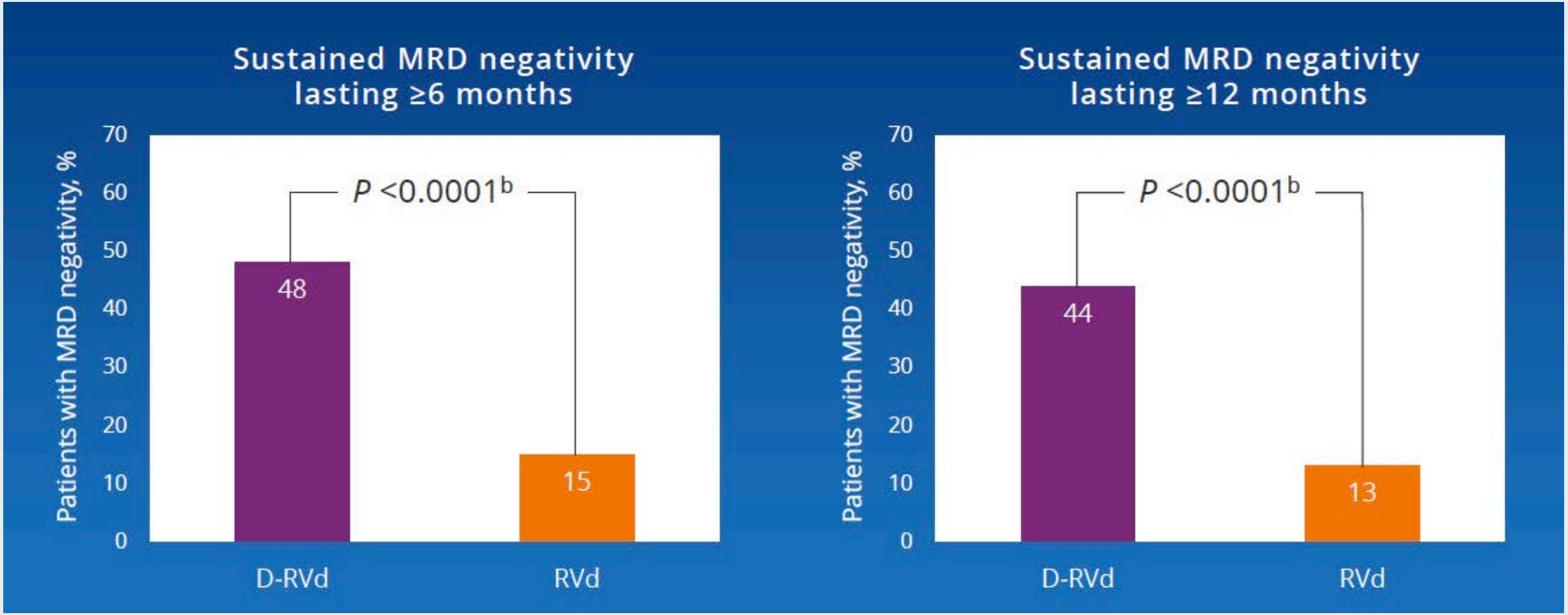


- Similarly, MRD-negativity (10^{-6}) rates favored D-RVd versus RVd in the ITT population (36% vs 15%, respectively; *P* = 0.0007), as well as among patients who achieved ≥CR (43% vs 22%; *P* = 0.0121)

MRD = minimal residual disease

Laubach JP et al. ASH 2021;Abstract 79.

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



Laubach JP et al. ASH 2021;Abstract 79.

RTP RESEARCH TO PRACTICE

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

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

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

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

SPM = second primary malignancy

Laubach JP et al. ASH 2021;Abstract 79.

UNIVERSITÄTS KLINIKUM HEIDELBERG

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

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

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

ASH 2021; Final Abstract Code: 463

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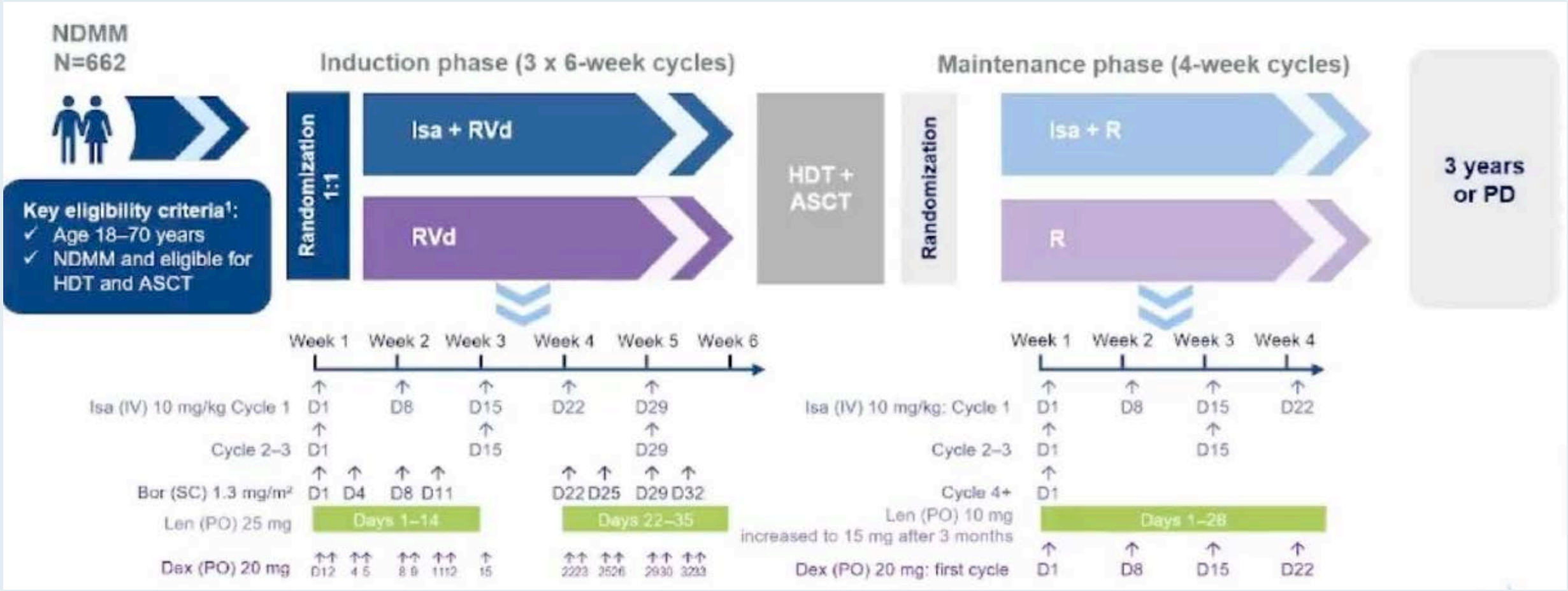
RTP RESEARCH TO PRACTICE

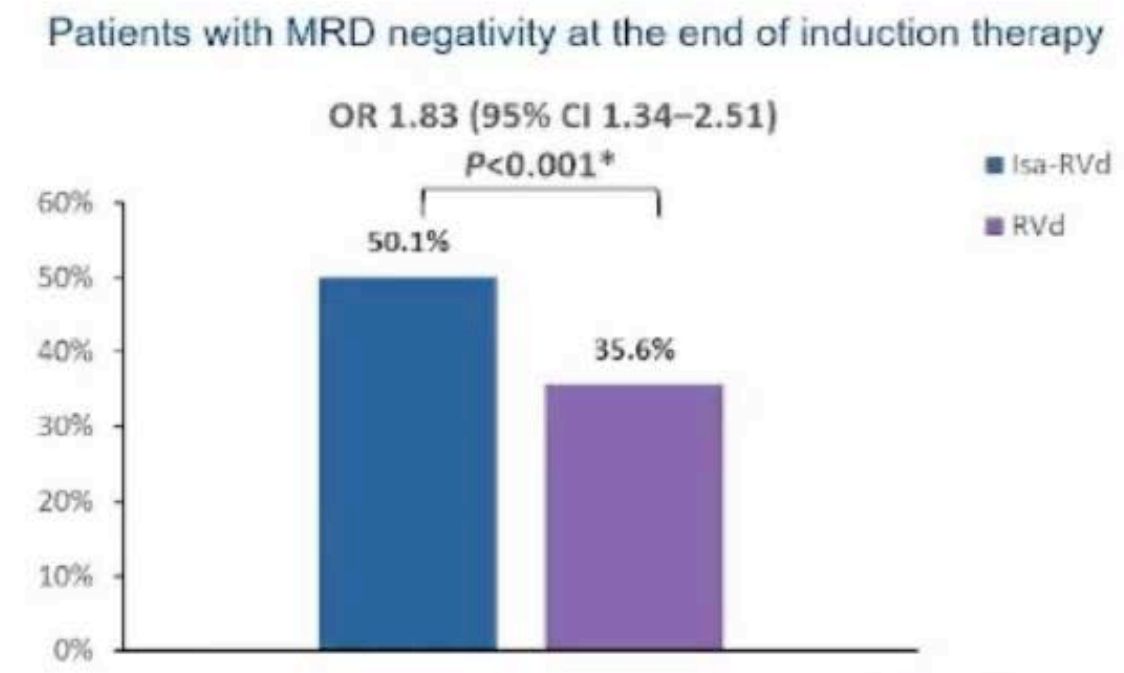
GMMG-HD7 Phase III Trial Design



Goldschmidt H et al. ASH 2021;Abstract 463.

RTP RESEARCH TO PRACTICE

GMMG-HD7: MRD Negativity at End of Induction Therapy

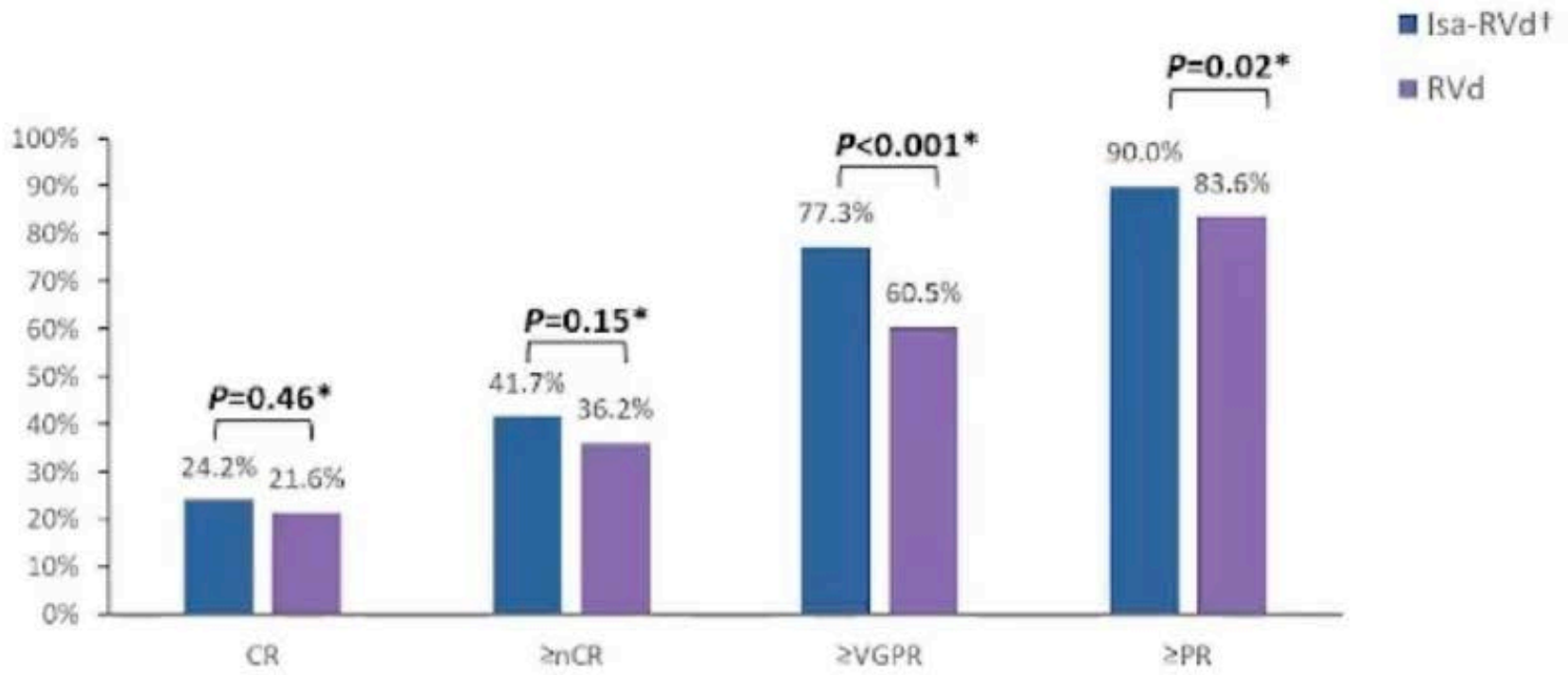


Low number of not assessable/missing† MRD status: Isa-RVd (10.6%) and RVd (15.2%)

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

Goldschmidt H et al. ASH 2021;Abstract 463.

GMMG-HD7: Response Rates After Induction Therapy



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

Goldschmidt H et al. ASH 2021;Abstract 463.

GMMG-HD7: Safety Profile

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

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

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

AE = adverse event

Goldschmidt H et al. ASH 2021;Abstract 463.

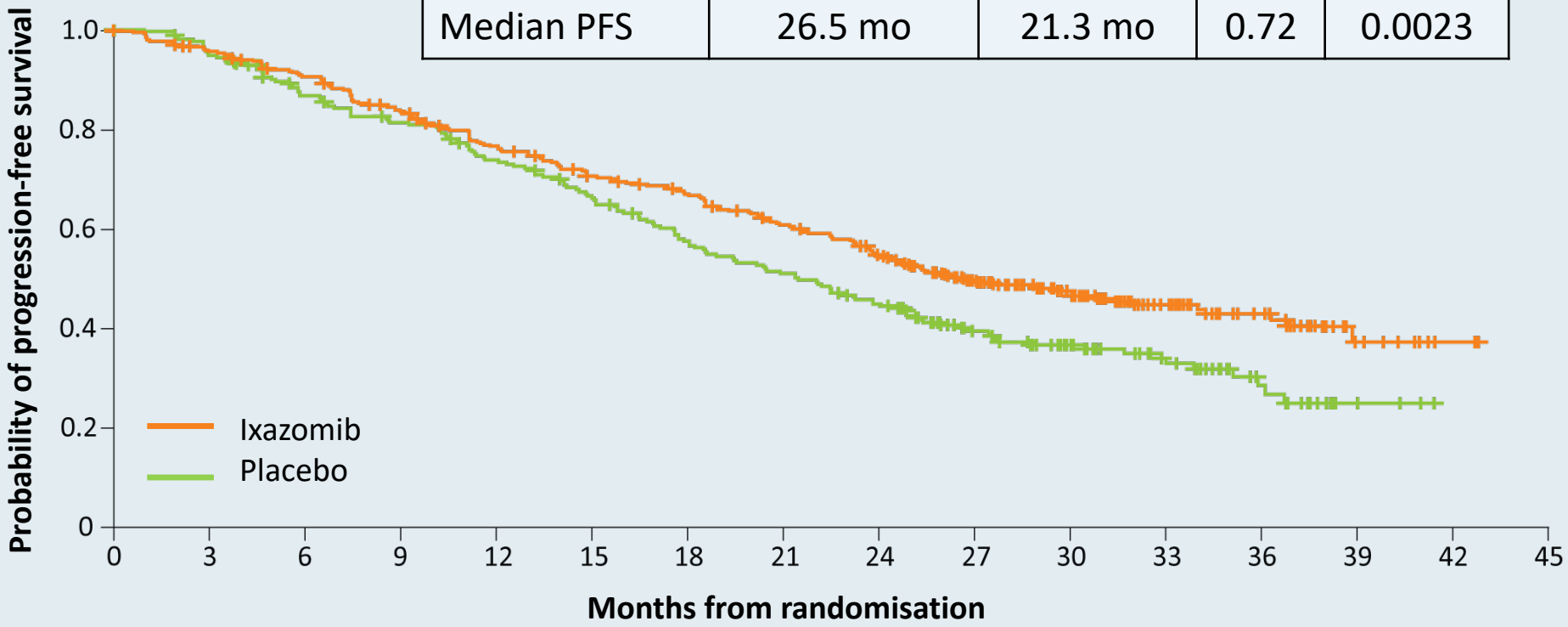
Oral ixazomib maintenance following autologous stem cell transplantation (TOURMALINE-MM3): a double-blind, randomised, placebo-controlled phase 3 trial

*Meletios A Dimopoulos, Francesca Gay, Fredrik Schjesvold, Meral Beksac, Roman Hajek, Katja Christina Weisel, Hartmut Goldschmidt, Vladimir Maisnar, Philippe Moreau, Chang Ki Min, Agnieszka Pluta, Wee-Joo Chng, Martin Kaiser, Sonja Zweegman, Maria-Victoria Mateos, Andrew Spencer, Shinsuke Iida, Gareth Morgan, Kaveri Suryanarayan, Zhaoyang Teng, Tomas Skacel, Antonio Palumbo, Ajeeta B Dash, Neeraj Gupta, Richard Labotka, S Vincent Rajkumar, on behalf of the TOURMALINE-MM3 study group**

Lancet 2019;393(10168):253-64.

TOURMALINE-MM3 Primary Endpoint: Progression-Free Survival (ITT)

	Ixazomib (n = 395)	Placebo (n = 261)	HR	*p*-value
Median PFS	26.5 mo	21.3 mo	0.72	0.0023



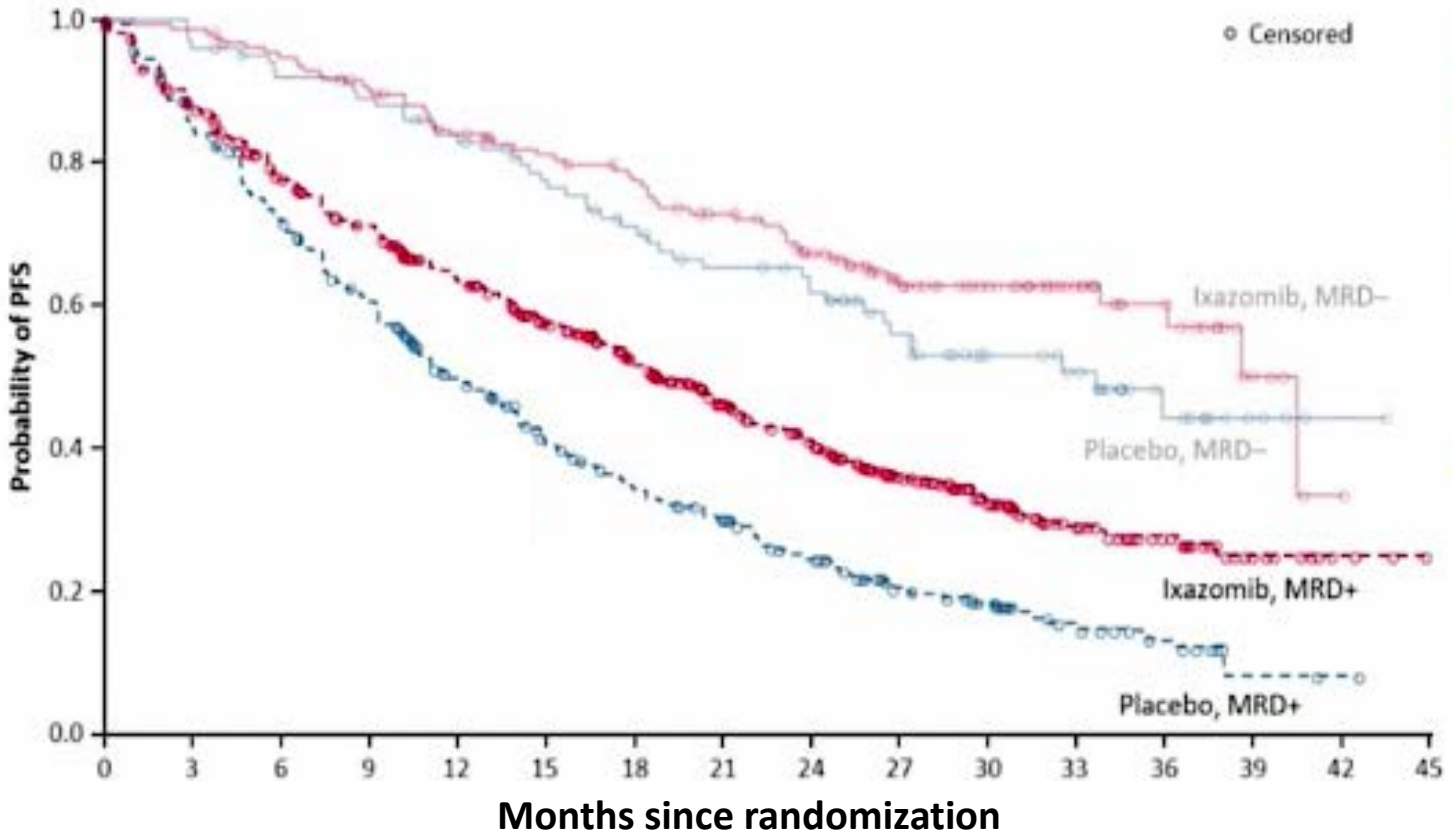
Dimopoulos MA et al. *Lancet* 2019;393(10168):253-64.

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

Paiva B et al.

ESMO 2021;Abstract S184.

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



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

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

Paiva B et al. ESMO 2021;Abstract S184.

RTP RESEARCH TO PRACTICE

Pooled Analysis of TOURMALINE-MM3 and MM4
Conclusions

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

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

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

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

Paiva B et al. EHA 2021;Abstract S184.

Agenda

Module 1: Treatment of MM in Transplant-Ineligible Patients

Module 2: Treatment of MM in Transplant-Eligible Patients

Module 3: Management of Relapsed/Refractory MM

Module 4: BCMA CAR T-Cell Therapy

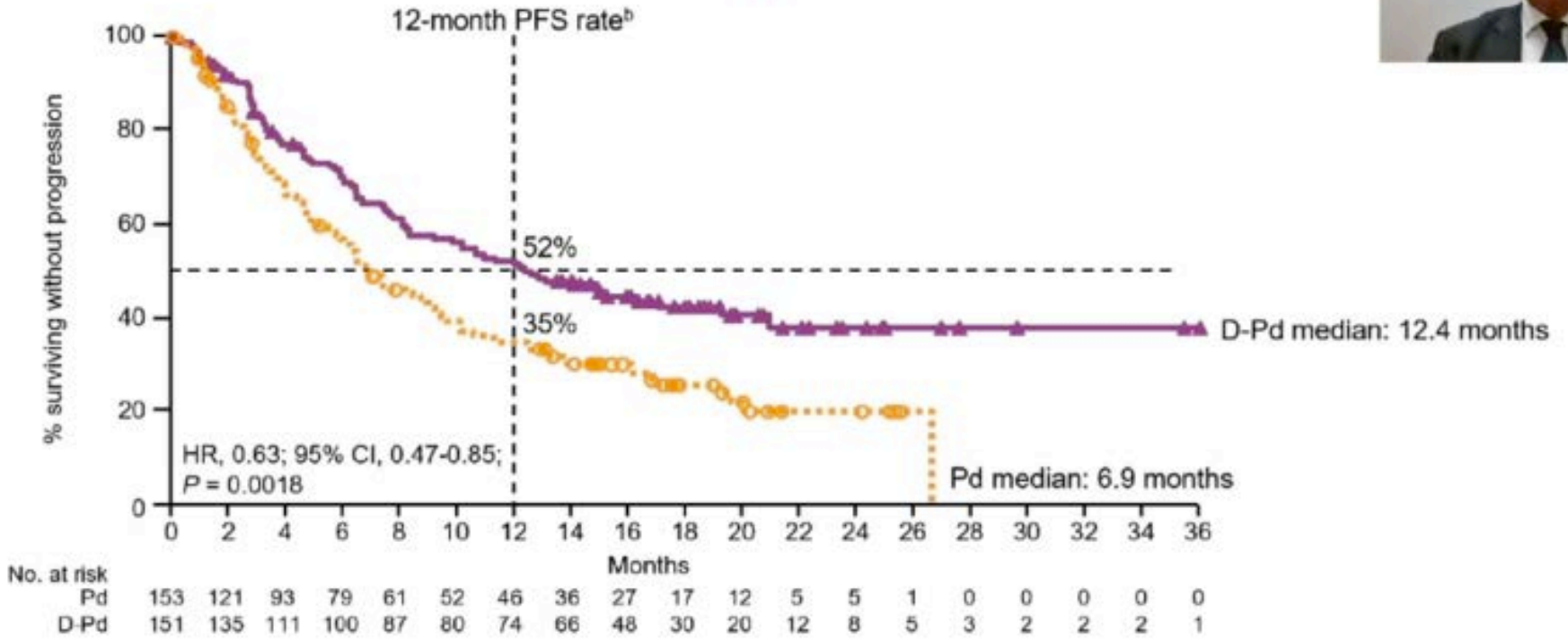
Module 5: Other Novel Agents and Strategies

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

Dimopoulos MA et al.

ASH 2020;Abstract 412.

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



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

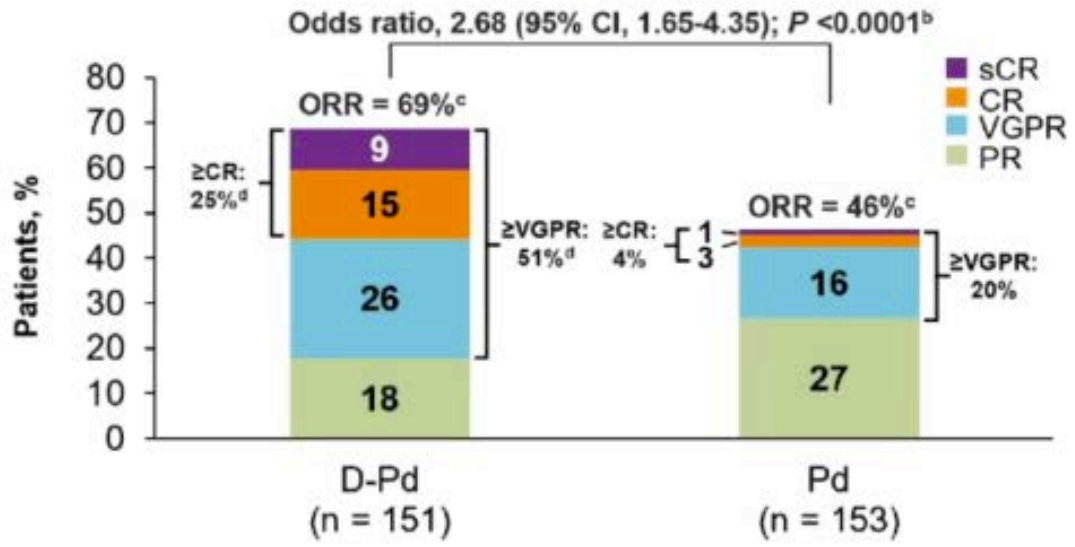
Addition of DARA SC to Pd improved PFS, with a 37% reduction in the risk of progression or death

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

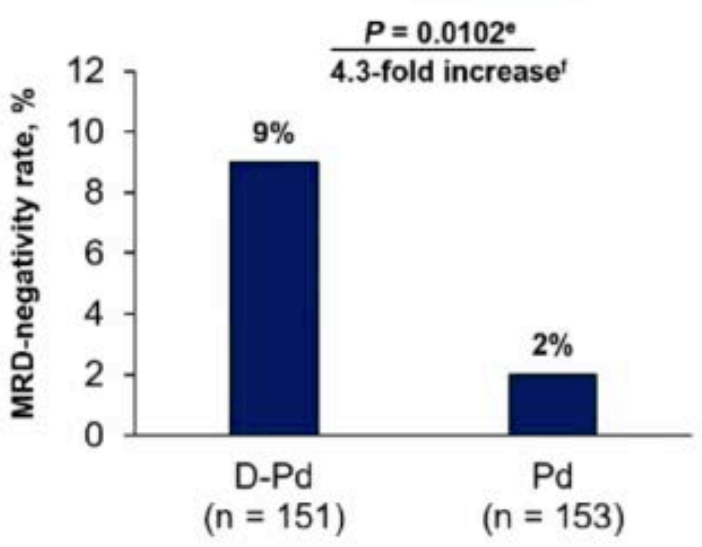
Dimopoulos MA et al. ASH 2020;Abstract 412.

Depth of Response[a]

Hematologic response



MRD negativity



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

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

Dimopoulos MA et al. ASH 2020;Abstract 412.

FDA Approves Daratumumab and Hyaluronidase-fihj with Pomalidomide and Dexamethasone for R/R MM

Press Release – July 9, 2021

"The Food and Drug Administration approved daratumumab and hyaluronidase-fihj in combination with pomalidomide and dexamethasone for adult patients with multiple myeloma who have received at least one prior line of therapy including lenalidomide and a proteasome inhibitor.

Efficacy was evaluated in APOLLO (NCT03180736), an open-label, active-controlled trial with 304 patients randomized (1:1) to daratumumab and hyaluronidase-fihj with pomalidomide and dexamethasone (Pd) vs Pd alone. Patients received daratumumab and hyaluronidase-fihj 1,800 mg/30,000 units (1,800 mg daratumumab and 30,000 units hyaluronidase) administered subcutaneously once weekly from Weeks 1 to 8, once every 2 weeks from Weeks 9 to 24 and once every 4 weeks starting with Week 25 until disease progression or unacceptable toxicity with pomalidomide 4 mg once daily orally on days 1-21 of each 28-day cycle; and dexamethasone 40 mg per week (or a reduced dose of 20 mg per week for patients >75 years).

The main efficacy outcome measure was progression-free survival (PFS). The median PFS was 12.4 months in the daratumumab and hyaluronidase-fihj-Pd treatment group and 6.9 months in the Pd treatment group (HR 0.63; 95% CI: 0.47, 0.85; p=0.0018), representing a 37% reduction in the risk of disease progression or death for patients treated with daratumumab and hyaluronidase-fihj-Pd versus Pd."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-daratumumab-and-hyaluronidase-fihj-pomalidomide-and-dexamethasone-multiple-myeloma

RTP RESEARCH TO PRACTICE

FDA Approves Daratumumab and Hyaluronidase-fihj with Carfilzomib and Dexamethasone for R/R MM

Press Release – November 30, 2021

"The Food and Drug Administration approved daratumumab + hyaluronidase-fihj and carfilzomib plus dexamethasone for adult patients with relapsed or refractory multiple myeloma who have received 1 to 3 prior lines of therapy.

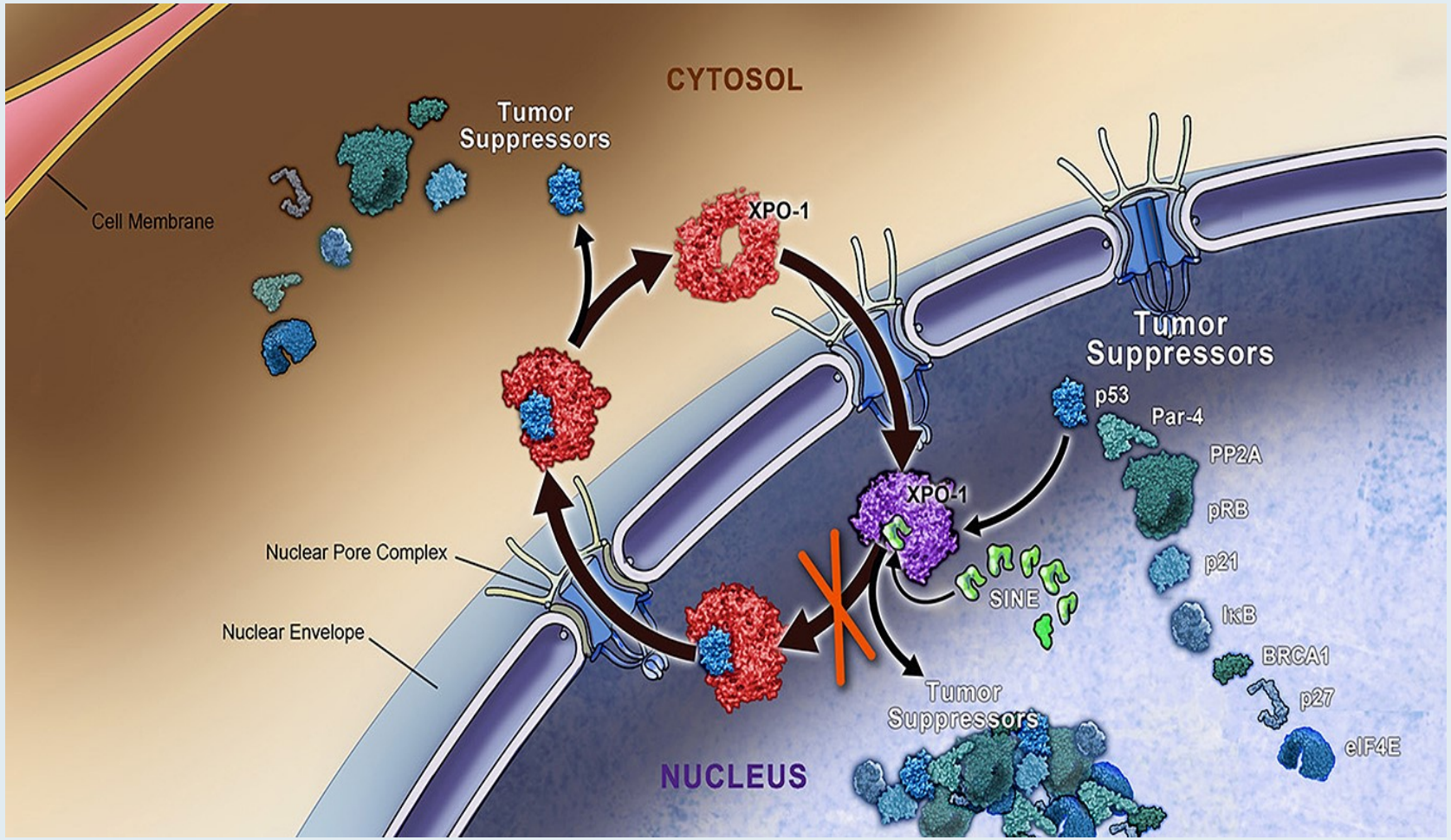
Efficacy was evaluated in a single-arm cohort of PLEIADES (NCT03412565), a multi-cohort, open-label trial. This cohort enrolled 66 patients with relapsed or refractory multiple myeloma who received at least one prior line of therapy. Patients received daratumumab + hyaluronidase-fihj 1,800 mg/30,000 units (1,800 mg daratumumab and 30,000 units hyaluronidase) administered subcutaneously in combination with carfilzomib (20/70 mg/m^2 once weekly regimen) and dexamethasone.

The main efficacy outcome measure was overall response rate (ORR). The ORR was 84.8%. At a median follow-up of 9.2 months, the median duration of response had not been reached and an estimated 85.2% maintained response for at least 6 months and 82.5% maintained response for at least 9 months."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-darzalex-faspro-kyprolis-and-dexamethasone-multiple-myeloma

RTP RESEARCH TO PRACTICE

Selinexor Mechanism of Action



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

Bahlis N et al. EHA 2016;Abstract P277.

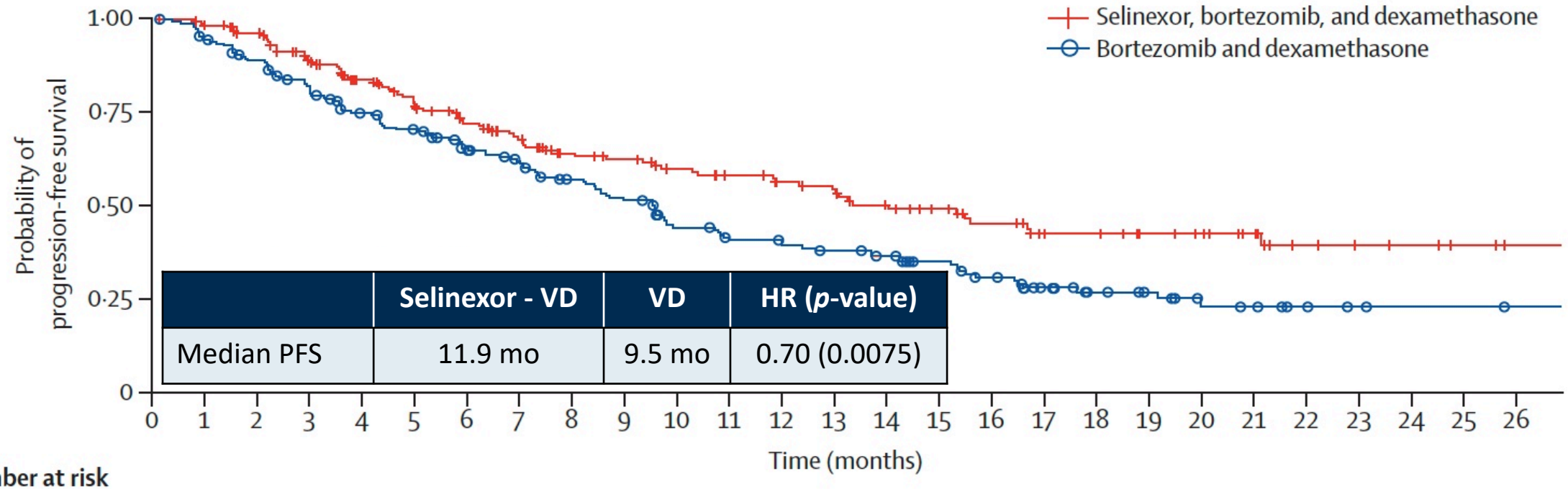
RTP RESEARCH TO PRACTICE

Lancet 2020;396:1563-73

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

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

BOSTON: Progression-Free Survival (ITT)



	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.

RTP RESEARCH TO PRACTICE

BOSTON: Select Adverse Events

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

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

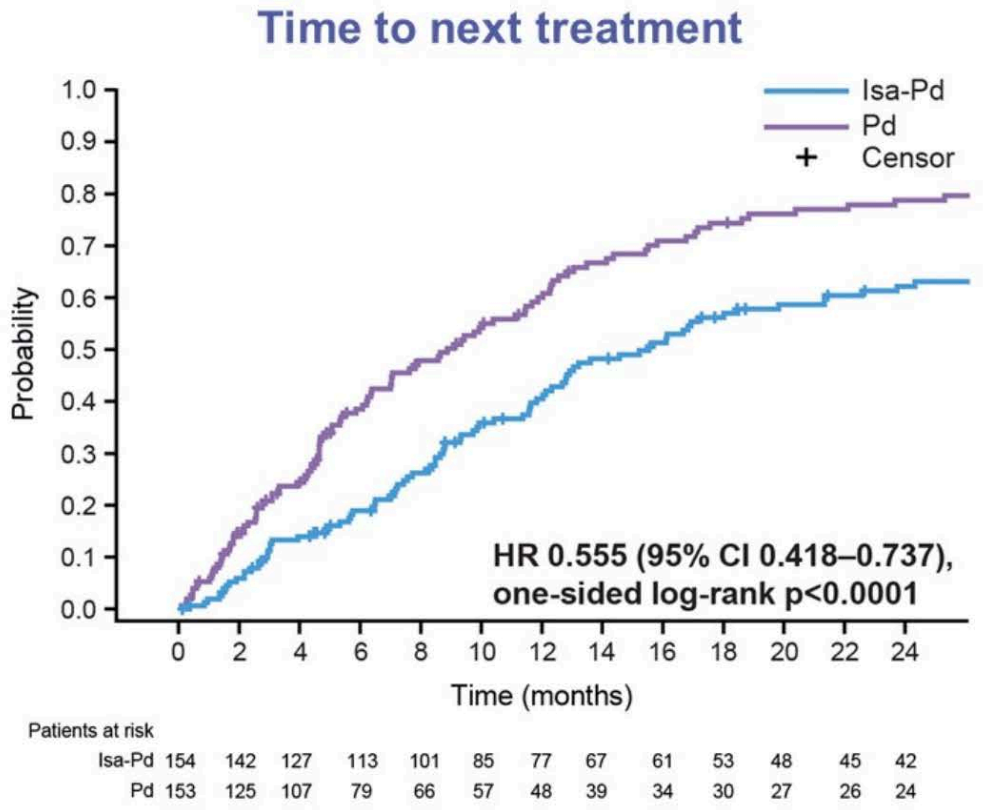
Updates from ICARIA-MM, a Phase 3 Study of Isatuximab (Isa) plus Pomalidomide and Low-Dose Dexamethasone (Pd) versus Pd in Relapsed and Refractory Multiple Myeloma (RRMM)

Richardson PD et al.

ASCO 2021;Abstract 8017.

ICARIA-MM: Progression-Free Survival and Time to Next Treatment

With prolonged follow-up, Isa-Pd continues to improve PFS[a]:
mPFS 11.1 months vs 5.8 months with Pd alone (HR 0.599, p<0.0001)



Patients who proceeded to subsequent therapy:

Isa-Pd: 60%
Pd: 72%

Patients who went on to receive subsequent daratumumab:

Isa-Pd: 23.9% (n=22/92)
Pd: 58.2% (n=64/110)

Median Time to next treatment:

15.5 months (Isa-Pd) vs 8.9 months (Pd)

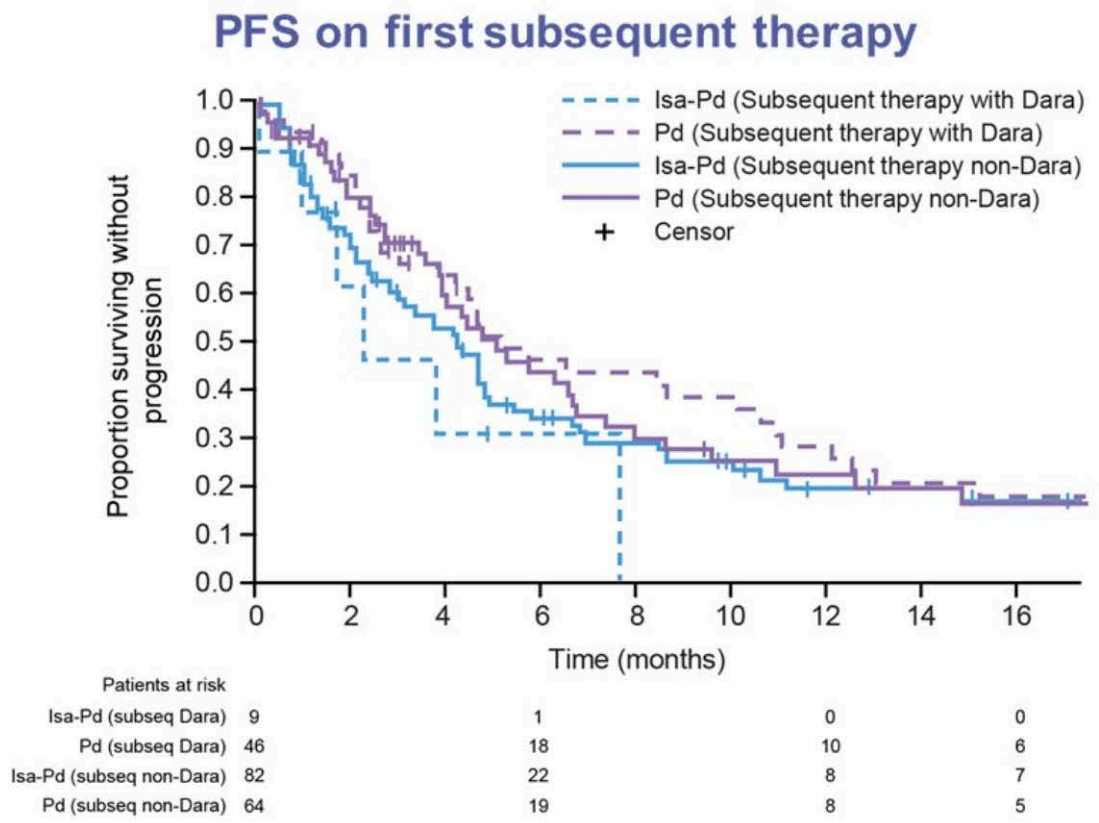
Richardson PD et al. ASCO 2021;Abstract 8017.

ICARIA-MM: Effect of Subsequent Daratumumab Therapy

First subsequent therapy	mPFS	
	Isa-Pd (n=82)	Pd (n=64)
Non-daratumumab	4.2 months	5.0 months
First subsequent therapy	**Isa-Pd (n=9)**	**Pd (n=46)**
Daratumumab	2.2 months	5.1 months

ORR in patients who received subsequent daratumumab therapy

Daratumumab regimen	Isa-Pd (n=22)	Pd (n=64)
Monotherapy or combined with steroids	14.3%	37.9%
Combined with a PI, IMiD, or alkylating agent	30.8%	31.8%



Richardson PD et al. ASCO 2021;Abstract 8017.

FDA Approves Isatuximab-irfc in Combination with Carfilzomib and Dexamethasone for R/R MM

Press Release – March 31, 2021

"The Food and Drug Administration approved isatuximab-irfc in combination with carfilzomib and dexamethasone, for the treatment of adult patients with relapsed or refractory multiple myeloma who have received one to three prior lines of therapy.

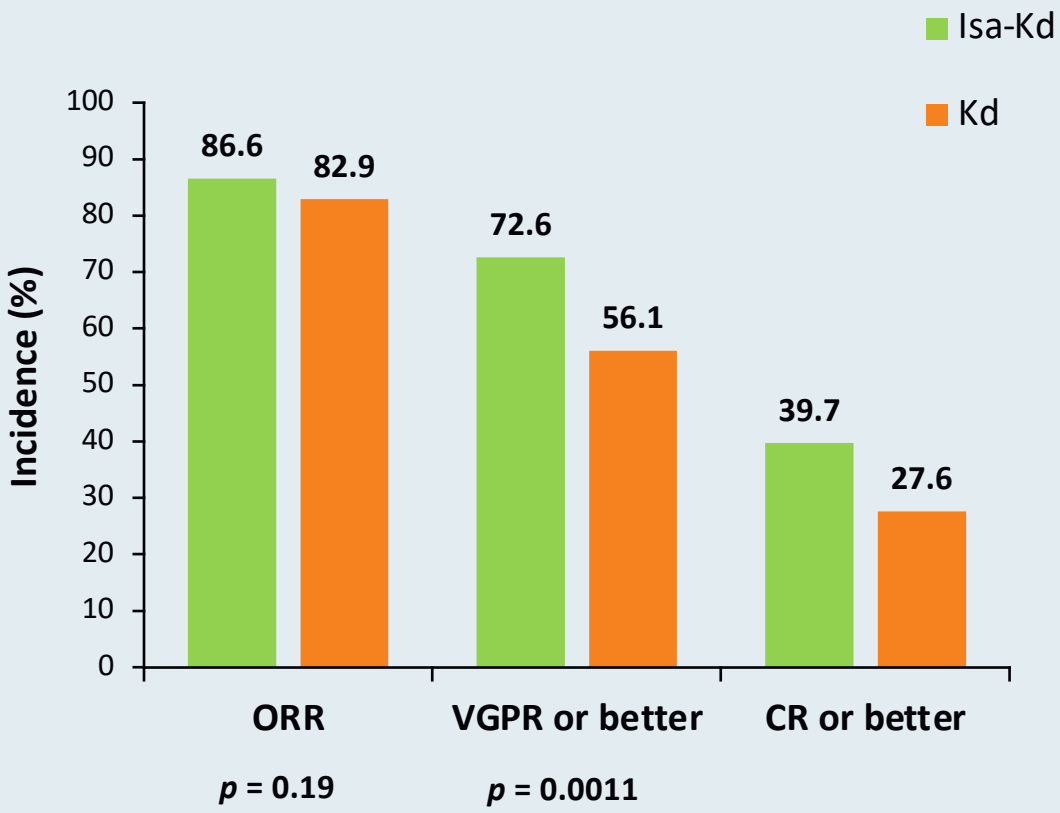
The efficacy and safety of isatuximab-irfc in combination with carfilzomib and dexamethasone was evaluated in IKEMA (NCT03275285), a multicenter, multinational, randomized, open-label, two-arm, phase 3 trial in patients with relapsed and/or refractory multiple myeloma who had received one to three prior lines of therapy. The trial randomized 302 patients (3:2) to receive isatuximab-irfc with carfilzomib and dexamethasone (Isa-Kd) or carfilzomib and dexamethasone (Kd).

The main efficacy outcome measure was progression-free survival (PFS), assessed by an independent response committee based on central laboratory data for M-protein and central radiologic imaging review using International Myeloma Working Group criteria. Median PFS was not reached in the Isa-Kd arm and was 20.27 months (95% CI: 15.77-NR) in the Kd arm (HR 0.548; p=0.0032), representing a 45% reduction in the risk of disease progression or death in patients treated with Kd."

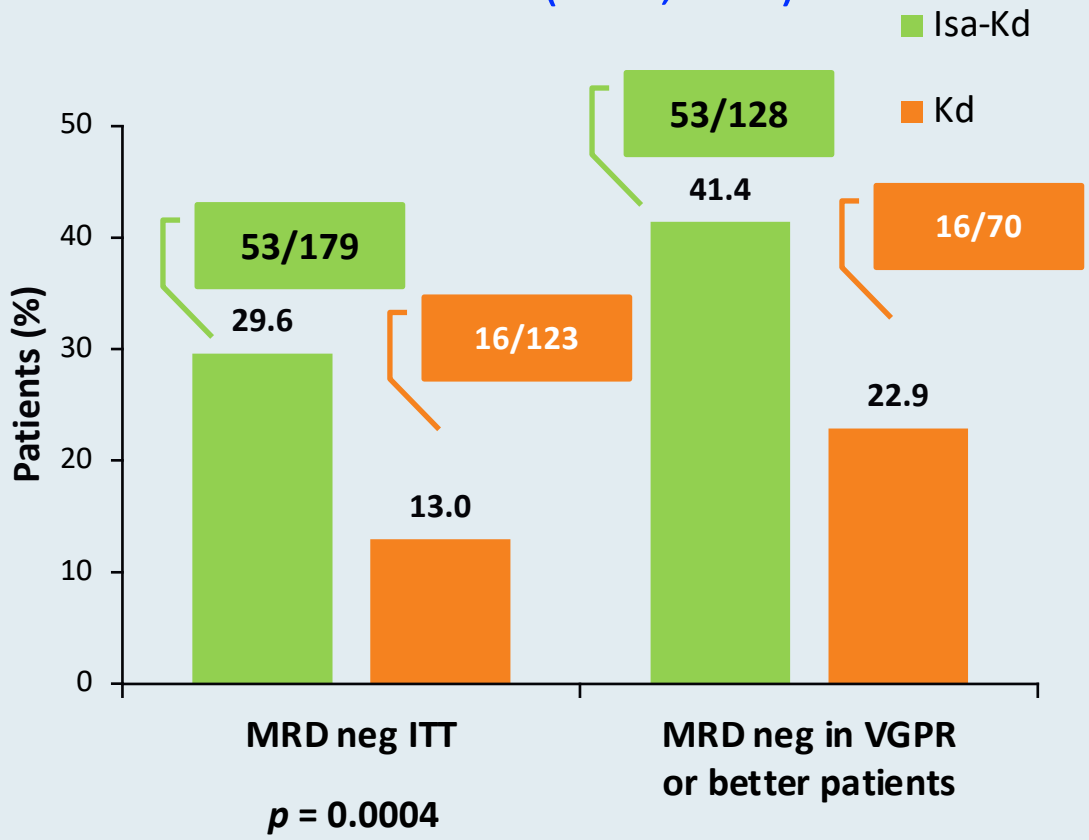
https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-isatuximab-irfc-multiple-myeloma

IKEMA: Isatuximab + Kd
Depth of Response

Best overall response



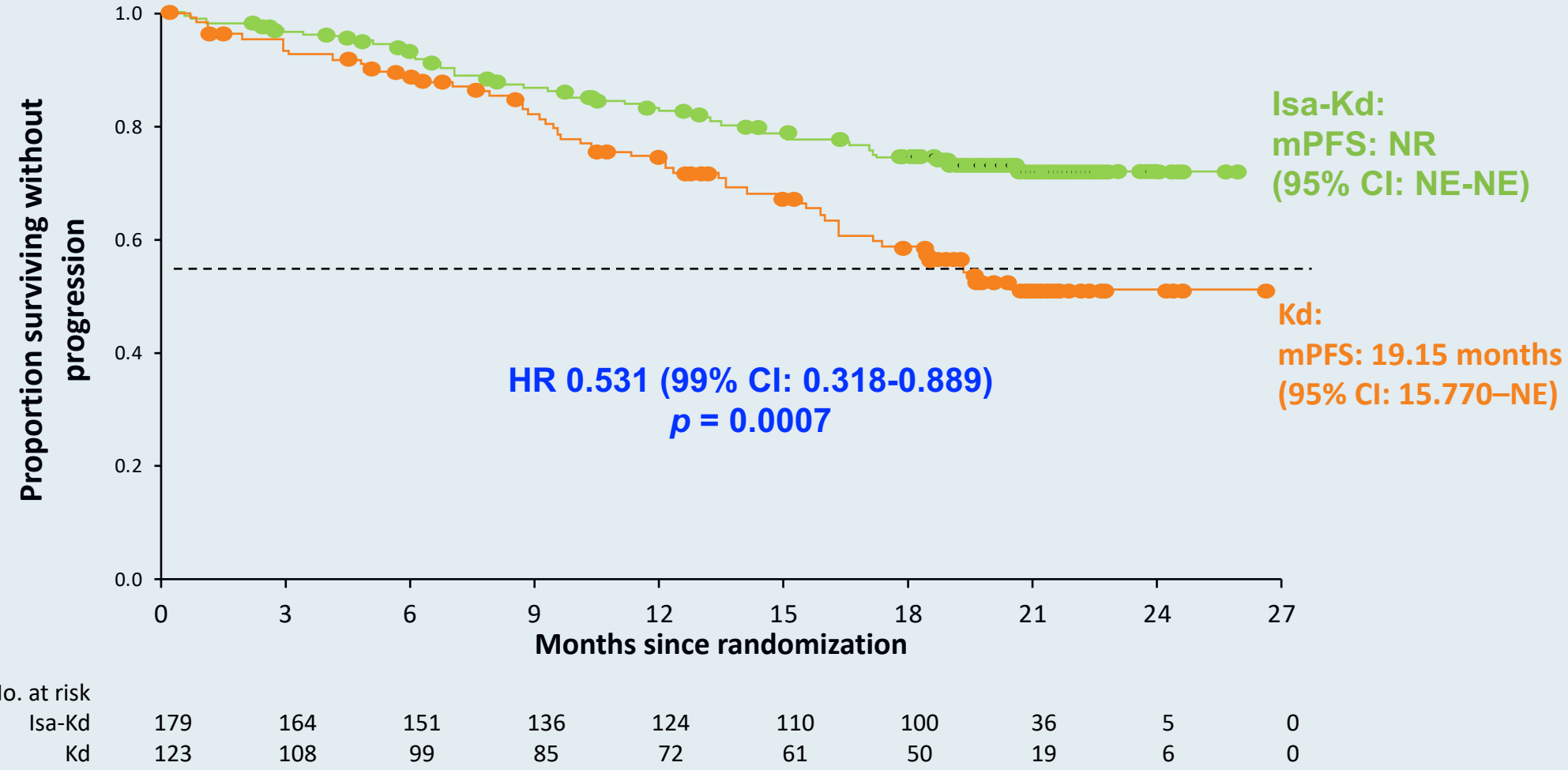
MRD rate (NGS, 10^{-5})



Moreau P et al. EHA 2020;Abstract LBA2603.

RTP RESEARCH TO PRACTICE

IKEMA: PFS



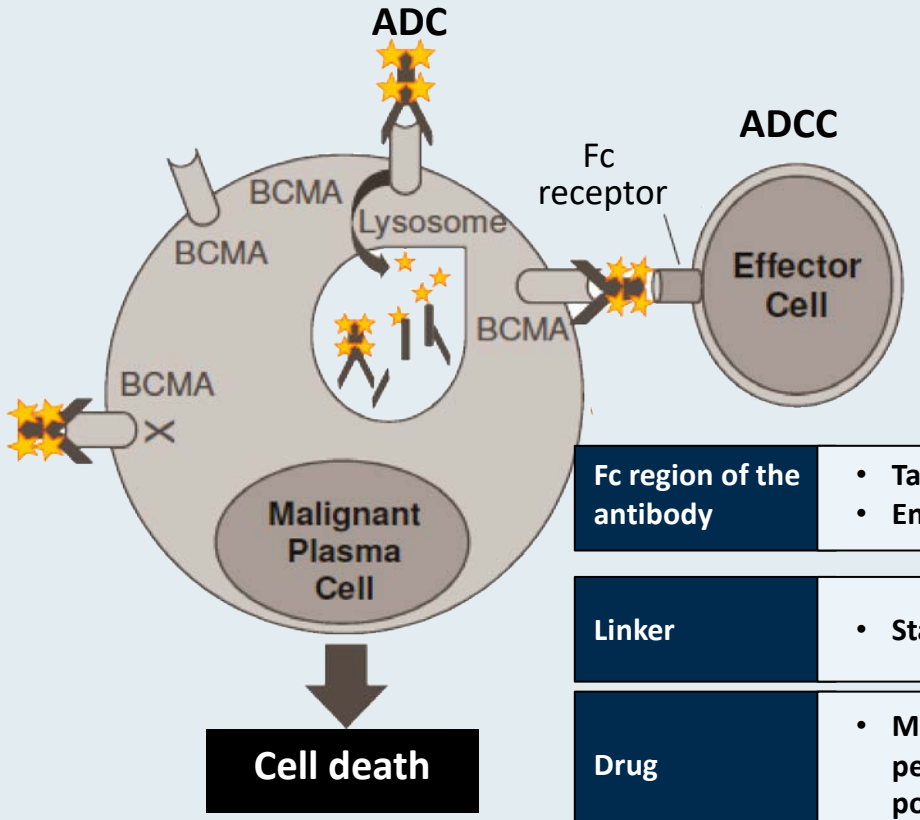
No. at risk										
Isa-Kd	179	164	151	136	124	110	100	36	5	0
Kd	123	108	99	85	72	61	50	19	6	0

One-sided *p*-value, level of significance <0.005

Moreau P et al. EHA 2020;Abstract LBA2603.

Belantamab Mafodotin: Anti-BCMA Antibody-Drug Conjugate

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



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

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

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

RTP RESEARCH TO PRACTICE

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

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

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

RTP RESEARCH TO PRACTICE

DREAMM-2: Single-Agent Belantamab Mafodotin Efficacy Outcomes

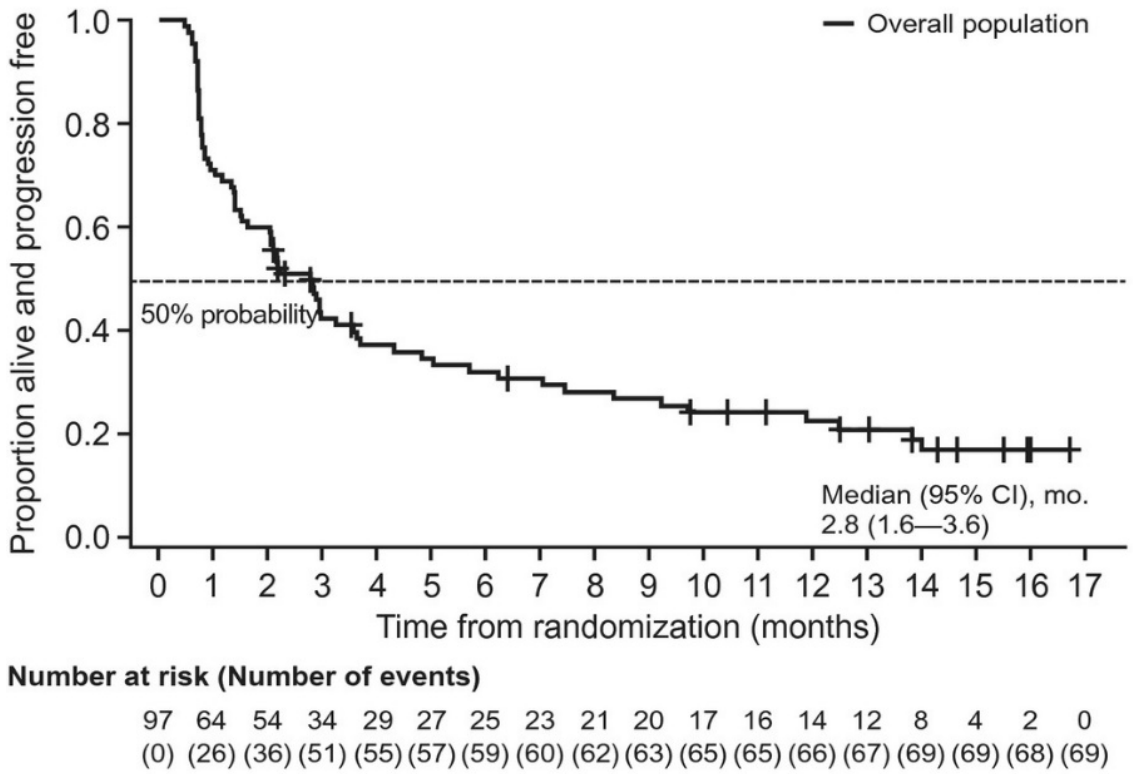
	Patients with 3-6 prior therapies (n = 47)	Patients with ≥7 prior therapies (n = 50)
ORR, % (97.5% CI)	32 (21.7-43.6)	30 (16.5-46.6)
Median DoR (95% CI estimates), months	11.0 (4.2-NR)	13.1 (4.0-NR)
Probability of DoR ≥6 months, % (95% CI estimates)	63 (31-83)	73 (44-89)
Median PFS (95% CI estimates),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

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

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

DREAMM-2: Longitudinal Outcomes

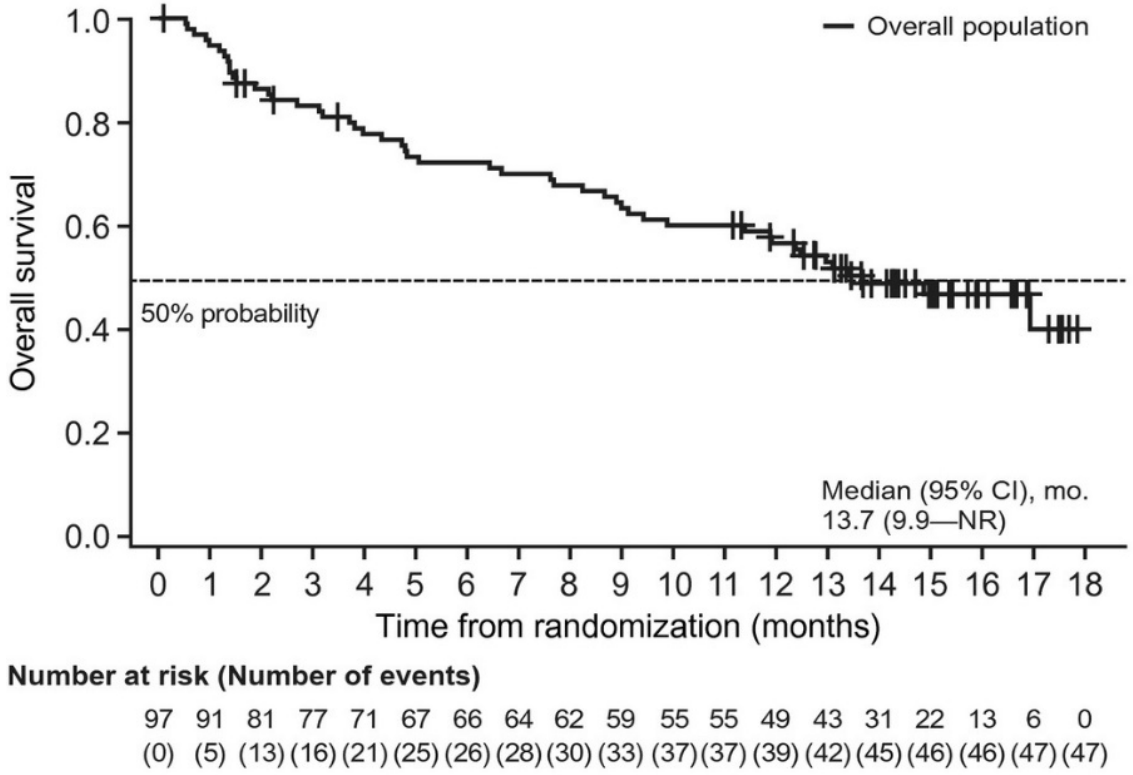
Progression-Free Survival



Number at risk (Number of events)

97	64	54	34	29	27	25	23	21	20	17	16	14	12	8	4	2	0
(0)	(26)	(36)	(51)	(55)	(57)	(59)	(60)	(62)	(63)	(65)	(65)	(66)	(67)	(69)	(69)	(68)	(69)

Overall Survival



Number at risk (Number of events)

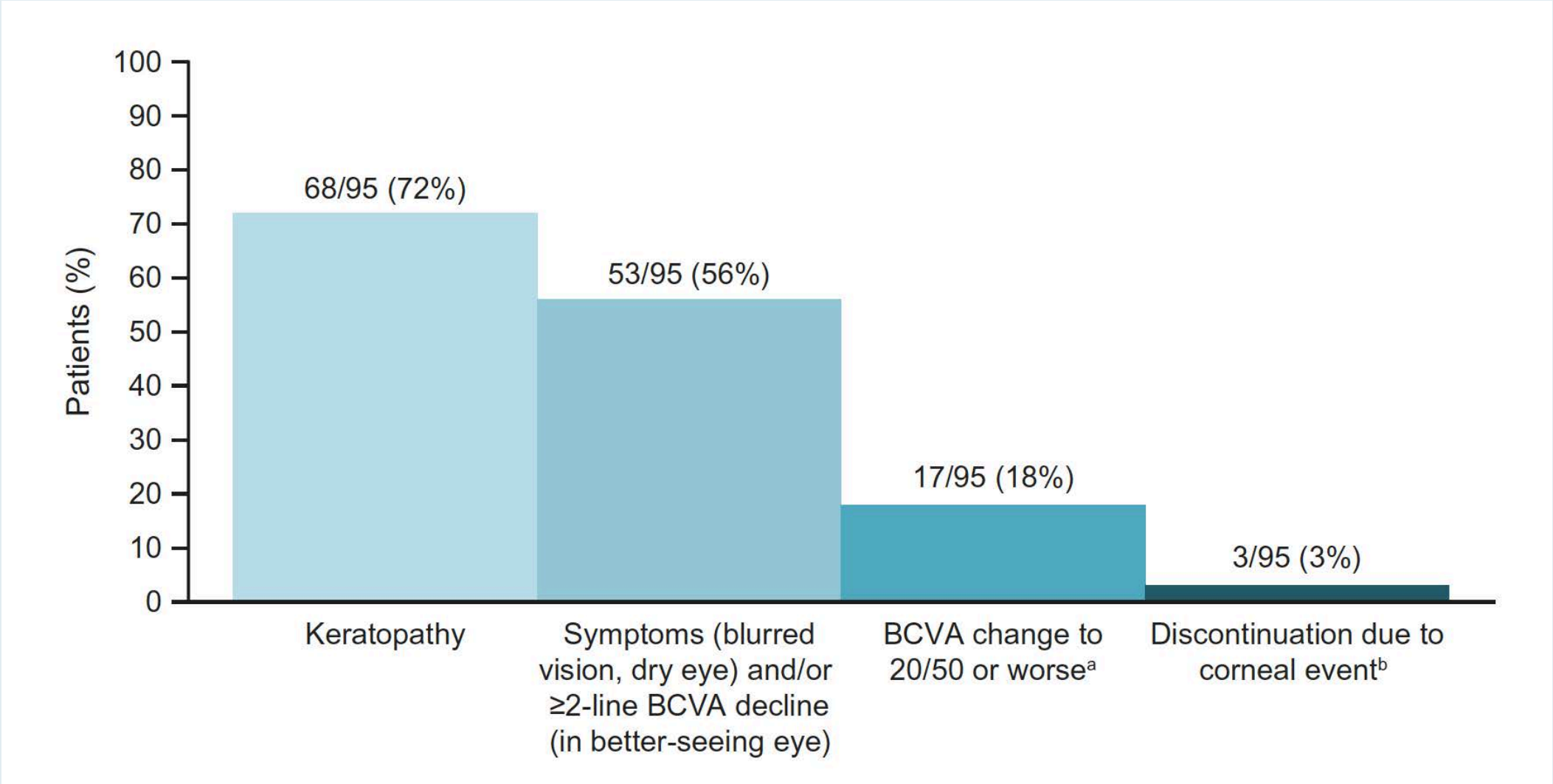
97	91	81	77	71	67	66	64	62	59	55	55	49	43	31	22	13	6	0
(0)	(5)	(13)	(16)	(21)	(25)	(26)	(28)	(30)	(33)	(37)	(37)	(39)	(42)	(45)	(46)	(46)	(47)	(47)

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

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

RTP RESEARCH TO PRACTICE

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



BCVA = best corrected visual acuity

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

RTP RESEARCH TO PRACTICE

Corneal Events: Mitigation Strategy

- Corticosteroid eye drops are not beneficial for prophylaxis or treatment
- Lubricating eye drops ≥4 times per day throughout duration of the treatment period
- No contact lens use during treatment period
- Eye examination with BCVA assessment and slit lamp examination with fluorescein staining prior to each planned dose
- Dose delays and dose reductions per recommendations

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

Belantamab Mafodotin Dose Modifications for Corneal Toxicity

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

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

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

DREAMM-6: Investigator-Assessed Best Confirmed Response with Belantamab Mafodotin + Vd

Figure 3. Investigator-assessed* best confirmed response

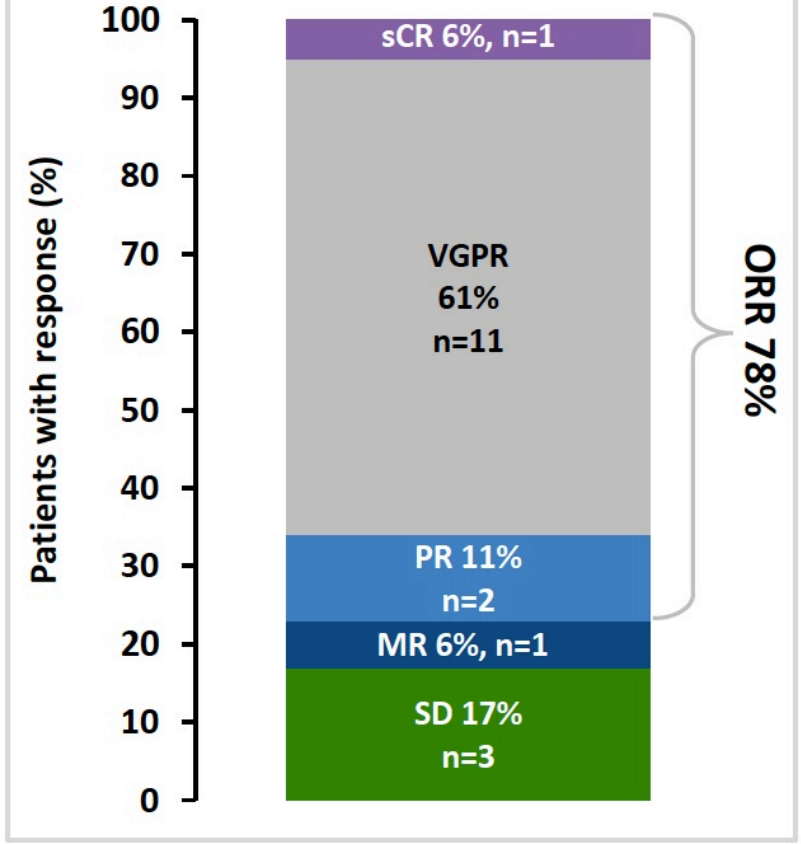
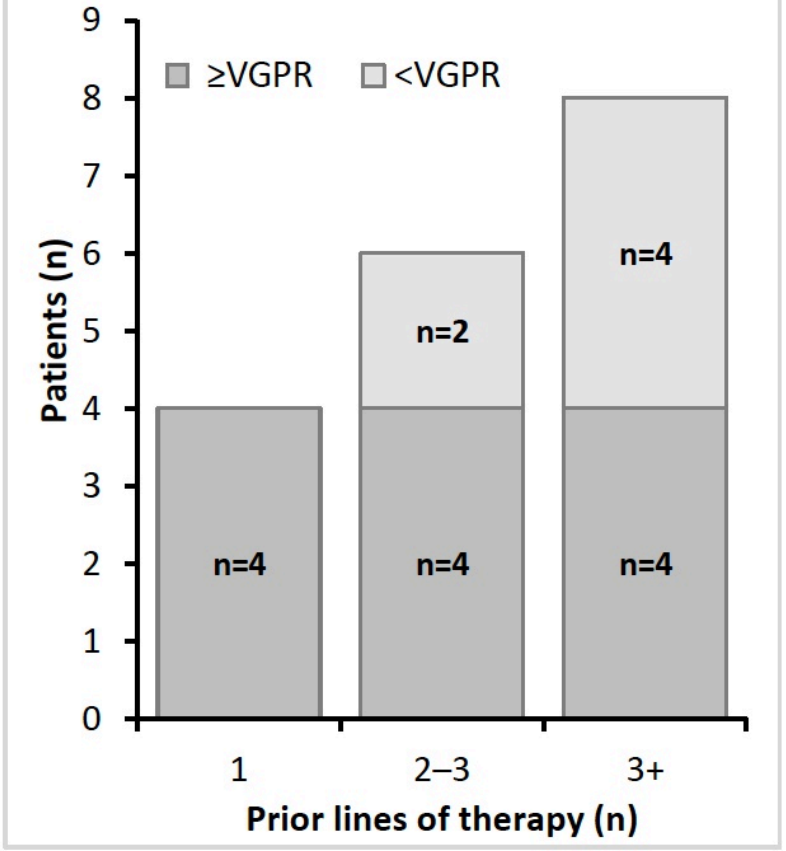


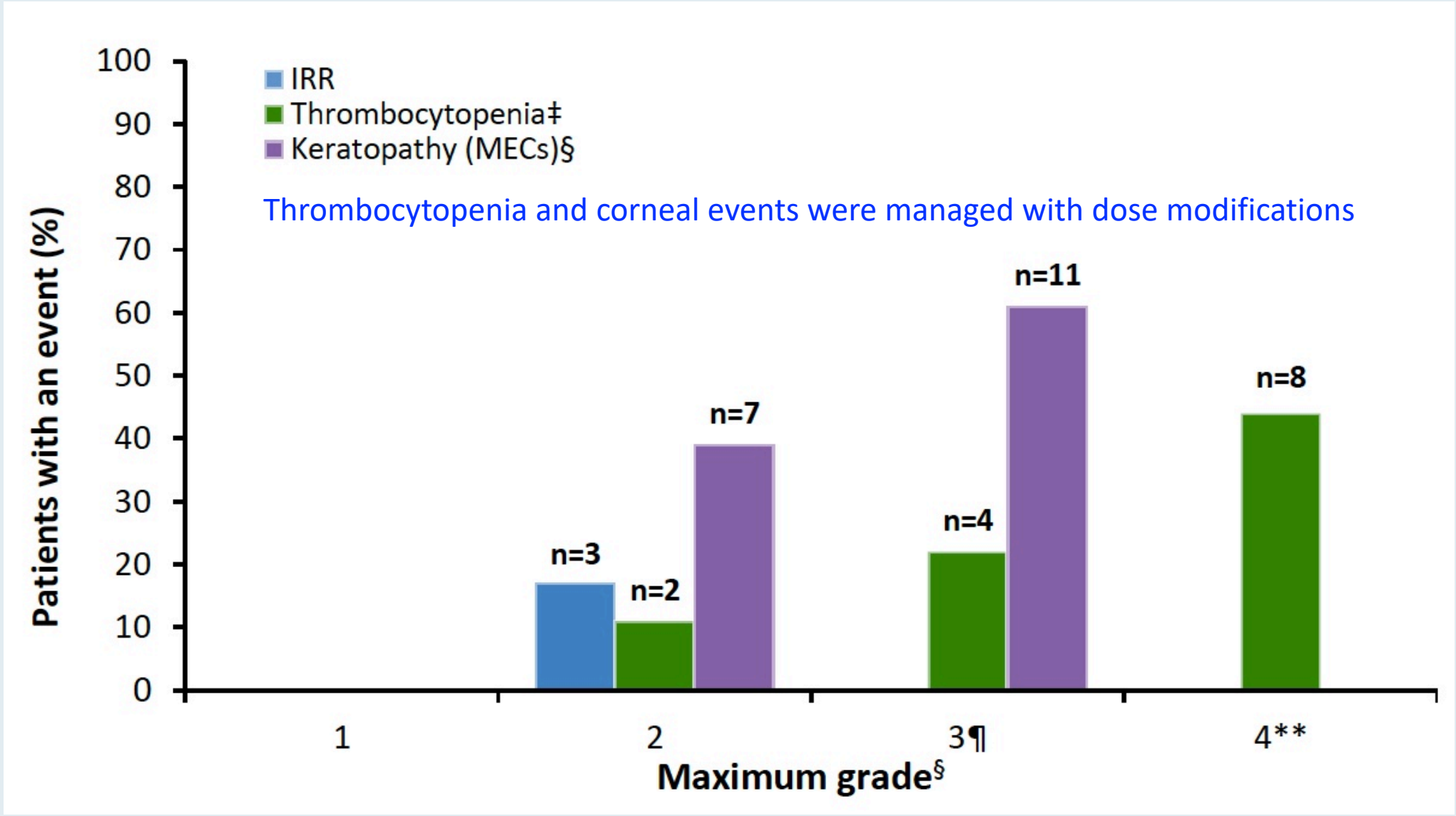
Figure 4. Investigator-assessed* best confirmed response per prior number of LOT



Popat R et al. ASH 2020;Abstract 1419.

RTP RESEARCH TO PRACTICE

DREAMM-6: Adverse Events of Special Interest



Popat R et al. ASH 2020;Abstract 1419.

Agenda

Module 1: Treatment of MM in Transplant-Ineligible Patients

Module 2: Treatment of MM in Transplant-Eligible Patients

Module 3: Management of Relapsed/Refractory MM

Module 4: BCMA CAR T-Cell Therapy

Module 5: Other Novel Agents and Strategies

FDA Approves Idecabtagene Vicleucel for R/R MM

Press Release – March 26, 2021

"The Food and Drug Administration approved idecabtagene vicleucel for the treatment of adult patients with relapsed or refractory multiple myeloma after four or more prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody. This is the first FDA-approved cell-based gene therapy for multiple myeloma.

Idecabtagene vicleucel is a B-cell maturation antigen (BCMA)-directed genetically modified autologous chimeric antigen receptor (CAR) T-cell therapy. Each dose is customized using a patient's own T-cells, which are collected and genetically modified, and infused back into the patient.

Safety and efficacy were evaluated in a multicenter study of 127 patients with relapsed and refractory multiple myeloma who received at least three prior lines of antimyeloma therapies; 88% had received four or more prior lines of therapies. Efficacy was evaluated in 100 patients who received idecabtagene vicleucel in the dose range of 300 to 460 x 106 CAR-positive T cells. Efficacy was established based on overall response rate (ORR), complete response (CR) rate, and duration of response (DOR), as evaluated by an Independent Response committee using the International Myeloma Working Group Uniform Response Criteria for Multiple Myeloma.

The ORR was 72% (95% CI: 62%, 81%) and CR rate was 28% (95% CI 19%, 38%). An estimated 65% of patients who achieved CR remained in CR for at least 12 months."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-idecabtagene-vicleucel-multiple-myeloma

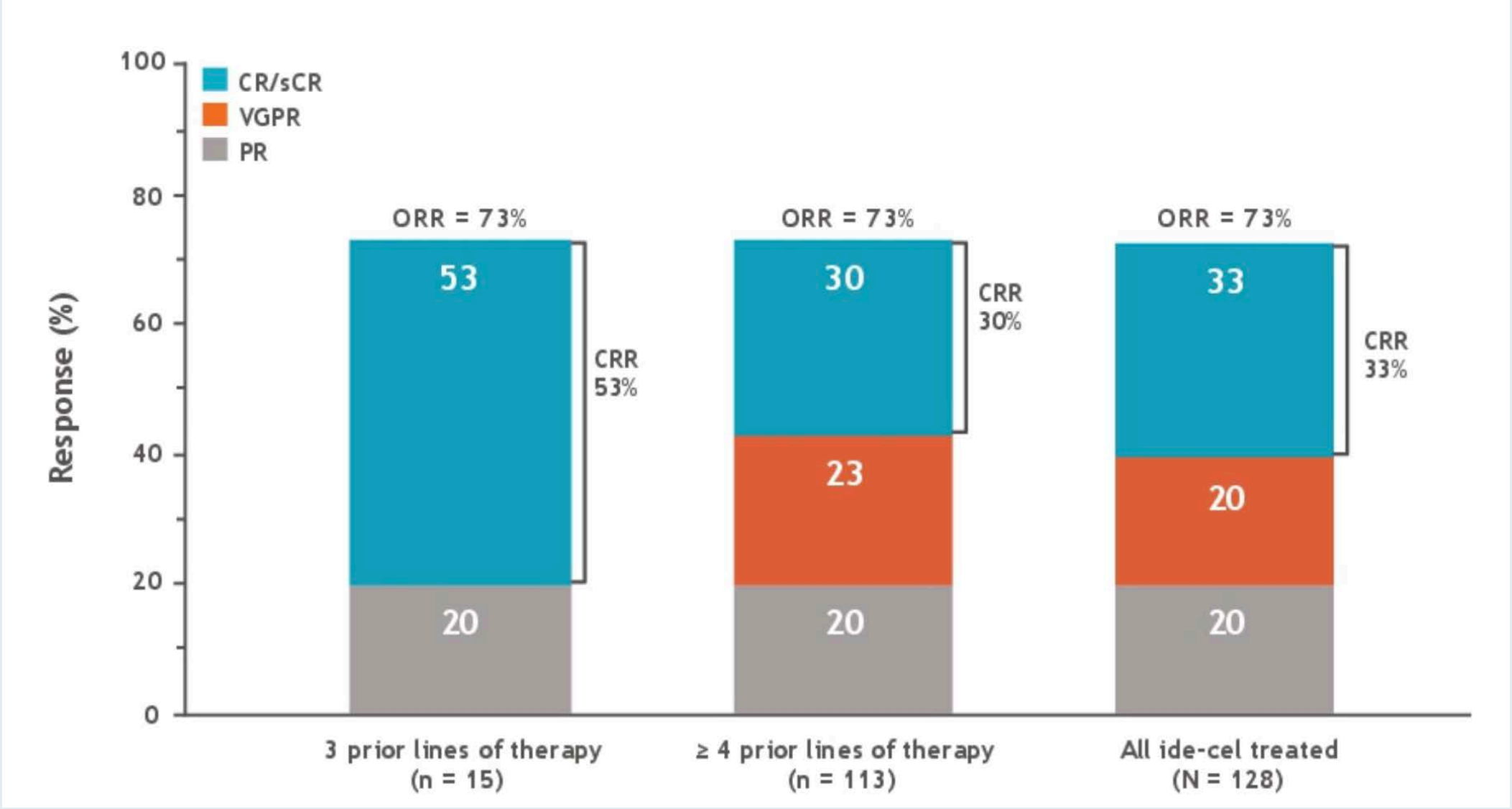
RTP RESEARCH TO PRACTICE

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

Anderson LD et al.

ASCO 2021;Abstract 8016.

KarMMa: Best Overall Response



Anderson LD et al. ASCO 2021;Abstract 8016.

KarMMa: Incidence of CRS and Neurotoxicity

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

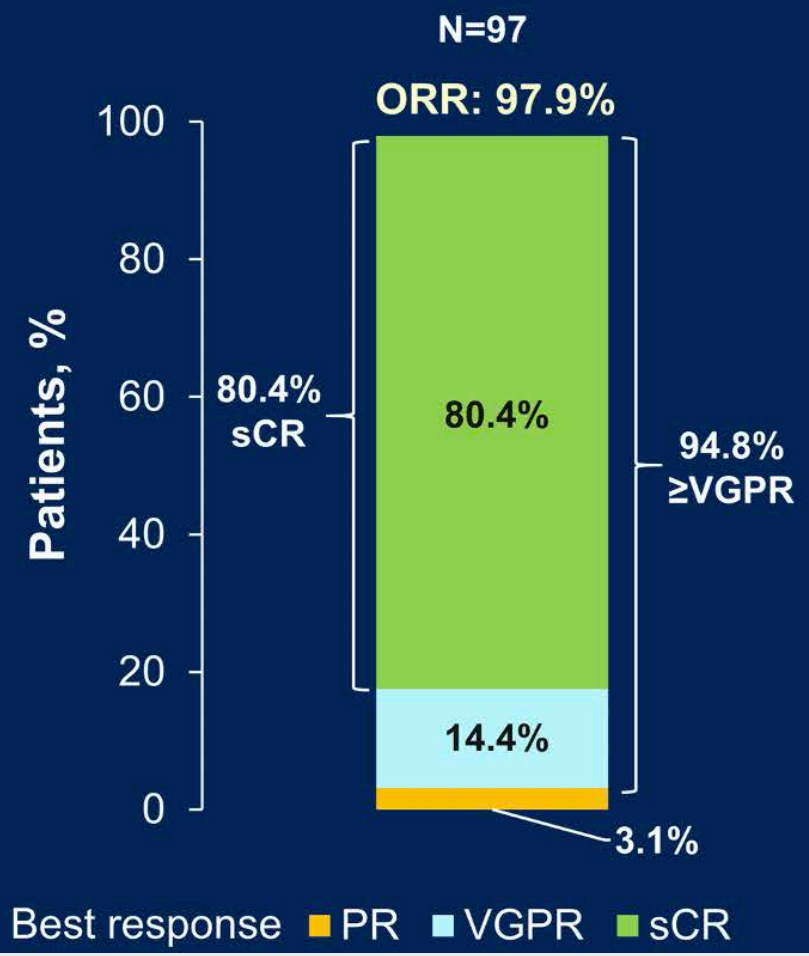
Anderson LD et al. ASCO 2021;Abstract 8016.

Ciltacabtagene Autoleucel, a B-Cell Maturation Antigen (BCMA)-Directed Chimeric Antigen Receptor T-Cell (CAR-T) Therapy, in Relapsed/Refractory Multiple Myeloma (R/R MM): Updated Results from CARTITUDE-1

Usmani SZ et al.

ASCO 2021;Abstract 8005.

CARTITUDE-1: Overall Response Rate



With longer follow-up, responses deepened with increasing rate of sCR

- Median time to first response: 1 month (range, 0.9–10.7)
- Median time to best response: 2.6 months (range, 0.9–15.2)
- Median time to ≥CR: 2.6 months (range, 0.9–15.2)
- Median duration of response: 21.8 months (95% CI, 21.8–NE)
  - Estimated 73% of responders have not progressed or died at 12 months
  - Median duration of response not reached in patients with sCR
- Response rates were comparable (range, 95–100%) across different subgroups (eg, number of prior lines of therapy, refractoriness, extramedullary plasmacytomas, and cytogenetic risk)[a]

Usmani SZ et al. ASCO 2021;Abstract 8005.

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.

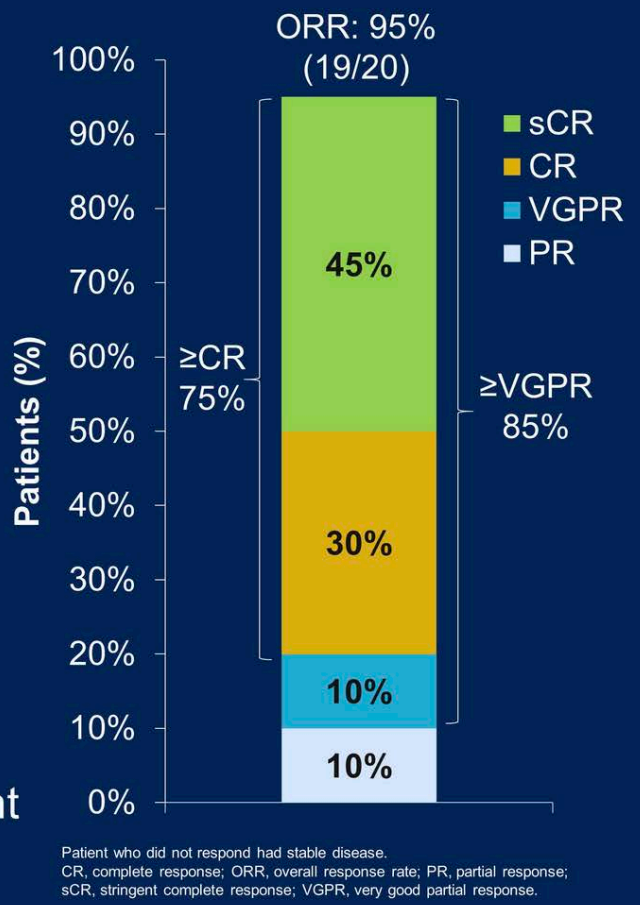
CARTITUDE-2: Ciltacabtagene Autoleucel After 1 to 3 Prior Lines of Therapy

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.

Agenda

Module 1: Treatment of MM in Transplant-Ineligible Patients

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Module 4: BCMA CAR T-Cell Therapy

Module 5: Other Novel Agents and Strategies

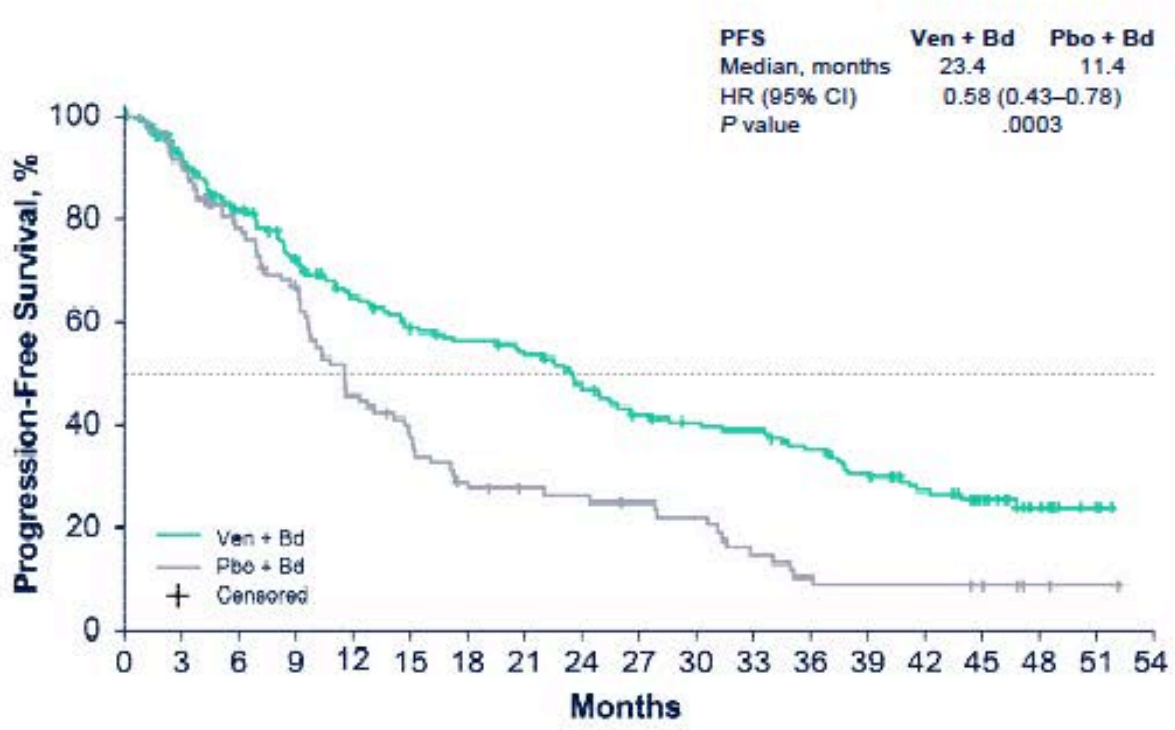
ASH 2021;Abstract 84

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

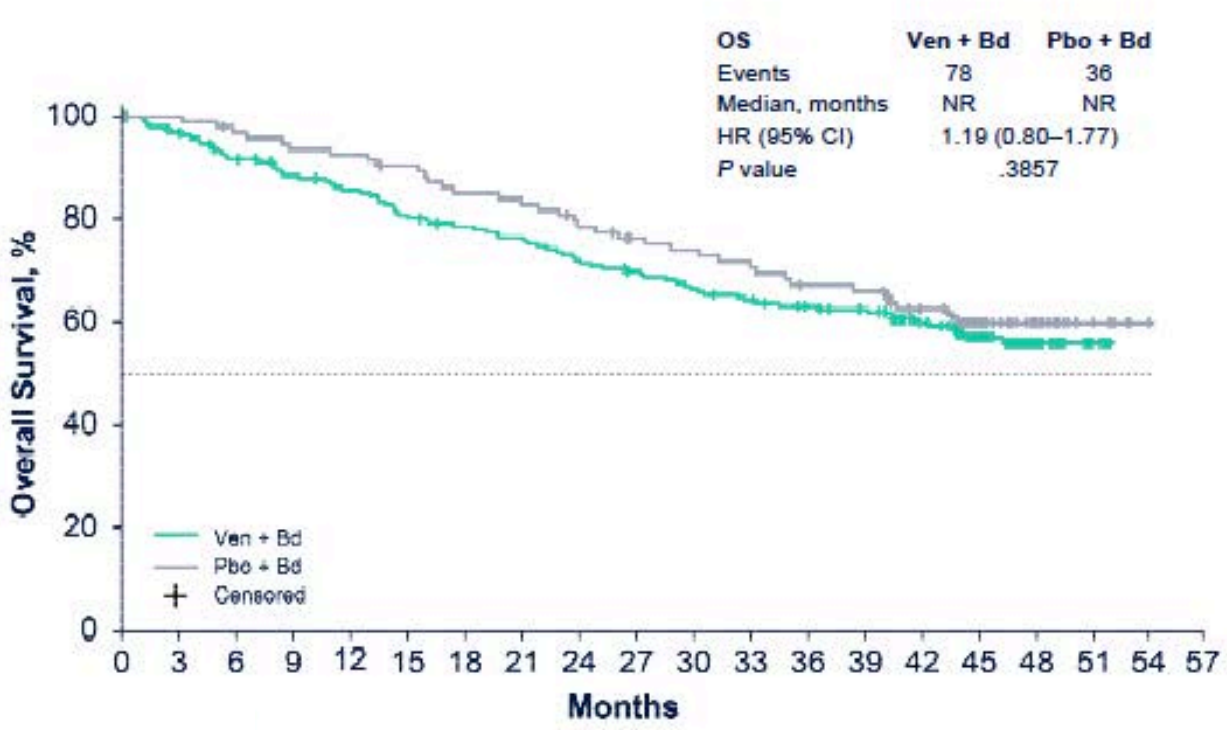
Shaji K. Kumar,[1] Simon J. Harrison,[2] Michele Cavo,[3] Javier de la Rubia,[4] Rakesh Popat,[5] Cristina Gasparetto,[6] Vania Hungria,[7] Hans Salwender,[8] Kenshi Suzuki,[9] Inho Kim,[10] Maika Onishi,[11] Grace Ku,[11] Rajvineeth Pothacamury,[12] Vasudha Sehgal,[12] Abdullah Masud,[12] Jeremy A.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

BELLINI: Updated Survival Results

Investigator-Assessed PFS in All Patients



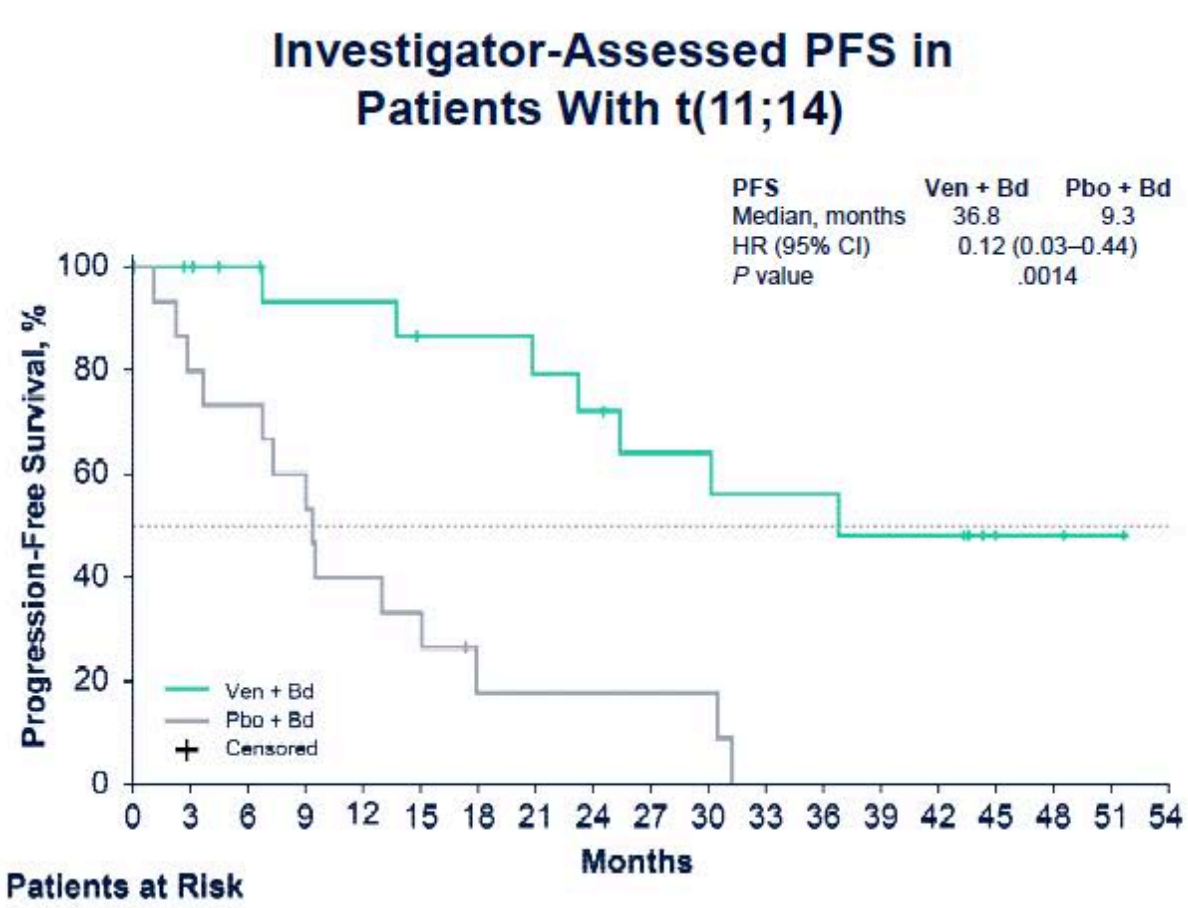
OS in All Patients

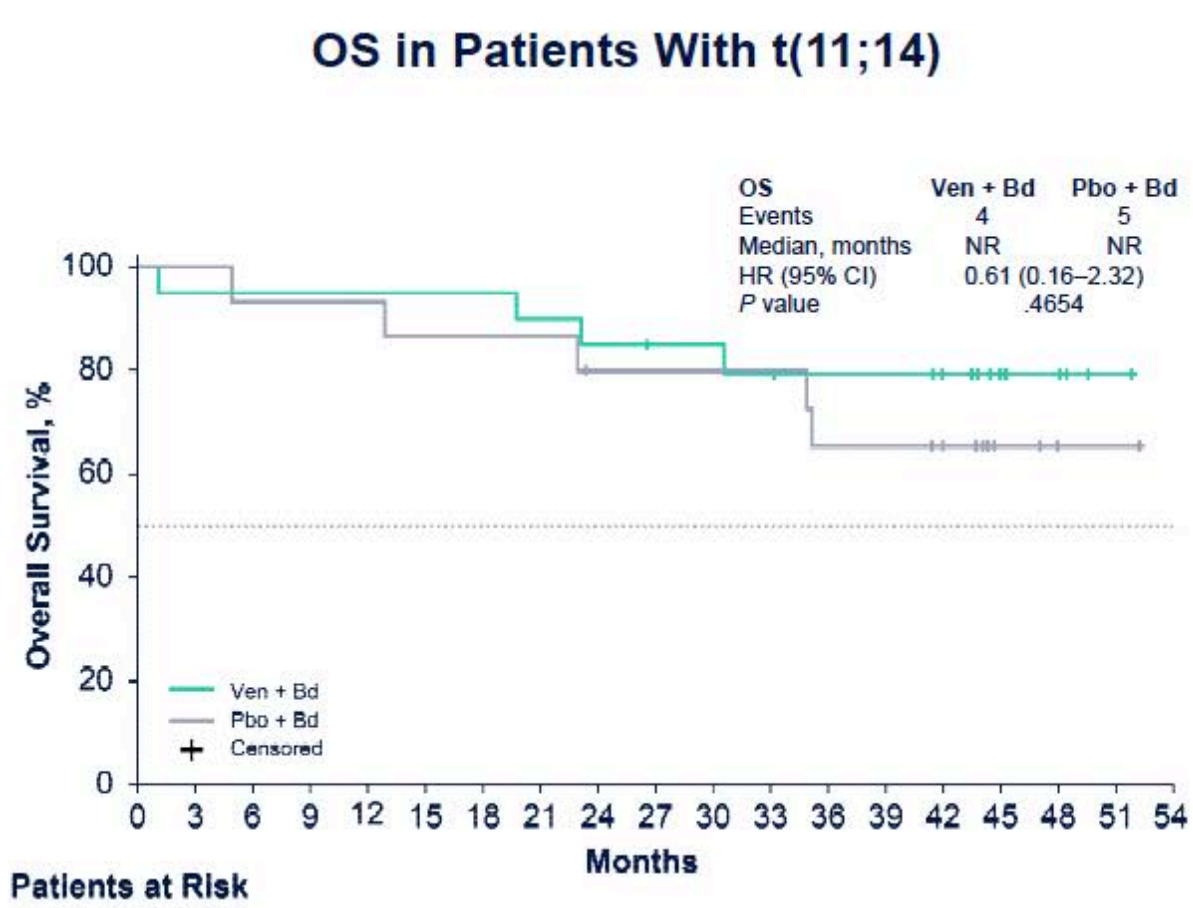


Kumar SK et al. ASH 2021;Abstract 84.

RTP RESEARCH TO PRACTICE

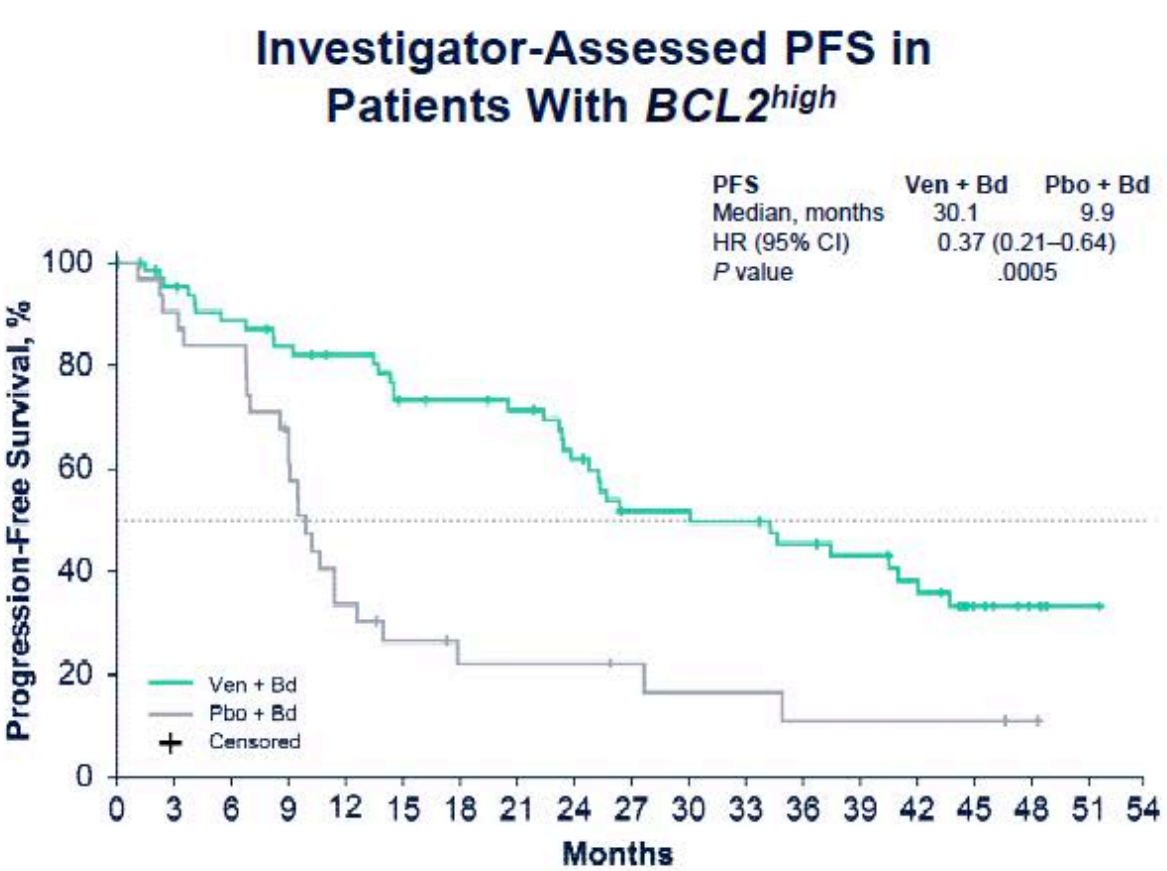
BELLINI: Updated Survival Results for Patients with t(11;14)

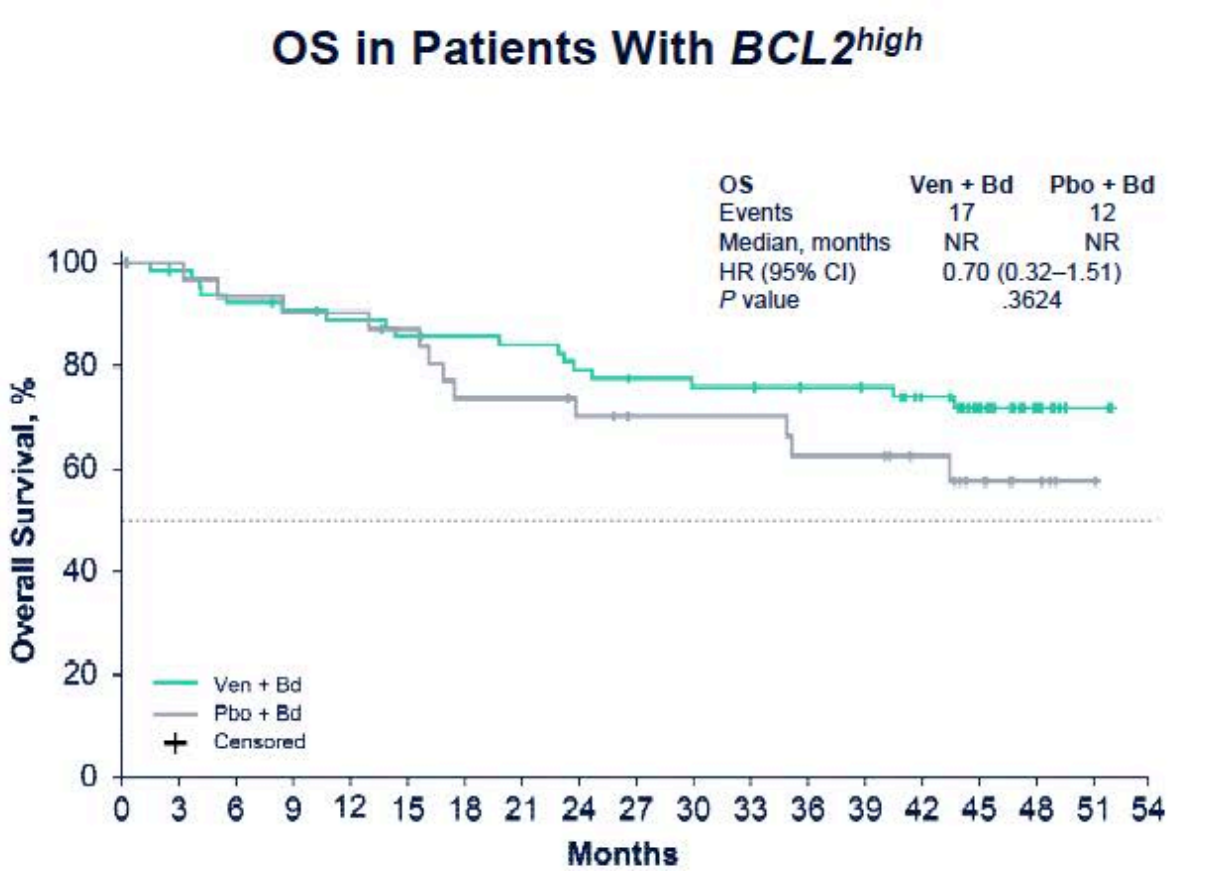




Kumar SK et al. ASH 2021;Abstract 84.

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





Kumar SK et al. ASH 2021;Abstract 84.

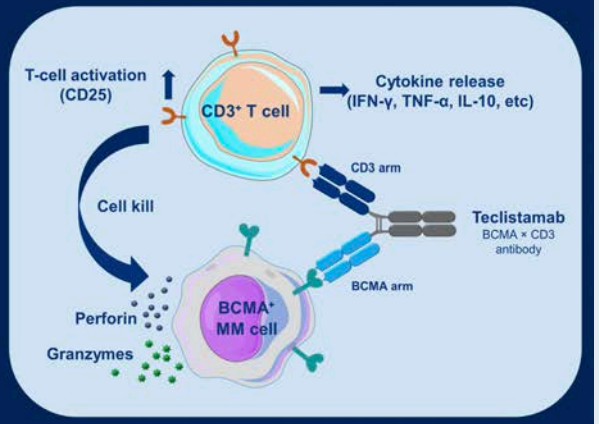
RTP RESEARCH TO PRACTICE

Bispecific Antibodies for R/R MM

TECLISTAMAB

BCMA × CD3 Bispecific Antibody

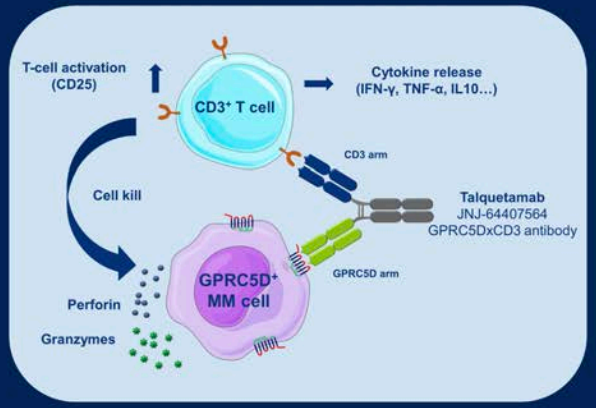
- Standard treatments and newly approved therapies for RRMM have limitations[1-3]
- Agents with new MOAs, including BCMA-targeted immunotherapies, offer considerable promise for RRMM
- Teclistamab (JNJ-64007957) is an off-the-shelf, full-size, BCMA × CD3, T-cell redirecting, bispecific antibody
- In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

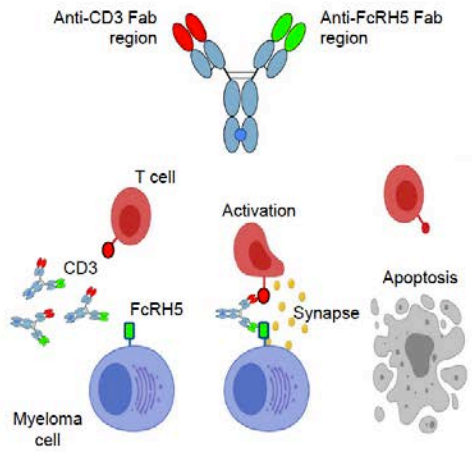
GPRC5D × CD3 Bispecific Antibody

- 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

Teclistamab, a B-cell maturation antigen × CD3 bispecific antibody, in patients with relapsed or refractory multiple myeloma (MajesTEC-1): a multicentre, open-label, single-arm, phase 1 study

Saad Z Usmani, Alfred L Garfall, Niels W C J van de Donk, Hareth Nahi, Jesus F San-Miguel, Albert Oriol, Laura Rosinol, Ajai Chari, Manisha Bhutani, Lionel Karlin, Lotfi Benboubker, Lixia Pei, Raluca Verona, Suzette Girgis, Tara Stephenson, Yusri Elsayed, Jeffrey Infante, Jenna D Goldberg, Arnob Banerjee, María-Victoria Mateos, Amrita Krishnan

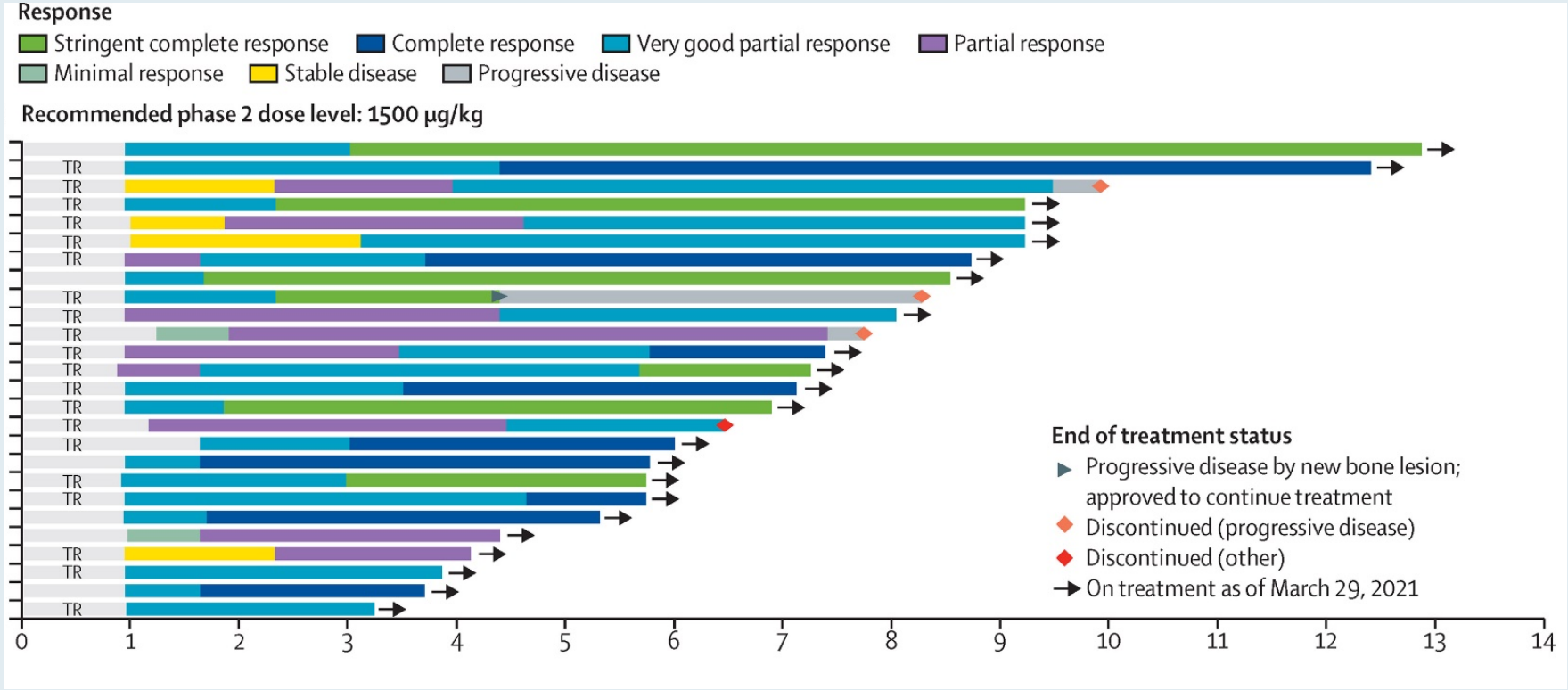
Lancet 2021; 398: 665–74

MajesTEC-1: A Phase I Study of Teclistamab in R/R MM

Teclistamab: A BCMA-targeted bispecific IgG4 mAb
Baseline characteristics: median prior regimens, 5 (4-6); high-risk cytogenetics, 37%; extramedullary disease, 20%; triple refractory, 83%.

Response at RP2D (%)	N = 40
ORR	65%
sCR	18%
CR	23%
VGPR	18%
PR	8%

69% of CR/sCR patients MRD-



- CRS at RP2D (recommended Phase II dose): 70% (0% Grade ≥3)
- 1 patient with Grade 1 neurotoxicity at the RP2D

Usmani S et al. *Lancet* 2021;398:665-74.

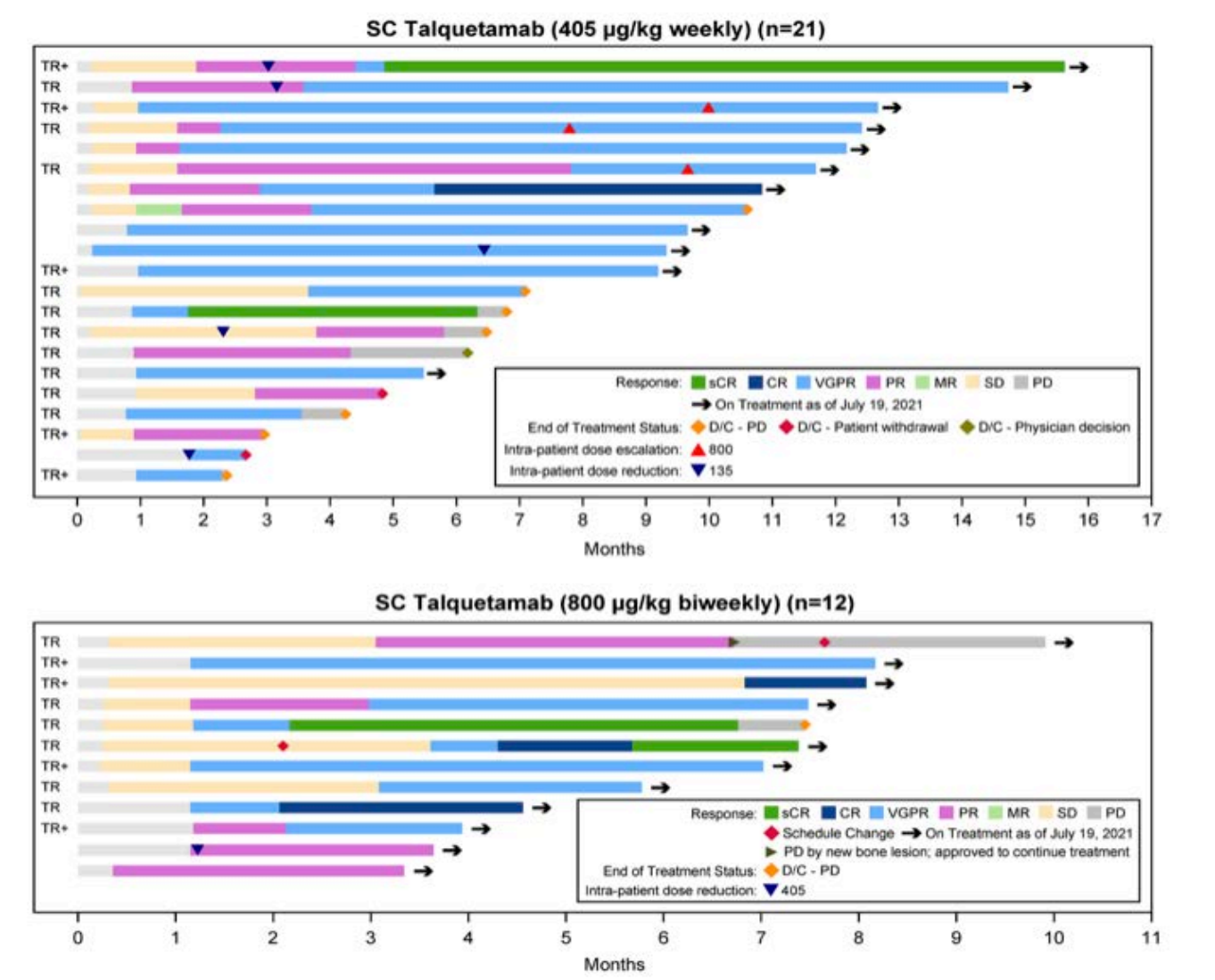
RTP RESEARCH TO PRACTICE

Updated Phase 1 Results from MonumenTAL-1: First-in-Human Study of Talquetamab, a G Protein-Coupled Receptor Family C Group 5 Member D x CD3 Bispecific Antibody, in Patients with Relapsed/Refractory Multiple Myeloma

Krishnan AY et al.

ASH 2021;Abstract 158.

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



Krishnan AY et al. ASH 2021;Abstract 158.

RTP RESEARCH TO PRACTICE

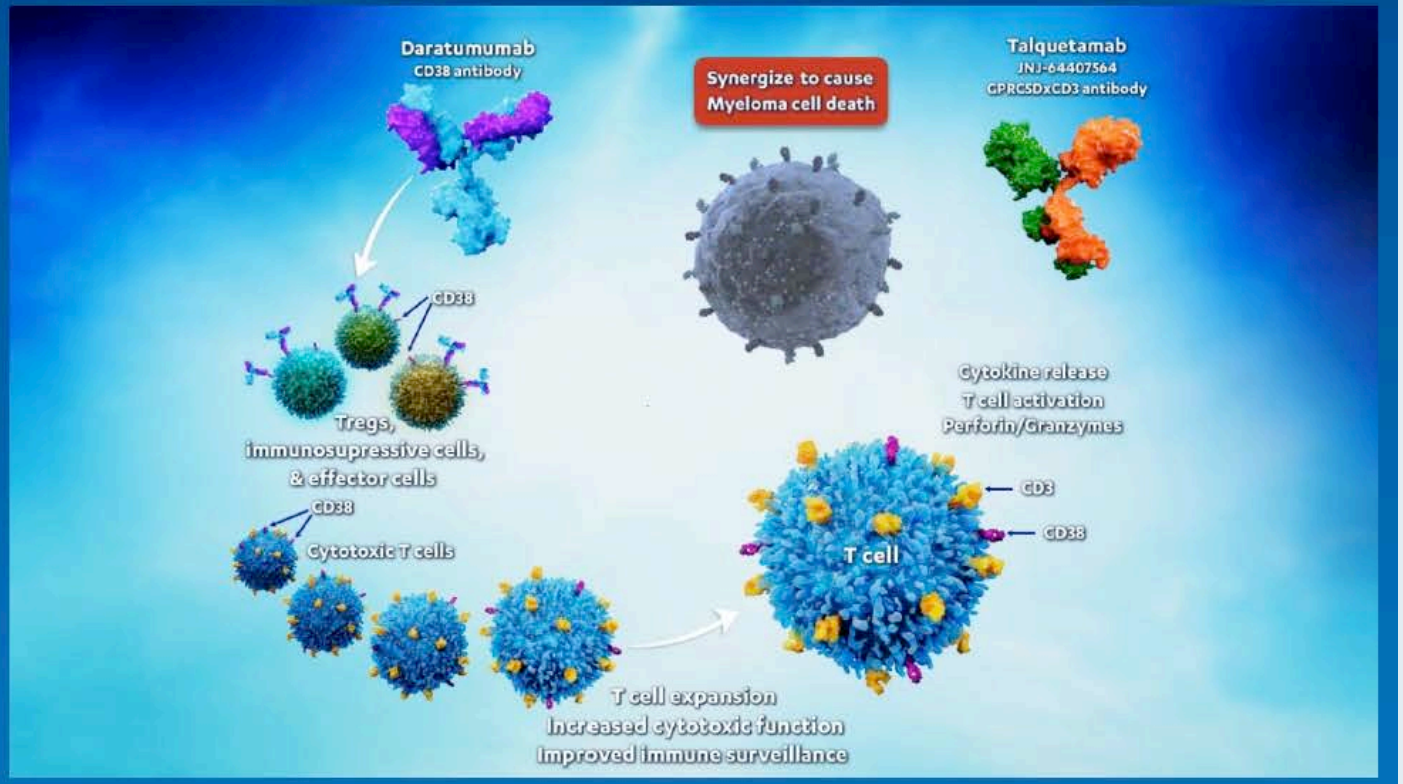
ASH 2021;Abstract 161

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]

Rationale for Combining Talquetamab and Daratumumab

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



Chari A et al. ASH 2021;Abstract 161.

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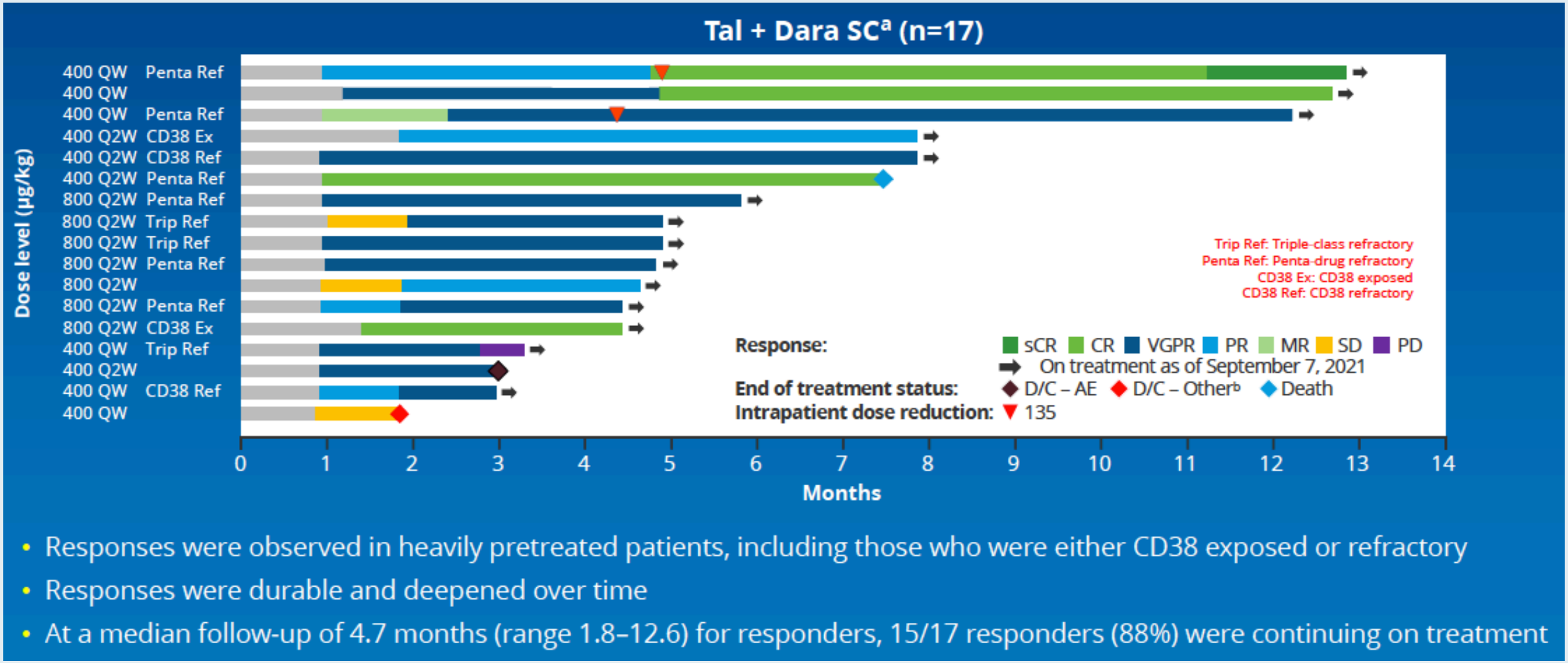
TRIMM-2: Overall Response

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

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

Chari A et al. ASH 2021;Abstract 161.

