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

Fifteenth Annual RTP Symposium Series Held During the Annual ONS Congress

Chronic Lymphocytic Leukemia

Thursday, April 27, 2023
12:15 PM – 1:45 PM

Faculty

John N Allan, MD
Jacqueline Broadway-Duren, PhD, DNP, APRN, FNP-BC
Corinne Hoffman, MS, APRN-CNP, AOCNP
Adam S Kittai, MD

Moderator

Neil Love, MD

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Faculty

John N Allan, MD
Associate Professor of Clinical Medicine
Weill Cornell Medicine
New York, New York

Adam S Kittai, MD
Assistant Professor
Division of Hematology
The Ohio State University
The OSUCCC – James
Columbus, Ohio

Jacqueline Broadway-Duren, PhD, DNP, APRN, FNP-BC
Family Nurse Practitioner
Department of Leukemia
The University of Texas MD Anderson Cancer Center
Houston, Texas

Moderator

Neil Love, MD
Research To Practice
Miami, Florida

Corinne Hoffman, MS, APRN-CNP, AOCNP
Nurse Practitioner, Hematology
The James Comprehensive Cancer Center
The Ohio State University Wexner Medical Center
Columbus, Ohio

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Dr Allan — Disclosures

Consulting Agreements	AbbVie Inc, ADC Therapeutics, AstraZeneca Pharmaceuticals LP, BeiGene Ltd, Epizyme Inc, Genentech, a member of the Roche Group, Janssen Biotech Inc, Lilly, Pharmacyclics LLC, an AbbVie Company, TG Therapeutics Inc
Contracted Research	BeiGene Ltd, Celgene Corporation, Genentech, a member of the Roche Group, Janssen Biotech Inc, TG Therapeutics Inc
Nonpromotional Disease State Awareness Speaking	AbbVie Inc, BeiGene Ltd, Janssen Biotech Inc, Pharmacyclics LLC, an AbbVie Company

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Dr Broadway-Duren — Disclosures

Advisory Roles	AbbVie Inc, Pharmacyclics LLC, an AbbVie Company

Ms Hoffman — Disclosures

Advisory Board	BeiGene Ltd, Pharmacyclics LLC, an AbbVie Company

Dr Kittai — Disclosures

Advisory Committee	AbbVie Inc, AstraZeneca Pharmaceuticals LP, BeiGene Ltd, Bristol-Myers Squibb Company, Janssen Biotech Inc, Kite, A Gilead Company, Lilly
Consulting Agreement	AbbVie Inc
Contracted Research	AstraZeneca Pharmaceuticals LP
Speakers Bureau	BeiGene Ltd

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Commercial Support

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

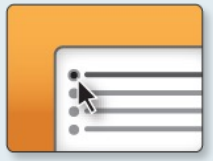
Research To Practice NCPD Planning Committee Members, Staff and Reviewers

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

Clinicians in the Meeting Room

Networked iPads are available.

Review Program Slides: Tap the Program Slides button to review speaker presentations and other program content.



Answer Survey Questions: Complete the pre- and postmeeting surveys. Survey questions will be discussed throughout the meeting.

Ask a Question: Tap Ask a Question to submit a challenging case or question for discussion. We will aim to address as many questions as possible during the program.

Complete Your Evaluation: Tap the NCPD Evaluation button to complete your evaluation electronically to receive credit for your participation.

For assistance, please raise your hand. Devices will be collected at the conclusion of the activity.

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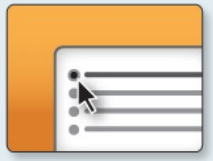
Clinicians Attending via Zoom

Review Program Slides: A link to the program slides will be posted in the chat room at the start of the program.



Answer Survey Questions: Complete the pre- and postmeeting surveys. Survey questions will be discussed throughout the meeting.

Ask a Question: Submit a challenging case or question for discussion using the Zoom chat room.

Get NCPD Credit: An NCPD credit link will be provided in the chat room at the conclusion of the program.

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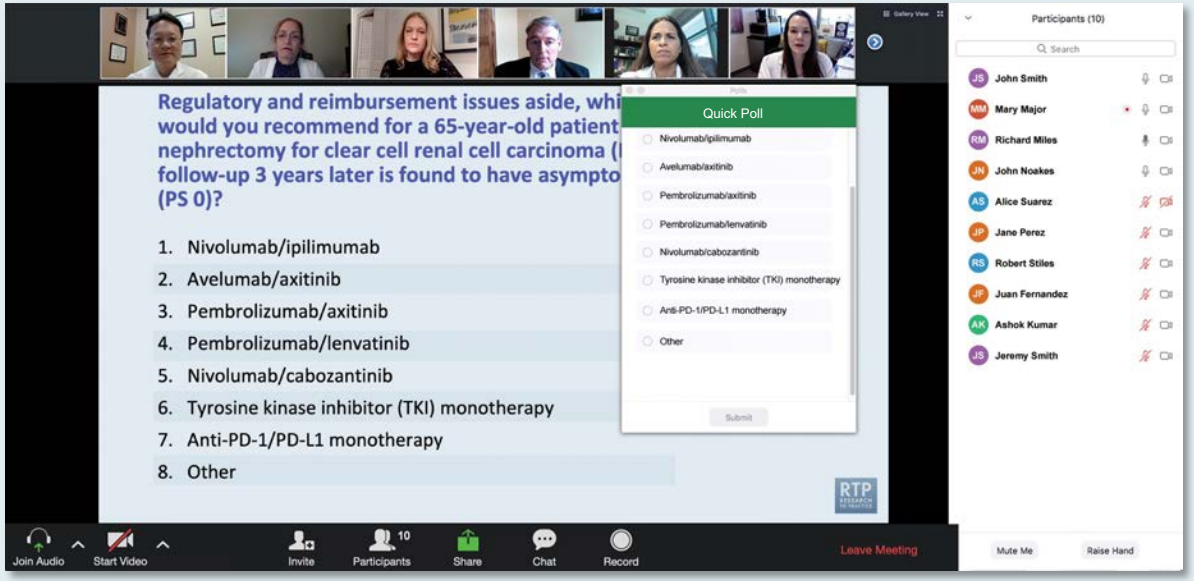
Clinicians, Please Complete the Pre- and Postmeeting Surveys



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About the Enduring Program

- The live meeting is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based video/PowerPoint program.
  An email will be sent to all attendees when the activity is available.
- To learn more about our education programs, visit our website, **www.ResearchToPractice.com**

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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

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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The James Comprehensive Cancer Center
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Columbus, Ohio

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Agenda

Module 1: Overview of Chronic Lymphocytic Leukemia (CLL)

Module 2: First-Line Therapy for CLL

Module 3: Use of Venetoclax in Combination with an Anti-CD20 Antibody

Module 4: Choice of BTK Inhibitor; BTK Inhibitor Toxicity

Module 5: Noncovalent BTK Inhibitors

Module 6: CAR T-Cell Therapy; Transformation

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Jacqueline Broadway-Duren, PhD, DNP, APRN, FNP-BC

70-year-old woman with CLL who received first-line therapy with obinutuzumab x 3 followed by acalabrutinib

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Dr Allan
New York, New York

Clinical Research Background

Dr Kittai
Columbus, Ohio

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

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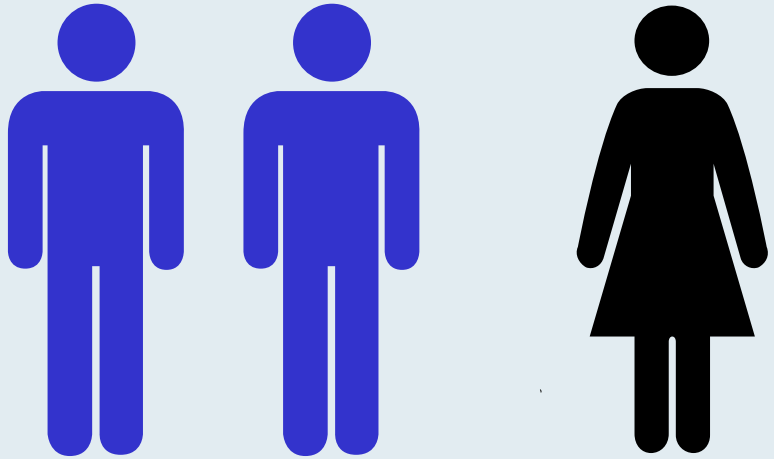
CLL Affects a Significant Number of Patients Worldwide, and Predominantly Older Patients

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

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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

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Module 5: Noncovalent BTK Inhibitors

Module 6: CAR T-Cell Therapy; Transformation

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Corinne Hoffman, MS, APRN-CNP, AOCNP

70-year-old woman with del13q CLL and PMH of headaches who received first-line therapy with zanubrutinib

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Dr Allan
New York, New York

Clinical Research Background

Dr Kittai
Columbus, Ohio

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

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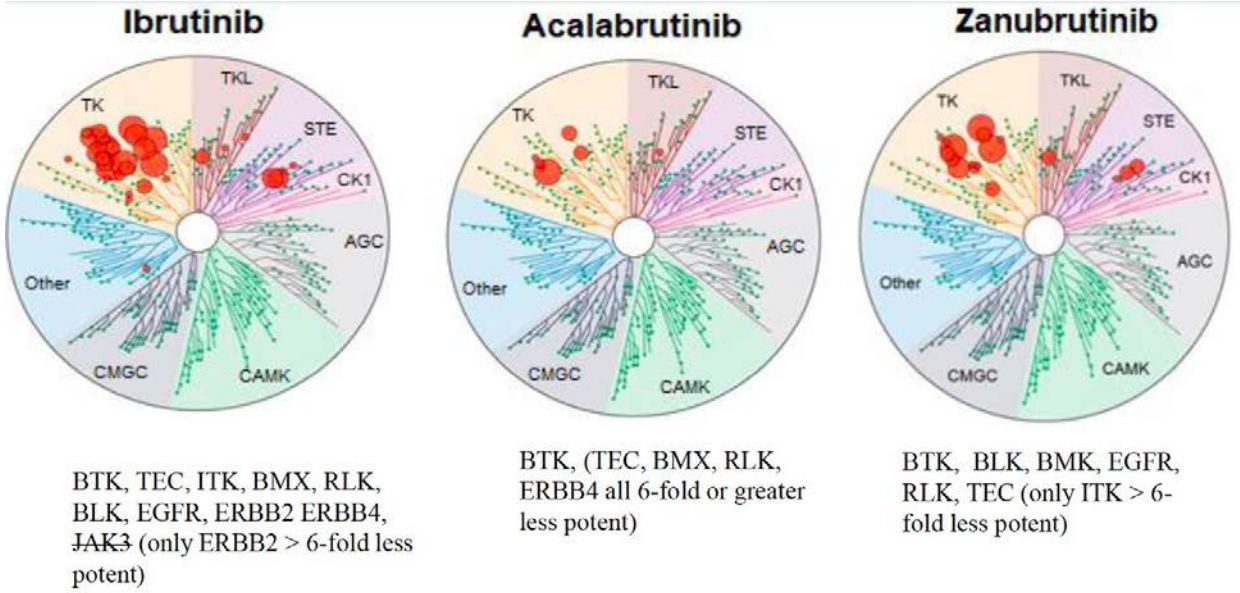
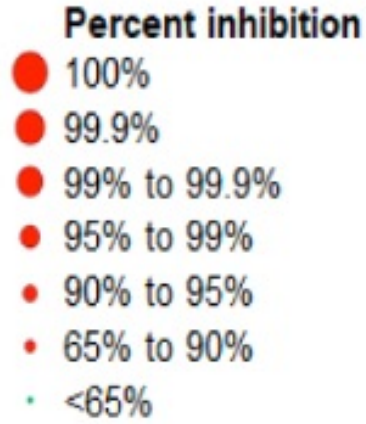
Irreversible and Reversible Bruton Tyrosine Kinase Inhibitors in CLL

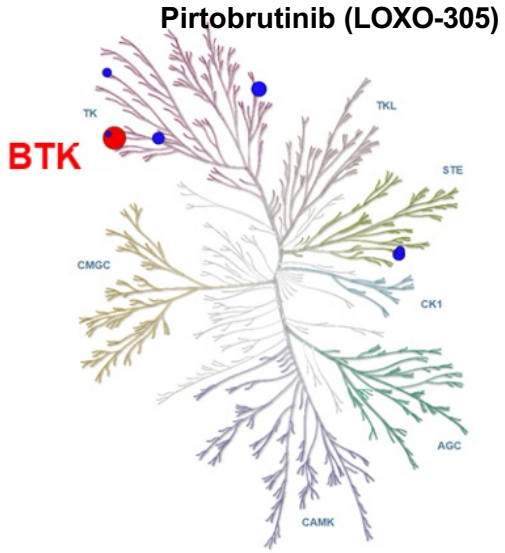
BTKi	Binding	T1/2 (hours)	IC50 (nM)	Dosing
Ibrutinib	Covalent irreversible C481	4-8	0.5	420 mg
Acalabrutinib	Covalent irreversible C481	0.9	5.1	100 mg BID
Zanubrutinib	Covalent irreversible C481	2-4	0.5	160 or 320 mg BID
Pirtobrutinib	Noncovalent reversible	Not available	0.85	200 mg

Irreversible



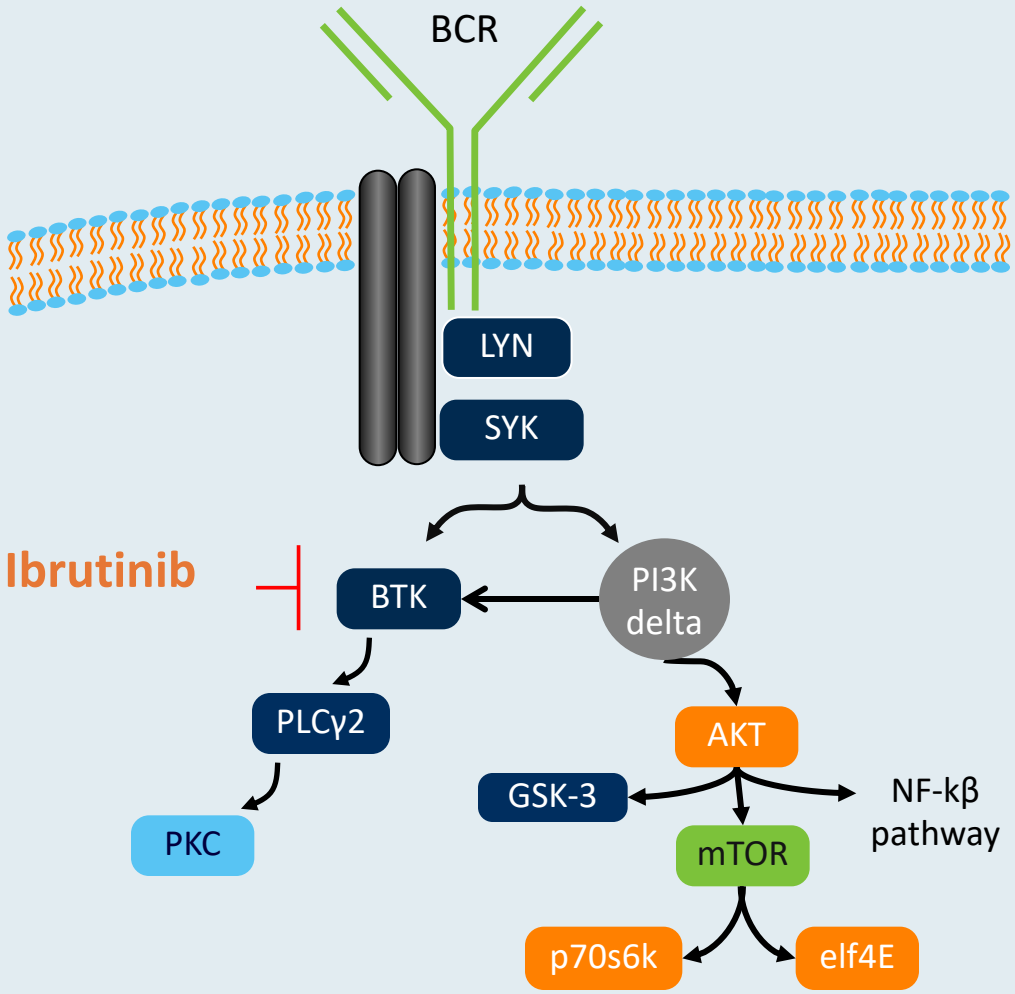


Reversible



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

Mechanism of Action of Ibrutinib



Woyach JA et al. *Blood* 2012;120(6):1175-84.

