Thank you for joining us.
The program will begin momentarily.

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Optimizing the Selection and Sequencing of Therapy for Patients with Chronic Lymphocytic Leukemia

A Meet The Professor Series

Jeff Sharman, MD
Willamette Valley Cancer Institute and Research Center
Medical Director of Hematology Research
US Oncology
Eugene, Oregon

Commercial Support

These activities are supported by educational grants from AbbVie Inc and AstraZeneca Pharmaceuticals LP.

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Dr Love — Disclosures

Dr Love is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following commercial interests: AbbVie Inc, Acerta Pharma — A member of the AstraZeneca Group, Adaptive Biotechnologies Corporation, Agendia Inc, Agios Pharmaceuticals Inc, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Biodesix Inc, bioTheranostics Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Daiichi Sankyo Inc, Dendreon Pharmaceuticals Inc, Eisai Inc, EMD Serono Inc, Exelixis Inc, Foundation Medicine, Genentech, a member of the Roche Group, Genmab, Genomic Health Inc, Gilead Sciences Inc, GlaxoSmithKline, Grail Inc, Guardant Health, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Infinity Pharmaceuticals Inc, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Kite, A Gilead Company, Lexicon Pharmaceuticals Inc, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Merrimack Pharmaceuticals Inc, Myriad Genetic Laboratories Inc, Natera Inc, Novartis, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Prometheus Laboratories Inc, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sandoz Inc, a Novartis Division, Sanofi Genzyme, Seattle Genetics, Sirtex Medical Ltd, Spectrum Pharmaceuticals Inc, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro, A GSK Company, Teva Oncology, Tokai Pharmaceuticals Inc and Verastem Inc.

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

Dr Sharman — Disclosures

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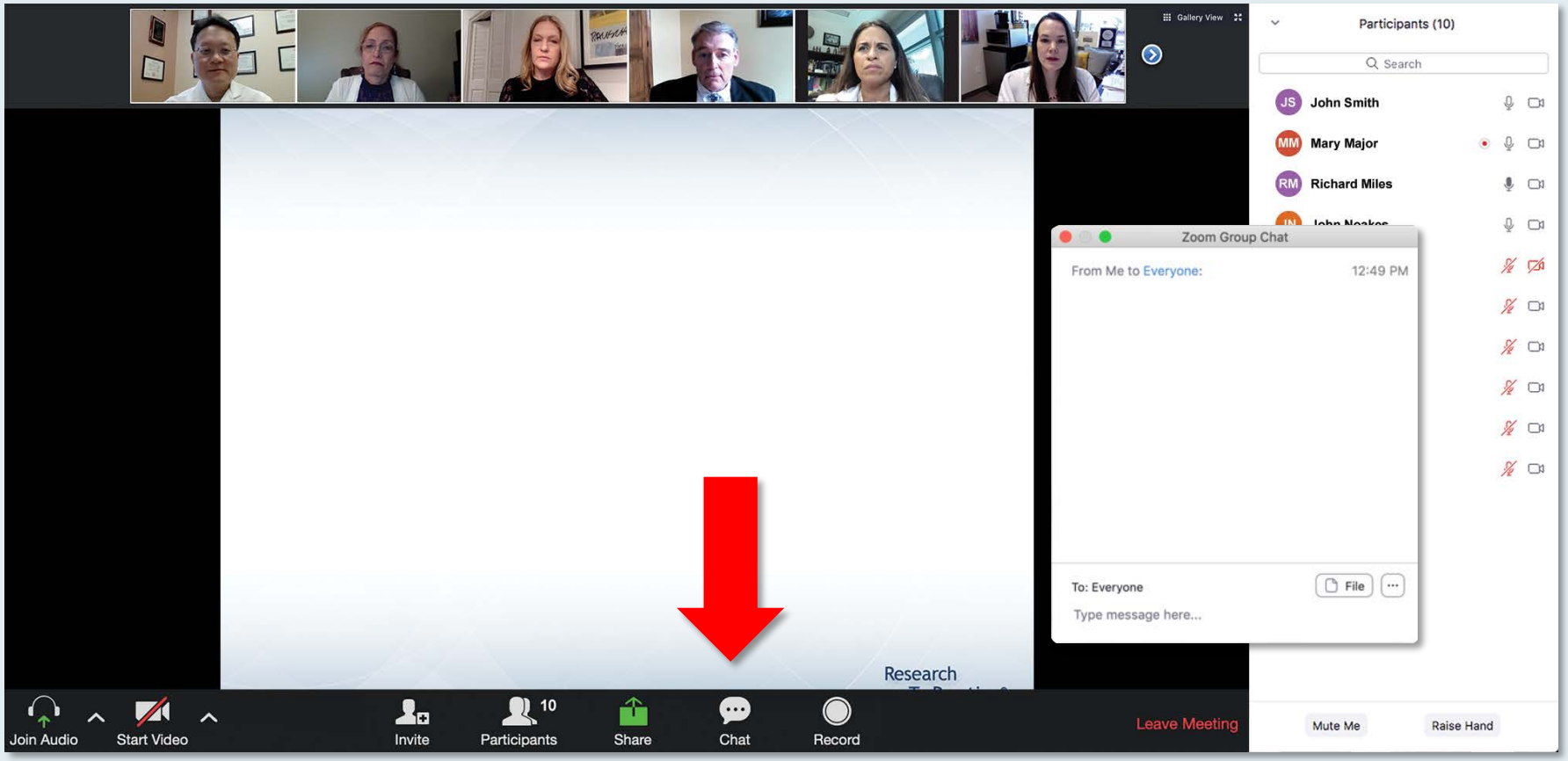
We Encourage Clinicians in Practice to Submit Questions



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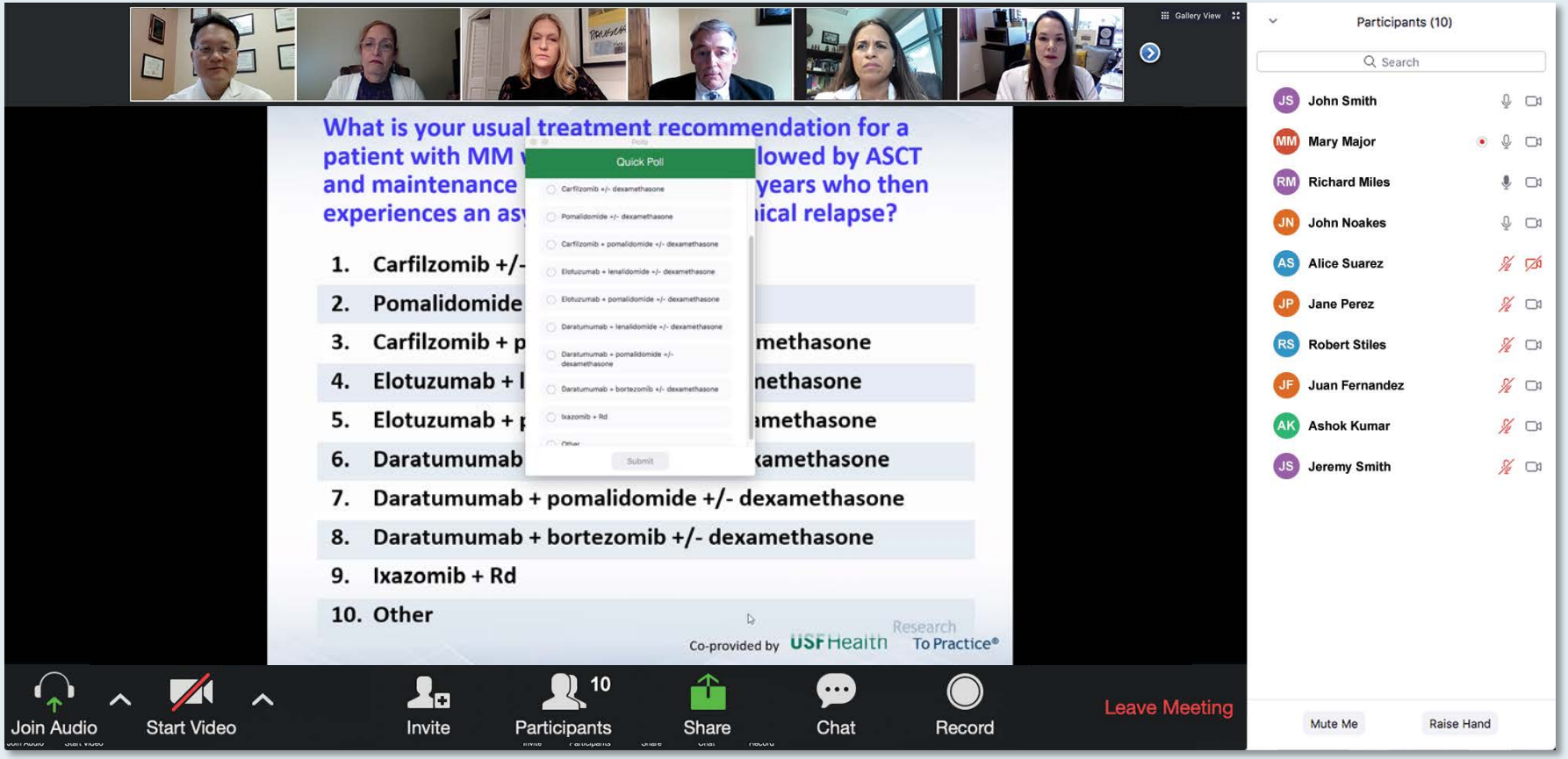
How to answer poll questions



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RTP RESEARCH TO PRACTICE

Upcoming Live Webinars

Thursday, September 24, 2020
12:00 PM – 1:00 PM ET

Exploring the Role of Immune Checkpoint Inhibitor Therapy and Other Novel Strategies in Gynecologic Cancers

Faculty
David M O'Malley, MD

Moderator
Neil Love, MD

Tuesday, September 29, 2020
12:00 PM – 1:00 PM ET

Current Questions and Controversies in the Management of Lung Cancer

Faculty
Benjamin Levy, MD

Moderator
Neil Love, MD

Upcoming Live Webinars

Thursday, October 1, 2020
12:00 PM – 1:00 PM ET

Clinical Investigator Perspectives on the Current and Future Role of PARP Inhibition in the Management of Ovarian Cancer

Faculty
Ursula Matulonis, MD

Moderator
Neil Love, MD

Friday, October 2, 2020
12:00 PM – 1:00 PM ET

Optimizing the Selection and Sequencing of Therapy for Patients with Chronic Lymphocytic Leukemia

Faculty
William G Wierda, MD, PhD

Moderator
Neil Love, MD

Thank you for joining us!

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

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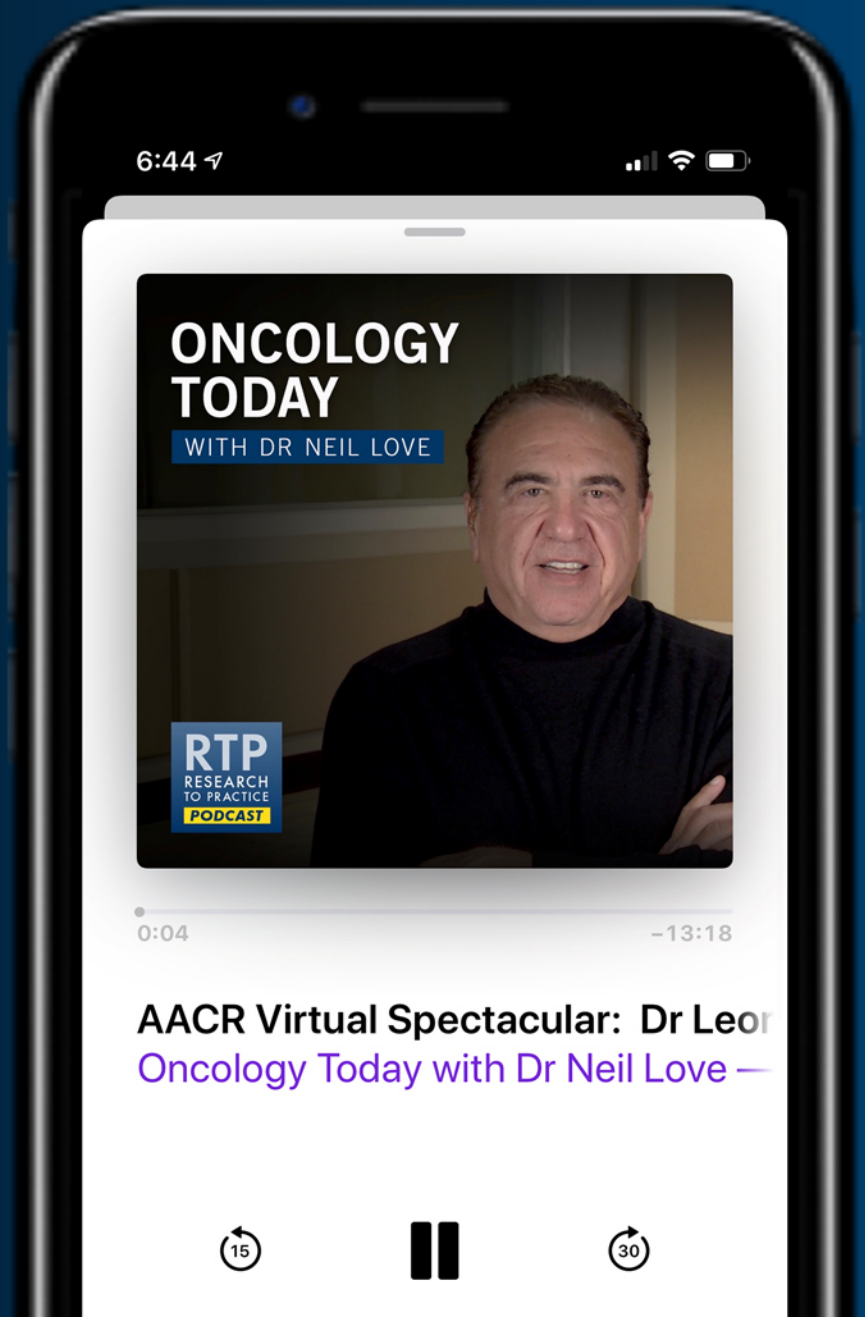

