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

Tuesday, August 9, 2022

5:00 PM – 6:30 PM ET

Faculty

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

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Meet The Professor

Optimizing the Management of Small Cell Lung Cancer

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

Faculty

Jacob Sands, MD

Moderator

Neil Love, MD

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In-Person and Zoom Audience Clinician Survey

In-person audience

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

Zoom participants

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

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Agenda

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

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

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

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

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

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

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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

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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 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)

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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)

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Chronic Lymphocytic Leukemia and Lymphomas Agenda

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Module 2: Chronic Lymphocytic Leukemia (CLL)

Module 3: Hodgkin Lymphoma

Module 4: Mantle Cell Lymphoma (MCL)

Module 5: Follicular Lymphoma (FL)

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Discussion Question

Regulatory and reimbursement issues aside, which first-line therapy would you generally recommend for an otherwise healthy, younger patient with Stage IV GCB-subtype diffuse large B-cell lymphoma (DLBCL)?

- R-CHOP
- R-CHP + polatuzumab vedotin
- Dose-adjusted R-EPOCH
- Other

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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

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TO PRACTICE

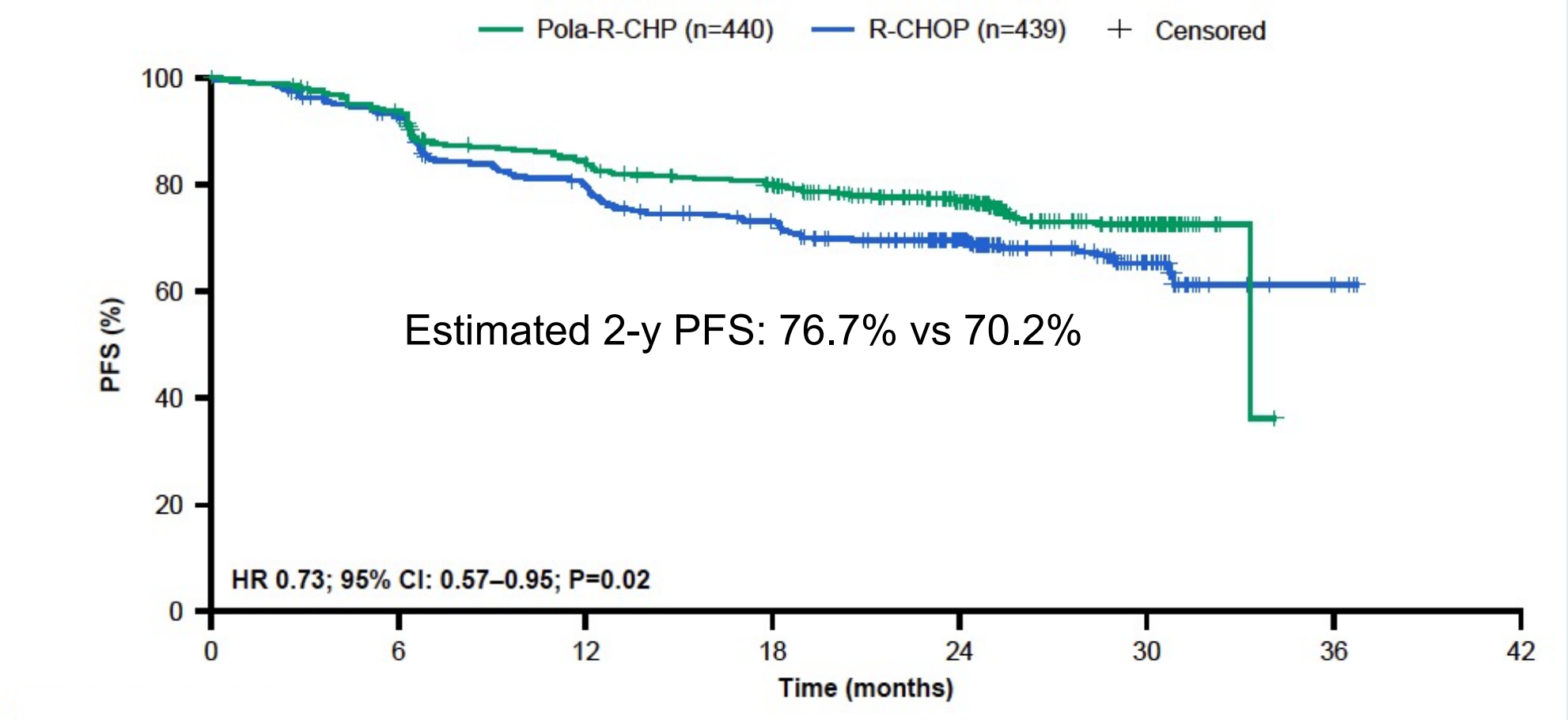
Polatuzumab Vedotin plus Rituximab, Cyclophosphamide, Doxorubicin, and Prednisone (Pola-R-CHP) Versus Rituximab, Cyclophosphamide, Doxorubicin, Vincristine and Prednisone (R-CHOP) Therapy in Patients with Previously Untreated Diffuse Large B-cell Lymphoma (DLBCL): Results from the Phase III POLARIX Study

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

RTP RESEARCH TO PRACTICE

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



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

RTP RESEARCH TO PRACTICE

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]

RTP RESEARCH TO PRACTICE

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
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Discussion Question

For patients with relapsed/refractory DLBCL to whom you are planning to administer CAR T-cell therapy, do you generally have a preference for which agent will be utilized?

- No
- Yes, axicabtagene ciloleucel
- Yes, lisocabtagene maraleucel
- Yes, tisagenlecleucel
- I don’t know

RTP RESEARCH TO PRACTICE

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

RTP RESEARCH TO PRACTICE

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

RTP RESEARCH TO PRACTICE

Lisocabtagene maraleucel as second-line therapy in adults with relapsed or refractory large B-cell lymphoma who were not intended for haematopoietic stem cell transplantation (PILOT): An open-label, phase 2 study

Alison Sehgal, Daanish Hoda, Peter A Riedell, Nilanjan Ghosh, Mehdi Hamadani, Gerhard C Hildebrandt, John E Godwin, Patrick M Reagan, Nina Wagner-Johnston, James Essell, Rajneesh Nath, Scott R Solomon, Rebecca Champion, Edward Licitra, Suzanne Fanning, Neel Gupta, Ronald Dubowy, Aleco D'Andrea, Lei Wang, Ken Ogasawara, Jerill Thorpe, Leo I Gordon

Summary

Background Patients with relapsed or refractory large B-cell lymphoma after first-line treatment who are not intended for haematopoietic stem-cell transplantation (HSCT) have poor outcomes and limited treatment options. We assessed the antitumour activity and safety of lisocabtagene maraleucel, an autologous, CD19-directed chimeric antigen receptor (CAR) T-cell product, as second-line treatment in adults with relapsed or refractory large B-cell lymphoma not intended for HSCT.

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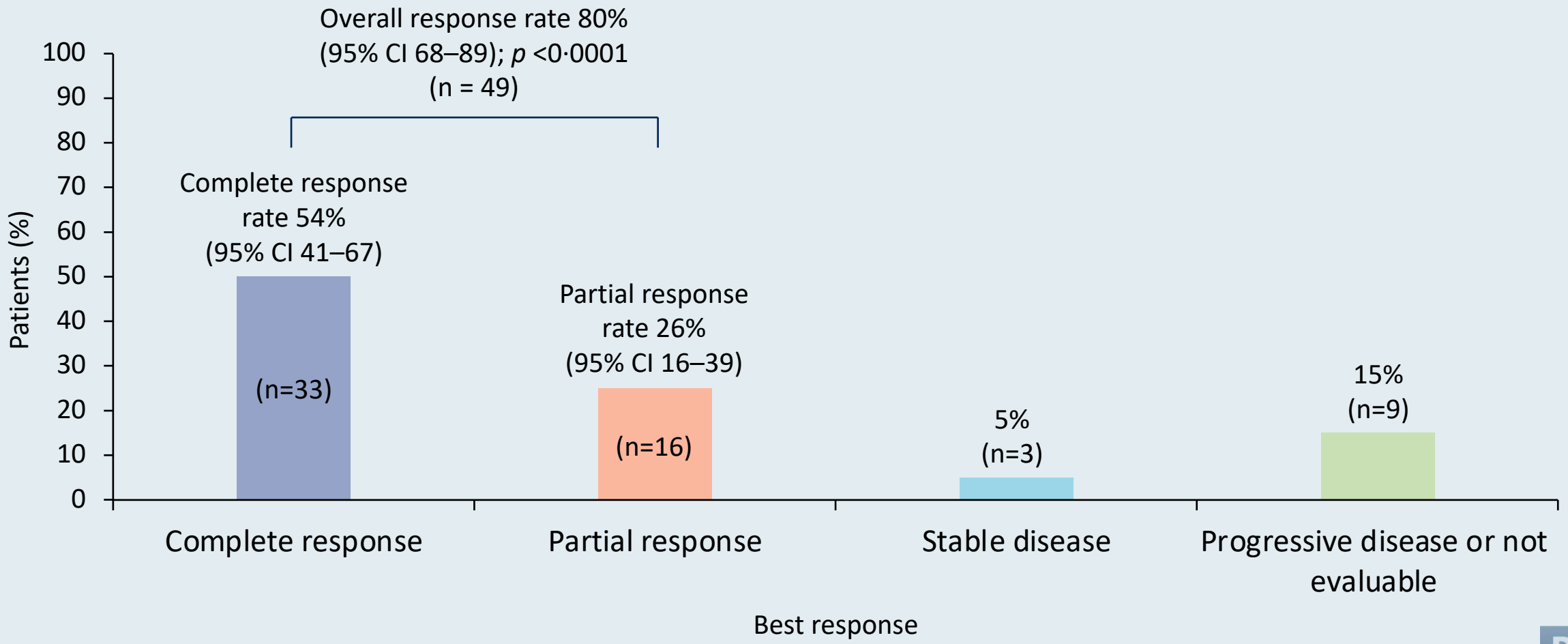
Best response by independent review committee assessment in the efficacy analysis set



* Including one patient in the efficacy analysis set who was not evaluable for response.

Patients who received lisocabtagene maraleucel (n = 61)

Transplantation not intended criteria	
Cytokine release syndrome	30 (49%)
Any grade	23 (38%)
Grade 1	11 (18%)
Grade 2	11 (18%)
Grade 3	1 (2%)
Grade 4 or 5	0
Time to onset,* days	4 (3-7)
Time to resolution,† days	4 (2-5)
Tocilizumab, corticosteroids, or both for cytokine release syndrome‡	16 (26%)
Tocilizumab only	6 (10%)
Tocilizumab and corticosteroids	10 (16%)
Corticosteroids only	0

* Time to onset was calculated from the lisocabtagene maraleucel infusion date to the first onset of cytokine release syndrome or a neurological event. Any cytokine release syndrome or a neurological event that started and stopped within 7 days was considered as a single episode.

† Time to resolution of cytokine release syndrome or a neurological event was defined as the number of days from onset to when the last event of the first episode ended. Patients with an unresolved event in the first episode were excluded from the summary.

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

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

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

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

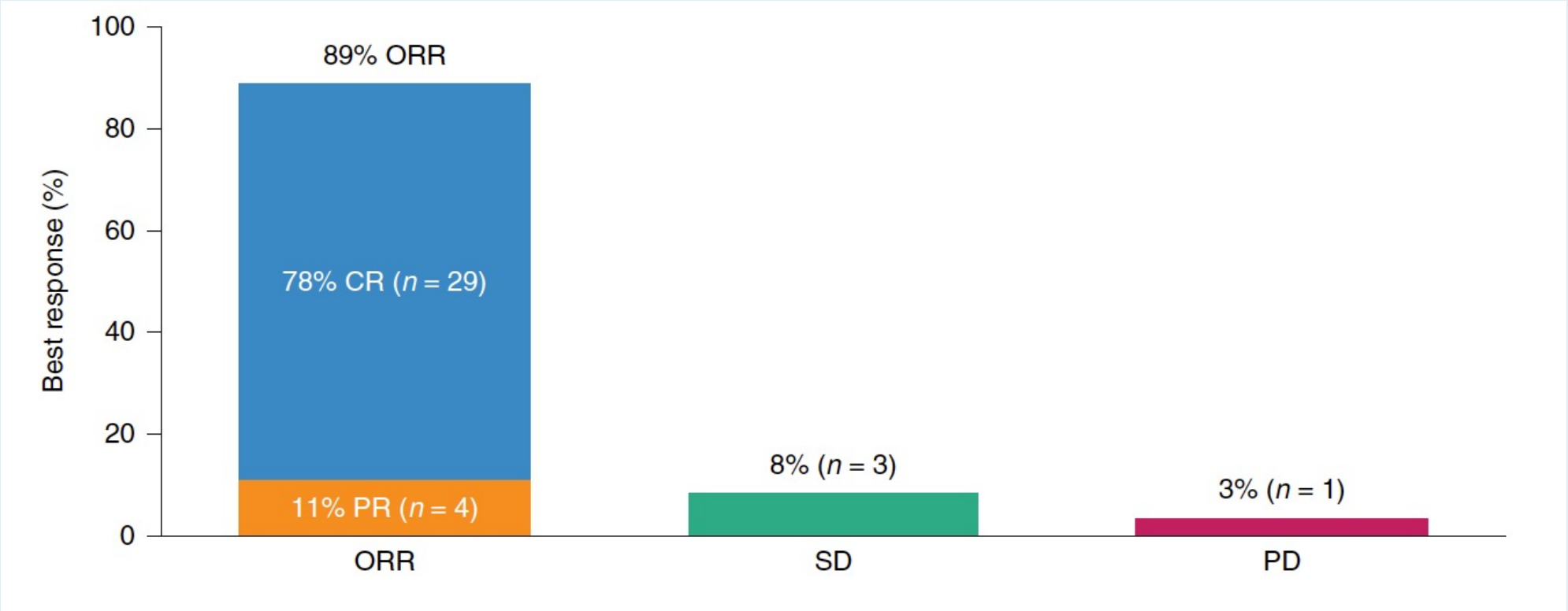
Sattva S. Neelapu[1]✉, Michael Dickinson[2], Javier Munoz[3], Matthew L. Ulrickson[3], Catherine Thieblemont[4,5], Olalekan O. Oluwole[6], Alex F. Herrera[7], Chaitra S. Ujjani[8], Yi Lin[9], Peter A. Riedell[10], Natasha Kekre[11], Sven de Vos[12], Christine Lui[13], Francesca Milletti[13], Jinghui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

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

RTP RESEARCH TO PRACTICE

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.

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

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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]

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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]

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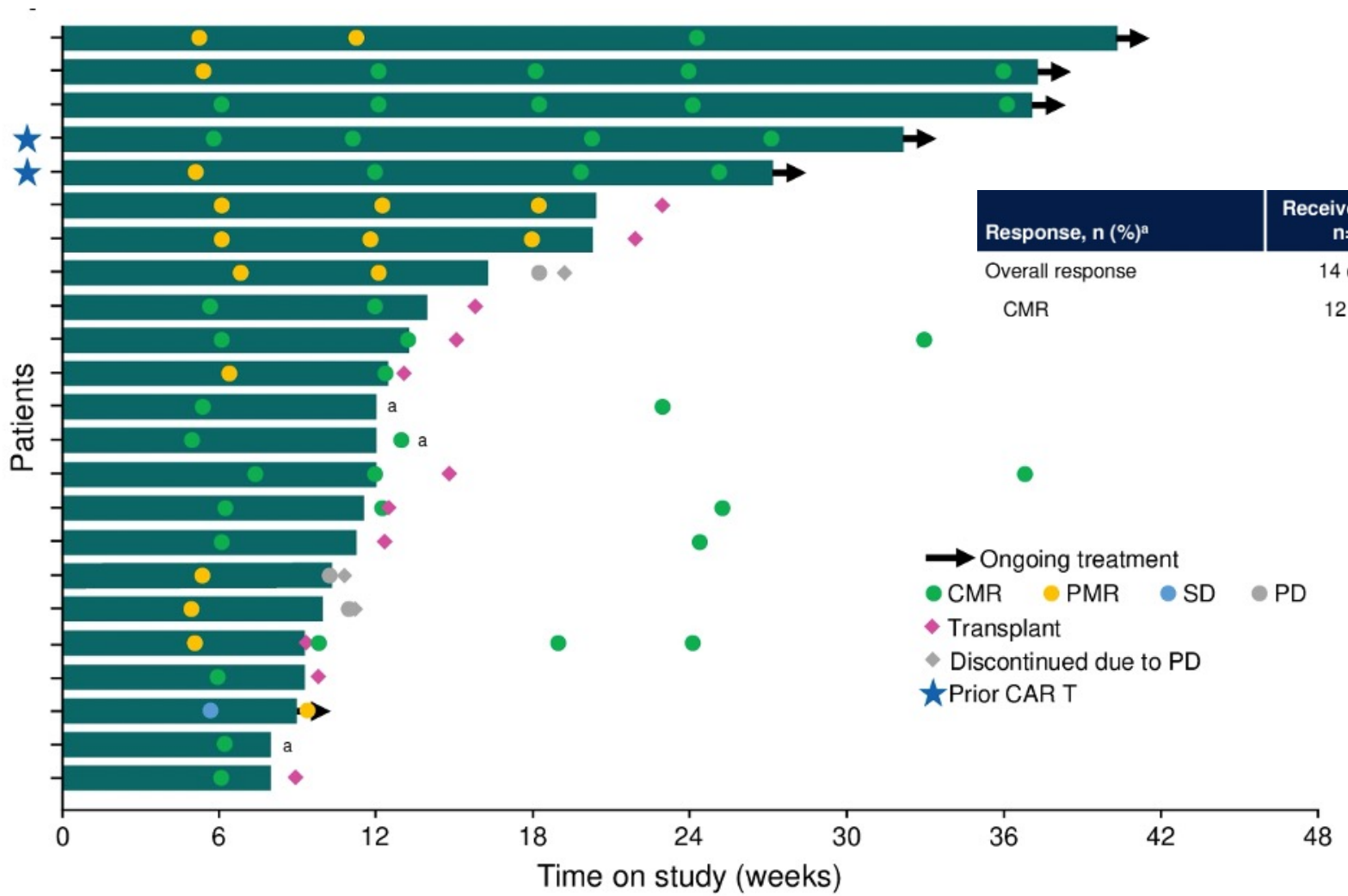
EPCORE NHL-2 Arm 4: Response Profile



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.

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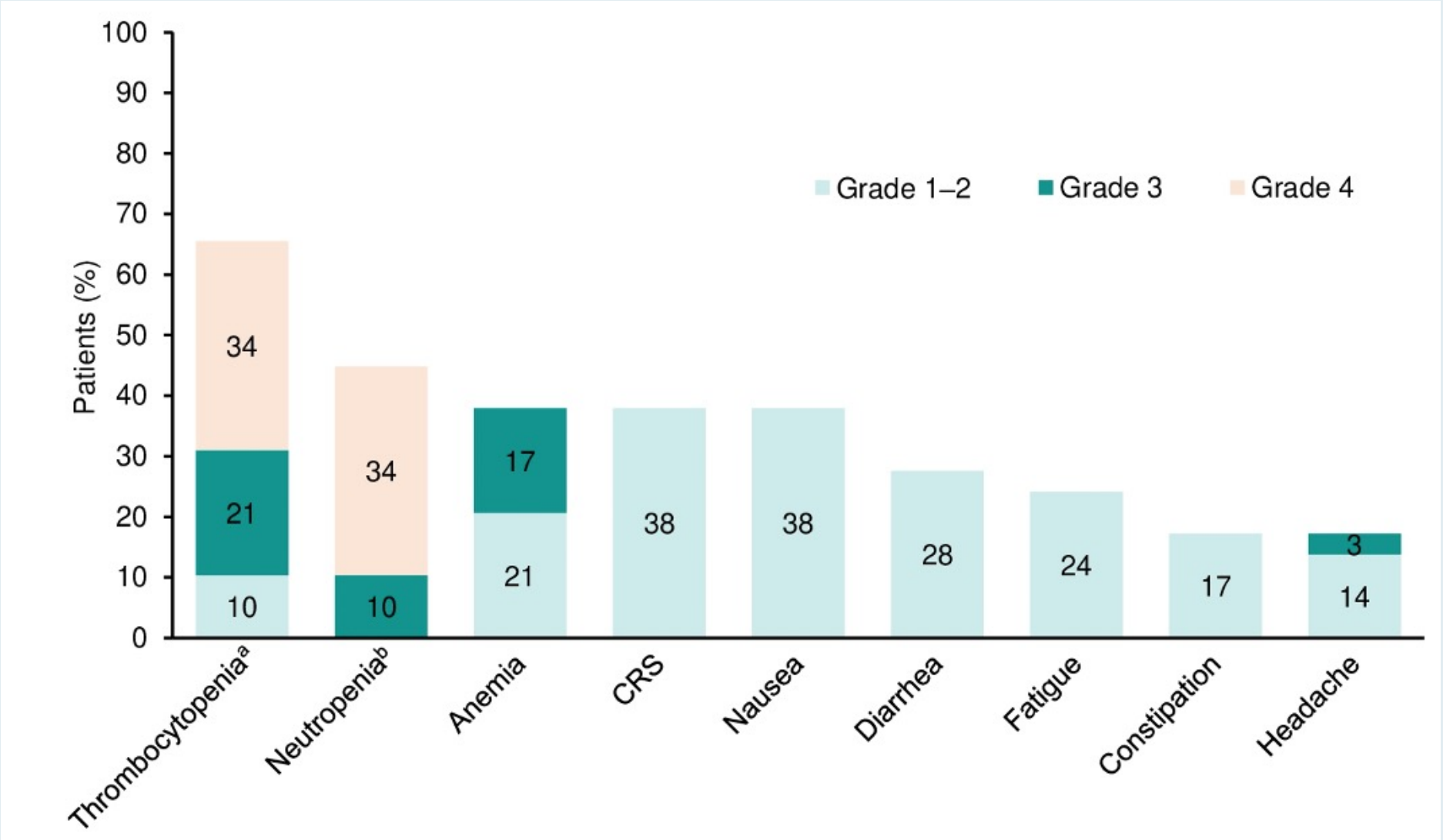
EPCORE NHL-2 Arm 4: Treatment-Emergent Adverse Events (≥15%)



Abrisqueta P et al. ASCO 2022;Abstract 7528.

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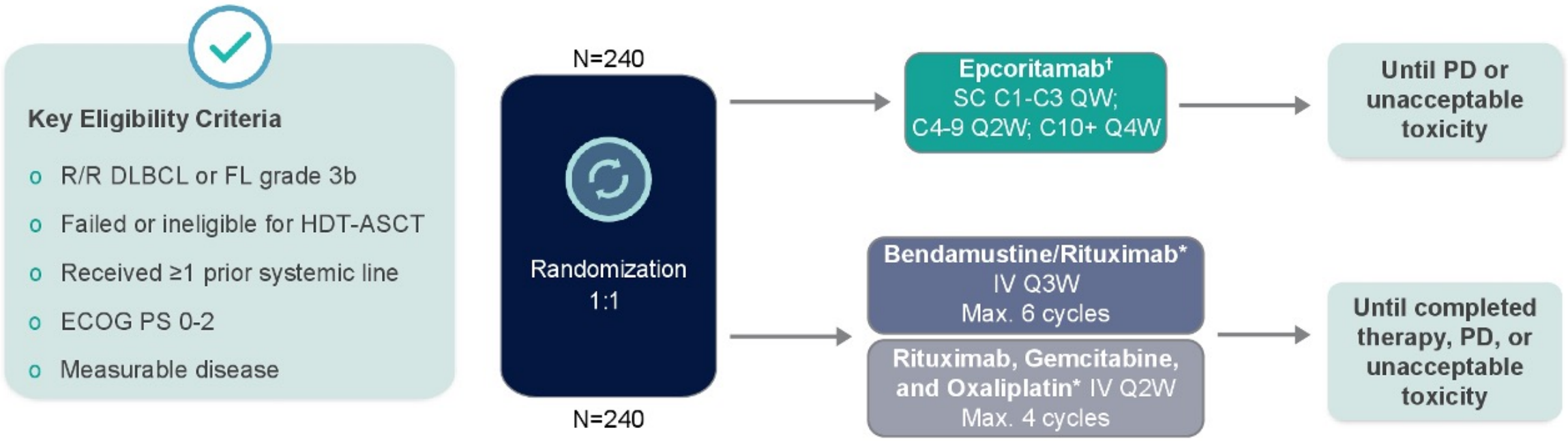
EPCORE DLBCL-1 Pivotal Phase III Trial Design



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.

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Module 2: Chronic Lymphocytic Leukemia (CLL)

Module 3: Hodgkin Lymphoma

Module 4: Mantle Cell Lymphoma (MCL)

Module 5: Follicular Lymphoma (FL)

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Discussion Question

What second-line therapy would you generally recommend for a 77-year-old patient with relapsed DLBCL who is ineligible for CART or autologous stem cell transplant?

- Selinexor
- Loncastuximab tesirine
- Tafasitamab and lenalidomide
- Lenalidomide and rituximab
- Polatuzumab/rituximab/bendamustine
- Other

RTP RESEARCH TO PRACTICE

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)

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- Noncovalent BTK inhibitors (pirtobrutinib) in relapsed disease

Module 3: Hodgkin Lymphoma

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Module 5: Follicular Lymphoma (FL)

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Discussion Question

Regulatory and reimbursement issues aside, what would you generally recommend as first-line treatment for a younger symptomatic patient with IGHV-unmutated CLL?

- Acalabrutinib
- Ibrutinib
- Zanubrutinib
- Venetoclax/obinutuzumab
- Ibrutinib/venetoclax
- Other

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Discussion Question

Regulatory and reimbursement issues aside, what would you generally recommend as first-line treatment for an 80-year-old patient with IGHV-unmutated CLL with a history of atrial fibrillation on apixaban?

- Acalabrutinib
- Ibrutinib
- Zanubrutinib
- Chlorambucil
- Chlorambucil/obinotuzumab
- Venetoclax/obinutuzumab
- Ibrutinib/venetoclax
- Other

RTP RESEARCH TO PRACTICE

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.

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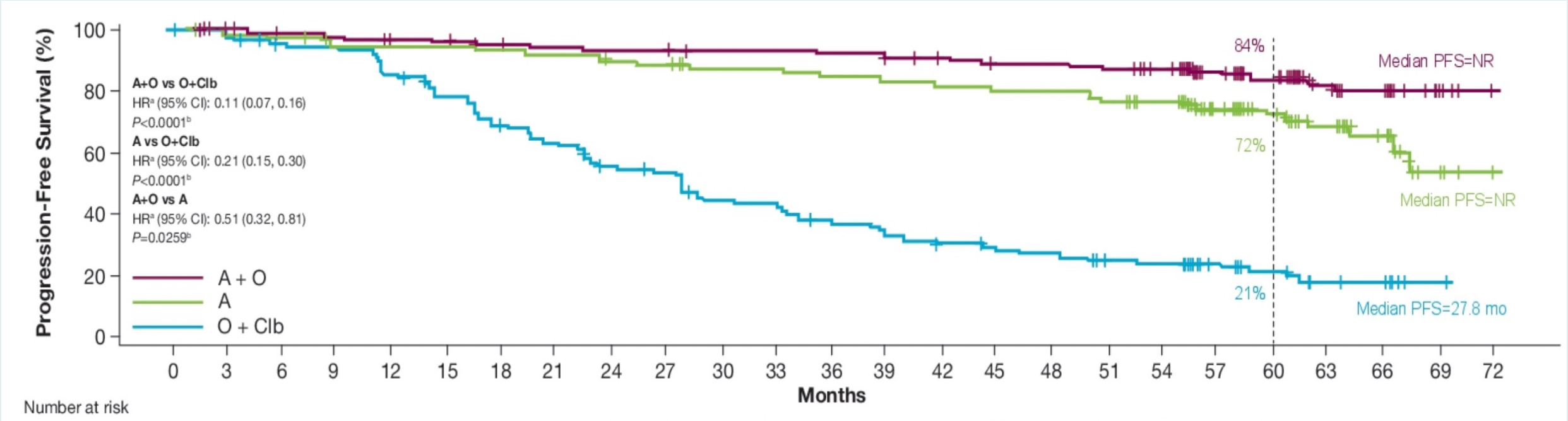
TO PRACTICE

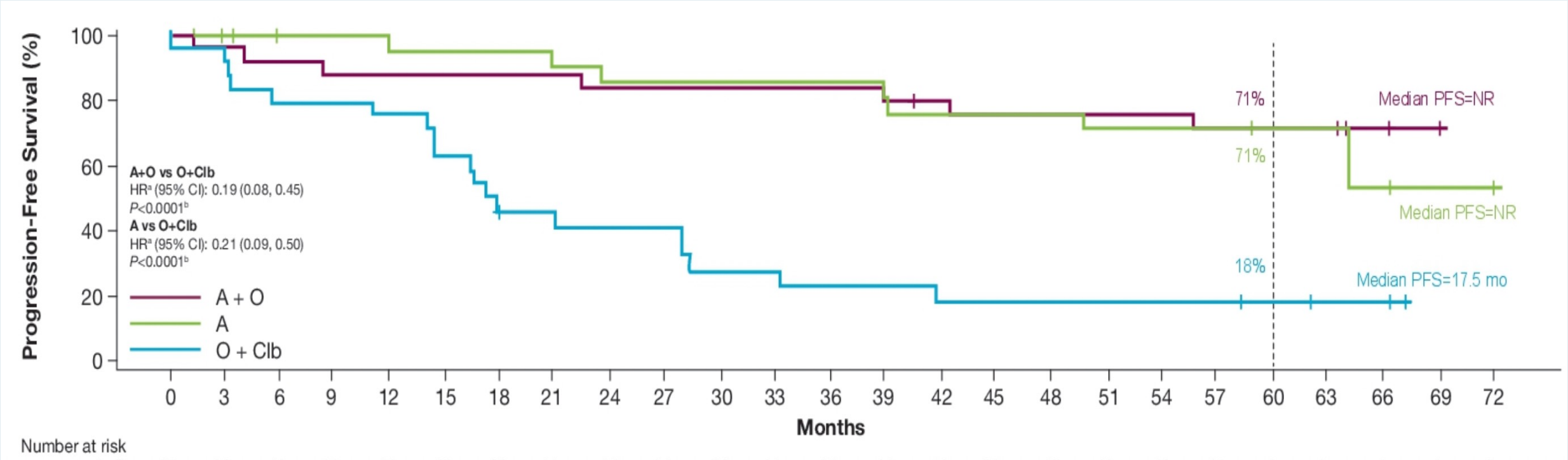
ELEVATE-TN: Investigator-Assessed PFS



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

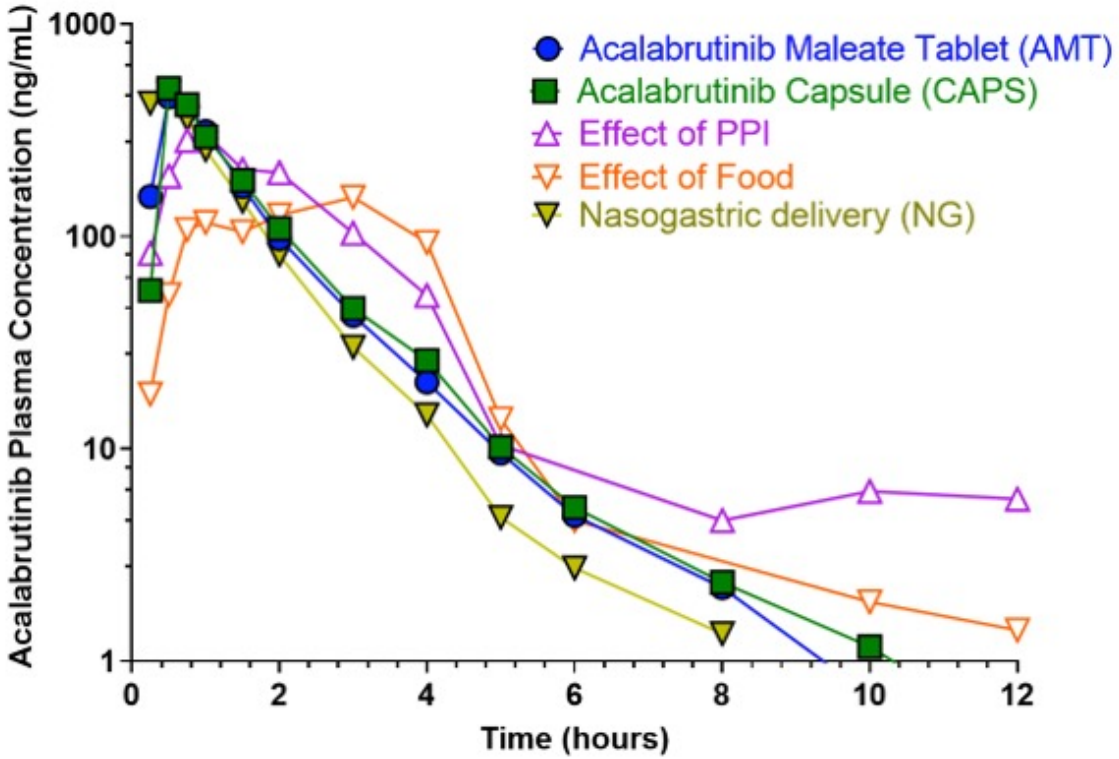
New Acalabrutinib Formulation Enables Co-Administration with Proton Pump Inhibitors and Dosing in Patients Unable to Swallow Capsules (ELEVATE-PLUS)

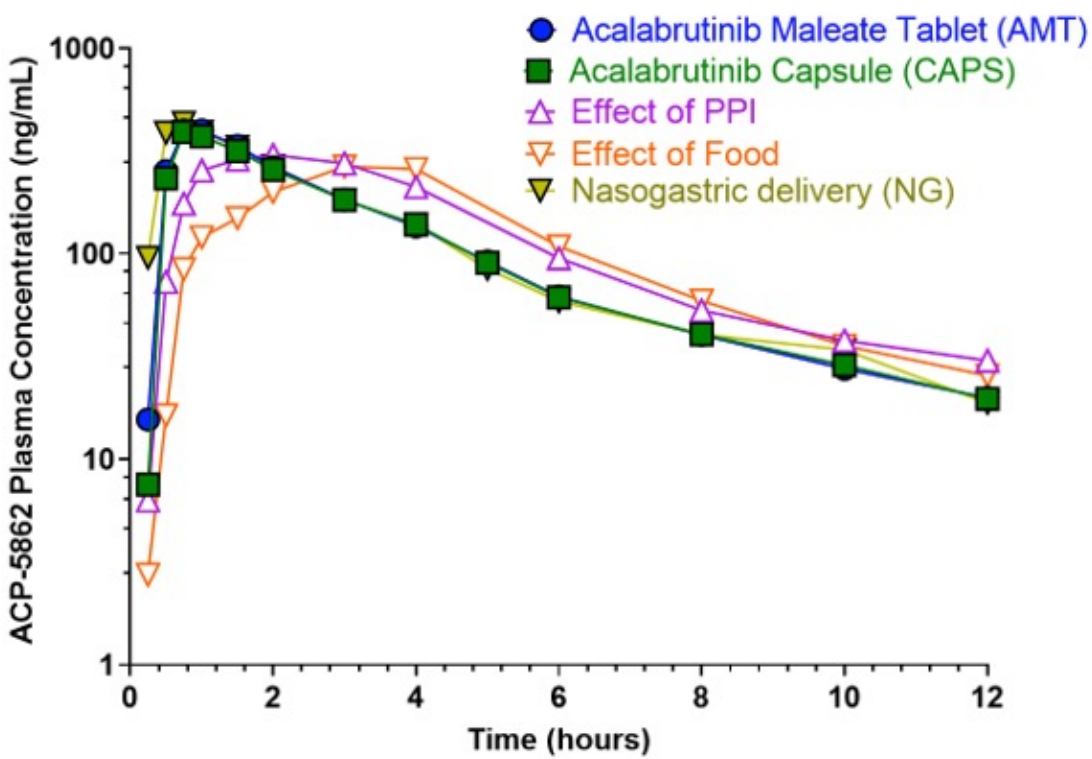
Sharma S et al.

ASH 2021;Abstract 4365.

RTP
RESEARCH
TO PRACTICE

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





Sharma S et al. ASH 2021;Abstract 4365.

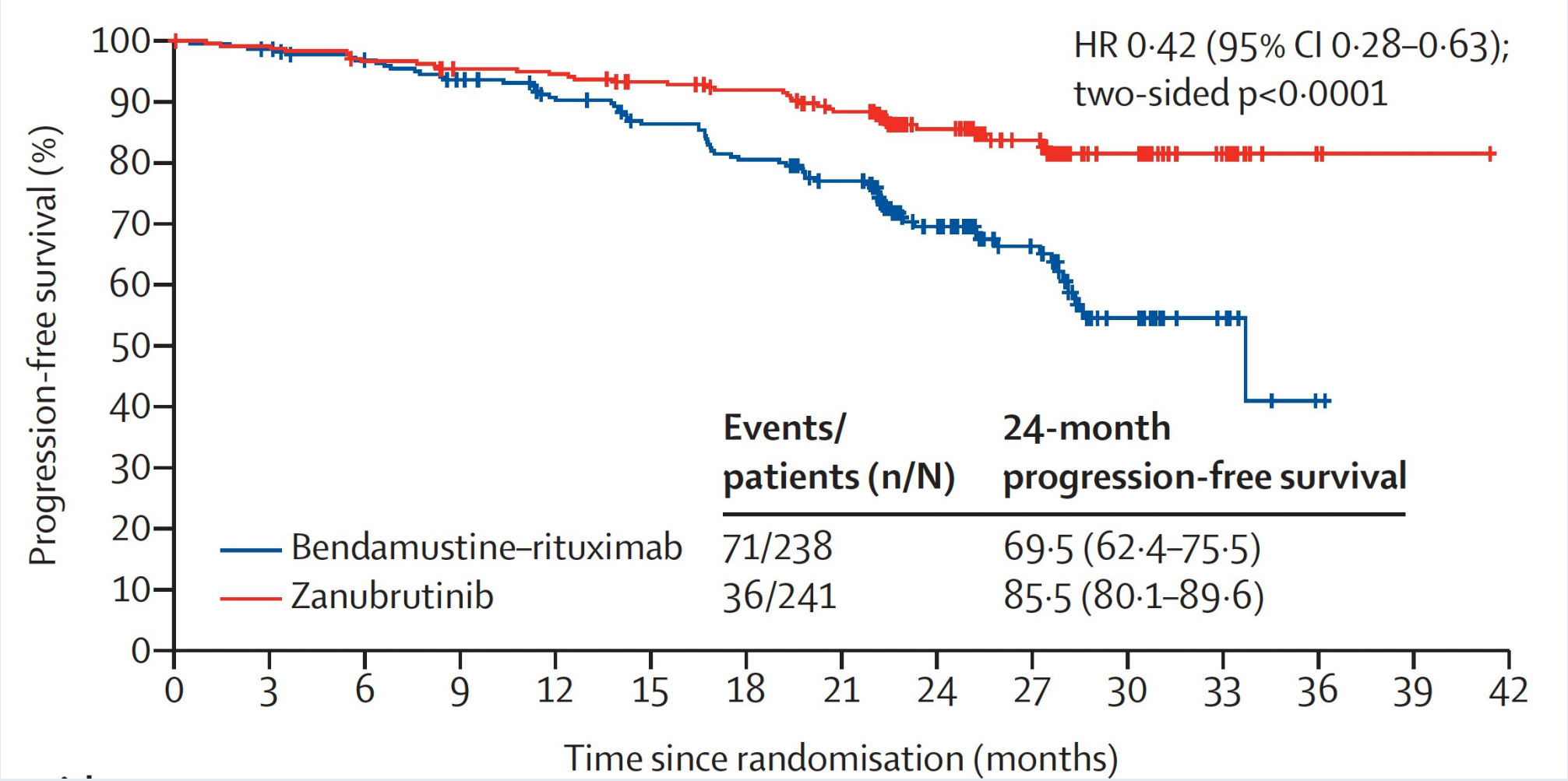
RTP RESEARCH TO PRACTICE

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].

RTP RESEARCH TO PRACTICE

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

DEUTSCHE STUDIENGRUPPE

Abstract S148

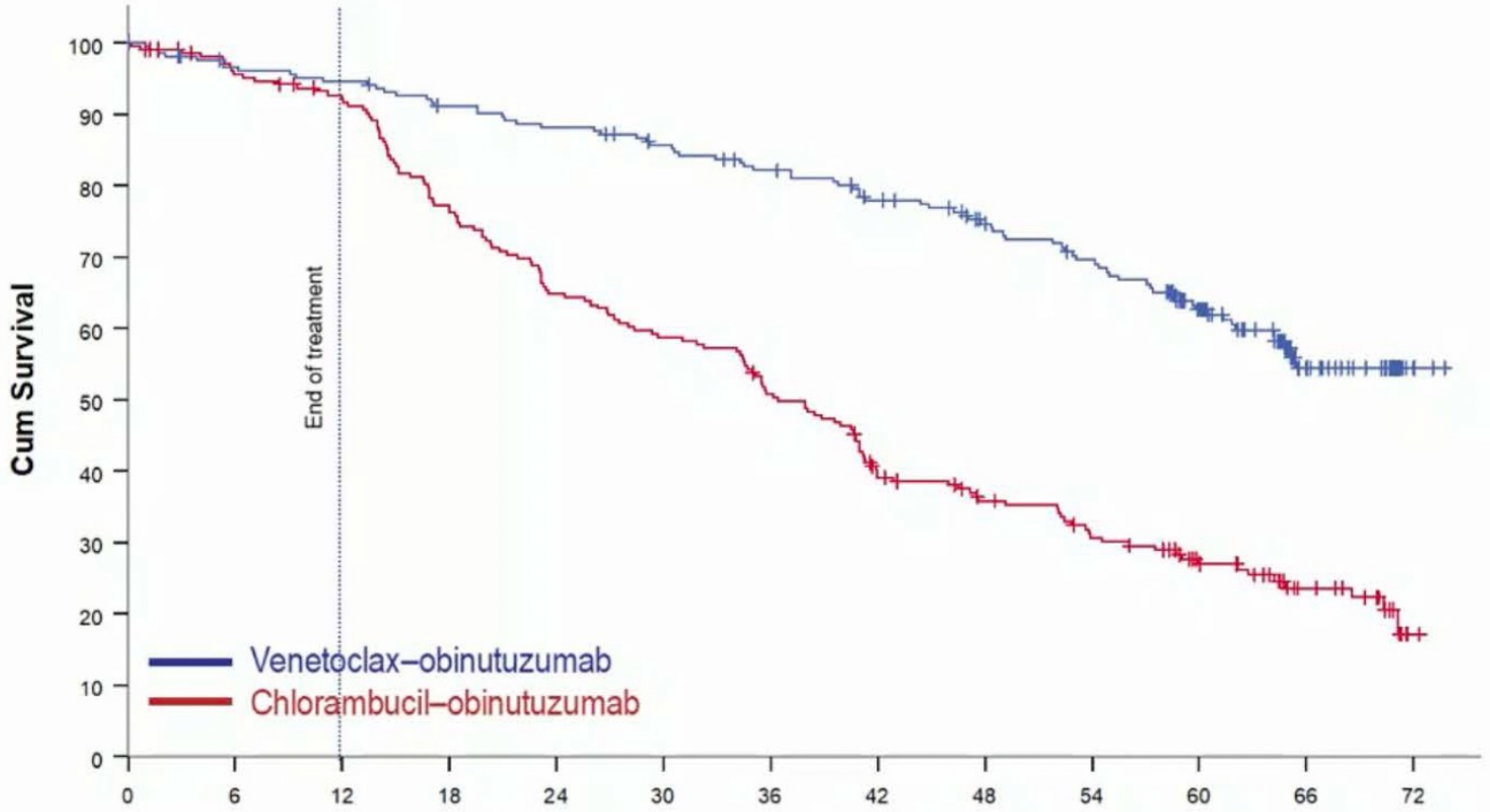
Venetoclax-Obinutuzumab for previously untreated chronic lymphocytic leukemia: 5-year results of the randomized CLL14 study

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

RTP RESEARCH TO PRACTICE

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

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

Rogers KA et al.

ASCO 2022;Abstract 7540.

