Summer Oncology Nursing Series

A Complimentary NCPD-Accredited Virtual Curriculum

Chronic Lymphocytic Leukemia: Session 2

Thursday, August 5, 2021
5:00 PM – 6:00 PM ET

Faculty

John M Pagel, MD, PhD
Lesley Camille Ballance, MSN, FNP-BC

Moderator

Neil Love, MD

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Chronic Lymphocytic Leukemia Faculty

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

Moderator
Neil Love, MD
Research To Practice
Miami, Florida

Lesley Camille Ballance, MSN, FNP-BC
Sarah Cannon Center for Blood Cancer
Tennessee Oncology
Nashville, Tennessee

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Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Genentech, a member of the Roche Group, and Pharmacyclics LLC, an AbbVie Company and Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC.

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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 companies: AbbVie Inc, Adaptive Biotechnologies Corporation, ADC Therapeutics, Agios Pharmaceuticals Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Coherus BioSciences, Daiichi Sankyo Inc, Eisai Inc, Epizyme Inc, Exact Sciences Inc, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, Genentech, a member of the Roche Group, Gilead Sciences Inc, GlaxoSmithKline, Grail Inc, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Novartis, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, Seagen Inc, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc and Verastem Inc.

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

Dr Pagel — Disclosures

Consulting Agreements	AstraZeneca Pharmaceuticals LP, BeiGene Ltd, Epizyme Inc, Gilead Sciences Inc, MorphoSys, Seagen Inc

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Ms Ballance — Disclosures

Consulting Agreement	AbbVie Inc
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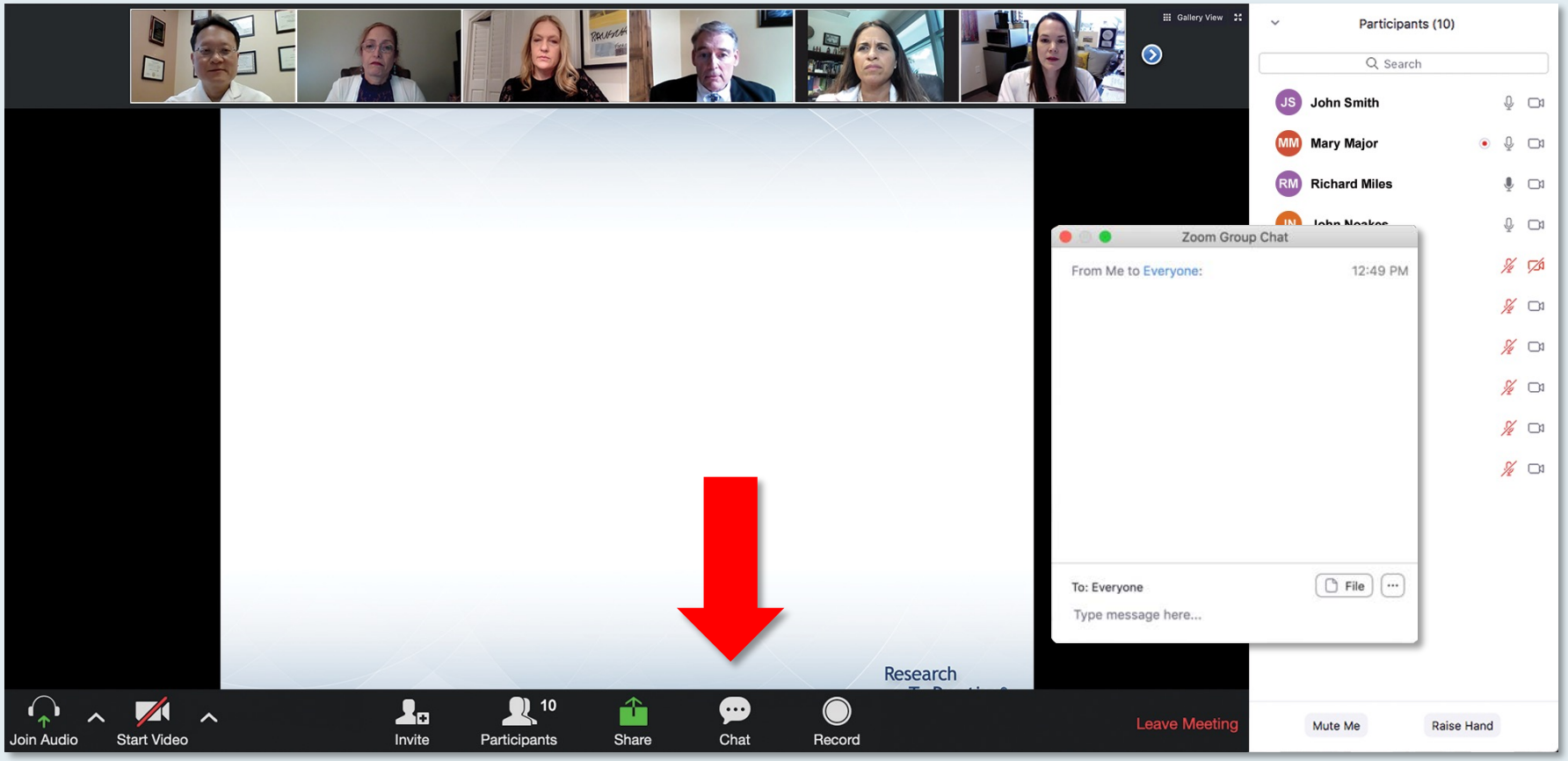
We Encourage Clinicians in Practice to Submit Questions



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

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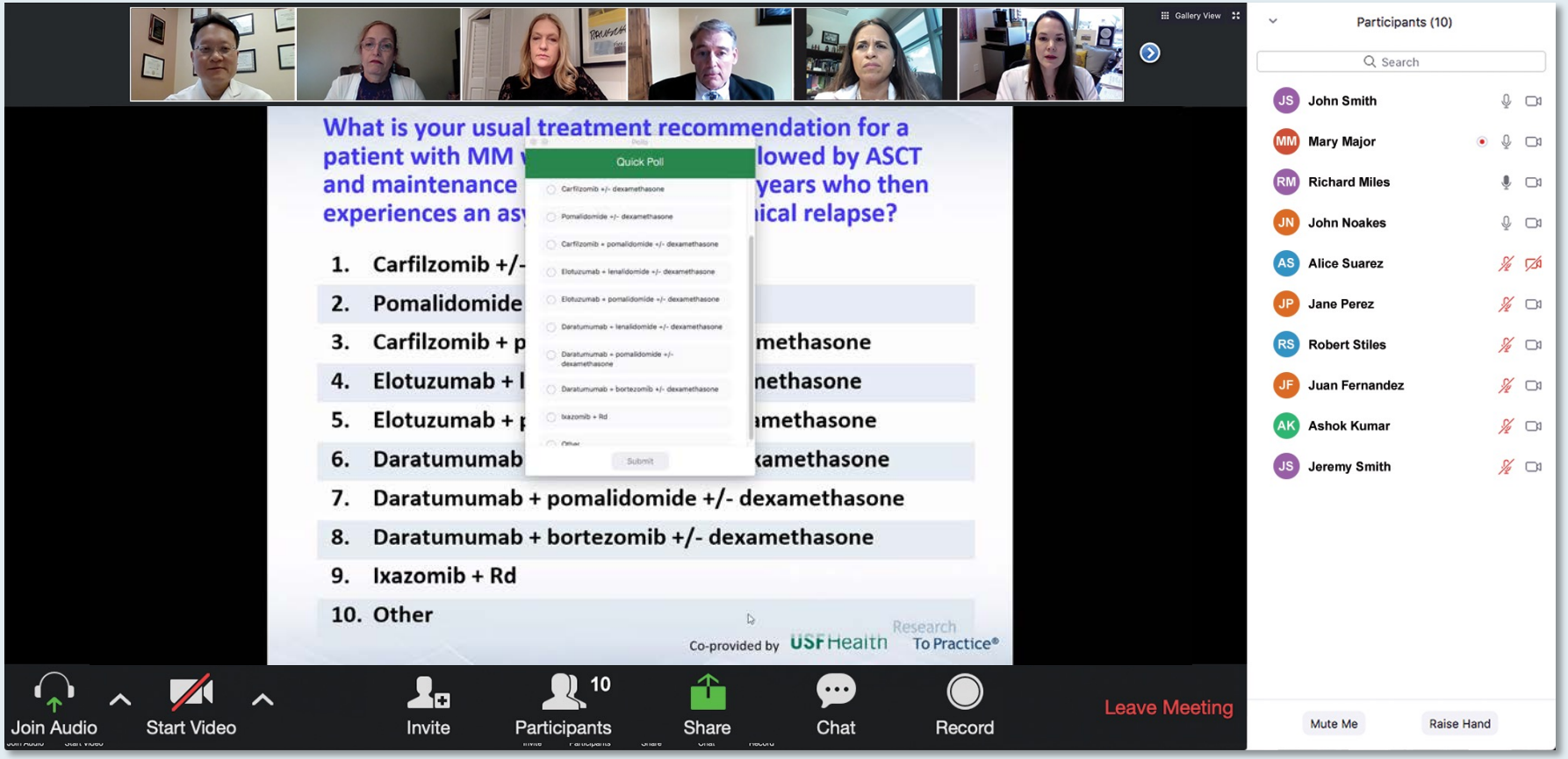
Familiarizing Yourself with the Zoom Interface

How to answer poll questions



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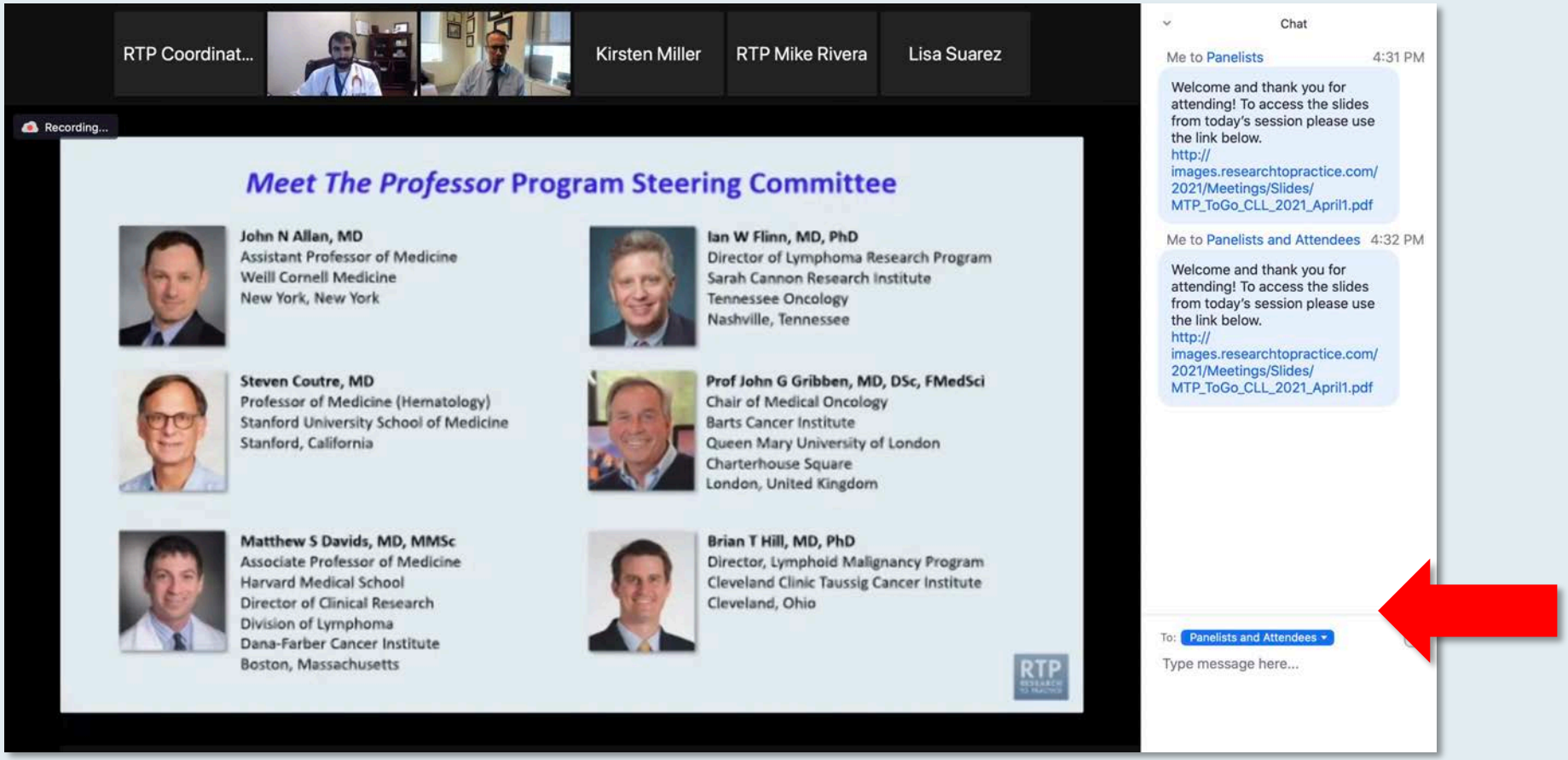
Familiarizing Yourself with the Zoom Interface

Expand chat submission box



Drag the white line above the submission box up to create more space for your message.

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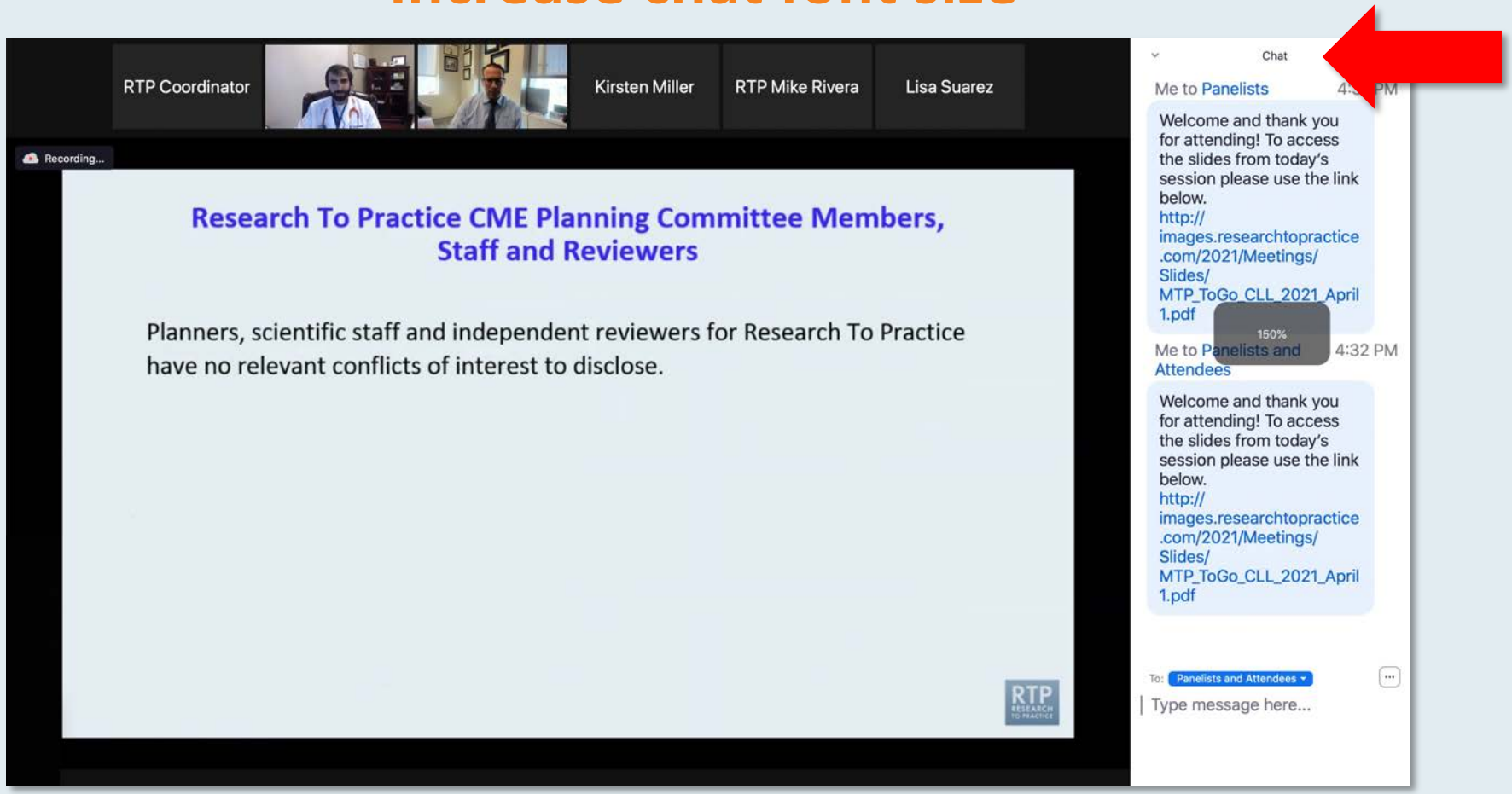
Familiarizing Yourself with the Zoom Interface

Increase chat font size



Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.