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Jeff Sharman, MD
Willamette Valley Cancer Institute and Research Center
Medical Director of Hematology Research
US Oncology
Eugene, Oregon

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Matthew S Davids, MD, MMSc
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Director of Clinical Research
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Brian T Hill, MD, PhD
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Ian W Flinn, MD, PhD
Director of Lymphoma Research Program
Sarah Cannon Research Institute
Tennessee Oncology
Nashville, Tennessee

Brad S Kahl, MD
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Washington University School of Medicine
Director, Lymphoma Program
Siteman Cancer Center
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Meet The Professor Program Participating Faculty

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Kerry Rogers, MD
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The Ohio State University
Columbus, Ohio

John M Pagel, MD, PhD
Chief of Hematologic Malignancies
Center for Blood Disorders and Stem Cell Transplantation
Swedish Cancer Institute
Seattle, Washington

Jeff Sharman, MD
Willamette Valley Cancer Institute and Research Center
Medical Director of Hematology Research
US Oncology
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Meet The Professor Program Participating Faculty

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Associate Center Director for Clinical Investigations
Director, Division of Hematology and Oncology
GW Cancer Center
Washington, DC

Jennifer Woyach, MD
Professor
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William G Wierda, MD, PhD
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Houston, Texas

Project Chair
Neil Love, MD
Research To Practice
Miami, Florida

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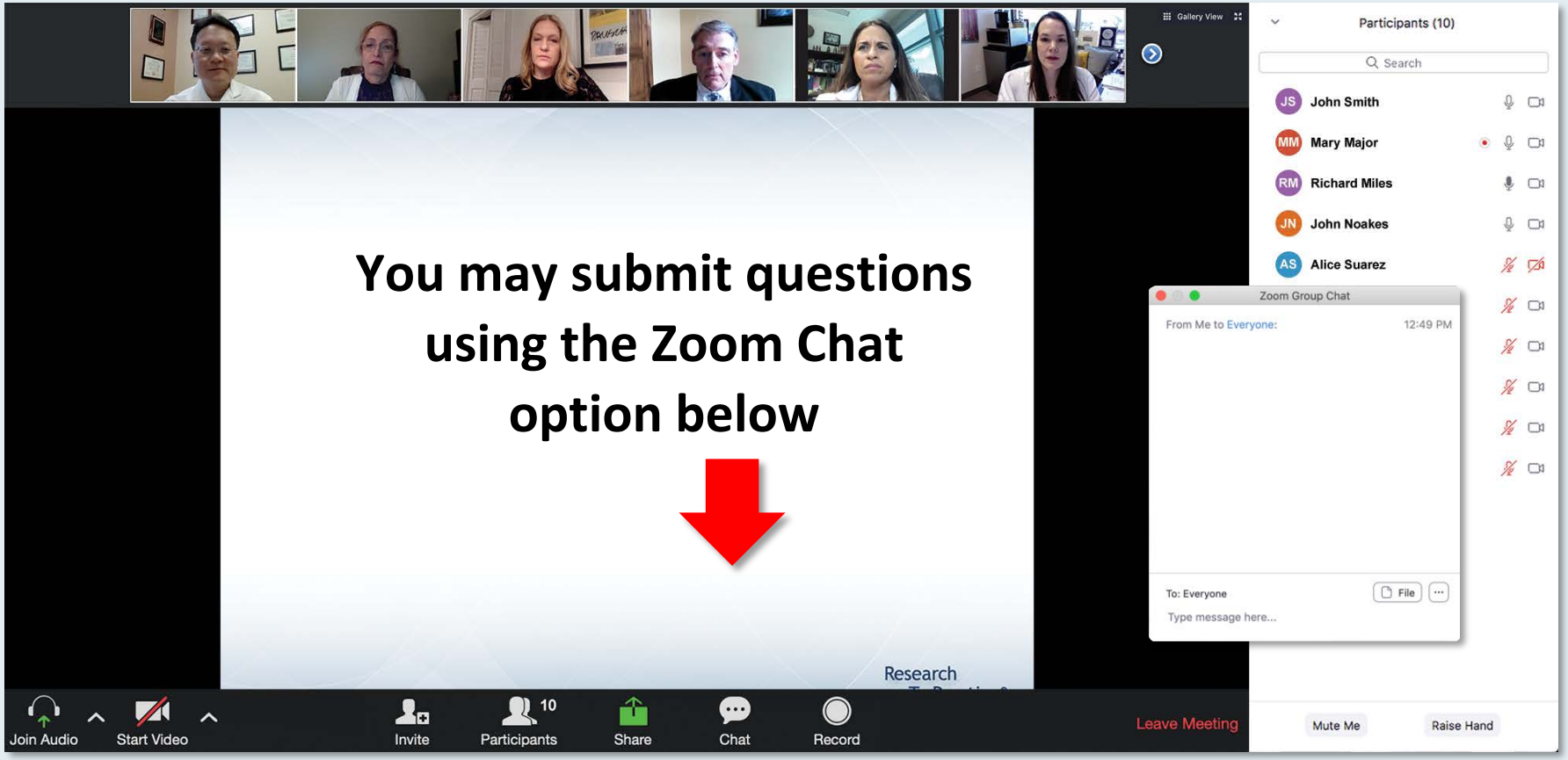
We Encourage Clinicians in Practice to Submit Questions



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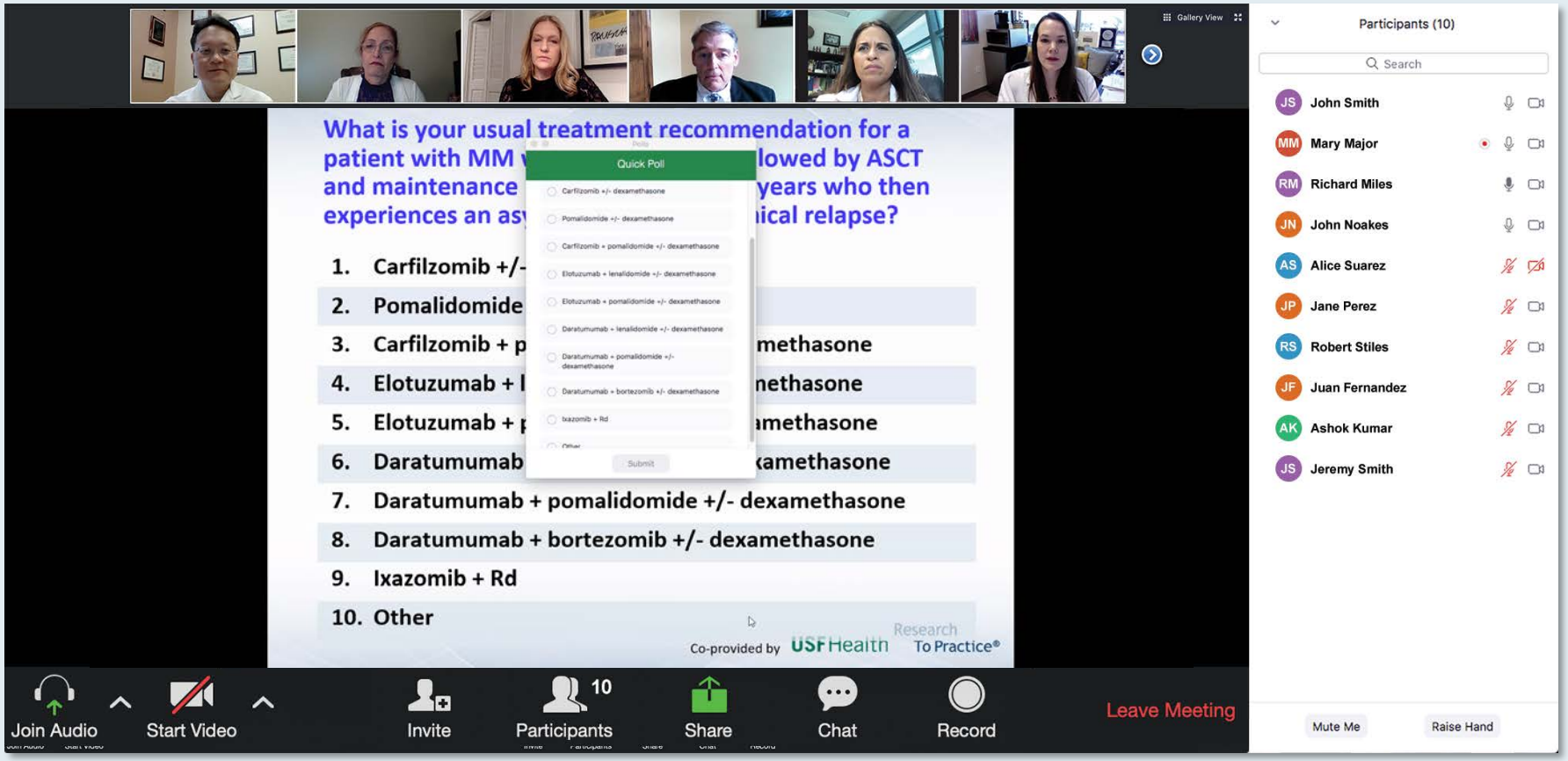

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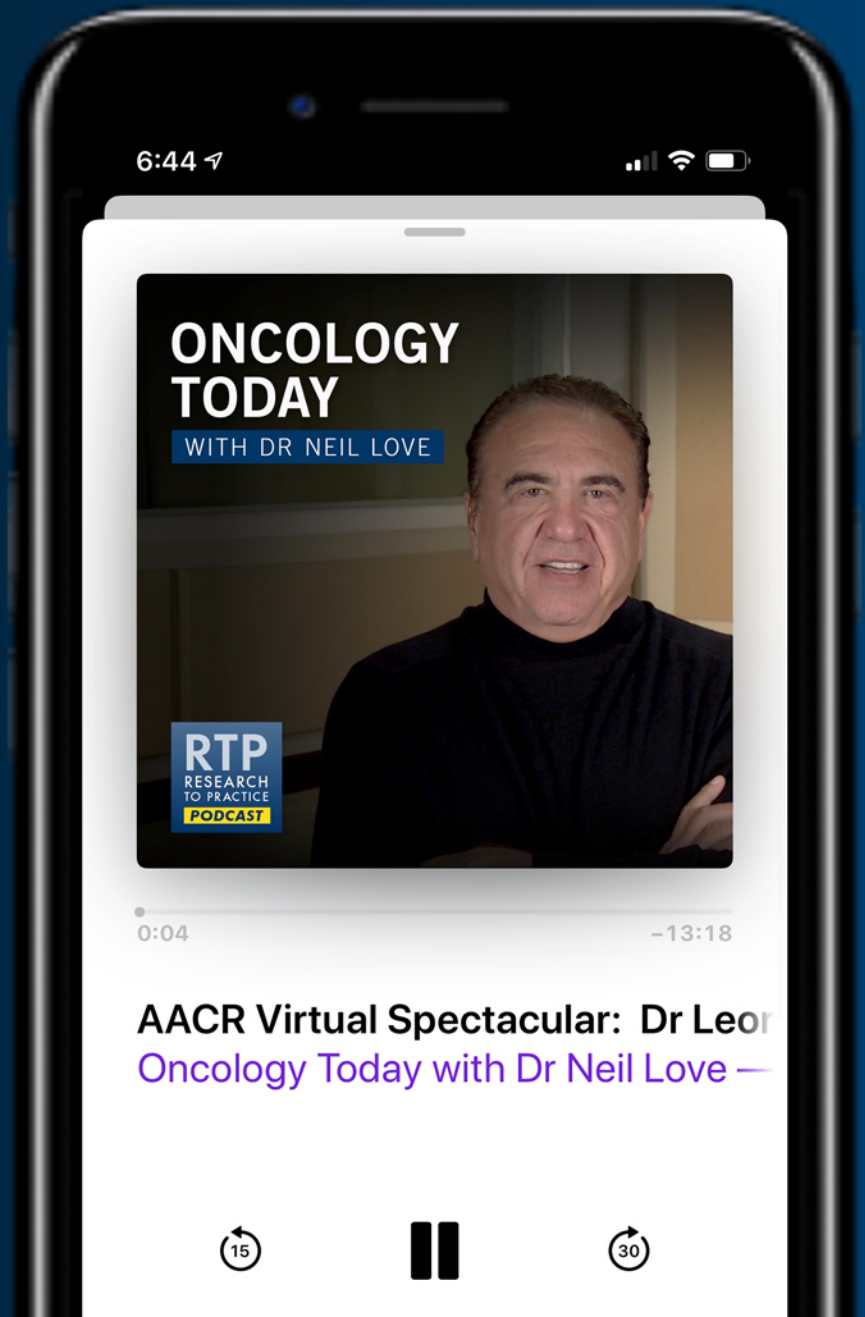

