

**Thank you for joining us.  
The program will commence momentarily.**

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

*A Meet The Professor Series*

**Kerry Rogers, MD**

Assistant Professor in the Division of Hematology  
The Ohio State University  
Columbus, Ohio

## Commercial Support

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

## 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, Boston Biomedical 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, Taiho Oncology Inc, Takeda Oncology, Tesaro, A GSK Company, Teva Oncology, Tokai Pharmaceuticals Inc, Tolero Pharmaceuticals and Verastem Inc.

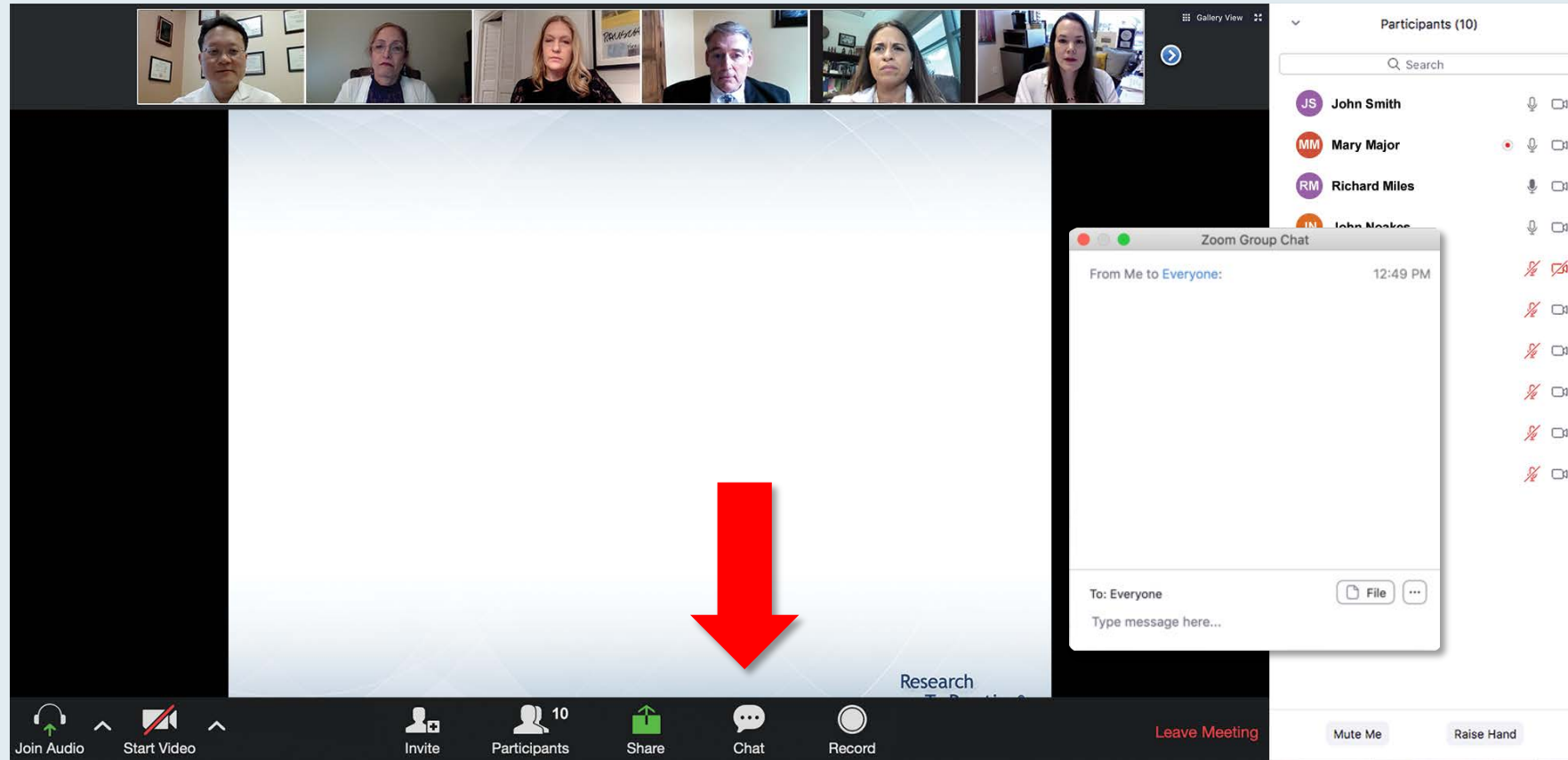
# Research To Practice CME Planning Committee Members, Staff and Reviewers

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

# Dr Rogers — Disclosures

<b>Consulting Agreements</b>	AbbVie Inc, Acerta Pharma — A member of the AstraZeneca Group, AstraZeneca Pharmaceuticals LP, Pharmacyclics LLC, an AbbVie Company
<b>Contracted Research</b>	AbbVie Inc, Genentech, a member of the Roche Group, Janssen Biotech Inc
<b>Travel</b>	AstraZeneca Pharmaceuticals LP

# We Encourage Clinicians in Practice to Submit Questions



**Feel free to submit questions now before the program commences and throughout the program.**

# Familiarizing Yourself with the Zoom Interface

## How to answer poll questions

The screenshot displays a Zoom meeting interface. At the top, a gallery view shows six participants. The main screen displays a poll question: "What is your usual treatment recommendation for a patient with MM who has been followed by ASCT for 1-5 years who then experiences an asymptomatic relapse?". Below the question is a list of ten treatment options, each preceded by a number. A "Quick Poll" overlay is visible, showing a list of radio button options corresponding to the numbered list. The bottom of the screen features a toolbar with icons for "Join Audio", "Start Video", "Invite", "Participants" (showing 10), "Share", "Chat", "Record", and a "Leave Meeting" button. On the right side, a "Participants (10)" list is visible, showing names and status icons.

What is your usual treatment recommendation for a patient with MM who has been followed by ASCT for 1-5 years who then experiences an asymptomatic relapse?

Quick Poll

- ☐ Carfilzomib +/- dexamethasone
- ☐ Pomalidomide +/- dexamethasone
- ☐ Carfilzomib + pomalidomide +/- dexamethasone
- ☐ Elotuzumab + lenalidomide +/- dexamethasone
- ☐ Elotuzumab + pomalidomide +/- dexamethasone
- ☐ Daratumumab + lenalidomide +/- dexamethasone
- ☐ Daratumumab + pomalidomide +/- dexamethasone
- ☐ Daratumumab + bortezomib +/- dexamethasone
- ☐ Ixazomib + Rd
- ☐ Other

Submit

Co-provided by USF Health Research To Practice®

Join Audio Start Video Invite Participants 10 Share Chat Record Leave Meeting Mute Me Raise Hand

Participants (10)

Search

- JS John Smith
- MM Mary Major
- RM Richard Miles
- JN John Noakes
- AS Alice Suarez
- JP Jane Perez
- RS Robert Stiles
- JF Juan Fernandez
- AK Ashok Kumar
- JS Jeremy Smith

When a poll question pops up, click your answer choice from the available options.  
Results will be shown after everyone has answered.



# Upcoming Live Webinars

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**Friday, September 11, 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**

Robert L Coleman, MD

**Moderator**

Neil Love, MD

***Thank you for joining us!***

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

# ONCOLOGY TODAY

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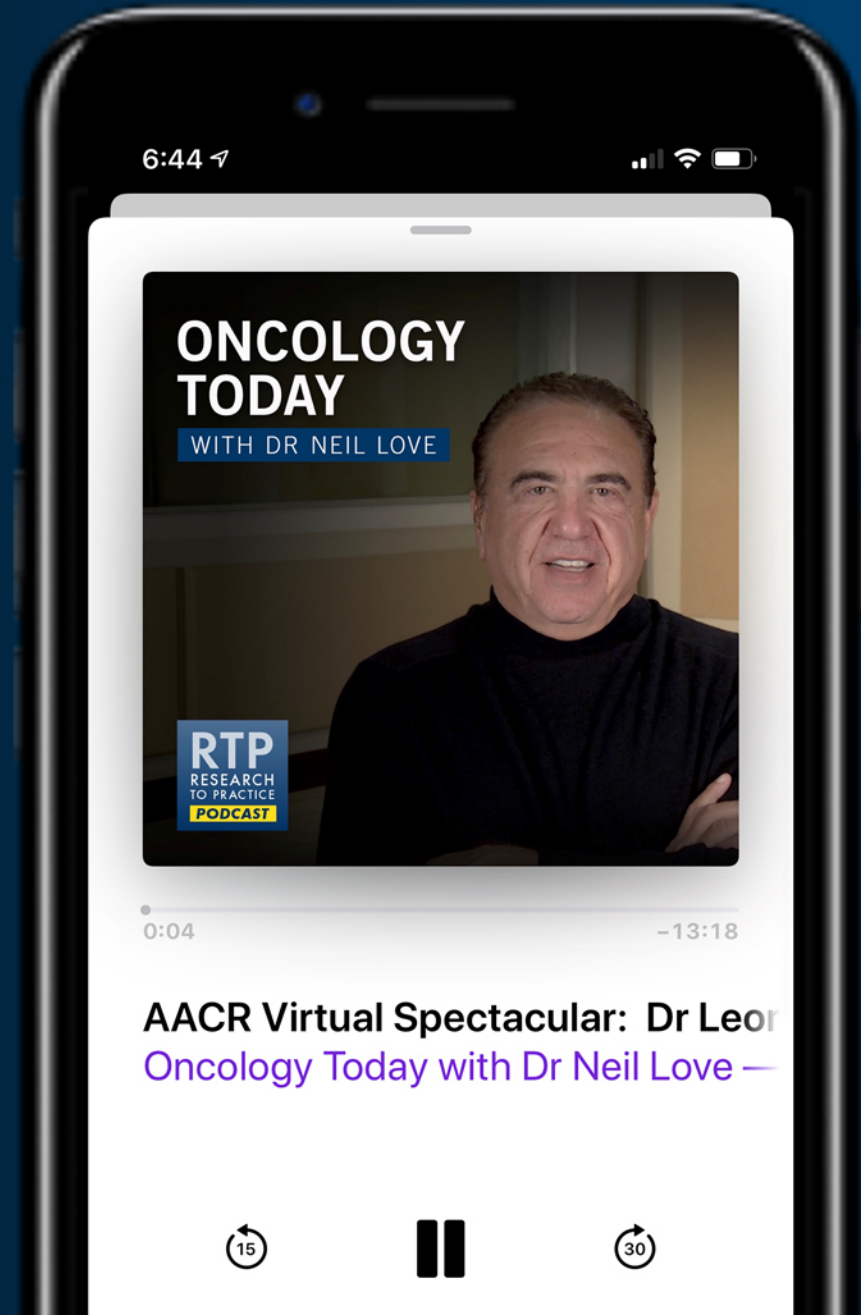
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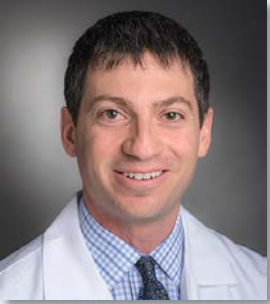
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**Kerry Rogers, MD**

Assistant Professor in the Division of Hematology  
The Ohio State University  
Columbus, Ohio

# *Meet The Professor Program Participating Faculty*



**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



**Brian T Hill, MD, PhD**  
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Cleveland Clinic Taussig Cancer Institute  
Cleveland, Ohio



**Ian W Flinn, MD, PhD**  
Director of Lymphoma Research Program  
Sarah Cannon Research Institute  
Tennessee Oncology  
Nashville, Tennessee

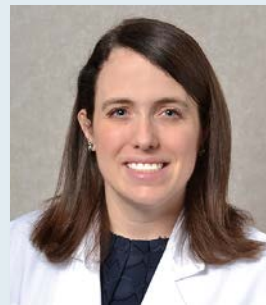


**Brad S Kahl, MD**  
Professor of Medicine  
Washington University School of Medicine  
Director, Lymphoma Program  
Siteman Cancer Center  
St Louis, Missouri

# *Meet The Professor Program Participating Faculty*



**Anthony R Mato, MD, MSCE**  
Associate Attending  
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**Kerry Rogers, MD**  
Assistant Professor in the Division of Hematology  
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  
Eugene, Oregon

# *Meet The Professor Program Participating Faculty*



**Mitchell R Smith, MD, PhD**

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



**Jennifer Woyach, MD**

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



**William G Wierda, MD, PhD**

DB Lane Cancer Research  
Distinguished Professor  
Department of Leukemia  
Division of Cancer Medicine  
The University of Texas  
MD Anderson Cancer Center  
Houston, Texas

# *Meet The Professor* Program Moderator



***Project Chair***

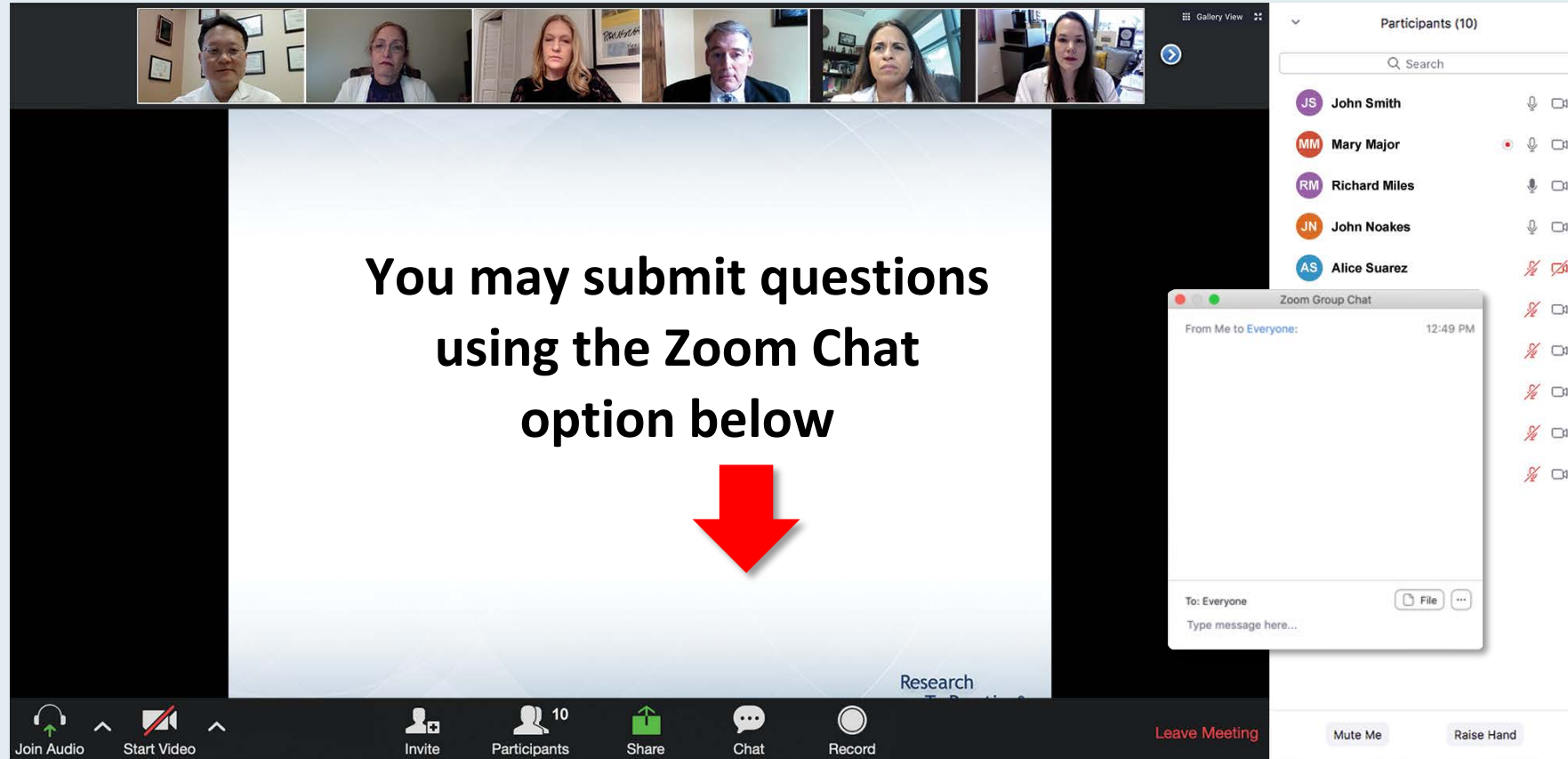
**Neil Love, MD**

Research To Practice

Miami, Florida



# We Encourage Clinicians in Practice to Submit Questions



The screenshot displays a Zoom meeting interface. At the top, a gallery view shows six participants. The main screen displays a presentation slide with the text: "You may submit questions using the Zoom Chat option below". A large red arrow points downwards from this text. On the right side, a "Participants (10)" list is visible, showing names like John Smith, Mary Major, Richard Miles, John Noakes, and Alice Suarez. Below the participants list, a "Zoom Group Chat" window is open, showing a message from "Me to Everyone" at 12:49 PM. The bottom toolbar includes icons for "Join Audio", "Start Video", "Invite", "Participants", "Share", "Chat", and "Record". A "Leave Meeting" button is also present.

