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

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

A Meet The Professor Series

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

Commercial Support

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

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Dr Love — Disclosures

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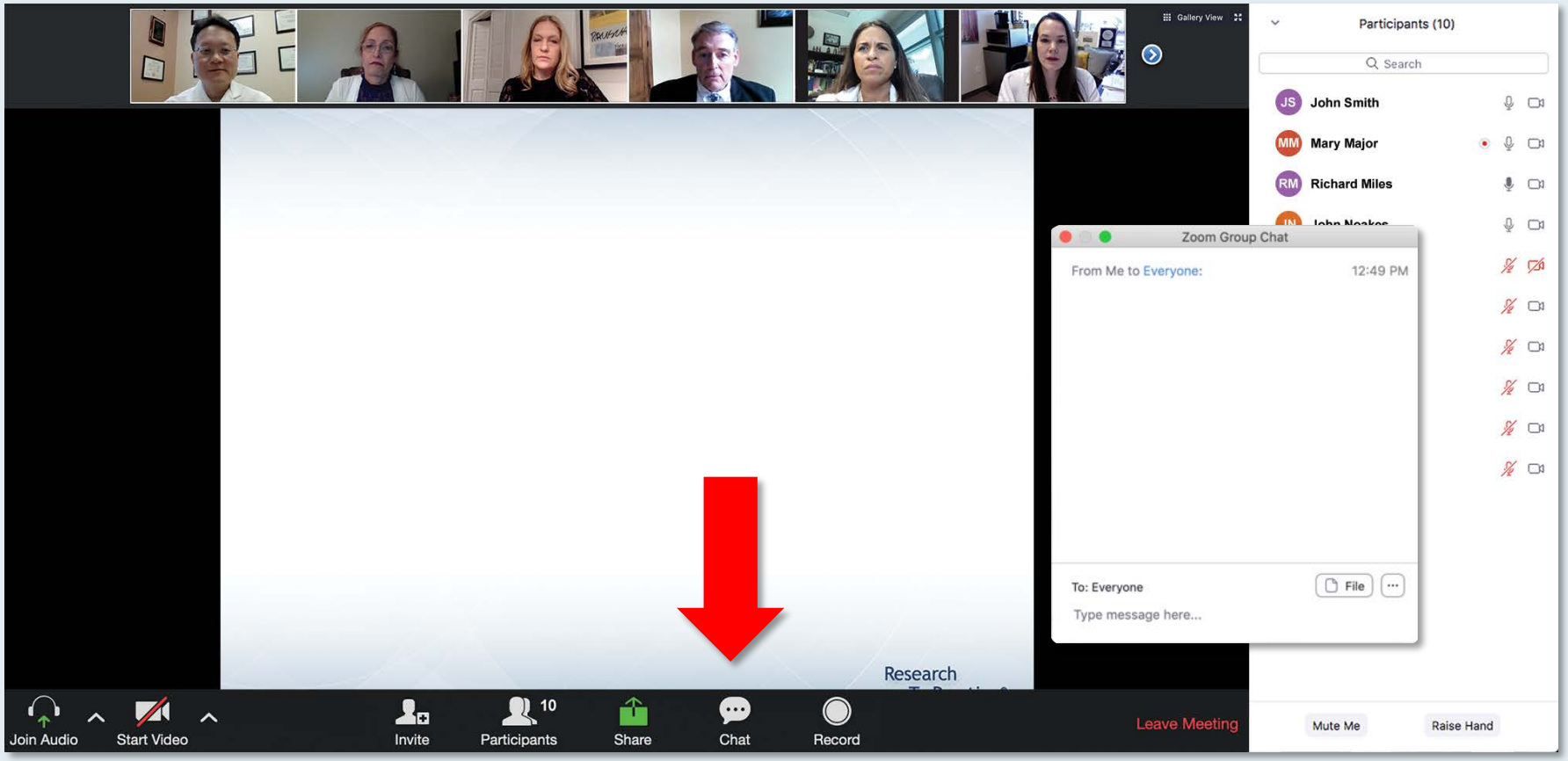

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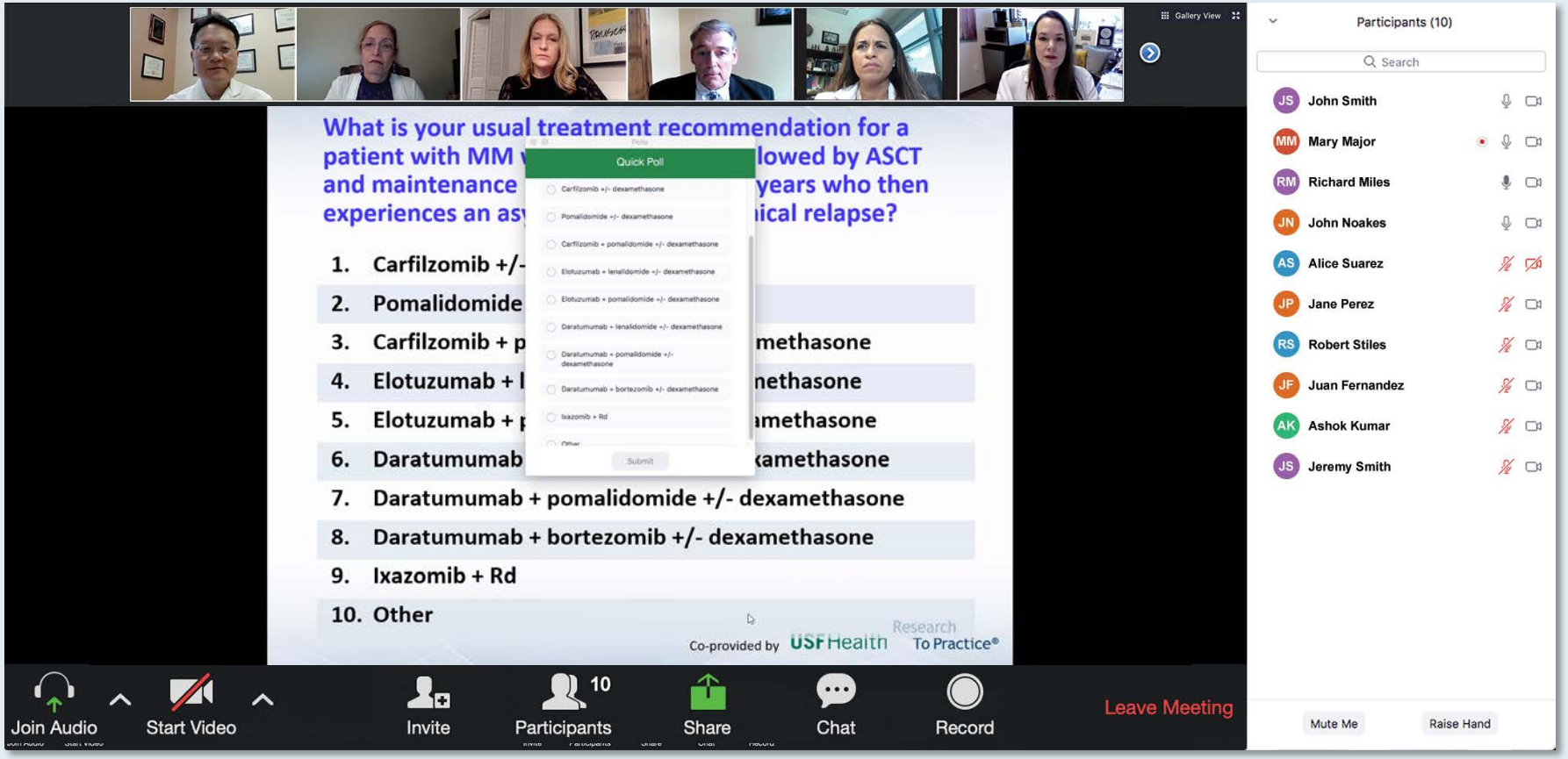

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Upcoming Live Webinars

Monday, September 21, 2020
12:00 PM – 1:00 PM ET

Clinical Investigator Perspectives on the Current and Future Management of Multiple Myeloma

Faculty
Ola Landgren, MD, PhD

Moderator
Neil Love, MD

Tuesday, September 22, 2020
12:00 PM – 1:00 PM ET

Current Questions and Controversies in the Management of Lung Cancer

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

Faculty
David M O'Malley, MD

Moderator
Neil Love, MD

Thank you for joining us!

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

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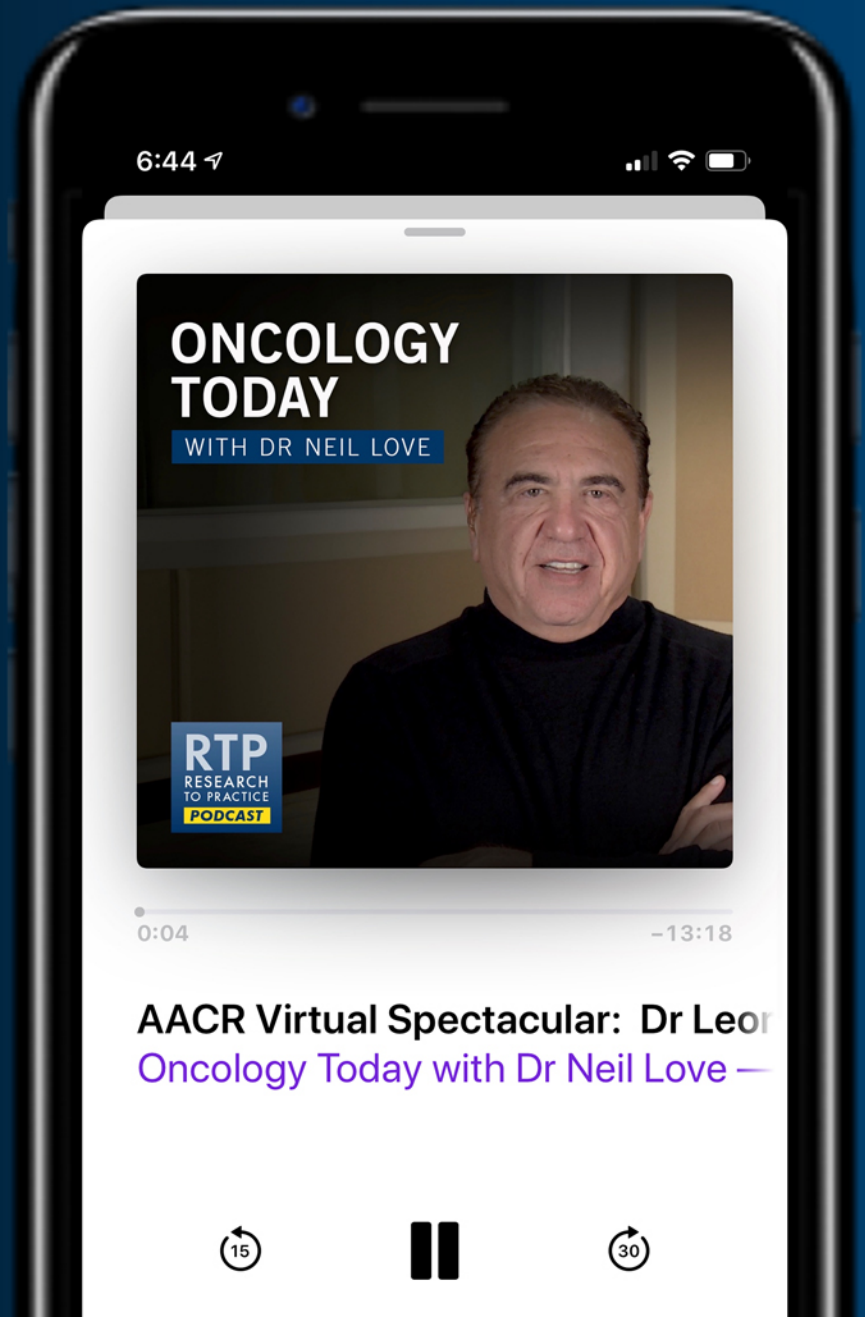

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Meet The Professor Program Participating Faculty

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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
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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
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Meet The Professor Program Participating Faculty

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

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Center for Blood Disorders and Stem Cell Transplantation
Swedish Cancer Institute
Seattle, Washington

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

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Meet The Professor Program Participating Faculty

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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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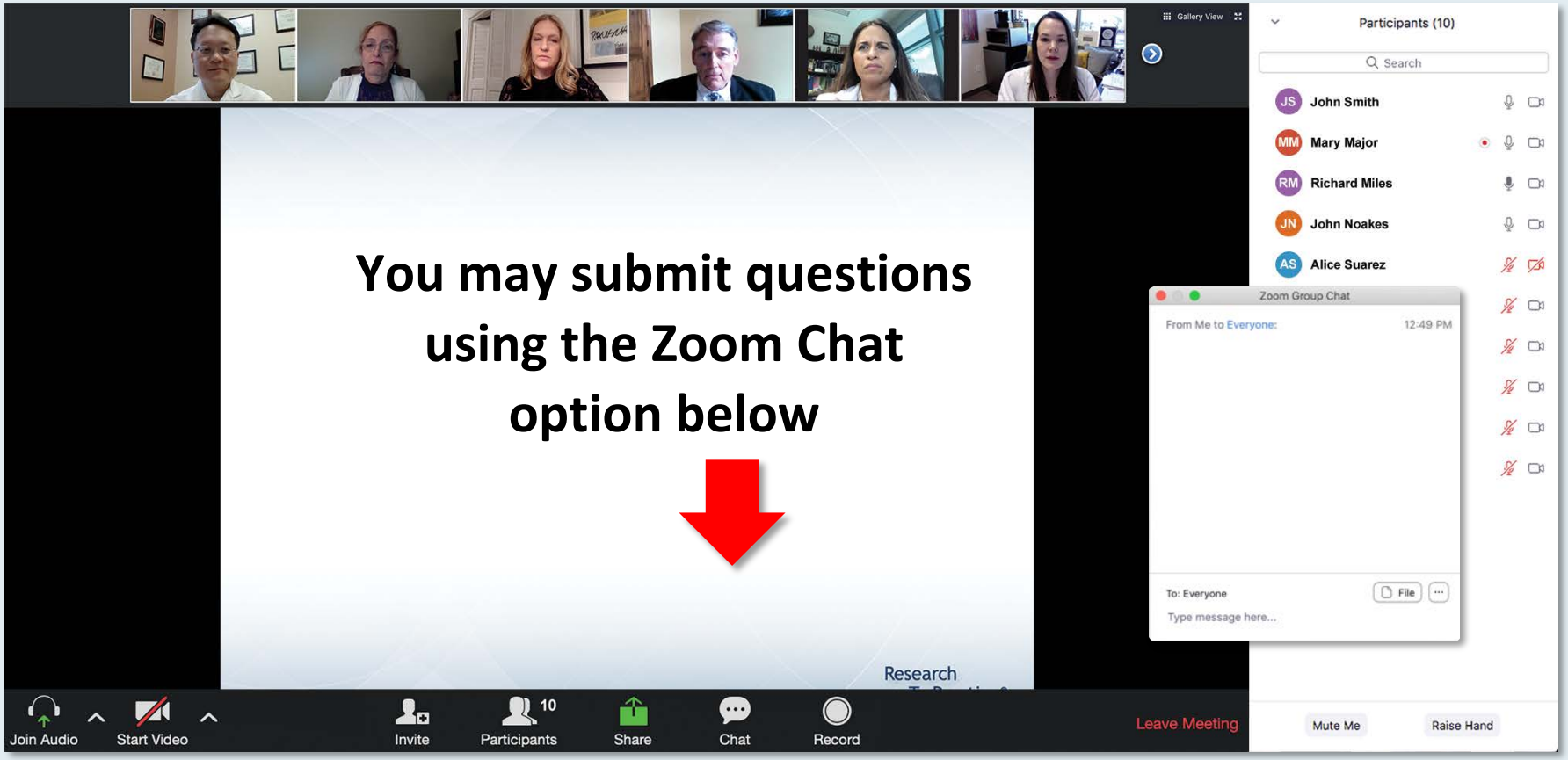