TRIMM-2: Duration of Response



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

Chari A et al. ASH 2021;Abstract 161.

TRIMM-2: Hematologic Safety Profile

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

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

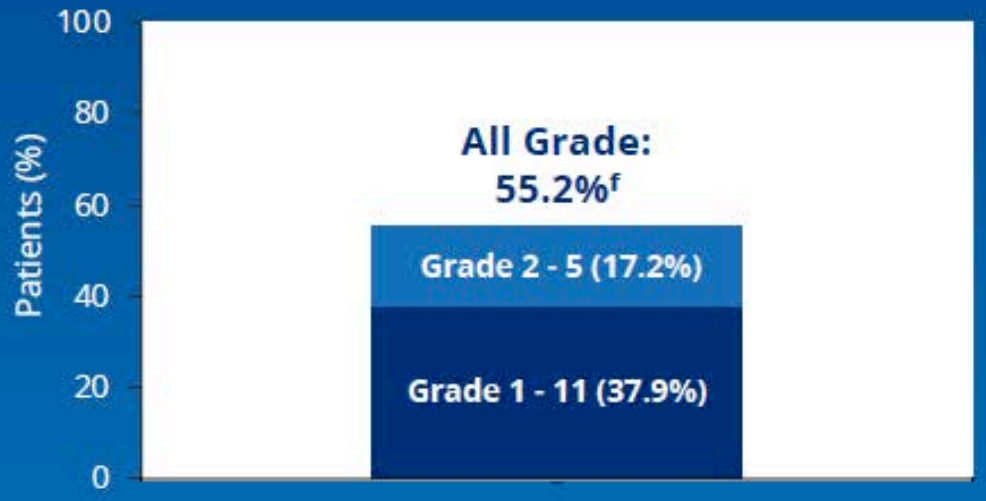
- The majority of AEs were grade 1 or 2
- No overlapping toxicities were observed
- 1 patient (3.4%) discontinued due to an AE
- Cytopenias were mostly confined to step-up and cycle 1/2 doses
  - Cytopenias resolved in the majority of patients
  - Neutropenias generally resolved within 1 week and were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

Chari A et al. ASH 2021;Abstract 161.

TRIMM-2: Cytokine Release Syndrome (CRS)

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

Maximum CRS Grade[e]

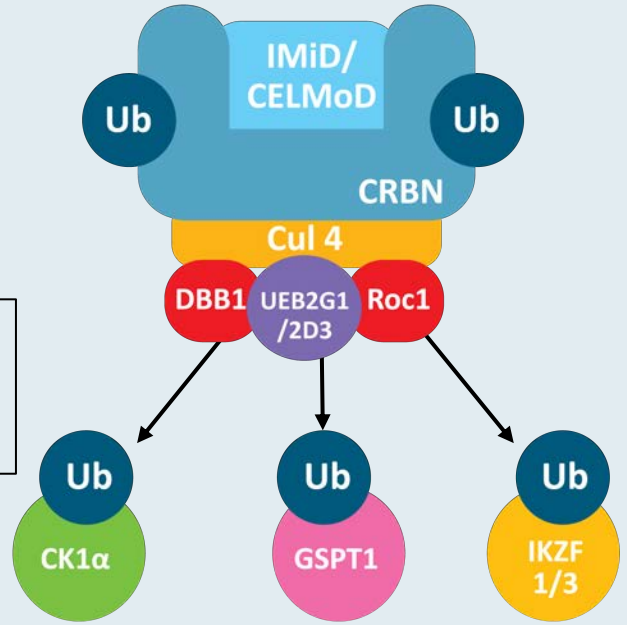


- **No grade 3/4 CRS events were observed**
  - All but 1 event of CRS occurred with step-up doses
- **CRS resolved in all patients, with no d/c due to CRS**
  - Only 1 patient received 2 doses of tocilizumab for a single CRS event[g]

Chari A et al. ASH 2021;Abstract 161.

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

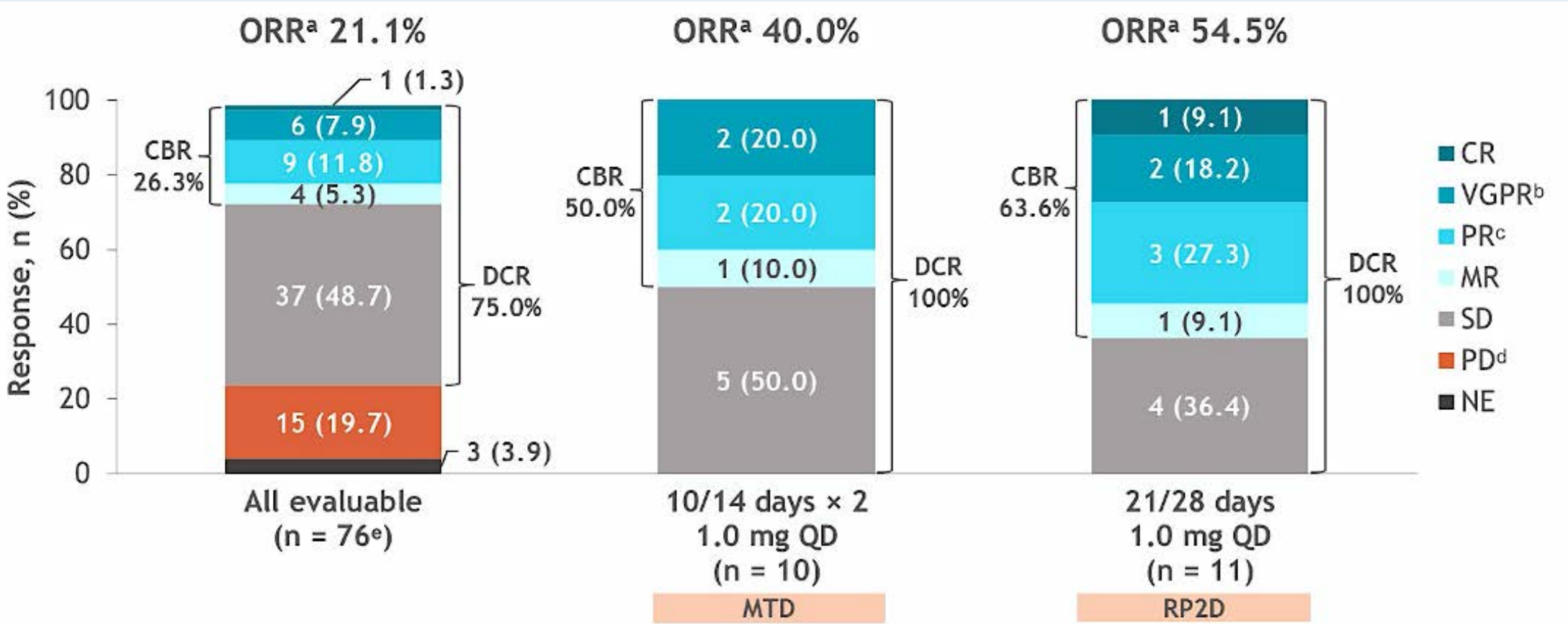
RTP RESEARCH TO PRACTICE

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

Richardson PG et al. ASCO 2020;Abstract 8500.

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.

Thank you for joining us!

CME and MOC 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 North Carolina Oncology Association and the South Carolina Oncology Society

A CME/MOC- and NCPD-Accredited Event

Saturday, February 12, 2022
8:30 AM – 4:00 PM ET

RTP
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TO PRACTICE

Agenda

Module 1 — Chronic Lymphocytic Leukemia and Lymphomas: *Drs Flinn and LaCasce*

Module 2 — Multiple Myeloma: *Drs Callander and Rajkumar*

Module 3 — Genitourinary Cancers: *Drs Dreicer and Heath*

Module 4 — Breast Cancer: *Drs Borges and Jhaveri*

Module 5 — Gastrointestinal Cancers: *Drs Hochster and Messersmith*

Module 6 — Lung Cancer: *Drs Govindan and Johnson*

Genitourinary Cancers Faculty

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

Elisabeth I Heath, MD
Associate Center Director, Translational Sciences
Chair, Genitourinary Oncology Multidisciplinary Team
Professor of Oncology and Medicine
Hartmann Endowed Chair for Prostate Cancer Research
Director, Prostate Cancer Research
Karmanos Cancer Institute
Wayne State University School of Medicine
Detroit, Michigan

MODULE 3: Genitourinary Cancers

Co-Moderator

Justin Peter Favaro, MD, PhD
Oncology Specialists of Charlotte
Charlotte, North Carolina

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RESEARCH
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Contributing General Medical Oncologists

Jennifer L Dallas, MD
Novant Health Cancer Institute
Charlotte, North Carolina

Joanna Metzner-Sadurski, MD
Self Regional Healthcare Cancer Center
Greenwood, South Carolina

Justin Peter Favaro, MD, PhD
Oncology Specialists of Charlotte
Charlotte, North Carolina

William R Mitchell, MD
Southern Oncology Specialists
Charlotte, North Carolina

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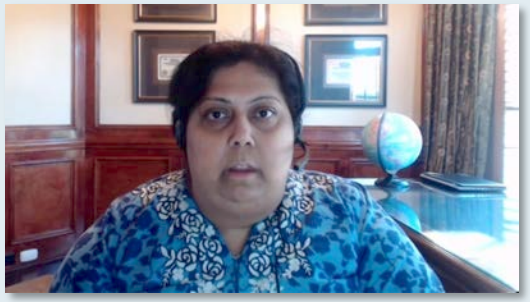
Contributing General Medical Oncologists



Niyati A Nathwani, MD
Carolina Blood and Cancer Care Associates
Charlotte, North Carolina

Nasfat Shehadeh, MD
Oncology Specialists of Charlotte, PA
Charlotte, North Carolina

Julia Saylors, MD
Charleston Oncology
North Charleston, South Carolina

RTP RESEARCH TO PRACTICE

Agenda

Module 1: Urothelial Bladder Carcinoma

Module 2: Prostate Cancer

Module 3: Renal Cell Carcinoma (RCC)

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RESEARCH
TO PRACTICE

Agenda

Module 1: Urothelial Bladder Carcinoma

Module 2: Prostate Cancer

Module 3: Renal Cell Carcinoma (RCC)

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RESEARCH
TO PRACTICE

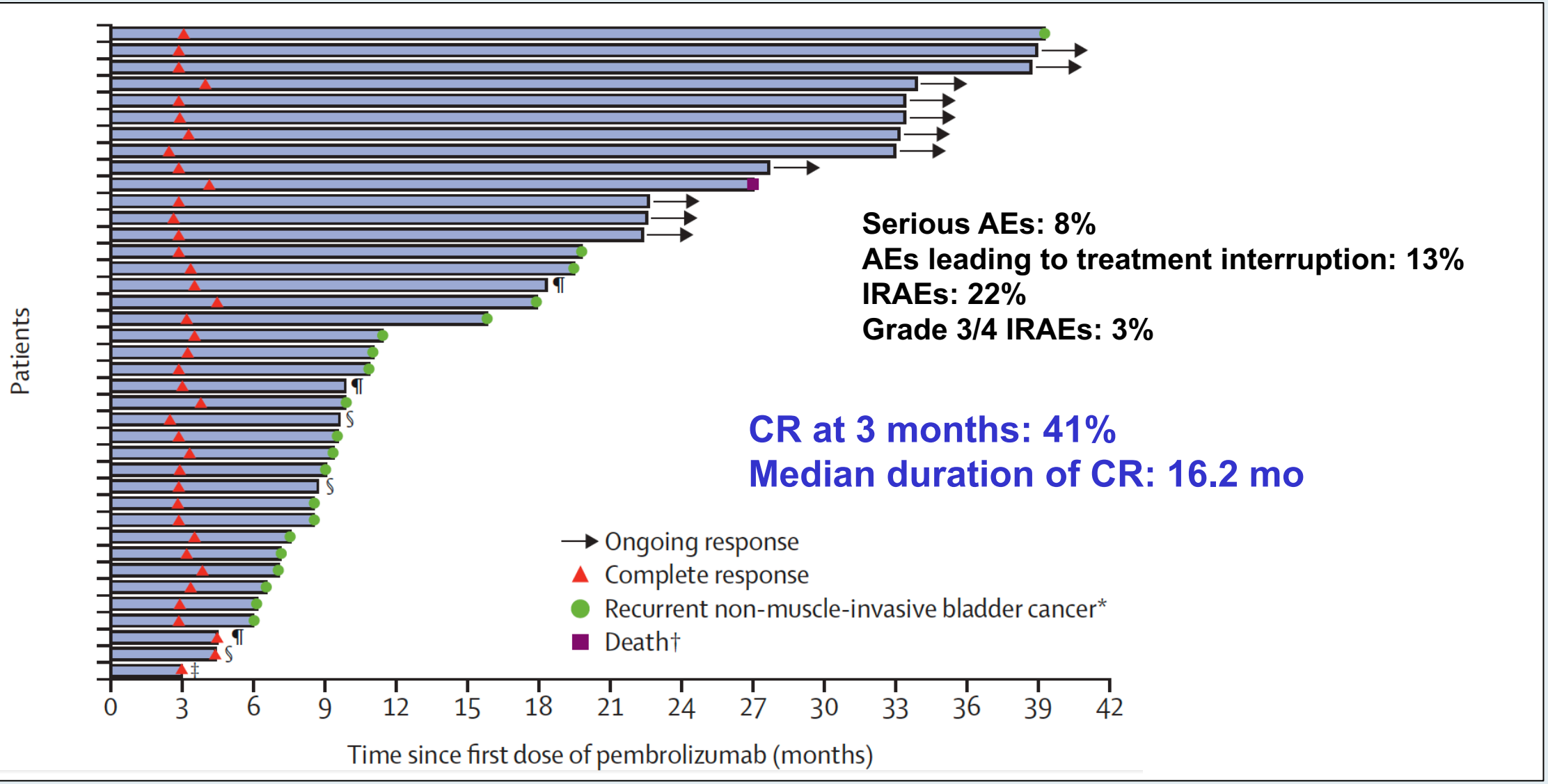
Pembrolizumab monotherapy for the treatment of high-risk non-muscle-invasive bladder cancer unresponsive to BCG (KEYNOTE-057): an open-label, single-arm, multicentre, phase 2 study

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;22:919-30.**

RTP RESEARCH TO PRACTICE

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



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

FDA Approves Nivolumab for Adjuvant Treatment of Urothelial Carcinoma

Press Release – August 19, 2021

"The Food and Drug Administration approved nivolumab for the adjuvant treatment of patients with urothelial carcinoma (UC) who are at high risk of recurrence after undergoing radical resection.

This is the first FDA approval for adjuvant treatment of patients with high-risk UC. The results supporting this approval also supported the conversion of nivolumab's accelerated approval for advanced/metastatic UC to a regular approval.

Nivolumab was investigated in CHECKMATE-274 (NCT02632409), a randomized, double-blind, placebo-controlled trial in patients who were within 120 days of radical resection of UC of the bladder or upper urinary tract (renal pelvis or ureter) at high risk of recurrence. Patients were randomized (1:1) to receive nivolumab 240 mg or placebo by intravenous infusion every 2 weeks until recurrence or until unacceptable toxicity for a maximum treatment duration of 1 year."

www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-nivolumab-adjuvant-treatment-urothelial-carcinoma

The NEW ENGLAND JOURNAL of MEDICINE

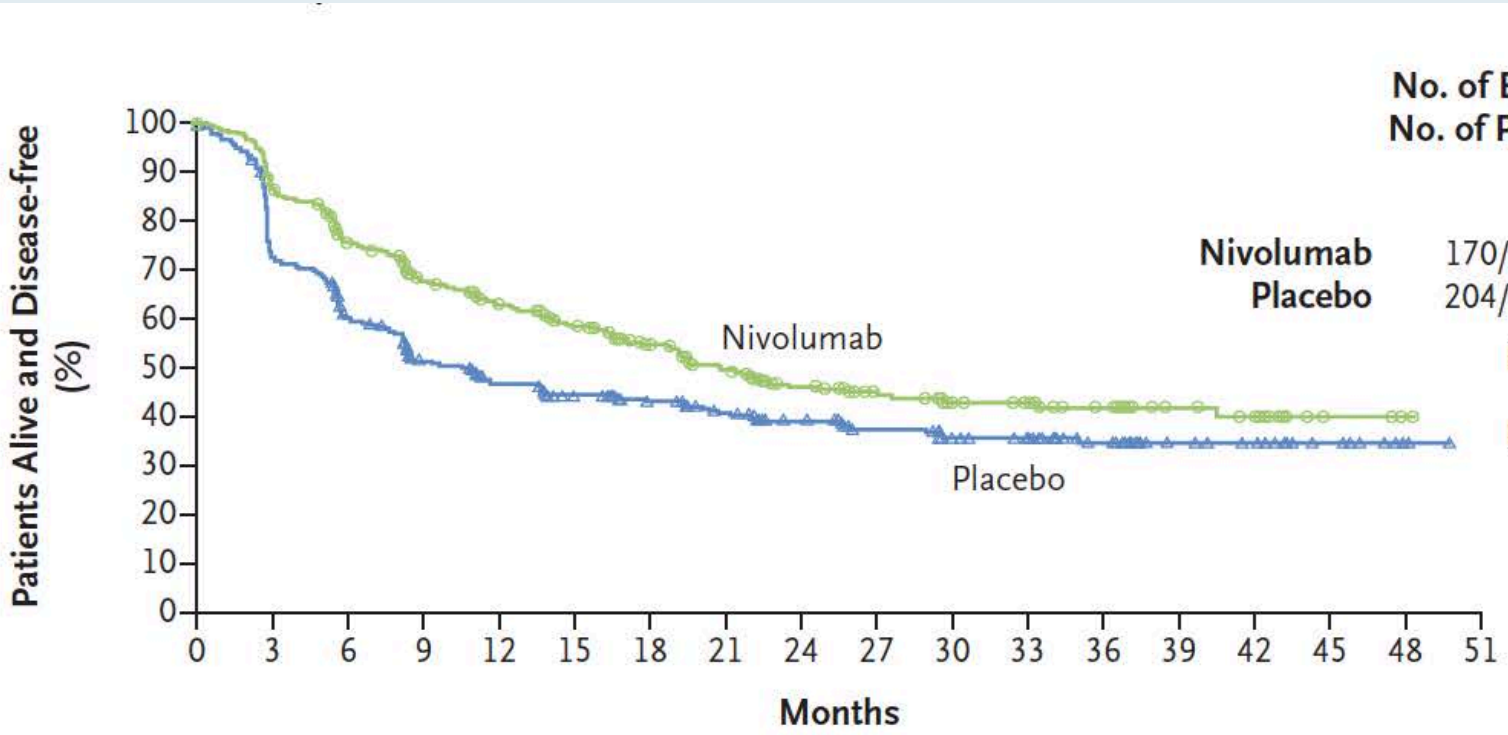
ORIGINAL ARTICLE

Adjuvant Nivolumab versus Placebo in Muscle-Invasive Urothelial Carcinoma

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

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

CheckMate 274: Disease-Free Survival in the ITT Population

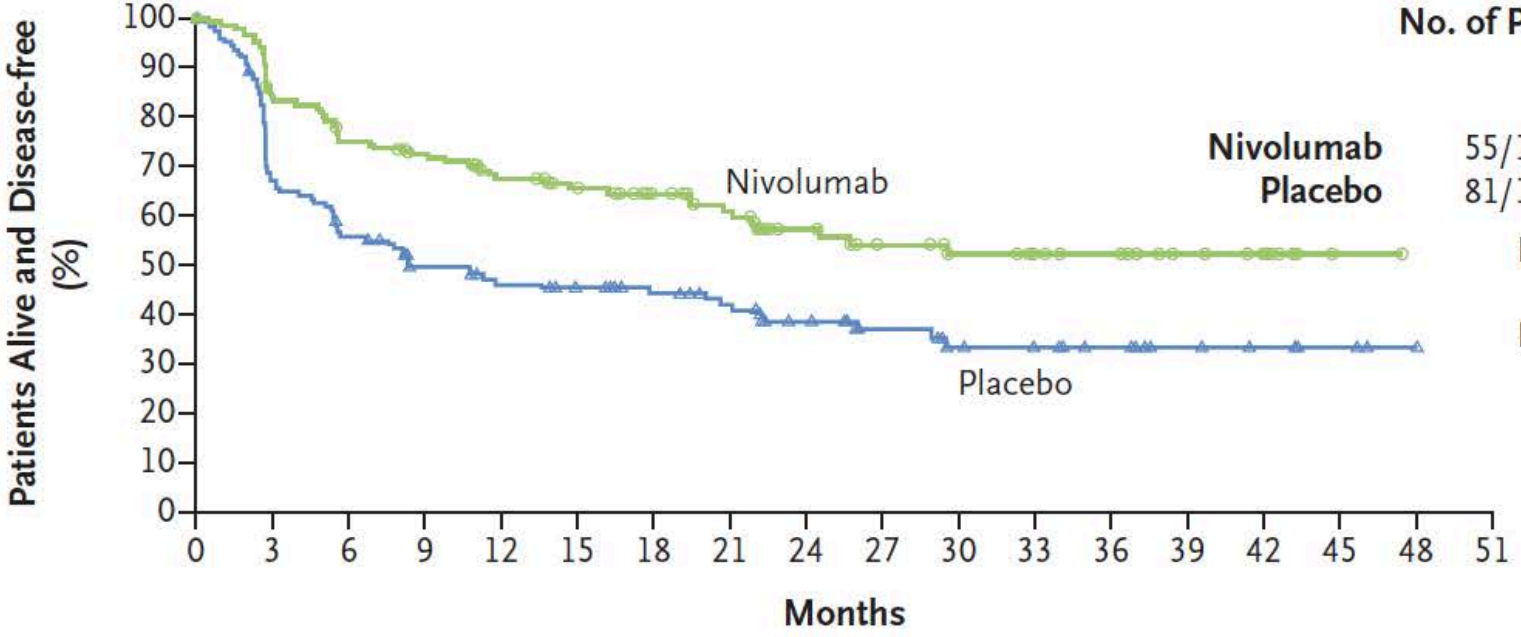


	No. of Events/ No. of Patients	Disease-free Survival at 6 Mo (95% CI)	Disease-free Survival at 12 Mo (95% CI)
		%	
Nivolumab	170/353	74.9 (69.9–79.2)	62.8 (57.3–67.8)
Placebo	204/356	60.3 (54.9–65.3)	46.6 (41.1–51.9)

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

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

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



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

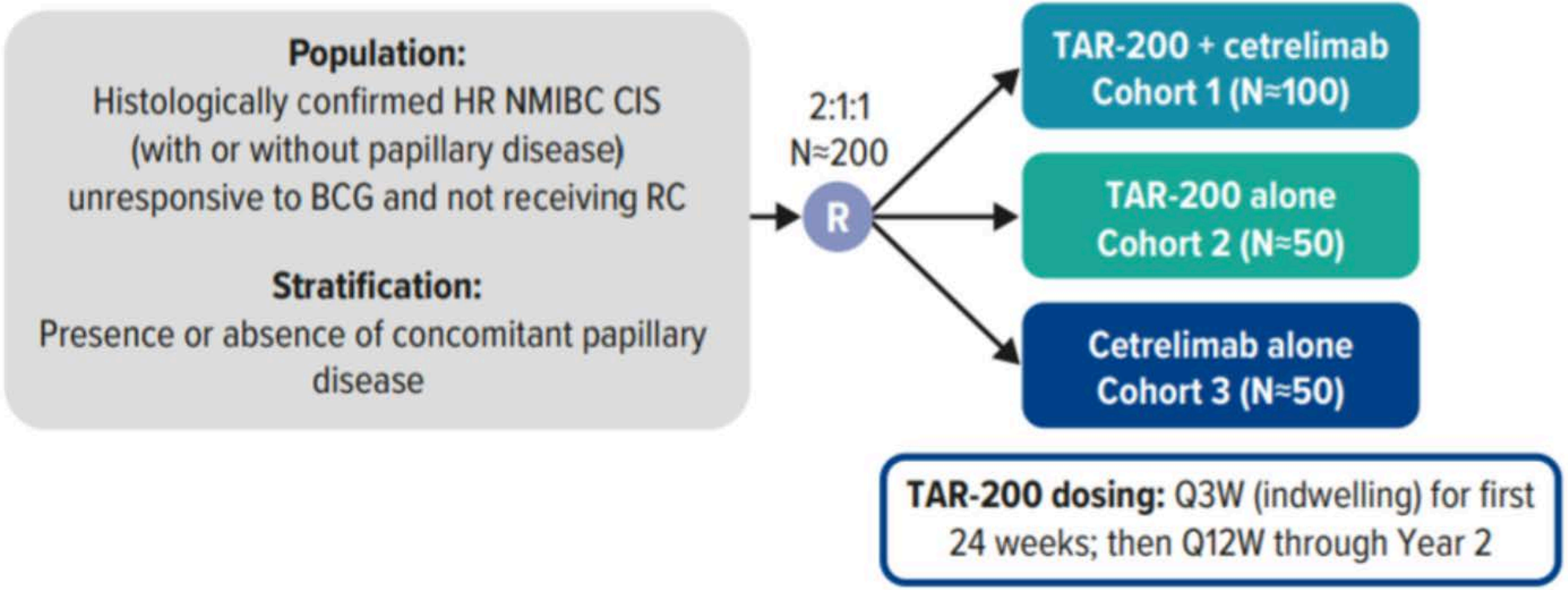
Hazard ratio for disease recurrence or death, 0.55 (98.72% CI, 0.35–0.85)
P<0.001

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

RTP RESEARCH TO PRACTICE

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

Clinical Trial Identifier: NCT04640623



Primary Endpoint: Overall clinical response rate

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

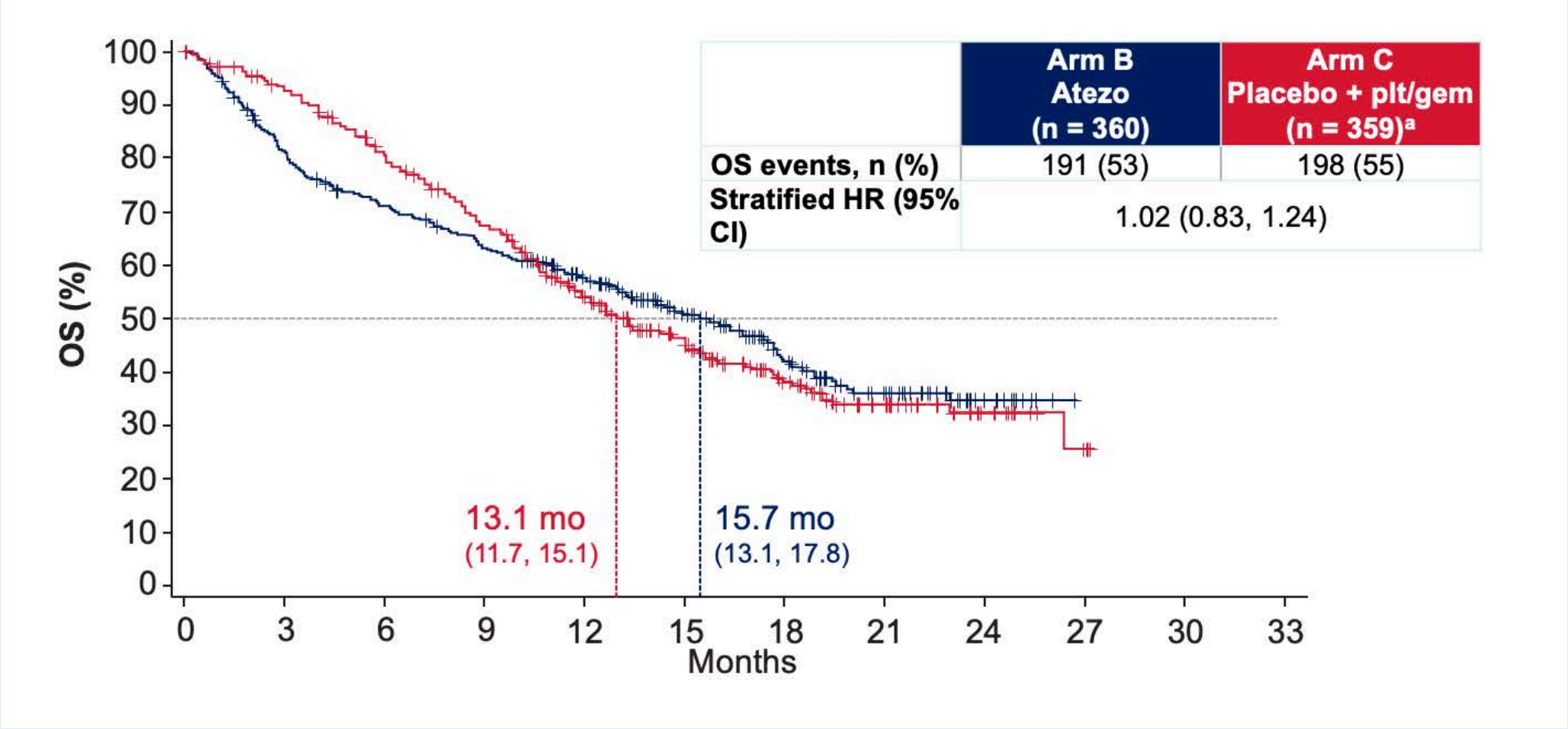
RTP RESEARCH TO PRACTICE

Atezolizumab with or without chemotherapy in metastatic urothelial cancer (IMvigor130): a multicentre, randomised, placebo-controlled phase 3 trial

Matthew D Galsky, José Ángel Arranz Arija, Aristotelis Bamias, Ian D Davis, Maria De Santis, Eiji Kikuchi, Xavier Garcia-del-Muro, Ugo De Giorgi, Marina Mencinger, Kouji Izumi, Stefano Panni, Mahmut Gumus, Mustafa Özgüroğlu, Arash Rezazadeh Kalebasty, Se Hoon Park, Boris Alekseev, Fabio A Schutz, Jian-Ri Li, Dingwei Ye, Nicholas J Vogelzang, Sandrine Bernhard, Darren Tayama, Sanjeev Mariathasan, Almut Mecke, AnnChristine Thåström, Enrique Grande, for the IMvigor130 Study Group†*

***Lancet* 2020;395:1547-57.**

IMvigor130: Overall Survival (OS) with Monotherapy (Arm B vs Arm C)

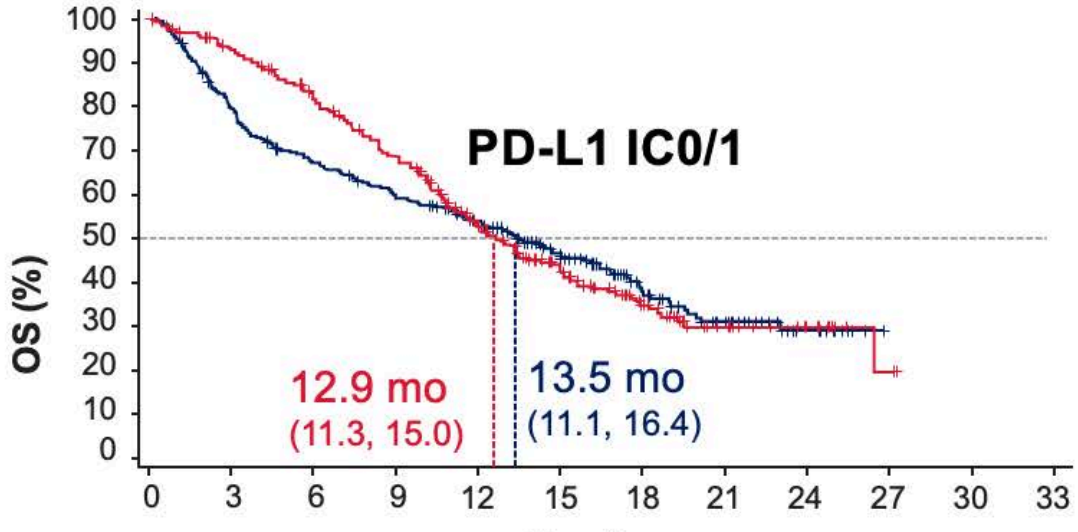


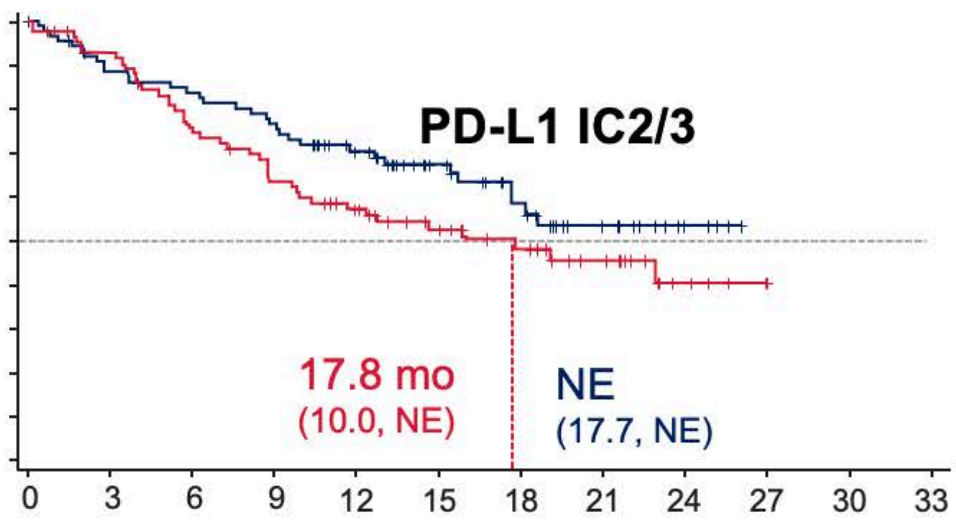
	Arm B Atezo (n = 360)	Arm C Placebo + plt/gem (n = 359)[a]
OS events, n (%)	191 (53)	198 (55)
Stratified HR (95% CI)	1.02 (0.83, 1.24)	

Galsky MD et al. *Lancet* 2020;395(10236):1547-57.

RTP RESEARCH TO PRACTICE

IMvigor130: OS by PD-L1 Status





No. at Risk												
Atezo	272	210	175	152	124	85	48	28	11	NE	NE	NE
Placebo + plt/gem	274	246	212	173	116	73	41	21	10	2	NE	NE

	Arm B Atezo (n = 272)	Arm C Placebo + plt/gem (n = 274)
OS events, n (%)	158 (58)	156 (57)
Unstratified HR (95% CI)	1.07 (0.86, 1.33)	

	88	75	70	64	49	35	24	14	5	NE	NE	NE
	85	76	62	51	42	30	21	14	5	1	NE	NE

	Arm B Atezo (n = 88)	Arm C Placebo + plt/gem (n = 85)
OS events, n (%)	33 (38)	42 (49)
Stratified HR (95% CI)	0.68 (0.43, 1.08)	

Galsky MD et al. *Lancet* 2020;395(10236):1547-57.

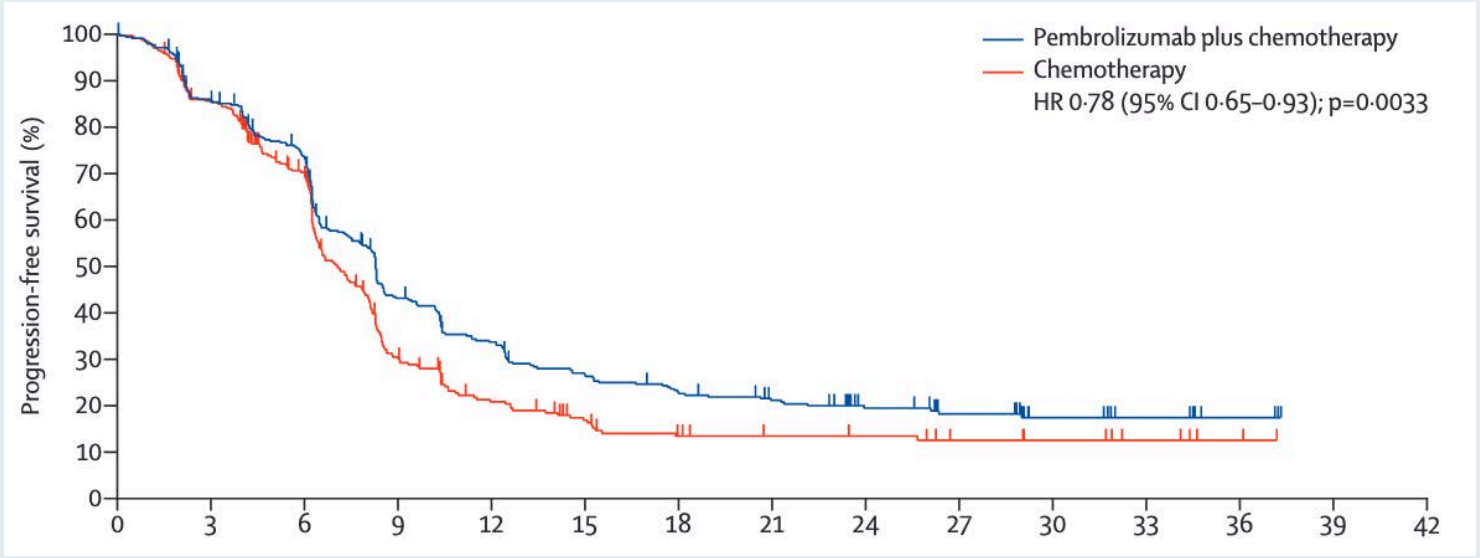
Pembrolizumab alone or combined with chemotherapy versus chemotherapy as first-line therapy for advanced urothelial carcinoma (KEYNOTE-361): a randomised, open-label, phase 3 trial

*Thomas Powles, Tibor Csőszi, Mustafa Özgüroğlu, Nobuaki Matsubara, Lajos Géczi, Susanna Y-S Cheng, Yves Fradet, Stephane Oudard, Christof Vulsteke, Rafael Morales Barrera, Aude Fléchon, Seyda Gunduz, Yohann Loriot, Alejo Rodriguez-Vida, Ronac Mamtani, Evan Y Yu, Kijoeng Nam, Kentaro Imai, Blanca Homet Moreno, Ajjai Alva, for the KEYNOTE-361 Investigators**

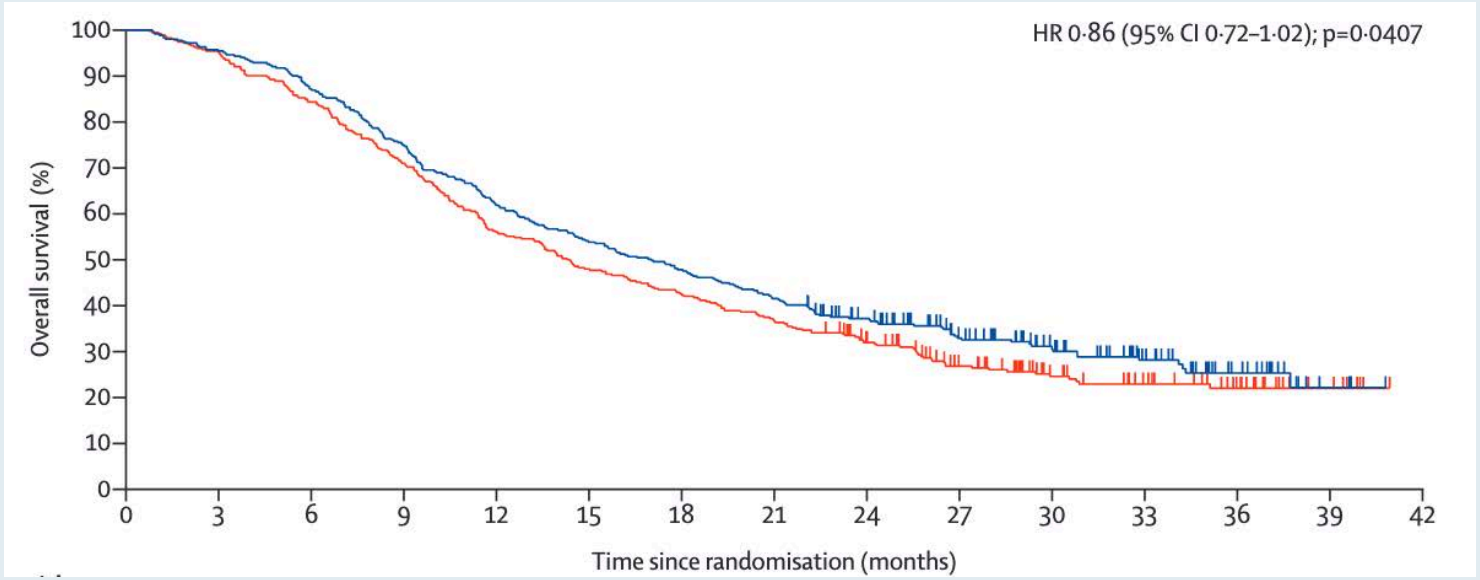
***Lancet Oncol* 2021;22:931-45.**

KEYNOTE-361: PFS and OS with Pembrolizumab and Chemotherapy

PFS



OS

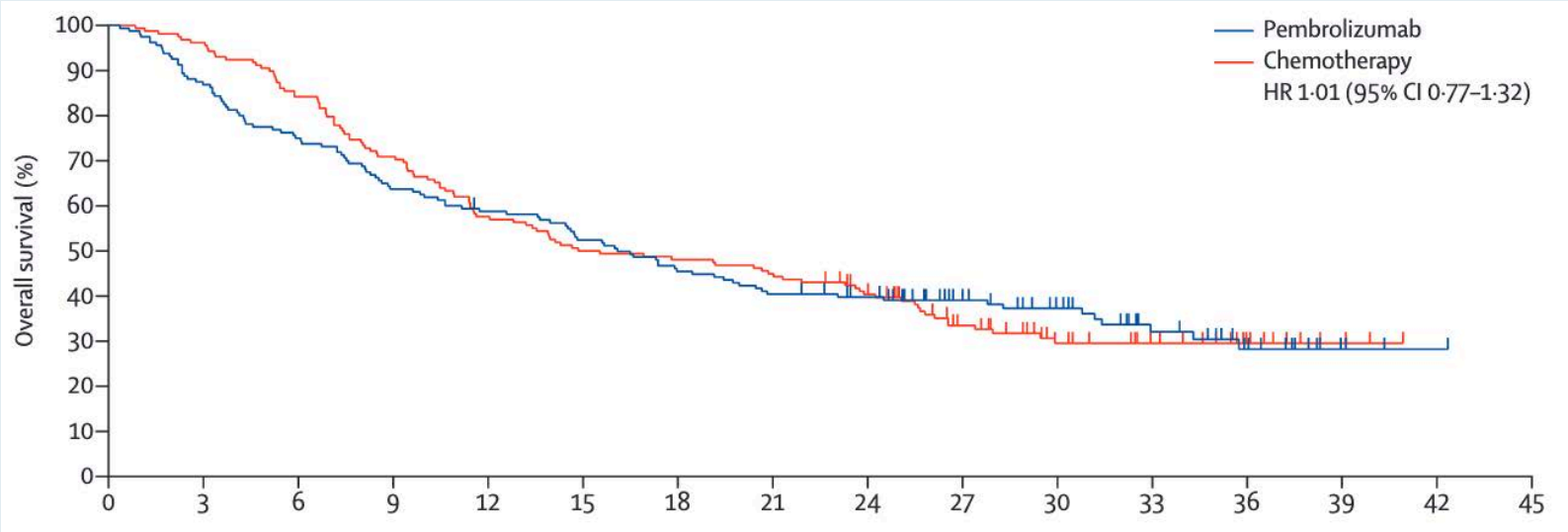


Powles T et al. *Lancet Oncol* 2021;22:931-45.

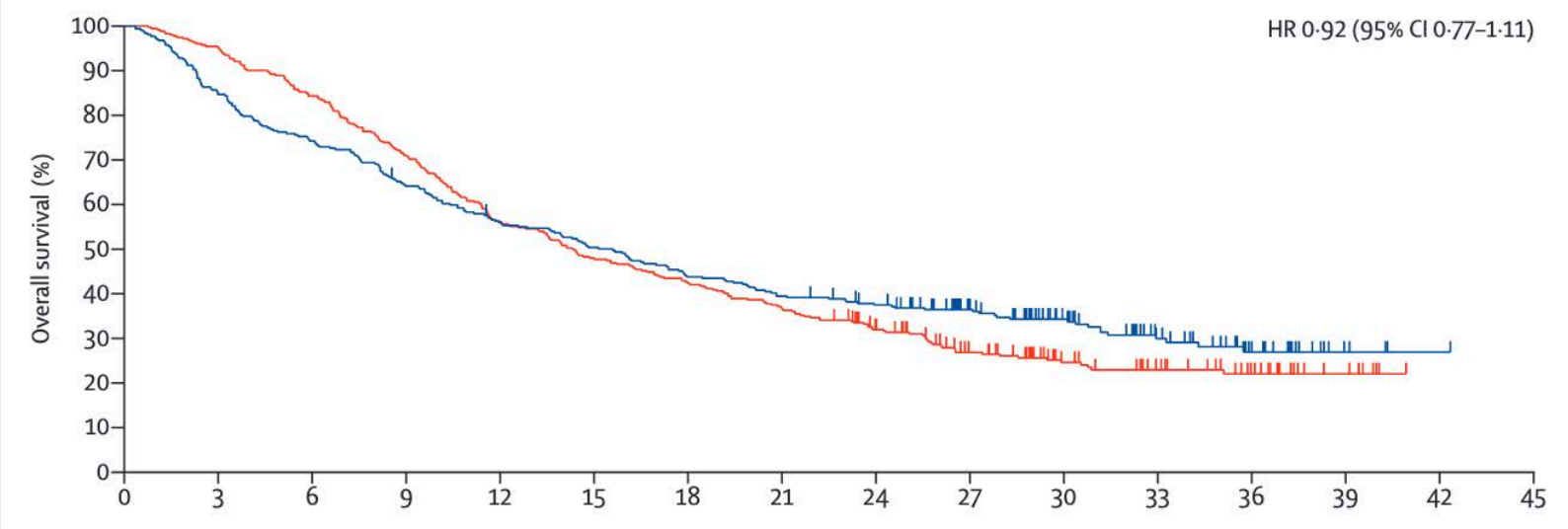
RTP RESEARCH TO PRACTICE

KEYNOTE-361: OS with Pembrolizumab Alone

PD-L1 CPS ≥10



ITT



Powles T et al. *Lancet Oncol* 2021;22:931-45.

RTP RESEARCH TO PRACTICE

N Engl J Med 2020;383:1218-30.

The NEW ENGLAND JOURNAL of MEDICINE

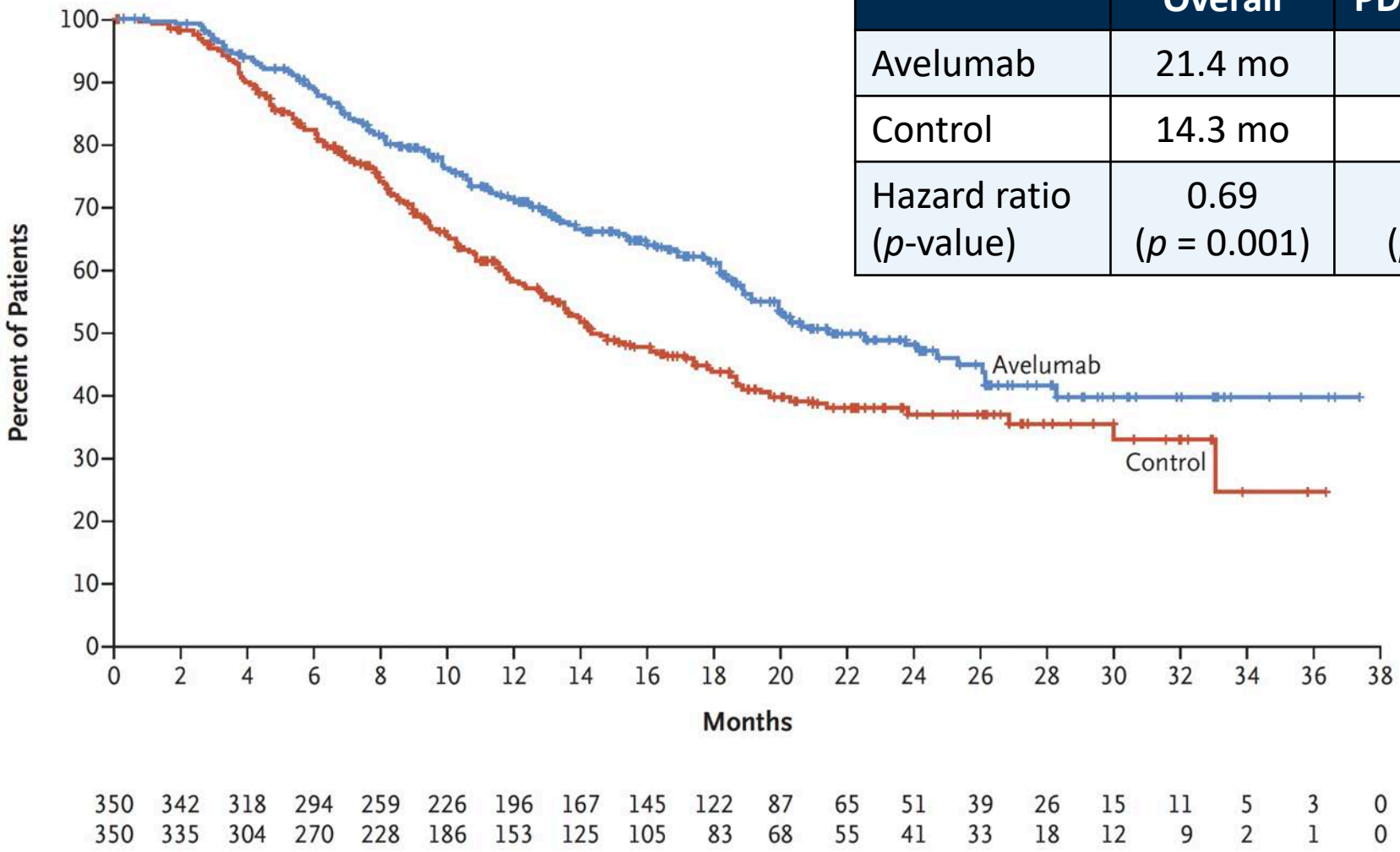
ORIGINAL ARTICLE

Avelumab Maintenance Therapy for Advanced or Metastatic Urothelial Carcinoma

T. Powles, S.H. Park, E. Voog, C. Caserta, B.P. Valderrama, H. Gurney, H. Kalofonos, S. Radulović, W. Demey, A. Ullén, Y. Loriot, S.S. Sridhar, N. Tsuchiya, E. Kopyltsov, C.N. Sternberg, J. Bellmunt, J.B. Aragon-Ching, D.P. Petrylak, R. Laliberte, J. Wang, B. Huang, C. Davis, C. Fowst, N. Costa, J.A. Blake-Haskins, A. di Pietro, and P. Grivas

JAVELIN Bladder 100 Primary Endpoint: Overall Survival

	Overall	PD-L1-positive
Avelumab	21.4 mo	NE
Control	14.3 mo	17.1 mo
Hazard ratio (*p*-value)	0.69 ($p = 0.001$)	0.56 ($p < 0.001$)



Powles T et al. *N Engl J Med* 2020;383:1218-30.

RTP RESEARCH TO PRACTICE

Avelumab First-Line (1L) Maintenance for Advanced Urothelial Carcinoma (UC): Long-Term Follow-Up Results from the JAVELIN Bladder 100 Trial

Powles T et al.

Genitourinary Cancers Symposium 2022;Abstract 487.

Poster Session B: Urothelial Carcinoma

Level 1, West Hall

Friday, Feb 18, 2022

8:15 PM – 9:15 PM EST

FDA Grants Regular Approval to Enfortumab Vedotin-ejfv for Locally Advanced or Metastatic Urothelial Cancer

Press Release – July 9, 2021

"The Food and Drug Administration approved enfortumab vedotin-ejfv, a Nectin-4-directed antibody and microtubule inhibitor conjugate, for adult patients with locally advanced or metastatic urothelial cancer who

- have previously received a programmed death receptor-1 (PD-1) or programmed death-ligand (PD-L1) inhibitor and platinum-containing chemotherapy, or
- are ineligible for cisplatin-containing chemotherapy and have previously received one or more prior lines of therapy.

Trial EV-301 (NCT03474107) was an open-label, randomized, multicenter trial required to confirm the clinical benefit of the 2019 accelerated approval. This trial enrolled 608 patients with locally advanced or metastatic urothelial cancer who received a prior PD-1 or PD-L1 inhibitor and platinum-based chemotherapy. Patients were randomized (1:1) to receive either enfortumab vedotin-ejfv (EV) 1.25 mg/kg on days 1, 8 and 15 of a 28-day cycle or investigator's choice of single-agent chemotherapy (docetaxel, paclitaxel, or vinflunine)."

www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-regular-approval-enfortumab-vedotin-ejfv-locally-advanced-or-metastatic-urothelial-cancer

The NEW ENGLAND JOURNAL of MEDICINE

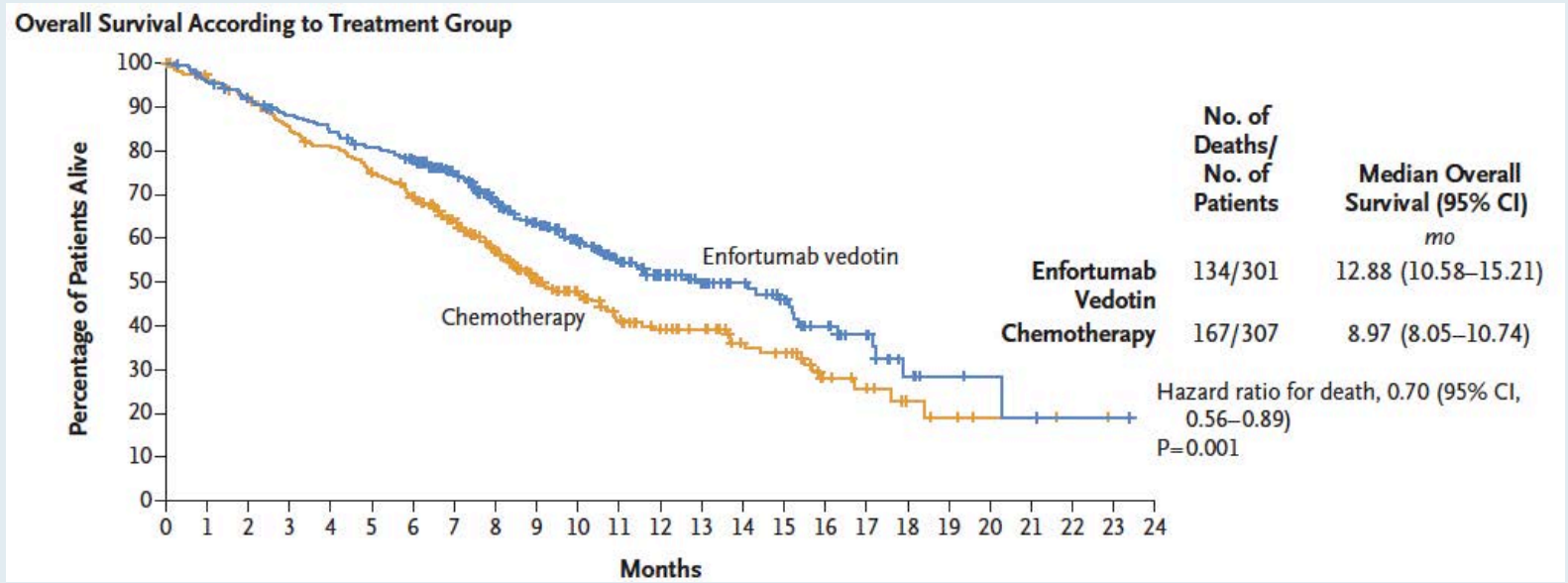
ORIGINAL ARTICLE

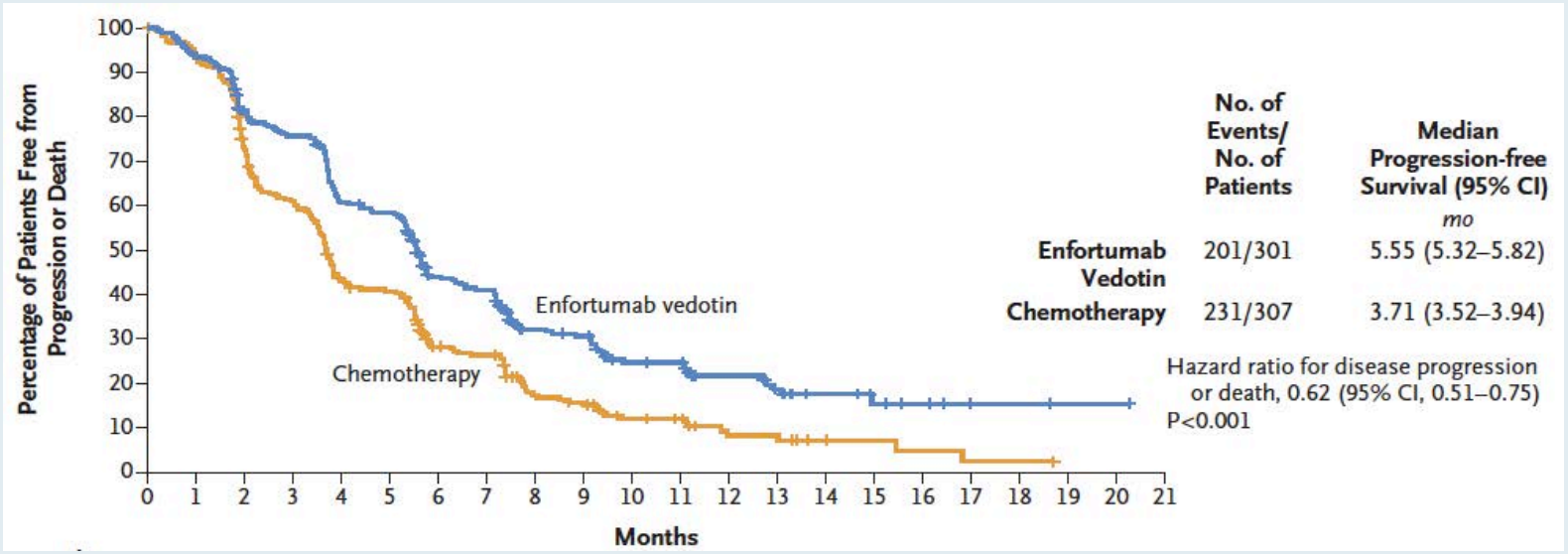
Enfortumab Vedotin in Previously Treated Advanced Urothelial Carcinoma

Thomas Powles, M.D., Jonathan E. Rosenberg, M.D., Guru P. Sonpavde, M.D., Yohann Loriot, M.D., Ph.D., Ignacio Durán, M.D., Ph.D., Jae-Lyun Lee, M.D., Ph.D., Nobuaki Matsubara, M.D., Christof Vulsteke, M.D., Ph.D., Daniel Castellano, M.D., Chunzhang Wu, Ph.D., Mary Campbell, M.D., Maria Matsangou, M.B., Ch.B., M.D., and Daniel P. Petrylak, M.D.

N Engl J Med 2021;384(12):1125-35.

EV-301: Survival and Response Analyses





	EV (n = 301)	Chemo (n = 307)
ORR	40.6%	17.9%
DCR	71.9%	53.4%

Incidence of treatment-related adverse events was similar in the 2 groups:

- 93.9% versus 91.8%

Incidence of events of Grade 3 or higher was also similar in the 2 groups:

- 51.4% versus 49.8%

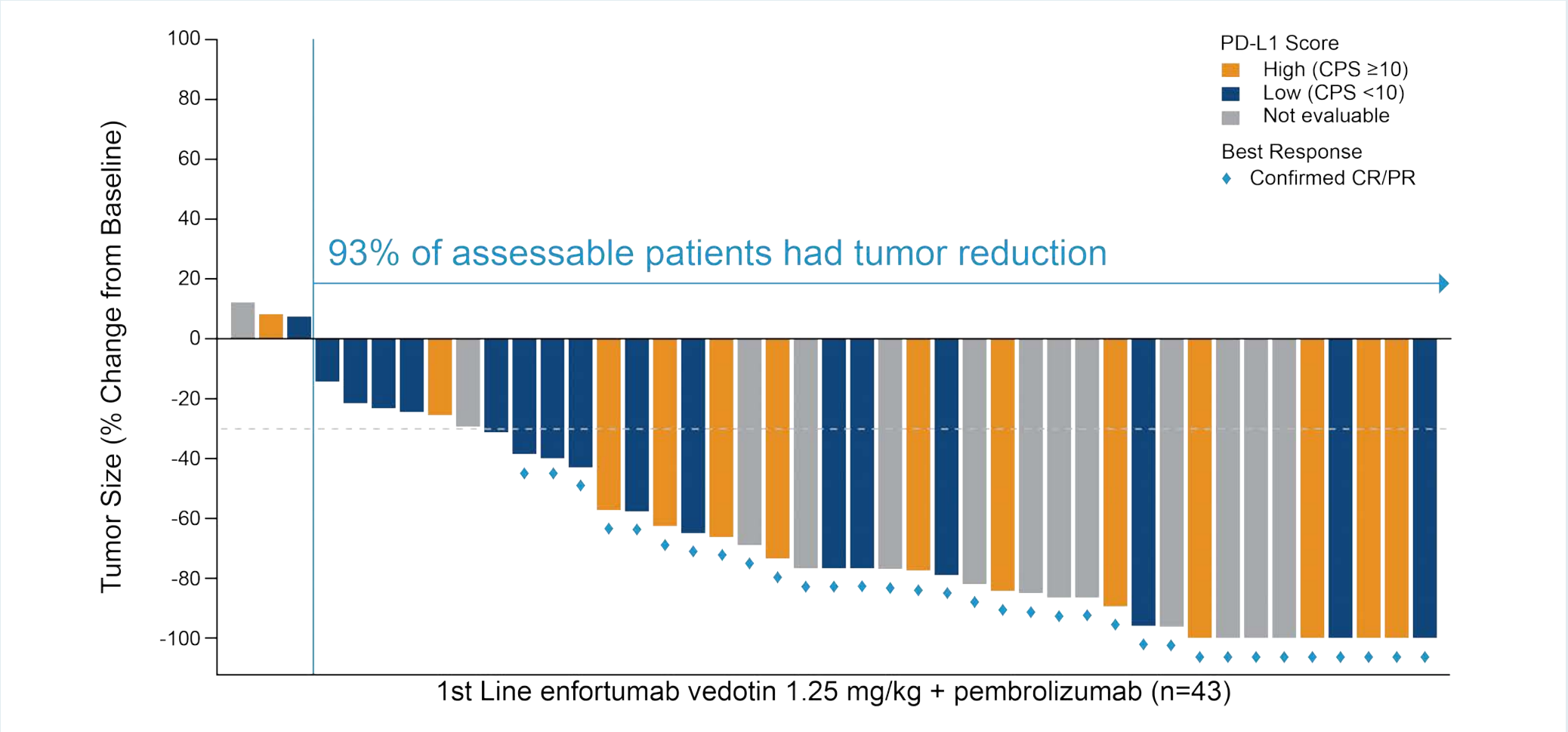
Powles T et al. *N Engl J Med* 2021;384(12):1125-35.

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

Friedlander TW et al.

ASCO 2021;Abstract 4528.

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

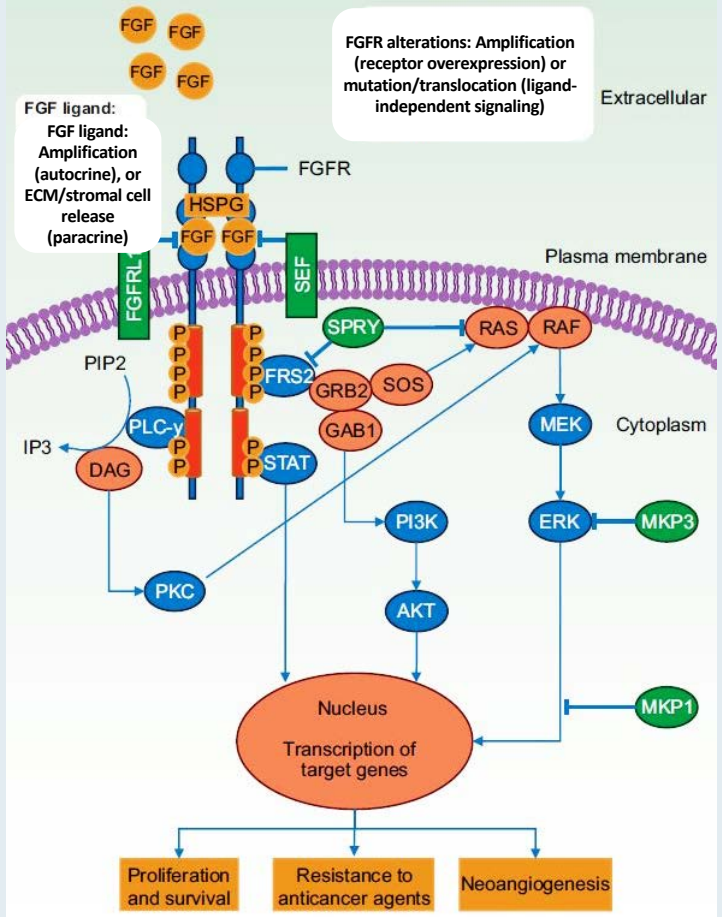


Friedlander TW et al. ASCO 2021;Abstract 4528.

RTP RESEARCH TO PRACTICE

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

FGFR Signaling Pathway[3]



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

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

1. The Cancer Genome Atlas (TCGA) genomic alteration database: https://tcga-data.nci.nih.gov/docs/publications/tcga/. Accessed February 6, 2020.
2. Genomics Evidence Neoplasia Information Exchange (GENIE) genomic alteration database: https://www.aacr.org/Research/Research/pages/aacr-project-genie.aspx. Accessed February 6, 2020. 3. Touat M et al. *Clin Cancer Res*. 2015;21:2684-2694. 4. Rodriguez-Vida A et al. *J Hematol Oncol*. 2015;8:119. 5. Li Q et al. *Curr Urol Rep*. 2016;17:12.

Courtesy of Arjun Balar, MD

ERDAFITINIB in Locally Advanced or Metastatic Urothelial Carcinoma (mUC): Long-Term Outcomes in BLC2001

Siefker-Radtke AO et al.

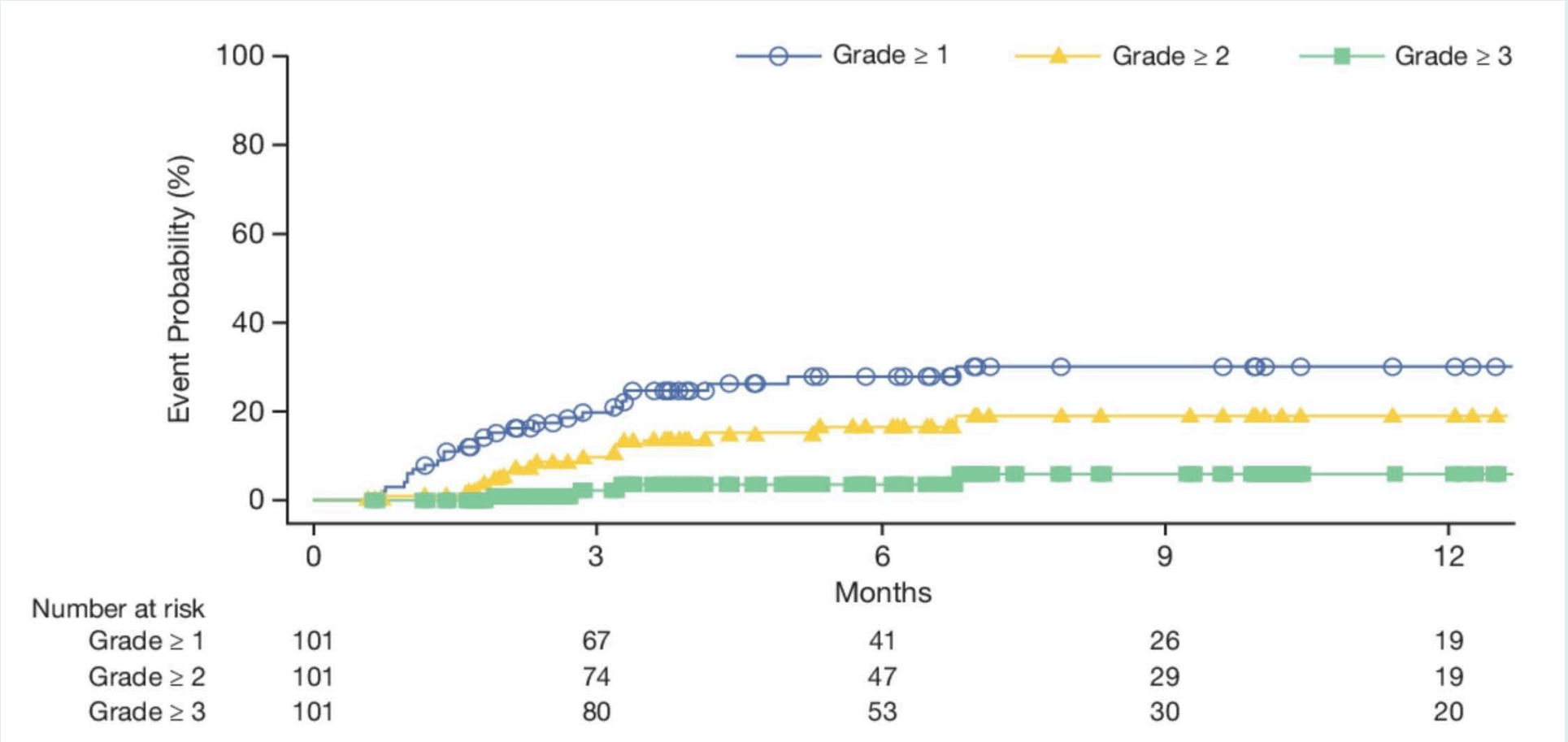
ASCO 2020;Abstract 5015.

Long-Term Outcomes from the Phase II BLC2001 Study: Erdafitinib for Locally Advanced or Metastatic Urothelial Carcinoma

Clinical endpoint	Erdafitinib (N = 101)
Objective response rate	39%
Median duration of response	6.0 months
Median progression-free survival	5.5 months
Median overall survival	11.3 months

Siefker-Radtke AO et al. ASCO 2020;Abstract 5015.

Long-Term Outcomes from the Phase II BLC2001 Study: Central Serous Retinopathy



Siefker-Radtke AO et al. ASCO 2020;Abstract 5015.

RTP RESEARCH TO PRACTICE

FDA Grants Accelerated Approval to Sacituzumab Govitecan for Advanced Urothelial Cancer

Press Release – April 13, 2021

"The Food and Drug Administration granted accelerated approval to sacituzumab govitecan for patients with locally advanced or metastatic urothelial cancer (mUC) who previously received a platinum-containing chemotherapy and either a programmed death receptor-1 (PD-1) or a programmed death-ligand 1 (PD-L1) inhibitor.

Efficacy and safety were evaluated in TROPHY (IMMU-132-06; NCT03547973), a single-arm, multicenter trial that enrolled 112 patients with locally advanced or mUC who received prior treatment with a platinum-containing chemotherapy and either a PD-1 or PD-L1 inhibitor. Patients received sacituzumab govitecan, 10 mg/kg intravenously, on days 1 and 8 of a 21-day treatment cycle."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-sacituzumab-govitecan-advanced-urothelial-cancer

RTP RESEARCH TO PRACTICE

TROPHY-U-01: A Phase II Open-Label Study of Sacituzumab Govitecan in Patients With Metastatic Urothelial Carcinoma Progressing After Platinum-Based Chemotherapy and Checkpoint Inhibitors

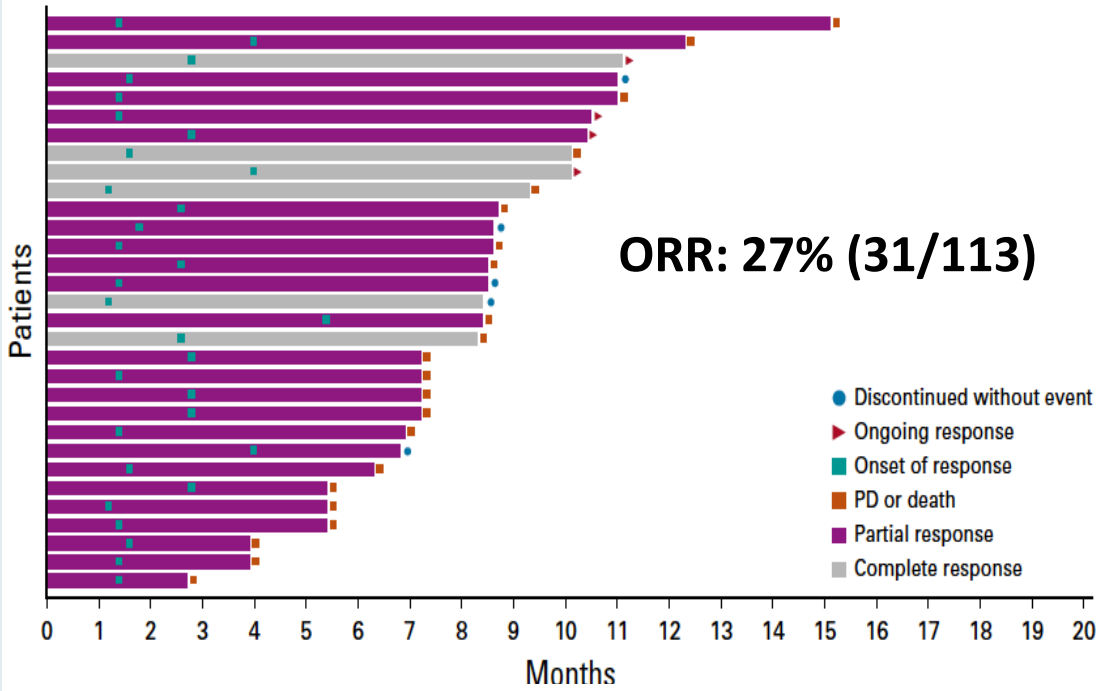
Scott T. Tagawa, MD, MS[1]; Arjun V. Balar, MD[2]; Daniel P. Petrylak, MD[3]; Arash Rezazadeh Kalebasty, MD[4]; Yohann Loriot, MD, PhD[5]; Aude Fléchon, MD, PhD[6]; Rohit K. Jain, MD[7]; Neeraj Agarwal, MD[8]; Manojkumar Bupathi, MD, MS[9]; Philippe Barthelemy, MD, PhD[10]; Philippe Beuzeboc, MD, PhD[11]; Phillip Palmbos, MD, PhD[12]; Christos E. Kyriakopoulos, MD[13]; Damien Pouessel, MD, PhD[14]; Cora N. Sternberg, MD[1]; Quan Hong, MD[15]; Trishna Goswami, MD[15]; Loretta M. Itri, MD[15]; and Petros Grivas, MD, PhD[16]

J Clin Oncol 2021;[Online ahead of print].

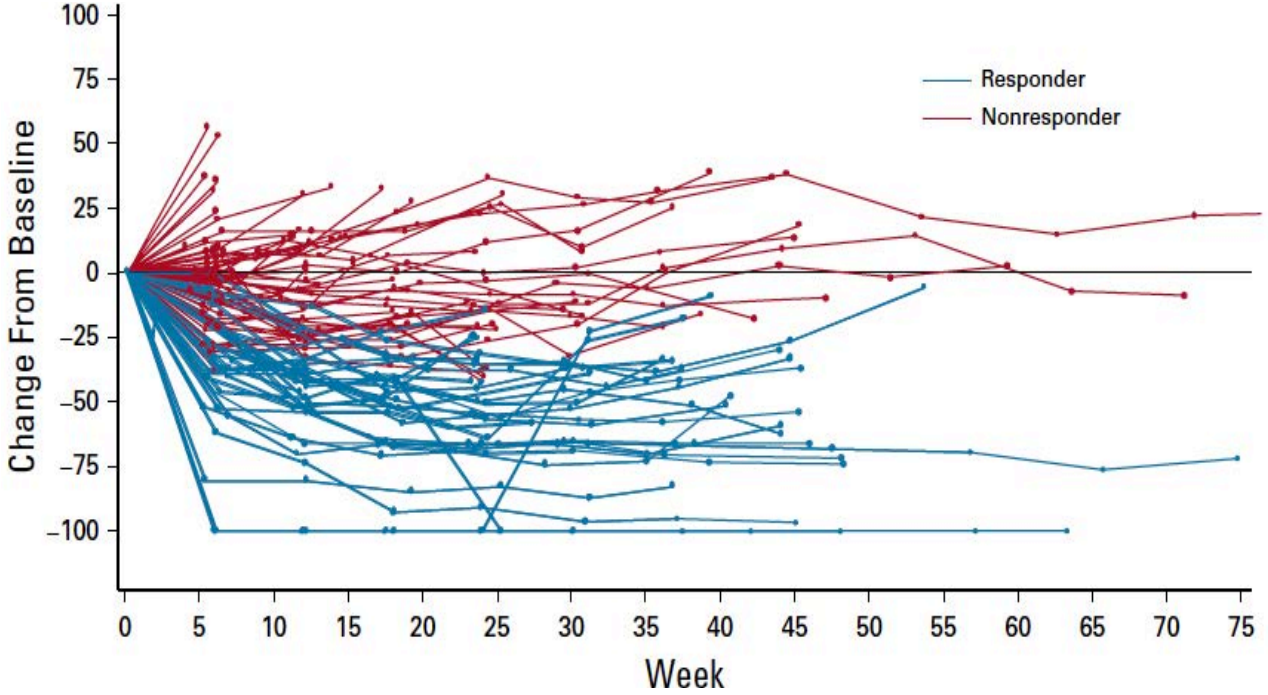
TROPHY U-01 (Cohort 1): ORR, Duration of Response and Survival

Median DOR: 7.2 mo

Median time to onset of response: 1.6 mo



ORR: 27% (31/113)



Median PFS: 5.4 mo

Median OS: 10.9 mo

Tagawa ST et al. *J Clin Oncol* 2021;[Online ahead of print]; Loriot Y et al. ESMO 2020;Abstract LBA24.

RTP RESEARCH TO PRACTICE

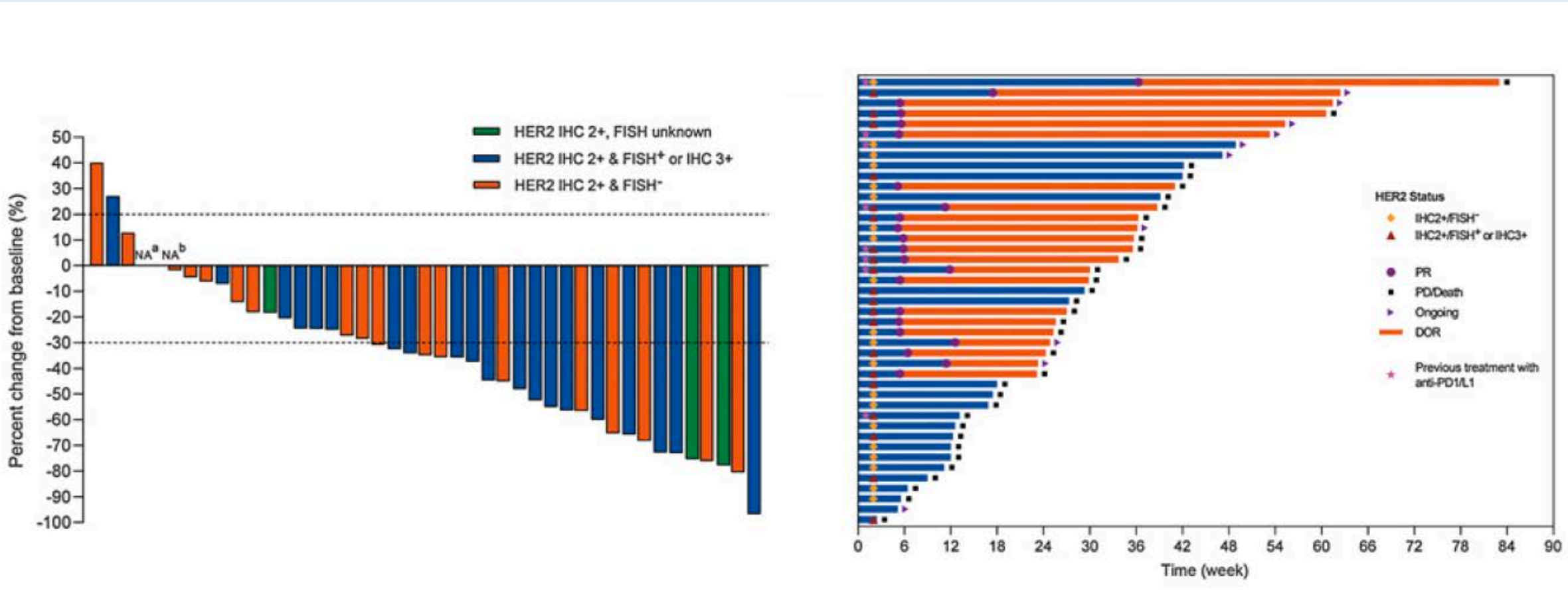
CLINICAL CANCER RESEARCH | CLINICAL TRIALS: TARGETED THERAPY

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;27:43-51.

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



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

RTP RESEARCH TO PRACTICE

Agenda

Module 1: Urothelial Bladder Carcinoma

Module 2: Prostate Cancer

Module 3: Renal Cell Carcinoma (RCC)

FDA Approves Relugolix for Advanced Prostate Cancer

Press Release – December 18, 2020

"On December 18, 2020, the US Food and Drug Administration approved the first oral gonadotropin-releasing hormone (GnRH) receptor antagonist, relugolix, for adult patients with advanced prostate cancer.

Efficacy was evaluated in HERO (NCT03085095), a randomized, open label trial in men requiring at least one year of androgen deprivation therapy with either prostate cancer recurrence following radiation or surgery or newly diagnosed castration-sensitive advanced prostate cancer.

Patients (N = 934) were randomized (2:1) to receive relugolix 360 mg oral loading dose on the first day, followed by daily oral doses of 120 mg, or leuprolide acetate 22.5 mg injection subcutaneously every 3 months for 48 weeks."

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-relugolix-advanced-prostate-cancer

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

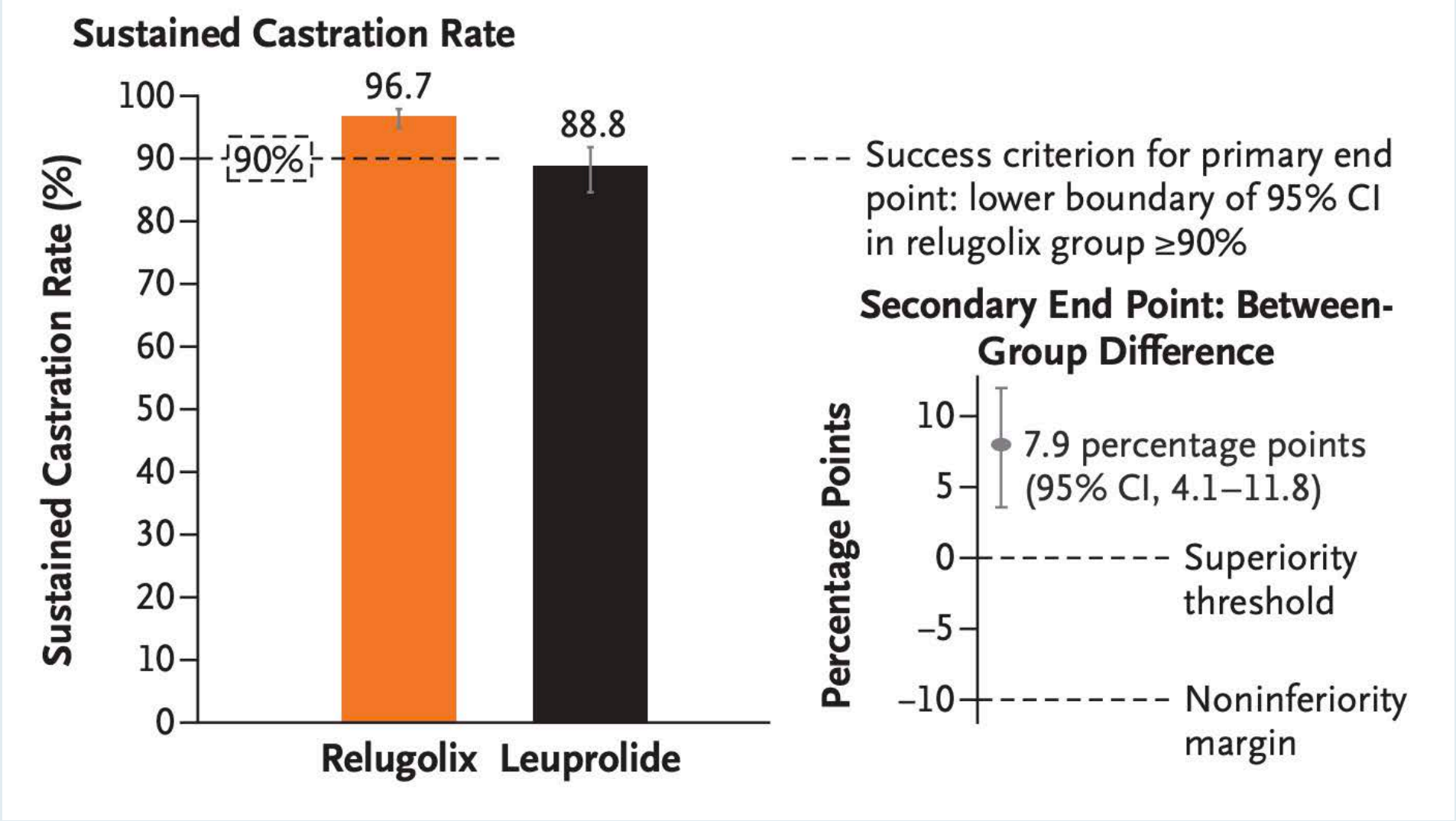
Oral Relugolix for Androgen-Deprivation Therapy in Advanced Prostate Cancer[2]

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

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

RTP RESEARCH TO PRACTICE

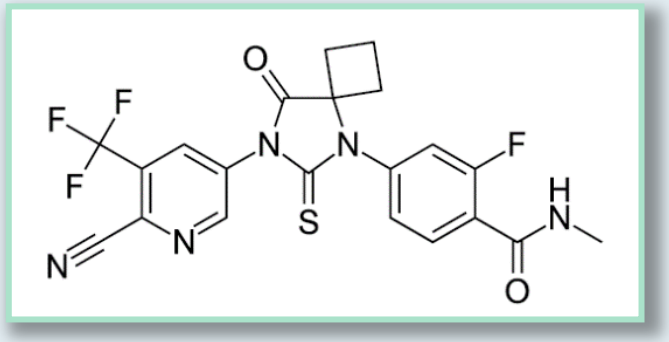
HERO Study: Oral Relugolix versus Leuprolide Acetate for Androgen-Deprivation Therapy



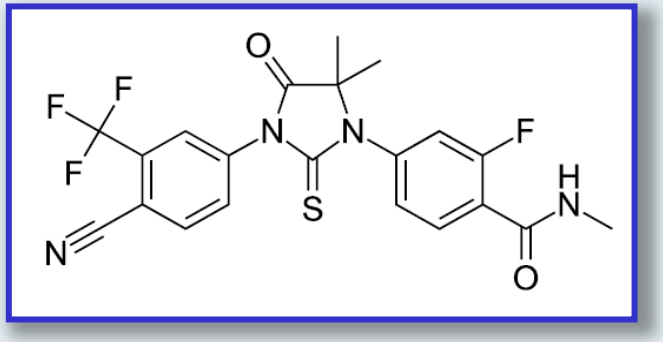
Shore ND et al. *N Engl J Med* 2020;382:2187-96.

Next-Generation Androgen Receptor Inhibitors

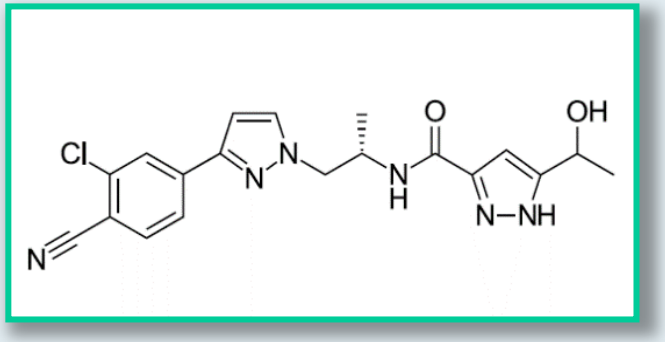
Apalutamide



Enzalutamide



Darolutamide



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

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

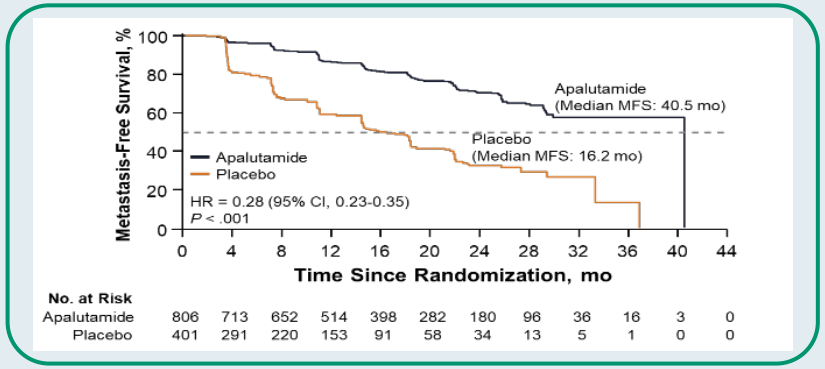
FDA Approvals of Next-Generation Antiandrogens for Nonmetastatic Castration-Resistant Prostate Cancer (CRPC)

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

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

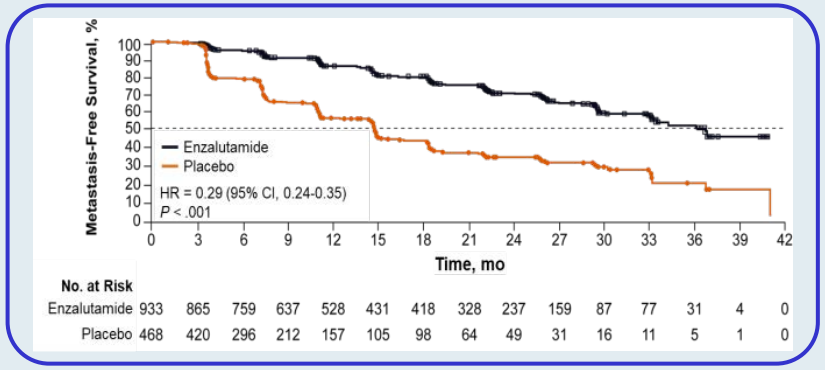
Primary Endpoint: Metastasis-Free Survival (MFS) in Nonmetastatic CRPC

SPARTAN[1]
Apalutamide



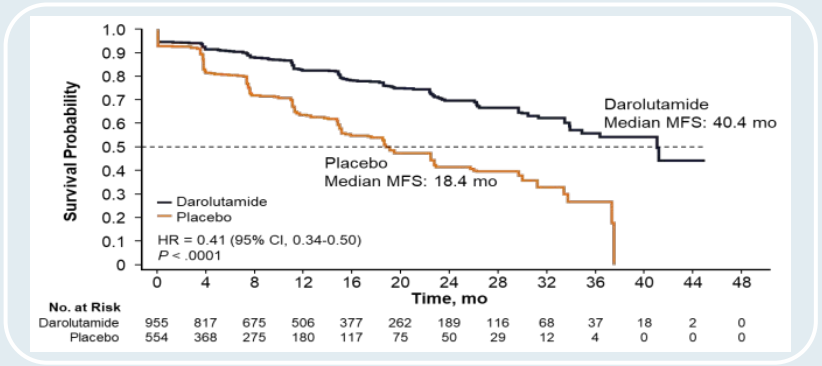
- 72% reduction of distant progression or death
- Median MFS: APA 40.5 vs PBO 16.2 months
- 24-month MFS benefit

PROSPER[2]
Enzalutamide



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

ARAMIS[3]
Darolutamide



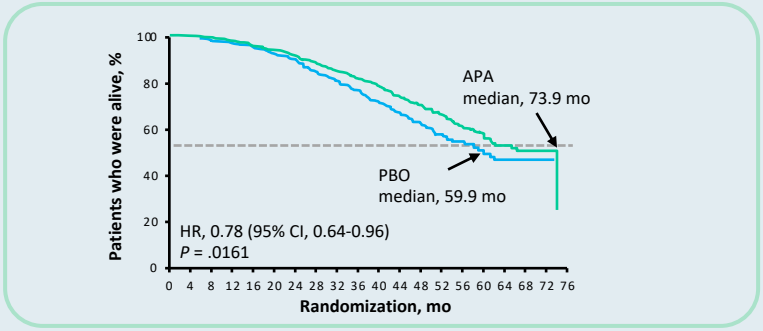
- 59% reduction of distant progression or death
- Median MFS: DARO 40.4 vs PBO 18.4 months
- 22-month MFS benefit

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

RTP RESEARCH TO PRACTICE

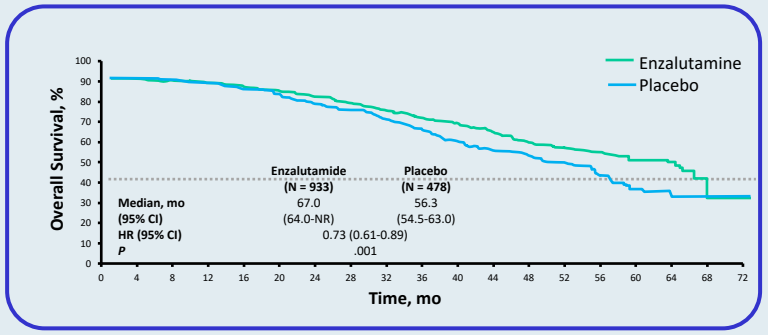
Secondary Endpoint: Overall Survival in Nonmetastatic CRPC

SPARTAN1[1] Apalutamide



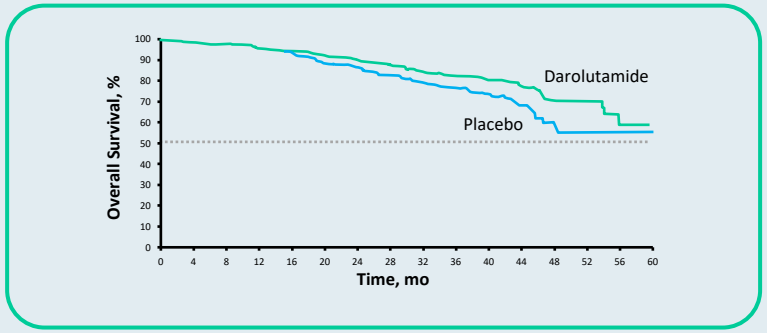
- 22% reduction in risk of death
- Median follow-up of 52.0 mo
- Median OS was significantly longer for apalutamide vs placebo
  - 73.9 mo vs 59.9 mo
  - **HR = 0.78 (95% CI 0.64-0.96); *p* = .016**

PROSPER[2] Enzalutamide



- 27% reduction in risk of death
- Median follow-up of 48 mo
- Median OS was significantly longer for enzalutamide vs placebo
  - 67.0 mo vs 56.3 mo
  - **HR = 0.73 (95% CI 0.61-0.89); *p* = .001**

ARAMIS[3] Darolutamide



- 31% reduction in risk of death
- Median follow-up of 29.0 mo
- Median OS was significantly longer for darolutamide vs placebo
  - **HR = 0.69 (95% CI, 0.53-0.88); *p* = .003**

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

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

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

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

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

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

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

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

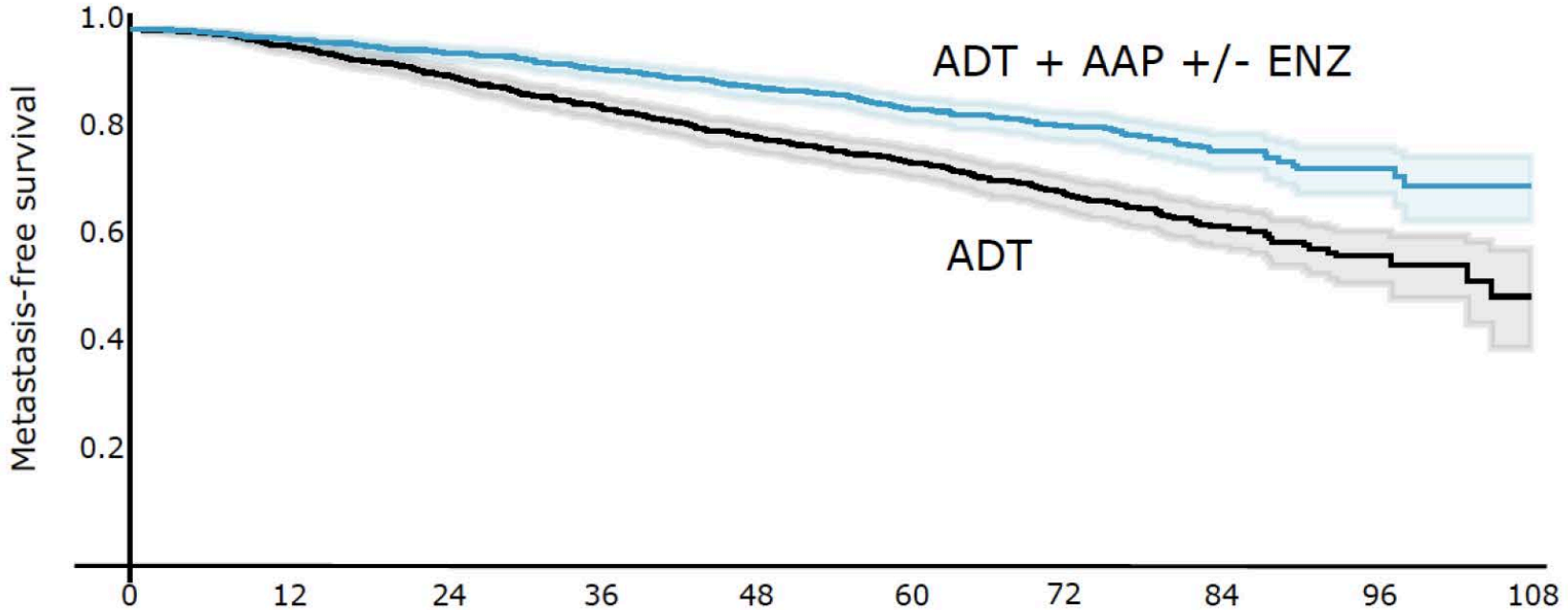
*113 U.K. and Swiss sites: list of investigators and collaborators at www.stampedetrial.org

www.stampedetrial.org

2021 ESMO congress

ESMO 2021;Abstract LBA4_PR.

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



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

Events

180 ADT + AAP +/- ENZ
306 ADT

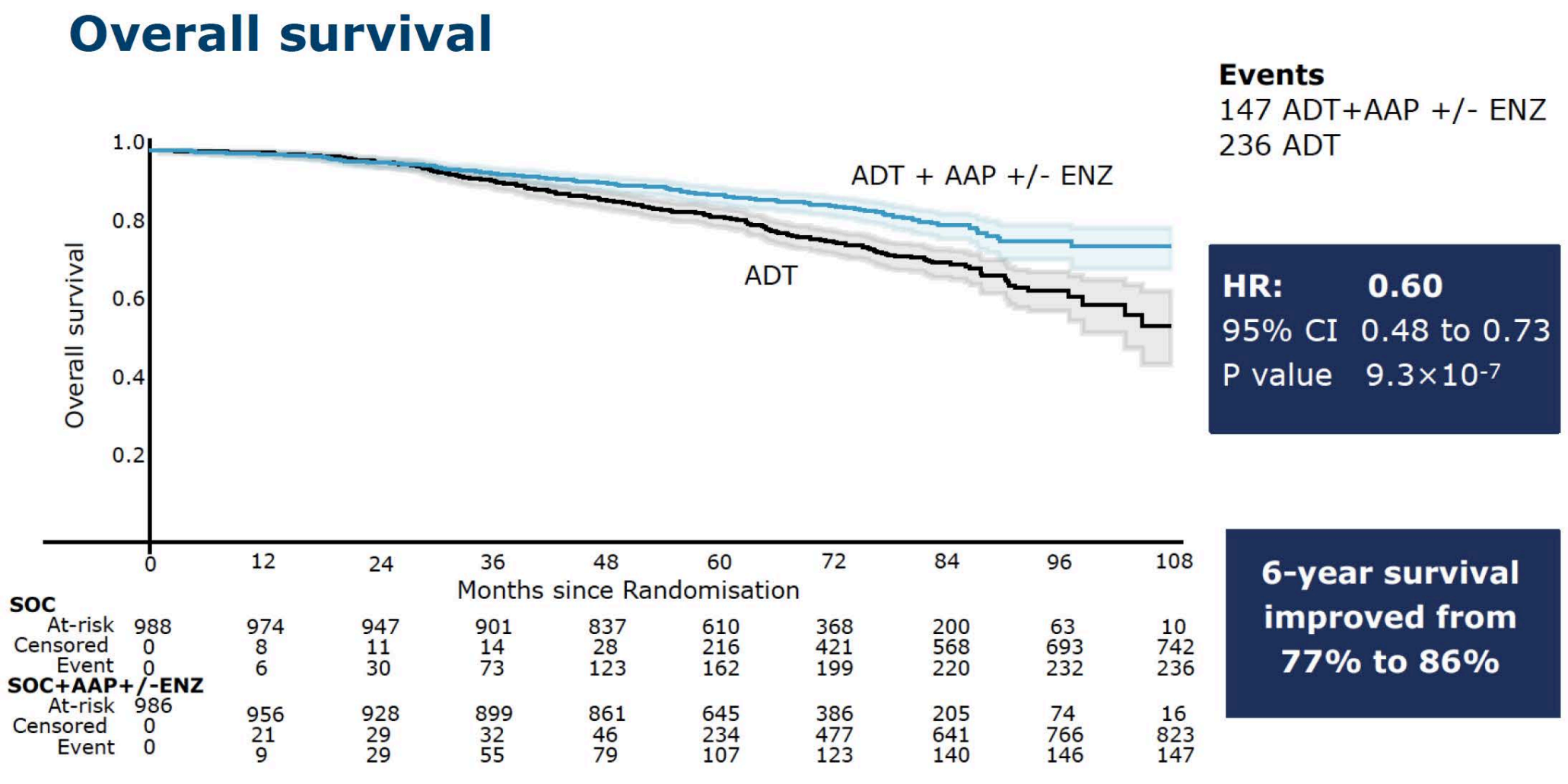
HR:	**0.53**
95% CI:	0.44-0.64
P value	2.9×10^{-11}

6-year MFS improved from 69% to 82%

Attard G et al. ESMO 2021;Abstract LBA4_PR.

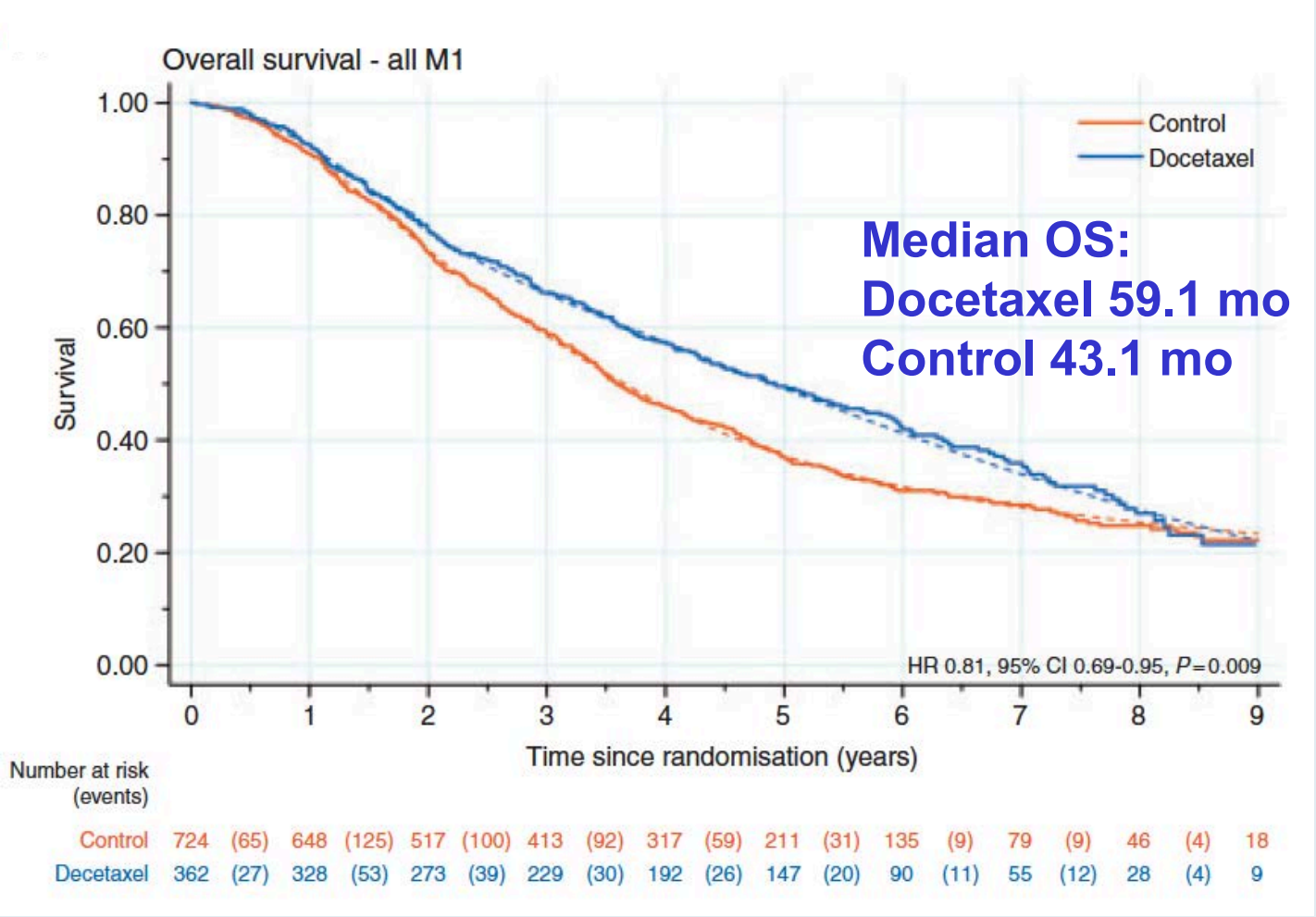
RTP RESEARCH TO PRACTICE

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



Attard G et al. ESMO 2021;Abstract LBA4_PR.

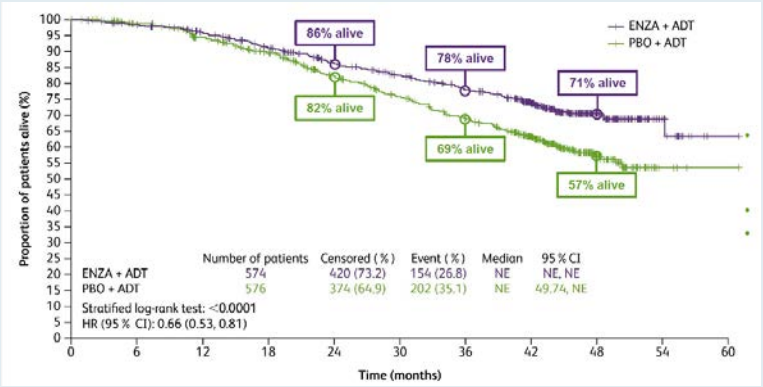
STAMPEDE: Long-Term Overall Survival Results with the Addition of Docetaxel to Hormone Therapy for Metastatic Hormone-Sensitive Prostate Cancer (mHSPC)



Clarke HW et al. *Ann Oncol* 2019;30(12):1992-2003.

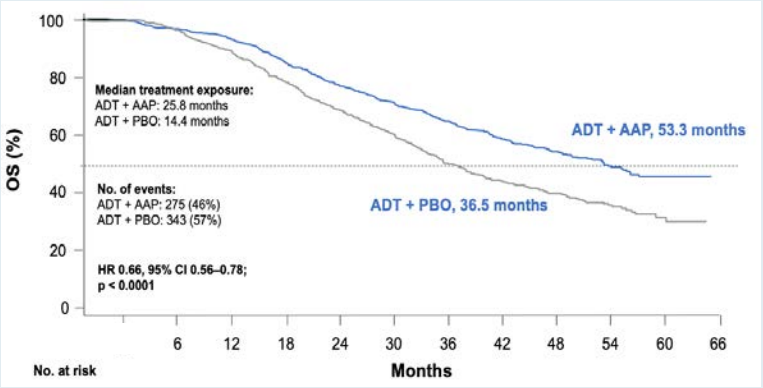
Final OS Analyses: Enzalutamide, Abiraterone and Apalutamide for mHSPC

ARCHES[1]
Enzalutamide + ADT



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

LATITUDE[2]
Abiraterone + ADT



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

TITAN[3]
Apalutatmide + ADT

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

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

RTP RESEARCH TO PRACTICE

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

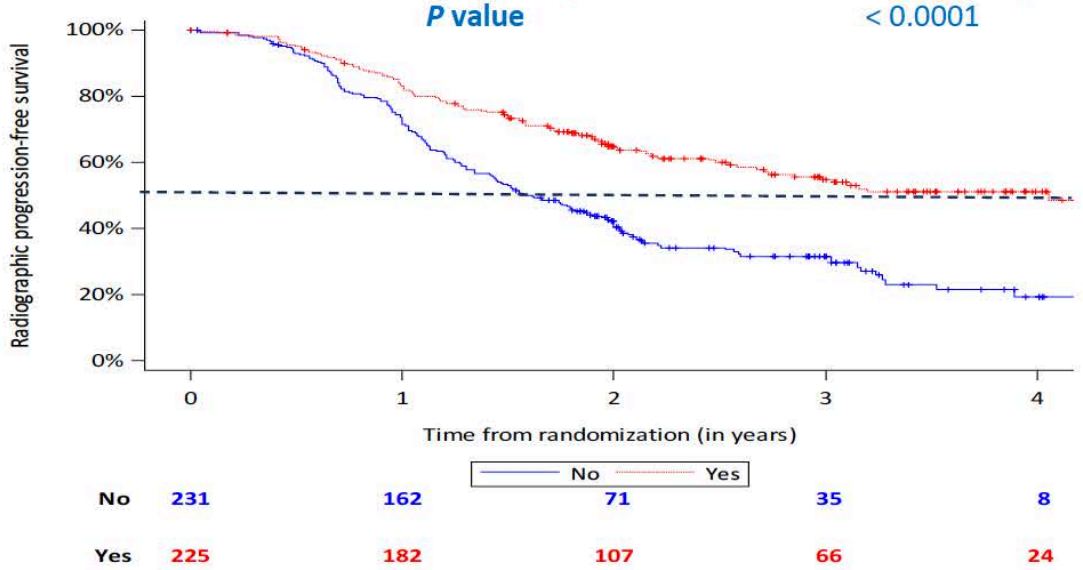
Karim Fizazi, Joan Carles, Stéphanie Foulon, Guilhem Roubaud, Ray McDermott, Aude Fléchon, Bertrand Tombal, Stéphane Supiot, Dominik Berthold, Philippe Ronchin, Gabriel Kacsó, Gwenaëlle Gravis, Fabio Calabro, Jean-François Berdah, Ali Hasbini, Marlon Silva, Antoine Thiery-Vuillemin, Igor Latorzeff, Isabelle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

Abstract LBA5

PEACE-1: Radiographic PFS by Metastatic Burden

« High Volume »

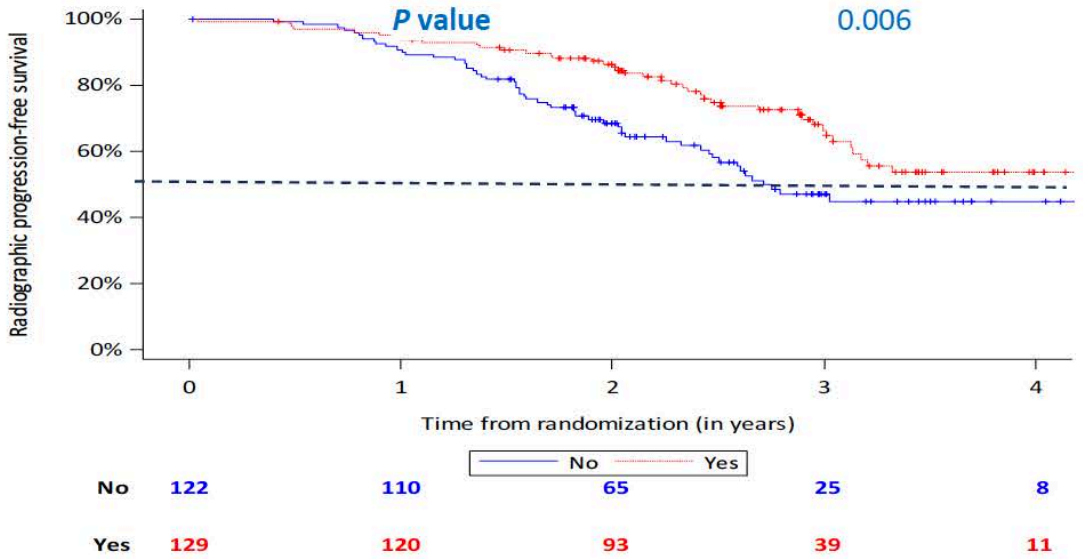
	SOC+Abi (n = 225)	SOC (n = 231)
Median, y (95% CI)	4.1 (2.7-NE)	1.6 (1.4-2.0)
Events	97	156
HR (95% CI)*	0.47 (0.36-0.60)	
P value	< 0.0001	



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

« Low Volume »

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



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

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

2021 ESMO congress

Karim Fizazi

Fizazi K et al. ESMO 2021;Abstract LBA5.

RTP RESEARCH TO PRACTICE

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

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

Fizazi K et al. ESMO 2021;Abstract LBA5.

Phase III ARASENS Trial of Darolutamide in Combination with Docetaxel and ADT Meets Primary Overall Survival Endpoint in mCRPC

Press Release – December 3, 2021

"The Phase III ARASENS trial investigating the use of the oral androgen receptor inhibitor darolutamide in metastatic hormone-sensitive prostate cancer (mHSPC) has met its primary endpoint. In the ARASENS trial, darolutamide in combination with docetaxel and androgen deprivation therapy (ADT) significantly increased overall survival (OS) compared to docetaxel and ADT. The overall incidence of reported adverse events was similar between treatment arms. Detailed results of the study are planned to be presented at an upcoming scientific congress."

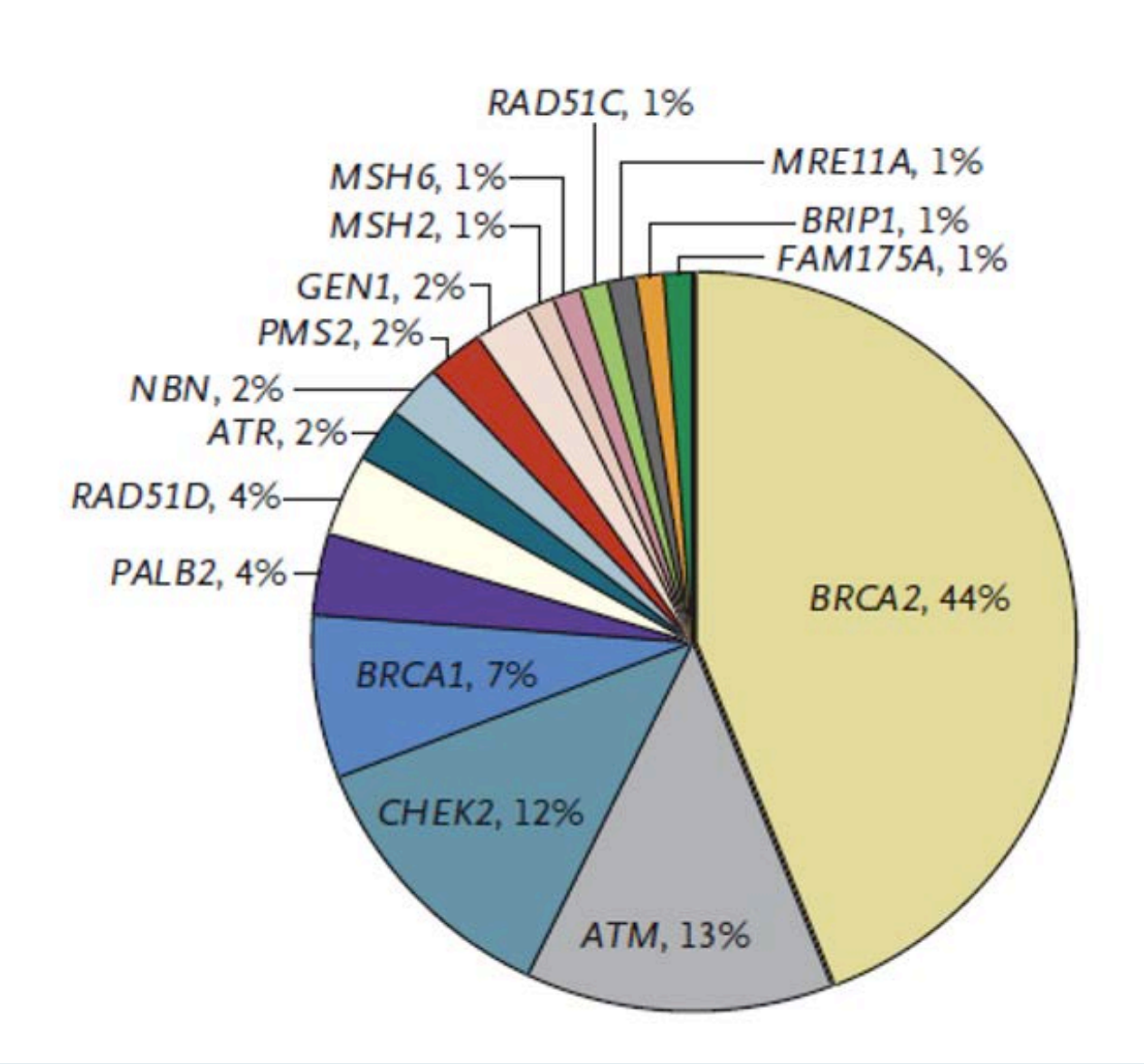
https://media.bayer.com/baynews/baynews.nsf/id/6AA96A64B2A1105DC125879F002A70DD?open&ref=irrefndcd

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

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

Oral Abstract Session A: Prostate Cancer
Level 3, Ballroom
Thursday, Feb 17, 2022
4:00 PM – 5:30 PM EST

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 mCRPC

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

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

RTP RESEARCH TO PRACTICE

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

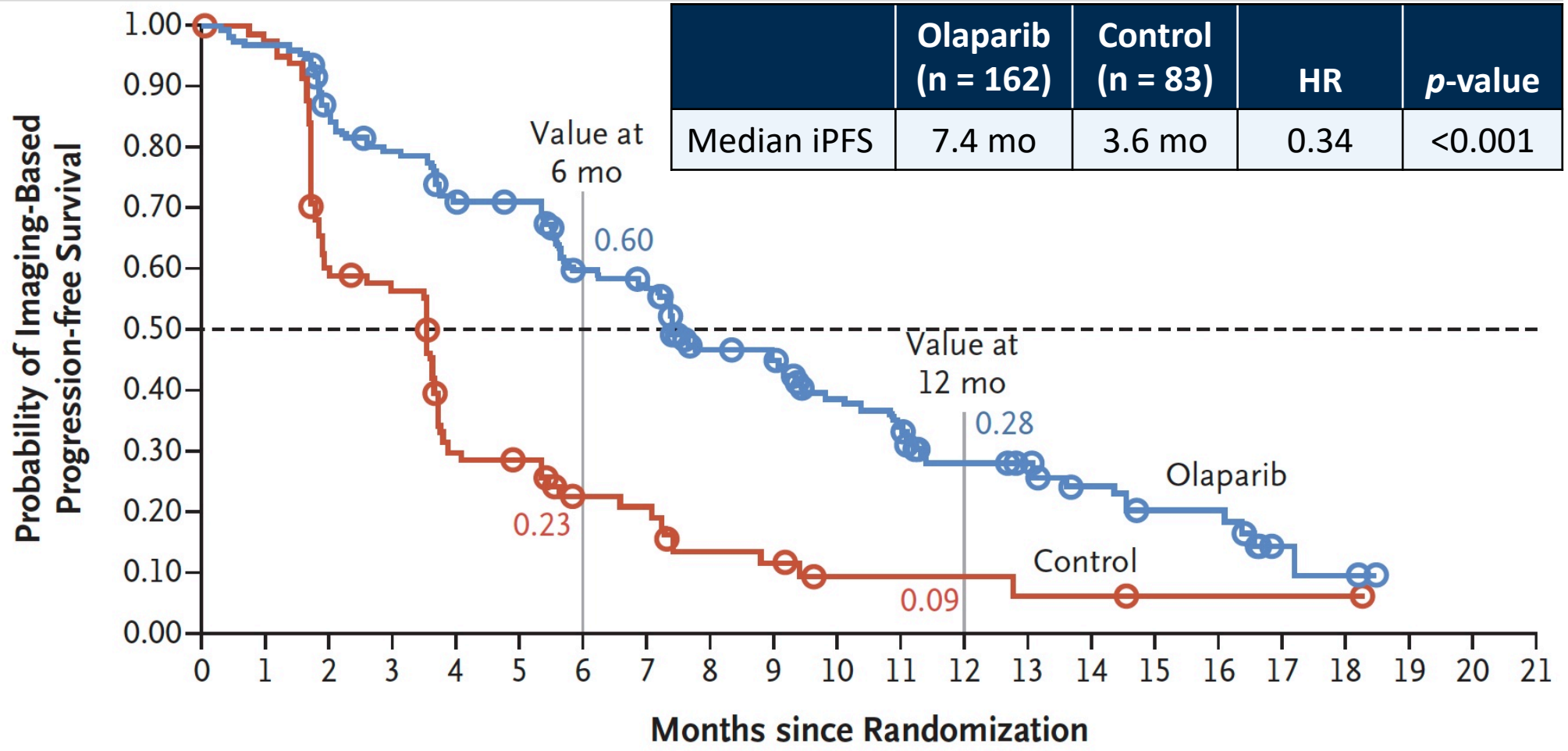
Olaparib for Metastatic Castration-Resistant Prostate Cancer

J. de Bono, J. Mateo, K. Fizazi, F. Saad, N. Shore, S. Sandhu, K.N. Chi, O. Sartor, N. Agarwal, D. Olmos, A. Thiery-Vuillemin, P. Twardowski, N. Mehra, C. Goessl, J. Kang, J. Burgents, W. Wu, A. Kohlmann, C.A. Adelman, and M. Hussain

***N Engl J Med* 2020;382:2091-102.**

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

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



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

RTP RESEARCH TO PRACTICE

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

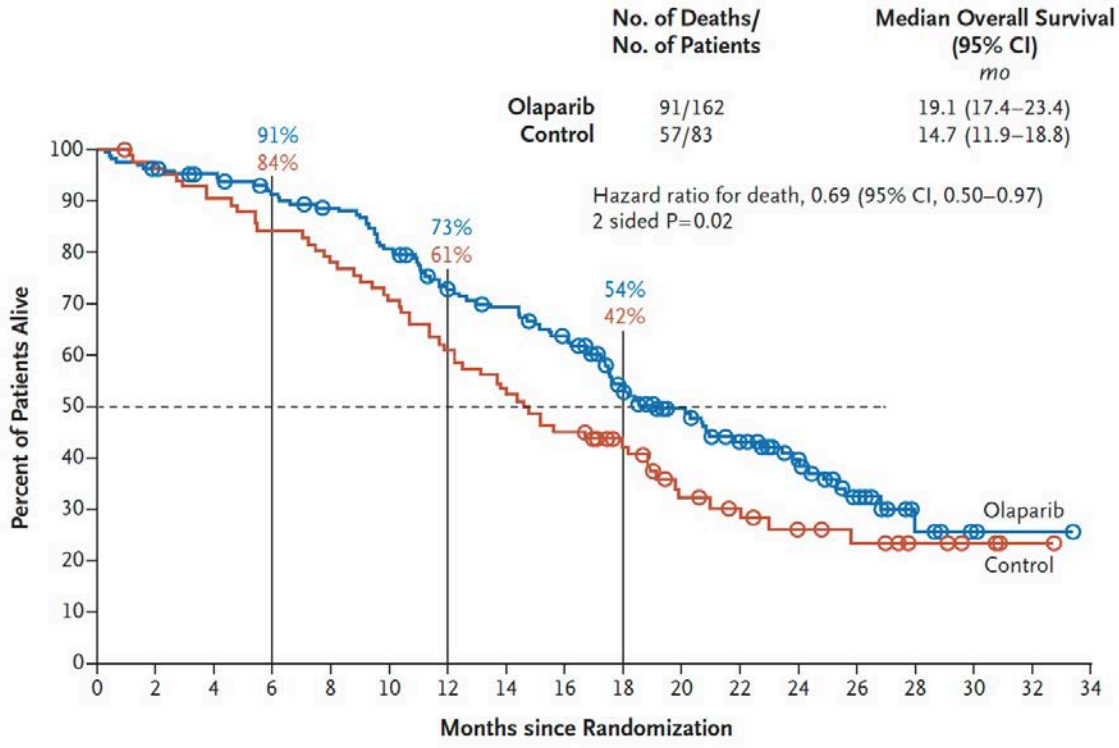
Survival with Olaparib in Metastatic Castration-Resistant Prostate Cancer

M. Hussain, J. Mateo, K. Fizazi, F. Saad, N. Shore, S. Sandhu, K.N. Chi, O. Sartor, N. Agarwal, D. Olmos, A. Thiery-Vuillemin, P. Twardowski, G. Roubaud, M. Özgüroğlu, J. Kang, J. Burgents, C. Gresty, C. Corcoran, C.A. Adelman, and J. de Bono, for the PROfound Trial Investigators*

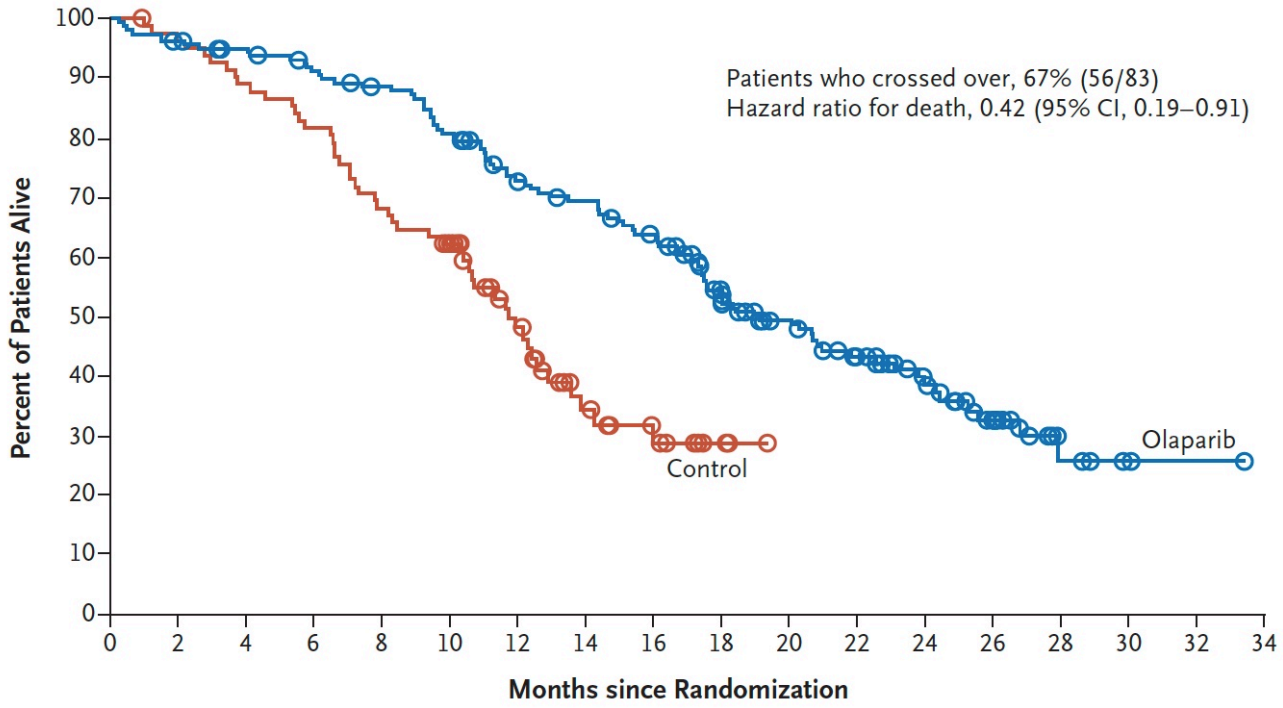
***N Engl J Med* 2020;383(24):2345-57.**

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

Overall survival



Crossover-adjusted overall survival



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

Positive Results Announced for the PROpel Phase III Trial of Olaparib with Abiraterone as First-Line Treatment for mCRPC

Press Release – September 24, 2021

"Positive high-level results from the PROpel Phase III trial showed that olaparib in combination with abiraterone demonstrated a statistically significant and clinically meaningful improvement in radiographic progression-free survival (rPFS) versus standard-of-care abiraterone as a 1st-line treatment for men with metastatic castration-resistant prostate cancer (mCRPC) with or without homologous recombination repair (HRR) gene mutations.

