

Meet The Professor

Management of Chronic Lymphocytic Leukemia

Prof John G Gribben, MD, DSc, FMedSci

Chair of Medical Oncology

Barts Cancer Institute

Queen Mary University of London

Charterhouse Square

London, United Kingdom

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, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Daiichi Sankyo Inc, Dendreon Pharmaceuticals Inc, Eisai Inc, EMD Serono Inc, Epizyme 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, Karyopharm Therapeutics, 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, Oncoceptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Prometheus Laboratories Inc, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sandoz Inc, a Novartis Division, Sanofi Genzyme, Seagen Inc, 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.

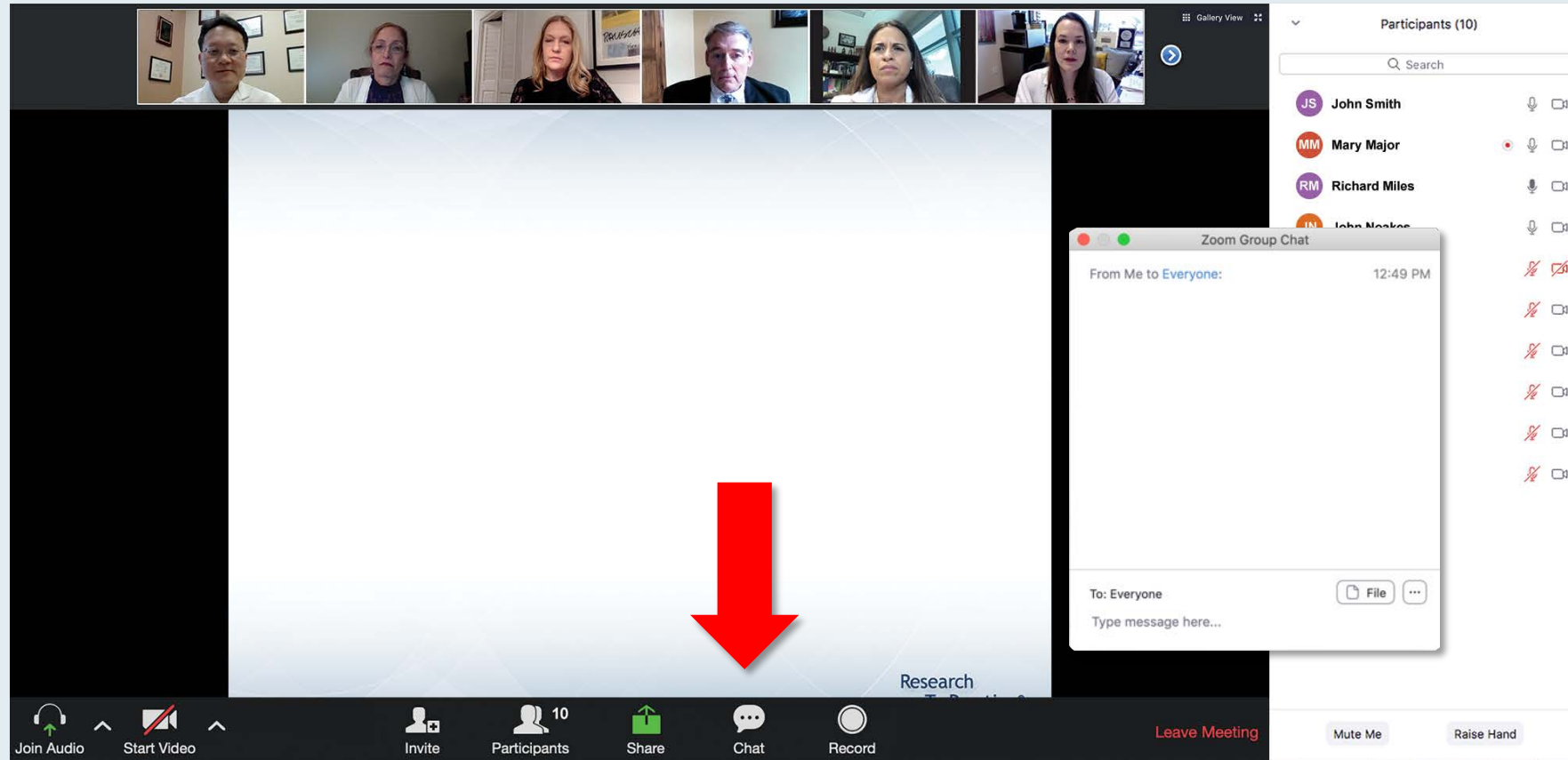
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Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

Prof Gribben — Disclosures

Advisory Committee	AbbVie Inc, AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Janssen Biotech Inc, Karyopharm Therapeutics, Kite, A Gilead Company, MorphoSys, Novartis
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We Encourage Clinicians in Practice to Submit Questions



Feel free to submit questions now before the program begins 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 options are: 1. Carfilzomib +/- dexamethasone, 2. Pomalidomide +/- dexamethasone, 3. Carfilzomib + pomalidomide +/- dexamethasone, 4. Elotuzumab + lenalidomide +/- dexamethasone, 5. Elotuzumab + pomalidomide +/- dexamethasone, 6. Daratumumab + lenalidomide +/- dexamethasone, 7. Daratumumab + pomalidomide +/- dexamethasone, 8. Daratumumab + bortezomib +/- dexamethasone, 9. Ixazomib + Rd, and 10. Other. The "Submit" button is at the bottom of the poll overlay. On the right side, the "Participants (10)" list is visible, showing names and icons for audio, video, and chat. At the bottom, the Zoom control bar includes buttons for "Join Audio", "Start Video", "Invite", "Participants", "Share", "Chat", "Record", and "Leave Meeting".

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

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Join Audio Start Video Invite Participants Share Chat Record Leave Meeting

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

Mute Me Raise Hand

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

Upcoming Webinars

**Monday, November 23, 2020
12:00 PM – 1:00 PM ET**

**Meet The Professor:
Management of Ovarian
Cancer**

Faculty

Deborah K Armstrong, MD

Moderator

Neil Love, MD

**Tuesday, December 1, 2020
5:00 PM – 6:00 PM ET**

**Year in Review: Clinical Investigators
Provide Perspectives on the Most
Relevant New Publications, Data Sets
and Advances in Oncology
Prostate Cancer**

Faculty

Emmanuel S Antonarakis, MD

Andrew J Armstrong, MD, ScM

Moderator

Neil Love, MD

Upcoming Webinars

Friday, December 4, 2020

**Consensus or Controversy?
Investigators Discuss Clinical
Practice Patterns and Available
Research Data Guiding the
Management of Hematologic Cancers**

A 4-Part Friday Satellite Symposia Live Webinar
Series Preceding the 62nd ASH Annual Meeting

Moderator

Neil Love, MD

Thank you for joining us!

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

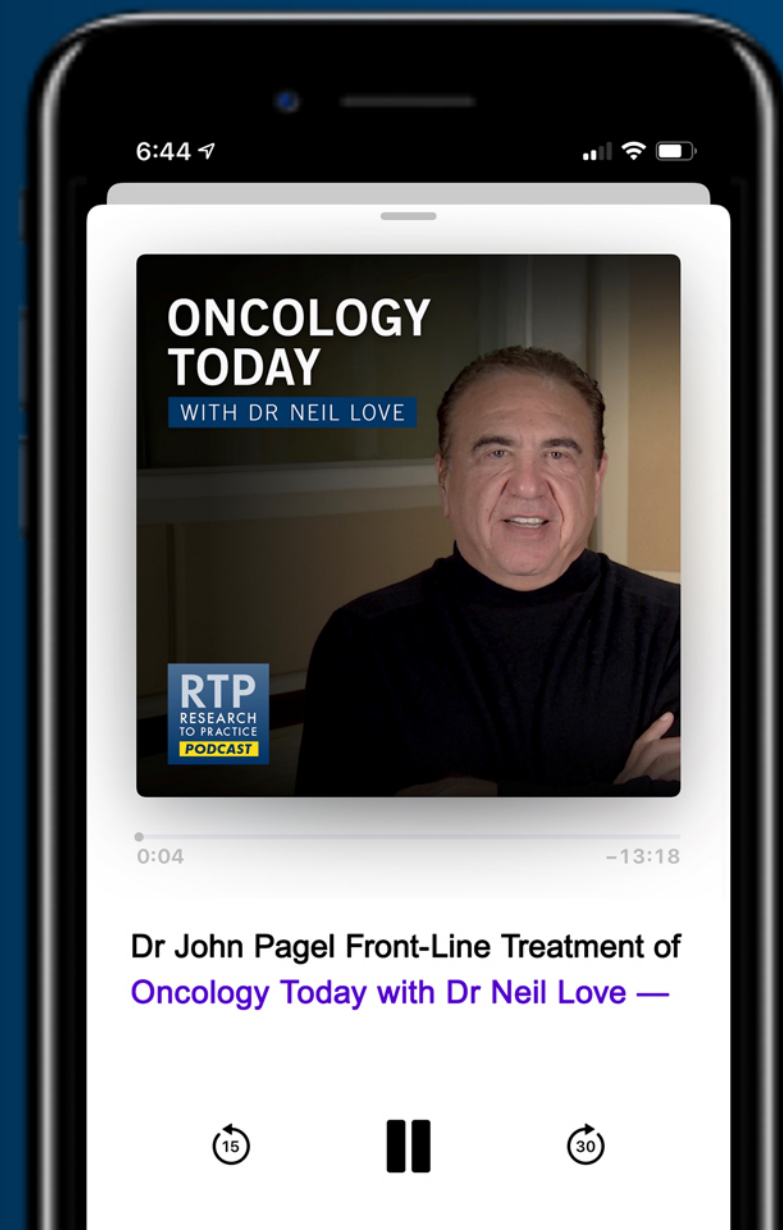
ONCOLOGY TODAY

SPECIAL EDITION: FRONT-LINE TREATMENT OF CHRONIC LYMPHOCYTIC LEUKEMIA

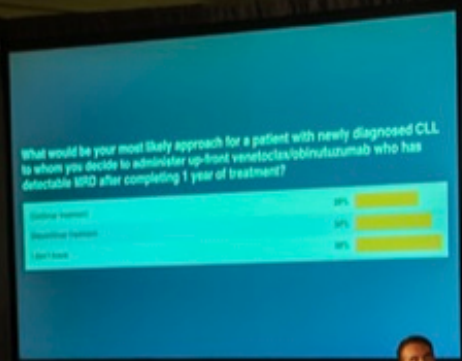
WITH DR NEIL LOVE



DR JOHN PAGEL
SWEDISH CANCER INSTITUTE
SEATTLE, WASHINGTON









Meet The Professor

Management of Chronic Lymphocytic Leukemia

Prof John G Gribben, MD, DSc, FMedSci

Chair of Medical Oncology

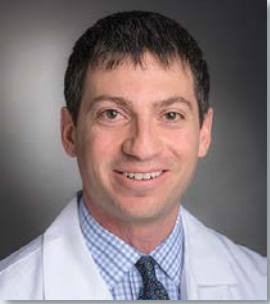
Barts Cancer Institute

Queen Mary University of London

Charterhouse Square

London, United Kingdom

Meet The Professor Program Participating Faculty



Matthew S Davids, MD, MMSc
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Harvard Medical School
Director of Clinical Research
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Dana-Farber Cancer Institute
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Director, Lymphoid Malignancy Program
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



Prof John G Gribben, MD, DSc, FMedSci
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Barts Cancer Institute
Queen Mary University of London
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London, United Kingdom

Meet The Professor Program Participating Faculty



Anthony R Mato, MD, MSCE
Associate Attending
Director, Chronic Lymphocytic Leukemia
Program
Memorial Sloan Kettering Cancer Center
New York, New York



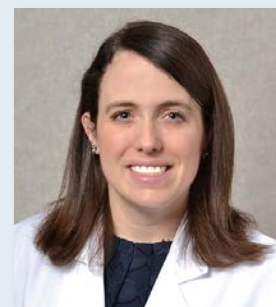
Jeff Sharman, MD
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Research Center
Medical Director of Hematology Research
US Oncology
Eugene, Oregon



John M Pagel, MD, PhD
Chief of Hematologic Malignancies
Center for Blood Disorders and Stem
Cell Transplantation
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Director, Chronic Lymphocytic Leukemia Program
Department of Hematology and Hematopoietic Cell
Transplantation
City of Hope National Medical Center
Duarte, California



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

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

Professor

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



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DB Lane Cancer Research

Distinguished Professor

Department of Leukemia

Division of Cancer Medicine

The University of Texas
MD Anderson Cancer Center
Houston, Texas



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 begins and throughout the program.

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What is your usual treatment recommendation for a patient with MM followed by ASCT 1-3 years who then experiences an asy... clinical relapse?