**Feel free to submit questions now before the program commences and throughout the program.**

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**Quick Poll**

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- ☐ Daratumumab + lenalidomide +/- dexamethasone
- ☐ Daratumumab + pomalidomide +/- dexamethasone
- ☐ Daratumumab + bortezomib +/- dexamethasone
- ☐ Ixazomib + Rd
- ☐ Other

**Participants (10)**

Name	Status
JS John Smith	Microphone On, Video On
MM Mary Major	Microphone On, Video On
RM Richard Miles	Microphone On, Video On
JN John Noakes	Microphone On, Video On
AS Alice Suarez	Microphone Off, Video Off
JP Jane Perez	Microphone Off, Video Off
RS Robert Stiles	Microphone Off, Video Off
JF Juan Fernandez	Microphone Off, Video Off
AK Ashok Kumar	Microphone Off, Video Off
JS Jeremy Smith	Microphone Off, Video Off

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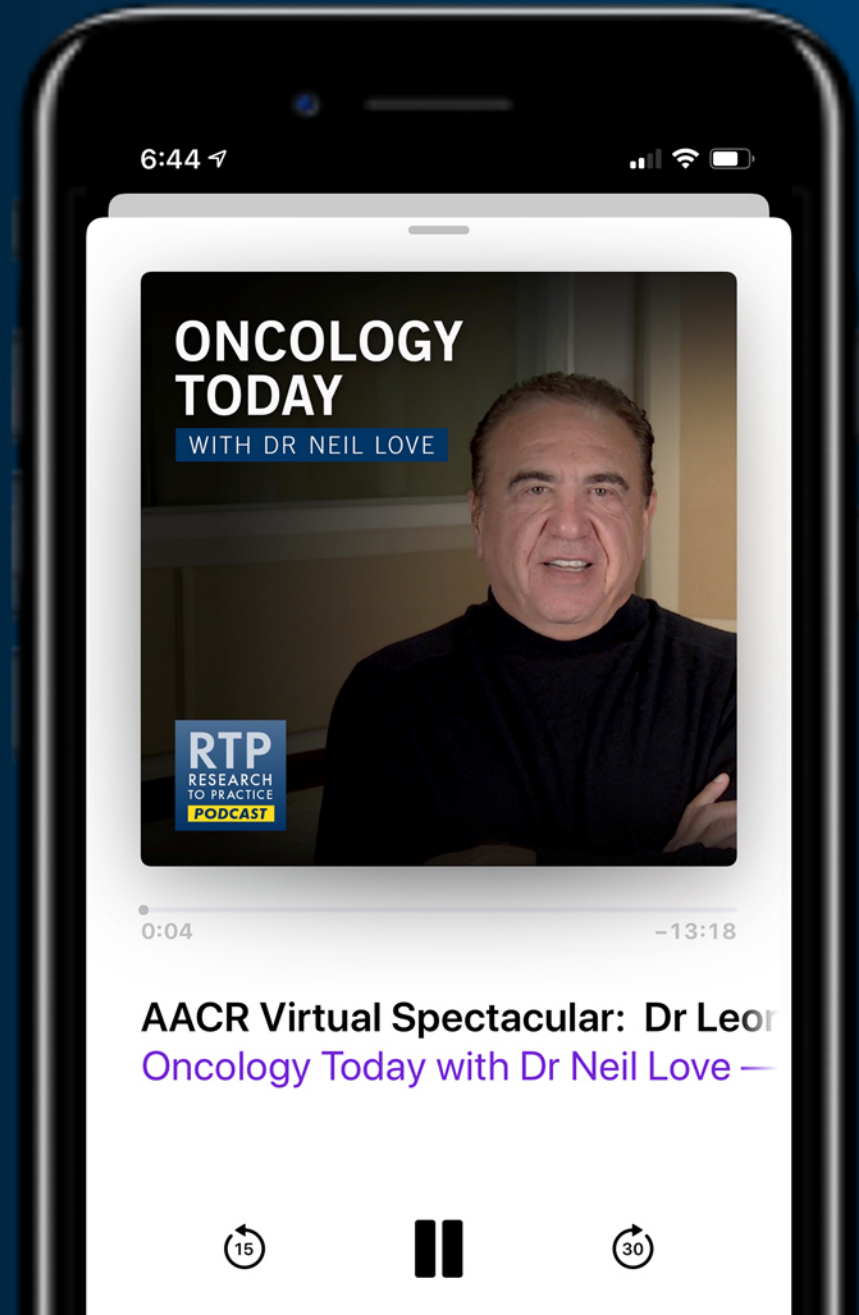
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# **Clinical Investigator Perspectives on the Current and Future Role of PARP Inhibition in the Management of Ovarian Cancer**

*A Meet The Professor Series*

**Friday, September 11, 2020  
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**Faculty**

**Robert L Coleman, MD**

**Moderator**

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Assistant Professor in the Division of Hematology  
The Ohio State University  
Columbus, Ohio



**Erik J Rupard, MD**  
Chief, Section of Hematology-Oncology  
McGlinn Cancer Institute  
Reading Hospital and Medical Center  
West Reading, Pennsylvania

# Meet The Professor with Dr Rogers

## **MODULE 1: Cases from the Community – Dr Rupard**

- A 39-year-old woman with newly diagnosed CLL
- Questions: Considerations for the up-front treatment of CLL
- A 48-year-old woman with cutaneous CLL
- A 67-year-old man with CLL and del(17p)

## **MODULE 2: Beyond the Guidelines – Clinical Investigator Approaches to Common Clinical Scenarios**

## **MODULE 3: Key Recent Data Sets**

- PFS and rate and duration of MRD negativity with venetoclax/obinutuzumab (CLL14 trial)
- FDA approval of acalabrutinib (ELEVATE-TN trial)
- Ibrutinib/rituximab in older (Alliance A041202 trial) and younger (ECOG-E1912 trial) patients
- CAPTIVATE MRD cohort
- Available data and current clinical role of ibrutinib/obinutuzumab (iLLUMINATE trial)
- Venetoclax/rituximab (MURANO trial)
- Acalabrutinib (ASCEND trial)
- Side effects associated with BTK inhibitors and venetoclax-associated toxicities



# Case Presentation – Dr Rupard: A 39-year-old woman with newly diagnosed CLL



**Dr Eric Rupard**

- 2018: Slowly declining Hgb, fatigue. Diagnosed with CLL, with 13q
- Ibrutinib 420 mg daily, with quadrupling of WBC (see image)
  - 6 months later: Slow decline in WBC
  - 6 months later: Slight increase in WBC
  - Improvement in fatigue
- Patient desires to continue treatment with ibrutinib

## Questions

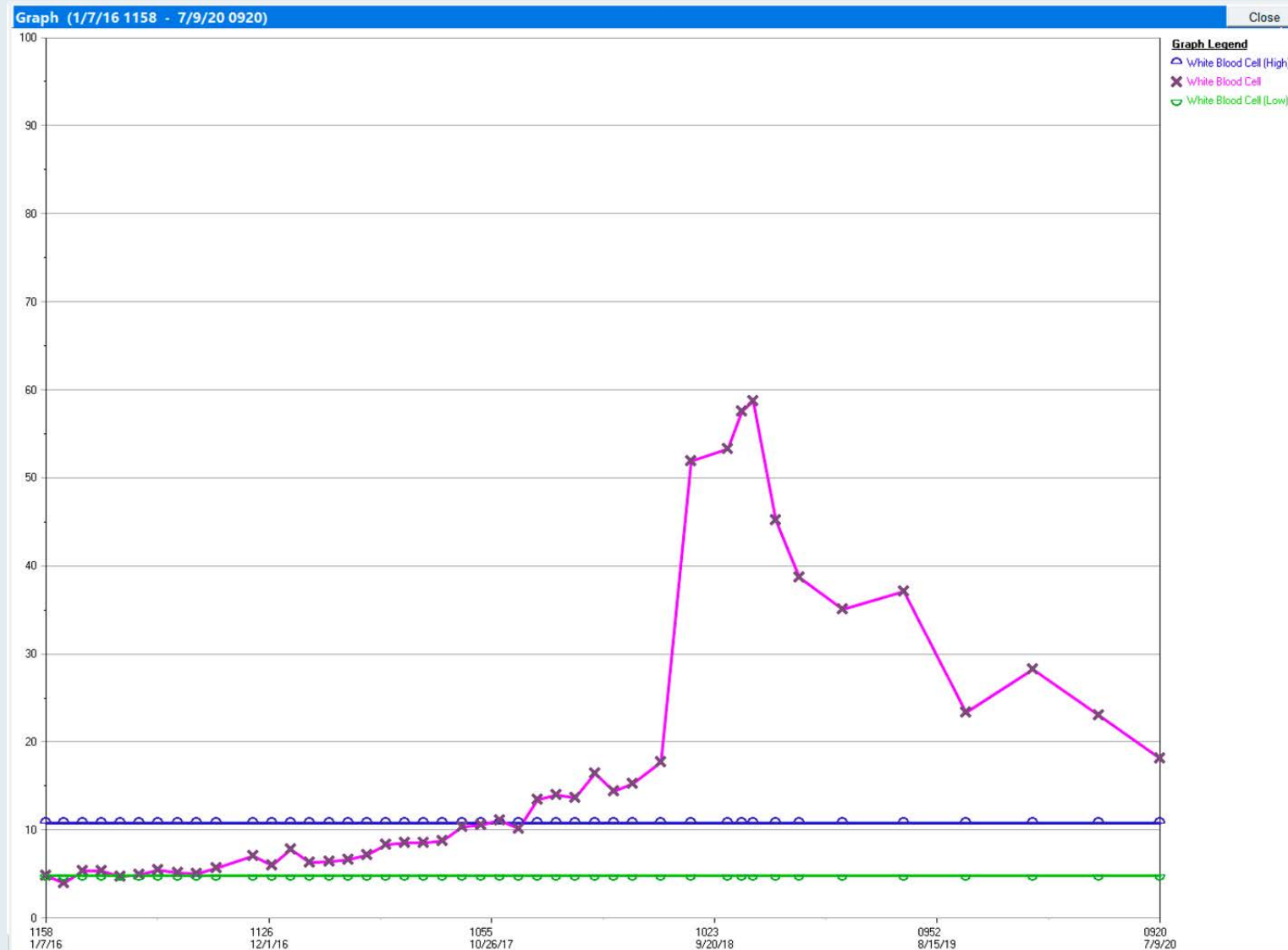
- Have you seen patients with very prolonged, ongoing white blood cell/lymphocyte responses to Bruton tyrosine kinase inhibitors?
- At what point do you decide that the BTK inhibitor is not working and move on to another treatment?



# Case Presentation Continued: WBC count over time on ibrutinib



**Dr Eric Rupard**



## Comments and Questions: Considerations for the up-front treatment of CLL



**Dr Eric Rupard**

# Case Presentation – Dr Rupard: A 48-year-old woman with cutaneous CLL

- 2013: Diagnosed with CLL, with del 13q → Observation
- 2015: Developed cutaneous disease (see pics)
- Bendamustine/rituximab, with resolution of leukemia cutis in one week (see after pic) → Lost to follow up
- 2018: Fatigue, pain, weight loss LUQ pain and visible spleen (massive)
- Bendamustine monotherapy (traveling the next day) → Lost to follow up
- 7/2020: Mild cutaneous CLL recurrence
- Ibrutinib 420 mg daily



**Dr Eric Rupard**

## Case Presentation Continued: A 48-year-old woman with cutaneous CLL



**Dr Eric Rupard**



# Case Presentation – Dr Rupard: A 67-year-old man with CLL and del(17p)



**Dr Eric Rupard**

- 2008: Diagnosed with CLL, CD-38-negative, del(17p) → BR, with CR
- 2015: WBC rising, platelets falling, bothersome LAD
- Rituximab monotherapy (Ibrutinib not feasible financially)
  - Complicated by necrotizing fasciitis, s/p BKA LLE → Recovered
- 2017: Ibrutinib, with remission in about 4 months
- 7/2019: Cellulitis of left leg stump, atrial fibrillation → Ibrutinib discontinued
- 1/2020: b-sxs (NS/fatigue/LOW) plus LAD → Acalabrutinib 100 mg daily
- 7/2020: Admit SOB, pericardial effusion; CT CAP: Bulky disease chest/abd; Biopsy: DLBCL
- Recommended R-CHOP, but due to second tele-opinion: Gem/carbo, with minimal response → Hospice

## Questions

- Have you seen this kind of infectious complication shortly after rituximab?
- Do you rechallenge patients who have had atrial fibrillation on ibrutinib and have been cardioverted out of it? Or, do you try to avoid the BTK inhibitors in the future?
- What is the safety of acalabrutinib in somebody who had previously had atrial fibrillation on ibrutinib?



# Meet The Professor with Dr Rogers

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- Side effects associated with BTK inhibitors and venetoclax-associated toxicities

**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?**

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 unmutated IGHV and no del(17p) or TP53 mutation who requires treatment?