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Meet The Professor with Dr Sharman

MODULE 1: Cases from Dr Rogers

- Comments and Questions: Impact of COVID-19 on treatment decision-making
- A 57-year-old man with relapsed/refractory (R/R) CLL
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MODULE 2: CLL Journal Club with Dr Sharman

- BTK inhibitors in patients with severe COVID-19
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MODULE 3: Beyond the Guidelines – Clinical Investigator Approaches to Common Clinical Scenarios

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Comments and Questions: Impact of COVID-19 on treatment decision-making

Dr Kerry Rogers

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Science Immunology

RESEARCH ARTICLES

Cite as: M. Roschewski *et al.*, *Sci. Immunol.* 10.1126/sciimmunol.abd0110 (2020).

CORONAVIRUS

Inhibition of Bruton tyrosine kinase in patients with severe COVID-19

Mark Roschewski[1*], Michail S. Lionakis[2*], Jeff P. Sharman[3*], Joseph Roswarski[4*], Andre Goy[5], M. Andrew Monticelli[6], Michael Roshon[7], Stephen H. Wrzesinski[8], Jigar V. Desai[2], Marissa A. Zarakas[2], Jacob Collen[9], Keith Rose[5], Ahmed Hamdy[10], Raquel Izumi[10], George W. Wright[11], Kevin K. Chung[9], Jose Baselga[12], Louis M. Staudt[1#], Wyndham H. Wilson[1#†]

Meet The Professor with Dr Sharman

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Case Presentation – Dr Rogers: A 57-year-old man with relapsed/refractory CLL

Dr Kerry Rogers

- 2013: Presented to ENT with enlarged cervical lymph nodes for 2 or 3 years
- Excisional lymph node biopsy: CLL/SLL, no constitutional symptoms
  - IGHV unmutated; Cytogenetics: FISH + del11q, karyotype del11q
  - Bendamustine/rituximab x 6, with all lymph nodes resolved → Observation
- 4/2019: Enlarged cervical lymph nodes → Ibrutinib due to fewer treatment visits
- 6/2019: Multiple painful swollen joints (inflammatory arthritis) → Prednisone x 2 weeks, hold ibrutinib
- 7/2019: Ibrutinib restarted at 280 mg PO daily → Recurrent joint inflammation, panniculitis

Case Presentation – Dr Rogers: A 57-year-old man with relapsed/refractory CLL (continued)

Dr Kerry Rogers

- 2013: Presented to ENT with enlarged cervical lymph nodes for 2 or 3 years
- Excisional lymph node biopsy: CLL/SLL, no constitutional symptoms
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- 4/2019: Enlarged cervical lymph nodes → Ibrutinib due to fewer treatment visits
- 6/2019: Multiple painful swollen joints (inflammatory arthritis) → Prednisone x 2 weeks, hold ibrutinib
- 7/2019: Ibrutinib restarted at 280 mg PO daily → Recurrent joint inflammation, panniculitis
  - Second course of prednisone, ibrutinib discontinued
- 7/2019: Returns feeling better, enlarged cervical lymph nodes → Acalabrutinib
- 2020: Continues to tolerate acalabrutinib well (minor headaches, increased bruising)

Questions

- Do you dose reduce either ibrutinib or acalabrutinib for side effects?
- What are your thoughts about the choice between BTK inhibitors compared to venetoclax/rituximab for patients who relapse after chemoimmunotherapy?

Case Presentation – Dr Rogers: A 44-year-old man with newly diagnosed CLL – Del(17p)

Dr Kerry Rogers

- 1/2020: Lymphocytosis, small but enlarged cervical nodes, mild fatigue
- 6/2020: Fatigue x 6 months, cervical lymph nodes enlarging, visible to friends, ~25 lb weight loss since January, feeling poorly
- Peripheral blood immunophenotyping: CLL
  - IGHV unmutated; FISH: del17p, complex karyotype
  - NGS: TP53 mutation (VAF 98.8%)
  - PET scan: All SUV < 5
- Ibrutinib due to daily dosing and no interactions with PPI
- Discussed future use of CAR-T or allotransplant

Questions

- How many people would prescribe a BTK inhibitor over obinutuzumab/venetoclax for a patient with high-risk disease?

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Comments and Questions: Optimal timing for referral to CAR-T therapy or allogeneic stem cell transplant

Dr Kerry Rogers

RTP RESEARCH TO PRACTICE

Case Presentation – Dr Rogers: A 65-year-old man with relapsed/refractory CLL

Dr Kerry Rogers

- 2010: Diagnosed with CLL in pulmonary clinic (COPD, sarcoidosis)
  - Cervical lymph nodes and lymphocytosis noted, >20% weight loss
  - IGHV unmutated (0%)
  - Cytogenetics: del11q, normal karyotype
- FCR x 6, with partial remission → Observation
- 2019: Enlarging cervical lymph node (8 x 6-cm) but otherwise feels well
- Repeat cytogenetics: FISH +del11q, complex karyotype
- Venetoclax/rituximab, with outpatient venetoclax dose escalation

Questions

Does everyone consider warfarin a contraindication for BTK inhibitors – either ibrutinib or acalabrutinib?

Are there patients to whom you would prescribe a BTK inhibitor, who had to take warfarin due to mechanical heart valves?

When do you decide to do inpatient versus outpatient venetoclax dose escalation?

Meet The Professor with Dr Sharman

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Br J Haematol 2019;186:130-95

Tumour debulking and reduction in predicted risk of tumour lysis syndrome with single-agent ibrutinib in patients with chronic lymphocytic leukaemia

William G. Wierda[1]
John C. Byrd[2]
Susan O'Brien[3]
Steven Coutre[4]
Paul M. Barr[5]
Richard R. Furman[6]
Thomas J. Kipps[7]
Jan A. Burger[1]
Don A. Stevens[8]
Jeff Sharman[9]
Paolo Ghia[10]
Ian W. Flinn[11]
Cathy Zhou[12]
Joi Ninomoto[12]
Danelle F. James[12]
Constantine S. Tam[13]

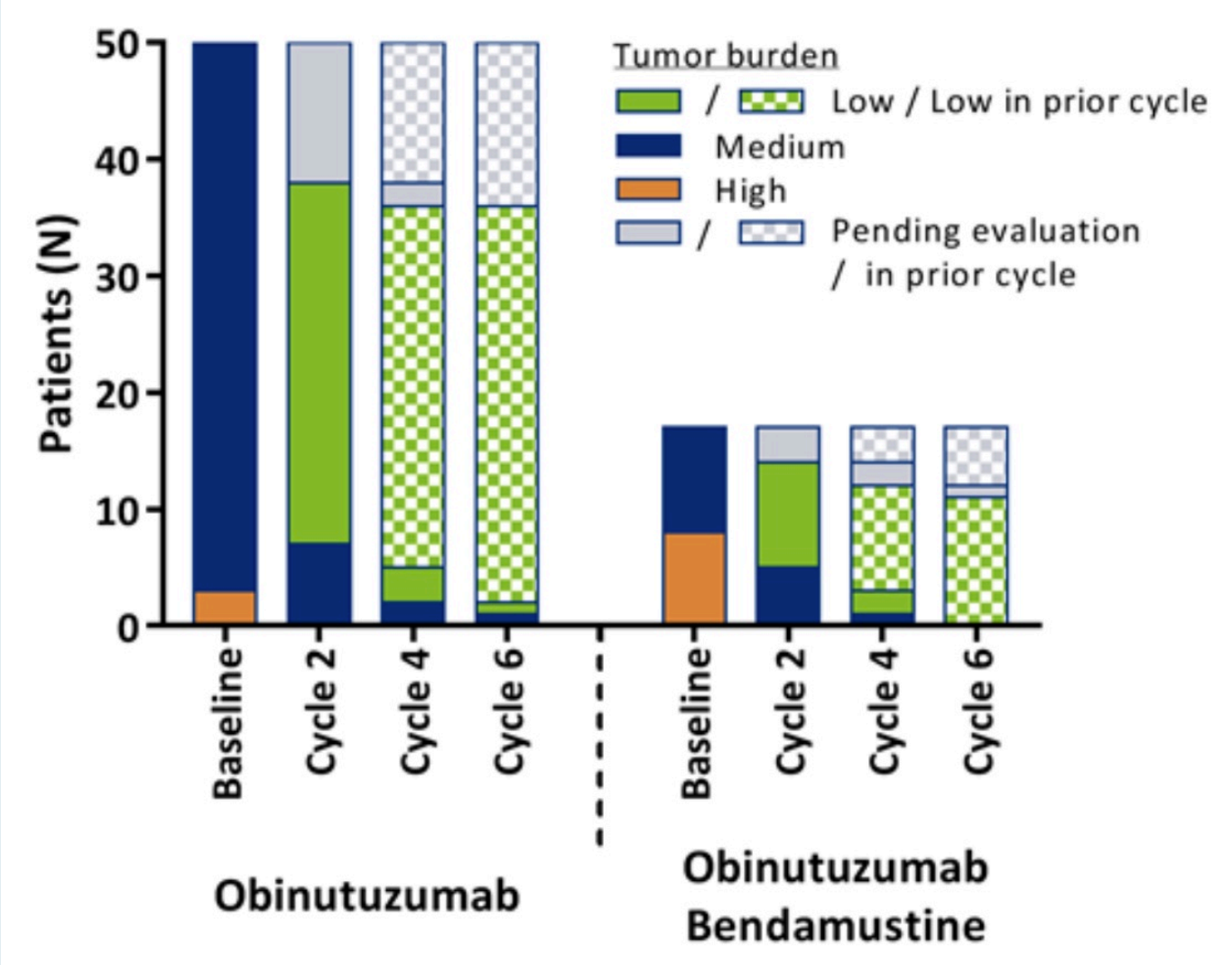
[1]University of Texas, MD Anderson Cancer Center, Houston, TX, [2]The Ohio State University Medical Center, Columbus, OH, [3]University of California Irvine, Irvine, [4]Stanford University School of Medicine, Stanford, CA, [5]Wilmot Cancer Institute, University of Rochester Medical Center, Rochester, [6]Weill Cornell Medical College, New York, NY, [7]University of California San Diego, Moores Cancer Center, San Diego, CA, [8]Norton Cancer Institute, Louisville, KY, [9]Willamette Valley Cancer Institute & Research Center/US Oncology Research, Eugene, OR, [10]Università Vita-Salute San Raffaele and IRCCS Istituto Scientifico San Raffaele, Milano, Italy, [11]Sarah Cannon Research Institute,

Debulking Eliminates Need for Hospitalization Prior to Initiating Frontline Venetoclax Therapy in Previously Untreated CLL Patients: A Phase 3b Study

Sharman JP et al.

ASH 2019;Abstract 3042.

Proportion of Patients Achieving Low Tumor Burden by Number of Treatment Cycles



Sharman JP et al. ASH 2019;Abstract 3042.

Phase 2 Study of Acalabrutinib in Ibrutinib (IBR)-Intolerant Patients (pts) with Relapsed/Refractory (R/R) Chronic Lymphocytic Leukemia (CLL)

Rogers KA et al.

ASCO 2019;Abstract 7530.

Impact of Premature Venetoclax (Ven) Discontinuation/Interruption on Outcomes in Relapsed/Refractory (R/R) Chronic Lymphocytic Leukemia (CLL): Phase III MURANO Study Results

Mato AR et al.

ASCO 2020;Abstract 8028.