ONCOLOGY TODAY

WITH DR NEIL LOVE

Key Presentations on Chronic Lymphocytic Leukemia and Follicular Lymphoma from the 2020 ASH Annual Meeting

DR ANN LACASCE

DANA-FARBER CANCER INSTITUTE

BOSTON, MASSACHUSETTS

Listen on Apple Podcasts

Spotify

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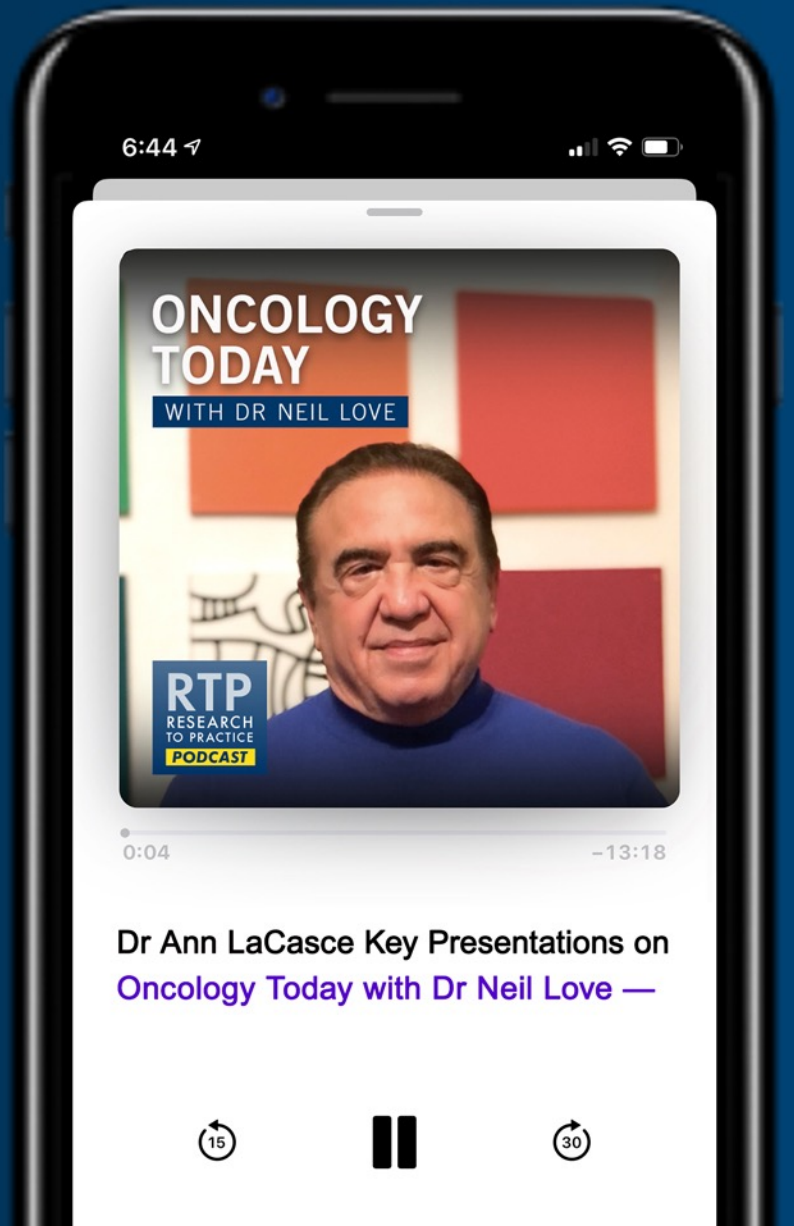

Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with Renal Cell Carcinoma

Friday, August 6, 2021
12:00 PM – 1:00 PM ET

Faculty

Thomas Powles, MBBS, MRCP, MD

Moderator

Neil Love, MD

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Three Exciting Educational Events Held in Conjunction with the 2021 Pan Pacific Lymphoma Conference

A Physician and Nurse Education Series in Partnership with the University of Nebraska Medical Center

Expert Second Opinion — Acute Myeloid Leukemia and Myelodysplastic Syndromes

Monday, August 9, 2021
7:00 PM – 8:30 PM ET

Faculty
Krishna Gundabolu, MD
Richard M Stone, MD
Eunice S Wang, MD

Moderator
Harry Paul Erba, MD, PhD

Beyond the Guidelines — Chronic Lymphocytic Leukemia

Tuesday, August 10, 2021
7:00 PM – 9:00 PM ET

Faculty
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Susan O'Brien, MD
Sonali M Smith, MD
Julie M Vose, MD, MBA

Moderator
Matthew S Davids, MD, MMSc

Cases from the Community — Multiple Myeloma

Thursday, August 12, 2021
7:00 PM – 8:30 PM ET

Faculty
Muhamed Baljevic, MD
Joseph Mikhael, MD
Nina Shah, MD

Moderator
Robert Z Orlowski, MD, PhD

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Expert Second Opinion — Investigators Discuss How They and Their Colleagues Navigate Emerging Clinical Research and Challenging Patients with Acute Myeloid Leukemia and Myelodysplastic Syndromes

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Optimizing the Selection and Sequencing of Therapy for Patients with HER2-Positive Breast Cancer

Tuesday, August 10, 2021
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Karen A Gelmon, MD

Moderator

Neil Love, MD

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Beyond the Guidelines — Investigator Perspectives on the Management of Patients with Chronic Lymphocytic Leukemia

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RTP RESEARCH TO PRACTICE

A Conversation with the Investigators: Perspectives on the Management of Head and Neck Cancer

Wednesday, August 11, 2021
5:00 PM – 6:00 PM ET

Faculty

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Ezra Cohen, MD
Robert L Ferris, MD, PhD

Moderator

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Prostate Cancer

Thursday, August 12, 2021
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A Oliver Sartor, MD
Ronald Stein, JD, MSN, NP-C, AOCNP

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Cases from the Community — Investigators Discuss Emerging Research and Actual Patients with Multiple Myeloma

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Thank you for joining us!

NCPD credit information will be emailed to each participant shortly.

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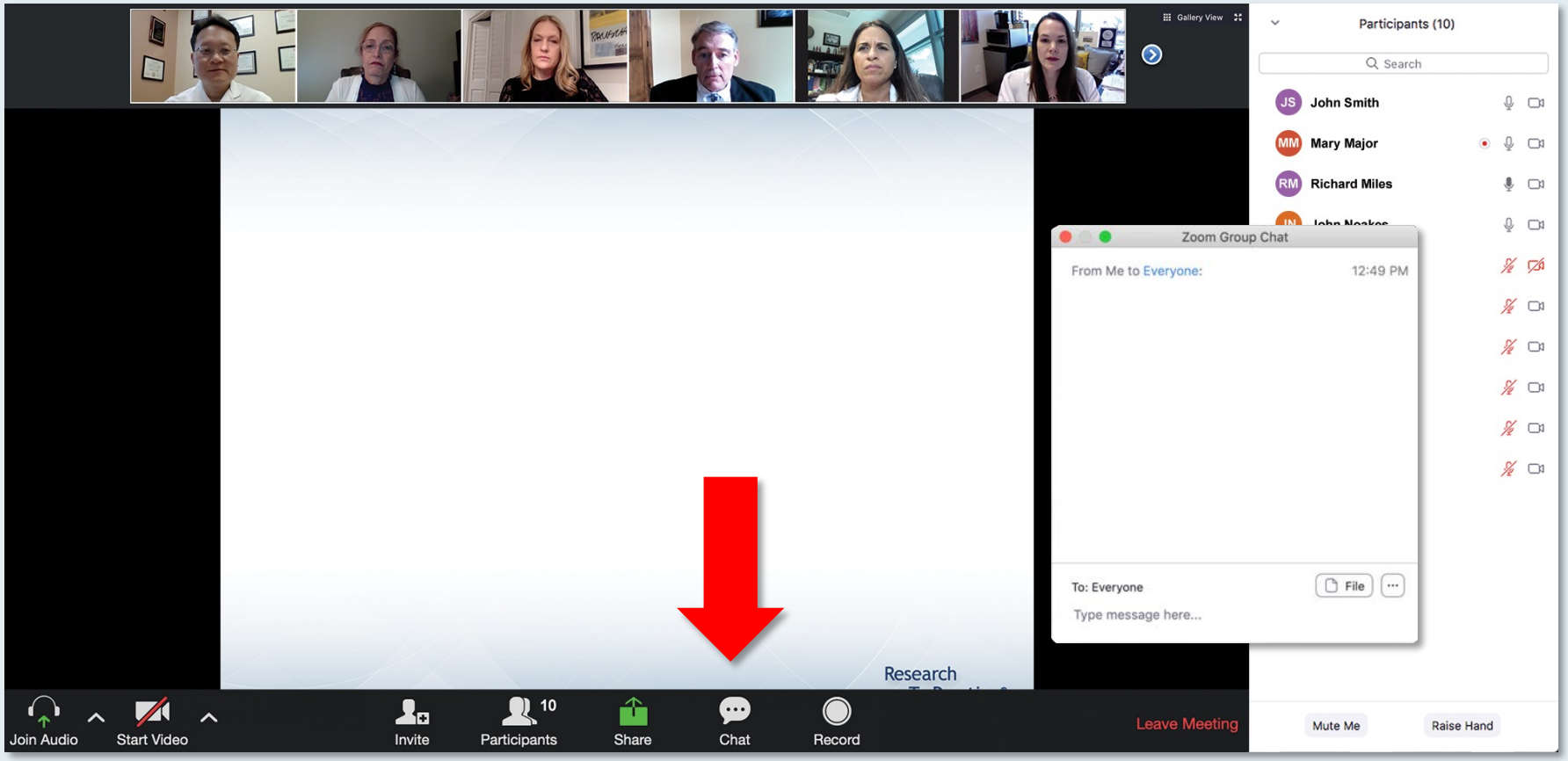

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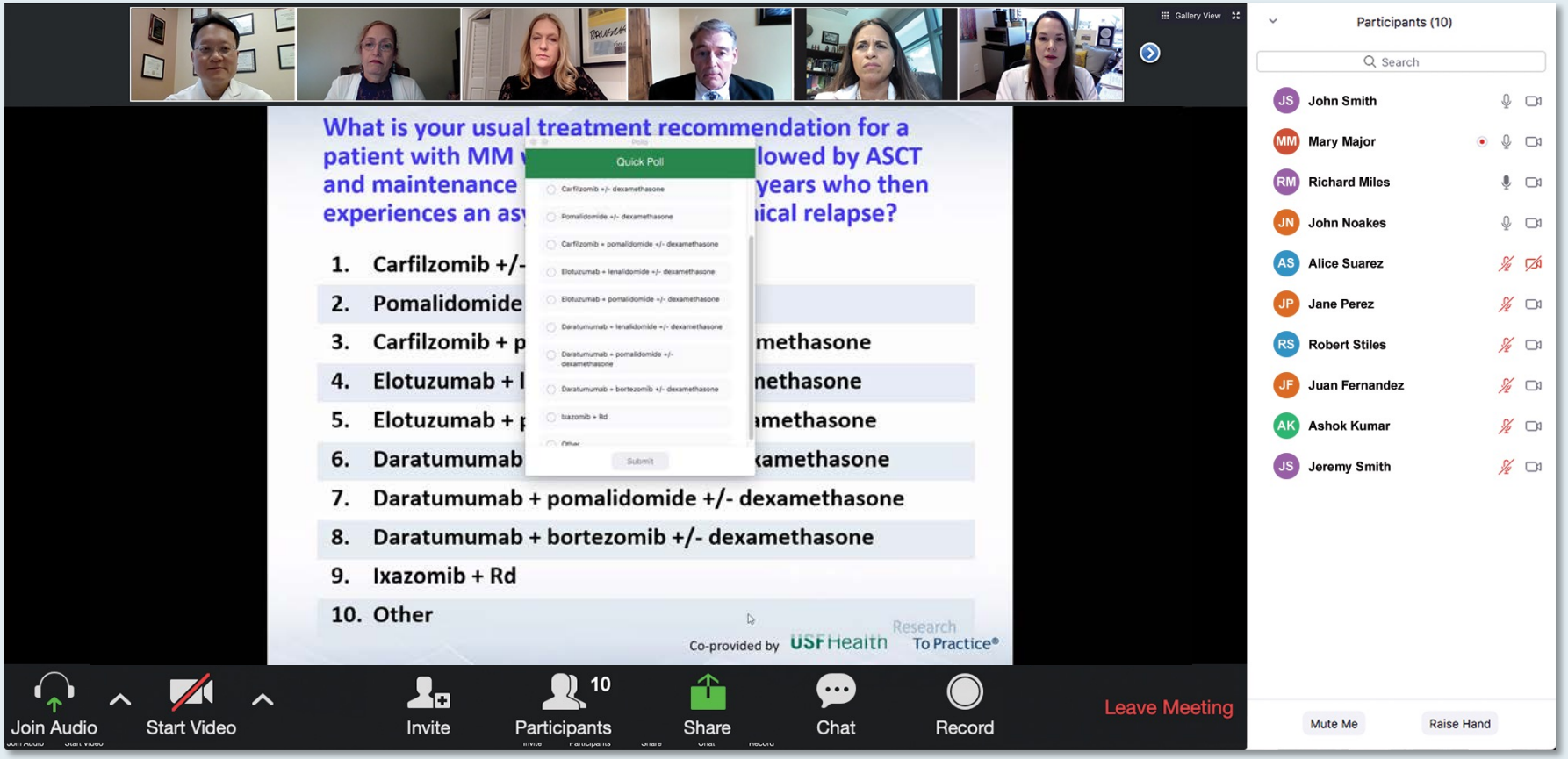

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Oncology Grand Rounds Nursing Webinar Series

April 2021

Monday	Tuesday	Wednesday	Thursday	Friday
19	20 Breast Ca 8:30 AM Lung Ca 5:00 PM	21 AML 12:00 PM CRC and GE Ca 4:45 PM	22 Prostate Ca 8:30 AM Lymphomas 5:00 PM	23
26	27 Multiple Myeloma 8:30 AM Gynecologic Ca 5:00 PM	28 Bladder Ca 12:00 PM	29 CLL 8:30 AM CAR-T 5:00 PM	30

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13th Annual Oncology Grand Rounds

A Complimentary NCPD Live Webinar Series
Held During the 46th Annual ONS Congress

Chronic Lymphocytic Leukemia

Thursday, April 29, 2021
8:30 AM – 10:00 AM ET

Medical Oncologists

Brian T Hill, MD, PhD
John M Pagel, MD, PhD
Jennifer Woyach, MD

Oncology Nurse Practitioners

Lesley Camille Ballance, MSN, FNP-BC
Kristen E Battiato, AGNP-C
Corinne Hoffman, MS, APRN-CNP, AOCNP

Moderator

Neil Love, MD

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Camille Ballance, MSN, FNP-BC
Kristen E Battiato, AGNP-C
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Research To Practice Education Platform

Oncology Nurse Practitioners

Case Presentations

- Key patient-education issues
- Biopsychosocial considerations:
  - Family/loved ones
  - The bond that heals

Clinical Investigators

Oncology Strategy

- New agents and regimens
- Predictive biomarkers
- Ongoing research and implications

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Agenda

Introduction: The Recent History of CLL Treatment

Module 1: BTK Inhibitors

- Case: A 51-year-old woman with previously untreated CLL who receives acalabrutinib
- Case: A 64-year-old woman with previously untreated CLL/SLL
- Key relevant data sets

Module 2: Venetoclax Combinations

- Case: A 44-year-old woman with CLL who was initially observed off treatment
- Case: A 61-year-old man with favorable-risk, IGHV-mutated CLL – 13q deletion
- Key relevant data sets

Module 3: Future Directions in CLL (U2 Regimen, Pirtobrutinib, CAR T-Cell Therapy)

- Case: A 71-year-old woman with multiregimen-relapsed CLL
- Key relevant data sets

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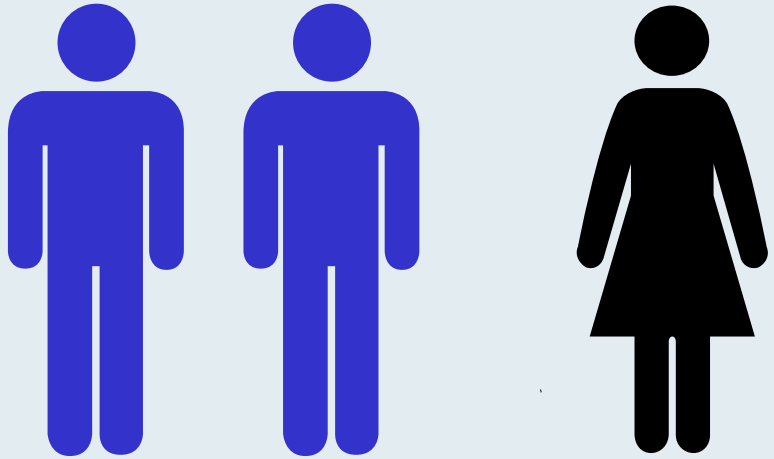
CLL Impacts a Significant Number of Patients Worldwide, Predominantly Affecting Older Patients

