# Meet The Professors Live: Clinical Investigators Provide Perspectives on Actual Cases of Patients with Lymphoma, Chronic Lymphocytic Leukemia and Multiple Myeloma

*A CME Symposium Held in Conjunction with the 2023 ASCO® Annual Meeting*

**Sunday, June 4, 2023**

**7:00 PM – 9:30 PM CT**

## Faculty

**John N Allan, MD**
**Shaji K Kumar, MD**
**Ann S LaCasce, MD, MMSc**
**Sagar Lonial, MD**
**Loretta J Nastoupil, MD**
**Susan O'Brien, MD**

## Moderator

**Neil Love, MD**

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# Multiple Myeloma Faculty

**Shaji K Kumar, MD**
Mark and Judy Mullins Professor
of Hematological Malignancies
Consultant, Division of Hematology
Professor of Medicine
Mayo Clinic
Rochester, Minnesota

**Sagar Lonial, MD**
Chair and Professor
Department of Hematology and Medical Oncology
Chief Medical Officer
Winship Cancer Institute
Emory University
Atlanta, Georgia

**Moderator**
**Neil Love, MD**
Research To Practice
Miami, Florida

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# Lymphoma Faculty

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

**Loretta J Nastoupil, MD**
Associate Professor
Section Chief, Indolent Lymphoma
Department of Lymphoma/Myeloma
The University of Texas MD Anderson Cancer Center
Houston, Texas

**Moderator**
**Neil Love, MD**
Research To Practice
Miami, Florida

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# Chronic Lymphocytic Leukemia Faculty

**John N Allan, MD**
Associate Professor of Clinical Medicine
Weill Cornell Medicine
New York, New York

**Susan O'Brien, MD**
Professor, Division of Hematology/Oncology
School of Medicine
UCI Chao Family Comprehensive Cancer Center
Orange, California

**Moderator**
**Neil Love, MD**
Research To Practice
Miami, Florida

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# Contributing General Medical Oncologists

**Lowell L Hart, MD**
Florida Cancer Specialists
and Research Institute
Fort Myers, Florida

**Priya Rudolph, MD, PhD**
Georgia Cancer Specialists
Northside Hospital Cancer Institute
Athens, Georgia

**Eric H Lee, MD, PhD**
Compassionate Cancer Care
Medical Group
Fountain Valley, California

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# Dr Allan — Disclosures

| | |
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| **Nonpromotional Disease State Awareness Speaking** | AbbVie Inc, BeiGene Ltd, Janssen Biotech Inc, Pharmacyclics LLC, an AbbVie Company |

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# Dr Hart — Disclosures

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# Dr Kumar — Disclosures

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# Dr LaCasce — Disclosures

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# Dr Lee — Disclosures

No relevant conflicts of interest to disclose

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# Dr Lonial — Disclosures

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# Dr Nastoupil — Disclosures

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# Dr O’Brien — Disclosures

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| **Nonrelevant Financial Relationship** | Alliance Pharma Inc, DynaMed, Nova Research Inc |

# Dr Rudolph — Disclosures

| | |
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## Commercial Support

This activity is supported by educational grants from AbbVie Inc, Genentech, a member of the Roche Group, Genmab US Inc, Karyopharm Therapeutics, Lilly, Regeneron Pharmaceuticals Inc, Sanofi, and Seagen Inc.

## Research To Practice CME Planning Committee Members, Staff and Reviewers

Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

| | |
|---|---|
| Friday<br>June 2 | **Gastroesophageal Cancers**<br>11:45 AM – 12:45 PM CT (12:45 PM – 1:45 PM ET) |
| | **Non-Small Cell Lung Cancer**<br>6:30 PM – 9:00 PM CT (7:30 PM – 10:00 PM ET) |
| Saturday<br>June 3 | **Hepatobiliary Cancers**<br>6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET) |
| | **Prostate Cancer**<br>7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET) |
| Sunday<br>June 4 | **Ovarian Cancer**<br>6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET) |
| | **Lymphoma, Chronic Lymphocytic Leukemia and Multiple Myeloma**<br>7:00 PM – 9:30 PM CT (8:00 PM – 10:30 PM ET) |
| Monday<br>June 5 | **Urothelial Bladder Cancer**<br>6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET) |
| | **Breast Cancer**<br>7:00 PM – 9:30 PM CT (8:00 PM – 10:30 PM ET) |
| Tuesday<br>June 6 | **Renal Cell Carcinoma (Webinar)**<br>7:00 AM – 8:00 AM CT (8:00 AM – 9:00 AM ET) |

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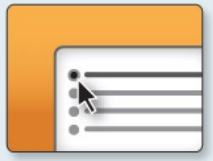
# Clinicians in the Meeting Room

**Networked iPads are available.**

**Review Program Slides: Tap the Program Slides button to review speaker presentations and other program content.**



**Answer Survey Questions: Complete the pre- and postmeeting surveys.**

**Ask a Question: Tap Ask a Question to submit a challenging case or question for discussion. We will aim to address as many questions as possible during the program.**

**Complete Your Evaluation: Tap the CME Evaluation button to complete your evaluation electronically to receive credit for your participation.**

***For assistance, please raise your hand. Devices will be collected at the conclusion of the activity.***

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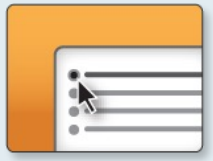
# Clinicians Attending via Zoom

**Review Program Slides: A link to the program slides will be posted in the chat room at the start of the program.**



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**Ask a Question: Submit a challenging case or question for discussion using the Zoom chat room.**

**Get CME Credit: A CME credit link will be provided in the chat room at the conclusion of the program.**

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# PREMEETING SURVEY – Available Now

***Clinicians in Attendance: If you have not already done so, please take a moment to complete the premeeting survey on the iPads for attendees in the room and on Zoom for those attending virtually. Your input on this survey will be integral to the program today.***

***A postmeeting survey will be posted toward the end of the session.***

***Thank you for your input.***

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# About the Enduring Program

- The live meeting is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based video/PowerPoint program.
  An email will be sent to all attendees when the activity is available.
- To learn more about our education programs, visit our website, **www.ResearchToPractice.com**

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# Meet The Professors Live: Clinical Investigators Provide Perspectives on Actual Cases of Patients with Multiple Myeloma

*A CME Symposium Held in Conjunction with the 2023 ASCO® Annual Meeting*


## Faculty

**Shaji K Kumar, MD**

**Sagar Lonial, MD**

## Moderator

**Neil Love, MD**


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# Agenda

## Module 1 — Initial Treatment of Newly Diagnosed Multiple Myeloma (MM)

- Up-front treatment for transplant eligible patients
- Up-front treatment for patients not eligible for transplant
- Current approach to maintenance therapy

## Module 2 — Sequencing of Therapies for Relapsed/Refractory MM

- Anti-CD38 antibodies
- Bispecific antibodies
- CAR T-cell therapy
- Selinexor
- Venetoclax and other strategies

# Agenda

## Module 1 — Initial Treatment of Newly Diagnosed Multiple Myeloma (MM)

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- Selinexor
- Venetoclax and other strategies

2022 ASCO ANNUAL MEETING

# RVd ± ASCT and Lenalidomide Maintenance to Progression for NDMM

## The Phase 3 DETERMINATION Trial

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

The NEW ENGLAND JOURNAL of MEDICINE

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

ORIGINAL ARTICLE

## Triplet Therapy, Transplantation, and Maintenance until Progression in Myeloma

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

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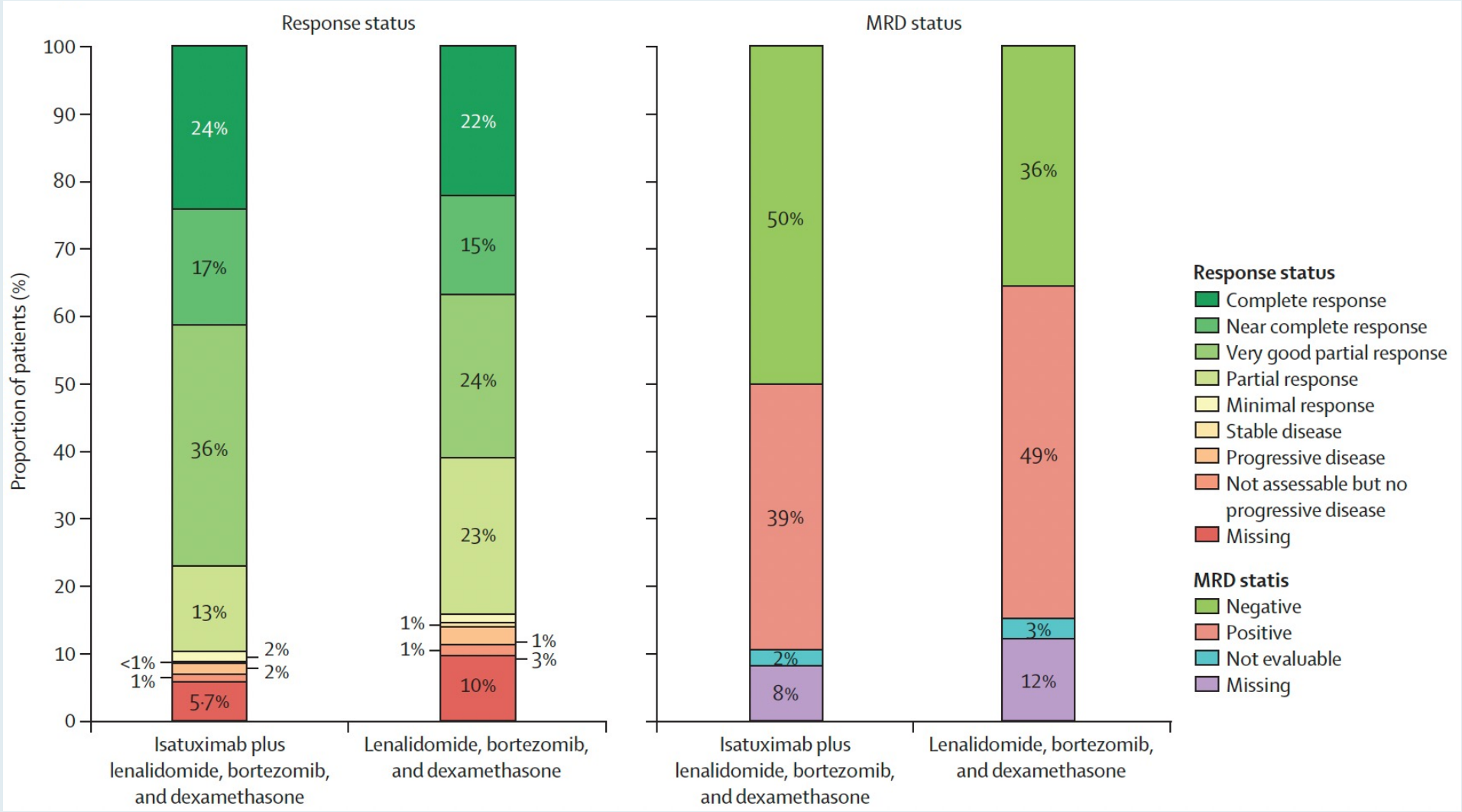
Articles

# Addition of isatuximab to lenalidomide, bortezomib, and dexamethasone as induction therapy for newly diagnosed, transplantation-eligible patients with multiple myeloma (GMMG-HD7): part 1 of an open-label, multicentre, randomised, active-controlled, phase 3 trial

*Hartmut Goldschmidt*, Elias K Mai*, Uta Bertsch, Roland Fenk, Eva Nievergall, Diana Tichy, Britta Besemer, Jan Dürig, Roland Schroers, Ivana von Metzler, Mathias Hänel, Christoph Mann, Anne M Asemissen, Bernhard Heilmeier, Niels Weinhold, Stefanie Huhn, Katharina Kriegsmann, Steffen P Luntz, Tobias A W Holderried, Karolin Trautmann-Grill, Deniz Gezer, Maika Klaiber-Hakimi, Martin Müller, Cyrus Khandanpour, Wolfgang Knauf, Christof Scheid, Markus Munder, Thomas Geer, Hendrik Riesenberg, Jörg Thomalla, Martin Hoffmann, Marc S Raab, Hans J Salwender, Katja C Weisel, for the German-Speaking Myeloma Multicenter Group (GMMG) HD7 investigators†*

*Lancet Haematol* 2022;9(11):e810-21.

# GMMG-HD7: Minimum Residual Disease Status and Response Rates after Induction Therapy in the Intent-to-Treat Population




Goldschmidt H et al. *Lancet Haematol* 2022;9(11):e810-21.

# Maintenance Therapy with Carfilzomib, Pomalidomide, and Dexamethasone (KPd) in High-Risk Myeloma Patients (Pts): A Phase 2 Study with Safety Run-in

Nooka AJ et al.

ASCO 2023;Abstract 8001.

Saturday, June 3; 1:27 PM CDT

# Daratumumab Plus Lenalidomide and Dexamethasone (D-Rd) Versus Lenalidomide and Dexamethasone (Rd) Alone in Transplant-ineligible Patients With Newly Diagnosed Multiple Myeloma (NDMM): Updated Analysis of the Phase 3 MAIA Study

**Shaji K. Kumar,[1] Philippe Moreau,[2] Nizar Bahlis,[3] Thierry Facon,[4] Torben Plesner,[5] Robert Z. Orlowski,[6] Supratik Basu,[7] Hareth Nahi,[8] Cyrille Hulin,[9] Hang Quach,[10] Hartmut Goldschmidt,[11] Michael O'Dwyer,[12] Aurore Perrot,[13] Christopher P. Venner,[14,15] Katja Weisel,[16] Noopur Raje,[17] Mourad Tiab,[18] Margaret Macro,[19] Laurent Frenzel,[20] Xavier Leleu,[21] George Wang,[22] Huiling Pei,[23] Maria Krevvata,[22] Robin Carson,[22] Fredrik Borgsten,[24] Saad Z. Usmani[25]**

[1]Department of Hematology, Mayo Clinic Rochester, Rochester, MN, USA; [2]Hematology Department, University Hospital Hôtel-Dieu, Nantes, France; [3]Arnie Charbonneau Cancer Research Institute, University of Calgary, Calgary, AB, Canada; [4]University of Lille, CHU Lille, Service des Maladies du Sang, Lille, France; [5]Vejle Hospital and University of Southern Denmark, Vejle, Denmark; [6]Department of Lymphoma & Myeloma, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [7]Royal Wolverhampton NHS Trust and University of Wolverhampton, CRN West Midlands, NIHR, Wolverhampton, UK; [8]Karolinska Institute, Department of Medicine, Division of Hematology, Karolinska University Hospital at Huddinge, Stockholm, Sweden; [9]Department of Hematology, Hôpital Haut Lévêque, University Hospital, Pessac, France; [10]University of Melbourne, St Vincent's Hospital, Melbourne, Australia; [11]GMMG-Study Group at University Hospital Heidelberg, Internal Medicine V, Heidelberg, Germany; [12]Department of Medicine/Haematology, NUI, Galway, Republic of Ireland; [13]CHU de Toulouse, IUCT-O, Université de Toulouse, UPS, Service d'Hématologie, Toulouse, France; [14]Department of Medical Oncology, Cross Cancer Institute, University of Alberta, Edmonton, AB, Canada; [15]BC Cancer – Vancouver Centre Group, Vancouver, BC, Canada; [16]Department of Oncology, Hematology and Bone Marrow Transplantation with Section of Pneumology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany; [17]Center for Multiple Myeloma, Massachusetts General Hospital Cancer Center, Boston, MA, USA; [18]CHD Vendée, La Roche sur Yon, France; [19]Centre Hospitalier Universitaire (CHU) de Caen, Caen, France; [20]Hôpital Necker-Enfants Malades, Paris, France; [21]CHU Poitiers, Hôpital la Milétrie, Poitiers, France; [22]Janssen Research & Development, LLC, Spring House, PA, USA; [23]Janssen Research & Development, LLC, Titusville, NJ, USA; [24]Janssen Research & Development, LLC, Raritan, NJ, USA; [25]Memorial Sloan Kettering Cancer Center, New York, NY, USA.

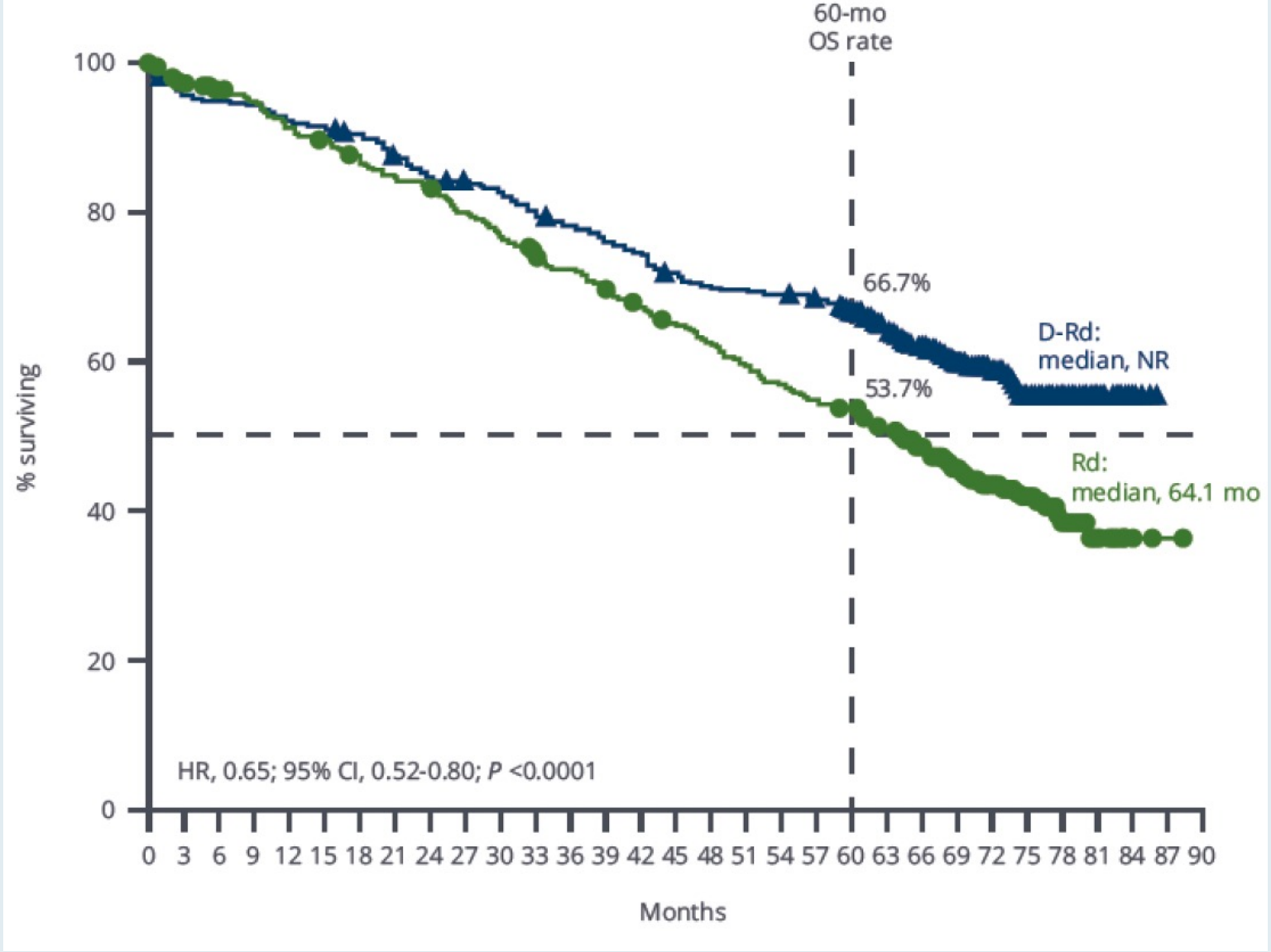
Presented at the 64th American Society of Hematology (ASH) Annual Meeting & Exposition; December 10-13, 2022; New Orleans, LA, USA.





Kumar S et al. ASH 2022;Abstract 4559.

# MAIA: Overall Survival in the ITT Population




Kumar S et al. ASH 2022;Abstract 4559.

RTP RESEARCH TO PRACTICE

# Agenda

## Module 1 — Initial Treatment of Newly Diagnosed Multiple Myeloma (MM)

- Up-front treatment for transplant-eligible patients
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- Current approach to maintenance therapy

## Module 2 — Sequencing of Therapies for Relapsed/Refractory MM

- Anti-CD38 antibodies
- Bispecific antibodies
- CAR T-cell therapy
- Selinexor
- Venetoclax and other strategies

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Blood Cancer Journal

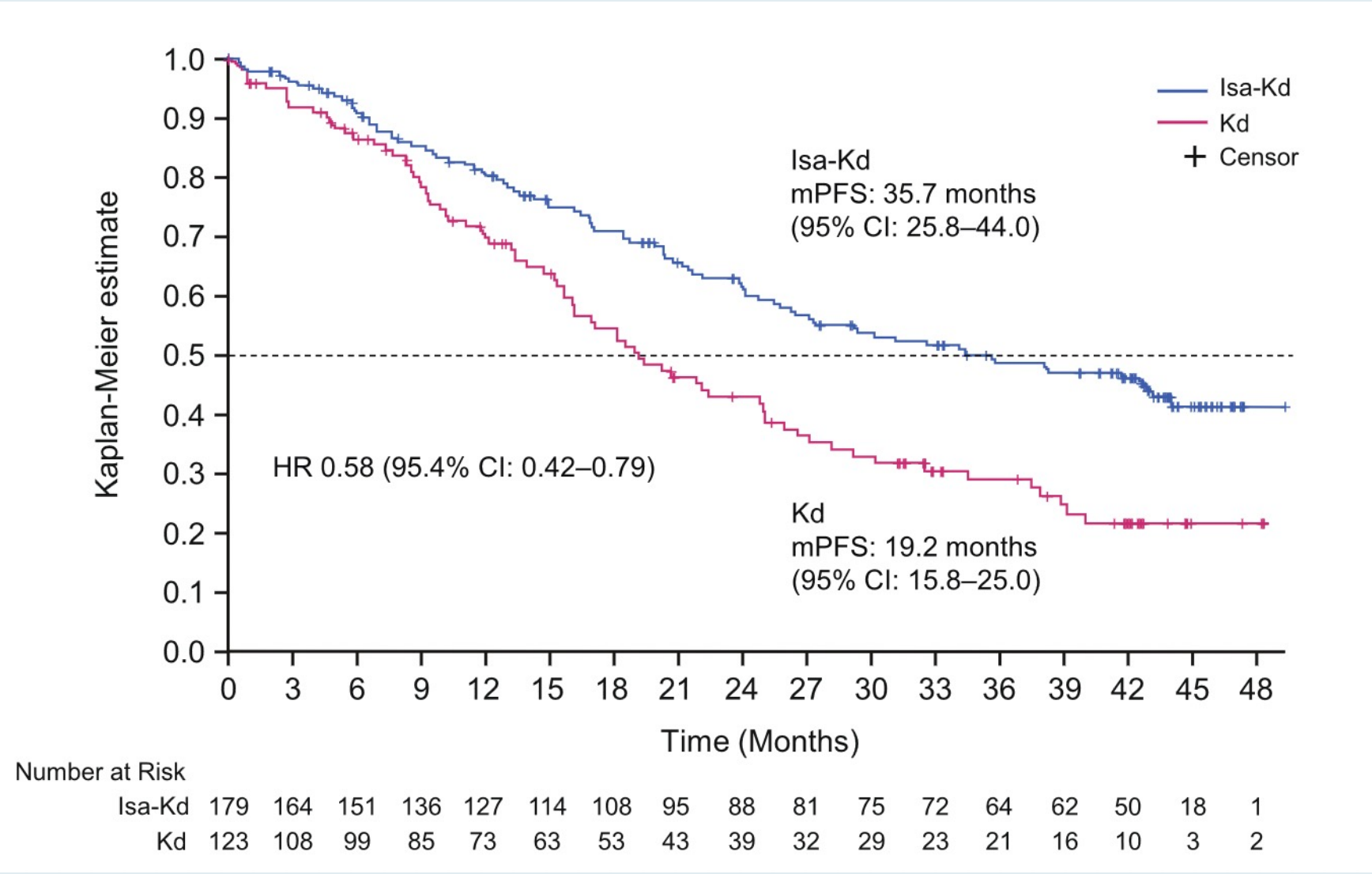
www.nature.com/bcj

ARTICLE OPEN

# Isatuximab, carfilzomib, and dexamethasone in patients with relapsed multiple myeloma: updated results from IKEMA, a randomized Phase 3 study

Thomas Martin[1,22]✉, Meletios-Athanasios Dimopoulos[2], Joseph Mikhael[3], Kwee Yong[4], Marcelo Capra[5], Thierry Facon[6], Roman Hajek[7], Ivan Špička[8], Ross Baker[9], Kihyun Kim[10], Gracia Martinez[11], Chang-Ki Min[12], Ludek Pour[13], Xavier Leleu[14], Albert Oriol[15], Youngil Koh[16], Kenshi Suzuki[17], France Casca[18], Sandrine Macé[19], Marie-Laure Risse[20] and Philippe Moreau[21,22]

# IKEMA: Updated PFS in the ITT Population




PFS = progression-free survival; ITT = intent-to-treat; Isa-Kd = isatuximab/carfilzomib/dexamethasone; Kd = carfilzomib/dexamethasone; mPFS = median PFS

Martin T et al. *Blood Cancer J* 2023;13(1):72.