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Ibrutinib

Mechanism of action

- BTK inhibitor

Indication

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

Recommended dose

- 420 mg po QD swallowed whole with water

Key issues

- Dose reduction guidelines

Ibrutinib package insert, 8/2022.

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Acalabrutinib

Mechanism of action

- **BTK inhibitor**

Indication

- **For patients with CLL or SLL**

Recommended dose

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

Key issues

- **Dose reduction guidelines**

Acalabrutinib package insert, 8/2022.

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Zanubrutinib

Mechanism of action

- **BTK inhibitor**

Indication

- **For patients with CLL or SLL**

Recommended dose

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

Key issues

- **Dose reduction guidelines**

Zanubrutinib package insert, 1/2023.

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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

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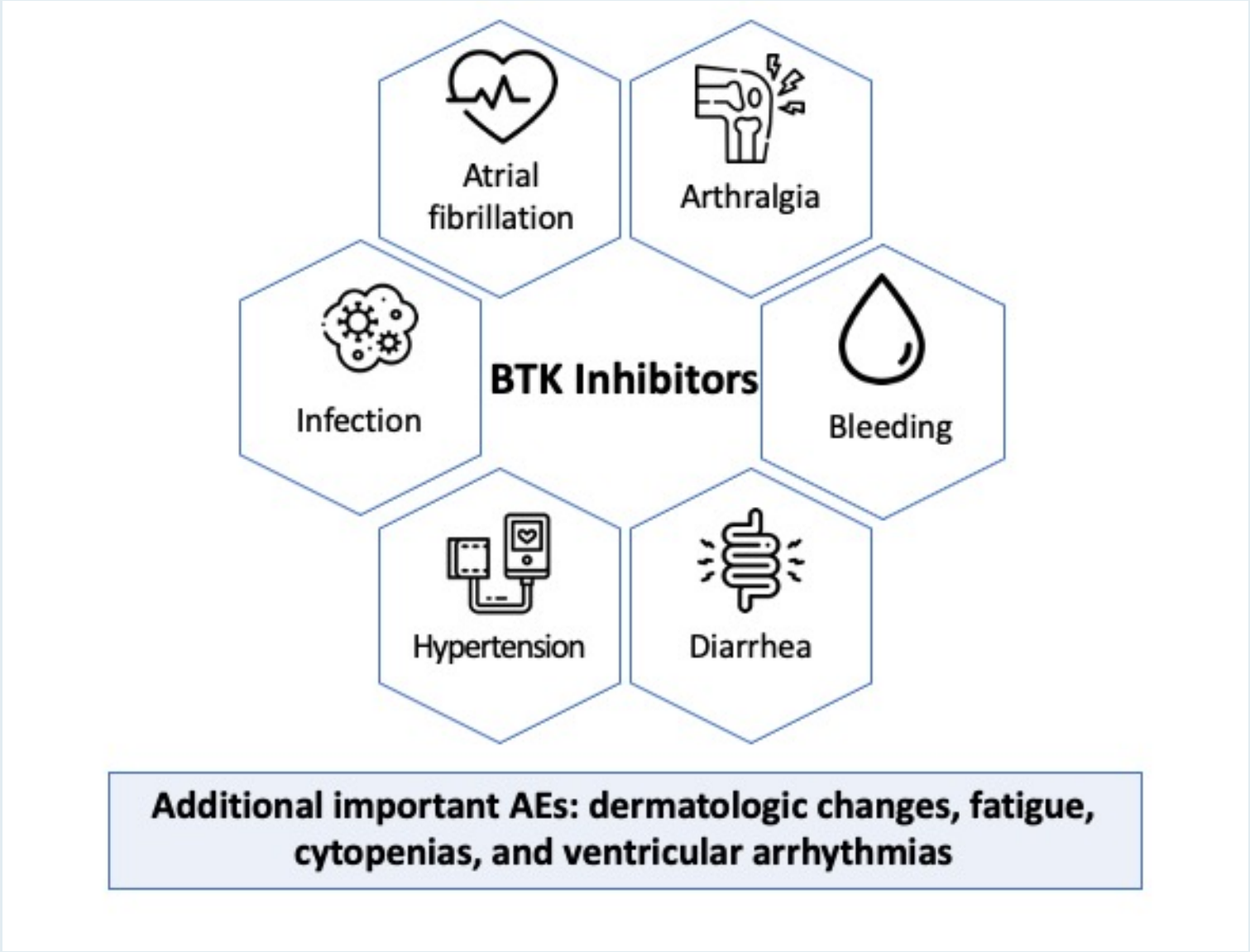
Summary of Adverse Events with BTK Inhibitors



Courtesy of Matthew S Davids, MD, MMSc 2022

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Jacqueline Broadway-Duren, PhD, DNP, APRN, FNP-BC

65-year-old woman with CLL who received first-line therapy with obinutuzumab/venetoclax

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Dr Allan
New York, New York

Clinical Research Background

Dr Kittai
Columbus, Ohio

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

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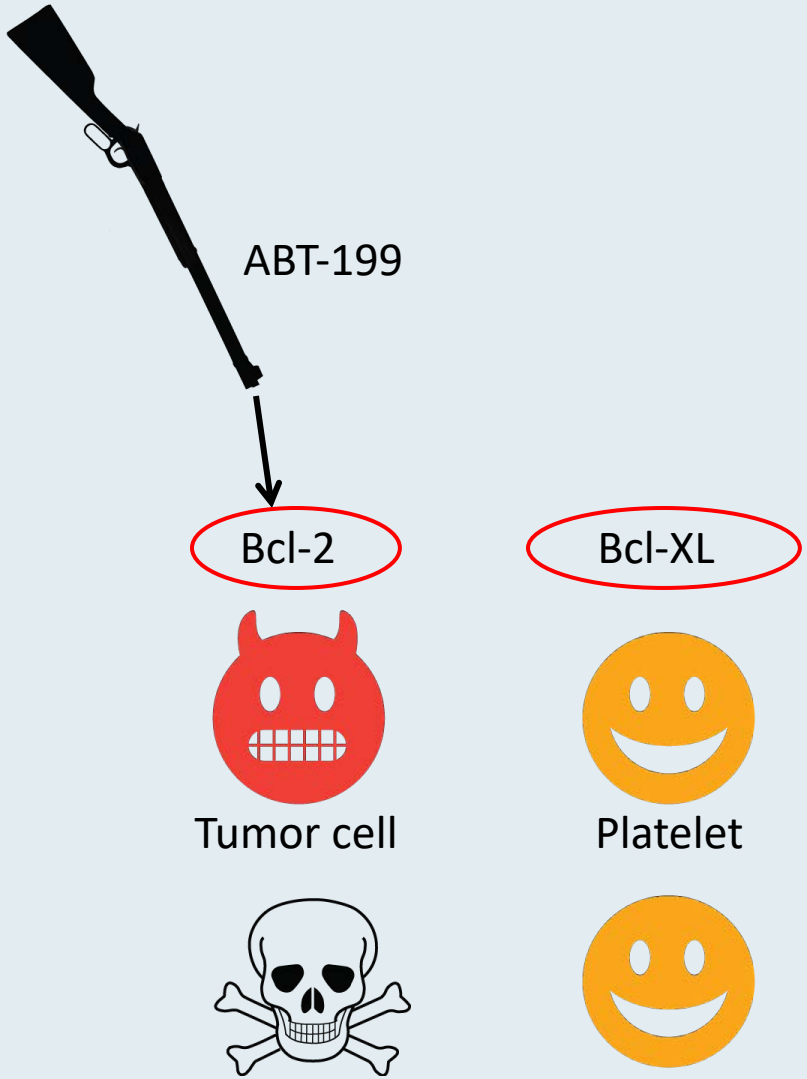
Mechanism of Action of Venetoclax (ABT-199)



- **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.

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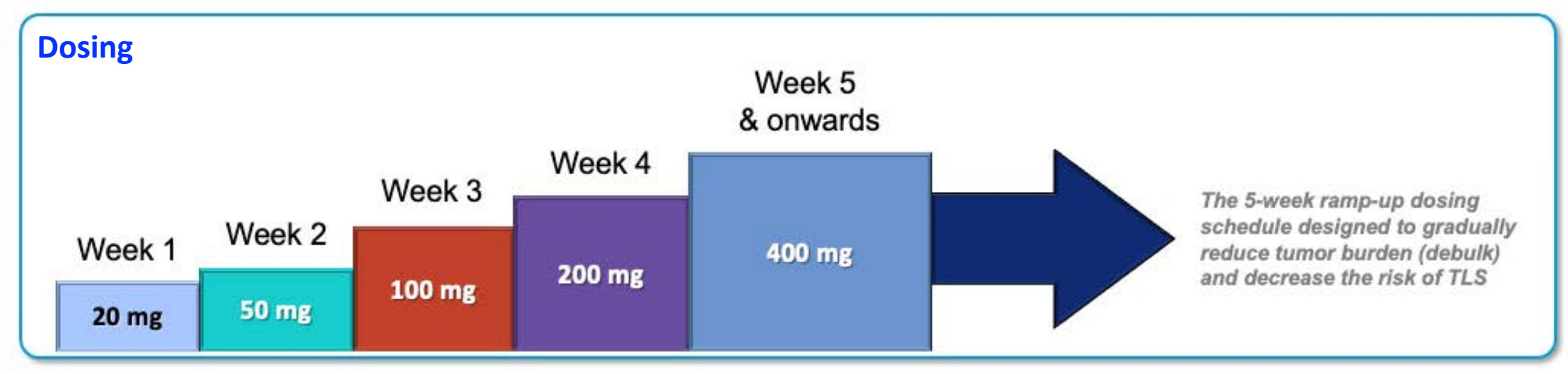
Venetoclax

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**

Courtesy of Robin Klebig, APRN, CNP, AOCNP

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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

- prn antiemetic

Diarrhea

- Loperamide prn
- Record # stools per day at baseline

Cytopenias

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

Courtesy of Robin Klebig, APRN, CNP, AOCNP

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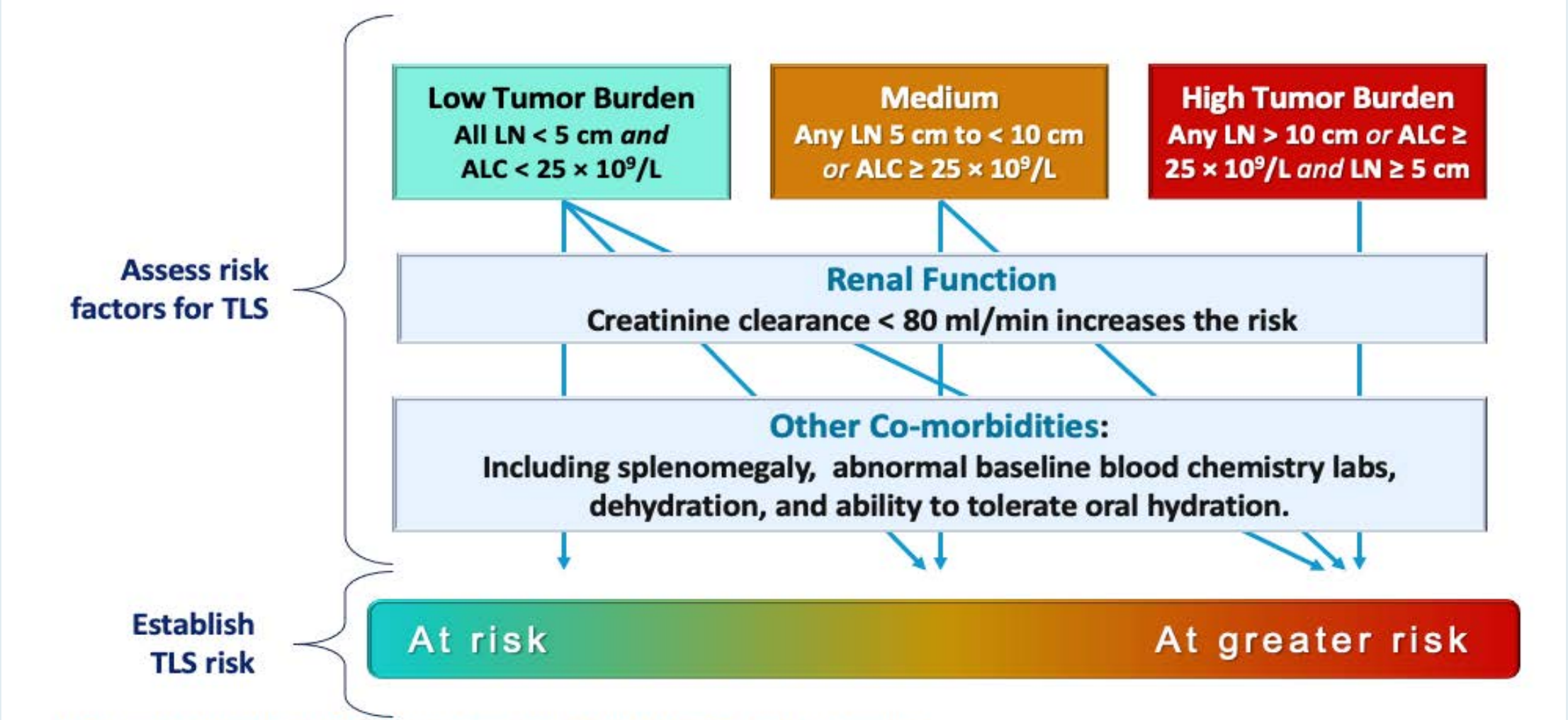
TLS Risk with Venetoclax Is a Continuum Based on Multiple Factors



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

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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

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Module 6: CAR T-Cell Therapy; Transformation

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Corinne Hoffman, MS, APRN-CNP, AOCNP

65-year-old woman with CLL who received ibrutinib and developed atrial fibrillation

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Dr Allan
New York, New York

Clinical Research Background

Dr Kittai
Columbus, Ohio

- **Choice of BTK inhibitor; BTK inhibitor toxicity**

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Corinne Hoffman, MS, APRN-CNP, AOCNP

68-year-old man with relapsed CLL who received obinutuzumab/venetoclax and developed neutropenia and thrombocytopenia

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Clinical Research Background

