What I Tell My Patients: Faculty Physicians and Nurses Discuss Patient Education About New Treatments and Clinical Trials

Part 3 of a 3-Part Complimentary NCPD Webinar Series
in Partnership with the 2023 ONS Congress

Chronic Lymphocytic Leukemia

Thursday, July 6, 2023
5:00 PM – 6:00 PM ET

Faculty

Kristen E Battiato, AGNP-C
Jennifer Woyach, MD

Moderator

Neil Love, MD

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RESEARCH TO PRACTICE

Faculty

Kristen E Battiato, AGNP-C
Advanced Practice Providers
Memorial Sloan Kettering Cancer Center
New York, New York

Moderator
Neil Love, MD
Research To Practice
Miami, Florida

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

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Commercial Support

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Dr Love — Disclosures

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

Ms Battiato — Disclosures

No relevant conflicts of interest to disclose.

Dr Woyach — Disclosures

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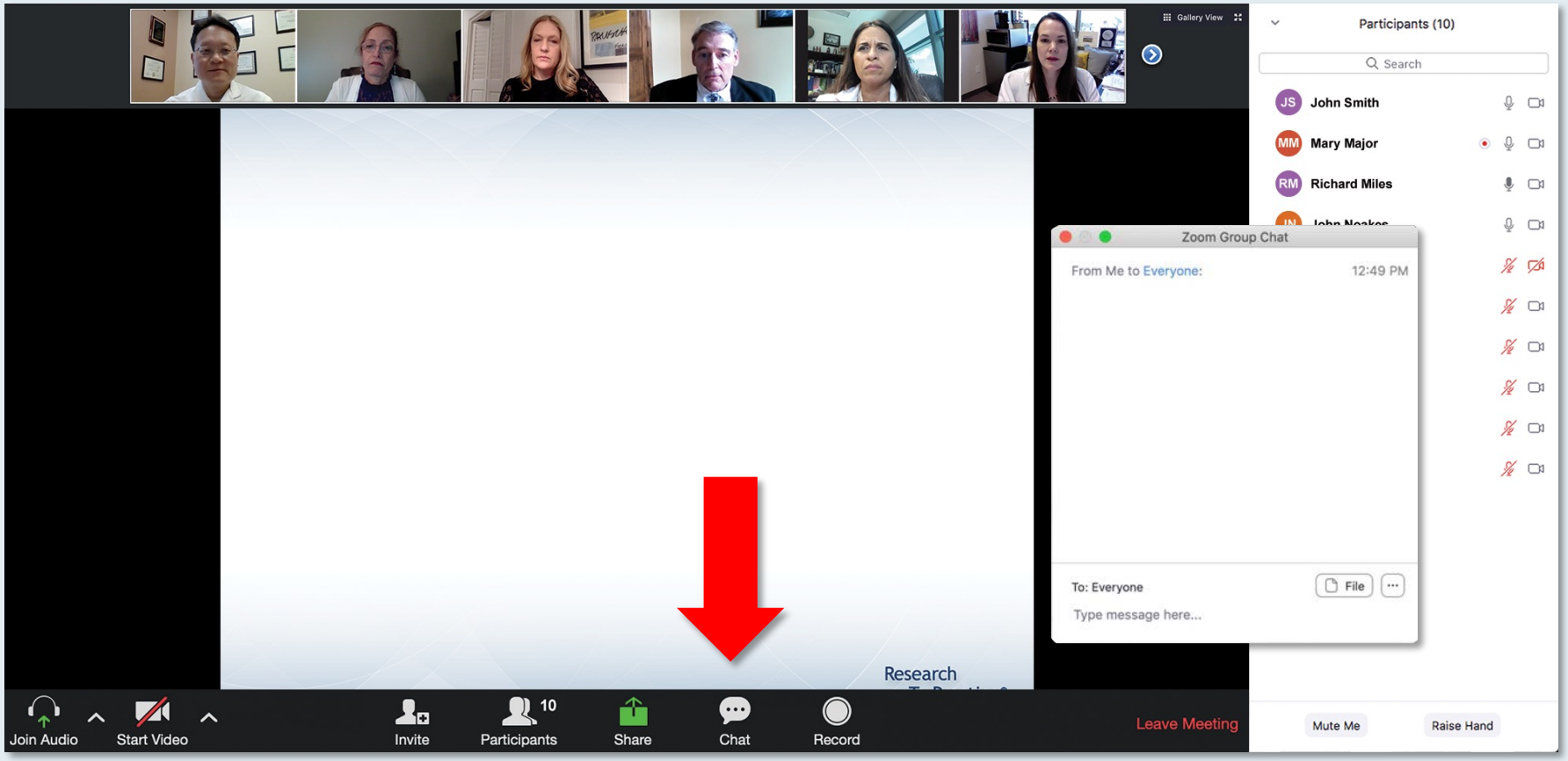

Feel free to submit questions now before the program begins and throughout the program.

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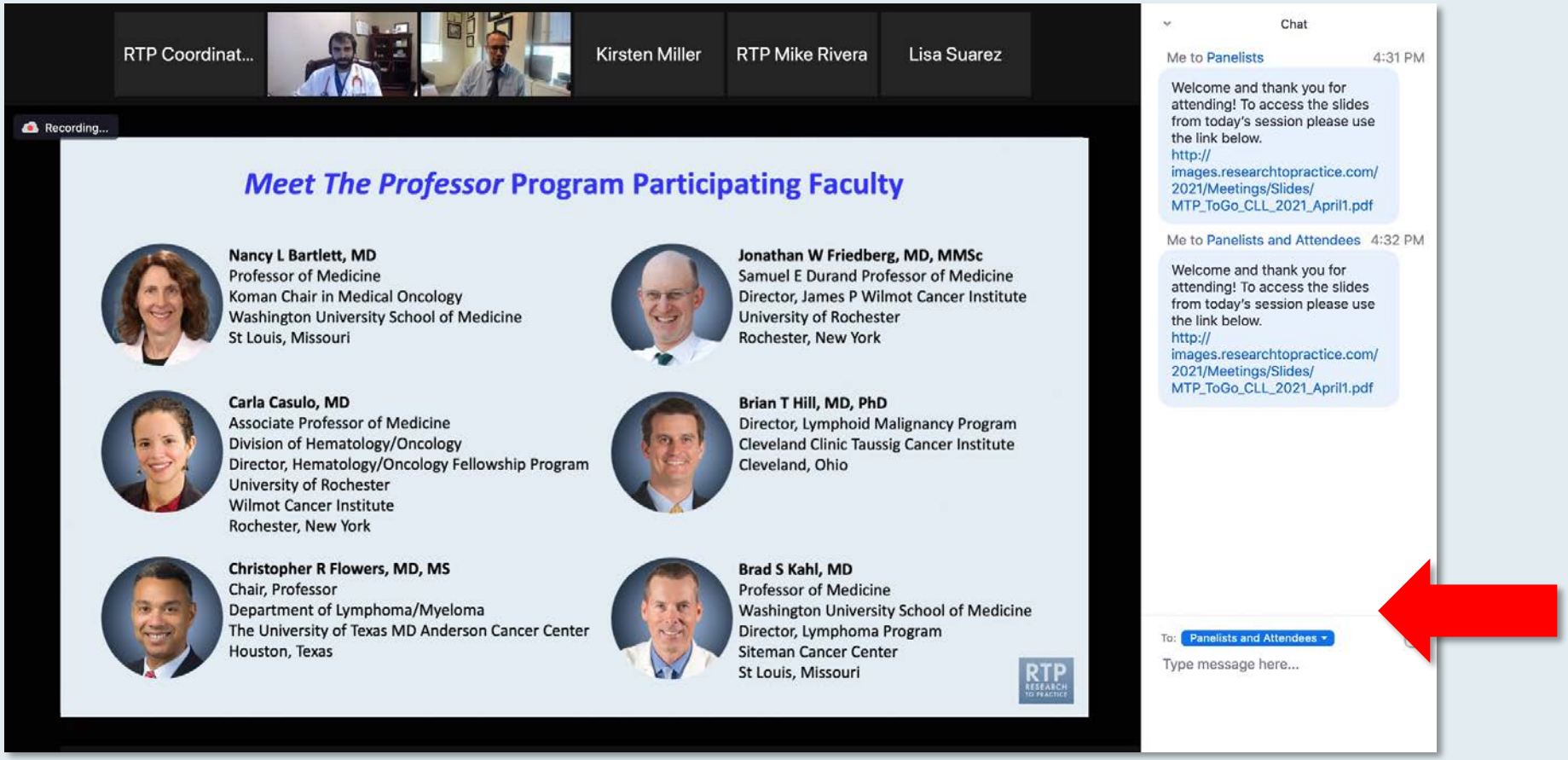
Familiarizing Yourself with the Zoom Interface

Expand chat submission box



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

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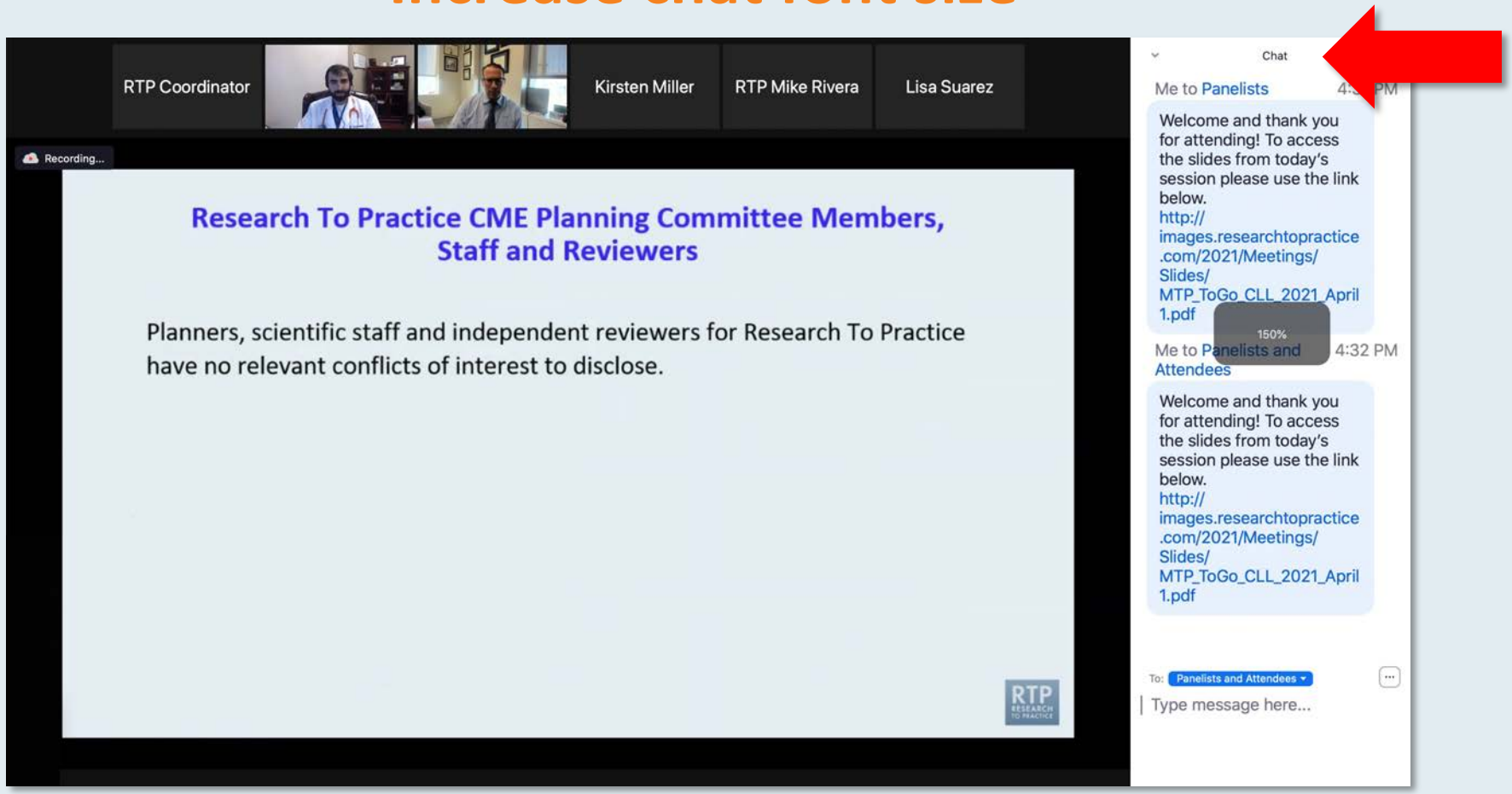
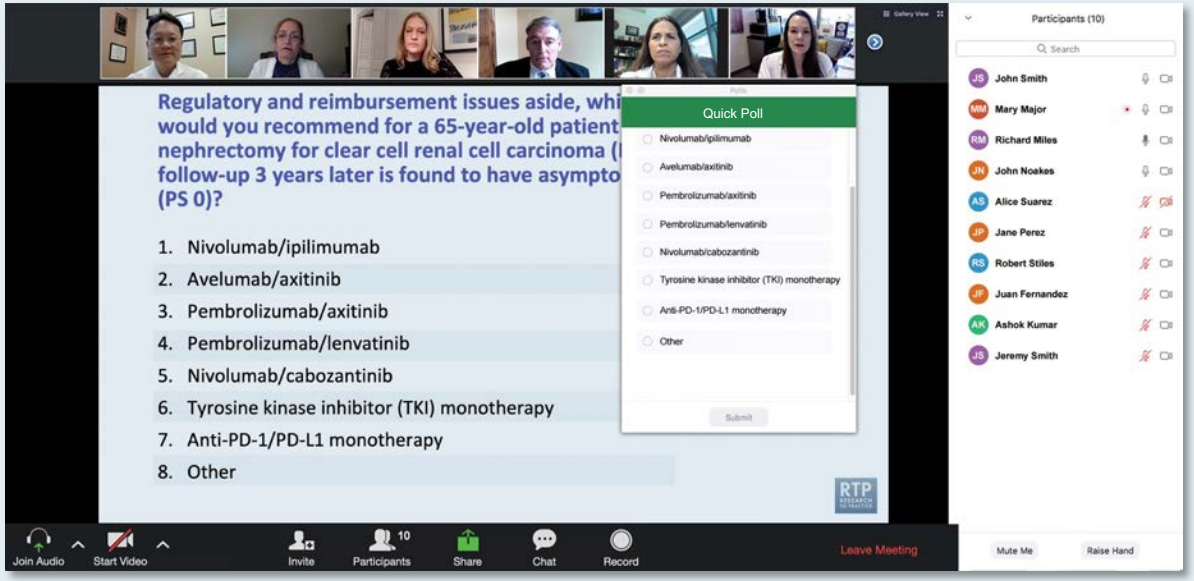
Familiarizing Yourself with the Zoom Interface

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.