At a planned interim analysis, the Independent Data Monitoring Committee concluded that the trial met the primary endpoint of rPFS in men with mCRPC who had not received treatment in the 1st-line setting including with new hormonal agents or chemotherapy.

The data will be presented at an upcoming medical meeting."

https://www.astrazeneca.com/media-centre/press-releases/2021/lynparza-propel-trial-meets-primary-endpoint.html

RTP RESEARCH TO PRACTICE

PROpel: Phase III Trial of Olaparib (ola) and Abiraterone (abi) versus Placebo (pbo) and Abi as First-Line (1L) Therapy for Patients (pts) with Metastatic Castration-Resistant Prostate Cancer (mCRPC)

Saad F et al.

Genitourinary Cancers Symposium 2022;Abstract 11.

Oral Abstract Session A: Prostate Cancer

Level 3, Ballroom

Thursday, Feb 17, 2022

4:00 PM – 5:30 PM EST

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

Chi KN et al.

Genitourinary Cancers Symposium;Abstract 12.

Oral Abstract Session A: Prostate Cancer

Level 3, Ballroom

Thursday, Feb 17, 2022

4:00 PM – 5:30 PM EST

rapid communications

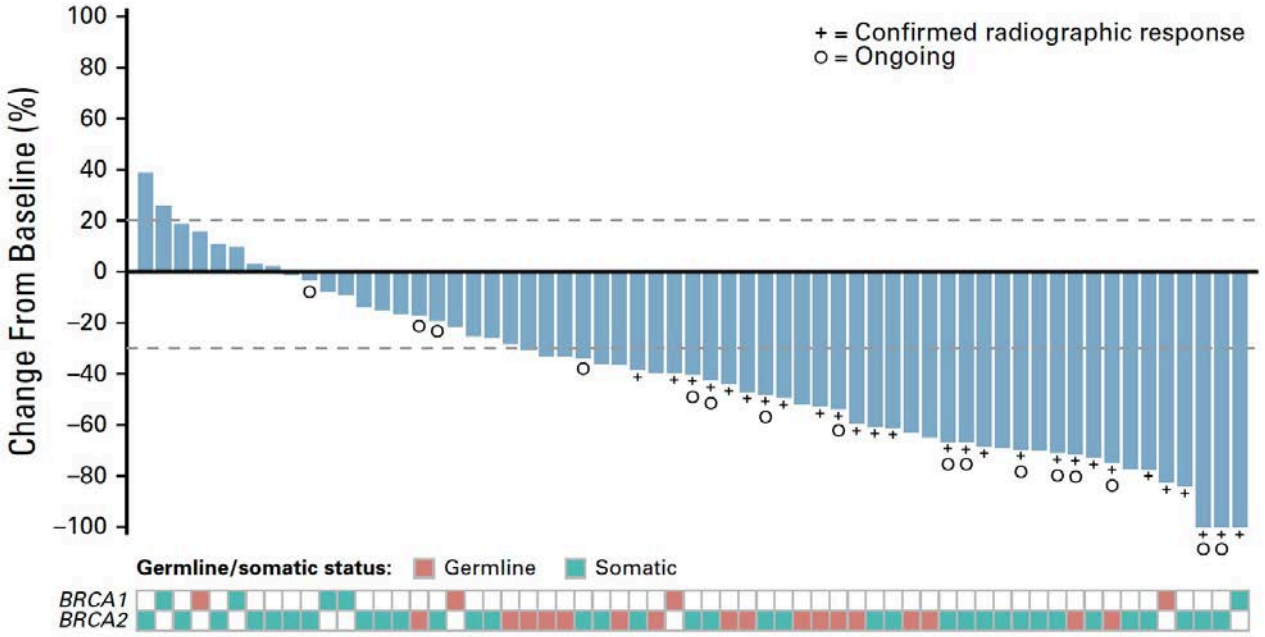
Rucaparib in Men With Metastatic Castration-Resistant Prostate Cancer Harboring a *BRCA1* or *BRCA2* Gene Alteration

Wassim Abida, MD, PhD[1]; Akash Patnaik, MD, PhD, MMSc[2]; David Campbell, MBBS[3]; Jeremy Shapiro, MBBS[4]; Alan H. Bryce, MD[5]; Ray McDermott, MD, PhD, MBA[6]; Brieuc Sautois, MD, PhD[7]; Nicholas J. Vogelzang, MD[8]; Richard M. Bambury, MD[9]; Eric Voog, MD[10]; Jingsong Zhang, MD, PhD[11]; Josep M. Piulats, MD[12]; Charles J. Ryan, MD[13]; Axel S. Merseburger, PhD[14]; Gedske Daugaard, DMSc[15]; Axel Heidenreich, MD[16]; Karim Fizazi, MD, PhD[17]; Celestia S. Higano, MD[18]; Laurence E. Krieger, MBChB[19]; Cora N. Sternberg, MD[20]; Simon P. Watkins, PhD[21]; Darrin Despain, MStat[22]; Andrew D. Simmons, PhD[23]; Andrea Loehr, PhD[23]; Melanie Dowson, BA[24]; Tony Golsorkhi, MD[25]; and Simon Chowdhury, MD, PhD[26,27]; on behalf of the TRITON2 investigators

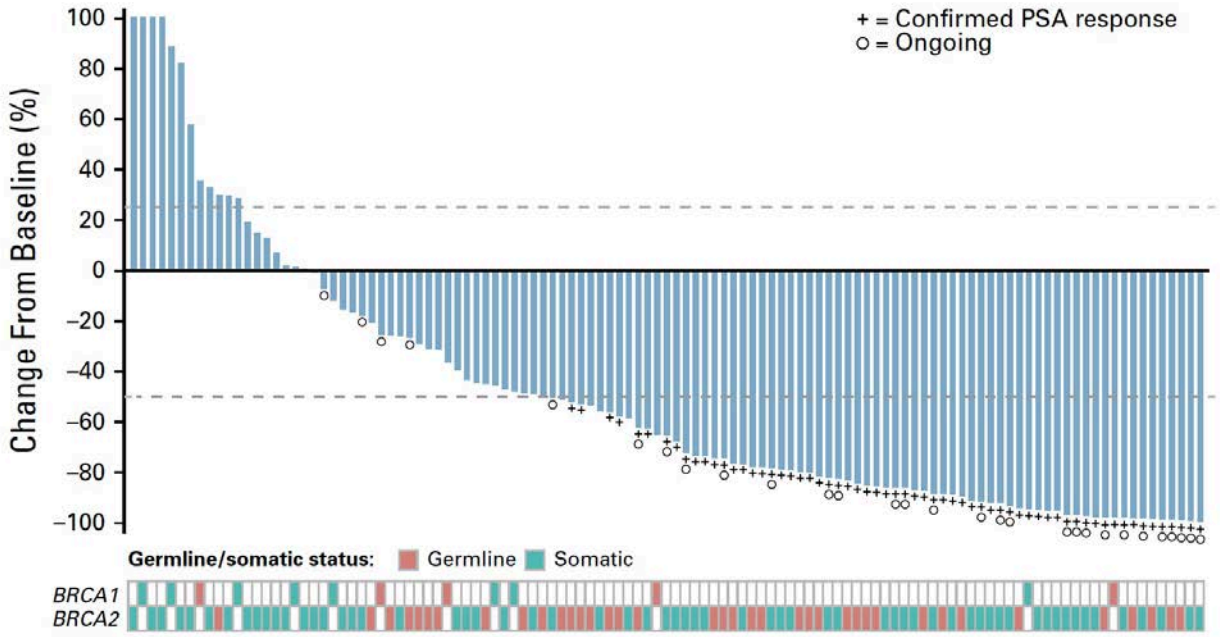
J Clin Oncol 2020;38(22):3763-72.

TRITON2: Response to Rucaparib in Patients with mCRPC Harboring a BRCA1 or BRCA2 Gene Alteration

ORR per independent radiology review: 43.5%



Confirmed PSA response rate: 54.8%



ORR = objective response rate

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

Articles

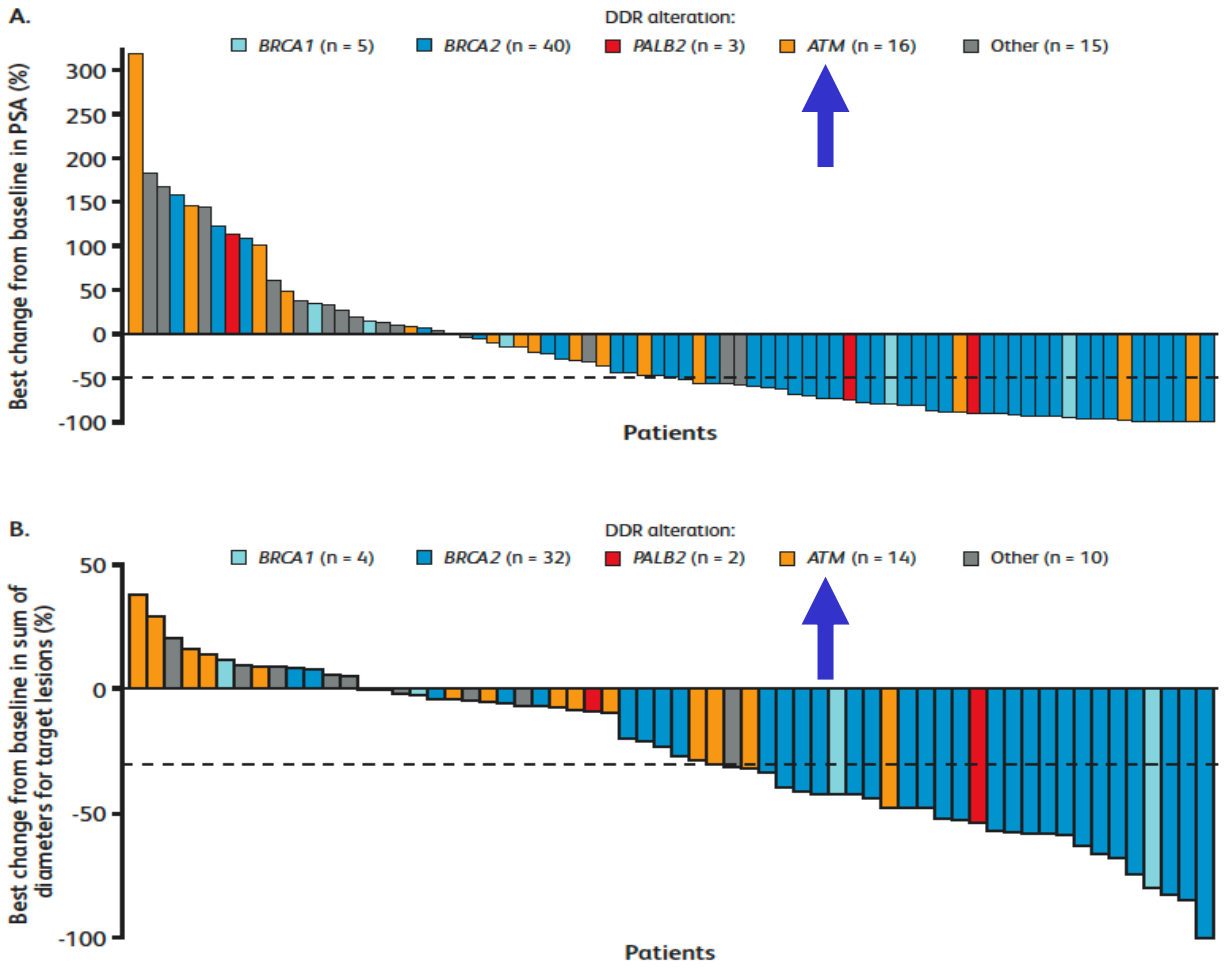
Talazoparib monotherapy in metastatic castration-resistant prostate cancer with DNA repair alterations (TALAPRO-1): an open-label, phase 2 trial

Johann S de Bono, Niven Mehra, Giorgio V Scagliotti, Elena Castro, Tanya Dorff, Adam Stirling, Arnulf Stenzl, Mark T Fleming, Celestia S Higano, Fred Saad, Consuelo Buttigliero, Inge M van Oort, A Douglas Laird, Marielena Mata, Hsiang-Chun Chen, Cynthia G Healy, Akos Czibere, Karim Fizazi

***Lancet Oncol* 2021;22(9):1250-64.**

TALAPRO-1: A Phase II Trial of Talazoparib for mCRPC

Figure 4. Best Change From Baseline in A. PSA and B. RECIST[a]



[a]DDR deficient population includes DDR patients who received treatment for ≥16 weeks; for panel A (n = 79) and for panel B (n = 62).
Abbreviations: DDR, DNA damage repair; PSA, prostate-specific antigen; RECIST, Response Evaluation Criteria in Solid Tumors version 1.1.

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

RTP RESEARCH TO PRACTICE

FDA Grants Breakthrough Therapy Designation to ^{177}Lu-PSMA-617 for the Treatment of mCRPC

Press Release – June 16, 2021

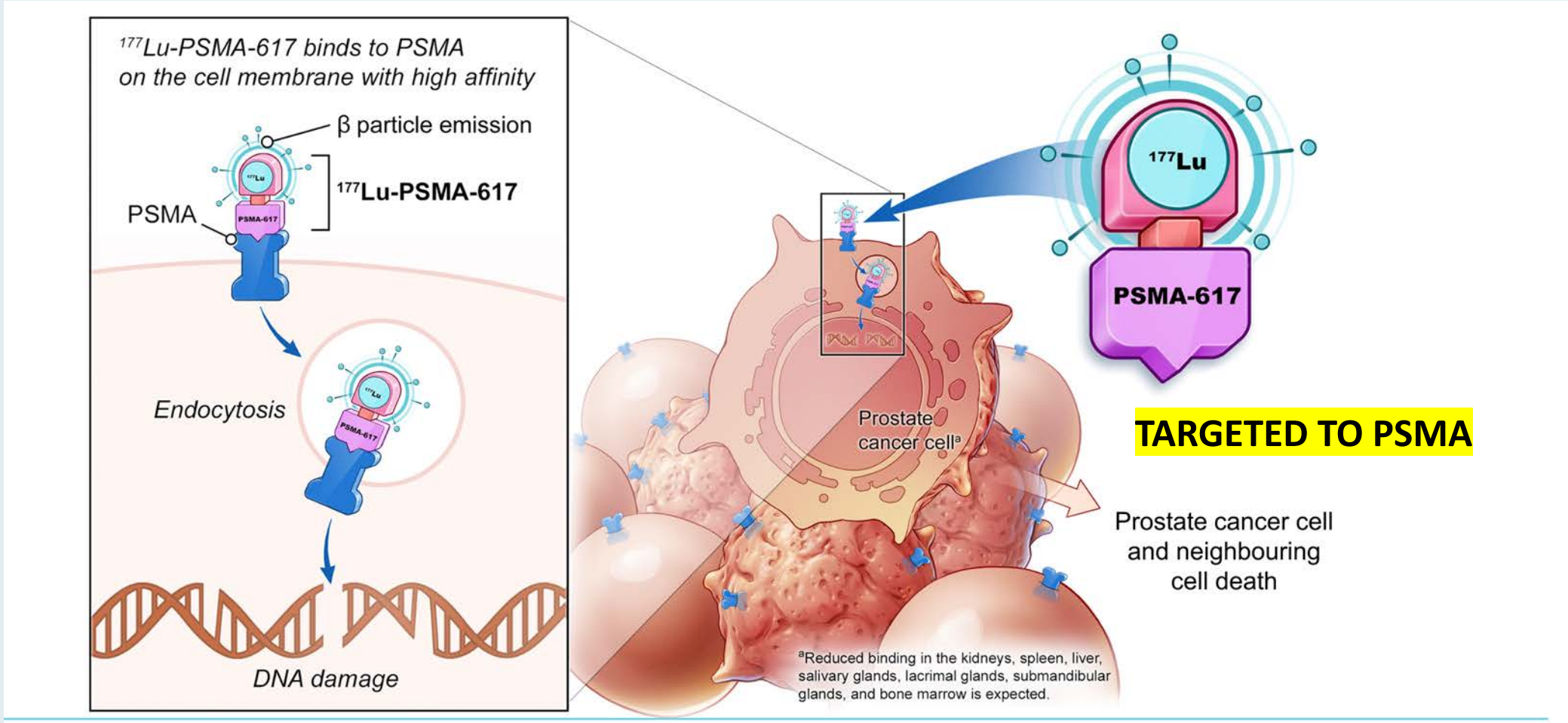
"The US Food and Drug Administration has granted Breakthrough Therapy designation to ^{177}Lu-PSMA-617, an investigational radioligand therapy for the treatment of metastatic castration-resistant prostate cancer (mCRPC). Breakthrough Therapy designation is granted to medicines being evaluated for serious conditions where early clinical evidence indicates the potential for substantial improvement over available therapy.

Breakthrough therapy designation was granted based on positive data from the pivotal, Phase III VISION study evaluating ^{177}Lu-PSMA-617, a targeted radioligand therapy, plus standard of care (SOC), compared to SOC alone, in patients with progressive PSMA-positive mCRPC."

https://www.novartis.com/news/novartis-receives-fda-breakthrough-therapy-designation-investigational-177lu-psma-617-patients-metastatic-castration-resistant-prostate-cancer-mcrpc

RTP RESEARCH TO PRACTICE

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



Morris MJ et al. ASCO 2021;Abstract LBA4.

N Engl J Med 2021;385:1091-103

The NEW ENGLAND JOURNAL of MEDICINE

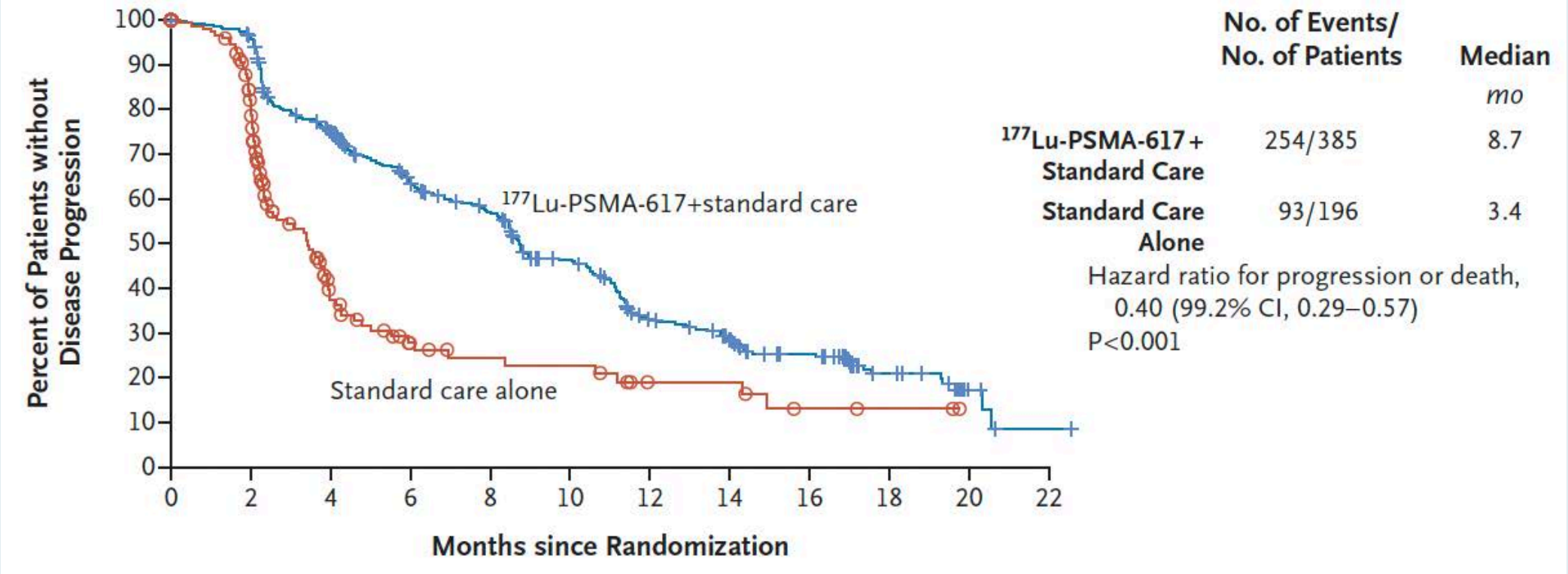
ORIGINAL ARTICLE

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

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

VISION: Efficacy Summary

Imaging–based PFS



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

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

RTP RESEARCH TO PRACTICE

VISION: Selected Adverse Events

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

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

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

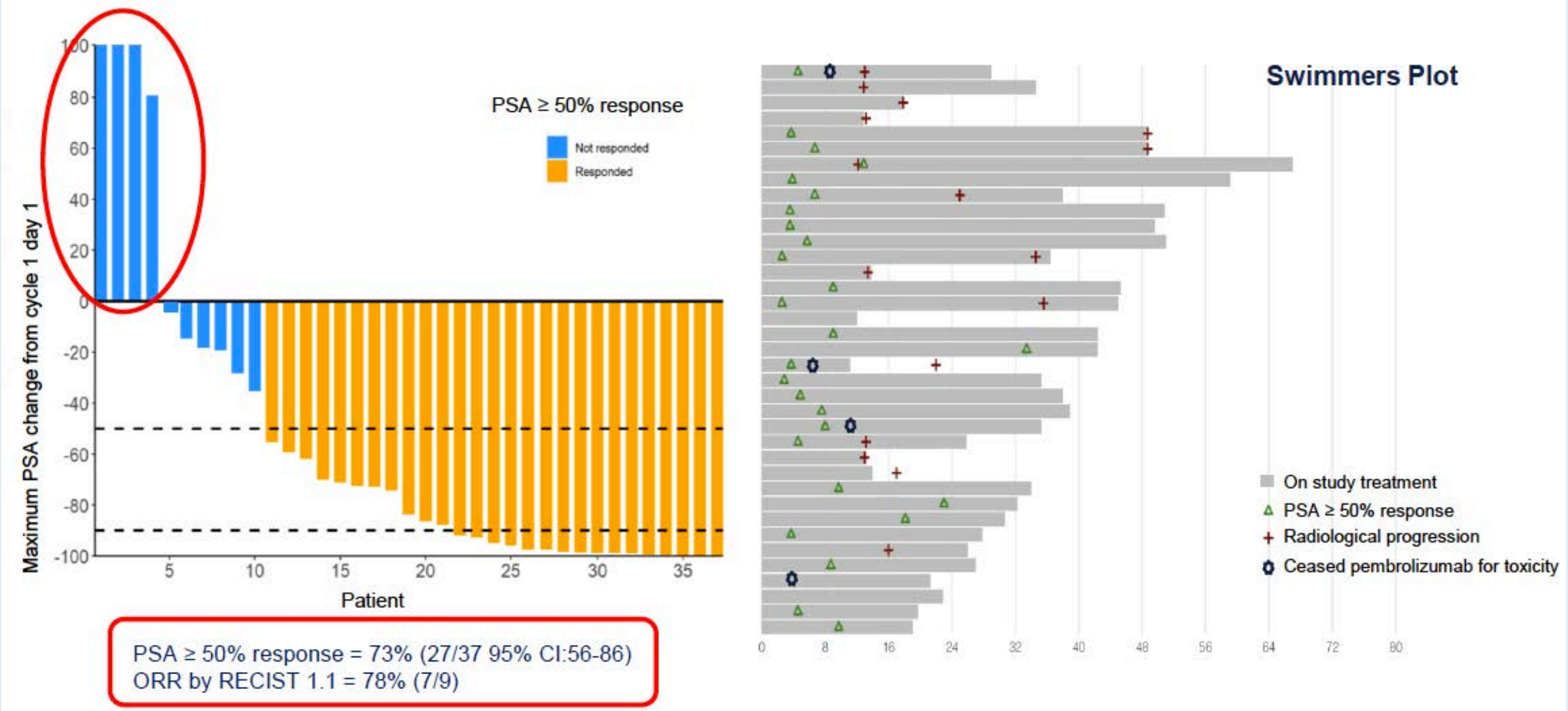
Shahneen Sandhu, Anthony M. Joshua, Louise Emmett, Lavinia Spain, Lisa G. Horvath, Megan Crumbaker, Arsha Anton, Roslyn Wallace, Anupama Pasam, Mathias Bressel, Erin Cassidy, Patricia Banks, Aravind Ravi Kumar, Ramin Alipour, Tim Akhurst, Grace Kong, Ian D. Davis, Scott Williams, Rod Hicks, Michael S.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

Abstract 577O

2021 ESMO congress

Presented by: Shahneen Sandhu

PRINCE: PSA Response Rate (Primary Endpoint)



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

Immune Checkpoint Inhibitors in mCRPC

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

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

2021 ESMO congress

Abstract LBA24

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

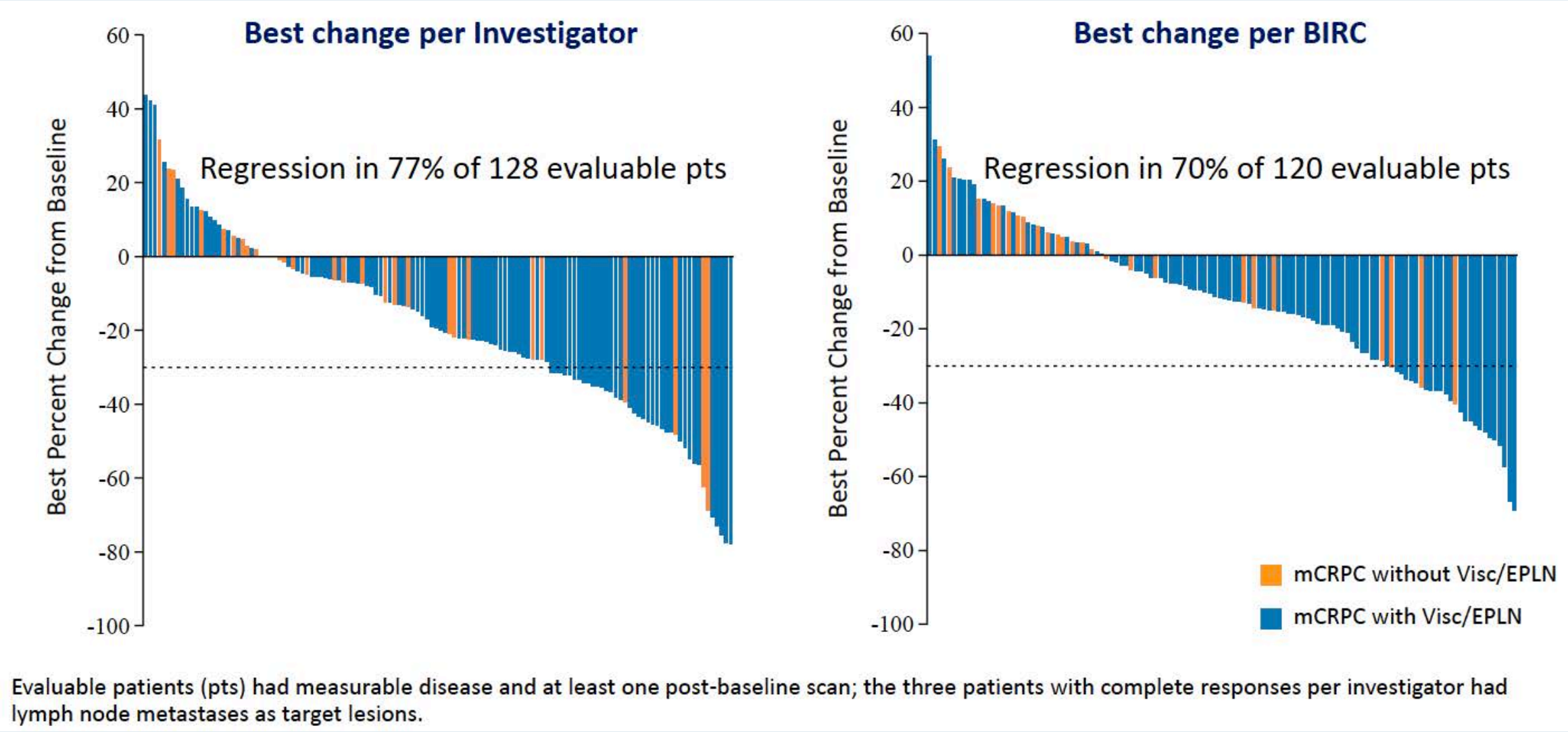
Neeraj Agarwal,[1] Bradley McGregor,[2] Benjamin L. Maughan,[1] Tanya B. Dorff,[3] William Kelly,[4] Bruno Fang,[5] Rana R. McKay,[6] Parminder Singh,[7] Lance Pagliaro,[8] Robert Dreicer,[9] Sandy Srinivas,[10] Yohann Loriot,[11] Ulka Vaishampayan,[12] Sanjay Goel,[13] Dominic Curran,[14] Ashok Panneerselvam,[14]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

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

*Co-senior authors

RTP RESEARCH TO PRACTICE

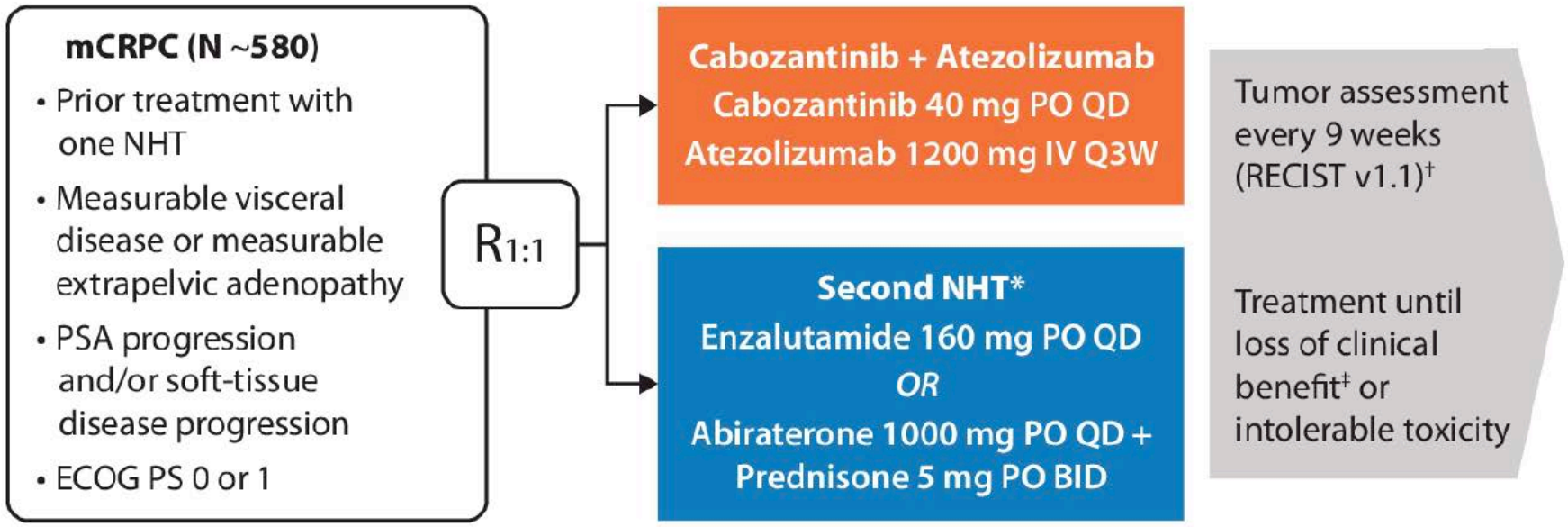
COSMIC-021: Best Change from Baseline in Sum of Target Lesions



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

Agarwal et al. ESMO 2021;Abstract LBA24.

CONTACT-02: Phase III Trial Schema



Stratification

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

Primary Endpoints

- PFS per RECIST v1.1 by BIRC
- OS

Secondary Endpoint

- ORR per RECIST v1.1 by BIRC

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

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

Agenda

Module 1: Urothelial Bladder Carcinoma

Module 2: Prostate Cancer

Module 3: Renal Cell Carcinoma (RCC)

RTP
RESEARCH
TO PRACTICE

FDA Approves Pembrolizumab for Adjuvant Treatment of Renal Cell Carcinoma

Press Release – November 17, 2021

"On November 17, 2021, the Food and Drug Administration approved pembrolizumab for the adjuvant treatment of patients with renal cell carcinoma (RCC) at intermediate-high or high risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions.

Efficacy was evaluated in KEYNOTE-564 (NCT03142334), a multicenter, randomized (1:1), double-blind, placebo-controlled trial in 994 patients with intermediate-high or high risk of recurrence of RCC, or M1 no evidence of disease. Patients were randomized to pembrolizumab 200 mg intravenously every 3 weeks or placebo for up to 1 year until disease recurrence or unacceptable toxicity.

The recommended pembrolizumab dose is 200 mg every 3 weeks or 400 mg every 6 weeks until disease recurrence, unacceptable toxicity, or up to 12 months."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-pembrolizumab-adjuvant-treatment-renal-cell-carcinoma

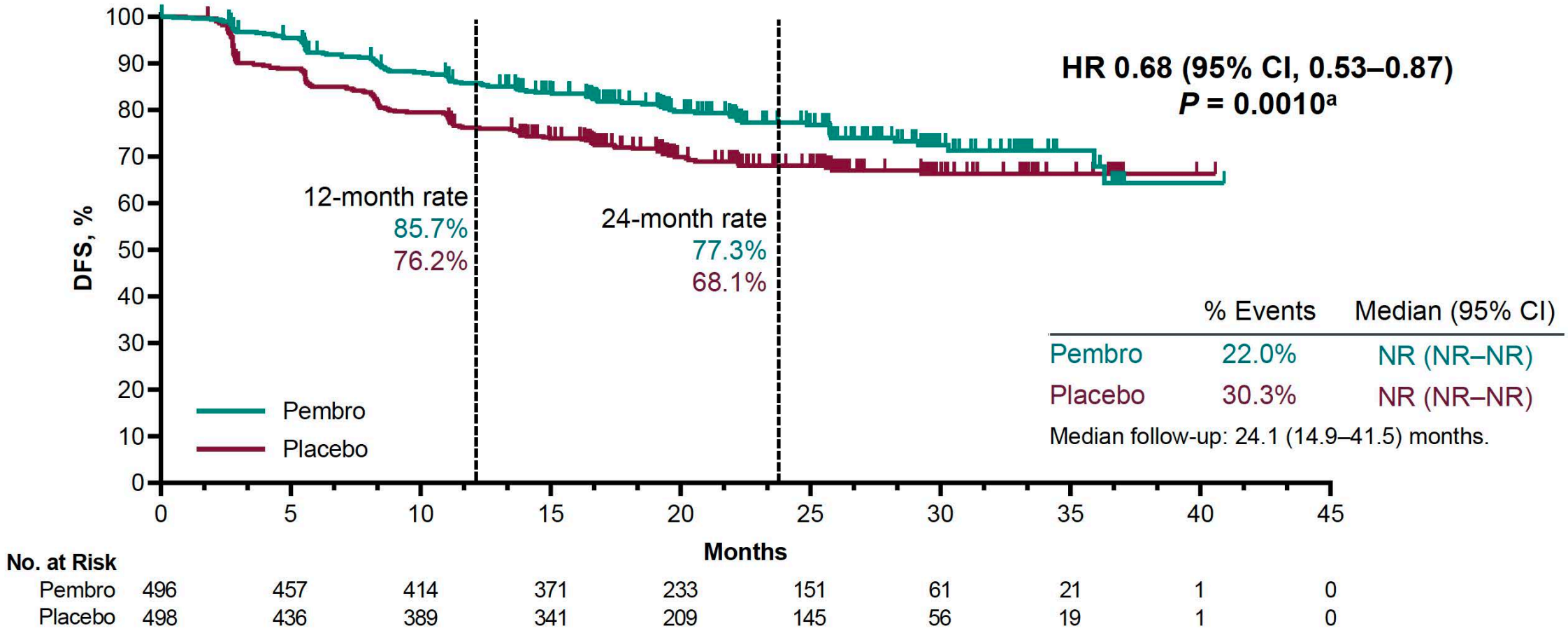
Pembrolizumab vs Placebo as Adjuvant Therapy for Patients with Renal Cell Carcinoma: Patient-Reported Outcomes in KEYNOTE-564

Toni K. Choueiri[1]; Piotr Tomczak[2]; Se Hoon Park[3]; Balaji Venugopal[4]; Stefan Symeonides[5]; Jaroslav Hajek[6]; Thomas Ferguson[7]; Yen-Hwa Chang[8]; Jae Lyun Lee[9]; Naomi Haas[10]; Piotr Sawrycki[11]; Naveed Sarwar[12]; Marine Gross-Goupil[13]; Antoine Thiery-Vuillemin[14]; Mauricio Mahave[15]; Rodolfo F. Perini[16]; Todd L. Saretsky[16]; Pingye Zhang[16]; Jaqueline Willemann-Rogerio[16]; David Quinn[17]; Thomas Powles[18]; on behalf of the KEYNOTE-564 investigators.

[1]Dana-Farber Cancer Institute, Boston, MA, USA; [2]Poznań University of Medical Sciences, Poznań, Poland; [3]Sungkyunkwan University, Samsung Medical Center, Seoul, South Korea; [4]Beatson West of Scotland Cancer Centre and University of Glasgow, Glasgow, UK; [5]Edinburgh Cancer Centre and University of Edinburgh, UK; [6]Fakultni Nemocnice Ostrava, Ostrava, Czech Republic; [7]Fiona Stanley Hospital, Perth, Australia; [8]Taipei Veterans General Hospital, Taipei, Taiwan; [9]Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea; [10]Abramson Cancer Center, Philadelphia, PA, USA; [11]Wojewodzki Szpital Zespolony im. L. Rydygiera w Toruniu, Torun, Poland; [12]Imperial College Healthcare NHS Trust, London, UK; [13]University Hospital Bordeaux-Hôpital Saint-André, Bordeaux, France; [14]University Hospital Jean Minjoz, Besançon, France; [15]Fundacion Arturo Lopez Perez FALP, Santiago, Chile; [16]Merck & Co., Inc., Kenilworth, NJ, USA; [17]USC Norris Comprehensive Cancer Center, Los Angeles, CA, USA; [18]Royal Free Hospital NHS Trust, University College London, London, UK.

Abstract 653O

KEYNOTE-564: Pembrolizumab as Adjuvant Therapy for Patients with RCC – Disease-Free Survival



Choueiri TK et al. ESMO 2021;Abstract 653O.

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

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

[a] Albiges L et al. *ESMO Open* 2020;5(6):e001079. [b] Powles T et al. *Lancet Oncol* 2020;21:1563-73.
[c] Choueiri TK et al. *Ann Oncol* 2020;31(8):1030-39.

FDA Approves Lenvatinib with Pembrolizumab for Advanced RCC

Press Release – August 10, 2021

"The Food and Drug Administration approved the combination of lenvatinib plus pembrolizumab for first-line treatment of adult patients with advanced renal cell carcinoma (RCC).

The efficacy of this combination was investigated in CLEAR (Study 307/KEYNOTE-581; NCT02811861), a multicenter, open-label, randomized phase 3 trial in patients with advanced RCC in the first-line setting. Patients were enrolled regardless of PD-L1 tumor expression status. The efficacy population supporting this approval included patients randomized to lenvatinib plus pembrolizumab (n = 355) compared with those randomized to single-agent sunitinib (n = 357)."

www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-lenvatinib-plus-pembrolizumab-advanced-renal-cell-carcinoma

The NEW ENGLAND JOURNAL of MEDICINE

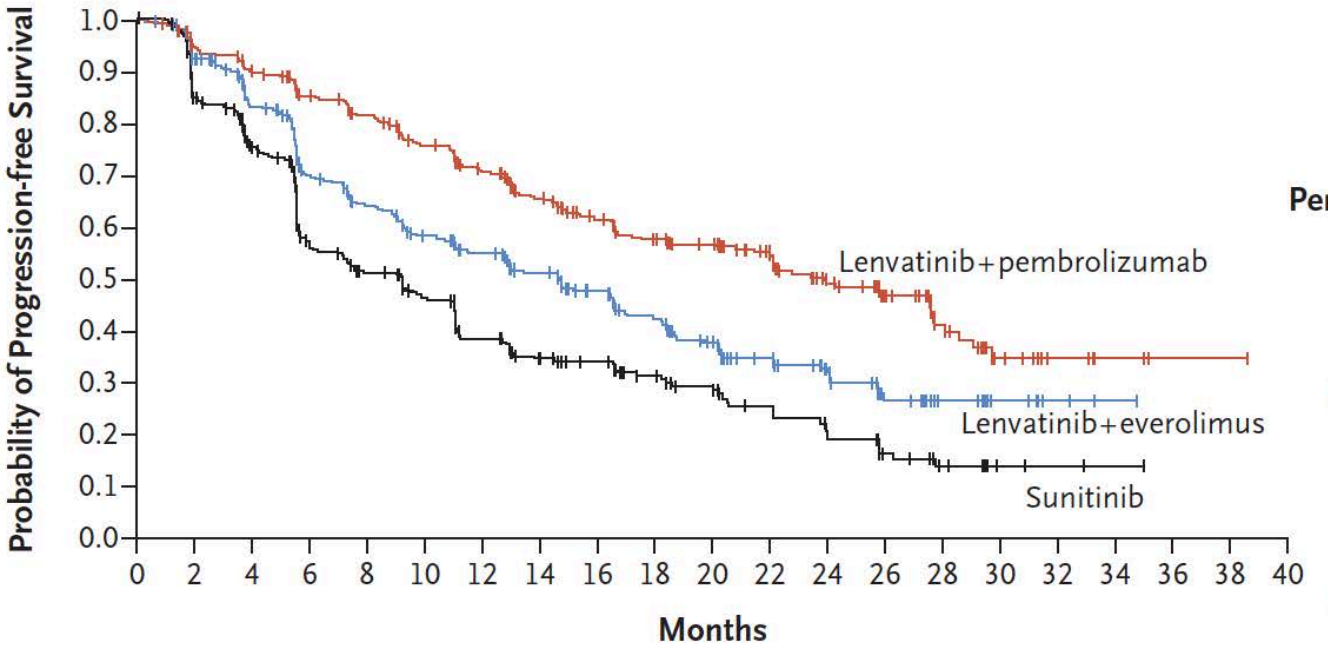
ESTABLISHED IN 1812 APRIL 8, 2021 VOL. 384 NO. 14

Lenvatinib plus Pembrolizumab or Everolimus for Advanced Renal Cell Carcinoma

R. Motzer, B. Alekseev, S.-Y. Rha, C. Porta, M. Eto, T. Powles, V. Grünwald, T.E. Hutson, E. Kopyltsov, M.J. Méndez-Vidal, V. Kozlov, A. Alyasova, S.-H. Hong, A. Kapoor, T. Alonso Gordoa, J.R. Merchan, E. Winquist, P. Maroto, J.C. Goh, M. Kim, H. Gurney, V. Patel, A. Peer, G. Procopio, T. Takagi, B. Melichar, F. Rolland, U. De Giorgi, S. Wong, J. Bedke, M. Schmidinger, C.E. Dutcus, A.D. Smith, L. Dutta, K. Mody, R.F. Perini, D. Xing, and T.K. Choueiri, for the CLEAR Trial Investigators*

CLEAR: Progression-Free Survival Analyses

Progression-free survival



No. at Risk

Lenvatinib+pembrolizumab	355	321	300	276	259	235	213	186	160	136	126	106	80	56	30	14	6	3	1	1	0
Lenvatinib+everolimus	357	305	259	207	185	163	149	125	105	85	70	53	37	20	13	7	3	1	0		
Sunitinib	357	262	218	145	124	107	85	69	62	49	42	32	25	16	9	3	2	1	0		

Median Progression-free Survival (95% CI)

	mo
Lenvatinib+ Pembrolizumab	23.9 (20.8–27.7)
Lenvatinib+ Everolimus	14.7 (11.1–16.7)
Sunitinib	9.2 (6.0–11.0)

Hazard ratio for disease progression or death (lenvatinib+ pembrolizumab vs. sunitinib), 0.39 (95% CI, 0.32–0.49); P<0.001

Hazard ratio for disease progression or death (lenvatinib+ everolimus vs. sunitinib), 0.65 (95% CI, 0.53–0.80); P<0.001

Overall survival was longer with lenvatinib and pembrolizumab than with sunitinib (HR 0.66; $p = 0.005$) but was not longer with lenvatinib and everolimus than with sunitinib (HR 1.15; $p = 0.30$).

Motzer R et al. *N Engl J Med* 2021;384(14):1289-300.

CLEAR: Updated OS by Risk Group and Treatment Arm

	MEDIAN OS, MONTHS		
Subgroup	Lenvatinib/pembrolizumab	Sunitinib	HR (95% CI)
All patients	NE	NE	0.72 (0.55-0.93)
MSKCC favorable risk	NE	NE	1.00 (0.51-1.96)
MSKCC intermediate risk	43.0	41.1	0.71 (0.52-0.97)
MSKCC poor risk	33.0	17.1	0.50 (0.25-1.02)
IMDC favorable risk	NE	NE	1.22 (0.66-2.26)
IMDC intermediate risk	43.0	41.1	0.72 (0.52-1.00)
IMDC poor risk	36.9	10.4	0.39 (0.20-0.77)

IMDC, International Metastatic Renal Cell Carcinoma Database Consortium criteria; MSKCC, Memorial Sloan Kettering Cancer Center criteria; OS, overall survival.

Choueiri TK et al. 2021 International Kidney Cancer Symposium;Abstract E41.

FDA Approves Nivolumab with Cabozantinib for Advanced RCC

Press Release – January 22, 2021

"The Food and Drug Administration approved the combination of nivolumab and cabozantinib as first-line treatment for patients with advanced renal cell carcinoma (RCC).

Efficacy was evaluated in CHECKMATE-9ER (NCT03141177), a randomized, open-label trial in patients with previously untreated advanced RCC. Patients were randomized to receive either nivolumab 240 mg over 30 minutes every 2 weeks in combination with cabozantinib 40 mg orally once daily (n = 323) or sunitinib 50 mg orally daily for the first 4 weeks of a 6-week cycle (4 weeks on treatment followed by 2 weeks off) (n = 328)."

www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-nivolumab-plus-cabozantinib-advanced-renal-cell-carcinoma

RTP RESEARCH TO PRACTICE

The NEW ENGLAND JOURNAL of MEDICINE

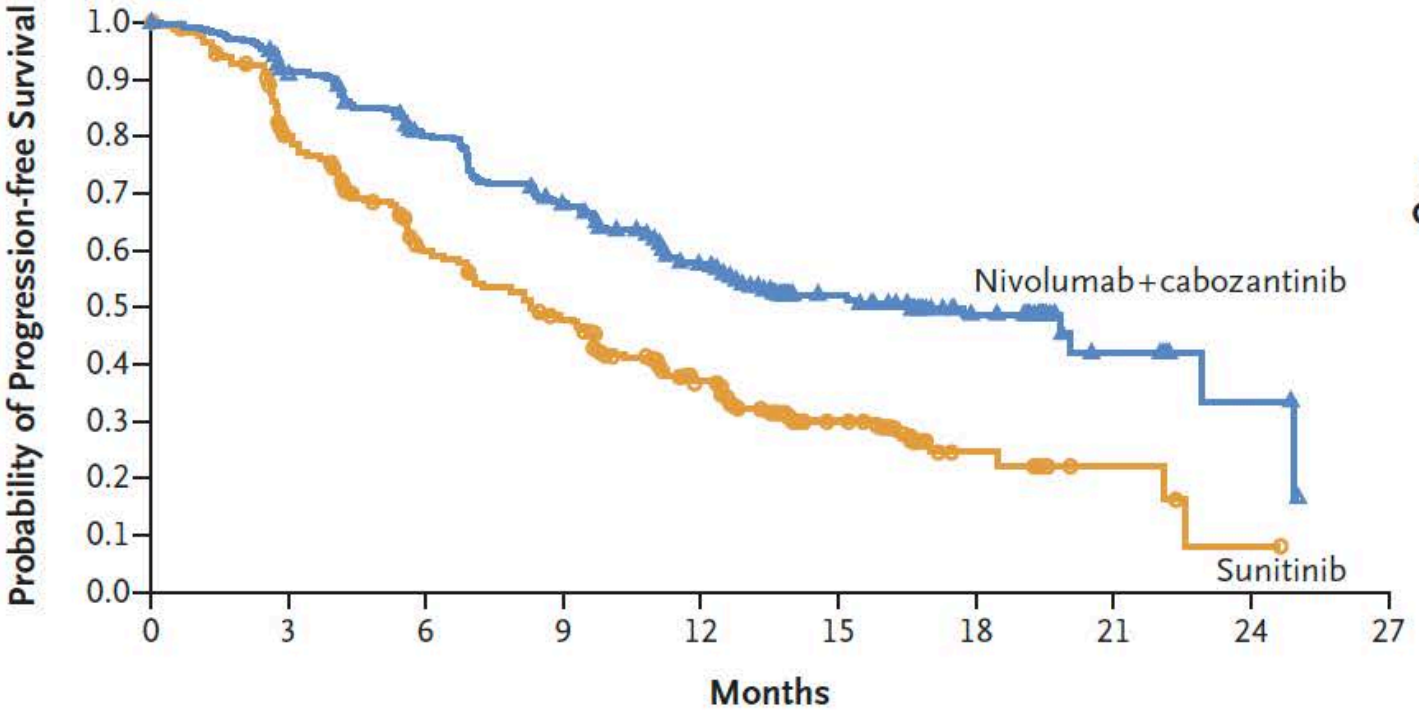
ORIGINAL ARTICLE

Nivolumab plus Cabozantinib versus Sunitinib for Advanced Renal-Cell Carcinoma

T.K. Choueiri, T. Powles, M. Burotto, B. Escudier, M.T. Bourlon, B. Zurawski, V.M. Oyervides Juárez, J.J. Hsieh, U. Basso, A.Y. Shah, C. Suárez, A. Hamzaj, J.C. Goh, C. Barrios, M. Richardet, C. Porta, R. Kowalyszyn, J.P. Feregrino, J. Żołnierek, D. Pook, E.R. Kessler, Y. Tomita, R. Mizuno, J. Bedke, J. Zhang, M.A. Maurer, B. Simsek, F. Ejzykowicz, G.M. Schwab, A.B. Apolo, and R.J. Motzer, for the CheckMate 9ER Investigators*

N Engl J Med 2021;384(9):829-41.

CheckMate 9ER: Progression-Free Survival



	No. of Patients	Median (95% CI) *mo*
Nivolumab+ Cabozantinib	323	16.6 (12.5–24.9)
Sunitinib	328	8.3 (7.0–9.7)

Hazard ratio for disease progression or death, 0.51 (95% CI, 0.41–0.64)
P<0.001

No. at Risk										
Nivolumab+cabozantinib	323	279	234	196	144	77	35	11	4	0
Sunitinib	328	228	159	122	79	31	10	4	1	0

Choueiri TK et al. *N Engl J Med* 2021;384(9):829-41.

FDA Approves Tivozanib for Relapsed or Refractory Advanced RCC

Press Release – March 10, 2021

"The Food and Drug Administration approved tivozanib, a kinase inhibitor, for adult patients with relapsed or refractory advanced renal cell carcinoma (RCC) following two or more prior systemic therapies.

Efficacy was evaluated in TIVO-3 (NCT02627963), a randomized (1:1), open-label, multicenter trial of tivozanib versus sorafenib in patients with relapsed or refractory advanced RCC who received two or three prior systemic treatments,including at least one VEGFR kinase inhibitor other than sorafenib or tivozanib. Patients were randomized to either tivozanib 1.34 mg orally once daily for 21 consecutive days every 28 days or sorafenib 400 mg orally twice a day continuously, until disease progression or unacceptable toxicity."

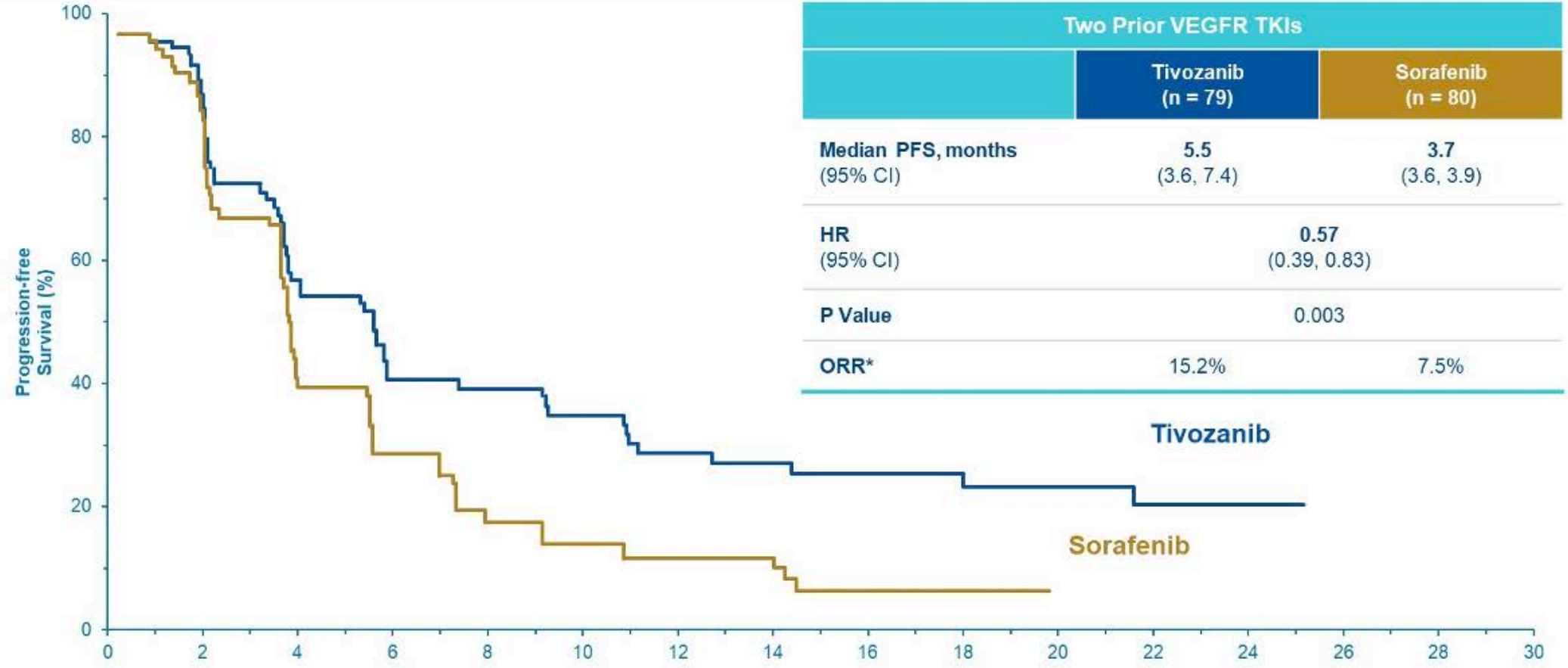
www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-tivozanib-relapsed-or-refractory-advanced-renal-cell-carcinoma

TIVO-3: Tivozanib in Patients with Advanced Renal Cell Carcinoma (aRCC) Who Have Progressed After Treatment with Axitinib

Rini BI et al.

Genitourinary Cancers Symposium 2021;Abstract 278.

TIVO-3: Progression-Free Survival and ORR in Patient Subgroup with 2 Prior Tyrosine Kinase Inhibitors (TKIs)



Two Prior VEGFR TKIs		
	Tivozanib (n = 79)	Sorafenib (n = 80)
Median PFS, months (95% CI)	5.5 (3.6, 7.4)	3.7 (3.6, 3.9)
HR (95% CI)	0.57 (0.39, 0.83)	
P Value	0.003	
ORR*	15.2%	7.5%

Rini BI et al. Genitourinary Cancers Symposium 2021;Abstract 278.

TIVO-3: Tivozanib After Axitinib

RCC Population	N (subjects)		mPFS (months)		HR	ORR	
	Tivo	Sor	Tivo	Sor		Tivo	Sor
ITT	175	175	5.6	3.9	0.73	18%	8%
3rd Line Any Prior Axitinib	47	46	5.5	3.9	0.71	16%	6%
4th Line Any Prior Axitinib	36	43	5.5	3.6	0.64	11%	10%
3rd and 4th Line Any Prior Axitinib	83	89	5.5	3.7	0.68	13%	8%

Rini BI et al. Genitourinary Cancers Symposium 2021;Abstract 278.

TIVO-3: Durability of Response and Updated Overall Survival of Tivozanib versus Sorafenib in Metastatic Renal Cell Carcinoma (mRCC)

Verzoni et al.
ASCO 2021;Abstract 4546.

"Tivozanib demonstrated clinically meaningful and statistically significant improvement in ORR and DoR with similar OS to sorafenib in patients with highly relapsed or refractory mRCC"

- *Median DoR was 20.3 months with tivozanib, twice that observed with sorafenib*

RTP RESEARCH TO PRACTICE

FDA Approves Belzutifan for Cancers Associated with von Hippel-Lindau Disease

Press Release – August 13, 2021

"On August 13, 2021, the Food and Drug Administration approved belzutifan, a hypoxia-inducible factor inhibitor for adult patients with von Hippel-Lindau (VHL) disease who require therapy for associated renal cell carcinoma (RCC), central nervous system (CNS) hemangioblastomas, or pancreatic neuroendocrine tumors (pNET), not requiring immediate surgery.

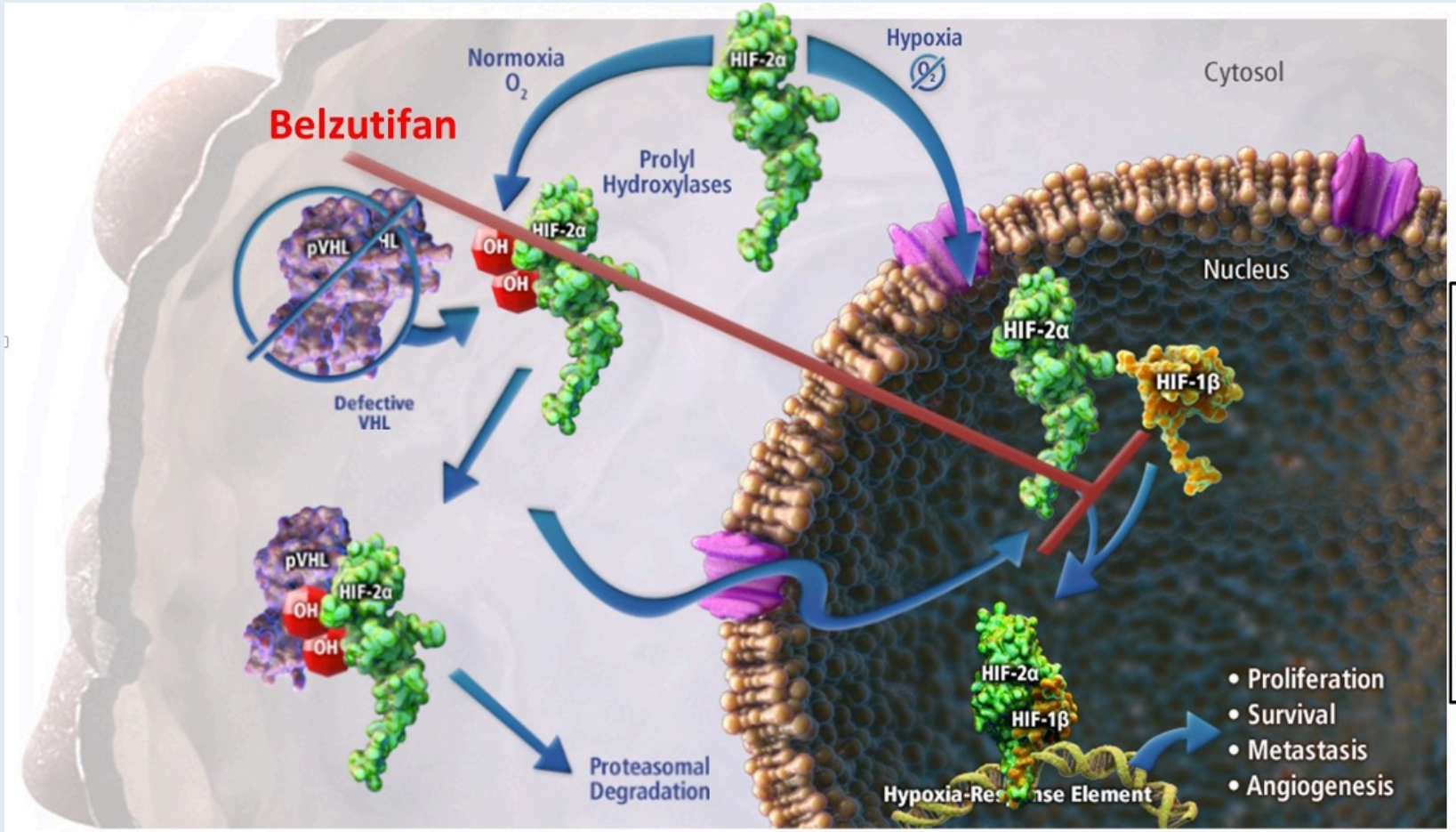
Belzutifan was investigated in the ongoing Study 004 (NCT03401788), an open-label clinical trial in 61 patients with VHL-associated RCC (VHL-RCC) diagnosed based on a VHL germline alteration and with at least one measurable solid tumor localized to the kidney. Enrolled patients had other VHL-associated tumors, including CNS hemangioblastomas and pNET. Patients received belzutifan 120 mg once daily until disease progression or unacceptable toxicity.

The recommended belzutifan dosage is 120 mg administered orally once daily with or without food."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-belzutifan-cancers-associated-von-hippel-lindau-disease

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.

The NEW ENGLAND JOURNAL of MEDICINE

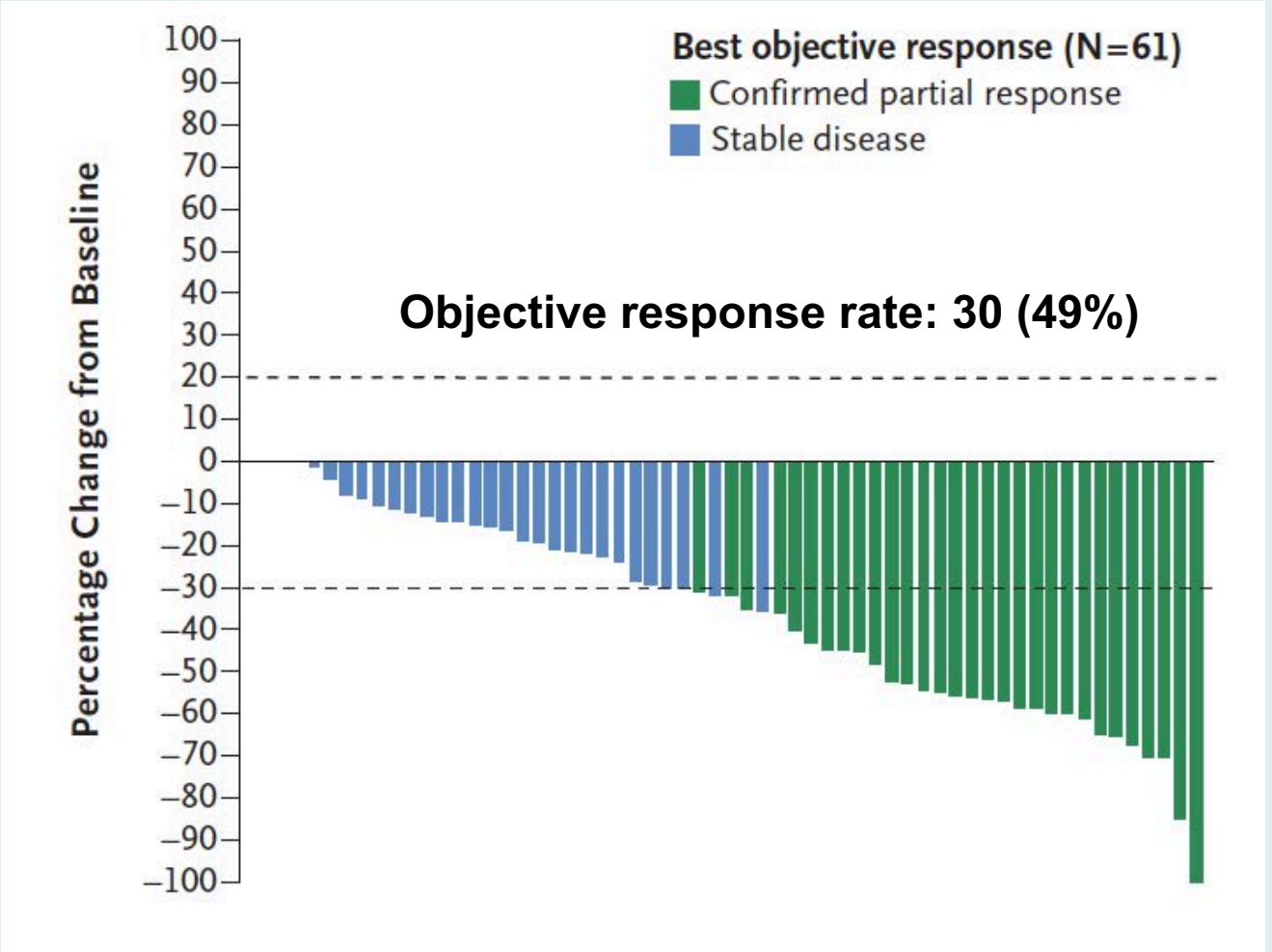
ORIGINAL ARTICLE

Belzutifan for Renal Cell Carcinoma in von Hippel–Lindau Disease

Eric Jonasch, M.D., Frede Donskov, M.D., Ph.D., Othon Iliopoulos, M.D., W. Kimryn Rathmell, M.D., Ph.D., Vivek K. Narayan, M.D., Benjamin L. Maughan, M.D., Stephane Oudard, M.D., Tobias Else, M.D., Jodi K. Maranchie, M.D., Sarah J. Welsh, M.D., Sanjay Thamake, Ph.D., Eric K. Park, M.D., Rodolfo F. Perini, M.D., W. Marston Linehan, M.D., and Ramaprasad Srinivasan, M.D., Ph.D., for the MK-6482-004 Investigators*

N Engl J Med 2021;385:2036-46.

Phase II Trial of Belzutifan: Maximum Change in Target Renal Tumors



Jonasch E et al. *N Engl J Med* 2021;385:2036-46.

Phase II Trial of Belzutifan: Select Adverse Events

Adverse event (n = 61)	Any grade	Grade 3
Anemia	55 (90%)	5 (8%)
Fatigue	40 (66%)	3 (5%)
Dyspnea	14 (23%)	1 (2%)
Myalgia	12 (20%)	1 (2%)
Hypertension	10 (16%)	5 (8%)
Diarrhea	8 (13%)	1 (2%)

Jonasch E et al. *N Engl J Med* 2021;385:2036-46.

Thank you for joining us!

CME and MOC 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 North Carolina Oncology Association and the South Carolina Oncology Society

A CME/MOC- and NCPD-Accredited Event

Saturday, February 12, 2022
8:30 AM – 4:00 PM ET

RTP
RESEARCH
TO PRACTICE

Agenda

Module 1 — Chronic Lymphocytic Leukemia and Lymphomas: *Drs Flinn and LaCasce*

Module 2 — Multiple Myeloma: *Drs Callander and Rajkumar*

Module 3 — Genitourinary Cancers: *Drs Dreicer and Heath*

Module 4 — Breast Cancer: *Drs Borges and Jhaveri*

Module 5 — Gastrointestinal Cancers: *Drs Hochster and Messersmith*

Module 6 — Lung Cancer: *Drs Govindan and Johnson*

Breast Cancer Faculty

Virginia F Borges, MD, MMSc
Professor of Medicine with Tenure
Robert F and Patricia Young-Connor Endowed Chair in Young Women's Breast Cancer Research
Deputy Head, Division of Medical Oncology
Director, Breast Cancer Research Program and Young Women's Breast Cancer Translational Program
University of Colorado Cancer Center
Aurora, Colorado

Komal Jhaveri, MD
Associate Attending Physician
Breast Medicine Service and Early Drug Development Service
Section Head, Endocrine Therapy Research Program
Clinical Director, Early Drug Development Service
Department of Medicine
Memorial Sloan Kettering Cancer Center
Assistant Professor of Medicine
Weill Cornell College of Medicine
New York, New York

RTP
RESEARCH TO PRACTICE

MODULE 4: Breast Cancer

Co-Moderator

Emily Z Touloukian, DO
Coastal Cancer Center
Myrtle Beach, South Carolina

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Contributing General Medical Oncologists

Jennifer L Dallas, MD
Novant Health Cancer Institute
Charlotte, North Carolina

Joanna Metzner-Sadurski, MD
Self Regional Healthcare Cancer Center
Greenwood, South Carolina

Justin Peter Favaro, MD, PhD
Oncology Specialists of Charlotte
Charlotte, North Carolina

William R Mitchell, MD
Southern Oncology Specialists
Charlotte, North Carolina

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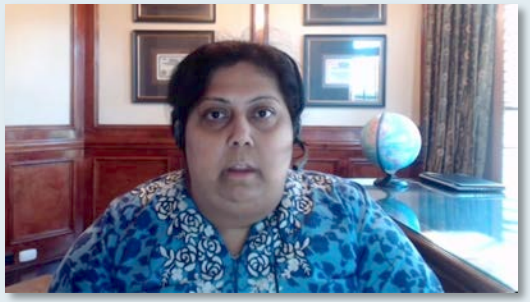
Contributing General Medical Oncologists



Niyati A Nathwani, MD
Carolina Blood and Cancer Care Associates
Charlotte, North Carolina

Nasfat Shehadeh, MD
Oncology Specialists of Charlotte, PA
Charlotte, North Carolina

Julia Saylors, MD
Charleston Oncology
North Charleston, South Carolina

Contributing Clinical Investigator

Gretchen G Kimmick, MD
Duke Cancer Institute
Durham, North Carolina

RTP RESEARCH TO PRACTICE

Agenda

Module 1: HER2-Positive

Module 2: ER/PR-Positive, HER2-Negative

Module 3: Triple-Negative

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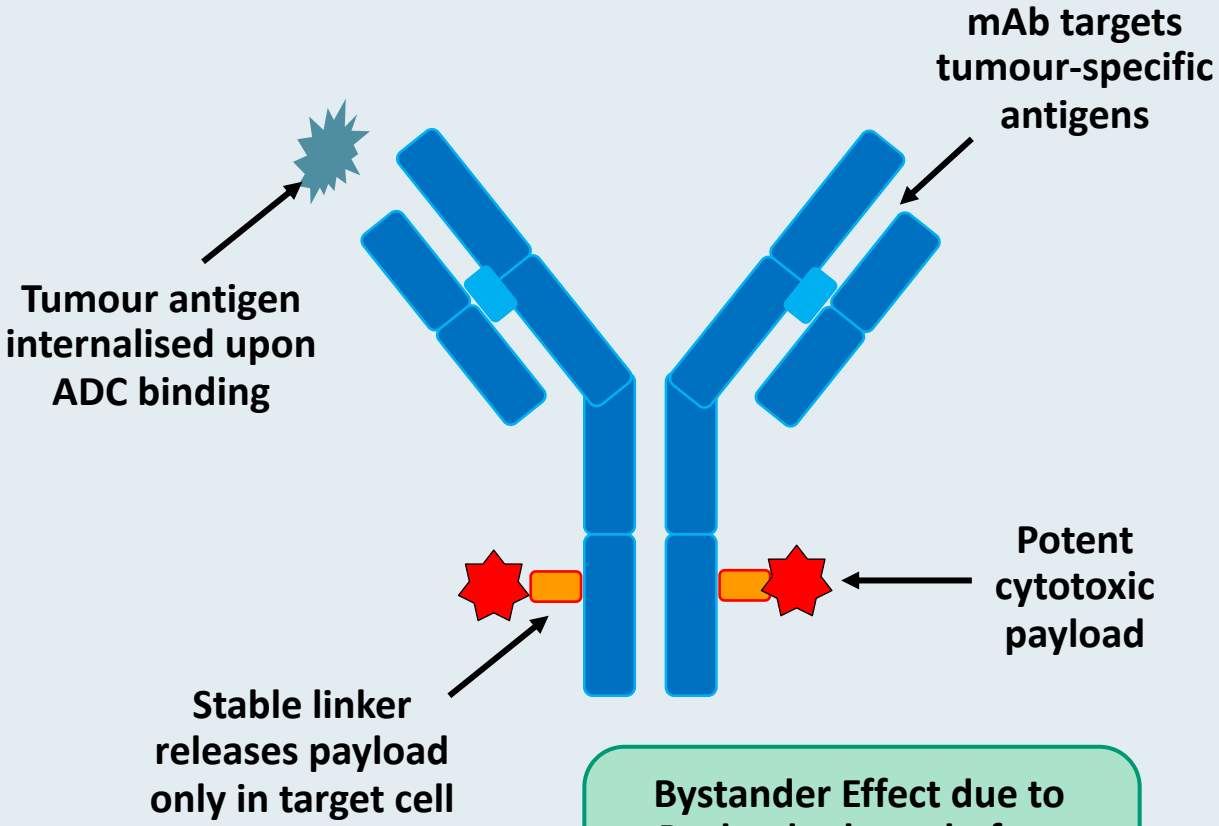
TO PRACTICE

HER2-Targeting Antibody-Drug Conjugates (ADCs)



Bystander Effect due to Payload release before internalisation or membrane permeability

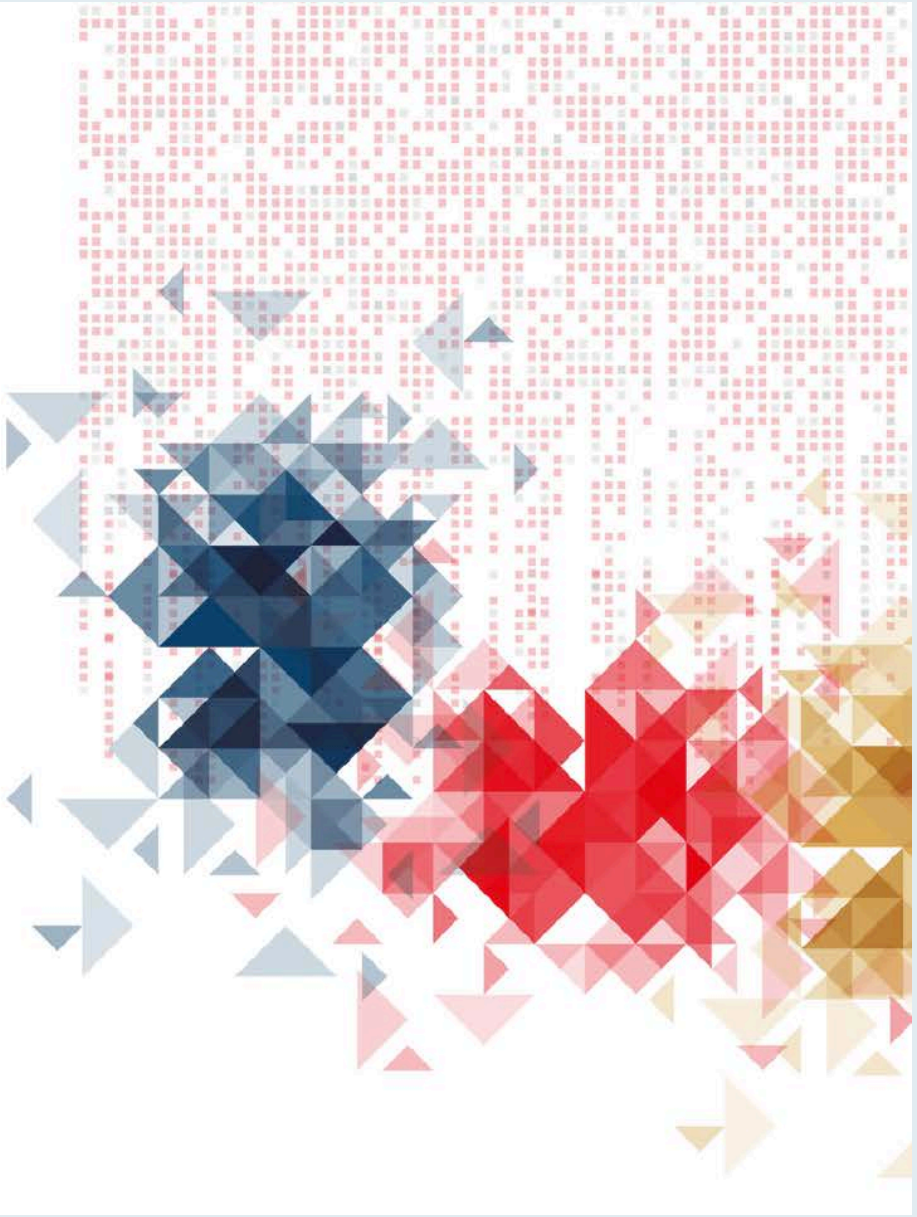
ADC Attributes	T-DM1[3-5]	T-DXd[1-4,a]
Payload MoA	Anti-microtubule	Topoisomerase I inhibitor
Drug-to-antibody ratio	~3.5:1	~8:1
Tumor-selective cleavable linker?	No	Yes
Evidence of bystander antitumor effect?	No	Yes

2021 ESMO congress

Trastuzumab Deruxtecan (T-DXd) vs Trastuzumab Emtansine (T-DM1) in Patients With HER2+ Metastatic Breast Cancer: Results of the Randomized, Phase 3 Study DESTINY-Breast03

Javier Cortés, MD[a], Sung-Bae Kim, Wei-Pang Chung, Seock-Ah Im, Yeon Hee Park, Roberto Hegg, Min-Hwan Kim, Ling-Ming Tseng, Vanessa Petry, Chi-Feng Chung, Hiroji Iwata, Erika Hamilton, Giuseppe Curigliano, Binghe Xu, Caleb Lee, Yali Liu, Jillian Cathcart, Emarjola Bako, Sunil Verma, Sara Hurvitz
On behalf of the DESTINY-Breast03 investigators

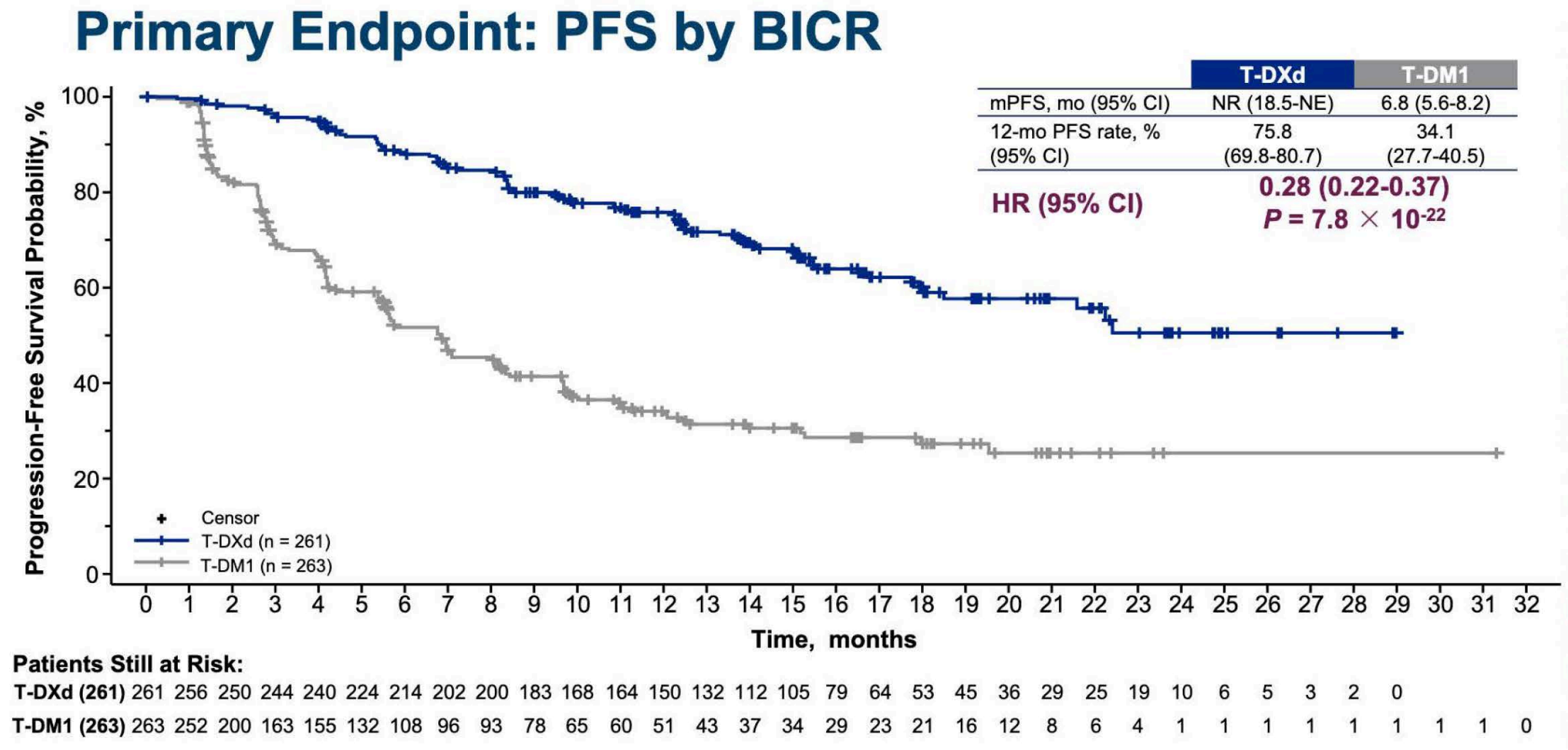
[a]Medical Oncology, International Breast Cancer Center (IBCC), Quironsalud Group, and Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; Universidad Europea de Madrid, Faculty of Biomedical and Health Sciences, Department of Medicine, Madrid, Spain.



Abstract LBA1

RTP RESEARCH TO PRACTICE

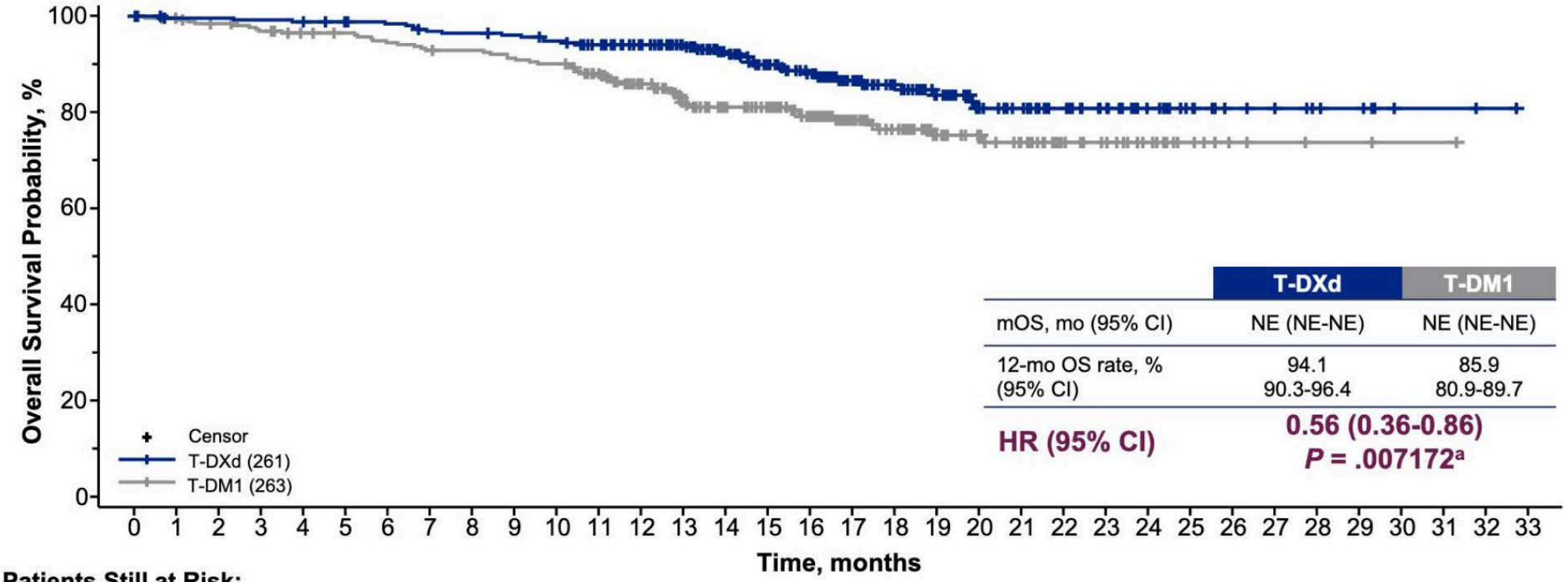
DESTINY-Breast03: Progression-Free Survival by Blinded Independent Central Review



Cortés J et al. ESMO 2021;Abstract LBA1.

DESTINY-Breast03: Overall Survival by BICR

Key Secondary Endpoint: OS



	T-DXd	T-DM1
mOS, mo (95% CI)	NE (NE-NE)	NE (NE-NE)
12-mo OS rate, % (95% CI)	94.1 90.3-96.4	85.9 80.9-89.7
HR (95% CI)	**0.56 (0.36-0.86)**	
	***P* = .007172[a]**	

Patients Still at Risk:

T-DXd (261)	261	256	256	255	254	251	249	244	243	241	237	230	218	202	180	158	133	108	86	71	56	50	42	33	24	18	11	10	7	6	2	2	1	0
T-DM1 (263)	263	258	253	248	243	241	236	232	231	227	224	210	188	165	151	140	120	91	75	58	52	44	32	27	18	11	5	4	3	3	1	1	0	

2021 ESMO congress

Early OS data with relatively few events (33 in the T-DXd arm, 53 in the T-DM1 arm)

[a]*P* = .007172, but does not cross pre-specified boundary of *P* < .000265

Cortés J et al. ESMO 2021;Abstract LBA1.

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DESTINY-Breast03: Drug-Related Treatment-Emergent Adverse Events in ≥20% of Patients

System Organ Class Preferred term, n (%)	T-DXd (n = 257)		T-DM1 (n = 261)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Blood and lymphatic system disorders				
Neutropenia[a]	110 (42.8)	49 (19.1)	29 (11.1)	8 (3.1)
Anemia[b]	78 (30.4)	15 (5.8)	37 (14.2)	11 (4.2)
Leukopenia[c]	77 (30.0)	17 (6.6)	20 (7.7)	1 (0.4)
Thrombocytopenia[d]	64 (24.9)	18 (7.0)	135 (51.7)	65 (24.9)
Gastrointestinal disorders				
Nausea	187 (72.8)	17 (6.6)	72 (27.6)	1 (0.4)
Vomiting	113 (44.0)	4 (1.6)	15 (5.7)	1 (0.4)
Diarrhea	61 (23.7)	1 (0.4)	10 (3.8)	1 (0.4)
Constipation	58 (22.6)	0	25 (9.6)	0
General disorders				
Fatigue[e]	115 (44.7)	13 (5.1)	77 (29.5)	2 (0.8)
Investigations				
AST increased	60 (23.3)	2 (0.8)	97 (37.2)	13 (5.0)
ALT increased	50 (19.5)	4 (1.6)	71 (27.2)	12 (4.6)
Metabolism and nutrition disorders				
Decreased appetite	67 (26.1)	3 (1.2)	33 (12.6)	0
Skin and subcutaneous tissue disorders				
Alopecia[f]	93 (36.2)	1 (0.4)	6 (2.3)	0

Cortés J et al. ESMO 2021;Abstract LBA1.

DESTINY-Breast03: Adverse Events of Special Interest

Adjudicated as drug-related ILD/pneumonitis[a], n (%)						
n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any Grade
T-DXd (n = 257)	7 (2.7)	18 (7.0)	2 (0.8)	0	0	27 (10.5)
T-DM1 (n = 261)	4 (1.5)	1 (0.4)	0	0	0	5 (1.9)

- There were no grade 4 or 5 adjudicated drug-related ILD/pneumonitis events observed with T-DXd

LVEF decrease, n (%)						
n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any Grade
T-DXd (n = 257)	1 (0.4)[b]	6 (2.3)[c]	0	0	0	7 (2.7)
T-DM1 (n = 261)	0	1 (0.4)[c]	0	0	0	1 (0.4)

- In the T-DXd arm, all reported adverse events of LVEF decrease were asymptomatic and no cases of cardiac failure occurred

Cortés J et al. ESMO 2021;Abstract LBA1.

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

Trastuzumab Deruxtecan (T-DXd) Versus Trastuzumab Emtansine (T-DM1) in Patients With HER2+ Metastatic Breast Cancer: Subgroup Analyses From the Randomized Phase 3 Study DESTINY-Breast03

Sara A. Hurvitz, MD[a], Sung-Bae Kim, Wei-Pang Chung, Seock-Ah Im, Yeon Hee Park, Roberto Hegg, Min-Hwan Kim, Ling-Ming Tseng, Vanessa Petry, Chi-Feng Chung, Hiroji Iwata, Erika Hamilton, Giuseppe Curigliano, Binghe Xu, Caleb Lee, Yali Liu, Jillian Cathcart, Emarjola Bako, Sunil Verma, Javier Cortes

On behalf of the DESTINY-Breast03 investigators

[a]Department of Medicine, David Geffen School of Medicine, University of California, Los Angeles, Jonsson Comprehensive Cancer Center, Los Angeles, CA USA

SABCS 2021;Abstract GS3-01.

DESTINY-Breast03: Progression-Free Survival (PFS) and Objective Response Rate (ORR) with T-DXd versus T-DM1 by Subgroup

	PFS by BICR, HR (95% CI)	Absolute ORR difference T-DXd, T-DM1 (95% CI)
All patients (N = 524)	0.28 (0.22-0.37)	45.5 (37.6-53.4)
Hormone receptor		
Positive (n = 272)	0.32 (0.22-0.46)	47.3 (36.1-58.4)
Negative (n = 248)	0.30 (0.20-0.44)	43.2 (31.5-55.0)
Prior pertuzumab		
Yes (n = 320)	0.31 (0.22-0.43)	46.7 (36.5-56.9)
No (n = 204)	0.30 (0.19-0.47)	43.6 (30.5-56.7)
Prior lines of therapy		
0-1 (n = 258)	0.33 (0.23-0.48)	39.3 (27.3-51.2)
≥2 (n = 266)	0.28 (0.19-0.41)	51.6 (40.9-62.4)
Visceral disease		
Yes (n = 384)	0.28 (0.21-0.38)	48.3 (39.1-57.6)
No (n = 140)	0.32 (0.17-0.58)	39.1 (23.6-54.6)
Brain metastases at baseline		
Yes (n = 82)	0.25 (0.13-0.45)	46.9 (25.6-68.3)
No (n = 442)	0.30 (0.22-0.40)	45.5 (36.9-54.1)

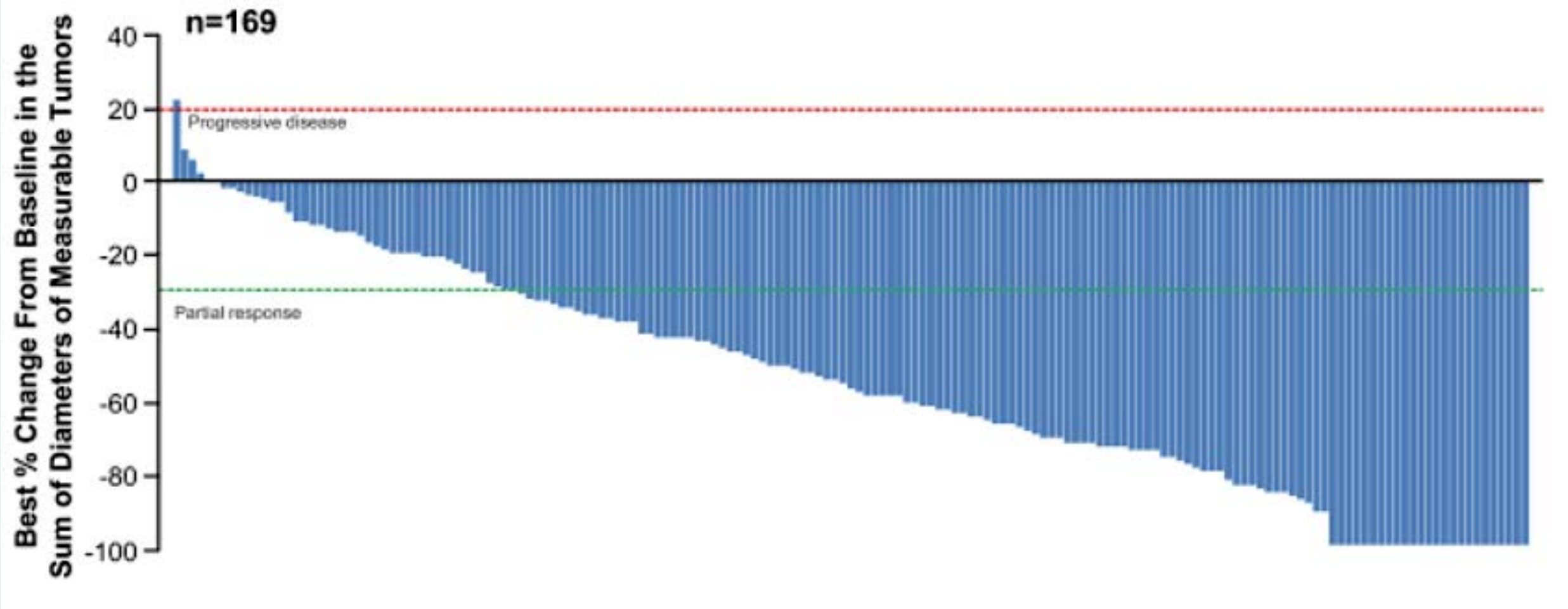
Hurvitz S et al. SABCS 2021;Abstract GS3-01.

Updated Results from DESTINY-Breast01, a Phase 2 Trial of Trastuzumab Deruxtecan (T-DXd) in HER2-Positive Metastatic Breast Cancer

Modi S et al.

SABCS 2020;Abstract PD3-06.

DESTINY-Breast01: Best Percent Change in Tumor Size from Baseline



Modi S et al. SABCS 2020;Abstract PD3-06.

RTP RESEARCH TO PRACTICE

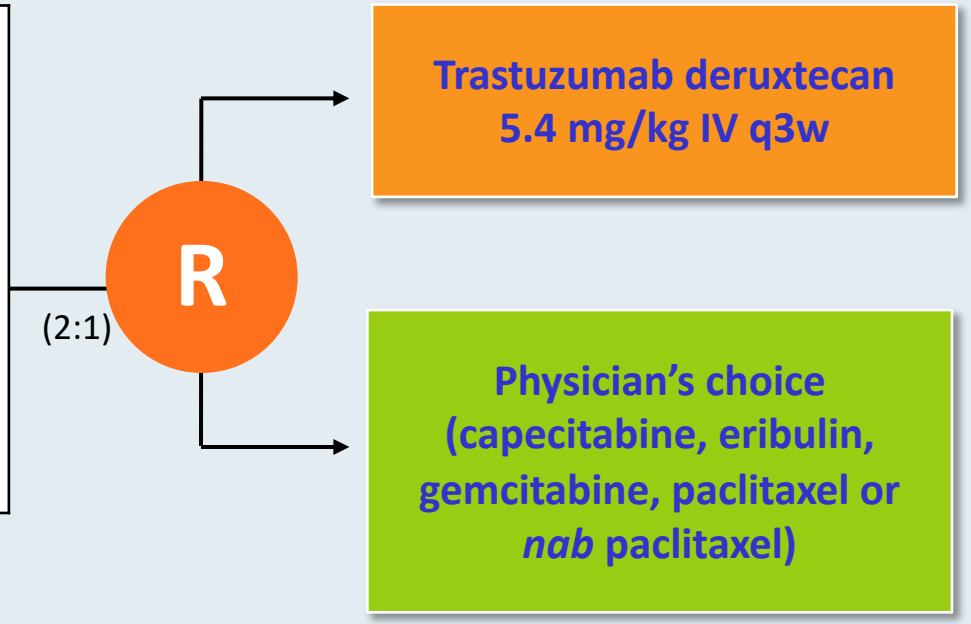
DESTINY-Breast04: Phase III Trial Schema

Target Accrual: 557

Unresectable and/or metastatic HER2-low BC
(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

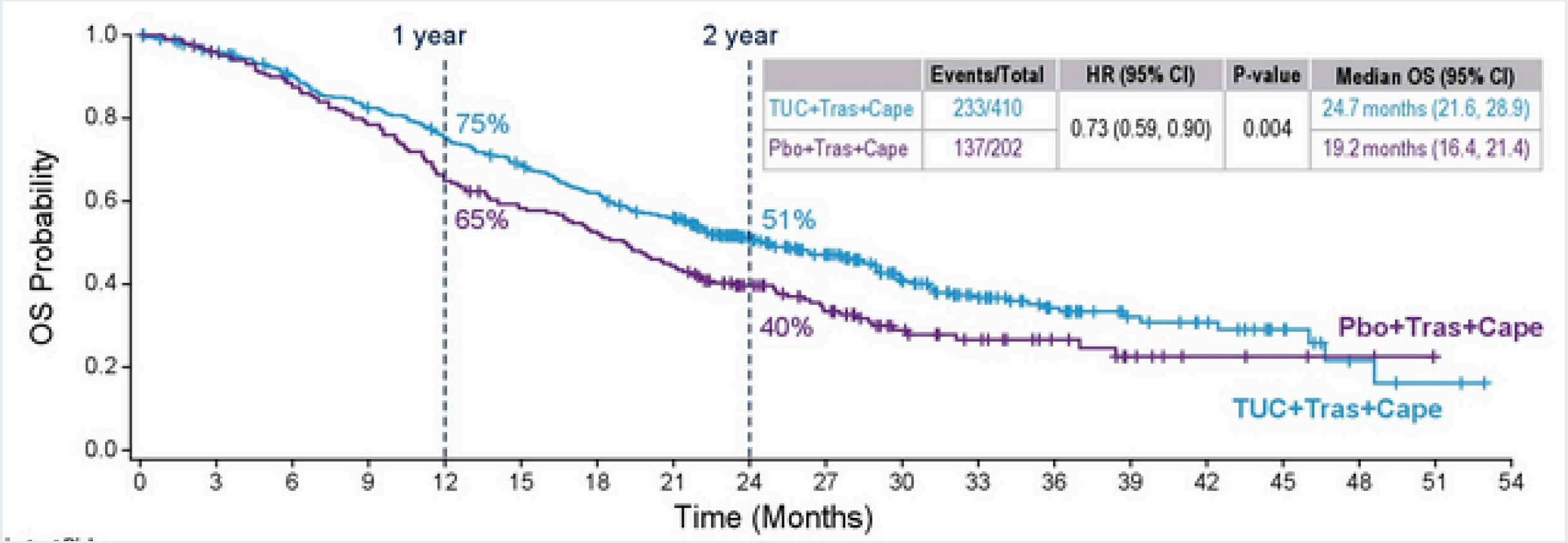
www.clinicaltrials.gov; Accessed February 2022.

Updated Results of Tucatinib versus Placebo Added to Trastuzumab and Capecitabine for Patients with Pretreated HER2-Positive Metastatic Breast Cancer with and without Brain Metastases (HER2CLIMB)

Curigliano G et al.

ASCO 2021;Abstract 1043.

HER2CLIMB: Overall Survival (OS)



	Events/Total	HR (95% CI)	P-value	Median OS (95% CI)
TUC+Tras+Cape	233/410	0.73 (0.59, 0.90)	0.004	24.7 months (21.6, 28.9)
Pbo+Tras+Cape	137/202			19.2 months (16.4, 21.4)

Curigliano G et al. ASCO 2021;Abstract 1043.

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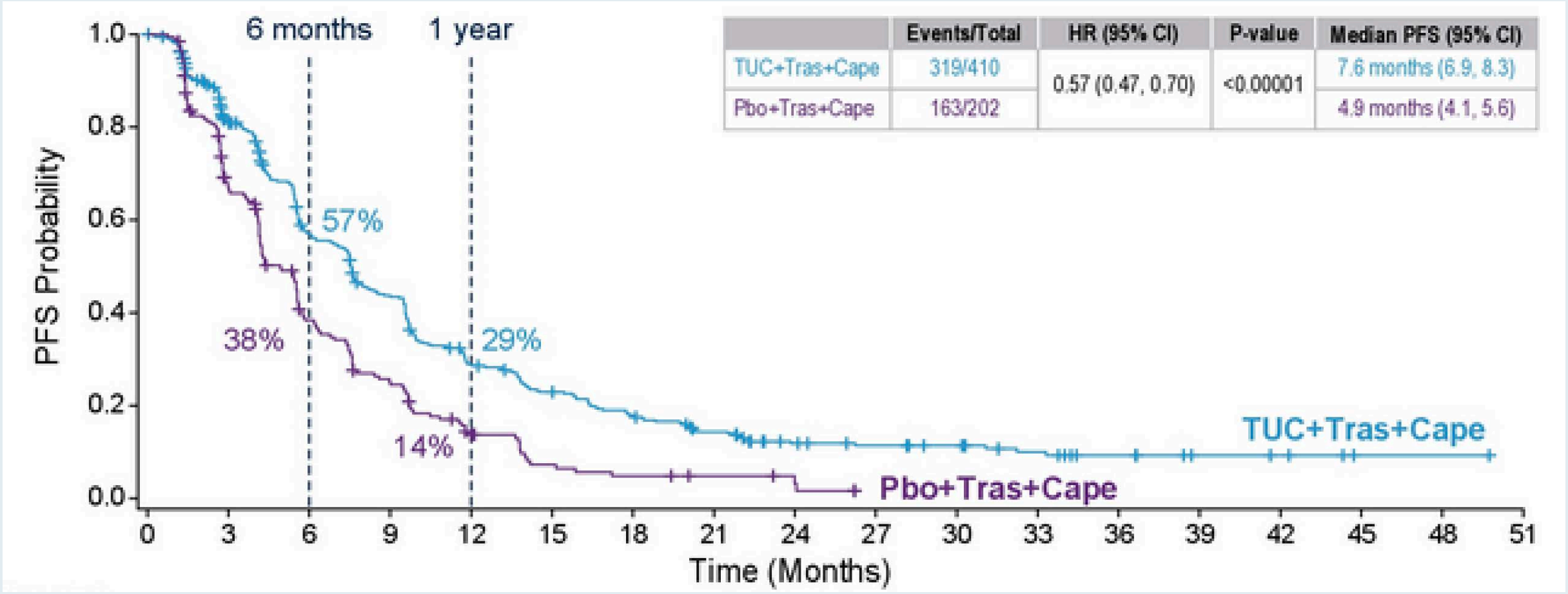
HER2CLIMB: Progression-Free Survival (PFS)

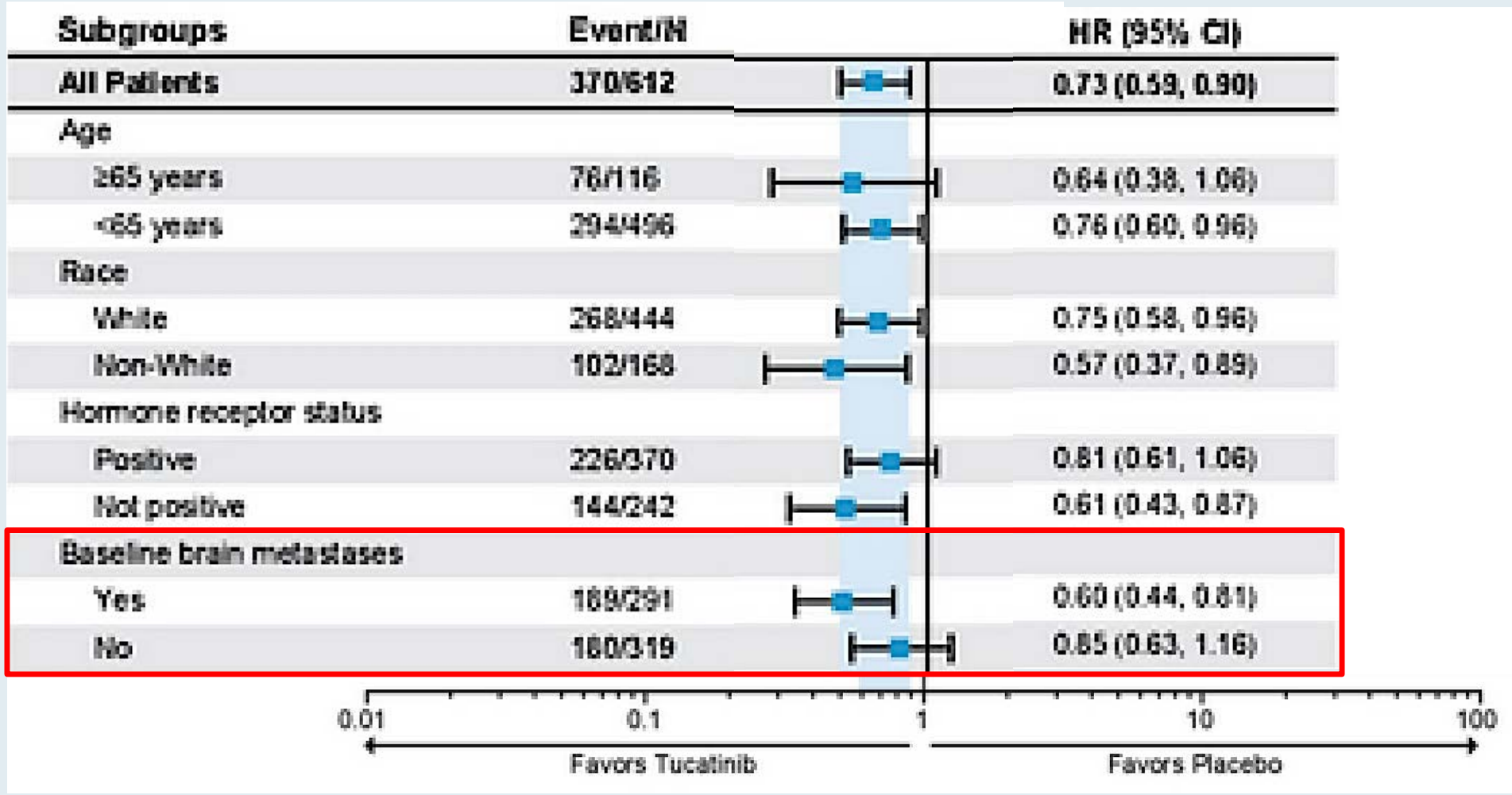


	Events/Total	HR (95% CI)	P-value	Median PFS (95% CI)
TUC+Tras+Cape	319/410	0.57 (0.47, 0.70)	<0.00001	7.6 months (6.9, 8.3)
Pbo+Tras+Cape	163/202			4.9 months (4.1, 5.6)

Curigliano G et al. ASCO 2021;Abstract 1043.

RTP RESEARCH TO PRACTICE

HER2CLIMB: Overall Survival for Patients with Baseline Brain Metastases



Curigliano G et al. ASCO 2021;Abstract 1043.

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HER2CLIMB: Safety Outcomes

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

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

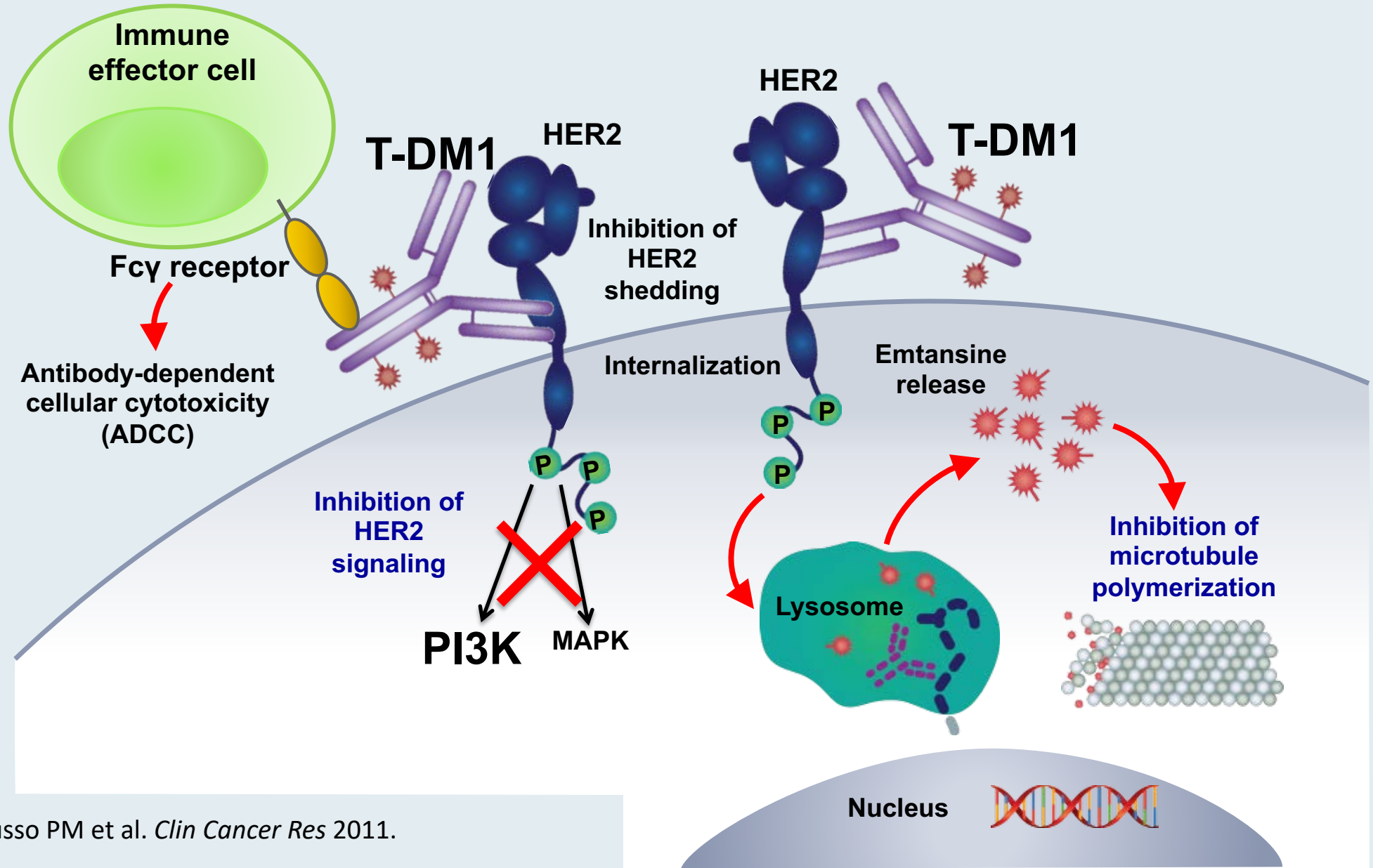
FDA-Approved Agents for Localized HER2-Positive Breast Cancer

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

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

Choong GM et al. *CA Cancer J Clin* 2020;70:355-374.

Trastuzumab Emtansine (T-DM1): Mechanisms of Action



Adapted from LoRusso PM et al. *Clin Cancer Res* 2011.

ARTICLE IN PRESS

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Ann Oncol 2021;[Online ahead of print]

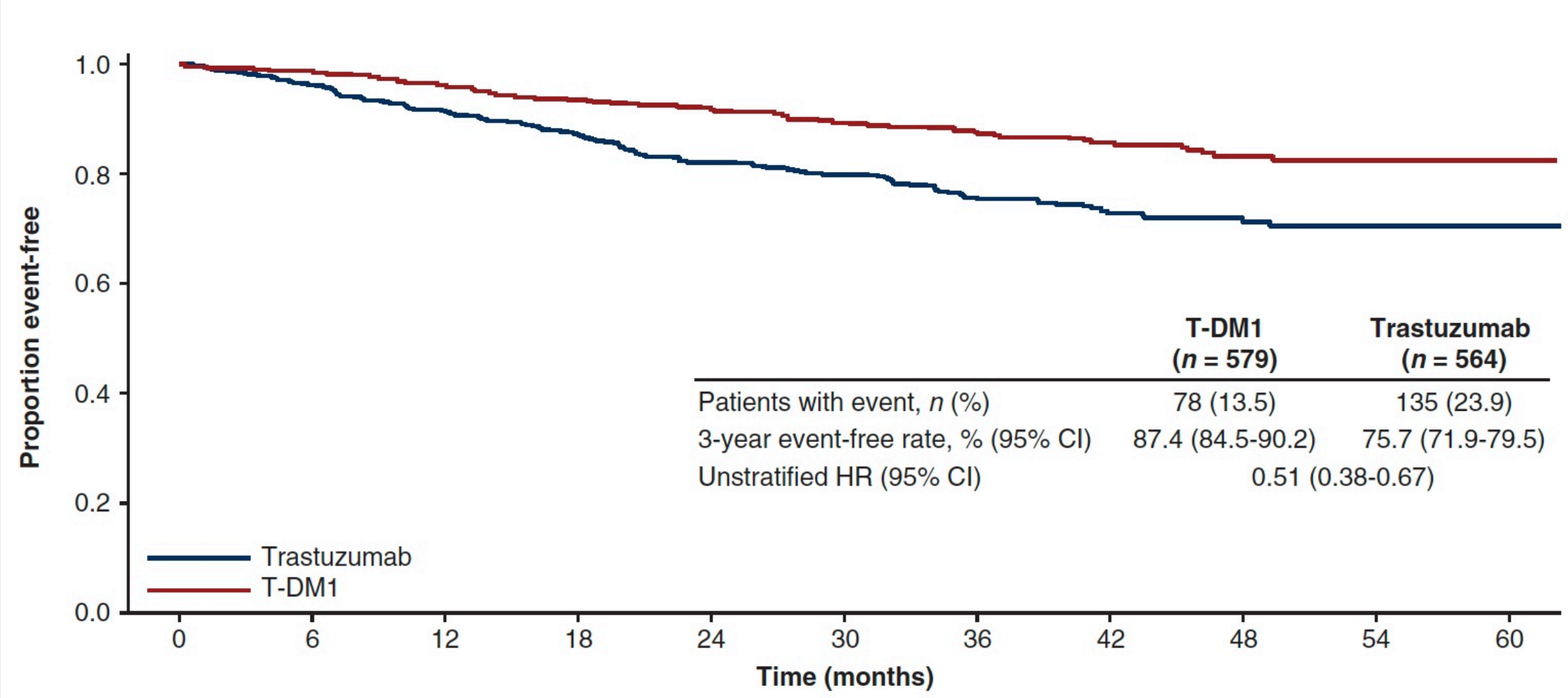
ANNALS OF ONCOLOGY driving innovation in oncology

ORIGINAL ARTICLE

Adjuvant T-DM1 versus trastuzumab in patients with residual invasive disease after neoadjuvant therapy for HER2-positive breast cancer: subgroup analyses from KATHERINE

E. P. Mamounas[1,2*], M. Untch[3], M. S. Mano[4], C.-S. Huang[5], C. E. Geyer Jr[1,6], G. von Minckwitz[7], N. Wolmark[1,8], X. Pivot[9], S. Kuemmel[10,11], M. P. DiGiovanna[12], B. Kaufman[13], G. Kunz[7,14], A. K. Conlin[1,15], J. C. Alcedo[16], T. Kuehn[17], I. Wapnir[1,18], A. Fontana[19], J. Hackmann[7,20], J. Polikoff[1,21], M. Saghatchian[22], A. Brufsky[1,23], Y. Yang[24], M. Zimovjanova[25], T. Boulet[26], H. Liu[27], D. Tesarowski[28], L. H. Lam[28], C. Song[28], M. Smitt[28,29] & S. Loibl[7,30]

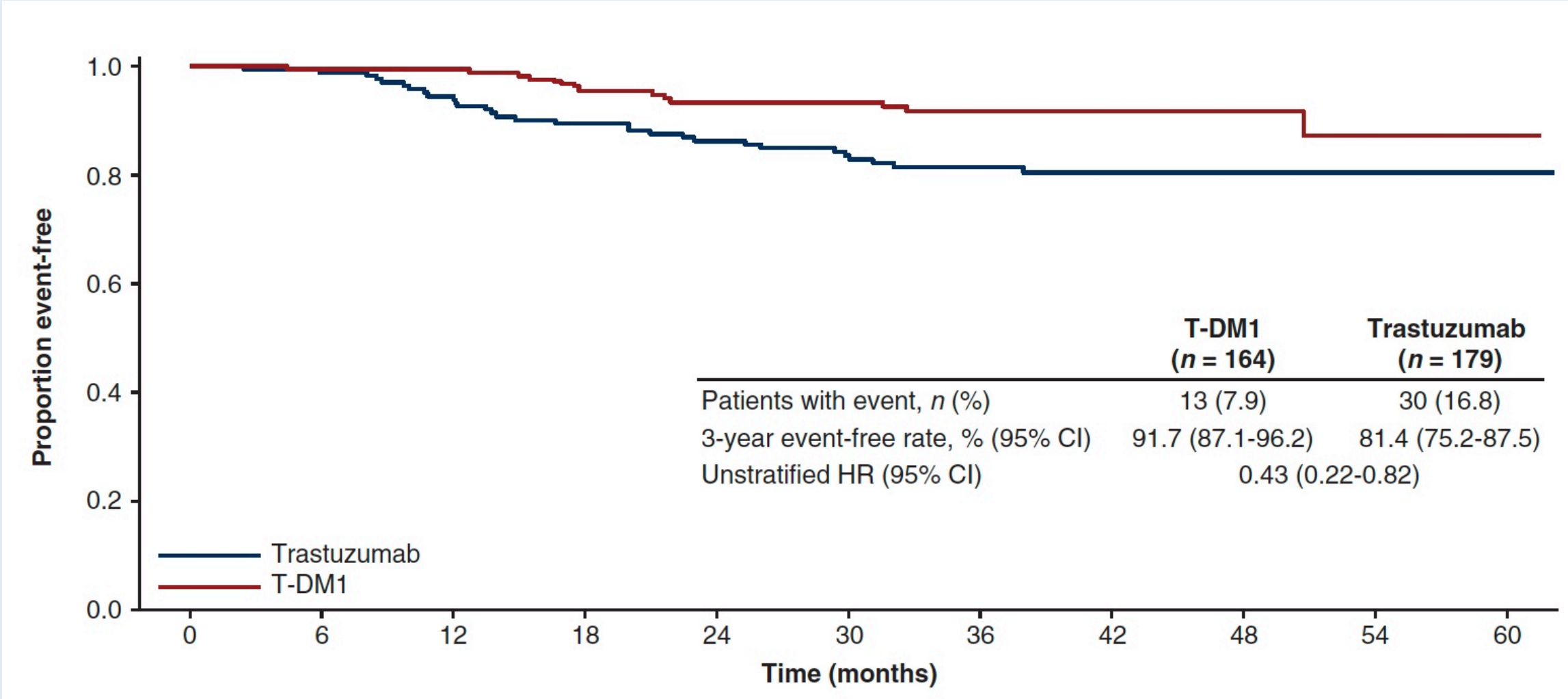
Time to First Invasive Disease-Free Survival Event for Patients Who Received Anthracycline-Based Neoadjuvant Therapy



	T-DM1 (*n* = 579)	Trastuzumab (*n* = 564)
Patients with event, *n* (%)	78 (13.5)	135 (23.9)
3-year event-free rate, % (95% CI)	87.4 (84.5-90.2)	75.7 (71.9-79.5)
Unstratified HR (95% CI)	0.51 (0.38-0.67)	

Mamounas EP et al. *Ann Oncol* 2021;[Online ahead of print].

Time to First Invasive Disease-Free Survival Event for Patients Who Received Non-Anthracycline-Based Neoadjuvant Therapy



Mamounas EP et al. *Ann Oncol* 2021;[Online ahead of print].

RTP RESEARCH TO PRACTICE

KATHERINE: Central Nervous System Recurrence Events

	T-DM1 (n = 743)	Trastuzumab (n = 743)
Patients with CNS recurrence	45 (6.1%)	40 (5.4%)
At first IDFS event[a]	44 (5.9%)	32 (4.3%)
After first IDFS event[b]	1 (0.1%)	8 (1.1%)
Patients with CNS as only event[c]	36 (4.8%)	21 (2.8%)
Median time to CNS recurrence	17.5 months	11.9 months

T-DM1 = trastuzumab emtansine; CNS = central nervous system; IDFS = invasive disease-free survival
CNS recurrence [a]within or [b]after 61 days of first IDFS event or at [c]any time

Mamounas EP et al. *Ann Oncol* 2021;32(8):1005-14.

original reports

Adjuvant Trastuzumab Emtansine Versus Paclitaxel in Combination With Trastuzumab for Stage I HER2-Positive Breast Cancer (ATEMPT): A Randomized Clinical Trial

Sara M. Tolaney, MD, MPH[1,2]; Nabihah Tayob, PhD[1]; Chau Dang, MD[3]; Denise A. Yardley, MD[4]; Steven J. Isakoff, MD, PhD[5]; Vicente Valero, MD[6]; Meredith Faggen, MD[1]; Therese Mulvey, MD[5]; Ron Bose, MD, PhD[7]; Jiani Hu, MSc[1]; Douglas Weckstein, MD[1]; Antonio C. Wolff, MD[8]; Katherine Reeder-Hayes, MD, MBA, MSc[9]; Hope S. Rugo, MD[10]; Bhuvaneswari Ramaswamy, MD[11]; Dan Zuckerman, MD[12]; Lowell Hart, MD[13]; Vijayakrishna K. Gadi, MD, PhD[14]; Michael Constantine, MD[1]; Kit Cheng, MD[15]; Frederick Briccetti, MD[1]; Bryan Schneider, MD[16]; Audrey Merrill Garrett, MD[17]; Kelly Marcom, MD[18]; Kathy Albain, MD[19]; Patricia DeFusco, MD[20]; Nadine Tung, MD[2,21]; Blair Ardman, MD[22]; Rita Nanda, MD[23]; Rachel C. Jankowitz, MD[24]; Mothaffar Rimawi, MD[25]; Vandana Abramson, MD[26]; Paula R. Pohlmann, MD, PhD, MSc[27]; Catherine Van Poznak, MD[28]; Andres Forero-Torres, MD[29]; Minetta Liu, MD[30]; Kathryn Ruddy, MD[30]; Yue Zheng, MSc[1]; Shoshana M. Rosenberg, ScD, MPH[1,2]; Richard D. Gelber, PhD[1,2]; Lorenzo Trippa, PhD[1,2]; William Barry, PhD[1]; Michelle DeMeo, BS[1]; Harold Burstein, MD, PhD[1,2]; Ann Partridge, MD, MPH[1,2]; Eric P. Winer, MD[1,2]; and Ian Krop, MD, PhD[1,2]

J Clin Oncol 2021;[Online ahead of print].

ATEMPT: Invasive Disease-Free Survival (IDFS) and Recurrence-Free Interval (RFI)

Outcome	T-DM1 (n = 383)	TH (n = 114)
Three-year IDFS	97.8%	93.4%
Three-year RFI	99.2%	94.3%

Tolaney SM et al. *J Clin Oncol* 2021;[Online ahead of print].

ATEMPT: Clinically Relevant Toxicity

Clinically Relevant Toxicity	T-DM1 (n = 383)	TH (n = 114)
Grade ≥3 nonhematologic toxicity	9%	11%
Grade ≥2 neurotoxicity	11%	23%
Grade ≥4 hematologic toxicity	1%	0%
Febrile neutropenia	0%	2%
Any toxicity requiring dose delay	28%	26%
Any toxicity requiring early discontinuation	17%	6%
Total	46%	47%

Tolaney SM et al. *J Clin Oncol* 2021;[Online ahead of print].