Targeting CD20: teaching an old dog new tricks

Jeff P. Sharman

Willamette Valley Cancer Institute/US Oncology, Eugene, OR

***Hematology Am Soc Hematol Educ Program* 2019;2019(1):273-8**

original report

Final Results of a Randomized, Phase III Study of Rituximab With or Without Idelalisib Followed by Open-Label Idelalisib in Patients With Relapsed Chronic Lymphocytic Leukemia

Jeff P. Sharman, MD[1]; Steven E. Coutre, MD[2]; Richard R. Furman, MD[3]; Bruce D. Cheson, MD[4]; John M. Pagel, MD, PhD[5]; Peter Hillmen, MBChB, PhD[6]; Jacqueline C. Barrientos, MS, MD[7]; Andrew D. Zelenetz, MD, PhD[8]; Thomas J. Kipps, MD, PhD[9]; Ian W. Flinn, MD, PhD[10]; Paolo Ghia, MD, PhD[11]; Herbert Eradat, MD[12]; Thomas Ervin, MD[13]; Nicole Lamanna, MD[14]; Bertrand Coiffier, MD, PhD[15†]; Andrew R. Pettitt, MA, Mb, BChir, PhD[16]; Shuo Ma, MD, PhD[17]; Eugen Tausch, MD[18]; Paula Cramer, MD[19]; Julie Huang, PhD[20]; Siddhartha Mitra, MD, PhD[20]; Michael Hallek, MD[19]; Susan M. O'Brien, MD[21]; and Stephan Stilgenbauer, MD[18]

J Clin Oncol 2019;37:1391-402

Trial in Progress: A Phase II, Multicenter, Single-Arm Study of Zanubrutinib (BGB-3111) in Patients with Previously Treated Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Intolerant of Prior Treatment with Ibrutinib

Flinn I et al.

ASCO 2020;Abstract TPS8066.

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RTP RESEARCH TO PRACTICE

What is your usual preferred initial regimen for a 60-year-old patient with CLL with IGHV mutation but no del(17p) or TP53 mutation who requires treatment?

1. FCR
2. Ibrutinib
3. Ibrutinib + rituximab
4. Ibrutinib + obinutuzumab
5. Acalabrutinib
6. Acalabrutinib + obinutuzumab
7. Venetoclax + obinutuzumab
8. Other

What is your usual preferred initial regimen for a 60-year-old patient with CLL with IGHV mutation but no del(17p) or TP53 mutation who requires treatment?

 MATTHEW S DAVIDS, MD, MMSC	Venetoclax + obinutuzumab
 IAN W FLINN, MD, PHD	Venetoclax + obinutuzumab
 BRIAN T HILL, MD, PHD	Venetoclax + obinutuzumab or BR
 BRAD S KAHL, MD	Venetoclax + obinutuzumab
 ANTHONY R MATO, MD, MSCE	FCR
 JOHN M PAGEL, MD, PHD	Acalabrutinib
 KERRY A ROGERS, MD	Ibrutinib or FCR
 JEFF SHARMAN, MD	FCR
 MITCHELL R SMITH, MD, PHD	FCR
 WILLIAM G WIERDA, MD, PHD	FCR
 JENNIFER WOYACH, MD	Venetoclax + obinutuzumab

BR = bendamustine/rituximab; FCR = fludarabine/cyclosphosphamide/rituximab (FCR)

What is your usual preferred initial regimen for a 75-year-old patient with CLL with IGHV mutation but no del(17p) or TP53 mutation who requires treatment?

 MATTHEW S DAVIDS, MD, MMSC	Venetoclax + obinutuzumab
 IAN W FLINN, MD, PHD	Acalabrutinib
 BRIAN T HILL, MD, PHD	Obinutuzumab
 BRAD S KAHL, MD	Venetoclax + obinutuzumab
 ANTHONY R MATO, MD, MSCE	Acalabrutinib
 JOHN M PAGEL, MD, PHD	Acalabrutinib
 KERRY A ROGERS, MD	Acalabrutinib or venetoclax + obinutuzumab
 JEFF SHARMAN, MD	Venetoclax + obinutuzumab
 MITCHELL R SMITH, MD, PHD	Ibrutinib
 WILLIAM G WIERDA, MD, PHD	Venetoclax + obinutuzumab
 JENNIFER WOYACH, MD	Ibrutinib

RTP RESEARCH TO PRACTICE

What is your usual preferred initial regimen for a 60-year-old patient with CLL with unmutated IGHV and no del(17p) or TP53 mutation who requires treatment?

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 JOHN M PAGEL, MD, PHD	Acalabrutinib
 KERRY A ROGERS, MD	Acalabrutinib or venetoclax + obinutuzumab
 JEFF SHARMAN, MD	Acalabrutinib
 MITCHELL R SMITH, MD, PHD	Venetoclax + obinutuzumab
 WILLIAM G WIERDA, MD, PHD	Venetoclax + obinutuzumab
 JENNIFER WOYACH, MD	Ibrutinib

RTP RESEARCH TO PRACTICE

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 MATTHEW S DAVIDS, MD, MMSC	Venetoclax + obinutuzumab
 IAN W FLINN, MD, PHD	Acalabrutinib
 BRIAN T HILL, MD, PHD	Venetoclax + obinutuzumab
 BRAD S KAHL, MD	Venetoclax + obinutuzumab
 ANTHONY R MATO, MD, MSCE	Acalabrutinib
 JOHN M PAGEL, MD, PHD	Acalabrutinib
 KERRY A ROGERS, MD	Acalabrutinib or venetoclax + obinutuzumab
 JEFF SHARMAN, MD	Acalabrutinib
 MITCHELL R SMITH, MD, PHD	Ibrutinib
 WILLIAM G WIERDA, MD, PHD	Acalabrutinib
 JENNIFER WOYACH, MD	Ibrutinib

RTP RESEARCH TO PRACTICE

What is your usual preferred initial regimen for a 75-year-old patient with CLL with unmutated IGHV and no del(17p) or TP53 mutation who requires treatment and has bulky disease?

 MATTHEW S DAVIDS, MD, MMSC	Venetoclax + obinutuzumab
 IAN W FLINN, MD, PHD	Acalabrutinib
 BRIAN T HILL, MD, PHD	Venetoclax + obinutuzumab
 BRAD S KAHL, MD	Venetoclax + obinutuzumab
 ANTHONY R MATO, MD, MSCE	Acalabrutinib + obinutuzumab
 JOHN M PAGEL, MD, PHD	Acalabrutinib
 KERRY A ROGERS, MD	Acalabrutinib
 JEFF SHARMAN, MD	Acalabrutinib
 MITCHELL R SMITH, MD, PHD	Venetoclax + obinutuzumab
 WILLIAM G WIERDA, MD, PHD	Acalabrutinib
 JENNIFER WOYACH, MD	Ibrutinib

RTP RESEARCH TO PRACTICE

What is your usual preferred initial regimen for a 60-year-old patient with del(17p) CLL who requires treatment?

 MATTHEW S DAVIDS, MD, MMSC	Ibrutinib
 IAN W FLINN, MD, PHD	Acalabrutinib
 BRIAN T HILL, MD, PHD	Acalabrutinib
 BRAD S KAHL, MD	Acalabrutinib + obinutuzumab
 ANTHONY R MATO, MD, MSCE	Acalabrutinib
 JOHN M PAGEL, MD, PHD	Acalabrutinib
 KERRY A ROGERS, MD	Ibrutnib
 JEFF SHARMAN, MD	Acalabrutinib
 MITCHELL R SMITH, MD, PHD	Venetoclax + obinutuzumab
 WILLIAM G WIERDA, MD, PHD	Acalabrutinib
 JENNIFER WOYACH, MD	Ibrutinib

RTP RESEARCH TO PRACTICE

What would be your most likely approach for a patient with newly diagnosed CLL to whom you administer up-front venetoclax/obinutuzumab who has detectable MRD after 1 year of treatment?

1. Continue treatment
2. Discontinue treatment

What would be your most likely approach for a patient with newly diagnosed CLL to whom you administer up-front venetoclax/obinutuzumab who has detectable minimal residual disease (MRD) after 1 year of treatment?

 MATTHEW S DAVIDS, MD, MMSC	Discontinue treatment
 IAN W FLINN, MD, PHD	Discontinue treatment
 BRIAN T HILL, MD, PHD	Discontinue treatment
 BRAD S KAHL, MD	Discontinue treatment
 ANTHONY R MATO, MD, MSCE	Continue treatment
 JOHN M PAGEL, MD, PHD	Continue treatment
 KERRY A ROGERS, MD	Discontinue treatment
 JEFF SHARMAN, MD	Discontinue treatment
 MITCHELL R SMITH, MD, PHD	Discontinue treatment
 WILLIAM G WIERDA, MD, PHD	Continue treatment
 JENNIFER WOYACH, MD	Discontinue treatment

RTP RESEARCH TO PRACTICE

What would be your most likely approach for a patient with newly diagnosed CLL to whom you administer up-front venetoclax/obinutuzumab who has achieved undetectable MRD status after 1 year of treatment?

 MATTHEW S DAVIDS, MD, MMSC	Discontinue treatment
 IAN W FLINN, MD, PHD	Discontinue treatment
 BRIAN T HILL, MD, PHD	Discontinue treatment
 BRAD S KAHL, MD	Discontinue treatment
 ANTHONY R MATO, MD, MSCE	Discontinue treatment
 JOHN M PAGEL, MD, PHD	Discontinue treatment
 KERRY A ROGERS, MD	Discontinue treatment
 JEFF SHARMAN, MD	Discontinue treatment
 MITCHELL R SMITH, MD, PHD	Discontinue treatment
 WILLIAM G WIERDA, MD, PHD	Discontinue treatment
 JENNIFER WOYACH, MD	Discontinue treatment

RTP RESEARCH TO PRACTICE

Which second-line systemic therapy would you recommend for a 60-year-old patient with CLL with no IGHV mutation and no del(17p) or TP53 mutation who responds to ibrutinib and then experiences disease progression 3 years later?

1. Acalabrutinib
2. Acalabrutinib + obinutuzumab
3. Venetoclax
4. Venetoclax + rituximab
5. Venetoclax + obinutuzumab
6. Idelalisib
7. Duvelisib
8. Other

Which second-line systemic therapy would you recommend for a 60-year-old patient with CLL with unmutated IGHV and no del(17p) or TP53 mutation who responds to ibrutinib and then experiences disease progression 3 years later?

 MATTHEW S DAVIDS, MD, MMSC	Venetoclax + rituximab
 IAN W FLINN, MD, PHD	Venetoclax + obinutuzumab
 BRIAN T HILL, MD, PHD	Venetoclax + rituximab
 BRAD S KAHL, MD	Venetoclax + rituximab
 ANTHONY R MATO, MD, MSCE	Venetoclax + rituximab
 JOHN M PAGEL, MD, PHD	Venetoclax
 KERRY A ROGERS, MD	Venetoclax + rituximab
 JEFF SHARMAN, MD	Venetoclax + rituximab
 MITCHELL R SMITH, MD, PHD	Venetoclax + obinutuzumab
 WILLIAM G WIERDA, MD, PHD	Venetoclax + rituximab
 JENNIFER WOYACH, MD	Venetoclax + rituximab

RTP RESEARCH TO PRACTICE

Which second-line systemic therapy would you recommend for a 60-year-old patient with CLL with no IGHV mutation and no del(17p) or TP53 mutation who responds to venetoclax/obinutuzumab and then experiences disease progression 3 years later?

1. Ibrutinib
2. Ibrutinib + rituximab
3. Ibrutinib + obinutuzumab
4. Acalabrutinib
5. Acalabrutinib + obinutuzumab
6. Idelalisib
7. Duvelisib
8. Other

Which second-line systemic therapy would you recommend for a 60-year-old patient with CLL with unmutated IGHV and no del(17p) or TP53 mutation who responds to venetoclax/obinutuzumab and then experiences disease progression 3 years later?

 MATTHEW S DAVIDS, MD, MMSC	Venetoclax + obinutuzumab
 IAN W FLINN, MD, PHD	Acalabrutinib
 BRIAN T HILL, MD, PHD	Acalabrutinib
 BRAD S KAHL, MD	Acalabrutinib
 ANTHONY R MATO, MD, MSCE	Venetoclax + rituximab
 JOHN M PAGEL, MD, PHD	Acalabrutinib
 KERRY A ROGERS, MD	Ibrutinib
 JEFF SHARMAN, MD	Acalabrutinib
 MITCHELL R SMITH, MD, PHD	Ibrutinib
 WILLIAM G WIERDA, MD, PHD	Venetoclax + rituximab
 JENNIFER WOYACH, MD	Ibrutinib

RTP RESEARCH TO PRACTICE

A 60-year-old patient with CLL, an absolute lymphocyte count of 20,000 and several involved lymph nodes that are smaller than 2 centimeters is about to receive venetoclax. What preemptive measures, if any, would you take to address tumor lysis syndrome prior to the initiation of therapy?