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



# 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?

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

# 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?

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

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

BR = bendamustine/rituximab; FCR = fludarabine/cyclophosphamide/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	 KERRY A ROGERS, MD	Acalabrutinib or venetoclax + obinutuzumab
 IAN W FLINN, MD, PHD	Acalabrutinib	 JEFF SHARMAN, MD	Venetoclax + obinutuzumab
 BRIAN T HILL, MD, PHD	Obinutuzumab	 MITCHELL R SMITH, MD, PHD	Ibrutinib
 BRAD S KAHL, MD	Venetoclax + obinutuzumab	 WILLIAM G WIERDA, MD, PHD	Venetoclax + obinutuzumab
 ANTHONY R MATO, MD, MSCE	Acalabrutinib	 JENNIFER WOYACH, MD	Ibrutinib
 JOHN M PAGEL, MD, PHD	Acalabrutinib		

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

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



**Based on current clinical trial data and your personal experience, how would you compare the global efficacy of acalabrutinib to that of ibrutinib for CLL?**

 <b>MATTHEW S DAVIDS, MD, MMSC</b>	<b>About the same</b>	 <b>KERRY A ROGERS, MD</b>	<b>About the same</b>
 <b>IAN W FLINN, MD, PHD</b>	<b>About the same</b>	 <b>JEFF SHARMAN, MD</b>	<b>Not enough data are currently available</b>
 <b>BRIAN T HILL, MD, PHD</b>	<b>About the same</b>	 <b>MITCHELL R SMITH, MD, PHD</b>	<b>About the same</b>
 <b>BRAD S KAHL, MD</b>	<b>About the same</b>	 <b>WILLIAM G WIERDA, MD, PHD</b>	<b>About the same</b>
 <b>ANTHONY R MATO, MD, MSCE</b>	<b>About the same</b>	 <b>JENNIFER WOYACH, MD</b>	<b>About the same</b>
 <b>JOHN M PAGEL, MD, PHD</b>	<b>About the same</b>		

Based on current clinical trial data and your personal experience, how would you compare the global efficacy of a single-agent Bruton tyrosine kinase (BTK) inhibitor to that of venetoclax/obinutuzumab for CLL?

 <div>MATTHEW S DAVIDS, MD, MMSC</div>	Not enough data are currently available	 <div>KERRY A ROGERS, MD</div>	Not enough data are currently available
 <div>IAN W FLINN, MD, PHD</div>	About the same	 <div>JEFF SHARMAN, MD</div>	A single-agent BTK inhibitor is more efficacious
 <div>BRIAN T HILL, MD, PHD</div>	A single-agent BTK inhibitor is more efficacious	 <div>MITCHELL R SMITH, MD, PHD</div>	Not enough data are currently available
 <div>BRAD S KAHL, MD</div>	About the same	 <div>WILLIAM G WIERDA, MD, PHD</div>	I don't know
 <div>ANTHONY R MATO, MD, MSCE</div>	About the same	 <div>JENNIFER WOYACH, MD</div>	Not enough data are currently available
 <div>JOHN M PAGEL, MD, PHD</div>	Venetoclax/obinutuzumab is more efficacious		



**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	 KERRY A ROGERS, MD	Discontinue treatment
 IAN W FLINN, MD, PHD	Discontinue treatment	 JEFF SHARMAN, MD	Discontinue treatment
 BRIAN T HILL, MD, PHD	Discontinue treatment	 MITCHELL R SMITH, MD, PHD	Discontinue treatment
 BRAD S KAHL, MD	Discontinue treatment	 WILLIAM G WIERDA, MD, PHD	Continue treatment
 ANTHONY R MATO, MD, MSCE	Continue treatment	 JENNIFER WOYACH, MD	Discontinue treatment
 JOHN M PAGEL, MD, PHD	Continue 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 achieved undetectable MRD status after 1 year of treatment?

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

**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?

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

**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?

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



**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**



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?

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

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

 <b>MATTHEW S DAVIDS, MD, MMSC</b>	<b>8 days</b>	 <b>KERRY A ROGERS, MD</b>	<b>2 nights for each dose escalation</b>
 <b>IAN W FLINN, MD, PHD</b>	<b>2 days</b>	 <b>JEFF SHARMAN, MD</b>	<b>2 days</b>
 <b>BRIAN T HILL, MD, PHD</b>	<b>2 days (&lt;48 hours)</b>	 <b>MITCHELL R SMITH, MD, PHD</b>	<b>1- 2 days</b>
 <b>BRAD S KAHL, MD</b>	<b>2 days</b>	 <b>WILLIAM G WIERDA, MD, PHD</b>	<b>2 days</b>
 <b>ANTHONY R MATO, MD, MSCE</b>	<b>2-3 days</b>	 <b>JENNIFER WOYACH, MD</b>	<b>2 days or rapid escalation to full dose over 5 days</b>
 <b>JOHN M PAGEL, MD, PHD</b>	<b>1 day</b>		

Based on current clinical trial data and your personal experience, how would you compare the tolerability/toxicity of acalabrutinib to that of ibrutinib for CLL?



MATTHEW S DAVIDS, MD,  
MMSC

**Acalabrutinib has less toxicity**



IAN W FLINN, MD, PHD

**Acalabrutinib has less toxicity**



BRIAN T HILL, MD, PHD

**Acalabrutinib has less toxicity**



BRAD S KAHL, MD

**Acalabrutinib has less toxicity**



ANTHONY R MATO, MD, MSCE

**Acalabrutinib has less toxicity**



JOHN M PAGEL, MD, PHD

**Acalabrutinib has less toxicity**



KERRY A ROGERS, MD

**Acalabrutinib has less toxicity**



JEFF SHARMAN, MD

**Acalabrutinib has less toxicity**



MITCHELL R SMITH, MD, PHD

**Acalabrutinib has less toxicity**



WILLIAM G WIERDA, MD, PHD












**Acalabrutinib has less toxicity**



JENNIFER WOYACH, MD

**Acalabrutinib has less toxicity**

Based on current clinical trial data and your personal experience, how would you compare the tolerability/toxicity of a single-agent BTK inhibitor to that of venetoclax/obinutuzumab for CLL?

 <div>MATTHEW S DAVIDS, MD, MMSC</div>	Venetoclax/obinutuzumab has less toxicity	 <div>KERRY A ROGERS, MD</div>	Venetoclax/obinutuzumab has less toxicity
 <div>IAN W FLINN, MD, PHD</div>	Venetoclax/obinutuzumab has less toxicity	 <div>JEFF SHARMAN, MD</div>	Venetoclax/obinutuzumab has less toxicity
 <div>BRIAN T HILL, MD, PHD</div>	Venetoclax/obinutuzumab has less toxicity	 <div>MITCHELL R SMITH, MD, PHD</div>	A single-agent BTK inhibitor has less toxicity
 <div>BRAD S KAHL, MD</div>	Venetoclax/obinutuzumab has less toxicity	 <div>WILLIAM G WIERDA, MD, PHD</div>	Venetoclax/obinutuzumab has less toxicity
 <div>ANTHONY R MATO, MD, MSCE</div>	Venetoclax/obinutuzumab has less toxicity	 <div>JENNIFER WOYACH, MD</div>	About the same
 <div>JOHN M PAGEL, MD, PHD</div>	About the same		

# Meet The Professor with Dr Rogers

## **MODULE 1: Cases from the Community – Dr Rupard**

- A 39-year-old woman with newly diagnosed CLL
- Questions: Considerations for the up-front treatment of CLL
- A 48-year-old woman with cutaneous CLL
- A 67-year-old man with CLL and del(17p)

## **MODULE 2: Beyond the Guidelines – Clinical Investigator Approaches to Common Clinical Scenarios**

## **MODULE 3: Key Recent Data Sets**

- PFS and rate and duration of MRD negativity with venetoclax/obinutuzumab (CLL14 trial)
- FDA approval of acalabrutinib (ELEVATE-TN trial)
- Ibrutinib/rituximab in older (Alliance A041202 trial) and younger (ECOG-E1912 trial) patients
- CAPTIVATE MRD cohort
- Available data and current clinical role of ibrutinib/obinutuzumab (iLLUMINATE trial)
- Venetoclax/rituximab (MURANO trial)
- Acalabrutinib (ASCEND trial)
- Side effects associated with BTK inhibitors and venetoclax-associated toxicities





## How I Treat

# How I manage CLL with venetoclax-based treatments

William G. Wierda<sup>1</sup> and Francesco Paolo Tambaro<sup>2</sup>

<sup>1</sup>Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, TX; and <sup>2</sup>Unità Operativa di Trapianto di Midollo Osseo e Servizio Trasfusionale, Azienda Ospedaliera di Rilievo Nazionale Santobono-Pausilipon, Napoli, Italy



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# Strategy for Selecting First-Line CLL Treatment

<b>TP53 status (del(17p)/TP53 mutation)</b>	<b>Age/ fitness</b>	<b>IGHV MS</b>	<b>First-line treatment (in order of authors' preference)</b>
TP53 intact	Younger/ fit	Mutated	(1) FCR (fixed duration), (2) VEN + OBIN (fixed duration), (3) BTKi ± OBIN (continuous)
		Unmutated	(1) VEN + OBIN (fixed-duration), (2) BTKi ± OBIN (continuous)
	Older/ unfit	Mutated	(1) VEN + OBIN (fixed duration), (2) BTKi ± OBIN (continuous)
		Unmutated	(1) BTKi ± OBIN (continuous), (2) VEN + OBIN (fixed-duration)

<b>TP53 status (del(17p)/TP53 mutation)</b>	<b>Age/ fitness</b>	<b>IGHV MS</b>	<b>First-line treatment (in order of authors' preference)</b>
TP53 deleted and/ or mutated	All	Either	(1) BTKi ± OBIN (continuous), (2) VEN + OBIN (fixed duration), no CIT

# Strategy for Selecting Treatment of R/R CLL

Prior treatment			Recommendation for next treatment	Allo-SCT planning
CIT	BCL2i	BTKi		
Yes	No	No	VEN + RIT (fixed duration) or BTKi (continuous)	No
		Yes (intolerant)	Alternative BTKi (continuous) or PI3Ki ± CD20 mAb (continuous)	No
		Yes (refractory)	VEN + RIT	Short-term
	Yes	No	BTKi (continuous)	Yes
		Yes (intolerant)	Alternative BTKi (continuous) or PI3Ki ± CD20 mAb (continuous)	Yes
		Yes (refractory)	Clinical trial CIT if no TP53 abnormality to debulk	Immediate

Prior treatment			Recommendation for next treatment	Allo-SCT planning
CIT	BCL2i	BTKi		
No	No	Yes (intolerant)	Alternative BTKi (continuous) or PI3Ki ± CD20 mAb (continuous)	No
		Yes (refractory)	VEN + RIT (fixed duration)	Yes
	Yes	No	BTKi (continuous)	No
		Yes (intolerant)	Alternative BTKi (continuous) or PI3Ki ± CD20 mAb (continuous)	No
		Yes (refractory)	Clinical trial CIT if no TP53 abnormality to debulk	Immediate



# Venetoclax in the Treatment of Chronic Lymphocytic Leukemia: Evidence, Expectations, and Future Prospects

Saba Tariq <sup>1</sup>, Sundus Tariq <sup>2</sup>, Maliha Khan <sup>3</sup>, Aysha Azhar <sup>4</sup>, Mukhtiar Baig <sup>5</sup>

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***Cureus* 2020 Jun 29;12(6):e8908.**

The NEW ENGLAND JOURNAL of MEDICINE

N Engl J Med 2020;383:460-73

REVIEW ARTICLE

Dan L. Longo, M.D., *Editor*

# Treatment of Chronic Lymphocytic Leukemia

Jan A. Burger, M.D., Ph.D.

# How to select a treatment for an individual patient?

## Menu

- Immunochemotherapy
  - FCR
  - BR
  - Chlorambucil/Obinutuzumab
- Novel Agents
  - Ibrutinib  $\pm$  obinutuzumab
  - Acalabrutinib  $\pm$  obinutuzumab
  - Venetoclax + Obinutuzumab

## Considerations

- If deletion 17p or p53 mutation
  - Chemo not very effective, better off with novel agents
- If IgHV unmutated
  - Chemo less effective than novel agents
- If IgHV mutated
  - Chemo and novel agents are similarly effective

Courtesy of Brad Kahl, MD

# Scenario #1

- 52 yo man with CLL requiring treatment.
  - No p53 mutation or 17p deletion.
  - IgHV unmutated.
- Best options include
  1. Venetoclax plus obinutuzumab
  2. BTKi plus obinutuzumab
- Pro's and Con's to each

Courtesy of Brad Kahl, MD

# Scenario #2

- 52 yo man with CLL requiring treatment.
  - No p53 mutation by sequencing
  - No 17p deletion or 11q deletion by FISH.
  - IgHV mutated.
- Best options include
  1. FCR
  2. Venetoclax plus obinutuzumab
  3. BTKi plus obinutuzumab
- Pro's and Con's to each

Courtesy of Brad Kahl, MD

# Scenario #3

- 72 yo man with CLL requiring treatment.
  - No p53 mutation.
  - No 17p deletion or 11q deletion.
  - IgHV unmutated.
- Best options include
  1. Venetoclax plus obinutuzumab
  2. BTKi
- Pro's and Con's to each.

Courtesy of Brad Kahl, MD

# Scenario #4

- 72 yo man with CLL requiring treatment.
  - No p53 mutation or 17p deletion.
  - IgHV mutated.
- Best options include
  1. Venetoclax plus obinutuzumab
  2. BR
  3. BTKi
- Pro's and Con's to each.

Courtesy of Brad Kahl, MD

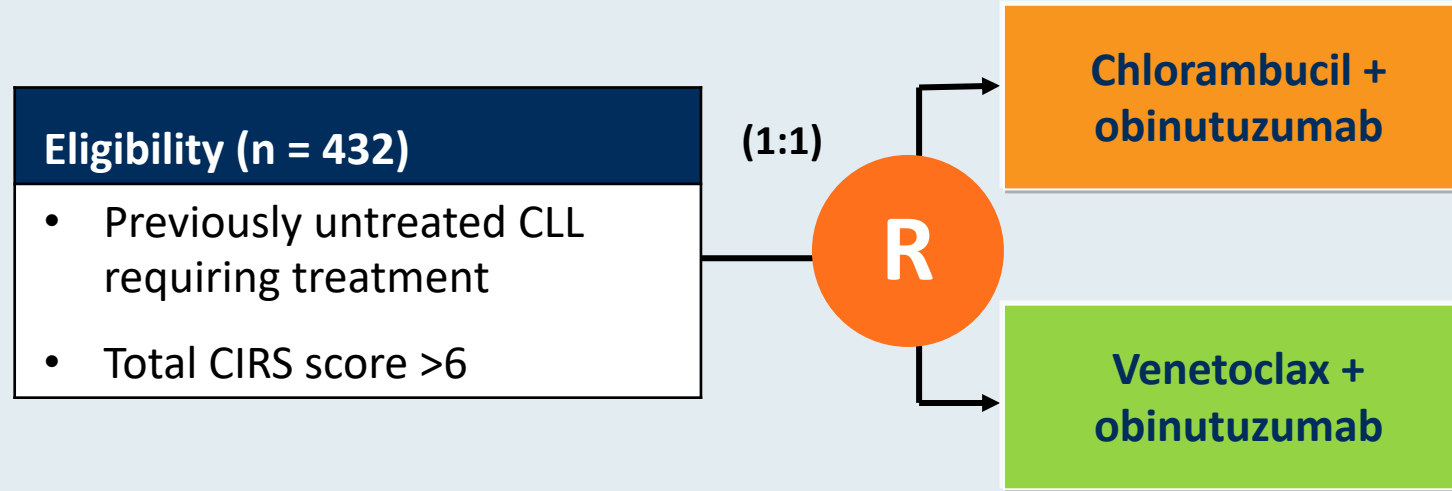
# Scenario #5

- 72 yo man with CLL requiring treatment.
- 17p deletion by FISH
- BTKi plus obinutuzumab
- This is the one scenario where I favor indefinite therapy over time limited therapy

