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

A CME/MOC- and NCPD-Accredited Hybrid Event

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

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Agenda

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

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

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

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

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

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

Chronic Lymphocytic Leukemia and Lymphomas Faculty

Brad S Kahl, MD
Professor of Medicine
Washington University School of Medicine
Director, Lymphoma Program
Siteman Cancer Center
St Louis, Missouri

Craig Moskowitz, MD
Physician in Chief and Interim Deputy Cancer Center Director
Sylvester Comprehensive Cancer Center
Professor of Medicine, Miller School of Medicine
University of Miami Health System
Miami, Florida

Co-Moderators

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

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

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

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

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

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

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MODULE 4: CLL and Lymphomas

Co-Moderator

Jeanna L Knoble, MD
Zangmeister Cancer Center
Columbus, Ohio

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Chronic Lymphocytic Leukemia and Lymphomas Agenda

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

Module 2: Chronic Lymphocytic Leukemia (CLL)

Module 3: Hodgkin Lymphoma

Module 4: Mantle Cell Lymphoma (MCL)

Module 5: Follicular Lymphoma (FL)

Chronic Lymphocytic Leukemia and Lymphomas Agenda

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

- Benefits and risks of the POLARIX regimen (ie, polatuzumab vedotin/R-CHP) as first-line treatment of DLBCL
- Timing and selection of patients for CAR T-cell therapy (and possibly T-cell-engaging bispecific antibodies in the future) versus transplant
- Sequencing of regimens for relapsed DLBCL (eg, loncastuximab tesirine, tafasitamab/lenalidomide, selinexor)

Module 2: Chronic Lymphocytic Leukemia (CLL)

Module 3: Hodgkin Lymphoma

Module 4: Mantle Cell Lymphoma (MCL)

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

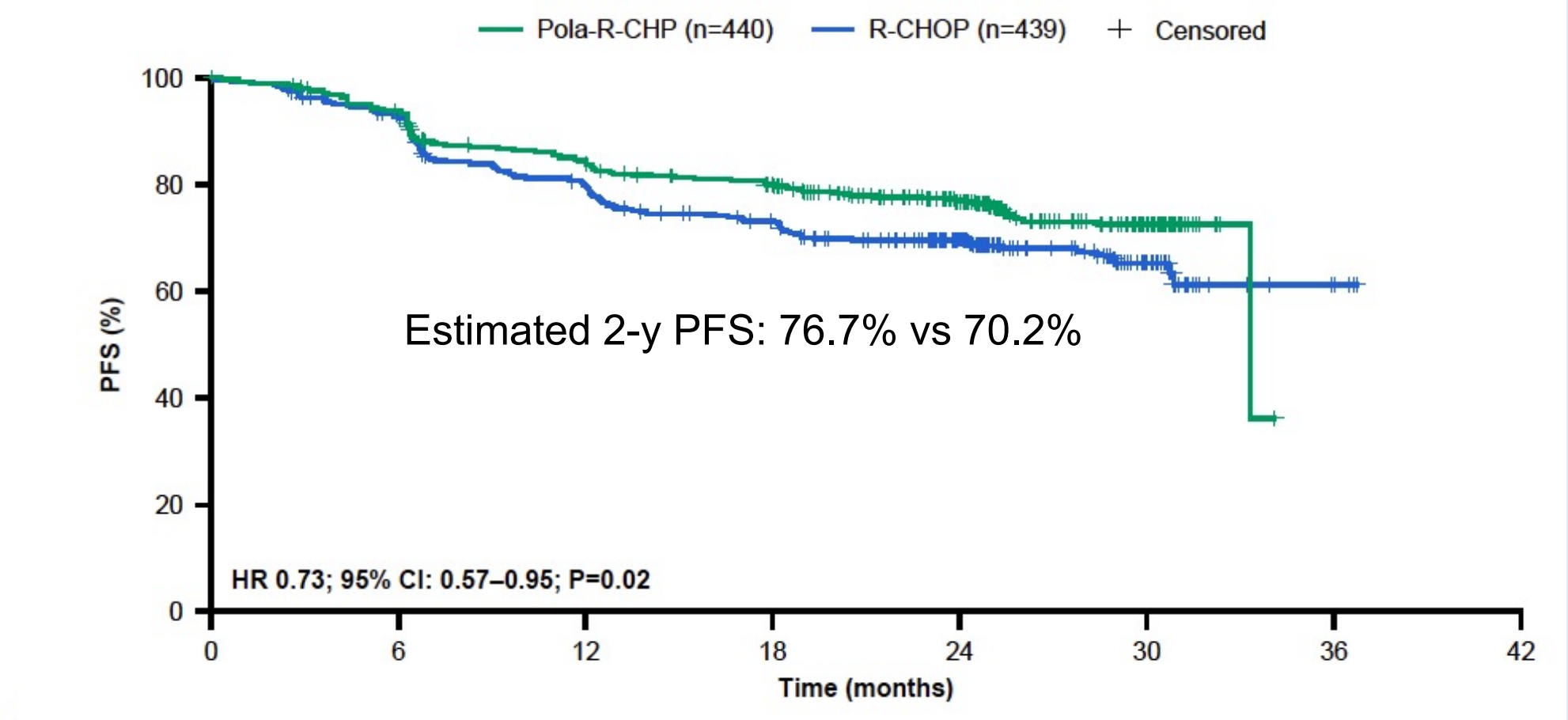
H. Tilly, F. Morschhauser, L.H. Sehn, J.W. Friedberg, M. Trněný, J.P. Sharman, C. Herbaux, J.M. Burke, M. Matasar, S. Rai, K. Izutsu, N. Mehta-Shah, L. Oberic, A. Chauchet, W. Jurczak, Y. Song, R. Greil, L. Mykhalska, J.M. Bergua-Burgués, M.C. Cheung, A. Pinto, H.-J. Shin, G. Hapgood, E. Munhoz, P. Abrisqueta,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

Polatuzumab Vedotin plus Rituximab, Cyclophosphamide, Doxorubicin, and Prednisone (Pola-R-CHP) Versus Rituximab, Cyclophosphamide, Doxorubicin, Vincristine and Prednisone (R-CHOP) Therapy in Patients with Previously Untreated Diffuse Large B-cell Lymphoma (DLBCL): Results from the Phase III POLARIX Study

Neha Mehta-Shah,[1] Hervé Tilly,[2] Franck Morschhauser,[3] Laurie H. Sehn,[4] Jonathan W. Friedberg,[5] Marek Trněný,[6] Jeff P. Sharman,[7] Charles Herbaux,[8] John M. Burke,[9] Matthew Matasar,[10] Shinya Rai,[11] Koji Izutsu,[12] Lucie Oberic,[13] Adrien Chauchet,[14] Wojciech Jurczak,[15] Yuqin Song,[16] Richard Greil,[17] Larysa Mykhalska,[18] Juan Miguel Bergua-Burgués,[19] Matthew C. Cheung,[20] Antonio Pinto,[21] Ho-Jin Shin,[22] Greg Hapgood,[23] Eduardo Munhoz,[24] Pau Abrisqueta,[25] Jyh-Pyng Gau,[26] Jamie Hirata,[27] Yanwen Jiang,[27] Mark Yan,[28] Calvin Lee,[27] Christopher Flowers,[29] Gilles Salles[30]

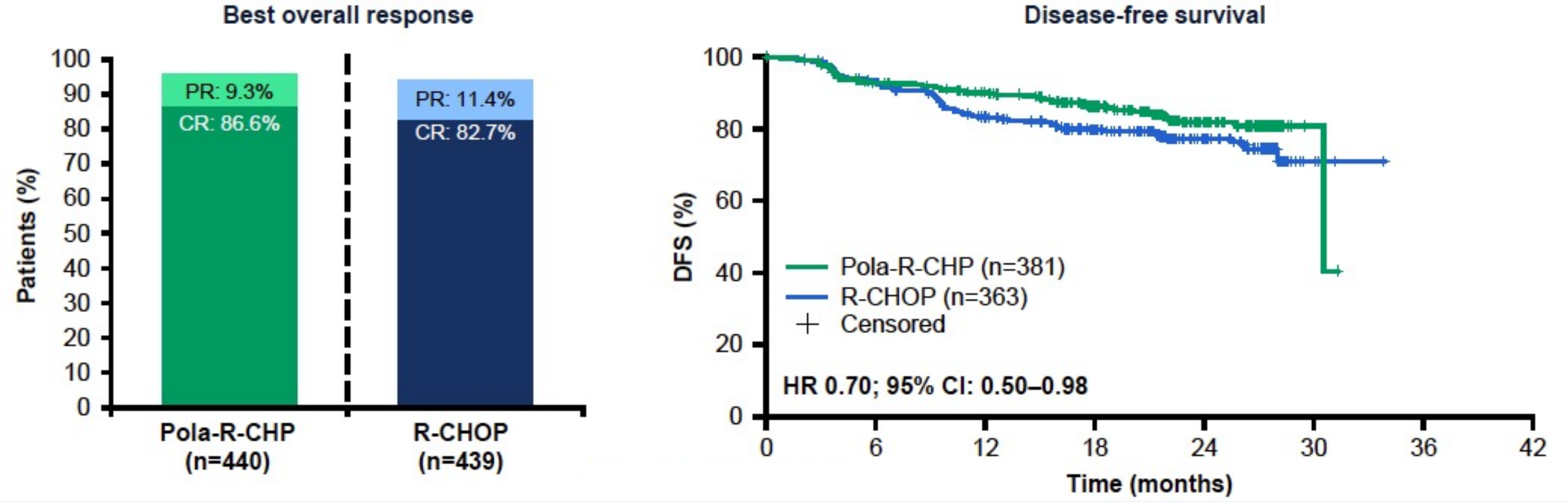
Pan Pacific Lymphoma Conference 2022

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



Mehta-Shah N et al. Pan Pacific Lymphoma Conference 2022.

POLARIX: Key Secondary Endpoints



PR = partial response; CR = complete response

- There was no difference in overall survival between treatment arms

Mehta-Shah N et al. Pan Pacific Lymphoma Conference 2022.

P7517

ASCO 2022

Outcomes by BCL2 and MYC expression and rearrangements in untreated diffuse large B-cell lymphoma (DLBCL) from the POLARIX trial

Franck Morschhauser,[1] Yanwen Jiang,[2] Fabrice Jardin,[3] Alex F. Herrera,[4] Laurie H. Sehn,[5] Charles Herbaux,[6] Christopher Flowers,[7] Tycel Phillips,[8] Armando López Guillermo,[9] Catherine Diefenbach,[10] Gareth P. Gregory,[11] Austin Kim,[12] Anna Maria Barbui,[13] Sandhya Balasubramanian,[2] Will Harris,[2] Jamie Hirata,[2] Joseph N. Paulson,[2] Calvin Lee,[2] Georg Lenz[14]

Summary

POLARIX (NTC03274492) is a Phase III international study of Pola-R-CHP vs R-CHOP in patients with previously untreated DLBCL and IPI 2–5.

This is a **pre-specified exploratory analysis** of the prognostic significance of BCL2 and MYC protein expression, and *BCL2*, *BCL6*, and *MYC* gene rearrangements.

The **poor prognostic impact associated with DEL** appears reduced in patients receiving Pola-R-CHP vs R-CHOP.

DEL, double-expressor lymphoma

Multivariate analyses **support the benefit of Pola-R-CHP** in patients with DLBCL that has BCL2 or MYC protein overexpression.

Morschhauser F et al. ASCO 2022;Abstract 7517.

N Engl J Med 2022;386(7):640-54.

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*

Lancet 2022;399:2294-308.

Lisocabtagene maraleucel 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 (TRANSFORM): results from an interim analysis of an open-label, randomised, phase 3 trial

Manali Kamdar, Scott R Solomon, Jon Arnason, Patrick B Johnston, Bertram Glass, Veronika Bachanova, Sami Ibrahimi, Stephan Mielke, Pim Mutsaers, Francisco Hernandez-Ilizaliturri, Koji Izutsu, Franck Morschhauser, Matthew Lunning, David G Maloney, Alessandro Crotta, Sandrine Montheard, Alessandro Previtali, Lara Stepan, Ken Ogasawara, Timothy Mack, Jeremy S Abramson, for the TRANSFORM Investigators†*

N Engl J Med 2022;386(7):629-39.

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

Randomized Trials Comparing Second-Line CAR T-Cell to Standard Therapy for Patients with Transplant-Eligible DLBCL with Primary Refractory Disease or Relapse within 1 Year of First-Line Therapy

	ZUMA-7	TRANSFORM	BELINDA
CAR T-cell therapy	Axicabtagene ciloleucel	Lisocabtagene maraleucel	Tisagenlecleucel
n	359	184	322
Patients infused in CAR arm	94%	98%	96%
Median EFS	8.3 mo vs 2 mo	10.1 mo vs 2.3 mo	3 mo vs 3 mo
Hazard ratio	0.398 ($p < 0.0001$)	0.349 ($p < 0.0001$)	1.07 ($p = 0.69$)
Median follow-up	25 mo	6 mo	10 mo
CR rate	65% vs 32%	66% vs 39%	28% vs 28%
Grade ≥3 CRS/NT	6%/21%	1%/4%	5%/3%
	Locke et al. ASH 2021;Abstract 2	Kamdar et al. ASH 2021;Abstract 91	Bishop et al. ASH 2021;Abstract LBA-6

Content Courtesy of Jeremy Abramson, MD

Recent FDA Approvals of CAR (Chimeric Antigen Receptor) T-Cell Therapy as Second-Line Treatment for Large B-Cell Lymphoma

6-24-22: "The FDA approved lisocabtagene maraleucel for adult patients with large B-cell lymphoma (LBCL) who have refractory disease to first-line chemoimmunotherapy or relapse within 12 months of first-line chemoimmunotherapy; or refractory disease to first-line chemoimmunotherapy or relapse after first-line chemoimmunotherapy and are not eligible for hematopoietic stem cell transplantation (HSCT) due to comorbidities or age. It is not indicated for the treatment of patients with primary central nervous system lymphoma." Based on the TRANSFORM study

4-01-22: "The FDA approved axicabtagene ciloleucel for adult patients with large B-cell lymphoma (LBCL) that is refractory to first-line chemoimmunotherapy or relapses within 12 months of first-line chemoimmunotherapy. It is not indicated for the treatment of patients with primary central nervous system lymphoma." Based on the ZUMA-7 study

www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-lisocabtagene-maraleucel-second-line-treatment-large-b-cell-lymphoma
www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-axicabtagene-ciloleucel-second-line-treatment-large-b-cell-lymphoma

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nature medicine

FOCUS | ARTICLES

https://doi.org/10.1038/s41591-022-01731-4

OPEN

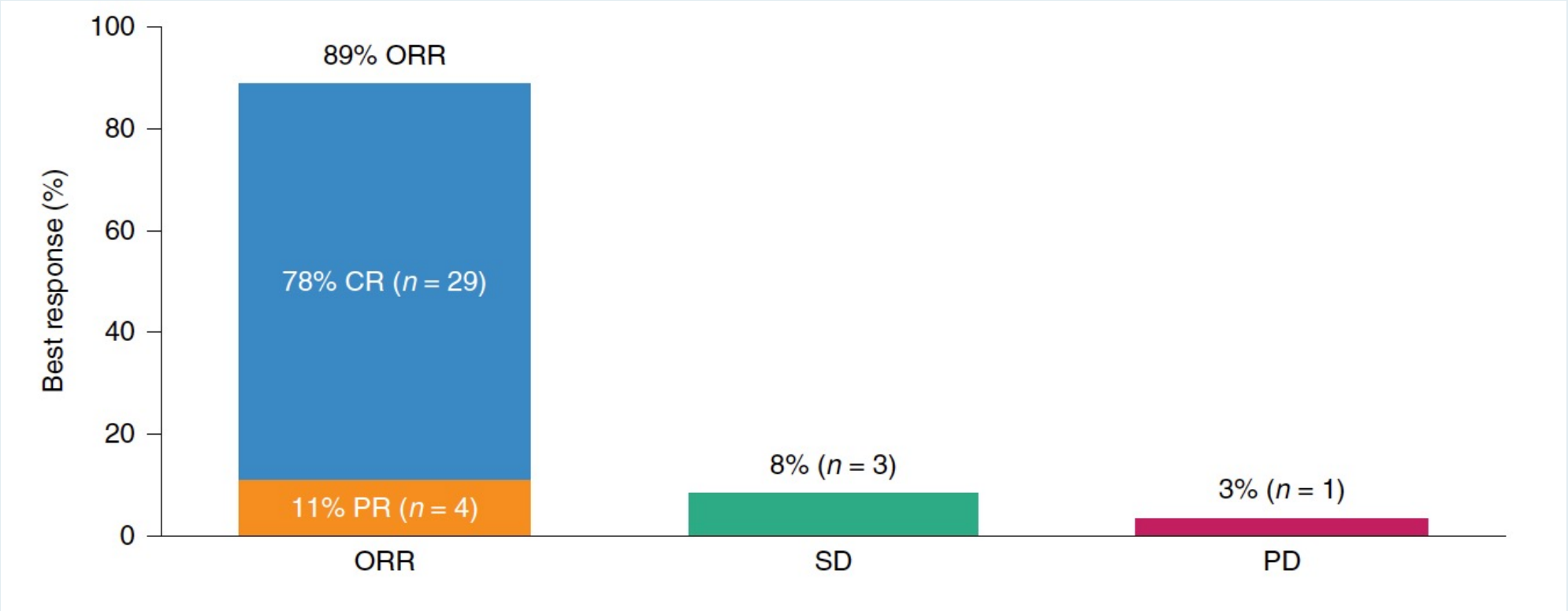
Axicabtagene ciloleucel as first-line therapy in high-risk large B-cell lymphoma: the phase 2 ZUMA-12 trial

Sattva S. Neelapu[1]✉, Michael Dickinson[2], Javier Munoz[3], Matthew L. Ulrickson[3], Catherine Thieblemont[4,5], Olalekan O. Oluwole[6], Alex F. Herrera[7], Chaitra S. Ujjani[8], Yi Lin[9], Peter A. Riedell[10], Natasha Kekre[11], Sven de Vos[12], Christine Lui[13], Francesca Milletti[13], Jinghui Dong[13], Hairong Xu[13] and Julio C. Chavez[14]

Nat Med 2022;28(4):735-42.

ZUMA-12: Efficacy Results with Axi-cel as First-Line Treatment

Objective response rate (ORR) and complete response (CR) for efficacy-evaluable patients (N = 37)



- At median follow-up of 15.9 months, 73% of patients remained in objective response
- Median duration of response, event-free survival and progression-free survival were not reached

Neelapu SS et al. *Nat Med* 2022;28(4):735-42.

ZUMA-12: Adverse Events of Interest in ≥15% of Patients Receiving Treatment

Adverse event[a], *n* (%)	Grade 1	Grade 2	Grade ≥3	Total
Subjects with any CRS[a]	27 (68)	10 (25)	3 (8)	40 (100)
Pyrexia	8 (20)	28 (70)	4 (10)	40 (100)
Hypotension	7 (18)	5 (13)	0 (0)	12 (30)
Chills	9 (23)	1 (3)	0 (0)	10 (25)
Hypoxia	2 (5)	2 (5)	5 (13)	9 (23)
Sinus tachycardia	6 (15)	0 (0)	0 (0)	6 (15)
Subjects with any neurologic events	14 (35)	6 (15)	9 (23)	29 (73)
Confusional state	7 (18)	2 (5)	2 (5)	11 (28)
Encephalopathy	2 (5)	2 (5)	6 (15)	10 (25)
Tremor	8 (20)	2 (5)	0 (0)	10 (25)

[a]Adverse events include those with onset on or after axi-cel infusion date and coded using MedDRA v.23.1. Neurologic events were identified using the modified blinatumomab registrational study[35]. CRS was graded according to Lee et al.[36]. The severity of all adverse events, including neurologic events and symptoms of CRS, was graded according to CTCAE v.5.0.

Neelapu SS et al. *Nat Med* 2022;28(4):735-42.

Novel Agents Recently Approved for Relapsed/Refractory DLBCL

	Pola-BR	Selinexor	Tafasitamab/ lenalidomide	Loncastuximab tesirine
Mechanism of action	Anti-CD79b ADC	XPO-1 inhibitor	Anti-CD19 MAb/immunomodulator	Anti-CD19 ADC
ORR	45%	28%	58%	48%
CR rate	40%	10%	40%	24%
PFS	9.2 mo	2.6 mo	11.6 mo	4.9 mo
DOR	12.6 mo	9.3 mo	43.9 mo	10.3 mo
OS	12.4 mo	NR	33.5 mo	9.9 mo

Pola-BR = polatuzumab vedotin with bendamustine/rituximab; ADC = antibody-drug conjugate; mAb = monoclonal antibody

Content Courtesy of Laurie H Sehn MD, MPH

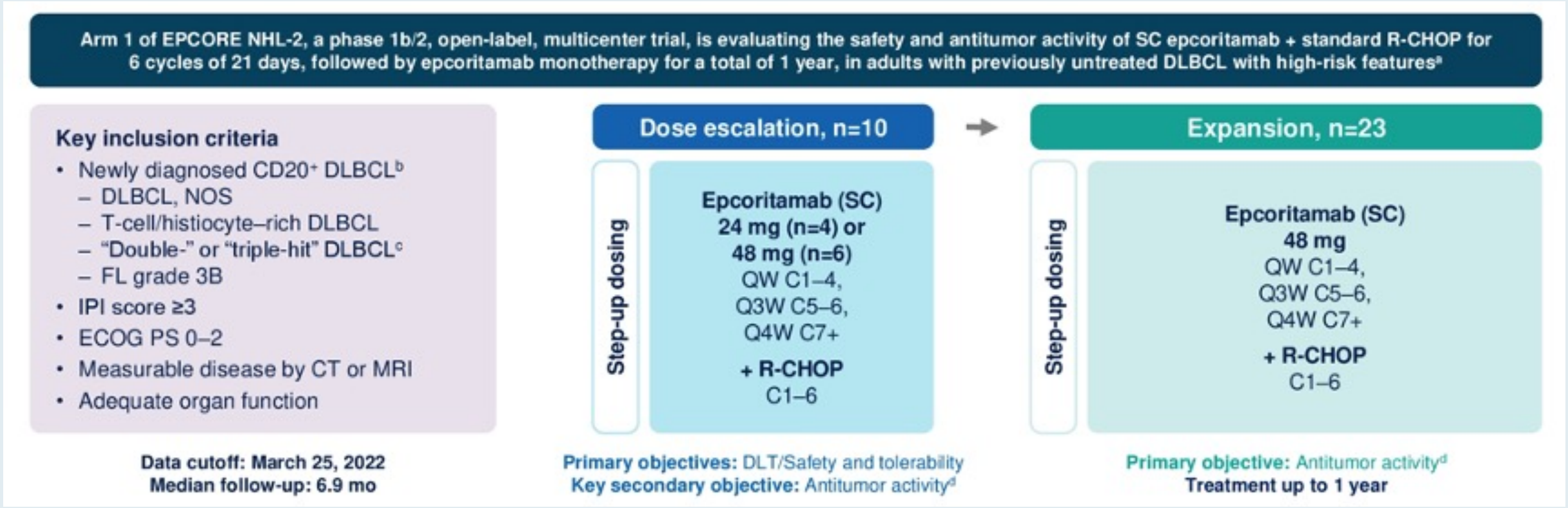
7523

ASCO 2022

First-line treatment (Tx) with subcutaneous (SC) epcoritamab (epco) + R-CHOP in patients (pts) with high-risk diffuse large B-cell lymphoma (DLBCL): phase 1/2 data update

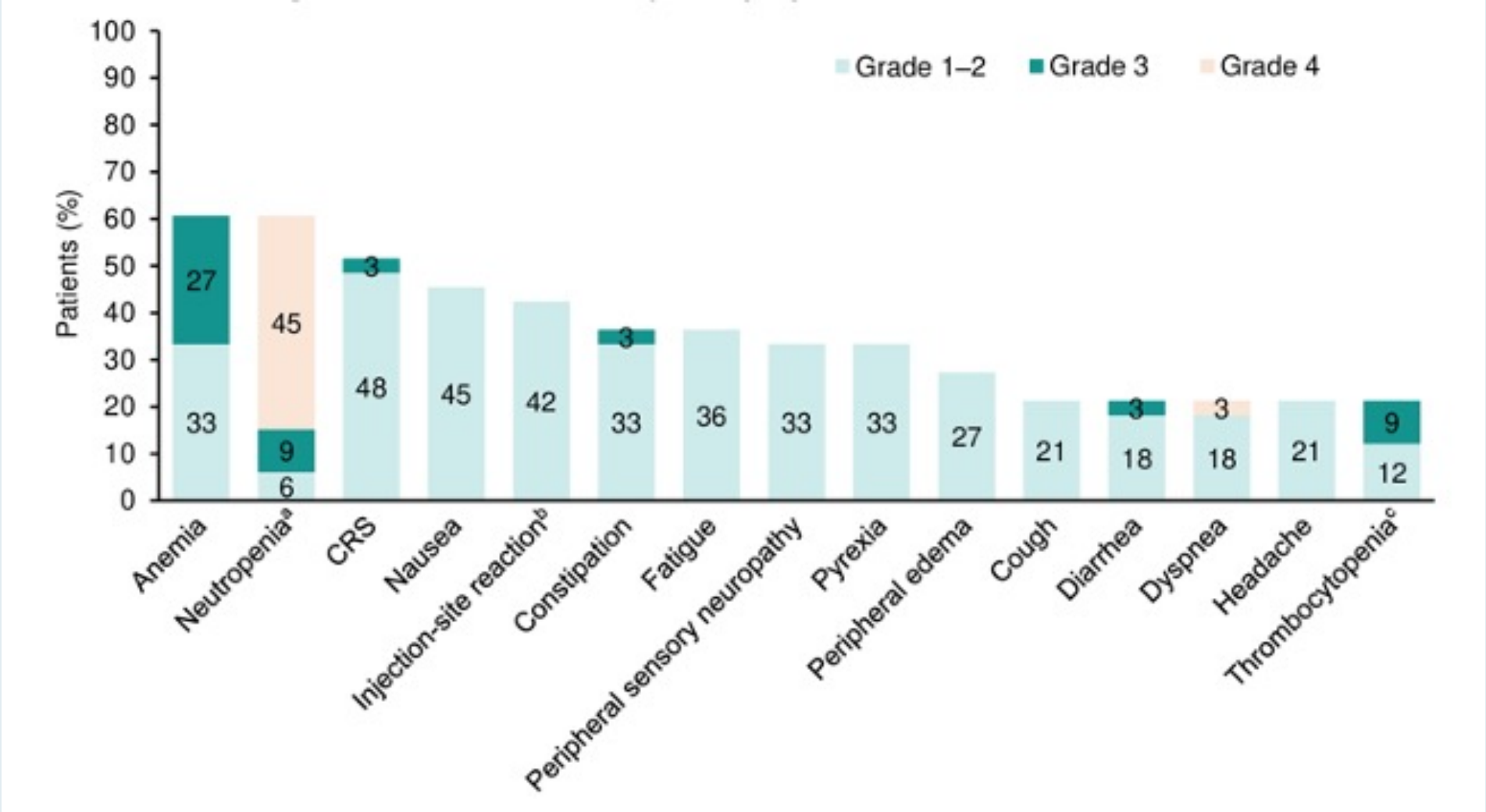
Lorenzo Falchi, MD,[1*] Fritz Offner, MD, PhD,[2] David Belada, MD, PhD,[3] Joshua Brody, MD,[4] Kim M. Linton, MBChB, PhD,[5] Yasmin Karimi, MD,[6] Raul Cordoba, MD, PhD,[7] Sylvia Snauwaert, MD, PhD,[8] Aqeel Abbas, MS,[9] Liwei Wang, PhD,[9] Jun Wu, MD, MS,[10] Brian Elliott, MD,[9] Michael Roost Clausen, MD, PhD[11]

EPCORE™ NHL-2 Arm 1 Study Design



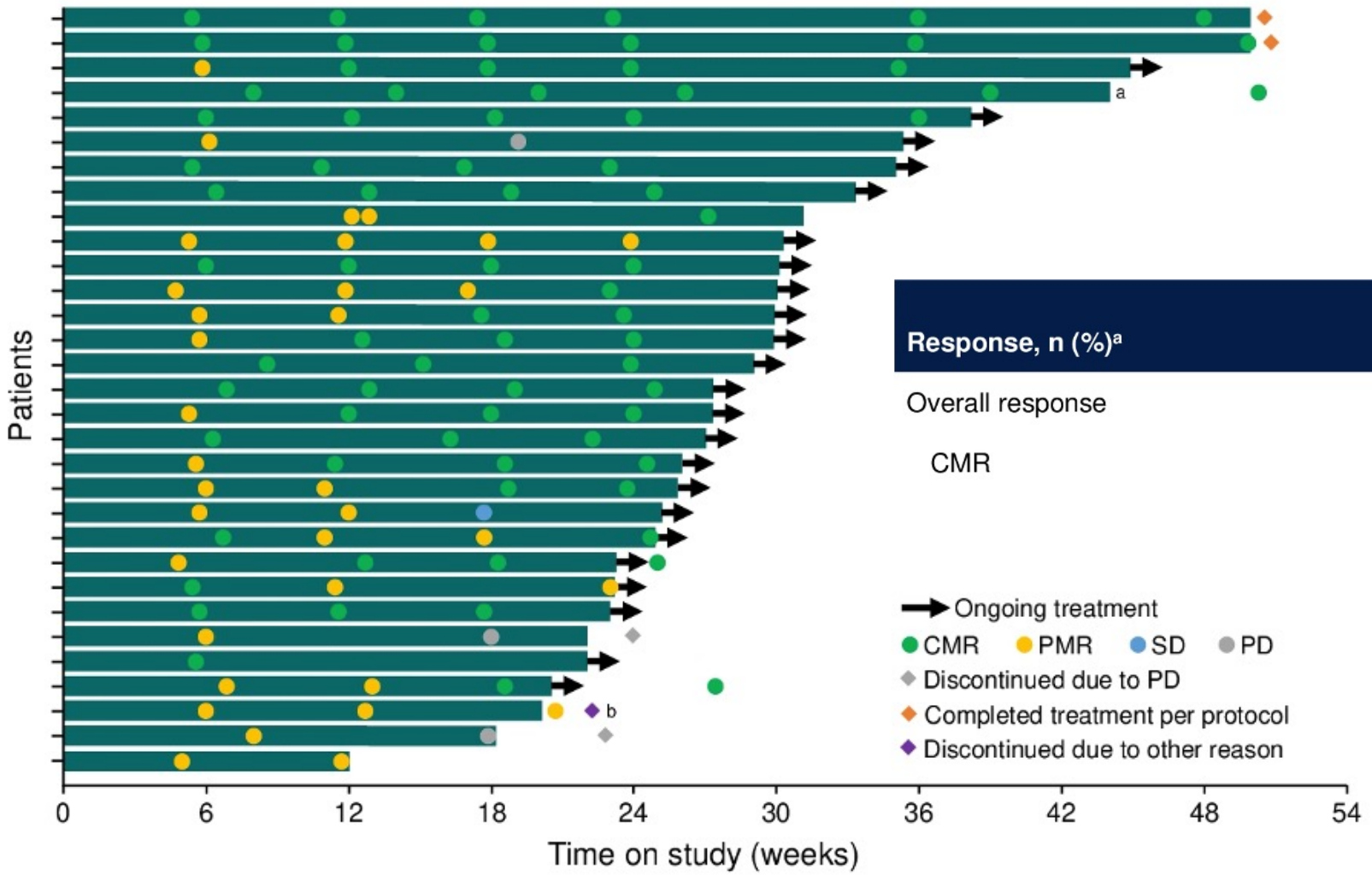
Falchi L et al. ASCO 2022;Abstract 7523.

EPCORE NHL-2 Arm 1: Treatment-Emergent Adverse Events



Falchi L et al. ASCO 2022; Abstract 7523.

EPCORE NHL-2 Arm 1: Response Profile



Response, n (%)[a]	Total n=31
Overall response	31 (100)
CMR	24 (77)

Falchi L et al. ASCO 2022; Abstract 7523.

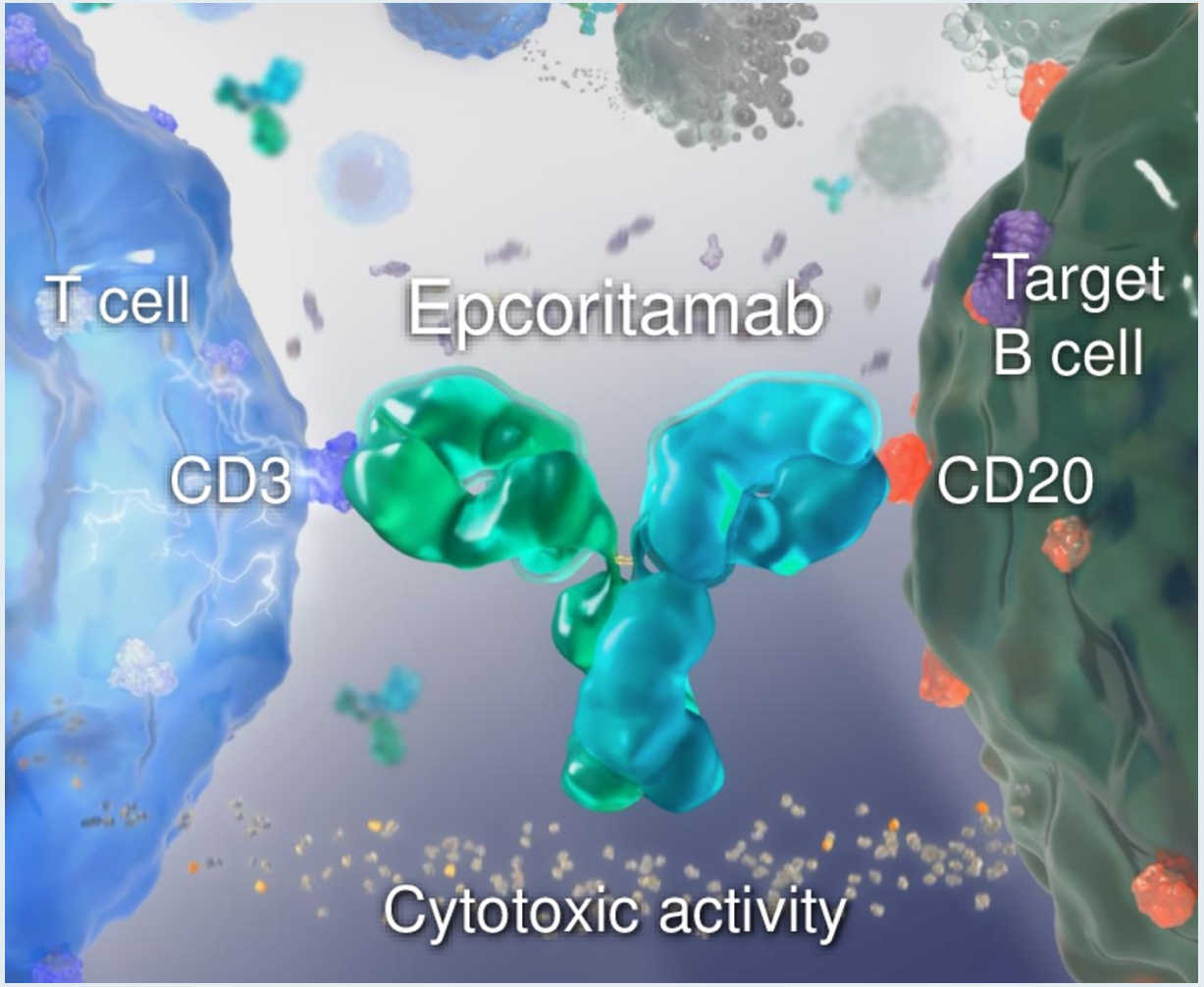
7528

ASCO 2022

Subcutaneous epcoritamab + R-DHAX/C in patients (pts) with relapsed or refractory (R/R) diffuse large B-cell lymphoma (DLBCL) eligible for autologous stem cell transplant (ASCT): preliminary phase 1/2 results

Pau Abrisqueta, MD, PhD,[1*] Lorenzo Falchi, MD,[2] Tycel Phillips, MD,[3] Sven de Vos, MD, PhD,[4] Marcel Nijland, MD, PhD,[5] Fritz Offner, MD, PhD,[6] Irina Bykhovski, PharmD,[7] Jun Wu, MD, MS,[8] Liwei Wang, PhD,[7] Ali Rana, MD, PhD,[7] Raul Cordoba, MD, PhD[9]

Mechanism of Action of the Subcutaneous Bispecific Antibody Epcoritamab



Falchi L et al. ASCO 2022;Abstract 7524.

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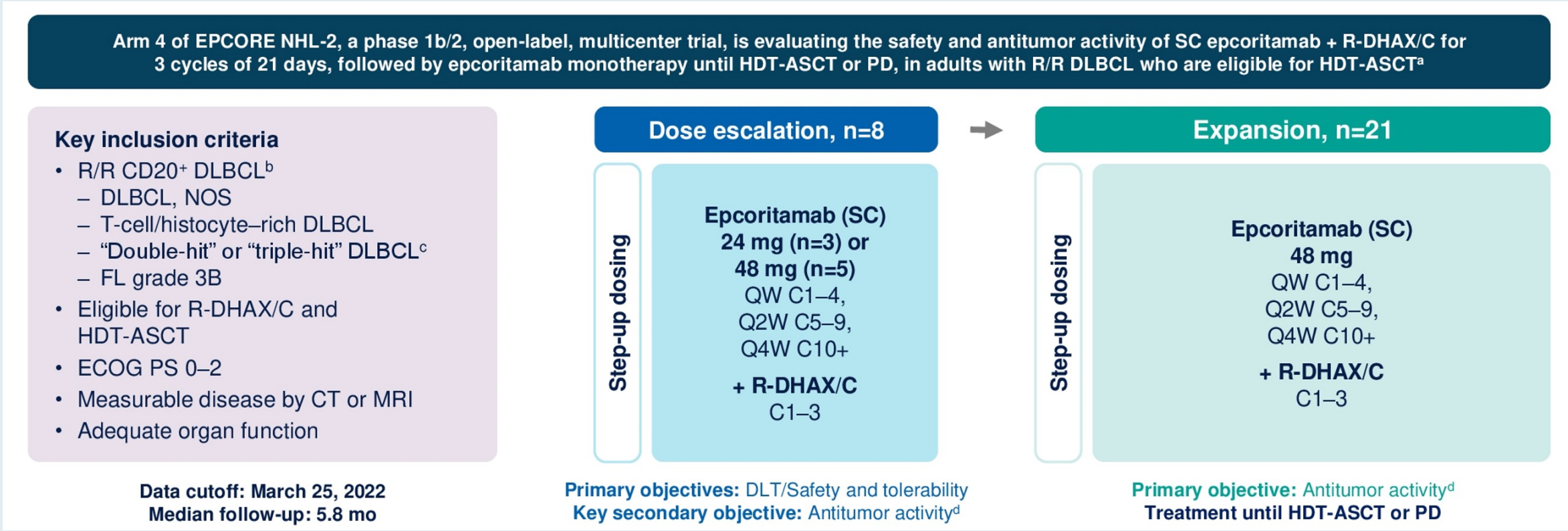
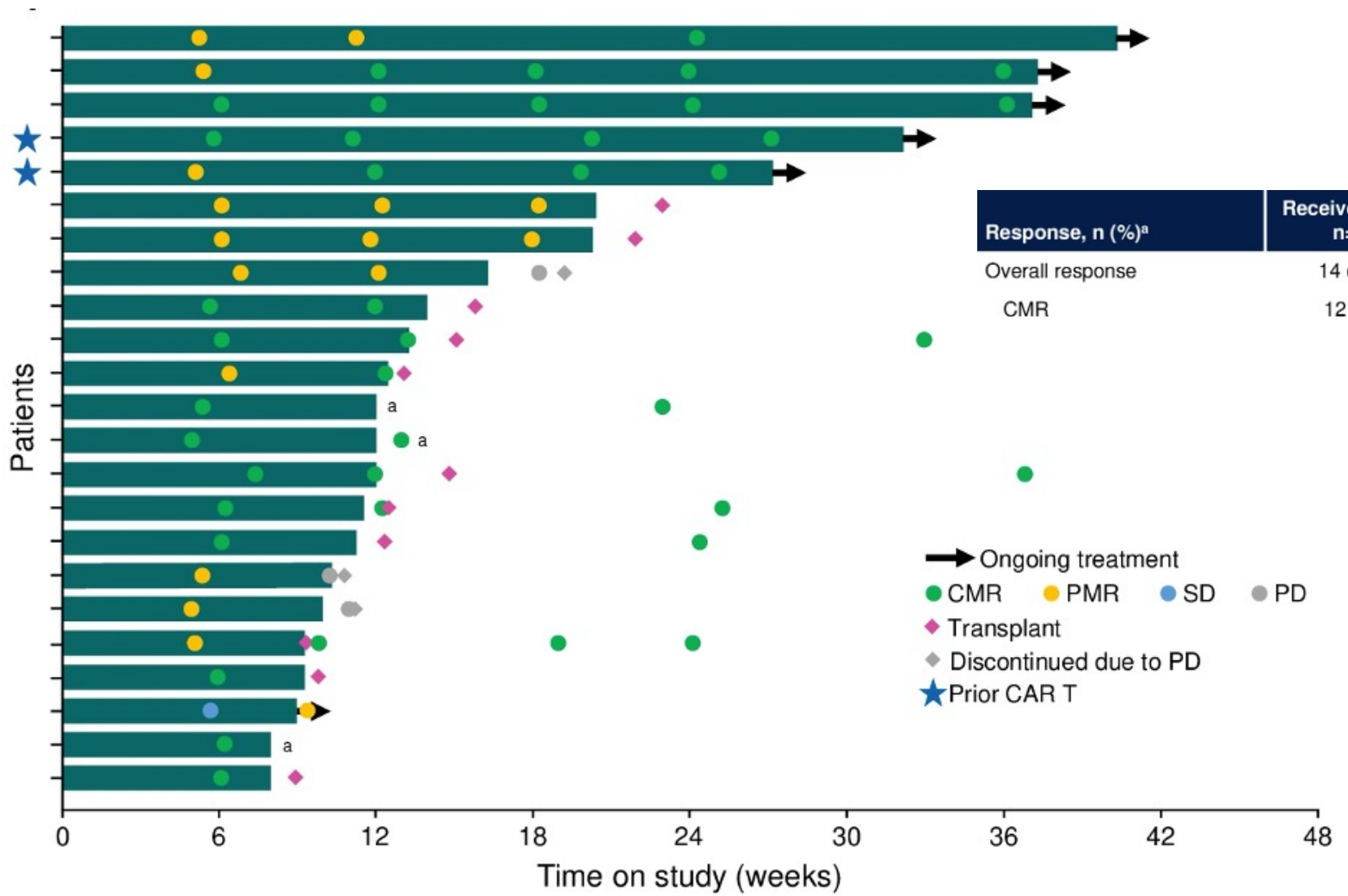
EPCORE NHL-2 Arm 4 Study Design



Abrisqueta P et al. ASCO 2022;Abstract 7528.

EPCORE NHL-2 Arm 4: Response Profile



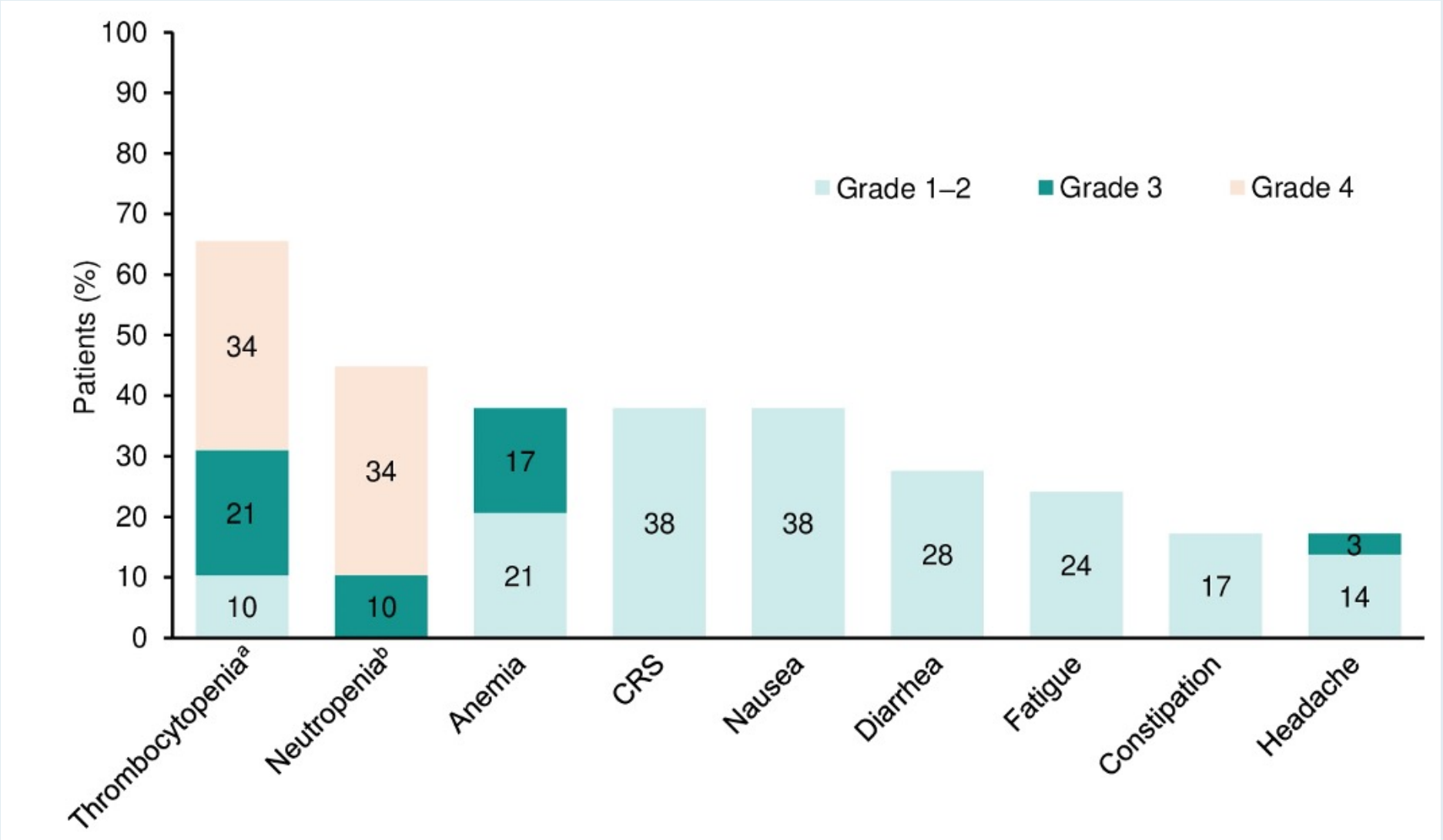
Response, n (%)[a]	Received ASCT n=14	Did not receive ASCT n=12	Total n=26
Overall response	14 (100)	9 (75)	23 (88)
CMR	12 (86)	5 (42)[b]	17 (65)

CMR = complete metabolic response; PMR = partial metabolic response; SD = stable disease; PD = progressive disease

Abrisqueta P et al. ASCO 2022;Abstract 7528.

RTP RESEARCH TO PRACTICE

EPCORE NHL-2 Arm 4: Treatment-Emergent Adverse Events (≥15%)



Abrisqueta P et al. ASCO 2022;Abstract 7528.

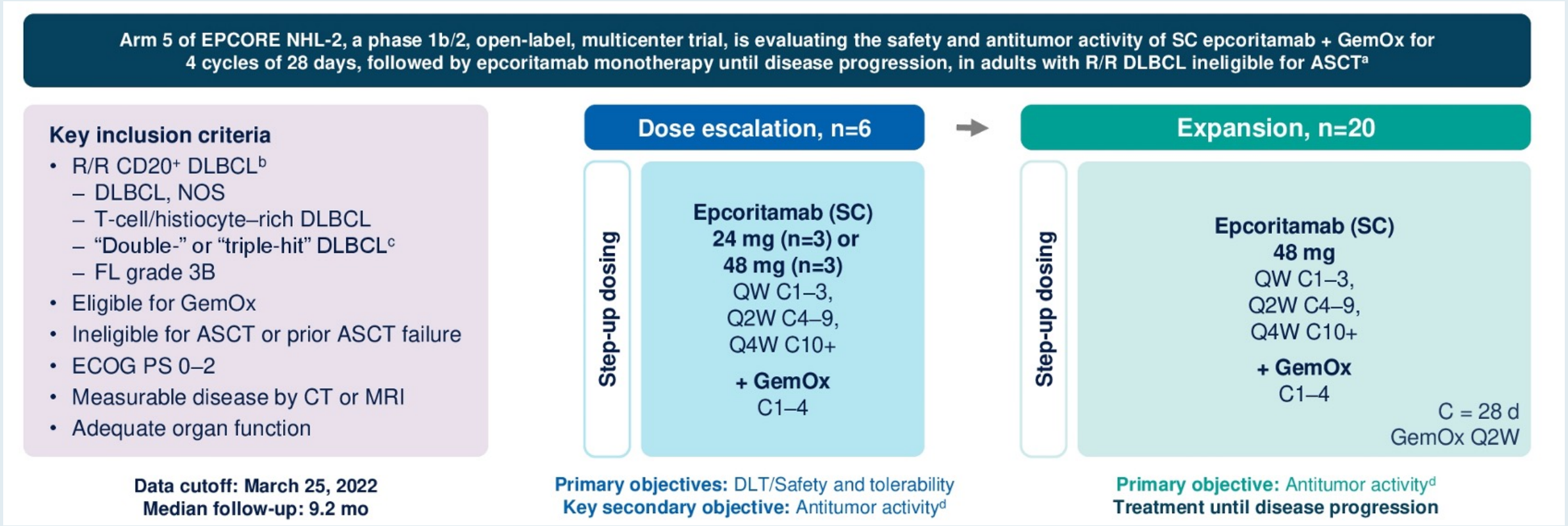
7527

ASCO 2022

Epcoritamab (epco) with gemcitabine + oxaliplatin (GemOx) in patients (pts) with relapsed or refractory (R/R) diffuse large B-cell lymphoma (DLBCL) ineligible for autologous stem cell transplant (ASCT) induces high response rate even in pts failing CAR T therapy

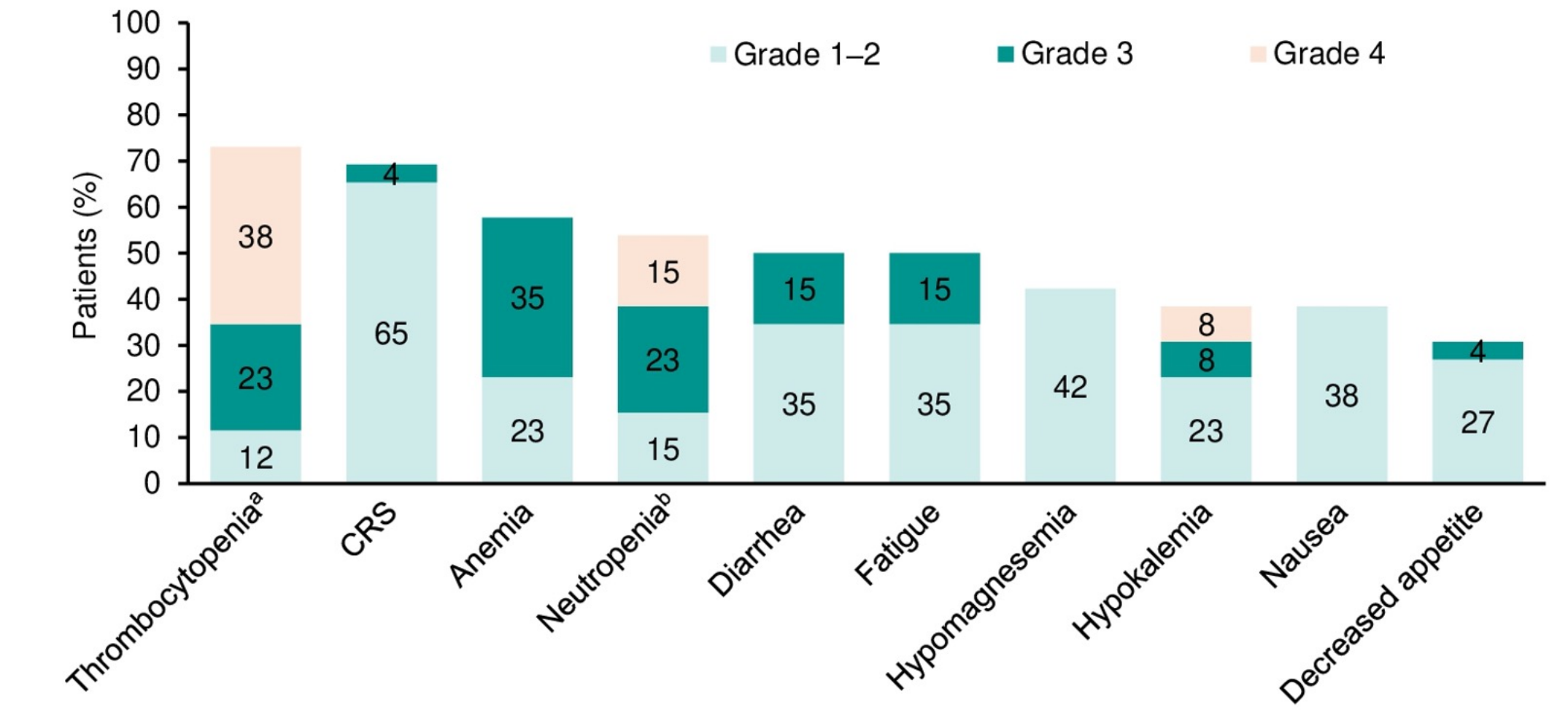
Joshua Brody, MD,[1]* Björn E. Wahlin, MD, PhD,[2] Tycel Phillips, MD,[3]
Régis Costello, MD, PhD,[4] Pieternella Lugtenburg, MD, PhD,[5]
Raul Cordoba, MD, PhD,[6] Liwei Wang, PhD,[7] Jun Wu, MD, MS,[8]
Brian Elliott, MD,[7] Aqeel Abbas, MS,[7] Judit Jørgensen, MD, PhD[9]

EPCORE NHL-2 Arm 5 Study Design



Brody J et al. ASCO 2022;Abstract 7527.

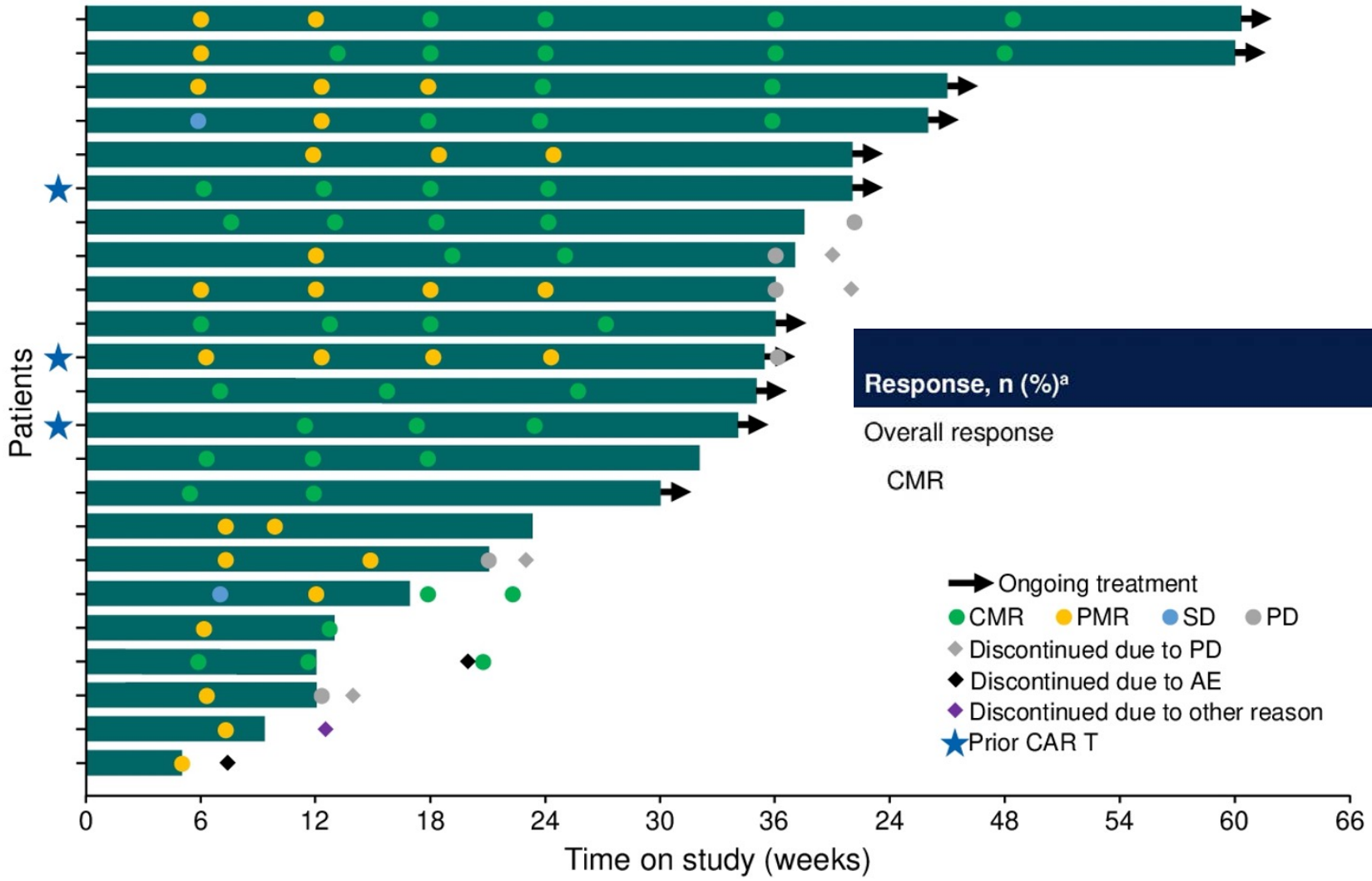
EPCORE NHL-2 Arm 5: Treatment-Emergent Adverse Events



CRS = cytokine release syndrome

Brody J et al. ASCO 2022;Abstract 7527.

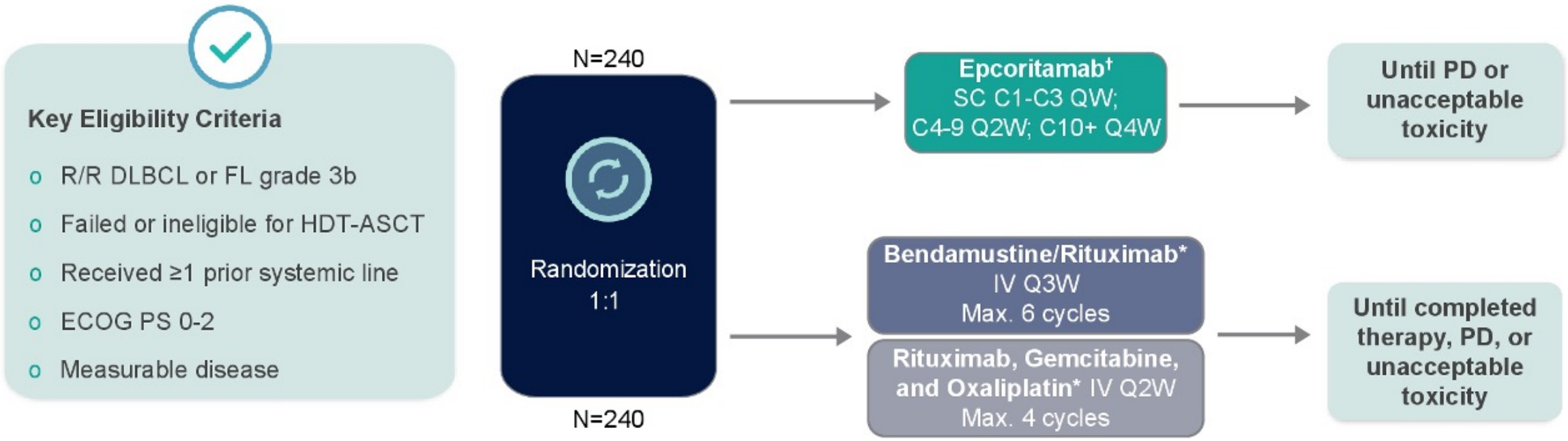
EPCORE NHL-2 Arm 5: Response Profile



Response, n (%)[a]	Total n=25
Overall response	23 (92)
CMR	15 (60)

Brody J et al. ASCO 2022;Abstract 7527.

EPCORE DLBCL-1 Pivotal Phase III Trial Design



Primary Endpoint: Overall Survival
Key Secondary Endpoints: ORR, CR, PFS, DOR and TTR

ORR = overall survival; CR = complete response; PFS = progression-free survival; DOR = duration of response; TTR = time to response

Thieblemont C et al. ASCO 2022;Abstract TPS7569.

Chronic Lymphocytic Leukemia and Lymphomas Agenda

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

Module 2: Chronic Lymphocytic Leukemia (CLL)

- Selection of first-line treatment strategy: Risk and benefits of BTK, Venetoclax/anti-CD20, BTKi + venetoclax; Choice of BTKi
- Noncovalent BTK inhibitors (pirtobrutinib) in relapsed disease

Module 3: Hodgkin Lymphoma

Module 4: Mantle Cell Lymphoma (MCL)

Module 5: Follicular Lymphoma (FL)

Current Approaches to Treatment of Treatment-Naïve CLL: NCCN Guidelines®

Without Del(17p)/*TP53* Mutation

Patients age ≥65 years OR patients age <65 years with significant comorbidities (CrCl <70 mL/min)

Preferred

- Acalabrutinib ± obinutuzumab[a]
- Ibrutinib[a]
- Venetoclax + obinutuzumab[a]
- Zanubrutinib

Other Regimens

- Bendamustine + anti-CD20
- Chlorambucil + obinutuzumab
- Obinutuzumab
- High-dose methylprednisolone + rituximab or obinutuzumab
- Ibrutinib + obinutuzumab
- Chlorambucil
- Rituximab

Patients age <65 years without significant comorbidities

Preferred

- Acalabrutinib ± obinutuzumab[a]
- Ibrutinib[a]
- Venetoclax + obinutuzumab
- Zanubrutinib

Other Regimens

- Bendamustine + anti-CD20
- Fludarabine + cyclophosphamide + rituximab[b]
- Ibrutinib + rituximab
- Fludarabine + rituximab
- High-dose methylprednisolone + rituximab or obinutuzumab

With Del(17p)/*TP53* Mutation

Preferred

- Acalabrutinib ± obinutuzumab
- Ibrutinib
- Venetoclax + obinutuzumab
- Zanubrutinib

Other Regimens

- Alemtuzumab ± rituximab
- High-dose methylprednisolone + rituximab
- Obinutuzumab

[a] Category 1 preferred regimen. [b] Preferred for patients with *IGHV*-mutated CLL.

NCCN Clinical Practice Guidelines® in Oncology for Chronic Lymphocytic Leukemia V.2.2022.

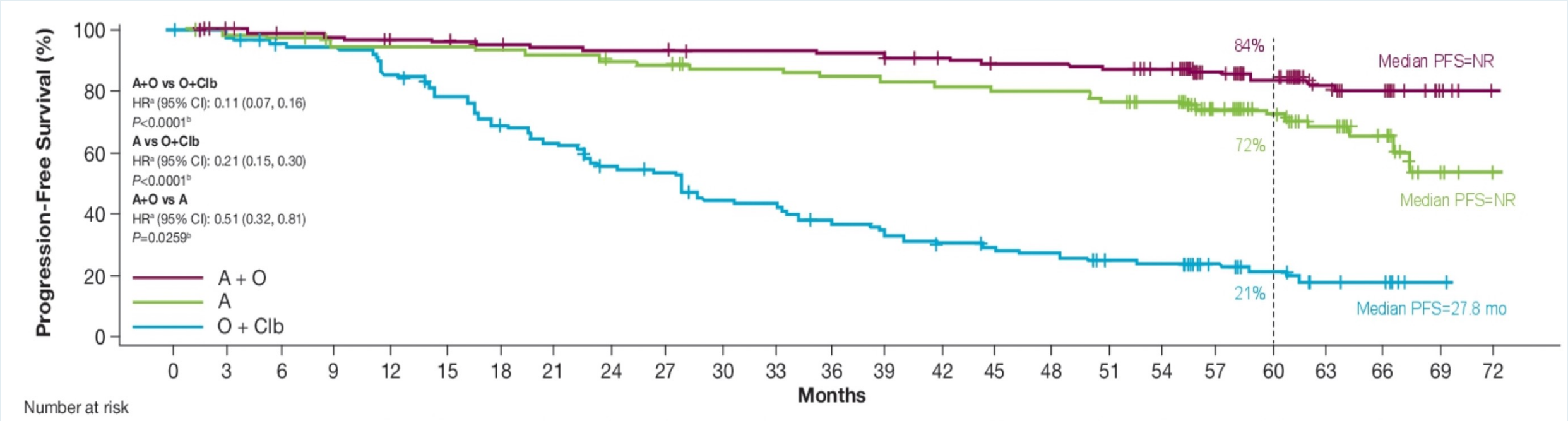
Courtesy of Ian W Flinn, MD, PhD

Acalabrutinib ± Obinutuzumab versus Obinutuzumab + Chlorambucil in Treatment-Naïve Chronic Lymphocytic Leukemia: Five-Year Follow-Up of ELEVATE-TN

Sharman JP et al.

ASCO 2022;Abstract 7539.

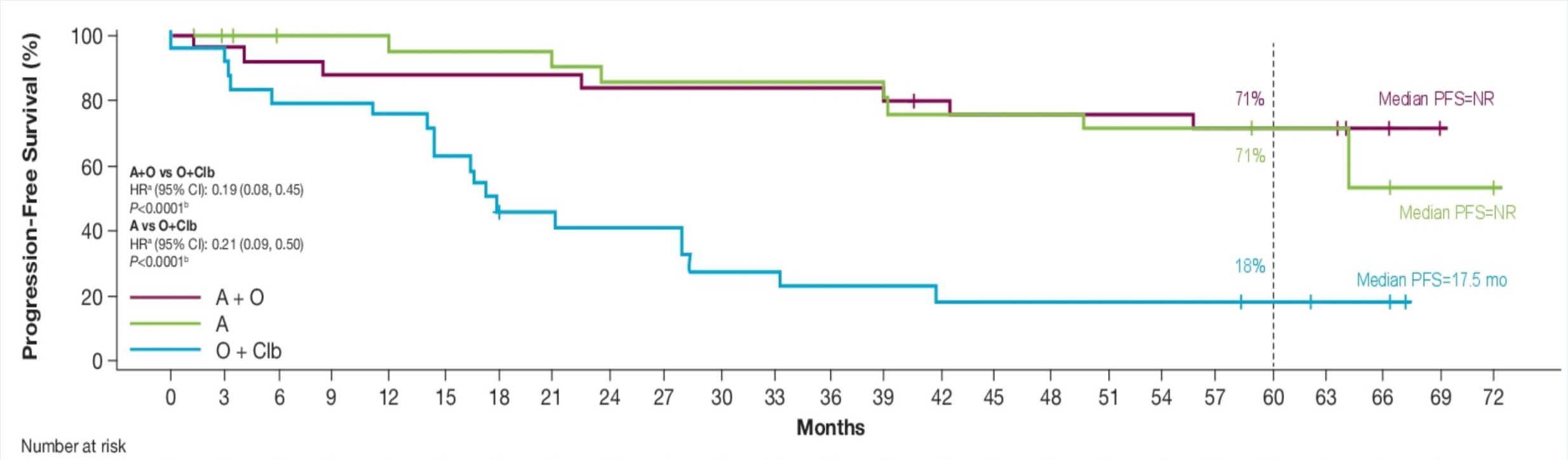
ELEVATE-TN: Investigator-Assessed PFS



Sharman JP et al. ASCO 2022;Abstract 7539.

RTP RESEARCH TO PRACTICE

ELEVATE-TN: Investigator-Assessed PFS for Patients with Del(17p) Disease and/or TP53 Mutation



Sharman JP et al. ASCO 2022;Abstract 7539.

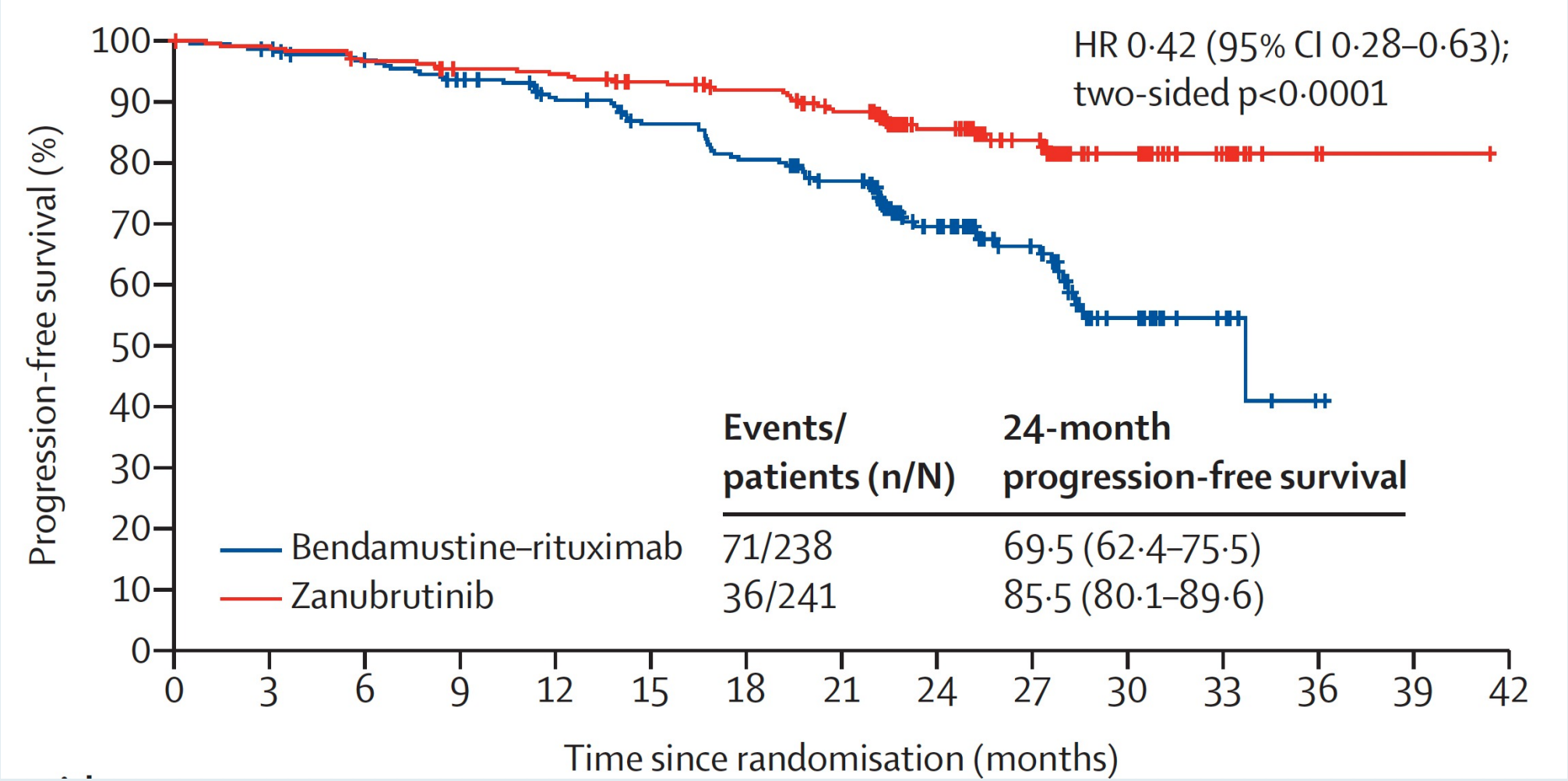
RTP RESEARCH TO PRACTICE

Lancet Oncol 2022;[Online ahead of print].

Zanubrutinib versus bendamustine and rituximab in untreated chronic lymphocytic leukaemia and small lymphocytic lymphoma (SEQUOIA): a randomised, controlled, phase 3 trial

Constantine S Tam, Jennifer R Brown, Brad S Kahl, Paolo Ghia, Krzysztof Giannopoulos, Wojciech Jurczak, Martin Šimkovič, Mazyar Shadman, Anders Österborg, Luca Laurenti, Patricia Walker, Stephen Opat, Henry Chan, Hanna Ciepluch, Richard Greil, Monica Tani, Marek Trněný, Danielle M Brander, Ian W Flinn, Sebastian Grosicki, Emma Verner, Alessandra Tedeschi, Jianyong Li, Tian Tian, Lei Zhou, Carol Marimpietri, Jason C Paik, Aileen Cohen, Jane Huang, Tadeusz Robak, Peter Hillmen**

SEQUOIA: PFS by Independent Review Committee (ITT Population)



Tam CS et al. *Lancet Oncol* 2022;[Online ahead of print].

UNIKLINIK KÖLN | Department I of Internal Medicine University Hospital of Cologne

DEUTSCHE STUDIENGRUPPE

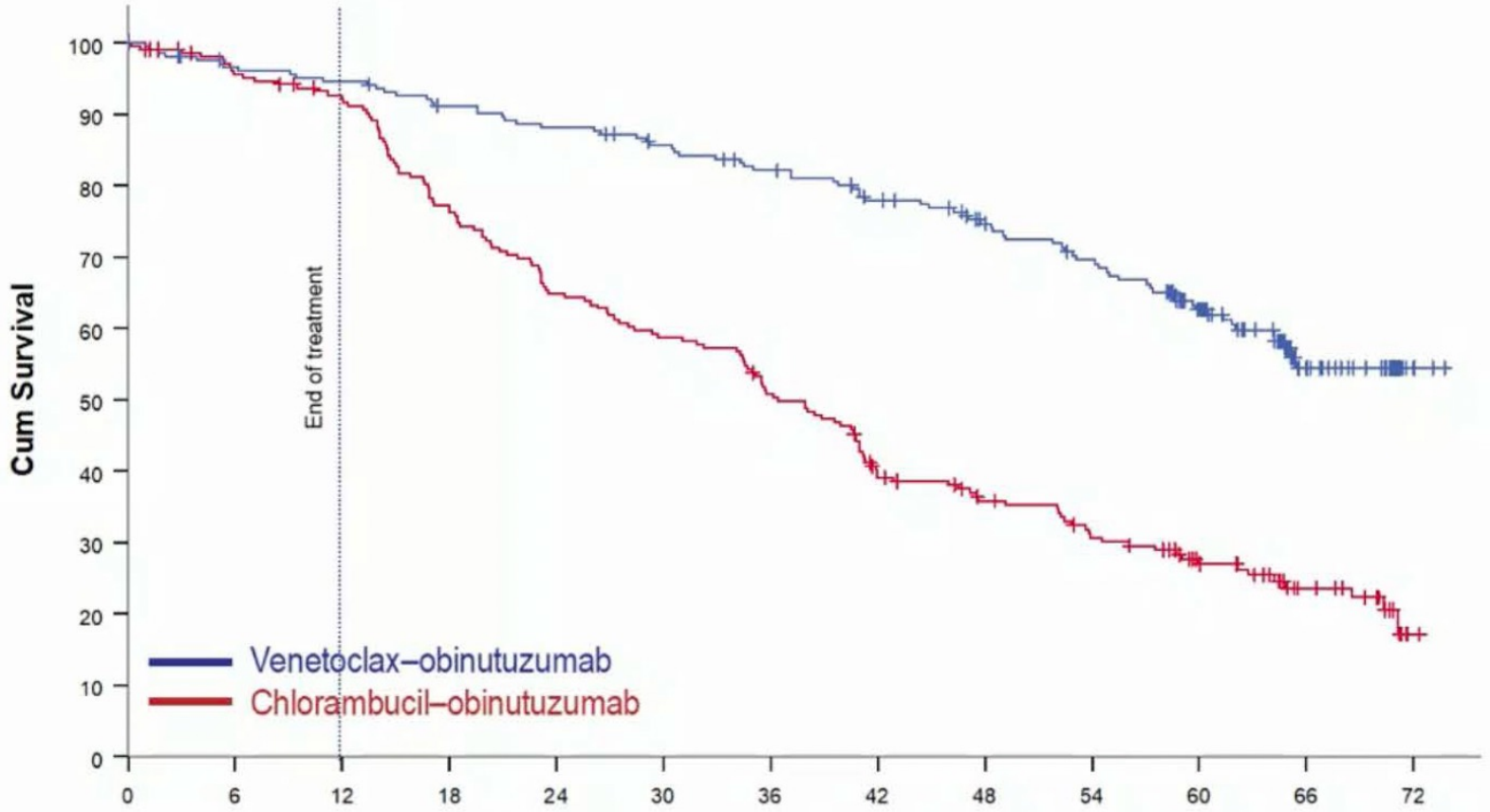
Abstract S148

Venetoclax-Obinutuzumab for previously untreated chronic lymphocytic leukemia: 5-year results of the randomized CLL14 study

Othman Al-Sawaf, Can Zhang, Sandra Robrecht, Alex Kotak, Naomi Chang, Anna Maria Fink, Eugen Tausch, Christof Schneider, Matthias Ritgen, Karl-Anton Kreuzer, Brenda Chyla, Barbara Eichhorst, Yanwen Jiang, Stephan Stilgenbauer, Michael Hallek, Kirsten Fischer

June 12th, 2022
Clinical CLL Session

CLL14: Progression-Free Survival



Median PFS

Ven-Obi: not reached

Clb-Obi: 36.4 months

5-year PFS rate

Ven-Obi: 62.6%

Clb-Obi: 27.0%

HR 0.35, 95% CI [0.26-0.46]
P<0.0001

Al-Sawaf O et al. EHA 2022;Abstract S148.

RTP RESEARCH TO PRACTICE

CLINICAL TRIALS AND OBSERVATIONS

Blood 2022 June 2;139(22):3229-30.

Comment on Tam et al, page 3278

A CAPTIVATE-ing new regimen for CLL

Kerry A. Rogers and Jennifer A. Woyach | The Ohio State University

Blood 2022 June 2;139(22):3278-89.

CLINICAL TRIALS AND OBSERVATIONS

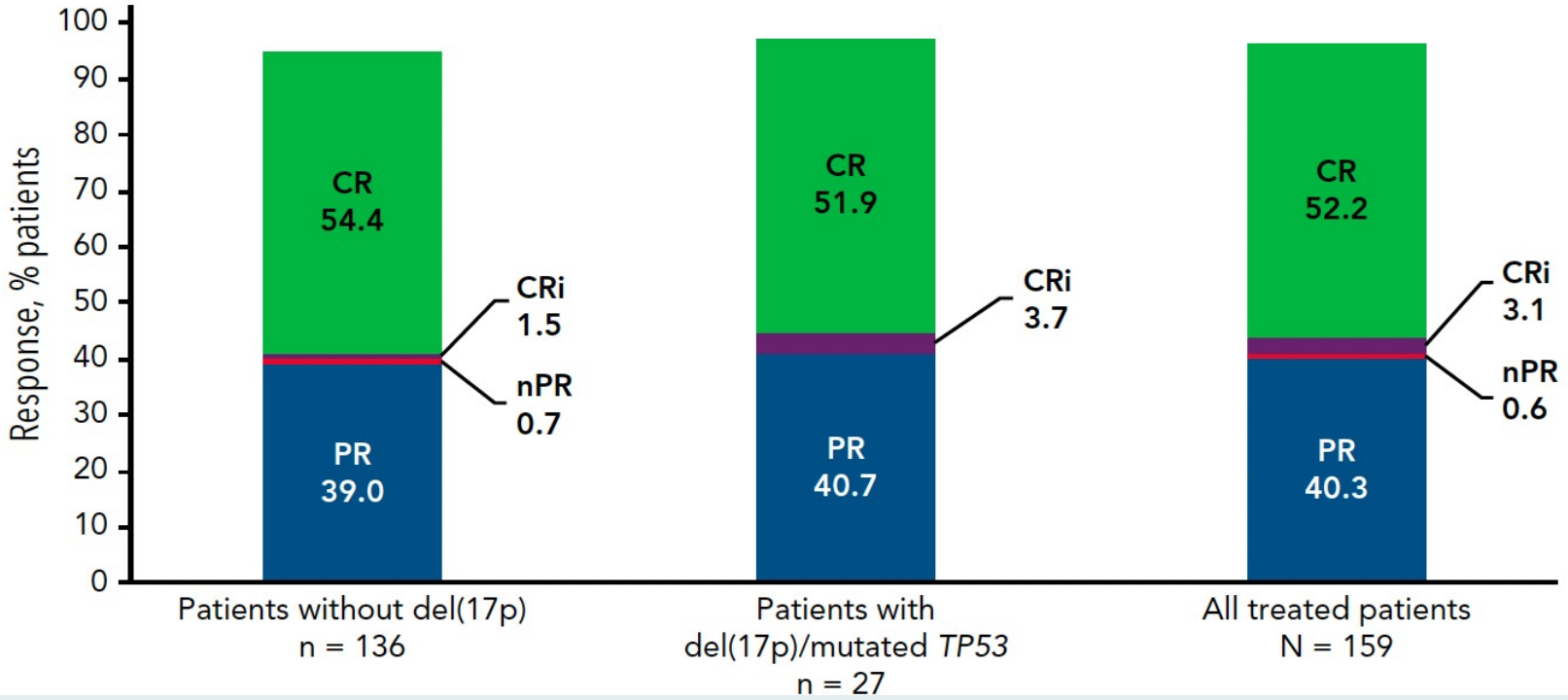
Fixed-duration ibrutinib plus venetoclax for first-line treatment of CLL: primary analysis of the CAPTIVATE FD cohort

Constantine S. Tam,[1-3] John N. Allan,[4] Tanya Siddiqi,[5] Thomas J. Kipps,[6] Ryan Jacobs,[7] Stephen Opat,[8] Paul M. Barr,[9] Alessandra Tedeschi,[10] Livio Trentin,[11] Rajat Bannerji,[12] Sharon Jackson,[13] Bryone J. Kuss,[14] Carol Moreno,[15] Edith Szafer-Glusman,[16] Kristin Russell,[16] Cathy Zhou,[16] Joi Ninomoto,[16] James P. Dean,[16] William G. Wierda,[17,*] and Paolo Ghia[18,19,*]

RTP RESEARCH TO PRACTICE

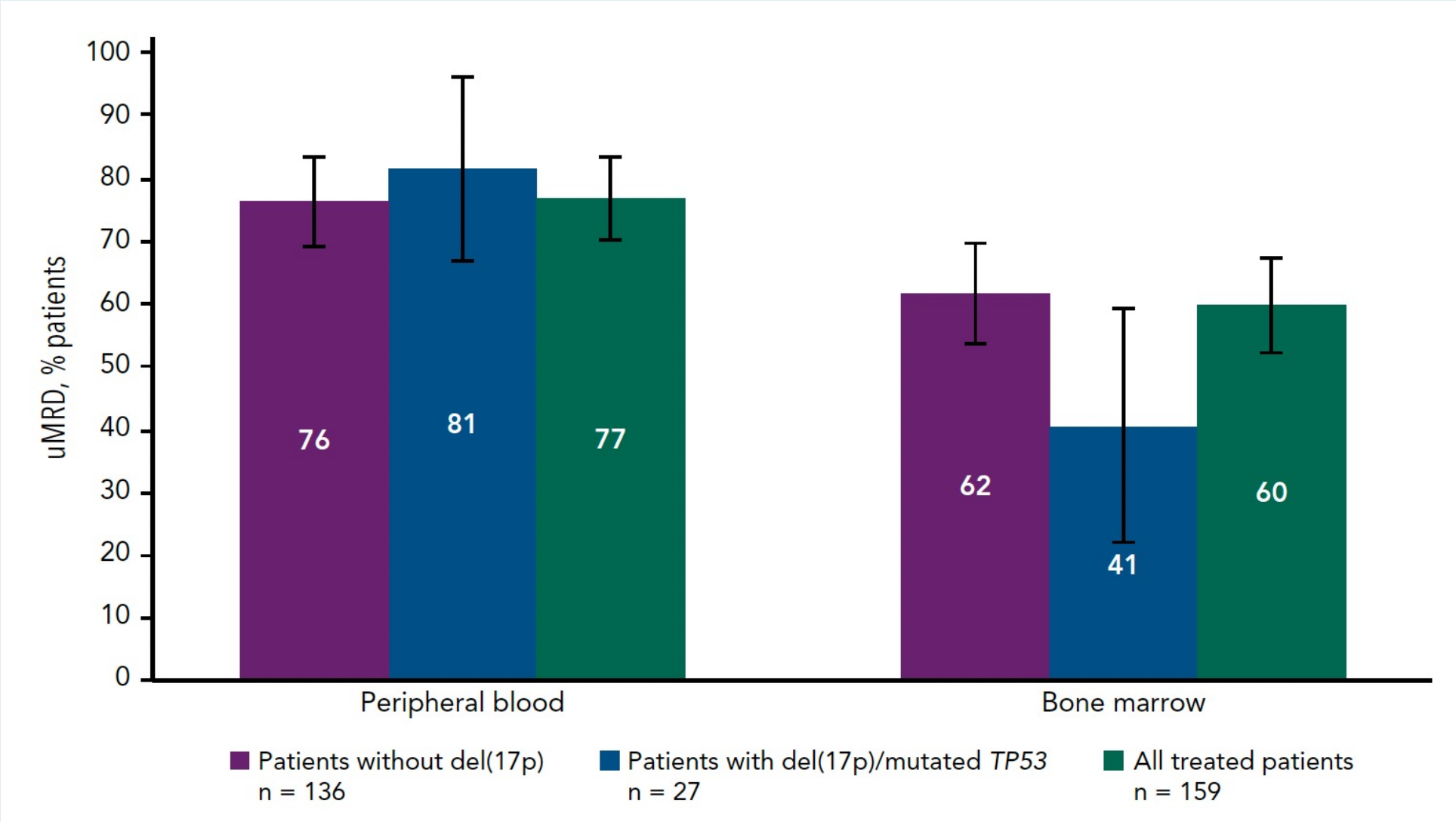
CAPTIVATE FD (Fixed Duration) Cohort: Best Overall Response

	Patients without del(17p) n = 136	Patients with del(17p)/mutated *TP53* n = 27	All treated patients N = 159
Best response, % (95% CI)			
CR/CRi	56 (48-64)	56 (37-74)	55 (48-63)
ORR	96 (92-99)	96 (89-100)	96 (93-99)
Duration of CR ≥12 cycles, n/N (%)	66/76 (87)	13/15 (87)	78/88 (89)*



Tam CS et al. *Blood* 2022 June 2;139(22):3278-89.

CAPTIVATE FD Cohort: Best MRD Response



uMRD = undetectable minimal residual disease

Tam CS et al. *Blood* 2022 June 2;139(22):3278-89.

NEJM Evidence

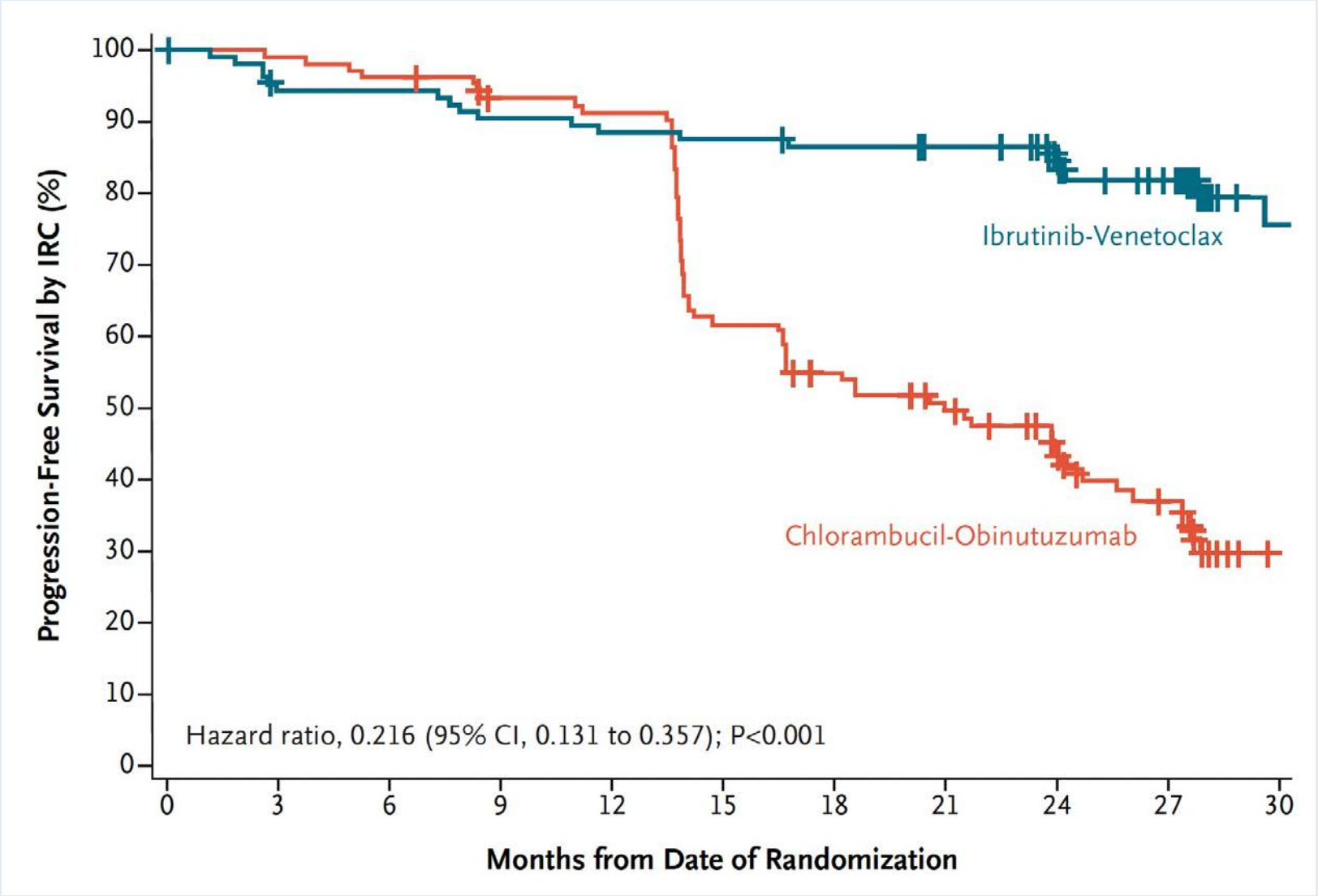
Published May 13, 2022

ORIGINAL ARTICLE

Fixed-Duration Ibrutinib-Venetoclax in Patients with Chronic Lymphocytic Leukemia and Comorbidities (27.7 months follow up)

Arnon P. Kater, M.D., Ph.D.,[1] Carolyn Owen, M.D.,[2] Carol Moreno, M.D.,[3] George Follows, B.M.Bch., Ph.D.,[4] Talha Munir, M.B.B.S.,[5] Mark-David Levin, M.D.,[6] Ohad Benjamini, M.D.,[7] Ann Janssens, M.D., Ph.D.,[8] Anders Osterborg, M.D., Ph.D.,[9] Tadeusz Robak, M.D., Ph.D.,[10] Martin Simkovic, M.D., Ph.D.,[11] Don Stevens, M.D.,[12] Sergey Voloshin, M.D., Ph.D.,[13] Vladimir Vorobyev, Ph.D.,[14] Loic Ysebaert, M.D., Ph.D.,[15] Rui Qin, Ph.D.,[16] Andrew J. Steele, Ph.D.,[17] Natasha Schuier, M.D.,[18] Kurt Baeten, Ph.D.,[19] Donne Bennett Caces, M.D., Ph.D.,[16] and Carsten U. Niemann, M.D., Ph.D.,[20] for the GLOW Investigators*

GLOW Primary Endpoint: PFS by Independent Review Committee (IRC)



Kater AP et al. *NEJM Evid* 2022;1(7). Published May 13.