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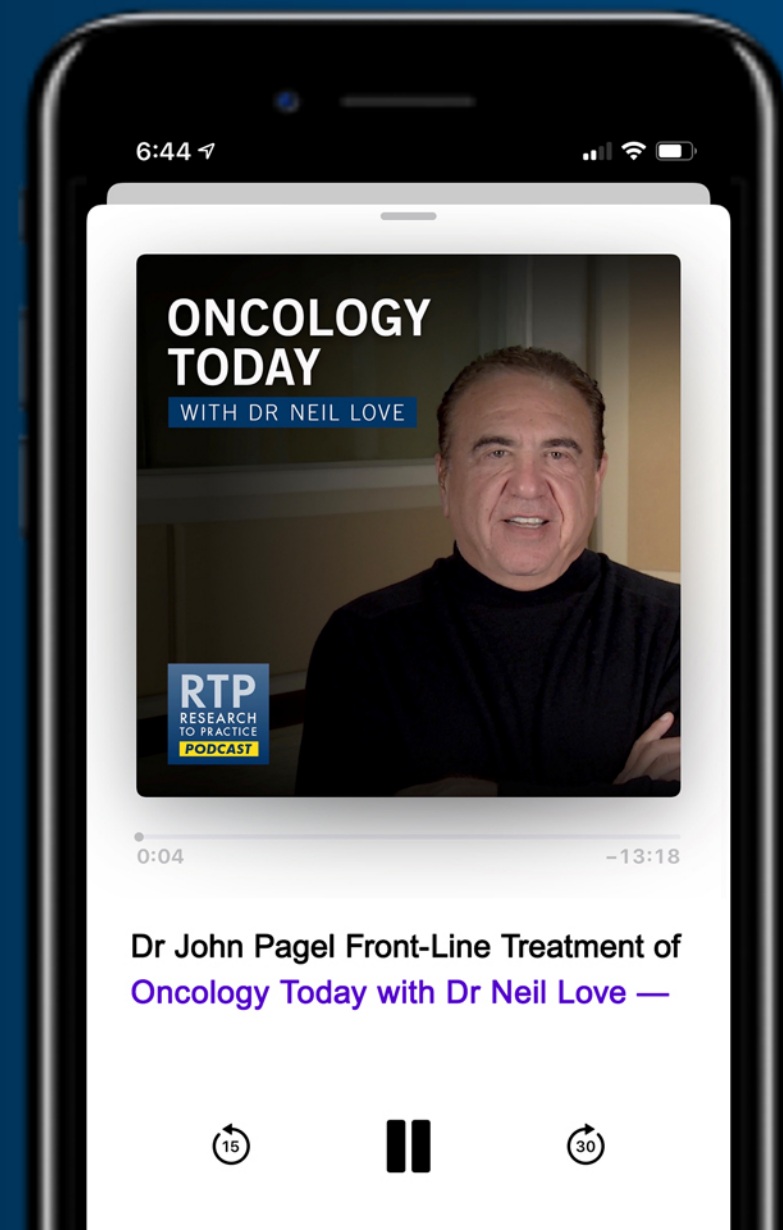
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Prostate Cancer

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**Emmanuel S Antonarakis, MD
Andrew J Armstrong, MD, ScM**

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Consensus or Controversy? Investigators Discuss Clinical Practice Patterns and Available Research Data Guiding the Management of Hematologic Cancers

A 4-Part Friday Satellite Symposia Live Webinar Series Preceding
the 62nd ASH Annual Meeting

Friday, December 4, 2020

Multiple Myeloma

8:30 AM – 10:00 AM Pacific Time
(11:30 AM – 1:00 PM ET)

Chronic Lymphocytic Leukemia

12:00 PM – 1:30 PM Pacific Time
(3:00 PM – 4:30 PM ET)

Acute Myeloid Leukemia

3:00 PM – 4:30 PM Pacific Time
(6:00 PM – 7:30 PM ET)

Hodgkin and Non-Hodgkin Lymphoma

7:00 PM – 8:30 PM Pacific Time
(10:00 PM – 11:30 PM ET)

Meet The Professor

Management of Chronic Lymphocytic Leukemia

Prof John G Gribben, MD, DSc, FMedSci

Chair of Medical Oncology

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Queen Mary University of London

Charterhouse Square

London, United Kingdom



Namrata I Peswani, MD

Hematologist Oncologist

UT Southwestern/Harold C Simmons Comprehensive Cancer Center

Richardson, Texas



Kerry Rogers, MD

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

Meet The Professor with Prof Gribben

MODULE 1: Cases from Drs Peswani and Rogers

- Dr Peswani: A 60-year-old man (30 pack-year smoking history) with CLL and non-small cell lung cancer
- Dr Rogers: A 71-year-old man with high-risk, relapsed/refractory CLL – del(17p), no IGHV mutation – Part 1
- Dr Rogers: A 71-year-old man with high-risk, relapsed/refractory CLL – del(17p), no IGHV mutation – Part 2
- Dr Peswani: A 52-year-old woman with CLL – IGHV mutation
- Dr Peswani: A 63-year-old man with CLL and ZAP70+, IGHV mutation – Primary refractory to ibrutinib – Part 1
- Dr Peswani: A 63-year-old man with CLL and ZAP70+, IGHV mutation – Primary refractory to ibrutinib – Part 2

MODULE 2: CLL Journal Club with Prof Gribben

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

MODULE 4: Key Recent Data Sets

Case Presentation – Dr Peswani: A 60-year-old man (30 pack-year smoking history) with CLL and non-small cell lung cancer



Dr Namrata Peswani

- Diagnosed with CLL, del(13q), IGHV mutated (ALC 8,000)
- Observation x 3 months → New rash, anemia, thrombocytopenia
 - CT: Extensive adenopathy, including hilar and mediastinal LNs, right lung infiltrate
 - Bronchoscopy: CLL
- Ibrutinib → (ALC 4,500), with response in lymphadenopathy except hilar and mediastinal nodes
- 3 months later: Scan and biopsy of RLL nodule: NSCLC, PD-L1 100%

Questions

- Could this patient be treated with pembrolizumab in order to control his NSCLC along with his CLL?

Case Presentation – Dr Rogers: A 71-year-old man with high-risk, relapsed/refractory CLL – del(17p), no IGHV mutation – Part 1



Dr Kerry Rogers

- 2008: Diagnosed with CLL after donating platelets, but no enlarged lymph nodes; Asymptomatic → Observation
- 2009: Bulky lymph nodes → FCR x 6
- 2012: Bedamustine/rituximab → relapsed <6 months later → Sent to referral center
- Cytogenetics: FISH del(17p), normal karyotype, IGHV unmutated

Case Presentation – Dr Rogers: A 71-year-old man with high-risk, relapsed/refractory CLL – del(17p), no IGHV mutation – Part 2



Dr Kerry Rogers

- 2008: Diagnosed with CLL after donating platelets, but no enlarged lymph nodes; Asymptomatic → Observation
- 2009: Bulky lymph nodes → FCR x 6
- 2012: Bedamustine/rituximab → relapsed <6 months later → Sent to referral center
- Cytogenetics: FISH del(17p), normal karyotype, IGHV unmutated
- ***Dinaciclib/ofatumumab on clinical trial***
- ***2015: Enlarged lymph nodes, cytogenetics unchanged***
- ***Acalabrutinib on clinical trial***
 - ***5/2017: BTK C481S noted on testing, VAF 0.4%***
 - ***2/2018: Small enlarged lymph nodes, BTK C481S VAF 87%***
- ***2020: Venetoclax ongoing, BTK C481S VAF 0%***

Questions

- What clinical testing for ibrutinib resistance mutations are you doing in your practice?

Case Presentation – Dr Peswani: A 52-year-old woman with CLL – IGHV mutation



Dr Namrata Peswani

- Diagnosed with CLL, del(13q), IGHV mutated
- ALC 15,000 and palpable, small cervical LAD, mild anemia (Hgb: 11), Platelets: 130,000
- Observation x 6 months → 50% increase in ALC, rapid increase in adenopathy, Hgb<10, Platelets: 80,000
- Offered ibrutinib but patient declines long-term medication
- FCR x 6 months, with CR, but patient is now anxious about not receiving any medication and requests ibrutinib

Questions

- Is there any role for maintenance therapy after chemoimmunotherapy?

Case Presentation – Dr Peswani: A 63-year-old man with CLL and ZAP70+, IGHV mutation – Primary refractory to ibrutinib – Part 1



Dr Namrata Peswani

- 6/2019: Bilateral lower extremity edema, scrotal edema, extensive bulky retroperitoneal lymphadenopathy (17-cm), lymphocyte count: 10,000
- Biopsy: CLL/SLL, trisomy 12, deletion 11q, ZAP70-positive, IGHV mutated
- 9/2019: Ibrutinib 420 mg, with improvement in edema and initial decrease in leukocytosis
 - Rash, eye changes, nail changes, hypertension, AV block
- Second opinion due to plateau of symptoms, “not feeling well” on ibrutinib
- 7/2020: Bulky retroperitoneal LAD (16-cm), normal WBC/ALC, Hgb 10, platelets 80,000

Case Presentation – Dr Peswani: A 63-year-old man with CLL and ZAP70+, IGHV mutation – Primary refractory to ibrutinib – Part 2



Dr Namrata Peswani

- 6/2019: Bilateral lower extremity edema, scrotal edema, extensive bulky retroperitoneal lymphadenopathy (17-cm), lymphocyte count: 10,000
- Biopsy: CLL/SLL, trisomy 12, deletion 11q, ZAP70-positive, IGHV mutated
- 9/2019: Ibrutinib 420 mg, with improvement in edema and initial decrease in leukocytosis
- Second opinion due to plateau of symptoms, “not feeling well” on ibrutinib
 - Rash, eye changes, nail changes, hypertension
- 7/2020: Bulky retroperitoneal LAD (16-cm), normal WBC/ALC, Hgb 10, platelets 80,000
- HTN, AV block, nasal lesion, skin rash and nail changes since starting ibrutinib
- ***Discussed switching to venetoclax/rituximab, but patient is reluctant***

Questions

- What are your thoughts about reducing the dose of ibrutinib to better manage side effects?
- What are your thoughts about switching therapy to acalabrutinib?

Meet The Professor with Prof Gribben

MODULE 1: Cases from Drs Peswani and Rogers

MODULE 2: CLL Journal Club with Prof Gribben

- Clinical outcomes of COVID-19 in patients with hematologic cancers
- Effect of ibrutinib on obinutuzumab-induced cytokine secretion
- Assessment and practical management of venetoclax-associated tumor lysis syndrome (TLS)
- CLARITY trial: Ibrutinib/venetoclax
- Umbralisib with ublituximab for CLL
- EHA position paper on personalized treatment for hematologic diseases
- Bone marrow niches in hematologic cancers
- iLLUMINATE trial: Ibrutinib/obinutuzumab
- Minimal residual disease response after obinutuzumab/bendamustine in the GADOLIN trial
- Ibrutinib versus chlorambucil/obinutuzumab in previously untreated CLL
- GALLIUM trial: Obinutuzumab/chemotherapy versus rituximab/chemotherapy
- Measuring clinical benefit of treatments
- Do we need to analyze everything at CLL diagnosis?
- Biosimilar agents in hematology
- Growth dynamics in naturally progressing CLL

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

MODULE 4: Key Recent Data Sets

Clinical outcome of coronavirus disease 2019 in haemato-oncology patients

Aries J et al. *Br J Haematol* 2020;190(2):e64-7.

Ibrutinib Decreases Obinutuzumab-Induced Secretion of Cytokines Associated with Infusion-Related Reactions in Patients with CLL: Analysis from the Illuminate Study

Greil R et al.

ICML 2019;Abstract 163.