Clinicians in the Audience, Please Complete the Pre- and Postmeeting Surveys



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ONCOLOGY TODAY

WITH DR NEIL LOVE

Key Presentations from the 64th American Society of Hematology (ASH) Annual Meeting: Chronic Lymphocytic Leukemia Edition

JOHN N ALLAN, MD
WEILL CORNELL MEDICINE

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Inside the Issue: Novel Agents, Approaches and Strategies in the Management of Higher-Risk Myelodysplastic Syndromes

A CME/MOC-Accredited Live Webinar

Tuesday, July 11, 2023
5:00 PM – 6:00 PM ET

Faculty

Guillermo Garcia-Manero, MD
David Sallman, MD

Moderator

Neil Love, MD

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RESEARCH TO PRACTICE

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Data Sets and Advances in Oncology

A Multitumor CME/MOC-Accredited Live Webinar Series

Melanoma and Nonmelanoma Skin Cancers

Thursday, July 13, 2023
5:00 PM – 6:00 PM ET

Faculty

Omid Hamid, MD

Evan J Lipson, MD

Moderator

Neil Love, MD

RTP Year in Review 2023

Inside the Issue: Integrating Bispecific Antibodies into the Management of Multiple Myeloma — Patient Selection and Toxicity Management

A CME/MOC-Accredited Live Webinar

Tuesday, July 18, 2023
5:00 PM – 6:00 PM ET

Faculty

Hans Lee, MD
Saad Zafar Usmani, MD, MBA

Moderator

Neil Love, MD

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RESEARCH TO PRACTICE

Inside the Issue: Current and Future Management of ER-Positive Metastatic Breast Cancer After Disease Progression on a CDK4/6 Inhibitor

A CME/MOC-Accredited Live Webinar

Thursday, July 20, 2023
5:00 PM – 6:00 PM ET

Faculty

Aditya Bardia, MD, MPH
Erika Hamilton, MD

Moderator

Neil Love, MD

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RESEARCH TO PRACTICE

Meet The Professor

Optimizing the Management of Soft Tissue Sarcoma and Related Connective Tissue Disorders

Tuesday, July 25, 2023
5:00 PM – 6:00 PM ET

Faculty

Richard F Riedel, MD

Moderator

Neil Love, MD

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Thank you for joining us!

NCPD credit information will be emailed to each participant within 5 business days.

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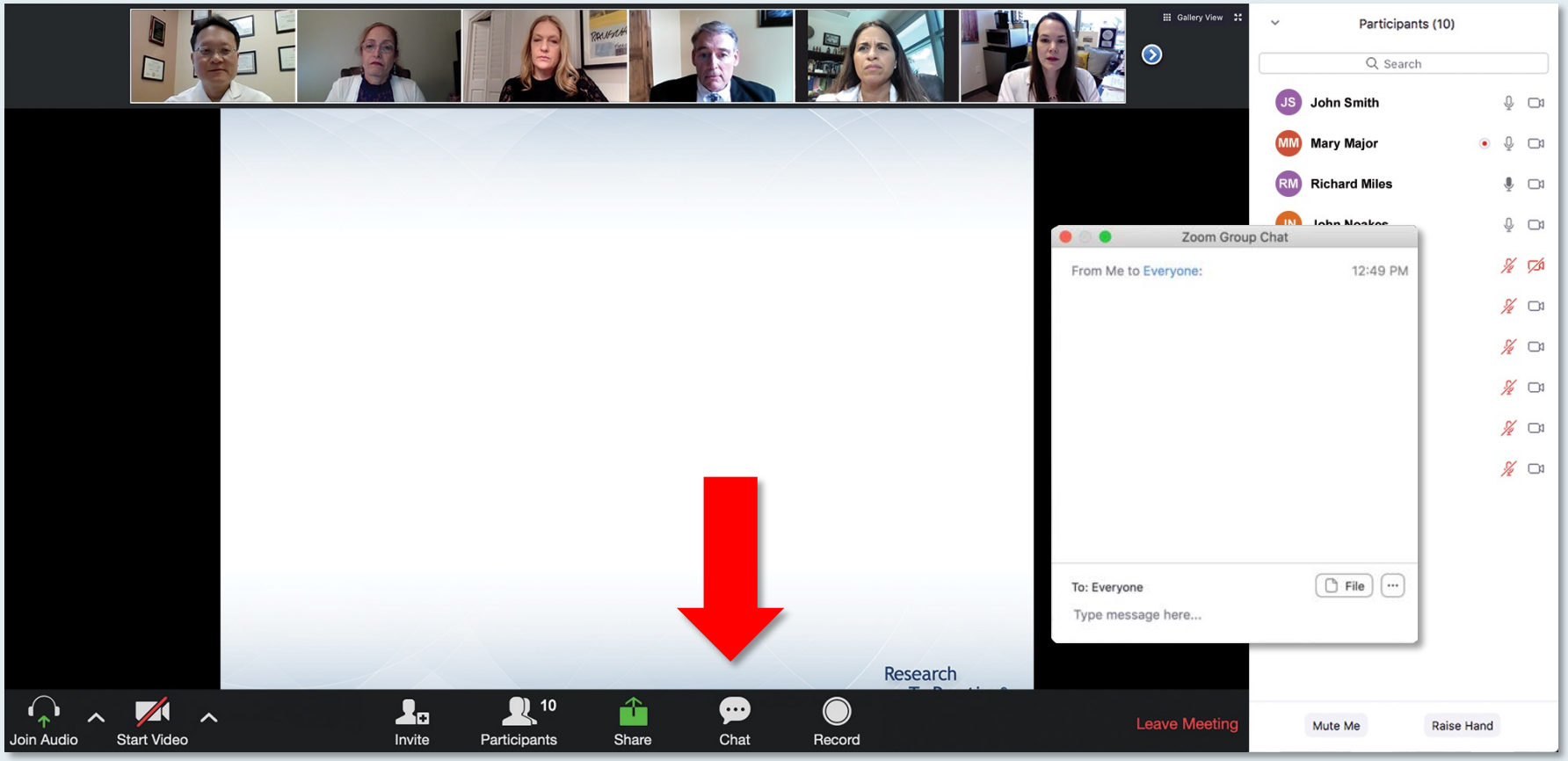

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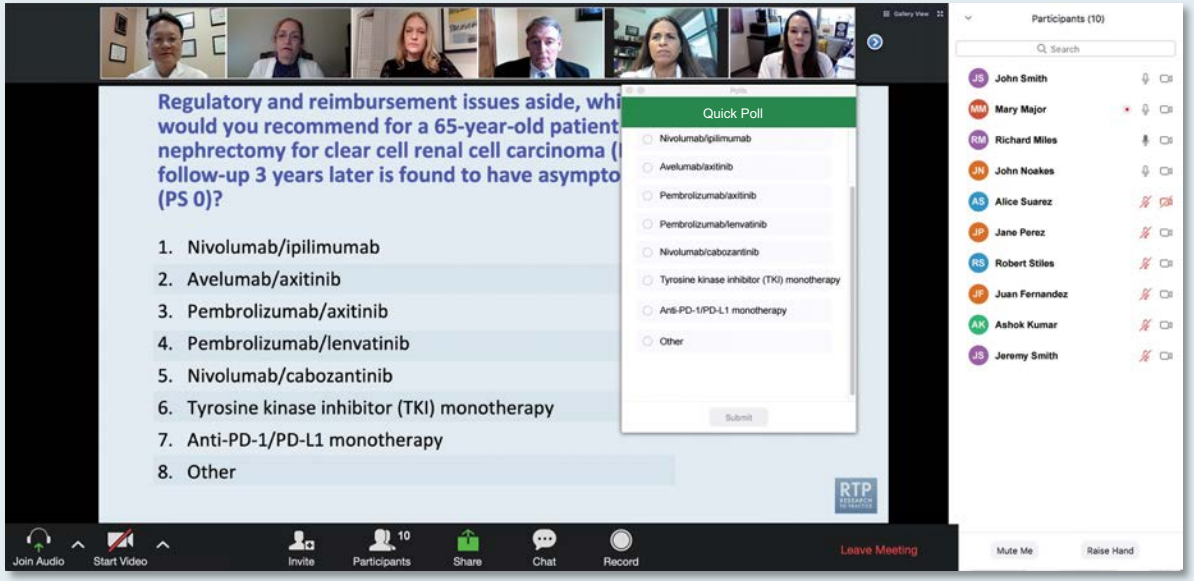

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“What I Tell My Patients”
Fifteenth Annual RTP-ONS NCPD Symposium Series
ONS Congress, San Antonio, Texas — April 26 to 29, 2023

Wednesday April 26	**Cervical and Endometrial Cancer** 11:15 AM – 12:45 PM CT (12:15 PM – 1:45 PM ET)
	Breast Cancer 6:00 PM – 8:00 PM CT (7:00 PM – 9:00 PM ET)
Thursday April 27	**Diffuse Large B-Cell Lymphoma** 6:00 AM – 7:30 AM CT (7:00 AM – 8:30 AM ET)
	Chronic Lymphocytic Leukemia 12:15 PM – 1:45 PM CT (1:15 PM – 2:45 PM ET)
	HER2-Targeted Antibody-Drug Conjugates 6:00 PM – 7:30 PM CT (7:00 PM – 8:30 PM ET)
Friday April 28	**Hepatobiliary Cancers** 6:00 AM – 7:30 AM CT (7:00 AM – 8:30 AM ET)
	Ovarian Cancer 12:15 PM – 1:45 PM CT (1:15 PM – 2:45 PM ET)
	Lung Cancer 6:00 PM – 8:00 PM CT (7:00 PM – 9:00 PM ET)
Saturday April 29	**Acute Myeloid Leukemia, Myelodysplastic Syndromes and Myelofibrosis** 6:00 AM – 7:30 AM CT (7:00 AM – 8:30 AM ET)
	Prostate Cancer 12:15 PM – 1:45 PM CT (1:15 PM – 2:45 PM ET)

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What I Tell My Patients:
New Treatments and Clinical Trials

An NCPD Webinar Series in Partnership with the 2023 ONS Congress

Urothelial Bladder Cancer

Thursday, May 25, 2023

Faculty

Brenda Martone, MSN, NP-BC, AOCNP
Jonathan E Rosenberg, MD

Moderator

Neil Love, MD

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TO PRACTICE

What I Tell My Patients:
New Treatments and Clinical Trials

An NCPD Webinar Series in Partnership with the 2023 ONS Congress

Colorectal and Gastroesophageal Cancers

Wednesday, June 14, 2023

Faculty

Kristen K Ciombor, MD, MSCI
Amanda K Wagner, APRN-CNP, AOCNP

Moderator

Neil Love, MD

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What I Tell My Patients

2023 ONS Congress

San Antonio, Texas

Symposia Themes

- New agents and therapies; ongoing trials related to specific clinical scenarios
- Patient education: Preparing to receive new therapies
- The bond that heals
- THANKS! (Great job)

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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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Ms Battiato — Disclosures

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Case 1: 73-year-old woman responding to ibrutinib for 4 years

Case 2: 81-year-old woman with TP53-mutant, del(17p) disease responding to acalabrutinib

Case 3: 55-year-old man with CLL/SLL treated for a year with obinutuzumab → venetoclax, NED for 3 years

Case 4: 66-year-old Cuban woman with multiregimen-recurrent disease, now on venetoclax

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SCIENCE BEHIND THE STUDY

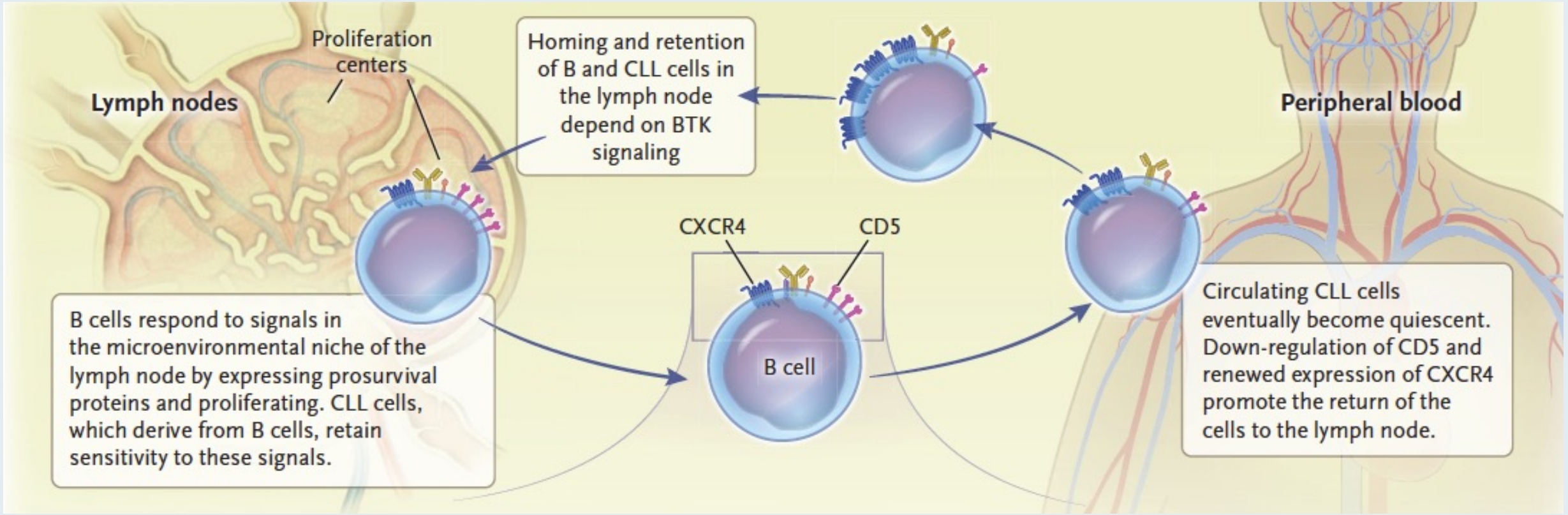
Elizabeth G. Phimister, Ph.D., *Editor*

Inhibiting BTK in Chronic Lymphocytic Leukemia

Arnon P. Kater, M.D., Ph.D., and Barbara Eichhorst, M.D.