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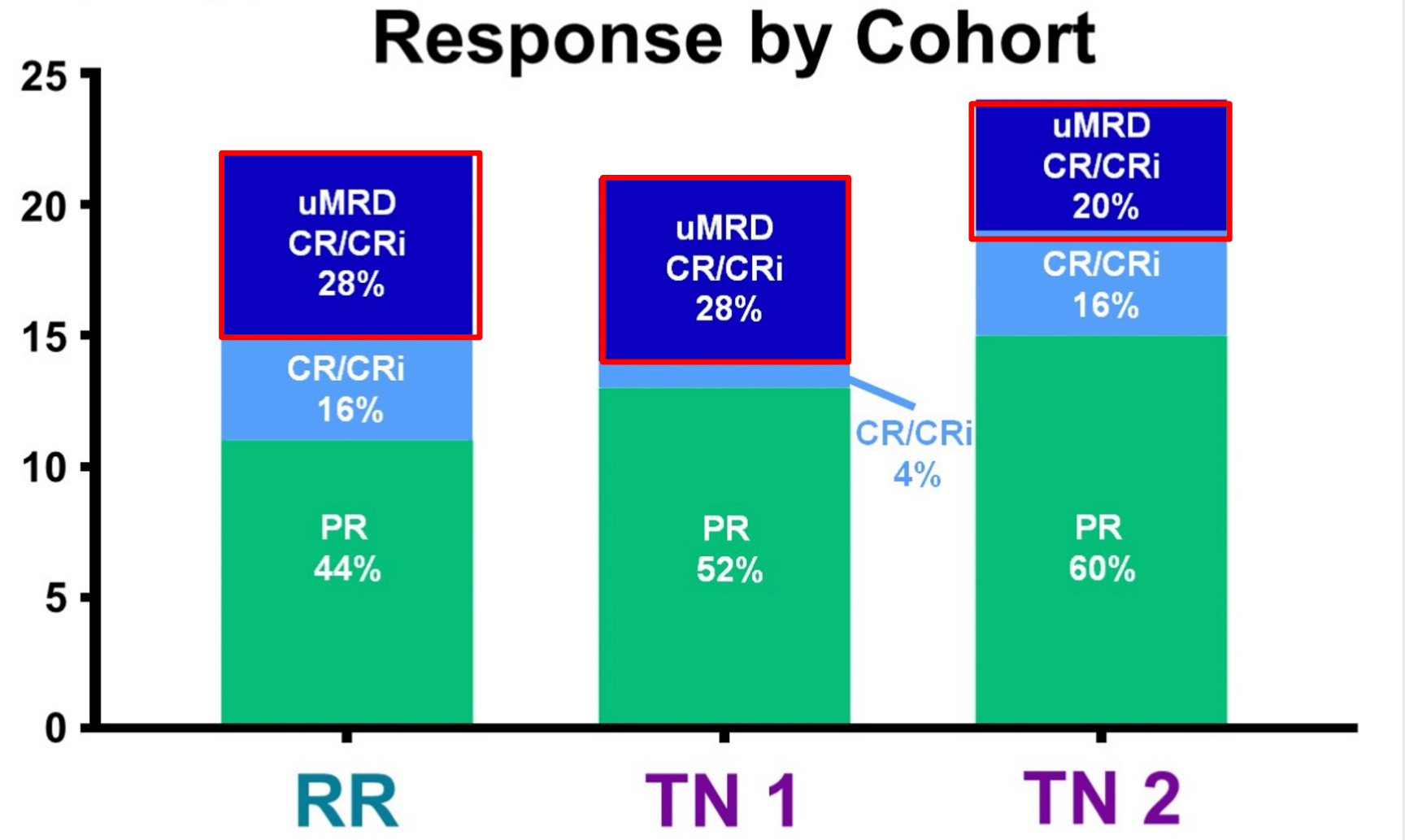
Primary Endpoint: Complete Response with Undetectable MRD (uMRD)



Rogers KA et al. ASCO 2022;Abstract 7540.

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

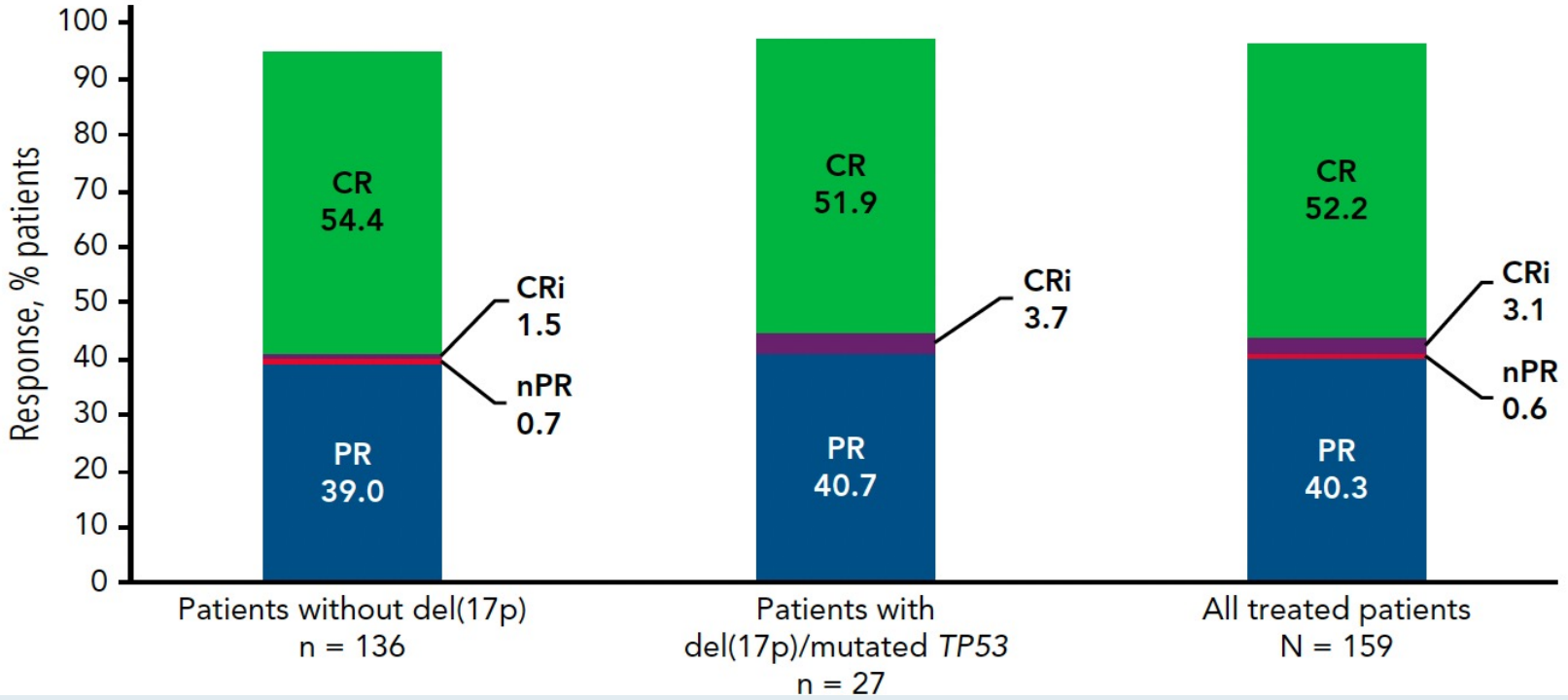
Fixed-duration ibrutinib plus venetoclax for first-line treatment of CLL: primary analysis of the CAPTIVATE FD cohort

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.

NEJM Evidence

Published May 13, 2022

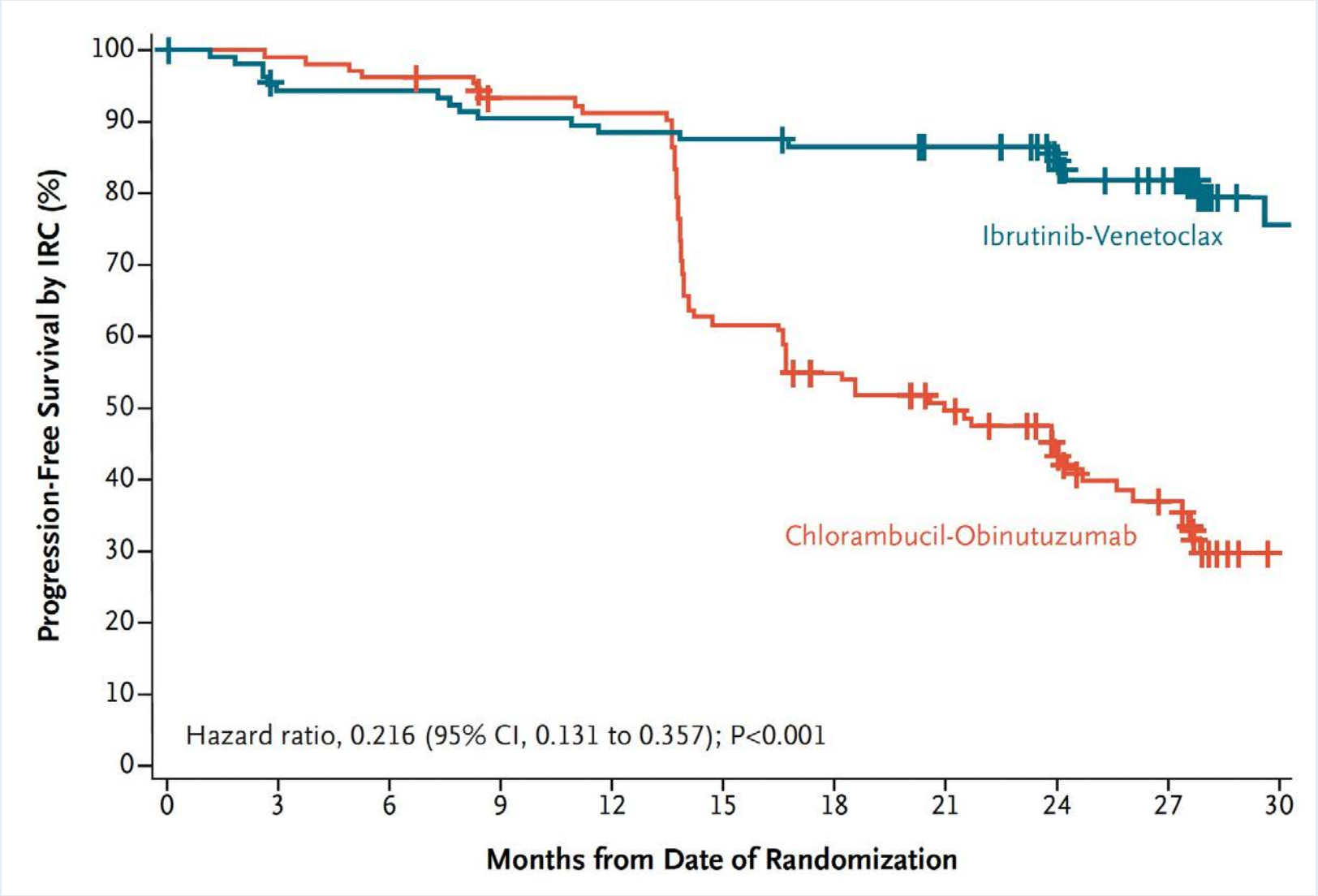
ORIGINAL ARTICLE

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*

RTP RESEARCH TO PRACTICE

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

Discussion Question

Regulatory and reimbursement issues aside and assuming all were available, which therapy would you recommend for a patient with CLL with disease progression on ibrutinib and then on second-line venetoclax/obinutuzumab?

- Chemoimmunotherapy
- Venetoclax + BTK inhibitor
- Idelalisib
- Duvelisib
- Pirtobrutinib
- CAR T-cell therapy
- Other

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.

RTP
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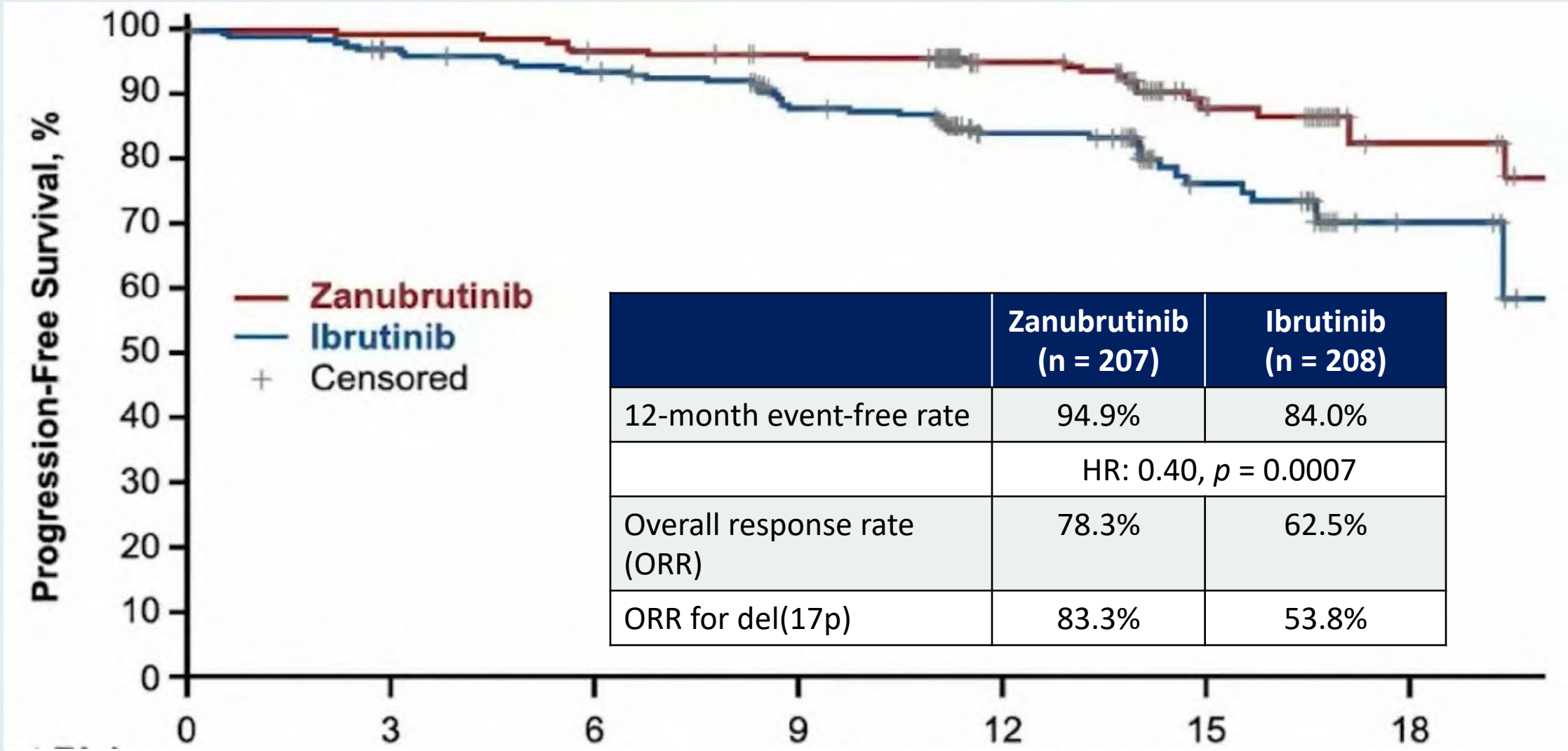
TO PRACTICE

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.

RTP RESEARCH TO PRACTICE

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)

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TO PRACTICE

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]

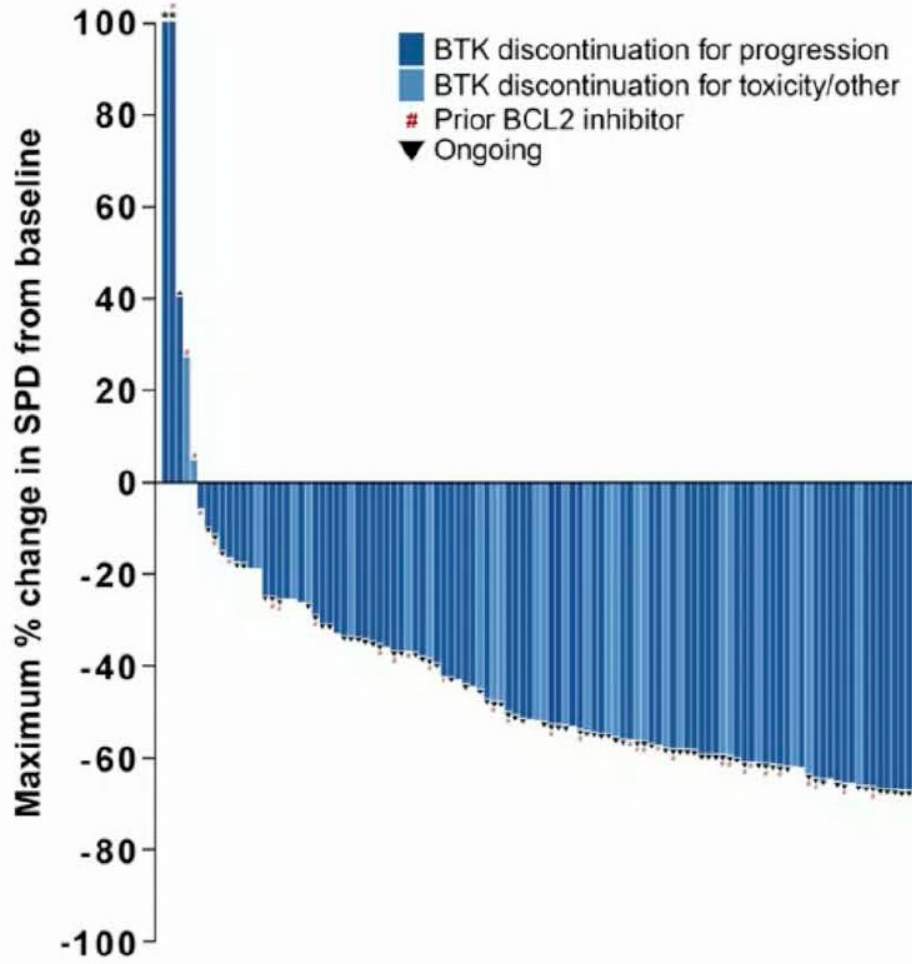
[1]Memorial Sloan Kettering Cancer Center, New York, USA; [2]Swedish Cancer Institute, Seattle, USA; [3]University of North Carolina at Chapel Hill, Chapel Hill, USA; [4]Medical College of Wisconsin, Milwaukee, USA; [5]Herbert Irving Comprehensive Cancer Center, Columbia University, New York, USA; [6]Department 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

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

Chronic Lymphocytic Leukemia and Lymphomas Agenda

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

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Module 4: Mantle Cell Lymphoma (MCL)

Module 5: Follicular Lymphoma (FL)

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Discussion Question

What initial treatment would you likely recommend for a younger patient with standard-risk classical Hodgkin lymphoma?

- Doxorubicin/bleomycin/vinblastine/dacarbazine (ABVD)
- PET-adapted ABVD
- Brentuximab vedotin + AVD
- AVD
- BEACOP
- Other

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TO PRACTICE

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

The NEW ENGLAND JOURNAL of MEDICINE

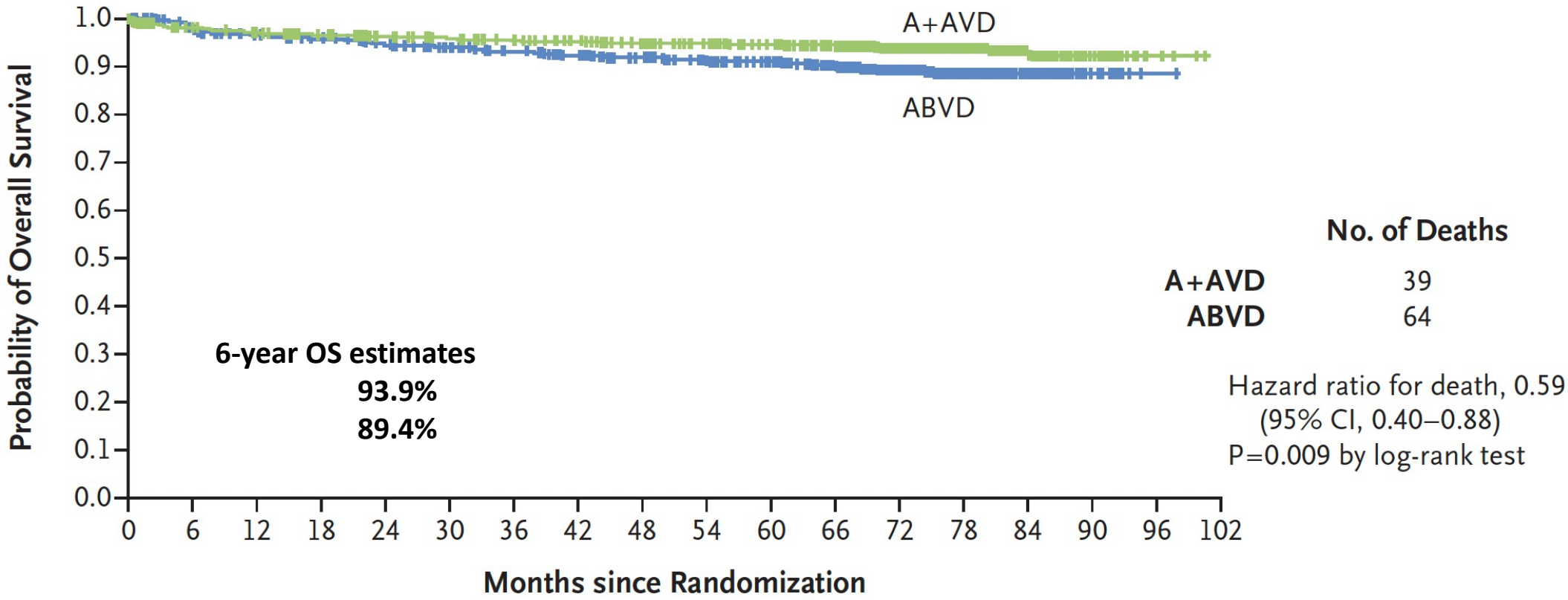
ORIGINAL ARTICLE

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*

RTP RESEARCH TO PRACTICE

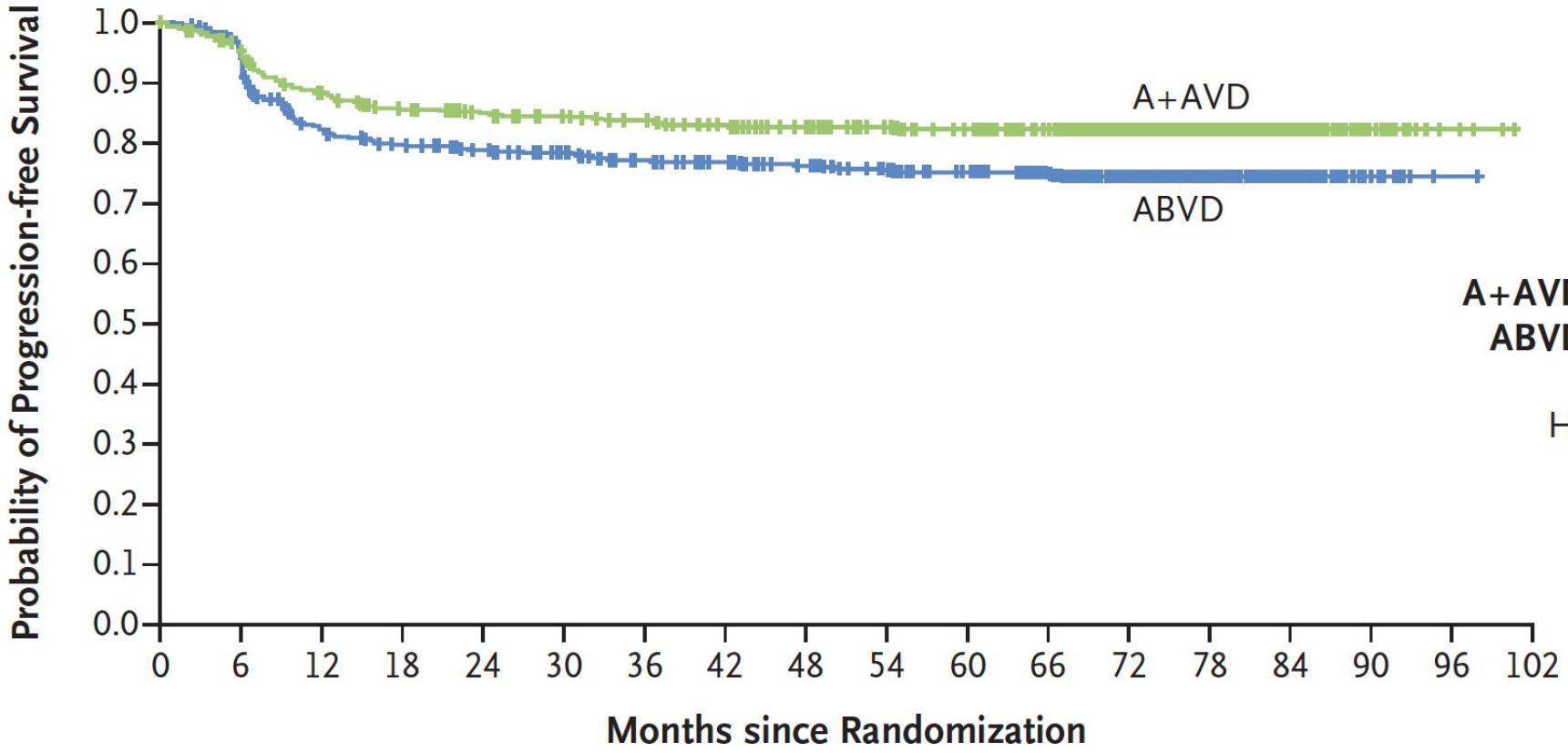
ECHELON-1 Primary Endpoint: Overall Survival (ITT Population)



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].

RTP RESEARCH TO PRACTICE

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

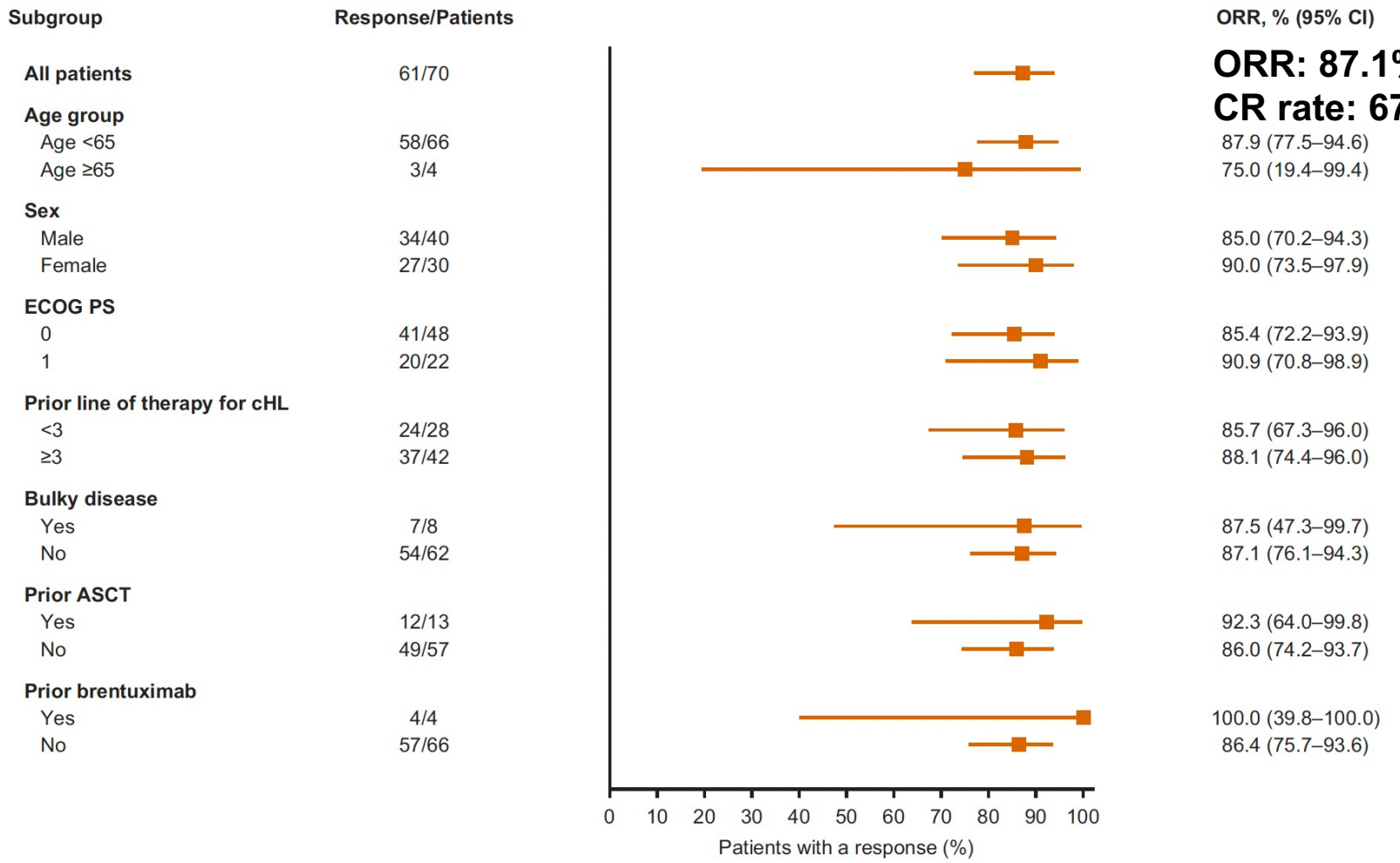
CLINICAL CANCER RESEARCH | CLINICAL TRIALS: IMMUNOTHERAPY

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]

RTP RESEARCH TO PRACTICE

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.

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)

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Discussion Question

What initial treatment would you recommend for a 78-year-old patient with classical Hodgkin lymphoma?

- Brentuximab vedotin
- Brentuximab vedotin/IO
- IO
- Brentuximab vedotin/DTIC
- Other

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Chronic Lymphocytic Leukemia and Lymphomas Agenda

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- 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)

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Module 5: Follicular Lymphoma (FL)

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Discussion Question

Regulatory and reimbursement issues aside, what would be your likely first-line recommendation for an 80-year-old asymptomatic patient with MCL?

- Ibrutinib
- BR/ibrutinib
- BR (bendamustine/rituximab)
- Acalabrutinib/BR
- Acalabrutinib
- Zanubrutinib
- Zanubrutinib/BR
- Other

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Discussion Question

Regulatory and reimbursement issues aside, what would be your preferred next-line therapy for a 65-year-old patient with MCL who experiences disease progression after receiving ibrutinib/BR?

- Venetoclax
- Lenalidomide
- Bortezomib
- CAR T-cell therapy
- Chemotherapy → ASCT
- Other

RTP RESEARCH TO PRACTICE

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.

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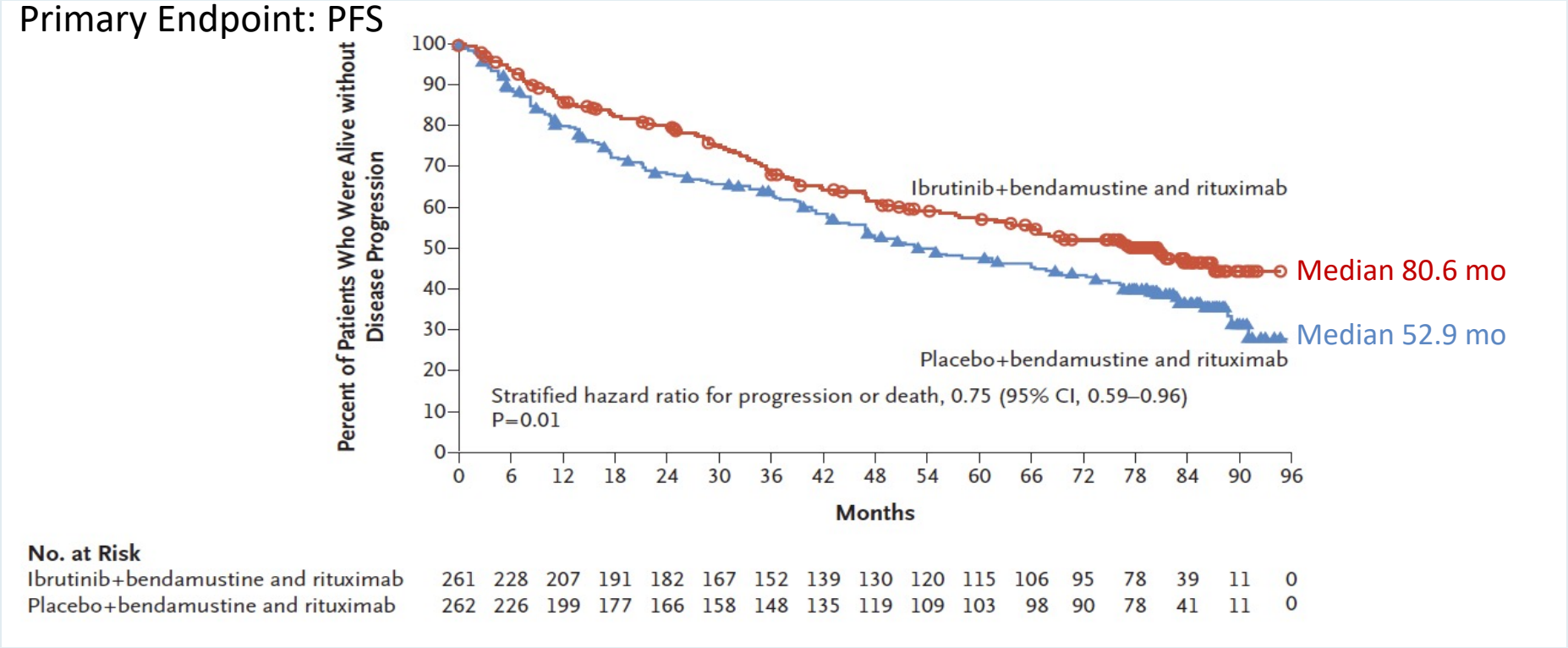
SHINE: A Phase III Trial of Ibrutinib with Bendamustine and Rituximab for MCL

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

Chronic Lymphocytic Leukemia and Lymphomas Agenda

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Module 5: Follicular Lymphoma (FL)

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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.

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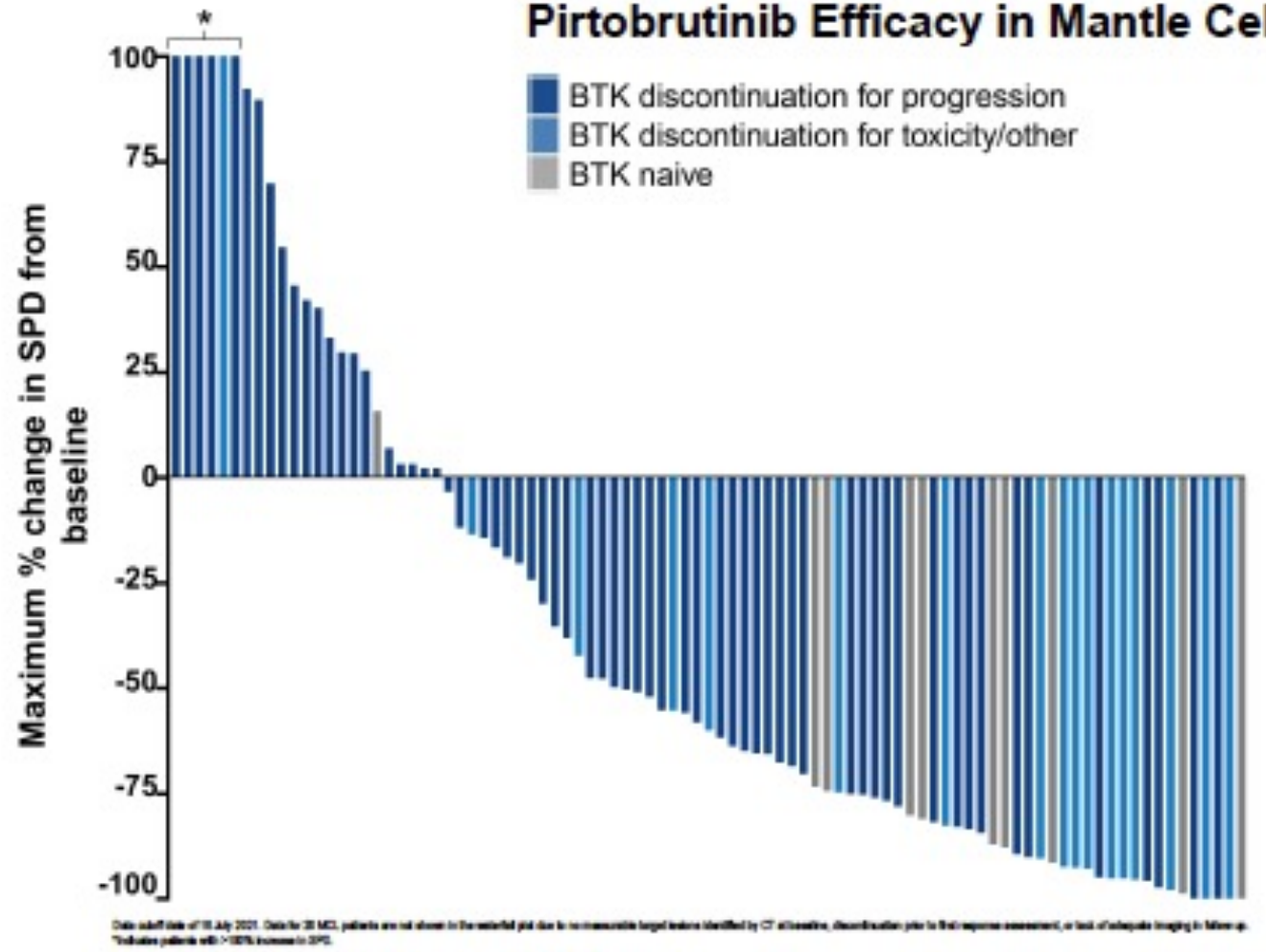
BRUIN: Updated Results with Pirtobrutinib for MCL



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.

RTP RESEARCH TO PRACTICE

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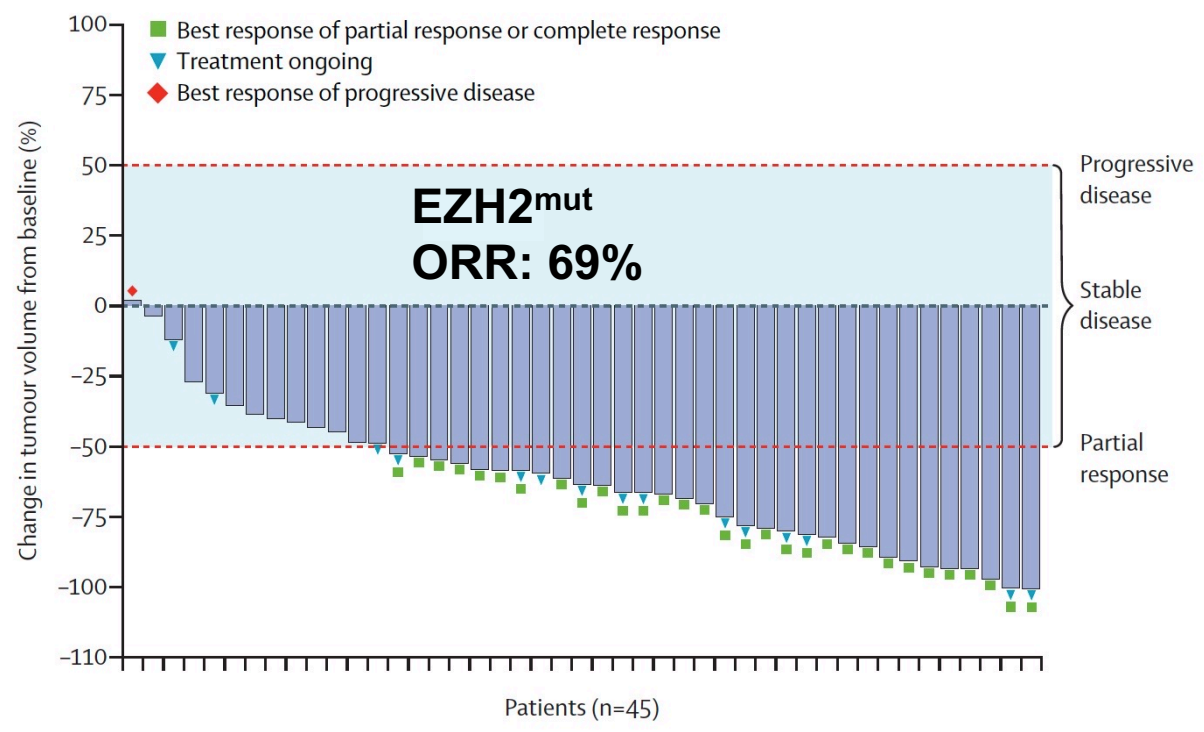
RTP RESEARCH TO PRACTICE

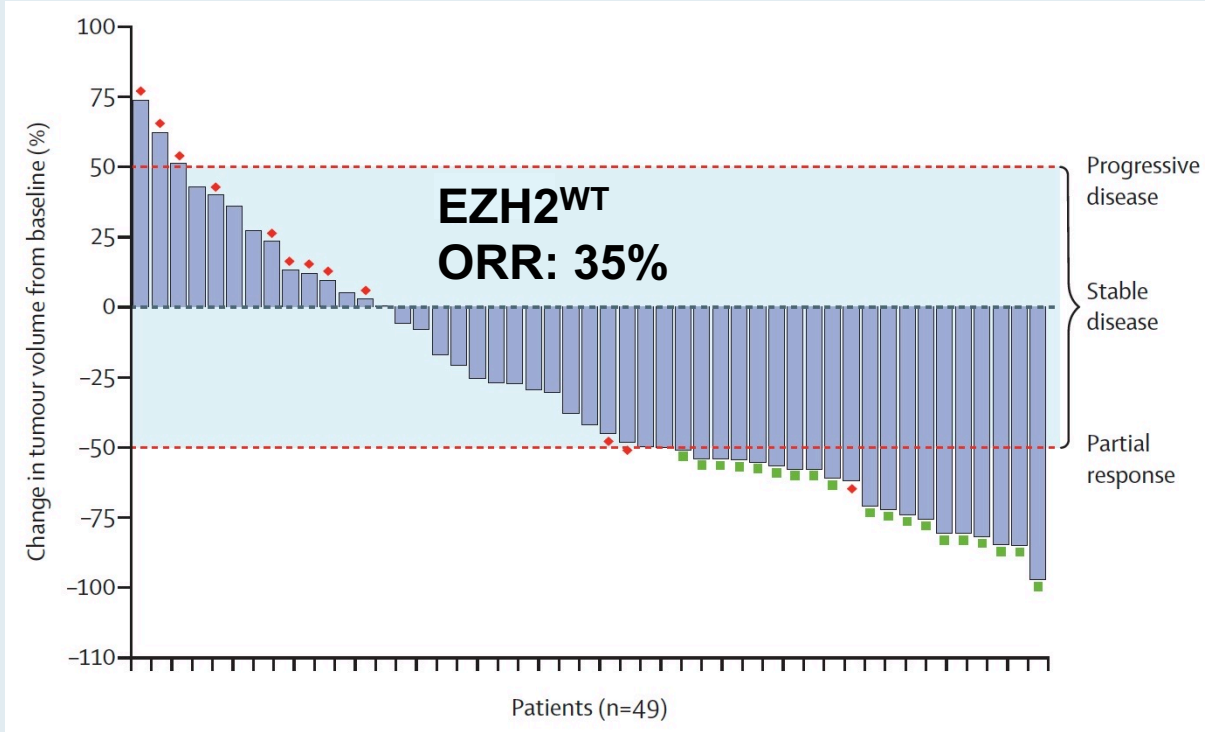
Lancet Oncol 2020;21(11):1433-42.

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

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

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





ORR = objective response rate

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

RTP RESEARCH TO PRACTICE

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.

RTP
RESEARCH
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RTP RESEARCH TO PRACTICE

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

RTP RESEARCH TO PRACTICE

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

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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.

RTP RESEARCH TO PRACTICE

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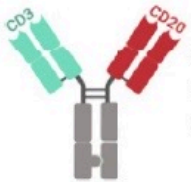
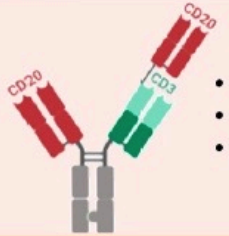
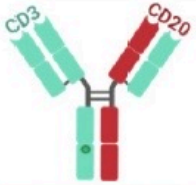
Structure of Selected Bispecific Antibodies

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.

RTP RESEARCH TO PRACTICE

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

RTP RESEARCH TO PRACTICE

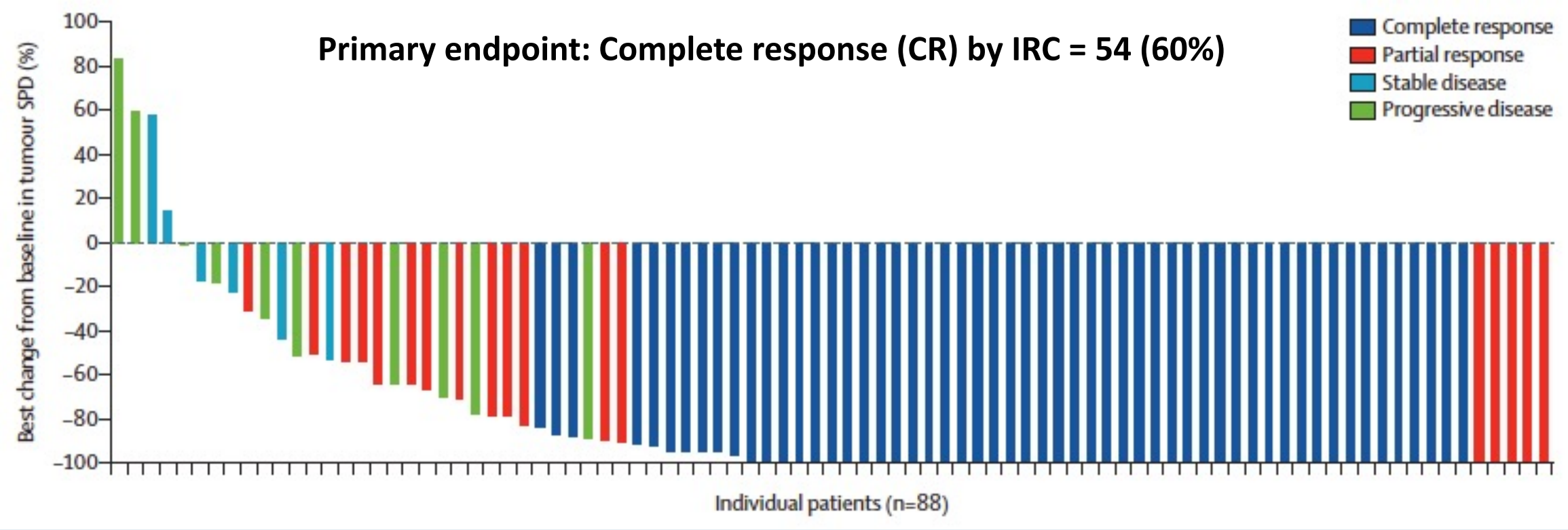
Lancet Oncol 2022;[Online ahead of print].