Dr Allan
New York, New York

Dr Kittai
Columbus, Ohio

- **Obinutuzumab versus rituximab**
- **Pirtobrutinib**

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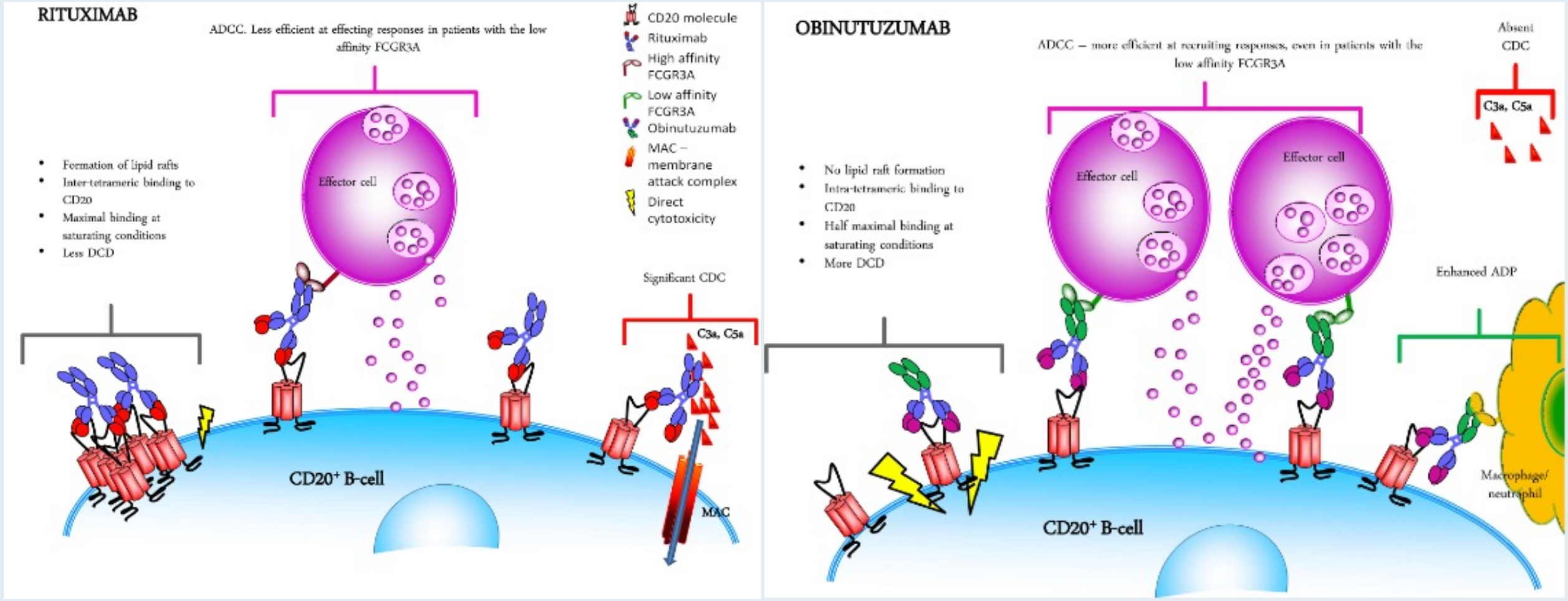
Mechanisms of Action of Rituximab and Obinutuzumab



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

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.

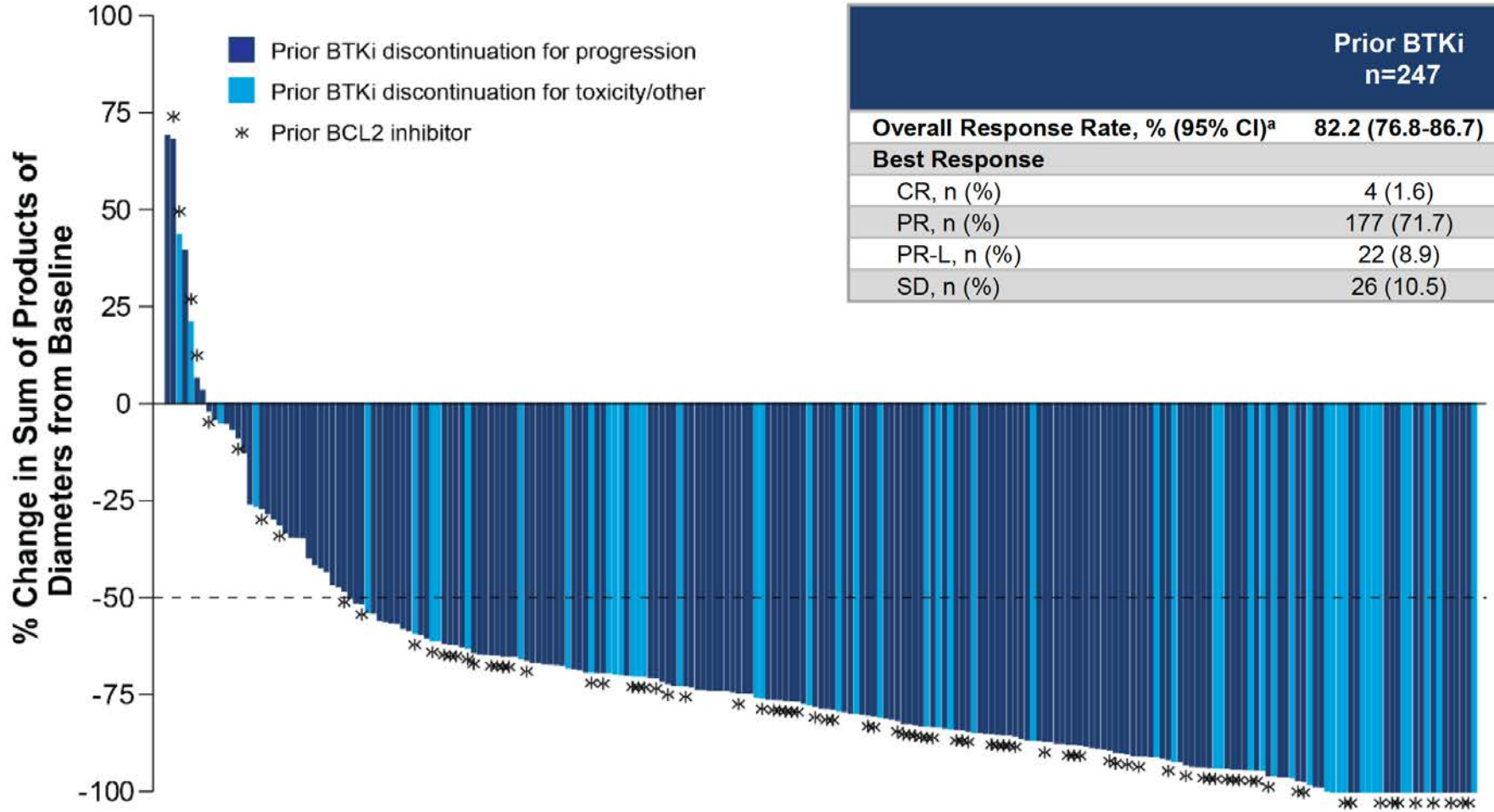
The main efficacy measures were overall response rate (ORR) and duration of response (DOR), as assessed by an independent review committee using Lugano criteria. The ORR was 50% (95% CI: 41, 59) with a complete response rate of 13%. The estimated median DOR was 8.3 months (95% CI: 5.7, NE), and the estimated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

BRUIN: Pirtobrutinib Efficacy in Patients with CLL/SLL Who Received Prior BTKi Treatment



	Prior BTKi n=247	Prior BTKi+BCL2i n=100
Overall Response Rate, % (95% CI)[a]	**82.2 (76.8-86.7)**	**79.0 (69.7-86.5)**
Best Response		
CR, n (%)	4 (1.6)	0 (0.0)
PR, n (%)	177 (71.7)	70 (70.0)
PR-L, n (%)	22 (8.9)	9 (9.0)
SD, n (%)	26 (10.5)	11 (11.0)

Mato AR et al. ASH 2022;Abstract 961.

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Agenda

Module 1: Overview of Chronic Lymphocytic Leukemia (CLL)

Module 2: First-Line Therapy for CLL

Module 3: Use of Venetoclax in Combination with an Anti-CD20 Antibody

Module 4: Choice of BTK Inhibitor; BTK Inhibitor Toxicity

Module 5: Noncovalent BTK Inhibitors

Module 6: CAR T-Cell Therapy; Transformation

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Jacqueline Broadway-Duren, PhD, DNP, APRN, FNP-BC

59-year-old man with CLL and a NOTCH1 mutation who received pirtobrutinib/obinutuzumab/venetoclax

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Clinical Research Background

Dr Allan
New York, New York

Dr Kittai
Columbus, Ohio

- **CAR T-cell therapy**
- **Transformation**

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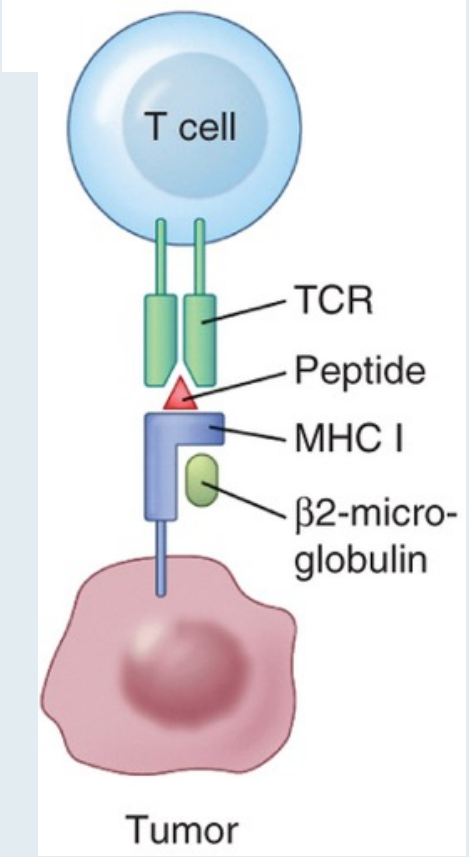
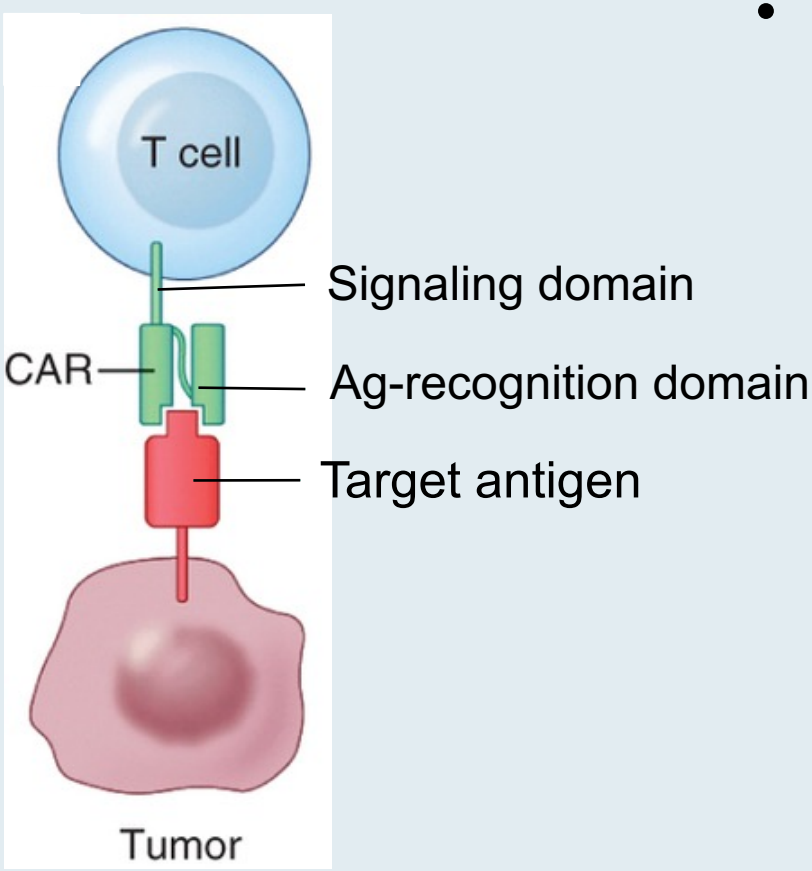
Chimeric Antigen Receptor (CAR) Modified T Cells

Normal T cell



CAR T cell



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

Courtesy of Sattva S Neelapu, MD

Adapted from Hinrichs & Restifo. *Nat Biotech* 2013

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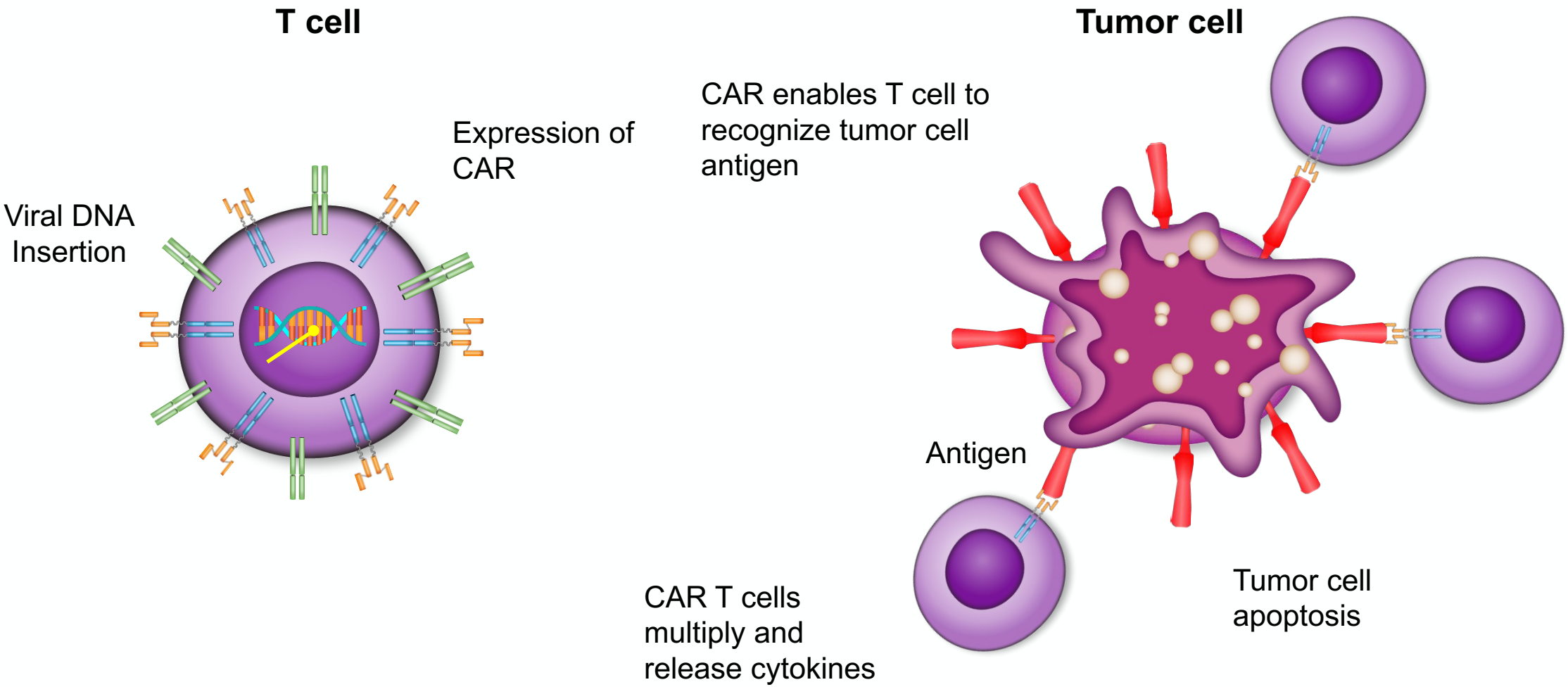
CAR T Cells: Mechanism of Action