RTP RESEARCH TO PRACTICE

# Agenda

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# CD3 x BCMA Bispecific Antibodies for MM

| | Teclistamab[1,2,3] | Linvoseltamab[4] | ABBV-383[5,6] | Elranatamab[7,8] | Alnuctamab[9] | REGN5459[10] |
|---|---|---|---|---|---|---|
| **Trial** | MajesTEC-1 | Phase I/II | Phase I | MagnetisMM-3 | Phase I | Phase I/II |
| **Population** | 165<br>Median 5 LOT<br>78% triple refractory | 252*<br>Median 6 LOT<br>90% triple refractory | 174*<br>Median 5 LOT<br>80% triple refractory | 123<br>Median 5 LOT<br>97% triple refractory<br>32% EMD | 68*<br>Median 4 LOT<br>63% triple refractory | 43 |
| **Safety all grade (Grade 3+)** | CRS 72% (0.6%)<br>Neurotoxicity 14.5% (0)<br>ICANS 3% (0)<br>Infections 76% (45%) | CRS 44% (1%)<br>Neurotoxicity: 5.6% (1.2%)<br>Infections: 54% (29%) | CRS 70% (2%)<br>ICANS : 6 pts (1 pt)<br>Infections 43% (22%) | CRS 56% (0)<br>ICANS 3% (0)<br>Infections 67% (35%) | CRS 53% (0)<br>ICANS 3% (0)<br>Infections 34% (9%) | CRS 54% (5%)<br>Infections: 61% (37%) |
| **Response ORR (VGPR+)** | 63% | 64% at 200mg | 61% at 60mg | 61% | 65% at 30mg dose | 67%<br>(90.5% at 2 highest doses) |

LOT = lines of therapy; CRS = cytokine release syndrome; pt = patient; ORR = overall response rate; VGPR = very good partial response

[1] Moreau et al. *N Engl J Med* 2022;387(6):495-505. [2] Nooka et al. ASCO 2022;Abstract 8007. [3] Touzeau et al. ASCO 2022;Abstract 8013. [4] Bumma et al. ASH 2022;Abstract 4555; AACR 2023. [5] Voorhees et al. ASH 2022;Abstract 1919. [6] Voorhees P et al. 19th International Myeloma Society Annual Meeting 2022;Abstract OAB-055. [7] Bahlis et al. ASH 2022;Abstract 159. [8] Raje et al. ASH 2022;Abstract 158. [9] Wong et al. ASH 2022;Abstract 162. [10] Suvannasankha A et al. AACR 2023;Abstract CT013.

# First Results from the RedirecTT-1 Study with Teclistamab (Tec) + Talquetamab (Tal) Simultaneously Targeting BCMA and GPRC5D in Patients (Pts) with Relapsed/Refractory Multiple Myeloma (RRMM)

Cohen YC et al.

ASCO 2023;Abstract 8002.

Saturday, June 3; 1:39 PM CDT

# LINKER-MM1 Study: Linvoseltamab (REGN5458) in Patients with Relapsed/Refractory Multiple Myeloma

Lee HC et al.

ASCO 2023;Abstract 8006.

Saturday, June 3; 3:15 PM CDT

# Efficacy and Safety of Elranatamab in Patients with Relapsed/Refractory Multiple Myeloma (RRMM) and Prior B-Cell Maturation Antigen (BCMA)-Directed Therapies: A Pooled Analysis from MagnetisMM Studies

Nooka AK et al.

ASCO 2023;Abstract 8008.

Saturday, June 3; 3:39 PM CDT

# Cevostamab is Efficacious and Well Tolerated in Patients Aged <65 and ≥65 Years with Relapsed/Refractory Multiple Myeloma

Krishnan A et al.

International Myeloma Society Annual Meeting 2022;Abstract P-012.

# RG6234, a GPRC5DxCD3 T-Cell Engaging Bispecific Antibody, Is Highly Active in Patients (pts) with Relapsed/Refractory Multiple Myeloma (RRMM): Updated Intravenous (IV) and First Subcutaneous (SC) Results from a Phase I Dose-Escalation Study

Carlo-Stella C et al.

ASH 2022;Abstract 161.

# Agenda

**Module 1 — Initial Treatment of Newly Diagnosed Multiple Myeloma (MM)**

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- Anti-CD38 antibodies
- Bispecific antibodies
- CAR T-cell therapy
- Selinexor
- Venetoclax and other strategies

# First Phase 3 Results from CARTITUDE-4: Cilta-Cel versus Standard of Care (PVd or DPd) in Lenalidomide-Refractory Multiple Myeloma

Dhakal B et al.

ASCO 2023;Abstract LBA106.

Monday, June 5; 9:57 AM CDT

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# Ide-cel or Standard Regimens in Relapsed and Refractory Multiple Myeloma

P. Rodriguez-Otero, S. Ailawadhi, B. Arnulf, K. Patel, M. Cavo, A.K. Nooka, S. Manier, N. Callander, L.J. Costa, R. Vij, N.J. Bahlis, P. Moreau, S.R. Solomon, M. Delforge, J. Berdeja, A. Truppel-Hartmann, Z. Yang, L. Favre-Kontula, F. Wu, J. Piasecki, M. Cook, and S. Giralt

2023;388:1002-14.

# Agenda

**Module 1 — Initial Treatment of Newly Diagnosed Multiple Myeloma**

- Up-front treatment for transplant-eligible patients
- Up-front treatment for patients not eligible for transplant
- Current approach to maintenance therapy

**Module 2 — Sequencing of Therapies for Relapsed/Refractory MM**

- Anti-CD38 antibodies
- Bispecific antibodies
- CAR T-cell therapy
- Selinexor
- Venetoclax and other strategies

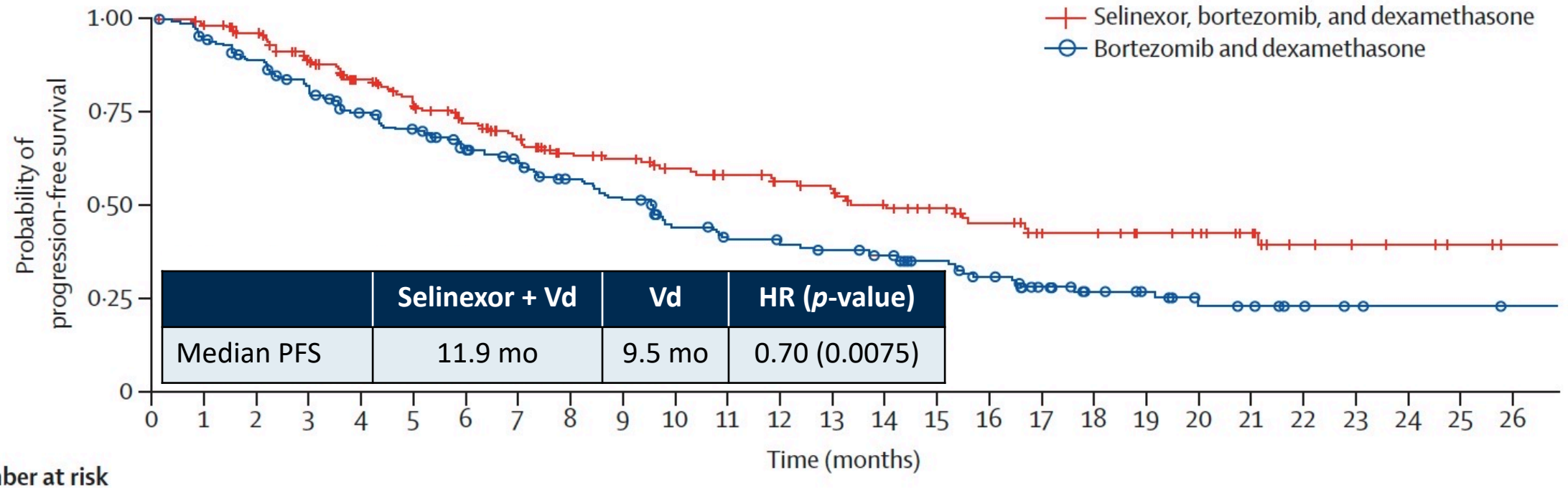
*Lancet* 2020;396(10262):1563-73.



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

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

# BOSTON: Progression-Free Survival (ITT Population)




| | Selinexor + Vd | Vd | HR (*p*-value) |
|---|---|---|---|
| Median PFS | 11.9 mo | 9.5 mo | 0.70 (0.0075) |

**Number at risk (number censored)**

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

ITT = intent-to-treat; Vd = bortezomib/dexamethasone

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

RTP RESEARCH TO PRACTICE

# BOSTON: Select Adverse Events

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

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

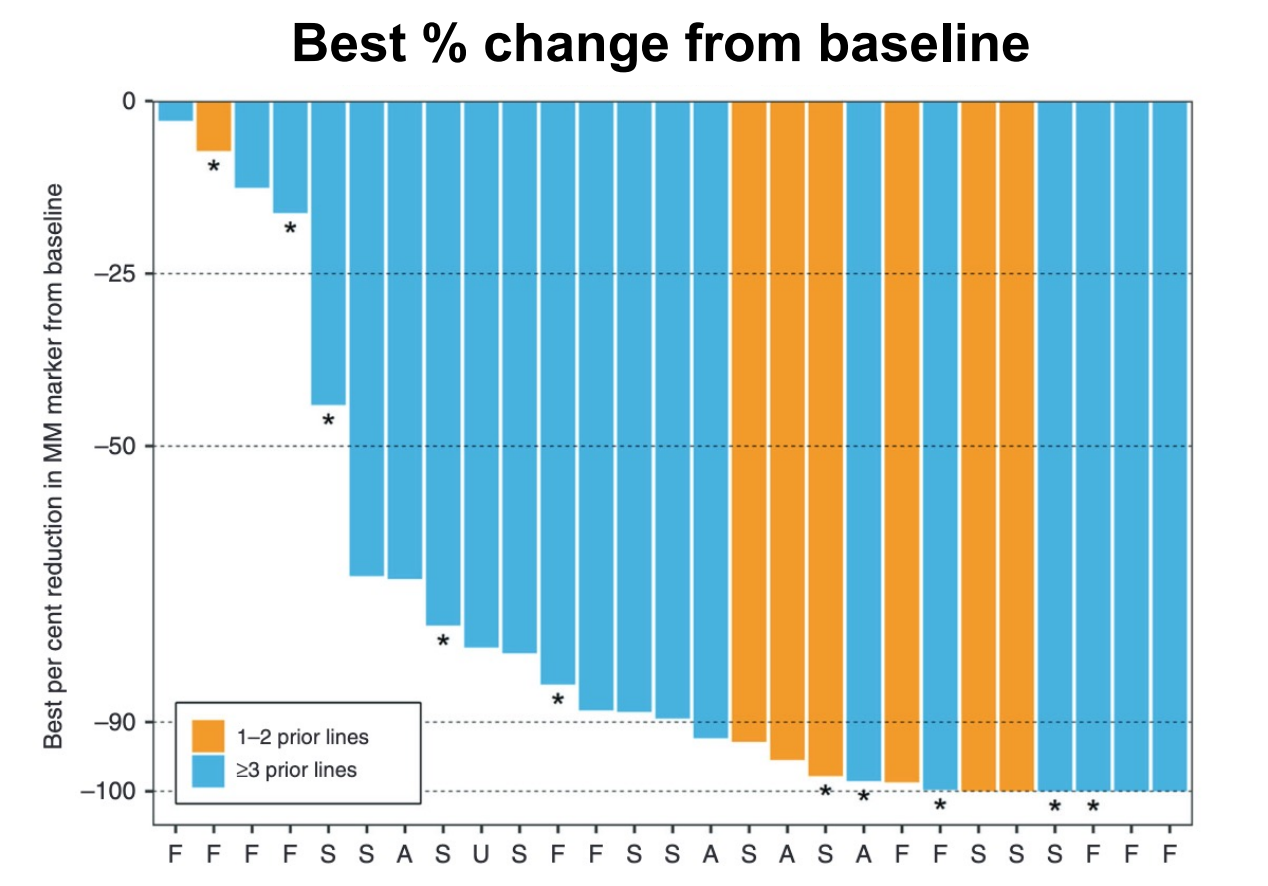
RTP RESEARCH TO PRACTICE

# Once weekly selinexor, carfilzomib and dexamethasone in carfilzomib non-refractory multiple myeloma patients

Cristina Gasparetto[1]✉, Gary J. Schiller[2], Sascha A. Tuchman[3], Natalie S. Callander[4], Muhamed Baljevic[5], Suzanne Lentzsch[6], Adriana C. Rossi[7], Rami Kotb[8], Darrell White[9], Nizar J. Bahlis[10], Christine I. Chen[11], Heather J. Sutherland[12], Sumit Madan[13], Richard LeBlanc[14], Michael Sebag[15], Christopher P. Venner[16], William I. Bensinger[17], Noa Biran[18], Sonia Ammu[19], Osnat Ben-Shahar[19], Andrew DeCastro[19], Dane Van Domelen[19], Tianjun Zhou[19], Chris Zhang[19], Ohad S. Bentur[19], Jatin Shah[19], Sharon Shacham[19], Michael Kauffman[19] and Brea Lipe[20]

***British Journal of Cancer* 2022;126:718-725**

# Depth of Response to Selinexor, Carfilzomib and Dexamethasone in Patients with Relapsed or Refractory Multiple Myeloma




**ORR: 78.1%**

**F free light chain, S SPEP, U UPEP, A IgA**

Gasperetto C et al. *Br J Cancer* 2022;126:718-725.

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- Anti-CD38 antibodies
- Bispecific antibodies
- CAR T-cell therapy
  Selinexor
- Venetoclax and other strategies

RTP RESEARCH TO PRACTICE

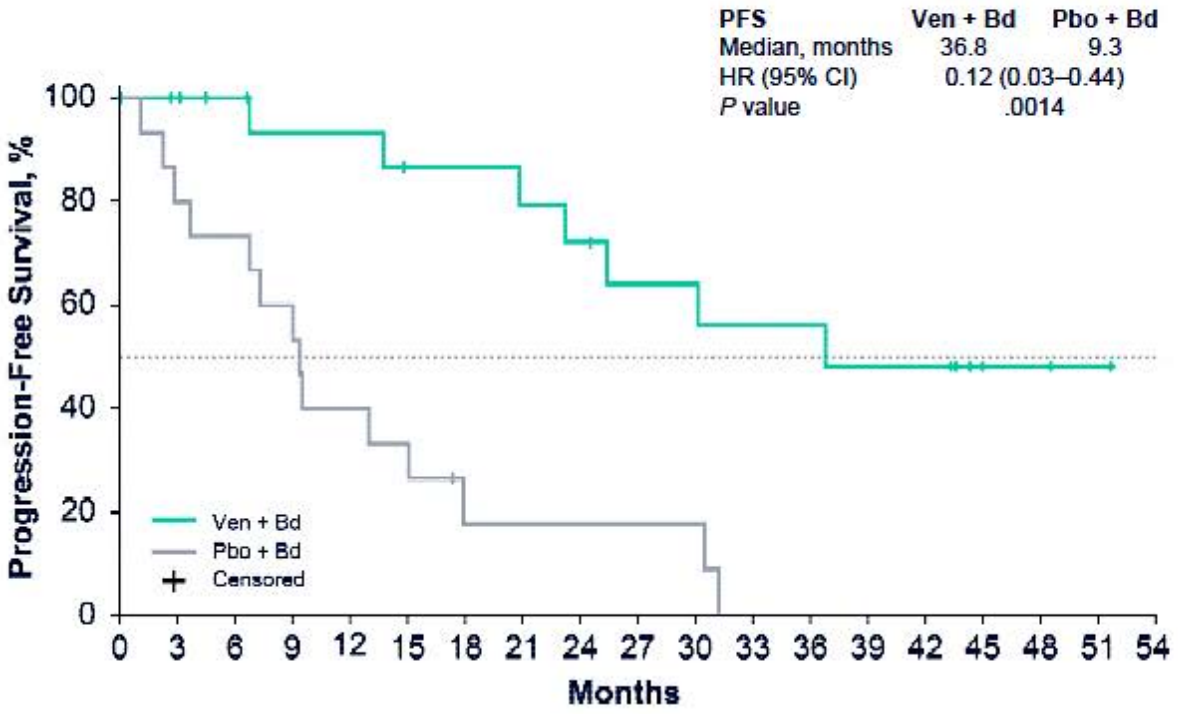
ASH 2021;Abstract 84.

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

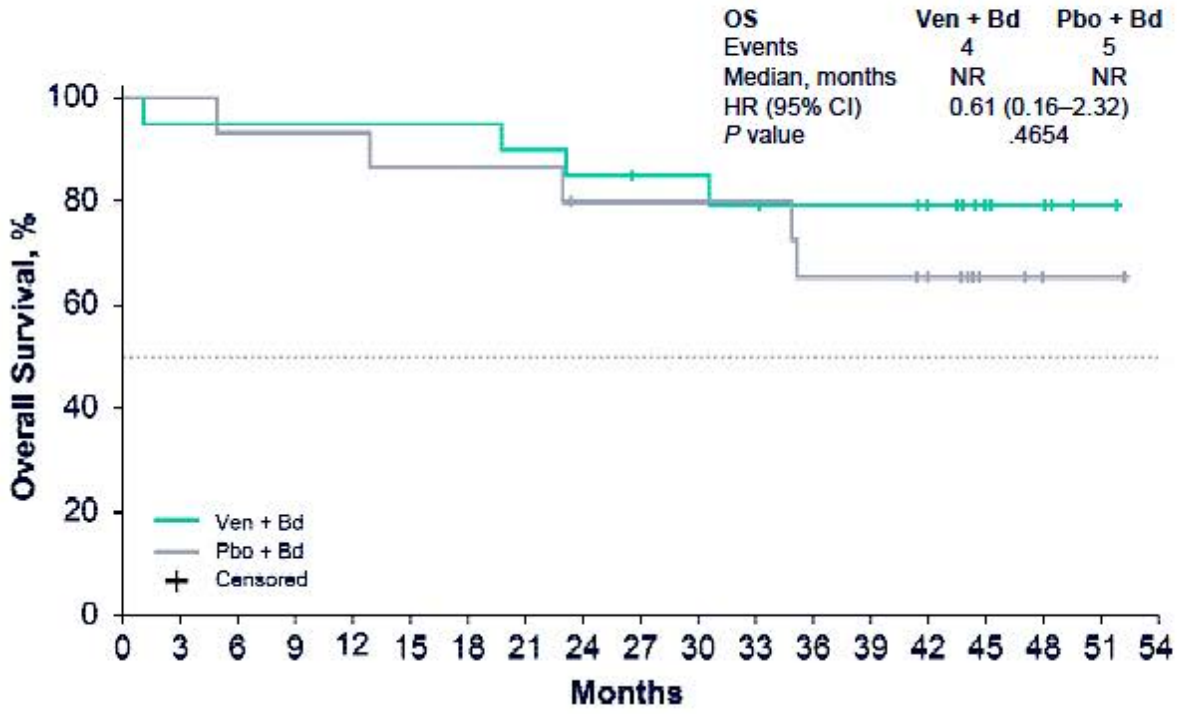
**Shaji K. Kumar,**[1] Simon J. Harrison,[2] Michele Cavo,[3] Javier de la Rubia,[4] Rakesh Popat,[5] Cristina Gasparetto,[6] Vania Hungria,[7] Hans Salwender,[8] Kenshi Suzuki,[9] Inho Kim,[10] Maika Onishi,[11] Grace Ku,[11] Rajvineeth Pothacamury,[12] Vasudha Sehgal,[12] Abdullah Masud,[12] Jeremy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

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

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



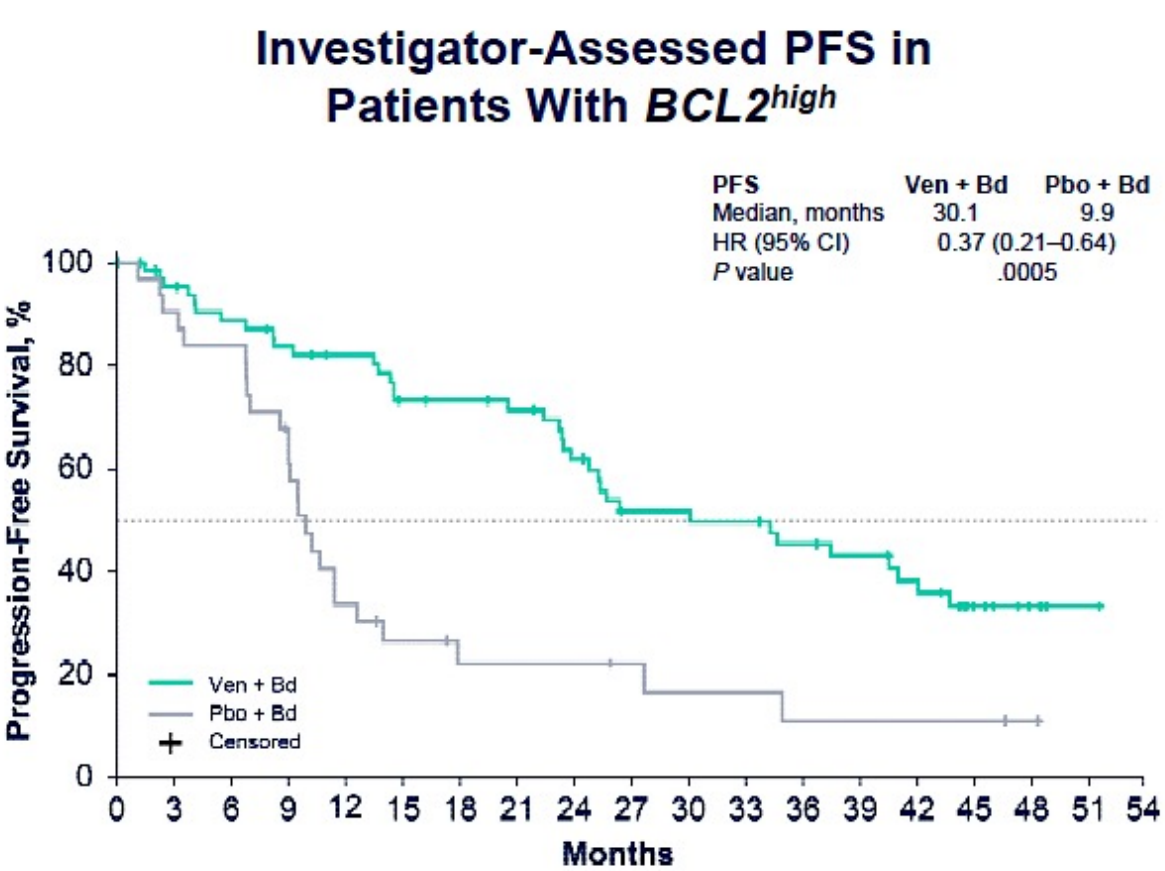

## OS in Patients With t(11;14)

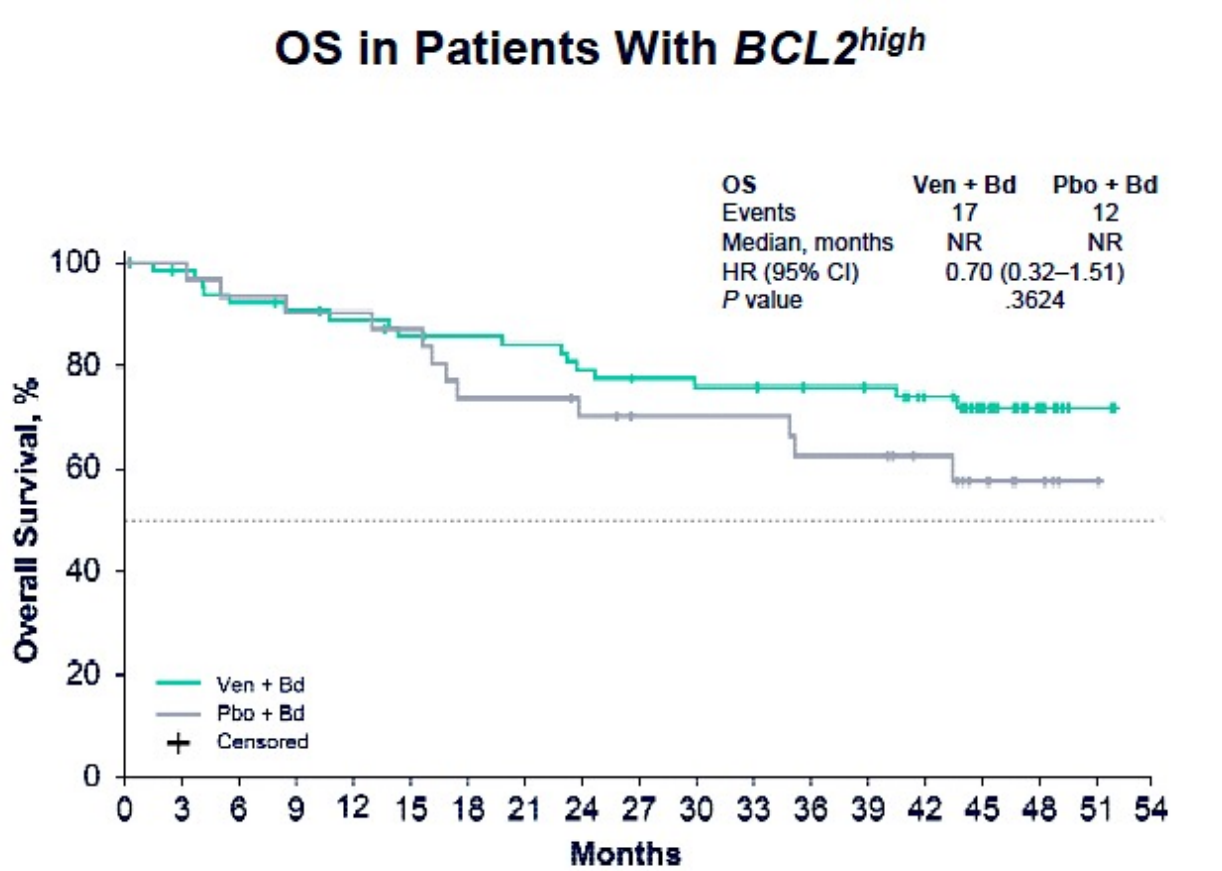



Kumar SK et al. ASH 2021;Abstract 84.