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].

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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].

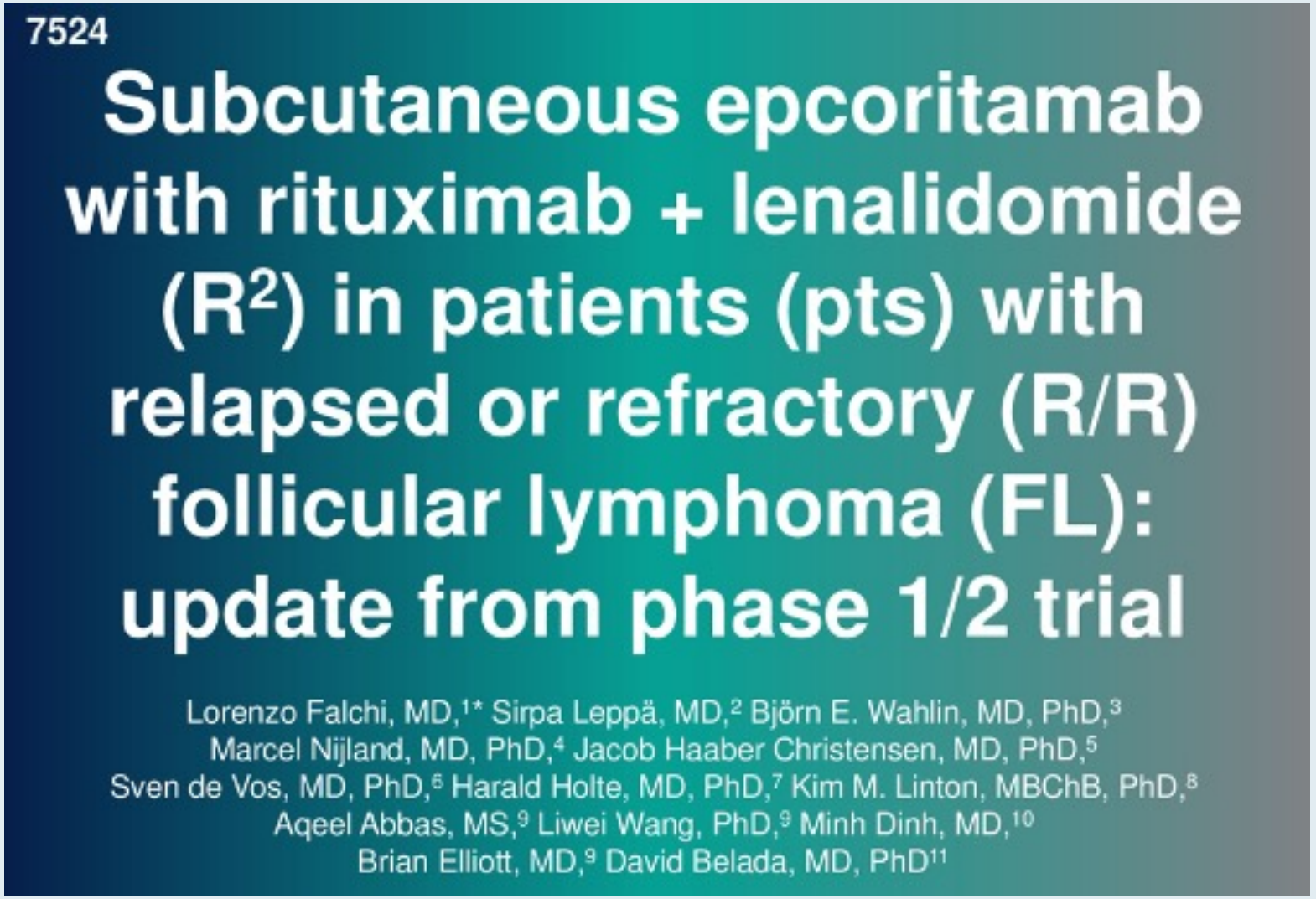
RTP RESEARCH TO PRACTICE

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



ASCO 2022;Abstract 7524.

RTP RESEARCH TO PRACTICE

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.

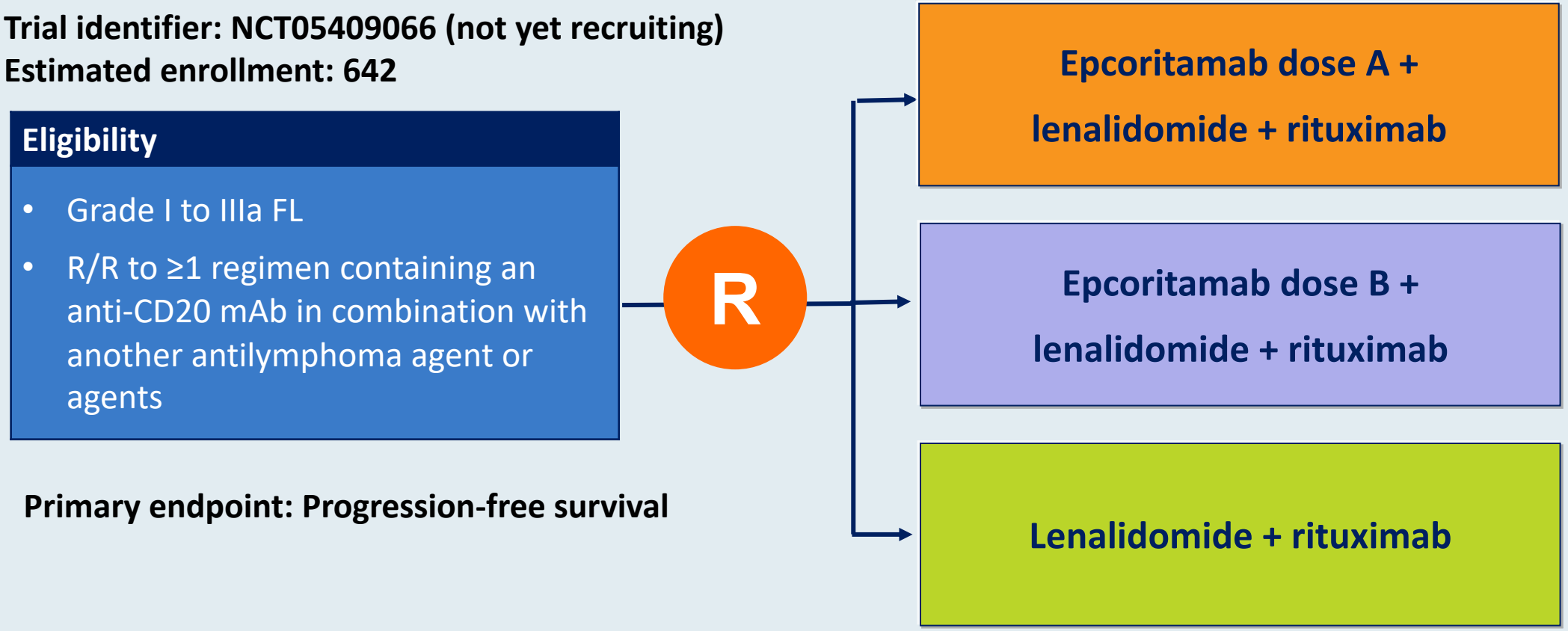
CMR = complete metabolic response; PMR = partial metabolic response

Falchi L et al. ASCO 2022;Abstract 7524.

RTP RESEARCH TO PRACTICE

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.

RTP RESEARCH TO PRACTICE

rapid communications

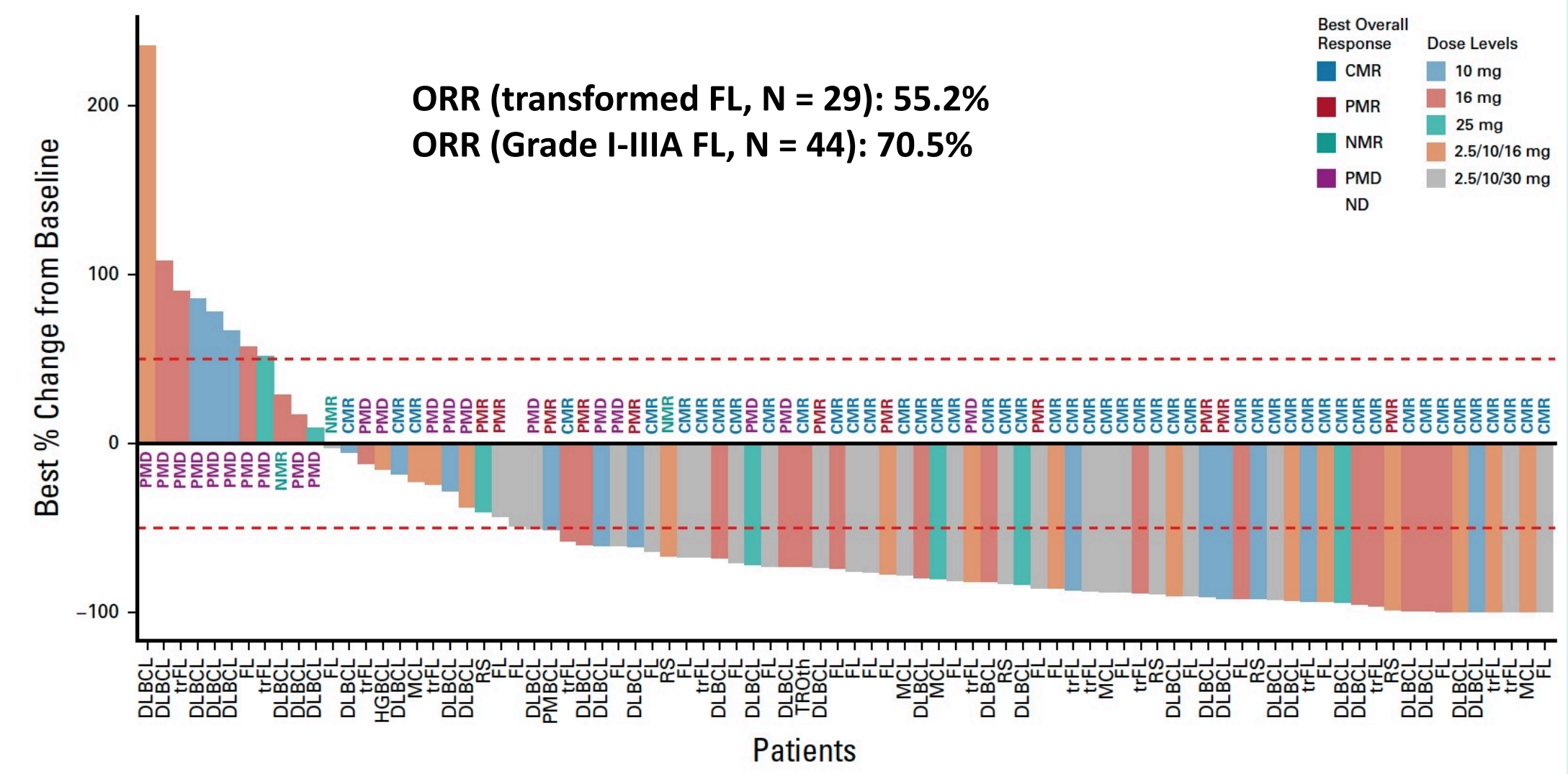
Glofitamab, a Novel, Bivalent CD20-Targeting T-Cell–Engaging Bispecific Antibody, Induces Durable Complete Remissions in Relapsed or Refractory B-Cell Lymphoma: A Phase I Trial

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]

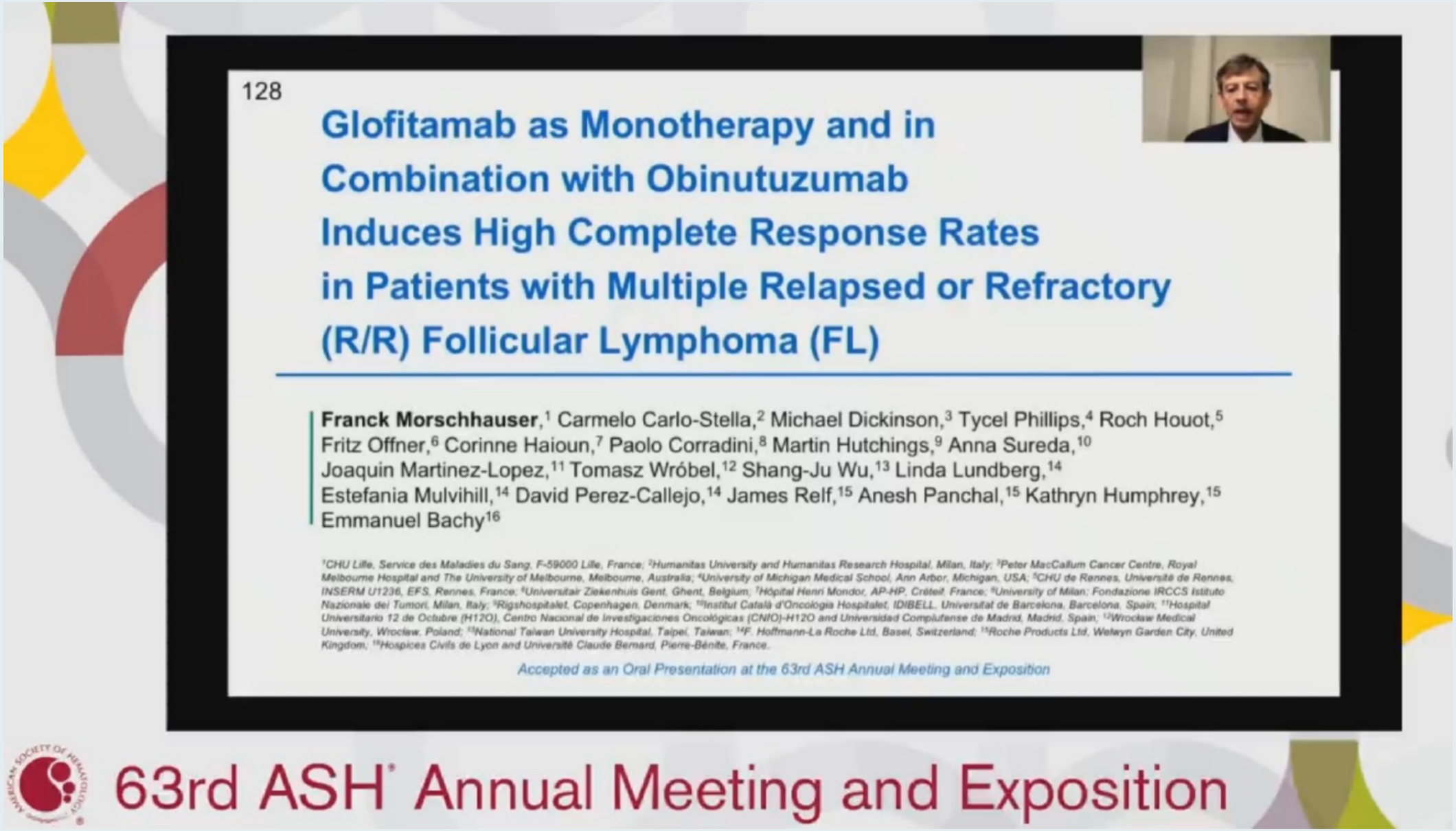
J Clin Oncol 2021;39(18):1959-70.

RTP RESEARCH TO PRACTICE

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

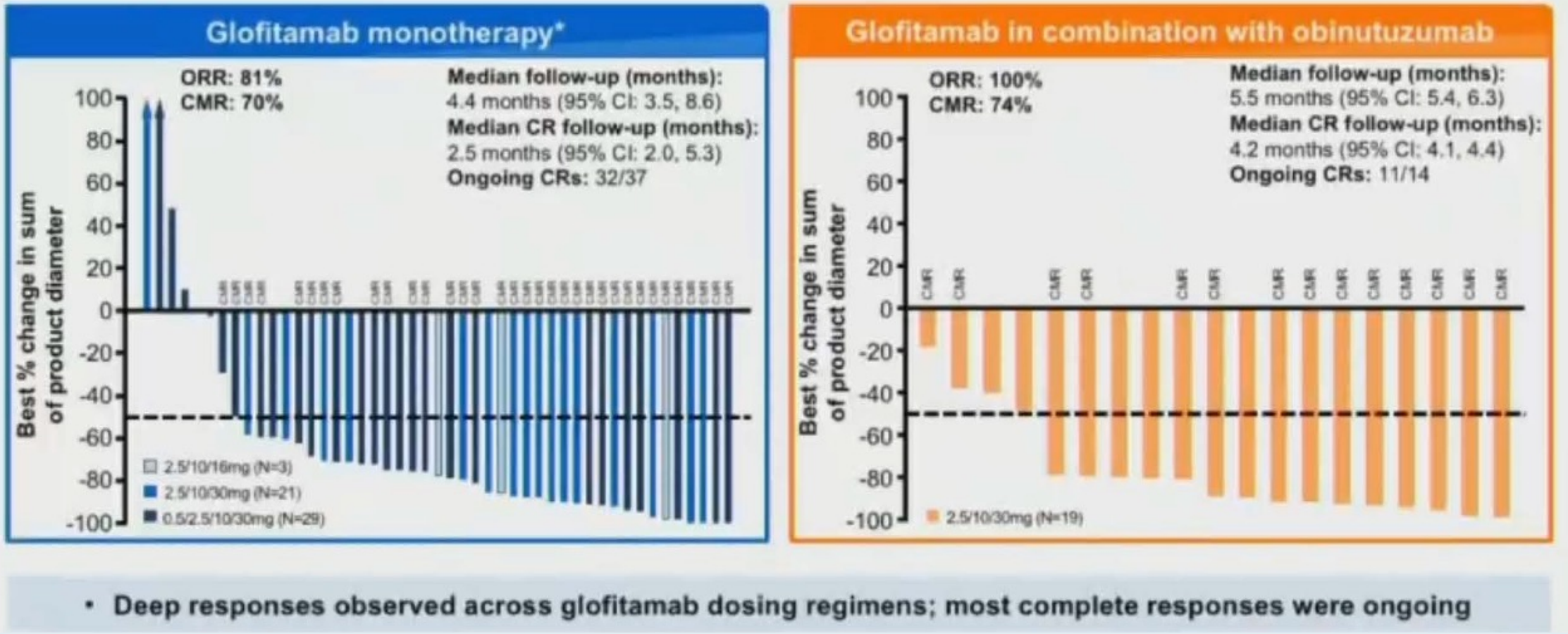


Hutchings M et al. *J Clin Oncol* 2021;39(18):1959-70.



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.

RTP RESEARCH TO PRACTICE

Approved PI3K Inhibitors for FL: Indication and Dosing

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

* 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.

RTP RESEARCH TO PRACTICE

Thank you for joining us!

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

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*

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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

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Gastrointestinal Cancers Agenda

Module 1: Colorectal Cancer

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Module 2: Upper Gastrointestinal Cancers

Module 3: Hepatocellular and Biliary Tract Cancers

Module 4: Pancreatic Adenocarcinoma

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Discussion Question

Have you used or would you use a ctDNA assay (eg, Signatera) to guide decision-making regarding adjuvant treatment for patients with colorectal cancer?

- I have
- I have not but would for the right patient
- I have not and would not
- I don’t know

RTP RESEARCH TO PRACTICE

CLINICAL CANCER RESEARCH | PRECISION MEDICINE AND IMAGING

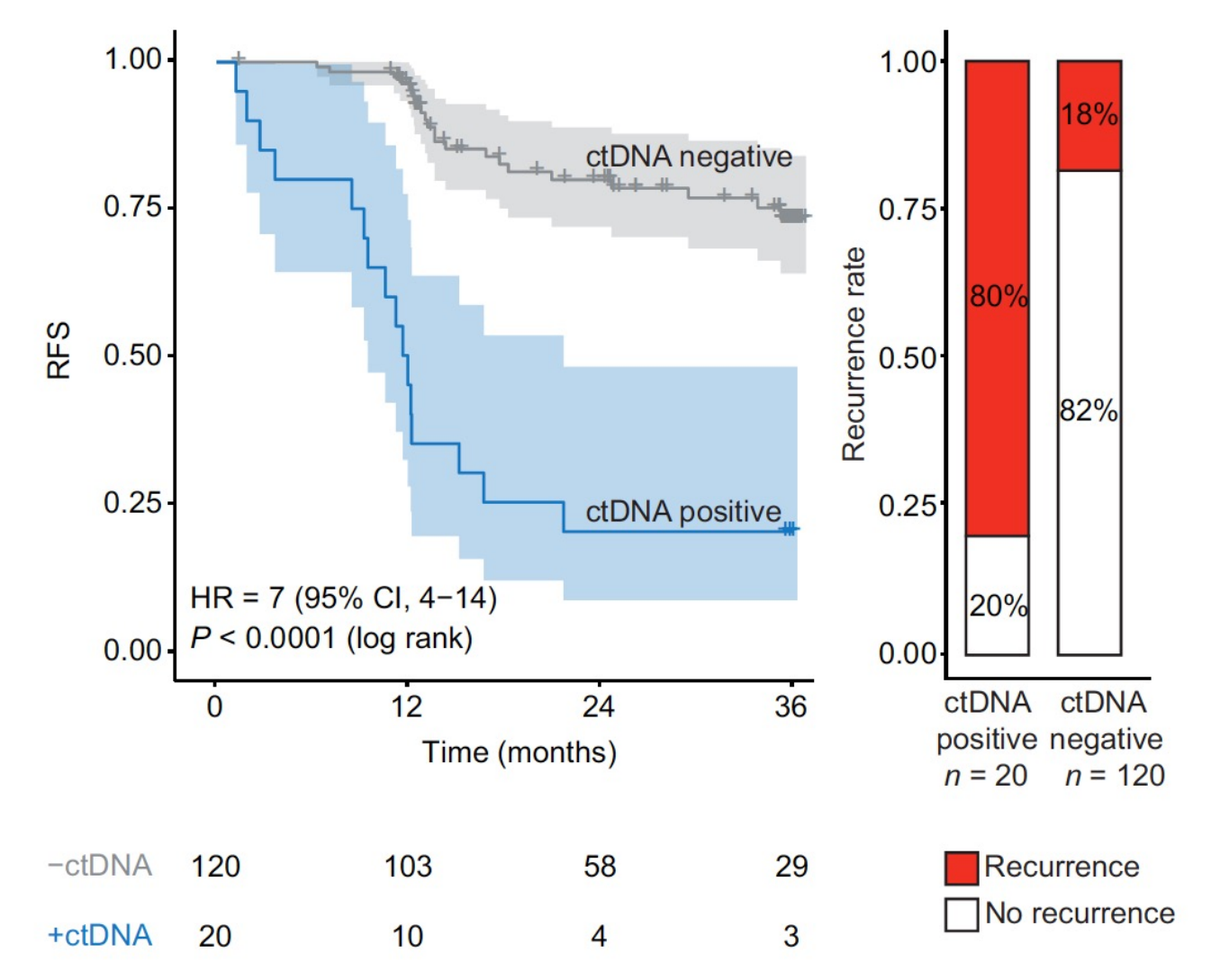
Circulating Tumor DNA in Stage III Colorectal Cancer, beyond Minimal Residual Disease Detection, toward Assessment of Adjuvant Therapy Efficacy and Clinical Behavior of Recurrences

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.

RTP RESEARCH TO PRACTICE

Detection of ctDNA After Surgery and Recurrence Rates



Henriksen TV et al. *Clin Cancer Res* 2022;28(3):507-17.

Gastrointestinal Cancers Agenda

Module 1: Colorectal Cancer

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- Management of metastatic disease: BRAF mutant

Module 2: Upper Gastrointestinal Cancers

Module 3: Hepatocellular and Biliary Tract Cancers

Module 4: Pancreatic Adenocarcinoma

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Discussion Question

Reimbursement and regulatory issues aside, what would be your preferred initial treatment strategy for a patient with resectable MSI-high rectal cancer?

- Total neoadjuvant therapy
- Concurrent chemoradiation therapy
- Immunotherapy
- Other

RTP RESEARCH TO PRACTICE

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

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ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

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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

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.

RTP RESEARCH TO PRACTICE

Gastrointestinal Cancers Agenda

Module 1: Colorectal Cancer

- Adjuvant systemic treatment: Role of ctDNA (Signatera)
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- 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

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Discussion Question

In general, which biologic treatment would you most likely combine with chemotherapy as first-line treatment for a patient with left-sided KRAS wild-type mCRC and potentially resectable liver metastases?

- EGFR antibody
- Bevacizumab
- Either regimen – coin flip
- I'm not sure

RTP RESEARCH TO PRACTICE

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

Gastrointestinal Cancers Agenda

Module 1: Colorectal Cancer

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Discussion Question

Regulatory and reimbursement issues aside, for a patient with HER2-overexpressing mCRC to whom you would administer HER2-targeted therapy, what would be your preferred initial treatment?

- Trastuzumab deruxtecan
- Trastuzumab/pertuzumab
- Trastuzumab/lapatinib
- Trastuzumab/tucatinib
- T-DM1
- Other

RTP RESEARCH TO PRACTICE

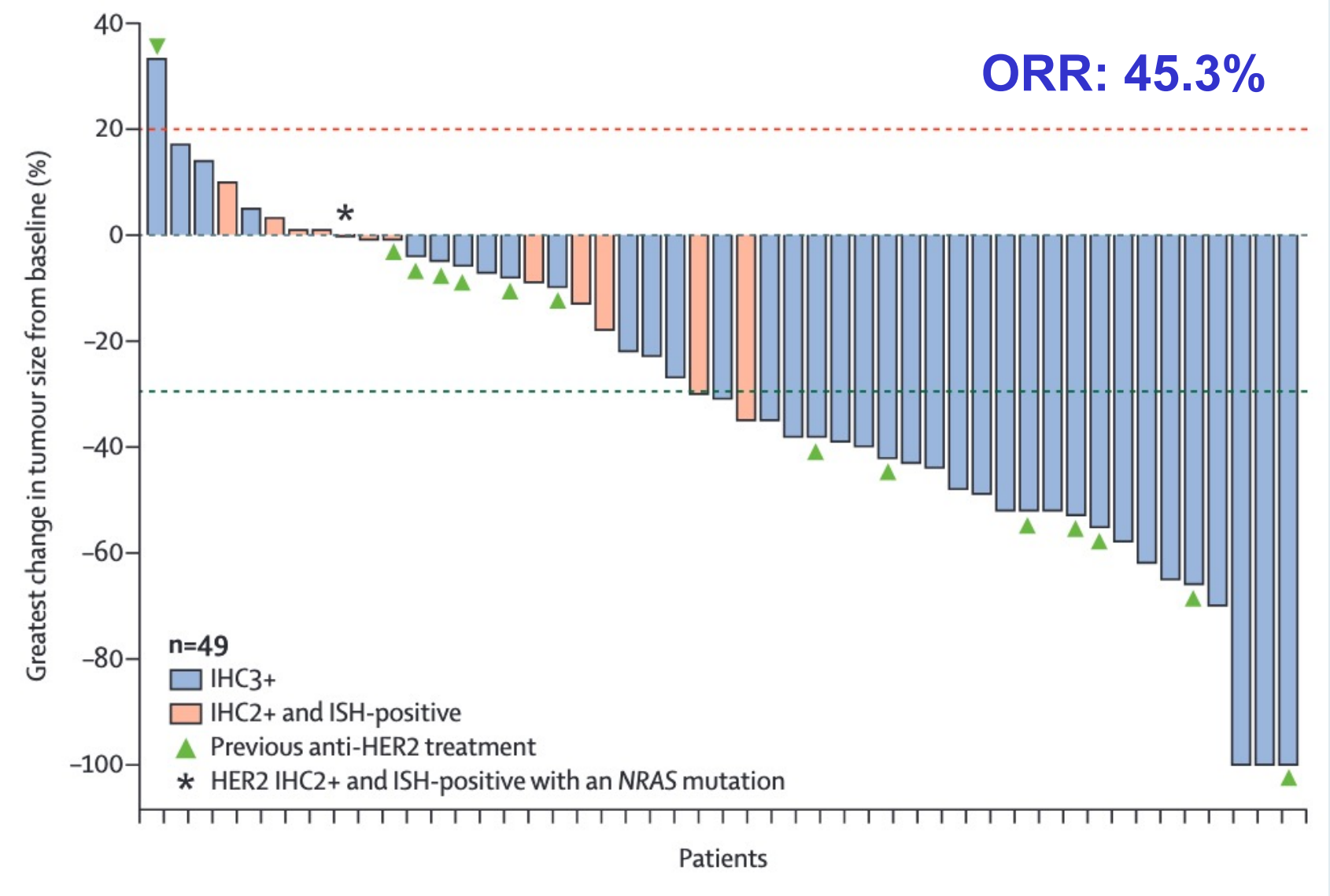
Lancet Oncol 2021;22(6):779-89.

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

RTP RESEARCH TO PRACTICE

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.

RTP RESEARCH TO PRACTICE

Results from Pivotal MOUNTAINEER Trial Demonstrating Clinically Meaningful Antitumor Activity of Tucatinib in Combination with Trastuzumab in Previously Treated HER2-Positive Metastatic Colorectal Cancer

Press Release – July 2, 2022

"…Today announced full results from the pivotal phase 2 MOUNTAINEER trial, which showed tucatinib in combination with trastuzumab was well-tolerated with durable responses in patients with previously treated HER2-positive metastatic colorectal cancer (mCRC).

At a median duration of follow-up of 20.7 months (interquartile range: 11.7, 39.0), results of the MOUNTAINEER trial showed a 38.1% confirmed objective response rate (cORR) (95% Confidence Interval [CI]: 27.7, 49.3) per blinded independent central review (BICR) in the HER2-positive patients who were assigned to receive tucatinib in combination with trastuzumab (n=84 with a median age of 55.0 years [range 24 to 77]). In these patients, the median duration of response (DoR) per BICR was 12.4 months (95% CI: 8.5, 20.5). Median progression-free survival per BICR was 8.2 months (95% CI: 4.2, 10.3), and median overall survival was 24.1 months (95% CI: 20.3, 36.7)."

https://finance.yahoo.com/news/seagen-announces-results-pivotal-mountaineer-103500806.html

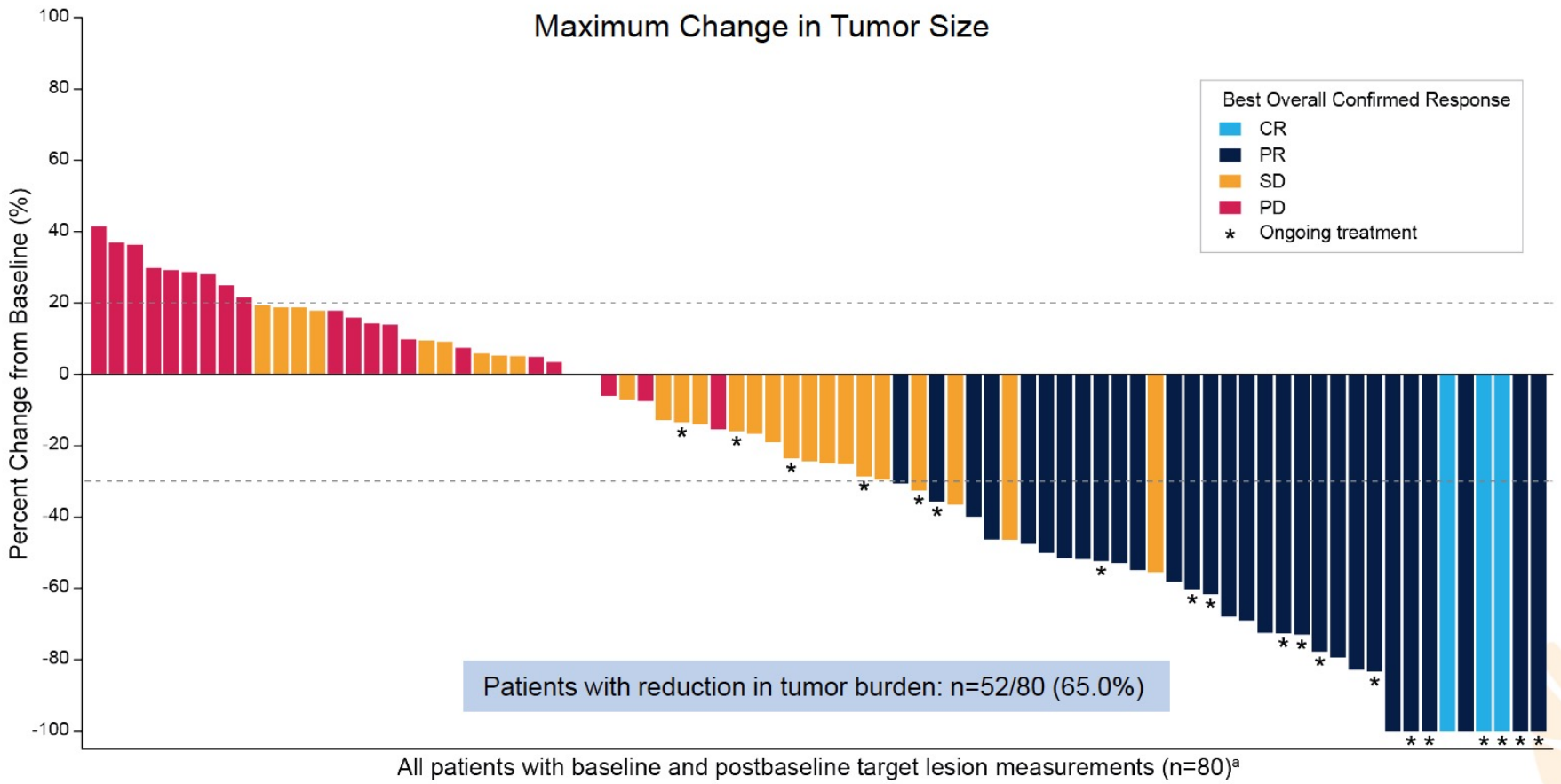
RTP RESEARCH TO PRACTICE

Primary analysis of MOUNTAINEER: A phase 2 study of tucatinib and trastuzumab for HER2-positive mCRC

John H. Strickler, Andrea Cercek, Salvatore Siena, Thierry Andre, Kimmie Ng, Eric Van Cutsem, Christina Wu, Andrew Scott Paulson, Joleen M. Hubbard, Andrew L. Coveler, Christos Fountzilas, Adel Kardosh, Pashtoon Murtaza Kasi, Heinz-Josef Lenz, Kristen Ciombor, Elena Elez, David L. Bajor, Michael Stecher, Wentao Feng, Tanios S. Bekaii-Saab

European Society of Medical Oncology World Congress on Gastrointestinal Cancer. Jun 29-Jul 2, 2022. Abstract LBA-2

Tucatinib + Trastuzumab: Change in Tumor Size



a Four patients who did not have baseline and/or post-baseline target lesion measurements are excluded
CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease.
Data cutoff: 28 Mar 2022

Strickler JH et al. ESMO GI 2022;Abstract LBA-2.

Gastrointestinal Cancers Agenda

Module 1: Colorectal Cancer

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Module 2: Upper Gastrointestinal Cancers

Module 3: Hepatocellular and Biliary Tract Cancers

Module 4: Pancreatic Adenocarcinoma

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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*

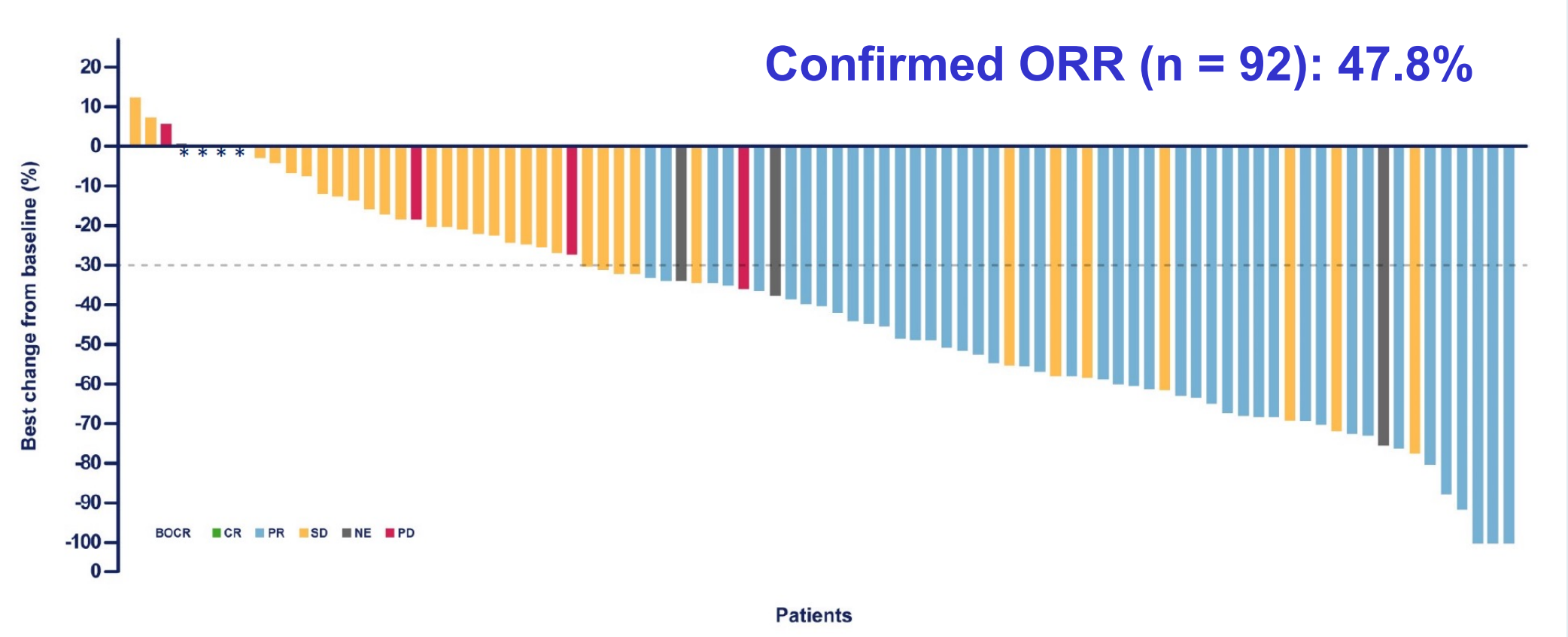
** University Hospitals Leuven, Belgium*

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.

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.

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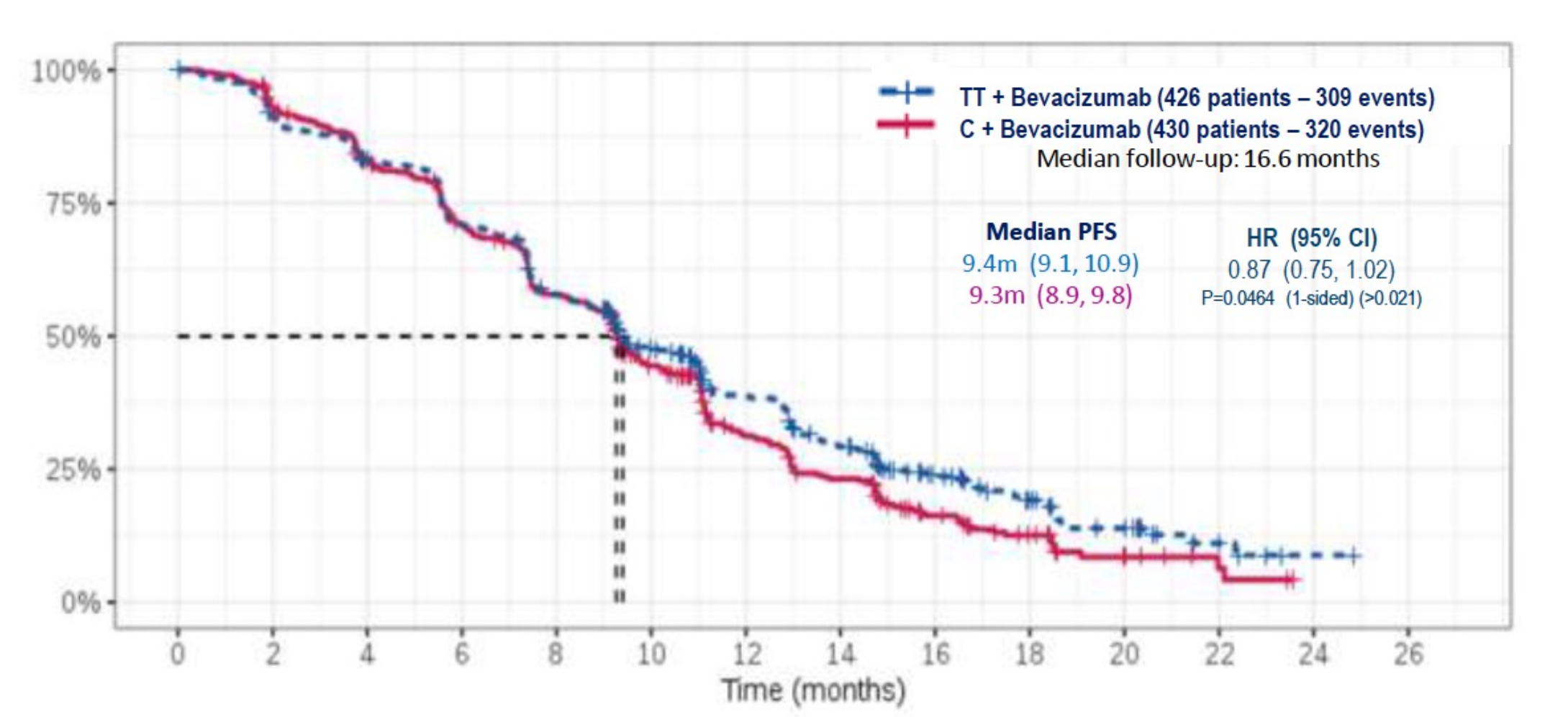
SOLSTICE Primary Endpoint: PFS by Investigator's Assessment



PFS = progression-free survival

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

RTP RESEARCH TO PRACTICE

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 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

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Gastrointestinal Cancers Agenda

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Module 4: Pancreatic Adenocarcinoma

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Discussion Question

Regulatory and reimbursement issues aside, for a patient with HER2-overexpressing mCRC to whom you would administer HER2-targeted therapy, what would be your preferred initial treatment?

- Trastuzumab deruxtecan
- Trastuzumab/pertuzumab
- Trastuzumab/lapatinib
- Trastuzumab/tucatinib
- T-DM1
- Other

RTP RESEARCH TO PRACTICE

2021 ASCO ANNUAL MEETING

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

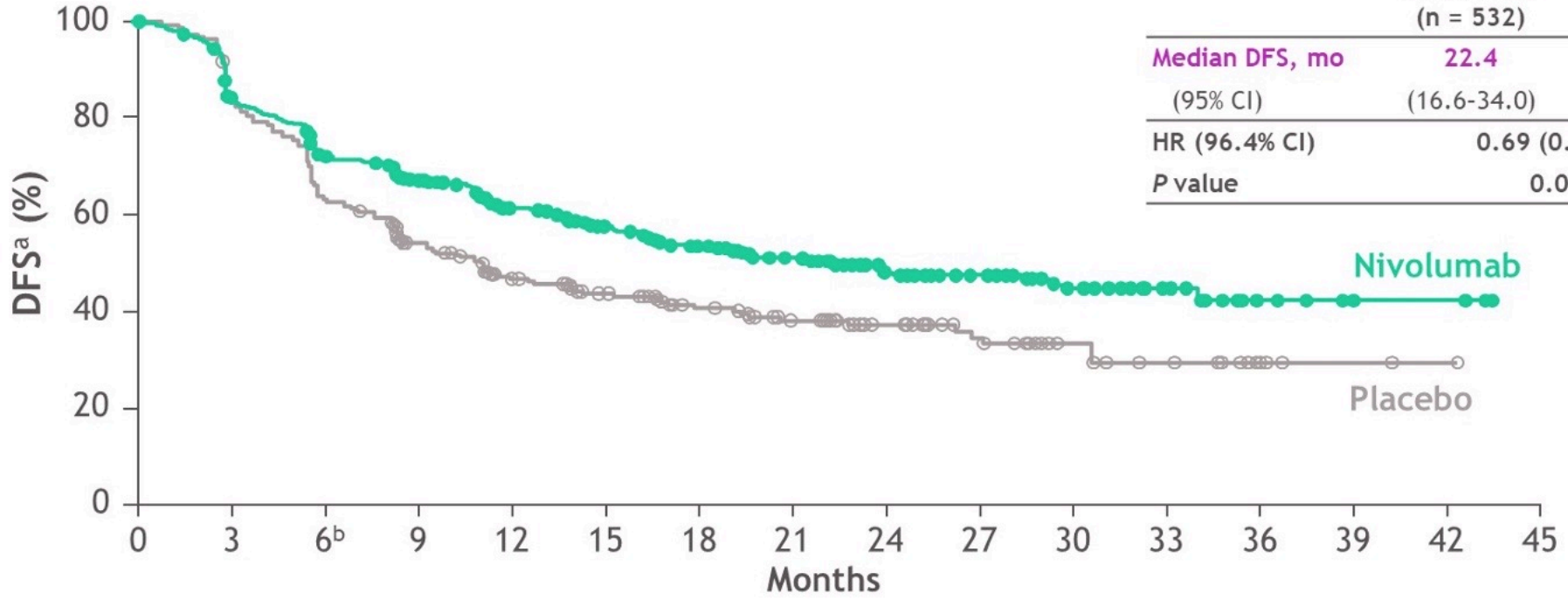
Ronan J. Kelly,[1] Jaffer A. Ajani,[2] Jaroslaw Kuzdzal,[3] Thomas Zander,[4] Eric Van Cutsem,[5] Guillaume Piessen,[6] Guillermo Mendez,[7] Josephine Feliciano,[8] Satoru Motoyama,[9] Astrid Lièvre,[10] Hope Uronis,[11] Elena Elimova,[12] Cecile Grootscholten,[13] Karen Geboes,[14] Jenny Zhang,[15] 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

RTP RESEARCH TO PRACTICE

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.