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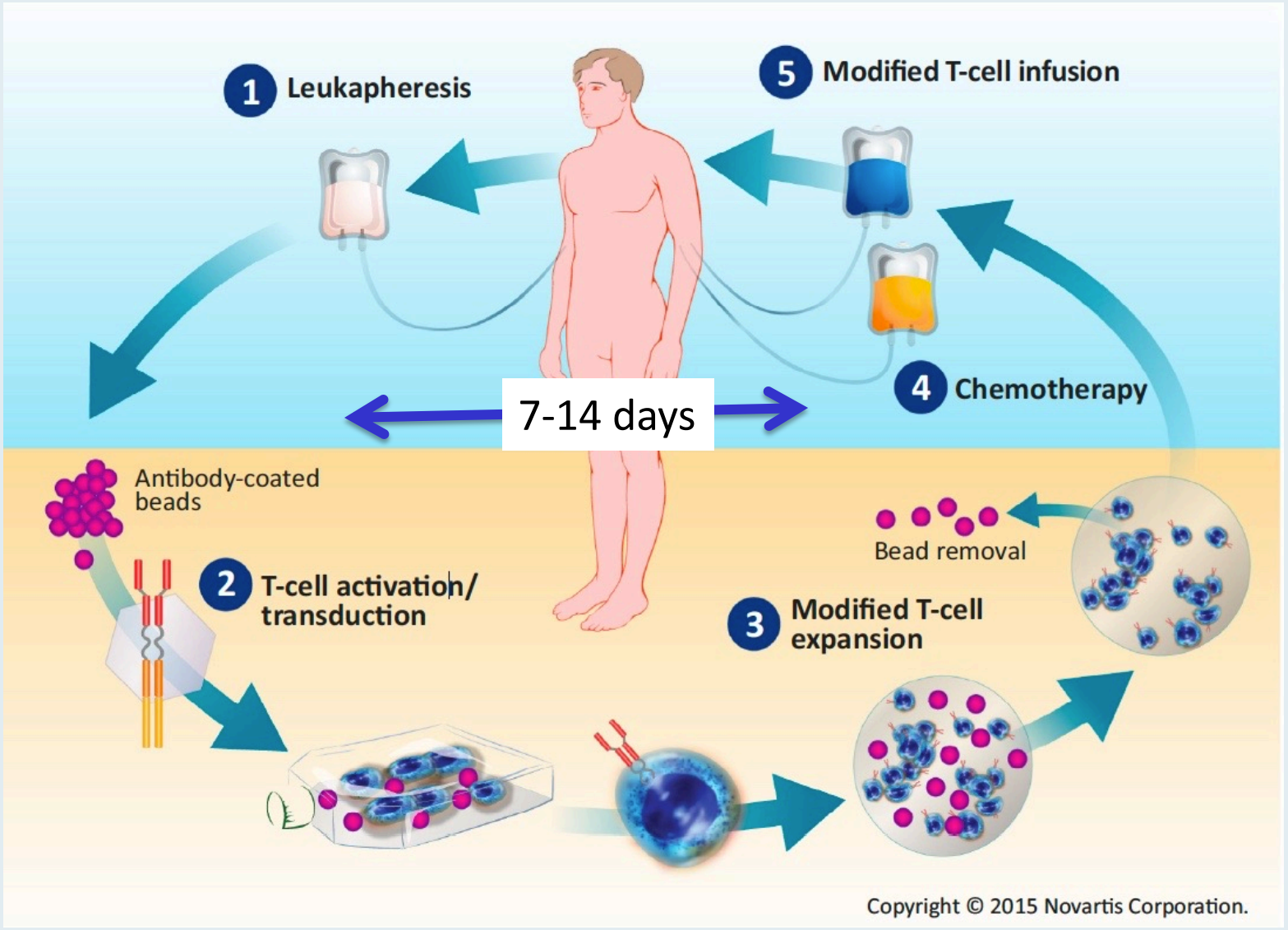
Overview of CAR T-Cell Therapy



Modification, Courtesy of David Porter, MD

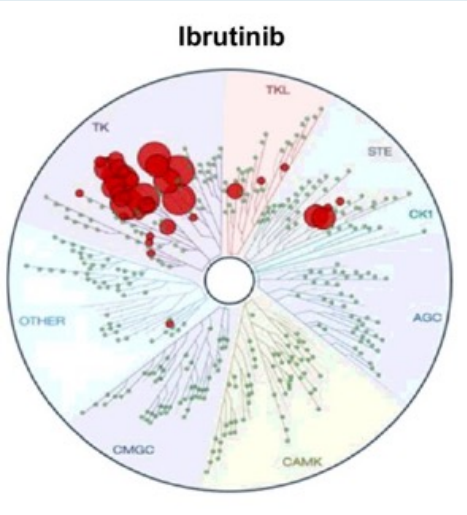
RTP RESEARCH TO PRACTICE

APPENDIX

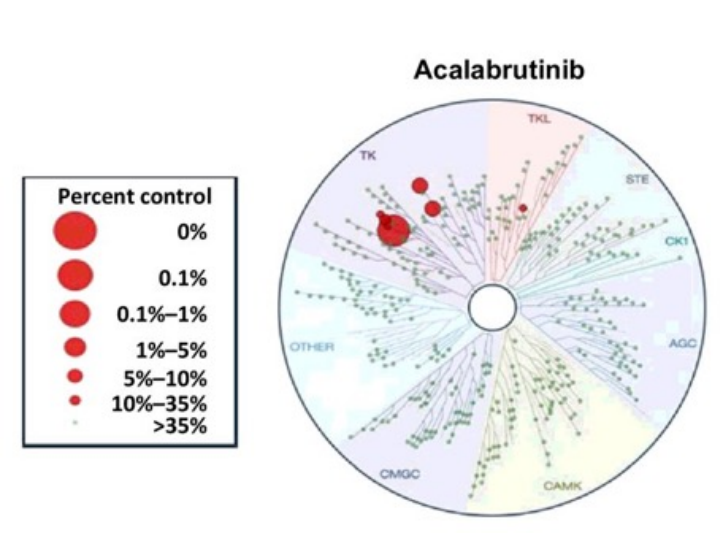
Overview of BTK Inhibitors for CLL

Irreversible

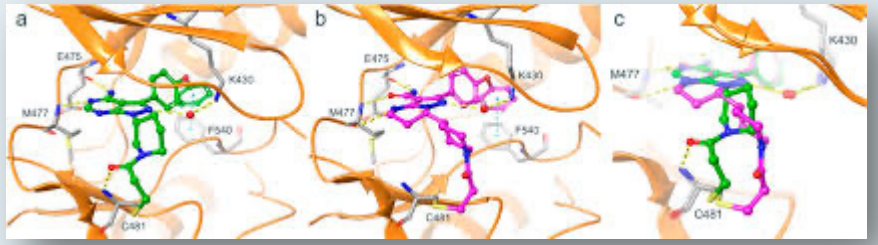
Ibrutinib



Acalabrutinib

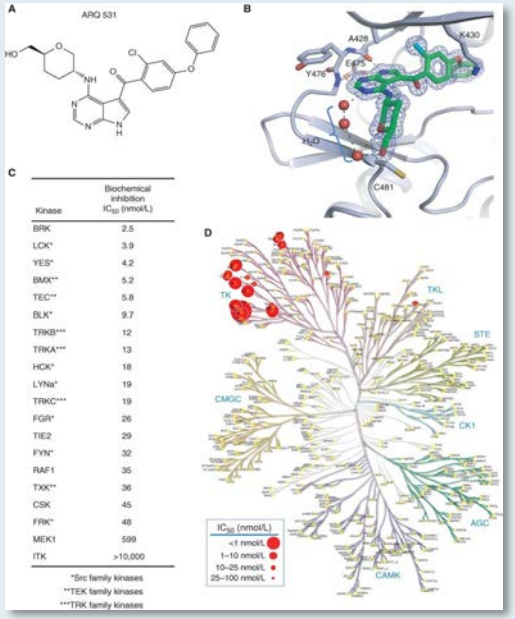


Zanubrutinib

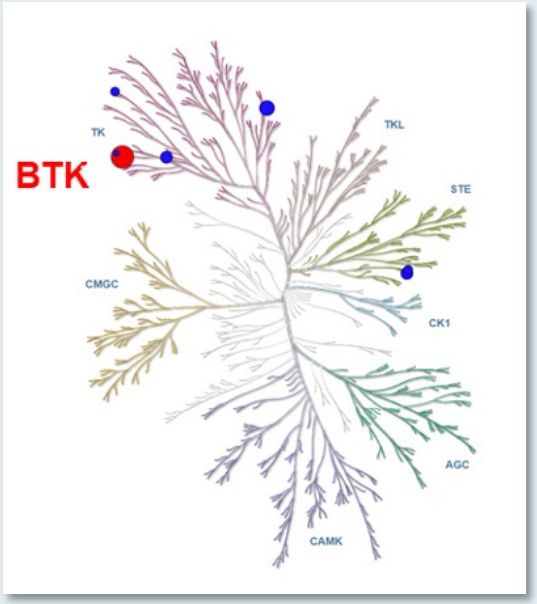


Reversible

ARQ-531 (MK-1026)



Pirtobrutinib



Courtesy of Matthew S Davids, MD, MMSc

RTP RESEARCH TO PRACTICE

ELEVATE-TN: First-Line Acalabrutinib +/- Obinutuzumab versus Obinutuzumab/Chlorambucil

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Acalabrutinib ± Obinutuzumab versus Obinutuzumab + Chlorambucil in Treatment-Naïve Chronic Lymphocytic Leukemia: Five-Year Follow-Up of ELEVATE-TN

Sharman JP et al.

ASCO 2022;Abstract 7539.

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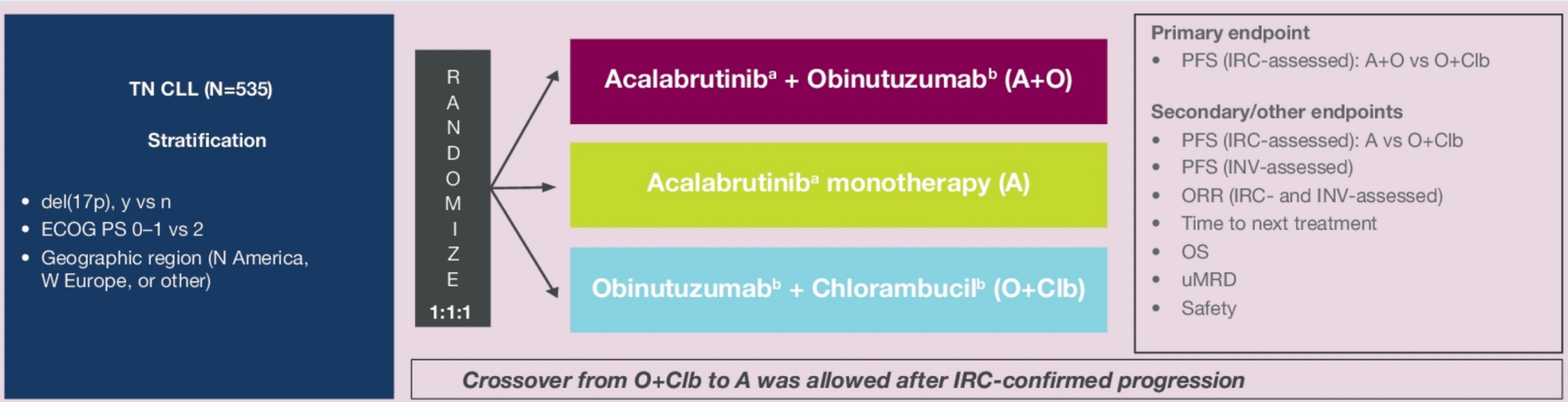
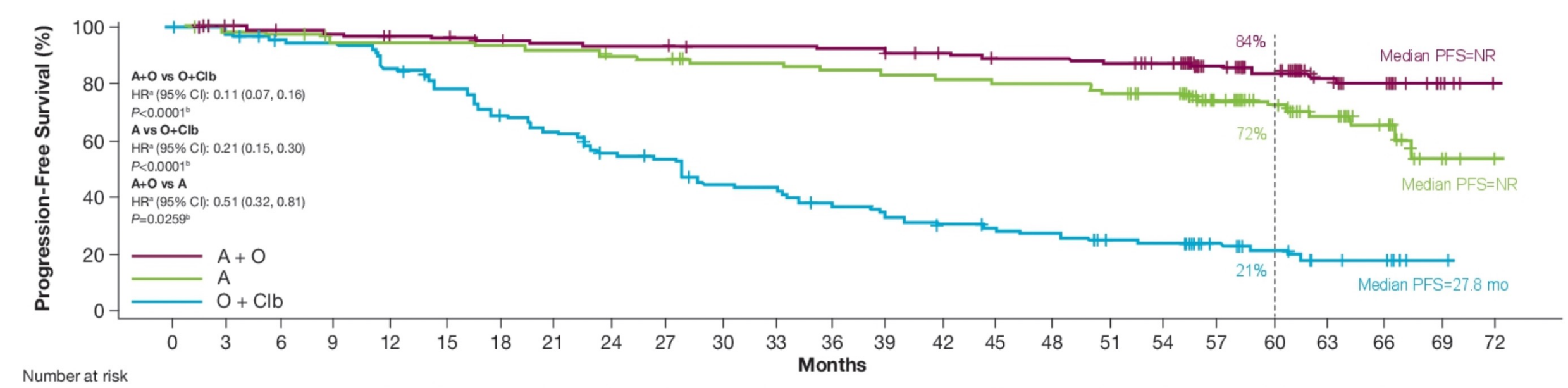
ELEVATE-TN Study Design



Note: After interim analysis,[7] PFS assessments were by investigator only

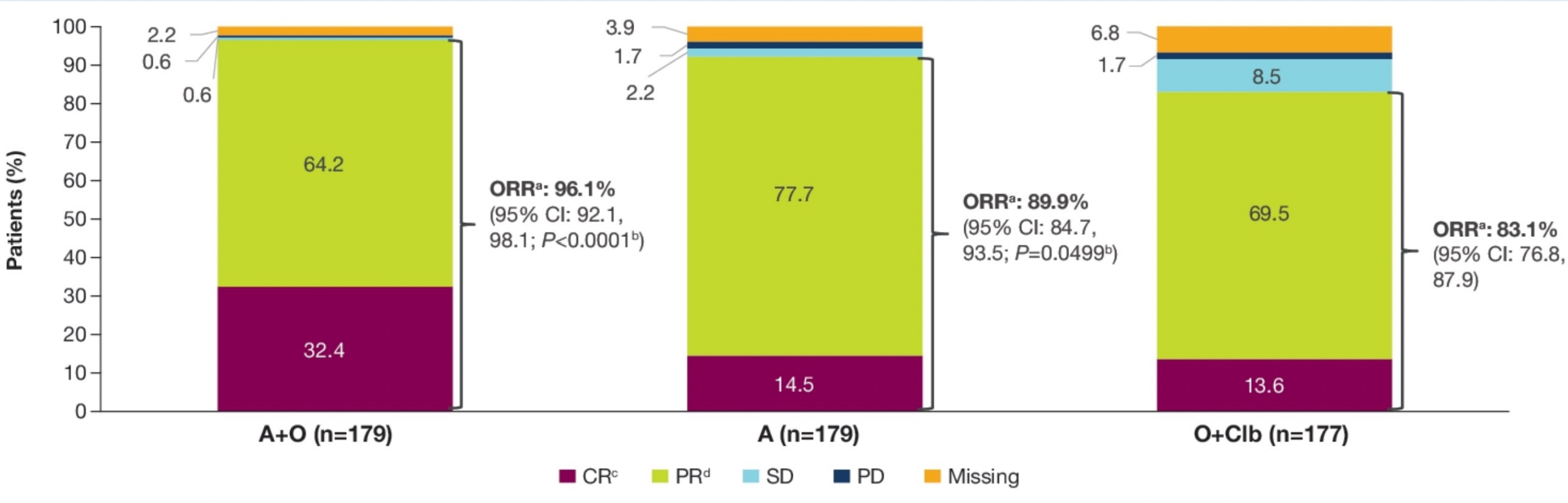
Sharman JP et al. ASCO 2022;Abstract 7539.