With an estimated 191,000 new cases globally, CLL represents 22% to 30% of all leukemia worldwide, being the most common leukemia in Western countries[1,2]

Median age at diagnosis[3]:

~90% of patients diagnosed with CLL are >55 years old[4]

Men are ~2X more likely to develop CLL[5]



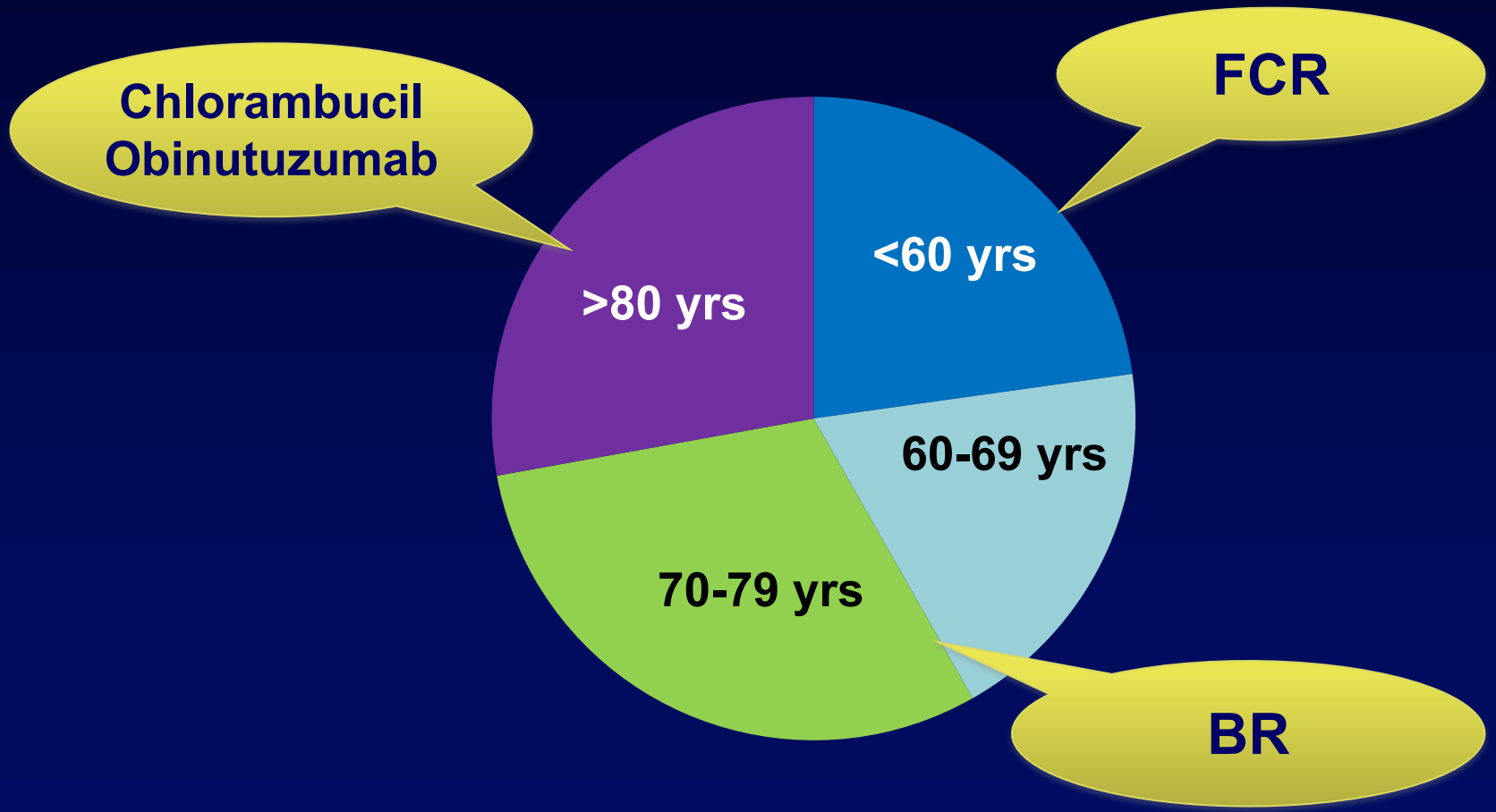
1. Union for International Cancer Control. https://www.who.int/selection_medicines/committees/expert/20/applications/CLL.pdf. Accessed November 6, 2019. 2. Combest AJ, et al. *J Hematol Oncol Pharm*. 2016;6(2):54-56. 3. Eichhorst B, et al. *Ann Oncol*. 2015;26(suppl 5):v78-v84. 4. Lymphoma Coalition. https://lymphomacoalition.org/images/subtype-reports/CLL_Europe _2017_Report.pdf. Accessed November 6, 2019. 5. Scarfò L, et al. *Crit Rev Oncol Hematol*. 2016;104:169-182.

Courtesy of John M Pagel, MD, PhD

Patients with newly diagnosed chronic lymphocytic leukemia (CLL) who feel well and are asymptomatic require treatment if…

1. Del(17p)/TP53 mutation is detected
2. White blood cell count exceeds 200,000
3. Both 1 and 2
4. Neither 1 nor 2
5. I don’t know

A simplistic (and outdated) approach to CLL



Courtesy of Brad S Kahl, MD

Novel agents in CLL have recently revolutionized therapy

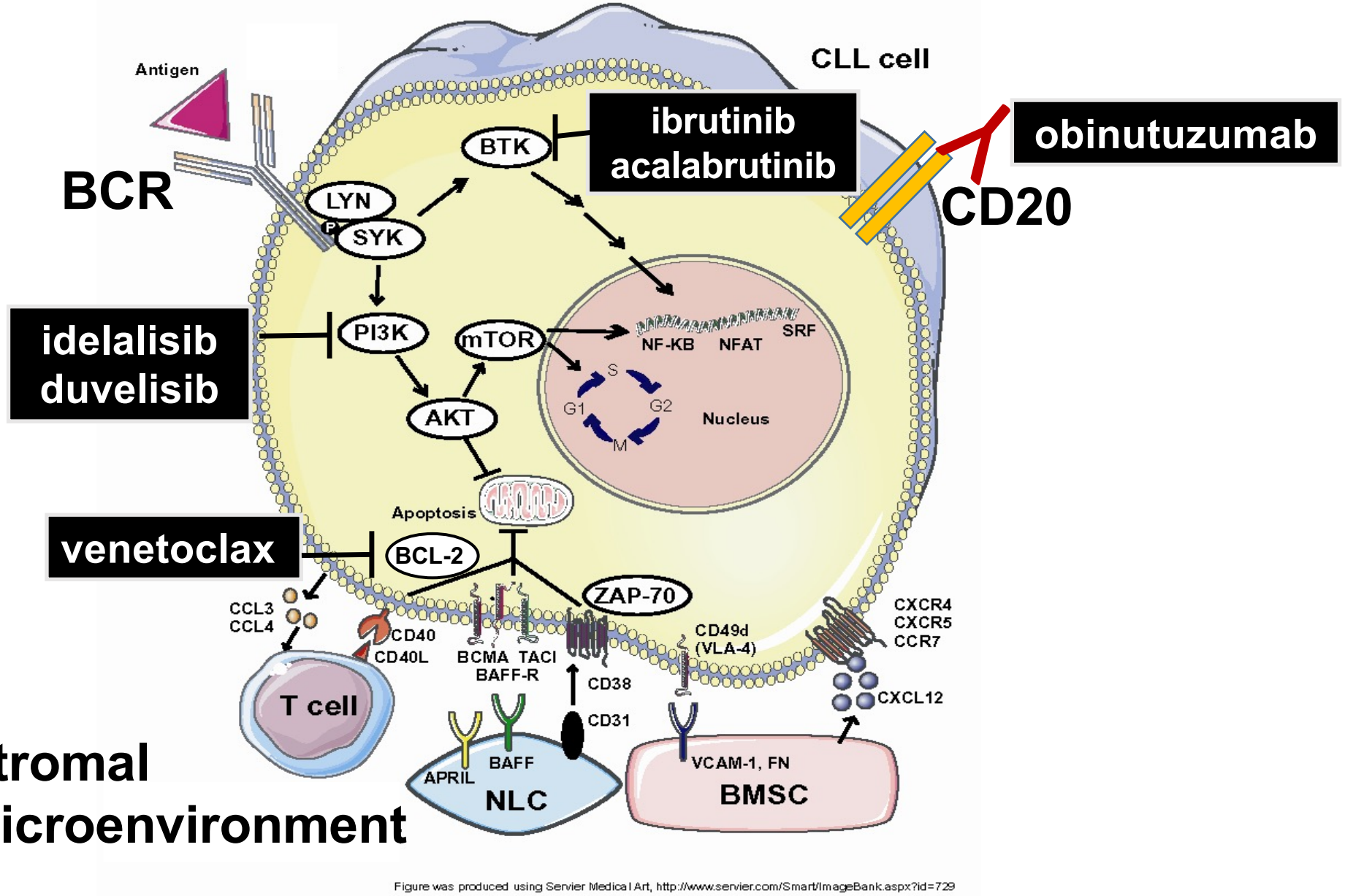


Figure was produced using Servier Medical Art, http://www.servier.com/Smart/ImageBank.aspx?id=729

Courtesy of Matthew S Davids, MD

Adapted from Davids and Brown, *Leuk Lymphoma*, 2012

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The use of anticoagulant therapy is an absolute contraindication to the use of ibrutinib for patients with CLL.

1. Agree
2. Disagree
3. I’m not sure

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BTK inhibitors should be temporarily discontinued in patients scheduled to undergo surgical procedures.

1. Agree
2. Disagree
3. I’m not sure

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In separate head-to-head trials evaluating acalabrutinib and zanubrutinib, each in comparison to ibrutinib, both agents demonstrated…

1. A significantly lower risk of atrial fibrillation versus ibrutinib
2. A significantly higher risk of atrial fibrillation versus ibrutinib
3. An equivalent risk of atrial fibrillation versus ibrutinib
4. I'm not sure

Case Presentation: A 51-year-old woman with previously untreated CLL who receives acalabrutinib

- 2014: Diagnosed with CLL, on watch and wait past 6 years
- In the past few months, WBC increasing, Hgb <11, platelets decreasing, asymptomatic
- IGHV mutated, del(13q)
- Prefers oral medication
- Reluctant to begin treatment
- Acalabrutinib
- Very active mother, who homeschools her children; informed them she has a chronic disease
- Educated the patient about acalabrutinib-related headache, lymphocytosis, importance of adherence

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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Case Presentation: A 64-year-old woman with previously untreated CLL/SLL

- 2017: Diagnosed with SLL, initially on watch and wait
- In the past few months, became anemic and had painful cervical lymph nodes
- IGHV unmutated, 13q, trisomy 12, borderline 17p
- Discussed frontline CLL treatment options
- Caregiver for her mother and opted for oral therapy
  - Acalabrutinib → adenopathy resolved within a week

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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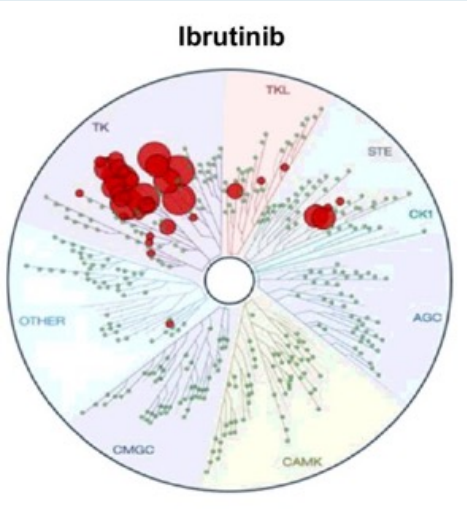
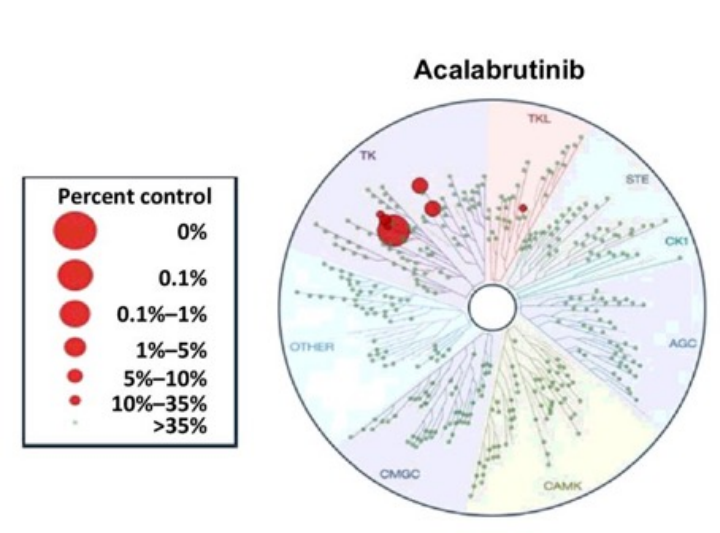
Overview of BTK Inhibitors in CLL

Irreversible

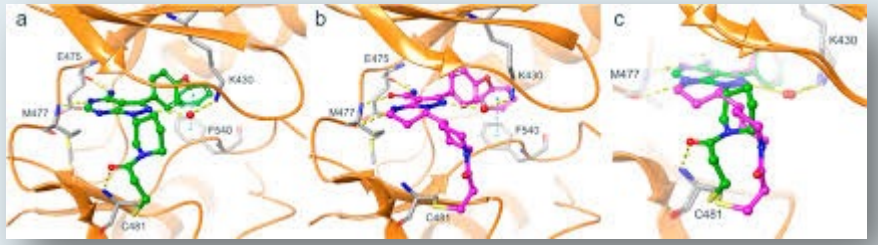
Ibrutinib



Acalabrutinib

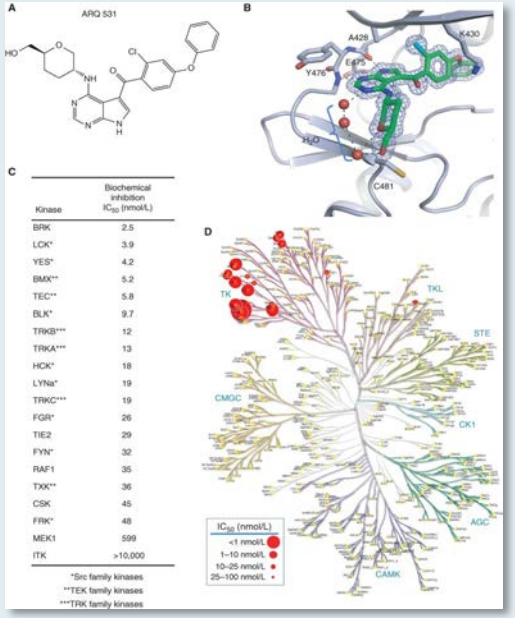


Zanubrutinib

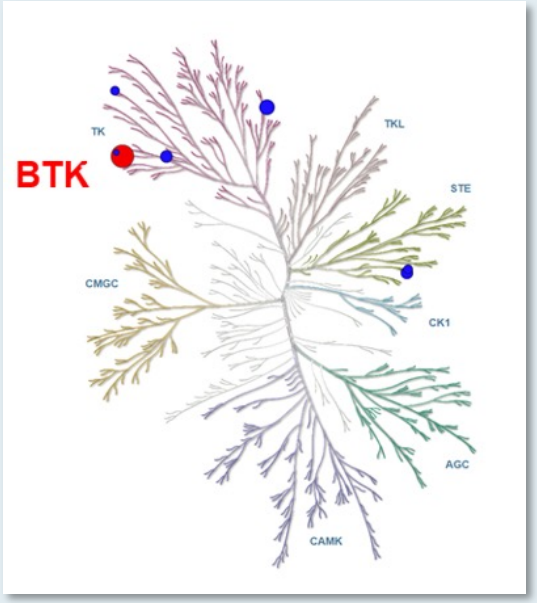


Reversible

ARQ-531 (MK-1026)



Pirtobrutinib (LOXO-305)



