Meet The Professor

Optimizing the Management of Chronic Lymphocytic Leukemia

Tuesday, November 5, 2024
5:00 PM – 6:00 PM ET

Faculty

Nicole Lamanna, MD

Moderator

Neil Love, MD

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Commercial Support

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Dr Love — Disclosures

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Nonrelevant Financial Relationship	UpToDate

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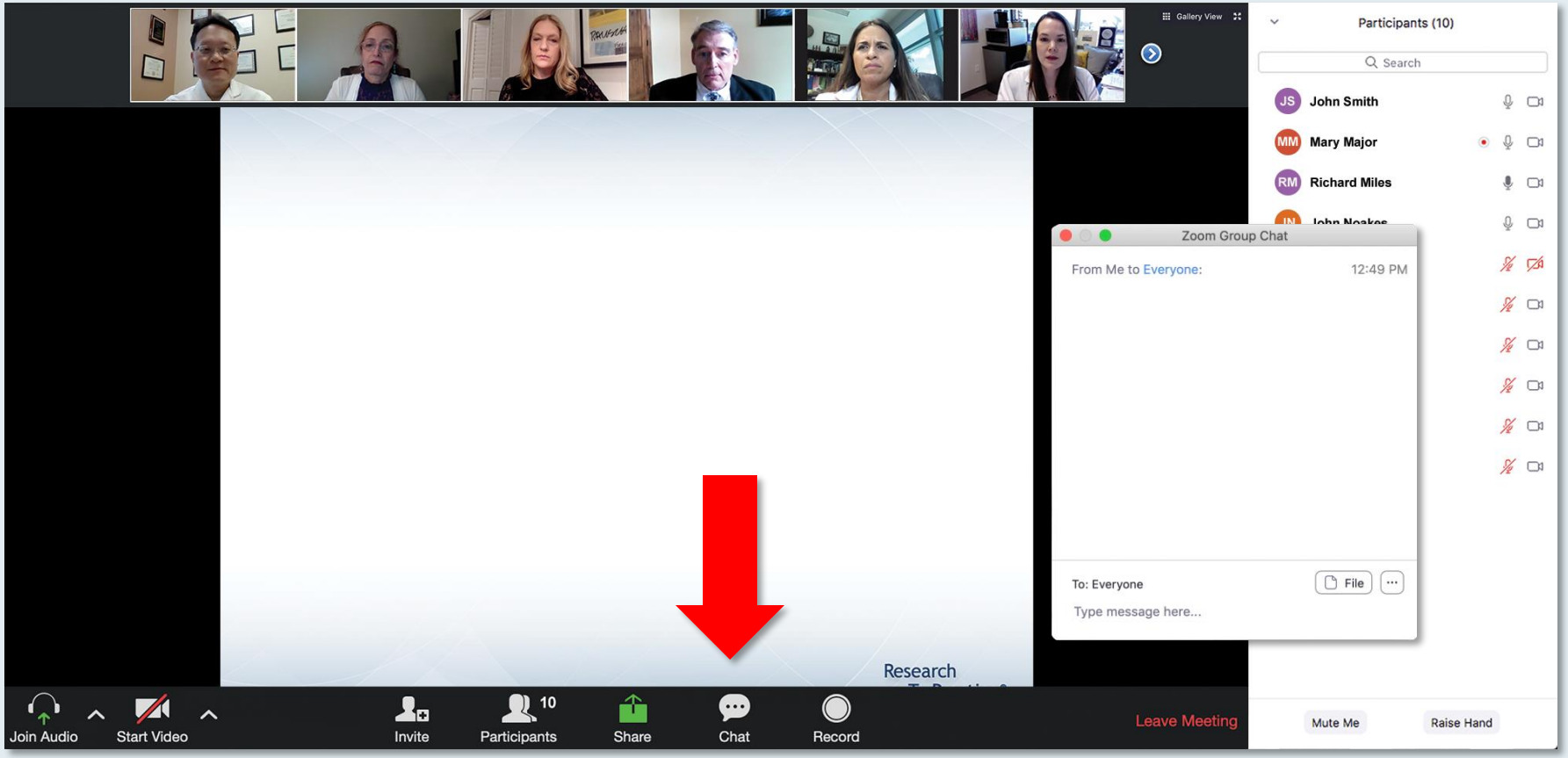

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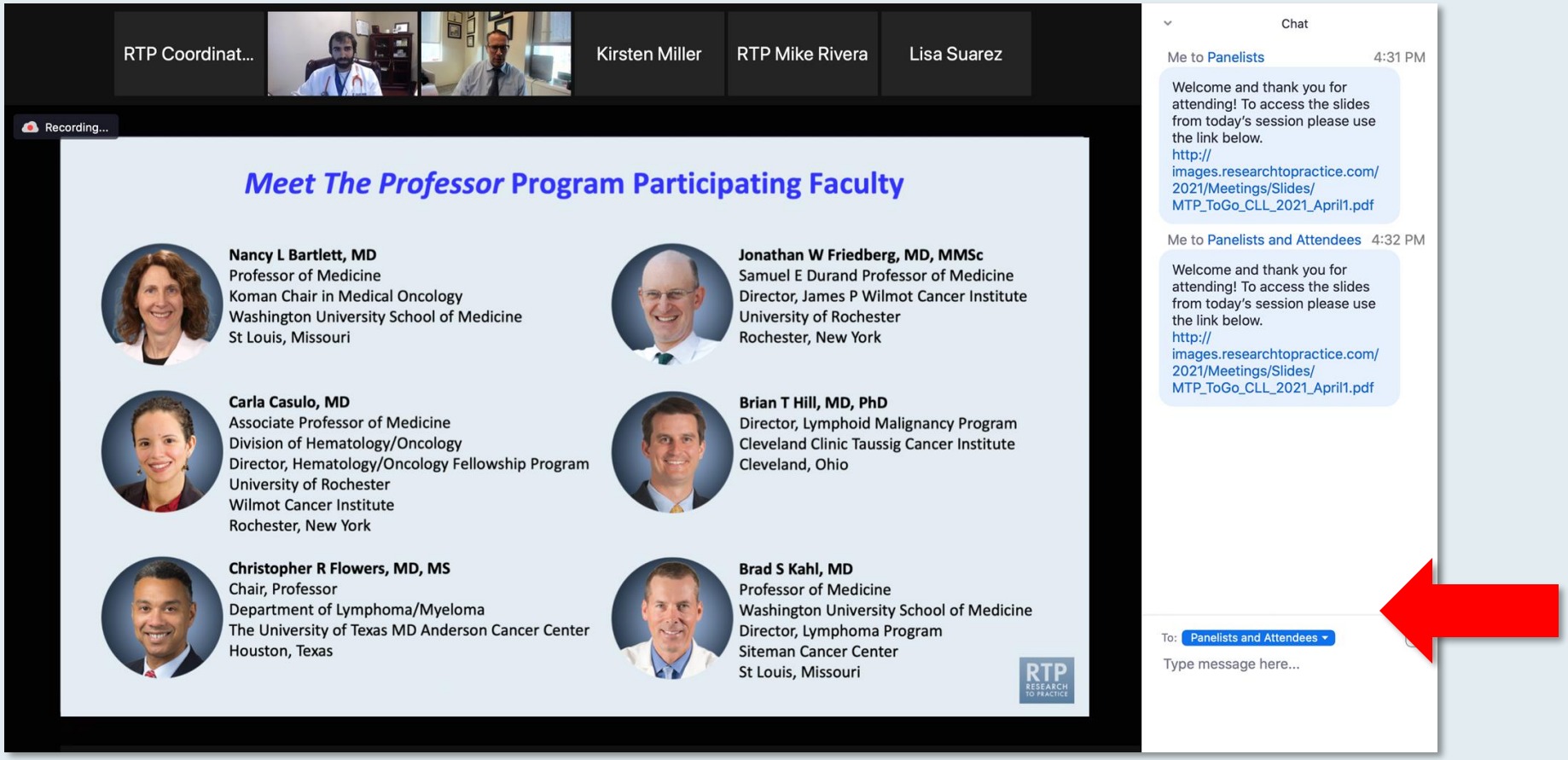

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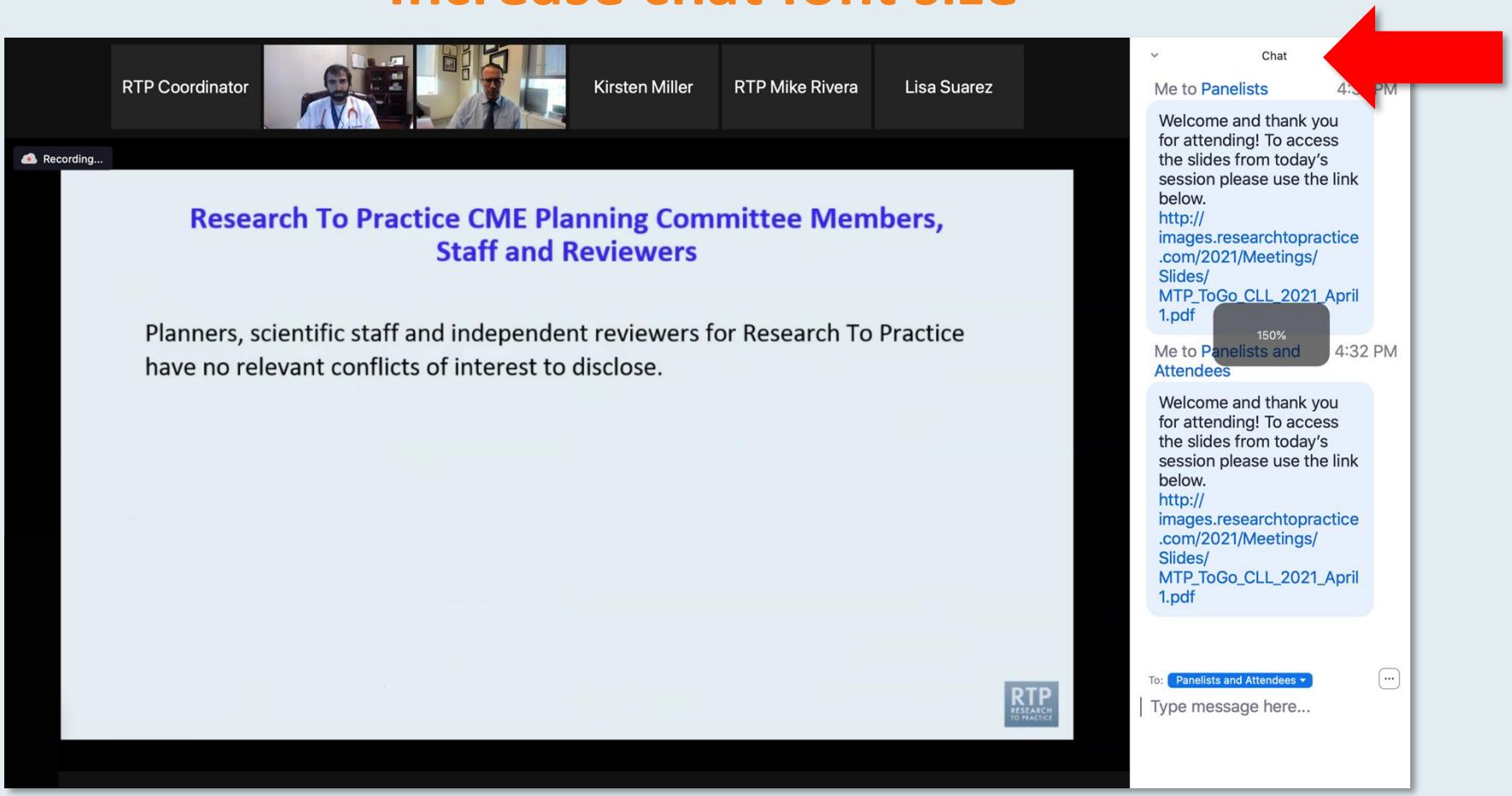

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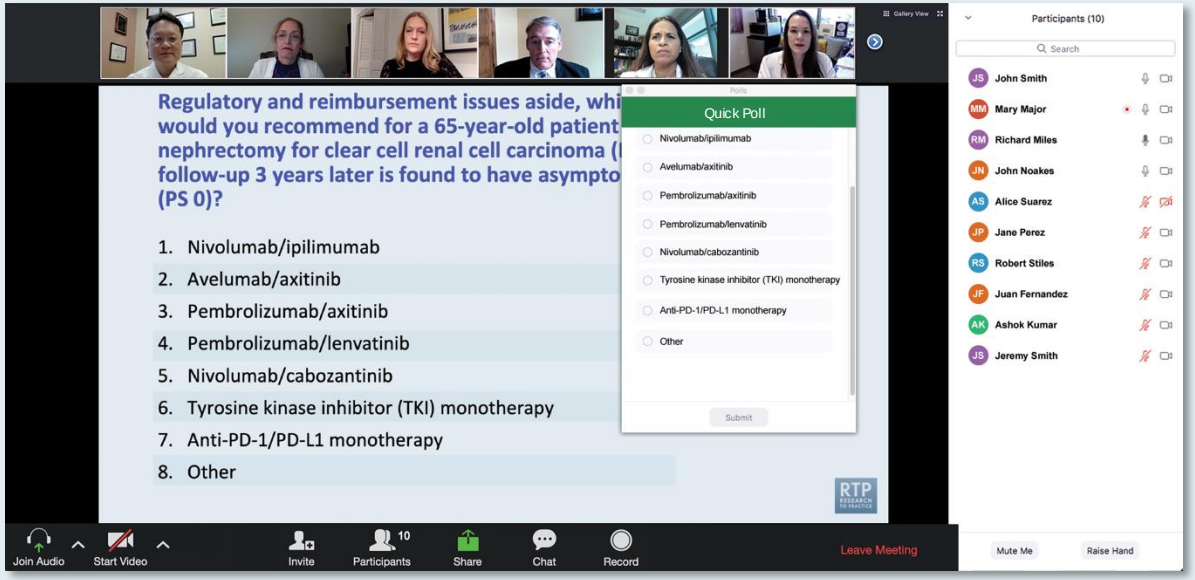

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Key Presentations on Chronic Lymphocytic Leukemia from Recent Major Conferences

