Meet The Professor
Management of Chronic Lymphocytic Leukemia

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

Commercial Support

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

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Dr Love — Disclosures

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

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Research To Practice CME Planning Committee Members, Staff and Reviewers

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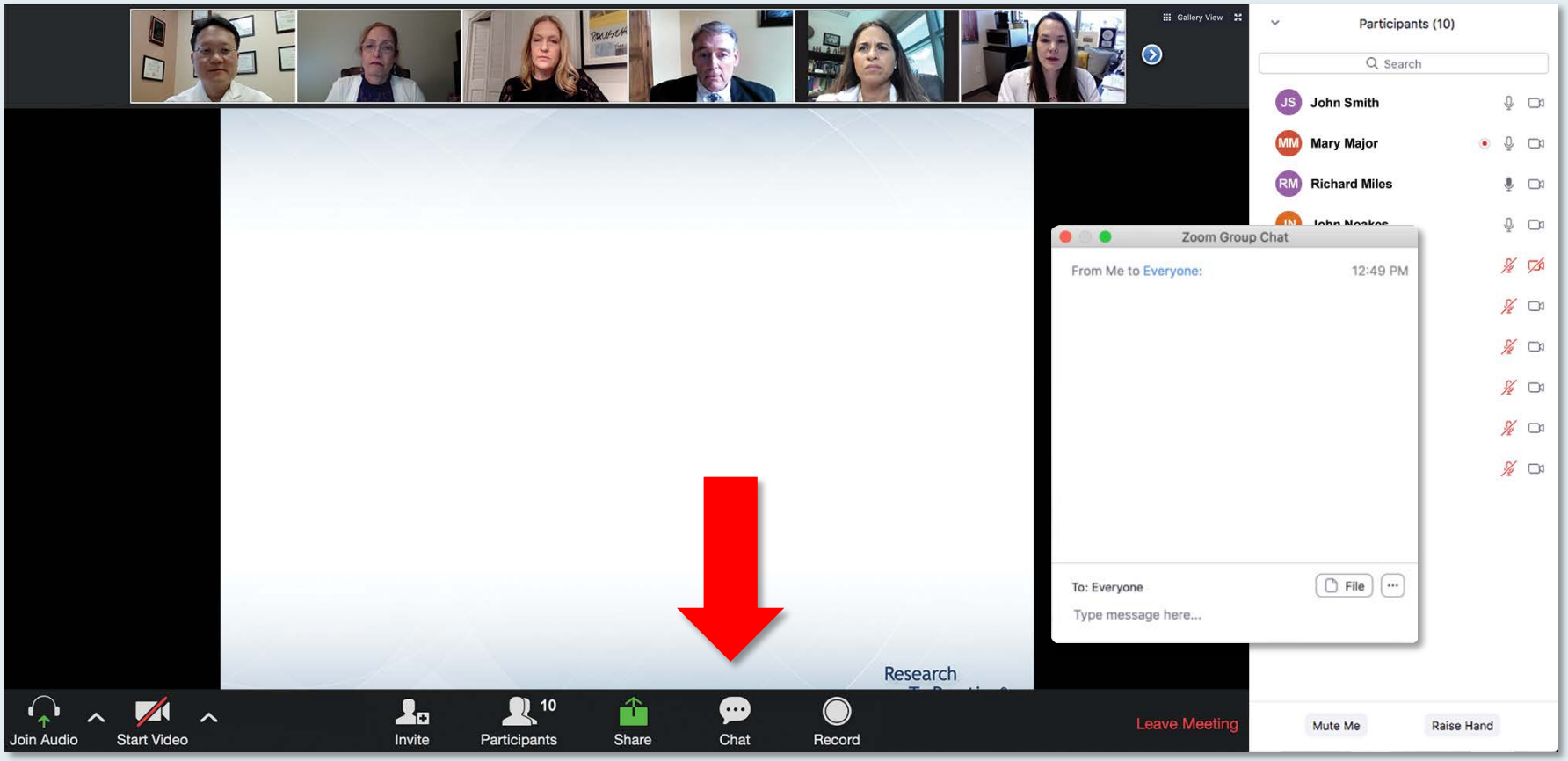
Dr Pagel — Disclosures

Consulting Agreements	AstraZeneca Pharmaceuticals LP, BeiGene, Gilead Sciences Inc, Takeda Oncology

We Encourage Clinicians in Practice to Submit Questions



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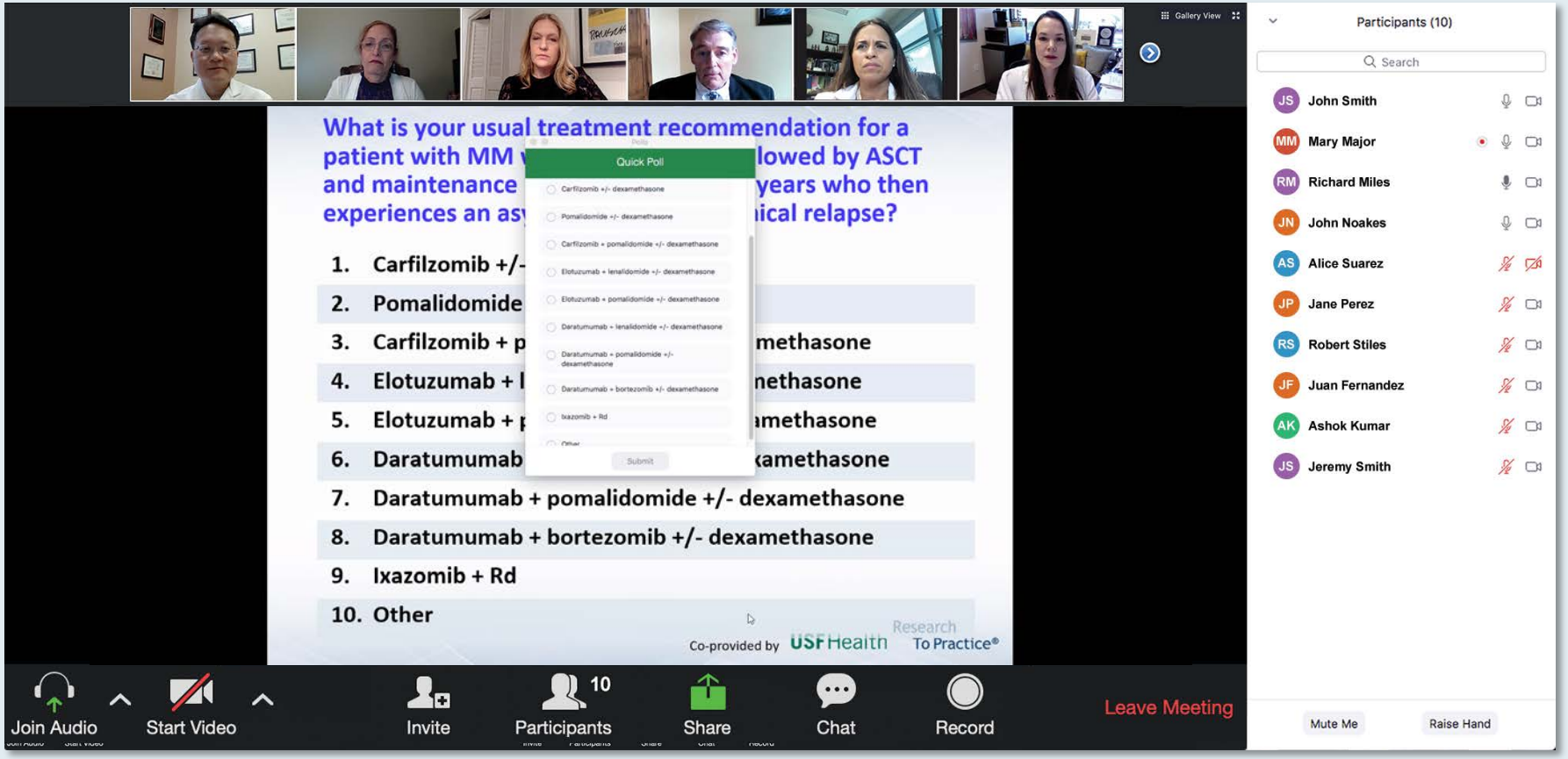
Familiarizing Yourself with the Zoom Interface

How to answer poll questions



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Upcoming Webinars

Thursday, October 15, 2020
12:00 PM – 1:00 PM ET

Meet The Professor: Management of Ovarian Cancer

Faculty
Kathleen Moore, MD

Moderator
Neil Love, MD

Friday, October 16, 2020
11:00 AM – 12:00 PM ET

Addressing Current Questions and Controversies in the Management of Non-Small Cell Lung Cancer with an EGFR Mutation

Faculty
Roy S Herbst, MD, PhD
Suresh S Ramalingam, MD
Helena Yu, MD

Moderator
Neil Love, MD

Upcoming Webinars

Tuesday, October 20, 2020
5:00 PM – 6:00 PM ET

Optimizing the Role of Radiation Oncologists and Other Multidisciplinary Team Members in the Management of Locally Advanced Non-Small Cell Lung Cancer

Faculty
Walter J Curran Jr, MD
Camille Usher, MS, APRN, NP-C

Moderator
Neil Love, MD

Thursday, October 22, 2020
12:00 PM – 1:00 PM ET

Meet The Professor: Management of Multiple Myeloma

Faculty
Krina K Patel, MD, MSc

Moderator
Neil Love, MD

Upcoming Webinars

Saturday, October 24, 2020
8:30 AM – 4:30 PM ET

Current Concepts and Recent Advances in Oncology: A Daylong Clinical Summit Hosted in Partnership with Florida Cancer Specialists

Moderator
Neil Love, MD

Thank you for joining us!

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

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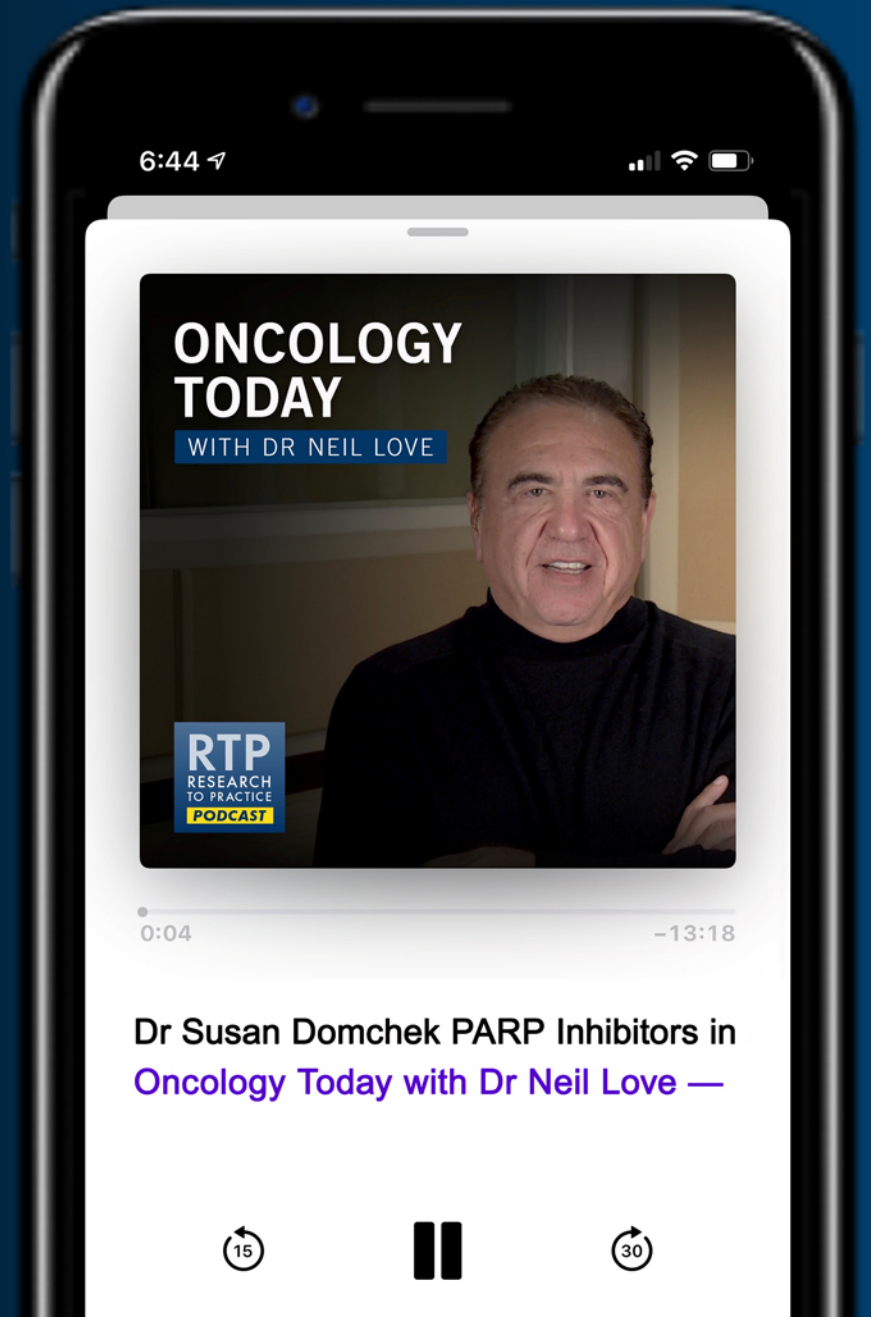

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Meet The Professor Program Participating Faculty

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Harvard Medical School
Director of Clinical Research
Division of Lymphoma
Dana-Farber Cancer Institute
Boston, Massachusetts

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

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Chief of Hematologic Malignancies
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US Oncology
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Meet The Professor Program Participating Faculty