Courtesy of Brad Kahl, MD



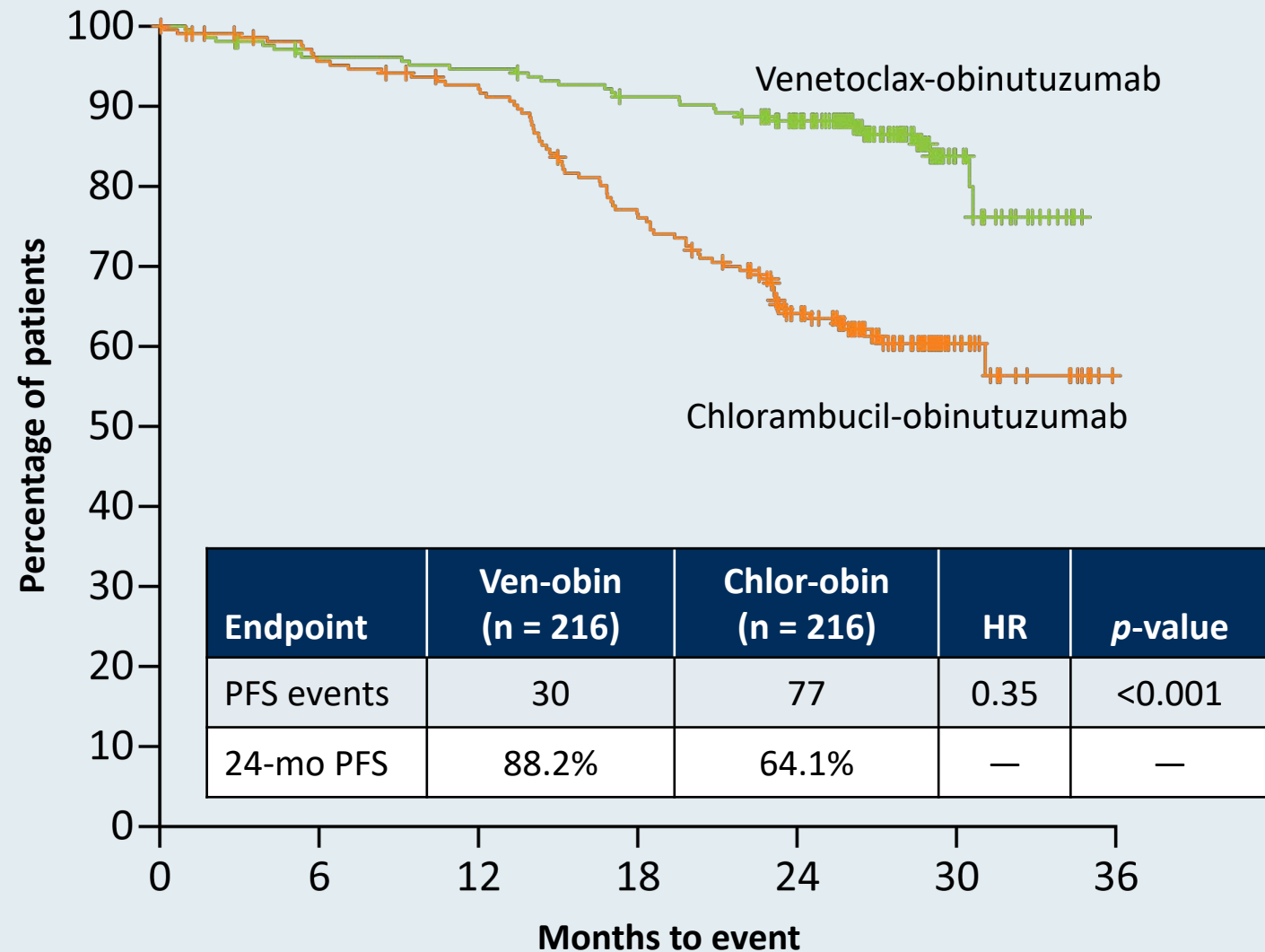
# CLL14 Phase III Study Schema



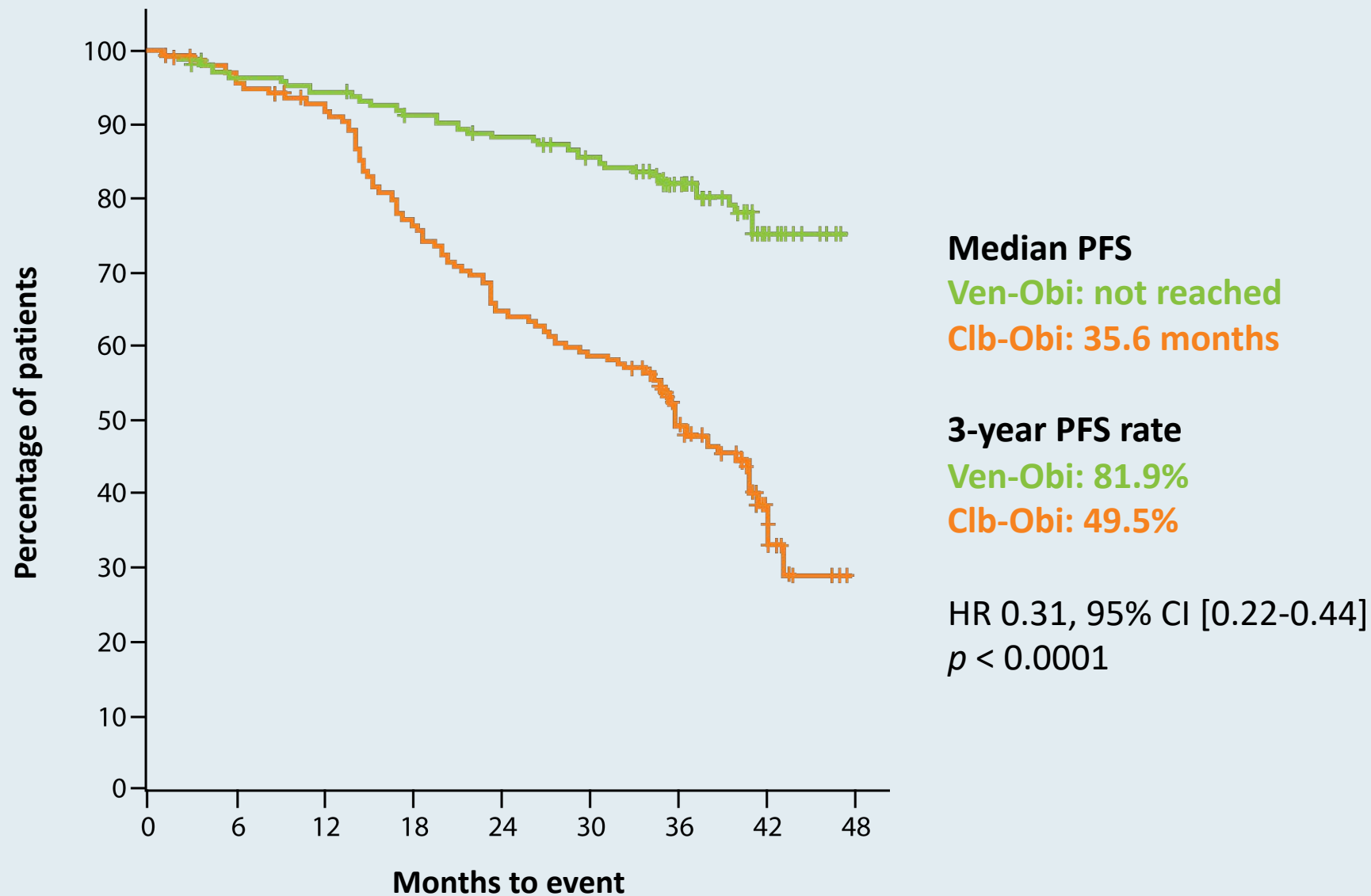
**Primary endpoint:** Progression-free survival

- 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

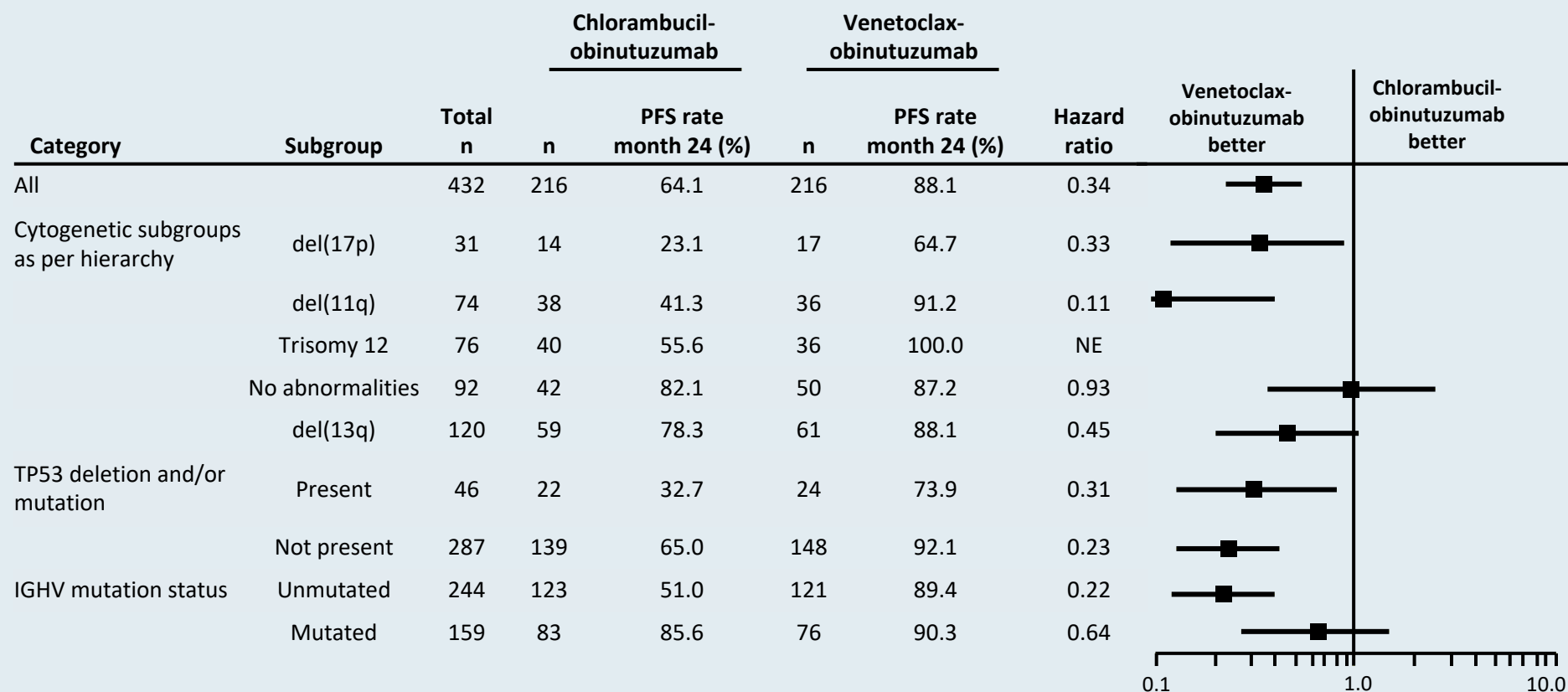
# CLL14: Investigator-Assessed Progression-Free Survival