DR BITA FAKHRI
STANFORD UNIVERSITY

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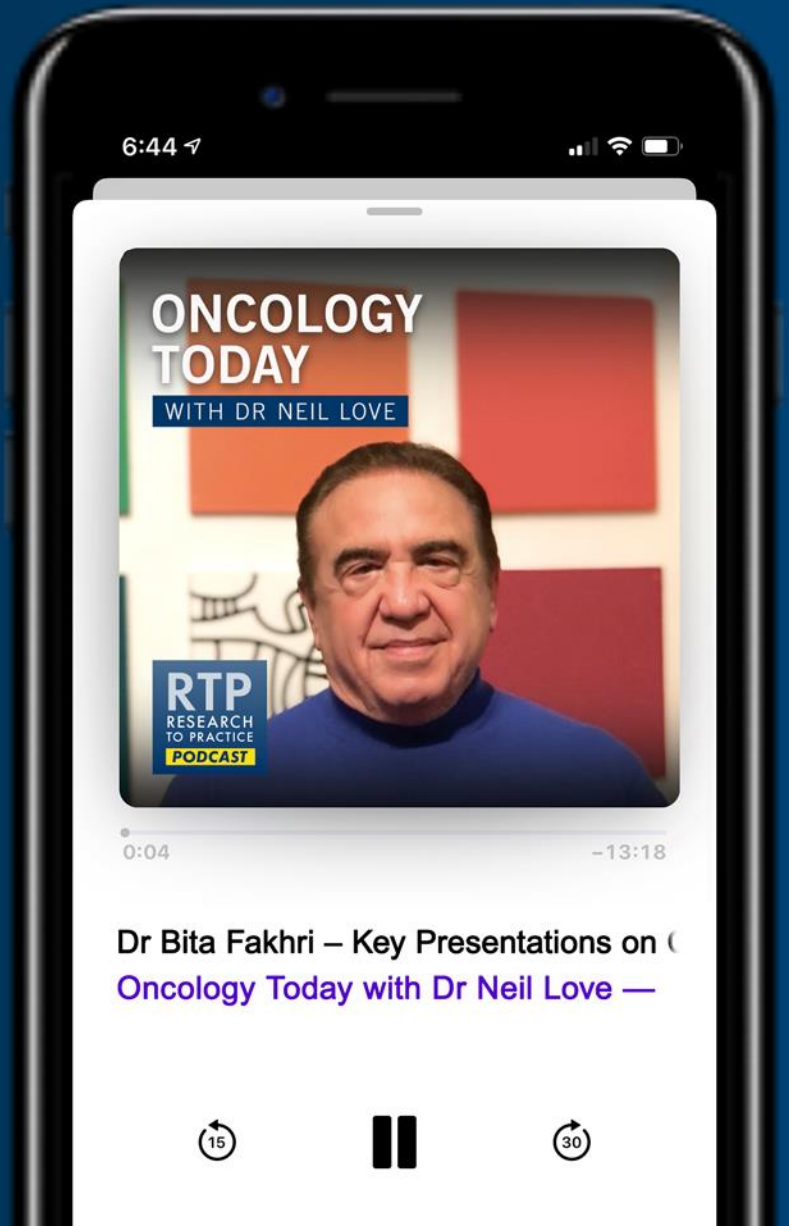

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Cases from the Community: Integrating New Research Findings into Practice

A Multitumor Educational Symposium in Partnership with the American Oncology Network

Saturday, November 16, 2024

Lung Cancer Update: Antibody-Drug Conjugates and New Approaches

Faculty

Edward B Garon, MD, MS

Leukemia and Myelodysplastic Syndromes

Faculty

Harry Paul Erba, MD, PhD

Moderator

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Sara M Tolaney, MD, MPH

Moderator

Neil Love, MD

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Thank you for joining us!

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MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

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Contributing Faculty

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Division of Hematology/Oncology
Department of Medicine
UCI Health
Orange County, California

Matthew S Davids, MD, MMSc
Associate Professor of Medicine
Harvard Medical School
Director of Clinical Research
Division of Lymphoma
Dana-Farber Cancer Institute
Boston, Massachusetts

Adam Kittai, MD
Associate Professor
Division of Hematology and Medical Oncology
Assistant Director of Lymphoma Clinical Research
CLL Clinical Research Leader
Icahn School of Medicine at Mount Sinai Hospital
New York, New York

Chaitra Ujjani, MD
Clinical Director of Lymphoma
Fred Hutchinson Cancer Center
Clinical Professor
University of Washington
Seattle, Washington

Jennifer Woyach, MD
Professor
Division of Hematology
Department of Internal Medicine
The Ohio State University Comprehensive Cancer Center
Columbus, Ohio

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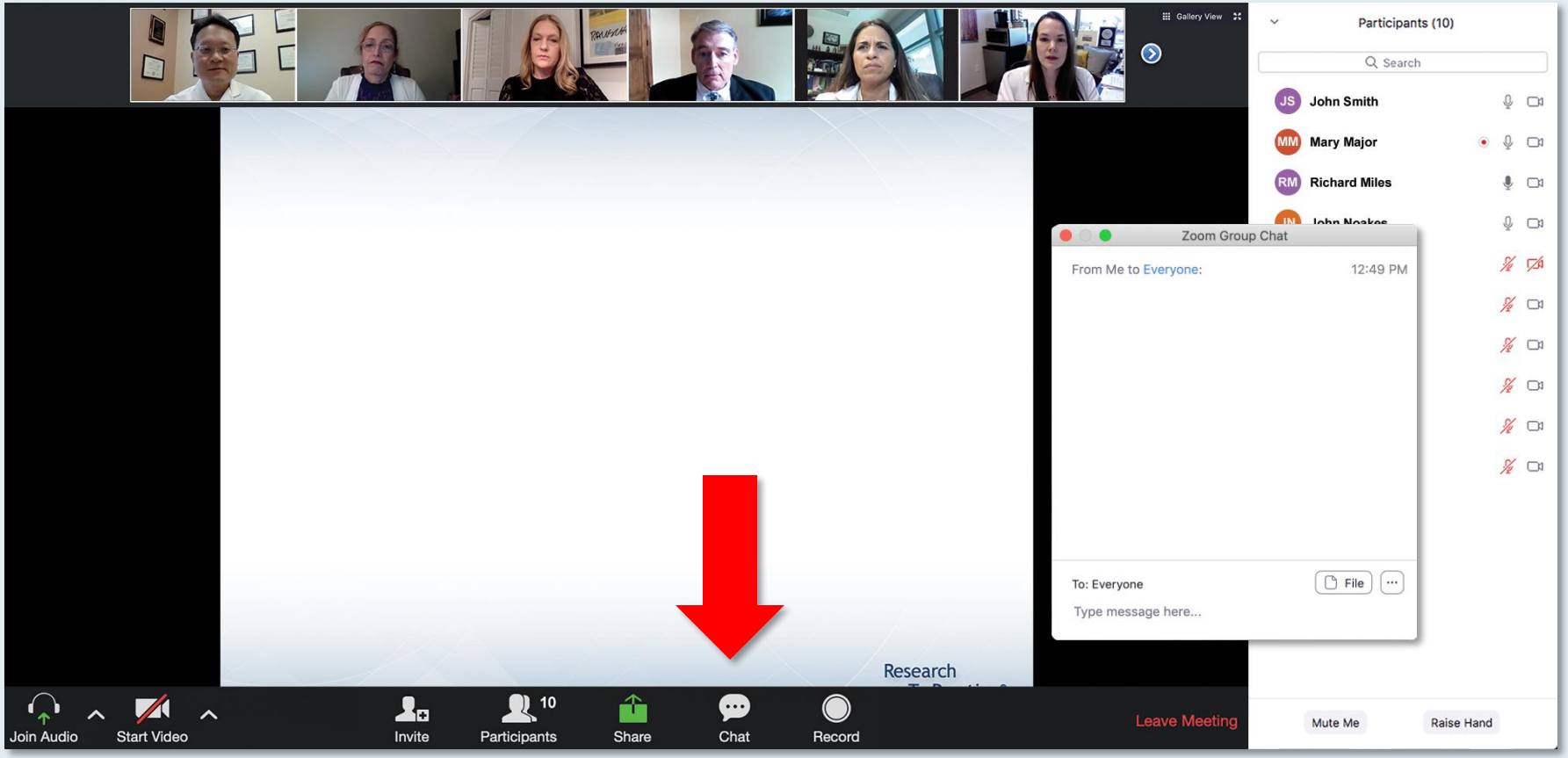

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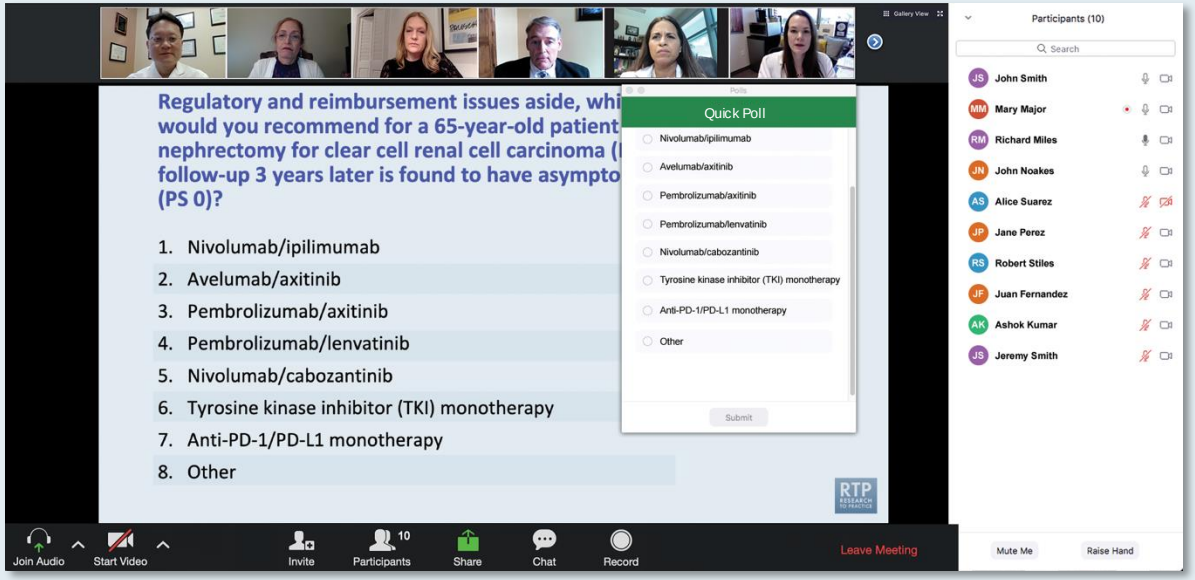

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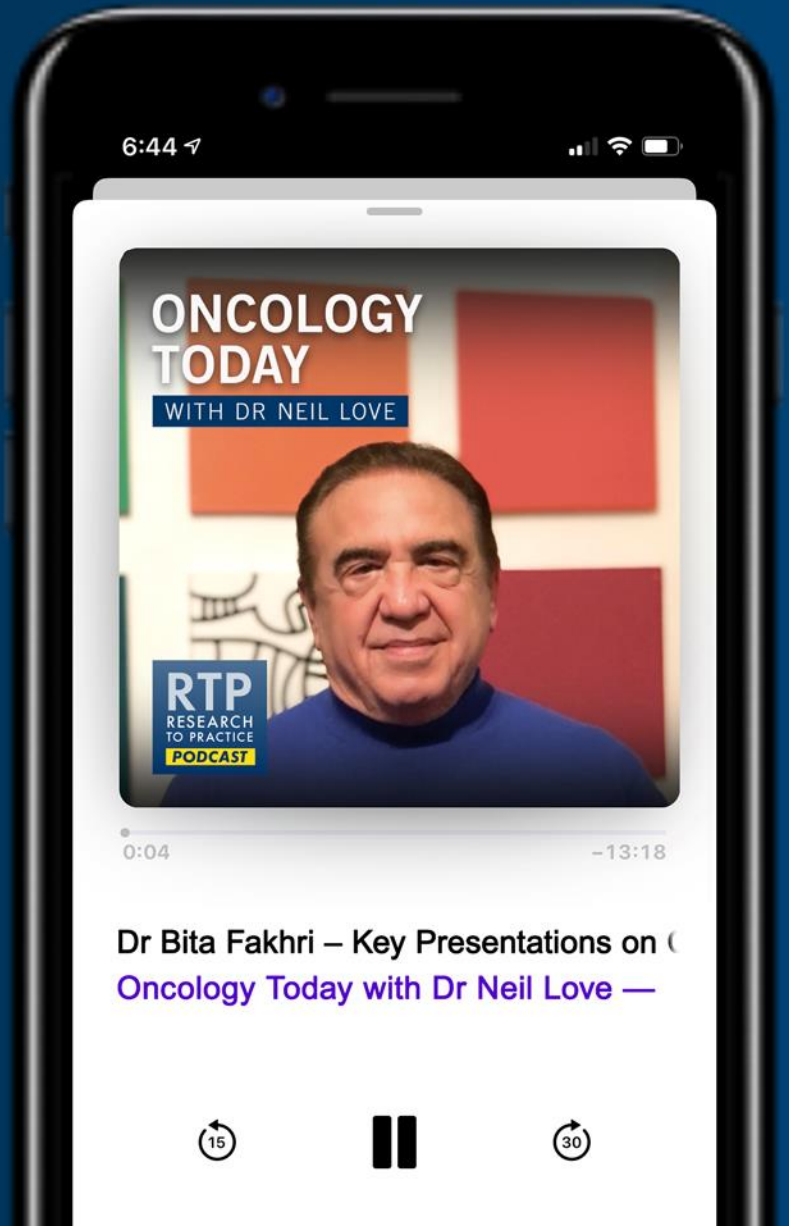

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WVU Cancer Institute
Wheeling, West Virginia

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Tennessee Oncology
Murfreesboro, Tennessee

Shams Bufalino, MD
Advocate Aurora Health
Park Ridge, Illinois

Erik Rupard, MD
Intermountain Health
St George, Utah

Warren S Brenner, MD
Lynn Cancer Institute
Boca Raton, Florida

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Meet The Professor with Dr Lamanna

Case Presentations and Questions for the Faculty:

- Dr Bhatnagar – 67-year-old man with IGHV-mutated CLL (trisomy 12) and progressive adenopathy
- Dr Rupard – 74-year-old woman with IGHV-unmutated, del(13q) CLL and fatigue
- Dr Bufalino – 85-year-old woman with del(13q) CLL under watchful waiting and progressive symptoms
- Dr Brenner – 62-year-old woman diagnosed with SLL now with disease progression on ibrutinib
- Dr Ma – 46-year-old man with SLL who received second-line venetoclax/rituximab
- Dr Brenner – Current role of pirtobrutinib; CAR T-cell therapy; Richter's transformation
- Dr Rupard – 46-year-old African American man with progressive lymphadenopathy in the neck is diagnosed with CLL/SL
- Dr Bhatnagar – 77-year-old man with newly diagnosed IGHV-unmutated CLL (TP53 mutation) receives acalabrutinib

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- **Dr Brenner – 62-year-old woman diagnosed with SLL now with disease progression on ibrutinib**
- **Dr Ma – 46-year-old man with SLL who received second-line venetoclax/rituximab**
- **Dr Brenner – Current role of pirtobrutinib; CAR T-cell therapy; Richter's transformation**
- **Dr Rupard – 46-year-old African American man with progressive lymphadenopathy in the neck is diagnosed with CLL/SL**
- **Dr Bhatnagar – 77-year-old man with newly diagnosed IGHV-unmutated CLL (TP53 mutation) receives acalabrutinib**

RTP
RESEARCH TO PRACTICE

Case Presentation: 67-year-old man with recent myocardial infarction and 6-vessel CABG, IGHV-mutated CLL (trisomy 12) and progressive cervical and intra-abdominal adenopathy

Dr Tina Bhatnagar (Wheeling, West Virginia)

RTP RESEARCH TO PRACTICE

Positive High-Level Results from the Phase III AMPLIFY Trial Announced

Press Release: July 29, 2024

"Positive high-level results from an interim analysis of the AMPLIFY Phase III trial showed a fixed duration of acalabrutinib in combination with venetoclax, with or without obinutuzumab, demonstrated a statistically significant and clinically meaningful improvement in progression-free survival (PFS) compared to standard-of-care chemoimmunotherapy in previously untreated adult patients with chronic lymphocytic leukemia (CLL).