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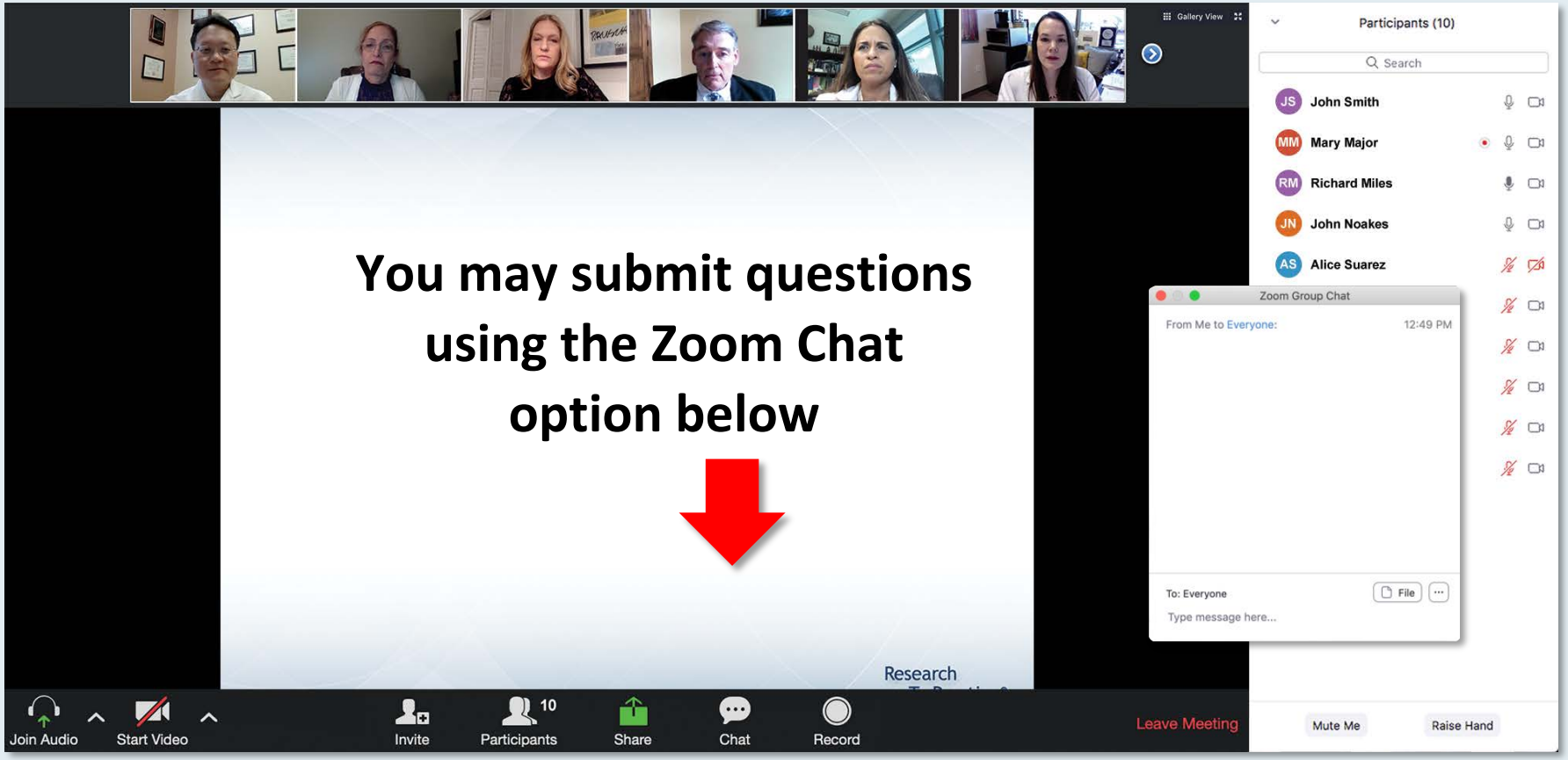

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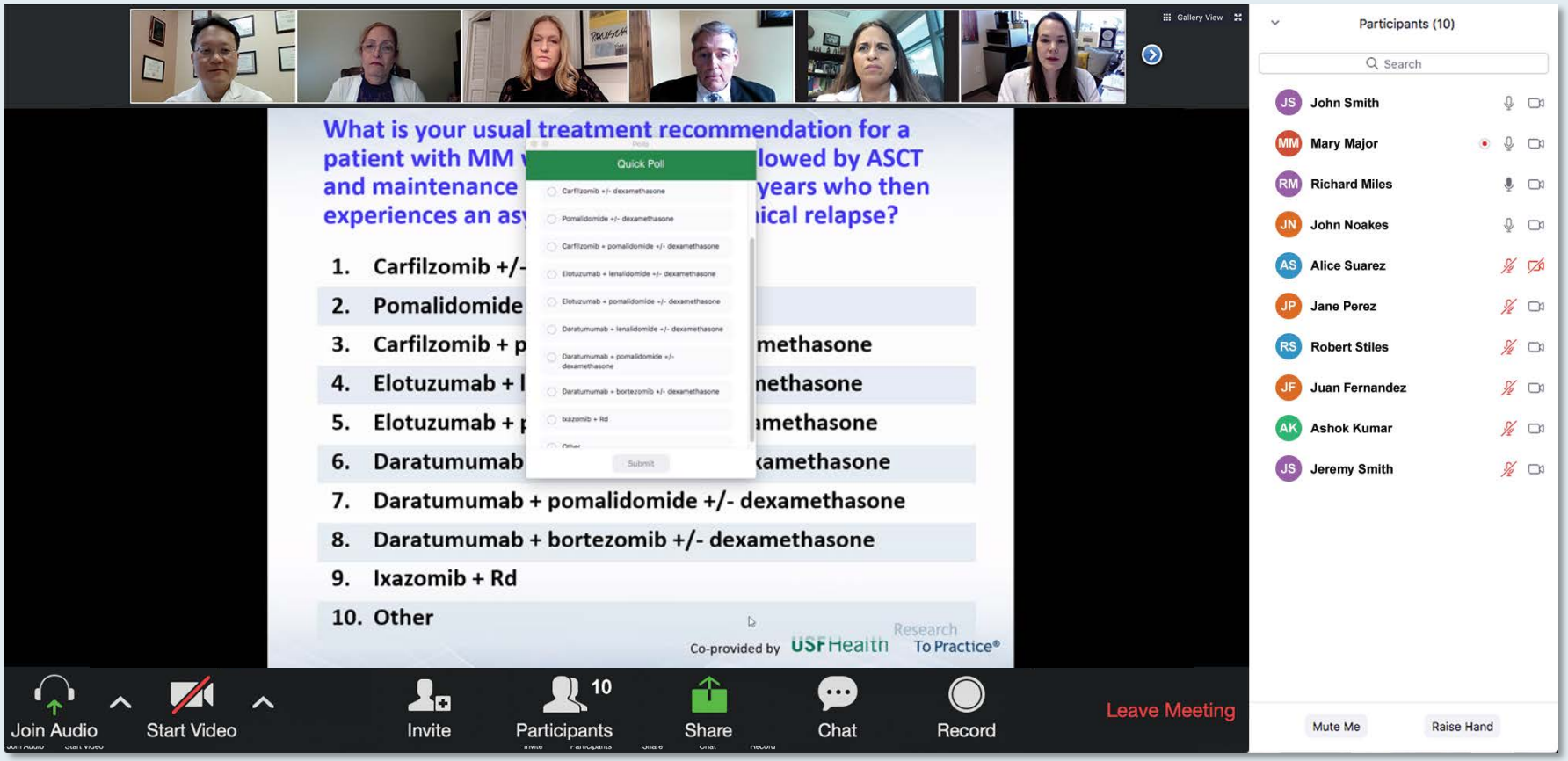

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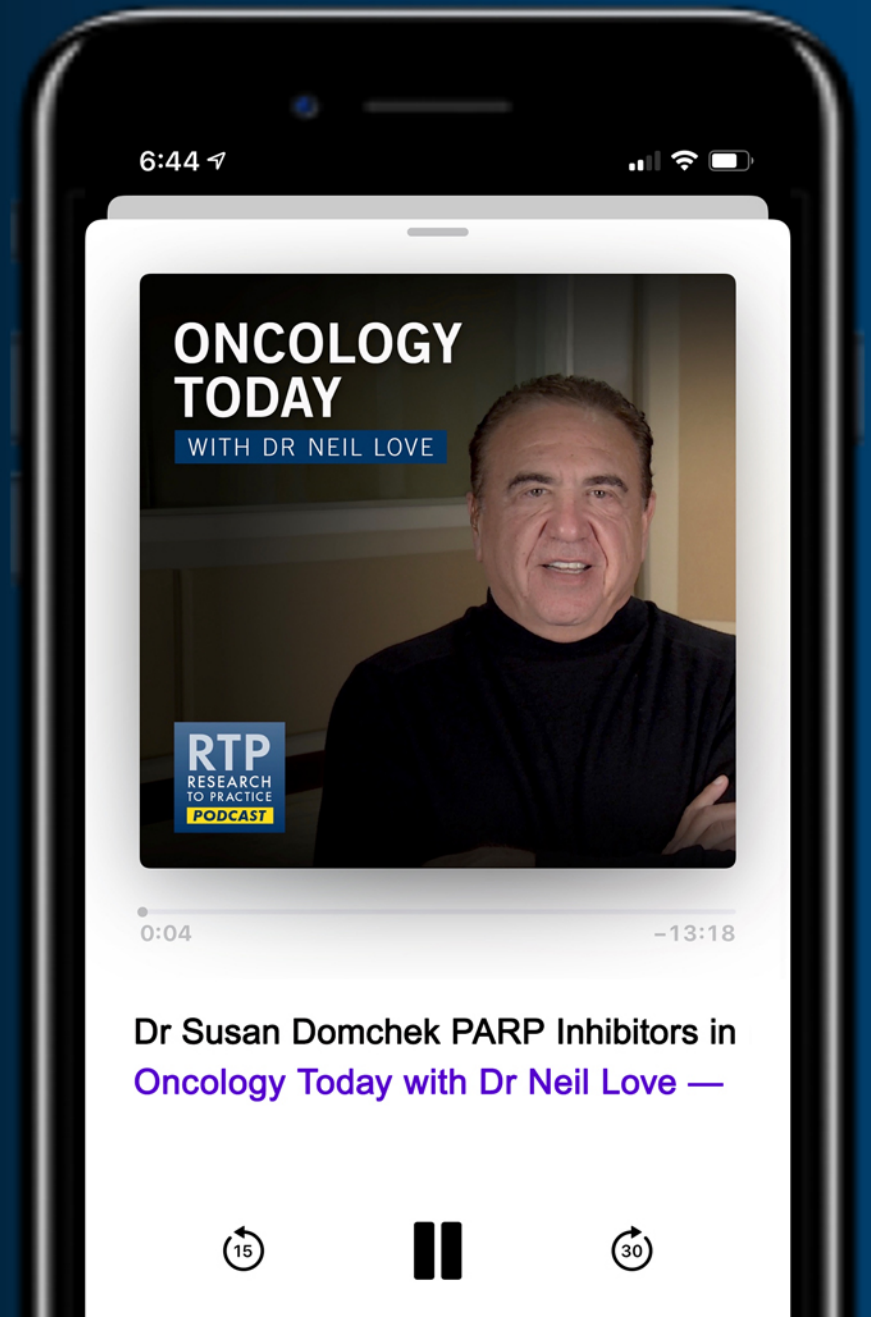

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William K Oh, MD
David M O'Malley, MD
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Gregory J Riely, MD, PhD
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Sara M Tolaney, MD, MPH

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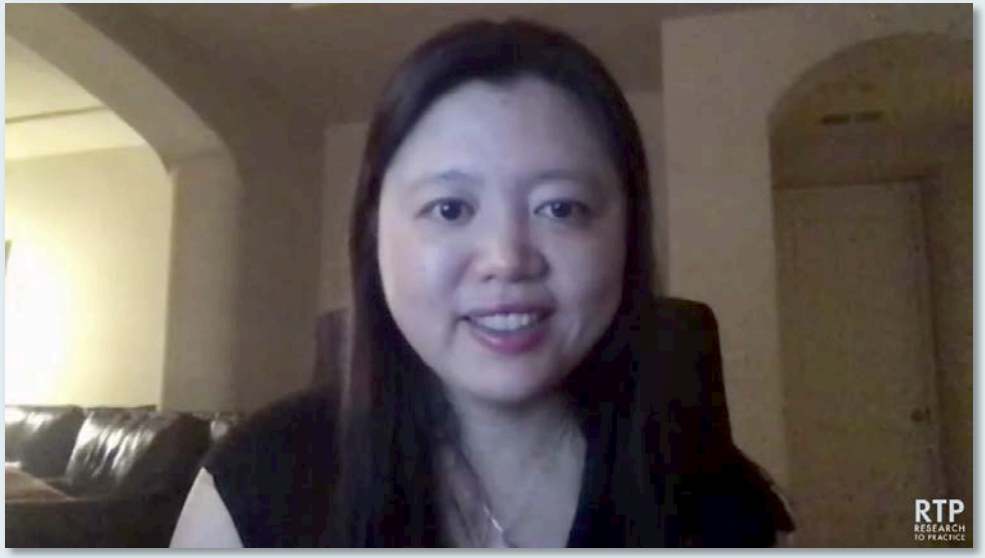

Gigi Chen, MD
Diablo Valley Oncology and
Hematology Medical Group
Pleasant Hill, California

Laurie Matt-Amaral, MD, MPH
Attending Physician
Cleveland Clinic Akron General Medical Center
Akron, Ohio

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Meet The Professor

Management of Lung Cancer

Professor Tony SK Mok, MD
Chairman, Department of Clinical Oncology
The Chinese University of Hong Kong
Hong Kong, China

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Meet The Professor with Dr Pagel

MODULE 1: Cases from Drs Chen and Matt-Amaral

- Dr Matt-Amaral: A 65-year-old woman with CLL and response to ibrutinib but plateau in absolute lymphocyte count
- Questions and Comments: Preference of ibrutinib, acalabrutinib or venetoclax
- Dr Chen: A 66-year-old woman with newly diagnosed CLL receives acalabrutinib
- Dr Chen: An 89-year-old woman with CLL develops congestive heart failure on ibrutinib
- Dr Matt-Amaral: A 77-year-old man with CLL and significant lymphadenopathy and splenomegaly
- Dr Chen: A 75-year-old woman with recurrent CLL after obinutuzumab/chlorambucil

MODULE 2: CLL Journal Club with Dr Pagel

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

MODULE 4: Key Recent Data Sets

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Case Presentation – Dr Matt-Amaral: A 65-year-old woman with CLL and response to ibrutinib but plateau in absolute lymphocyte count (ALC)

Dr Laurie Matt-Amaral

- Presented after routine visit to PCP; asymptomatic with some lymphadenopathy in the neck
  - WBC 111.8; ALC 103K
  - Bone marrow biopsy: Trisomy 12 with 90-95% involvement
- April 2019: Ibrutinib initiated
- Most recent labwork: WBC 181.8; ALC 177.07
- Patient remains asymptomatic; lymphadenopathy has disappeared and anemia has resolved

Questions

- As long as the patient is still responding and her white blood cell count is dropping, would you consider continuing her on ibrutinib, or would you consider switching to another agent because there may be resistance of some kind?