RTP RESEARCH TO PRACTICE

Gastrointestinal Cancers Agenda

Module 1: Colorectal Cancer

Module 2: Upper Gastrointestinal Cancers

- Adjuvant and postneoadjuvant use of immunotherapy
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Module 4: Pancreatic Adenocarcinoma

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RESEARCH
TO PRACTICE

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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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]✉

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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.

RTP RESEARCH TO PRACTICE

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.

RTP RESEARCH TO PRACTICE

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

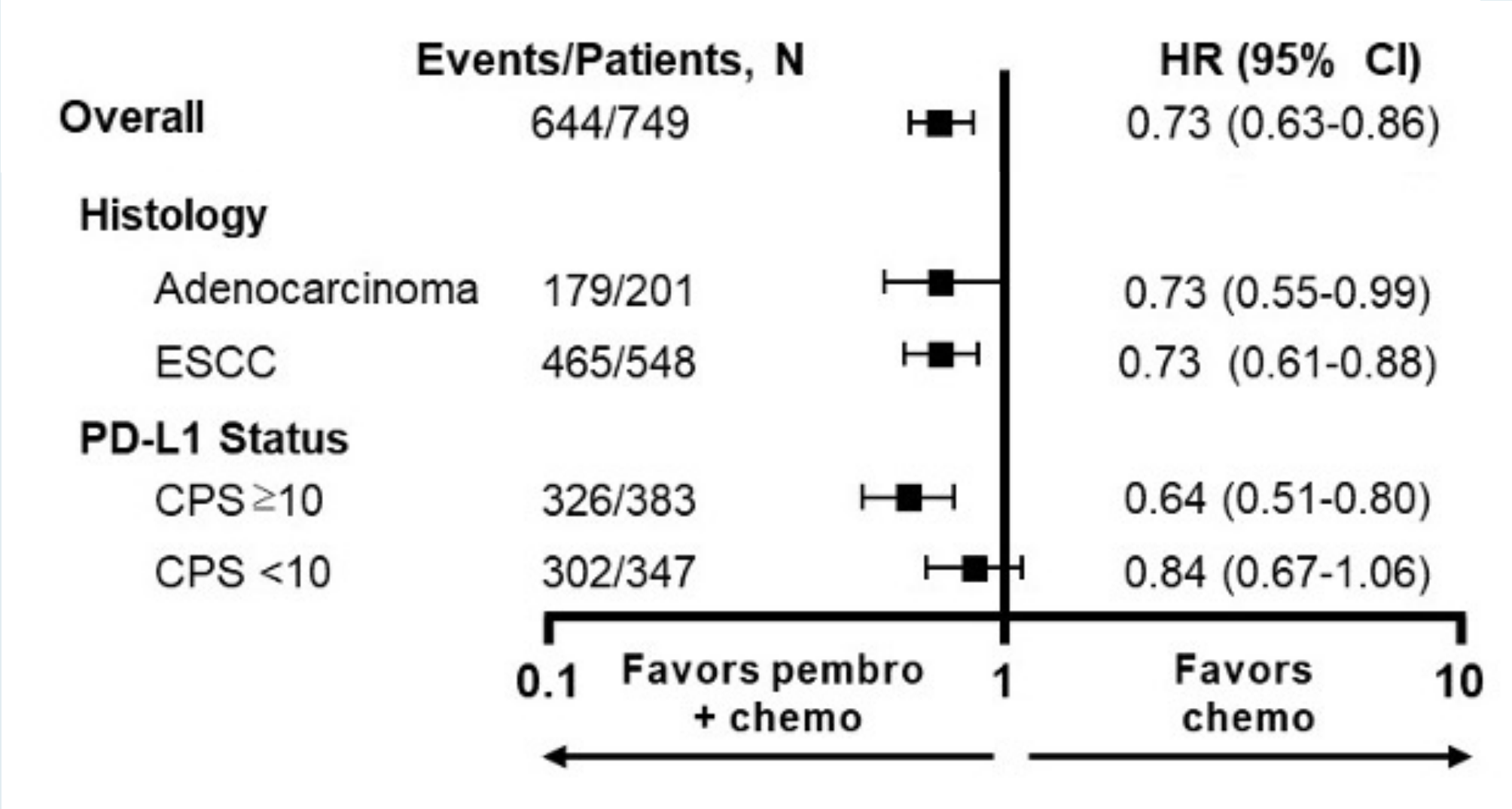
Jean-Philippe Metges,[1] Ken Kato,[2] Jong-Mu Sun,[3] Manish A. Shah,[4] Peter Enzinger,[5] Antoine Adenis,[6] Toshihiko Doi,[7] Takashi Kojima,[7] Zhigang Li,[8] Sung-Bae Kim,[9] Byoung Chul Cho,[10] Wasat Mansoor,[11] Shau-Hsuan Li,[12] Patrapim Sunpaweravong,[13] Maria Alsina Maqueda,[14] Gary L.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

RTP RESEARCH TO PRACTICE

KEYNOTE-590: Overall Survival in Select Subgroups



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

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 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

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Discussion Question

Regulatory and reimbursement issues aside, what would you recommend as second-line therapy for a patient with metastatic HER2-positive, MSS gastric adenocarcinoma (PD-L1 CPS ≥1) and disease progression on FOLFOX/trastuzumab/pembrolizumab?

- Ramucirumab
- Ramucirumab/paclitaxel
- Paclitaxel/trastuzumab
- Trastuzumab deruxtecan
- Other chemotherapy
- Other chemotherapy/trastuzumab
- Tucatinib/trastuzumab
- Other

RTP RESEARCH TO PRACTICE

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

PRESENTED BY: Kensei Yamaguchi, MD

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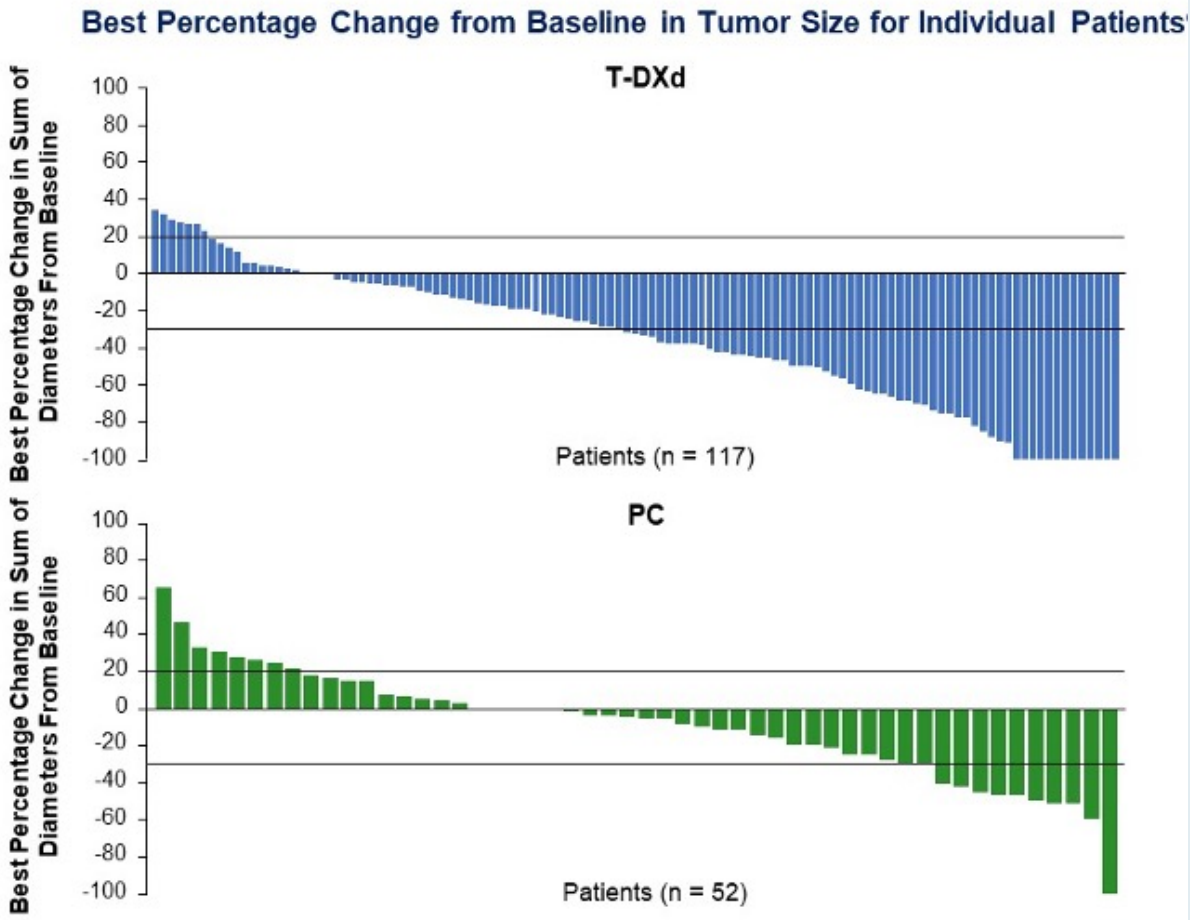
DESTINY-Gastric01: Antitumor Activity

	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.

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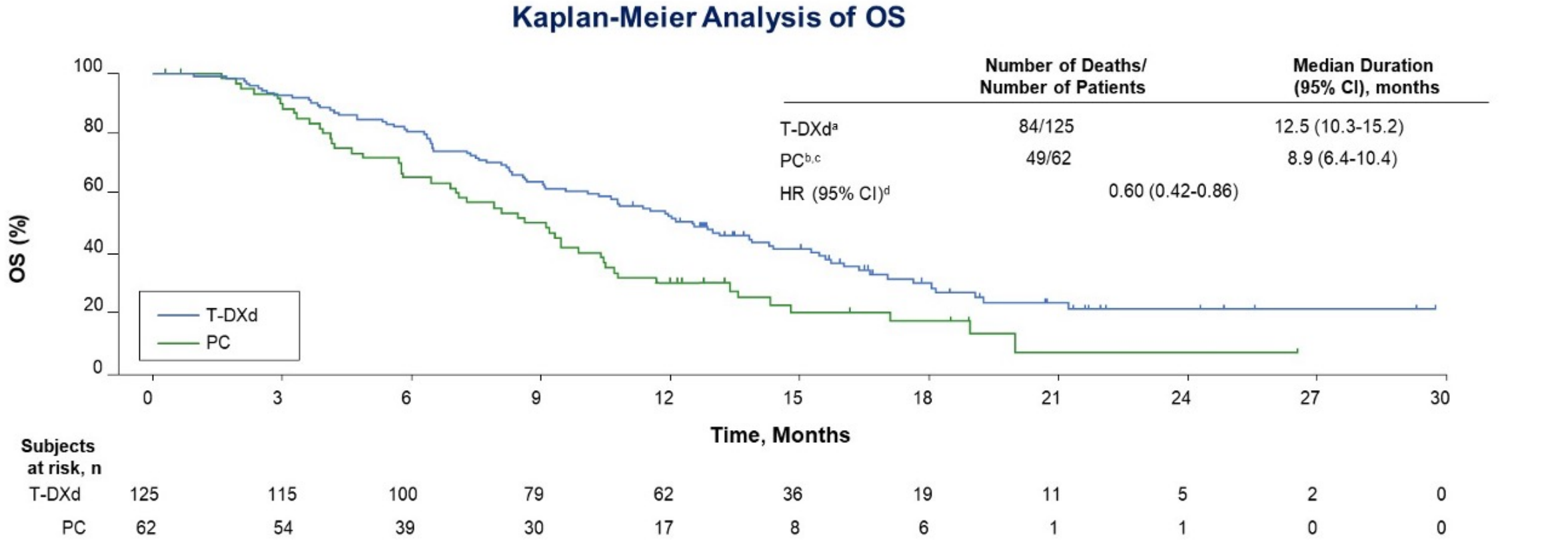
DESTINY-Gastric01: Final Overall Survival (OS)



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.

RTP RESEARCH TO PRACTICE

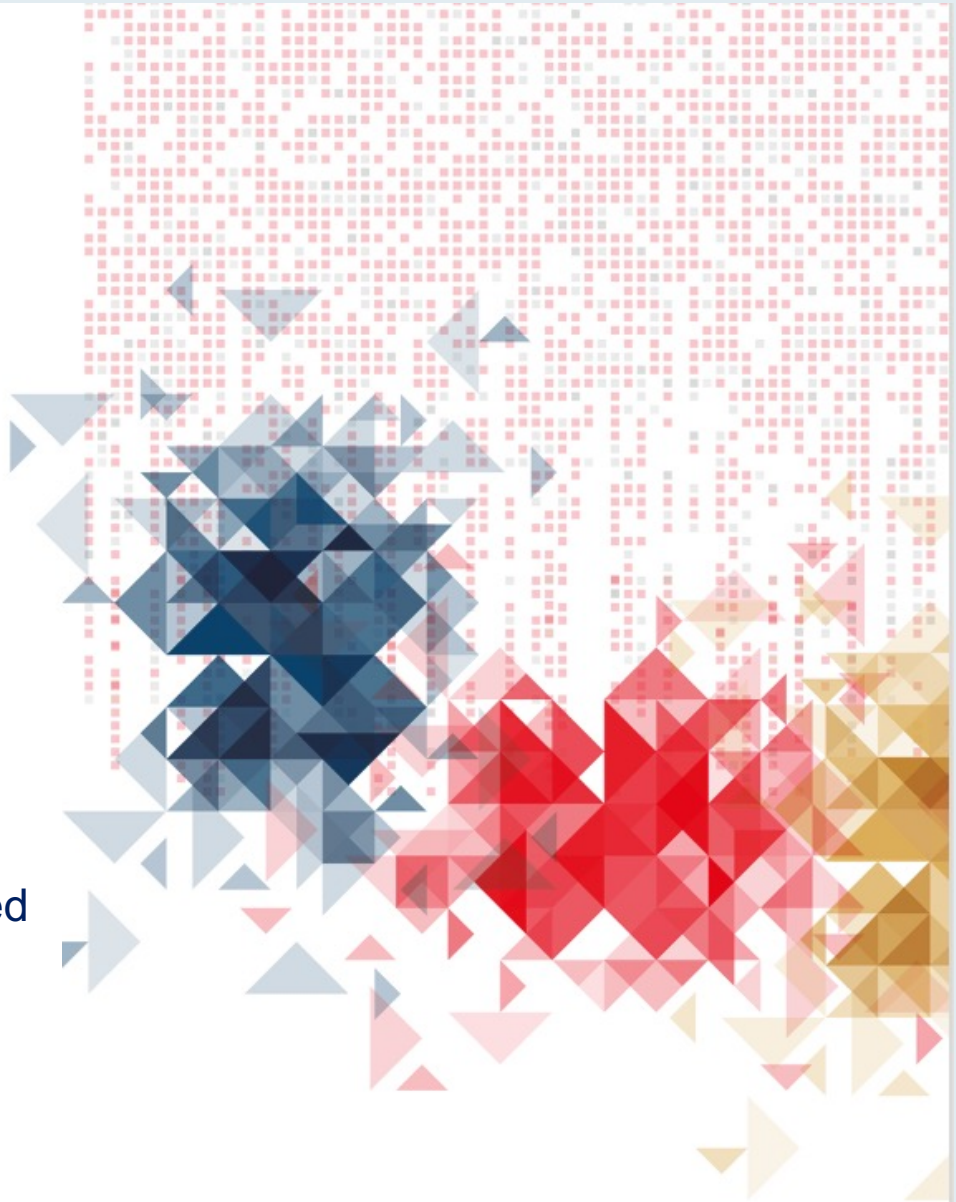
2021 ESMO congress

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

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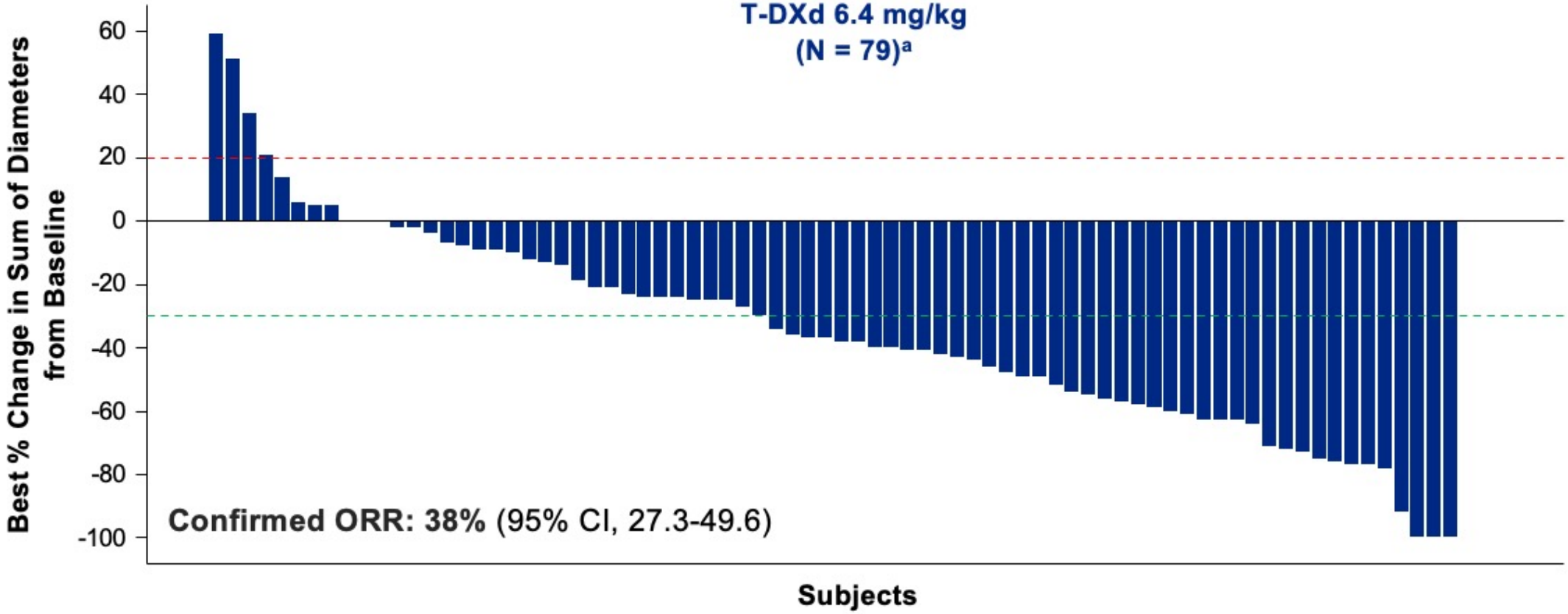
DESTINY-Gastric02: Best Percentage Change of Tumor Size from Baseline



Van Cutsem E et al. ESMO 2021;Abstract LBA55.

RTP RESEARCH TO PRACTICE

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

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

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TO PRACTICE

Gastrointestinal Cancers Agenda

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- Current and novel treatment approaches (eg, immunotherapy and HER2-targeted therapy) for advanced biliary tract cancers

Module 4: Pancreatic Adenocarcinoma

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TO PRACTICE

Discussion Question

Regulatory and reimbursement issues aside, which systemic regimen would you prefer for a 65-year-old man with metastatic hepatocellular carcinoma (HCC) and Grade 1 esophageal varices?

- STRIDE regimen (durvalumab and tremelimumab)
- Atezolizumab and bevacizumab
- Either regimen – coin flip
- I'm not sure

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Discussion Question

In the Phase III HIMALAYA study, what was the dose and schedule of tremelimumab used in combination with durvalumab for the treatment of advanced HCC?

- Single dose of 300 mg administered in the first cycle only
- 75 mg every 4 weeks
- Single dose of 75 mg administered in the first cycle only
- 300 mg every 4 weeks
- I'm not sure

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TO PRACTICE

NEJM Evidence

Published June 6, 2022

DOI: 10.1056/EVIDoa2100070

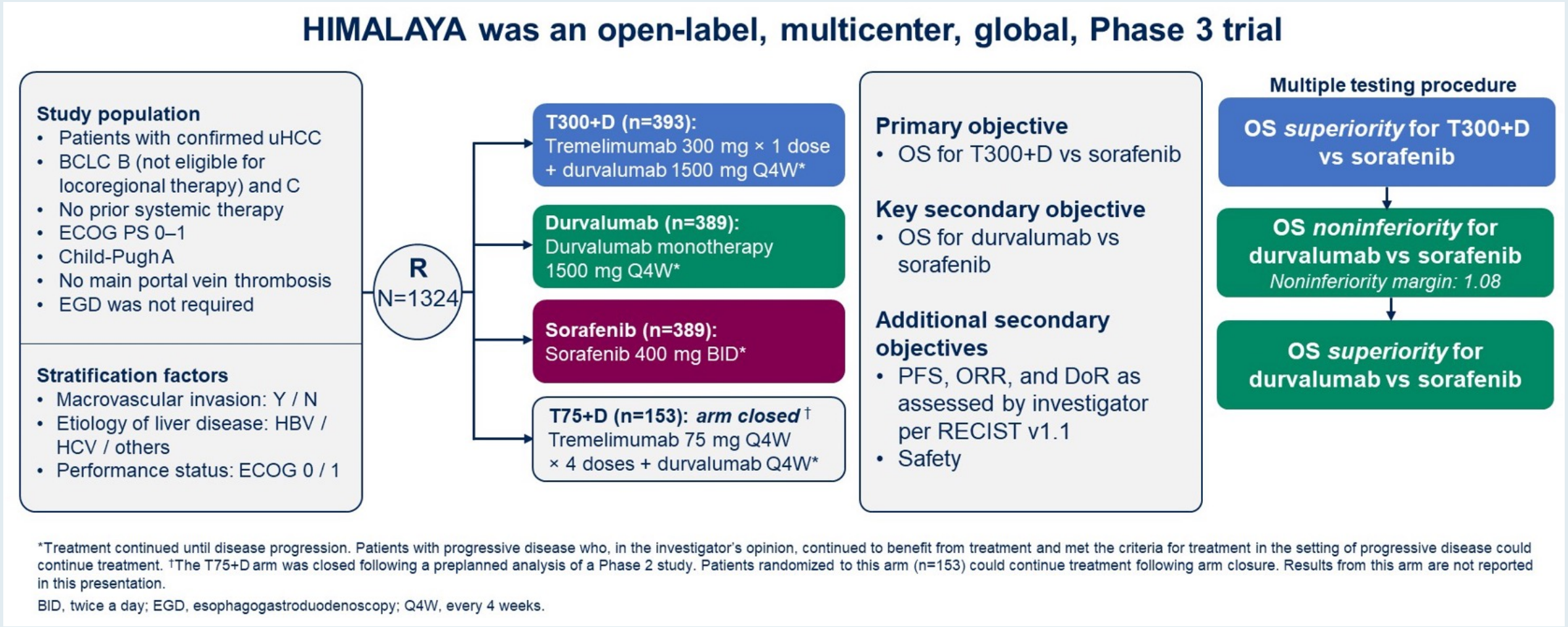
ORIGINAL ARTICLE

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]

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

HIMALAYA Phase III Trial Schema



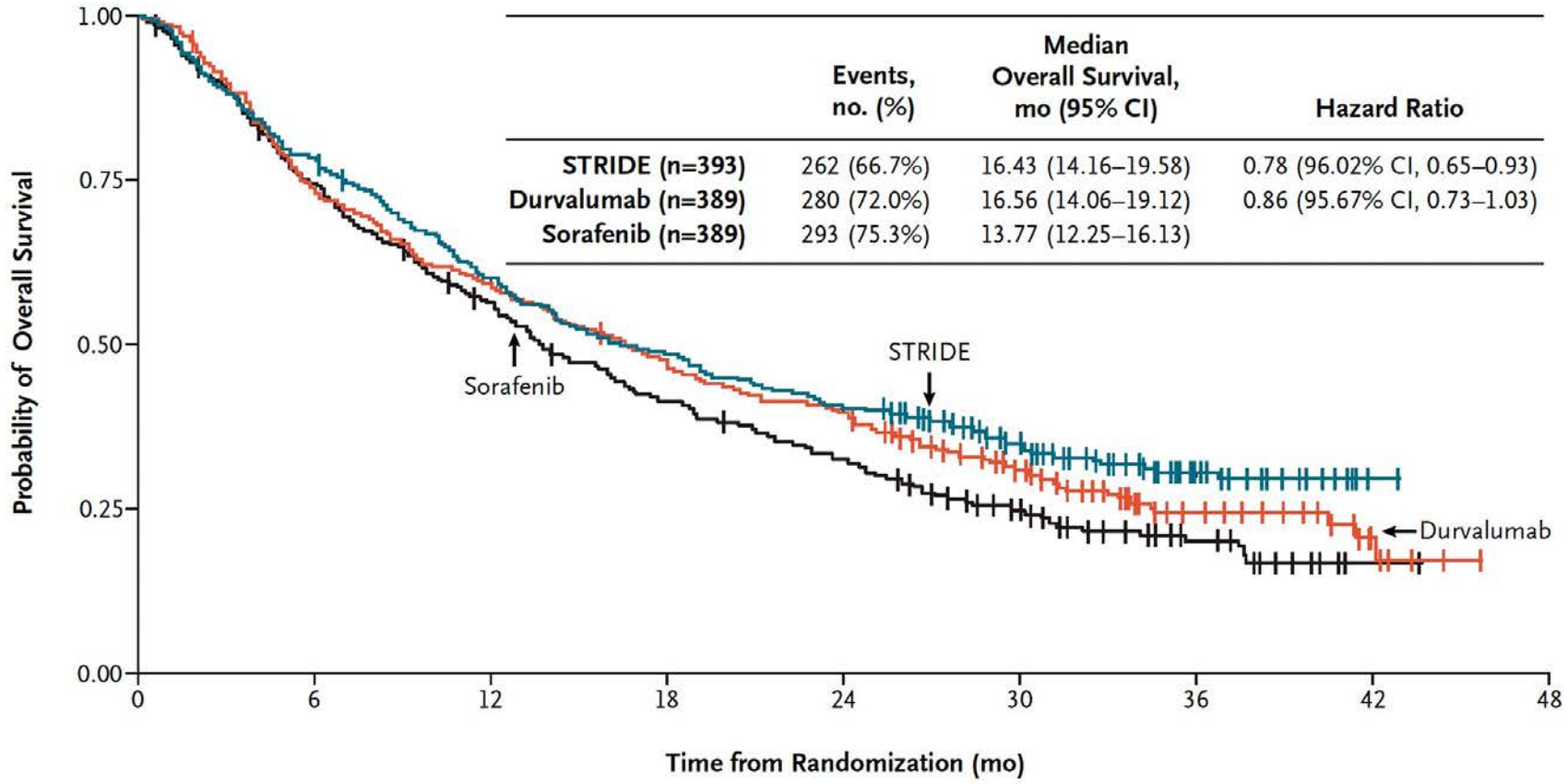
*Treatment continued until disease progression. Patients with progressive disease who, in the investigator's opinion, continued to benefit from treatment and met the criteria for treatment in the setting of progressive disease could continue treatment. †The T75+D arm was closed following a preplanned analysis of a Phase 2 study. Patients randomized to this arm (n=153) could continue treatment following arm closure. Results from this arm are not reported in this presentation.

BID, twice a day; EGD, esophagogastroduodenoscopy; Q4W, every 4 weeks.

Abou-Alfa GK et al. Gastrointestinal Cancers Symposium 2022;Abstract 379.

RTP RESEARCH TO PRACTICE

HIMALAYA: Overall Survival

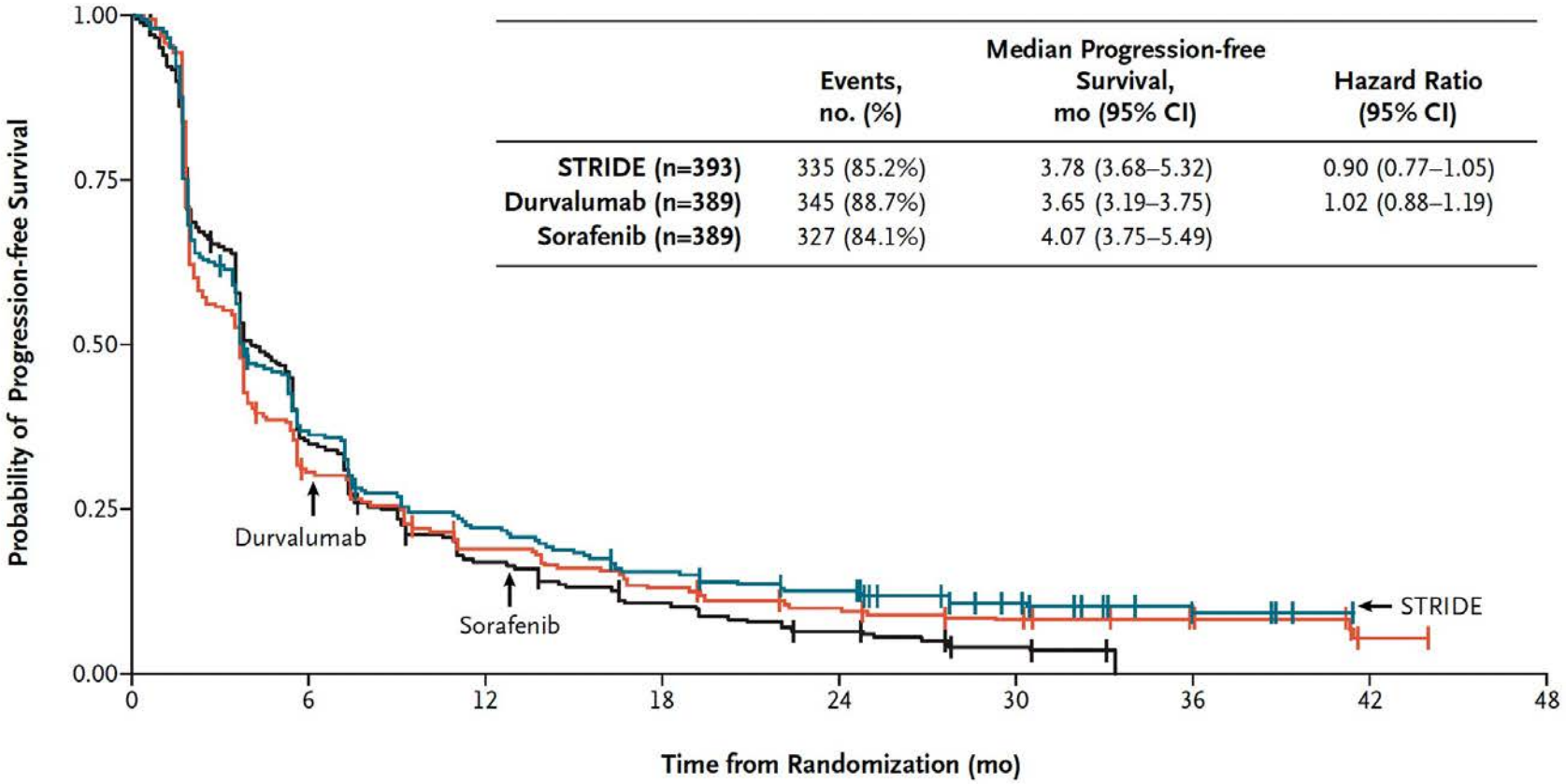


	Events, no. (%)	Median Overall Survival, mo (95% CI)	Hazard Ratio
STRIDE (n=393)	262 (66.7%)	16.43 (14.16–19.58)	0.78 (96.02% CI, 0.65–0.93)
Durvalumab (n=389)	280 (72.0%)	16.56 (14.06–19.12)	0.86 (95.67% CI, 0.73–1.03)
Sorafenib (n=389)	293 (75.3%)	13.77 (12.25–16.13)	

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

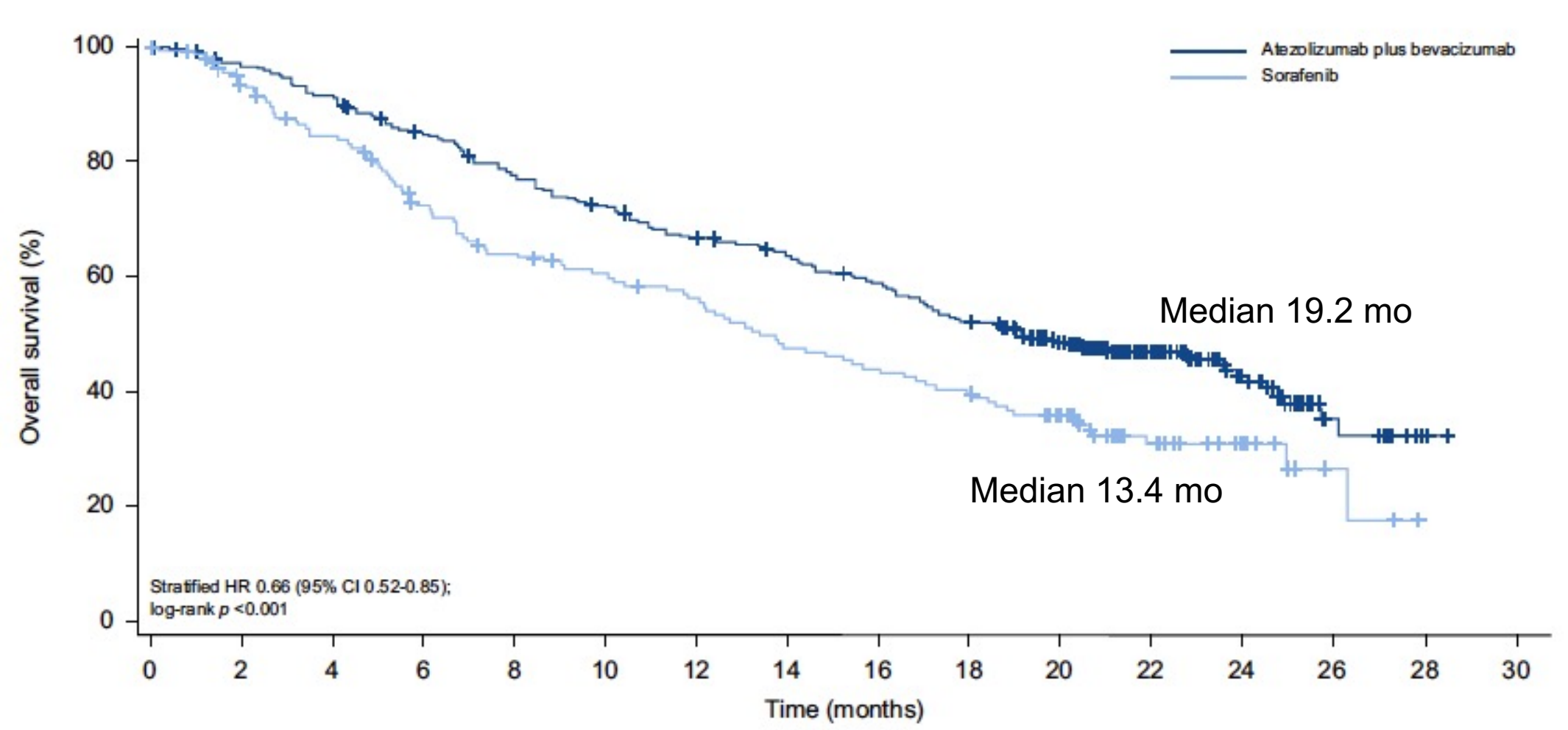
Updated efficacy and safety data from IMbrave150: Atezolizumab plus bevacizumab *vs.* sorafenib for unresectable hepatocellular carcinoma

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.

RTP
RESEARCH
TO PRACTICE

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

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

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

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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

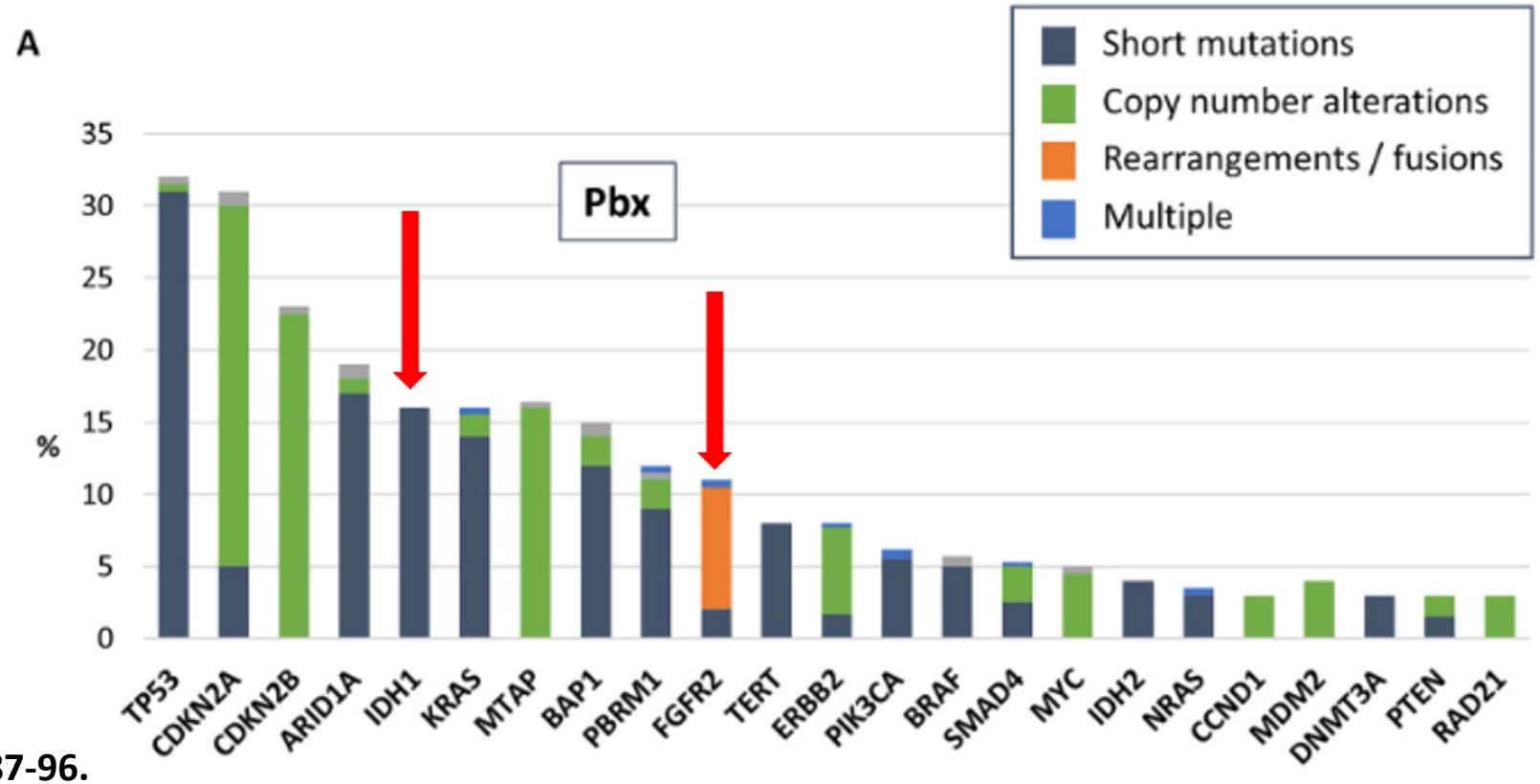
MSI = microsatellite instability; MMR = mismatch repair

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

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

RTP RESEARCH TO PRACTICE

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

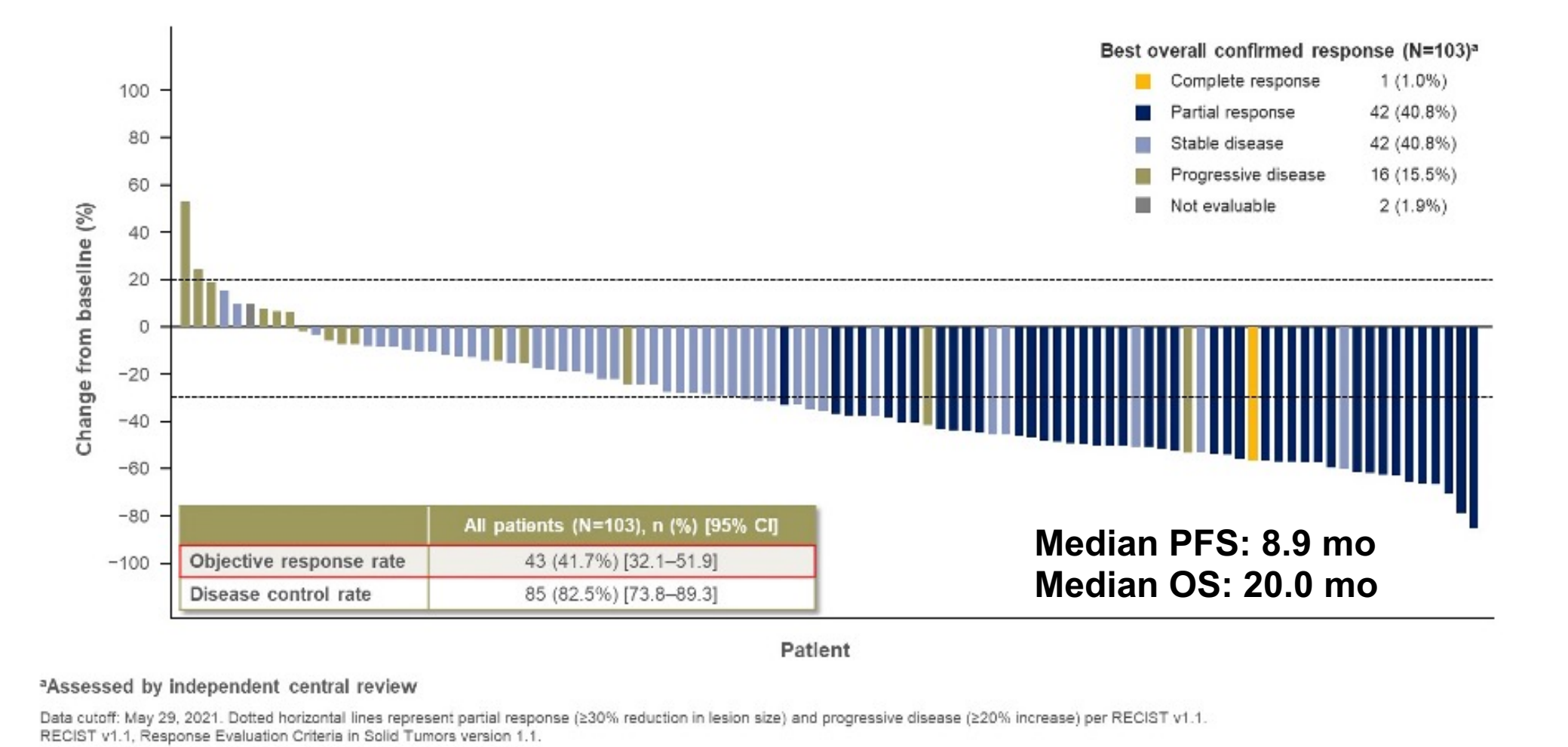
Lipika Goyal,[1] Funda Meric-Bernstam,[2] Antoine Hollebecque,[3] Chigusa Morizane,[4] Juan W. Valle,[5] Thomas B. Karasic,[6] Thomas A. Abrams,[7] Robin Kate Kelley,[8] Philippe Cassier,[9] Junji Furuse,[10] Heinz-Josef Klümpen,[11] Heung-Moon Chang,[12] Li-Tzong Chen,[13] Yoshito Komatsu,[14] Kunihiro 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: A Phase II Study of Futibatinib for Intrahepatic Cholangiocarcinoma with FGFR2 Fusions/Rearrangements

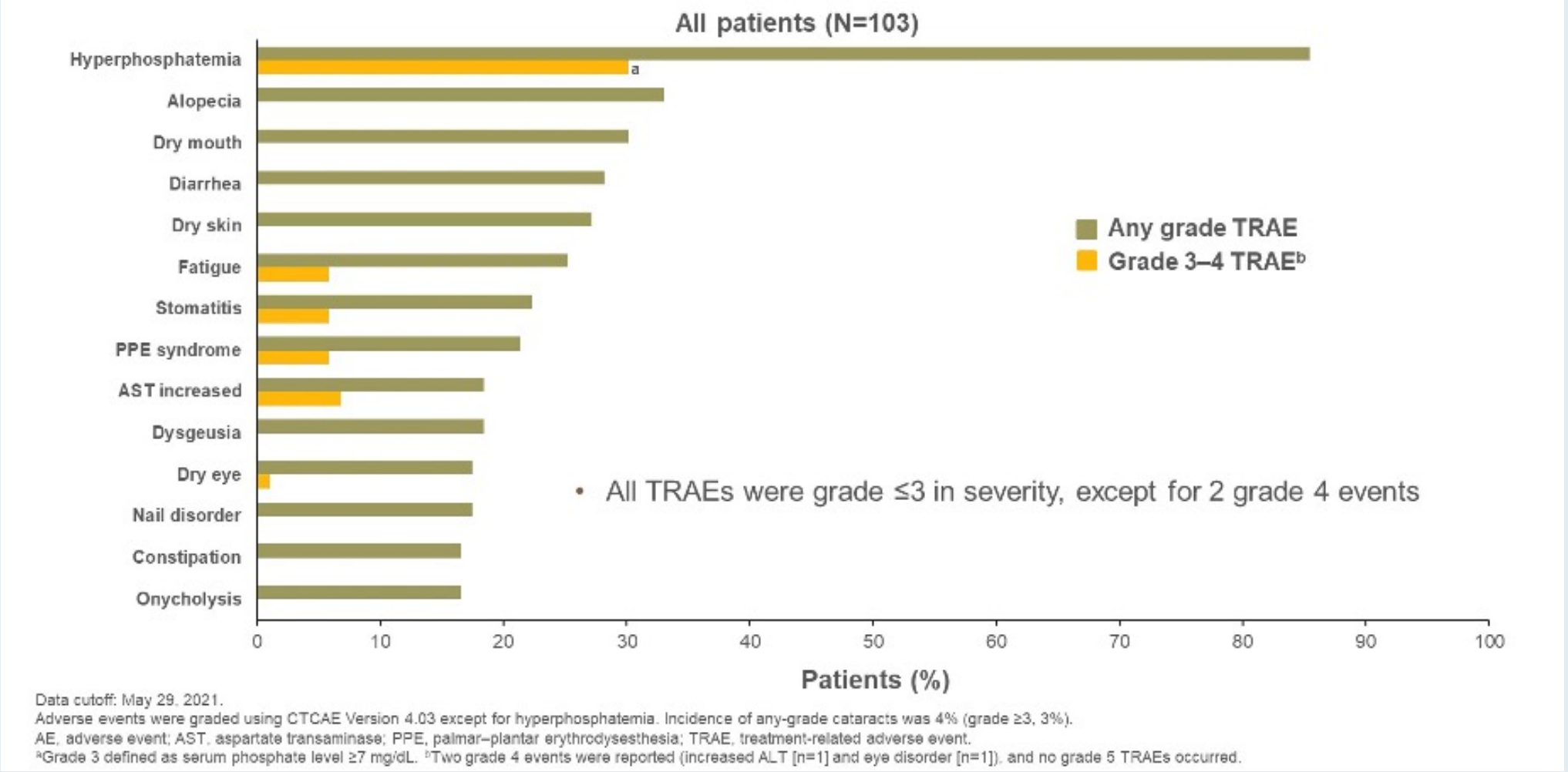


PFS = progression-free survival; OS = overall survival

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

Gastrointestinal Cancers Agenda

Module 1: Colorectal Cancer

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- 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

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Discussion Question

Regulatory and reimbursement issues aside, what initial therapy would you recommend for a fit 60-year-old woman with newly diagnosed metastatic cholangiocarcinoma?