 MATTHEW S DAVIDS, MD, MMSC	Encourage oral hydration and allopurinol
 IAN W FLINN, MD, PHD	IV hydration and allopurinol
 BRIAN T HILL, MD, PHD	Encourage oral hydration and allopurinol
 BRAD S KAHL, MD	Encourage oral hydration and allopurinol
 ANTHONY R MATO, MD, MSCE	IV hydration and allopurinol
 JOHN M PAGEL, MD, PHD	Encourage oral hydration and allopurinol
 KERRY A ROGERS, MD	Encourage oral hydration and allopurinol
 JEFF SHARMAN, MD	Give the obinutuzumab first to debulk, then after 1 month can start as outpatient with hydration and allopurinol
 MITCHELL R SMITH, MD, PHD	Encourage oral hydration and allopurinol
 WILLIAM G WIERDA, MD, PHD	Encourage oral hydration and allopurinol
 JENNIFER WOYACH, MD	Encourage oral hydration and allopurinol

RTP RESEARCH TO PRACTICE

A 60-year-old patient with CLL, an absolute lymphocyte count of 80,000 and several involved lymph nodes that are larger than 5 centimeters is about to receive venetoclax. What preemptive measures, if any, would you take to address tumor lysis syndrome prior to the initiation of therapy?

 MATTHEW S DAVIDS, MD, MMSC	Admit to hospital
 IAN W FLINN, MD, PHD	Debulk with obinutuzumab
 BRIAN T HILL, MD, PHD	Admit to hospital
 BRAD S KAHL, MD	Admit to hospital
 ANTHONY R MATO, MD, MSCE	Admit to hospital
 JOHN M PAGEL, MD, PHD	Admit to hospital
 KERRY A ROGERS, MD	Admit to hospital
 JEFF SHARMAN, MD	Obinutuzumab for 1 month to lower patient risk, then outpatient hydration and allopurinol
 MITCHELL R SMITH, MD, PHD	Admit to hospital
 WILLIAM G WIERDA, MD, PHD	Admit to hospital
 JENNIFER WOYACH, MD	IV hydration and allopurinol

RTP RESEARCH TO PRACTICE

For your patients with CLL whom you admit to the hospital to receive venetoclax, for how long do you typically admit them?

 MATTHEW S DAVIDS, MD, MMSC	8 days
 IAN W FLINN, MD, PHD	2 days
 BRIAN T HILL, MD, PHD	2 days (<48 hours)
 BRAD S KAHL, MD	2 days
 ANTHONY R MATO, MD, MSCE	2-3 days
 JOHN M PAGEL, MD, PHD	1 day

 KERRY A ROGERS, MD	2 nights for each dose escalation
 JEFF SHARMAN, MD	2 days
 MITCHELL R SMITH, MD, PHD	1- 2 days
 WILLIAM G WIERDA, MD, PHD	2 days
 JENNIFER WOYACH, MD	2 days or rapid escalation to full dose over 5 days

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Sharman

MODULE 1: Cases from Dr Rogers

- Comments and Questions: Impact of COVID-19 on treatment decision-making
- A 57-year-old man with relapsed/refractory (R/R) CLL
- A 44-year-old man with newly diagnosed CLL – Del(17p)
- Comments and Questions: Optimal timing for referral to CAR-T therapy or allogeneic stem cell transplant
- A 65-year-old man with R/R CLL

MODULE 2: CLL Journal Club with Dr Sharman

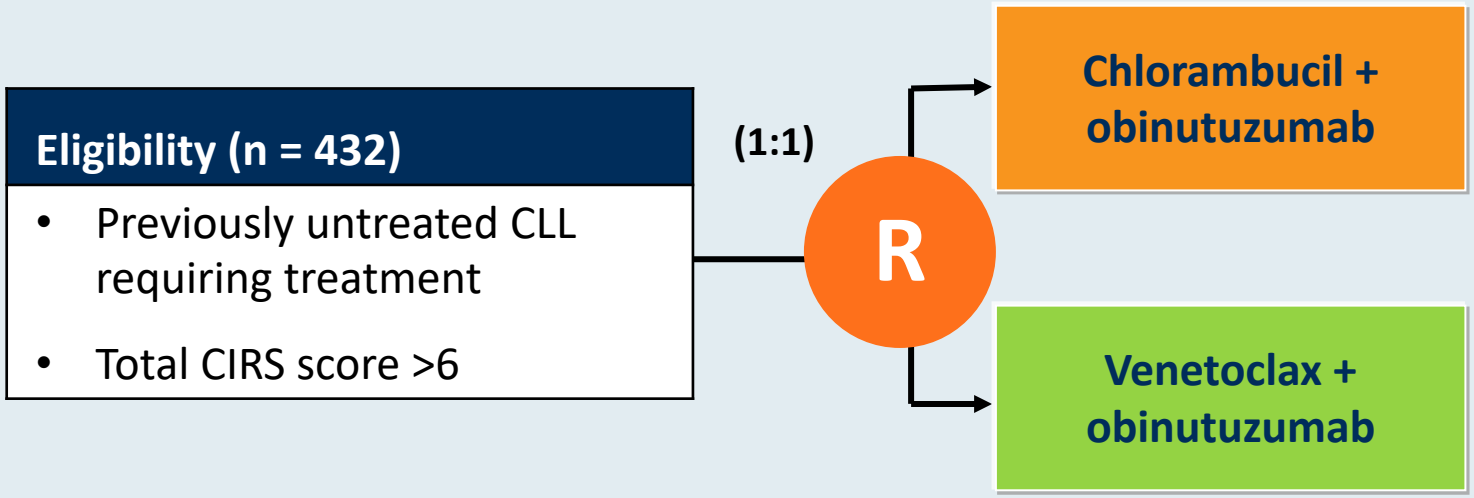
- BTK inhibitors in patients with severe COVID-19
- Tumor reduction and risk of tumor lysis syndrome in patients receiving ibrutinib
- Debulking to eliminate the need for hospitalization before initiating front-line venetoclax
- Acalabrutinib in ibrutinib-intolerant patients with R/R CLL
- Impact of premature venetoclax discontinuation or interruption on outcomes in R/R CLL: MURANO trial
- Targeting CD20: Teaching an old dog new tricks
- Trial in progress: Zanubrutinib for patients with R/R CLL and ibrutinib intolerance

MODULE 3: Beyond the Guidelines – Clinical Investigator Approaches to Common Clinical Scenarios

MODULE 4: Key Recent Data Sets and Approvals

RTP RESEARCH TO PRACTICE

CLL14 Phase III Study Schema

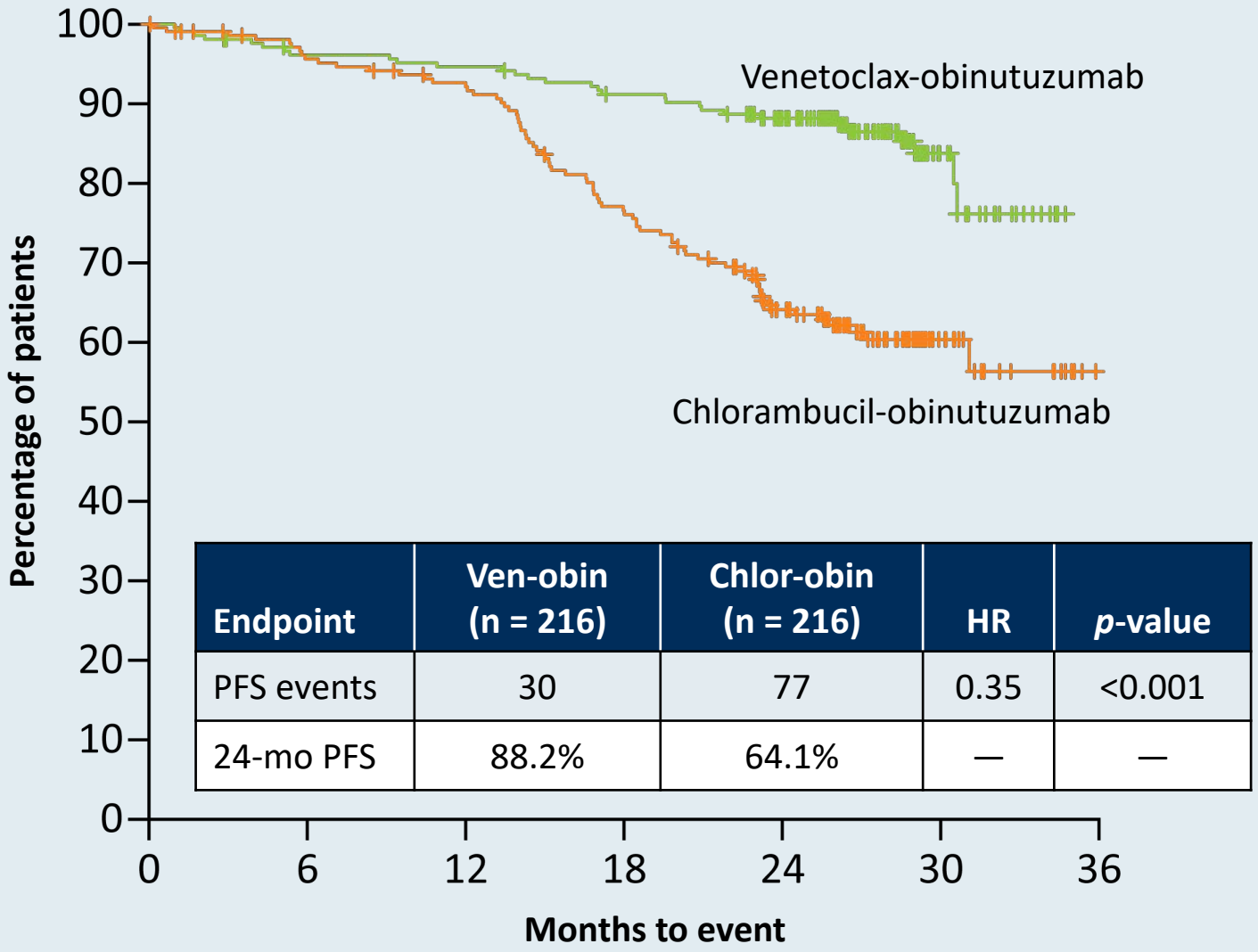


Primary endpoint: Progression-free survival

- Treatment duration in both groups: 12 cycles, 28 days each
- No crossover was allowed
- Daily oral venetoclax regimen:
  - Initiated on day 22 of cycle 1, starting with a 5-week dose ramp-up (1 week each of 20, 50, 100 and 200 mg, then 400 mg daily for 1 week)
  - Thereafter continuing at 400 mg daily until completion of cycle 12

www.clinicaltrials.gov (NCT02242942). Accessed August 2020.
Fischer K et al. *N Engl J Med* 2019;380(23):2225-36.

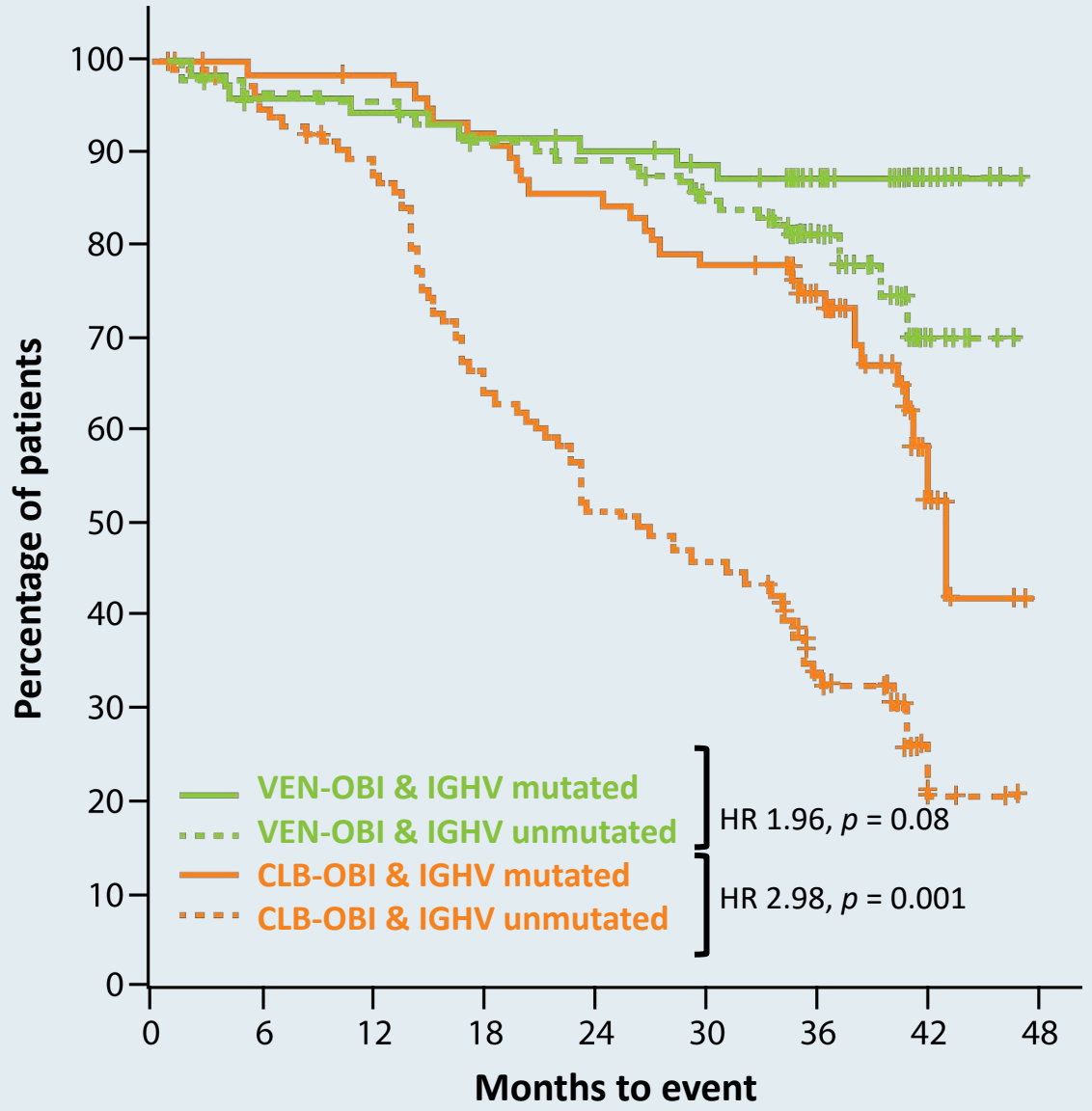
CLL14: Investigator-Assessed Progression-Free Survival



Endpoint	Ven-obin (n = 216)	Chlor-obin (n = 216)	HR	*p*-value
PFS events	30	77	0.35	<0.001
24-mo PFS	88.2%	64.1%	—	—

Fischer K et al. *N Engl J Med* 2019;380(23):2225-36.