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Questions and Comments: Preference of ibrutinib, acalabrutinib or venetoclax

Dr Laurie Matt-Amaral

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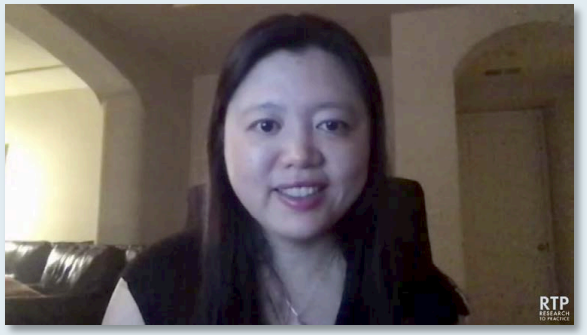
Case Presentation – Dr Chen: A 66-year-old woman with newly diagnosed CLL receives acalabrutinib



Dr Gigi Chen

- March 2012: Diagnosed with CLL → 1 cycle of FCR → switched to BR x 5 cycles due to FCR side effects
- 2020: Patient presents with new lymphadenopathy in neck and is experiencing night sweats
  - PET/CT: Recurrent CLL with hypermetabolic lymphadenopathy seen in the neck, chest, abdomen, and pelvis
  - Bone marrow biopsy: CLL/FL
  - FISH: Trisomy 12
- Acalabrutinib therapy initiated

Questions

- How do you select the best treatment for a patient such as this with higher-risk CLL? If this patient had presented today instead of in 2012, would the best initial treatment still be FCR?
- What is the role of MRD testing?

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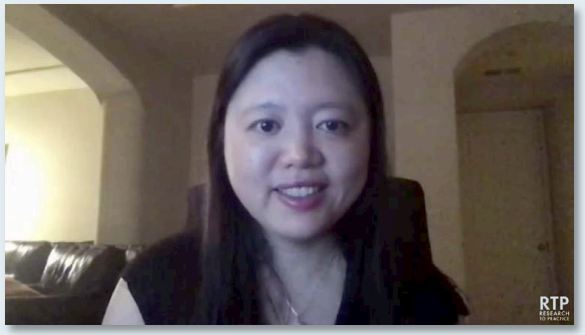
Case Presentation – Dr Chen: An 89-year-old woman with CLL develops congestive heart failure (CHF) on ibrutinib



Dr Gigi Chen

- 2010: Diagnosed with CLL with normal cytogenetics
  - Single agent rituximab administered
- Patient has now been on ibrutinib therapy for some time and was more recently hospitalized for CHF, atrial fibrillation → anti-coagulation therapy initiated
- Patient also has chronic kidney disease, creatinine clearance 30-40 mL/min
- CLL has been under control with no new lymphadenopathy and patient desires to continue treatment

Questions

- What would be the best treatment option for this patient? Is venetoclax an option?
- How would you initiate venetoclax in this patient with significant comorbidities if she were to develop symptomatic disease with lymphadenopathy?

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Case Presentation – Dr Matt-Amaral: A 77-year-old man with CLL and significant lymphadenopathy and splenomegaly

Dr Laurie Matt-Amaral

- 2014: Initial diagnosis of Rai 0 Stage II CLL → observation
- 2020: Presents with pneumonia-type symptoms and WBC > 500K
  - RAI 3, Stage IV with elevated ALC, lymphadenopathy, splenomegaly, and anemia
  - FISH: del(11q)
- Allopurinol/hydroxyurea → rituximab weekly x 3 while waiting for insurance approval for ibrutinib
- Ibrutinib initiated

Questions

- Would you have initiated treatment with hydroxyurea in this patient who was asymptomatic, or approached the patient differently? What would be other ideal therapies for him given that he seems to be responding to ibrutinib?
- Do you agree with using rituximab for a short period of time to get a reduction in his ALC, or would you prefer to wait for the oral agent?

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REGULAR ARTICLE

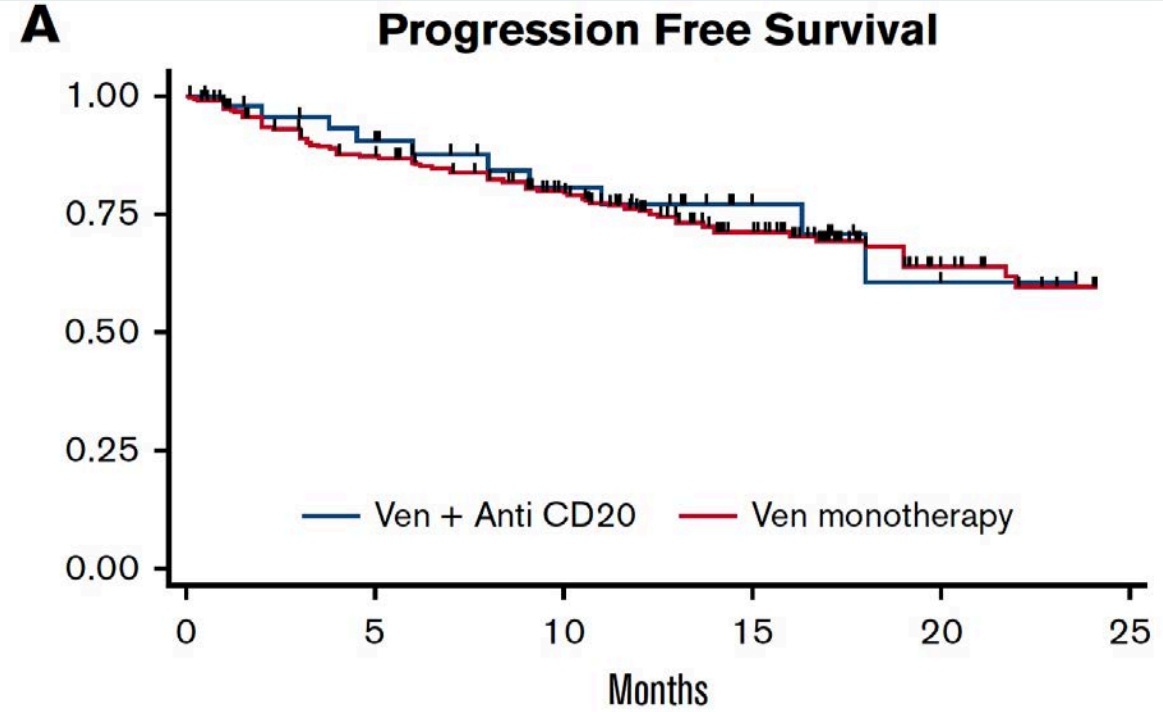
blood advances

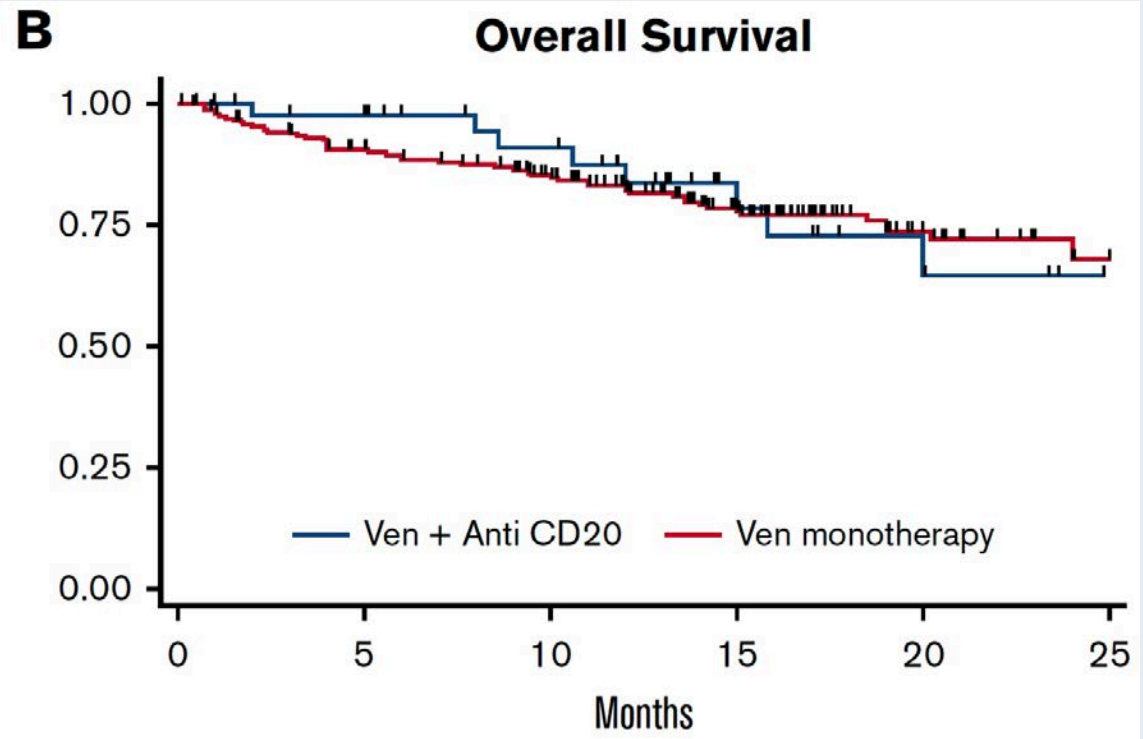
A retrospective comparison of venetoclax alone or in combination with an anti-CD20 monoclonal antibody in R/R CLL

Anthony R. Mato,[1,*] Lindsey E. Roeker,[1,*] Toby A. Eyre,[2] Chadi Nabhan,[3] Nicole Lamanna,[4] Brian T. Hill,[5] Danielle M. Brander,[6] Paul M. Barr,[7] Frederick Lansigan,[8] Bruce D. Cheson,[9] Arun K. Singavi,[10] Maryam Sarraf Yazdy,[9] Nirav N. Shah,[10] John N. Allan,[11] Erica B. Bhavsar,[11] Joanna Rhodes,[12] Kaitlin Kennard,[12] Stephen J. Schuster,[12] AnnaLynn M. Williams,[7] Alan P. Skarbnik,[13] Andre H. Goy,[13] Julie M. Goodfriend,[1] Colleen Dorsey,[1] Catherine C. Coombs,[14] Hande Tuncer,[15] Chaitra S. Ujjani,[16] Ryan Jacobs,[17] Allison M. Winter,[5] John M. Pagel,[18] Neil Bailey,[18] Anna Schuh,[2] Mazyar Shadman,[16] Andrea Sitlinger,[6] Hanna Weissbrot,[4] Sivraj Muralikrishnan,[8] Andrew Zelenetz,[1] Amy A. Kirkwood,[19] and Christopher P. Fox[20]

Blood Adv 2019;3(10):1568-73

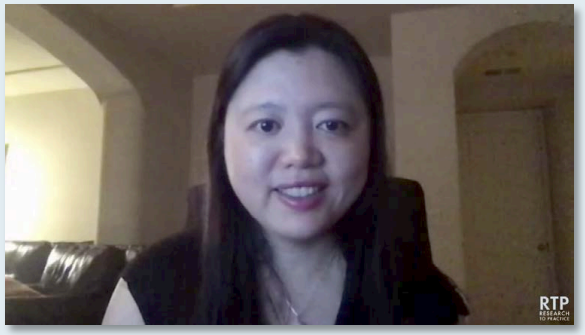
PFS (A) and OS (B) Stratified by Venetoclax Monotherapy and Venetoclax with Anti-CD20 Therapy for R/R CLL





Mato AR et al. *Blood Adv* 2019;3(10):1568-73.

Case Presentation – Dr Chen: A 75-year-old woman with recurrent CLL after obinutuzumab/ chlorambucil



Dr Gigi Chen

- 2010: Diagnosed with CLL → observation
- December 2016: Presents with weight loss, massive splenomegaly, increased lymphadenopathy
- Ibrutinib initiated but later discontinued due to patient development of severe constipation, nausea and vomiting requiring hospitalization
- Enrollment on INFORM clinical trial → obinutuzumab/chlorambucil → chlorambucil held due to cytopenia → obinutuzumab x 6 cycles
- July 2019: Admitted due to autoimmune hemolytic anemia with Hb 4.1 g/dL
  - Blood transfusion → rituximab
- 2020: Recurrence of lymphadenopathy and splenomegaly

Questions

- If you were to consider venetoclax now for this patient, would you consider it with obinutuzumab or a different agent, given that she has progressed on obinutuzumab previously?

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Meet The Professor with Dr Pagel

MODULE 1: Cases from Drs Chen and Matt-Amaral

MODULE 2: CLL Journal Club with Dr Pagel

- Toxicities and outcomes with acalabrutinib for treatment-naïve and relapsed/refractory (R/R) CLL
- First-in-human, proof-of-concept Phase I trial of LOXO-305 for pretreated B-cell cancers
- Ongoing results of a Phase IB/II dose-escalation and cohort-expansion study of vecabrutinib
- Tumor lysis, adverse events and dose adjustments with venetoclax in routine clinical practice
- Efficacy and safety of venetoclax in elderly patients with R/R CLL
- Comparative analysis of targeted novel agents for R/R CLL
- Efficacy of therapies after venetoclax
- Venetoclax alone or combined with anti-CD20 therapy for R/R CLL
- Future of PI3K inhibitors in CLL
- GIMEMA trial: Efficacy of BR for untreated CLL — Indirect comparison to ibrutinib in a real-world setting
- Pembrolizumab for R/R Richter syndrome
- COVID-19: Respiratory failure, use of convalescent plasma and outcomes and management of CLL

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

MODULE 4: Key Recent Data Sets

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Toxicities and Outcomes of Acalabrutinib-Treated Patients with Chronic Lymphocytic Leukemia: A Retrospective Analysis of Real World Patients

Yazdy MS et al.

ASH 2019;Abstract 4311.