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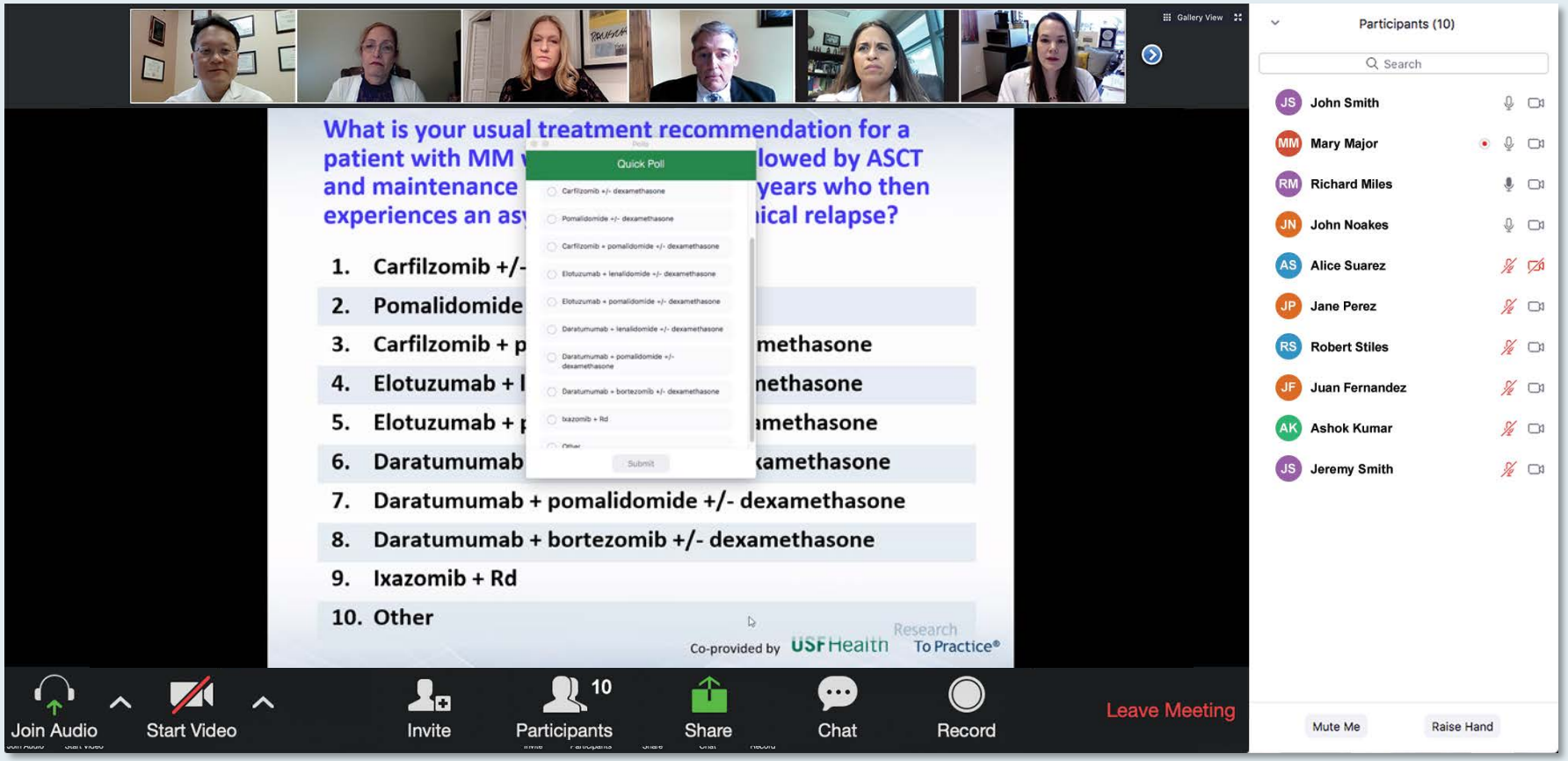

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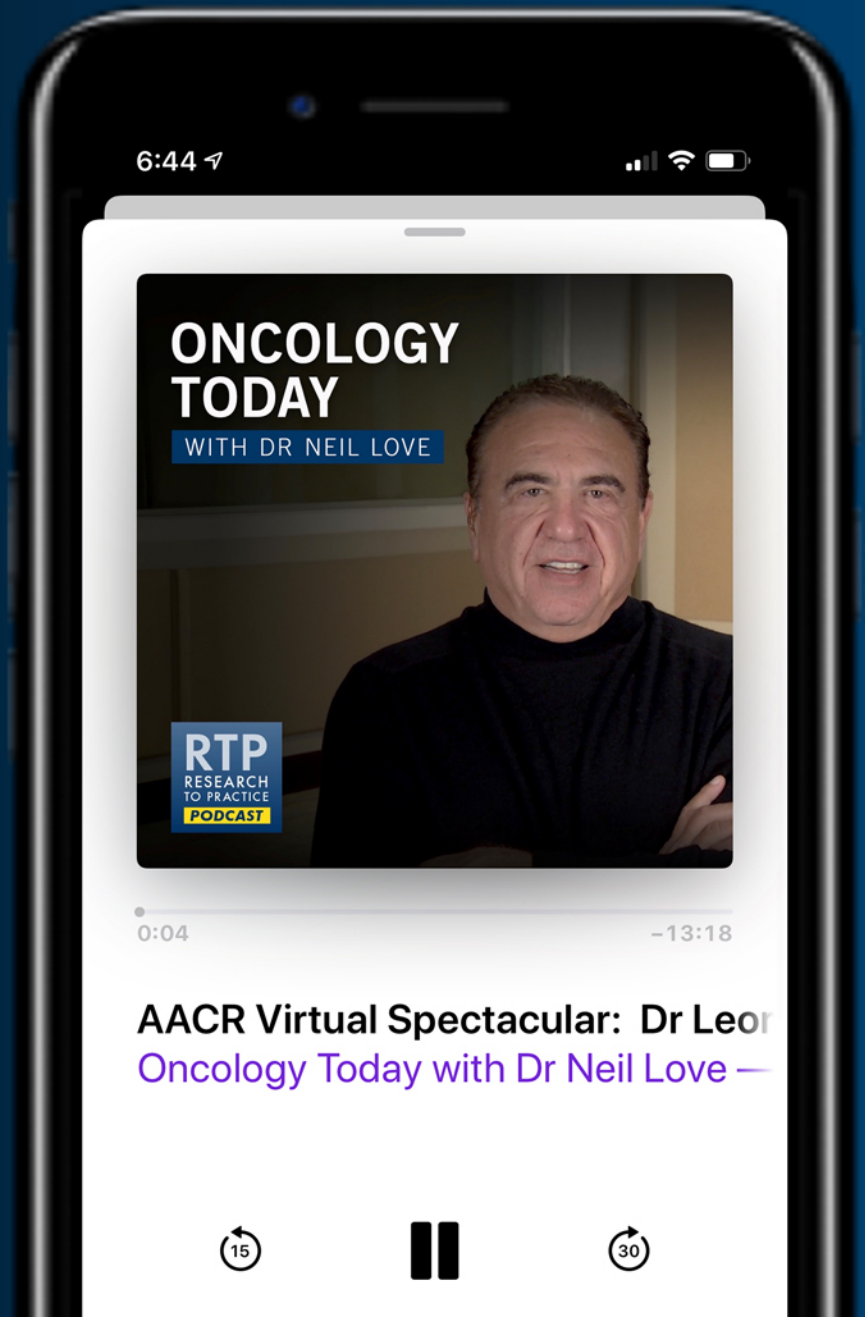

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Matthew S Davids, MD, MMSc
Associate Professor of Medicine, Harvard Medical School
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Dana-Farber Cancer Institute
Boston, Massachusetts

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

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COVID-19 AND CLL

MAY 21, 2020

Understanding the Impact of COVID-19 on the Care of Patients with Chronic Lymphocytic Leukemia – A Live CME Webinar

Moderator
Neil Love, MD

Faculty
Matthew S Davids, MD, MMSc
Anthony R Mato, MD, MSCE
Jeff Sharman, MD

Blood 2020;136(10):1134-1143

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,†]

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

Am J Hematol 2020 Aug;95(8):E199-E203.

CLINICAL CANCER RESEARCH | PERSPECTIVES

BTK Inhibitors in Cancer Patients with COVID-19: "The Winner Will be the One Who Controls That Chaos" (Napoleon Bonaparte)

Elise A. Chong[1], Lindsey E. Roeker[2], Mazyar Shadman[3], Matthew S. Davids[4], Stephen J. Schuster[1], and Anthony R. Mato[2]

Clin Cancer Res 2020 Jul 15;26(14):3514-6.

Meet The Professor with Dr Davids

MODULE 1: Cases from the Community – Dr Brenner

- A 77-year-old woman with Stage I CLL – Del(13q), IGHV mutation
- A 77-year-old man with Stage I CLL – Del(13q), IGHV rearrangement
- An 84-year-old woman with relapsed CLL
- A 76-year-old woman with relapsed CLL – Del(17p)

MODULE 2: Journal Club

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

Case Presentation – Dr Brenner: A 77-year-old woman with Stage I CLL – Del(13q), IGHV mutation

Dr Warren S Brenner

- June 2018: Stage I CLL with del13q, IGHV mutation
- Observation
- 2020: Rapidly rising WBC, progressive anemia

Questions

- Does the COVID-19 pandemic impact decision making regarding use of oral agents or whether to consider regimens such as venetoclax/obinutuzumab?
- In patients who receive a BTK inhibitor, should a CD20 monoclonal antibody be added? Do these improve efficacy? MRD rate?
- What drives you to go with a BTK inhibitor versus venetoclax?

RTP RESEARCH TO PRACTICE

Case Presentation – Dr Brenner: A 77-year-old man with Stage I CLL – Del(13q), IGHV rearrangement

Dr Warren S Brenner

- 2000: SLL in pelvic lymph node dissection during surgery for prostate cancer
- Observation
- Stage I CLL del13q, IGHV rearrangement
- June 4 2020: Initiation of obinutuzumab with venetoclax dose ramp-up June 25, 2020

Questions

- In a patient who receives obinutuzumab and venetoclax in the front-line setting, after they complete their therapy, should we be doing MRD testing? Do you ever use MRD testing to make a decision about whether or not to continue venetoclax-based therapy? Or is it safe to discontinue venetoclax at that point?

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Case Presentation – Dr Brenner: An 84-year-old woman with relapsed CLL

Dr Warren S Brenner

- Diagnosed with CLL >30 years ago (Disease and treatment course unknown)
- CVP, tolerated poorly
- 2010: Bendamustine/rituximab
- 2016: Rituximab monotherapy
- Feb – April 2016: Ibrutinib, poorly tolerated and discontinued
- 2016: Resumed rituximab
- March 2019: Re-initiation of ibrutinib, but discontinued after one month
  - Massive skin purpura over the entire right side of her face
- May 2019: Re-initiation of ibrutinib, dose reduced to 280 mg daily
- Currently, progressive disease – patient declines IV treatment due to COVID-19

Questions

- Has the faculty ever observed the skin side effects she experienced with a BTK inhibitor?
- What is the role of BTK resistance testing? Should this be done in the community?
- In a patient who developed such a significant bleeding event on ibrutinib, is there a role to re-challenge with acalabrutinib? When would they use PI3K inhibitors?

Case Presentation – Dr Brenner: A 76-year-old woman with relapsed CLL – Del(17p)

Dr Warren S Brenner

- 1990s: Initially diagnosed with CLL → Observation
- 2005: Fludarabine/rituximab x 4 → PD in 2009: BR x 4, with good response
- 6/2014: Ibrutinib
  - 8/2015: Atrial fibrillation requiring cardioversion, anticoagulant → recurrent afib → cardioversion
- 2017: Progressive elevation of WBC → BR x 6
- 11/2017: Genetic profiling: del17p, biallelic del13q, 3 missense mutations in p53
- 2/2018: Progressive disease
- 1/2019: Venetoclax → discontinued in June due to progressive diarrhea, numerous other side effects
- 6/2020: Progressive disease

Questions

- In a patient who develops atrial fibrillation on ibrutinib, particularly those on anticoagulants, do you ever rechallenge with ibrutinib? Would you use acalabrutinib instead?
- In a patient who developed toxicity from a BTK inhibitor and did not tolerate venetoclax-based therapy, would you use PI3K inhibitors? Do you prefer one versus the others? Any pearls regarding management of side effects?