RTP RESEARCH TO PRACTICE

original reports

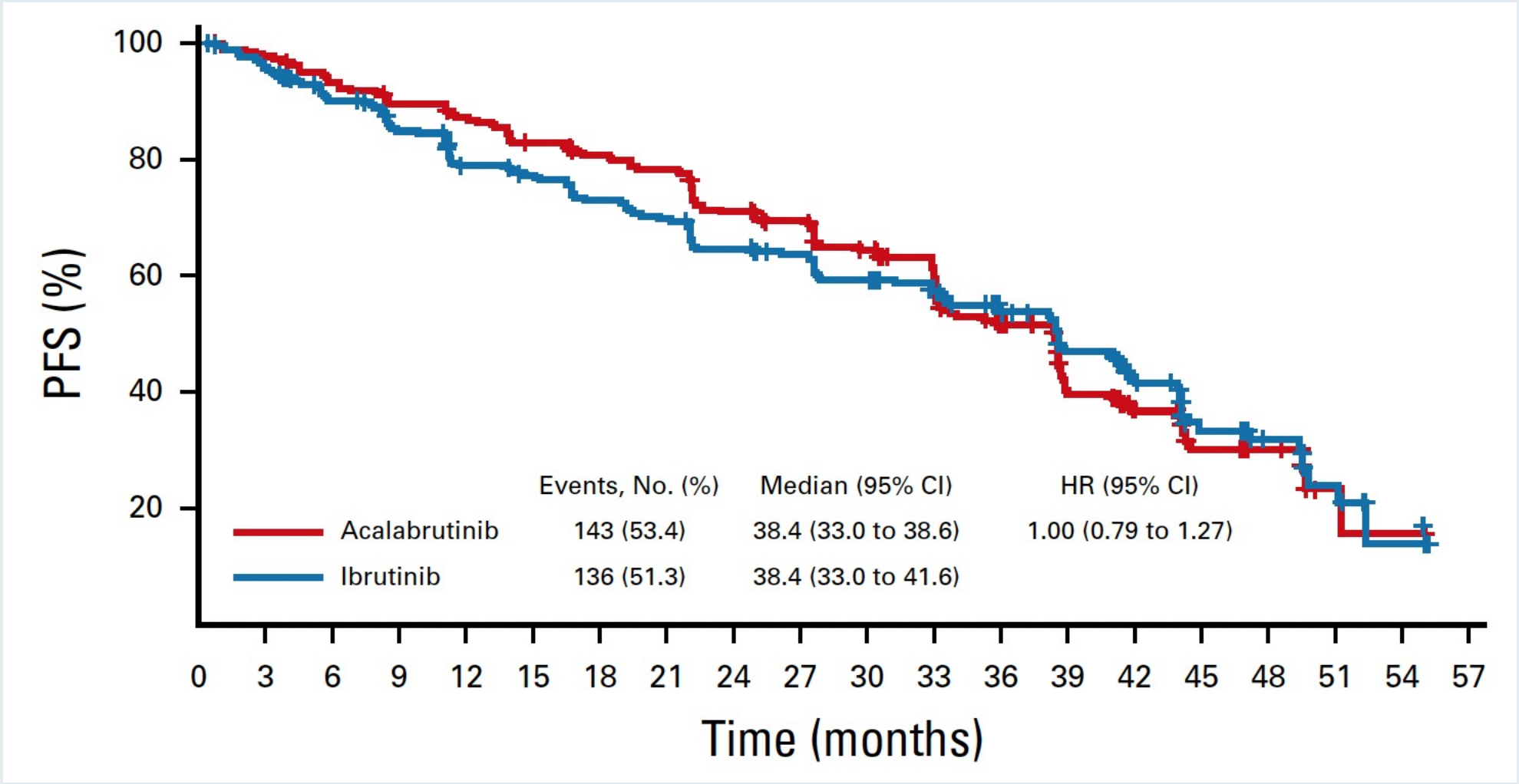
Acalabrutinib Versus Ibrutinib in Previously Treated Chronic Lymphocytic Leukemia: Results of the First Randomized Phase III Trial

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.

RTP RESEARCH TO PRACTICE

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%[j]	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

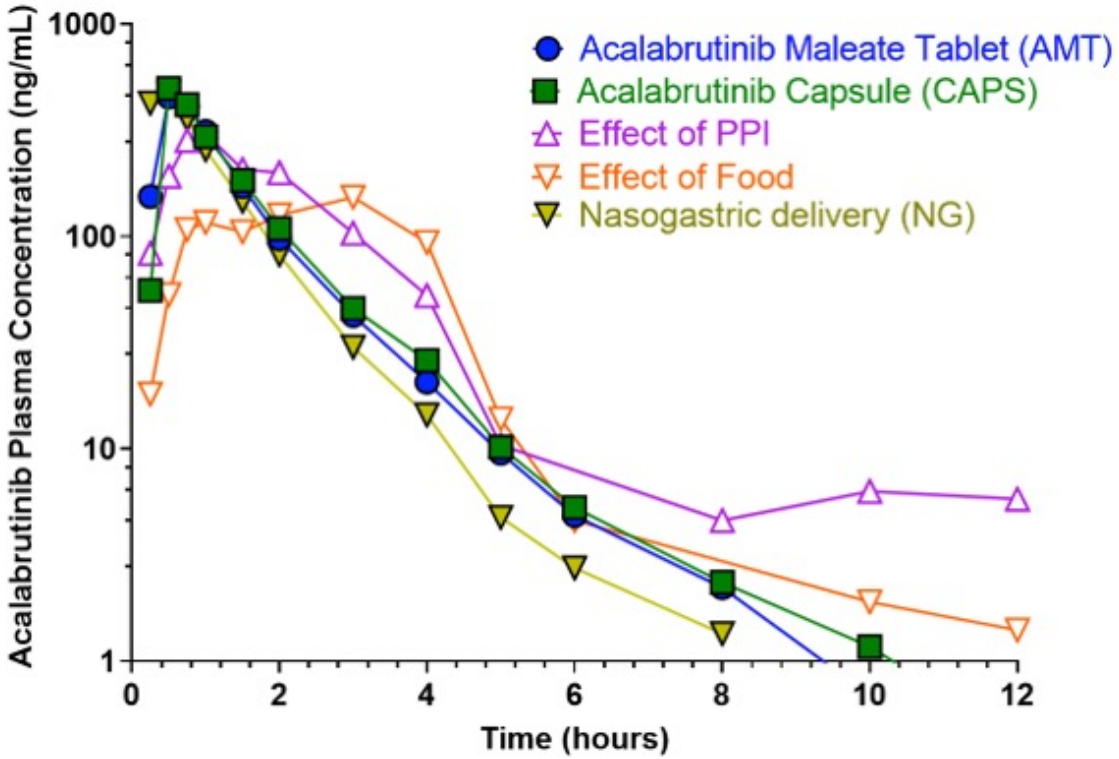
Seymour JF et al. ASH 2021;Abstract 3721.

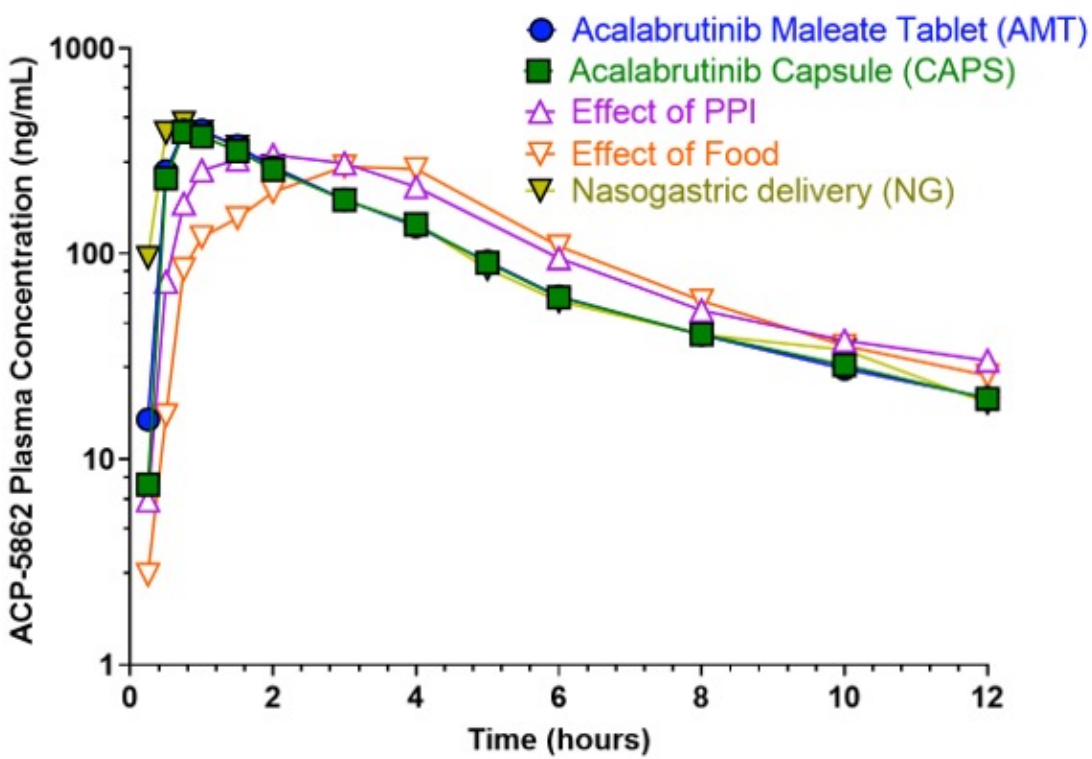
New Acalabrutinib Formulation Enables Co-Administration with Proton Pump Inhibitors and Dosing in Patients Unable to Swallow Capsules (ELEVATE-PLUS)

Sharma S et al.

ASH 2021;Abstract 4365.

ELEVATE-PLUS: Pharmacokinetic Profiles of Acalabrutinib and Its Major Pharmacologically Active Metabolite Across 3 Clinical Trials





Sharma S et al. ASH 2021;Abstract 4365.

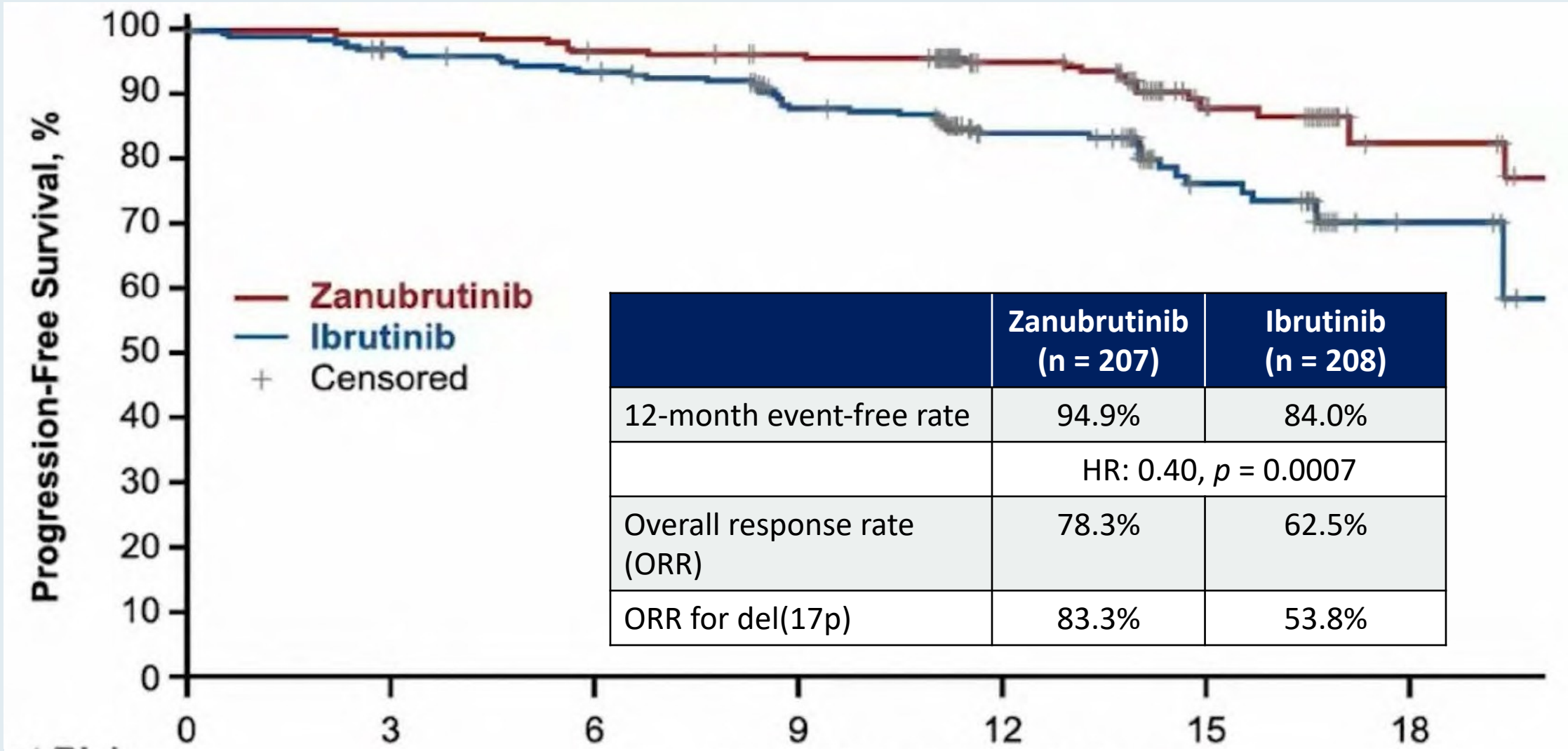
RTP RESEARCH TO PRACTICE

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	
Overall response rate (ORR)	78.3%	62.5%
ORR for del(17p)	83.3%	53.8%

Hillmen P et al. EHA 2021;Abstract LBA1900.

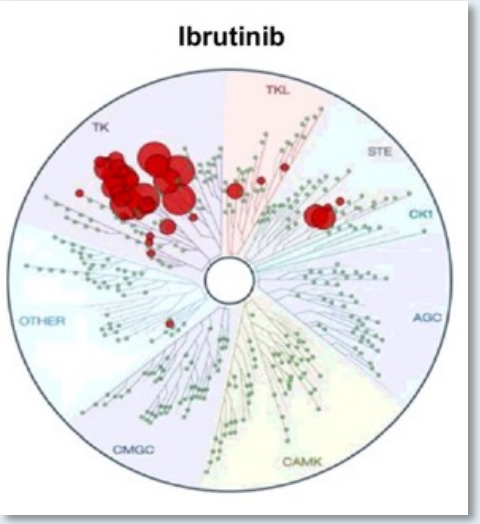
ALPINE: Adverse Events of Special Interest

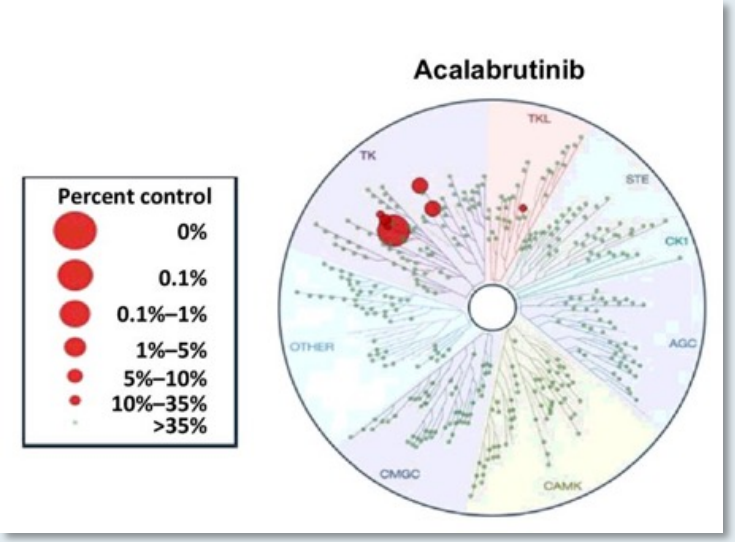
Safety Analysis Population	Zanubrutinib (n=204), n (%)		Ibrutinib (n=207), n (%)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Cardiac disorders[a]	28 (13.7)	5 (2.5)	52 (25.1)	14 (6.8)
Atrial fibrillation and flutter (key 2º endpoint)	**5 (2.5)**	**2 (1.0)**	**21 (10.1)**	**4 (1.9)**
Hemorrhage	73 (35.8)	6 (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.

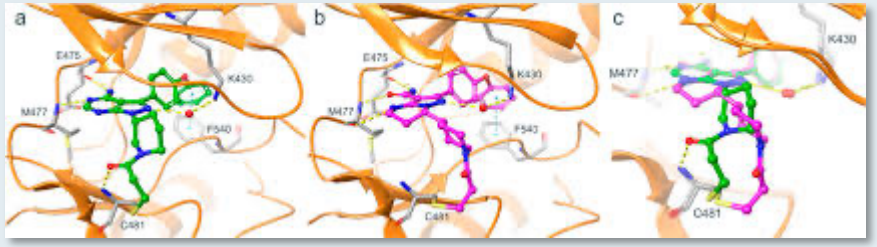
Overview of BTK Inhibitors in CLL

Irreversible



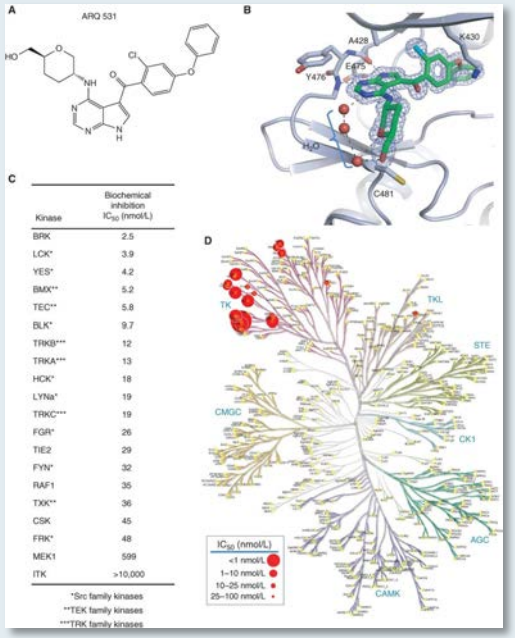


Zanubrutinib

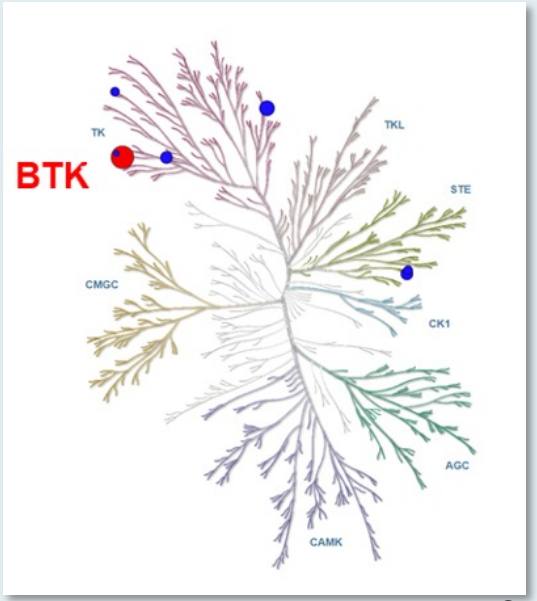


Reversible

ARQ-531 (MK-1026)



Pirtobrutinib (LOXO-305)



Courtesy of Matthew S Davids, MD, MMSc

EHA EUROPEAN HEMATOLOGY ASSOCIATION

EHA2022 HYBRID JUNE 9-17 VIENNA

Pirtobrutinib, A Highly Selective, Non-Covalent (Reversible) BTK Inhibitor In Previously Treated CLL/SLL: Updated Results From The Phase 1/2 BRUIN Study

Anthony R. Mato[1], John M. Pagel[2], Catherine C. Coombs[3], Nirav N. Shah[4], Nicole Lamanna[5], Talha Munir[6], Ewa Lech-Maranda[7], Toby A. Eyre[8], Jennifer A. Woyach[9], William G. Wierda[10], Chan Y. Cheah[11], Jonathon B. Cohen[12], Lindsey E. Roeker[1], Manish R. Patel[13], Bita Fakhri[14], Minal A. Barve[15], Constantine S. Tam[16], David J. Lewis[17], James N. Gerson[18], Alvaro J. Alencar[19], Chaitra S. Ujjani[20], Ian W. Flinn[21], Suchitra Sundaram[22], Shuo Ma[23], Deepa Jagadeesh[24], Joanna M. Rhodes[25], Justin Taylor[19], Omar Abdel-Wahab[1], Paolo Ghia[26], Stephen J. Schuster[18], Denise Wang[27], Binoj Nair[27], Edward Zhu[27], Donald E. Tsai[27], Matthew S. Davids[28], Jennifer R. Brown[28], Wojciech Jurczak[29]

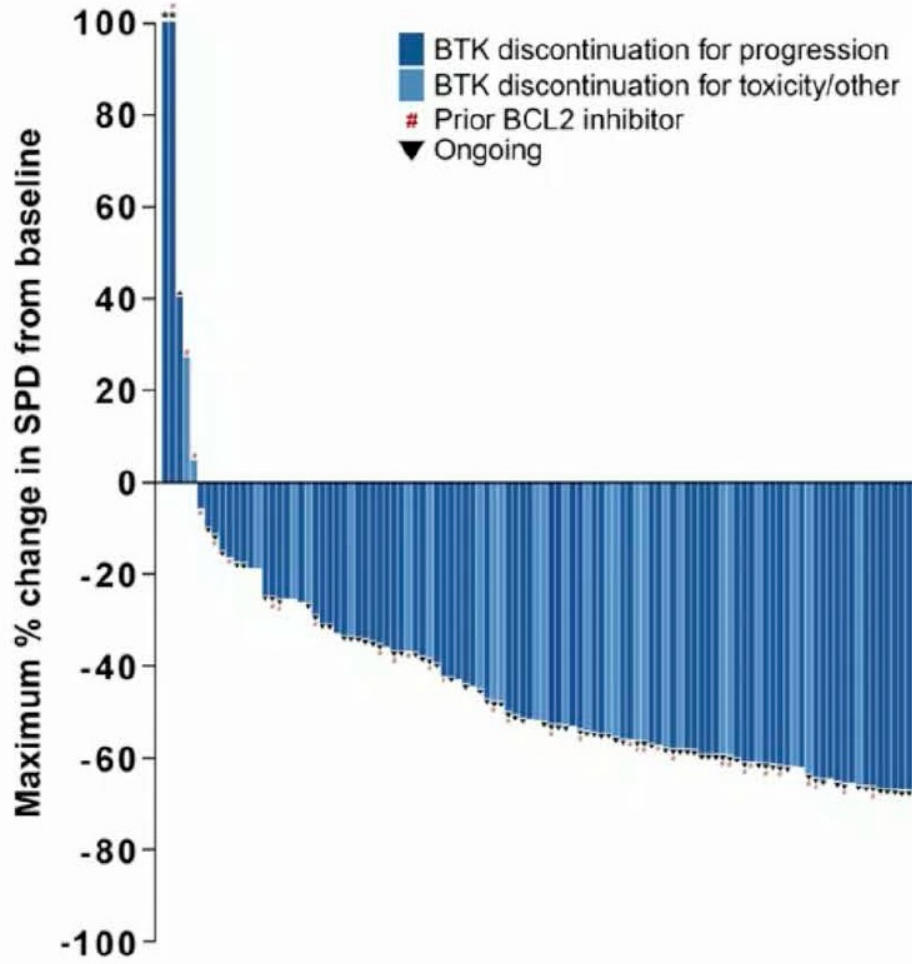
[1]Memorial Sloan Kettering Cancer Center, New York, USA; [2]Swedish Cancer Institute, Seattle, USA; [3]University of North Carolina at Chapel Hill, Chapel Hill, USA; [4]Medical College of Wisconsin, Milwaukee, USA; [5]Herbert Irving Comprehensive Cancer Center, Columbia University, New York, USA; [6]Department of Haematology, St. James's University Hospital, Leeds, UK; [7]Institute of Hematology and Transfusion Medicine, Warsaw, Poland; [8]Oxford University Hospitals NHS Foundation Trust, Churchill Cancer Center, Oxford, UK; [9]The Ohio State University Comprehensive Cancer Center, Columbus, USA; [10]MD Anderson Cancer Center, Houston, USA; [11]Linear Clinical Research and Sir Charles Gairdner Hospital, Perth, Australia; [12]Winship Cancer Institute, Emory University, Atlanta, GA, USA; [13]Florida Cancer Specialists/Sarah Cannon Research Institute, Sarasota, USA; [14]University of California San Francisco, San Francisco, USA; [15]Mary Crowley Cancer Research, Dallas, USA; [16]Peter MacCallum Cancer Center, Royal Melbourne Hospital, and University of Melbourne, Melbourne, Australia; [17]Plymouth Hospitals NHS Trust - Derriford Hospital, Plymouth, UK; [18]Lymphoma Program, Abramson Cancer Center, University of Pennsylvania, Philadelphia, USA; [19]University of Miami Miller School of Medicine, Miami, USA; [20]Fred Hutchinson Cancer Research Center, [21]Sarah Cannon Research Institute, Nashville, USA; [22]Department of Hematology and Medical Oncology, Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, NY, [23]Robert H. Lurie Comprehensive Cancer Center of Northwestern University, Chicago, IL, USA; [24]Cleveland Clinic, Cleveland, OH, USA; [25]Northwell Health Cancer Institute, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell Health, New Hyde Park, NY; [26]Università Vita-Salute San Raffaele and IRCCS Ospedale San Raffaele, Milan, Italy; [27]Loxo Oncology at Lilly, Stamford, CT, USA; [28]Dana-Farber Cancer Institute and Harvard Medical School, Boston, USA; [29]Maria Sklodowska-Curie National Research Institute of Oncology, Krakow, Poland

Anthony R. Mato

Abstract S147

RTP RESEARCH TO PRACTICE

BRUIN: Pirtobrutinib Efficacy in BTK-Pretreated CLL/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. EHA 2022;Abstract S147.

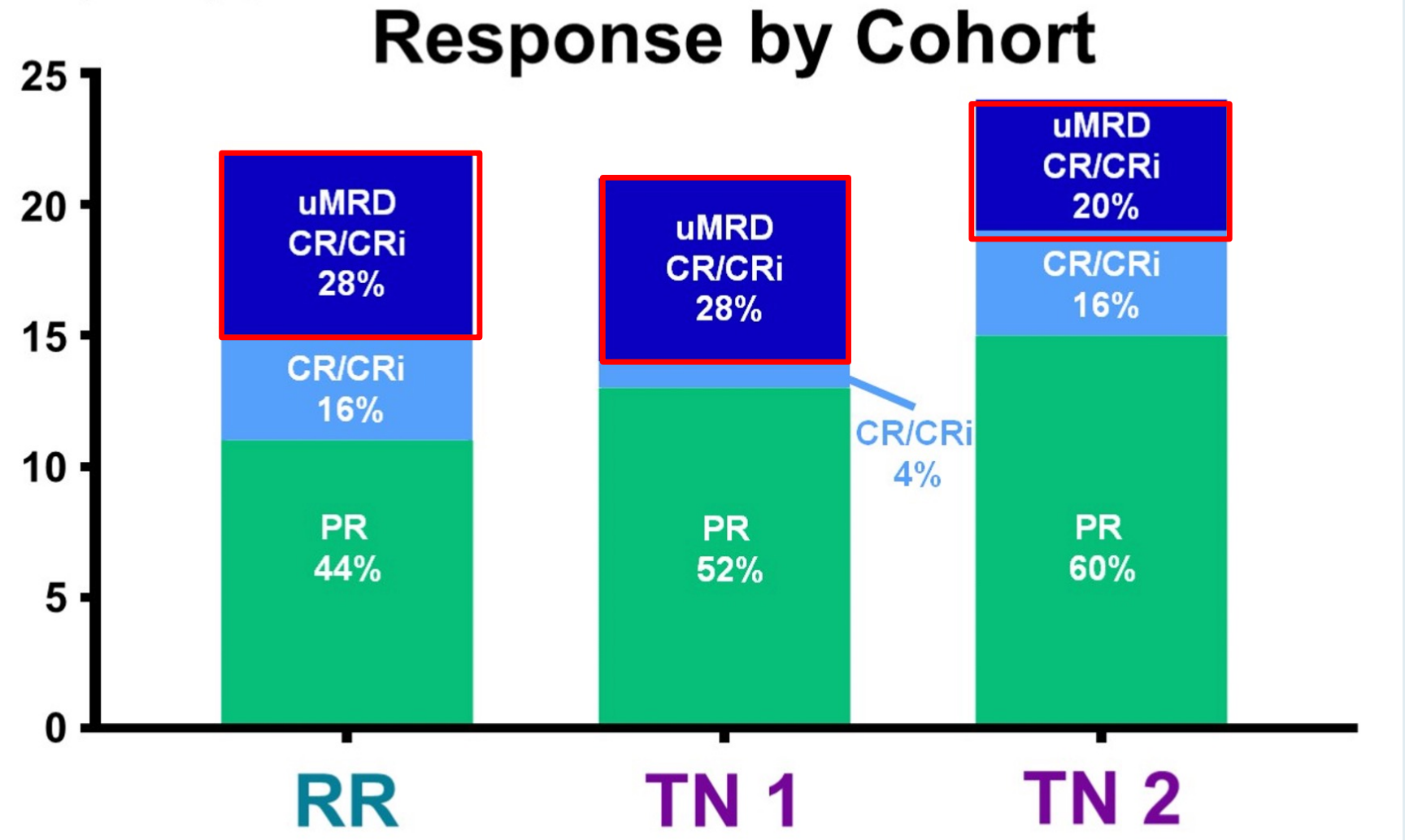
RTP RESEARCH TO PRACTICE

Four-Year Follow-Up from a Phase 2 Study of Obinutuzumab, Ibrutinib, and Venetoclax in CLL

Rogers KA et al.

ASCO 2022;Abstract 7540.

Primary Endpoint: Complete Response with Undetectable MRD (uMRD)



Rogers KA et al. ASCO 2022;Abstract 7540.

RTP RESEARCH TO PRACTICE

Chronic Lymphocytic Leukemia and Lymphomas Agenda

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

Module 2: Chronic Lymphocytic Leukemia (CLL)

Module 3: Hodgkin Lymphoma

- Front-line management of advanced-stage HL: ABVD vs BV-AVD
- Older patients with HL; role of IOs

Module 4: Mantle Cell Lymphoma (MCL)

Module 5: Follicular Lymphoma (FL)

RTP RESEARCH TO PRACTICE

N Engl J Med July 13 2022;[Online ahead of print].

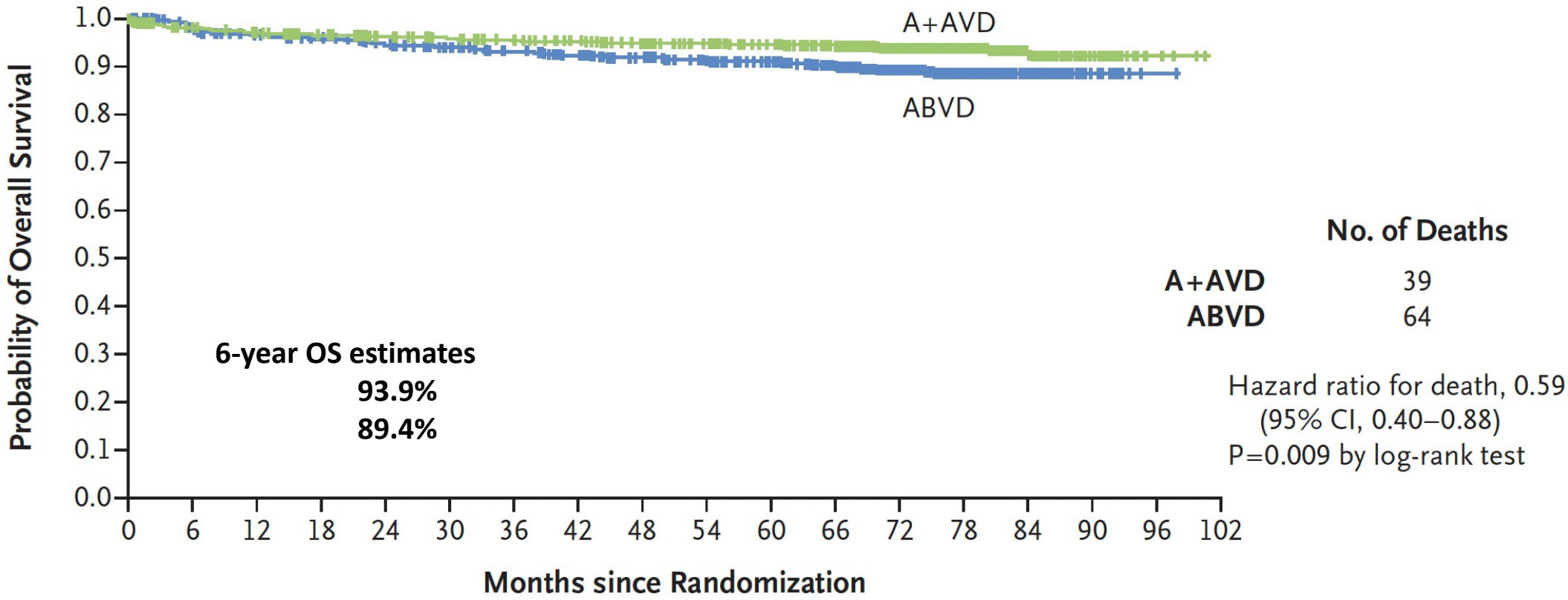
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Overall Survival with Brentuximab Vedotin in Stage III or IV Hodgkin's Lymphoma

Stephen M. Ansell, M.D., Ph.D., John Radford, M.D., Joseph M. Connors, M.D., Monika Długosz-Danecka, M.D., Ph.D., Won-Seog Kim, M.D., Andrea Gallamini, M.D., Radhakrishnan Ramchandren, M.D., Jonathan W. Friedberg, M.D., Ranjana Advani, M.D., Martin Hutchings, Ph.D., Andrew M. Evens, D.O., Piotr Smolewski, M.D., Ph.D., Kerry J. Savage, M.D., Nancy L. Bartlett, M.D., Hyeon-Seok Eom, M.D., Ph.D., Jeremy S. Abramson, M.D., Cassie Dong, Ph.D., Frank Campana, M.D., Keenan Fenton, M.D., Markus Puhlmann, M.D., and David J. Straus, M.D., for the ECHELON-1 Study Group*

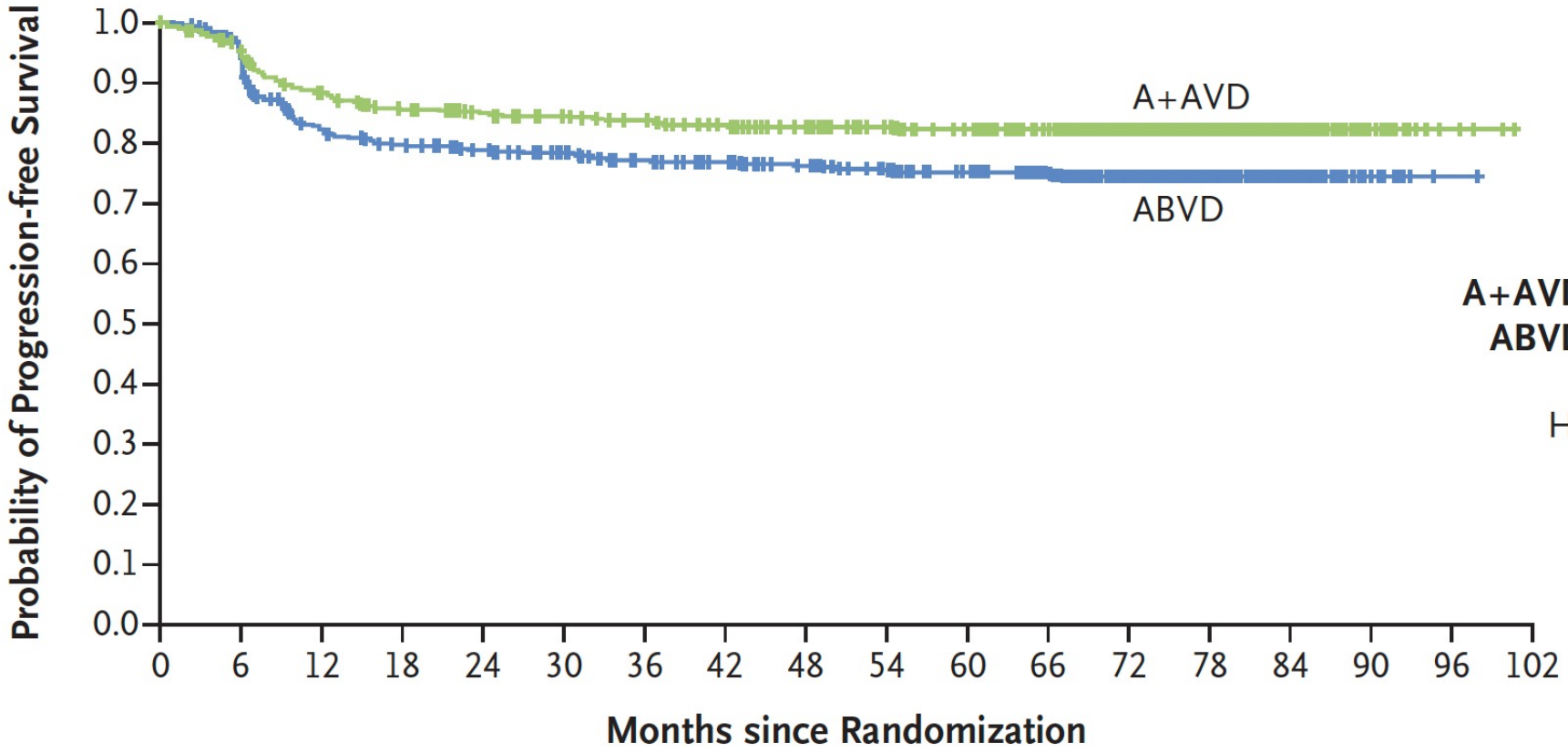
ECHELON-1 Primary Endpoint: Overall Survival (ITT Population)



A + AVD = brentuximab vedotin with doxorubicin, vinblastine and dacarbazine; ABVD = doxorubicin, bleomycin, vinblastine and dacarbazine

Ansell SM et al. *N Engl J Med* July 13 2022;[Online ahead of print].

ECHELON-1: Progression-Free Survival (ITT Population)



No. of Events

A+AVD	112
ABVD	159

Hazard ratio for disease progression or death, 0.68 (95% CI, 0.53–0.86)

No. at Risk

A+AVD	664	619	563	537	520	508	496	480	463	448	428	400	305	179	86	24	4	0
ABVD	670	612	520	501	485	465	442	432	414	391	371	338	245	154	67	9	1	0

A + AVD = brentuximab vedotin with doxorubicin, vinblastine and dacarbazine; ABVD = doxorubicin, bleomycin, vinblastine and dacarbazine

Ansell SM et al. *N Engl J Med* July 13 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

original reports

Brentuximab Vedotin Plus AVD for First-Line Treatment of Early-Stage Unfavorable Hodgkin Lymphoma (BREACH): A Multicenter, Open-Label, Randomized, Phase II Trial

Luc-Matthieu Fornecker, MD, PhD[1]; Julien Lazarovici, MD[2]; Igor Aurer, MD, PhD[3]; René-Olivier Casasnovas, MD[4]; Anne-Claire Gac, MD[5]; Christophe Bonnet, MD[6]; Krimo Bouabdallah, MD[7]; Pierre Feugier, MD[8]; Lena Specht, MD[9]; Lysiane Molina, MD[10]; Mohamed Touati, MD[11]; Cécile Borel, MD[12]; Aspasia Stamatoullas, MD[13]; Emmanuelle Nicolas-Virelizier, MD[14]; Laurent Pascal, MD[15]; Pieternella Lugtenburg, MD, PhD[16]; Nicola Di Renzo, MD[17]; Thierry Vander Borght, MD, PhD[18]; Alexandra Traverse-Glehen, MD[19]; Peggy Dartigues, MD[2]; Martin Hutchings, MD[20]; Annibale Versari, MD[21]; Michel Meignan, MD[22]; Massimo Federico, MD[23]; and Marc André, MD[18] for the LYSA-FIL-EORTC Intergroup

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

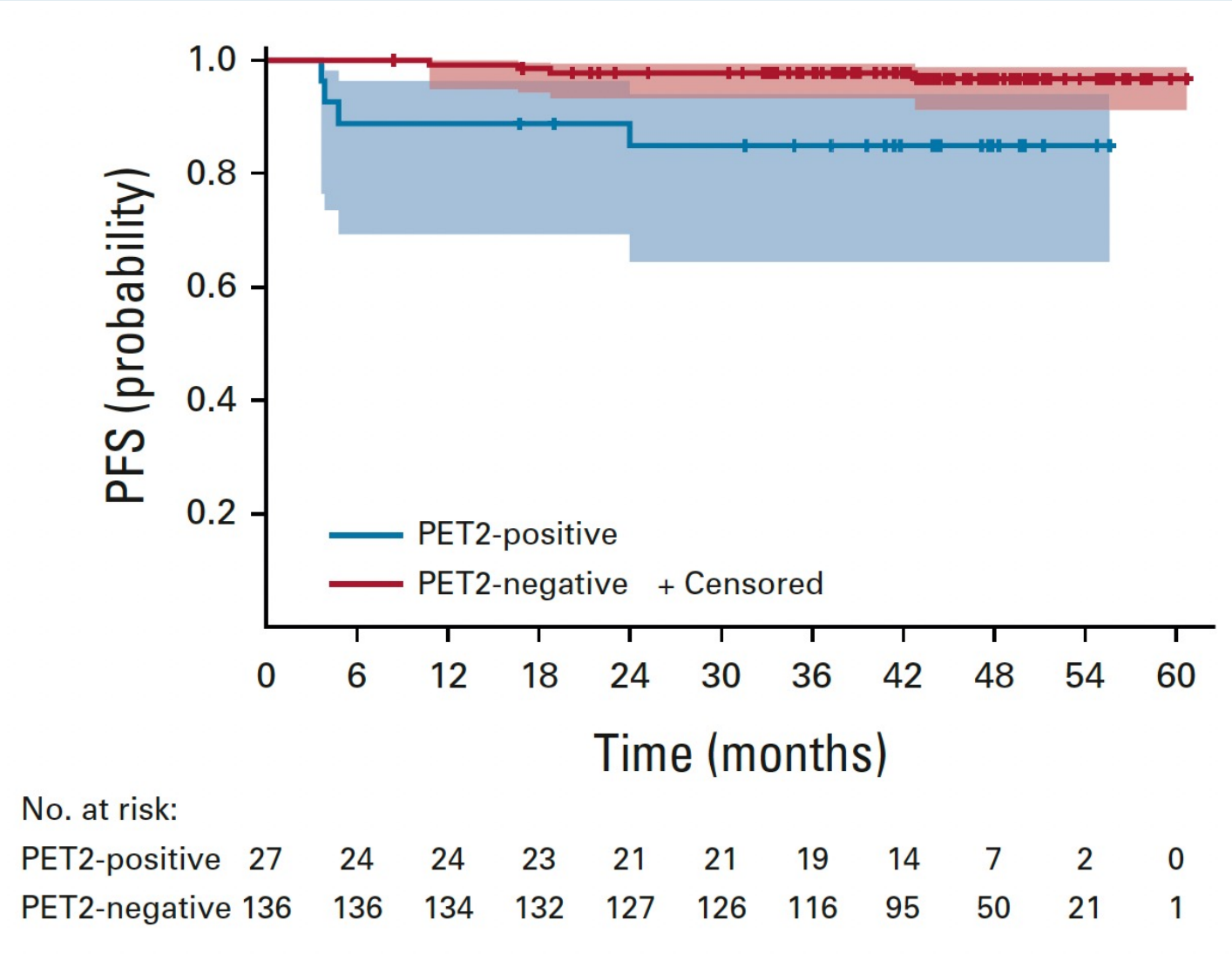
BREACH: PET Response After 2 Cycles

Response	BV-AVD (n = 113)	ABVD (n = 57)
PET response after two cycles		
Deauville 1	4 (4)	4 (7)
Deauville 2	34 (30)	22 (39)
Deauville 3	55 (49)	17 (30)
Deauville 4	13 (12)	8 (14)
Deauville 5	3 (3)	3 (5)
Not evaluated	4 (4)	3 (5)

BV-AVD = brentuximab vedotin with doxorubicin, vinblastine and dacarbazine; ABVD = doxorubicin, bleomycin, vincristine and dacarbazine

Fornecker LM et al. *J Clin Oncol* 2022;[Online ahead of print].

BREACH: PFS by PET Status After 2 Cycles



No. at risk:

PET2-positive	27	24	24	23	21	21	19	14	7	2	0
PET2-negative	136	136	134	132	127	126	116	95	50	21	1

Fornecker LM et al. *J Clin Oncol* 2022;[Online ahead of print].

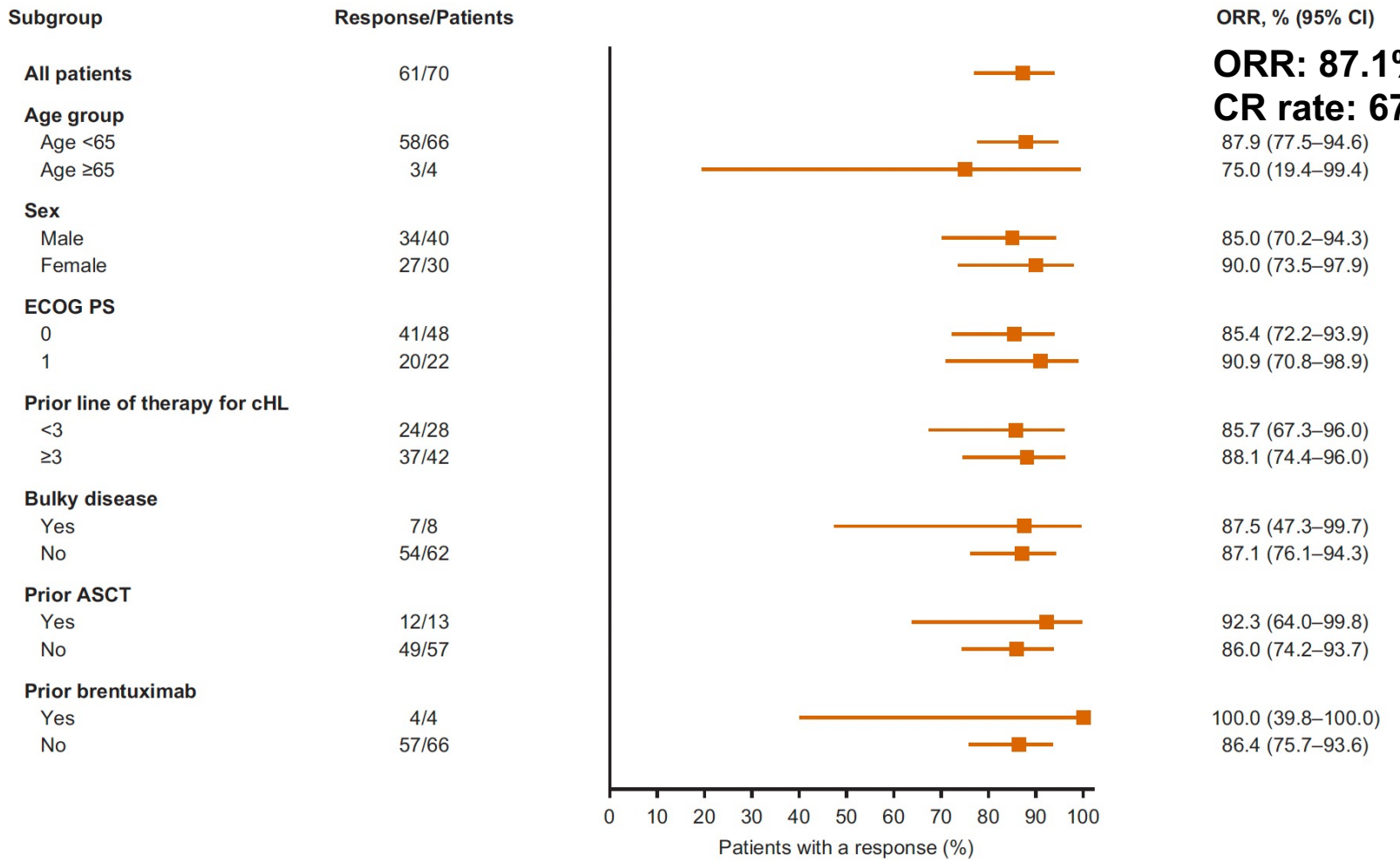
Clin Cancer Res 2022;28(6):1147-56.

CLINICAL CANCER RESEARCH | CLINICAL TRIALS: IMMUNOTHERAPY

Tislelizumab for Relapsed/Refractory Classical Hodgkin Lymphoma: 3-Year Follow-up and Correlative Biomarker Analysis

Yuqin Song[1], Quanli Gao[2], Huilai Zhang[3], Lei Fan[4], Jianfeng Zhou[5], Dehui Zou[6], Wei Li[7], Haiyan Yang[8], Ting Liu[9], Quanshun Wang[10], Fangfang Lv[11], Haiyi Guo[12], Xia Zhao[12], Dan Wang[12], Pei Zhang[12], Yidi Wang[12], Lei Wang[12], Tengfei Liu[12], Yun Zhang[12], Zhirong Shen[12], Jane Huang[12], and Jun Zhu[1]

Response and Survival with Tislelizumab for Relapsed/Refractory Classical Hodgkin Lymphoma



ORR: 87.1%
CR rate: 67.1%

mPFS: 31.5 mo
3-y PFS: 40.8%
3-y OS: 84.8%

ORR = overall response rate

Song U et al. *Clin Cancer Res* 2022;28(6):1147-56.

RTP RESEARCH TO PRACTICE

Tislelizumab: Treatment-Emergent and Treatment-Related Adverse Events

	Tislelizumab ($N = 70$)			
	TEAE		TRAE	
N (%)	All grades	Grade ≥3	All grades	Grade ≥3
Patients with ≥1 AE	68 (97.1)	29 (41.4)	68 (97.1)	22 (31.4)
Pyrexia	40 (57.1)	0	38 (54.3)	0
Upper respiratory tract infection	27 (38.6)	2 (2.9)	17 (24.3)	0
Hypothyroidism	26 (37.1)	0	26 (37.1)	0
Weight increased	24 (34.3)	2 (2.9)	19 (27.1)	2 (2.9)
White blood cell count decreased	15 (21.4)	1 (1.4)	14 (20.0)	0
Cough	15 (21.4)	0	9 (12.9)	0
Alanine aminotransferase increased	14 (20.0)	0	14 (20.0)	0
Pruritus	13 (18.6)	0	12 (17.1)	0
Weight decreased	12 (17.1)	0	8 (11.4)	0
Aspartate aminotransferase increased	11 (15.7)	0	8 (11.4)	0
Rash	11 (15.7)	1 (1.4)	11 (15.7)	1 (1.4)
Neutrophil count decreased	10 (14.3)	2 (2.9)	9 (12.9)	1 (1.4)
Hyperuricemia	10 (14.3)	0	7 (10.0)	0
Diarrhea	10 (14.3)	0	6 (8.6)	0
Anemia	9 (12.9)	1 (1.4)	4 (5.7)	0
Blood creatine phosphokinase increased	8 (11.4)	2 (2.9)	8 (11.4)	2 (2.9)
Blood thyroid stimulating hormone increased	8 (11.4)	0	8 (11.4)	0
Blood bilirubin increased	7 (10.0)	0	7 (10.0)	0
Platelet count decreased	7 (10.0)	0	6 (8.6)	0
Pneumonia	7 (10.0)	2 (2.9)	6 (8.6)	1 (1.4)
Vomiting	7 (10.0)	0	5 (7.1)	0
Headache	7 (10.0)	1 (1.4)	5 (7.1)	1 (1.4)
Neutropenia	4 (5.7)	2 (2.9)	3 (4.3)	2 (2.9)
Hypertension	3 (4.3)	2 (2.9)	3 (4.3)	2 (2.9)
Lipase increased	2 (2.9)	2 (2.9)	2 (2.9)	2 (2.9)
Pneumonitis	2 (2.9)	2 (2.9)	2 (2.9)	2 (2.9)

Song U et al. *Clin Cancer Res* 2022;28(6):1147-56.

Chronic Lymphocytic Leukemia and Lymphomas Agenda

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

Module 2: Chronic Lymphocytic Leukemia (CLL)

Module 3: Hodgkin Lymphoma

Module 4: Mantle Cell Lymphoma (MCL)

- Addition of BTKi to first-line systemic treatment
- Second-line treatment, role of venetoclax; Timing and selection of patients for consideration of CAR T-cell therapy with brexucabtagene autoleucel

Module 5: Follicular Lymphoma (FL)

ORIGINAL ARTICLE

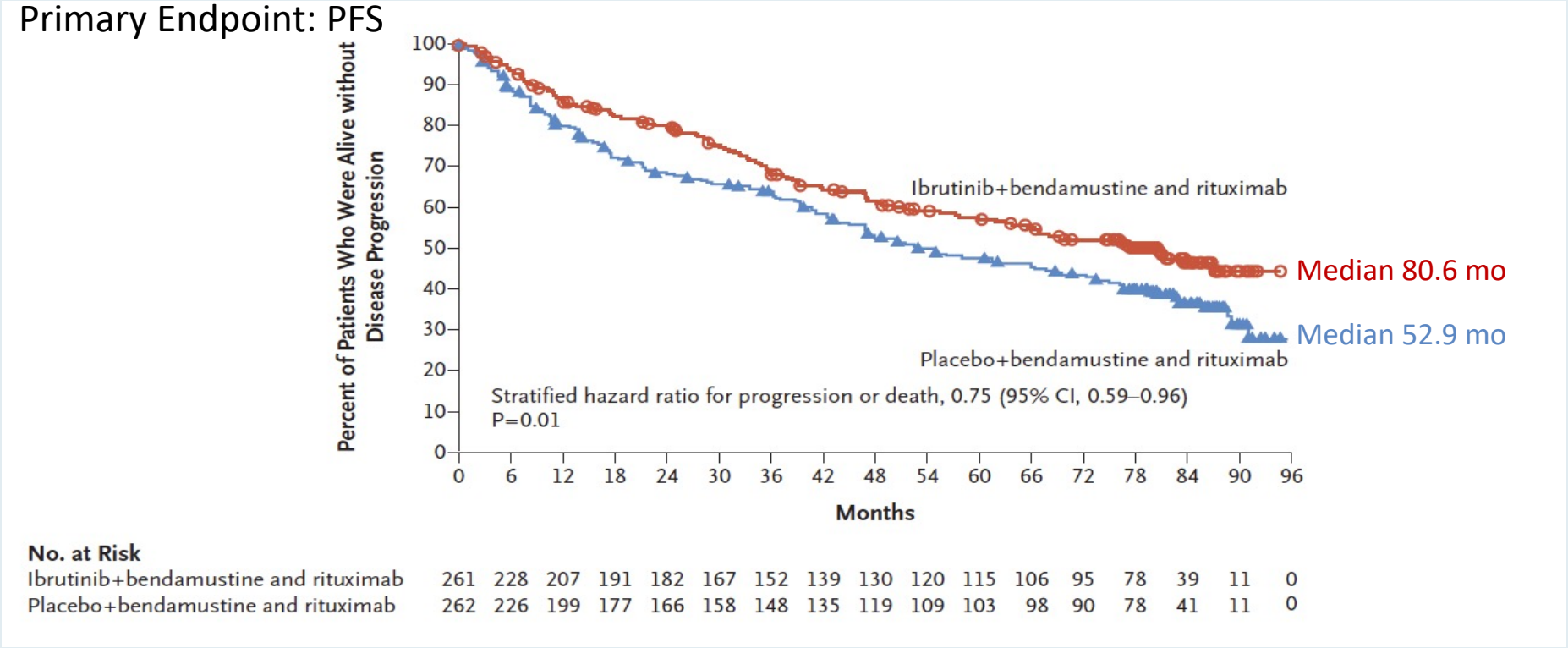
Ibrutinib plus Bendamustine and Rituximab in Untreated Mantle-Cell Lymphoma

Michael L. Wang, M.D., Wojciech Jurczak, M.D., Ph.D., Mats Jerkeman, M.D., Ph.D., Judith Trotman, F.R.A.C.P., Pier L. Zinzani, M.D., Ph.D., David Belada, M.D., Ph.D., Carola Boccomini, M.D., Ian W. Flinn, M.D., Ph.D., Pratyush Giri, F.R.A.C.P., Andre Goy, M.D., Paul A. Hamlin, M.D., Olivier Hermine, M.D., Ph.D., José-Ángel Hernández-Rivas, M.D., Ph.D., Xiaonan Hong, M.D., Seok Jin Kim, M.D., Ph.D., David Lewis, F.R.C.Path., Ph.D., Yuko Mishima, M.D., Ph.D., Muhit Özcan, M.D., Guilherme F. Perini, M.D., Christopher Pocock, M.D., Ph.D., Yuqin Song, M.D., Ph.D., Stephen E. Spurgeon, M.D., John M. Storring, M.D., Jan Walewski, M.D., Jun Zhu, M.D., Ph.D., Rui Qin, Ph.D., Todd Henninger, Ph.D., Sanjay Deshpande, M.D., Angela Howes, Ph.D., Steven Le Gouill, M.D., Ph.D., and Martin Dreyling, M.D., for the SHINE Investigators*

N Engl J Med 2022;386(26):2482-94.

SHINE: A Phase III Trial of Ibrutinib with Bendamustine and Rituximab for MCL

Primary Endpoint: PFS



- The proportion of patients with a complete response was 65.5% in the ibrutinib group and 57.6% in the placebo group (p = 0.06)
- Overall survival was similar in the 2 groups (HR 1.07)
- The safety profile of the combined therapy was consistent with the known profiles of the individual drugs

Wang ML et al. *N Engl J Med* 2022;386(26):2482-94.

RTP RESEARCH TO PRACTICE

original reports

Ibrutinib With Rituximab in First-Line Treatment of Older Patients With Mantle Cell Lymphoma

Preetesh Jain, MD, DM, PhD[1]; Shuangtao Zhao, PhD[2]; Hun Ju Lee, MD[1]; Holly A. Hill, MPH[1]; Chi Young Ok, MD[3]; Rashmi Kanagal-Shamanna, MD[3]; Fredrick B. Hagemeister, MD[1]; Nathan Fowler, MD[1]; Luis Fayad, MD[1]; Yixin Yao, PhD[1]; Yang Liu, PhD[1]; Omar B. Moghrabi, BS[1]; Lucy Navsaria, MBBS[1]; Lei Feng, MS[4]; Graciela M. Nogueras Gonzalez, MPH[4]; Guofan Xu, MD[5]; Selvi Thirumurthi, MD[6]; David Santos, MD[7]; Cezar Iliescu, MD[8]; Guilin Tang, MD, PhD[3]; L. Jeffrey Medeiros, MD[3]; Francisco Vega, MD, PhD[3]; Michelle Avellaneda, BS[1]; Maria Badillo, BS[1]; Christopher R. Flowers, MD[1]; Linghua Wang, PhD[2]; and Michael L. Wang, MD[1]

J Clin Oncol 2021;40:202-12.

RTP RESEARCH TO PRACTICE

Three-Year Follow-Up of Outcomes With KTE-X19 in Patients With Relapsed/Refractory Mantle Cell Lymphoma in ZUMA-2

Michael L. Wang, MD[1]; Javier Munoz, MD, MS, FACP[2]; Andre Goy, MD[3]; Frederick L. Locke, MD[4]; Caron A. Jacobson, MD, MMSc[5]; Brian T. Hill, MD, PhD[6]; John M. Timmerman, MD[7]; Houston Holmes, MD, MBA, FACP[8]; Ian W. Flinn, MD, PhD[9]; David B. Miklos, MD, PhD[10]; John M. Pagel, MD, PhD, DSc[11]; Marie José Kersten, MD, PhD[12]; Roch Houot, MD, PhD[13]; Amer Beitinjaneh, MD[14]; Weimin Peng, PhD[15]; Xiang Fang, PhD[15]; Rhine R. Shen, PhD[15]; Rubina Siddiqi, PhD[15]; Ioana Kloos, MD[15]; Patrick M. Reagan, MD[16]

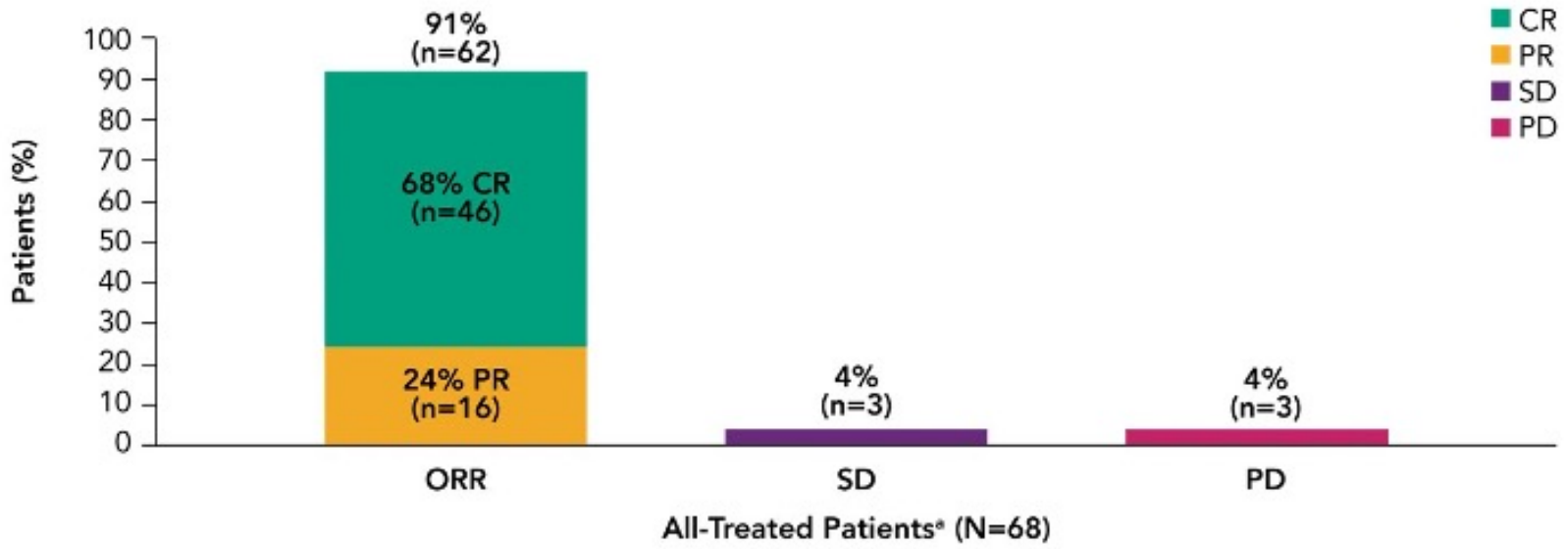
[1]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Banner MD Anderson Cancer Center, Gilbert, AZ, USA; [3]John Theurer Cancer Center, Hackensack University, Hackensack, NJ, USA; [4]Moffitt Cancer Center, Tampa, FL, USA; [5]Dana-Farber Cancer Institute, Boston, MA, USA; [6]Cleveland Clinic Foundation, Cleveland, OH, USA; [7]David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; [8]Texas Oncology, Dallas, TX, USA; [9]Sarah Cannon Research Institute and Tennessee Oncology, Nashville, TN, USA; [10]Stanford University School of Medicine, Stanford, CA, USA; [11]Swedish Cancer Institute, Seattle, WA, USA; [12]Amsterdam UMC, University of Amsterdam, Amsterdam, Cancer Center Amsterdam, The Netherlands, on behalf of HOVON/LLPC; [13]CHU Rennes, Université Rennes, INSERM & EFS, Rennes, France; [14]University of Miami, Miami, FL, USA; [15]Kite, a Gilead Company, Santa Monica, CA; and [16]University of Rochester Medical Center, Rochester, NY, USA

Disclosures

Michael L. Wang: honoraria from Janssen, Acerta Pharma, OMI, Physicians' Education Resources, Dava Oncology, CAHON, Hebei Cancer Prevention Federation, Clinical Care Options, Mumbai Hematology Group, Anticancer Association, Newbridge Pharmaceuticals; consultancy or advisory role for InnoCare, Loxo Oncology, Juno, Oncternal, CStone, AstraZeneca, Janssen, VelosBio, Pharmacyclics, Genentech, Bayer Healthcare; research funding from Kite, Pharmacyclics, Janssen, AstraZeneca, Celgene, Loxo Oncology, Juno, BioInvent, VelosBio, Acerta Pharma, Oncternal, Verastem, Molecular Templates, Lilly, InnoCare.

ASCO 2022;Abstract 7518

ZUMA-2 Three-Year Follow-Up: Objective Response Rate (ORR) with Brexucabtagene Autoleucel for All Patients Receiving Treatment (N = 68)

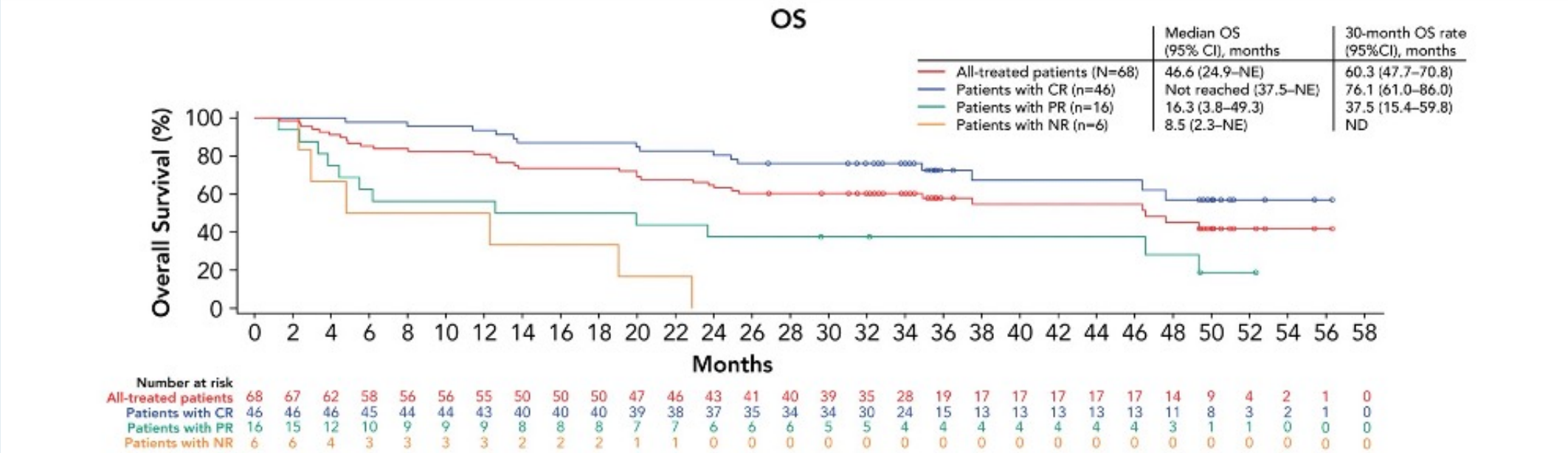


- After a median follow-up of 35.6 months (range, 25.9-56.3), the ORR (CR + partial response [PR]) was 91% (95% CI, 81.8-96.7), with a 68% CR rate (95% CI, 55.2-78.5) and a median DOR of 28.2 months (95% CI, 13.5-47.1)
- In the ITT population, ORR was 84% (95% CI, 73.4-91.3), with a 62% CR rate (95% CI, 50.1-73.2)

With 3-years of follow-up, these data demonstrate that a single infusion of KTE-X19 resulted in high rates of durable responses in R/R MCL.

Wang ML et al. ASCO 2022;Abstract 7518.

ZUMA-2 Three-Year Follow-Up: Overall Survival with Brexucabtagene Autoleucel for All Patients Receiving Treatment (N = 68)



- The median progression-free survival (PFS) was 25.8 months, as shown in the full poster
- In the ITT population (data not shown), the median PFS was 24.0 months and the median OS was 47.4 months

Median OS among treated patients was 46.6 months and was not reached among those who achieved CR.

Wang ML et al. ASCO 2022;Abstract 7518.

RTP RESEARCH TO PRACTICE

ZUMA-2 Three-Year Follow-Up: Overall Adverse Events (AEs) and AEs Occurring Since the Primary Analysis Report

	All-Treated Patients (N=68)				
	Overall AEs Occurring Since Infusion	AEs Occurring Since the Primary Analysis Report			
		Any Grade	Grade 3	Grade 4	Grade 5
AEs, n (%)					
Any	68 (100)	18 (26)	4 (6)	7 (10)	3 (4)
Any KTE-X19–related	66 (97)	9 (13)	2 (3)	6 (9)	0
Serious AEs, n (%)					
Any	48 (71)	8 (12)	4 (6)	0	3 (4)
Serious KTE-X19–related	37 (54)	2 (3)	2 (3)	0	0
CRS or neurologic events, n (%)	63 (93)	2 (3)	1 (1)	0	0
CRS[a]	62 (91)	0	0	0	0
Neurologic events	43 (63)	2 (3)	1 (1)[b]	0	0
Serious neurologic event	22 (32)	1 (1)	1 (1)[b]	0	0
Cytopenias, n (%)					
Thrombocytopenia	50 (74)	2 (3)	0	2 (3)	0
Neutropenia	59 (87)	8 (12)	1 (1)	7 (10)	0
Anemia	47 (69)	3 (4)	2 (3)	0	0
Infection, n (%)					
Any	36 (53)	7 (10)	3 (4)	0	1 (1)
Serious	21 (31)	4 (6)	3 (4)	0	1 (1)
COVID-19 associated viral	0	0	0	0	0
Non–COVID-19 associated viral	11 (16)	3 (4)	1 (1)	0	0
Hypogammaglobulinemia, n (%)	14 (21)	1 (1)	0	0	0
Tumor lysis syndrome, n (%)	1 (1)	0	0	0	0

Data cutoff for the primary analysis was July 19, 2019[1]; data cutoff for the present analysis was July 24, 2021. Numbers (percentage) of patients with worst grade of AE are shown; AEs occurring after retreatment are not included. [a]CRS events were graded per revised Lee et al. 2014 grading system[17]; all other AEs were graded per Common Terminology Criteria for Adverse Events version 4.03. [b]This serious neurologic event of encephalopathy began on day 397; the event resolved on day 408 and was considered unrelated to KTE-X19. AE, adverse event; CRS, cytokine release syndrome; KTE-X19, brexucabtagene autoleucel. 1. Wang M, et al. N Engl J Med. 2020;382:1331-1342.

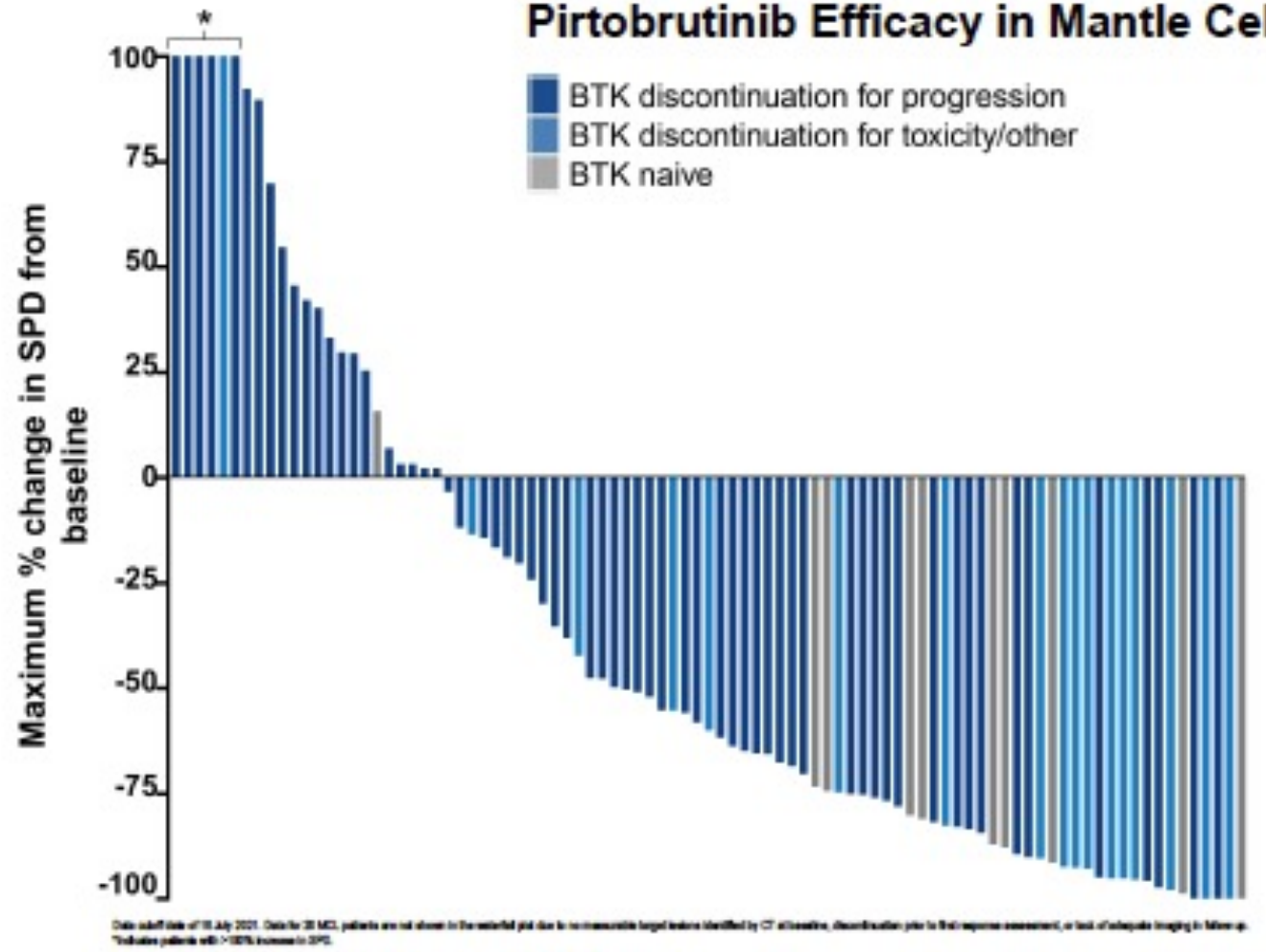
Wang ML et al. ASCO 2022;Abstract 7518.

Pirtobrutinib, a Highly Selective, Non-Covalent (Reversible) BTK Inhibitor in Previously Treated Mantle Cell Lymphoma: Updated Results from the Phase 1/2 BRUIN Study

Lewis K et al.

Pan Pacific Lymphoma Conference 2022.

BRUIN: Updated Results with Pirtobrutinib for MCL



BTK Pre-Treated MCL Patients[a]	n=100
Overall Response Rate[b], % (95% CI)	**51% (41-61)**
Best Response	
CR, n (%)	25 (25)
PR, n (%)	26 (26)
SD, n (%)	16 (16)
BTK Naive MCL Patients[a]	**n=11**
Overall Response Rate[b], % (95% CI)	**82% (48-98)**
Best Response	
CR, n (%)	2 (18)
PR, n (%)	7 (64)
SD, n (%)	1 (9)

- Efficacy also seen in patients with prior:
  - Stem cell transplant (n=28): ORR 64% (95% CI: 44-81)
  - CAR-T therapy (n=6): ORR 50% (95% CI: 12-88)

Lewis K et al. Pan Pacific Lymphoma Conference 2022.

BRUIN: Updated Safety Results with Pirtobrutinib for MCL

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%

Lewis K et al. Pan Pacific Lymphoma Conference 2022.

Chronic Lymphocytic Leukemia and Lymphomas Agenda

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

Module 2: Chronic Lymphocytic Leukemia (CLL)

Module 3: Hodgkin Lymphoma

Module 4: Mantle Cell Lymphoma (MCL)

Module 5: Follicular Lymphoma (FL)

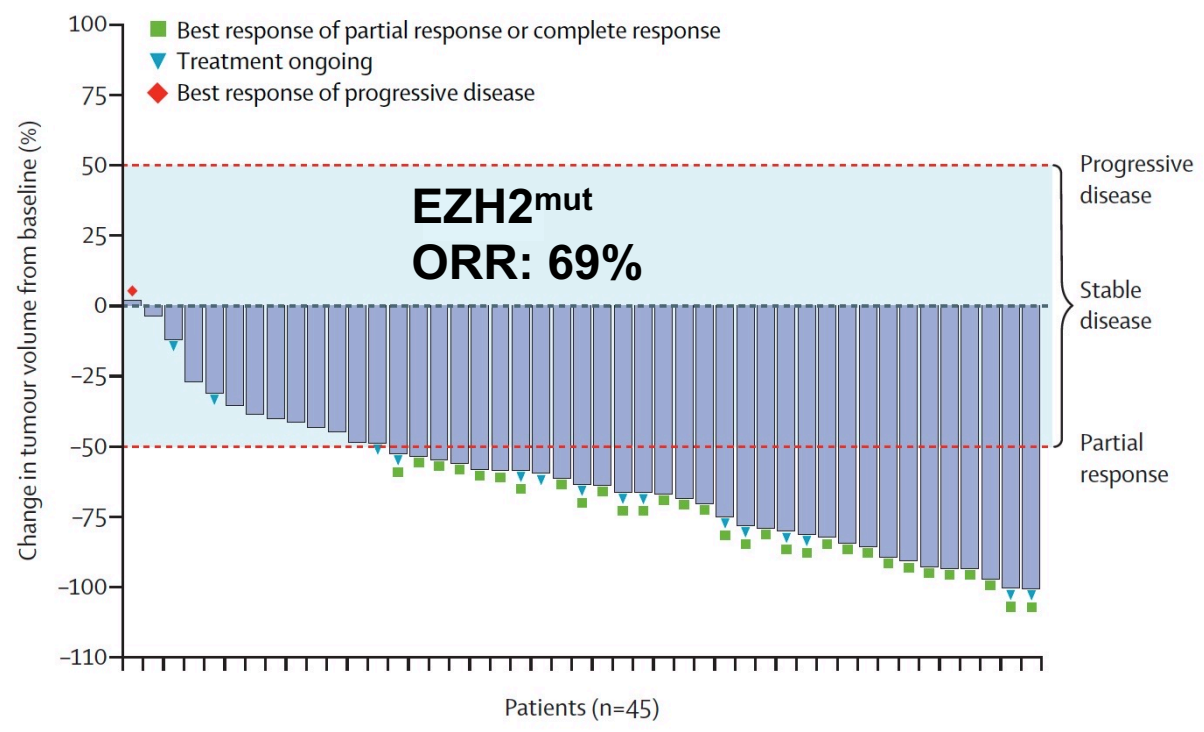
- Use of tazemetostat for the management for relapsed/refractory FL with and without EZH2 mutations
- CAR T-cell therapy for relapsed/refractory FL
- Potential clinical role of investigational bispecific antibodies (eg, mosunetuzumab, epcoritamab, glofitamab) for relapsed/refractory FL

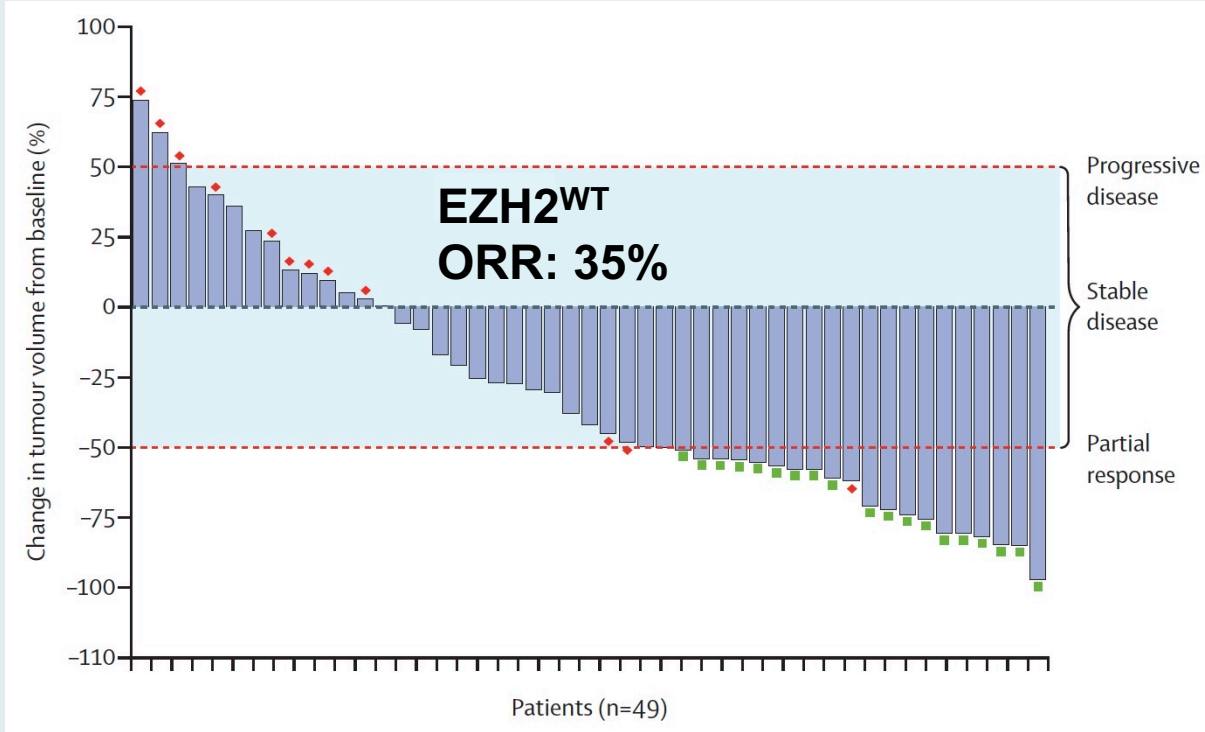
Lancet Oncol 2020;21(11):1433-42.

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 EZH2 Mutations or EZH2 Wild-Type Tumors





ORR = objective response rate

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

Updated Interim Analysis of the Randomized Phase 1b/3 Study of Tazemetostat in Combination with Lenalidomide and Rituximab in Patients with Relapsed/Refractory Follicular Lymphoma

Batlevi CL et al.

ASCO 2022;Abstract 7572.

Preliminary Efficacy in a Phase Ib/III Study of Tazemetostat with Lenalidomide and Rituximab for R/R FL

Best Overall Response,[a] n (%)	All Dosing Cohorts TAZ + R² (n=38)[b]
Objective response rate	36 (95)
Complete response[c]	19 (50)
Partial response	17 (45)
Stable disease	2 (5)

[a]Overall, there were 31 PET-CT–based responses and 7 CT-based responses. [b]6 patients were not included in the initial efficacy assessments. [c]For complete response, 18 were PET-CT–based responses and 1 was a CT-based response.
CT, computed tomography; PET, positron emission tomography; R², lenalidomide + rituximab; TAZ, tazemetostat.

- Median PFS and DOR were not reached, with a median follow-up of 5.7 months

Batlevi CL et al. ASCO 2022;Abstract 7572.

FDA Grants Accelerated Approval to Tisagenlecleucel for Relapsed or Refractory Follicular Lymphoma

Press Release – May 27, 2022

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

The approval was based on the ELARA trial (NCT03568461), a multicenter, single-arm, open-label trial evaluating tisagenlecleucel, a CD19-directed chimeric antigen receptor (CAR) T cell therapy, in adult patients who were refractory or relapsed within 6 months after completion of two or more lines of systemic therapy (including an anti-CD20 antibody and an alkylating agent) or relapsed after autologous hematopoietic stem cell transplant. Following lymphodepleting chemotherapy, tisagenlecleucel was administered as a single intravenous infusion with a target dose of 0.6 to 6.0 x 108 CAR-positive viable T cells."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-tisagenlecleucel-relapsed-or-refractory-follicular-lymphoma

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

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)**

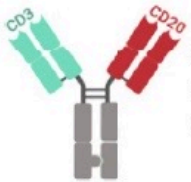
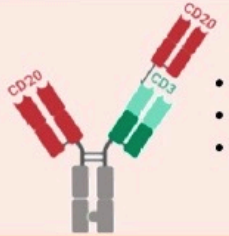
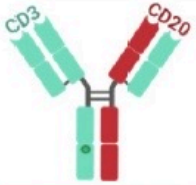
Efficacy Results of Extended Follow-up Analysis

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.

Structure of Selected Bispecific Antibodies

Bi-Specific Antibody	Targets	Design	Ig Fragment Formats
blinatumomab	CD19 x CD3		• two murine scFv joined by a glycine-serine linker • monovalent CD19 and monovalent CD3 binding • cloned from anti-CD19 (clone HD37) and anti-CD3 (clone L2K-07) murine mAbs
mosunetuzumab	CD20 x CD3		• humanized mouse heterodimeric IgG1-based antibody • monovalent CD20 and monovalent CD3ε binding • modified Fc devoid of FcγR and complement binding
glofitamab	$(CD20)_2$ x CD3		• humanized mouse IgG1-based antibody • bivalent CD20 and monovalent CD3ε binding • modified Fc devoid of FcγR and complement binding
odronextamab	CD20 x CD3		• fully human IgG4-based heterodimeric antibody • monovalent CD20 and monovalent CD3ε binding • Fc-dependent effector function-minimized antibody with Fc of the anti-CD3ε heavy chain modified to reduce Protein A binding • common κ light chain from anti-CD3ε mAb
epcoritamab	CD20 x CD3		• humanized mouse IgG1-based heterodimeric antibody • monovalent CD20 and monovalent CD3 binding • IgG1 Fc modified to minimize Fc-dependent effector functions and to control Fab-arm exchange of mAb half-molecules, resulting in high bispecific product yield

Ig, immunoglobulin; scFv, single-chain variable fragment; mAb, monoclonal antibody; Fc, fragment crystallizable; FcγR, Fc gamma receptor

Schuster SJ. *Hematol Oncol* 2021;39(S1):113-16.

FDA Grants Priority Review to the CD20 x CD3 Bispecific Antibody Mosunetuzumab for Relapsed/Refractory Follicular Lymphoma

Press Release — July 6, 2022

"The US Food and Drug Administration has accepted the Biologics License Application (BLA) and granted Priority Review for mosunetuzumab, a potential first-in-class CD20 x CD3 T-cell engaging bispecific antibody, for the treatment of adults with relapsed or refractory (R/R) follicular lymphoma (FL) who have received at least two prior systemic therapies.

The BLA is based on positive results from the pivotal phase I/II GO29781 study of mosunetuzumab, which showed high complete response (CR) rates, with the majority of responders (57% [95% CI: 49-70]) maintaining responses for at least 18 months, and manageable tolerability in people with heavily pretreated FL."

https://www.globenewswire.com/news-release/2022/07/06/2474498/0/en/FDA-grants-Priority-Review-to-Roche-s-Lunsumio-for-people-with-relapsed-or-refractory-follicular-lymphoma.html

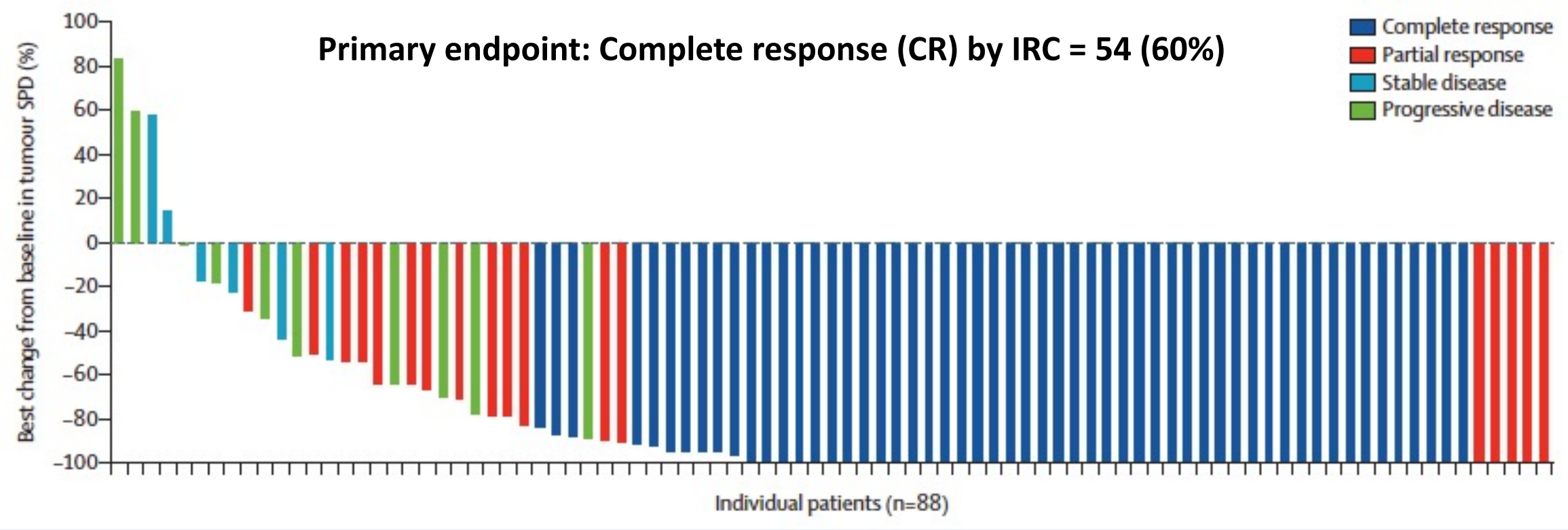
Lancet Oncol 2022;[Online ahead of print].

Articles

Safety and efficacy of mosunetuzumab, a bispecific antibody, in patients with relapsed or refractory follicular lymphoma: a single-arm, multicentre, phase 2 study

Lihua E Budde, Laurie H Sehn, Matthew Matasar, Stephen J Schuster, Sarit Assouline, Pratyush Giri, John Kuruvilla, Miguel Canales, Sascha Dietrich, Keith Fay, Matthew Ku, Loretta Nastoupil, Chan Yoon Cheah, Michael C Wei, Shen Yin, Chi-Chung Li, Huang Huang, Antonia Kwan, Elicia Penuel, Nancy L Bartlett

Response to Mosunetuzumab Monotherapy in Patients with R/R FL Who Have Received ≥2 Lines of Therapy



Budde LE et al. *Lancet Oncol* 2022;[Online ahead of print].

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Efficacy Summary for Mosunetuzumab Monotherapy in Patients with R/R FL Who Have Received ≥2 Lines of Therapy

	Response to mosunetuzumab per IRC (n = 90)
Objective response rate	72 (80%)
Complete response (CR)	54 (60%)
Median duration of response	22.8 months
Median duration of response in patients with CR	22.8 months
Median progression-free survival	17.9 months
Median overall survival	Not reached

Budde LE et al. *Lancet Oncol* 2022;[Online ahead of print].

Select Adverse Events Associated with Mosunetuzumab Monotherapy for Patients with R/R FL Who Have Received ≥2 Lines of Therapy

Treatment-emergent adverse event	N = 90
Any-grade cytokine release syndrome (CRS)	44%
Grade 3 or 4 neutropenia	26%
Grade 3 or 4 hypophosphatemia	17%

- Most CRS events occurred during cycle 1 and were Grade 1 or 2
- Neurological adverse events observed by investigator assessment and consistent with ICANS were confusional state (3 of 90 [3%]), disturbance in attention (1 [1%]), and cognitive disorder (1 [1%])
- All ICANS-like events were low grade and resolved

ICANS = immune effector cell-associated neurotoxicity syndrome

Budde LE et al. *Lancet Oncol* 2022;[Online ahead of print].

Lancet 2021;398:1157-69.