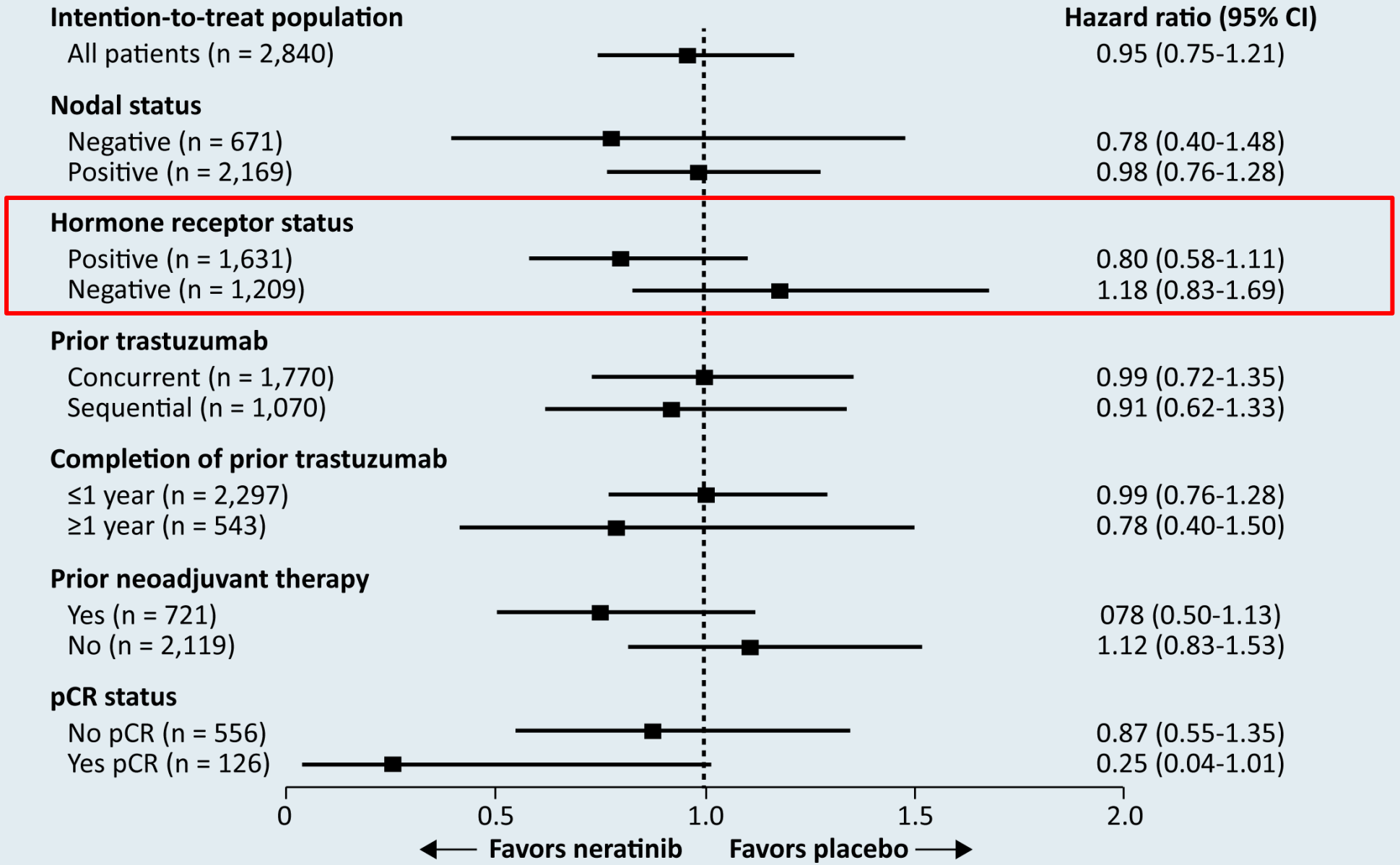
RTP RESEARCH TO PRACTICE

Continued Efficacy of Neratinib in Patients with HER2-Positive Early-Stage Breast Cancer: Final Overall Survival Analysis from the Randomized Phase 3 ExteNET Trial

Holmes FA et al.

SABCS 2020;Abstract PD3-03.

ExteNET: Final Overall Survival Analysis



Holmes FA et al. SABCS 2020;Abstract PD3-03.

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%
Prior neoadjuvant therapy (n = 1,334)				
No (n = 980)	3	6	0.7%	1.5%
Yes (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%

Holmes FA et al. SABCS 2020;Abstract PD3-03.

Agenda

Module 1: HER2-Positive

Module 2: ER/PR-Positive, HER2-Negative

Module 3: Triple-Negative

RTP
RESEARCH
TO PRACTICE

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

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

NCCN Guidelines. Breast Cancer. Version 6.2021. August 16, 2021.

N Engl J Med 2021;385:2336-47

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

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

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

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

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

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

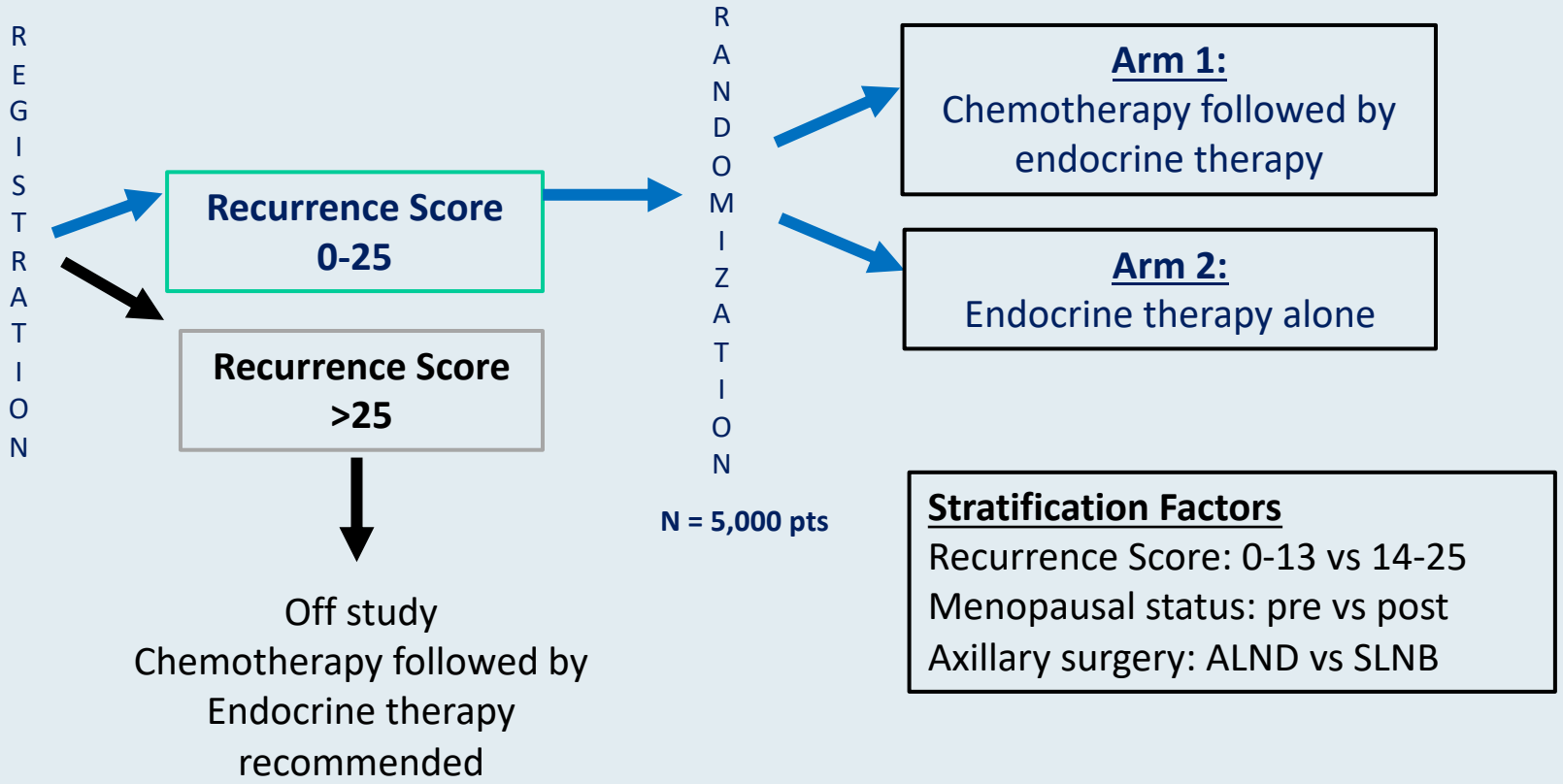
On Behalf of the RxPonder Investigators

SABCS 2021;Abstract GS2-07.

RxPONDER Trial Schema

Key Entry Criteria

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



Stratification Factors

Recurrence Score: 0-13 vs 14-25
Menopausal status: pre vs post
Axillary surgery: ALND vs SLNB

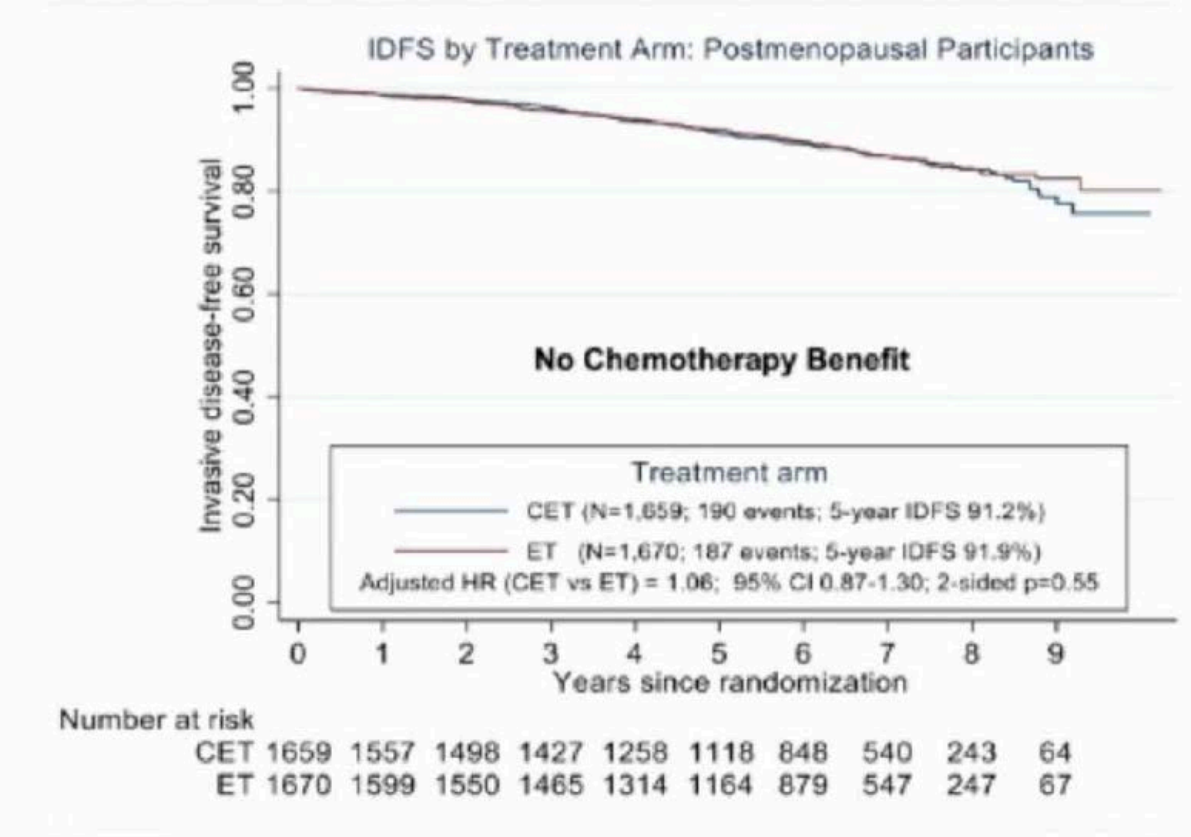
* After randomization of 2,493 pts, the protocol was amended to exclude enrollment of pts with pN1mic as only nodal disease.
† Approved chemotherapy regimens included TC, FAC (or FEC), AC/T (or EC/T), FAC/T (or FEC/T). AC alone or CMF not allowed.
SLNB = sentinel lymph node biopsy; ALND = axillary lymph node dissection

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

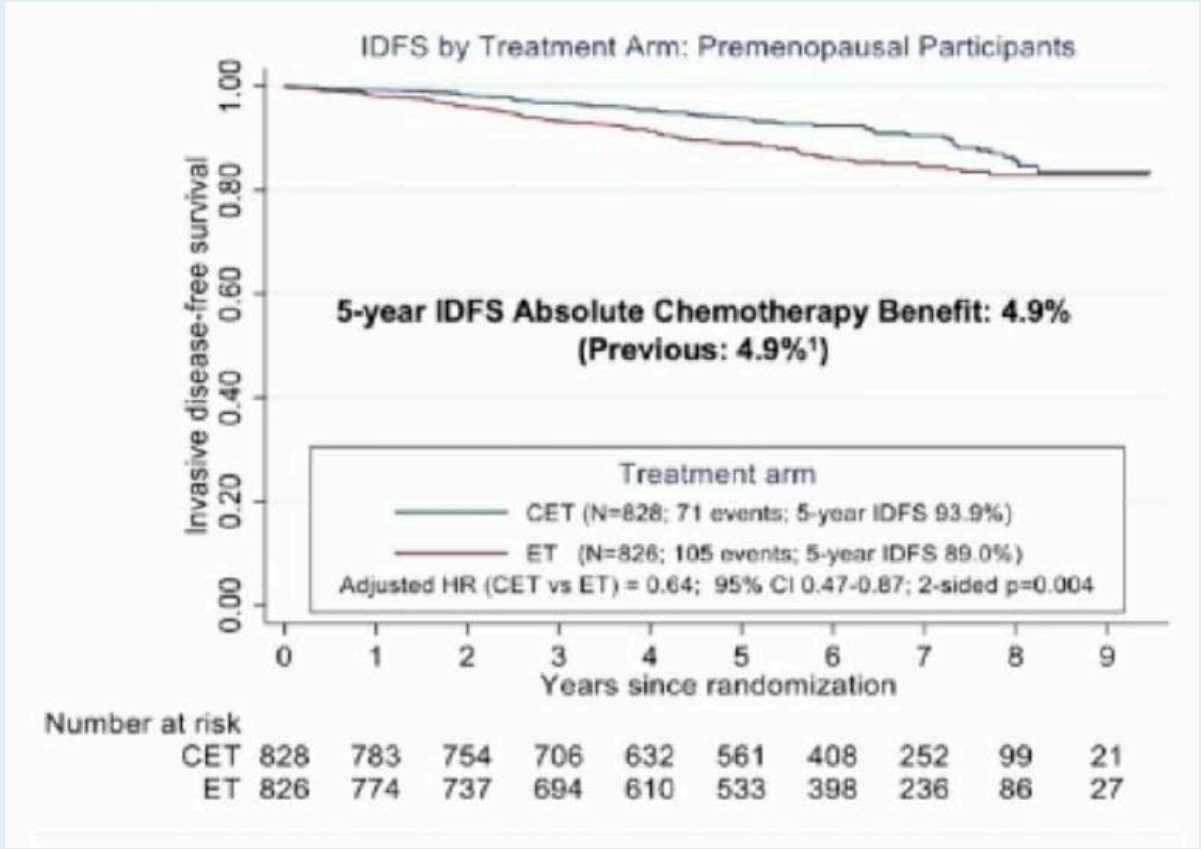
RTP RESEARCH TO PRACTICE

RxPONDER Updated Analysis: IDFS Stratified by Menopausal Status

Postmenopausal



Premenopausal



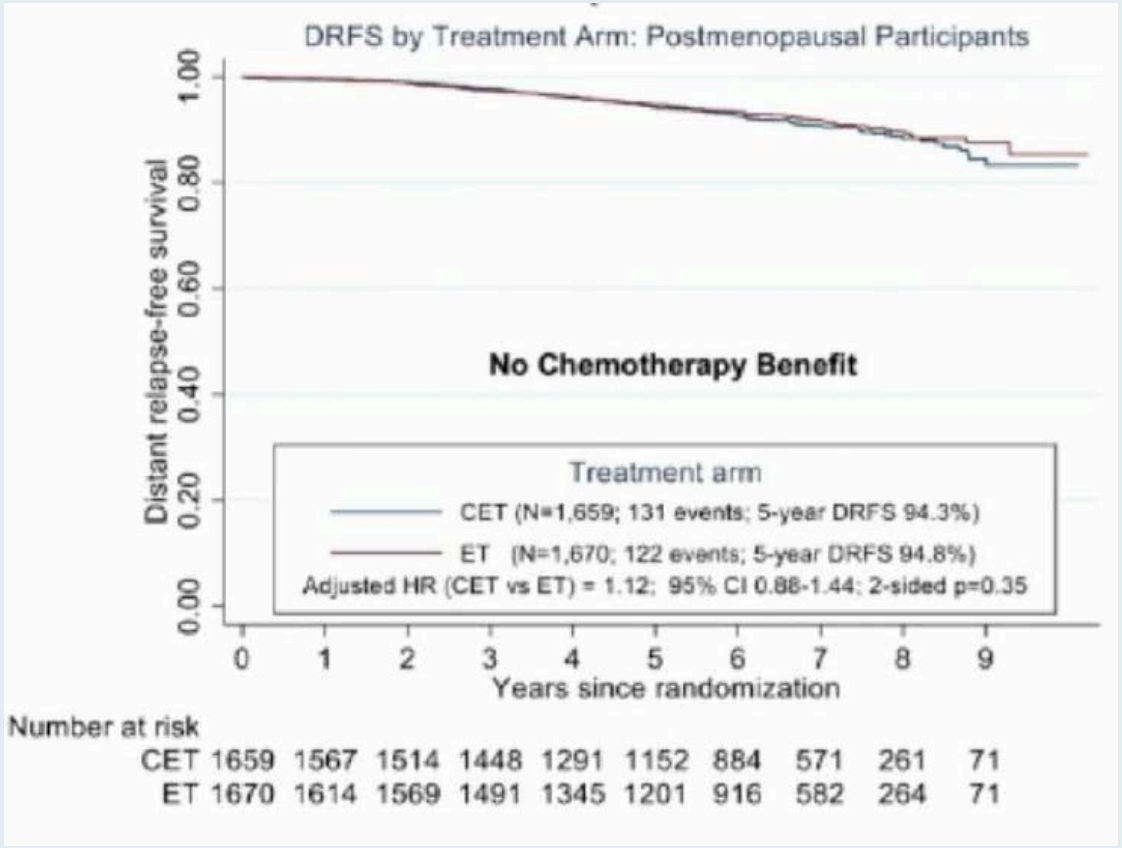
IDFS = invasive disease-free survival

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

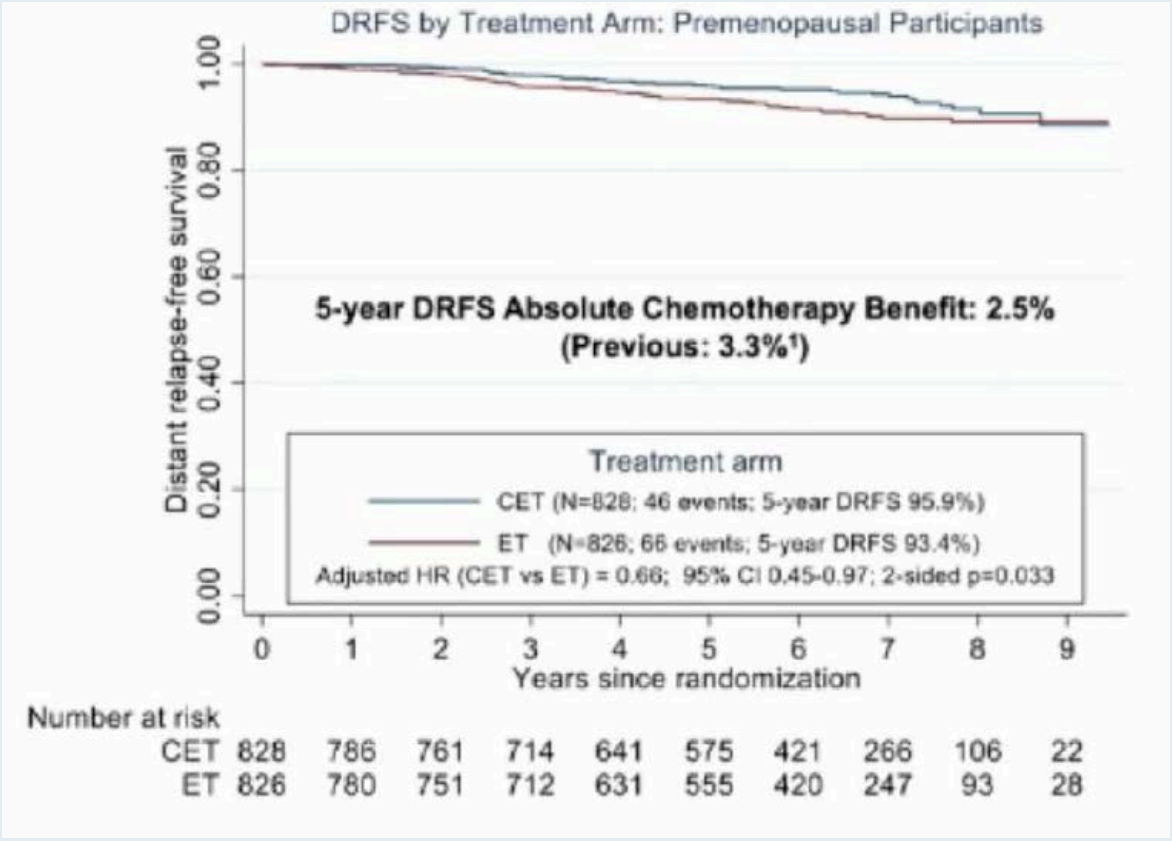
RTP RESEARCH TO PRACTICE

RxPONDER Updated Analysis: DRFS Stratified by Menopausal Status

Postmenopausal



Premenopausal



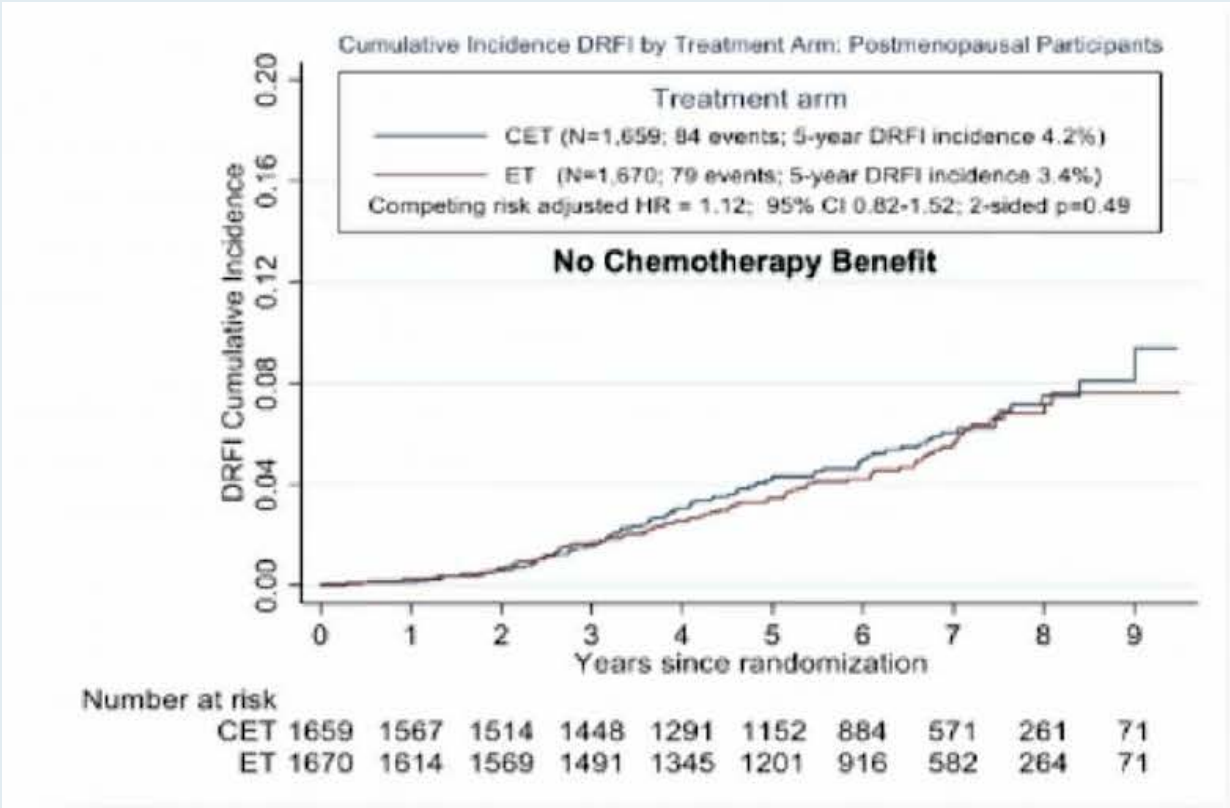
DRFS = distant recurrence-free survival

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

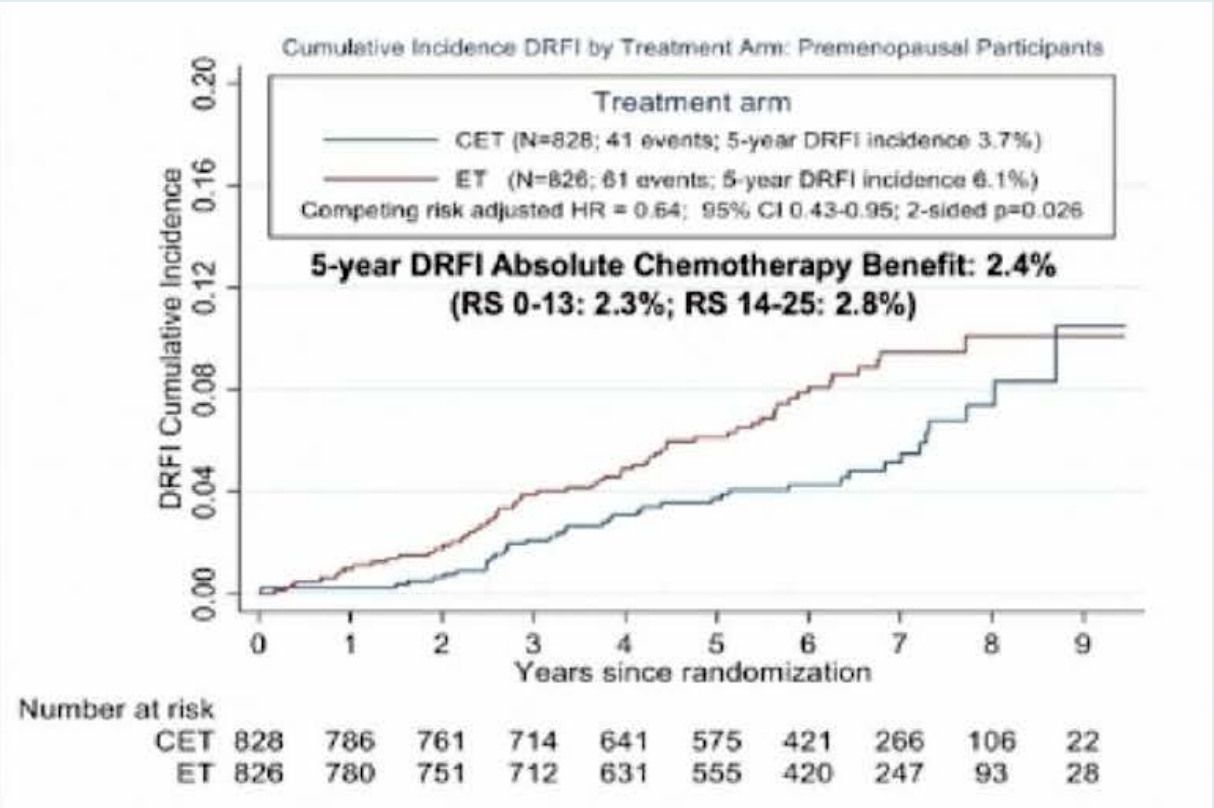
RTP RESEARCH TO PRACTICE

RxPONDER New Analysis: DRFI Stratified by Menopausal Status

Postmenopausal



Premenopausal



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

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

DRFI = distant recurrence-free interval

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

RTP RESEARCH TO PRACTICE

FDA Approves Adjuvant Abemaciclib with Endocrine Therapy for Localized Breast Cancer

Press Release – October 12, 2021

"The Food and Drug Administration approved abemaciclib with endocrine therapy (tamoxifen or an aromatase inhibitor) for adjuvant treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive, early breast cancer at high risk of recurrence and a Ki-67 score ≥20%, as determined by an FDA approved test. This is the first CDK 4/6 inhibitor approved for adjuvant treatment of breast cancer.

FDA also approved the Ki-67 IHC MIB-1 pharmDx assay as a companion diagnostic for selecting patients for this indication.

Efficacy was evaluated in monarchE (NCT03155997), a randomized (1:1), open-label, two-cohort multicenter trial that included adult women and men with HR-positive, HER2-negative, node-positive, resected, early breast cancer with clinical and pathological features consistent with a high risk of disease recurrence."

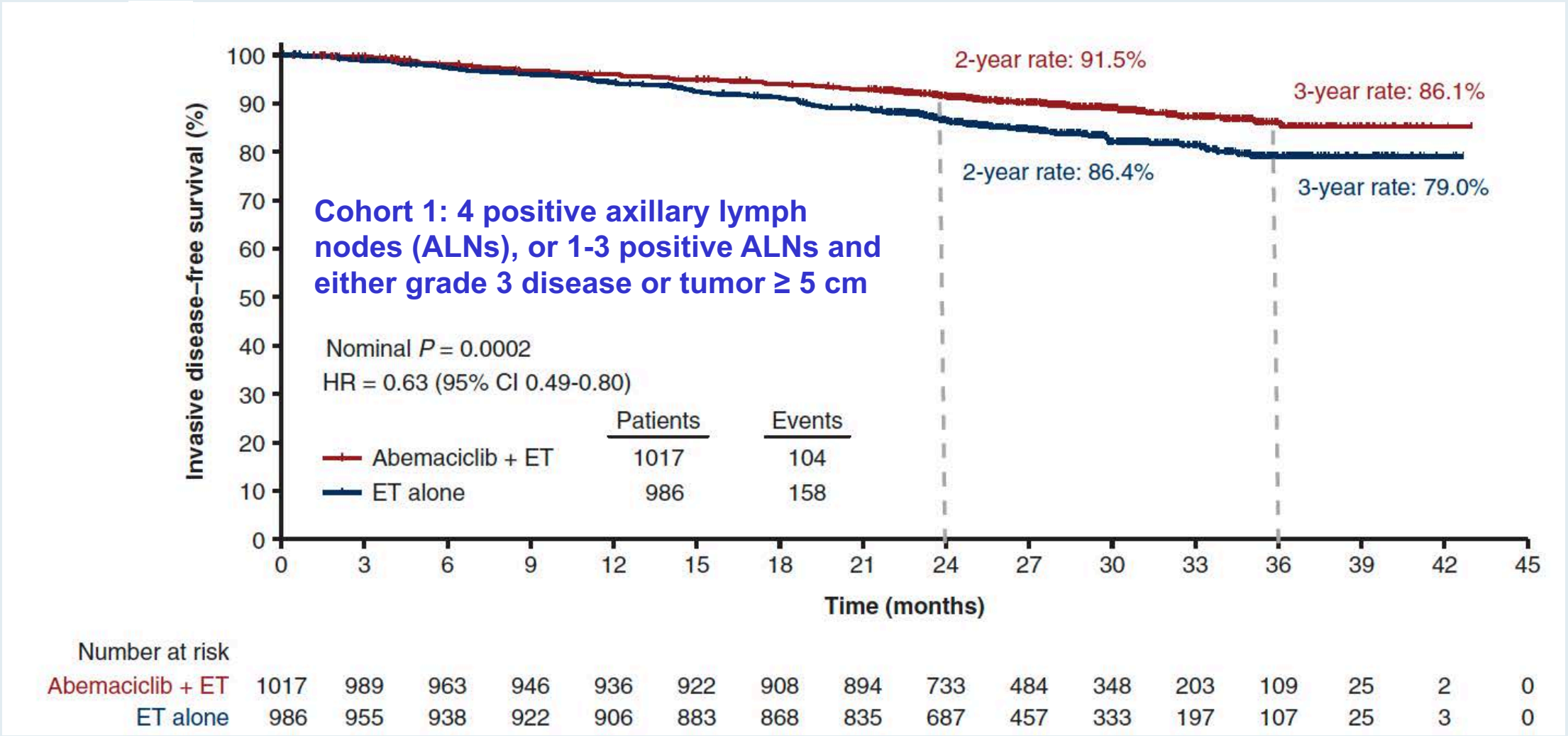
https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-abemaciclib-endocrine-therapy-early-breast-cancer

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).

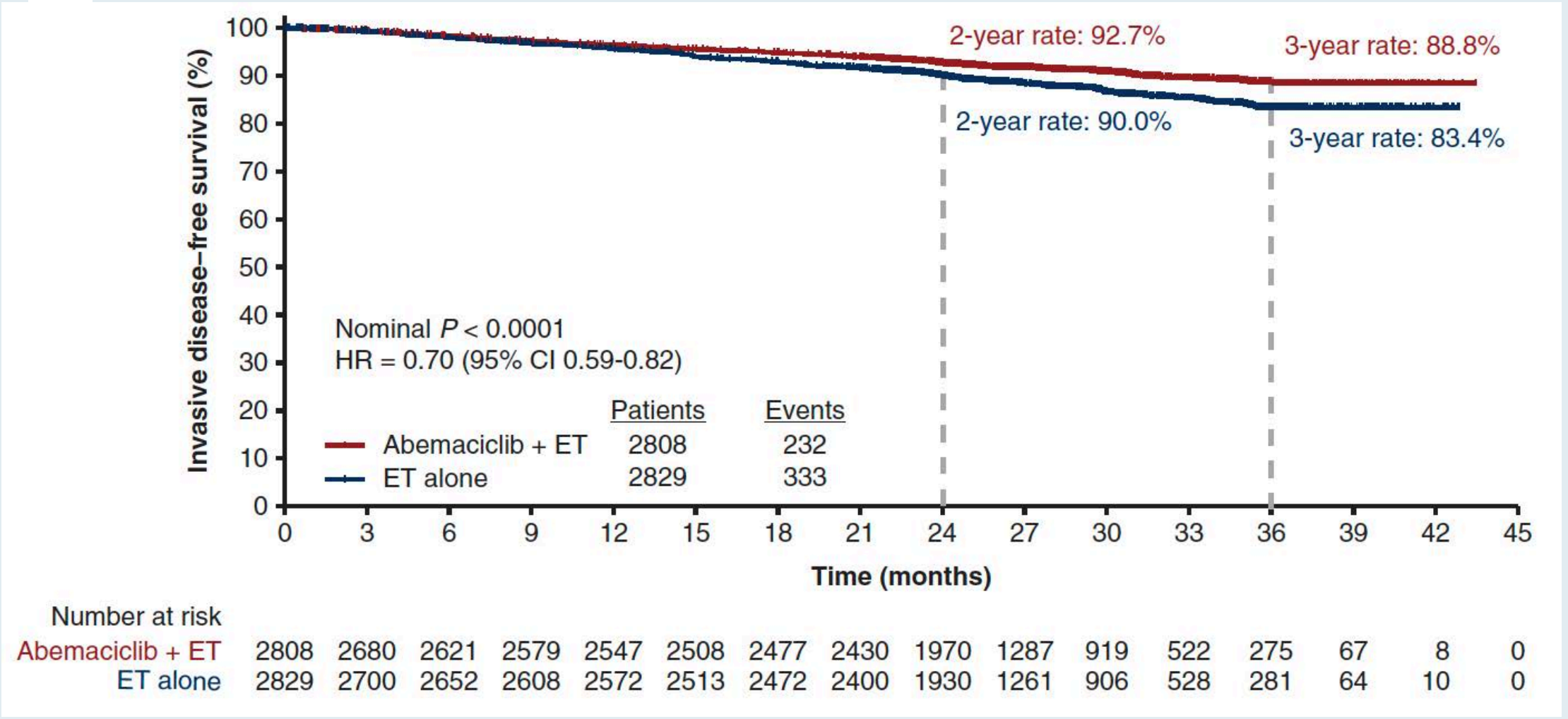
Harbeck N et al. *Ann Oncol* 2021;[Online ahead of print].
https://www.asco.org/practice-patients/guidelines/breast-cancer#/11081

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



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

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



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

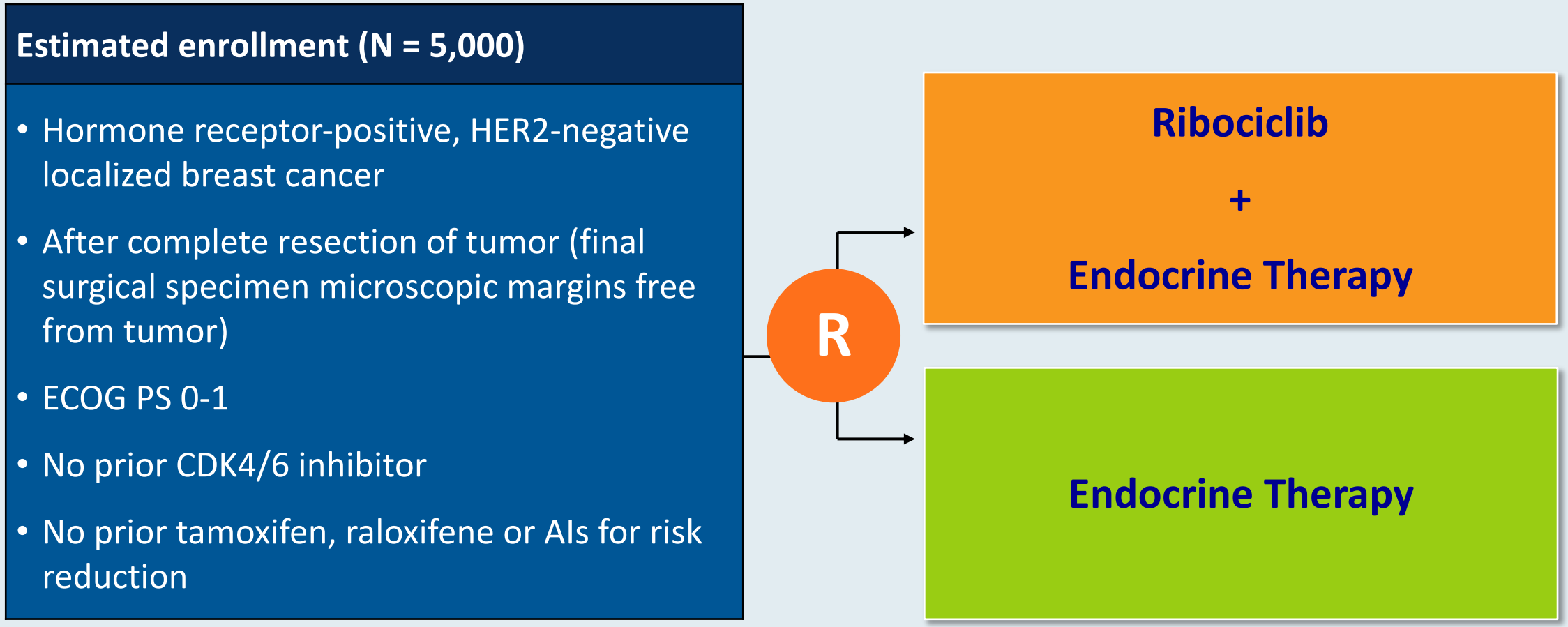
monarchE: Select Adverse Events (AEs)

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

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

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

NATALEE: Ongoing Adjuvant Phase III Trial Design



Primary endpoint: Invasive disease-free survival

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

www.clinicaltrials.gov. NCT03701334. Accessed August 2021.

Key Trials Exploring CDK4/6 Inhibitors in Localized Breast Cancer

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

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

RTP RESEARCH TO PRACTICE

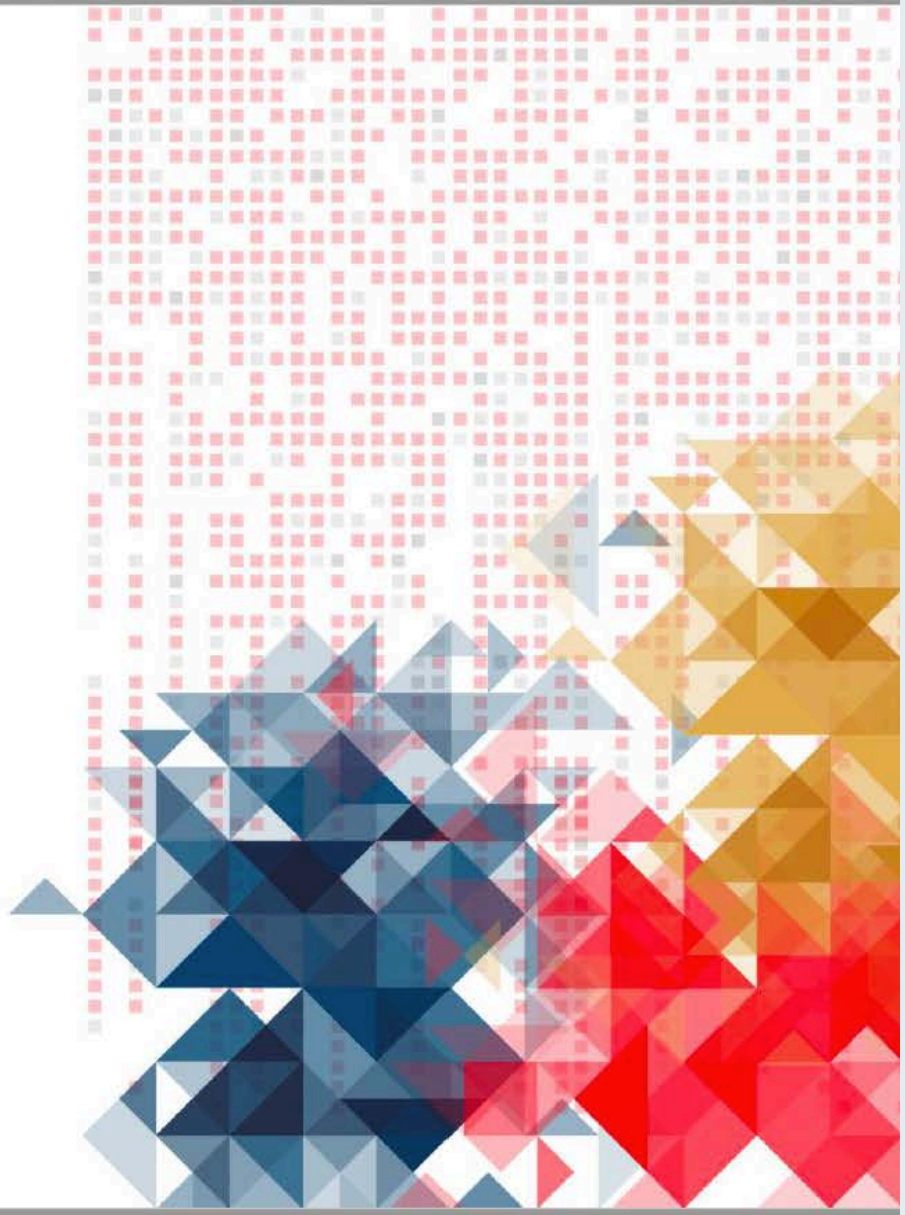
2021 ESMO congress

Abstract LBA17_PR

Overall Survival Results From the Phase III MONALEESA-2 Trial of Postmenopausal Patients With HR+/HER2− Advanced Breast Cancer Treated With Endocrine Therapy ± Ribociclib

Gabriel N. Hortobagyi,[1] Salomon M. Stemmer,[2] Howard A. Burris,[3] Yoon Sim Yap,[4] Gabe Sonke,[5] Lowell Hart,[6] Mario Campone,[7] Katarina Petrakova,[8] Eric P. Winer,[9] Wolfgang Janni,[10] Pierfranco Conte,[11] David A. Cameron,[12] Fabrice André,[13] Carlos Arteaga,[14] Juan Pablo Zarate,[15] Arunava Chakravartty,[15] Tetiana Taran,[16] Fabienne Le Gac,[16] Paolo Serra,[16] Joyce O'Shaughnessy[17]

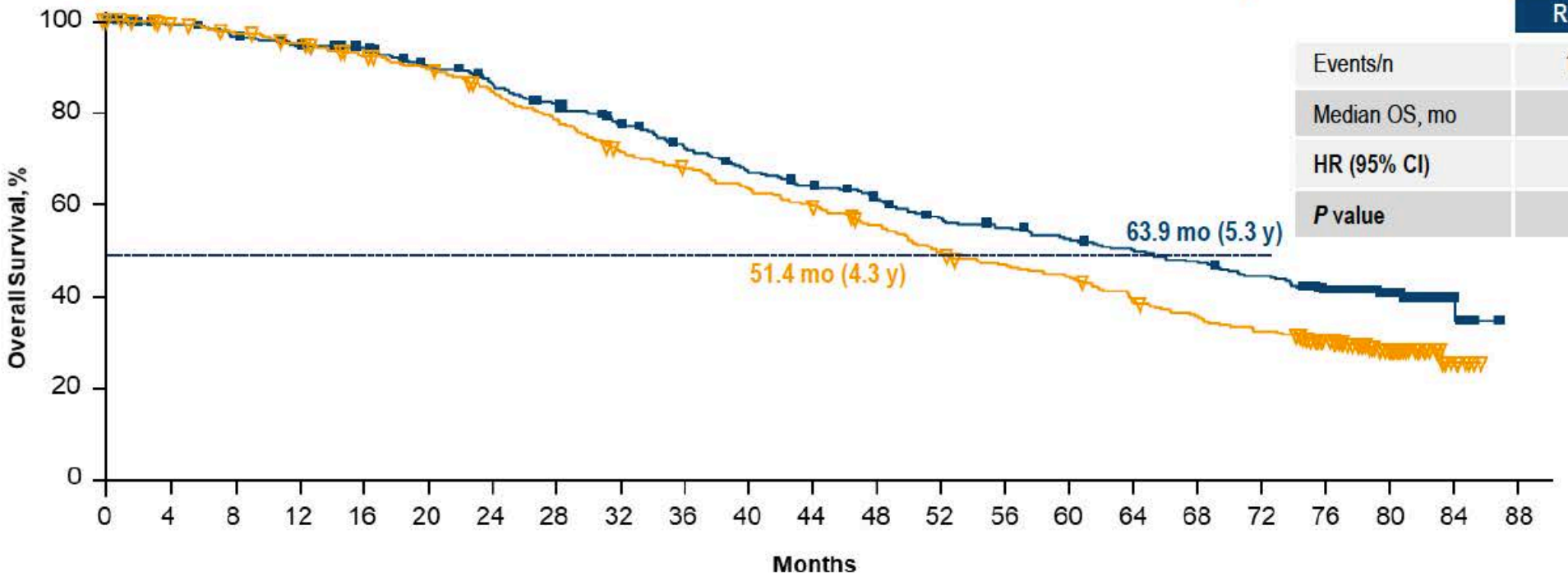
[1]Department of Breast Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; [2]Institute of Oncology, Davidoff Center, Rabin Medical Center, Tel Aviv University, Tel Aviv, Israel; [3]Sarah Cannon Research Institute, Nashville, TN; [4]Department of Medical Oncology, National Cancer Centre Singapore, Singapore; [5]Medical Oncology, Netherlands Cancer Institute and BOOG Study Center, Amsterdam, the Netherlands; [6]Florida Cancer Specialists, Sarah Cannon Research Institute, Fort Myers, FL, USA; [7]Department of Medical Oncology, Institut de Cancérologie de l'Ouest/René Gauducheau, Saint-Herblain, France; [8]Department of Comprehensive Cancer Care, Masaryk Memorial Cancer Institute, Brno, Czech Republic; [9]Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA; [10]Department of Gynecology, University of Ulm, Ulm, Germany; [11]Department of Surgery, Oncology and Gastroenterology, University of Padua and Division of Medical Oncology 2, Istituto Oncologico Veneto, IRCCS, Padua, Italy; [12]Edinburgh Cancer Research Centre, Institute of Genomics and Cancer, University of Edinburgh, Edinburgh, UK; [13]Department of Medical Oncology, Institut Gustave Roussy, Medical School, Université Paris Saclay, Villejuif, France; [14] UT Southwestern Simmons Comprehensive Cancer Center, UT Southwestern Medical Center, Dallas, TX; [15]Novartis Pharmaceuticals Corporation, East Hanover, NJ; [16]Novartis Pharma AG, Basel, Switzerland; [17]Baylor University Medical Center, Texas Oncology, US ONCOLOGY, Dallas, TX



RTP RESEARCH TO PRACTICE

MONALEESA-2: Overall Survival (OS)

Improvement in median OS was 12.5 months with ribociclib plus letrozole



	RIB + LET	PBO + LET
Events/n	181/334	219/334
Median OS, mo	63.9	51.4
HR (95% CI)	0.76 (0.63-0.93)	
P value	.004	

No. at risk

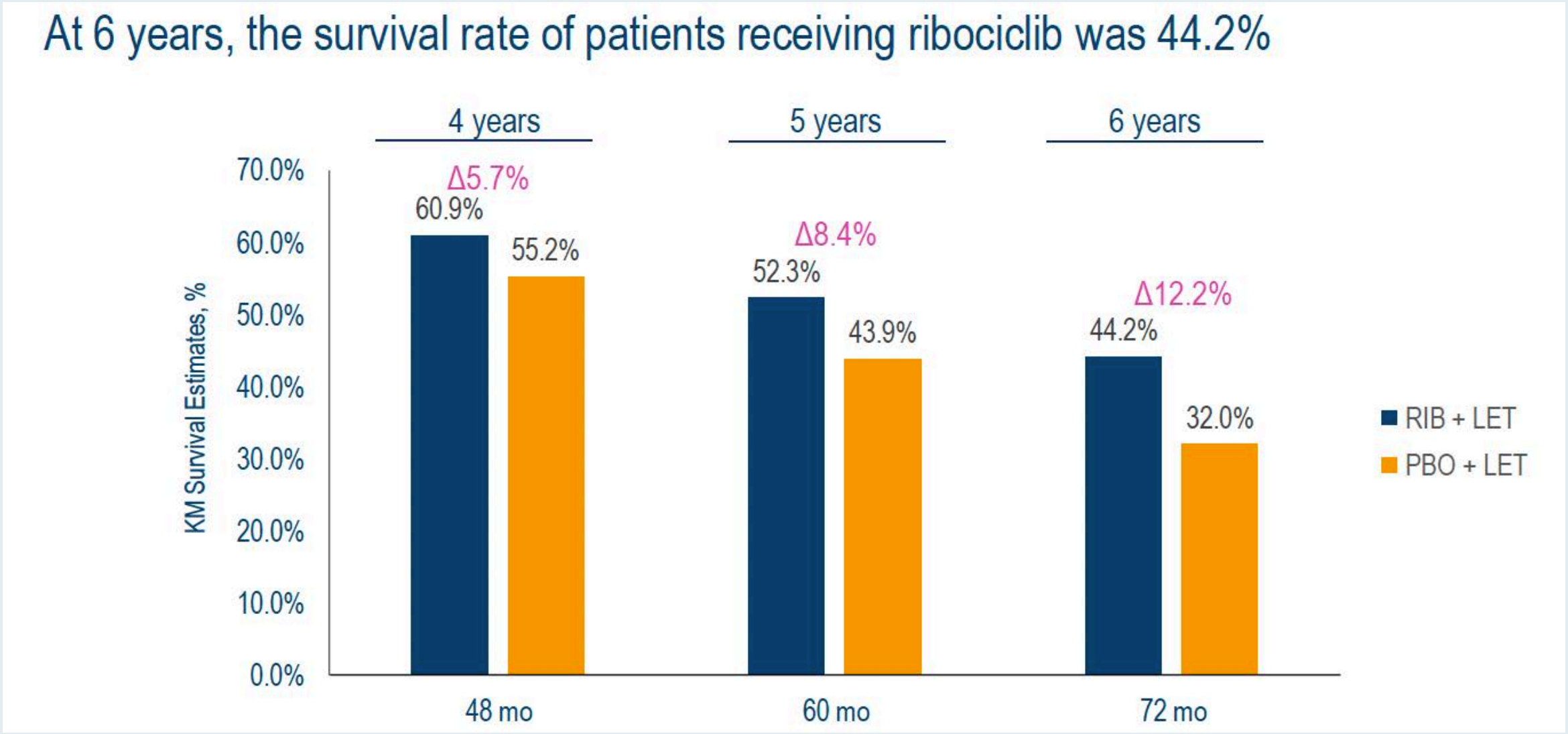
RIB + LET	334	323	315	305	300	284	270	253	237	220	202	191	180	165	158	150	142	135	125	101	48	8	0
PBO + LET	334	326	316	306	293	283	265	244	222	209	195	183	167	149	139	131	114	104	94	73	38	6	0

The P value of .004 crossed the prespecified boundary to claim superior efficacy

Hortobagyi GN et al. ESMO 2021;Abstract LBA17_PR.

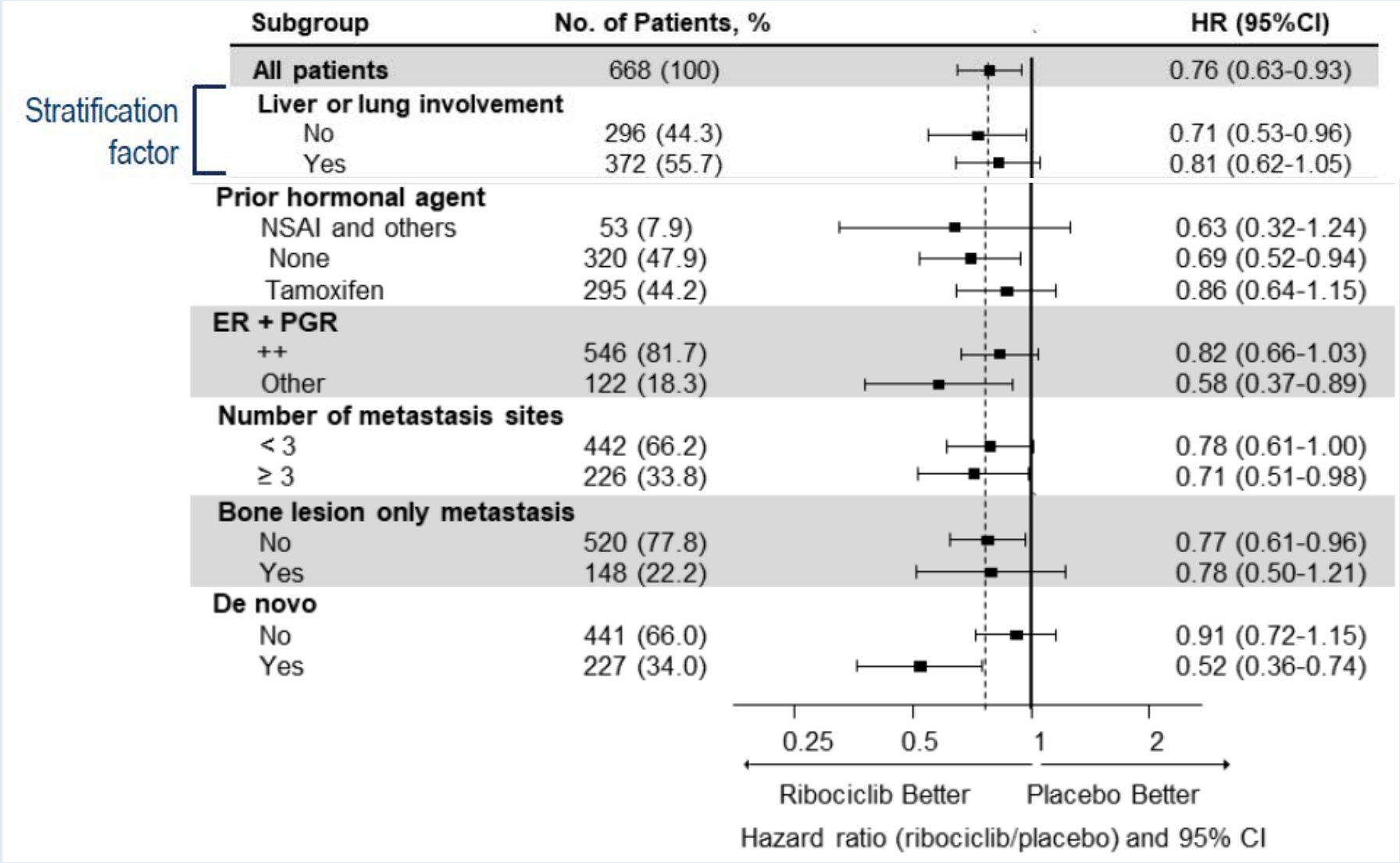
RTP RESEARCH TO PRACTICE

MONALEESA-2: The OS Benefit Increased Over Time



Hortobagyi GN et al. ESMO 2021;Abstract LBA17_PR.

MONALEESA-2: OS Benefit Across Key Subgroups



Hortobagyi GN et al. ESMO 2021;Abstract LBA17_PR.

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

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

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

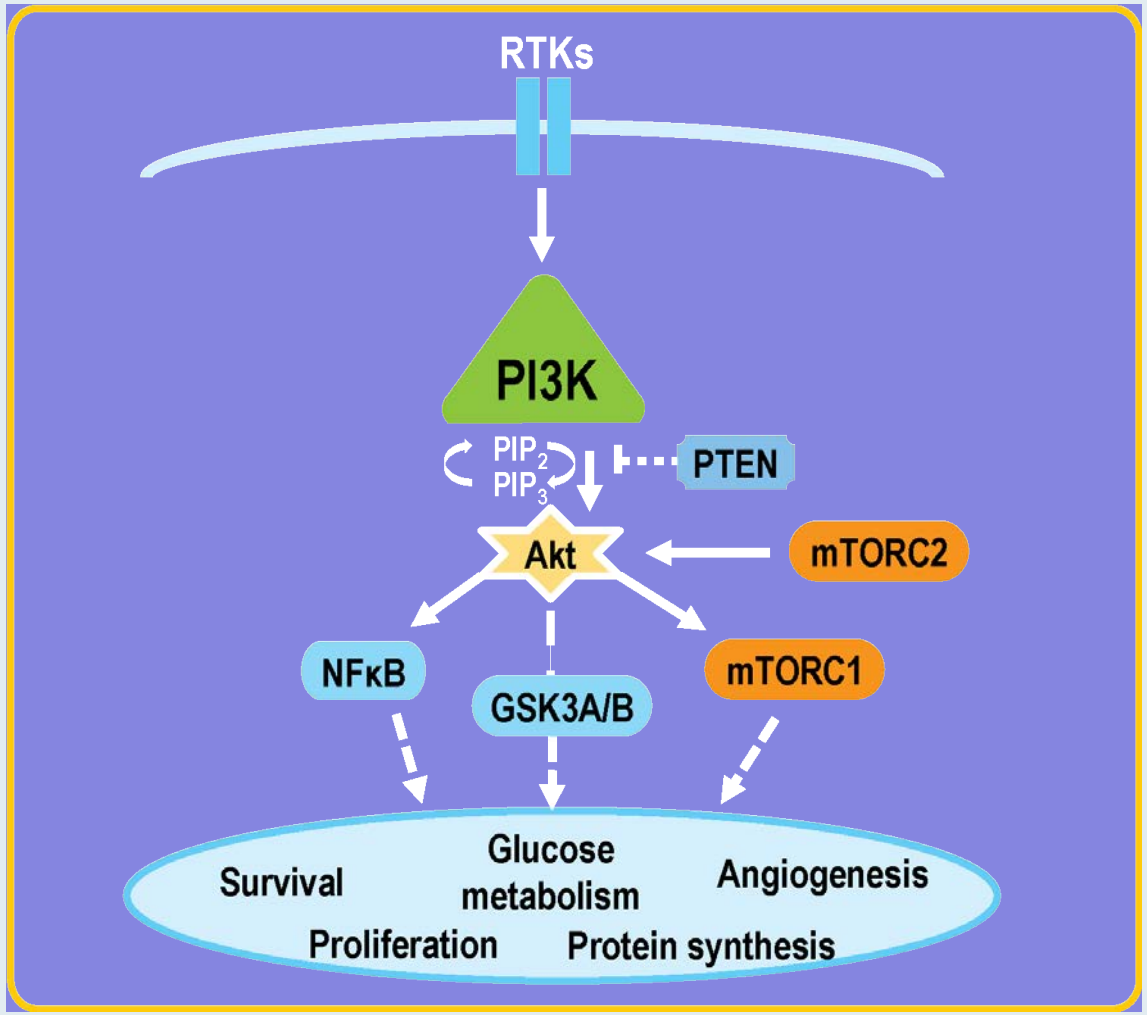
RTP RESEARCH TO PRACTICE

Common Side Effects and Dosing of CDK4/6 Inhibitors

	Palbociclib		Abemaciclib		Ribociclib	
Dosing	125 mg qd 3 wk on, 1 wk off		200 mg BID continuously		600 mg qd 3 wk on, 1 wk off	
Common adverse events	**All grades**	**Grade 3/4**	**All grades**	**Grade 3/4**	**All grades**	**Grade 3/4**
Neutropenia Thrombocytopenia	95% 76%	54% 19%	88% 42%	27% 2%	46% 37%	29% 10%
Diarrhea Nausea Vomiting	16% 23% 5%	0 0 0	90% 65% 35%	20% 5% 2%	22% 46% 25%	3% 2% 0

Barroso-Sousa R et al. *Breast Care* 2016;11:167-73.

PI3K Inhibitors: Mechanism of Action



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

André F et al. ESMO 2018;Abstract LBA3_PR.

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

ORIGINAL ARTICLE

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

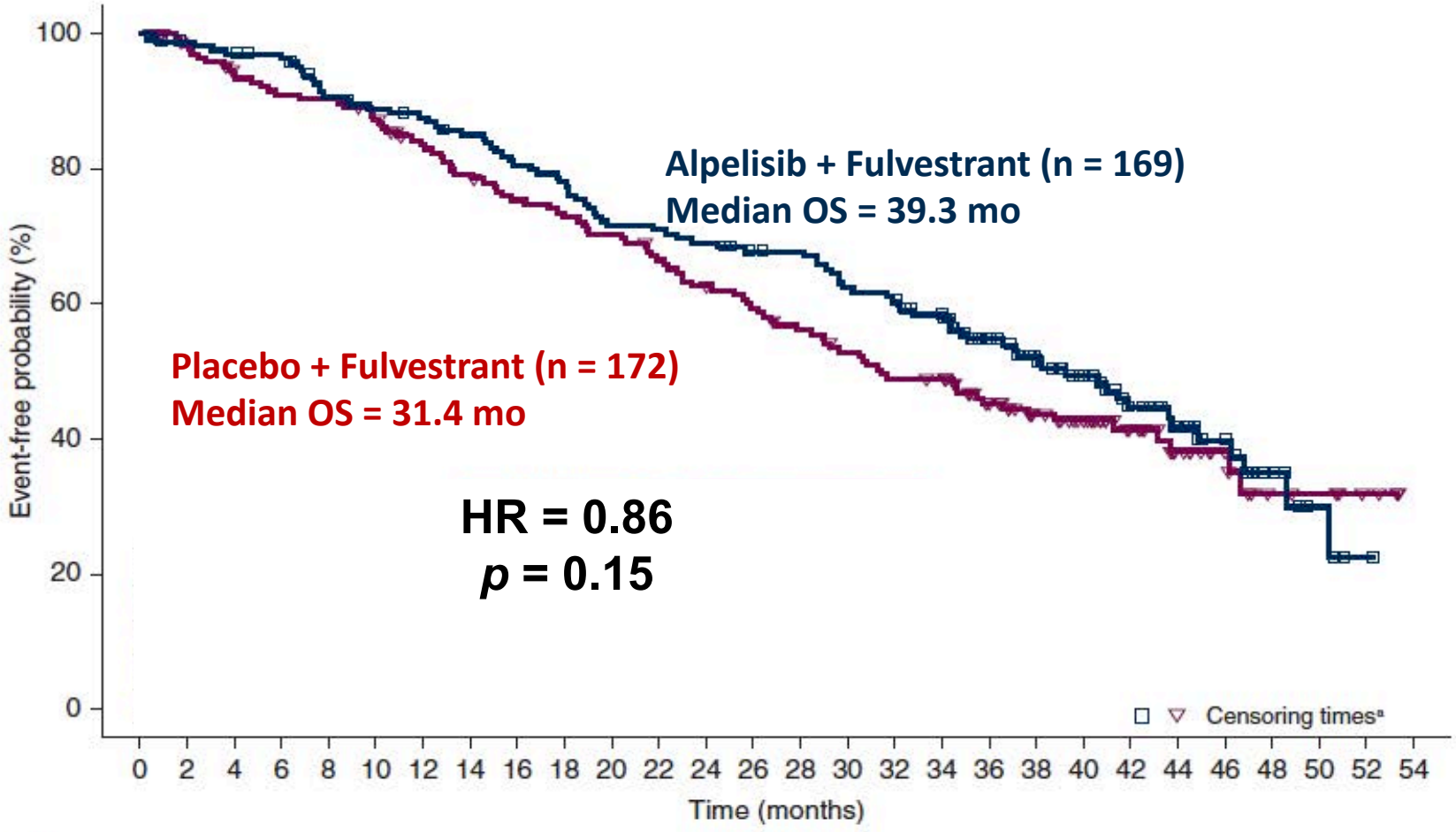
F. André[1*], E. M. Ciruelos[2], D. Juric[3], S. Loibl[4], M. Campone[5], I. A. Mayer[6], G. Rubovszky[7], T. Yamashita[8], B. Kaufman[9], Y.-S. Lu[10], K. Inoue[11], Z. Pápai[12], M. Takahashi[13], F. Ghaznawi[14], D. Mills[15], M. Kaper[14], M. Miller[14], P. F. Conte[16], H. Iwata[17] & H. S. Rugo[18]

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

Available online 25 November 2020

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

SOLAR-1: OS for Patients with Advanced Breast Cancer with a PIK3CA Mutation



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

RTP RESEARCH TO PRACTICE

SOLAR-1: Select Adverse Events in Overall Patient Population

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

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

Lancet Oncol 2021;22:489-98.

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

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

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

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

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

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

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

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

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

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

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

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

Treatment crossover between cohorts is not permitted

Primary endpoint

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

(assessed in each cohort)

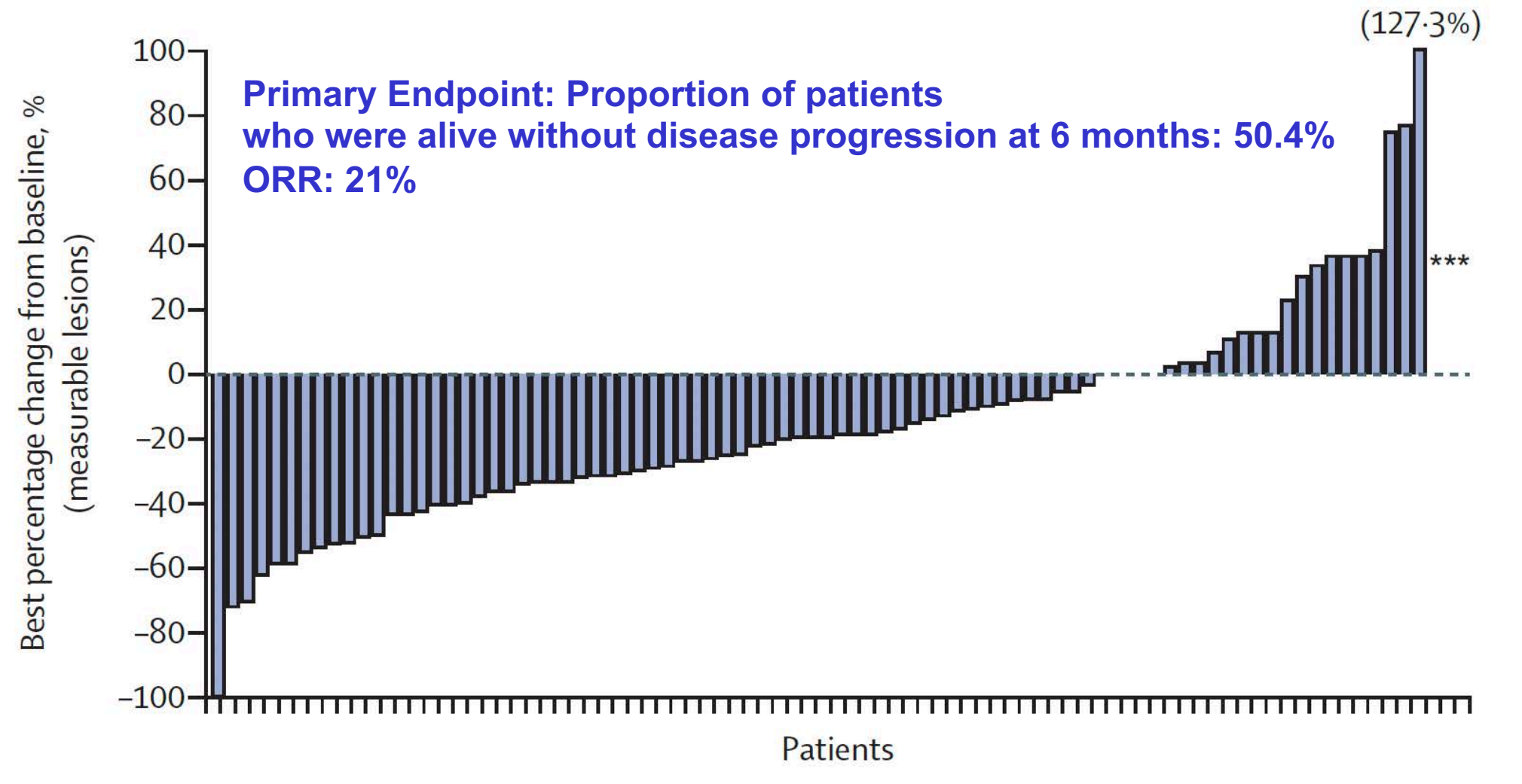
- PFS
- PFS2
- ORR, CBR, DOR
- OS
- Safety

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

Cohort A: Rugo HS et al. *Lancet Oncol* 2021.

RTP RESEARCH TO PRACTICE

BYLieve Efficacy Outcomes



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

New Phase III HARMONIA Trial Will Compare Palbociclib to Ribociclib for HR-Positive, HER2-Negative Advanced Breast Cancer

Press Release – September 19, 2021

"HARMONIA, an international, randomized, Phase III, multicenter, open-label study of ribociclib versus palbociclib, both in combination with endocrine therapy, in patients with hormone receptor-positive, human epidermal growth factor receptor 2-negative (HR+/HER2-) advanced or metastatic breast cancer with a HER2-enriched (HER2E) intrinsic subtype [has been announced]. HARMONIA is the first prospective Phase III trial to enroll patients selected by RNA-based molecular subtyping of their tumors and the first to directly compare two CDK4/6 inhibitors in patients with HR+/HER2- advanced breast cancer.

The primary endpoint of HARMONIA is progression free survival, and the study will evaluate if ribociblib positively alters tumor biology, enabling a better response to endocrine therapy compared to palbociclib.

HARMONIA enrollment is expected to begin in Q1 2022. Patients with the basal-like subtype may also enroll. This exploratory cohort of patients will be treated with a chemotherapy-based regimen as these tumors behave more like triple-negative breast cancer."

https://www.novartis.com/news/media-releases/novartis-announces-collaboration-harmonia-phase-iii-head-head-trial-evaluating-kisqali-vs-ibrance-patients-hrher2-advanced-breast-cancer

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

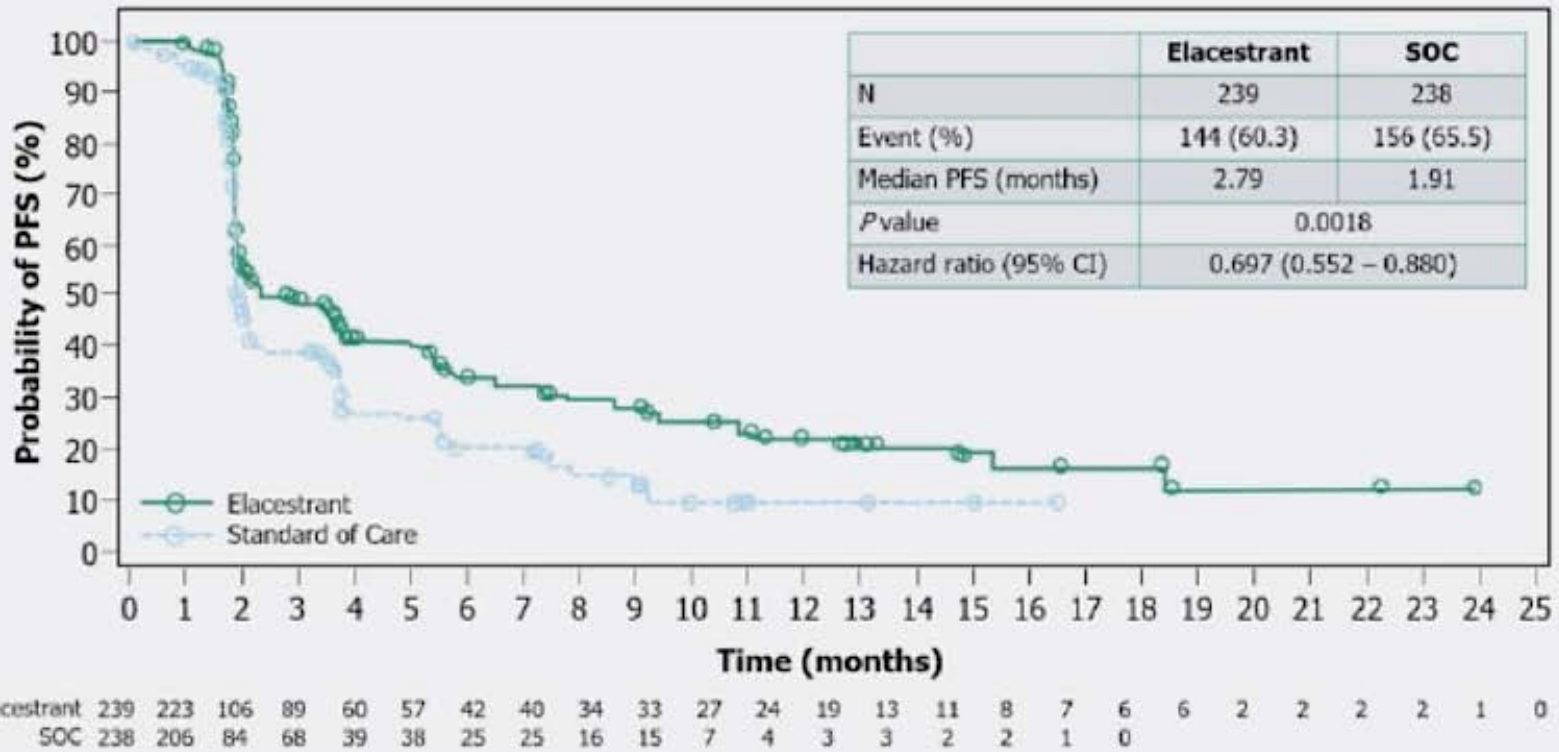
Elacestrant, an oral selective estrogen receptor degrader (SERD), vs investigator's choice of endocrine monotherapy for ER+/HER2- advanced/metastatic breast cancer (mBC) following progression on prior endocrine and CDK4/6 inhibitor therapy: Results of EMERALD phase 3 trial

Bardia A,[1] Neven P,[2] Streich G,[3] Montero AJ,[4] Forget F,[5] Mouret-Reynier MA,[6] Sohn JH,[7] Vuylsteke P,[8] Harnden KK,[9] Khong H,[10] Kocsis J,[11] Dalenc F,[12] Kaklamani V,[13] Dillon P,[14] Babu S,[15] Waters S,[16] Deleu I,[17] Garcia-Saenz J,[18] Bria E,[19] Cazzaniga M,[20] Lu J,[21] Aftimos P,[22] Cortes J,[23] Liu S,[24] Laurent D,[25] Conlan MG,[26] Bidard FC[27]

SABCS 2021;Abstract GS2-02.

EMERALD: Progression-Free Survival (PFS) by IRC

All Patients (ITT)



	Elacestrant	SOC
N	239	238
Event (%)	144 (60.3)	156 (65.5)
Median PFS (months)	2.79	1.91
P value	0.0018	
Hazard ratio (95% CI)	0.697 (0.552 – 0.880)	

Elacestrant is associated with a 30% reduction in the risk of progression or death in all patients with ER+/HER2- mBC

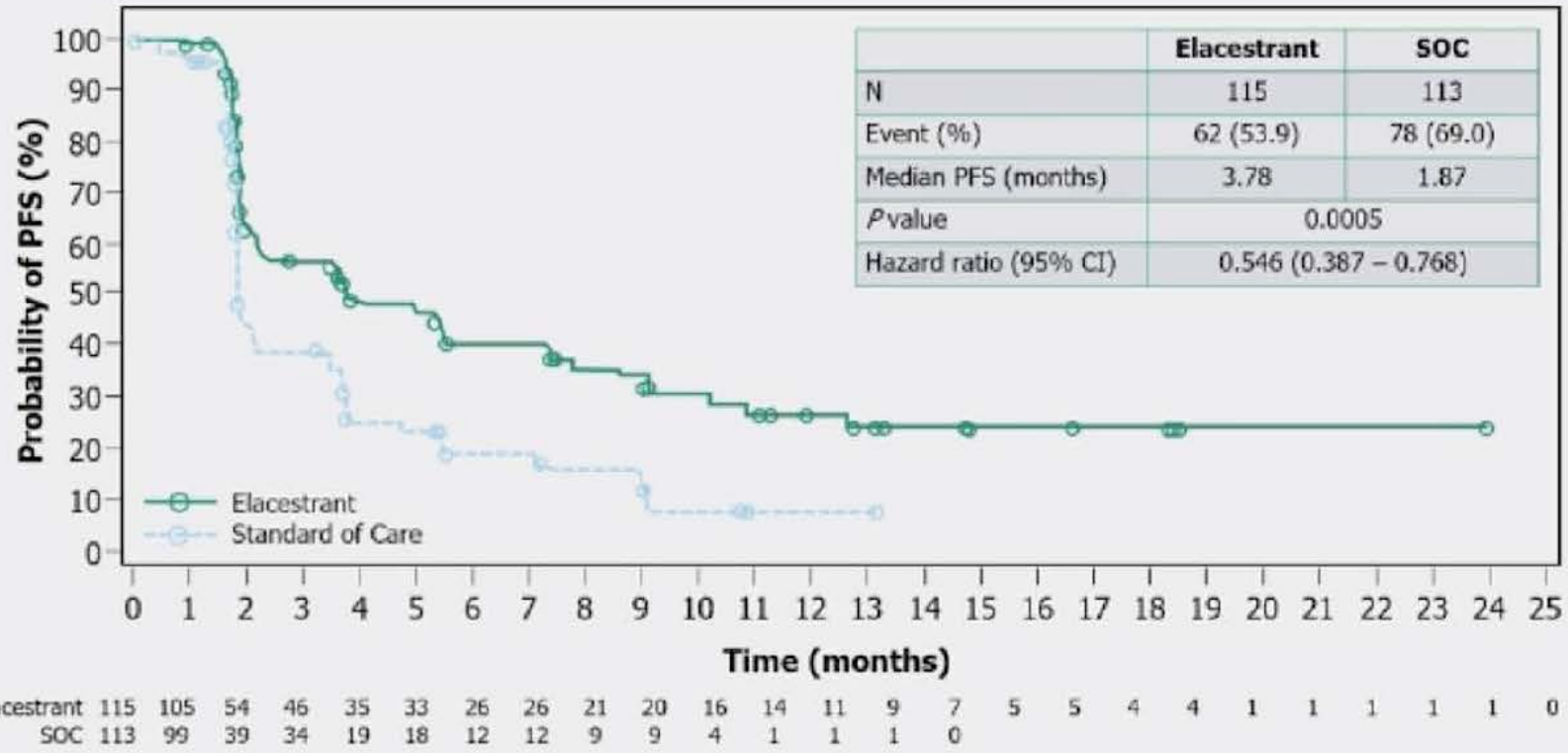
Elacestrant demonstrated a significant improvement versus SOC in all patients with ER+/HER2- advanced/metastatic breast cancer following CDK4/6i therapy

Bardia A et al. SABCS 2021;Abstract GS2-02.

RTP RESEARCH TO PRACTICE

EMERALD: PFS by IRC (continued)

Patients With Tumors Harboring *mESR1*



	Elacestrant	SOC
N	115	113
Event (%)	62 (53.9)	78 (69.0)
Median PFS (months)	3.78	1.87
P value	0.0005	
Hazard ratio (95% CI)	0.546 (0.387 – 0.768)	

Elacestrant is associated with a 45% reduction in the risk of progression or death in patients harboring *mESR1*

Elacestrant demonstrated a significant improvement versus SOC in patients with ER+/HER2- advanced/metastatic breast cancer and *mESR1* following CDK4/6i therapy

Bardia A et al. SABCS 2021;Abstract GS2-02.

RTP RESEARCH TO PRACTICE

EMERALD: Treatment-Emergent Adverse Events

	Elacestrant N = 237, n (%)		SOC					
			Total N = 229, n (%)		Fulvestrant N = 161, n (%)		AI N = 68, n (%)	
Preferred Term	All Grades	Grade 3/4	All Grades	Grade 3/4	All Grades	Grade 3/4	All Grades	Grade 3/4
Nausea	83 (35.0)	6 (2.5)	43 (18.8)	2 (0.9)	26 (16.1)	-	17 (25.0)	2 (2.9)
Fatigue	45 (19.0)	2 (0.8)	43 (18.8)	2 (0.9)	35 (21.7)	1 (0.6)	8 (11.8)	1 (1.5)
Vomiting	45 (19.0)	2 (0.8)	19 (8.3)	-	12 (7.5)	-	7 (10.3)	-
Decreased appetite	35 (14.8)	2 (0.8)	21 (9.2)	1 (0.4)	12 (7.5)	-	9 (13.2)	1 (1.5)
Arthralgia	34 (14.3)	2 (0.8)	37 (16.2)	-	28 (17.4)	-	9 (13.2)	-
Diarrhea	33 (13.9)	-	23 (10.0)	2 (0.9)	14 (8.7)	1 (0.6)	9 (13.2)	1 (1.5)
Back pain	33 (13.9)	6 (2.5)	22 (9.6)	1 (0.4)	16 (9.9)	1 (0.6)	6 (8.8)	-
Aspartate aminotransferase increased	31 (13.1)	4 (1.7)	28 (12.2)	2 (0.9)	20 (12.4)	2 (1.2)	8 (11.8)	-
Headache	29 (12.2)	4 (1.7)	26 (11.4)	-	18 (11.2)	-	8 (11.8)	-
Constipation	29 (12.2)	-	15 (6.6)	-	10 (6.2)	-	5 (7.4)	-
Hot flush	27 (11.4)	-	19 (8.3)	-	15 (9.3)	-	4 (5.9)	-
Dyspepsia	24 (10.1)	-	6 (2.6)	-	4 (2.5)	-	2 (2.9)	-
Alanine aminotransferase increased	22 (9.3)	5 (2.1)	23 (10.0)	1 (0.4)	17 (10.6)	-	6 (8.8)	1 (1.5)

Bardia A et al. SABCS 2021;Abstract GS2-02.

Select Ongoing Phase II/III Trials of Oral SERDs in Development for ER-Positive, HER2-Negative Advanced Breast Cancer

Drug	Trial name (phase)	Treatment arms	Setting	Estimated study completion date
Amcenestrant (SAR439859)	AMEERA-3 (Phase II)	• Amcenestrant • Endocrine monotherapy	Prior hormonal tx	July 2025
Amcenestrant (SAR439859)	AMEERA-5 (Phase III)	• Amcenestrant + Palbociclib • Letrozole + Palbociclib	Untreated ABC	May 2027
Camizestrant (AZD9833)	SERENA-4 (Phase III)	• Camizestrant + Palbociclib • Anastrozole + Palbociclib	Untreated ABC	February 2029
Giredestrant (GDC-9545)	acelERA (Phase II)	• Giredestrant • Endocrine monotherapy	Prior systemic and/or targeted tx	January 2024
Giredestrant (GDC-9545)	persevERA (Phase III)	• Giredestrant + Palbociclib • Letrozole + Palbociclib	Untreated ABC	March 2027

SERD: Selective ER degrader

www.clinicaltrials.gov. Accessed August 2021

RTP RESEARCH TO PRACTICE

Agenda

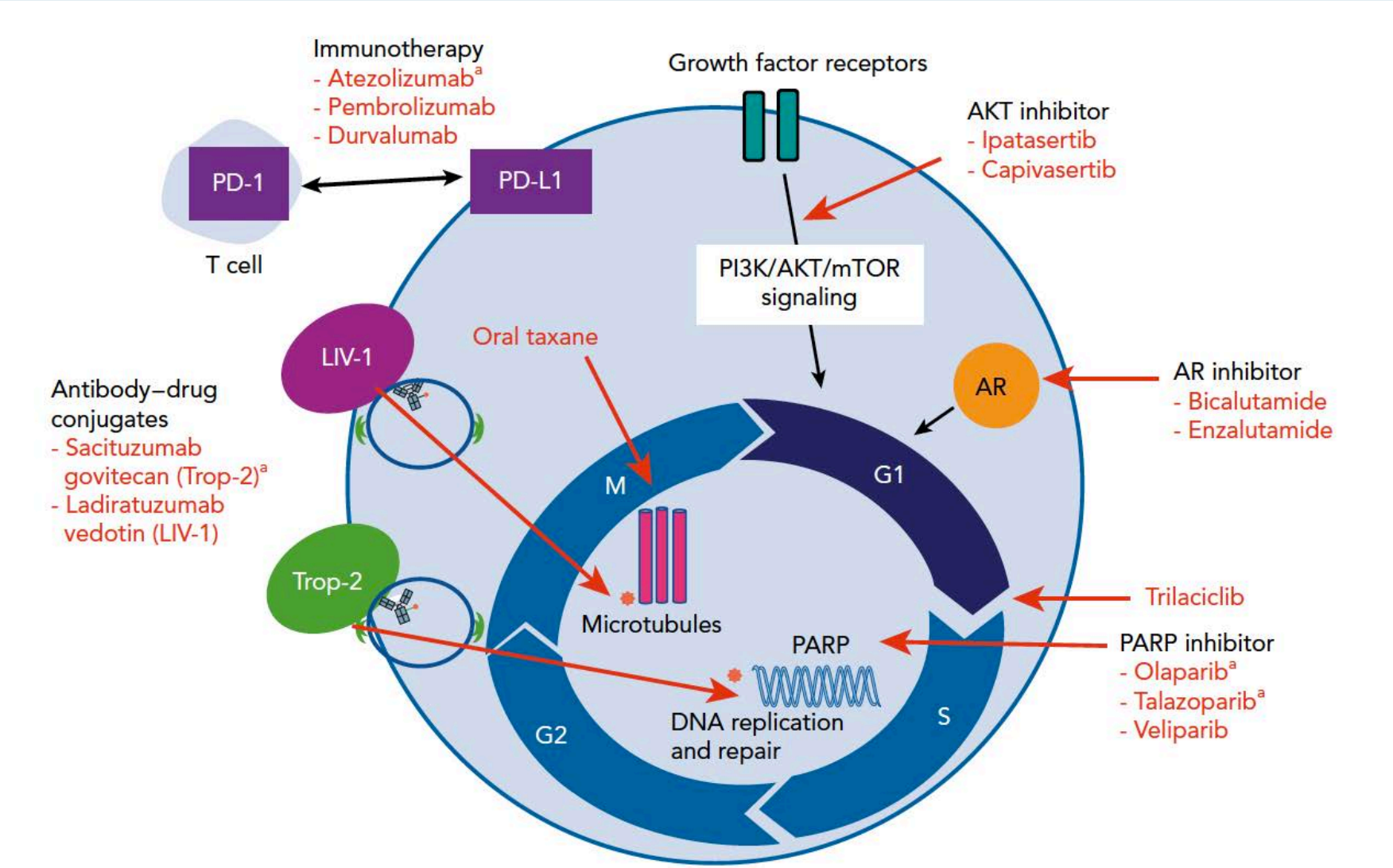
Module 1: HER2-Positive

Module 2: ER/PR-Positive, HER2-Negative

Module 3: Triple-Negative

RTP
RESEARCH
TO PRACTICE

Novel Targets for Therapeutic Intervention in Triple-Negative Breast Cancer



Vidula N et al. *J Natl Compr Canc Netw* 2020;1-9.

RTP RESEARCH TO PRACTICE

J Clin Oncol 2021;[Online ahead of print].

ASCO rapid recommendations

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

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

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

ASCO 2021 Adjuvant PARP Inhibitor Updated Recommendations

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

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

N Engl J Med 2021;384:2394-405

The NEW ENGLAND JOURNAL of MEDICINE

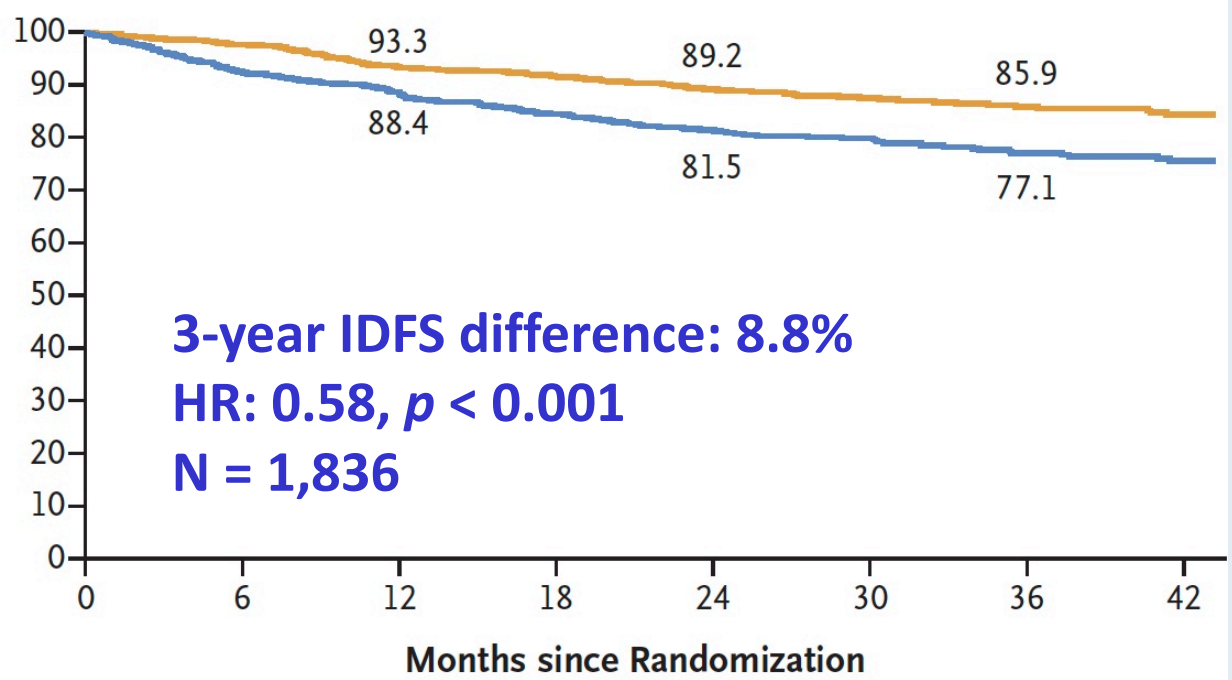
ORIGINAL ARTICLE

Adjuvant Olaparib for Patients with *BRCA1*- or *BRCA2*-Mutated Breast Cancer

A.N.J. Tutt, J.E. Garber, B. Kaufman, G. Viale, D. Fumagalli, P. Rastogi, R.D. Gelber, E. de Azambuja, A. Fielding, J. Balmaña, S.M. Domchek, K.A. Gelmon, S.J. Hollingsworth, L.A. Korde, B. Linderholm, H. Bandos, E. Senkus, J.M. Suga, Z. Shao, A.W. Pippas, Z. Nowecki, T. Huzarski, P.A. Ganz, P.C. Lucas, N. Baker, S. Loibl, R. McConnell, M. Piccart, R. Schmutzler, G.G. Steger, J.P. Costantino, A. Arahmani, N. Wolmark, E. McFadden, V. Karantza, S.R. Lakhani, G. Yothers, C. Campbell, and C.E. Geyer, Jr., for the OlympiA Clinical Trial Steering Committee and Investigators*

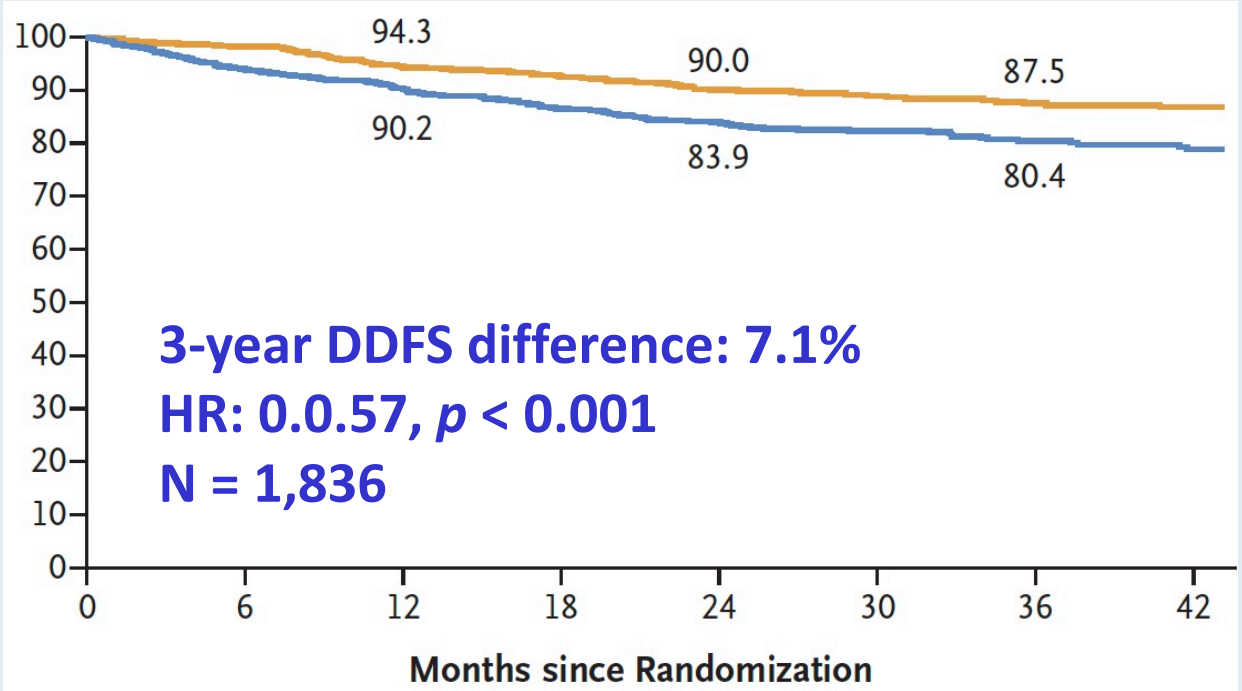
OlympiA: Invasive and Distant Disease-Free Survival

Invasive DFS (IDFS)



3-year IDFS difference: 8.8%
HR: 0.58, $p < 0.001$
N = 1,836

Distant DFS (DDFS)



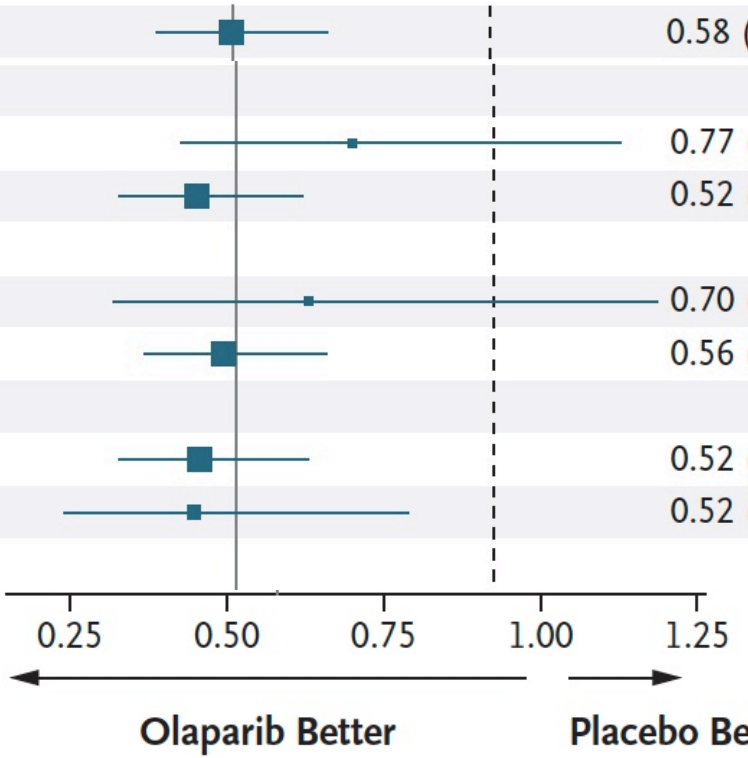
3-year DDFS difference: 7.1%
HR: 0.0.57, $p < 0.001$
N = 1,836

Tutt ANJ et al. *N Engl J Med* 2021;384:2394-405.

RTP RESEARCH TO PRACTICE

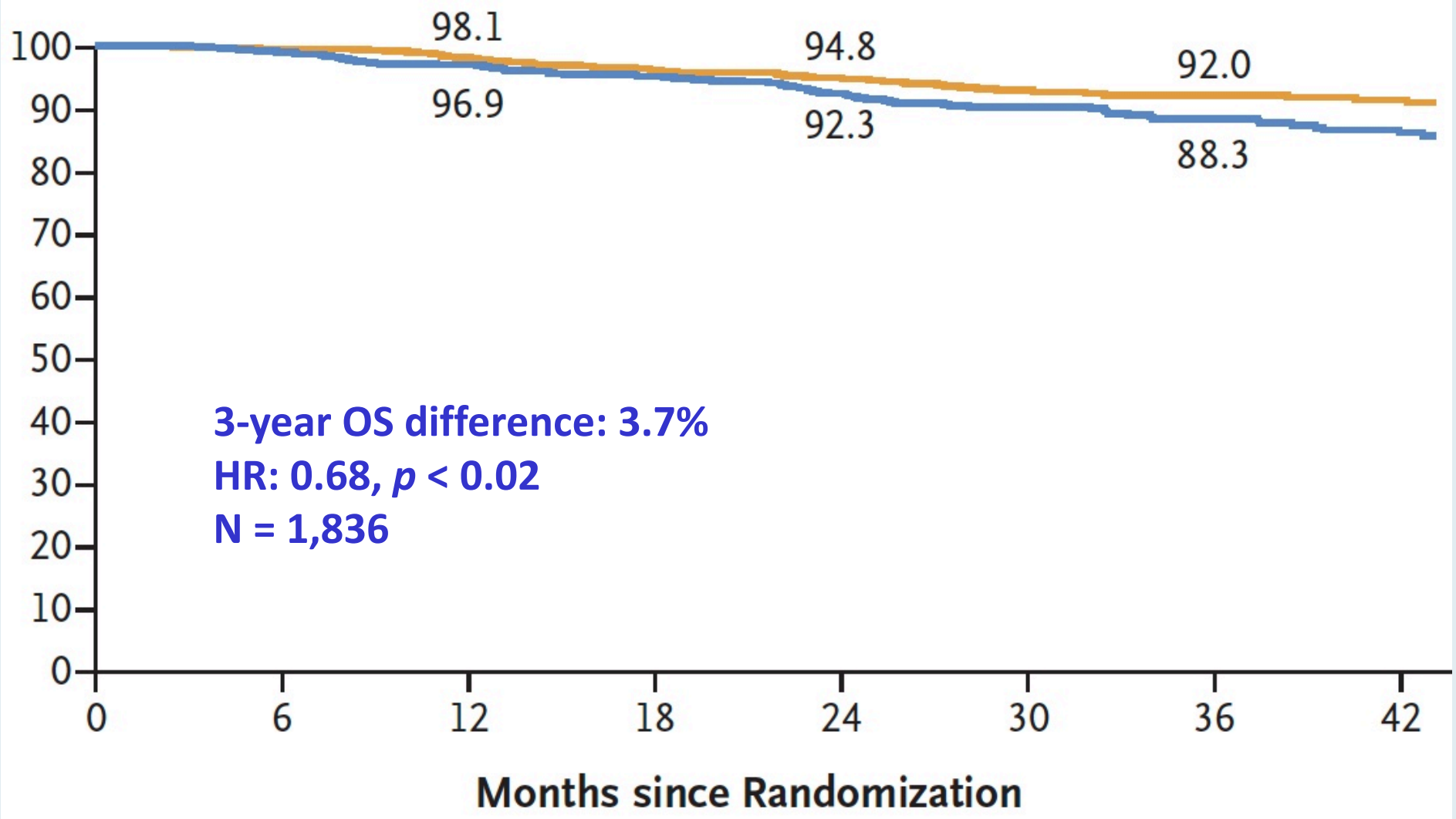
OlympiA: 3-Year IDFS

Subgroup	Olaparib	Placebo	3-Yr Invasive Disease–free Survival		Stratified Hazard Ratio for Invasive Disease or Death (95% CI)
			Olaparib	Placebo	
	no. of patients with an event/total no.		%		
All patients	106/921	178/915	85.9	77.1	0.58 (0.46–0.74)
Previous platinum-based chemotherapy					
Yes	34/247	43/239	82.0	77.0	0.77 (0.49–1.21)
No	72/674	135/676	87.3	77.1	0.52 (0.39–0.69)
Hormone-receptor status					
HR+ and HER2–	19/168	25/157	83.5	77.2	0.70 (0.38–1.27)
TNBC	87/751	153/758	86.1	76.9	0.56 (0.43–0.73)
Germline *BRCA* mutation					
BRCA1	70/558	126/558	85.0	73.4	0.52 (0.39–0.70)
BRCA2	22/230	38/209	88.6	78.0	0.52 (0.30–0.86)
BRCA1 and *BRCA2*	0/1	0/3	NC	NC	NC



Tutt ANJ et al. *N Engl J Med* 2021;384:2394-405.

OlympiA: Overall Survival (OS)



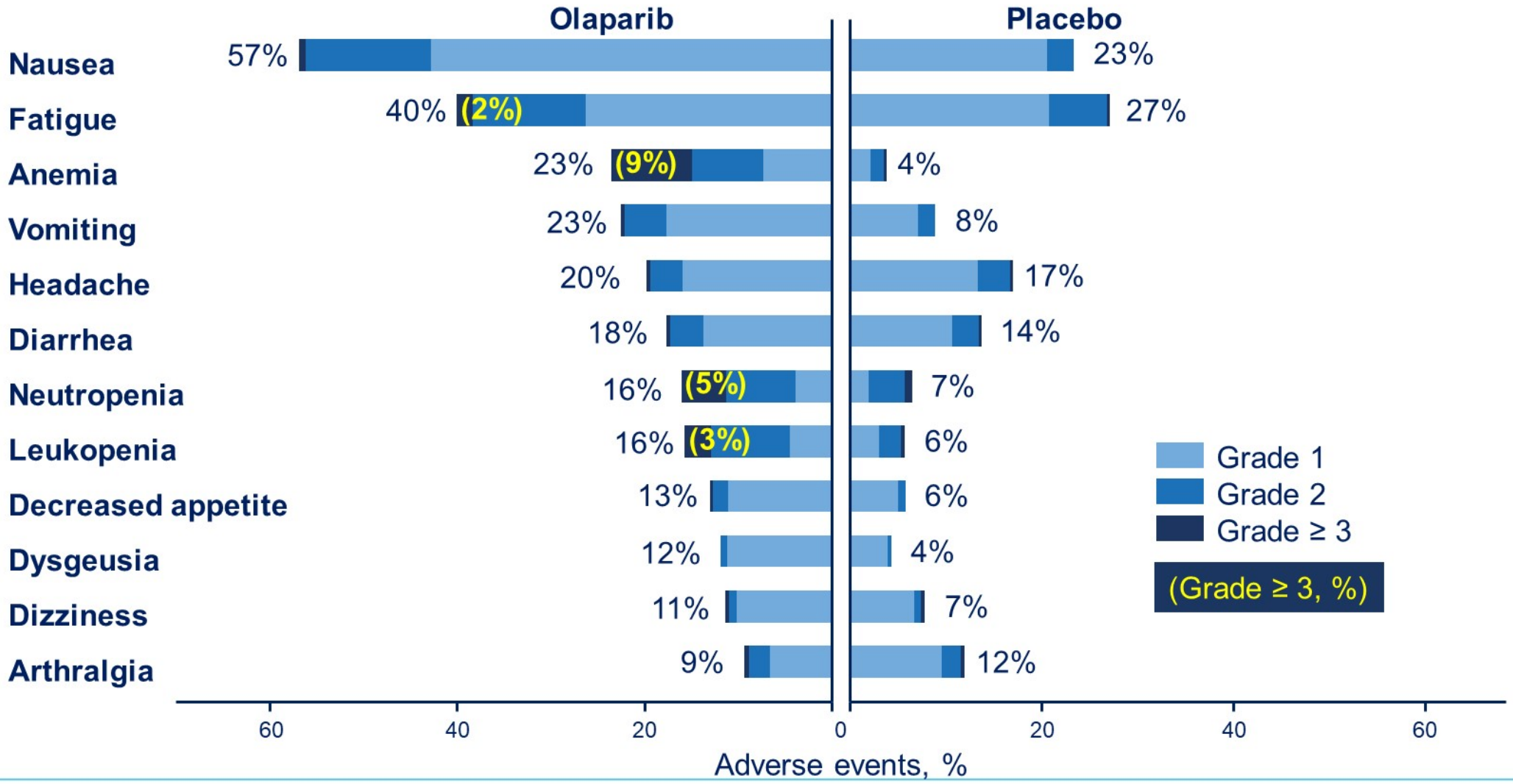
Tutt ANJ et al. *N Engl J Med* 2021;384:2394-405.

OlympiA: Summary of Adverse Events

Adverse Event	Olaparib (N = 911)	Placebo (N = 904)
	no. of patients (%)	
Any adverse event	835 (91.7)	753 (83.3)
Serious adverse event	79 (8.7)	76 (8.4)
Adverse event of special interest†	30 (3.3)	46 (5.1)
MDS or AML	2 (0.2)	3 (0.3)
Pneumonitis‡	9 (1.0)	11 (1.2)
New primary cancer§	19 (2.1)	32 (3.5)
Grade ≥3 adverse event	221 (24.3)	102 (11.3)
Grade 4 adverse event¶	17 (1.9)	4 (0.4)
Adverse event leading to permanent discontinuation of olaparib or placebo‖	90 (9.9)	38 (4.2)
Adverse event leading to death**	1 (0.1)	2 (0.2)

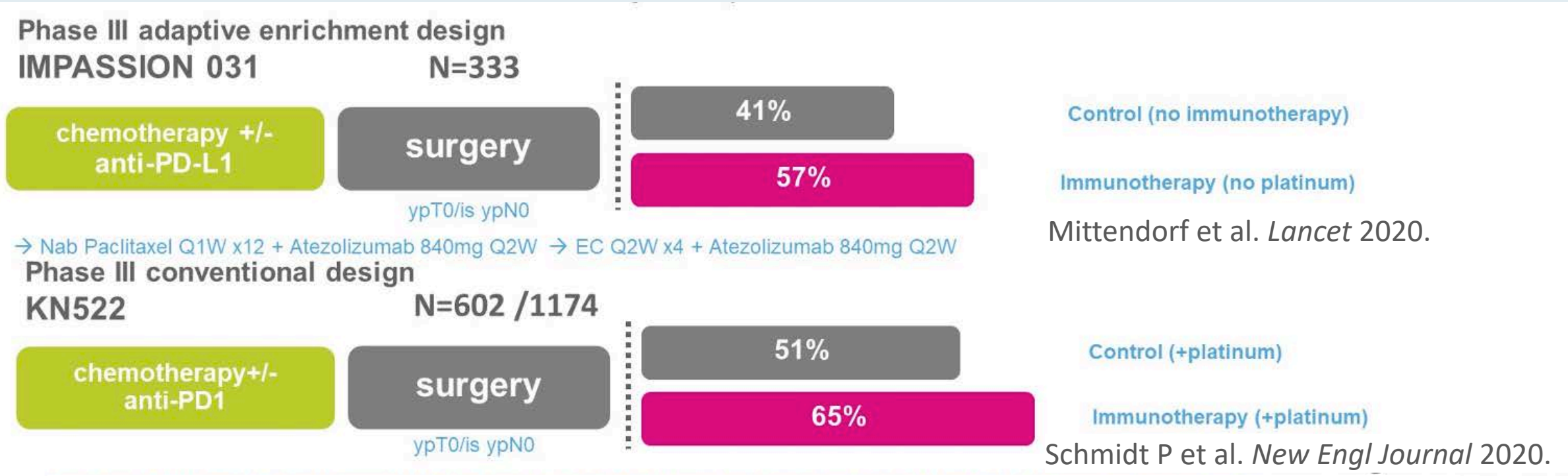
Tutt ANJ et al. *N Engl J Med* 2021;384:2394-405.

OlympiA: Adverse events of any grade ≥ 10%



Presented By: Andrew Tutt MB ChB PhD FMedSci
The Institute of Cancer Research and Kings College London

Phase III Studies of Neoadjuvant Chemotherapy with Anti-PD-1/PD-L1 Antibodies: IMpassion031 and KEYNOTE-522



Mittendorf et al. *Lancet* 2020.

Schmidt P et al. *New Engl Journal* 2020.

Loibl S et al. ASCO 2021;Abstract 506.

Primary Endpoints of Phase III Studies of Neoadjuvant Immunotherapy with Chemotherapy

Change in pCR rate	Overall	PD-L1 positive	PD-L1 negative
KEYNOTE-522[1] (Pembrolizumab + CT vs Placebo + CT)	+13.6%	+14%	+18%
IMpassion 031[2] (Atezolizumab + CT vs Placebo + CT)	+17%	+20%	+14%

pCR = pathologic complete response

Event-free survival	Median FU	Events	HR
KEYNOTE-522[3] (Pembrolizumab + CT vs Placebo + CT)	39.1 mo	15.7% vs 23.8%	0.63
IMpassion 031[2] (Atezolizumab + CT vs Placebo + CT)*	20.6 mo	10.3% vs 13.1%	0.76

*IMpassion031 not powered for event-free survival, disease-free survival or overall survival

[1] Schmid et al. *NEJM* 2020; [2] Mittendorf et al. *Lancet* 2020; [3] Schmid et al. ESMO 2021 Virtual Plenary.

FDA Approves Pembrolizumab for High-Risk Localized Triple-Negative Breast Cancer

Press Release – July 26, 2021

"The Food and Drug Administration approved pembrolizumab for high-risk, early-stage, triple-negative breast cancer (TNBC) in combination with chemotherapy as neoadjuvant treatment, and then continued as a single agent as adjuvant treatment after surgery.

FDA also granted regular approval to pembrolizumab in combination with chemotherapy for patients with locally recurrent unresectable or metastatic TNBC whose tumors express PD-L1 (Combined Positive Score [CPS] ≥10) as determined by an FDA approved test. FDA granted accelerated approval to pembrolizumab for this indication in November 2020.

The following trial was the basis of the neoadjuvant and adjuvant approval, as well as the confirmatory trial for the accelerated approval.

The efficacy of pembrolizumab in combination with neoadjuvant chemotherapy followed by surgery and continued adjuvant treatment with pembrolizumab as a single agent was investigated in KEYNOTE-522 (NCT03036488), a randomized, multicenter, double-blind, placebo-controlled trial conducted in 1174 patients with newly diagnosed previously untreated high-risk early-stage TNBC (tumor size >1 cm but ≤2 cm in diameter with nodal involvement or tumor size >2 cm in diameter regardless of nodal involvement). Patients were enrolled regardless of tumor PD-L1 expression."

www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-pembrolizumab-high-risk-early-stage-triple-negative-breast-cancer?utm_medium=email&utm_source=govdelivery

RTP RESEARCH TO PRACTICE

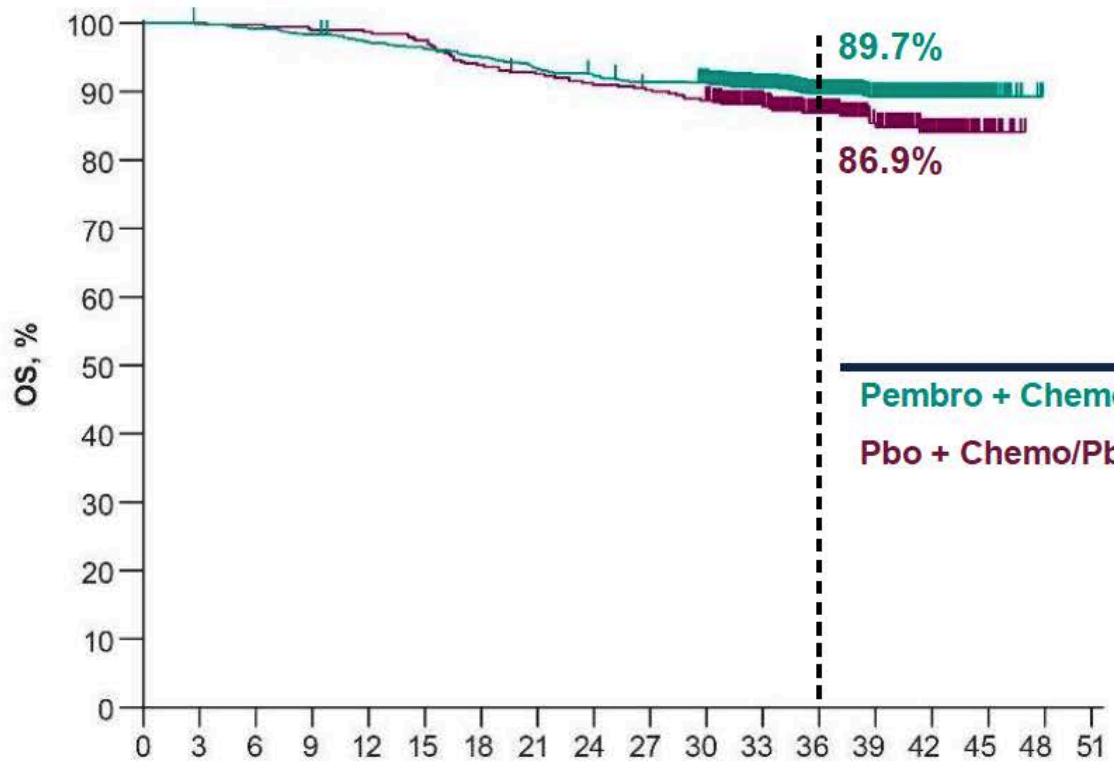
ESMO VIRTUAL PLENARY

KEYNOTE-522: Phase 3 Study of Neoadjuvant Pembrolizumab + Chemotherapy versus Placebo + Chemotherapy, Followed by Adjuvant Pembrolizumab versus Placebo for Early-Stage Triple-Negative Breast Cancer

Peter Schmid[1], Javier Cortes[2], Rebecca Dent[3], Lajos Pusztai[4], Heather McArthur[5], Sherko Kümmel[6], Jonas Bergh[7], Carsten Denkert[8], Yeon Hee Park[9], Rina Hui[10], Nadia Harbeck[11], Masato Takahashi[12], Michael Untch[13], Peter A. Fasching[14], Fatima Cardoso[15], Yu Ding[16], Konstantinos Tryfonidis[17], Gursel Aktan[17], Vassiliki Karantza[17], Joyce O'Shaughnessy[18]

1. Centre for Experimental Cancer Medicine, Barts Cancer Institute, Queen Mary University London, London, UK; 2. International Breast Cancer Center, Quirón Group, Madrid and Barcelona, Spain and Vall d'Hebron Institute of Oncology, Barcelona, Spain; 3. National Cancer Center Singapore, Duke–National University of Singapore Medical School, Singapore; 4. Yale School of Medicine, Yale Cancer Center, New Haven, CT, USA; 5. Breast Oncology, Cedars-Sinai Medical Center, Los Angeles, CA, USA; 6. Breast Unit, Kliniken Essen-Mitte, Essen, Germany; 7. Department of Oncology-Pathology, Karolinska Institutet and Breast Cancer Centre, Cancer theme, Karolinska University Hospital, Solna, Sweden; 8. Institute of Pathology, Philipps-University Marburg and University Hospital Marburg (UKGM), Marburg, Germany; 9. Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; 10. Westmead Breast Cancer Institute, Westmead Hospital and the University of Sydney, Sydney, NSW, Australia; 11. Breast Center, LMU University Hospital, Munich, Germany; 12. Department of Breast Surgery, Hokkaido Cancer Center, Sapporo, Japan; 13. Breast Cancer Center, Helios Klinikum Berlin-Buch, Berlin, Germany; 14. University Hospital Erlangen, Comprehensive Cancer Center Erlangen-EMN, Erlangen, Germany; 15. Breast Unit, Champalimaud Clinical Center/Champalimaud Foundation, Lisbon, Portugal; 16. Biostatistics, Merck & Co., Inc., Kenilworth, NJ, USA; 17. Merck Research Laboratories, Merck & Co., Inc., Kenilworth, NJ, USA; 18. Baylor University Medical Center, Texas Oncology, US Oncology, Dallas, TX, USA

KEYNOTE-522: Updated OS (Median Follow-Up 39.1 Months)



	Events	HR (95% CI)	*P*-value
Pembro + Chemo/Pembro	10.2%	0.72[a] (0.51-1.02)	0.03214[b]
Pbo + Chemo/Pbo	14.1%		

No. at Risk																		
Pembro + Chemo/Pembro	784	782	777	770	759	752	742	729	720	712	701	586	461	323	178	30	0	0
Pbo + Chemo/Pbo	390	390	389	386	385	380	366	360	354	350	343	286	223	157	89	17	0	0

[a]Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors. [b]Prespecified *P*-value boundary of 0.00086 not reached at this analysis.
Data cutoff date: March 23, 2021.

Schmid P et al. ESMO 2021 Virtual Plenary.

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

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

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

RTP RESEARCH TO PRACTICE

OlympiAD and EMBRACA: Efficacy Summary

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

TPC = treatment of physician's choice

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

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

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

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

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

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

Phase III KEYNOTE-355 Trial Met Primary Endpoint of Overall Survival for Patients with Metastatic Triple-Negative Breast Cancer Whose Tumors Expressed PD-L1 (CPS ≥10)

Press Release – July 27, 2021

"Positive overall survival (OS) results [were announced] from the pivotal Phase 3 KEYNOTE-355 trial evaluating pembrolizumab in combination with chemotherapy for the treatment of patients with metastatic triple-negative breast cancer (mTNBC). Findings from the final analysis show first-line treatment with pembrolizumab in combination with chemotherapy (*nab*-paclitaxel, paclitaxel or gemcitabine/carboplatin) demonstrated a statistically significant and clinically meaningful improvement in OS compared with chemotherapy alone in patients with mTNBC whose tumors expressed PD-L1 (Combined Positive Score [CPS] ≥10). No new safety signals were identified. These OS results will be presented at an upcoming medical meeting and submitted to regulatory authorities."

https://www.merck.com/news/merck-announces-phase-3-keynote-355-trial-met-primary-endpoint-of-overall-survival-os-in-patients-with-metastatic-triple-negative-breast-cancer-whose-tumors-expressed-pd-l1-cps-%e2%89%a510/

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

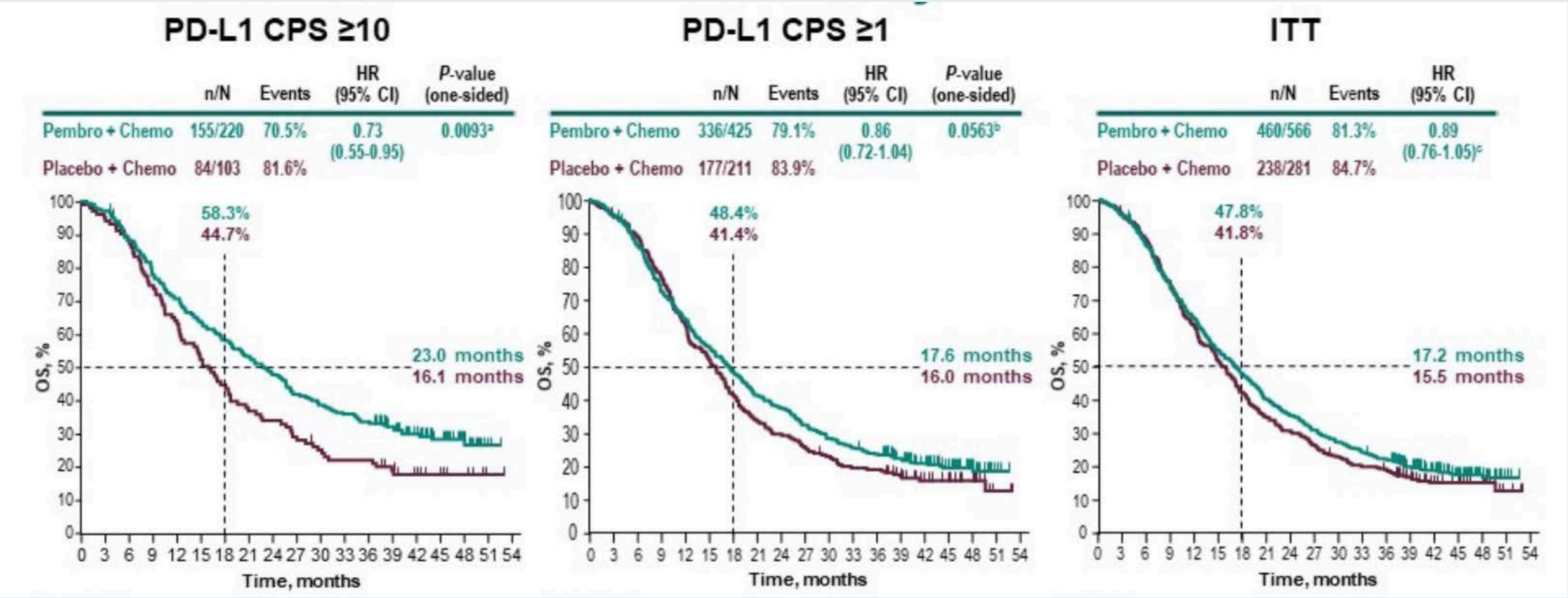
Efficacy of Pembrolizumab + Chemotherapy vs Placebo + Chemotherapy by PD-L1 Combined Positive Score 1-9, 10-19, and ≥20 for Previously Untreated Locally Recurrent Inoperable or Metastatic Triple-Negative Breast Cancer: KEYNOTE-355 Subgroup Analysis

Javier Cortes[1], David W. Cescon[2], Hope S. Rugo[3], Zbigniew Nowecki[4], Seock-Ah Im[5], Mastura Md Yusof[6], Carlos Gallardo[7], Oleg Lipatov[8], Carlos Henrique Barrios[9], Jose Perez-Garcia[10], Hiroji Iwata[11], Norikazu Masuda[12], Marco Torregroza Otero[13], Erhan Gokmen[14], Sherene Loi[15], Zifang Guo[16], Xuan Zhou[16], Vassiliki Karantza[16] Wilbur Pan[16], Peter Schmid[17]

1. International Breast Cancer Center (IBCC), Quiron Group, Madrid and Barcelona, Spain and Vall d'Hebron Institute of Oncology, Barcelona, Spain, Universidad Europea de Madrid, Faculty of Biomedical and Health Sciences, Department of Medicine, Madrid, Spain; 2. Princess Margaret Cancer Centre, University of Toronto, Toronto, Ontario, Canada; 3. University of California San Francisco Comprehensive Cancer Center, San Francisco, CA, USA; 4. Maria Sklodowska-Curie Memorial Cancer Centre and Institute of Oncology, Warsaw, Poland; 5. Seoul National University Hospital, Seoul, Republic of Korea; 6. Cancer Center at Pantai Hospital, Kuala Lumpur, Malaysia; 7. Arturo Lopez Perez Foundation, Santiago, Chile; 8. Republican Clinical Oncology Dispensary, Republic of Bashkortostan, Russian Federation; 9. Oncology Research Unit, Hospital São Lucas, PUCRS, Porto Alegre, Brazil; 10. International Breast Cancer Center (IBCC), Quiron Group, Barcelona, Spain; 11. Aichi Cancer Center Hospital, Nagoya, Japan; 12. Nagoya University Graduate School of Medicine, Nagoya, Japan; 13. Oncomedica S.A., Monteria, Colombia; 14. Ege University Medical School, Izmir, Turkey; 15. Division of Cancer Research, Peter MacCallum Cancer Centre, Melbourne, Australia; The Sir Peter MacCallum Department of Medical Oncology, University of Melbourne, Parkville, Australia; 16. Merck & Co., Inc., Kenilworth, NJ, USA; 17. Barts Cancer Institute, Centre for Experimental Cancer Medicine, London, UK

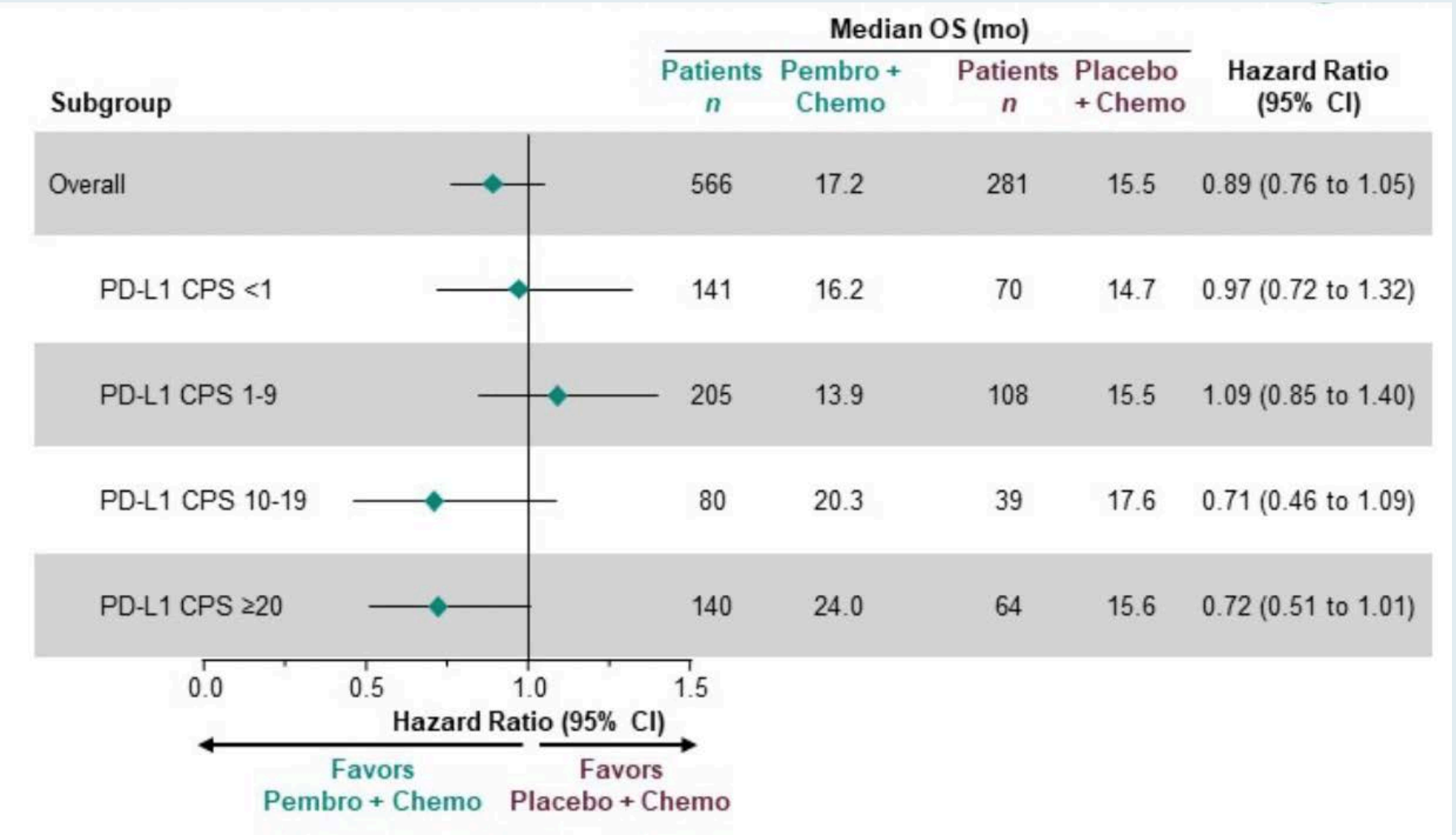
Abstract GS1-02

KEYNOTE-355: Overall Survival (OS) at Final Analysis



Cortes J et al. SABCS 2021;Abstract GS1-02.