REGULAR ARTICLE

blood advances

Acalabrutinib monotherapy in patients with chronic lymphocytic leukemia who are intolerant to ibrutinib

Farrukh T. Awan,[1] Anna Schuh,[2] Jennifer R. Brown,[3] Richard R. Furman,[4] John M. Pagel,[5] Peter Hillmen,[6] Deborah M. Stephens,[7] Jennifer Woyach,[8] Elena Bibikova,[9] Prista Charuworn,[9] Melanie M. Frigault,[9,10] Ahmed Hamdy,[9] Raquel Izumi,[9] Bolan Linghu,[11] Priti Patel,[9] Min Hui Wang,[9] and John C. Byrd[8]

Blood Adv 2019;3(9):1553-62

Acalabrutinib in Treatment-Naïve Chronic Lymphocytic Leukemia: Mature Results from Phase II Study Demonstrating Durable Remissions and Long-Term Tolerability

Byrd JC et al.

ASCO 2020;Abstract 8024.

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Regular Article

CLINICAL TRIALS AND OBSERVATIONS

Acalabrutinib monotherapy in patients with relapsed/refractory chronic lymphocytic leukemia: updated phase 2 results

John C. Byrd,[1,*] William G. Wierda,[2] Anna Schuh,[3] Stephen Devereux,[4] Jorge M. Chaves,[5] Jennifer R. Brown,[6] Peter Hillmen,[7] Peter Martin,[8] Farrukh T. Awan,[9] Deborah M. Stephens,[10] Paolo Ghia,[11,12] Jacqueline Barrientos,[13] John M. Pagel,[14] Jennifer A. Woyach,[1] Kathleen Burke,[15] Todd Covey,[16] Michael Gulrajani,[16] Ahmed Hamdy,[16] Raquel Izumi,[16] Melanie M. Frigault,[16] Priti Patel,[16] Wayne Rothbaum,[16] Min Hui Wang,[16] Susan O'Brien,[17,*] and Richard R. Furman[8,*]

Blood 2020;135(15):1204-13

Investigator-Assessed Best Response to Acalabrutinib

	N = 134	
	n/n	% (95% CI*) or n (%)
ORR: CR + PR+ PRL		94 (89, 97)
ORR: CR + PR		88 (81, 93)
Best response		
CR		6 (4)
PR		112 (84)
PRL		8 (6)
Stable disease		2 (1)
PD		2 (1)
Unknown†		4 (3)
ORR by high-risk subgroup: CR + PR + PRL		
del(17)(p13.1)	25/27	93 (76, 99)
del(11)(q22.3)	20/21	95 (76, 100)
Unmutated IGHV	77/81	95 (88, 99)
Complex karyotype, ≥3 abnormalities	18/20	90 (68, 99)

*The 95% exact binomial CI.

†Patients did not have on-treatment assessments.

Byrd JC, et al. *Blood* 2020;135(15):1204-13.

Results from a First-in-Human, Proof-of-Concept Phase 1 Trial in Pretreated B-Cell Malignancies for Loxo-305, a Next-Generation, Highly Selective, Non-Covalent BTK Inhibitor

Mato AR et al.

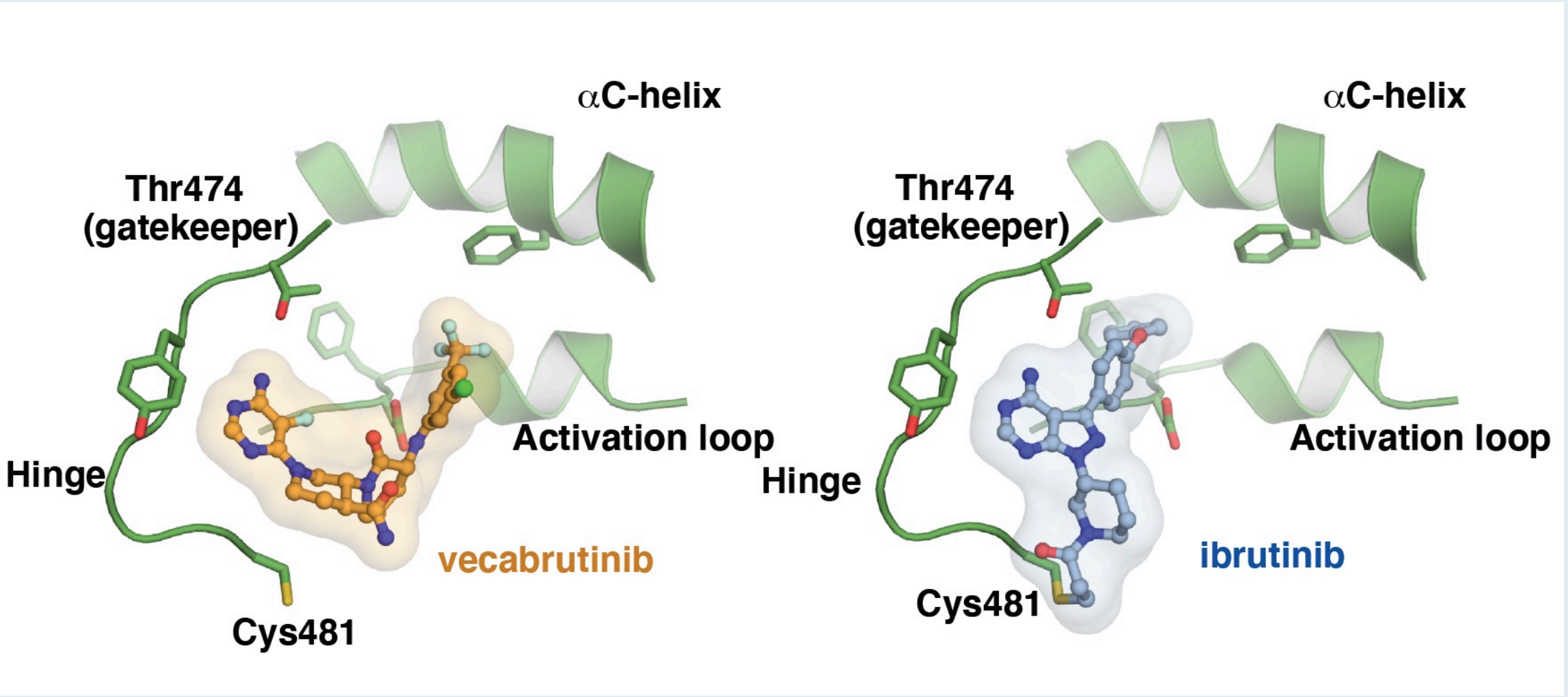
ASH 2019;Abstract 501.

Ongoing Results of a Phase 1B/2 Dose-Escalation and Cohort-Expansion Study of the Selective, Noncovalent, Reversible Bruton's Tyrosine Kinase Inhibitor, Vecabrutinib, in B-Cell Malignancies

Allan JN et al.

ASH 2019;Abstract 3041.

Vecabrutinib's BTK Domain Interaction Differentiated from Ibrutinib



Allan JN et al. ASH 2019;Abstract 3041.

Precision Medicine and Imaging

Clinical Cancer Research

Tumor Lysis, Adverse Events, and Dose Adjustments in 297 Venetoclax-Treated CLL Patients in Routine Clinical Practice

Lindsey E. Roeker[1], Christopher P. Fox[2], Toby A. Eyre[3], Danielle M. Brander[4], John N. Allan[5], Stephen J. Schuster[6], Chadi Nabhan[7], Brian T. Hill[8], Nirav N. Shah[9], Frederick Lansigan[10], Maryam Yazdy[11], Bruce D. Cheson[11], Nicole Lamanna[12], Arun K. Singavi[9], Catherine C. Coombs[13], Paul M. Barr[14], Alan P. Skarbnik[15], Mazyar Shadman[16], Chaitra S. Ujjani[16], Hande H. Tuncer[17], Allison M. Winter[8], Joanna Rhodes[6], Colleen Dorsey[1], Hannah Morse[1], Charlene Kabel[1], John M. Pagel[18], Annalynn M. Williams[14], Ryan Jacobs[19], Andre Goy[15], Sivraj Muralikrishnan[10], Laurie Pearson[17], Andrea Sitlinger[4], Neil Bailey[18], Anna Schuh[3], Amy A. Kirkwood[20], and Anthony R. Mato[1]

Clin Cancer Res 2019;25(14):4264-70

The efficacy and safety of venetoclax therapy in elderly patients with relapsed, refractory chronic lymphocytic leukaemia

Toby A. Eyre[1,†], Lindsey E. Roeker[2,†], Christopher P. Fox[3], Satyen H. Gohill[4], Renata Walewska[5], Harriet S. Walter[6], Francesco Forconi[7,8], Angus Broom[9], Arvind Arumainathan[10], Danielle M. Brander[11], John N. Allan[12], Stephen J. Schuster[13], Brian T. Hill[14], Frederick Lansigan[15], Bruce D. Cheson[16], Nicole Lamanna[17], Catherine C. Coombs[18], Paul M. Barr[19], Alan P. Skarbnik[20], Mazyar Shadman[21], Chaitra S. Ujjani[21], Laurie Pearson[22], John M. Pagel[23], Ryan Jacobs[24], Anthony R. Mato[2]

Br J Haematol 2020;188(6):918-23

haematologica
Journal of The Ferrata Storti Foundation

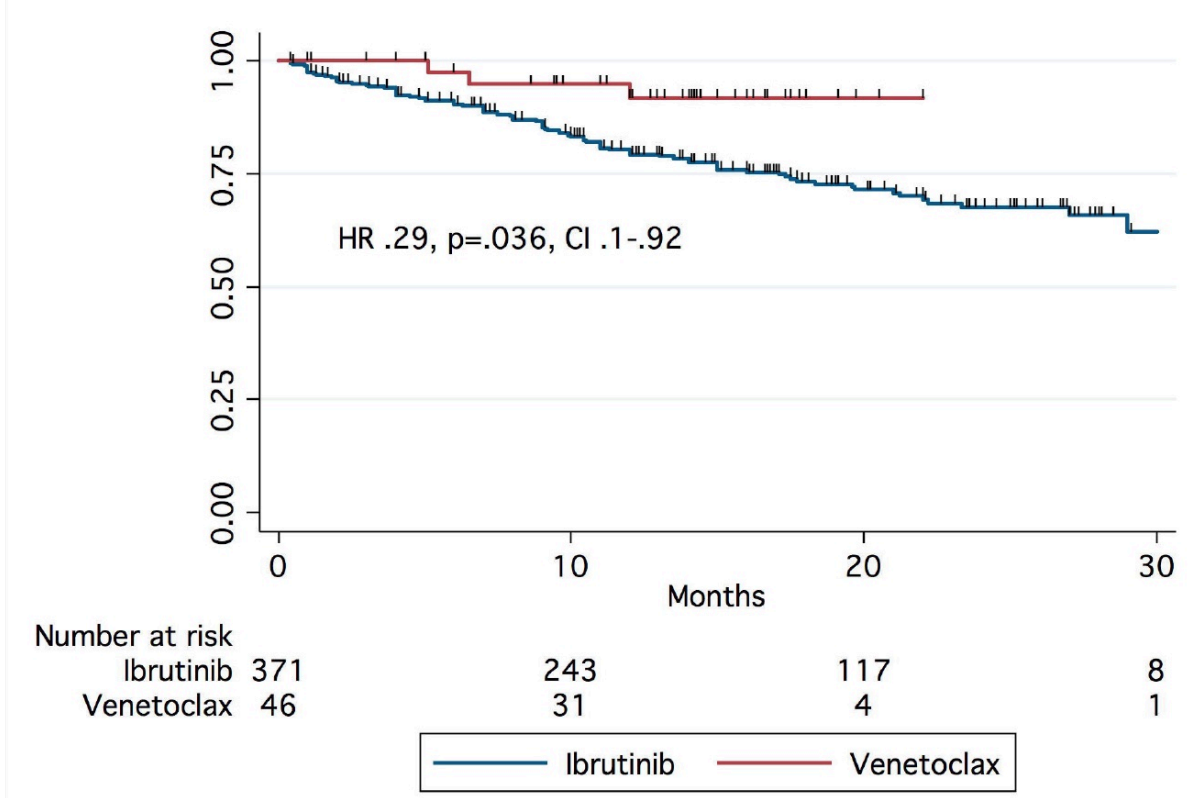
Comparative analysis of targeted novel therapies in relapsed, refractory chronic lymphocytic leukaemia

by Toby A. Eyre, Nicole Lamanna, Lindsey E. Roeker, Chaitra S. Ujjani, Brian T. Hill, Paul M. Barr, Erick Lansigan, Bruce D. Cheson, Maryam Yazdy, John N. Allan, Joanna Rhodes, Stephen J. Schuster, Chadi Nabhan, Alan Skarbnik, Lori Leslie, Prioty Islam, Katherine Whitaker, Catherine C. Coombs, Hande H. Tuncer, John M. Pagel, Ryan Jacobs, Allison M. Winter, Neil Bailey, Andrea Sitlinger, Anna H. Schuh, George Follows, Christopher P. Fox, Danielle M. Brander, Mazyar Shadman, and Anthony R. Mato

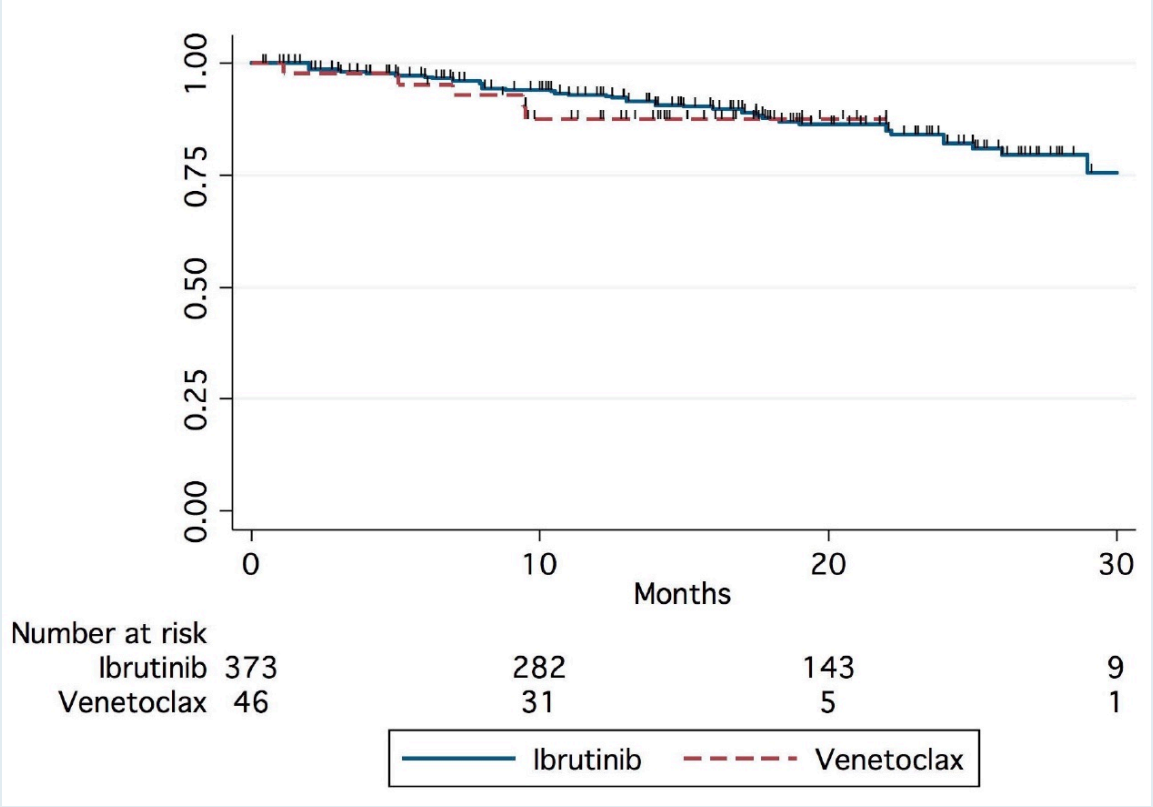
Haematologica **2020;[Online ahead of print]**

Survival Outcomes for Patients with Relapsed, Refractory CLL According to First Novel Agent Received

Progression-free survival according to novel targeted agent



Overall survival according to novel targeted agent



Eyre TA et al. *Haematologica* 2020;[Online ahead of print].