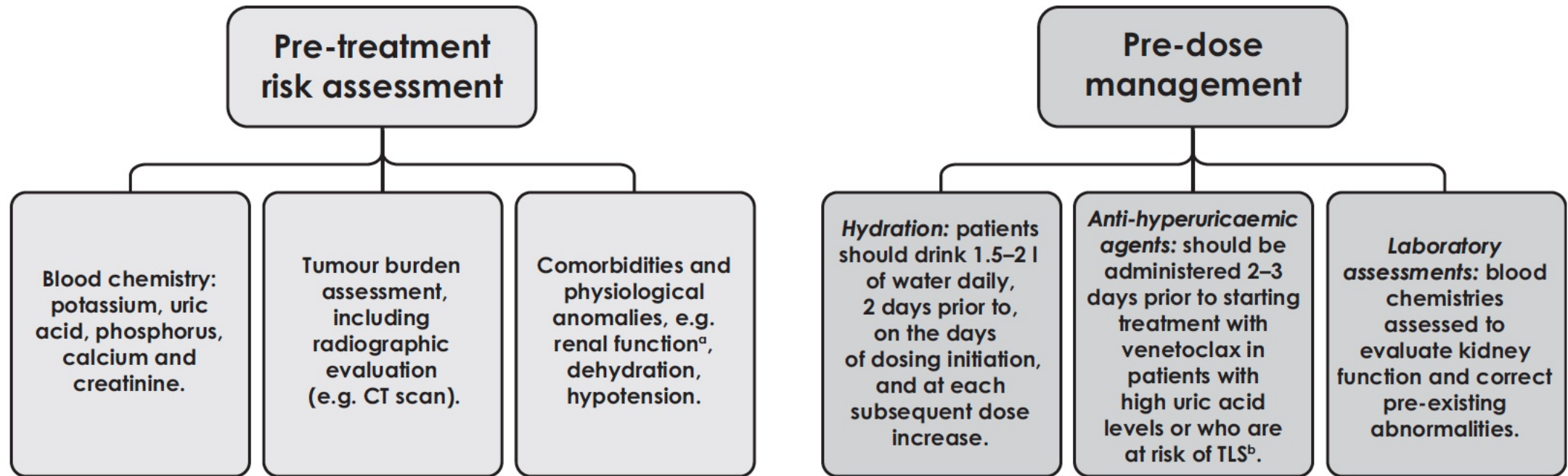
***Br J Haematol* 2020;188(6):844-51**

bjh emergencies in haematology

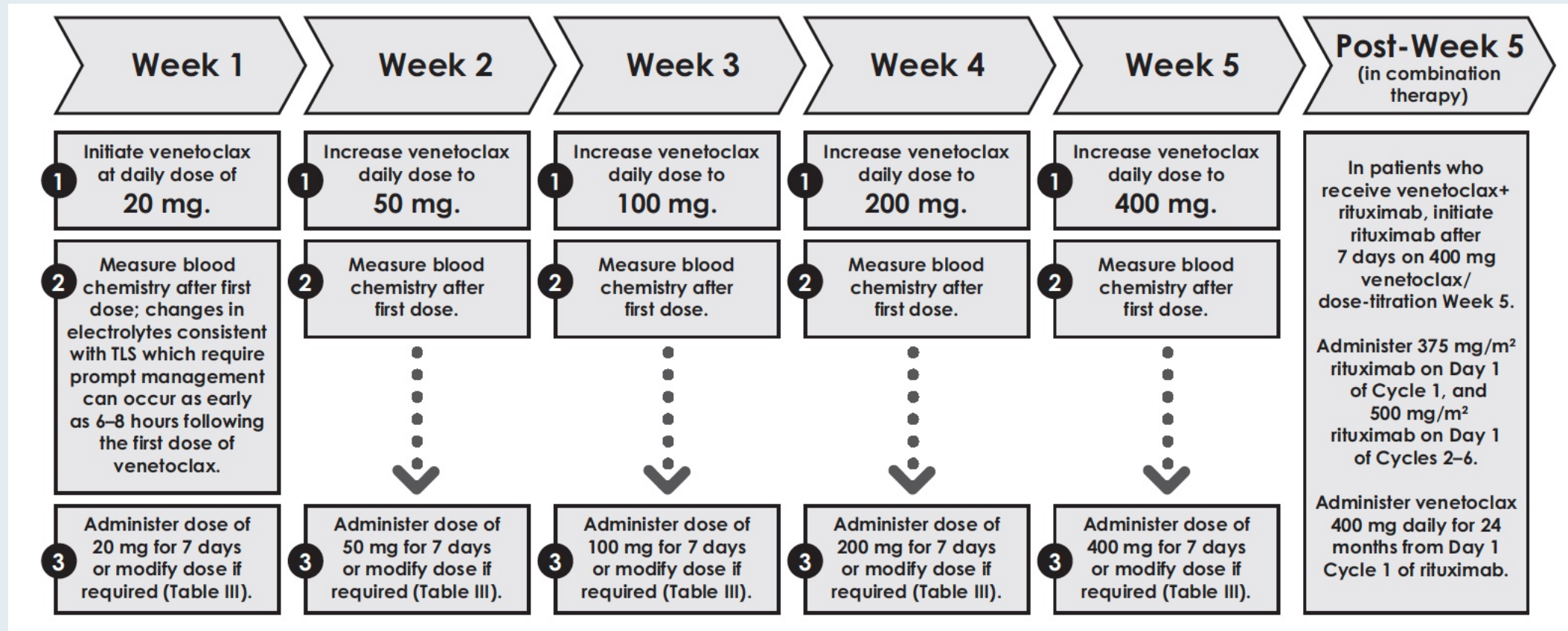
Practical management of tumour lysis syndrome in venetoclax-treated patients with chronic lymphocytic leukaemia

John G. Gribben

Predose Initiation for Venetoclax



Venetoclax 5-Week Dose Titration Schedule



Ibrutinib Plus Venetoclax in Relapsed/Refractory Chronic Lymphocytic Leukemia: The CLARITY Study

Peter Hillmen, MBChB, PhD^{1,2}; Andy C. Rawstron, PhD²; Kristian Brock, MSc³; Samuel Muñoz-Vicente, MSc³; Francesca J. Yates, PhD³; Rebecca Bishop³; Rebecca Boucher, MSc³; Donald MacDonald, PhD⁴; Christopher Fegan, MD^{5,6}; Alison McCaig, PhD⁷; Anna Schuh, MD, PhD⁸; Andrew Pettitt, MA, MB BChir, PhD⁹; John G. Gribben, MD, DSc¹⁰; Piers E.M. Patten, MBChB, PhD^{11,15}; Stephen Devereux, PhD¹¹; Adrian Bloor, MA, MB BChir, PhD¹²; Christopher P. Fox, MBChB, PhD¹³; Francesco Forconi, MD, DM, PhD^{14,16}; and Talha Munir, MBBS²

J Clin Oncol 2019 Oct 20;37(30):2722-2729

Continued Long Term Responses to Ibrutinib + Venetoclax Treatment for Relapsed/Refractory CLL in the Blood Cancer UK TAP Clarity Trial

Hillmen P et al.

ASH 2019;Abstract 124.

Umbralisib plus Ublituximab (U2) Is Superior to Obinutuzumab plus Chlorambucil (O + Chl) in Patients with Treatment Naïve (TN) and Relapsed/Refractory (R/R) Chronic Lymphocytic Leukemia (CLL): Results from the Phase 3 Unity-CLL Study

Gribben JG et al.

ASH 2020;Abstract 543.

Personalized Treatment for Hematologic Diseases in Europe: An EHA Position Paper

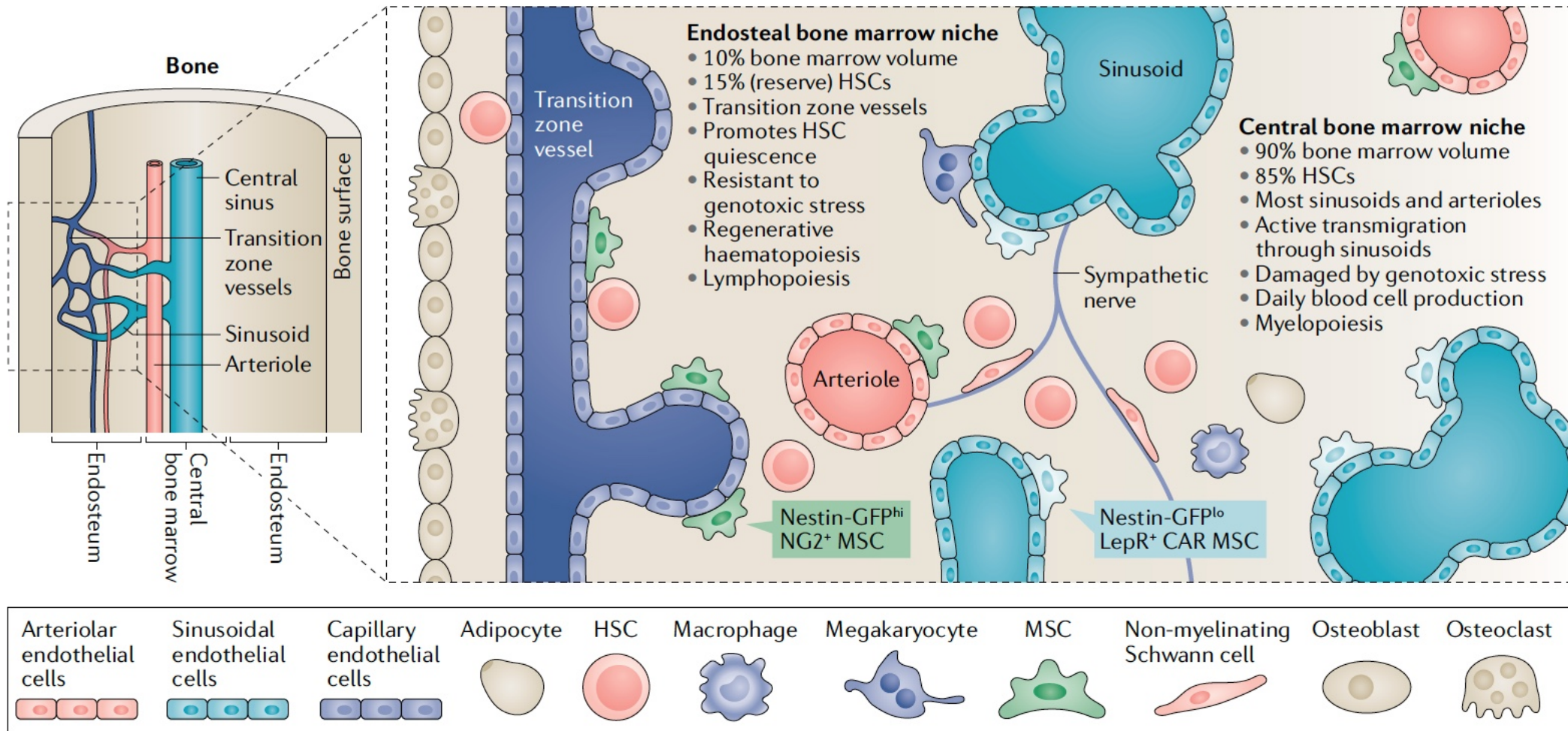
Ulrich Jäger¹, Peter Kapitein², John Gribben³

Hemasphere 2020;4(5):e474

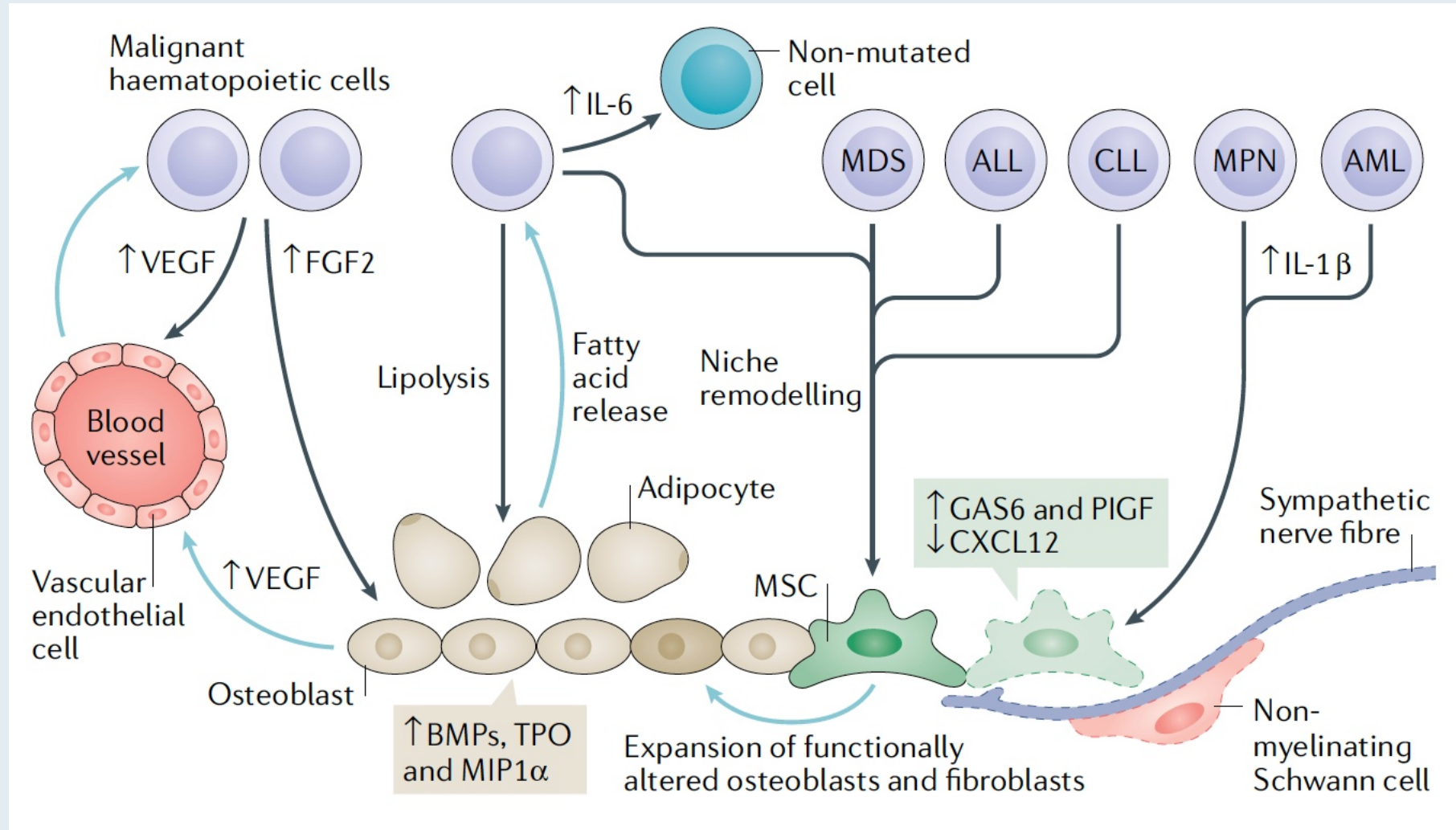
Bone marrow niches in haematological malignancies

Simón Méndez-Ferrer^{iD}, Dominique Bonnet^{iD}, David P. Steensma, Robert P. Hasserjian, Irene M. Ghobrial^{iD}, John G. Gribben^{iD}, Michael Andreeff and Daniela S. Krause^{iD}