Articles

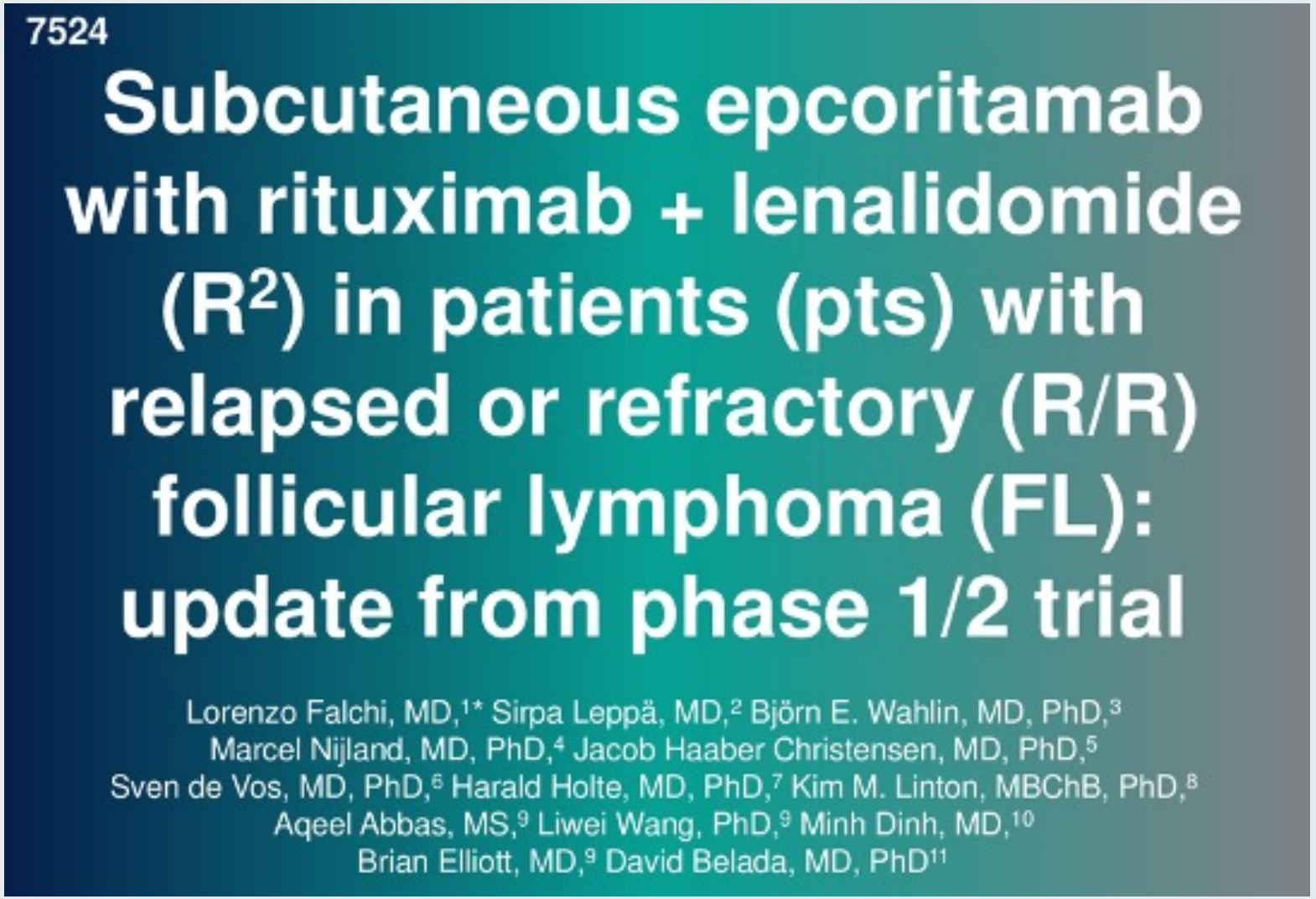
Dose escalation of subcutaneous epcoritamab in patients with relapsed or refractory B-cell non-Hodgkin lymphoma: an open-label, phase 1/2 study

Martin Hutchings, Rogier Mous, Michael Roost Clausen, Peter Johnson, Kim M Linton, Martine E D Chamuleau, David John Lewis, Anna Sureda Balari, David Cunningham, Roberto S Oliveri, Brian Elliott, Dena DeMarco, Ada Azaryan, Christopher Chiu, Tommy Li, Kuo-mei Chen, Tahamtan Ahmadi, Pieternella J Lugtenburg

Phase I/II Study Response Rates with Subcutaneous Epcoritamab in Patient Subgroup with R/R FL

	Epcoritamab 0.76 – 48 mg (n = 10)	Epcoritamab 48 mg (n = 1)
Overall response rate	9 (90%)	0
Complete response	5 (50%)	0
Partial response	4 (40%)	0
Time to response	1.9 months	NA

Hutchings M et al. *Lancet* 2021;398:1157-69.



ASCO 2022;Abstract 7524.

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EPCORE NHL-2 Arm 2a: Best Overall Response at Any Time and at 6 Weeks (First Assessment)

Response, n (%)[a]	At any time Arm 2a n=28[b]	At 6 weeks Arm 2a n=27	At 6 weeks Arm 2b n=28
Overall response	28 (100)	25 (93)	26 (93)
CMR	27 (96)	19 (70)	17 (61)
PMR	1 (4)	6 (22)	9 (32)
Stable disease	0	2 (7)	1 (4)
Progressive disease	0	0	1 (4)

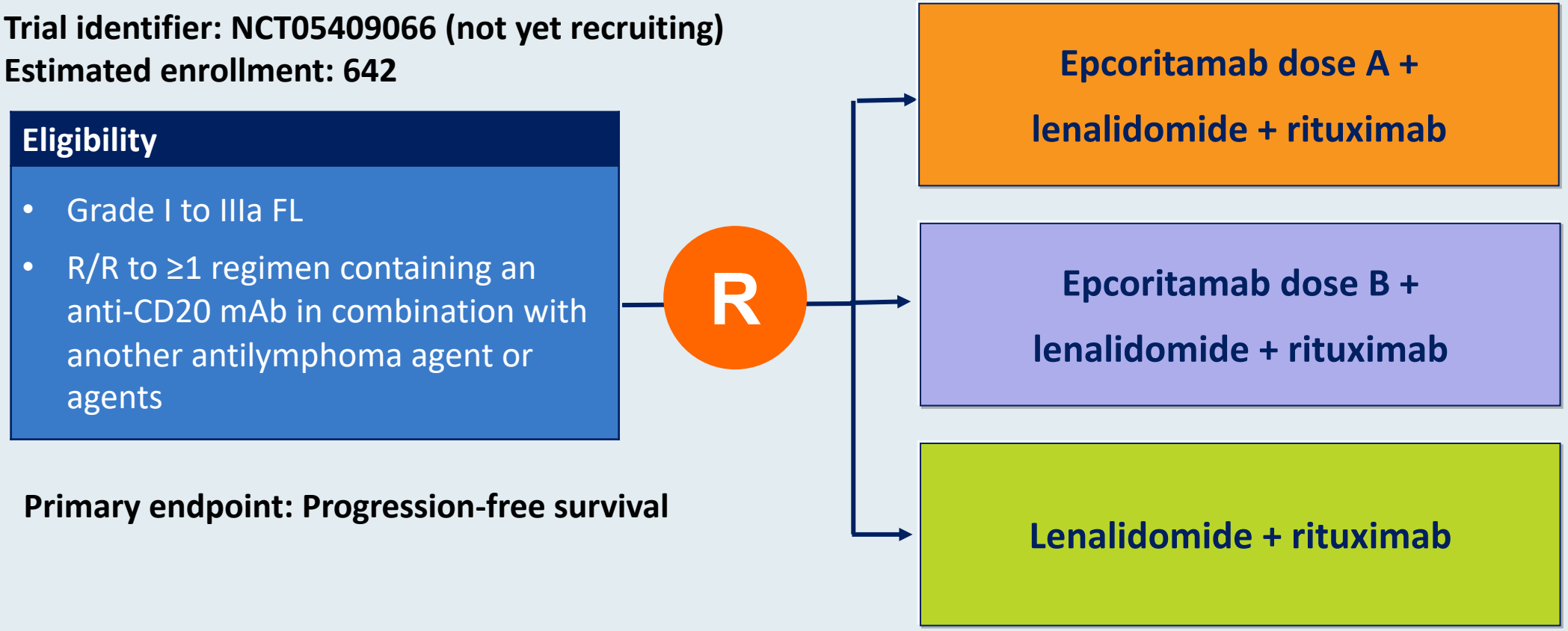
Data cutoff: March 25, 2022. [a]Based on modified response-evaluable population, defined as patients with ≥1 target lesion at baseline and ≥1 postbaseline response evaluation and patients who died within 60 d of first dose. [b]Excludes 2 patients who discontinued before first assessment.

CMR = complete metabolic response; PMR = partial metabolic response

Falchi L et al. ASCO 2022;Abstract 7524.

EPCORE FL-1: A Phase III Trial of Epcoritamab with Lenalidomide and Rituximab for R/R FL

Trial identifier: NCT05409066 (not yet recruiting)
Estimated enrollment: 642



Primary endpoint: Progression-free survival

www.clinicaltrials.gov. Accessed July 2022.

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rapid communications

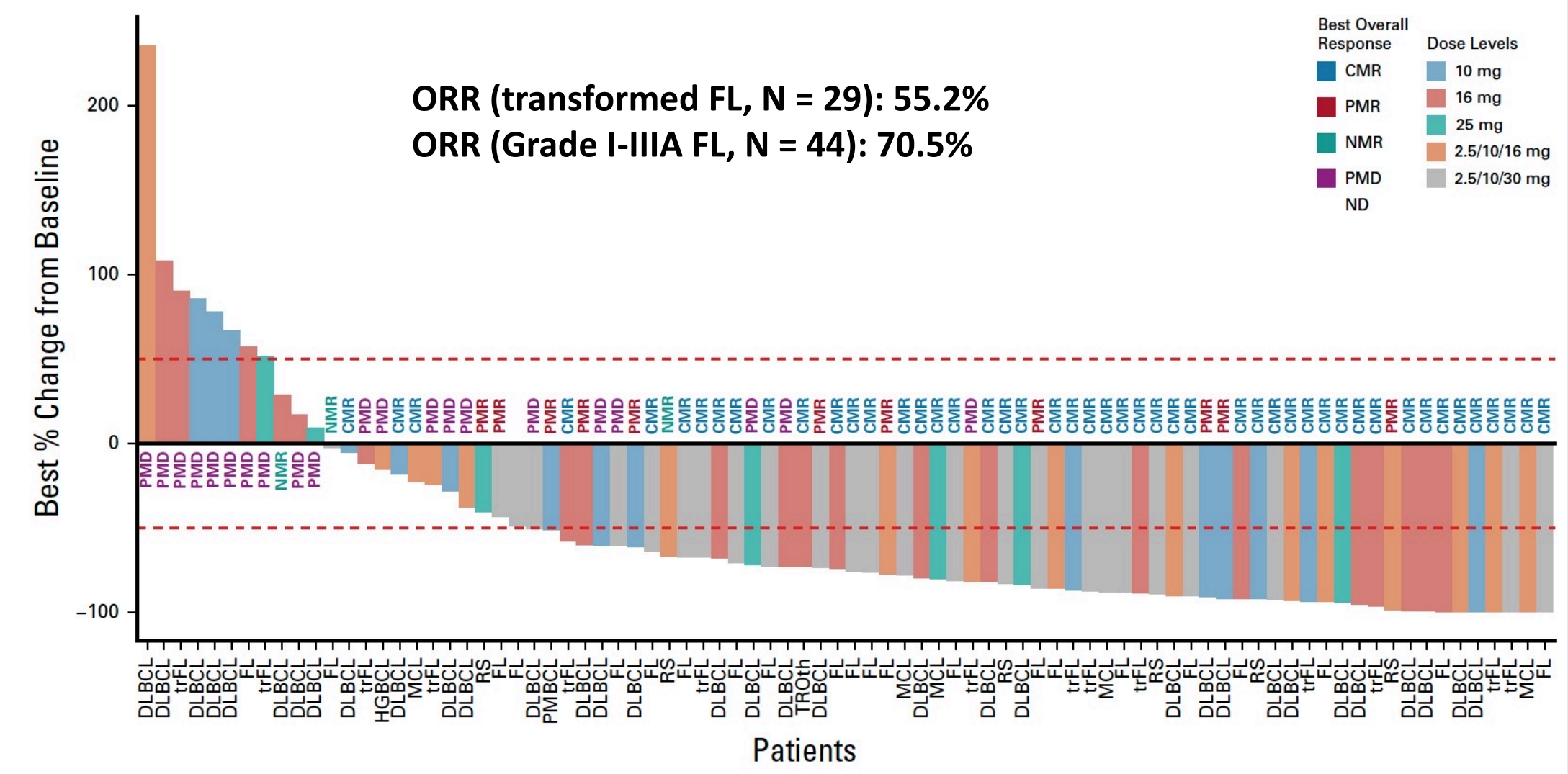
Glofitamab, a Novel, Bivalent CD20-Targeting T-Cell–Engaging Bispecific Antibody, Induces Durable Complete Remissions in Relapsed or Refractory B-Cell Lymphoma: A Phase I Trial

Martin Hutchings, PhD[1]; Franck Morschhauser, MD, PhD[2]; Gloria Iacoboni, MD[3,4]; Carmelo Carlo-Stella, MD[5]; Fritz C. Offner, MD, PhD[6]; Anna Sureda, MD, PhD[7]; Gilles Salles, MD[8]; Joaquín Martínez-Lopez, MD, PhD, MBA[9]; Michael Crump, MD[10]; Denise N. Thomas, MSc[11]; Peter N. Morcos, PharmD[11]; Cristiano Ferlini, MD[11]; Ann-Marie E. Bröske, PhD[12]; Anton Belousov, PhD[13]; Marina Bacac, PhD[13]; Natalie Dimier, PhD[14]; David J. Carlile, PhD[14]; Linda Lundberg, PhD[15]; David Perez-Callejo, MD, PhD[15]; Pablo Umaña, PhD[13]; Tom Moore, MD[12]; Martin Weisser, MD[12]; and Michael J. Dickinson, MBBS, DMedSci[16]

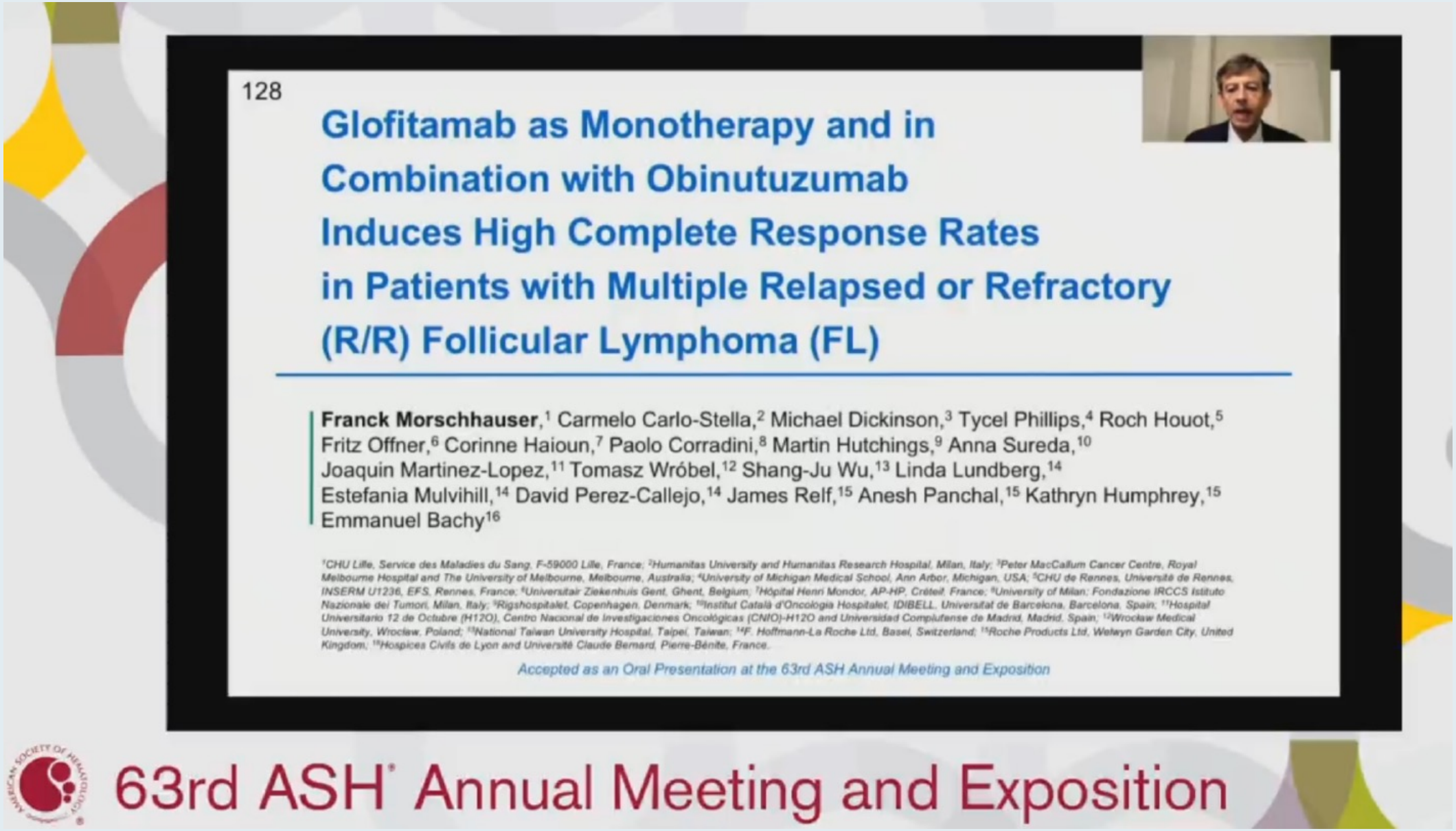
J Clin Oncol 2021;39(18):1959-70.

RTP RESEARCH TO PRACTICE

Response to Glofitamab in Patients with R/R B-Cell Lymphomas

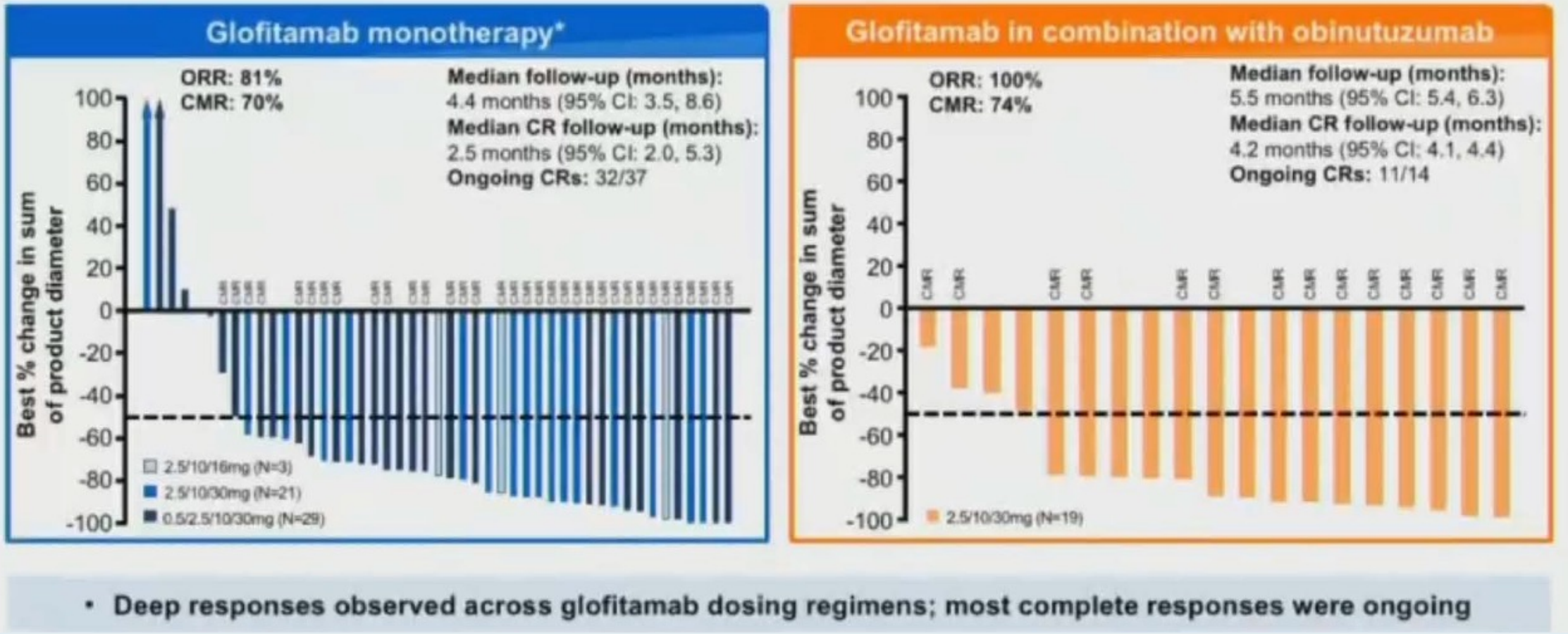


Hutchings M et al. *J Clin Oncol* 2021;39(18):1959-70.



ASH 2021;Abstract 128.

Phase I/II Study of Glofitamab as Monotherapy or in Combination with Obinutuzumab for R/R FL



- Myelosuppression was more common with the combination
- CRS rates were high and comparable, and cases were mainly low grade

Morschhauser F et al. ASH 2021;Abstract 128.

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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

* Indications in FL were withdrawn for idelalisib (Jan 2022), duvelisib (Dec 2021) and umbralisib (June 2022)

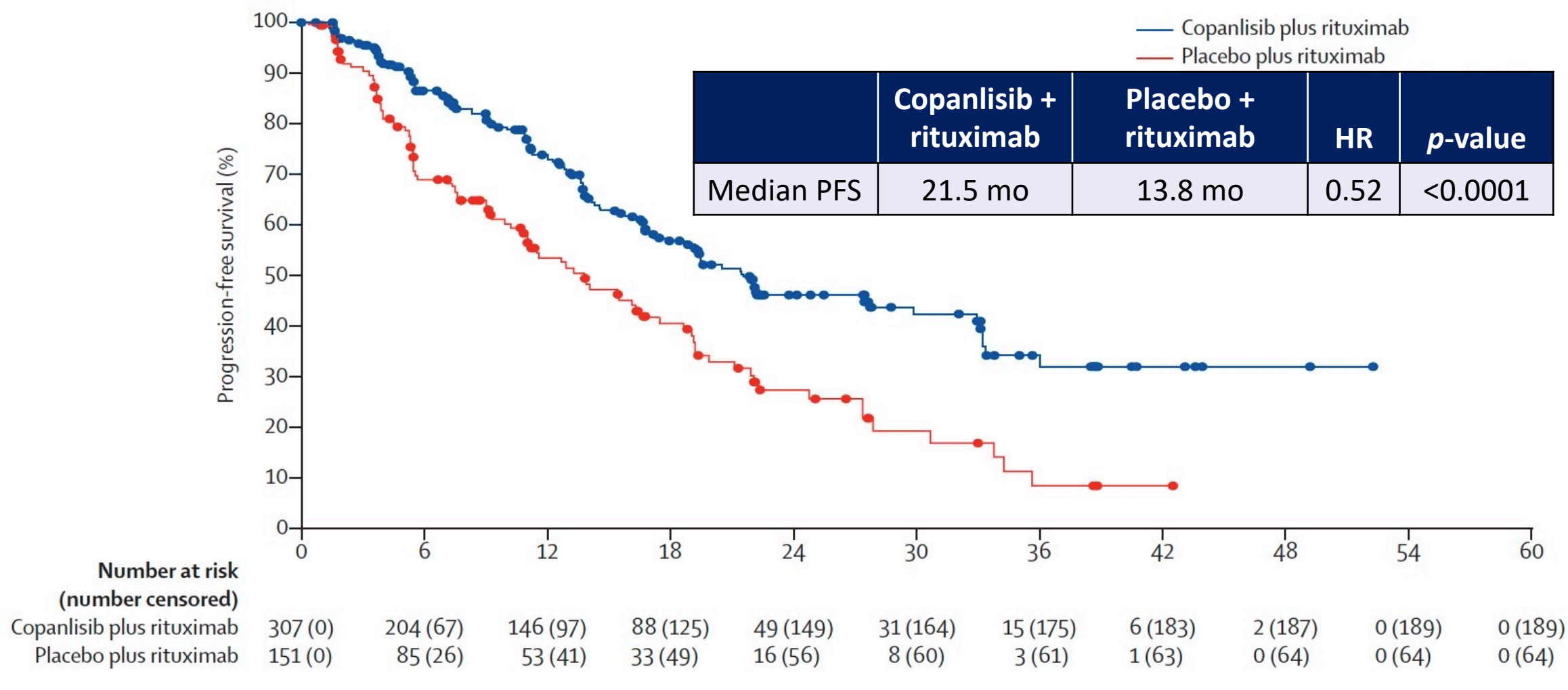
[1] Gopal AK et al. *N Engl J Med* 2014;370(11):1008-18; Idelalisib package insert, January 2018.
[2] Dreyling M et al. *J Clin Oncol* 2017;35(35):3898-905; Copanlisib package insert, September 2017.
[3] Flinn IW et al. *J Clin Oncol* 2019;[Online ahead of print]; Zinzani PL et al. EHA 2017;Abstract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

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 for Patients with Relapsed/Refractory (R/R) Indolent Non-Hodgkin Lymphoma



	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.

Thank you for joining us!

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

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

A CME/MOC- and NCPD-Accredited Hybrid Event

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

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Agenda

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

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

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

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

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

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

Gastrointestinal Cancers Faculty

Rutika Mehta, MD, MPH
Assistant Member in the Department
of Gastrointestinal Oncology
Moffitt Cancer Center
Assistant Professor in the Department
of Oncologic Sciences
University of South Florida
Tampa, Florida

Philip A Philip, MD, PhD, FRCP
Professor of Oncology and Pharmacology
Leader, GI and Neuroendocrine Oncology
Henry Ford Cancer Institute
Wayne State University
Detroit, Michigan

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Co-Moderators

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

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

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

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

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

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

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MODULE 5: Gastrointestinal Cancers

Co-Moderator

Pavani Ellipeddi, MD
Hematology Oncology Clinic
Baton Rouge, Louisiana

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Gastrointestinal Cancers Agenda

Module 1: Colorectal Cancer

Module 2: Upper Gastrointestinal Cancers

Module 3: Hepatocellular and Biliary Tract Cancers

Module 4: Pancreatic Adenocarcinoma

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Gastrointestinal Cancers Agenda

Module 1: Colorectal Cancer

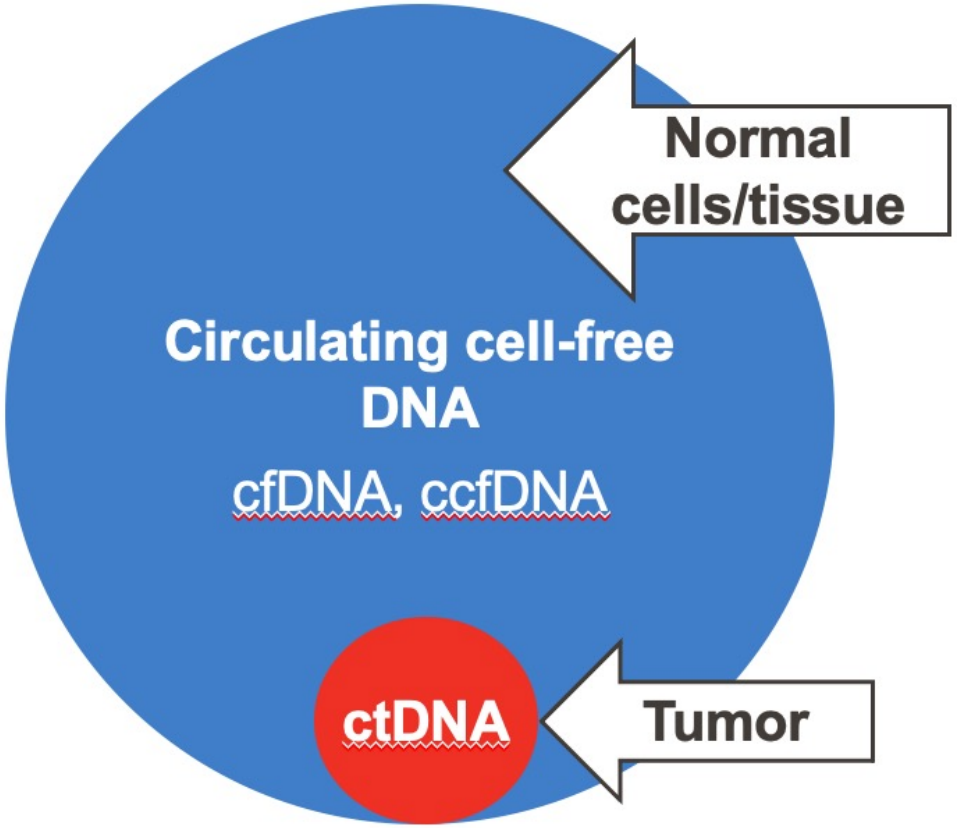
- Adjuvant systemic treatment: Role of ctDNA (Signatera)
- Management of MSI-high disease: Adjuvant and metastatic settings
- Management of metastatic disease: First-line EGFR antibodies versus bevacizumab
- Management of metastatic disease: HER2-positive
- Management of metastatic disease: BRAF mutant

Module 2: Upper Gastrointestinal Cancers

Module 3: Hepatocellular and Biliary Tract Cancers

Module 4: 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

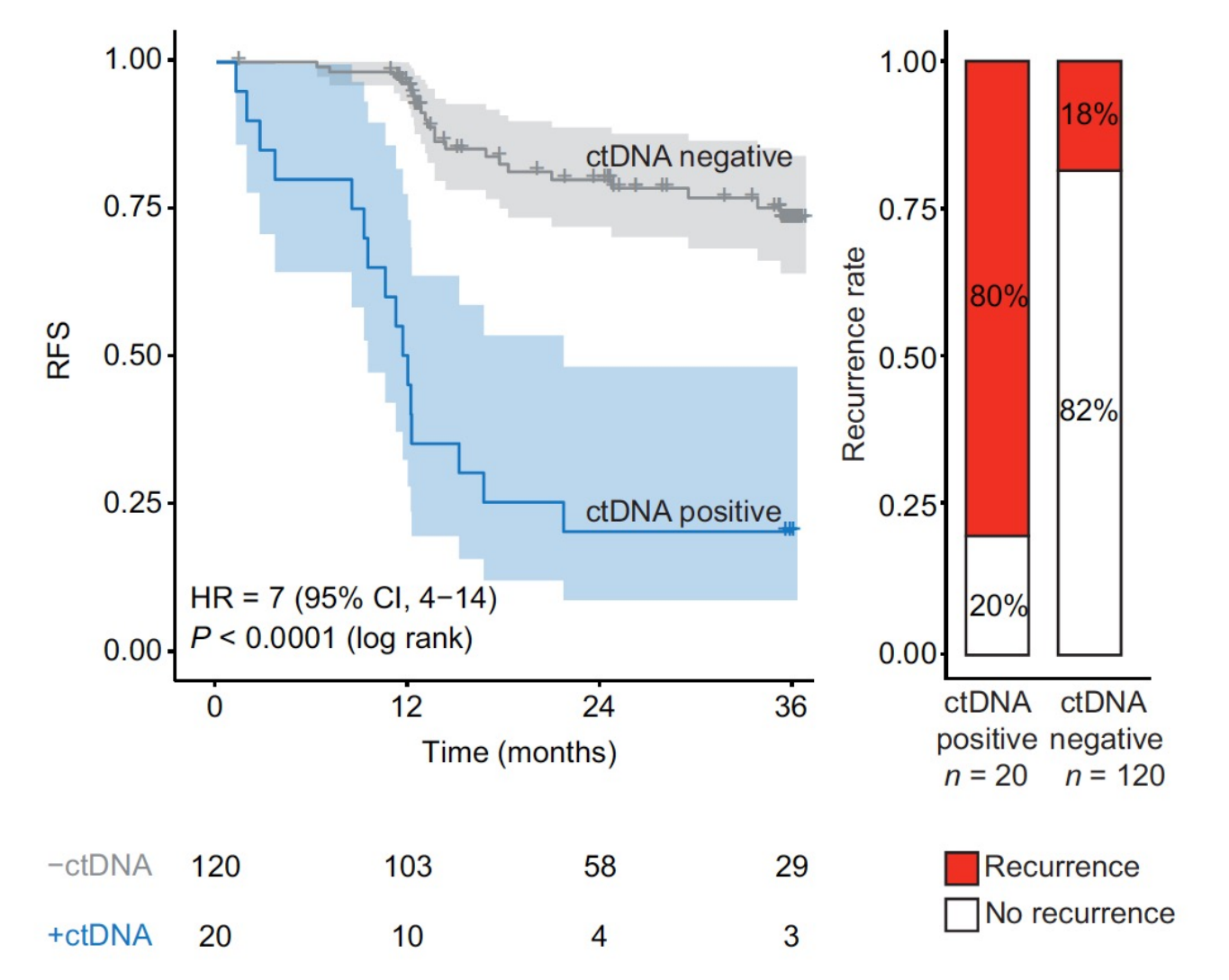
CLINICAL CANCER RESEARCH | PRECISION MEDICINE AND IMAGING

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.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 23, 2022 VOL. 386 NO. 25

PD-1 Blockade in Mismatch Repair–Deficient, Locally Advanced Rectal Cancer

A. Cercek, M. Lumish, J. Sinopoli, J. Weiss, J. Shia, M. Lamendola-Essel, I.H. El Dika, N. Segal, M. Shcherba, R. Sugarman, Z. Stadler, R. Yaeger, J.J. Smith, B. Rousseau, G. Argiles, M. Patel, A
K. Iyer, J. Zhang, N. Gianino, C. Crane, P.B. Romesser, E.P. Pappou, P. Paty, J.
M. Gollub, M.R. Weiser, K.A. Schalper, and L.A. Diaz,

2022 ASCO ANNUAL MEETING

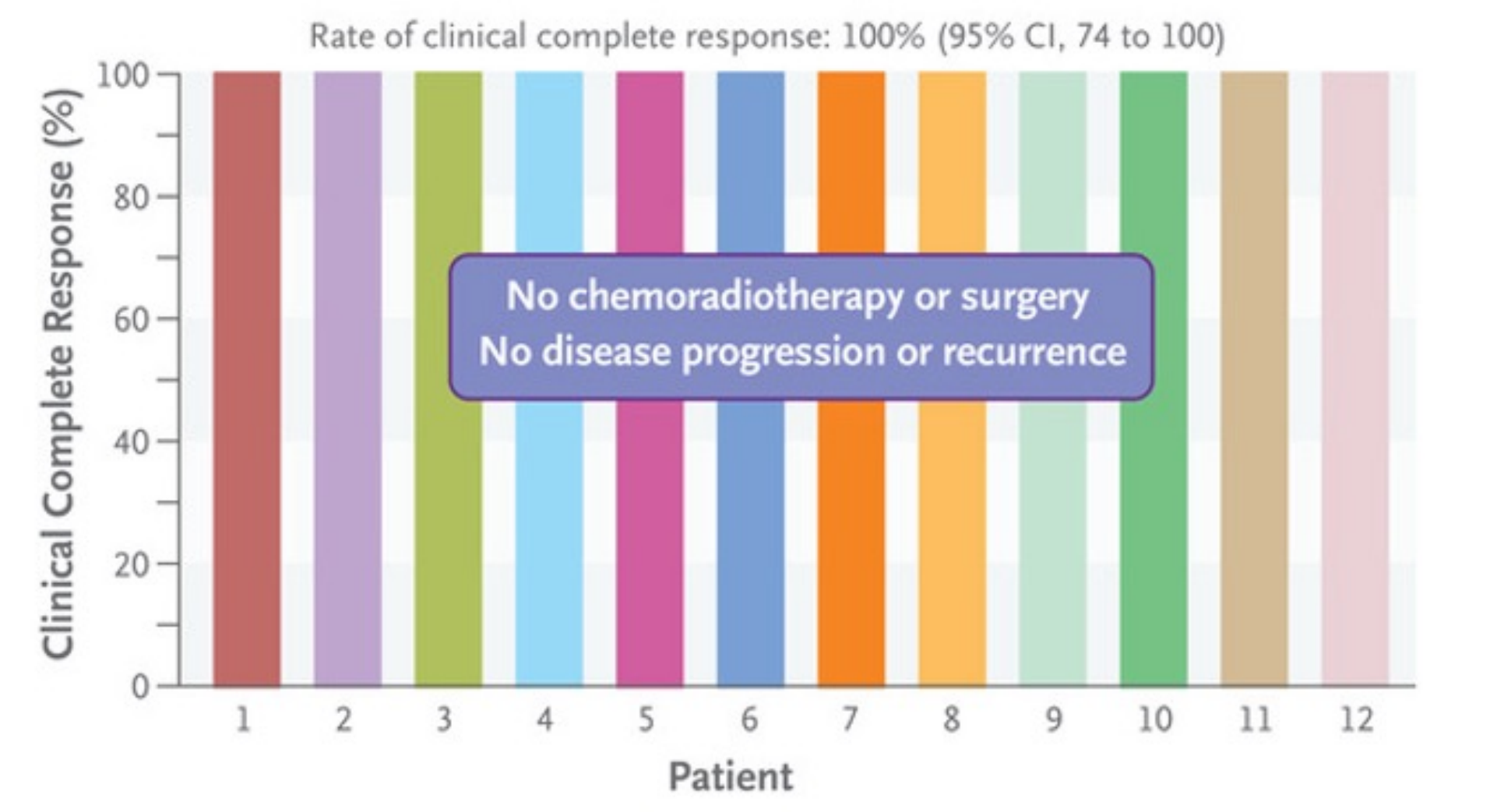
Abstract LBA5.

Late breaking abstract

PD-1 blockade as curative-intent therapy in mismatch repair deficient locally advanced rectal cancer

Andrea Cercek, MD
Head, Colorectal Cancer Section
Co-Director Center for Young Onset Colorectal and Gastrointestinal Cancers
Memorial Sloan Kettering Cancer Center

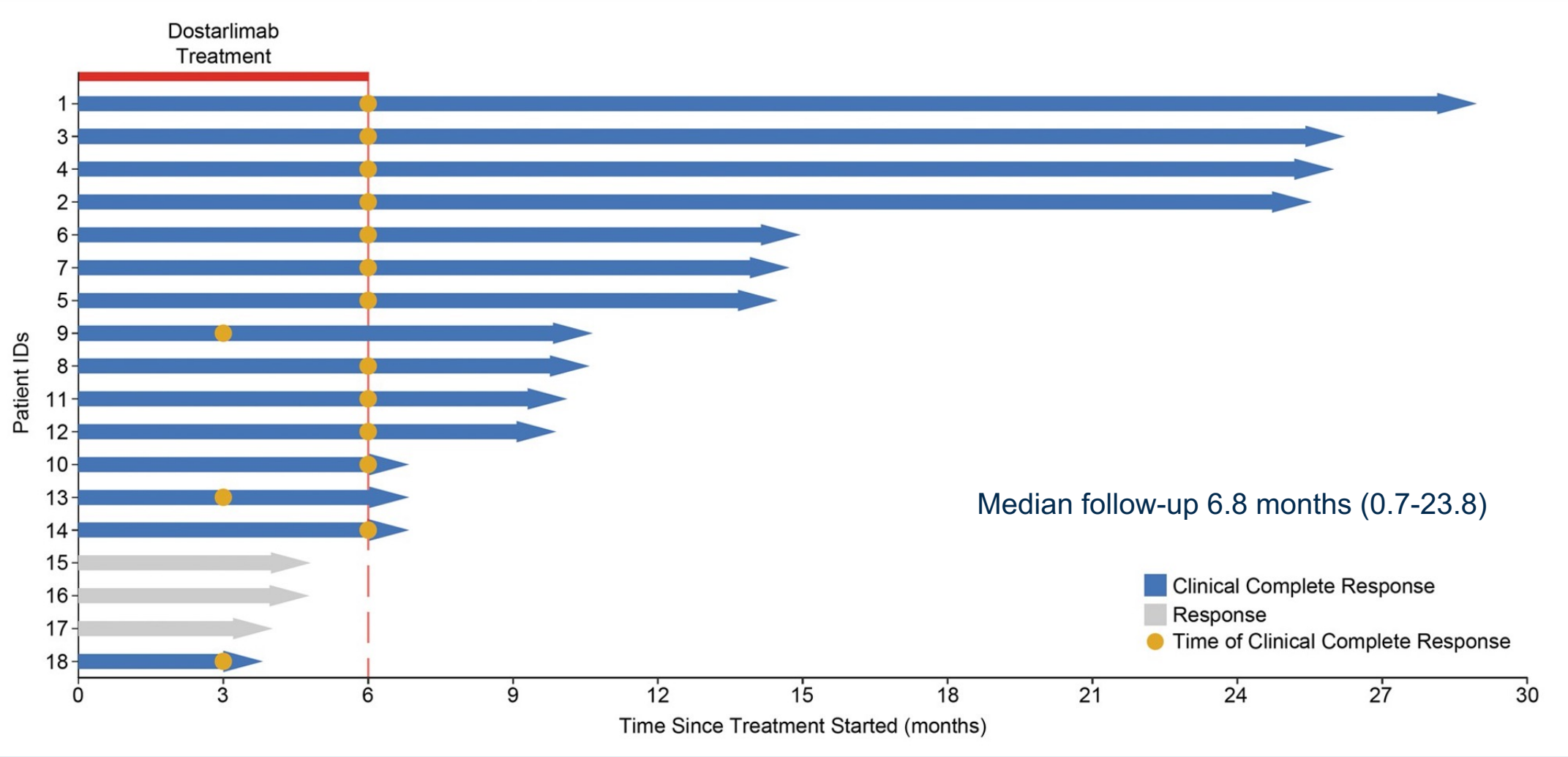
Rate of Clinical Response



CI = confidence interval

Cercek A et al. *N Engl J Med* 2022;386(25):2363-76. Cercek A et al. ASCO 2022;Abstract LBA5.

Duration of Response



Cercek A et al. *N Engl J Med* 2022;386(25):2363-76. Cercek A et al. ASCO 2022;Abstract LBA5.

RTP RESEARCH TO PRACTICE

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

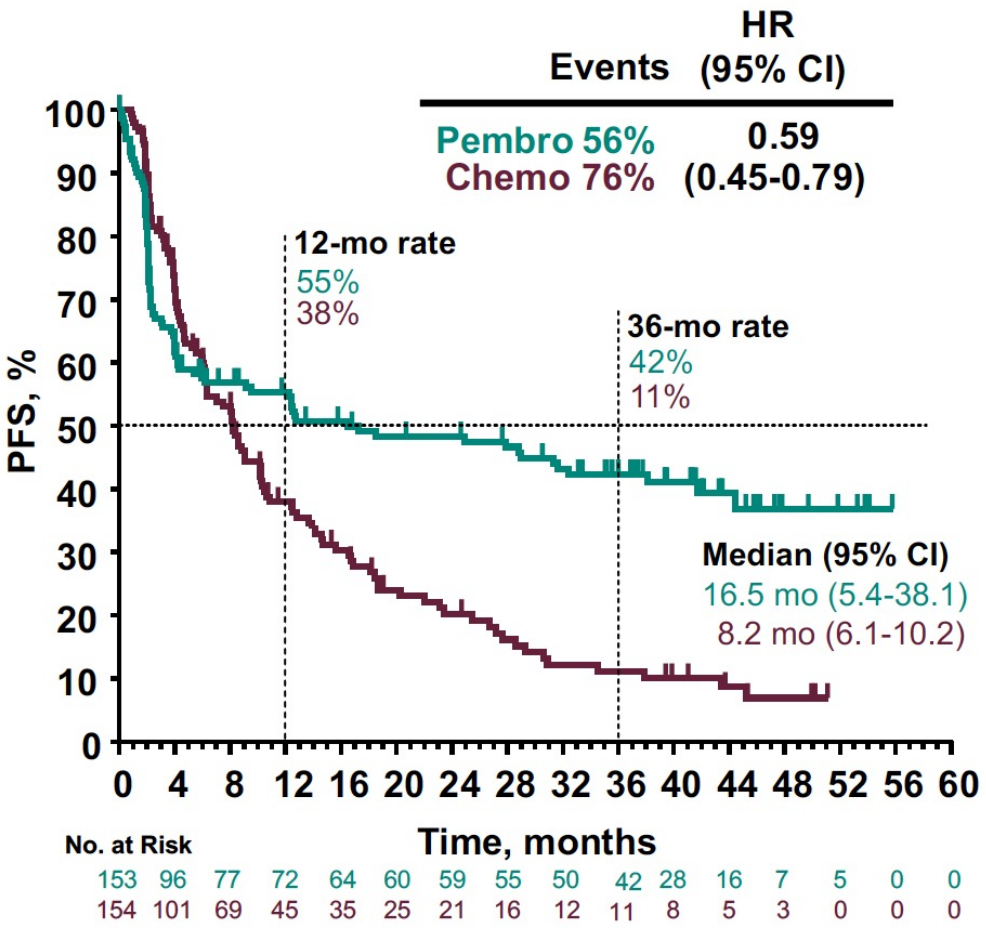
Thierry André,[1] Kai-Keen Shiu,[2] Tae Won Kim,[3] Benny Vittrup Jensen,[4] Lars Henrik Jensen,[5] Cornelis Punt,[6] Denis Smith,[7] Rocio Garcia-Carbonero,[8] Julia Alcaide-Garcia,[9] Peter Gibbs,[10] Christelle de la Fouchardiere,[11] Fernando Rivera,[12] Elena Elez,[13] Johanna Bendell,[14] Dung T. Le,[15] Takayuki Yoshino,[16] Wenyan Zhong,[17] David Fogelman,[18] Patricia Marinello,[18] Luis A. Diaz Jr[19]

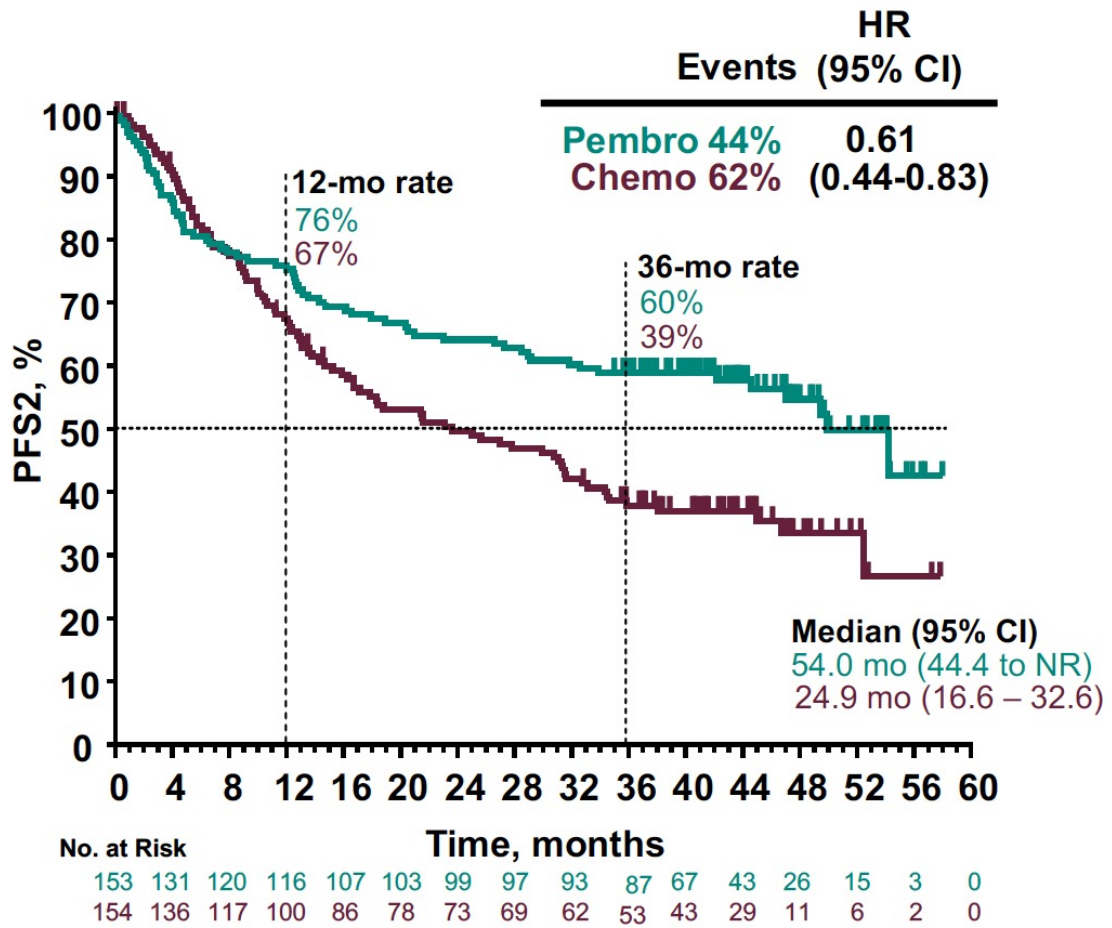
[1]Sorbonne Université and Hôpital Saint Antoine, Paris, France; [2]University College Hospital, NHS Foundation Trust, London, United Kingdom; [3]Asan Medical Center, University of Ulsan, Seoul, Republic of Korea; [4]Herlev and Gentofte Hospital, Herlev, Denmark; [5]University Hospital of Southern Denmark, 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

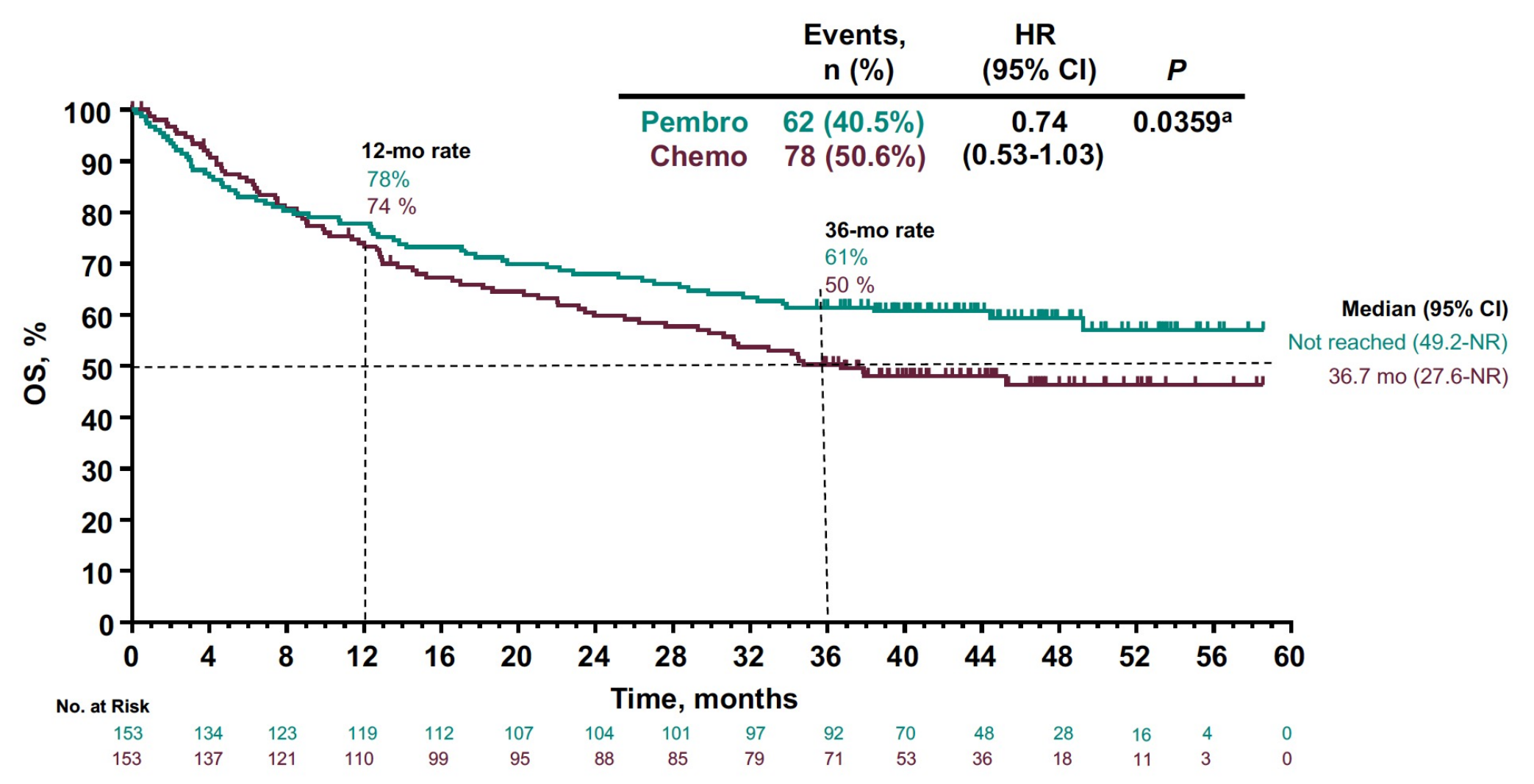
KEYNOTE-177: Progression-Free Survival (PFS)





André T et al. ESMO World Congress on Gastrointestinal Cancer 2021;Abstract O-8.

KEYNOTE-177: Overall Survival (OS)



André T et al. ESMO World Congress on Gastrointestinal Cancer 2021;Abstract O-8.

original reports

First-Line Nivolumab Plus Low-Dose Ipilimumab for Microsatellite Instability-High/ Mismatch Repair-Deficient Metastatic Colorectal Cancer: The Phase II CheckMate 142 Study

Heinz-Josef Lenz, MD[1]; Eric Van Cutsem, MD, PhD[2]; Maria Luisa Limon, MD[3]; Ka Yeung Mark Wong, PhD[4]; Alain Hendlisz, MD, PhD[5]; Massimo Aglietta, MD, PhD[6]; Pilar García-Alfonso, MD[7]; Bart Neyns, MD, PhD[8]; Gabriele Luppi, MD[9]; Dana B. Cardin, MD[10]; Tomislav Dragovich, MD, PhD[11]; Usman Shah, MD[12]; Sandzhar Abdullaev, MD, PhD[13]; Joseph Gricar, MS[13]; Jean-Marie Ledeine, MS[13]; Michael James Overman, MD[14]; and Sara Lonardi, MD[15]

J Clin Oncol 2022;40(2):161-70.

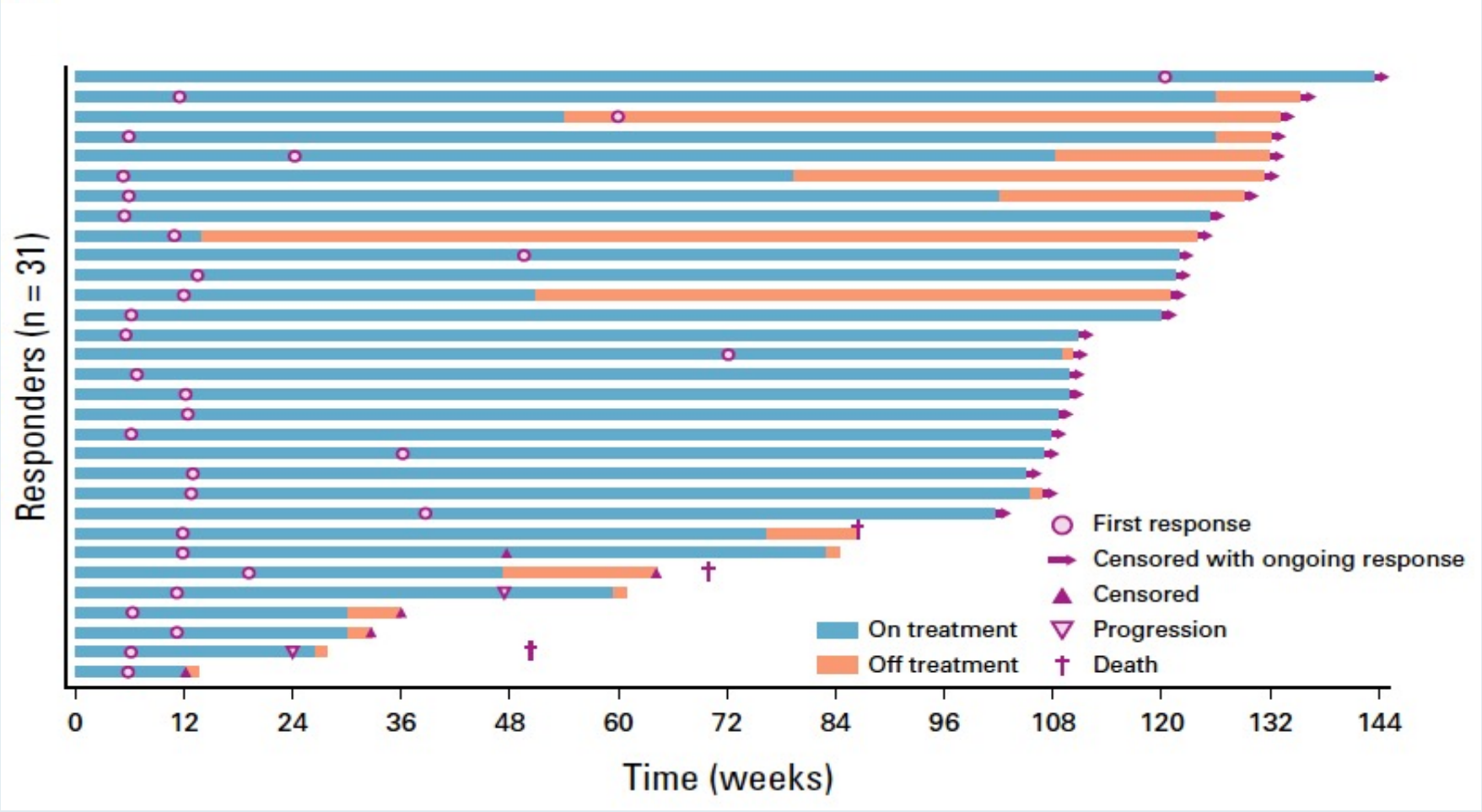
CheckMate 142: ORR, Best Overall Response, DCR and Median DOR (N = 45)

Response	Investigator Assessed	BICR Assessed
ORR,[a] No. (%)	31 (69)	28 (62)
95% CI	53 to 82	46.5 to 76.2
ORR by *BRAF* and/or *KRAS* mutation status,[b] No. (%)		
BRAF and *KRAS* wild-type (n = 13)	8 (62)	7 (54)
BRAF mutation (n = 17)	13 (76)	14 (82)
KRAS mutation (n = 10)	8 (80)	7 (70)
Best overall response,[c] No. (%)		
CR	6 (13)	11 (24)
PR	25 (56)	17 (38)
SD	7 (16)	8 (18)
PD	6 (13)	7 (16)
Not determined	1 (2)	2 (4)
DCR,[d] No. (%)	38 (84)	35 (78)
95% CI	70.5 to 93.5	63 to 89
Median DOR, months (range)[e]	NR (1.4+ to 29.0+)	NR (3.3+ to 29.0+)

ORR = overall response rate; DCR = disease control rate; DOR = duration of response; CR = complete response; PR = partial response; SD = stable disease; PD = disease progression

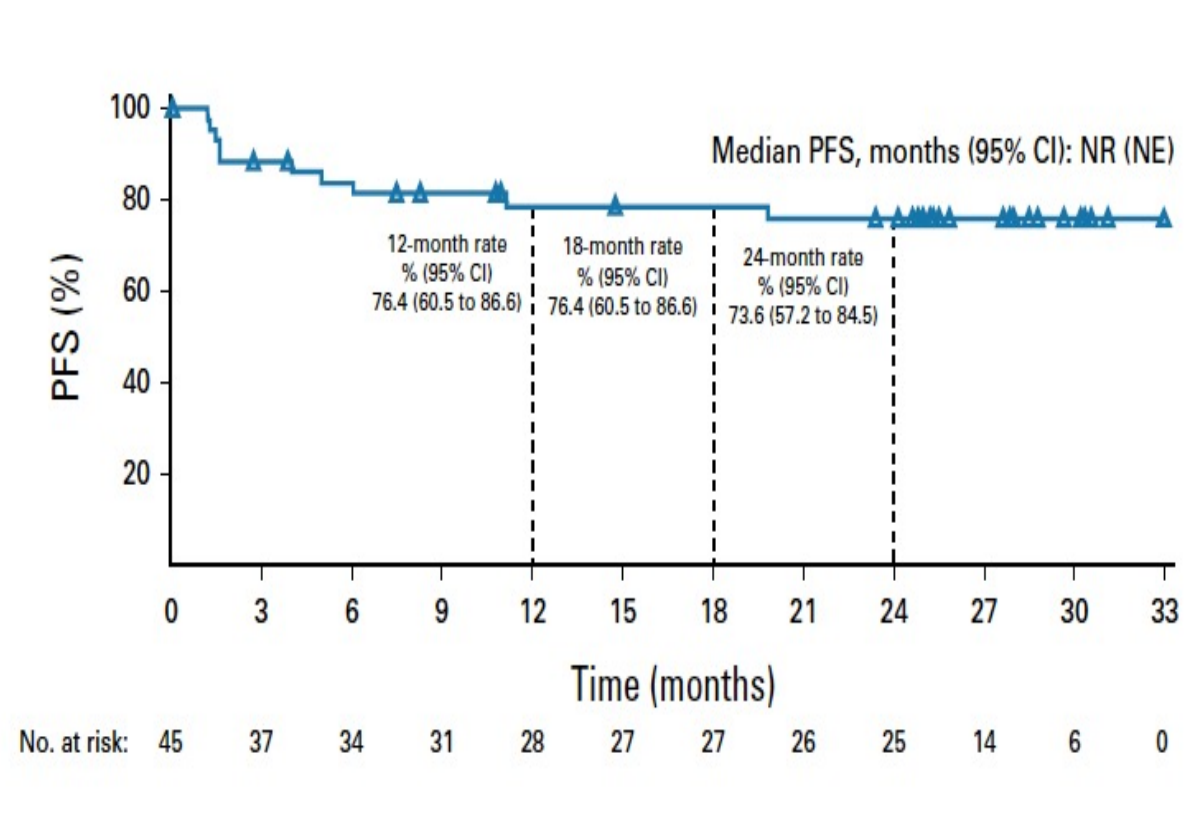
Lenz H-J et al. *J Clin Oncol* 2022;40(2):161-70.

CheckMate 142: Characterization of Patients with a Response

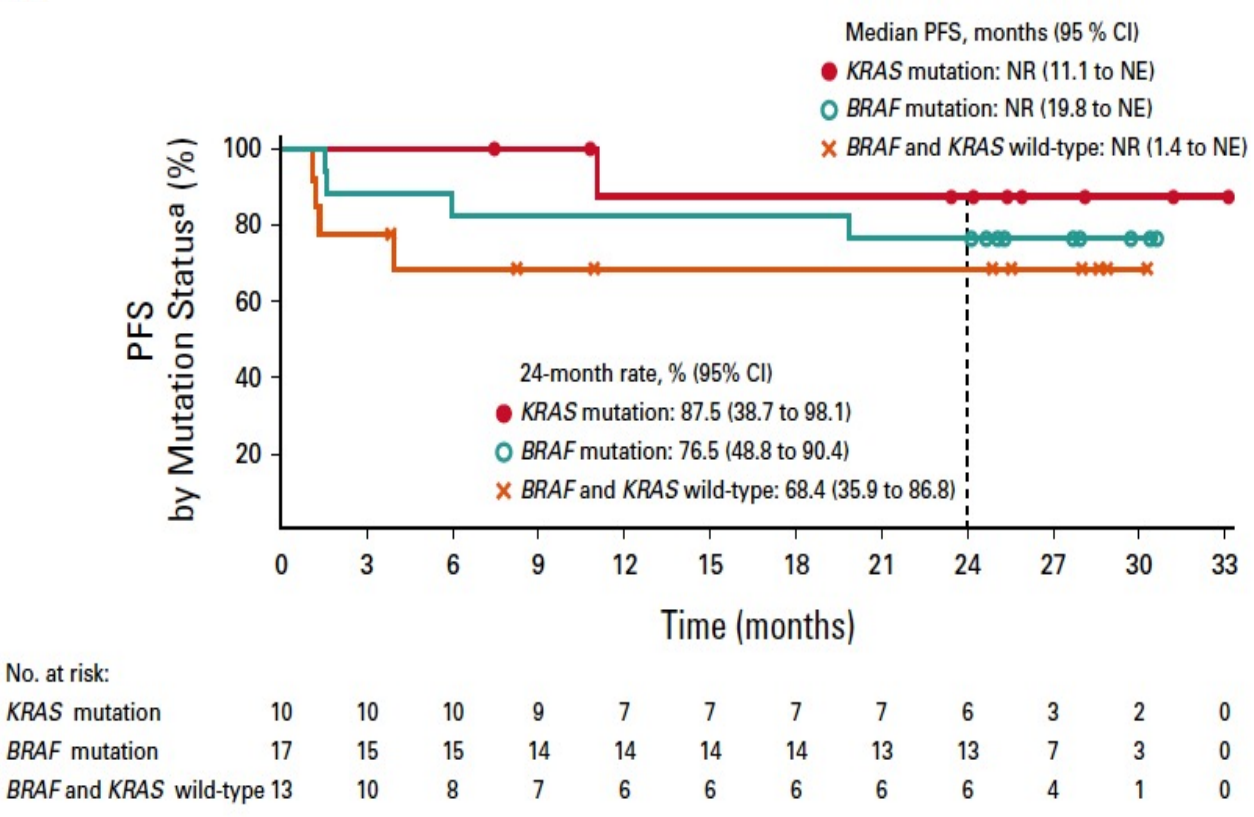


Lenz H-J et al. *J Clin Oncol* 2022;40(2):161-70.

CheckMate 142: Progression-Free Survival (PFS)



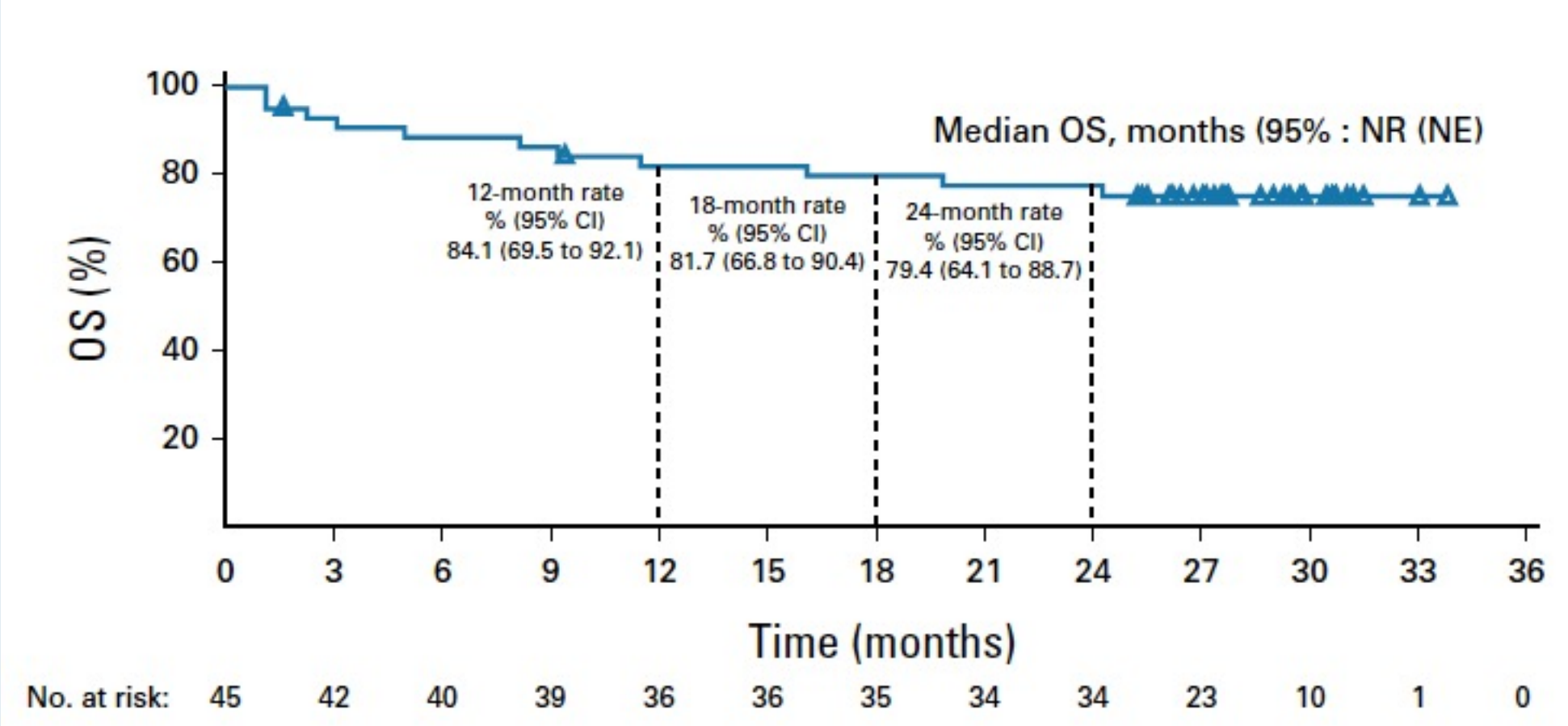
Per investigator assessment



Per investigator assessment by mutation status

Lenz H-J et al. *J Clin Oncol* 2022;40(2):161-70.

CheckMate 142: Overall Survival (OS)



Lenz H-J et al. *J Clin Oncol* 2022;40(2):161-70.

2022 ASCO® ANNUAL MEETING

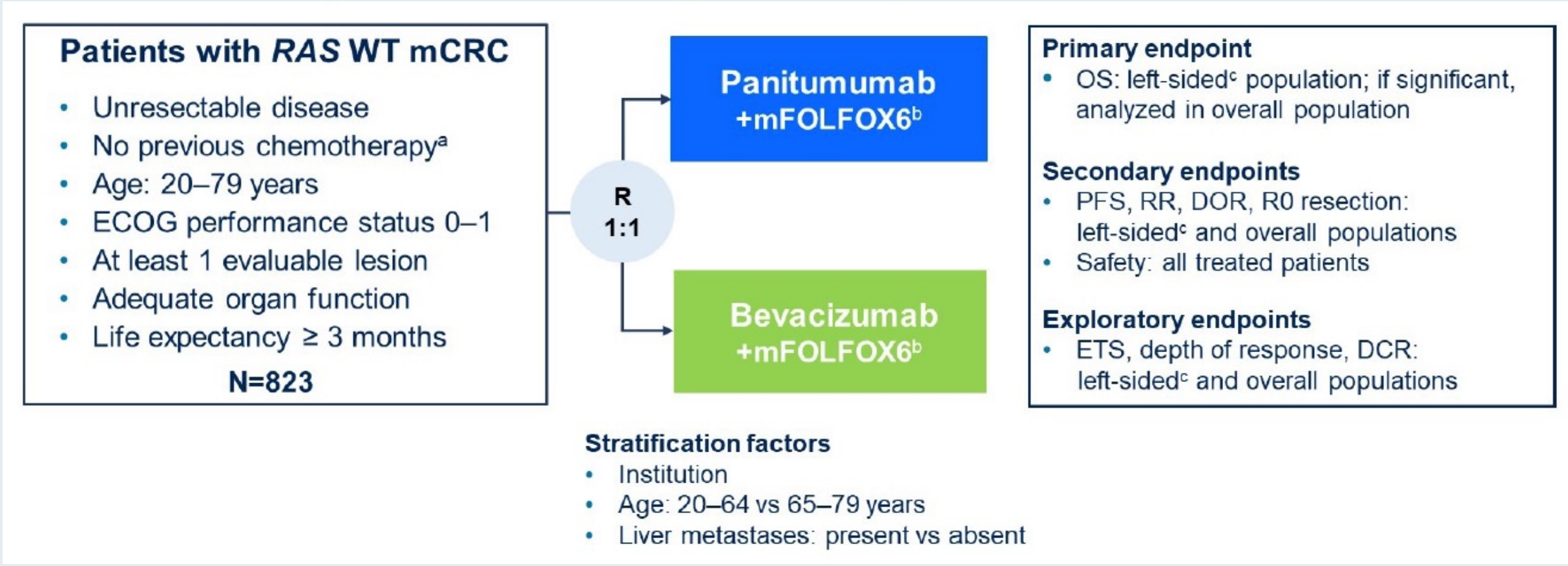
Abstract LBA1

Panitumumab plus mFOLFOX6 versus Bevacizumab plus mFOLFOX6 as first-line treatment in patients with *RAS* wild-type metastatic colorectal cancer: results from the phase 3 PARADIGM trial

Takayuki Yoshino[1], Jun Watanabe[2], Kohei Shitara[1], Kentaro Yamazaki[3], Hisatsugu Ohori[4], Manabu Shiozawa[5], Hirofumi Yasui[4], Eiji Oki[6], Takeo Sato[7], Takeshi Naitoh[8], Yoshito Komatsu[9], Takeshi Kato[10], Masamitsu Hihara[11], Junpei Soeda[11], Kouji Yamamoto[12], Kiwamu Akagi[13], Atsushi Ochiai[14], Hiroyuki Uetake[15], Katsuya Tsuchihara[16], Kei Muro[17]

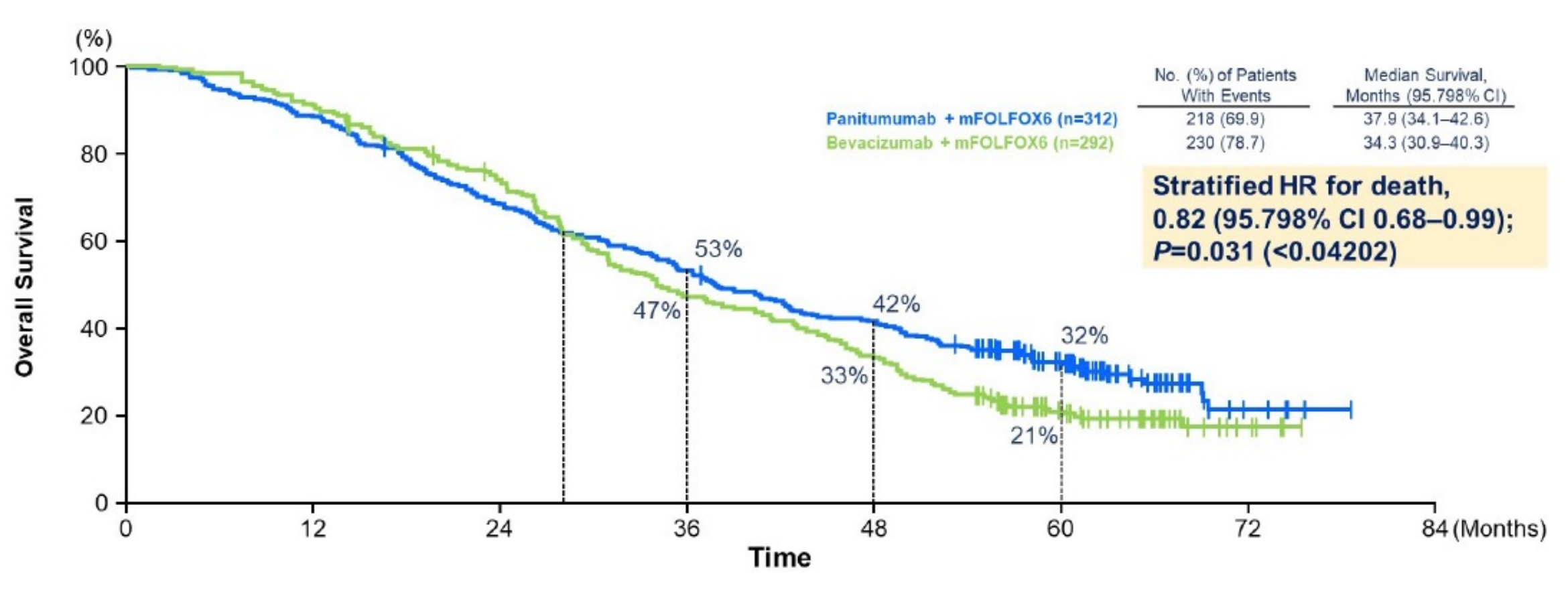
RTP RESEARCH TO PRACTICE

PARADIGM: Phase III Study Design



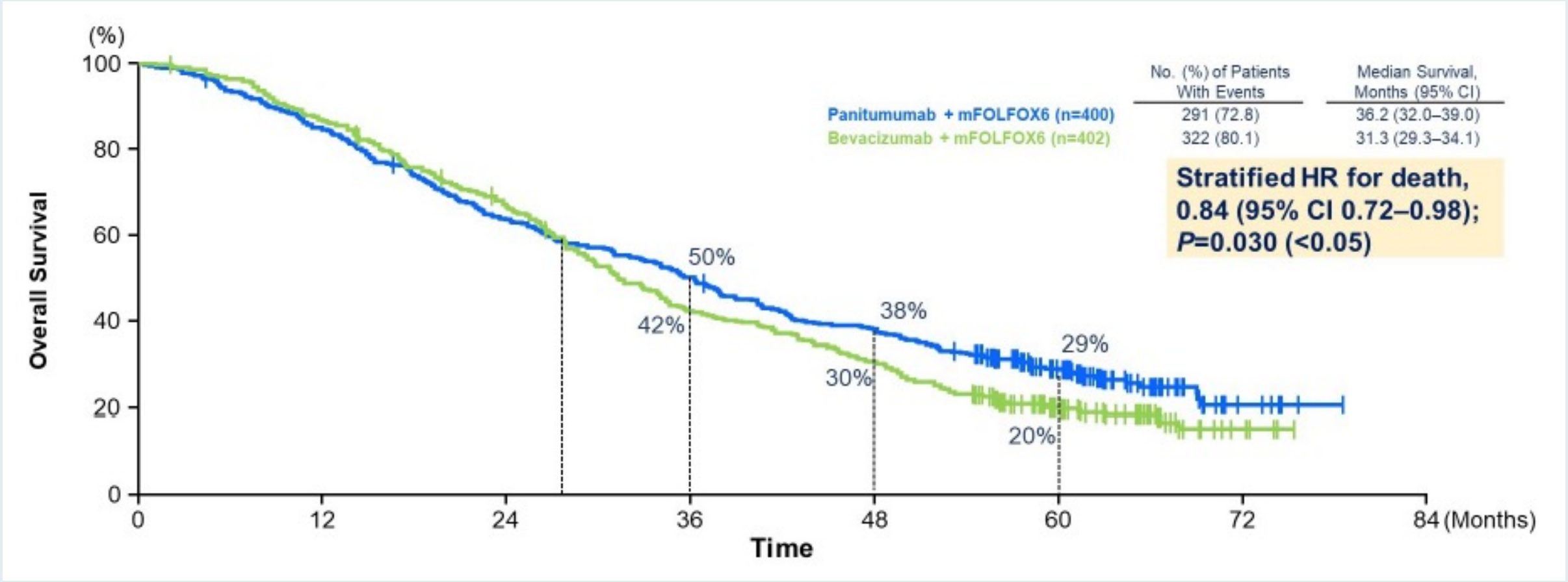
Yoshino T et al. ASCO 2022;Abstract LBA1.

PARADIGM: Overall Survival in Left-Sided Population (Primary Endpoint 1)



Yoshino T et al. ASCO 2022;Abstract LBA1.

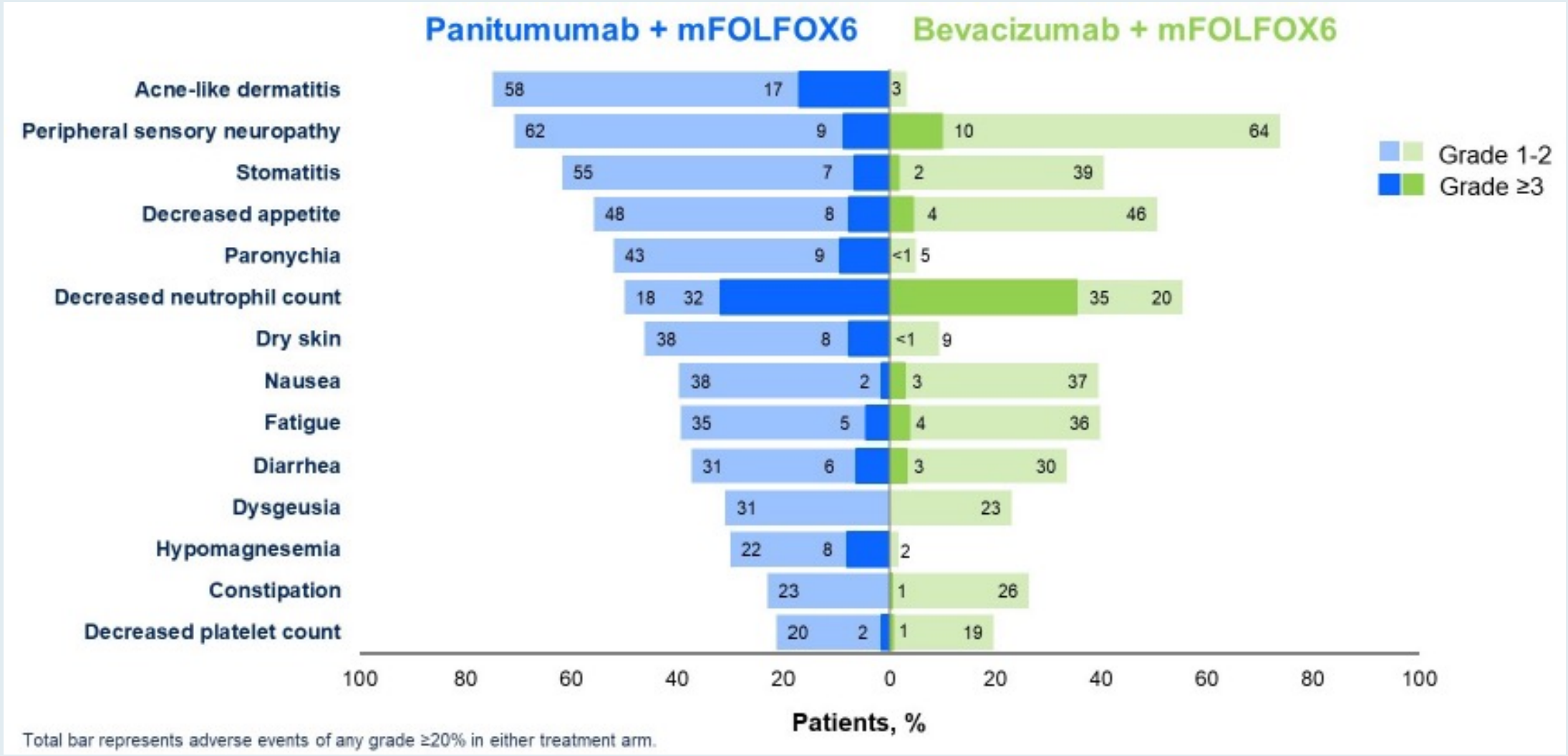
PARADIGM: Overall Survival in Overall Population (Primary Endpoint 2)



Yoshino T et al. ASCO 2022;Abstract LBA1.

RTP RESEARCH TO PRACTICE

PARADIGM: Adverse Events Reported in ≥20% of Patients



Yoshino T et al. ASCO 2022;Abstract LBA1.

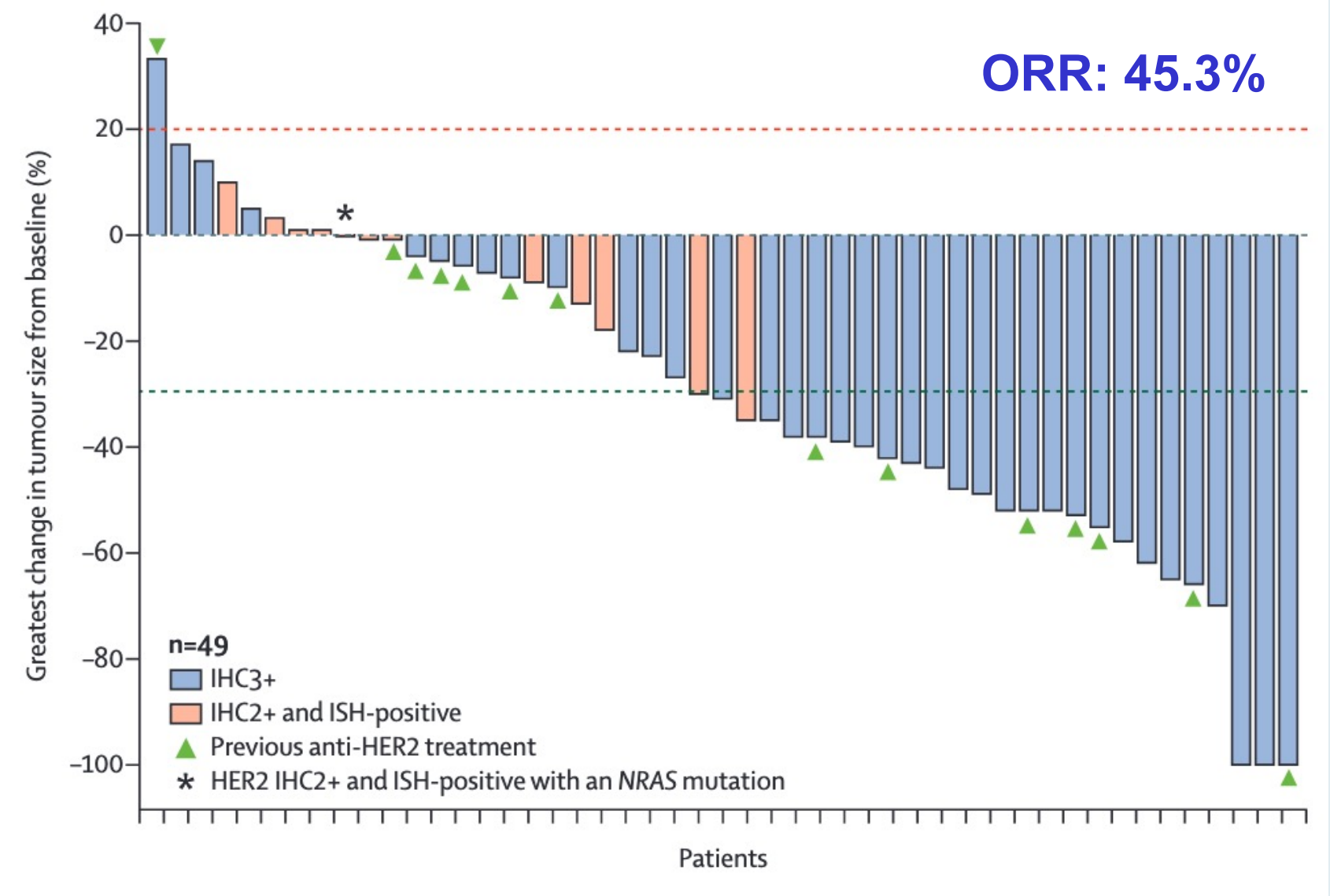
RTP RESEARCH TO PRACTICE

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.

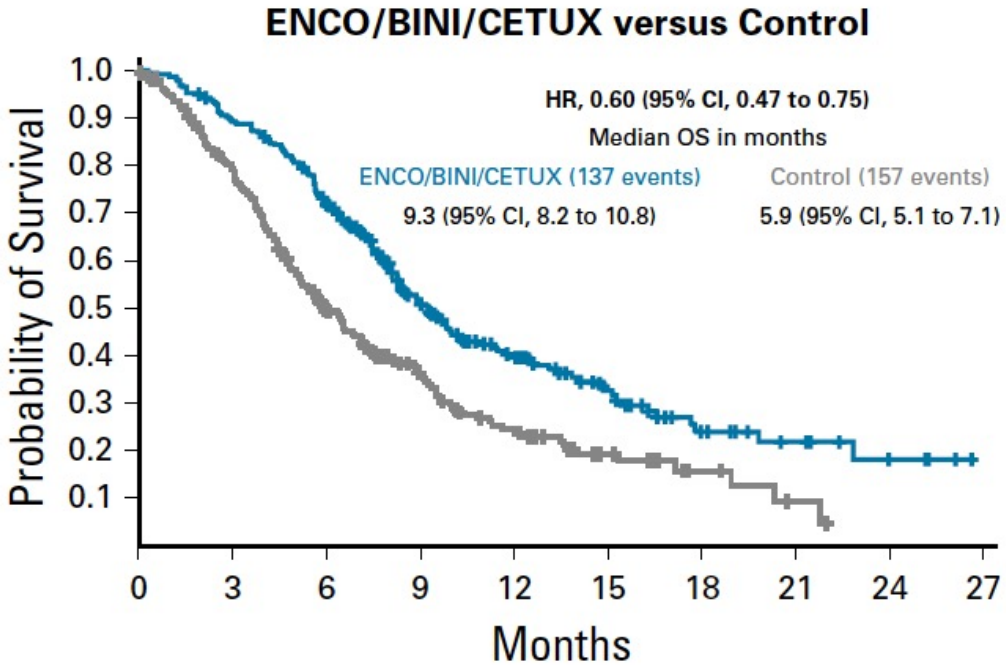
rapid communications

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]

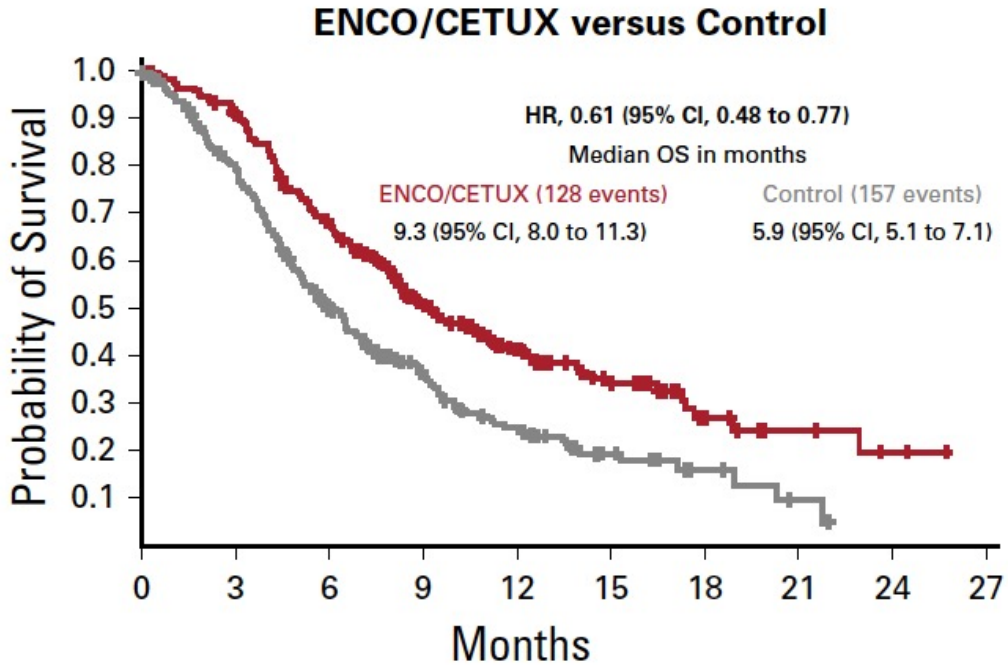
J Clin Oncol 2021;39(4):273-84.

BEACON: Overall Survival Results



Number of patients at risk

ENCO/BINI/CETUX	224	198	157	89	56	33	15	9	4	0
Control	221	166	98	54	33	15	6	2	0	0

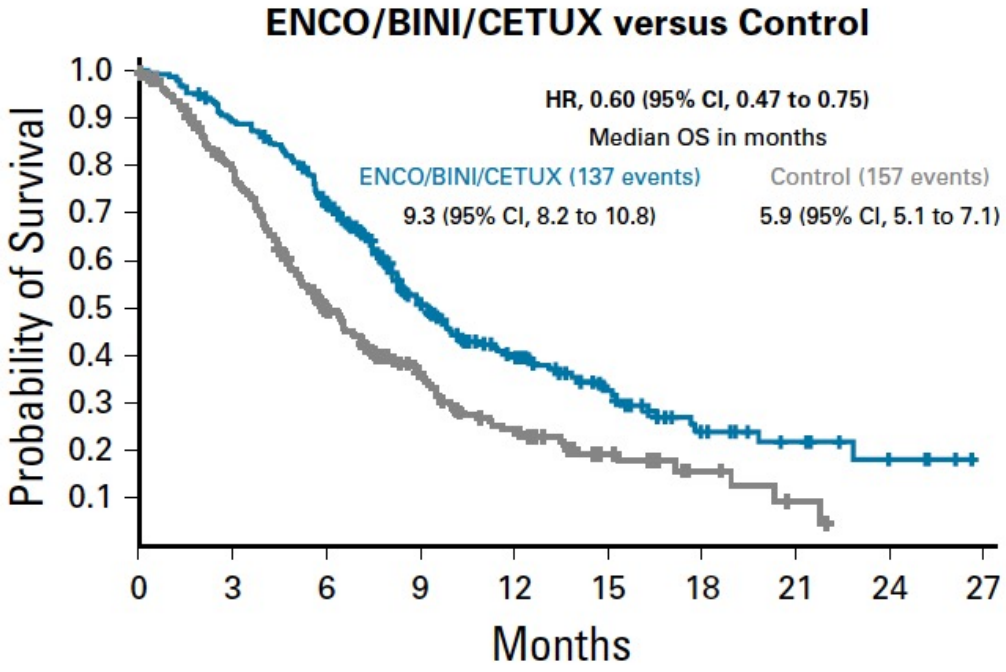


Number of patients at risk

ENCO/CETUX	220	197	143	83	47	28	13	7	2	0
Control	221	166	98	54	33	15	6	2	0	0

Tabanero J et al. *J Clin Oncol* 2021;39(4):273-84.