Meet The Professor with Dr Davids

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REGULAR ARTICLE

blood advances

Pneumocystis jirovecii pneumonia and institutional prophylaxis practices in CLL patients treated with BTK inhibitors

Christine E. Ryan,[1,2] Matthew P. Cheng,[2,3] Nicolas C. Issa,[2,3] Jennifer R. Brown,[1,2] and Matthew S. Davids[1,2]

[1]Department of Medicine, Brigham and Women's Hospital, Boston, MA; [2]Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA; and [3]Division of Infectious Diseases, Department of Medicine, Brigham and Women's Hospital, Boston, MA

14 APRIL 2020 | VOLUME 4, NUMBER 7

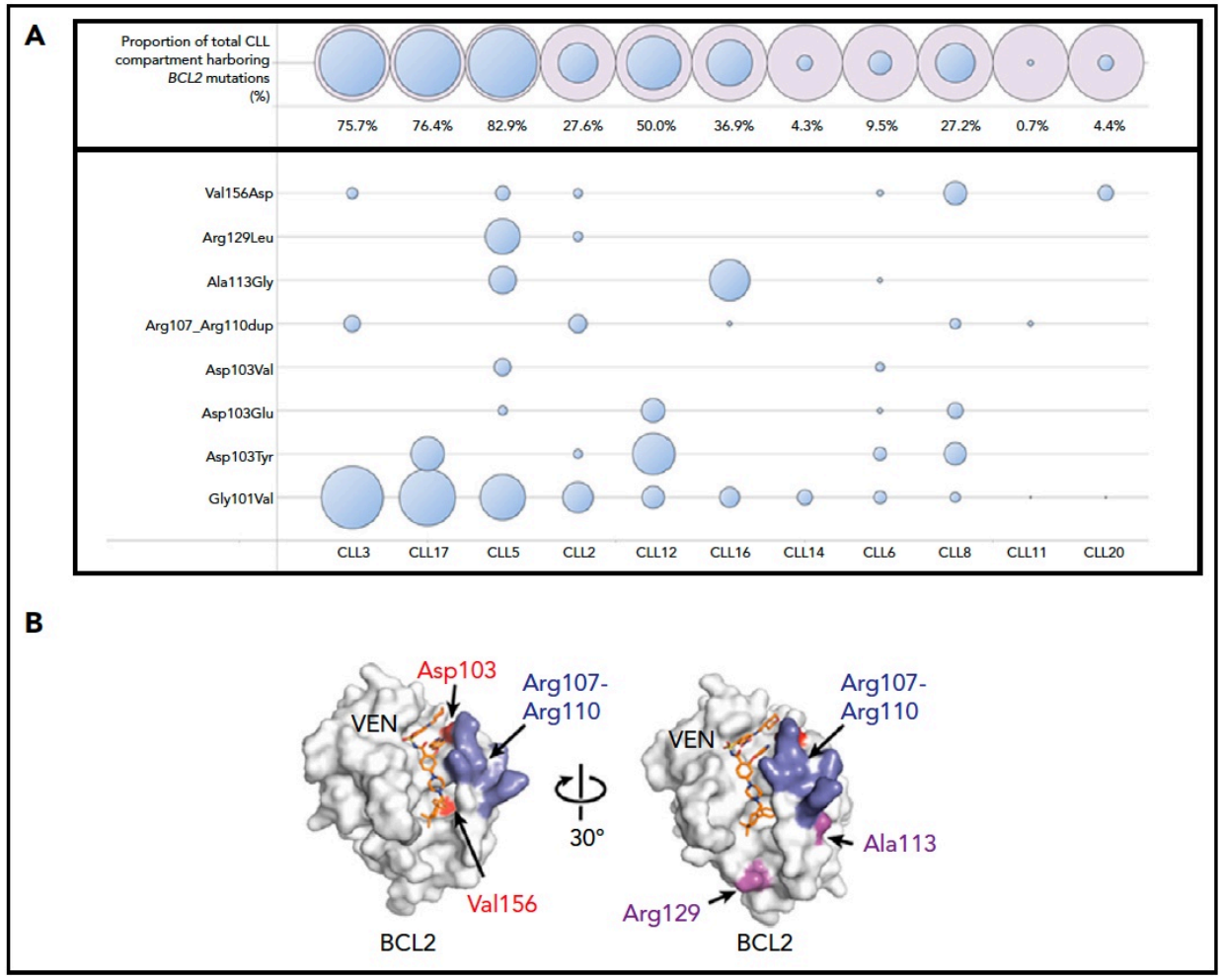
TO THE EDITOR:

Multiple *BCL2* mutations cooccurring with Gly101Val emerge in chronic lymphocytic leukemia progression on venetoclax

Piers Blombery,[1-3] Ella R. Thompson,[1,3] Tamia Nguyen,[1] Richard W. Birkinshaw,[3,4] Jia-nan Gong,[3,4] Xiangting Chen,[1] Michelle McBean,[1] Rachel Thijssen,[3,4] Thomas Conway,[1] Mary Ann Anderson,[2-4] John F. Seymour,[2,3] David A. Westerman,[1-3] Peter E. Czabotar,[3,4] David C. S. Huang,[3,4] and Andrew W. Roberts[2-4]

[1]Department of Pathology, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; [2]Clinical Haematology, The Royal Melbourne Hospital and Peter MacCallum Cancer Centre, Parkville, VIC, Australia; [3]University of Melbourne, Melbourne, VIC, Australia; and [4]The Walter and Eliza Hall Institute of Medical Research, Melbourne, VIC, Australia

BCL2 Mutations in Patients with Progressive CLL on Venetoclax



(A) BCL2 mutations in a cohort of patients with CLL progression on venetoclax. Patients are ordered in descending Gly101Val cancer cell fraction (CCF). CCF was determined as (VAF/disease burden determined by flow cytometry) x 2 (assuming heterozygosity). Area of blue circles is proportional to CCF mutated. The top row shows the total CCF harboring BCL2 mutations (the sum of individual CCF and assumes occurrence in mutually exclusive cells).

(B) Structure of BCL2 protein with venetoclax bound (PDB ID 6O0K) illustrating the positions of the mutated residues Asp103, Val156, Arg107 to Arg110, Ala113, and Arg129.

Blombery P et al. *Blood* 2020;135(10):773.

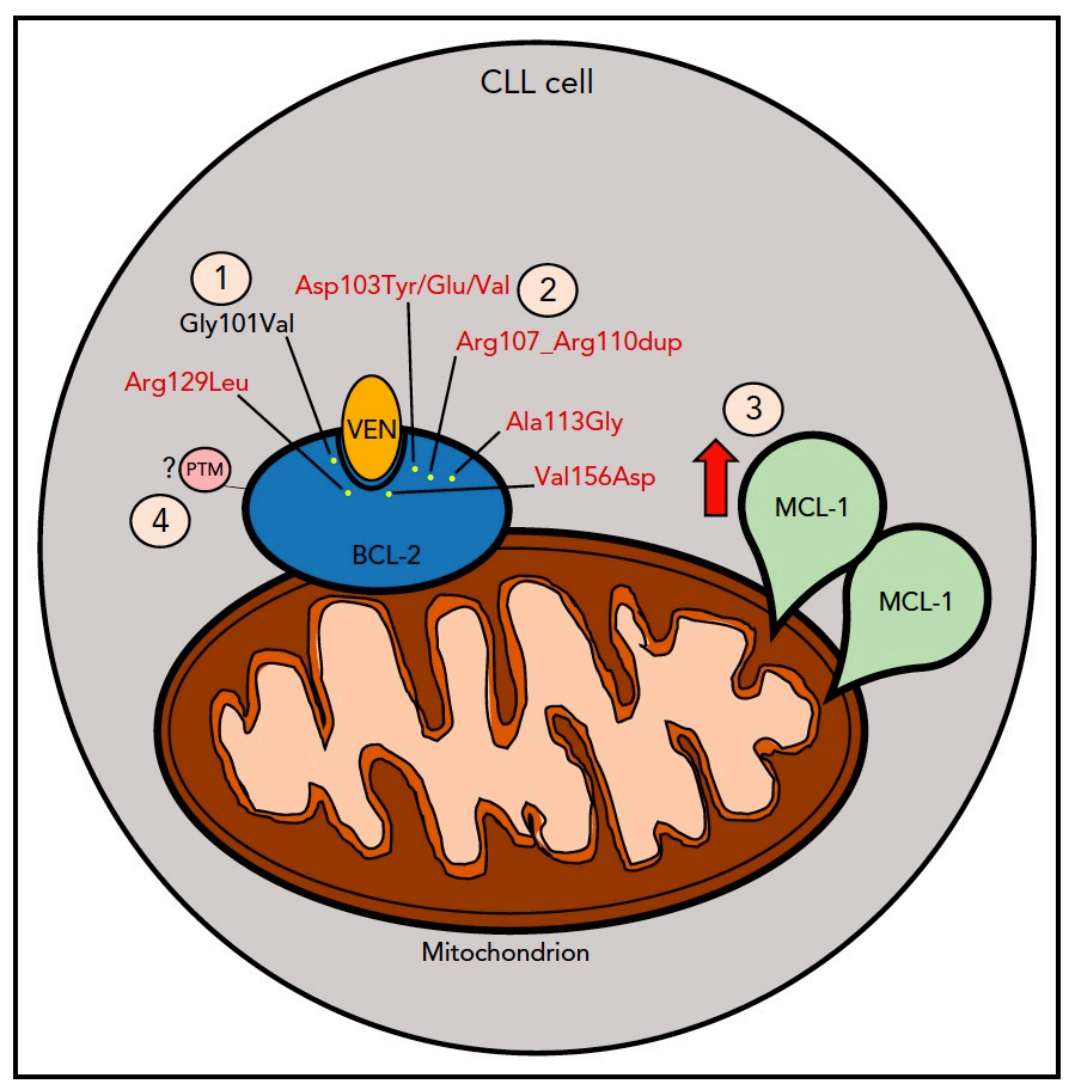
Comment on Blombery et al, page 773

Breaking through BCL-2 inhibition in CLL

Stephen J. F. Chong and Matthew S. Davids | Dana-Farber Cancer Institute

In this issue of *Blood*, Blombery and colleagues have identified multiple novel somatic mutations in *BCL-2* occurring concurrently with the recently reported Gly101Val *BCL-2* resistance mutation in patients with chronic lymphocytic leukemia (CLL) receiving venetoclax.[1] Their study demonstrates that, in addition to functional resistance mechanisms such as aberrant expression of other antiapoptotic proteins, multiple acquired resistance mutations in *BCL-2* can occur in different CLL cells in a single patient.

Mechanisms Contributing to Venetoclax (VEN) Resistance



(1) Gly101Val mutation (in black) acquired following venetoclax treatment as previously described.

(2) New mutations (in red) identified concomitantly with Gly101Val, as described by Blombery and colleagues.

(3) MCL-1 overexpression following VEN treatment.

(4) Potential post-translational modification (PTM) that may contribute to VEN resistance (eg, phosphorylation events).

Chong SJF, Davids MS. *Blood* 2020 Mar 5;135(10):709-11.

RTP RESEARCH TO PRACTICE

blood

Regular Article

CLINICAL TRIALS AND OBSERVATIONS

Venetoclax plus R- or G-CHOP in non-Hodgkin lymphoma: results from the CAVALLI phase 1b trial

Andrew D. Zelenetz,[1] Gilles Salles,[2,3] Kylie D. Mason,[4] Carla Casulo,[5] Steven Le Gouill,[6] Laurie H. Sehn,[7] Herve Tilly,[8] Guillaume Cartron,[9] Martine E. D. Chamuleau,[10] Andre Goy,[11] Constantine S. Tam,[12,13] Pieternella J. Lugtenburg,[14] Adam M. Petrich,[15] Arijit Sinha,[16] Divya Samineni,[17] Sylvia Herter,[18] Ellen Ingalla,[17] Edith Szafer-Glusman,[17] Christian Klein,[18] Deepak Sampath,[17] Martin Kornacker,[19] Mehrdad Mobasher,[17] and Franck Morschhauser[20]

Comment on Zelenetz et al, page 1964

Venetoclax: R-CHOP rocket booster?

Charles Herbaux and Matthew S. Davids | Dana-Farber Cancer Institute

In this issue of *Blood*, Zelenetz et al[1] report the results of the phase 1b portion of the CAVALLI study, one of the first trials to explore a novel strategy of chemosensitization, by adding the B-cell leukemia/lymphoma-2 (BCL2) inhibitor venetoclax to chemoimmunotherapy for patients with non-Hodgkin lymphoma (NHL).

Neutropenia Analysis of Venetoclax Monotherapy in Patients with Relapsed or Refractory Chronic Lymphocytic Leukemia: Pooled Data from VENICE-I and -II Phase IIIb Trials

Anderson MN, Davids MS et al.

ASCO 2020;Abstract e20011.

Preliminary Safety and Efficacy Results from a Phase 2 Study of Acalabrutinib, Venetoclax and Obinutuzumab in Patients with Previously Untreated Chronic Lymphocytic Leukemia (CLL)

Lampson BL, Davids MS et al.

ASH 2019;Abstract 32.

An Innovative Telemedicine Platform to Provide Expert Access to Patients with Chronic Lymphocytic Leukemia (CLL)

Koffman B, Davids MS et al.

ASH 2019;Abstract 4716.

How to select a treatment for an individual patient?

Menu

- Immunochemotherapy
  - FCR
  - BR
  - Chlorambucil/Obinutuzumab
- Novel Agents
  - Ibrutinib ± obinutuzumab
  - Acalabrutinib ± obinutuzumab
  - Venetoclax + Obinutuzumab

Considerations

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

Courtesy of Brad Kahl, MD

Scenario #1

- 52 yo man with CLL requiring treatment.
  - No p53 mutation or 17p deletion.
  - IgHV unmutated.

- Best options include
  1. Venetoclax plus obinutuzumab
  2. BTKi plus obinutuzumab

- Pro's and Con's to each

Courtesy of Brad Kahl, MD

Scenario #2

- 52 yo man with CLL requiring treatment.
  - No p53 mutation by sequencing
  - No 17p deletion or 11q deletion by FISH.
  - IgHV mutated.

- Best options include
  1. FCR
  2. Venetoclax plus obinutuzumab
  3. BTKi plus obinutuzumab
- Pro's and Con's to each

Courtesy of Brad Kahl, MD

Scenario #3

- 72 yo man with CLL requiring treatment.
  - No p53 mutation.
  - No 17p deletion or 11q deletion.
  - IgHV unmutated.

- Best options include
  1. Venetoclax plus obinutuzumab
  2. BTKi

- Pro's and Con's to each.

Courtesy of Brad Kahl, MD

Scenario #4

- 72 yo man with CLL requiring treatment.
  - No p53 mutation or 17p deletion.
  - IgHV mutated.

- Best options include
  1. Venetoclax plus obinutuzumab
  2. BR
  3. BTKi

- Pro's and Con's to each.