RTP RESEARCH TO PRACTICE

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




Kumar SK et al. ASH 2021;Abstract 84.

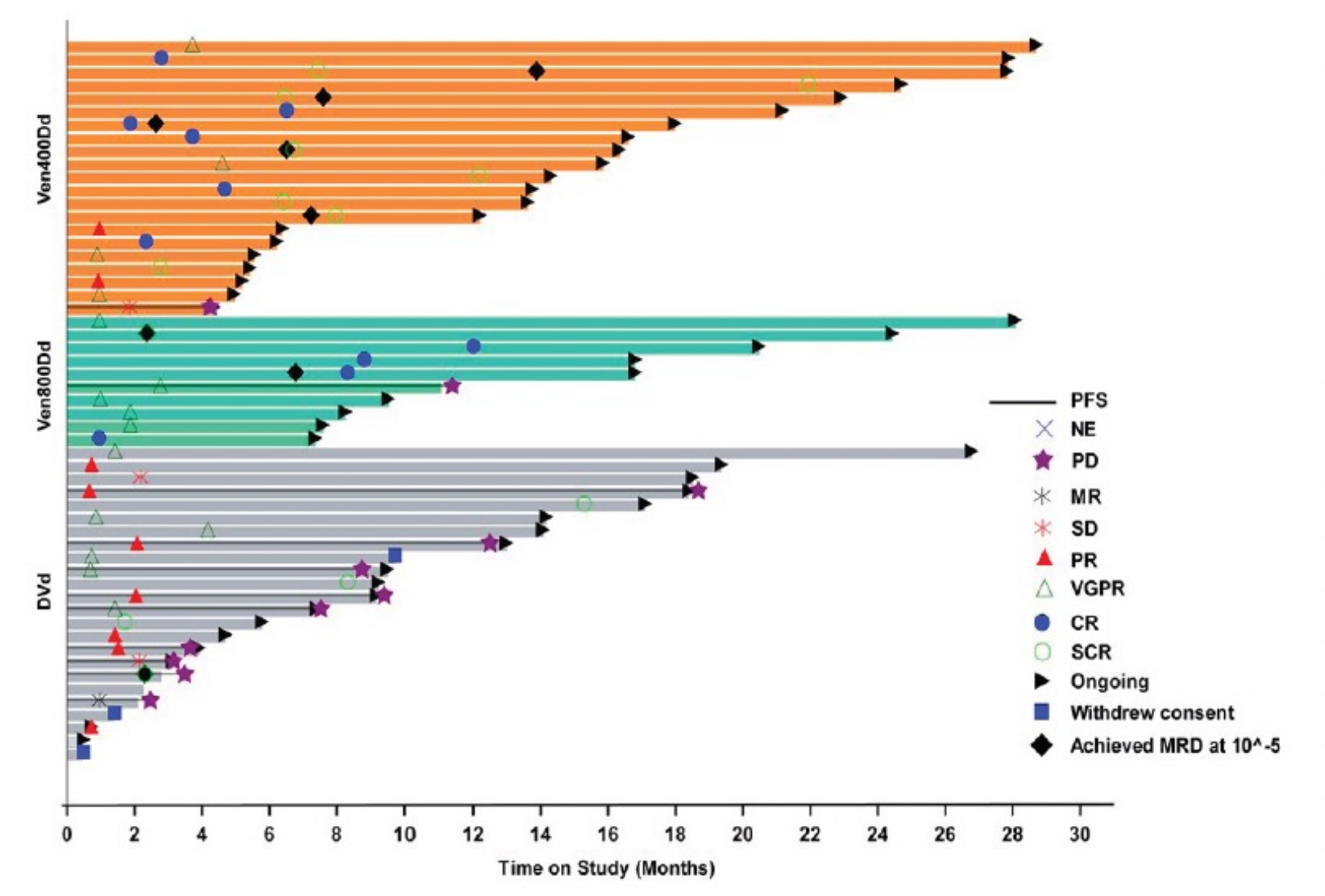
RTP RESEARCH TO PRACTICE

ASH 2022 Abstract 3232

# An Updated Safety and Efficacy Analysis of Venetoclax Plus Daratumumab and Dexamethasone in an Expansion Cohort of a Phase 1/2 Study of Patients With t(11;14) Relapsed/Refractory Multiple Myeloma

Jonathan L. Kaufman,[1] Hang Quach,[2] Rachid Baz,[3] Annette Juul Vangsted,[4] Shir-Jing Ho,[5] Simon J. Harrison,[6] Torben Plesner,[7] Philippe Moreau,[8] Simon Gibbs,[9] Eva Medvedova,[10] Muhammad Jalaluddin,[11] Jeremy A. Ross,[11] Leanne L Fleming,[11] Yan Luo,[11] Nizar J. Bahlis[12]

# Venetoclax, Daratumumab and Dexamethasone (VenDd) Responses




Kaufman JL et al. ASH 2022; Abstract 3232.

RTP RESEARCH TO PRACTICE

# A Phase 3, Open-Label, Randomized Study to Evaluate the Efficacy and Safety of Single-Agent Belantamab Mafodotin (Belamaf) Compared to Pomalidomide plus Low-Dose Dexamethasone (Pd) in Patients (Pts) with Relapsed/Refractory Multiple Myeloma (RRMM): DREAMM-3

Weisel K et al.

ASCO 2023;Abstract 8007.

Saturday, June 3; 3:27 PM CDT

# Meet The Professors Live: Clinical Investigators Provide Perspectives on Actual Cases of Patients with Lymphoma

*A CME Symposium Held in Conjunction with the 2023 ASCO® Annual Meeting*


## Faculty

**Ann S LaCasce, MD, MMSc**

**Loretta J Nastoupil, MD**

## Moderator

**Neil Love, MD**


RTP RESEARCH TO PRACTICE

# Agenda

## Module 1 — Hodgkin Lymphoma

- First-line therapy

## Module 2 — Diffuse Large B-Cell Lymphoma

- First-line therapy
- Bispecific antibodies
- CAR T-cell therapy
- Selinexor

## Module 3 — Follicular Lymphoma

- Bispecific antibodies

## Module 4 — Mantle Cell Lymphoma

- BTK inhibitors
- CAR T-cell therapy

RTP
RESEARCH
TO PRACTICE

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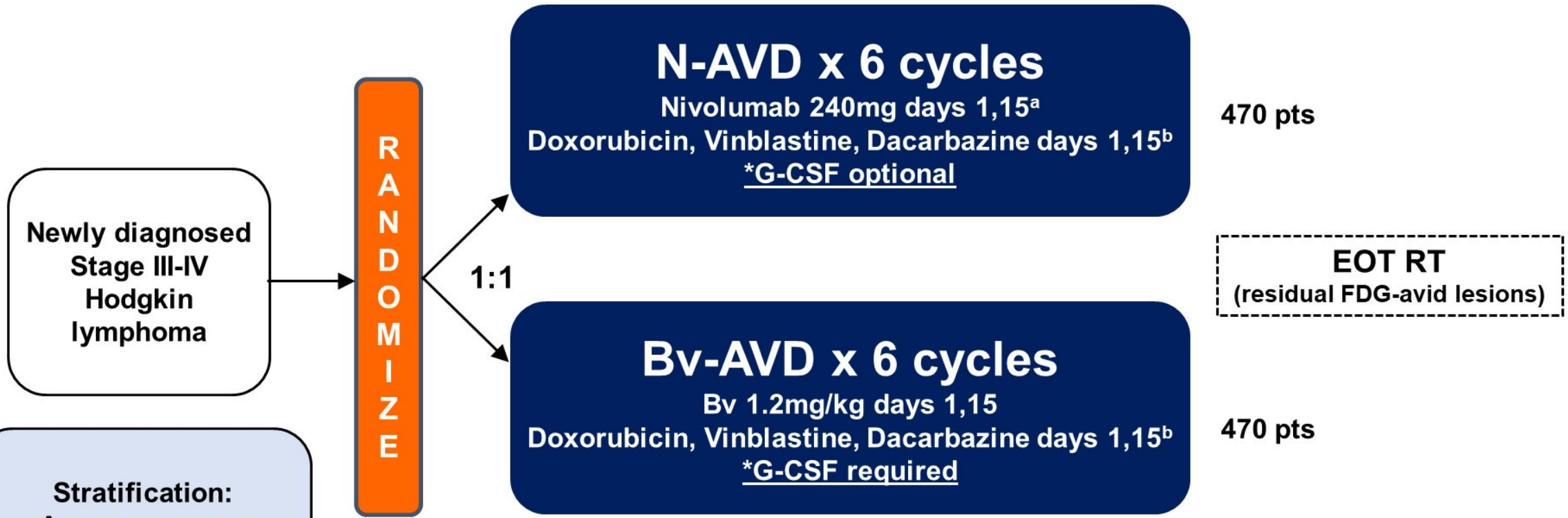
2023 ASCO ANNUAL MEETING

# SWOG S1826, a Randomized Study of Nivolumab(N)-AVD Versus Brentuximab Vedotin(Bv)-AVD in Advanced Stage Classic Hodgkin Lymphoma (cHL)

***Alex F. Herrera, MD***[1], *Michael L. LeBlanc, PhD*[2], *Sharon M. Castellino, MD, MSc*[3], *Hongli Li, MS*[2], *Sarah C. Rutherford, MD*[4], *Andrew M Evens, DO, MSc*[5], *Kelly Davison, MD*[6], *Angela Punnett, MD*[7], *David C. Hodgson, MD, MPH, FRCPC*[8], *Susan K Parsons, MD, MRP*[9], *Sairah Ahmed, MD*[10], *Carla Casulo, MD*[11], *Nancy L. Bartlett, MD*[12], *Joo Y. Song, MD*[13], *Richard F. Little*[14], *Brad S. Kahl, MD*[12], *John P. Leonard, MD*[4], *Sonali M. Smith, MD*[15], *Kara M. Kelly, MD*[16], *and Jonathan W. Friedberg, MD, MSSc*[11]

*[1]City of Hope, Duarte, CA, [2]SWOG Statistical Center, Fred Hutchinson Cancer Center, Seattle, WA, [3]Emory University, Aflac Cancer and Blood Disorders Center, Children's Healthcare of Atlanta, Atlanta, GA, [4]Weill Cornell Medicine-New York Presbyterian Hospital, New York, NY, [5]Rutgers Cancer Institute of New Jersey, New Brunswick, NJ, [6]McGill University, Montreal, QC, Canada, [7]Hospital for Sick Children, Toronto, ON, Canada, [8]Department of Radiation Oncology, Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada, [9]Tufts Medical Center, Tufts University School of Medicine, Boston, MA, [10] University of Texas M.D. Anderson Cancer Center, Houston, TX, [11]Division of Hematology/Oncology, University of Rochester, Rochester, NY [11]Division of Medical Oncology and Hematology, Princess Margaret Cancer Centre, Toronto, ON, Canada, [12]Washington University School of Medicine in St. Louis, St. Louis, MO, [13]Department of Pathology, City of Hope, CA [14]Cancer Therapy Evaluation Program, National Cancer Institute, Bethesda, MD [15] Department of Oncology, University of Chicago, Chicago, IL, [16]Department of Pediatric Oncology, Roswell Park Comprehensive Cancer Center, Buffalo, NY*

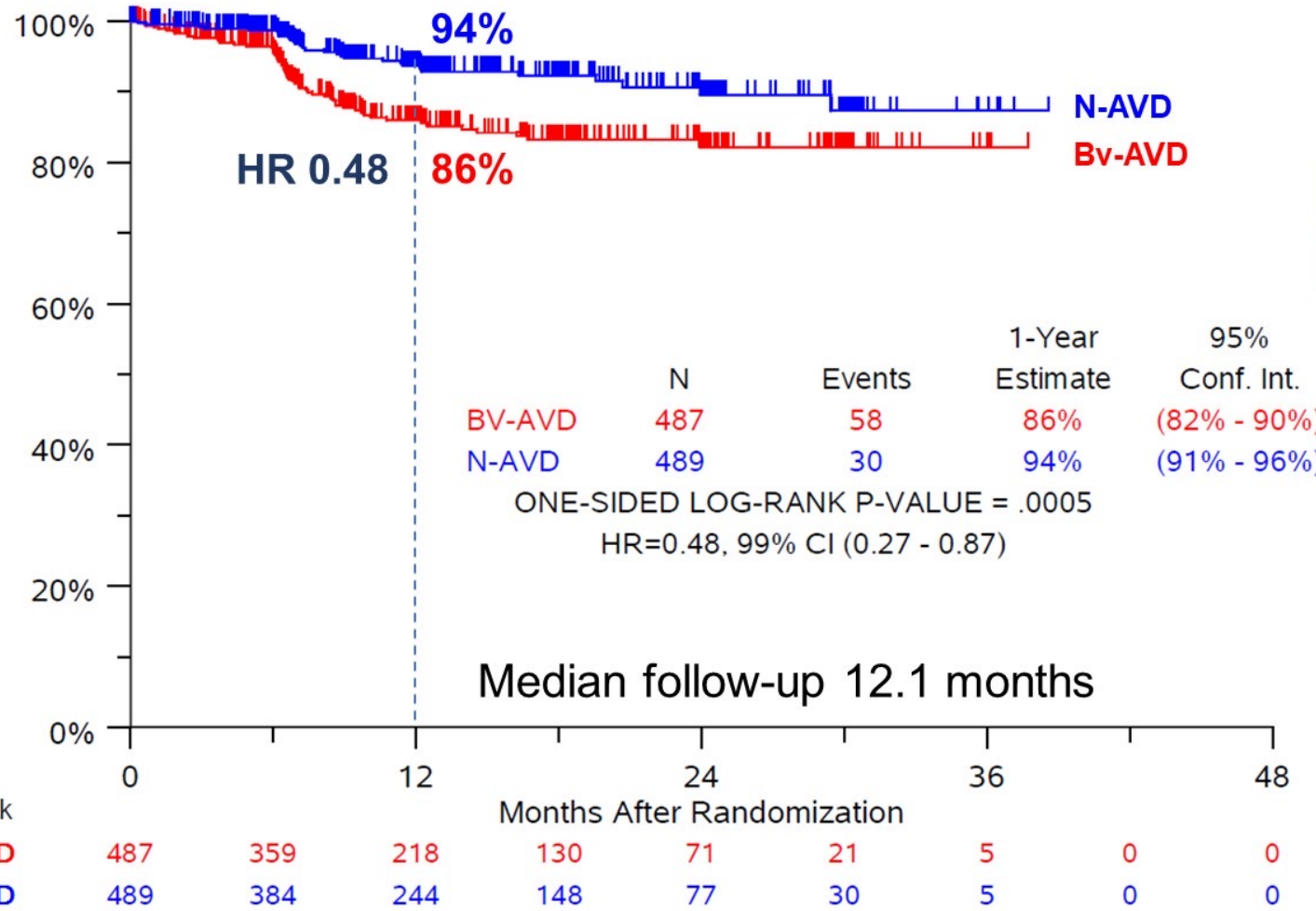
# S1826 Study Design




- Primary endpoint: PFS
- Assume 84% 2-year PFS for BV-AVD, 90% 2-year PFS in N-AVD, final analysis @ 179 events

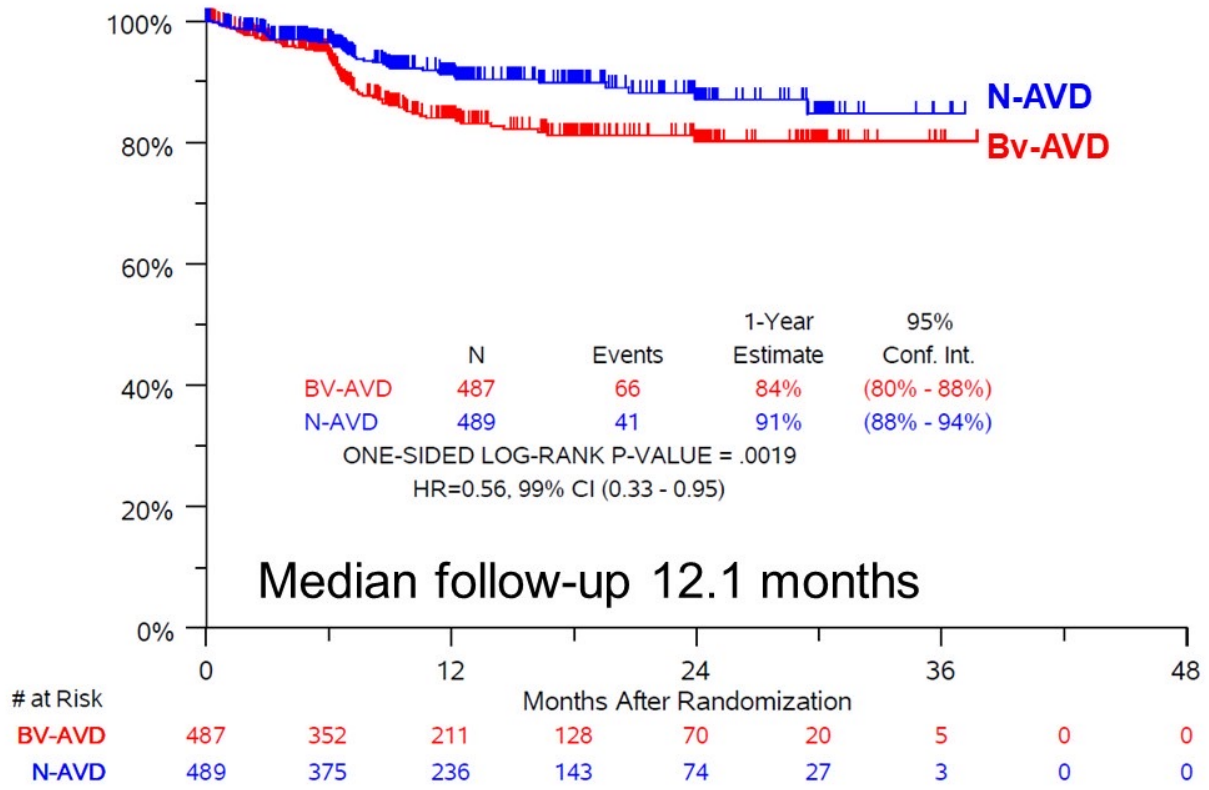
[a] Nivolumab 3mg/kg for ages ≤ 17, max 240mg
[b] Conventional doses of AVD: Stephens DM et al Blood 2019, Ansell SM et al NEJM 2022

# N-AVD improves PFS compared to Bv-AVD




**1-year PFS**
**N-AVD 94%**
**Bv-AVD 86%**

# Event-Free Survival



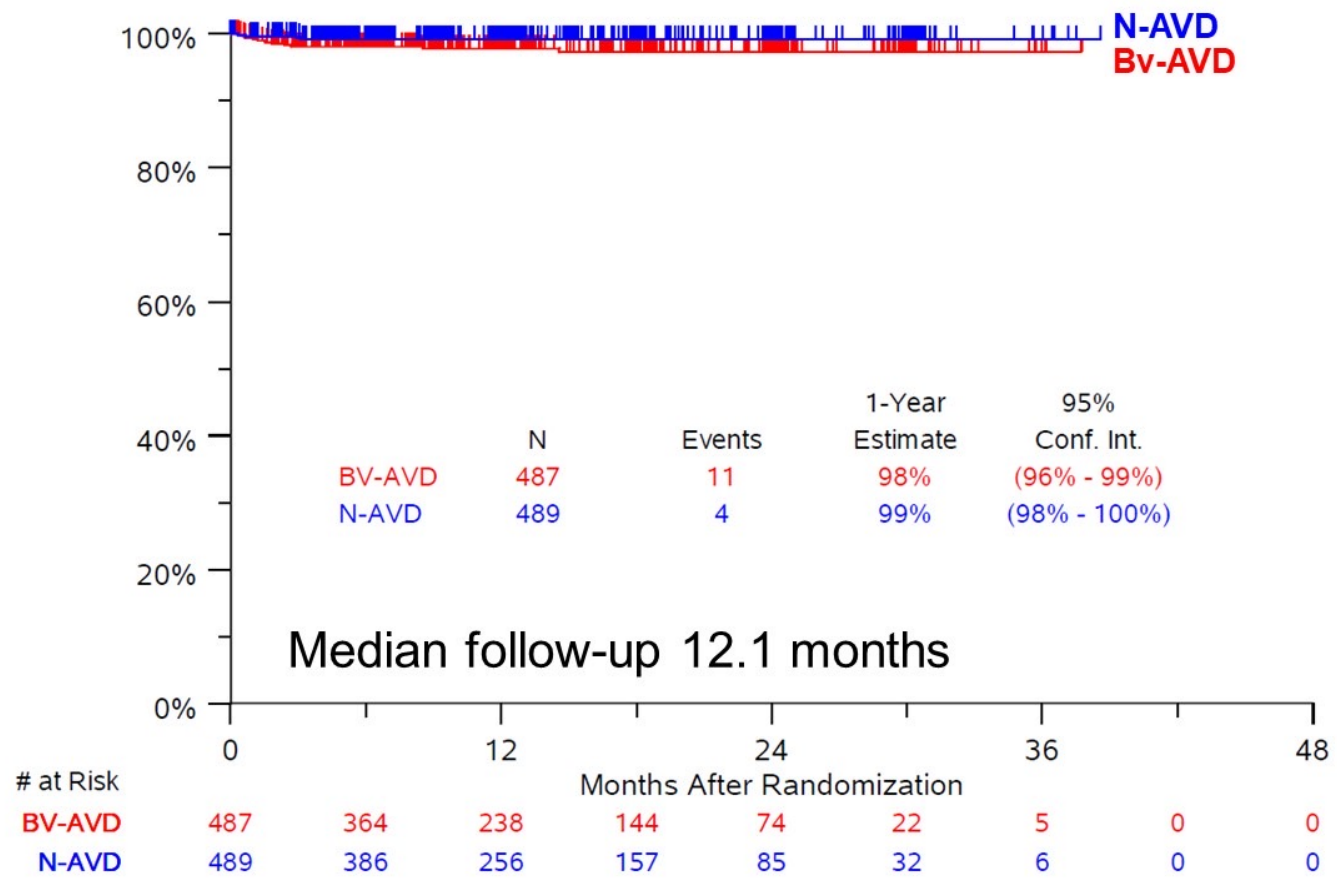

**1-year EFS**
**N-AVD 91%**
**Bv-AVD 84%**

EFS events: death, progression, non-protocol treatment before progression

| EFS event | N-AVD | Bv-AVD |
|---|---|---|
| Non-protocol chemo before PD | 9 | 6 |
| Non-protocol immunotx before PD | 1 | 0 |
| Non-protocol RT prior to PD | 1* | 3** |
| Progression/Relapse | **26** | **47** |
| Death without progression | **4** | **10** |
| Total EFS Event | **41** | **66** |

* Intended for RT, EOT DS=3, received RT anyways
**1/3 intended for RT, 1 with EOT DS=2 and off tx due to AE then received RT, 2 with EOT DS=3 and received RT anyways