RTP RESEARCH TO PRACTICE

Efficacy of Therapies Following Venetoclax Discontinuation in CLL: Focus on B-Cell Receptor Signal Transduction Inhibitors and Cellular Therapies

Mato AR et al.

ASH 2019;Abstract 502.

Current Hematologic Malignancy Reports (2019) 14:292–301
https://doi.org/10.1007/s11899-019-00525-9

CHRONIC LYMPHOCYTIC LEUKEMIAS (N JAIN, SECTION EDITOR)

Exploring a Future for PI3K Inhibitors in Chronic Lymphocytic Leukemia

Krish Patel[1] · John M. Pagel[1]

ORIGINAL RESEARCH

Cancer Medicine Open Access WILEY

Efficacy of bendamustine and rituximab in unfit patients with previously untreated chronic lymphocytic leukemia. Indirect comparison with ibrutinib in a real-world setting. A GIMEMA-ERIC and US study

Antonio Cuneo[1] | Anthony R. Mato[2] | Gian Matteo Rigolin[1]* | Alfonso Piciocchi[3] | Massimo Gentile[4] | Luca Laurenti[5] | John N. Allan[6] | John M. Pagel[7] | Danielle M. Brander[8] | Brian T. Hill[9] | Allison Winter[9] | Nicole Lamanna[10] | Constantine S. Tam[11] | Ryan Jacobs[12] | Frederick Lansigan[13] | Paul M. Barr[14] | Mazyar Shadman[15] | Alan P. Skarbnik[16] | Jeffrey J. Pu[17] | Alison R. Sehgal[18] | Stephen J. Schuster[19] | Nirav N. Shah[20] | Chaitra S. Ujjani[15] | Lindsey Roeker[2] | Ester Maria Orlandi[21] | Atto Billio[22] | Livio Trentin[23] | Martin Spacek[24] | Monia Marchetti[25] | Alessandra Tedeschi[26] | Fiorella Ilariucci[27] | Gianluca Gaidano[28] | Michael Doubek[29] | Lucia Farina[30] | Stefano Molica[31] | Francesco Di Raimondo[32] | Marta Coscia[33] | Francesca Romana Mauro[34] | Javier de la Serna[35] | Angeles Medina Perez[36] | Isacco Ferrarini[37] | Giuseppe Cimino[38] | Maurizio Cavallari[1] | Rosalba Cucci[3] | Marco Vignetti[3] | Robin Foà[34] | Paolo Ghia[39] | the GIMEMA, European Research Initiative (ERIC) on CLL, US study group

Cancer Med 2020;[Online ahead of print]

Pembrolizumab in relapsed or refractory Richter syndrome

Armand P et al. *Br J Haematol* 2020;190(2):e117-20

ASAIO Journal 2020

Case Report

COVID-19 Respiratory Failure: Targeting Inflammation on VV-ECMO Support

Matthew E. Hartman,*† Roland A. Hernandez,‡ Krish Patel,§ Teresa E. Wagner,¶ Tony Trinh,|| Anne B. Lipke,# Eric T. Yim,** Juan N. Pulido,††‡‡ John M. Pagel,§§ Samuel J. Youssef,‡ and John L. Mignone*

***ASAIO J* 2020;66(6):603-6**

TO THE EDITOR:

Use of convalescent plasma in hospitalized patients with COVID-19: case series

Livia Hegerova,[1] Ted A. Gooley,[2] Kelly A. Sweerus,[3] Cynthia Maree,[4] Neil Bailey,[1] Megumi Bailey,[1] Vanessa Dunleavy,[1] Krish Patel,[1] Kirsten Alcorn,[5] Rebecca Haley,[5] Jill M. Johnsen,[5,6] Barbara A. Konkle,[5,6] Annamarie C. Lahti,[7] Morgan L. Alexander,[7] Jason D. Goldman,[4] Anne Lipke,[3] Sun-jung Lim,[3] Mark D. Sullivan,[3] John S. Pauk,[4] and John M. Pagel[1]

***Blood* 2020;136(6):759-62**

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DOI: 10.1002/ajh.25851

CORRESPONDENCE

Management of CLL patients early in the COVID-19 pandemic: An international survey of CLL experts

Koffman B et al. *Am J Hematol* 2020;95(8):E199-203

blood®

Regular Article

CLINICAL TRIALS AND OBSERVATIONS

Outcomes of COVID-19 in patients with CLL: a multicenter international experience

Anthony R. Mato,[1,*] Lindsey E. Roeker,[1,*] Nicole Lamanna,[2] John N. Allan,[3] Lori Leslie,[4] John M. Pagel,[5] Krish Patel,[5] Anders Osterborg,[6] Daniel Wojenski,[7] Manali Kamdar,[8] Scott F. Huntington,[9] Matthew S. Davids,[10] Jennifer R. Brown,[10] Darko Antic,[11] Ryan Jacobs,[12] Inhye E. Ahn,[13] Jeffrey Pu,[14] Krista M. Isaac,[15] Paul M. Barr,[16] Chaitra S. Ujjani,[17] Mark B. Geyer,[1] Ellin Berman,[1] Andrew D. Zelenetz,[1] Nikita Malakhov,[3] Richard R. Furman,[3] Michael Koropsak,[4] Neil Bailey,[5] Lotta Hanson,[6] Guilherme F. Perini,[18] Shuo Ma,[7] Christine E. Ryan,[10] Adrian Wiestner,[13] Craig A. Portell,[15] Mazyar Shadman,[17] Elise A. Chong,[19] Danielle M. Brander,[20] Suchitra Sundaram,[21] Amanda N. Seddon,[22] Erlene Seymour,[23] Meera Patel,[23] Nicolas Martinez-Calle,[24] Talha Munir,[25] Renata Walewska,[26] Angus Broom,[27] Harriet Walter,[28] Dima El-Sharkawi,[29] Helen Parry,[30] Matthew R. Wilson,[31] Piers E. M. Patten,[32] José-Ángel Hernández-Rivas,[33] Fatima Miras,[34] Noemi Fernández Escalada,[35] Paola Ghione,[1] Chadi Nabhan,[36] Sonia Lebowitz,[1] Erica Bhavsar,[3] Javier López-Jiménez,[37|] Daniel Naya,[38] Jose Antonio Garcia-Marco,[39] Sigrid S. Skånland,[40] Raul Cordoba,[41,†] and Toby A. Eyre[42,†]

Blood 2020;136(10):1134-43

Meet The Professor with Dr Pagel

MODULE 1: Cases from Drs Chen and Matt-Amaral

MODULE 2: CLL Journal Club with Dr Pagel

- Toxicities and outcomes with acalabrutinib for treatment-naïve and relapsed/refractory (R/R) CLL
- First-in-human, proof-of-concept Phase I trial of LOXO-305 for pretreated B-cell cancers
- Ongoing results of a Phase IB/II dose-escalation and cohort-expansion study of vecabrutinib
- Tumor lysis, adverse events and dose adjustments with venetoclax in routine clinical practice
- Efficacy and safety of venetoclax in elderly patients with R/R CLL
- Comparative analysis of targeted novel agents for R/R CLL
- Efficacy of therapies after venetoclax
- Venetoclax alone or combined with anti-CD20 therapy for R/R CLL
- Future of PI3K inhibitors in CLL
- GIMEMA trial: Efficacy of BR for untreated CLL — Indirect comparison to ibrutinib in a real-world setting
- Pembrolizumab for R/R Richter syndrome
- COVID-19: Respiratory failure, use of convalescent plasma and outcomes and management of CLL

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

MODULE 4: Key Recent Data Sets

RTP
RESEARCH
TO PRACTICE

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

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

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

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

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

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

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

RTP RESEARCH TO PRACTICE

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

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

RTP RESEARCH TO PRACTICE

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

RTP RESEARCH TO PRACTICE

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

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

RTP RESEARCH TO PRACTICE

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

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

RTP RESEARCH TO PRACTICE

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

1. Continue treatment
2. Discontinue treatment

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

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

RTP RESEARCH TO PRACTICE

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

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

RTP RESEARCH TO PRACTICE

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

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

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

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

RTP RESEARCH TO PRACTICE

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

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

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

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

RTP RESEARCH TO PRACTICE

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

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

RTP RESEARCH TO PRACTICE

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

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

RTP RESEARCH TO PRACTICE

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

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

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

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Pagel

MODULE 1: Cases from Drs Chen and Matt-Amaral

MODULE 2: CLL Journal Club with Dr Pagel

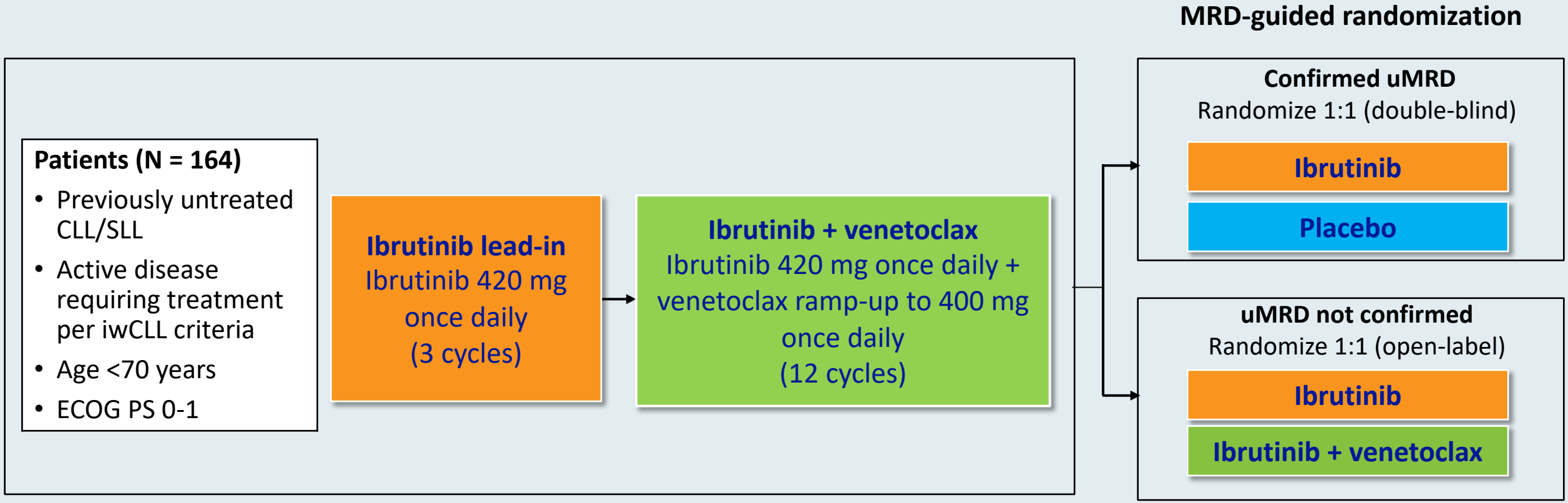
- Toxicities and outcomes with acalabrutinib for treatment-naïve and relapsed/refractory (R/R) CLL
- First-in-human, proof-of-concept Phase I trial of LOXO-305 for pretreated B-cell cancers
- Ongoing results of a Phase IB/II dose-escalation and cohort-expansion study of vecabrutinib
- Tumor lysis, adverse events and dose adjustments with venetoclax in routine clinical practice
- Efficacy and safety of venetoclax in elderly patients with R/R CLL
- Comparative analysis of targeted novel agents for R/R CLL
- Efficacy of therapies after venetoclax
- Venetoclax alone or combined with anti-CD20 therapy for R/R CLL
- Future of PI3K inhibitors in CLL
- GIMEMA trial: Efficacy of BR for untreated CLL — Indirect comparison to ibrutinib in a real-world setting
- Pembrolizumab for R/R Richter syndrome
- COVID-19: Respiratory failure, use of convalescent plasma and outcomes and management of CLL