Courtesy of Brad Kahl, MD

Scenario #5

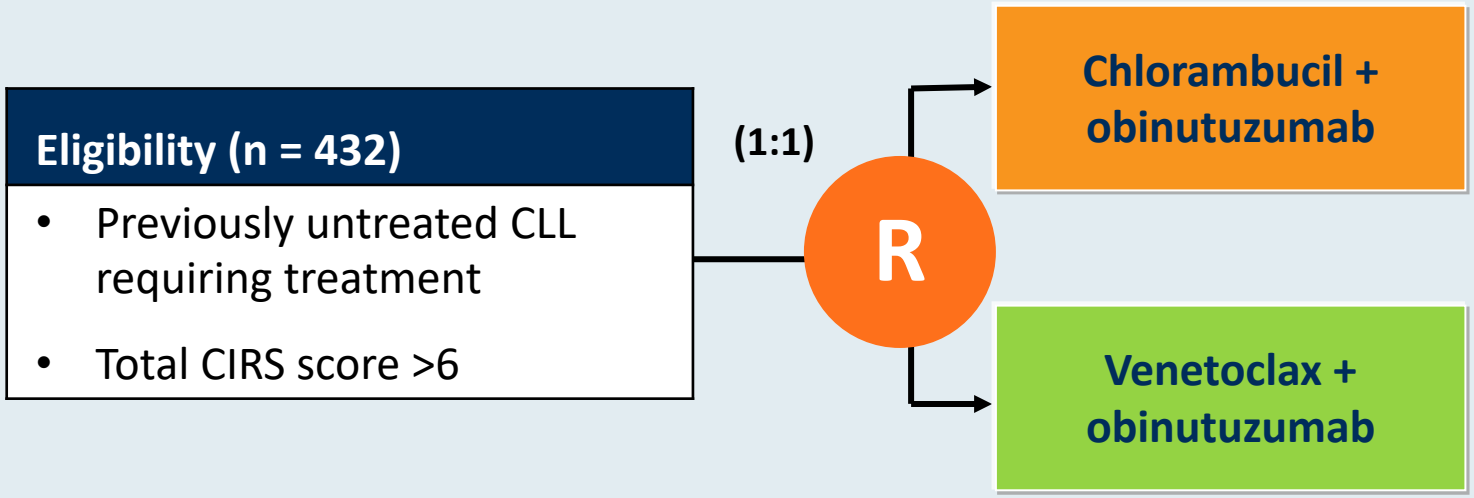
- 72 yo man with CLL requiring treatment.
- 17p deletion by FISH

- BTKi plus obinutuzumab

- This is the one scenario where I favor indefinite therapy over time limited therapy

Courtesy of Brad Kahl, MD

CLL14 Phase III Study Schema

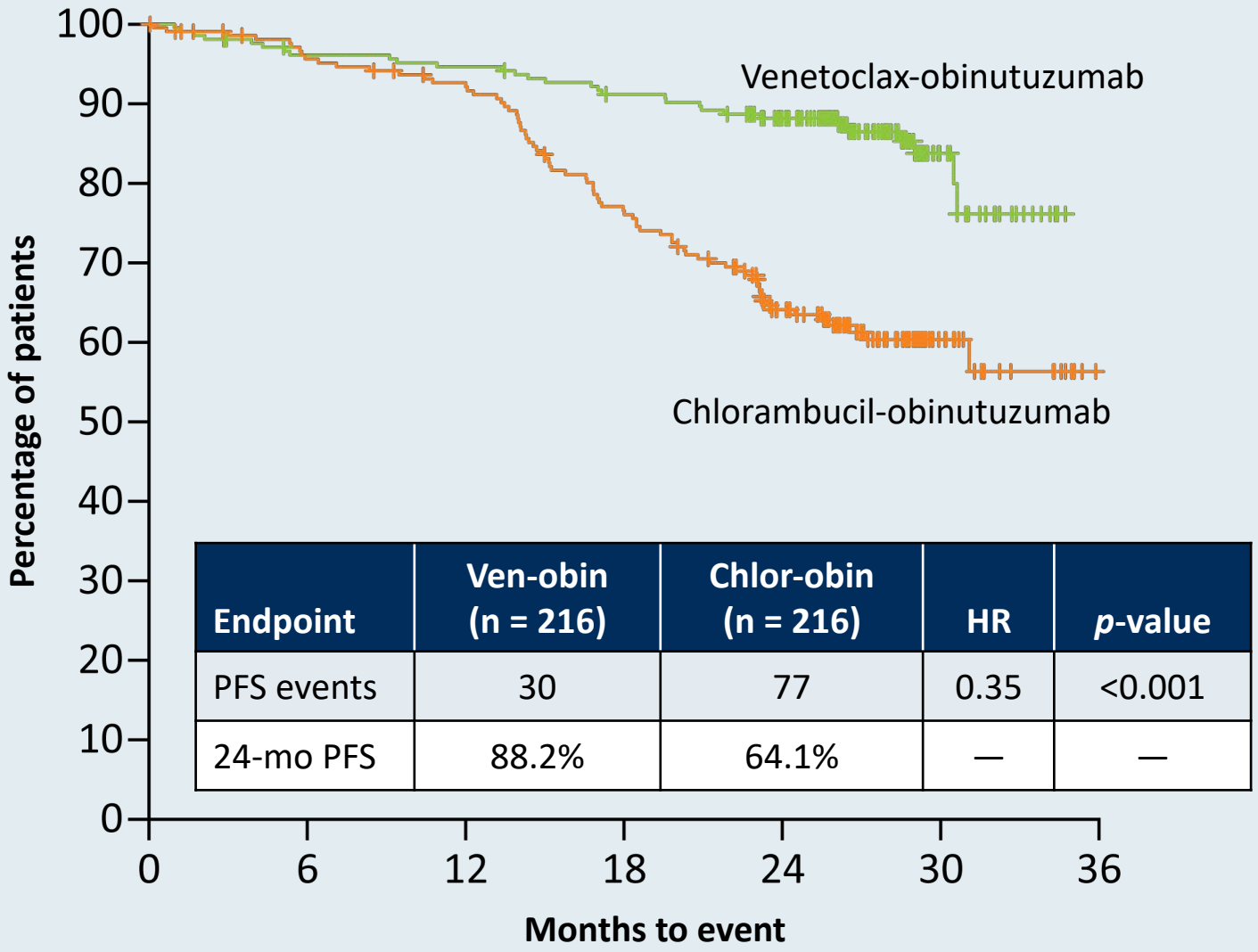


Primary endpoint: Progression-free survival

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

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

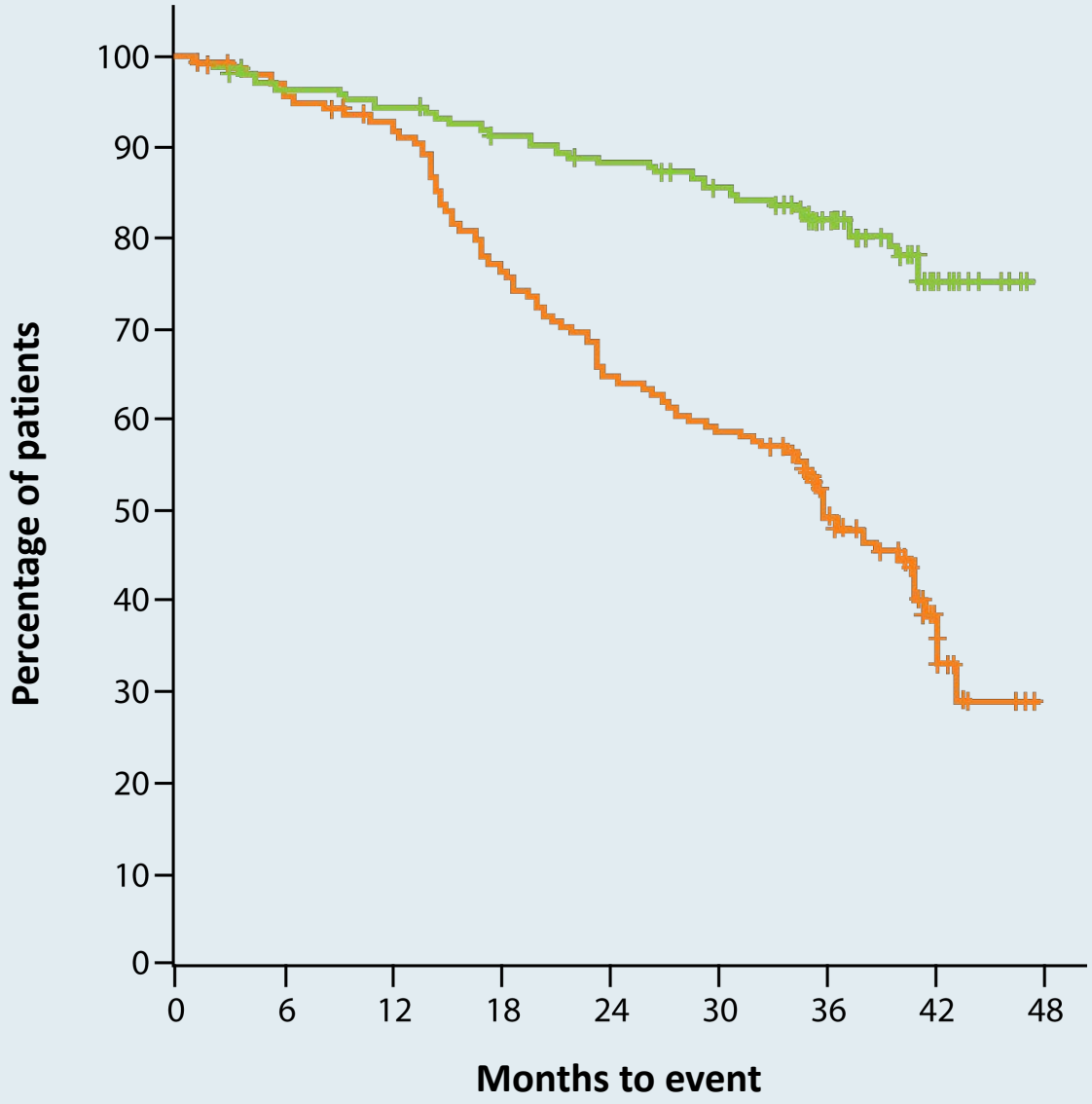
CLL14: Investigator-Assessed Progression-Free Survival



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: Updated 3-Year PFS



Median PFS

Ven-Obi: not reached

Clb-Obi: 35.6 months

3-year PFS rate

Ven-Obi: 81.9%

Clb-Obi: 49.5%

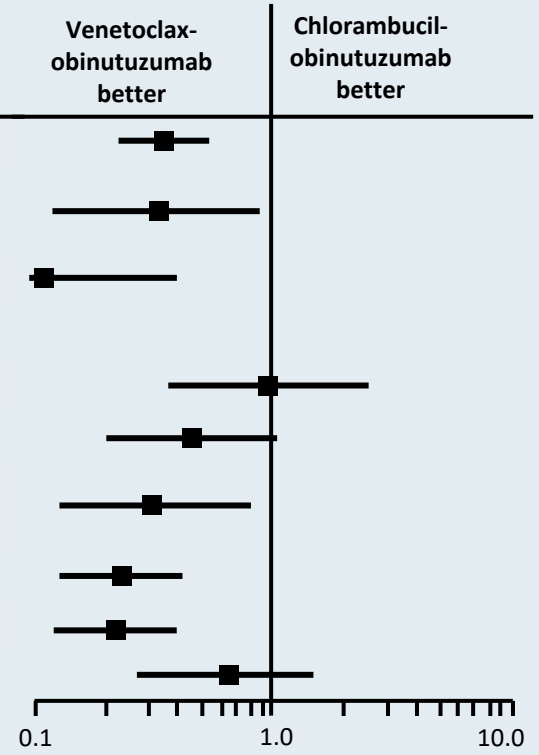
HR 0.31, 95% CI [0.22-0.44]

$p < 0.0001$

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

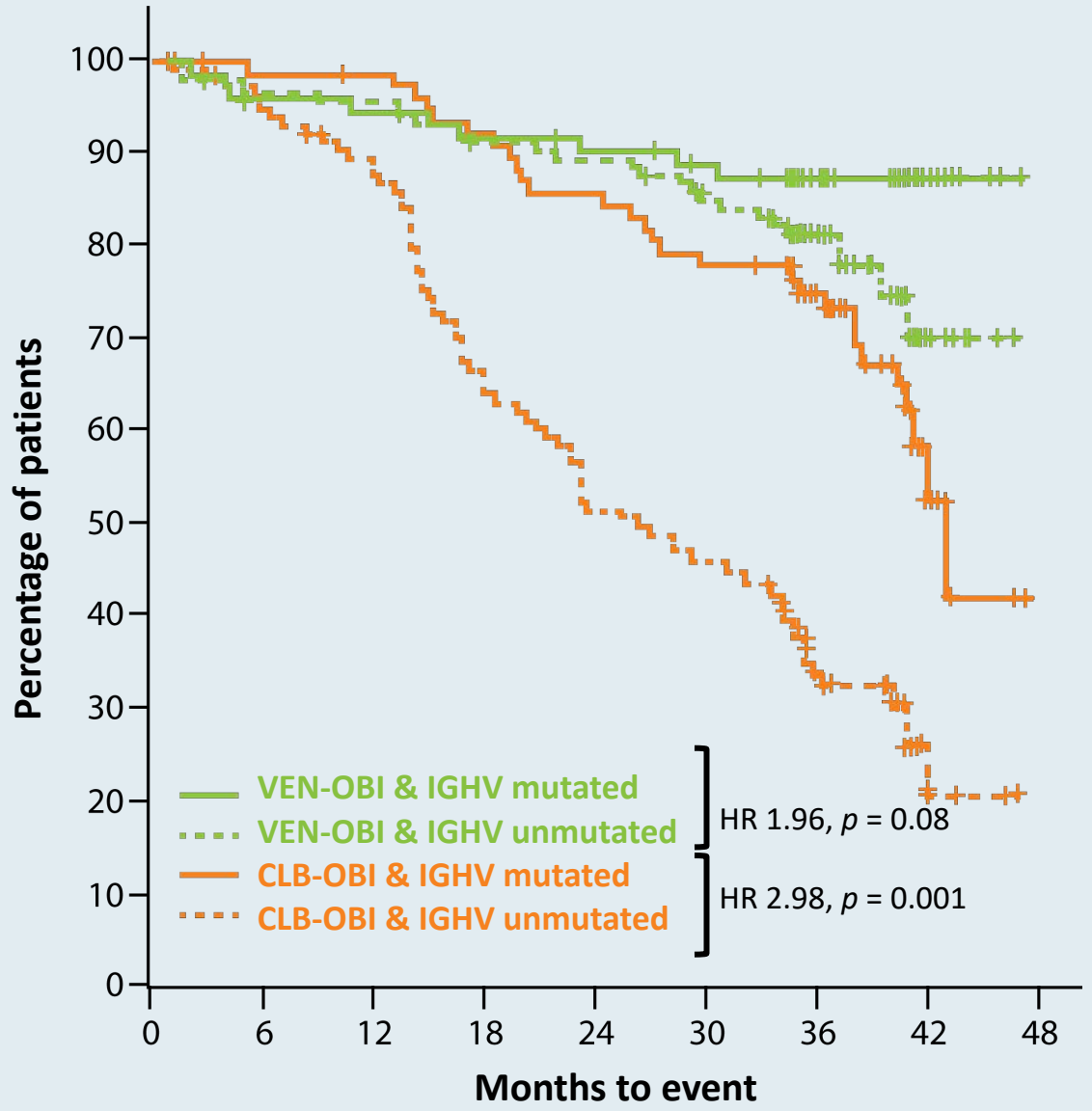
CLL14: Investigator-Assessed Progression-Free Survival by Prognostic Subgroup