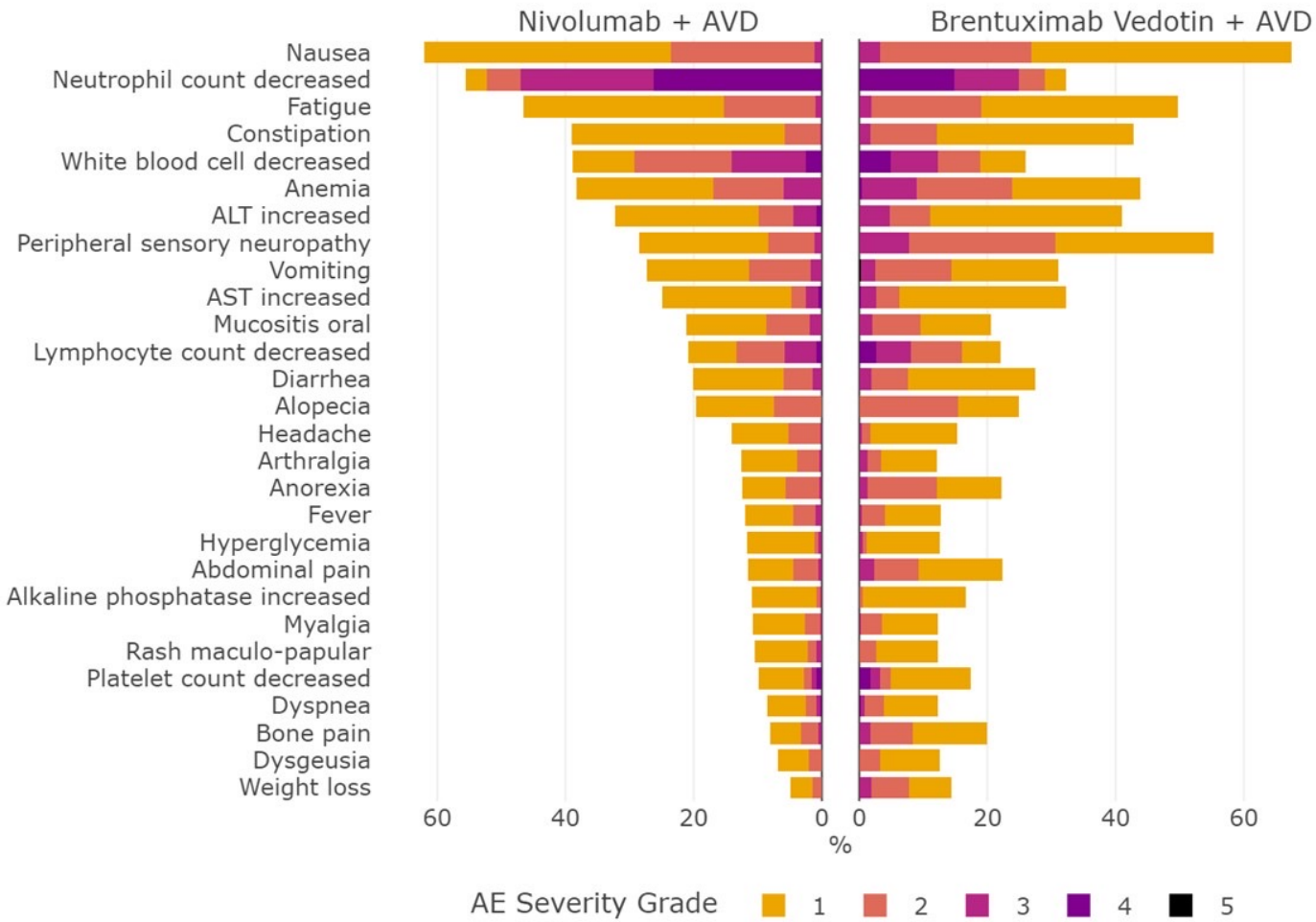
# Overall Survival




| Cause of death | N-AVD | Bv-AVD |
|---|---|---|
| Infection | 2 | 4 |
| Sepsis | 1 | 2* |
| Cardiac arrest | 0 | 1 |
| Pneumonitis | 0 | 1 |
| Dehydration, vomiting, cHL | 0 | 1 |
| cHL | 1** | 0 |
| Unknown | 1 | 2 |
| **Total OS events** | **4** | **11** |

* 1 death from COVID-19/sepsis
** never received treatment, ineligible on C1D1

# Adverse Events in ≥ 10% patients by Arm






PRESENTED BY: Alex F. Herrera, MD

# S1826 Conclusions

- **N-AVD improved PFS compared to Bv-AVD in advanced stage cHL**
  - N-AVD improved EFS versus Bv-AVD
- N-AVD was well-tolerated
  - Few immune-related adverse events
- < 1% of patients received consolidative RT
  - May reduce late effects
- Follow-up ongoing to confirm durability of PFS, assess long-term safety, OS, and PROs
- Key step towards harmonizing pediatric and adult therapy of cHL
- **N-AVD is poised to be a new standard therapy for advanced stage cHL**


PRESENTED BY: Alex F. Herrera, MD

The NEW ENGLAND JOURNAL of MEDICINE

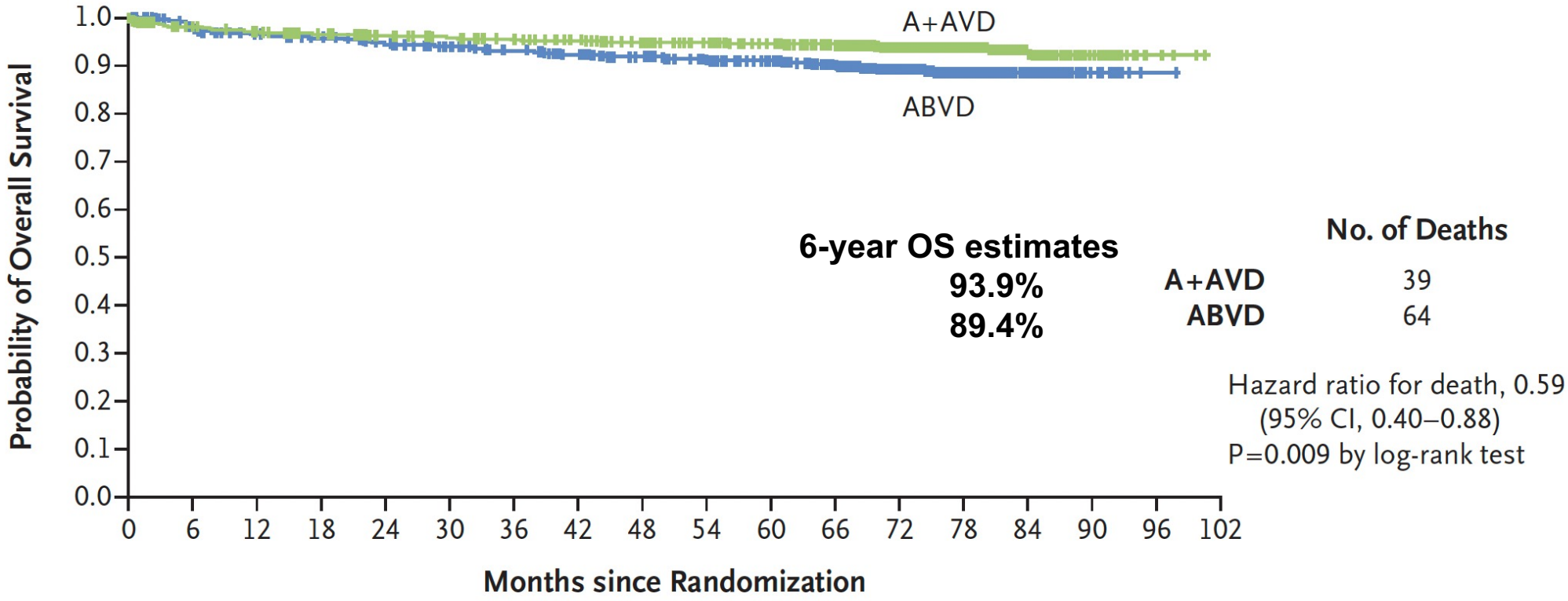
ORIGINAL ARTICLE

# 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*

2022;387(4):310-20.

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




**No. at Risk**

| | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| A+AVD | 664 | 638 | 626 | 612 | 598 | 584 | 572 | 557 | 538 | 517 | 494 | 461 | 350 | 209 | 97 | 27 | 4 | 0 |
| ABVD | 670 | 634 | 614 | 604 | 587 | 567 | 545 | 527 | 505 | 479 | 454 | 411 | 308 | 191 | 84 | 11 | 1 | 0 |

A+AVD = brentuximab vedotin/doxorubicin/vinblastine/dacarbazine; ABVD = doxorubicin/bleomycin/vinblastine/dacarbazine

Ansell SM et al. *N Engl J Med* 2022;387(4):310-20.

# Agenda

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RTP RESEARCH TO PRACTICE

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# FDA Approves Polatuzumab Vedotin-piiq for Previously Untreated Diffuse Large B-Cell Lymphoma, Not Otherwise Specified and High-Grade B-Cell Lymphoma

## Press Release: April 19, 2023

"The Food and Drug Administration approved polatuzumab vedotin-piiq with a rituximab product, cyclophosphamide, doxorubicin, and prednisone (R-CHP) for adult patients who have previously untreated diffuse large B-cell lymphoma (DLBCL), not otherwise specified (NOS), or high-grade B-cell lymphoma (HGBL) and who have an International Prognostic Index (IPI) score of 2 or greater.

Approval was based on POLARIX (NCT03274492), a randomized, double-blind, placebo-controlled trial in 879 patients with previously untreated large B-cell lymphoma and an IPI score of 2-5. The trial evaluated the superiority of substituting polatuzumab vedotin for vincristine in the R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) regimen. Patients were randomized (1:1) to receive either polatuzumab vedotin plus R-CHP (pola + R-CHP) or R-CHOP for six 21-day cycles, followed by two additional cycles of rituximab alone in both arms. The main diagnoses were de novo DLBCL, NOS (84%) and HGBL (11%)."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-polatuzumab-vedotin-piiq-previously-untreated-diffuse-large-b-cell-lymphoma-not

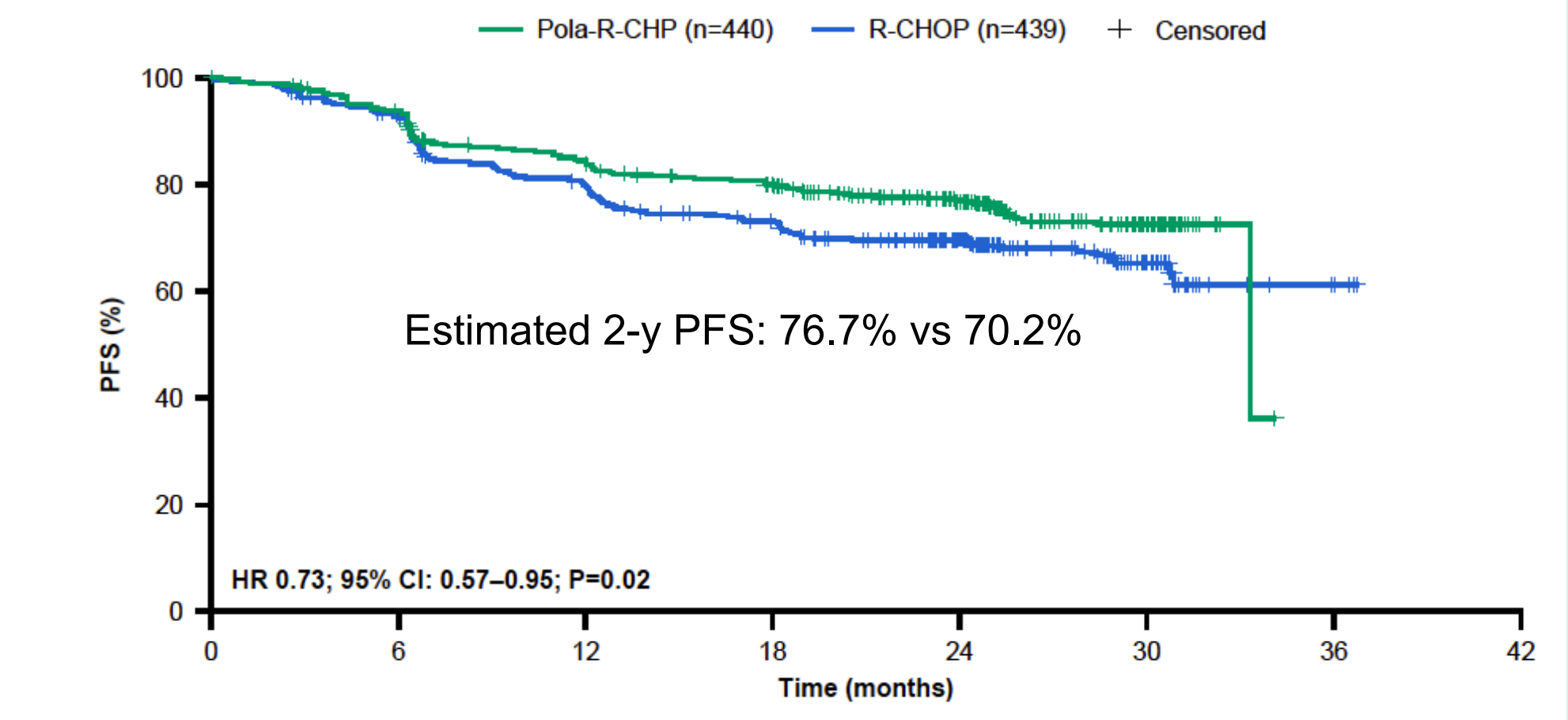
RTP RESEARCH TO PRACTICE

# 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

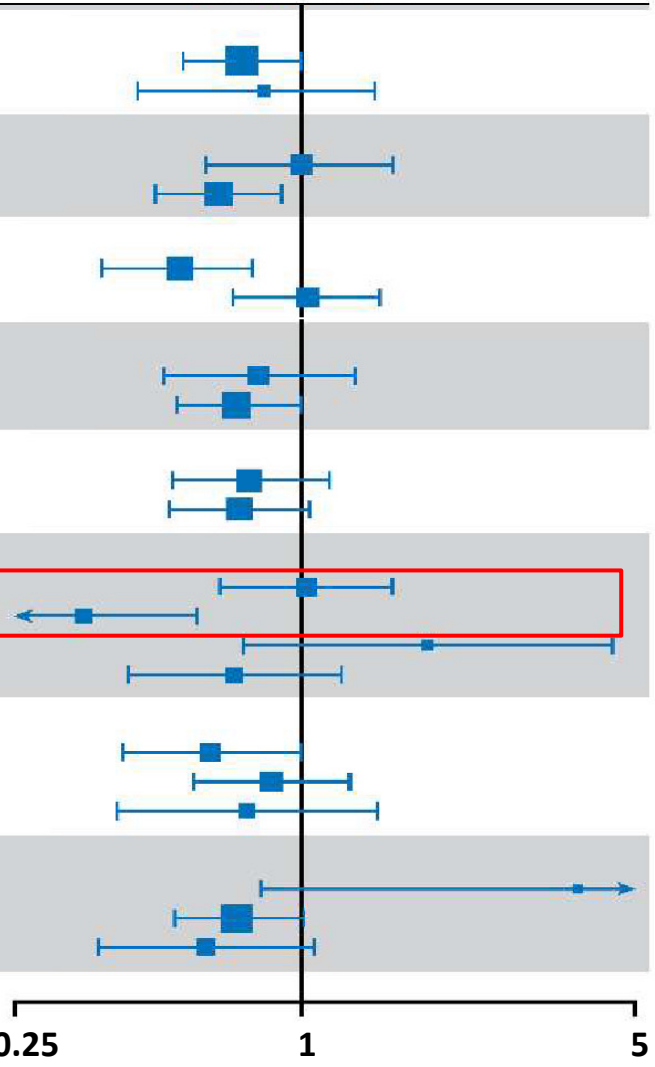
# POLARIX: Investigator-Assessed Progression-Free Survival (PFS) — Primary Endpoint




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

# POLARIX: Subgroup Analysis

| Baseline Risk Factors | Total N | Pola-R-CHP (N=440) n | Pola-R-CHP (N=440) 2-year Rate | R-CHOP (N=439) n | R-CHOP (N=439) 2-year Rate | Hazard Ratio | 95% Wald CI |
|---|---|---|---|---|---|---|---|
| ECOG PS | | | | | | | |
| 0-1 | 737 | 374 | 78.4 | 363 | 71.2 | 0.8 | (0.6 to 1.0) |
| 2 | 141 | 66 | 67.2 | 75 | 65.0 | 0.8 | (0.5 to 1.4) |
| IPI score | | | | | | | |
| IPI 2 | 334 | 167 | 79.3 | 167 | 78.5 | 1.0 | (0.6 to 1.6) |
| IPI 3-5 | 545 | 273 | 75.2 | 272 | 65.1 | 0.7 | (0.5 to 0.9) |
| Bulky disease | | | | | | | |
| Absent | 494 | 247 | 82.7 | 247 | 70.7 | 0.6 | (0.4 to 0.8) |
| Present | 385 | 193 | 69.0 | 192 | 69.7 | 1.0 | (0.7 to 1.5) |
| Baseline LDH | | | | | | | |
| ≤ULN | 300 | 146 | 78.9 | 154 | 75.6 | 0.8 | (0.5 to 1.3) |
| >ULN | 575 | 291 | 75.4 | 284 | 67.2 | 0.7 | (0.5 to 1.0) |
| No. of extranodal sites | | | | | | | |
| 0-1 | 453 | 227 | 80.2 | 226 | 74.5 | 0.8 | (0.5 to 1.1) |
| ≥2 | 426 | 213 | 73.0 | 213 | 65.8 | 0.7 | (0.5 to 1.0) |
| Cell-of-origin | | | | | | | |
| GCB | 352 | 184 | 75.1 | 168 | 76.9 | 1.0 | (0.7 to 1.5) |
| ABC | 221 | 102 | 83.9 | 119 | 58.8 | 0.4 | (0.2 to 0.6) |
| Unclassified | 95 | 44 | 73.0 | 51 | 86.2 | 1.9 | (0.8 to 4.5) |
| Unkown | 211 | 110 | 73.8 | 101 | 64.3 | 0.7 | (0.4 to 1.2) |
| Double expressor by IHC | | | | | | | |
| DEL | 290 | 139 | 75.5 | 151 | 63.1 | 0.6 | (0.4 to 1.0) |
| Non DEL | 438 | 223 | 77.7 | 215 | 75.7 | 0.9 | (0.6 to 1.3) |
| Unknown | 151 | 78 | 76.0 | 73 | 69.8 | 0.8 | (0.4 to 1.5) |
| Double- or triple-hit lymphoma | | | | | | | |
| Yes | 45 | 26 | 69.0 | 19 | 889 | 3.8 | (0.8 to 17.6) |
| No | 620 | 305 | 76.8 | 315 | 70.3 | 0.7 | (0.5 to 1.0) |
| Unknown | 214 | 109 | 78.5 | 105 | 66.4 | 0.6 | (0.4 to 1.1) |




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

RTP RESEARCH TO PRACTICE

# Agenda

**Module 1 — Hodgkin Lymphoma**

- First-line therapy

**Module 2 — Diffuse Large B-Cell Lymphoma**

- First-line therapy
- Bispecific antibodies
- CAR T-cell therapy
- Selinexor

**Module 3 — Follicular Lymphoma**

- Bispecific antibodies

**Module 4 — Mantle Cell Lymphoma**

- BTK inhibitors
- CAR T-cell therapy

RTP RESEARCH TO PRACTICE

# FDA grants accelerated approval to epcoritamab-bysp for relapsed or refractory diffuse large B-cell lymphoma and high-grade B-cell lymphoma

## Press Release: May 19, 2023

"On May 19, 2023, the Food and Drug Administration granted accelerated approval to epcoritamab-bysp for relapsed or refractory diffuse large B-cell lymphoma (DLBCL) not otherwise specified, including DLBCL arising from indolent lymphoma, and high-grade B-cell lymphoma after two or more lines of systemic therapy.

Epcoritamab-bysp, a bispecific CD20-directed CD3 T-cell engager, was evaluated in EPCORE NHL-1 (NCT03625037), an open-label, multi-cohort, multicenter, single-arm trial in patients with relapsed or refractory B-cell lymphoma. The efficacy population consisted of 148 patients with relapsed or refractory DLBCL, not otherwise specified, including DLBCL arising from indolent lymphoma, and high-grade B-cell lymphoma after two or more lines of systemic therapy, including at least one anti-CD20 monoclonal antibody-containing therapy.

The main efficacy outcome measure was overall response rate (ORR) determined by Lugano 2014 criteria, as assessed by an Independent Review Committee. The ORR was 61% (95% CI: 53, 69) with 38% of patients achieving complete responses. With a median follow-up of 9.8 months among responders, the estimated median duration of response (DOR) was 15.6 months (95%CI: 9.7, not reached)."

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-grants-accelerated-approval-epcoritamab-bysp-relapsed-or-refractory-diffuse-large-b-cell

RTP RESEARCH TO PRACTICE

ASH 2022;Abstract 444.

# Odronextamab in Patients with Relapsed/Refractory (R/R) Diffuse Large B-Cell Lymphoma (DLBCL): Results from a Prespecified Analysis of the Phase 2 Study ELM-2

**Won Seog Kim[1], Tae Min Kim[2], Seok-Goo Cho[3], Isidro Jarque[4], Elżbieta Iskierka[5], Michelle Poon[6], H. Miles Prince[7], Sung Yong Oh[8], Francesca Lim[9], Cecilia Carpio[10], Tran-Der Tan[11], Sabarish Ayyappan[12], Antonio Gutierrez[13], Jingjin Li[14], Melanie Ufkin[14], Min Zhu[14], Aafia Chaudhry[14], Hesham Mohamed[14], Srikanth Ambati[14], Jan Walewski[15], on behalf of ELM-2 Investigators**

*[1]Samsung Medical Center, Center for Hematologic Malignancy, Seoul, South Korea; [2]Seoul National University Hospital, Seoul, South Korea; [3]The Catholic University of Korea, Seoul St. Mary's Hospital Hematology, Seoul, South Korea; [4]Hospital Universitari i Politècnic La Fe, Valencia, Spain; [5]Copernicus Memorial Hospital, Department of Hematology, Medical University of Łódź, Łódź, Poland; [6]Hematology Oncology National University Hospital, Singapore; [7]Epworth Healthcare and University of Melbourne, East Melbourne, Australia; [8]Dong-A University Hospital, Busan, South Korea; [9]Singapore General Hospital, Singapore; [10]Department of Hematology, Vall d'Hebron Institute of Oncology (VHIO), University Hospital Vall d'Hebron, Autonomous University of Barcelona (UAB), Barcelona, Spain; [11]Hematology and Medical Oncology Koo Foundation Sun Yat Sen Cancer Center, Taipei City, Taiwan; [12]University of Iowa Hospital and Clinics, Iowa City, IA, USA; [13]Hospital Universitari Son Espases, IdISBa Palma, Spain; [14]Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA; [15]Narodowy Instytut Onkologii im. Marii Skłodowskiej-Curie Państwowy Instytut Badawczy, Warszawa, Poland*

ClinicalTrials.gov ID: NCT03888105

# ELM-2: DLBCL Cohort – Objective Response Rate

| Best overall response | Independent central review N=130* | Investigator evaluation N=130* |
|---|---|---|
| Objective response rate (ORR)† | **49.2%** [95% CI 40.4%–58.1%] | **50.0%** [95% CI 41.1%–58.9%] |
| Complete response | **30.8%** | **36.2%** |
| Partial response | 18.5% | 13.8% |
| Stable disease | 3.8% | 3.1% |
| Progressive disease | 22.3% | 21.5% |

| Week 12 response assessment by independent central review | 1/20 step-up regimen N=67 | 0.7/4/20 step-up regimen N=63 |
|---|---|---|
| ORR | 46.3% [95% CI: 34.0–58.9%] | 42.9% [95% CI: 30.5–56.0%] |
| Complete response | 26.9% | 20.6% |

- 63% of responders achieved a complete response
- Consistent efficacy observed at Week 12 regardless of Cycle 1 step-up regimen

- Median opportunity of follow-up: 21.3 months (range 2.6–29.8)

Kim WS et al. ASH 2022;Abstract 444.