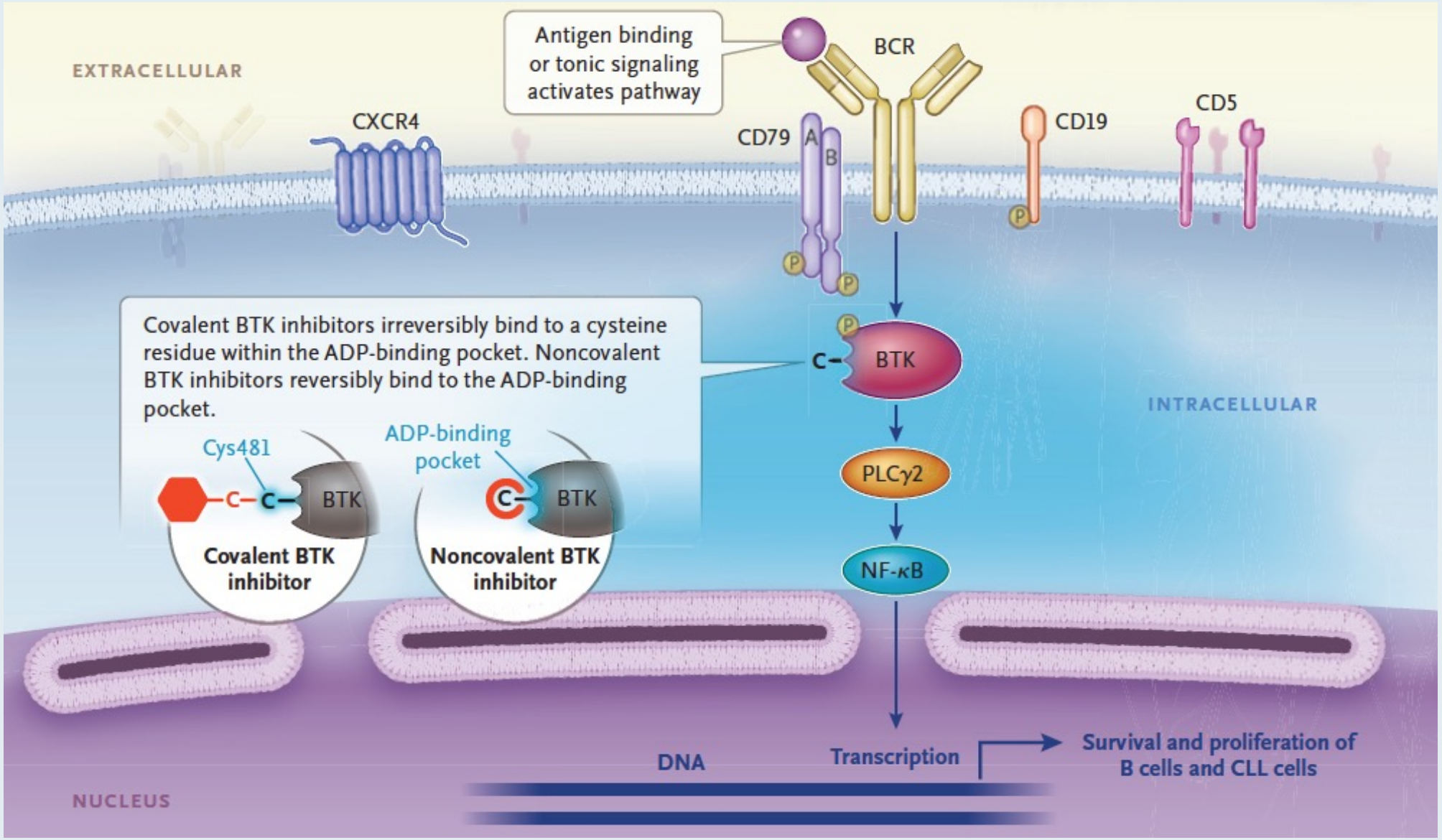
***N Engl J Med* 2023;389:83-6.**

Recirculation of CLL Cells Between Blood and Lymphoid Tissue



Kater AP, Eichhorst B. *N Engl J Med* 2023;389:83-6.

BCR Signaling Pathway



Kater AP, Eichhorst B. *N Engl J Med* 2023;389:83-6.

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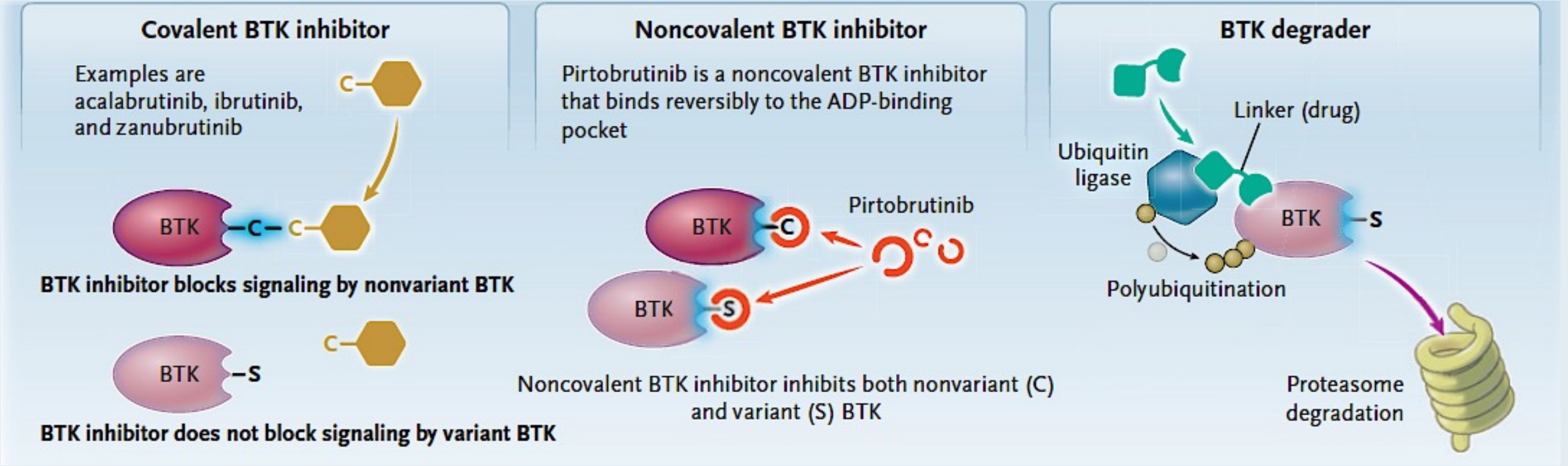
Current and Future BTK Inhibitor Therapies



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Kristen E Battiato, AGNP-C

73-year-old woman, a retired schoolteacher with a history of GERD who has had CLL since 2015. She lives 2 hours away and cares for her 90-year-old mother. She is receiving ibrutinib with ongoing response after initial lymphocytosis.

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Dr Woyach
Columbus, Ohio

Clinical Research Background

- **Indications to treat**
- **Infections/vaccinations**
- **Autoimmune issues**

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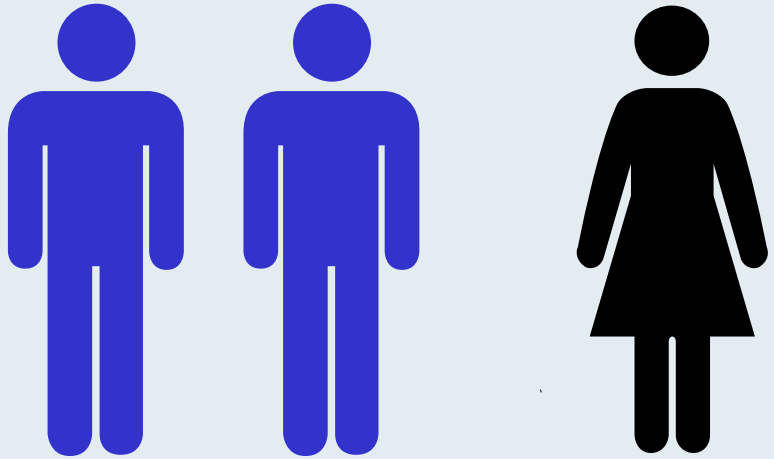
CLL Affects a Significant Number of People Worldwide, Predominantly Older People

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.

Content courtesy of John M Pagel, MD, PhD

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Indications for treatment:

- Disease-related symptoms
  - Fatigue can by tricky
- Progressive bulky disease
  - spleen > 6 cm below costal margin; LN > 10 cm
- Progressive bone marrow failure, manifesting as anemia or thrombocytopenia
- Autoimmune complications poorly responsive to steroids
- Progressive lymphocytosis: Lymphocyte doubling time < 6 months, or increase in ≥ 50% in a two-month period

*Note: Absolute lymphocyte count alone not an indication for treatment

Courtesy of Brad S Kahl, MD

CLL special considerations

- High frequency of AI complications
  - ITP, AIHA, neutropenia
- High frequency of infections
  - Check Ig levels
  - Consider IVIg replacement therapy if recurrent infections and IgG < 300
- High rate of skin cancer
  - Low threshold to send to Dermatology

Courtesy of Brad S Kahl, MD

Dr Woyach
Columbus, Ohio

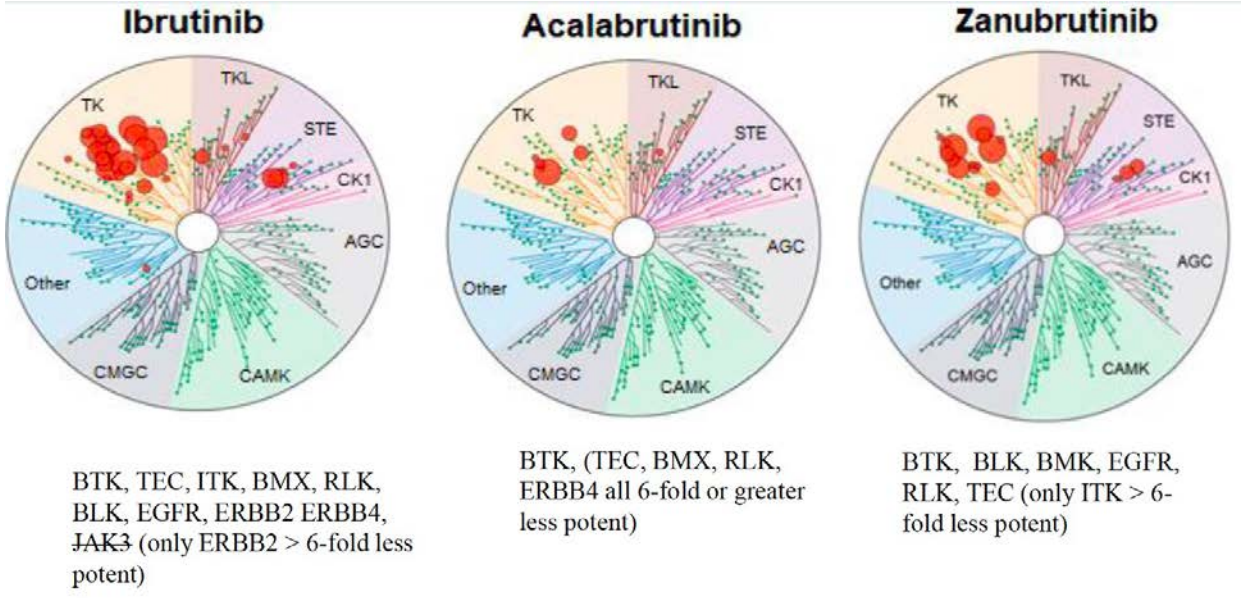
Clinical Research Background

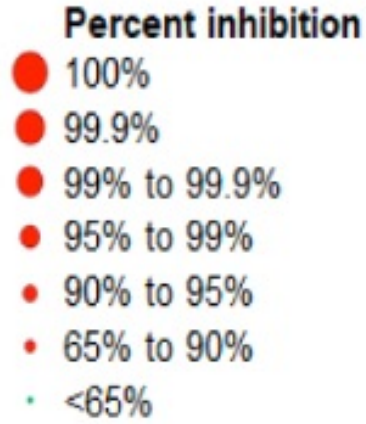
- **First-line therapy: BTK inhibitor versus venetoclax/obinutuzumab; BTK inhibitor with venetoclax? Use of anti-CD20 antibodies?**

Irreversible and Reversible Bruton Tyrosine Kinase Inhibitors in CLL

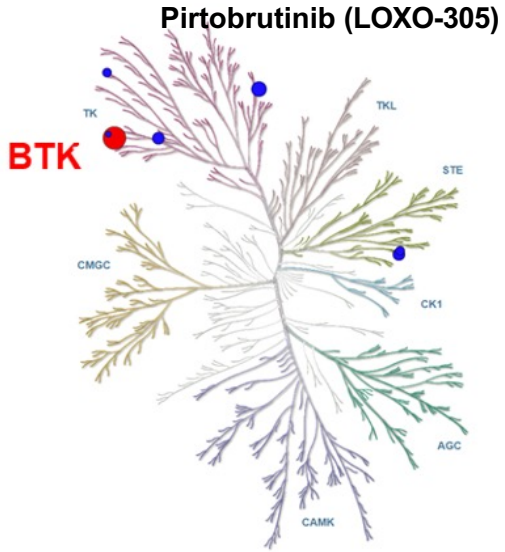
BTKi	Binding	T1/2 (hours)	IC50 (nM)	Dosing
Ibrutinib	Covalent irreversible C481	4-8	0.5	420 mg
Acalabrutinib	Covalent irreversible C481	0.9	5.1	100 mg BID
Zanubrutinib	Covalent irreversible C481	2-4	0.5	160 mg BID or 320 mg once daily
Pirtobrutinib	Noncovalent reversible	Not available	0.85	200 mg

Irreversible





Reversible



Robak T et al. *Cancers* 2022 February 2;14(3):771.

FDA Approves Zanubrutinib for Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma

Press Release: January 19, 2023

"On January 19, 2023, the Food and Drug Administration approved zanubrutinib for chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).