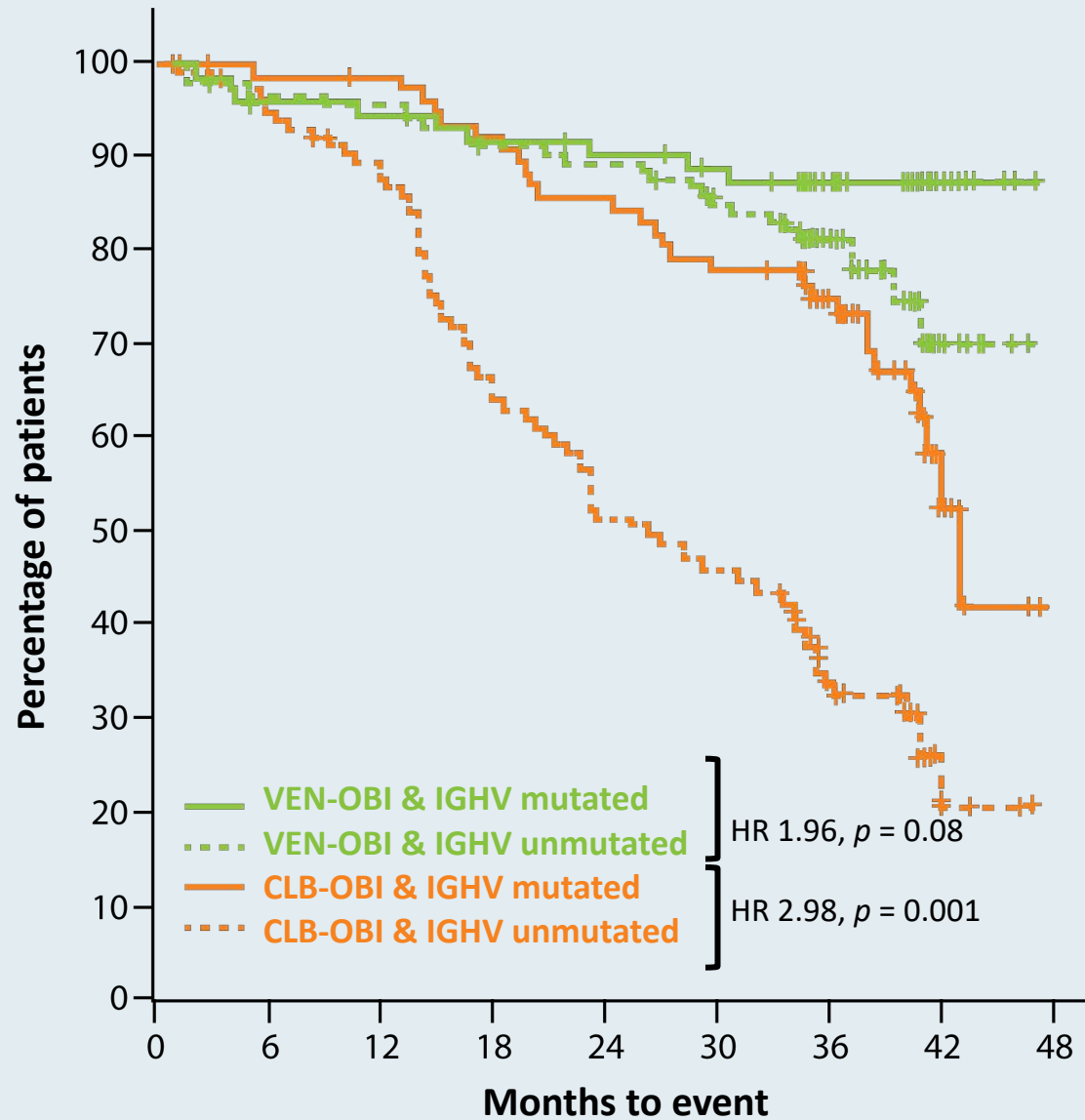
## CLL14: Updated 3-Year PFS



# CLL14: Investigator-Assessed Progression-Free Survival by Prognostic Subgroup



# CLL14: PFS by IGHV Mutation and TP53 Status



## Median PFS

Ven-Obi & IGHVmut: not reached

Ven-Obi & IGHVunmut: not reached

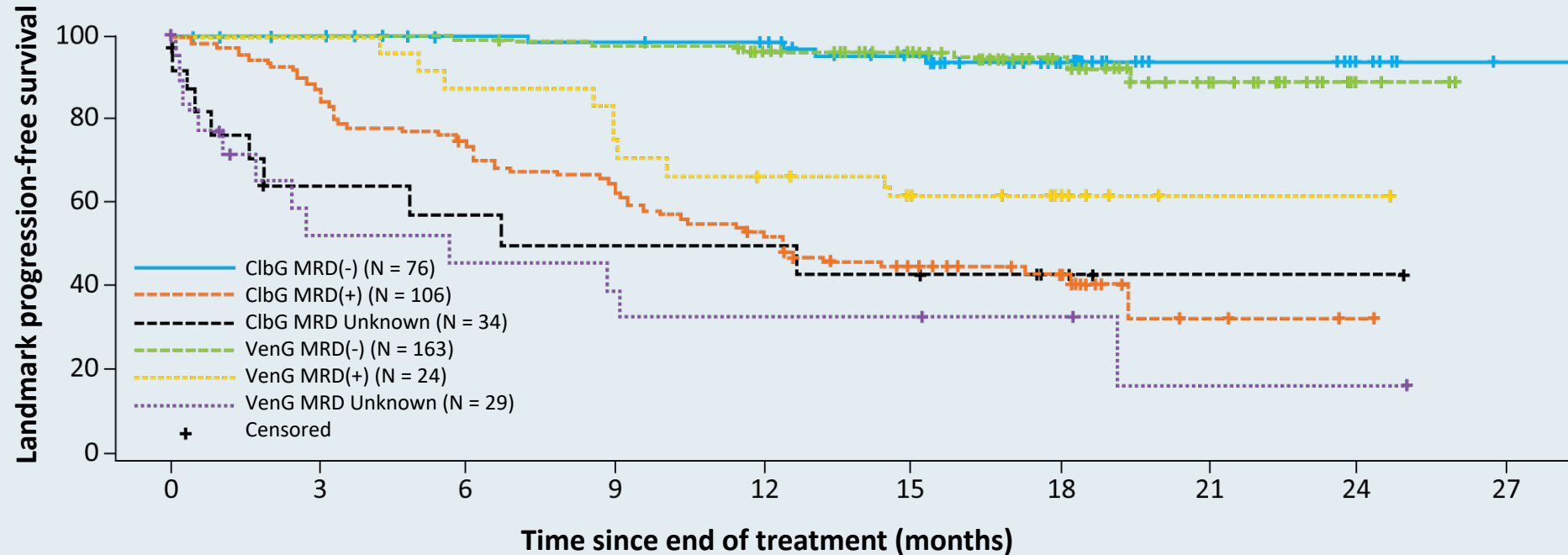
CLb-Obi & IGHVmut: 42.9 months

CLb-Obi & IGHVunmut: 26.3 months

## CLL14: Minimal Residual Disease 3 Months After Treatment

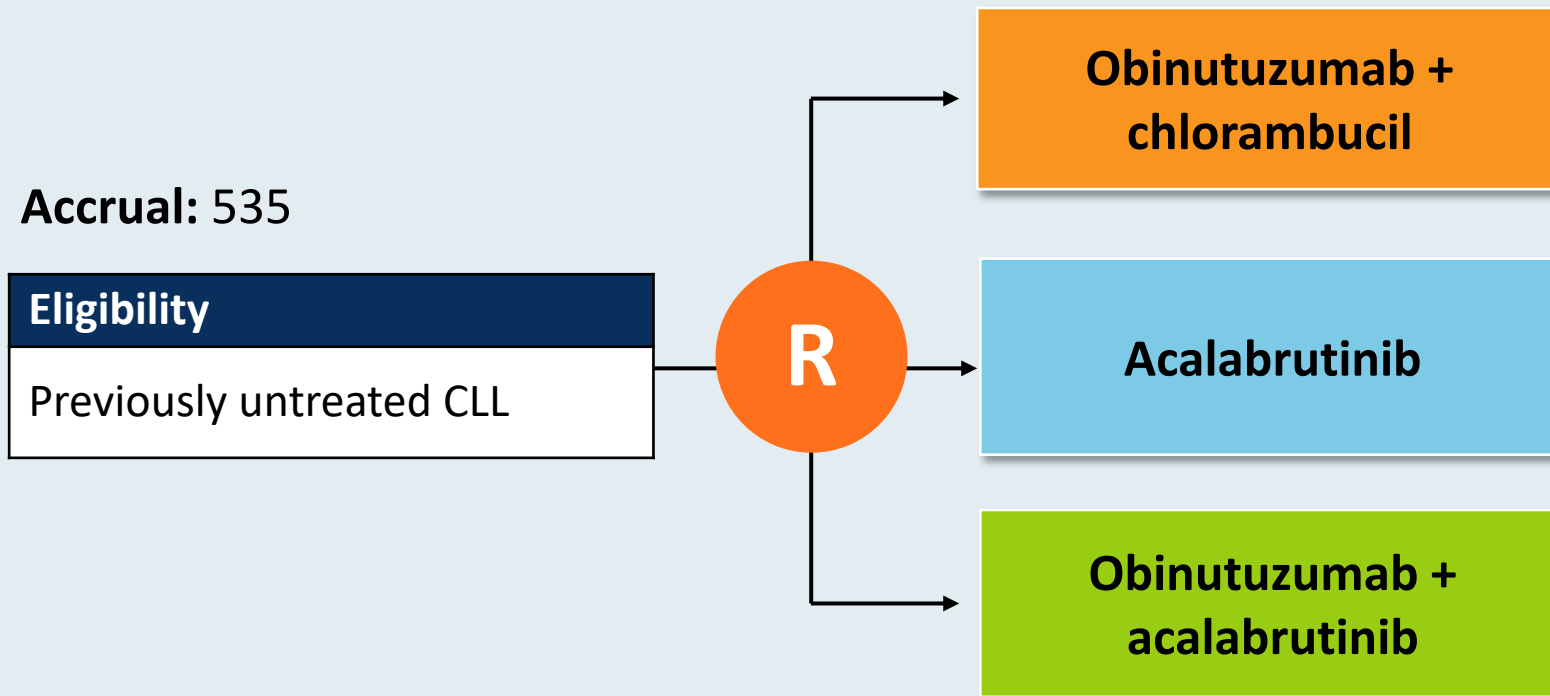
MRD 3 months after treatment	MRD-negative		MRD responders	
	Veneto/obin (N = 216)	Chloram/obin (N = 216)	Veneto/obin (N = 216)	Chloram/obin (N = 216)
MRD in bone marrow	56.9%	17.1%	33.8%	10.6%
Odds ratio, <i>p</i> -value	OR: 6.4, <i>p</i> < 0.0001		OR: 4.3, <i>p</i> < 0.0001	
MRD in peripheral blood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

# 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.

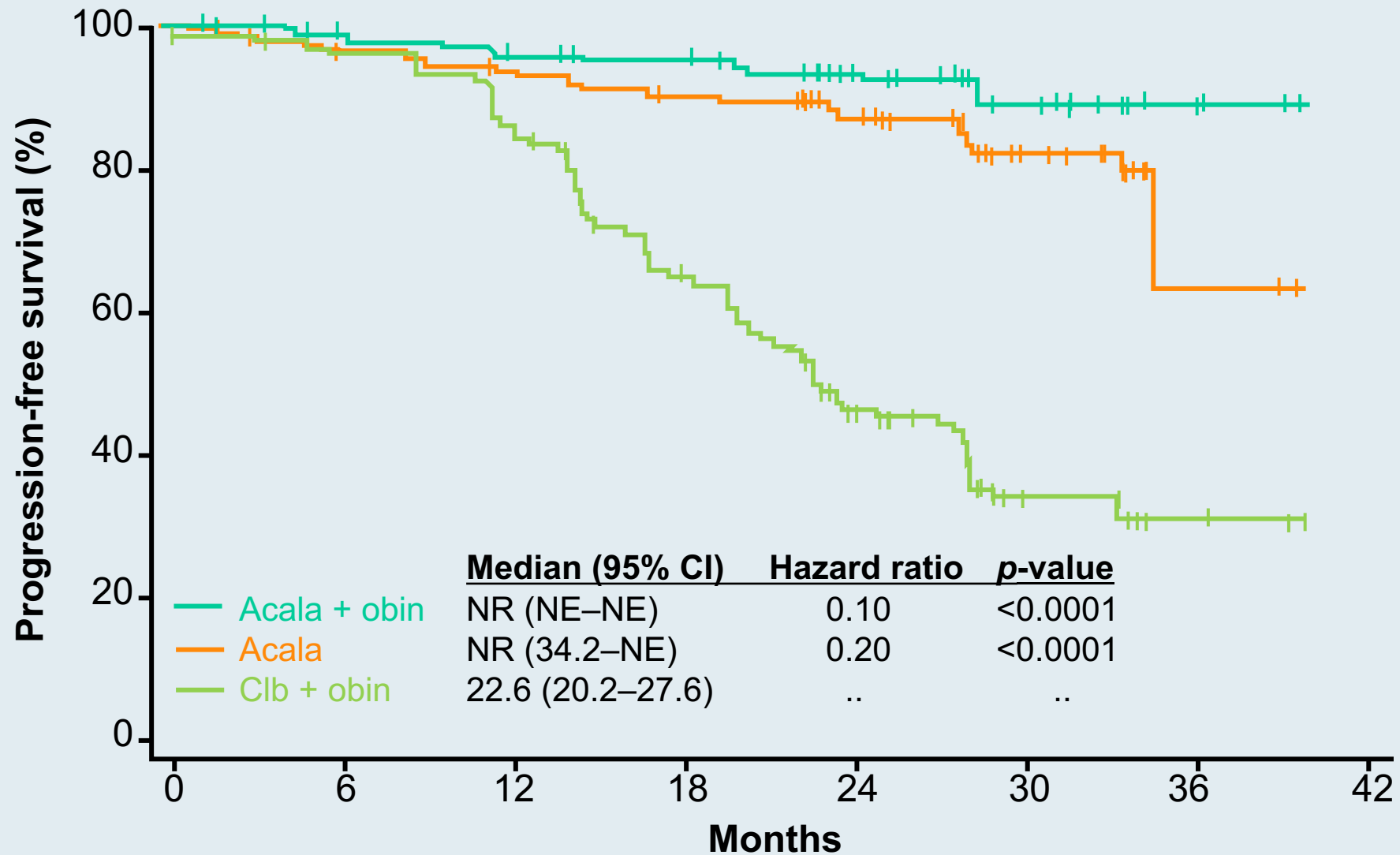
# ELEVATE-TN Phase III Trial Schema



**Primary endpoint:** Progression-free survival



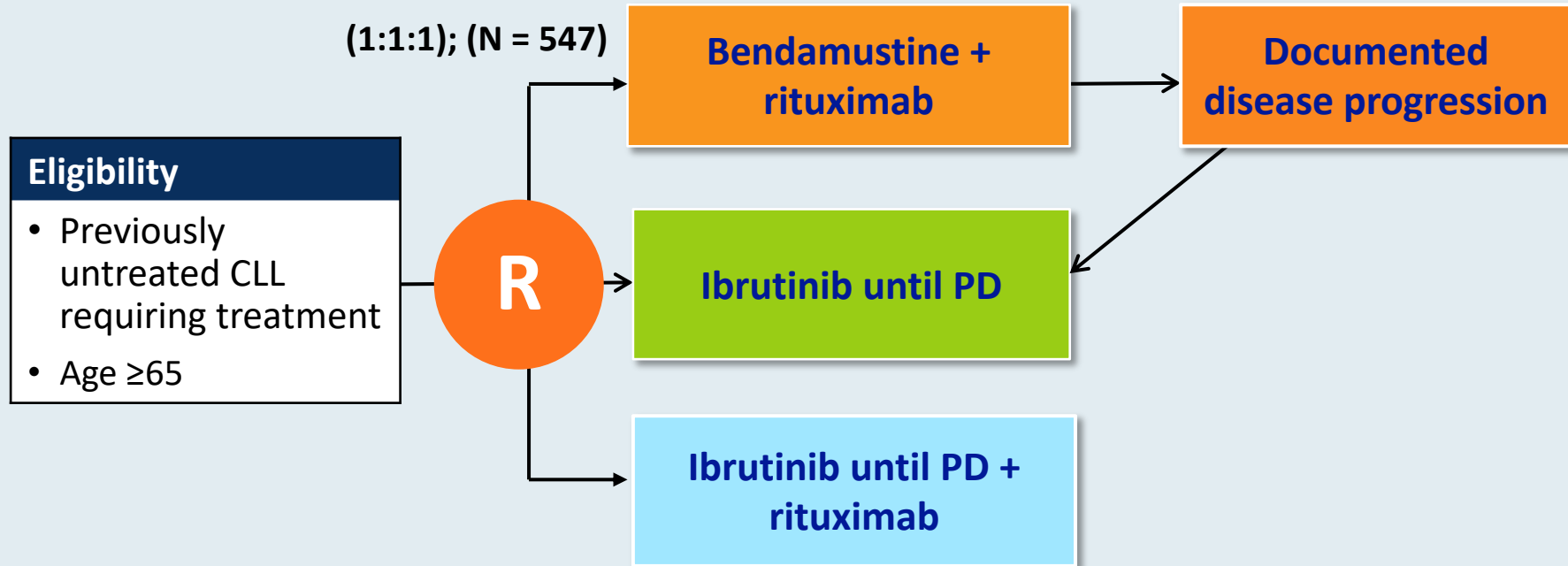
## ELEVATE-TN: PFS (IRC)



## ELEVATE-TN: Select Safety Parameters

	Acalabrutinib/obinutuzumab (n = 178)		Acalabrutinib (n = 179)		Obinutuzumab/chlorambucil (n = 169)	
	Grade 1-2	Grade ≥3	Grade 1-2	Grade ≥3	Grade 1-2	Grade ≥3
Any AE	26%	70%	45%	50%	29%	70%
Serious AE	6%	33%	2%	30%	2%	20%
AE leading to drug discontinuation	11%		9%		14%	
Neutropenia	2%	30%	1%	10%	4%	41%
Grade ≥3 infections						
Infusion-related reactions	11%	2%	0	0	34%	5%