- Gemcitabine and cisplatin
- Gemcitabine, cisplatin and durvalumab
- FOLFOX
- Gemcitabine monotherapy
- Other

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TO PRACTICE

NEJM Evidence

Published June 1, 2022

DOI: 10.1056/EVIDoa2200015

ORIGINAL ARTICLE

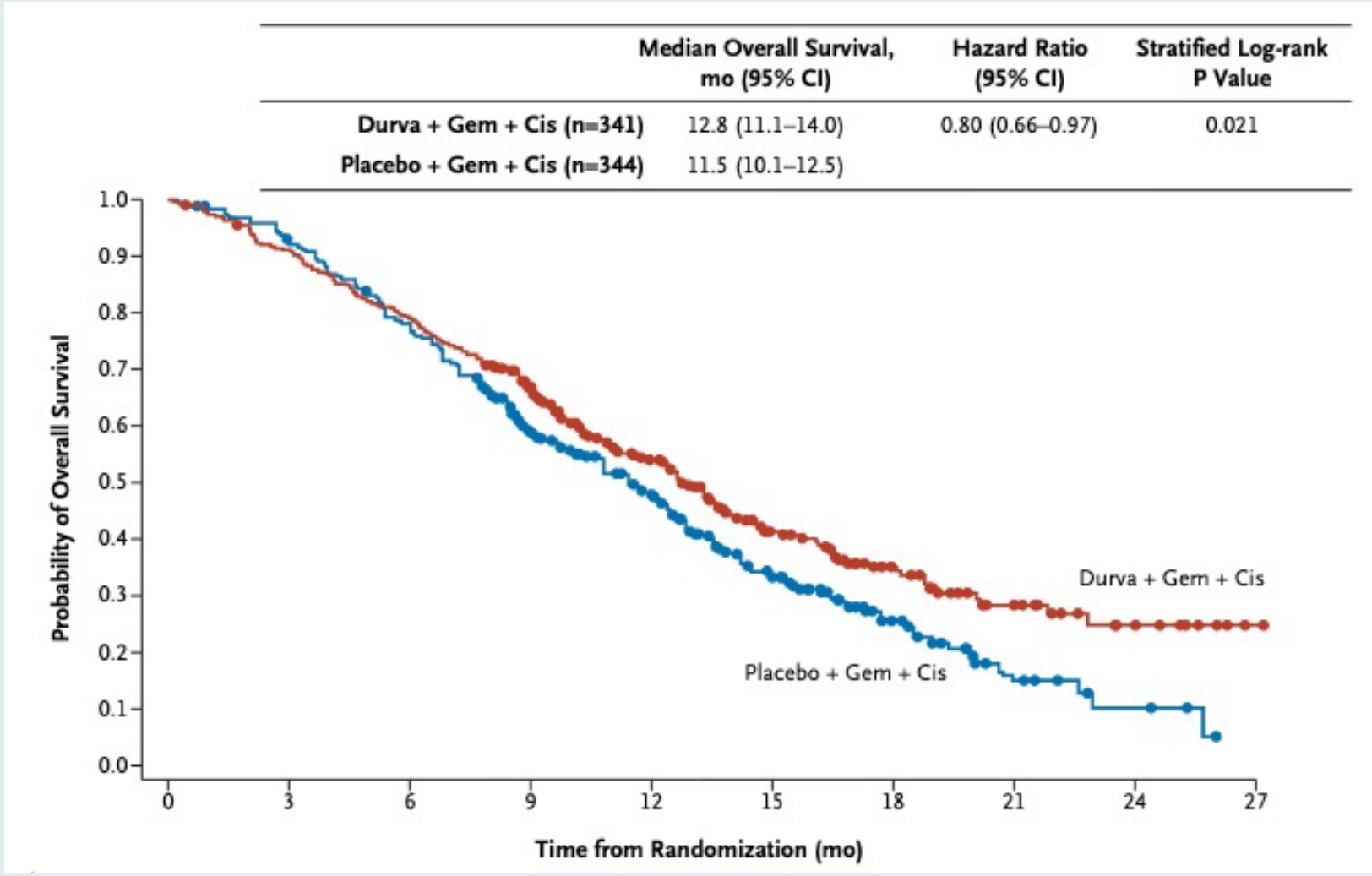
Durvalumab plus Gemcitabine and Cisplatin in Advanced Biliary Tract Cancer

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]

RTP RESEARCH TO PRACTICE

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

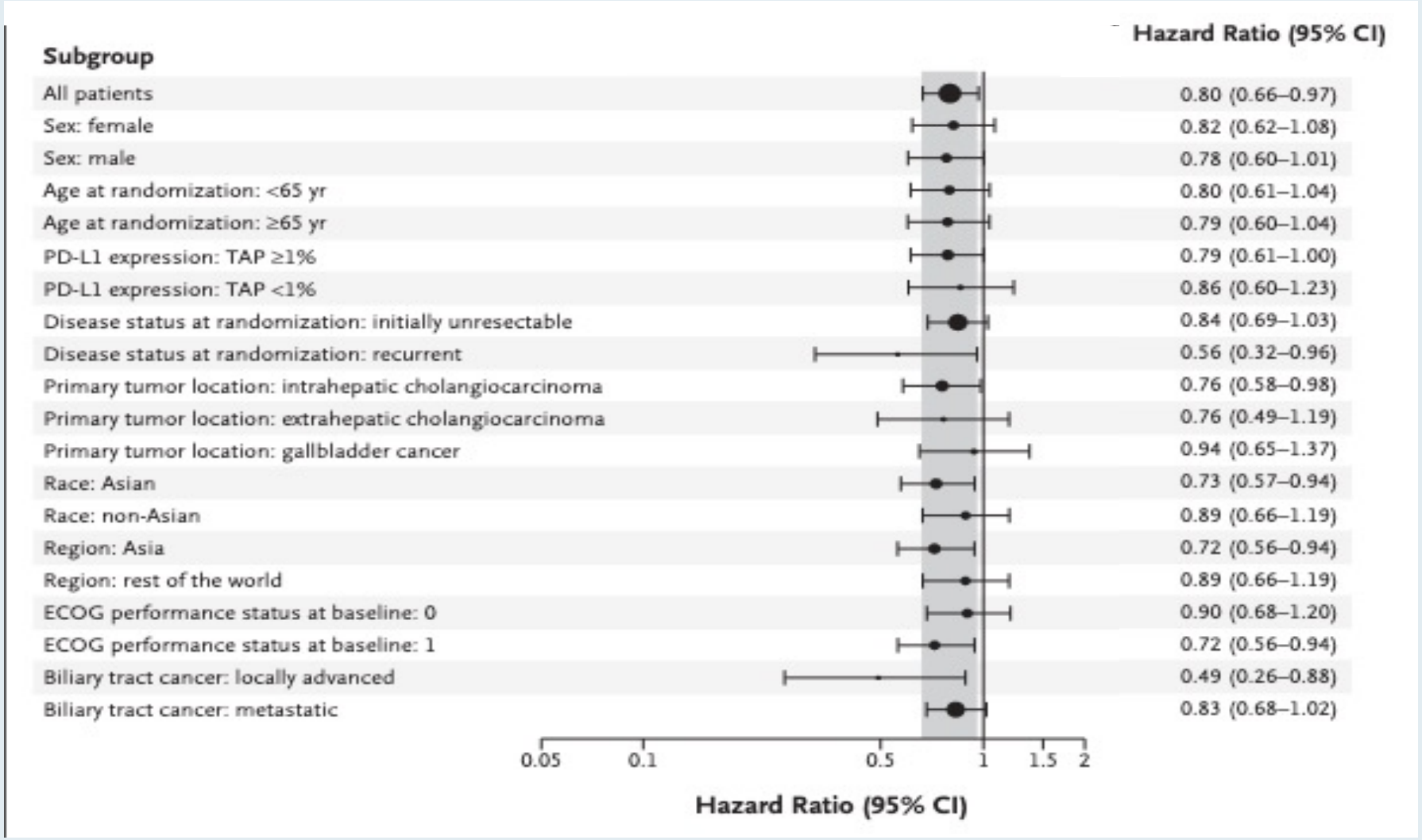
	Median Overall Survival, mo (95% CI)	Hazard Ratio (95% CI)	Stratified Log-rank P Value
Durva + Gem + Cis (n=341)	12.8 (11.1–14.0)	0.80 (0.66–0.97)	0.021
Placebo + Gem + Cis (n=344)	11.5 (10.1–12.5)		



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

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

RTP RESEARCH TO PRACTICE

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.

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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.

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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

- 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

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RESEARCH
TO PRACTICE

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- Potential future role of KRAS-targeted treatment of metastatic pancreatic cancer

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TO PRACTICE

Discussion Question

Have you used or would you use a PARP inhibitor for a patient with metastatic pancreatic cancer?

- I have
- I have not but would for the right patient
- I have not and would not
- I don’t know

RTP RESEARCH TO PRACTICE

original reports

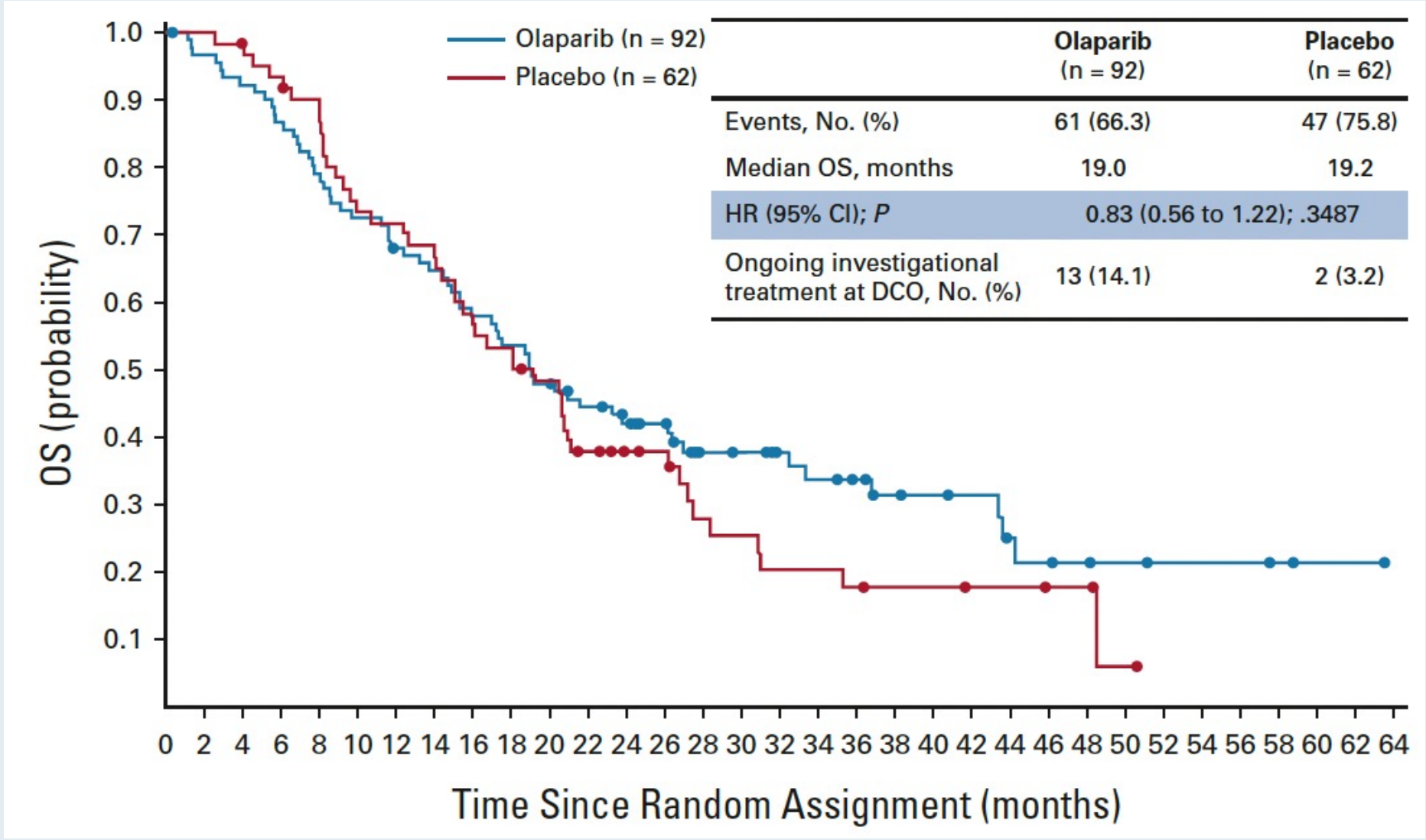
Overall Survival Results From the POLO Trial: A Phase III Study of Active Maintenance Olaparib Versus Placebo for Germline BRCA-Mutated Metastatic Pancreatic Cancer

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].

RTP RESEARCH TO PRACTICE

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].

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

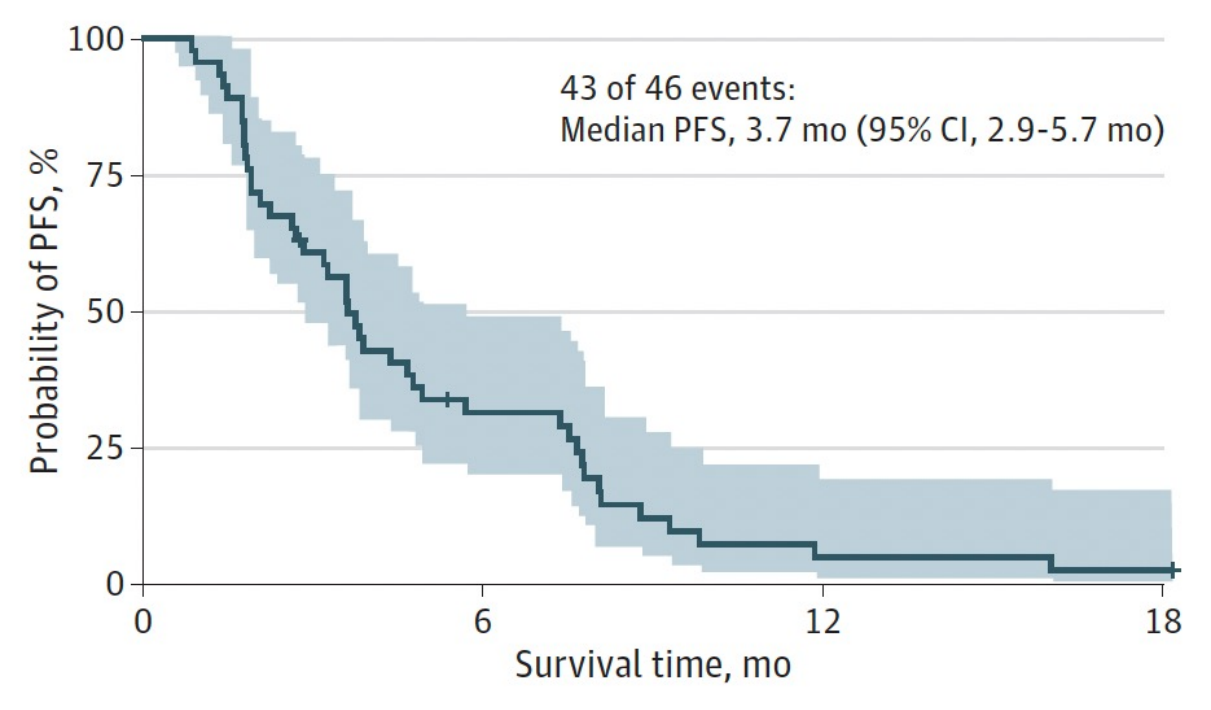
Findings From 2 Phase 2 Nonrandomized Clinical Trials

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

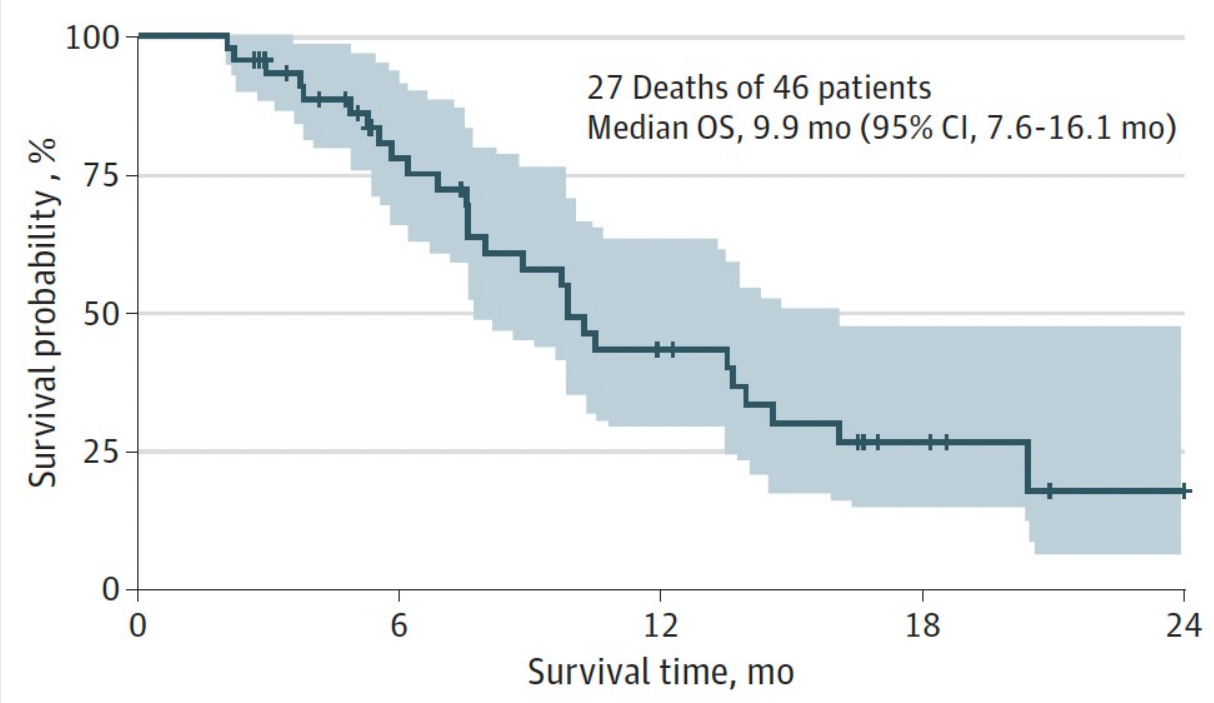
RTP RESEARCH TO PRACTICE

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

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

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RESEARCH
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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

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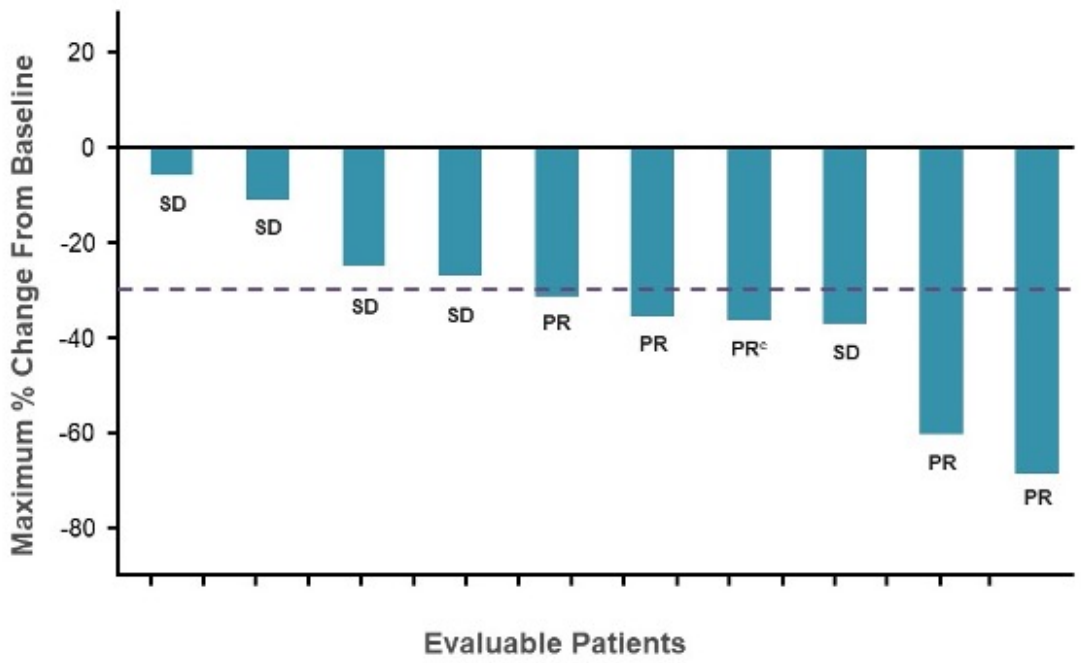
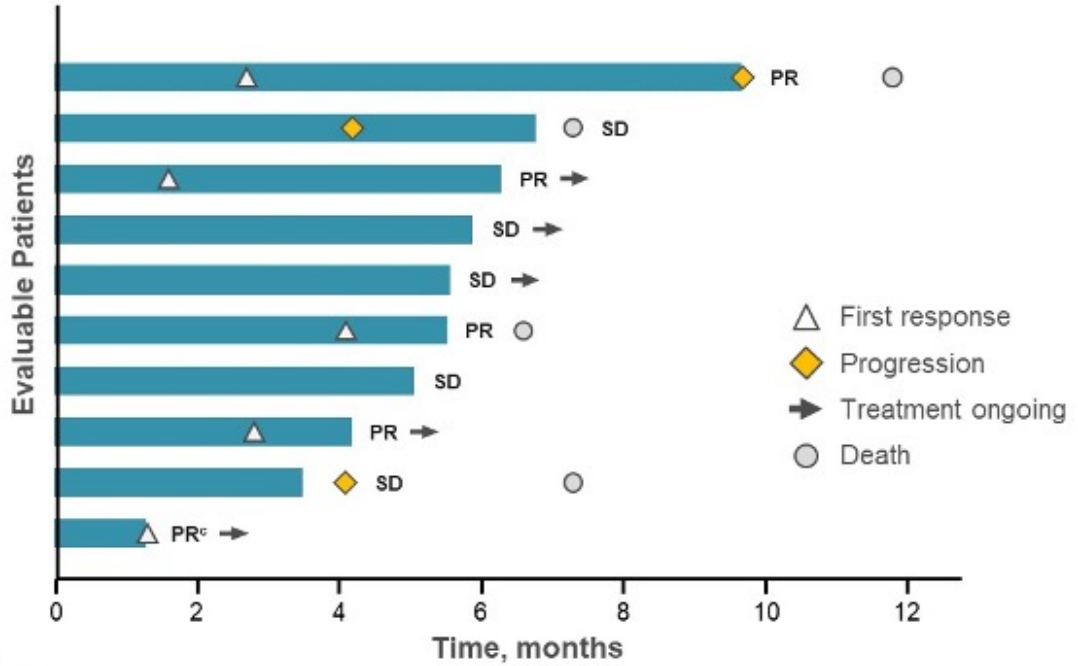
KRYSTAL-1: Best Tumor Change from Baseline and Duration of Treatment with Adagrasib for Unresectable or Metastatic PDAC

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.

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Thank you for joining us!

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

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

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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*

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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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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

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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

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Module 2: Targeted Treatment of NSCLC

Module 3: Small Cell Lung Cancer

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Discussion Question

Have you used or would you use neoadjuvant IO with chemotherapy for a patient with localized NSCLC?

- I have
- I have not, but I would for the right patient
- I have not and would not
- I'm not sure

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Discussion Question

Regulatory and reimbursement issues aside, what initial therapy would you recommend for an otherwise fit 60-year-old patient with T1N2M0, Stage IIIA NSCLC without a driver mutation (PD-1 10%)?

- Chemotherapy/nivolumab followed by surgery
- Surgery followed by adjuvant chemotherapy, then atezolizumab
- Concurrent chemoradiation therapy followed by consolidation durvalumab
- Other

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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

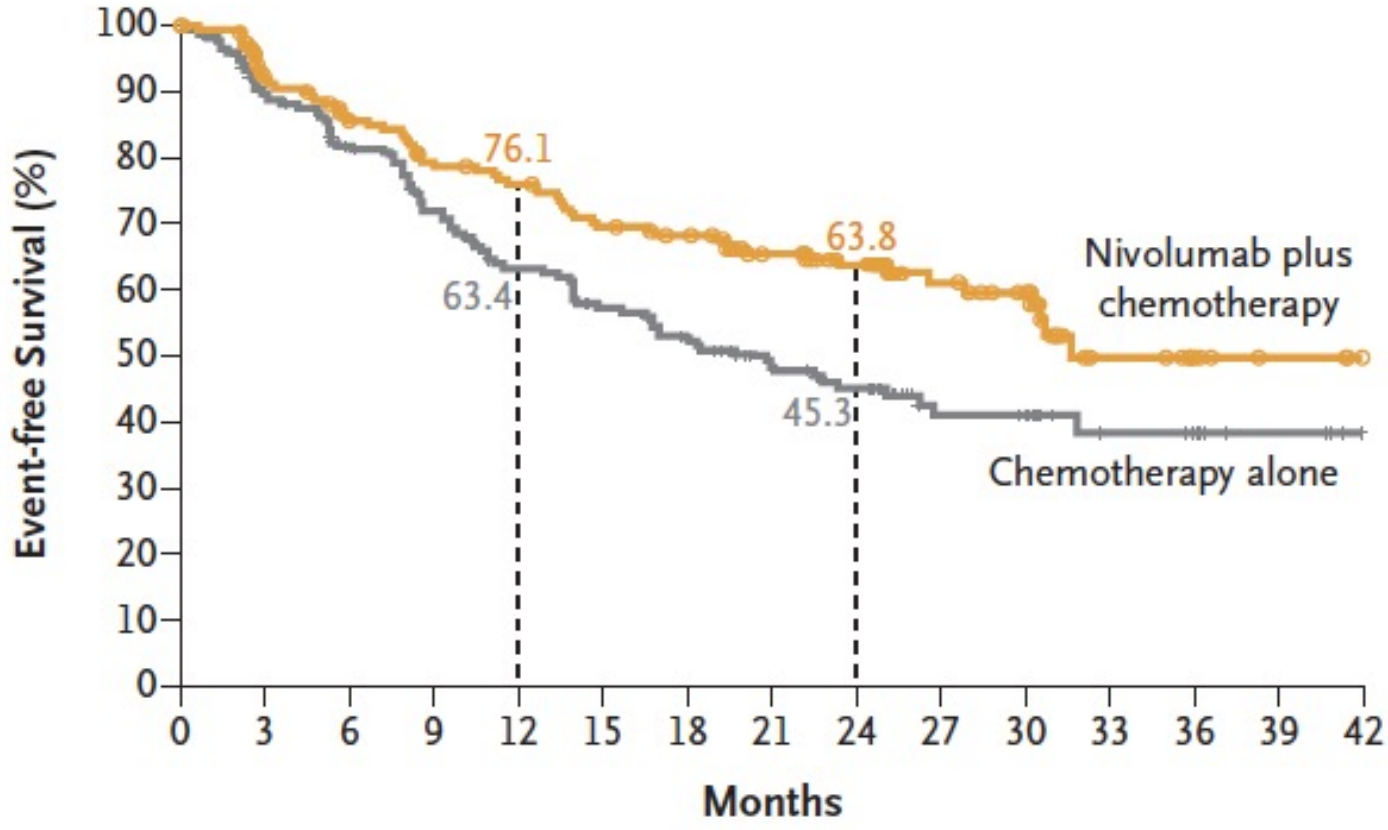
Neoadjuvant Nivolumab plus Chemotherapy in Resectable Lung Cancer

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.**

RTP RESEARCH TO PRACTICE

CheckMate 816 Coprimary Endpoint: Event-Free Survival

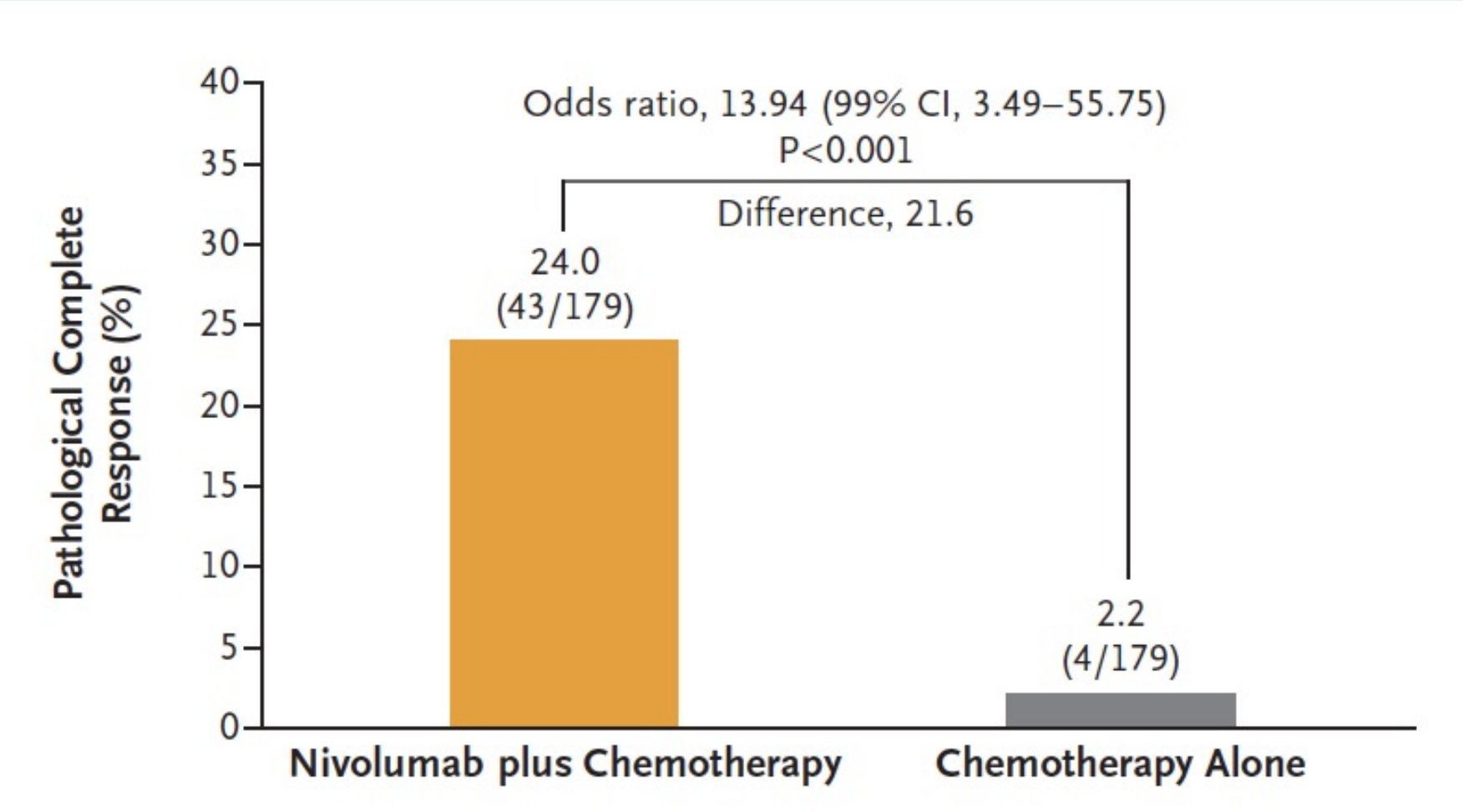


	No. of Patients	Median Event-free Survival (95% CI) *mo*
Nivolumab plus Chemotherapy	179	31.6 (30.2–NR)
Chemotherapy Alone	179	20.8 (14.0–26.7)

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

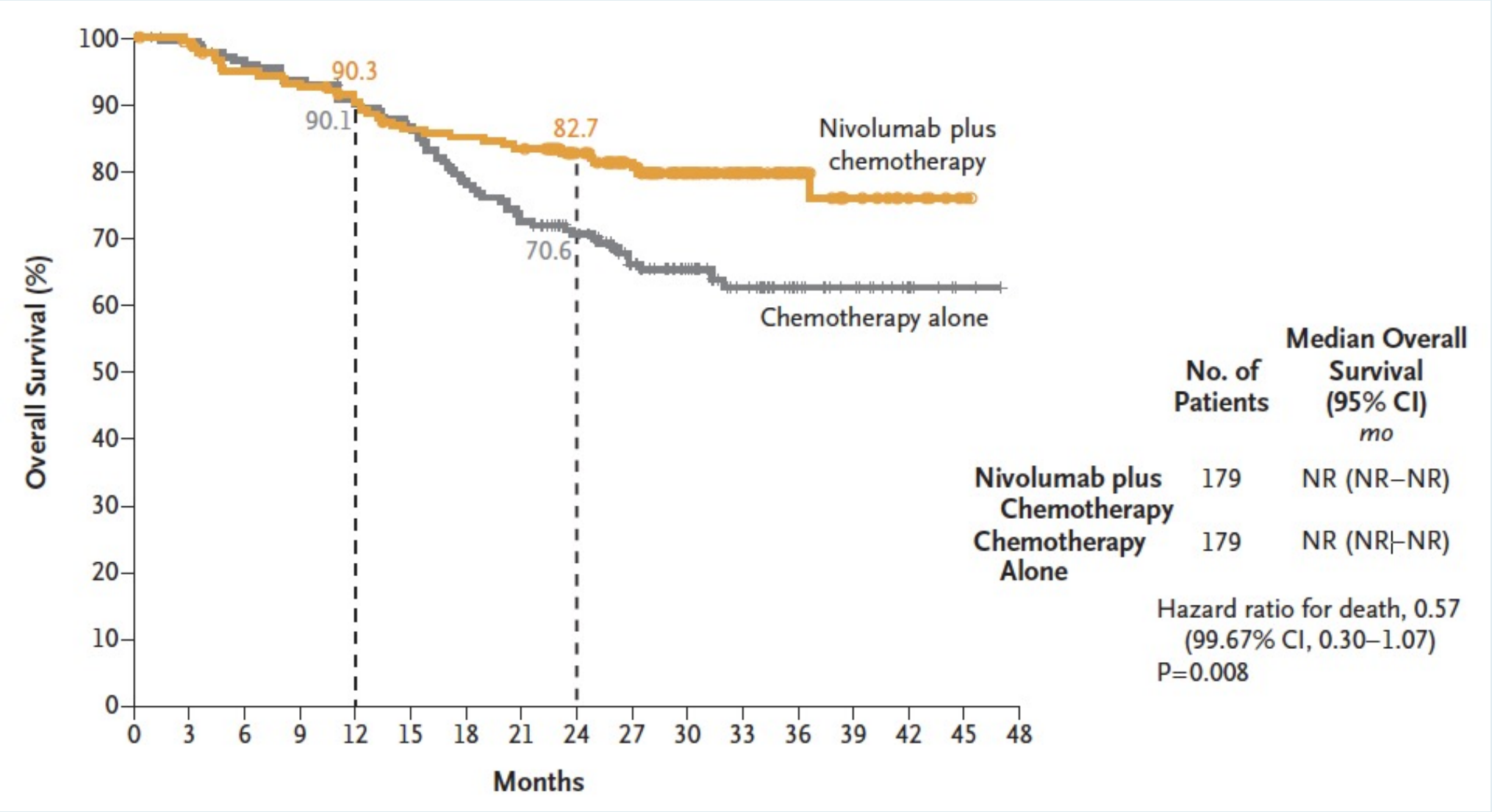
Forde PM et al. *N Engl J Med* 2022;386(21):1973-85.

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.

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

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ESMO VIRTUAL PLENARY

EORTC European Organisation for Research and Treatment of Cancer
The future of cancer therapy

etop
Information | Research

Pembrolizumab Versus Placebo For Early-Stage NSCLC Following Complete Resection and Adjuvant Chemotherapy When Indicated: Randomized, Triple-Blind, Phase 3 EORTC-1416-LCG/ETOP 8-15 – PEARLS/KEYNOTE-091 Study

L. Paz-Ares,[1*] M. O'Brien,[2*] M. Mauer,[3] U. Dafni,[4] K. Oselin,[5] L. Havel,[6] E. Esteban,[7] D. Isla,[8] A. Martinez-Marti,[9] M. Faehling,[10] M. Tsuboi,[11] J.S. Lee,[12] K. Nakagawa,[13] J. Yang,[14] S.M. Keller,[14] N. Jha,[3] S. Marreaud,[3] R. Stahel,[15] S. Peters,[16**] B. Besse[17**] on behalf of the PEARLS/KEYNOTE-091 Investigators

[1]Hospital Universitario 12 de Octubre, CNIO, Ciberonc & Universidad Complutense, Madrid, Spain; [2]Royal Marsden Hospital, London, UK; [3]European Organisation for Research and Treatment of Cancer, Headquarters Brussels, Belgium; [4]National and Kapodistrian University of Athens and Frontier Science Foundation Hellas; [5]North Estonia Medical Centre, Tallinn, Estonia; [6]Charles University and Thomayer Hospital, Prague, Czech Republic; [7]Hospital Universitario Central de Asturias, Oviedo, Spain; [8]University Hospital Lozano Blesa, IIS Aragon, Zaragoza, Spain; [9]Vall d'Hebron Institute of Oncology (VHIO), Vall d'Hebron University Hospital, Barcelona, Spain; [10]Klinikum Esslingen, Esslingen, Germany; [11]National Cancer Center Hospital East, Kashiwa, Japan; [12]Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, South Korea; [13]Kindai University Faculty of Medicine, Osaka, Japan; [14]Merck & Co., Inc., Kenilworth, NJ, USA; [15]European Thoracic Oncology Platform, Bern, Switzerland; [16]Lausanne University Hospital, Lausanne, Switzerland; [17]Institut Gustave Roussy, Villejuif, France
*Drs. Paz-Ares and O'Brien contributed equally to this presentation. **Drs. Peters and Besse contributed equally to this presentation.

ESMO

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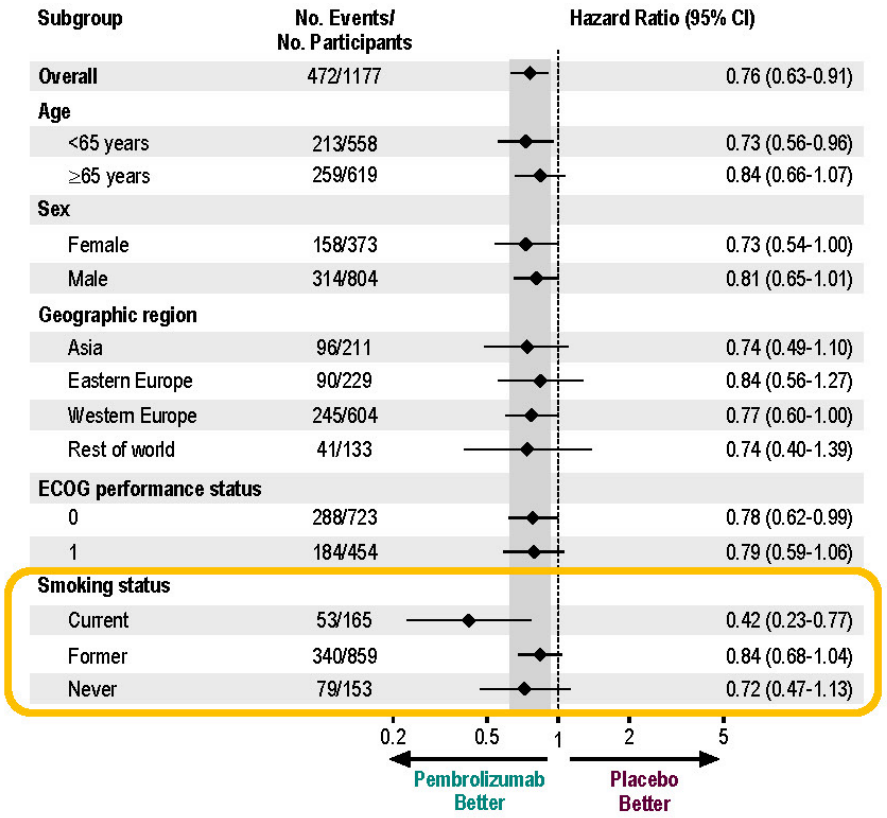
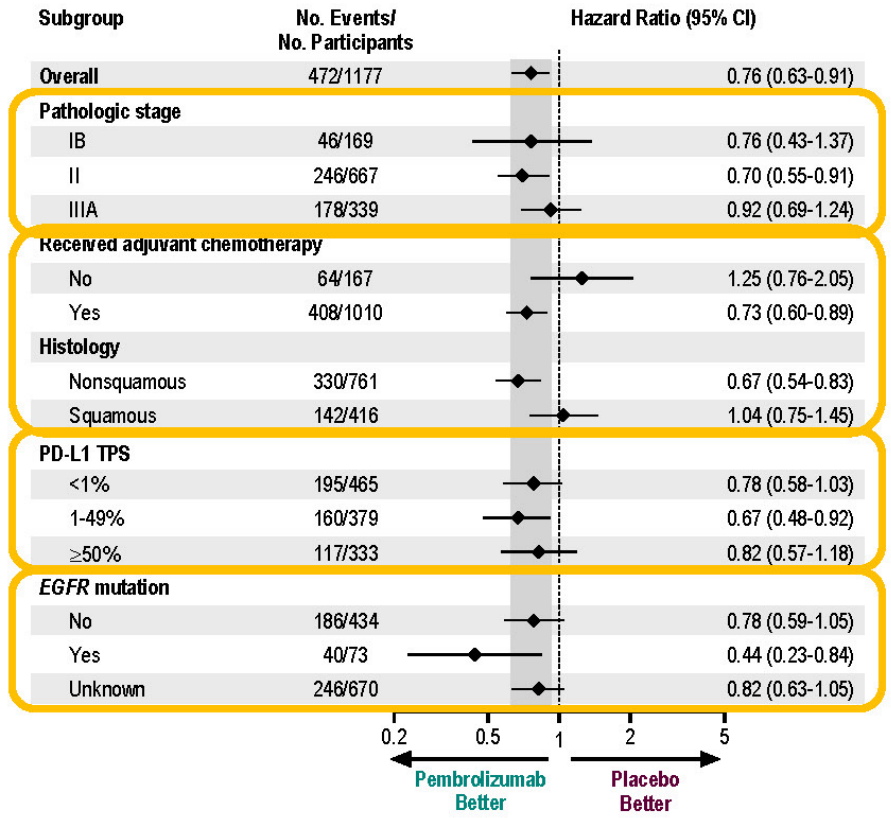
DFS in Key Subgroups, Overall Population





ESMO VIRTUAL PLENARY

Response assessed per RECIST v1.1 by investigator review.
Data cutoff date: September 20, 2021

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Summary and Conclusions

- Pembrolizumab provided statistically significant, clinically meaningful DFS improvement versus placebo in the overall population
  - Median DFS of 53.6 months with pembrolizumab vs 42.0 months with placebo (HR, 0.76)
  - Generally consistent DFS benefit in participants with PD-L1 TPS <1%, 1-49%, and ≥50%
  - OS data are immature
  - DFS in the PD-L1-defined populations and OS will be tested at future analyses according to the analysis plan
- Pembrolizumab safety profile as expected
- **Data suggest pembrolizumab has the potential to be a new adjuvant treatment option for patients with stage IB (T ≥4 cm) to IIIA NSCLC following complete resection and adjuvant chemotherapy when recommended, regardless of PD-L1 expression**

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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.