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

MODULE 4: Key Recent Data Sets

RTP RESEARCH TO PRACTICE

CAPTIVATE MRD Cohort: Study Design

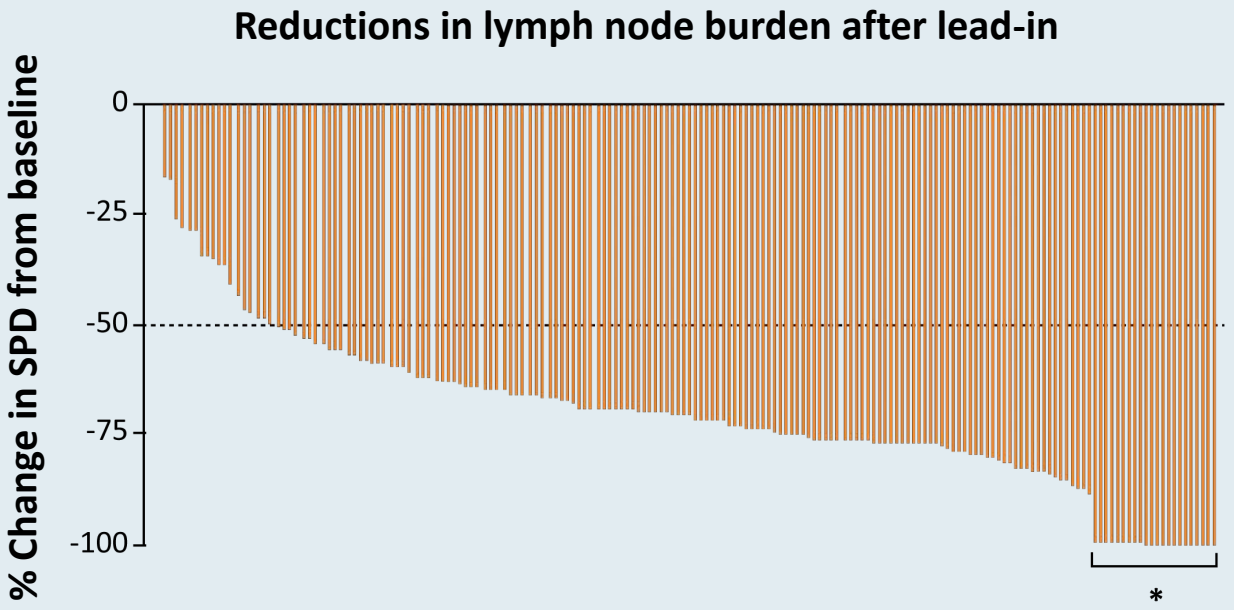


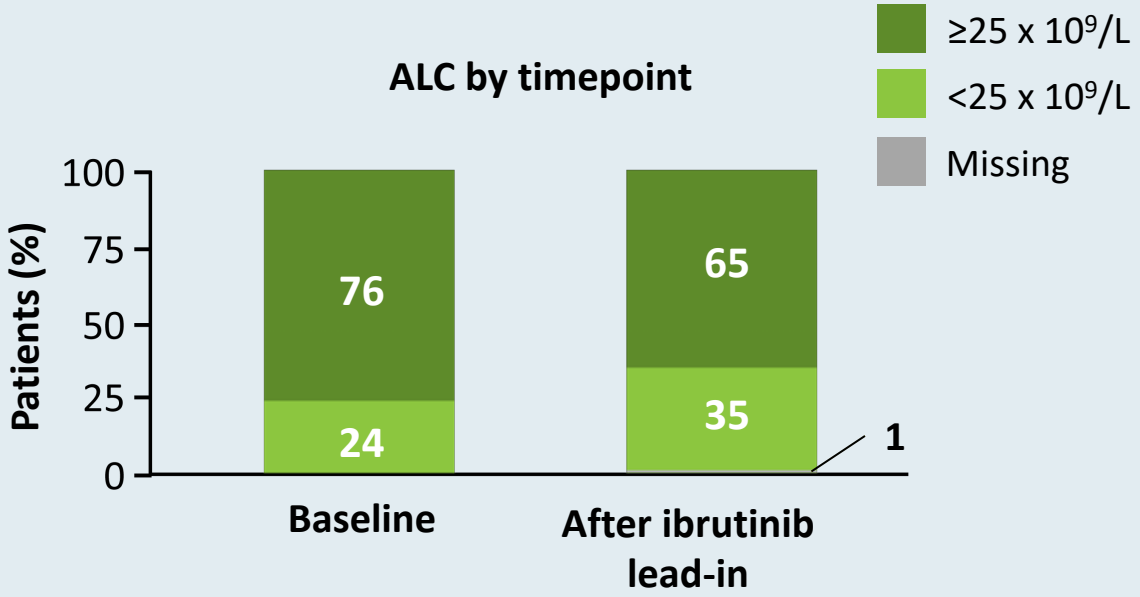
uMRD = undetectable minimal residual disease

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

Siddiqi S et al. EHA 2020;Abstract S158.

CAPTIVATE MRD Cohort: 3 Cycles of Ibrutinib Lead-In





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

Siddiqi S et al. EHA 2020;Abstract S158.

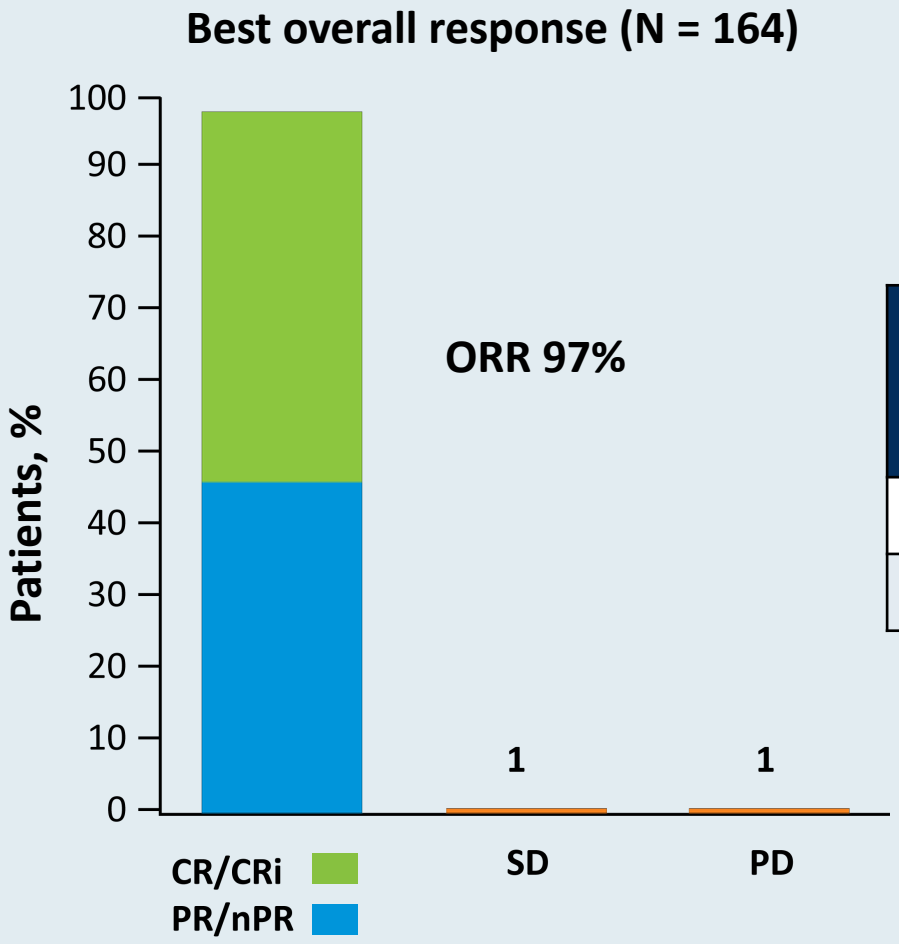
CAPTIVATE MRD Cohort: Undetectable MRD Rate

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

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

Siddiqi S et al. EHA 2020;Abstract S158.

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



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

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

Siddiqi S et al. EHA 2020;Abstract S158.

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

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

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

Siddiqi S et al. EHA 2020;Abstract S158.