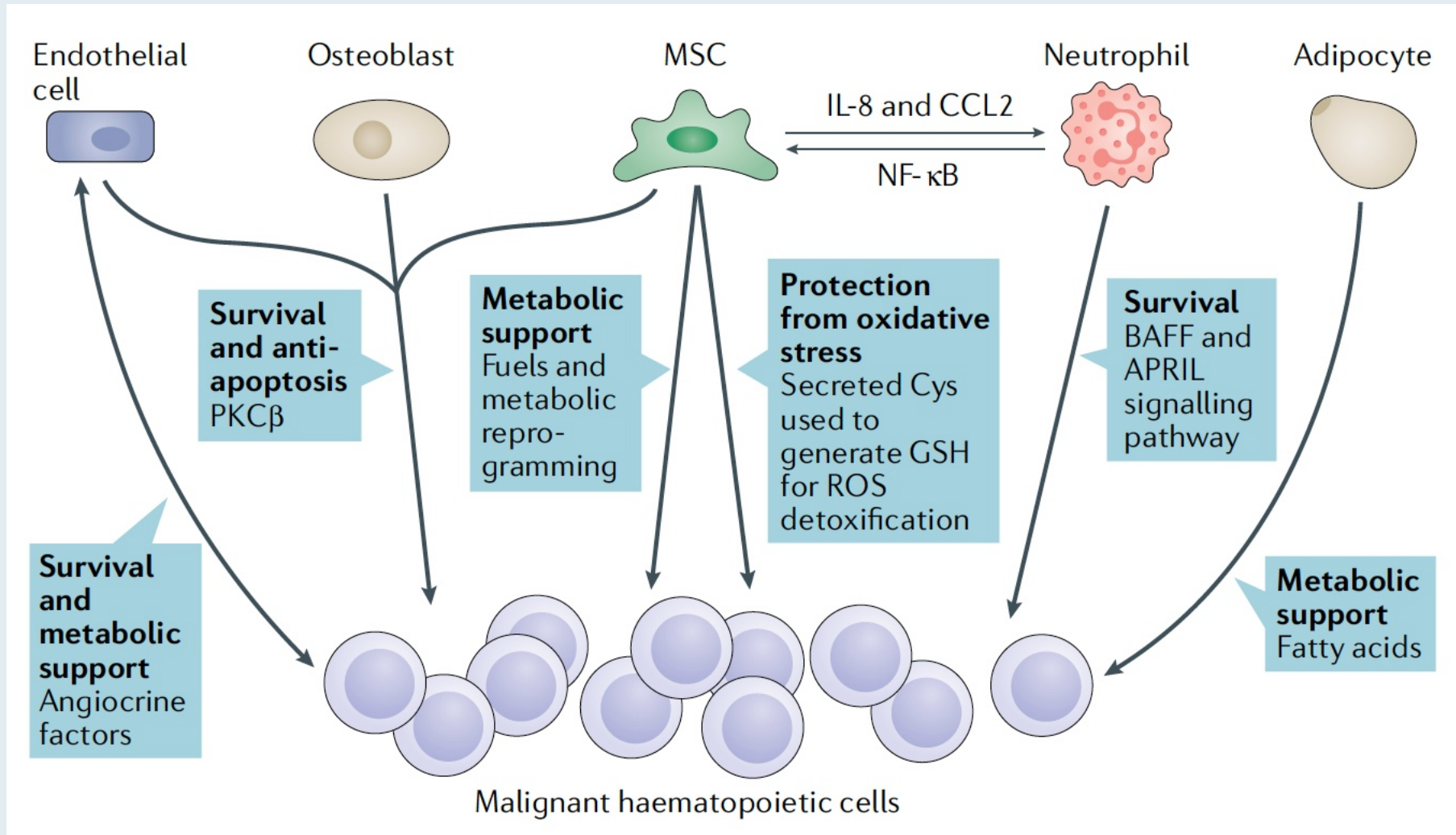
Features of Anatomically Defined Hematopoietic Stem Cell Niches in Mouse Bone Marrow



Bone Marrow Niche Remodeling Favors Disease Progression in Hematologic Cancer



Contributions of the Bone Marrow Niche to Survival and Chemoresistance of Malignant Hematopoietic Cells



Lancet Oncol 2019;20(1):43-56

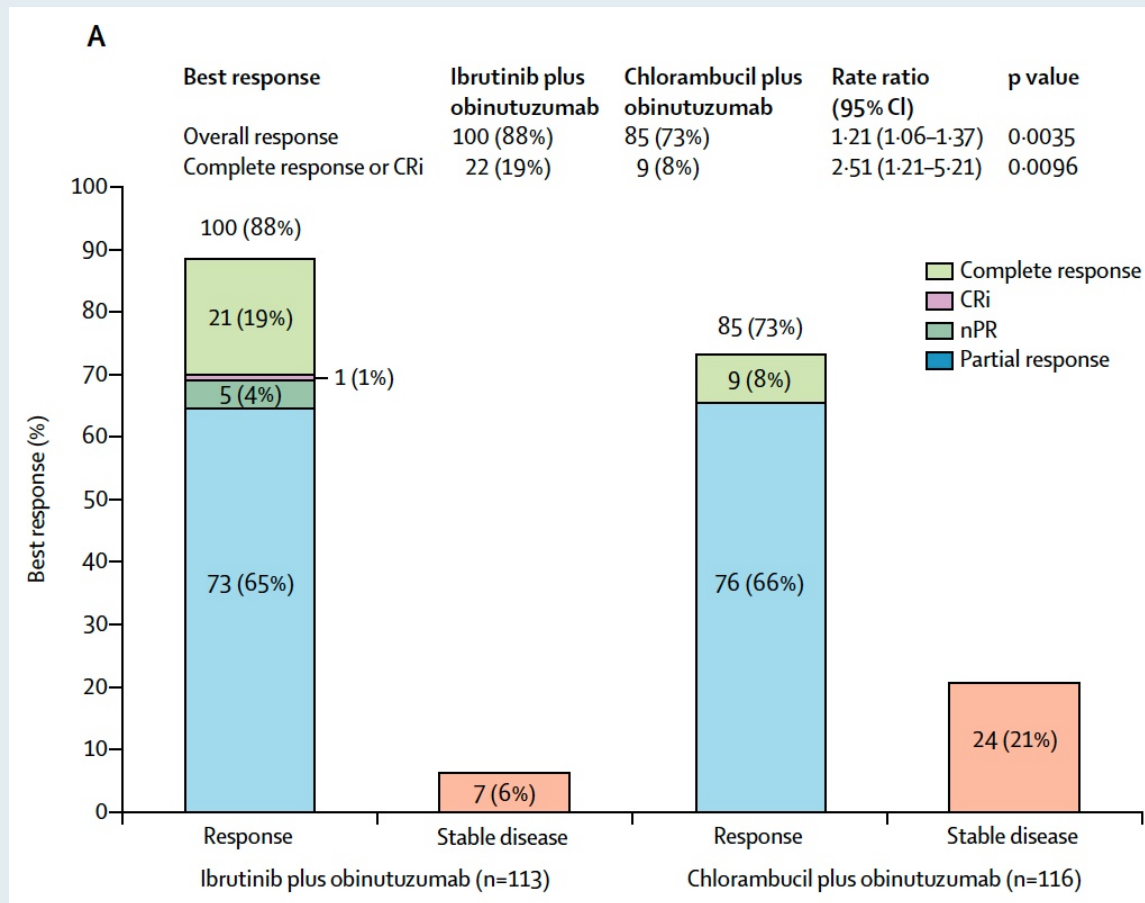
Ibrutinib plus obinutuzumab versus chlorambucil plus obinutuzumab in first-line treatment of chronic lymphocytic leukaemia (iLLUMINATE): a multicentre, randomised, open-label, phase 3 trial



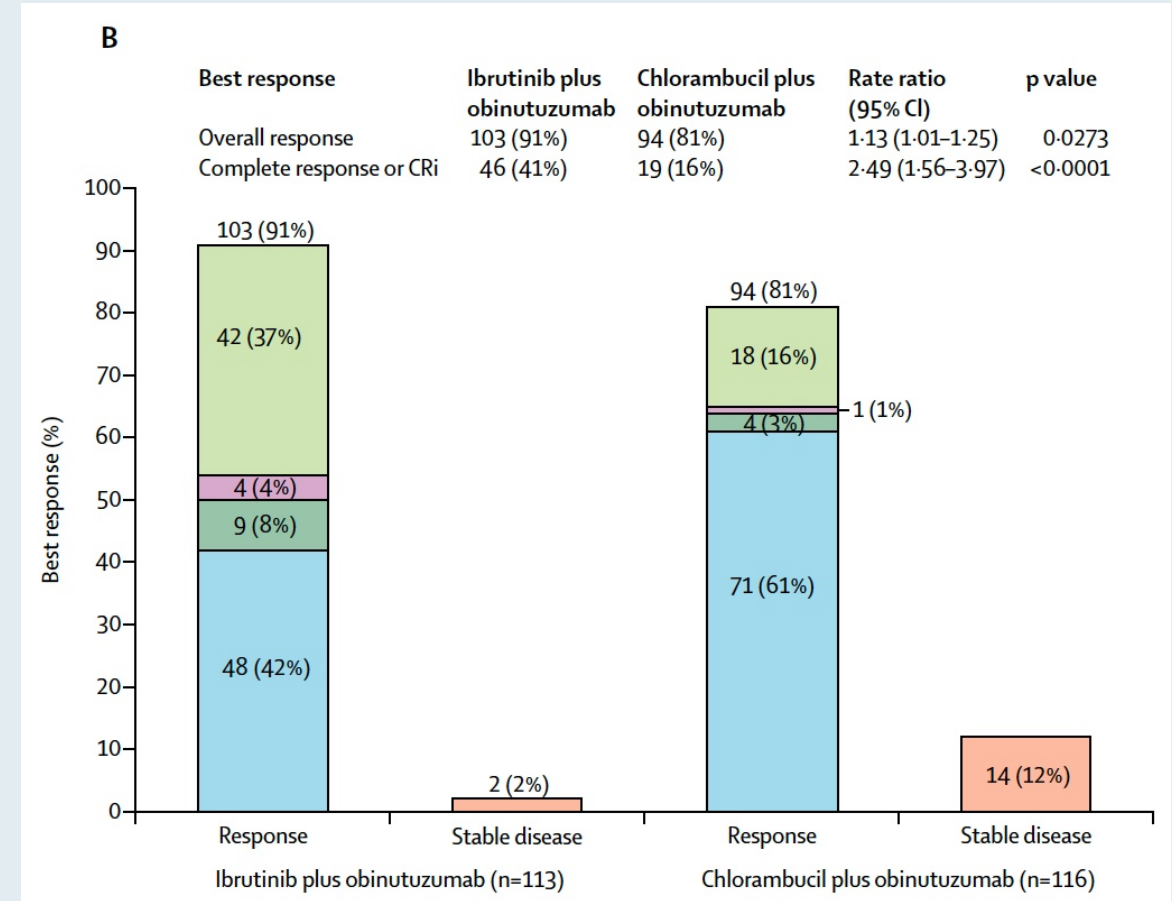
Carol Moreno, Richard Greil, Fatih Demirkan, Alessandra Tedeschi, Bertrand Anz, Loree Larratt, Martin Simkovic, Olga Samoilova, Jan Novak, Dina Ben-Yehuda, Vladimir Strugov, Devinder Gill, John G Gribben, Emily Hsu, Chih-Jian Lih, Cathy Zhou, Fong Clow, Danelle F James, Lori Styles, Ian W Flinn

Best Overall Response: Ibrutinib and Obinutuzumab versus Chlorambucil and Obinutuzumab

IRC Assessed



Investigator Assessed



Leukemia (2020) 34:522–532

<https://doi.org/10.1038/s41375-019-0559-9>

ARTICLE

Lymphoma

MRD response in relapsed/refractory FL after obinutuzumab plus bendamustine or bendamustine alone in the GADOLIN trial

Christiane Pott¹ · Laurie H. Sehn² · David Belada³ · John Gribben⁴ · Eva Hoster⁵ · Brad Kahl⁶ · Britta Kehden¹ · Emmanuelle Nicolas-Virelizier⁷ · Nathalie Spielewoy⁸ · Guenter Fingerle-Rowson⁸ · Chris Harbron⁹ · Kirsten Mundt⁸ · Elisabeth Wassner-Fritsch⁸ · Bruce D. Cheson¹⁰

Assessment of Tumor Lysis Syndrome in Patients with Chronic Lymphocytic Leukemia Treated with Venetoclax in the Clinical Trial and Post-Marketing Settings

Seymour JF et al.

ASH 2020;Abstract 2231.

LETTERS TO THE EDITOR

Tedeschi A et al. *Haematologica* 2020 Apr;105(4):e164-e168

A cross-trial comparison of single-agent ibrutinib versus chlorambucil-obinutuzumab in previously untreated patients with chronic lymphocytic leukemia or small lymphocytic lymphoma

Comparison of Efficacy and Safety with Obinutuzumab plus Chemotherapy versus Rituximab plus Chemotherapy in Patients with Previously Untreated Follicular Lymphoma: Updated Results from the Phase III Gallium Study

Townsend W et al.

ASCO 2020;Abstract 8023.

Measuring Clinical Benefit of Treatments for Hematologic Malignancies: Critical First Steps Accomplished—What is Next?

John G. Gribben¹, Elisabeth de Vries², Nathan I. Cherny³, Pieter Sonneveld⁴

bjh commentary

Do we need to analyse everything at diagnosis in chronic lymphocytic leukaemia?

John G. Gribben 

***Br J Haematol* 2020 May;189(4):603-604**

Here to Stay: Biosimilars in Hematology

John Gribben¹, Giampaolo Merlini², Anton Hagenbeek³, On behalf of EHA

Nature. 2019 June ; 570(7762): 474–479.