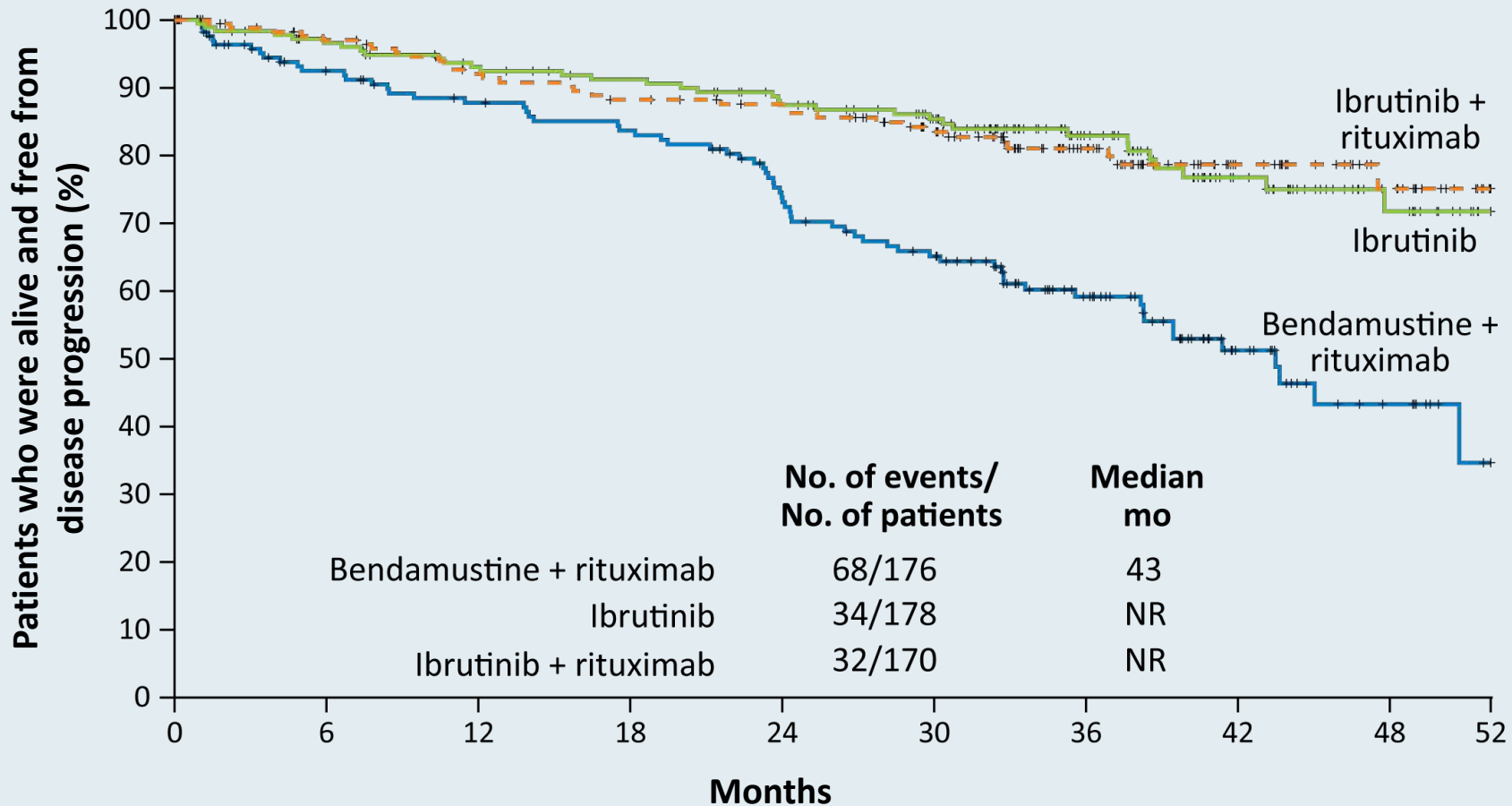
# Phase III Alliance A041202 Study Design



**Primary endpoint:** Progression-free survival (PFS)

**Secondary endpoints:** OS, ORR, Impact of MRD on PFS and OS, Duration of response, Toxicity and Tolerability

# Alliance A041202: Efficacy with Ibrutinib Alone or in Combination with Rituximab Compared to Bendamustine/Rituximab



## Alliance A041202: Grade 3 to 5 Adverse Events of Special Interest

Adverse event	Bendamustine + rituximab (N = 176)	Ibrutinib (N = 180)	Ibrutinib + rituximab (N = 181)	p-value
<b>Hematologic – Any Grade 3-4</b>	<b>61%</b>	<b>41%</b>	<b>39%</b>	<b>&lt;0.001</b>
Anemia	12%	12%	6%	0.09
Decreased neutrophil count	40%	15%	21%	<0.001
Decreased platelet count	15%	7%	5%	0.008
<b>Nonhematologic – Any Grade 3-5</b>	<b>63%</b>	<b>74%</b>	<b>74%</b>	<b>0.04</b>
Bleeding	0	2%	3%	0.46
Infections	15%	20%	21%	0.62
Febrile neutropenia	7%	2%	1%	<0.001
Atrial fibrillation	3%	9%	6%	0.05
Hypertension	15%	29%	34%	<0.001

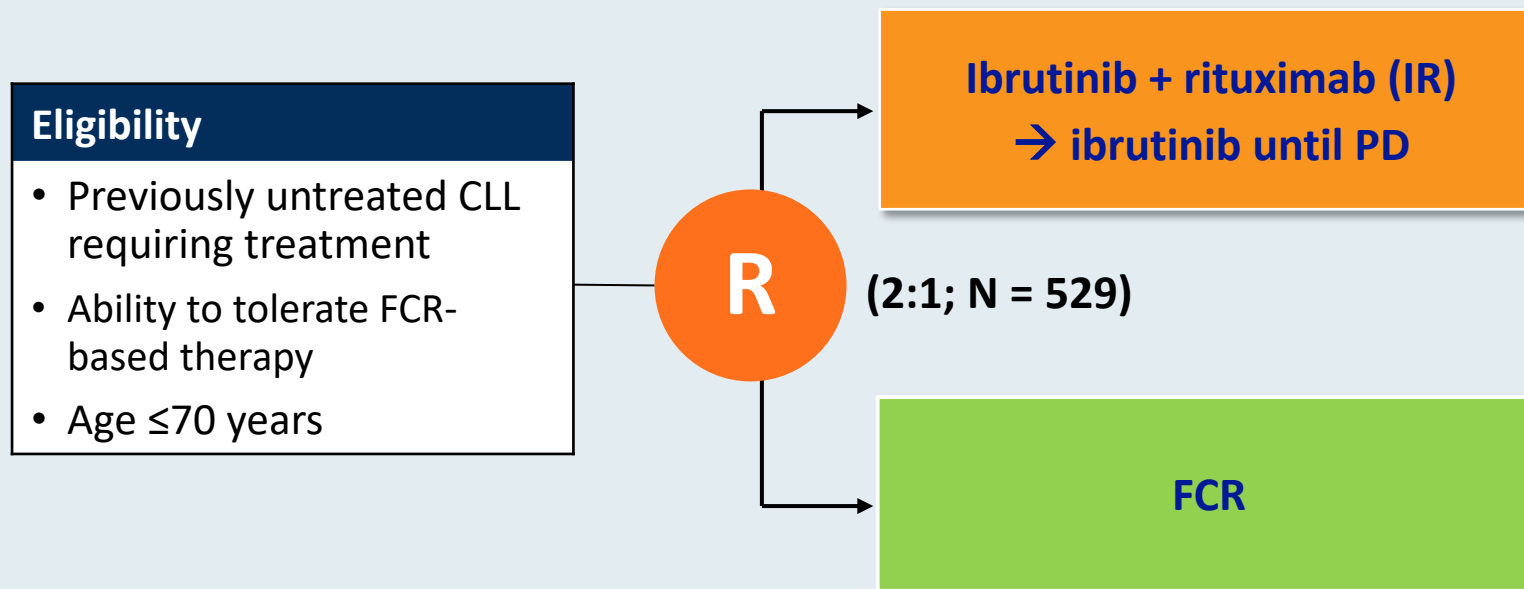
# FDA Approval of Ibrutinib with Rituximab for Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma

Press Release – April 21, 2020

“The Food and Drug Administration expanded the indication of ibrutinib to include its combination with rituximab for the initial treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).

Approval was based on the E1912 trial (NCT02048813), a 2:1 randomized, multicenter, open-label, actively controlled trial of ibrutinib with rituximab compared to fludarabine, cyclophosphamide, and rituximab (FCR) in 529 adult patients 70 years or younger with previously untreated CLL or SLL requiring systemic therapy. Patients with 17p deletion were excluded. Ibrutinib was administered at 420 mg daily until disease progression or unacceptable toxicity.”

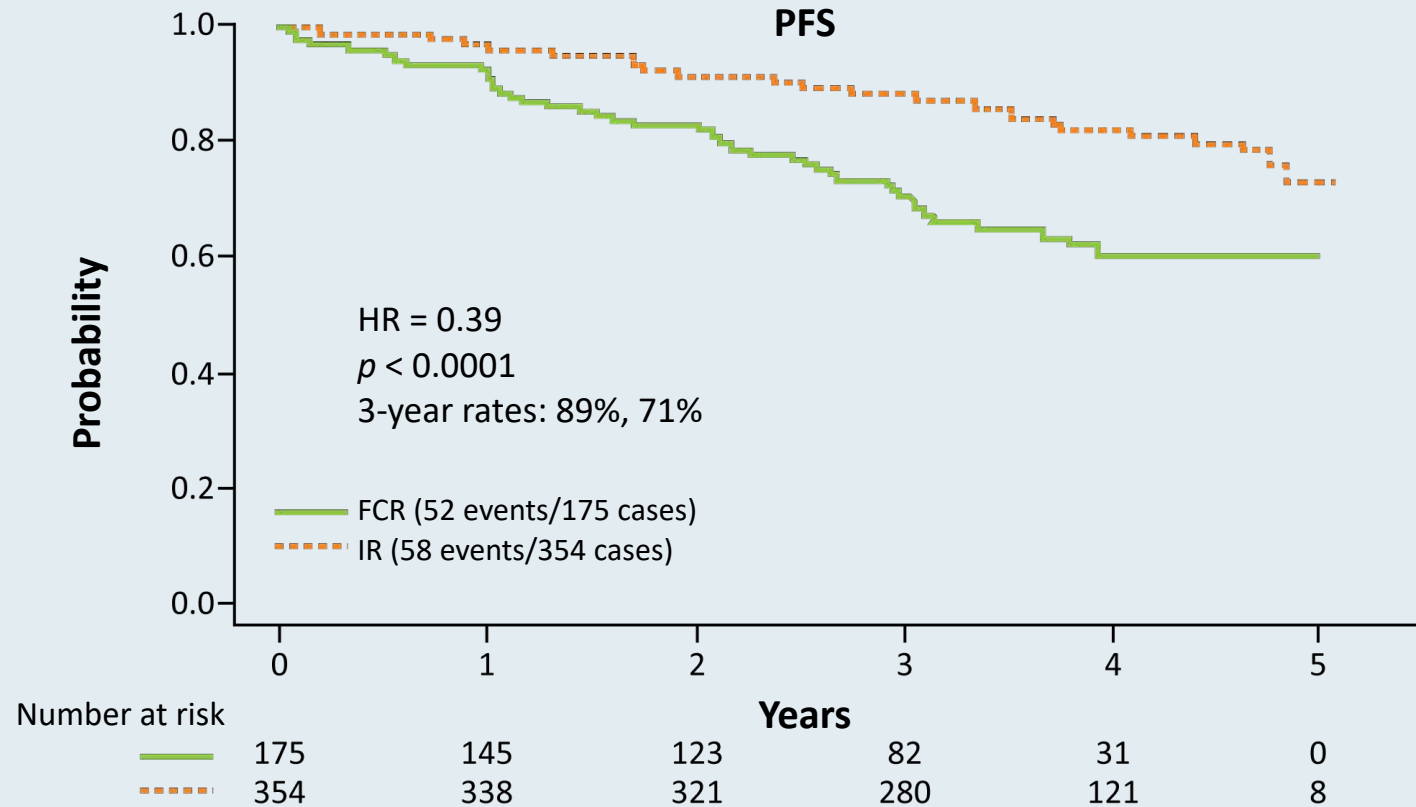
# Phase III ECOG-ACRIN E1912 Study Design



**Primary endpoint:** PFS

**Secondary endpoints:** OS, ORR, Toxicity and Tolerability

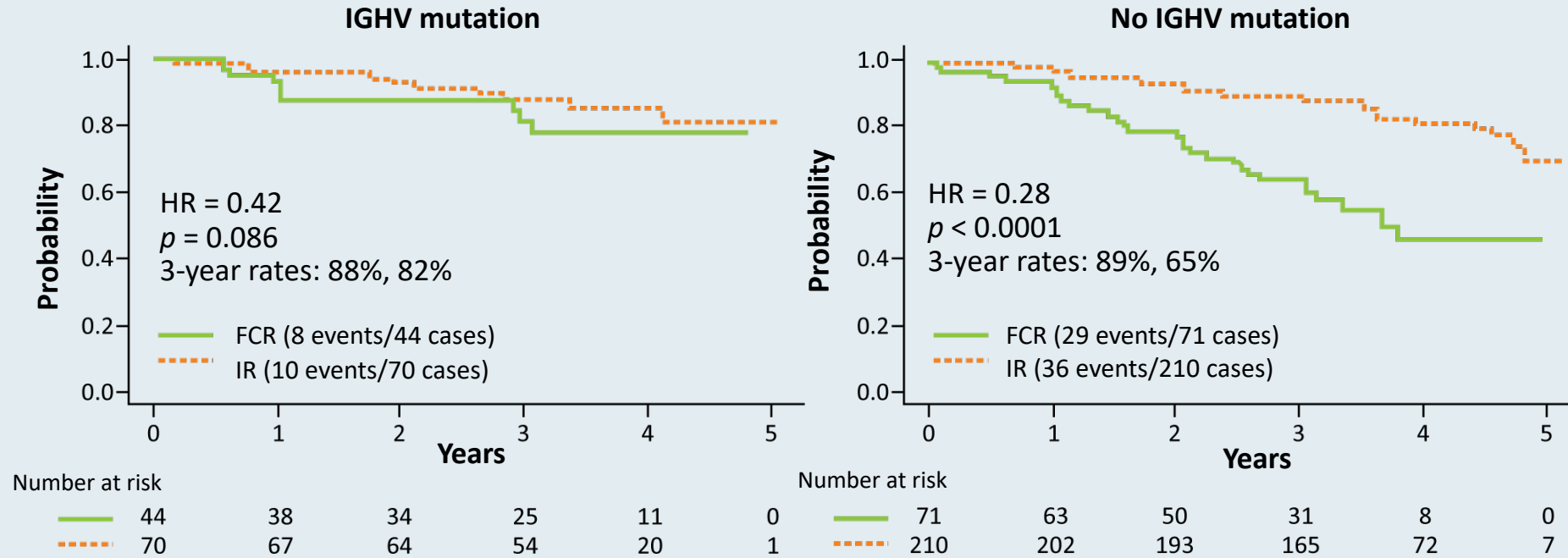
# ECOG-ACRIN E1912 Extended Follow-Up: Up-Front IR Compared to FCR for Younger Patients with CLL



- Grade  $\geq 3$  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.