KEYNOTE-355: OS in Additional PD-L1 CPS Subgroups



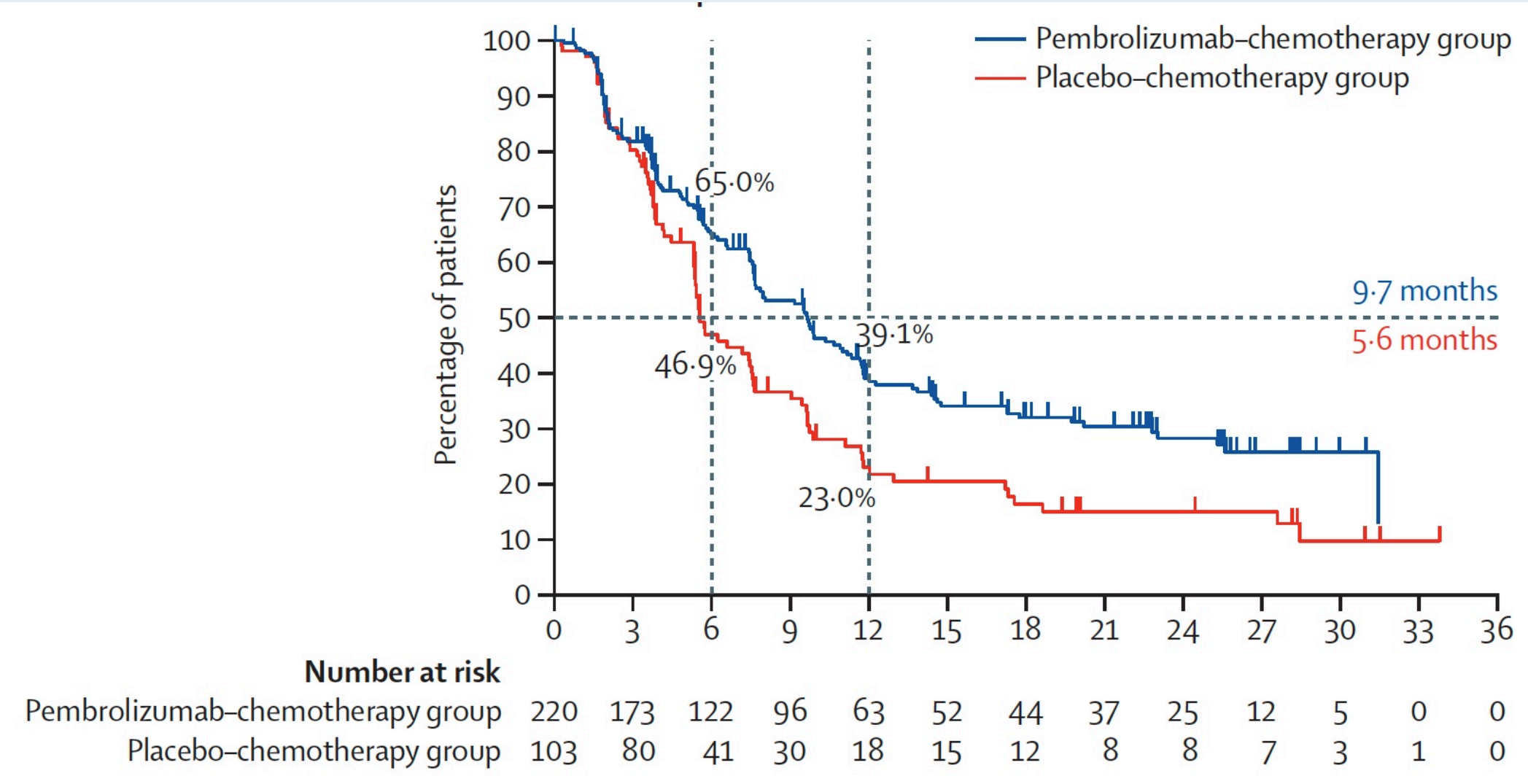
Cortes J et al. SABCS 2021;Abstract GS1-02.

Lancet 2020;396:1817-28

Pembrolizumab plus chemotherapy versus placebo plus chemotherapy for previously untreated locally recurrent inoperable or metastatic triple-negative breast cancer (KEYNOTE-355): a randomised, placebo-controlled, double-blind, phase 3 clinical trial

*Javier Cortes, David W Cescon, Hope S Rugo, Zbigniew Nowecki, Seock-Ah Im, Mastura Md Yusof, Carlos Gallardo, Oleg Lipatov, Carlos H Barrios, Esther Holgado, Hiroji Iwata, Norikazu Masuda, Marco Torregroza Otero, Erhan Gokmen, Sherene Loi, Zifang Guo, Jing Zhao, Gursel Aktan, Vassiliki Karantza, Peter Schmid, for the KEYNOTE-355 Investigators**

KEYNOTE-355: Progression-Free Survival (Combined Positive Score ≥10)



Cortes J et al. *Lancet* 2020;396:1817-28.

Withdrawal of Accelerated Approval of Atezolizumab in Combination with Chemotherapy for Unresectable Locally Advanced or Metastatic Triple-Negative Breast Cancer

Press Release – August 27, 2021

"Accelerated approval has been voluntarily withdrawn in the United States for atezolizumab in combination with chemotherapy (*nab* paclitaxel) for the treatment of unresectable locally advanced or metastatic TNBC in adult patients whose tumors express PD-L1 as determined by an FDA-approved test.

The decision was made in consultation with the FDA after failure of the confirmatory IMpassion131 trial to meet its primary endpoint of PFS for the initial (first-line) treatment of mTNBC in the PD-L1-positive population."

https://www.gene.com/media/press-releases/14927/2021-08-27/genentech-provides-update-on-tecentriq-u

FDA Grants Regular Approval to Sacituzumab Govitecan for Triple-Negative Breast Cancer

Press Release – April 7, 2021

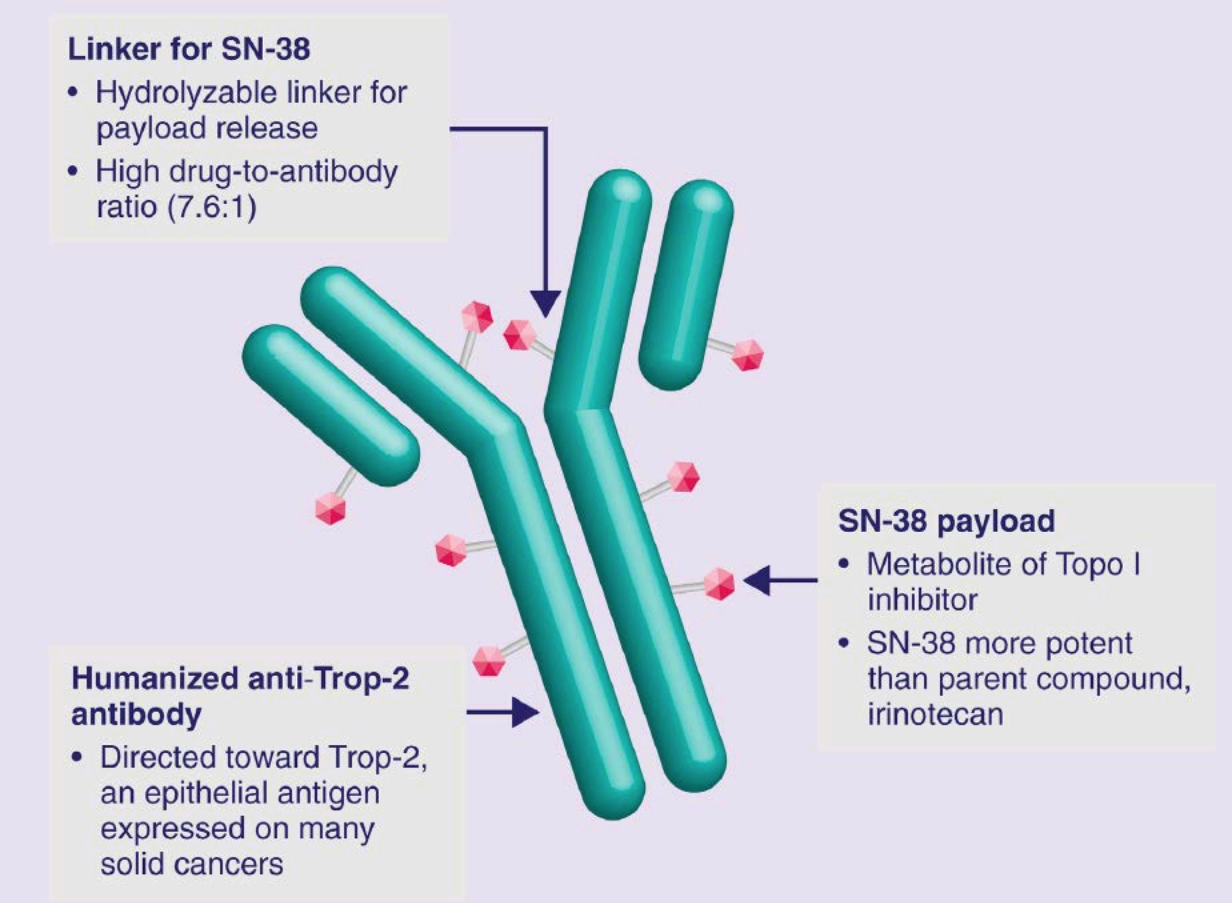
"The Food and Drug Administration granted regular approval to sacituzumab govitecan for patients with unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC) who have received two or more prior systemic therapies, at least one of them for metastatic disease.

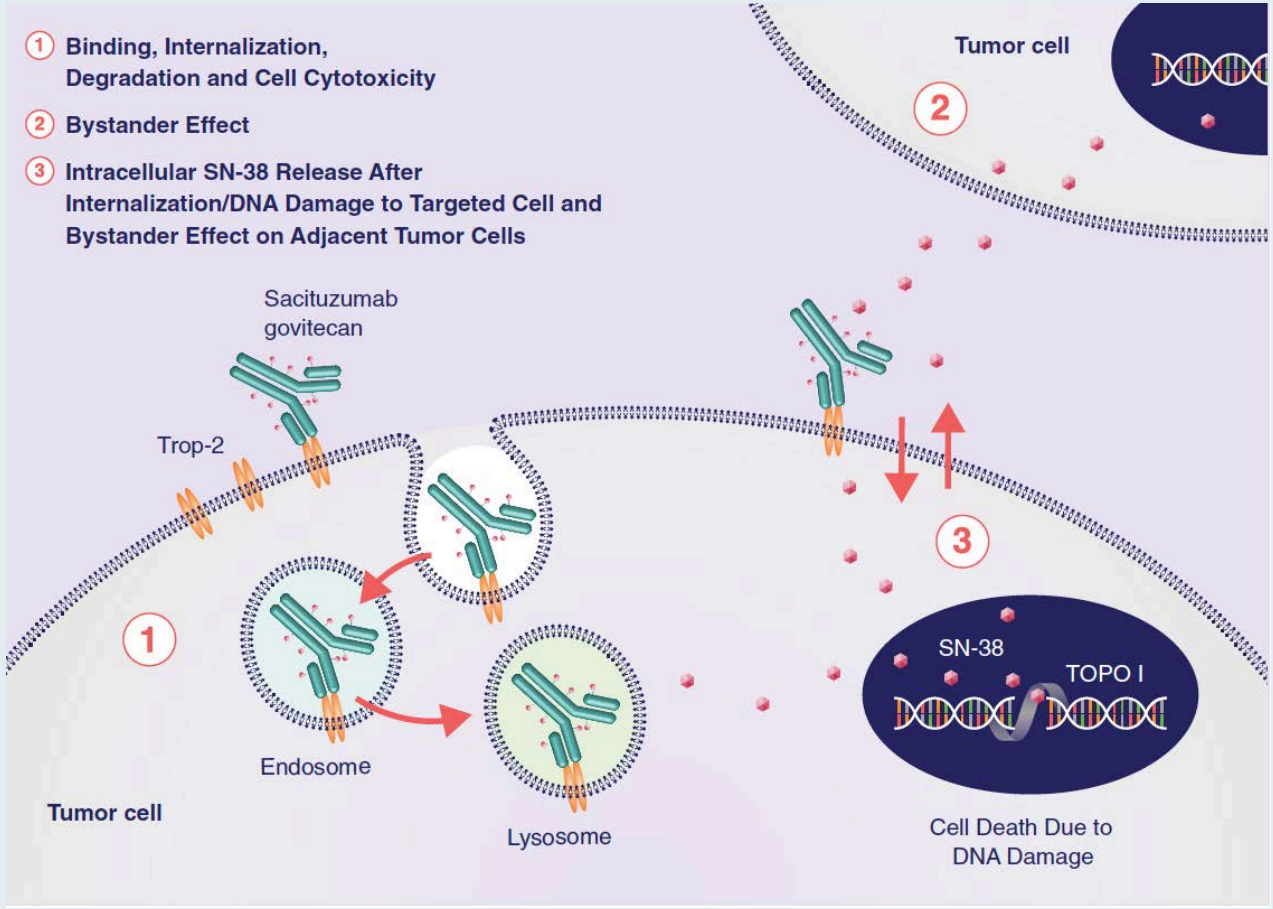
Efficacy and safety were evaluated in a multicenter, open-label, randomized trial (ASCENT; NCT02574455) conducted in 529 patients with unresectable locally advanced or mTNBC who had relapsed after at least two prior chemotherapies, one of which could be in the neoadjuvant or adjuvant setting, if progression occurred within 12 months. Patients were randomized (1:1) to receive sacituzumab govitecan, 10 mg/kg as an intravenous infusion, on days 1 and 8 of a 21-day (n = 267) cycle or physician's choice of single agent chemotherapy (n = 262)."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-regular-approval-sacituzumab-govitecan-triple-negative-breast-cancer

RTP RESEARCH TO PRACTICE

Sacituzumab Govitecan Is a First-in-Class TROP-2-Directed Antibody-Drug Conjugate





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

N Engl J Med 2021;384:1529-41.

The NEW ENGLAND JOURNAL of MEDICINE

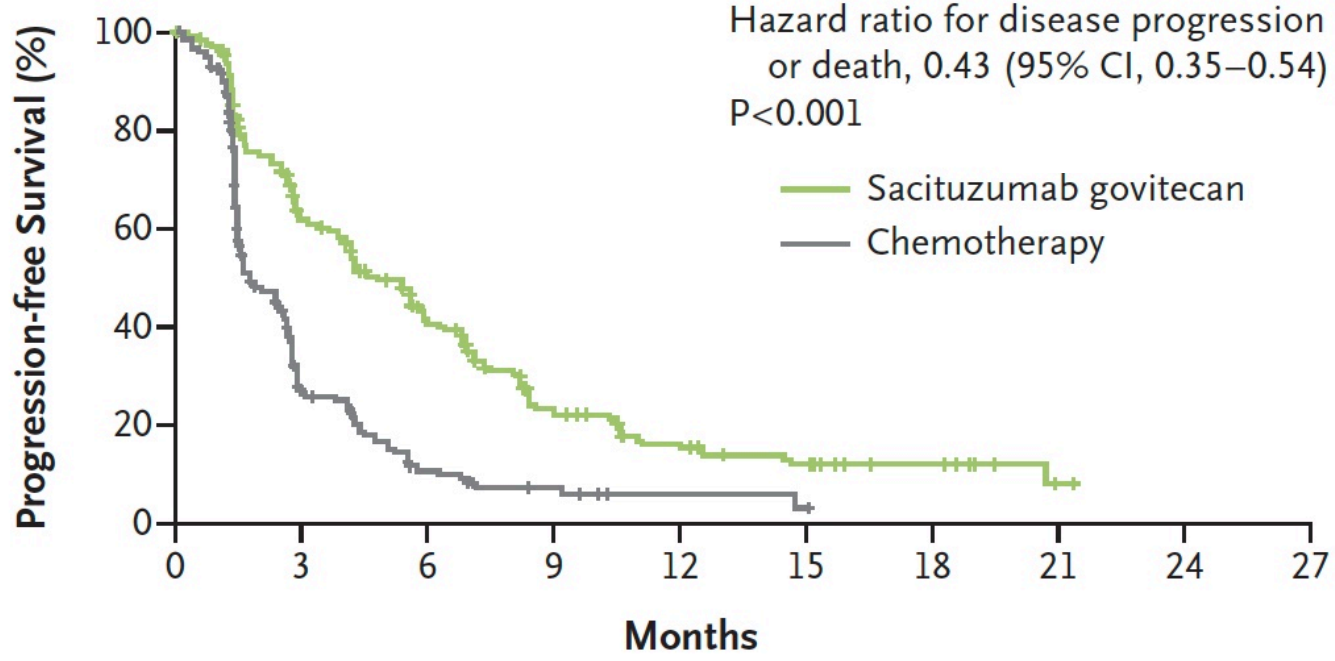
ORIGINAL ARTICLE

Sacituzumab Govitecan in Metastatic Triple-Negative Breast Cancer

A. Bardia, S.A. Hurvitz, S.M. Tolaney, D. Loirat, K. Punie, M. Oliveira, A. Brufsky, S.D. Sardesai, K. Kalinsky, A.B. Zelnak, R. Weaver, T. Traina, F. Dalenc, P. Aftimos, F. Lynce, S. Diab, J. Cortés, J. O'Shaughnessy, V. Diéras, C. Ferrario, P. Schmid, L.A. Carey, L. Gianni, M.J. Piccart, S. Loibl, D.M. Goldenberg, Q. Hong, M.S. Olivo, L.M. Itri, and H.S. Rugo, for the ASCENT Clinical Trial Investigators*

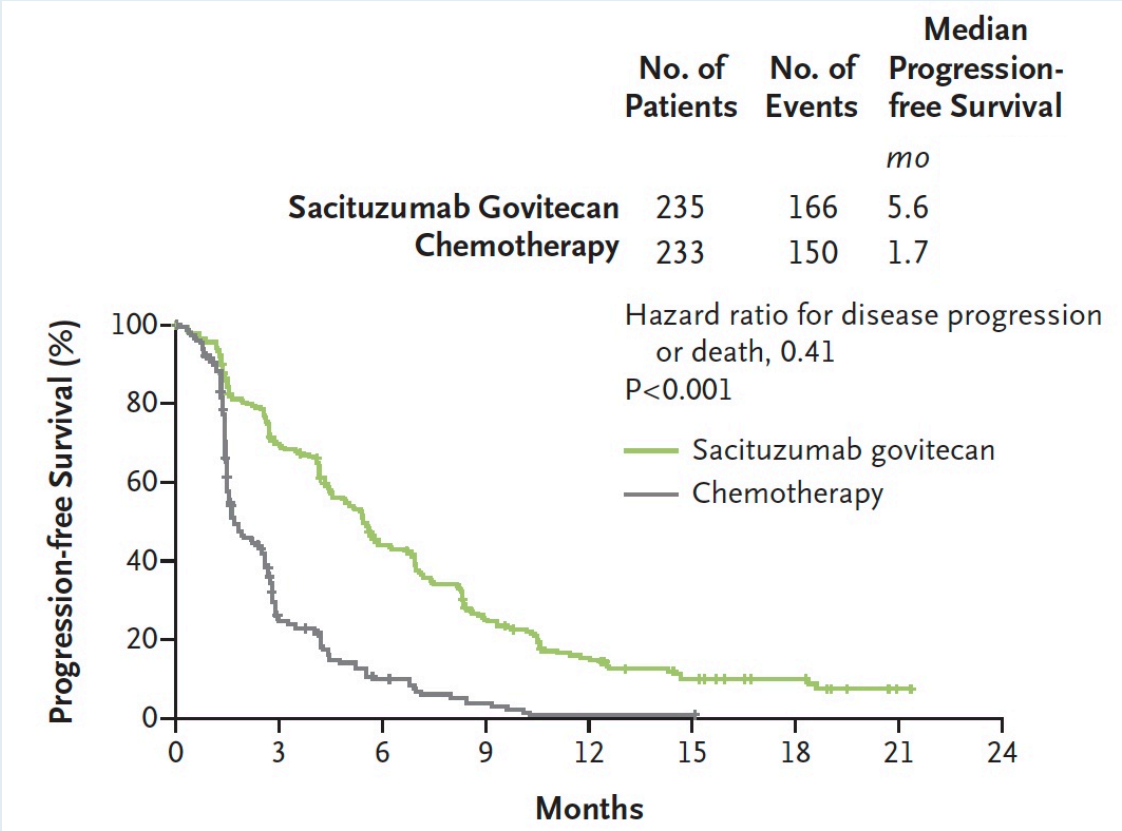
ASCENT: Progression-Free Survival (Overall Population)

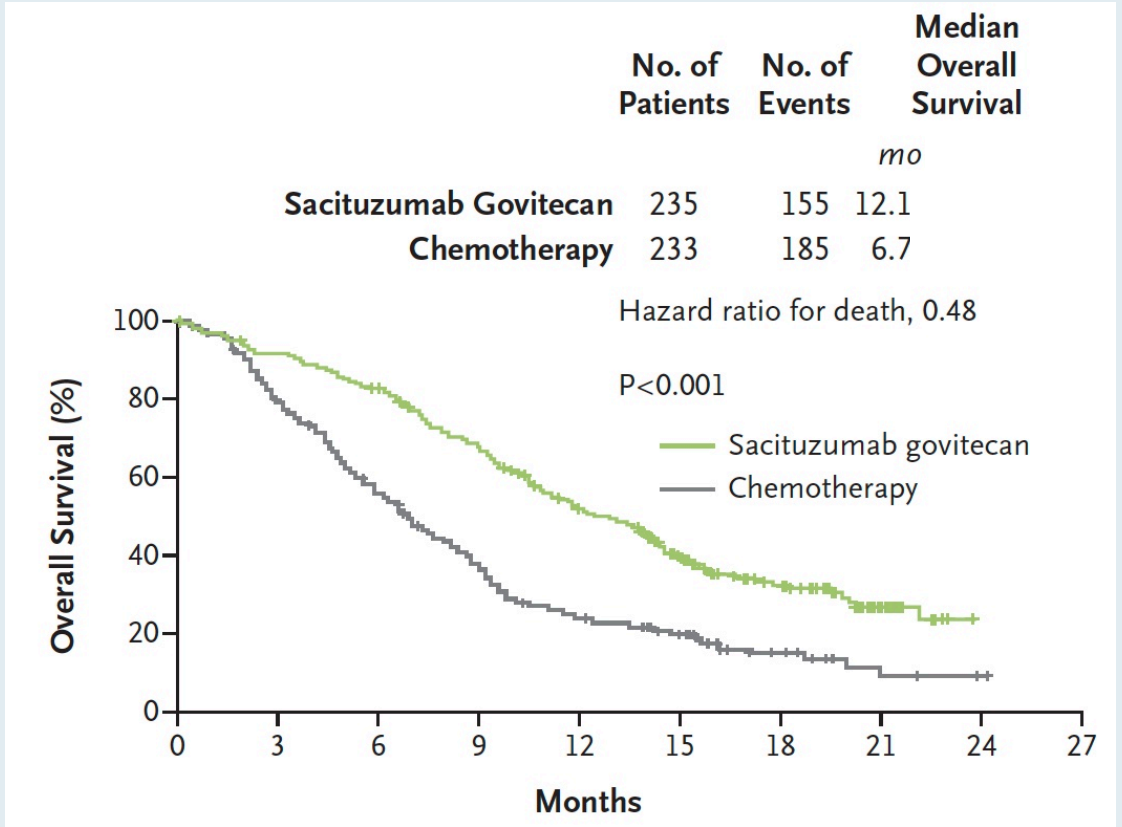
	No. of Patients	No. of Events	Median Progression-free Survival
			mo
Sacituzumab Govitecan	267	190	4.8
Chemotherapy	262	171	1.7



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

ASCENT: PFS and OS Among Patients without Brain Metastases





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

RTP RESEARCH TO PRACTICE

ASCENT: Selected Adverse Events

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

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

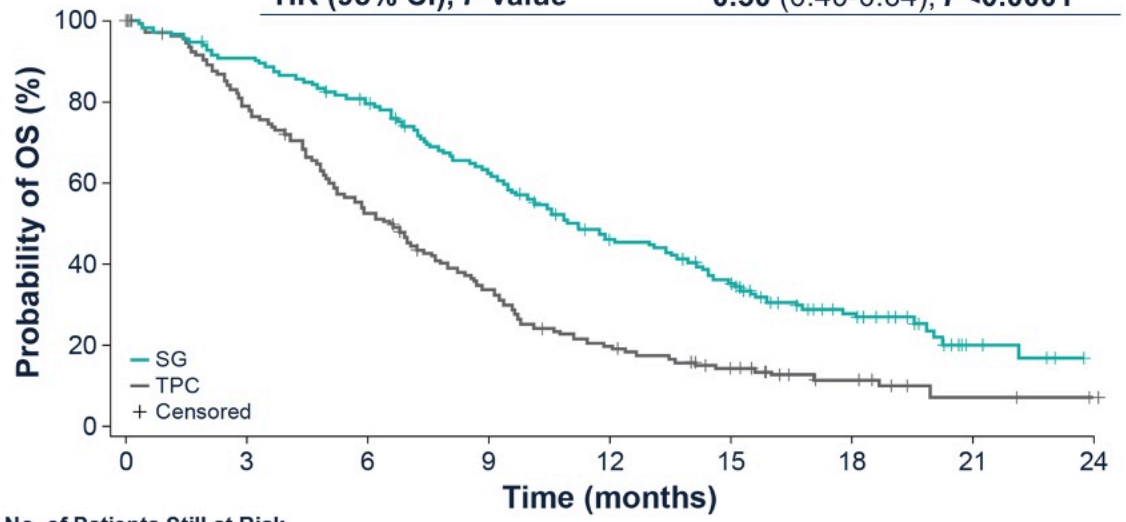
Outcomes in Patients (pts) Aged ≥65 Years in the Phase 3 ASCENT Study of Sacituzumab Govitecan (SG) in Metastatic Triple-Negative Breast Cancer (mTNBC)

Kalinsky K et al.

ASCO 2021;Abstract 1011.

ASCENT: Overall Survival for Young and Older Patients with mTNBC Treated with Sacituzumab Govitecan

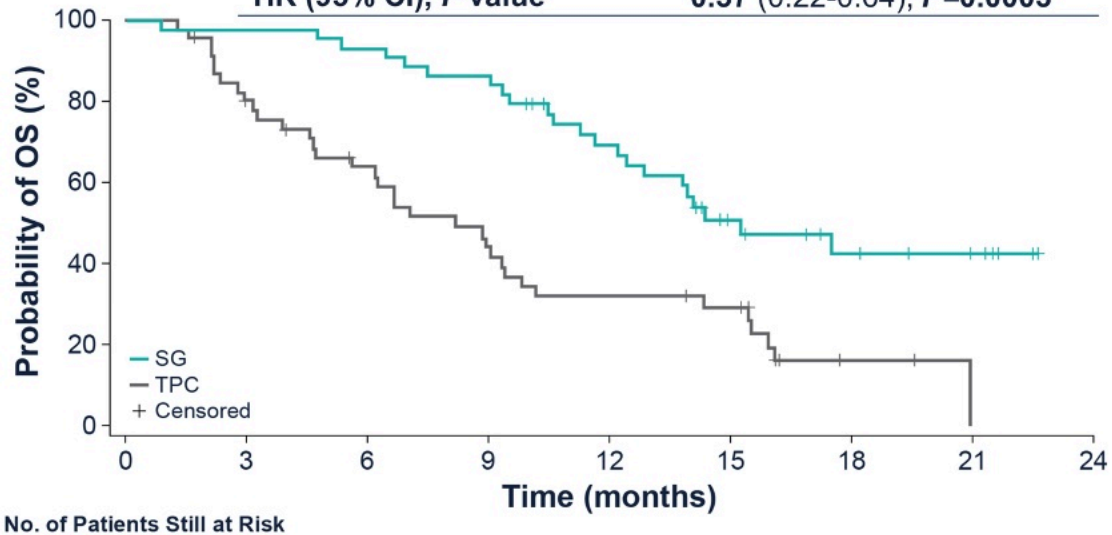
	<65 y	
	SG (n=191)	TPC (n=187)
No. of events	133	150
Median OS—mo (95% CI)	11.2 (9.9-13.4)	6.6 (5.3-7.4)
HR (95% CI), *P* value	**0.50** (0.40-0.64), ***P*<0.0001**	



No. of Patients Still at Risk

SG	191	185	177	171	163	155	149	135	123	115	102	89	80	77	68	56	40	32	28	22	14	7	6	1	0
TPC	187	168	157	138	125	106	91	77	66	56	42	37	32	28	25	19	14	11	9	5	3	3	3	2	1

	≥65 y	
	SG (n=44)	TPC (n=46)
No. of events	22	35
Median OS—mo (95% CI)	15.3 (12.4-NE)	8.2 (5.6-9.8)
HR (95% CI), *P* value	**0.37** (0.22-0.64), ***P*=0.0003**	



No. of Patients Still at Risk

SG	44	43	43	43	43	42	41	39	38	38	33	29	27	24	22	14	12	11	9	8	7	6	2	0
TPC	46	46	43	35	31	28	26	22	21	18	14	13	13	13	12	11	6	3	2	2	1	0	0	0

- In patients aged ≥65 years, improvement in median OS with SG vs TPC treatment was comparable with that of the overall population (12.1 vs 6.7 months)[1]

Kalinsky K et al. ASCO 2021;Abstract 1011.

RTP RESEARCH TO PRACTICE

San Antonio Breast Cancer Symposium 2020;Abstract GS3-06

Biomarker Evaluation in the Phase 3 ASCENT Study of Sacituzumab Govitecan Versus Chemotherapy in Patients With Metastatic Triple-Negative Breast Cancer

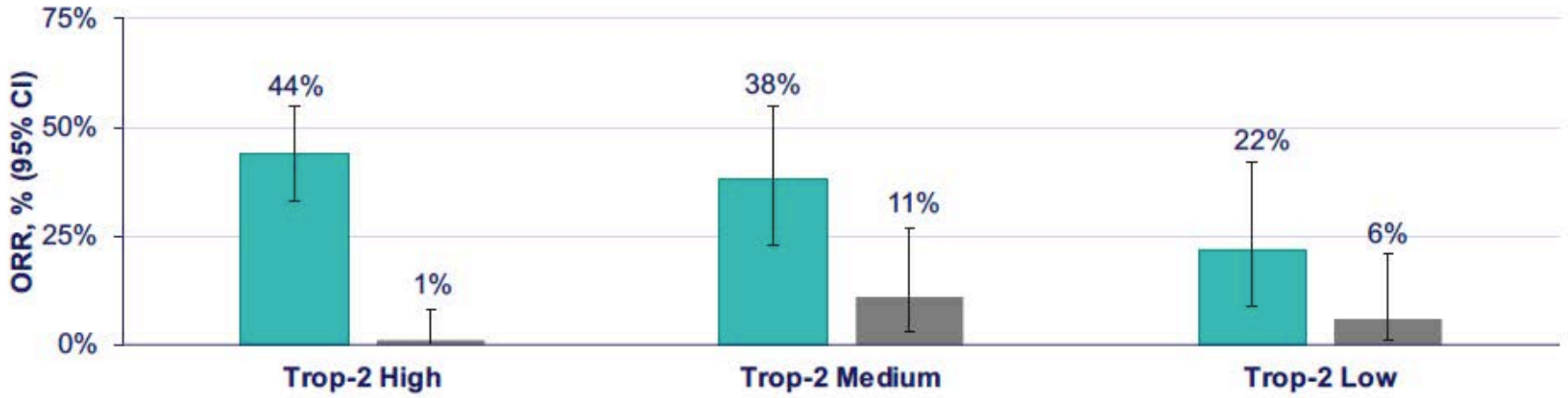
Sara A. Hurvitz,[1] Sara M. Tolaney,[2] Kevin Punie,[3] Delphine Loirat,[4] Mafalda Oliveira,[5] Kevin Kalinsky,[6] Amelia Zelnak,[7] Philippe Aftimos,[8] Florence Dalenc,[9] Sagar Sardesai,[10] Erika Hamilton,[11] Priyanka Sharma,[12] Sabela Recalde,[13] Eva Ciruelos Gil,[14] Tiffany Traina,[15] Joyce O'Shaughnessy,[16] Javier Cortes,[17] Michaela Tsai,[18] Linda Vahdat,[19] Véronique Diéras,[20] Lisa Carey,[21] Hope S. Rugo,[22] David M. Goldenberg,[23] Quan Hong,[23] Martin Olivo,[23] Loretta M. Itri,[23] and Aditya Bardia[24]

[1]Medical Oncology, University of California, Los Angeles, Jonsson Comprehensive Cancer Center, Los Angeles, CA, USA; [2]Dana-Farber Cancer Institute, Boston, MA, USA; [3]Department of General Medical Oncology, University Hospitals Leuven, Leuven, Belgium; [4]Institut Curie, Paris, France; [5]Hospital Universitari Vall d'Hebron, Barcelona, Spain; [6]Winship Cancer Institute, Emory University, Atlanta, GA, USA; [7]Northside Hospital, Atlanta, GA, USA; [8]Institut Jules Bordet, Brussels, Belgium; [9]Institut Claudius Regaud, Toulouse, France; [10]The Ohio State University Wexner Medical Center, Columbus, OH, USA; [11]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN, USA; [12]University of Kansas Cancer Center - The Richard and Annette Bloch Cancer Care Pavilion, Kansas City, KS, USA; [13]Institut Catala d'Oncologia Hospitalet, Barcelona, Spain; [14]Hospital Universitario 12 de Octubre, Madrid, Spain; [15]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [16]Texas Oncology - Baylor Charles A. Sammons Cancer Center, Dallas, TX, USA; [17]IOB Institute of Oncology, Quiron Group, Madrid & Barcelona, Spain; [18]VPCI Oncology Research, Minneapolis, MN, USA; [19]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [20]Centre Eugène-Marquis, Rennes, France; [21]University of North Carolina Lineberger Comprehensive Cancer Center, Chapel Hill, NC, USA; [22]University of California San Francisco Comprehensive Cancer Center, San Francisco, CA, USA; [23]Immunomedics, Morris Plains, NJ, USA; and [24]Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

To obtain presentation, https://bit.ly/2020hurvitzgs3-06

ClinicalTrials.gov Number: NCT02574455

ORR by Trop-2 Expression



	Trop-2 High H-score: 200-300 (n=157)		Trop-2 Medium H-score: 100-200 (n=74)		Trop-2 Low H-score: <100 (n=59)	
	SG (n=85)	TPC (n=72)	SG (n=39)	TPC (n=35)	SG (n=27)	TPC (n=32)
ORR—% (no.)	44% (37)	1% (1)	38% (15)	11% (4)	22% (6)	6% (2)
95% CI	33-55	0-8	23-55	3-27	9-42	1-21

Assessed in the brain metastases-negative population. ORR and PFS are assessed by BICR. Trop-2 expression determined in archival samples by validated immunohistochemistry assay and H-scoring.
BICR, blind independent central review; H-score, histochemical-score; ORR, objective response rate; SG, sacituzumab govitecan; TPC, treatment of physician's choice; Trop-2, trophoblast cell surface antigen-2.

Hurvitz SA et al. SABCS 2020;Abstract GS3-06.

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

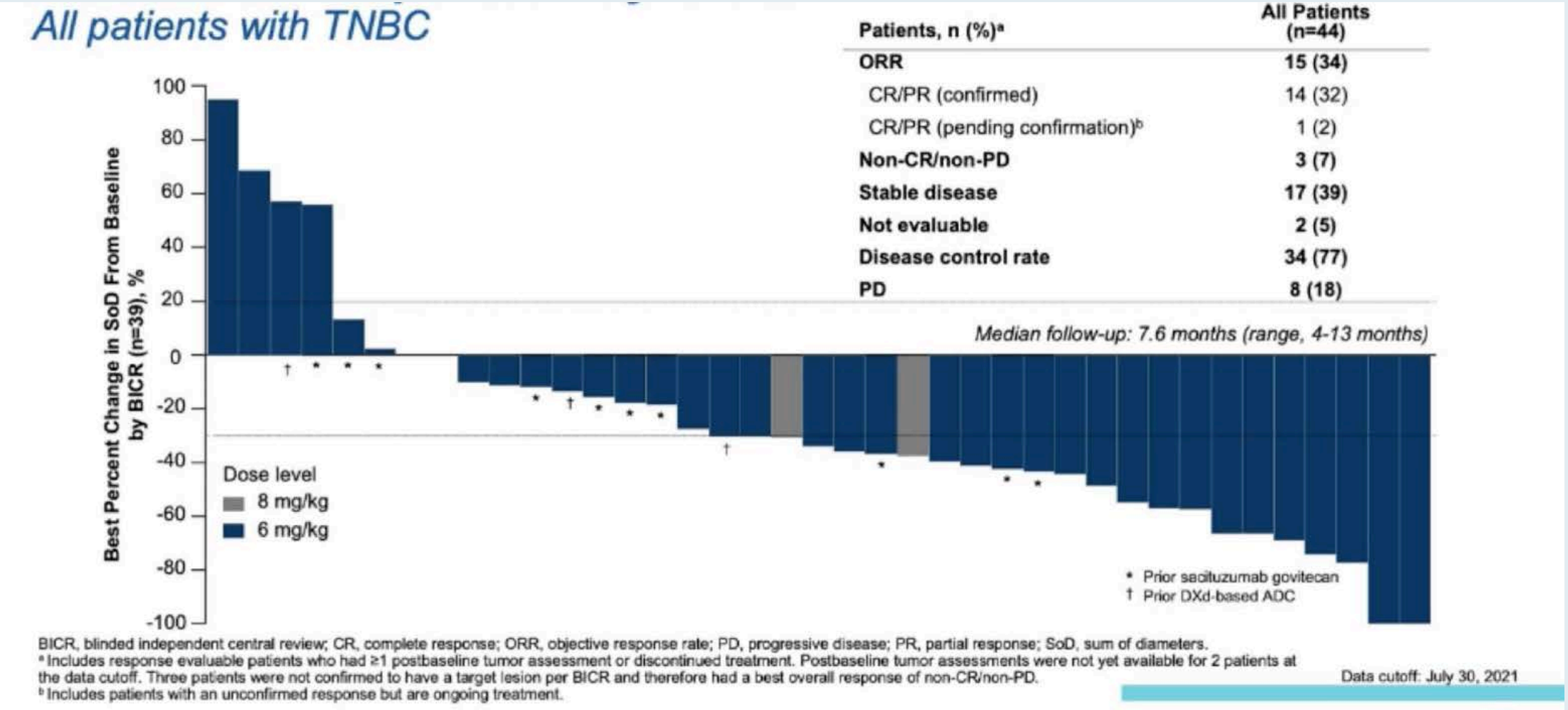
Datopotamab Deruxtecan (Dato-DXd) in Advanced/Metastatic HER2 Negative Breast Cancer: Triple Negative Breast Cancer Results from the Phase 1 TROPION-PanTumor01 Study

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

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

Abstract GS1-05

TROPION-PanTumor01: Antitumor Response in 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)**

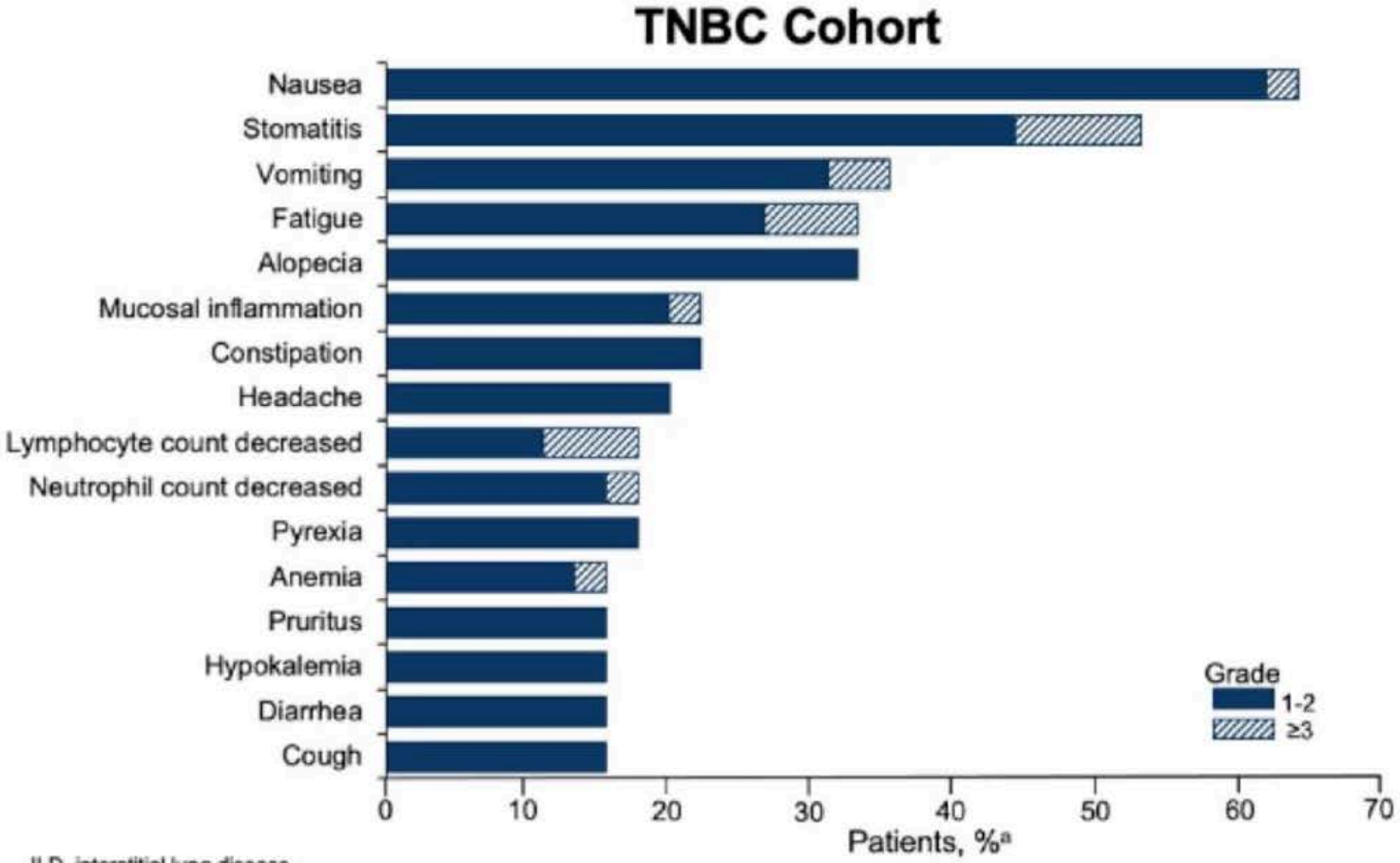
BICR, blinded independent central review; CR, complete response; ORR, objective response rate; PD, progressive disease; PR, partial response; SoD, sum of diameters.
[a] Includes response evaluable patients who had ≥1 postbaseline tumor assessment or discontinued treatment. Postbaseline tumor assessments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

Thank you for joining us!

CME and MOC 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 North Carolina Oncology Association and the South Carolina Oncology Society

A CME/MOC- and NCPD-Accredited Event

Saturday, February 12, 2022
8:30 AM – 4:00 PM ET

RTP
RESEARCH
TO PRACTICE

Agenda

Module 1 — Chronic Lymphocytic Leukemia and Lymphomas: *Drs Flinn and LaCasce*

Module 2 — Multiple Myeloma: *Drs Callander and Rajkumar*

Module 3 — Genitourinary Cancers: *Drs Dreicer and Heath*

Module 4 — Breast Cancer: *Drs Borges and Jhaveri*

Module 5 — Gastrointestinal Cancers: *Drs Hochster and Messersmith*

Module 6 — Lung Cancer: *Drs Govindan and Johnson*

Gastrointestinal Cancers Faculty

Howard S Hochster, MD
Distinguished Professor of Medicine
Rutgers Robert Wood Johnson Medical School
Rutgers-CINJ Associate Director, Clinical Research
Director, Clinical Oncology Research
RWJBarnabas Health System
New Brunswick, New Jersey

Wells A Messersmith, MD
Chief Medical Officer, Cancer Center
Associate Director of Clinical Services
University of Colorado Cancer Center
Aurora, Colorado

RTP
RESEARCH
TO PRACTICE

MODULE 5: Gastrointestinal Cancers

Co-Moderator

Nasfat Shehadeh, MD
Medical Oncologist
Oncology Specialists of Charlotte, PA
Charlotte, North Carolina

Contributing General Medical Oncologists

Jennifer L Dallas, MD
Novant Health Cancer Institute
Charlotte, North Carolina

Joanna Metzner-Sadurski, MD
Self Regional Healthcare Cancer Center
Greenwood, South Carolina

Justin Peter Favaro, MD, PhD
Oncology Specialists of Charlotte
Charlotte, North Carolina

William R Mitchell, MD
Southern Oncology Specialists
Charlotte, North Carolina

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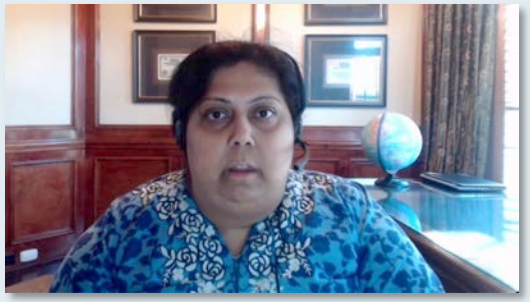
Contributing General Medical Oncologists



Niyati A Nathwani, MD
Carolina Blood and Cancer Care Associates
Charlotte, North Carolina

Nasfat Shehadeh, MD
Oncology Specialists of Charlotte, PA
Charlotte, North Carolina

Julia Saylors, MD
Charleston Oncology
North Charleston, South Carolina

RTP RESEARCH TO PRACTICE

Agenda

Module 1: Gastric and Gastroesophageal Cancers

Module 2: Hepatocellular Cancer

Module 3: Biliary Tract Cancers

Module 4: Colorectal Cancer

Module 5: Pancreatic Adenocarcinoma

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RESEARCH
TO PRACTICE

Agenda

Module 1: Gastric and Gastroesophageal Cancers

Module 2: Hepatocellular Cancer

Module 3: Biliary Tract Cancers

Module 4: Colorectal Cancer

Module 5: Pancreatic Adenocarcinoma

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RESEARCH
TO PRACTICE

- CheckMate 577: Adjuvant nivolumab in resect esophageal/GEJ cancers
- KEYNOTE-590:

FDA Approves Nivolumab for Resected Esophageal or GEJ Cancer

Press Release – May 20, 2021

"The Food and Drug Administration approved nivolumab for patients with completely resected esophageal or gastroesophageal junction (GEJ) cancer with residual pathologic disease who have received neoadjuvant chemoradiotherapy.

Efficacy was evaluated in CHECKMATE-577 (NCT02743494), a randomized, multicenter, double-blind trial in 794 patients with completely resected (negative margins) esophageal or GEJ cancers who had residual pathologic disease following concurrent chemoradiotherapy. Patients were randomized (2:1) to receive either nivolumab 240 mg or placebo every 2 weeks for 16 weeks followed by 480 mg of nivolumab or placebo every 4 weeks beginning at week 17 for up to one year of treatment.

The recommended nivolumab dose for adjuvant treatment of resected esophageal or GEJ cancer is 240 mg every 2 weeks or 480 mg every 4 weeks for a total treatment duration of 1 year. Both doses are administered as 30-minute intravenous infusions."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-nivolumab-resected-esophageal-or-gej-cancer

2021 ASCO ANNUAL MEETING

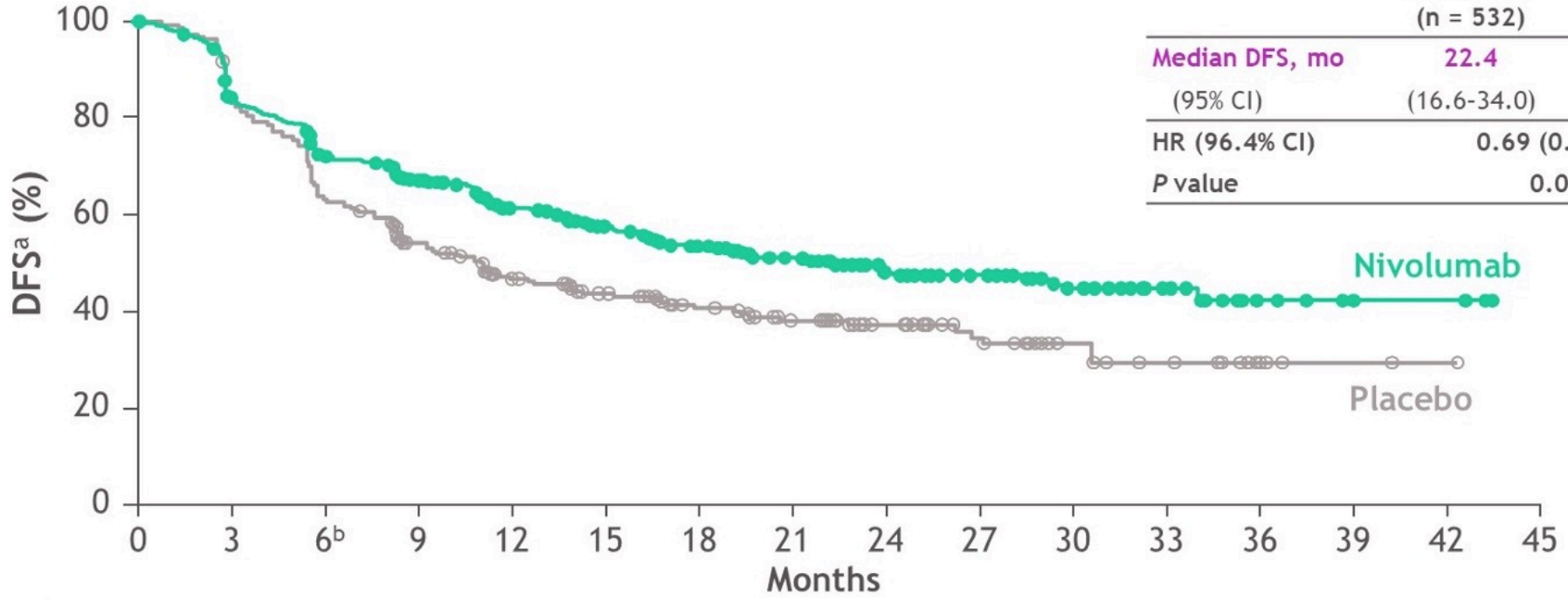
Adjuvant nivolumab in resected esophageal or gastroesophageal junction cancer following neoadjuvant chemoradiotherapy: expanded efficacy and safety analyses from CheckMate 577

Ronan J. Kelly,[1] Jaffer A. Ajani,[2] Jaroslaw Kuzdzal,[3] Thomas Zander,[4] Eric Van Cutsem,[5] Guillaume Piessen,[6] Guillermo Mendez,[7] Josephine Feliciano,[8] Satoru Motoyama,[9] Astrid Lièvre,[10] Hope Uronis,[11] Elena Elimova,[12] Cecile Grootscholten,[13] Karen Geboes,[14] Jenny Zhang,[15] Samira Soleymani,[15] Ming Lei,[15] Prianka Singh,[15] James M. Cleary,[16] Markus Moehler[17]

[1]The Charles A. Sammons Cancer Center at Baylor University Medical Center, Dallas, TX; [2]The University of Texas MD Anderson Cancer Center, Houston, TX; [3]Jagiellonian University, John Paul II Hospital, Cracow, Poland; [4]University Hospital of Cologne, Cologne, Germany; [5]University Hospitals Gasthuisberg, Leuven and KULeuven, Leuven, Belgium; [6]University of Lille, Claude Huriez University Hospital, Lille, France; [7]Fundacion Favaloro, Buenos Aires, Argentina; [8]Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD; [9]Akita University Hospital, Akita, Japan; [10]CHU Pontchaillou, Rennes 1 University, Rennes, France; [11]Duke Cancer Institute, Durham, NC; [12]Princess Margaret Cancer Centre, Toronto, ON, Canada; [13]Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; [14]UZ Gent, Gent, Belgium; [15]Bristol Myers Squibb, Princeton, NJ; [16]Dana Farber Cancer Institute, Boston, MA; [17]Johannes-Gutenberg University Clinic, Mainz, Germany

Abstract number 4003

CheckMate 577: Disease-Free Survival (DFS)



	Nivolumab (n = 532)	Placebo (n = 262)
Median DFS, mo	22.4	11.0
(95% CI)	(16.6-34.0)	(8.3-14.3)
HR (96.4% CI)	0.69 (0.56-0.86)	
P value	0.0003[c]	

No. at risk																
Nivolumab	532	430	364	306	249	212	181	147	92	68	41	22	8	4	3	0
Placebo	262	214	163	126	96	80	65	53	38	28	17	12	5	2	1	0

- Nivolumab provided superior DFS with a 31% reduction in the risk of recurrence or death and a doubling in median DFS versus placebo

Kelly RJ et al. ASCO 2021;Abstract 4003.

FDA Approves Pembrolizumab in Combination with Chemotherapy for Esophageal or GEJ Carcinoma

Press Release – March 22, 2021

"The Food and Drug Administration approved pembrolizumab in combination with platinum and fluoropyrimidine-based chemotherapy for patients with metastatic or locally advanced esophageal or gastroesophageal (GEJ) (tumors with epicenter 1 to 5 centimeters above the gastroesophageal junction) carcinoma who are not candidates for surgical resection or definitive chemoradiation.

Efficacy was evaluated in KEYNOTE-590 (NCT03189719), a multicenter, randomized, placebo-controlled trial that enrolled 749 patients with metastatic or locally advanced esophageal or gastroesophageal junction carcinoma who were not candidates for surgical resection or definitive chemoradiation.

The recommended pembrolizumab dose for esophageal cancer is 200 mg every 3 weeks or 400 mg every 6 weeks."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-pembrolizumab-esophageal-or-gej-carcinoma

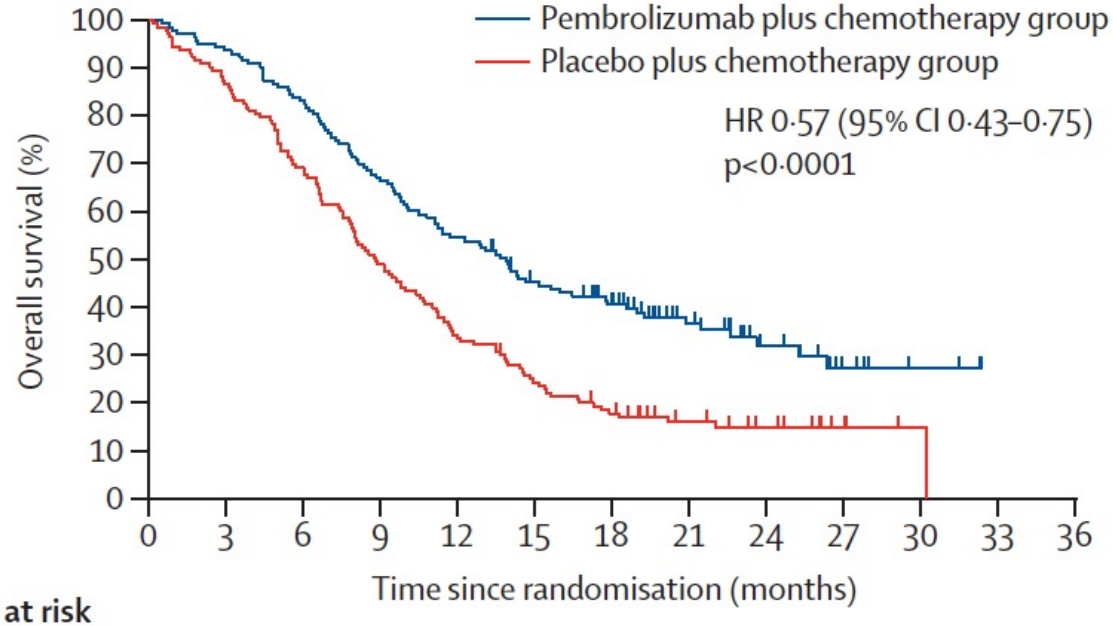
Lancet 2021;398(10302):759-71.

Pembrolizumab plus chemotherapy versus chemotherapy alone for first-line treatment of advanced oesophageal cancer (KEYNOTE-590): a randomised, placebo-controlled, phase 3 study

*Jong-Mu Sun, Lin Shen, Manish A Shah, Peter Enzinger, Antoine Adenis, Toshihiko Doi, Takashi Kojima, Jean-Philippe Metges, Zhigang Li, Sung-Bae Kim, Byoung Chul Cho, Wasat Mansoor, Shau-Hsuan Li, Patrapim Sunpaweravong, Maria Alsina Maqueda, Eray Goekkurt, Hiroki Hara, Luis Antunes, Christos Fountzilas, Akihito Tsuji, Victor Castro Oliden, Qi Liu, Sukrut Shah, Pooja Bhagia, Ken Kato, on behalf of the KEYNOTE-590 Investigators**

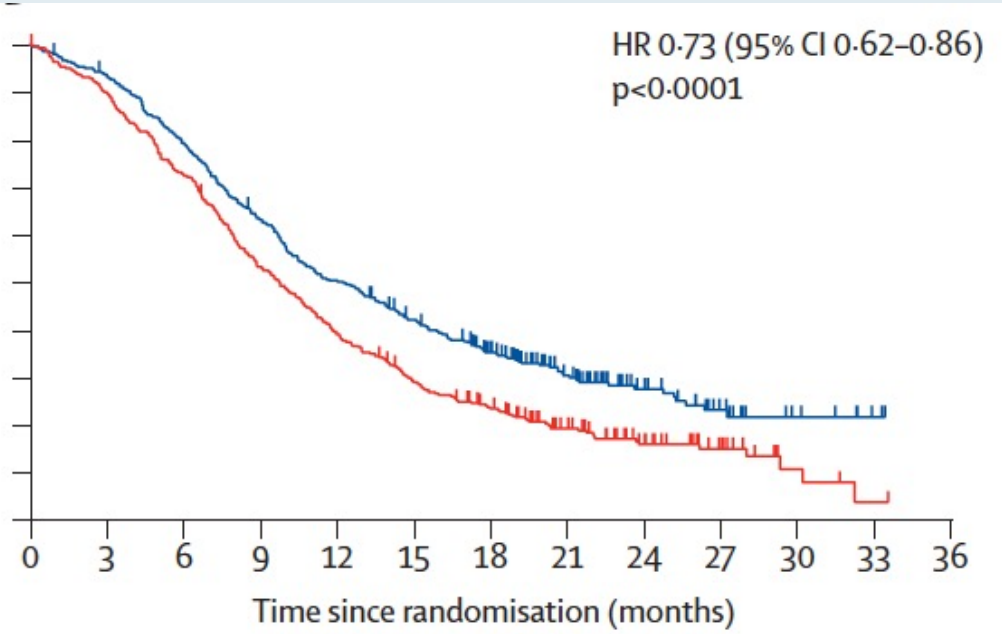
KEYNOTE-590: Overall Survival (OS)

PD-L1 Combined Positive Score (CPS) ≥10



Number at risk (number censored)													
Pembrolizumab plus chemotherapy group	143 (0)	134 (0)	119 (0)	96 (0)	78 (0)	61 (4)	51 (8)	29 (25)	16 (35)	7 (42)	3 (46)	0 (49)	0 (49)
Placebo plus chemotherapy group	143 (0)	124 (0)	99 (0)	70 (0)	48 (0)	34 (1)	24 (2)	15 (9)	10 (13)	4 (19)	1 (22)	0 (22)	0 (22)

All Randomized Patients



	373 (0)	348 (2)	295 (2)	235 (3)	187 (3)	151 (9)	118 (17)	68 (54)	36 (81)	17 (95)	7 (104)	2 (109)	0 (111)
	376 (0)	338 (1)	274 (1)	200 (2)	147 (2)	108 (5)	82 (11)	51 (28)	28 (44)	15 (56)	4 (65)	1 (66)	0 (67)

Sun JM et al. *Lancet* 2021;398(10302):759-71.

RTP RESEARCH TO PRACTICE

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

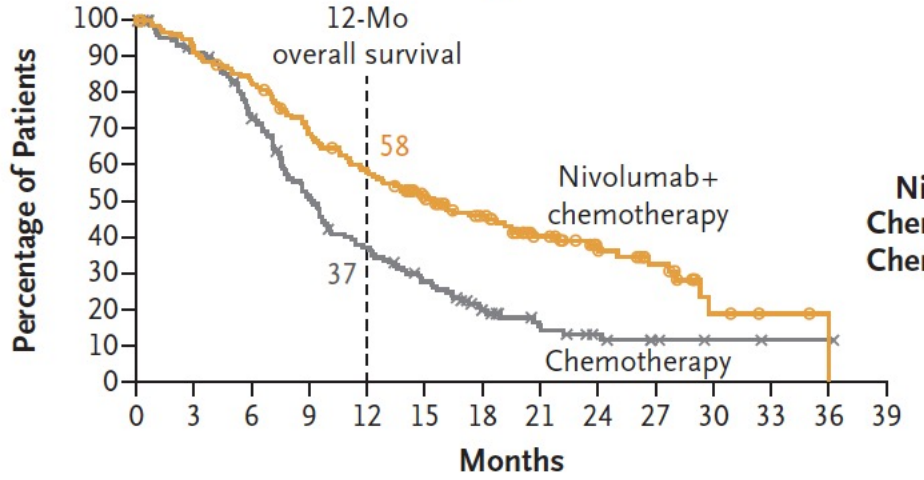
Nivolumab Combination Therapy in Advanced Esophageal Squamous-Cell Carcinoma

Y. Doki, J.A. Ajani, K. Kato, J. Xu, L. Wyrwicz, S. Motoyama, T. Ogata, H. Kawakami, C.-H. Hsu, A. Adenis, F. El Hajbi, M. Di Bartolomeo, M.I. Braghiroli, E. Holtved, S.A. Ostoich, H.R. Kim, M. Ueno, W. Mansoor, W.-C. Yang, T. Liu, J. Bridgewater, T. Makino, I. Xynos, X. Liu, M. Lei, K. Kondo, A. Patel, J. Gricar, I. Chau, and Y. Kitagawa, for the CheckMate 648 Trial Investigators*

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

CheckMate 648: OS for Patients with PD-L1 ≥1% (Primary Endpoint with PFS in PD-L1 ≥1%) and in Overall Population

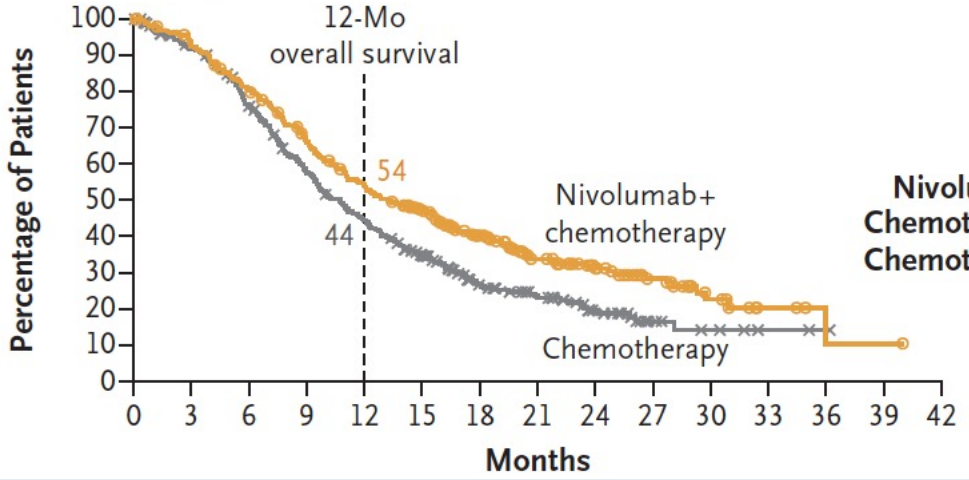
Overall Survival in Patients with Tumor-Cell PD-L1 Expression of ≥1%



	No. of Patients	Median Overall Survival (95% CI)
		mo
Nivolumab+ Chemotherapy	158	15.4 (11.9–19.5)
Chemotherapy	157	9.1 (7.7–10.0)

Hazard ratio for death, 0.54
(99.5% CI, 0.37–0.80)
P<0.001

Overall Survival in the Overall Population



	No. of Patients	Median Overall Survival (95% CI)
		mo
Nivolumab+ Chemotherapy	321	13.2 (11.1–15.7)
Chemotherapy	324	10.7 (9.4–11.9)

Hazard ratio for death, 0.74
(99.1% CI, 0.58–0.96)
P=0.002

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

RTP RESEARCH TO PRACTICE

2021 ESMO congress

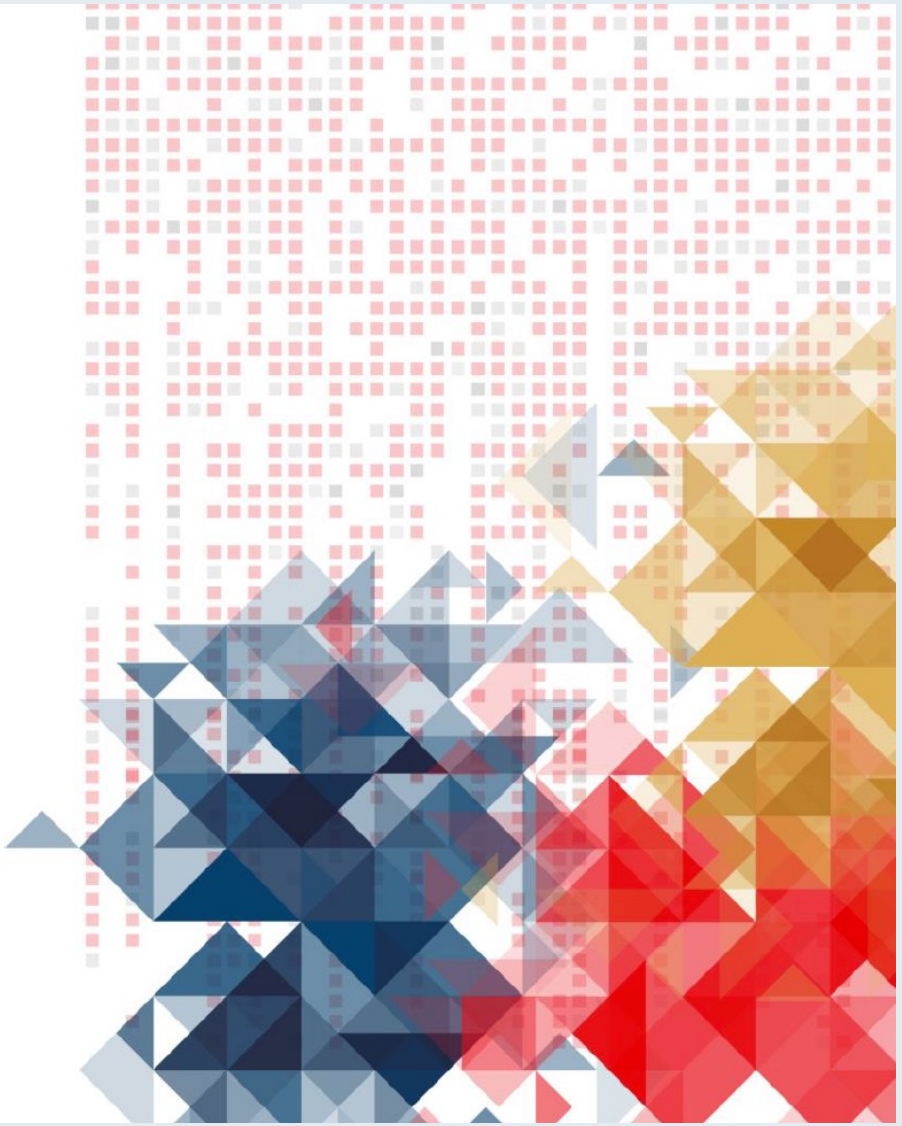
JUPITER-06:

A Randomized, Double-blind, Phase 3 Study of Toripalimab versus Placebo In Combination with First-Line Chemotherapy for Treatment Naive Advanced or Metastatic Esophageal Squamous Cell Carcinoma (ESCC)

R.-H. Xu[1], F. Wang[1], C. Cui[2], J. Yao[3], Y. Zhang[4], G. Wang[5], J. Feng[6], S. Yang[7], Y. Fan[8], J. Shi[9], X.Zhang[10], L. Shen[11], Y.Shu[12], C. Wang[13], T. Dai[14], T. Mao[15], L. Chen[16], Z. Guo[17], B. Liu[18], H. Pan[19], Coherus Biosciences and Shanghai Junshi Biosciences.

[1]Department of Medical Oncology, Sun Yat-Sen University Cancer Center; State Key Laboratory of Oncology in South China; Collaborative Innovation Center of Cancer Medicine, Guangzhou, China; [2]Medical Oncology, Cancer Hospital Chinese Academy of Medical Sciences, Beijing, China, [3]Medical Oncology, The First Affiliated Hospital of Henan University of Science and Technology, Luoyang, China, [4]Gastroenterology, Harbin Medical University Cancer Hospital, Harbin, China, [5]MedicalOncology, Army Medical Center of PLA, Chongqing, China, [6]Medical Oncology Department, Jiangsu Cancer Hospital, Nanjing, China, [7]Department of Internal Medicine, Henan Cancer Hospital & Affiliated Cancer Hospital of Zhengzhou University, Zhengzhou, China, [8]Department of Medical Oncology, Zhejiang Cancer Hospital, Hangzhou, China,[9]Medical Oncology, Linyi Cancer Hospital, Linyi, China, [10]Medical Oncology, The Northern Jiangsu People's Hospital, Yangzhou, China, [11]Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education), Peking University Cancer Hospital and Institute, Beijing, China, [12]Cancer Center, Jiangsu Province Hospital, The First Affiliated Hospital of Nanjing Medical University, Nanjing, China, [13]Medical Oncology, Zhongda Hospital Southeast University, Nanjing, China, [14]Medical Oncology, The Affiliated Hospital of Southwest Medical University, Luzhou, China, [15]Medical Oncology, Shanghai Chest Hospital, Shanghai, China, [16]Medical Oncology, Guangxi Medical University Affiliated Tumor Hospital, Nanning, China, [17]Medical Oncology, Fujian Cancer Hospital, Fuzhou, China,[18]Medical Oncology, Shandong Cancer Hospital, Jinan, China, [19]Medical Oncology, Sir Run Run Shaw Hospital, Zhejiang University, Hangzhou, China

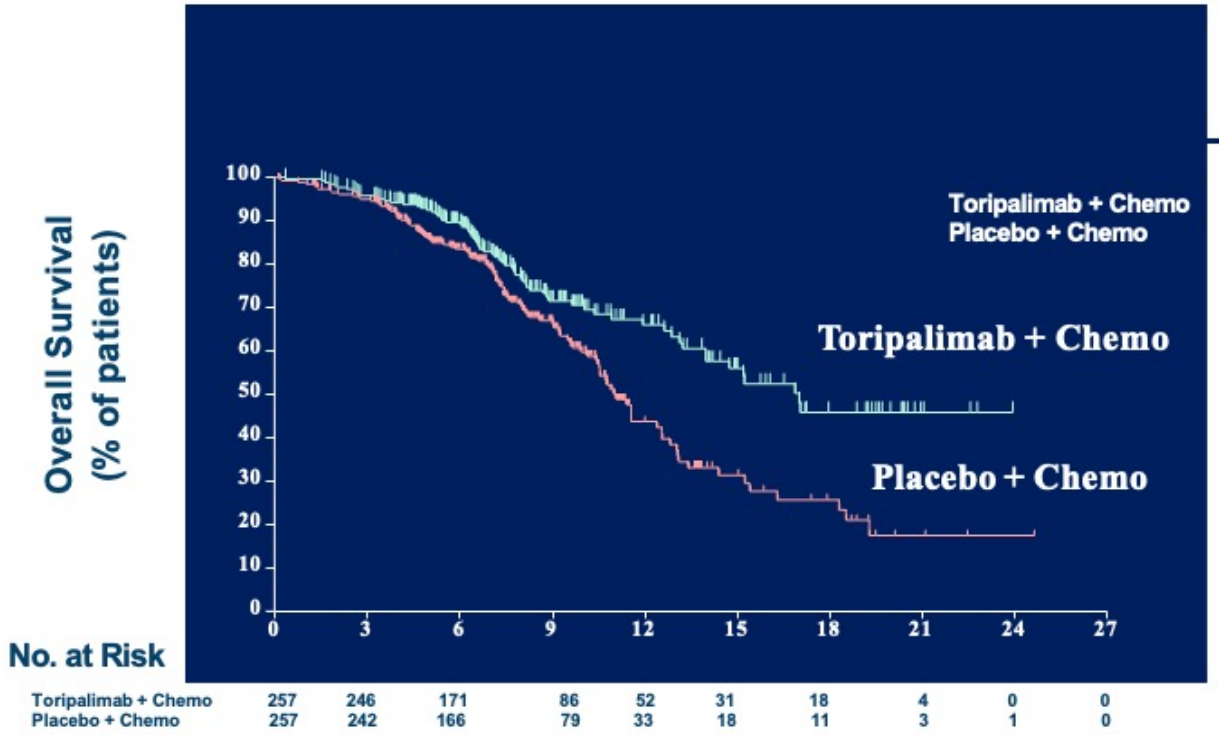
Presented by Feng Wang MD, PhD at 2021 ESMO Annual Meeting



Abstract 1373MO

RTP RESEARCH TO PRACTICE

JUPITER-06: OS with Toripalimab and Chemotherapy in Advanced or Metastatic Esophageal Squamous Cell Carcinoma (ESCC)



No. of Deaths/ Total No. of Patients	Median Overall Survival (95% CI) *mo*	1-Yr Overall Survival Rate % (95% CI)	2-Yr Overall Survival Rate % (95% CI)
70/257	**17.0 (14.0, NE)**	**66.0 (57.5, 73.2)**	**NE (NE, NE)**
103/257	11.0 (10.4, 12.6)	43.7 (34.4, 52.6)	17.5 (8.7, 28.9)

Stratified HR for death,

0.58 (95% CI 0.425, 0.783);
P=0.00036

PD-L1 expression subgroups:

CPS ≥ 1: 15.2 vs. 10.9 months, HR=0.61 (95%CI 0.435, 0.870)

CPS < 1: NE vs. 11.6 months, HR=0.61 (95%CI 0.297, 1.247)

Wang F et al. ESMO 2021;Abstract 1373MO.

RTP RESEARCH TO PRACTICE

2021 ESMO congress

Sintilimab plus chemotherapy versus chemotherapy as first-line therapy in patients with advanced or metastatic esophageal squamous cell cancer: First Results of the Phase 3 ORIENT-15 study

Lin Shen[1], Zhihao Lu[2], Junye Wang[3], Yongqian Shu[4], Li Kong[5], Lei Yang[6], Buhai Wang[7], Zhiwu Wang[8], Yinghua Ji[9], Guochun Cao[10], Hu Liu[11], Tongjian Cui[12], Na Li[13], Wensheng Qiu[14], Zhuo Ma[15], Yuling Chen[15], Haoyu Li[15], Xing Sun[15], Yan Wang[15], Hui Zhou[15]

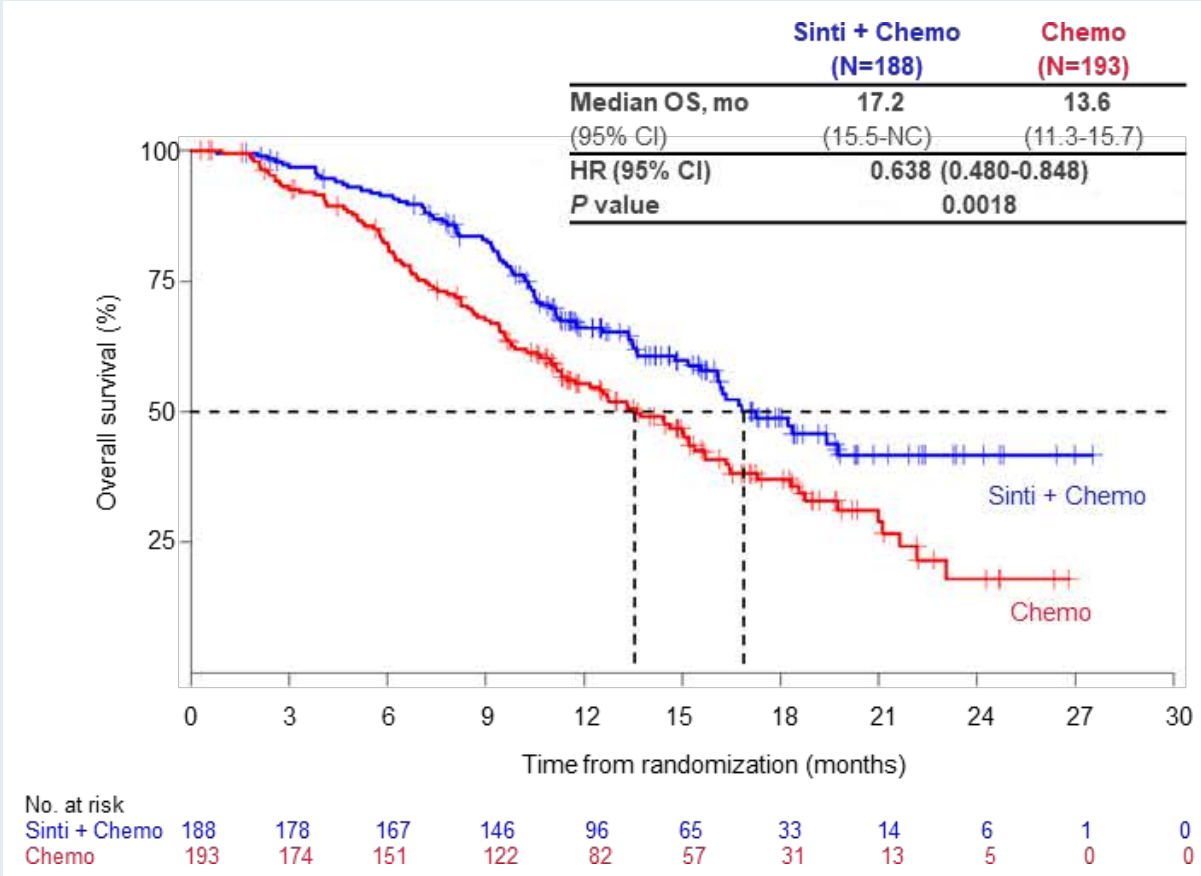
[1]Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education), Peking University Cancer Hospital and Institute, Beijing, China, [2]Department of Gastrointestinal Oncology, Peking University Cancer Hospital & Institute, Beijing, China, [3]Department of Oncology, The Affiliated Hospital of Jining Medical College, Jining, China, [4]Department of Medical Oncology, The First Affiliated Hospital of Nanjing Medical University, Nanjing, China, [5]Special Needs Ward, Shandong Cancer Hospital and Institute, Shandong First Medical University and Shandong Academy of Medical Sciences, Jinan, China, [6]Department of Medical Oncology, Nantong Cancer Hospital, Nantong, China, [7]Department of Medical Oncology, Northern Jiangsu People's Hospital, Affiliated Hospital to Yangzhou University, Yangzhou, China, [8]Department of Radiotherapy and Chemotherapy, Tangshan People Hospital, Tangshan, China, [9]Department of Medical Oncology, The First Affiliated Hospital of Xinxiang Medical University, Xinxiang, China, [10]Department of Oncology, Jiangsu Cancer Hospital, Nanjing Medical University, Nanjing, China, [11]Department of Medical Oncology, Anhui provincial Cancer Hospital, University of Science and Technology of China, Hefei, China, [12]Department of Oncology, Fujian Provincial Hospital, Fuzhou, China, [13]Department of Medical Oncology, Suining Central Hospital, Suining, China, [14]Department of Medical Oncology, The Affiliated Hospital of Qingdao University, Qingdao, China, [15]Medical Oncology, Innovent Biologics, Inc., Suzhou, China, [16]Biostatistics, Innovent Biologics, Inc., Suzhou, China

Abstract LBA52

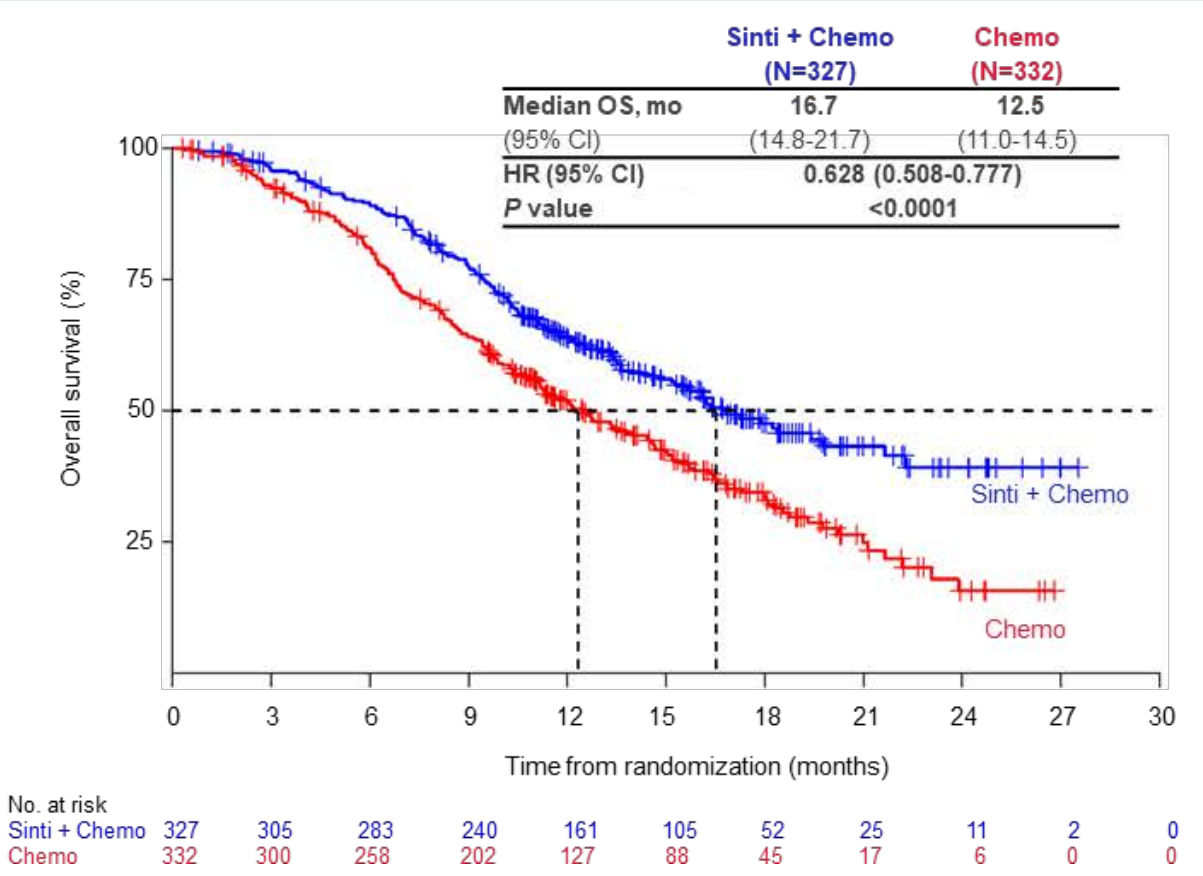
RTP RESEARCH TO PRACTICE

ORIENT-15: OS with Sintilimab and Chemotherapy in Advanced or Metastatic ESCC

PD-L1 CPS ≥10



All patients



Shen L et al. ESMO 2021;Abstract LBA52.

RTP RESEARCH TO PRACTICE

FDA Approves Nivolumab with Chemotherapy for Front-Line Advanced Gastric, GEJ and Esophageal Cancer

Press Release – April 16, 2021

"The FDA approved nivolumab in combination with certain types of chemotherapy for the frontline treatment of patients with advanced or metastatic gastric cancer, gastroesophageal junction cancer and esophageal adenocarcinoma, making it the first approved immunotherapy for this patient population.

The agency based the approval on data from the randomized, multicenter, open-label phase 3 CheckMate-649 trial, designed to evaluate nivolumab – a monoclonal antibody that inhibits tumor growth by enhancing T-cell function – plus chemotherapy in 1,581 patients with previously untreated advanced or metastatic gastric cancer, gastroesophageal junction cancer and esophageal adenocarcinoma.

Of the 789 patients treated in the nivolumab arm, median overall survival was 13.8 months, compared with 11.6 months for patients who received chemotherapy alone."

https://www.cancernetwork.com/view/fda-approves-nivolumab-plus-chemo-for-frontline-advanced-gastric-cancer

RTP RESEARCH TO PRACTICE

ASCO Gastrointestinal Cancers Symposium 2022

Nivolumab plus chemotherapy versus chemotherapy as first-line treatment for advanced gastric cancer/gastroesophageal junction cancer/esophageal adenocarcinoma: expanded analyses from 24-month follow-up of CheckMate 649

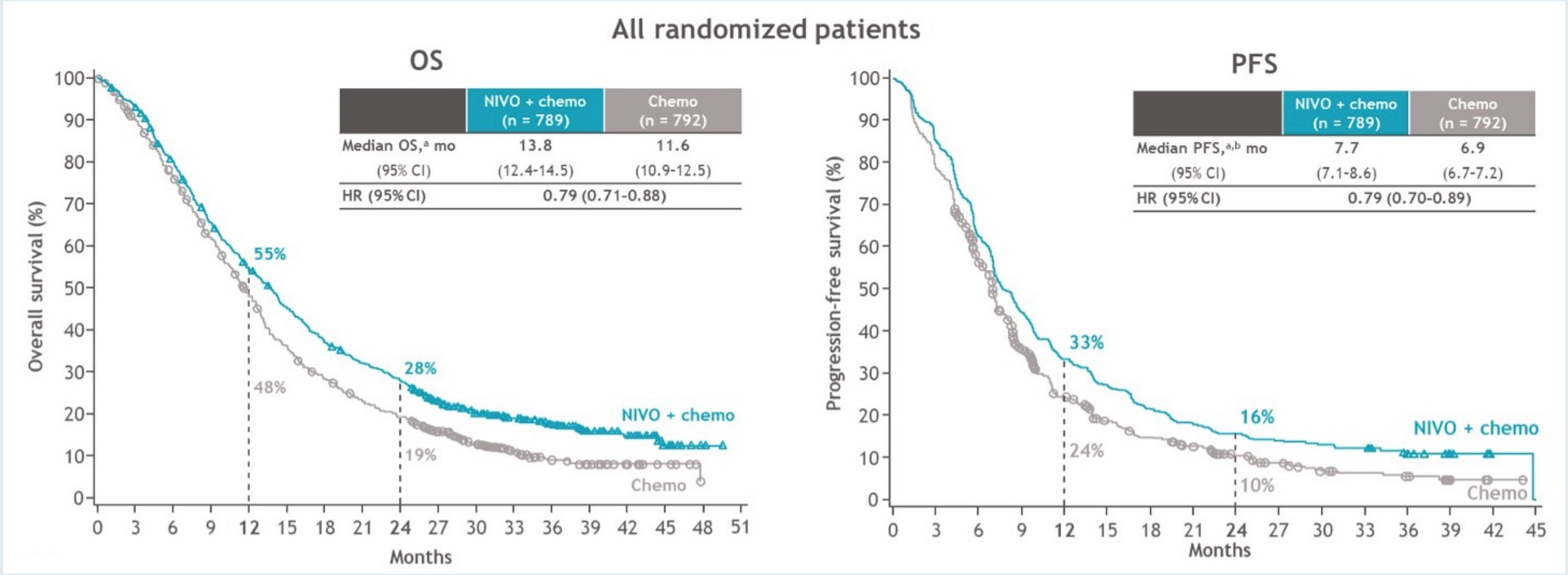
Kohei Shitara,[1] Yelena Y. Janjigian,[2] Markus Moehler,[3] Marcelo Garrido,[4] Carlos Gallardo,[5] Lin Shen,[6] Kensei Yamaguchi,[7] Lucjan Wyrwicz,[8] Tomasz Skoczylas,[9] Arinilda Bragagnoli,[10] Tianshu Liu,[11] Mustapha Tehfe,[12] Elena Elimova,[13] Samira Soleymani,[14] Ming Lei,[14] Kaoru Kondo,[14] Mingshun Li,[14] Jaffer A. Ajani[15]

[1]National Cancer Center Hospital East, Kashiwa, Japan; [2]Memorial Sloan Kettering Cancer Center and Weill Cornell Medical College, New York, NY, USA; [3]Johannes-Gutenberg University Clinic, Mainz, Germany; [4]Clinica San Carlos de Apoquindo, Pontificia Universidad Católica, Santiago, Chile; [5]Fundacion Arturo Lopez Perez, Santiago, Chile; [6]Department of Gastrointestinal Oncology, Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Peking University Cancer Hospital and Institute, Beijing, China; [7]Cancer Institute Hospital of JFCR, Tokyo, Japan; [8]Klinika Onkologii i Radioterapii, Narodowy Instytut Onkologii, Warszawa, Poland; [9]II Klinika Chirurgii Ogólnej, Gastroenterologicznej i Nowotworów Układu Pokarmowego, Medical University of Lublin, Lublin, Poland; [10]Fundacao Pio Xii Hosp Cancer De Barretos, Barretos, Brazil; [11]Zhongshan Hospital Fudan University, Shanghai, China; [12]Oncology Center - Centre Hospitalier de l'Universite de Montreal, Montreal, QC, Canada; [13]Princess Margaret Cancer Centre, Toronto, ON, Canada; [14]Bristol Myers Squibb, Princeton, NJ, USA; [15]The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Abstract number 240

RTP RESEARCH TO PRACTICE

CheckMate 649: Overall and Progression-Free Survival

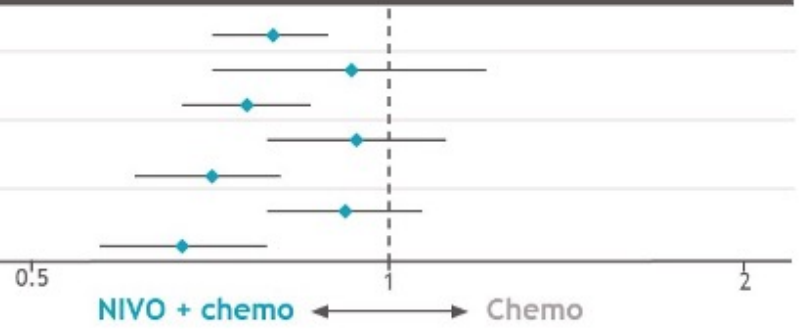


Shitara K et al. Gastrointestinal Cancers Symposium 2022;Abstract 240.

CheckMate 649: Efficacy Subgroup Analysis by PD-L1 CPS Excluding Patients with Microsatellite Instability-High Tumors

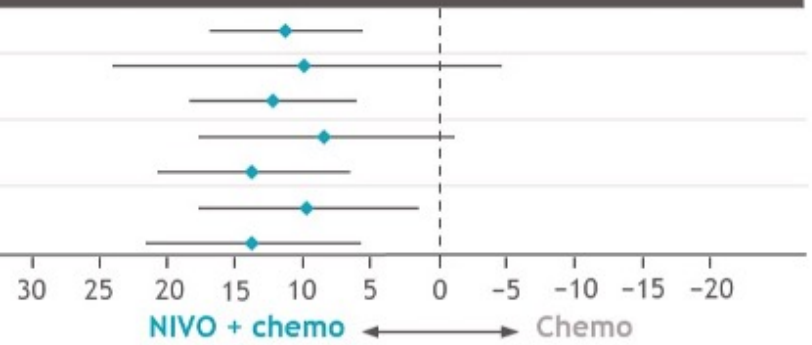
Overall survival

PD-L1 CPS[a]	Number of patients	Median, months		Unstratified HR[b]	Unstratified HR (95% CI)
		NIVO + chemo	Chemo		
Overall (N = 1537)		13.5	11.6	0.80	
< 1	262	13.4	12.5	0.93	
≥ 1	1256	13.6	11.4	0.76	
< 5	597	12.4	12.1	0.94	
≥ 5	921	14.2	11.1	0.71	
< 10	779	12.4	12.6	0.92	
≥ 10	739	14.4	10.9	0.67	



Objective response rate

PD-L1 CPS[c]	Number of patients	Objective response rate, %		Unweighted ORR difference,[d] %	Unweighted ORR difference, % (95% CI)
		NIVO + chemo	Chemo		
Overall (n = 1172)		58	46	12	
< 1	176	52	41	11	
≥ 1	982	60	47	13	
< 5	418	55	46	9	
≥ 5	740	60	46	14	
< 10	563	57	47	10	
≥ 10	595	59	45	14	



- OS and ORR benefits were consistent with the all randomized population when excluding patients with MSI-H tumors[e]

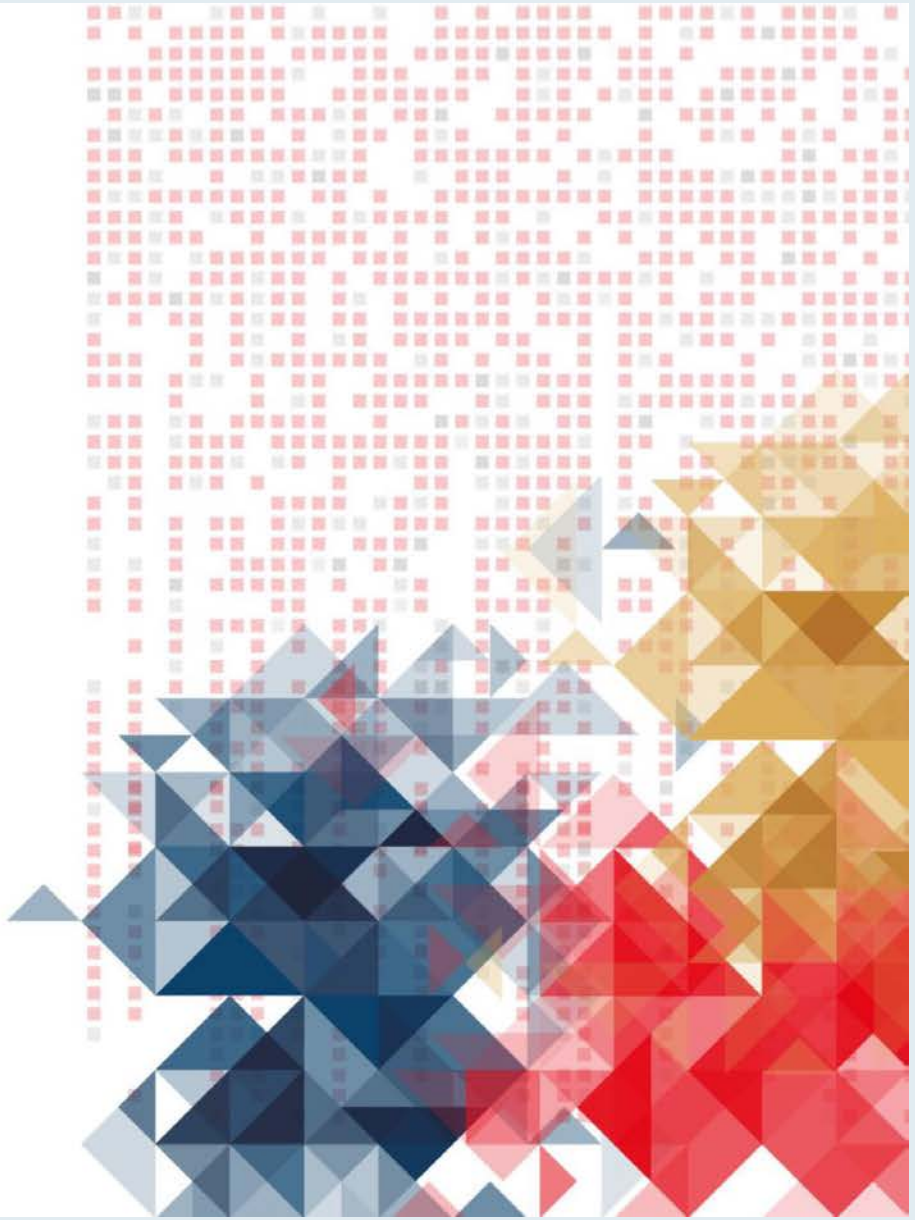
Shitara K et al. Gastrointestinal Cancers Symposium 2022;Abstract 240.

2021 ESMO congress

Sintilimab plus chemotherapy (chemo) versus chemo as the first-line treatment for advanced gastric or gastroesophageal junction (G/GEJ) adenocarcinoma (ORIENT-16)

Jianming Xu*, Haiping Jiang, Yueyin Pan, Kangsheng Gu, Sundong Cang, Lei Han, Yongqian Shu, Jiayi Li, Junhui Zhao, Hongming Pan, Suxia Luo, Yanru Qin, Qunyi Guo, Yuxian Bai, Yang Ling, Yingmei Guo, Ziran Li, Ying Liu, Yan Wang, Hui Zhou

*, presenting author, MD, The Fifth Medical Center, Chinese PLA General Hospital



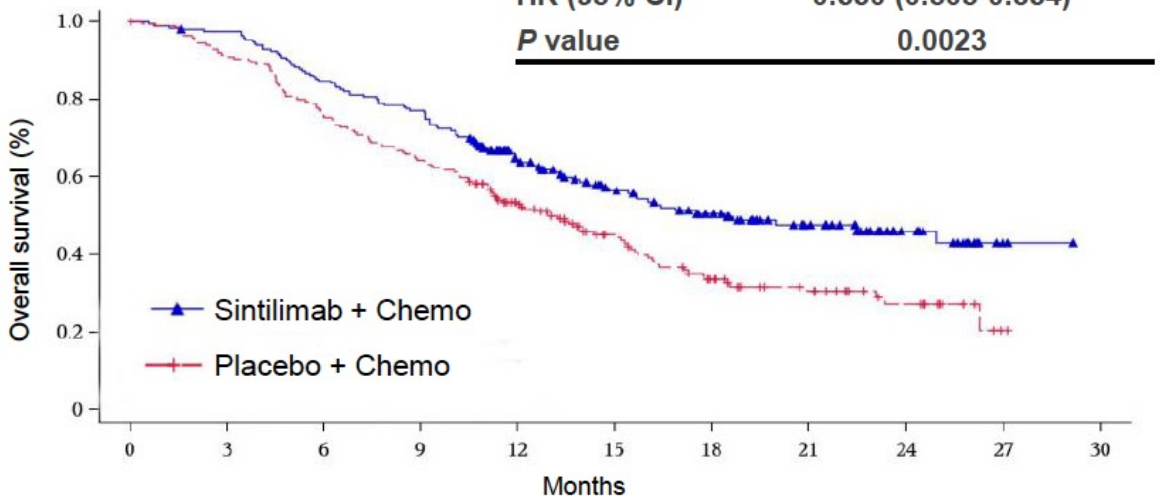
Abstract LBA53

RTP RESEARCH TO PRACTICE

ORIENT-16: OS with Sintilimab and Chemotherapy in Advanced Gastric or GEJ Adenocarcinoma

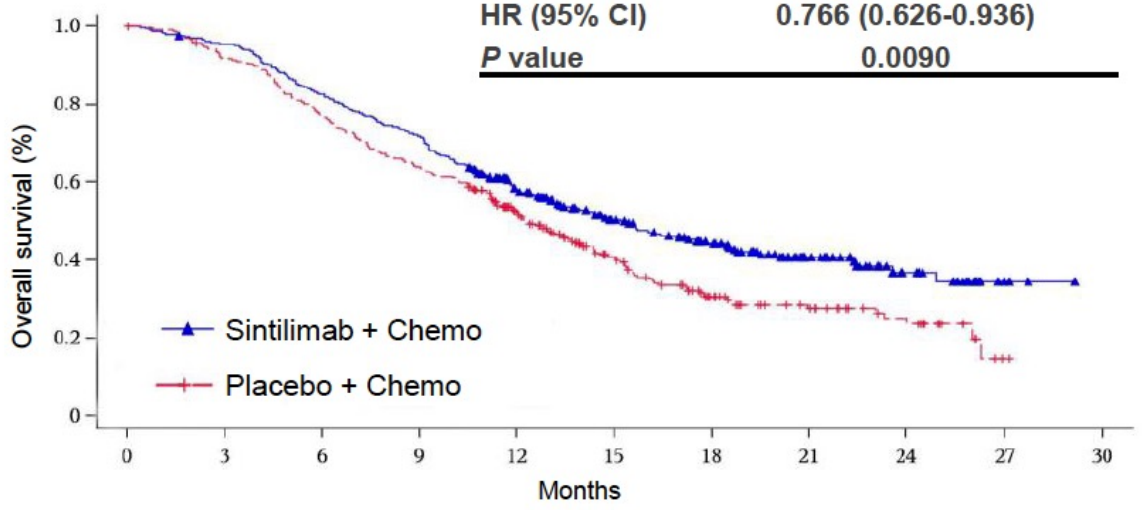
PD-L1 CPS ≥5

	Sin + Chemo (N=197)	Chemo (N=200)
Median OS, mo (95% CI)	18.4 (14.6-NC)	12.9 (11.1-.15.4)
HR (95% CI)	0.660 (0.505-0.864)	
P value	0.0023	



All patients

	Sin + Chemo (N=327)	Chemo (N=323)
Median OS, mo (95% CI)	15.2 (12.9-18.4)	12.3 (11.3-.13.8)
HR (95% CI)	0.766 (0.626-0.936)	
P value	0.0090	



Xu J et al. ESMO 2021;Abstract LBA53.

FDA Grants Accelerated Approval to Pembrolizumab with Trastuzumab and Chemotherapy as First-Line Therapy for HER2-Positive Gastric Cancer

Press Release – May 5, 2021

"The Food and Drug Administration granted accelerated approval to pembrolizumab in combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy for the first-line treatment of patients with locally advanced unresectable or metastatic HER2 positive gastric or gastroesophageal junction (GEJ) adenocarcinoma.

Approval was based on the prespecified interim analysis of the first 264 patients of the ongoing KEYNOTE-811 (NCT03615326) trial, a multicenter, randomized, double-blind, placebo-controlled trial in patients with HER2-positive advanced gastric or gastroesophageal junction (GEJ) adenocarcinoma who had not previously received systemic therapy for metastatic disease. Patients were randomized (1:1) to receive pembrolizumab 200 mg or placebo every 3 weeks, in combination with trastuzumab and either fluorouracil plus cisplatin or capecitabine plus oxaliplatin.

The main efficacy measure for this analysis was overall response rate (ORR) assessed by blinded independent review committee. The ORR was 74% in the pembrolizumab arm and 52% in the placebo arm (one-sided p-value < 0.0001, statistically significant). The median duration of response (DoR) was 10.6 months for patients treated with pembrolizumab and 9.5 months for those in the placebo arm."

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-grants-accelerated-approval-pembrolizumab-her2-positive-gastric-cancer

RTP RESEARCH TO PRACTICE

Nature 2021;600(7890):727-30.

Article

The KEYNOTE-811 trial of dual PD-1 and HER2 blockade in HER2-positive gastric cancer

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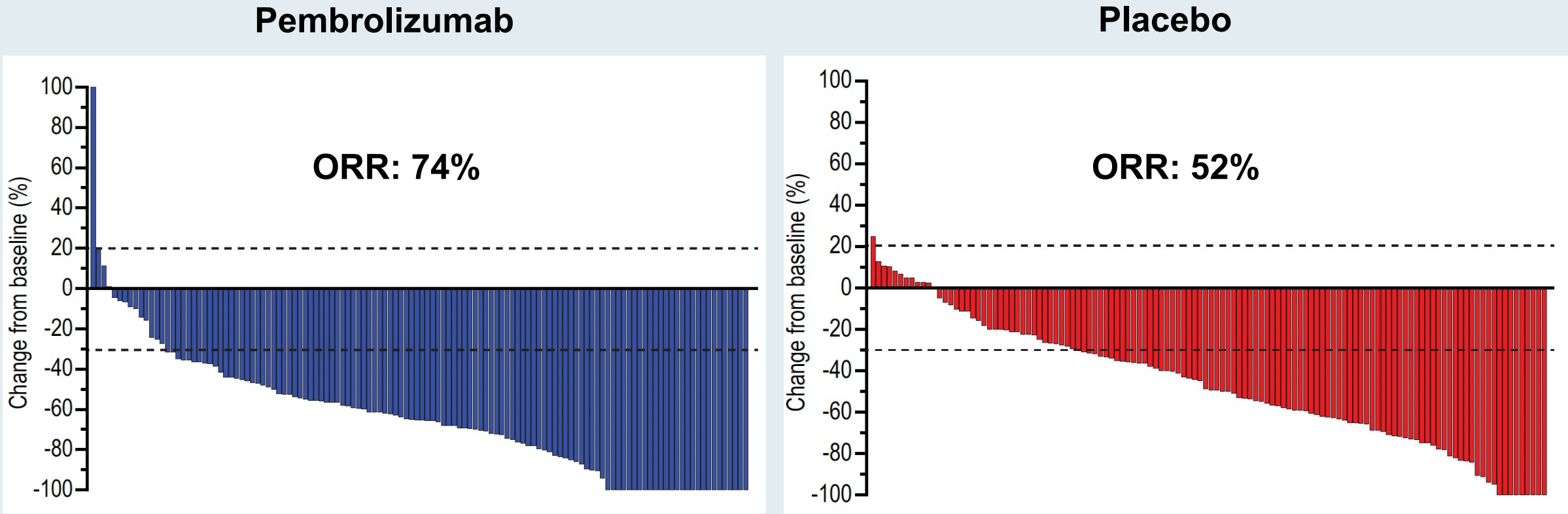
Yelena Y. Janjigian[1]✉, Akihito Kawazoe[2], Patricio Yañez[3], Ning Li[4], Sara Lonardi[5], Oleksii Kolesnik[6], Olga Barajas[7], Yuxian Bai[8], Lin Shen[9], Yong Tang[10], Lucjan S. Wyrwicz[11], Jianming Xu[12], Kohei Shitara[2], Shukui Qin[13], Eric Van Cutsem[14], Josep Tabernero[15], Lie Li[16], Sukrut Shah[16], Pooja Bhagia[16] & Hyun Cheol Chung[17]

KEYNOTE-811: Overall Response Rate



Janjigian YY et al. *Nature* 2021;600(7890):727-30.

RTP RESEARCH TO PRACTICE

ESMO WORLD CONGRESS ON Gastrointestinal Cancer

Pembrolizumab Plus Trastuzumab and Chemotherapy for HER2+ Metastatic Gastric or Gastroesophageal Junction Cancer: Initial Findings of the Global Phase 3 KEYNOTE-811 Study

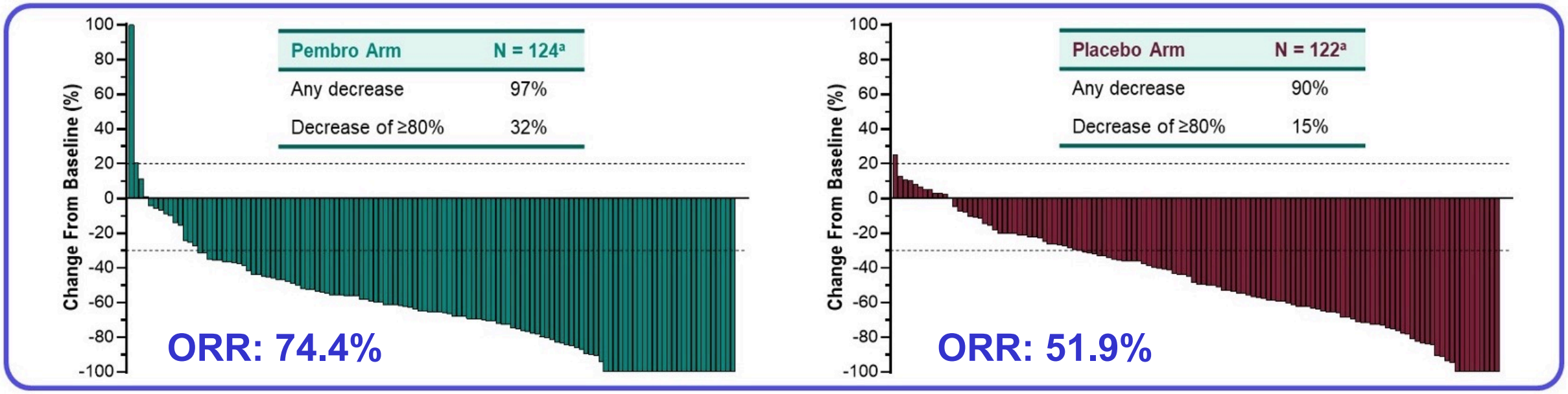
Yelena Y. Janjigian,[1] Akihito Kawazoe,[2] Patricio Yañez,[3] Suxia Luo,[4] Sara Lonardi,[5] Oleksii Kolesnik,[6] Olga Barajas,[7] Yuxian Bai,[8] Lin Shen,[9] Yong Tang,[10] Lucjan S. Wyrwicz,[11] Kohei Shitara,[2] Shukui Qin,[12] Eric Van Cutsem,[13] Josep Tabernero,[14] Lie Li,[15] Chie-Schin Shih,[15] Pooja Bhagia,[15] Hyun Cheol Chung,[16] on behalf of the KEYNOTE-811 Investigators

[1]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]National Cancer Center Hospital East, Kashiwa, Japan; [3]Universidad de La Frontera, James Lind Cancer Research Center, Temuco, Chile; [4]Henan Cancer Hospital, the Affiliated Cancer Hospital of Zhengzhou University, Zhengzhou, China; [5]Istituto Oncologico Veneto IOV-IRCCS, Padova, Italy; [6]Medical Center "Oncolife", Zaporizhzhia, Ukraine; [7]Arturo López Pérez Foundation, Santiago, Chile; [8]Harbin Medical University Cancer Hospital, Harbin, China; [9]Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Peking University Cancer Hospital & Institute, Beijing, China; [10]Cancer Hospital Affiliated to Xinjiang Medical University, Xinjiang, China; [11]Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Warsaw, Poland; [12]Cancer Center of People's Liberation Army, Nanjing, China; [13]University Hospitals Gasthuisberg and KU Leuven, Leuven, Belgium; [14]Vall d'Hebron Hospital Campus and Institute of Oncology (VHIO), IOB-Quiron, UVic-UCC, Barcelona, Spain; [15]Merck & Co., Inc., Kenilworth, NJ, USA; [16]Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea

ESMO World Congress on Gastrointestinal Cancer 2021;Abstract LBA4.

RTP RESEARCH TO PRACTICE

KEYNOTE-811: Confirmed Response at First Interim Analysis



Janjigian YY et al. ESMO World Congress on Gastrointestinal Cancer 2021;Abstract LBA4.

FDA Approves Trastuzumab Deruxtecan for HER2-Positive Gastric Adenocarcinomas

Press Release – January 15, 2021

"The Food and Drug Administration approved fam-trastuzumab deruxtecan-nxki for adult patients with locally advanced or metastatic HER2-positive gastric or gastroesophageal (GEJ) adenocarcinoma who have received a prior trastuzumab-based regimen.

Efficacy was evaluated in a multicenter, open-label, randomized trial (DESTINY-Gastric01, NCT03329690) in patients with HER2-positive locally advanced or metastatic gastric or GEJ adenocarcinoma who had progressed on at least two prior regimens, including trastuzumab, a fluoropyrimidine- and a platinum-containing chemotherapy. A total of 188 patients were randomized (2:1) to receive fam-trastuzumab deruxtecan-nxki 6.4 mg/kg intravenously every 3 weeks or physician's choice of either irinotecan or paclitaxel monotherapy."

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-fam-trastuzumab-deruxtecan-nxki-her2-positive-gastric-adenocarcinomas

2021 ASCO ANNUAL MEETING

Abstract 4048

DESTINY-Gastric01

Trastuzumab deruxtecan (T-DXd; DS-8201) in patients with human epidermal growth factor receptor 2–positive advanced gastric cancer or gastroesophageal junction adenocarcinoma: final overall survival results from a randomized, multicenter, open-label, phase 2 study (DESTINY-Gastric01)

Kensei Yamaguchi

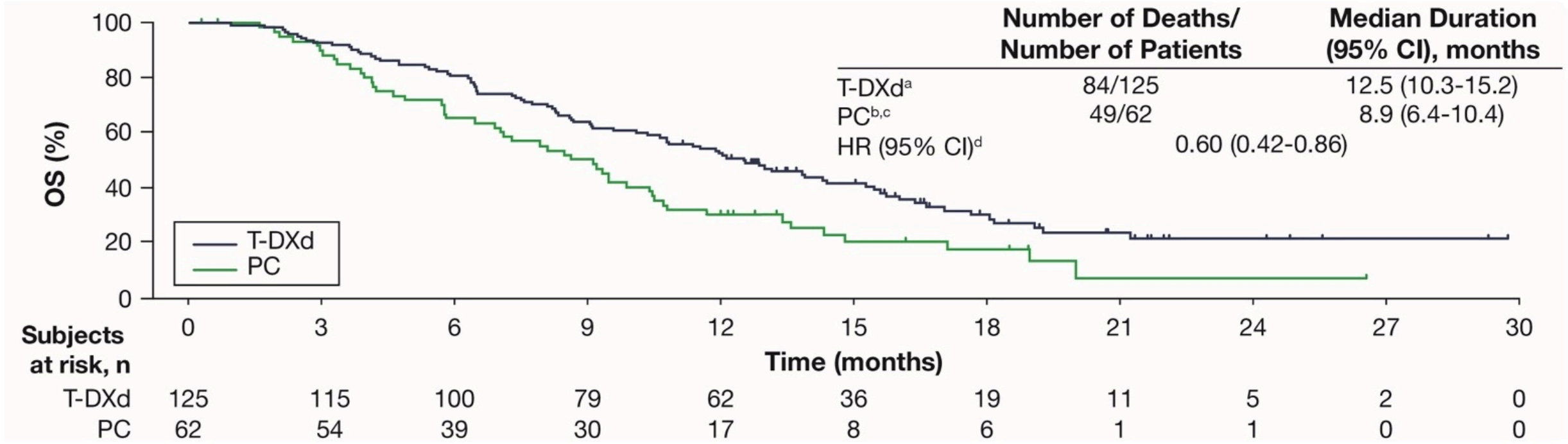
The Cancer Institute Hospital of JFCR, Tokyo, Japan

June 2021

ON BEHALF OF THE DESTINY-Gastric01 INVESTIGATORS

Additional authors: Yung-Jue Bang, Satoru Iwasa, Naotoshi Sugimoto, Min-Hee Ryu, Daisuke Sakai, Hyun Cheol Chung, Hisato Kawakami, Hiroshi Yabusaki, Jeeyun Lee, Kaku Saito Yoshinori Kawaguchi, Takahiro Kamio, Akihito Kojima, Masahiro Sugihara, Kohei Shitara

DESTINY-Gastric01: Final OS Analysis



As in the primary analysis (101 OS events; 54.0% maturity), in this updated analysis (133 OS events; 71.1% maturity), trastuzumab deruxtecan (T-DXd) showed superior antitumor activity compared to physician's choice.

Yamaguchi K et al. ASCO 2021;Abstract 4048.

DESTINY-Gastric01: Exploratory Biomarker Analysis of OS in HER2-Positive or HER2-Low Advanced Gastric or GEJ Cancer

Exploratory Biomarker in Primary HER2-Positive Cohort	Median Overall Survival
Plasma HER2 amplification	
Not Amplified	12.1 mo
Amplified	13.0 mo
Plasma HER2 copy number*	
Above 6.0	21.2 mo
Below 6.0	12.0 mo
Exploratory Biomarker in Exploratory HER2-Low Cohort	
Plasma HER2 extracellular domain**	
Above 11.6 ng/mL	10.1 mo
Below 11.6 ng/mL	4.3 mo

*An exploratory cutoff (copy number = 6.0) value was determined, which minimized *p*-value, estimated by log-rank test. Below 6.0 includes patients without amplification; **An exploratory cutoff value of 11.6 ng/mL in exploratory cohorts was determined, which minimized *p*-value, estimated by log-rank test.

Shitari K et al. ESMO World Congress on Gastrointestinal Cancer 2021;Abstract O-14.

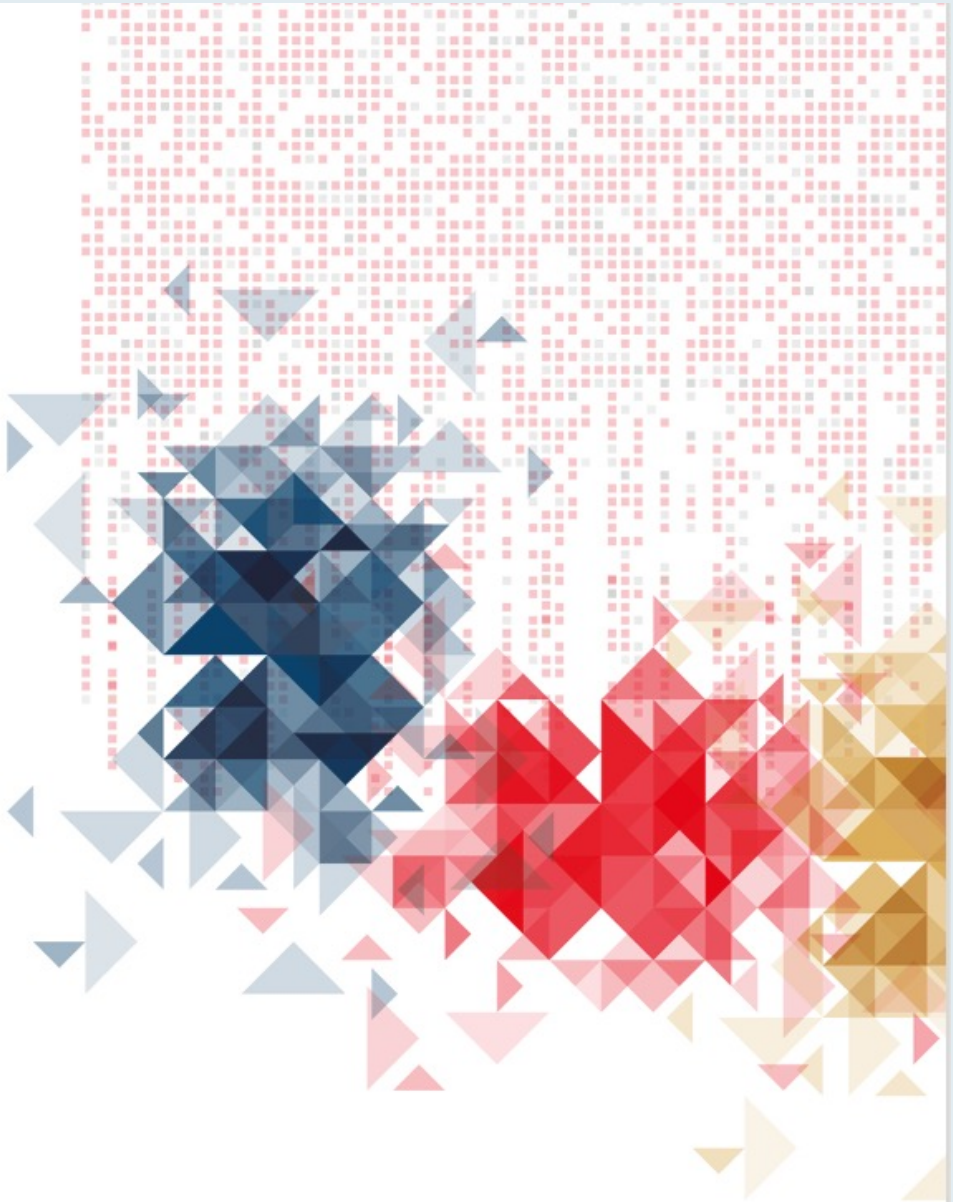
2021 ESMO congress

Primary Analysis of a Phase 2 Single-Arm Trial of Trastuzumab Deruxtecan (T-DXd) in Western Patients With HER2-Positive (HER2+) Unresectable or Metastatic Gastric or Gastroesophageal Junction (GEJ) Cancer Who Progressed on or After a Trastuzumab-containing Regimen

Eric Van Cutsem, MD[a], Maria di Bartolomeo, Elizabeth Smyth, Ian Chau, Haeseong Park, Salvatore Siena, Sara Lonardi, Zev A. Wainberg, Jaffer Ajani, Joseph Chao, Jabed Seraj, Yoshinori Kawaguchi, Amy Qin, Jasmeet Singh, Gerold Meinhardt, Geoffrey Ku

On behalf of the DESTINY-Gastric02 investigators

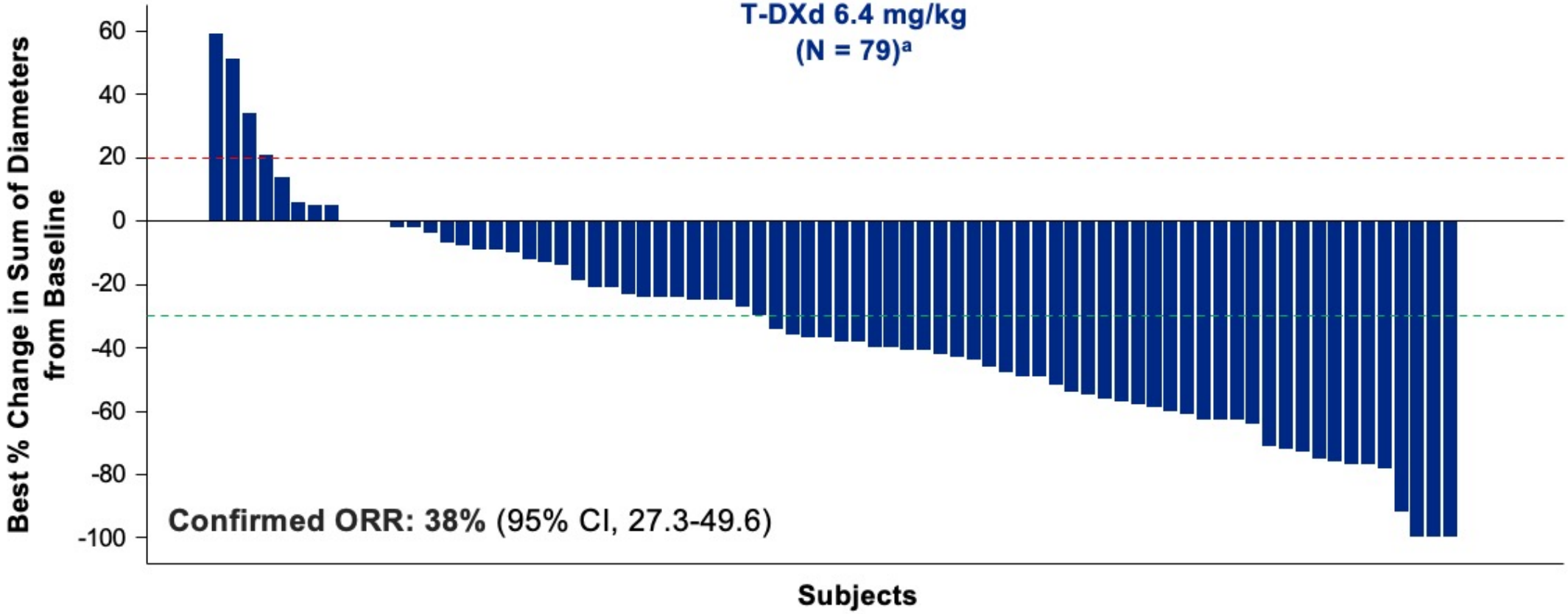
[a]University Hospital Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium



Abstract LBA55

RTP RESEARCH TO PRACTICE

DESTINY-Gastric02: Best Percentage Change of Tumor Size from Baseline



Van Cutsem E et al. ESMO 2021;Abstract LBA55.

FDA Grants Bemarituzumab Breakthrough Therapy Designation as First-Line Treatment for Gastric and Gastroesophageal Cancers that Overexpress FGFR2b

Press Release – April 19, 2021

"The US Food and Drug Administration (FDA) granted Breakthrough Therapy Designation for investigational bemarituzumab as first-line treatment for patients with fibroblast growth factor receptor 2b (FGFR2b) overexpressing and human epidermal growth factor receptor 2 (HER2)-negative metastatic and locally advanced gastric and gastroesophageal (GEJ) adenocarcinoma in combination with modified FOLFOX6 (fluoropyrimidine, leucovorin, and oxaliplatin), based on an FDA-approved companion diagnostic assay showing at least 10% of tumor cells overexpressing FGFR2b."