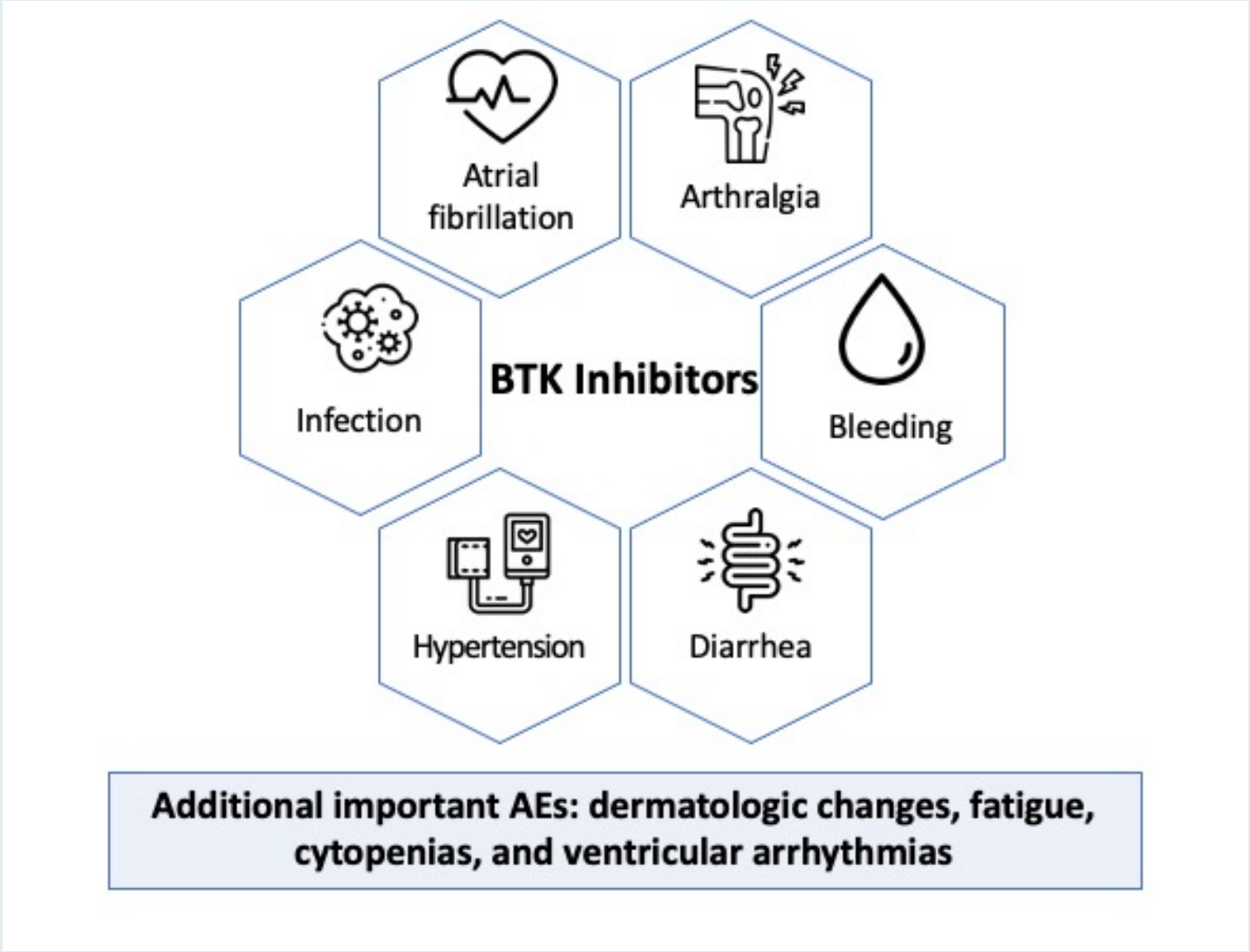
Efficacy in patients with treatment-naïve CLL/SLL was evaluated in SEQUOIA (NCT03336333). In the randomized cohort including patients without 17p deletion, a total of 479 patients were randomized 1:1 to receive either zanubrutinib until disease progression or unacceptable toxicity or bendamustine plus rituximab (BR) for 6 cycles.

Efficacy in patients with relapsed or refractory CLL/SLL was evaluated in ALPINE (NCT03734016). A total of 652 patients were randomized 1:1 to receive either zanubrutinib or ibrutinib.

The recommended zanubrutinib dosage is 160 mg taken orally twice daily or 320 mg taken orally once daily until disease progression or unacceptable toxicity."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-zanubrutinib-chronic-lymphocytic-leukemia-or-small-lymphocytic-lymphoma

Summary of Adverse Events (AEs) with BTK Inhibitors



Content courtesy of Matthew S Davids, MD, MMSc 2022

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Kristen E Battiato, AGNP-C

Extremely anxious 81-year-old woman, a retired tailor, with CLL since 2019. TP53 mutated, del17p, with a large burden of intra-abdominal disease. She is responding to acalabrutinib and soon to visit her family in Italy.

“Pack your acalabrutinib, wear a mask, eat outside, and enjoy your life!”

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original reports

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

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 November 1;39(31):3441-52.

original reports

Zanubrutinib Versus Ibrutinib in Relapsed/ Refractory Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma: Interim Analysis of a Randomized Phase III Trial

Peter Hillmen, MBChB, PhD[1]; Barbara Eichhorst, MD[2]; Jennifer R. Brown, MD, PhD[3]; Nicole Lamanna, MD[4]; Susan M. O'Brien, MD[5]; Constantine S. Tam, MBBS, MD[6-9]; Lugui Qiu, MD, PhD[10]; Maciej Kazmierczak, MD, PhD[11]; Keshu Zhou, MD, PhD[12]; Martin Šimkovič, MD, PhD[13,14]; Jiří Mayer, MD[15]; Amanda Gillespie-Twardy, MD[16]; Mazyar Shadman, MD, MPH[17,18]; Alessandra Ferrajoli, MD[19]; Peter S. Ganly, BMBCh, PhD[20]; Robert Weinkove, MBBS, PhD[21,22]; Sebastian Grosicki, MD, PhD[23]; Andrzej Mital, MD, PhD[24]; Tadeusz Robak, MD, PhD[25]; Anders Österborg, MD, PhD[26,27]; Habte A. Yimer, MD[28]; Tommi Salmi, MD[29]; Meng Ji, MD[30]; Jessica Yecies, PhD[29]; Adam Idoine, PhD[29]; Kenneth Wu, PhD[29]; Jane Huang, MD[29]; and Wojciech Jurczak, MD, PhD[31]

J Clin Oncol 2023;[Online ahead of print].

Agenda

Introduction

Case 1: 73-year-old woman responding to ibrutinib for 4 years

Case 2: 81-year-old woman with TP53-mutant, del(17p) disease responding to acalabrutinib

Case 3: 55-year-old man with CLL/SLL treated for a year with obinutuzumab → venetoclax, NED for 3 years

Case 4: 66-year-old Cuban woman with multiregimen-recurrent disease, now on venetoclax

Kristen E Battiato, AGNP-C

55-year-old man who works in finance. He has had CLL/SLL since 2018 when he was told by his employer not to come to work because "you're scaring the clients with your neck!"

Treated for a year with obinutuzumab/venetoclax and now has been observed off treatment in complete remission for 3 years. Experienced fever, rigors, nausea/vomiting with first infusion of obinutuzumab.

RTP
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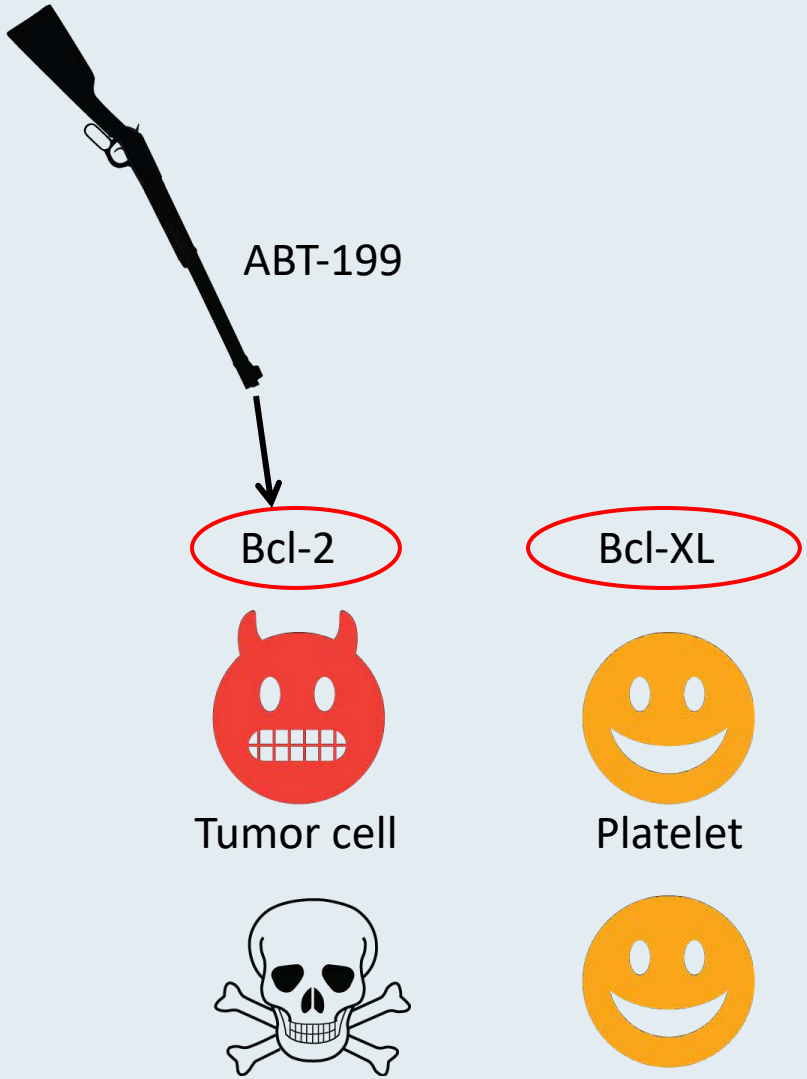
TO PRACTICE

Dr Woyach
Columbus, Ohio

Clinical Research Background

- **Venetoclax with an anti-CD20 antibody**
- **First line versus second line**
- **Obinutuzumab debulking**
- **Obinutuzumab toxicity, including tumor lysis syndrome (TLS)**

Mechanism of Action of Venetoclax (ABT-199)



- **Bcl-2 functions to prevent cell death by apoptosis**
- **Venetoclax is specific for Bcl-2 and inhibits its function, thereby removing the block on apoptosis**

Adapted from Davids MS, Letai A. *Cancer Cell* 2013;23(2):139-41.

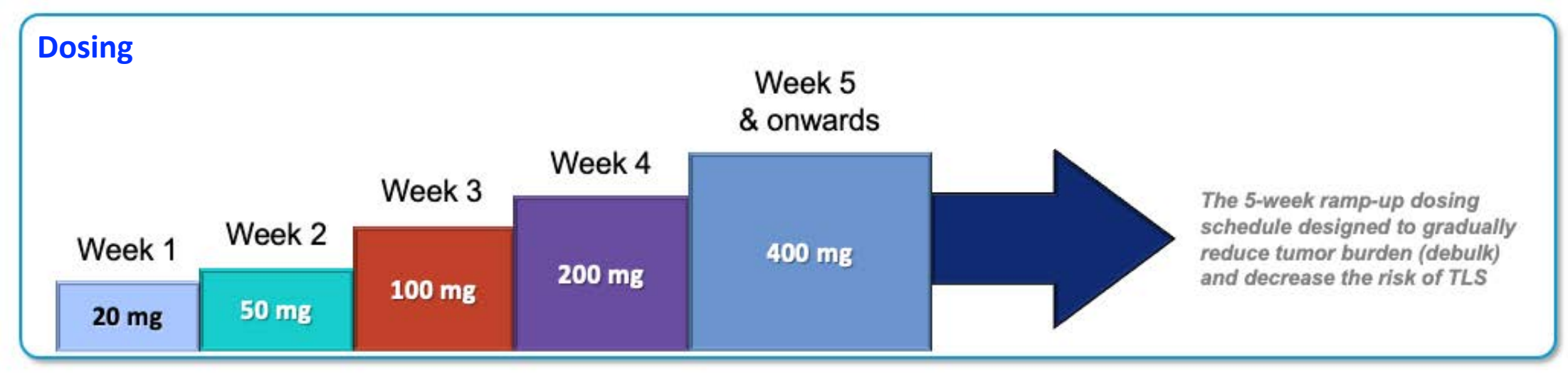
Venetoclax

Mechanism of action

- **Bcl-2 inhibitor**

Indication

- **For patients with CLL or SLL**



- **In combination with obinutuzumab: After ramp-up, continue venetoclax 400 mg once daily until the last day of cycle 12**
- **In combination with rituximab: After ramp-up, continue venetoclax 400 mg once daily for 24 months**
- **As monotherapy: After ramp-up, continue venetoclax 400 mg once daily until disease progression or unacceptable toxicity**

Venetoclax package insert, 6/2022.

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Patient Education: Venetoclax

- Pharmacy consultation re potential drug interactions
  - CYP3A4 interactions – Avoid strong inhibitors and inducers
    - Azole antifungals, mycin antibiotics, protease inhibitors, etc
    - Moderate – consider dose adjustment
    - Avoid grapefruit/juice, Seville oranges, and starfruit
- Take with food and water, same time each day

Content courtesy of Robin Klebig, APRN, CNP, AOCNP

Patient Education: Venetoclax (Continued)

Potential for tumor lysis syndrome

- 5-week ramp-up to goal dose
- Hospitalization for weekly ramp-up (bulky)
- TLS lab monitoring q8h x 24 hours
- Allopurinol
- Hydration

Nausea

- Antiemetic prn

Diarrhea

- Loperamide prn
- Record # stools per day at baseline

Cytopenias

- Neutropenia
  - Increased infection risk
- Thrombocytopenia
  - Bleeding risk
- Anemia
  - Typically not transfusion requiring

Content courtesy of Robin Klebig, APRN, CNP, AOCNP

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.	