RTP RESEARCH TO PRACTICE

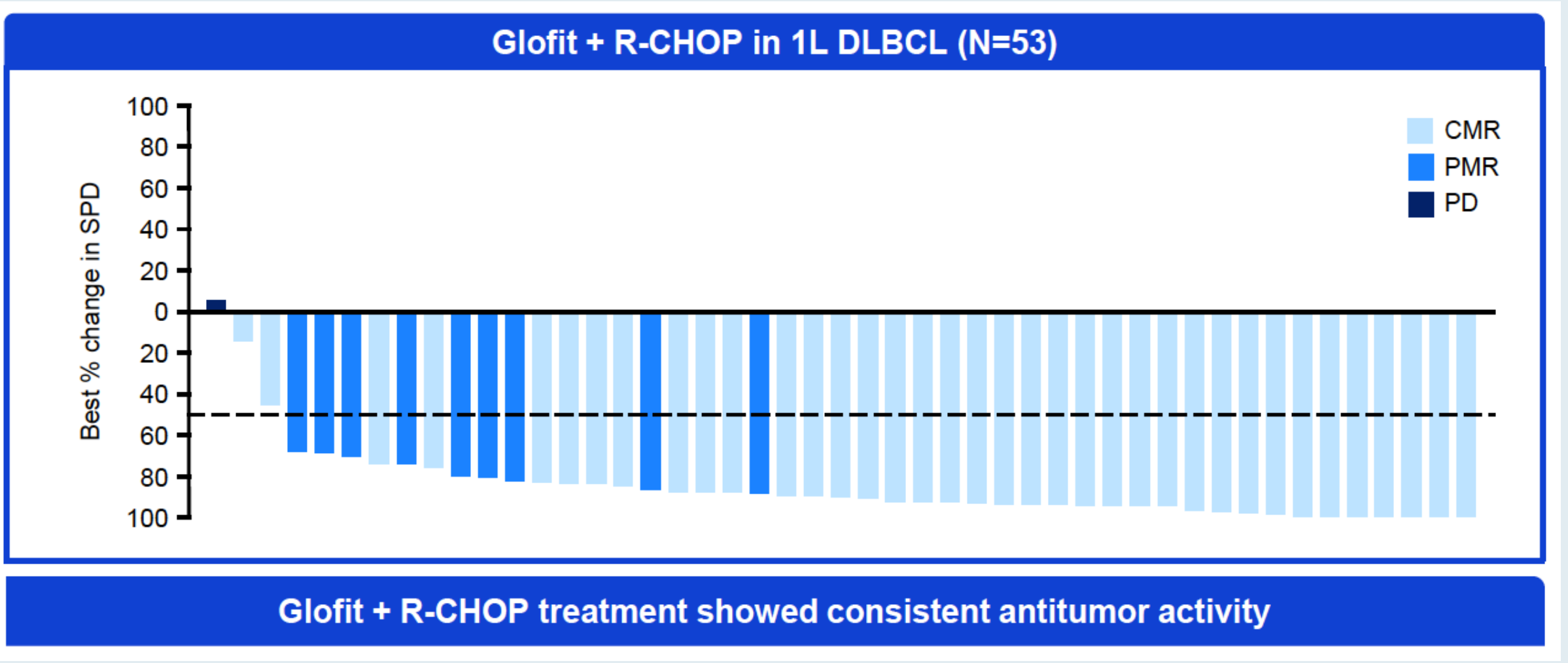
# Glofitamab Plus R-CHOP Induces High Response Rates and a Favorable Safety Profile in Patients with Previously Untreated Diffuse Large B-Cell Lymphoma (DLBCL): Results from a Phase Ib Study

**Max S. Topp**,[1] Monica Tani,[2] Michael Dickinson,[3] Nilanjan Ghosh,[4] Armando Santoro,[5] Antonio Pinto,[6] Francesc Bosch,[7] Christopher P. Fox,[8] Armando Lopez Guillermo,[9] Claudia Carlucci,[10] Chun Wu,[11] Kathryn Humphrey,[10] Pauline Baumlin,[12] Martin Barrett,[10] Naseer Qayum,[10] Franck Morschhauser[13]

*[1]Universitätsklinikum Würzburg, Würzburg, Germany; [2]Ospedale Santa Maria delle Croci, Ravenna, Italy; [3]The Peter MacCallum Cancer Centre, Royal Melbourne Hospital and The University of Melbourne, Melbourne, Australia; [4]Levine Cancer Institute/Atrium Health, Charlotte, NC, USA; [5]Humanitas University and IRCCS Humanitas Research Hospital, Humanitas Cancer Center, Milan, Italy; [6]Istituto Nazionale Tumori, Fondazione 'G. Pascale', IRCCS, Naples, Italy; [7]Department of Hematology Hospital Vall d'Hebron, Barcelona, Spain; [8]Nottingham University Hospitals NHS Trust, Nottingham, United Kingdom; [9]Hospital Clínic de Barcelona, Barcelona, Spain; [10]Roche Products Ltd, Welwyn Garden City, United Kingdom; [11]Roche (China) Holding Ltd, Shanghai, China; [12]F. Hoffmann-La Roche Ltd, Basel, Switzerland; [13]Hôpital Claude Huriez Universitaire Lille, CHU Lille, ULR 7365 - GRITA - Groupe de Recherche sur les formes Injectables et les Technologies Associées and Centre Hospitalier Régional Universitaire de Lille, Lille, France.*

**ASH 2022;Abstract 737.**

# First-Line Glofitamab plus R-CHOP: Antitumor Activity




CMR = complete molecular response; PMR = partial molecular response; PD = progressive disease

Topp MS et al. ASH 2022;Abstract 737.

# Agenda

**Module 1 — Hodgkin Lymphoma**

- First-line therapy

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- First-line therapy
- Bispecific antibodies
- CAR T-cell therapy
- Selinexor

**Module 3 — Follicular Lymphoma**

- Bispecific antibodies

**Module 4 — Mantle Cell Lymphoma**

- BTK inhibitors
- CAR T-cell therapy

RTP
RESEARCH
TO PRACTICE

# Primary Overall Survival Analysis of the Phase 3 Randomized ZUMA-7 Study of Axicabtagene Ciloleucel versus Standard-of-Care Therapy in Relapsed/Refractory Large B-Cell Lymphoma

Westin J et al.

ASCO 2023;Abstract LBA107.

Monday, June 5; 10:09 AM CDT

# Agenda

**Module 1 — Hodgkin Lymphoma**

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- Bispecific antibodies

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- BTK inhibitors
- CAR T-cell therapy

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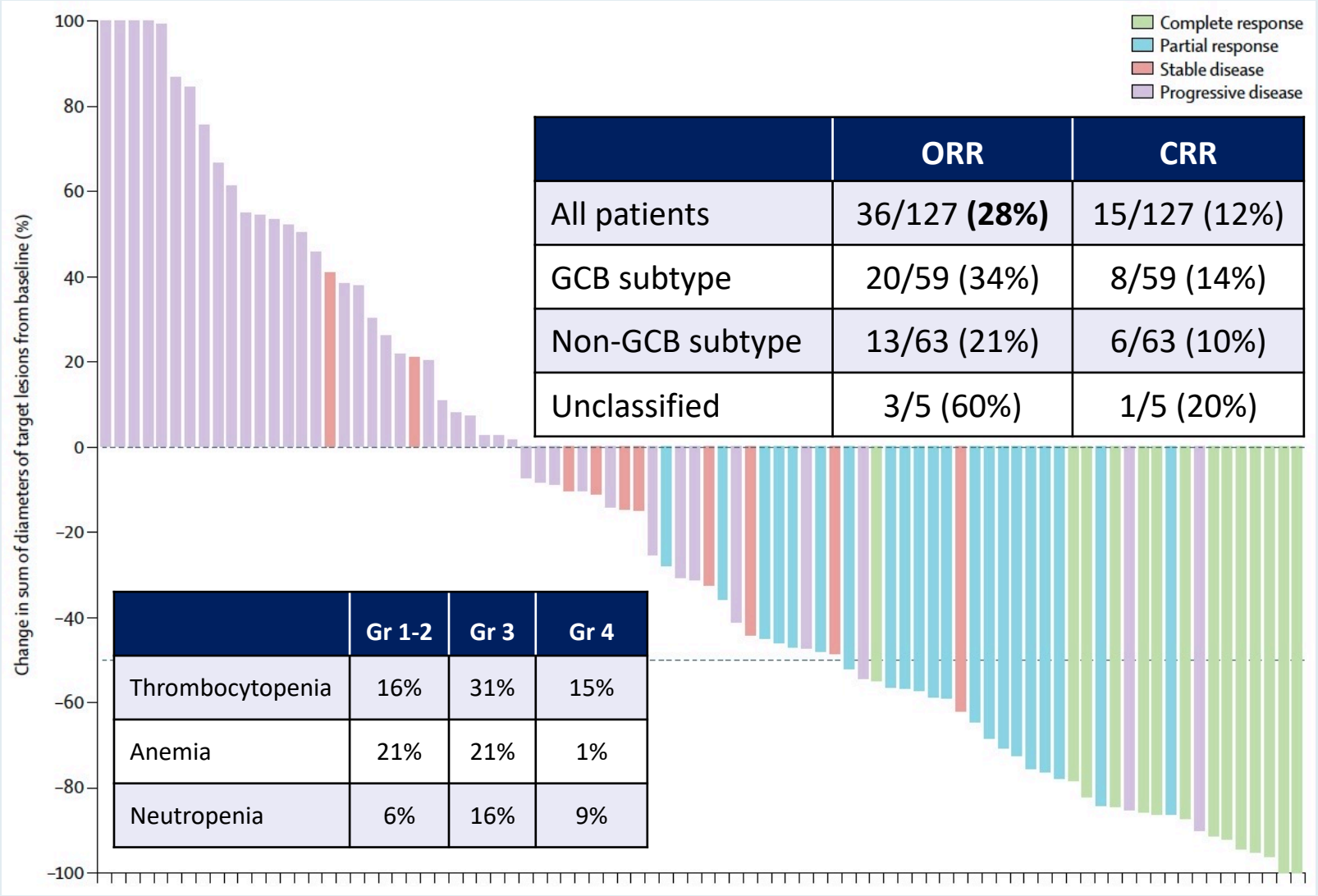
RESEARCH
TO PRACTICE

*Lancet Haematol* 2020;7:e511-22.

# Selinexor in patients with relapsed or refractory diffuse large B-cell lymphoma (SADAL): a single-arm, multinational, multicentre, open-label, phase 2 trial

*Nagesh Kalakonda*, Marie Maerevoet*, Federica Cavallo, George Follows, Andre Goy, Joost S P Vermaat, Olivier Casasnovas, Nada Hamad, Josée M Zijlstra, Sameer Bakhshi, Reda Bouabdallah, Sylvain Choquet, Ronit Gurion, Brian Hill, Ulrich Jaeger, Juan Manuel Sancho, Michael Schuster, Catherine Thieblemont, Fátima De la Cruz, Miklos Egyed, Sourav Mishra, Fritz Offner, Theodoros P Vassilakopoulos, Krzysztof Warzocha, Daniel McCarthy, Xiwen Ma, Kelly Corona, Jean-Richard Saint-Martin, Hua Chang, Yosef Landesman, Anita Joshi, Hongwei Wang, Jatin Shah, Sharon Shacham, Michael Kauffman, Eric Van Den Neste, Miguel A Canales*

# SADAL: Efficacy and Safety of Selinexor for R/R DLBCL After at Least 2 Previous Lines of Chemoimmunotherapy




| | ORR | CRR |
|---|---|---|
| All patients | 36/127 **(28%)** | 15/127 (12%) |
| GCB subtype | 20/59 (34%) | 8/59 (14%) |
| Non-GCB subtype | 13/63 (21%) | 6/63 (10%) |
| Unclassified | 3/5 (60%) | 1/5 (20%) |

| | Gr 1-2 | Gr 3 | Gr 4 |
|---|---|---|---|
| Thrombocytopenia | 16% | 31% | 15% |
| Anemia | 21% | 21% | 1% |
| Neutropenia | 6% | 16% | 9% |

ORR = overall response rate; CRR = complete response rate

Kalakonda N et al. *Lancet Haematol* 2020;7:e511-22.

RTP RESEARCH TO PRACTICE

# Agenda

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RTP
RESEARCH
TO PRACTICE

# Epcoritamab + R2 Regimen and Responses in High-Risk Follicular Lymphoma, Regardless of POD24 Status

Merryman R et al.

ASCO 2023;Abstract 7506.

Monday, June 5; 11:45 AM CDT

ASH 2022;Abstract 610.

# Mosunetuzumab Monotherapy Demonstrates Durable Efficacy with a Manageable Safety Profile in Patients with Relapsed/Refractory Follicular Lymphoma who Received ≥2 Prior Therapies: Updated Results from a Pivotal Phase II Study

Nancy L. Bartlett,[1] Laurie H. Sehn,[2] Matthew Matasar,[3] Stephen J. Schuster,[4] Sarit Assouline,[5] Pratyush Giri,[6] John Kuruvilla,[7] Miguel Canales,[8] Sascha Dietrich,[9] Keith Fay,[10] Matthew Ku,[11] Loretta Nastoupil,[12] Michael C. Wei,[13] Shen Yin,[13] Iris To,[13] Huang Huang,[14] Juliana Min,[15] Elicia Penuel,[13] Christopher R. Bolen,[13] L. Elizabeth Budde[16]

*[1]Siteman Cancer Center, Washington University School of Medicine, St. Louis, MO, USA; [2]BC Cancer Centre for Lymphoid Cancer and University of British Columbia, Vancouver, BC, Canada; [3]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [4]Lymphoma Program, Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA, USA; [5]Jewish General Hospital, McGill University, Montreal, QC, Canada; [6]Royal Adelaide Hospital, Adelaide, Australia; [7]Princess Margaret Cancer Centre, Toronto, ON, Canada; [8]Hospital Universitario La Paz, Madrid, Spain; [9]Universitat Heidelberg, Heidelberg, Germany; [10]St Vincent's Hospital and Royal North Shore Hospital, Sydney, Australia; [11]St Vincent's Hospital, University of Melbourne, Melbourne, Australia; [12]MD Anderson Cancer Center, Houston, TX, USA; [13]Genentech, Inc., South San Francisco, CA, USA; [14]Hoffmann-La Roche Ltd, Mississauga, Canada; [15]Roche Products Ltd, Welwyn Garden City, United Kingdom; [16]City of Hope National Medical Center, Duarte, CA, USA.*

*Presented at the 64th ASH Annual Meeting | December 10–13, 2022*

# Odronextamab in Patients with Relapsed/Refractory (R/R) Follicular Lymphoma (FL) Grade 1–3a: Results from a Prespecified Analysis of the Phase 2 Study ELM-2

**Tae Min Kim[1], Michal Taszner[2], Seok-Goo Cho[3], Silvana Novelli[4], Steven Le Gouill[5], Michelle Poon[6], Jose C. Villasboas[7], Rebecca Champion[8], Emmanuel Bachy[9], Stephanie Guidez[10], Aranzazu Alonso[11], Deepa Jagadeesh[12], Michele Merli[13], David Tucker[14], Jingxian Cai[15], Carolina Leite de Oliveira[15], Min Zhu[15], Aafia Chaudhry[15], Hesham Mohamed[15], Srikanth Ambati[15], Stefano Luminari[16], on behalf of ELM-2 Investigators**

*[1]Seoul National University Hospital, Seoul, South Korea; [2]Department of Haematology and Transplantology, Faculty of Medicine, Medical University of Gdańsk, Gdańsk, Poland; [3]The Catholic University of Korea, Seoul St. Mary's Hospital Hematology, Seoul, South Korea; [4]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [5]Service d'Hématologie Clinique, Centre Hospitalier Universitaire de Nantes, Nantes, France (currently at Institut Curie, Paris, France and Université UVSQ, France); [6]Hematology Oncology National University Hospital, Singapore; [7]Mayo Clinic Rochester, Rochester, MN, USA; [8]Norton Cancer Institute, Louisville, KY, USA; [9]Hospices Civils de Lyon and Université Claude Bernard Lyon 1, Lyon, France;[10]Centre Hospitalier Universitaire (CHU) de Poitiers, Poitiers, France; [11]Hospital Universitario Quiron Salud Madrid, Madrid, Spain; [12]Cleveland Clinic Main Campus, Cleveland, OH, USA; [13]Ospedale di Circolo e Fondazione Macchi, Varese, Italy; [14]Royal Cornwall Hospital, Cornwall, United Kingdom; [15]Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA; [16]Division of Hematology, Azienda Unità Sanitaria Locale-IRCCS, Reggio Emilia, Italy*

ClinicalTrials.gov ID: NCT03888105

This study was funded by Regeneron Pharmaceuticals, Inc.

Medical writing support was provided by Lewis Cawkwell of Arc, a division of Spirit Medical Communications Group Limited, and funded by Regeneron Pharmaceuticals, Inc.

*Presented at the 64th American Society of Hematology (ASH) Annual Meeting and Exposition, December 10–13, 2022, New Orleans, LA, USA.*



Kim TM et al. ASH 2022;Abstract 949.

# Agenda

**Module 1 — Hodgkin Lymphoma**

- First-line therapy

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- First-line therapy
- Bispecific antibodies
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- Selinexor

**Module 3 — Follicular Lymphoma**

- Bispecific antibodies

**Module 4 — Mantle Cell Lymphoma**

- BTK inhibitors
- CAR T-cell therapy

RTP RESEARCH TO PRACTICE

# Agenda

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RTP RESEARCH TO PRACTICE

# Update on Ibrutinib US Accelerated Approvals for Mantle Cell Lymphoma and Marginal Zone Lymphoma Indications

## Press Release: April 6, 2023

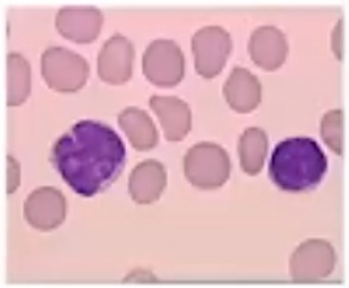
"The manufacturer announced today the intent to voluntarily withdraw, in the U.S., accelerated ibrutinib approvals for patients with the blood cancers mantle cell lymphoma (MCL) who have received at least one prior therapy and with marginal zone lymphoma (MZL) who require systemic therapy and have received at least one prior anti-CD20-based therapy.

Other approved indications for ibrutinib in the U.S. are not affected. This voluntary action is due to requirements related to the accelerated approval status granted by the U.S. FDA for MCL and MZL. These indications were approved via this pathway based on overall response rates in Phase 2 clinical studies. To confirm clinical benefit following accelerated approvals, additional studies are required by the FDA."

https://news.abbvie.com/news/press-releases/update-on-imbruvica-ibrutinib-us-accelerated-approvals-for-mantle-cell-lymphoma-and-marginal-zone-lymphoma-indications.htm

# TRIANGLE:

## AUTOLOGOUS TRANSPLANTATION AFTER A RITUXIMAB/IBRUTINIB/ARA-C CONTAINING INDUCTION IN GENERALIZED MANTLE CELL LYMPHOMA – A RANDOMIZED EUROPEAN MCL NETWORK TRIAL



M Dreyling, J Doorduijn, E Giné, M Jerkeman, J Walewski, M Hutchings, U Mey, J Riise, M Trneny, V Vergote, M Celli, O Shpilberg, M Gomes da Silva, S Leppa, L Jiang, C Pott, W Klapper, D Gözel, C Schmidt, M Unterhalt, M Ladetto*, E Hoster*

LMU University Hospital Munich, Germany; Erasmus MC Cancer Institute, University Medical Center Rotterdam, Netherlands; Hospital Clinic of Barcelona, Spain; Skane University Hospital and Lund University, Lund, Sweden; Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland; Rigshospitalet, Copenhagen University Hospital, Denmark; Kantonsspital Graubuenden, Chur, Switzerland; Oslo University Hospital, Oslo, Norway; Charles University and General University Hospital, Prague, Czech Republic; University Hospitals Leuven, Belgium; Ospedale degli Infermi di Rimini, Italy; Assuta Ramat Hahayal Medical Center, Tel Aviv, Israel; Instituto Português de Oncologia, Lisboa, Portugal; Helsinki University Hospital Comprehensive Cancer Center, Finland; IBE, LMU University Munich, Germany; University of Schleswig-Holstein, Kiel, Germany; Az Ospedaliera Santi Antonio e Biagio e Cesare Arrigo, Alessandria, Italy

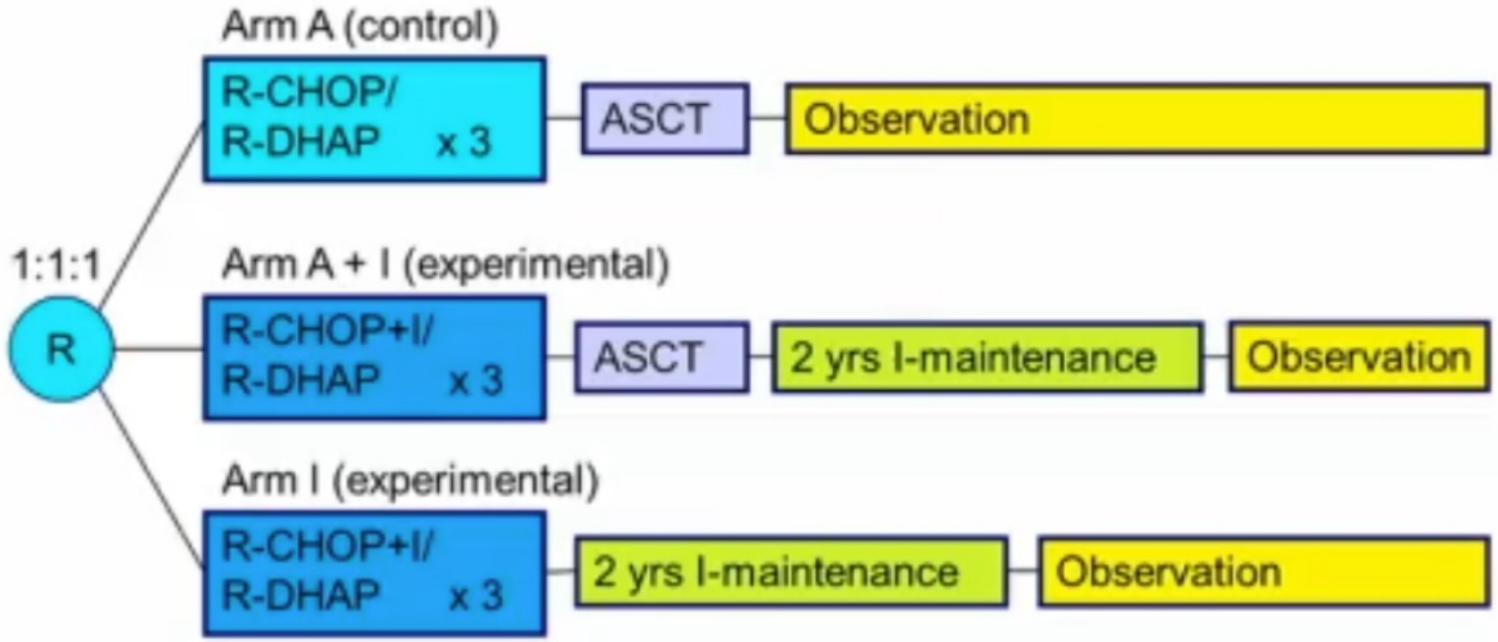
**ASH 2022;Abstract 1.**

# TRIANGLE Phase III Trial Design

- MCL patients
- previously untreated
- stage II-IV
- younger than 66 years
- suitable for HA and ASCT
- ECOG 0-2

- Primary outcome: FFS

- Secondary outcomes:
  - Response rates
  - PFS, RD
  - OS
  - Safety




- R maintenance was added following national guidelines in all 3 trial arms
- Rituximab maintenance (without or with Ibrutinib) was started in 168 (58 %)/165 (57 %)/158 (54 %) of A/A+I/I randomized patients.

Dreyling M et al. ASH 2022;Abstract 1.

ORIGINAL ARTICLE

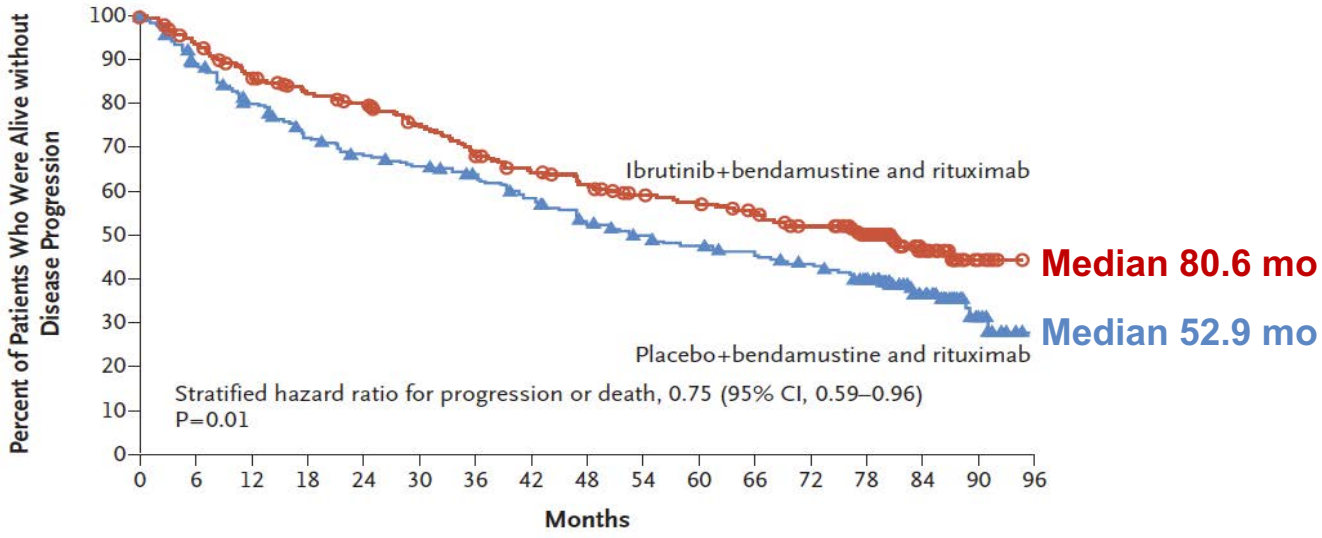
# Ibrutinib plus Bendamustine and Rituximab in Untreated Mantle-Cell Lymphoma

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):2482-2494.