Ongoing Phase III EA9161 Trial Schema

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

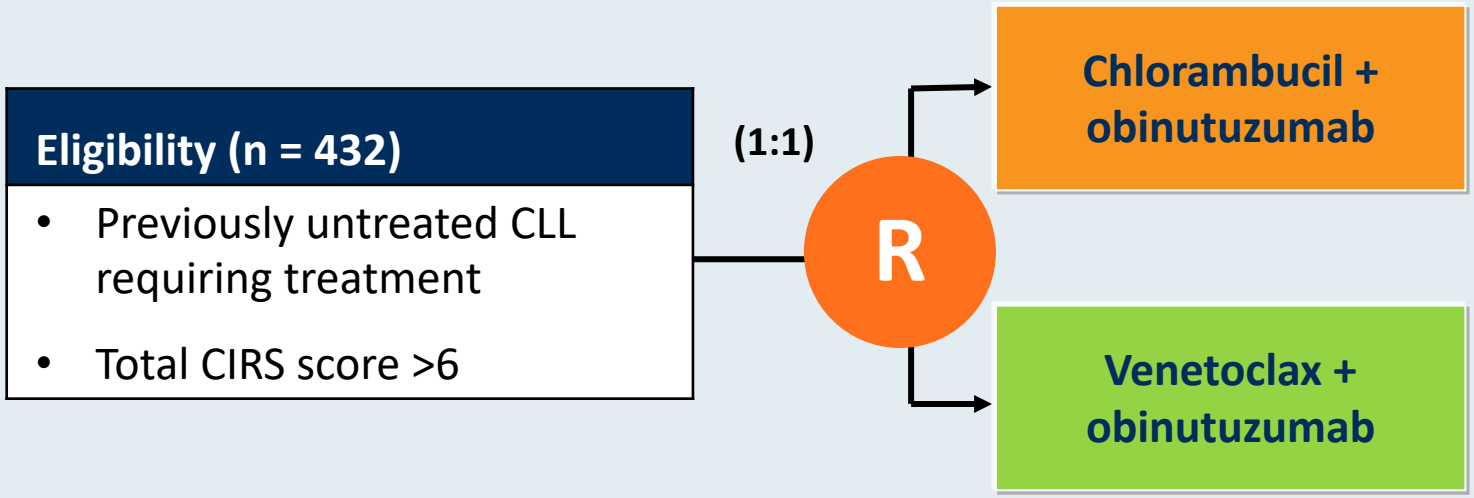
Randomize

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

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

Courtesy of Brad Kahl, MD

CLL14 Phase III Study Schema

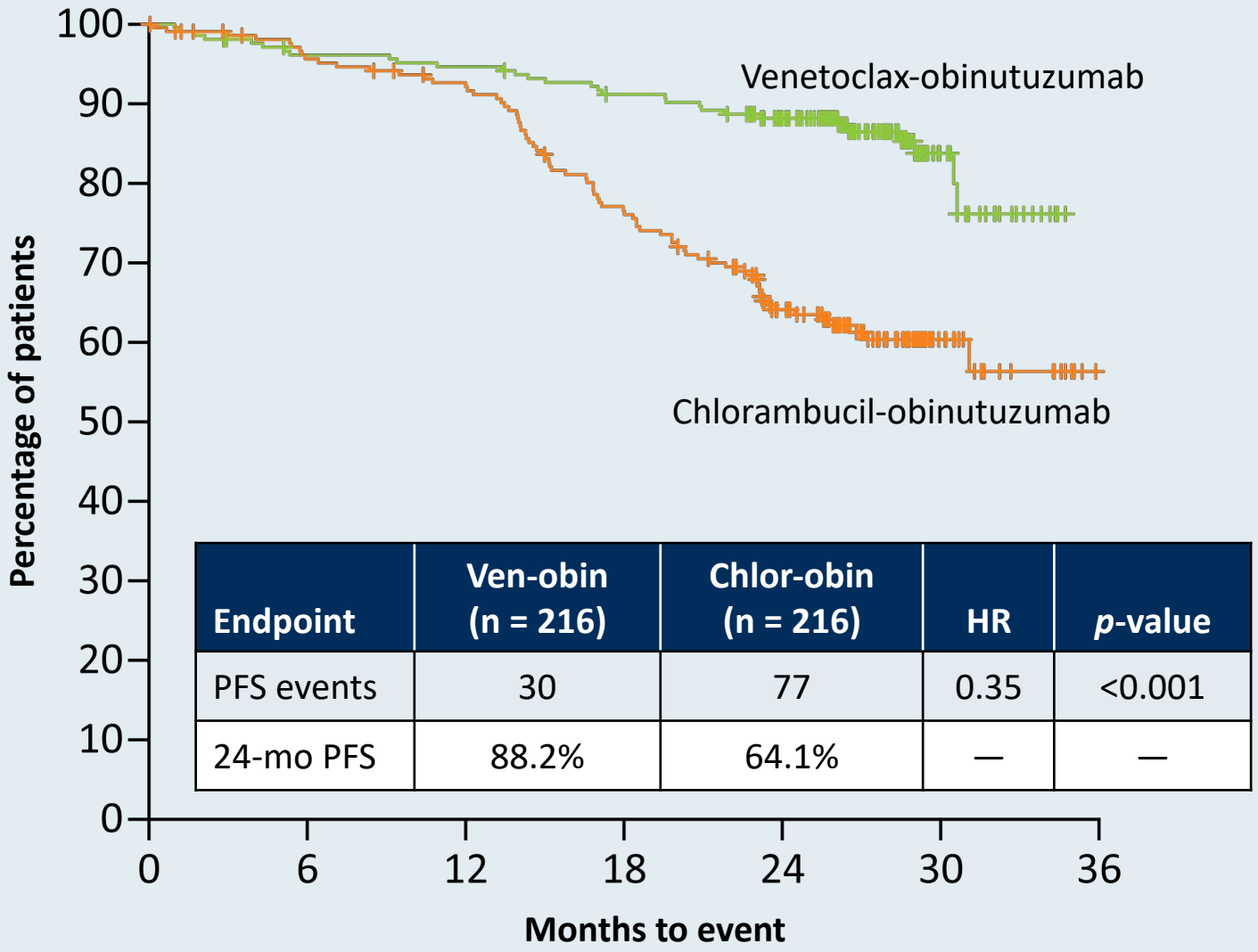


Primary endpoint: Progression-free survival

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

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

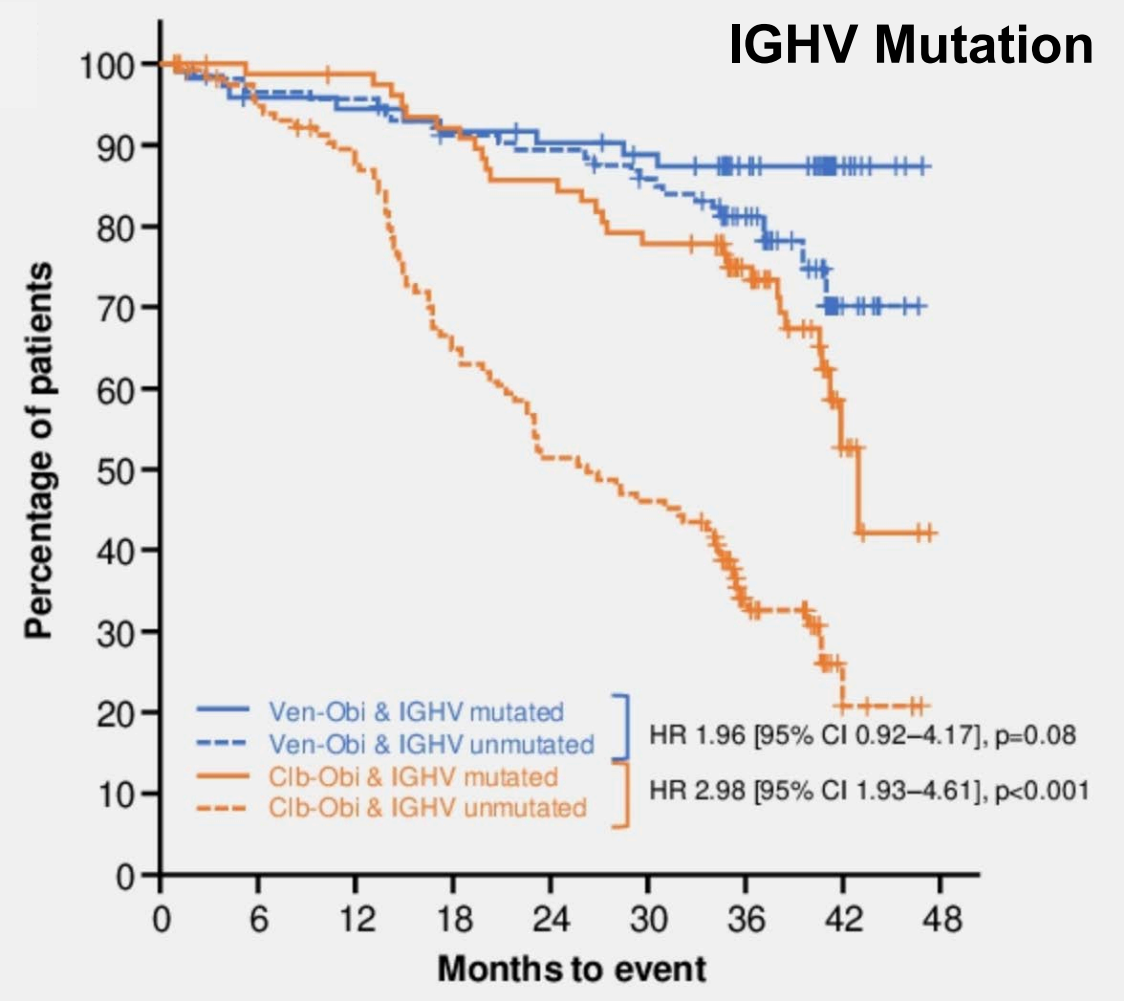
CLL14: Investigator-Assessed Progression-Free Survival

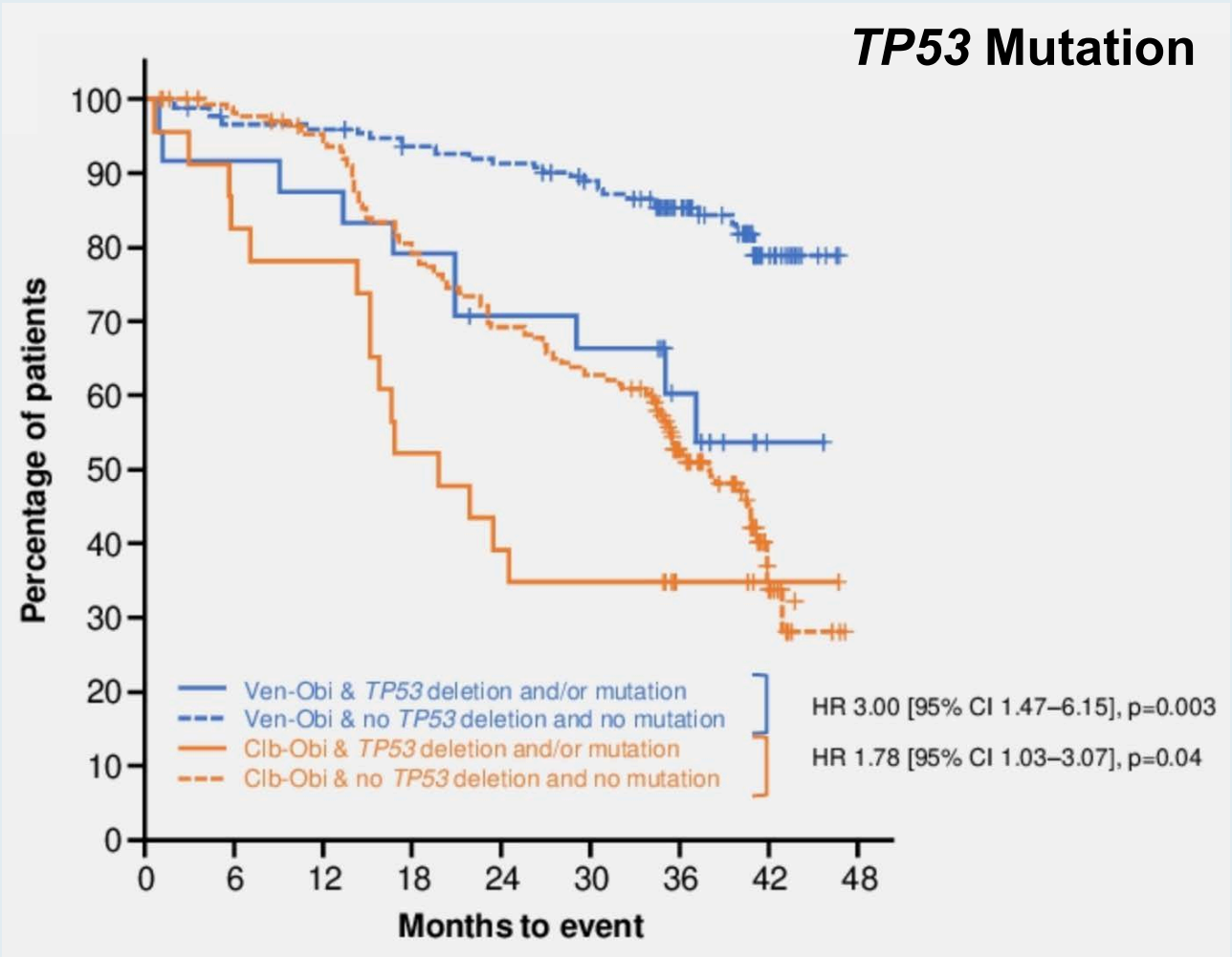


Endpoint	Ven-obin (n = 216)	Chlor-obin (n = 216)	HR	*p*-value
PFS events	30	77	0.35	<0.001
24-mo PFS	88.2%	64.1%	—	—

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

CLL14: PFS by IGHV and TP53 Mutation Status





Al-Sawaf O et al. ASCO 2020;Abstract 8027.

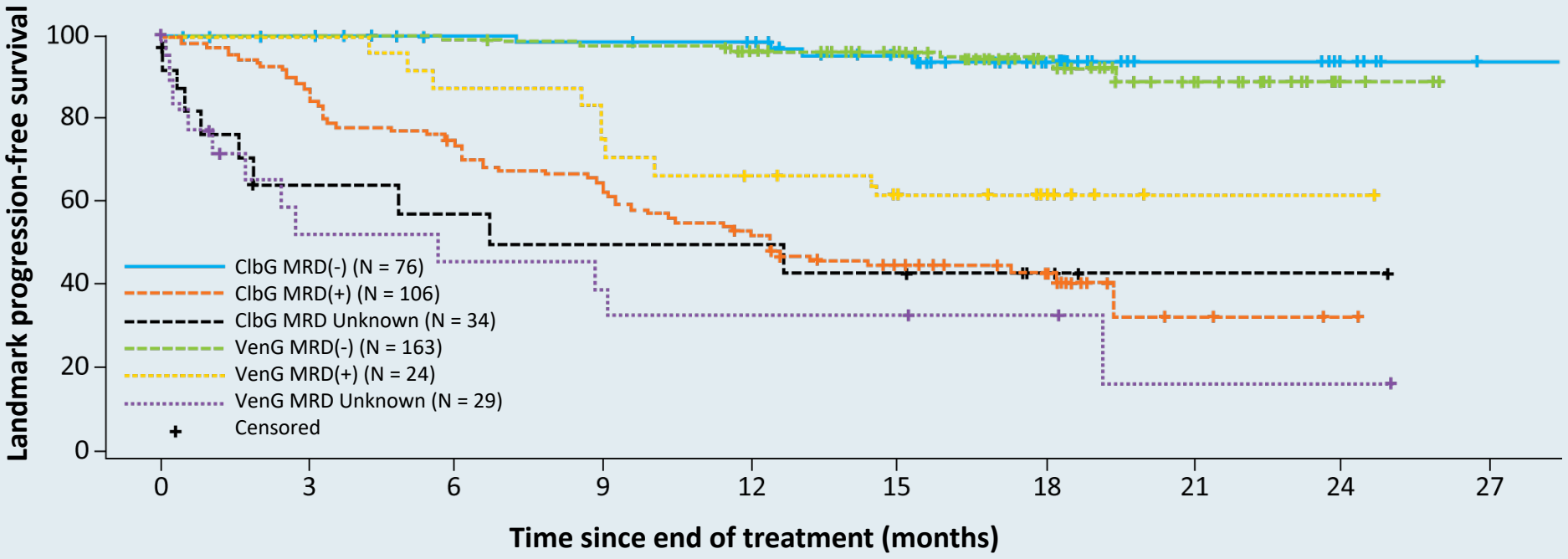
RTP RESEARCH TO PRACTICE

CLL14: Minimal Residual Disease 3 Months After Treatment

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

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

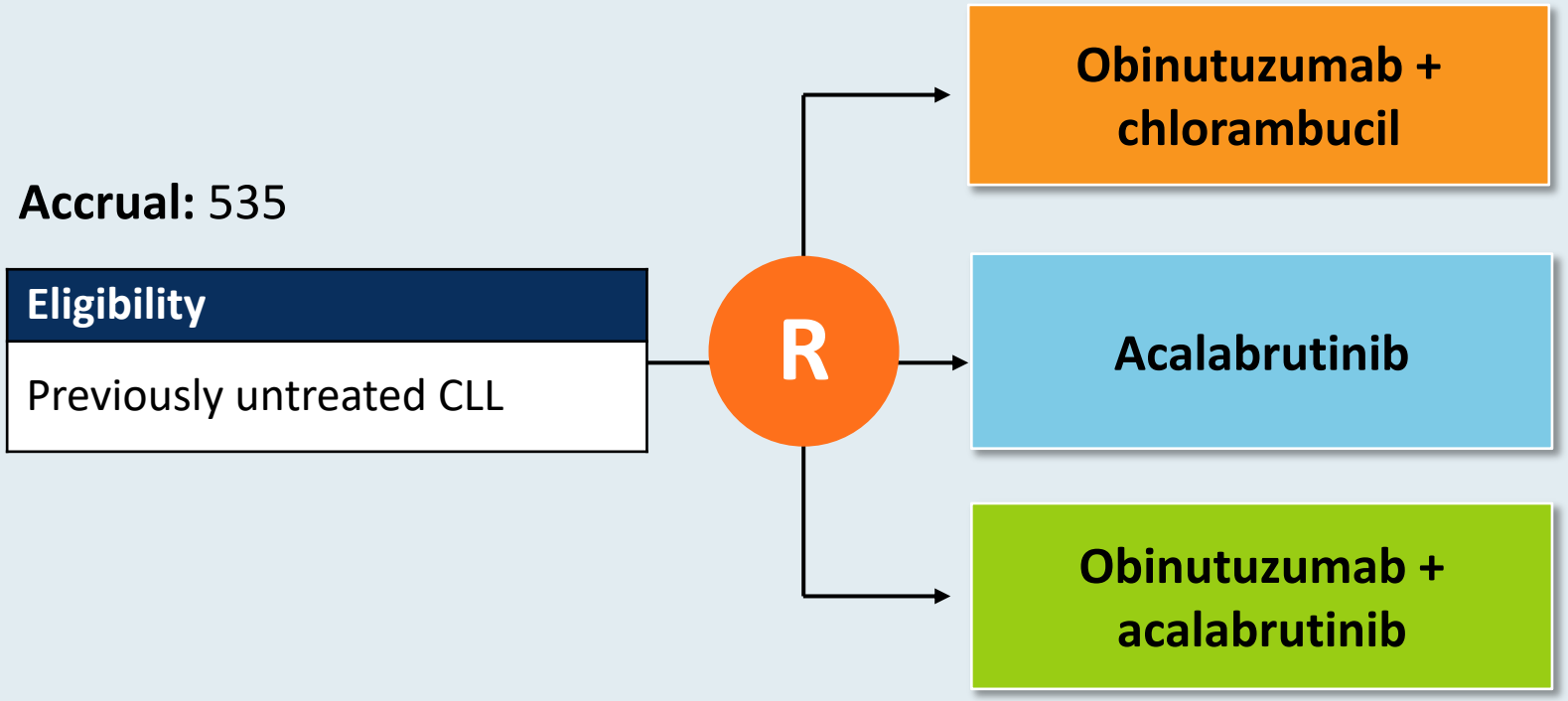
CLL14: Landmark Analysis from End of Therapy PFS by MRD Group



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

Fischer K et al. ASH 2019;Abstract 36.