ELEVATE-TN: Investigator-Assessed PFS



Sharman JP et al. ASCO 2022;Abstract 7539.

ELEVATE-TN: Investigator-Assessed ORR



Sharman JP et al. ASCO 2022;Abstract 7539.

ELEVATE-TN: Adverse Events of Clinical Interest

	A+O (n=178)		A (n=179)		O+Clb (n=169)	
	Any Grade	**Grade ≥3**	**Any Grade**	**Grade ≥3**	**Any Grade**	**Grade ≥3**
Cardiac events	43 (24.2)	17 (9.6)	39 (21.8)	18 (10.1)	13 (7.7)	3 (1.8)
Atrial fibrillation	11 (6.2)	2 (1.1)	13 (7.3)	2 (1.1)	1 (0.6)	0
Bleeding	88 (49.4)	8 (4.5)	78 (43.6)	6 (3.4)	20 (11.8)	0
Major bleeding[a]	12 (6.7)	8 (4.5)	8 (4.5)	6 (3.4)	2 (1.2)	0
Hypertension	17 (9.6)	8 (4.5)	16 (8.9)	7 (3.9)	6 (3.6)	5 (3.0)
Infections	140 (78.7)	50 (28.1)	135 (75.4)	35 (19.6)	75 (44.4)	14 (8.3)
SPMs	31 (17.4)	14 (7.9)	27 (15.1)	7 (3.9)	7 (4.1)	3 (1.8)
SPMs excluding non-melanoma skin	17 (9.6)	12 (6.7)	13 (7.3)	5 (2.8)	3 (1.8)	2 (1.2)

Sharman JP et al. ASCO 2022;Abstract 7539.

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CLL14: First-Line Venetoclax/Obinutuzumab

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EHA EUROPEAN HEMATOLOGY ASSOCIATION

EHA2022 HYBRID JUNE 9-17 VIENNA

EHA EUROPEAN HEMATOLOGY ASSOCIATION

Abstract S148

EHA2022 HYBRID VIRTUAL

UNIKLINIK KÖLN | Department I of Internal Medicine University Hospital of Cologne

DEUTSCHE STUDIENGRUPPE CLL

Othman Al-Sawaf

Abstract S148

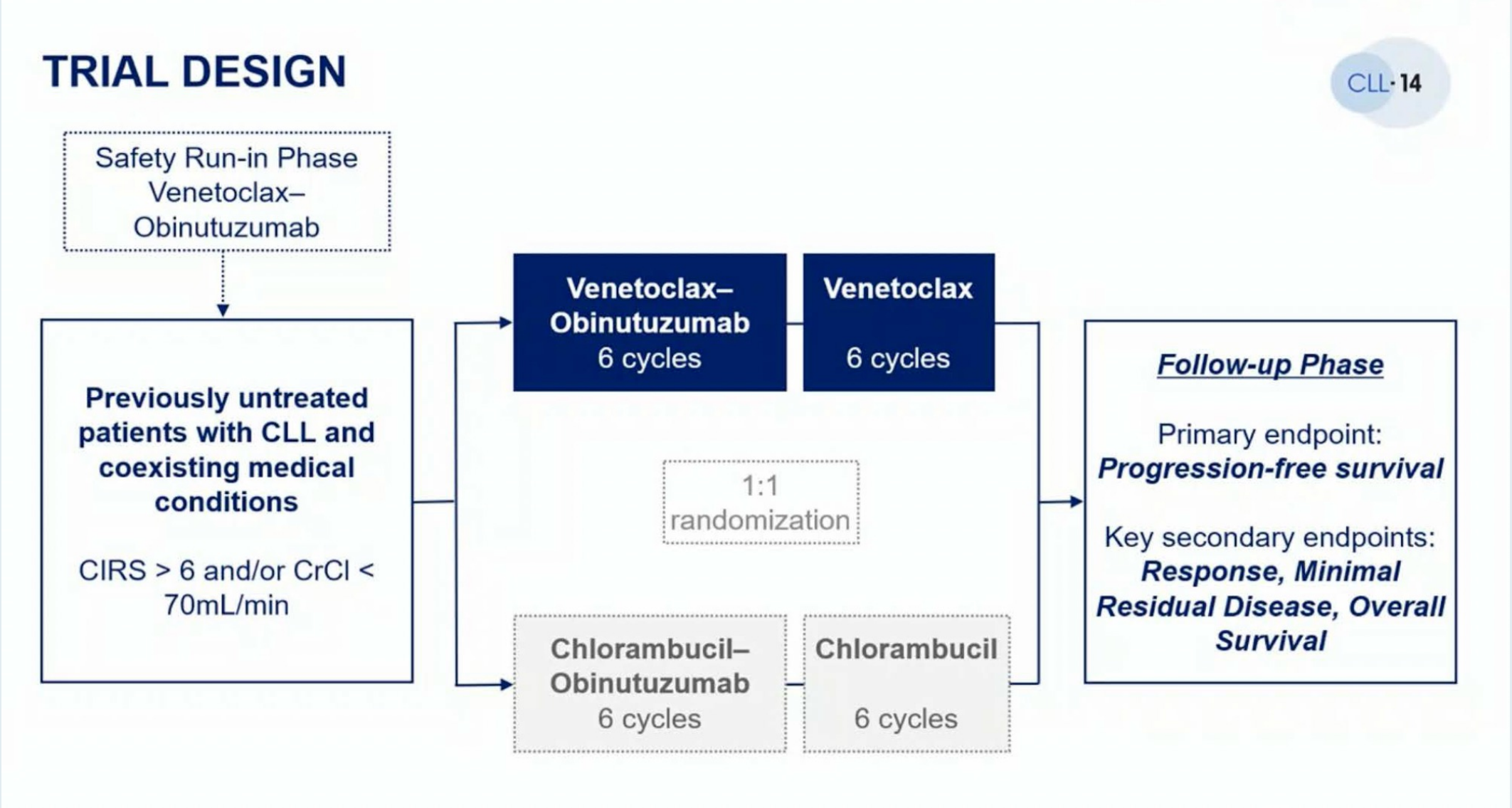
Venetoclax-Obinutuzumab for previously untreated chronic lymphocytic leukemia: 5-year results of the randomized CLL14 study

Othman Al-Sawaf, Can Zhang, Sandra Robrecht, Alex Kotak, Naomi Chang, Anna Maria Fink, Eugen Tausch, Christof Schneider, Matthias Ritgen, Karl-Anton Kreuzer, Brenda Chyla, Barbara Eichhorst, Yanwen Jiang, Stephan Stilgenbauer, Michael Hallek, Kirsten Fischer

June 12th, 2022
Clinical CLL Session

RTP RESEARCH TO PRACTICE

CLL14 Trial Design



Al-Sawaf O et al. EHA 2022;Abstract S148.

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CLL14: Most Frequent Grade ≥III Adverse Events

	Venetoclax-obinutuzumab (N=212)		Chlorambucil-obinutuzumab (N=214)	
	During Treatment	After Treatment	During Treatment	After Treatment
Neutropenia	51.9%	4.0%	47.2%	1.9%
Thrombocytopenia	14.2%	0.5%	15.0%	0.0%
Anemia	7.5%	2.0%	6.1%	0.5%
Febrile neutropenia	4.2%	1.0%	3.3%	0.5%
Leukopenia	2.4%	0.0%	4.7%	0.0%
Pneunomia	3.8%	3.0%	3.3%	1.4%
Infusion-related reaction	9.0%	0.0%	9.8%	0.5%
Tumour lysis syndrome	1.4%	0.0%	3.3%	0.0%

Al-Sawaf O et al. EHA 2022;Abstract S148.

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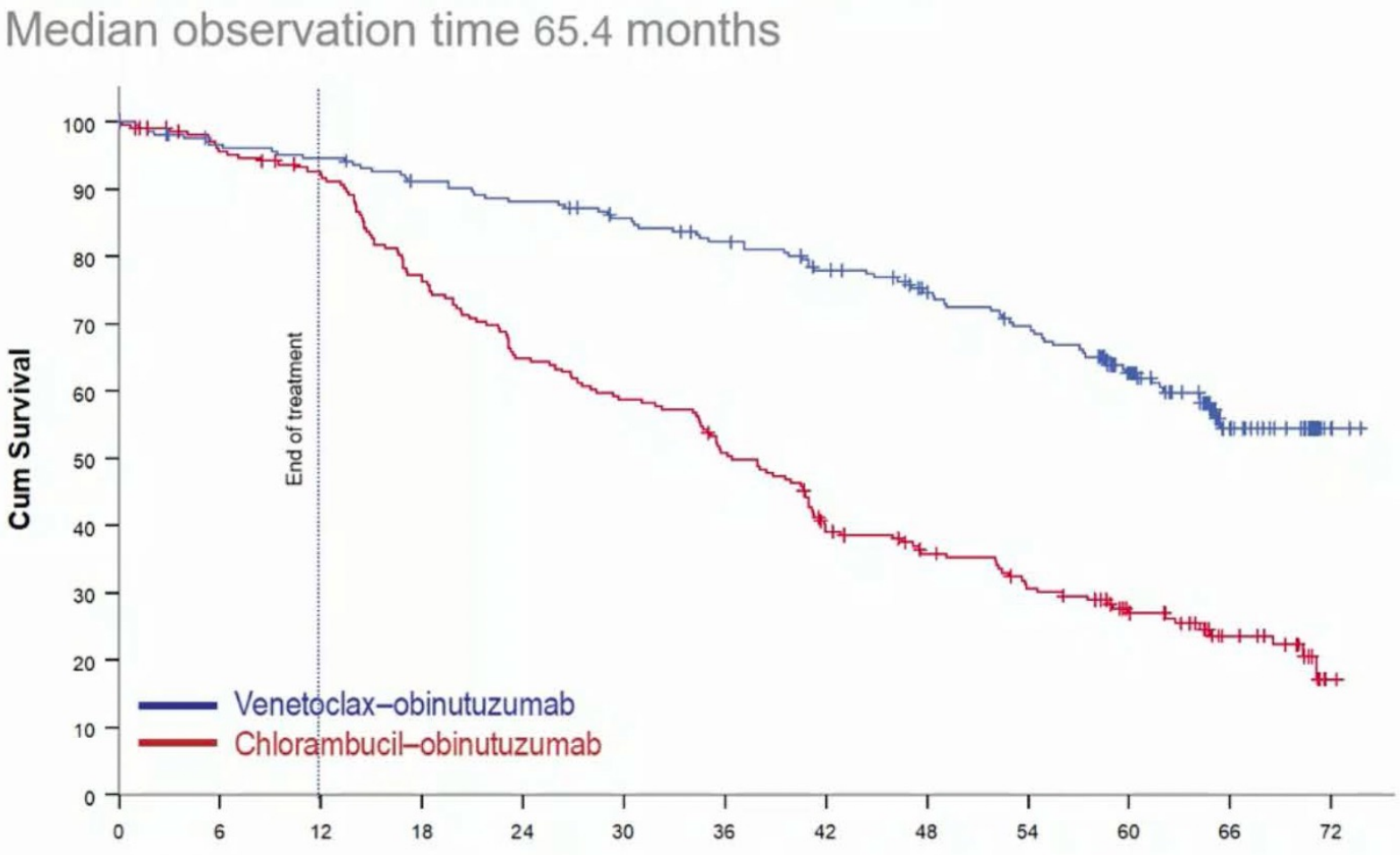
CLL14: Progression-Free Survival



Median PFS

Ven-Obi: not reached

Clb-Obi: 36.4 months

5-year PFS rate

Ven-Obi: 62.6%

Clb-Obi: 27.0%

HR 0.35, 95% CI [0.26-0.46]

P<0.0001

Al-Sawaf O et al. EHA 2022;Abstract S148.

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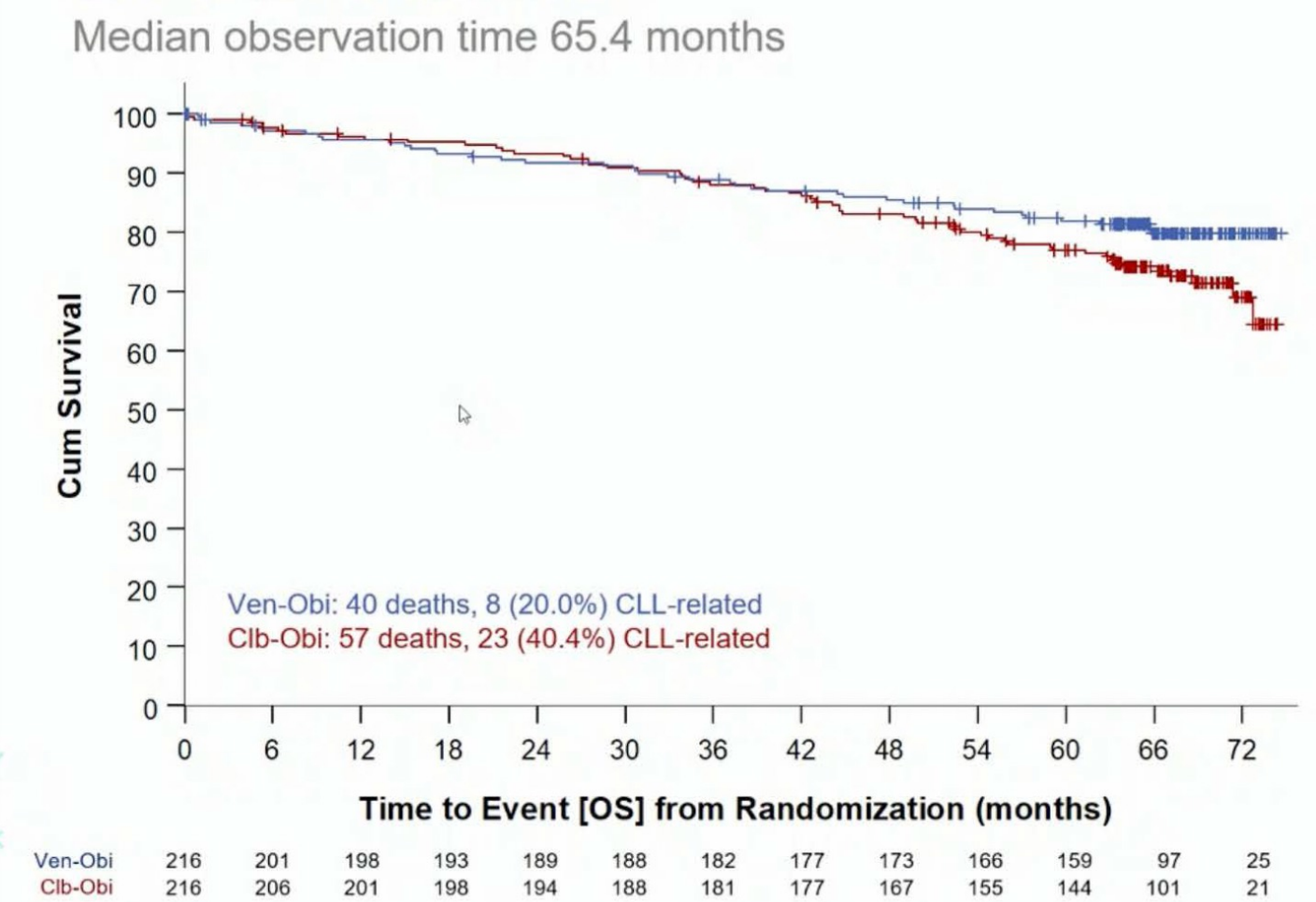
CLL14: Overall Survival



Median OS
Ven-Obi: not reached
Clb-Obi: not reached

5-year OS rate
Ven-Obi: 81.9%
Clb-Obi: 77.0%

HR 0.72, 95% CI [0.48-1.09]
P=0.12

Al-Sawaf O et al. EHA 2022;Abstract S148.