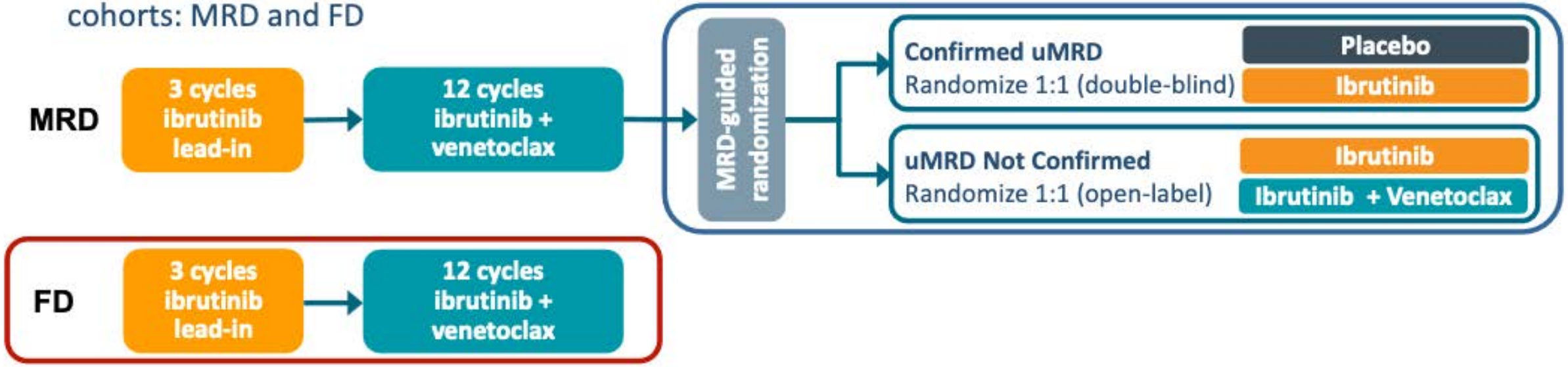
[a]Administer intravenous hydration for any patient who cannot tolerate oral hydration; [b]Evaluate blood chemistries (potassium, uric acid, phosphorus, calcium, and creatinine); review in real time; [c]For patients at risk of TLS, monitor blood chemistries at 6–8 hours and at 24 hours at each subsequent 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

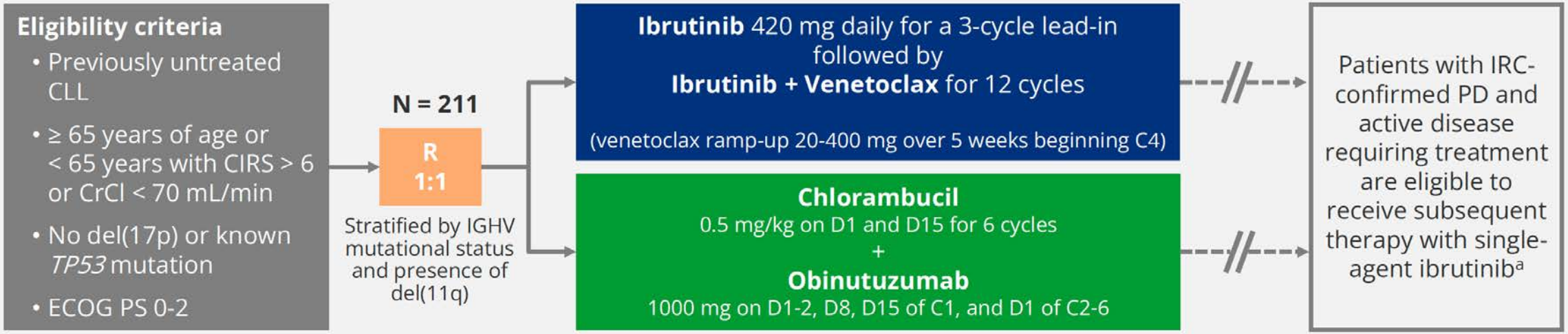
CAPTIVATE: A Phase II Study Evaluating Ibrutinib Followed by Ibrutinib and Venetoclax for Previously Untreated CLL

- CAPTIVATE (PCYC-1142) is an international, multicenter phase 2 study evaluating first-line treatment with 3 cycles of ibrutinib followed by 12 cycles of combined ibrutinib + venetoclax that comprises 2 cohorts: MRD and FD



Allan JN et al. EHA 2021;Abstract S147.

GLOW: A Phase III Trial of Fixed-Duration Ibrutinib and Venetoclax for Older Patients with Previously Untreated CLL

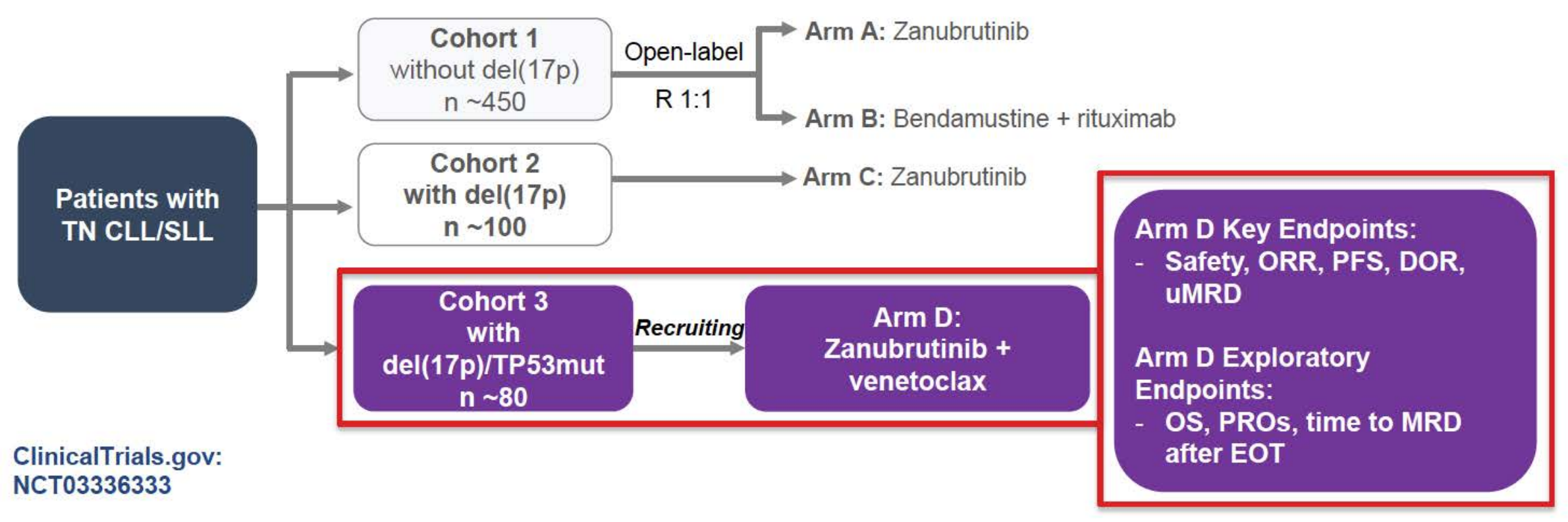


- **Primary end point: IRC-assessed PFS**
- Key secondary end points: uMRD rates, response rates, overall survival, time to next treatment, and safety
- Current analysis
  - Median study follow-up of 46 months (range, 1.7-51.7)
  - MRD assessed in peripheral blood in responders by NGS

CIRS = cumulative illness rating scale; CrCl = creatinine clearance; IRC = independent review committee; PD = progressive disease; PFS = progression-free survival; MRD = minimal residual disease; uMRD = undetectable MRD; NGS = next-generation sequencing

Niemann CU et al. ASH 2022;Abstract 93.

SEQUOIA Trial Design Arm D: Zanubrutinib and Venetoclax for Treatment-Naïve CLL/SLL

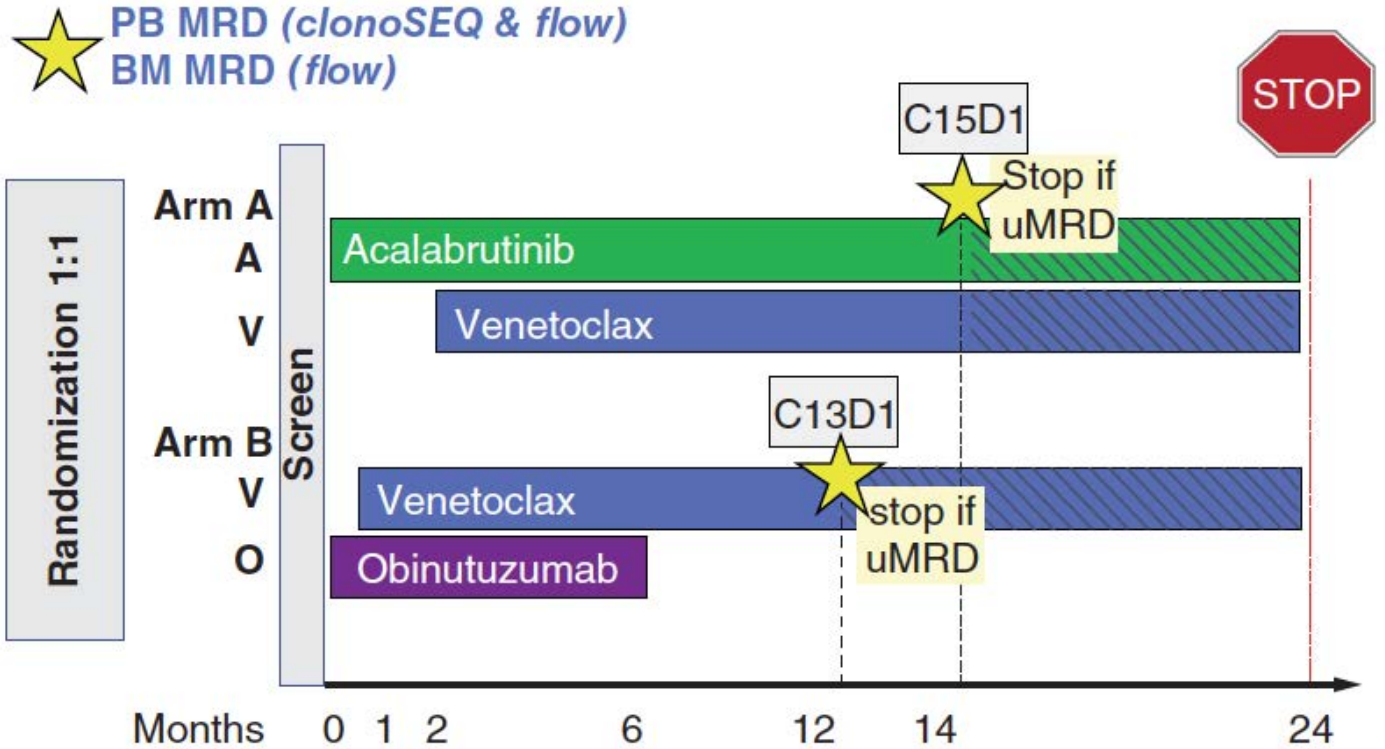


Tedeschi A et al. ASH 2021;Abstract 67.

MAJIC: An Ongoing Phase III Trial Evaluating Acalabrutinib with Venetoclax versus Venetoclax with Obinutuzumab for Previously Untreated CLL/SLL

Arm A **Acalabrutinib (A)** 100 mg po BID,
Venetoclax (V) 400 mg po daily (C3D1–C14), including 5 week ramp up
STOP if uMRD and at least PR. If MRD+ continue AV to 24 months

Arm B **Venetoclax (V)** 400 mg po daily (C1D22–C12), including 5 week ramp up
Obinutuzumab (O) 1000 mg IV (C1D1-2/8/15, C2-6 D1)
STOP if uMRD and at least PR. If MRD+ continue V to 24 months



Ryan CE et al. *Future Oncol* 2022;18(33):3689-99.

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Case 4: 66-year-old Cuban woman with multiregimen-recurrent disease, now on venetoclax

Kristen E Battiato, AGNP-C

66-year-old Cuban woman with CLL diagnosed in 2008; s/p bendamustine/rituximab, ibrutinib, Murano regimen (rituximab/venetoclax) and venetoclax maintenance for 2 years.

She is very mistrusting of the medical community. A retired school administrator, she lives with her son and has an extensive social support network of family and friends.

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FDA Grants Accelerated Approval to Pirtobrutinib for Relapsed or Refractory Mantle Cell Lymphoma

Press Release: January 27, 2023

"On January 27, 2023, the Food and Drug Administration (FDA) granted accelerated approval to pirtobrutinib for relapsed or refractory mantle cell lymphoma (MCL) after at least two lines of systemic therapy, including a BTK inhibitor.

Efficacy was evaluated in BRUIN (NCT03740529), an open-label, multicenter, single-arm trial of pirtobrutinib monotherapy that included 120 patients with MCL previously treated with a BTK inhibitor.

The main efficacy measures were overall response rate (ORR) and duration of response (DOR), as assessed by an independent review committee using Lugano criteria. The ORR was 50% (95% CI: 41, 59) with a complete response rate of 13%. The estimated median DOR was 8.3 months (95% CI: 5.7, NE), and the estimated DOR rate at 6 months was 65.3% (95% CI: 49.8, 77.1).

The recommended pirtobrutinib dosage is 200 mg orally once daily until disease progression or unacceptable toxicity."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-pirtobrutinib-relapsed-or-refractory-mantle-cell-lymphoma.