Growth dynamics in naturally progressing chronic lymphocytic leukaemia

Michaela Gruber^{1,2,3}, Ivana Bozic⁴, Ignaty Leshchiner², Dimitri Livitz², Kristen Stevenson⁵, Laura Rassenti⁶, Daniel Rosebrock², Amaro Taylor-Weiner², Oriol Olive¹, Reaha Goyetche¹, Stacey M. Fernandes¹, Jing Sun¹, Chip Stewart², Alicia Wong², Carrie Cibulskis², Wandu Zhang¹, Johannes G. Reiter⁷, Jeffrey M. Gerold⁷, John G. Gribben⁸, Kanti R. Rai⁹, Michael J. Keating¹⁰, Jennifer R. Brown^{1,11,12}, Donna Neuberg⁵, Thomas J. Kipps⁶, Martin A. Nowak^{7,13}, Gad Getz^{2,12,14,15}, and Catherine J. Wu^{1,2,11,12}

Meet The Professor with Prof Gribben

MODULE 1: Cases from Drs Peswani and Rogers

MODULE 2: CLL Journal Club with Prof Gribben

- Clinical outcomes of COVID-19 in patients with hematologic cancers
- Effect of ibrutinib on obinutuzumab-induced cytokine secretion
- Assessment and practical management of venetoclax-associated tumor lysis syndrome (TLS)
- CLARITY trial: Ibrutinib/venetoclax
- Umbralisib with ublituximab for CLL
- EHA position paper on personalized treatment for hematologic diseases
- Bone marrow niches in hematologic cancers
- iLLUMINATE trial: Ibrutinib/obinutuzumab
- Minimal residual disease response after obinutuzumab/bendamustine in the GADOLIN trial
- Ibrutinib versus chlorambucil/obinutuzumab in previously untreated CLL
- GALLIUM trial: Obinutuzumab/chemotherapy versus rituximab/chemotherapy
- Measuring clinical benefit of treatments
- Do we need to analyze everything at CLL diagnosis?
- Biosimilar agents in hematology
- Growth dynamics in naturally progressing CLL

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

MODULE 4: Key Recent Data Sets

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	 KERRY A ROGERS, MD	Ibrutinib or FCR
 IAN W FLINN, MD, PhD	Venetoclax + obinutuzumab	 JEFF SHARMAN, MD	FCR
 PROF JOHN G GRIBBEN, MD, DSC, FMedSci	FCR	 TANYA SIDDIQI, MD	Venetoclax + obinutuzumab
 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
 PROF JOHN G GRIBBEN, MD, DSC, FMedSci	Venetoclax + obinutuzumab	 TANYA SIDDIQI, MD	Acalabrutinib + 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 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?

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

 MATTHEW S DAVIDS, MD, MMSC	Venetoclax + obinutuzumab	 KERRY A ROGERS, MD	Acalabrutinib or venetoclax + obinutuzumab
 IAN W FLINN, MD, PHD	Acalabrutinib	 JEFF SHARMAN, MD	Acalabrutinib
 PROF JOHN G GRIBBEN, MD, DSC, FMedSci	Ibrutinib	 TANYA SIDDIQI, MD	Acalabrutinib + obinutuzumab
 BRIAN T HILL, MD, PHD	Venetoclax + obinutuzumab	 MITCHELL R SMITH, MD, PHD	Ibrutinib
 BRAD S KAHL, MD	Venetoclax + obinutuzumab	 WILLIAM G WIERDA, MD, PHD	Acalabrutinib
 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 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	 KERRY A ROGERS, MD	Acalabrutinib
 IAN W FLINN, MD, PHD	Acalabrutinib	 JEFF SHARMAN, MD	Acalabrutinib
 PROF JOHN G GRIBBEN, MD, DSC, FMedSci	Ibrutinib	 TANYA SIDDIQI, MD	Acalabrutinib + obinutuzumab
 BRIAN T HILL, MD, PHD	Venetoclax + obinutuzumab	 MITCHELL R SMITH, MD, PHD	Venetoclax + obinutuzumab
 BRAD S KAHL, MD	Venetoclax + obinutuzumab	 WILLIAM G WIERDA, MD, PHD	Acalabrutinib
 ANTHONY R MATO, MD, MSCE	Acalabrutinib + obinutuzumab	 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?

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

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
 PROF JOHN G GRIBBEN, MD, DSC, FMedSci	Discontinue treatment	 TANYA SIDDIQI, MD	Continue 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?

 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
 PROF JOHN G GRIBBEN, MD, DSC, FMedSci	Discontinue treatment	 TANYA SIDDIQI, 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	Discontinue treatment
 ANTHONY R MATO, MD, MSCE	Discontinue treatment	 JENNIFER WOYACH, MD	Discontinue treatment
 JOHN M PAGEL, MD, PHD	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?

 MATTHEW S DAVIDS, MD, MMSC	Venetoclax + rituximab	 KERRY A ROGERS, MD	Venetoclax + rituximab
 IAN W FLINN, MD, PHD	Venetoclax + obinutuzumab	 JEFF SHARMAN, MD	Venetoclax + rituximab
 PROF JOHN G GRIBBEN, MD, DSC, FMedSci	Venetoclax + rituximab	 TANYA SIDDIQI, MD	Ibrutinib + obinutuzumab OR venetoclax + obinutuzumab
 BRIAN T HILL, MD, PHD	Venetoclax + rituximab	 MITCHELL R SMITH, MD, PHD	Venetoclax + obinutuzumab
 BRAD S KAHL, MD	Venetoclax + rituximab	 WILLIAM G WIERDA, MD, PHD	Venetoclax + rituximab
 ANTHONY R MATO, MD, MSCE	Venetoclax + rituximab	 JENNIFER WOYACH, MD	Venetoclax + rituximab
 JOHN M PAGEL, MD, PHD	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?

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



PROF JOHN G GRIBBEN, MD,
DSC, FMedSci

**Encourage oral 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**



TANYA SIDDIQI, MD

**Encourage oral 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?

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

 MATTHEW S DAVIDS, MD, MMSC	8 days	 KERRY A ROGERS, MD	2 nights for each dose escalation
 IAN W FLINN, MD, PHD	2 days	 JEFF SHARMAN, MD	2 days
 PROF JOHN G GRIBBEN, MD, DSC, FMedSci	1 day	 TANYA SIDDIQI, MD	1-2 days each week during early ramp-up
 BRIAN T HILL, MD, PHD	2 days (<48 hours)	 MITCHELL R SMITH, MD, PHD	1- 2 days
 BRAD S KAHL, MD	2 days	 WILLIAM G WIERDA, MD, PHD	2 days
 ANTHONY R MATO, MD, MSCE	2-3 days	 JENNIFER WOYACH, MD	2 days or rapid escalation to full dose over 5 days
 JOHN M PAGEL, MD, PHD	1 day		

Meet The Professor with Prof Gribben

MODULE 1: Cases from Drs Peswani and Rogers

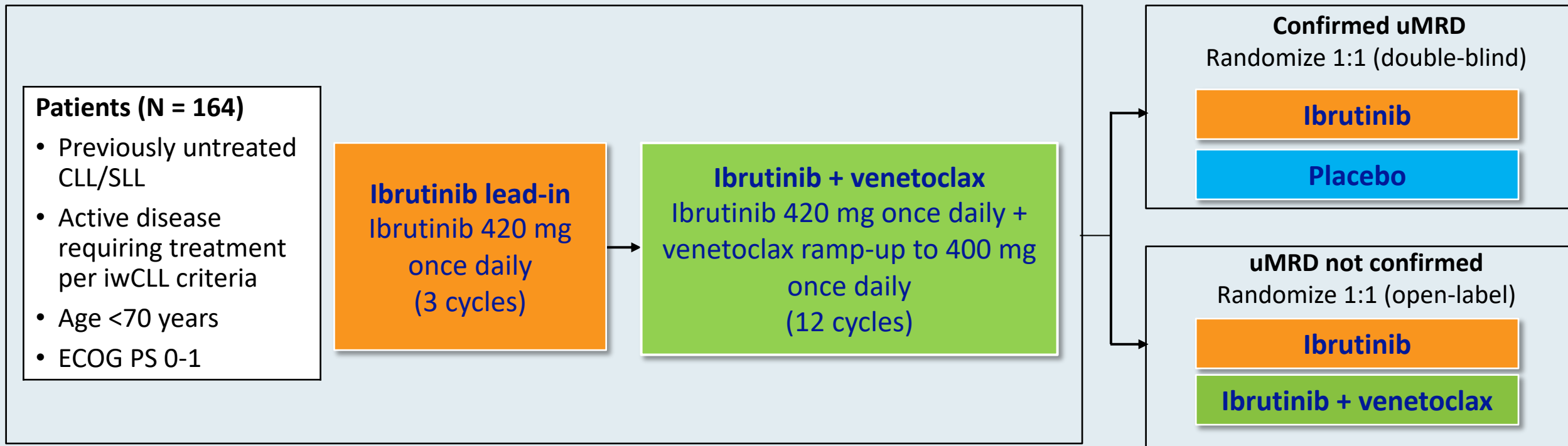
MODULE 2: CLL Journal Club with Prof Gribben

- Clinical outcomes of COVID-19 in patients with hematologic cancers
- Effect of ibrutinib on obinutuzumab-induced cytokine secretion
- Assessment and practical management of venetoclax-associated tumor lysis syndrome (TLS)
- CLARITY trial: Ibrutinib/venetoclax
- Umbralisib with ublituximab for CLL
- EHA position paper on personalized treatment for hematologic diseases
- Bone marrow niches in hematologic cancers
- iLLUMINATE trial: Ibrutinib/obinutuzumab
- Minimal residual disease response after obinutuzumab/bendamustine in the GADOLIN trial
- Ibrutinib versus chlorambucil/obinutuzumab in previously untreated CLL
- GALLIUM trial: Obinutuzumab/chemotherapy versus rituximab/chemotherapy
- Measuring clinical benefit of treatments
- Do we need to analyze everything at CLL diagnosis?
- Biosimilar agents in hematology
- Growth dynamics in naturally progressing CLL

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

MODULE 4: Key Recent Data Sets

CAPTIVATE MRD Cohort: Study Design

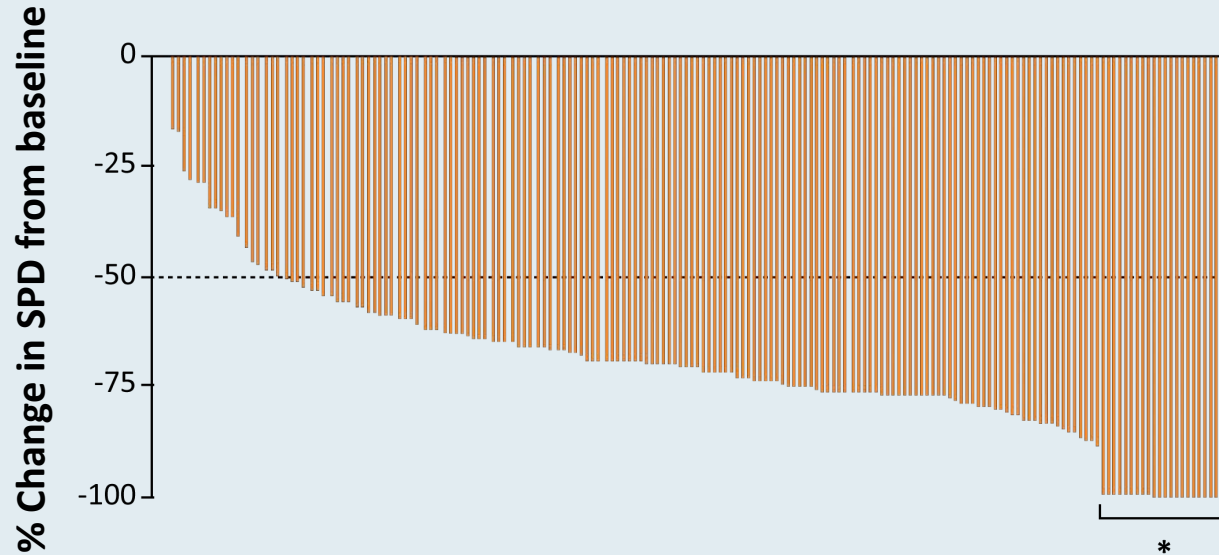


uMRD = undetectable minimal residual disease

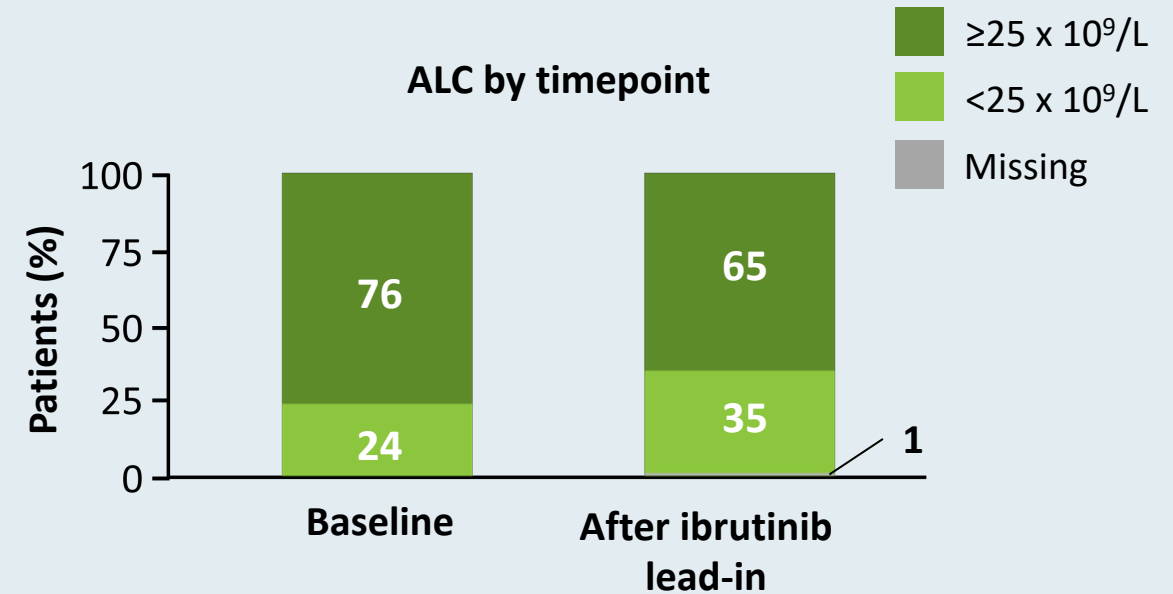
Results presented for prerandomization phase of the MRD cohort (n = 164) with 12 cycles of ibrutinib + venetoclax prior to MRD-guided randomization