Courtesy of Matthew S Davids, MD, MMSc

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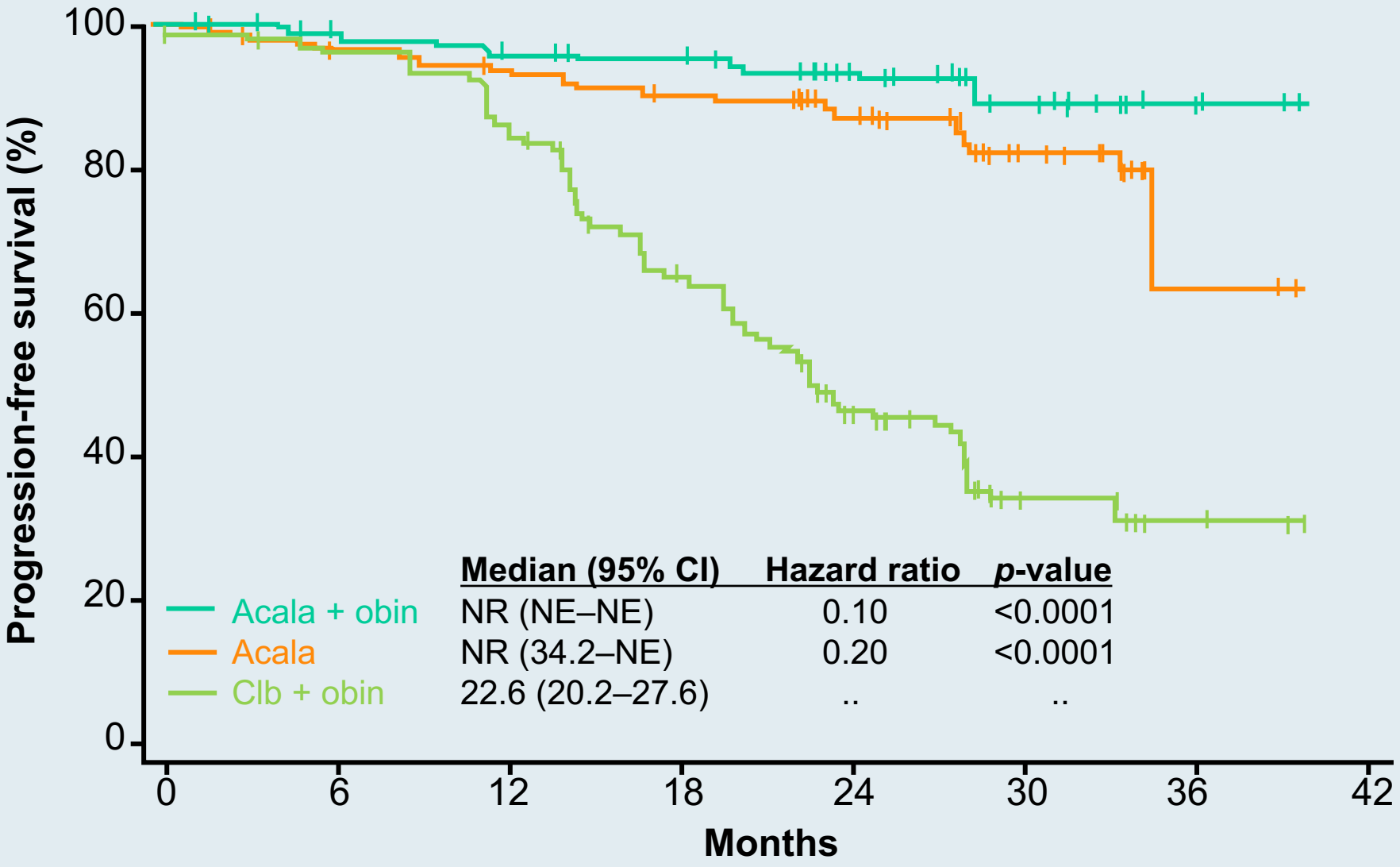
Articles

Acalabrutinib with or without obinutuzumab versus chlorambucil and obinutuzumab for treatment-naive chronic lymphocytic leukaemia (ELEVATE-TN): a randomised, controlled, phase 3 trial

Jeff P Sharman, Miklos Egyed, Wojciech Jurczak, Alan Skarbnik, John M Pagel, Ian W Flinn, Manali Kamdar, Talha Munir, Renata Walewska, Gillian Corbett, Laura Maria Fogliatto, Yair Herishanu, Versha Banerji, Steven Coutre, George Follows, Patricia Walker, Karin Karlsson, Paolo Ghia, Ann Janssens, Florence Cymbalista, Jennifer A Woyach, Gilles Salles, William G Wierda, Raquel Izumi, Veerendra Munugalavadla, Priti Patel, Min Hui Wang, Sofia Wong, John C Byrd

Lancet 2020;395(10232):1278-91.

ELEVATE-TN: PFS (IRC)



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

original reports

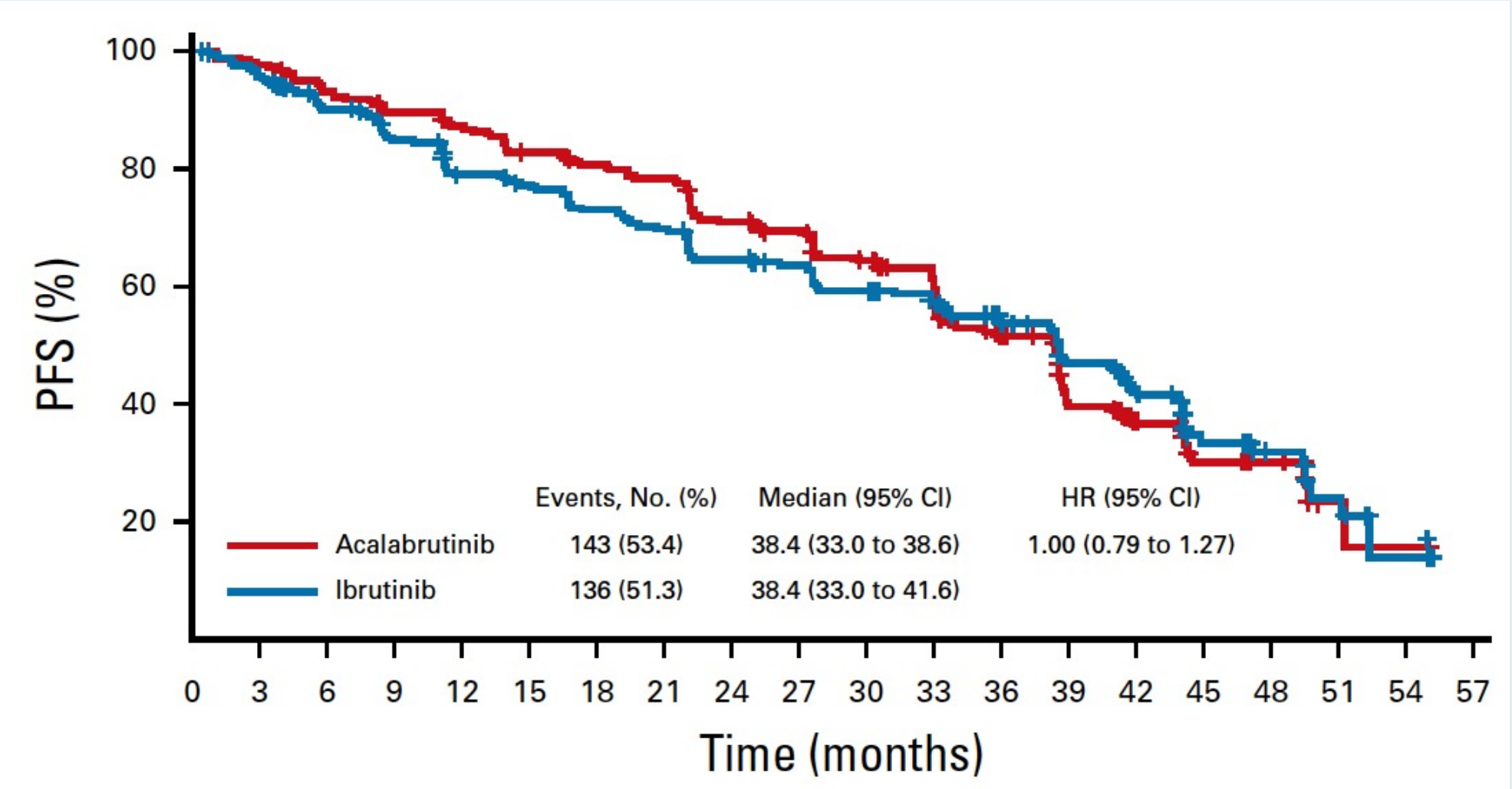
Acalabrutinib Versus Ibrutinib in Previously Treated Chronic Lymphocytic Leukemia: Results of the First Randomized Phase III Trial

John C. Byrd, MD[1]; Peter Hillmen, MD, MBChB, PhD[2]; Paolo Ghia, MD, PhD[3,4]; Arnon P. Kater, MD, PhD[5]; Asher Chanan-Khan, MD[6]; Richard R. Furman, MD[7]; Susan O'Brien, MD[8]; Mustafa Nuri Yenerel, MD[9]; Arpad Illés, MD[10]; Neil Kay, MD[11]; Jose A. Garcia-Marco, MD, PhD[12]; Anthony Mato, MD[13]; Javier Pinilla-Ibarz, MD, PhD[14]; John F. Seymour, PhD[15]; Stephane Lepretre, MD[16,17]; Stephan Stilgenbauer, MD[18]; Tadeusz Robak, PhD[19]; Wayne Rothbaum, MS[20]; Raquel Izumi, PhD[20]; Ahmed Hamdy, MD[20]; Priti Patel, MD[21]; Kara Higgins, MS[21]; Sophia Sohoni, MD[21]; and Wojciech Jurczak, MD, PhD[22]

J Clin Oncol 2021;[Online ahead of print].

RTP RESEARCH TO PRACTICE

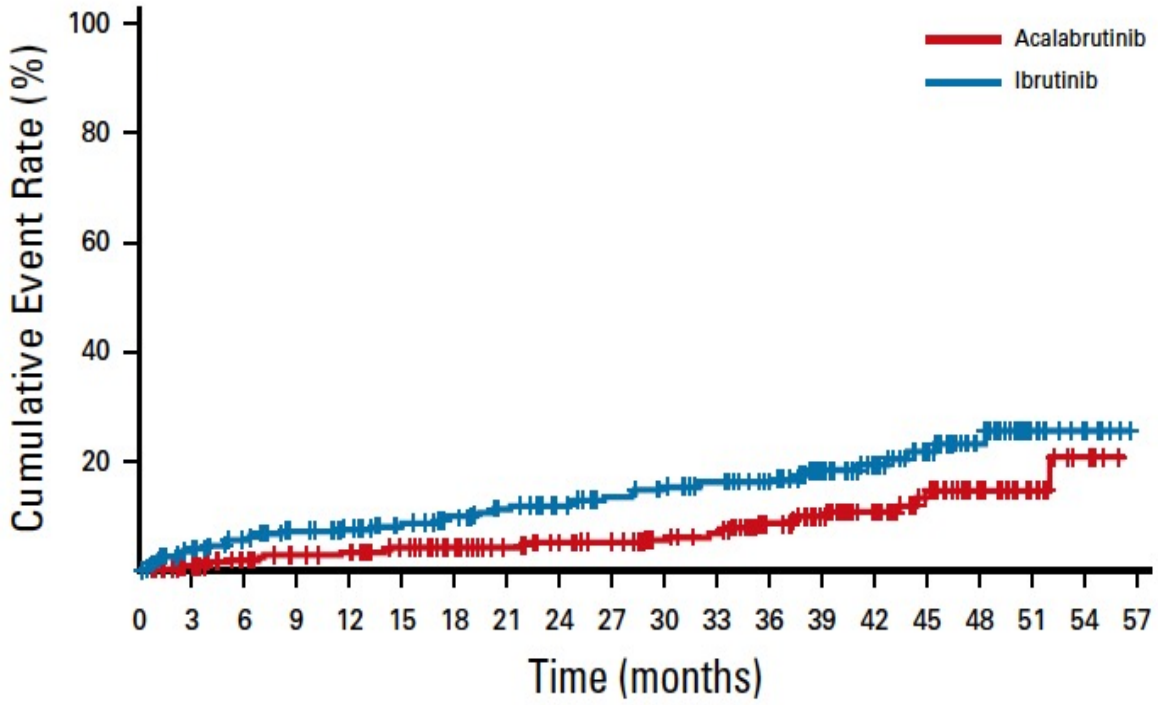
ELEVATE-RR: Primary Endpoint – Noninferiority Met on IRC-Assessed PFS



Byrd JC et al. *J Clin Oncol* 2021;[Online ahead of print]; ASCO 2021;Abstract 7500.

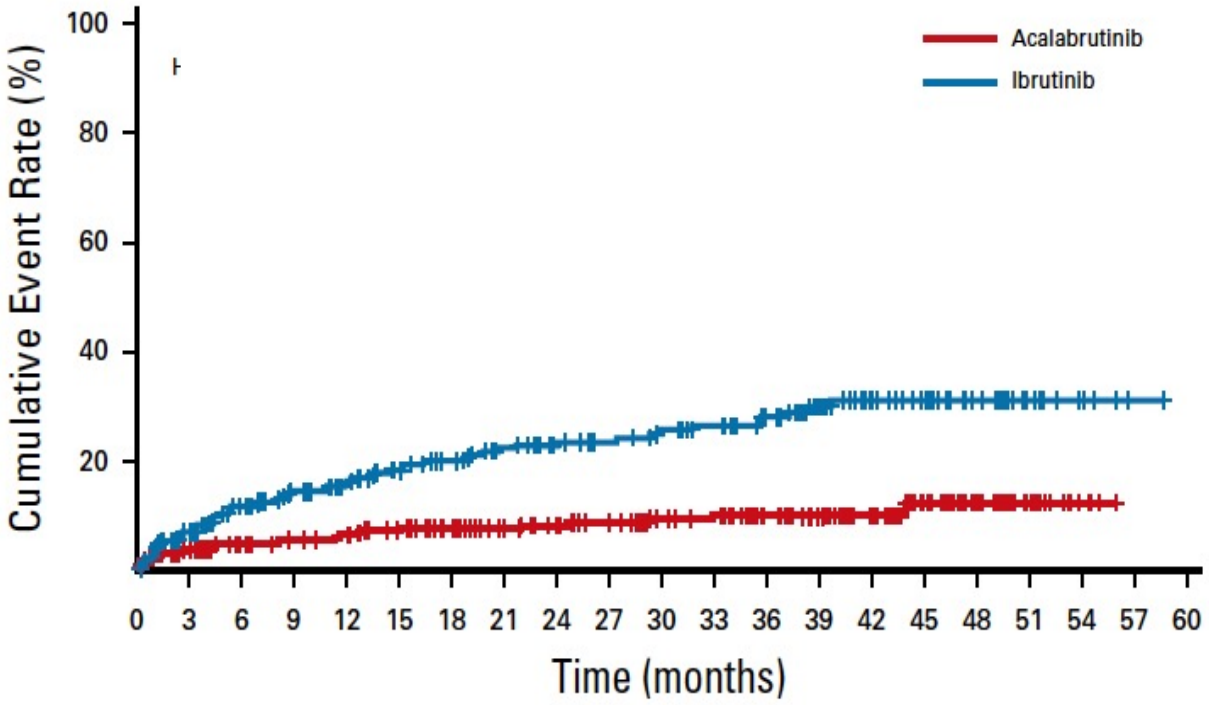
ELEVATE-RR: Cumulative Incidences of Atrial Fibrillation and Hypertension with Acalabrutinib versus Ibrutinib

Atrial Fibrillation



Acalabrutinib:Ibrutinib
HR (95% CI): 0.52 (0.32 to 0.86)

Hypertension



Acalabrutinib:Ibrutinib
HR (95% CI): 0.34 (0.21 to 0.54)

Byrd JC et al. *J Clin Oncol* 2021;[Online ahead of print]; ASCO 2021;Abstract 7500.

RTP RESEARCH TO PRACTICE

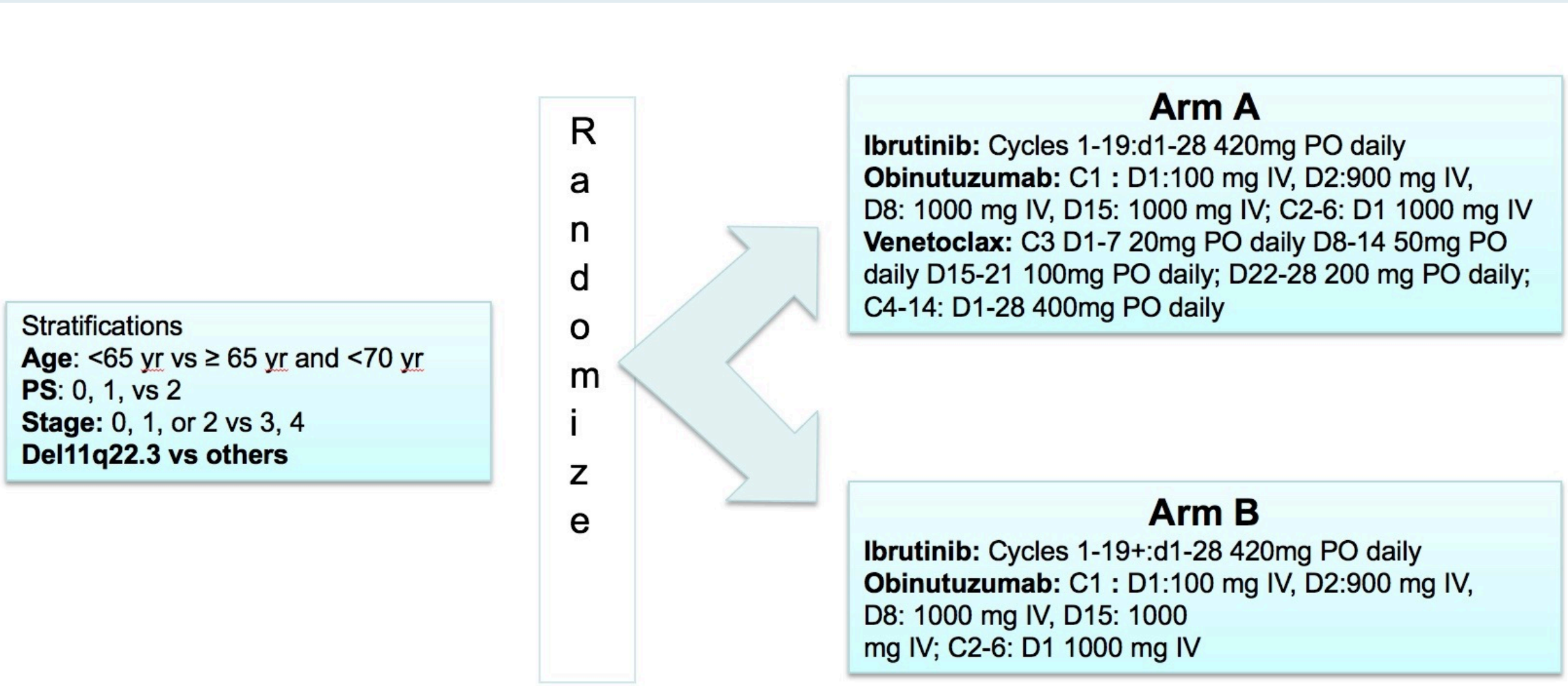
ELEVATE-RR: Adverse Events of Special Interest

Adverse events (AEs)	Acalabrutinib (n = 266)		Ibrutinib (n = 263)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Cardiac events	24.1%	8.6%	30.0%	9.5%
Atrial fibrillation	9.4%	4.9%	**16.0%**	3.8%
Ventricular tachyarrhythmias	0	0	0.4%	0.4%
Hypertension	9.4%	4.1%	**23.2%**	9.1%
Bleeding events	38.0%	3.8%	51.3%	4.6%
Major bleeding events	4.5%	3.8%	5.3%	4.6%
Infections	78.2%	30.8%	81.4%	30.0%
SPMs	9.0%	6.0%	7.6%	5.3%
Headache	34.6%		20.2%	
AEs leading to treatment discontinuation	14.7%		21.3%	

SPMs = Second primary malignancies, excluding nonmelanoma skin cancers

Byrd JC et al. ASCO 2021;Abstract 7500.