For the secondary endpoint of overall survival (OS), a trend was observed in favour of acalabrutinib in combination with venetoclax, with or without obinutuzumab, versus standard-of-care chemoimmunotherapy. The OS data were not mature at the time of this analysis and the trial will continue to assess OS as a key secondary endpoint.

The safety and tolerability were consistent with the known safety profile of each medicine. No new safety signals were identified, with low rates of cardiac toxicity observed. The data will be presented at a forthcoming medical meeting and shared with global regulatory authorities."

https://www.astrazeneca.com/media-centre/press-releases/2024/calquence-fixed-duration-combo-improved-1l-cll-pfs.html

RTP RESEARCH TO PRACTICE

Abstract 1009

ASH | Annual Meeting & Exposition

1009 Fixed-Duration Acalabrutinib Plus Venetoclax with or without Obinutuzumab Versus Chemoimmunotherapy for First-Line Treatment of Chronic Lymphocytic Leukemia: Interim Analysis of the Multicenter, Open-Label, Randomized, Phase 3 AMPLIFY Trial

Program: Oral and Poster Abstracts
Type: Oral
Session: 642. Chronic Lymphocytic Leukemia: Clinical and Epidemiological: Frontline Targeted Therapy Combinations
Hematology Disease Topics & Pathways:
Research, Clinical trials, Lymphoid Leukemias, CLL, Clinical Research, Diseases, Lymphoid Malignancies

Monday, December 9, 2024: 4:30 PM

Jennifer R. Brown, MD, PhD[1], *John F. Seymour, MBBS, PhD*[2], *Wojciech Jurczak, MD, PhD*[3], *Andrew Aw, MD*[4*], *Malgorzata Wach, MD*[5*], *Arpad Illes, MD*[6*], *Alessandra Tedeschi, MD*[7*], *Carolyn Owen, MD*[8], *Alan P Skarbnik, MD*[9], *Daniel Lysak, MD*[10*], *Ki-Seong Eom, MD, PhD*[11*], *Martin Å imkoviÄ, MD*[12*], *Miguel Arturo Pavlovsky, MD*[13], *Arnon P. Kater, MD, PhD*[14], *Barbara F. Eichhorst, MD*[15], *Kara Miller, MS*[16*], *Veerendra Munugalavadla, PhD*[16], *Ting Yu, MD*[16], *Marianne de Borja, MS*[17*] *and Paolo Ghia, MD, PhD*[18,19]

RTP RESEARCH TO PRACTICE

AMPLIFY: An Ongoing Phase III Trial of Fixed-Duration Acalabrutinib and Venetoclax with or without Obinutuzumab for Previously Untreated CLL without Del(17p) or TP53 Mutation

Trial identifier: NCT03836261 (active, not recruiting)
Estimated enrollment: 984

Eligibility

- Diagnosis of CLL requiring active treatment
- ECOG PS 0-2
- No detected del(17p) or TP53 mutation
- No prior CLL-specific therapies

R

Acalabrutinib + venetoclax

Acalabrutinib + venetoclax + obinutuzumab

Investigator choice of FCR or bendamustine/rituximab

FCR = fludarabine, cyclophosphamide and rituximab

Primary endpoint: Progression-free survival by independent central review

www.clinicaltrials.gov. Accessed August 2024.

RTP RESEARCH TO PRACTICE

AMPLIFY: Abstract Summary

- N = 867 patients randomized (acalabrutinib and venetoclax [AV], n = 291; acalabrutinib, venetoclax and obinutuzumab [AVO], n = 286; FCR with bendamustine/rituximab [BR], n = 290)
- Median follow-up 41 months
- **Primary endpoint**: Blinded independent central review (BICR)-assessed progression-free survival (PFS) with AV versus FCR/BR in ITT population
- **Secondary endpoints** include BICR-assessed PFS (AVO versus FCR/BR) and overall survival (OS)
- AV and AVO provided a statistically significant improvement in BICR-assessed PFS over the control arm (HR versus FCR/BR: 0.65 and 0.42, $p = 0.0038$ and $p < 0.0001$, respectively)
    - Median PFS: Not reached in AV or AVO arm, 47.6 months in FCR/BR arm
    - AV demonstrated an OS benefit trend over FCR/BR (HR 0.33, nominal $p < 0.0001$)

Conclusions

- AMPLIFY met its primary endpoint, demonstrating superior BICR-assessed PFS with AV versus FCR/BR, with similar findings seen with AVO versus FCR/BR
- The combinations AV and AVO provided deep and durable responses with manageable safety profiles
- AV offers the first all-oral fixed-duration regimen that combines venetoclax with a second-generation BTK inhibitor for fit patients with treatment-naïve CLL

Brown JR et al. ASH 2024;Abstract 1009.

RTP RESEARCH TO PRACTICE

Combination of Zanubrutinib + Venetoclax for Treatment-naive CLL/SLL With del(17p) and/or *TP53*: Preliminary Results From SEQUOIA Arm D

Shuo Ma,[1] Talha Munir,[2] Masa Lasica,[3] Mazyar Shadman,[4,5] Alessandra Tedeschi,[6] Emmanuelle Ferrant,[7] Ian W. Flinn,[8] Wojciech Janowski,[9] Monica Tani,[10] Tadeusz Robak,[11] Jennifer R. Brown,[12] Constantine S. Tam,[13] Tian Tian,[14] Emily Mantovani,[14] Stephanie Agresti,[14] Linlin Xu,[14] Aileen Cohen,[14] Wojciech Jurczak,[15] **Paolo Ghia**[16,17]

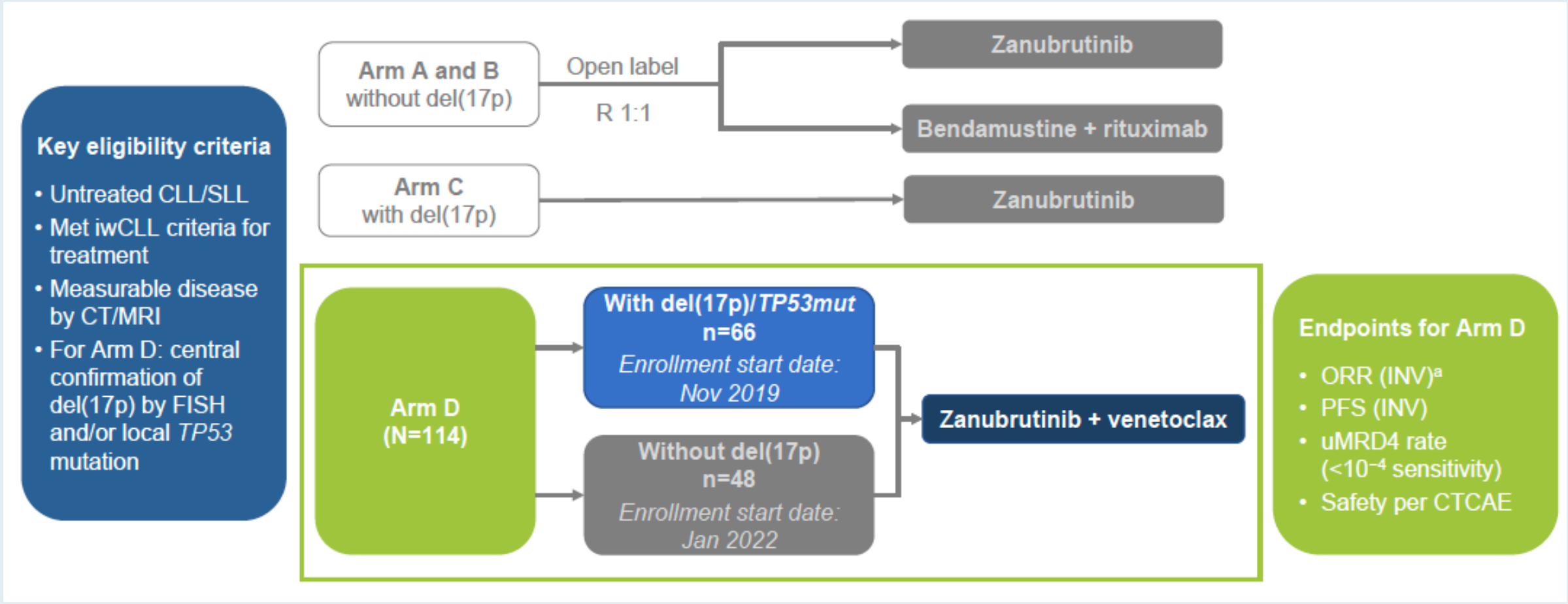
[1]Robert H. Lurie Comprehensive Cancer Center, Northwestern University Feinberg School of Medicine, Chicago, IL, USA; [2]Leeds Teaching Hospitals NHS Trust, Leeds, UK; [3]St Vincent's Hospital Melbourne, Fitzroy, VIC, Australia; [4]Fred Hutchinson Cancer Research Center, Seattle, WA, USA; [5]University of Washington, Seattle, WA, USA; [6]ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy; [7]Département Hématologie, CHU de Lyon-Sud, Lyon-Sud, France; [8]Tennessee Oncology/OneOncology, Nashville, TN, USA; [9]Calvary Mater Newcastle Hospital, Waratah, NSW, Australia; [10]Hematology Unit, Santa Maria delle Croci Hospital, Ravenna, Italy; [11]Medical University of Łódź, Copernicus Memorial Hospital, Łódź, Poland; [12]Dana-Farber Cancer Institute, Boston, MA, USA; [13]Alfred Hospital and Monash University, Melbourne, VIC, Australia; [14]BeiGene USA, Inc, San Mateo, CA, USA; [15]Maria Sklodowska-Curie National Research Institute of Oncology, Kraków, Poland; [16]IRCCS Ospedale San Raffaele, Milan, Italy; [17]Università Vita-Salute San Raffaele, Milan, Italy

Presented at the EHA2024 Hybrid Congress; June 13-16, 2024; Madrid, Spain

Abstract S160

RTP RESEARCH TO PRACTICE

SEQUOIA Study Design: Arm D Cohort with Del(17p) and/or TP53 Mutation



Ma S et al. EHA 2024;Abstract S160.

SEQUOIA Arm D: Author Conclusions

- Preliminary results for treatment with zanubrutinib + venetoclax in patients with high-risk TN CLL/SLL with del(17p) and/or *TP53* mutation showed favorable safety and tolerability
  - Rates of atrial fibrillation/flutter and hypertension were low (2% and 9%, respectively)
- Promising efficacy was seen in this high-risk population with deep and durable responses
  - An ORR of 100% and a high rate of uMRD were achieved
  - With a median follow-up of 31.6 months, high 12- and 24-month PFS estimates were seen (95% and 94%, respectively)
- The study is ongoing and results in patients who meet MRD-guided early stopping rules will be reported as data mature
- The ongoing phase 3 CELESTIAL-TNCLL trial (BGB-11417-301) is evaluating zanubrutinib in combination with sonrotoclax, a next-generation and potent BCL2 inhibitor, as fixed duration therapy in patients with TN CLL

Ma S et al. EHA 2024;Abstract S160.

RTP RESEARCH TO PRACTICE

Select Ongoing First-Line Phase III Trials

Trial	Subgroup	N	Status*	MRD	Treatment arms			
GAIA/CLL13 (NCT02950051)	Fit pts	926	Enrolled	Co-Primary	IbrVenOb	VenOb	VenR	FCR/BR
EA9161 (NCT03701282)	Fit, 18-69 yo	720	Enrolled	Secondary	IbrVenOb	IbrOb		
A041702 (NCT03737981)	≥70 yo	454	Enrolled	Secondary	IbrVenOb	IbrOb		
CRISTALLO (NCT04285567)	Fit pts [no del(17p)]	166	Enrolled	Primary	VenOb			FCR/BR
CLL17 (NCT04608318)	All pts	897	Enrolled	Secondary	IbrVen	VenOb	Ibr	
ACE-CL-311 (NCT03836261)	All pts	984	Enrolled	Secondary	AcaVenOb	AcaVen		FCR/BR
GCLLSG (NCT05197192)	High-risk	650	Enrolling	Secondary	AcaVenOb	VenOb		
MAJIC (NCT05057494)	All	607	Enrolling	Secondary	AcaVen	VenOb		

* Status as of August 2024

Content Courtesy of William G Wierda, MD, PhD; adapted

RTP RESEARCH TO PRACTICE

When you are going to administer a Bruton tyrosine kinase (BTK) inhibitor as initial treatment for a patient with CLL, which would you generally prefer?

 Dr Coombs	Zanubrutinib
 Dr Davids	Acalabrutinib
 Dr Kittai	Acalabrutinib
 Dr Lamanna	Acalabrutinib or zanubrutinib
 Dr Ujjani	Zanubrutinib
 Dr Woyach	Acalabrutinib or zanubrutinib

RTP RESEARCH TO PRACTICE

Based on current clinical trial data and/or your personal experience, how would you compare the global efficacy and tolerability/toxicity of ibrutinib, acalabrutinib and zanubrutinib for patients with newly diagnosed CLL?

	Efficacy	Tolerability/toxicity
 Dr Coombs	About the same	Acalabrutinib has the least toxicity
 Dr Davids	Zanubrutinib is the most efficacious	Acalabrutinib has the least toxicity
 Dr Kittai	About the same	Acalabrutinib has the least toxicity
 Dr Lamanna	About the same	Toxicity profiles differ*
 Dr Ujjani	There are not enough available data at this time	Zanubrutinib has the least toxicity
 Dr Woyach	About the same	Acalabrutinib has the least toxicity

*Bruising is similar among all 3. Less cardiac toxicity with acalabrutinib and zanubrutinib. More headache with acalabrutinib, more myelosuppression with zanubrutinib

What is your initial treatment for a 63-year-old patient with newly diagnosed CLL with no IGHV mutation but with del(17p) and with atrial fibrillation that is well controlled with apixaban?