CAPTIVATE MRD Cohort: 3 Cycles of Ibrutinib Lead-In

Reductions in lymph node burden after lead-in



ALC by timepoint



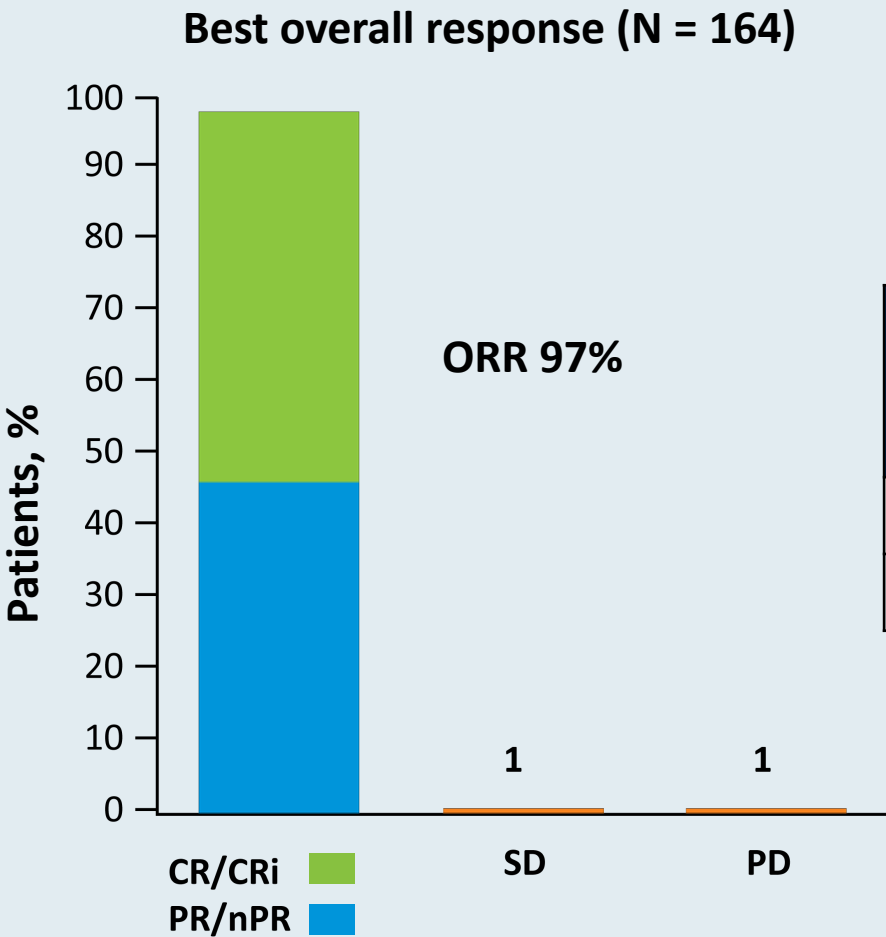
Three cycles of ibrutinib lead-in reduces TLS risk and indication for hospitalization

CAPTIVATE MRD Cohort: Undetectable MRD Rate

	Peripheral blood n = 163	Bone marrow n = 155
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

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)

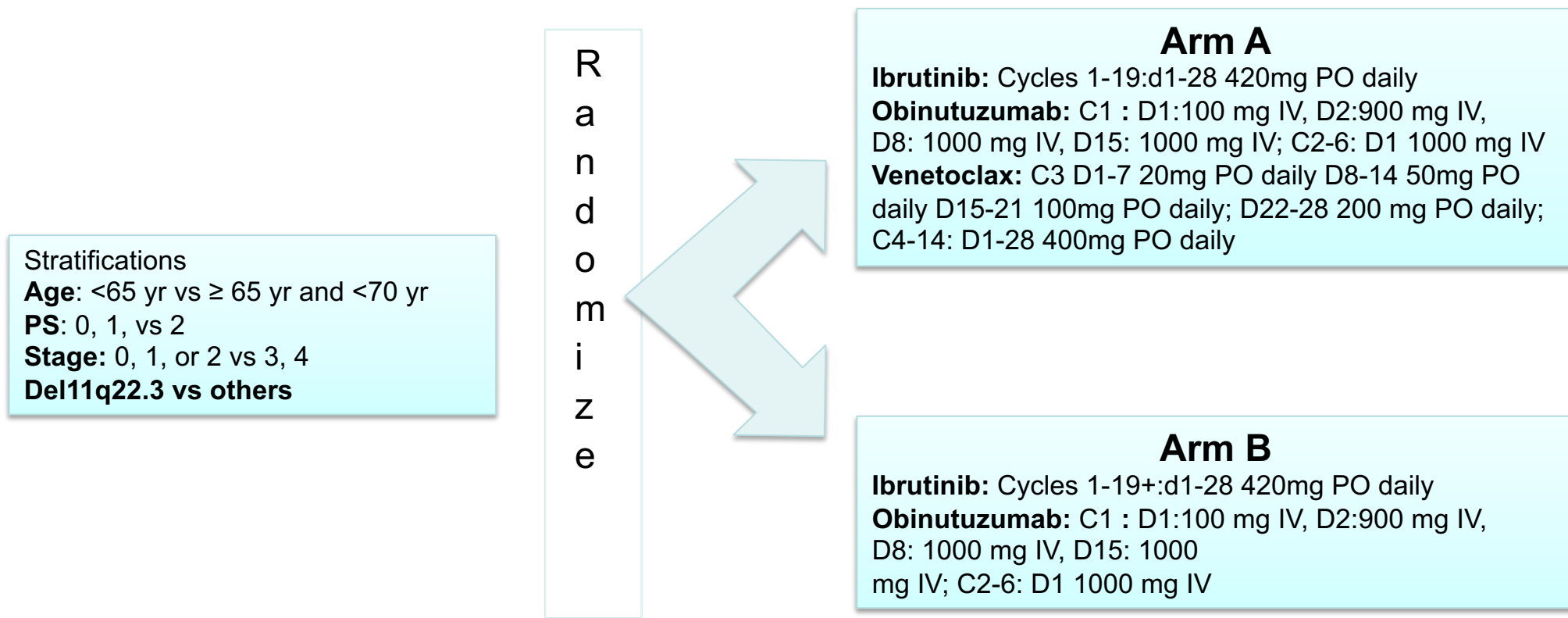
At 15 months, 98% of patients were progression free with no deaths

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)

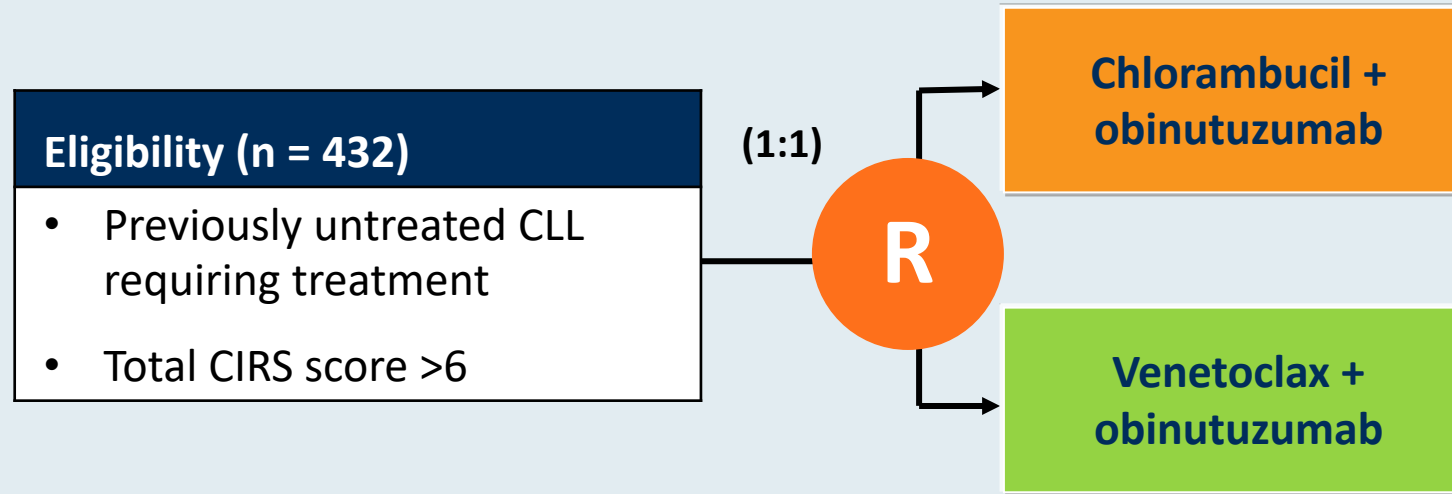
- Low rates of Grade 3 atrial fibrillation, major hemorrhage, infections, febrile neutropenia and laboratory TLS (no Grade 4 event)
- No patients developed clinical TLS
 - Laboratory TLS reported as AE in 3 patients (only 1 met Howard criteria)
- No fatal AEs