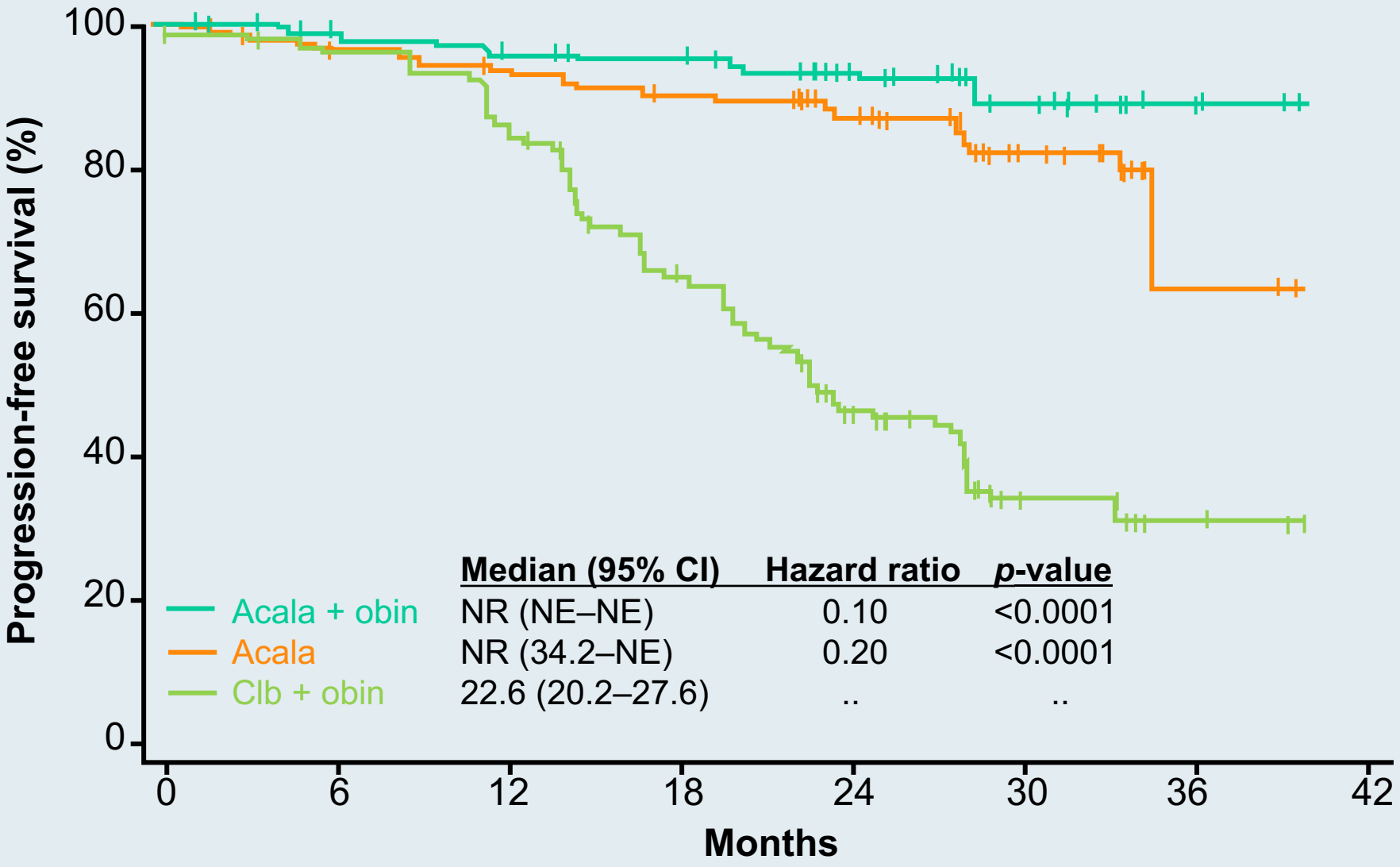
ELEVATE-TN Phase III Trial Schema



Primary endpoint: Progression-free survival

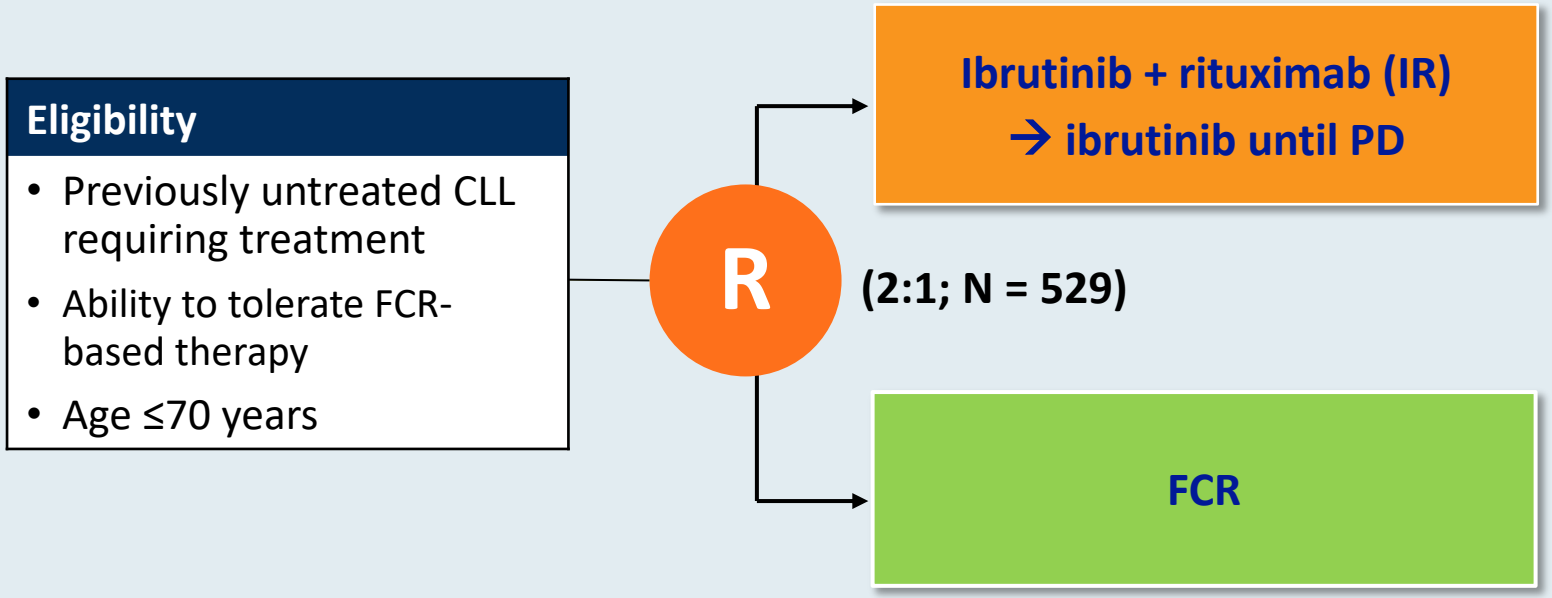
www.clinicaltrials.gov (NCT02475681). Accessed August 2020.

ELEVATE-TN: PFS (IRC)



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

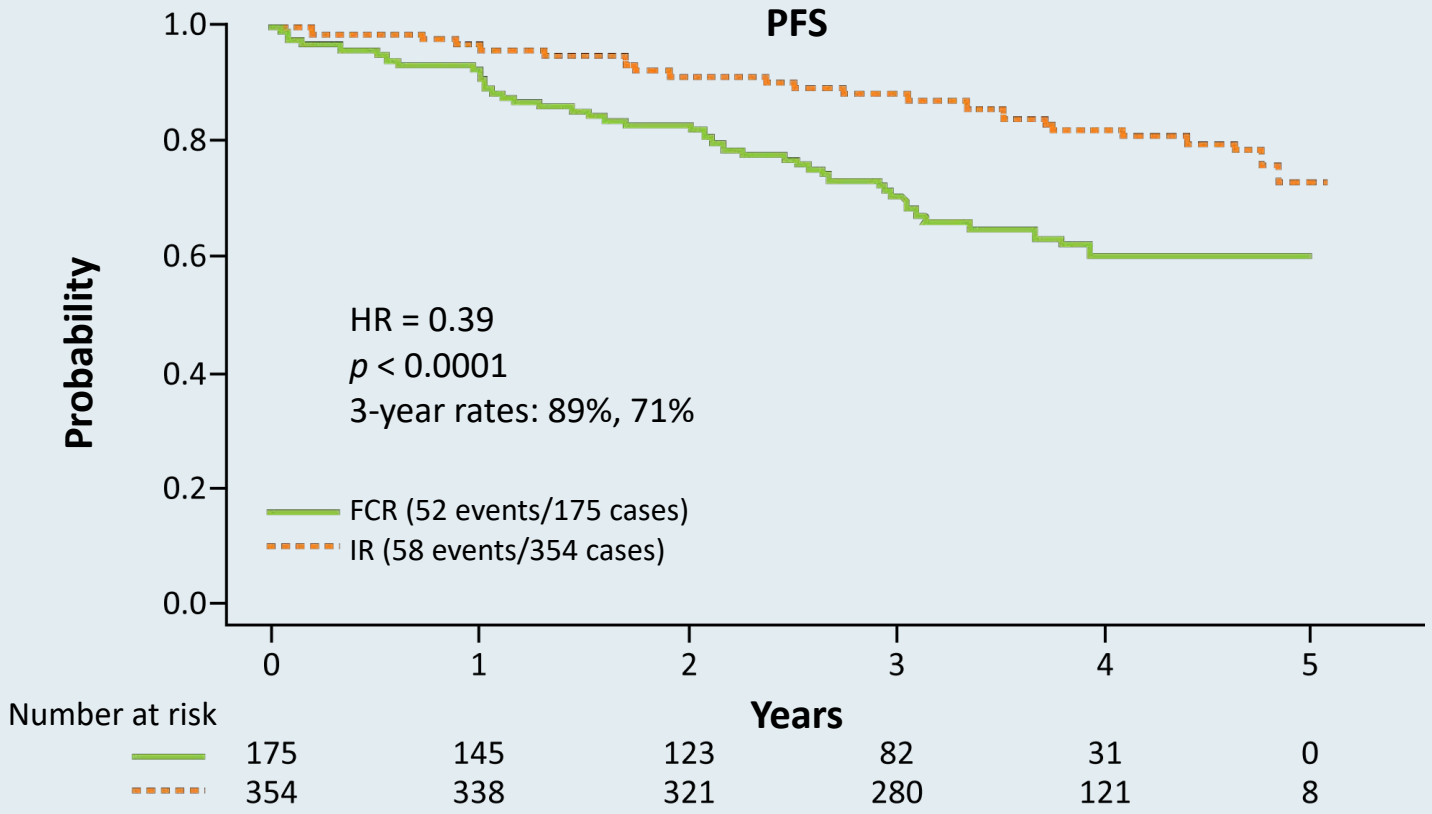
Phase III ECOG-ACRIN E1912 Study Design



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

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

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

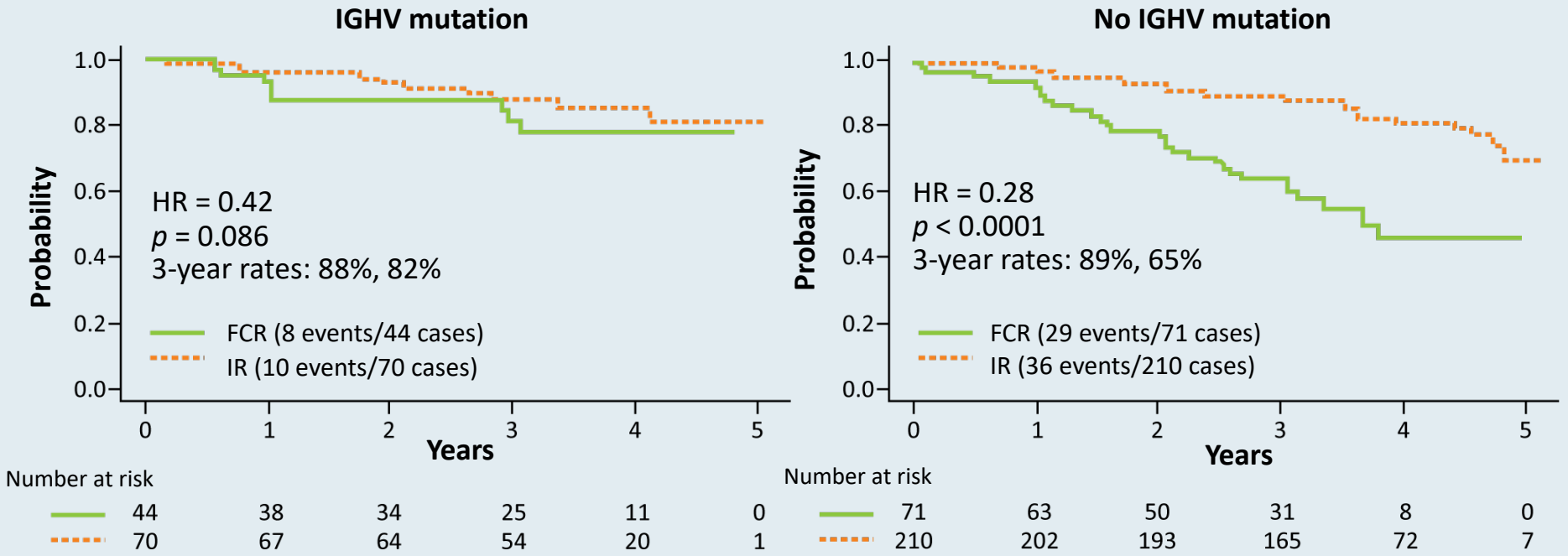


- Grade ≥3 treatment-related AEs were reported in 70% of patients receiving IR and 80% of patients receiving FCR (odds ratio = 0.56; $p = 0.013$).
- Among the 95 patients who discontinued ibrutinib, the most common cause was AE or complication.

Shanafelt TD et al. ASH 2019;Abstract 33.

RTP RESEARCH TO PRACTICE

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



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

Shanafelt TD et al. ASH 2019;Abstract 33.

What are your thoughts about the video clips of oncologists presenting cases that we are using in these webinars?

1. Better to skip it
2. Useful but do less of it
3. Leave it the way it currently is
4. There should be more

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Meet The Professor
Management of Ovarian Cancer

Thursday, October 15, 2020
12:00 PM – 1:00 PM ET

Faculty

Kathleen Moore, MD

Moderator

Neil Love, MD

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Thank you for joining us!

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

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