Category	Subgroup	Total n	Chlorambucil-obinutuzumab n	Chlorambucil-obinutuzumab PFS rate month 24 (%)	Venetoclax-obinutuzumab n	Venetoclax-obinutuzumab PFS rate month 24 (%)	Hazard ratio
All		432	216	64.1	216	88.1	0.34
Cytogenetic subgroups as per hierarchy	del(17p)	31	14	23.1	17	64.7	0.33
	del(11q)	74	38	41.3	36	91.2	0.11
	Trisomy 12	76	40	55.6	36	100.0	NE
	No abnormalities	92	42	82.1	50	87.2	0.93
	del(13q)	120	59	78.3	61	88.1	0.45
TP53 deletion and/or mutation	Present	46	22	32.7	24	73.9	0.31
	Not present	287	139	65.0	148	92.1	0.23
IGHV mutation status	Unmutated	244	123	51.0	121	89.4	0.22
	Mutated	159	83	85.6	76	90.3	0.64



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

CLL14: PFS by IGHV Mutation and TP53 Status



Median PFS

Ven-Obi & IGHVmut: not reached

Ven-Obi & IGHVunmut: not reached

Clb-Obi & IGHVmut: 42.9 months

Clb-Obi & IGHVunmut: 26.3 months

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

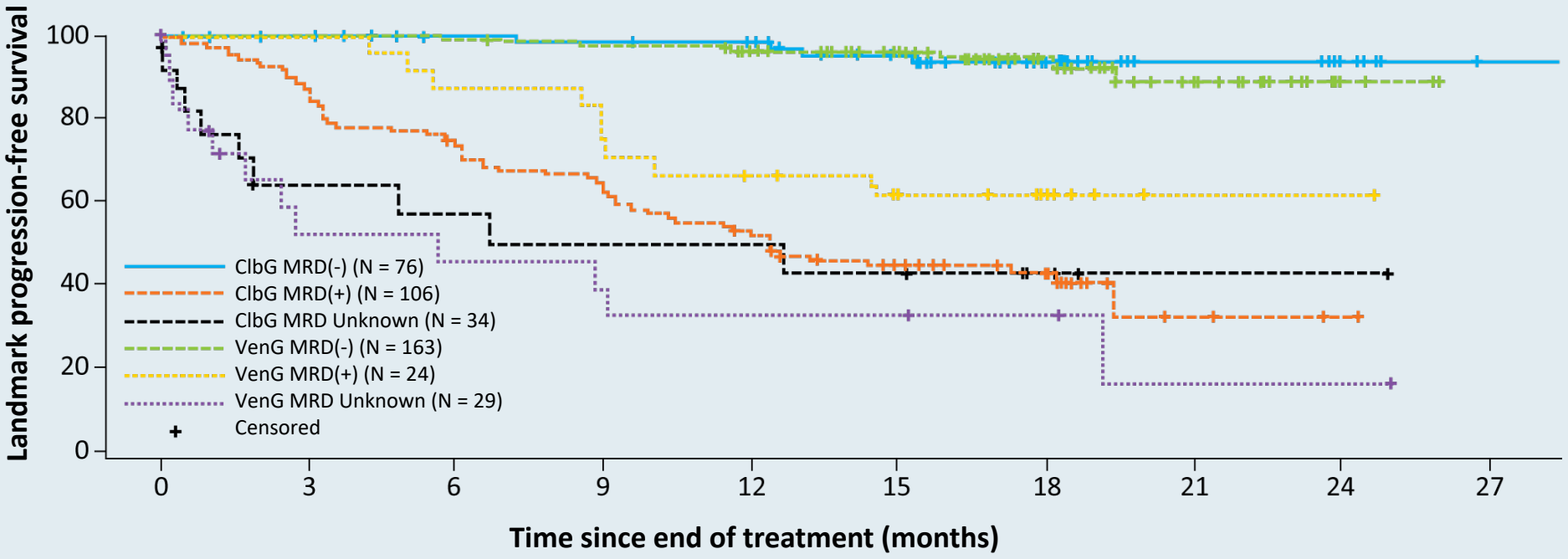
RTP RESEARCH TO PRACTICE

CLL14: Minimal Residual Disease 3 Months After Treatment

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

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

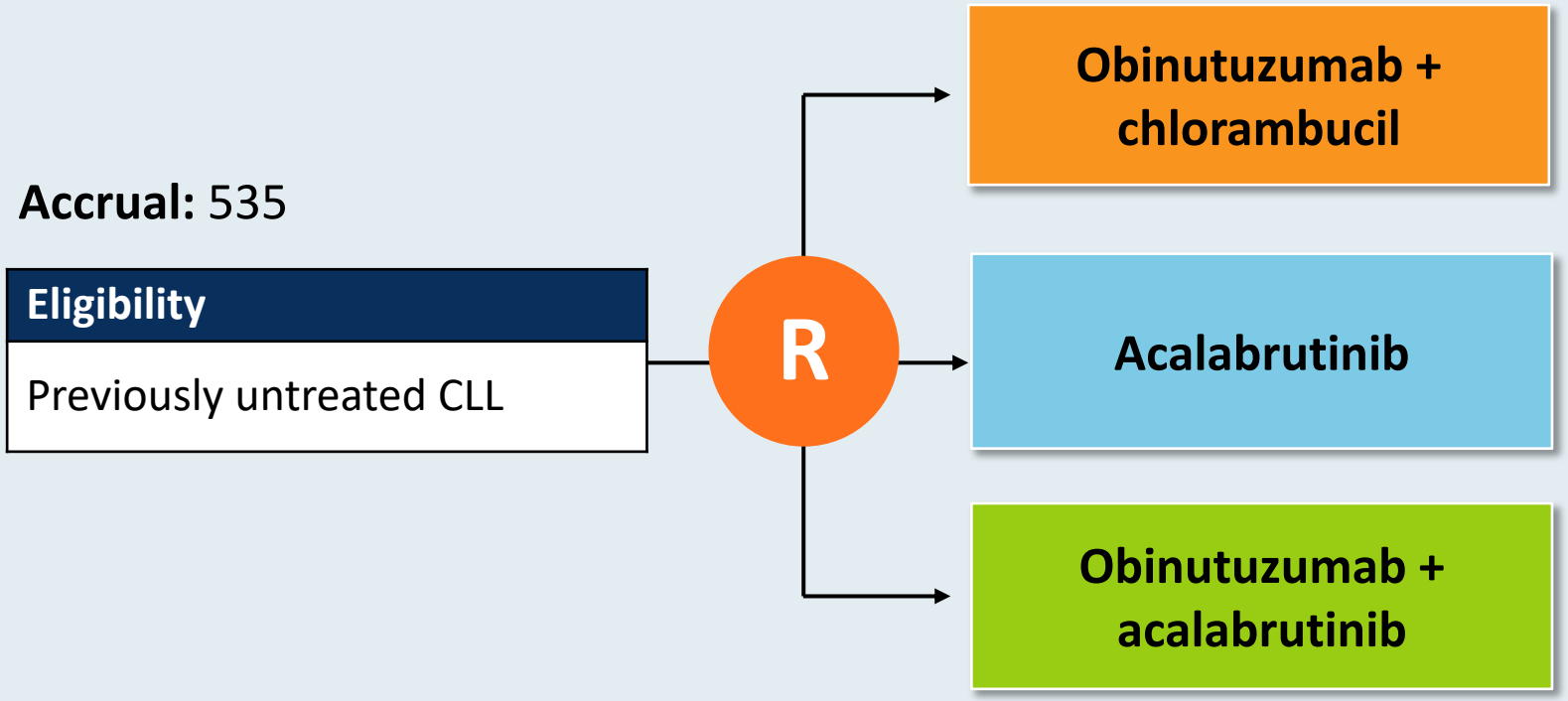
CLL14: Landmark Analysis from End of Therapy PFS by MRD Group



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

Fischer K et al. ASH 2019;Abstract 36.

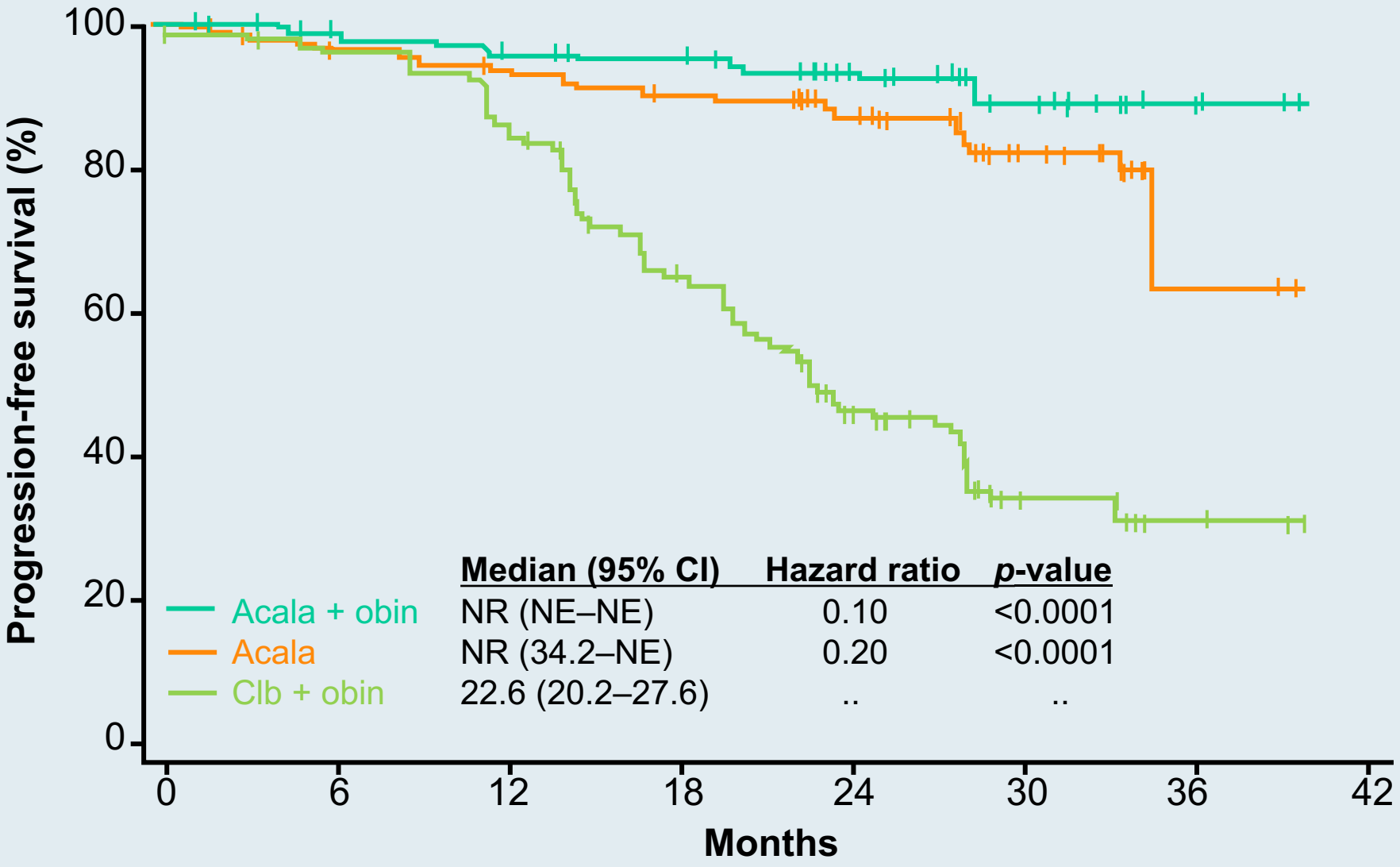
ELEVATE-TN Phase III Trial Schema



Primary endpoint: Progression-free survival

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

ELEVATE-TN: PFS (IRC)



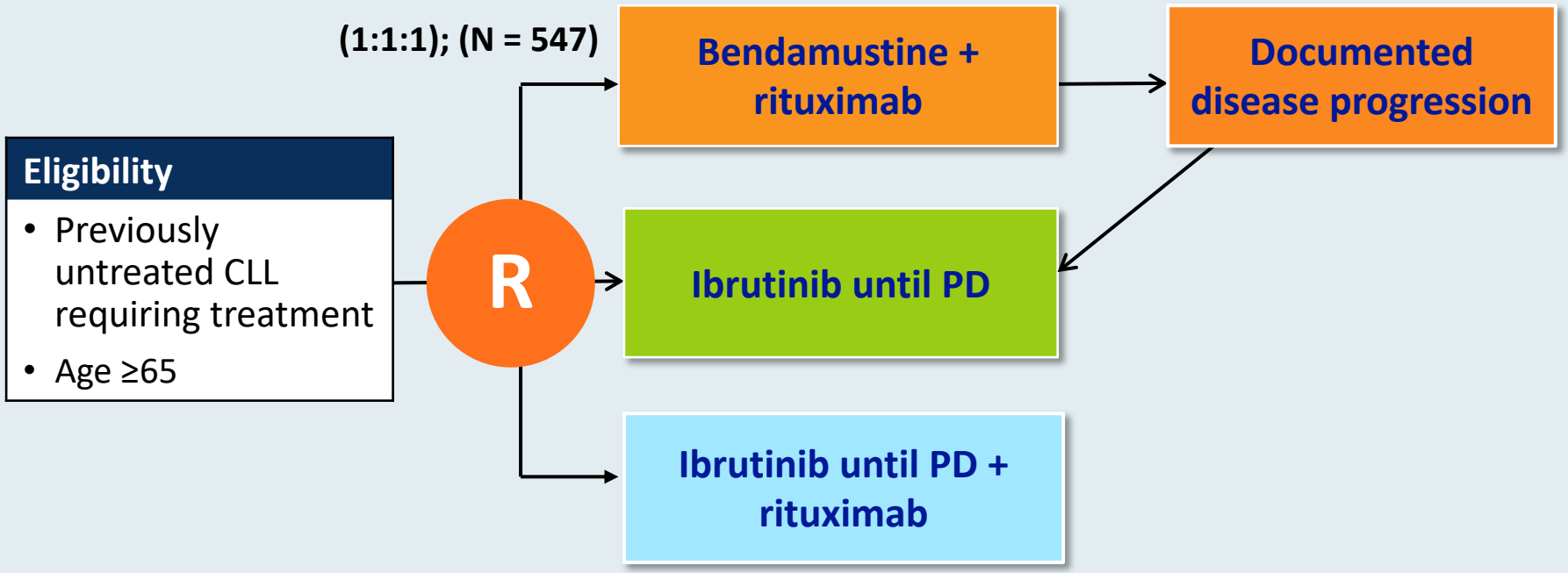
Sharman JP et al. *Lancet* 2020;395:1278-91.