RTP RESEARCH TO PRACTICE

SEQUOIA: First-Line Zanubrutinib versus BR

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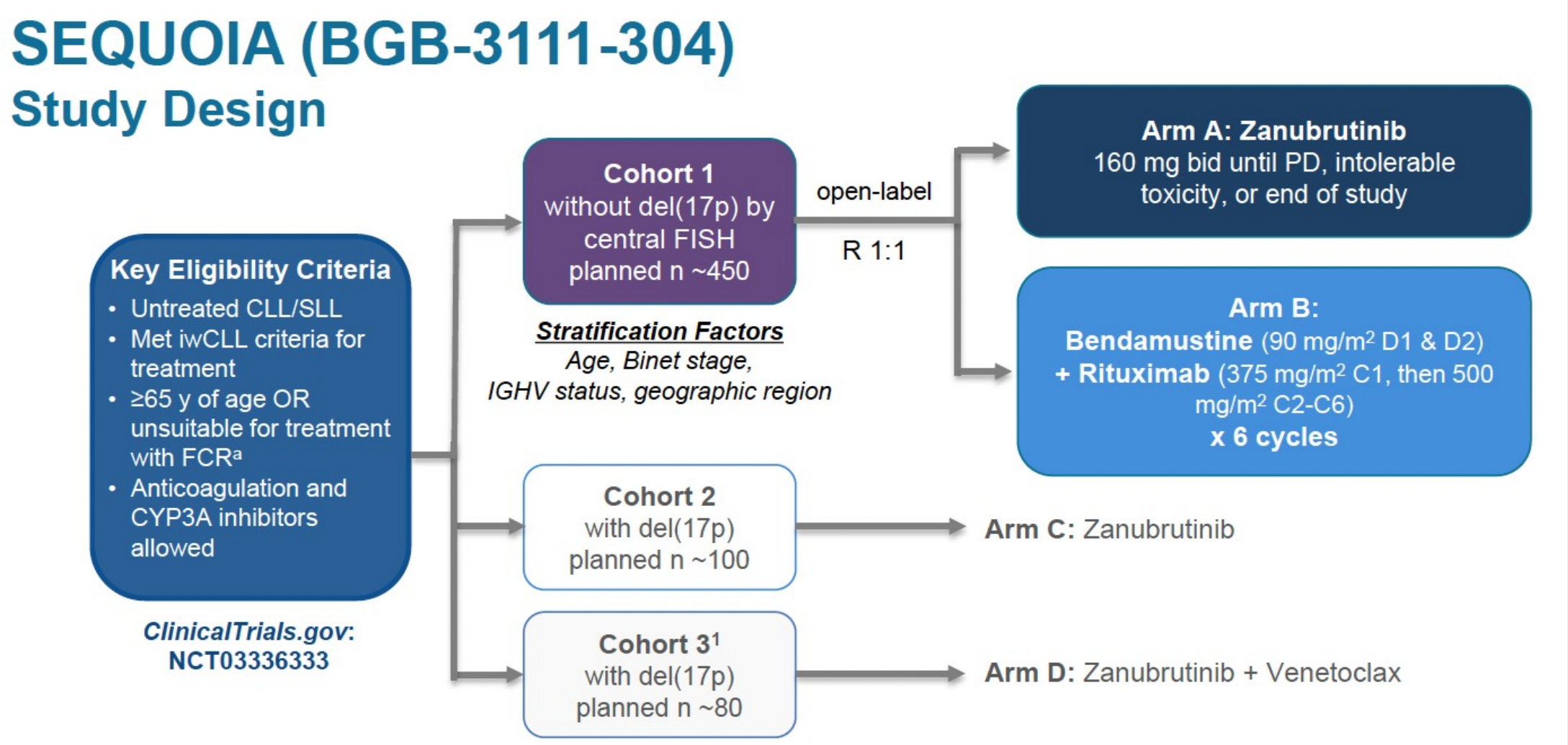
Lancet Oncol 2022 August;23(8):1031-43.

Zanubrutinib versus bendamustine and rituximab in untreated chronic lymphocytic leukaemia and small lymphocytic lymphoma (SEQUOIA): a randomised, controlled, phase 3 trial

Constantine S Tam, Jennifer R Brown, Brad S Kahl, Paolo Ghia, Krzysztof Giannopoulos, Wojciech Jurczak, Martin Šimkovič, Mazyar Shadman, Anders Österborg, Luca Laurenti, Patricia Walker, Stephen Opat, Henry Chan, Hanna Ciepluch, Richard Greil, Monica Tani, Marek Trněný, Danielle M Brander, Ian W Flinn, Sebastian Grosicki, Emma Verner, Alessandra Tedeschi, Jianyong Li, Tian Tian, Lei Zhou, Carol Marimpietri, Jason C Paik, Aileen Cohen, Jane Huang, Tadeusz Robak, Peter Hillmen**

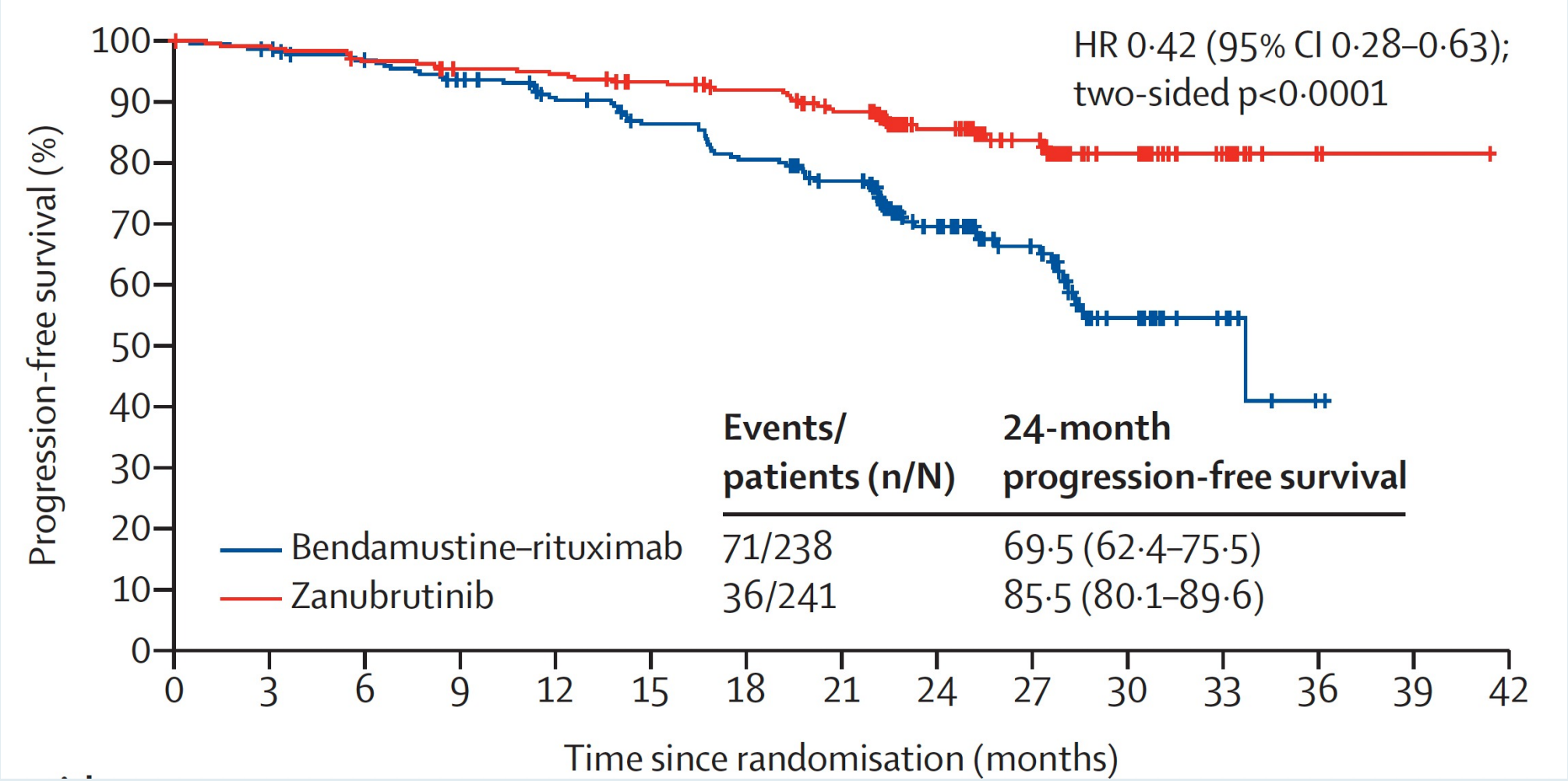
SEQUOIA Phase III Study Design



Tam CS et al. ASH 2021;Abstract 396.

RTP RESEARCH TO PRACTICE

SEQUOIA: Progression-Free Survival by IRC (ITT Population)



Tam CS et al. *Lancet Oncol* 2022 August;23(8):1031-43.

SEQUOIA: Adverse Events of Interest

	Patients Without del(17p)				Patients With del(17p)	
	Group A Zanubrutinib (n=240[a])		Group B Bendamustine-rituximab (n=227[b])		Group C Zanubrutinib (n=111)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any AEI, n (%)	207 (86·3)	96 (40·0)	206 (90·7)	156 (68·7)	103 (92·8)	46 (41·4)
Anaemia	11 (4·6)	1 (0·4)	44 (19·4)	4 (1·8)	6 (5·4)	0 (0·0)
Arthralgia	32 (13·3)	2 (0·8)	20 (8·8)	1 (0·4)	22 (19·8)	1 (0·9)
Atrial fibrillation	8 (3·3)	1 (0·4)	6 (2·6)	3 (1·3)	5 (4·5)	4 (3·6)
Bleeding	108 (45·0)	9 (3·8)	25 (11·0)	4 (1·8)	57 (51·4)	6 (5·4)
Bruising	58 (24·2)	0 (0·0)	9 (4·0)	0 (0·0)	28 (25·2)	0 (0·0)
Major Bleeding	12 (5·0)	9 (3·8)	4 (1·8)	4 (1·8)	8 (7·2)	6 (5·4)
Minor Bleeding	68 (28·3)	0 (0·0)	15 (6·6)	0 (0·0)	34 (30·6)	0 (0·0)
Petechiae	18 (7·5)	1 (0·4)	0 (0·0)	0 (0·0)	5 (4·5)	0 (0·0)
Diarrhoea	33 (13·8)	2 (0·8)	31 (13·7)	5 (2·2)	19 (17·1)	1 (0·9)
Hypertension	34 (14·2)	15 (6·3)	24 (10·6)	11 (4·8)	12 (10·8)	6 (5·4)
Infections	149 (62·1)	39 (16·3)	127 (55·9)	43 (18·9)	79 (71·2)	19 (17·1)
Myalgia	9 (3·8)	0 (0·0)	3 (1·3)	0 (0·0)	6 (5·4)	1 (0·9)
Neutropenia	38 (15·8)	28 (11·7)	129 (56·8)	116 (51·1)	21 (18·9)	18 (16·2)
Other cancers	31 (12·9)	17 (7·1)	20 (8·8)	7 (3·1)	24 (21·6)	7 (6·3)
Dermatologic other cancers	16 (6·7)	2 (0·8)	10 (4·4)	2 (0·9)	17 (15·3)	2 (1·8)
Thrombocytopenia	11 (4·6)	5 (2·1)	40 (17·6)	18 (7·9)	8 (7·2)	1 (0·9)

Tam CS et al. *Lancet Oncol* 2022 August;23(8):1031-43.

RTP RESEARCH TO PRACTICE

ELEVATE-RR and ALPINE

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original reports

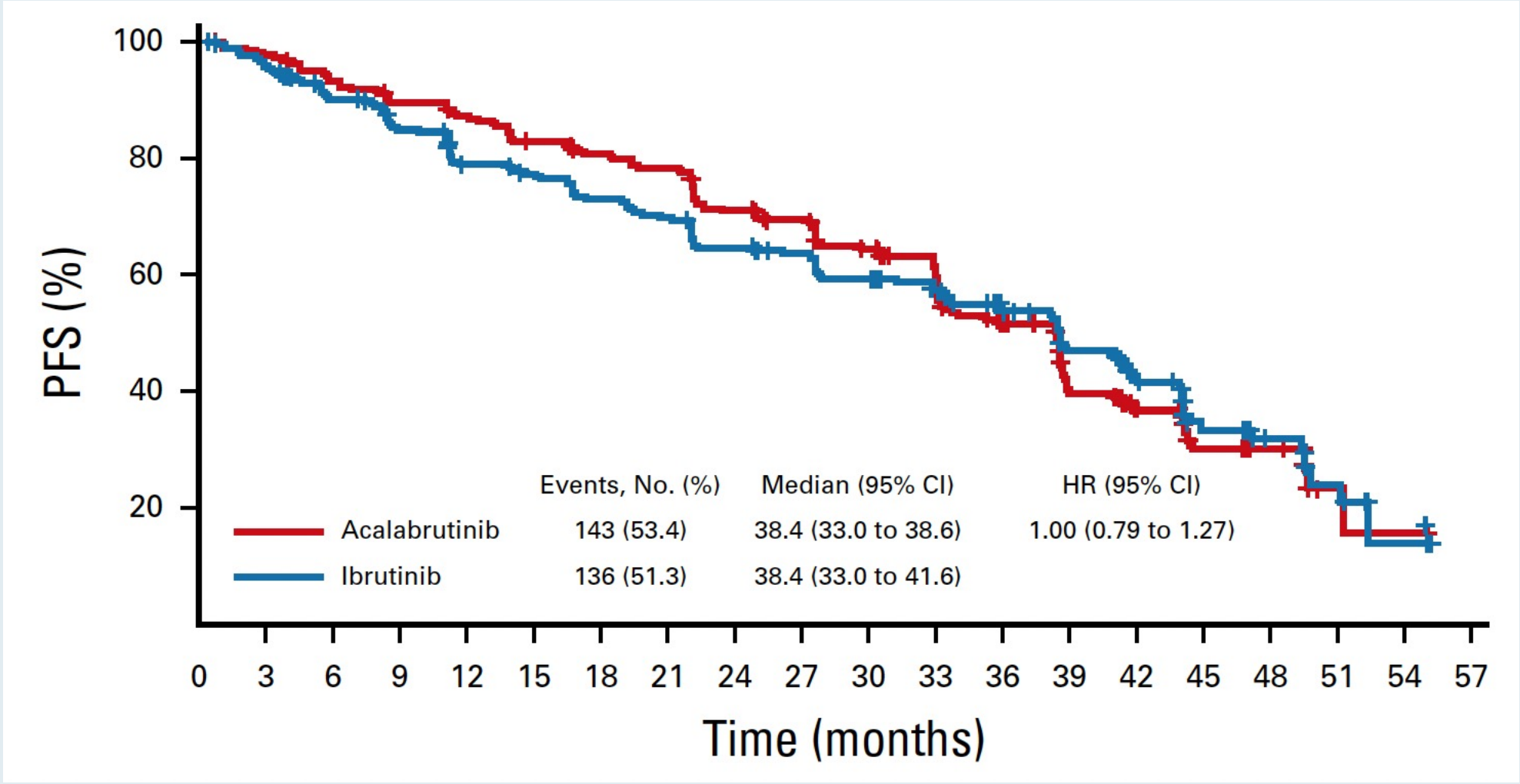
Acalabrutinib Versus Ibrutinib in Previously Treated Chronic Lymphocytic Leukemia: Results of the First Randomized Phase III Trial