# SHINE: Phase III Trial of Ibrutinib Plus Bendamustine and Rituximab in MCL

**Primary Endpoint: PFS**




**No. at Risk**

| | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ibrutinib+bendamustine and rituximab | 261 | 228 | 207 | 191 | 182 | 167 | 152 | 139 | 130 | 120 | 115 | 106 | 95 | 78 | 39 | 11 | 0 |
| Placebo+bendamustine and rituximab | 262 | 226 | 199 | 177 | 166 | 158 | 148 | 135 | 119 | 109 | 103 | 98 | 90 | 78 | 41 | 11 | 0 |

- The percentage 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 two 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):2482-2494.

RTP RESEARCH TO PRACTICE

# FDA Grants Accelerated Approval to Pirtobrutinib for Patients with Relapsed or Refractory Mantle Cell Lymphoma

## Press Release: January 27, 2023

On January 27, 2023, the Food and Drug Administration (FDA) granted accelerated approval to pirtobrutinib for relapsed or refractory mantle cell lymphoma (MCL) after at least 2 lines of systemic therapy, including a BTK inhibitor.

“Pirtobrutinib was approved under the FDA's Accelerated Approval pathway based on response rate from the open-label, single-arm, international, Phase 1/2 study, called the BRUIN trial. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.”

“In the BRUIN Phase 1/2 trial, covalent BTK inhibitor pre-treated patients with relapsed or refractory MCL achieved an overall response rate of 50%, with 13% of patients achieving a complete response [with pirtobrutinib].”

“Pirtobrutinib, a highly selective kinase inhibitor, utilizes a novel binding mechanism and is the first and only FDA approved non-covalent (reversible) BTK inhibitor. Pirtobrutinib can reestablish BTK inhibition in MCL patients previously treated with a covalent BTK inhibitor (ibrutinib, acalabrutinib, or zanubrutinib) and extend the benefit of targeting the BTK pathway.”

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-pirtobrutinib-relapsed-or-refractory-mantle-cell-lymphoma?utm_medium=email&utm_source=govdelivery; https://finance.yahoo.com/news/u-fda-approves-jaypirca-pirtobrutinib-190700019.html

RTP RESEARCH TO PRACTICE

4218

# Efficacy of Pirtobrutinib in Covalent BTK-Inhibitor Pre-Treated Relapsed / Refractory Mantle Cell Lymphoma: Additional Patients and Extended Follow-up from the Phase 1/2 BRUIN Study

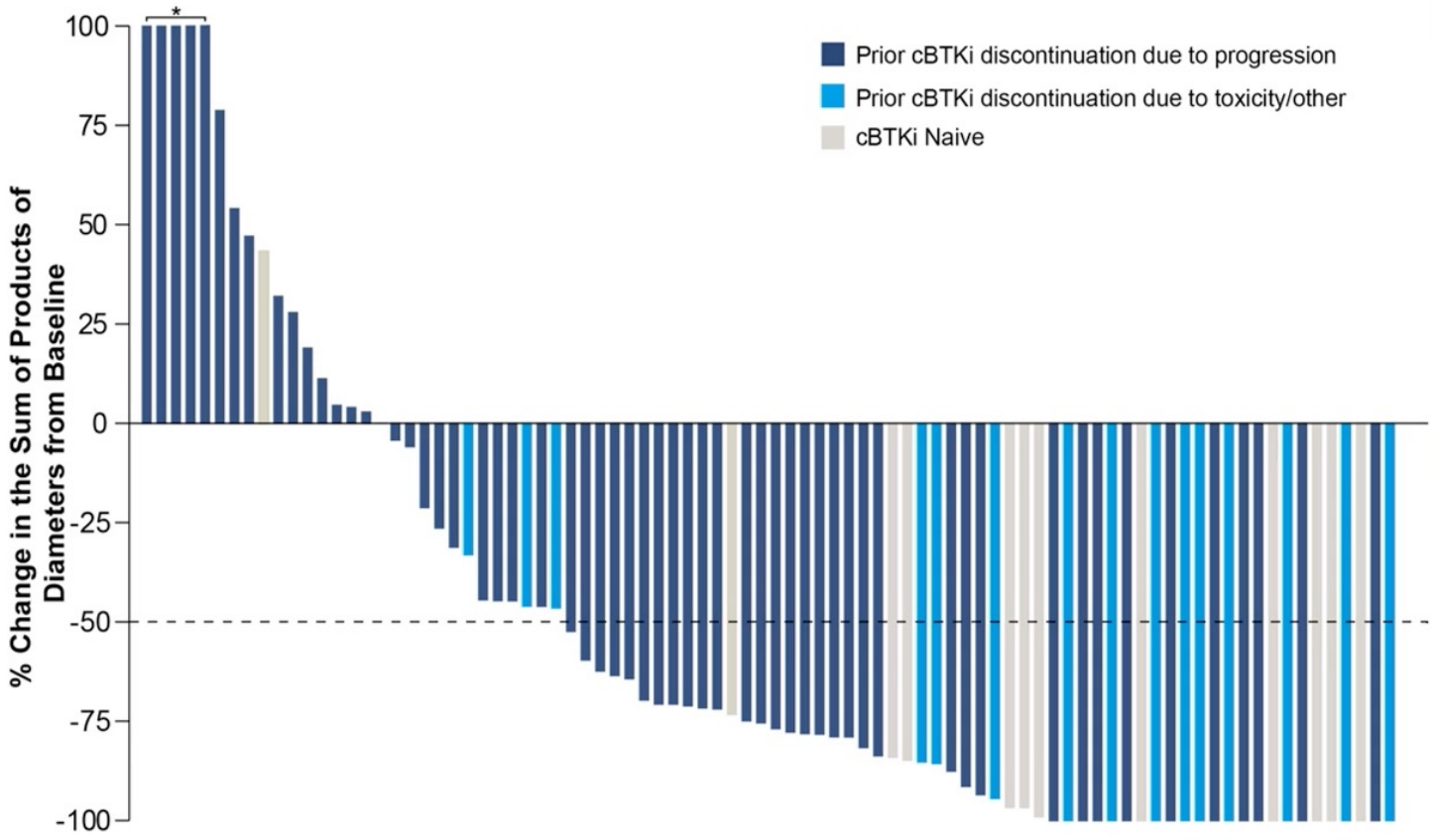

Michael L. Wang[1], Nirav N. Shah[2], Wojciech Jurczak[3], Pier Luigi Zinzani[4], Toby A. Eyre[5], Chan Y. Cheah[6], Chaitra S. Ujjani[7], Youngil Koh[8], Koji Izutsu[9], James N. Gerson[10], Ian Flinn[11], Benoit Tessoulin[12], Alvaro J. Alencar[13], Shuo Ma[14], Ewa Lech-Maranda[15], Joanna Rhodes[16], Krish Patel[17], Jennifer Woyach[18], Nicole Lamanna[19], Yucai Wang[20], Constantine Tam[21], Talha Munir[22], Hirokazu Nagai[23], Francisco Hernandez-Ilizaliturri[24], Anita Kumar[25], John F. Seymour[21], Andrew Zelenetz[25], Preteesh Jain[26], Binoj Nair[27], Donald E. Tsai[27], Minna Balbas[27], Richard A. Walgren[27], Paolo Abada[27], Chunxiao Wang[28], Junjie Zhao[27], Anthony R. Mato[25]

[1]MD Anderson Cancer Center, Houston, USA; [2]Medical College of Wisconsin, Milwaukee, USA ; [3]Maria Sklodowska-Curie National Research Institute of Oncology, Krakow, Poland; [4]Institute of Hematology "Seràgnoli" University of Bologna, Bologna Italy; [5]Oxford University Hospitals NHS Foundation Trust, Churchill Cancer Center, Oxford, UK; [6]Linear Clinical Research and Sir Charles Gairdner Hospital, Perth, Australia; [7]Fred Hutchinson Cancer Research Center, University of Washington, USA; [8]Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea; [9]National Cancer Center Hospital, Tokyo, Japan; [10]Lymphoma Program, Abramson Cancer Center, USA; [11]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, USA; [12]Haematology Department, University Hospital, Nantes, France; [13]Sylvester Comprehensive Cancer Center, Miami, USA; [14]Robert H. Lurie Comprehensive Cancer Center, Division of Hematology-Oncology, Northwestern University Feinberg School of Medicine, Chicago, USA; [15]Institute of Hematology and Transfusion Medicine, Warsaw, Poland; [16]Division of Hematology and Oncology, Department of Medicine, Hospital of the University of Pennsylvania, Philadelphia, USA; [17]Center for Blood Disorders and Cellular Therapy, Swedish Cancer Institute, Seattle, USA; [18]The Ohio State University Comprehensive Cancer Center, Columbus, USA; [19]Herbert Irving Comprehensive Cancer Center, Columbia University, USA; [20]Division of Hematology, Mayo Clinic, Rochester, USA; [21]Peter MacCallum Cancer Centre, Royal Melbourne Hospital and University of Melbourne, Melbourne, Victoria, Australia; [22]Department of Haematology, St. James's University Hospital, Leeds, UK; [23]Department of Hematology, National Hospital Organization Nagoya Medical Center, Aichi, Japan; [24]Department of Medicine, Roswell Park Comprehensive Cancer Center, Buffalo, USA; [25]Memorial Sloan Kettering Cancer Center, New York, USA; [26]Department of Lymphoma and Myeloma, University of Texas MD Anderson Cancer Center, Houston, USA; [27]Loxo@Lilly, Indianapolis, USA; [28]Eli Lilly and Company, Indianapolis, USA




**ASH 2022;Abstract 4218.**

# Pirtobrutinib Efficacy in Patients with MCL




| Prior cBTKi MCL Patients | n=90 |
|---|---|
| **Overall Response Rate[a], % (95% CI)** | **57.8% (46.9-68.1)** |
| **Best Response[b]** | |
| CR, n (%) | 18 (20.0) |
| PR, n (%) | 34 (37.8) |
| SD, n (%) | 14 (15.6) |
| PD, n (%) | 15 (16.7) |

| cBTKi Naïve MCL Patients | n=14 |
|---|---|
| **Overall Response Rate[a], % (95% CI)** | **85.7% (57.2-98.2)** |
| **Best Response[c]** | |
| CR, n (%) | 5 (35.7) |
| PR, n (%) | 7 (50.0) |
| SD, n (%) | 0 (0.0) |
| PD, n (%) | 1 (7.1) |

Data cutoff date of 31 January 2022. Data for 18 patients are not shown in the waterfall plot due to no measurable target lesions identified by CT at baseline, discontinuation prior to first response assessment, or lack of adequate imaging in follow-up. *Indicates patients with >100% increase in SPD. [a]ORR includes patients with a best response of CR and PR. [b]9 cBTKi pre-treated MCL patients were not evaluable. [c]1 cBTKi naïve patient was not evaluable. Response status per Lugano 2014 criteria based on IRC assessment.



cBTKi = covalent Bruton tyrosine kinase inhibitor; CR = complete response; PR = partial response; SD = stable disease; PD = progressive disease

Wang ML et al. ASH 2022;Abstract 4218.

Wang *et al. J Hematol Oncol* (2021) 14:179
https://doi.org/10.1186/s13045-021-01188-x

Journal of Hematology & Oncology

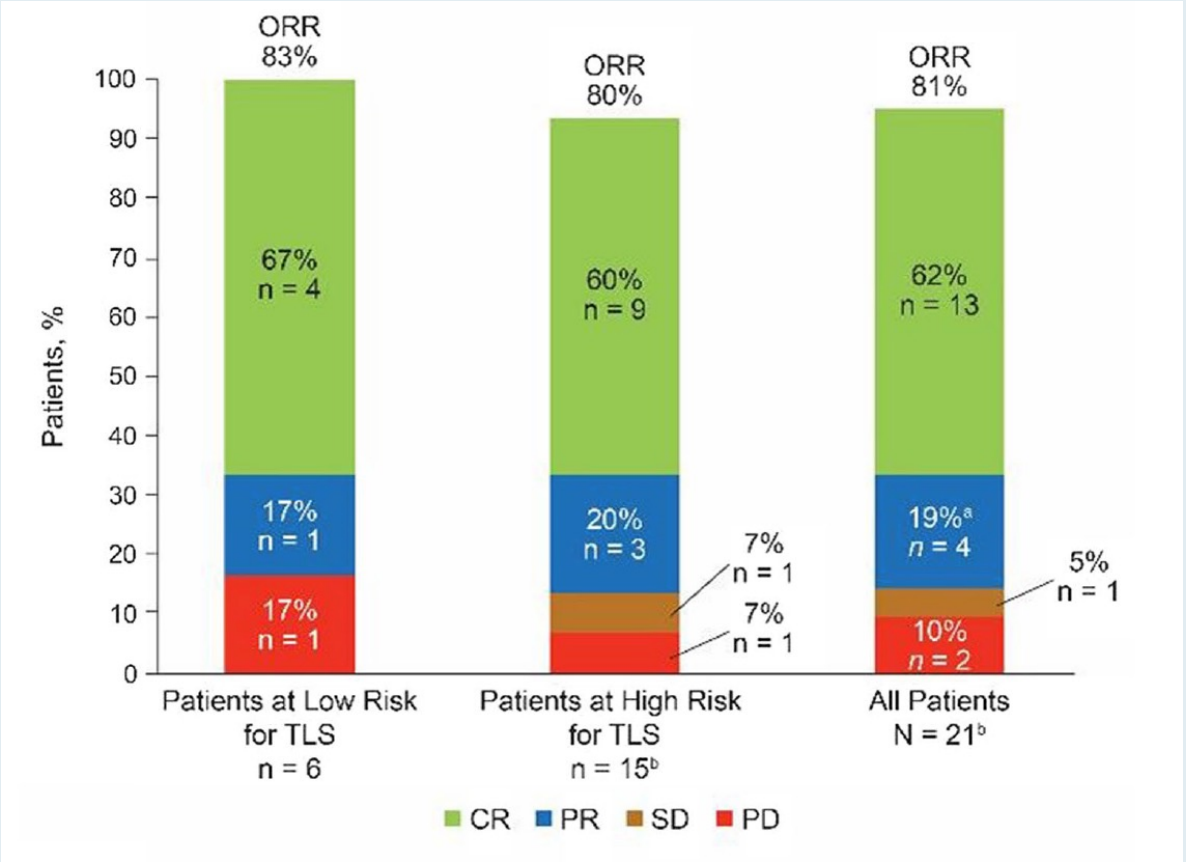
RAPID COMMUNICATION

Open Access

# Concurrent ibrutinib plus venetoclax in relapsed/refractory mantle cell lymphoma: the safety run-in of the phase 3 SYMPATICO study

Michael Wang[1*], Radhakrishnan Ramchandren[2], Robert Chen[3], Lionel Karlin[4], Geoffrey Chong[5], Wojciech Jurczak[6], Ka Lung Wu[7], Mark Bishton[8], Graham P. Collins[9], Paul Eliadis[10], Frédéric Peyrade[11], Yihua Lee[12], Karl Eckert[12], Jutta K. Neuenburg[12] and Constantine S. Tam[13]

# SYMPATICO: Efficacy Outcomes with Concurrent Ibrutinib and Venetoclax in Relapsed/Refractory MCL




- Median duration of response was 32.3 months
- Median progression-free survival was 35.0 months
- Median overall survival was also 35.0 months

Wang M et al. *J Hematol Oncol* 2021;14(1):179.

RTP RESEARCH TO PRACTICE

*Blood* 2021;137(7):877-87.

Plenary Paper

CLINICAL TRIALS AND OBSERVATIONS

# Ibrutinib, obinutuzumab, and venetoclax in relapsed and untreated patients with mantle cell lymphoma: a phase 1/2 trial

Steven Le Gouill,[1] Franck Morschhauser,[2] David Chiron,[3] Krimo Bouabdallah,[4] Guillaume Cartron,[5] Olivier Casasnovas,[6] Caroline Bodet-Milin,[7] Sylviane Ragot,[8] Céline Bossard,[9] Nathalie Nadal,[6] Charles Herbaux,[10] Benoit Tessoulin,[1] Emmanuelle Tchernonog,[11] Cédric Rossi,[6] Rory McCulloch,[12] Thomas Gastinne,[13] Mary B. Callanan,[8,*] and Simon Rule[12,*]

# Ibrutinib, Obinutuzumab and Venetoclax for Relapsed and Untreated MCL: Response at End of Cycle 6

| | Cohort A: relapsed patients, ibrutinib and obinutuzumab (n = 9) | Cohort B: relapsed patients, ibrutinib, obinutuzumab, and venetoclax (n = 24) | Cohort C: untreated patients, ibrutinib, obinutuzumab, and venetoclax (n = 15) |
|---|---|---|---|
| **Response at end of cycle 6 (Cheson 99)** | | | |
| CR/CRu | 7 (78) | 16 (67) | 12 (80) |
| PR | 0 (0) | 2 (8) | 2 (13) |
| SD | 1 (11) | — | — |
| PD | 1 (11) | 4 (17) | 1 (7) |
| Not done | — | 2 (8)† | — |
| **Response at end of cycle 6 (Lugano)** | | | |
| CR | 7 (78) | 16 (67) | 13 (86) |
| PR | 1 (11) | 1 (4) | 1 (7) |
| PD | 1 (11) | 5 (21) | 1 (7) |
| Not done | — | 2 (8)† | — |

Le Gouill S et al. *Blood* 2021;137(7):877-87.

# Agenda

**Module 1 — Hodgkin Lymphoma**

- First-line therapy

**Module 2 — Diffuse Large B-Cell Lymphoma**

- First-line therapy
- Bispecific antibodies
- CAR T-cell therapy
- Selinexor

**Module 3 — Follicular Lymphoma**

- Bispecific antibodies

**Module 4 — Mantle Cell Lymphoma**

- BTK inhibitors
- CAR T-cell therapy

# Real-world outcomes of brexucabtagene autoleucel (brexu-cel) for relapsed or refractory (R/R) mantle cell lymphoma (MCL): A CIBMTR subgroup analysis by prior treatment.

Kambhampati S et al.

ASCO 2023;Abstract 7507.

Monday, June 5; 11:57 AM CDT

# Meet The Professors Live: Clinical Investigators Provide Perspectives on Actual Cases of Patients with Chronic Lymphocytic Leukemia

*A CME Symposium Held in Conjunction with the 2023 ASCO® Annual Meeting*


## Faculty

**John N Allan, MD**

**Susan O'Brien, MD**

## Moderator

**Neil Love, MD**


RTP RESEARCH TO PRACTICE

# Agenda

**Module 1 — First-Line Treatment of Chronic Lymphocytic Leukemia**

- BTK inhibitors
- Venetoclax combinations

**Module 2 — Relapsed/Refractory Disease**

- BTK inhibitors
- Venetoclax combinations

**Module 3 — Richter's Transformation**

# Agenda

## Module 1 — First-Line Treatment of Chronic Lymphocytic Leukemia

- BTK inhibitors
- Venetoclax combinations

## Module 2 — Relapsed/Refractory Disease

- BTK inhibitors
- Venetoclax combinations

## Module 3 — Richter's Transformation

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# Frontline Phase III Randomized Trials in CLL

| BTKi | BCL2i | Novel-novel |
|---|---|---|
| **RESONATE-2** (>65 or comorbidities)<br>Ibrutinib *vs.* **Chlorambucil** | **CLL14** (CIRS >6; CrCl <70 mL/min)<br>Venetoclax + O *vs.* **Chlorambucil + O** | **GLOW** (>65 or comorbidities)<br>Ibrutinib + Venetoclax *vs.* **Chlorambucil + O** |
| **iLLUMINATE** (PCYC-1130) (>65 or comorbidities)<br>Ibrutinib + O *vs.* **Chlorambucil + O** | | **CLL13** (>65yo or ≤65yo with comorbidities)<br>I+V+O *vs.* Ven+O *vs.* Ven+R *vs.* **FCR/BR** |
| **ECOG E1912** [<70; non-del(17p)]<br>Ibrutinib + R *vs.* **FCR** | | |
| **Alliance** A041202 (>65)<br>Ibrutinib *vs.* Ibrutinib + R *vs.* **BR** | | |
| **ELEVATE-TN** (>65 or comorbidities)<br>Acala *vs.* Acala + O *vs.* **Chlorambucil + O** | | |
| **SEQUOIA** [≥65 OR comorbidities; non-del(17p)]<br>Zanubrutinib *vs.* **BR** | | |
| **FLAIR** [≤75; non-del(17p)]<br>Ibrutinib + R *vs.* **FCR** | | |

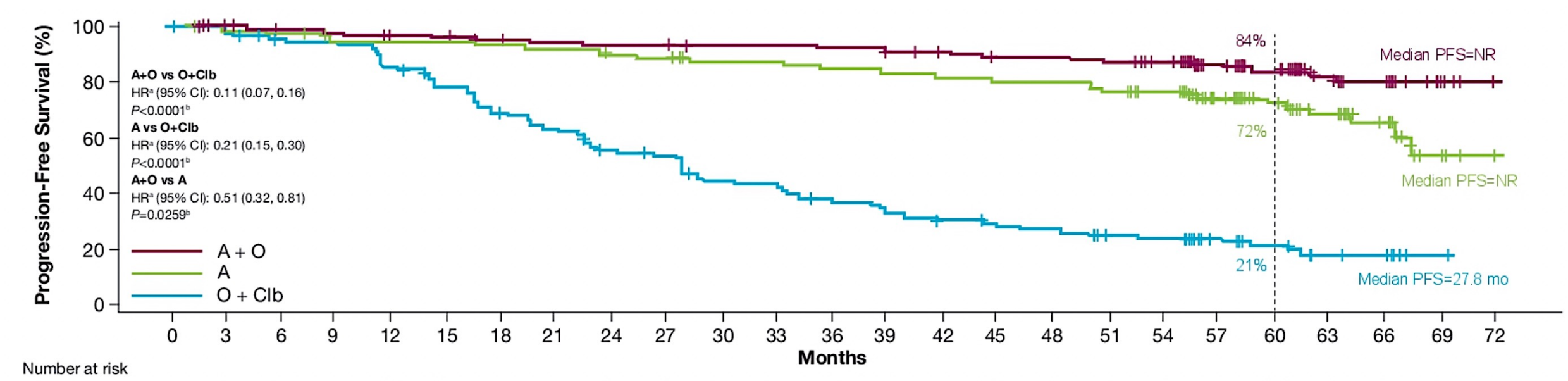
Courtesy of Alexy Danilov, MD, PhD

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

Sharman JP et al.

ASCO 2022;Abstract 7539.

# ELEVATE-TN: Investigator-Assessed PFS




Sharman JP et al. ASCO 2022;Abstract 7539.

# FDA Approves Zanubrutinib for Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma

## Press Release: January 19, 2023

“On January 19, 2023, the Food and Drug Administration approved zanubrutinib for chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).