 Dr Coombs	Venetoclax + obinutuzumab
 Dr Davids	Zanubrutinib
 Dr Kittai	Acalabrutinib
 Dr Lamanna	Acalabrutinib or zanubrutinib*
 Dr Ujjani	Zanubrutinib
 Dr Woyach	Zanubrutinib

*Discuss possible need for increased cardiac medications to control fibrillation; if that is not desired by patient, I would discuss venetoclax-based therapy with possible continuation of venetoclax as monotherapy.

RTP RESEARCH TO PRACTICE

Do you have a preferred BTK inhibitor for a patient with a history of the conditions listed below?

	Migraine headache	Difficult-to-control hypertension
 Dr Coombs	Yes, zanubrutinib	Yes, zanubrutinib
 Dr Davids	Yes, zanubrutinib	Yes, acalabrutinib
 Dr Kittai	Yes, zanubrutinib	Yes, acalabrutinib
 Dr Lamanna	Yes, zanubrutinib	Yes, acalabrutinib
 Dr Ujjani	Yes, acalabrutinib or zanubrutinib, depending on availability	Yes, acalabrutinib
 Dr Woyach	Yes, zanubrutinib	Yes, acalabrutinib

Meet The Professor with Dr Lamanna

Case Presentations and Questions for the Faculty:

- Dr Bhatnagar – 67-year-old man with IGHV-mutated CLL (trisomy 12) and progressive adenopathy
- **Dr Rupard – 74-year-old woman with IGHV-unmutated, del(13q) CLL and fatigue**
- Dr Bufalino – 85-year-old woman with del(13q) CLL under watchful waiting and progressive symptoms
- Dr Brenner – 62-year-old woman diagnosed with SLL now with disease progression on ibrutinib
- Dr Ma – 46-year-old man with SLL who received second-line venetoclax/rituximab
- Dr Brenner – Current role of pirtobrutinib; CAR T-cell therapy; Richter's transformation
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- Dr Bhatnagar – 77-year-old man with newly diagnosed IGHV-unmutated CLL (TP53 mutation) receives acalabrutinib

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RESEARCH TO PRACTICE

Case Presentation: 74-year-old woman with IGHV-unmutated, del(13q) CLL, Rai Stage 0, with fatigue as only symptom

Dr Erik Rupard (St George, Utah)

RTP
RESEARCH TO PRACTICE

ASH | Annual Meeting & Exposition

4625 Treatment Outcomes of Patients Treated with Venetoclax-Obinutuzumab Therapy Vs Btki Therapies in 1L CLL: An International Real-World Study

Program: Oral and Poster Abstracts
Session: 642. Chronic Lymphocytic Leukemia: Clinical and Epidemiological: Poster III
Hematology Disease Topics & Pathways:
Lymphoid Leukemias, CLL, Diseases, Lymphoid Malignancies

Monday, December 9, 2024, 6:00 PM-8:00 PM

***Nicole Lamanna, MD*[1*], *Jennifer R. Brown, MD, PhD*[2], *Chaitra S. Ujjani, MD*[3], *Toby A. Eyre*[4*], *Beenish Manzoor*[5*], *Nilanjan Ghosh*[6*], *Lindsey Roeker, MD*[7], *Matthew S. Davids, MD, MMSc*[2], *Catherine C Coombs, MD*[8*], *Alan P Skarbnik, MD*[9], *Brian T. Hill, MD, PhD*[10], *Hande H. Tuncer, MD*[2], *Lori A. Leslie, MD*[11*], *Joanna M. Rhodes, MD, MSCE*[12*], *Isabelle Fleury, MD, MSc*[13], *Paul M Barr, MD*[14], *Nnadozie Emechebe*[5*], *Nicolas Martinez-Calle*[15*], *Christopher E. Jensen*[16*], *Yun Choi*[17*], *Dureshahwar Jawaid*[5*], *Laurie K Pearson, MD*[18], *Meghan C. Thompson, MD*[7], *Steven E Marx*[5*], *Wendy Sinai, PharmD*[19*], *Frederick Lansigan, MD*[20*], *Bita Fakhri, MD, MPH*[21], *Deborah M. Stephens, DO*[22], *Stephen J. Schuster, MD*[23], *Michael Coyle*[24*], *Irina Pivneva, PhD*[25*], *Talissa Watson*[25*], *Annie Guerin, MSc*[25*] *and Mazyar Shadman*[3*]

Abstract 4625

RTP RESEARCH TO PRACTICE

Abstract Conclusions

- This study is one of the first to demonstrate advantages in clinical outcomes for patients using venetoclax-obinutuzumab (VO) versus covalent BTKi therapy in the first-line setting for time to next treatment or death.
- Considering that 19% of patients who received a BTKi switched therapy, largely due to intolerance, this highlights the need for future studies to assess VO versus second-generation BTKis in the first-line setting with longer follow-up time and larger cohorts.

Lamanna N et al. ASH 2024;Abstract 4625.

RTP RESEARCH TO PRACTICE

Real-World Treatment Effectiveness in High-Risk Patients with Chronic Lymphocytic Leukemia (CLL) Receiving Venetoclax-Based Therapy: An International Study

Coombs CC et al.

EHA 2024;Abstract P665.

Regulatory and reimbursement issues aside, what would be your preferred initial regimen for a 70-year-old patient with IGHV-unmutated CLL who requires treatment and has the mutation status described below?

	Without del(17p) or TP53 mutation	With del(17p) or TP53 mutation
 Dr Coombs	Venetoclax + obinutuzumab	Zanubrutinib
 Dr Davids	Venetoclax + obinutuzumab	Zanubrutinib
 Dr Kittai	Acalabrutinib	Acalabrutinib
 Dr Lamanna	Acalabrutinib or zanubrutinib or venetoclax/obinutuzumab	Acalabrutinib or zanubrutinib
 Dr Ujjani	Venetoclax + obinutuzumab	Zanubrutinib
 Dr Woyach	Venetoclax + obinutuzumab	Acalabrutinib or zanubrutinib

Approximately what proportion of your patients would prefer to receive time-limited therapy with venetoclax and obinutuzumab?

	Younger patients (eg, age 60)	Older patients (eg, age 80)
 Dr Coombs	70%	20%
 Dr Davids	90%	20%
 Dr Kittai	30%	5%
 Dr Lamanna	20%	10%
 Dr Ujjani	50%	50%
 Dr Woyach	50%	20%

Meet The Professor with Dr Lamanna

Case Presentations and Questions for the Faculty:

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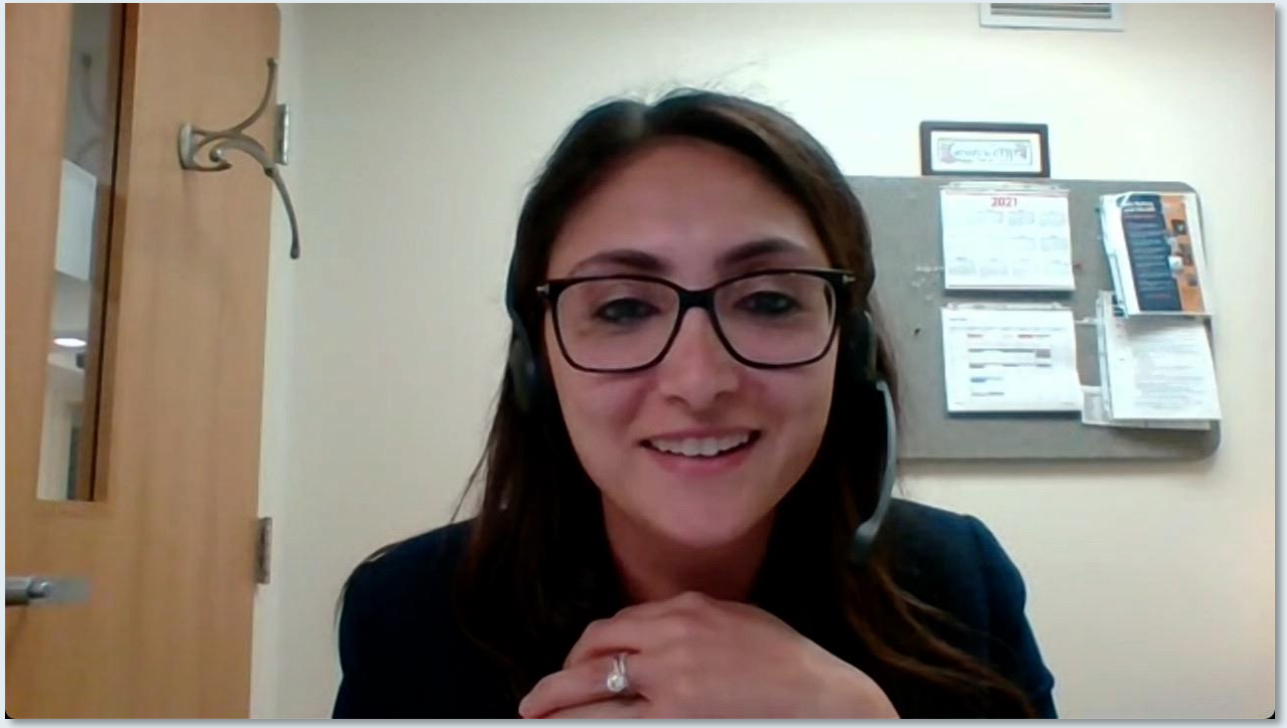
- Dr Bhatnagar – 77-year-old man with newly diagnosed IGHV-unmutated CLL (TP53 mutation) receives acalabrutinib

RTP RESEARCH TO PRACTICE

Case Presentation: 85-year-old woman with del(13q) CLL under watchful waiting develops progressive fatigue, weight loss and rising WBC with doubling time less than 5 months



Dr Shams Bufalino (Park Ridge, Illinois)

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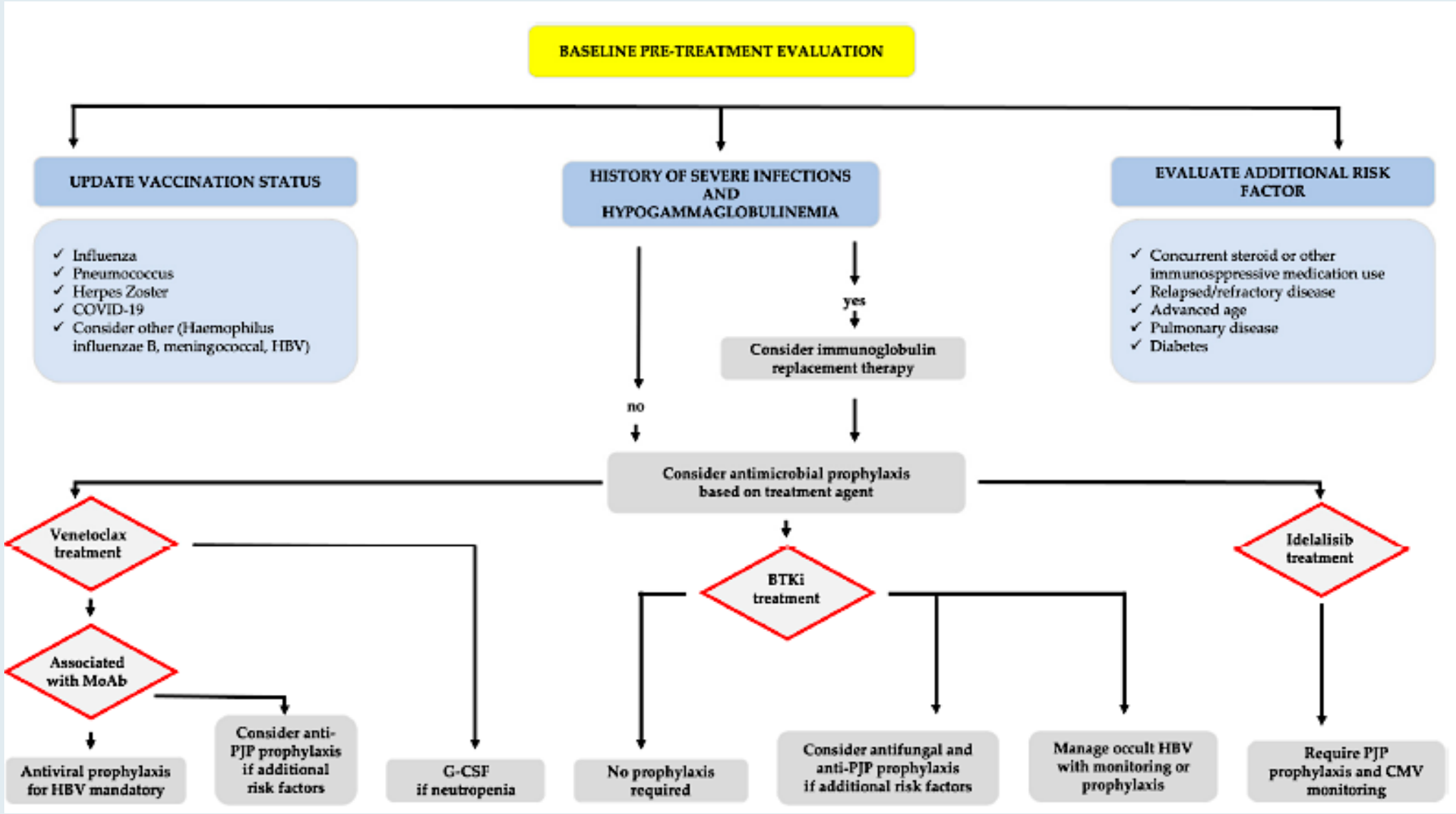
TO PRACTICE

Management of Infectious Risk for Patients with CLL Undergoing Treatment with BTK or Bcl-2 Inhibitors



Galitzia A et al. *Cancers* 2024;16:1996.