Phase III EA9161 Schema



Clinicaltrials.gov/ct2/show/NCT03701282?term=EA9161&draw=2&rank=1, Accessed March 1, 2021

FIRST INTERIM ANALYSIS OF ALPINE STUDY: RESULTS OF A PHASE 3 RANDOMIZED STUDY OF ZANUBRUTINIB VS IBRUTINIB IN PATIENTS WITH RELAPSED/REFRACTORY CHRONIC LYMPHOCYTIC LEUKEMIA/ SMALL LYMPHOCYTIC LYMPHOMA

Peter Hillmen, MBChB, PhD[1]; Barbara Eichhorst, MD[2]; Jennifer R. Brown, MD, PhD[3]; Nicole Lamanna MD[4]; Susan O'Brien, MD[5]; Constantine S. Tam, MBBS, MD[6,7,8,9]; Lugui Qiu, MD, PhD[10]; Maciej Kazmierczak, MD, PhD[11]; Keshu Zhou, MD, PhD[12]; Martin Šimkovič, MD, PhD[13,14]; Jiri Mayer, MD[15]; Amanda Gillespie-Twardy, MD[16], Mazyar Shadman, MD, MPH[17,18]; Alessandra Ferrajoli, MD[19]; Peter S. Ganly, BMBCh, PhD[20,21]; Robert Weinkove, MBBS, PhD[22,23]; Tommi Salmi, MD[24]; Meng Ji, MD[24]; Jessica Yecies, PhD[24]; Kenneth Wu, PhD[24]; William Novotny, MD[24]; Jane Huang, MD[24]; Wojciech Jurczak, MD, PhD[25]

[1]St James's University Hospital, Leeds, United Kingdom; [2]Department of Internal Medicine, University of Cologne, Cologne, Germany; [3]Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA, USA; [4]Herbert Irving Comprehensive Cancer Center, Columbia University, New York, NY, USA; [5]Chao Family Comprehensive Cancer Center, University of California, Irvine, CA, USA; [6]Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia; [7]University of Melbourne, Parkville, Victoria, Australia; [8]St Vincent's Hospital, Fitzroy, Victoria, Australia; [9]Royal Melbourne Hospital, Parkville, Victoria, Australia; [10]Chinese Academy of Medical Sciences, Peking Union Medical College, Tianjin, China; [11]Department of Hematology and Bone Marrow Transplantation, Poznan University of Medical Sciences, Poznan, Poland; [12]Affiliated Cancer Hospital of Zhengzhou University, Henan Cancer Hospital, Zhengzhou, China; [13]4th Department of Internal Medicine - Hematology, University Hospital, Hradec Kralove, Czech Republic; [14]Faculty of Medicine, Charles University, Prague, Czech Republic; [15]Department of Internal Medicine-Hematology and Oncology, Masaryk University and University Hospital, Brno, Czech Republic; [16]Blue Ridge Cancer Care, Roanoke, VA, USA; [17]Fred Hutchinson Cancer Research Center, Seattle, WA, USA; [18]Department of Medicine, University of Washington, Seattle, WA, USA; [19]Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [20]Department of Haematology, Christchurch Hospital, Christchurch, New Zealand; [21]Department of Pathology and Biomedical Science, University of Otago, Christchurch, New Zealand; [22]Wellington Blood and Cancer Centre, Capital and Coast District Health Board, Wellington, New Zealand; [23]Malaghan Institute of Medical Research, Wellington, New Zealand; [24]BeiGene (Beijing) Co, Ltd., Beijing, China and BeiGene USA, Inc, San Mateo, CA, USA; and [25]Maria Sklodowska-Curie National Institute of Oncology, Krakow, Poland

June 11, 2021
Presidential Symposium (Abstract LB1900)

EHA

EHA2021 VIRTUAL

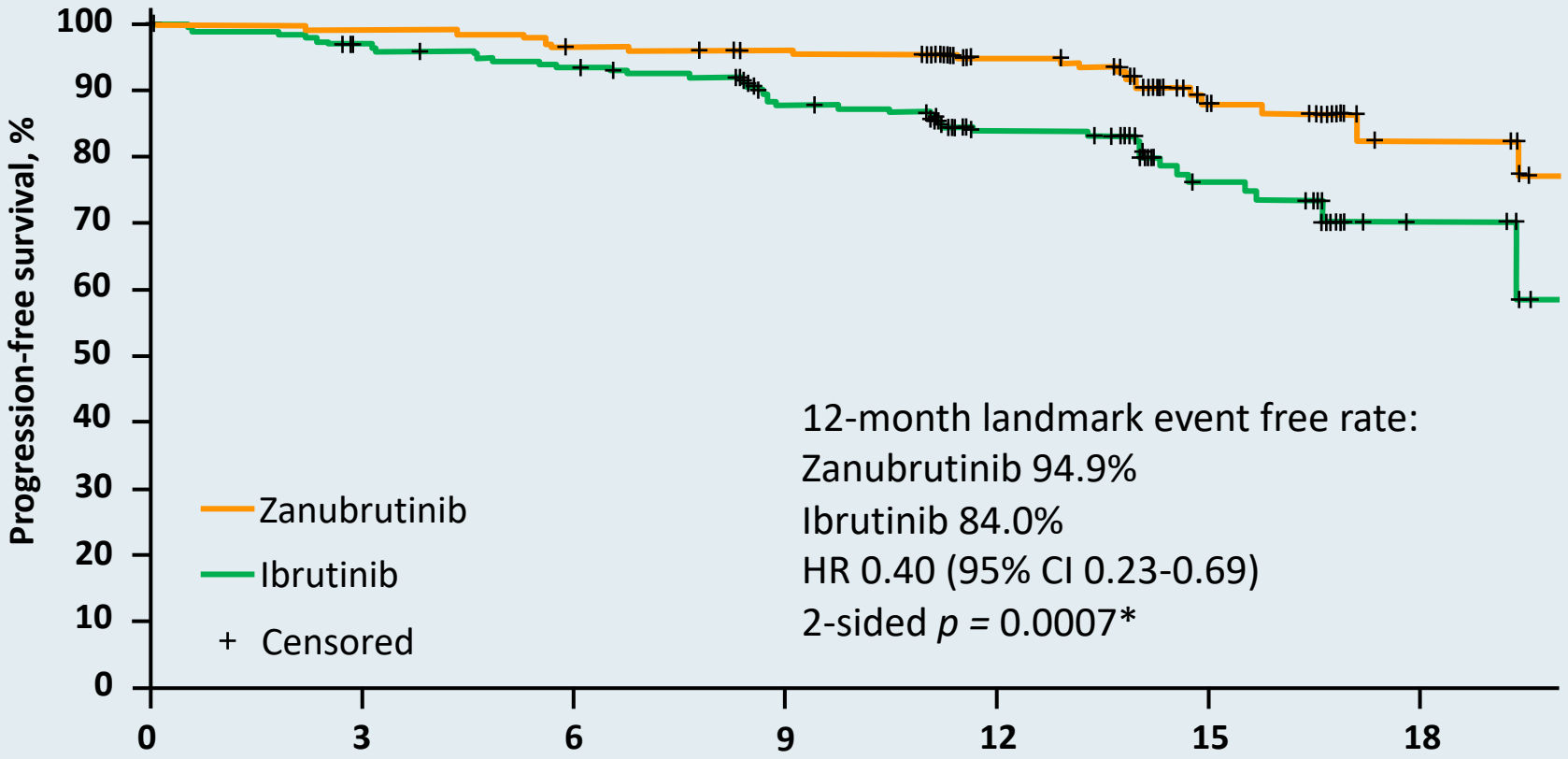
RTP RESEARCH TO PRACTICE

ALPINE: Primary Endpoint – ORR by Investigator Assessment

	Zanubrutinib (n = 207), n (%)	Ibrutinib (n = 208), n (%)
Primary endpoint: ORR (PR + CR)	162 **(78.3)** 95% CI: 72.0, 83.7	130 **(62.5)** 95% CI: 55.5, 69.1
	Superiority 2-sided *p* = 0.0006 compared with prespecified alpha of 0.0099	
CR/CRi	4 (1.9)	3 (1.4)
nPR	1 (0.5)	0
PR	157 (75.8)	127 (61.1)
ORR (PR-L + PR + CR)	*183 (88.4)*	*169 (81.3)*
PR-L	21 (10.1)	39 (18.8)
SD	17 (8.2)	28 (13.5)
PD	1 (0.5)	2 (1.0)
Discontinued or new therapy prior to first assessment	6 (2.9)	9 (4.3)
	Del(17p) (n = 24), n (%)	**Del(17p) (n = 26), n (%)**
ORR (PC + CR)	20 (83.3)	14 (53.8)

Hillmen P et al. EHA 2021;Abstract LB1900.

ALPINE: PFS by Investigator Assessment



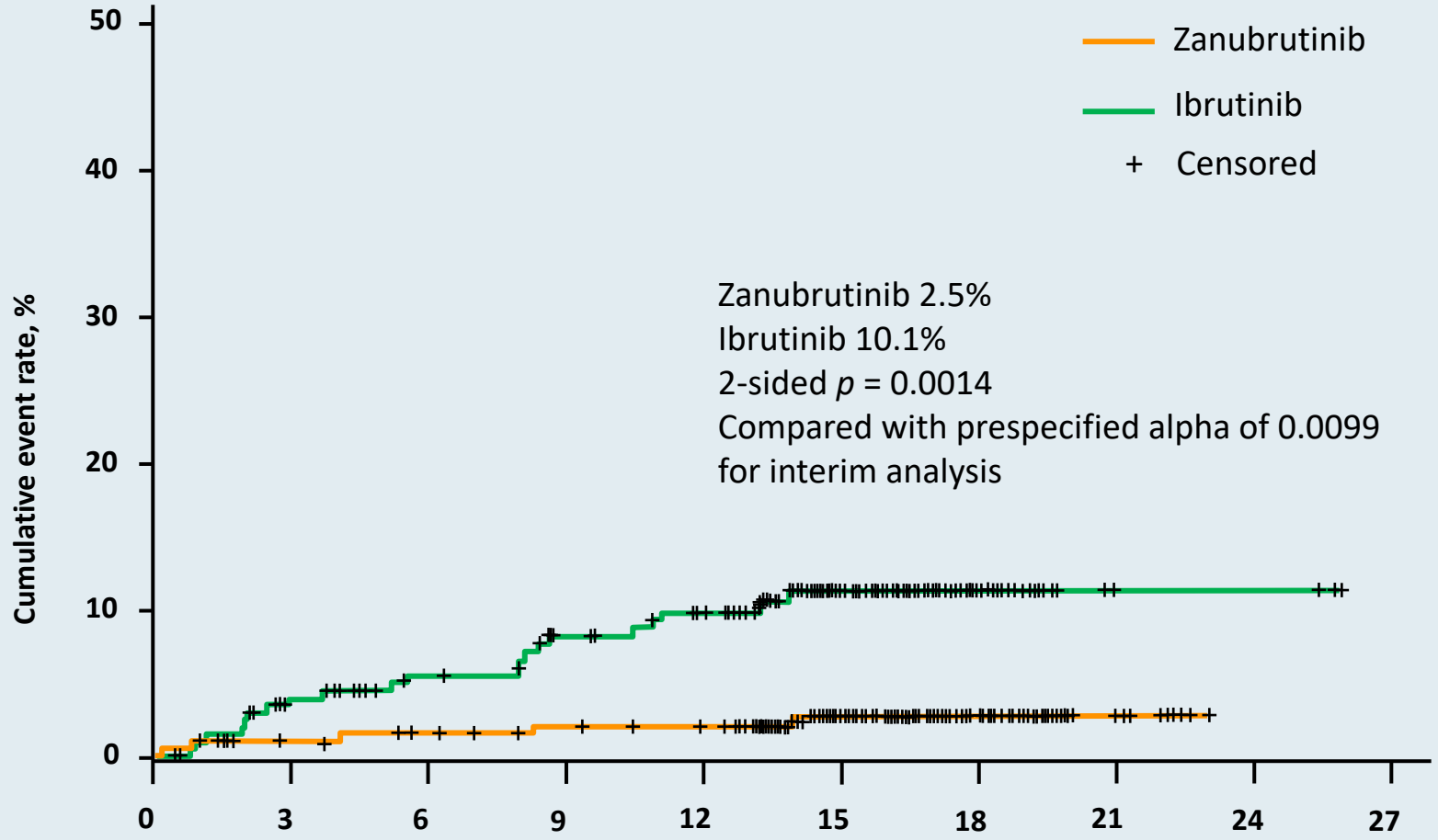
Patients at Risk							
Zanubrutinib	207	200	194	190	152	70	19
Ibrutinib	208	196	188	170	125	57	8

- Although not a pre-specified analysis, the overall 12-month PFS was higher with zanubrutinib vs ibrutinib (94.9% vs 84.0%)

*Not a prespecified analysis; formal analysis of PFS will be based on all patients when the target number of events are reached.

Hillmen P et al. EHA 2021;Abstract LB1900.

ALPINE: Incidence of Atrial Fibrillation with Zanubrutinib versus Ibrutinib



Patients at Risk										
Zanubrutinib	204	197	194	190	187	114	40	9	0	0
Ibrutinib	207	190	179	168	160	91	26	3	3	0

Hillmen P et al. EHA 2021;Abstract LB1900.

RTP RESEARCH TO PRACTICE

ALPINE: Adverse Events of Special Interest

Safety Analysis Population	Zanubrutinib (n=204), n (%)		Ibrutinib (n=207), n (%)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Cardiac disorders[a]	28 (13.7)	5 (2.5)	52 (25.1)	14 (6.8)
Atrial fibrillation and flutter (key 2º endpoint)	**5 (2.5)**	**2 (1.0)**	**21 (10.1)**	**4 (1.9)**
Hemorrhage Major hemorrhage[b]	73 (35.8) 6 (2.9)	6 (2.9) 6 (2.9)	75 (36.2) 8 (3.9)	6 (2.9) 6 (2.9)
Hypertension	34 (16.7)	22 (10.8)	34 (16.4)	22 (10.6)
Infections	122 (59.8)	26 (12.7)	131 (63.3)	37 (17.9)
Neutropenia[c]	58 (28.4)	38 (18.6)	45 (21.7)	31 (15.0)
Thrombocytopenia[c]	19 (9.3)	7 (3.4)	26 (12.6)	7 (3.4)
Secondary primary malignancies Skin cancers	17 (8.3) 7 (3.4)	10 (4.9) 3 (1.5)	13 (6.3) 10 (4.8)	4 (1.9) 2 (1.0)

[a]Cardiac disorders leading to treatment discontinuation: zanubrutinib 0 patients and ibrutinib 7 (3.4%) patients.
[b]Includes serious or Grade ≥3 hemorrhage or any Grade CNS hemorrhage
[c]Pooled terms including neutropenia, neutrophil count decreased, and febrile neutropenia; thrombocytopenia and platelet count decreased.

Hillmen P et al. EHA 2021;Abstract LB1900.