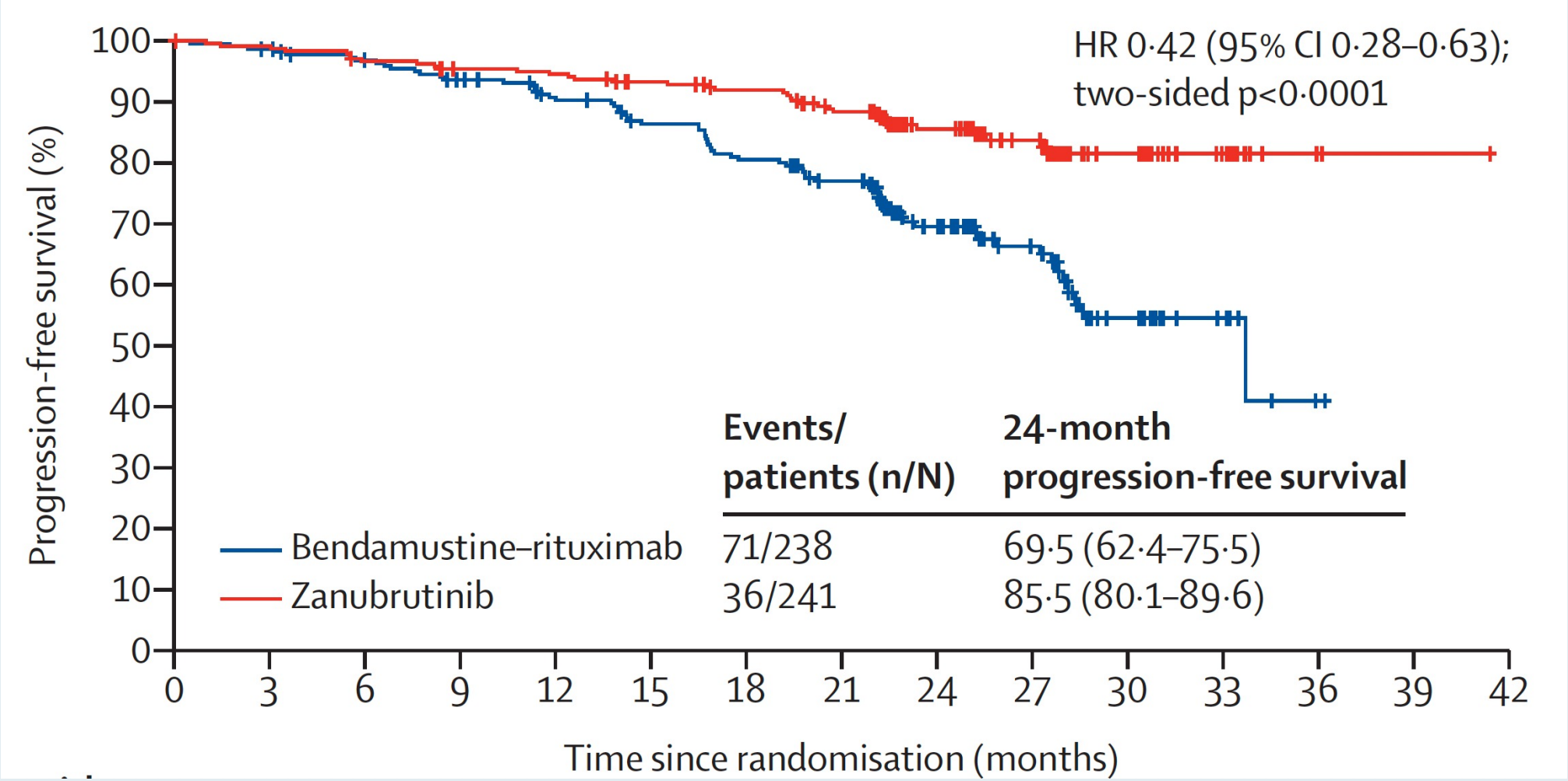
Efficacy in patients with treatment-naïve CLL/SLL was evaluated in SEQUOIA (NCT03336333). In the randomized cohort including patients without 17p deletion, a total of 479 patients were randomized 1:1 to receive either zanubrutinib until disease progression or unacceptable toxicity or bendamustine plus rituximab (BR) for 6 cycles.

Efficacy in patients with relapsed or refractory CLL/SLL was evaluated in ALPINE (NCT03734016). A total of 652 patients were randomized 1:1 to receive either zanubrutinib or ibrutinib.

The recommended zanubrutinib dosage is 160 mg taken orally twice daily or 320 mg taken orally once daily until disease progression or unacceptable toxicity.”

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-zanubrutinib-chronic-lymphocytic-leukemia-or-small-lymphocytic-lymphoma

# SEQUOIA: Progression-Free Survival by IRC (ITT)




Tam CS et al. *Lancet Oncol* 2022 Aug;23(8):1031-1043.

# Frequency of Adverse Events in Landmark Studies of Currently Approved BTKis in Treatment-Naïve CLL

| Adverse event | Ibrutinib | | Acalabrutinib | | Zanubrutinib* | |
|---|---|---|---|---|---|---|
| | RESONATE2 TN (n = 135) | | ELEVATE-TN TN (n = 179) | | SEQUOIA TN (n = 240) | |
| | All grades | Grade ≥ 3 | All grades | Grade ≥ 3 | All grades | Grade ≥ 3 |
| Atrial fibrillation | 10% | 4% | 3.6% | NR | 3.3% | 0.4% |
| Bleeding | 7% | 6% | 39% | 2% | 41% | 3% |
| Hypertension | 14% | 4% | 5% | 2% | 6% | 6% |
| Arthralgia | 20% | 2% | 16% | 0.6% | 13% | 1% |
| Infection | NR | 23% | 65% | 14% | 62.2% | 16.3% |
| Diarrhea | 42% | 4% | 35% | 0.6% | 13% | 1% |

* In patients without del(1)(p13.1)

Lipsky A, Lamanna N. *Hematology Am Soc Hematol Educ Program* 2020 Dec 4;2020(1):336-45. Tam CS et al. *Lancet Oncol* 2022;23:1031-43.

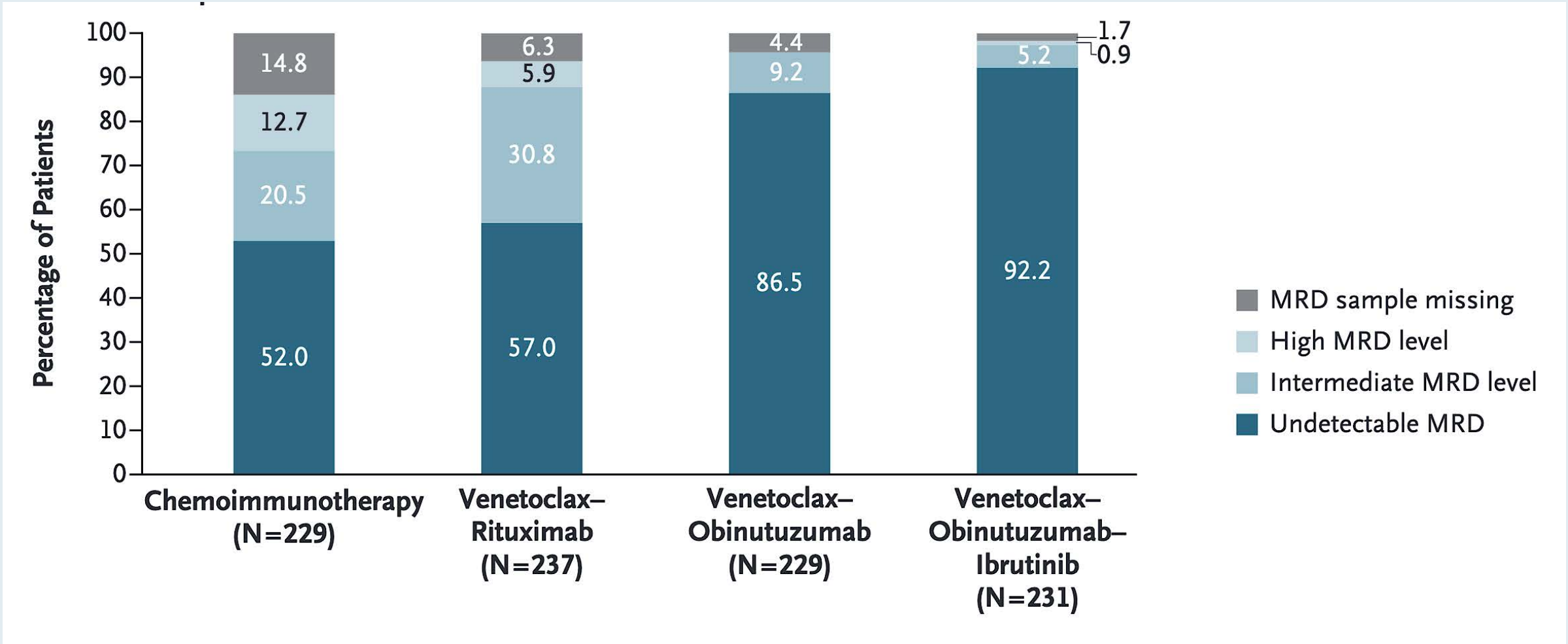
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 11, 2023 VOL. 388 NO. 19 1739-54.

# First-Line Venetoclax Combinations in Chronic Lymphocytic Leukemia

B. Eichhorst, C.U. Niemann, A.P. Kater, M. Fürstenau, J. von Tresckow, C. Zhang, S. Robrecht, M. Gregor, G. Juliusson, P. Thornton, P.B. Staber, T. Tadmor, V. Lindström, C. da Cunha-Bang, C. Schneider, C.B. Poulsen, T. Illmer, B. Schöttker, T. Nösslinger, A. Janssens, I. Christiansen, M. Baumann, H. Frederiksen, M. van der Klift, U. Jäger, M.B.L. Leys, M. Hoogendoorn, K. Lotfi, H. Hebart, T. Gaska, H. Koene, L. Enggaard, J. Goede, J.C. Regelink, A. Widmer, F. Simon, N. De Silva, A.-M. Fink, J. Bahlo, K. Fischer, C.-M. Wendtner, K.A. Kreuzer, M. Ritgen, M. Brüggemann, E. Tausch, M.-D. Levin, M. van Oers, C. Geisler, S. Stilgenbauer, and M. Hallek, for the GCLLSG, the HOVON and Nordic CLL Study Groups, the SAKK, the Israeli CLL Association, and Cancer Trials Ireland*

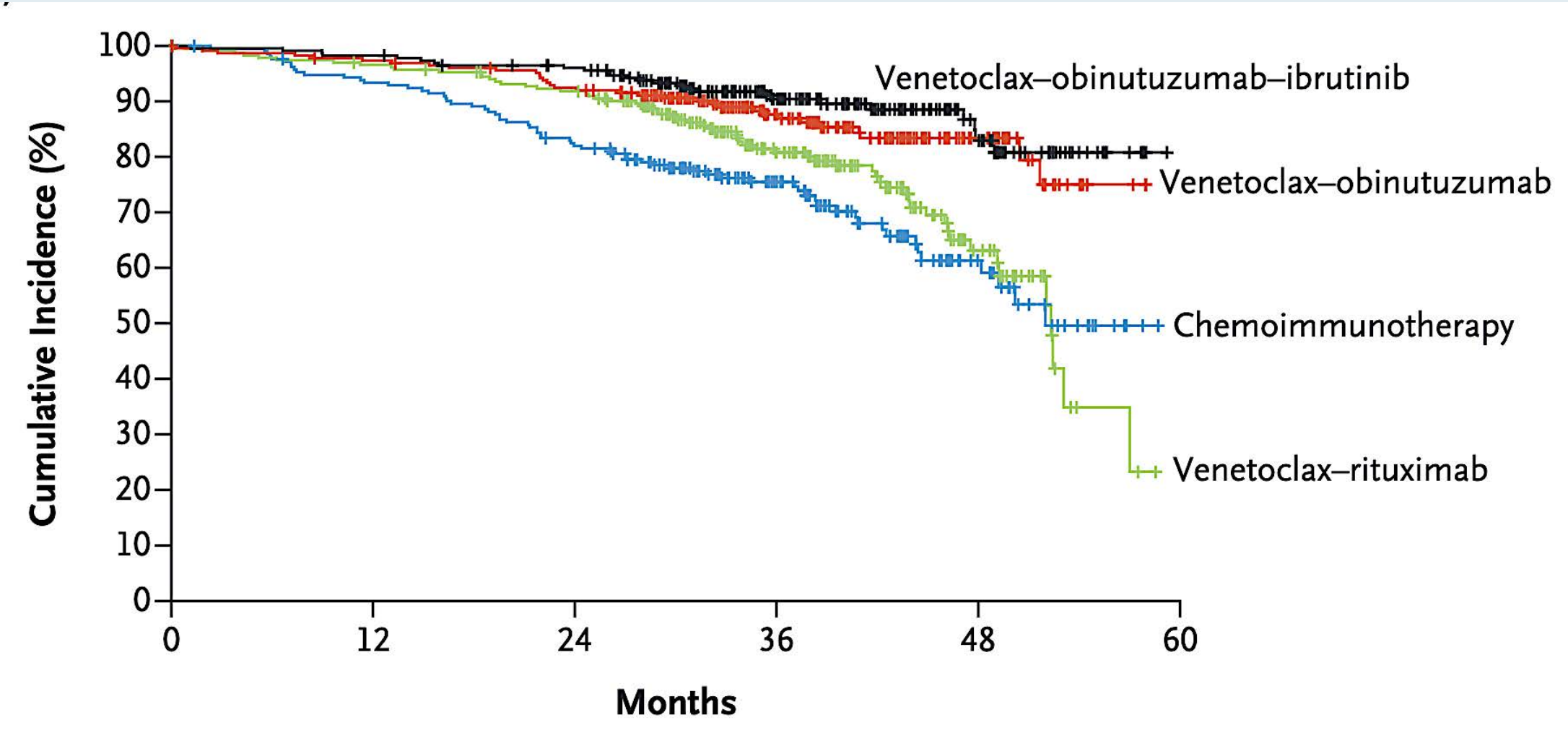
# CLL13/GAIA: MRD in Peripheral Blood at Month 15




MRD = minimal residual disease

Eichhorst Bet al. *N Engl J Med* 2023;388(19):1739-54.

# CLL13/GAIA: Progression-Free Survival in All Patients




Eichhorst Bet al. *N Engl J Med* 2023;388(19):1739-54.

# Agenda

**Module 1 — First-Line Treatment of Chronic Lymphocytic Leukemia**

- BTK inhibitors
- Venetoclax combinations

**Module 2 — Relapsed/Refractory Disease**

- BTK inhibitors
- Venetoclax combinations

**Module 3 — Richter's Transformation**

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original reports

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

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

*J Clin Oncol* 2021 Nov 1;39(31):3441-52.

original reports

# Zanubrutinib Versus Ibrutinib in Relapsed/ Refractory Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma: Interim Analysis of a Randomized Phase III Trial

Peter Hillmen, MBChB, PhD[1]; Barbara Eichhorst, MD[2]; Jennifer R. Brown, MD, PhD[3]; Nicole Lamanna, MD[4]; Susan M. O'Brien, MD[5]; Constantine S. Tam, MBBS, MD[6-9]; Lugui Qiu, MD, PhD[10]; Maciej Kazmierczak, MD, PhD[11]; Keshu Zhou, MD, PhD[12]; Martin Šimkovič, MD, PhD[13,14]; Jiří Mayer, MD[15]; Amanda Gillespie-Twardy, MD[16]; Mazyar Shadman, MD, MPH[17,18]; Alessandra Ferrajoli, MD[19]; Peter S. Ganly, BMBCh, PhD[20]; Robert Weinkove, MBBS, PhD[21,22]; Sebastian Grosicki, MD, PhD[23]; Andrzej Mital, MD, PhD[24]; Tadeusz Robak, MD, PhD[25]; Anders Österborg, MD, PhD[26,27]; Habte A. Yimer, MD[28]; Tommi Salmi, MD[29]; Meng Ji, MD[30]; Jessica Yecies, PhD[29]; Adam Idoine, PhD[29]; Kenneth Wu, PhD[29]; Jane Huang, MD[29]; and Wojciech Jurczak, MD, PhD[31]

*J Clin Oncol* 2023;[Online ahead of print].

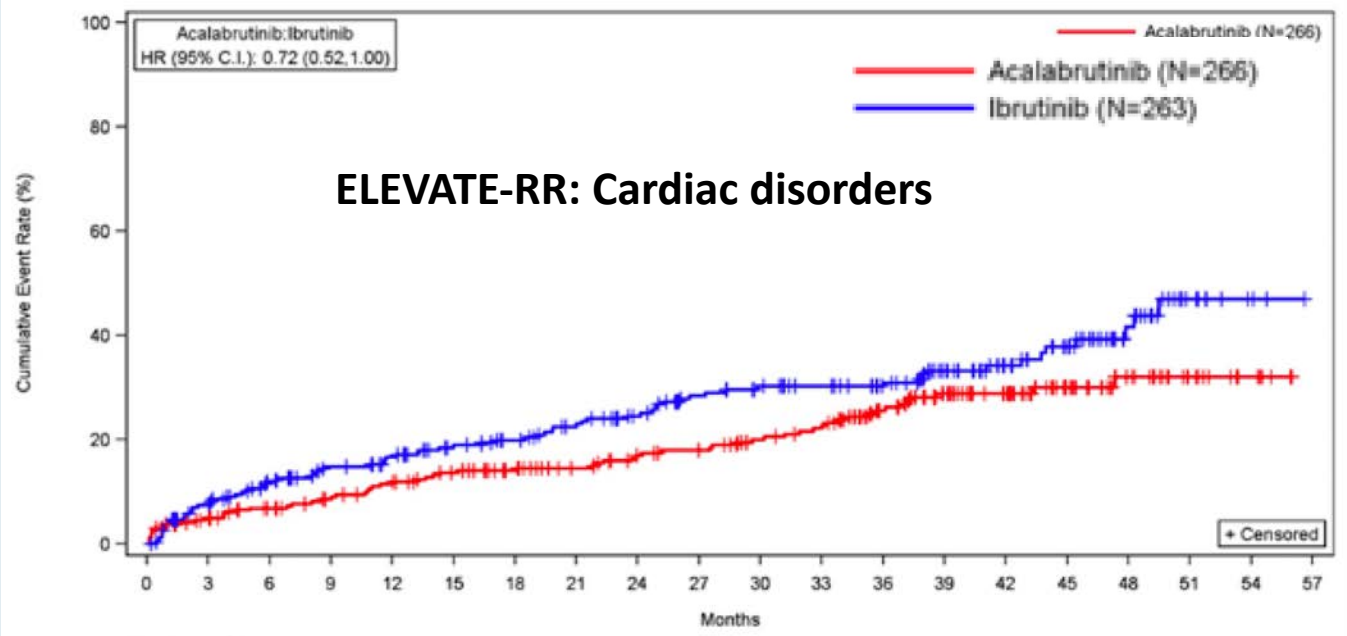
# ELEVATE-RR and ALPINE: Cardiac, Hypertension and Bleeding Events

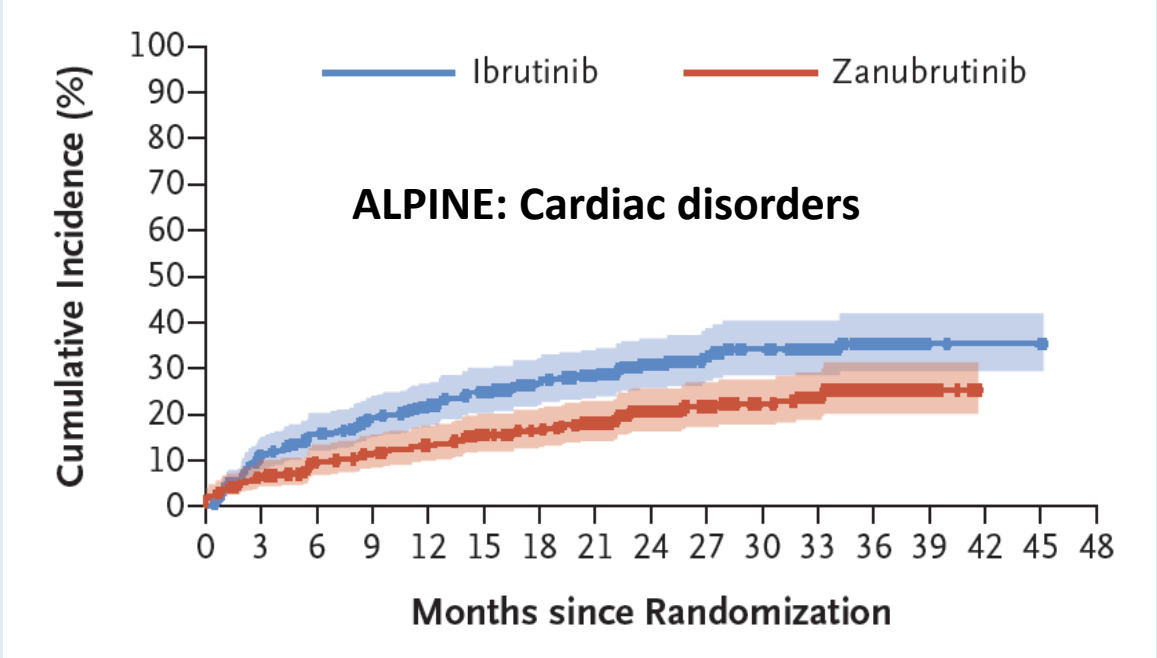
| | ELEVATE-RR[1] | | | | ALPINE[2] | | | |
|---|---|---|---|---|---|---|---|---|
| | Acalabrutinib (n = 266) | | Ibrutinib (n = 263) | | Zanubrutinib (n = 324) | | Ibrutinib (n = 324) | |
| | Any grade | Grade ≥3 | Any grade | Grade ≥3 | Any grade | Grade ≥3 | Any grade | Grade ≥3 |
| Any cardiac event | 24.1% | 8.6% | 30.0% | 9.5% | 21.3% | NR | 29.6% | NR |
| Atrial fibrillation/flutter | 9.4% | 4.9% | 16.4% | 3.8% | 5.2% | 2.5% | 13.3% | 4.0$ |
| Hypertension | 8.6% | 4.1% | 23.2% | 9.1% | 23.5% | 15.1% | 22.8% | 13.6% |
| Hemorrhage | 38.0% | 3.8% | 51.3% | 4.6% | 42.3% | 3.4% | 41.4% | 3.7% |

NR = not reported

[1] Byrd JC et al. *J Clin Oncol* 2021;39:3441-2452; [2] Brown JR et al. *N Engl J Med* 2022 Dec 13;[Online ahead of print].

# ELEVATE-RR and ALPINE: Any-Grade Cardiac Event



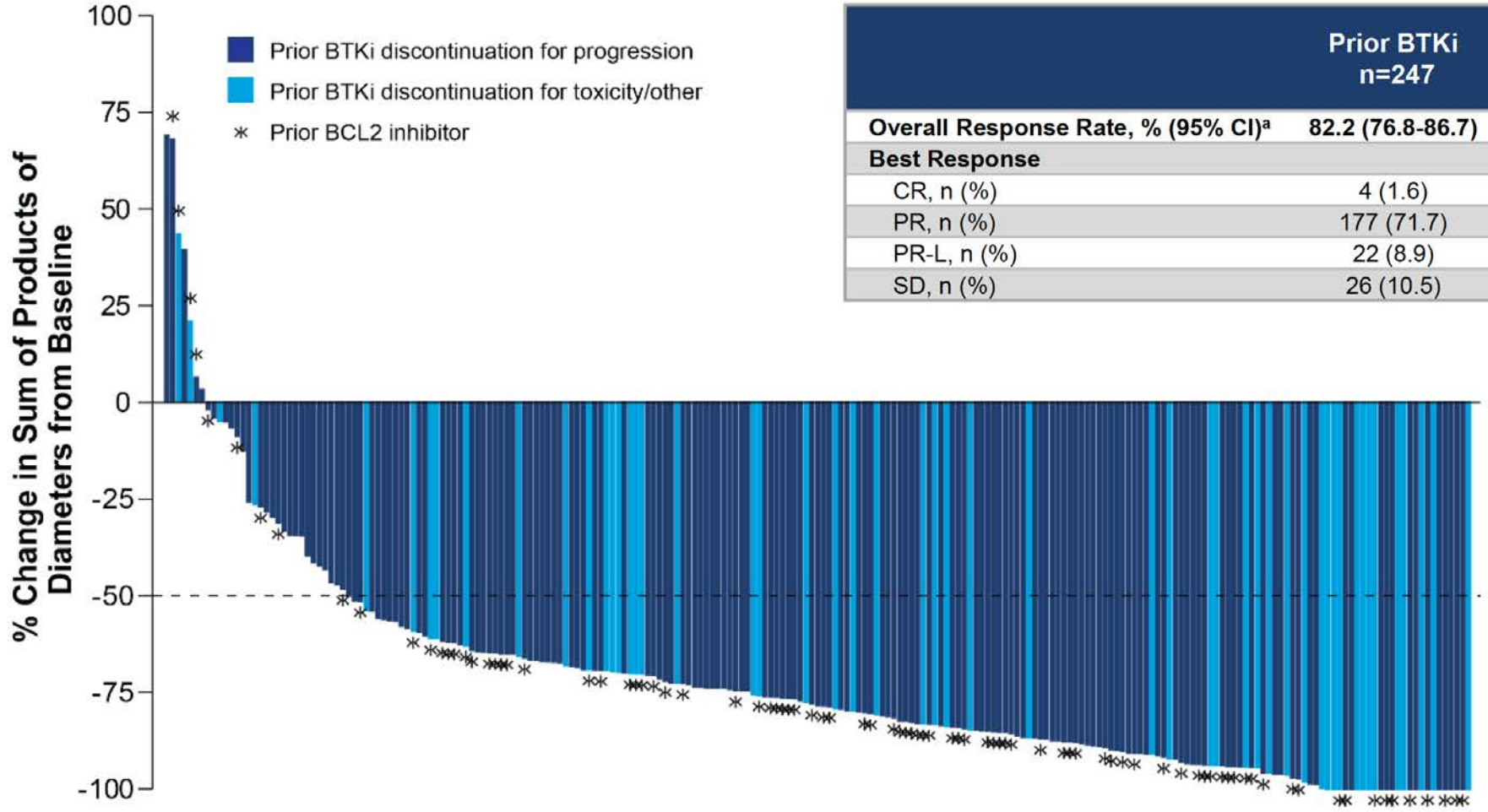

[1] Byrd JC et al. *J Clin Oncol* 2021;39:3441-2452; [2] Brown JR et al. *N Engl J Med* 2022 Dec 13;[Online ahead of print].

ASH 2022;Abstract 961.