This designation is supported by results from the Phase 2 FIGHT trial.

https://www.amgen.com/newsroom/press-releases/2021/04/amgens-investigational-targeted-treatment-bemarituzumab-granted-breakthrough-therapy-designation

RTP RESEARCH TO PRACTICE

2021 ASCO ANNUAL MEETING

Abstract 4010

FIGHT: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PHASE 2 STUDY OF BEMARITUZUMAB (BEMA) COMBINED WITH MODIFIED FOLFOX6 IN 1L FGFR2B+ ADVANCED GASTRIC/GASTROESOPHAGEAL JUNCTION ADENOCARCINOMA (GC) (NCT03694522)

Presenter: Daniel Catenacci, MD
University of Chicago

Authors: Catenacci DV[1], Kang YK[2], Saeed A[3], Yamaguchi K[4], Qin S[5], Lee KW[6], Kim IH[7], Oh SC[8], Li J[9], Turk HM[10], Teixeira AC[11], Borg C[12], Hitre E[13], Udrea AA[14], Cardellino GG[15], Guardeño Sanchez R[16], Mitra S[17], Yang Y[17], Enzinger PC[18], Wainberg ZA[19]

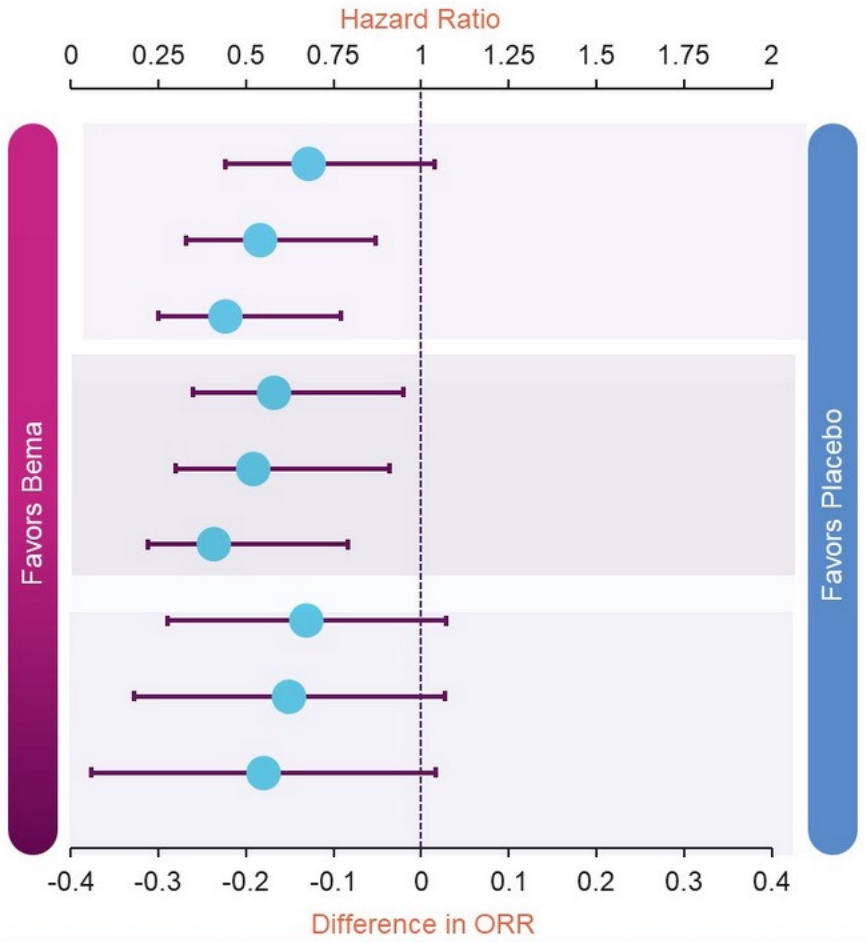
[1]University of Chicago, Chicago, USA; [2]Asan Medical Center, Seoul, South Korea; [3]Kansas University Cancer Center, Westwood, KS, USA; [4]The Cancer Institute Hospital of JFCR, Koto-Ku , Tokyo, Japan; [5]81 Hospital Nanjing University of Chinese Medicine, Nanjing, China; [6]Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Gyeonggi-do, South Korea; [7]The Catholic University of Korea, Seoul St. Mary's Hospital, Seoul, South Korea; [8]Korea University Guro Hospital, Seoul, South Korea; [9]Shanghai East Hospital, Shanghai, China; [10]Department of Medical Oncology, Bezmialem Vakif University, School of Medicine, Istanbul, Turkey; [11]Hospital Senhora Da Oliveira, Guimarães, Portugal; [12]Centre Hospitalier Régional Universitaire de Besançon, Besançon France; [13]National Institute of Oncology, Budapest, Hungary; [14]SC Medisprof SRL, Cluj-Napoca, Romania; [15]Department of Oncology, Azienda Sanitaria Universitaria Friuli Centrale, Udine, Italy; [16]Institut Català d'Oncologia, Girona, Spain; [17]FivePrime Therapeutics, Inc., South San Francisco, USA; [18]Dana Farber Cancer Institute, Boston, USA; [19]University of California, Los Angeles, USA

RTP RESEARCH TO PRACTICE

FIGHT: Efficacy of First-Line Bemarituzumab with Modified FOLFOX6 for Gastric/GEJ Adenocarcinoma

Endpoint	Subgroup	Median PFS/OS (months) Response rate	HR (95% CI) Difference in ORR (95% CI)
PFS	Overall*	Bema: 9.5 Placebo: 7.4	0.68 (0.44, 1.04)
	IHC 2+ or 3+ ≥5%†	Bema: 10.2 Placebo: 7.3	0.54 (0.33, 0.87)
	IHC 2+ or 3+ ≥10%‡	Bema: 14.1 Placebo: 7.3	0.44 (0.25, 0.77)
OS	Overall	Bema: NR Placebo: 12.9	0.58 (0.35, 0.95)
	IHC 2+ or 3+ ≥5%	Bema: NR Placebo: 12.5	0.52 (0.30, 0.91)
	IHC 2+ or 3+ ≥10%	Bema: NR Placebo: 11.1	0.41 (0.22, 0.79)
ORR	Overall	Bema: 36 (46.8%) Placebo: 26 (33.3%)	-13.1%§ (-29.0%, 2.8%)
	IHC 2+ or 3+ ≥5%	Bema: 30 (51.7%) Placebo: 22 (36.7%)	-15.1%§ (-32.8%, 2.7%)
	IHC 2+ or 3+ ≥10%	Bema: 24 (54.5%) Placebo: 19 (36.5%)	-18.0%§ (-37.7%, 1.7%)

*N = 155; †N = 118; ‡N = 96; §difference in ORR is calculated by (placebo ORR – Bema ORR).
NR, not reached.



- Median OS was reached in the overall population with longer follow-up – 5.7-mo improvement

Catenacci DV et al. ASCO 2021;Abstract 4010.

RTP RESEARCH TO PRACTICE

FIGHT: Selected Treatment-Related Adverse Event Summary

Selected AE (Preferred term)	Any Grade		Grade ≥3	
	Bema (N = 76)	Placebo (N = 77)	Bema (N = 76)	Placebo (N = 77)
Total Events	**76 (100.0%)**	**76 (98.7%)**	**63 (82.9%)**	**57 (74.0%)**
Nausea	36 (47.4%)	41 (53.2%)	0	3 (3.9%)
Vomiting	22 (28.9%)	24 (31.2%)	2 (2.6%)	2 (2.6%)
Diarrhea	31 (40.8%)	24 (31.2%)	2 (2.6%)	1 (1.3%)
Stomatitis	24 (31.6%)	10 (13.0%)	7 (9.2%)	1 (1.3%)
Peripheral sensory neuropathy	15 (19.7%)	15 (19.5%)	4 (5.3%)	3 (3.9%)
Neutrophil count decreased	31 (40.8%)	33 (42.9%)	23 (30.3%)	27 (35.1%)
Platelet count decreased	14 (18.4%)	21 (27.3%)	1 (1.3%)	0
Aspartate aminotransferase increased	23 (30.3%)	15 (19.5%)	4 (5.3%)	2 (2.6%)
Alanine aminotransferase increased	22 (28.9%)	11 (14.3%)	2 (2.6%)	1 (1.3%)
Dry eye	20 (26.3%)	5 (6.5%)	2 (2.6%)	0

AE, adverse event.

Catenacci DV et al. ASCO 2021;Abstract 4010.

RTP RESEARCH TO PRACTICE

Agenda

Module 1: Gastric and Gastroesophageal Cancers

Module 2: Hepatocellular Cancer

Module 3: Biliary Tract Cancers

Module 4: Colorectal Cancer

Module 5: Pancreatic Adenocarcinoma

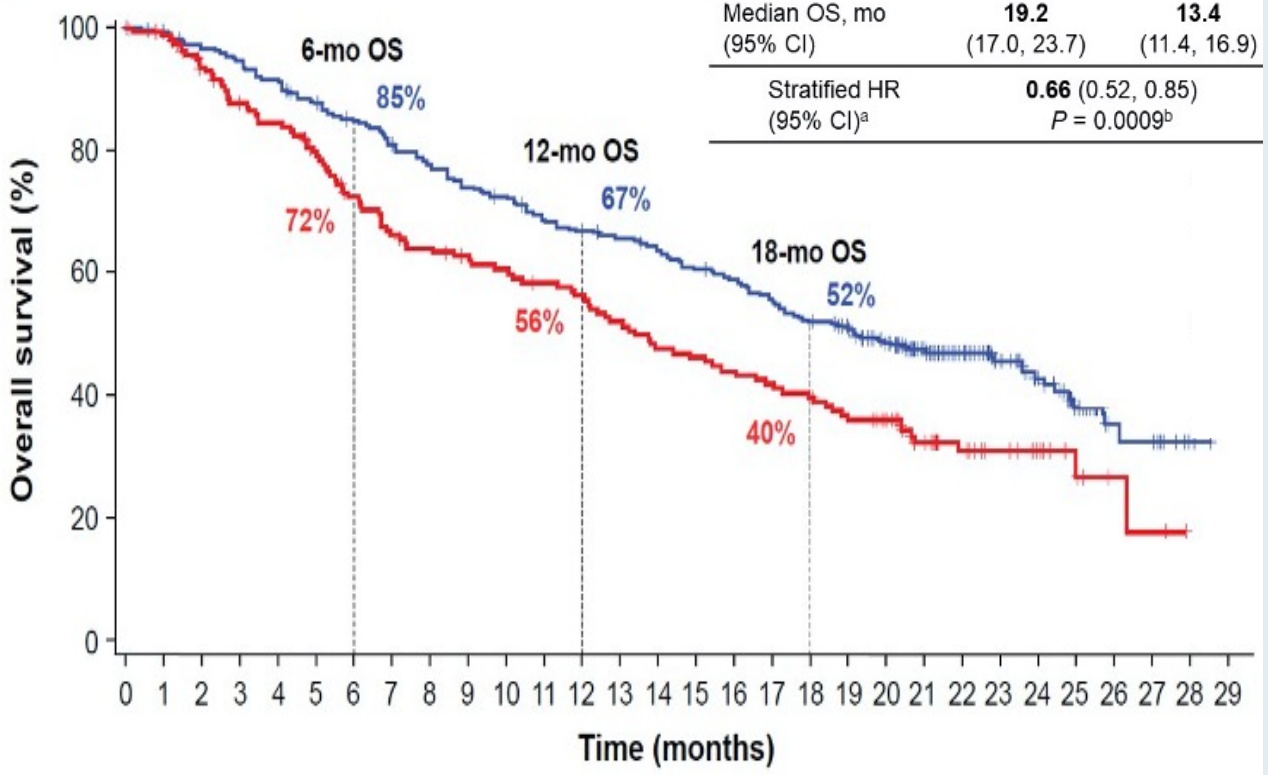
IMbrave150: Updated Overall Survival (OS) Data from a Global, Randomized, Open-Label Phase III Study of Atezolizumab (atezo) + Bevacizumab (bev) versus Sorafenib (sor) in Patients (pts) with Unresectable Hepatocellular Carcinoma (HCC)

Finn RS et al.

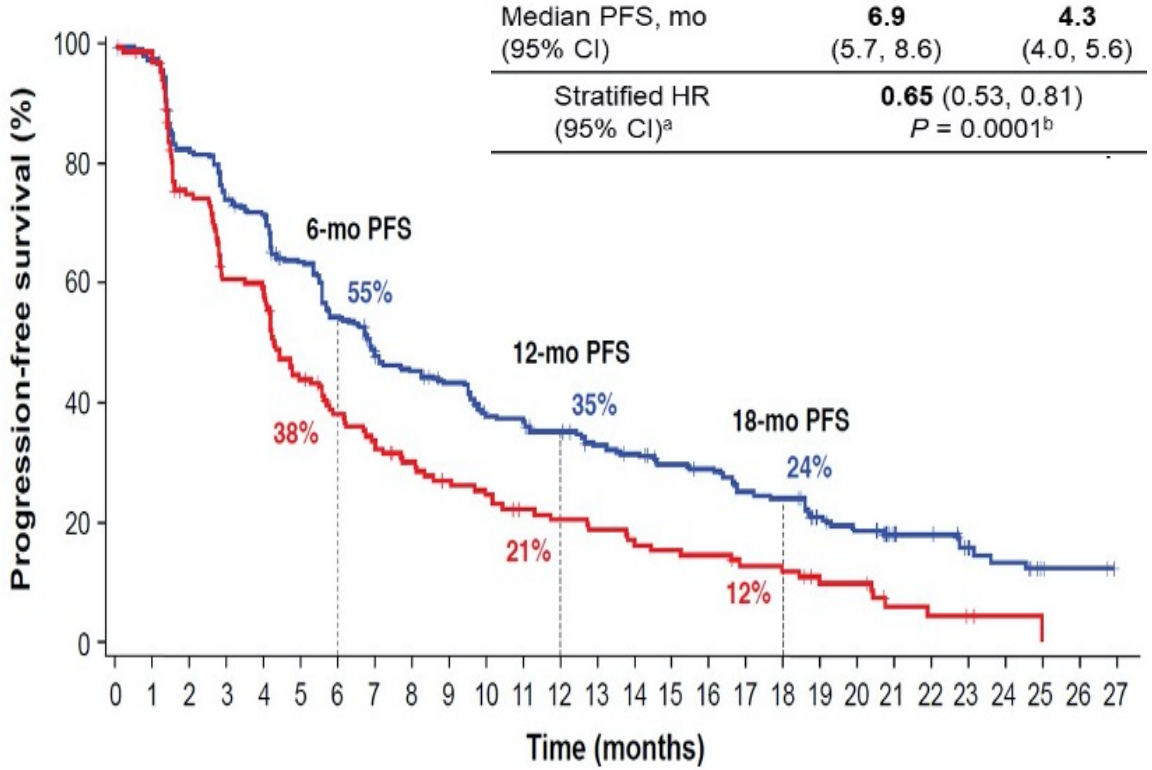
Gastrointestinal Cancers Symposium 2021;Abstract 267.

IMbrave150: Updated OS and PFS (Median Follow-Up = 15.6 Months)

Updated OS	Atezo + Bev (n = 336)	Sorafenib (n = 165)
OS events, n (%)	180 (54)	100 (61)
Median OS, mo (95% CI)	**19.2** (17.0, 23.7)	**13.4** (11.4, 16.9)
Stratified HR (95% CI)[a]	**0.66** (0.52, 0.85) *P* = 0.0009[b]	



Updated PFS	Atezo + Bev (n = 336)	Sorafenib (n = 165)
PFS events, n (%)	257 (76)	130 (79)
Median PFS, mo (95% CI)	**6.9** (5.7, 8.6)	**4.3** (4.0, 5.6)
Stratified HR (95% CI)[a]	**0.65** (0.53, 0.81) *P* = 0.0001[b]	



Finn RS et al. Gastrointestinal Cancers Symposium 2021;Abstract 267.

RTP RESEARCH TO PRACTICE

ASCO Gastrointestinal Cancers Symposium

Abstract 379

Phase 3 randomized, open-label, multicenter study of tremelimumab and durvalumab as first-line therapy in patients with unresectable hepatocellular carcinoma: HIMALAYA

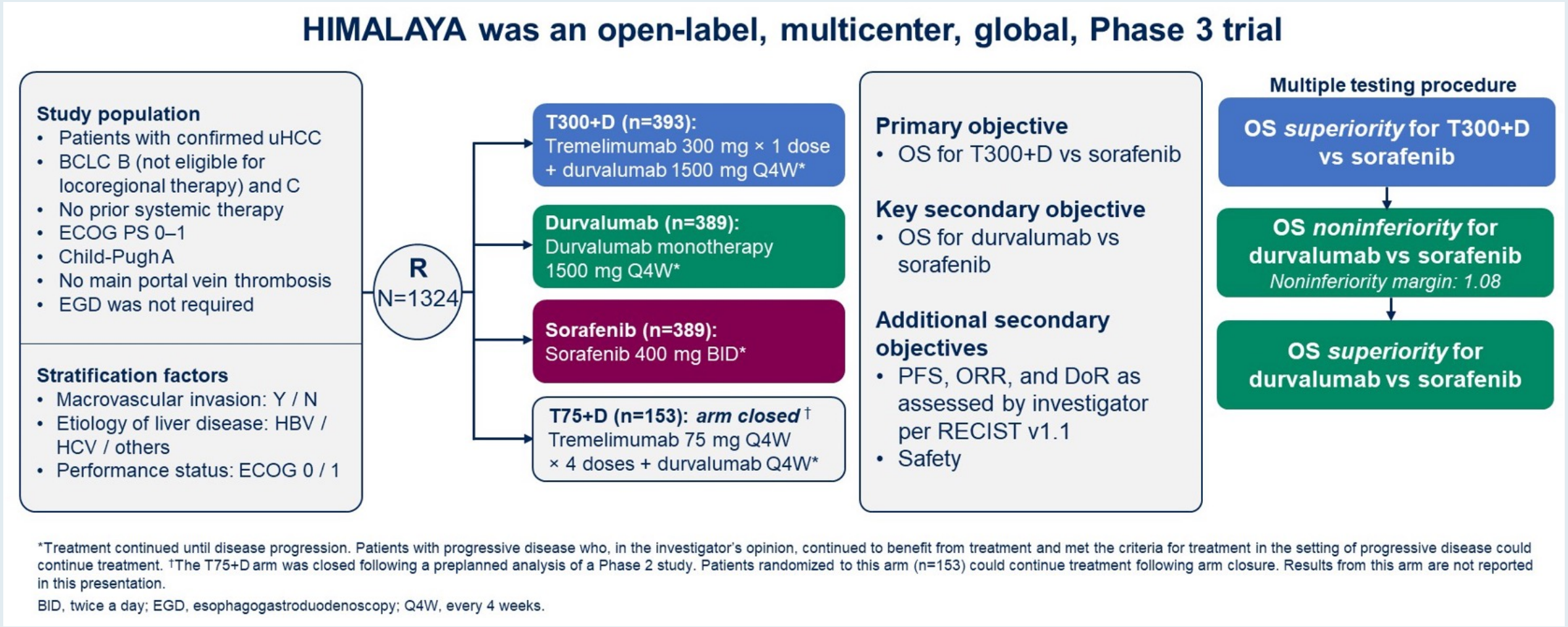
Ghassan K Abou-Alfa,[1,2*] Stephen L Chan,[3*] Masatoshi Kudo,[4*] George Lau,[5*] Robin Kate Kelley,[6] Junji Furuse,[7] Wattana Sukeepaisarnjaroen,[8] Yoon-Koo Kang,[9] Tu V Dao,[10] Enrico N De Toni,[11] Lorenza Rimassa,[12,13] Valery Breder,[14] Alexander Vasilyev,[15] Alexandra Heurgué,[16] Vincent C Tam,[17] Kabir Mody,[18] Satheesh Chiradoni Thungappa,[19] Philip He,[20] Alejandra Negro,[20] and Bruno Sangro[21]

[1]Department of Medicine, Memorial Sloan Kettering Center, New York, NY, USA; [2]Weill Medical College, Cornell University, New York, NY, USA; [3]State Key Laboratory of Translational Oncology, Department of Clinical Oncology, Sir Yue-Kong Pao Center for Cancer, The Chinese University of Hong Kong, Hong Kong, China; [4]Department of Gastroenterology and Hepatology, Kindai University Faculty of Medicine, Osaka, Japan; [5]Humanity and Health Clinical Trial Center, Humanity and Health Medical Group, Hong Kong, China; [6]Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco, CA, USA; [7]Department of Medical Oncology, Kyorin University Faculty of Medicine, Mitaka, Japan; [8]Department of Medicine, Srinagarind Hospital, Khon Kaen University, Khon Kaen, Thailand; [9]Department of Oncology, University of Ulsan College of Medicine, Asan Medical Center, Seoul, South Korea; [10]Cancer Research and Clinical Trial Center, National Cancer Hospital, Hanoi, Vietnam; [11]Department of Medicine II, University Hospital, LMU Munich, Munich, Germany; [12]Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Milan, Italy; [13]Humanitas Cancer Center, IRCCS Humanitas Research Hospital, Rozzano, Milan, Italy; [14]Chemotherapy Department No17, N.N. Blokhin Russian Cancer Research Center, Moscow, Russia; [15]Railway Clinical Hospital, St. Petersburg, Russia; [16]Service d'Hépato-Gastro-entérologie, Hôpital Robert-Debré, Reims, France; [17]Tom Baker Cancer Centre, University of Calgary, Calgary, AB, Canada; [18]Division of Hematology/Oncology, Department of Medicine, Mayo Clinic, Jacksonville, FL, USA; [19] Sri Venkateshwara Hospital, Bangalore, India; [20]AstraZeneca, Gaithersburg, MD, USA; [21]Liver Unit and HPB Oncology Area, Clinica Universidad de Navarra and CIBEREHD, Pamplona, Spain

*Drs Ghassan K Abou-Alfa, Stephen L Chan, Masatoshi Kudo, and George Lau contributed equally to this work.

RTP RESEARCH TO PRACTICE

HIMALAYA Phase III Trial Schema



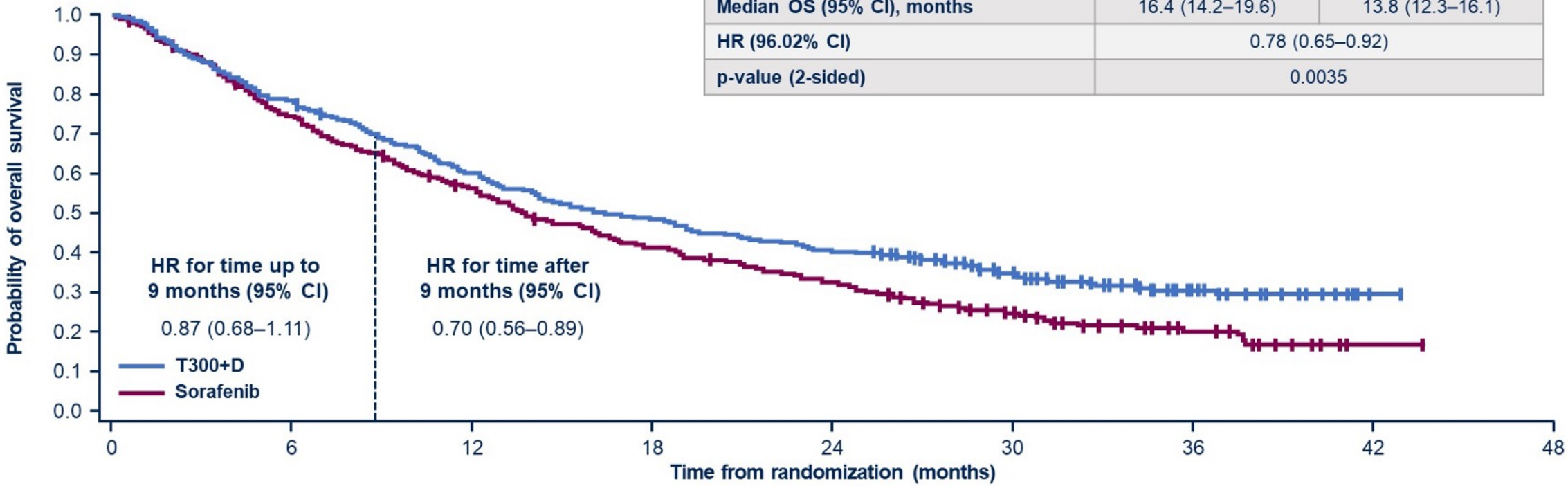
*Treatment continued until disease progression. Patients with progressive disease who, in the investigator's opinion, continued to benefit from treatment and met the criteria for treatment in the setting of progressive disease could continue treatment. †The T75+D arm was closed following a preplanned analysis of a Phase 2 study. Patients randomized to this arm (n=153) could continue treatment following arm closure. Results from this arm are not reported in this presentation.

BID, twice a day; EGD, esophagogastroduodenoscopy; Q4W, every 4 weeks.

Abou-Alfa GK et al. Gastrointestinal Cancers Symposium 2022;Abstract 379.

HIMALAYA Primary Endpoint: OS for Tremelimumab 300 and Durvalumab as First-Line Therapy in Unresectable HCC

	T300+D (n=393)	Sorafenib (n=389)
OS events, n (%)	262 (66.7)	293 (75.3)
Median OS (95% CI), months	16.4 (14.2–19.6)	13.8 (12.3–16.1)
HR (96.02% CI)	0.78 (0.65–0.92)	
p-value (2-sided)	0.0035	



Abou-Alfa GK et al. Gastrointestinal Cancers Symposium 2022;Abstract 379.

RTP RESEARCH TO PRACTICE

HIMALAYA: Safety and Tolerability

Event, n (%)	T300+D (n=388)	Durvalumab (n=388)	Sorafenib (n=374)
Any AE	378 (97.4)	345 (88.9)	357 (95.5)
Any TRAE*	294 (75.8)	202 (52.1)	317 (84.8)
Any grade 3/4 AE	196 (50.5)	144 (37.1)	196 (52.4)
Any grade 3/4 TRAE	100 (25.8)	50 (12.9)	138 (36.9)
Any serious TRAE	68 (17.5)	32 (8.2)	35 (9.4)
Any TRAE leading to death	9 (2.3)†	0	3 (0.8)‡
Any TRAE leading to discontinuation	32 (8.2)	16 (4.1)	41 (11.0)

Includes AEs with onset or increase in severity on or after the date of the first dose through 90 days following the date of the last dose or the date of initiation of the first subsequent therapy.

*Treatment-related was as assessed by investigator. †Nervous system disorder (n=1), acute respiratory distress syndrome (n=1), hepatitis (n=1), myocarditis (n=1), immune-mediated hepatitis (n=2), pneumonitis (n=1), hepatic failure (n=1), myasthenia gravis (n=1). ‡Hematuria (n=1), cerebral hematoma (n=1), hepatic failure (n=1).

AE, adverse event; SMQ, Standardized MedDRA Query; T300+D, tremelimumab 300 mg × 1 dose + durvalumab 1500 mg Q4W; TRAE, treatment-related adverse event.

Abou-Alfa GK et al. Gastrointestinal Cancers Symposium 2022;Abstract 379.

ESMO ASIA VIRTUAL ONCOLOGY WEEK

ESMO VIRTUAL PLENARY

ABSTRACT VP10-2021

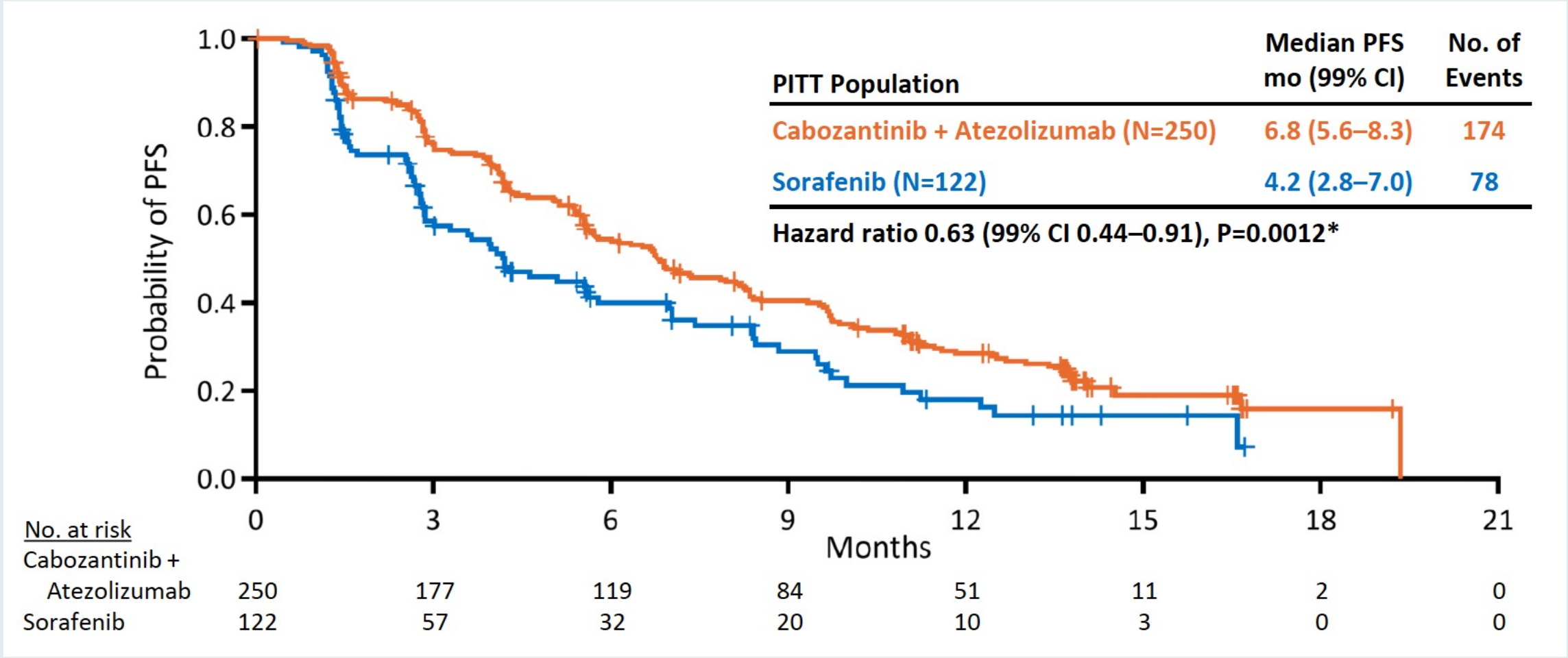
Cabozantinib plus atezolizumab versus sorafenib as first-line systemic treatment for advanced hepatocellular carcinoma: results from the randomized phase 3 COSMIC-312 trial

Robin Kate Kelley, Thomas Yau, Ann-Lii Cheng, Ahmed Kaseb, Shukui Qin, Andrew Zhu, Stephen Chan, Wattana Sukeepaisarnjaroen, Valery Breder, Gontran Verset, Edward Gane, Ivan Borbath, Jose David Gomez Rangel, Philippe Merle, Fawzi Benzaghou, Kamalika Banerjee, Saswati Hazra, Jonathan Fawcett, Lorenza Rimassa

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

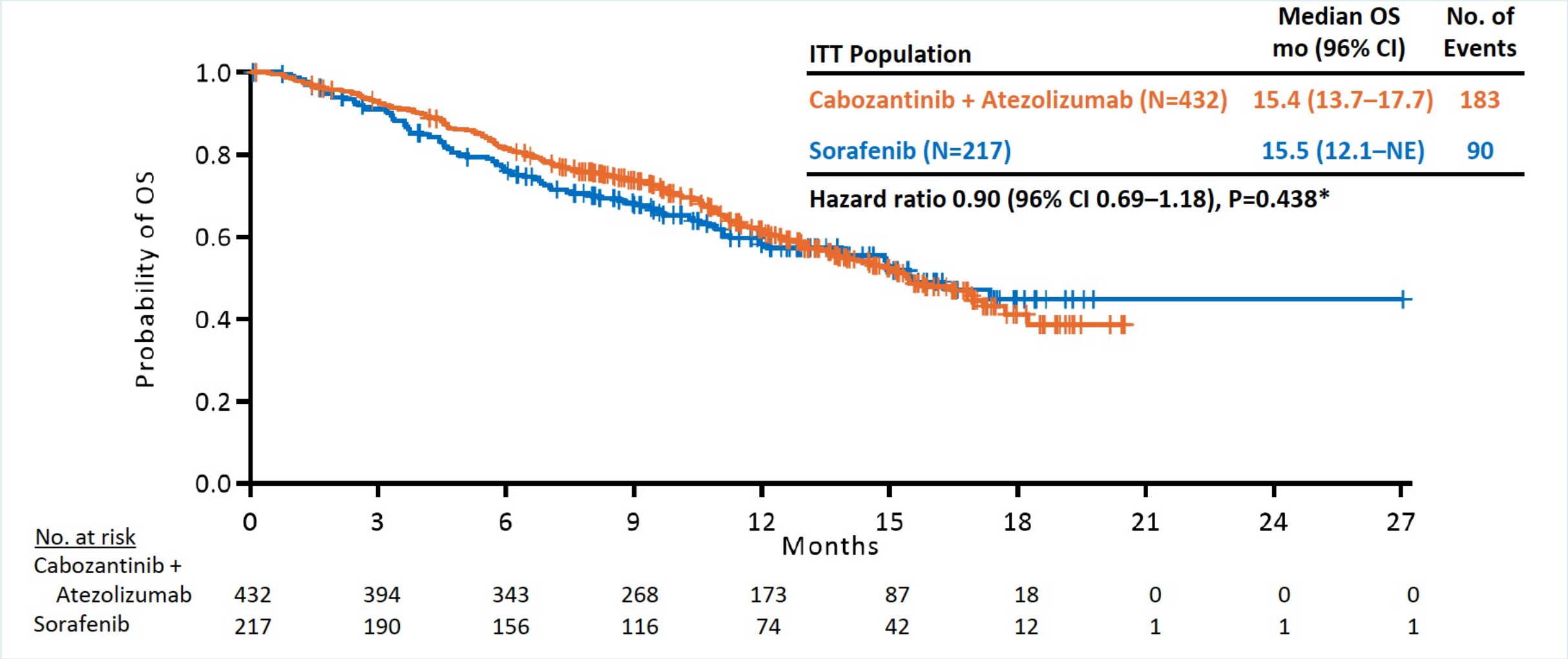
RTP RESEARCH TO PRACTICE

COSMIC-312 Primary Endpoint of PFS: Final Analysis



Kelley RK et al. ESMO Asia Virtual Oncology Week 2021;Abstract VP10-2021.

COSMIC-312 Primary Endpoint of OS: Interim Analysis



Kelley RK et al. ESMO Asia Virtual Oncology Week 2021;Abstract VP10-2021.

Agenda

Module 1: Gastric and Gastroesophageal Cancers

Module 2: Hepatocellular Cancer

Module 3: Biliary Tract Cancers

Module 4: Colorectal Cancer

Module 5: Pancreatic Adenocarcinoma

ASCO Gastrointestinal Cancers Symposium

Abstract 378

A Phase 3 randomized, double-blind, placebo-controlled study of durvalumab in combination with gemcitabine plus cisplatin in patients with advanced biliary tract cancer: TOPAZ-1

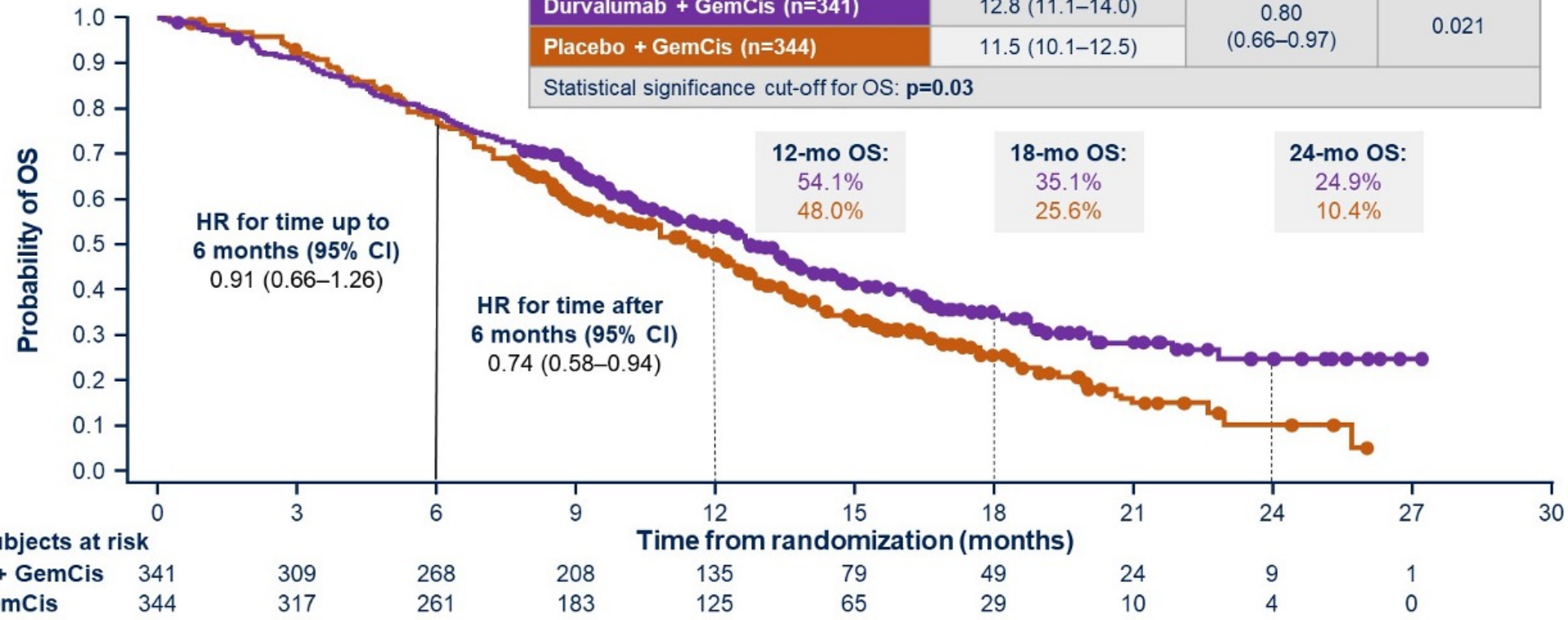
Do-Youn Oh,[1] Aiwu Ruth He,[2] Shukui Qin,[3] Li-Tzong Chen,[4] Takuji Okusaka,[5] Arndt Vogel,[6] Jin Won Kim,[7] Thatthan Suksomboon charoen,[8] Myung Ah Lee,[9] Masayuki Kitano,[10] Howard Burris,[11] Mohamed Bouattour,[12] Suebpong Tanasanvimon,[13] Renata Zaucha,[14] Antonio Avallone,[15] Juan Cundom,[16] Nana Rokutanda,[17] Julia Xiong,[17] Gordon Cohen,[17] Juan W. Valle[18]

[1]Division of Medical Oncology, Department of Internal Medicine, Seoul National University Hospital, Cancer Research Institute, Seoul National University College of Medicine, Seoul, South Korea; [2]Division of Hematology and Oncology, Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC, USA; [3]Cancer Center of Nanjing, Jinling Hospital, Nanjing, China; [4]Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, and National Institute of Cancer Research, Tainan, and National Cheng Kung University Hospital, National Cheng Kung University, Tainan, Taiwan; [5]Department of Hepatobiliary and Pancreatic Oncology, National Cancer Center Hospital, Tokyo, Japan; [6]Gastroenterology, Hepatology and Endocrinology, Hannover Medical School, Hannover, Germany; [7]Division of Medical Oncology, Department of Internal Medicine, Seoul National University Bundang Hospital, Seoul, South Korea; [8]Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand; [9]Division of Medical Oncology, Department of Internal Medicine, Seoul St. Mary's Hospital, College of Medicine, The Catholic University, Seoul, South Korea; [10]Second Department of Internal Medicine, Wakayama Medical University, Wakayama, Japan; [11]Sarah Cannon Research Institute, Tennessee Oncology, Nashville, TN, USA; [12]Department of Liver Cancer Unit, AP-HP Hôpital Beaujon, Paris, France; [13]Department of Internal Medicine, Faculty of Medicine, Chulalongkorn University, King Chulalongkorn Memorial Hospital, Bangkok, Thailand; [14]Department of Oncology and Radiotherapy, Medical University of Gdańsk, Gdańsk, Poland; [15]Istituto Nazionale Tumori-IRCCS Fondazione G. Pascale, Naples, Italy; [16]Instituto de Investigaciones Metabólicas, Buenos Aires, Argentina; [17]AstraZeneca, Gaithersburg, MD, USA; [18]Division of Cancer Sciences, The University of Manchester and The Christie NHS Foundation Trust, Manchester, UK

RTP RESEARCH TO PRACTICE

TOPAZ-1 Primary Endpoint: OS

	Median OS (95% CI), months	Hazard ratio (95% CI)	p-value
Durvalumab + GemCis (n=341)	12.8 (11.1–14.0)	0.80 (0.66–0.97)	0.021
Placebo + GemCis (n=344)	11.5 (10.1–12.5)		
Statistical significance cut-off for OS: **p=0.03**			

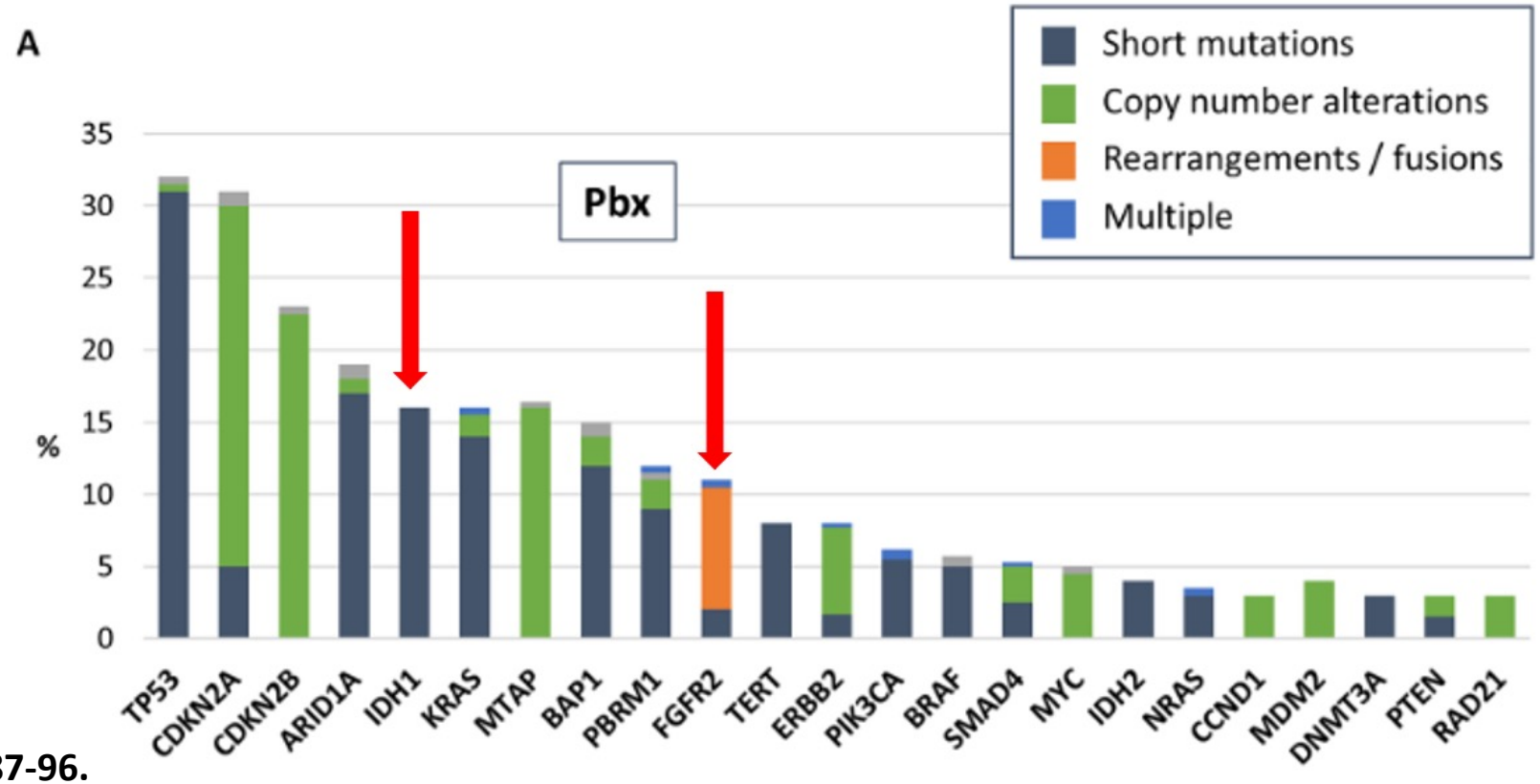


Median duration of follow-up (95% CI) was 16.8 (14.8–17.7) months with durvalumab + GemCis and 15.9 (14.9–16.9) months with placebo + GemCis.
CI, confidence interval; GemCis, gemcitabine and cisplatin; HR, hazard ratio; mo, month; OS, overall survival.

Oh D-Y et al. Gastrointestinal Cancers Symposium 2022;Abstract 378.

Emerging Targets in Cholangiocarcinoma: Focus on FGFR2 and IDH1

- Mutation profiling of N=1632 iCCA using Foundation Medicine panel
  - n=1048 with primary tumor biopsy (Pbx)
  - *FGFR2* fusion or rearrangement: 9%
  - *IDH1* mutation: 16%



Israel MA et al. *Oncologist* 2021;26(9):787-96.

Courtesy of Katie Kelley, MD.

RTP RESEARCH TO PRACTICE

FDA Grants Accelerated Approval to Infigratinib for Metastatic Cholangiocarcinoma

Press Release – May 28, 2021

"The Food and Drug Administration granted accelerated approval to infigratinib, a kinase inhibitor for adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement as detected by an FDA-approved test.

The FDA also approved FoundationOne® CDx for selection of patients with FGFR2 fusion or other rearrangement as a companion diagnostic device for treatment with infigratinib.

Efficacy was demonstrated in CBGJ398X2204 (NCT02150967), a multicenter open-label single-arm trial, that enrolled 108 patients with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with an FGFR2 fusion or rearrangement as determined by local or central testing. Patients received infigratinib 125 mg orally once daily for 21 consecutive days followed by 7 days off therapy, in 28-day cycles until disease progression or unacceptable toxicity."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-infigratinib-metastatic-cholangiocarcinoma

RTP RESEARCH TO PRACTICE

Lancet Gasteroenterol Hepatol 2021;6(10):803-15.

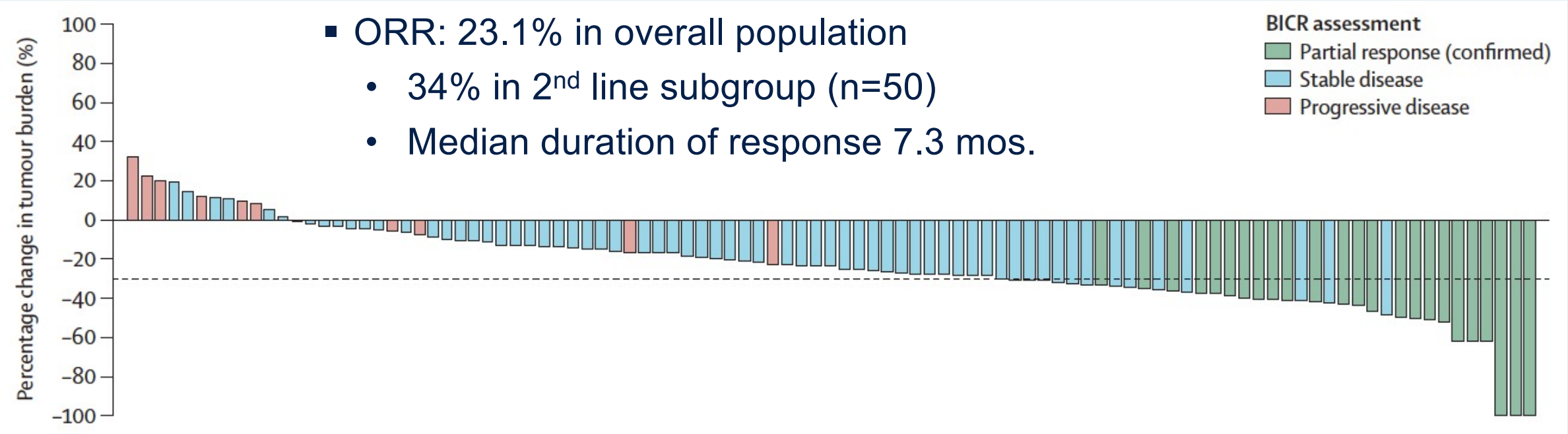
Articles

Infigratinib (BGJ398) in previously treated patients with advanced or metastatic cholangiocarcinoma with *FGFR2* fusions or rearrangements: mature results from a multicentre, open-label, single-arm, phase 2 study

Milind Javle, Sameek Roychowdhury, Robin Kate Kelley, Saeed Sadeghi, Teresa Macarulla, Karl Heinz Weiss, Dirk-Thomas Waldschmidt, Lipika Goyal, Ivan Borbath, Anthony El-Khoueiry, Mitesh J Borad, Wei Peng Yong, Philip A Philip, Michael Bitzer, Surbpong Tanasanvimon, Ai Li, Amit Pande, Harris S Soifer, Stacie Peacock Shepherd, Susan Moran, Andrew X Zhu, Tanios S Bekaii-Saab, Ghassan K Abou-Alfa

Phase II Study of Infigratinib in Advanced or Metastatic Cholangiocarcinoma Harboring FGFR2 Fusions or Rearrangements

- ORR: 23.1% in overall population
  - 34% in 2nd line subgroup (n=50)
  - Median duration of response 7.3 mos.



Javle M et al. *Lancet Gasteroenterol Hepatol* 2021;6(10):803-15.

RTP RESEARCH TO PRACTICE

Pemigatinib for Previously Treated Locally Advanced or Metastatic Cholangiocarcinoma: Update of FIGHT-202

Abou-Alfa GK,[1,2] Sahai V,[3] Hollebecque A,[4] Vaccaro G,[5] Melisi D,[6] Al-Rajabi R,[7] Paulson AS,[8] Borad MJ,[9] Gallinson D,[10] Murphy AG,[11] Oh D-Y,[12] Dotan E,[13] Catenacci DV,[14] Van Cutsem E,[15] Lihou C,[16] Zhen H,[16] Féliz L,[17] Vogel A[18]

[1]Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]Weill Medical College at Cornell University, New York, NY, USA; [3]Division of Hematology and Oncology, Department of Internal Medicine, University of Michigan, Ann Arbor, MI, USA; [4]Department of Adult Medicine, Gustave Roussy, Villejuif, France; [5]Providence Cancer Center Oncology and Hematology Care Clinic, Portland, OR, USA; [6]Digestive Molecular Clinical Oncology Research Unit, Department of Medicine, Università degli studi di Verona, Verona, Italy; [7]Department of Internal Medicine, Division of Hematology/Oncology, University of Kansas Cancer Center, Kansas City, KS, USA; [8]Baylor Charles A. Sammons Cancer Center, Baylor University Medical Center, Dallas, TX, USA; [9]Department of Internal Medicine, Mayo Clinic Cancer Center, Scottsdale, AZ, USA; [10]Department of Hematology/Oncology, Morristown Memorial Hospital, Carol Cancer Center, Morristown, NJ, USA; [11]Department of Oncology, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine, Baltimore, MD, USA; [12]Department of Internal Medicine, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, South Korea; [13]Department of Hematology/Oncology, Fox Chase Cancer Center, Philadelphia, PA, USA; [14]Department of Medicine, University of Chicago Medicine, Chicago, IL, USA; [15]Department of Digestive Oncology, University Hospitals Leuven and KU Leuven, Leuven, Belgium; [16]Incyte Corporation, Wilmington, DE, USA; [17]Incyte Biosciences International Sàrl, Morges, Switzerland; [18]Department of Gastroenterology, Hepatology and Endocrinology, Hannover Medical School, Hannover, Niedersachsen, Germany

2021 American Society of Clinical Oncology (ASCO) Annual Meeting, June 4–8, 2021: Poster 4086

FIGHT-202: Pemigatinib for Previously Treated Locally Advanced or Metastatic Cholangiocarcinoma

- The ORR for cohort A was 37.0% in this updated analysis with 4 complete responses (CRs) and 36 partial responses (PRs), and a median duration of response of 8.1 months (**Table 1**)
- The updated median PFS was 7.0 months, and the updated median OS was 17.5 months (**Table 1**)
- No changes in the numbers of patients with CR or PR occurred in cohorts B and C in the current vs the primary analysis

Table 1. Efficacy Outcomes in Patients With *FGFR2* Fusions or Rearrangements (Cohort A)

Variable	Primary Analysis[1] (n = 107)	Current Analysis (n = 108)*
ORR (95% CI), %	35.5 (26.5–45.4)	**37.0 (27.9–46.9)**
Best OR, † n (%)		
CR	3 (2.8)	4 (3.7)
PR	35 (32.7)	36 (33.3)
SD	50 (46.7)	49 (45.4)
PD	16 (14.9)	16 (14.8)
Not evaluable‡	3 (2.8)	3 (2.8)
DCR (95% CI), %	82 (74–89)	82.4 (73.9–89.1)
mDOR (95% CI), mo	7.5 (5.7–14.5)	8.1 (5.7–13.1)
mPFS (95% CI), mo	6.9 (6.2–9.6)	7.0 (6.1–10.5)
mOS (95% CI), mo	21.1 (14·8–NE)§	17.5 (14.4–23.0)
Responders	–	30.1 (21.5–NE)
Nonresponders	–	13.7 (9.6–16.2)

*Includes 1 patient from Japan who was enrolled in cohort A after the primary cutoff date (enrollment was held open in Japan for this patient because they were already in screening). †Assessed and confirmed by independent central review. ‡Postbaseline tumor assessment was not performed owing to study discontinuation (2 participants in cohort A, 4 participants in cohort B, 3 participants in cohort C) or was performed prior to the minimum interval of 39 days for an assessment of SD (1 patient in cohort A, 1 patient in cohort B). §OS not mature at data cutoff used for the primary analysis (March 22, 2019).
mDOR, median duration of response; mOS, median overall survival; mPFS, median progression-free survival; NE, not estimable; OR, objective response; PD, progressive disease; SD, stable disease.

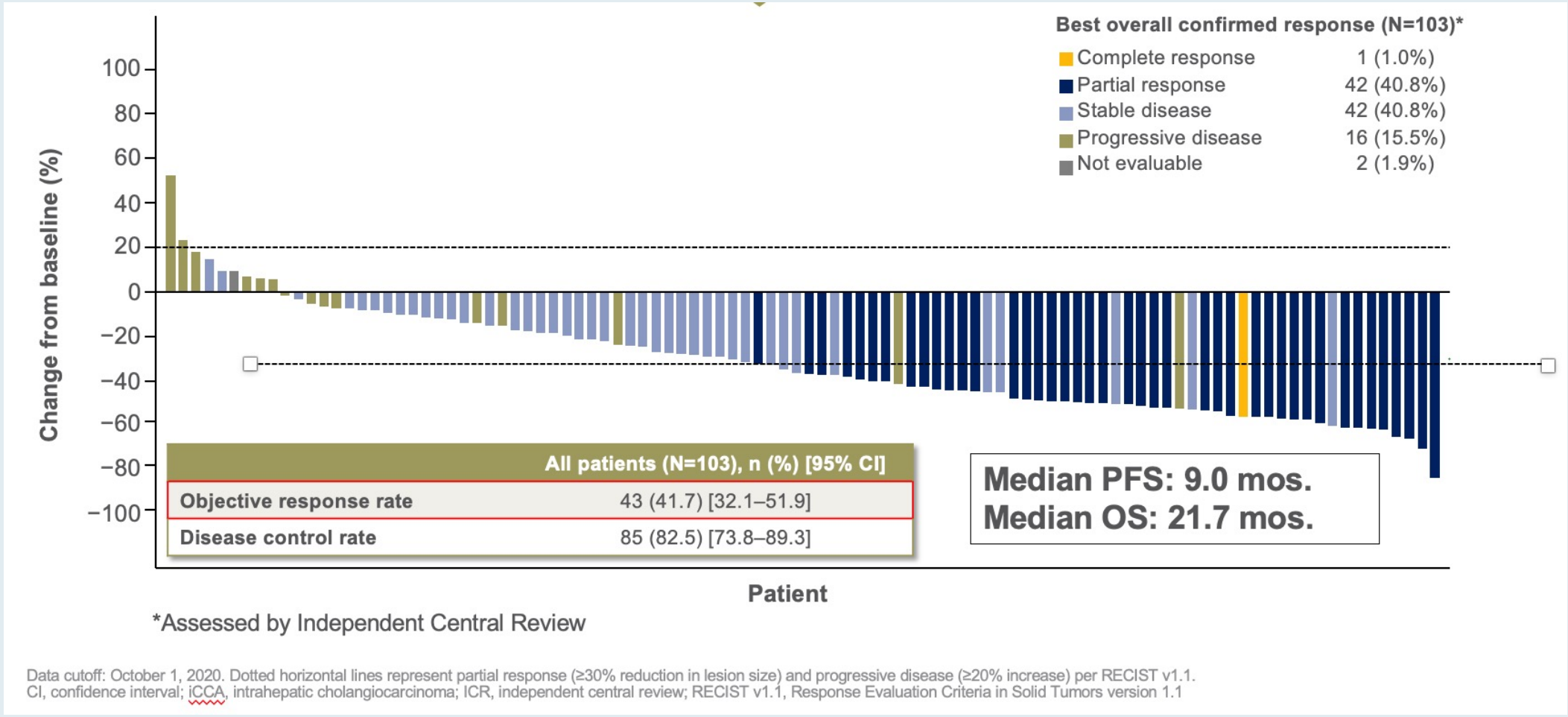
1. Abou-Alfa GK, et al. *Lancet Oncol.* 2020;21:671–668.

About-Alfa GK et al. ASCO 2021;Abstract 4086.

Primary Results of Phase 2 FOENIX-CCA2: The Irreversible FGFR1-4 Inhibitor Futibatinib in Intrahepatic Cholangiocarcinoma (iCCA) with FGFR2 Fusions/Rearrangements

Goyal L et al.
AACR 2021;Abstract CT010.

FOENIX-CCA2: Phase II Study of Futibatinib in Intrahepatic Cholangiocarcinoma with FGFR2 Fusions/Rearrangements



Data cutoff: October 1, 2020. Dotted horizontal lines represent partial response (≥30% reduction in lesion size) and progressive disease (≥20% increase) per RECIST v1.1.
CI, confidence interval; iCCA, intrahepatic cholangiocarcinoma; ICR, independent central review; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1

Goyal L et al. AACR 2021;Abstract CT010.

RTP RESEARCH TO PRACTICE

FDA Approves Ivosidenib for Advanced or Metastatic Cholangiocarcinoma

Press Release – August 25, 2021

"The Food and Drug Administration approved ivosidenib for adult patients with previously treated, locally advanced or metastatic cholangiocarcinoma with an isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test.

Today, the FDA also approved the Oncomine Dx Target Test as a companion diagnostic device to aid in selecting patients with cholangiocarcinoma for treatment with ivosidenib.

Ivosidenib was investigated in a randomized (2:1), multicenter, double-blind, placebo-controlled clinical trial (Study AG120-C-005, NCT02989857) of 185 adult patients with locally advanced or metastatic cholangiocarcinoma with an IDH1 mutation. The patient's disease must have progressed following at least one, but not more than two prior regimens, including at least one gemcitabine- or 5-flurouracil-containing regimen. Patients were randomized to receive either ivosidenib 500 mg orally once daily or matched placebo until disease progression or unacceptable toxicity."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-ivosidenib-advanced-or-metastatic-cholangiocarcinoma

RTP RESEARCH TO PRACTICE

Research

JAMA Oncology | Original Investigation

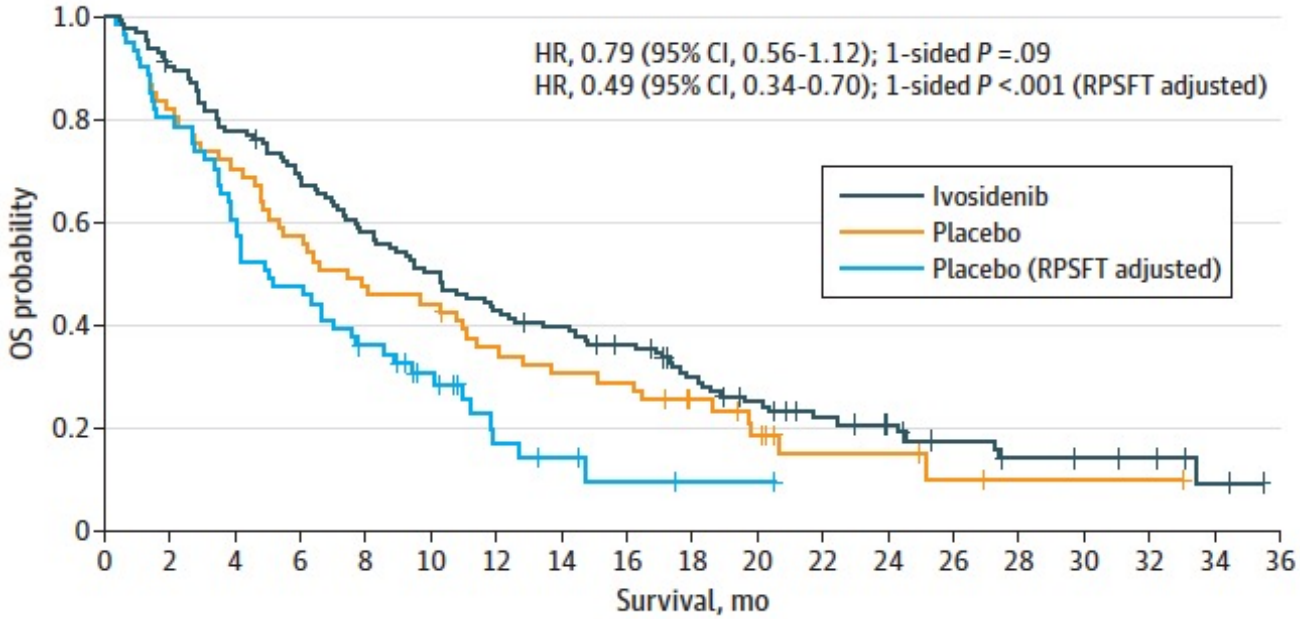
Final Overall Survival Efficacy Results of Ivosidenib for Patients With Advanced Cholangiocarcinoma With *IDH1* Mutation

The Phase 3 Randomized Clinical ClarIDHy Trial

Andrew X. Zhu, MD, PhD; Teresa Macarulla, MD; Milind M. Javle, MD; R. Kate Kelley, MD; Sam J. Lubner, MD; Jorge Adeva, MD; James M. Cleary, MD; Daniel V. T. Catenacci, MD; Mitesh J. Borad, MD; John A. Bridgewater, PhD; William P. Harris, MD; Adrian G. Murphy, MD; Do-Youn Oh, MD; Jonathan R. Whisenant, MD; Maeve A. Lowery, MD; Lipika Goyal, MD; Rachna T. Shroff, MD; Anthony B. El-Khoueiry, MD; Christina X. Chamberlain, PhD; Elia Aguado-Fraile, PhD; Sung Choe, PhD; Bin Wu, PhD; Hua Liu, PhD; Camelia Gliser, BS; Shuchi S. Pandya, MD; Juan W. Valle, MD; Ghassan K. Abou-Alfa, MD

JAMA Oncol 2021;7(11):1669-77.

ClarIDHy: Final OS with Ivosidenib for Patients with Advanced Cholangiocarcinoma with IDH1 Mutation



No. at risk

Ivosidenib	126	113	97	85	72	62	53	48	42	32	25	18	14	10	7	6	5	2
Placebo	61	50	43	35	29	27	21	18	17	12	8	4	4	2	1	1	1	
Placebo (RPSFT adjusted)	61	49	37	29	21	14	6	4	2	1	1							

Treatment group	Events/patients, No.	OS, median (95% CI), mo
Ivosidenib	100/126	10.3 (7.8-12.4)
Placebo	50/61	7.5 (4.8-11.1)
Placebo adjusted by RPSFT	49/61	5.1 (3.8-7.6)

Zhu AX et al. *JAMA Oncol* 2021;7(1):1669-77.

Agenda

Module 1: Gastric and Gastroesophageal Cancers

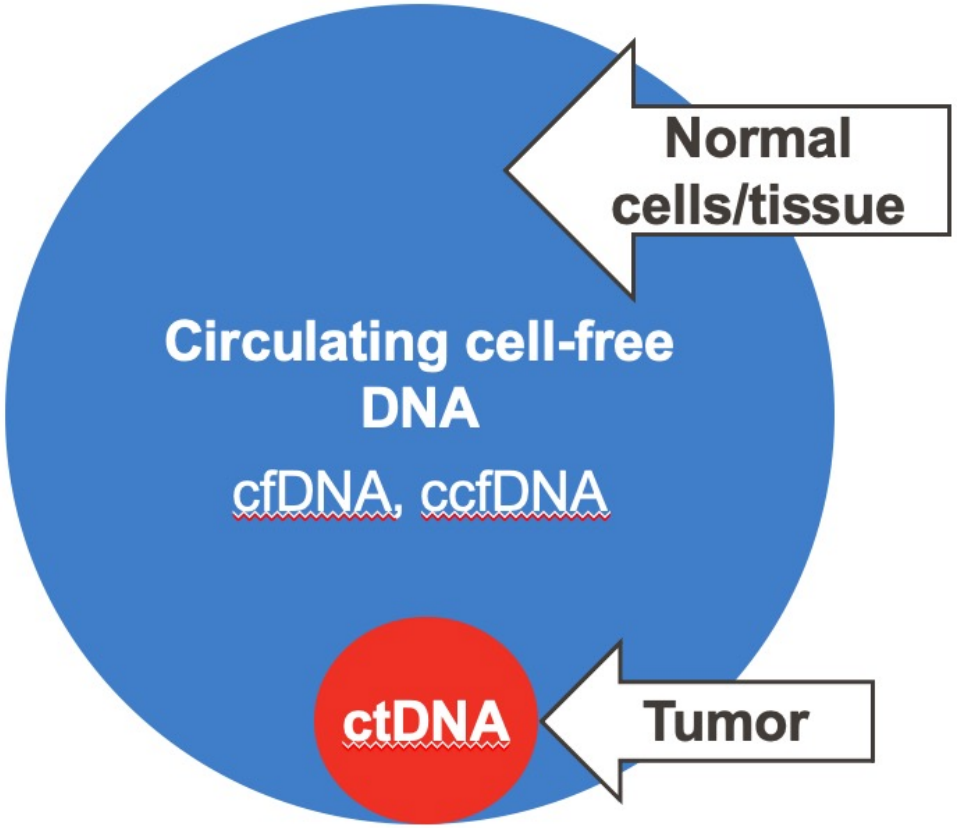
Module 2: Hepatocellular Cancer

Module 3: Biliary Tract Cancers

Module 4: Colorectal Cancer

Module 5: Pancreatic Adenocarcinoma

Characteristics and Terminology for Circulating Tumor DNA (ctDNA)



Initially described by Madel and Metais in 1948
Half-life: ~ 0.5 hours

Two Main Ways to Test ctDNA:

- "Tumor-informed testing"
  - Sequencing the tumor and looking for those mutations
- "Tumor-naïve testing"
  - Casting a wide net and looking for tumor mutations

Chandrananda D et al. *BMC Med Genomics.* 2015;8:29; Wyllie AH. *Nature.* 1980;284(5756):555-556; Mandel P & Metais P. *C R*

Courtesy of Christopher Lieu, MD

CONSENSUS STATEMENT

OPEN

Check for updates

ctDNA applications and integration in colorectal cancer: an NCI Colon and Rectal–Anal Task Forces whitepaper

Arvind Dasari[1,40]✉, Van K. Morris[1,40], Carmen J. Allegra[2], Chloe Atreya[3], Al B. Benson III[4], Patrick Boland[5], Ki Chung[6], Mehmet S. Copur[7], Ryan B. Corcoran[8], Dustin A. Deming[9], Andrea Dwyer[10], Maximilian Diehn[11], Cathy Eng[1], Thomas J. George[12], Marc J. Gollub[13], Rachel A. Goodwin[14], Stanley R. Hamilton[15], Jaclyn F. Hechtman[16], Howard Hochster[17], Theodore S. Hong[18], Federico Innocenti[19], Atif Iqbal[20], Samuel A. Jacobs[21], Hagen F. Kennecke[22], James J. Lee[23], Christopher H. Lieu[24], Heinz-Josef Lenz[25], O. Wolf Lindwasser[26], Clara Montagut[27], Bruno Odisio[28], Fang-Shu Ou[29], Laura Porter[30], Kanwal Raghav[1], Deborah Schrag[31], Aaron J. Scott[32], Qian Shi[29], John H. Strickler[33], Alan Venook[34], Rona Yaeger[35], Greg Yothers[36], Y. Nancy You[37], Jason A. Zell[38,39] and Scott Kopetz[1]

Nat Rev Clin Oncol 2020;17(12):757-70.

RTP RESEARCH TO PRACTICE

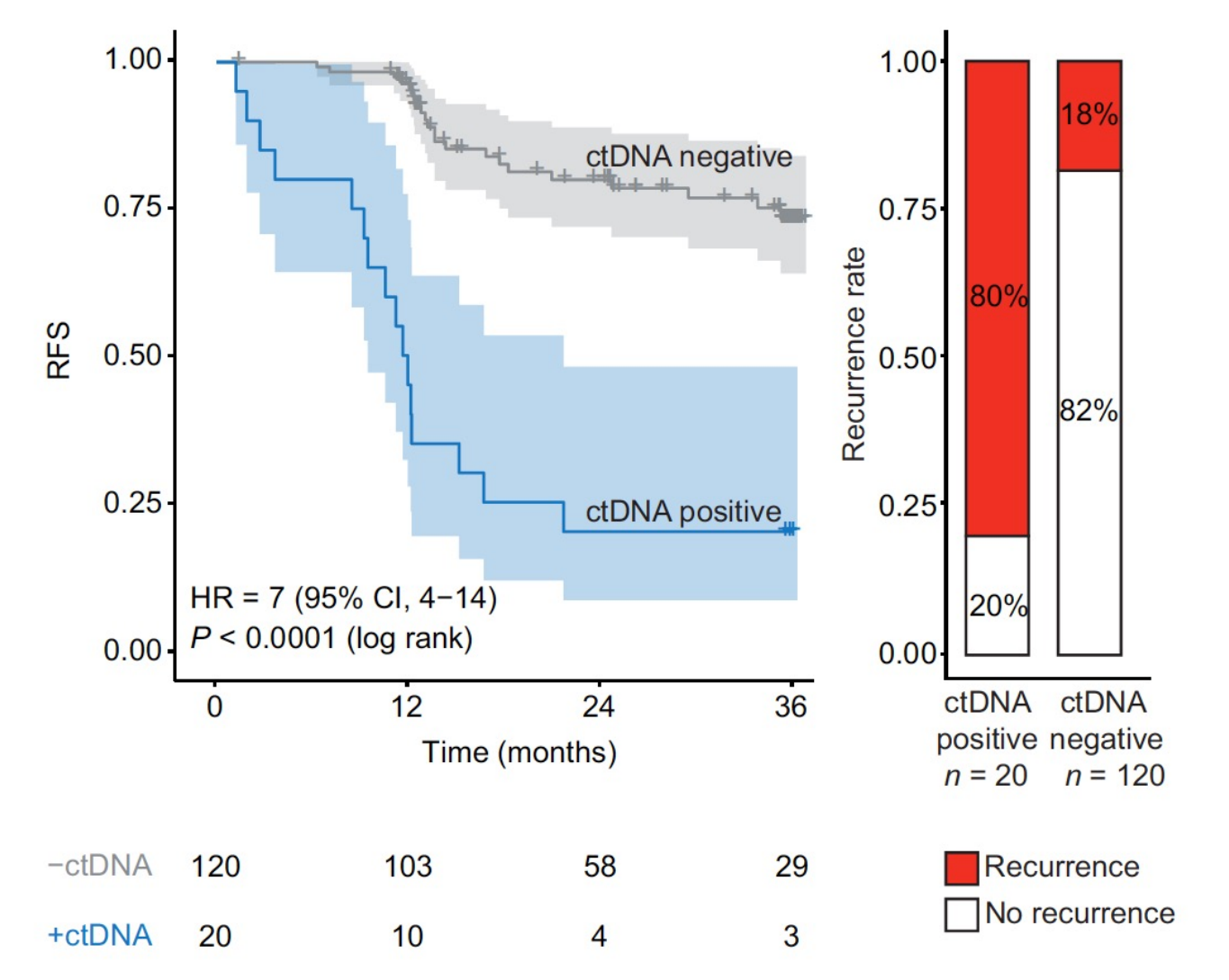
CLINICAL CANCER RESEARCH | PRECISION MEDICINE AND IMAGING

Circulating Tumor DNA in Stage III Colorectal Cancer, beyond Minimal Residual Disease Detection, toward Assessment of Adjuvant Therapy Efficacy and Clinical Behavior of Recurrences

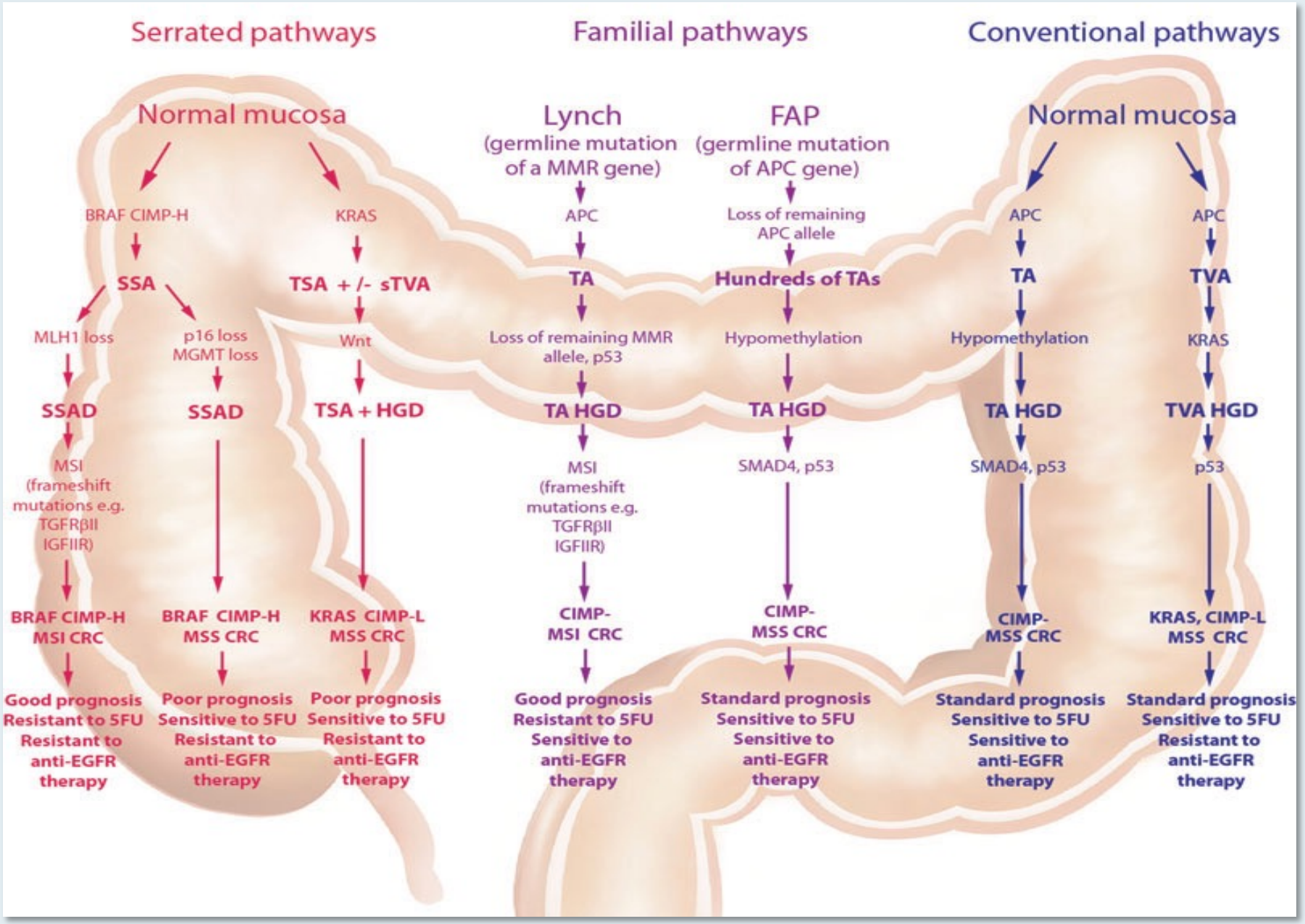
Tenna Vesterman Henriksen[1,2], Noelia Tarazona[3,4], Amanda Frydendahl[1,2], Thomas Reinert[1,2], Francisco Gimeno-Valiente[3], Juan Antonio Carbonell-Asins[3,5], Shruti Sharma[6], Derrick Renner[6], Dina Hafez[6], Desamparados Roda[3,4], Marisol Huerta[3], Susana Roselló[3,4], Anders Husted Madsen[7], Uffe S. Løve[8], Per Vadgaard Andersen[9], Ole Thorlacius-Ussing[10], Lene Hjerrild Iversen[11], Kåre Andersson Gotschalck[12], Himanshu Sethi[6], Alexey Aleshin[6], Andres Cervantes[3,4], and Claus Lindbjerg Andersen[1,2]

Clin Cancer Res 2022;28(3):507-17.

Detection of ctDNA After Surgery and Recurrence Rates

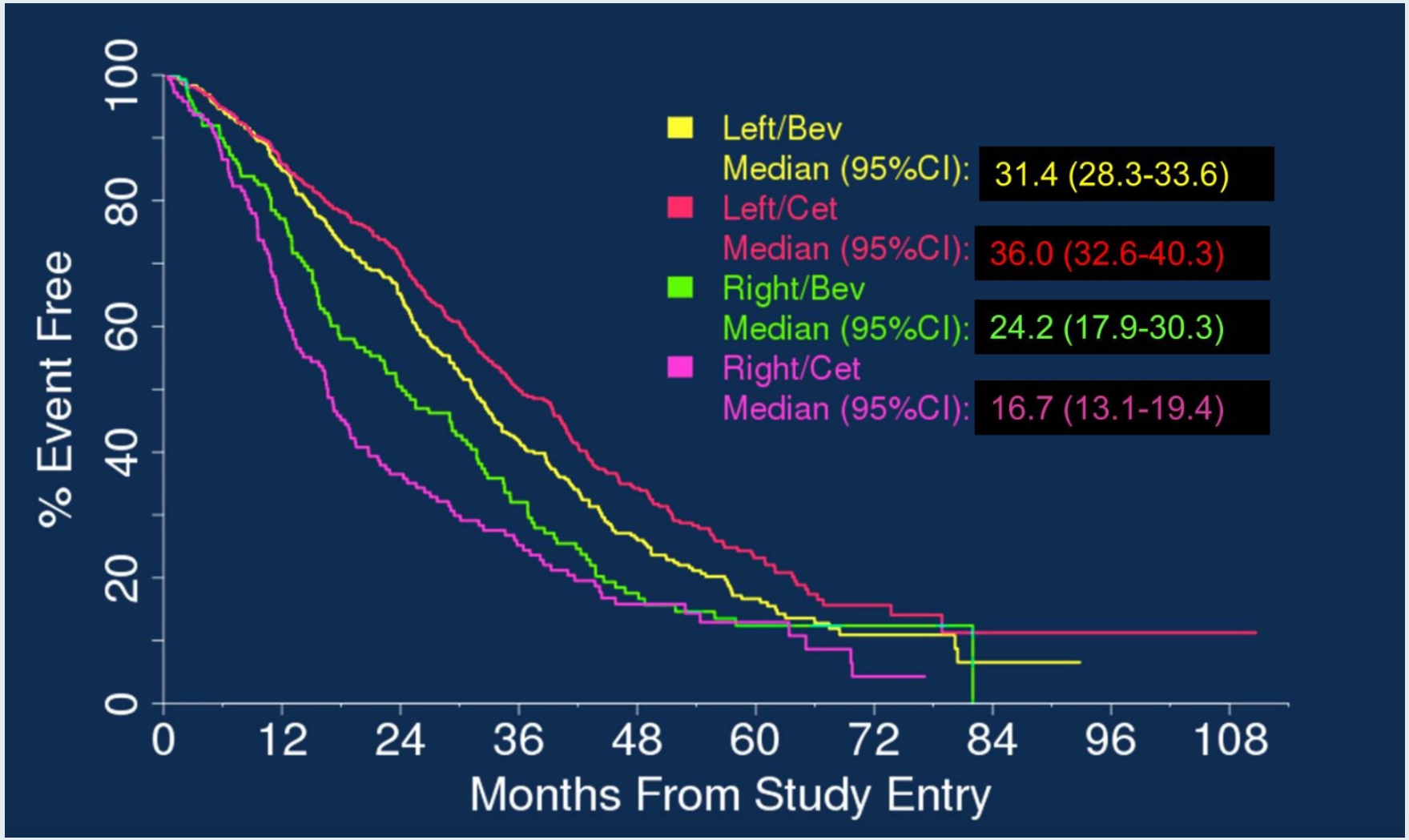


Henriksen TV et al. *Clin Cancer Res* 2022;28(3):507-17.



Courtesy of Christopher Lieu, MD.

CALGB/SWOG-80405: OS by Tumor Location and Biologic Agent (RAS Wild Type)



Venook A et al. ASCO 2016;Abstract 3504.

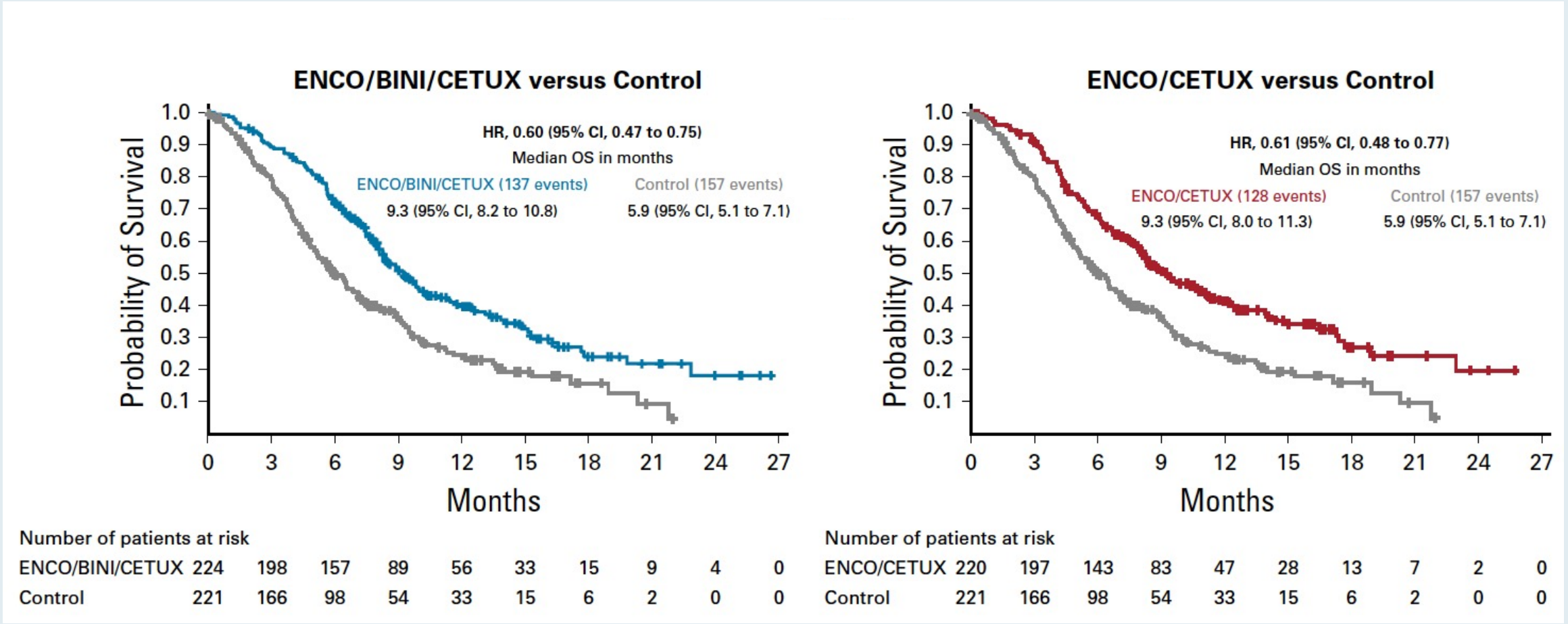
rapid communications

Encorafenib Plus Cetuximab as a New Standard of Care for Previously Treated *BRAF* V600E–Mutant Metastatic Colorectal Cancer: Updated Survival Results and Subgroup Analyses from the BEACON Study

Josep Tabernero, MD, PhD[1]; Axel Grothey, MD[2]; Eric Van Cutsem, MD, PhD[3]; Rona Yaeger, MD[4]; Harpreet Wasan, MD[5]; Takayuki Yoshino, MD, PhD[6]; Jayesh Desai, MBBS[7]; Fortunato Ciardiello, MD, PhD[8]; Fotios Loupakis, MD, PhD[9]; Yong Sang Hong, MD, PhD[10]; Neeltje Steeghs, MD, PhD[11]; Tormod Kyrre Guren, MD, PhD[12]; Hendrik-Tobias Arkenau, MD, PhD[13]; Pilar Garcia-Alfonso, MD[14]; Elena Elez, MD, PhD[1]; Ashwin Gollerkeri, MD[15]; Kati Maharry, PhD[15]; Janna Christy-Bittel, MSN[15]; and Scott Kopetz, MD, PhD[16]

J Clin Oncol 2021;39(4):273-84.

BEACON: OS Results



Tabanero J et al. *J Clin Oncol* 2021;39(4):273-84.

ESMO WORLD CONGRESS ON Gastrointestinal Cancer

ANCHOR CRC: a single-arm, phase 2 study of encorafenib, binimetinib plus cetuximab in previously untreated *BRAF*^{V600E}–mutant metastatic colorectal cancer

Eric Van Cutsem, Julien Taieb, Rona Yaeger, Takayuki Yoshino, Evaristo Maiello, Elena Elez Fernandez, Jeroen Dekervel, Paul Ross, Ana Ruiz Casado, Janet Graham, Takeshi Kato, Jose Carlos Ruffinelli, Thierry André, Edith Carrière Roussel, Isabelle Klauck, Mélanie Groc, Axel Grothey, Jean-Claude Vedovato, Josep Tabernero*

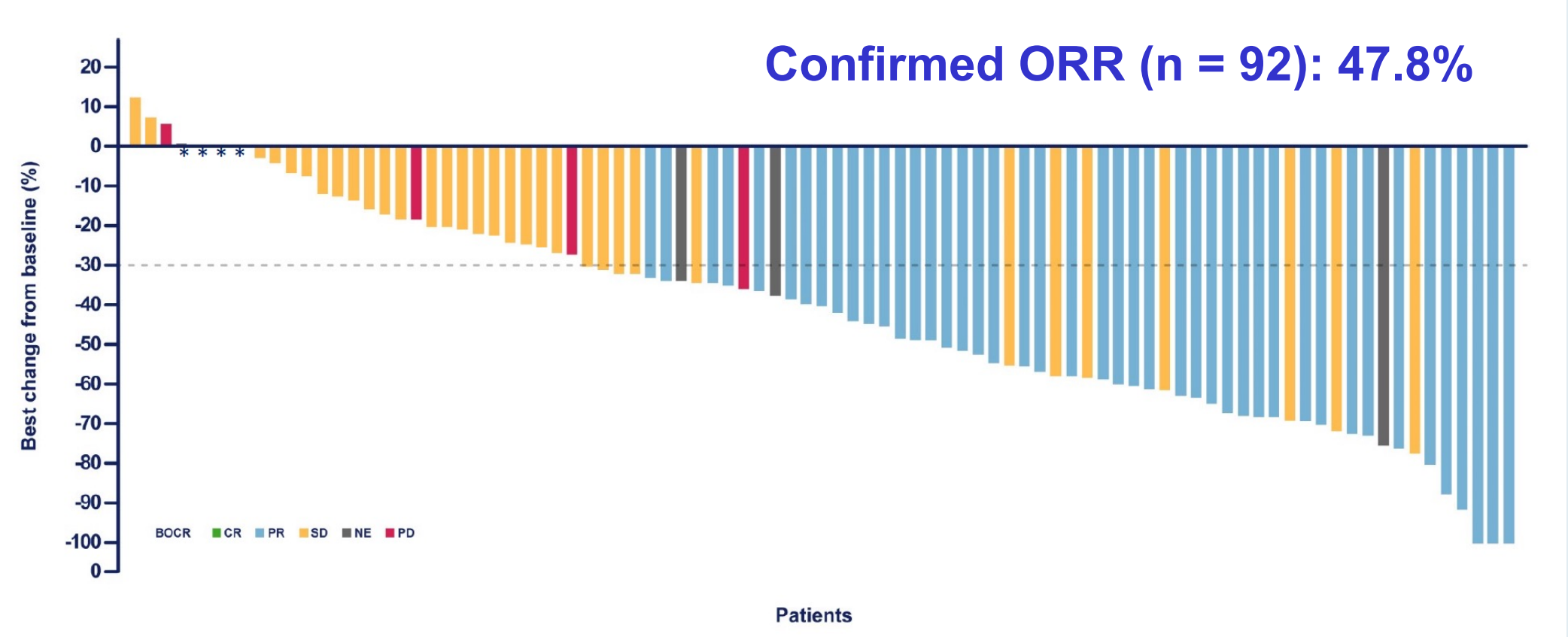
** University Hospitals Leuven, Belgium*

ANCHOR CRC: encorAfenib, biNimetinib and Cetuximab in subjects witH previOusly untreated BRAF-mutant ColoRectal Cancer

ESMO World Congress on Gastrointestinal Cancer 2021;Abstract O-10.

RTP RESEARCH TO PRACTICE

ANCHOR CRC: Results Summary



ORR, objective response rate.

- OS was 17.2 mos (with a median follow-up of 14.4 mos)
- The triplet combination was well-tolerated and there were no unexpected toxicities

Van Cutsem E et al. ESMO World Congress on Gastrointestinal Cancer 2021;Abstract O-10.

BREAKWATER Study Design

An open-label, multicenter, randomized phase 3 study of 1st line encorafenib plus cetuximab with or without chemotherapy versus standard of care therapy in patients with metastatic *BRAF* V600E-mutant mCRC

Safety lead-in

Patients with *BRAF*^{V600E} mutant mCRC with 0 to 1 prior regimens in the metastatic setting

Phase 3

Patients with *BRAF*^{V600E} mutant mCRC and no prior systemic therapy in the metastatic setting

Encorafenib + cetuximab + mFOLFOX6
N=30
Encorafenib + cetuximab + FOLFIRI
N=30

Dosages
- Encorafenib, 300 mg PO QD
- Cetuximab, 500 mg/m² IV Q2W
- **FOLFOX, full dose IV Q2W**
- FOLFIRI, full dose IV Q2W

Randomize 1:1:1*

Arm A**
Encorafenib + cetuximab, N=290

Arm B**
Encorafenib + cetuximab + FOLFOX or FOLFIRI$^{\beta}$, N=290

Control arm§
Physician's choice: FOLFOX, FOLFIRI, FOLFOXIRI, CAPOX, all ± anti-VEGF antibody, N=290

PRIMARY ENDPOINTS
PFS (BICR) Arm A vs Control
AND
PFS (BICR) Arm B vs Control
(BICR, blinded independent central review)

KEY SECONDARY ENDPOINTS
OS Arm A vs Control
AND
OS Arm B vs Control

OTHER ENDPOINTS
- Incidence of DLTs, adverse events, dose modifications/discontinuations due to AEs
- PK including drug-drug interactions

BREAKWATER STUDY

*Stratified by: ECOG PS 0 v. 1, Region US/Canada v. Western Europe v. ROW
**Same dosing as SLI; $^{\beta}$FOLFOX or FOLFIRI based on SLI results; § No crossover.
ClinicalTrials.gov Identifier: NCT04607421

Van Cutsem E et al. ESMO World Congress on Gastrointestinal Cancer 2021;Abstract O-10.

ESMO WORLD CONGRESS ON Gastrointestinal Cancer

Final Overall Survival for the Phase 3 KN177 Study: Pembrolizumab Versus Chemotherapy in Microsatellite Instability-High/Mismatch Repair Deficient Metastatic Colorectal Cancer

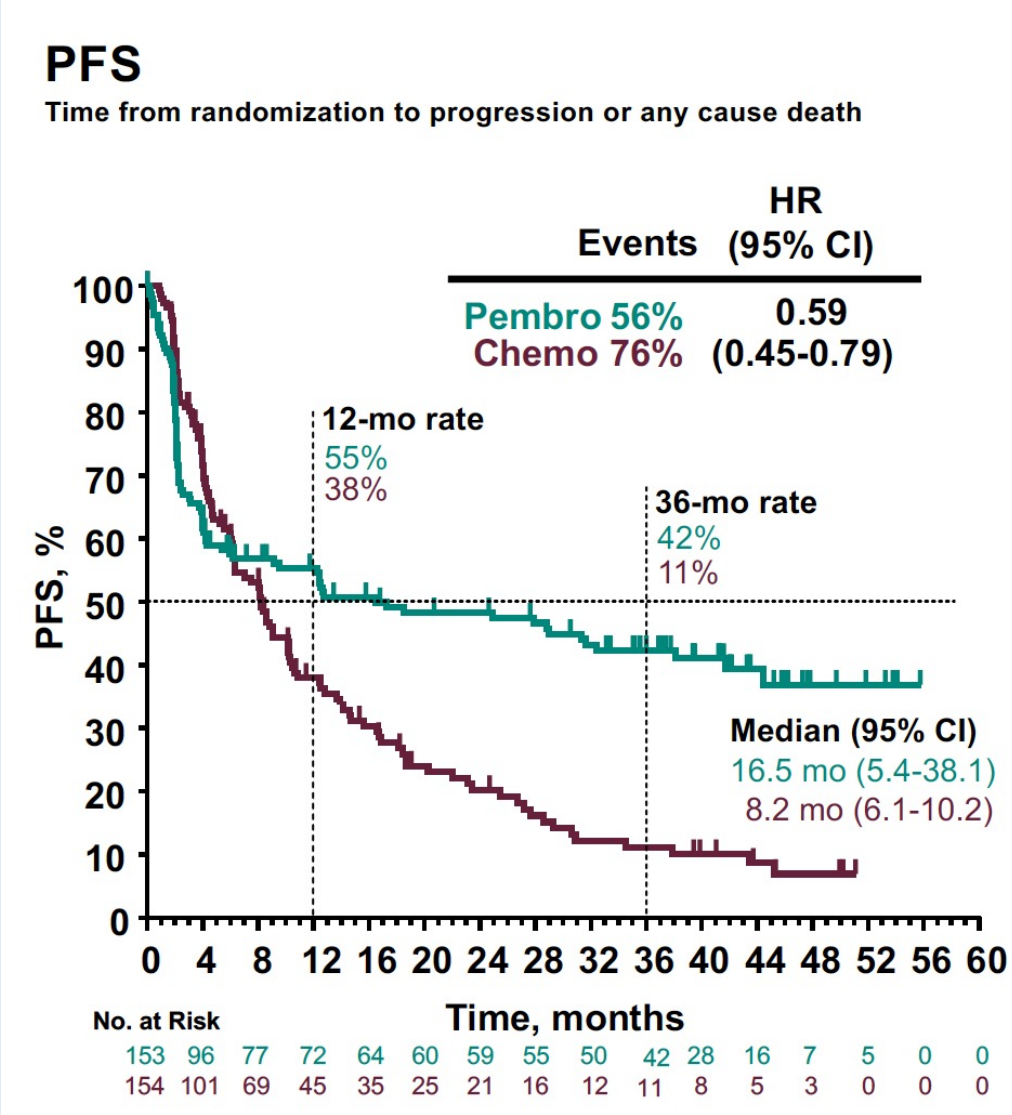
Thierry André,[1] Kai-Keen Shiu,[2] Tae Won Kim,[3] Benny Vittrup Jensen,[4] Lars Henrik Jensen,[5] Cornelis Punt,[6] Denis Smith,[7] Rocio Garcia-Carbonero,[8] Julia Alcaide-Garcia,[9] Peter Gibbs,[10] Christelle de la Fouchardiere,[11] Fernando Rivera,[12] Elena Elez,[13] Johanna Bendell,[14] Dung T. Le,[15] Takayuki Yoshino,[16] Wenyan Zhong,[17] David Fogelman,[18] Patricia Marinello,[18] Luis A. Diaz Jr[19]

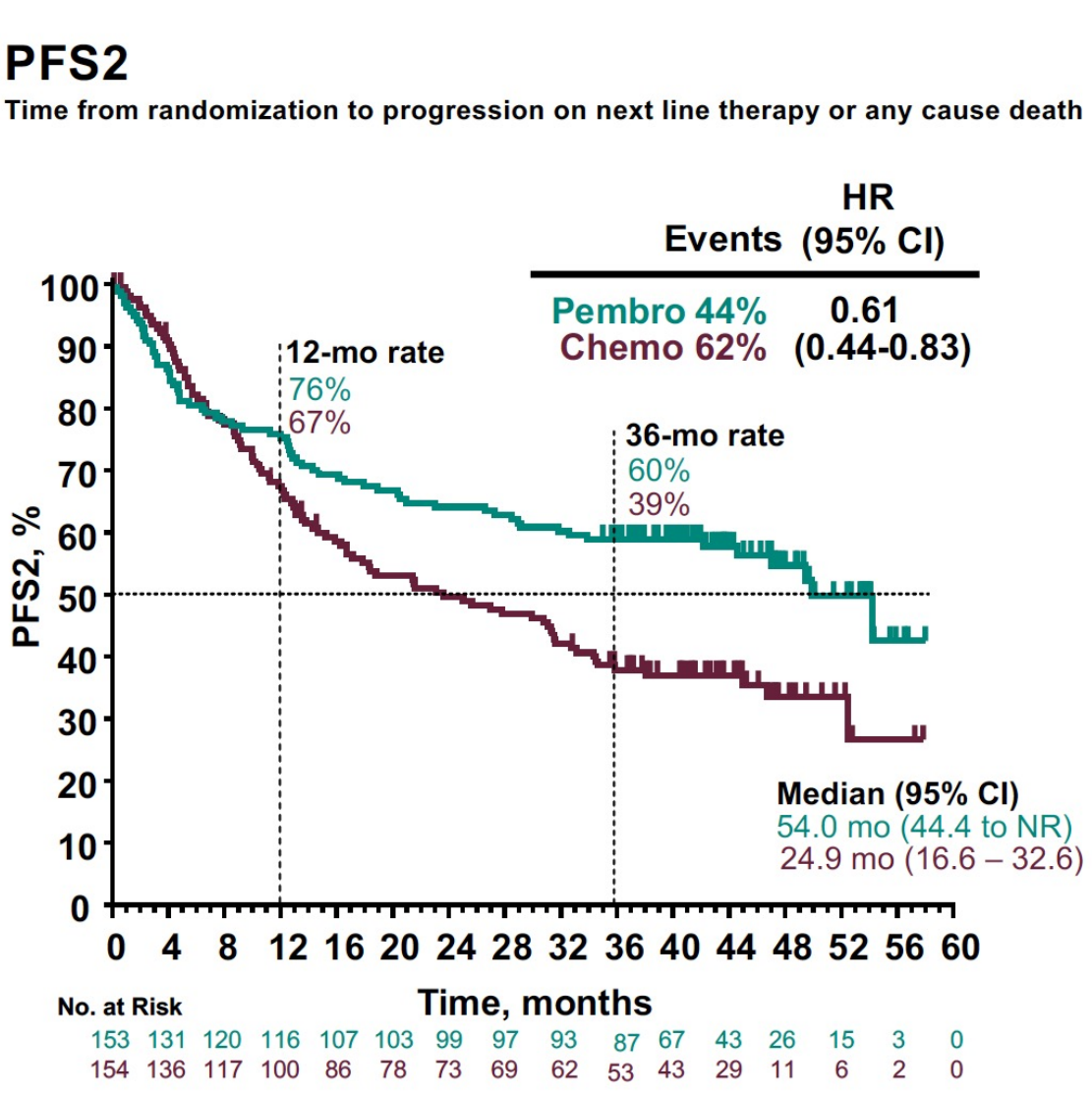
[1]Sorbonne Université and Hôpital Saint Antoine, Paris, France; [2]University College Hospital, NHS Foundation Trust, London, United Kingdom; [3]Asan Medical Center, University of Ulsan, Seoul, Republic of Korea; [4]Herlev and Gentofte Hospital, Herlev, Denmark; [5]University Hospital of Southern Denmark, Vejle, Denmark; [6]Amsterdam University Medical Centers, University of Amsterdam, Amsterdam, Netherlands; [7]Bordeaux University Hospital, Bordeaux, France; [8]Hospital Universitario 12 de Octubre, Imas12, CNIO, UCM, Madrid, Spain; [9]Hospital Regional Universitario de Malaga, Malaga, Spain; [10]Western Health, St Albans, Australia; [11]Léon Bérard Center, Lyon, France; [12]Hospital Universitario Marques de Valdecilla, IDIVAL, Santander, Spain; [13]Vall d'Hebron Institute of Oncology, Barcelona, Spain; [14]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN, USA; [15]Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD, USA; [16]National Cancer Center Hospital East, Kashiwa, Japan; [17]MSD China, Beijing, China; [18]Merck & Co., Inc. Kenilworth, NJ, USA; [19]Memorial Sloan Kettering Cancer Center, New York, NY, USA

ESMO World Congress on Gastrointestinal Cancer 2021;Abstract O-8.

RTP RESEARCH TO PRACTICE

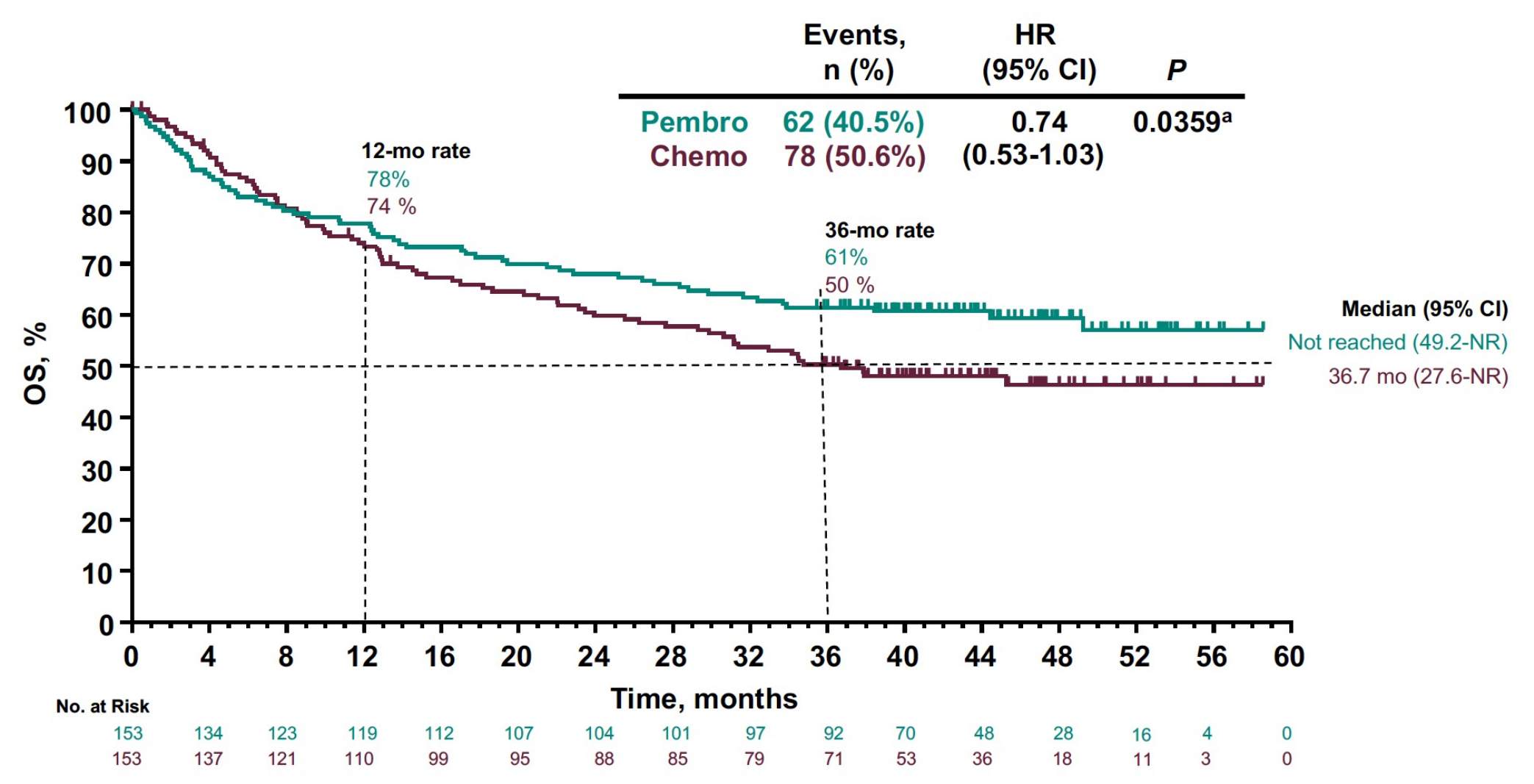
KEYNOTE-177: Progression-Free Survival





André T et al. ESMO World Congress on Gastrointestinal Cancer 2021;Abstract O-8.

KEYNOTE-177: Overall Survival



André T et al. ESMO World Congress on Gastrointestinal Cancer 2021;Abstract O-8.

ESMO WORLD CONGRESS ON Gastrointestinal Cancer

NIVOLUMAB PLUS LOW-DOSE IPILIMUMAB IN PREVIOUSLY TREATED PATIENTS WITH MICROSATELLITE INSTABILITY-HIGH/ MISMATCH REPAIR-DEFICIENT METASTATIC COLORECTAL CANCER: 4-YEAR FOLLOW-UP FROM CHECKMATE 142

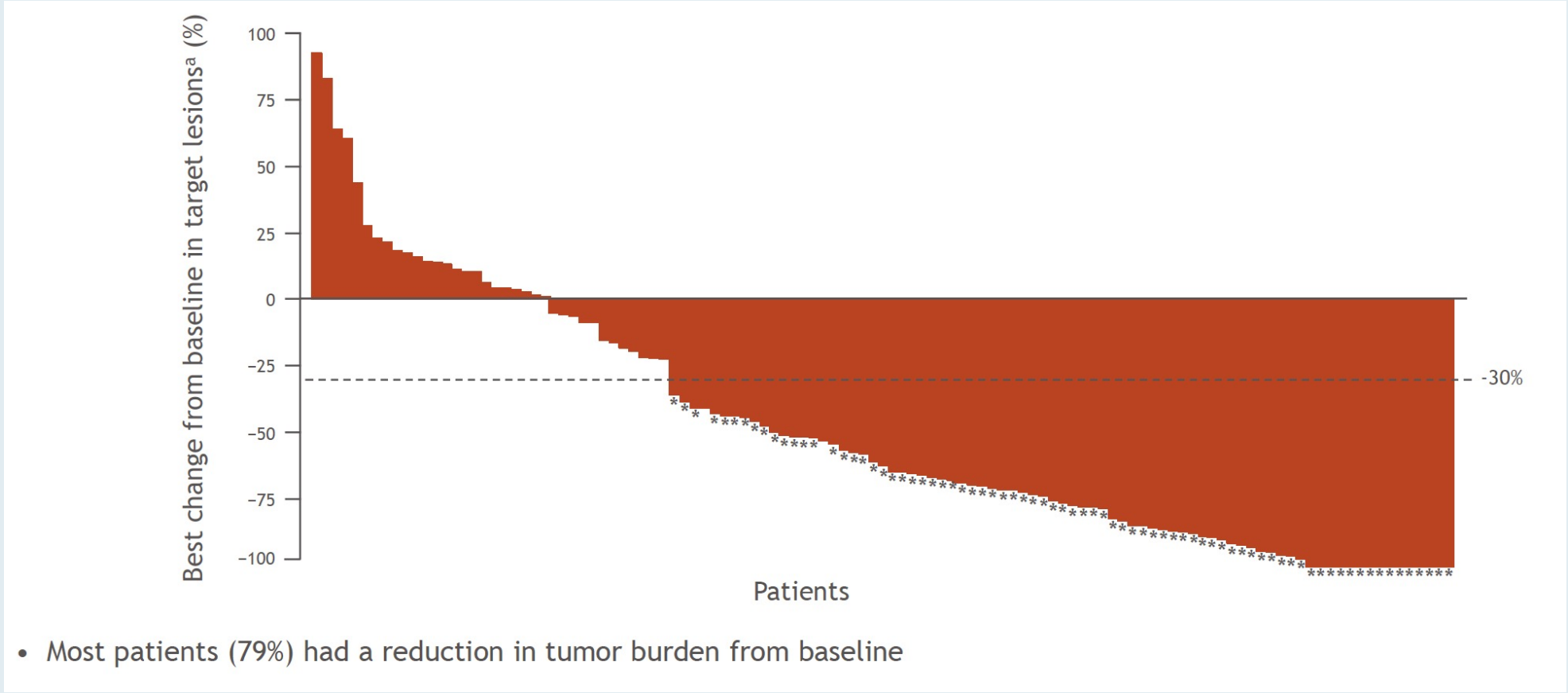
Thierry André,[1] Sara Lonardi,[2] Ka Yeung Mark Wong,[3] Heinz-Josef Lenz,[4] Fabio Gelsomino,[5] Massimo Aglietta,[6] Michael A. Morse,[7] Eric Van Cutsem,[8] Ray McDermott,[9] Andrew Hill,[10] Michael B. Sawyer,[11] Alain Hendlisz,[12] Bart Neyns,[13] Sandzhar Abdullaev,[14] Arteid Memaj,[14] Ming Lei,[14] Scott Kopetz,[15] Michael Overman[15]

[1]Hôpital Saint Antoine, Assistance Publique Hôpitaux de Paris and Sorbonne Université, Paris, France; [2]Istituto Oncologico Veneto IOV-IRCSS, Padova, Italy; [3]Westmead Hospital, Sydney, NSW, Australia; [4]University of Southern California Norris Comprehensive Cancer Center, Los Angeles, CA, USA; [5]University Hospital of Modena, Modena, Italy; [6]Candiolo Cancer Institute and University of Torino Medical School, Candiolo, Italy; [7]Duke University Medical Center, Durham, NC, USA; [8]University Hospitals Gasthuisberg/ Leuven and KU Leuven, Leuven, Belgium; [9]St Vincent's University Hospital and Cancer Trials Ireland, Dublin, Ireland; [10]Tasman Oncology Research, Ltd., Southport, QLD, Australia; [11]Cross Cancer Institute and University of Alberta, Edmonton, AB, Canada; [12]Institut Jules Bordet, Brussels, Belgium; [13]Universitair Ziekenhuis Brussel, Brussels, Belgium; [14]Bristol Myers Squibb, Princeton, NJ, USA; [15]MD Anderson Cancer Center, Houston, TX, USA

ESMO World Congress on Gastrointestinal Cancer 2021;Abstract SO-27.

RTP RESEARCH TO PRACTICE

CheckMate 142: Four-Year Update of Nivolumab/Ipilimumab as First-Line Therapy for Microsatellite Instability-High/Mismatch Repair-Deficient (dMMR) Metastatic Colorectal Cancer (mCRC)



- Most patients (79%) had a reduction in tumor burden from baseline

- Median PFS and OS were not reached
- 48-month PFS rate: 53%
- 48-month OS rate: 70.5%

André T et al. World Congress on Gastrointestinal Cancer 2021;Abstract SO-27.

FDA Grants Accelerated Approval to Dostarlimab-gxly for dMMR Advanced Solid Tumors

Press Release – August 17, 2021

"The Food and Drug Administration granted accelerated approval to dostarlimab-gxly for adult patients with mismatch repair deficient (dMMR) recurrent or advanced solid tumors, as determined by an FDA-approved test, that have progressed on or following prior treatment and who have no satisfactory alternative treatment options.

Today, the FDA also approved the VENTANA MMR RxDx Panel as a companion diagnostic device to select patients with dMMR solid tumors for treatment with dostarlimab-gxly.

The efficacy of dostarlimab was evaluated in the GARNET Trial (NCT02715284), a non-randomized, multicenter, open-label, multi-cohort trial. The efficacy population consisted of 209 patients with dMMR recurrent or advanced solid tumors who progressed following systemic therapy and had no satisfactory alternative treatment."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-dostarlimab-gxly-dmmr-advanced-solid-tumors

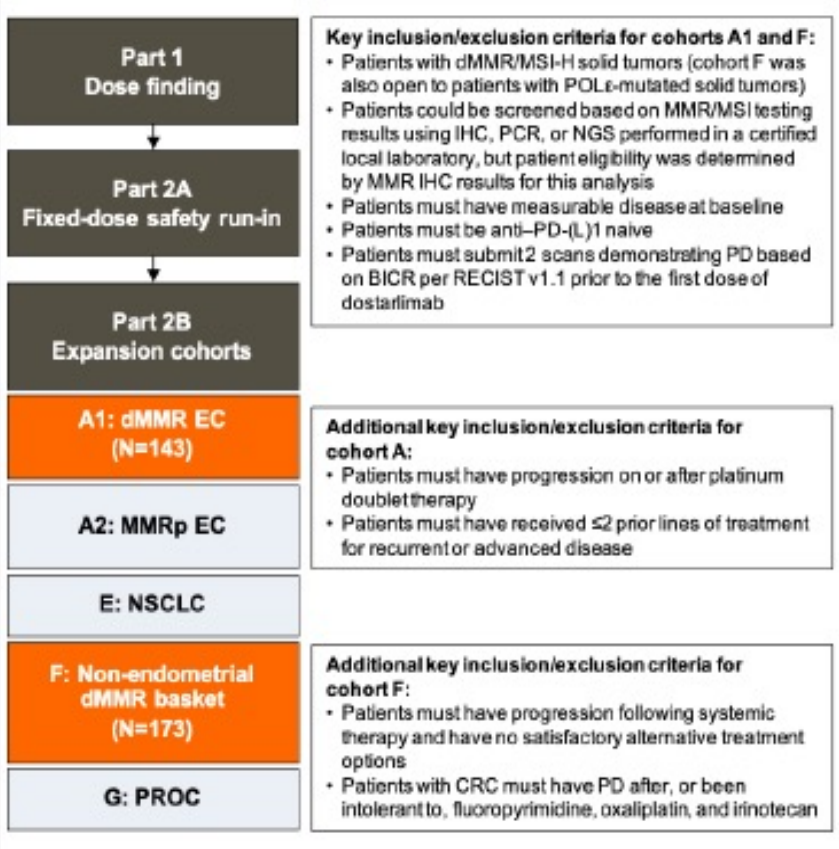
Antitumor Activity of Dostarlimab in Patients with Mismatch Repair–Deficient (dMMR) Tumors: A Combined Analysis of 2 Cohorts in the GARNET Study

Berton D et al.

ASCO 2021;Abstract 2564.

GARNET: Trial Design and Antitumor Activity

Trial Design



Primary Endpoint Analysis

Variable	Cohort A1 (n=103)	Cohort F (n=106)	Cohorts A1 + F (n=209)
Median follow-up time, mo[a]	20.4	16.7	17.5
Confirmed responses, n	46	41	87
ORR, % (95% CI)[b]	44.7 (34.9–54.8)	38.7 (29.4–48.6)	41.6 (34.9–48.6)
CR, n (%)	11 (10.7)	8 (7.5)	19 (9.1)
PR, n (%)	35 (34.0)	33 (31.1)	68 (32.5)
SD, n (%)	13 (12.6)	26 (24.5)	39 (18.7)
PD, n (%)	39 (37.9)	32 (30.2)	71 (34.0)
NE, n (%)	5 (4.9)	7 (6.6)	3 (1.4)
Disease control rate, % (95% CI)[c]	57.3 (47.2–67.0)	63.2 (53.3–72.4)	60.3 (53.3–67.0)
Duration of response, median (range), mo	34.7 (2.63 to 35.78+)	NR (5.59 to 30.13+)	34.7 (2.63 to 35.78+)

Antitumor Activity by Tumor Type

		Confirmed ORR (RECIST v1.1)	
Tumor type	**Patients, N**	**n (%)**	**95% CI, %**
Overall	**209**	**87 (41.6)**	**(34.9–48.6)**
EC	**103**	**46 (44.7)**	**(34.9–54.8)**
CRC	**69**	**25 (36.2)**	**(25.0–48.7)**
Non-CRC	**37**	**16 (43.2)**	**(27.1–60.5)**
Small-intestinal cancer	12	4 (33.3)	(9.9–65.1)
Gastric and gastroesophageal junction cancer	8	3 (37.5)	(8.5–75.5)
Pancreatic carcinoma	4	SD, 3 PD	
Ovarian cancer	2	PR, SD	
Hepatocellular carcinoma	2	PR, PD	
Biliary neoplasm	2	2 CR	
Breast cancer	1	CR	
Adrenal cortical carcinoma	1	PR	
Malignant neoplasm of the female genitals	1	PR	
Pleural cancer	1	PR	
Unknown origin	1	PR	
Renal cell carcinoma	1	SD	
Esophageal cancer	1	PD	

Berton D et al. ASCO 2021;Abstract 2564.

RTP RESEARCH TO PRACTICE

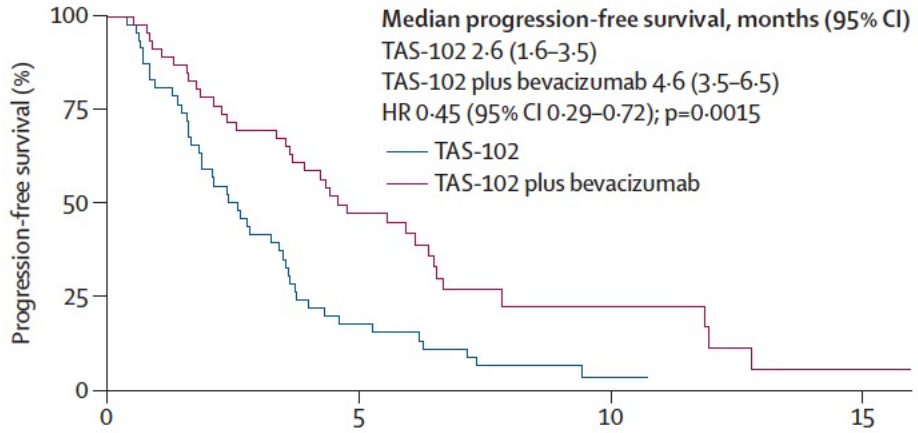
Lancet Oncol 2020;21(3):412-20.

Articles

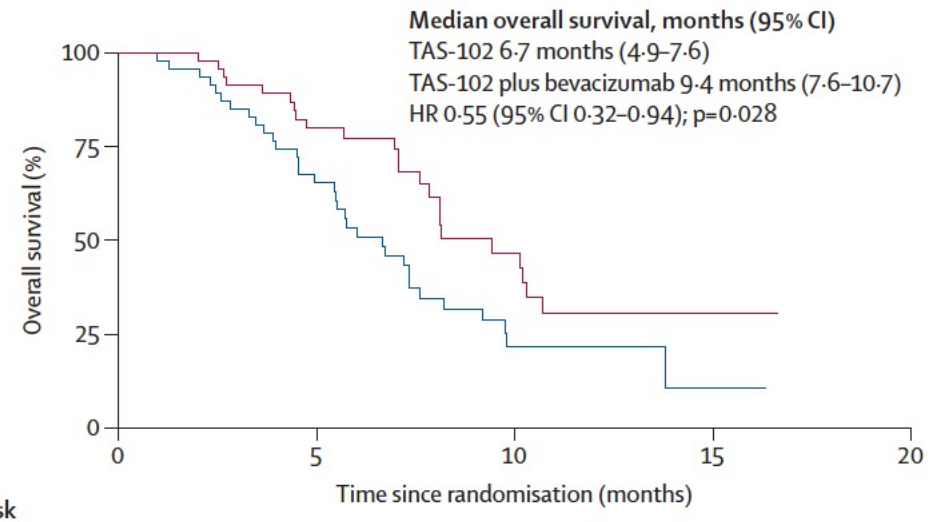
TAS-102 with or without bevacizumab in patients with chemorefractory metastatic colorectal cancer: an investigator-initiated, open-label, randomised, phase 2 trial

Per Pfeiffer, Mette Yilmaz, Sören Möller, Daniela Zitnjak, Merete Krogh, Lone Nørgård Petersen, Laurids Østergaard Poulsen, Stine Braendegaard Winther, Karina Gravgaard Thomsen, Camilla Qvortrup

TAS-102 with or without Bevacizumab for Refractory mCRC



Number at risk (number censored)				
TAS-102	47 (38)	8 (6)	1 (0)	0
TAS-102 plus bevacizumab	46 (24)	20 (8)	5 (3)	1



Number at risk (number censored)					
TAS-102	47 (16)	29 (16)	6 (1)	1 (0)	0
TAS-102 plus bevacizumab	46 (9)	34 (10)	12 (4)	2 (0)	0

Pfeiffer P et al. *Lancet Oncol* 2020;21(3):412-20.

RTP RESEARCH TO PRACTICE

ESMO VIRTUAL PLENARY

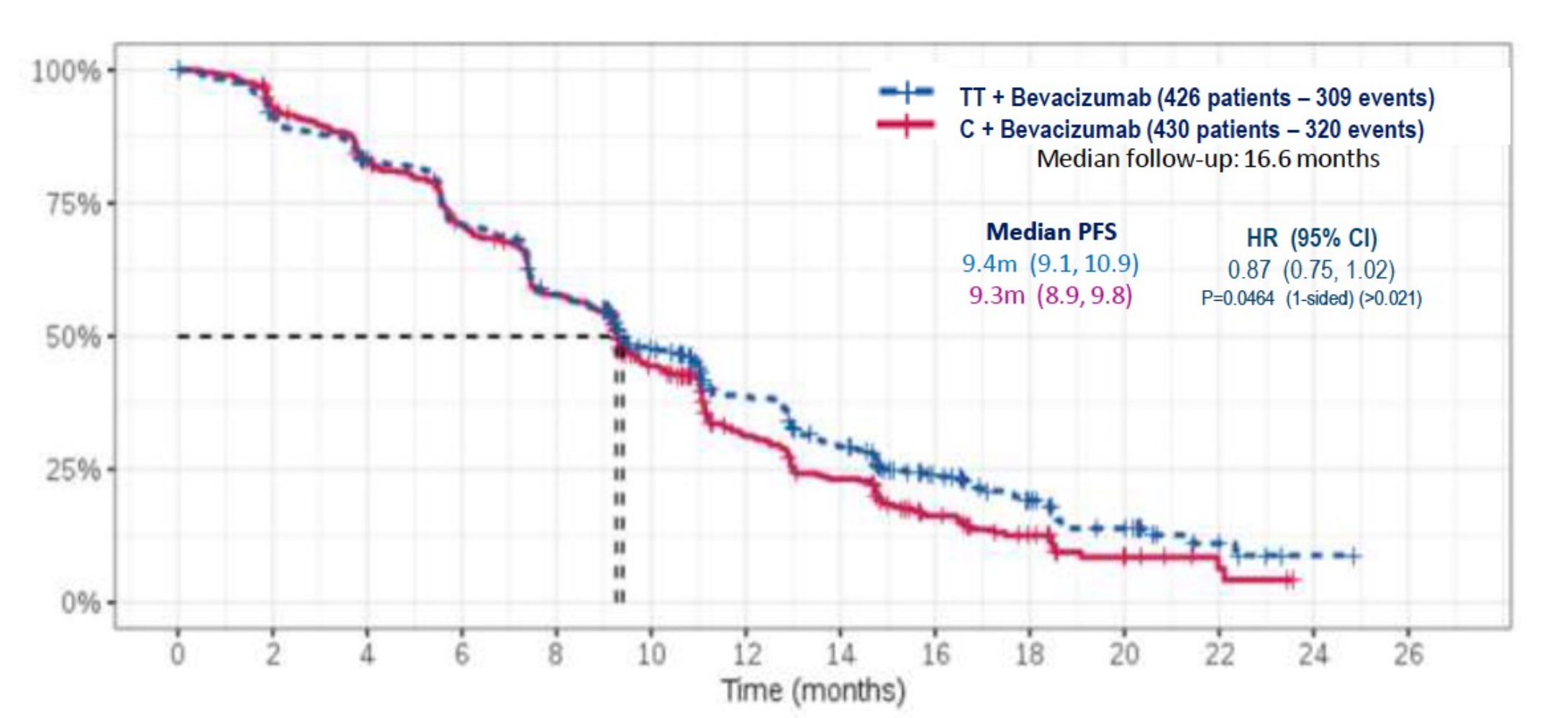
TRIFLURIDINE/TIPIRACIL PLUS BEVACIZUMAB VS CAPECITABINE PLUS BEVACIZUMAB AS FIRST LINE TREATMENT FOR PATIENTS WITH METASTATIC COLORECTAL CANCER (mCRC) INELIGIBLE FOR INTENSIVE THERAPY: THE PHASE III RANDOMIZED SOLSTICE STUDY

T. ANDRÉ,[1] A. FALCONE,[2] Y. SHPARYK,[3] F. MOISEENKO,[4] E. POLO-MARQUES,[5] T. CSOSZI,[6] A. CAMPOS-BRAGAGNOLI,[7] G. LIPOSITS,[8] E. CHMIELOWSKA,[9] P. AUBEL,[10] L. MARTÍN,[10] R. FOUGERAY,[10] N. AMELLAL,[10] M. SAUNDERS[11]

[1]Sorbonne University and Saint-Antoine Hospital, Paris, France; [2]University Hospital of Pisa, Pisa, Italy; [3]Lviv Regional Oncology Center, Lviv, Ukraine; [4]Saint Petersburg Scientific Practical Centre for Specialized Medical Care, St Petersburg, Russia; [5]University Hospital Miguel Servet, Zaragoza, Spain; [6]Hetenyi County Oncology Centre Szolnok, Hungary; [7]Barretos Cancer Hospital, Barretos, Brazil; [8]Herning Regional Hospital, Herning, Denmark; [9]Nu-Med Center for Diagnostics and Oncological Therapy, Tomaszów Mazowiecki, Poland; [10]Servier International Research Institute, Suresnes, France; [11]Christie Hospital NHS Foundation Trust, Manchester, United Kingdom

ESMO Virtual Plenary 2021;Abstract VP-11.

SOLSTICE Primary Endpoint: PFS by Investigator's Assessment



André T et al. *ESMO Virtual Plenary* 2021;22:Abstract VP-11.

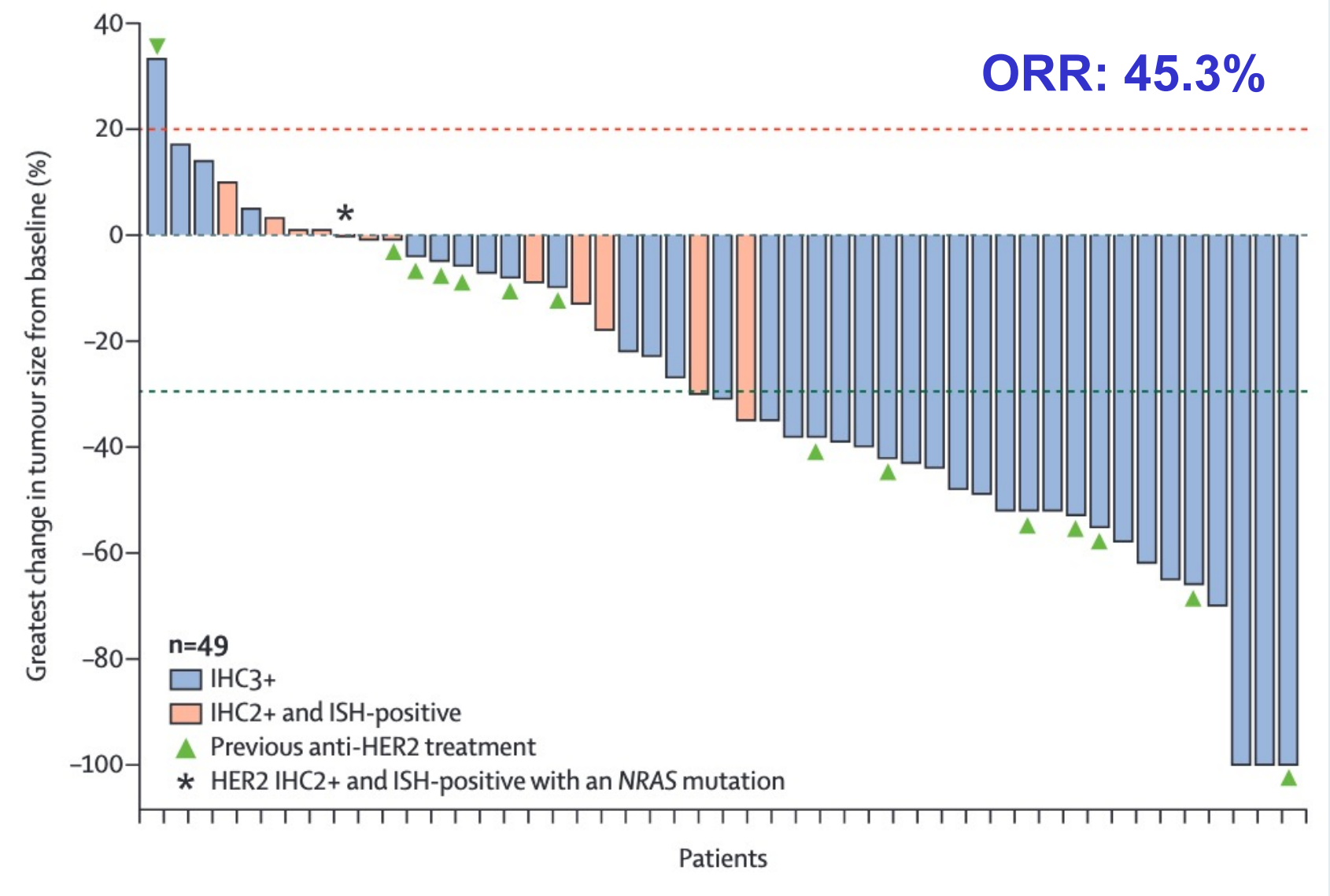
RTP RESEARCH TO PRACTICE

Lancet Oncol 2021;22(6):779-89.