Positive Topline Results Announced from the Phase III SEQUOIA Trial: Zanubrutinib versus BR for Treatment-Naïve CLL

Press Release: July 29, 2021

"The SEQUOIA trial met the primary endpoint at interim analysis, with zanubrutinib significantly prolonging progression-free survival compared to chemoimmunotherapy, and safety and tolerability consistent with its known profile. SEQUOIA is the second positive global Phase 3 trial of zanubrutinib in chronic lymphocytic leukemia, following ALPINE in the relapsed or refractory setting.

With a median follow-up of 25.8 months, the SEQUOIA trial met the primary endpoint of progression-free survival (PFS) as assessed by independent review committee (IRC), as zanubrutinib achieved a highly statistically significant improvement in PFS compared to B + R.

In addition, the trial demonstrated a statistically significant improvement in PFS per investigator assessment, a secondary endpoint. Zanubrutinib was also generally well-tolerated, consistent with its known safety profile."

https://www.businesswire.com/news/home/20210729006225/en/BeiGene-Announces-Positive-Topline-Results-from-Phase-3-SEQUOIA-Trial-Comparing-BRUKINSA%C2%AE-Zanubrutinib-to-Bendamustine-Plus-Rituximab-in-Patients-with-Treatment-Na%C3%AFve-Chronic-Lymphocytic-Leukemia

Agenda

Introduction: The Recent History of CLL Treatment

Module 1: BTK Inhibitors

- Case: A 51-year-old woman with previously untreated CLL who receives acalabrutinib
- Case: A 64-year-old woman with previously untreated CLL/SLL
- Key relevant data sets

Module 2: Venetoclax Combinations

- Case: A 44-year-old woman with CLL who was initially observed off treatment
- Case: A 61-year-old man with favorable-risk, IGHV-mutated CLL – 13q deletion
- Key relevant data sets

Module 3: Future Directions in CLL (U2 Regimen, Pirtobrutinib, CAR T-Cell Therapy)

- Case: A 71-year-old woman with multiregimen-relapsed CLL
- Key relevant data sets

Case Presentation: A 44-year-old woman with CLL who was initially observed off treatment

- 2017: Research nurse diagnosed with CLL → Observation
- Doubling of WBC in the past 6 months
  - IGHV mutated, trisomy 12
- Obinutuzumab/venetoclax completed beginning 2021
  - WBC decreased, but significant fatigue
- Counseling patient about what to expect from obinutuzumab/venetoclax
- Explaining tumor lysis syndrome

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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Case Presentation: A 61-year-old man with favorable-risk, IGHV-mutated CLL – 13q deletion

- 2018: Presented with axillary adenopathy, enlarged spleen and thrombocytopenia
- Bone marrow biopsy: 65% CLL cells
- Treated with venetoclax/obinutuzumab on the Phase III CLL14 trial
  - Minimal tumor lysis syndrome during ramp up period
- Now off therapy, in complete remission and MRD-negative

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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TO PRACTICE

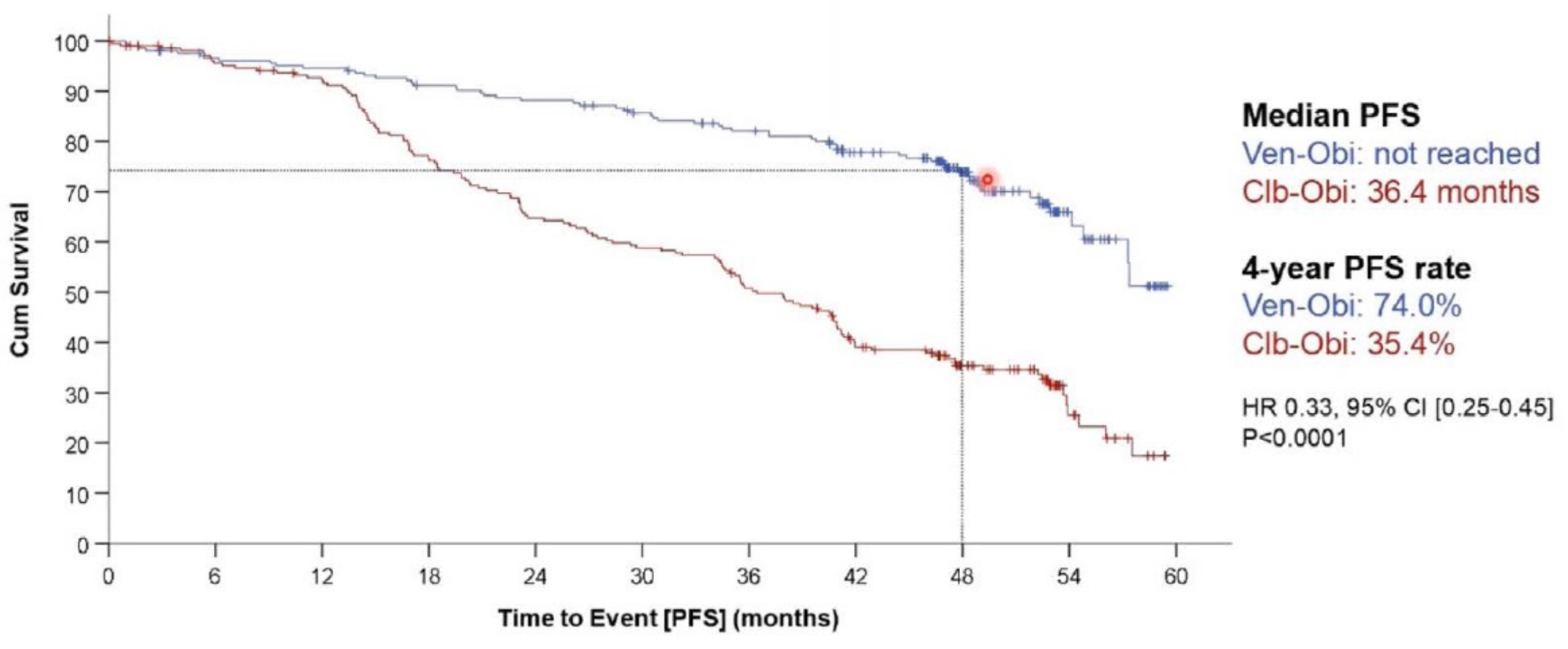
Articles

Venetoclax plus obinutuzumab versus chlorambucil plus obinutuzumab for previously untreated chronic lymphocytic leukaemia (CLL14): follow-up results from a multicentre, open-label, randomised, phase 3 trial

Othman Al-Sawaf, Can Zhang, Maneesh Tandon, Arijit Sinha, Anna-Maria Fink, Sandra Robrecht, Olga Samoylova, Anna M Liberati, Javier Pinilla-Ibarz, Stephen Opat, Liliya Sivcheva, Katell Le Dû, Laura M Fogliatto, Carsten U Niemann, Robert Weinkove, Sue Robinson, Thomas J Kipps, Eugen Tausch, William Schary, Matthias Ritgen, Clemens-Martin Wendtner, Karl-Anton Kreuzer, Barbara Eichhorst, Stephan Stilgenbauer, Michael Hallek, Kirsten Fischer**

Lancet Oncol 2020;21(9):1188-200.

CLL14: Updated 4-Year PFS



Median observation time: 52.4 months

Al-Sawaf O et al. ASH 2020;Abstract 127 .

RTP RESEARCH TO PRACTICE

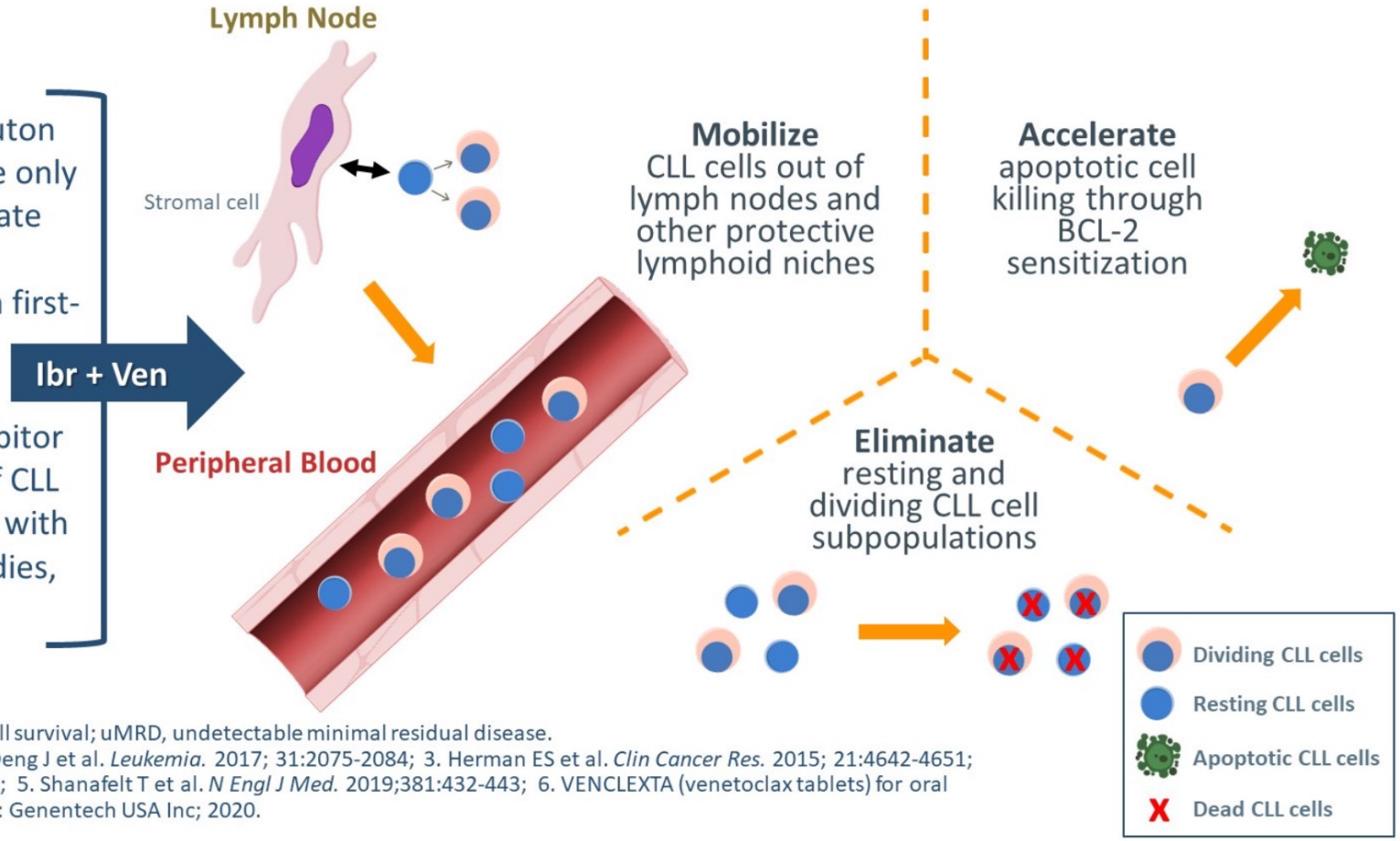
Fixed-Duration (FD) First-Line Treatment With Ibrutinib Plus Venetoclax for Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma: Primary Analysis of the FD Cohort of the Phase 2 CAPTIVATE Study

Paolo Ghia, MD, PhD[1]; John N. Allan, MD[2]; Tanya Siddiqi, MD[3]; Thomas J. Kipps, MD, PhD[4]; Ryan Jacobs, MD[5]; Stephen Opat, FRACP, FRCPA, MBBS[6]; Paul M. Barr, MD[7]; Alessandra Tedeschi, MD[8]; Livio Trentin, MD[9]; Rajat Bannerji, MD, PhD[10]; Sharon Jackson, MD[11]; Bryone Kuss, MBBS, PhD, FRACP, FRCPA[12]; Carol Moreno, MD, PhD[13]; Edith Szafer-Glusman, PhD[14]; Kristin Russell, BS[14]; Cathy Zhou, MS[14]; Joi Ninomoto, PharmD[14]; James P. Dean, MD, PhD[14]; William G. Wierda, MD, PhD[15]; Constantine Tam, MBBS, MD[16]

[1]Division of Experimental Oncology, Università Vita-Salute San Raffaele and IRCCS Ospedale San Raffaele, Milan, Italy; [2]Weill Cornell Medicine, New York, NY, USA; [3]City of Hope National Medical Center, Duarte, CA, USA; [4]UCSD Moores Cancer Center, San Diego, CA, USA; [5]Levine Cancer Institute, Charlotte, NC, USA; [6]Monash University, Clayton, VIC, Australia; [7]Wilmot Cancer Institute, University of Rochester Medical Center, Rochester, NY, USA; [8]ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy; [9]Hematology and Clinical Immunology Unit, Department of Medicine, University of Padova, Padova, Italy; [10]Rutgers Cancer Institute of New Jersey, New Brunswick, NJ, USA; [11]Middlemore Hospital, Auckland, New Zealand; [12]Flinders University and Medical Centre, Bedford Park, SA, Australia; [13]Hospital de la Santa Creu i Sant Pau, Autonomous University of Barcelona, Barcelona, Spain; [14]Pharmacyclics LLC, an AbbVie Company, Sunnyvale, CA, USA; [15]Department of Leukemia, University of Texas MD Anderson Cancer Center, Houston, TX, USA; [16]Peter MacCallum Cancer Center & St. Vincent's Hospital and the University of Melbourne, Melbourne, VIC, Australia

Rationale: Ibrutinib and Venetoclax Have Distinct and Complementary Modes of Action That Work Synergistically[1-3]

- Ibrutinib, a once-daily oral Bruton tyrosine kinase inhibitor, is the only targeted therapy to demonstrate significant OS benefit in randomized phase 3 studies in first-line CLL[4,5]
- Venetoclax, an oral BCL-2 inhibitor approved for the treatment of CLL as a single agent or combined with anti-CD20 monoclonal antibodies, achieves high rates of uMRD[6]

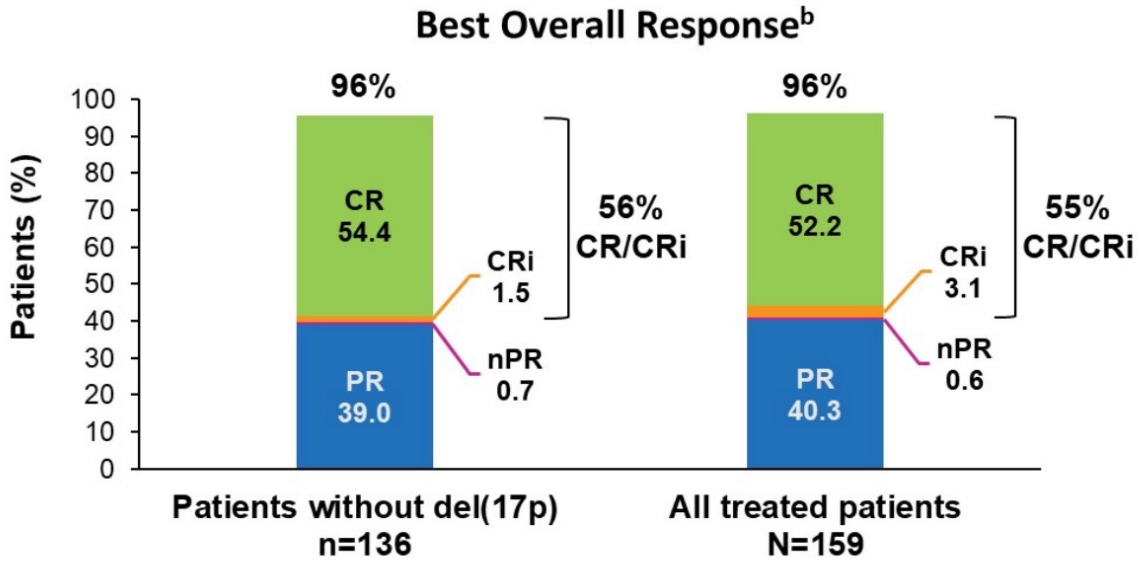


CLL, chronic lymphocytic leukemia; OS, overall survival; uMRD, undetectable minimal residual disease.

1. Lu P et al. *Blood Cancer J.* 2021; 11:39; 2. Deng J et al. *Leukemia.* 2017; 31:2075-2084; 3. Herman ES et al. *Clin Cancer Res.* 2015; 21:4642-4651; 4. Burger JA et al. *Leukemia.* 2020;34:787-798; 5. Shanafelt T et al. *N Engl J Med.* 2019;381:432-443; 6. VENCLEXTA (venetoclax tablets) for oral use [package insert]. South San Francisco, CA: Genentech USA Inc; 2020.

Ghia P et al. ASCO 2021;Abstract 7501.

Primary Endpoint of CR Rate[a]: Fixed-Duration Treatment with Ibrutinib + Venetoclax Provides Deep, Durable Responses



DOCR ≥12 cycles n/N (%)	66/76 (87)	78/88 (89)*

- Primary endpoint was met: 56% (95% CI, 48–64) CR rate[a] in patients without del(17p)
  - Significantly excludes 37% minimum rate (P<0.0001)
  - Meaningful improvement over 40% rate of historical comparator of FCR in CLL10[1]

*After achieving CR[a], 9 patients with <1 year of follow-up were not evaluable; 1 patient died 7 months after CR and completion of therapy.

nPR, nodular partial response; PR, partial response; DOCR, duration of complete response.
[a]Proportion of patients with CR or CRi. [b]Overall response was assessed at the end of Cycle 3, on Day 1 of Cycles 7, 10, 13, 19, 25, 28, and 31, and every 6 months thereafter.