CLL14: PFS by IGHV Mutation and TP53 Status



Median PFS

Ven-Obi & IGHVmut: not reached

Ven-Obi & IGHVunmut: not reached

Clb-Obi & IGHVmut: 42.9 months

Clb-Obi & IGHVunmut: 26.3 months

Al-Sawaf O et al. EHA 2020;Abstract S155.

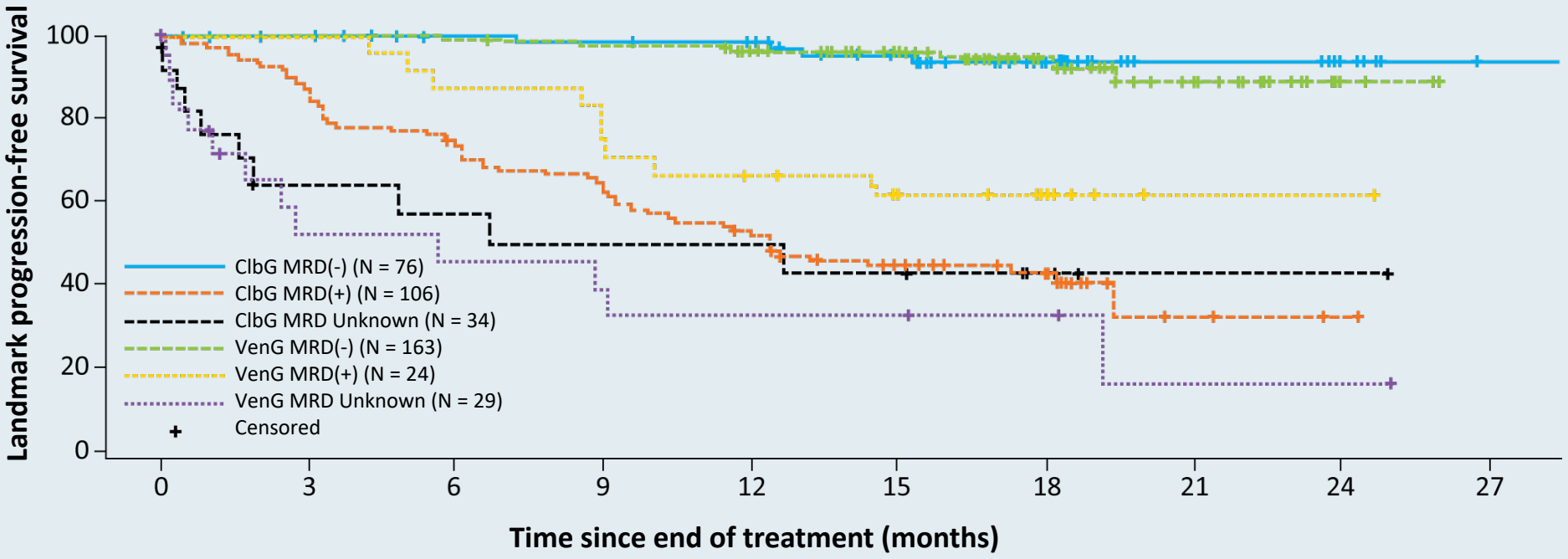
RTP RESEARCH TO PRACTICE

CLL14: Minimal Residual Disease 3 Months After Treatment

MRD 3 months after treatment	MRD-negative		MRD responders	
	Veneto/obin (N = 216)	Chloram/obin (N = 216)	Veneto/obin (N = 216)	Chloram/obin (N = 216)
MRD in bone marrow	56.9%	17.1%	33.8%	10.6%
Odds ratio, *p*-value	OR: 6.4, $p < 0.0001$		OR: 4.3, $p < 0.0001$	
MRD in peripheral blood	75.7%	35.2%	42.1%	14.4%
Odds ratio, *p*-value	OR: 5.7, $p < 0.0001$		OR: 4.3, $p < 0.0001$	

Fischer K et al. *N Engl J Med* 2019;380(23):2225-36.

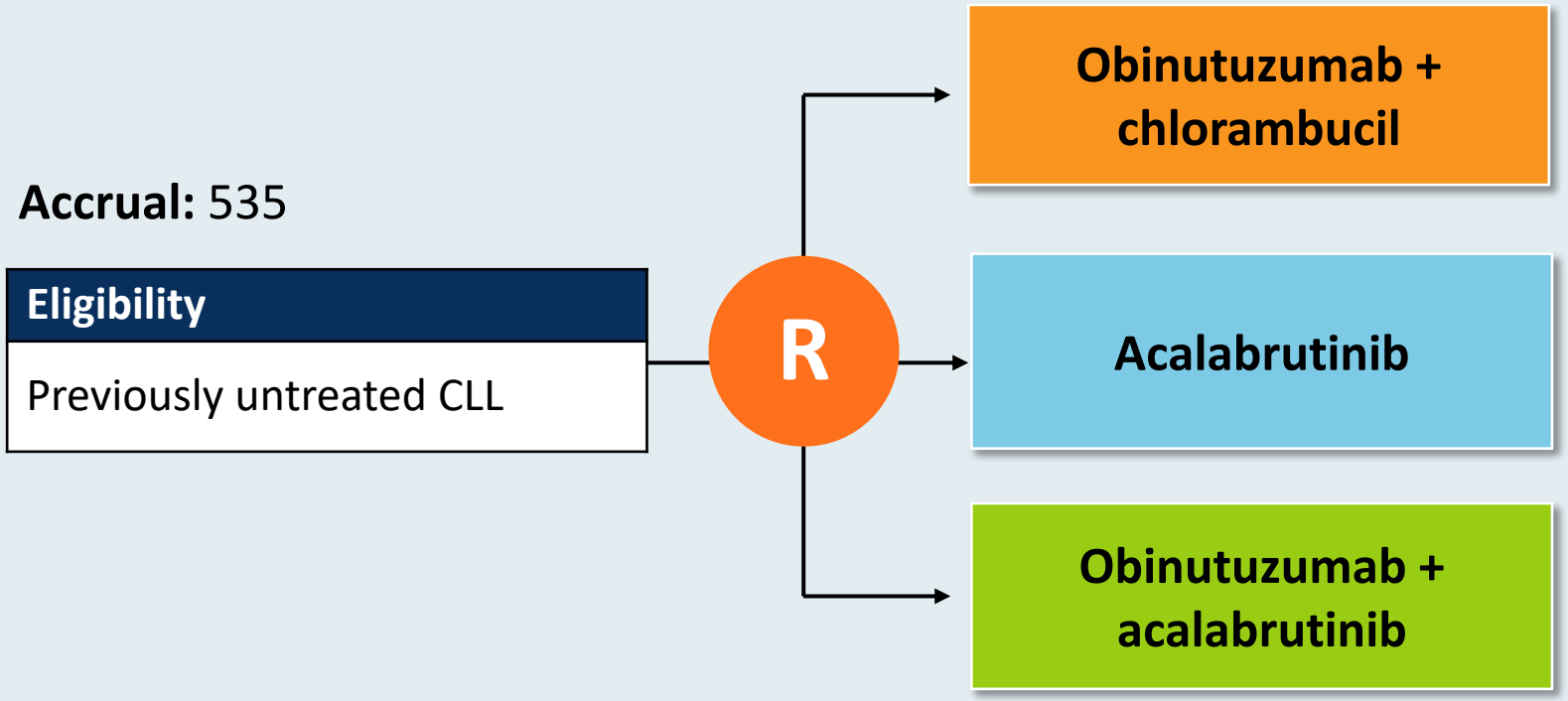
CLL14: Landmark Analysis from End of Therapy PFS by MRD Group



Further landmark analysis of PFS by MRD status showed that undetectable MRD translated into improved PFS regardless of the clinical response status at end of therapy.

Fischer K et al. ASH 2019;Abstract 36.