ELEVATE-TN: Select Safety Parameters

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

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

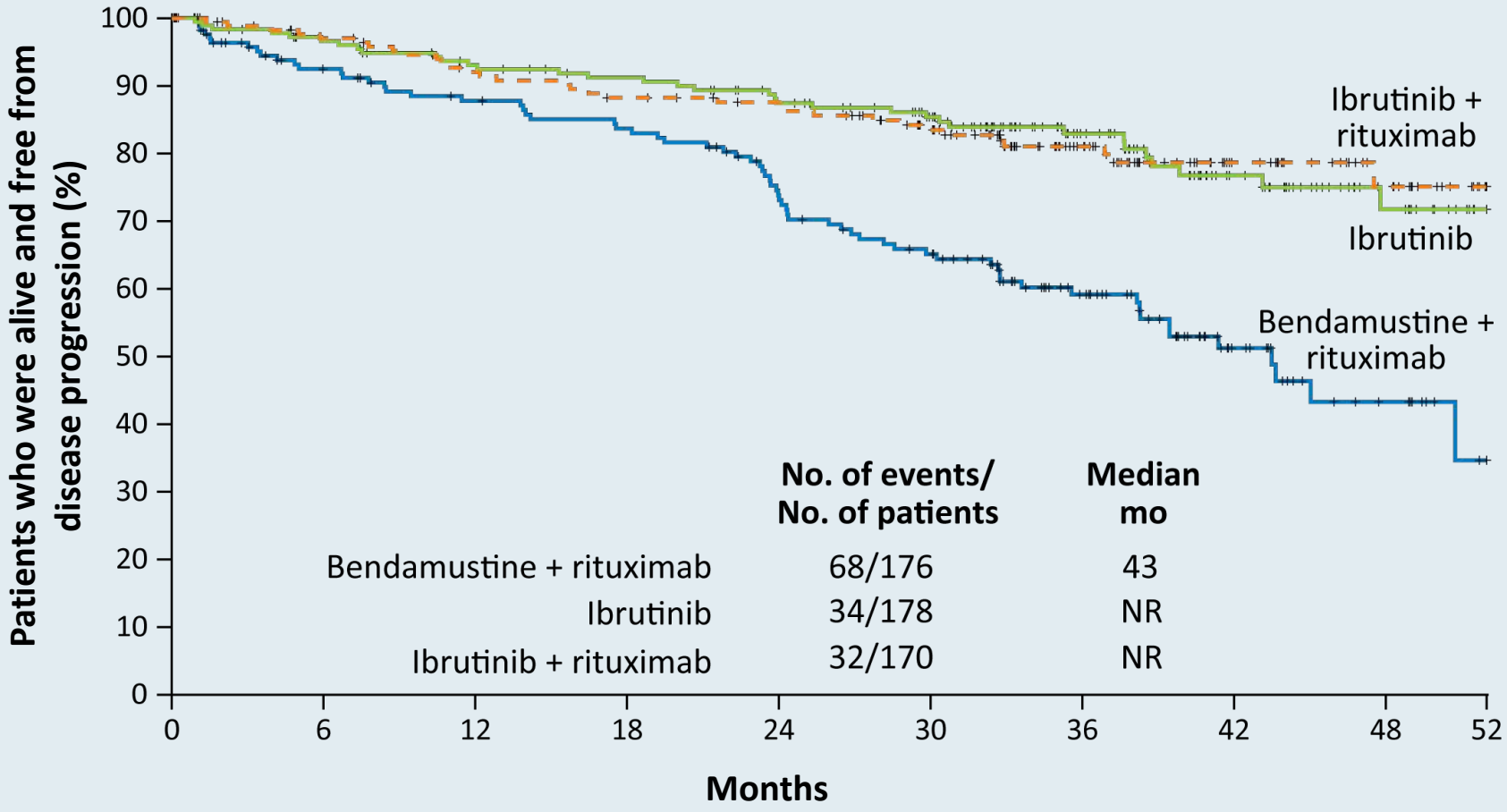
Phase III Alliance A041202 Study Design



Primary endpoint: Progression-free survival (PFS)
Secondary endpoints: OS, ORR, Impact of MRD on PFS and OS, Duration of response, Toxicity and Tolerability

Woyach JA et al. *N Engl J Med* 2018;379(26):2517-28.
Woyach J et al. Alliance Fall Group Meeting, November 5, 2015.

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



Woyach JA et al. *N Engl J Med* 2018;379(26):2517-28.

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

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

Woyach JA et al. *N Engl J Med* 2018;379(26):2517-28.

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

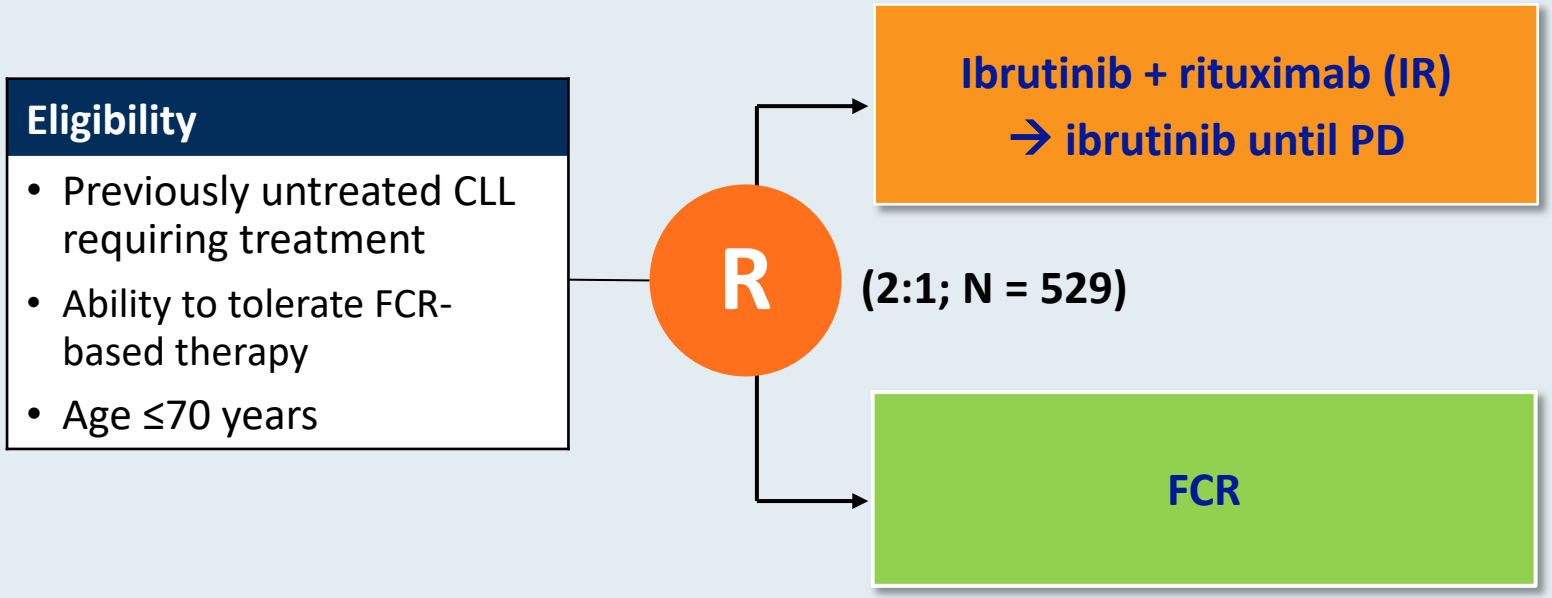
Press Release – April 21, 2020

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

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

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-ibrutinib-plus-rituximab-chronic-lymphocytic-leukemia

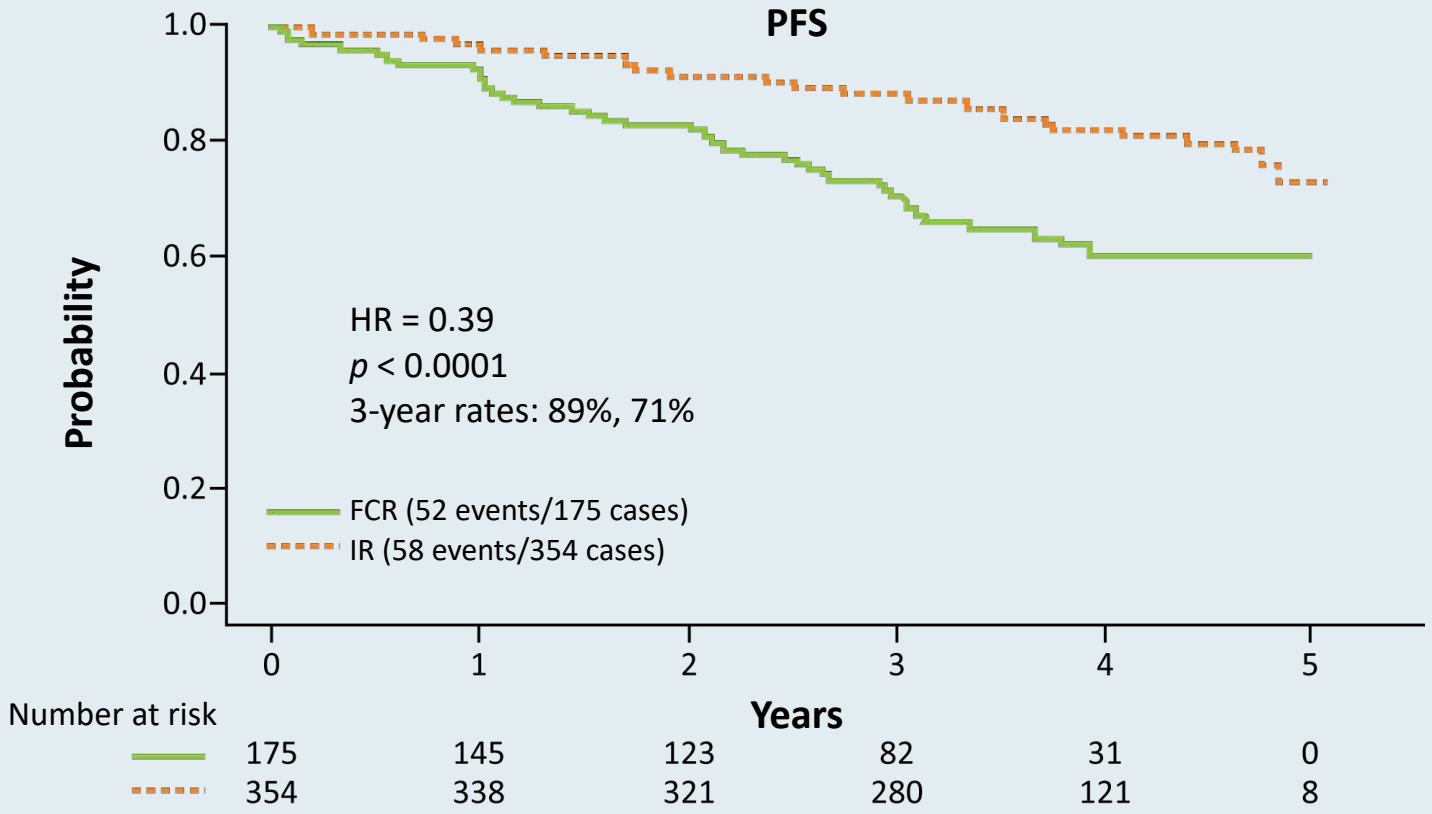
Phase III ECOG-ACRIN E1912 Study Design



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

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

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

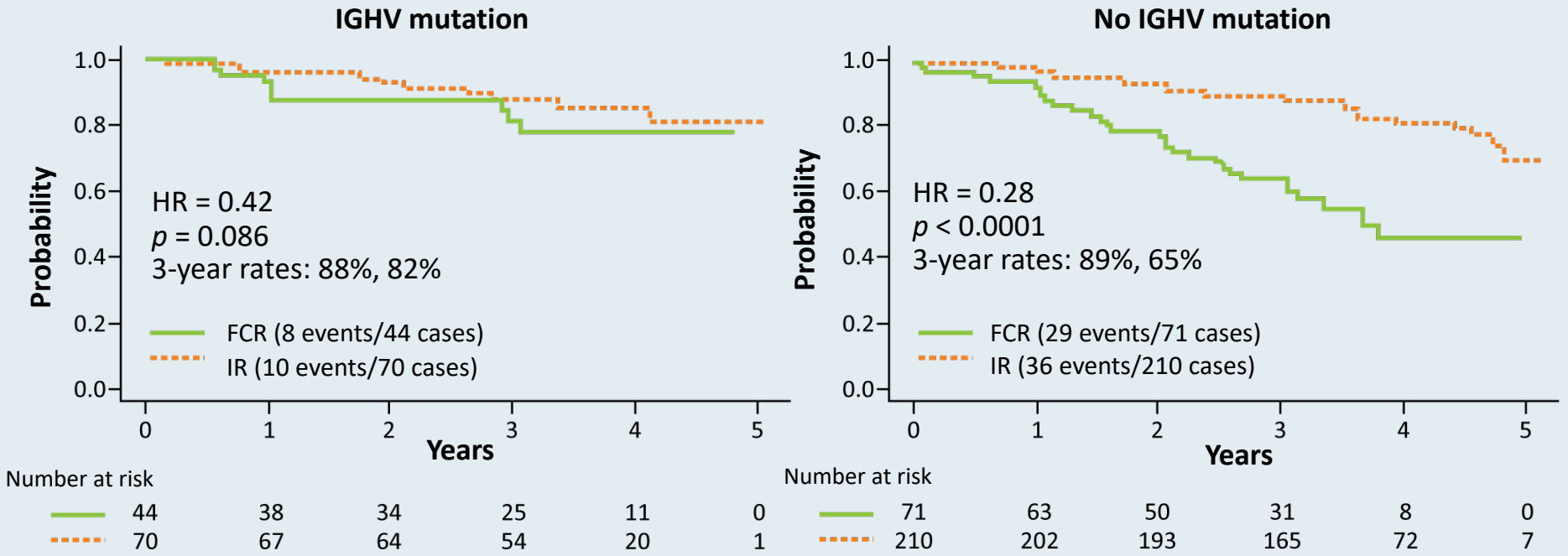


- Grade ≥3 treatment-related AEs were reported in 70% of patients receiving IR and 80% of patients receiving FCR (odds ratio = 0.56; $p = 0.013$).
- Among the 95 patients who discontinued ibrutinib, the most common cause was AE or complication.