1. Eichhorst B et al. *Lancet Oncol.* 2016;17:928-942.

ASCO 2021, CAPTIVATE-FD; Ghia et al.

Ghia P et al. ASCO 2021;Abstract 7501.

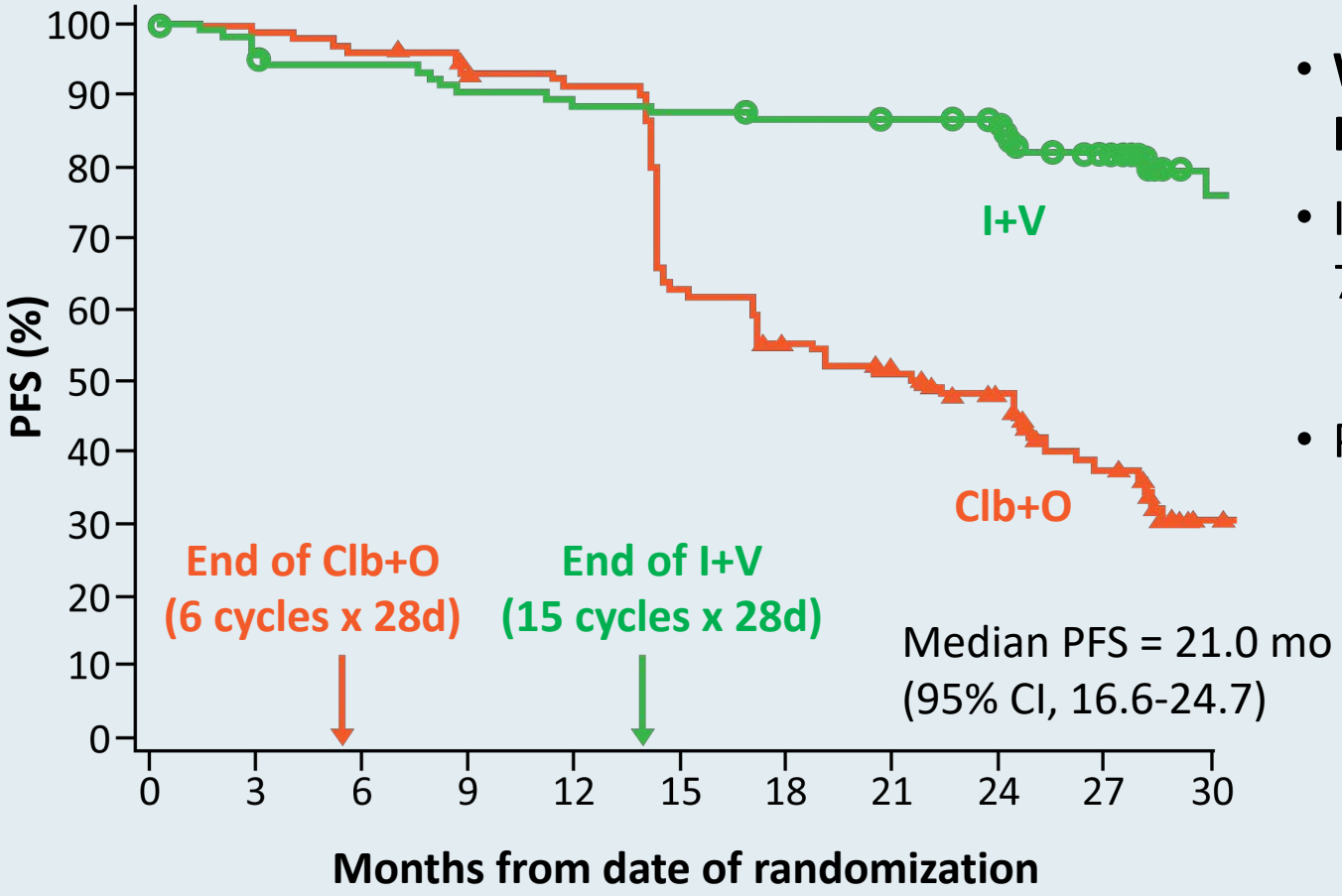
FIXED-DURATION IBRUTINIB PLUS VENETOCLAX (I+V) VERSUS CHLORAMBUCIL PLUS OBINUTUZUMAB (CLB+O) FOR FIRST-LINE TREATMENT OF CHRONIC LYMPHOCYTIC LEUKEMIA (CLL): PRIMARY ANALYSIS OF THE PHASE 3 GLOW STUDY

Arnon P. Kater,[1] Carolyn Owen,[2] Carol Moreno,[3] George Follows,[4] Talha Munir,[5] Mark-David Levin,[6] Ohad Benjamini,[7] Ann Janssens,[8] Anders Osterborg,[9] Tadeusz Robak,[10] Martin Simkovic,[11] Don Stevens,[12] Sergey Voloshin,[13] Vladimir Vorobyev,[14] Munci Yagci,[15] Loic Ysebaert,[16] Rui Qin,[17] Sriram Balasubramanian,[18] Natasha Schuier,[19] Kurt Baeten,[20] Donne Bennett Caces,[17] Carsten U. Niemann[21]

[1]Amsterdam University Medical Centers, Amsterdam, Netherlands; [2]Tom Baker Cancer Centre, Calgary, Canada; [3]Hospital de la Santa Creu i Sant Pau, Autonomous University of Barcelona, Spain; [4]Addenbrookes Hospital, Cambridge, UK; [5]St James's Hospital, Leeds, UK; [6]Albert Schweitzer Hospital, Dordrecht, Netherlands; [7]Sheba Medical Center, Ramat Gan, Israel; [8]UZ Leuven Gasthuisberg, Leuven, Belgium; [9]Karolinska University Hospital, Stockholm, Sweden; [10]Medical University of Lodz, Copernicus Memorial Hospital, Lodz, Poland; [11]University Hospital Hradec Kralove, Hradec Kralove, Czech Republic; [12]Norton Cancer Institute, Louisville, KY, USA; [13]Russian Scientific and Research Institute of Hematology and Transfusiology, St. Petersburg, Russia; [14]S.P. Botkin Moscow City Clinical Hospital, Moscow, Russia; [15]Gazi Universitesi Tip Fakultesi, Ankara, Turkey; [16]Institut Universitaire du Cancer Toulouse Oncopole, Toulouse, France; [17]Janssen Research & Development, Raritan, NJ, USA; [18]Janssen Research & Development, San Diego, CA, USA; [19]Janssen Research & Development, Düsseldorf, Germany; [20]Janssen Research & Development, Beerse, Belgium; [21]Rigshospitalet Copenhagen University Hospital, Copenhagen, Denmark

Kater AP et al. EHA 2021;Abstract LB1902.

GLOW: Progression-Free Survival by IRC

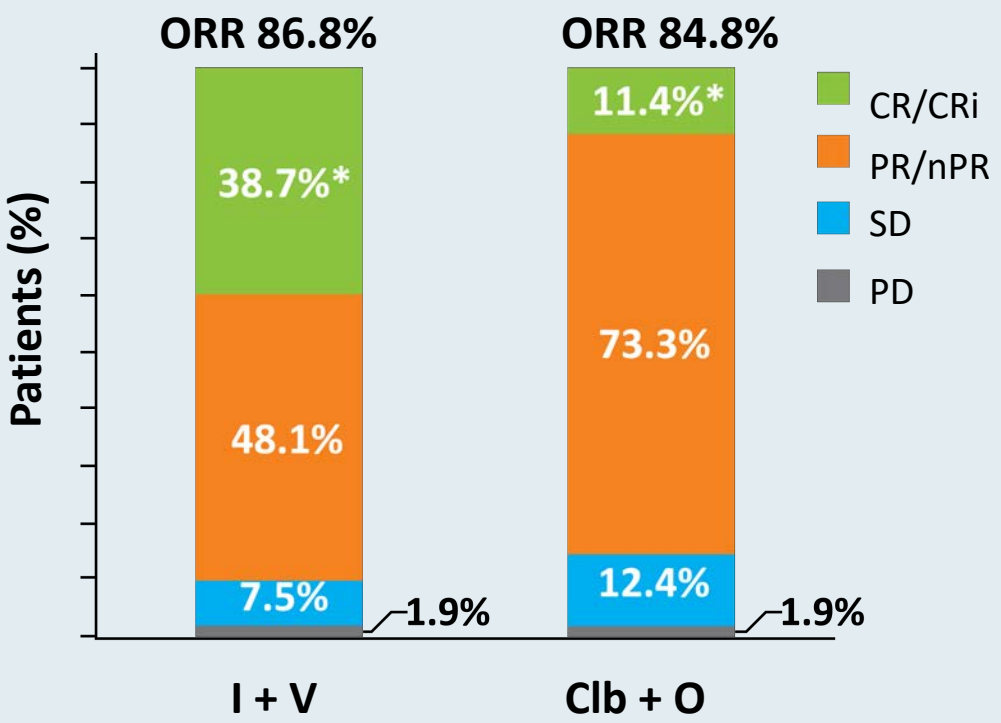


- **With a median follow up of 27.7 months, IRC-assessed PFS for I + V was superior to Clb + O**
- I + V reduced the risk of progression or death by 78% vs Clb + O
  - **HR 0.216** (95% CI, 0.131-0.357; $p < 0.0001$)
- PFS by INV assessment was consistent with IRC
  - **HR 0.207** (95% CI, 0.120-0.357; $p < 0.0001$)

Kater AP et al. EHA 2021;Abstract LB1902.

GLOW: Overall Response Rates

Response by IRC



* $p < 0.0001$

- CR/CRi rates were significantly higher for I + V vs Clb + O by both IRC and INV assessments:
  - 38.7% vs 11.4% by IRC ($p < 0.0001$)
  - 45.3% vs 13.3% by IRC ($p < 0.0001$)
- Responses to I + V were more durable:
  - 90% of responders in the I + V arm sustained IRC response 24 months after initial response vs 41% in Clb + O arm

Kater AP et al. EHA 2021;Abstract LB1902.

GLOW: Summary of Adverse Events and TLS Risk

	I + V (N = 106)	Clb + O (N = 105)
Median exposure, mo (range)	13.8 (0.7-19.5)	5.1 (1.8-7.9)
Any, %	75.5	69.5
Neutropenia	34.9	49.5
Infections	17.0	11.4
Thrombocytopenia	5.7	20.0
Diarrhea	10.4	1.0
Hypertension	5.7	0
TLS	0	5.7

- After 3 cycles of ibrutinib lead-in, <2% of patients remained at risk for TLS based on high tumor burden
- 2 (1.9%) patients in I + V arm discontinued ibrutinib due to atrial fibrillation
- SAEs in ≥5% of patients for I + V vs Clb + O: Infections (12.3% vs 8.6%) and atrial fibrillation (6.6% vs 0%)
- Rate of secondary malignancies at time of analysis: 8.5% for I + V vs 10.5% for Clb + O
  - NMSC: 3.8% vs 1.9%
  - Other: 4.7% vs 8.6%

Kater AP et al. EHA 2021;Abstract LB1902.

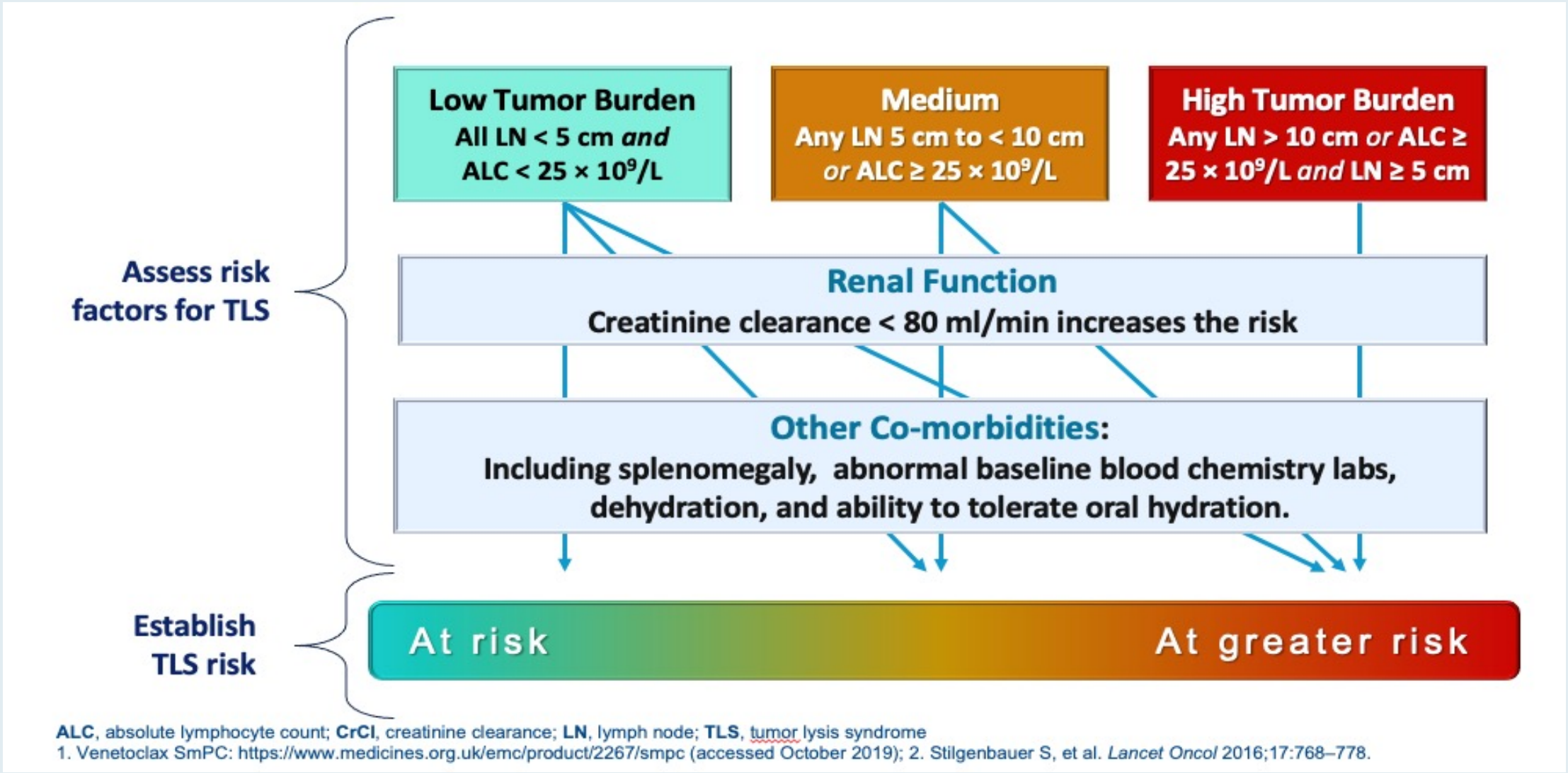
Which of the following disease-related factors is critical in attempting to determine an individual's risk of developing tumor lysis syndrome from treatment with venetoclax for CLL?

1. White blood cell count
2. Size of lymph nodes
3. Tumor grade
4. All of the above
5. Only 1 and 2
6. Only 1 and 3
7. Only 2 and 3
8. I'm not sure

Which of the following patient-related factors is most important in attempting to determine an individual's risk of developing tumor lysis syndrome from treatment with venetoclax for CLL?

1. Hepatic function
2. Renal function
3. Body mass index
4. I'm not sure

TLS Risk with Venetoclax Is a Continuum Based on Multiple Factors

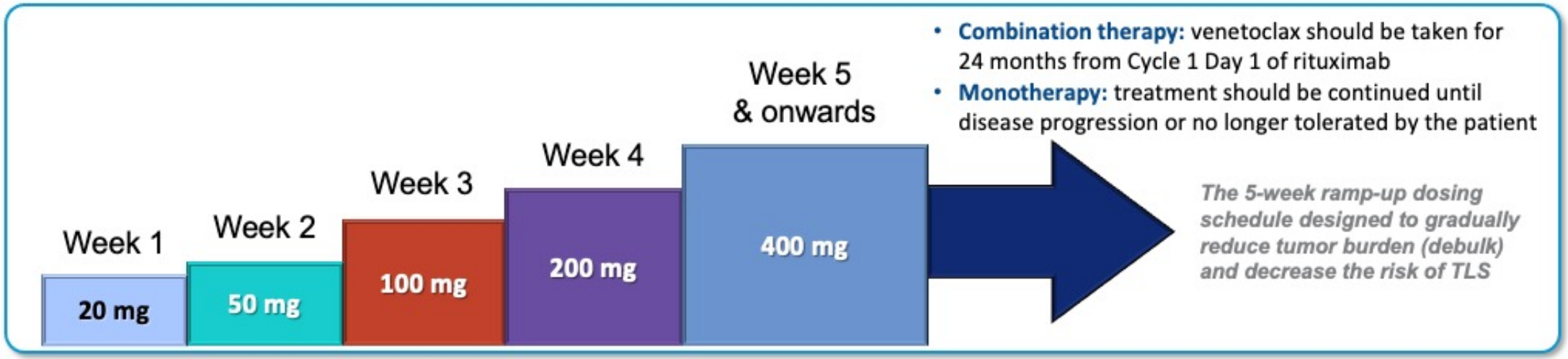


ALC, absolute lymphocyte count; **CrCl**, creatinine clearance; **LN**, lymph node; **TLS**, tumor lysis syndrome

1. Venetoclax SmPC: https://www.medicines.org.uk/emc/product/2267/smpc (accessed October 2019); 2. Stilgenbauer S, et al. *Lancet Oncol* 2016;17:768–778.