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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
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Module 2: Targeted Treatment of NSCLC

Module 3: Small Cell Lung Cancer

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Discussion Question

What would you likely recommend as consolidation treatment after chemoradiation therapy for a patient with Stage III NSCLC with an EGFR exon 19 activating mutation?

- Osimertinib
- Durvalumab
- Chemotherapy followed by osimertinib
- None
- Other
- I do not know

RTP RESEARCH TO PRACTICE

original reports

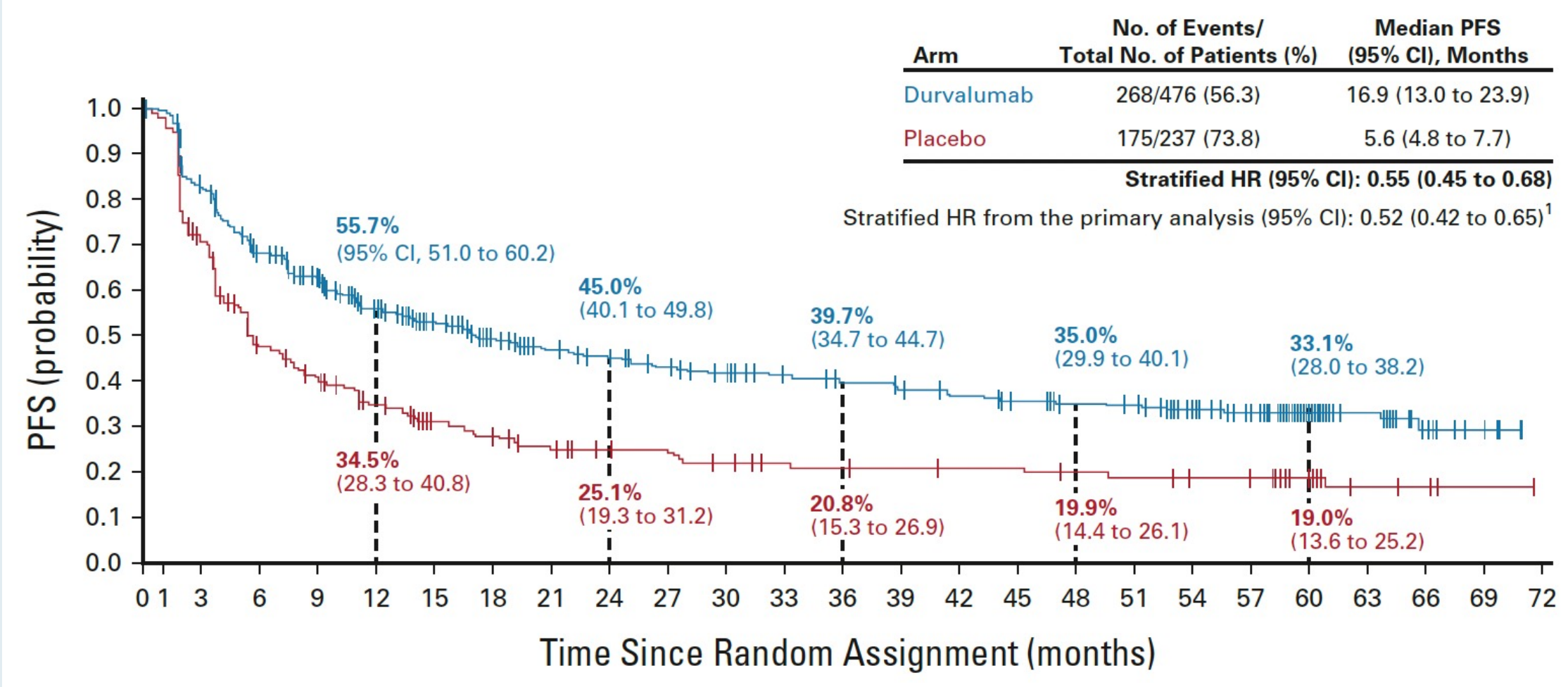
Five-Year Survival Outcomes From the PACIFIC Trial: Durvalumab After Chemoradiotherapy in Stage III Non–Small-Cell Lung Cancer

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.

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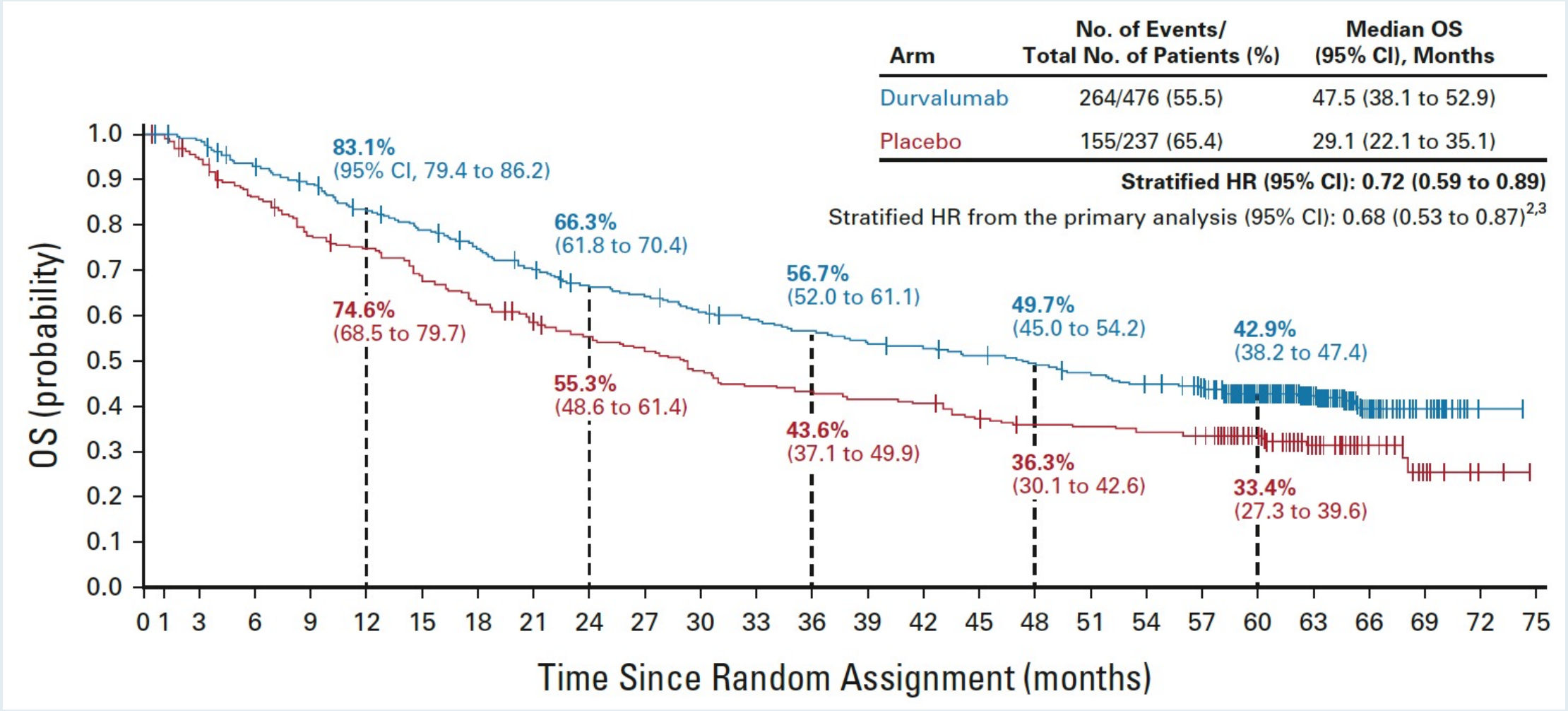
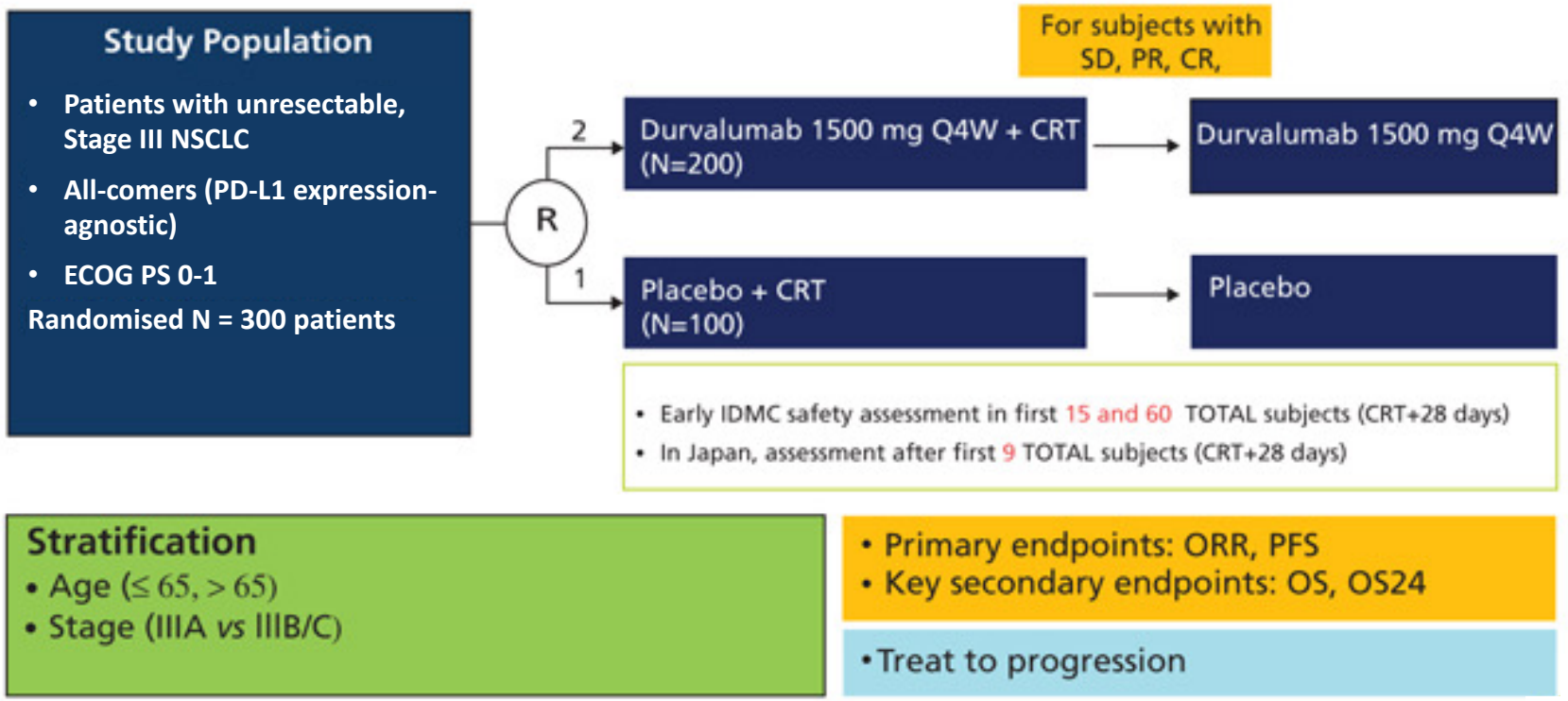
PACIFIC: Five-Year Overall Survival (OS) with Durvalumab After Chemoradiation Therapy for Stage III NSCLC



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

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].

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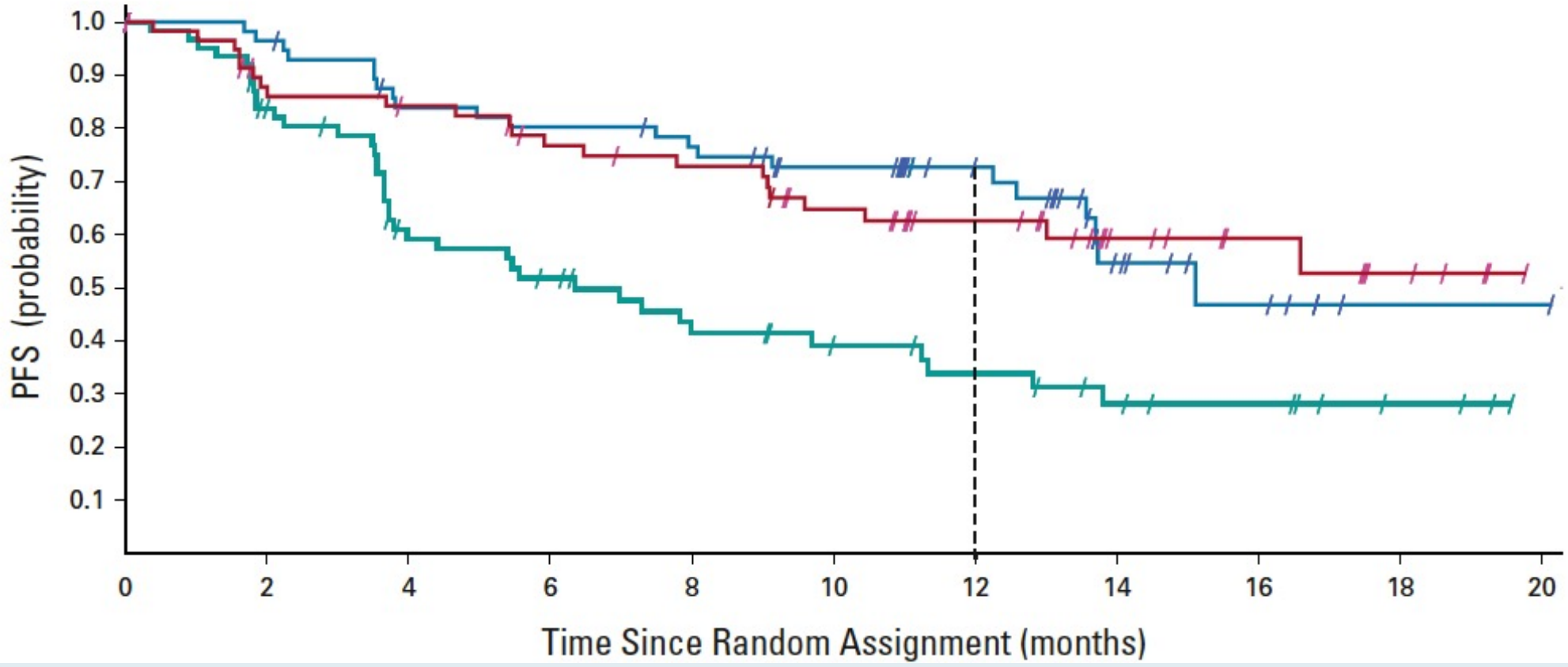
COAST: Progression-Free Survival

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].

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Lung Cancer Agenda

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- 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

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Discussion Question

What first-line treatment would you likely recommend to a 60-year-old asymptomatic patient with low-volume, nonvisceral disease, a PD-1 level of 65% and no actionable driver mutations?

- Pembrolizumab
- Ipilimumab and nivolumab
- Cemiplimab
- Pembrolizumab and chemotherapy
- Atezolizumab
- Atezolizumab, bevacizumab and chemotherapy
- Other

RTP RESEARCH TO PRACTICE

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.

RTP RESEARCH TO PRACTICE

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.

RTP RESEARCH TO PRACTICE

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 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.

RTP RESEARCH TO PRACTICE

Durvalumab ± Tremelimumab + Chemotherapy as First-Line Treatment for mNSCLC: Results from the Phase 3 POSEIDON Study

Melissa L Johnson,[1] Byoung Chul Cho,[2] Alexander Luft,[3] Jorge Alatorre-Alexander,[4] Sarayut Lucien Geater,[5] Konstantin Laktionov,[6] Aleksandr Vasiliev,[7] Dmytro Trukhin,[8] Sang-We Kim,[9] Grygorii Ursol,[10] Maen Hussein,[11] Farah Louise Lim,[12] Cheng-Ta Yang,[13] Luiz Henrique Araujo,[14] Haruhiro Saito,[15] Niels Reinmuth,[16] Xiaojin Shi,[17] Lynne Poole,[18] Solange Peters,[19] Edward B Garon,[20] Tony Mok[21]

[1]Sarah Cannon Research Institute, Tennessee Oncology, PLLCC, Nashville, TN, USA; [2]Yonsei Cancer Center, Seoul, Korea; [3]Leningrad Regional Clinical Hospital, St Petersburg, Russia; [4]Health Pharma Professional Research, Mexico City, Mexico; [5]Prince of Songkla University, Songkhla, Thailand; [6]Federal State Budgetary Institution "N.N. Blokhin National Medical Research Center of Oncology" of the Ministry of Health of the Russian Federation (N.N. Blokhin NMRCO), Moscow, Russia; [7]"Private Health Institution "Clinical Hospital" RZD-Medicine", St Petersburg, Russia; [8]Odessa Regional Oncological Dispensary, Odessa, Ukraine; [9]Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; [10]Acinus, Kropyvnytskyi, Ukraine; [11]Florida Cancer Specialists – Sarah Cannon Research Institute, Leesburg, FL, USA; [12]Queen Mary University of London, London, United Kingdom; [13]Chang Gung Memorial Hospital, Taoyuan City, Taiwan; [14]Instituto Nacional de Cancer-INCA, Rio de Janeiro, Brazil; [15]Kanagawa Cancer Center, Yokohama, Japan; [16]Asklepios Lung Clinic, Munich-Gauting, Germany; [17]AstraZeneca, Gaithersburg, MD, USA; [18]AstraZeneca, Cambridge, UK; [19]Centre Hospitalier Universitaire Vaudois, Lausanne University, Lausanne, Switzerland; [20]David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; [21]Chinese University of Hong Kong, Hong Kong, China

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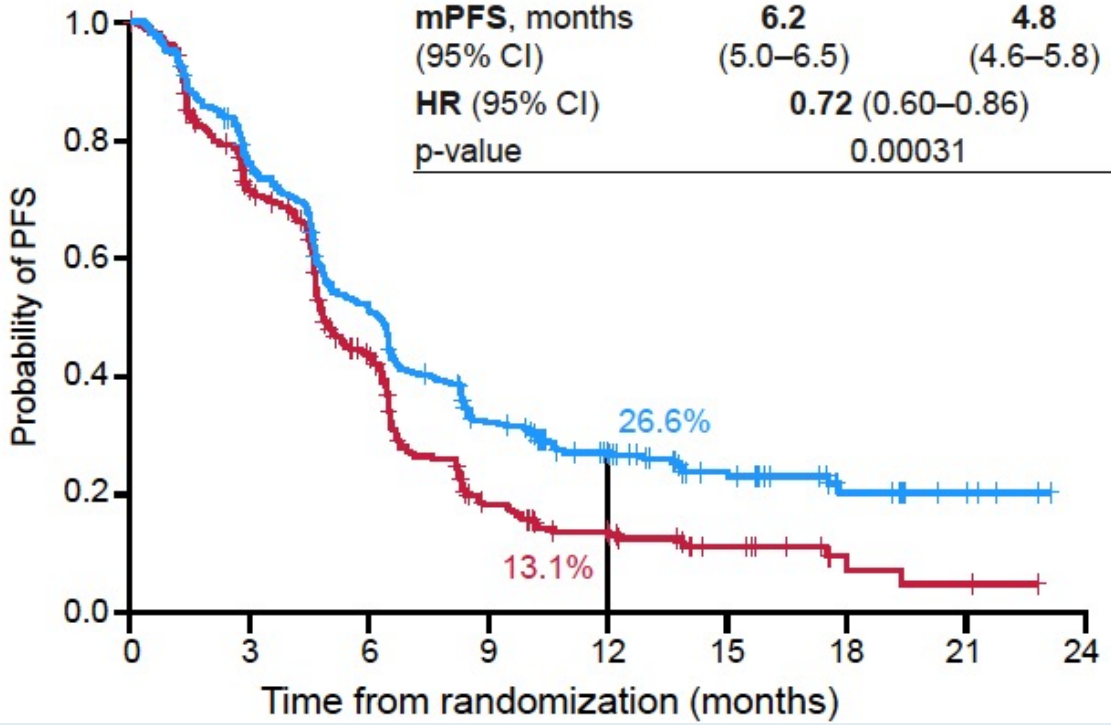
Abstract PL02.01

RTP RESEARCH TO PRACTICE

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

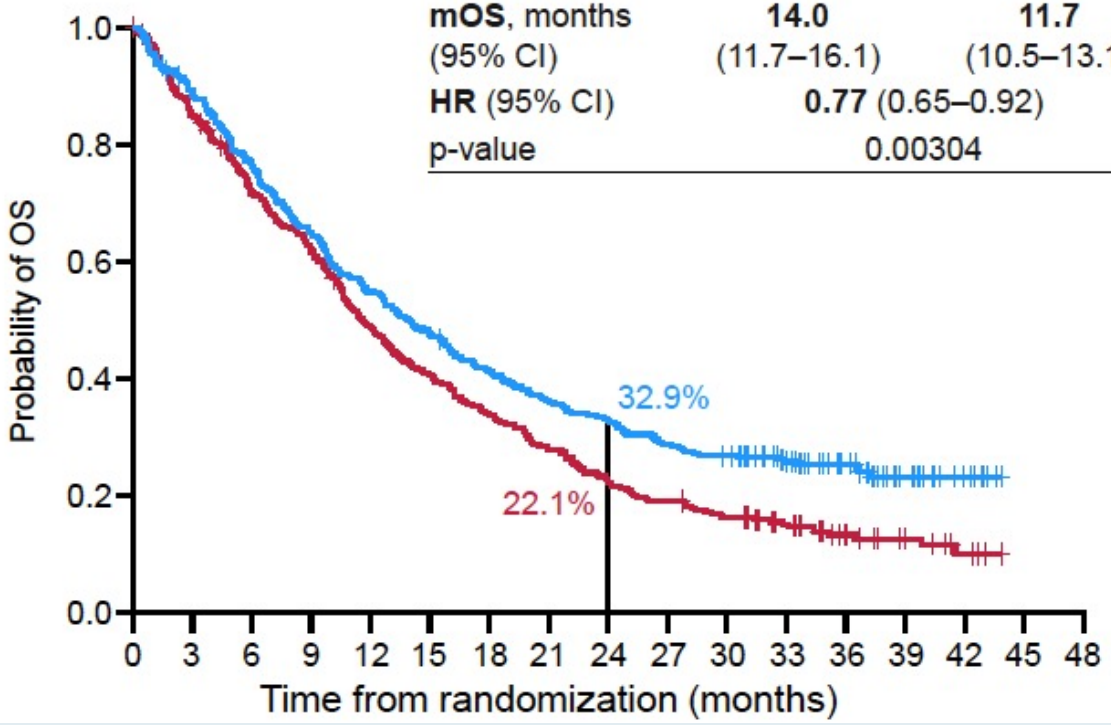
PFS

	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

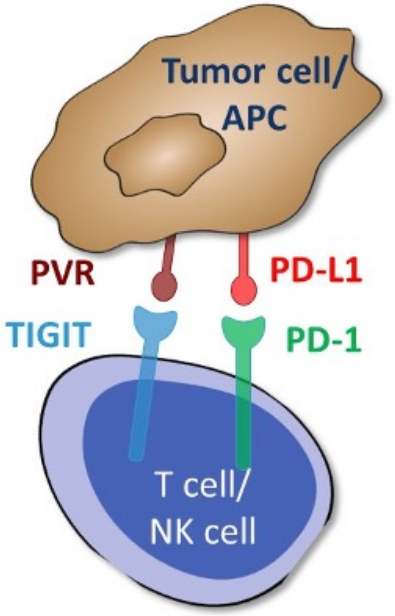


Figure adapted from Manieri et al. *Trends Immunology* 2017

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.

RTP RESEARCH TO PRACTICE

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

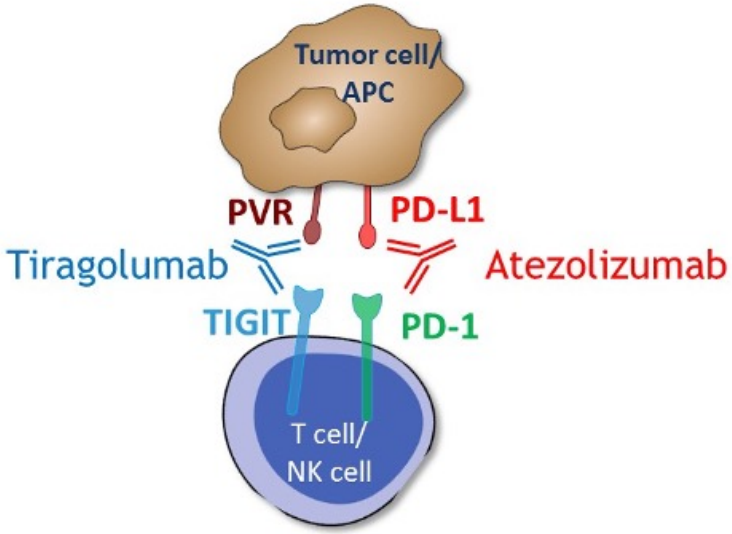
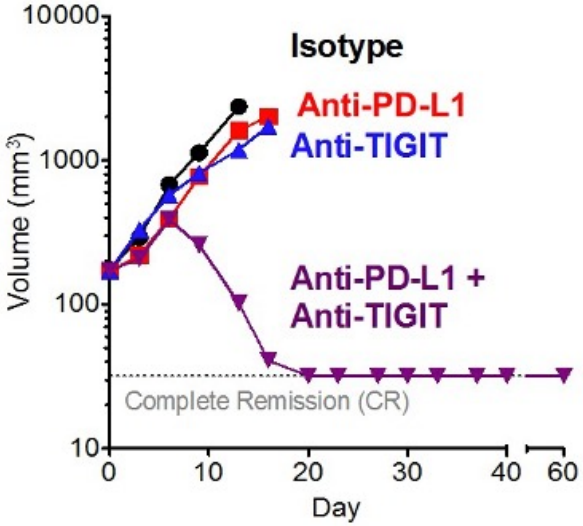


Figure adapted from Manieri et al. *Trends Immunology* 2017

- 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

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Rodriguez-Abreu D et al. ASCO 2020;Abstract 9503.

RTP RESEARCH TO PRACTICE

ESMO IMMUNO-ONCOLOGY 2021

Onsite and Online Congress

Updated analysis and patient-reported outcomes from CITYSCAPE: a randomised, double-blind, Phase II study of the anti-TIGIT antibody tiragolumab + atezolizumab vs placebo + atezolizumab as first-line treatment for PD-L1+ NSCLC

Byoung Chul Cho,[1] Delvys Rodriguez-Abreu,[2] Maen Hussein,[3] Manuel Cobo,[4] Anjan Patel,[5] Nevena Secen,[6] Gregory Gerstner,[7] Dong-Wan Kim,[8] Yun-Gyoo Lee,[9] Wu-Chou Su,[10] Elizabeth Huang,[11] Namrata Patil,[12] Meilin Huang,[12] Zoe Zhang,[12] Xiaohui Wen,[12] Diana Mendus,[12] Tien Hoang,[12] Raymond Meng,[12] Melissa Johnson[13]

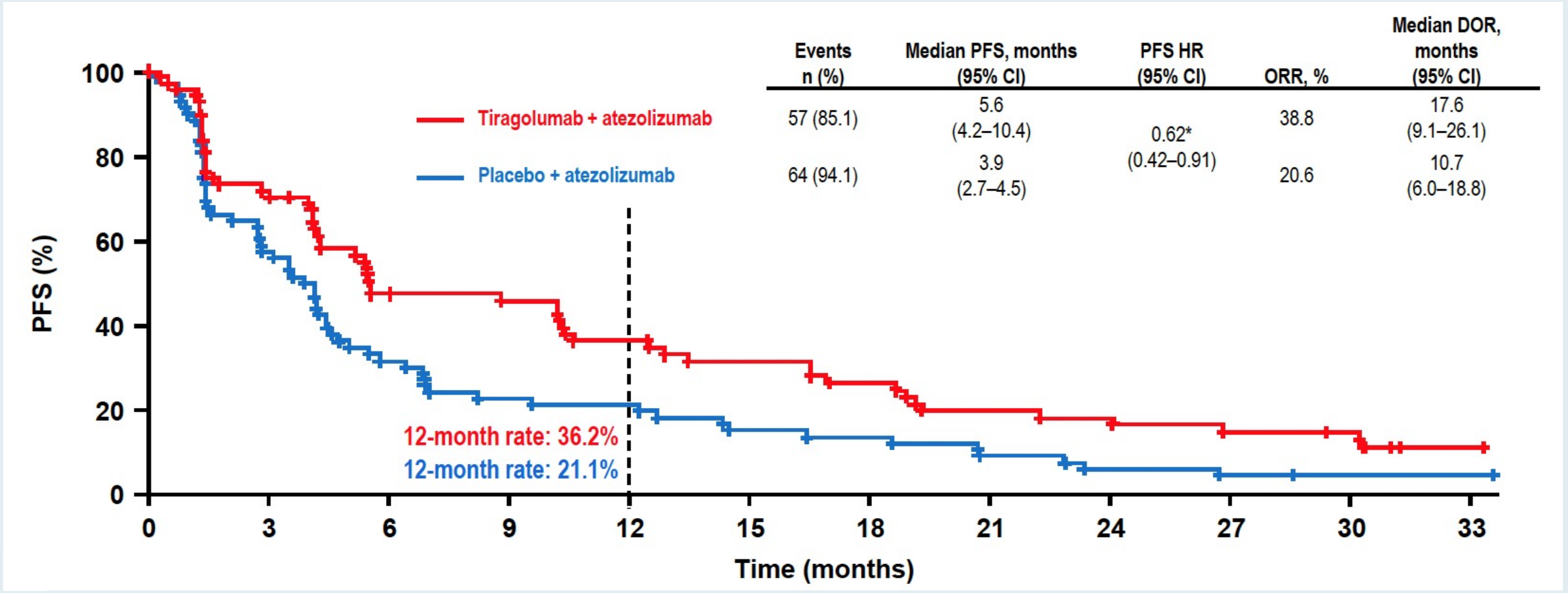
1. Severance Hospital, Yonsei University Health System, Seoul, Korea; 2. Hospital Universitario Gran Canaria, Las Palmas, Spain; 3. Florida Cancer Specialists, Leesburg, Florida, USA; 4. Hospital Regional Universitario de Malaga, Malaga, Spain; 5. Florida Cancer Specialists, Sarasota, Florida, USA; 6. Institute of Lung Diseases Vojvodina, Sremska Kamenica, Serbia; 7. Illinois Cancer Care, Peoria, Illinois, USA; 8. Seoul National University College of Medicine and Seoul National University Hospital, Seoul, South Korea; 9. Sungkyunkwan University School of Medicine, Kangbuk Samsung Hospital Seoul, South Korea; 10. National Cheng Kung University Hospital, Tainan City, Taiwan; 11. Roche Products Ltd., Welwyn Garden City, UK; 12. Genentech, Inc., South San Francisco, USA; 13. Sarah Cannon Research Institute and Tennessee Onc., PLLC Nashville, Tennessee, USA

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Abstract LBA2

RTP RESEARCH TO PRACTICE

CITYSCAPE: Investigator-Assessed PFS (ITT 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

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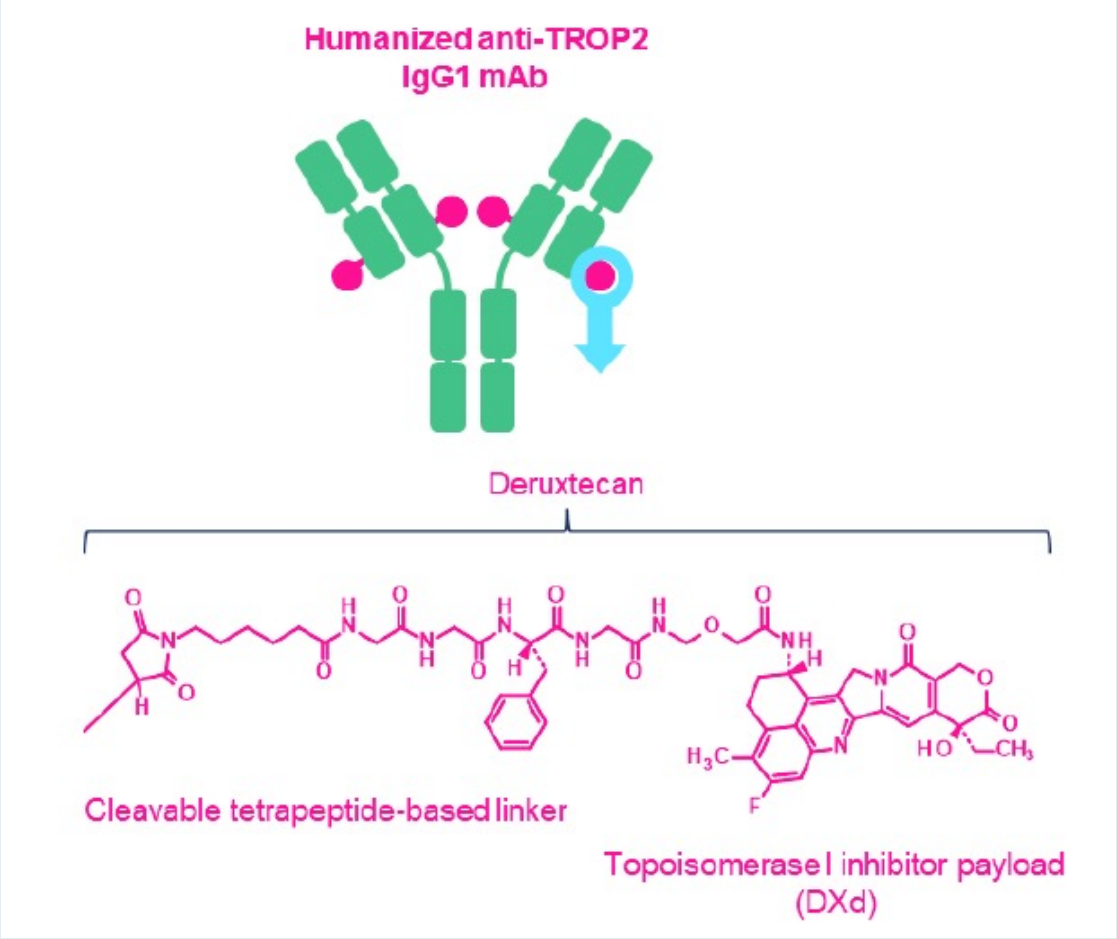
Targeting TROP2 with Datopotamab Deruxtecan (Data-DXd)

- 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.

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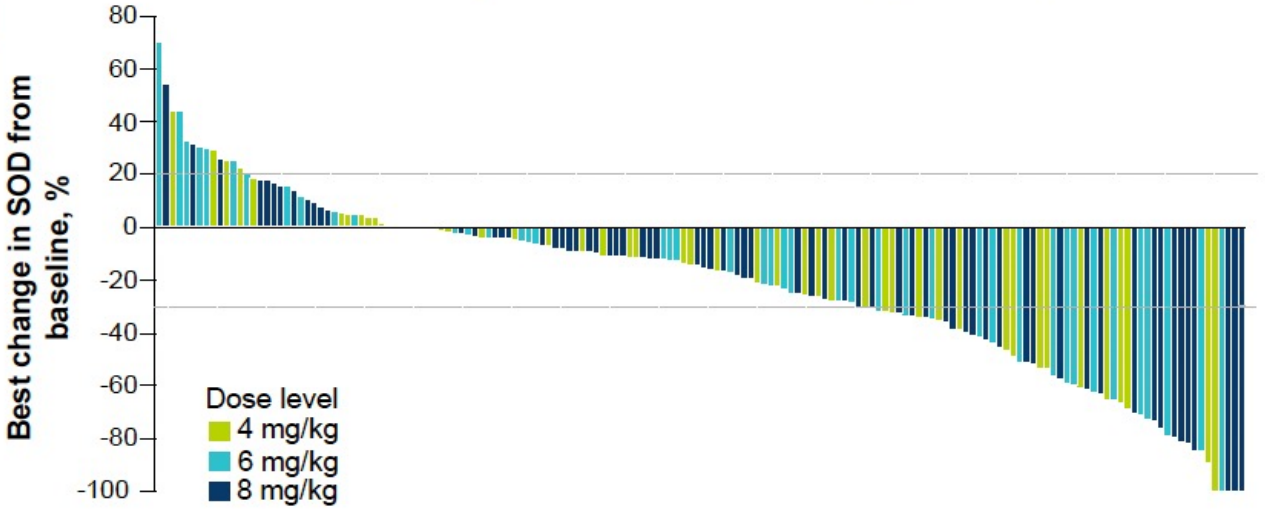
TROPION-PanTumor01: Antitumor Activity of Data-DXd

Best Overall Response (BICR)

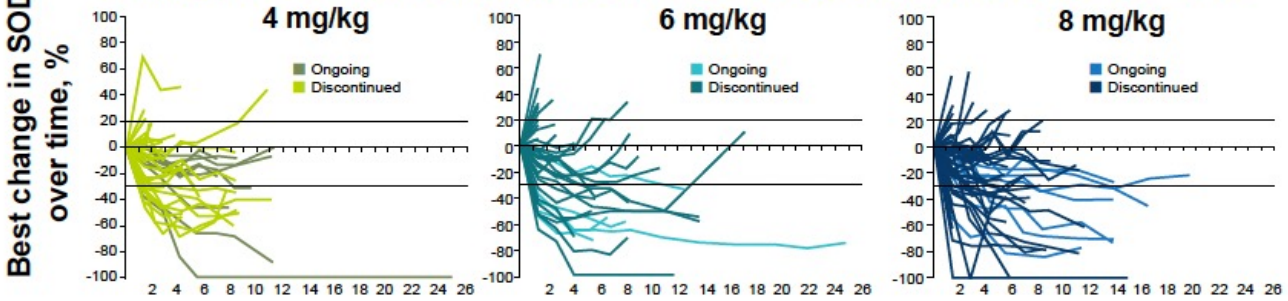
Patients[a]	Dato-DXd dose		
	4 mg/kg (n=50)	6 mg/kg (n=50)	8 mg/kg (n=80)
ORR, n (%)[b]	12 (24)	14 (28)	19 (24)
CR, n (%)	0	0	1 (1)
PR, n (%)[b]	12 (24)	14 (28)	18 (23)
SD, n (%)	25 (50)	20 (40)	42 (53)
Non-CR/PD, n (%)	1 (2)	2 (4)	2 (3)
PD, n (%)	7 (14)	10 (20)	8 (10)
NE, n (%)	5 (10)	5 (10)	9 (11)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

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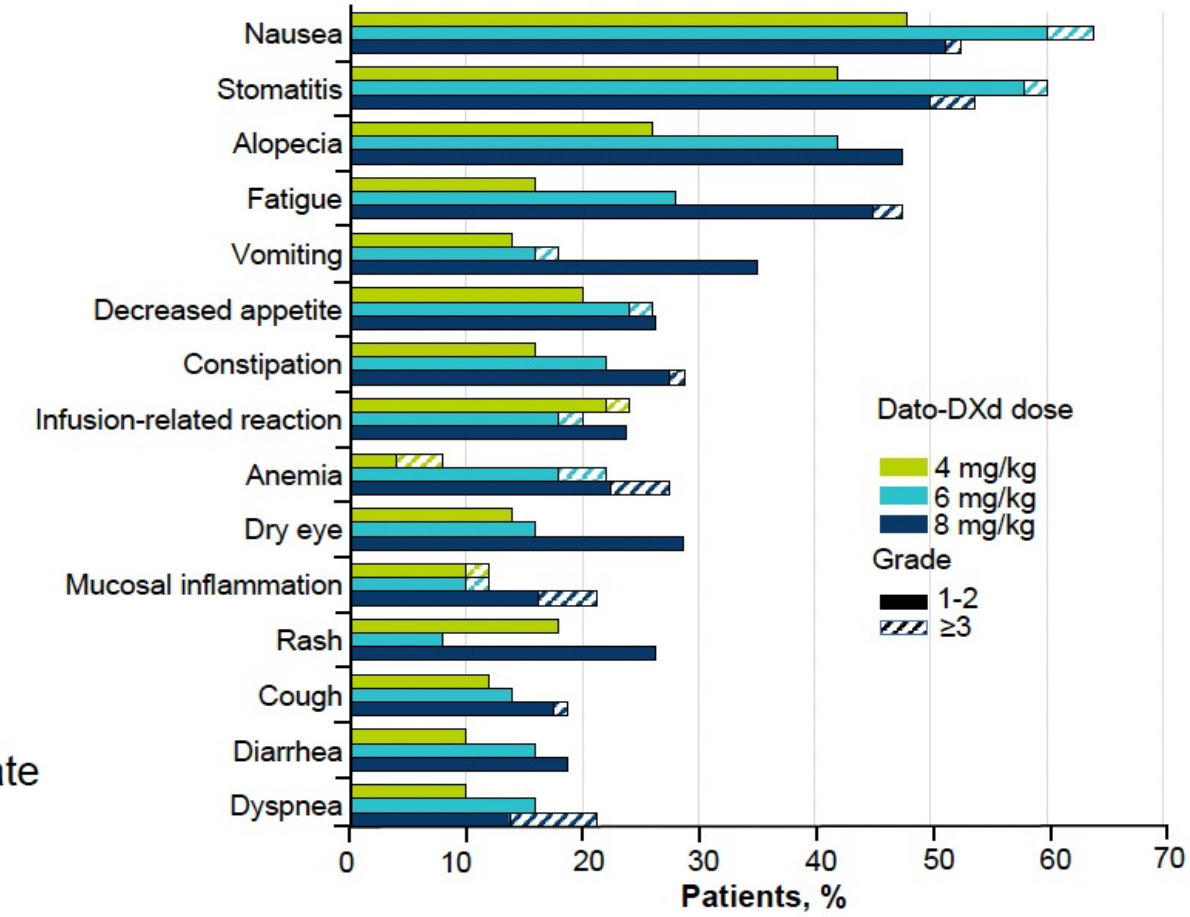
TROPION-PanTumor01: Safety and Treatment-Emergent Adverse Events

Overall Safety Summary

Patients, n (%)	Dato-DXd dose 4 mg/kg (n=50)	6 mg/kg (n=50)	8 mg/kg (n=80)
TEAE	49 (98)	49 (98)	80 (100)
Grade ≥3	15 (30)	27 (54)	46 (58)
Drug-related TEAE	47 (94)	41 (82)	78 (98)
Grade ≥3	7 (14)	13 (26)	28 (35)
Serious TEAE	10 (20)	24 (48)	40 (50)
Grade ≥3	10 (20)	18 (36)	37 (46)
Dose adjustments			
TEAEs associated with discontinuation	8 (16)	7 (14)	19 (24)
TEAEs associated with dose interruption	4 (8)	15 (30)	29 (36)
TEAEs associated with dose reduction	1 (2)	5 (10)	23 (29)
ILD adjudicated as drug related[a]	5 (10)	3 (6)	11 (14)
Grade ≤2	4 (8)	2 (4)	7 (9)
Grades 3-4	1 (2)	1 (2)	1 (1)
Grade 5	0	0	3 (4)

- The safety profile was manageable with mainly mild/moderate toxicity; TEAEs were primarily nonhematologic

TEAEs in ≥15% of Patients[b]



Garon EB et al. 2021 WCLC;Abstract MA03.02.