Meet The Professor with Dr Lamanna

Case Presentations and Questions for the Faculty:

- Dr Bhatnagar – 67-year-old man with IGHV-mutated CLL (trisomy 12) and progressive adenopathy
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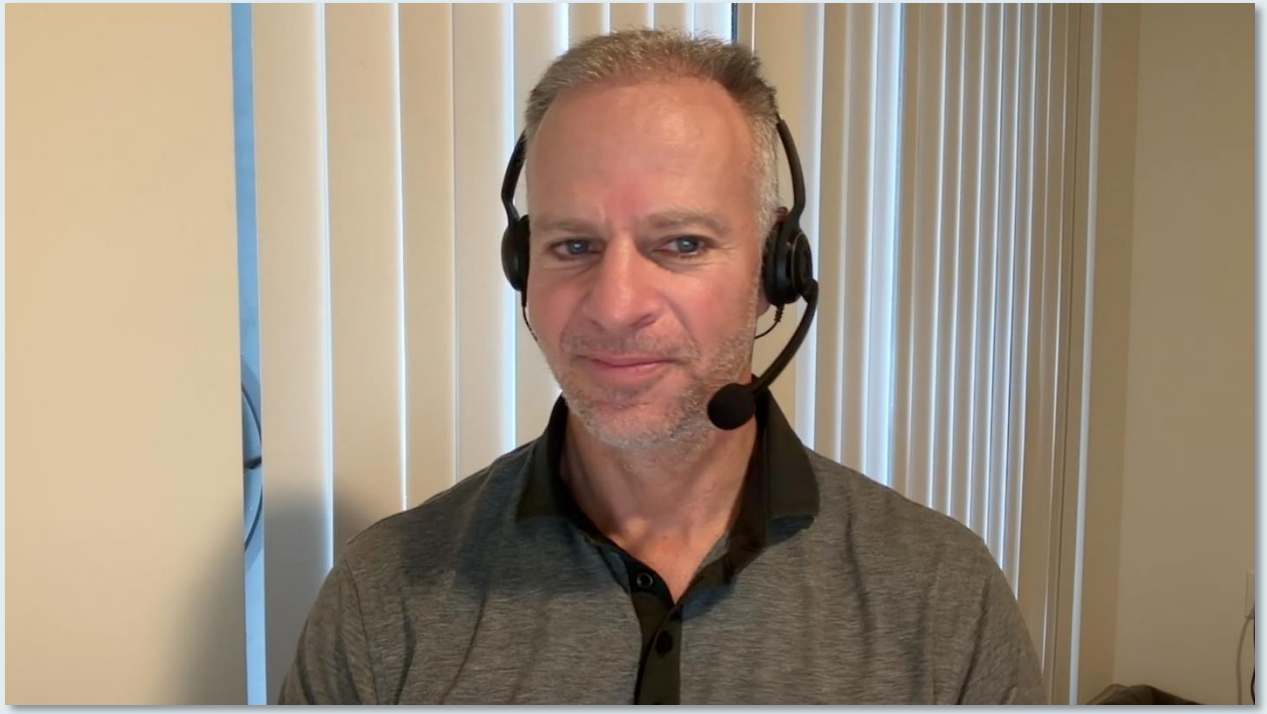
- Dr Rupard – 46-year-old African American man with progressive lymphadenopathy in the neck is diagnosed with CLL/SL
- Dr Bhatnagar – 77-year-old man with newly diagnosed IGHV-unmutated CLL (TP53 mutation) receives acalabrutinib

RTP RESEARCH TO PRACTICE

Case Presentation: 62-year-old woman diagnosed with SLL in 2010, treated with FCR, develops disease relapse in 2015 (now Notch1 and TP53 mutations) and receives ibrutinib; now with disease progression



Dr Warren Brenner (Boca Raton, Florida)

RTP
RESEARCH
TO PRACTICE

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

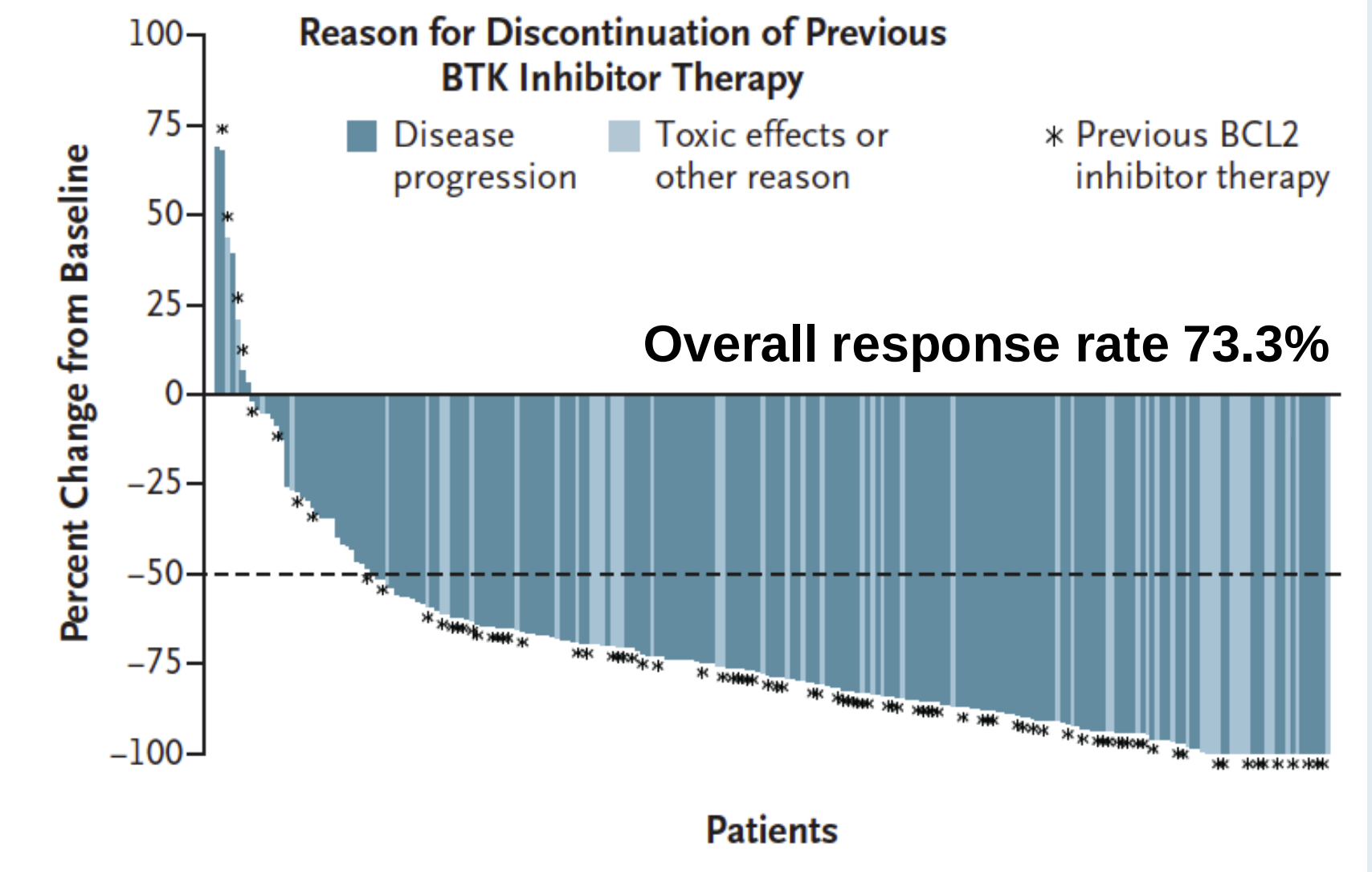
Pirtobrutinib after a Covalent BTK Inhibitor in Chronic Lymphocytic Leukemia

A.R. Mato, J.A. Woyach, J.R. Brown, P. Ghia, K. Patel, T.A. Eyre, T. Munir, E. Lech-Maranda, N. Lamanna, C.S. Tam, N.N. Shah, C.C. Coombs, C.S. Ujjani, B. Fakhri, C.Y. Cheah, M.R. Patel, A.J. Alencar, J.B. Cohen, J.N. Gerson, I.W. Flinn, S. Ma, D. Jagadeesh, J.M. Rhodes, F. Hernandez-Ilizaliturri, P.L. Zinzani, J.F. Seymour, M. Balbas, B. Nair, P. Abada, C. Wang, A.S. Ruppert, D. Wang, D.E. Tsai, W.G. Wierda, and W. Jurczak

2023;389:33-44.

RTP RESEARCH TO PRACTICE

BRUIN: Pirtobrutinib Efficacy in Patients with CLL or SLL Who Received Prior BTK Inhibitor Treatment



Mato et al. *N Engl J Med* 2023;389:33-44.

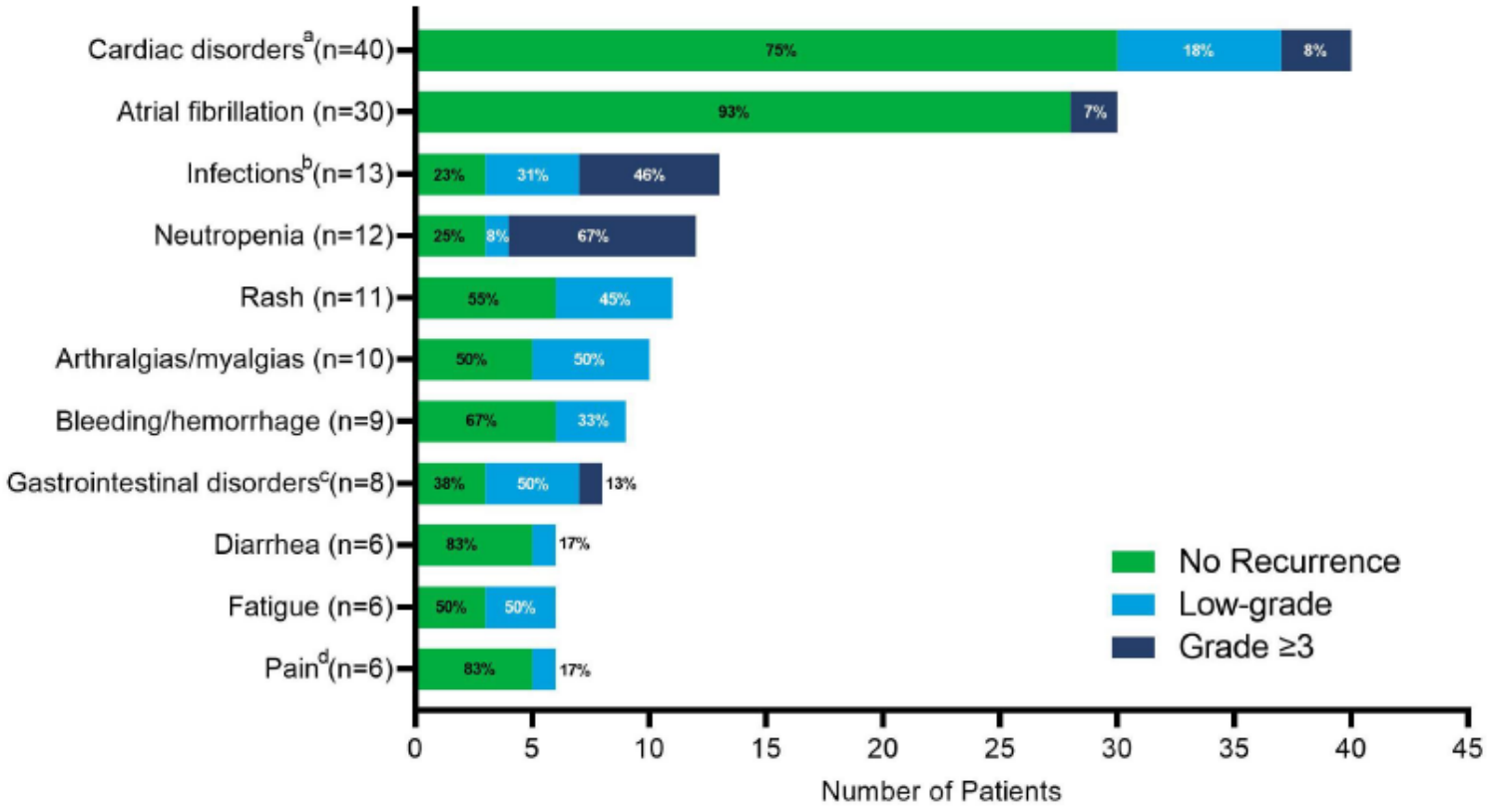
Safety and Tolerability of Pirtobrutinib Monotherapy in Patients with B-Cell Malignancies Who Were Previously Intolerant to a Covalent BTK Inhibitor: Results from the Phase 1/2 BRUIN Study

Shah NN et al.

ASH 2022;Abstract 1797.

JC JOURNAL CLUB
RTP RESEARCH TO PRACTICE

Pirtobrutinib TEAEs Recurring in Patients Who Previously Experienced TEAEs Leading to BTK Inhibitor Discontinuation



- No patient who discontinued a prior BTKi due to a TEAE had to discontinue pirtobrutinib for the same TEAE
- Of the 62 patients who discontinued pirtobrutinib, the majority did so for progressive disease (55%, n=34)
  - Discontinuations for pirtobrutinib related AEs occurred in 7 patients (1 each) including: COVID-19 pneumonia, myalgia, neutropenia, platelet count decreased, rash maculo-papular, skin necrosis, and staphylococcal sepsis
  - Other reasons for non-PD, non-pirtobrutinib related AE discontinuations included: AEs unrelated to treatment (n=13, including 7 deaths), intercurrent illness (n=1), alternative treatment per investigator (n=2), consent withdrawal (n=4), and other (n=1)
- Median relative dose intensity of pirtobrutinib was 97% (IQR, 92-100)
- 93% of patients received ≥1 pirtobrutinib dose at or above the RP2D of 200 mg daily

Most common TEAE categories that led to discontinuation of prior cBTKi are shown; an individual patient may be counted in more than one category. [a]Cardiac disorders include atrial fibrillation. [b]Prior discontinuation infection types were not specified for most patients, so any infection recurrence was investigated. Eleven grade ≥3 infections in the 6 patients with an infection recurrence included: pneumonia (n=6, including COVID-19 pneumonia, n=2 and fungal pneumonia, n=1), bacteremia, diarrhea, salmonellosis, septic shock, and COVID-19 (n=1 each). [c]Gastrointestinal disorders include diarrhea. [d]1 had recurrence of pain in the same site, 3 had new/different pain, and 2 had no pain; no patient discontinued pirtobrutinib for pain.

TEAE = treatment-emergent adverse event

Shah NN et al. ASH 2022;Abstract 1797.

Received: 16 May 2024 | Revised: 20 August 2024 | Accepted: 26 August 2024

DOI: 10.1002/jha2.1013

eJHaem

British Society for Haematology

RESEARCH ARTICLE

Evaluation of bleeding risk in patients who received pirtobrutinib in the presence or absence of antithrombotic therapy

Nicole Lamanna[1] | Constantine S. Tam[2,3] | Jennifer A. Woyach[4] | Alvaro J. Alencar[5] | M. Lia Palomba[6] | Pier Luigi Zinzani[7,8] | Ian W. Flinn[9] | Bita Fakhri[10] | Jonathon B. Cohen[11] | Arrin Kontos[12] | Heiko Konig[12] | Amy S. Ruppert[13] | Anindya Chatterjee[12] | Richard Sizelove[13] | Livia Compte[13] | Donald E. Tsai[12] | Wojciech Jurczak[14]

2024;5(5):929-39.