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

RTP RESEARCH TO PRACTICE

ELEVATE-RR: Independent Review Committee-Assessed PFS



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

RTP RESEARCH TO PRACTICE

ELEVATE-RR: Characterization of Adverse Events with Acalabrutinib versus Ibrutinib

	Incidence, %				Exposure-Adjusted Incidence[b]				Exposure-Adjusted Time With Event[c]			
	Any grade		Grade ≥3		Any grade		Grade ≥3		Any grade		Grade ≥3	
	Acala[d]	Ibru[e]	Acala[d]	Ibru[e]	Acala[d]	Ibru[e]	Acala[d]	Ibru[e]	Acala[d]	Ibru[e]	Acala[d]	Ibru[e]
ECIs												
Cardiac events	24%	30%	9%	10%	1.2	1.9	0.4	0.5	7.1	13.0	0.4	0.2
Afib/flutter	9%	**16%***	5%	4%	0.4	0.7	0.2	0.1	1.3	3.8	0.3	0.1
HTN[f]	9%	**23%***	4%	**9%***	0.4	1.2	0.1	0.4	4.1	15.0	1.6	4.0
Bleeding events[g]	38%	**51%***	4%	5%	2.4	3.8	0.1	0.2	13.7	24.6	0.1	0.1
Major bleeding events[h]	5%[i]	5%[j]	4%	5%	0.2	0.2	0.1	0.2	0.1	0.3	0.1	0.1
Infections[k]	78%	81%	31%	30%	8.9	10.4	1.6	2.0	14.6	15.6	1.5	1.1
Selected Common AEs (preferred term)												
Diarrhea	35%	**46%***	1%	**5%***	1.9	2.8	<0.1	0.2	6.7	9.6	<0.1	0.1
Headache	**35%***	20%	**2%***	0	1.8	1.1	<0.1	0	7.8	5.4	<0.1	0
Cough	**29%***	21%	1%	<1%	1.3	1.1	<0.1	<0.1	5.6	4.9	<0.1	<0.1
Fatigue	20%	17%	**3%***	0%	0.9	0.9	0.1	0	7.4	7.0	0.6	0
Arthralgia	16%	**23%***	0	1%	0.6	1.3	0	<0.1	7.5	10.4	0	<0.1
Back pain	8%	**13%***	0	1%	0.3	0.5	0	<0.1	1.9	3.2	0	0.1
Muscle spasms	6%	**13%***	0	1%	0.2	0.7	0	<0.1	0.8	10.0	0	0.1
Dyspepsia	4%	**12%***	0	0	0.1	0.5	0	0	1.0	2.4	0	0

Seymour JF et al. ASH 2021;Abstract 3721.

RTP RESEARCH TO PRACTICE

original reports

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

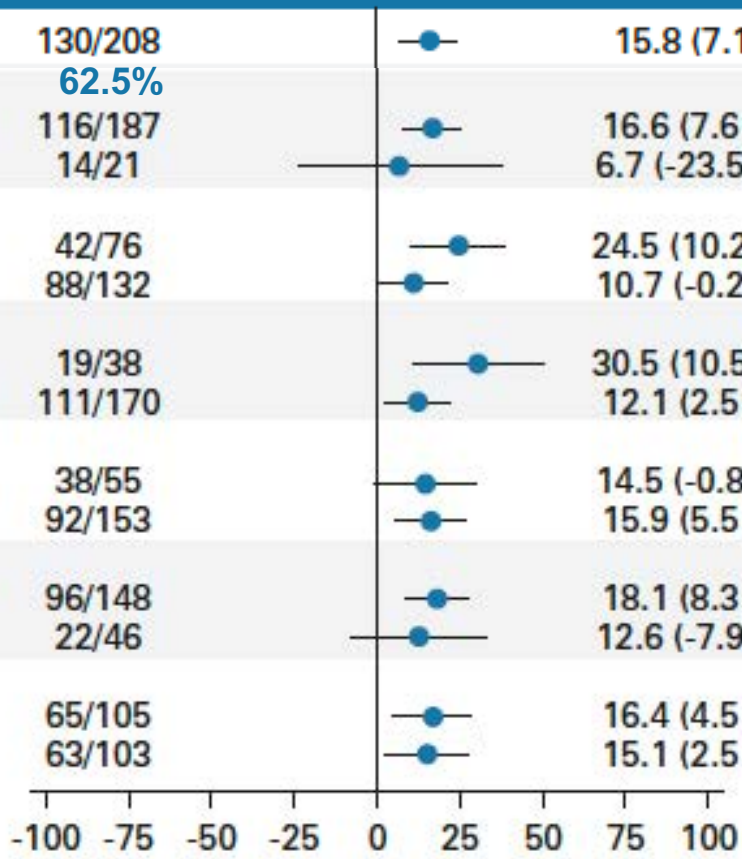
Peter Hillmen, MBChB, PhD[1]; Barbara Eichhorst, MD[2]; Jennifer R. Brown, MD, PhD[3]; Nicole Lamanna, MD[4]; Susan M. O'Brien, MD[5]; Constantine S. Tam, MBBS, MD[6-9]; Lugui Qiu, MD, PhD[10]; Maciej Kazmierczak, MD, PhD[11]; Keshu Zhou, MD, PhD[12]; Martin Šimkovič, MD, PhD[13,14]; Jiří Mayer, MD[15]; 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 February 10;41(5):1035-45.

RTP RESEARCH TO PRACTICE

ALPINE: Forest Plot of Overall Response

Subgroup	Response/Patients		Favors Ibrutinib	Favors Zanubrutinib	Rate Difference, % (95% CI)
	Zanubrutinib	Ibrutinib			
All patients	162/207	130/208			15.8 (7.1 to 24.4)
Prior lines of therapy	78.3%	62.5%			
1-3	151/192	116/187			16.6 (7.6 to 25.7)
> 3	11/15	14/21			6.7 (-23.5 to 36.8)
Baseline ECOG performance status					
0	63/79	42/76			24.5 (10.2 to 38.7)
≥ 1	99/128	88/132			10.7 (-0.2 to 21.5)
Baseline del(17p)/*TP53* mutation status					
Present	33/41	19/38			30.5 (10.5 to 50.5)
Absent	127/164	111/170			12.1 (2.5 to 21.7)
del(11q) mutation status					
Deleted/abnormal	51/61	38/55			14.5 (-0.8 to 29.9)
Not deleted/normal	111/146	92/153			15.9 (5.5 to 26.3)
Baseline IGHV mutation status					
Unmutated	122/147	96/148			18.1 (8.3 to 27.9)
Mutated	26/43	22/46			12.6 (-7.9 to 33.2)
Bulky disease					
≥ 5 cm	85/106	65/105			16.4 (4.5 to 28.3)
< 5 cm	77/101	63/103			15.1 (2.5 to 27.6)

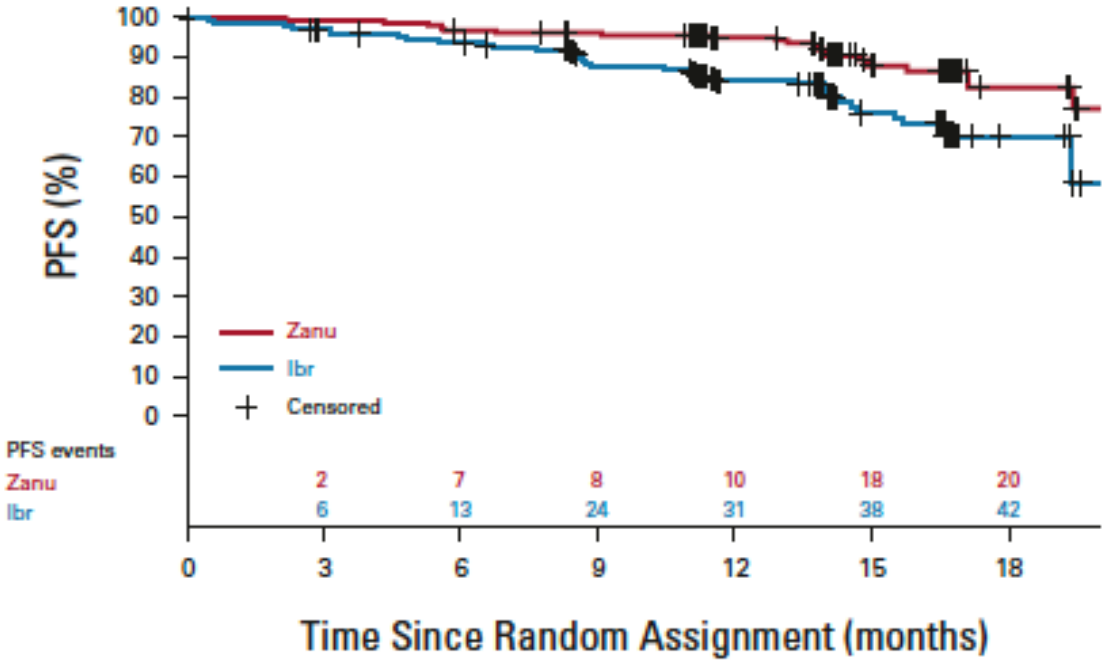


Hillmen P et al. *J Clin Oncol* 2023 February 10;41(5):1035-45.

RTP RESEARCH TO PRACTICE

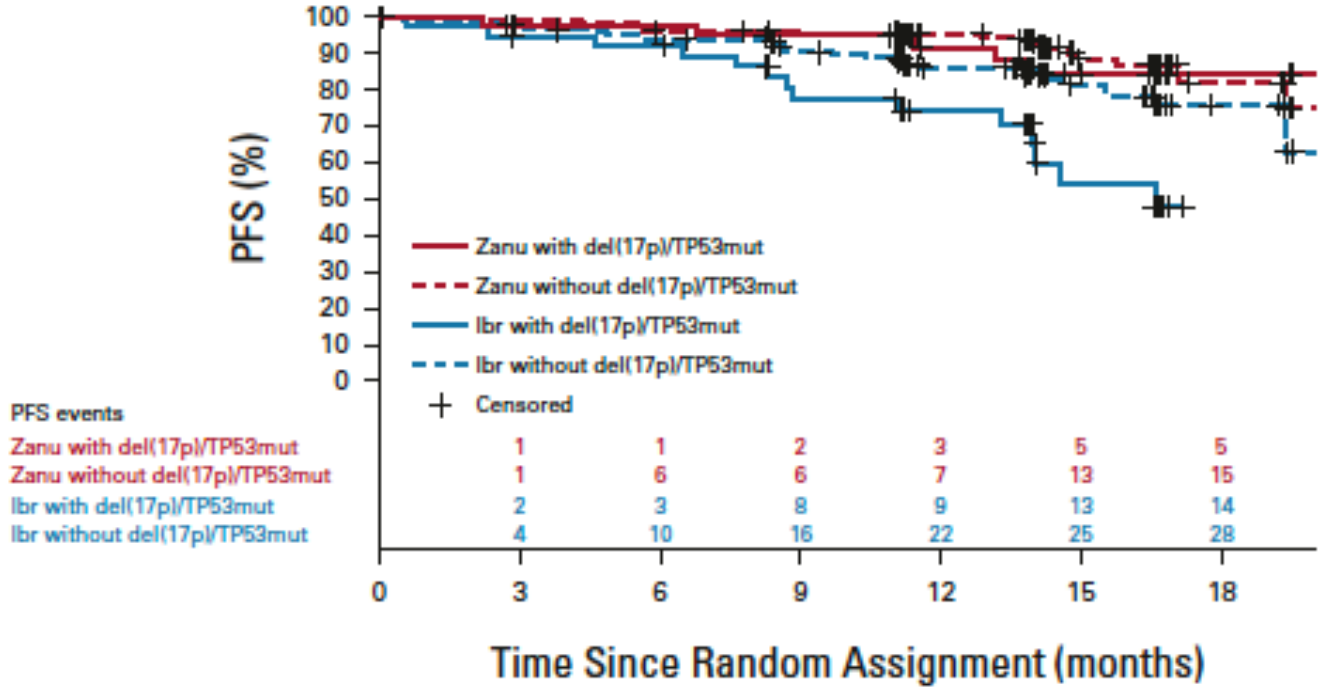
ALPINE: Progression-Free Survival

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.

RTP RESEARCH TO PRACTICE

ALPINE: Select Adverse Events

Adverse event (AE)	Zanubrutinib (n = 204)	Ibrutinib (n = 207)
AE leading to treatment discontinuation	7.8%	13.0%
Atrial fibrillation/flutter	2.5%	10.1%
Cardiac disorder	13.7%	25.1%
Neutropenia	28.4%	21.7%
Grade ≥3 infections	12.7%	17.9%
Major hemorrhagic events	2.9%	3.9%

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

RTP RESEARCH TO PRACTICE

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].

RTP RESEARCH TO PRACTICE

ELEVATE-RR and ALPINE: Cardiac, Hypertension and Bleeding Events

	ELEVATE-RR[1]				ALPINE[2]			
	Acalabrutinib (n = 266)		Ibrutinib (n = 263)		Zanubrutinib (n = 324)		Ibrutinib (n = 324)	
	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3
Any cardiac event	24.1%	8.6%	30.0%	9.5%	21.3%	NR	29.6%	NR
Atrial fibrillation/flutter	9.4%	4.9%	16.4%	3.8%	5.2%	2.5%	13.3%	4.0$
Hypertension	8.6%	4.1%	23.2%	9.1%	23.5%	15.1%	22.8%	13.6%
Hemorrhage	38.0%	3.8%	51.3%	4.6%	42.3%	3.4%	41.4%	3.7%

NR = not reported

[1] Byrd JC et al. *J Clin Oncol* 2021;39:3441-2452; [2] Brown JR et al. *N Eng J Med* 2022 December 13;[Online ahead of print].

RTP RESEARCH TO PRACTICE

ELEVATE-RR and ALPINE: Cytopenias and Infections

	ELEVATE-RR[1]				ALPINE[2]			
	Acalabrutinib (n = 266)		Ibrutinib (n = 263)		Zanubrutinib (n = 324)		Ibrutinib (n = 324)	
	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3
Anemia	21.8%	11.7%	18.6%	12.9%	15.4%	2.2%	16.4%	2.5%
Thrombocytopenia	15.8%	10.2%	13.7%	6.8%	13.0%	3.4%	15.4%	5.2%
Neutropenia	23.3%	21.8%	25.9%	24.0%	29.3%	21.0%	24.4%	18.2%
Infections	78.2%	30.8%	81.4%	30.0%	71.3%	26.5%	73.1%	28.1%
ILD/pneumonitis*	2.6%	0.4%	6.5%	0.8%	5.9%	NR	8.0%	NR

NR = not reported
* Pneumonia only

[1] Byrd JC et al. *J Clin Oncol* 2021;39:3441-2452; [2] Brown JR et al. *N Eng J Med* 2022 December 13;[Online ahead of print].