Ongoing Phase III EA9161 Trial Schema



Courtesy of Brad Kahl, MD

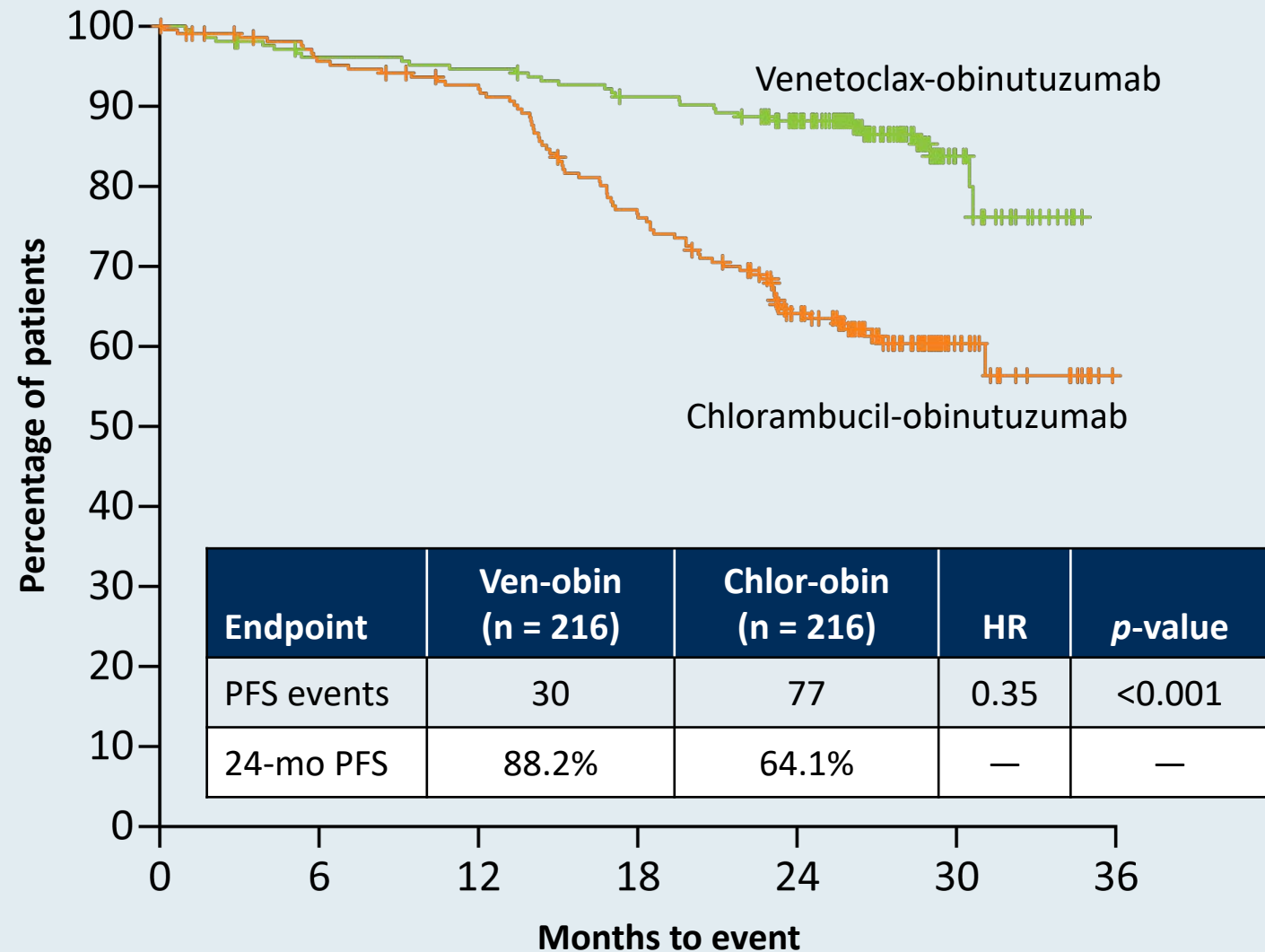
CLL14 Phase III Study Schema



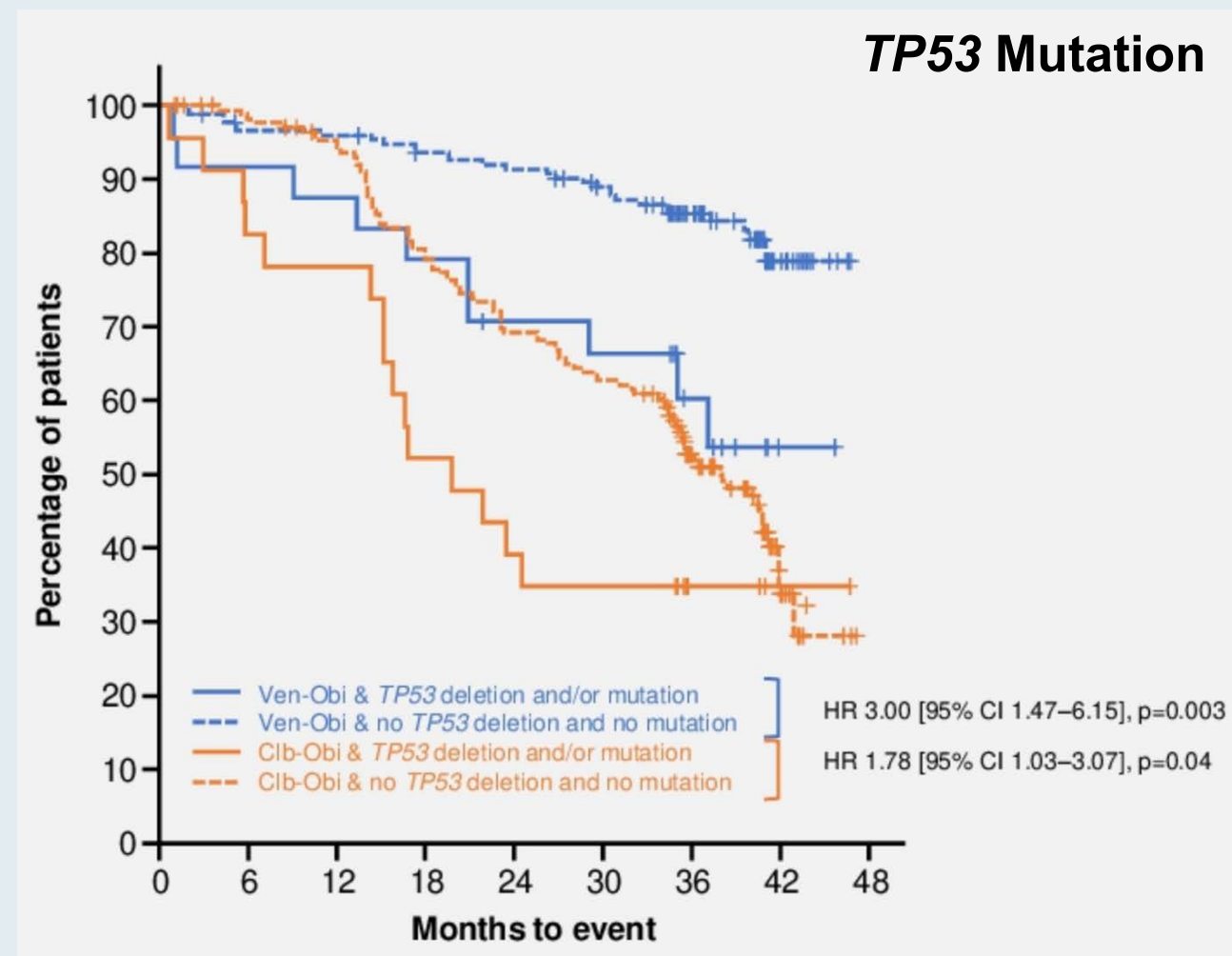
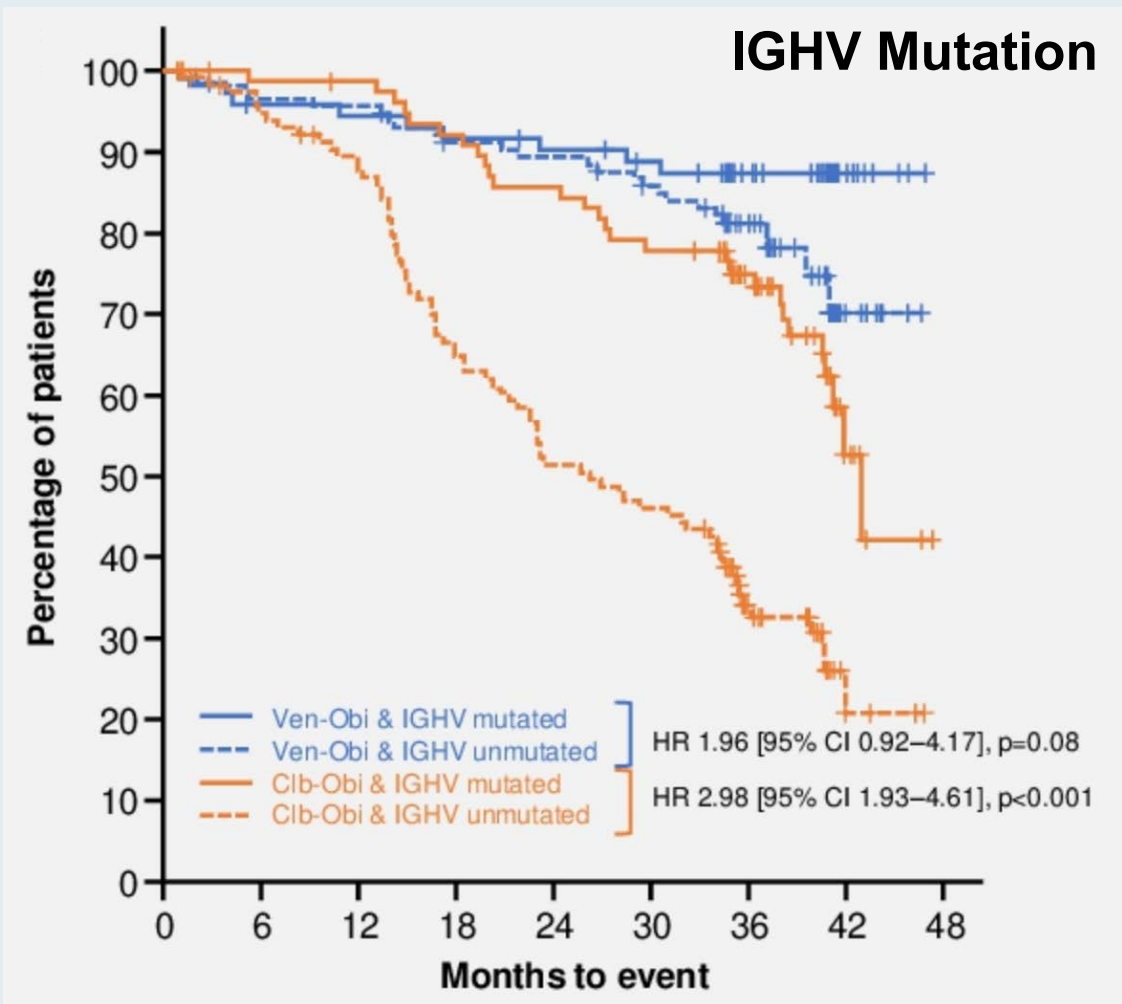
Primary endpoint: Progression-free survival

- 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



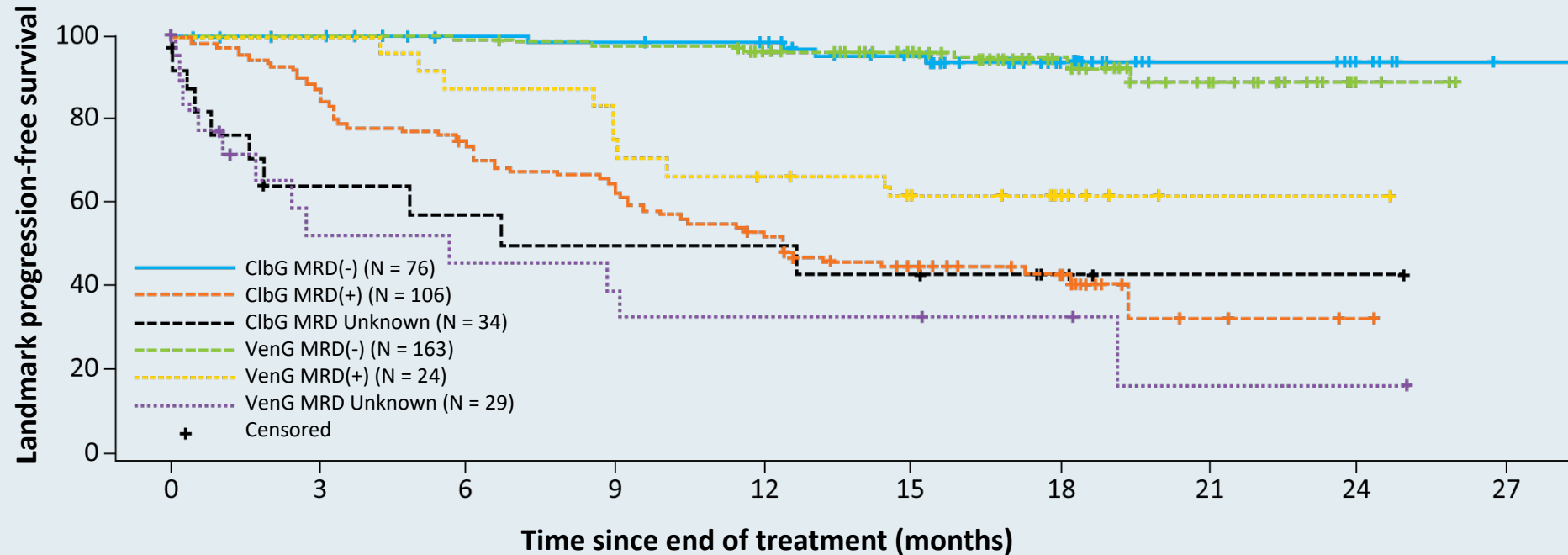
CLL14: PFS by IGHV and TP53 Mutation Status



CLL14: Minimal Residual Disease 3 Months After Treatment

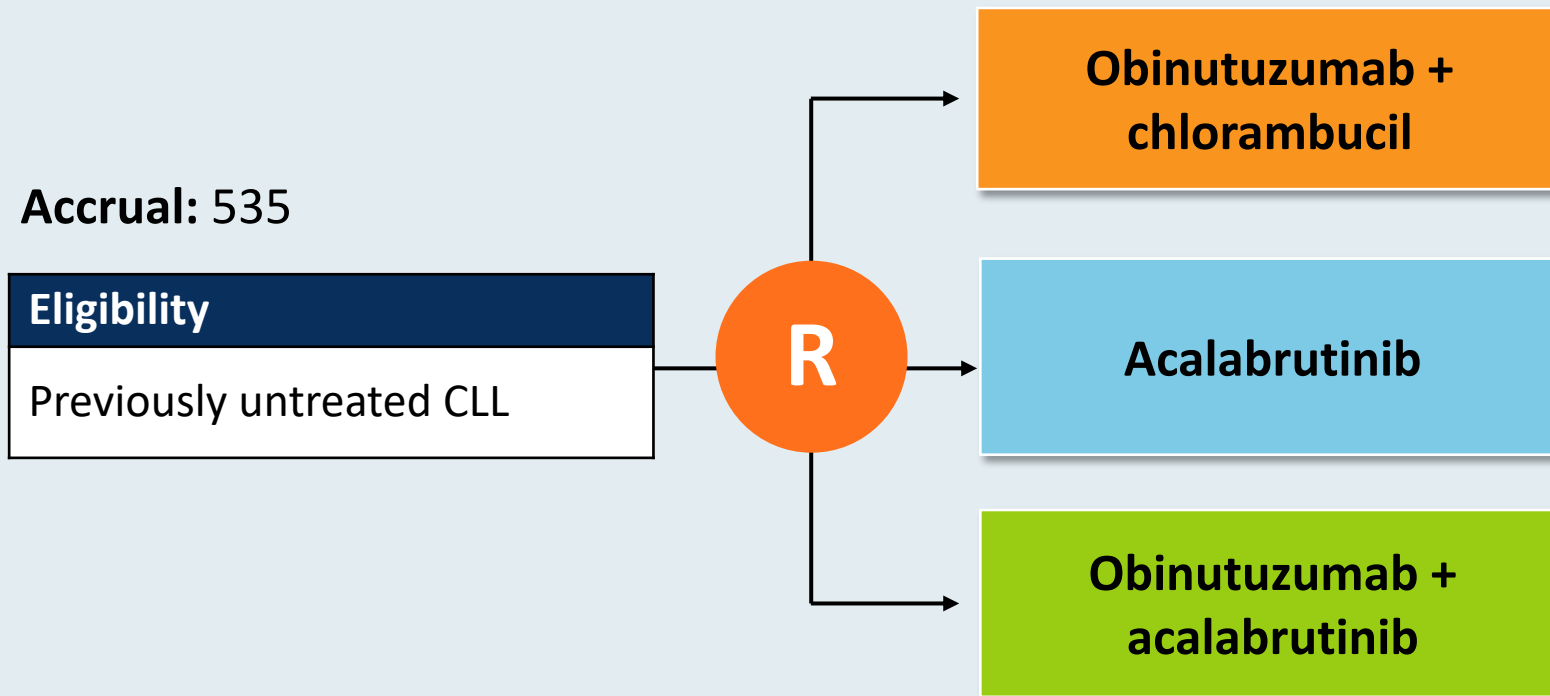
MRD 3 months after treatment	MRD-negative		MRD responders	
	Veneto/obin (N = 216)	Chloram/obin (N = 216)	Veneto/obin (N = 216)	Chloram/obin (N = 216)
MRD in bone marrow	56.9%	17.1%	33.8%	10.6%
Odds ratio, <i>p</i> -value	OR 6.4, <i>p</i> < 0.0001		OR 4.3, <i>p</i> < 0.0001	
MRD in peripheral blood	75.7%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