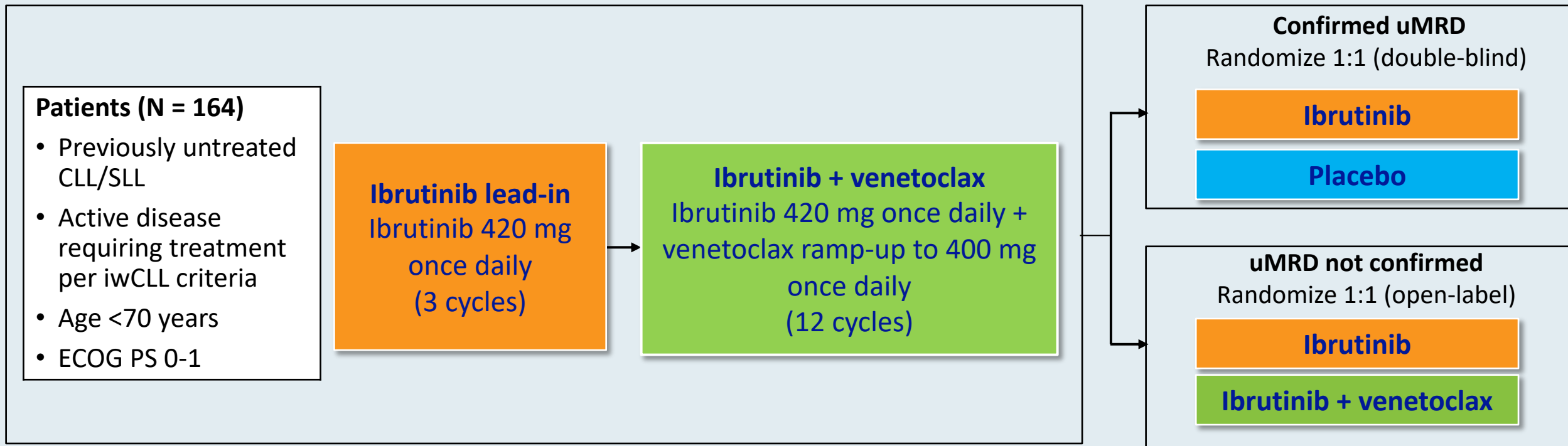


# ECOG-ACRIN E1912 Extended Follow-Up: PFS by IGHV Mutation Status



- 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;  $p = 0.086$ ).

# CAPTIVATE MRD Cohort: Study Design

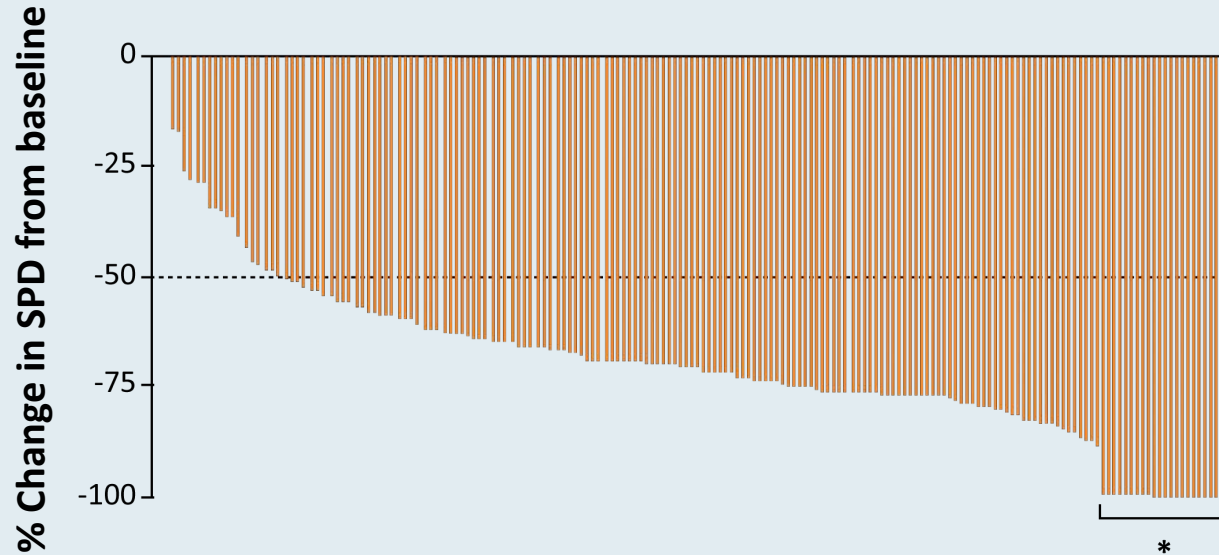


uMRD = undetectable minimal residual disease

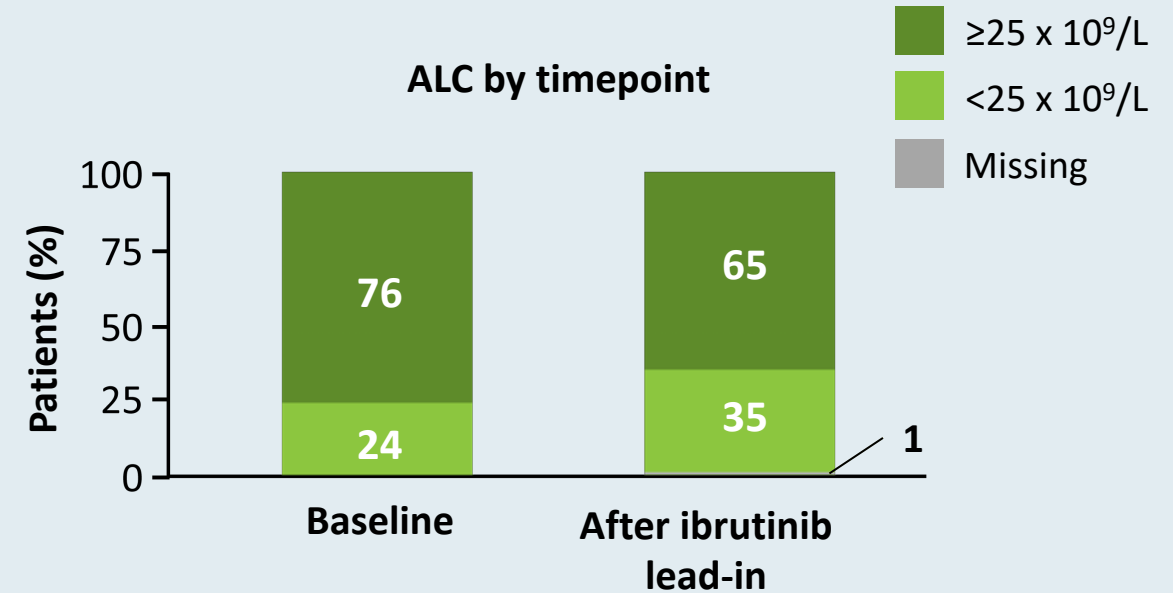
Results presented for prerandomization phase of the MRD cohort (n = 164) with 12 cycles of ibrutinib + venetoclax prior to MRD-guided randomization

# CAPTIVATE MRD Cohort: 3 Cycles of Ibrutinib Lead-In

Reductions in lymph node burden after lead-in



ALC by timepoint



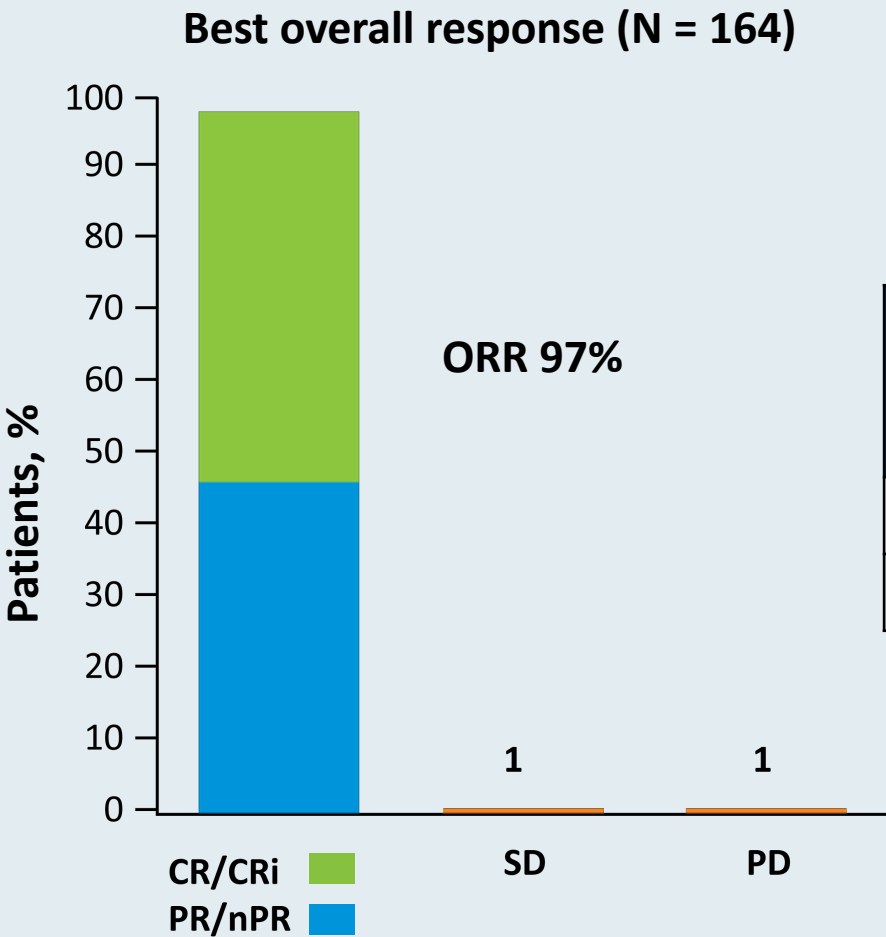
Three cycles of ibrutinib lead-in reduces TLS risk and indication for hospitalization

## CAPTIVATE MRD Cohort: Undetectable MRD Rate

	Peripheral blood n = 163	Bone marrow n = 155
<b>Best response of undetectable MRD in evaluable patients</b> (95% CI)	<b>75%</b> (68-82)	<b>72%</b> (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

# 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)

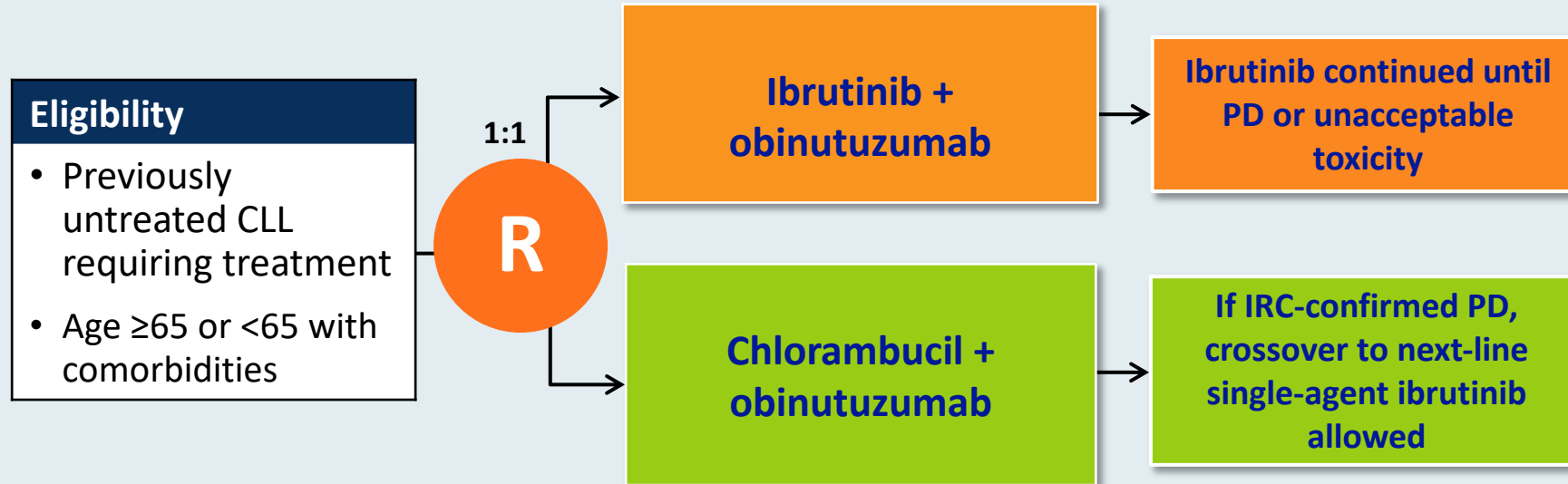
At 15 months, 98% of patients were progression free with no deaths

# 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

# Phase III iLLUMINATE Study Design



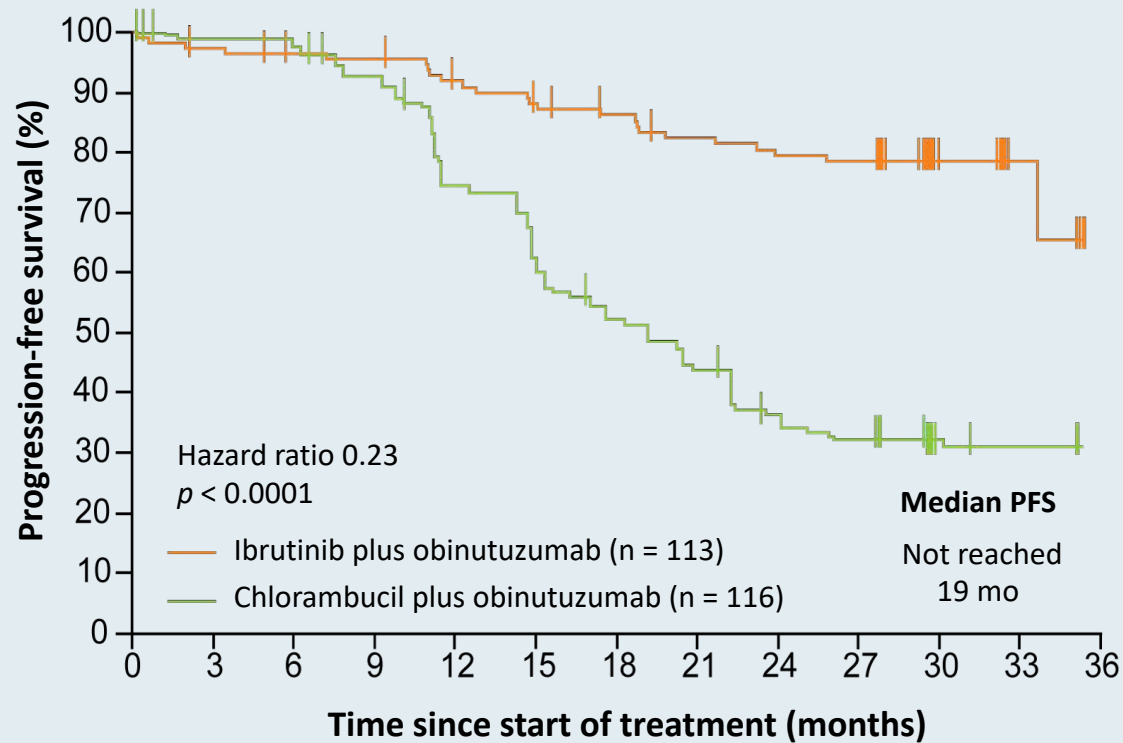
## Stratification

- ECOG PS (0-1 vs 2)
- Del(17p)/del(11q) (+/+ vs +/- vs -/+ vs -/-)

**Primary endpoint:** PFS by IRC in ITT

**Secondary endpoints:** PFS for patients at high risk (positive for del(17p) or TP53 mutation, del(11q), or no IGHV mutation), MRD, ORR, OS, IRRs, safety