Trastuzumab deruxtecan (DS-8201) in patients with HER2-expressing metastatic colorectal cancer (DESTINY-CRC01): a multicentre, open-label, phase 2 trial

Salvatore Siena, Maria Di Bartolomeo, Kanwal Raghav, Toshiki Masuishi, Fotios Loupakis, Hisato Kawakami, Kensei Yamaguchi, Tomohiro Nishina, Marwan Fakih, Elena Elez, Javier Rodriguez, Fortunato Ciardiello, Yoshito Komatsu, Taito Esaki, Ki Chung, Zev Wainberg, Andrea Sartore-Bianchi, Kapil Saxena, Eriko Yamamoto, Emarjola Bako, Yasuyuki Okuda, Javad Shahidi, Axel Grothey, Takayuki Yoshino, on behalf of the DESTINY-CRC01 investigators

DESTINY-CRC01: Best Change in Tumor Size in Cohort A



Siena S et al. *Lancet Oncol* 2021;22(6):779-89.

RTP RESEARCH TO PRACTICE

DESTINY-CRC01 Adverse Events of Special Interest: Interstitial Lung Disease (ILD)

All Patients (N=86)	n (%)
Grade 1	0
Grade 2	4 (4.7)
Grade 3	1 (1.2)
Grade 4	0
Grade 5	3 (3.5)[a]
Any Grade/Total	8 (9.3)[b,c]

Adjudicated drug-related ILDs:

- Median time to adjudicated onset was 61.0 days (range, 9-165 days)
- 8 of 8 patients received corticosteroids
- 4 patients with grade 2 recovered and 1 patient with grade 3 did not recover (later died due to disease progression)
- Median time from adjudicated onset date to initiation of steroid treatment in the 8 ILD cases was 3.5 days, (range 0-50)

Grade 5 ILDs:

- In the 3 fatal cases adjudicated as drug-related ILD, onset was from 9 days to 120 days (median: 22 days); and death occurred 6-19 days after diagnosis (median: 6 days)

Updated ILD/pneumonitis guidelines recommend to monitor for symptoms, interrupt or discontinue T-DXd, conduct imaging (as clinically indicated), and start steroids as soon as ILD is suspected.

Yoshino T et al. ASCO 2021;Abstract 3500.

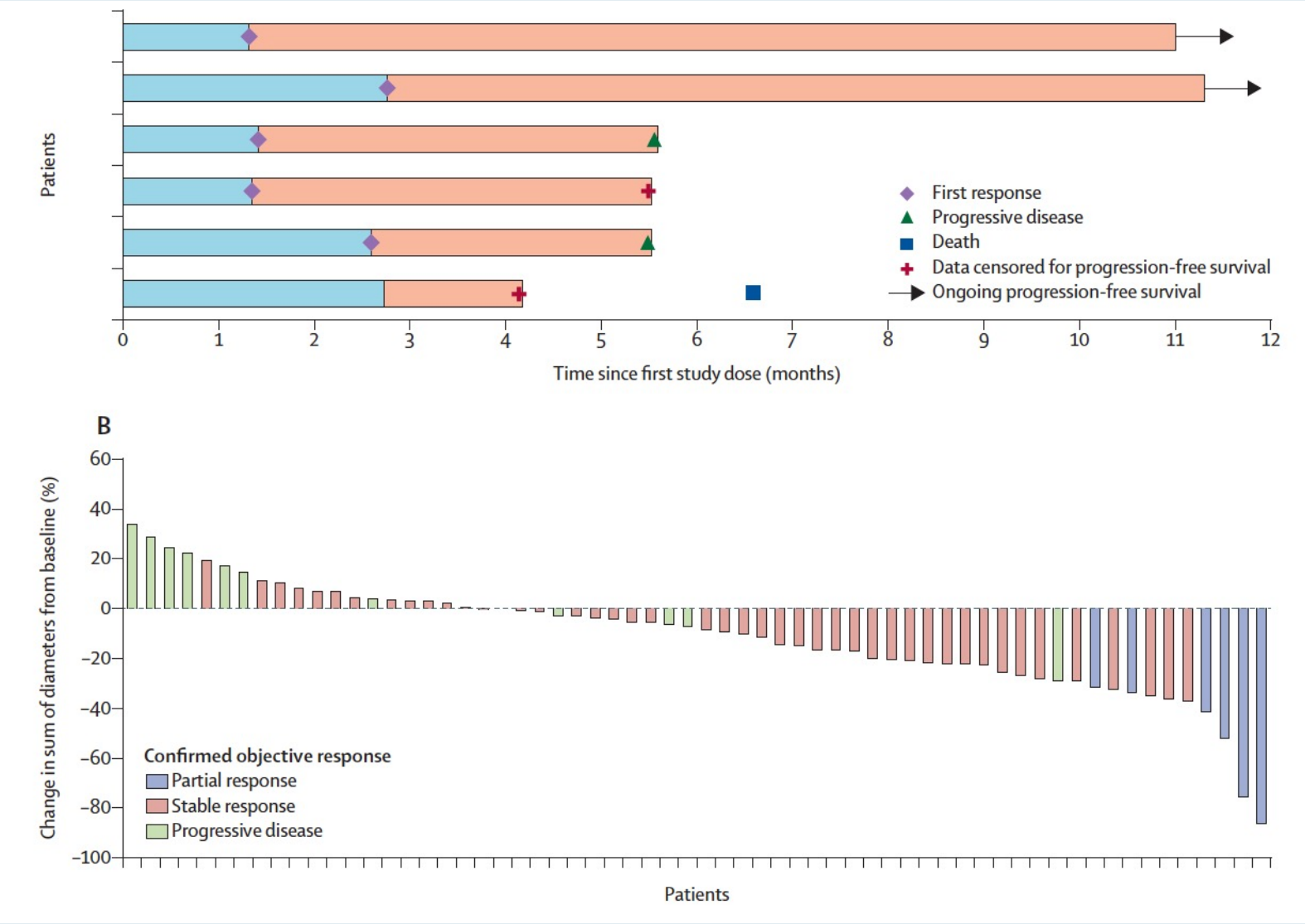
Lancet Oncol 2022;23(1):115-24.

Articles

Sotorasib for previously treated colorectal cancers with *KRAS*^{G12C} mutation (CodeBreaK100): a prespecified analysis of a single-arm, phase 2 trial

Marwan G Fakih, Scott Kopetz*, Yasutoshi Kuboki, Tae Won Kim, Pamela N Munster, John C Krauss, Gerald S Falchook, Sae-Won Han, Volker Heinemann, Kei Muro, John H Strickler, David S Hong, Crystal S Denlinger, Gustavo Girotto, Myung-Ah Lee, Haby Henary, Qui Tran, Joseph K Park, Gataree Ngarmchamnanrith, Hans Prenen, Timothy J Price*

CodeBreak100: Efficacy of Sotorasib



Fakih MG et al. Lancet Oncol 2022;23(1):115-24.

Agenda

Module 1: Gastric and Gastroesophageal Cancers

Module 2: Hepatocellular Cancer

Module 3: Biliary Tract Cancers

Module 4: Colorectal Cancer

Module 5: Pancreatic Adenocarcinoma

Final overall survival results from the phase 3 POLO trial: maintenance olaparib for germline BRCA-mutated metastatic pancreatic cancer

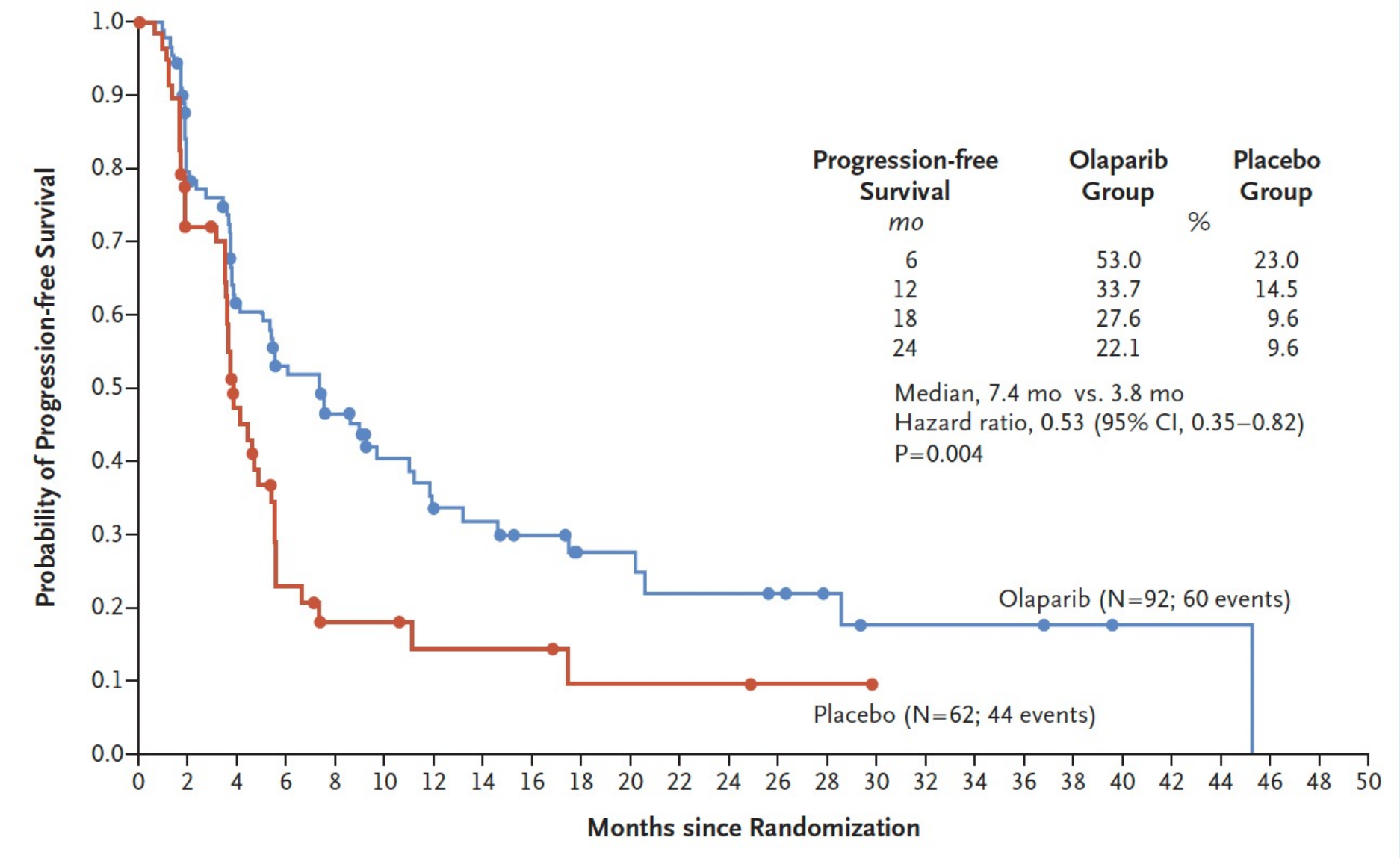
Talia Golan (presenter),[1] Pascal Hammel,[2] Michele Reni,[3] Eric Van Cutsem,[4] Teresa Macarulla,[5] Michael J Hall,[6] Joon Oh Park,[7] Daniel Hochhauser,[8] Dirk Arnold,[9] Do-Youn Oh,[10] Anke Reinacher-Schick,[11] Giampaolo Tortora,[12] Hana Algül,[13] Eileen M O'Reilly,[14] David McGuinness,[15] Karen Cui,[16] Katia Schlienger,[17] Gershon Y Locker,[16] Hedy L Kindler[18]

[1]Institute of Oncology, Sheba Medical Center, Tel Aviv University, Tel Aviv, Israel; [2]Hôpital Beaujon (Assistance Publique–Hôpitaux de Paris), Clichy, and University Paris VII, Paris, France; [3]IRCCS Ospedale San Raffaele Scientific Institute, Milan, Italy; [4]University Hospitals Gasthuisberg and KU Leuven, Leuven, Belgium; [5]Vall d'Hebron University Hospital and Vall d'Hebron Institute of Oncology, Barcelona, Spain; [6]Fox Chase Cancer Center, Philadelphia, PA, USA; [7]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; [8]University College London Cancer Institute, London, UK; [9]Asklepios Tumorzentrum Hamburg Asklepios Klinik Altona, Hamburg, Germany; [10]Seoul National University Hospital, Cancer Research Institute, Seoul National University College of Medicine, Seoul, South Korea; [11]St. Josef-Hospital, Ruhr University Bochum, Bochum, Germany; [12]Medical Oncology Unit, Fondazione Policlinico Gemelli IRCCS, Rome, Italy; [13]Klinikum rechts der Isar, Comprehensive Cancer Center Munich TUM, Technische Universität Munich, Munich, Germany; [14]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [15]AstraZeneca, Cambridge, UK; [16]AstraZeneca, Gaithersburg, MD, USA; [17]Merck & Co., Inc., Kenilworth, NJ, USA; [18]University of Chicago, Chicago, IL, USA

PRESENTED AT: Gastrointestinal Cancers Symposium

#GI21

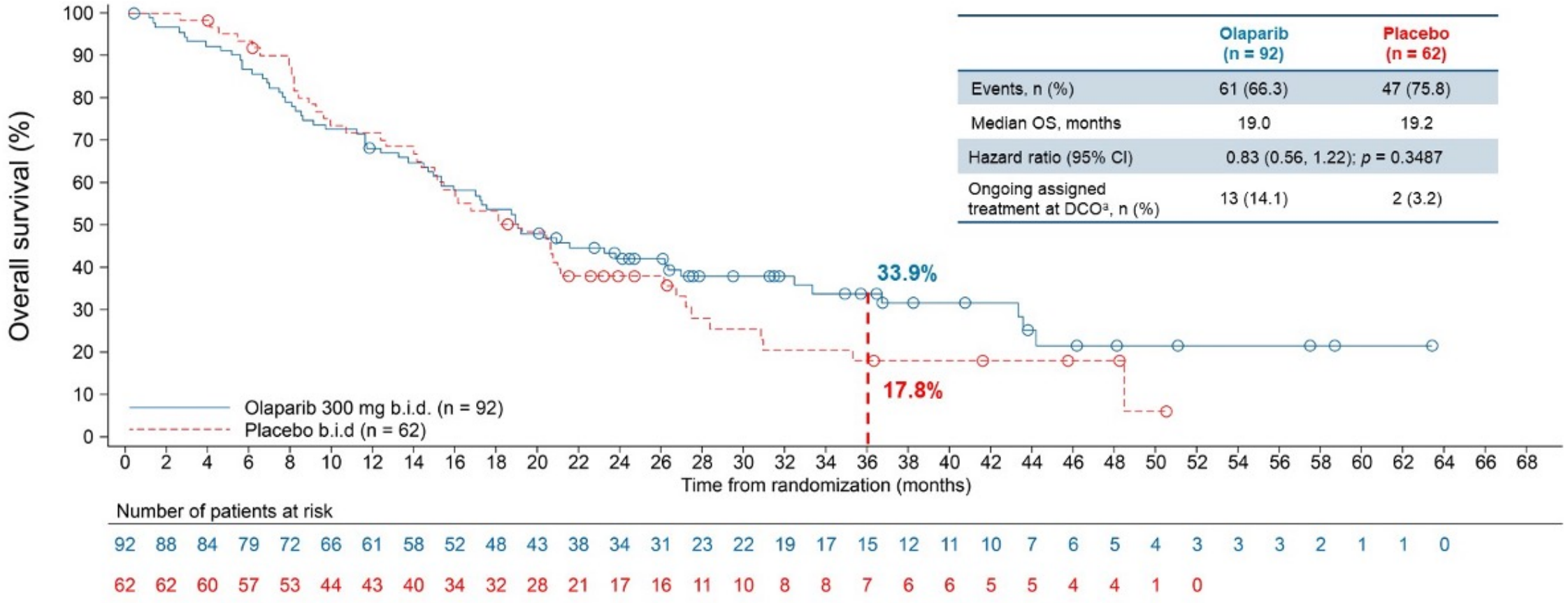
POLO: Initial Report of PFS



Progression-free Survival	Olaparib Group	Placebo Group
mo	%	
6	53.0	23.0
12	33.7	14.5
18	27.6	9.6
24	22.1	9.6

Golan T et al. *N Engl J Med* 2019;381(4):317-27.

POLO: Final OS Analysis



	Olaparib (n = 92)	Placebo (n = 62)
Events, n (%)	61 (66.3)	47 (75.8)
Median OS, months	19.0	19.2
Hazard ratio (95% CI)	0.83 (0.56, 1.22); $p = 0.3487$	
Ongoing assigned treatment at DCO[a], n (%)	13 (14.1)	2 (3.2)

Golan T et al. GI Cancers Symposium 2021;Abstract 378.

RTP RESEARCH TO PRACTICE

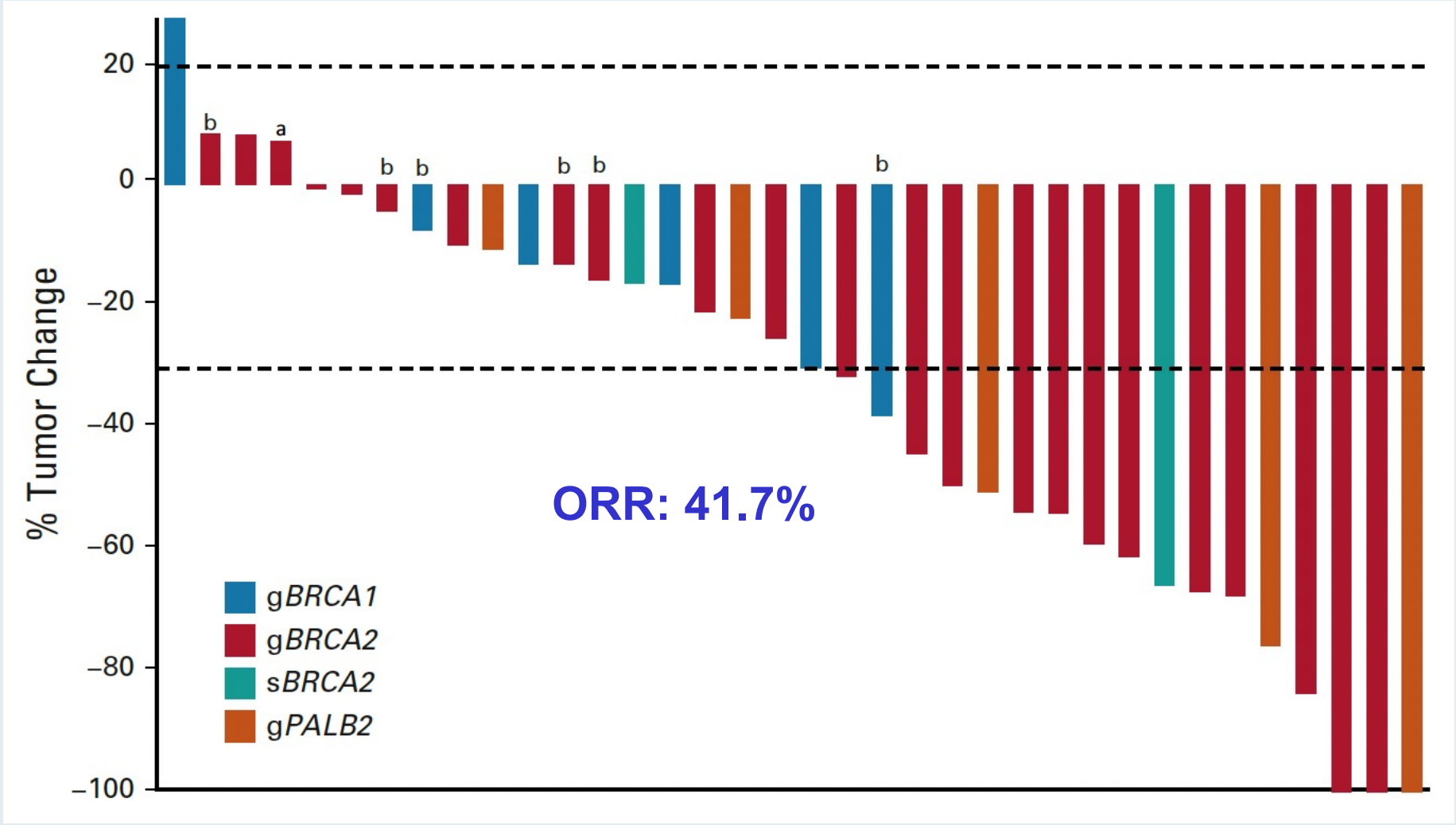
original reports

Phase II Study of Maintenance Rucaparib in Patients With Platinum-Sensitive Advanced Pancreatic Cancer and a Pathogenic Germline or Somatic Variant in *BRCA1*, *BRCA2*, or *PALB2*

Kim A. Reiss, MD[1,2]; Rosemarie Mick, MS[1,3]; Mark H. O'Hara, MD[1,2]; Ursina Teitelbaum, MD[1,2]; Thomas B. Karasic, MD[1,2]; Charles Schneider, MD[1,2]; Stacy Cowden, RN[1]; Traci Southwell, RN[1]; Janae Romeo, MBE[1]; Natallia Izgur, RN[1]; Zain M. Hannan, BA[1]; Rashmi Tondon, MD[1,4]; Katherine Nathanson, MD[1,2]; Robert H. Vonderheide, MD, DPhil[1,2]; Max M. Wattenberg, MD[1,2]; Gregory Beatty, MD, PhD[1,2]; and Susan M. Domchek, MD[1,2]

J Clin Oncol 2021;39(22):2497-505.

Maintenance Rucaparib in Platinum-Sensitive Advanced Pancreatic Cancer



Reiss KA et al. *J Clin Oncol* 2021;39(22):2497-505.

RTP RESEARCH TO PRACTICE

Research

JAMA Oncol 2021;7(5):693-9.

JAMA Oncology | Original Investigation

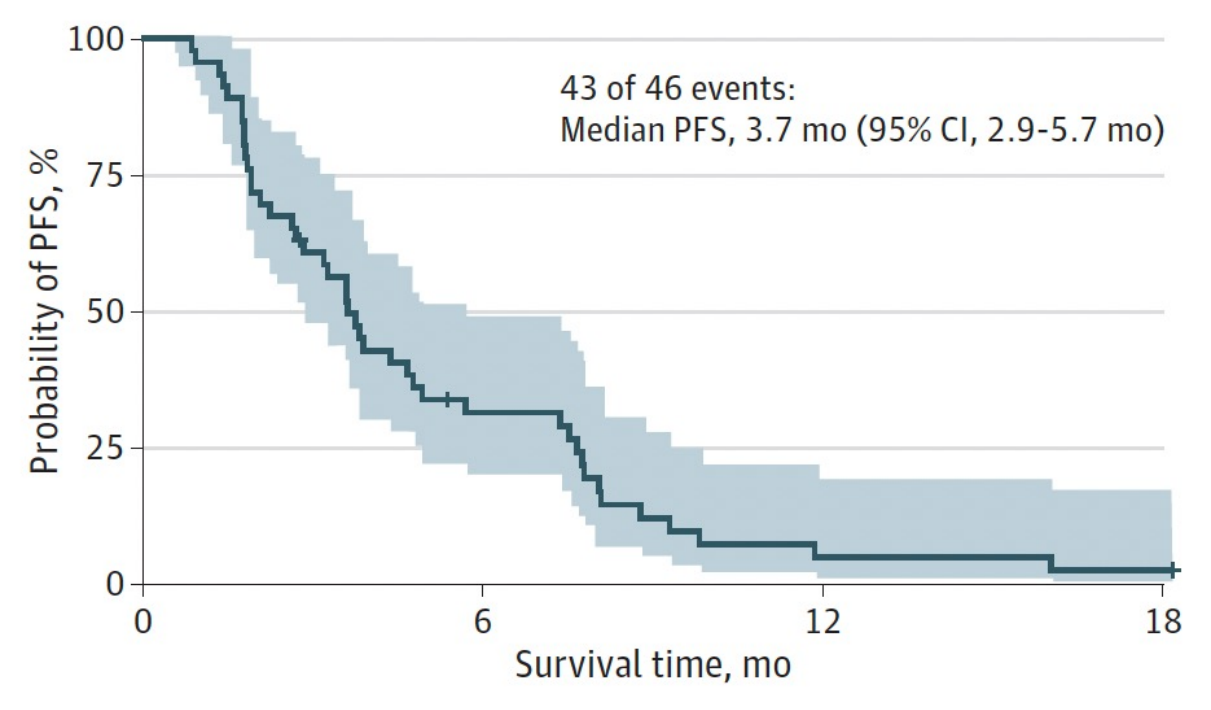
Olaparib Monotherapy for Previously Treated Pancreatic Cancer With DNA Damage Repair Genetic Alterations Other Than Germline *BRCA* Variants

Findings From 2 Phase 2 Nonrandomized Clinical Trials

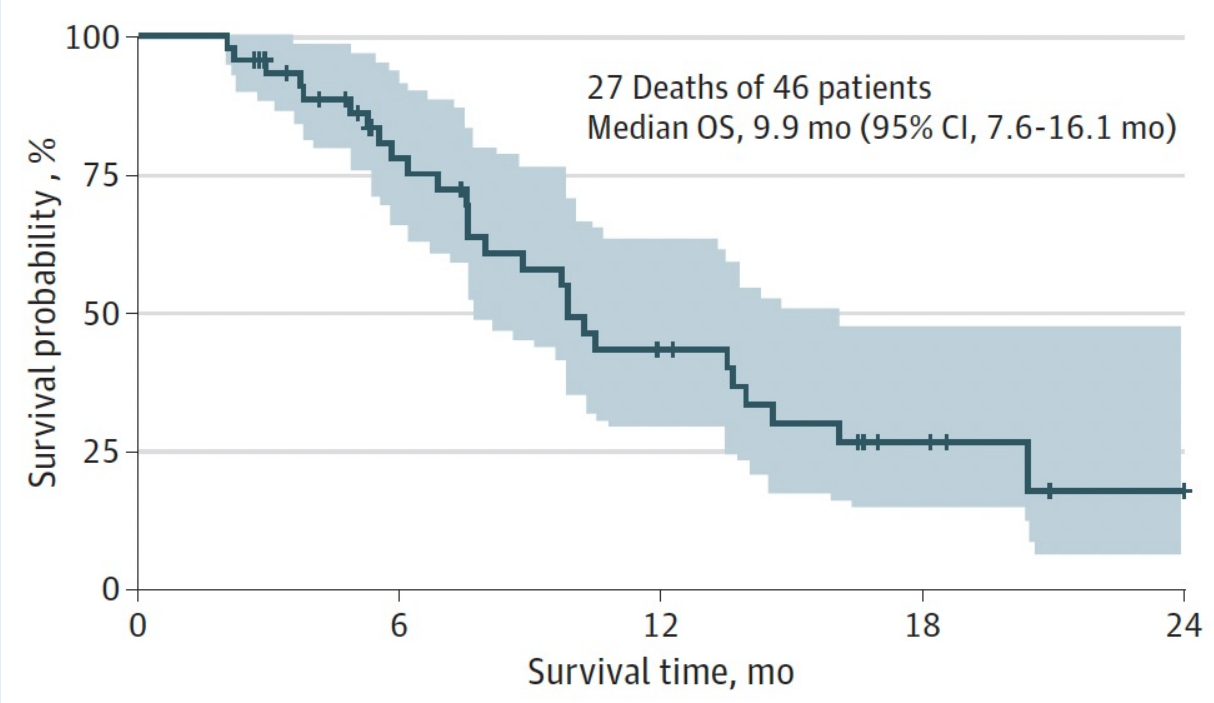
Milind Javle, MD; Einat Shacham-Shmueli, MD; Lianchun Xiao, MS; Gauri Varadhachary, MBBS, MD; Naama Halpern, MD, MBA; David Fogelman, MD; Ben Boursi, MD; Syeda Uruba, MBBS, MPH; Ofer Margalit, MD, PhD; Robert A. Wolff, MD; Talia Golan, MD

Olaparib Monotherapy for Previously Treated Pancreatic Cancer with DNA Damage Repair Genetic Alterations Other Than Germline BRCA Variants

Progression-Free Survival



Overall Survival



Javle M et al. *JAMA Oncol* 2021;7(5):693-9.

RTP RESEARCH TO PRACTICE

Gastrointestinal Cancers Symposium 2021

Abstract 639

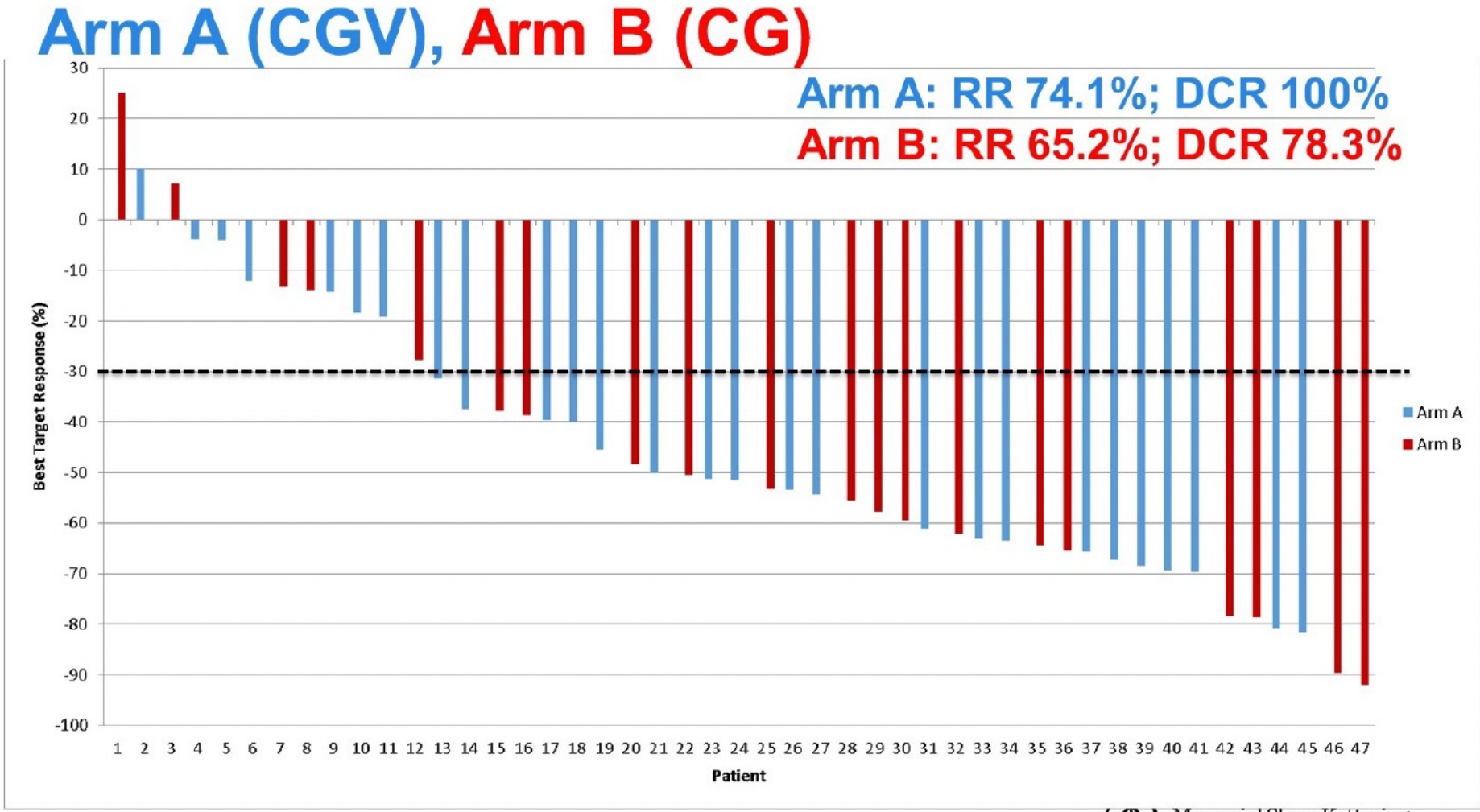
Memorial Sloan Kettering Cancer Center

Randomized, Multicenter, Phase II Trial of Gemcitabine, Cisplatin +/- Veliparib in Patients with Pancreas Adenocarcinoma and a known Germline *BRCA/PALB2* Mutation

Eileen M. O'Reilly, MD[1]; Jonathan W. Lee, MSc[1]; Mark Zalupski, MD[2]; Marinela Capanu[1]; Jennifer Park, BS[1]; Talia Golan, MD[3]; Esther Tahover, MD[4]; Maeve A. Lowery, MD[5]; Joanne F. Chou, MPH[1]; Vaibhav Sahai, MBBS, MS[2]; Robin Brenner, RN, BSN[1]; Hedy L. Kindler, MD[6]; Kenneth H. Yu, MD[1]; Alice Zervoudakis, MD[1]; Shreya Vemuri, BS[1]; Zsofia K. Stadler, MD[1]; Richard K. G. Do, MD, PhD[1]; Neesha Dhani, MD, PhD[7]; Alice P. Chen, MD[8]; and David P. Kelsen, MD[1]

[1]Memorial Sloan Kettering Cancer Center, New York, NY. [2]University of Michigan, Ann Arbor, MI. [3]Chaim Sheba Medical Center at Tel HaShomer, Tel HaShomer, Israel. [4]The Oncology Institute, Sha'are Zedek Medical Center, Jerusalem, Israel. [5]Trinity College, Dublin, Ireland. [6]University of Chicago, Chicago, IL. [7]Princess Margaret Cancer Centre-University Health Network, Toronto, Ontario, Canada. [8]National Cancer Institute, Bethesda, MD

Primary Endpoint: RECIST Response



RR: Response Rate; DCR: Disease Control Rate

O'Reilly EM et al. Gastrointestinal Cancers Symposium 2021;Abstract 639.

Abstract 599

GI Cancers Symposium 2022

Real-World Use of PARP inhibitors in *BRCA*-Mutated Pancreatic Cancer: A Retrospective Analysis

Suvina Amin[1], **Weiyan Li[1]**, Seongjung Joo[2], Gboyega Adeboyeje[2], Patricia DeArbeloa[3], Emanuel F Petricoin III[3,4], Edik M Blais[3], Michael J Pishvaian[3,5]

PARPi Usage Summary Relative to Platinum Sensitivity and Line of Therapy in a World-Wide Registry Study

More ← ← ← ← Less Platinum Exposure Before First PARPi Use (Real-World Scenarios Only)	PARPi-Switch Context	# PARPi-Users (N = 21, %)	Treatment settings of first platinum use	Treatment settings of first PARP inhibitor use
	Platinum-Naïve	2 (10%)	1st line (1); Censored (1)	1st line (2)
	Platinum-Exposed	5 (24%)	Neoadjuvant (3); 2nd line (1); Censored (1)	Neoadjuvant (1); 1st line (1); 2nd line (3)
	Platinum-Sensitive	8 (38%)	Neoadjuvant (1); 1st line (3); 2nd line (4)	1st line (3); 2nd line (3); 3rd line (2)
	Platinum-Resistant	6 (28%)	1st line (4); 2nd line (2)	2nd line (1); 3rd line (3); 5th line (2)

Amin S et al. GI Cancers Symposium 2022;Abstract 599.

RTP RESEARCH TO PRACTICE

Thank you for joining us!

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

RTP
RESEARCH
TO PRACTICE

Recent Advances and Real-World Implications in Medical Oncology: A Daylong Multitumor Educational Symposium in Partnership with the North Carolina Oncology Association and the South Carolina Oncology Society

A CME/MOC- and NCPD-Accredited Event

Saturday, February 12, 2022
8:30 AM – 4:00 PM ET

RTP
RESEARCH
TO PRACTICE

Agenda

Module 1 — Chronic Lymphocytic Leukemia and Lymphomas: *Drs Flinn and LaCasce*

Module 2 — Multiple Myeloma: *Drs Callander and Rajkumar*

Module 3 — Genitourinary Cancers: *Drs Dreicer and Heath*

Module 4 — Breast Cancer: *Drs Borges and Jhaveri*

Module 5 — Gastrointestinal Cancers: *Drs Hochster and Messersmith*

Module 6 — Lung Cancer: *Drs Govindan and Johnson*

Lung Cancer Faculty

Ramaswamy Govindan, MD
Professor of Medicine
Director, Section of Oncology
Anheuser-Busch Endowed Chair in Medical Oncology
Washington University School of Medicine
St Louis, Missouri

Melissa Johnson, MD
Director, Lung Cancer Research Program
Associate Director of Drug Development for the Drug Development Unit in Nashville
Sarah Cannon Research Institute
Nashville, Tennessee

RTP
RESEARCH TO PRACTICE

MODULE 6: Lung Cancer

Co-Moderator

Jimmy Ruiz, MD
Associate Professor of Medicine
Assistant Director for Clinical Research
Atrium Health Wake Forest Baptist
Comprehensive Cancer Center
Winston-Salem, North Carolina

Contributing General Medical Oncologists

Jennifer L Dallas, MD
Novant Health Cancer Institute
Charlotte, North Carolina

Joanna Metzner-Sadurski, MD
Self Regional Healthcare Cancer Center
Greenwood, South Carolina

Justin Peter Favaro, MD, PhD
Oncology Specialists of Charlotte
Charlotte, North Carolina

William R Mitchell, MD
Southern Oncology Specialists
Charlotte, North Carolina

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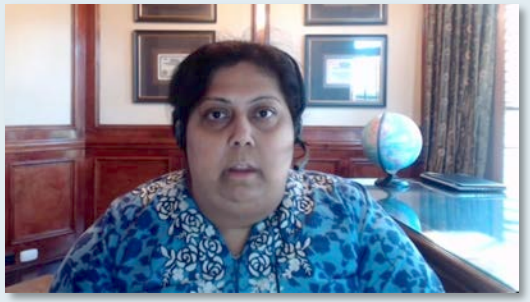
RESEARCH
TO PRACTICE

Contributing General Medical Oncologists



Niyati A Nathwani, MD
Carolina Blood and Cancer Care Associates
Charlotte, North Carolina

Nasfat Shehadeh, MD
Oncology Specialists of Charlotte, PA
Charlotte, North Carolina

Julia Saylors, MD
Charleston Oncology
North Charleston, South Carolina

RTP RESEARCH TO PRACTICE

Agenda

Module 1: Non-Small Cell Lung Cancer (NSCLC) with EGFR Mutations

Module 2: NSCLC with ALK Rearrangement

Module 3: NSCLC with RET, MET Exon 14 and HER2 Mutations

Module 4: NSCLC without Targetable Mutations

Module 5: Extensive-Stage Small Cell Lung Cancer

Agenda

Module 1: NSCLC with EGFR Mutations

Module 2: NSCLC with ALK Rearrangement

Module 3: NSCLC with RET, MET Exon 14 and HER2 Mutations

Module 4: NSCLC without Targetable Mutations

Module 5: Extensive-Stage Small Cell Lung Cancer

The NEW ENGLAND JOURNAL of MEDICINE

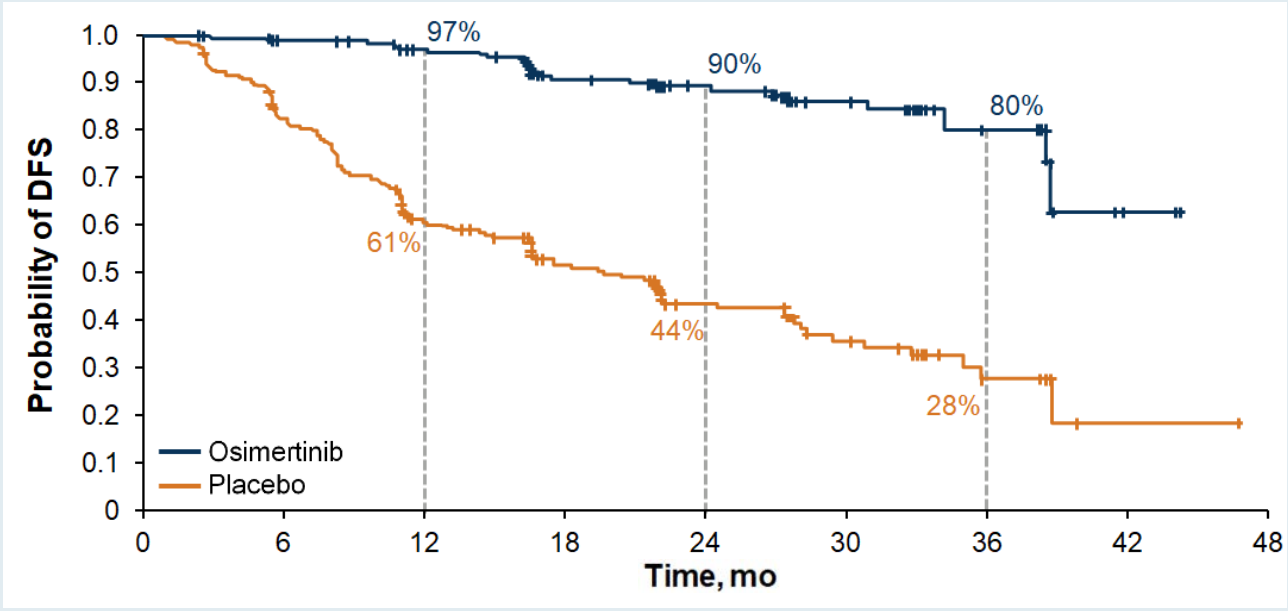
ESTABLISHED IN 1812 OCTOBER 29, 2020 VOL. 383 NO. 18

Osimertinib in Resected *EGFR*-Mutated Non–Small-Cell Lung Cancer

Yi-Long Wu, M.D., Masahiro Tsuboi, M.D., Jie He, M.D., Thomas John, Ph.D., Christian Grohe, M.D., Margarita Majem, M.D., Jonathan W. Goldman, M.D., Konstantin Laktionov, Ph.D., Sang-We Kim, M.D., Ph.D., Terufumi Kato, M.D., Huu-Vinh Vu, M.D., Ph.D., Shun Lu, M.D., Kye-Young Lee, M.D., Ph.D., Charuwan Akewanlop, M.D., Chong-Jen Yu, M.D., Ph.D., Filippo de Marinis, M.D., Laura Bonanno, M.D., Manuel Domine, M.D., Ph.D., Frances A. Shepherd, M.D., Lingmin Zeng, Ph.D., Rachel Hodge, M.Sc., Ajlan Atasoy, M.D., Yuri Rukazenkov, M.D., Ph.D., and Roy S. Herbst, M.D., Ph.D., for the ADAURA Investigators*

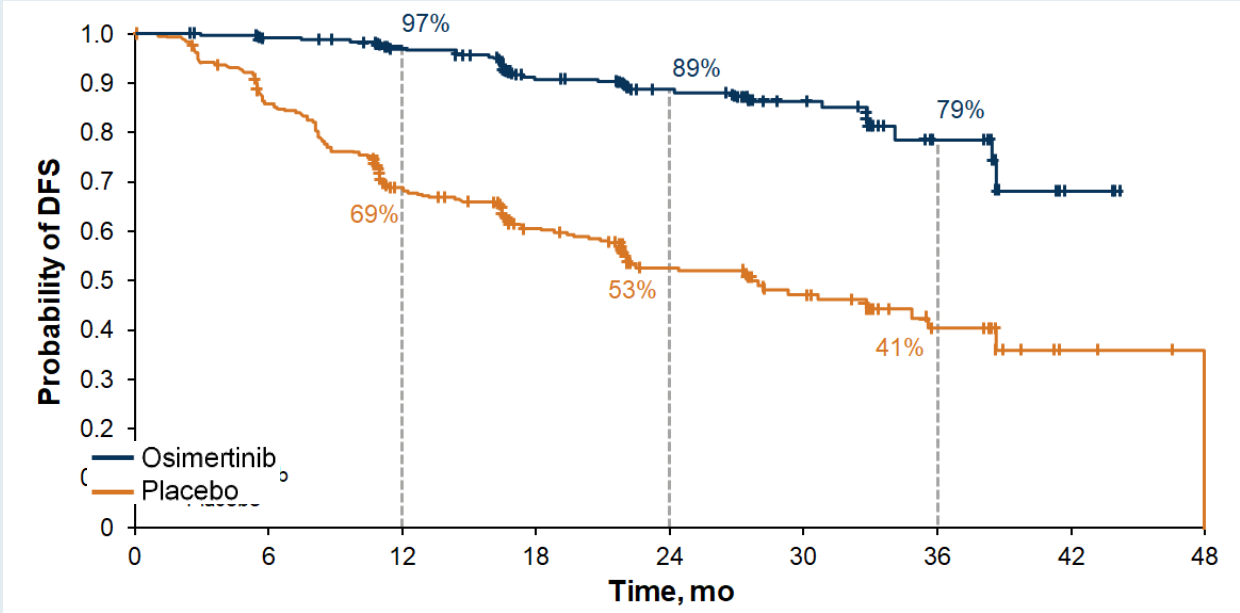
Phase III ADAURA Trial: Adjuvant Osimertinib

DFS: Stage II to IIIA Disease



HR = 0.17; $p < .001$) → 83% reduction in risk of disease recurrence or death

DFS: Stage IB to IIIA Disease

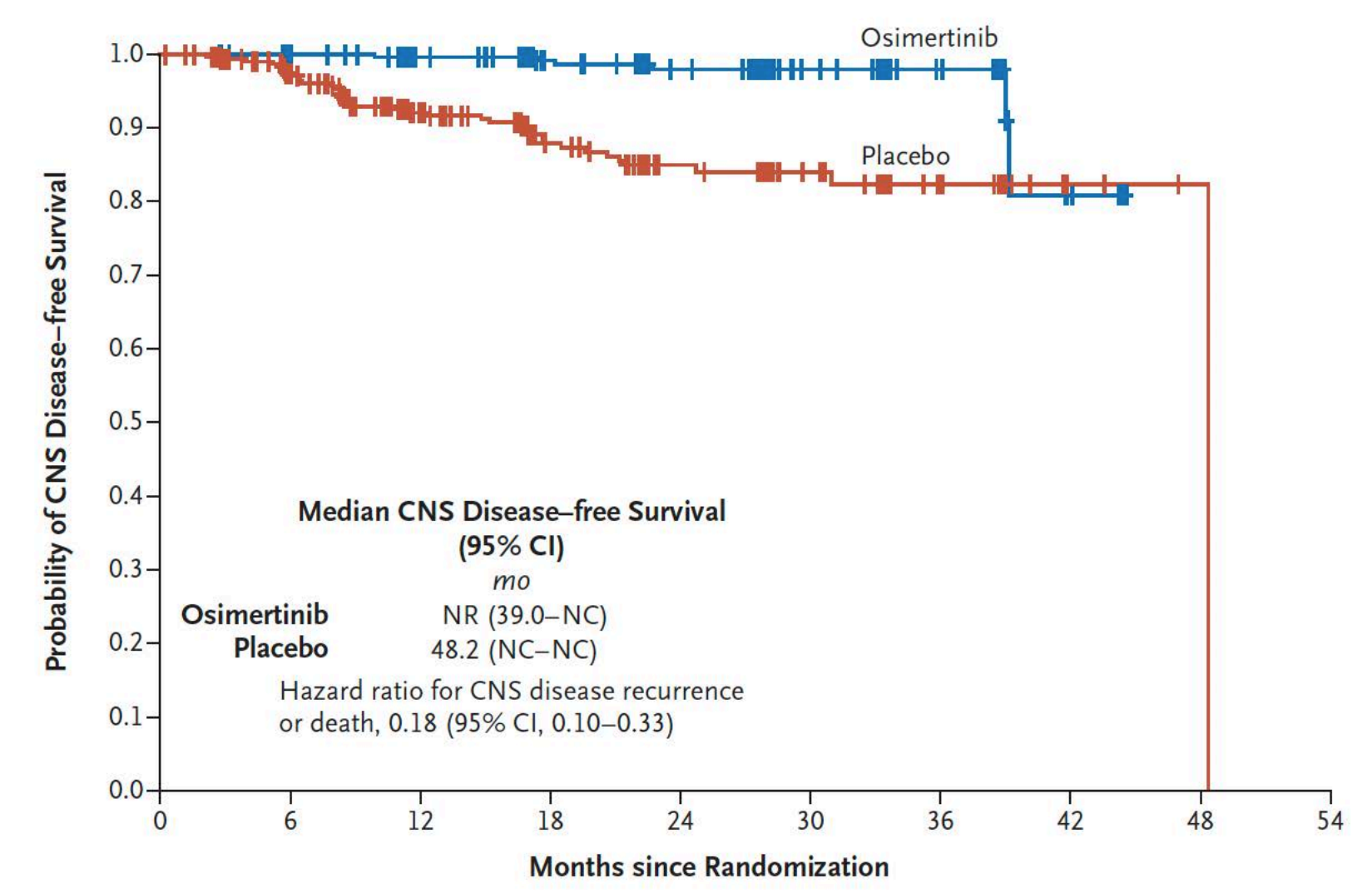


HR = 0.20; $p < .001$) → 80% reduction in risk of disease recurrence or death

Wu Y et al. *N Engl J Med* 2020;383:825-35.

RTP RESEARCH TO PRACTICE

ADAURA: CNS Disease-Free Survival According to Investigator Assessment in the Overall Population



Wu Y et al. *N Engl J Med* 2020;383:825-35.

RTP RESEARCH TO PRACTICE

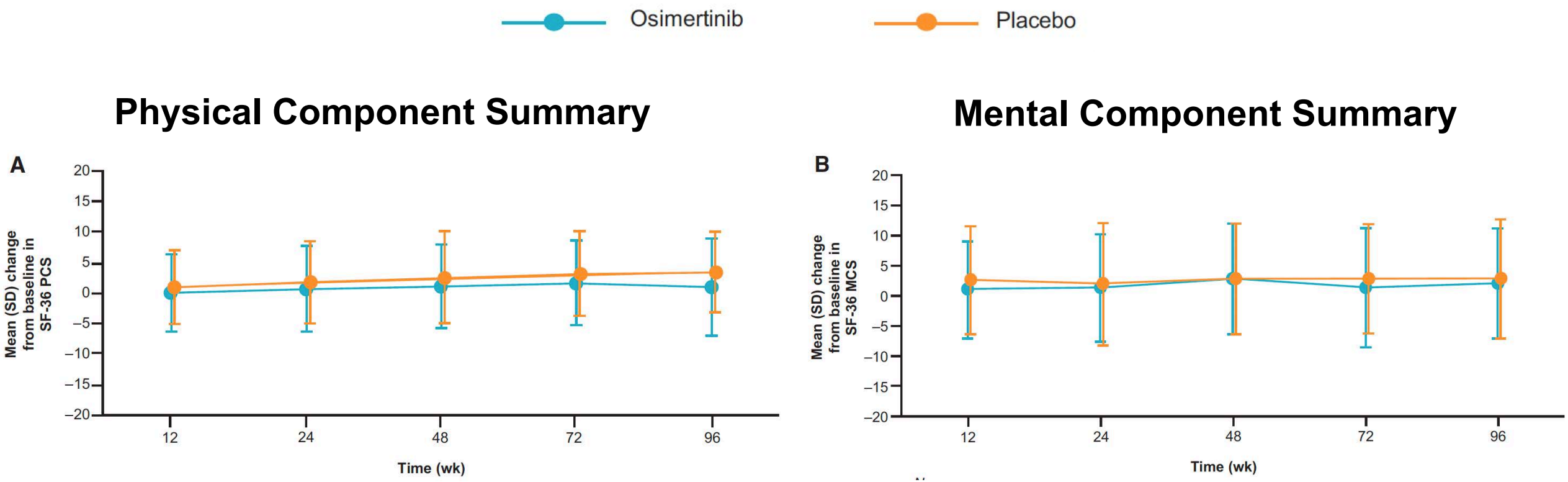
CLINICAL CANCER RESEARCH | CLINICAL TRIALS: TARGETED THERAPY

Health-Related Quality of Life Outcomes in Patients with Resected Epidermal Growth Factor Receptor–Mutated Non–Small Cell Lung Cancer Who Received Adjuvant Osimertinib in the Phase III ADAURA Trial

Margarita Majem[1], Jonathan W. Goldman[2], Thomas John[3], Christian Grohe[4], Konstantin Laktionov[5], Sang-We Kim[6], Terufumi Kato[7], Huu Vinh Vu[8], Shun Lu[9], Shanqing Li[10], Kye Young Lee[11], Charuwan Akewanlop[12], Chong-Jen Yu[13], Filippo de Marinis[14], Laura Bonanno[15], Manuel Domine[16], Frances A. Shepherd[17], Shinji Atagi[18], Lingmin Zeng[19], Dakshayini Kulkarni[20], Nenad Medic[21], Masahiro Tsuboi[22], Roy S. Herbst[23], and Yi-Long Wu[24]

***Clin Cancer Res* 2022;[Online ahead of print].**

ADAURA: Health-Related Quality of Life Over Time



Majem M et al. *Clin Cancer Res* 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

FDA Grants Breakthrough Therapy Status to Patritumab Deruxtecan for EGFR-Positive Metastatic NSCLC

Press Release – January 4, 2022

"Patritumab deruxtecan (U3-1402), a potential first-in-class HER3 directed antibody-drug conjugate, was granted breakthrough therapy designation by the FDA for the treatment of patients with metastatic or locally advanced, *EGFR*-mutant non–small cell lung cancer (NSCLC).

Data from a phase 1 trial (NCT03260491) assessing the efficacy of patritumab deruxtecan in a heavily pretreated population of patients with EGFR-mutant NSCLC that have become resistant to other TKIs were read out at the 2021 American Society of Clinical Oncology Annual Meeting: Lung Cancer.

A 5.6 mg/kg dose of the treatment resulted in a confirmed objective response rate of 39% in a population of patients who were previously treated with a TKI and platinum-based therapy (n = 57). Additionally, treatment with patritumab deruxtecan resulted in a disease control rate of 72%, as well as a median progression-free survival of 8.2 months (95% CI, 4.0–not evaluable)."

https://www.cancernetwork.com/view/fda-grants-breakthrough-therapy-status-to-patritumab-deruxtecan-for-egfr-metastatic-nsclc

RTP RESEARCH TO PRACTICE

RESEARCH ARTICLE

Cancer Discov 2022;12(1):74-89.

Efficacy and Safety of Patritumab Deruxtecan (HER3-DXd) in EGFR Inhibitor–Resistant, *EGFR*-Mutated Non–Small Cell Lung Cancer

Pasi A. Jänne[1], Christina Baik[2], Wu-Chou Su[3], Melissa L. Johnson[4], Hidetoshi Hayashi[5], Makoto Nishio[6], Dong-Wan Kim[7], Marianna Koczywas[8], Kathryn A. Gold[9], Conor E. Steuer[10], Haruyasu Murakami[11], James Chih-Hsin Yang[12], Sang-We Kim[13], Michele Vigliotti[14], Rong Shi[14], Zhenhao Qi[14], Yang Qiu[14], Lihui Zhao[14], David Sternberg[14], Channing Yu[14], and Helena A. Yu[15]

Summary of Adverse Events

TEAEs	Pooled RDE 5.6 mg/kg ($n=57$), n (%)	All patients 3.2/4.8/5.6/6.4 mg/kg ($n=81$), n (%)
Any TEAE	57 (100)	81 (100)
Grade ≥3 TEAEs	42 (74)	52 (64)
Serious TEAEs	25 (44)	32 (40)
TEAEs associated with treatment discontinuation	6 (11)[a]	7 (9)[b]
TEAEs associated with dose reduction	12 (21)	18 (22)
TEAEs associated with dose interruption	21 (37)	30 (37)
TEAEs associated with death	4 (7)[c]	5 (6)[d]
Treatment-related TEAEs	55 (96)	78 (96)
Grade ≥3 treatment-related TEAEs	31 (54)	38 (47)
Treatment-related TEAEs associated with death	0	0
Serious treatment-related TEAEs	12 (21)	15 (19)

RDE = recommended dose for expansion

Jänne PA et al. *Cancer Discov* 2022;12(1):74-89.

Responses by Blinded Independent Central Review

Characteristics	Pooled RDE (5.6 mg/kg)	
	All pooled ($n = 57$)	Prior PBC and osimertinib ($n = 44$)
Confirmed ORR, % (n) [95% CI]	39 (22) [26.0–52.4]	39 (17) [24.4–54.5]
BOR, n (%)		
CR	1 (2)	1 (2)
PR	21 (37)	16 (36)
SD	19 (33)	13 (30)
PD	9 (16)	8 (18)
NE	7 (12)	6 (14)
DCR,[a] % (n) [95% CI]	72 (41) [58.5–83.0]	68 (30) [52.4–81.4]
TTR, median (range), months	2.6 (1.2–5.4)	2.7 (1.2–5.4)
Duration of response, median (95% CI), months	6.9 (3.1–NE)	7.0 (3.1–NE)
Progression-free survival, median (95% CI), months	8.2 (4.4–8.3)	8.2 (4.0–NE)
Overall survival, median (95% CI), months	NE (9.4–NE)	NE (8.2–NE)

Abbreviation: PBC, platinum-based chemotherapy.

[a]DCR = rate of confirmed BOR of CR, PR, or SD.

Jänne PA et al. *Cancer Discov* 2022;12(1):74-89.

Select Grade ≥3 Treatment-Emergent Adverse Events (TEAEs)

TEAEs	Pooled RDE 5.6 mg/kg ($n = 57$), n (%)	All patients 3.2/4.8/5.6/6.4 mg/kg ($n = 81$), n (%)
Grade ≥3 TEAEs occurring in ≥5% of patients		
Platelet count decrease/thrombocytopenia	17 (30)	21 (26)
Neutrophil count decrease/neutropenia	11 (19)	12 (15)
Fatigue	8 (14)	8 (10)
Anemia/hemoglobin decrease	5 (9)	6 (7)
Dyspnea	5 (9)	5 (6)
Febrile neutropenia	5 (9)	5 (6)
Adjudicated ILD	5 (9)[e]	5 (6)[e]
Adjudicated treatment-related ILD	4 (7)[f]	4 (5)[f]

Jänne PA et al. *Cancer Discov* 2022;12(1):74-89.

FDA Grants Accelerated Approval to Mobocertinib for Metastatic NSCLC with EGFR Exon 20 Insertion Mutations

Press Release – September 15, 2021

"The Food and Drug Administration granted accelerated approval to mobocertinib for adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 20 insertion mutations, as detected by an FDA-approved test, whose disease has progressed on or after platinum-based chemotherapy.

Today, the FDA also approved the Oncomine Dx Target Test as a companion diagnostic device to select patients with the above mutations for mobocertinib treatment.

Approval was based on Study 101, an international, non-randomized, open-label, multicohort clinical trial (NCT02716116) which included patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations. Efficacy was evaluated in 114 patients whose disease had progressed on or after platinum-based chemotherapy. Patients received mobocertinib 160 mg orally daily until disease progression or intolerable toxicity."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-mobocertinib-metastatic-non-small-cell-lung-cancer-egfr-exon-20

RTP RESEARCH TO PRACTICE

Research

JAMA Oncol 2021;7(12):e214761.

JAMA Oncology | Original Investigation

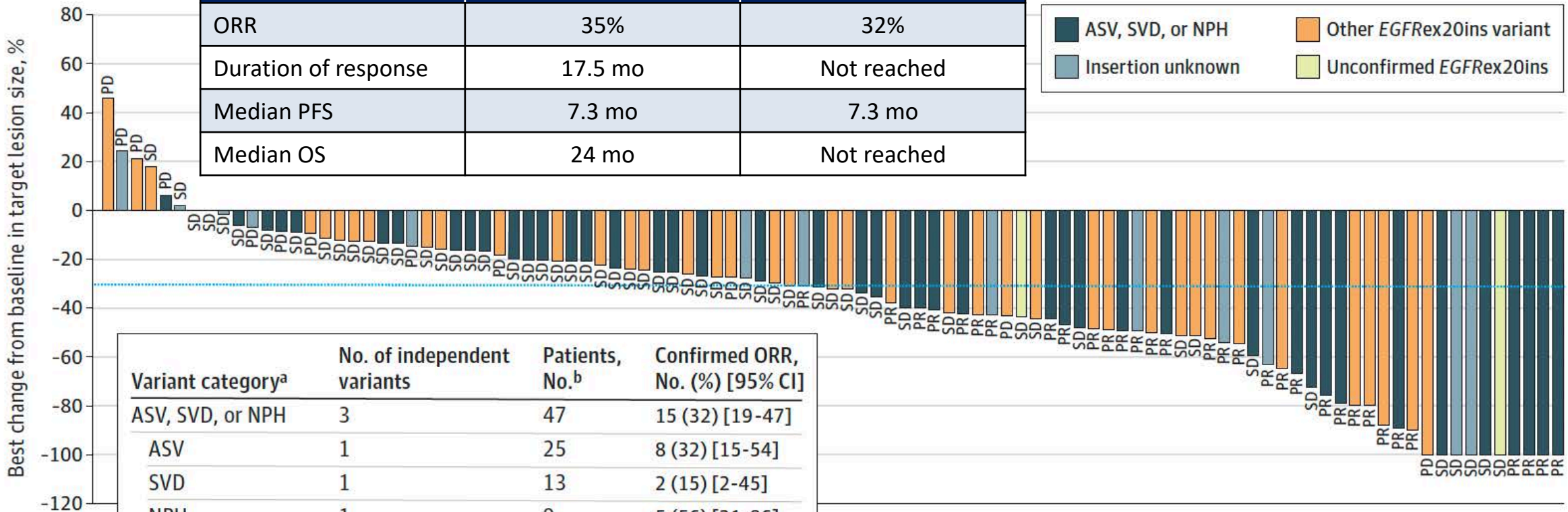
Treatment Outcomes and Safety of Mobocertinib in Platinum-Pretreated Patients With *EGFR* Exon 20 Insertion–Positive Metastatic Non–Small Cell Lung Cancer

A Phase 1/2 Open-label Nonrandomized Clinical Trial

Caicun Zhou, PhD, MD; Suresh S. Ramalingam, MD; Tae Min Kim, MD, PhD; Sang-We Kim, MD; James Chih-Hsin Yang, MD; Gregory J. Riely, MD; Tarek Mekhail, MD; Danny Nguyen, MD; Maria R. Garcia Campelo, MD; Enriqueta Felip, MD; Sylvie Vincent, PhD; Shu Jin, MS; Celina Griffin, PharmD; Veronica Bunn, PhD; Jianchang Lin, PhD; Huamao M. Lin, PhD; Minal Mehta, MBBS; Pasi A. Jänne, MD, PhD

Mobocertinib Activity in Patients with Platinum-Pretreated Metastatic NSCLC with EGFRex20ins Mutation (PPP Cohort)

	PPP cohort (n = 114)	EXCLAIM cohort (n = 96)
ORR	35%	32%
Duration of response	17.5 mo	Not reached
Median PFS	7.3 mo	7.3 mo
Median OS	24 mo	Not reached



Variant category[a]	No. of independent variants	Patients, No.[b]	Confirmed ORR, No. (%) [95% CI]
ASV, SVD, or NPH	3	47	15 (32) [19-47]
ASV	1	25	8 (32) [15-54]
SVD	1	13	2 (15) [2-45]
NPH	1	9	5 (56) [21-86]
Other *EGFR*ex20ins	29	48	12 (25) [14-40]
Insertion unknown		16	5 (31) [11-59]

Zhou C et al. *JAMA Oncol* 2021;7(12):e214761.

RTP RESEARCH TO PRACTICE

Summary of Adverse Events (AEs) and Most Common AEs

Adverse event	Patients, No. (%)			
	PPP cohort (n = 114)		EXCLAIM cohort (n = 96)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Overview of AEs				
Any	114 (100)	79 (69)	96 (100)	63 (66)
Any treatment-related	113 (99)	54 (47)	95 (99)	40 (42)
Serious	56 (49)	52 (46)	45 (47)	42 (44)
Leading to dose reduction	29 (25)	NA[a]	21 (22)	NA[a]
Leading to treatment discontinuation	19 (17)	NA[a]	10 (10)	NA[a]
Treatment-related AEs of any grade reported in ≥10% or of grade ≥3 reported in ≥3% of patients				
Diarrhea	104 (91)	24 (21)	89 (93)	15 (16)
Rash	51 (45)	0	43 (45)	0
Paronychia	43 (38)	1 (<1)	37 (39)	1 (1)

Zhou C et al. *JAMA Oncol* 2021;7(12):e214761.

FDA Grants Accelerated Approval to Amivantamab-vmjw for Metastatic NSCLC

Press Release – May 21, 2021

"The Food and Drug Administration granted accelerated approval to amivantamab-vmjw, a bispecific antibody directed against epidermal growth factor (EGF) and MET receptors, for adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 20 insertion mutations, as detected by an FDA-approved test, whose disease has progressed on or after platinum-based chemotherapy.

FDA also approved the Guardant360® CDx as a companion diagnostic for amivantamab-vmjw.

Approval was based on CHRYSALIS, a multicenter, non-randomized, open label, multicohort clinical trial (NCT02609776) which included patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations. Efficacy was evaluated in 81 patients with advanced NSCLC with EGFR exon 20 insertion mutations whose disease had progressed on or after platinum-based chemotherapy. Patients received amivantamab-vmjw once weekly for 4 weeks, then every 2 weeks thereafter until disease progression or unacceptable toxicity."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-amivantamab-vmjw-metastatic-non-small-cell-lung-cancer

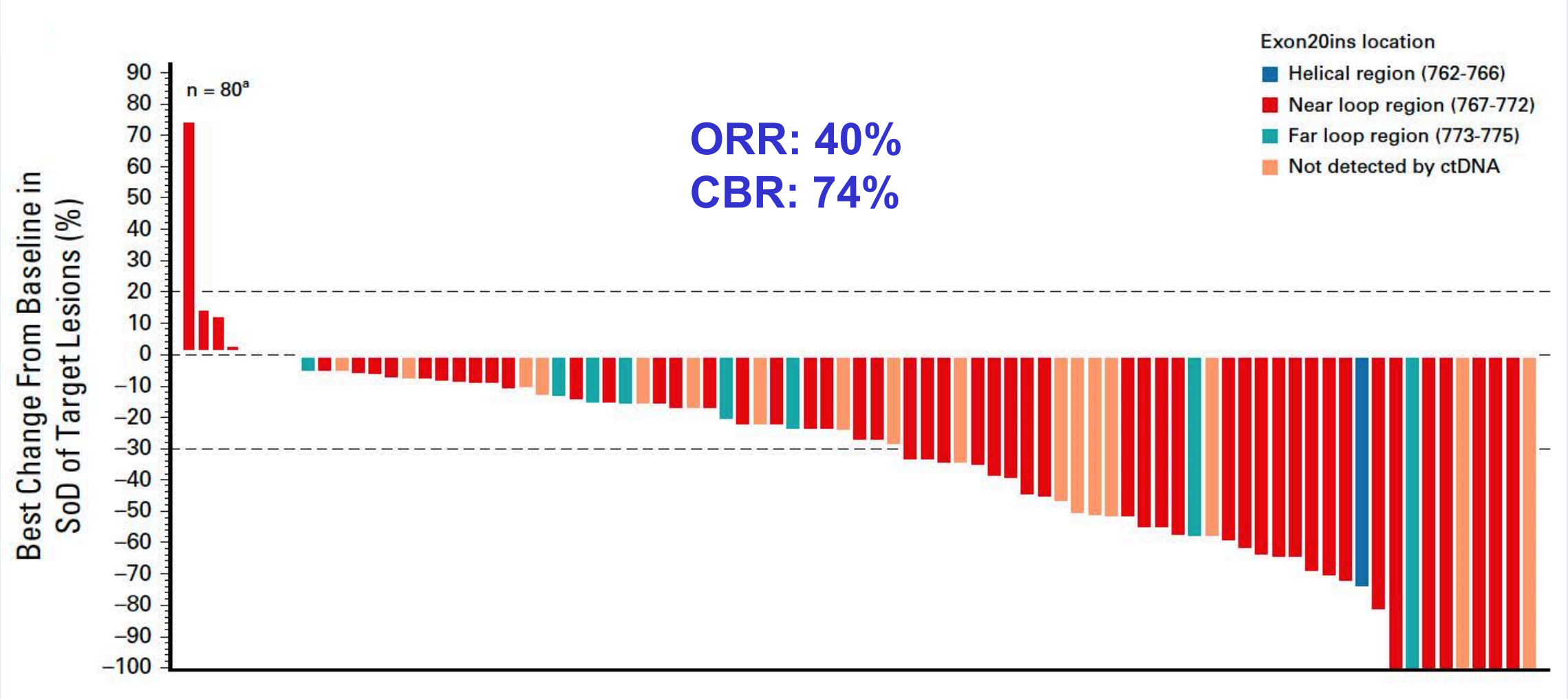
original reports

Amivantamab in EGFR Exon 20 Insertion–Mutated Non–Small-Cell Lung Cancer Progressing on Platinum Chemotherapy: Initial Results From the CHRYSALIS Phase I Study

Keunchil Park, MD, PhD[1]; Eric B. Haura, MD[2]; Natasha B. Leighl, MD[3]; Paul Mitchell, MD[4]; Catherine A. Shu, MD[5]; Nicolas Girard, MD, PhD[6]; Santiago Viteri, MD[7]; Ji-Youn Han, MD, PhD[8]; Sang-We Kim, MD, PhD[9]; Chee Khoon Lee, MD[10]; Joshua K. Sabari, MD[11]; Alexander I. Spira, MD, PhD[12]; Tsung-Ying Yang, MD, PhD[13]; Dong-Wan Kim, MD, PhD[14]; Ki Hyeong Lee, MD, PhD[15]; Rachel E. Sanborn, MD[16]; José Trigo, MD[17]; Koichi Goto, MD, PhD[18]; Jong-Seok Lee, MD, PhD[19]; James Chih-Hsin Yang, MD, PhD[20]; Ramaswamy Govindan, MD[21]; Joshua M. Bauml, MD[22]; Pilar Garrido, MD, PhD[23]; Matthew G. Krebs, MD, PhD[24]; Karen L. Reckamp, MD[25]; John Xie, PhD[26]; Joshua C. Curtin, PhD[26]; Nahor Haddish-Berhane, PhD[26]; Amy Roshak, BS[26]; Dawn Millington, MS[26]; Patricia Lorenzini, MS[26]; Meena Thayu, MD[26]; Roland E. Knoblauch, MD, PhD[26]; and Byoung Chul Cho, MD, PhD[27]

J Clin Oncol 2021;39:3391-402.

CHRYSALIS: Tumor Reduction and Response



Park K et al. *J Clin Oncol* 2021;39:3391-402.

RTP RESEARCH TO PRACTICE

CHRYSALIS: Summary of Adverse Events (AEs) and Most Common AEs

Event	Safety Population (n = 114), No. (%)	Patients Treated at the RP2D (n = 258), No. (%)
Any AE	113 (99)	257 (100)
Grade ≥ 3 AE	40 (35)	101 (39)
Serious AE	34 (30)	79 (31)
AE leading to death	8 (7)	13 (5)
AE leading to discontinuation	11 (10)	17 (7)
AE leading to dose reduction	15 (13)	26 (10)
AE leading to dose interruption[a]	40 (35)	88 (34)

Most Common AEs in the Safety Population

Adverse Events	Any Grade	Grade ≥3
Rash	86%	4%
Infusion-related reactions	66%	3%
Paronychia	45%	1%

Park K et al. *J Clin Oncol* 2021;39:3391-402.

RTP RESEARCH TO PRACTICE

Agenda

Module 1: NSCLC with EGFR Mutations

Module 2: NSCLC with ALK Rearrangement

Module 3: NSCLC with RET, MET Exon 14, KRAS G12C or HER2 Mutations

Module 4: NSCLC without Targetable Mutations

Module 5: Extensive-Stage Small Cell Lung Cancer

Activity of ALK Tyrosine Kinase Inhibitors (TKIs) in the First-Line Setting for Advanced NSCLC with ALK Rearrangement

ALK TKI	Median PFS	Overall response rate	Intracranial response
Crizotinib	10.9 mo	74%	NA
Ceritinib	16.6 mo	72.5%	72.7%
Alectinib	34.8 mo	82.9%	82.9%
Brigatinib	29.4 mo	71%	78%
Lorlatinib	Not reached	90%	66.7%
Ensartinib	26.2 mo	80%	64.3%

Xia B et al. *Transl Lung Cancer Res* 2020;9(6):2521-34.

RTP RESEARCH TO PRACTICE

Common and Unique Adverse Effects of ALK TKIs

ALK TKI	Most common adverse effects
Crizotinib	Vision disorders, nausea, diarrhea, vomiting, edema, constipation, elevated transaminases, fatigue, decreased appetite, upper respiratory infection, dizziness and neuropathy
Ceritinib	Diarrhea, nausea, vomiting, fatigue, abdominal pain, decreased appetite and weight loss
Alectinib	Constipation, fatigue, edema, myalgia and anemia
Brigatinib	Diarrhea, fatigue, nausea, rash, cough, myalgia, headache, hypertension, vomiting and dyspnea
Lorlatinib	Hypercholesterolemia, hypertriglyceridemia, edema, peripheral neuropathy, weight gain, cognitive effects, fatigue, dyspnea, arthralgia and diarrhea
Ensartinib	Rash, nausea, pruritus and vomiting

Crizotinib PI, rev 1/2021; Ceritinib PI, rev 3/2019; Alectinib PI, rev 1/2021; Brigatinib PI, rev 5/2020; Lorlatinib PI, rev 3/2021
Xia B et al. *Transl Lung Cancer Res* 2020;9(6):2521-253; Gristina V et al. *Pharmaceuticals* 2020;13:474.

FDA Approves Lorlatinib for Metastatic ALK-Positive NSCLC

Press Release – March 3, 2021

"The Food and Drug Administration granted regular approval to lorlatinib for patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive, detected by an FDA-approved test.

The FDA also approved the Ventana ALK (D5F3) CDx Assay as a companion diagnostic for lorlatinib.

Lorlatinib received accelerated approval in November 2018 for the second- or third-line treatment of ALK-positive metastatic NSCLC. This current approval is based on data from Study B7461006 (NCT03052608), a randomized, multicenter, open-label, active-controlled trial conducted in 296 patients with ALK-positive metastatic NSCLC who had not received prior systemic therapy for metastatic disease. Patients were required to have ALK-positive tumors detected by the VENTANA ALK (D5F3) CDx assay. Patients were randomized 1:1 to receive lorlatinib 100 mg orally once daily (n = 149) or crizotinib 250 mg orally twice daily (n = 147)."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-lorlatinib-metastatic-alk-positive-nsclc

RTP RESEARCH TO PRACTICE

The NEW ENGLAND JOURNAL of MEDICINE

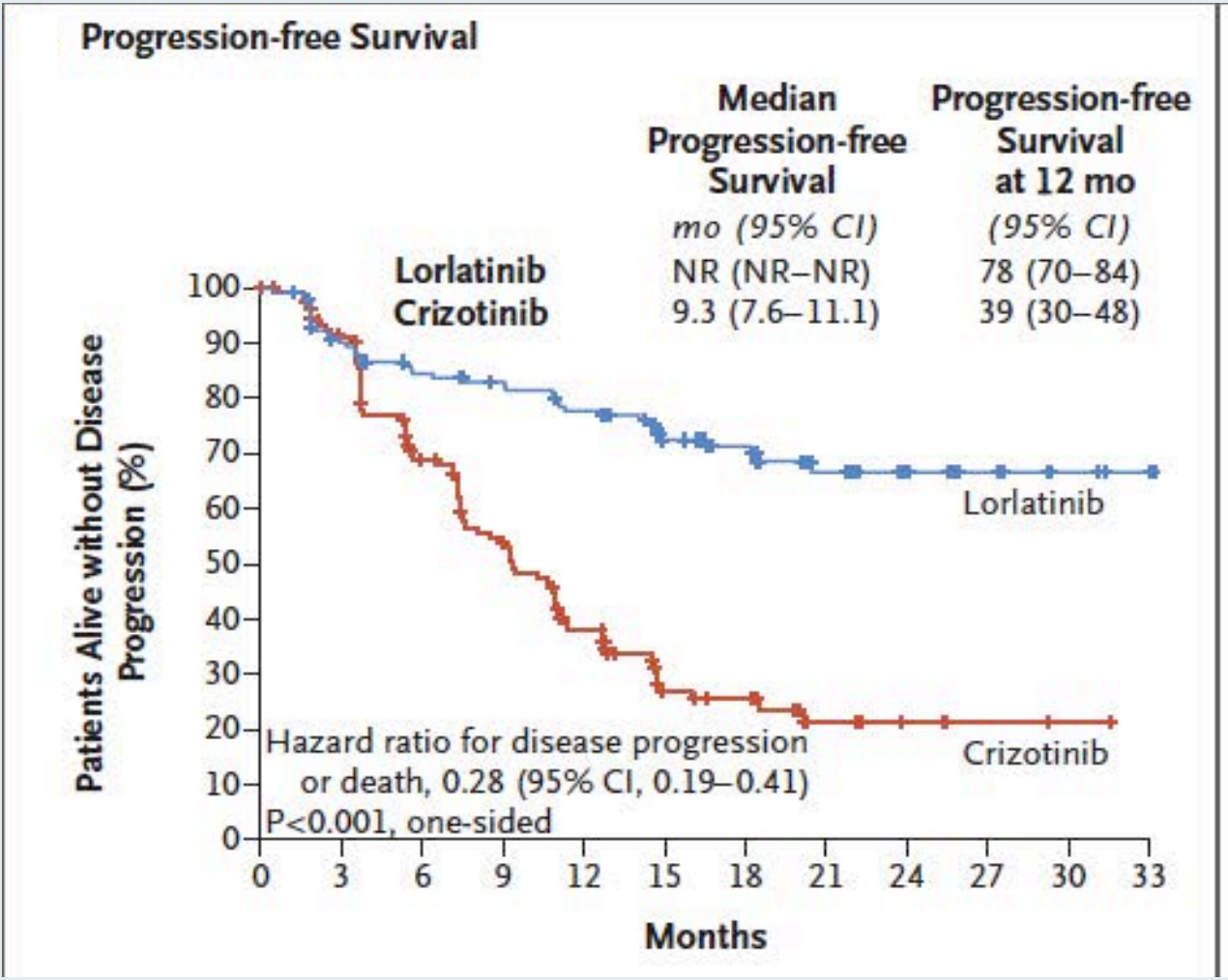
ORIGINAL ARTICLE

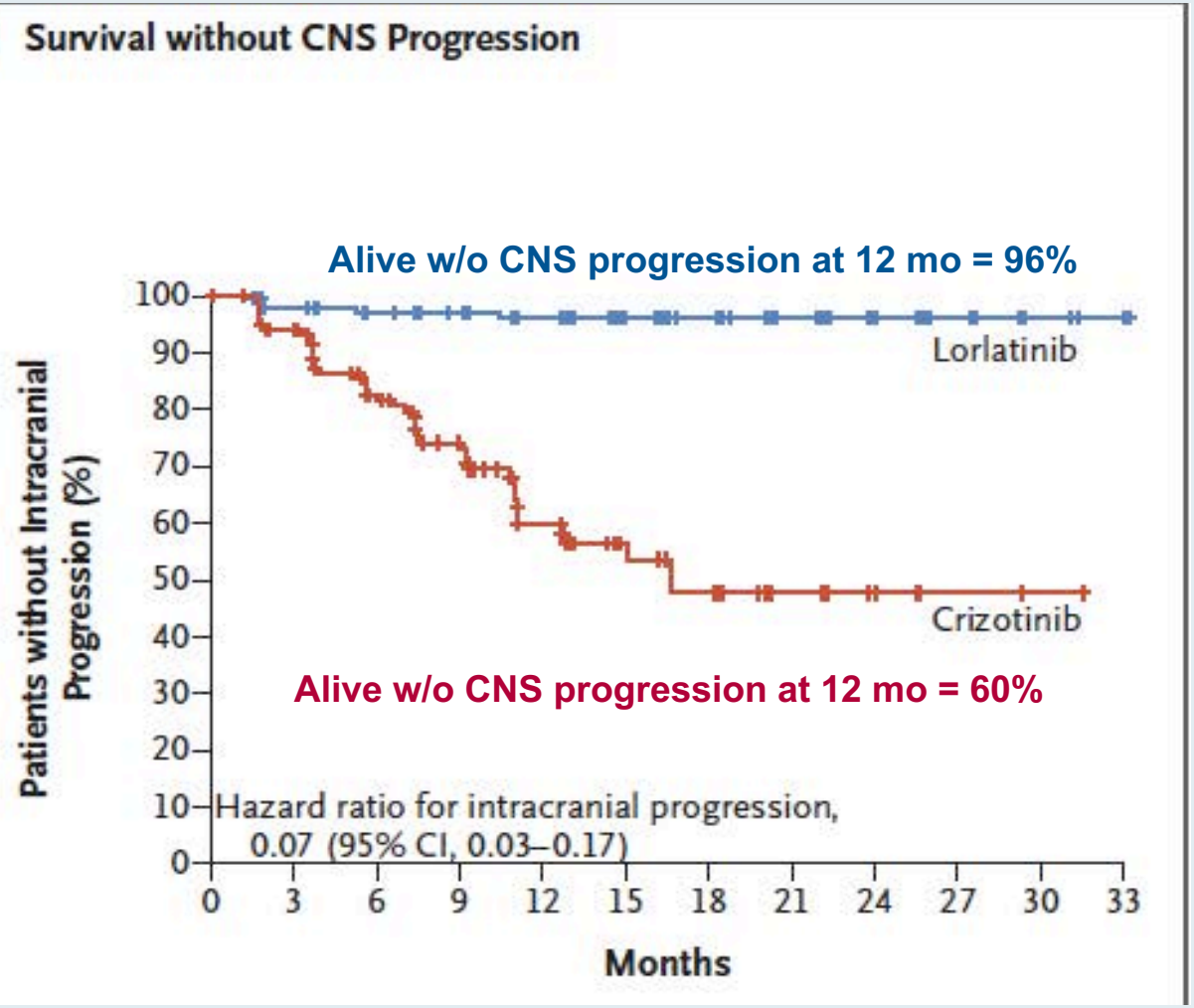
First-Line Lorlatinib or Crizotinib in Advanced *ALK*-Positive Lung Cancer

Alice T. Shaw, M.D., Ph.D., Todd M. Bauer, M.D., Filippo de Marinis, M.D., Ph.D., Enriqueta Felip, M.D., Ph.D., Yasushi Goto, M.D., Ph.D., Geoffrey Liu, M.D., Julien Mazieres, M.D., Ph.D., Dong-Wan Kim, M.D., Ph.D., Tony Mok, M.D., Anna Polli, B.Sc., Holger Thurm, M.D., Anna M. Calella, Ph.D., Gerson Peltz, M.D., M.P.H., and Benjamin J. Solomon, M.B., B.S., Ph.D., for the CROWN Trial Investigators*

N Engl J Med 2020;383(21):2018-29.

CROWN: PFS and Survival without Intracranial Progression



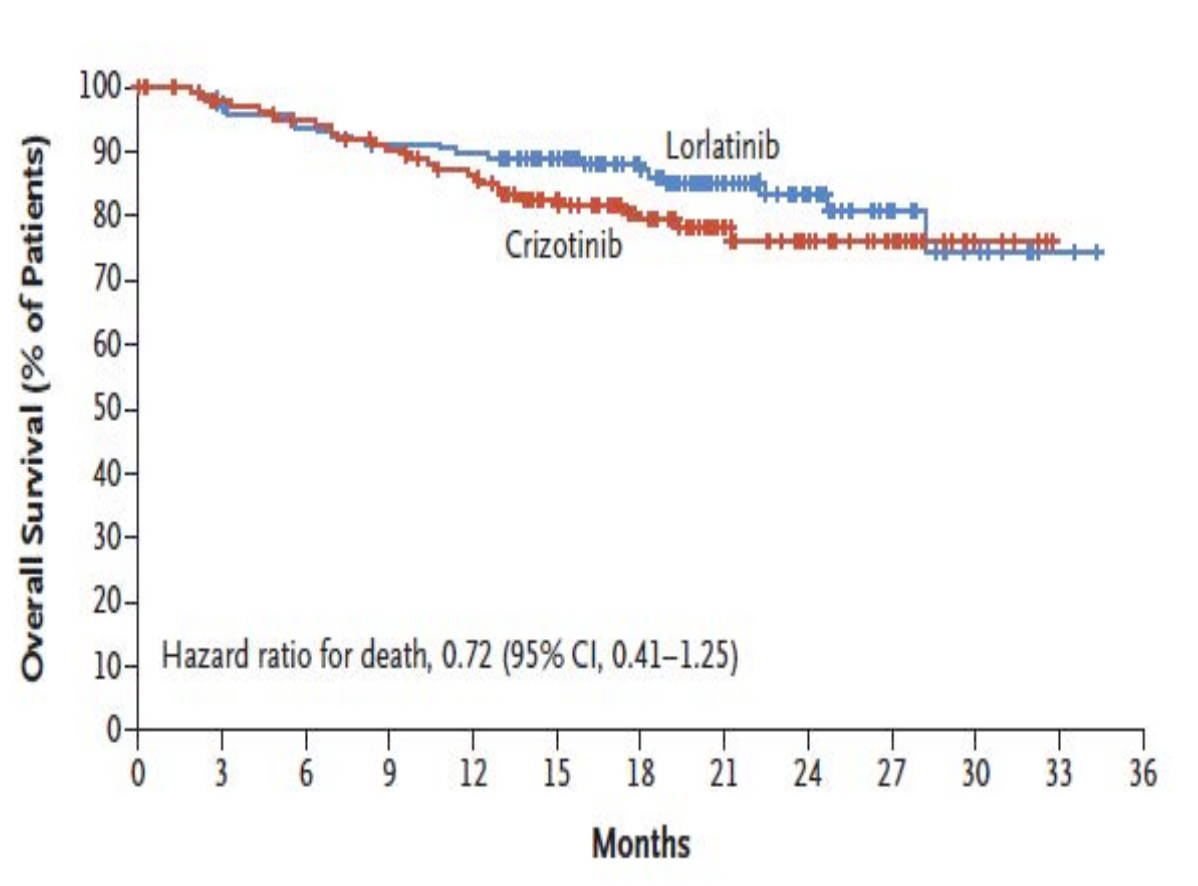


Shaw AT et al. *N Engl J Med* 2020;383(21):2018-29.

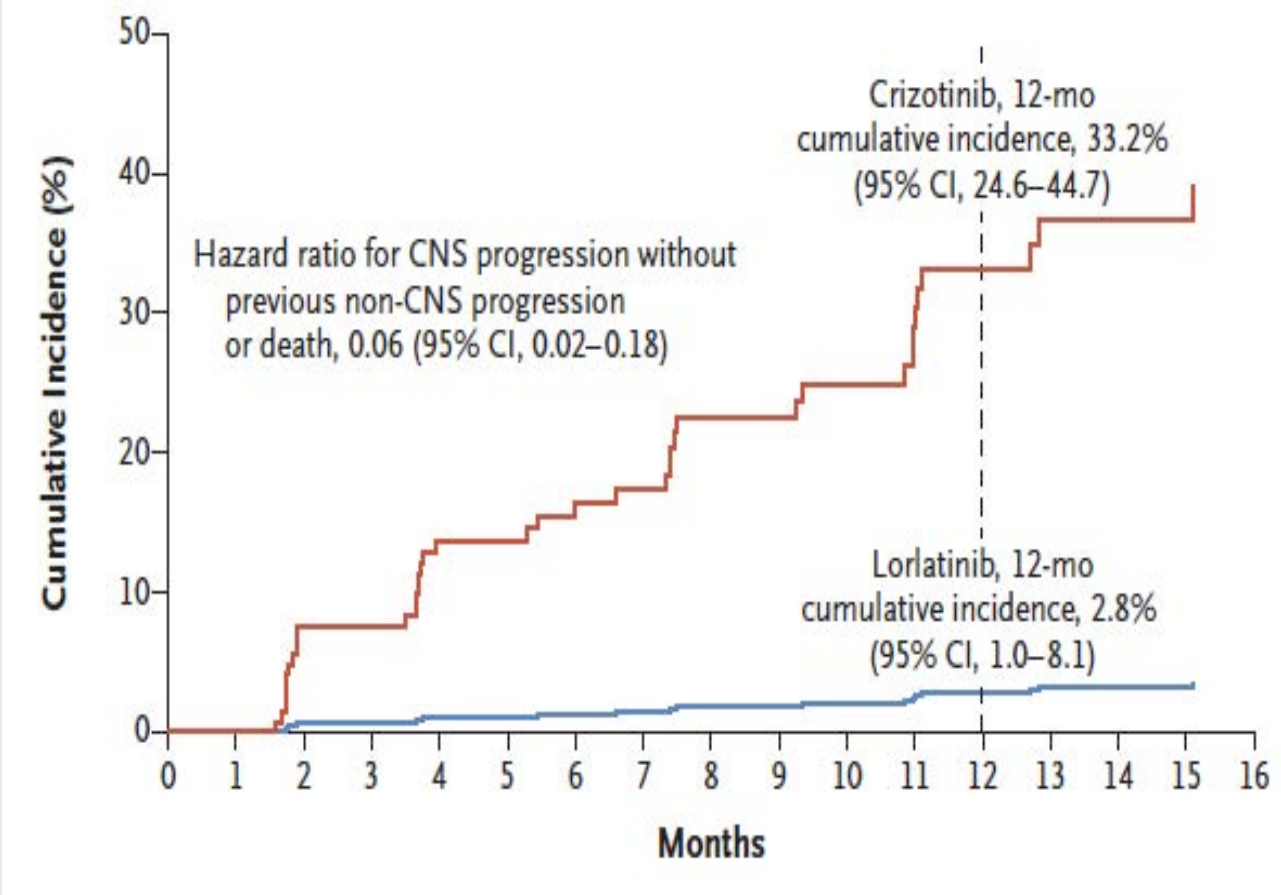
RTP RESEARCH TO PRACTICE

CROWN: Overall Survival and Cumulative Incidence of CNS Progression

Overall Survival



Cumulative Incidence of CNS Progression as First Event



Shaw AT et al. *N Engl J Med* 2020;383(21):2018-29.

RTP RESEARCH TO PRACTICE

Agenda

Module 1: NSCLC with EGFR Mutations

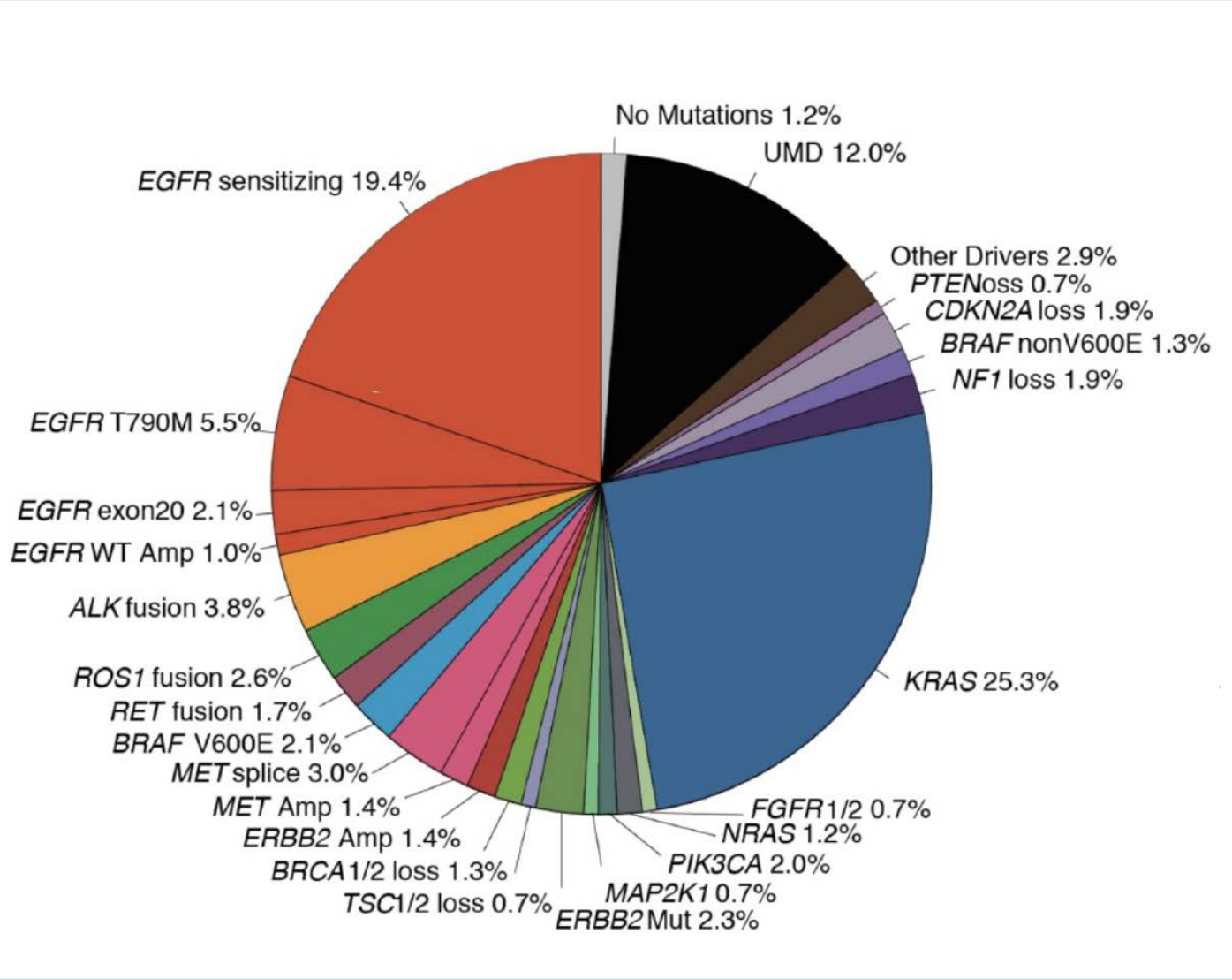
Module 2: NSCLC with ALK Rearrangement

Module 3: NSCLC with RET, MET Exon 14 and HER2 Mutations

Module 4: NSCLC without Targetable Mutations

Module 5: Extensive-Stage Small Cell Lung Cancer

MSK-IMPACT: Prospective Comprehensive Molecular Characterization of Lung Adenocarcinomas



EGFR sensitizing	19.4%
EGFR T790M	5.5%
EGFR exon20	2.1%
KRAS	25.3%
ALK fusion	3.8%
ROS1 fusion	2.6%
RET fusion	1.7%
BRAF V600E	2.1%
BRAF nonV600E	1.3%
MET splice	3.0%
MET Amp	1.4%
ERBB2 Amp	1.4%
ERBB2 Mut	2.3%

Jordan EJ et al. *Cancer Discovery* 2017;7(6):596-609.

RTP RESEARCH TO PRACTICE

original reports

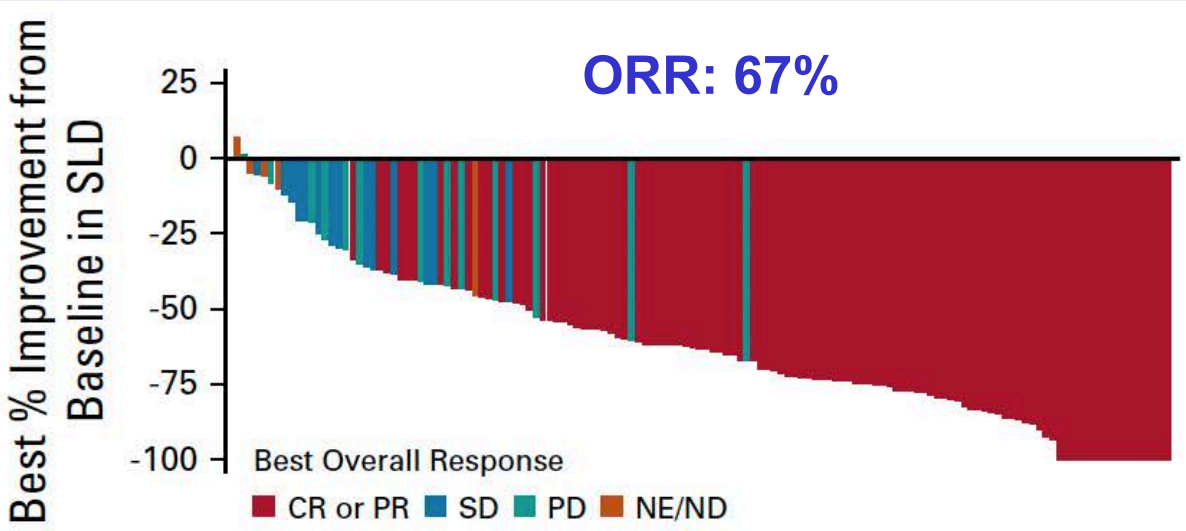
Updated Integrated Analysis of the Efficacy and Safety of Entrectinib in Locally Advanced or Metastatic *ROS1* Fusion–Positive Non–Small-Cell Lung Cancer

Rafal Dziadziuszko, MD, PhD[1]; Matthew G. Krebs, MD, PhD[2]; Filippo De Braud, MD[3,4]; Salvatore Siena, MD[3,5]; Alexander Drilon, MD[6]; Robert C. Doebele, MD, PhD[7]; Manish R. Patel, DO[8]; Byoung Chul Cho, MD, PhD[9]; Stephen V. Liu, MD[10]; Myung-Ju Ahn, MD, PhD[11]; Chao-Hua Chiu, MD[12]; Anna F. Farago, MD, PhD[13]; Chia-Chi Lin, MD[14]; Christos S. Karapetis, MBBS, MMedSc[15]; Yu-Chung Li, MD[16]; Bann-mo Day, PhD[17]; David Chen, PharmD[17]; Timothy R. Wilson, PhD[17]; and Fabrice Barlesi, MD, PhD[18,19]

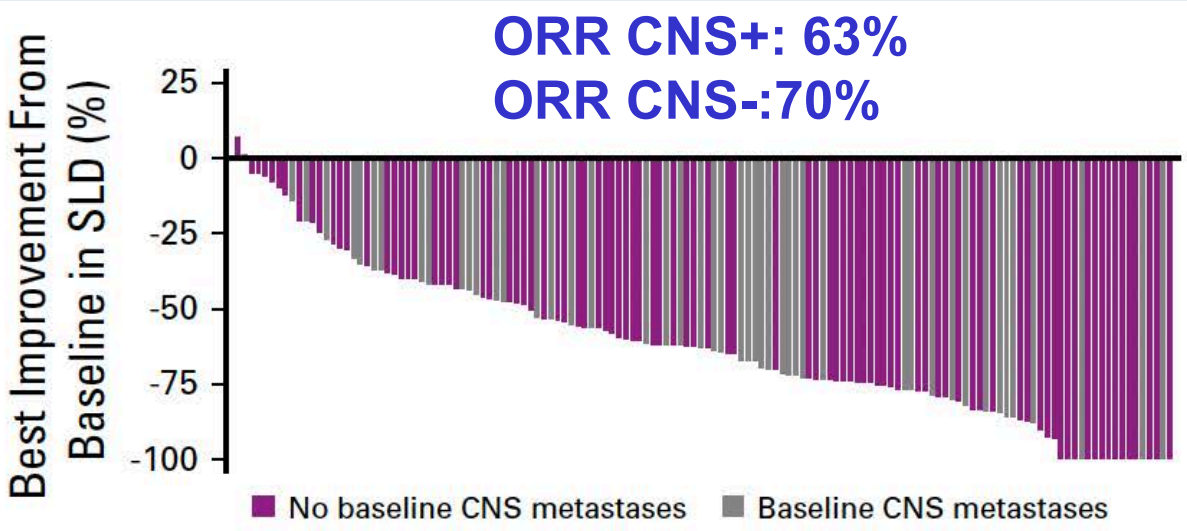
J Clin Oncol 2021;39(11):1253-63.

Integrated Analysis of ALKA-372-001, STARTRK-1, STARTRK-2, and STARTRK-NG

Efficacy Evaluable Population (N = 161)



Patients with (n = 56) and without (n = 105) CNS Metastases at Baseline



ORR = objective response rate

Dziadziuszko R et al. *J Clin Oncol* 2021;39(11):1253-63.

Lancet Oncol 2021;22:959-69.

Pralsetinib for *RET* fusion-positive non-small-cell lung cancer (ARROW): a multi-cohort, open-label, phase 1/2 study

Justin F Gainor, Giuseppe Curigliano, Dong-Wan Kim, Dae Ho Lee, Benjamin Besse, Christina S Baik, Robert C Doebele, Philippe A Cassier, Gilberto Lopes, Daniel S W Tan, Elena Garralda, Luis G Paz-Ares, Byoung Chul Cho, Shirish M Gadgeel, Michael Thomas, Stephen V Liu, Matthew H Taylor, Aaron S Mansfield, Viola W Zhu, Corinne Clifford, Hui Zhang, Michael Palmer, Jennifer Green, Christopher D Turner, Vivek Subbiah

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 27, 2020 VOL. 383 NO. 9

Efficacy of Selpercatinib in *RET* Fusion–Positive Non–Small-Cell Lung Cancer

A. Drilon, G.R. Oxnard, D.S.W. Tan, H.H.F. Loong, M. Johnson, J. Gainor, C.E. McCoach, O. Gautschi, B. Besse, B.C. Cho, N. Peled, J. Weiss, Y.-J. Kim, Y. Ohe, M. Nishio, K. Park, J. Patel, T. Seto, T. Sakamoto, E. Rosen, M.H. Shah, F. Barlesi, P.A. Cassier, L. Bazhenova, F. De Braud, E. Garralda, V. Velcheti, M. Satouchi, K. Ohashi, N.A. Pennell, K.L. Reckamp, G.K. Dy, J. Wolf, B. Solomon, G. Falchook, K. Ebata, M. Nguyen, B. Nair, E.Y. Zhu, L. Yang, X. Huang, E. Olek, S.M. Rothenberg, K. Goto, and V. Subbiah

Selpercatinib and Pralsetinib for Advanced NSCLC with RET Fusion

	Selpercatinib	Pralesetinib
Pivotal study	LIBRETTO-001 Phase I/II (N = 105)	ARROW Phase I/II (N = 233)
FDA approval	May 8, 2020	September 4, 2020
ORR	64%	61%
Median duration of response	17.5 months	Not reached
Common Grade ≥3 adverse events	Hypertension (14%) Increased ALT (12%) and AST (10%) levels Hyponatremia (6%) Lymphopenia (6%)	Neutropenia (18%) Hypertension (11%) Anemia (10%) Decreased WBC (6%)

[1] Drilon A et al. *N Engl J Med* 2020;383:813-24. [2] Gainor JF et al. *Lancet Oncol* 2021;22:959-69.

RTP RESEARCH TO PRACTICE

FDA Grants Accelerated Approval to Tepotinib for Metastatic NSCLC

Press Release – February 3, 2021

"The Food and Drug Administration granted accelerated approval to tepotinib for adult patients with metastatic non-small cell lung cancer (NSCLC) harboring mesenchymal-epithelial transition (MET) exon 14 skipping alterations.

Efficacy was demonstrated in the VISION trial (NCT02864992), a multicenter, non-randomized, open-label, multicohort study enrolling 152 patients with advanced or metastatic NSCLC with MET exon 14 skipping alterations. Patients received tepotinib 450 mg orally once daily until disease progression or unacceptable toxicity."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-tepotinib-metastatic-non-small-cell-lung-cancer

RTP RESEARCH TO PRACTICE

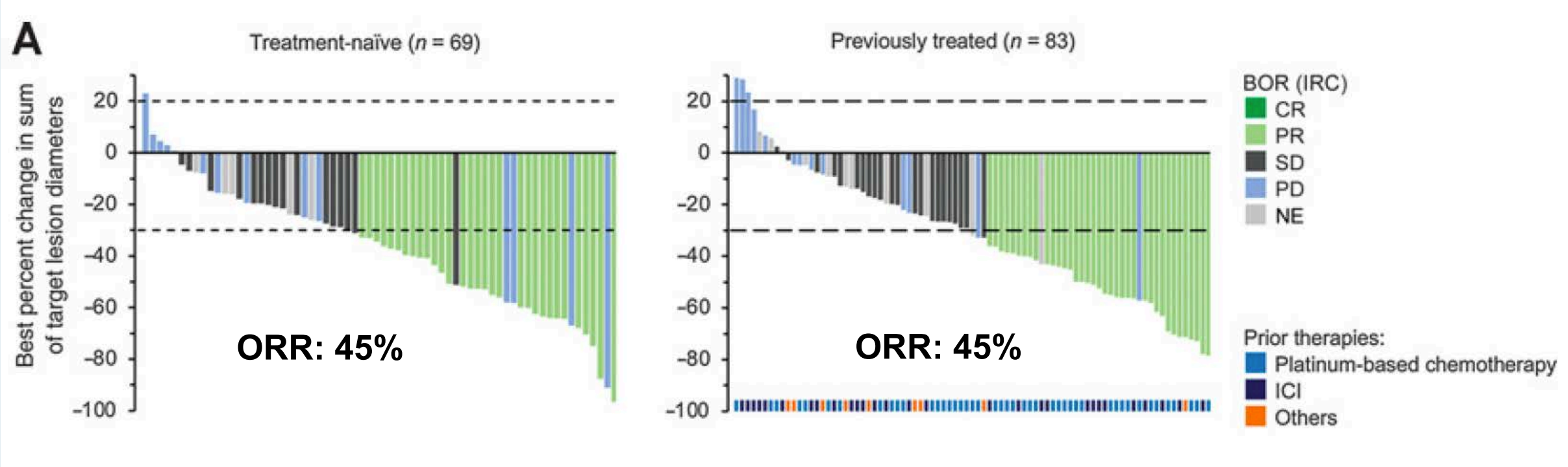
CLINICAL CANCER RESEARCH | CLINICAL TRIALS: TARGETED THERAPY

Tepotinib Efficacy and Safety in Patients with *MET* Exon 14 Skipping NSCLC: Outcomes in Patient Subgroups from the VISION Study with Relevance for Clinical Practice

Xiuning Le[1], Hiroshi Sakai[2], Enriqueta Felip[3], Remi Veillon[4], Marina Chiara Garassino[5,6], Jo Raskin[7], Alexis B. Cortot[8], Santiago Viteri[9], Julien Mazieres[10], Egbert F. Smit[11], Michael Thomas[12], Wade T. Iams[13], Byoung Chul Cho[14], Hye Ryun Kim[14], James Chih-Hsin Yang[15], Yuh-Min Chen[16], Jyoti D. Patel[17], Christine M. Bestvina[18], Keunchil Park[19], Frank Griesinger[20], Melissa Johnson[21], Maya Gottfried[22], Christian Britschgi[23], John Heymach[1], Elif Sikoglu[24], Karin Berghoff[25], Karl-Maria Schumacher[26], Rolf Bruns[27], Gordon Otto[26], and Paul K. Paik[28,29]

***Clin Cancer Res* 2021;[Online ahead of print].**

VISION: Tepotinib in Advanced NSCLC with MET Exon 14 Skipping Mutations



Le X et al. *Clin Cancer Res* 2021;[Online ahead of print].

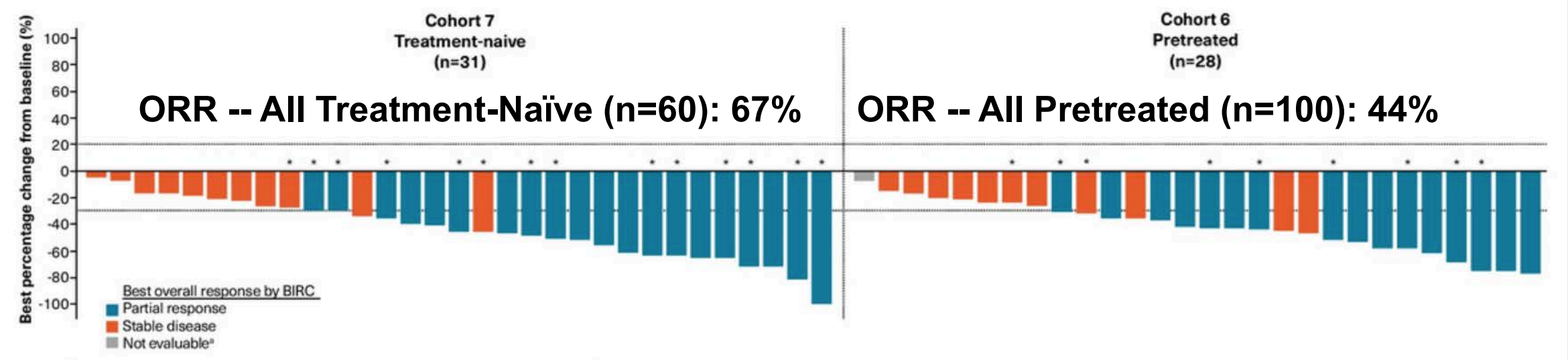
RTP RESEARCH TO PRACTICE

Capmatinib in *MET* Exon 14-Mutated, Advanced NSCLC: Updated Results from the GEOMETRY mono-1 Study

Wolf J et al.

ASCO 2021;Abstract 9020.

GEOMETRY mono-1



Wolf J et al. ASCO 2021;Abstract 9020.

RTP RESEARCH TO PRACTICE

N Engl J Med 2022;386:241-51.

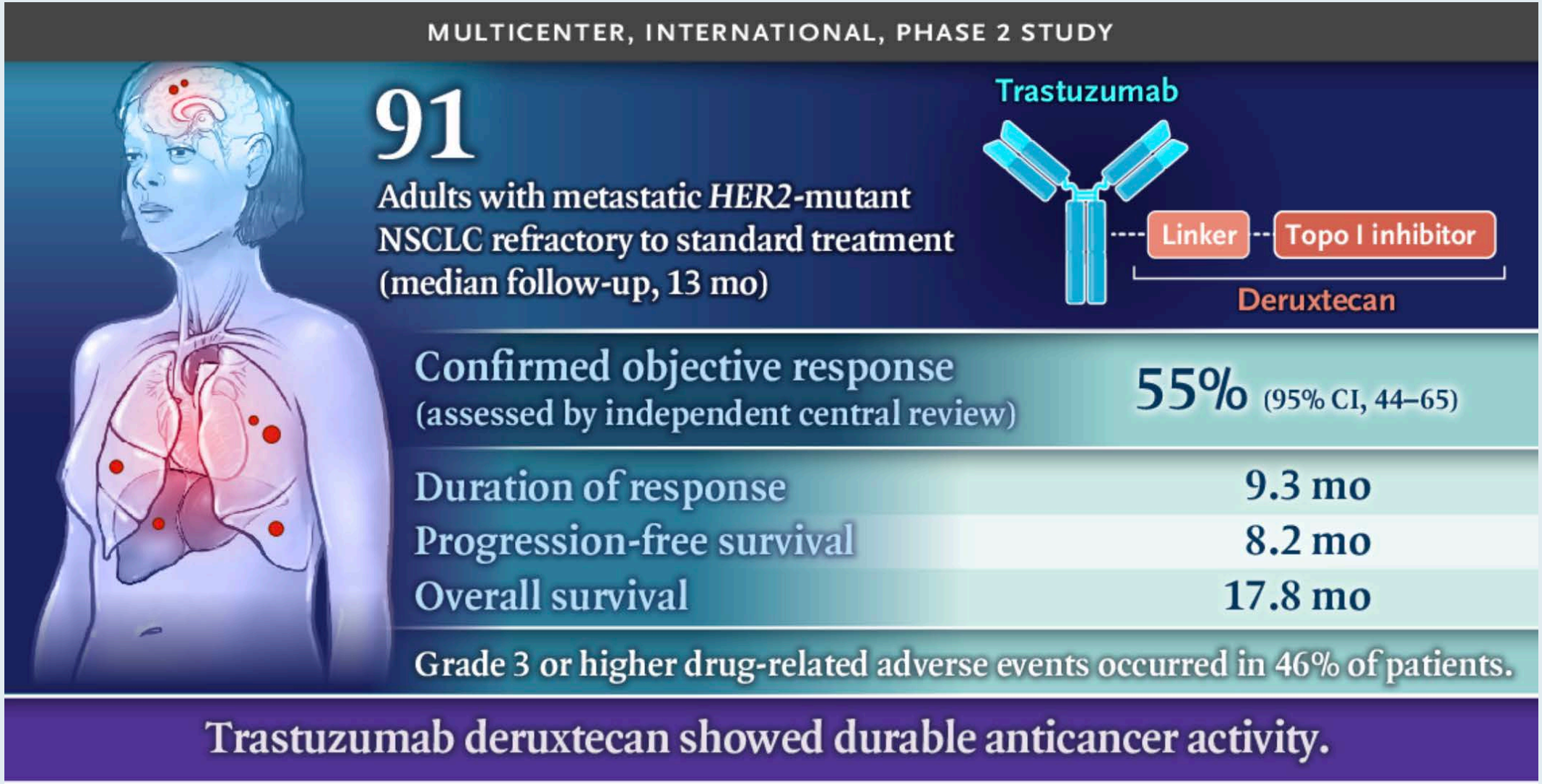
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Trastuzumab Deruxtecan in *HER2*-Mutant Non–Small-Cell Lung Cancer

Bob T. Li, M.D., Ph.D., M.P.H., Egbert F. Smit, M.D., Ph.D., Yasushi Goto, M.D., Ph.D., Kazuhiko Nakagawa, M.D., Hibiki Udagawa, M.D., Julien Mazières, M.D., Misako Nagasaka, M.D., Ph.D., Lyudmila Bazhenova, M.D., Andreas N. Saltos, M.D., Enriqueta Felip, M.D., Ph.D., Jose M. Pacheco, M.D., Maurice Pérol, M.D., Luis Paz-Ares, M.D., Kapil Saxena, M.D., Ryota Shiga, B.Sc., Yingkai Cheng, M.D., Ph.D., Suddhasatta Acharyya, Ph.D., Patrik Vitazka, M.D., Ph.D., Javad Shahidi, M.D., David Planchard, M.D., Ph.D., and Pasi A. Jänne, M.D., Ph.D., for the DESTINY-Lung01 Trial Investigators*

DESTINY-Lung01 Study



Li BT et al. *N Engl J Med* 2022;386(3):241-51.

FDA Grants Accelerated Approval to Sotorasib for NSCLC with KRAS G12C Mutation

Press Release – May 28, 2021

"The Food and Drug Administration granted accelerated approval to sotorasib, a RAS GTPase family inhibitor, for adult patients with KRAS G12C-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC), as determined by an FDA-approved test, who have received at least one prior systemic therapy.

FDA also approved the QIAGEN therascreen® KRAS RGQ PCR kit (tissue) and the Guardant360® CDx (plasma) as companion diagnostics for sotorasib. If no mutation is detected in a plasma specimen, the tumor tissue should be tested.

Approval was based on CodeBreaK 100, a multicenter, single-arm, open label clinical trial (NCT03600883) which included patients with locally advanced or metastatic NSCLC with KRAS G12C mutations. Efficacy was evaluated in 124 patients whose disease had progressed on or after at least one prior systemic therapy. Patients received sotorasib 960 mg orally daily until disease progression or unacceptable toxicity."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-sotorasib-kras-g12c-mutated-nsclc

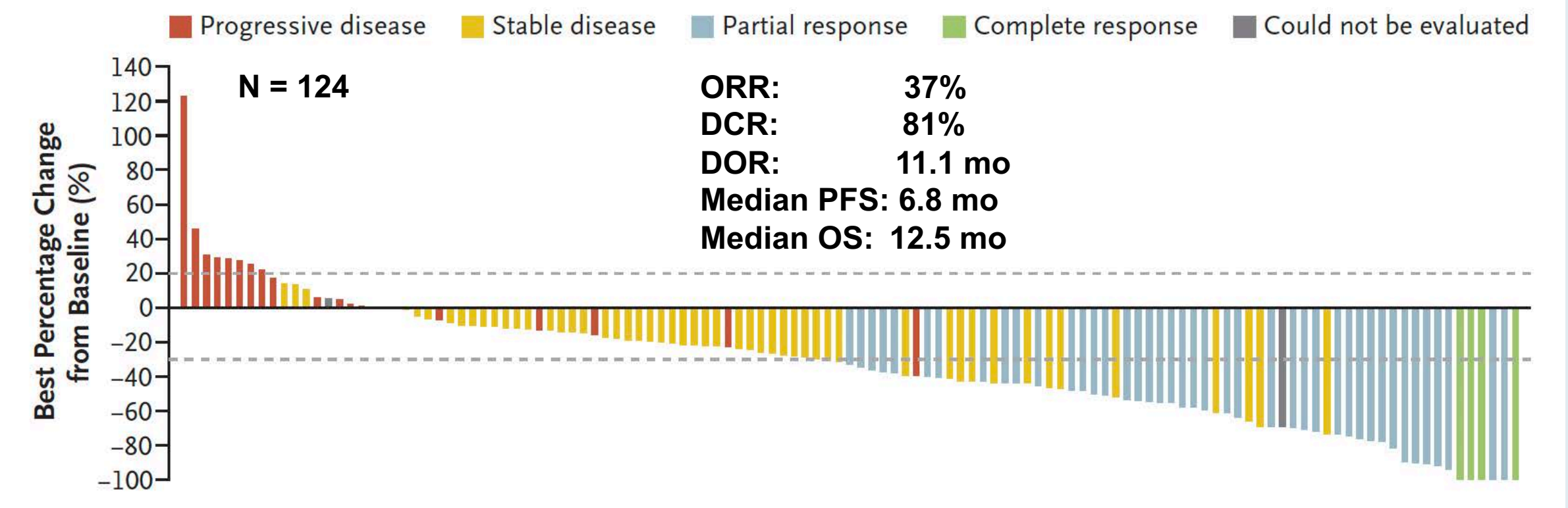
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 24, 2021 VOL. 384 NO. 25

Sotorasib for Lung Cancers with *KRAS* p.G12C Mutation

F. Skoulidis, B.T. Li, G.K. Dy, T.J. Price, G.S. Falchook, J. Wolf, A. Italiano, M. Schuler, H. Borghaei, F. Barlesi, T. Kato, A. Curioni-Fontecedro, A. Sacher, A. Spira, S.S. Ramalingam, T. Takahashi, B. Besse, A. Anderson, A. Ang, Q. Tran, O. Mather, H. Henary, G. Ngarmchamnanrith, G. Friberg, V. Velcheti, and R. Govindan

CodeBreaK 100: Sotorasib for Previously Treated Metastatic NSCLC with KRAS p.G12C Mutation



Skoulidis F et al. *N Engl J Med* 2021;384(25):2371-81.

RTP RESEARCH TO PRACTICE

Agenda

Module 1: NSCLC with EGFR Mutations

Module 2: NSCLC with ALK Rearrangement

Module 3: NSCLC with RET, MET Exon 14 and HER2 Mutations

Module 4: NSCLC without Targetable Mutations

Module 5: Extensive-Stage Small Cell Lung Cancer

FDA Approves Atezolizumab as Adjuvant Treatment for NSCLC

Press Release – October 15, 2021

"The Food and Drug Administration approved atezolizumab for adjuvant treatment following resection and platinum-based chemotherapy in patients with stage II to IIIA non-small cell lung cancer (NSCLC) whose tumors have PD-L1 expression on ≥ 1% of tumor cells, as determined by an FDA-approved test.

Today, the FDA also approved the VENTANA PD-L1 (SP263) Assay as a companion diagnostic device to select patients with NSCLC for adjuvant treatment with atezolizumab.

The major efficacy outcome measure was disease-free survival (DFS) as assessed by the investigator in the primary efficacy analysis population (n = 476) of patients with stage II-IIIA NSCLC with PD-L1 expression on ≥1% of tumor cells (PD-L1 ≥1% TC). Median DFS was not reached in patients on the atezolizumab arm compared with 35.3 months on the BSC arm (HR 0.66; p = 0.004). In a pre-specified secondary subgroup analysis of patients with PD-L1 TC ≥ 50% stage II-IIIA NSCLC, the DFS HR was 0.43. In an exploratory subgroup analysis of patients with PD-L1 TC 1-49% stage II-IIIA NSCLC, the DFS HR was 0.87.

The recommended atezolizumab dose for this indication is 840 mg every 2 weeks, 1,200 mg every 3 weeks, or 1,680 mg every 4 weeks for up to 1 year."

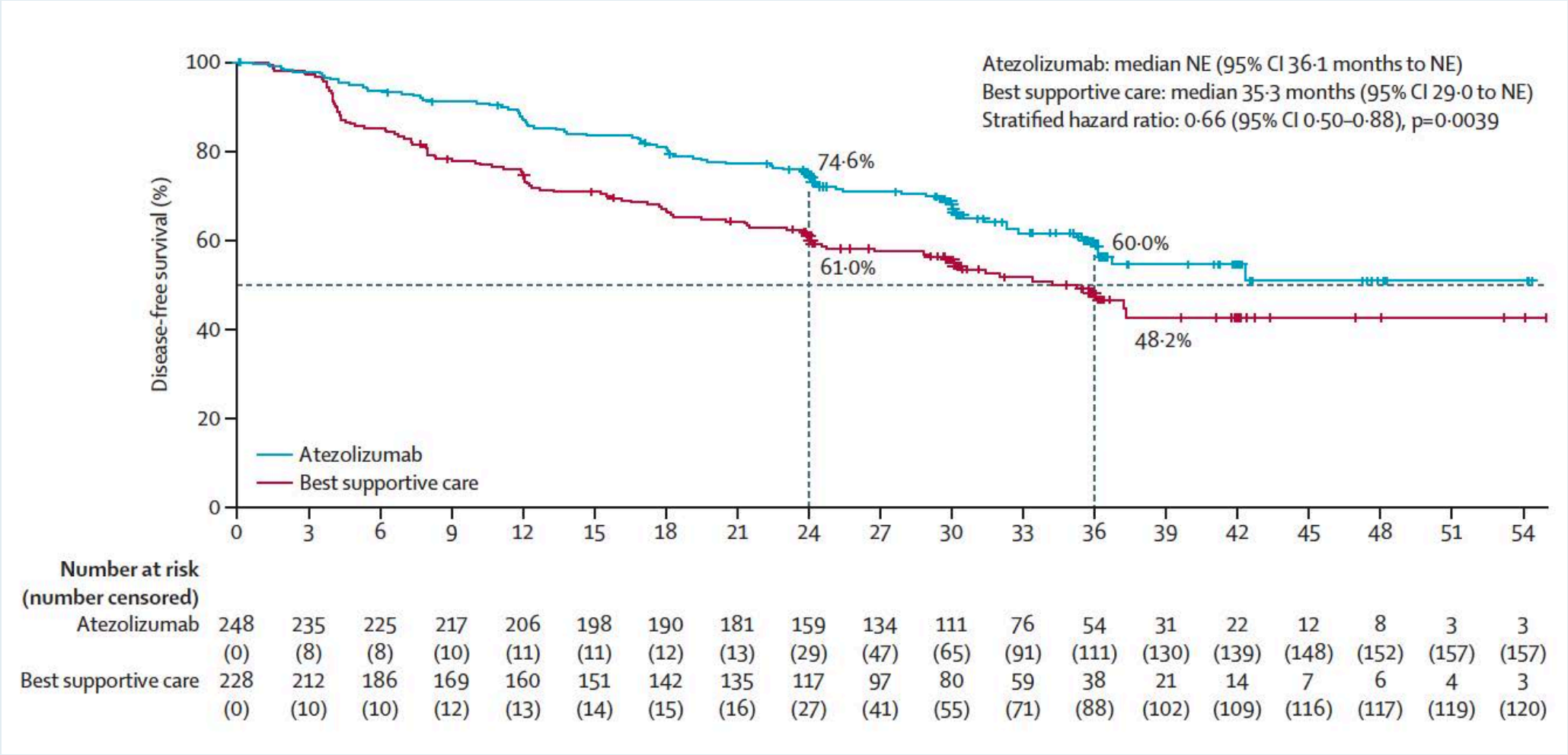
https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-atezolizumab-adjuvant-treatment-non-small-cell-lung-cancer

Lancet 2021;398:1344-57.

Adjuvant atezolizumab after adjuvant chemotherapy in resected stage IB–IIIA non-small-cell lung cancer (IMpower010): a randomised, multicentre, open-label, phase 3 trial

*Enriqueta Felip, Nasser Altorki, Caicun Zhou, Tibor Csőszi, Ihor Vynnychenko, Oleksandr Goloborodko, Alexander Luft, Andrey Akopov, Alex Martinez-Marti, Hirotsugu Kenmotsu, Yuh-Min Chen, Antonio Chella, Shunichi Sugawara, David Voong, Fan Wu, Jing Yi, Yu Deng, Mark McCleland, Elizabeth Bennett, Barbara Gitlitz, Heather Wakelee, for the IMpower010 Investigators**

IMpower010 Primary Endpoint: Disease-Free Survival in the PD-L1 ≥1% Tumor Cells Stage II-IIIA Population



Felip E et al. *Lancet* 2021;398(10308):1344-57.

IMpower010: Efficacy Summary

	Atezolizumab	BSC	HR (*p*-value)
TC PD-L1 ≥1%, Stage II-IIIA (n = 248, 228)			
Median disease-free survival (DFS)	Not estimable	35.3 mo	0.66 (0.0039)
2-year DFS rate	75%	61%	—
3-year DFS rate	60%	48%	—
All randomized Stage II-IIIA (n = 442, 440)			
Median DFS	42.3 mo	35.3 mo	0.79 (0.020)
2-year DFS rate	70%	62%	—
3-year DFS rate	56%	50%	—
ITT population (n = 507, 598)			
Median DFS	Not estimable	37 mo	0.81 (0.040)
2-year DFS rate	71%	64%	—
3-year DFS rate	58%	53%	—

BSC = best supportive care; TC = tumor cells

Overall survival data in the ITT population were immature and not formally tested.

Felip E et al. *Lancet* 2021;398(10308):1344-57.