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Bleeding/Bruising Treatment-Emergent Adverse Events

Patient-level summary	AT-E cohort ($n = 216$)	AT-NE cohort ($n = 557$)
Bleeding/bruising, *n* (%)		
Any grade	97 (44.9)	181 (32.5)
Grade ≥3	6 (2.8)	11 (2.0)
Serious bleeding/bruising, *n* (%)	6 (2.8)	10 (1.8)
Bleeding/bruising requiring		
Dose interruption, *n* (%)	8 (3.7)	14 (2.5)
Dose reduction, *n* (%)	0	1 (0.2)
Dose discontinuation, *n* (%)	0	0
Hospitalization[a], *n* (%)	5 (2.3)	9 (1.6)
Median time to first onset of bleeding/bruising, weeks (IQR)	8.1 (2.6–24.0)	4.1 (1.3–16.1)
Event-level summary		
Total number of bleeding/bruising events	157	296
Recovered/resolved, *n* (%)	90 (57.3)	164 (55.4)
With treatment	10 (6.4)	17 (5.7)
Without treatment	80 (51.0)	147 (49.7)
Median duration[b], weeks (IQR)	2.1 (0.6–4.3)	4.0 (1.1–7.9)

Abbreviations: AT-E, antithrombotic exposed; AT-NE, antithrombotic non-exposed; IQR, interquartile range.
[a]Including prolonged hospitalization.
[b]Duration was calculated for 88 and 159 recovered/resolved adverse events with nonmissing end dates for the AT-E cohort and AT-NE cohorts, respectively.

Lamanna N et al. *EJHaem* 2024;5(5):929-39.

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Which third-line therapy would you generally prefer for a patient with double-refractory CLL?

 Dr Coombs	Pirtobrutinib
 Dr Davids	Pirtobrutinib
 Dr Kittai	Pirtobrutinib
 Dr Lamanna	Pirtobrutinib
 Dr Ujjani	Lisocabtagene maraleucel
 Dr Woyach	Pirtobrutinib

RTP RESEARCH TO PRACTICE

In which line of therapy are you currently using pirtobrutinib for your patients with CLL?

 Dr Coombs	Third line
 Dr Davids	Third line
 Dr Kittai	Third line
 Dr Lamanna	Third line
 Dr Ujjani	Fourth line
 Dr Woyach	Third line

RTP RESEARCH TO PRACTICE

Based on current clinical trial data and your personal experience, how would you compare the global efficacy and tolerability/toxicity of pirtobrutinib to that of ibrutinib, acalabrutinib and zanubrutinib for patients with relapsed/refractory (R/R) CLL?

	Efficacy	Tolerability/toxicity
 Dr Coombs	There are not enough available data at this time	Pirtobrutinib has the least toxicity
 Dr Davids	About the same	Pirtobrutinib has the least toxicity
 Dr Kittai	There are not enough available data at this time	There are not enough available data at this time
 Dr Lamanna	There are not enough available data at this time	Pirtobrutinib has the least toxicity
 Dr Ujjani	There are not enough available data at this time	Pirtobrutinib has the least toxicity
 Dr Woyach	There are not enough available data at this time	Pirtobrutinib has the least toxicity

Meet The Professor with Dr Lamanna

Case Presentations and Questions for the Faculty:

- Dr Bhatnagar – 67-year-old man with IGHV-mutated CLL (trisomy 12) and progressive adenopathy
- Dr Rupard – 74-year-old woman with IGHV-unmutated, del(13q) CLL and fatigue
- Dr Bufalino – 85-year-old woman with del(13q) CLL under watchful waiting and progressive symptoms
- Dr Brenner – 62-year-old woman diagnosed with SLL now with disease progression on ibrutinib
- Dr Ma – 46-year-old man with SLL who received second-line venetoclax/rituximab
- Dr Brenner – Current role of pirtobrutinib; CAR T-cell therapy; Richter's transformation
- Dr Rupard – 46-year-old African American man with progressive lymphadenopathy in the neck is diagnosed with CLL/SL
- Dr Bhatnagar – 77-year-old man with newly diagnosed IGHV-unmutated CLL (TP53 mutation) receives acalabrutinib

RTP
RESEARCH TO PRACTICE

Case Presentation: 46-year-old man with SLL treated with BR → R and second-line venetoclax/rituximab x 3 years with residual tumor by MRD assay

Dr Yanjun Ma (Murfreesboro, Tennessee)

RTP
RESEARCH
TO PRACTICE

Currently Applied Methods for MRD Assessment

Method	Sensitivity	Features	Advantages	Disadvantages
Flow cytometry				
4-color flow	10^{-4}	Detection of surface markers by established antibody panels	ERIC consensus guidelines available, widely accessible, relatively affordable, quantitative results, relatively quick	Fresh (<48 h) peripheral blood or bone marrow samples necessary, sufficient number of cells required to achieve sensitivity
≥6-color flow	10^{-5}			
8-color flow	10^{-6}			
10-color flow	10^{-5}			
Polymerase chain reaction (PCR)				
ASO (allele-specific oligonucleotide) PCR	10^{-5}	Quantification based on allele- and patient-specific primers for hypervariable CDR3 of IgH	Good sensitivity, use of DNA (instead of fresh material), quantitative results	Patient-specific primers required, baseline reference sample necessary, relatively time and labor intensive
Next-generation sequencing				
clonoSEQ®	10^{-6}	Measurement of CLL-specific IgH sequences based on consensus primers	High sensitivity, use of DNA, tracking of clones possible, quantitative results	Relatively expensive, baseline reference sample necessary, not widely used yet

ERIC = European Research Initiative on CLL

Al-Sawaf O et al. *Hematol Oncol Clin N Am* 2021;35(4):775-91. Wierda WG et al. *Leukemia* 2021;35:3059-72.

RTP RESEARCH TO PRACTICE

Real-World Treatment Effectiveness in Patients with Chronic Lymphocytic Leukemia (CLL) Receiving Venetoclax-Based Therapy After Bruton Tyrosine Kinase Inhibitors: An International Study

Ghosh N et al.

EHA 2024;Abstract P671.

JC JOURNAL CLUB
RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, which second-line systemic therapy would you recommend for a 70-year-old patient with IGHV-unmutated CLL without del(17p) or TP53 mutations who responds to ibrutinib and then experiences disease progression 3 years later?

 Dr Coombs	Venetoclax + obinutuzumab
 Dr Davids	Venetoclax + obinutuzumab
 Dr Kittai	Venetoclax + obinutuzumab
 Dr Lamanna	Venetoclax + obinutuzumab or venetoclax + rituximab
 Dr Ujjani	Venetoclax + obinutuzumab
 Dr Woyach	Venetoclax + obinutuzumab

RTP RESEARCH TO PRACTICE

For patients with CLL who are receiving obinutuzumab/venetoclax as initial therapy, do you generally order a minimal residual disease (MRD) assay at the end of 12 months? What would be your most likely approach if after completing 12 months of treatment the patient had detectable MRD versus undetectable MRD?

	MRD assay?	Detectable MRD	Undetectable MRD
 Dr Coombs	Yes	Discontinue treatment	Discontinue treatment
 Dr Davids	Yes	Discontinue treatment	Discontinue treatment
 Dr Kittai	Yes	Discontinue treatment	Discontinue treatment
 Dr Lamanna	Yes	Continue treatment, but if MRD is persistent will discontinue	Discontinue treatment
 Dr Ujjani	Yes	Discontinue treatment	Discontinue treatment
 Dr Woyach	Yes	Discontinue treatment	Discontinue treatment

Meet The Professor with Dr Lamanna

Case Presentations and Questions for the Faculty:

- Dr Bhatnagar – 67-year-old man with IGHV-mutated CLL (trisomy 12) and progressive adenopathy
- Dr Rupard – 74-year-old woman with IGHV-unmutated, del(13q) CLL and fatigue
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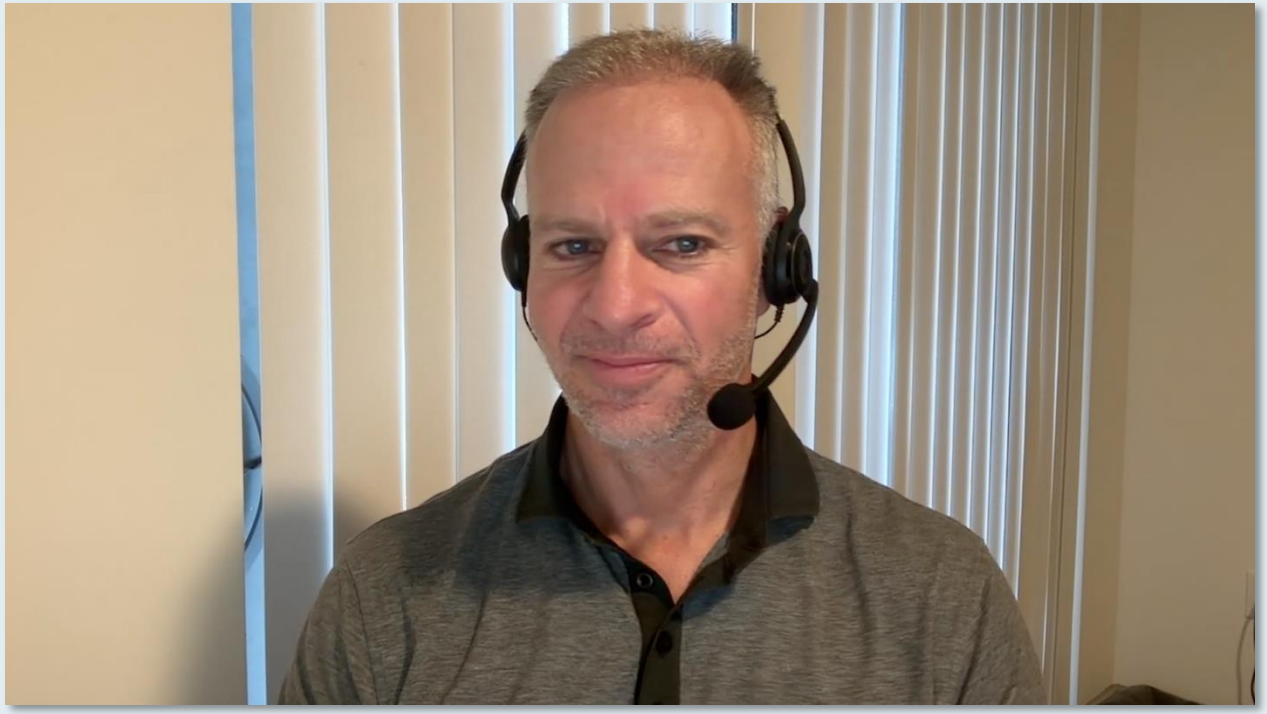
- Dr Brenner – 62-year-old woman diagnosed with SLL now with disease progression on ibrutinib
- Dr Ma – 46-year-old man with SLL who received second-line venetoclax/rituximab
- **Dr Brenner – Current role of pirtobrutinib; CAR T-cell therapy; Richter's transformation**
- Dr Rupard – 46-year-old African American man with progressive lymphadenopathy in the neck is diagnosed with CLL/SL
- Dr Bhatnagar – 77-year-old man with newly diagnosed IGHV-unmutated CLL (TP53 mutation) receives acalabrutinib

RTP RESEARCH TO PRACTICE

Questions for the Faculty: Current role of pirtobrutinib, unique toxicities; CAR T-cell therapy for the treatment of CLL, management of Richter's transformation



Dr Warren Brenner (Boca Raton, Florida)

RTP
RESEARCH TO PRACTICE

ASH | Annual Meeting & Exposition

1870 Outcomes of Therapies Following Discontinuation of Non-Covalent Brutonâ€™s Tyrosine Kinase Inhibitors for Patients with Chronic Lymphocytic Leukemia and Richter Transformation: Results from an International, Multicenter Study

Program: Oral and Poster Abstracts
Session: 642. Chronic Lymphocytic Leukemia: Clinical and Epidemiological: Poster I
Hematology Disease Topics & Pathways:
Research, Lymphoid Leukemias, Adult, CLL, Clinical Research, Diseases, Lymphoid Malignancies, Study Population, Human

Saturday, December 7, 2024, 5:30 PM-7:30 PM

Meghan C. Thompson, MD[1], *Seema A. Bhat, MD*[2*], *Wojciech Jurczak, MD, PhD*[3], *Krish Patel, MD*[4], *Nirav N. Shah, MD*[5], *Jennifer A. Woyach, MD*[6], *Catherine C. Coombs, MD*[7], *Toby A. Eyre*[8*], *Michal Danecki*[3*], *Monika Dlugosz-Danecka, MD, PhD*[3*], *Neil Bailey, MSc*[4], *Joanna M. Rhodes, MD, MSCE*[9*], *Nicole Lamanna, MD*[10], *Andrew H. Lipsky, MD*[10], *Jeffrey Jensen, MD, PhD*[11], *Adam Kidwell, MD*[5*], *Eytan M. Stein, MD*[1], *Monica Shah, BA*[1*], *Jennifer R. Brown, MD, PhD*[12], *Andriy Derkach, PhD*[13*], *Anthony R. Mato, MD*[14,15*] *and Lindsey Roeker, MD*[1]

Abstract 1870

RTP RESEARCH TO PRACTICE

Abstract Conclusions

- PFS for treatment following non-covalent BTKi (ncBTKi) dc was relatively short for patients with CLL (15 months) and patients with Richter's transformation (2 months).
- For patients with CLL, venetoclax-based therapy resulted in a high overall response rate (72%). The median PFS for venetoclax as first therapy after following ncBTKi dc was 23 months in this population whose disease was largely venetoclax-naïve, but heavily pretreated, supporting that venetoclax may be sequenced after ncBTKi dc.
- There is an unmet need for novel therapeutic approaches for patients with CLL and Richter's transformation after ncBTKi dc.

Thompson MC et al. ASH 2024;Abstract 1870.