BEACON: Overall Survival Results



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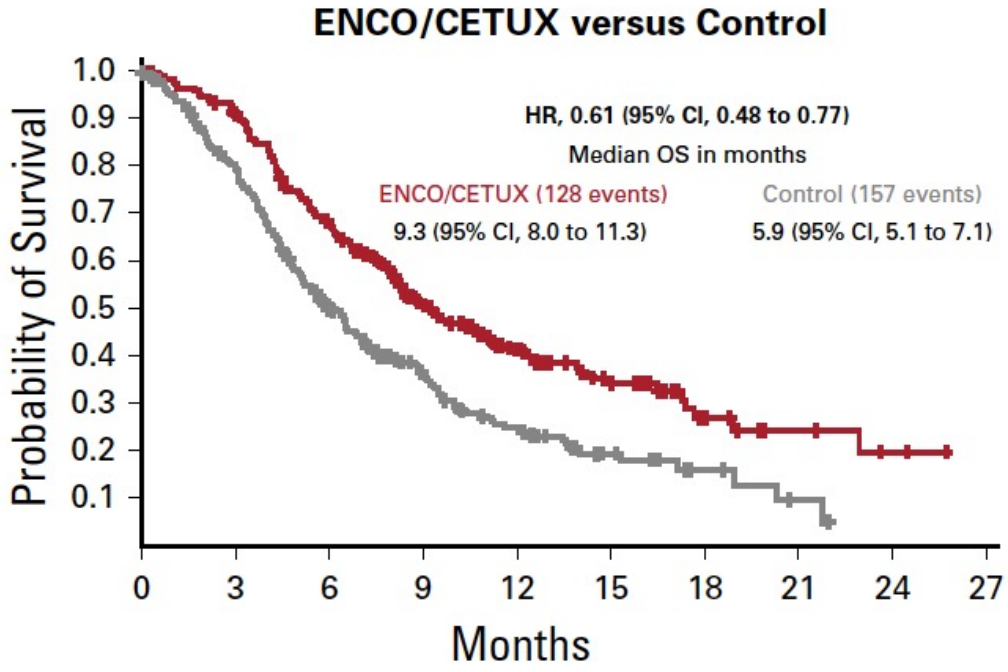

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Tabanero J et al. *J Clin Oncol* 2021;39(4):273-84.

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*

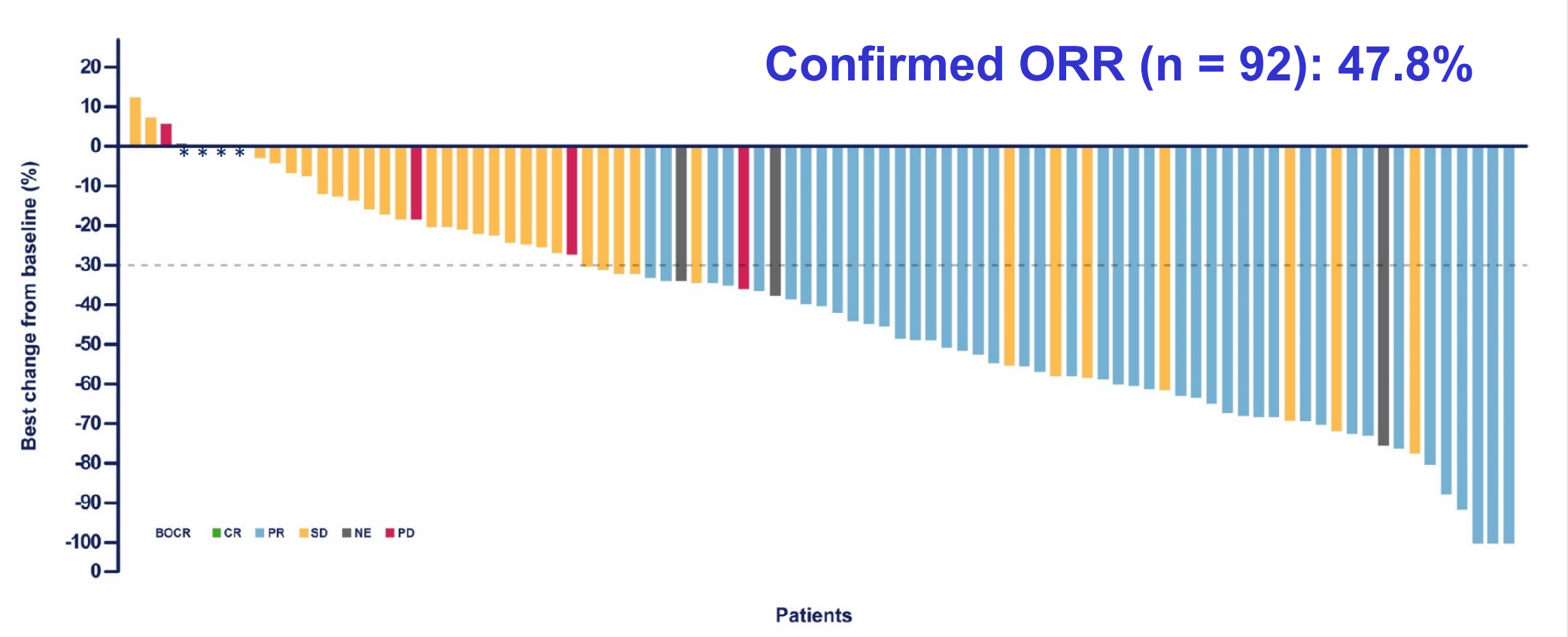
** University Hospitals Leuven, Belgium*

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.

- Overall survival was 17.2 mo (with a median follow-up of 14.4 mo)
- 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 FOLFIRIβ, 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; βFOLFOX 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.

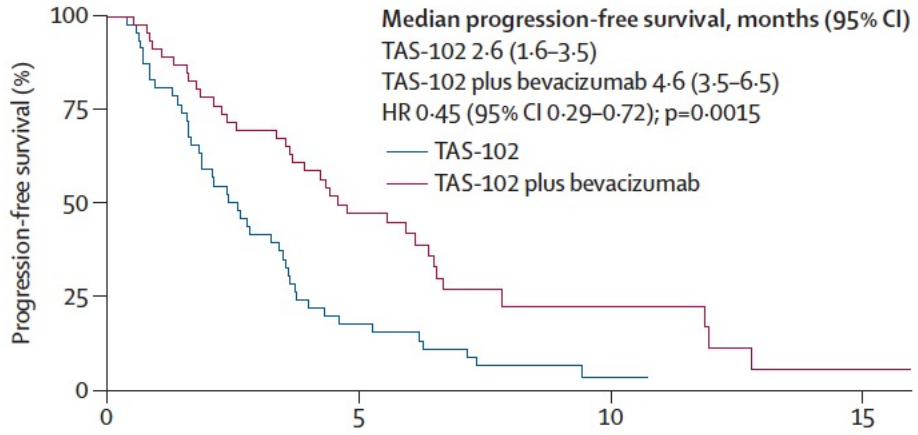
Lancet Oncol 2020;21(3):412-20.

Articles

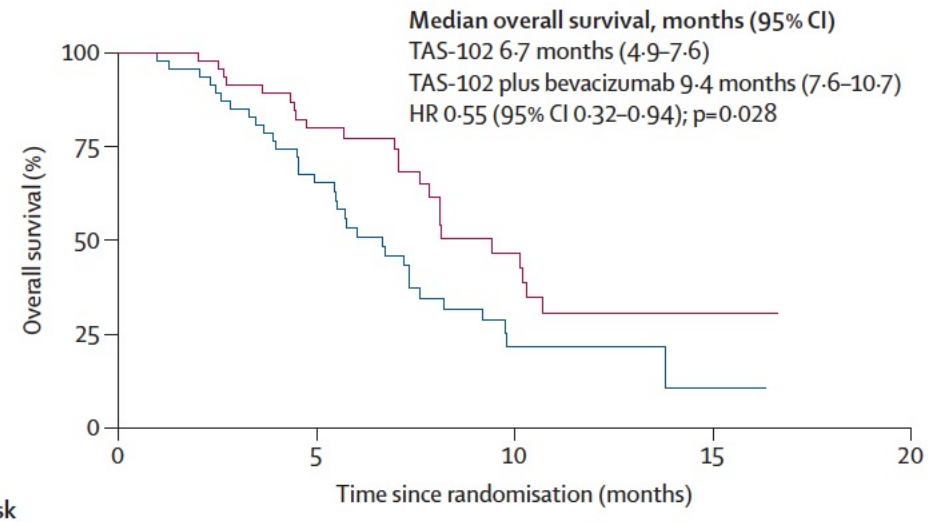
TAS-102 with or without bevacizumab in patients with chemorefractory metastatic colorectal cancer: an investigator-initiated, open-label, randomised, phase 2 trial

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 Metastatic Colorectal Cancer



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

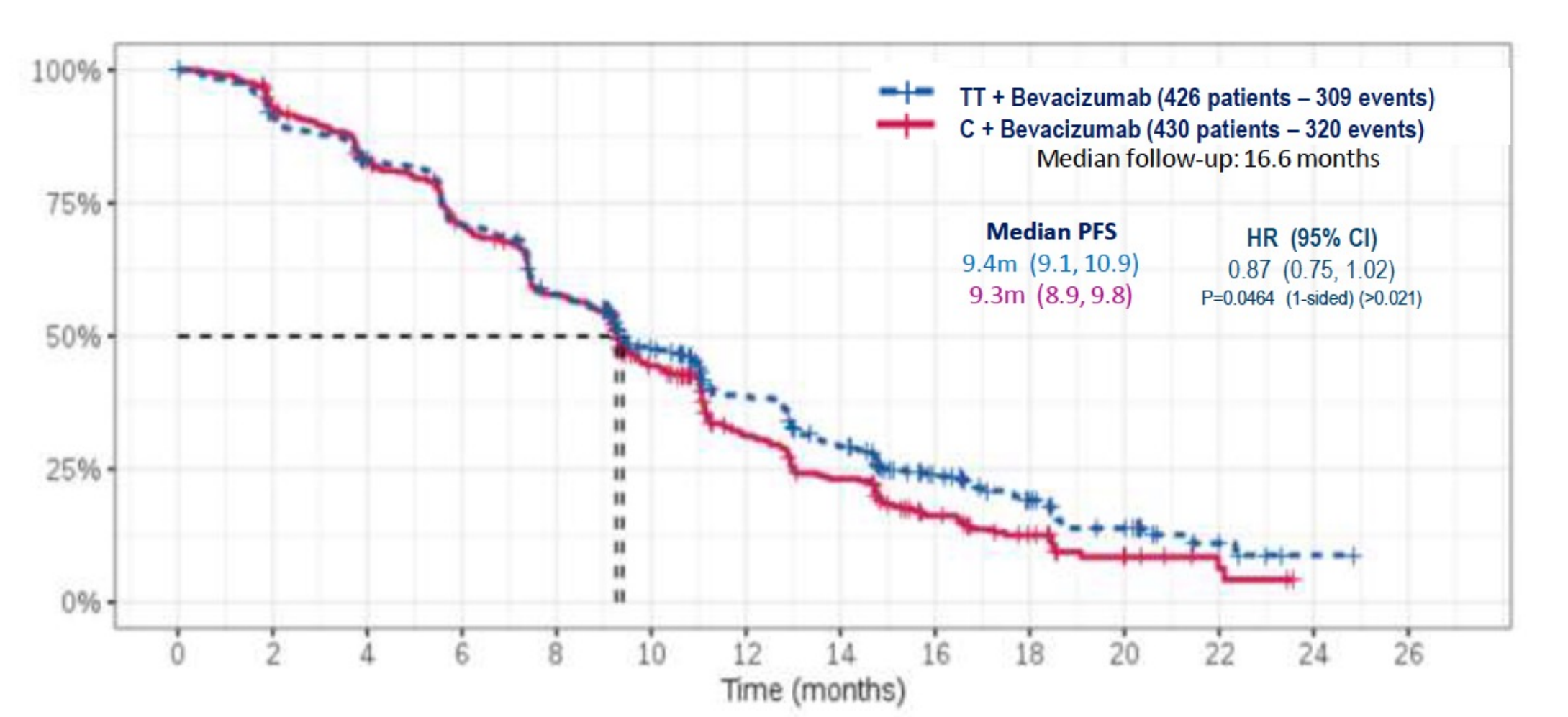
TRIFLURIDINE/TIPIRACIL PLUS BEVACIZUMAB VS CAPECITABINE PLUS BEVACIZUMAB AS FIRST LINE TREATMENT FOR PATIENTS WITH METASTATIC COLORECTAL CANCER (mCRC) INELIGIBLE FOR INTENSIVE THERAPY: THE PHASE III RANDOMIZED SOLSTICE STUDY

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

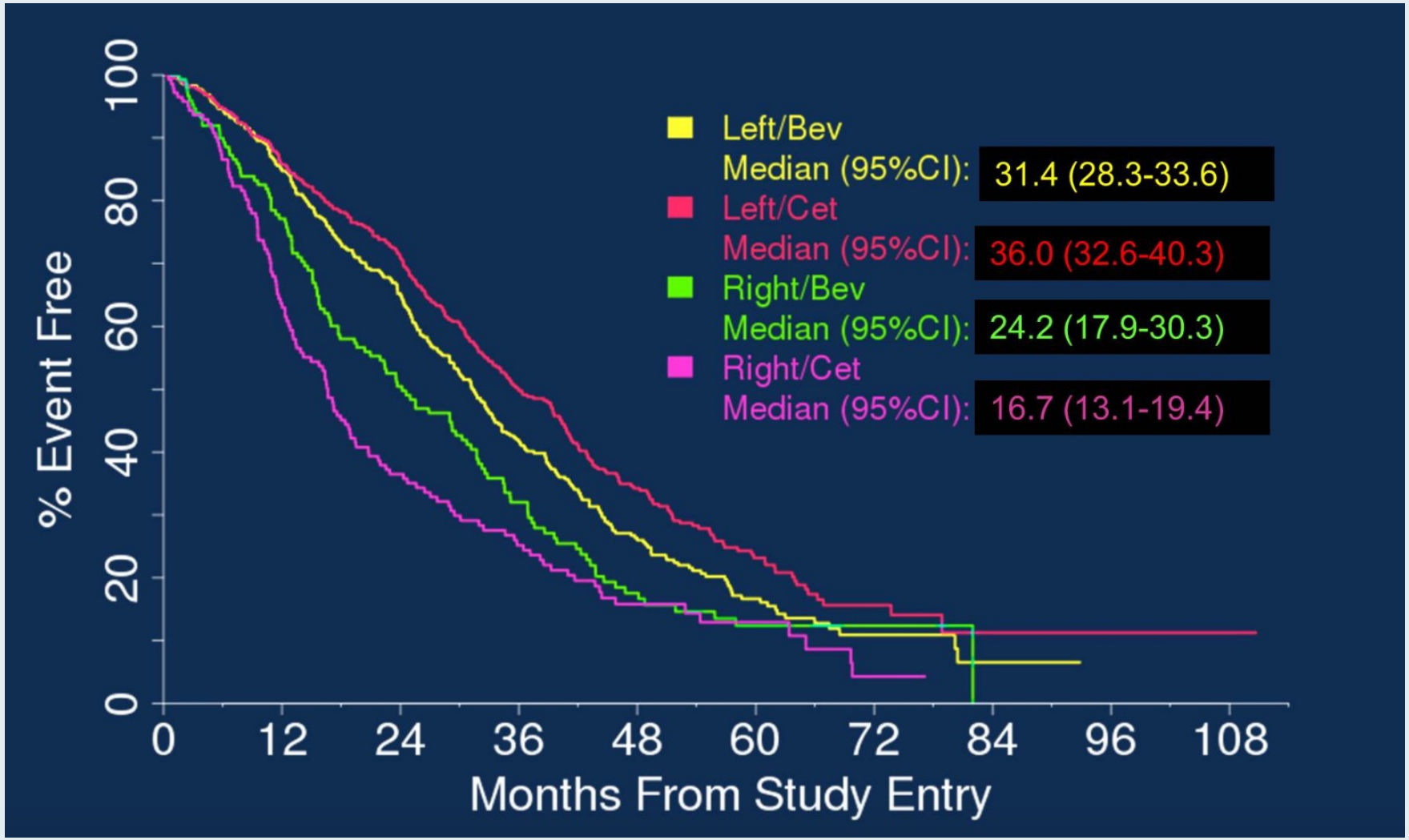


PFS = progression-free survival

André T et al. *ESMO Virtual Plenary* 2021;22:Abstract VP-11.

RTP RESEARCH TO PRACTICE

CALGB/SWOG-80405: Overall Survival by Tumor Location and Biologic Agent (RAS Wild Type)



Venook A et al. ASCO 2016;Abstract 3504.

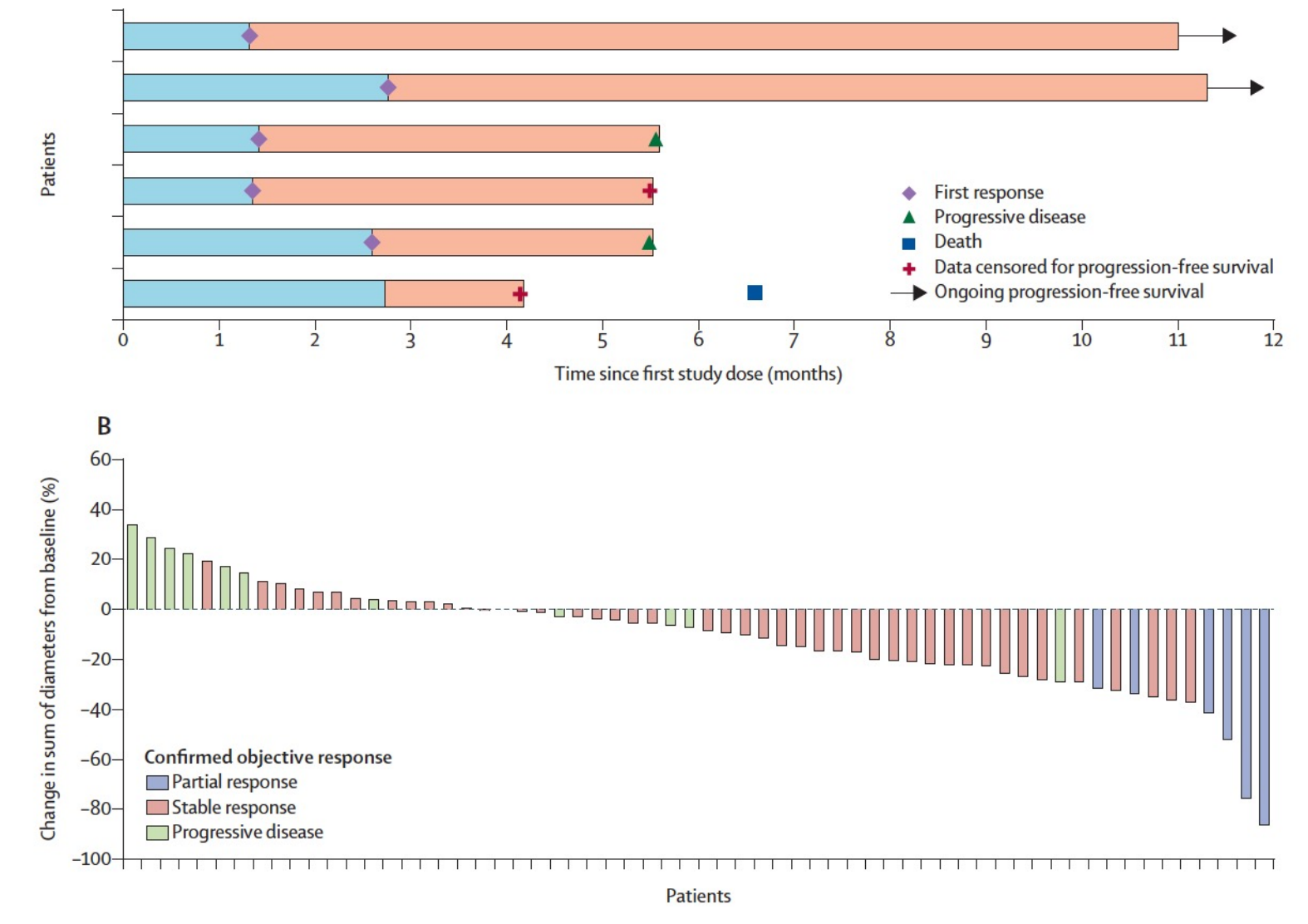
Lancet Oncol 2022;23(1):115-24.

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*

CodeBreaK 100: Efficacy of Sotorasib



Fakih MG et al. *Lancet Oncol* 2022;23(1):115-24.

Gastrointestinal Cancers Agenda

Module 1: Colorectal Cancer

Module 2: Upper Gastrointestinal Cancers

- Adjuvant and postneoadjuvant use of immunotherapy
- First-line treatment of metastatic disease: Patient selection for immunotherapy alone or in combination with chemotherapy
- Sequential treatment of HER2-positive metastatic disease; role of T-DXd

Module 3: Hepatocellular and Biliary Tract Cancers

Module 4: Pancreatic Adenocarcinoma

Checkpoint Inhibitor Approvals for HER2-Negative Gastric, Gastroesophageal Junction (GEJ) and Esophageal Cancers

Regimen/FDA approval date/pivotal trial	Location	Histology	Setting	PD-L1
Nivolumab 5/20/21 (CM-577)	Esophageal, GEJ	Adenocarcinoma and squamous	• Completed resected, with residual pathologic disease after neoadjuvant chemoradiation	Not required
Pembrolizumab + cisplatin/5-FU 3/22/2021 (KN-590)	Esophageal, GEJ	Adenocarcinoma and squamous	• Recurrent locally advanced or metastatic • Not amenable to surgical resection or definitive chemoradiation	Not required
Nivolumab + mFOLFOX6 or CAPOX 4/16/2021 (CM-649)	Gastric, GEJ, esophageal	Adenocarcinoma	• Advanced or metastatic gastric, GEJ or esophageal adenocarcinoma	Not required
Pembrolizumab 7/30/2019 (KN-181)	Esophageal, GEJ	Squamous	• Recurrent locally advanced or metastatic • Not amenable to surgical resection or definitive chemoradiation • After ≥1 prior lines of systemic therapy	CPS ≥10
Nivolumab 6/10/2020 (ATTRACTION-3)	Esophageal	Squamous	• Unresectable advanced, recurrent or metastatic • After prior fluoropyrimidine- and platinum-based chemotherapy	Not required

Kelly RJ et al. *New Engl J Med* 2021;384(13):1191-203. Sun J et al. *Lancet* 2021;398(10302):759-71. Janjigian YY et al. *Lancet* 2021;398(10294):27-40. Kojima T et al. *J Clin Oncol* 2020;38(35):4138-48. Kato K et al. *Lancet Oncol* 2019;20(11):1506-17.

2021 ASCO ANNUAL MEETING

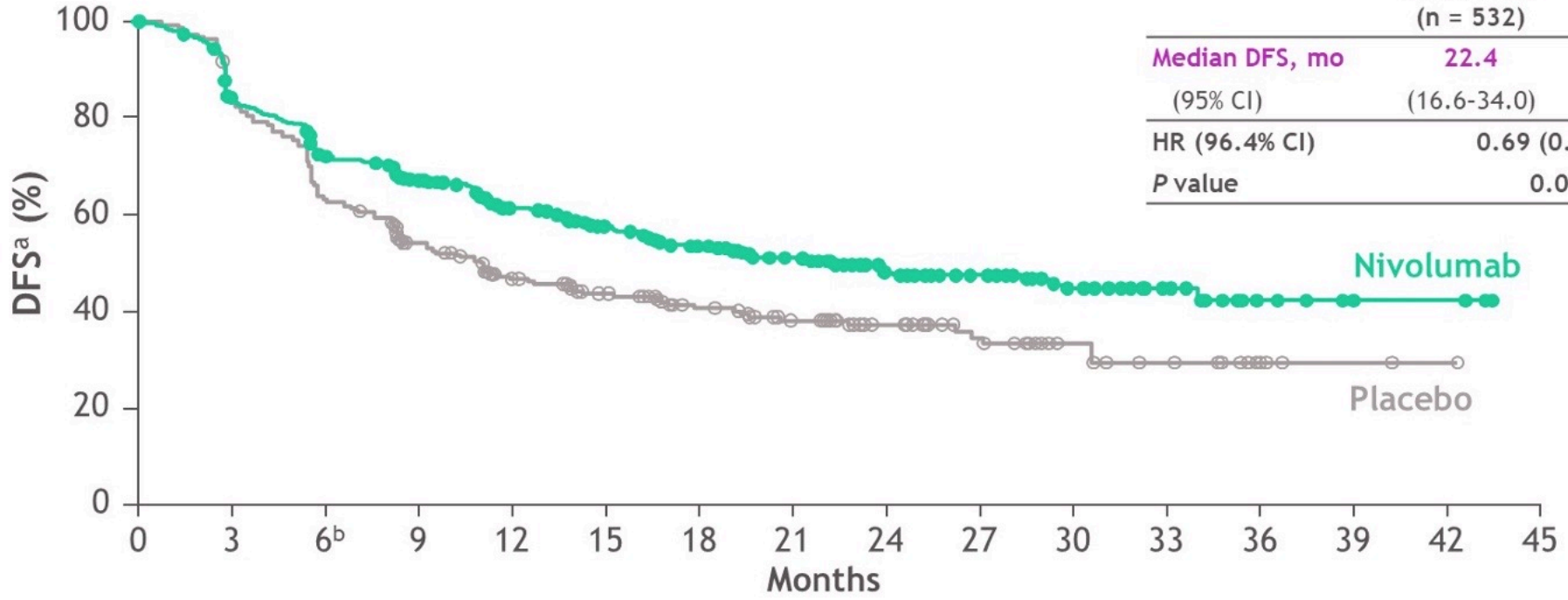
Adjuvant nivolumab in resected esophageal or gastroesophageal junction cancer following neoadjuvant chemoradiotherapy: expanded efficacy and safety analyses from CheckMate 577

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.

Article

Nature 2022;603(7903):942-8.

Nivolumab plus chemotherapy or ipilimumab in gastro-oesophageal cancer

https://doi.org/10.1038/s41586-022-04508-4

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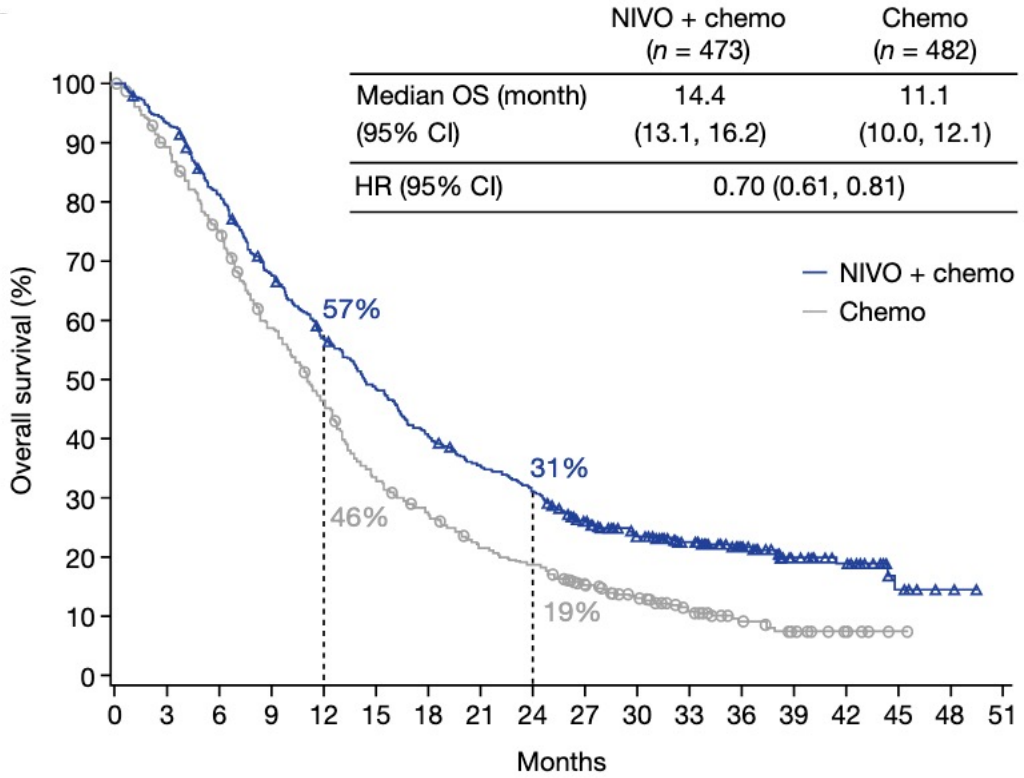
Published online: 23 March 2022

Open access

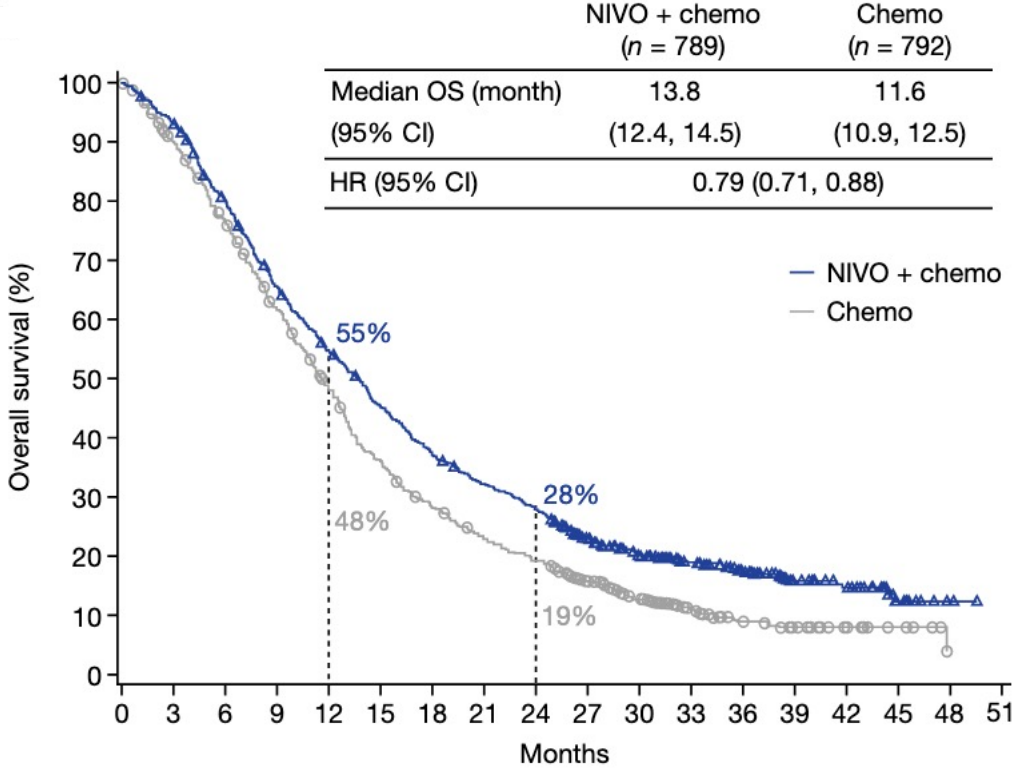
Kohei Shitara[1], Jaffer A. Ajani[2], Markus Moehler[3], Marcelo Garrido[4], Carlos Gallardo[5], Lin Shen[6], Kensei Yamaguchi[7], Lucjan Wyrwicz[8], Tomasz Skoczylas[9], Arinilda Campos Bragagnoli[10], Tianshu Liu[11], Mustapha Tehfe[12], Elena Elimova[13], Ricardo Bruges[14], Thomas Zander[15], Sergio de Azevedo[16], Ruben Kowalyszyn[17], Roberto Pazo-Cid[18], Michael Schenker[19], James M. Cleary[20], Patricio Yanez[21], Kynan Feeney[22], Michalis V. Karamouzis[23], Valerie Poulart[24], Ming Lei[24], Hong Xiao[24], Kaoru Kondo[24], Mingshun Li[24] & Yelena Y. Janjigian[25]✉

CheckMate 649: Overall Survival

PD-L1 CPS ≥5



All randomly assigned patients

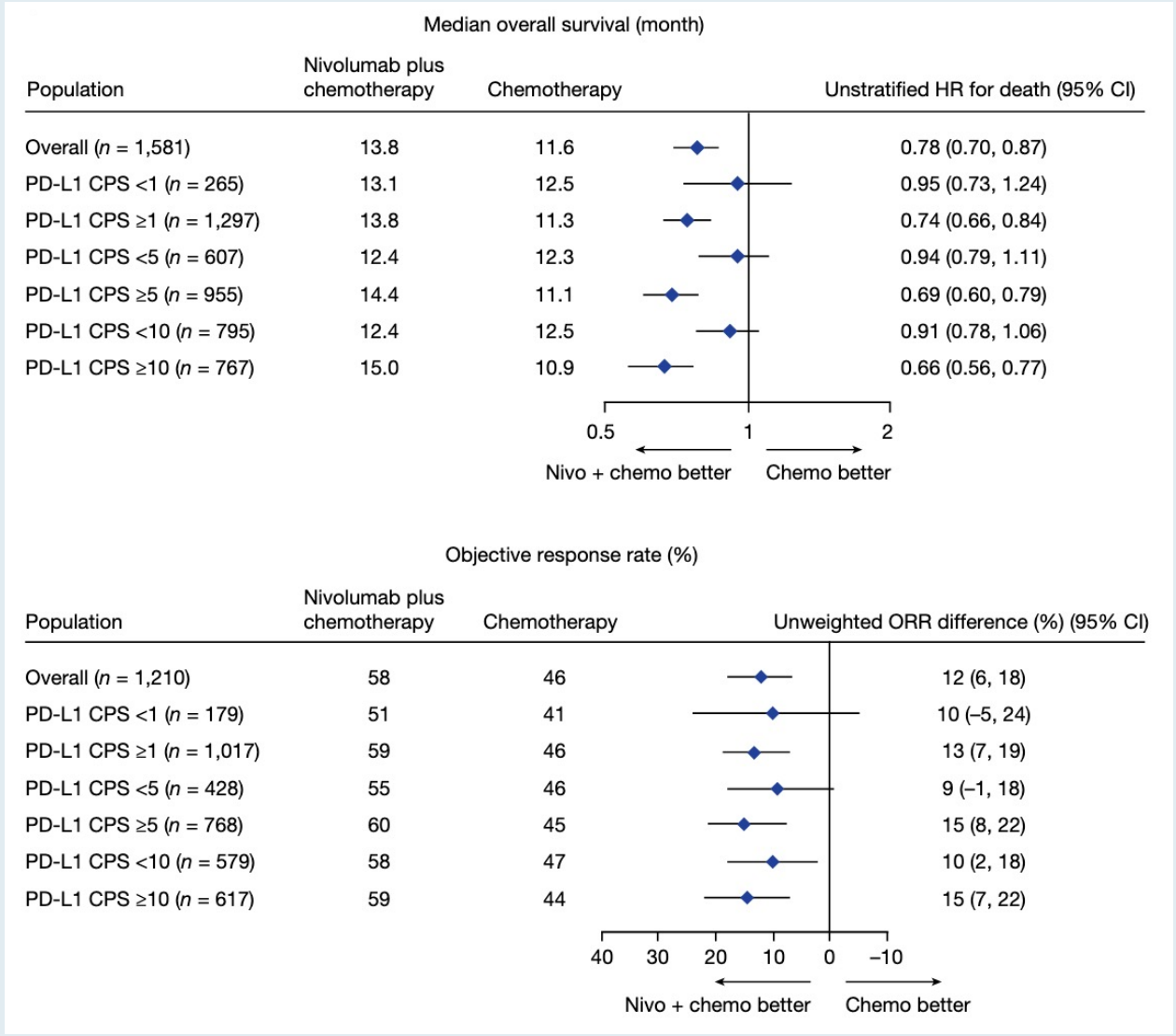


CPS = combined positive score; OS = overall survival; NIVO = nivolumab

Shitara K et al. *Nature* 2022;603(7903):942-8.

RTP RESEARCH TO PRACTICE

CheckMate 649: Efficacy Subgroup Analysis by PD-L1 CPS Excluding Patients with MSI-High Tumors



Shitara K et al. *Nature* 2022;603(7903):942-8.

CPS = combined positive score; MSI = microsatellite instability

RTP RESEARCH TO PRACTICE

The NEW ENGLAND JOURNAL of MEDICINE

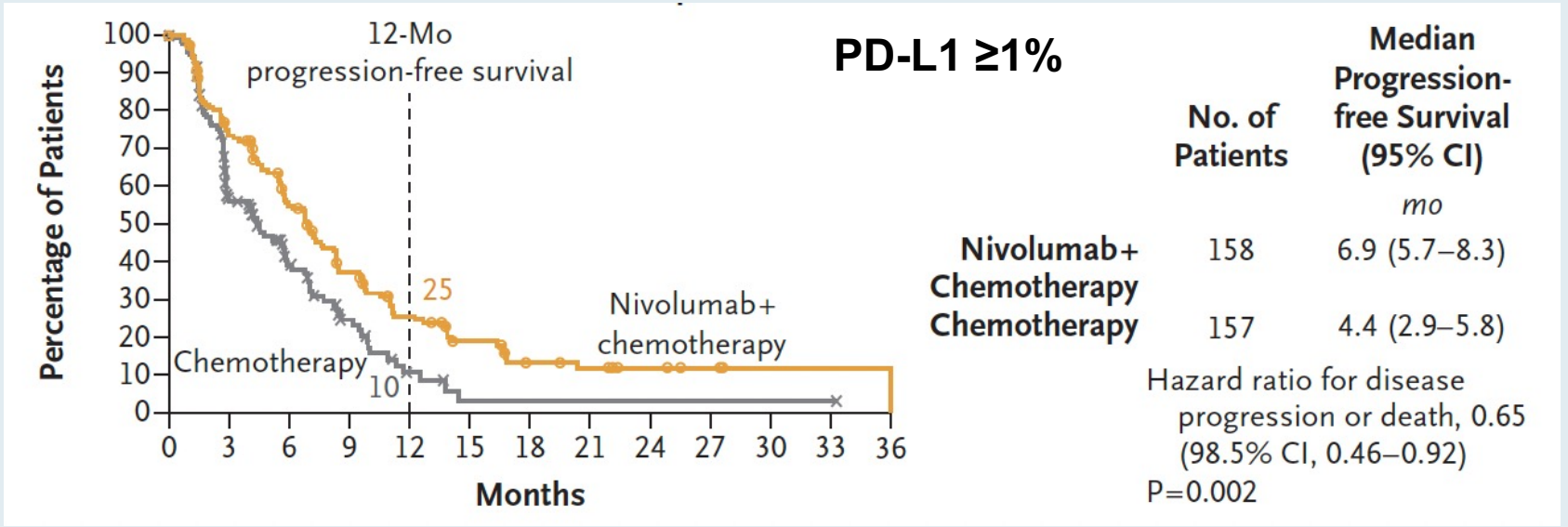
ORIGINAL ARTICLE

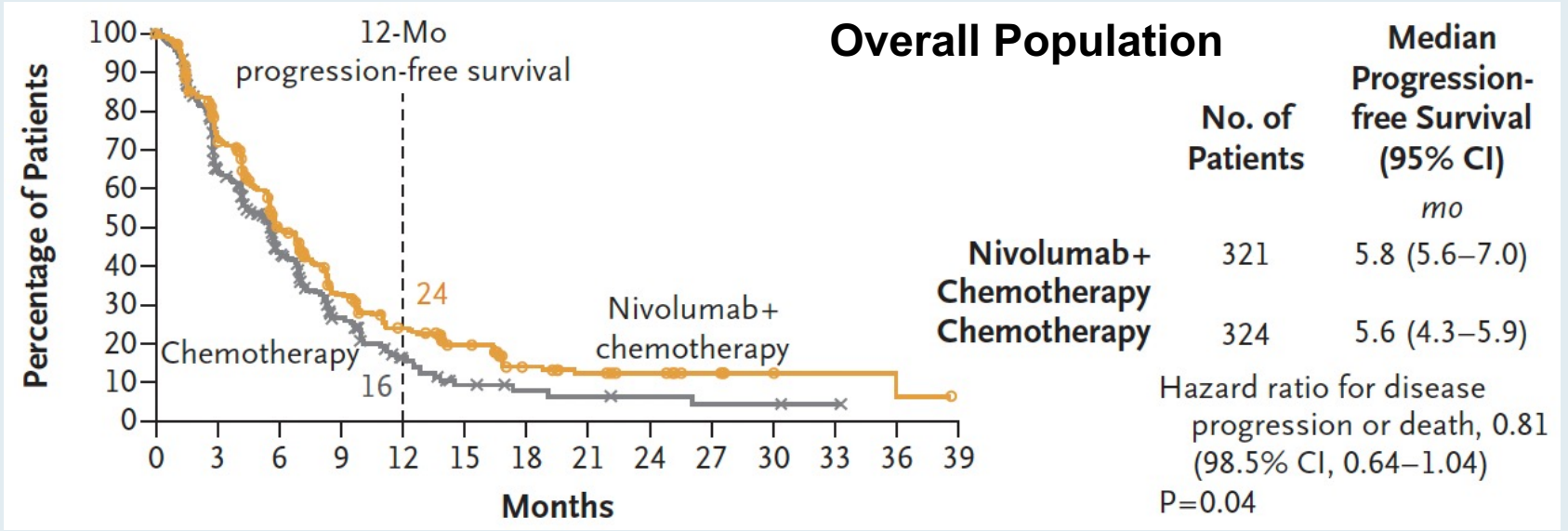
Nivolumab Combination Therapy in Advanced Esophageal Squamous-Cell Carcinoma

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*

New Engl J Med 2022;386(5):449-62.

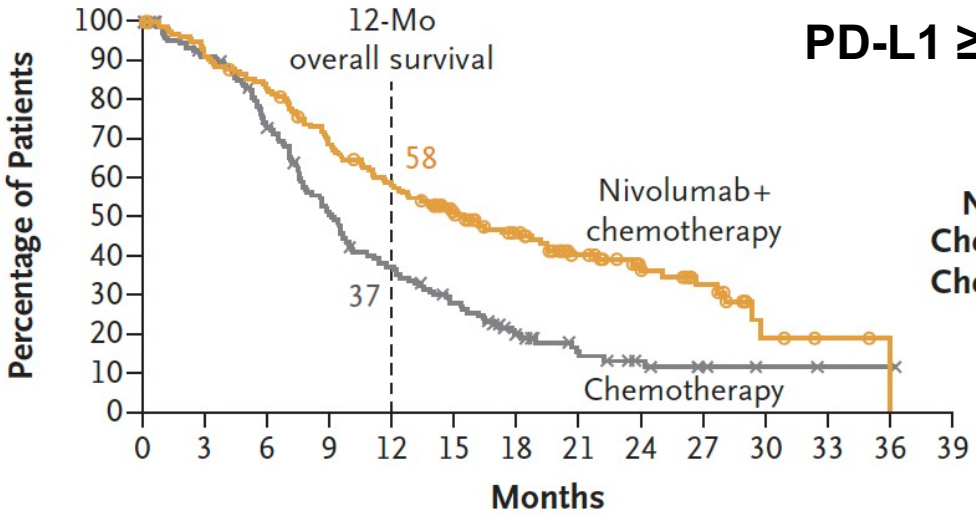
CheckMate 648: Progression-Free Survival for PD-L1 ≥1% and in the Overall Population — Nivolumab and Chemotherapy





Doki Y et al. *N Engl J Med* 2022;386(5):449-62.

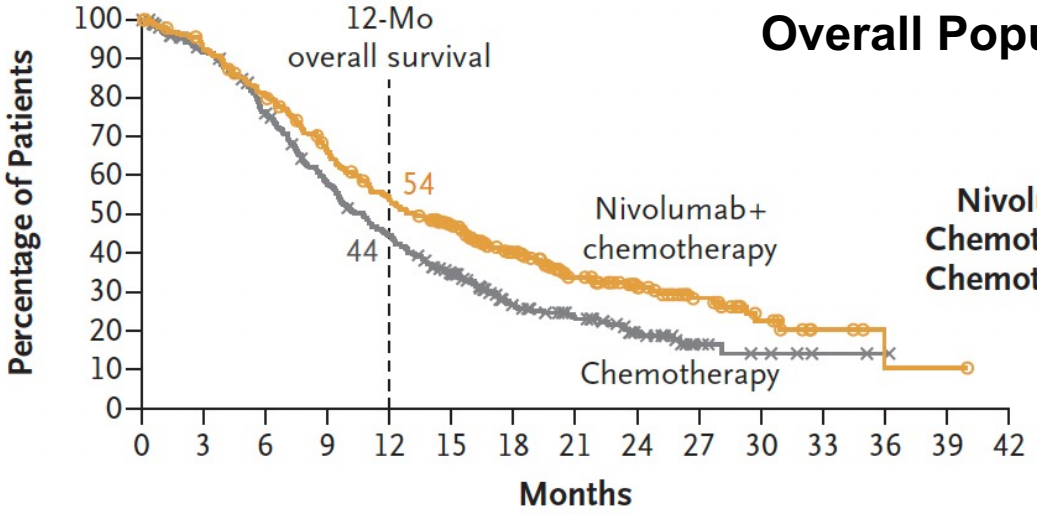
CheckMate 648: Overall Survival for PD-L1 ≥1% and in the Overall Population — Nivolumab and Chemotherapy



PD-L1 ≥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 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)

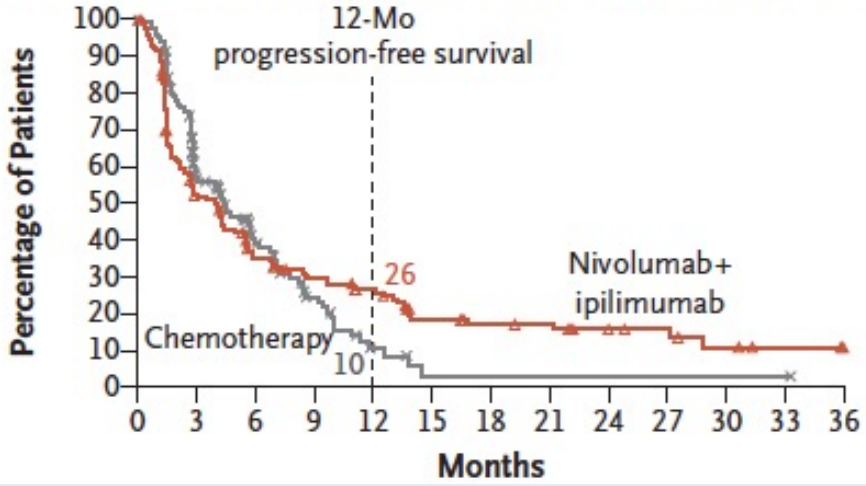
Hazard ratio for death, 0.74
(99.1% CI, 0.58–0.96)
P=0.002

Doki Y et al. *N Engl J Med* 2022;386(5):449-62.

RTP RESEARCH TO PRACTICE

CheckMate 648: Progression-Free Survival for PD-L1 ≥1% and in the Overall Population — Nivolumab and Ipilimumab

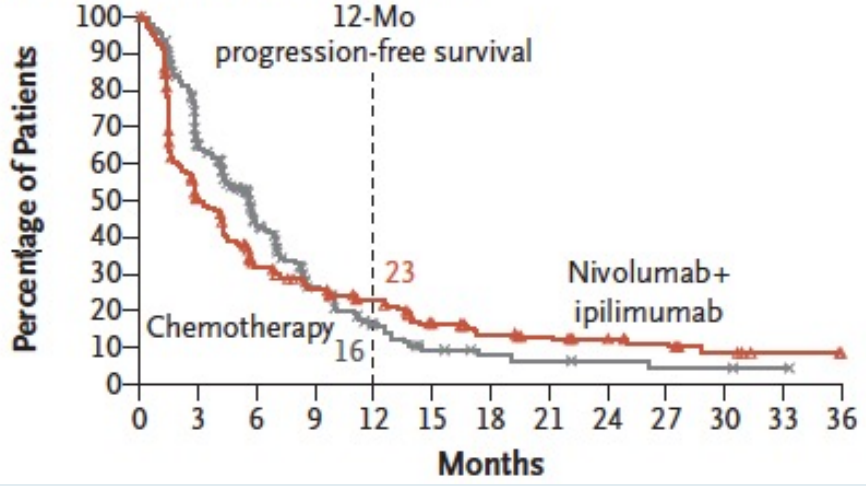
Progression-free Survival in Patients with Tumor-Cell PD-L1 Expression of ≥1%



	No. of Patients	Median Progression-free Survival (95% CI)
		mo
Nivolumab+ Ipilimumab	158	4.0 (2.4–4.9)
Chemotherapy	157	4.4 (2.9–5.8)

Hazard ratio for disease progression or death, 1.02 (98.5% CI, 0.73–1.43)
P=0.90

Progression-free Survival in the Overall Population



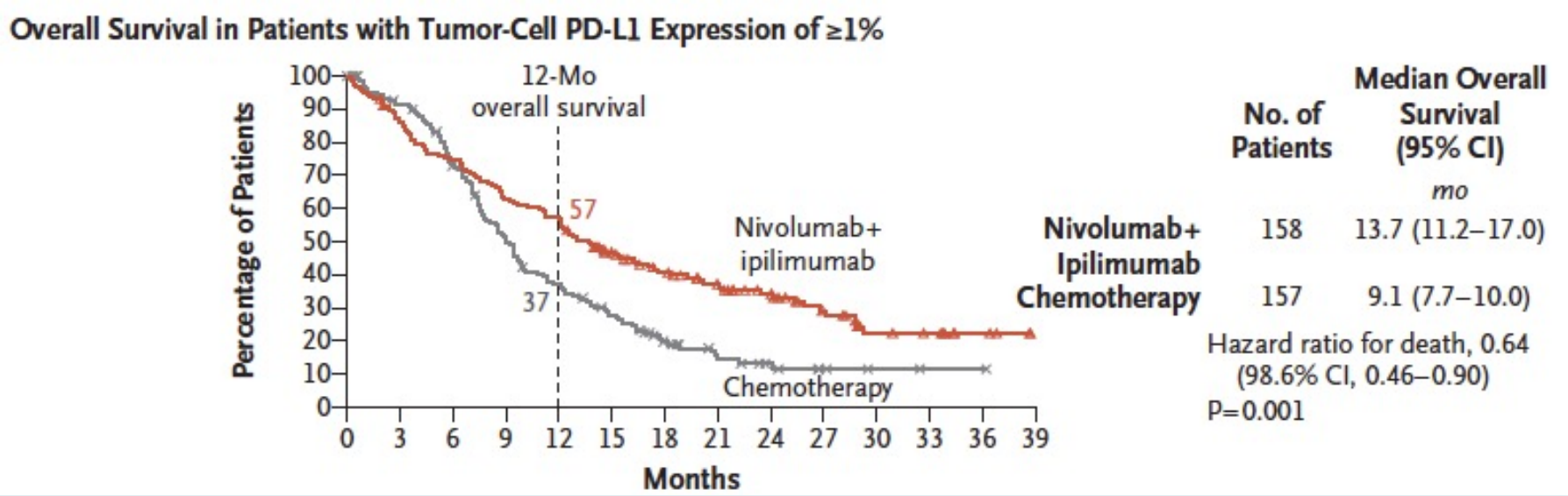
	No. of Patients	Median Progression-free Survival (95% CI)
		mo
Nivolumab+ Ipilimumab	325	2.9 (2.7–4.2)
Chemotherapy	324	5.6 (4.3–5.9)

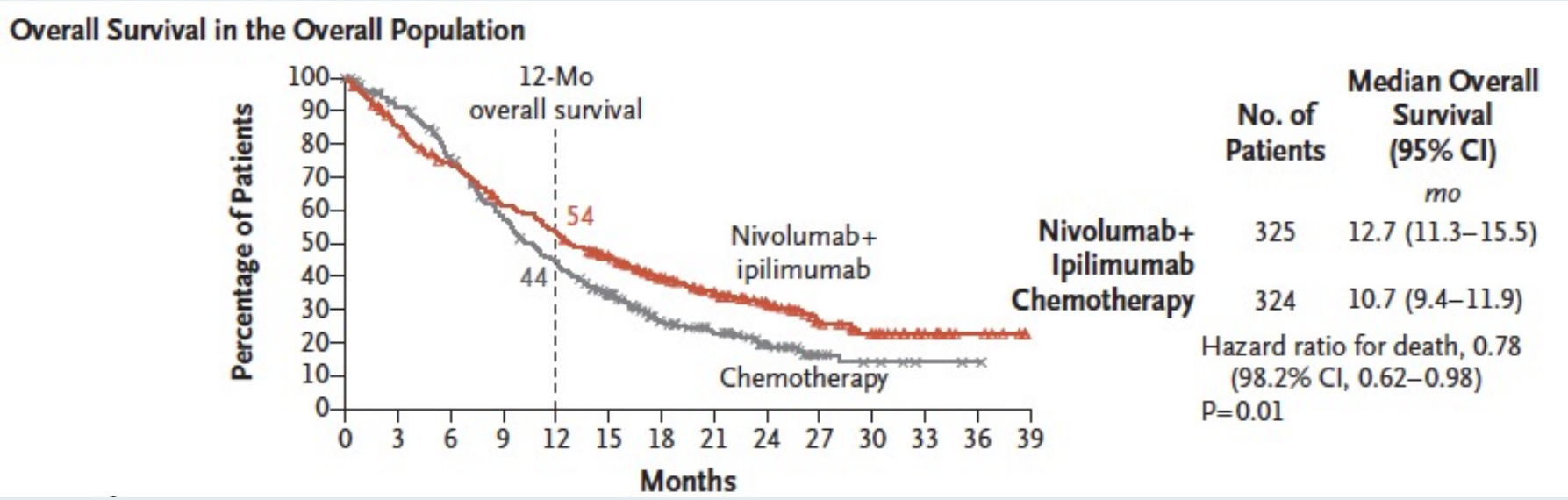
Hazard ratio for disease progression or death, 1.26 (95% CI, 1.04–1.52)
P value not tested

Doki Y et al. *New Engl J Med* 2022;386(5):449-62.

RTP RESEARCH TO PRACTICE

CheckMate 648: Overall Survival for PD-L1 ≥1% and in the Overall Population — Nivolumab and Ipilimumab





Doki Y et al. *New Engl J Med* 2022;386(5):449-62.

CheckMate 648: Antitumor Activity (BICR)

Endpoint	PD-L1 ≥1%			Overall population		
	Nivo/chemo (n = 158)	Nivo/ipi (n = 158)	Chemotherapy (n = 157)	Nivo/chemo (n = 321)	Nivo/ipi (n = 325)	Chemotherapy (n = 324)
ORR	53%	35%	20%	47%	28%	27%
Best overall response						
CR	16%	18%	5%	13%	11%	6%
PR	37%	18%	15%	34%	17%	21%
SD	25%	27%	46%	32%	32%	46%
PD	14%	30%	15%	13%	32%	12%
Median DoR	8.4 mo	11.8 mo	5.7 mo	8.2 mo	11.1 mo	7.1 mo
Pts with ongoing response	13%	25%	3%	17%	22%	6%

BICR = blinded independent central review; nivo = nivolumab; ipi = ipilimumab; ORR = objective response rate; CR = complete response; PR = partial response; SD = stable disease; PD = disease progression; DoR = duration of response

Doki Y et al. *N Engl J Med* 2022;386(5):449-62.

CheckMate 648: Select Treatment-Related Adverse Events

Endpoint	Nivolumab/chemotherapy (N = 310)		Nivolumab/ipilimumab (N = 322)		Chemotherapy (N = 304)	
	Any grade	Grade 3 or 4	Any grade	Grade 3 or 4	Any grade	Grade 3 or 4
Serious AEs	53%	35%	20%	47%	28%	27%
AEs leading to discontinuation	16%	18%	5%	13%	11%	6%
Nausea	59%	4%	8%	<1%	52%	3%
Stomatitis	32%	6%	4%	0	23%	2%
Anemia	30%	10%	4%	1%	22%	6%
Decreased neutrophils	21%	8%	1%	0	17%	8%
Decreased white cells	14%	4%	1%	0	9%	2%

AEs = adverse events

Doki Y et al. *N Engl J Med* 2022;386(5):449-62.

Checkmate-649 versus Checkmate-648

CM-649 - Gastric cancer

NIVO (1 mg/kg) + IPI (3 mg/kg) Q3W × 4 then NIVO 240 mg Q2W[e]

Different schedules!

CM-648 - Esophageal cancer

NIVO (3 mg/kg) Q2W + IPI (1 mg/kg) Q6W

CM-649: Treatment-related Adverse Events

All treated,[a] n (%)	NIVO + chemo (n = 782)[b]		Chemo (n = 767)[b]		NIVO + IPI (n = 403)[c]		Chemo (n = 389)[c]	
	Any grade	Grade 3-4	Any grade	Grade 3-4	Any grade	Grade 3-4	Any grade	Grade 3-4
Any TRAEs[d]	739 (95)	471 (60)	682 (89)	344 (45)	323 (80)	155 (38)	356 (92)	180 (46)
Serious TRAEs[d]	175 (22)	133 (17)	94 (12)	77 (10)	122 (30)	93 (23)	54 (14)	45 (12)
TRAEs leading to discontinuation[d,e]	300 (38)	141 (18)	188 (25)	70 (9)	88 (22)	68 (17)	101 (26)	37 (10)
Treatment-related deaths[f]	16 (2)[g]		4 (< 1)[h]		10 (2)[i]		3 (< 1)[j]	

NIVO = nivolumab; IPI = ipilimumab; TRAEs = treatment-related adverse events

Lordick F. ESMO 2021;Discussant.

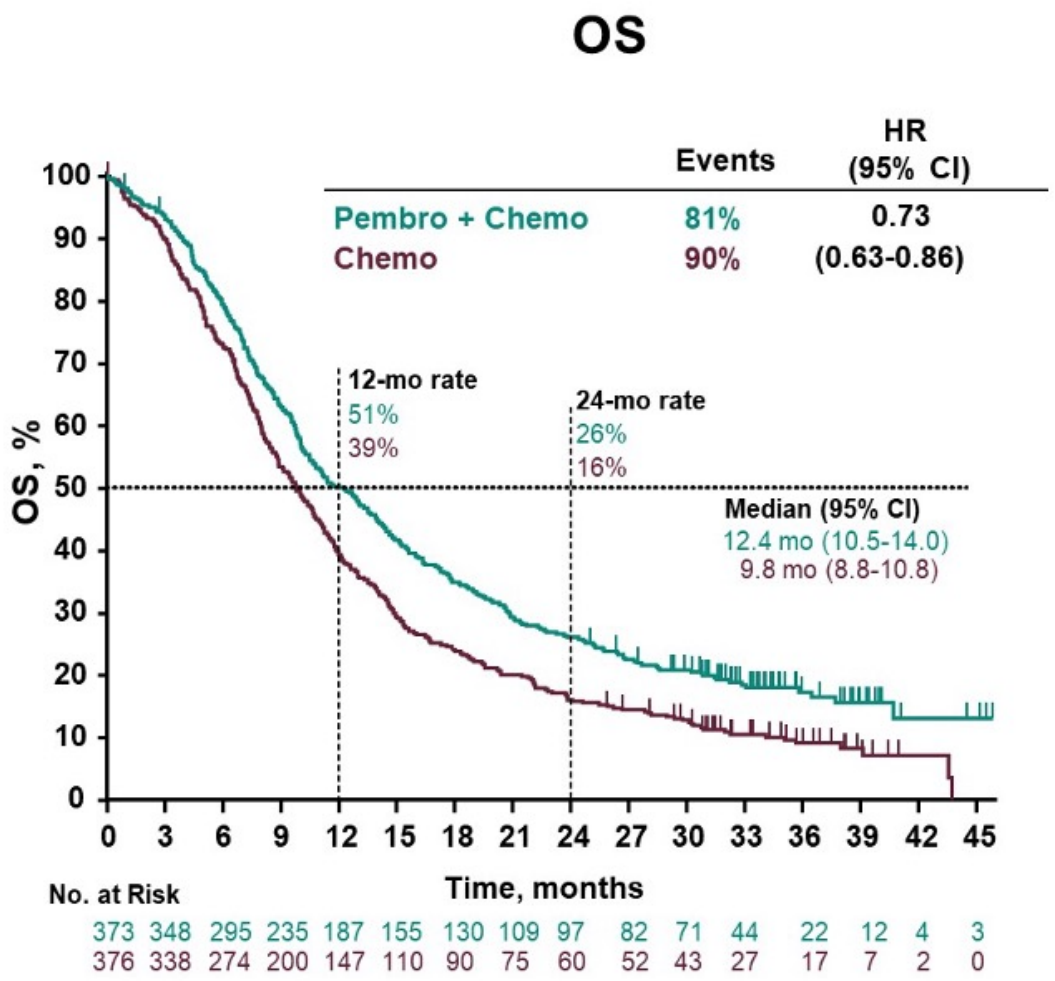
First-line Pembrolizumab Plus Chemotherapy Versus Chemotherapy in Advanced Esophageal Cancer: Longer-term Efficacy, Safety, and Quality-of-life Results From the Phase 3 KEYNOTE-590 Study

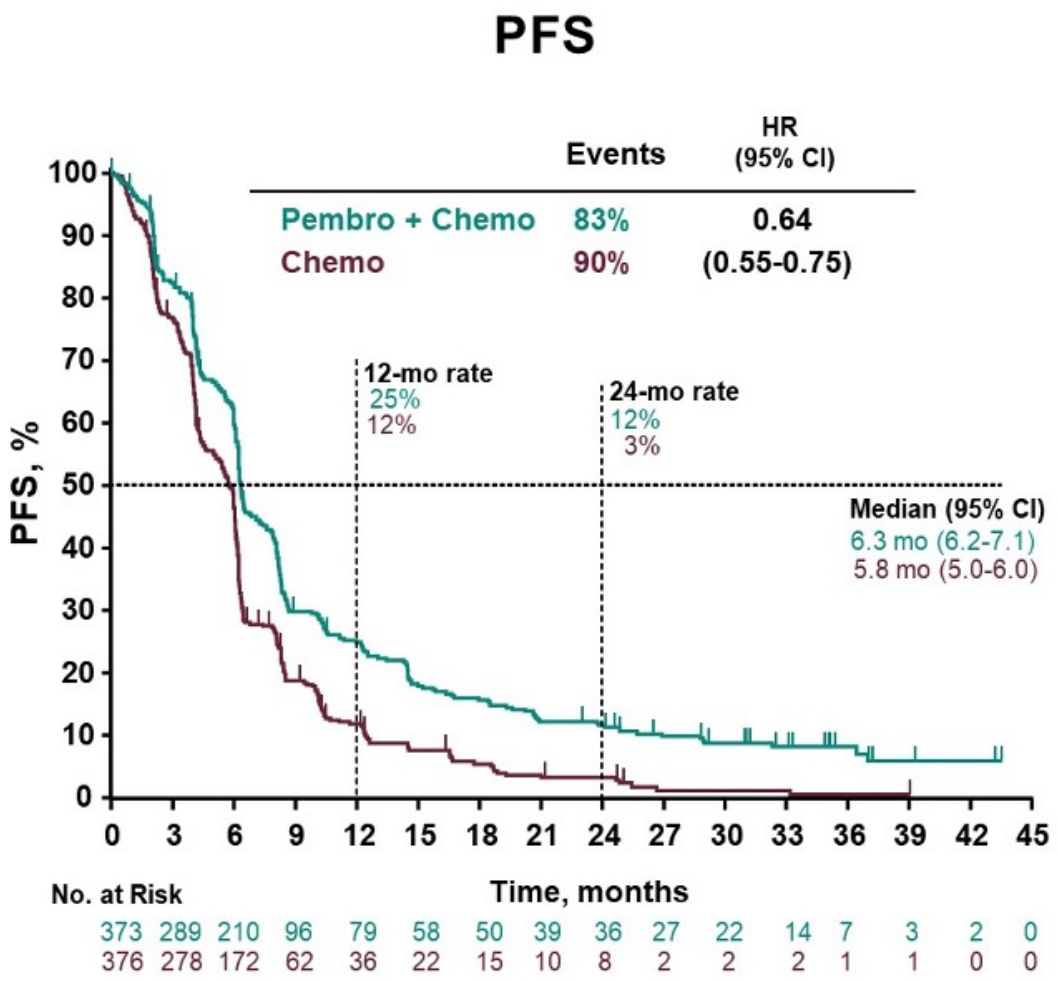
Jean-Philippe Metges,[1] Ken Kato,[2] Jong-Mu Sun,[3] Manish A. Shah,[4] Peter Enzinger,[5] Antoine Adenis,[6] Toshihiko Doi,[7] Takashi Kojima,[7] Zhigang Li,[8] Sung-Bae Kim,[9] Byoung Chul Cho,[10] Wasat Mansoor,[11] Shau-Hsuan Li,[12] Patrapim Sunpaweravong,[13] Maria Alsina Maqueda,[14] Gary L. Buchschacher, Jr,[15] Wu Jimin,[16] Sukrut Shah,[16] Pooja Bhagia,[16] Lin Shen[17]

[1]CHU Brest – Institut de Cancerologie et d'Hematologie ARPEGO Network, Brest, France; [2]National Cancer Center Hospital, Tokyo, Japan; [3]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [4]Weill Cornell Medical College, New York, NY, USA; [5]Dana Farber Cancer Institute, Boston, MA, USA; [6]IRCM, Inserm, Université Montpellier, ICM, Montpellier, France; [7]National Cancer Center Hospital East, Kashiwa, Japan; [8]Shanghai Chest Hospital Esophageal Disease Center, Shanghai, China; [9]Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; [10]Severance Hospital, Yonsei University Health System, Seoul, Republic of Korea; [11]Christie Hospital NHS Trust, Manchester, United Kingdom; [12]Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan; [13]Prince of Songkla University Hospital, Songkhla, Thailand; [14]Vall d'Hebron Institute of Oncology, Barcelona, Spain; [15]Kaiser Permanente Southern California, Los Angeles Medical Center, Los Angeles, CA, USA; [16]Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA; [17]Peking University Cancer Hospital & Institute; Beijing, China

Gastrointestinal Cancers Symposium 2022;Abstract 241.

KEYNOTE-590: Survival Analyses (All Patients)



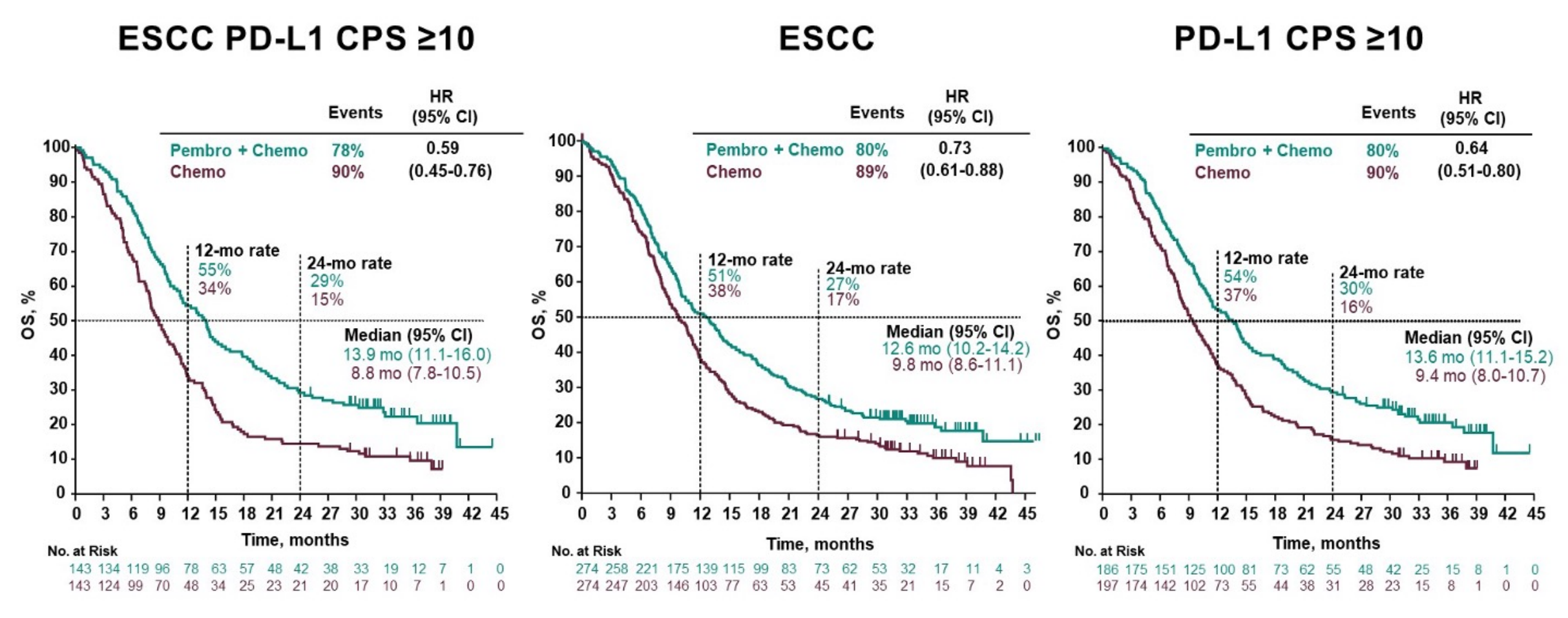


OS = overall survival; PFS = progression-free survival

Metges JP et al. Gastrointestinal Cancers Symposium 2022;Abstract 241.

RTP RESEARCH TO PRACTICE

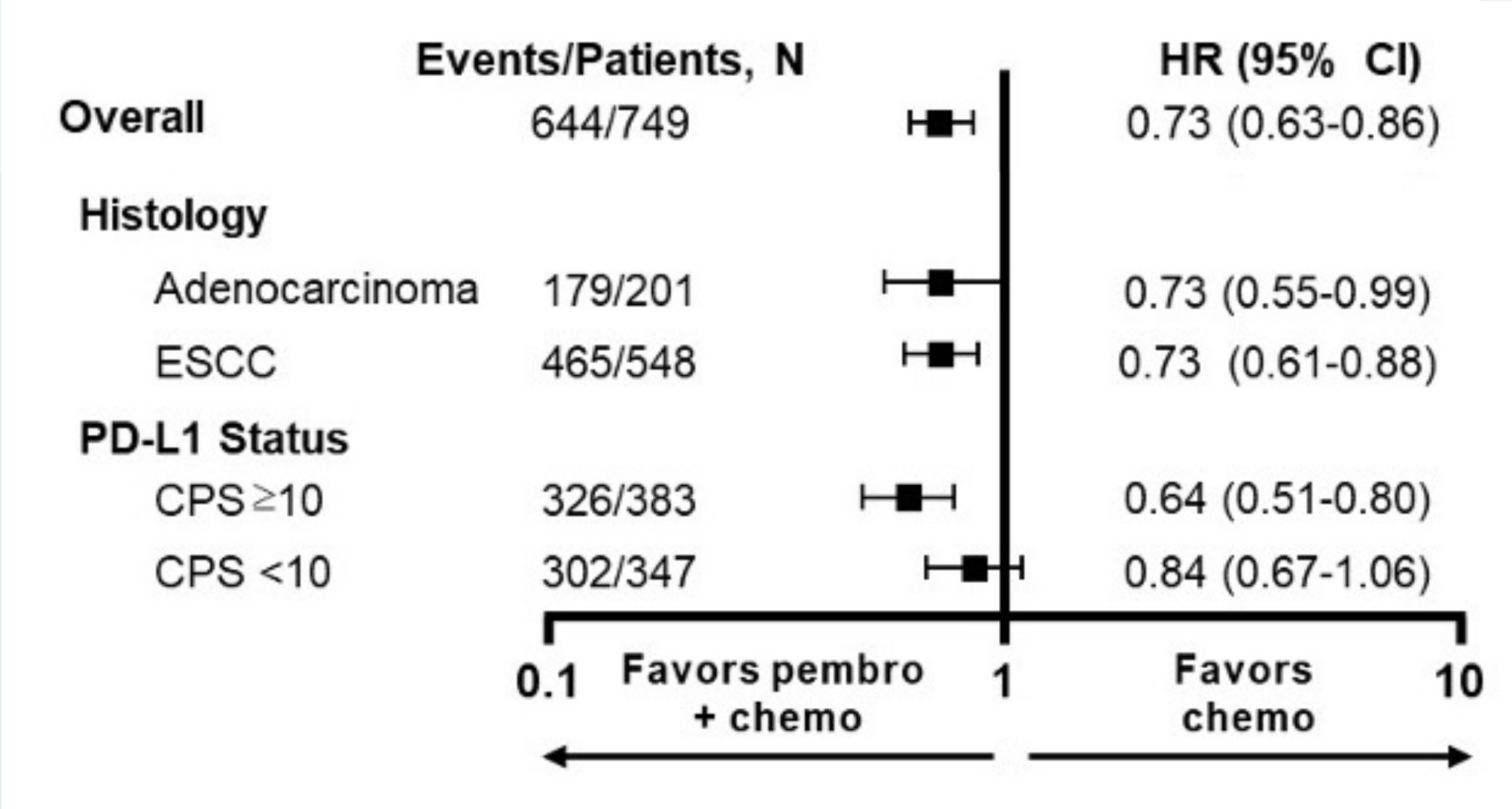
KEYNOTE-590: Overall Survival (OS) in Prespecified Subgroups



ESCC = esophageal squamous cell carcinoma

Metges JP et al. Gastrointestinal Cancers Symposium 2022;Abstract 241.

KEYNOTE-590: Overall Survival in Select Subgroups



Metges JP et al. Gastrointestinal Cancers Symposium 2022;Abstract 241.

KEYNOTE-590: Antitumor Response

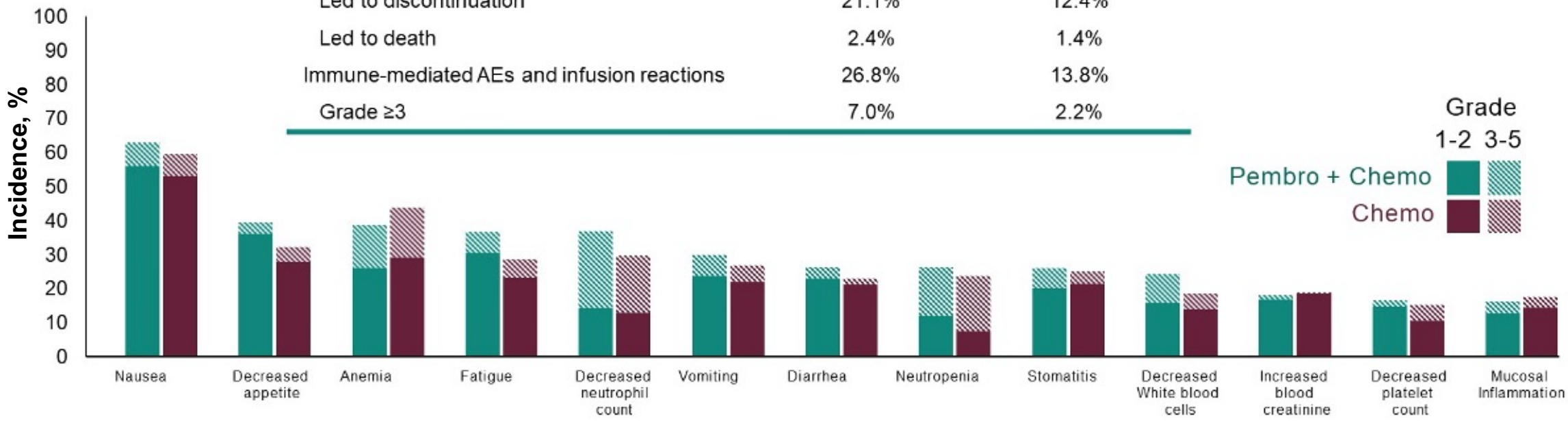
Best response, n (%)	Pembro + Chemo N = 373	Chemo N = 376
ORR, n (%)	**168 (45.0)**	**110 (29.3)**
Complete response	25 (6.7)	9 (2.4)
Partial response	143 (38.3)	101 (26.9)
Stable disease	126 (33.8)	174 (46.3)
Disease control rate	294 (78.8)	284 (75.5)
Progressive disease	43 (11.5)	59 (15.7)
Not evaluable/no assessment	36 (9.6)	33 (8.7)
Median DOR (range), mo	8.3 (1.2+ to 41.7+)	6.0 (1.5+ to 34.9+)
≥ 24 months response duration, %	**20.4**	**6.2**

ORR = objective response rate; DOR = duration of response

Metges JP et al. Gastrointestinal Cancers Symposium 2022;Abstract 241.

KEYNOTE-590: Adverse Events (AEs) Summary

Events, n (%)	Pembro + Chemo N = 373	Chemo N = 376
Any	100%	99.5%
Treatment-related	98.4%	97.3%
Grade ≥3	71.9%	67.6%
Led to discontinuation	21.1%	12.4%
Led to death	2.4%	1.4%
Immune-mediated AEs and infusion reactions	26.8%	13.8%
Grade ≥3	7.0%	2.2%



Metges JP et al. Gastrointestinal Cancers Symposium 2022;Abstract 241.

Poster 242

ASCO Gastrointestinal Cancers Symposium 2022

Trastuzumab Deruxtecan (T-DXd; DS-8201) in Patients With HER2–Positive Advanced Gastric or Gastroesophageal Junction (GEJ) Adenocarcinoma: Final Overall Survival (OS) Results From a Randomized, Multicenter, Open-Label, Phase 2 Study (DESTINY-Gastric01)

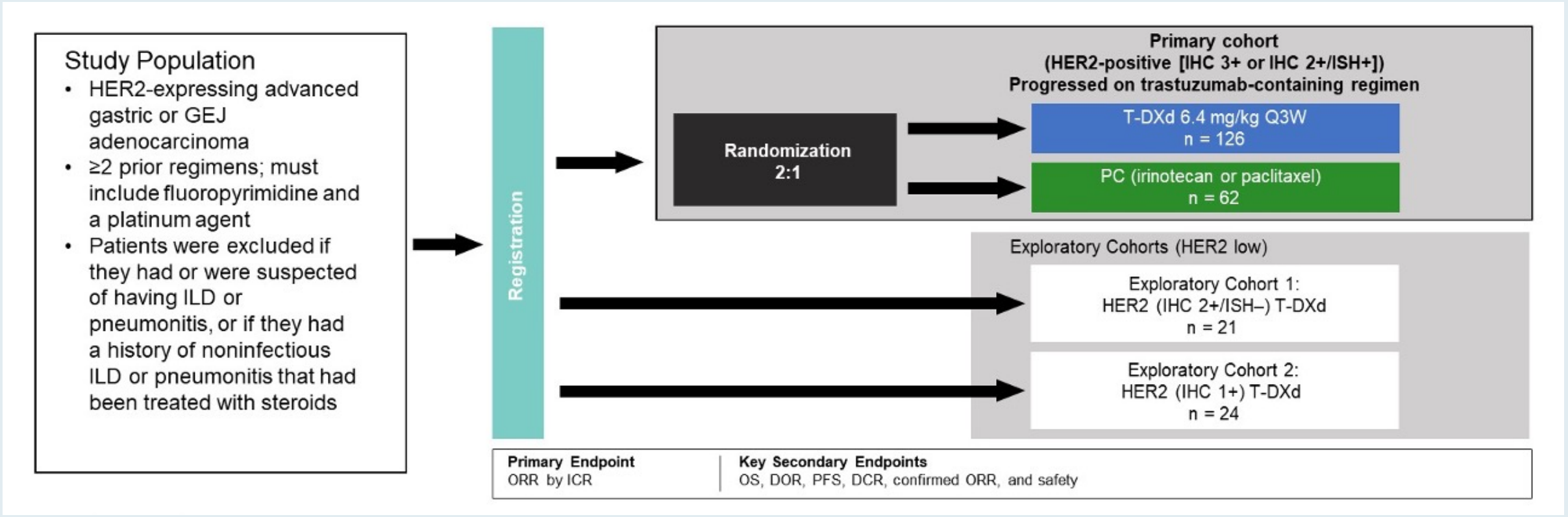
Kensei Yamaguchi

The Cancer Institute Hospital of JFCR, Tokyo, Japan

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 Randomized, Phase II Study Design

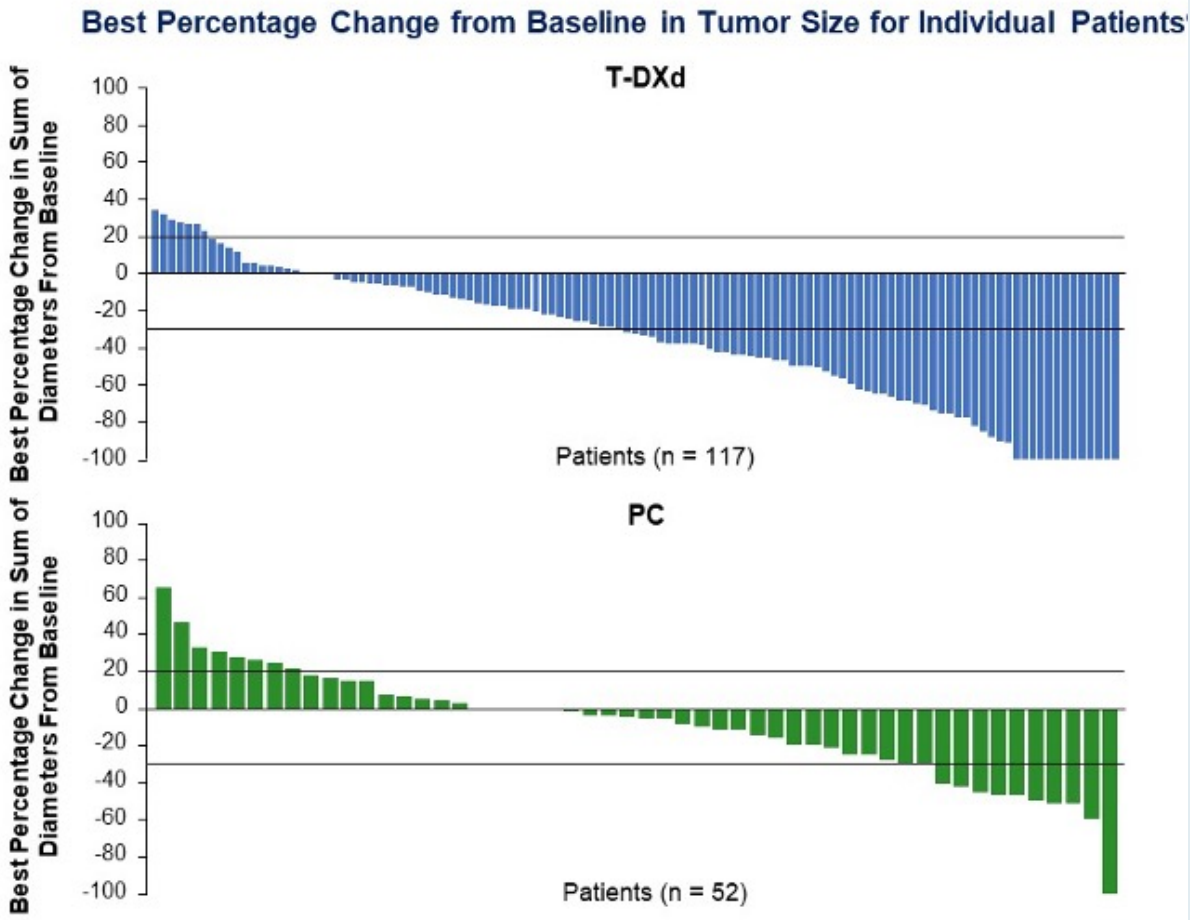


GEJ = gastroesophageal junction; ILD = interstitial lung disease; IHC = immunohistochemistry; PC = physician's choice; ORR = objective response rate; ICR = independent central review; OS = overall survival; DOR = duration of response; PFS = progression-free survival; DCR = disease control rate

Yamaguchi K et al. Gastrointestinal Cancers Symposium 2022;Abstract 242.

DESTINY-Gastric01: Antitumor Activity

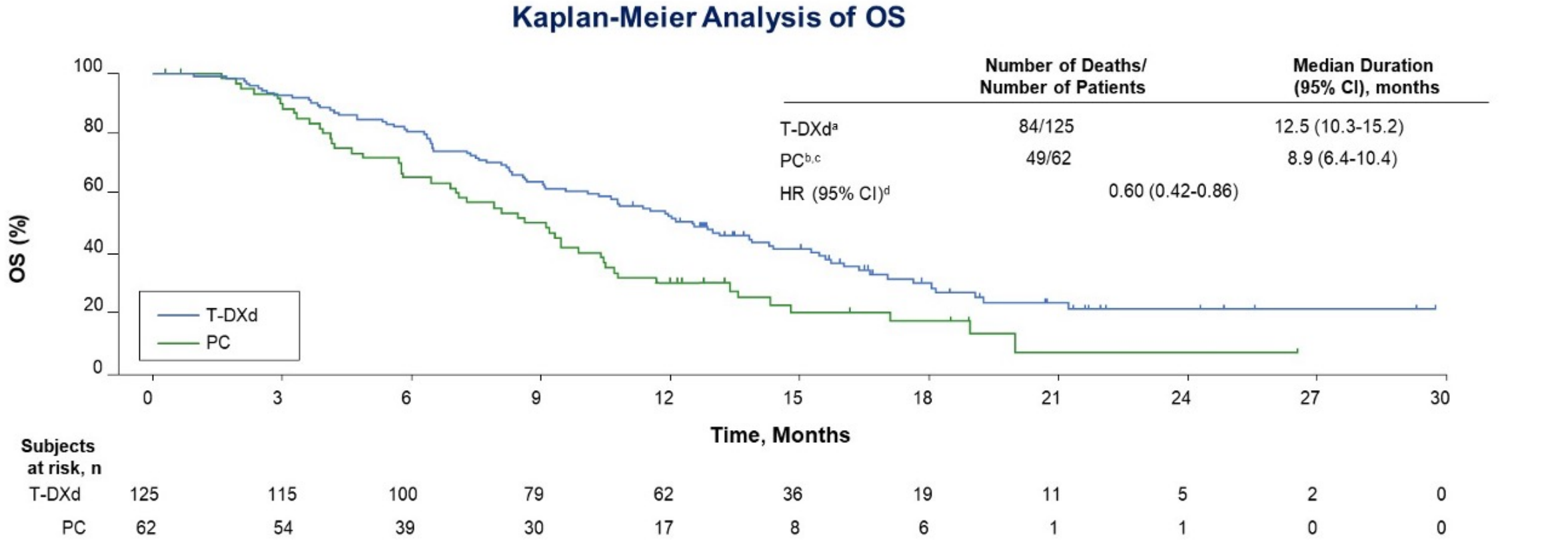
	T-DXd n = 119	PC Overall n = 56
ORR (CR + PR) by ICR, n (%)[a]	**61 (51.3) 95% CI, 41.9-60.5**	**8 (14.3) 95% CI, 6.4-26.2**
	P < 0.0001[b]	
CR	11 (9.2)	0
PR	50 (42.0)	8 (14.3)
SD	42 (35.3)	27 (48.2)
PD	14 (11.8)	17 (30.4)
Not evaluable	2 (1.7)	4 (7.1)
Confirmed ORR (CR + PR) by ICR, n (%)[a]	50 (42.0) 95% CI, 33.0-51.4	7 (12.5) 95% CI, 5.2-24.1
CR	10 (8.4)	0
PR	40[c] (33.6)	7 (12.5)
SD	52 (43.7)	28 (50.0)
PD	14 (11.8)	17 (30.4)
Not evaluable	3 (2.5)	4 (7.1)
Confirmed DCR (CR + PR + SD), n (%)[a]	102 (85.7) 95% CI, 78.1-91.5	35 (62.5) 95% CI, 48.5-75.1
Confirmed DOR, median, months	12.5 95% CI, 5.6-NE	3.9 95% CI, 3.0-4.9
TTR, median, months	1.5 95% CI, 1.4-1.7	1.6 95% CI, 1.3-1.7



PC = physician's choice; ORR = objective response rate; CR = complete response; PR = partial response; ICR = independent central review; SD = stable disease; PD = disease progression; DCR = disease control rate; DOR = duration of response; TTR = time to repsonse

Yamaguchi K et al. Gastrointestinal Cancers Symposium 2022;Abstract 242.

DESTINY-Gastric01: Final Overall Survival (OS)



As in the primary analysis (101 OS events; 54.0% maturity), in this updated analysis (133 OS events; 71.1% maturity), T-DXd showed superior antitumor activity compared to PC

PC = physician's choice

Yamaguchi K et al. Gastrointestinal Cancers Symposium 2022;Abstract 242.

DESTINY-Gastric01: Select Adverse Events

Adverse event	T-DXd (n = 125)		Physician's choice overall (n = 62)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Neutrophil count decrease	65%	51%	36%	24%
Nausea	63%	6%	47%	2%
Decreased appetite	61%	17%	45%	13%
Anemia	58%	38%	31%	23%
Platelet count decrease	40%	11%	7%	3%
WBC count decrease	38%	21%	36%	11%
Lymphocyte count decrease	23%	12%	3%	2%

16 patients (13%) had T-DXd-related interstitial lung disease/pneumonitis

- 13/16 were Grade 1 or 2
- Median time to first onset: 102.5 days

Yamaguchi K et al. Gastrointestinal Cancers Symposium 2022;Abstract 242.

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, Maria di Bartolomeo, Elizabeth Smyth, Ian Cha, 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

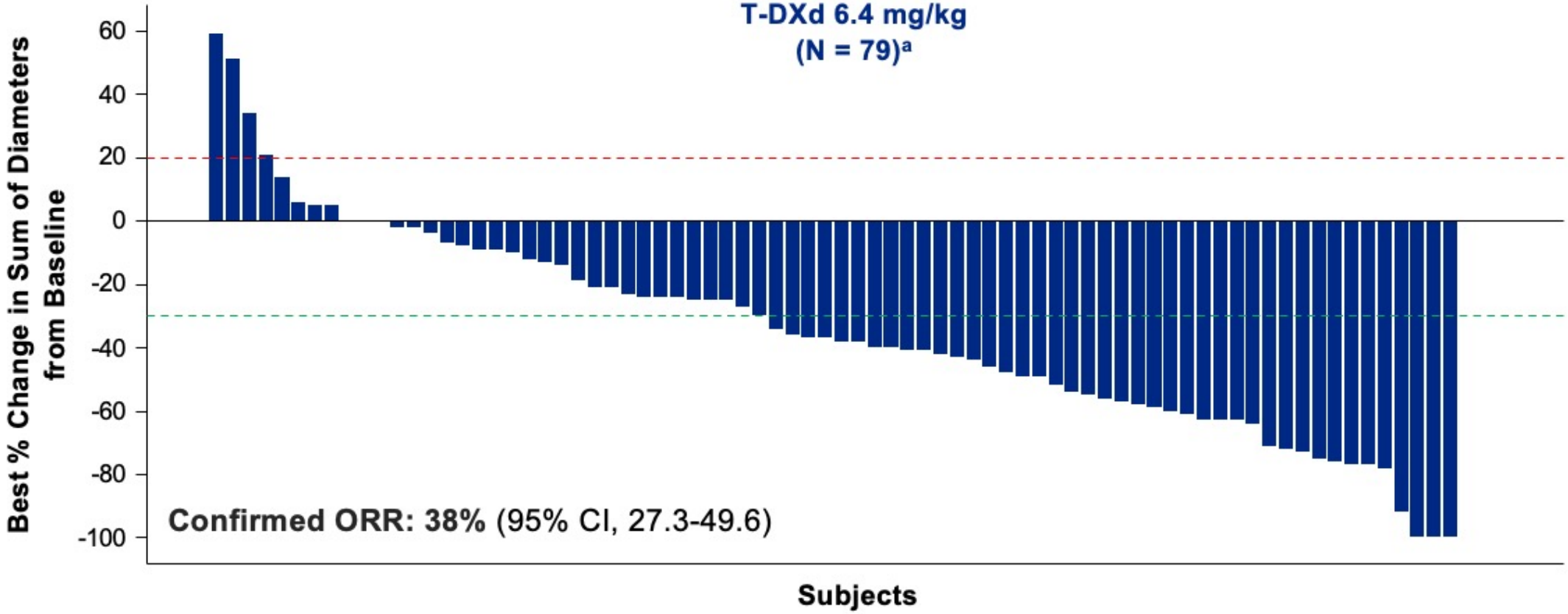
On behalf of the DESTINY-Gastric02 investigators

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.