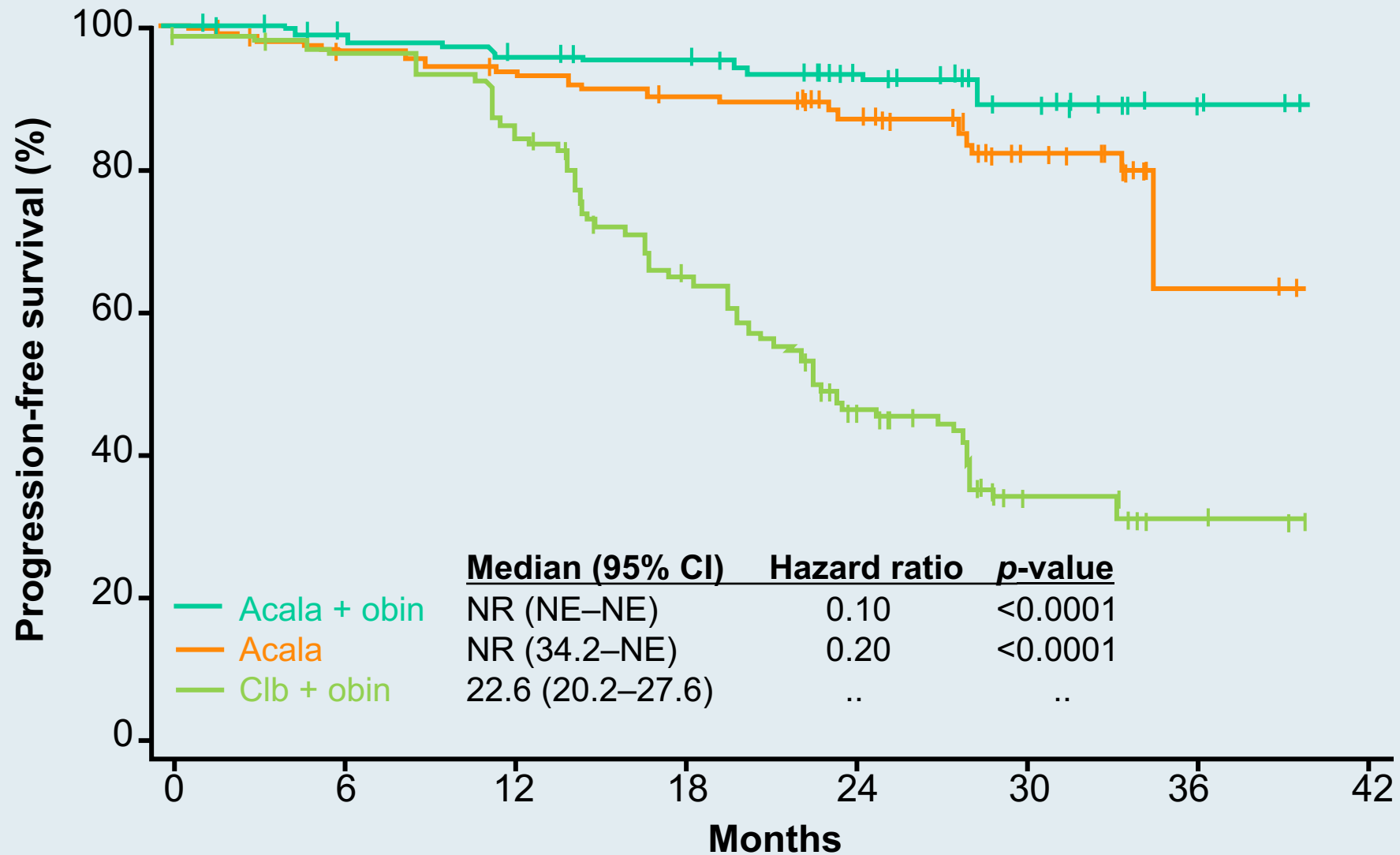
Further landmark analysis of PFS by MRD status showed that undetectable MRD translated into improved PFS regardless of the clinical response status at end of therapy.

ELEVATE-TN Phase III Trial Schema

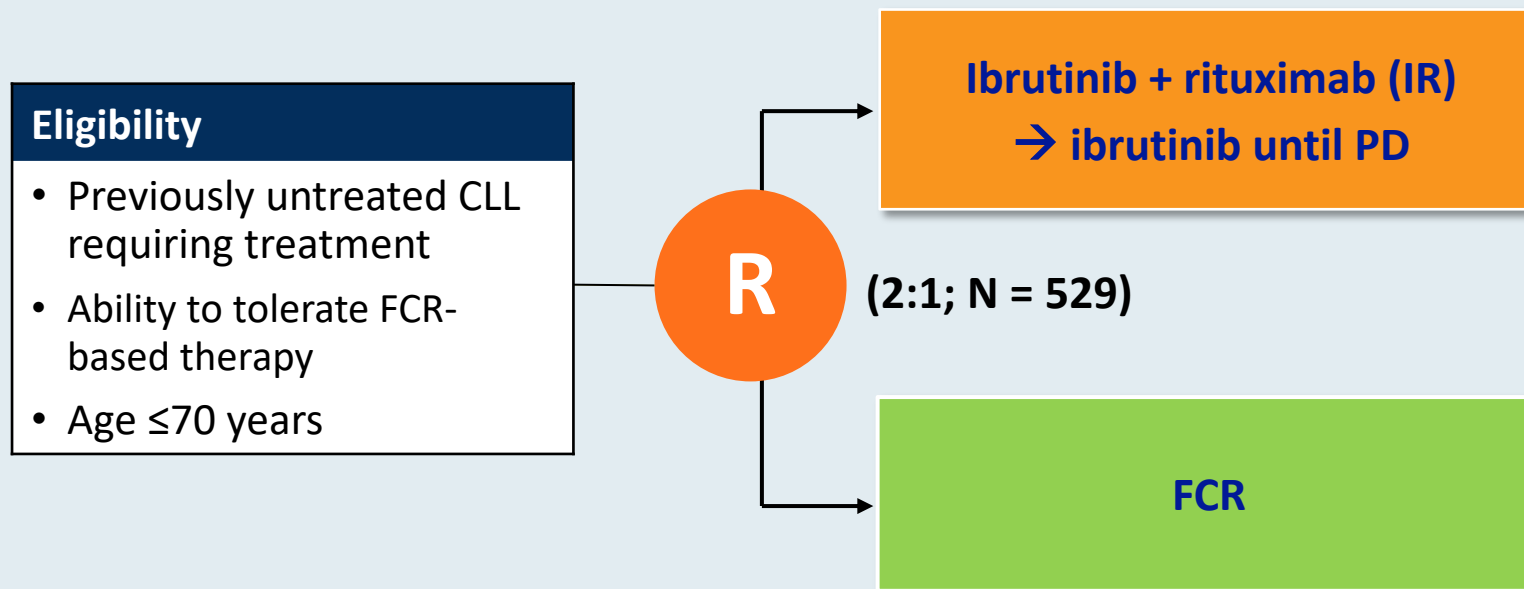


Primary endpoint: Progression-free survival

ELEVATE-TN: PFS (IRC)



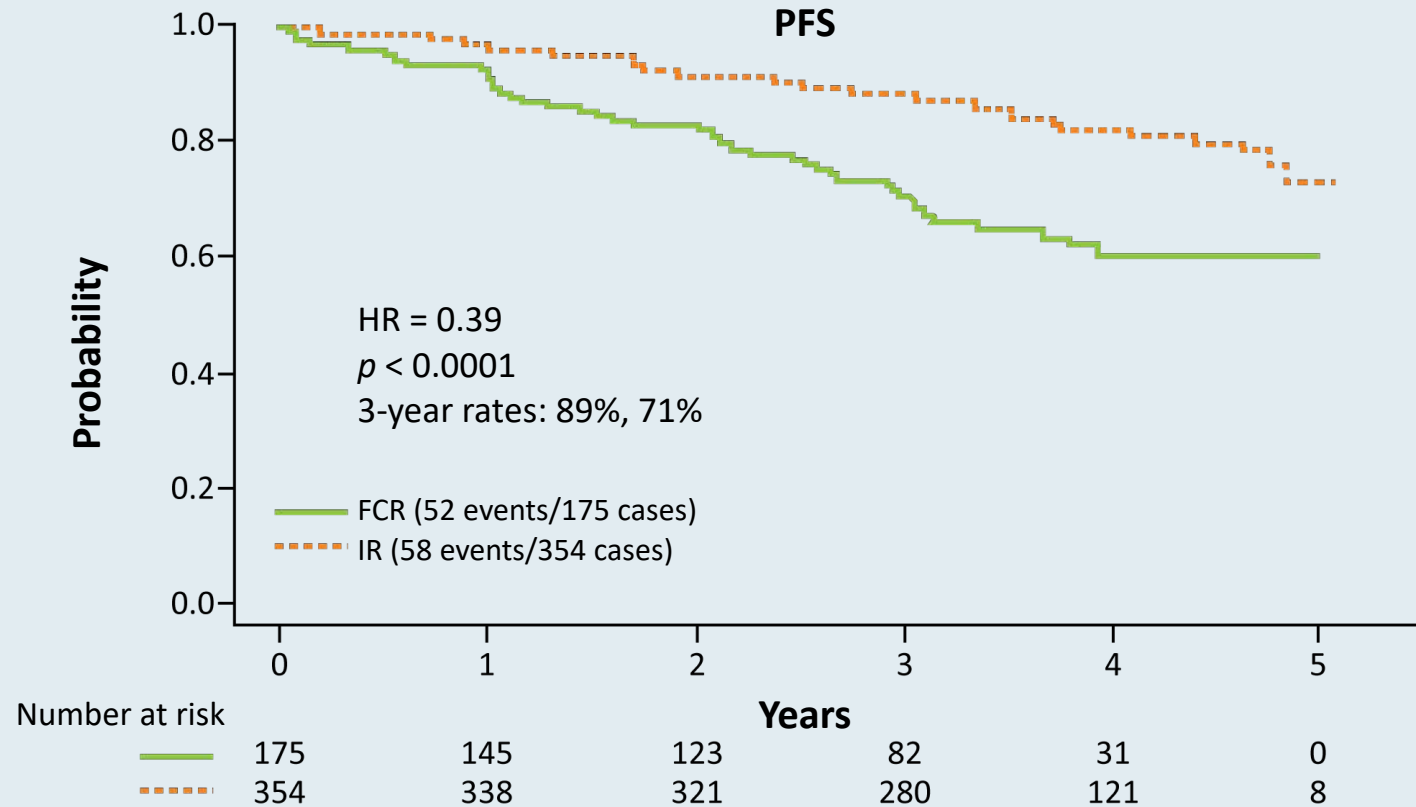
Phase III ECOG-ACRIN E1912 Study Design



Primary endpoint: PFS

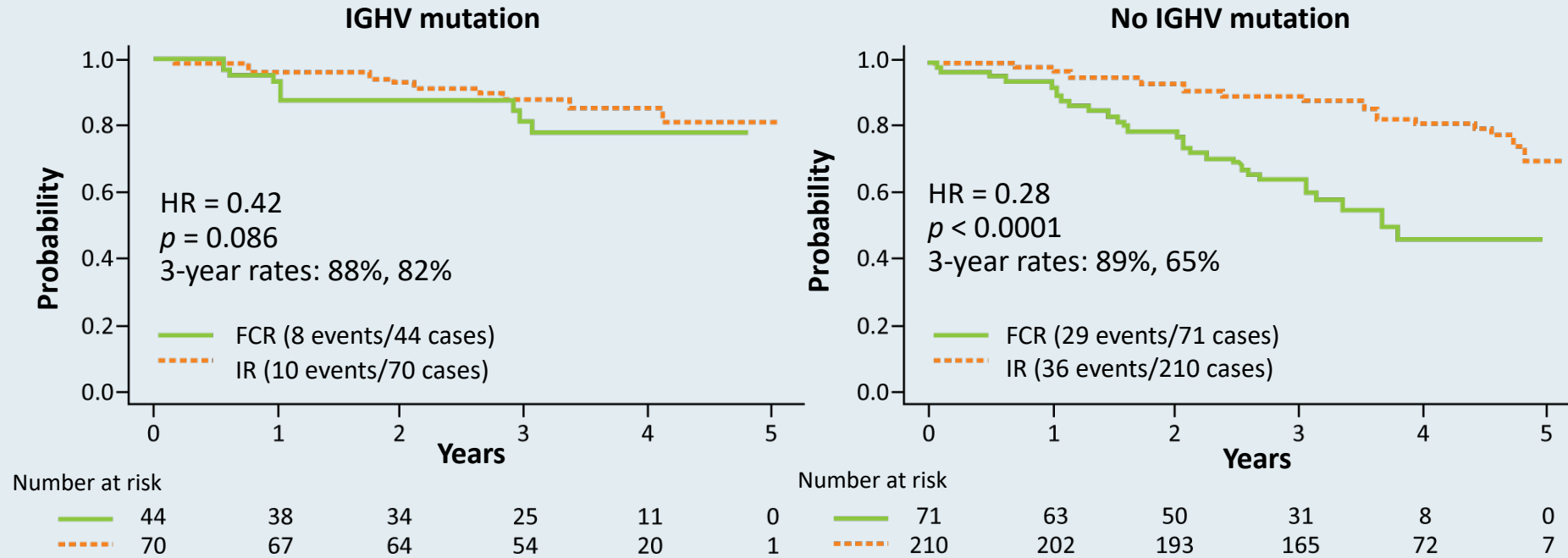
Secondary endpoints: OS, ORR, Toxicity and Tolerability

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



- Grade ≥ 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; $p = 0.086$).

Meet The Professor

Management of Lung Cancer

Wednesday, October 28, 2020
12:00 PM – 1:00 PM ET

Faculty

Professor Solange Peters, MD, PhD

Moderator

Neil Love, MD

Thank you for joining us!

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