RTP RESEARCH TO PRACTICE

The NEW ENGLAND JOURNAL of MEDICINE

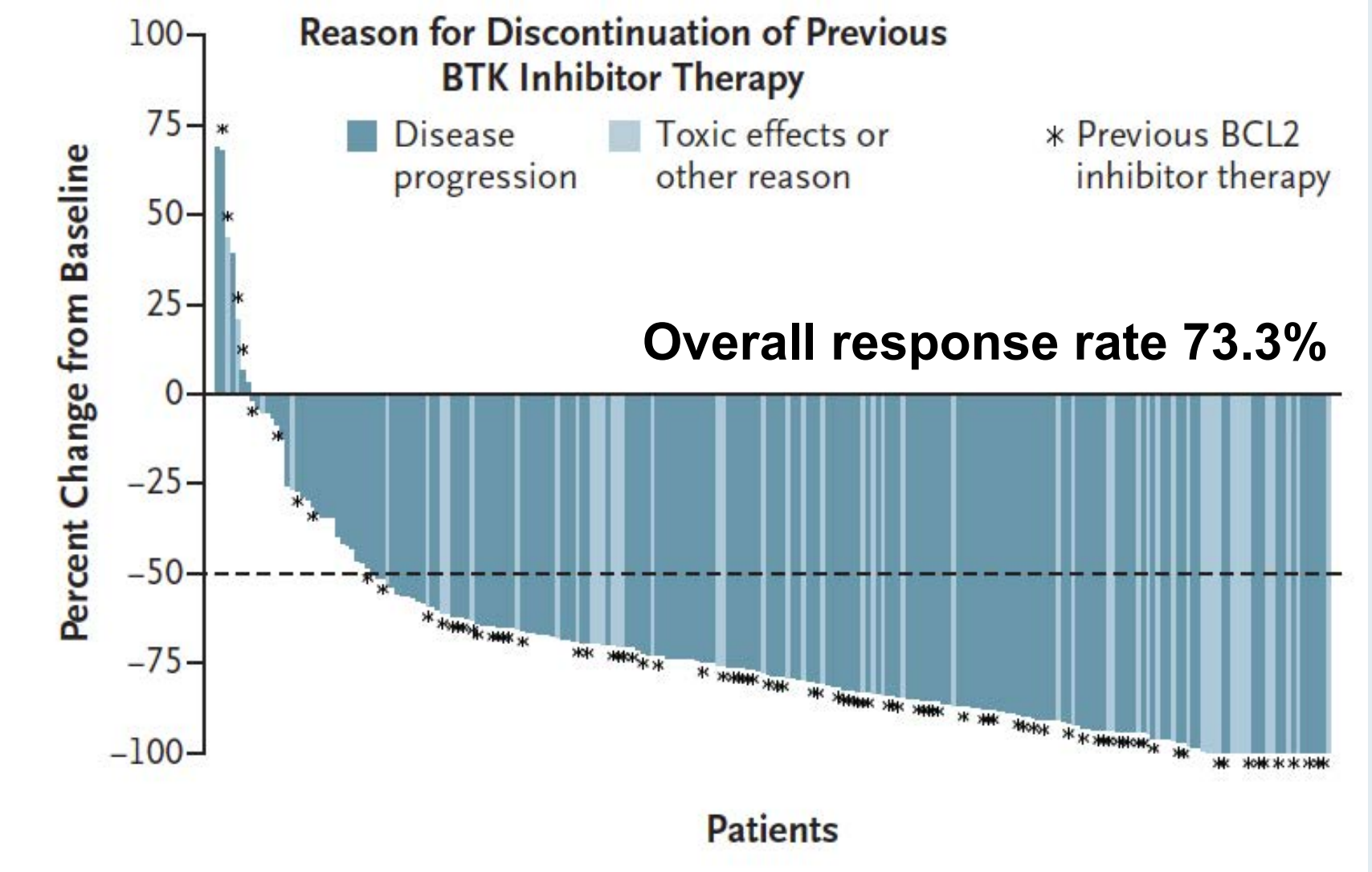
ORIGINAL ARTICLE

Pirtobrutinib after a Covalent BTK Inhibitor in Chronic Lymphocytic Leukemia

A.R. Mato, J.A. Woyach, J.R. Brown, P. Ghia, K. Patel, T.A. Eyre, T. Munir, E. Lech-Maranda, N. Lamanna, C.S. Tam, N.N. Shah, C.C. Coombs, C.S. Ujjani, B. Fakhri, C.Y. Cheah, M.R. Patel, A.J. Alencar, J.B. Cohen, J.N. Gerson, I.W. Flinn, S. Ma, D. Jagadeesh, J.M. Rhodes, F. Hernandez-Ilizaliturri, P.L. Zinzani, J.F. Seymour, M. Balbas, B. Nair, P. Abada, C. Wang, A.S. Ruppert, D. Wang, D.E. Tsai, W.G. Wierda, and W. Jurczak

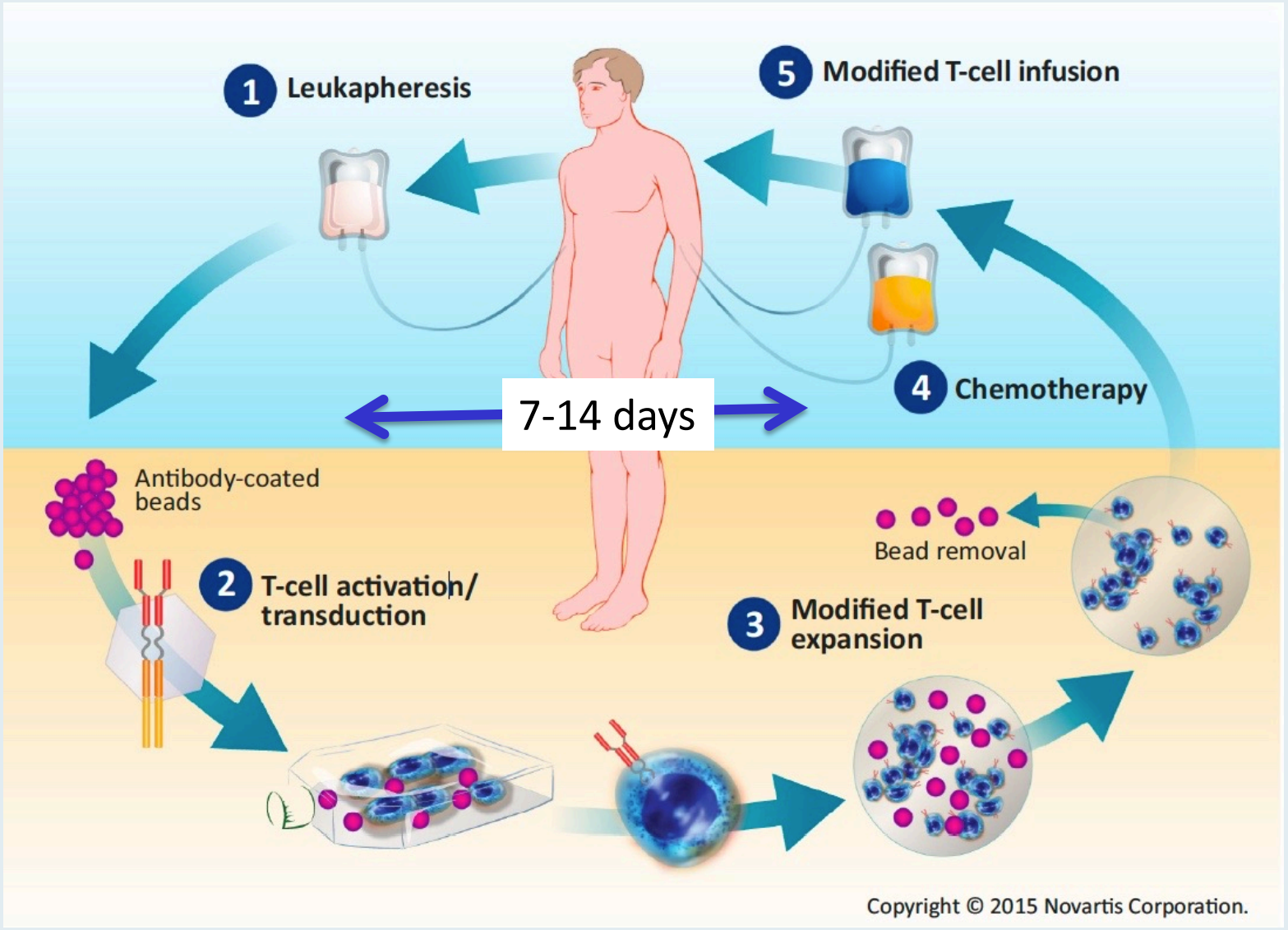
2023;389:33-44.

BRUIN Trial: Pirtobrutinib Efficacy in Patients with CLL or SLL Who Received Prior BTK Inhibitor Treatment



Mato AR et al. *N Engl J Med* 2023;389:33-44.

Overview of CAR T-Cell Therapy



Modification, Courtesy of David Porter, MD

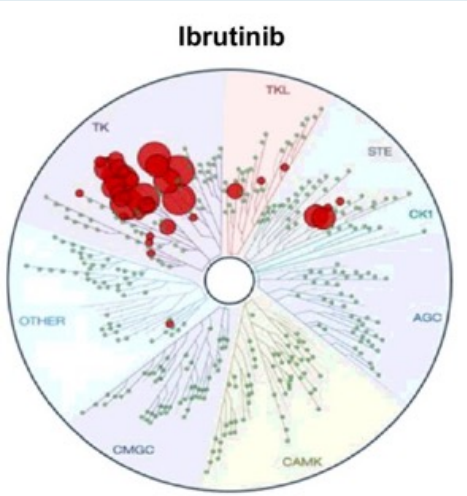
RTP RESEARCH TO PRACTICE

APPENDIX

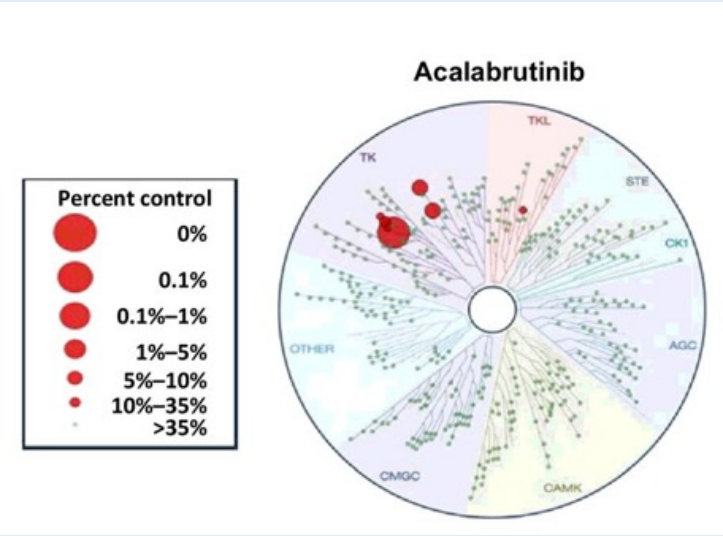
Overview of BTK Inhibitors for CLL

Irreversible

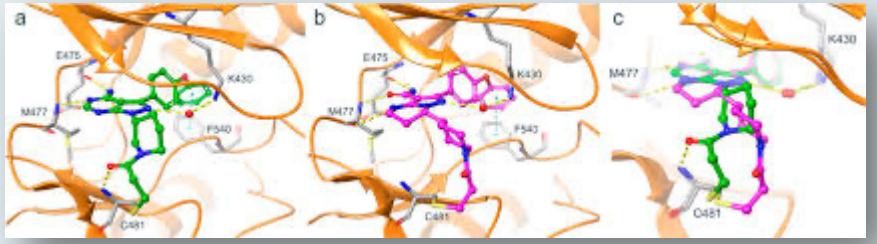
Ibrutinib



Acalabrutinib

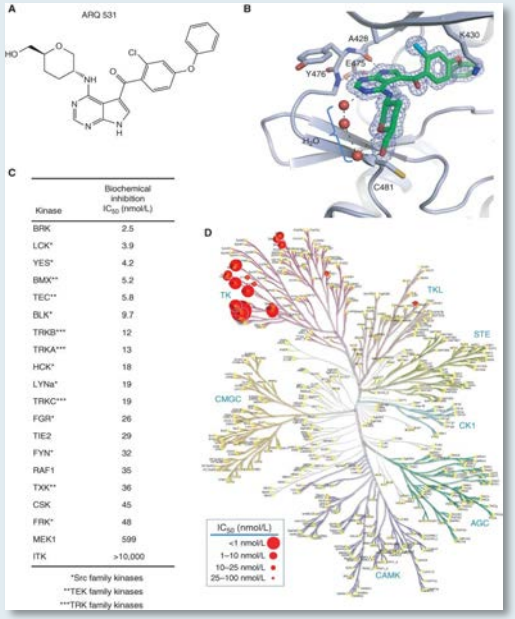


Zanubrutinib

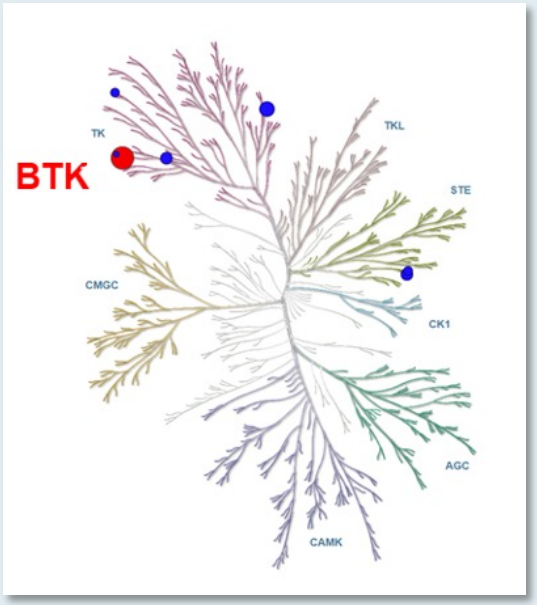


Reversible

ARQ-531 (MK-1026)



Pirtobrutinib



Content courtesy of Matthew S Davids, MD, MMSc

RTP RESEARCH TO PRACTICE

Ibrutinib

Mechanism of action

- BTK inhibitor

Indication

- For patients with CLL or small lymphocytic lymphoma (SLL)

Recommended dose

- 420 mg qd swallowed whole with water

Key issues

- Dose reduction guidelines

Ibrutinib package insert, 8/2022.