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

WORLD CONGRESS ON Gastrointestinal Cancer

SO-7

Co-occurring HER2 and PD-L1 expression in patients with HER2-positive trastuzumab-refractory gastric cancer (GC)/gastroesophageal junction adenocarcinoma (GEJA): biomarker analysis from the trastuzumab deruxtecan (T-DXd) DESTINY-Gastric03 trial

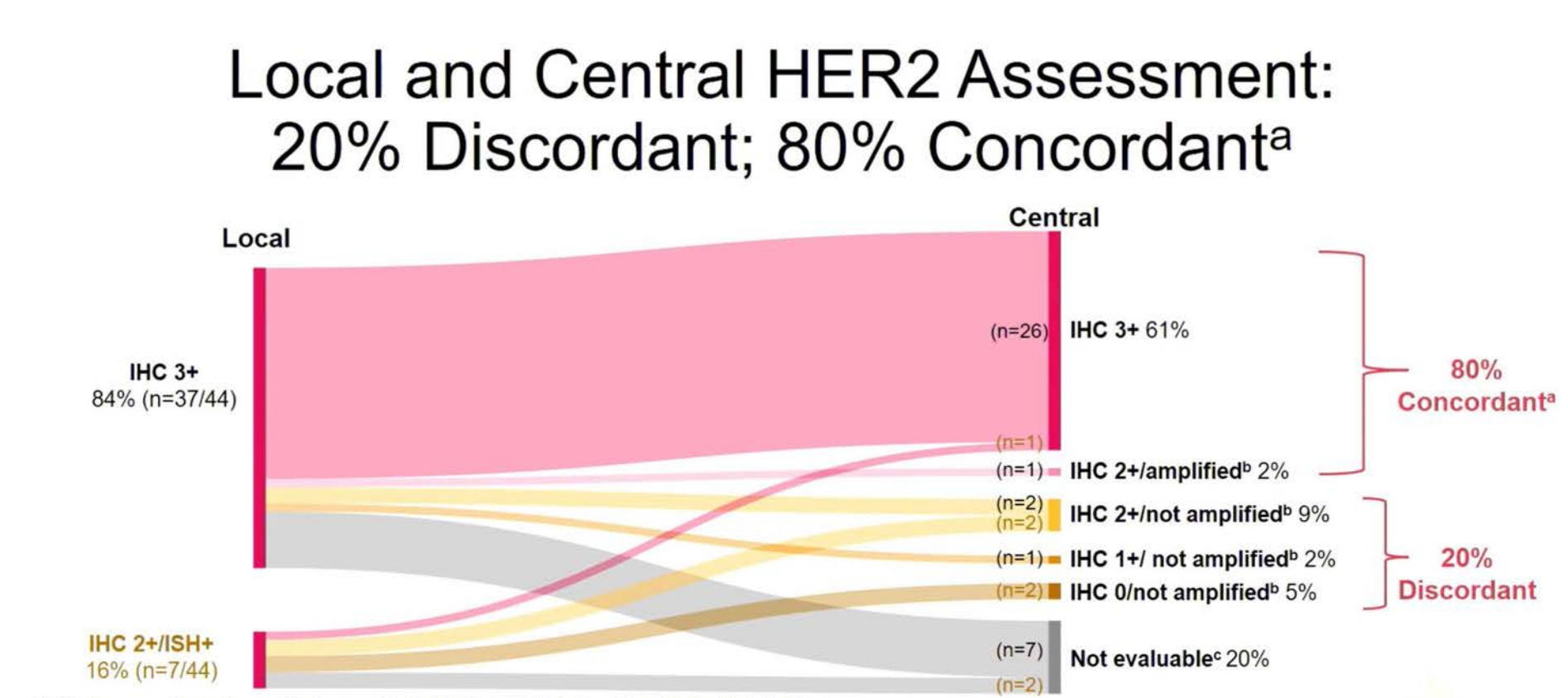
Yelena Y. Janjigian, MD[1]; Sun Young Rha, MD, PhD[2]; Do-Youn Oh, MD, PhD[3]; Marc Díez García, MD[4]; Hanneke van Laarhoven, MD, PhD[5]; Yee Chao, MD, PhD[6]; Maria Di Bartolomeo, MD[7]; Nadia Haj Mohammad, MD, PhD[8]; Wenyan Zhong, PhD[9]; Elizabeth Croydon, MD[10]; Fabiola Cecchi, PhD, PharmD[9]; Jeeyun Lee, MD[11]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]Yonsei Cancer Center, Yonsei University College of Medicine, Seodaemun-gu, Seoul, Korea; [3]Seoul National University Hospital, Seoul National University College of Medicine, Jongno-gu, Seoul, Korea; [4]Vall d'Hebron University Hospital-VHIO, Barcelona, Spain; [5]Cancer Center Amsterdam, Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands; [6]Taipei Veterans General Hospital, National Yang Ming Chiao Tung University, Taipei, Taiwan; [7]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [8]University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands; [9]AstraZeneca Pharmaceuticals LP, Gaithersburg, MD, USA; [10]AstraZeneca Pharmaceuticals LP, Cambridge, UK; [11]Samsung Medical Center, Sungkyunkwan University School of Medicine, Gangnam-gu, Seoul, Korea

ESMO World Congress on Gastrointestinal Cancer 2022, June 29-July 2, 2022, Barcelona, Spain

RTP RESEARCH TO PRACTICE

Discordant HER2 Assessment



HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization.

[a] Concordance rate was defined as the percentage of samples classified as HER2 positive by both local and central assessment.

[b] HER2 amplification using FoundationOne® (F1CDx).

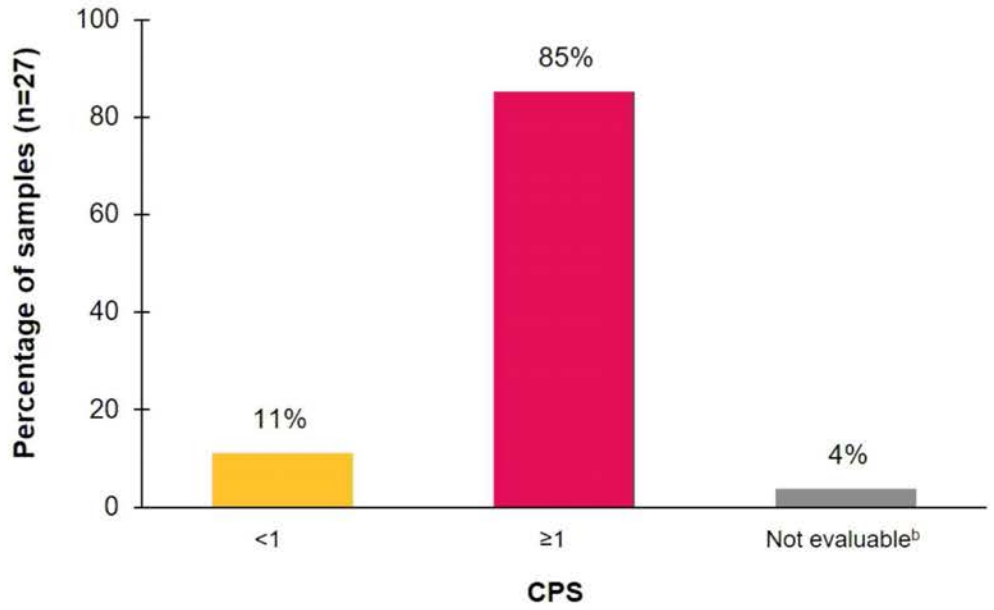
[c] Samples with missing IHC/amplification data due to an insufficient number of tumor cells (<100) on the tissue section for HER2 IHC assessment or insufficient tumor content collected for next-generation sequencing.

Janjigian YY, et al. Co-occurring HER2 and PD-L1 expression in patients with HER2-positive trastuzumab-refractory gastric cancer (GC)/gastroesophageal junction adenocarcinoma (GEJA): biomarker analysis from the trastuzumab deruxtecan (T-DXd) DESTINY-Gastric03 trial. Presented at ESMO World Congress on Gastrointestinal Cancer; June 29-July 2, 2022; Barcelona, Spain. Abstract SO-7.

Janjigian YY et al. ESMO World Congress on Gastrointestinal Cancers;Abstract SO-7.

PD-L1 Expression and HER2 Coexpression

PD-L1 Expression by Central Assessment[a]: 85% PD-L1 Positive



CPS	% (n/N)
CPS <1	11 (3/27)
CPS ≥1	85 (23/27)
CPS ≥1 to <5	37 (10/27)
CPS ≥5	48 (13/27)
Not evaluable[b]	4 (1/27)

CPS, combined positive score; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; PD-L1, programmed death ligand 1.

[a] PD-L1 expression was centrally assessed using a verified IHC assay (PD-L1 IHC 22C3 pharmDx; Agilent Technologies).

[b] There was an insufficient number of viable tumor cells (<100) present for PD-L1 testing.

Janjigian YY, et al. Co-occurring HER2 and PD-L1 expression in patients with HER2-positive trastuzumab-refractory gastric cancer (GC)/gastroesophageal junction adenocarcinoma (GEJA): biomarker analysis from the trastuzumab deruxtecan (T-DXd) DESTINY-Gastric03 trial. Presented at ESMO World Congress on Gastrointestinal Cancer; June 29-July 2, 2022; Barcelona, Spain. Abstract SO-7.

Janjigian YY et al. ESMO World Congress on Gastrointestinal Cancers;Abstract SO-7.

Support for Dual Anti-HER2 and Anti-PD-L1 Therapy

Conclusions

- In a subset of patients with GC/GEJA in the ongoing DESTINY-Gastric03 trial, 20% discordance was observed between local and central HER2 testing, consistent with previously reported data in GC[1]
  - Discordance may be attributed to tissue heterogeneity
- Substantial overlap (85%) was observed between HER2 and PD-L1 positivity in this GC/GEJA population, consistent with earlier studies[2]
- These data support dual anti-HER2 and anti–PD-L1 therapy in HER2-positive GC/GEJA

GC, gastric cancer; GEJA, gastroesophageal junction adenocarcinoma; HER2, human epidermal growth factor receptor 2; PD-L1, programmed death ligand 1.

1. Huemer F, et al. *J Clin Med*. 2020;9(4):935. 2. Janjigian YY, et al. *Nature*. 2021;600:727-730.

Janjigian YY, et al. Co-occurring HER2 and PD-L1 expression in patients with HER2-positive trastuzumab-refractory gastric cancer (GC)/gastroesophageal junction adenocarcinoma (GEJA): biomarker analysis from the trastuzumab deruxtecan (T-DXd) DESTINY-Gastric03 trial. Presented at ESMO World Congress on Gastrointestinal Cancer; June 29-July 2, 2022; Barcelona, Spain. Abstract SO-7.

Janjigian YY et al. ESMO World Congress on Gastrointestinal Cancers;Abstract SO-7.

2021 ESMO congress

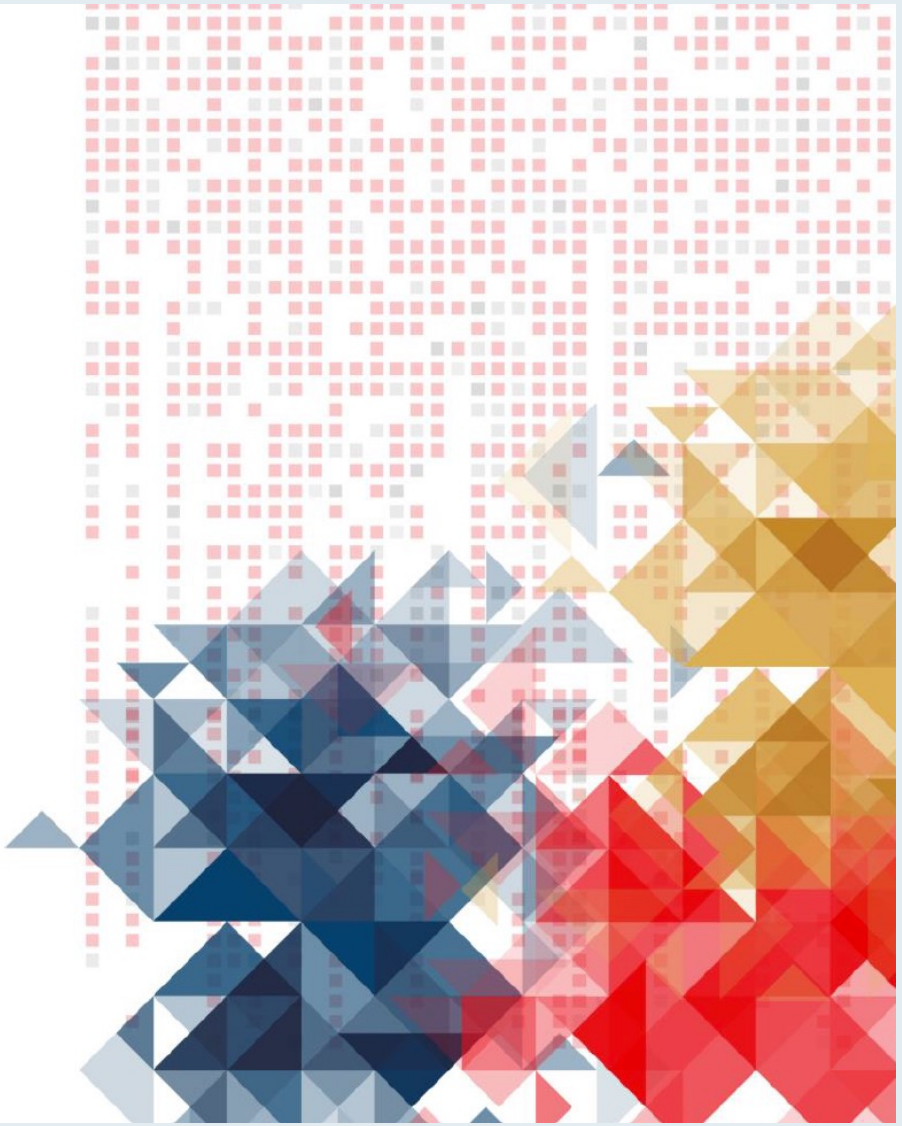
JUPITER-06:

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

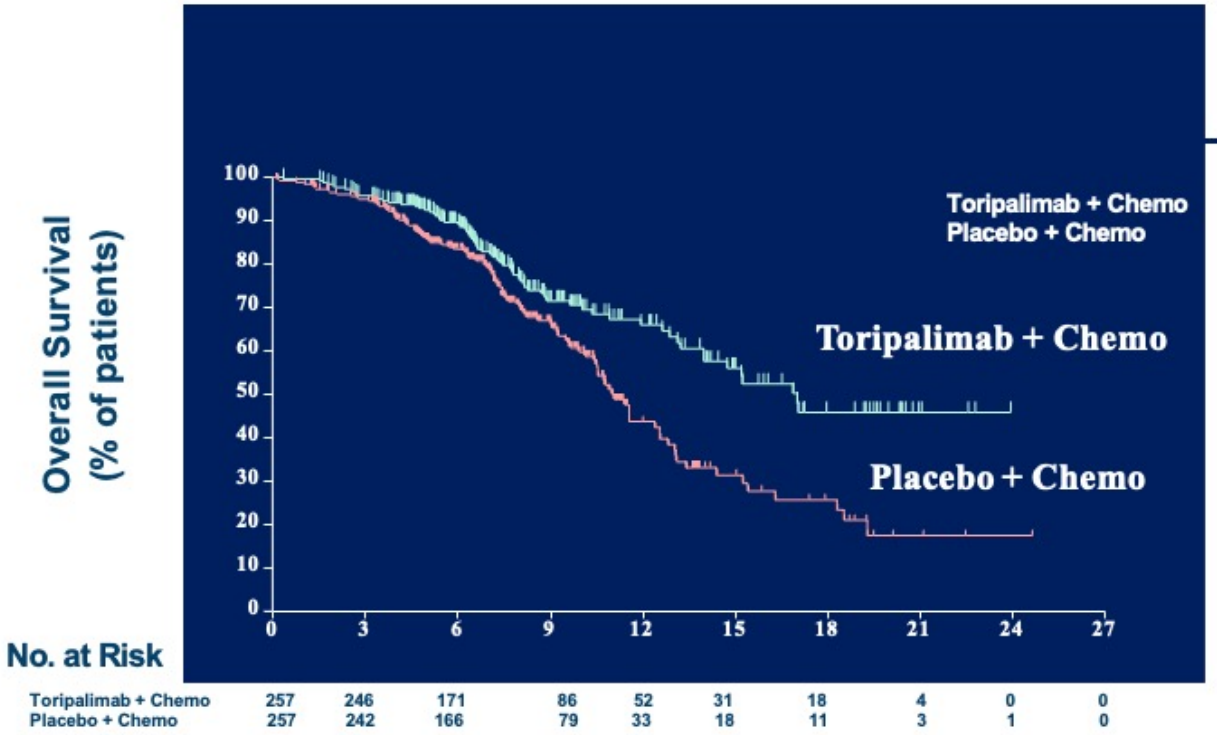
Presented by Feng Wang MD, PhD at 2021 ESMO Annual Meeting



Abstract 1373MO

RTP RESEARCH TO PRACTICE

JUPITER-06: Overall Survival with Toripalimab and Chemotherapy for 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)
Toripalimab + Chemo	70/257	17.0 (14.0, NE)	66.0 (57.5, 73.2)	NE (NE, NE)
Placebo + Chemo	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]

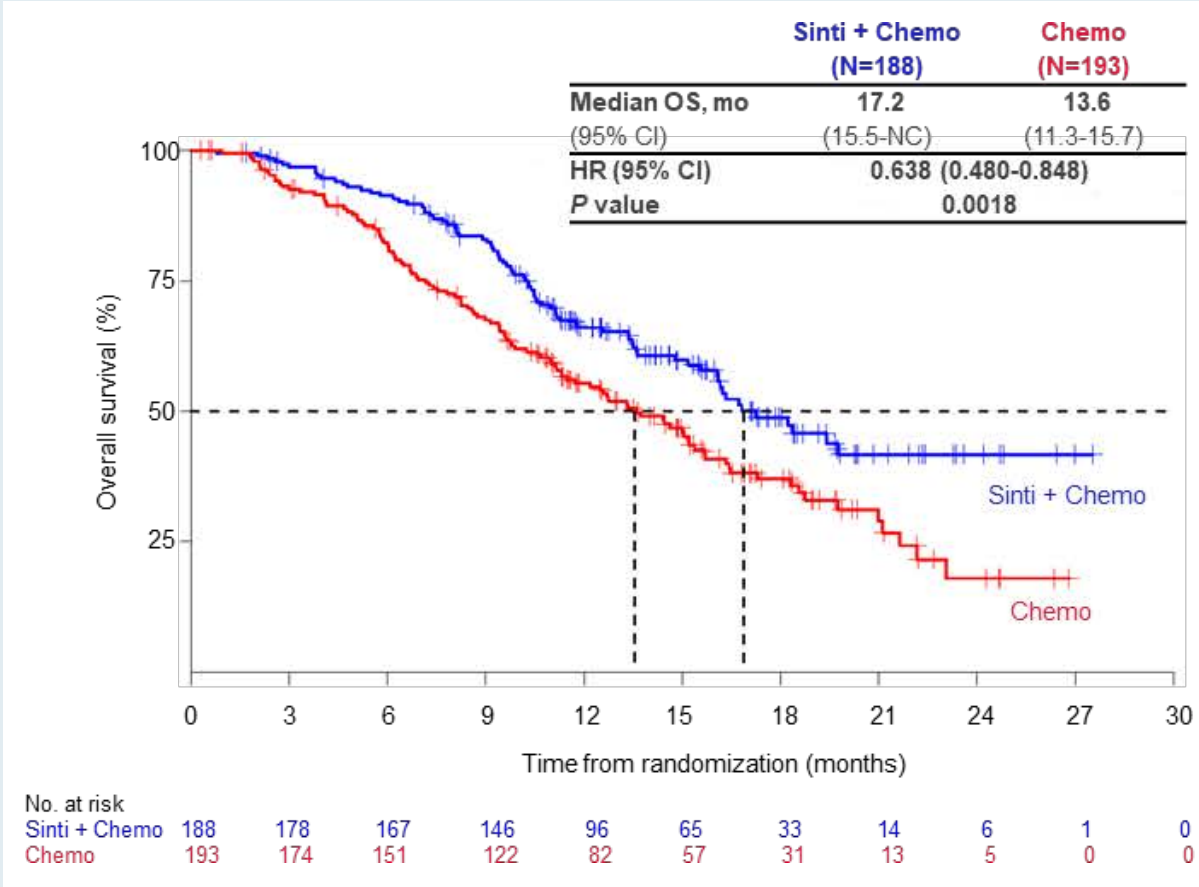
[1]Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education), Peking University Cancer Hospital and Institute, Beijing, China, [2]Department of Gastrointestinal Oncology, Peking University Cancer Hospital & Institute, Beijing, China, [3]Department of Oncology, The Affiliated 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

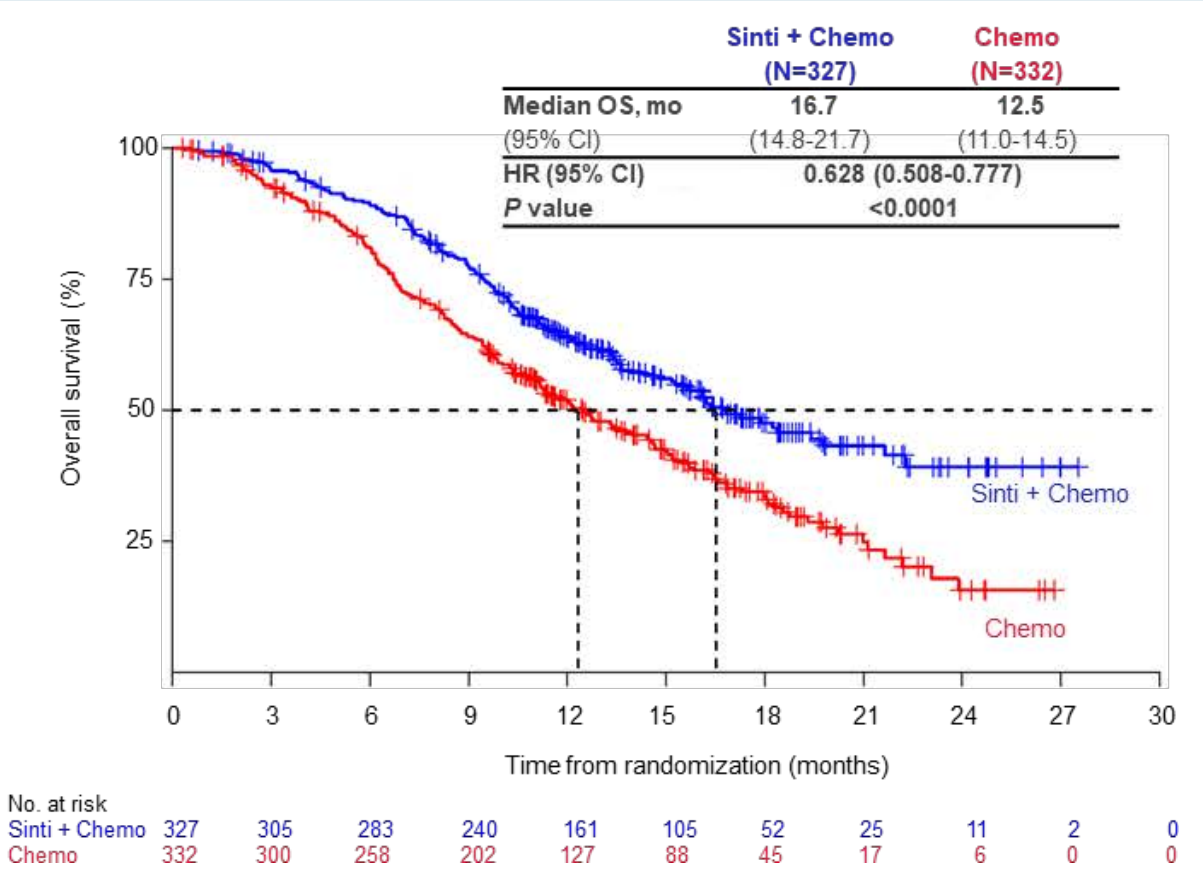
RTP RESEARCH TO PRACTICE

ORIENT-15: OS with Sintilimab and Chemotherapy for Advanced or Metastatic ESCC

PD-L1 CPS ≥10



All patients



OS = overall survival; ESCC = esophageal squamous cell carcinoma; sinti = sintilimab

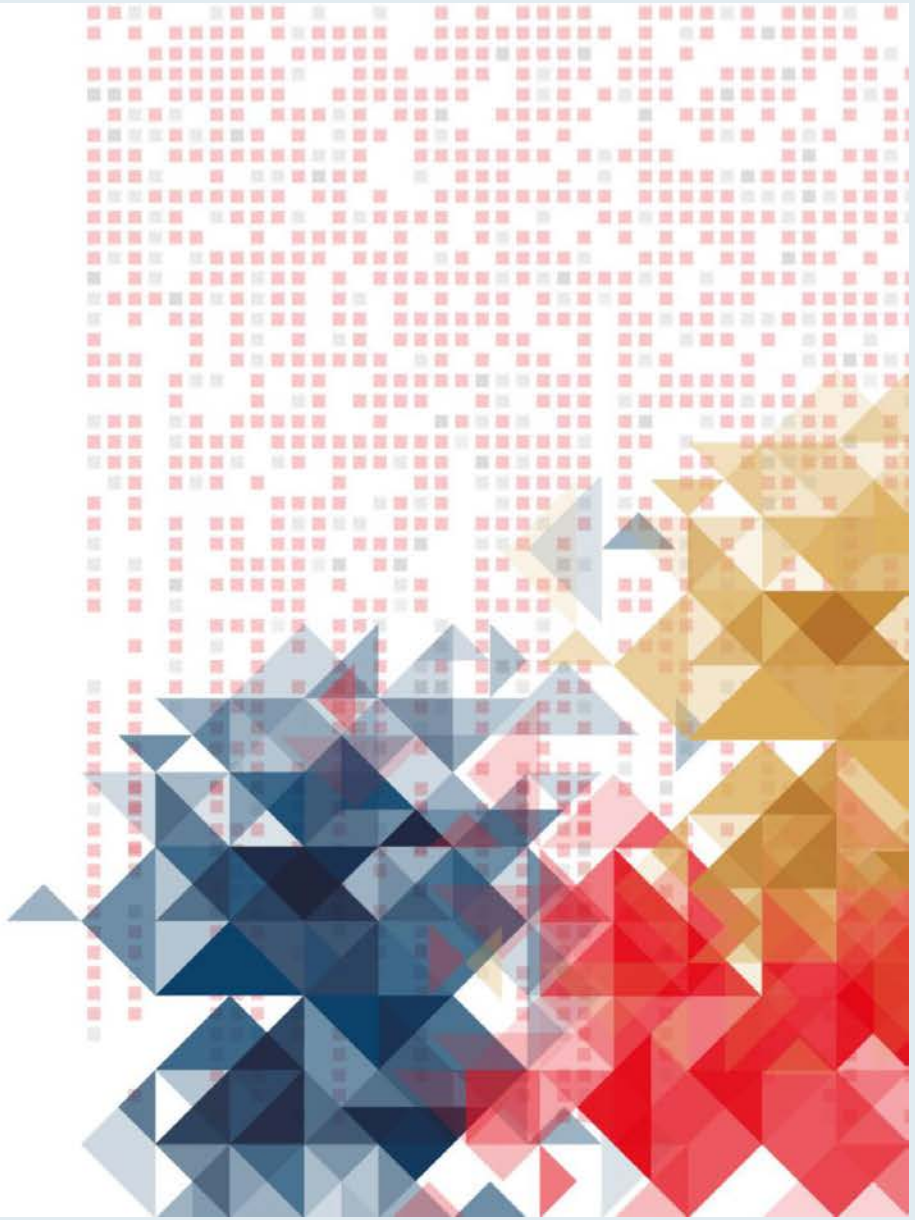
Shen L et al. ESMO 2021;Abstract LBA52.

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



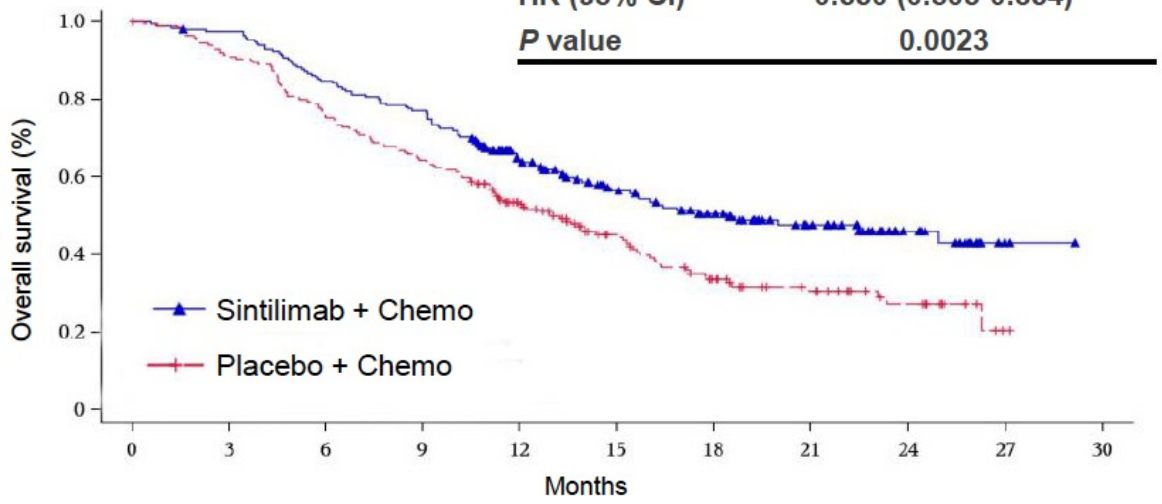
Abstract LBA53

RTP RESEARCH TO PRACTICE

ORIENT-16: OS with Sintilimab and Chemotherapy for Advanced Gastric or GEJ Adenocarcinoma

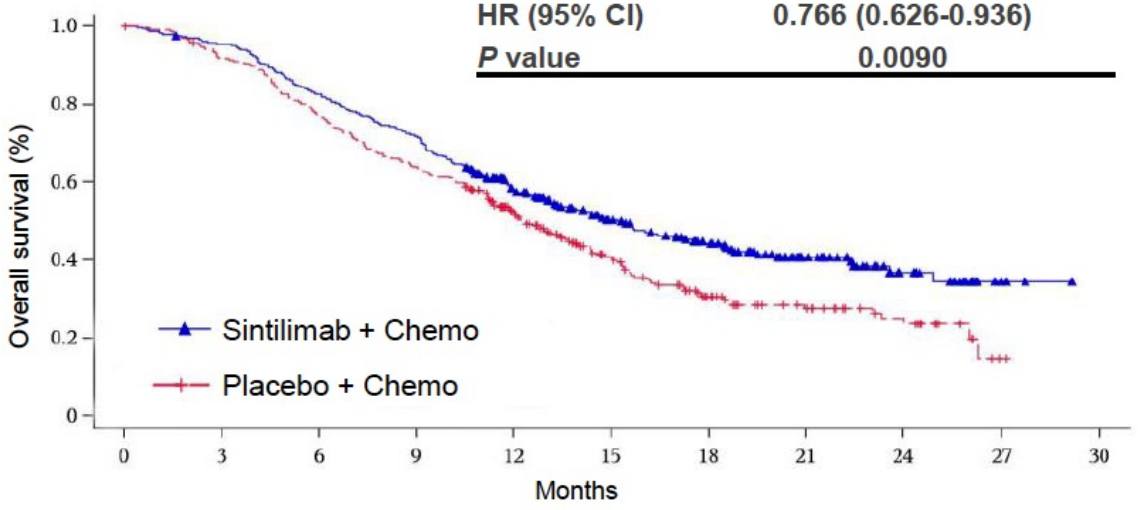
PD-L1 CPS ≥5

	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	



OS = overall survival; GEJ = gastroesophageal junction; sin = sintilimab

Xu J et al. ESMO 2021;Abstract LBA53.

Gastrointestinal Cancers Agenda

Module 1: Colorectal Cancer

Module 2: Upper Gastrointestinal Cancers

Module 3: Hepatocellular and Biliary Tract Cancers

- First-line therapy for patients with unresectable advanced HCC; implications of the Phase III HIMALAYA study results for the STRIDE regimen (durvalumab/tremelimumab)
- Optimal management of previously treated, unresectable advanced cholangiocarcinoma with targetable FGFR2 or IDH1 genetic alterations; potential clinical role of futibatinib
- Current and novel treatment approaches (eg, immunotherapy and HER2-targeted therapy) for advanced biliary tract cancers

Module 4: Pancreatic Adenocarcinoma

Update on Phase III LEAP-002 Trial Evaluating Pembrolizumab with Lenvatinib versus Lenvatinib Monotherapy for Patients with Unresectable HCC

Press Release: August 3, 2022

"Today [it was] announced that the Phase 3 LEAP-002 trial investigating pembrolizumab plus lenvatinib, the orally available multiple receptor tyrosine kinase inhibitor, versus lenvatinib monotherapy did not meet its dual primary endpoints of overall survival (OS) and progression-free survival (PFS) as a first-line treatment for patients with unresectable hepatocellular carcinoma (uHCC). There were trends toward improvement in OS and PFS for patients who received pembrolizumab plus lenvatinib versus lenvatinib monotherapy; however, these results did not meet statistical significance per the pre-specified statistical plan.

The median OS of the lenvatinib monotherapy arm in LEAP-002 was longer than that observed in previously reported clinical trials evaluating lenvatinib monotherapy in uHCC. The safety profile of pembrolizumab plus lenvatinib was consistent with previously reported data on the combination. [The companies] plan to present these data at an upcoming medical conference."

https://finance.yahoo.com/news/merck-eisai-phase-3-leap-104500062.html

RTP RESEARCH TO PRACTICE

Combined Immunotherapy and VEGF Pathway-Targeted Agents as First-Line Treatment for Advanced, Unresectable HCC

Phase III Study Design	IMbrave150[a,b] (N = 501)	ORIENT-32[c] (N = 595)	COSMIC-312[d] (N = 837)
Treatment arms	Atezolizumab + bev Sorafenib	Sintilimab + bev biosimilar Sorafenib	Atezolizumab + cabozantinib* Sorafenib* Cabozantinib
Patient population	Global patient population HBV-associated HCC (~48%)	Asian patient population HBV-associated HCC (94%)	Global patient population HBV-associated HCC (~30%)
Median PFS	6.9 mo vs 4.3 mo HR: 0.65, $p < 0.001$	4.6 mo vs 2.8 mo HR: 0.56, $p < 0.0001$	6.8 mo vs 4.2 mo* HR: 0.63, $p = 0.0012$
Median OS	19.2 mo vs 13.4 mo HR: 0.66, $p < 0.001$	Not reached vs 10.4 mo HR: 0.57, $p < 0.0001$	(Combination arm vs sorafenib): 15.4 mo vs 15.5 mo HR: 0.90, $p = 0.44$
Confirmed ORR	27.3% vs 11.9%	21.0% vs 4.0%	13.0% vs 5.0% vs 11.0%

HCC = hepatocellular cancer; bev = bevacizumab; HBV = hepatitis B virus; PFS = progression-free survival; OS = overall survival; ORR = objective response rate

* PFS ITT population

[a] Cheng A-L et al. *J Hepatol* 2022;76(4):862-73; [b] Finn RS et al. *N Engl J Med* 2020;382:1894-905; [c] Ren Z et al. *Lancet Oncol* 2021;22:977-90; [d] Kelley RK et al. *Lancet Oncol* 2022;[Online ahead of print].

Combined Immunotherapy and VEGF Pathway-Targeted Agents as First-Line Treatment for Advanced, Unresectable HCC (continued)

Phase III Study Design	IMbrave150[a,b] (N = 501)	ORIENT-32[c] (N = 595)	HIMALAYA[d,e] (N = 1,171)
Treatment arms	Atezolizumab + bev Sorafenib	Sintilimab + bev biosimilar Sorafenib	Durvalumab + tremelimumab* Durvalumab Sorafenib*
Patient population	Global patient population HBV-associated HCC (~48%)	Asian patient population HBV-associated HCC (94%)	Global patient population HBV-associated HCC (~31%)
Median PFS	6.9 mo vs 4.3 mo HR: 0.65, $p < 0.001$	4.6 mo vs 2.8 mo HR: 0.56, $p < 0.0001$	3.8 mo vs 3.7 mo vs 4.1 mo
Median OS	19.2 mo vs 13.4 mo HR: 0.66, $p < 0.001$	Not reached vs 10.4 mo HR: 0.57, $p < 0.0001$	(Combination arm vs sorafenib)*: 16.4 mo vs 13.8 mo HR: 0.78, $p = 0.0035$
Confirmed ORR	27.3% vs 11.9%	21.0% vs 4.0%	20.1% vs 17.0% vs 5.1%

HCC = hepatocellular cancer; bev = bevacizumab; HBV = hepatitis B virus; PFS = progression-free survival; OS = overall survival; ORR = objective response rate

* **Primary study objective:** OS for T300 + D vs sorafenib; **Secondary objective**: OS for durvalumab vs sorafenib (16.6 mo vs 13.8 mo, HR: 0.86)

[a] Cheng A-L et al. *J Hepatol* 2022;76(4):862-73; [b] Finn RS et al. *N Engl J Med* 2020;382:1894-905; [c] Ren Z et al. *Lancet Oncol* 2021;22:977-90; [d] Abou-Alfa GK et al. Gastrointestinal Cancers Symposium 2022;Abstract 379; [e] Abou-Alfa G et al. *NEJM Evidence* 2022;[Online ahead of print].

NEJM Evidence

Published June 6, 2022

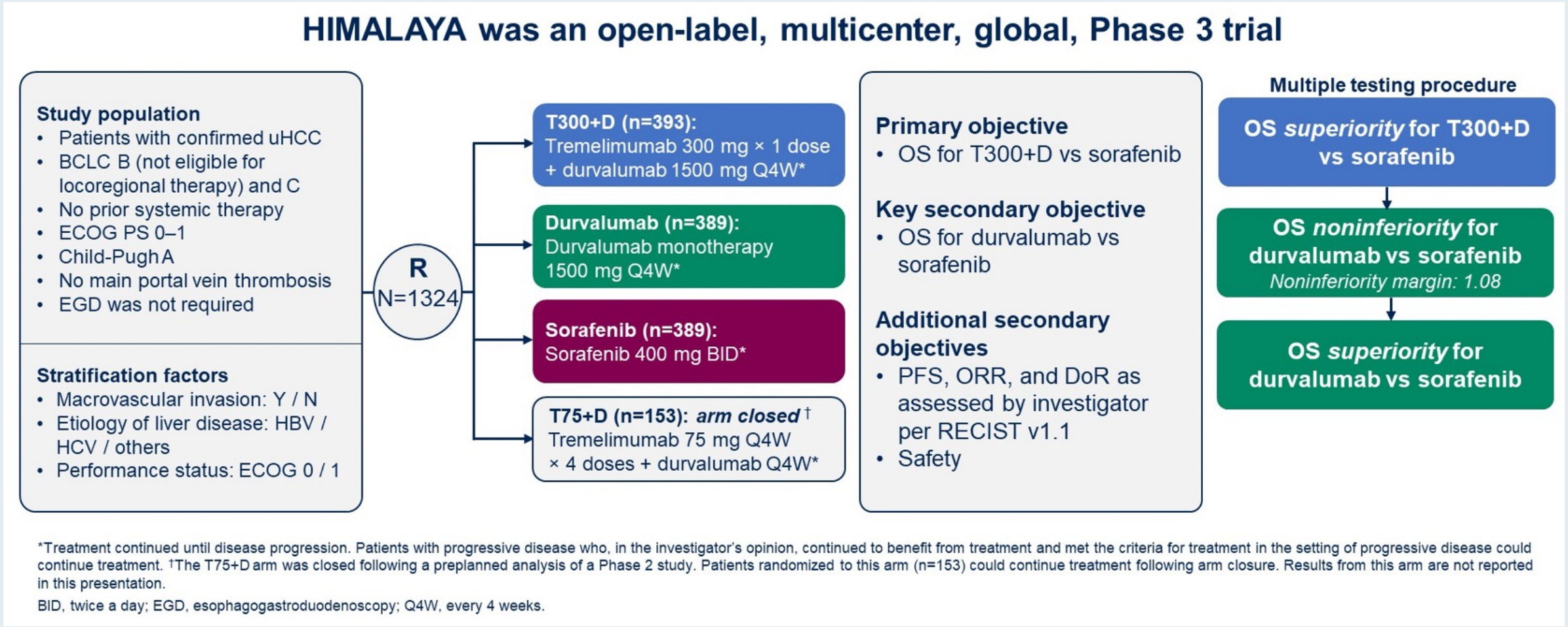
DOI: 10.1056/EVIDoa2100070

ORIGINAL ARTICLE

Tremelimumab Plus Durvalumab in Unresectable Hepatocellular Carcinoma

Ghassan K. Abou-Alfa, M.D., M.B.A.,[1,2] George Lau, M.D., F.R.C.P.,[3] Masatoshi Kudo, M.D., Ph.D.,[4] Stephen L. Chan, M.D.,[5] Robin Kate Kelley, M.D.,[6] Junji Furuse, M.D., Ph.D.,[7] Wattana Sukeepaisarnjaroen, M.D.,[8] Yoon-Koo Kang, M.D., Ph.D.,[9] Tu Van Dao, M.D., Ph.D.,[10] Enrico N. De Toni, M.D., Ph.D.,[11] Lorenza Rimassa, M.D.,[12,13] Valeriy Breder, M.D., Ph.D.,[14] Alexander Vasilyev, M.D.,[15] Alexandra Heurgué, M.D.,[16] Vincent C. Tam, M.D.,[17] Kabir Mody, M.D.,[18] Satheesh Chiradoni Thungappa, M.D.,[19] Yuriy Ostapenko, M.D.,[20] Thomas Yau, M.D.,[21] Sergio Azevedo, M.D.,[22] María Varela, M.D., Ph.D.,[23] Ann-Lii Cheng, M.D., Ph.D.,[24] Shukui Qin, M.D., Ph.D.,[25] Peter R. Galle, M.D., Ph.D.,[26] Sajid Ali, M.D.,[27] Michelle Marcovitz, Ph.D.,[27] Mallory Makowsky, Pharm.D.,[27] Philip He, Ph.D.,[27] John F. Kurland, Ph.D.,[27] Alejandra Negro, Ph.D.,[27] and Bruno Sangro, M.D., Ph.D.[28]

HIMALAYA Phase III Trial Schema

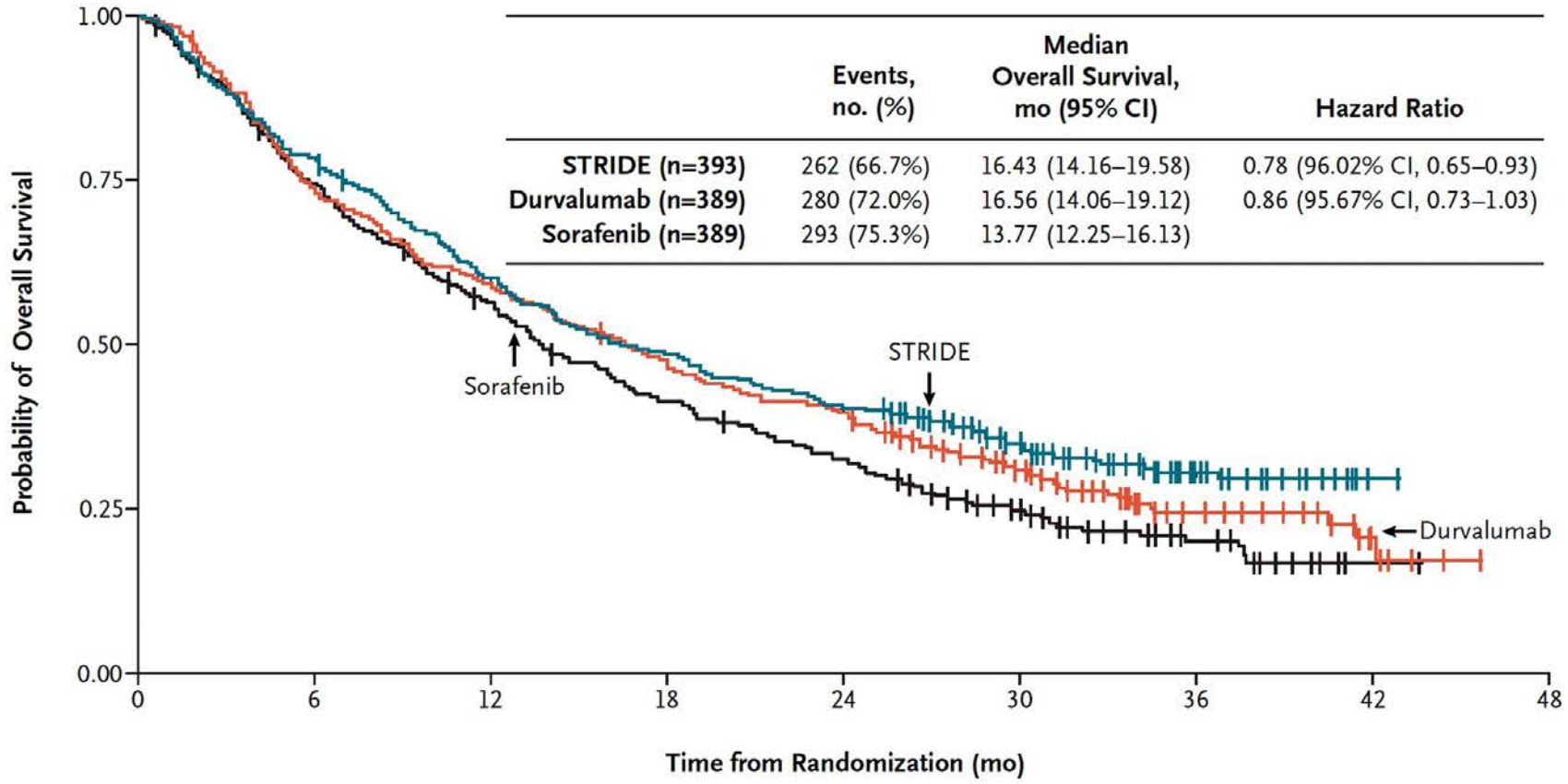


*Treatment continued until disease progression. Patients with progressive disease who, in the investigator's opinion, continued to benefit from treatment and met the criteria for treatment in the setting of progressive disease could continue treatment. †The T75+D arm was closed following a preplanned 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: Overall Survival

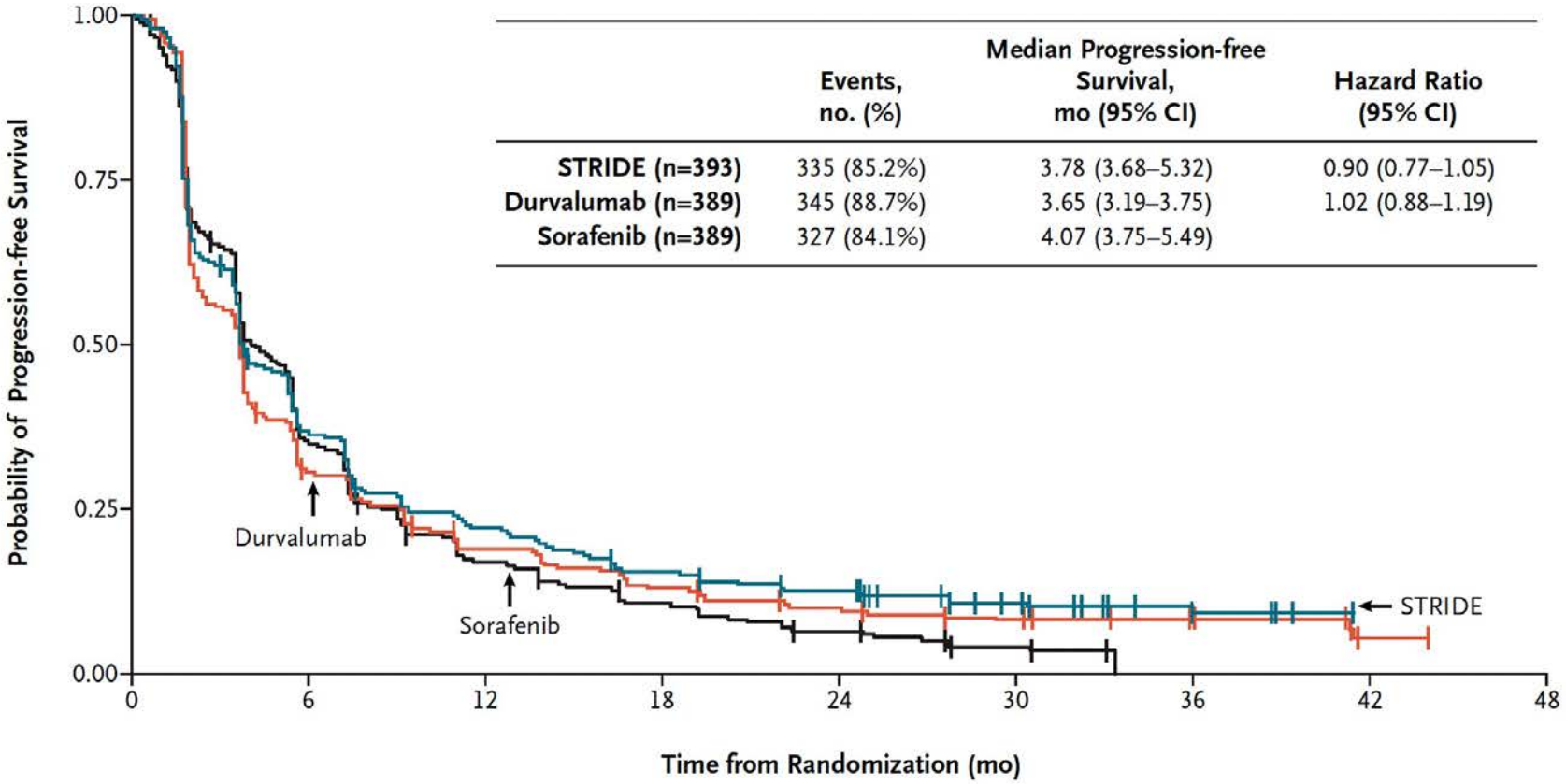


	Events, no. (%)	Median Overall Survival, mo (95% CI)	Hazard Ratio
STRIDE (n=393)	262 (66.7%)	16.43 (14.16–19.58)	0.78 (96.02% CI, 0.65–0.93)
Durvalumab (n=389)	280 (72.0%)	16.56 (14.06–19.12)	0.86 (95.67% CI, 0.73–1.03)
Sorafenib (n=389)	293 (75.3%)	13.77 (12.25–16.13)	

No. at Risk									
STRIDE	393	308	235	190	158	98	32	1	0
Durvalumab	389	286	230	183	153	87	27	6	0
Sorafenib	389	283	211	155	121	62	21	1	0

Abou-Alfa G et al. *NEJM Evidence*, June 6, 2022.

HIMALAYA: Progression-Free Survival



	Events, no. (%)	Median Progression-free Survival, mo (95% CI)	Hazard Ratio (95% CI)
STRIDE (n=393)	335 (85.2%)	3.78 (3.68–5.32)	0.90 (0.77–1.05)
Durvalumab (n=389)	345 (88.7%)	3.65 (3.19–3.75)	1.02 (0.88–1.19)
Sorafenib (n=389)	327 (84.1%)	4.07 (3.75–5.49)	

No. at Risk									
STRIDE	393	135	81	55	43	26	7	0	0
Durvalumab	389	115	68	47	34	20	6	1	0
Sorafenib	389	118	53	31	18	6	0	0	0

Abou-Alfa G et al. *NEJM Evidence*, June 6, 2022.

HIMALAYA: Response Outcomes (Intent-to-Treat Population)

Parameter	STRIDE (n=393)	Durvalumab (n=389)	Sorafenib (n=389)
Response — no. (%)			
Objective†	79 (20.1)	66 (17.0)	20 (5.1)
Complete	12 (3.1)	6 (1.5)	0
Partial	67 (17.0)	60 (15.4)	20 (5.1)
Stable disease — no. (%)	157 (39.9)	147 (37.8)	216 (55.5)
Disease control rate — %	236 (60.1)	213 (54.8)	236 (60.7)
Duration of response — mo‡			
Median	22.34	16.82	18.43
IQR	8.54–NR	7.43–NR	6.51–25.99
Time to response — mo			
Median	2.17	2.09	3.78

Abou-Alfa G et al. *NEJM Evidence*, June 6, 2022.

Research Article
Hepatic and Biliary Cancer

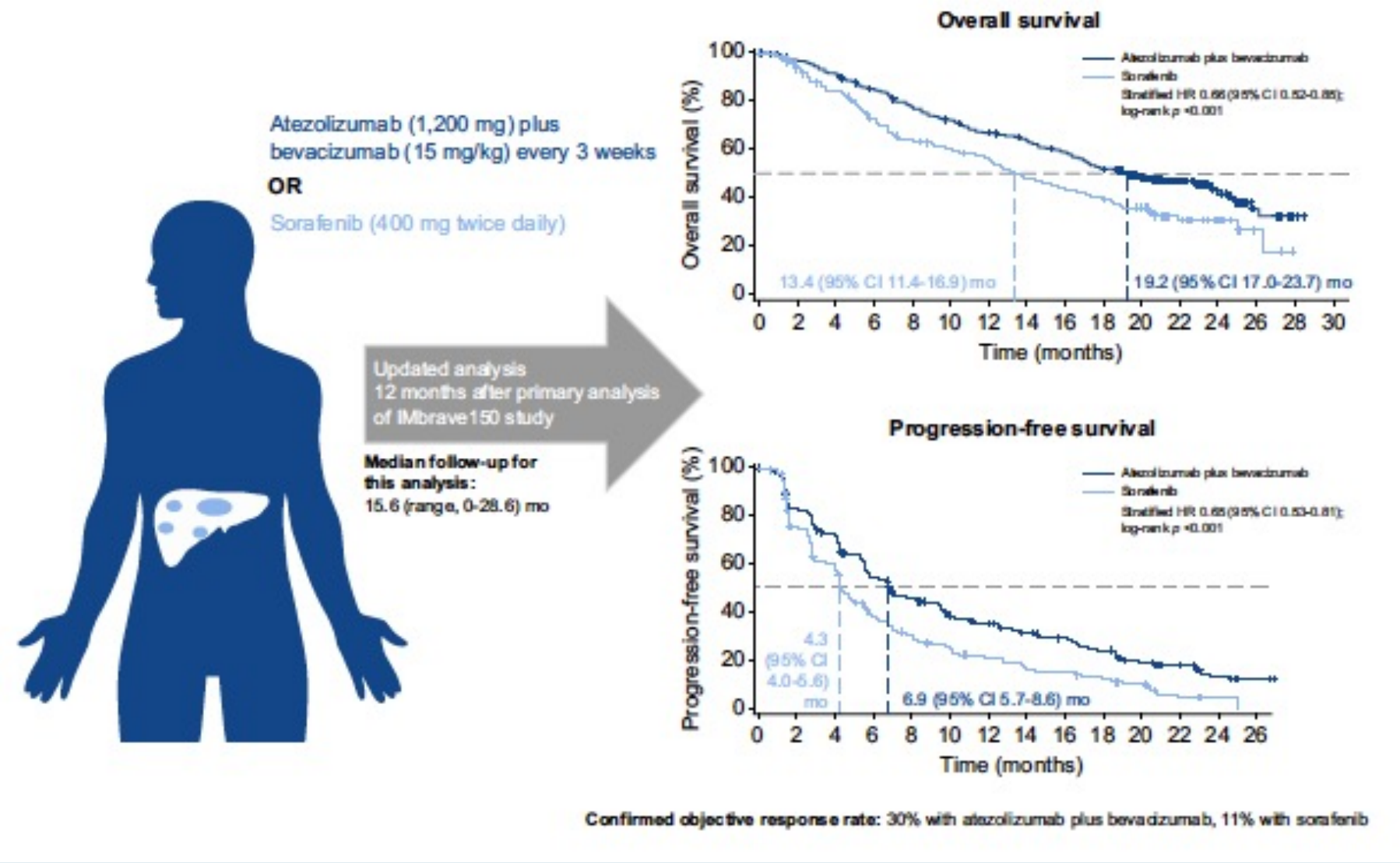
JOURNAL
OF HEPATOLOGY

Updated efficacy and safety data from IMbrave150: Atezolizumab plus bevacizumab *vs.* sorafenib for unresectable hepatocellular carcinoma

Ann-Lii Cheng[1,*], Shukui Qin[2], Masafumi Ikeda[3], Peter R. Galle[4], Michel Ducreux[5], Tae-You Kim[6], Ho Yeong Lim[7], Masatoshi Kudo[8], Valeriy Breder[9], Philippe Merle[10], Ahmed O. Kaseb[11], Daneng Li[12], Wendy Verret[13], Ning Ma[14], Alan Nicholas[15], Yifan Wang[16], Lindong Li[17], Andrew X. Zhu[18,19], Richard S. Finn[20,*]

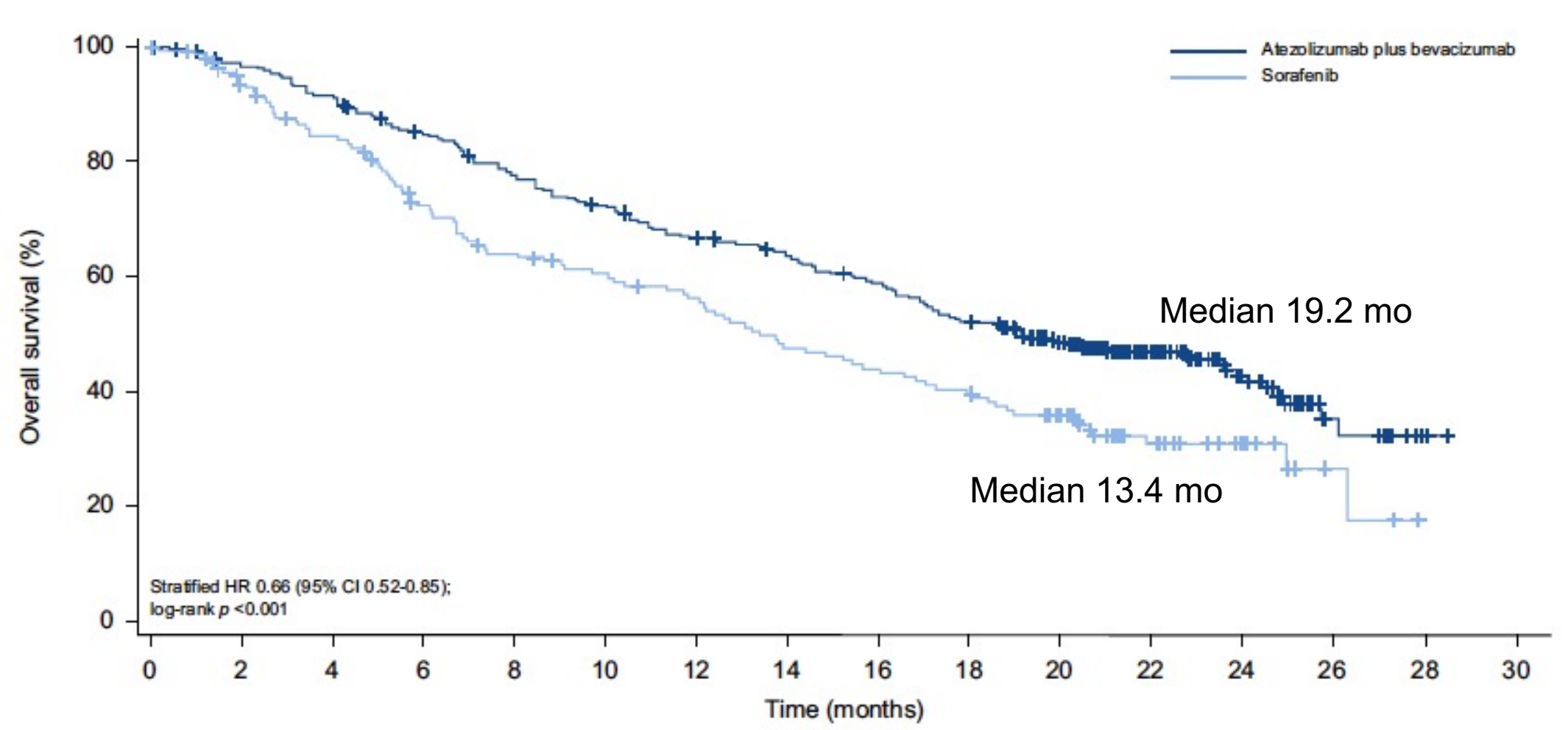
J Hepatol 2022;76(4):862-73.

IMbrave150: Updated 5-Year OS and PFS with Atezolizumab and Bevacizumab (Median Follow-Up = 15.6 Months)



Cheng A-L et al. *J Hepatol* 2022;76(4):862-73.

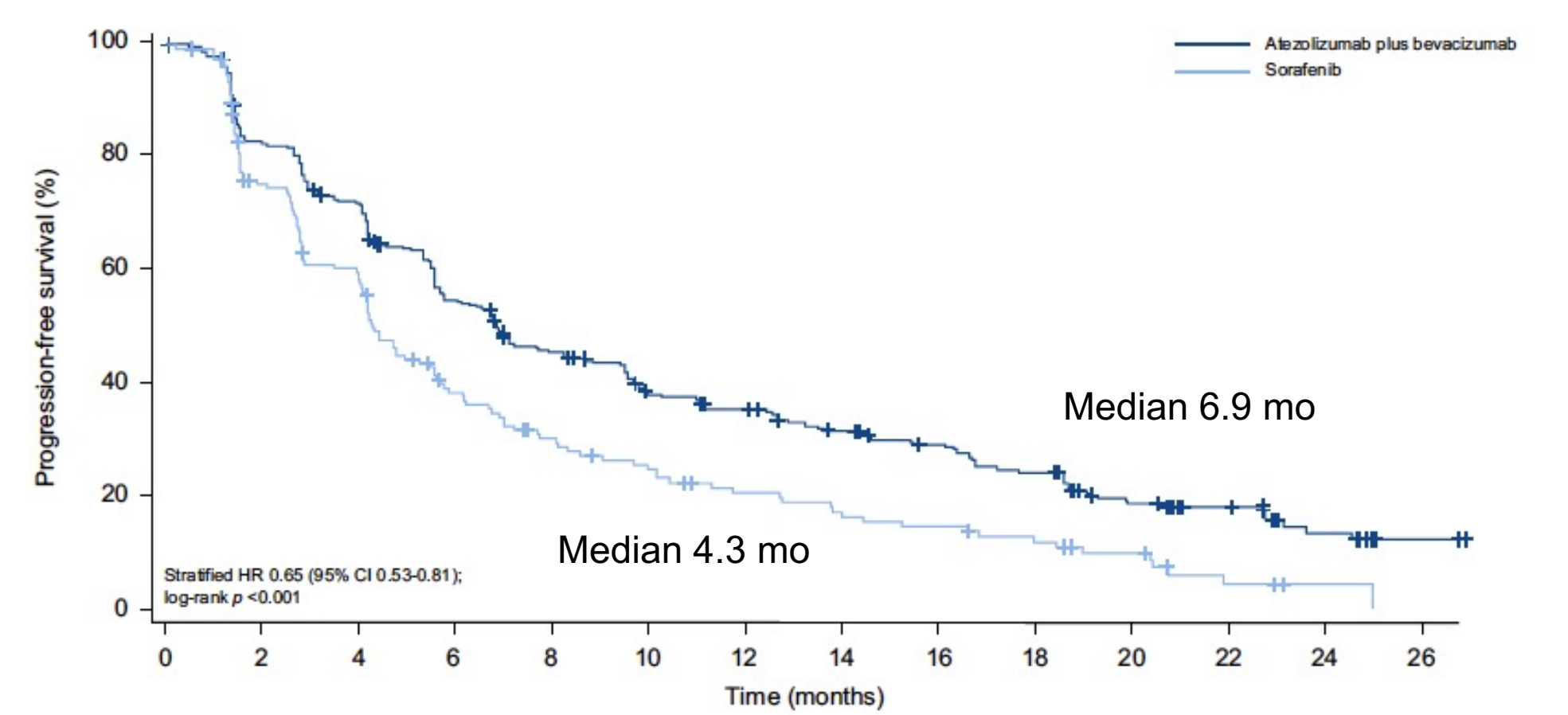
IMbrave150: Updated 5-Year OS with Atezolizumab and Bevacizumab (Median Follow-Up = 15.6 Months)



Cheng A-L et al. *J Hepatol* 2022;76(4):862-73.

RTP RESEARCH TO PRACTICE

IMbrave150: Updated 5-Year PFS with Atezolizumab and Bevacizumab (Median Follow-Up = 15.6 Months)



Cheng A-L et al. *J Hepatol* 2022;76(4):862-73.

RTP RESEARCH TO PRACTICE

Therapeutic Targets and Approach to Molecular Profiling for Biliary Tract Cancers

Target	Frequency	Targeted agents	Molecular test
IDH1	***13%*** of intrahepatic cholangiocarcinomas	Ivosidenib	Tumor next-generation DNA sequencing or targeted sequencing for hotspot mutations in coding region of IDH1
FGFR pathway	**20%** of intrahepatic cholangiocarcinomas	Erdafitinib; futibatinib; infigratinib; pemigatinib	Tumor next-generation DNA sequencing including FGFR2 intronic region, targeted RNAseq or FISH testing for FGFR2 translocation
BRAF	**5%** of intrahepatic cholangiocarcinomas	Dabrafenib with trametinib; vemurafenib	Tumor next-generation DNA sequencing or targeted sequencing for hotspot mutations in coding region of BRAF
MSI-high or MMR deficiency	**2%** of biliary tract cancers	Pembrolizumab	Multiple testing modalities available: PCR, immunohistochemistry or tumor next-generation DNA sequencing
ERBB2 (HER2)	***15%-20%*** gallbladder cancer; extrahepatic cholangiocarcinomas		Multiple testing modalities available including immunohistochemistry and FISH for expression and amplification, tumor next-generation DNA sequencing for mutations

MSI = microsatellite instability; MMR = mismatch repair

Valle JW et al. *Lancet* 2021;397(10272):428-44.

NEJM Evidence

Published June 1, 2022

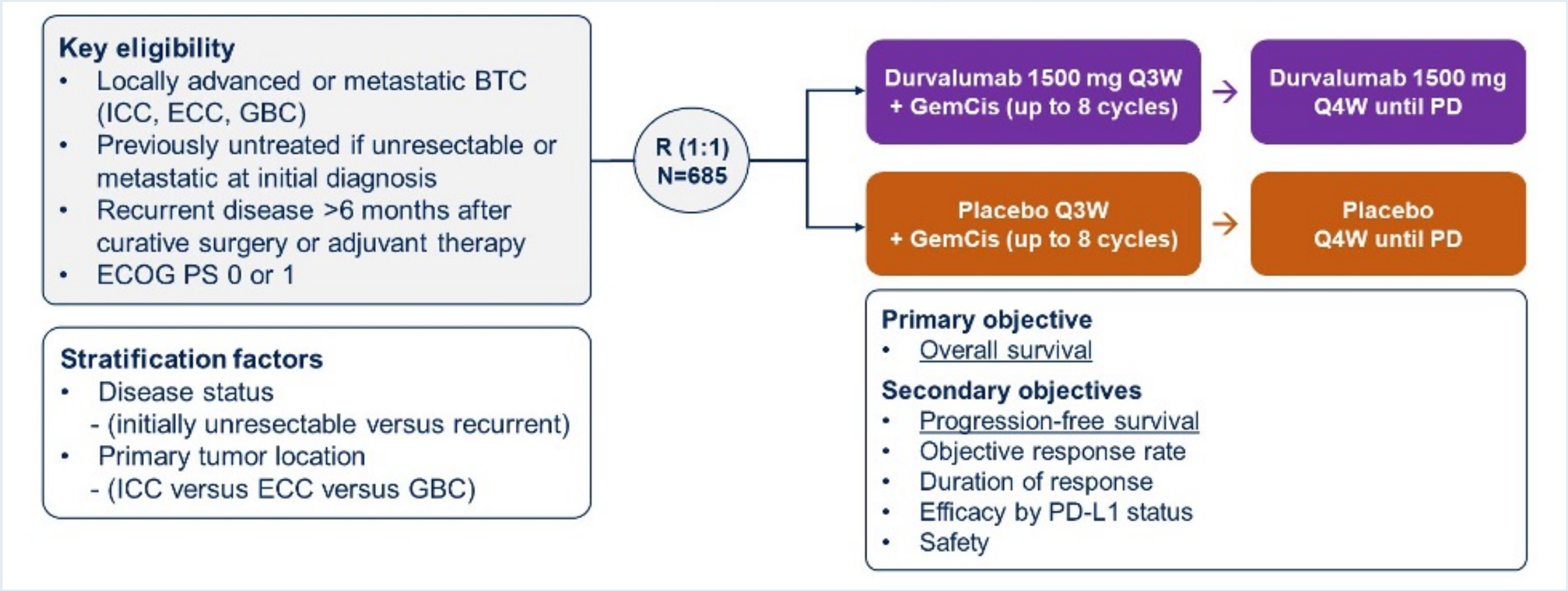
DOI: 10.1056/EVIDoa2200015

ORIGINAL ARTICLE

Durvalumab plus Gemcitabine and Cisplatin in Advanced Biliary Tract Cancer

Do-Youn Oh, M.D., Ph.D.,[1] Aiwu Ruth He, M.D., Ph.D.,[2] Shukui Qin, M.D.,[3] Li-Tzong Chen, M.D., Ph.D.,[4,5,6] Takuji Okusaka, M.D., Ph.D.,[7] Arndt Vogel, M.D.,[8] Jin Won Kim, M.D., Ph.D.,[9] Thatthan Suksomboon charoen, M.D.,[10] Myung Ah Lee, M.D., Ph.D.,[11] Masayuki Kitano, M.D., Ph.D.,[12] Howard Burris, M.D.,[13] Mohamed Bouattour, M.D.,[14] Suebpong Tanasanvimon, M.D.,[15] Mairéad G. McNamara, M.B., Ph.D.,[16] Renata Zaucha, M.D., Ph.D.,[17] Antonio Avallone, M.D.,[18] Benjamin Tan, M.D.,[19] Juan Cundom, M.D.,[20] Choong-kun Lee, M.D., Ph.D.,[21] Hidenori Takahashi, M.D., Ph.D.,[22] Masafumi Ikeda, M.D., Ph.D.,[23] Jen-Shi Chen, M.D.,[24] Julie Wang, Ph.D.,[25] Mallory Makowsky, Pharm.D.,[25] Nana Rokutanda, M.D., Ph.D.,[25] Philip He, Ph.D.,[25,26] John F. Kurland, Ph.D.,[25] Gordon Cohen, M.D., M.P.H.,[25] and Juan W. Valle, M.D.[16]

TOPAZ-1 Phase III Trial Schema

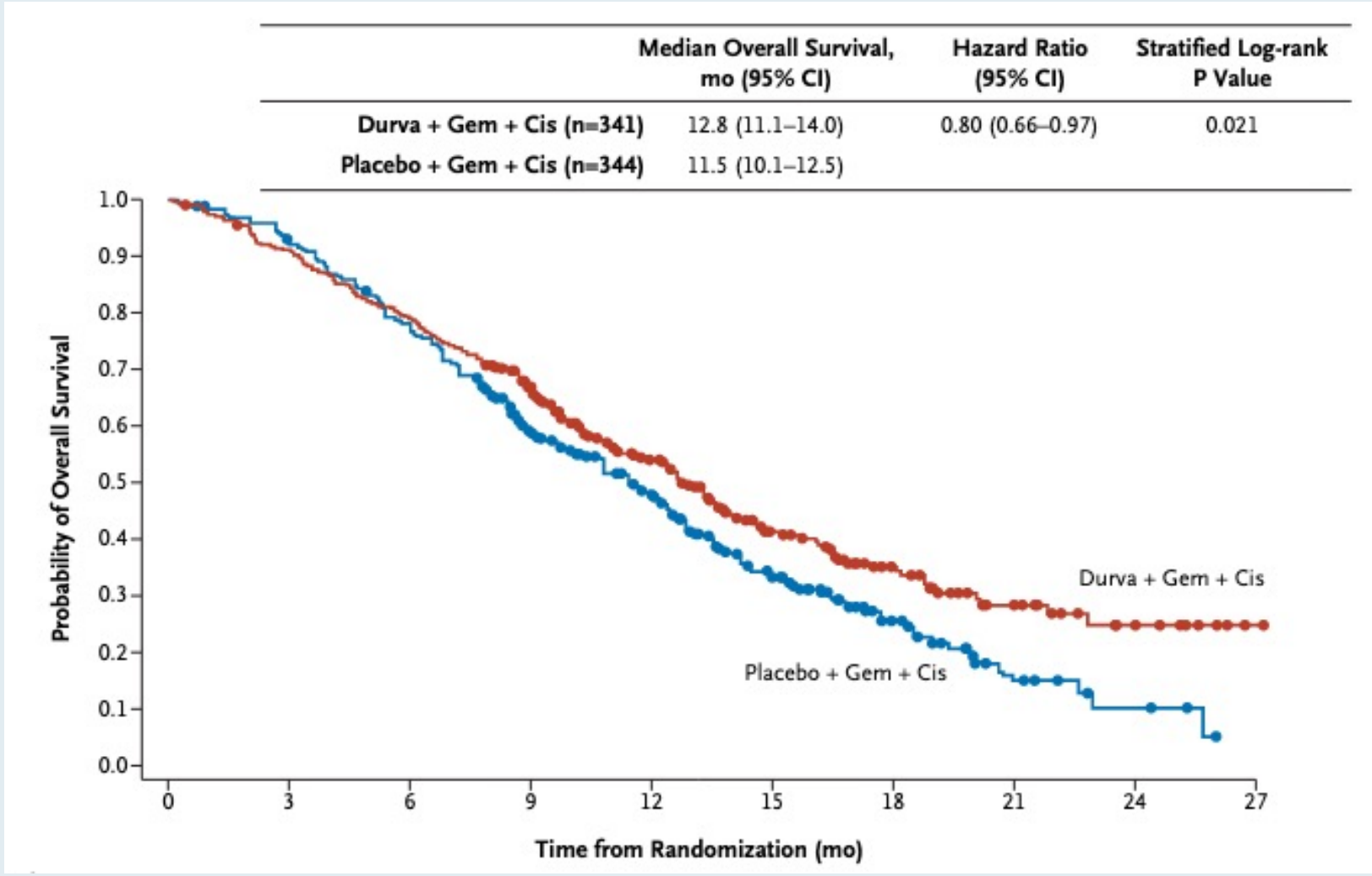


BTC = biliary tract cancer; ICC = intrahepatic cholangiocarcinoma; ECC = extrahepatic cholangiocarcinoma; GBC = gallbladder carcinoma

Oh D-Y et al. Gastrointestinal Cancers Symposium 2022;Abstract 378.

TOPAZ-1: Primary OS Endpoint with Durvalumab and Gemcitabine/Cisplatin for Advanced Biliary Tract Cancer

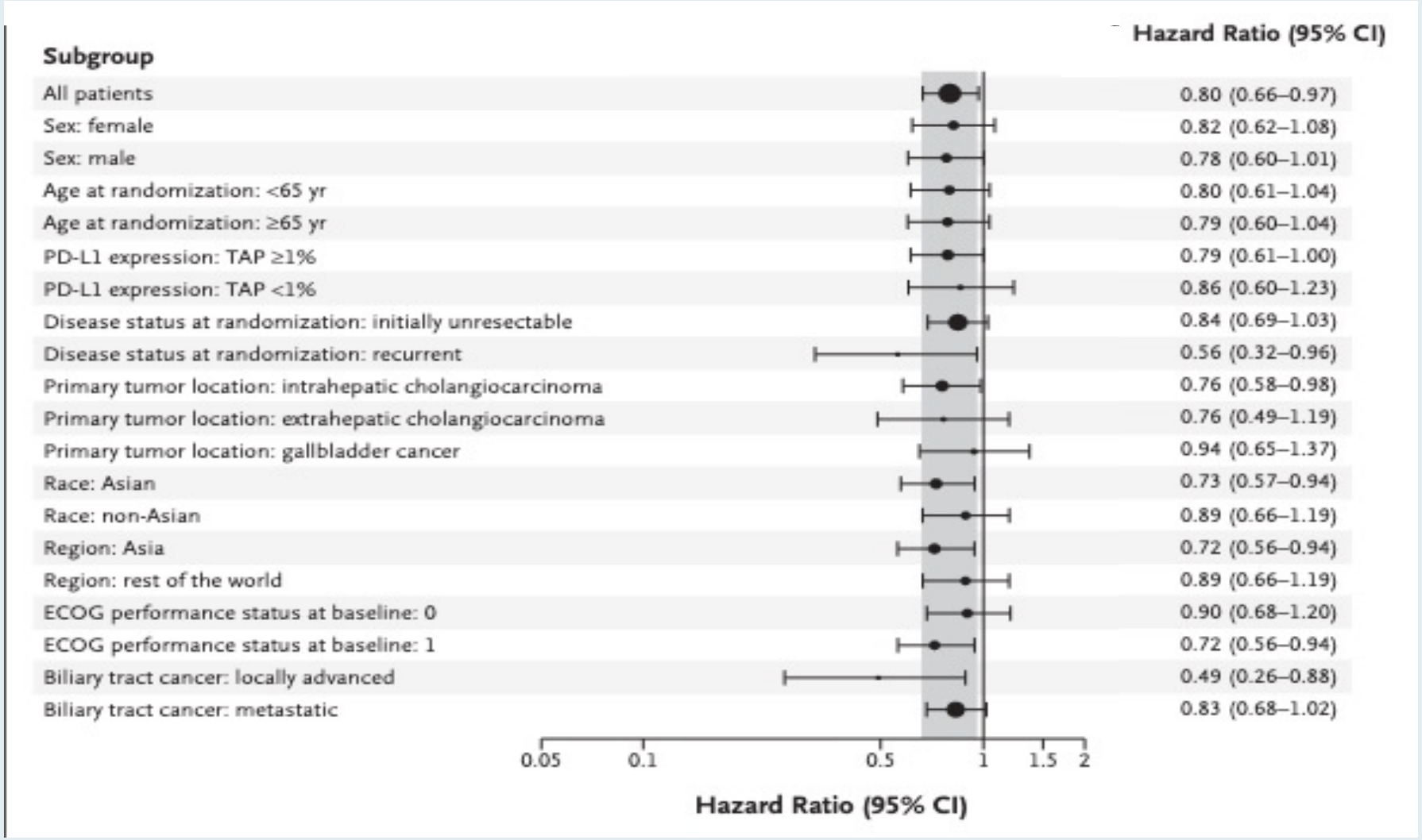
	Median Overall Survival, mo (95% CI)	Hazard Ratio (95% CI)	Stratified Log-rank P Value
Durva + Gem + Cis (n=341)	12.8 (11.1–14.0)	0.80 (0.66–0.97)	0.021
Placebo + Gem + Cis (n=344)	11.5 (10.1–12.5)		



Oh D-Y et al. *NEJM Evidence*, June 1, 2022.

RTP RESEARCH TO PRACTICE

TOPAZ-1: Overall Survival Subgroup Analysis



Oh D-Y et al. *NEJM Evidence*, June 1, 2022.

RTP RESEARCH TO PRACTICE

TOPAZ-1: Adverse Event Summary

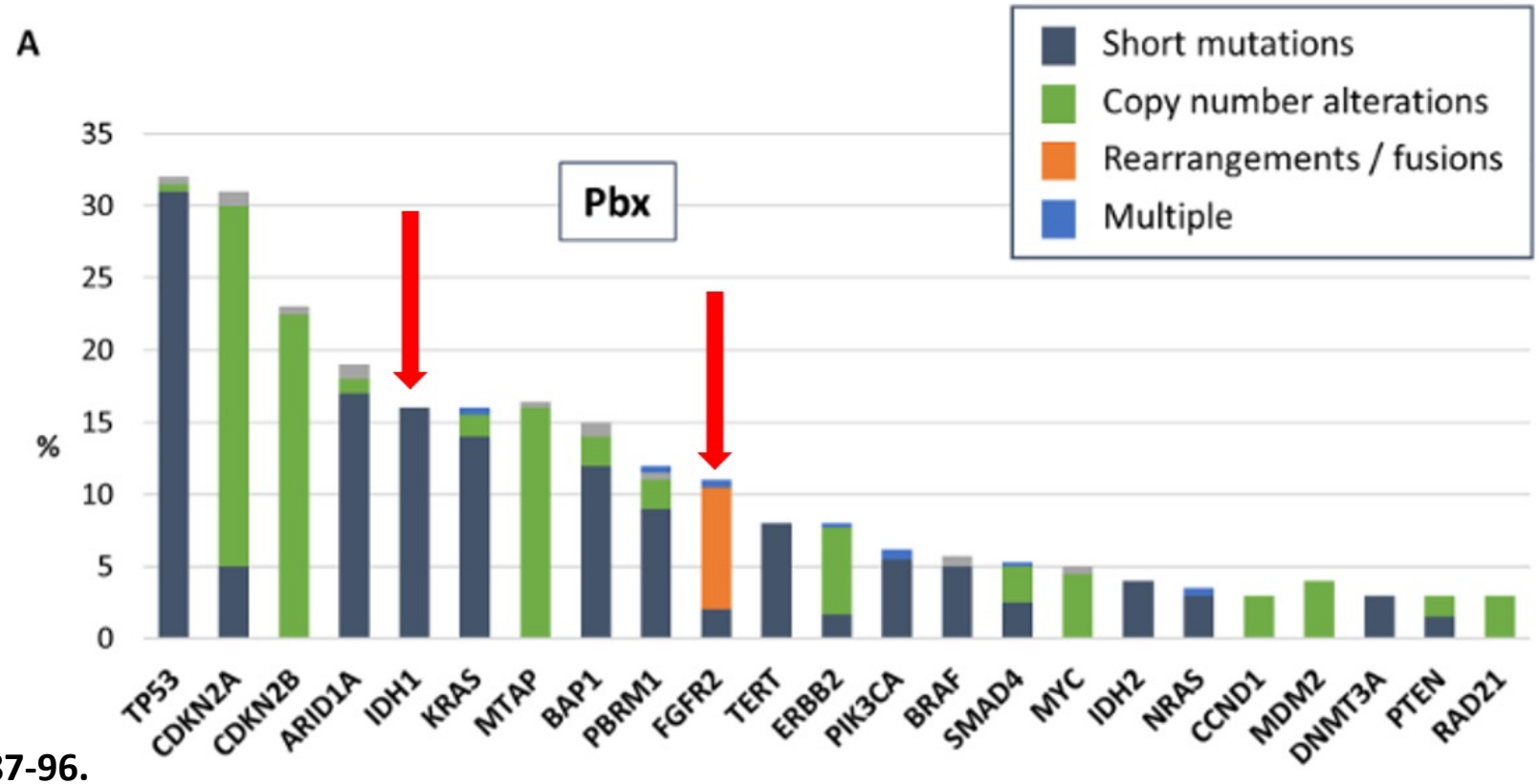
Parameter	Durvalumab plus Gemcitabine and Cisplatin (n=338)	Placebo plus Gemcitabine and Cisplatin (n=342)
Adverse events — no. (%)		
Any grade	336 (99.4)	338 (98.8)
Serious	160 (47.3)	149 (43.6)
Grade 3 or 4	256 (75.7)	266 (77.8)
Leading to discontinuation of any study treatment	44 (13.0)	52 (15.2)
Leading to death	12 (3.6)	14 (4.1)
Treatment-related adverse events — no. (%)		
Any grade	314 (92.9)	308 (90.1)
Serious	53 (15.7)	59 (17.3)
Grade 3 or 4	212 (62.7)	222 (64.9)
Leading to discontinuation of any study treatment	30 (8.9)	39 (11.4)
Leading to death*	2 (0.6)	1 (0.3)

Oh D-Y et al. *NEJM Evidence*, June 1, 2022.

RTP RESEARCH TO PRACTICE

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.

Content Courtesy of Katie Kelley, MD.

RTP RESEARCH TO PRACTICE

FGFR Inhibitor Efficacy for Cholangiocarcinoma Harboring FGFR2 Fusions

	Pemigatinib* (N = 107)	Infigratinib* (N = 108)	Futibatinib (N = 67)	Derazantinib (N = 29)
ORR	35.5%	23.1%	37.3%	20.7%
DCR	82.2%	84.3%	82.1%	82.8%
mPFS	6.9 mo	7.3 mo	7.2 mo	5.7 mo
mOS	21.1 mo	12.2 mo	NR	NR
Toxicities	Hyperphosphatemia, alopecia, diarrhea	Hyperphosphatemia, stomatitis, fatigue	Hyperphosphatemia, diarrhea, dry mouth	Hyperphosphatemia, fatigue, ocular

ORR = objective response rate; DCR = disease control rate; mPFS = median progression-free survival; mOS = median overall survival

*FDA approved

Abou-Alfa GK et al. *Lancet Oncol* 2020;21(5):671-84; Javle M et al. Gastrointestinal Cancers Symposium 2021; Goyal L et al. ASCO 2020; Mazzaferro V et al. *Br J Cancer* 2019;120(2):165-71.

Content Courtesy of Tanios Bekaii-Saab

FDA Accepts for Priority Review New Drug Application for Futibatinib for Cholangiocarcinoma

Press Release: March 30, 2022

“The US Food and Drug Administration (FDA) has accepted for priority review the New Drug Application (NDA) for futibatinib in the treatment of patients with previously treated locally advanced or metastatic cholangiocarcinoma (CCA) harboring FGFR2 gene rearrangements, including gene fusions. Futibatinib is an investigational, oral, potent, selective and irreversible small-molecule inhibitor of FGFR1, 2, 3 and 4. The FDA provided an anticipated Prescription Drug User Fee Act (PDUFA) action date of September 30, 2022.

The NDA is based on data from the pivotal Phase 2b FOENIX-CCA2 trial in 103 patients with locally advanced or metastatic unresectable intrahepatic (inside the liver) CCA, harboring FGFR2 gene rearrangements including fusions who had received one or more prior lines of systemic therapy. Patients in the trial received futibatinib 20 mg once daily until disease progression or unacceptable toxicity. The trial's primary endpoint was an objective response rate (ORR), which was 41.7% as assessed by independent central review. The key secondary endpoint of duration of response (DOR) demonstrated a median of 9.7 months (72% of responses ≥6 months). Common treatment-related adverse events (TRAEs) in the trial were hyperphosphatemia (85%), alopecia (33%) and dry mouth (30%). The only serious adverse reaction reported in more than one patient enrolled in the FOENIX-CCA2 trial was migraine (1.9%).”

https://www.prnewswire.com/news-releases/us-food-and-drug-administration-fda-accepts-for-priority-review-taiho-oncologys-new-drug-application-for-futibatinib-for-cholangiocarcinoma-301513278.html?tc=eml_cleartime

RTP RESEARCH TO PRACTICE

Updated Results of the FOENIX-CCA2 Trial: Efficacy and Safety of Futibatinib in Intrahepatic Cholangiocarcinoma Harboring *FGFR2* Fusions/Rearrangements

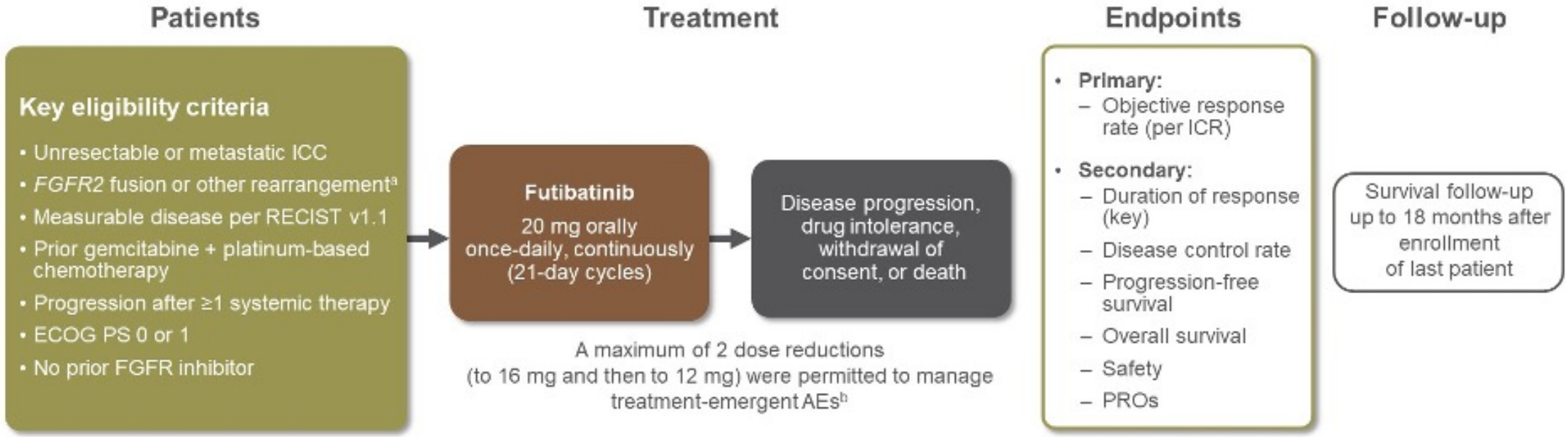
Lipika Goyal,[1] Funda Meric-Bernstam,[2] Antoine Hollebecque,[3] Chigusa Morizane,[4] Juan W. Valle,[5] Thomas B. Karasic,[6] Thomas A. Abrams,[7] Robin Kate Kelley,[8] Philippe Cassier,[9] Junji Furuse,[10] Heinz-Josef Klümpen,[11] Heung-Moon Chang,[12] Li-Tzong Chen,[13] Yoshito Komatsu,[14] Kunihiro Masuda,[15] Daniel Ahn,[16] Kate Li,[17] Karim A. Benhadji,[17] Volker Wacheck,[17] John A. Bridgewater[18]

[1]Massachusetts General Hospital Cancer Center, Boston, MA, USA; [2]University of Texas MD Anderson Cancer Center, Houston, TX, USA; [3]Gustave Roussy, Drug Development Department (DITEP), F-94805, Villejuif, France; [4]National Cancer Center Hospital, Tokyo, Japan; [5]University of Manchester and The Christie NHS Foundation Trust, Manchester, UK; [6]Hospital of the University of Pennsylvania, Philadelphia, PA, USA; [7]Dana-Farber Cancer Institute, Boston, MA, USA; [8]University of California, San Francisco, CA, USA; [9]Centre Léon-Bérard, Lyon, France; [10]Kyorin University, Faculty of Medicine, Tokyo, Japan; [11]Amsterdam University Medical Centers, University of Amsterdam, Amsterdam, The Netherlands; [12]Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea; [13]National Institute of Cancer Research, National Health Research Institutes, Tainan, Taiwan; [14]Hokkaido University Hospital Cancer Center, Hokkaido, Japan; [15]Tohoku University Graduate School of Medicine, Miyagi, Japan; [16]Mayo Clinic, Phoenix, AZ, USA; [17]Taiho Oncology, Inc., Princeton, NJ, USA; [18]UCL Cancer Institute, London, UK

ASCO 2022;Abstract 4009.

RTP RESEARCH TO PRACTICE

FOENIX-CCA2: Phase II Study Design

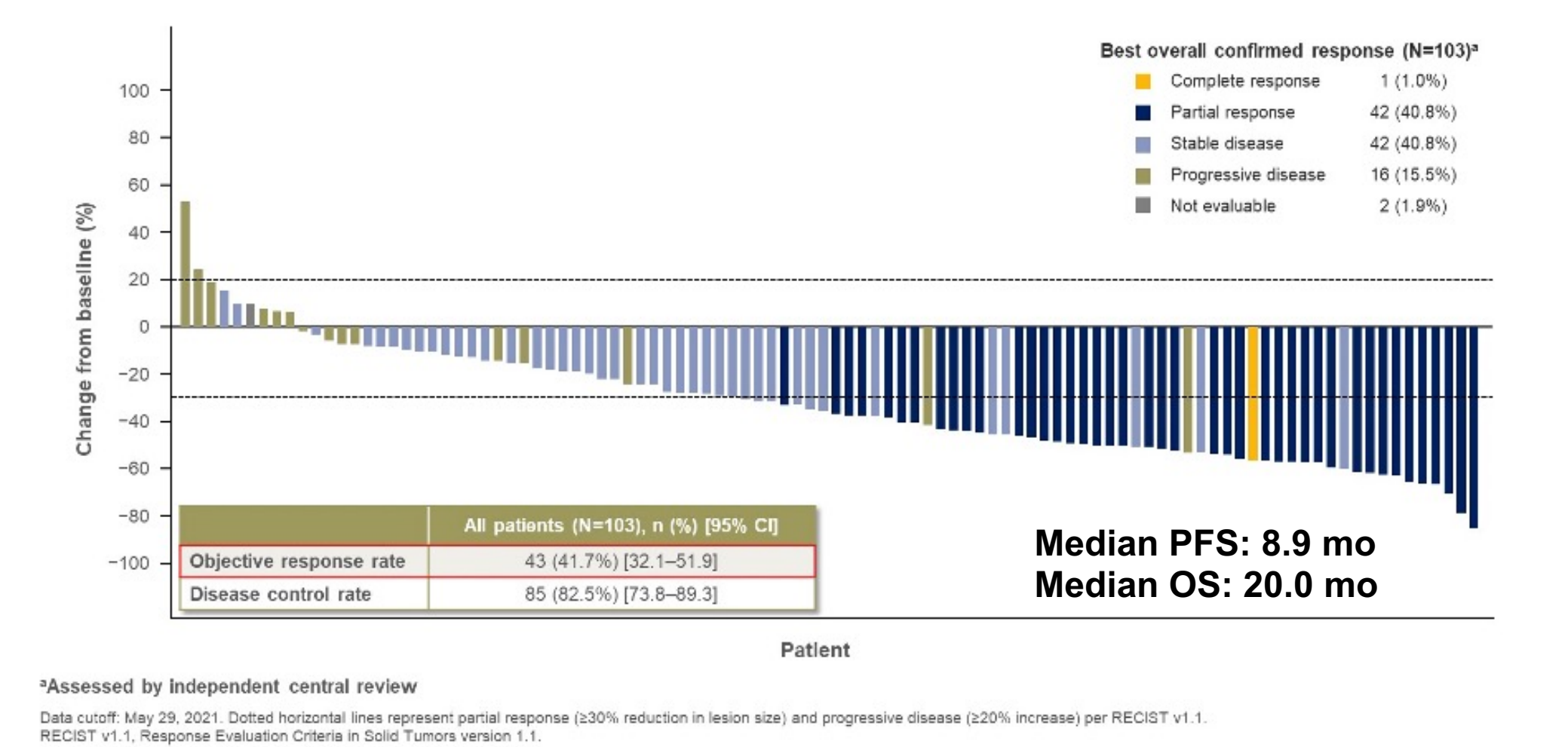


- At the time of the final data cutoff (May 29, 2021), median follow-up was 25.0 months, and 96/103 patients (93%) had discontinued treatment
- The median number of treatment cycles was 13.0, for a median treatment duration of 9.1 months

ICC = intrahepatic cholangiocarcinoma; AEs = adverse events; ICR = independent central review

Goyal L et al. ASCO 2022;Abstract 4009.