2021 ESMO congress

Abstract LBA49

Efficacy of Datopotamab Deruxtecan (Dato-DXd) in Patients With Advanced/Metastatic Non-Small Cell Lung Cancer (NSCLC) and Actionable Genomic Alterations (AGAs): Preliminary Results From the Phase 1 TROPION-PanTumor01 Study

Edward B. Garon,[1] Melissa L. Johnson,[2] Aaron E. Lisberg,[1] Alexander Spira,[3] Noboru Yamamoto,[4] Rebecca S. Heist,[5] Jacob M. Sands,[6] Kiyotaka Yoh,[7] Funda Meric-Bernstam,[8] Satoru Kitazono,[9] Jonathan Greenberg,[10] Fumiaki Kobayashi,[11] Yui Kawasaki,[11] Lori Jukofsky,[10] Kota Nakamura,[10] Toshio Shimizu[4]

[1]David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; [2]Sarah Cannon Research Institute, Tennessee Oncology, PLLC/OneOncology, Nashville, TN, USA; [3]Virginia Cancer Specialists, Fairfax, VA, USA; [4]Department of Experimental Therapeutics, National Cancer Center Hospital, Tokyo, Japan; [5]Massachusetts General Hospital, Boston, MA, USA; [6]Dana-Farber Cancer Institute, Boston, MA, USA; [7]National Cancer Center Hospital East, Chiba, Japan; [8]The University of Texas, MD Anderson Cancer Center, Houston, TX, USA; [9]The Cancer Institute Hospital of JFCR, Tokyo, Japan; [10]Daiichi Sankyo, Inc, Basking Ridge, NJ, USA; [11]Daiichi Sankyo Co, Ltd, Tokyo, Japan

RTP RESEARCH TO PRACTICE

Phase I TROPION-PanTumor01 (NSCLC Cohort): Antitumor Activity of Dato-DXd in NSCLC with Actionable Genomic Alterations

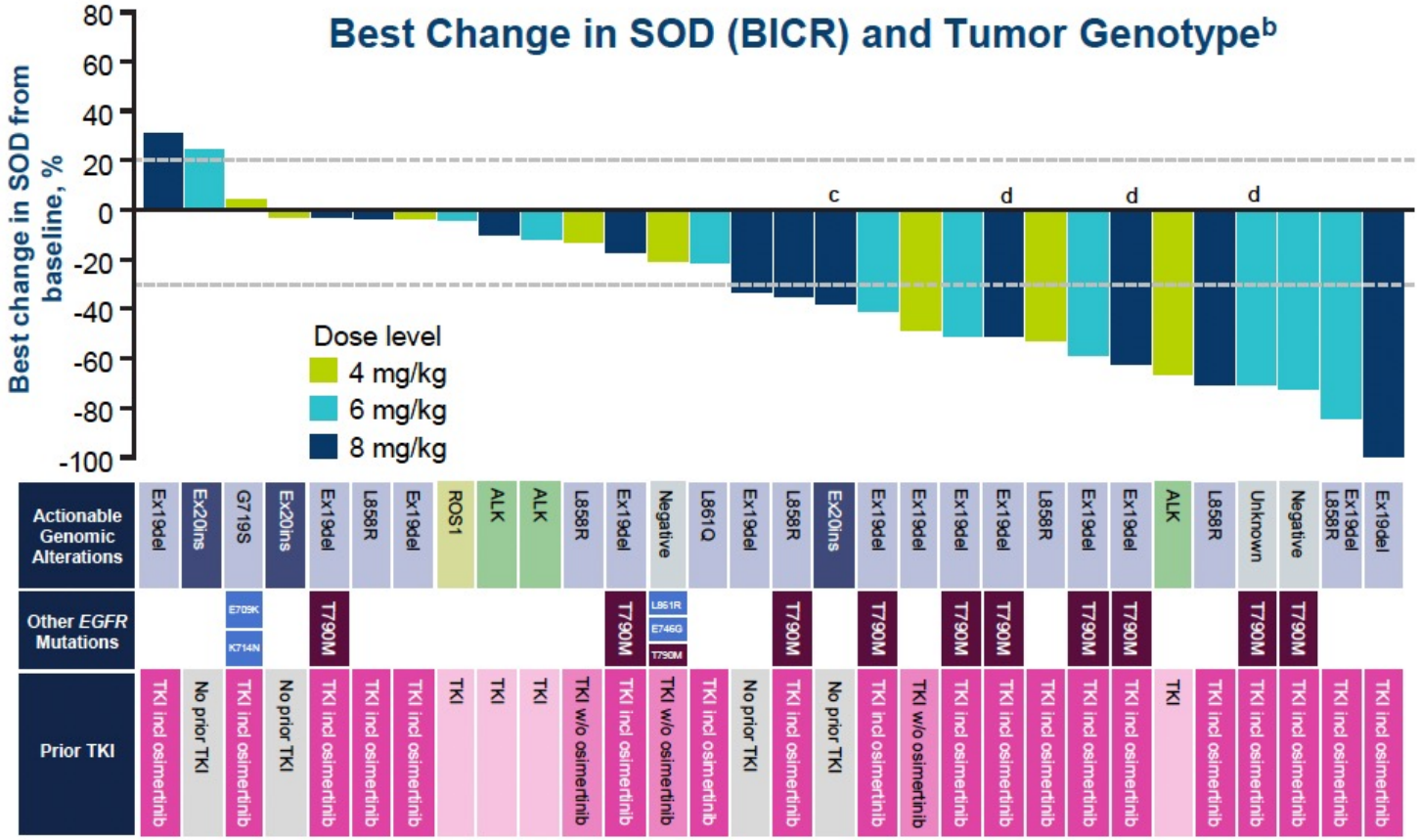
Best Overall Response (BICR)

Patients[a]	Dato-DXd n=34
ORR, n (%)	12 (35)
CR	0
PR	12 (35)
SD, n (%)	14 (41)
Non-CR/PD, n (%)	2 (6)
PD, n (%)	2 (6)
NE, n (%)	4 (12)
DOR, median (95% CI), mo	9.5 (3.3-NE)

- Clinical activity was observed in *EGFR* (Ex19del, L858R) including after osimertinib and across other AGAs

Data cutoff: April 6, 2021.

Best Change in SOD (BICR) and Tumor Genotype[b]



Garon EB et al. ESMO 2021;Abstract LBA49.

RTP RESEARCH TO PRACTICE

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

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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

- **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

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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

- **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

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Discussion Question

Regulatory and reimbursement issues aside, in general, what adjuvant treatment, if any, would you recommend for an otherwise healthy 65-year-old patient with Stage IB nonsquamous NSCLC with an EGFR exon 19 deletion and a PD-L1 TPS of 50%?

- None
- Chemotherapy
- Osimertinib
- Chemotherapy → osimertinib
- Chemotherapy → atezolizumab
- Chemotherapy → osimertinib + atezolizumab
- Atezolizumab
- Other

RTP RESEARCH TO PRACTICE

Discussion Question

In general, would you recommend durvalumab after chemoradiation therapy for a patient with a PD-L1 level of 0?

- Yes
- No
- I'm not sure

RTP RESEARCH TO PRACTICE

CLINICAL CANCER RESEARCH | CLINICAL TRIALS: TARGETED THERAPY

Health-Related Quality of Life Outcomes in Patients with Resected Epidermal Growth Factor Receptor–Mutated Non–Small Cell Lung Cancer Who Received Adjuvant Osimertinib in the Phase III ADAURA Trial

Margarita Majem[1], Jonathan W. Goldman[2], Thomas John[3], Christian Grohe[4], Konstantin Laktionov[5], Sang-We Kim[6], Terufumi Kato[7], Huu Vinh Vu[8], Shun Lu[9], Shanqing Li[10], Kye Young Lee[11], Charuwan Akewanlop[12], Chong-Jen Yu[13], Filippo de Marinis[14], Laura Bonanno[15], Manuel Domine[16], Frances A. Shepherd[17], Shinji Atagi[18], Lingmin Zeng[19], Dakshayini Kulkarni[20], Nenad Medic[21], Masahiro Tsuboi[22], Roy S. Herbst[23], and Yi-Long Wu[24]

***Clin Cancer Res* 2022;[Online ahead of print].**

RTP RESEARCH TO PRACTICE

FDA Grants Breakthrough Therapy Status to Patritumab Deruxtecan for EGFR-Positive Metastatic NSCLC

Press Release – January 4, 2022

"Patritumab deruxtecan (U3-1402), a potential first-in-class HER3 directed antibody-drug conjugate, was granted breakthrough therapy designation by the FDA for the treatment of patients with metastatic or locally advanced, *EGFR*-mutant non–small cell lung cancer (NSCLC).

Data from a phase 1 trial (NCT03260491) assessing the efficacy of patritumab deruxtecan in a heavily pretreated population of patients with EGFR-mutant NSCLC that have become resistant to other TKIs were read out at the 2021 American Society of Clinical Oncology Annual Meeting: Lung Cancer.

A 5.6 mg/kg dose of the treatment resulted in a confirmed objective response rate of 39% in a population of patients who were previously treated with a TKI and platinum-based therapy (n = 57). Additionally, treatment with patritumab deruxtecan resulted in a disease control rate of 72%, as well as a median progression-free survival of 8.2 months (95% CI, 4.0–not evaluable)."

https://www.cancernetwork.com/view/fda-grants-breakthrough-therapy-status-to-patritumab-deruxtecan-for-egfr-metastatic-nsclc

RTP RESEARCH TO PRACTICE

RESEARCH ARTICLE

Cancer Discov 2022;12(1):74-89.

Efficacy and Safety of Patritumab Deruxtecan (HER3-DXd) in EGFR Inhibitor–Resistant, *EGFR*-Mutated Non–Small Cell Lung Cancer

Pasi A. Jänne[1], Christina Baik[2], Wu-Chou Su[3], Melissa L. Johnson[4], Hidetoshi Hayashi[5], Makoto Nishio[6], Dong-Wan Kim[7], Marianna Koczywas[8], Kathryn A. Gold[9], Conor E. Steuer[10], Haruyasu Murakami[11], James Chih-Hsin Yang[12], Sang-We Kim[13], Michele Vigliotti[14], Rong Shi[14], Zhenhao Qi[14], Yang Qiu[14], Lihui Zhao[14], David Sternberg[14], Channing Yu[14], and Helena A. Yu[15]

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.

RTP RESEARCH TO PRACTICE

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

2022 ASCO® ANNUAL MEETING

Abstract 9006

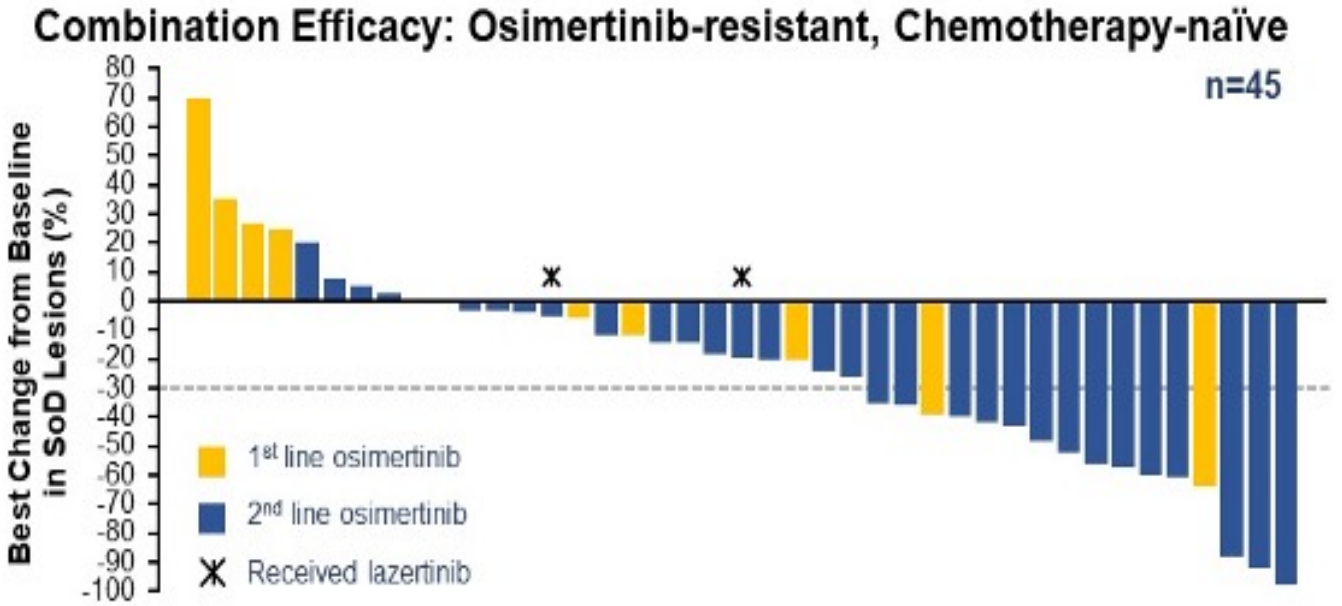
Amivantamab and lazertinib in patients with EGFR-mutant non-small cell lung cancer (NSCLC) after progression on osimertinib and platinum-based chemotherapy: Updated results from CHRYSALIS-2

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

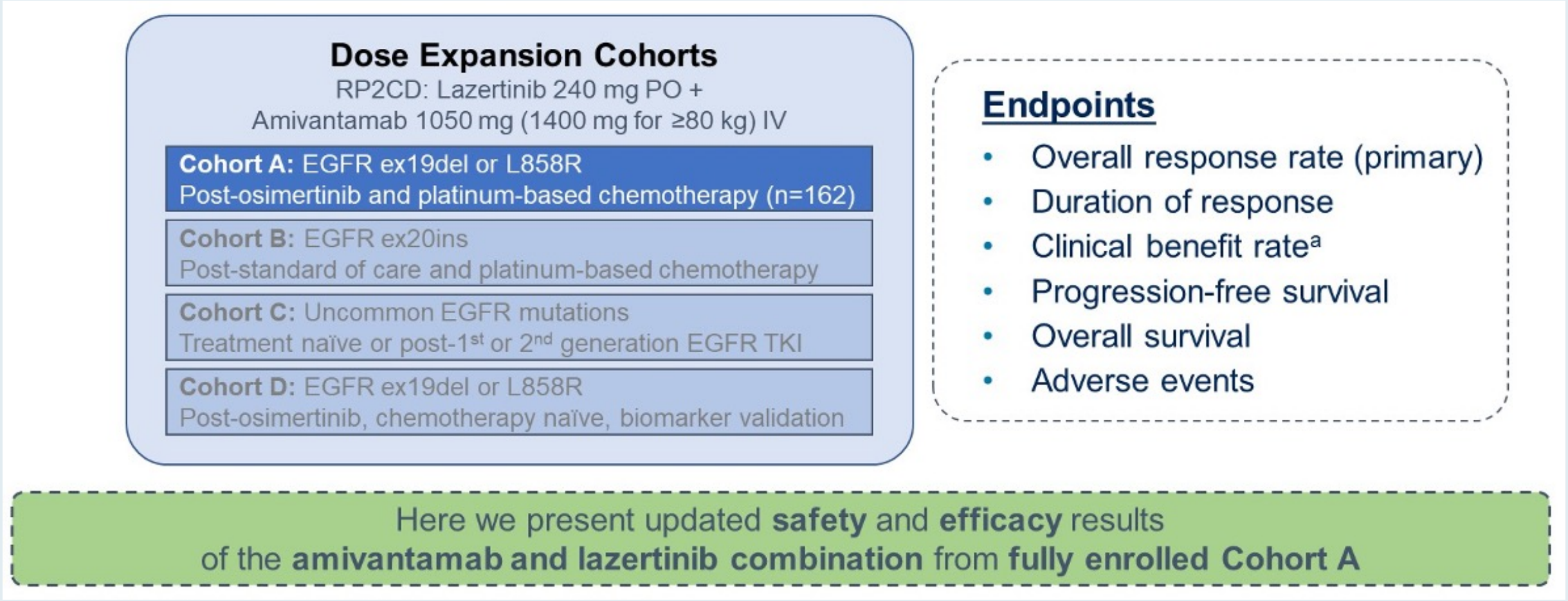
- Amivantamab[a] is an EGFR-MET bispecific antibody with immune cell-directing activity[1-3]
- Lazertinib is a highly selective, brain-penetrant, third-generation EGFR TKI with efficacy in activating EGFR mutations, T790M, and CNS disease[4,5]
- Preclinical studies demonstrate improved antitumor activity 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

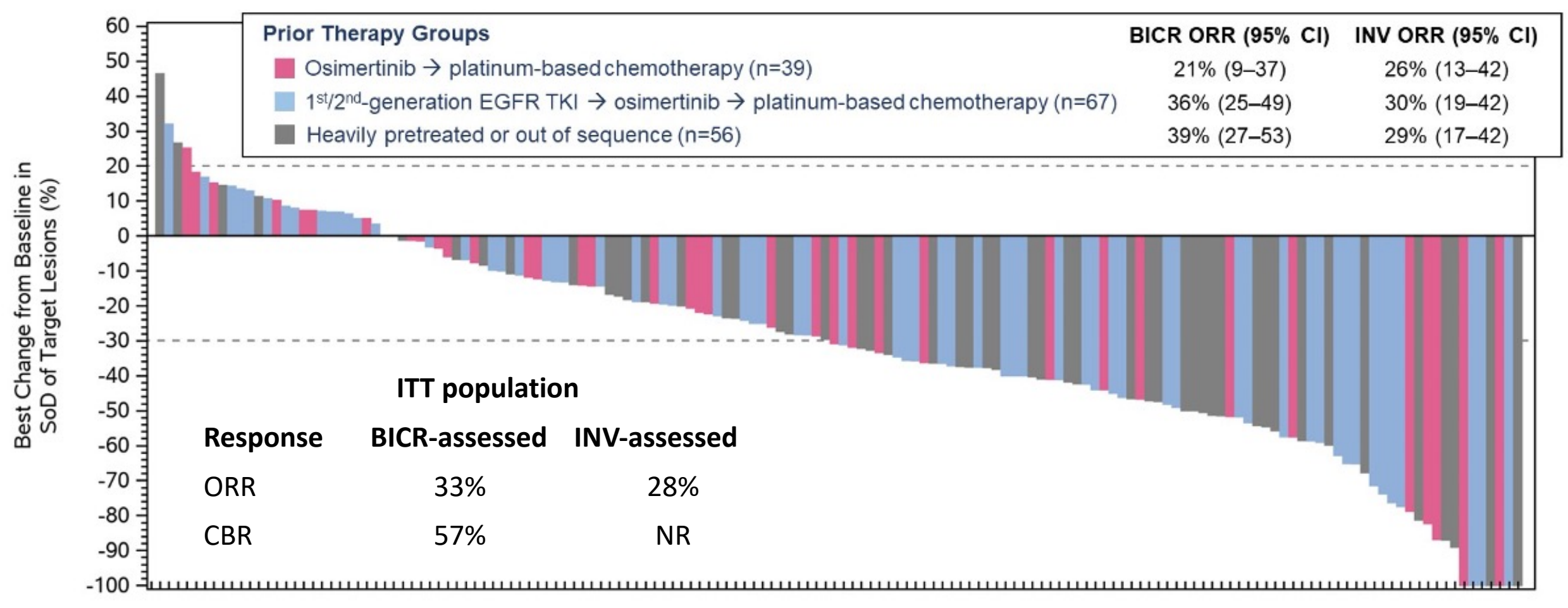
CHRYSALIS-2: Study Design



Shu CA et al. ASCO 2022;Abstract 9006.

RTP RESEARCH TO PRACTICE

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.

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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.

RTP RESEARCH TO PRACTICE

Discussion Question

Which therapy would you generally recommend first for a patient with metastatic NSCLC and an EGFR exon 20 insertion mutation — amivantamab or mobocertinib?

- Amivantamab
- Mobocertinib
- Either agent (coin flip)
- I’m not sure

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.

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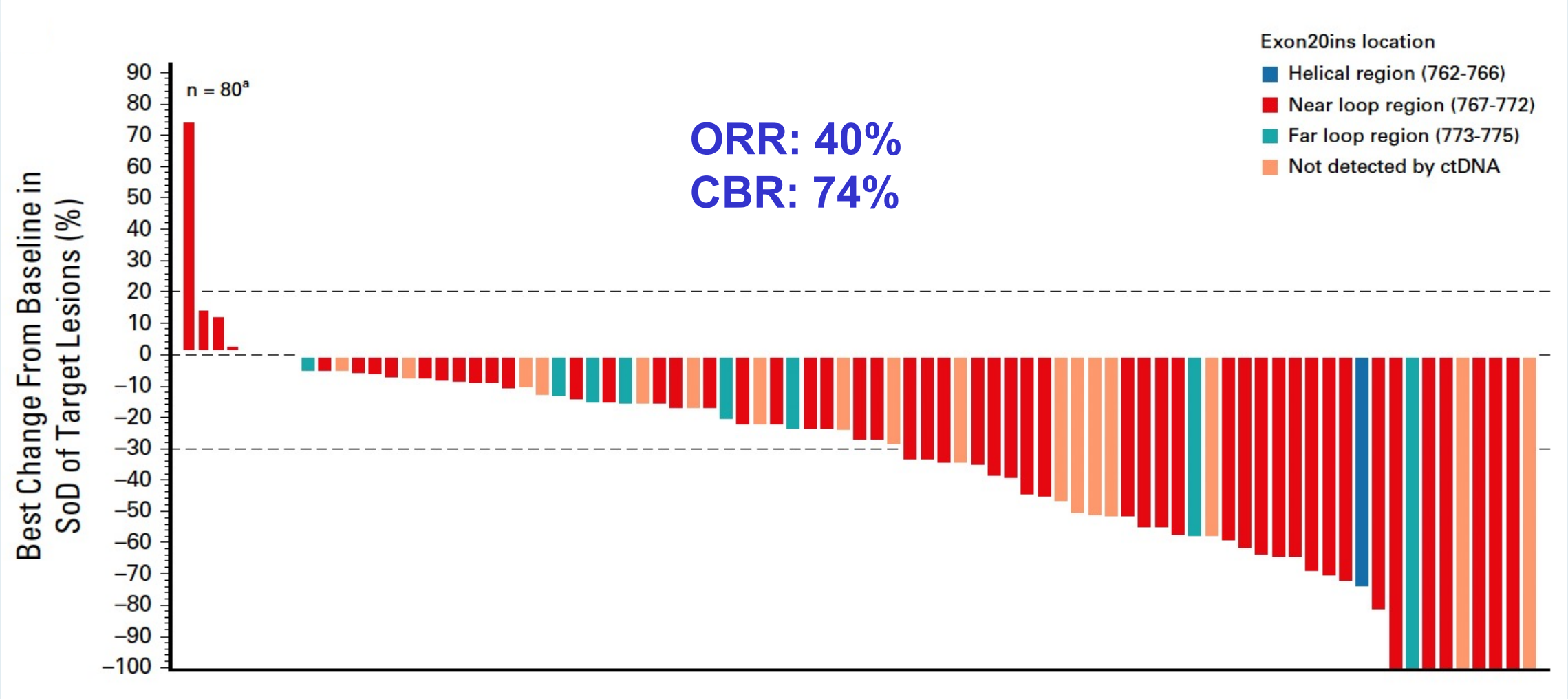
CHRYSALIS: Tumor Reduction and Response



Park K et al. *J Clin Oncol* 2021;39:3391-402.

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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

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.

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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

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

Module 3: Small Cell Lung Cancer

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Discussion Question

What is your usual first-line treatment recommendation for a patient with ALK-positive metastatic NSCLC?

- Alectinib
- Brigatinib
- Lorlatinib
- Crizotinib
- Ceritinib
- Other

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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.

RTP RESEARCH TO PRACTICE

Common and Unique Adverse Effects of ALK TKIs

ALK TKI	Most common adverse effects
Crizotinib	Vision disorders, nausea, diarrhea, vomiting, edema, constipation, elevated transaminases, fatigue, decreased appetite, upper respiratory infection, dizziness and neuropathy
Ceritinib	Diarrhea, nausea, vomiting, fatigue, abdominal pain, decreased appetite and weight loss
Alectinib	Constipation, fatigue, edema, myalgia and anemia
Brigatinib	Diarrhea, fatigue, nausea, rash, cough, myalgia, headache, hypertension, vomiting and dyspnea
Lorlatinib	Hypercholesterolemia, hypertriglyceridemia, edema, peripheral neuropathy, weight gain, cognitive effects, fatigue, dyspnea, arthralgia and diarrhea
Ensartinib	Rash, nausea, pruritus and vomiting

Crizotinib PI, rev 1/2021; Ceritinib PI, rev 3/2019; Alectinib PI, rev 1/2021; Brigatinib PI, rev 5/2020; Lorlatinib PI, rev 3/2021
Xia B et al. *Transl Lung Cancer Res* 2020;9(6):2521-253; Gristina V et al. *Pharmaceuticals* 2020;13:474.

RTP RESEARCH TO PRACTICE

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

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Discussion Question

In general, for a patient with bilateral brain metastases that would otherwise require whole-brain radiation therapy, the presence of which of the following driver mutations would make you more likely to recommend systemic therapy alone?

- RET
- Met exon 14
- BRAF
- ROS1
- EGFR
- ALK
- All the above
- All except MET exon 14
- All except MET exon 14 and BRAF

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Discussion Question

Regulatory and reimbursement issues aside, in which line of therapy would you generally offer trastuzumab deruxtecan to a patient with metastatic nonsquamous NSCLC (PD-L1 TPS 10%) with a HER2 mutation?

- First line
- Second line
- Third line
- Beyond third line
- I would not offer trastuzumab deruxtecan to this patient

RTP RESEARCH TO PRACTICE

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

The NEW ENGLAND JOURNAL of MEDICINE

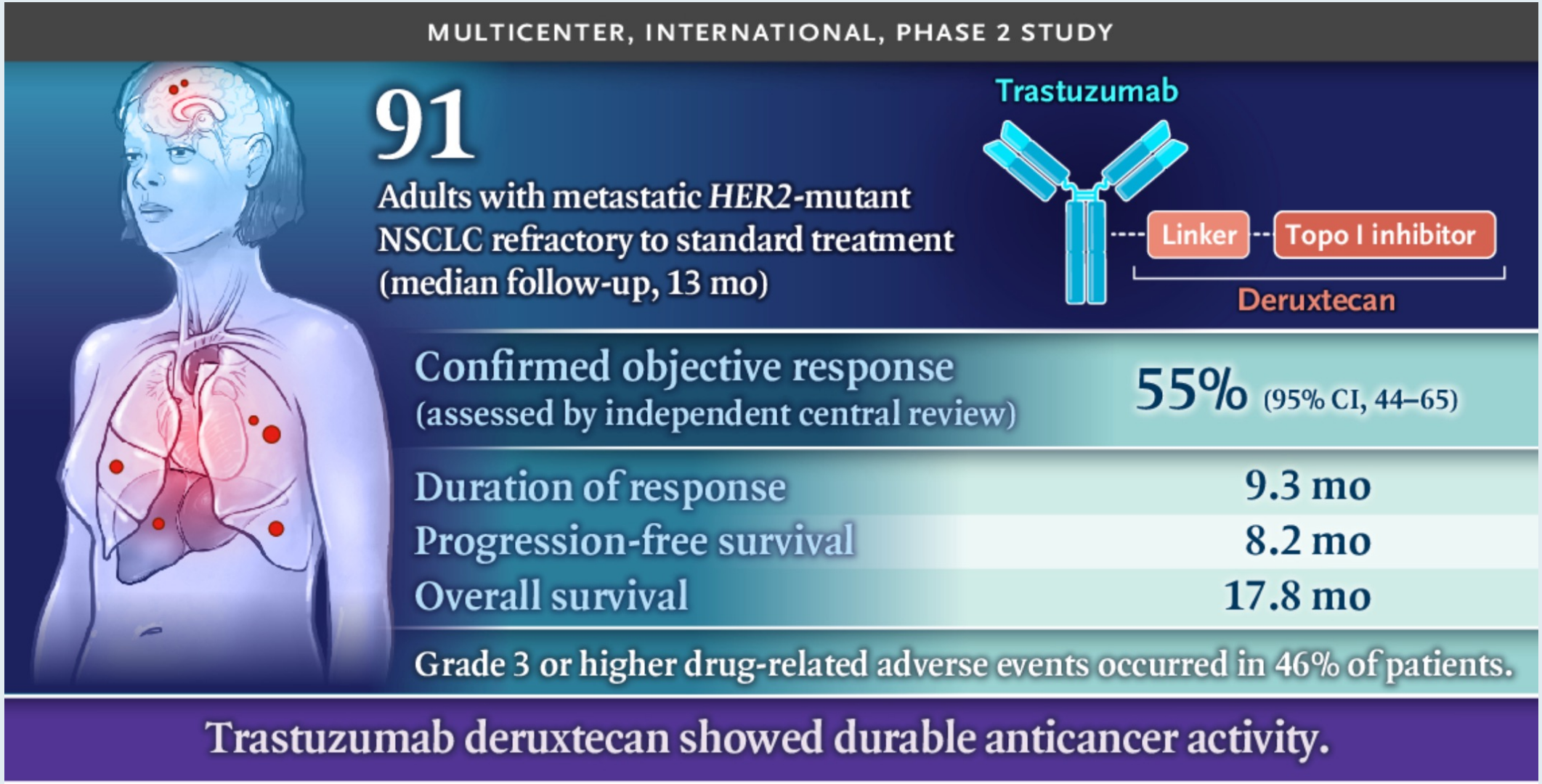
ORIGINAL ARTICLE

Trastuzumab Deruxtecan in *HER2*-Mutant Non–Small-Cell Lung Cancer

Bob T. Li, M.D., Ph.D., M.P.H., Egbert F. Smit, M.D., Ph.D., Yasushi Goto, M.D., Ph.D., Kazuhiko Nakagawa, M.D., Hibiki Udagawa, M.D., Julien Mazières, M.D., Misako Nagasaka, M.D., Ph.D., Lyudmila Bazhenova, M.D., Andreas N. Saltos, M.D., Enriqueta Felip, M.D., Ph.D., Jose M. Pacheco, M.D., Maurice Pérol, M.D., Luis Paz-Ares, M.D., Kapil Saxena, M.D., Ryota Shiga, B.Sc., Yingkai Cheng, M.D., Ph.D., Suddhasatta Acharyya, Ph.D., Patrik Vitazka, M.D., Ph.D., Javad Shahidi, M.D., David Planchard, M.D., Ph.D., and Pasi A. Jänne, M.D., Ph.D., for the DESTINY-Lung01 Trial Investigators*

RTP RESEARCH TO PRACTICE

DESTINY-Lung01 Study



Li BT et al. *N Engl J Med* 2022;386(3):241-51.

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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.

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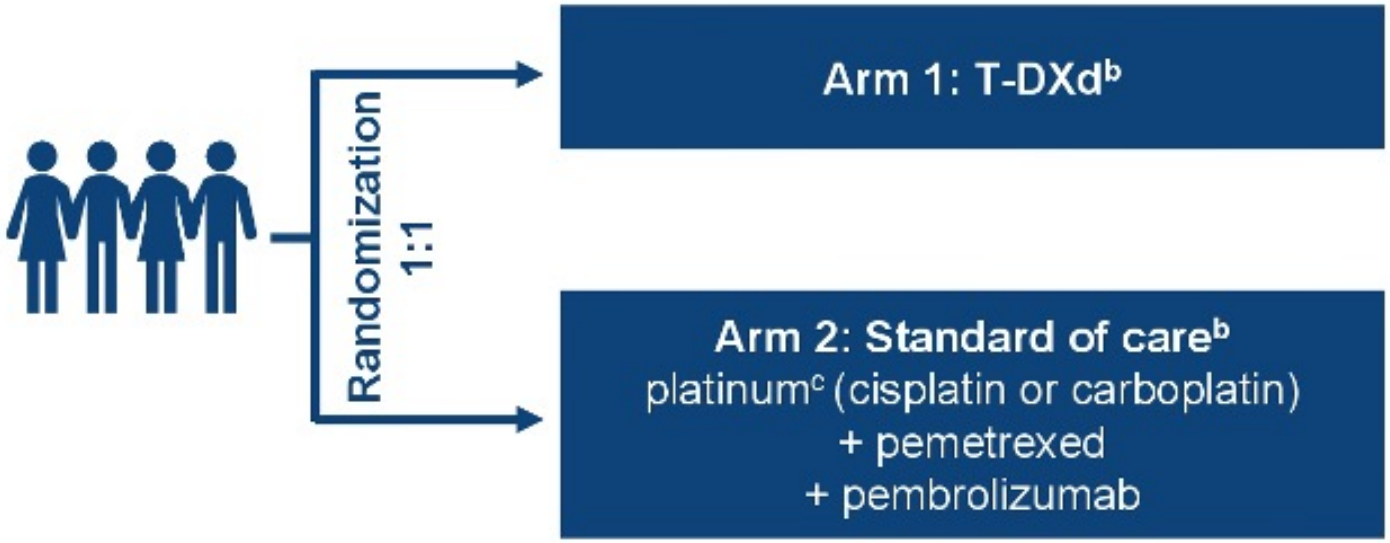
DESTINY-Lung04 Phase III Study Design

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.

RTP RESEARCH TO PRACTICE

CLINICAL CANCER RESEARCH | CLINICAL TRIALS: TARGETED THERAPY

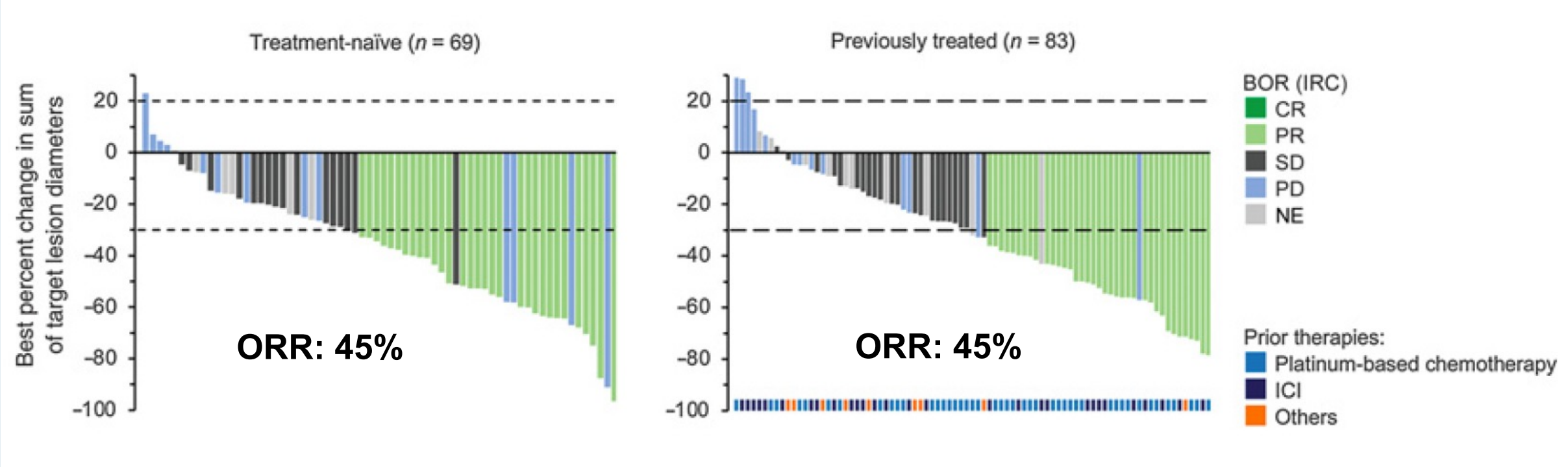
Tepotinib Efficacy and Safety in Patients with *MET* Exon 14 Skipping NSCLC: Outcomes in Patient Subgroups from the VISION Study with Relevance for Clinical Practice

Xiuning Le[1], Hiroshi Sakai[2], Enriqueta Felip[3], Remi Veillon[4], Marina Chiara Garassino[5,6], Jo Raskin[7], Alexis B. Cortot[8], Santiago Viteri[9], Julien Mazieres[10], Egbert F. Smit[11], Michael Thomas[12], Wade T. Iams[13], Byoung Chul Cho[14], Hye Ryun Kim[14], James Chih-Hsin Yang[15], Yuh-Min Chen[16], Jyoti D. Patel[17], Christine M. Bestvina[18], Keunchil Park[19], Frank Griesinger[20], Melissa Johnson[21], Maya Gottfried[22], Christian Britschgi[23], John Heymach[1], Elif Sikoglu[24], Karin Berghoff[25], Karl-Maria Schumacher[26], Rolf Bruns[27], Gordon Otto[26], and Paul K. Paik[28,29]

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

RTP RESEARCH TO PRACTICE

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.

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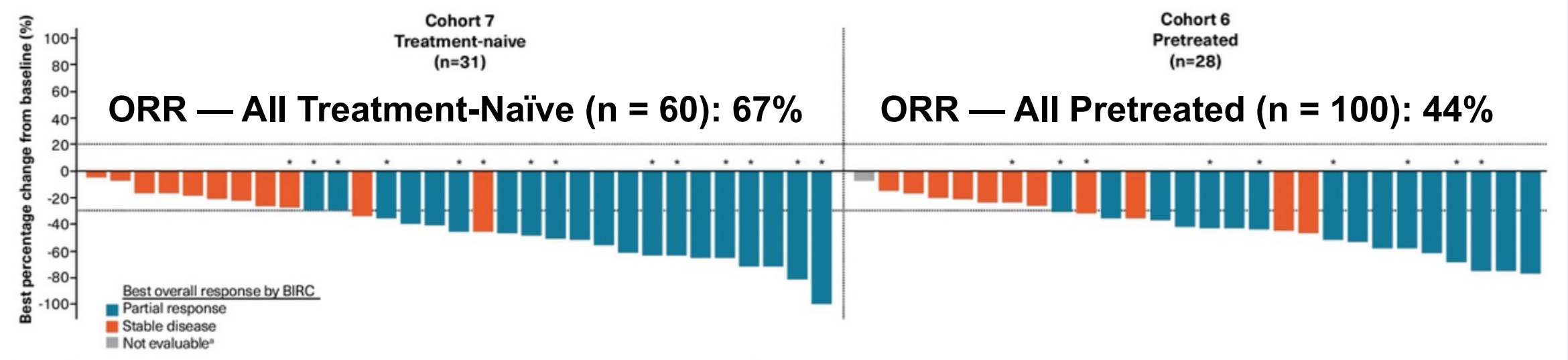
GEOMETRY mono-1



Wolf J et al. ASCO 2021;Abstract 9020.

RTP RESEARCH TO PRACTICE

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

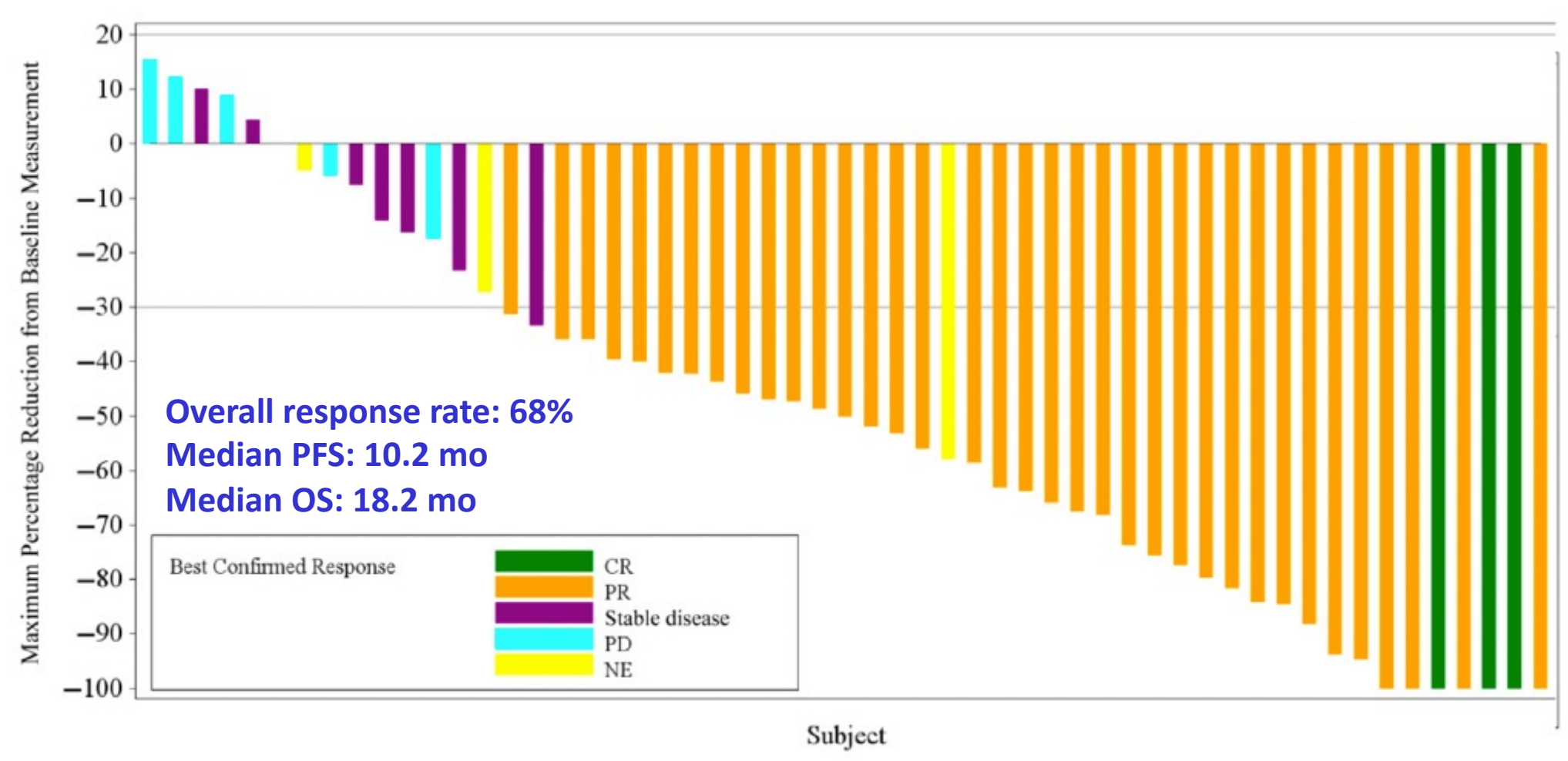
ORIGINAL ARTICLE

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)

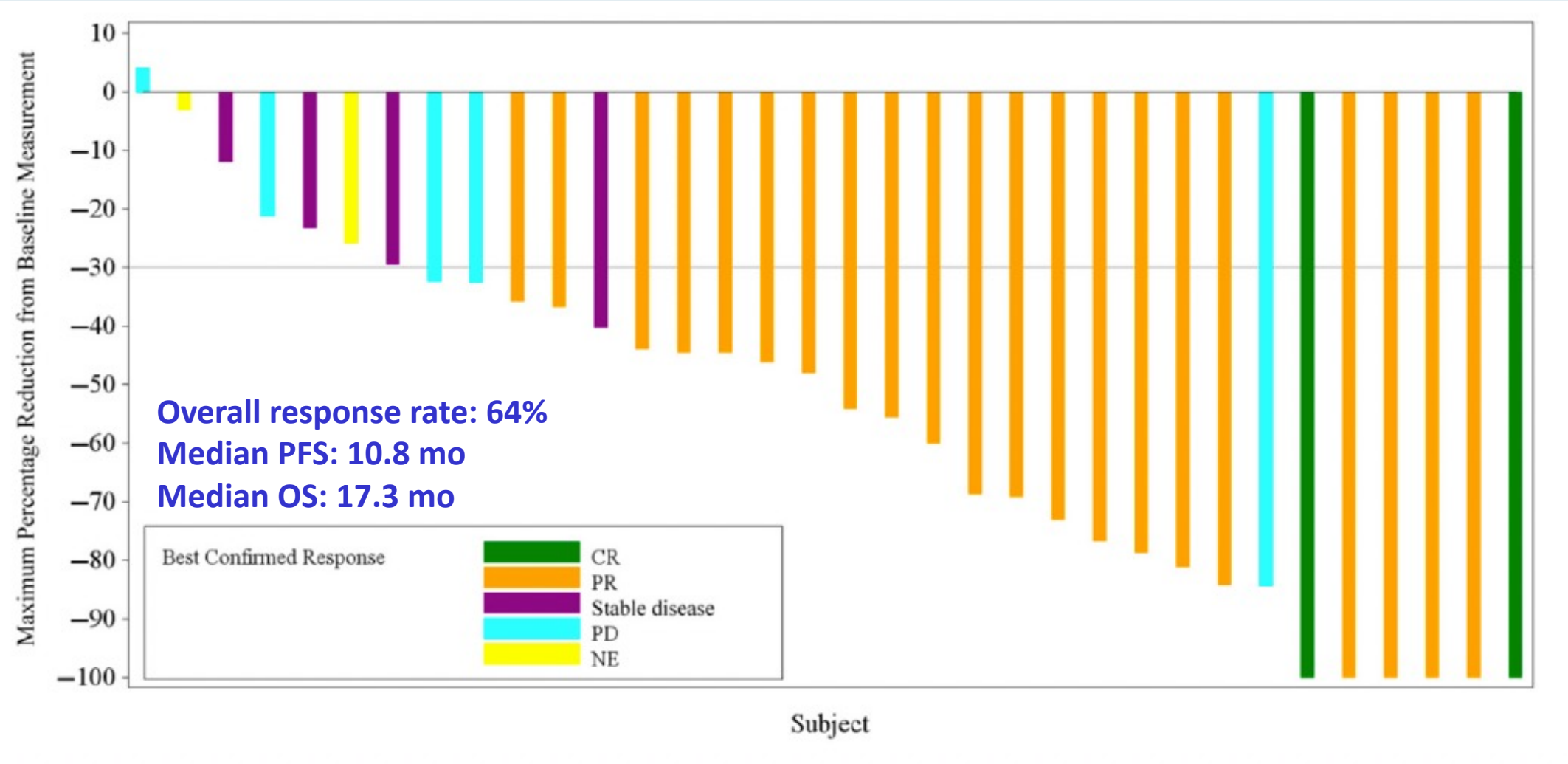


Planchard D et al. *J Thorac Oncol* 2022;17(1):103-15.

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

Discussion Question

Regulatory and reimbursement issues aside, in which line of therapy would you generally offer targeted treatment to a patient with metastatic nonsquamous NSCLC (PD-L1 TPS 50%) with a RET fusion?

- First line
- Second line
- Third line
- Beyond third line
- I would not offer targeted treatment to this patient

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

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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

RTP RESEARCH TO PRACTICE

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

Discussion Question

Regulatory and reimbursement issues aside, in which line of therapy would you generally offer targeted treatment to a patient with metastatic nonsquamous NSCLC (PD-L1 TPS 50%) with a KRAS G12C mutation?