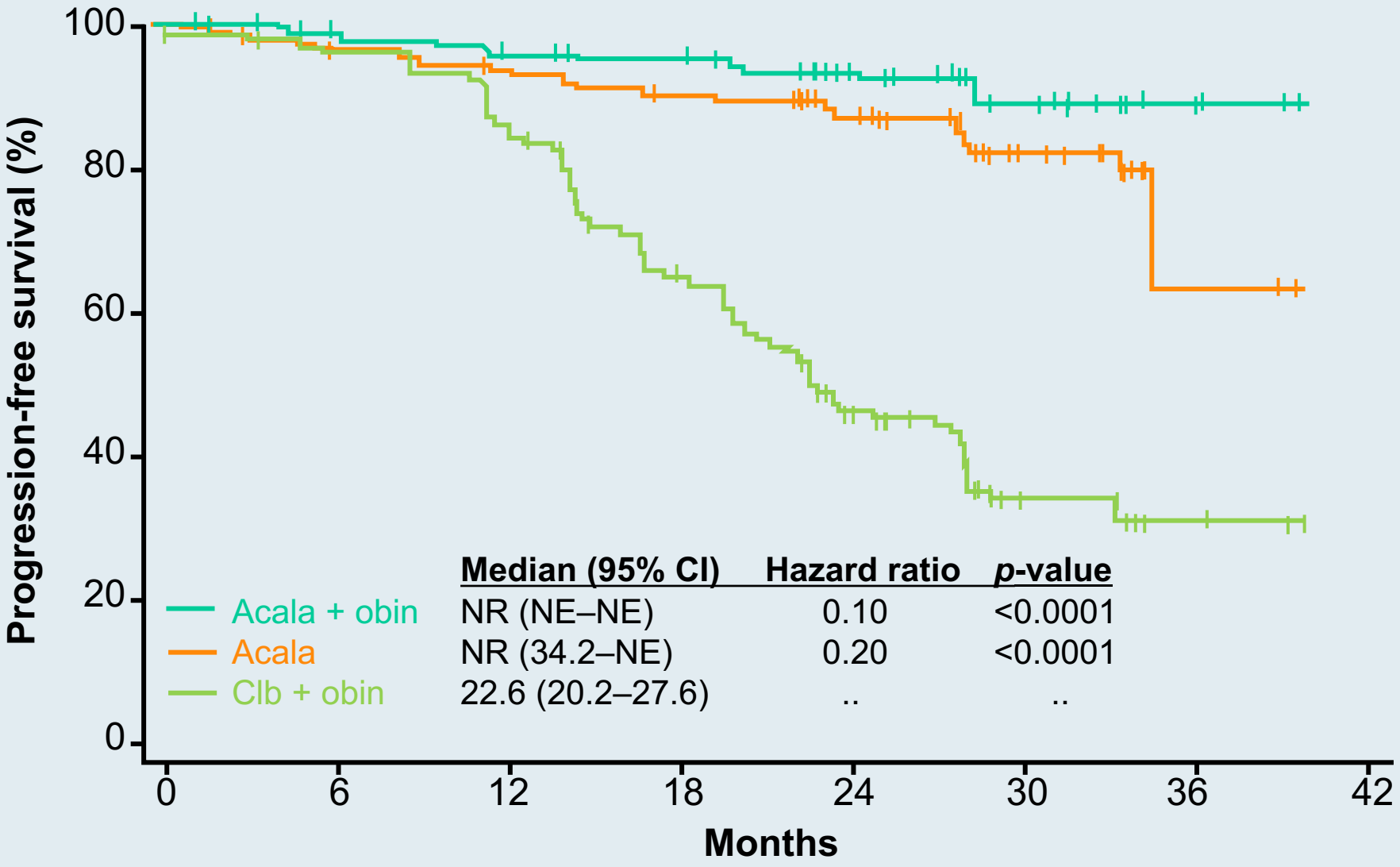
ELEVATE-TN Phase III Trial Schema



Primary endpoint: Progression-free survival

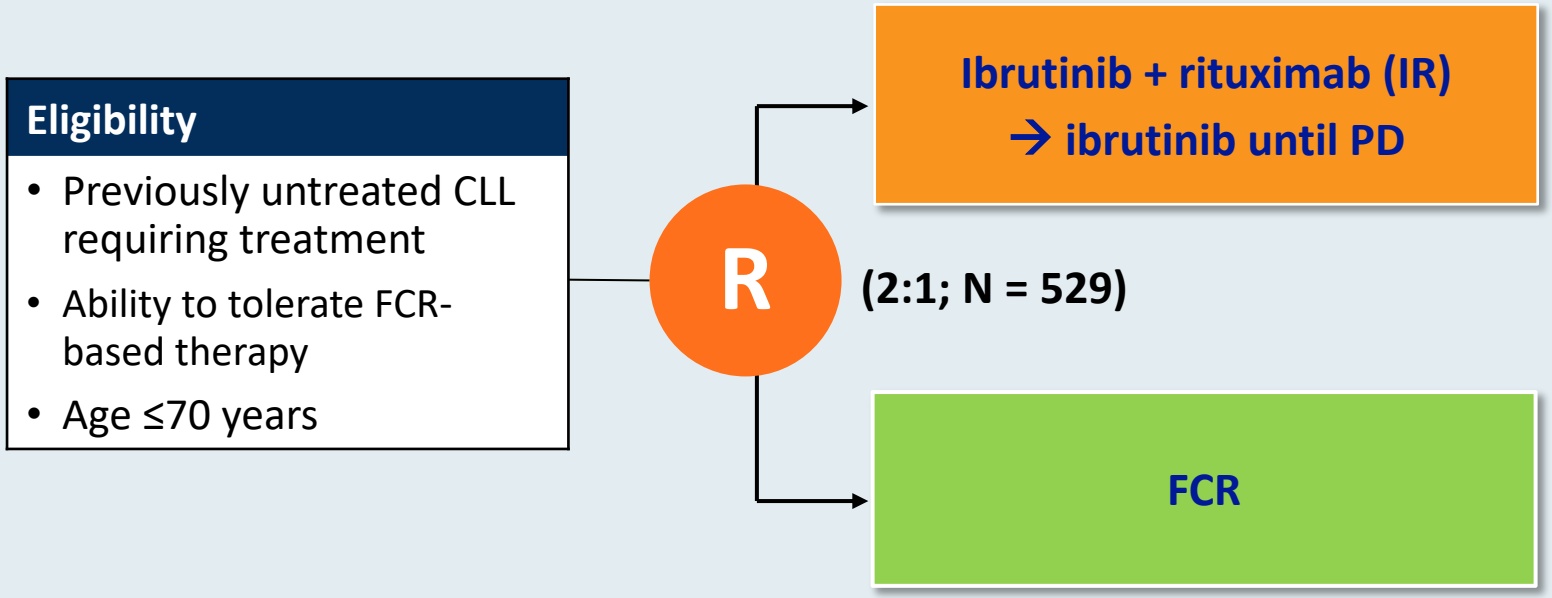
www.clinicaltrials.gov (NCT02475681). Accessed August 2020.

ELEVATE-TN: PFS (IRC)



Sharman JP et al. *Lancet* 2020;395:1278-91.

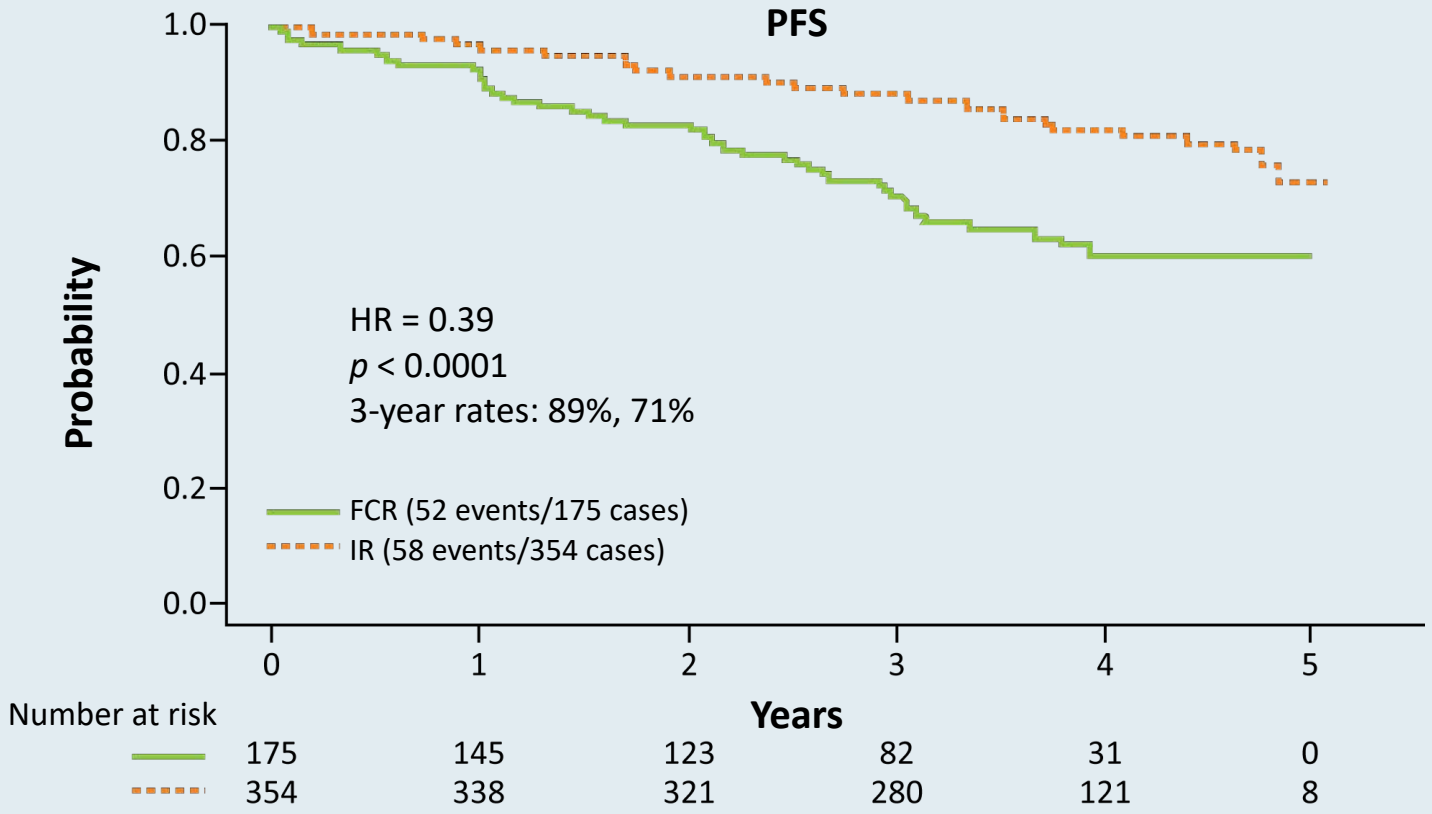
Phase III ECOG-ACRIN E1912 Study Design



Primary endpoint: PFS
Secondary endpoints: OS, ORR, Toxicity and Tolerability

ECOG-ACRIN E1912 Physician Fact Sheet, version 01/15/16;
www.clinicaltrials.gov (NCT02048813); Shanafelt TD et al. ASH 2018;Abstract LBA-4.

ECOG-ACRIN E1912 Extended Follow-Up: Up-Front IR Compared to FCR for Younger Patients with CLL

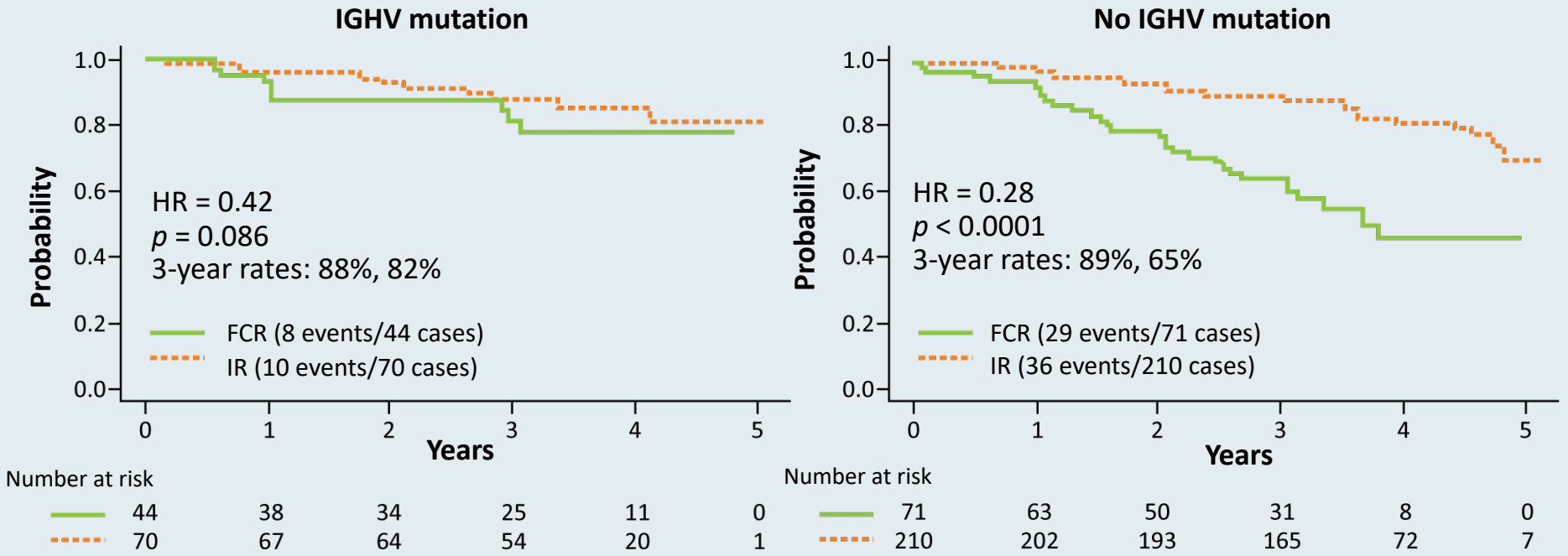


- Grade ≥3 treatment-related AEs were reported in 70% of patients receiving IR and 80% of patients receiving FCR (odds ratio = 0.56; $p = 0.013$).
- Among the 95 patients who discontinued ibrutinib, the most common cause was AE or complication.

Shanafelt TD et al. ASH 2019;Abstract 33.

RTP RESEARCH TO PRACTICE

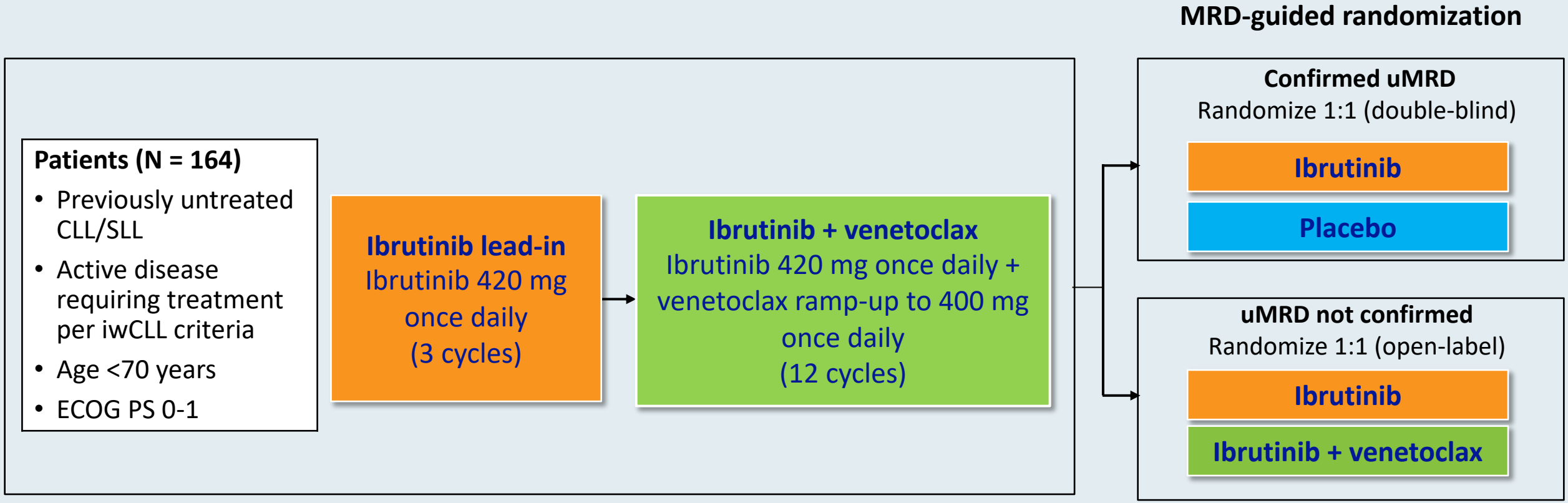
ECOG-ACRIN E1912 Extended Follow-Up: PFS by IGHV Mutation Status



- On subgroup analysis by IGHV mutation status, IR was superior to FCR for CLL with no IGHV mutation (HR = 0.28; $p < 0.0001$).
- With current follow-up the difference between IR and FCR is not significant for CLL with IGHV mutation (HR = 0.42; $p = 0.086$).