FOENIX-CCA2: A Phase II Study of Futibatinib for Intrahepatic Cholangiocarcinoma with FGFR2 Fusions/Rearrangements

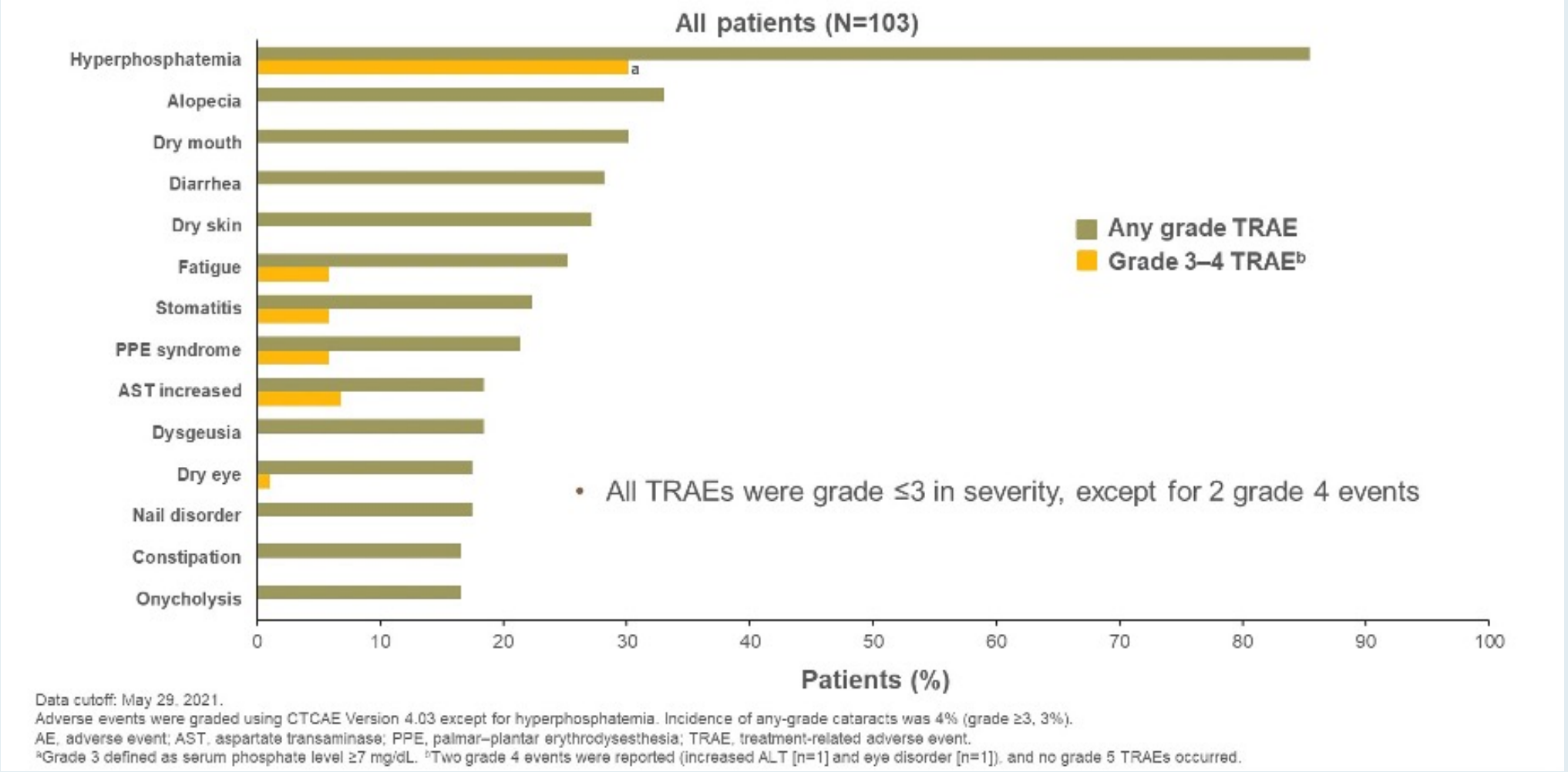


PFS = progression-free survival; OS = overall survival

Goyal L et al. ASCO 2022;Abstract 4009.

RTP RESEARCH TO PRACTICE

FOENIX-CCA2: Most Common (≥15%) Treatment-Related AEs with Futibatinib for Intrahepatic Cholangiocarcinoma



Data cutoff: May 29, 2021.
Adverse events were graded using CTCAE Version 4.03 except for hyperphosphatemia. Incidence of any-grade cataracts was 4% (grade ≥3, 3%).
AE, adverse event; AST, aspartate transaminase; PPE, palmar–plantar erythrodysesthesia; TRAE, treatment-related adverse event.
[a]Grade 3 defined as serum phosphate level ≥7 mg/dL. [b]Two grade 4 events were reported (increased ALT [n=1] and eye disorder [n=1]), and no grade 5 TRAEs occurred.

Goyal L et al. ASCO 2022;Abstract 4009.

RTP RESEARCH TO PRACTICE

FOENIX-CCA2: Adverse Events (AEs) of Special Interest with Futibatinib for Intrahepatic Cholangiocarcinoma

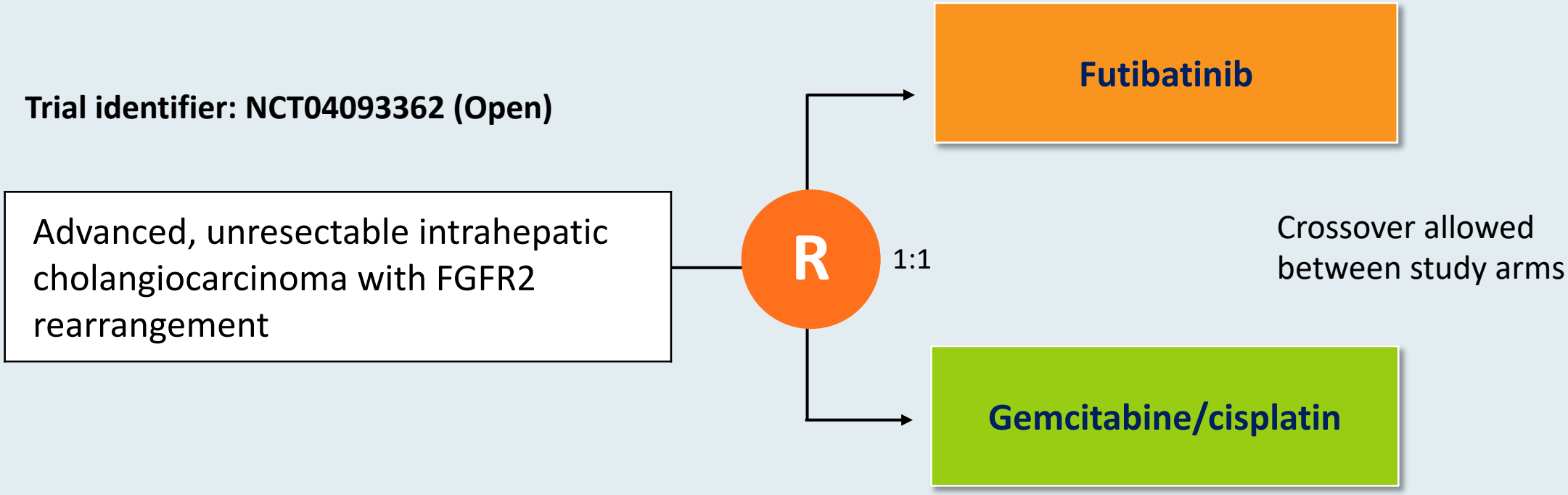
AE of special interest by group term	Safety population (N=103), n (%)		
	Any grade[a]	Grade 3	Grade 4
Hyperphosphatemia	94 (91)	32 (31)	0
Nail toxicities	54 (52)	2 (2)	0
Increased ALT and AST	28 (27)	12 (12)	1 (1)
Palmar–plantar erythrodysesthesia (PPE) syndrome	23 (22)	6 (6)	0
Rash	9 (9)	0	0
Retinal disorders	8 (8)	0	0

- One AE of special interest led to treatment discontinuation (PPE syndrome, grade 1)
- Hyperphosphatemia was manageable with phosphate-lowering therapy and dose modification
  - Median time to resolution of grade 3 hyperphosphatemia was 7.0 days (range, 2.0–26.0 days)

Goyal L et al. ASCO 2022;Abstract 4009.

FOENIX-CCA3: Phase III Study Design

Trial identifier: NCT04093362 (Open)



Primary endpoint: Progression-free survival

www.clinicaltrials.gov. NCT04093362. Accessed August 2022.

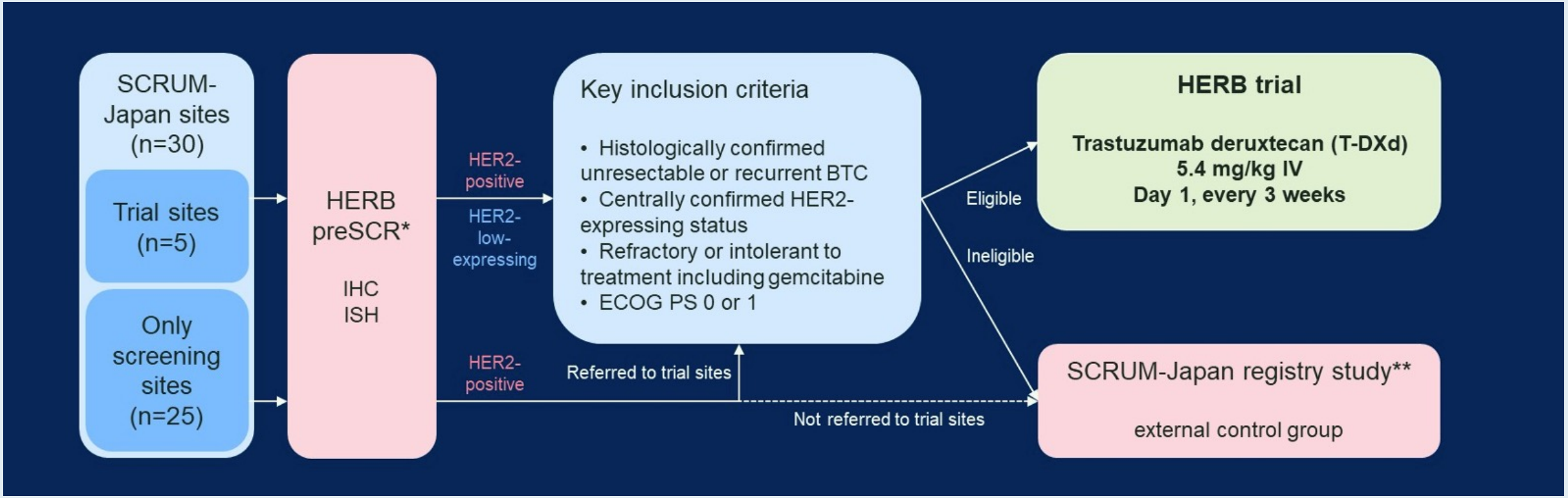
2022 ASCO ANNUAL MEETING

Trastuzumab deruxtecan (T-DXd; DS-8201) in patients (pts) with HER2-expressing unresectable or recurrent biliary tract cancer (BTC): An investigator-initiated multicenter phase 2 study (HERB trial)

Akihiro Ohba[1], Chigusa Morizane[1], Yasuyuki Kawamoto[2], Yoshito Komatsu[2], Makoto Ueno[3], Satoshi Kobayashi[3], Masafumi Ikeda[4], Mitsuhito Sasaki[4], Junji Furuse[5], Naohiro Okano[5], Nobuyoshi Hiraoka[1], Hiroshi Yoshida[1], Aya Kuchiba[1], Ryo Sadachi[1], Kenichi Nakamura[1], Naoko Matsui[1], Yoshiaki Nakamura[4], Wataru Okamoto[6], Takayuki Yoshino[4], Takuji Okusaka[1]

[1]National Cancer Center Hospital, [2]Hokkaido University Hospital, [3]Kanagawa Cancer Center, [4]National Cancer Center Hospital East, [5]Kyorin University Faculty of Medicine, [6]Hiroshima University Hospital

HERB: Phase II Study of Trastuzumab Deruxtecan (T-DXd) for HER2-Expressing Biliary Tract Cancer



Ohba A et al. ASCO 2022;Abstract 4006.

HERB Primary Endpoint: Confirmed ORR by BICR with T-DXd for Biliary Tract Cancer

- Tumor response

*: P =0.01

	HER2-positive (n=22)	HER2-low-expressing (n=8)	All pts (n=30)
Confirmed ORR (90% CI) (95% CI)	**36.4% (19.6-56.1)*** (17.2–59.3)	12.5% – (0.3–52.7)	30.0% – (14.7–49.4)
Confirmed DCR (95% CI)	81.8% (59.7–94.8)	75.0% (34.9–96.8)	80.0% (61.4–92.3)
Confirmed best response, n (%)			
CR	2 (9.1)	0 (0)	2 (6.7)
PR	6 (27.3)	1 (12.5)	7 (23.3)
SD	10 (45.5)	5 (62.5)	15 (50.0)
PD	3 (13.6)	1 (12.5)	4 (13.3)
NE	1 (4.5)	1 (12.5)	2 (6.7)

- Best percentage change

ORR = overall response rate; BICR = blinded independent central review; CR = complete response; PR = partial response; SD = stable disease; PD = disease progression; NE = not estimable

Ohba A et al. ASCO 2022;Abstract 4006.

HERB Secondary Endpoints: Progression-Free Survival (PFS) and Overall Survival (OS) with T-DXd for Biliary Tract Cancer

	HER2-positive disease (n = 22)	HER2-low expressing disease (n = 8)
Median PFS	5.1 mo	3.5 mo
6-month PFS rate	40.9%	0
Median OS	7.1 mo	8.9 mo
6-month OS rate	63.6%	75.0%

Ohba A et al. ASCO 2022;Abstract 4006.

HERB: Treatment-Emergent Adverse Events with T-DXd for Biliary Tract Cancer

Event	Any grade, n (%)	Grade ≥ 3, n (%)
Anemia	22 (68.8)	17 (53.1)
Neutrophil count decreased	18 (56.3)	10 (31.3)
White blood cell count decreased	18 (56.3)	10 (31.3)
Platelet count decreased	14 (43.8)	3 (9.4)
Nausea	14 (43.8)	0 (0)
Alopecia	13 (40.6)	0 (0)
Anorexia	12 (37.5)	1 (3.1)
Lymphocyte count decreased	11 (34.4)	7 (21.9)
Fatigue / Malaise	11 (34.4)	0 (0)
Interstitial lung disease / Pneumonitis	8 (25.0)	4 (12.5)
Hypoalbuminemia	7 (21.9)	1 (3.1)
Vomiting	7 (21.9)	0 (0)
Mucositis oral	5 (15.6)	0 (0)

Ohba A et al. ASCO 2022;Abstract 4006.

HERB: Interstitial Lung Disease (ILD)/Pneumonitis with T-DXd for Biliary Tract Cancer

	ILDs (n=8)*
Grade, n (%) 1 2 3 5	 3 (37.5) 1 (12.5) 2 (25.0) 2 (25.0)
Median time to onset (range), days	124 (35–247)**
Median Age (range), years	73 (51–75)
Sex, female, n (%)	3 (37.5)
Number of prior regimens, n (%) 1 ≥ 2	 4 (50.0) 4 (50.0)
HER2 status of IHC/ISH, n (%) 3+/+ 2+/+	 5 (62.5) 3 (37.5)
Lung metastasis, n (%)	3 (37.5)
Smoking history, n (%)	3 (37.5)
Biliary drainage, n (%)	4 (50.0)

Ohba A et al. ASCO 2022;Abstract 4006.

Lancet Gasteroenterol Hepatol 2021;6(10):803-15.

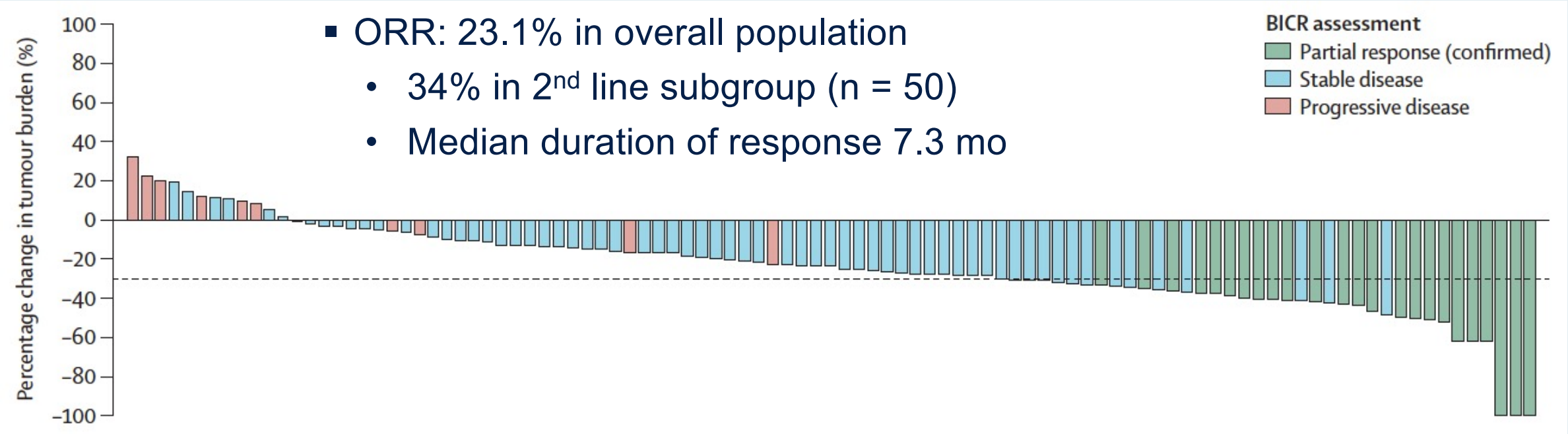
Articles

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 for 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 mo



Javle M et al. *Lancet Gasteroenterol Hepatol* 2021;6(10):803-15.

RTP RESEARCH TO PRACTICE

JCO Precis Oncol 2022;6:e2100414.

TARGETED DRUG THERAPY

original reports

Progression-Free Survival in Patients With Cholangiocarcinoma With or Without *FGF/FGFR* Alterations: A FIGHT-202 Post Hoc Analysis of Prior Systemic Therapy Response

Kristen Bibeau, MSPH, PhD[1]; Luis Féliz, MD[2]; Christine F. Lihou, BS[1]; Haobo Ren, PhD[1]; and Ghassan K. Abou-Alfa, MD[3,4]

FIGHT-202: PFS on Prior First- and Second-Line Therapy According to FGF/FGFR Genetic Alteration Status in Patients with Cholangiocarcinoma

Therapy	*FGFR2* Fusions/Rearrangements (n = 107)	Other *FGF/FGFR* Alterations (n = 20)	No *FGF/FGFR* Alterations (n = 18)
Prior first-line therapy			
Evaluable patients, No.	102	19	16
Median PFS (95% CI), months	5.5 (4.0 to 8.0)	4.4 (2.7 to 7.1)	2.8 (1.6 to 11.3)
Gemcitabine plus cisplatin, No.	69	12	13
Median PFS (95% CI), months	5.7 (4.6 to 9.1)	3.9 (1.6 to 6.4)	2.8 (1.6 to 17.7)
Not gemcitabine plus cisplatin, No.	33	7	3
Median PFS (95% CI), months	4.1 (2.3 to 6.5)	7.4 (3.1 to 14.0)	5.1 (1.3 to 5.5)
Prior second-line therapy			
Evaluable patients, No.	39	8	6
Median PFS (95% CI), months	4.2 (3.0 to 5.3)	3.0 (1.1 to 9.9)	5.9 (2.4 to 12.5)
Pemigatinib second-line therapy			
Evaluable patients, No.	65	12	12
Median PFS (95% CI), months	7.0 (4.9 to 11.1)	2.1 (1.2 to 6.9)	1.7 (1.2 to 2.0)

PFS = progression-free survival

Bibeau B et al. *JCO Precis Oncol* 2022;6:e2100414.

RTP RESEARCH TO PRACTICE

Research

JAMA Oncology | Original Investigation

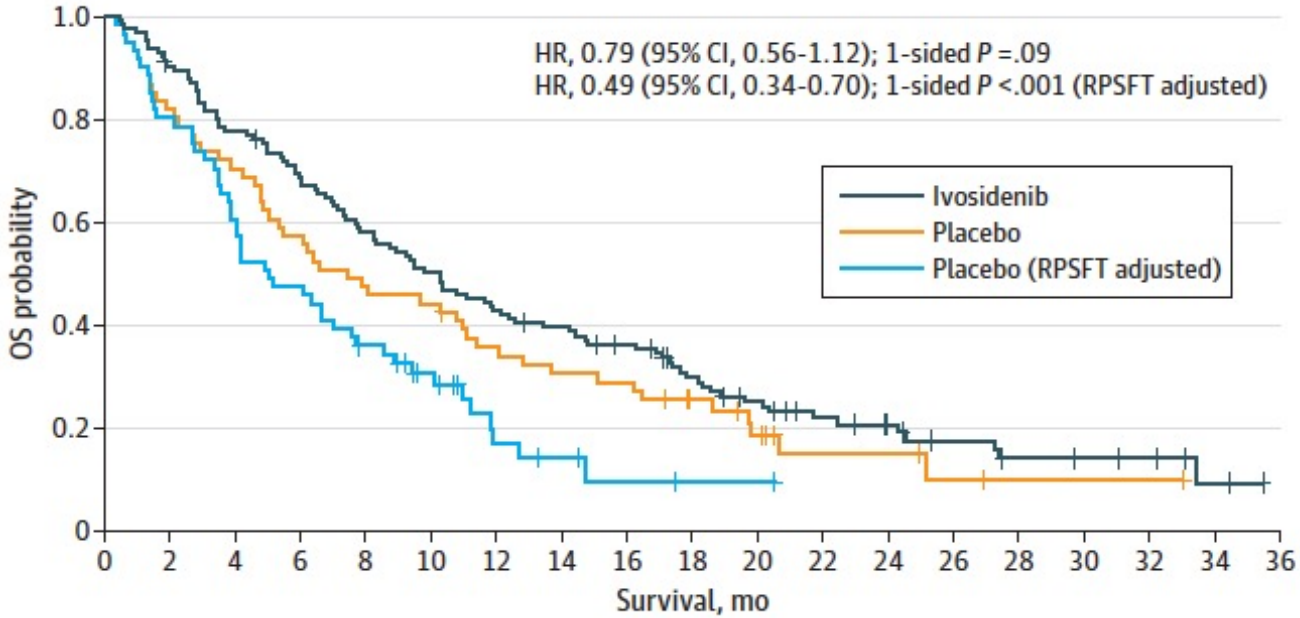
Final Overall Survival Efficacy Results of Ivosidenib for Patients With Advanced Cholangiocarcinoma With *IDH1* Mutation

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.

Gastrointestinal Cancers Agenda

Module 1: Colorectal Cancer

Module 2: Upper Gastrointestinal Cancers

Module 3: Hepatocellular and Biliary Tract Cancers

Module 4: Pancreatic Adenocarcinoma

- PARPi (maintenance olaparib) in patients with gBRCA-mutated metastatic pancreatic cancer; potential role of olaparib for patients with other DNA damage repair genetic alterations
- Potential future role of KRAS-targeted treatment of metastatic pancreatic cancer

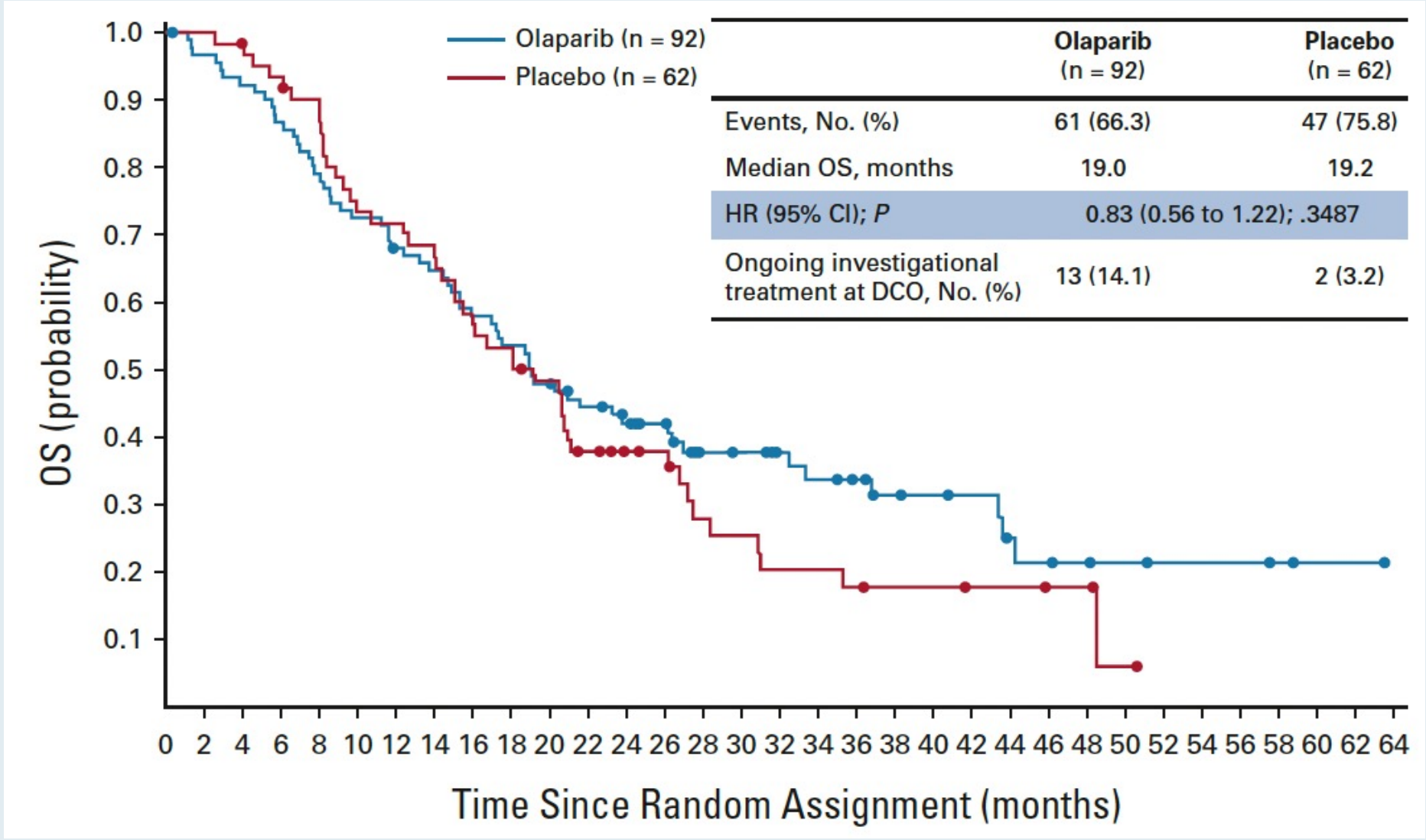
original reports

Overall Survival Results From the POLO Trial: A Phase III Study of Active Maintenance Olaparib Versus Placebo for Germline BRCA-Mutated Metastatic Pancreatic Cancer

Hedy L. Kindler, MD[1]; Pascal Hammel, MD, PhD[2]; Michele Reni, MD[3]; Eric Van Cutsem, MD, PhD[4]; Teresa Macarulla, MD, PhD[5]; Michael J. Hall, MD[6]; Joon Oh Park, MD, PhD[7]; Daniel Hochhauser, MD, PhD[8]; Dirk Arnold, MD, PhD[9]; Do-Youn Oh, MD, PhD[10]; Anke Reinacher-Schick, MD, PhD[11]; Giampaolo Tortora, MD, PhD[12]; Hana Algül, MD, PhD, MPH[13]; Eileen M. O'Reilly, MD[14]; Sonal Bordia, MD[15]; David McGuinness, MSc[16]; Karen Cui, MD, PhD[17]; Gershon Y. Locker, MD[17]; and Talia Golan, MD[18]

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

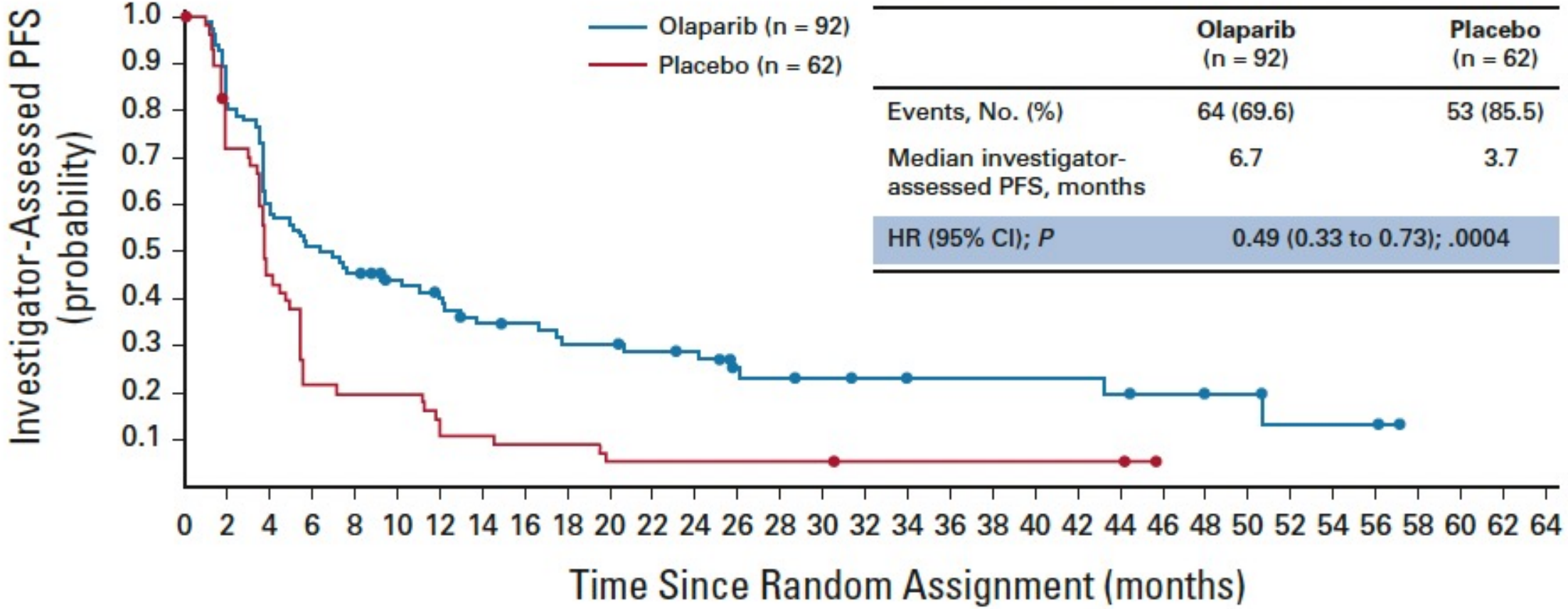
POLO: Overall Survival (OS)



	Olaparib (n = 92)	Placebo (n = 62)
Events, No. (%)	61 (66.3)	47 (75.8)
Median OS, months	19.0	19.2
HR (95% CI); *P*	0.83 (0.56 to 1.22); .3487	
Ongoing investigational treatment at DCO, No. (%)	13 (14.1)	2 (3.2)

Kindler HL et al. *J Clin Oncol* 2022;[Online ahead of print].

POLO: Investigator-Assessed Progression-Free Survival (PFS)



	Olaparib (n = 92)	Placebo (n = 62)
Events, No. (%)	64 (69.6)	53 (85.5)
Median investigator-assessed PFS, months	6.7	3.7
HR (95% CI); *P*	0.49 (0.33 to 0.73); .0004	

Kindler HL et al. *J Clin Oncol* 2022;[Online ahead of print].

POLO: Other Key Secondary Endpoints

	Olaparib (n = 92)	Placebo (n = 62)	Hazard ratio	*p*-value
PFS2	16.9 mo	9.3 mo	0.66	0.0613
TFST	9.0 mo	5.4 mo	0.44	<0.0001
TSST	14.9 mo	9.6 mo	0.61	0.011
TDT	7.5 mo	3.8 mo	0.43	<0.0001

TFST = time to first subsequent cancer therapy or death; TSST = time to second subsequent cancer therapy or death; TDT = time to discontinuation of treatment or death

Kindler HL et al. *J Clin Oncol* 2022;[Online ahead of print].

POLO: Summary of Adverse Events (AEs)

Event	Olaparib (n = 90)		Placebo (n = 61)	
	Any Grade, No. (%)	Grade ≥ 3, No. (%)	Any Grade, No. (%)	Grade ≥ 3, No. (%)
Any AE	89 (98.9)	44 (48.9)	56 (91.8)	15 (24.6)
Nausea	44 (48.9)	1 (1.1)	15 (24.6)	1 (1.6)
Fatigue	42 (46.7)	5 (5.6)	16 (26.2)	0 (0.0)
Diarrhea	34 (37.8)	1 (1.1)	10 (16.4)	0 (0.0)
Abdominal pain	29 (32.2)	3 (3.3)	16 (26.2)	1 (1.6)
Anemia	29 (32.2)	11 (12.2)	10 (16.4)	2 (3.3)
Constipation	25 (27.8)	0 (0.0)	7 (11.5)	0 (0.0)
Decreased appetite	25 (27.8)	3 (3.3)	4 (6.6)	0 (0.0)
Vomiting	23 (25.6)	2 (2.2)	10 (16.4)	1 (1.6)
Back pain	22 (24.4)	0 (0.0)	13 (21.3)	1 (1.6)
Arthralgia	16 (17.8)	1 (1.1)	7 (11.5)	0 (0.0)
Asthenia	16 (17.8)	1 (1.1)	6 (9.8)	1 (1.6)
Pyrexia	16 (17.8)	0 (0.0)	6 (9.8)	0 (0.0)

Event	Olaparib (n = 90)		Placebo (n = 61)	
	Any Grade, No. (%)	Grade ≥ 3, No. (%)	Any Grade, No. (%)	Grade ≥ 3, No. (%)
Serious AE	28 (31.1)	NA	10 (16.4)	NA
Death	1 (1.1)	NA	0 (0.0)	NA
Interruption of intervention because of AE	37 (41.1)	NA	4 (6.6)	NA
Dose reduction because of AE	16 (17.8)	NA	3 (4.9)	NA
Discontinuation of intervention because of AE	8 (8.9)	NA	1 (1.6)	NA

Kindler HL et al. *J Clin Oncol* 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

Research

JAMA Oncol 2021;7(5):693-9.

JAMA Oncology | Original Investigation

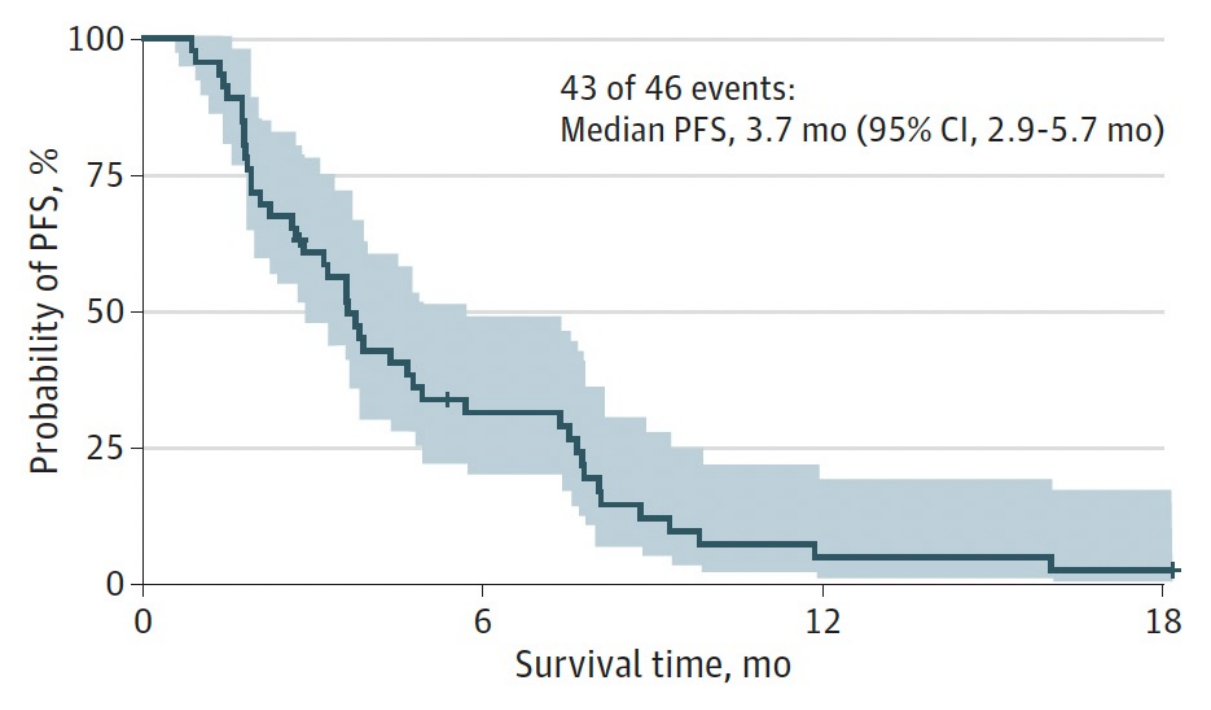
Olaparib Monotherapy for Previously Treated Pancreatic Cancer With DNA Damage Repair Genetic Alterations Other Than Germline *BRCA* Variants

Findings From 2 Phase 2 Nonrandomized Clinical Trials

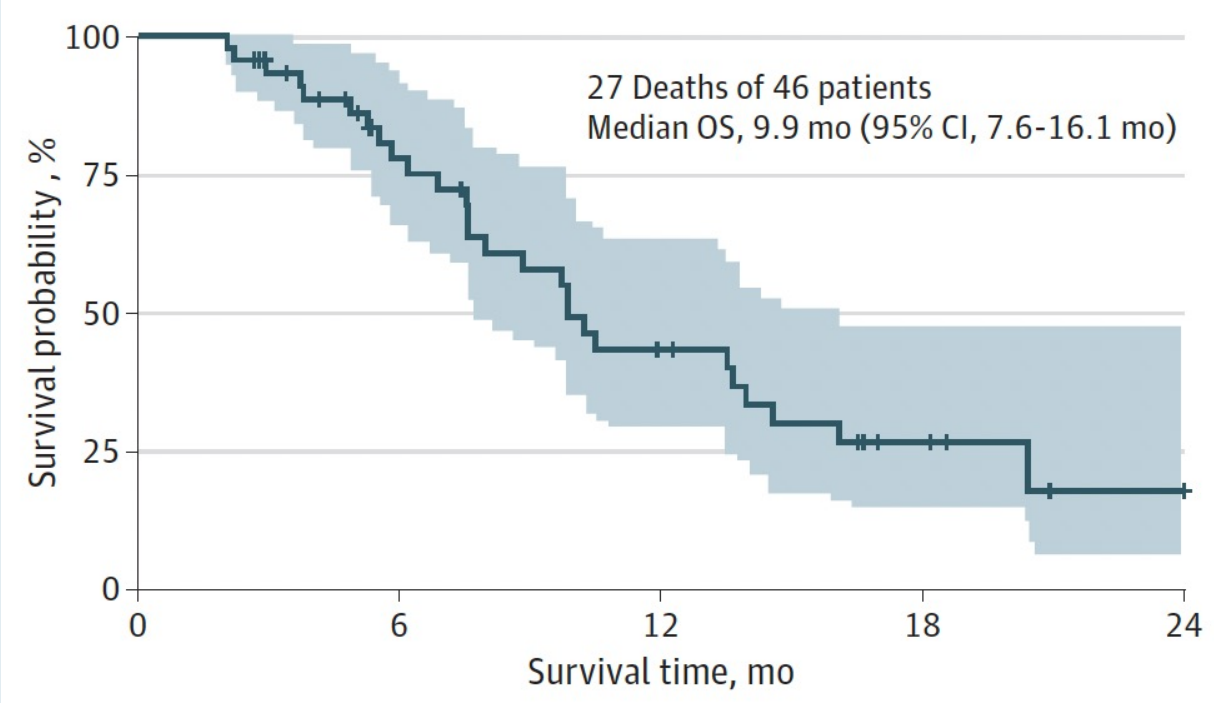
Milind Javle, MD; Einat Shacham-Shmueli, MD; Lianchun Xiao, MS; Gauri Varadhachary, MBBS, MD; Naama Halpern, MD, MBA; David Fogelman, MD; Ben Boursi, MD; Syeda Uruba, MBBS, MPH; Ofer Margalit, MD, PhD; Robert A. Wolff, MD; Talia Golan, MD

Olaparib Monotherapy for Previously Treated Pancreatic Cancer with DNA Damage Repair Genetic Alterations Other Than Germline BRCA Variants

Progression-free survival (PFS)



Overall survival (OS)



Javle M et al. *JAMA Oncol* 2021;7(5):693-9.

RTP RESEARCH TO PRACTICE

Abstract 599

Gastrointestinal 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]

PARP Inhibitor (PARPi) Usage Summary Relative to Platinum Sensitivity and Line of Therapy in a Worldwide 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. Gastrointestinal Cancers Symposium 2022;Abstract 599.

ASCO Gastrointestinal Cancers Symposium

Abstract 519

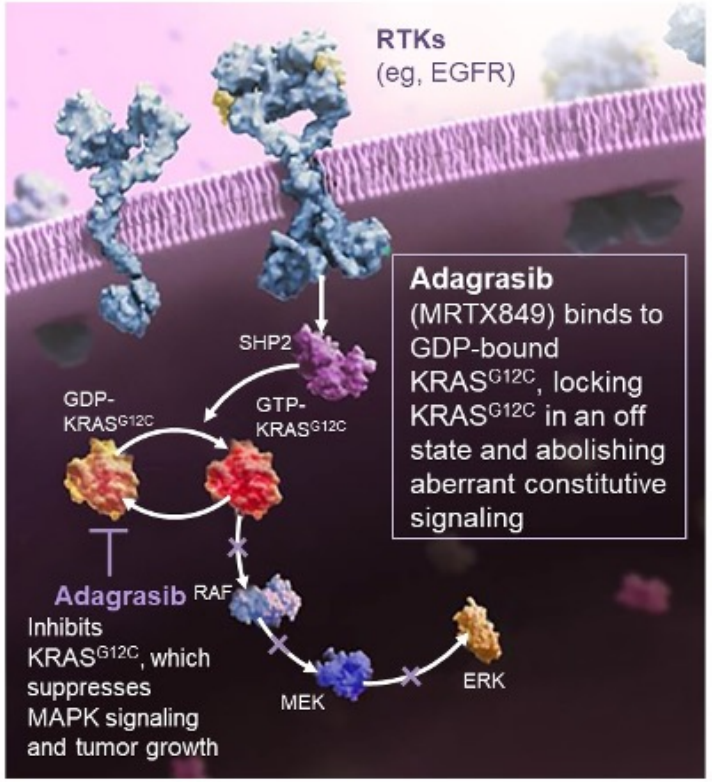
KRYSTAL-1: Updated Activity and Safety of Adagrasib (MRTX849) in Patients (Pts) With Unresectable or Metastatic Pancreatic Cancer (PDAC) and Other Gastrointestinal (GI) Tumors Harboring a KRAS^{G12C} Mutation

TS Bekaii-Saab[1], AI Spira[2], R Yaeger[3], GL Buchschacher Jr.[4], AJ McRee[5], JK Sabari[6], ML Johnson[7], M Barve[8], N Hafez[9], K Velastegui[10], JG Christensen[10], T Kheoh[10], H Der-Torossian[10], SM Gadgeel[11]

[1]Department of Medical Oncology and Hematology, Mayo Clinic, Scottsdale, Arizona, USA; [2]Virginia Cancer Specialists, Fairfax, Virginia, NEXT Oncology, Virginia, US Oncology Research, The Woodlands, Texas, USA; [3]Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, New York, USA; [4]Kaiser Permanente Southern California, Los Angeles, California, USA; [5]Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, NC, USA; [6]Perlmutter Cancer Center, New York University Langone Health, New York, New York, USA; [7]Sarah Cannon Research Institute, Tennessee Oncology, Nashville, Tennessee, USA; [8]Mary Crowley Cancer Research, Dallas, Texas, USA; [9]Yale Cancer Center, New Haven, Connecticut, USA; [10]Mirati Therapeutics, Inc., San Diego, California, USA; [11]Henry Ford Cancer Institute/Henry Ford Health System, Detroit, Michigan, USA

Adagrasib: A Differentiated, Selective Inhibitor of KRAS^{G12C}

- KRAS mutations occur in approximately 90% of pancreatic cancer[1]; ~2% of these are KRAS^{G12C} mutations[2]
- The KRAS protein cycles between GTP-on and GDP-off states and has a protein resynthesis half-life of ~24 hours[3,4]
- Adagrasib, a covalent inhibitor of KRAS^{G12C}, irreversibly and selectively binds KRAS^{G12C} in its inactive, GDP-bound state
- Adagrasib was optimized for desired properties of a KRAS^{G12C} inhibitor[5]:
  - Long half-life of ~24 hours
  - Dose-dependent PK
  - CNS penetration
- Maintaining continuous exposure of adagrasib above a target threshold enables inhibition of KRAS-dependent signaling for the complete dose interval and maximizes depth and duration of antitumor activity

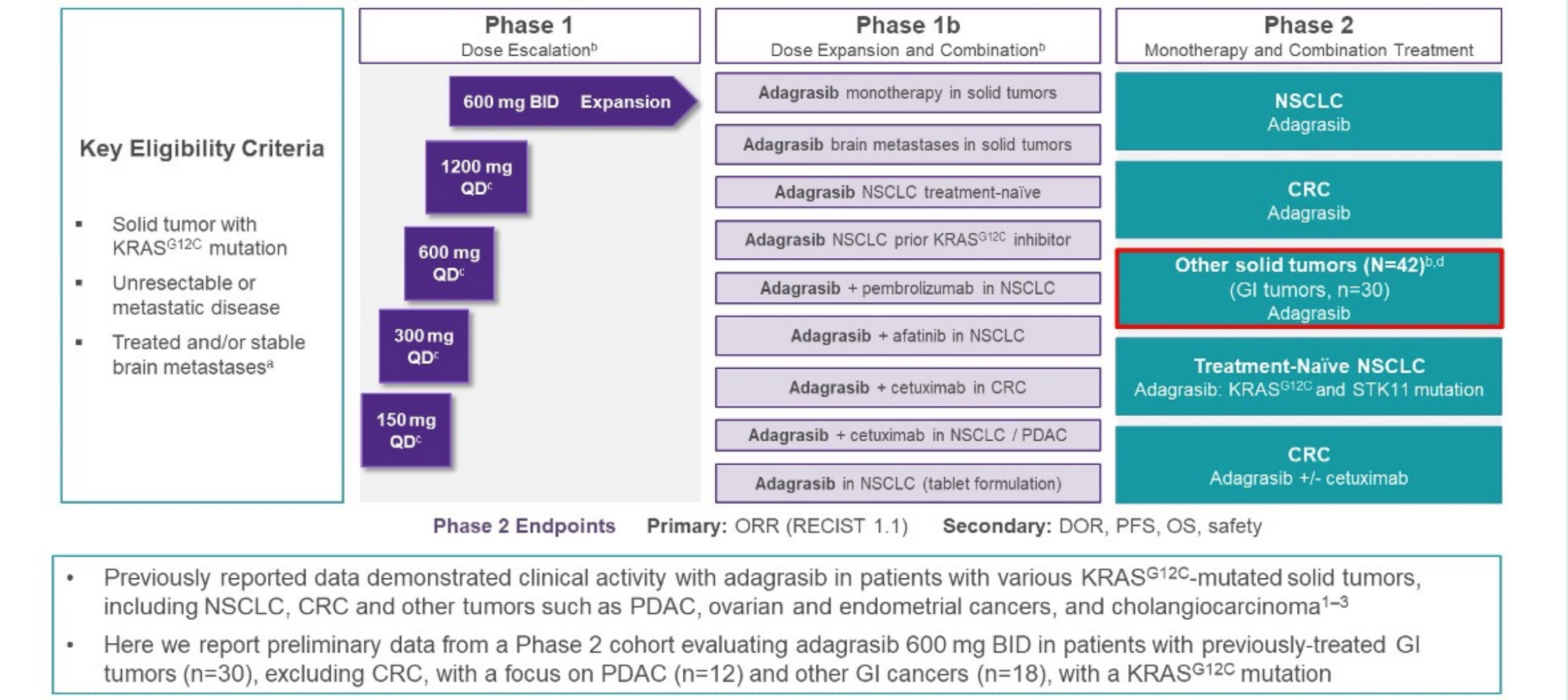


CNS, central nervous system; EGFR, epidermal growth factor receptor; PK, pharmacokinetics; RTK, receptor tyrosine kinase.

1. Prior IA, et al. *Cancer Res*. 2012;72(10):2457–2467. 2. Nollmann FI & Alexander Ruess D. *Biomedicines*. 2020;8(8):281. 3. Bos JL, et al. *Cell*. 2007;129:865–877. 4. Shukla S, et al. *Neoplasia*. 2014;16(2):115–128. 5. Hallin J, et al. *Cancer Discov*. 2020;10(1):54–71.

Bekaii-Saab TS et al. Gastrointestinal Cancers Symposium 2022;Abstract 519.

KRYSTAL-1 Study Design



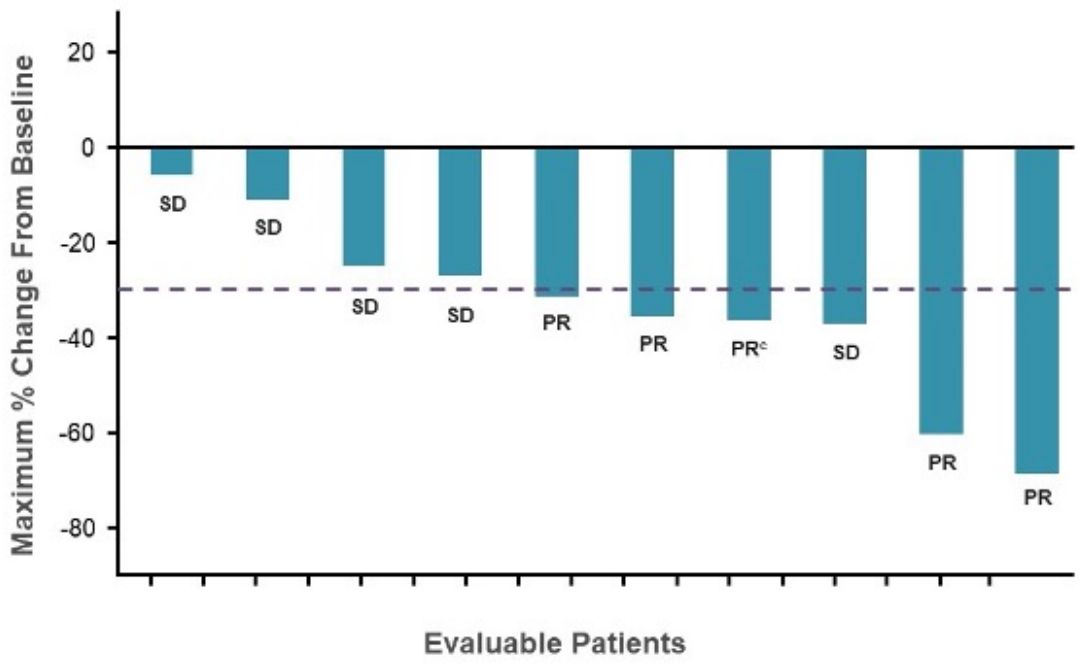
- Previously reported data demonstrated clinical activity with adagrasib in patients with various KRAS^{G12C}-mutated solid tumors, including NSCLC, CRC and other tumors such as PDAC, ovarian and endometrial cancers, and cholangiocarcinoma[1–3]
- Here we report preliminary data from a Phase 2 cohort evaluating adagrasib 600 mg BID in patients with previously-treated GI tumors (n=30), excluding CRC, with a focus on PDAC (n=12) and other GI cancers (n=18), with a KRAS^{G12C} mutation

NSCLC = non-small cell lung cancer; CRC = colorectal cancer; PDAC = pancreatic ductal adenocarcinoma

Bekaii-Saab TS et al. Gastrointestinal Cancers Symposium 2022;Abstract 519.

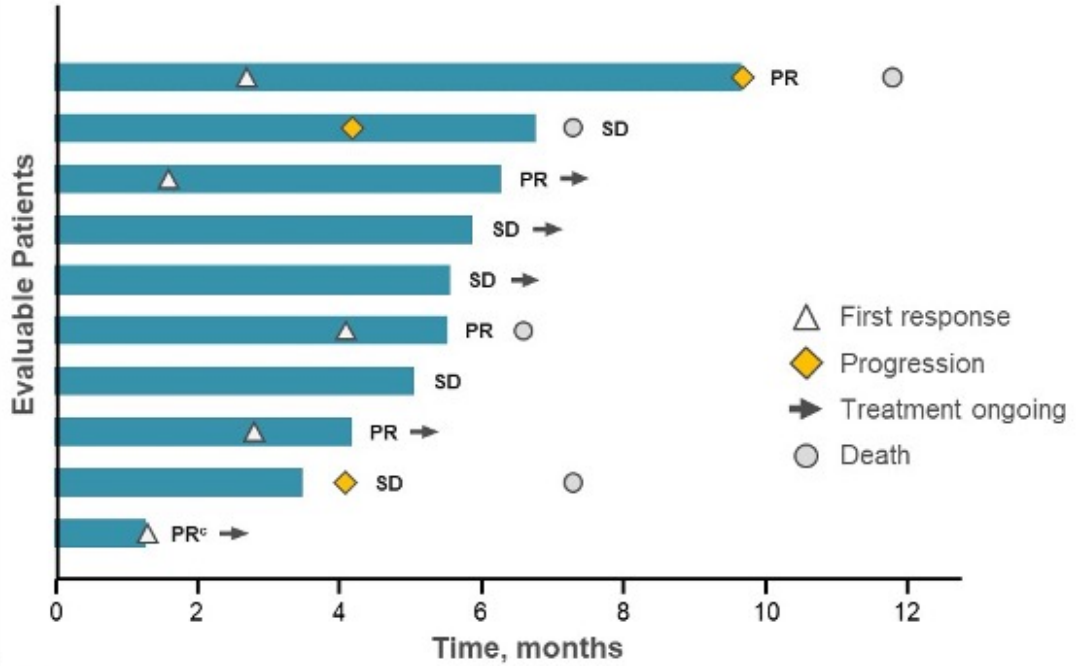
KRYSTAL-1: Best Tumor Change from Baseline and Duration of Treatment with Adagrasib for Unresectable or Metastatic PDAC

Best Tumor Change from Baseline (n = 10)



- Response rate: 50% (5/10), including 1 unconfirmed PR
- SD: 50% (5/10 patients)
- DCR: 100% (10/10 patients)

Duration of Treatment (n = 10)



- Median TTR: 2.8 months
- Median DOR: 6.97 months
- Median PFS: 6.6 months (95% CI 1.0–9.7)
- Treatment ongoing in 50% (5/10) of patients

PDAC = pancreatic ductal adenocarcinoma; SD = stable disease; DCR = disease control rate; PR = partial response; TTR = time to response; DOR = duration of response; PFS = progression-free survival

Bekaii-Saab TS et al. Gastrointestinal Cancers Symposium 2022;Abstract 519.

RTP RESEARCH TO PRACTICE

KRYSTAL-1: Incidence of Treatment-Related Adverse Events (TRAEs) with Adagrasib

Most Frequent TRAEs[b]	Overall (N=42)[c]		Overall GI cancers[d] (n=30)	
TRAEs, %	**Any Grade**	**Grade 3**	**Any Grade**	**Grade 3**
Any TRAEs	91	21	87	27
Most frequent TRAEs, %				
Nausea	48	2	50	3
Vomiting	43	0	40	0
Diarrhea	43	0	37	0
Fatigue	29	7	33	10
AST increase	19	2	20	3
Blood creatinine increase	19	0	17	0
Anemia	17	2	20	3
Peripheral edema	17	0	17	0
QT prolongation	14	5	13	7
ALT increase	12	2	13	3
Dysgeusia	12	0	13	0

- No Grade 4 or 5 TRAEs
- No TRAEs led to discontinuation

Bekaii-Saab TS et al. Gastrointestinal Cancers Symposium 2022;Abstract 519.

original reports

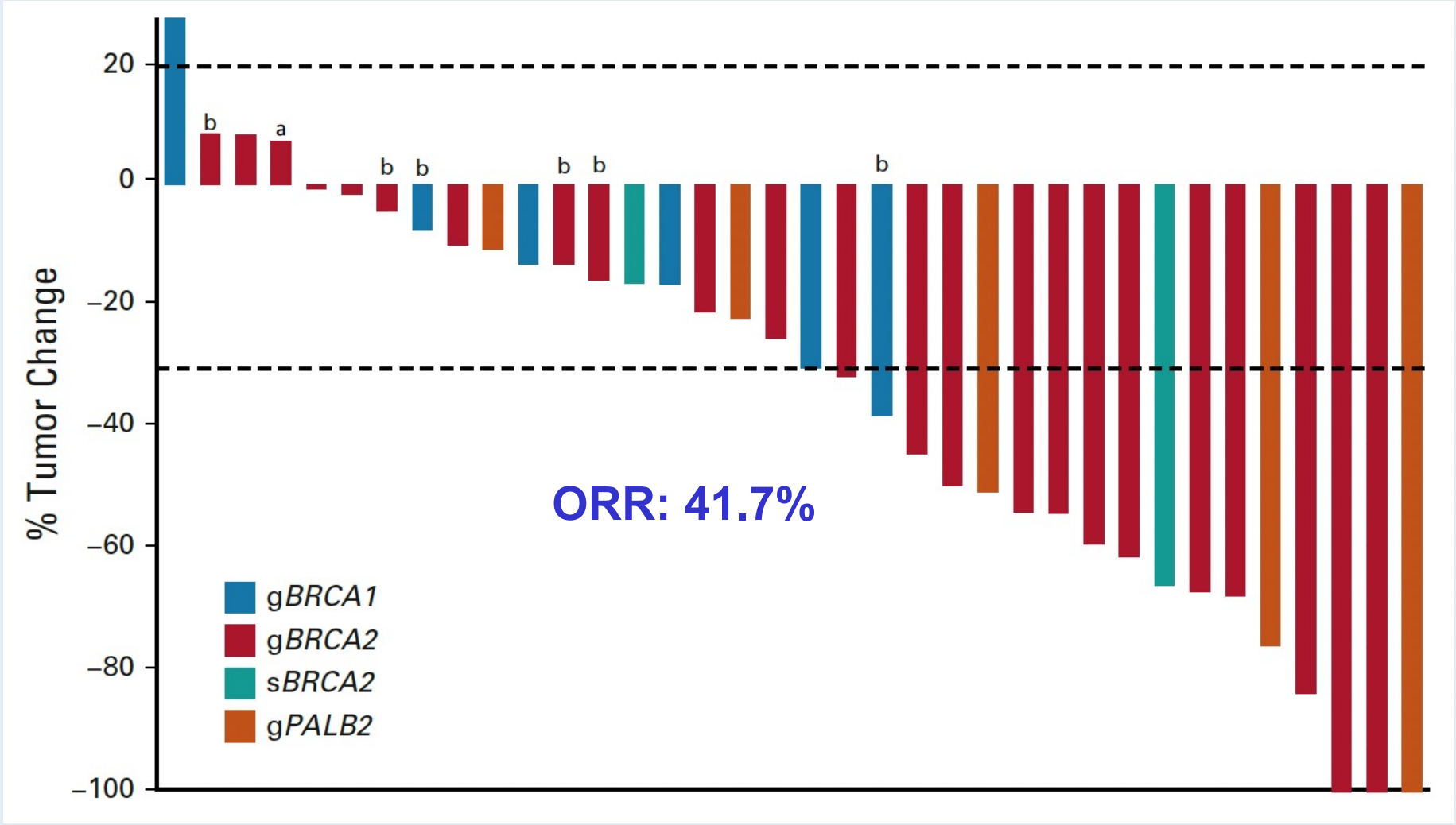
Phase II Study of Maintenance Rucaparib in Patients With Platinum-Sensitive Advanced Pancreatic Cancer and a Pathogenic Germline or Somatic Variant in *BRCA1*, *BRCA2*, or *PALB2*

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.

RTP RESEARCH TO PRACTICE

Maintenance Rucaparib for Platinum-Sensitive Advanced Pancreatic Cancer



Reiss KA et al. *J Clin Oncol* 2021;39(22):2497-505.

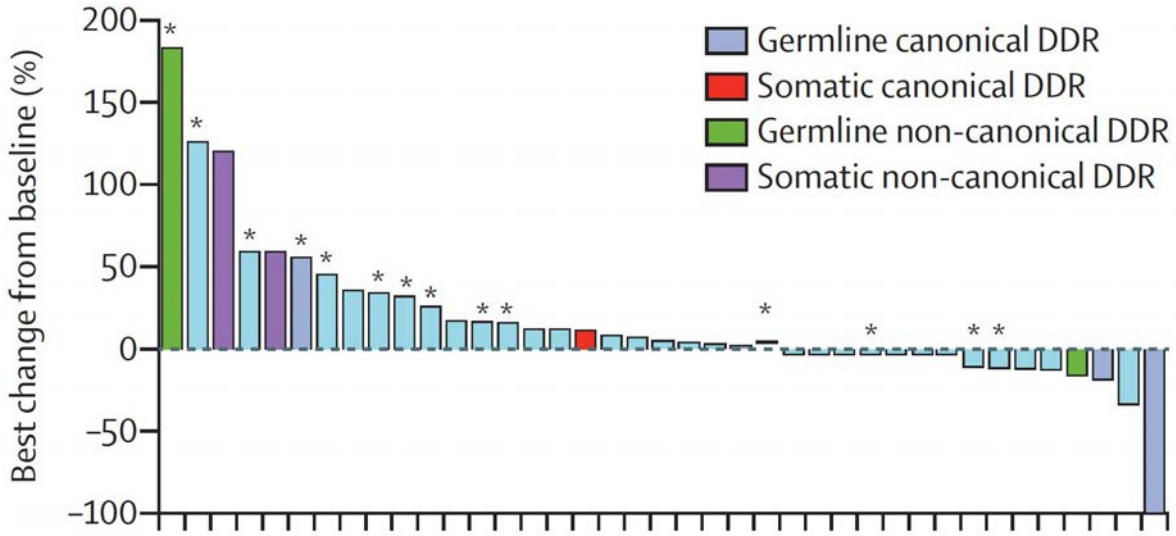
RTP RESEARCH TO PRACTICE

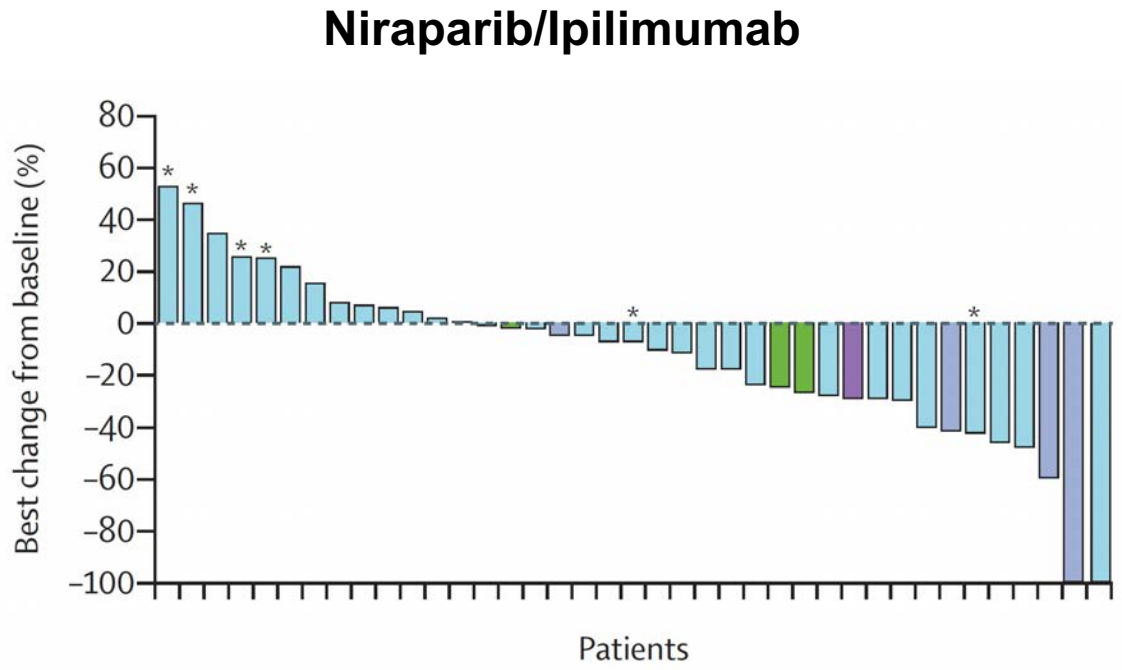
Lancet Oncol 2022;23(8):1009-20.

Niraparib plus nivolumab or niraparib plus ipilimumab in patients with platinum-sensitive advanced pancreatic cancer: a randomised, phase 1b/2 trial

Kim A Reiss, Rosemarie Mick, Ursina Teitelbaum, Mark O'Hara, Charles Schneider, Ryan Massa, Thomas Karasic, Rashmi Tondon, Chioma Onyiah, Mary Kate Gosselin, Alyssa Donze, Susan M Domchek, Robert H Vonderheide

Waterfall Plots of Best Responses of Patients with Measurable Disease at the Start of the Study





DDR = DNA damage repair

Reiss KA et al. *Lancet Oncol* 2022;23(8):1009-20.

Efficacy Data in All Patients and in Those Without Pathogenic Variants in DNA Damage Repair Genes

	Primary efficacy population				Patients without pathogenic BRCA1, BRCA2 or PALB2 variants		Patients without any DDR variants	
	6-month PFS	ORR	Median PFS	Median OS	Median PFS	Median OS	Median PFS	Median OS
Niraparib with nivolumab								
Patients	44	39	44	44	37	37	32	32
Outcome	20.6% vs 44% $p = 0.0002$	7.7%	1.9 mo	13.2 mo	1.9 mo	13.2 mo	1.8 mo	13.2 mo
Niraparib with ipilimumab								
Patients	40	39	40	40	33	33	30	30
Outcome	59.6% vs 44% $p = 0.045$	15.4%	8.1 mo	17.3 mo	7.6 mo	17.3 mo	7.6 mo	15.0 mo

DDR = DNA damage repair; PFS = progression-free survival; ORR = overall response rate; OS = overall survival

Reiss KA et al. *Lancet Oncol* 2022;23(8):1009-20.

Thank you for joining us!

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

We are taking a short break!

The program will resume at 3:25 PM PT (6:25 PM ET)

Up Next…

Drs Ibiayi Dagogo-Jack and Suresh Ramalingam discuss the management of lung cancer

RTP
RESEARCH
TO PRACTICE

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

A CME/MOC- and NCPD-Accredited Hybrid Event

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

RTP
RESEARCH
TO PRACTICE

Agenda

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

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

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

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

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

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

RTP RESEARCH TO PRACTICE

Lung Cancer Faculty

Ibiayi Dagogo-Jack, MD
Assistant Professor of Medicine
Harvard Medical School
Massachusetts General Hospital
Boston, Massachusetts

Suresh S Ramalingam, MD
Professor of Hematology and Medical Oncology
Roberto C Goizueta Chair for Cancer Research
Executive Director, Winship Cancer Institute
Emory University School of Medicine
Atlanta, Georgia

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TO PRACTICE

Co-Moderators

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

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

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

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

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

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

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MODULE 6: Lung Cancer

Co-Moderator

Ram Trehan, MD
George Washington University
Silver Spring, Maryland

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Lung Cancer Agenda

Module 1: Immunotherapy in Patients with Non-Small Cell Lung Cancer (NSCLC) without Targetable Mutations

Module 2: Targeted Treatment of NSCLC

Module 3: Small Cell Lung Cancer

Lung Cancer Agenda

Module 1: Immunotherapy in Patients with Non-Small Cell Lung Cancer (NSCLC) without Targetable Mutations

- Adjuvant immunotherapy (atezolizumab) and neoadjuvant IO (nivolumab)
- Consolidation immunotherapy (durvalumab/PACIFIC) after chemoradiation for locally advanced NSCLC
- IO alone or in combination with chemotherapy as first-line therapy for metastatic NSCLC

Module 2: Targeted Treatment of NSCLC

Module 3: Small Cell Lung Cancer

Positive Phase III IMscin001 Study Results Announced for Subcutaneous Atezolizumab for NSCLC

Press Release – August 2, 2022

"The Phase III IMscin001 study evaluating a subcutaneous formulation of atezolizumab met its co-primary endpoints. The study showed non-inferior levels of atezolizumab in the blood (pharmacokinetics), when injected subcutaneously, compared with intravenous (IV) infusion, in cancer immunotherapy-naïve patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) for whom prior platinum therapy has failed. The safety profile of the subcutaneous formulation was consistent with that of IV atezolizumab.

Administering atezolizumab subcutaneously reduces the treatment time to 3-8 minutes per injection, compared with 30-60 minutes for standard IV infusion.

Detailed findings of the IMscin001 study [will be shared] at an upcoming medical meeting and [submitted] for regulatory approval to health authorities globally, including the US Food and Drug Administration and European Medicines Agency."

https://www.globenewswire.com/news-release/2022/08/02/2489970/0/en/Roche-s-subcutaneous-formulation-of-Tecentriq-demonstrates-positive-Phase-III-results.html

RTP RESEARCH TO PRACTICE

FDA Approves Neoadjuvant Nivolumab and Platinum-Doublet Chemotherapy for Localized NSCLC

Press Release – March 4, 2022

"The Food and Drug Administration approved nivolumab with platinum-doublet chemotherapy for adult patients with resectable non-small cell lung cancer (NSCLC) in the neoadjuvant setting. This represents the first FDA approval for neoadjuvant therapy for early-stage NSCLC.

Efficacy was evaluated in CHECKMATE-816 (NCT02998528), a randomized, open label trial in patients with resectable, histologically confirmed Stage IB (≥4 cm), II, or IIIA NSCLC (AJCC/UICC staging criteria) and measurable disease (RECIST v1.1.). Patients were enrolled regardless of the tumor PD-L1 status. A total of 358 patients were randomized to receive either nivolumab plus platinum-doublet chemotherapy administered every 3 weeks for up to 3 cycles, or platinum-chemotherapy alone administered on the same schedule.

The main efficacy outcome measures were event-free survival (EFS) and pathologic complete response (pCR) by blinded independent central review. Median EFS was 31.6 months in the nivolumab plus chemotherapy arm and 20.8 months for those receiving chemotherapy alone. The hazard ratio was 0.63 (p=0.0052). The pCR rate was 24% in the nivolumab plus chemotherapy arm and 2.2% in the chemotherapy alone arm."

www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-neoadjuvant-nivolumab-and-platinum-doublet-chemotherapy-early-stage-non-small-cell-lung

RTP RESEARCH TO PRACTICE

The NEW ENGLAND JOURNAL of MEDICINE

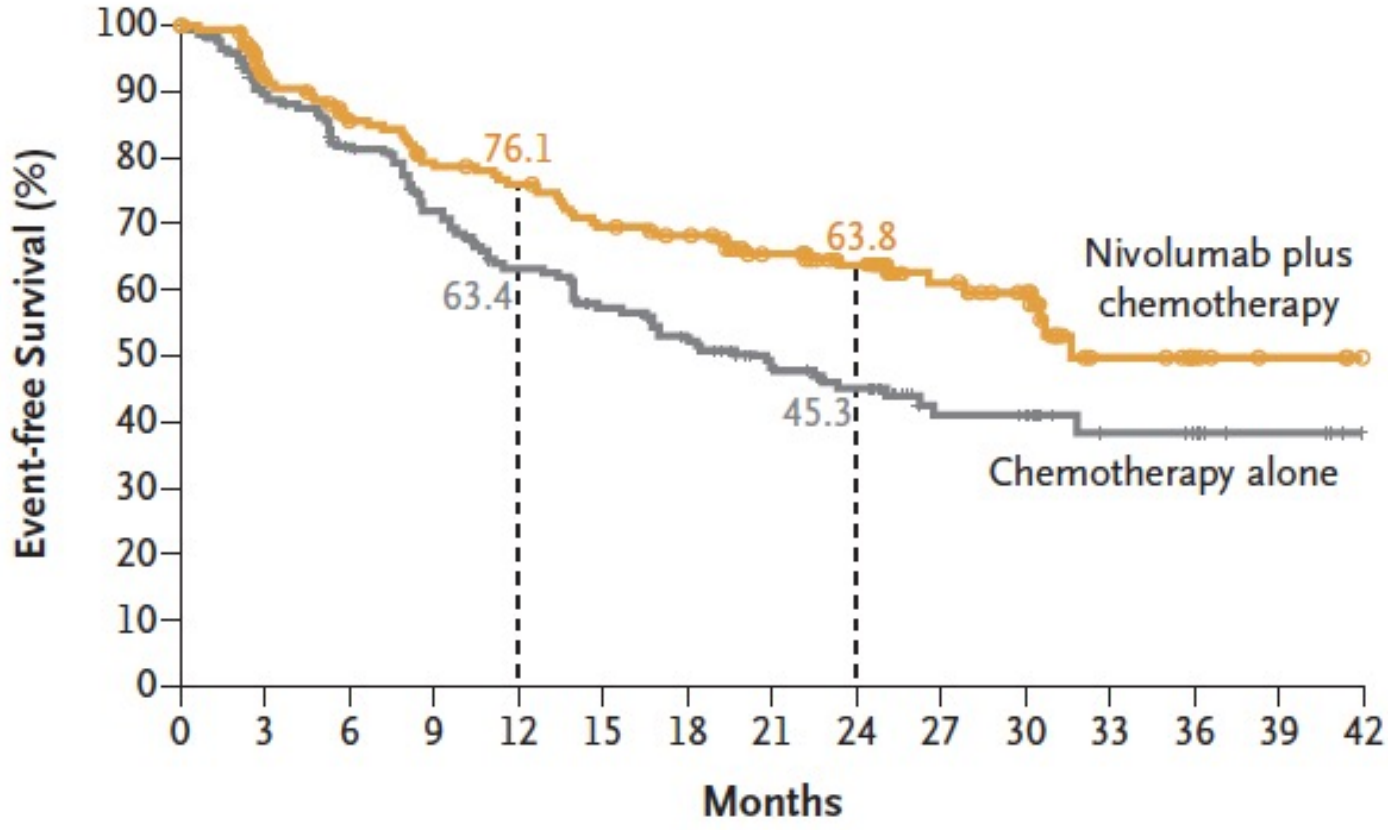
ORIGINAL ARTICLE

Neoadjuvant Nivolumab plus Chemotherapy in Resectable Lung Cancer

P.M. Forde, J. Spicer, S. Lu, M. Provencio, T. Mitsudomi, M.M. Awad, E. Felip, S.R. Broderick, J.R. Brahmer, S.J. Swanson, K. Kerr, C. Wang, T.-E. Ciuleanu, G.B. Saylors, F. Tanaka, H. Ito, K.-N. Chen, M. Liberman, E.E. Vokes, J.M. Taube, C. Dorange, J. Cai, J. Fiore, A. Jarkowski, D. Balli, M. Sausen, D. Pandya, C.Y. Calvet, and N. Girard, for the CheckMate 816 Investigators*

***N Engl J Med* 2022;386(21):1973-85.**

CheckMate 816 Coprimary Endpoint: Event-Free Survival

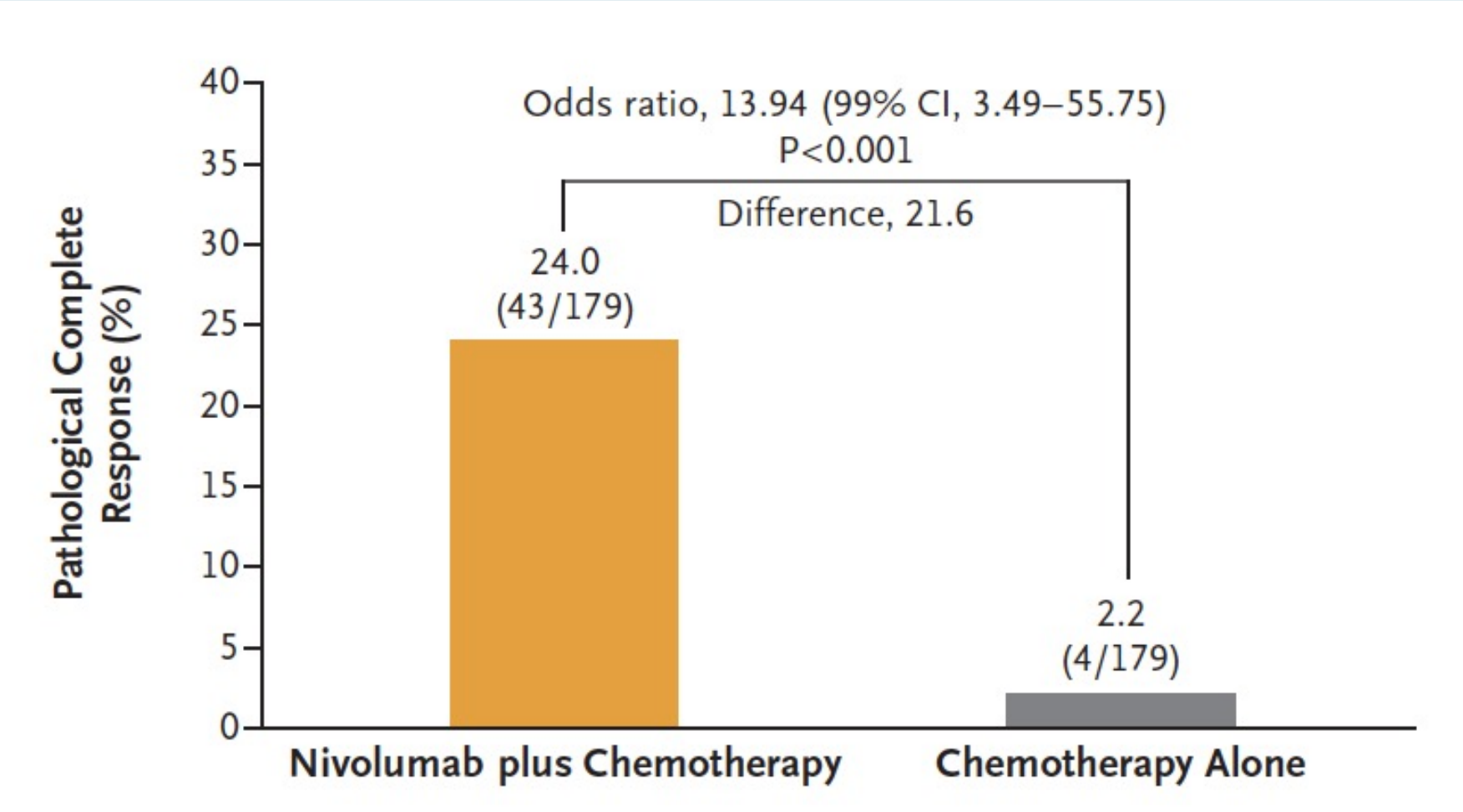


	No. of Patients	Median Event-free Survival (95% CI) *mo*
Nivolumab plus Chemotherapy	179	31.6 (30.2–NR)
Chemotherapy Alone	179	20.8 (14.0–26.7)

Hazard ratio for disease progression, disease recurrence, or death, 0.63 (97.38% CI, 0.43–0.91)
P=0.005

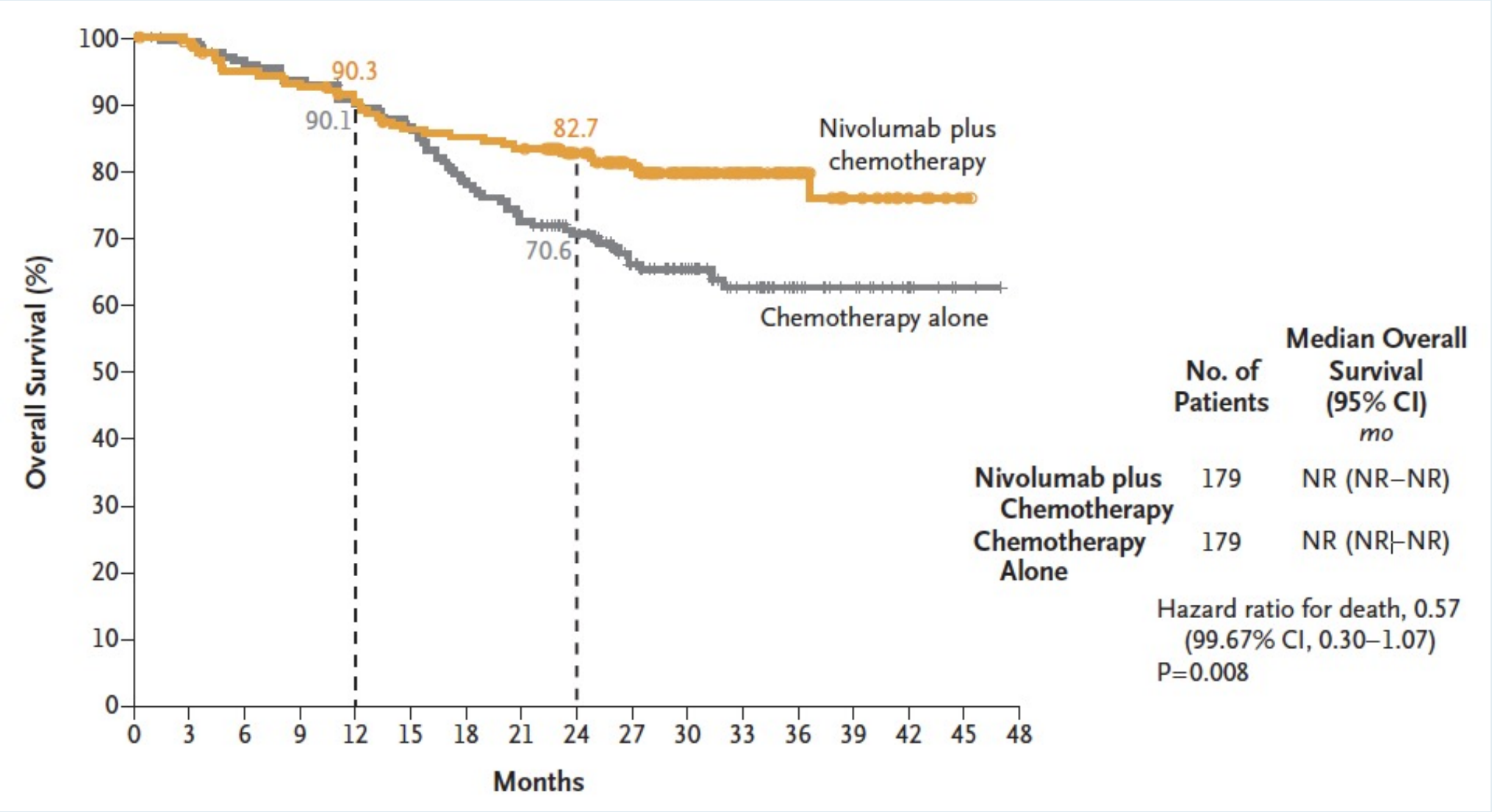
Forde PM et al. *N Engl J Med* 2022;386(21):1973-85.

CheckMate 816 Coprimary Endpoint: Pathologic Complete Response



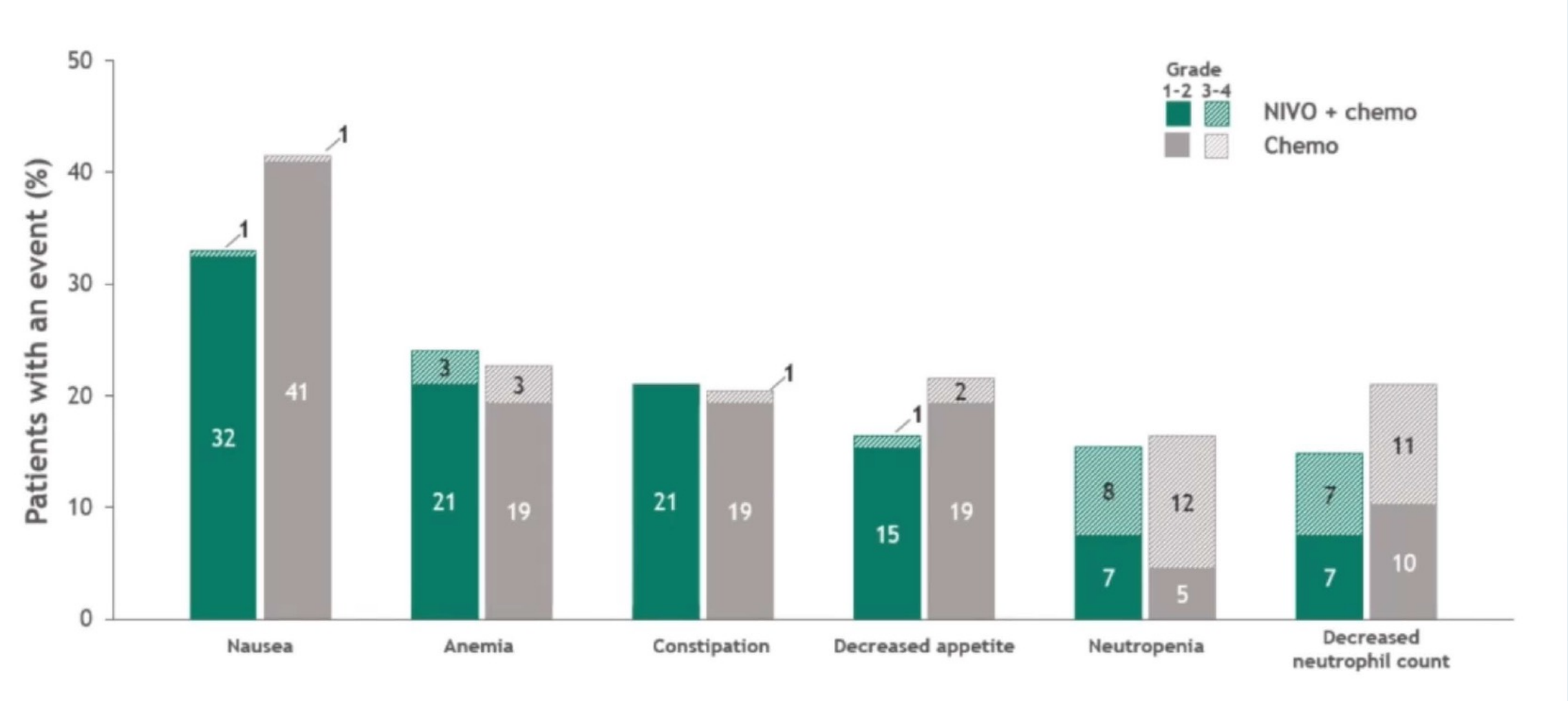
Forde PM et al. *N Engl J Med* 2022;386(21):1973-85.

CheckMate 816: Overall Survival



Forde PM et al. *N Engl J Med* 2022;386(21):1973-85.

CheckMate 816: Treatment-Related Adverse Events in ≥15% of Patients



Forde PM et al. AACR 2021;Abstract CT003.

RTP RESEARCH TO PRACTICE

Pembrolizumab Significantly Improves Disease-Free Survival versus Placebo as Adjuvant Therapy for Stage IB-IIIA NSCLC Regardless of PD-L1 Expression

Press Release – March 17, 2022

"Today results [were announced] from the pivotal Phase 3 KEYNOTE-091 trial, also known as EORTC-1416-LCG/ETOP-8-15 – PEARLS. The study found that adjuvant treatment with pembrolizumab significantly improved disease-free survival (DFS), one of the dual primary endpoints, reducing the risk of disease recurrence or death by 24% compared to placebo (hazard ratio [HR]=0.76; p=0.0014) in patients with stage IB (≥4 centimeters) to IIIA non-small cell lung cancer (NSCLC) following surgical resection regardless of PD-L1 expression. Median DFS was 53.6 months for pembrolizumab versus 42.0 months for placebo, an improvement of nearly one year. These data are being presented today during a European Society for Medical Oncology (ESMO) Virtual Plenary and will be shared with regulatory authorities worldwide.

'These are the first positive results for pembrolizumab in the adjuvant setting for non-small cell lung cancer, and represent the sixth positive pivotal study evaluating a pembrolizumab regimen in earlier stages of cancer,' said Dr Roy Baynes, senior vice president and head of global clinical development, chief medical officer, Merck Research Laboratories.

'Pembrolizumab has become foundational in the treatment of metastatic non-small cell lung cancer, and we are pleased to present these data showing the potential of pembrolizumab to help more patients with lung cancer in earlier stages of disease. We thank the patients, their caregivers and investigators for participating in this study.'"

https://finance.yahoo.com/news/merck-keytruda-pembrolizumab-significantly-improved-181500060.html

RTP RESEARCH TO PRACTICE

IMpower010: Overall Survival Interim Analysis of a Phase III Study of Atezolizumab vs Best Supportive Care in Resected NSCLC

Felip E et al.

IASLC 2022;Abstract PL03.09.

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 2022;40(12):1356-84.