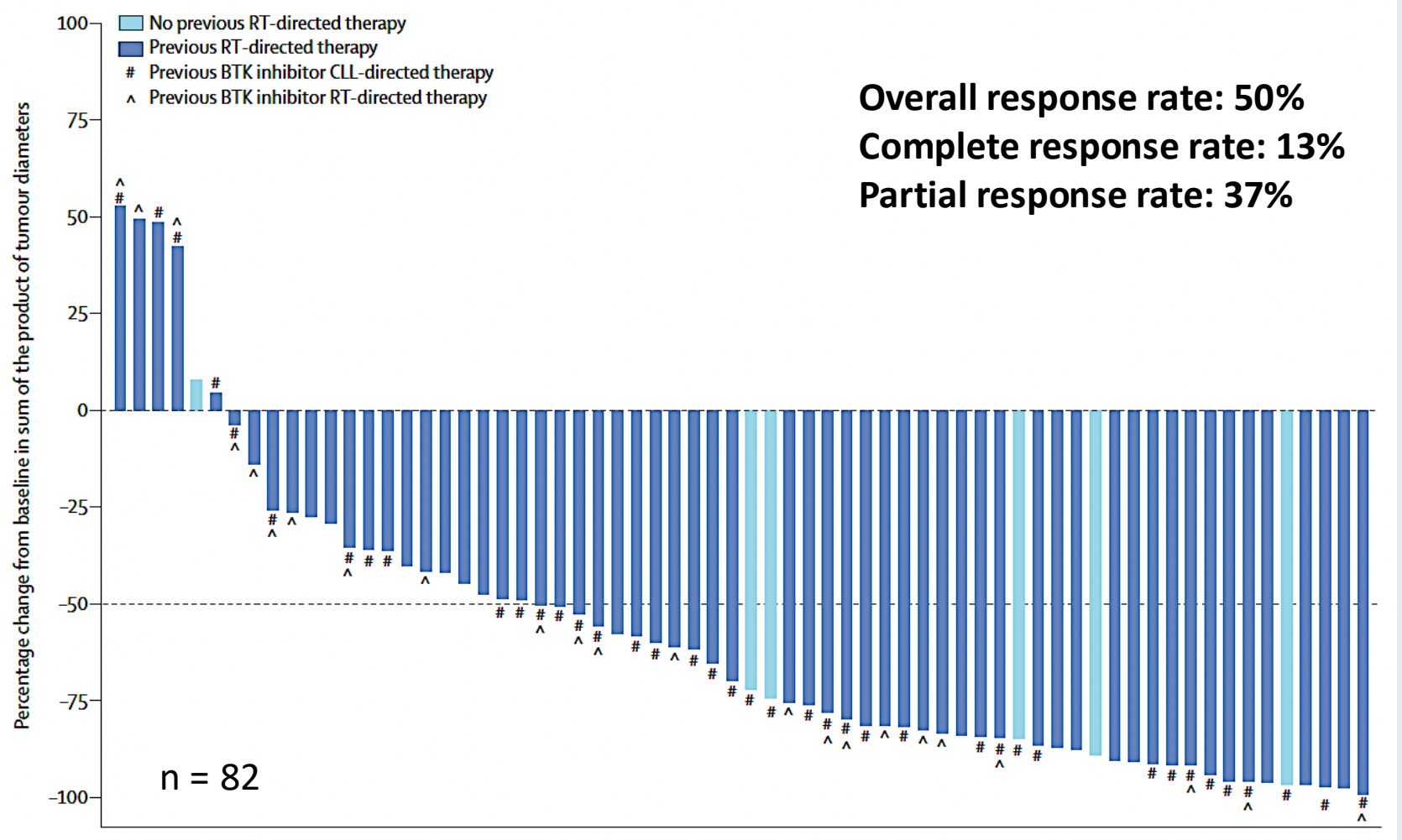
RTP RESEARCH TO PRACTICE

Pirtobrutinib, a highly selective, non-covalent (reversible) BTK inhibitor in patients with B-cell malignancies: analysis of the Richter transformation subgroup from the multicentre, open-label, phase 1/2 BRUIN study

William G Wierda, Nirav N Shah, Chan Y Cheah, David Lewis, Marc S Hoffmann, Catherine C Coombs, Nicole Lamanna, Shuo Ma, Deepa Jagadeesh, Talha Munir, Yucai Wang, Toby A Eyre, Joanna M Rhodes, Matthew McKinney, Ewa Lech-Maranda, Constantine S Tam, Wojciech Jurczak, Koji Izutsu, Alvaro J Alencar, Manish R Patel, John F Seymour, Jennifer A Woyach , Philip A Thompson, Paolo B Abada, Caleb Ho, Samuel C McNeely, Narasimha Marella, Bastien Nguyen, Chunxiao Wang, Amy S Ruppert, Binoj Nair, Hui Liu, Donald E Tsai, Lindsey E Roeker, Paolo Ghia

***Lancet Haematol* 2024 September;11(9):e682-92.**

BRUIN Subgroup Analysis: Activity of Pirtobrutinib in Patients with Richter's Transformation (RT)



- The most common Grade 3 or worse adverse event was neutropenia (n = 19).

Wierda WG et al. *Lancet Haematol* 2024 September;11(9):e682-92.

Epcoritamab in Patients with Relapsed or Refractory Chronic Lymphocytic Leukemia: Results from the Phase 1b/2 EPCORE CLL-1 Trial Expansion Cohort

Kater AP et al.

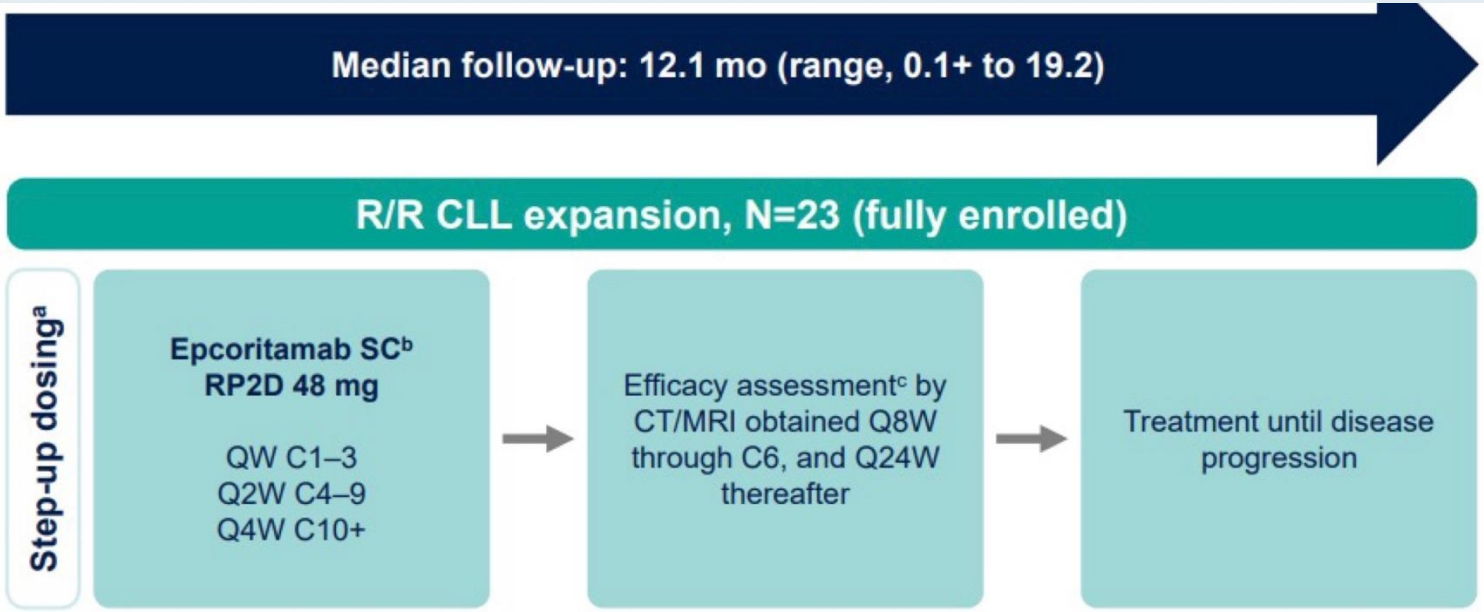
iwCLL 2023;Abstract 1546171.

RTP
RESEARCH TO PRACTICE

EPCORE CLL-1 Study Design

Key inclusion criteria

- CD20+ R/R CLL
- ≥2 prior lines of systemic therapy, including treatment with or intolerance to a BTK inhibitor
- ECOG PS 0–2
- Requiring treatment per iwCLL criteria
- Measurable disease with ≥5×10^9/L B lymphocytes or measurable lymphadenopathy or organomegaly
- No minimum life expectancy required



- **Primary endpoint:** Overall response rate (ORR)
- **Key secondary endpoints:** Complete response (CR) rate, time to response, and safety/tolerability

Data cutoff: July 5, 2023. Epcoritamab was administered in 28-d cycles. [a]Patients received epcoritamab SC with step-up dosing (ie, 0.16 mg priming and 0.8 mg intermediate doses before first full dose) and corticosteroid prophylaxis as previously described to mitigate CRS. [b]To ensure patient safety and better characterize CRS, inpatient monitoring was required for the first 4 doses of epcoritamab. [c]Based on iwCLL guidelines.

Kater AP et al. iwCLL 2023;Abstract 1546171.

RTP RESEARCH TO PRACTICE

EPCORE CLL-1: Response

Response, n (%)[a]	Total Efficacy Evaluable n=21	*TP53* Aberration n=14	Double-Exposed[b] n=17
Overall response[c]	**13 (62)**	**9 (64)**	**9 (53)**
Complete response	7 (33)	4 (29)	5 (29)
Partial response	6 (29)	5 (36)	4 (24)
Stable disease	4 (19)	2 (14)	4 (24)
Progressive disease	1 (5)	1 (7)	1 (6)
Not evaluable/no assessment[d]	3 (14)	2 (14)	3 (18)

Very encouraging overall and complete response rates observed, including in difficult-to-treat, high-risk R/R CLL patients

[a]Based on response-evaluable population, defined as patients who received ≥1 full dose of epcoritamab, had ≥1 postbaseline response evaluation, or died within 60 d of first dose.[b]Patients previously treated with both a BTK and a BCL-2 inhibitor. [c]Response assessment according to iwCLL criteria. [d]Two patients died without postbaseline assessment.

Kater AP et al. iwCLL 2023;Abstract 1546171.

RTP RESEARCH TO PRACTICE

Do you actively screen for BTK resistance mutations in your patients with CLL who experience disease progression on a BTK inhibitor?

 Dr Coombs	No
 Dr Davids	Yes, with in-house NGS assay
 Dr Kittai	Yes, with FoundationOne® NGS assay
 Dr Lamanna	Yes, NeoGenomics assay
 Dr Ujjani	Yes, with in-house NGS assay
 Dr Woyach	Yes, NGS assay

NGS = next-generation sequencing

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, what treatment would you recommend for a 75-year-old patient with IGHV-unmutated CLL and a TP53 mutation who developed Richter's transformation?

 Dr Coombs	R-CHOP + venetoclax
 Dr Davids	R-CHOP + venetoclax
 Dr Kittai	R-CHOP + venetoclax
 Dr Lamanna	Pirtobrutinib
 Dr Ujjani	R-CHOP
 Dr Woyach	R-CHOP + venetoclax

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Lamanna

Case Presentations and Questions for the Faculty:

- Dr Bhatnagar – 67-year-old man with IGHV-mutated CLL (trisomy 12) and progressive adenopathy
- Dr Rupard – 74-year-old woman with IGHV-unmutated, del(13q) CLL and fatigue
- Dr Bufalino – 85-year-old woman with del(13q) CLL under watchful waiting and progressive symptoms
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- **Dr Rupard – 46-year-old African American man with progressive lymphadenopathy in the neck is diagnosed with CLL/SL**
- Dr Bhatnagar – 77-year-old man with newly diagnosed IGHV-unmutated CLL (TP53 mutation) receives acalabrutinib

RTP RESEARCH TO PRACTICE

Case Presentation: 46-year-old African American man with progressive lymphadenopathy in the neck is diagnosed with CLL/SLL (trisomy 12, SF3B1 mutation) and starts receiving acalabrutinib with rapid response

Dr Erik Rupard (St George, Utah)

RTP RESEARCH TO PRACTICE

Racial Disparities in Real-World Treatment Patterns and Outcomes Among Patients with CLL

Rhodes J et al.

EHA 2023;Abstract P647.

JC JOURNAL CLUB
RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Lamanna

Case Presentations and Questions for the Faculty:

- Dr Bhatnagar – 67-year-old man with IGHV-mutated CLL (trisomy 12) and progressive adenopathy
- Dr Rupard – 74-year-old woman with IGHV-unmutated, del(13q) CLL and fatigue
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- Dr Rupard – 46-year-old African American man with progressive lymphadenopathy in the neck is diagnosed with CLL/SL
- Dr Bhatnagar – 77-year-old man with newly diagnosed IGHV-unmutated CLL (TP53 mutation) receives acalabrutinib

RTP RESEARCH TO PRACTICE

Case Presentation: 77-year-old man with newly diagnosed IGHV-unmutated CLL (TP53 mutation) receives acalabrutinib but experiences nausea, arthralgia, myalgia, joint swelling and rash

Dr Tina Bhatnagar (Wheeling, West Virginia)

RTP RESEARCH TO PRACTICE

Original Study

Treatment Discontinuation Patterns for Patients With Chronic Lymphocytic Leukemia in Real-World Settings: Results From a Multi-Center International Study

Mazyar Shadman,[1] Beenish S. Manzoor,[2] Kavita Sail,[2] Hande H. Tuncer,[3] John N. Allan,[4] Chaitra Ujjani,[1] Nnadozie Emechebe,[2] Rajesh Kamalakar,[2] Catherine C. Coombs,[5] Lori Leslie,[6] Paul M. Barr,[7] Jennifer R. Brown,[8] Toby A. Eyre,[9] Alexandros Rampotas,[9] Anna Schuh,[9] Nicole Lamanna,[10] Alan Skarbnik,[11] Lindsey E. Roeker,[12] Rajat Bannerji,[13] Barbara Eichhorst,[14] Isabelle Fleury,[15] Matthew S. Davids,[8] Hasan Alhasani,[2] Dingfeng Jiang,[2] Brian T. Hill,[16] Stephen J. Schuster,[17] Danielle M. Brander,[18] Irina Pivneva,[19] Rebecca Burne,[19] Annie Guerin,[19] Anthony R. Mato[12]

Clin Lymphoma Myeloma Leuk 2023;23(7):515-26.