# iLLUMINATE: A Phase III Trial of Ibrutinib and Obinutuzumab as First-Line Therapy for CLL



## Most common Grade 3 or 4 AEs

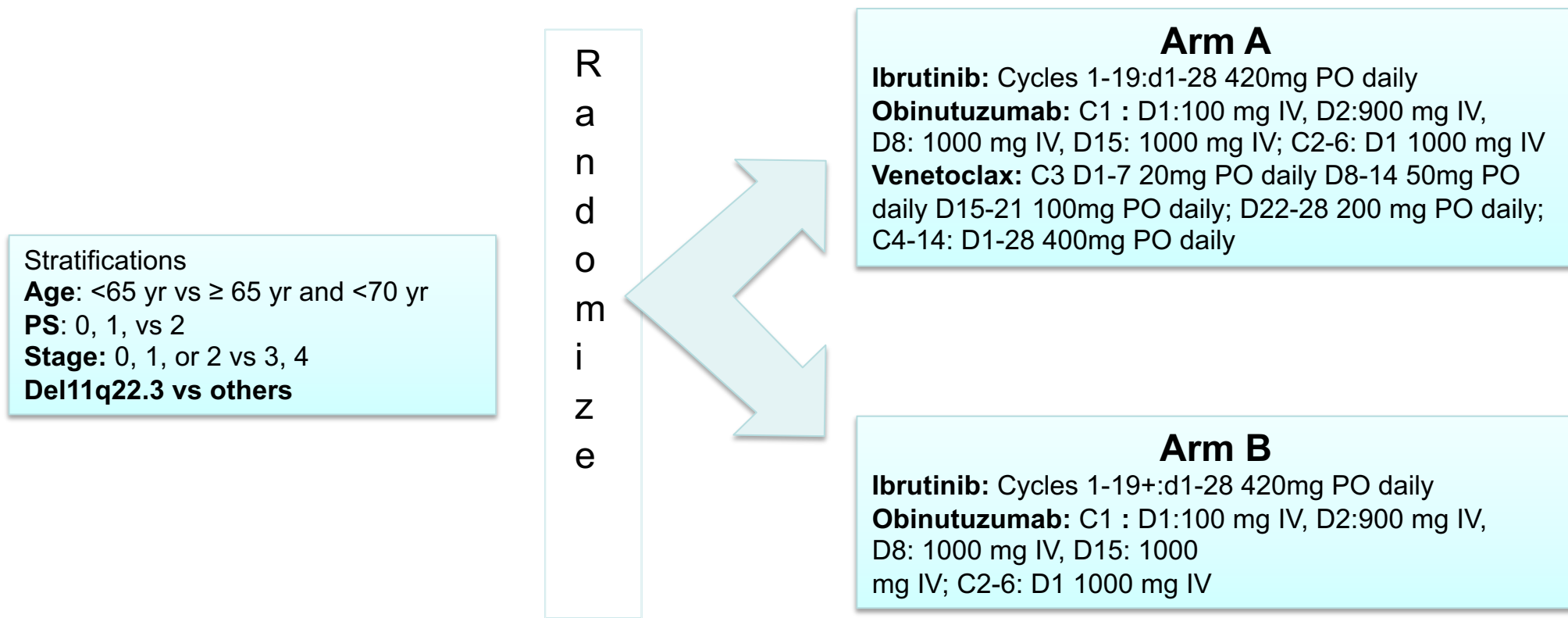
- Neutropenia
- Thrombocytopenia

## Serious AEs

- Ibrutinib/obinutuzumab: 58%
- Chlorambucil/obinutuzumab: 35%



# Ongoing Phase III EA9161 Trial Schema

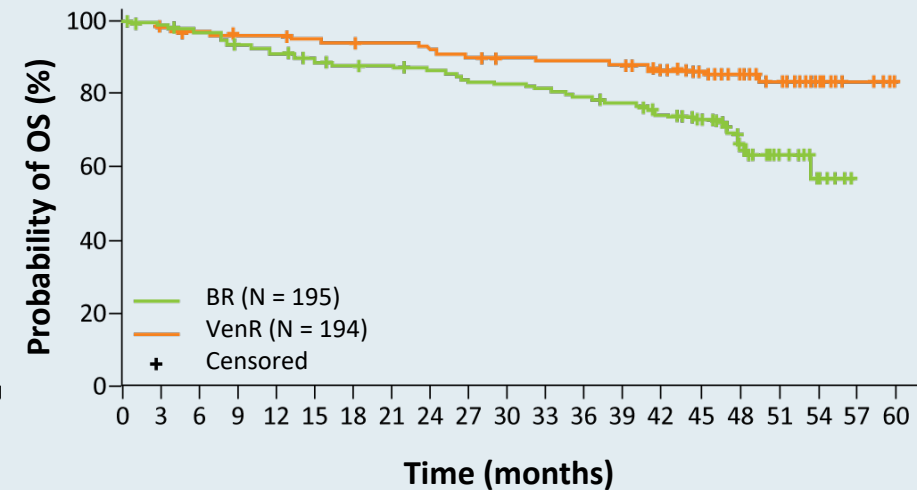
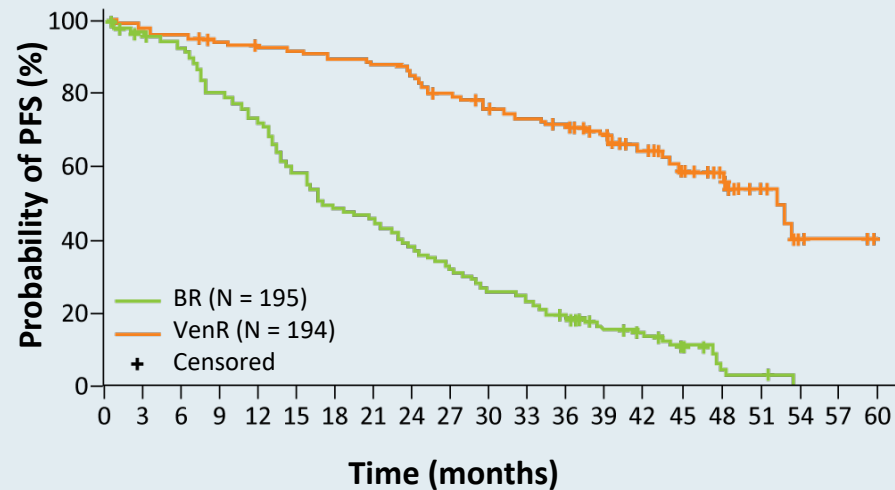


Courtesy of Brad Kahl, MD

## Relapsed/Refractory Disease

# MURANO Trial: Survival Analyses with Venetoclax/ Rituximab for R/R CLL (48-Month Median Follow-Up)

	VenR (n = 194)	BR (n = 195)	Hazard ratio	<i>p</i> -value
Four-year PFS	57.3%	4.6%	0.19	<0.0001
Four-year OS	85.3%	66.8%	0.41	<0.0001



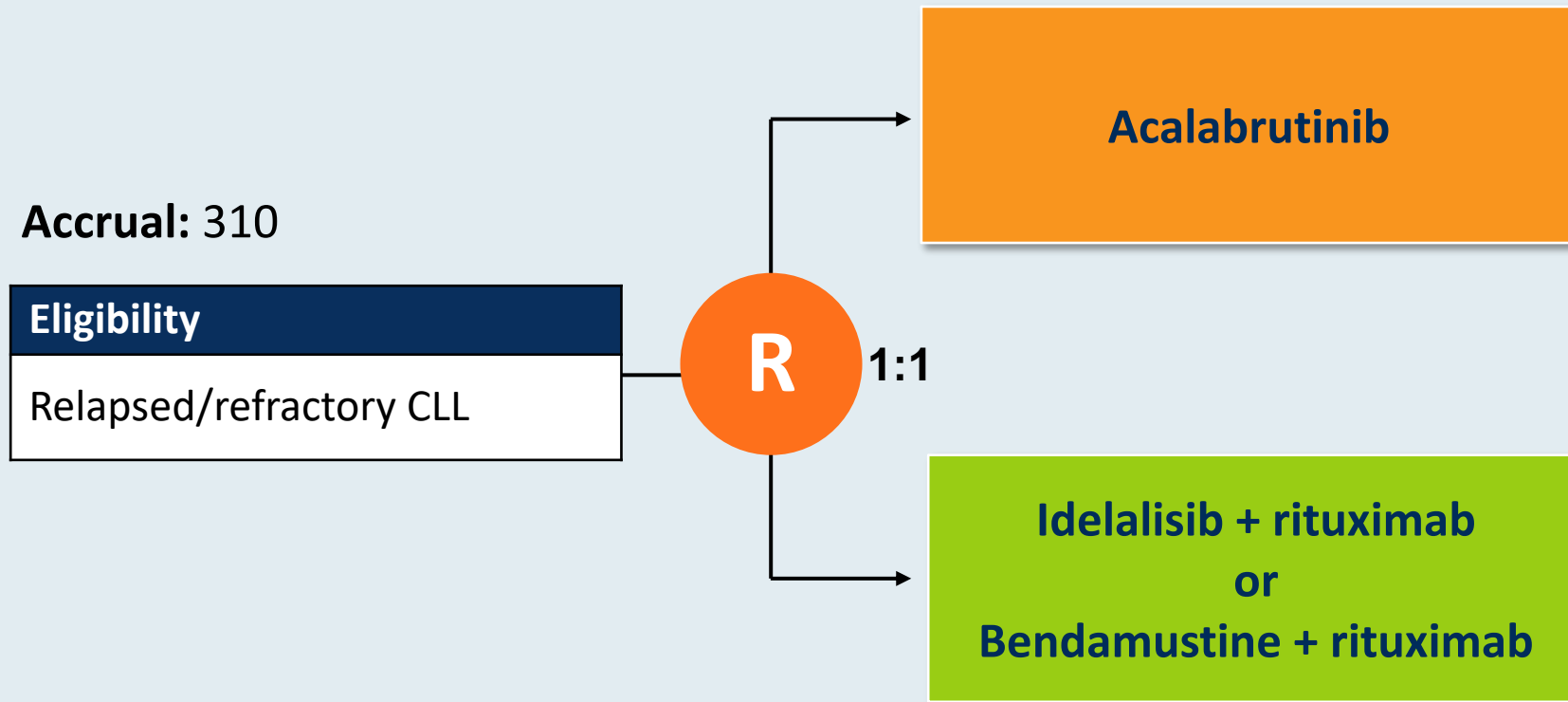
# FDA Approval of Acalabrutinib for Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma

Press Release – November 21, 2019

“The Food and Drug Administration approved acalabrutinib for adults with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL). This review was conducted under Project Orbis, an initiative of the FDA Oncology Center of Excellence. Project Orbis provides a framework for concurrent submission and review of oncology drugs among international partners.

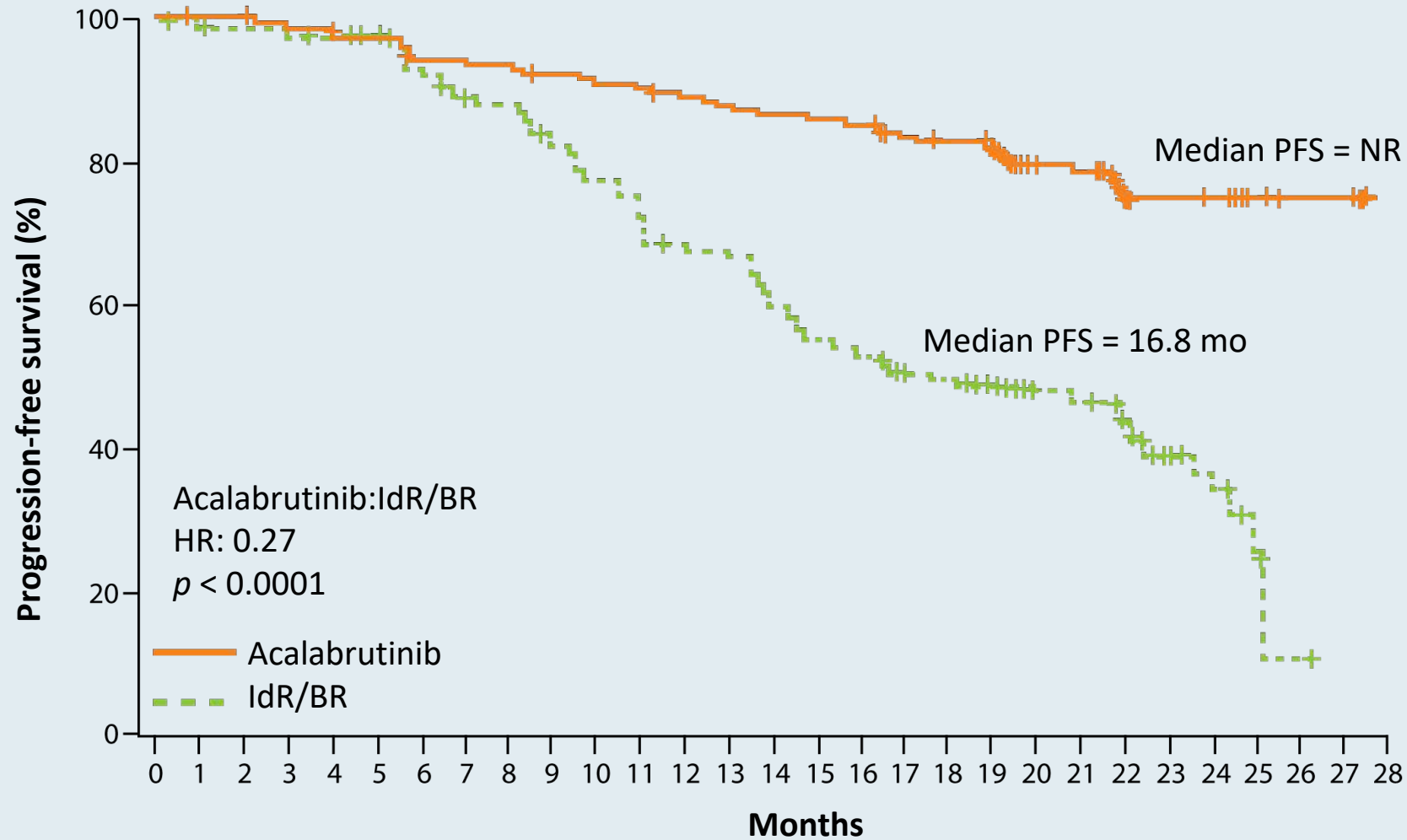
Approval was based on two randomized, actively controlled trials in patients with CLL: ELEVATE-TN (NCT02475681) and ASCEND (NCT02970318). Efficacy in both trials was based on progression-free survival (PFS) as assessed by independent review. The recommended dose is 100 mg orally every 12 hours.”

# ASCEND Phase III Trial Schema



**Primary endpoint:** Progression-free survival by IRC

# ASCEND: Final Analysis of Investigator-Assessed PFS



After a median of 22 months, acalabrutinib prolonged PFS vs investigator's choice of therapy (estimated 18-mo PFS: 82% and 48%, respectively)

## ASCEND: Adverse Events of Clinical Interest

Adverse event	Acalabrutinib (n = 154)		IdR (n = 118)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Atrial fibrillation	6%	1%	3%	1%
Hemorrhage	29%	3%	8%	3%
Major hemorrhage	3%	3%	3%	3%
Hypertension	5%	3%	4%	1%
Infections	63%	20%	65%	25%
Second primary cancer, excluding nonmelanoma skin carcinomas	5%	4%	2%	1%
Tumor lysis syndrome	1%	1%	1%	1%

IdR = rituximab/idelalisib



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

*A Meet The Professor Series*

**Friday, September 11, 2020  
12:00 PM – 1:00 PM ET**

**Faculty**

**Robert L Coleman, MD**

**Moderator**

**Neil Love, MD**

***Thank you for joining us!***

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