RTP RESEARCH TO PRACTICE

original reports

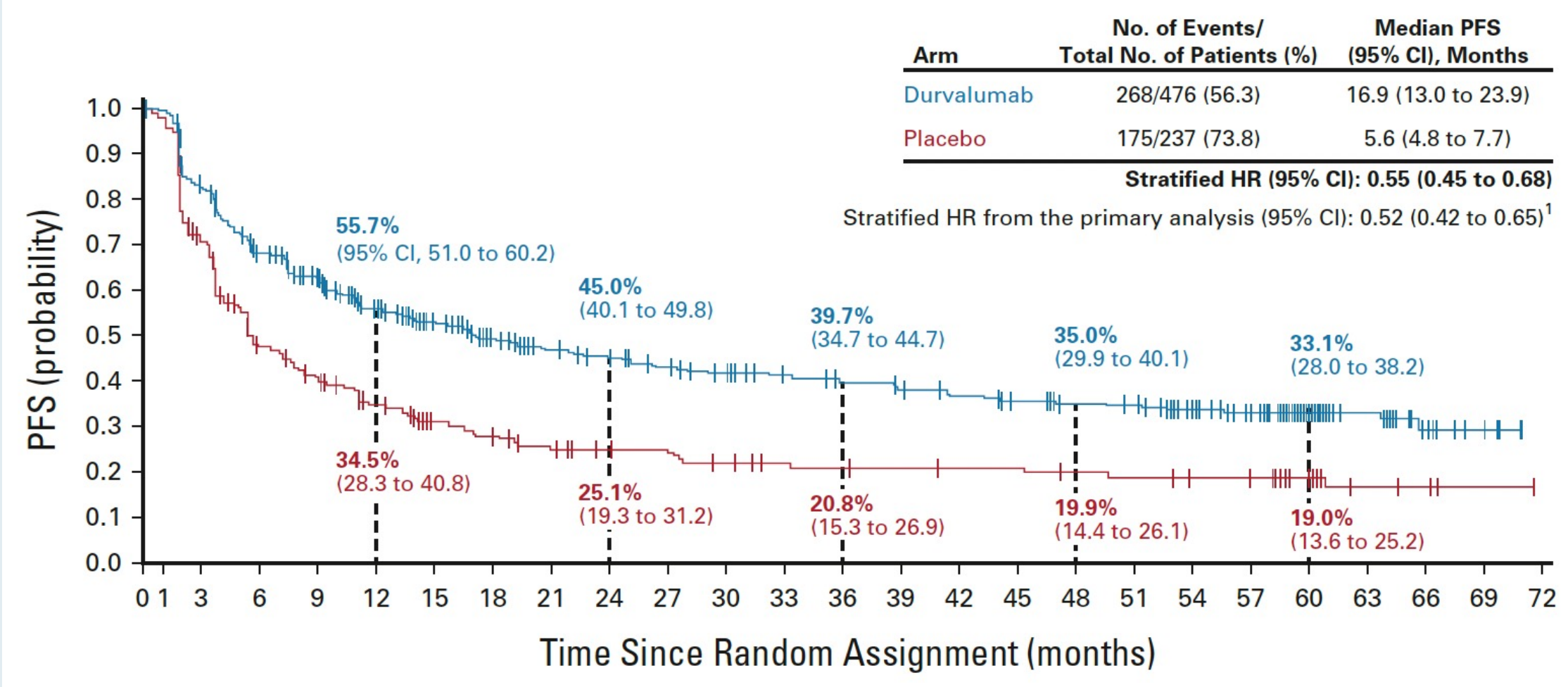
Five-Year Survival Outcomes From the PACIFIC Trial: Durvalumab After Chemoradiotherapy in Stage III Non–Small-Cell Lung Cancer

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;40(12):1301-11.

RTP RESEARCH TO PRACTICE

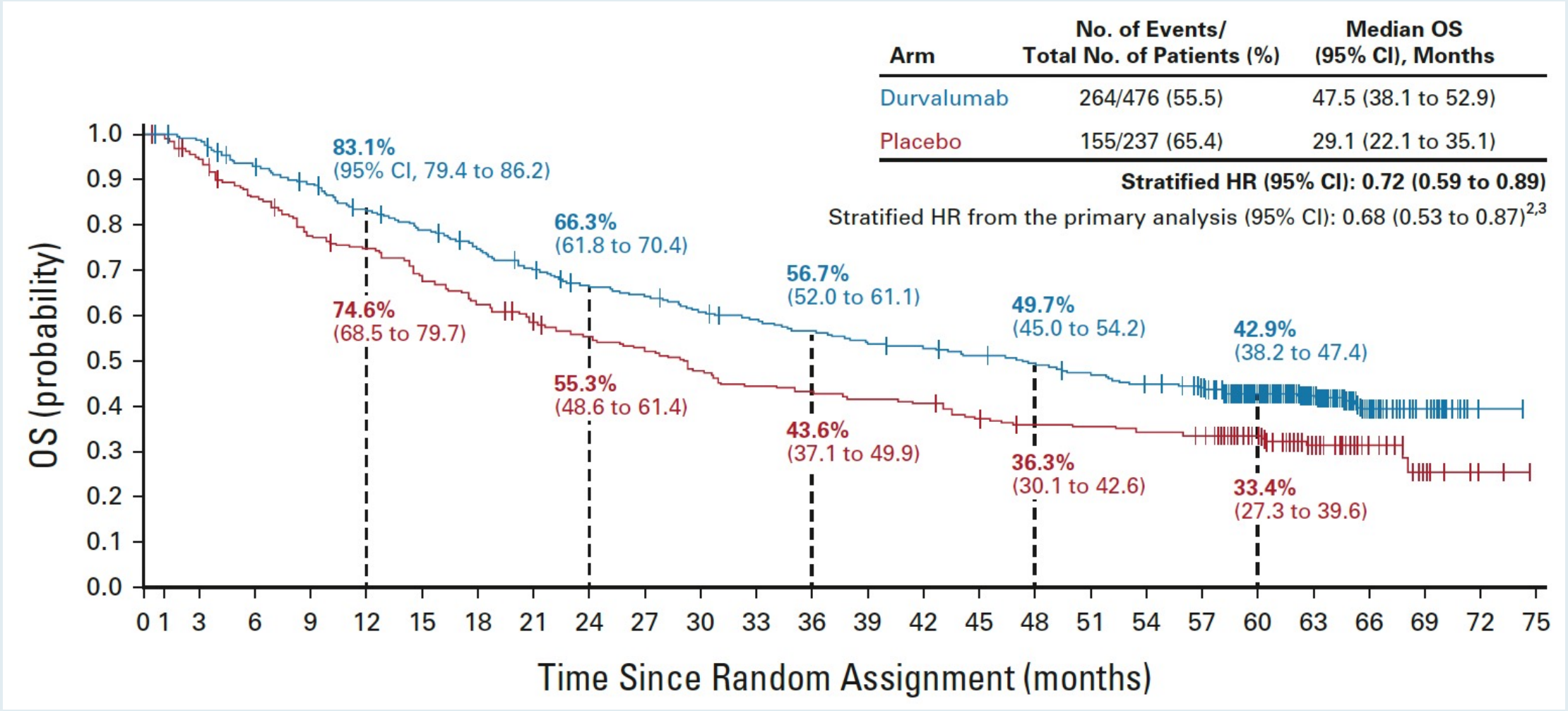
PACIFIC: Five-Year Progression-Free Survival (PFS) with Durvalumab After Chemoradiation Therapy for Stage III NSCLC



Spigel DR et al. *J Clin Oncol* 2022;40(12):1301-11.

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;40(12):1301-11.

editorials

Durvalumab Induces Sustained Survival Benefit After Concurrent Chemoradiotherapy in Stage III Non–Small-Cell Lung Cancer

Jean-Louis Pujol, MD, PhD[1]

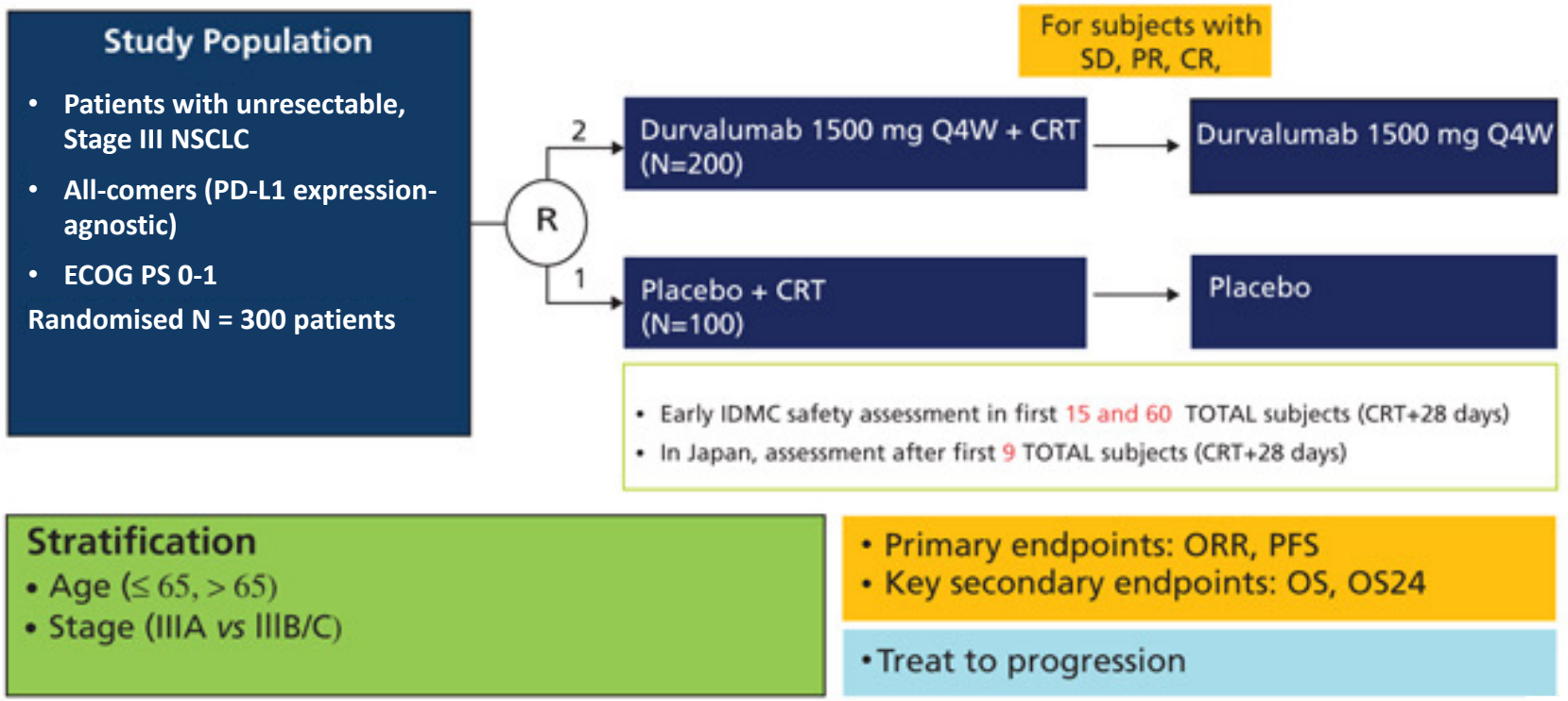
J Clin Oncol 2022;40(12):1271-74.

THE TAKEAWAY

In the article that accompanies this editorial by Spigel et al,[9] consolidation with durvalumab prolongs long-term survival of patients with unresectable stage III non–small-cell lung cancer whose disease has not progressed after concurrent chemotherapy and radiotherapy. This study provides a benchmark to which other regimens should be compared, and further studies determining the optimal duration of immune checkpoint inhibitor consolidation and investigating predictive biomarkers for immunotherapy response should be undertaken.

PACIFIC-2: An Ongoing Phase III Trial of Durvalumab with Chemoradiation Therapy for Patients with Unresectable NSCLC

Trial Identifier: NCT03519971



www.clinicaltrials.gov. Accessed August 2022.

RTP RESEARCH TO PRACTICE

original reports

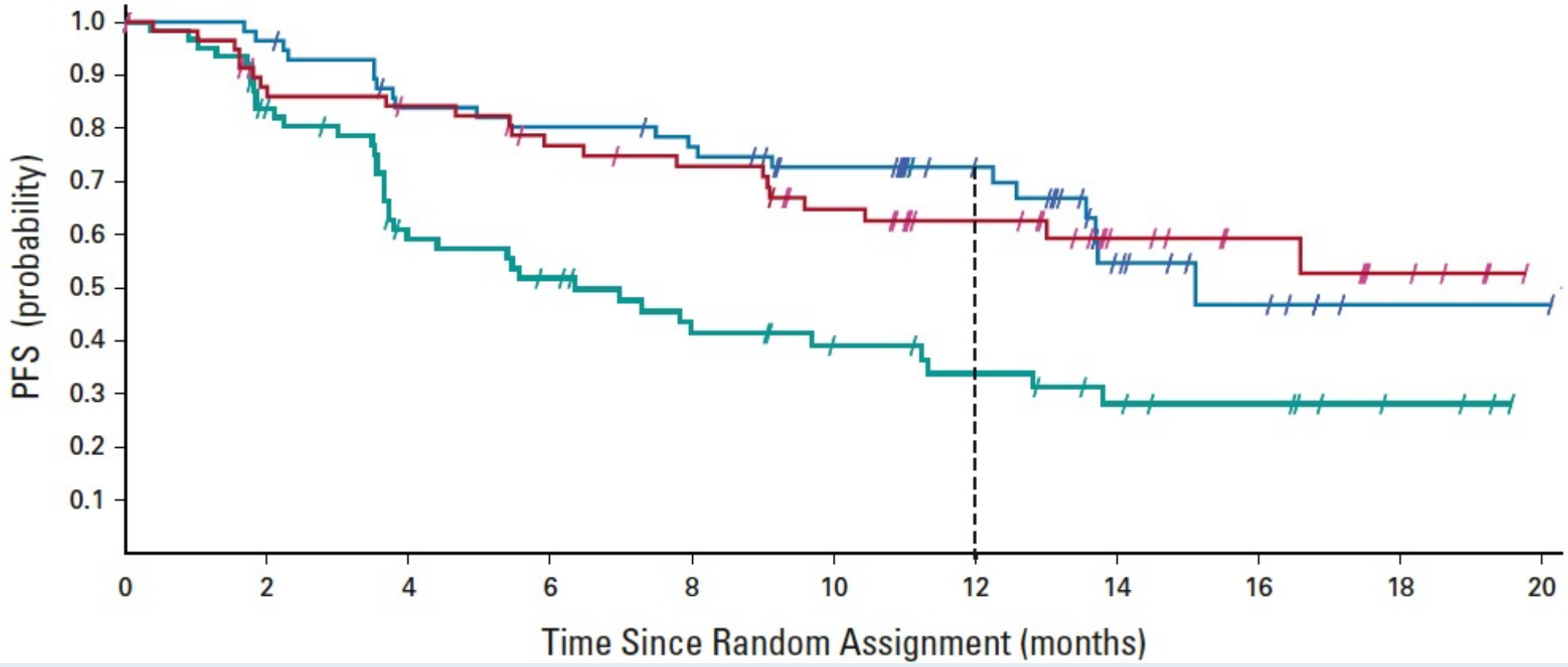
COAST: An Open-Label, Phase II, Multidrug Platform Study of Durvalumab Alone or in Combination With Oleclumab or Monalizumab in Patients With Unresectable, Stage III Non–Small-Cell Lung Cancer

Roy S. Herbst, MD, PhD[1]; Margarita Majem, MD, PhD[2]; Fabrice Barlesi, MD, PhD[3]; Enric Carcereny, MD[4]; Quincy Chu, MD[5]; Isabelle Monnet, MD, PhD[6]; Alfredo Sanchez-Hernandez, MD[7]; Shaker Dakhil, MD[8]; D. Ross Camidge, MD, PhD[9]; Leanne Winzer, MSc[10]; Yee Soo-Hoo, MPH[11]; Zachary A. Cooper, PhD[11]; Rakesh Kumar, MD, PhD[11]; John Bothos, PhD[11]; Charu Aggarwal, MD, MPH[12]; and Alex Martinez-Marti, MD[13]

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

COAST: Progression-Free Survival

Treatment Arm	No. of Events/ Total No. of Patients (%)	Median PFS, Months (95% CI)[a]	12-Month PFS Rate, % (95% CI)	HR, % (95% CI)[b,c]
Durvalumab + monalizumab	21/62 (33.9)	15.1 (13.6 to NE)	72.7 (58.8 to 82.6)	0.42 (0.24 to 0.72)
Durvalumab + oleclumab	22/60 (36.7)	NR (10.4 to NE)	62.6 (48.1 to 74.2)	0.44 (0.26 to 0.75)
Durvalumab	38/67 (56.7)	6.3 (3.7 to 11.2)	33.9 (21.2 to 47.1)	–



Herbst RS et al. *J Clin Oncol* 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

COAST: Antitumor Activity and Safety Summary

Antitumor Activity	Durvalumab (n = 67)	Durvalumab + Oleclumab (n = 60)	Durvalumab + Monalizumab (n = 62)
Confirmed ORR, % (95% CI)[a] (No.)	17.9 (9.6 to 29.2) (12)	30.0 (18.8 to 43.2) (18)	35.5 (23.7 to 48.7) (22)
Difference in confirmed ORR, % (95% CI)[b]	—	12.1 (–2.7 to 26.9)	16.7 (1.5 to 32.0)
Best overall response by RECIST,[c,d] No. (%)			
CR	2 (3.0)	1 (1.7)	3 (4.8)
PR	10 (14.9)	17 (28.3)	19 (30.6)
SD	37 (55.2)	32 (53.3)	31 (50.0)
PD	11 (16.4)	6 (10.0)	4 (6.5)
NE	7 (10.4)	4 (6.7)	4 (6.5)
DCR at 16 weeks, % (95% CI)[c,e] (No.)	55.2 (42.6 to 67.4) (37)	80.0 (67.7 to 89.2) (48)	77.4 (65.0 to 87.1) (48)
Median DoR, months (95% CI)[c] Range	NR (7.4 to NA) 1.9+ to 17.5+	NR (12.9 to NA) 1.8+ to 16.9+	NR (9.0 to NA) 1.9+ to 18.4+

Incidence	Durvalumab	Durvalumab + Oleclumab	Durvalumab + Monalizumab
Any TEAEs, No. (%)	65 (98.5)	57 (96.6)	61 (100)
Grade ≥ 3 TEAEs, No. (%)	26 (39.4)	24 (40.7)	17 (27.9)
Study drug-related AEs, No. (%)	49 (74.2)	46 (78.0)	50 (82.0)
Study drug-related SAEs, No. (%)	6 (9.1)	7 (11.9)	5 (8.2)
TEAEs leading to treatment discontinuation, No. (%)	11 (16.7)	9 (15.3)	9 (14.8)
Deaths[a,b], No. (%)	7 (10.6)	4 (6.8)	3 (4.9)

Herbst RS et al. *J Clin Oncol* 2022;[Online ahead of print].

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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. *Int J Radiat Oncol Biol Phys* 2021;111(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-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.

2022 ASCO® ANNUAL MEETING

Abstract 9000

FDA

Outcomes of anti-PD-(L)1 therapy with or without chemotherapy (chemo) for first-line (1L) treatment of advanced non-small cell lung cancer (NSCLC) with PD-L1 score ≥50%: FDA Pooled Analysis

Oladimeji Akinboro[1], Jonathon Vallejo[1], Erica Nakajima[1], Yi Ren[1], Pallavi Mishra-Kalyani[1], Erin Larkins[1], Paz Vellanki[1], Nicole Drezner[1], Mathieu Luckson[1], Shenghui Tang[1], Martha Donoghue[1,2], Richard Pazdur[1,2], Julia A. Beaver[1,2], Harpreet Singh[1,2]

[1]Center for Drug Evaluation and Research, U.S. Food and Drug Administration

[2]Oncology Center of Excellence, U.S. Food and Drug Administration

RTP RESEARCH TO PRACTICE

FDA-Approved Regimens for Advanced NSCLC Not Harboring Tumor Genomic Alterations

PD-L1 level	Regimen	Histology	Approval endpoint
≥ 50%	**Pembrolizumab**	NSCLC	**OS** & PFS
	Atezolizumab [a]	NSCLC	**OS**
	Cemiplimab	NSCLC	**OS** & PFS
≥ 1%	**Pembrolizumab**	NSCLC	**OS**
	Nivolumab + Ipilimumab	NSCLC	**OS**
None	**Pembrolizumab** + Platinum + Pemetrexed [b]	NSq-NSCLC	**OS** & PFS
	Pembrolizumab + Carboplatin + Paclitaxel	Sq-NSCLC	**OS** & PFS
	Atezolizumab + Bevacizumab + Carboplatin + Paclitaxel	NSq-NSCLC	**OS** & PFS
	Atezolizumab + Carboplatin + Nab-paclitaxel	NSq-NSCLC	**OS** & PFS
	Nivolumab + Ipilimumab + Platinum doublet	NSCLC	**OS**

Akinboro O et al. ASCO 2022;Abstract 9000.

Clinical Trials of First-Line Chemotherapy/Immuno-oncology (IO) and IO Regimens Included in FDA Pooled Analysis

Chemo-IO Trials		IO-only Trials	
Trial	Investigational Regimen	Trial	Investigational Regimen
KEYNOTE-021*	**Pembrolizumab** + Chemo**	CheckMate 026	**Nivolumab****
KEYNOTE-189	**Pembrolizumab** + Chemo**	KEYNOTE-024	**Pembrolizumab****
KEYNOTE-407	**Pembrolizumab** + Chemo**	KEYNOTE-042	**Pembrolizumab****
IMpower150	**Atezolizumab** + Bevacizumab + Chemo***	IMpower110	**Atezolizumab****
IMpower130	**Atezolizumab** + Chemo**	CheckMate 227	**Nivolumab** + **Ipilimumab****
CheckMate-9LA	**Nivolumab** + **Ipilimumab** + Chemo**	EMPOWER-Lung 1	**Cemiplimab****

Akinboro O et al. ASCO 2022;Abstract 9000.

FDA Pooled Analysis: Author Conclusions and Summary

- Our pooled analysis does not suggest a difference in OS for Chemo-IO vs IO-alone though there appears to be a slight numerical advantage favoring Chemo-IO
- Observed differences in PFS and ORR between Chemo-IO and IO-alone to be interpreted in the context of the OS findings and the exploratory nature of this analysis
- Older adults aged ≥75 years may have better OS and PFS outcomes with IO-only regimens
- These support shared decision-making in selecting a therapeutic approach

Akinboro O et al. ASCO 2022;Abstract 9000.

FDA Pooled Analysis: Limitations

- Retrospective exploratory pooled analyses
  - Results only hypothesis-generating
- Analyses do not explain the lack of concordance between OS and PFS/ORR results
  - Subsequent therapies in the IO-only arm
  - Deaths and treatment-discontinuation due to toxicity
- Potential heterogeneity across trials
  - Differences in PD-L1 assays
- Notable differences between clinical trial populations and real-world patients

Akinboro O et al. ASCO 2022;Abstract 9000.

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
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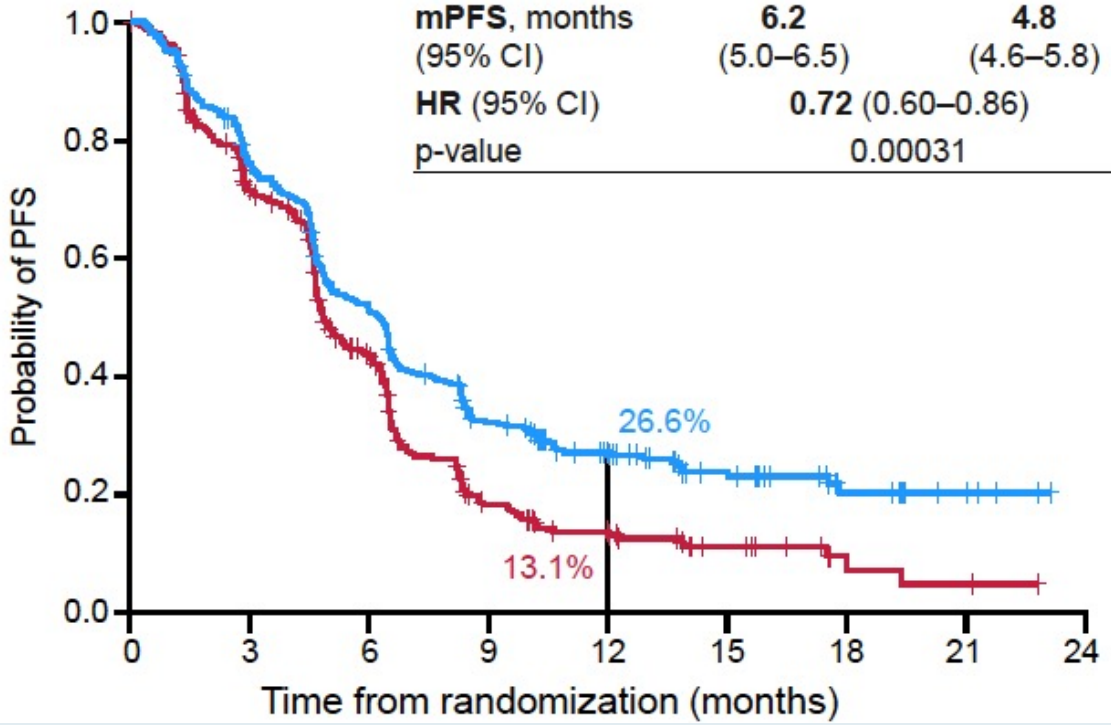
Abstract PL02.01

POSEIDON: First-Line Durvalumab with Tremelimumab and Chemotherapy for Advanced NSCLC

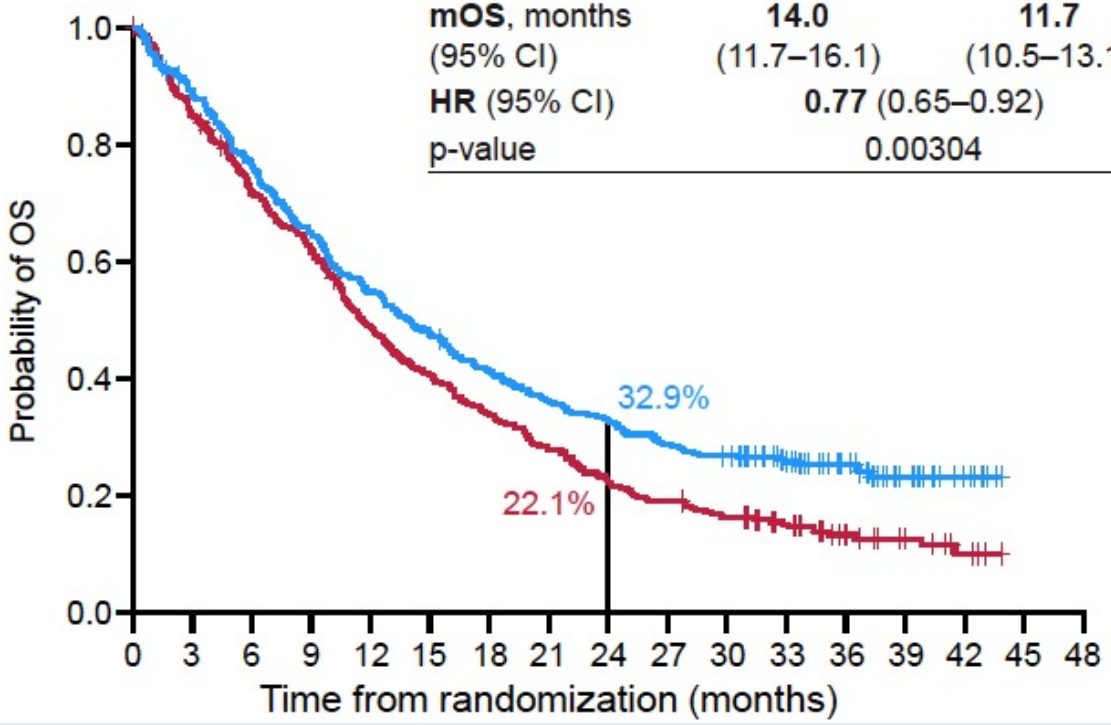
PFS

	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	



mPFS = median progression-free survival; mOS = median overall survival

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

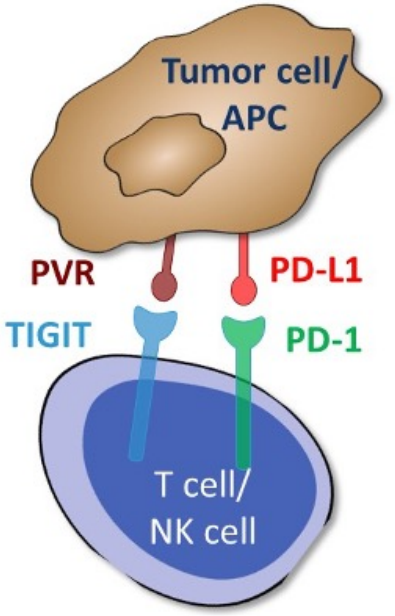


Figure adapted from Manieri et al. *Trends Immunology* 2017

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

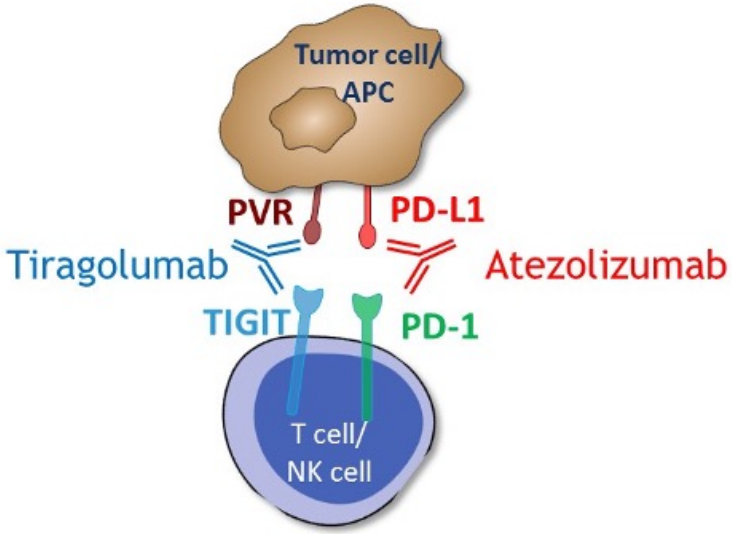
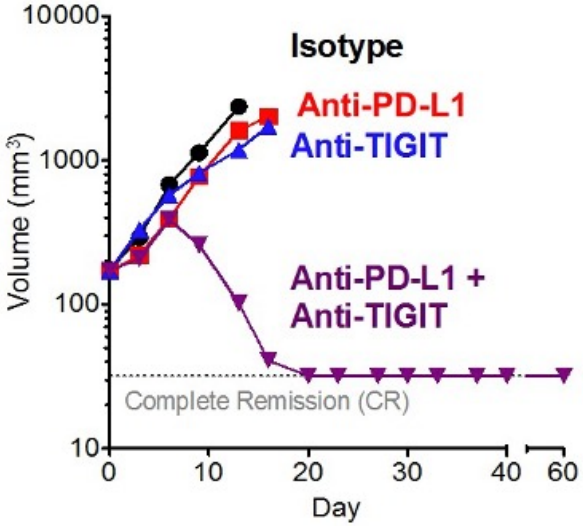


Figure adapted from Manieri et al. *Trends Immunology* 2017

- 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]

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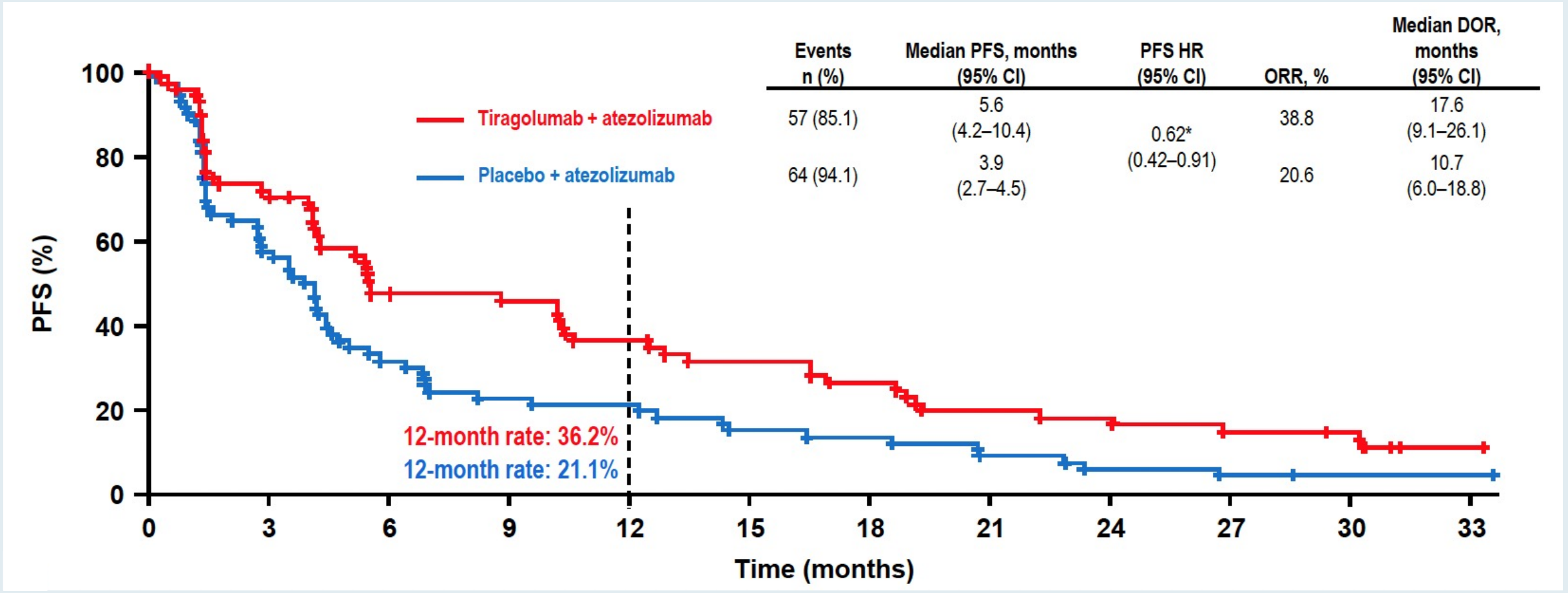
ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Abstract LBA2

CITYSCAPE: Investigator-Assessed PFS (ITT Population)



	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.

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

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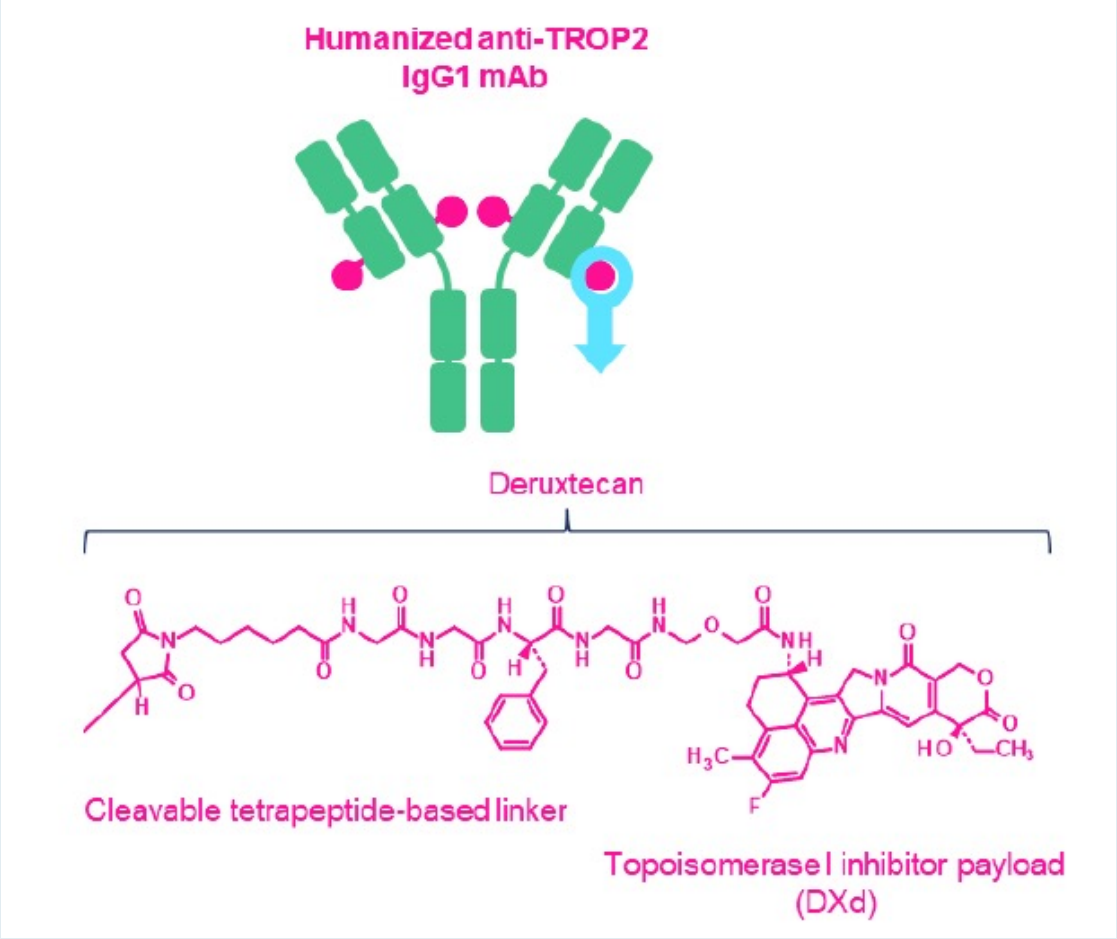
Abstract MA03.02

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.

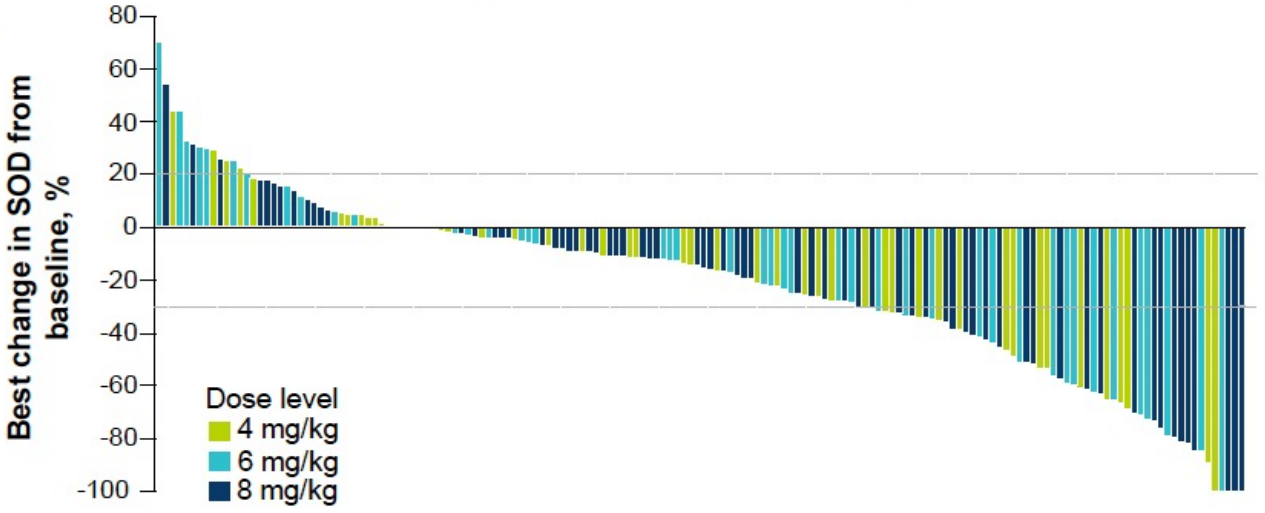
TROPION-PanTumor01: Antitumor Activity of Data-DXd

Best Overall Response (BICR)

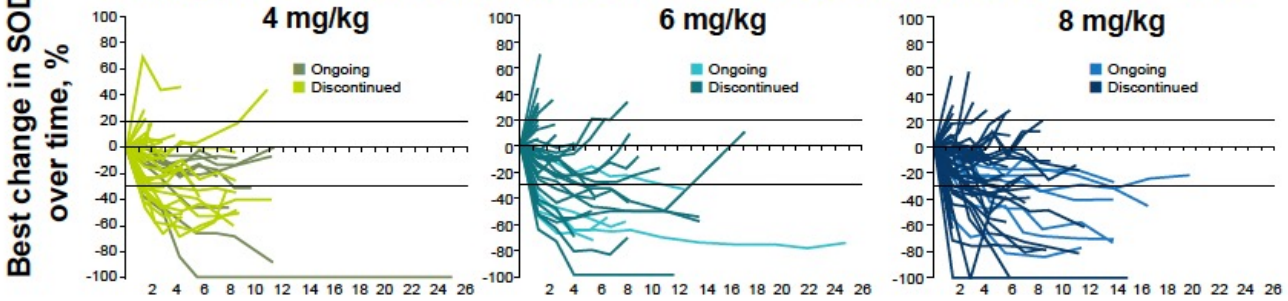
Patients[a]	Dato-DXd dose		
	4 mg/kg (n=50)	6 mg/kg (n=50)	8 mg/kg (n=80)
ORR, n (%)[b]	12 (24)	14 (28)	19 (24)
CR, n (%)	0	0	1 (1)
PR, n (%)[b]	12 (24)	14 (28)	18 (23)
SD, n (%)	25 (50)	20 (40)	42 (53)
Non-CR/PD, n (%)	1 (2)	2 (4)	2 (3)
PD, n (%)	7 (14)	10 (20)	8 (10)
NE, n (%)	5 (10)	5 (10)	9 (11)
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

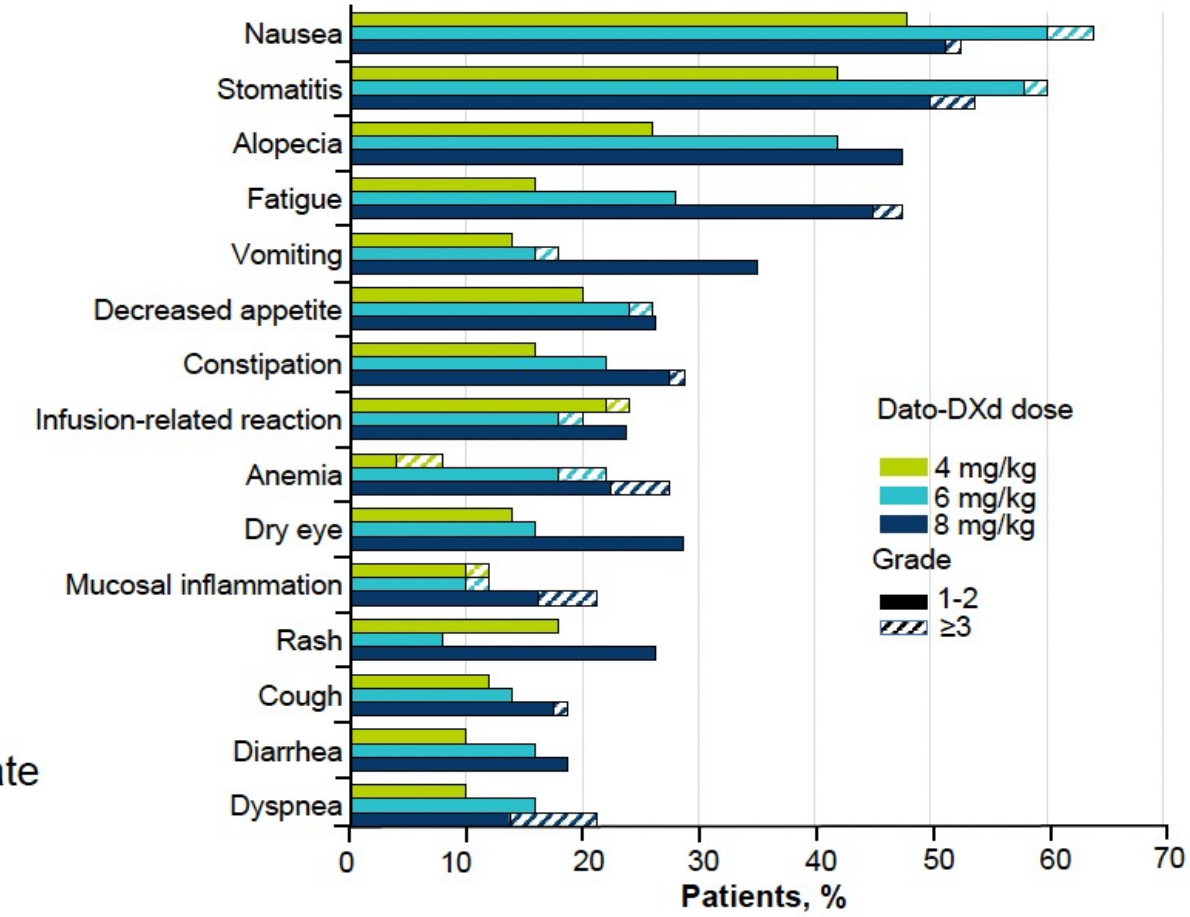
TROPION-PanTumor01: Safety and Treatment-Emergent Adverse Events

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

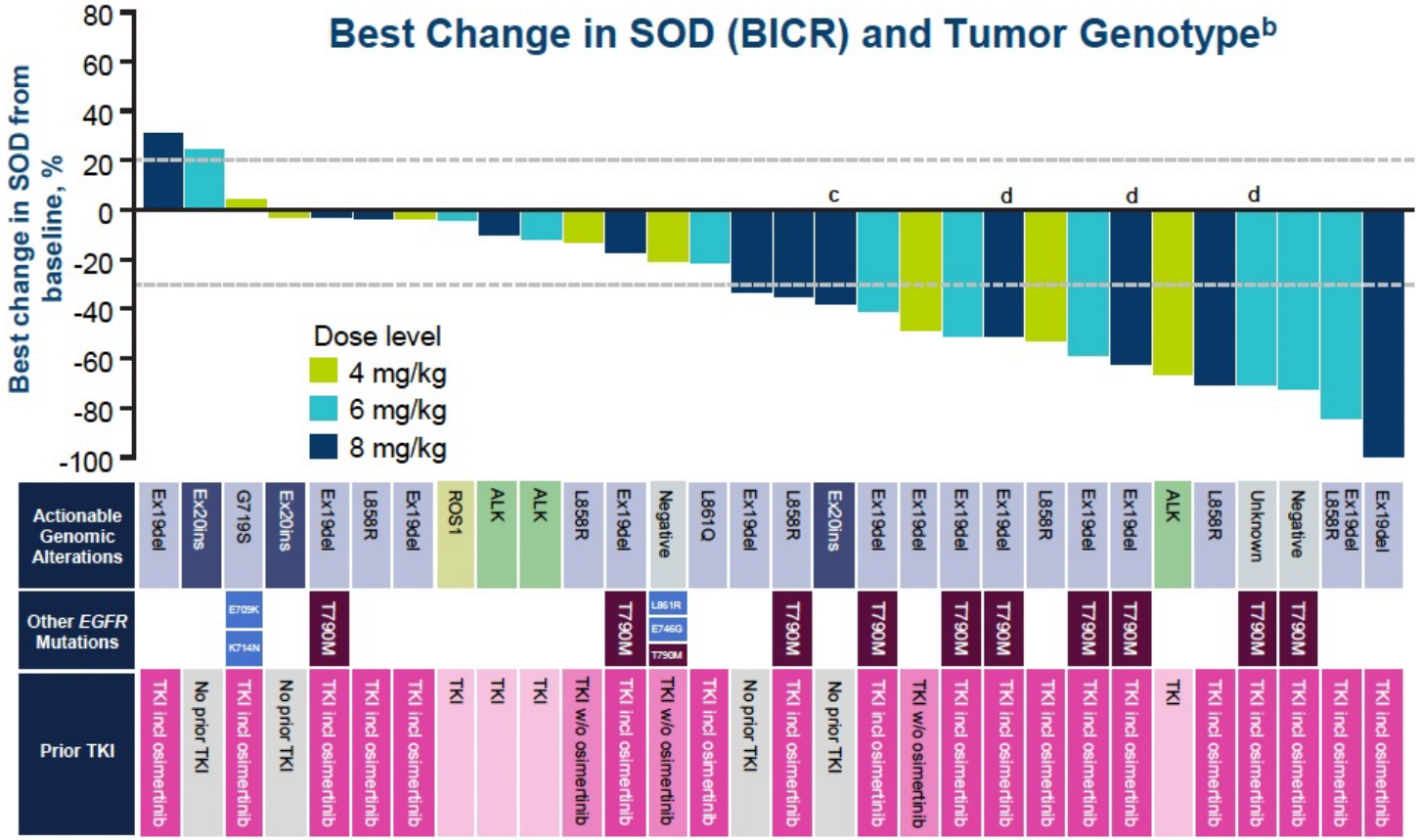
Best Overall Response (BICR)

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.

Lung Cancer Agenda

Module 1: Immunotherapy in Patients with Non-Small Cell Lung Cancer (NSCLC) without Targetable Mutations

Module 2: Targeted Treatment of NSCLC

Module 3: Small Cell Lung Cancer

Lung Cancer Agenda

Module 1: Immunotherapy in Patients with Non-Small Cell Lung Cancer (NSCLC) without Targetable Mutations

Module 2: Targeted Treatment of NSCLC

- **Generic Issues in Targeted Therapy**
  - Role of IOs in metastatic disease
  - Chemotherapy versus targeted treatment: First-line treatment of metastatic disease
  - Targeted treatment of brain metastases
  - Role of liquid biopsies; changes in biomarker status, resistance mutations
  - Adjuvant targeted therapy; postchemoradiaton therapy

Module 3: Small Cell Lung Cancer

Lung Cancer Agenda

Module 1: Immunotherapy in Patients with Non-Small Cell Lung Cancer (NSCLC) without Targetable Mutations

Module 2: Targeted Treatment of NSCLC

- **EGFR Mutations**
  - Optimal use of adjuvant osimertinib; patient selection and optimal incorporation into clinical practice; other adjuvant targeted options
  - Second-line treatment of metastatic disease
  - EGFR exon 20 insertion mutations

Module 3: Small Cell Lung Cancer

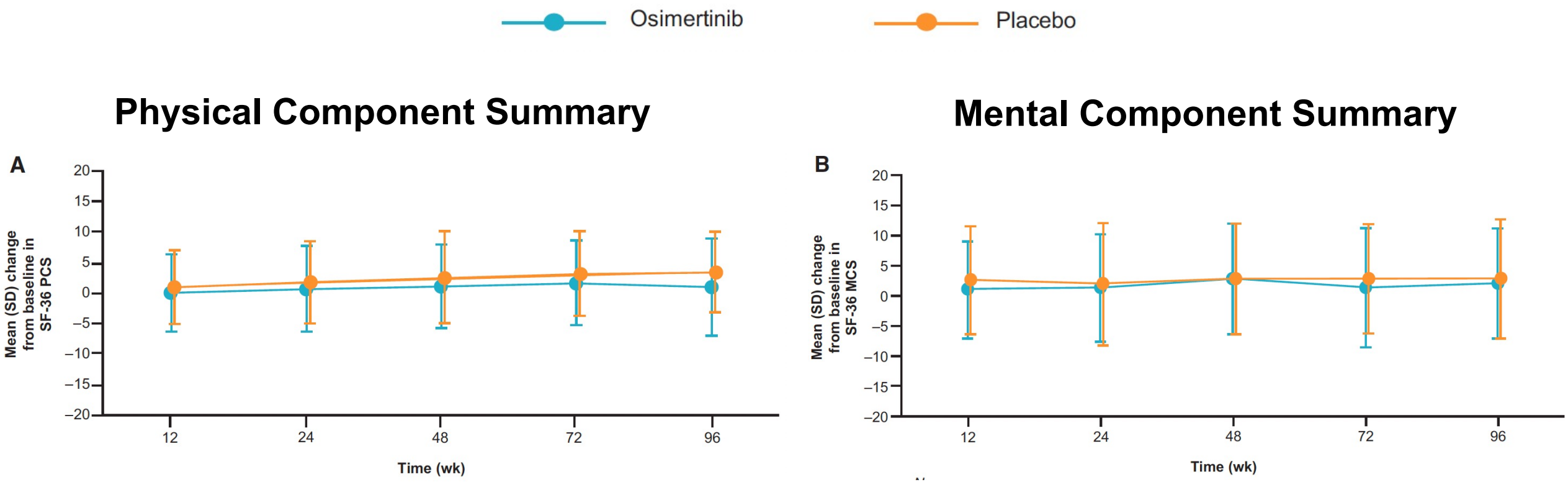
CLINICAL CANCER RESEARCH | CLINICAL TRIALS: TARGETED THERAPY

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

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]

Patritumab Deruxtecan: 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)

RDE = recommended dose for expansion; PBC = platinum-based chemotherapy; ORR = objective response rate; BOR = best overall response; CR = complete response; PR = partial response; SD = stable disease; PD = progressive disease; NE = not evaluated; DCR = disease control rate; TTR = time to response

[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) with Patritumab Deruxtecan

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]

ILD = interstitial lung disease

Jänne PA et al. *Cancer Discov* 2022;12(1):74-89.

RTP RESEARCH TO PRACTICE

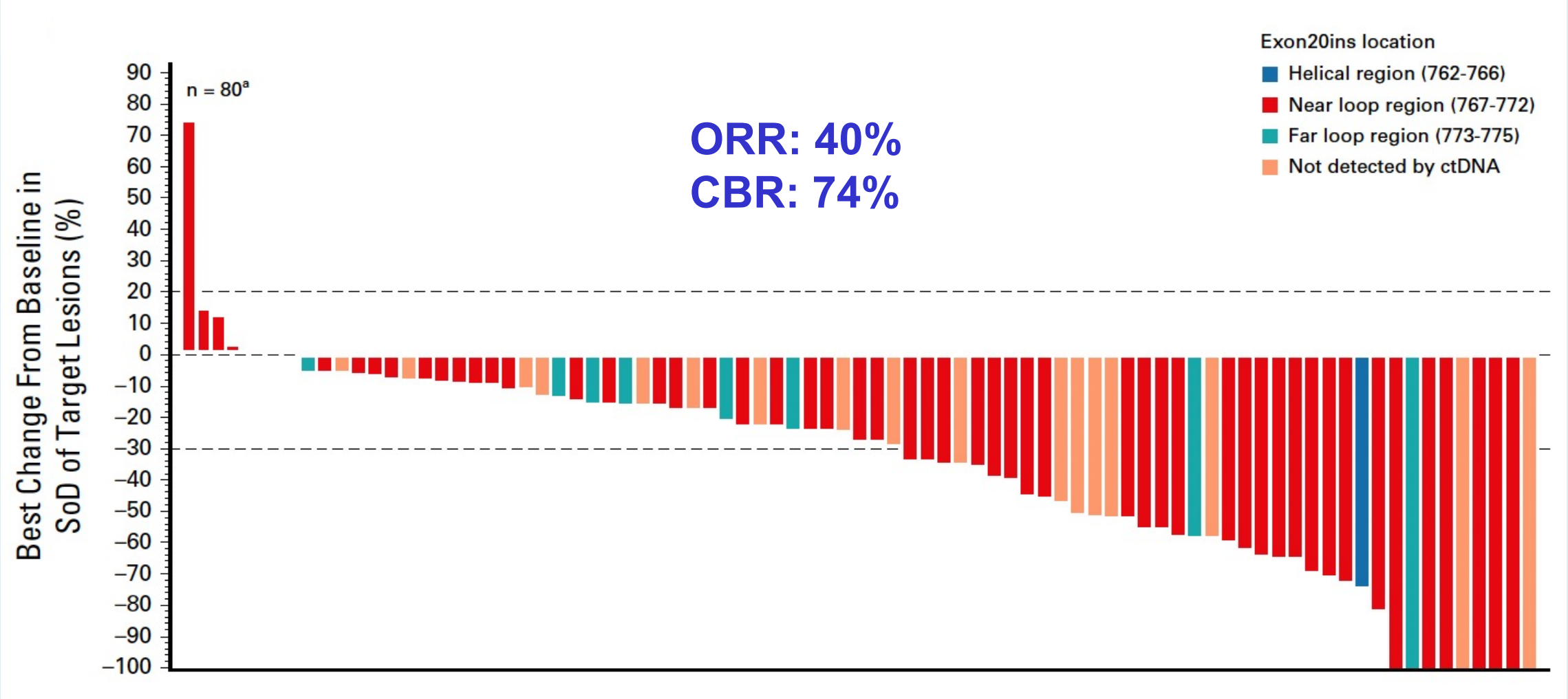
original reports

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

2022 ASCO® ANNUAL MEETING

Abstract 9006

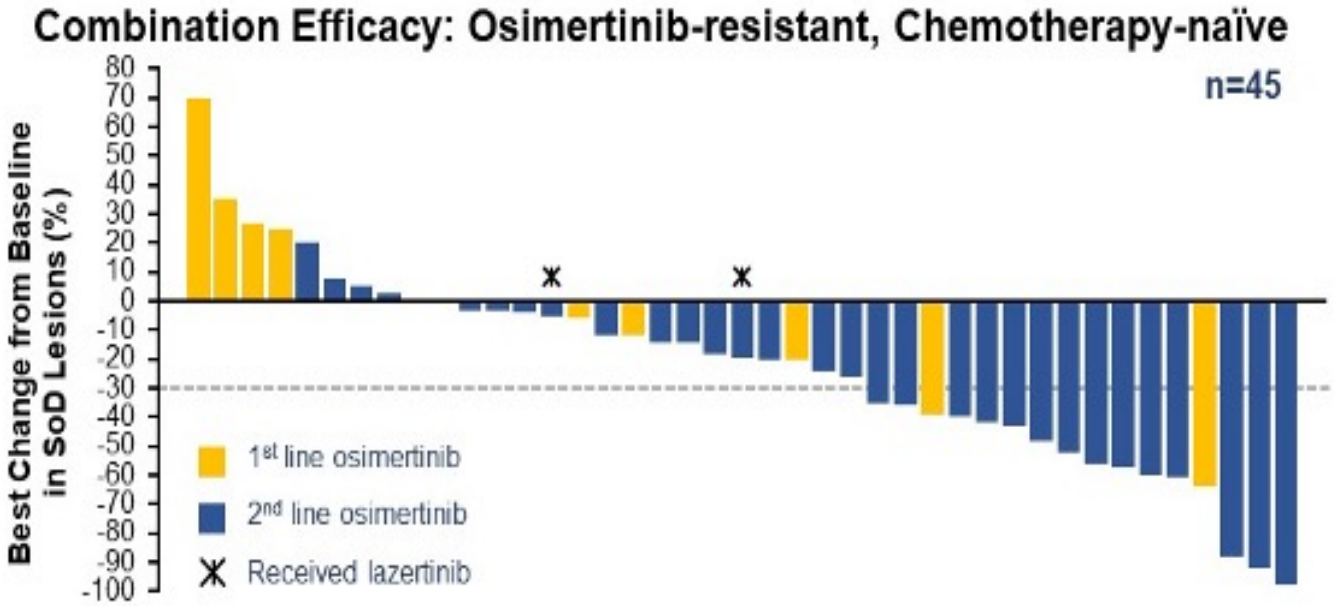
Amivantamab and lazertinib in patients with EGFR-mutant non-small cell lung cancer (NSCLC) after progression on osimertinib and platinum-based chemotherapy: Updated results from CHRYSALIS-2

Catherine A. Shu,[1] Koichi Goto,[2] Yuichiro Ohe,[3] Benjamin Besse,[4] Se-Hoon Lee,[5] Yongsheng Wang,[6] Frank Griesinger,[7] James Chih-Hsin Yang,[8] Enriqueta Felip,[9] Rachel E. Sanborn,[10] Reyes Bernabe Caro,[11] Joshua C. Curtin,[12] Jun Chen,[12] Janine Mahoney,[12] Leonardo Trani,[12] Joshua M. Bauml,[12] Meena Thayu,[12] Roland E. Knoblauch,[12] Byoung Chul Cho[13]

RTP RESEARCH TO PRACTICE

CHRYSALIS-2: Rationale for Combining Amivantamab and Lazertinib

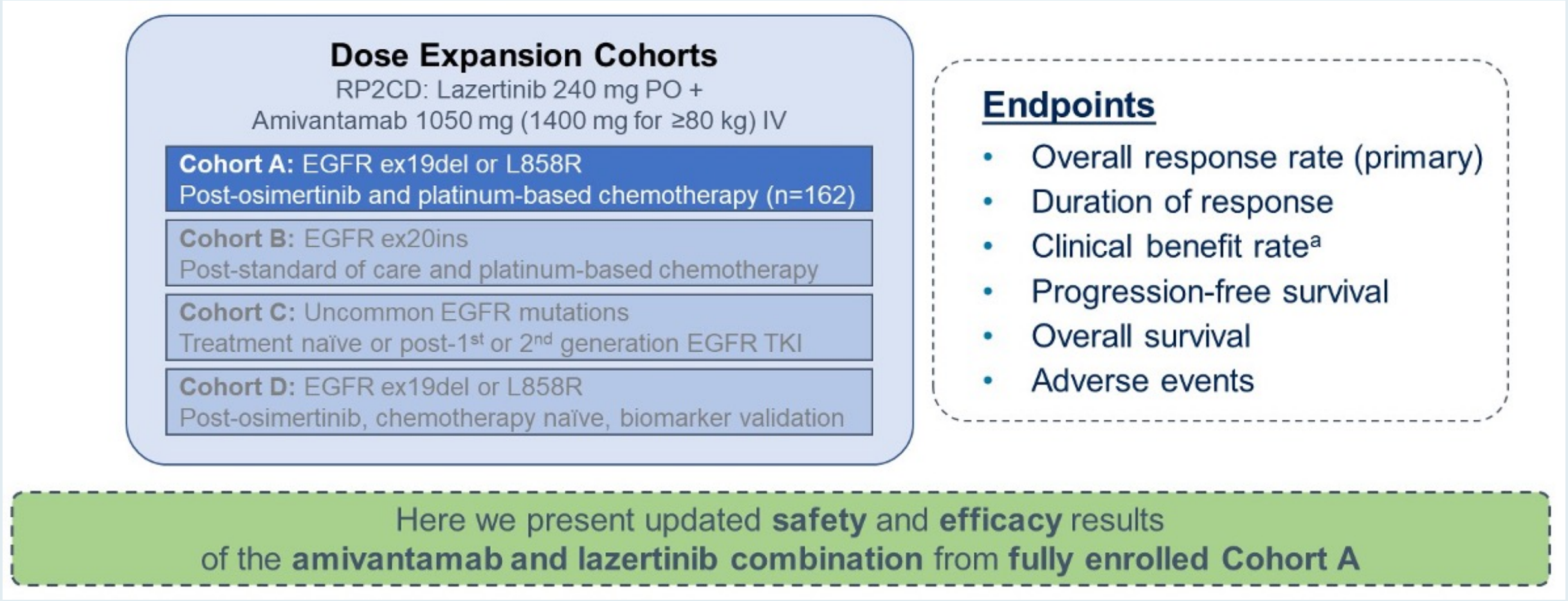
- Amivantamab[a] is an EGFR-MET bispecific antibody with immune cell-directing activity[1-3]
- Lazertinib is a highly selective, brain-penetrant, third-generation EGFR TKI with efficacy in activating EGFR mutations, T790M, and CNS disease[4,5]
- Preclinical studies demonstrate improved antitumor activity when both extracellular and catalytic EGFR domains are simultaneously targeted
- Among 45 patients who progressed on osimertinib but were chemotherapy naïve, the overall response rate was 36% and median DOR was 9.6 months without biomarker selection[6,7]
- This analysis explores the combination in patients with EGFRm NSCLC who have failed all standard of care (osimertinib and platinum-based chemotherapy)



Shu CA et al. ASCO 2022;Abstract 9006.

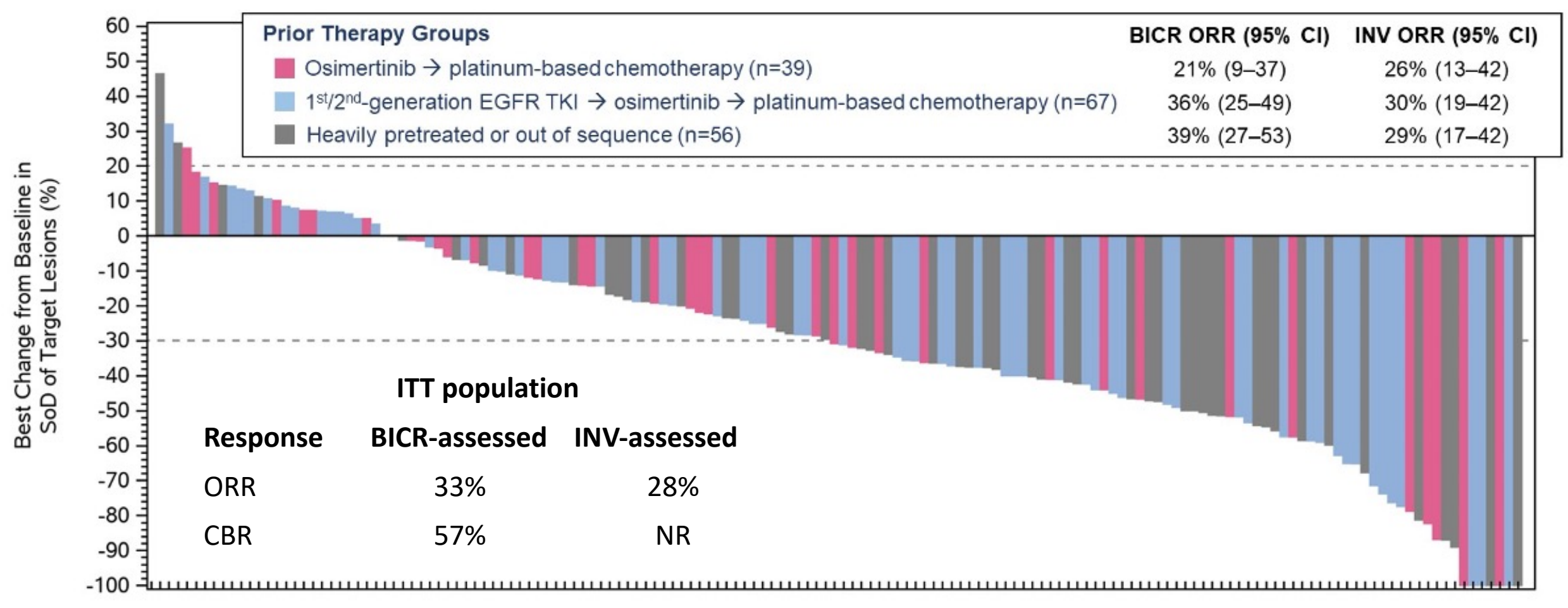
RTP RESEARCH TO PRACTICE

CHRYSALIS-2: Study Design



Shu CA et al. ASCO 2022;Abstract 9006.

CHRYSALIS-2: Best Antitumor Response and ORR by Prior Therapy



ORR = overall response rate; BICR = blinded independent central review; INV = investigator; CBR = clinical benefit rate

Shu CA et al. ASCO 2022;Abstract 9006.

RTP RESEARCH TO PRACTICE

CHRYSALIS-2: Adverse Events

TEAEs (≥15%) by Preferred Term, n (%)	n=162	
	All grade	Grade ≥3
EGFR-related		
Rash	71 (44)	4 (2)
Dermatitis acneiform	55 (34)	8 (5)
Paronychia	84 (52)	6 (4)
Stomatitis	63 (39)	2 (1)
Diarrhea	36 (22)	1 (1)
Pruritus	30 (19)	1 (1)
MET-related		
Hypoalbuminemia	70 (43)	11 (7)
Peripheral edema	43 (27)	2 (1)
Other		
Infusion related reaction	108 (67)	13 (8)
Increased ALT	46 (28)	5 (3)
Nausea	40 (25)	3 (2)
Decreased appetite	39 (24)	1 (1)
Constipation	38 (23)	0
Asthenia	37 (23)	7 (4)
Dry skin	37 (23)	0
Vomiting	36 (22)	1 (1)
Increased AST	35 (22)	3 (2)
Dyspnea	33 (20)	13 (8)
Thrombocytopenia	33 (20)	2 (1)
Fatigue	32 (20)	4 (2)
Headache	29 (18)	2 (1)
Anemia	27 (17)	4 (2)
Hypocalcemia	26 (16)	1 (1)

- Individual AEs were mostly grade 1-2
- Dose interruptions, reductions, and discontinuations of both amivantamab and lazertinib due to toxicity were seen in 57 (35%), 15 (9%), and 12 (7%) patients, respectively
- Pneumonitis/ILD was seen in 11 (7%) patients, of which 6 (4%) were grade ≥3 (no grade 5)
- Cumulative grouped rash-related AEs[a] occurred in 129 (80%) patients, with 17 grade ≥3 (10%)
- Safety profile consistent with what was previously reported; no new safety signals identified

Shu CA et al. ASCO 2022;Abstract 9006.

FDA Grants Breakthrough Therapy Status to CLN-081 for Locally Advanced or Metastatic NSCLC with EGFR Exon 20 Mutation

Press Release – January 4, 2022

"CLN-081, an orally available, irreversible epidermal growth factor receptor (EGFR) inhibitor, today received a Breakthrough Therapy Designation from the FDA for the treatment of locally advanced or metastatic NSCLC in patients harboring EGFR exon 20 insertion mutations and who have previously received platinum-based systemic chemotherapy.

CLN-081 functions by selectively targeting cells expressing EGFR exon 20 insertion mutations while sparing cells expressing wild type EGFR, according to a company statement. A phase 1/2 trial is underway to evaluate various doses in patients whose NSCLC has progressed on or after prior therapy.

The designation, which serves to expedite the development and review of drugs intended to treat a serious condition, is based off updated phase 1/2a data that showed CLN-081 led to a high response rate and durable response among heavily pretreated patients.

That data, which were released in December 2021, revealed that of the 36 patients enrolled in the 100-mg BID cohort 14 achieved a confirmed PR for a 39% confirmed response rate, with a median duration of response of greater than 15 months. In the initial cohort of phase 1 patients (n = 13), median progression-free survival was 12 months. When it comes to safety and tolerability, both diarrhea and rash have been limited to grade 1 and 2 events."

https://www.ajmc.com/view/cln-081-receives-breakthrough-therapy-designation-for-nsclc

RTP RESEARCH TO PRACTICE

PRO-CTCAE Analysis of Mobocertinib in EGFR Exon 20 Insertion–Positive Metastatic Non–Small Cell Lung Cancer (NSCLC)

Garcia R et al.

IASLC 2022;Abstract EP08.02-171.

Lung Cancer Agenda

Module 1: Immunotherapy in Patients with Non-Small Cell Lung Cancer (NSCLC) without Targetable Mutations

Module 2: Targeted Treatment of NSCLC

- **ALK Rearrangement**
  - First- and second-line therapy: Choice of agent, clinical management

Module 3: 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	ORR	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%

PFS = progression-free survival; ORR = overall response rate

Xia B et al. *Transl Lung Cancer Res* 2020;9(6):2521-34.

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.

Lung Cancer Agenda

Module 1: Immunotherapy in Patients with Non-Small Cell Lung Cancer (NSCLC) without Targetable Mutations

Module 2: Targeted Treatment of NSCLC

- **NSCLC with Other Targetable Mutations**
  - Trastuzumab deruxtecan (T-DXd) in HER2-mutant NSCLC
  - Published findings with and current clinical role of capmatinib and tepotinib in patients with MET exon 14 mutation-positive NSCLC
  - Reported clinical activity and safety data with dabrafenib and trametinib in patients with metastatic NSCLC with a BRAF V600E mutation
  - RET fusions: First-line therapy for metastatic disease, choice of agent
  - KRAS G12C: First-line therapy for metastatic disease, choice of agent

Module 3: Small Cell Lung Cancer

N Engl J Med 2022;386:241-51.

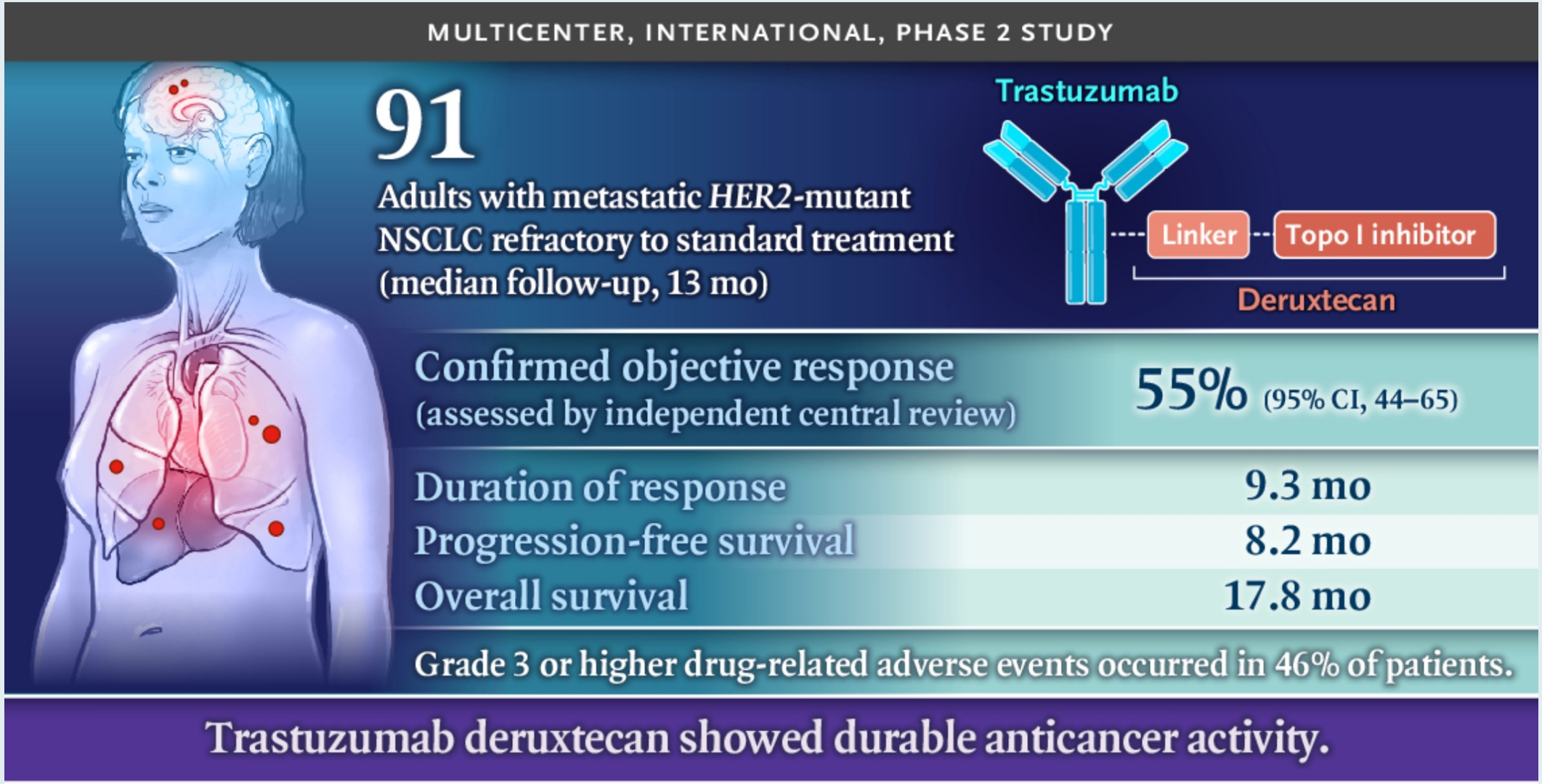
The NEW ENGLAND JOURNAL of MEDICINE

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.

Open-Label, Randomized, Multicenter, Phase 3 Study Evaluating Trastuzumab Deruxtecan (T-DXd) as First-Line Treatment in Patients with Unresectable, Locally Advanced, or Metastatic Non–Small Cell Lung Cancer (NSCLC) Harboring HER2 Exon 19 or 20 Mutations (DESTINY-Lung04)

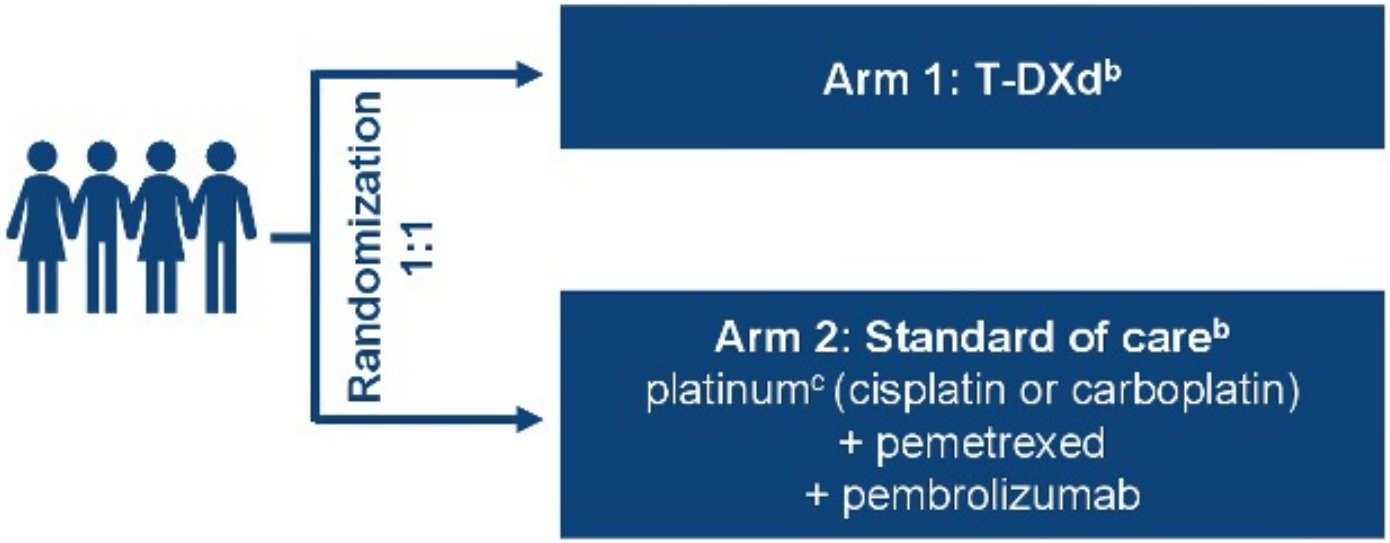
Li BT et al.

ASCO 2022;Abstract TPS9137.

DESTINY-Lung04 Phase III Study Design

Patient population (N≈264)

- Unresectable, locally advanced (not amenable to curative therapy), or metastatic nonsquamous NSCLC with *HER2* exon 19 or 20 mutations[a]
- Naive to systemic therapy in the locally advanced or metastatic setting
- No known other targetable oncogenic mutations/alterations



[a] *HER2* mutations may be detected in tissue or ctDNA.
[b] Crossover is not permitted.
[c] Investigator's choice of cisplatin or carboplatin.

Primary Endpoint: PFS by BICR

Li BT et al. ASCO 2022;Abstract TPS9137.

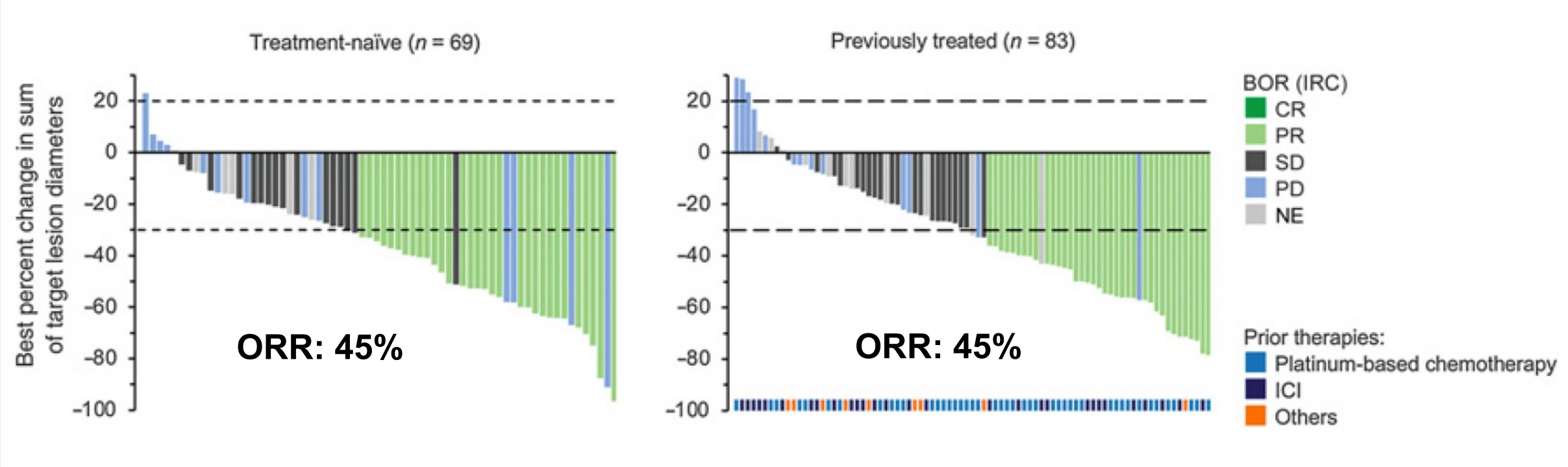
CLINICAL CANCER RESEARCH | CLINICAL TRIALS: TARGETED THERAPY

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* 2022;28(6):1117-26.**

VISION: Tepotinib for Advanced NSCLC with a MET Exon 14 Skipping Mutation



ORR = objective response rate

Le X et al. *Clin Cancer Res* 2022;28(6):1117-26.

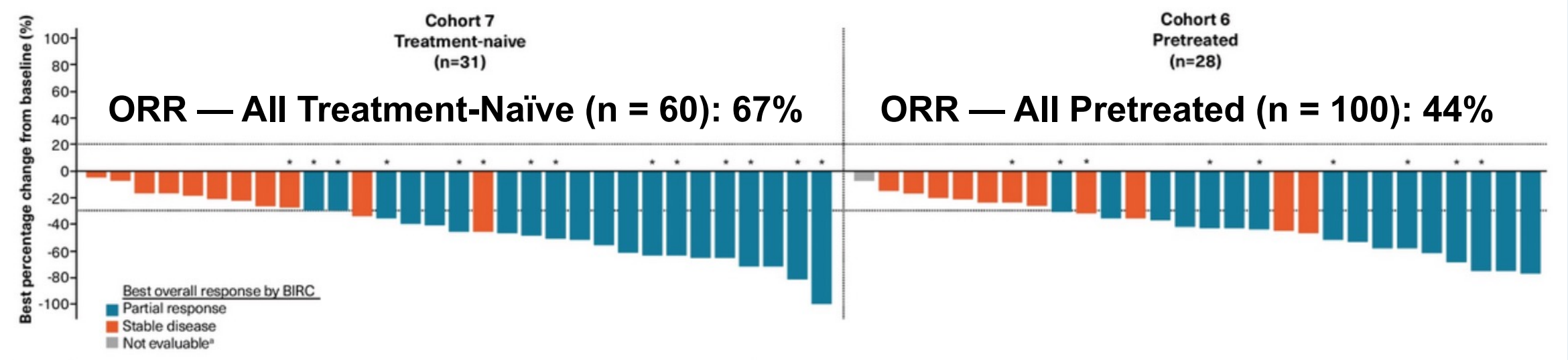
RTP RESEARCH TO PRACTICE

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

J Thorac Oncol 2022;17(1):103-15.

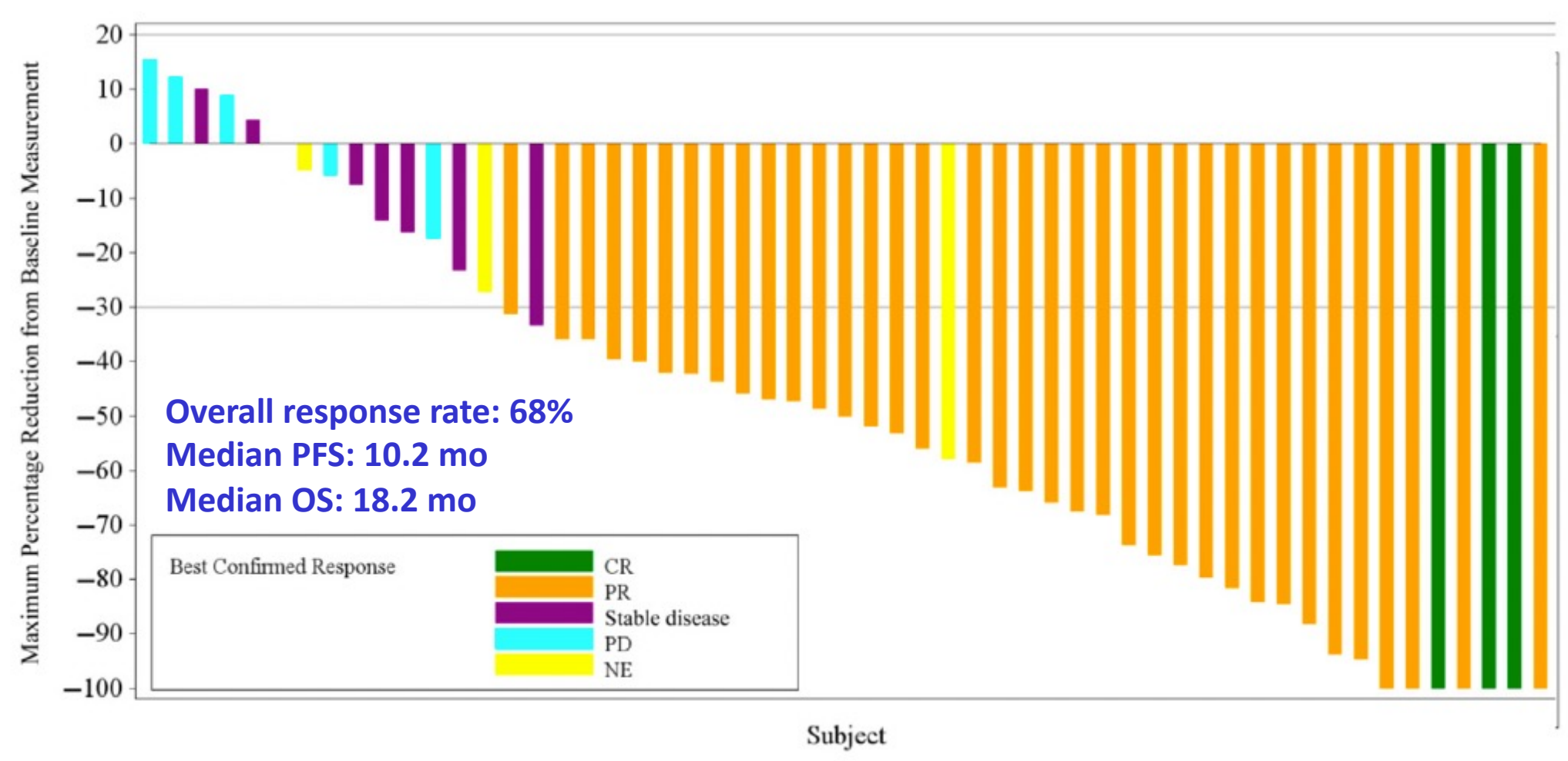
ORIGINAL ARTICLE

Phase 2 Study of Dabrafenib Plus Trametinib in Patients With *BRAF* V600E-Mutant Metastatic NSCLC: Updated 5-Year Survival Rates and Genomic Analysis

David Planchard, MD,[a] Benjamin Besse, MD,[a] Harry J. M. Groen, MD,[b] Sayed M. S. Hashemi, MD,[c] Julien Mazieres, MD,[d] Tae Min Kim, MD, PhD,[e] Elisabeth Quoix, MD, PhD,[f] Pierre-Jean Souquet, MD,[g] Fabrice Barlesi, MD, PhD,[a,h] Christina Baik, MD, MPH,[i] Liza C. Villaruz, MD,[j] Ronan J. Kelly, MD,[k] Shirong Zhang, PhD,[l] Monique Tan, MD,[l] Eduard Gasal, MD,[l] Libero Santarpia, MD, PhD,[m] Bruce E. Johnson, MD[n,*]

Five-Year Update — Phase II Study of Dabrafenib/Trametinib for Metastatic NSCLC with a BRAF V600E Mutation

Previously Treated Disease (N = 57)

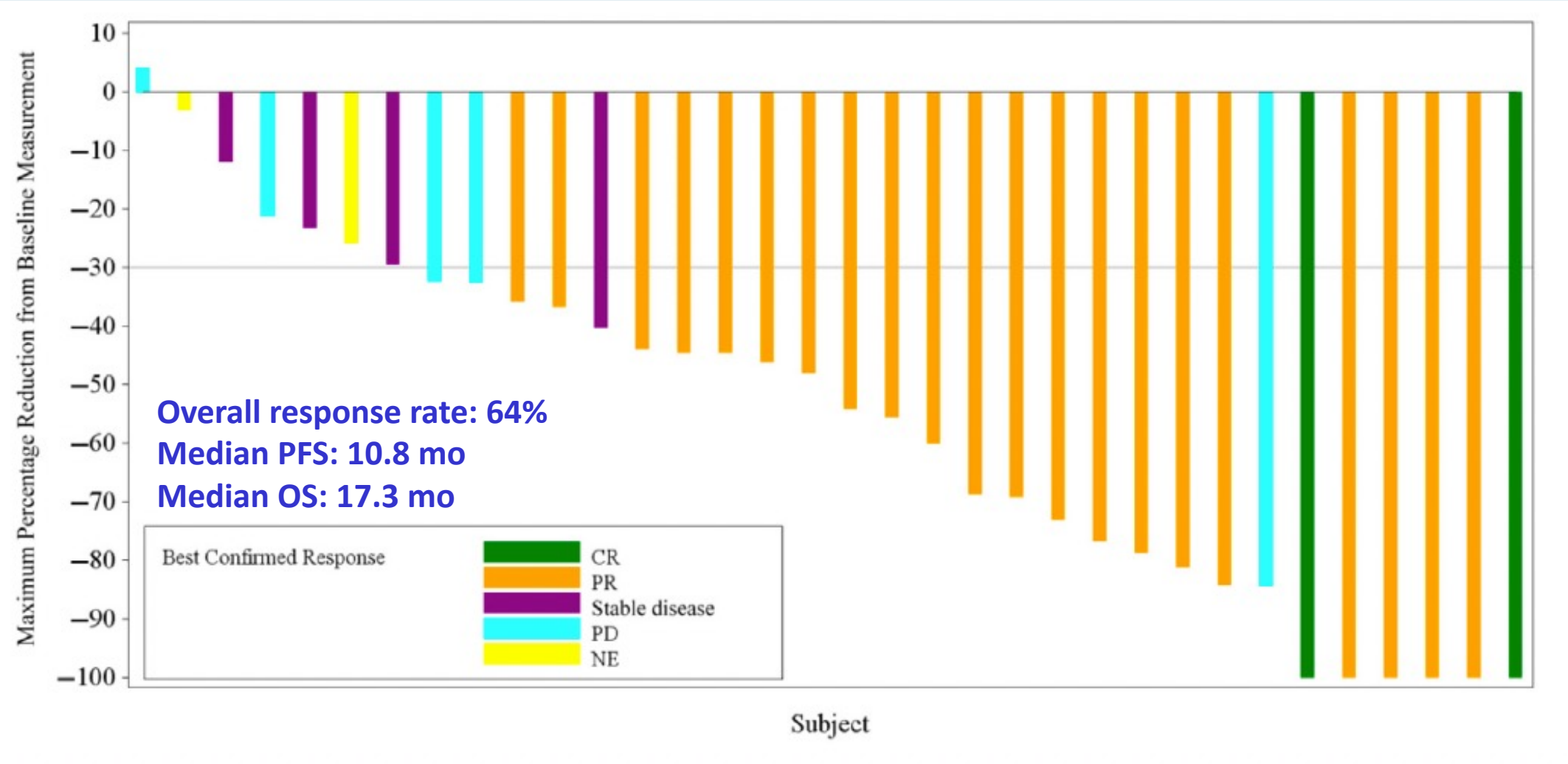


Planchard D et al. *J Thorac Oncol* 2022;17(1):103-15.

RTP RESEARCH TO PRACTICE

Five-Year Update — Phase II Study of Dabrafenib/Trametinib for Metastatic NSCLC with a BRAF V600E Mutation

Treatment-Naïve Disease (N = 36)



Planchard D et al. *J Thorac Oncol* 2022;17(1):103-15.

RTP RESEARCH TO PRACTICE

Five-Year Update — Phase II Study of Dabrafenib/Trametinib for Metastatic NSCLC with a BRAF V600E Mutation

Outcomes According to Genomic Alterations Detected by Next-Generation Sequencing

Cohort	Genetic Alterations	Cohort	Best Response	PFS, mo	OS, mo
Dabrafenib plus trametinib (cohort B; ORR, 68.4%; mPFS, 10.2 mo; mOS, 18.2 mo)	*BRAF* V600E+*IDH1*R132C	B	CR	6.9	40.7
	BRAF V600E+*KRAS*G13C	B	PR	58.1	58.1
	BRAF V600E+*IDH1*R132L[a,b]	B	PR	32.4	32.4
	BRAF V600E+*PIK3CA*E542K[c]	B	PR	16.7	55.2
	BRAF V600E+*cMET*ex14 skipping	B	PR	10.2	18.2
	BRAF V600E+*PIK3CA*E545K[c]	B	NE	1.4	3.8
	BRAF V600E+*PIK3CA*E545K[c]	B	PD	1.4	3.1
	*cMET*T1010I[d]	B	PR	27.6	59.4
	*JAK3*S493C[d]	B	PR	5.6	10.3
	*KRAS*G12V[d]	B	PD	2.9	4.4
Dabrafenib plus trametinib (cohort C; ORR, 63.9%; mPFS, 10.8 mo; mOS, 17.3 mo)	*BRAF* V600E+*mTOR*T1977K[c]	C	PR	7.0	7.0
	BRAF V600E+*IDH1*R132C	C	PR	10.4	17.3
	BRAF V600E+*IDH1*R132L	C	PR	5.5	8.2
	BRAF V600E+*BRAF*G466V	C	Stable disease	19.4	40.2
	ALK fusion[d,e]	C	Stable disease	13.8	40.9[f]
	*JAK3*S493C[d]	C	PR	19.3	51.2[f]

Planchard D et al. *J Thorac Oncol* 2022;17(1):103-15.