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

APPENDIX

Long-Term Safety with ≥12 Months of Pirtobrutinib in Relapsed/Refractory (R/R) B-Cell Malignancies

Wojciech Jurczak (Presenter)[1], Catherine C. Coombs[2], Nirav N. Shah[3], Jennifer Woyach[4], Chan Y. Cheah[5], Krish Patel[6], Kami Maddocks[4], Yucai Wang[7], Catherine E. Muehlenbein[8], Chunxiao Wang[9], Sarang Abhyankar[8], Donald E. Tsai[8], Toby A. Eyre[10]

[1]Maria Sklodowska-Curie National Research Institute of Oncology, Krakow, Poland; [2]UCI Health, Orange, CA, USA; [3]Medical College of Wisconsin, Milwaukee, WI, USA; [4]The Ohio State University Comprehensive Cancer Center, Columbus, USA; [5]Linear Clinical Research and Sir Charles Gairdner Hospital, Perth, Australia; [6]Center for Blood Disorders and Cellular Therapy, Swedish Cancer Institute, Seattle, WA, USA; [7]Division of Hematology, Mayo Clinic, Rochester, MN, USA; [8]Loxo@Lilly, Indianapolis, IN, USA; [9]Eli Lilly and Company, Indianapolis, IN, USA; [10]Oxford University Hospitals NHS Foundation Trust, Churchill Cancer Center, Oxford, United Kingdom

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RTP RESEARCH TO PRACTICE

BRUIN: Pirtobrutinib Safety Profile in Patients with ≥12 Months Treatment and in the Overall Safety Population

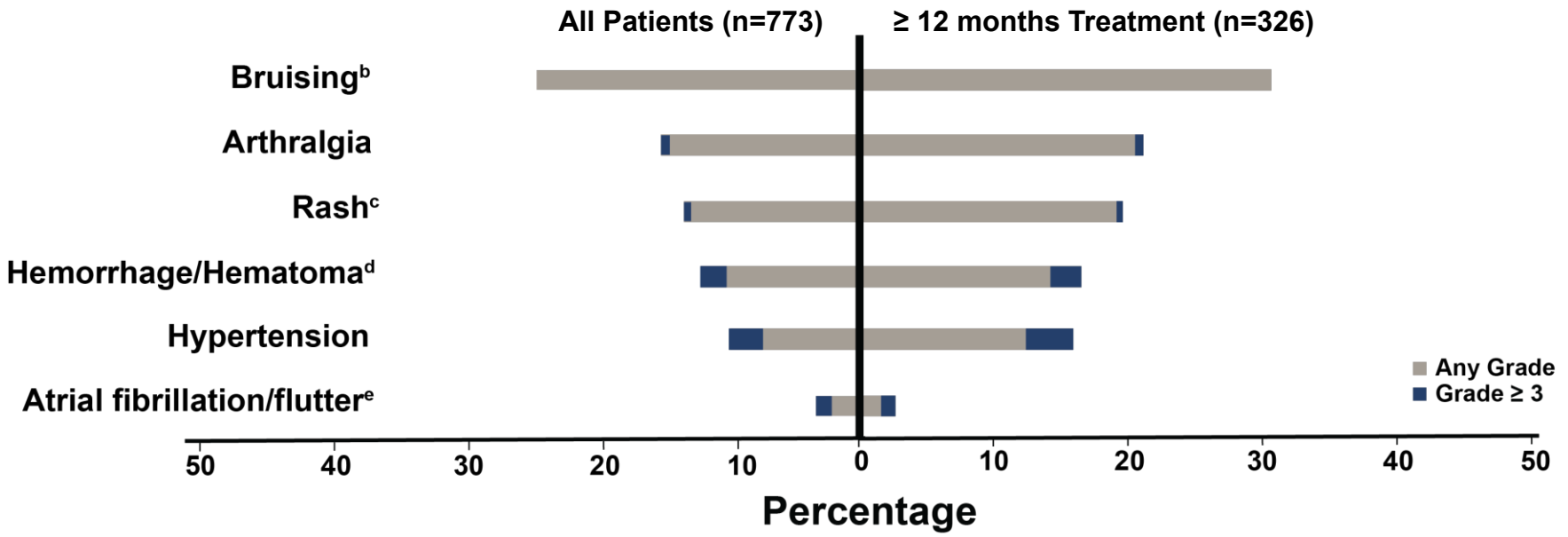
Treatment Emergent AEs (≥15%)	≥12 Months Treatment (N=326)				All Patients (N=773)			
	Any Grade TEAE (%)	Grade ≥3 TEAE (%)	Leading to Dose Reduction (%)	Leading to Drug Discontinuation (%)	Any Grade TEAE (%)	Grade ≥3 TEAE (%)	Leading to Dose Reduction (%)	Leading to Drug Discontinuation (%)
Fatigue	32.2	1.2	0	0	28.7	2.1	0.4	0.3
Diarrhea	30.7	1.2	0.3	0	24.2	0.9	0.3	0
Neutropenia[a]	29.8	23.9	3.1	0.6	25.0	20.3	2.1	0.5
Covid-19	28.5	4.3	0.3	0	16.7	2.7	0.1	0.4
Contusion	25.8	0	0.3	0	19.4	0	0.1	0
Cough	24.5	0	0	0	17.5	0.1	0.1	0
Back Pain	20.9	0.9	0	0	12.7	0.5	0	0
Headache	18.4	0.6	0	0	13.1	0.5	0.1	0
Upper Respiratory Tract Infection	18.1	0	0	0	9.8	0.1	0	0
Nausea	17.5	0.3	0	0	16.2	0.1	0.1	0.1
Dyspnea	17.2	0.6	0.3	0	15.5	1.0	0.1	0.1
Abdominal Pain	16.3	0.9	0	0	13.1	1.0	0	0.1
Constipation	16.3	0	0	0	13.6	0.3	0	0
AEs of Special Interest[b]	**Any Grade TEAE (%)**	**Grade ≥3 TEAE (%)**	**Leading to Dose Reduction (%)**	**Leading to Drug Discontinuation (%)**	**Any Grade TEAE (%)**	**Grade ≥3 TEAE (%)**	**Leading to Dose Reduction (%)**	**Leading to Drug Discontinuation (%)**
Bruising[c]	30.7	0	0.3	0	23.7	0	0.1	0
Arthralgia	21.2	0.6	0	0	14.4	0.6	0	0
Rash[d]	19.6	0.3	0	0	12.7	0.5	0.3	0.1
Hemorrhage/ Hematoma[e]	16.6	2.1	0	0	11.4	1.8	0	0
Hypertension	16.0	3.4	0.3	0	9.2	2.3	0.1	0
Atrial fibrillation/ flutter[f]	2.8	0.9	0	0	2.8	1.2	0	0

Data cutoff date of 29 July 2022. [a]Aggregate of neutropenia and neutrophil count decreased. [b]AEs of special interest are those that were previously associated with covalent BTK inhibitors. [c]Aggregate of contusion, petechiae, ecchymosis, and increased tendency to bruise. [d]Aggregate of all preferred terms including rash. [e]Aggregate of all preferred terms including hematoma or hemorrhage. [f]Aggregate of atrial fibrillation and atrial flutter.

Jurczak W et al. EHA 2023;Abstract P618.

RTP RESEARCH TO PRACTICE

BRUIN: Selected Adverse Events (AEs) of Special Interest



Data cutoff date of 29 July 2022. [a]AEs of special interest are those that were previously associated with covalent BTK inhibitors. [b]Aggregate of contusion, petechiae, ecchymosis, and increased tendency to bruise. [c]Aggregate of all preferred terms including rash. [d]Aggregate of all preferred terms including hematoma or hemorrhage. [e]Aggregate of atrial fibrillation and atrial flutter.

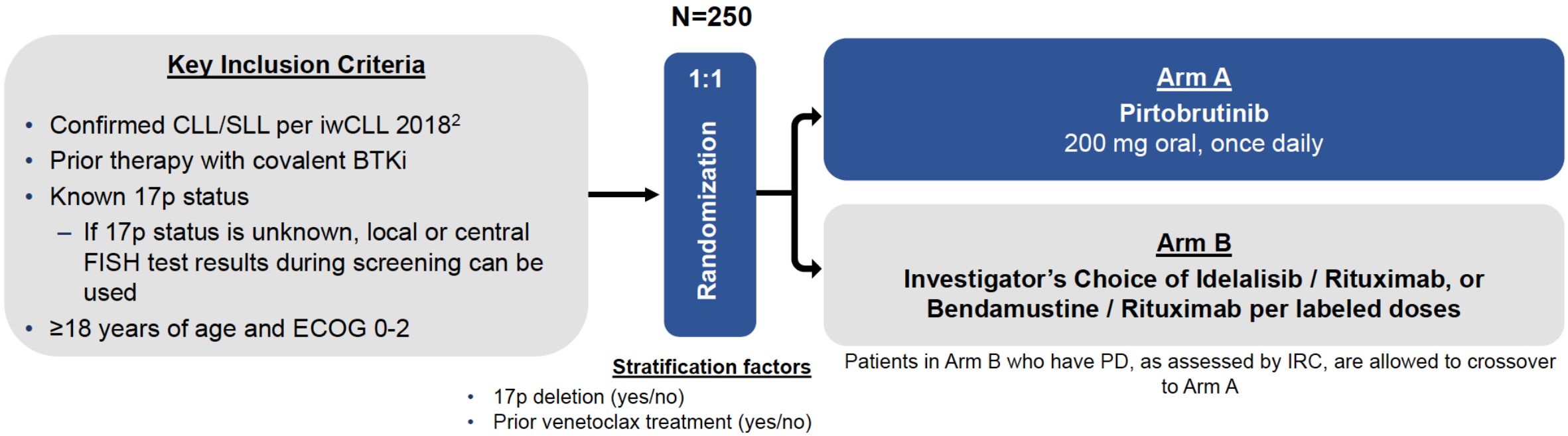
Among the 326 patients who received ≥12 months treatment:

- Most TEAEs and AEs of special interest were low grade and did not lead to dose reduction or discontinuation
- 42% of the patients with treatment-emergent hypertension had a pre-existing medical history of hypertension
- In total, across all TEAEs, dose reduction or discontinuation occurred in 23 (7%) and 11 (3%) patients, respectively
- **With additional treatment, the rates of selected AEs of special interest did not show clinically meaningful increases, particularly Grade ≥3**

TEAEs = treatment-emergent adverse events

Jurczak W et al. EHA 2023;Abstract P618.

BRUIN CLL-321: An Ongoing Phase III Trial of Pirtobrutinib Monotherapy for Relapsed/Refractory CLL



Primary endpoint: Progression-free survival per iwCLL 2018 by IRC

iwCLL = International Workshop on Chronic Lymphocytic Leukemia; IRC = independent review committee; FISH = fluorescence in situ hybridization; ECOG = Eastern Cooperative Oncology Group; PD = disease progression

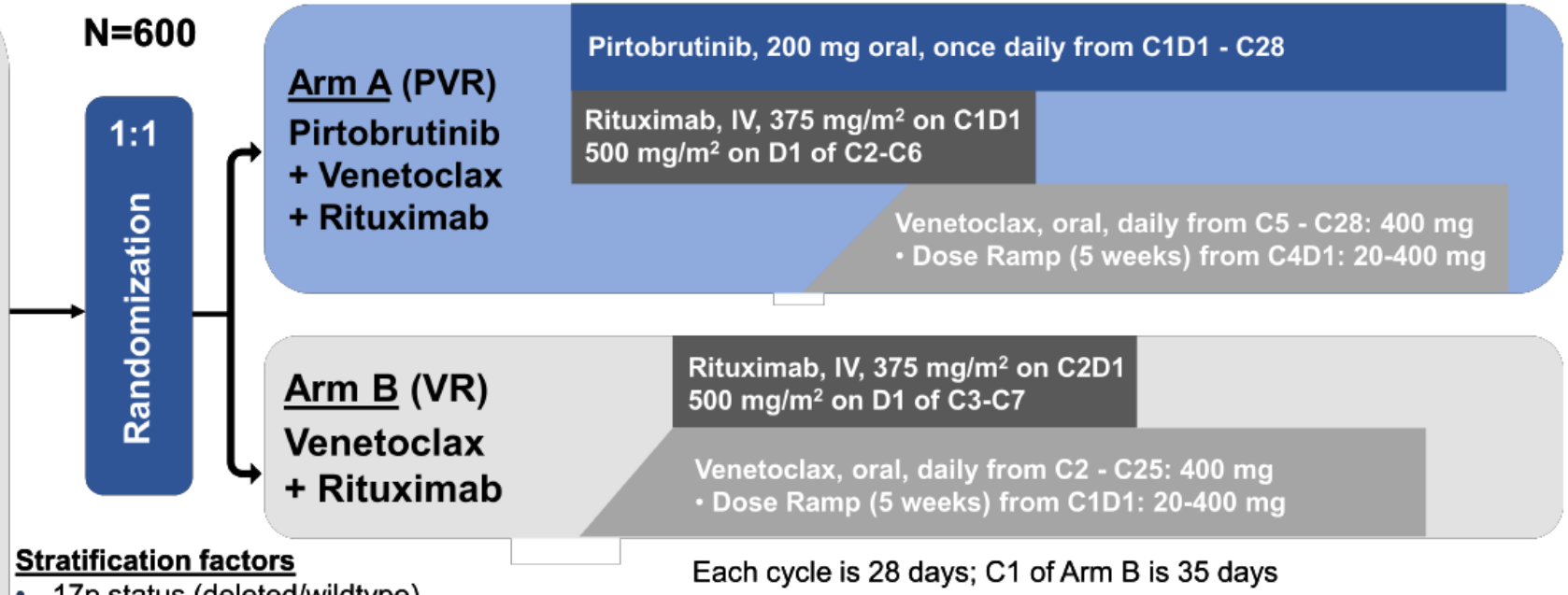
Follows G et al. ASCO 2023;Abstract TPS7582. Hill M et al. SOHO 2022;Abstract CLL-114.

RTP RESEARCH TO PRACTICE

BRUIN CLL-322: An Ongoing Phase III Trial of Pirtobrutinib and Venetoclax/Rituximab for Relapsed/Refractory CLL

Key Inclusion Criteria

- Confirmed CLL/SLL per iwCLL 2018[3]
- Previously treated CLL/SLL (including a covalent BTKi or covalent BTKi naïve [limited to 20% of total enrollment])
- Known 17p status
  - If 17p status is unknown, local or central FISH test results during screening can be used
- No prior venetoclax
- ≥18 years of age and ECOG 0-2



Stratification factors

- 17p status (deleted/wildtype)
- Prior experience of BTKi (discontinuation due to PD or other vs no prior BTKi)

Primary endpoint: Progression-free survival per iwCLL 2018 by IRC

RTP RESEARCH TO PRACTICE

Eyre TA et al. ASCO 2023;Abstract TPS7583. Wierda WG et al. SOHO 2022;Abstract CLL-322.

Bhavana (Tina) Bhatnagar, DO
WVU Cancer Institute
Wheeling, West Virginia

Yanjun Ma, MD
Tennessee Oncology
Murfreesboro, Tennessee

Shams Bufalino, MD
Advocate Aurora Health
Park Ridge, Illinois

Erik Rupard, MD
Intermountain Health
St George, Utah

Warren S Brenner, MD
Lynn Cancer Institute
Boca Raton, Florida

RTP
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TO PRACTICE

A Live Webinar for Patients

Cancer Q&A: Addressing Common Questions from Patients with Metastatic Triple-Negative Breast Cancer

Developed in Partnership with the Triple Negative Breast Cancer Foundation

Wednesday, November 13, 2024
6:00 PM – 7:00 PM ET

Faculty

Lisa A Carey, MD, ScM, FASCO
Rita Nanda, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Thank you for joining us!

Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to us. The survey will remain open for 5 minutes after the meeting ends.

Information on how to obtain CME and ABIM MOC credit is provided in the Zoom chat room. Attendees will also receive an email in 1 to 3 business days with these instructions.

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