# Efficacy of Pirtobrutinib in Covalent BTK-Inhibitor Pre-Treated Relapsed / Refractory CLL/SLL: Additional Patients and Extended Follow-up from the Phase 1/2 BRUIN Study

Anthony R. Mato[1], Jennifer A. Woyach[2], Jennifer R. Brown[3], Paolo Ghia[4], Krish Patel [5], Toby A. Eyre[6], Talha Munir[7], Ewa Lech-Maranda[8], Nicole Lamanna[9], Constantine S. Tam[10], Nirav N. Shah[11], Catherine C. Coombs[12], Chaitra S. Ujjani[13], Manish R. Patel[14], Bita Fakhri[15], Chan Y. Cheah[16], Alvaro J. Alencar[17], Jonathon B. Cohen[18], James N. Gerson[19], Ian W. Flinn[20], Shuo Ma[21], Deepa Jagadeesh[22], Joanna M. Rhodes[23], Francisco Hernandez-Ilizaliturri[24], John F. Seymour[10], Pier Luigi Zinzani[25], Minna Balbas[26], Binoj Nair[26], Paolo Abada[26], Chunxiao Wang[27], Amy S. Ruppert[27], Denise Wang[26], Donald E. Tsai[26], William G. Wierda[28], Wojciech Jurczak[29]

# BRUIN: Pirtobrutinib Efficacy in CLL/SLL Patients Who Received Prior Bruton Tyrosine Kinase Inhibitor (BTKi) Treatment

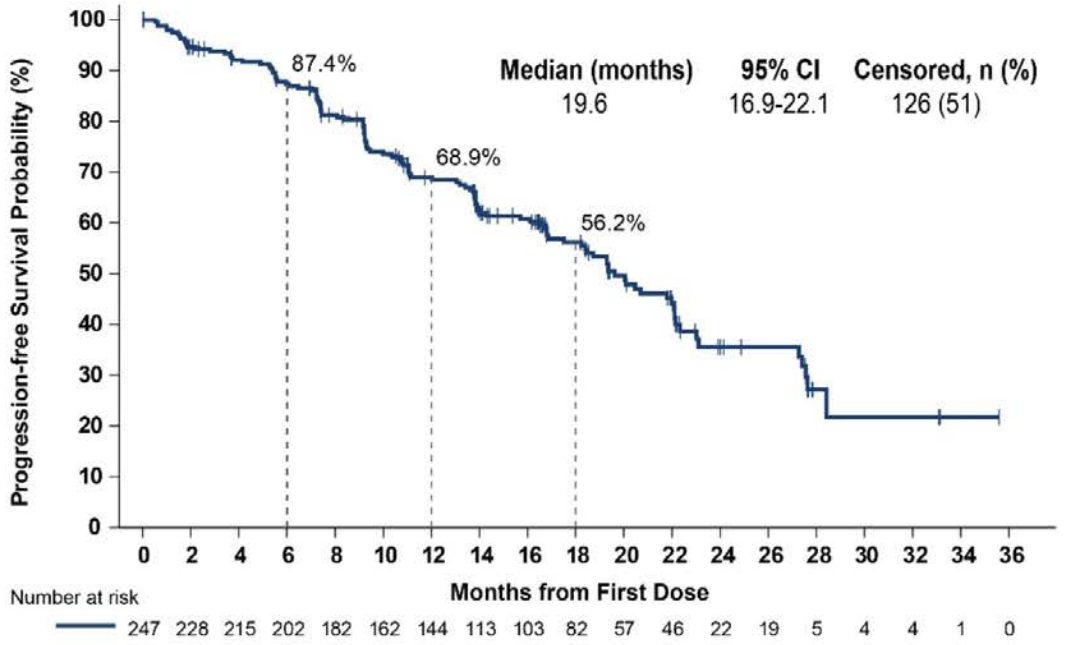



| | Prior BTKi n=247 | Prior BTKi+BCL2i n=100 |
|---|---|---|
| **Overall Response Rate, % (95% CI)[a]** | **82.2 (76.8-86.7)** | **79.0 (69.7-86.5)** |
| **Best Response** | | |
| CR, n (%) | 4 (1.6) | 0 (0.0) |
| PR, n (%) | 177 (71.7) | 70 (70.0) |
| PR-L, n (%) | 22 (8.9) | 9 (9.0) |
| SD, n (%) | 26 (10.5) | 11 (11.0) |

Mato AR et al. ASH 2022;Abstract 961.

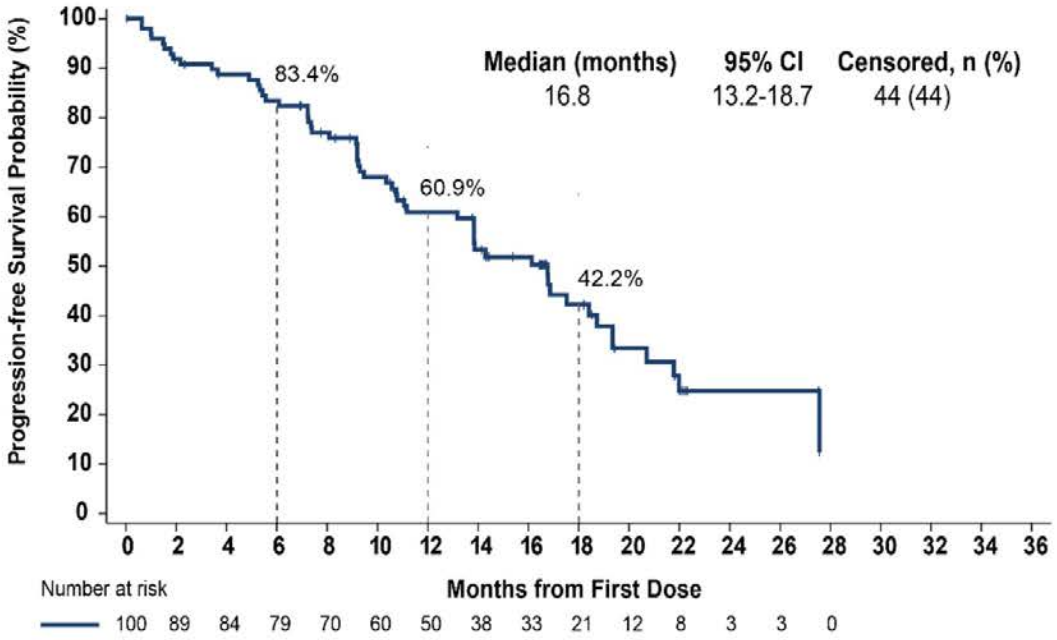
# BRUIN: Progression-Free Survival in CLL/SLL Patients Who Received Prior BTKi Treatment

**All prior BTKi patients**
**Median prior lines = 3**




- Median follow-up of 19.4 months for patients who received prior BTKi

**Prior BTKi and BCL2i patients**
**Median prior lines = 5**




- Median follow-up of 18.2 months for patients who received prior BTKi and BCL2i

Mato AR et al. ASH 2022;Abstract 961.

RTP RESEARCH TO PRACTICE

*Blood* 2022 Aug 25;140(8):839-850

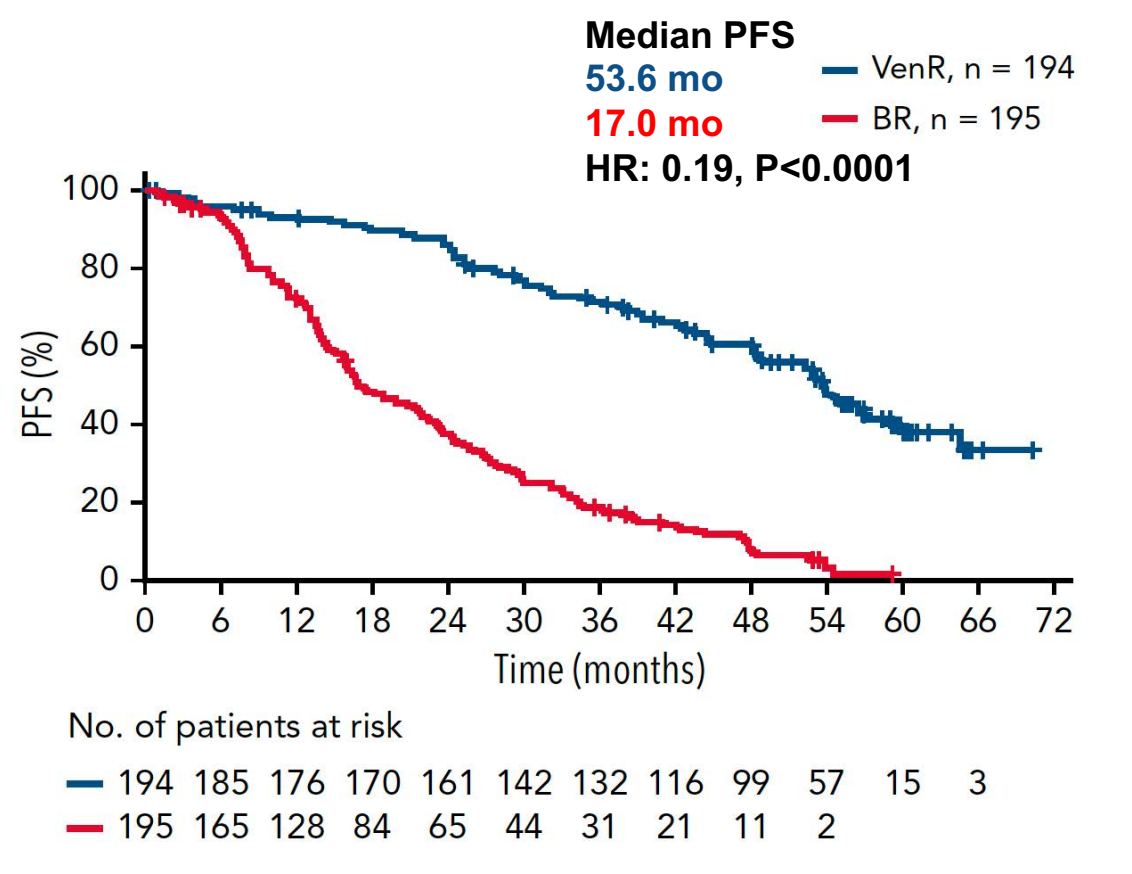
Regular Article

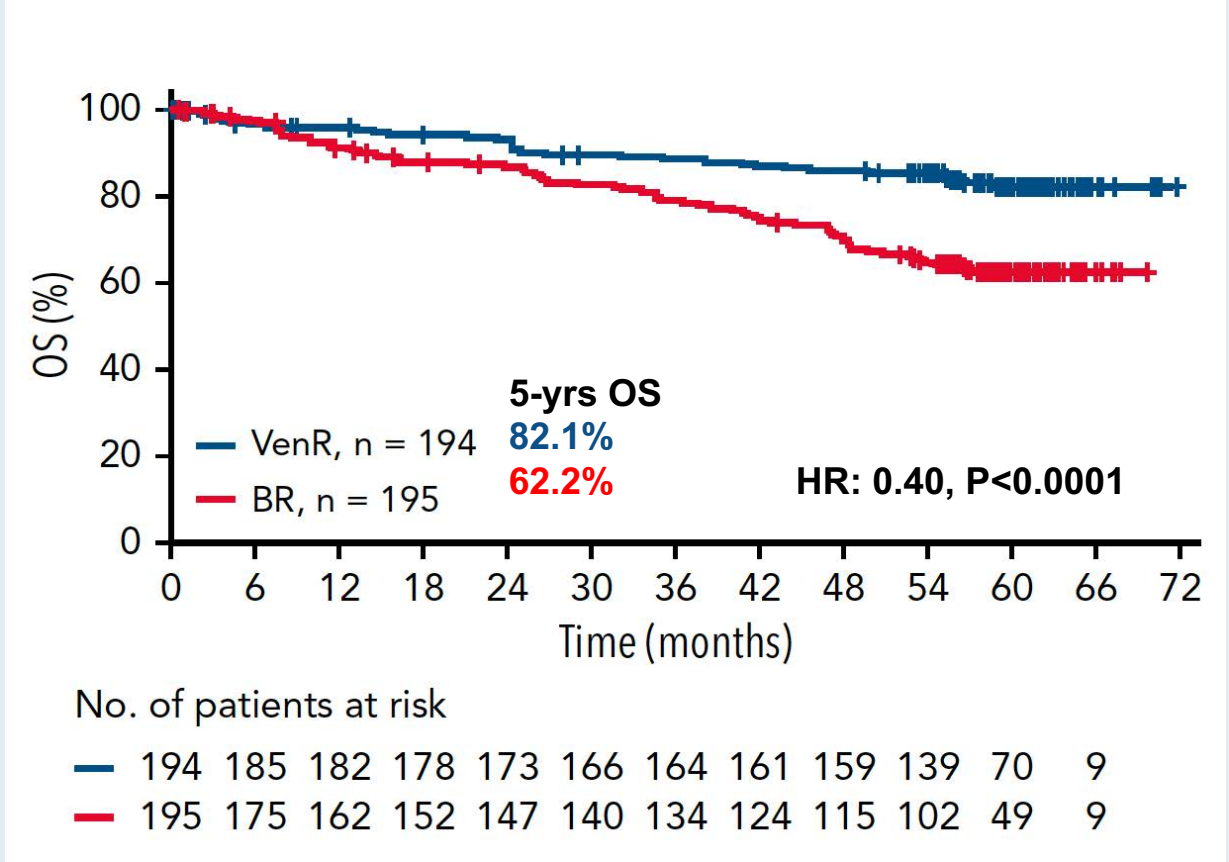
CLINICAL TRIALS AND OBSERVATIONS

# Enduring undetectable MRD and updated outcomes in relapsed/refractory CLL after fixed-duration venetoclax-rituximab

John F. Seymour,[1] Thomas J. Kipps,[2] Barbara F. Eichhorst,[3] James D'Rozario,[4] Carolyn J. Owen,[5] Sarit Assouline,[6] Nicole Lamanna,[7] Tadeusz Robak,[8] Javier de la Serna,[9] Ulrich Jaeger,[10] Guillaume Cartron,[11] Marco Montillo,[12] Clemens Mellink,[13] Brenda Chyla,[14] Anesh Panchal,[15] Tong Lu,[16] Jenny Q. Wu,[16] Yanwen Jiang,[16] Marcus Lefebure,[15] Michelle Boyer,[15] and Arnon P. Kater[17]

# MURANO: Median PFS and OS with 5 Years of Follow-Up




Seymour JF et al. Blood 2022 Aug 25;140(8):839-850.

RTP RESEARCH TO PRACTICE

# Agenda

**Module 1 — First-Line Treatment of Chronic Lymphocytic Leukemia**

- BTK inhibitors
- Venetoclax combinations

**Module 2 — Relapsed/Refractory Disease**

- BTK inhibitors
- Venetoclax combinations

**Module 3 — Richter's Transformation**

RTP RESEARCH TO PRACTICE

# Results of MOLTO, A Multicenter, Open Label, Phase II Clinical Trial Evaluating Venetoclax, Atezolizumab and Obinutuzumab Combination in Richter Syndrome

Frustaci AM et al.

ASCO 2023;Abstract 7502.

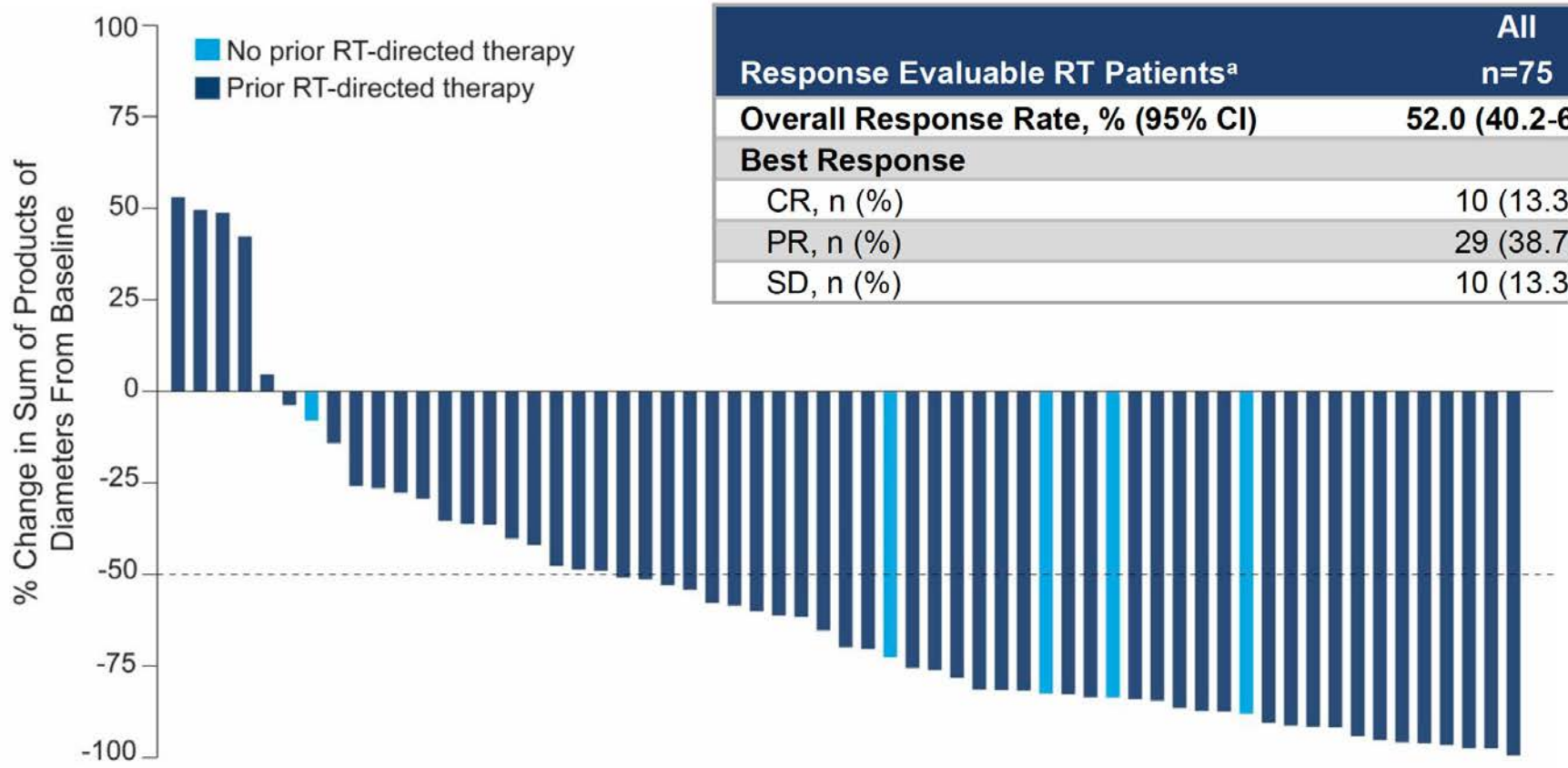
Monday, June 5; 10:09 AM CDT

ASH 2022; Abstract 347

# Efficacy of Pirtobrutinib, a Highly Selective, Non-Covalent (Reversible) BTK Inhibitor in Richter Transformation: Results From the Phase 1/2 BRUIN Study

William G. Wierda[1], David Lewis[2], Paolo Ghia[3], Nirav N. Shah[4], Catherine C. Coombs[5], Chan Y. Cheah[6], Jennifer Woyach[7], Nicole Lamanna[8], Joanna M. Rhodes[9], Marc S. Hoffmann[10], Shuo Ma[11], Toby A. Eyre[12], Talha Munir[13], Manish R. Patel[14], Alvaro J. Alencar[15], Constantine S. Tam[16], Wojciech Jurczak[17], Ewa Lech-Maranda[18], John F. Seymour[16], Lindsey E. Roeker[19], Philip A. Thompson[1], Paolo B. Abada[20], Chunxiao Wang[21], Amy S. Ruppert[21], Binoj Nair[20], Hui Liu[20], Donald E. Tsai[20], Anthony R. Mato[19]

# BRUIN: Pirtobrutinib Efficacy in RT Patients




| Response Evaluable RT Patients[a] | All n=75 | Prior RT Therapy n=68 |
|---|---|---|
| **Overall Response Rate, % (95% CI)** | **52.0 (40.2-63.7)** | **50.0 (37.6-62.4)** |
| **Best Response** | | |
| CR, n (%) | 10 (13.3) | 9 (13.2) |
| PR, n (%) | 29 (38.7) | 25 (36.8) |
| SD, n (%) | 10 (13.3) | 10 (14.7) |

- Among 75 response-evaluable patients, the median time-to-response was 1.8 months (range, 0.9-9.2), median time on study was 6.7 months (range, 0.7-29.1), and median time on treatment was 3.4 months (range, 0.2-26.7)

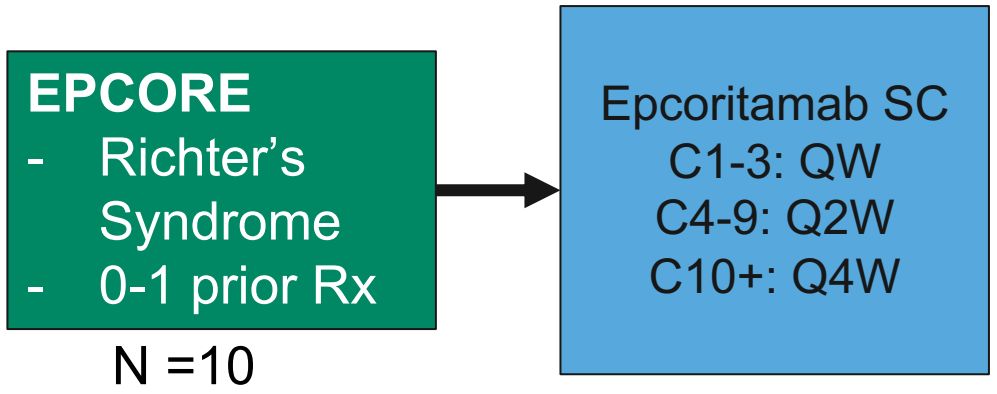
Wierda WG et al. ASH 2022; Abstract 347.

# BRUIN in RT: Conclusions

- This trial represents one of the largest prospective RT populations ever studied, comprised predominantly of heavily pretreated RT patients with an extremely poor expected overall survival
- Pirtobrutinib demonstrated promising efficacy, including among patients who received prior RT chemoimmunotherapy and cBTKi
  - Notably, pirtobrutinib demonstrated an ORR of 52% overall and 50% among patients who received prior RT therapy
  - Median OS was 13.1 months, regardless of prior RT therapy
  - DoR was 5.6 months, regardless of prior RT therapy
  - 6 responding patients discontinued in ongoing response to pursue curative intent transplant therapy
- Pirtobrutinib continues to be well-tolerated with low rates of Grade ≥3 AEs and discontinuation due to drug-related toxicity
  - Low rates of cBTKi-associated AEs were observed with pirtobrutinib

Wierda WG et al. ASH 2022; Abstract 347.

# EPCORE– Richter's Syndrome




Bispecific Antibody to CD3/CD20

Median Prior CLL Rx = 3 (0-7)

| | ORR | CRR |
|---|---|---|
| Responders, n (%) | 6/10 (60) | 5/10 (50) |

Cytokine Release Syndrome: n = 90% (all grade 1/2)

- First full dose given C1D15
- Median time from first full dose to CRS = 13 hrs
- Median time to resolution = 3 (2-9) days

Neurotoxicity = 0%

Kater, ASH 2022

Courtesy of Deborah Stephens, DO

# Meet The Professors Live: Clinical Investigators Provide Perspectives on Actual Cases of Patients with Lymphoma, Chronic Lymphocytic Leukemia and Multiple Myeloma

*A CME Symposium Held in Conjunction with the 2023 ASCO® Annual Meeting*

**Sunday, June 4, 2023**

**7:00 PM – 9:30 PM CT**

## Faculty

**John N Allan, MD**
**Shaji K Kumar, MD**
**Ann S LaCasce, MD, MMSc**
**Sagar Lonial, MD**
**Loretta J Nastoupil, MD**
**Susan O'Brien, MD**

## Moderator

**Neil Love, MD**

RTP RESEARCH TO PRACTICE

# Breakfast with the Investigators: Urothelial Bladder Cancer

*A CME Symposium Held in Conjunction with the 2023 ASCO® Annual Meeting*

**Monday, June 5, 2023**

**6:45 AM – 7:45 AM CT**

## Faculty

**Matthew D Galsky, MD**

**Andrea Necchi, MD**

**Scott T Tagawa, MD, MS**

## Moderator

**Neil Love, MD**

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# POSTMEETING SURVEY – Available Now

***Clinicians in Attendance: The postmeeting survey is now available on the iPads for attendees in the room and on Zoom for those attending virtually. We appreciate your completing this survey before the end of the program.***

***Thank you for your input.***

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**Thank you for joining us!**
**Your feedback is very important to us.**

**Please complete the survey currently up on the iPads for attendees in the room and on Zoom for those attending virtually. The survey will remain open up to 5 minutes after the meeting ends.**

***How to Obtain CME Credit***

***In-person attendees: Please refer to the program syllabus for the CME credit link or QR code. You may also use the iPads available in the meeting room to complete the course evaluation.***

***Online/Zoom attendees: The CME credit link is posted in the chat room.***

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