Shanafelt TD et al. ASH 2019;Abstract 33.

RTP RESEARCH TO PRACTICE

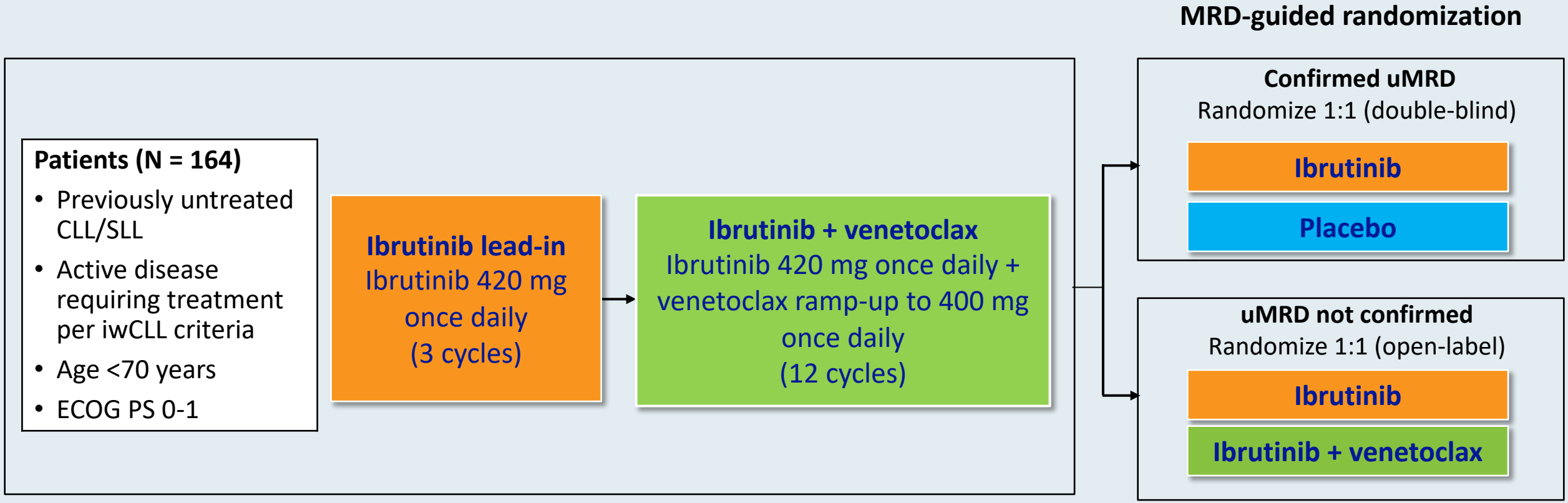
ECOG-ACRIN E1912 Extended Follow-Up: PFS by IGHV Mutation Status



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

Shanafelt TD et al. ASH 2019;Abstract 33.

CAPTIVATE MRD Cohort: Study Design

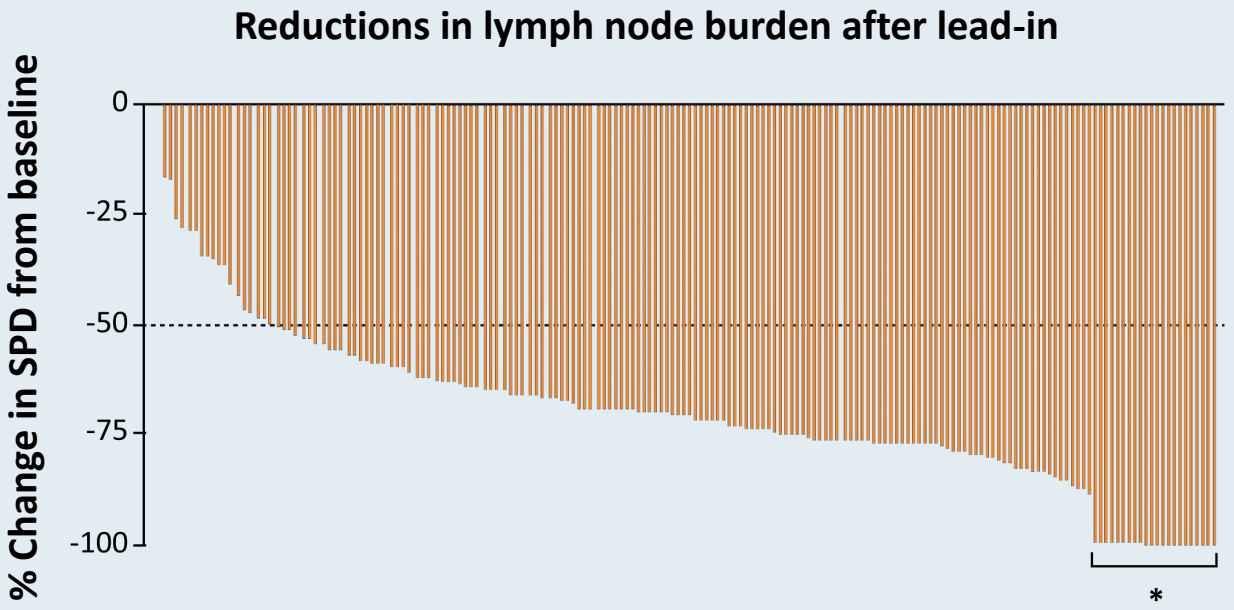


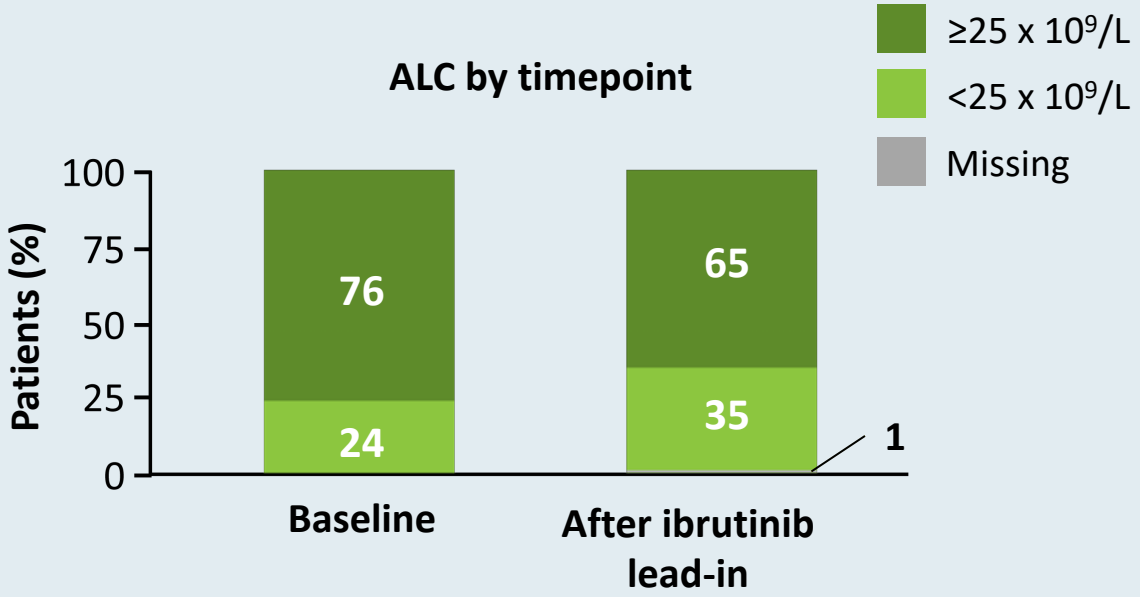
uMRD = undetectable minimal residual disease

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

Siddiqi S et al. EHA 2020;Abstract S158.

CAPTIVATE MRD Cohort: 3 Cycles of Ibrutinib Lead-In





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

Siddiqi S et al. EHA 2020;Abstract S158.

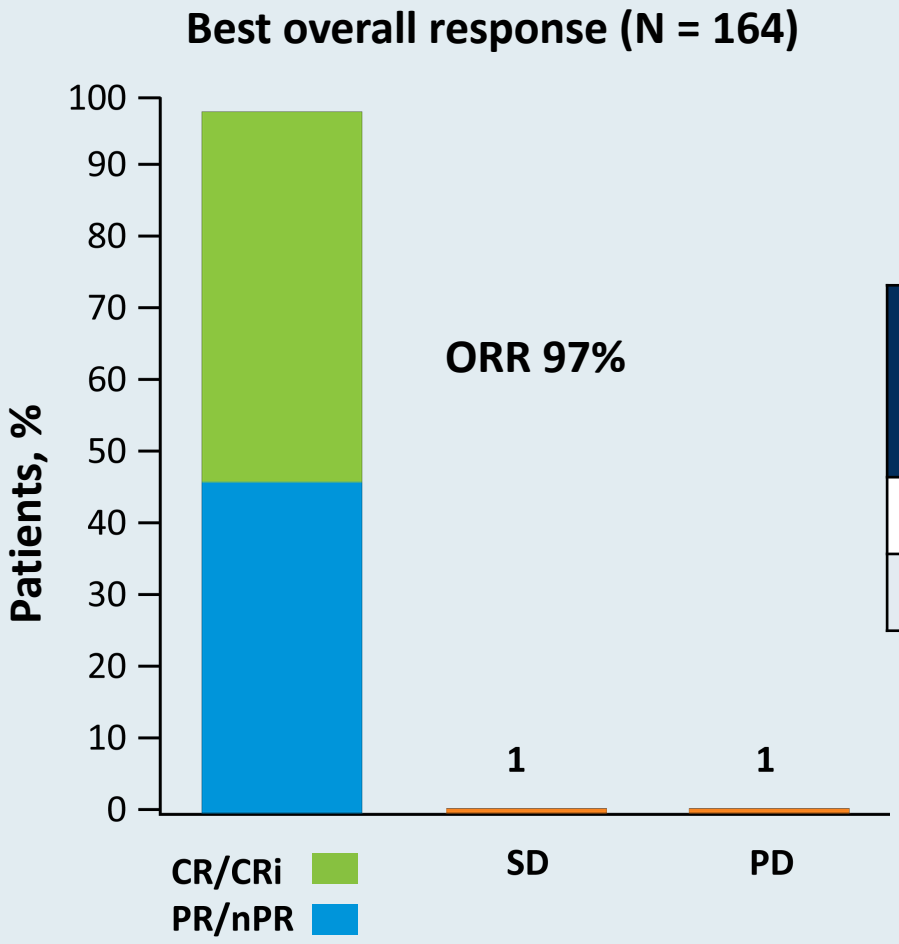
CAPTIVATE MRD Cohort: Undetectable MRD Rate

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

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

Siddiqi S et al. EHA 2020;Abstract S158.

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



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

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

Siddiqi S et al. EHA 2020;Abstract S158.

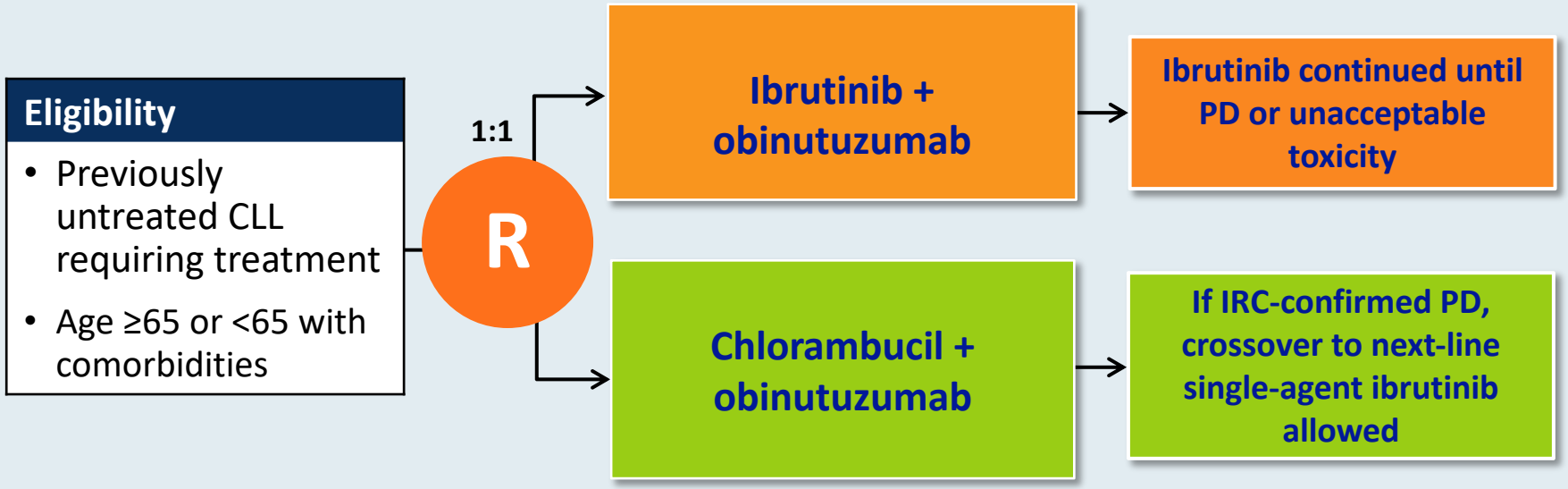
CAPTIVATE MRD Cohort: Summary of Grade 3 and 4 AEs of Interest

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

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

Siddiqi S et al. EHA 2020;Abstract S158.