Shanafelt TD et al. ASH 2019;Abstract 33.

CAPTIVATE MRD Cohort: Study Design

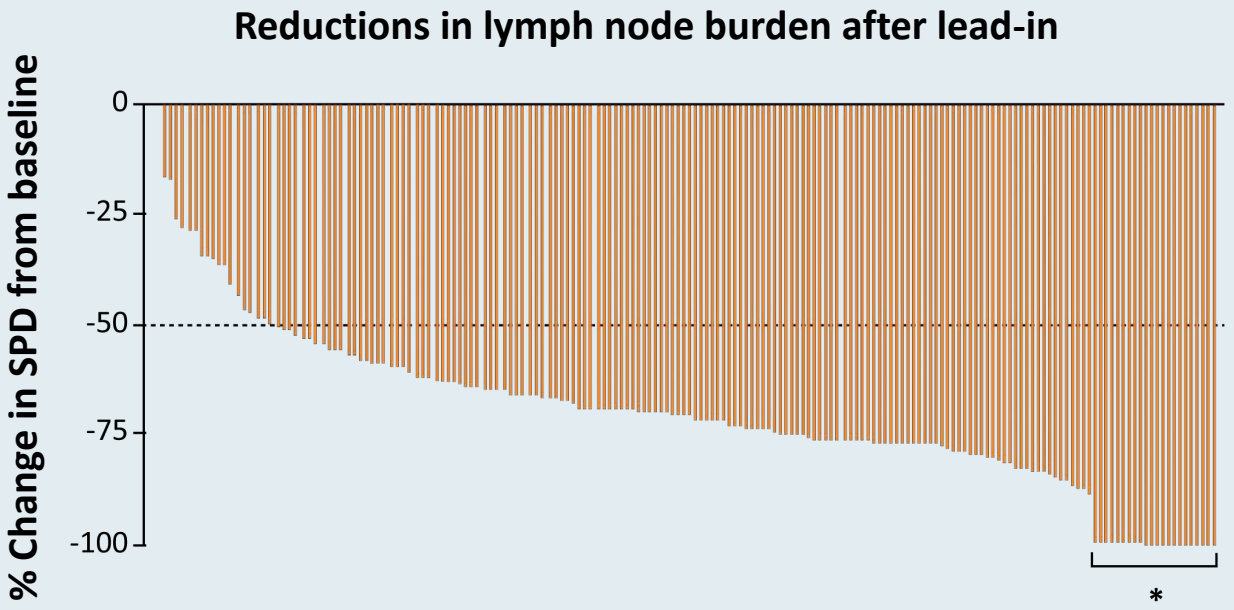


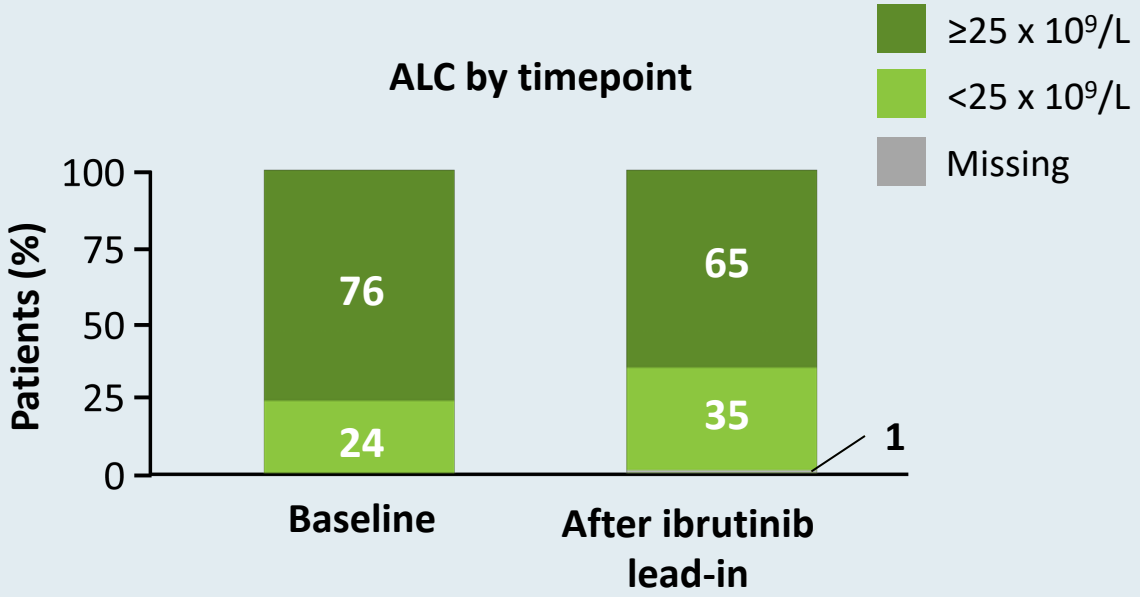
uMRD = undetectable minimal residual disease

Results presented for prerandomization phase of the MRD cohort (n = 164) with 12 cycles of ibrutinib + venetoclax prior to MRD-guided randomization

Siddiqi S et al. EHA 2020;Abstract S158.

CAPTIVATE MRD Cohort: 3 Cycles of Ibrutinib Lead-In





Three cycles of ibrutinib lead-in reduces TLS risk and indication for hospitalization

Siddiqi S et al. EHA 2020;Abstract S158.

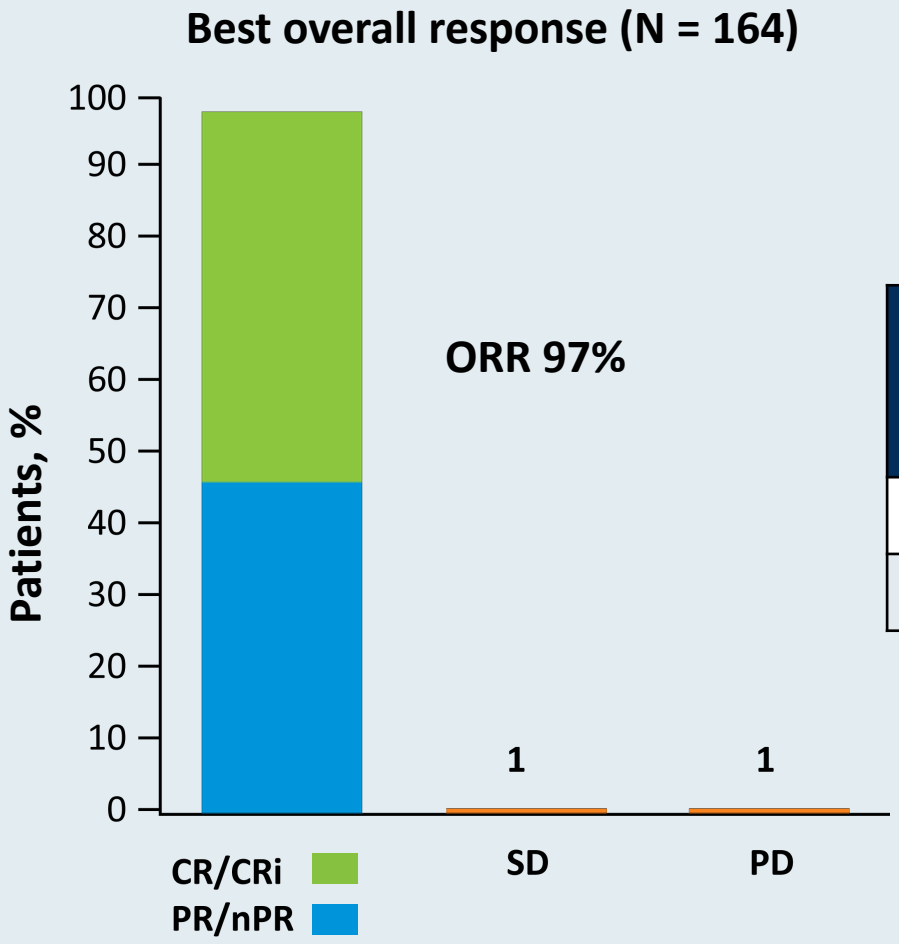
CAPTIVATE MRD Cohort: Undetectable MRD Rate

	Peripheral blood n = 163	Bone marrow n = 155
Best response of undetectable MRD in evaluable patients (95% CI)	**75%** (68-82)	**72%** (64-79)

- Rates of undetectable MRD in peripheral blood and bone marrow were highly concordant at Cycle 16 (91%)
- In the all-treated population (N = 164), undetectable MRD was achieved in 75% of patients in peripheral blood and in 68% of patients in bone marrow with up to 12 cycles of combination ibrutinib/venetoclax

Siddiqi S et al. EHA 2020;Abstract S158.

CAPTIVATE MRD Cohort: Undetectable MRD in Patients with CR/PR



Best overall response (up to Cycle 16)	CR n = 84	PR n = 75	ORR (CR + PR) n = 159
Undetectable MRD in PB, n (%)	71 (85)	52 (69)	123 (77)
Undetectable MRD in BM, n (%)	67 (80)	44 (59)	111 (70)

At 15 months, 98% of patients were progression free with no deaths

Siddiqi S et al. EHA 2020;Abstract S158.

CAPTIVATE MRD Cohort: Summary of Grade 3 and 4 AEs of Interest

AEs, n (%)	Ibrutinib lead-in (3 cycles) N = 164		Ibrutinib + venetoclax combination (12 cycles) N = 159		Overall (15 cycles) N = 164
	Grade 3	Grade 4	Grade 3	Grade 4	Grade 3-4
Atrial fibrillation	2 (1)	0	1 (1)	0	3 (2)
Major hemorrhage	0	0	1 (1)	0	1 (1)
Infections	4 (2)	0	10 (6)	0	14 (9)
Neutropenia	4 (2)	7 (4)	27 (17)	26 (16)	58 (35)
Febrile neutropenia	1 (1)	0	2 (1)	0	3 (2)
Laboratory TLS	0	0	2 (1)	0	2 (1)

- Low rates of Grade 3 atrial fibrillation, major hemorrhage, infections, febrile neutropenia and laboratory TLS (no Grade 4 event)
- No patients developed clinical TLS
  - Laboratory TLS reported as AE in 3 patients (only 1 met Howard criteria)
- No fatal AEs

Siddiqi S et al. EHA 2020;Abstract S158.

Ongoing Phase III EA9161 Trial Schema

Stratifications
Age: <65 yr vs ≥ 65 yr and <70 yr
PS: 0, 1, vs 2
Stage: 0, 1, or 2 vs 3, 4
Del11q22.3 vs others

Randomize

Arm A
Ibrutinib: Cycles 1-19:d1-28 420mg PO daily
Obinutuzumab: C1 **:** D1:100 mg IV, D2:900 mg IV, D8: 1000 mg IV, D15: 1000 mg IV; C2-6: D1 1000 mg IV
Venetoclax: C3 D1-7 20mg PO daily D8-14 50mg PO daily D15-21 100mg PO daily; D22-28 200 mg PO daily; C4-14: D1-28 400mg PO daily

Arm B
Ibrutinib: Cycles 1-19+:d1-28 420mg PO daily
Obinutuzumab: C1 **:** D1:100 mg IV, D2:900 mg IV, D8: 1000 mg IV, D15: 1000 mg IV; C2-6: D1 1000 mg IV

Courtesy of Brad Kahl, MD

Exploring the Role of Immune Checkpoint Inhibitor Therapy and Other Novel Strategies in Gynecologic Cancers

A Meet The Professor Series

Thursday, September 24, 2020
12:00 PM – 1:00 PM ET

Faculty
David M O'Malley, MD

Moderator
Neil Love, MD

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Thank you for joining us!

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

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