- First line
- Second line
- Third line
- Beyond third line
- I would not offer targeted treatment to this patient

RTP RESEARCH TO PRACTICE

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

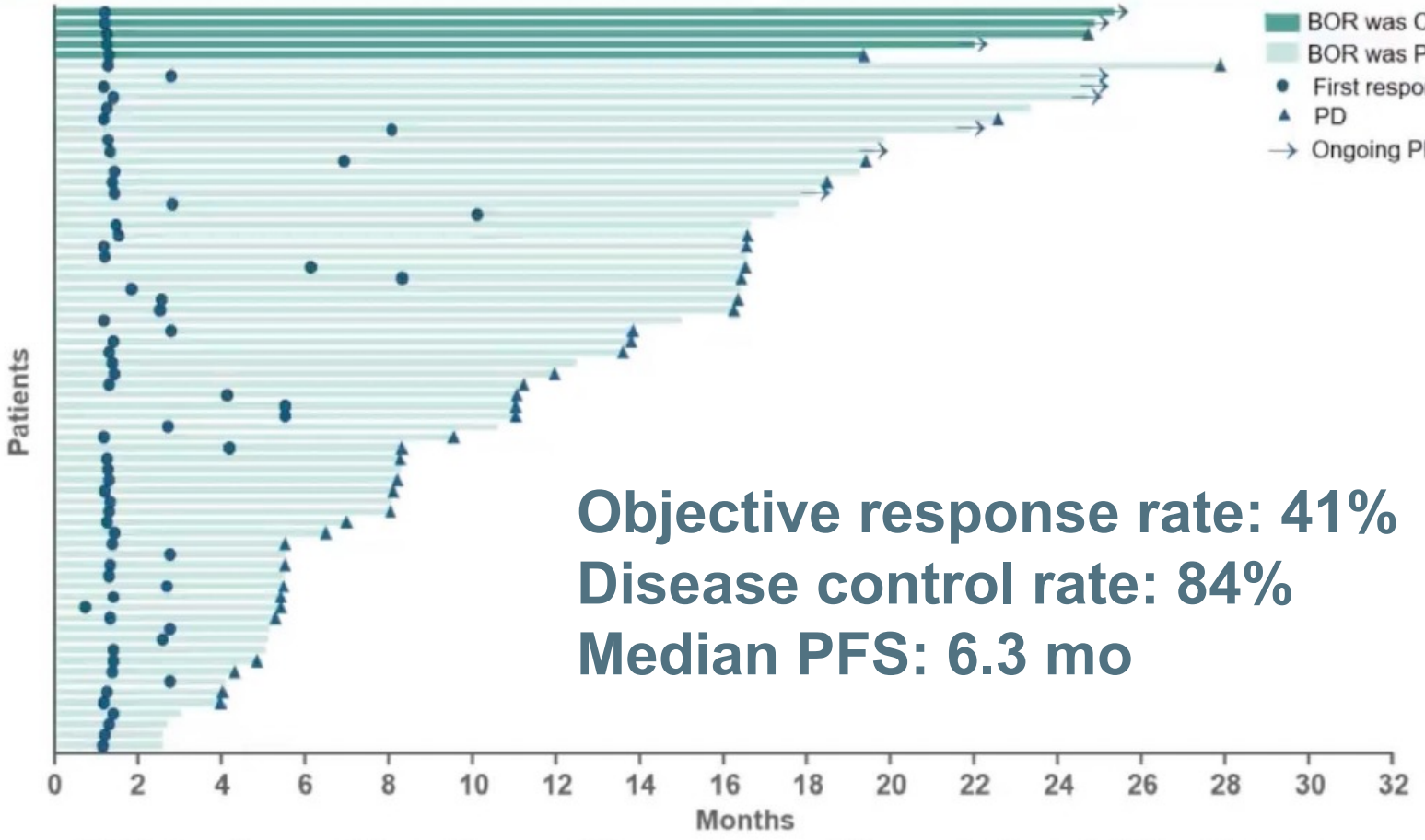
On behalf of: Ramaswamy Govindan[2], Vamsidhar Velcheti[3], Gerald S. Falchook[4], Antoine Italiano[5], Juergen Wolf[6], Adrian G. Sacher[7], Toshiaki Takahashi[8], Suresh S. Ramalingam[9], Christophe Dooms[10], Dong-Wan Kim[11], Alfredo Addeo[12], Jayesh Desai[13], Martin Schuler[14], Pascale Tomasini[15], 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**

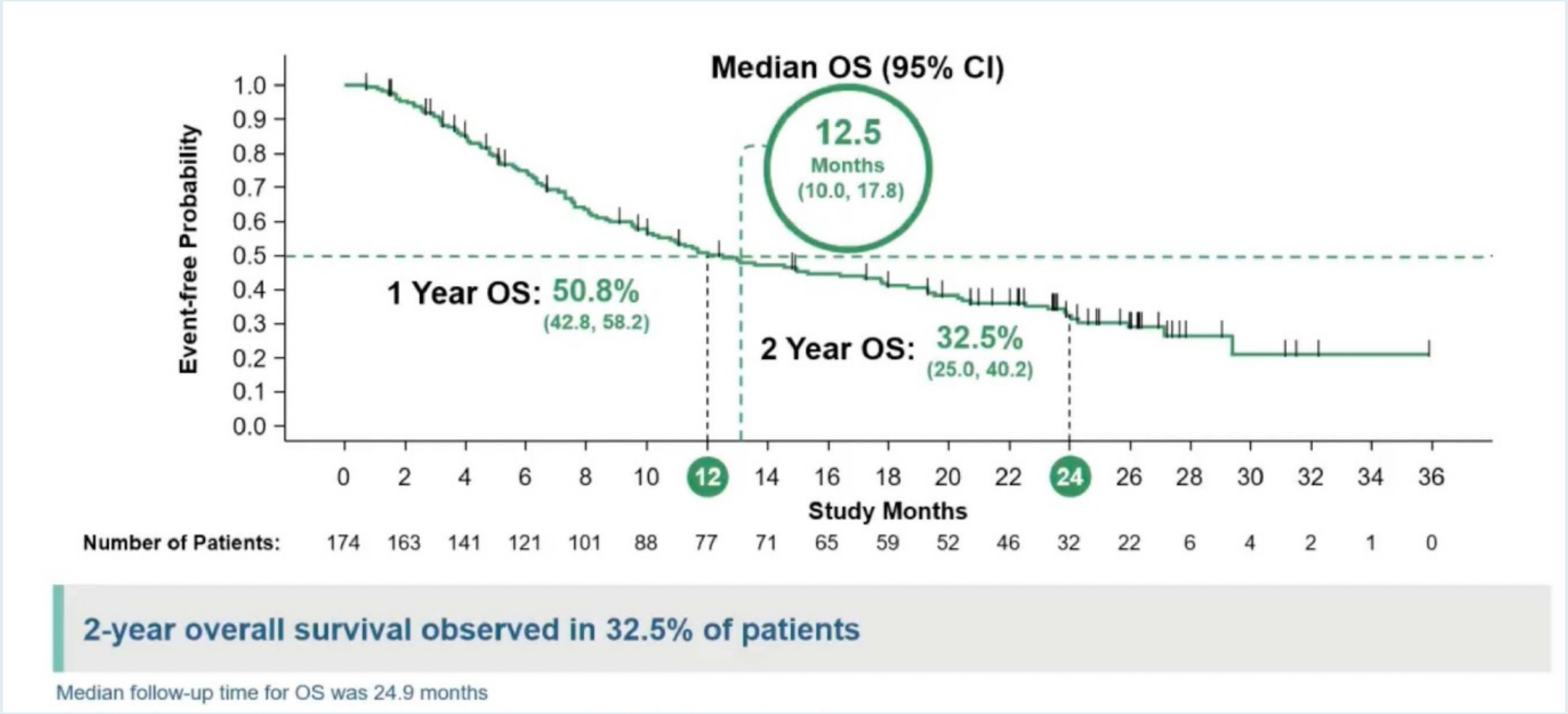
BOR, best overall response; CR, complete response; PD, progressive disease; PFS, progression-free survival; PR, partial response.

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

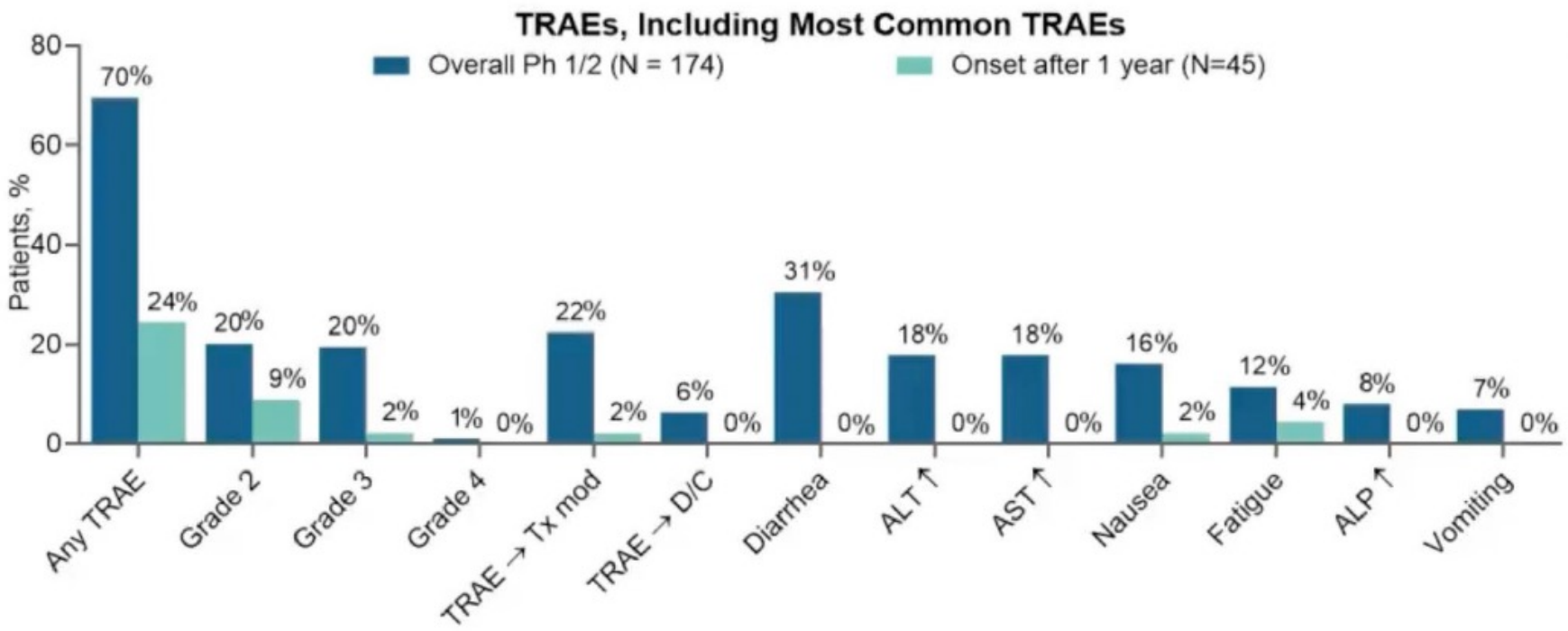
Median follow-up time for OS was 24.9 months

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

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.

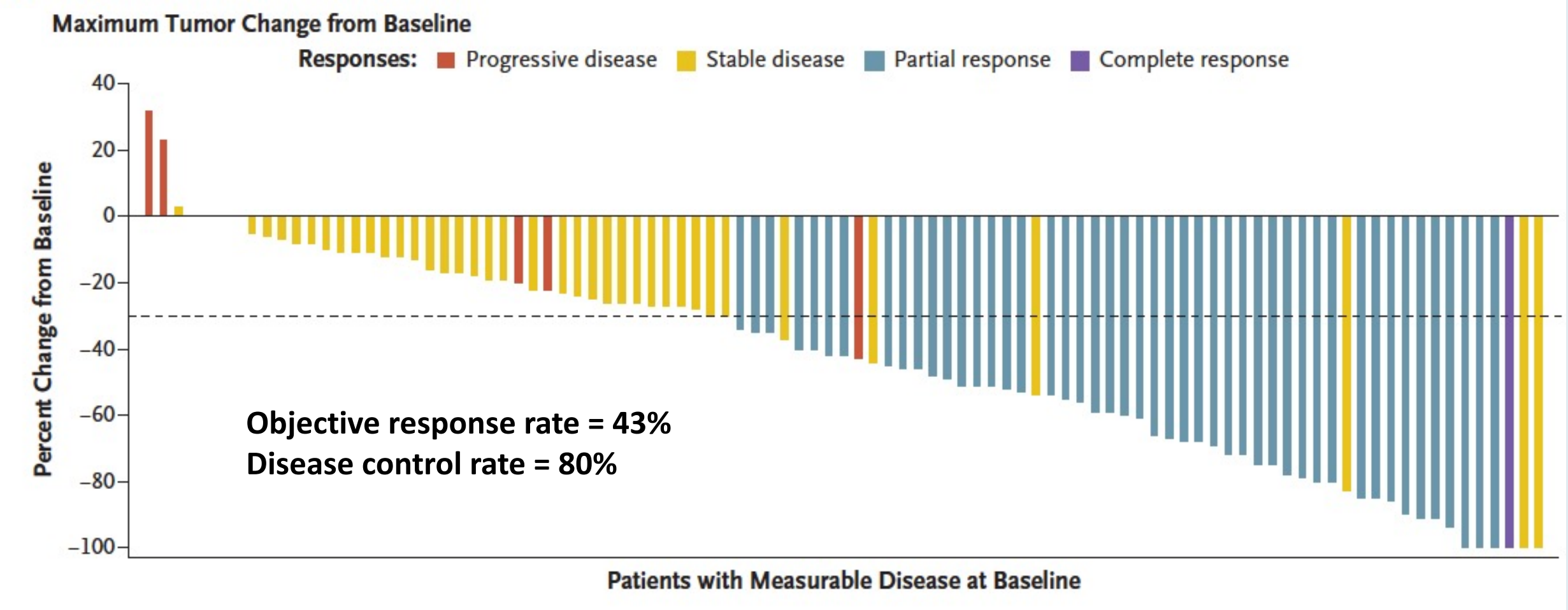
ORIGINAL ARTICLE

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

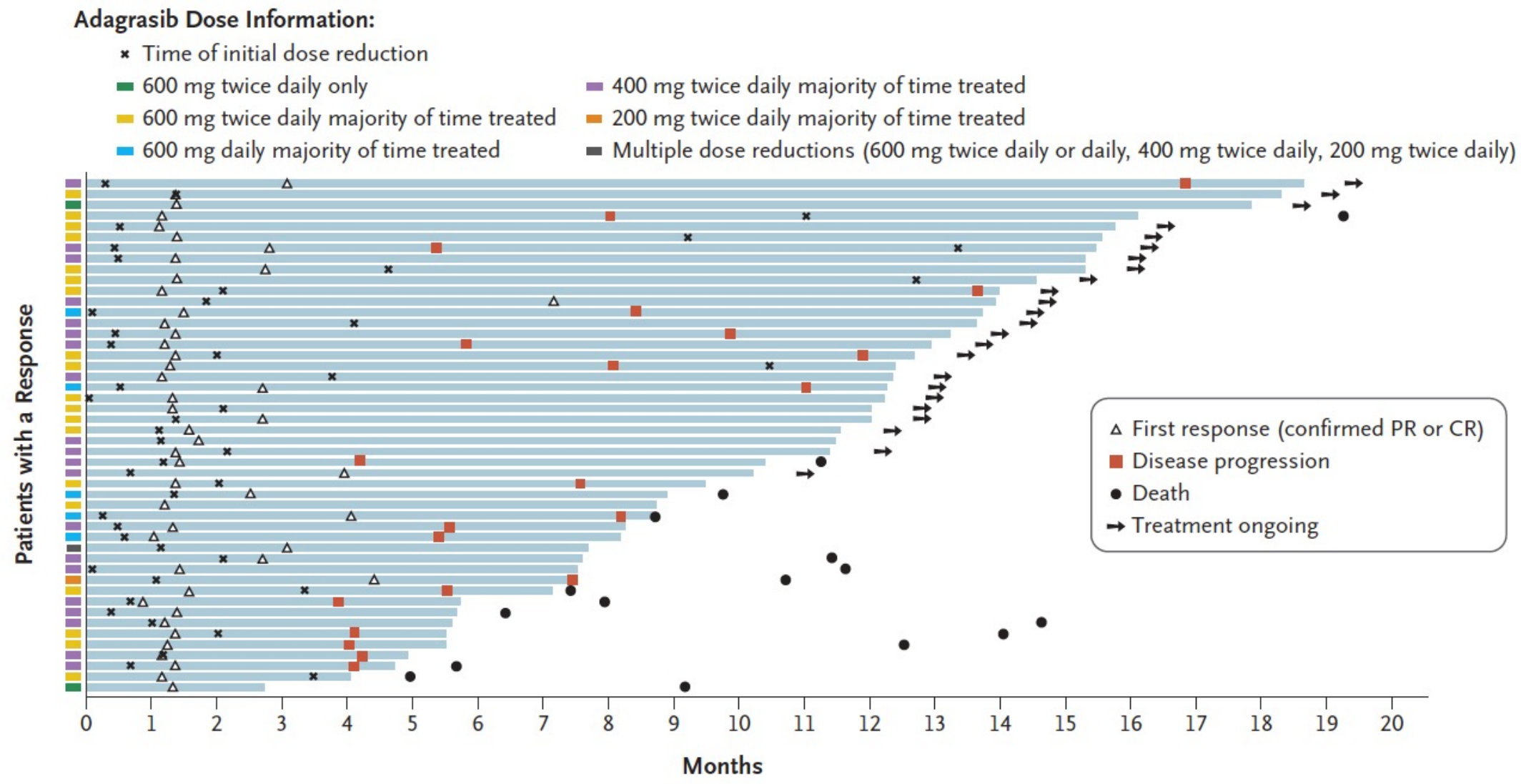
KRYSTAL-1: Tumor Response with Adagrasib for Advanced NSCLC Harboring a KRAS G12C Mutation



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

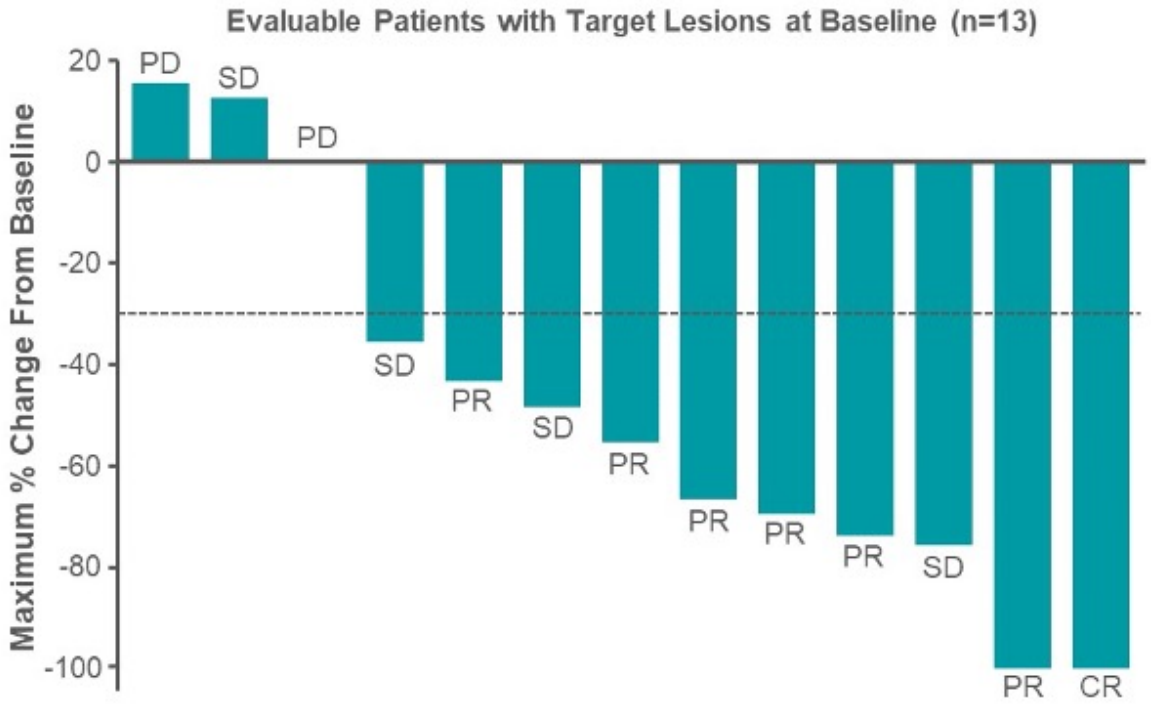


Jänne PA et al. *N Engl J Med* 2022;387(2):120-31; Spira AI et al. ASCO 2022;Abstract 9002.

RTP RESEARCH TO PRACTICE

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.

RTP RESEARCH TO PRACTICE

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.

RTP RESEARCH TO PRACTICE

2022 ASCO ANNUAL MEETING

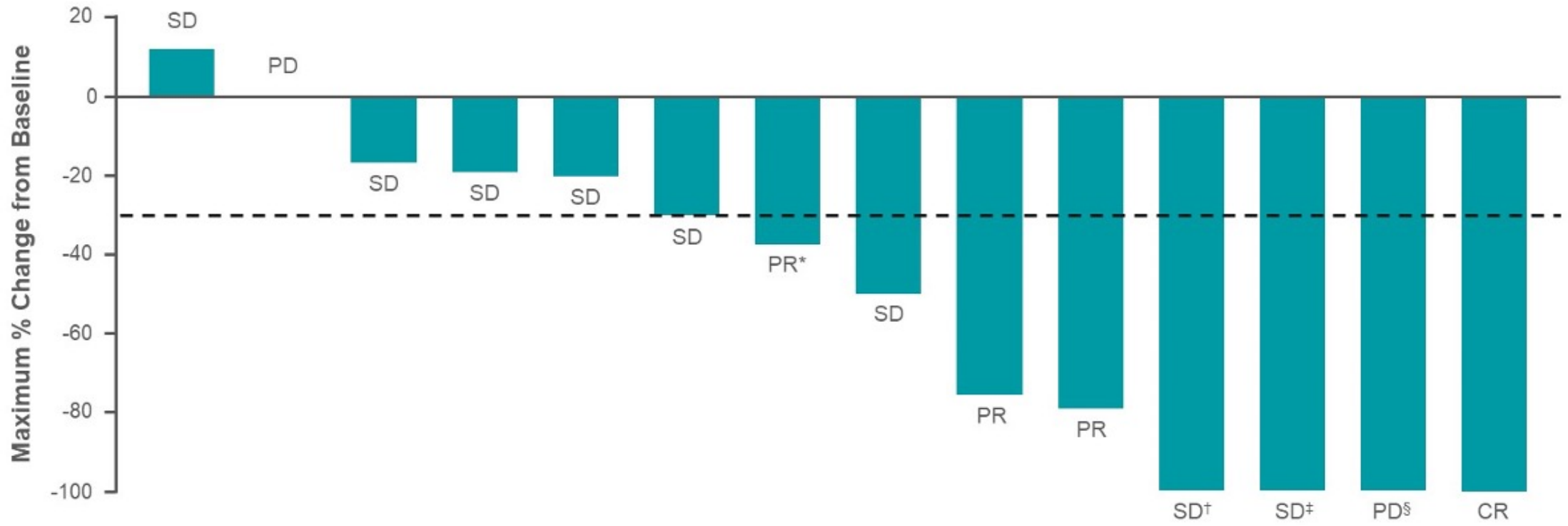
Abstract LBA9009

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: 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.

RTP RESEARCH TO PRACTICE

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.

RTP RESEARCH TO PRACTICE

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

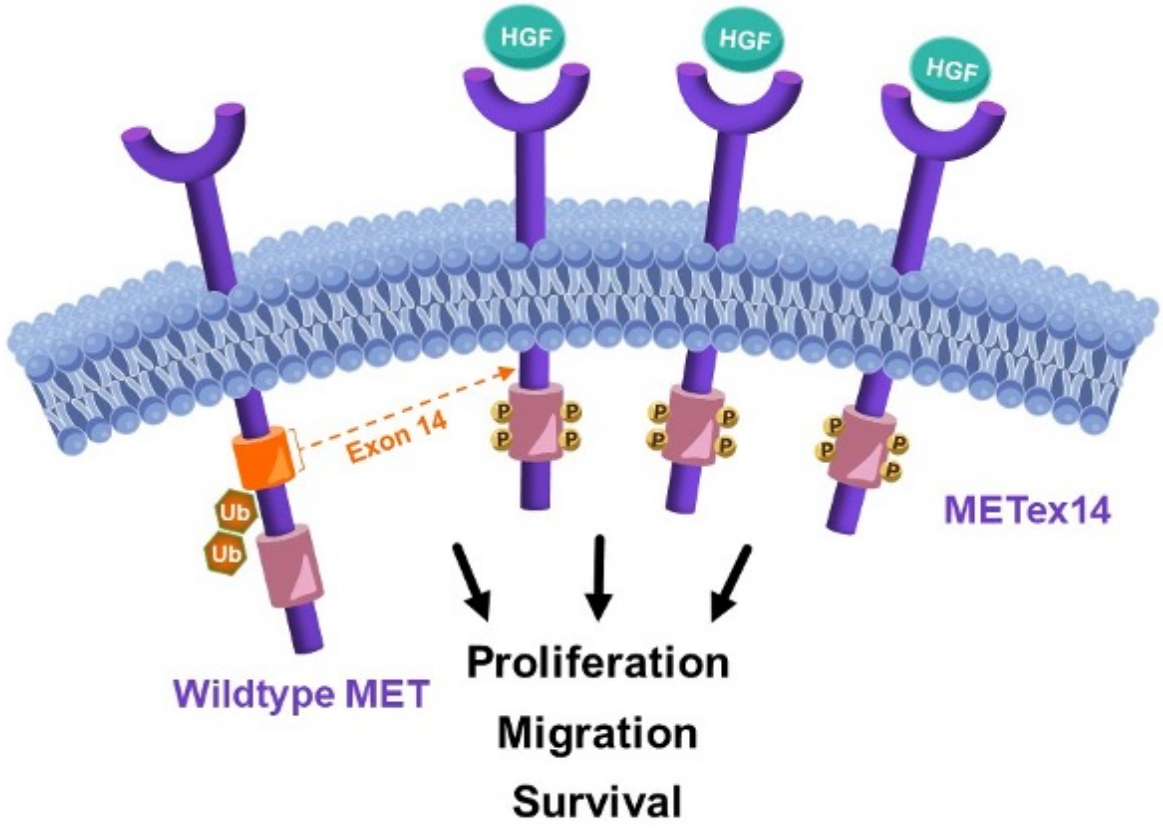
MET Exon 14 Skipping Mutations in NSCLC

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

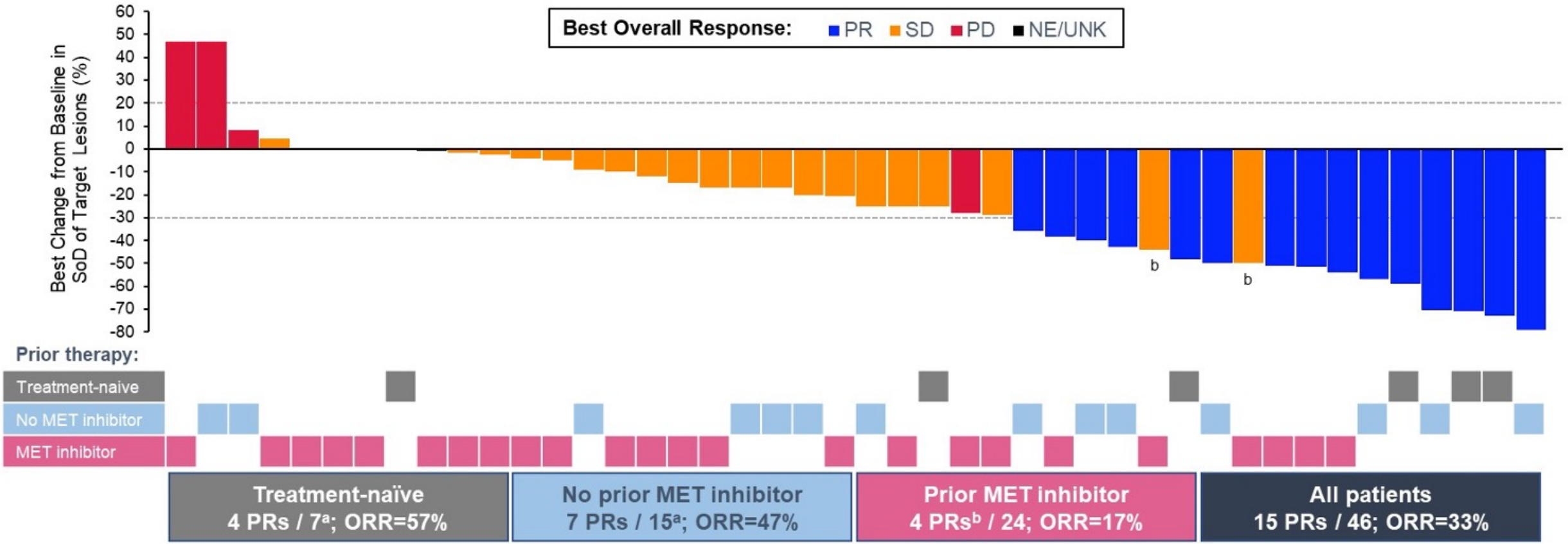


Krebs MG et al. ASCO 2022;Abstract 9008.

RTP RESEARCH TO PRACTICE

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.

RTP RESEARCH TO PRACTICE

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

RTP
RESEARCH
TO PRACTICE

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)

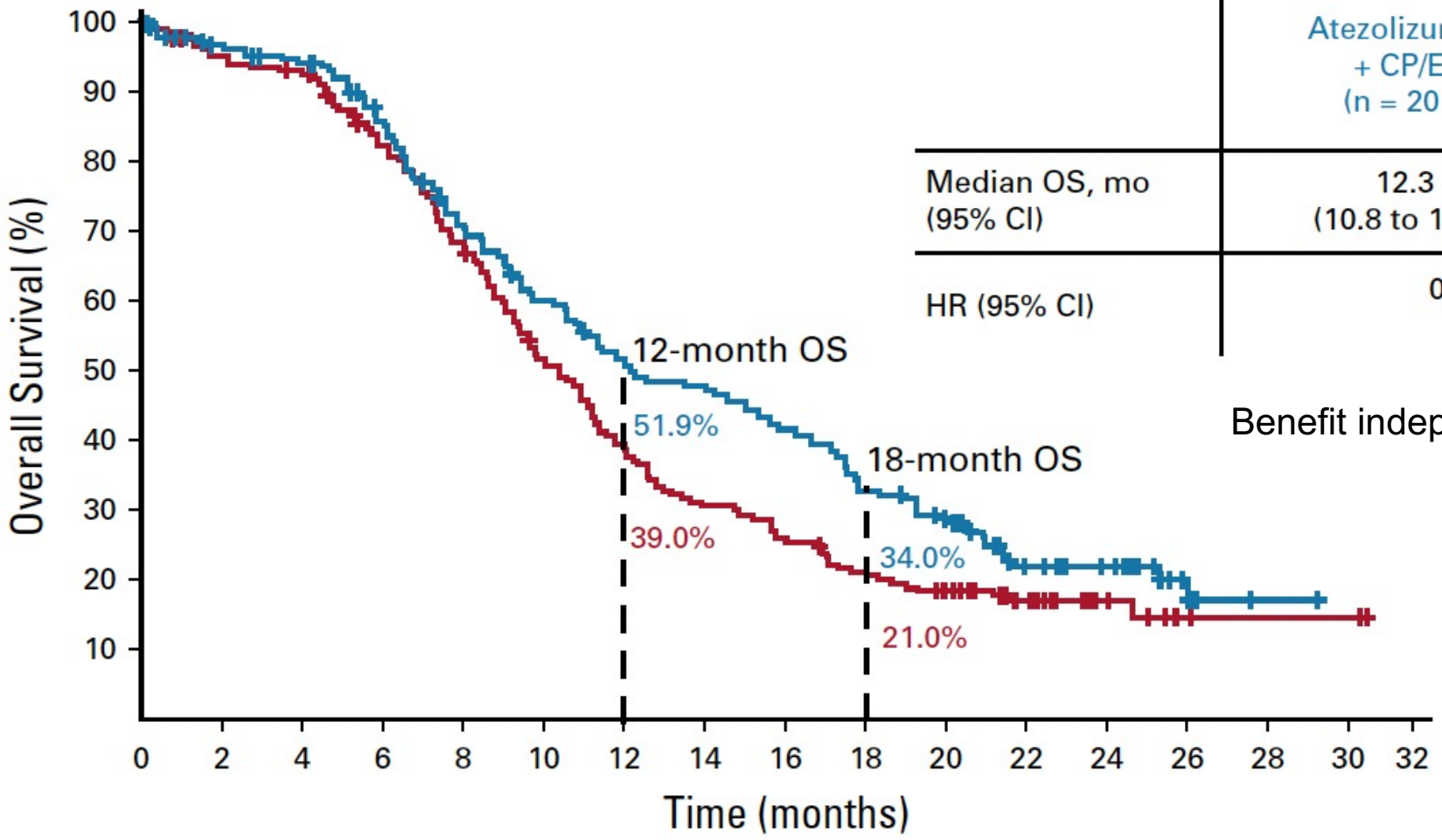
Stephen V. Liu, MD[1]; Martin Reck, MD, PhD[2]; Aaron S. Mansfield, MD[3]; Tony Mok, MD[4]; Arnaud Scherpereel, MD, PhD[5]; Niels Reinmuth, MD, PhD[6]; Marina Chiara Garassino, MD[7]; Javier De Castro Carpeno, MD[8]; Raffaele Califano, MD[9]; Makoto Nishio, MD[10]; Francisco Orlandi, MD[11]; Jorge Alatorre-Alexander, 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.

RTP RESEARCH TO PRACTICE

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.

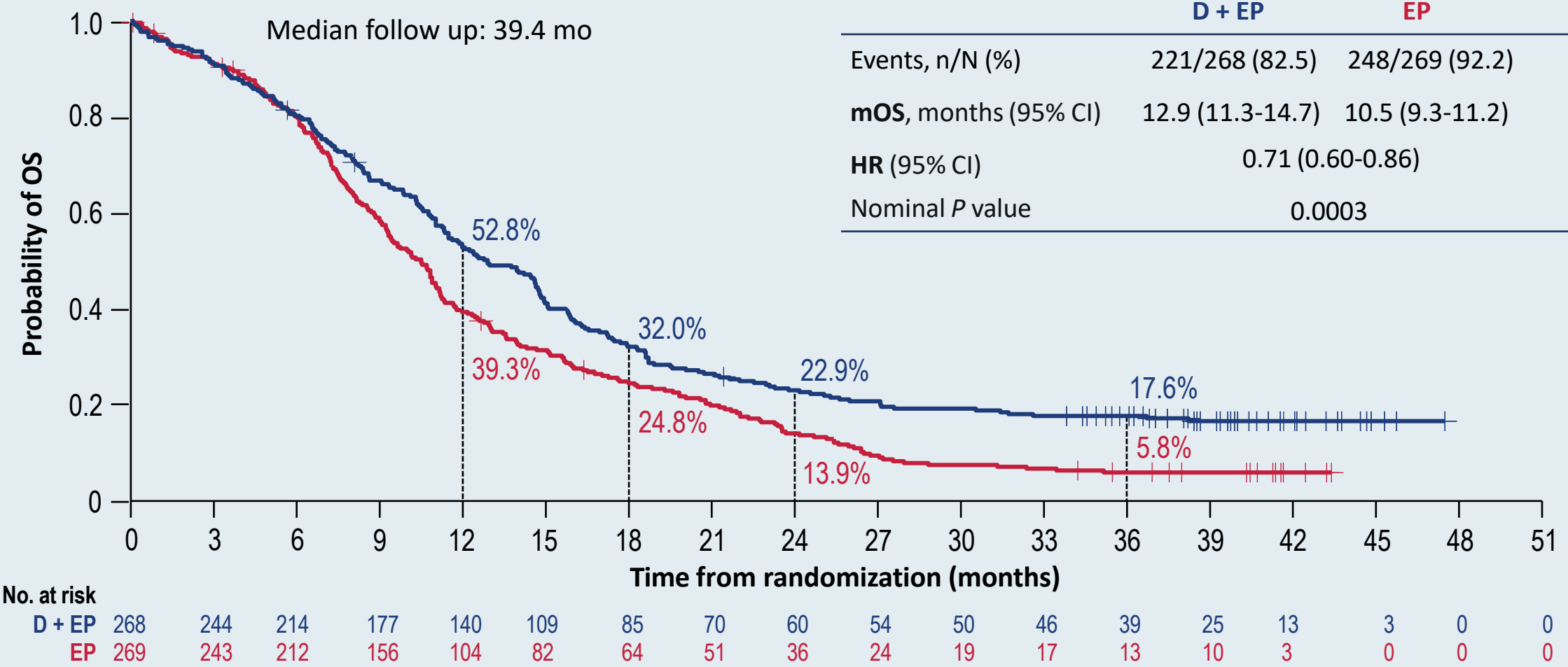
Durvalumab ± Tremelimumab + Platinum-Etoposide in First-Line Extensive-Stage SCLC (ES-SCLC): 3-Year Overall Survival Update from the Phase III CASPIAN Study

Paz-Ares L et al.

ESMO 2021;Abstract LBA61.

RTP
RESEARCH
TO PRACTICE

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.

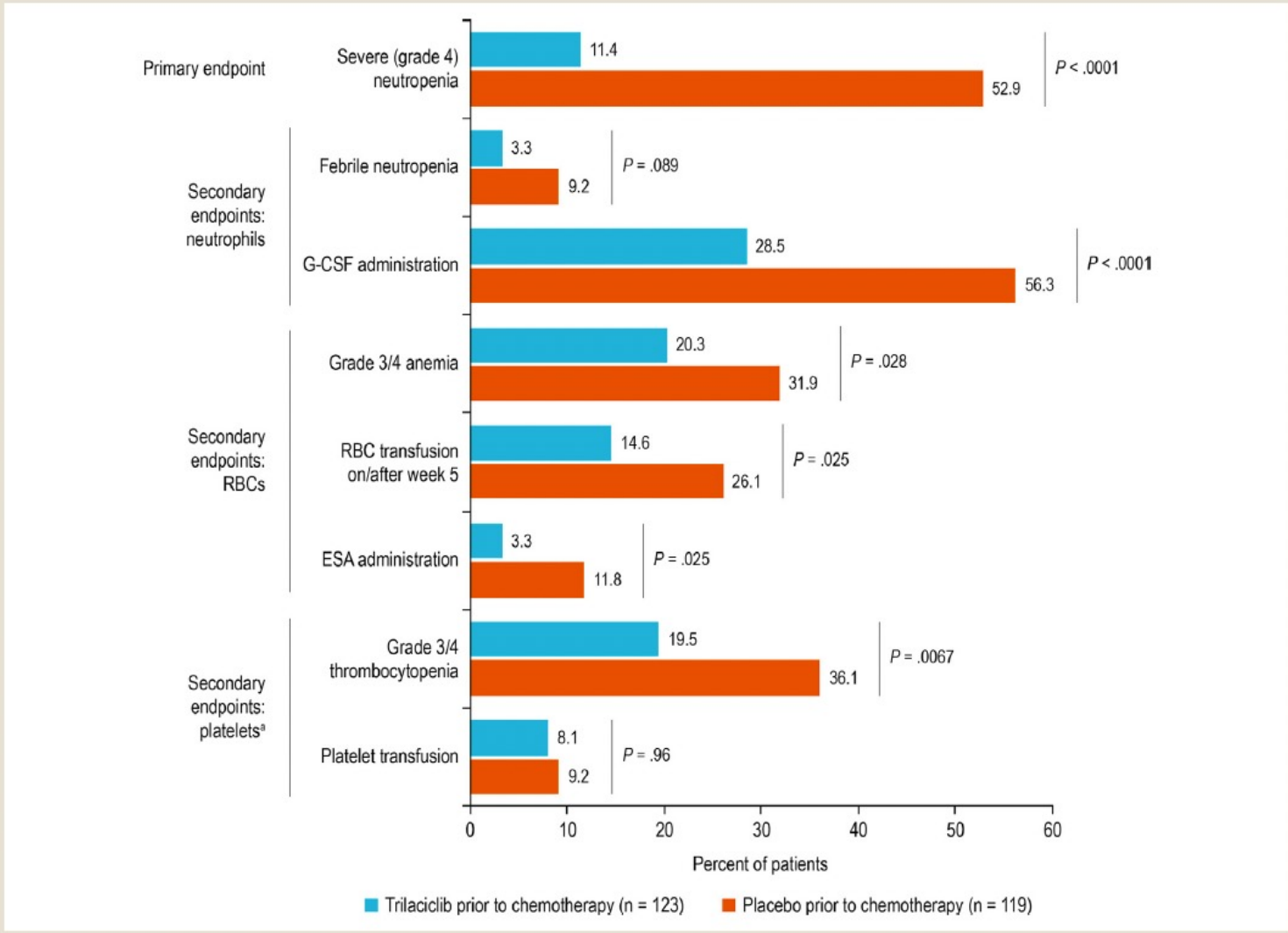
Original Study

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]

RTP RESEARCH TO PRACTICE

Myelopreservation Benefits with Trilaciclib Administered Prior to Chemotherapy



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

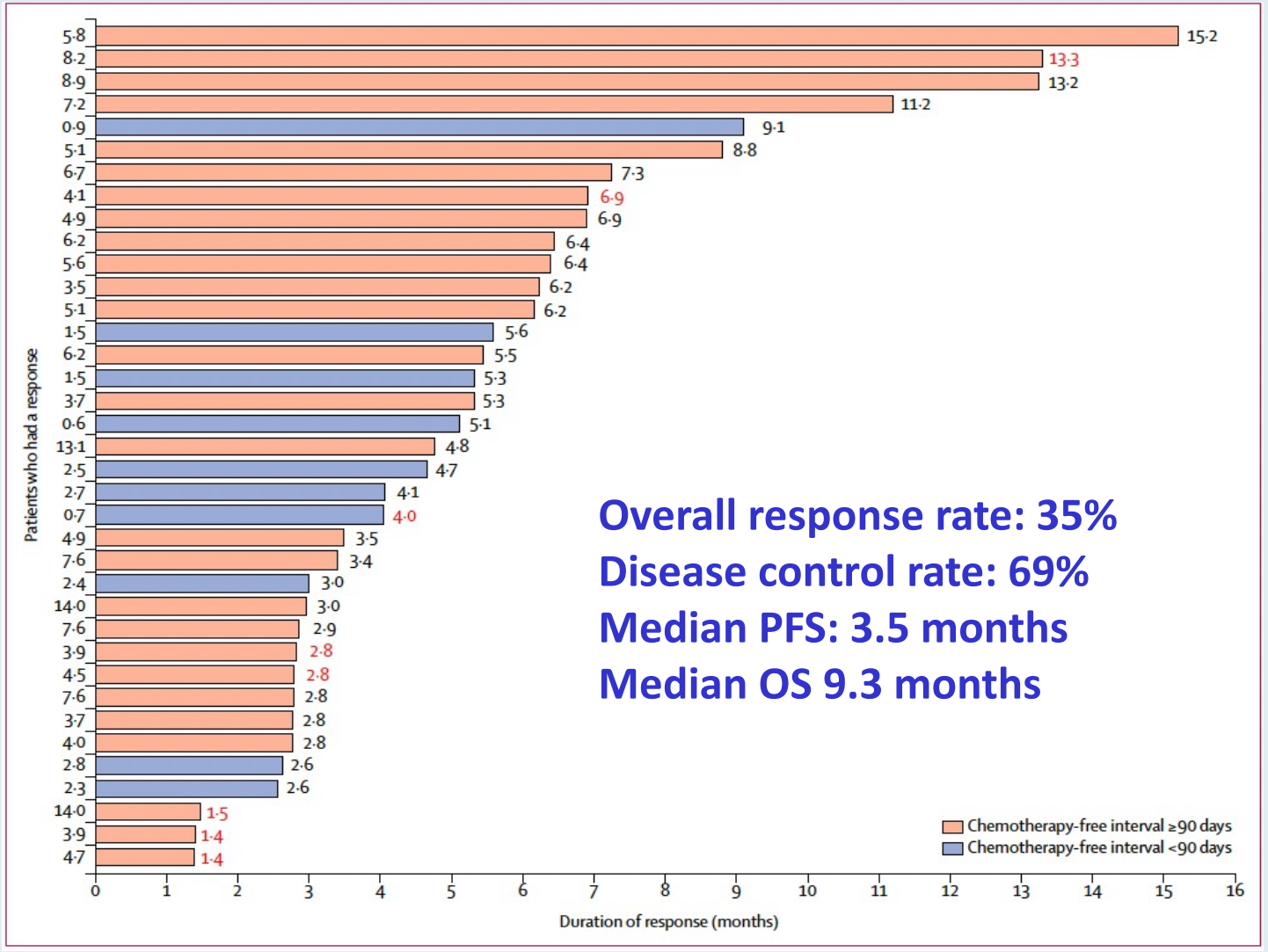
Lancet Oncol 2020;21:645-54.

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*

RTP RESEARCH TO PRACTICE

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.

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Thank you for joining us!

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