Phase III iLLUMINATE Study Design



Stratification

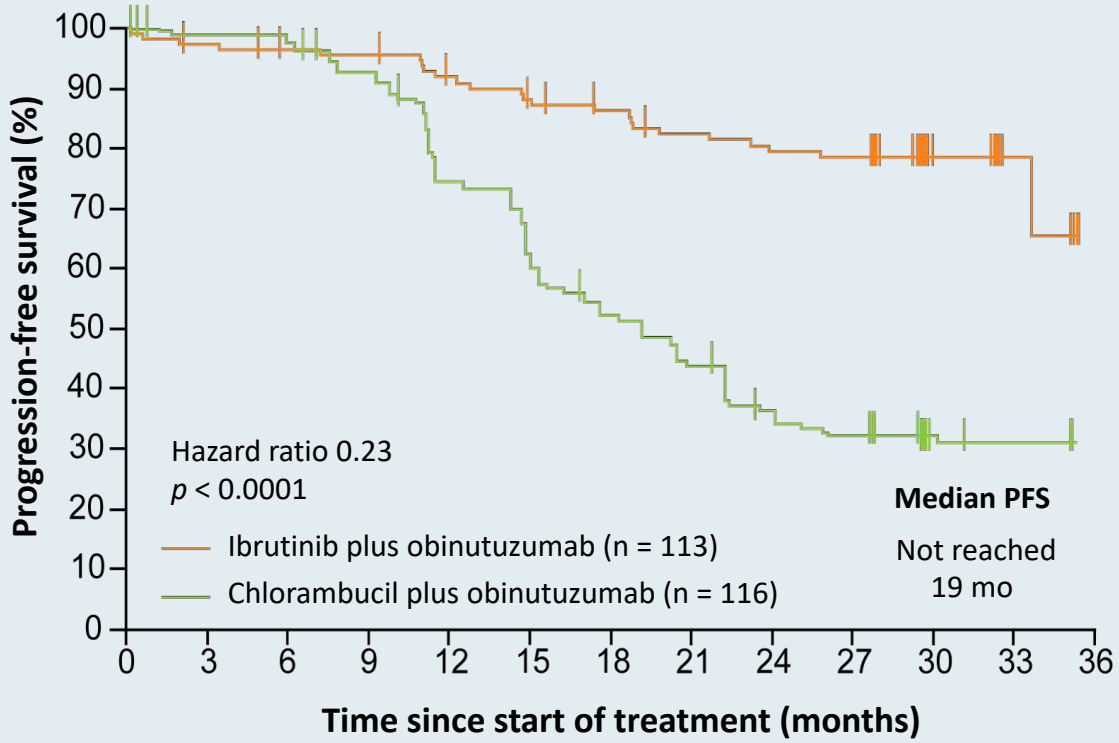
- ECOG PS (0-1 vs 2)
- Del(17p)/del(11q) (+/+ vs +/- vs -/+ vs -/-)

Primary endpoint: PFS by IRC in ITT

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

Moreno C et al. *Lancet Oncol* 2019;20(1):43-56.

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



Most common Grade 3 or 4 AEs

- Neutropenia
- Thrombocytopenia

Serious AEs

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

Moreno C et al. *Lancet Oncol* 2019;20(1):43-56.

RTP RESEARCH TO PRACTICE

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

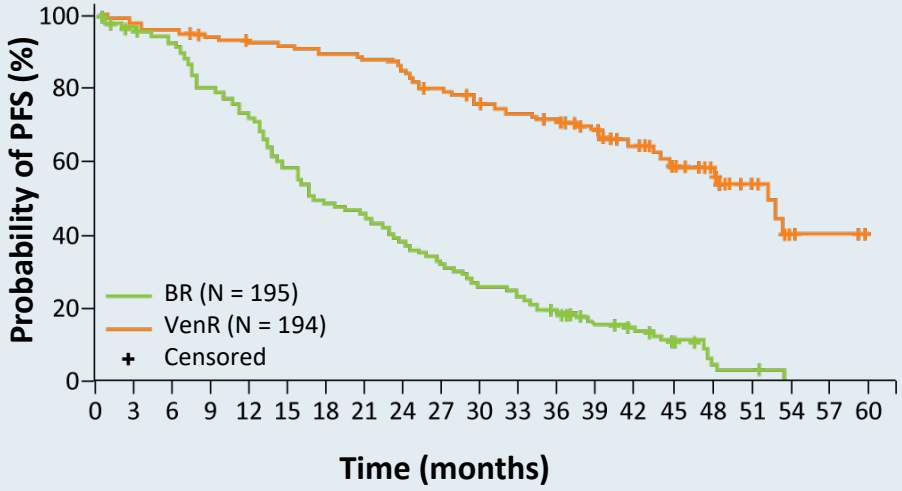
Arm B
Ibrutinib: Cycles 1-19+:d1-28 420mg PO daily
Obinutuzumab: C1 **:** D1:100 mg IV, D2:900 mg IV, D8: 1000 mg IV, D15: 1000 mg IV; C2-6: D1 1000 mg IV

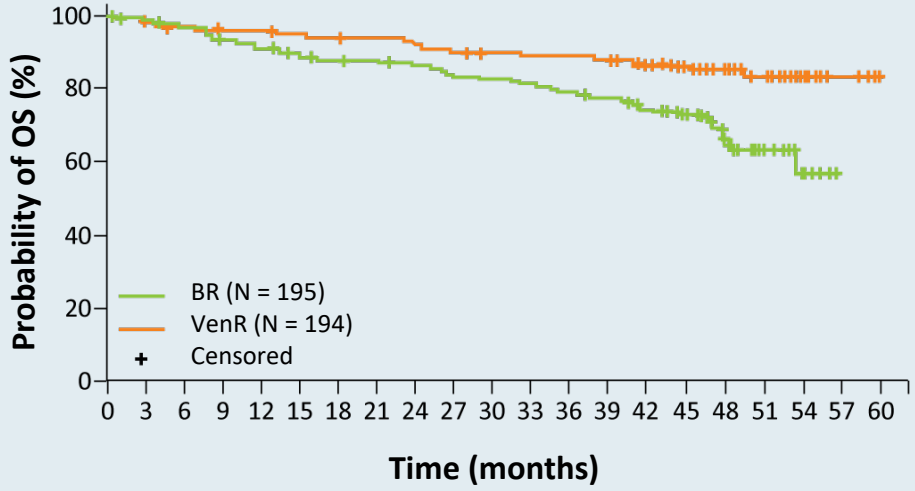
Courtesy of Brad Kahl, MD

Relapsed/Refractory Disease

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

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





Seymour JF et al. ASH 2019;Abstract 355.

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

Press Release – November 21, 2019

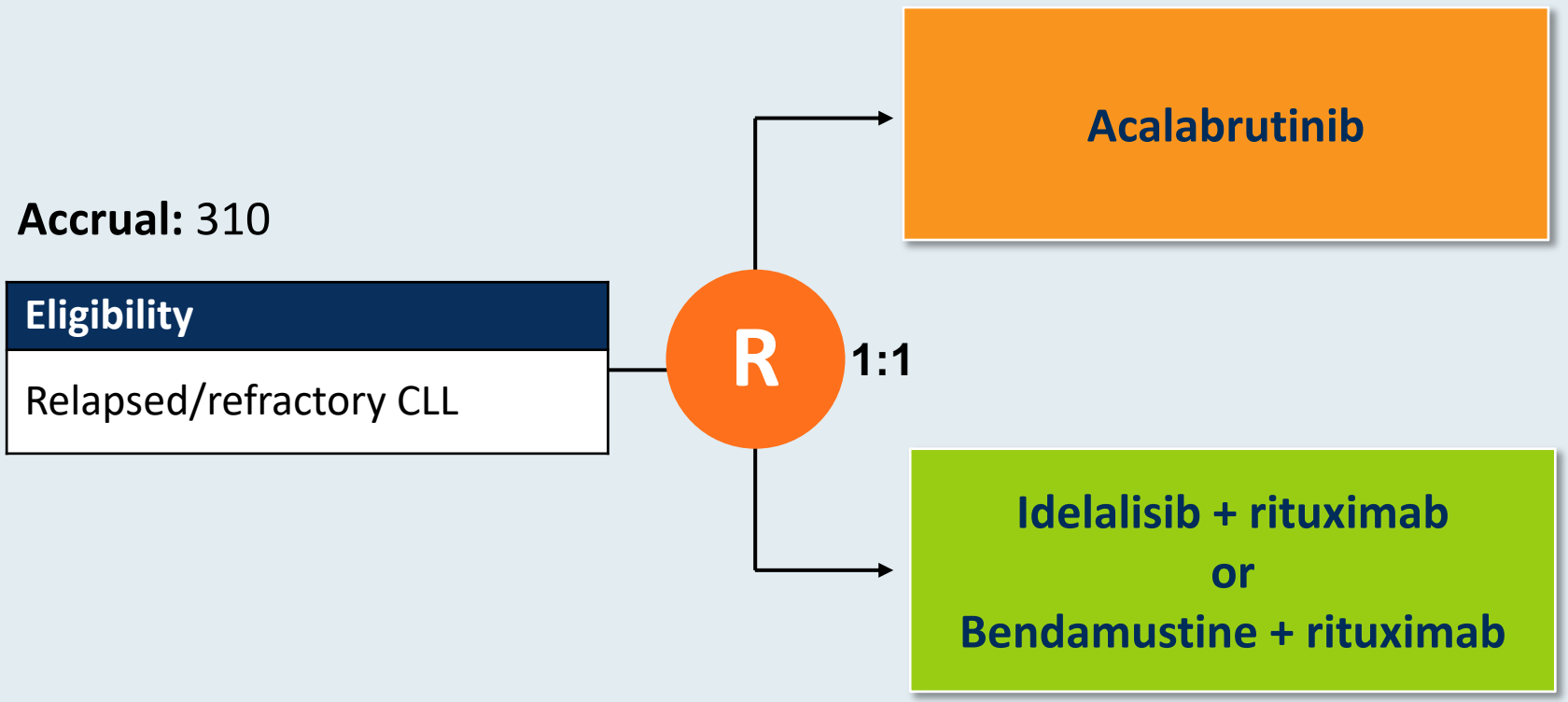
"The Food and Drug Administration approved acalabrutinib for adults with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL). This review was conducted under Project Orbis, an initiative of the FDA Oncology Center of Excellence. Project Orbis provides a framework for concurrent submission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

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

https://www.fda.gov/drugs/resources-information-approved-drugs/project-orbis-fda-approves-acalabrutinib-cll-and-sll

RTP RESEARCH TO PRACTICE

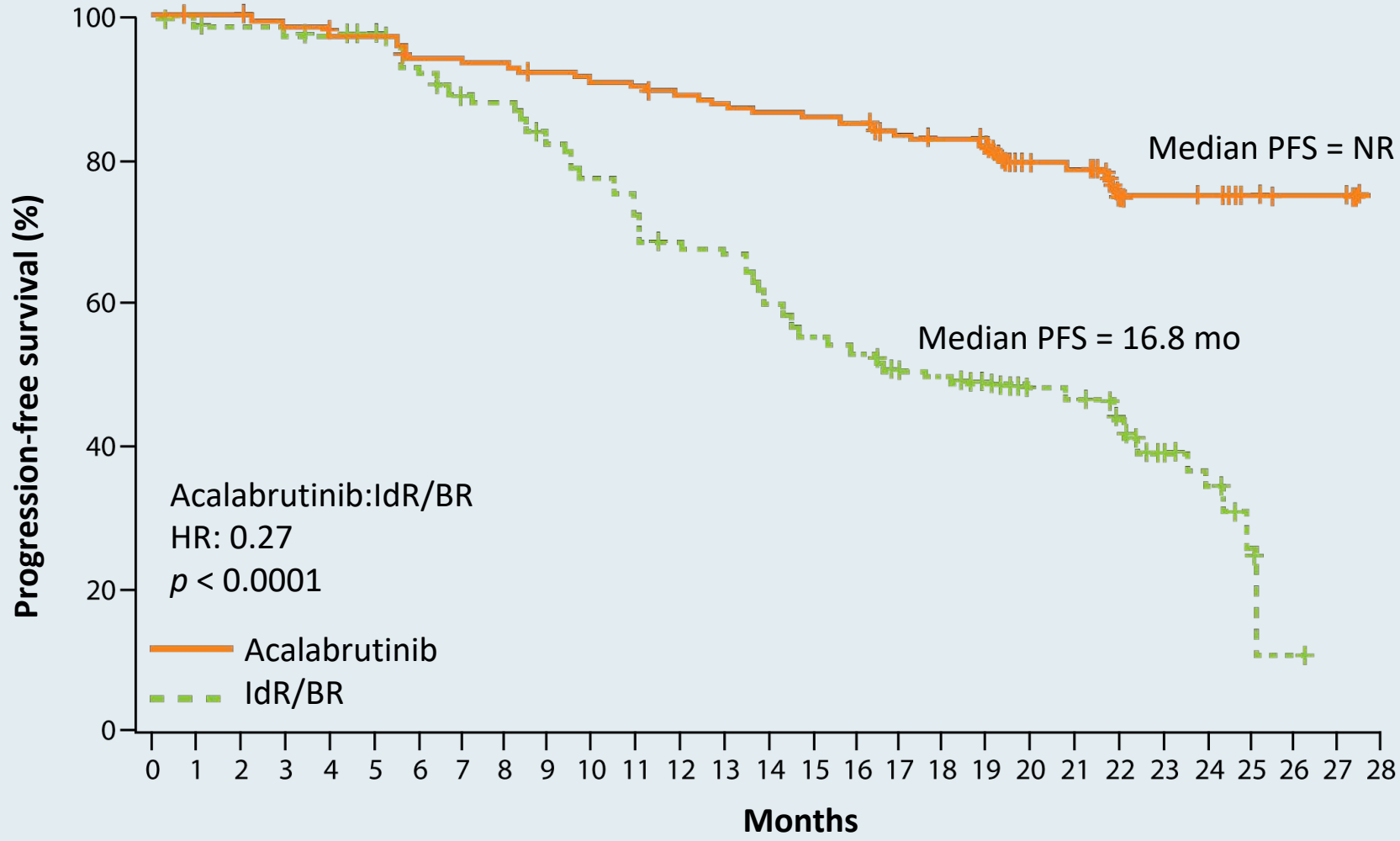
ASCEND Phase III Trial Schema



Primary endpoint: Progression-free survival by IRC

Ghia P et al. EHA 2019;Abstract LBA 2606.
www.clinicaltrials.gov (NCT02970318). Accessed August 2020.

ASCEND: Final Analysis of Investigator-Assessed PFS



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

Ghia P et al. EHA 2020;Abstract S159.

ASCEND: Adverse Events of Clinical Interest

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

IdR = rituximab/idelalisib

Ghia P et al. EHA 2020;Abstract S159.

Meet The Professor with Dr Davids

MODULE 1: Cases from the Community – Dr Brenner

- A 77-year-old woman with Stage I CLL – Del(13q), IGHV mutation
- A 77-year-old man with Stage I CLL – Del(13q), IGHV rearrangement
- An 84-year-old woman with relapsed CLL
- A 76-year-old woman with relapsed CLL – Del(17p)

MODULE 2: Journal Club

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

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 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 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

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

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

RTP RESEARCH TO PRACTICE

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

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

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

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

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

RTP RESEARCH TO PRACTICE

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

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

RTP RESEARCH TO PRACTICE

Clinical Investigator Perspectives on the Current and Future Management of Multiple Myeloma

A Meet The Professor Series

Monday, September 21, 2020
12:00 PM – 1:00 PM ET

Faculty
Ola Landgren, MD, PhD

Moderator
Neil Love, MD

Co-provided by USF Health

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Thank you for joining us!

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

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