RTP RESEARCH TO PRACTICE

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[1]	Pralesetinib[2]
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

Ongoing Phase III Trials of Selpercatinib or Pralsetinib for NSCLC with RET Fusion

Trial identifier	Setting	Treatment arms
LIBRETTO-431 (NCT04194944)	Untreated Stage IIIB-IIIC or Stage IV non-squamous NSCLC that is not suitable for radical surgery or radiation therapy	• Selpercatinib • Pemetrexed and platinum with or without pembrolizumab
LIBRETTO-432 (NCT04819100)	Stage IB, II or IIIA NSCLC after definitive locoregional therapy	• Selpercatinib • Placebo
AcceleRET-Lung (NCT04222972)	Locally advanced or metastatic NSCLC that has not been treated with systemic anticancer therapy for metastatic disease	• Pralsetinib • Platinum-based chemotherapy (with or without pembrolizumab)
NCT05170204	Unresectable Stage III NSCLC	<u>Cohort A3</u> • Pralsetinib • Durvalumab

www.clinicaltrials.gov; Accessed March 2022.

Abstract CT008

AACR American Association for Cancer Research ANNUAL MEETING 2022 New Orleans

Long-term Outcomes With Sotorasib in Pre-treated *KRAS* p.G12C Mutated NSCLC: 2-year Analysis of CodeBreaK 100

Presenter: Grace K. Dy[1], MD

[1]Roswell Park Comprehensive Cancer Center

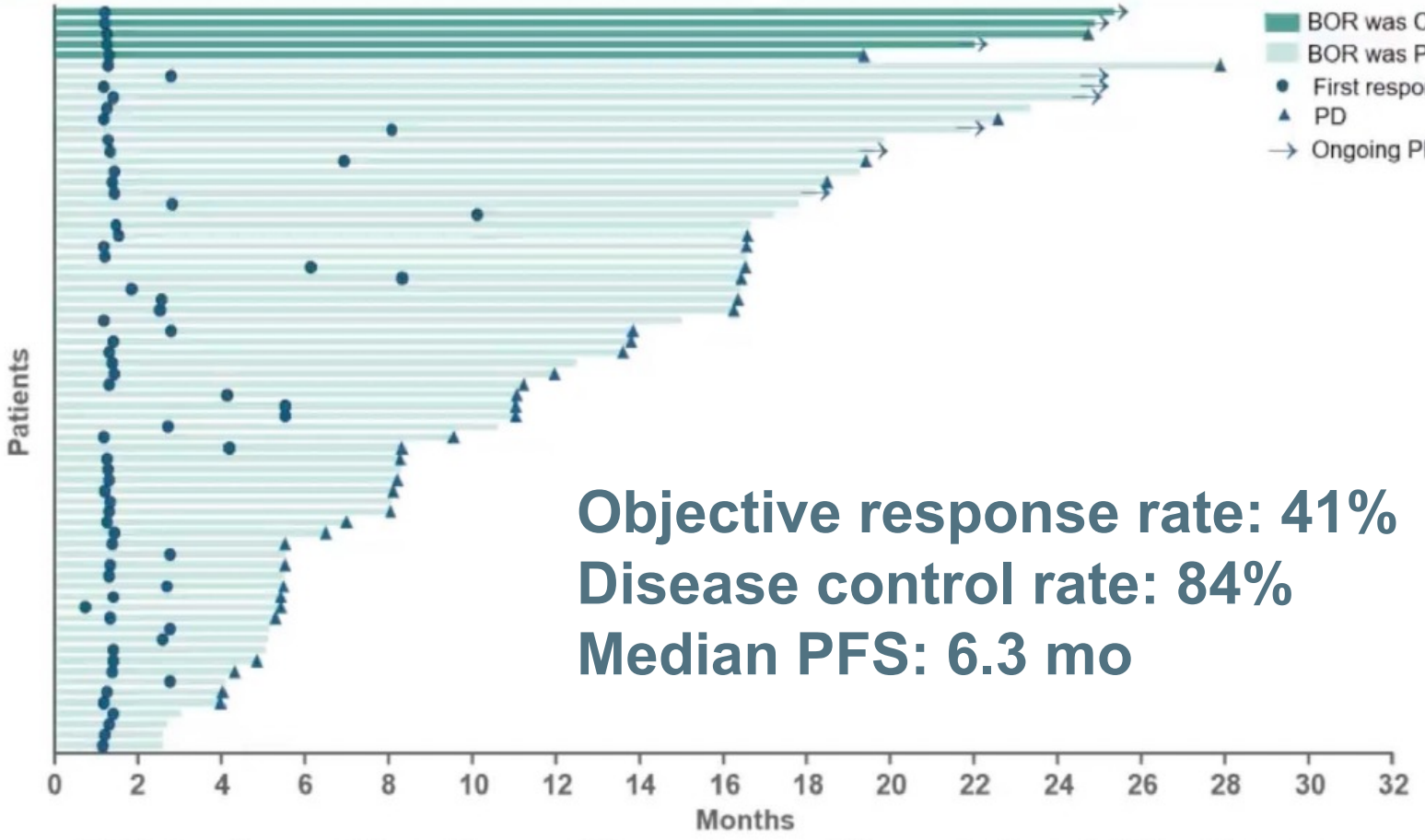
On behalf of: Ramaswamy Govindan[2], Vamsidhar Velcheti[3], Gerald S. Falchook[4], Antoine Italiano[5], Juergen Wolf[6], Adrian G. Sacher[7], Toshiaki Takahashi[8], Suresh S. Ramalingam[9], Christophe Dooms[10], Dong-Wan Kim[11], Alfredo Addeo[12], Jayesh Desai[13], Martin Schuler[14], Pascale Tomasini[15], Qui Tran[16], Simon Jones[16], Agnes Ang[16], Abraham Anderson[16], Antreas Hindoyan[16], David S. Hong[17], Bob T. Li[18]

[2]Washington University in St Louis, [3]New York University Langone, [4]Sarah Cannon Research Institute, [5]Institut Bergonie, [6]Universitatsklinikum Koln, [7]Princess Margaret Cancer Centre, [8]Shizuoka Cancer Center [9]Winship Cancer Institute, [10]Universitair Ziekenhuis Leuven [11]Seoul National University Hospital, [12]Hopitaux Universitaires de Geneve, [13]Peter MacCallum Cancer Centre, [14]Universitatsklinikum Essen, [15]Hopital de la Timone, [16]Amgen Inc., [17]MD Anderson Cancer Center, [18]Memorial Sloan Kettering Cancer Center

RTP RESEARCH TO PRACTICE

CodeBreaK 100: Long-Term Outcomes with Sotorasib for Pre-Treated Metastatic NSCLC with KRAS G12C Mutation

— *Durability of Response*



Objective response rate: 41%
Disease control rate: 84%
Median PFS: 6.3 mo

Median time to response: 6 weeks

- 70% of patients had a response at their first scan

Median duration of response: 12.3 months (95% CI: 7.1, 15.0)

50.6% (95% CI: 37.4, 62.4) **of responders remained in response for 12+ months**

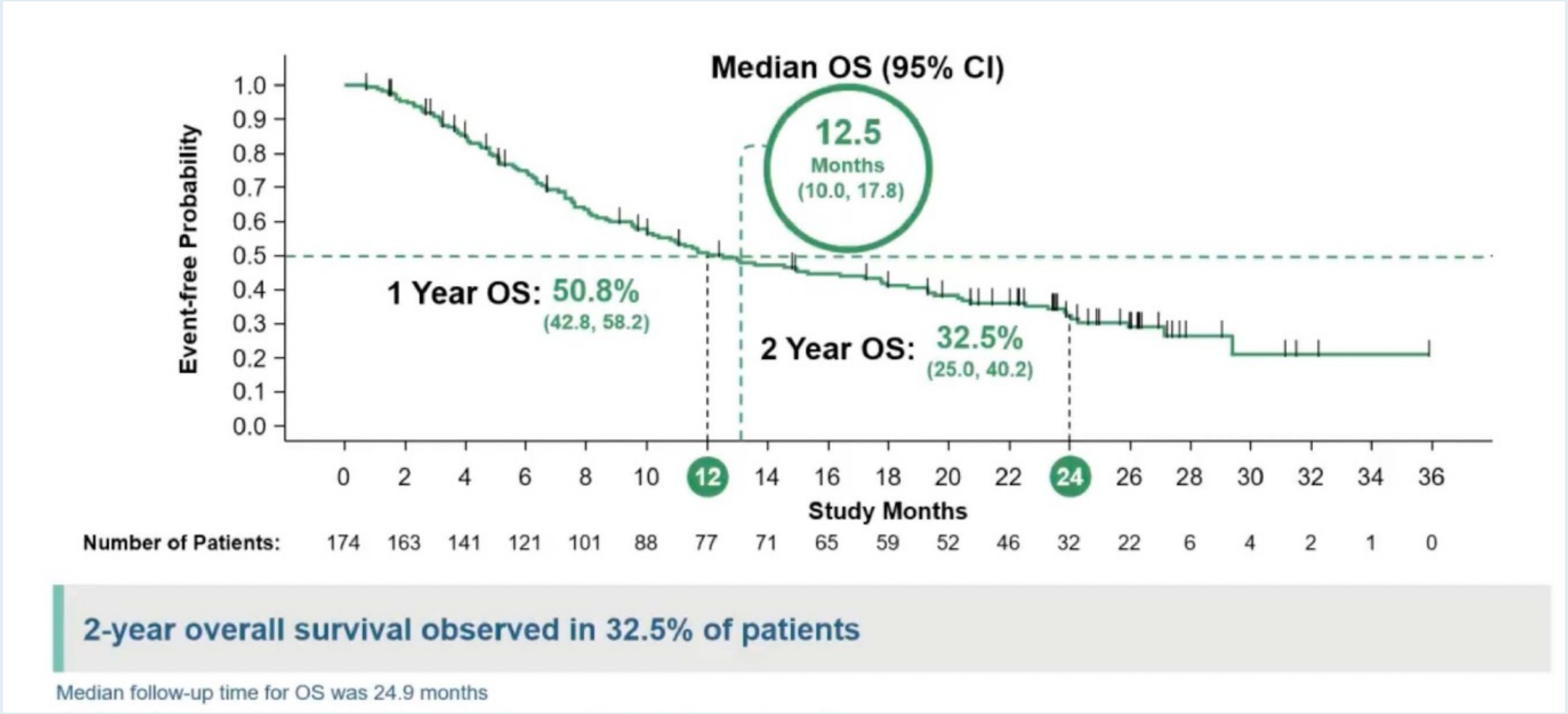
BOR, best overall response; CR, complete response; PD, progressive disease; PFS, progression-free survival; PR, partial response.

Dy GK et al. AACR 2022;Abstract CT008.

RTP RESEARCH TO PRACTICE

CodeBreaK 100: Long-Term Outcomes with Sotorasib for Pre-Treated Metastatic NSCLC with KRAS G12C Mutation

— *Overall Survival (OS)*



2-year overall survival observed in 32.5% of patients

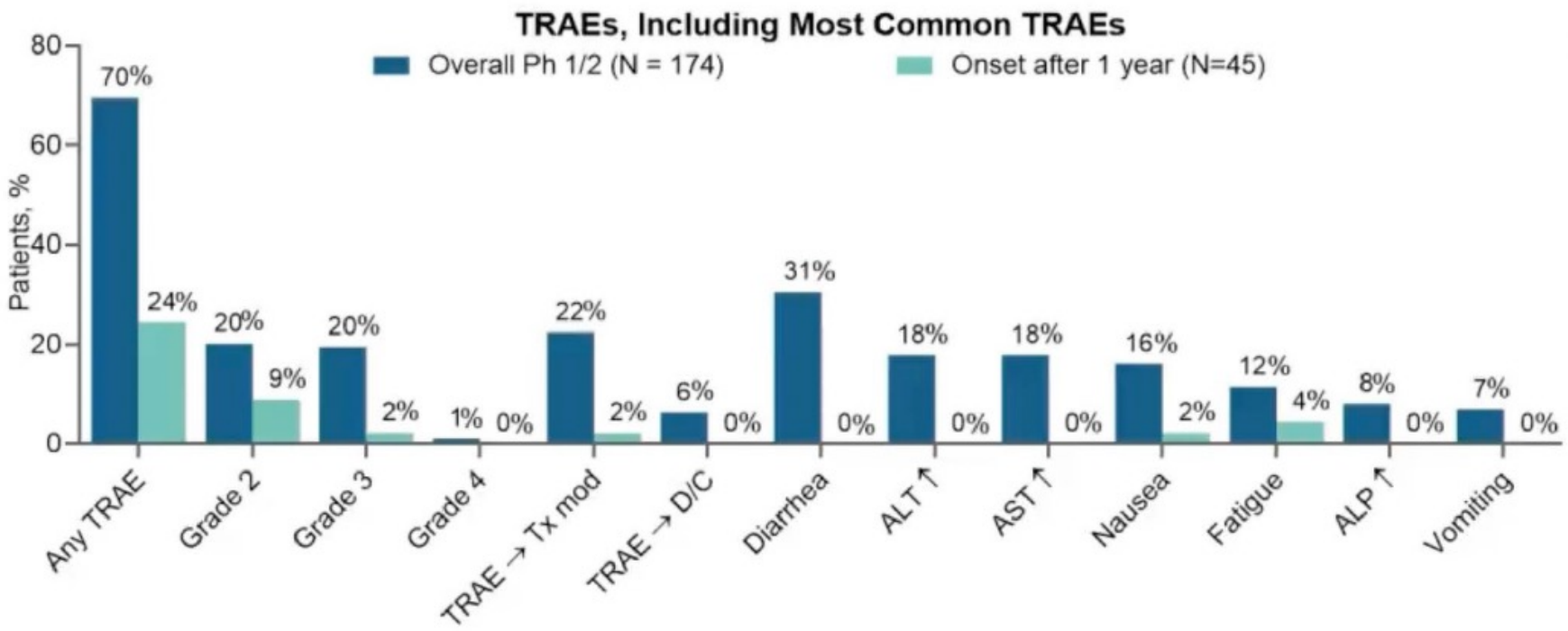
Median follow-up time for OS was 24.9 months

Dy GK et al. AACR 2022;Abstract CT008.

RTP RESEARCH TO PRACTICE

CodeBreaK 100: Long-Term Outcomes with Sotorasib for Pre-Treated Metastatic NSCLC with KRAS G12C Mutation

— *Treatment-Related Adverse Events (TRAEs)*



Grade 3 or 4 TRAEs occurred in 21% of patients

- One patient with new onset Grade 3 TRAE after 1 year (hemolytic anemia)

No fatal TRAEs occurred

- No TRAE leading to discontinuation after 1 year

Well-tolerated in the long-term: late-onset TRAEs were mild and manageable

Dy GK et al. AACR 2022;Abstract CT008.

RTP RESEARCH TO PRACTICE

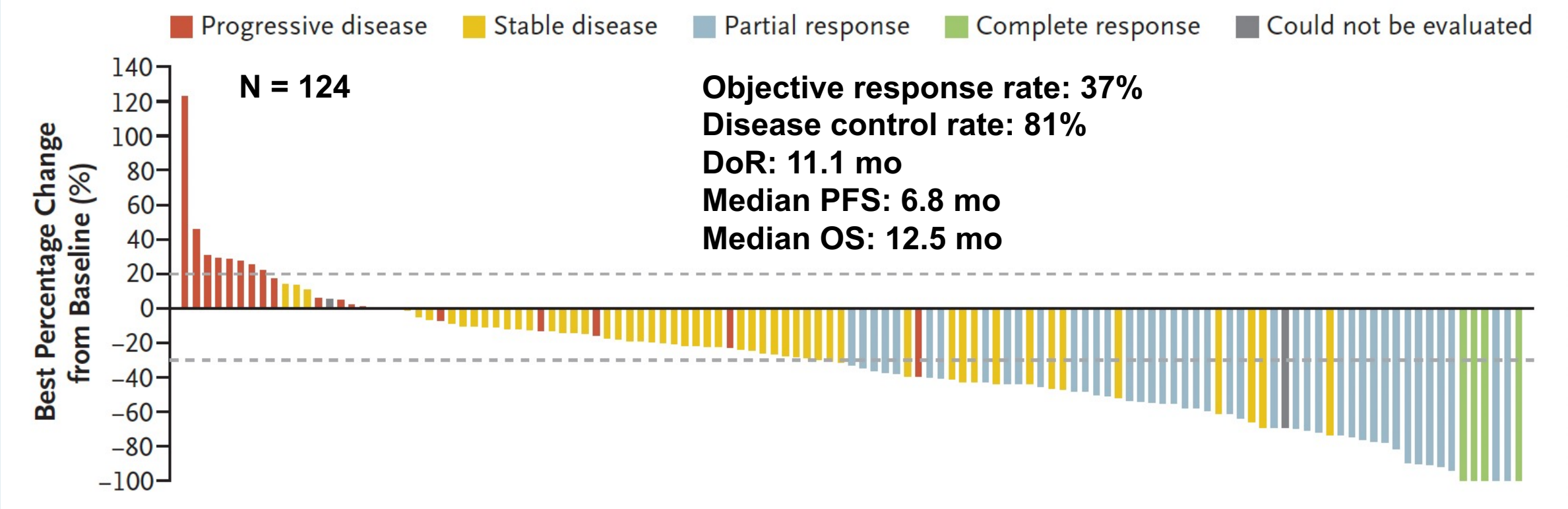
The NEW ENGLAND JOURNAL of MEDICINE

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

2022 ASCO ANNUAL MEETING

Abstract 9002

KRYSTAL-1: Activity and Safety of Adagrasib (MRTX849) in Patients with Advanced/Metastatic Non-Small Cell Lung Cancer Harboring a $KRAS^{G12C}$ Mutation

Alexander I. Spira[1], Gregory J. Riely[2], Shirish M. Gadgeel[3], Rebecca S. Heist[4], Sai-Hong Ignatius Ou[5], Jose M. Pacheco[6], Melissa L. Johnson[7], Joshua K. Sabari[8], Konstantinos Leventakos[9], Edwin Yau[10], Lyudmila Bazhenova[11], Marcelo V. Negrao[12], Nathan A. Pennell[13], Jun Zhang[14], Karen Velastegui[15], James G. Christensen[15], Xiaohong Yan[15], Kenna Anderes[15], Richard C. Chao[15], Pasi A. Jänne[16]

N Engl J Med 2022 Jul 14;387(2):120-31.

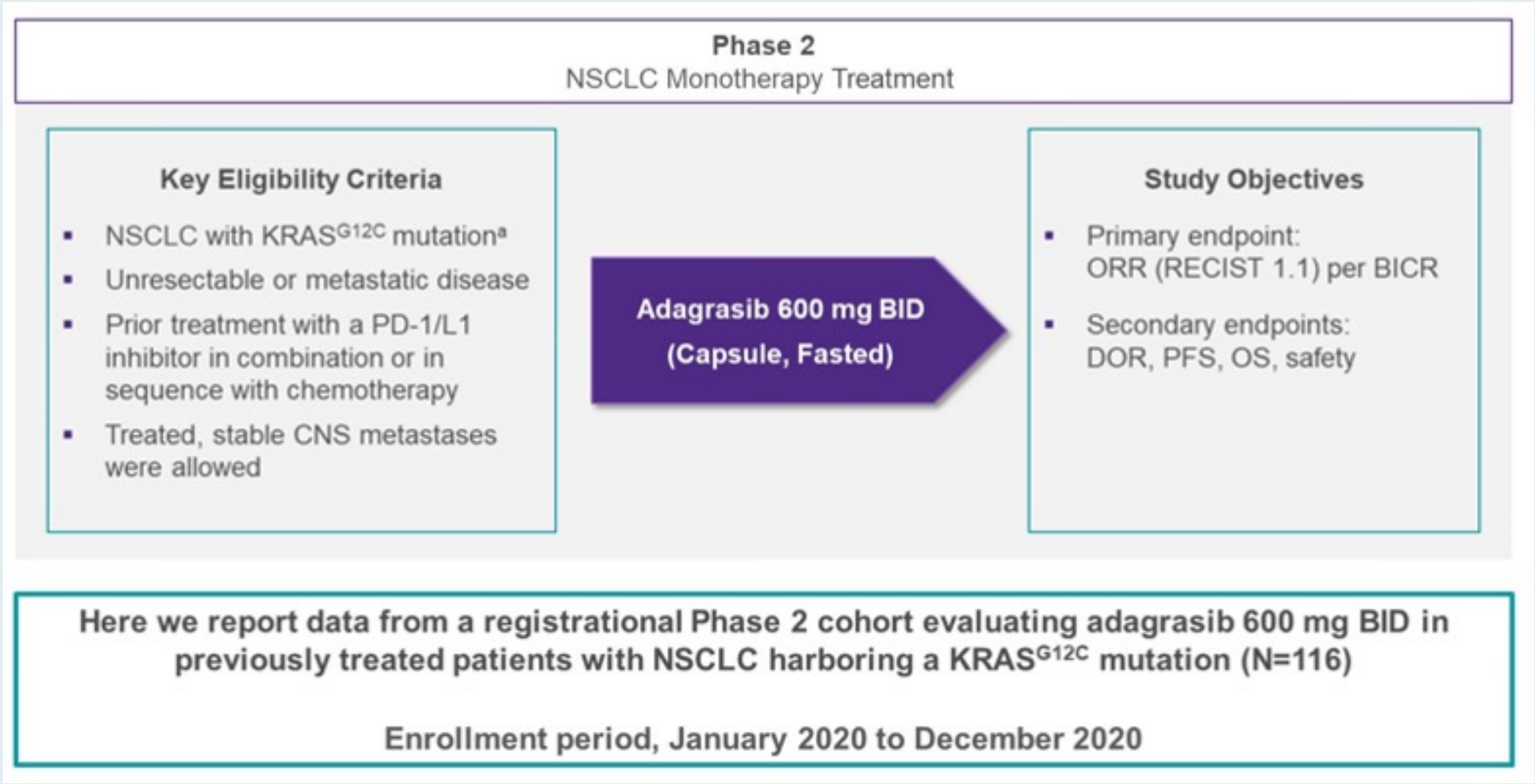
ORIGINAL ARTICLE

Adagrasib in Non–Small-Cell Lung Cancer Harboring a *KRAS*^{G12C} Mutation

Pasi A. Jänne, M.D., Ph.D., Gregory J. Riely, M.D., Ph.D., Shirish M. Gadgeel, M.D., Rebecca S. Heist, M.D., M.P.H., Sai-Hong I. Ou, M.D., Ph.D., Jose M. Pacheco, M.D., Melissa L. Johnson, M.D., Joshua K. Sabari, M.D., Konstantinos Leventakos, M.D., Ph.D., Edwin Yau, M.D., Ph.D., Lyudmila Bazhenova, M.D., Marcelo V. Negrao, M.D., Nathan A. Pennell, M.D., Ph.D., Jun Zhang, M.D., Ph.D., Kenna Anderes, Ph.D., Hirak Der-Torossian, M.D., Thian Kheoh, Ph.D., Karen Velastegui, B.Sc., Xiaohong Yan, Ph.D., James G. Christensen, Ph.D., Richard C. Chao, M.D., and Alexander I. Spira, M.D., Ph.D.

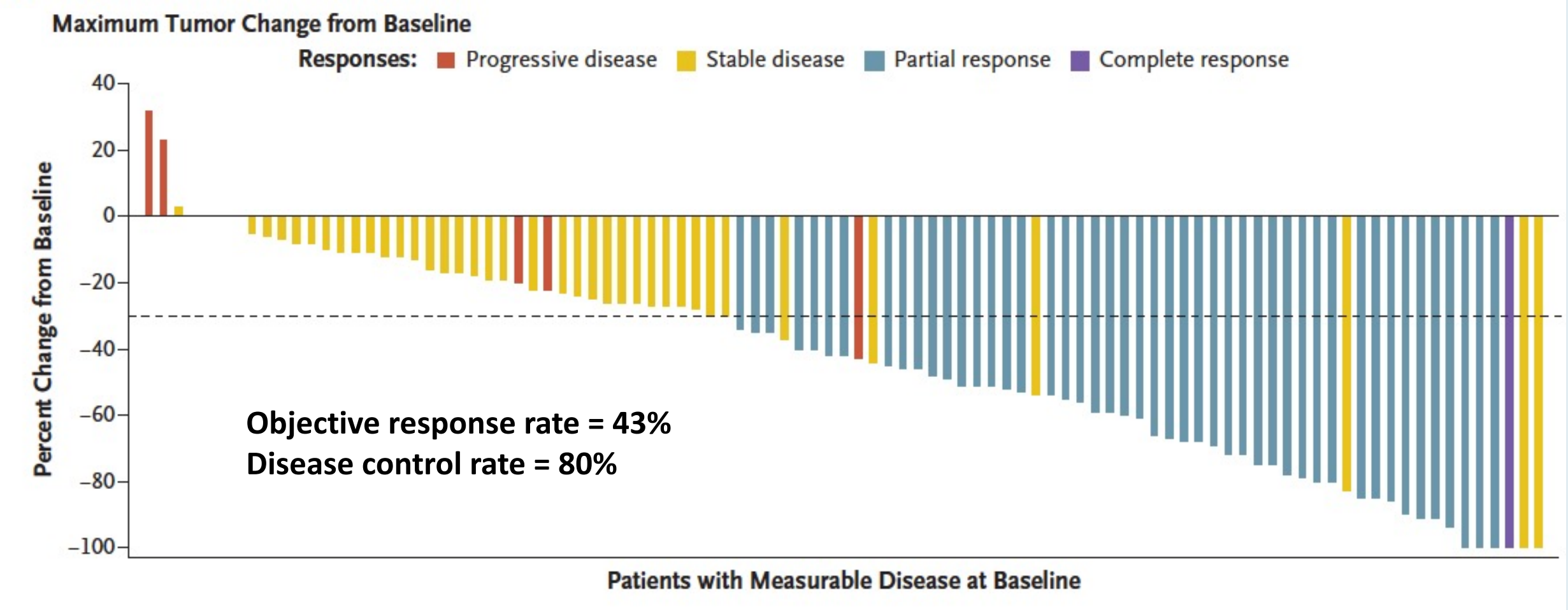
RTP RESEARCH TO PRACTICE

KRYSTAL-1: Phase II Cohort A Study Design



Spira AI et al. ASCO 2022;Abstract 9002.

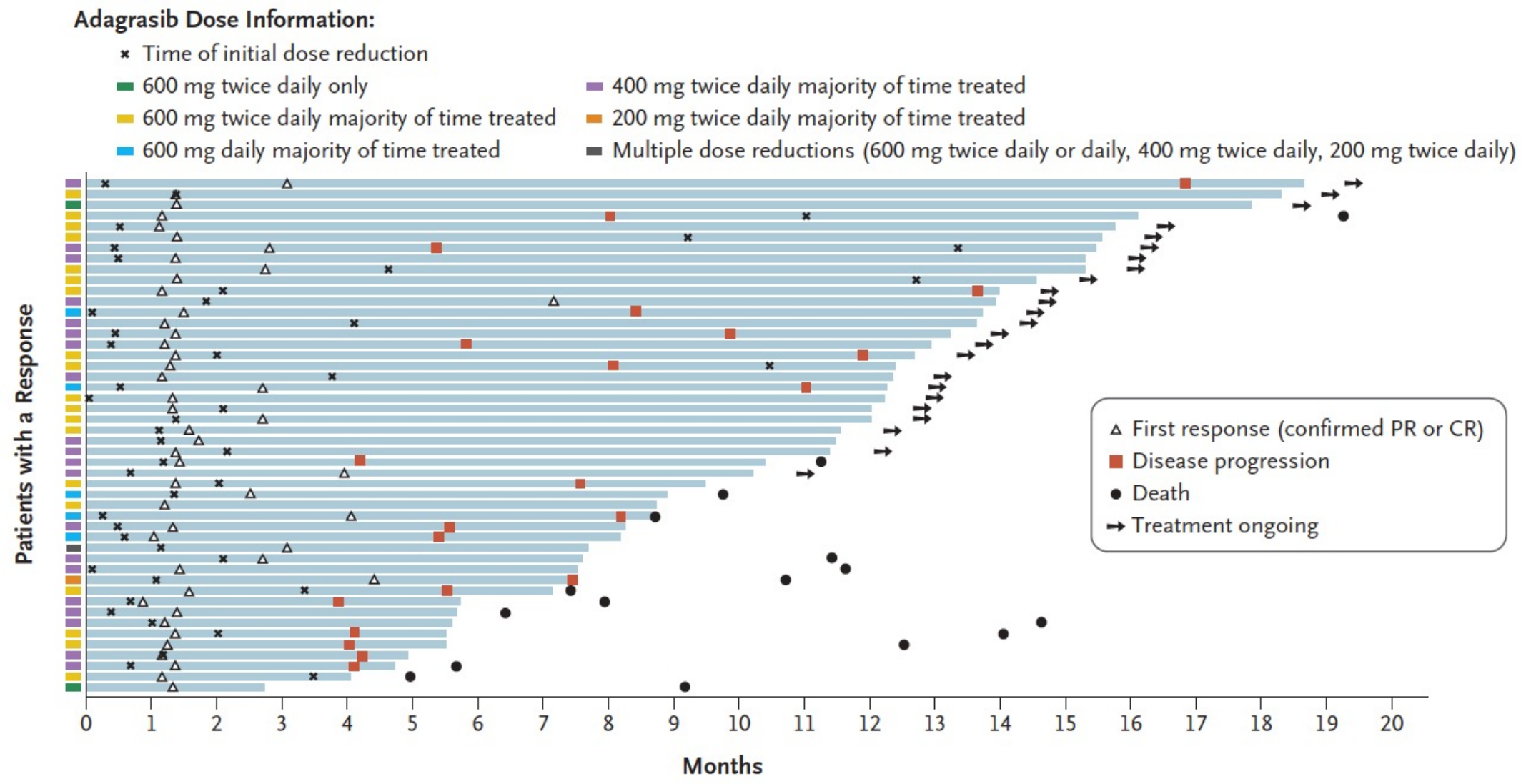
KRYSTAL-1: Tumor Response with Adagrasib for Advanced NSCLC Harboring a KRAS G12C Mutation



Jänne PA et al. *N Engl J Med* 2022;387(2):120-31; Spira AI et al. ASCO 2022;Abstract 9002.

RTP RESEARCH TO PRACTICE

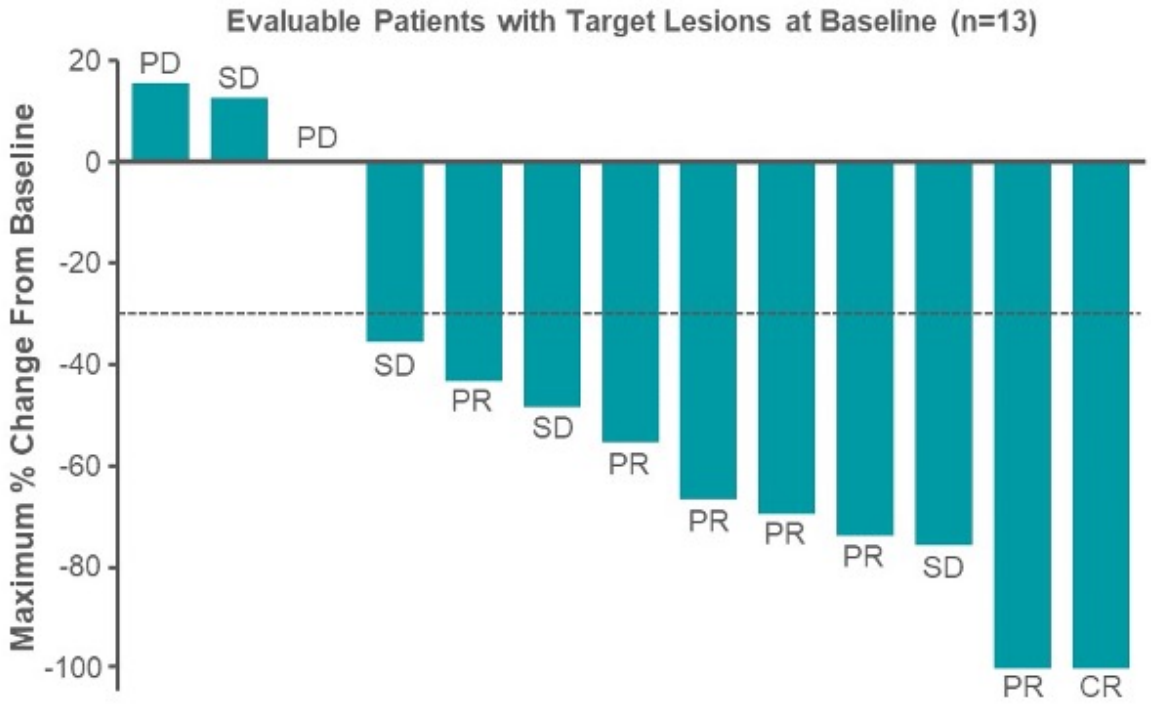
KRYSTAL-1: Time to Response and Duration of Response with Adagrasib for Advanced NSCLC Harboring a KRAS G12C Mutation



Jänne PA et al. *N Engl J Med* 2022;387(2):120-31; Spira AI et al. ASCO 2022;Abstract 9002.

KRYSTAL-1: Intracranial Response with Adagrasib in Patients with NSCLC and Treated, Stable CNS Metastases

Best Overall Response	Overall (n=33)[b]	Patients with Non-target Lesions Only (n=19)	Patients with Target Lesions (n=13)[c]
IC ORR, n (%)	**11 (33%)**	**4 (21%)**	**7 (54%)**
Complete response	5 (15%)	4 (21%)	1 (8%)
Partial response	6 (18%)	-	6 (46%)
Stable disease	17 (52%)	13 (68%)	4 (31%)
IC DCR, n (%)	**28 (85%)**	**17 (89%)**	**11 (85%)**



- IC ORR by modified RANO-BM was 33% (95% CI, 18–52); median IC DOR was 11.2 months (95% CI, 3.0–NE)
- IC DCR was 85% (95% CI, 68–95); median IC PFS was 5.4 months (95% CI, 3.3–11.6)

Spira AI et al. ASCO 2022;Abstract 9002.

KRYSTAL-1: Treatment-Related Adverse Events with Adagrasib in Patients with Advanced NSCLC Harboring a KRAS G12C Mutation

	Adagrasib Monotherapy (N=116) Capsule, Fasted	
TRAEs, n (%)	**Any Grade**	**Grades 3–4**
Any TRAEs	113 (97%)	50 (43%)
Most frequent TRAEs[a], n (%)		
Diarrhea	73 (63%)	1 (<1%)
Nausea	72 (62%)	5 (4%)
Vomiting	55 (47%)	1 (<1%)
Fatigue	47 (41%)	5 (4%)
ALT increase	32 (28%)	5 (4%)
Blood creatinine increase	30 (26%)	1 (<1%)
AST increase	29 (25%)	4 (3%)
Decreased appetite	28 (24%)	4 (3%)

- Grade 1–2 TRAEs occurred in 53% of patients
- There were 2 grade 5 TRAEs (cardiac failure [n=1] and pulmonary hemorrhage [n=1])
- TRAEs led to dose reduction in 60/116 (52%) patients[b] and to dose interruption in 71/116 (61%) patients
- TRAEs led to discontinuation of study drug in 8/116 (7%) patients

Spira AI et al. ASCO 2022;Abstract 9002.

2022 ASCO ANNUAL MEETING

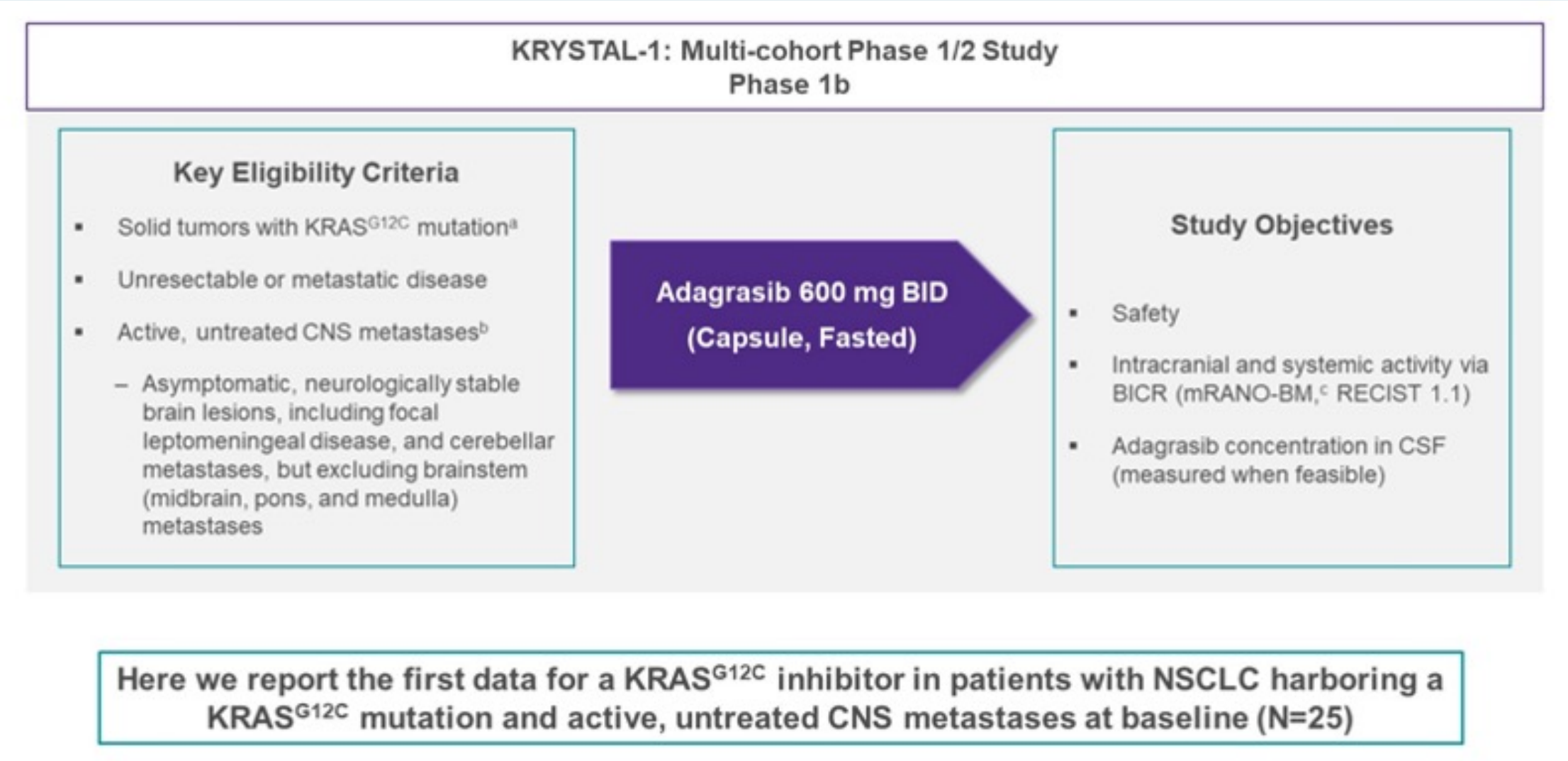
Abstract LBA9009

Activity of Adagrasib (MRTX849) in Patients with KRAS^{G12C}-Mutated NSCLC and Active, Untreated CNS Metastases in the KRYSTAL-1 Trial

Joshua K. Sabari,[1] Alexander I. Spira,[2] Rebecca S. Heist,[3] Pasi A. Jänne,[4] Jose M. Pacheco,[5] Jared Weiss,[6] Shirish M. Gadgeel,[7] Hirak Der-Torossian,[8] Karen Velastegui,[8] Thian Kheoh,[8] James G. Christensen,[8] Marcelo V. Negrao[9]

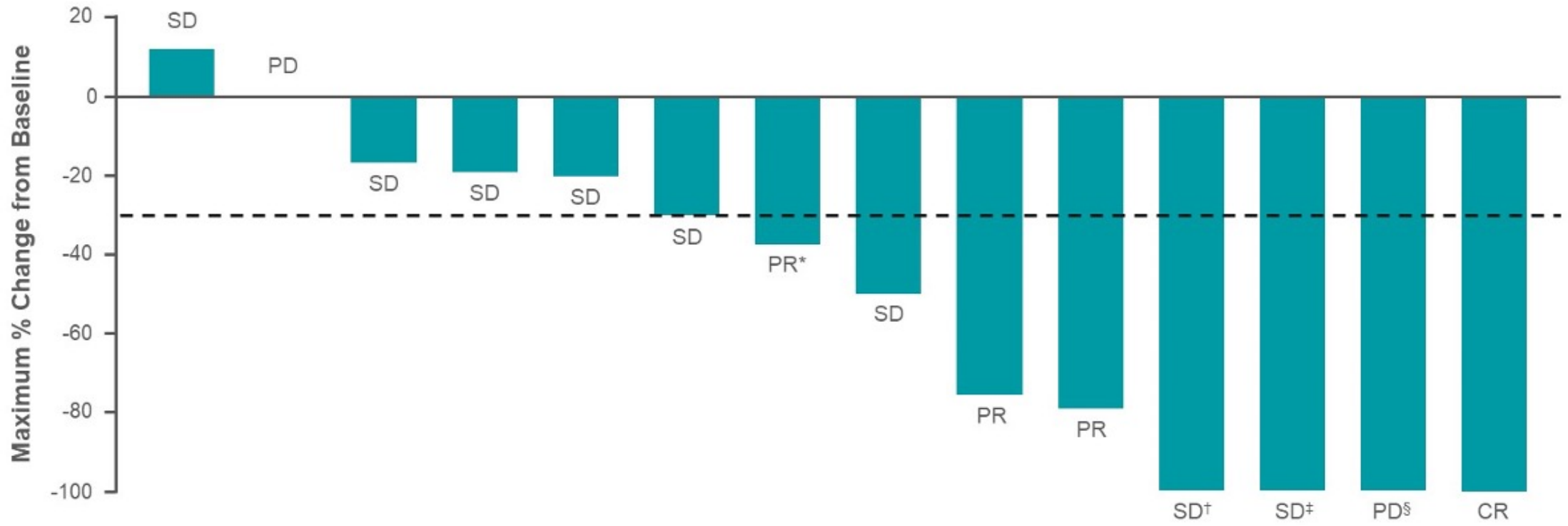
RTP RESEARCH TO PRACTICE

KRYSTAL-1: Active, Untreated CNS Metastases Cohort



Sabari JK et al. ASCO 2022;Abstract LBA9009.

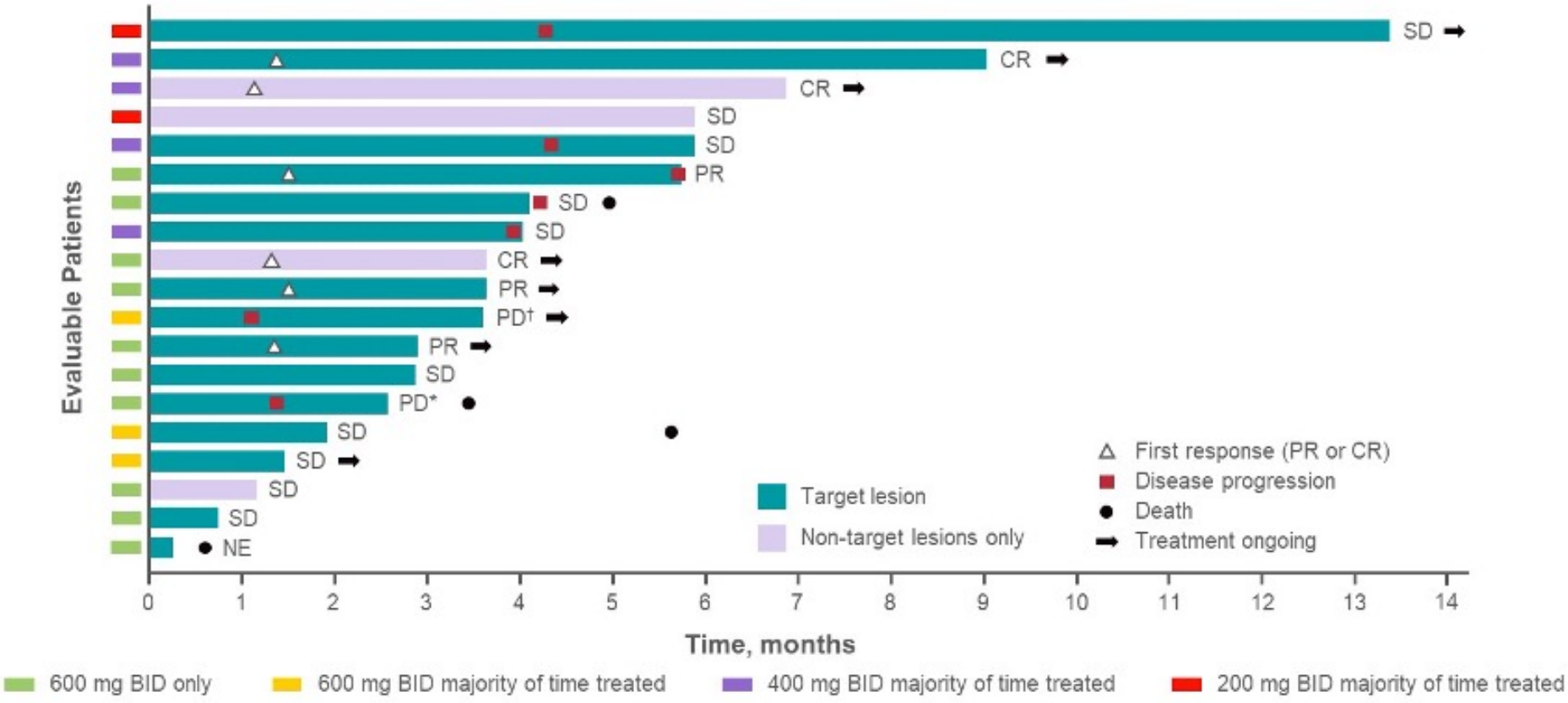
KRYSTAL-1: Intracranial Response with Adagrasib in Patients with NSCLC and Active, Untreated CNS Metastases



- Objective IC responses were observed in 32% (95% CI, 12.6–56.6)[a]
- IC DCR was 84% (95% CI, 60.4–96.6)

Sabari JK et al. ASCO 2022;Abstract LBA9009.

KRYSTAL-1: Duration of Treatment with Adagrasib for Patients with NSCLC and Active, Untreated CNS Metastases



- Median IC DOR was not reached (95% CI, 4.1–NE)[a]
- Median IC PFS was 4.2 months (95% CI, 3.8–NE)[b]; median OS had not been reached

Sabari JK et al. ASCO 2022;Abstract LBA9009.

RTP RESEARCH TO PRACTICE

KRYSTAL-1: Treatment-Related Adverse Events with Adagrasib in Patients with NSCLC and Active, Untreated CNS Metastases

	Adagrasib Monotherapy (N=25) Capsule, Fasted	
TRAEs, n (%)	**Any Grade**	**Grade 3**
Any TRAEs	24 (96%)	9 (36%)
Most frequent TRAEs,[a] n (%)		
Nausea	20 (80%)	2 (8%)
Diarrhea	20 (80%)	0
Vomiting	11 (44%)	3 (12%)
AST increase	10 (40%)	1 (4%)
ALT increase	9 (36%)	2 (8%)
Fatigue	8 (32%)	0
Anemia	6 (24%)	0
Blood alkaline phosphatase increase	6 (24%)	1 (4%)
Blood creatinine increase	6 (24%)	0
Decreased appetite	6 (24%)	0
Dizziness	5 (20%)	2 (8%)
Dysgeusia	5 (20%)	0

- Grade 1–2 TRAEs occurred in 60% of patients
- No grade 4/5 TRAEs
- TRAEs led to dose reduction/interruption in 12 (48%) patients and discontinuation in 1 (4%) patient
- CNS-specific TRAEs included dizziness (20%, n=5) and grade 1/2 aphasia and insomnia (4%, n=1)

Sabari JK et al. ASCO 2022;Abstract LBA9009.

Key Trials of ROS1 TKIs for TKI-Naïve NSCLC with ROS1 Fusions

ROS1 TKI	Study	Phase	ORR	Median DoR	Median PFS	Intracranial ORR
Crizotinib	PROFILE 1001	Ib	38/53 (72%)	25 mo	19 mo	—
	OxOnc	II	91/127 (72%)	20 mo	16 mo	—
	EUCROSS	II	21/30 (70%)	19 mo	20 mo	—
	AcSe	II	35/36 (69%)	—	6 mo	—
	METROS	II	17/26 (65%)	21 mo	23 mo	33%
Entrectinib	Drilon et al	I/II	41/53 (77%)	25 mo	19 mo	55%
Ceritinib	Lim et al	II	20/30 (67%)	21 mo	19 mo	29%
Brigatinib	Gettinger et al	I	1/1 (100%)	—	—	—
Lorlatinib	Shaw et al	I/II	13/21 (62%)	25 mo	21 mo	64%
Repotrectinib	Cho et al	I/II	10/11 (91%)	—	—	100%
Taletrectinib	Fujiwara et al	I	6/9 (67%)	—	—	—

ORR = objective response rate; DoR = duration of response

Drilon A et al. *Nat Rev Clin Oncol* 2021;18(1):35-55.

Key Trials of ROS1 TKIs for TKI-Pretreated NSCLC with ROS1 Fusions

ROS1 TKI	Study	Phase	ORR
Entrectinib (after crizotinib)	Drilon et al	I/II	0/6 (0%)
Ceritinib (after crizotinib)	Lim et al	II	0/2 (0%)
Brigatinib (after crizotinib)	Gettinger et al	I	0/2 (0%)
Lorlatinib	Shaw et al	I/II	After crizotinib: 14/40 (35%) After ≥2 prior TKIs: 0/6 (0%)
Repotrectinib	Drilon et al	I/II	After 1 prior TKI: 7/18 (39%) After ≥2 prior TKIs: 2/7 (29%)
Taletrectinib (after crizotinib)	Fujiwara et al	I	1/3 (33%)

Drilon A et al. *Nat Rev Clin Oncol* 2021;18(1):35-55.

2022 ASCO® ANNUAL MEETING

Abstract 9008

Amivantamab in NSCLC patients with MET exon 14 skipping mutation: Updated results from the CHRYSALIS study

Matthew G. Krebs,[1] Alexander I. Spira,[2] Byoung Chul Cho,[3] Benjamin Besse,[4] Jonathan W. Goldman,[5] Pasi A. Jänne,[6] Zhiyong Ma,[7] Aaron S. Mansfield,[8] Anna Minchom,[9] Sai-Hong Ignatius Ou,[10] Ravi Salgia,[11] Zhijie Wang,[12] Casilda Llacer Perez,[13] Grace Gao,[14] Joshua C. Curtin,[14] Amy Roshak,[14] Robert W. Schnepp,[14] Meena Thayu,[14] Roland E. Knoblauch,[14] Chee Khoon Lee[15]

RTP RESEARCH TO PRACTICE

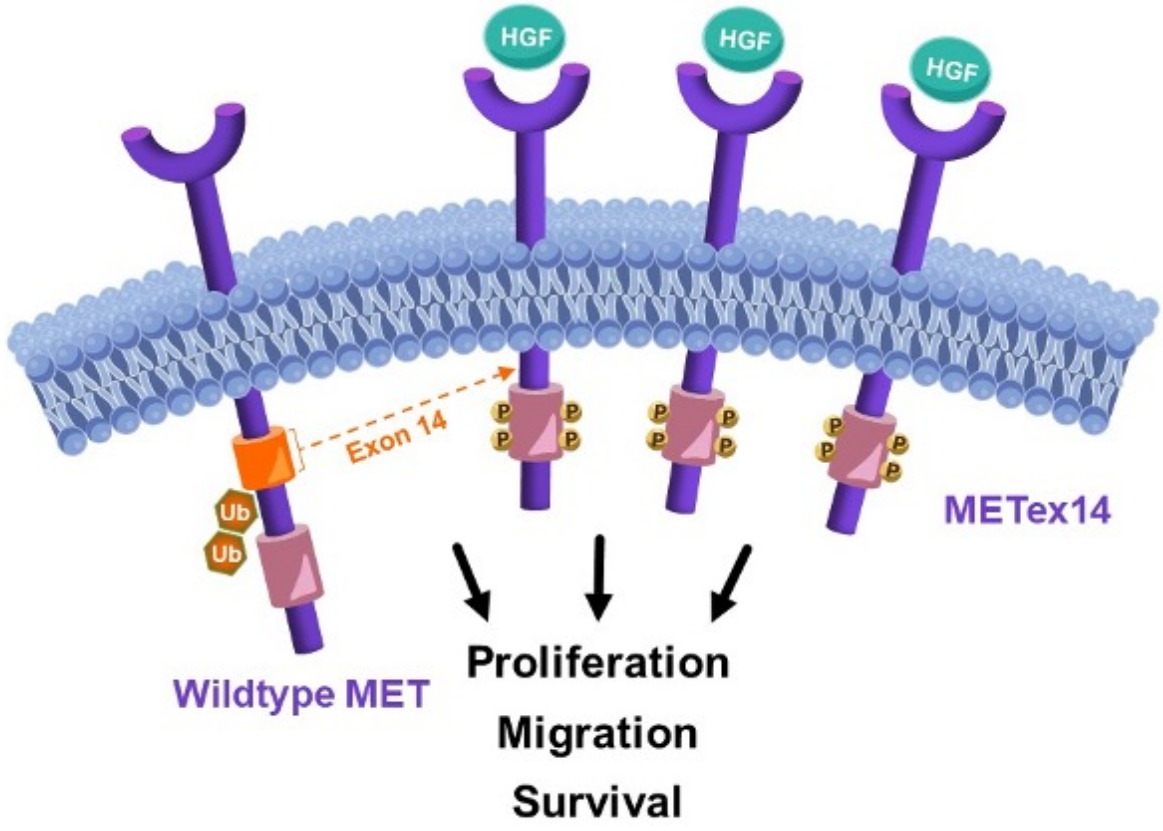
MET Exon 14 Skipping Mutations in NSCLC

MET Exon 14 Skipping Mutations (METex14)

- Found in ~3% of NSCLCs[1]
- Are generally more common in older patients (≥70 years), women, and non-smokers[2]
- Aberrant splicing of exon 14 disrupts degradation of MET receptors, resulting in constitutive activation of the MET pathway[3]

MET TKIs (Capmatinib and Tepotinib)

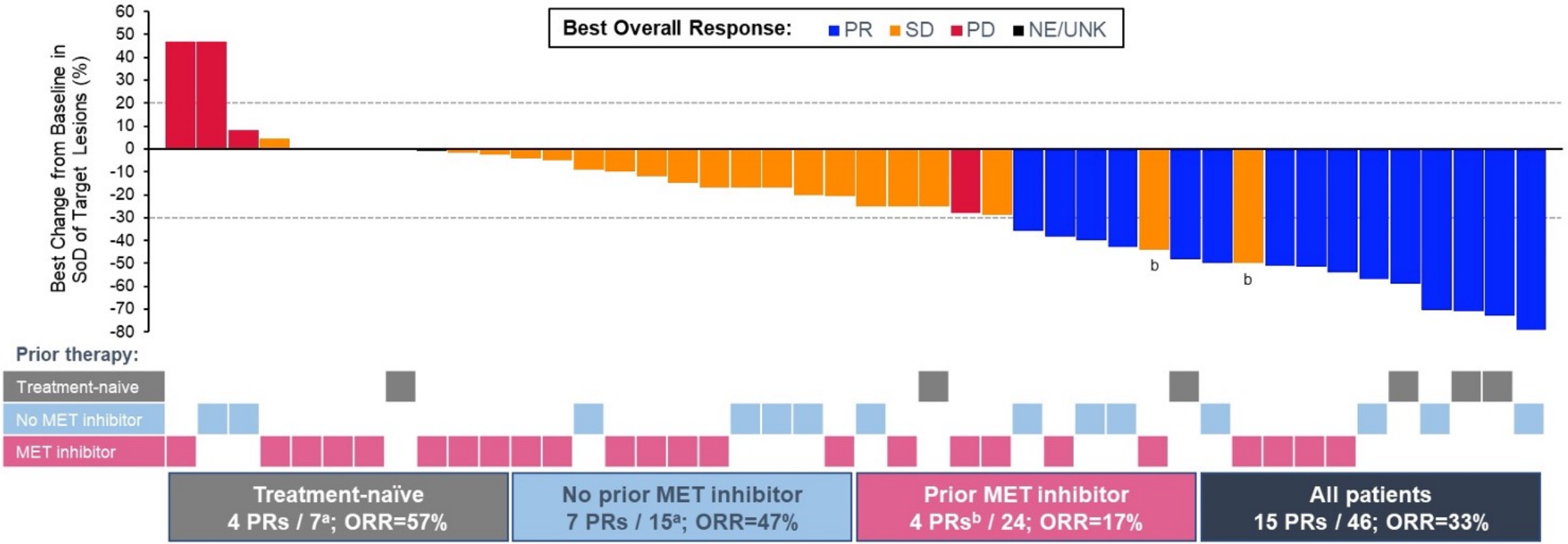
- Have accelerated approval
- ORR 41% to 43% in previously treated, MET TKI-naïve populations[4,5]
- Most patients develop acquired resistance[6]
  - Mechanisms may include secondary MET mutations or activation of bypass signalling



Krebs MG et al. ASCO 2022;Abstract 9008.

CHRYSALIS: Antitumor Activity of Amivantamab Monotherapy for Advanced NSCLC with MET Exon 14 Skipping Mutations

- A total of 46 patients were efficacy evaluable



Krebs MG et al. ASCO 2022;Abstract 9008.

RTP RESEARCH TO PRACTICE

CHRYSALIS: Safety Profile of Amivantamab Monotherapy for Advanced NSCLC with MET Exon 14 Skipping Mutations

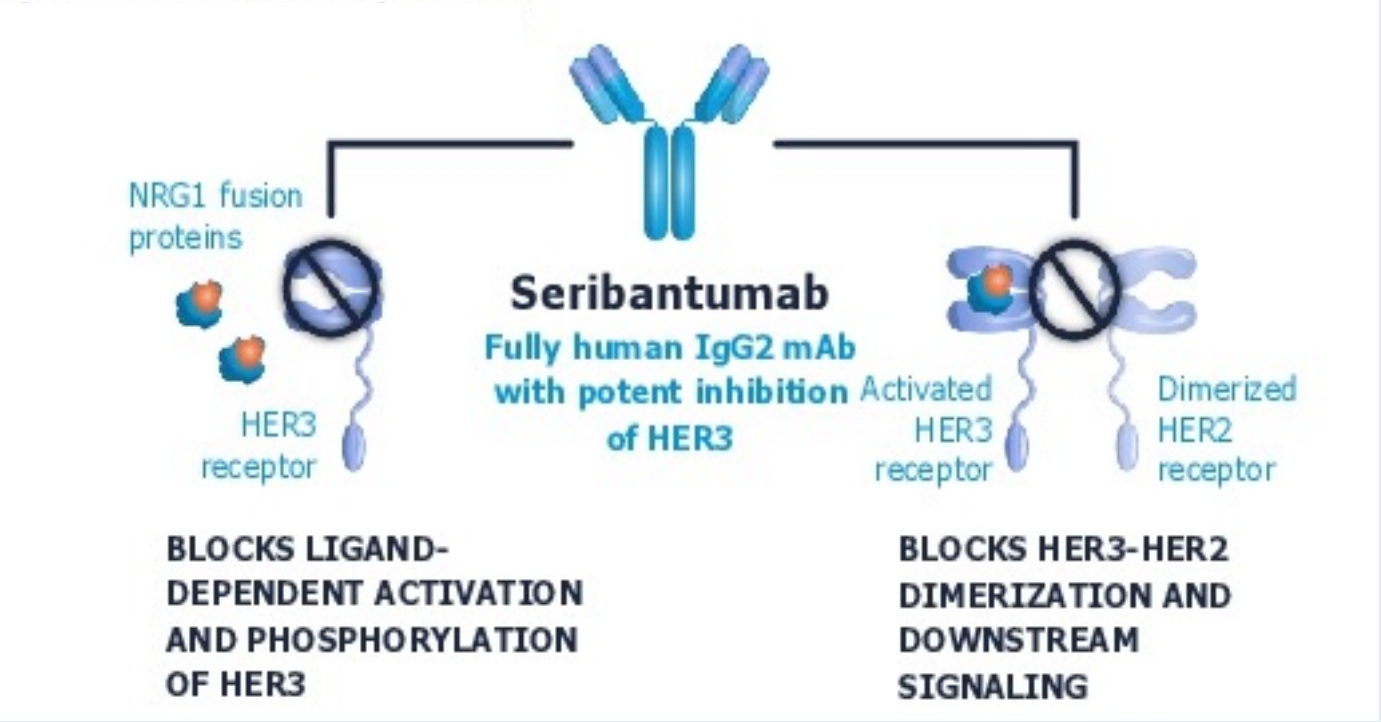
TEAE (≥15%) by Preferred Term, n (%)	RP2D (n=425) Median follow-up 11.8 months		METex14 Subset (n=55) Median follow up 5.1 months	
	All Grades	Grade ≥3	All Grades	Grade ≥3
Infusion related reaction	283 (67)	11 (3)	38 (69)	3 (5)
Rash	155 (36)	8 (2)	17 (31)	1 (2)
Dermatitis acneiform	155 (36)	4 (1)	22 (40)	0
Paronychia	193 (45)	7 (2)	21 (38)	0
Fatigue	93 (22)	8 (2)	17 (31)	2 (4)
Hypoalbuminemia	135 (32)	10 (2)	15 (27)	1 (2)
Stomatitis	91 (21)	2 (0.5)	15 (27)	0
Decreased appetite	76 (18)	2 (0.5)	12 (22)	0
Dyspnea	96 (23)	21 (5)	12 (22)	4 (7)
Peripheral edema	104 (24)	4 (1)	11 (20)	0
Pruritus	79 (19)	0	12 (22)	0
Nausea	104 (24)	2 (0.5)	11 (20)	0
Constipation	105 (25)	0	10 (18)	0
Hypomagnesemia	41 (10)	0	9 (16)	0
Aspartate aminotransferase increased	64 (15)	5 (1)	9 (16)	1 (2)
Alanine aminotransferase increased	72 (17)	10 (2)	8 (15)	1 (2)
Cough	78 (18)	0	3 (5)	0

- Treatment modifications due to toxicity (n=425): interruptions in 21%, reductions in 12%, and discontinuations in 5% of patients
  - Rates of pneumonitis/ILD was 4%
  - Cumulative grouped rash-related AEs[a] occurred in 322 (76%) patients, with 16 grade ≥3 (4%)
- Safety profile for METex14 subset is consistent with the larger CHRYSALIS safety population, with majority of events grade 1-2
- No new safety signals found

Krebs MG et al. ASCO 2022;Abstract 9008.

Neuregulin-1 (NRG1) Gene Fusions and Seribantumab Mechanism of Action

- NRG1 gene fusions are rare oncogenic drivers found in 0.2% of solid tumors, including lung, colorectal, breast and ovarian
- NRG1 fusion proteins predominantly retain an active EGF-like domain, which drives tumorigenesis and proliferation through aberrant HER3 activation
- Seribantumab is a fully human monoclonal antibody against HER3



Bendell JC et al. 2021 Gastrointestinal Cancers Symposium;Abstract TPS449.

FDA Grants Fast Track Designation to Seribantumab for Advanced Solid Tumors with NRG1 Fusions

Press Release – May 25, 2022

"The FDA has granted fast track designation to seribantumab as a tumor-agnostic treatment for patients with advanced solid tumors that harbor *NRG1* gene fusions. Seribantumab is currently being assessed in the ongoing phase 2 CRESTONE trial (NCT04383210) in adult patients with *NRG1* fusions in recurrent, locally advanced, or metastatic solid tumors. Initial data from the trial will be presented at the upcoming American Society of Clinical Oncology 2022 Annual Meeting.

There are currently no approved therapies that specifically target *NRG1* fusions, and therefore, receipt of fast track designation in a tumor-agnostic setting is a significant step in addressing this unmet need. Seribantumab is a fully human IgG2 monoclonal antibody that binds to HER3, which is activated through the binding of *NRG1* gene fusion when activated. Moreover, the *NRG1* fusion protein [can] activate the HER3 pathway and cause unregulated cell growth and proliferation.

The trial has an estimated enrollment of 75 patients who will be divided into 1 of 3 cohorts. The primary end point is objective response rate."

https://www.cancernetwork.com/view/fda-grants-fast-track-designation-of-seribantumab-for-nrg1-advanced-solid-tumors

RTP RESEARCH TO PRACTICE

2022 ASCO® ANNUAL MEETING

Abstract 3006

CRESTONE: Initial Efficacy and Safety of Seribantumab in Solid Tumors Harboring NRG1 Fusions

Daniel R. Carrizosa,[1] Mark E. Burkard,[2] Yasir Y. Elamin,[3] Jayesh Desai,[4] Shirish M. Gadgeel,[5] Jessica J. Lin,[6] Saiama N. Waqar,[7] David R. Spigel,[8] Young Kwang Chae,[9] Parneet K. Cheema,[10] Eric B. Haura,[11] Stephen V. Liu,[12] Danny Nguyen,[13] Karen L. Reckamp,[14] Frank Yung-Chin Tsai,[15] Valerie M. Jansen,[16] Alexander Drilon,[17] Sai-Hong Ignatius Ou,[18] D Ross Camidge,[19] Tejas Patil[19]

[1]Levine Cancer Institute/Atrium Health, Charlotte, NC; [2]University of Wisconsin Carbone Cancer Center, Madison, WI; [3]The University of Texas MD Anderson Cancer Center, Houston, TX; [4]Peter MacCallum Cancer Centre, Melbourne, Australia; [5]Henry Ford Cancer Institute/Henry Ford Health System, Detroit, MI; [6]Massachusetts General Hospital, Boston, MA; [7]Washington University School of Medicine, St. Louis, MO; [8]Sarah Cannon Research Institute, Nashville, TN; [9]Northwestern University, Chicago, IL; [10]William Osler Health System, Calgary, Canada; [11]H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL; [12]Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC; [13]City of Hope, Huntington Beach and Irvine, CA; [14]Cedars-Sinai Medical Center, Los Angeles, CA; [15]HonorHealth, Scottsdale, AZ; [16]Elevation Oncology, Inc. New York, NY; [17]Memorial Sloan Kettering Cancer Center, New York, NY; [18]Chao Family Comprehensive Cancer Center, University of CA-Irvine, Orange, CA; [19]University of Colorado Cancer Center, Aurora, CO

RTP RESEARCH TO PRACTICE

CRESTONE: An Ongoing Phase II Study of Seribantumab for Patients with Advanced Solid Tumors with NRG1 Fusions

Trial identifier: NCT04383210 (open)

Advanced solid tumor with an NRG1 gene fusion

Disease progression on or unresponsive to at least 1 prior standard therapy appropriate for tumor type and stage of disease

No further available curative therapy options

No prior pan-ERBB or any ERBB/HER2/HER3 directed therapy (Cohort 1 only)

Primary Endpoint: Objective response rate

Seribantumab
1-h IV infusion at various doses once weekly, every 2 weeks and every 3 weeks, during the induction, consolidation and maintenance dosing phases, respectively

Patient cohorts

Cohort 1: A minimum of 55 adult patients with advanced solid tumors harboring NRG1 gene fusions who have received prior standard treatment, excluding prior ERBB-directed therapy

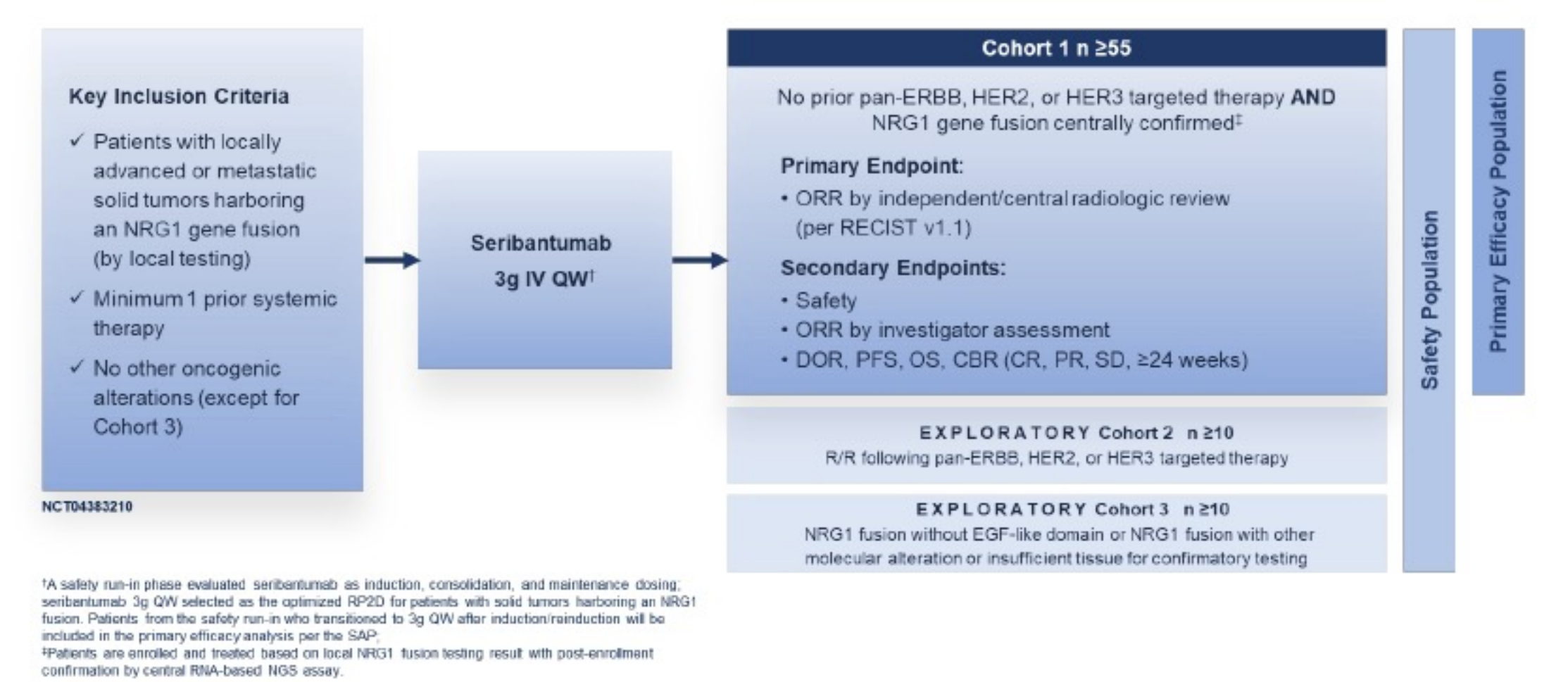
Cohort 2: Up to 10 adult patients with advanced solid tumors harboring NRG1 gene fusions who have received prior standard treatment, including prior ERBB-directed therapy

Cohort 3: Up to 10 adult patients with advanced solid tumors harboring NRG1 gene fusions lacking an EGF-like domain who have received prior standard treatment, which may have included prior ERBB-directed therapy

www.clinicaltrials.gov; Accessed April 2022.

RTP RESEARCH TO PRACTICE

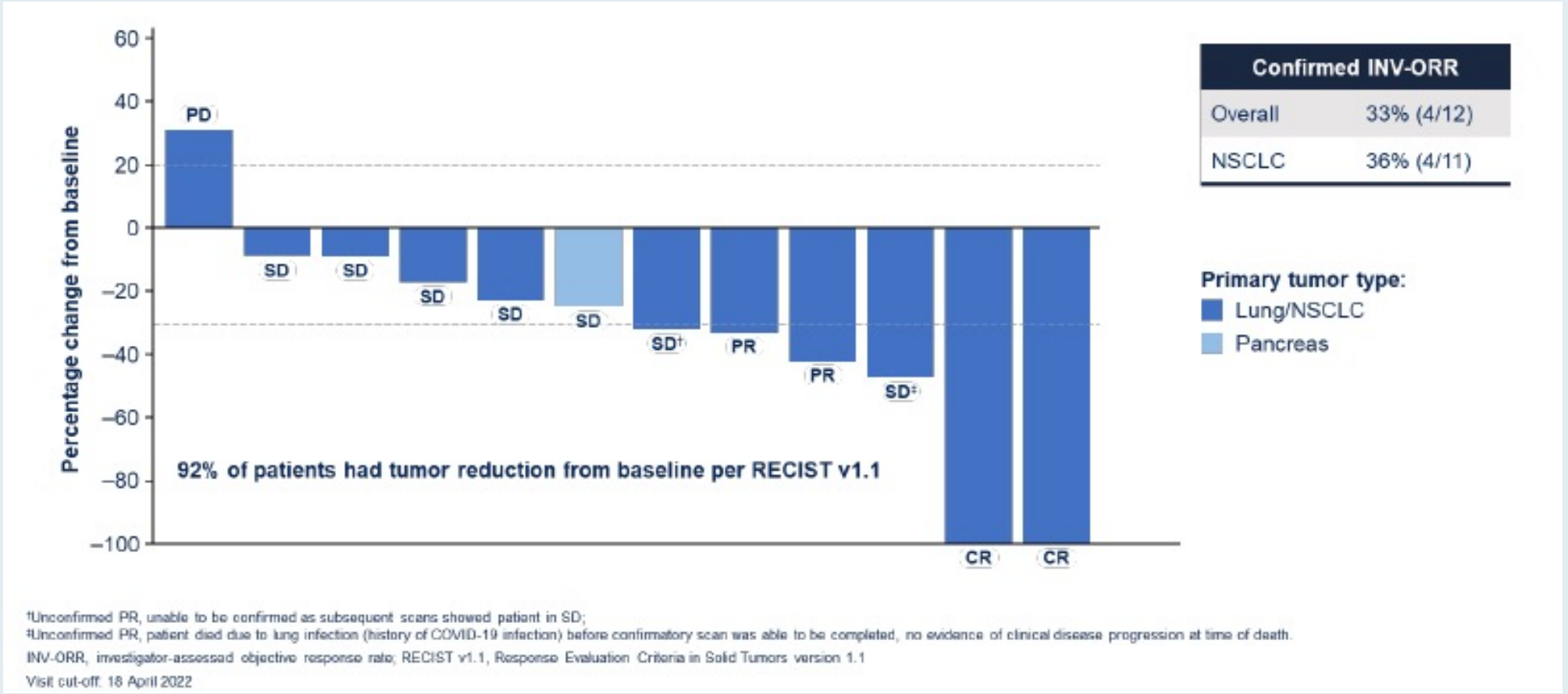
CRESTONE: A Phase II Study of Seribantumab for Patients with Advanced Solid Tumors Harboring NRG1 Fusions



QW = once weekly; ORR = objective response rate; DOR = duration of response; PFS = progression-free survival; OS = overall survival; CBR = clinical benefit rate; CR = complete response; PR = partial response; SD = stable disease

Carrizosa DR et al. ASCO 2022;Abstract 3006.

CRESTONE: Efficacy of Seribantumab for Patients with Advanced Solid Tumors Harboring NRG1 Fusions



PD = progressive disease; SD = stable disease; PR = partial response; CR = complete response

- Median DoR has not been reached

Carrizosa DR et al. ASCO 2022;Abstract 3006.

CRESTONE: Select Treatment-Related Adverse Events with Seribantumab in Patients with Advanced Solid Tumors Harboring NRG1 Fusions

Treatment-related adverse event (N = 35)	Any grade	Grade ≥3
Patients with ≥1 AE	30 (86%)	2 (6%)
Diarrhea	14 (40%)	1 (3%)
Fatigue	10 (29%)	0
Rash	9 (26%)	0
Hypokalemia	3 (9%)	0

Carrizosa DR et al. ASCO 2022;Abstract 3006.

Lung Cancer Agenda

Module 1: Immunotherapy in Patients with Non-Small Cell Lung Cancer (NSCLC) without Targetable Mutations

Module 2: Targeted Treatment of NSCLC

Module 3: Small Cell Lung Cancer

- First-line IO/chemotherapy: Durvalumab versus atezolizumab; role of trilaciclib
- Second-line treatment: Current clinical role of lurbinectedin

original reports

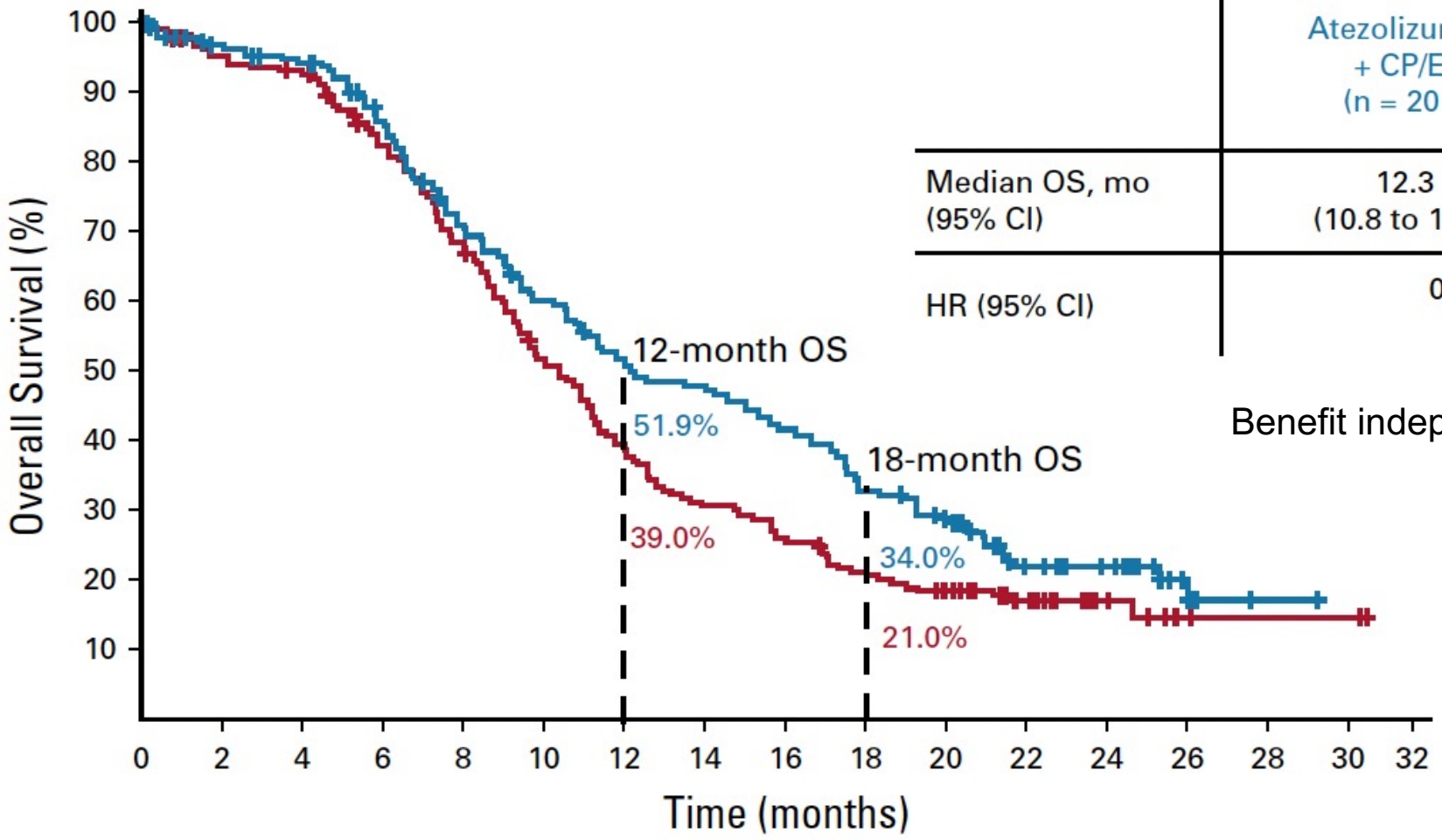
Updated Overall Survival and PD-L1 Subgroup Analysis of Patients With Extensive-Stage Small-Cell Lung Cancer Treated With Atezolizumab, Carboplatin, and Etoposide (IMpower133)

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

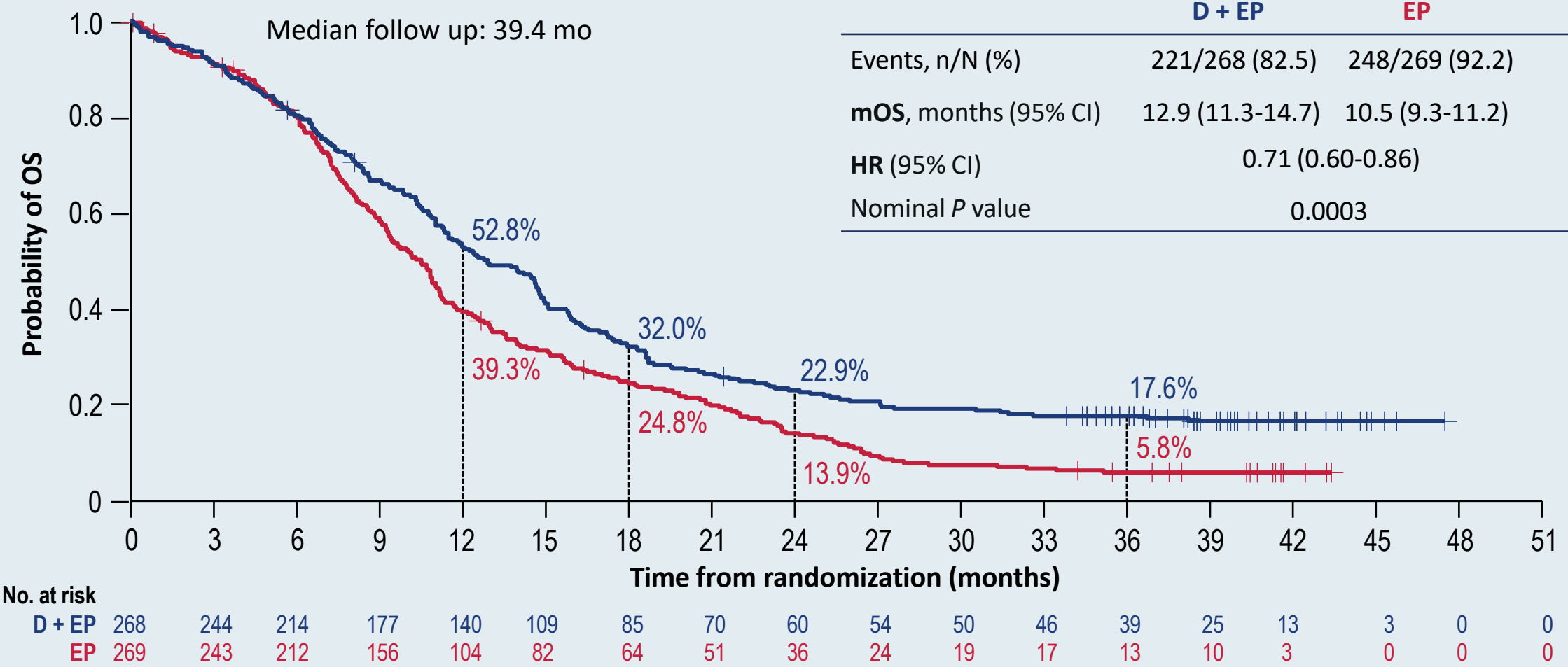
Liu SV et al. *J Clin Oncol* 2021;39(6):619-30.

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

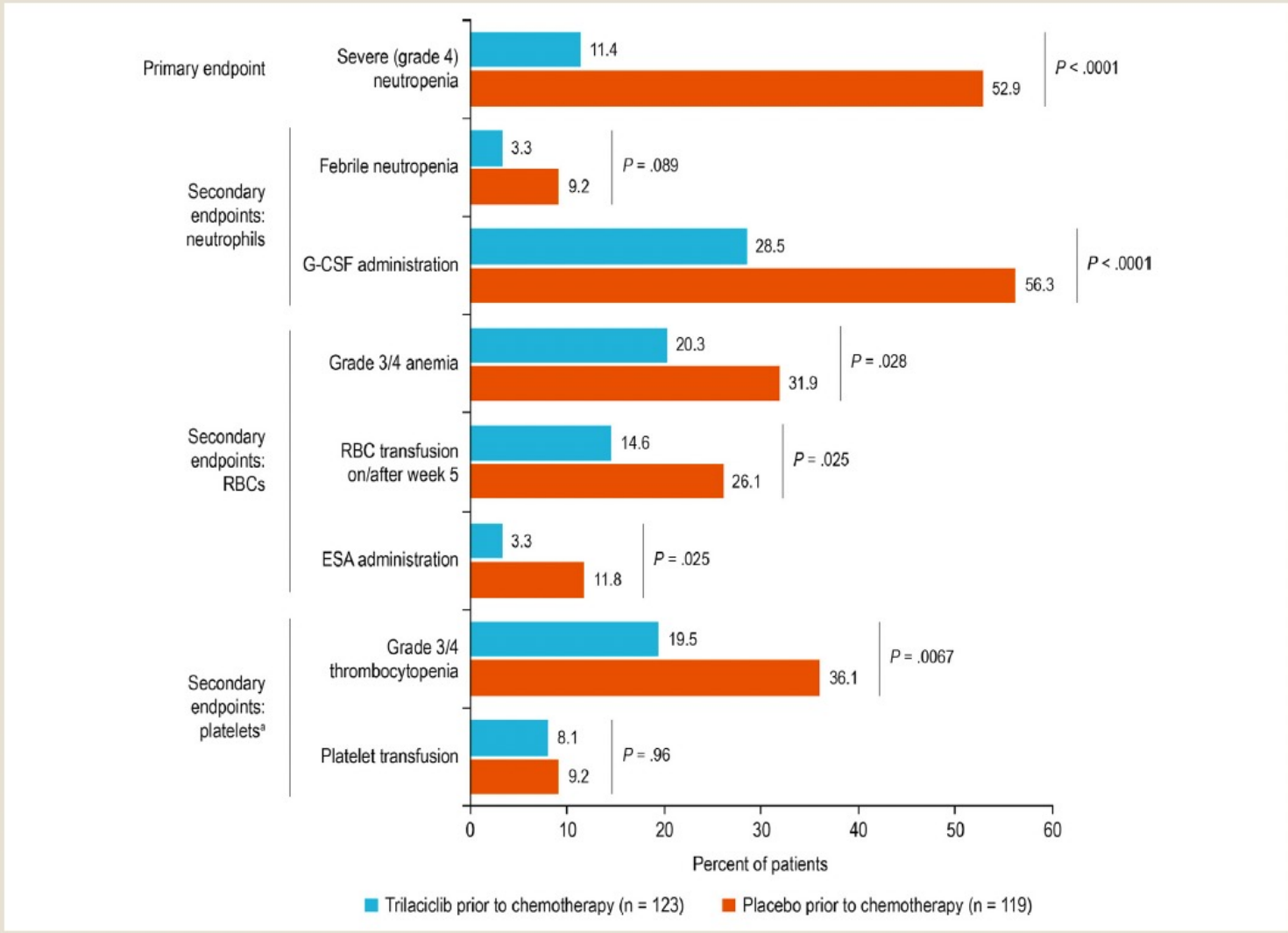
Clin Lung Cancer 2021;22(5):449-60.

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



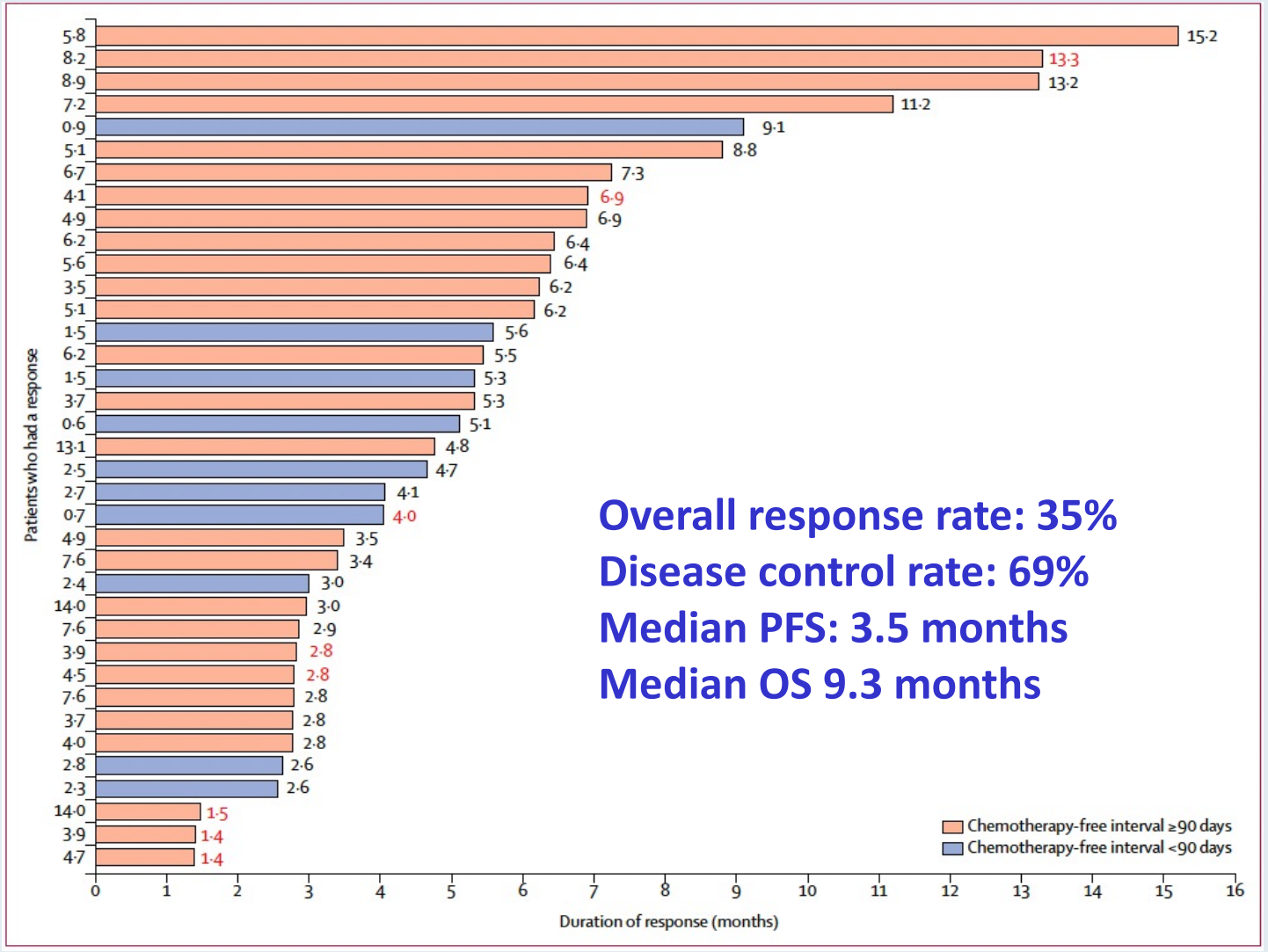
Weiss J et al. *Clin Lung Cancer* 2021;22(5):449-60.

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 1 Line of Chemotherapy



Overall response rate: 35%
Disease control rate: 69%
Median PFS: 3.5 months
Median OS 9.3 months

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

SKYSCRAPER-02: Primary Results of a Phase III, Randomized, Double-Blind, Placebo-Controlled Study of Atezolizumab (atezo) + Carboplatin + Etoposide (CE) with or without Tiragolumab (tira) in Patients (pts) with Untreated Extensive-Stage Small Cell Lung Cancer (ES-SCLC)

Rudin CM et al.

ASCO 2022;Abstract LBA8507.

SKYSCRAPER-02: Primary Survival Analysis

	Primary analysis set		Full analysis set	
	Tira + atezo + CE (n = 196)	Pbo + atezo + CE (n = 201)	Tira + atezo + CE (n = 243)	Pbo + atezo + CE (n = 247)
Median PFS	5.4 mo	5.6 mo	5.1 mo	5.4 mo
Stratified HR (*p*-value)	1.11 (0.3504)		1.08*	
Median OS	13.6 mo	13.6 mo	13.1 mo	12.9 mo
Stratified HR (*p*-value)	1.04 (0.7963)		1.02*	

* Not formally tested in full analysis set

Rubin CM et al. ASCO 2022;Abstract LBA8507.

Thank you for joining us!

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