Courtesy of Matthew S Davids, MD, MMSc

Venetoclax Dose Initiation



The 5-week dose-titration schedule is designed to gradually reduce tumour burden and decrease the risk of TLS

Combination therapy: recommended dose of venetoclax in combination with rituximab is 400 mg once daily; rituximab should be administered after the patient has completed the dose-titration schedule and has received the recommended daily dose of 400 mg venetoclax for 7 days.

Monotherapy: the recommended dose of venetoclax is 400 mg once daily.

Venetoclax SmPC: https://www.medicines.org.uk/emc/product/2267/smpc (accessed October 2019).

Courtesy of Matthew S Davids, MD, MMSc

Venetoclax: TLS Prophylaxis and Monitoring

[a] **HYDRATION**	**Oral** (1.5 – 2 L); start 2 days prior to treatment start.	**IV** if needed due to higher TLS risk
ANTI-HYPER-URICAEMIC AGENTS	Patients with high uric acid or TLS risk should be administered with anti-hyperuricaemic agents **2 to 3 days prior** to treatment start	
[b,c] **LABORATORY MONITORING**	• **Pre-dose, 6–8, 24 hours** (at 1st dose of 20 mg and 50 mg, and for patients who continue to be at risk • Pre-dose at subsequent ramp-up doses	Evaluate blood chemistries and review in real time
HOSPITALIZATION	Based on physician assessment, some patients consider hospitalisation on first dose of venetoclax for more intensive prophylaxis and monitoring during the first 24 hours.	

[a]Administer intravenous hydration for any patient who cannot tolerate oral hydration; [b]Evaluate blood chemistries (potassium, uric acid, phosphorus, calcium, and creatinine); review in real time; [c]For patients at risk of TLS, monitor blood chemistries at 6–8 hours and at 24 hours at each subsequent ramp-up dose. Changes in blood chemistries consistent with TLS that require prompt management can occur as early as 6-8 hours following the first dose of venetoclax, and at each dose increase. **LN,** lymph node; **ALC**, absolute lymphocyte count; **TLS**, tumour lysis syndrome; **VEN**, venetoclax

1. Venetoclax SPC https://www.medicines.org.uk/emc/product/2267/smpc (accessed October 2019); 2. Stilgenbauer S, et al. *Lancet Oncol*. 2016; 17:768–778

Courtesy of Matthew S Davids, MD, MMSc

Agenda

Introduction: The Recent History of CLL Treatment

Module 1: BTK Inhibitors

- Case: A 51-year-old woman with previously untreated CLL who receives acalabrutinib
- Case: A 64-year-old woman with previously untreated CLL/SLL
- Key relevant data sets

Module 2: Venetoclax Combinations

- Case: A 44-year-old woman with CLL who was initially observed off treatment
- Case: A 61-year-old man with favorable-risk, IGHV-mutated CLL – 13q deletion
- Key relevant data sets

Module 3: Future Directions in CLL (U2 Regimen, Pirtobrutinib, CAR T-Cell Therapy)

- Case: A 71-year-old woman with multiregimen-relapsed CLL
- Key relevant data sets

Case Presentation: A 71-year-old woman with multiregimen-relapsed CLL

- 2009: CLL diagnosis – IGHV unmutated, trisomy 12, del(13q)
- Initial treatment: FCR
- Subsequent therapies
  - Clinical trial with PI3K inhibitor – discontinued due to colitis
  - Venetoclax/obinutuzumab
  - Venetoclax/ibrutinib
- Current therapy: Venetoclax/acalabrutinib

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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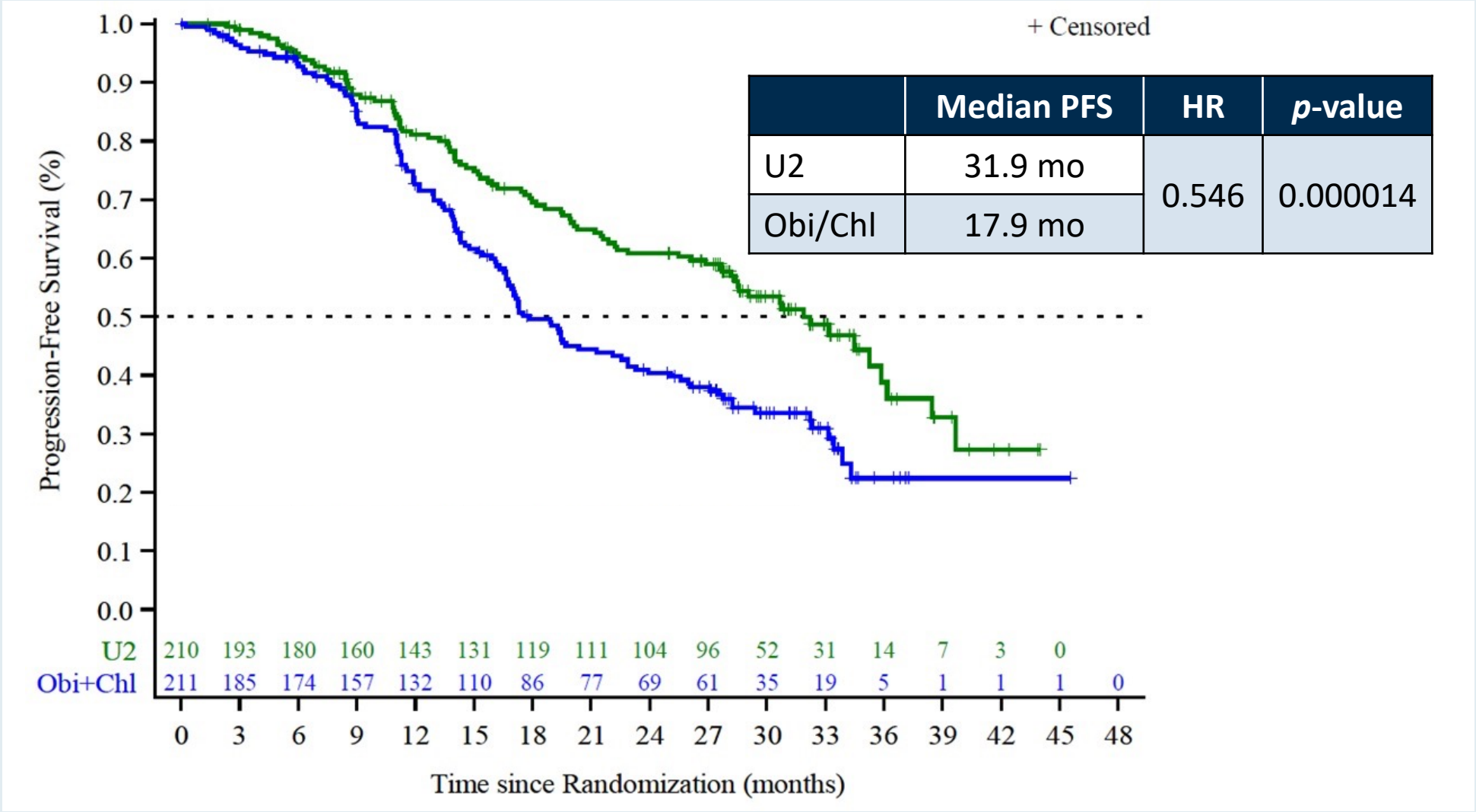
Umbralisib plus Ublituximab (U2) Is Superior to Obinutuzumab plus Chlorambucil (O + Chl) in Patients with Treatment Naïve (TN) and Relapsed/Refractory (R/R) Chronic Lymphocytic Leukemia (CLL): Results from the Phase 3 Unity-CLL Study

Gribben JG et al.

ASH 2020;Abstract 543.

UNITY-CLL: PFS with Umbralisib/Ublituximab (U2) versus Obinutuzumab/Chlorambucil



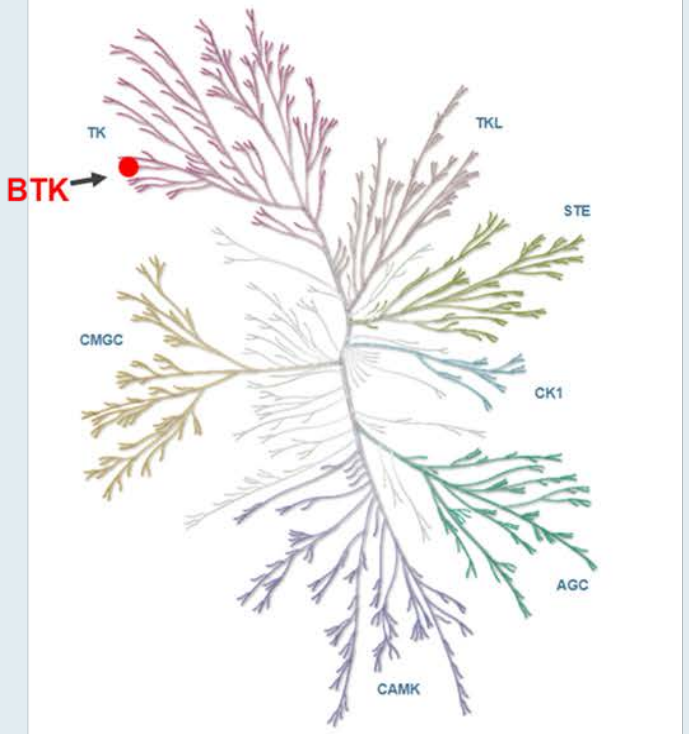
	Median PFS	HR	*p*-value
U2	31.9 mo	0.546	0.000014
Obi/Chl	17.9 mo		

Gribben JG et al. ASH 2020;Abstract 543.

LOXO-305 is a Highly Potent and Selective Non-Covalent BTK Inhibitor

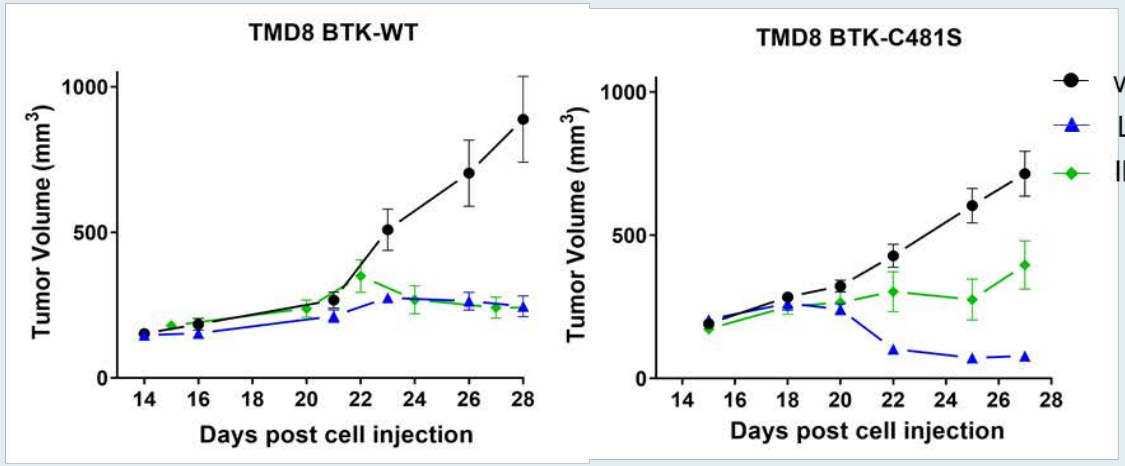
Kinome selectivity

Highly selective for BTK



Xenograft models

In vivo activity similarly efficacious as ibrutinib in WT; superior in C481S



- Nanomolar potency against WT & C481-mutant BTK in cell and enzyme assays[1,2]
- >300-fold selectivity for BTK vs 370 other kinases[1]
- Due to reversible binding mode, BTK inhibition not impacted by intrinsic rate of BTK turnover[1]
- Favorable pharmacologic properties allow sustained BTK inhibition throughout dosing interval[1]

BID, twice-daily; BTK, Bruton tyrosine kinase. Illustration reproduced courtesy of Cell Signaling Technology, Inc. (www.cellsignal.com). [1]Brandhuber et al. *Clin. Lymphoma Myeloma Leuk*. 2018;18:S216. [2]Mato et al. *Blood*. 2019:134 (Suppl 1):501.

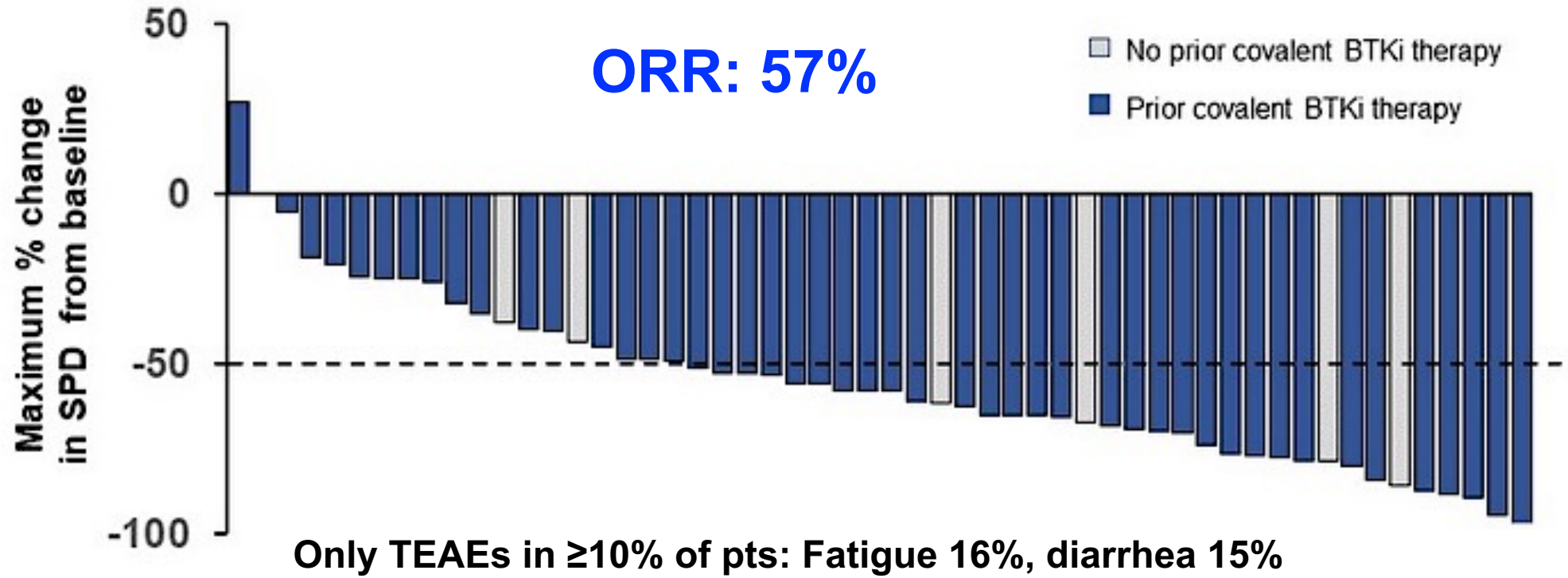
Mato AR et al. ASH 2020;Abstract 542.

LOXO-305, a Next Generation, Highly Selective, Non-Covalent BTK Inhibitor in Previously Treated CLL/SLL: Results from the Phase 1/2 BRUIN Study

Mato AR et al.

ASH 2020;Abstract 542.

BRUIN: Pirtobrutinib (LOXO-305) for Previously Treated CLL/SLL
(Median prior therapies: 4)



Only TEAEs in ≥10% of pts: Fatigue 16%, diarrhea 15%

* 11 efficacy-evaluable pts are not included in the waterfall plot, including 1 pt who discontinued prior to first response assessment, and 10 pts (4 pts with PR/PR-L and 6 pts with SD) with incomplete tumor lesion measurement data at the time of data cut

Mato AR et al. ASH 2020;Abstract 542.

Updated Follow-Up of Patients with Relapsed/Refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Treated with Lisocabtagene Maraleucel in the Phase 1 Monotherapy Cohort of Transcend CLL 004, Including High-Risk and Ibrutinib-Treated Patients

Siddiqi T et al.

ASH 2020;Abstract 546.

Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with Renal Cell Carcinoma

Friday, August 6, 2021
12:00 PM – 1:00 PM ET

Faculty

Thomas Powles, MBBS, MRCP, MD

Moderator

Neil Love, MD

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Thank you for joining us!

NCPD credit information will be emailed to each participant shortly.

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