Acalabrutinib

Mechanism of action

- **BTK inhibitor**

Indication

- **For patients with CLL or SLL**

Recommended dose

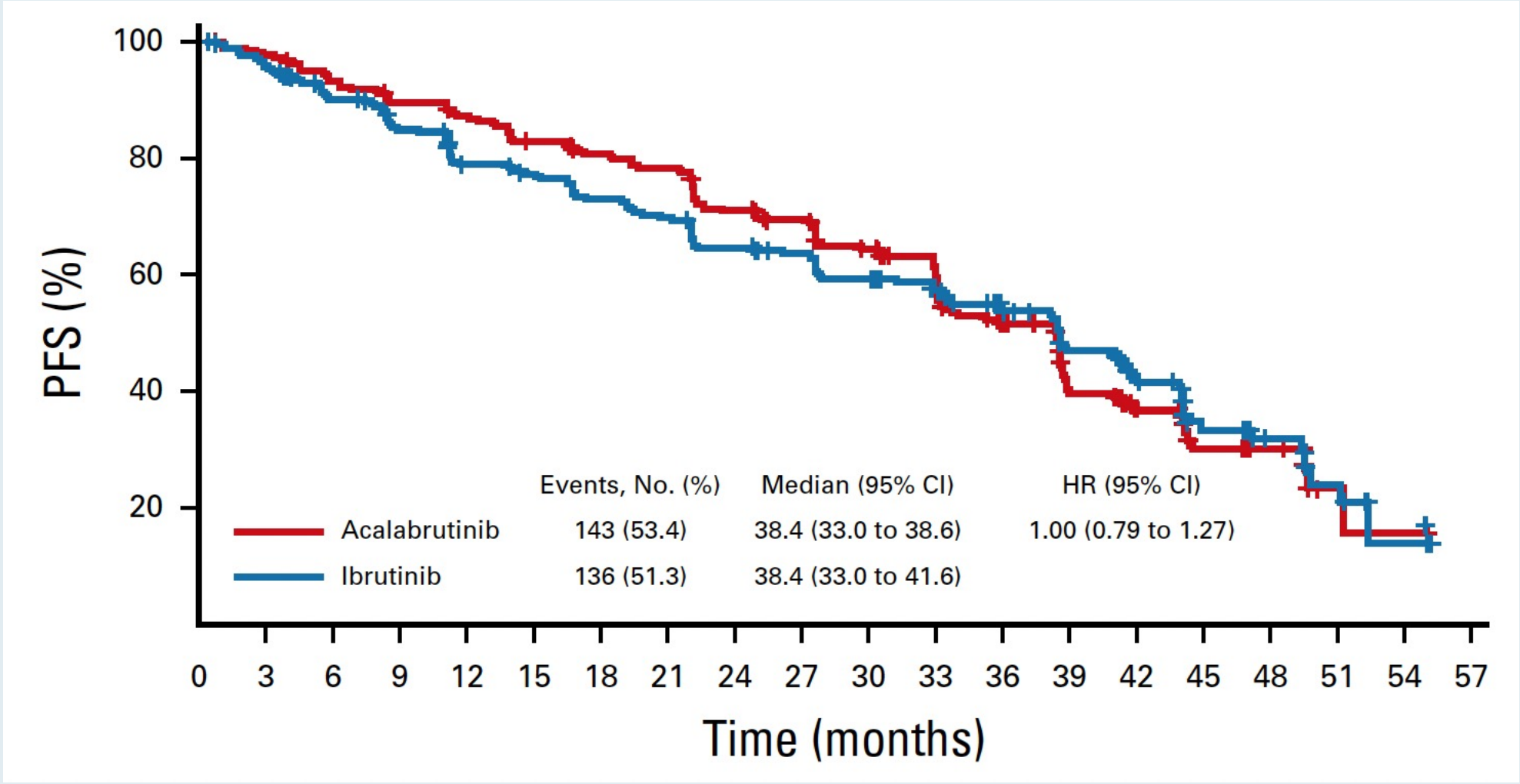
- **100 mg approximately every 12 hours swallowed whole with water, with or without food**

Key issues

- **Dose reduction guidelines**

Acalabrutinib package insert, 8/2022.

ELEVATE-RR: Independent Review Committee-Assessed PFS



Byrd JC et al. *J Clin Oncol* 2021;39(31):3441-52.

Zanubrutinib

Mechanism of action

- **BTK inhibitor**

Indication

- **For patients with CLL or SLL**

Recommended dose

- **160 mg twice daily or 320 mg once daily, swallowed whole with water, with or without food**

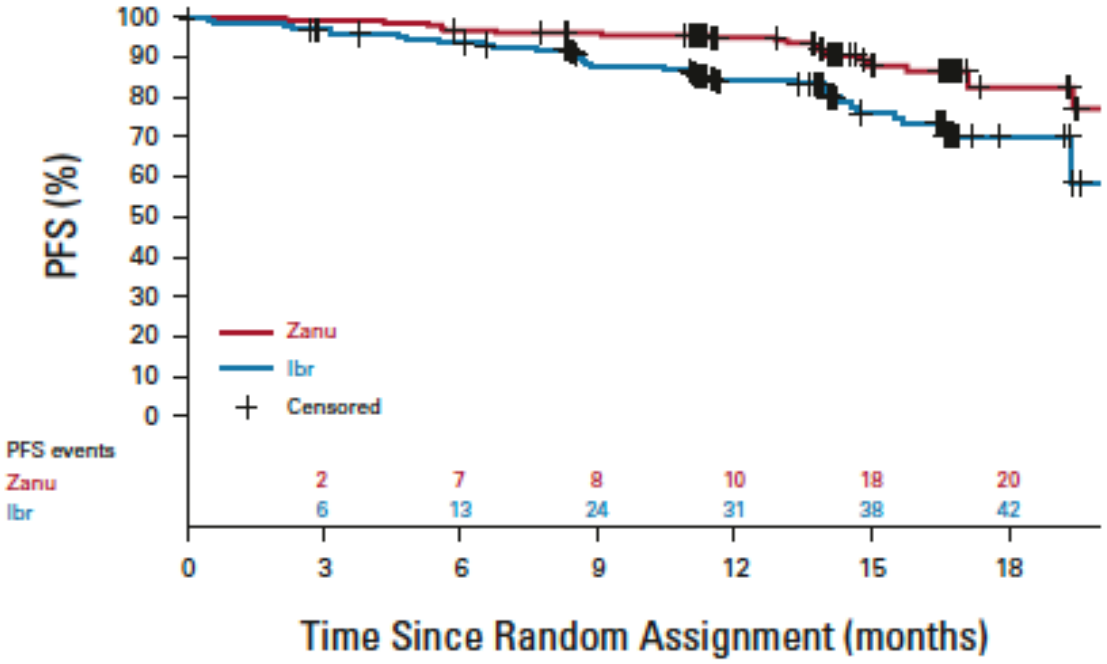
Key issues

- **Dose reduction guidelines**

Zanubrutinib package insert, 1/2023.

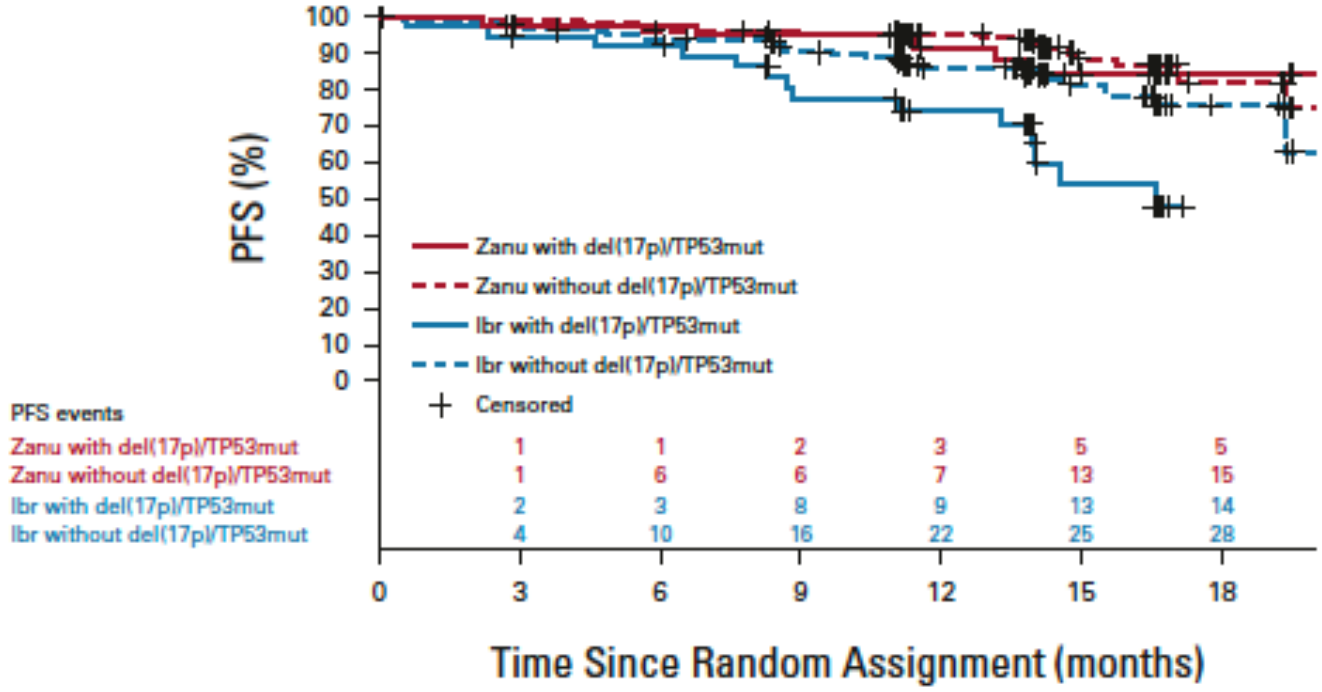
ALPINE: Progression-Free Survival

All Patients



	Zanubrutinib	Ibrutinib
12m PFS	94.9%	84.0%

Del(17p)/TP53

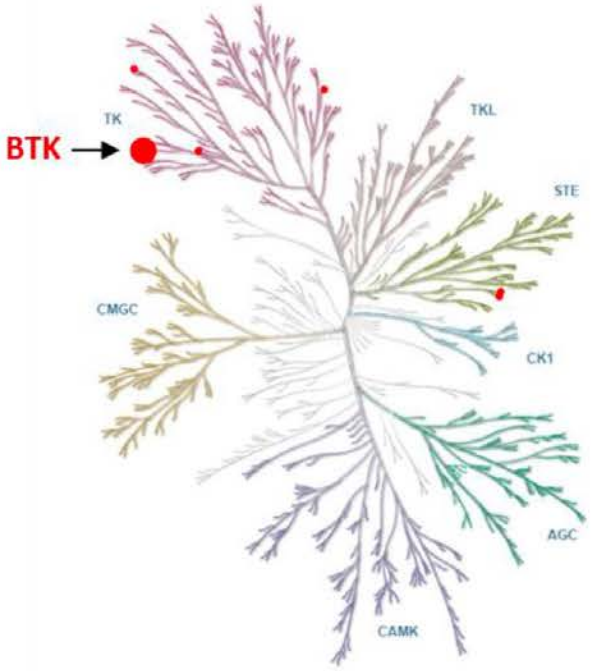


	Zanubrutinib	Ibrutinib
12m PFS	91.6%	74.4%

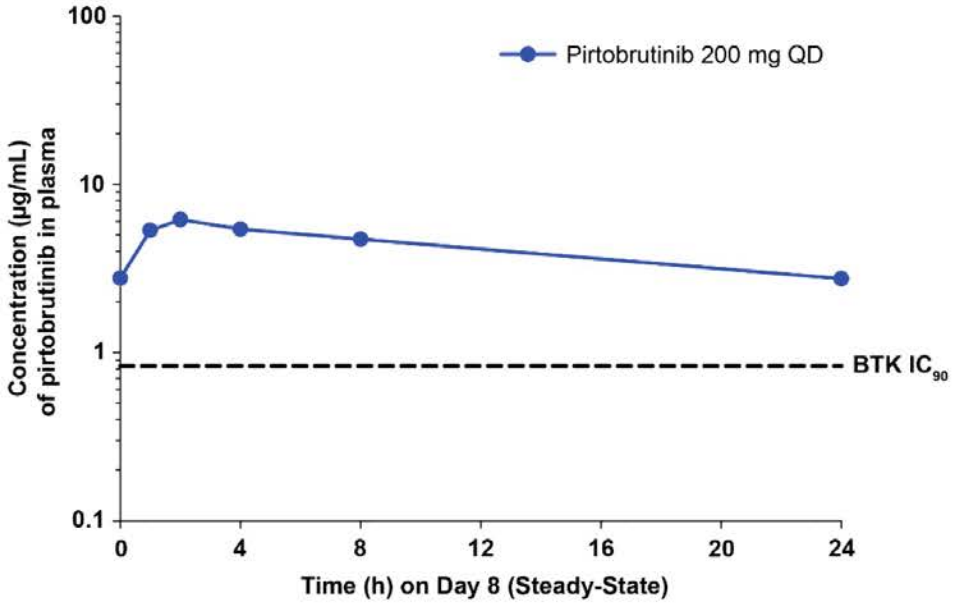
Hillmen P et al. *J Clin Oncol* 2023 February 10;41(5):1035-45.