IMpower010: Safety Summary

	Atezolizumab group (n=495)	Best supportive care group (n=495)
Adverse event		
Any grade	459 (93%)	350 (71%)
Grade 3–4	108 (22%)	57 (12%)
Serious	87 (18%)	42 (8%)
Grade 5	8 (2%)*	3 (1%)†
Led to dose interruption of atezolizumab	142 (29%)	..
Led to atezolizumab discontinuation	90 (18%)	..
Immune-mediated adverse events		
Any grade	256 (52%)	47 (9%)
Grade 3–4	39 (8%)	3 (1%)
Required the use of systemic corticosteroids‡	60 (12%)	4 (1%)
Led to discontinuation	52 (11%)	0

Data are n (%). *Interstitial lung disease, multiple organ dysfunction syndrome, myocarditis, and acute myeloid leukaemia (all four events related to atezolizumab), and pneumothorax, cerebrovascular accident, arrhythmia, and acute cardiac failure. †Pneumonia; pulmonary embolism; and cardiac tamponade and septic shock in the same patient. ‡Atezolizumab-related.

Felip E et al. *Lancet* 2021;398(10308):1344-57.

RTP RESEARCH TO PRACTICE

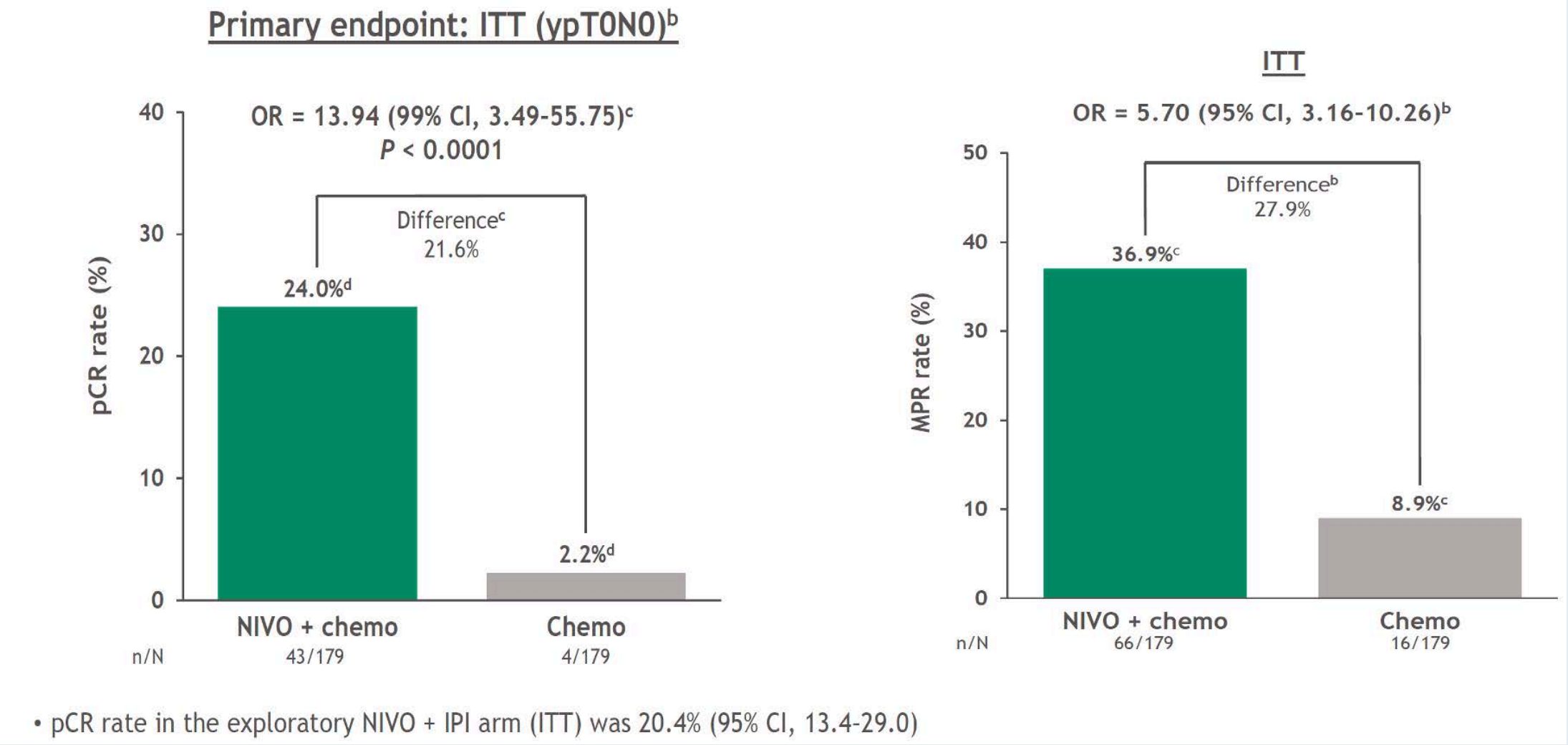
CheckMate 816 Met a Primary Endpoint of Improved Event-Free Survival with Neoadjuvant Nivolumab in Combination with Chemotherapy

Press Release – November 8, 2021

"The Phase 3 CheckMate-816 trial met the primary endpoint of improved event-free survival (EFS) in patients with resectable stage IB to IIIA non-small cell lung cancer (NSCLC). In a prespecified interim analysis, nivolumab plus chemotherapy showed a statistically significant and clinically meaningful improvement in EFS compared to chemotherapy alone when given before surgery. This combination previously showed a significant improvement of pathologic complete response (pCR), the trial's other primary endpoint. The safety profile of nivolumab plus chemotherapy was consistent with previously reported studies in NSCLC. CheckMate-816 is the first Phase 3 trial with an immunotherapy-based combination to demonstrate a statistically significant and clinically meaningful benefit as a neoadjuvant treatment for patients with non-metastatic non-small cell lung cancer."

https://news.bms.com/news/details/2021/Neoadjuvant-Opdivo-nivolumab-Plus-Chemotherapy-Significantly-Improves-Event-Free-Survival-in-Patients-with-Resectable-Non-Small-Cell-Lung-Cancer-in-Phase-3-CheckMate--816-Trial/default.aspx

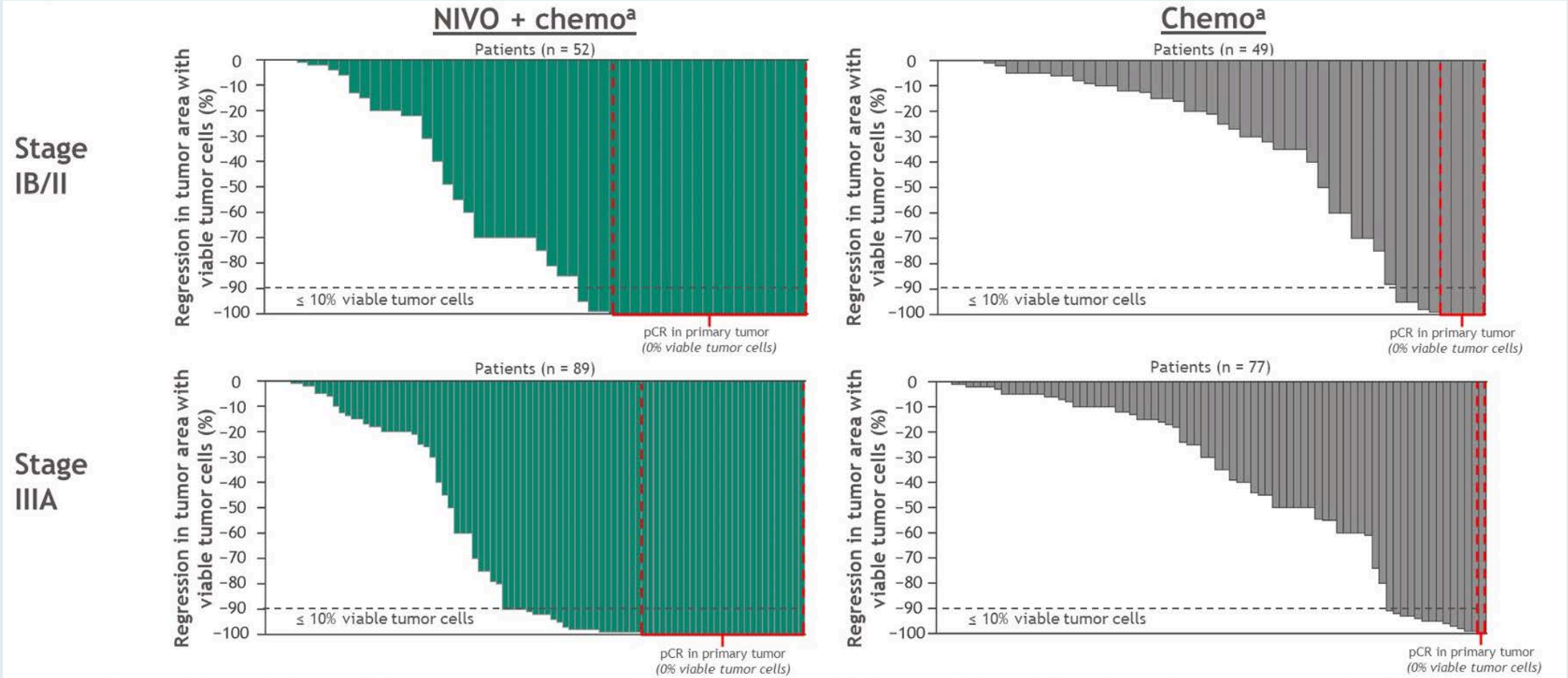
CheckMate 816 Coprimary Endpoint: Pathologic Complete Response (pCR)



- pCR rate in the exploratory NIVO + IPI arm (ITT) was 20.4% (95% CI, 13.4-29.0)

Forde PM et al. AACR 2021;Abstract CT003.

CheckMate 816: Depth of Pathologic Regression in Primary Tumor by Stage



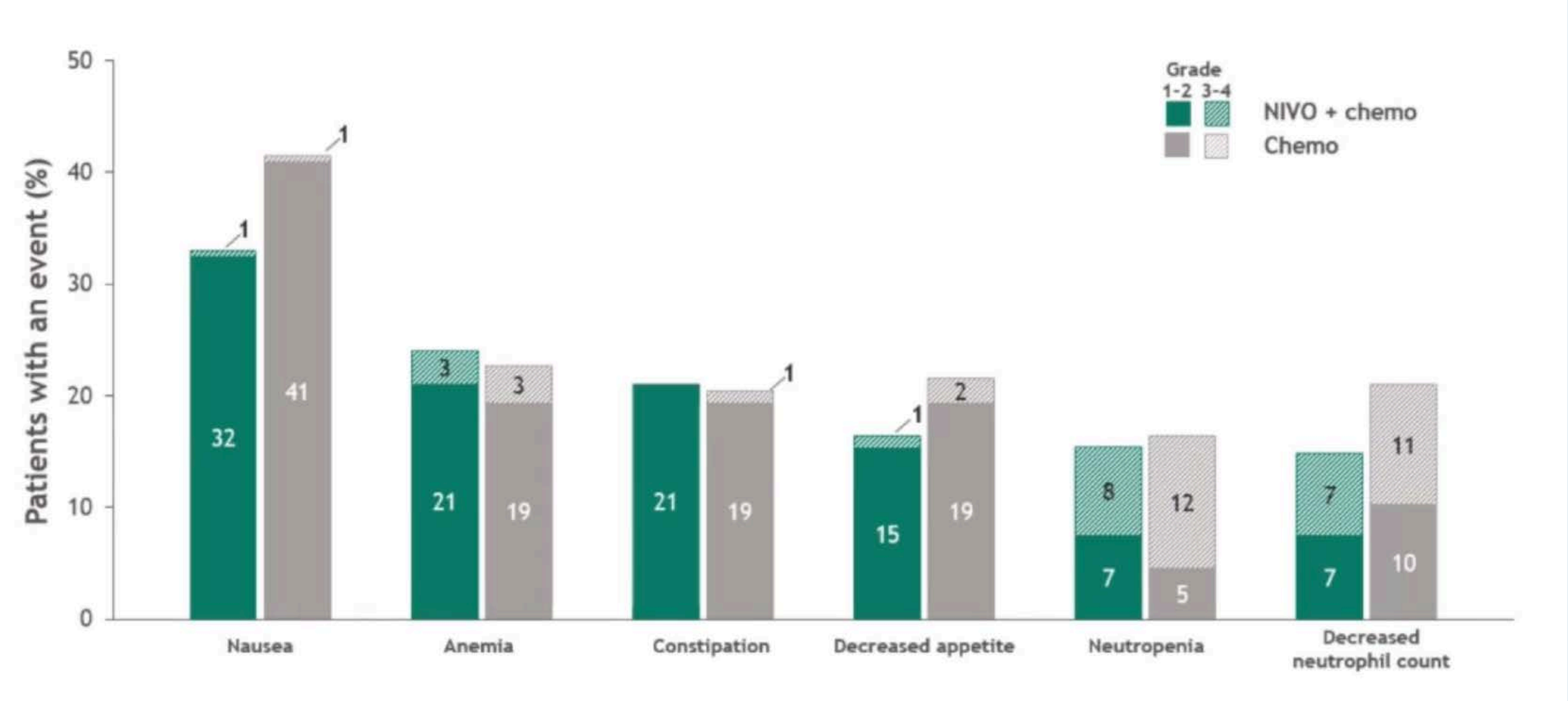
- The median residual viable tumor percentage in stage IB/II and IIIA was 28% and 8% with NIVO + chemo vs 79% and 70% with chemo, respectively

[a]Response-evaluable patients.

Spicer J et al. ASCO 2021;Abstract 8503.

RTP RESEARCH TO PRACTICE

CheckMate 816: Treatment-Related Adverse Events in ≥15% of Patients



Forde PM et al. AACR 2021;Abstract CT003.

ASCO special articles

Management of Stage III Non–Small-Cell Lung Cancer: ASCO Guideline

Megan E. Daly, MD[1]; Navneet Singh, MD, DM[2]; Nofisat Ismaila, MD, MSc[3]; Mara B. Antonoff, MD[4]; Douglas A. Arenberg, MD[5]; Jeffrey Bradley, MD[6]; Elizabeth David, MD[7]; Frank Detterbeck, MD[8]; Martin Früh, MD[9,10]; Matthew A. Gubens, MD, MS[11]; Amy C. Moore, PhD[12]; Sukhmani K. Padda, MD[13]; Jyoti D. Patel, MD[14]; Tanyanika Phillips, MD, MPH[15]; Angel Qin, MD[5]; Clifford Robinson, MD[16]; and Charles B. Simone II, MD[17]

J Clin Oncol 2021;[Online ahead of print].

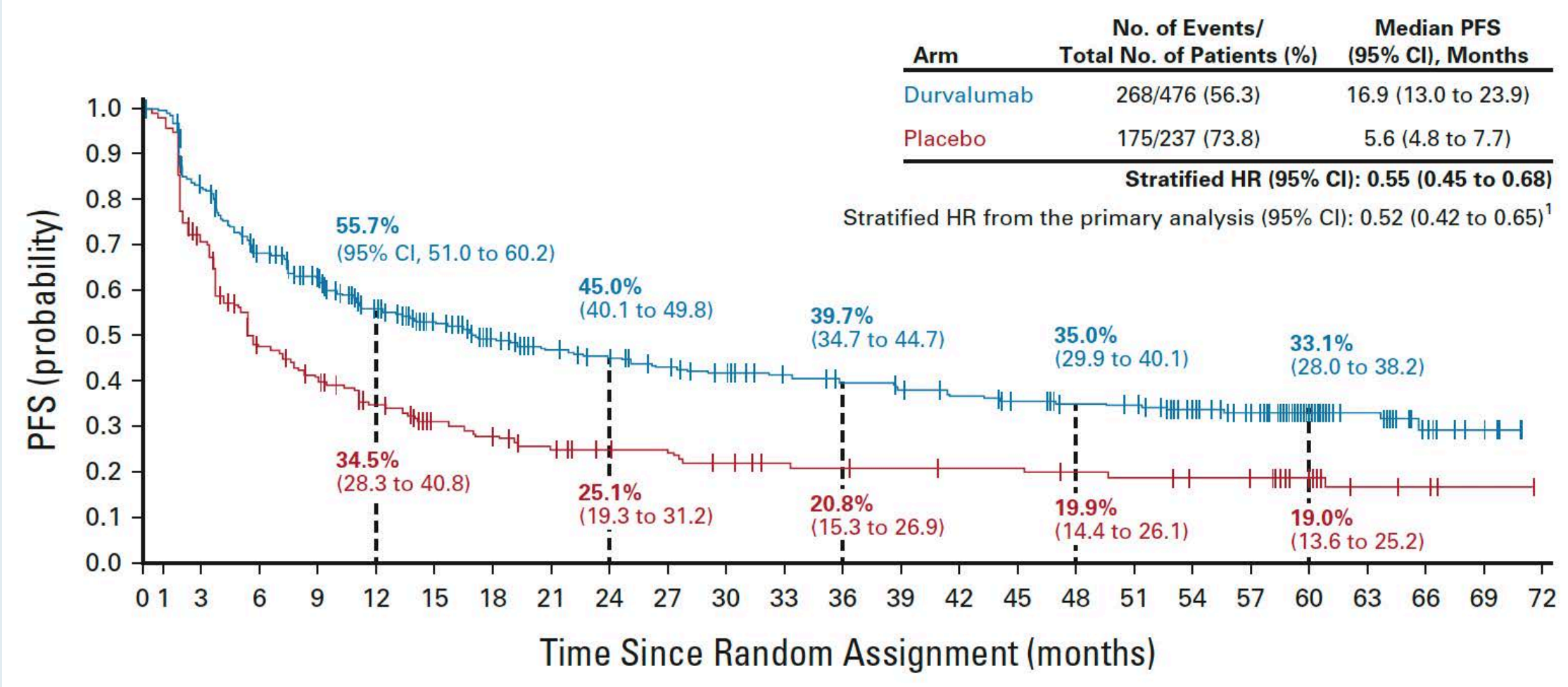
original reports

Five-Year Survival Outcomes From the PACIFIC Trial: Durvalumab After Chemoradiotherapy in Stage III Non–Small-Cell Lung Cancer

David R. Spigel, MD[1]; Corinne Faivre-Finn, MD, PhD[2]; Jhanelle E. Gray, MD[3]; David Vicente, MD[4]; David Planchard, MD, PhD[5]; Luis Paz-Ares, MD, PhD[6]; Johan F. Vansteenkiste, MD, PhD[7]; Marina C. Garassino, MD[8,9]; Rina Hui, PhD[10]; Xavier Quantin, MD, PhD[11]; Andreas Rimner, MD[12]; Yi-Long Wu, MD[13]; Mustafa Özgüroğlu, MD[14]; Ki H. Lee, MD[15]; Terufumi Kato, MD[16]; Maike de Wit, MD, PhD[17]; Takayasu Kurata, MD[18]; Martin Reck, MD, PhD[19]; Byoung C. Cho, MD, PhD[20]; Suresh Senan, PhD[21]; Jarushka Naidoo, MBBCH, MHS[22]; Helen Mann, MSc[23]; Michael Newton, PharmD[24]; Piruntha Thiyagarajah, MD[23]; and Scott J. Antonia, MD, PhD[3]; on behalf of the PACIFIC Investigators

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

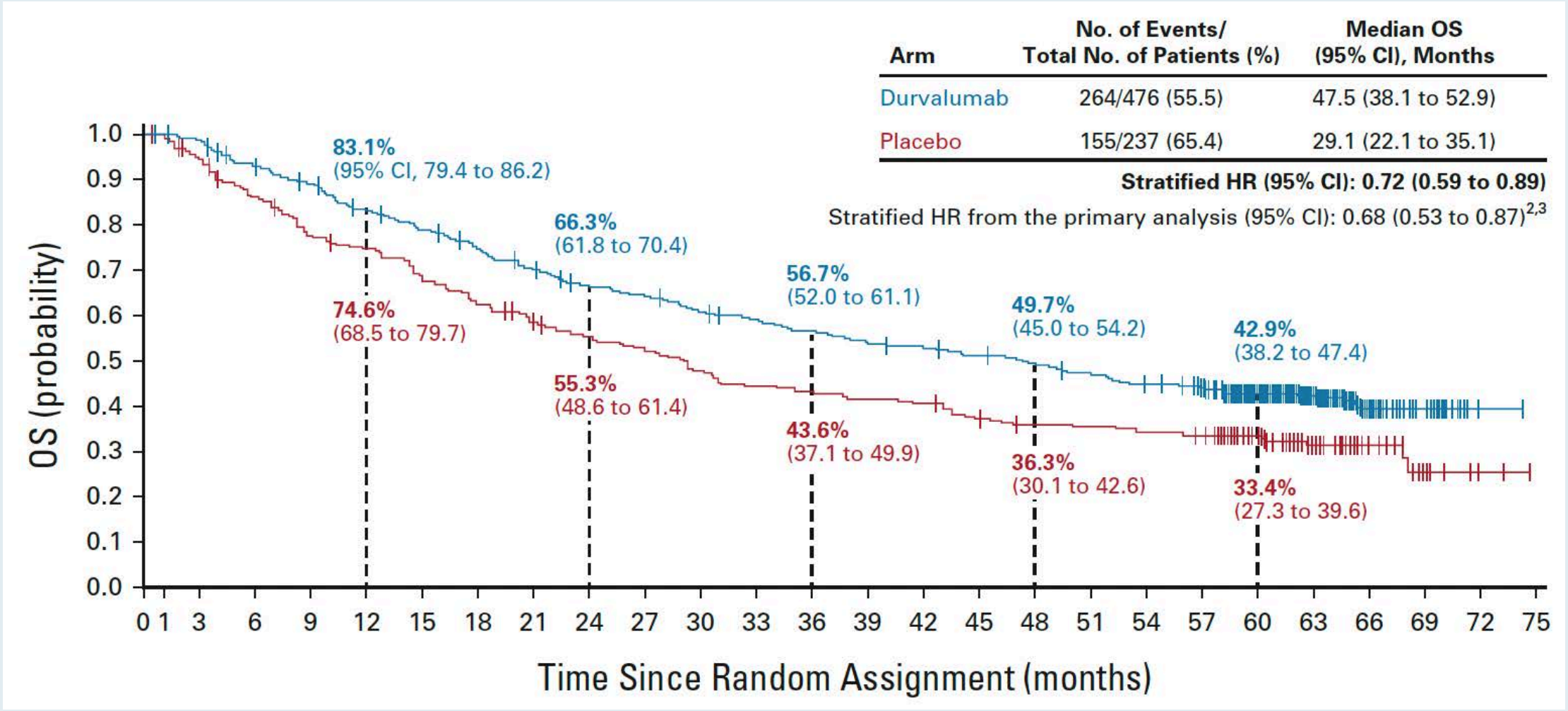
PACIFIC: Five-Year Progression-Free Survival (PFS) with Durvalumab After Chemoradiation Therapy for Stage III NSCLC



Spigel DR et al. *J Clin Oncol* 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

PACIFIC: Five-Year Overall Survival (OS) with Durvalumab After Chemoradiation Therapy for Stage III NSCLC



Spigel DR et al. *J Clin Oncol* 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

PACIFIC-R: Real-World Study of Durvalumab After Chemoradiation Therapy for Patients with Unresectable Stage III NSCLC

- International observational study (N = 1,155)
- Median PFS: 22.5 months
- Median duration of durvalumab treatment: 11 months

Summary of safety and pneumonitis	N = 1,155
Discontinuation of durvalumab due to AE	17.5%
Discontinuation of durvalumab due to pneumonitis Temporary Permanent	13.8% 5.1% 8.7%
Any-grade pneumonitis and/or interstitial lung disease Moderate severity Life threatening Fatal	18.5% 8.8% 0.2% 0.1%

Girard N et al. ESMO 2021;Abstract 1171MO.

RTP RESEARCH TO PRACTICE

FDA Approves Durvalumab for Fixed-Dose Use in NSCLC, Bladder Cancer Indications

Press Release – November 20, 2020

"The FDA has approved durvalumab for an additional dosing option, a fixed dose of 1500 mg every 4 weeks, in the approved indications of unresectable stage III non-small cell lung cancer after chemoradiation and previously treated advanced bladder cancer.

This new dosing option is consistent with the dosing for the agent that has been approved in extensive-stage small cell lung cancer (ES-SCLC); this will serve as an alternative option for patients who weigh more than 30 kg rather than the weight-based dosing of 10 mg/kg that is administered every 2 weeks.

The regulatory decision was based on data from several clinical trials examining the agent, including the phase 3 PACIFIC trial (NCT02125461), which supported the 2-week, weight-based dosing in patients with unresectable stage III NSCLC, and the phase 3 CASPIAN trial (NCT03043872), which examined a 4-week, fixed-dose during maintenance treatment in patients with ES-SCLC."

https://www.onclive.com/view/fda-approves-durvalumab-for-fixed-dose-use-in-nsclc-bladder-cancer-indications

RTP RESEARCH TO PRACTICE

INTERNATIONAL JOURNAL OF
RADIATION ONCOLOGY • BIOLOGY • PHYSICS
ASTRO

16 | VOLUME 111, ISSUE 3, SUPPLEMENT , S9-S10, NOVEMBER 01, 2021

Pembrolizumab Plus Platinum Chemotherapy and Radiotherapy for Unresectable, Locally Advanced, Stage 3 NSCLC: KEYNOTE-799

S.K. Jabbour • K.H. Lee • N. Frost • ... A. Samkari • S. Keller • M. Reck • Show all authors

Phase II KEYNOTE-799 Trial of Pembrolizumab with Concurrent Chemoradiation Therapy for Unresectable Stage III NSCLC

Coprimary Endpoints: Overall Response Rate (ORR) and Grade 3 or Higher Pneumonitis

	Cohort A (squamous and nonsquamous) (n = 112)	Cohort B (nonsquamous only) (n = 102)
ORR	70.5%	70.6%
12-month PFS	67.1%	71.6%
12-month OS	81.3%	87.0%
Grade ≥3 pneumonitis	8.0%	6.9%

Jabbour SK et al. *IJROBP* 2021;11(3, Suppl):9-10.

FDA-Approved Single-Agent Immunotherapy Options for First-Line Therapy

Monotherapy	FDA approval	Pivotal study	Histologic type	HR (OS)
Pembrolizumab[1,2] (q3wk or q6wk)	4/11/19 10/24/16	KEYNOTE-042 KEYNOTE-024	PD-L1 TPS ≥1%	0.63
Atezolizumab[3] (q2wk, q3wk or q4wk)	5/18/20	IMpower110	PD-L1 TPS ≥50, EGFR and/or ALK wt	0.59
Cemiplimab[4] (q3wk)	2/22/21	EMPOWER-Lung 1 (Study 1624)	PD-L1 TPS ≥50, EGFR and/or ALK and/or ROS1 wt	0.57

[1] Mok. *Lancet* 2019. [2] Reck. *J Clin Oncol* 2019. [3] Herbst. *N Engl J Med* 2020. [4] Sezer. *Lancet* 2021.

FDA Approves Cemiplimab-rwlc for NSCLC with High PD-L1 Expression

Press Release – February 22, 2021

"The Food and Drug Administration approved cemiplimab-rwlc for the first-line treatment of patients with advanced non-small cell lung cancer (NSCLC) (locally advanced who are not candidates for surgical resection or definitive chemoradiation or metastatic) whose tumors have high PD-L1 expression (Tumor Proportion Score [TPS] > 50%) as determined by an FDA-approved test, with no EGFR, ALK or ROS1 aberrations.

Efficacy was evaluated in Study 1624 (NCT03088540), a multi-center, randomized, open-label trial in 710 patients with locally advanced NSCLC who were not candidates for surgical resection or definitive chemoradiation or with metastatic NSCLC. Patients were randomized (1:1) to receive cemiplimab-rwlc 350 mg intravenously every 3 weeks for up to 108 weeks or a platinum-based chemotherapy. The main efficacy outcome measures were overall survival (OS) and progression-free survival (PFS) per blinded independent central review (BICR)."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-cemiplimab-rwlc-non-small-cell-lung-cancer-high-pd-l1-expression

RTP RESEARCH TO PRACTICE

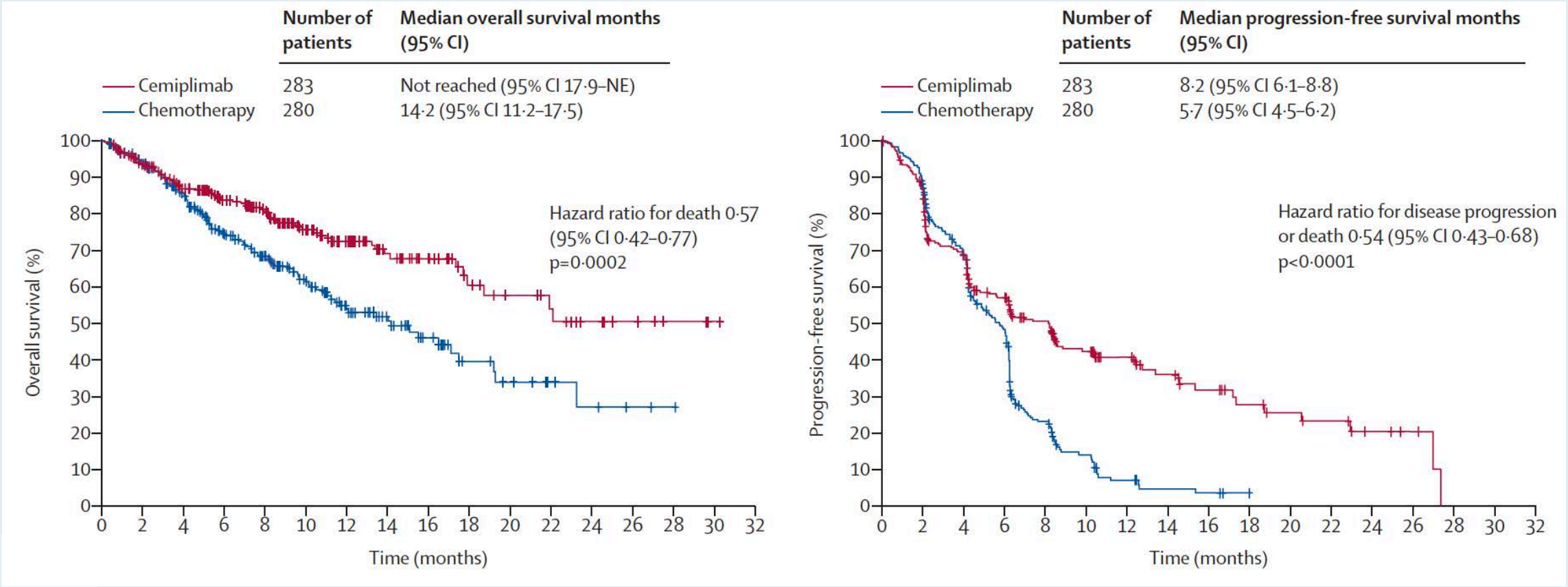
Lancet 2021;397:592-604.

Cemiplimab monotherapy for first-line treatment of advanced non-small-cell lung cancer with PD-L1 of at least 50%: a multicentre, open-label, global, phase 3, randomised, controlled trial

Ahmet Sezer, Saadettin Kilickap, Mahmut Gümüş, Igor Bondarenko, Mustafa Özgüroğlu, Miranda Gogishvili, Haci M Turk, Irfan Cicin, Dmitry Bentsion, Oleg Gladkov, Philip Clingan, Virote Sriuranpong, Naiyer Rizvi, Bo Gao, Siyu Li, Sue Lee, Kristina McGuire, Chieh-I Chen, Tamta Makharadze, Semra Paydas, Marina Nechaeva, Frank Seebach, David M Weinreich, George D Yancopoulos, Giuseppe Gullo, Israel Lowy, Petra Rietschel

EMPOWER-Lung 1: A Phase III Trial of Cemiplimab Monotherapy for First-Line Treatment of NSCLC with PD-L1 ≥50%

Overall Survival



Progression-Free Survival

Sezer A et al. *Lancet* 2021;397:592-604.

FDA-Approved Immunotherapy Combination Options for First-Line Therapy

Combination regimen	FDA approval	Pivotal study	Histologic type	HR (OS)
Pembrolizumab (q3wk or q6wk) + platinum and pemetrexed[1]	8/20/18	KEYNOTE-189	Nonsquamous	0.56
Pembrolizumab (q3wk or q6wk) + carboplatin, paclitaxel or *nab* paclitaxel[2]	10/30/18	KEYNOTE-407	Squamous	0.71
Atezolizumab (q3wk) + carboplatin and paclitaxel and bevacizumab[3]	12/6/18	IMpower150	Nonsquamous	0.80
Atezolizumab (q3wk) + carboplatin and *nab* paclitaxel[4]	12/3/19	IMpower130	Nonsquamous	0.79
Nivolumab (q2wk) + ipilimumab[5]	5/15/20	CheckMate 227	PD-L1 TPS ≥1, EGFR and/or ALK wt	0.76
Nivolumab (q3wk) + ipilimumab and chemotherapy[6]	5/26/20	CheckMate 9LA	EGFR and/or ALK wt	0.72

[1] Rodriguez-Abreu. *Ann Oncol* 2021. [2] Paz-Ares. *J Thorac Oncol* 2020. [3] Socinski *J Thorac Oncol* 2021. [4] West. *Lancet Oncol* 2019.
[5] Paz-Ares. ASCO 2021;Abstract 9016. [6] Reck. ASCO 2021;Abstract 9000.

2021 ESMO congress **Abstract LBA51**

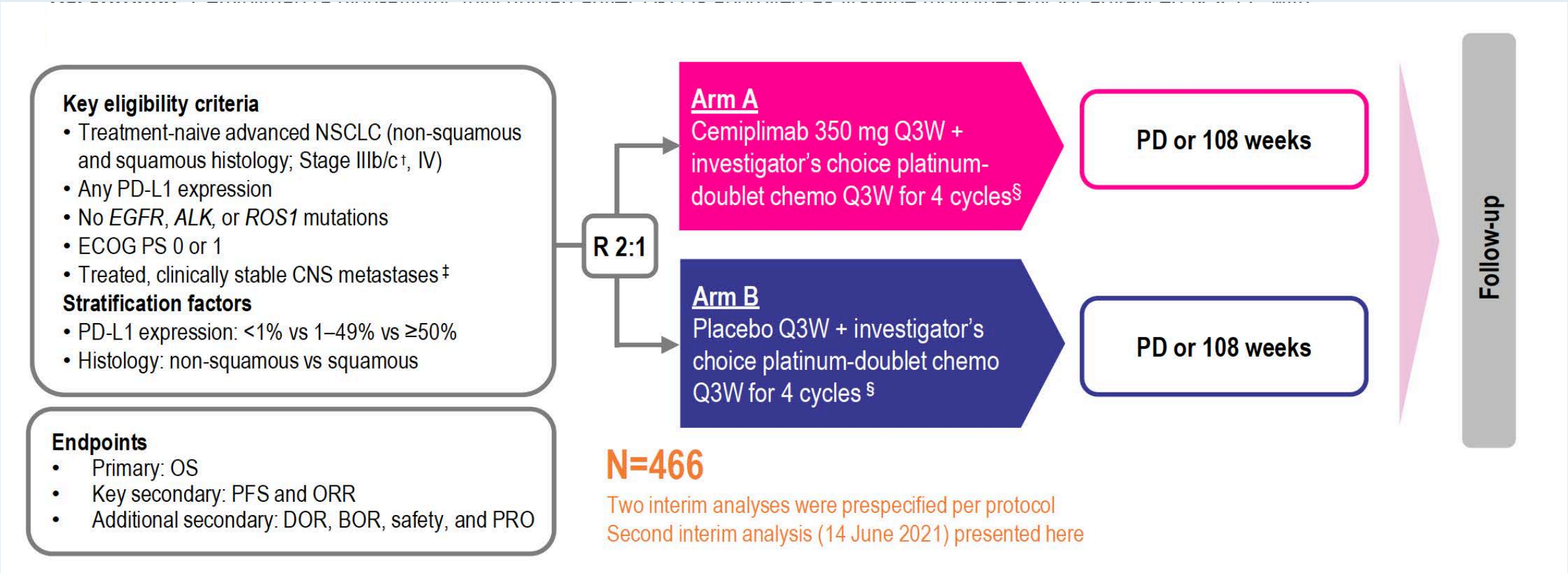
EMPOWER

EMPOWER-Lung 3: Cemiplimab in Combination With Platinum-Doublet Chemotherapy (Chemo) for First-Line (1L) Treatment of Advanced Non-Small Cell Lung Cancer (NSCLC)

Miranda Gogishvili,[1] Tamar Melkadze,[2] Tamta Makharadze,[3] David Giorgadze,[4] Mikhail Dvorkin,[5] Konstantin Penkov,[6] Konstantin Laktionov,[7] Gia Nemsadze,[8] Marina Nechaeva,[9] Irina Rozhkova,[10] Ewa Kalinka,[11] Christian Gessner,[12] Brizio Moreno-Jaime,[13] Rodolfo Passalacqua,[14] Siyu Li,[15] Kristina McGuire,[15] Ruben G. W. Quek,[15] Bo Gao,[15] Frank Seebach,[15] David M. Weinreich,[15] George D. Yancopoulos,[15] Israel Lowy,[15] Giuseppe Gullo,[15] Petra Rietschel[15]

[1]High Technology Medical Centre, University Clinic Ltd, Tbilisi, Georgia; [2]Georgia Medical Institute, Jonesboro, Georgia, USA; [3]LTD High Technology Hospital Med Center, Batumi, Georgia; [4]David Tvildiani Medical University, Tbilisi, Georgia; [5]State Budgetary Healthcare Institution of Omsk Region, Omsk, Russia; [6]Private Medical Institution Euromedservice, St Petersburg, Russia; [7]Federal State Budgetary Institution "N.N. Blokhin National Medical Research Center of Oncology" of the Ministry of Health of the Russian Federation (N.N. Blokhin NMRCO), Moscow, Russia; [8]The Institute of Clinical Oncology, Tbilisi, Georgia; [9]Chelyabinsk Regional Clinical Oncology Center, Chelyabinsk, Chelyabinsk Oblast, Russia; [10]State Budgetary Healthcare Institution of Kaluga Region, Kaluga, Russia; [11]Polish Mother's Memorial Hospital Research Institute, Łódź, Poland; [12]POIS Leipzig GbR Steffi Geßner, Leipzig, Germany; [13] Hospital Regional ISSSTE, León, Mexico; [14]Istituti Ospitalieri Di Cremona, Cremona, Italy; [15]Regeneron Pharmaceuticals, Inc, Tarrytown, New York

EMPOWER-Lung 3: First-Line Cemiplimab with Platinum-Doublet Chemotherapy for Advanced NSCLC



Gogishvili M et al. ESMO 2021;Abstract LBA51.

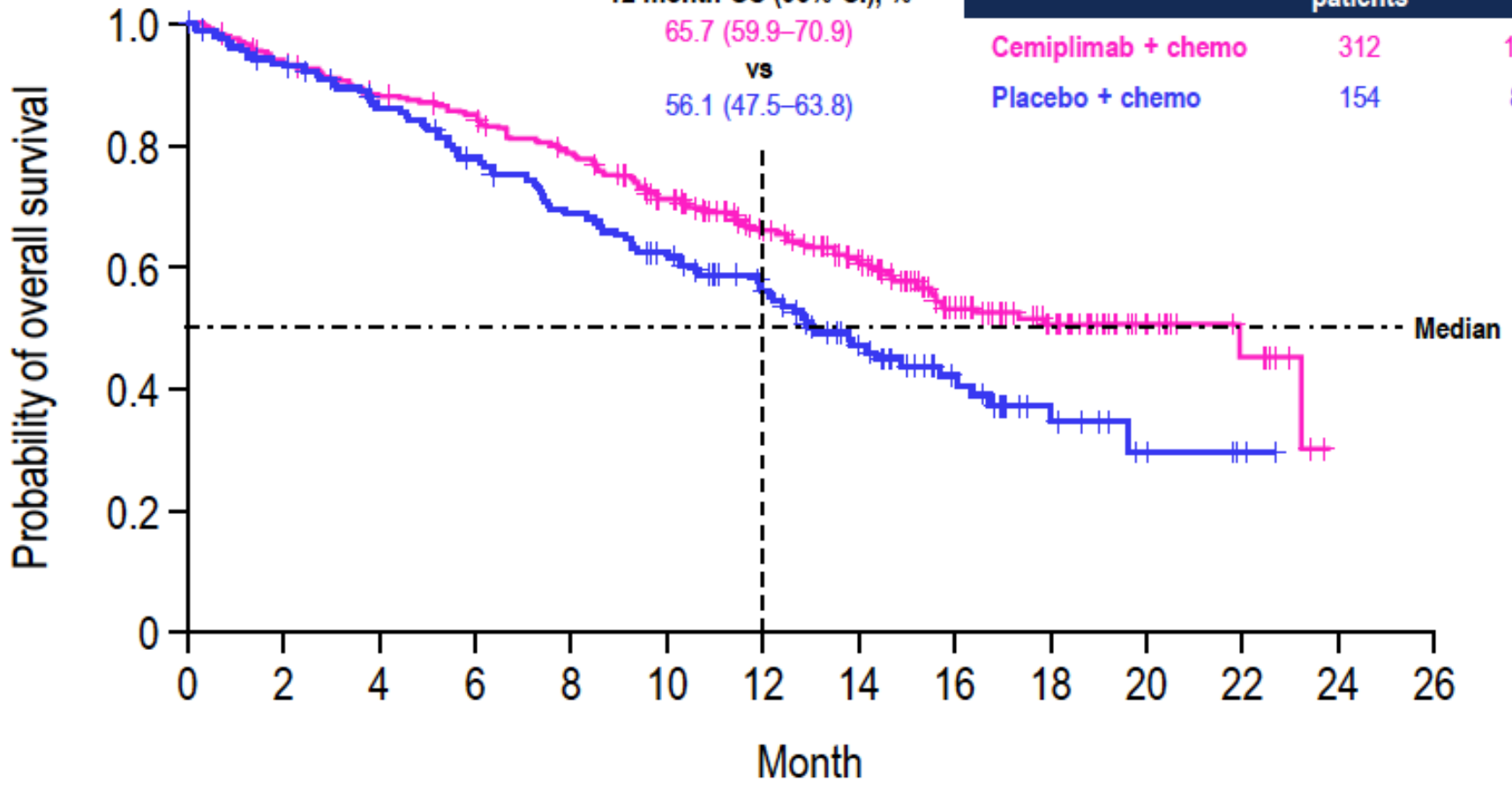
RTP RESEARCH TO PRACTICE

EMPOWER-Lung 3: First-Line Cemiplimab with Platinum-Doublet Chemotherapy for Advanced NSCLC

Median duration of follow-up (range): 16.4 (8.5–24.0) months

	No. of patients	No. of events, n (%)	OS, median (95% CI), months
Cemiplimab + chemo	312	132 (42.3)	21.9 (15.5–NE)
Placebo + chemo	154	82 (53.2)	13.0 (11.9–16.1)

HR (95% CI) = 0.71 (0.53–0.93); *P*=0.014



Gogishvili M et al. ESMO 2021;Abstract LBA51.

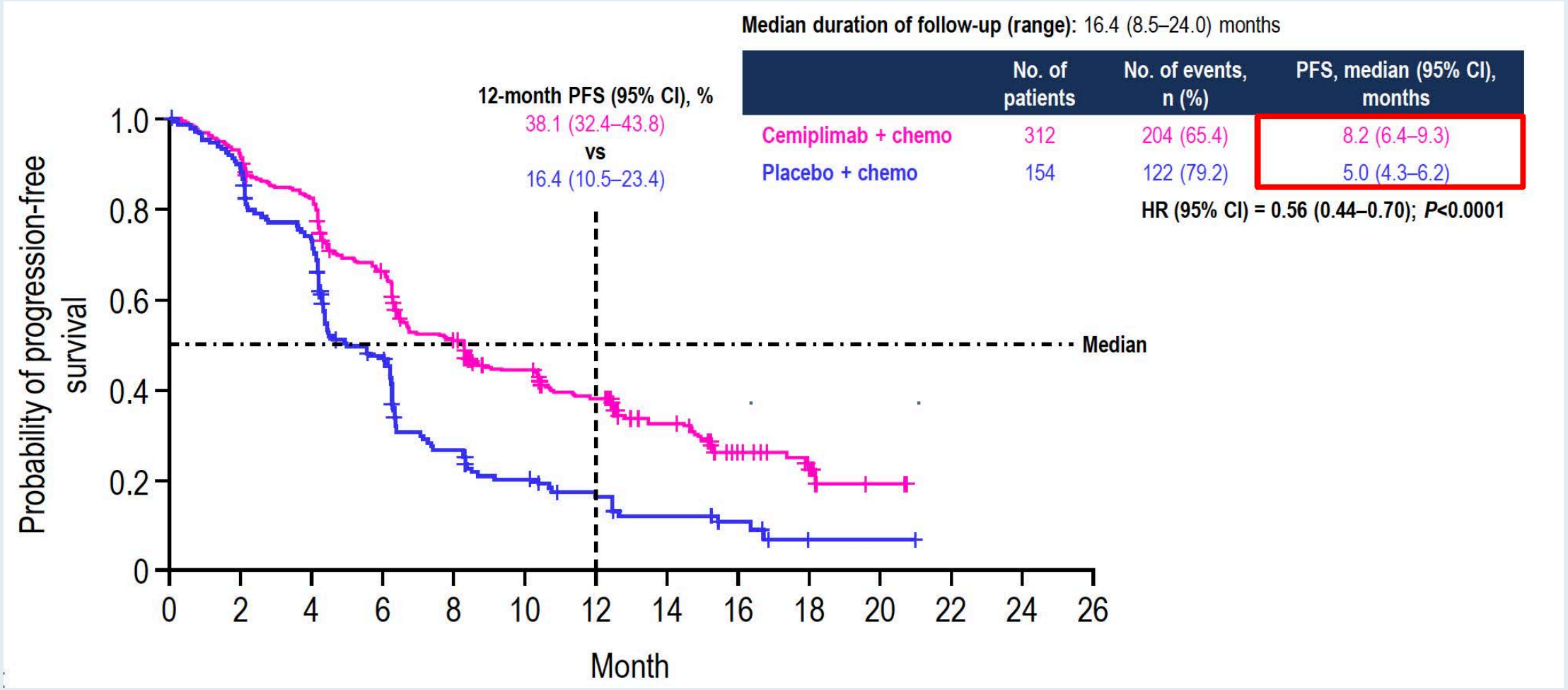
RTP RESEARCH TO PRACTICE

EMPOWER-Lung 3: Progression-Free Survival

Median duration of follow-up (range): 16.4 (8.5–24.0) months

	No. of patients	No. of events, n (%)	PFS, median (95% CI), months
Cemiplimab + chemo	312	204 (65.4)	8.2 (6.4–9.3)
Placebo + chemo	154	122 (79.2)	5.0 (4.3–6.2)

HR (95% CI) = 0.56 (0.44–0.70); *P*<0.0001



Gogishvili M et al. ESMO 2021;Abstract LBA51.

RTP RESEARCH TO PRACTICE

Durvalumab ± Tremelimumab + Chemotherapy as First-Line Treatment for mNSCLC: Results from the Phase 3 POSEIDON Study

Melissa L Johnson,[1] Byoung Chul Cho,[2] Alexander Luft,[3] Jorge Alatorre-Alexander,[4] Sarayut Lucien Geater,[5] Konstantin Laktionov,[6] Aleksandr Vasiliev,[7] Dmytro Trukhin,[8] Sang-We Kim,[9] Grygorii Ursol,[10] Maen Hussein,[11] Farah Louise Lim,[12] Cheng-Ta Yang,[13] Luiz Henrique Araujo,[14] Haruhiro Saito,[15] Niels Reinmuth,[16] Xiaojin Shi,[17] Lynne Poole,[18] Solange Peters,[19] Edward B Garon,[20] Tony Mok[21]

[1]Sarah Cannon Research Institute, Tennessee Oncology, PLLCC, Nashville, TN, USA; [2]Yonsei Cancer Center, Seoul, Korea; [3]Leningrad Regional Clinical Hospital, St Petersburg, Russia; [4]Health Pharma Professional Research, Mexico City, Mexico; [5]Prince of Songkla University, Songkhla, Thailand; [6]Federal State Budgetary Institution "N.N. Blokhin National Medical Research Center of Oncology" of the Ministry of Health of the Russian Federation (N.N. Blokhin NMRCO), Moscow, Russia; [7]"Private Health Institution "Clinical Hospital" RZD-Medicine", St Petersburg, Russia; [8]Odessa Regional Oncological Dispensary, Odessa, Ukraine; [9]Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; [10]Acinus, Kropyvnytskyi, Ukraine; [11]Florida Cancer Specialists – Sarah Cannon Research Institute, Leesburg, FL, USA; [12]Queen Mary University of London, London, United Kingdom; [13]Chang Gung Memorial Hospital, Taoyuan City, Taiwan; [14]Instituto Nacional de Cancer-INCA, Rio de Janeiro, Brazil; [15]Kanagawa Cancer Center, Yokohama, Japan; [16]Asklepios Lung Clinic, Munich-Gauting, Germany; [17]AstraZeneca, Gaithersburg, MD, USA; [18]AstraZeneca, Cambridge, UK; [19]Centre Hospitalier Universitaire Vaudois, Lausanne University, Lausanne, Switzerland; [20]David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; [21]Chinese University of Hong Kong, Hong Kong, China

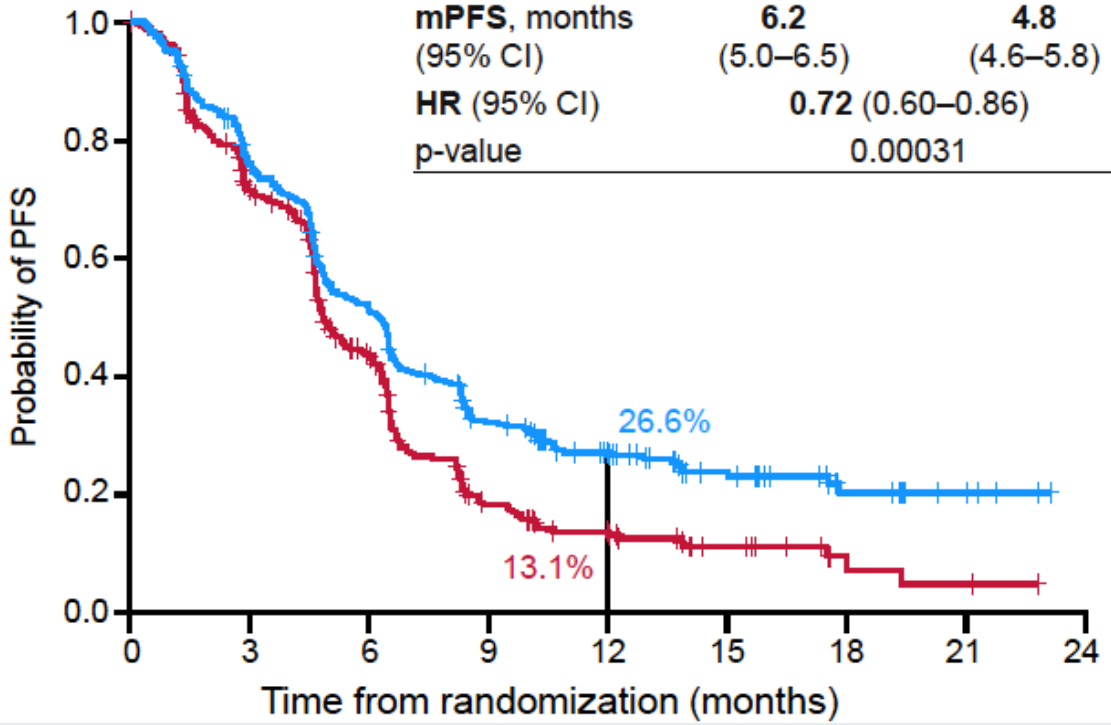
IASLC 2021 World Conference on Lung Cancer
SEPTEMBER 8 - 14, 2021 I WORLDWIDE VIRTUAL EVENT

Abstract PL02.01

POSEIDON: First-Line Durvalumab with Tremelimumab and Chemotherapy for Advanced NSCLC

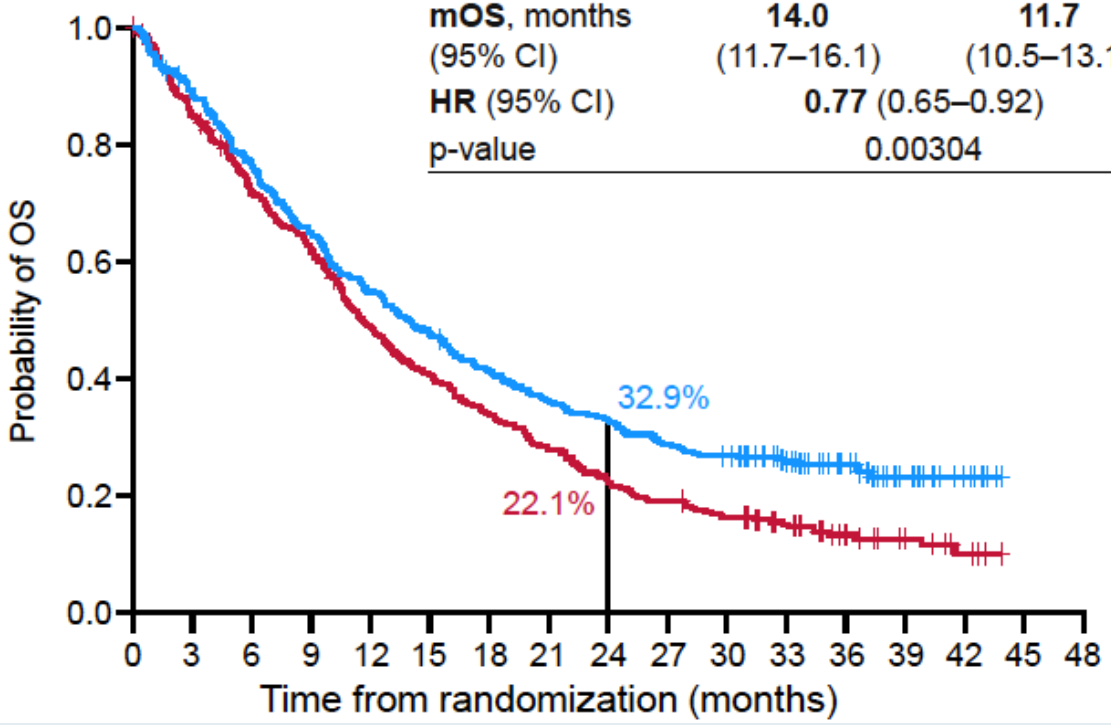
PFS

	D+T+CT	CT
Events, n/N (%)	238/338 (70.4)	258/337 (76.6)
mPFS, months (95% CI)	**6.2** (5.0–6.5)	**4.8** (4.6–5.8)
HR (95% CI)	**0.72** (0.60–0.86)	
p-value	0.00031	



OS

	D+T+CT	CT
Events, n/N (%)	251/338 (74.3)	285/337 (84.6)
mOS, months (95% CI)	**14.0** (11.7–16.1)	**11.7** (10.5–13.1)
HR (95% CI)	**0.77** (0.65–0.92)	
p-value	0.00304	



Johnson ML et al. WCLC 2021;Abstract PL02.01

RTP RESEARCH TO PRACTICE

Background: TIGIT Pathway

- TIGIT (T cell immunoreceptor with Ig and ITIM domains) is a novel inhibitory receptor expressed on multiple immune cells, including T cells and NK cells[1-3]
- TIGIT inhibits T cells and NK cells by binding to its ligand PVR on tumor cells and antigen-presenting cells (APCs)
- TIGIT expression strongly correlates with PD-1 expression, especially in tumor-infiltrating T cells in lung cancer
- *Hypothesis*: Anti-TIGIT antibodies, which prevent TIGIT from binding to its ligand, could restore the anti-tumor response and could complement the activity of anti-PD-L1/PD-1 antibodies

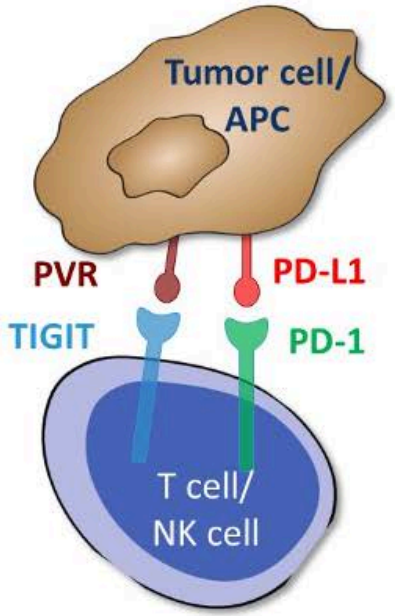


Figure adapted from Manieri et al. *Trends Immunology* 2017

NK, natural killer; PVR, poliovirus receptor

[1] Manieri et al. *Trends Immunology* 2017; [2] Rotte et al. *Annals of Oncology* 2018; [3] Yu et al. *Nature Immunology* 2009

Rodriguez-Abreu D et al. ASCO 2020;Abstract 9503.

Background: Tiragolumab, an Anti-TIGIT Antibody

- Tiragolumab is a fully human IgG1/kappa anti-TIGIT monoclonal antibody with an intact Fc region that blocks the binding of TIGIT to its receptor PVR

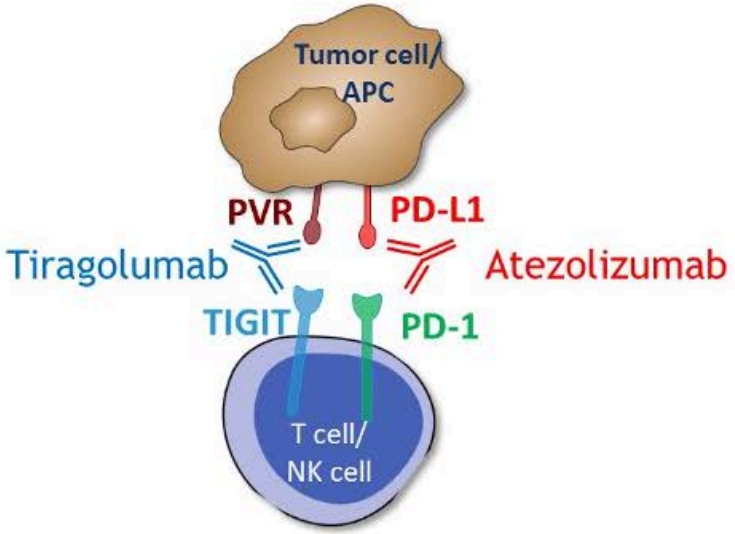
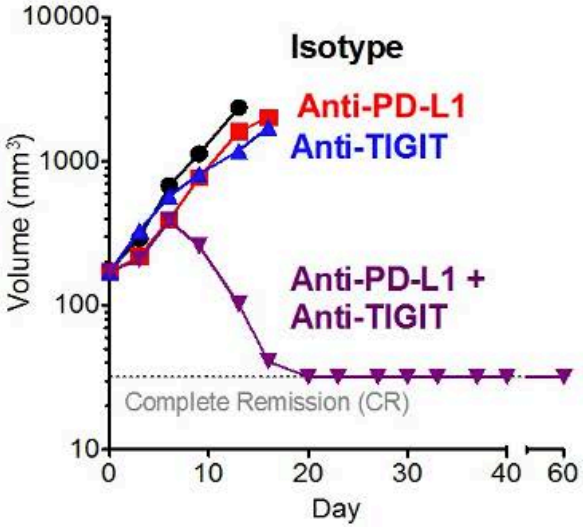


Figure adapted from Manieri et al. *Trends Immunology* 2017

- In preclinical models, combination treatment with anti-TIGIT and anti-PD-L1 antibodies synergistically improves tumor control and prolongs survival in mice[1]



[1] Johnston et al. *Cancer Cell* 2014

Rodriguez-Abreu D et al. ASCO 2020;Abstract 9503.

ESMO IMMUNO-ONCOLOGY 2021

Onsite and Online Congress

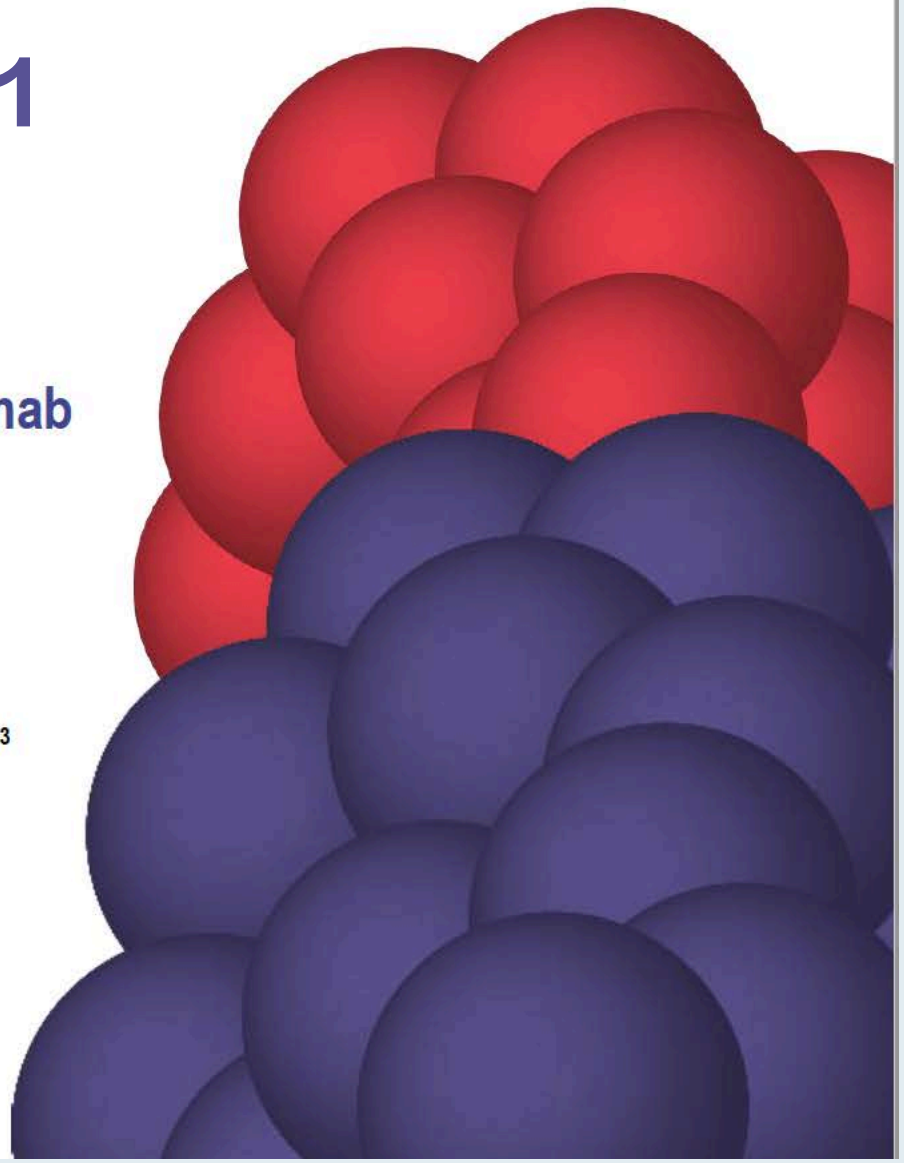
Updated analysis and patient-reported outcomes from CITYSCAPE: a randomised, double-blind, Phase II study of the anti-TIGIT antibody tiragolumab + atezolizumab vs placebo + atezolizumab as first-line treatment for PD-L1+ NSCLC

Byoung Chul Cho,[1] Delvys Rodriguez-Abreu,[2] Maen Hussein,[3] Manuel Cobo,[4] Anjan Patel,[5] Nevena Secen,[6] Gregory Gerstner,[7] Dong-Wan Kim,[8] Yun-Gyoo Lee,[9] Wu-Chou Su,[10] Elizabeth Huang,[11] Namrata Patil,[12] Meilin Huang,[12] Zoe Zhang,[12] Xiaohui Wen,[12] Diana Mendus,[12] Tien Hoang,[12] Raymond Meng,[12] Melissa Johnson[13]

1. Severance Hospital, Yonsei University Health System, Seoul, Korea; 2. Hospital Universitario Gran Canaria, Las Palmas, Spain; 3. Florida Cancer Specialists, Leesburg, Florida, USA; 4. Hospital Regional Universitario de Malaga, Malaga, Spain; 5. Florida Cancer Specialists, Sarasota, Florida, USA; 6. Institute of Lung Diseases Vojvodina, Sremska Kamenica, Serbia; 7. Illinois Cancer Care, Peoria, Illinois, USA; 8. Seoul National University College of Medicine and Seoul National University Hospital, Seoul, South Korea; 9. Sungkyunkwan University School of Medicine, Kangbuk Samsung Hospital Seoul, South Korea; 10. National Cheng Kung University Hospital, Tainan City, Taiwan; 11. Roche Products Ltd., Welwyn Garden City, UK; 12. Genentech, Inc., South San Francisco, USA; 13. Sarah Cannon Research Institute and Tennessee Onc., PLLC Nashville, Tennessee, USA

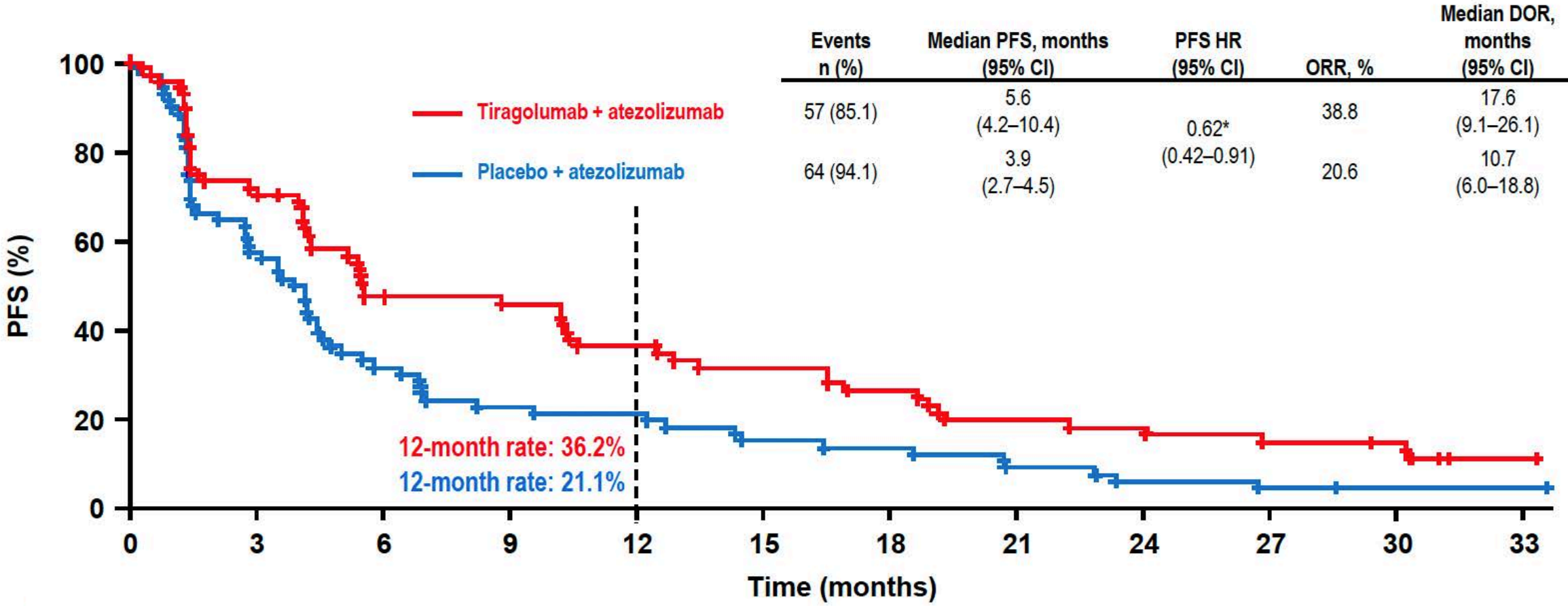
ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Abstract LBA2



RTP RESEARCH TO PRACTICE

CITYSCAPE: Investigator-Assessed PFS (ITT)



	Events n (%)	Median PFS, months (95% CI)	PFS HR (95% CI)	ORR, %	Median DOR, months (95% CI)
Tiragolumab + atezolizumab	57 (85.1)	5.6 (4.2–10.4)	0.62* (0.42–0.91)	38.8	17.6 (9.1–26.1)
Placebo + atezolizumab	64 (94.1)	3.9 (2.7–4.5)		20.6	10.7 (6.0–18.8)

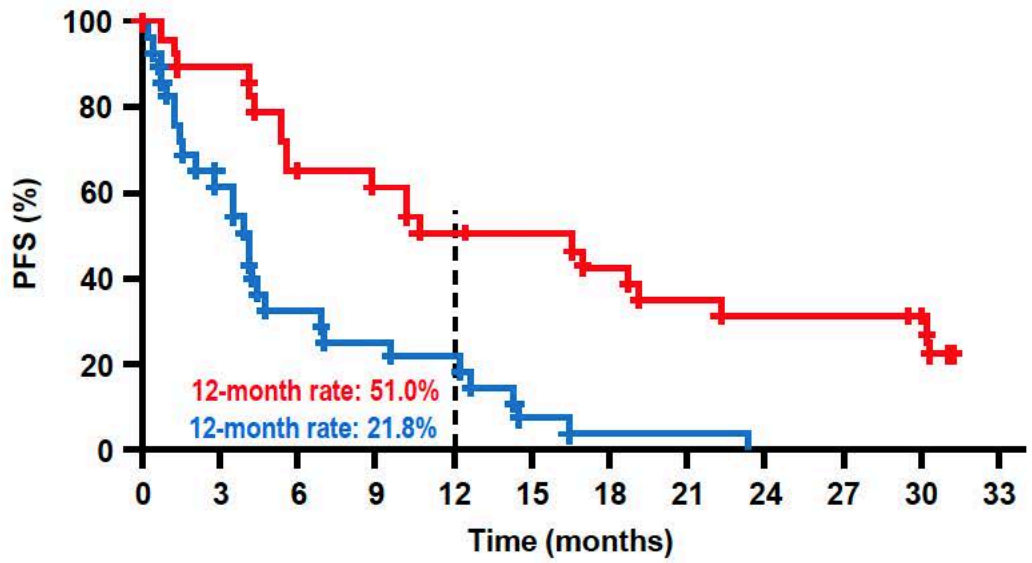
Cho BC et al. ESMO Immuno-Oncology 2021;Abstract LBA2.

RTP RESEARCH TO PRACTICE

CITYSCAPE: PFS by PD-L1 Subgroup

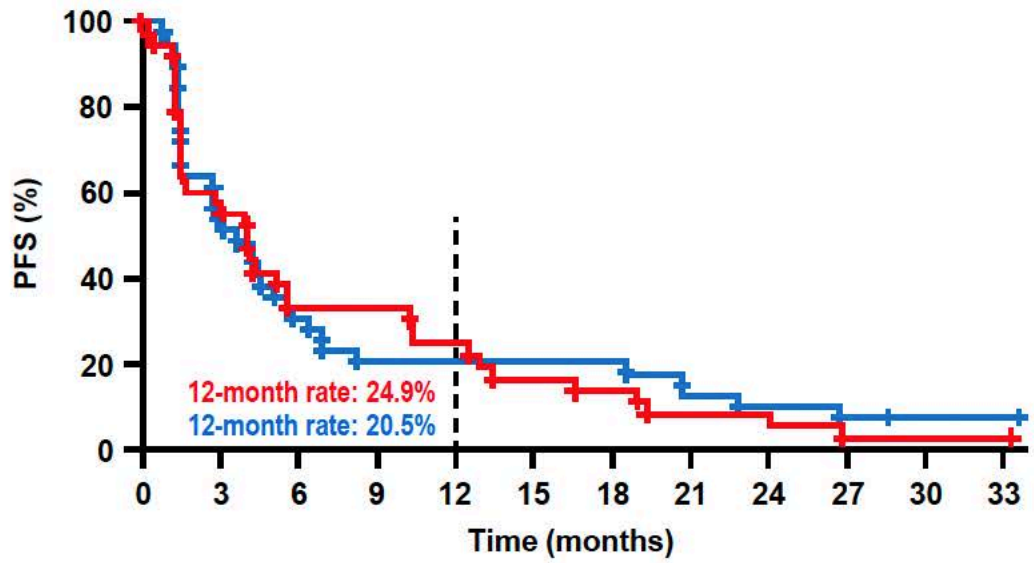
PD-L1 TPS ≥50% (n=58)

	Events n (%)	Median PFS, months (95% CI)	PFS HR (95% CI)	ORR, %	Median DOR, months (95% CI)
Tira + atezo	21 (72.4)	16.6 (5.5–22.3)	0.29* (0.15–0.53)	69.0	15.7 (9.1–NE)
Placebo + atezo	28 (96.6)	4.1 (2.1–6.8)		24.1	8.2 (5.6–10.4)



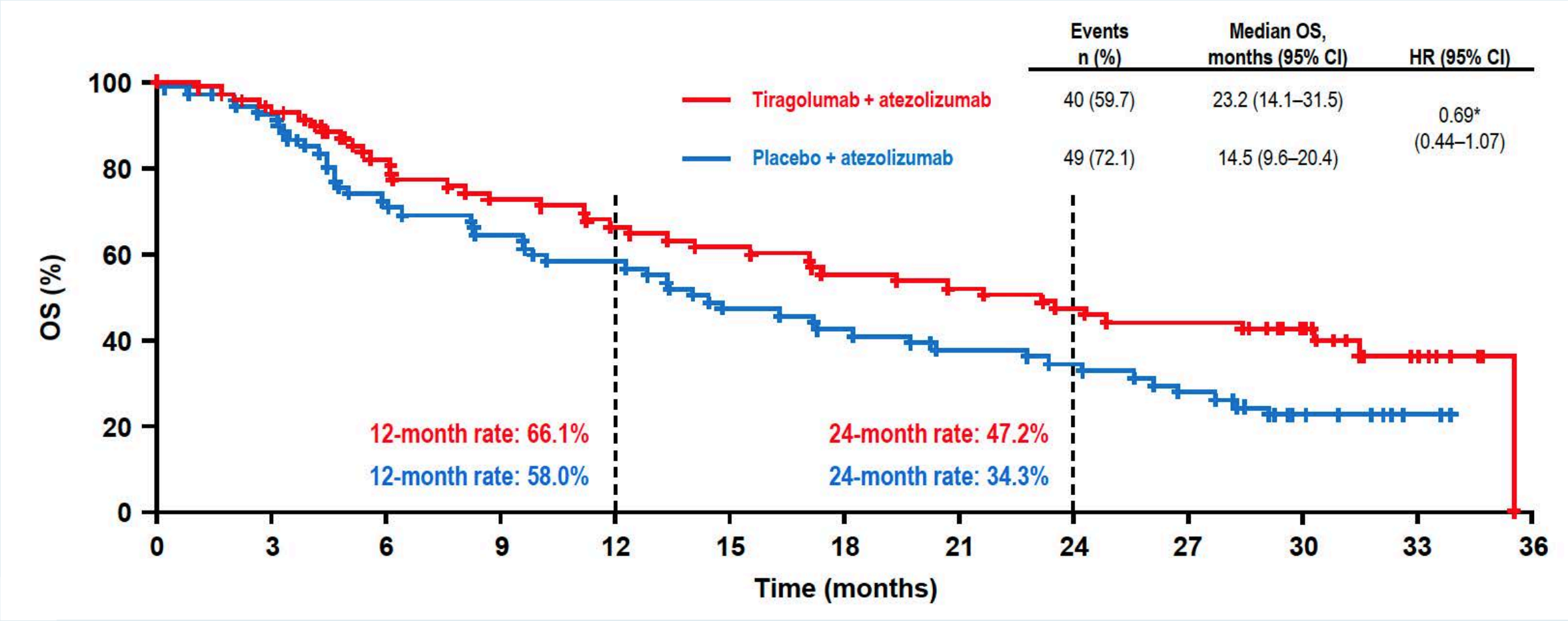
PD-L1 TPS 1–49% (n=77)

	Events n (%)	Median PFS, months (95% CI)	PFS HR (95% CI)	ORR, %	Median DOR, months (95% CI)
Tira + atezo	36 (94.7)	4.0 (1.6–5.6)	1.07* (0.67–1.71)	15.8	17.8 (8.3–24.2)
Placebo + atezo	36 (92.3)	3.6 (1.4–5.5)		17.9	18.8 (15.9–22.8)



Cho BC et al. ESMO Immuno-Oncology 2021;Abstract LBA2.

CITYSCAPE: Investigator-Assessed OS (ITT)

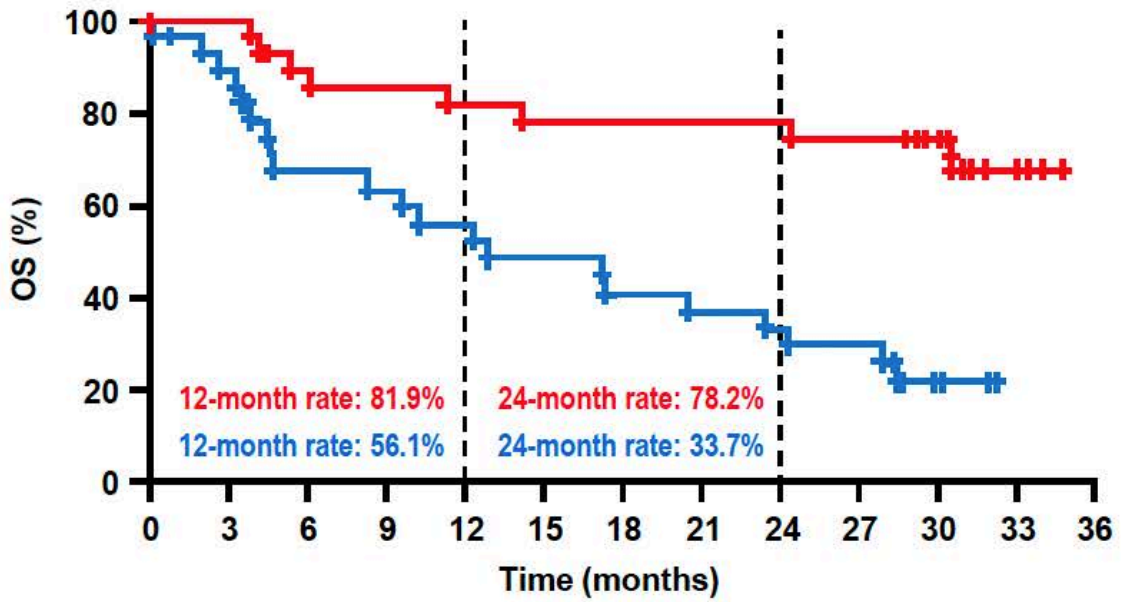


Cho BC et al. ESMO Immuno-Oncology 2021;Abstract LBA2.

CITYSCAPE: OS by PD-L1 Subgroup

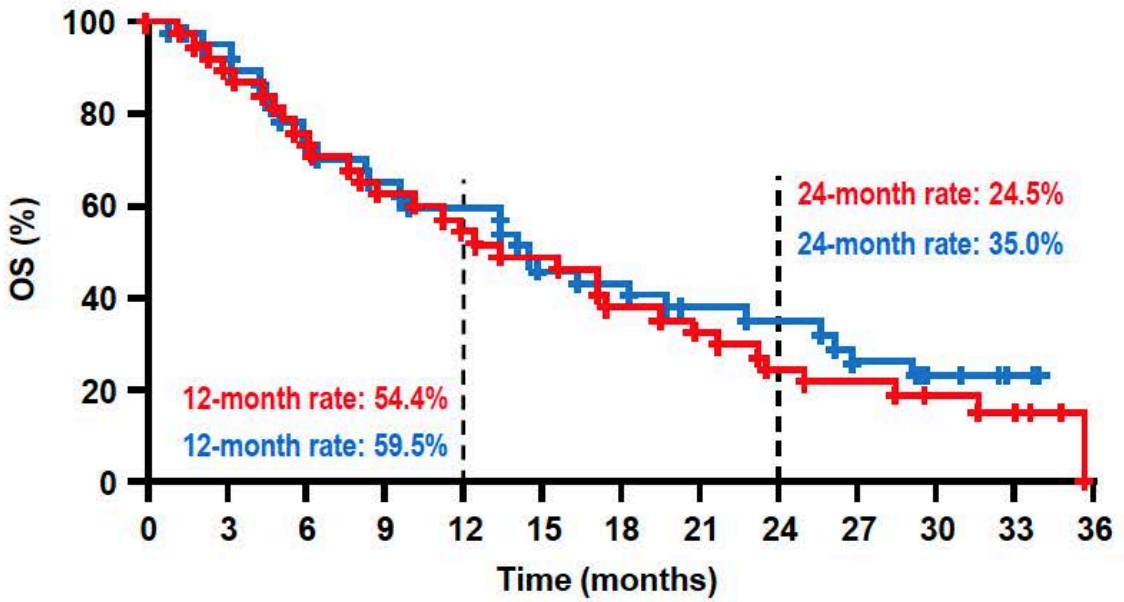
PD-L1 TPS ≥50% (n=58)

	Events n (%)	Median OS, months (95% CI)	HR (95% CI)
Tira + atezo	8 (27.6)	NE (30.3–NE)	0.23* (0.10–0.53)
Placebo + atezo	21 (72.4)	12.8 (4.7–24.2)	



PD-L1 TPS 1–49% (n=77)

	Events n (%)	Median OS, months (95% CI)	HR (95% CI)
Tira + atezo	32 (84.2)	13.3 (8.0–20.7)	1.16* (0.70–1.94)
Placebo + atezo	28 (71.8)	14.5 (8.3–25.6)	



Cho BC et al. ESMO Immuno-Oncology 2021;Abstract LBA2.

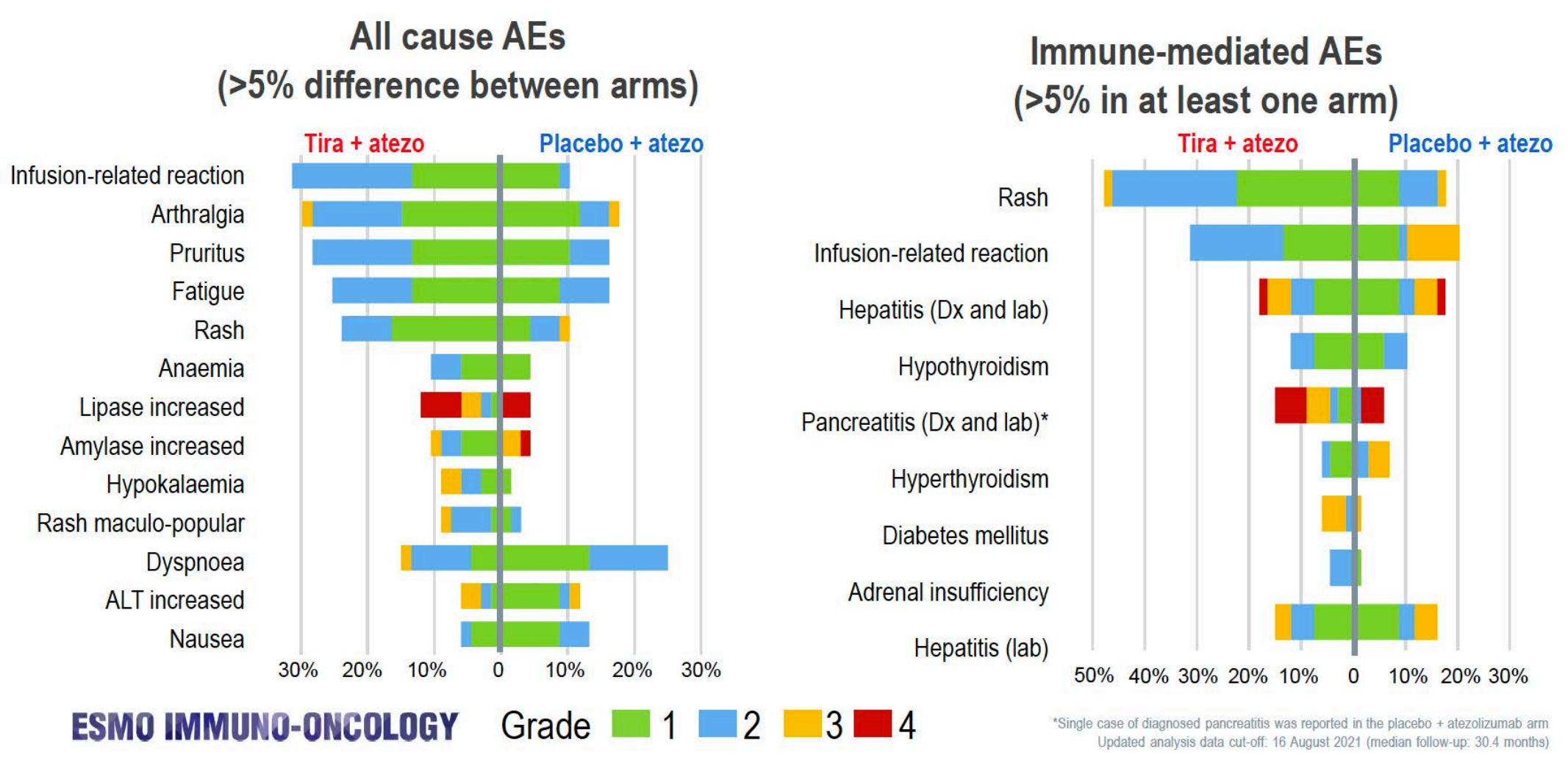
RTP RESEARCH TO PRACTICE

CITYSCAPE: Safety Summary

	Tiragolumab + atezolizumab (n=67)	Placebo + atezolizumab (n=68)
Median treatment duration, months (min–max)	4.99 (0–34.5)	2.81 (0–30.3)
Any-cause AEs, n (%)	66 (98.5)	66 (97.1)
Grade 3–4 AEs	35 (52.2)	27 (39.7)
Grade 5	3 (4.5)	7 (10.3)
Serious AEs	35 (52.2)	28 (41.2)
Treatment-related AEs, n (%)	55 (82.1)	48 (70.6)
Grade 3–4 AEs	15 (22.4)	17 (25.0)
Grade 5*	2 (3.0)	0
Serious AEs	14 (20.9)	12 (17.6)
Immune-mediated AEs, n (%)	51 (76.1)	32 (47.1)
Grade 3–4	13 (19.4)	11 (16.2)
AEs leading to dose modification/interruption, n (%)	33 (49.3)	24 (35.3)
AEs leading to treatment withdrawal, n (%)	10 (14.9)	9 (13.2)

Cho BC et al. ESMO Immuno-Oncology 2021;Abstract LBA2.

CITYSCAPE: Incidence of Adverse Events



Cho BC et al. ESMO Immuno-Oncology 2021;Abstract LBA2.

TROPION-PanTumor01: Updated Results From the NSCLC Cohort of the Phase 1 Study of Datopotamab Deruxtecan in Solid Tumors

Edward B. Garon, MD, MS

David Geffen School of Medicine at UCLA
Los Angeles, CA, USA

Edward B. Garon,[1] Melissa Johnson,[2] Aaron E. Lisberg,[1] Alexander Spira,[3] Noboru Yamamoto,[4] Rebecca S. Heist,[5] Jacob M. Sands,[6] Kiyotaka Yoh,[7] Funda Meric-Bernstam,[8] Satoru Kitazono,[9] Jonathan Greenberg,[10] Fumiaki Kobayashi,[11] Ferdinand Guevara,[10] Yui Kawasaki,[11] Toshio Shimizu[4]

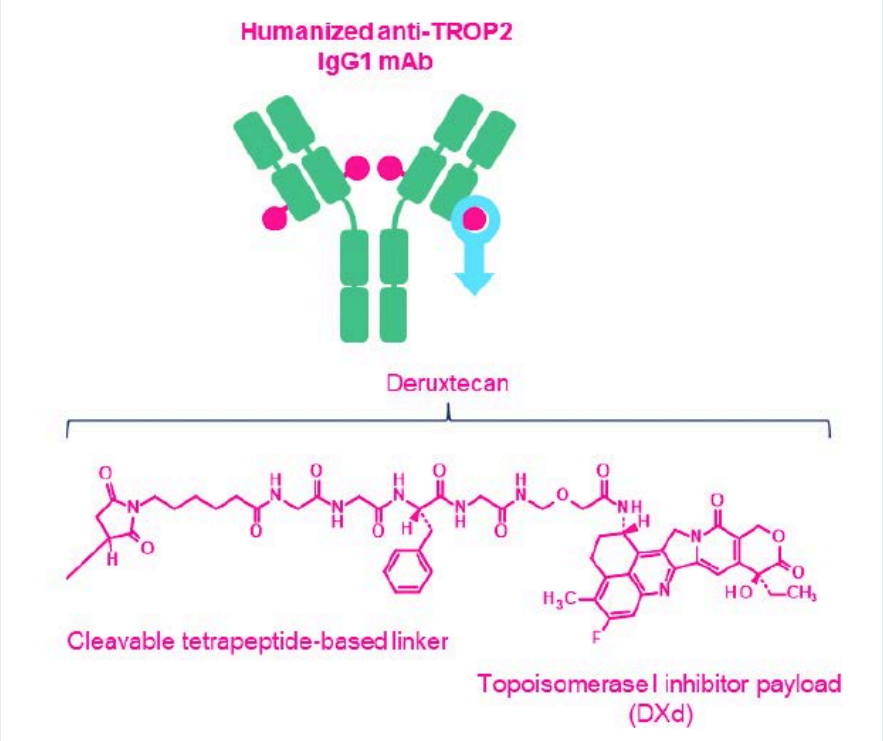
[1]David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; [2]Sarah Cannon Research Institute, Tennessee Oncology, PLLC, OneOncology, Nashville, TN, USA; [3]Virginia Cancer Specialists and US Oncology Research, Fairfax, VA, USA; [4]National Cancer Center Hospital, Tokyo, Japan; [5]Massachusetts General Hospital, Boston, MA, USA; [6]Dana-Farber Cancer Institute, Boston, MA, USA; [7]National Cancer Center Hospital East, Chiba, Japan; [8]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [9]The Cancer Institute Hospital of JFCR, Tokyo, Japan; [10]Daiichi Sankyo, Inc, Basking Ridge, NJ, USA; [11]Daiichi Sankyo Co, Ltd, Tokyo, Japan

IASLC | 2021 World Conference on Lung Cancer
SEPTEMBER 8 - 14, 2021 I WORLDWIDE VIRTUAL EVENT

Abstract MA03.02

Targeting TROP2 with Datopotamab Deruxtecan (Data-DXd)

- TROP2 is highly expressed in NSCLC, regardless of genomic mutation status, and has been associated with poor prognosis
- Data-DXd is an antibody-drug conjugate composed of a humanized anti-TROP2 monoclonal antibody conjugated to a potent topoisomerase I inhibitor payload via a stable tetrapeptide-based cleaver linker



Garon EB et al. 2021 WCLC;Abstract MA03.02.

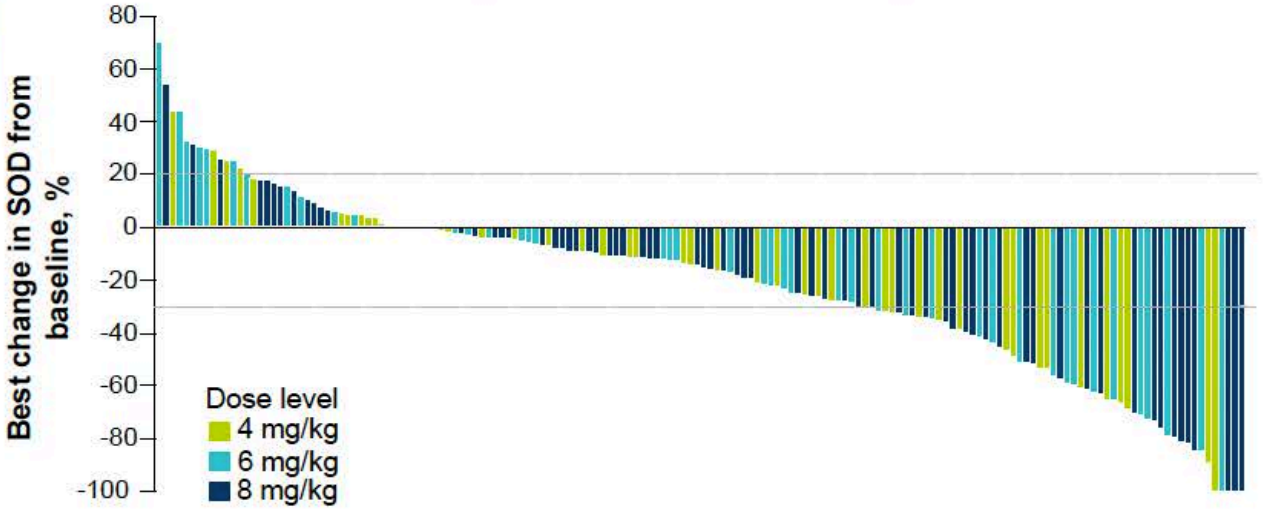
TROPION-PanTumor01: Antitumor Activity of Data-DXd

Best Overall Response (BICR)

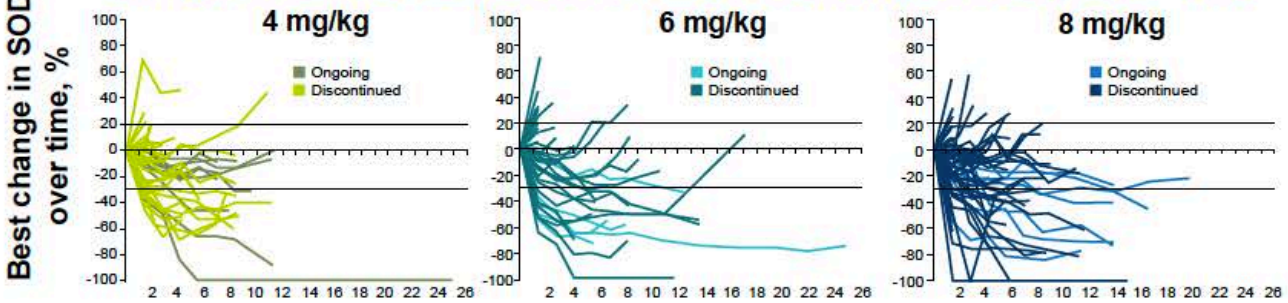
Patients[a]	Dato-DXd dose		
	4 mg/kg (n=50)	6 mg/kg (n=50)	8 mg/kg (n=80)
ORR, n (%)[b]	12 (24)	14 (28)	19 (24)
CR, n (%)	0	0	1 (1)
PR, n (%)[b]	12 (24)	14 (28)	18 (23)
SD, n (%)	25 (50)	20 (40)	42 (53)
Non-CR/PD, n (%)	1 (2)	2 (4)	2 (3)
PD, n (%)	7 (14)	10 (20)	8 (10)
NE, n (%)	5 (10)	5 (10)	9 (11)
DOR, median (95% CI), mo	NE (2.8-NE)	10.5 (5.6-NE)	9.4 (5.8-NE)

- Antitumor activity was observed at 4-, 6-, and 8-mg/kg doses of Dato-DXd
- Most responses were durable over time, including a median duration of response of 10.5 months in the 6-mg/kg cohort

Best Change in Sum of Diameters (per BICR)



Change in Sum of Diameters of Target Lesion (per BICR) Over Time



Garon EB et al. 2021 WCLC;Abstract MA03.02.

RTP RESEARCH TO PRACTICE

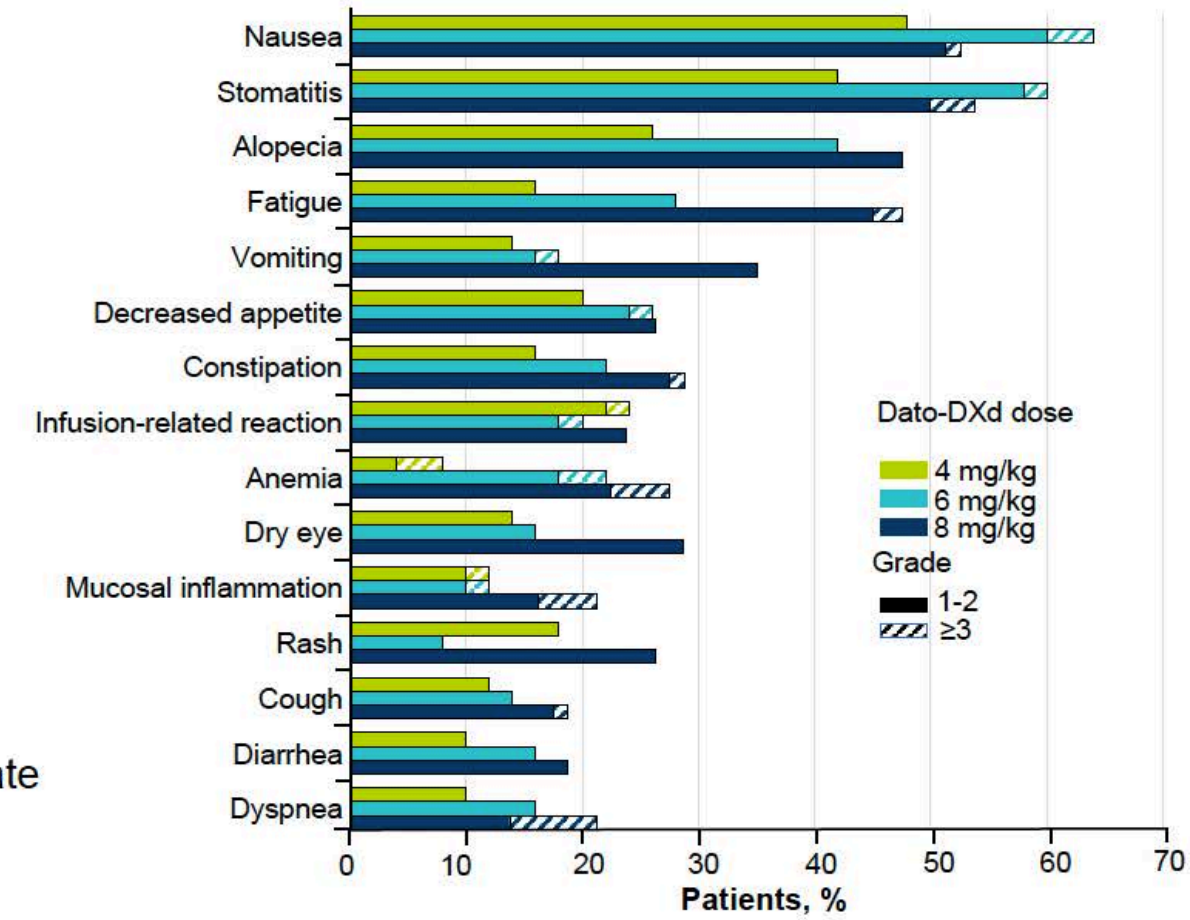
TROPION-PanTumor01: Safety and Treatment-Emergent Adverse Events

Overall Safety Summary

Patients, n (%)	Dato-DXd dose		
	4 mg/kg (n=50)	6 mg/kg (n=50)	8 mg/kg (n=80)
TEAE	49 (98)	49 (98)	80 (100)
Grade ≥3	15 (30)	27 (54)	46 (58)
Drug-related TEAE	47 (94)	41 (82)	78 (98)
Grade ≥3	7 (14)	13 (26)	28 (35)
Serious TEAE	10 (20)	24 (48)	40 (50)
Grade ≥3	10 (20)	18 (36)	37 (46)
Dose adjustments			
TEAEs associated with discontinuation	8 (16)	7 (14)	19 (24)
TEAEs associated with dose interruption	4 (8)	15 (30)	29 (36)
TEAEs associated with dose reduction	1 (2)	5 (10)	23 (29)
ILD adjudicated as drug related[a]	5 (10)	3 (6)	11 (14)
Grade ≤2	4 (8)	2 (4)	7 (9)
Grades 3-4	1 (2)	1 (2)	1 (1)
Grade 5	0	0	3 (4)

- The safety profile was manageable with mainly mild/moderate toxicity; TEAEs were primarily nonhematologic

TEAEs in ≥15% of Patients[b]



Garon EB et al. 2021 WCLC;Abstract MA03.02.

2021 ESMO congress

Abstract LBA49

Efficacy of Datopotamab Deruxtecan (Dato-DXd) in Patients With Advanced/Metastatic Non-Small Cell Lung Cancer (NSCLC) and Actionable Genomic Alterations (AGAs): Preliminary Results From the Phase 1 TROPION-PanTumor01 Study

Edward B. Garon,[1] Melissa L. Johnson,[2] Aaron E. Lisberg,[1] Alexander Spira,[3] Noboru Yamamoto,[4] Rebecca S. Heist,[5] Jacob M. Sands,[6] Kiyotaka Yoh,[7] Funda Meric-Bernstam,[8] Satoru Kitazono,[9] Jonathan Greenberg,[10] Fumiaki Kobayashi,[11] Yui Kawasaki,[11] Lori Jukofsky,[10] Kota Nakamura,[10] Toshio Shimizu[4]

[1]David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; [2]Sarah Cannon Research Institute, Tennessee Oncology, PLLC/OneOncology, Nashville, TN, USA; [3]Virginia Cancer Specialists, Fairfax, VA, USA; [4]Department of Experimental Therapeutics, National Cancer Center Hospital, Tokyo, Japan; [5]Massachusetts General Hospital, Boston, MA, USA; [6]Dana-Farber Cancer Institute, Boston, MA, USA; [7]National Cancer Center Hospital East, Chiba, Japan; [8]The University of Texas, MD Anderson Cancer Center, Houston, TX, USA; [9]The Cancer Institute Hospital of JFCR, Tokyo, Japan; [10]Daiichi Sankyo, Inc, Basking Ridge, NJ, USA; [11]Daiichi Sankyo Co, Ltd, Tokyo, Japan

RTP RESEARCH TO PRACTICE

Phase I TROPION-PanTumor01 (NSCLC Cohort): Antitumor Activity of Dato-DXd in NSCLC with Actionable Genomic Alterations

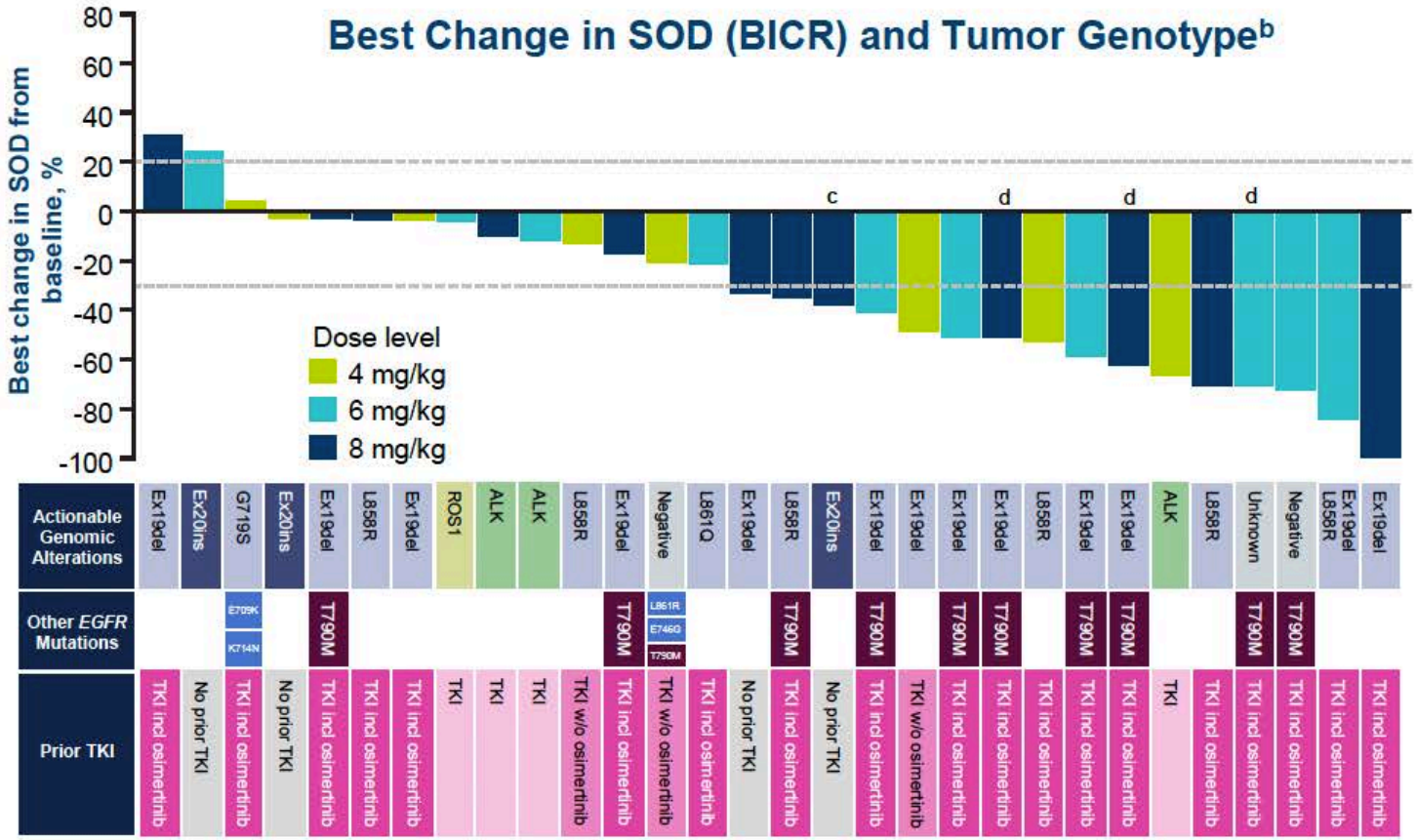
Best Overall Response (BICR)

Patients[a]	Dato-DXd n=34
ORR, n (%)	12 (35)
CR	0
PR	12 (35)
SD, n (%)	14 (41)
Non-CR/PD, n (%)	2 (6)
PD, n (%)	2 (6)
NE, n (%)	4 (12)
DOR, median (95% CI), mo	9.5 (3.3-NE)

- Clinical activity was observed in *EGFR* (Ex19del, L858R) including after osimertinib and across other AGAs

Data cutoff: April 6, 2021.

Best Change in SOD (BICR) and Tumor Genotype[b]



Garon EB et al. ESMO 2021;Abstract LBA49.

RTP RESEARCH TO PRACTICE

Agenda

Module 1: NSCLC with EGFR Mutations

Module 2: NSCLC with ALK Rearrangement

Module 3: NSCLC with RET, MET Exon 14 and HER2 Mutations

Module 4: NSCLC without Targetable Mutations

Module 5: Extensive-Stage Small Cell Lung Cancer

original reports

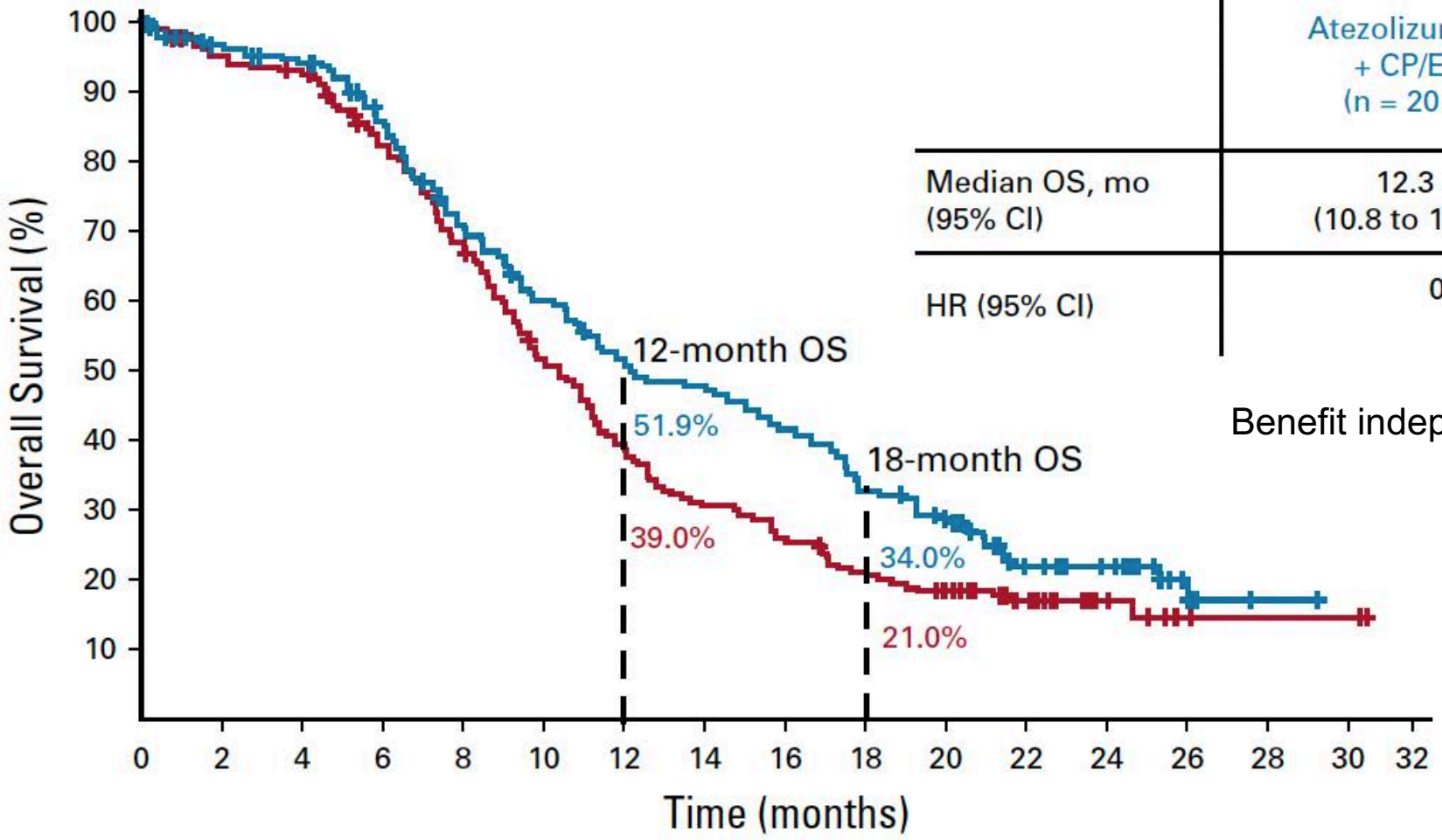
Updated Overall Survival and PD-L1 Subgroup Analysis of Patients With Extensive-Stage Small-Cell Lung Cancer Treated With Atezolizumab, Carboplatin, and Etoposide (IMpower133)

Stephen V. Liu, MD[1]; Martin Reck, MD, PhD[2]; Aaron S. Mansfield, MD[3]; Tony Mok, MD[4]; Arnaud Scherpereel, MD, PhD[5]; Niels Reinmuth, MD, PhD[6]; Marina Chiara Garassino, MD[7]; Javier De Castro Carpeno, MD[8]; Raffaele Califano, MD[9]; Makoto Nishio, MD[10]; Francisco Orlandi, MD[11]; Jorge Alatorre-Alexander, MD[12]; Ticiana Leal, MD[13]; Ying Cheng, MD[14]; Jong-Seok Lee, MD[15]; Sivuonthanh Lam, PharmD[16]; Mark McCleland, PhD[16]; Yu Deng, PhD[16]; See Phan, MD[16]; and Leora Horn, MD[17]

J Clin Oncol 2021;39(6):619-30.

IMpower133: Updated OS in Extensive-Stage Small Cell Lung Cancer Treated with First-Line Atezolizumab, Carboplatin and Etoposide

Median follow up: 22.9 mo



	Atezolizumab + CP/ET (n = 201)	Placebo + CP/ET (n = 202)
Median OS, mo (95% CI)	12.3 (10.8 to 15.8)	10.3 (9.3 to 11.3)
HR (95% CI)	0.76 (0.60 to 0.95) *P* = .0154*	

Benefit independent of PD-L1 status

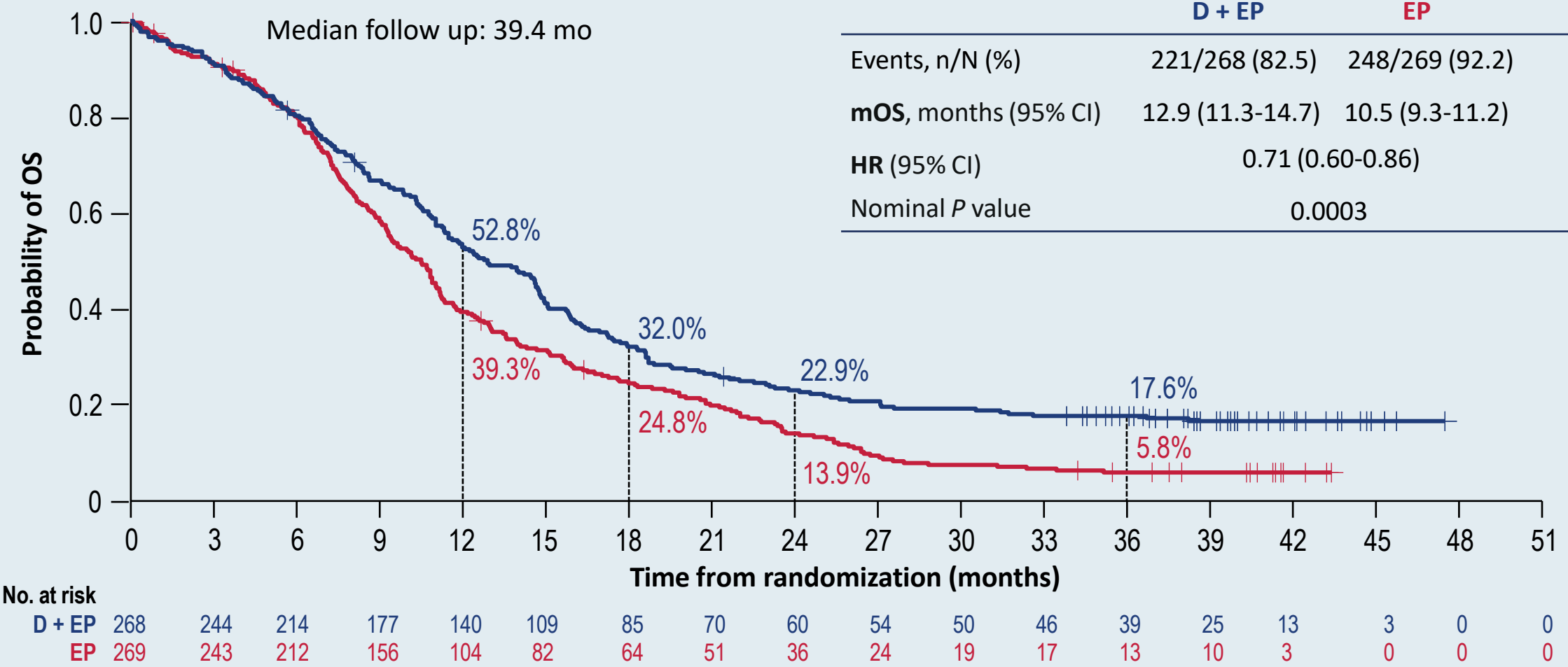
Liu SV et al. *J Clin Oncol* 2021;39(6):619-30.

Durvalumab ± Tremelimumab + Platinum-Etoposide in First-Line Extensive-Stage SCLC (ES-SCLC): 3-Year Overall Survival Update from the Phase III CASPIAN Study

Paz-Ares L et al.

ESMO 2021;Abstract LBA61.

CASPIAN: Three-Year Updated OS with First-Line Durvalumab, Platinum and Etoposide for ES-SCLC



	D + EP	EP
Events, n/N (%)	221/268 (82.5)	248/269 (92.2)
mOS, months (95% CI)	12.9 (11.3-14.7)	10.5 (9.3-11.2)
HR (95% CI)	0.71 (0.60-0.86)	
Nominal *P* value	0.0003	

Paz-Ares LG et al. ESMO 2021;Abstract LBA61.

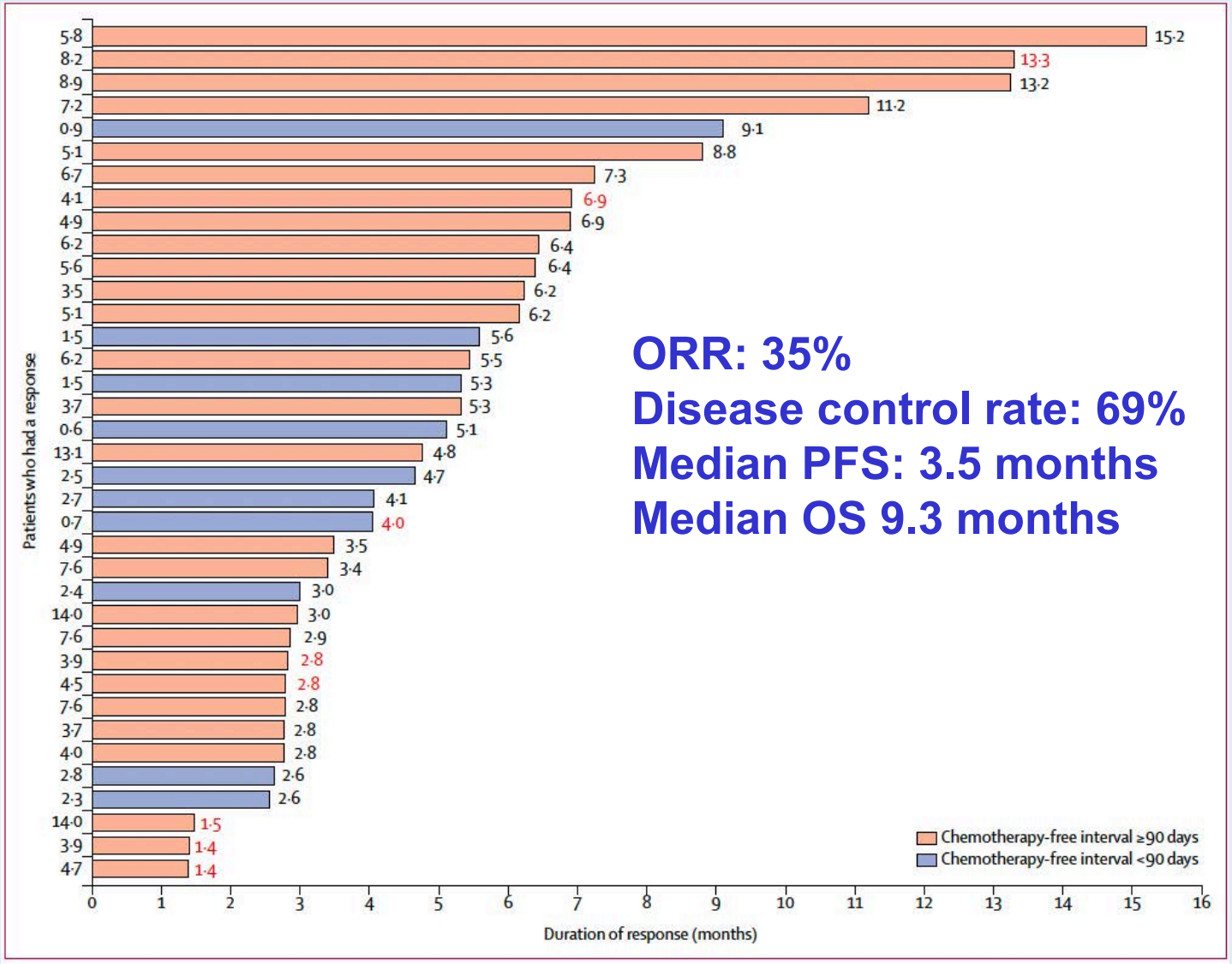
RTP RESEARCH TO PRACTICE

Lancet Oncol 2020;21:645-54.

Lurbinectedin as second-line treatment for patients with small-cell lung cancer: a single-arm, open-label, phase 2 basket trial

José Trigo, Vivek Subbiah*, Benjamin Besse, Victor Moreno, Rafael López, María Angeles Sala, Solange Peters, Santiago Ponce, Cristian Fernández, Vicente Alfaro, Javier Gómez, Carmen Kahatt, Ali Zeaiter, Khalil Zaman, Valentina Boni, Jennifer Arrondeau, Maite Martínez, Jean-Pierre Delord, Ahmad Awada, Rebecca Kristeleit, Maria Eugenia Olmedo, Luciano Wannesson, Javier Valdivia, María Jesús Rubio, Antonio Anton, John Sarantopoulos, Sant P Chawla, Joaquín Mosquera-Martinez, Manolo D'Arcangelo, Armando Santoro, Victor M Villalobos, Jacob Sands, Luis Paz-Ares*

Response, Survival and Common AEs in the Pivotal Phase II Study of Lurbinectedin for Patients with SCLC After One Line of Chemotherapy



Common treatment-related adverse events		
	Grade 1-2	Grade 3-4
Anemia	87%	9%
Leukopenia	50%	29%
Neutropenia	26%	46%
Thrombocytopenia	37%	7%

Trigo J et al. *Lancet Oncol* 2020;21:645-54.

RTP RESEARCH TO PRACTICE

FDA Approves Drug to Reduce Bone Marrow Suppression Caused by Chemotherapy

Press Release – February 12, 2021

"The US Food and Drug Administration approved trilaciclib as the first therapy in its class to reduce the frequency of chemotherapy-induced bone marrow suppression in adults receiving certain types of chemotherapy for extensive-stage (when the cancer has spread beyond the lungs) small cell lung cancer. Trilaciclib may help protect bone marrow cells from damage caused by chemotherapy by inhibiting cyclin-dependent kinase 4/6, a type of enzyme.

The effectiveness of trilaciclib was evaluated in three randomized, double-blind, placebo-controlled studies in patients with extensive-stage small cell lung cancer. Combined, these studies randomly assigned 245 patients to receive either an infusion of trilaciclib in their veins or a placebo before chemotherapy. The studies then compared the two groups for the proportion of patients with severe neutropenia (a very low count of white blood cells called neutrophils) and the duration of severe neutropenia in the first cycle of chemotherapy. In all three studies, patients who received trilaciclib had a lower chance of having severe neutropenia compared to patients who received a placebo. Among those who had severe neutropenia, patients who received trilaciclib, on average, had it for a shorter time than patients who received a placebo."

https://www.fda.gov/news-events/press-announcements/fda-approves-drug-reduce-bone-marrow-suppression-caused-chemotherapy

RTP RESEARCH TO PRACTICE

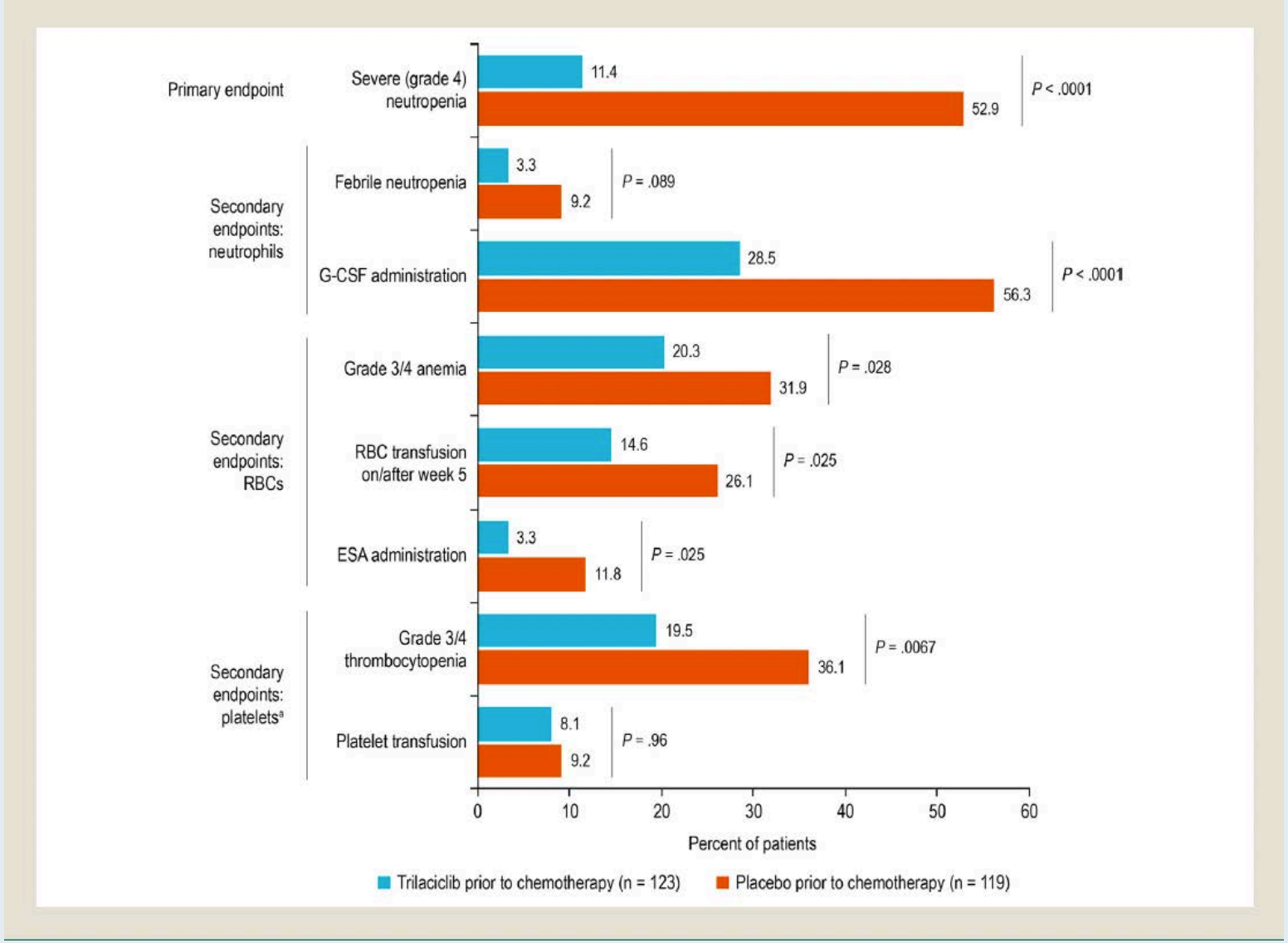
Clin Lung Cancer 2021;22(5):449-60.

Original Study

Effects of Trilaciclib on Chemotherapy-Induced Myelosuppression and Patient-Reported Outcomes in Patients with Extensive-Stage Small Cell Lung Cancer: Pooled Results from Three Phase II Randomized, Double-Blind, Placebo-Controlled Studies

Jared Weiss,[1] Jerome Goldschmidt,[2] Zoran Andric,[3] Konstantin H. Dragnev,[4] Chad Gwaltney,[5] Konstantina Skaltsa,[6] Yili Pritchett,[7] Joyce M. Antal,[7] Shannon R. Morris,[7] Davey Daniel[8,9]

Myelopreservation Benefits with Trilaciclib Administered Prior to Chemotherapy



Weiss J et al. *Clin Lung Cancer* 2021;22(5):449-60.

RTP RESEARCH TO PRACTICE

Thank you for joining us!

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