Pirtobrutinib Is a Highly Selective, Noncovalent (Reversible) BTK Inhibitor

Highly Selective for BTK[6,7]



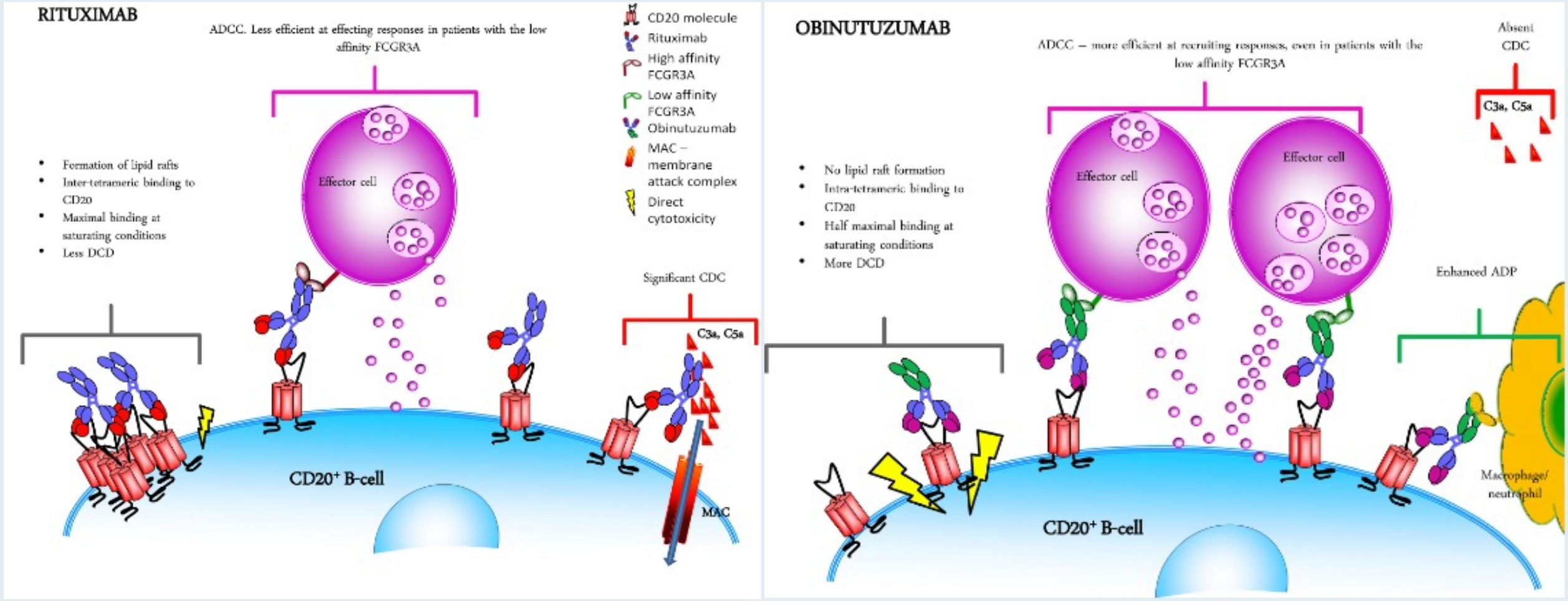
Plasma Exposures Exceeded BTK IC_{90} Throughout Dosing Interval



- Inhibits both wildtype and C481-mutant BTK with equal low nM potency, and has favorable oral pharmacology that enables continuous BTK inhibition throughout the dosing interval regardless of intrinsic rate of BTK turnover
- Pirtobrutinib is well tolerated and demonstrates promising efficacy in poor-prognosis B-cell malignancy patients following prior therapy, including prior cBTKi[1]

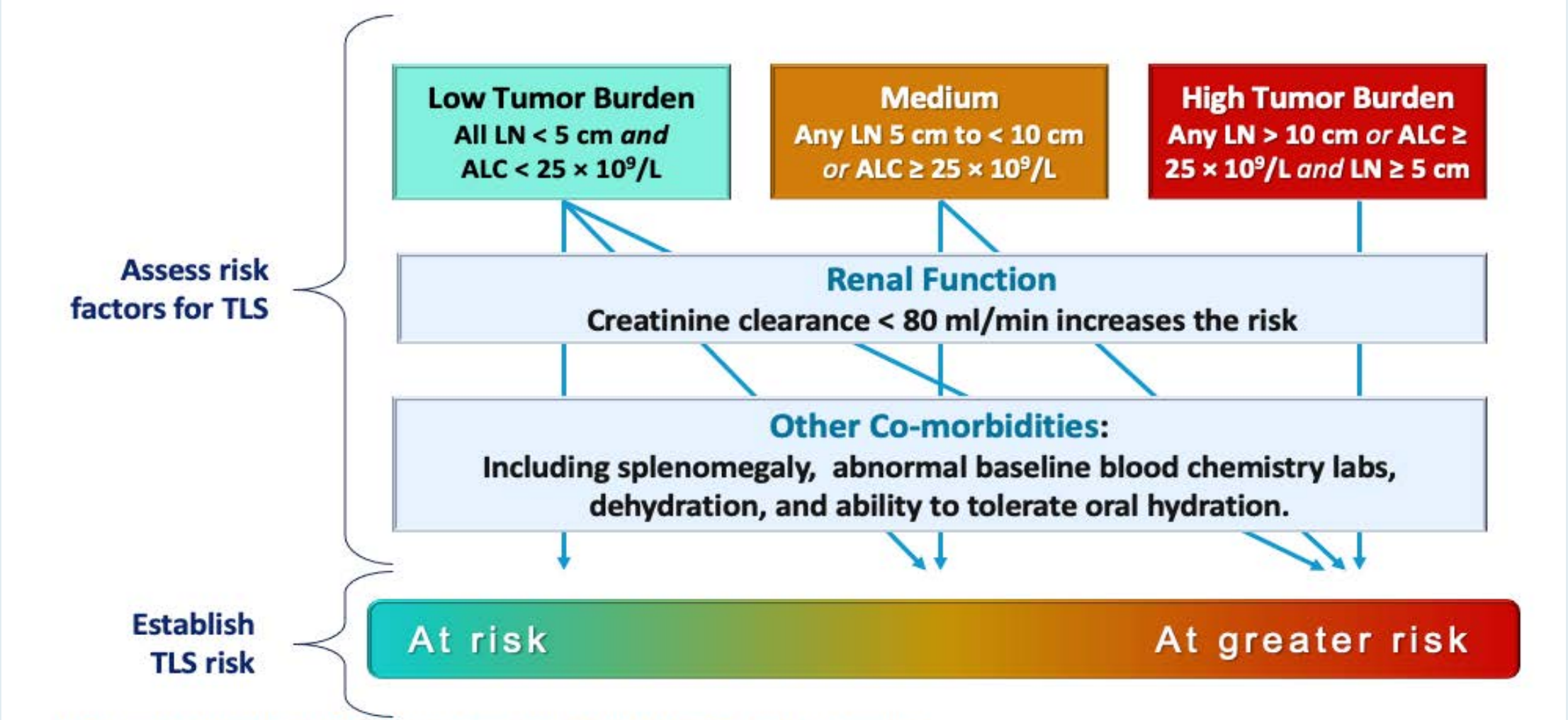
Mato AR et al. ASH 2022;Abstract 961.

Mechanisms of Action of Rituximab and Obinutuzumab



Freeman CL, Sehn LH. *Br J Hematol* 2018;182:29-45.

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.

Content courtesy of Matthew S Davids, MD, MMSc

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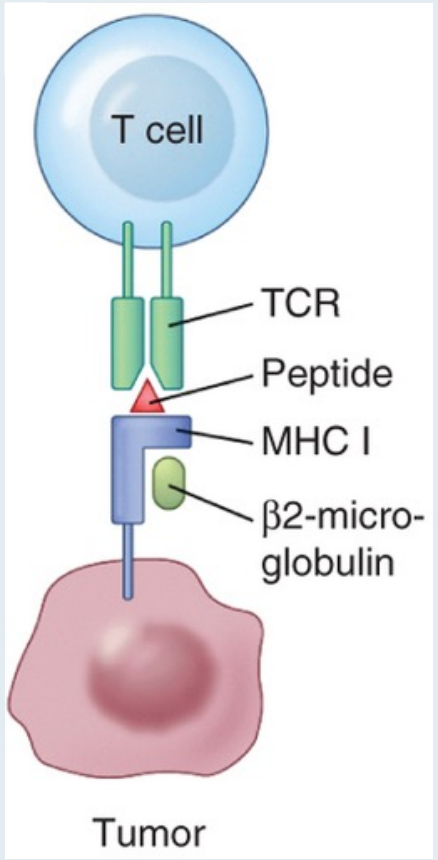
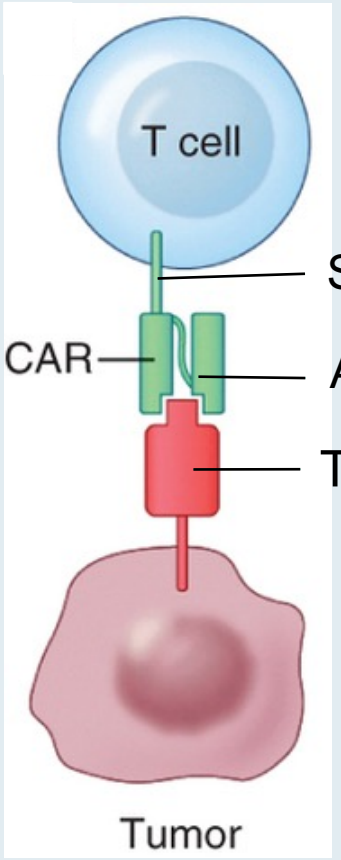
Chimeric Antigen Receptor (CAR) Modified T Cells

Normal T cell



CAR T cell



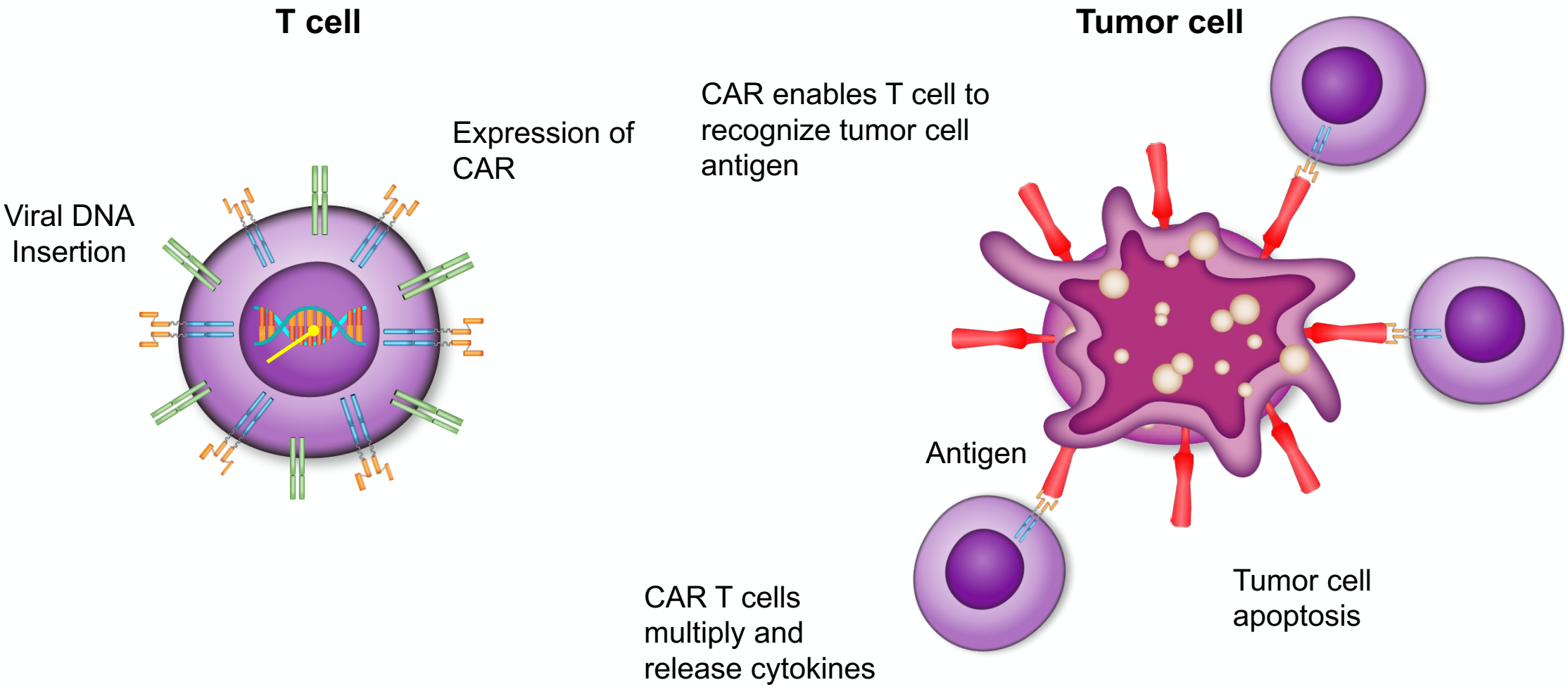
- **Genetically engineered T cells altered to express an artificial receptor, CAR**

Content courtesy of Sattva S Neelapu, MD

Adapted from Hinrichs & Restifo. *Nat Biotech* 2013

RTP RESEARCH TO PRACTICE

CAR T Cells: Mechanism of Action



TRANSCEND CLL 004: TEAEs, AESIs and Management of CRS and Neurological Events

- The most common grade ≥ 3 TEAEs (≥ 40%) were neutropenia (61%), anemia (52%), and thrombocytopenia (41%)

Patients with CRS and NEs	Full study population (n = 117)
CRS,[a] n (%)	99 (85)
Grade 1/2	43 (37)/46 (39)
Grade 3	10 (9)
Grade 4/5	0
Median (range) time to onset/resolution, days	4.0 (1–18)/6.0 (2–37)
NE,[b] n (%)	53 (45)
Grade 1/2	13 (11)/18 (15)
Grade 3	21 (18)
Grade 4	1 (1)
Grade 5	0
Median (range) time to onset/resolution, days	7.0 (1–21)/7.0 (1–83)

- 81 (69%) patients received tocilizumab and/or corticosteroids for management of CRS and/or NEs

Other AESIs, n (%)	Full study population (n = 117)
Prolonged cytopenia[c]	63 (54)
Grade ≥ 3 infections[d]	20 (17)
Hypogammaglobulinemia[e]	18 (15)
Tumor lysis syndrome	13 (11)
Second primary malignancy[e]	11 (9)
Macrophage activation syndrome	4 (3)

- 5 deaths due to TEAEs were reported
  - 4 considered unrelated to liso-cel by investigators (respiratory failure, sepsis, *Escherichia coli* infection, and invasive aspergillosis)
  - 1 considered related to liso-cel by investigators (macrophage activation syndrome)

[a]CRS was graded based on the Lee 2014 criteria; [b]NEs were defined as investigator-identified neurological AEs related to liso-cel; [c]Defined as grade ≥ 3 laboratory abnormalities of neutropenia, anemia, and/or thrombocytopenia at Day 30 after liso-cel infusion; [d]Includes grade ≥ 3 TEAEs from the infections and infestations (system organ class) by AE high-level group term; [e]AEs from the 90-day treatment-emergent period, posttreatment-emergent period, and long-term follow-up were included. AESI, adverse event of special interest; CRS, cytokine release syndrome; NE, neurological event; TEAE, treatment-emergent adverse event.

Siddiqi T et al. ASCO 2023;Abstract 7501; *Lancet* 2023 June 6;[Online ahead of print].

Inside the Issue: Novel Agents, Approaches and Strategies in the Management of Higher-Risk Myelodysplastic Syndromes

A CME/MOC-Accredited Live Webinar

Tuesday, July 11, 2023
5:00 PM – 6:00 PM ET

Faculty

Guillermo Garcia-Manero, MD
David Sallman, MD

Moderator

Neil Love, MD

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Thank you for joining us!

Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to us. The survey will remain open up to 5 minutes after the meeting ends.

NCPD credit information will be emailed to each participant within 5 business days.

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