RTP RESEARCH TO PRACTICE

ELEVATE-RR and ALPINE: Common Non-Hematologic Adverse Events

	ELEVATE-RR[1]				ALPINE[2,3]			
	Acalabrutinib (n = 266)		Ibrutinib (n = 263)		Zanubrutinib (n = 324)		Ibrutinib (n = 324)	
	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3
Diarrhea	34.6%	1.1%	**46.0%**	**4.9%**	16.0%	1.5%*	24.1%	0.9%*
Headache	**34.6%**	1.5%	20.2%	0	NR	NR	NR	NR
Fatigue	20.3%	**3.4%**	16.7%	0	9.6%	0.9%*	13.3%	0.9%
Arthralgia	15.8%	0	22.8%	0.8%	14.5%	NR	16.4%	NR
Rash	9.8%	0.8%	12.5%	0	10.2%	1.2%*	12.3%	0.9%*
Secondary primary malignancies	18.8%	8.6%	13.7%	5.7%	12.3%	13.3%	13.3%	5.2%

NR = not reported

[1] Byrd JC et al. *J Clin Oncol* 2021;39:3441-2452; [2] Brown JR et al. *N Eng J Med* 2022 December 13;[Online ahead of print];
[3] Hillmen P et al. EHA 2021;Abstract S145; * Zanubrutinib prescribing information, revised 1/2023.

RTP RESEARCH TO PRACTICE

BRUIN: Pirtobrutinib

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RESEARCH
TO PRACTICE

ASH 2022;Abstract 961.

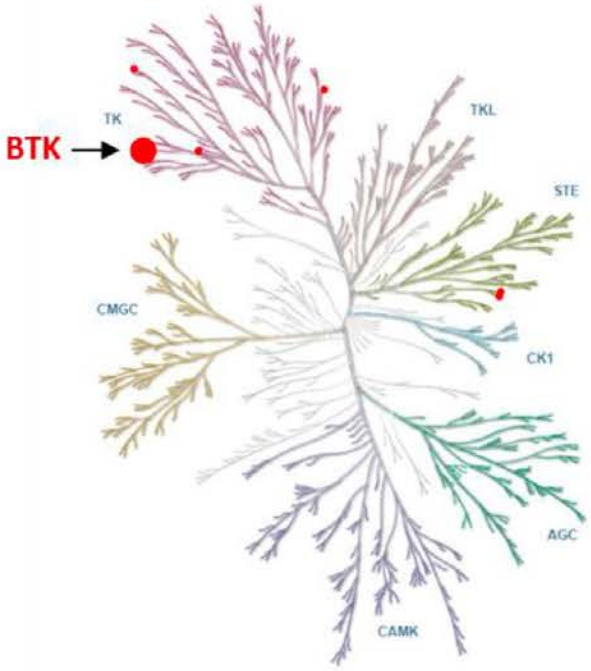
Efficacy of Pirtobrutinib in Covalent BTK-Inhibitor Pre-Treated Relapsed / Refractory CLL/SLL: Additional Patients and Extended Follow-up from the Phase 1/2 BRUIN Study

Anthony R. Mato[1], Jennifer A. Woyach[2], Jennifer R. Brown[3], Paolo Ghia[4], Krish Patel [5], Toby A. Eyre[6], Talha Munir[7], Ewa Lech-Maranda[8], Nicole Lamanna[9], Constantine S. Tam[10], Nirav N. Shah[11], Catherine C. Coombs[12], Chaitra S. Ujjani[13], Manish R. Patel[14], Bita Fakhri[15], Chan Y. Cheah[16], Alvaro J. Alencar[17], Jonathon B. Cohen[18], James N. Gerson[19], Ian W. Flinn[20], Shuo Ma[21], Deepa Jagadeesh[22], Joanna M. Rhodes[23], Francisco Hernandez-Ilizaliturri[24], John F. Seymour[10], Pier Luigi Zinzani[25], Minna Balbas[26], Binoj Nair[26], Paolo Abada[26], Chunxiao Wang[27], Amy S. Ruppert[27], Denise Wang[26], Donald E. Tsai[26], William G. Wierda[28], Wojciech Jurczak[29]

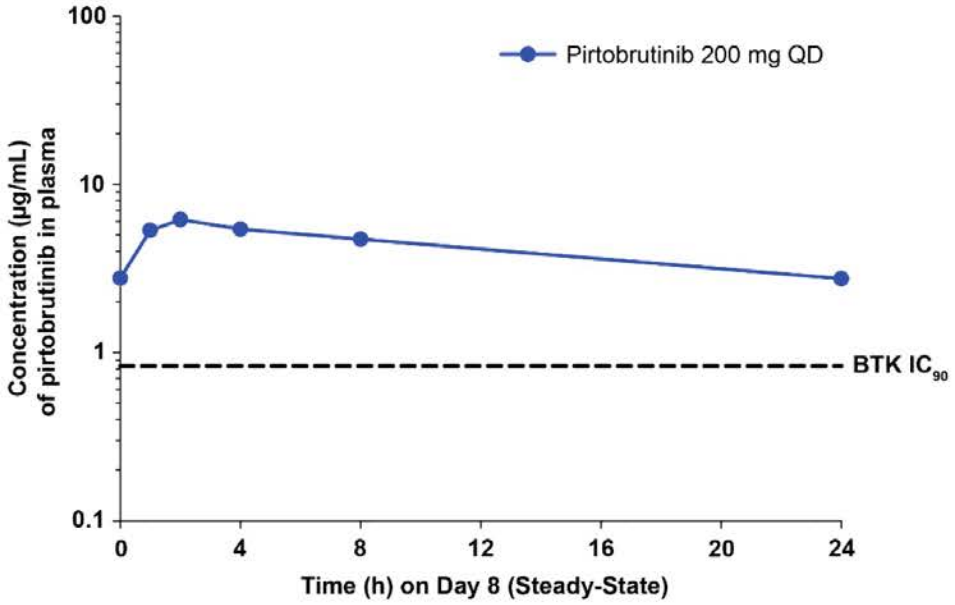
RTP RESEARCH TO PRACTICE

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

Highly Selective for BTK[6,7]



Plasma Exposures Exceeded BTK IC_{90} Throughout Dosing Interval

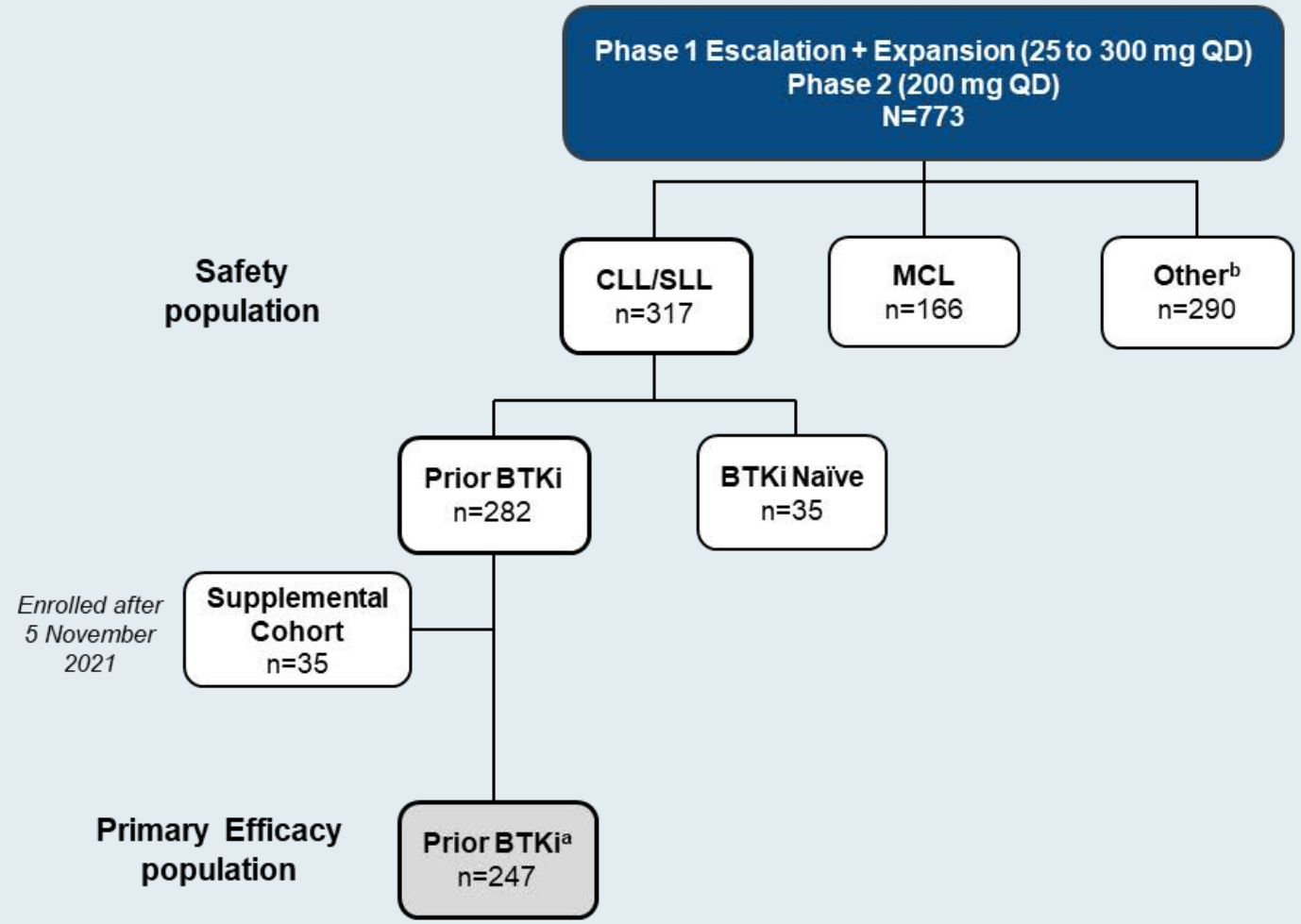


- Inhibits both wildtype and C481-mutant BTK with equal low nM potency, and has favorable oral pharmacology that enables continuous BTK inhibition throughout the dosing interval regardless of intrinsic rate of BTK turnover
- Pirtobrutinib is well tolerated and demonstrates promising efficacy in poor-prognosis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

Mato AR et al. ASH 2022;Abstract 961.

RTP RESEARCH TO PRACTICE

Phase I/II BRUIN Study Design



Phase 1 3+3 design

- 28-day cycles
- Intra-patient dose escalation allowed
- Cohort expansion permitted at doses deemed safe

Eligibility

- Age ≥18
- ECOG PS 0-2
- Active disease and in need of treatment
- Previously treated

Key endpoints

- Safety/tolerability
- Determine MTD and recommended phase 2 dose
- Pharmacokinetics
- Efficacy according to ORR and DOR (iwCLL) as assessed by IRC

Primary efficacy population[a]

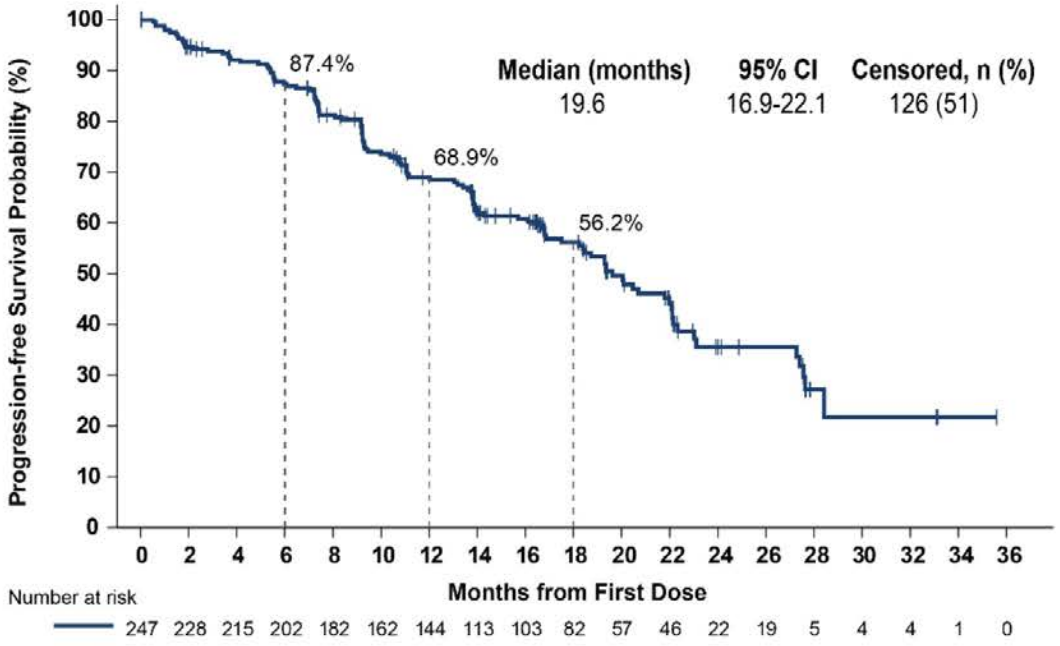
- Enrolled in phase 1 or 2
- Treated with prior BTK inhibitor containing regimen
- Received one or more doses of pirtobrutinib monotherapy

Mato AR et al. ASH 2022;Abstract 961.

RTP RESEARCH TO PRACTICE

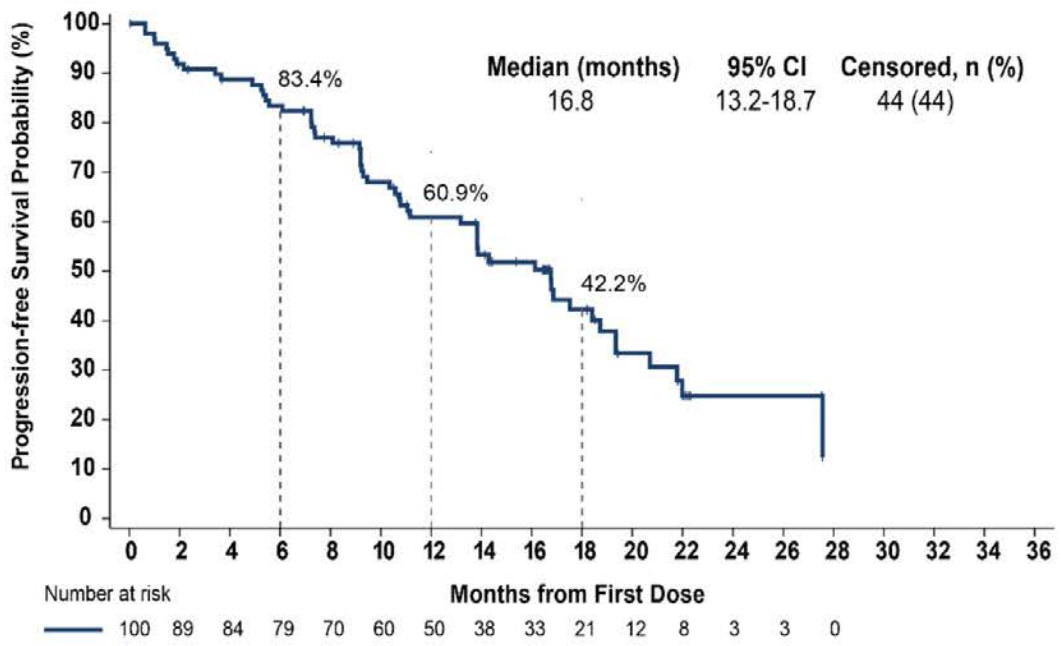
BRUIN: Progression-Free Survival in Patients with CLL/SLL Who Received Prior BTKi Treatment

All prior BTKi patients
Median prior lines = 3



- Median follow-up of 19.4 months for patients who received prior BTKi

Prior BTKi and BCL2i patients
Median prior lines = 5



- Median follow-up of 18.2 months for patients who received prior BTKi and BCL2i

Mato AR et al. ASH 2022;Abstract 961.

RTP RESEARCH TO PRACTICE

BRUIN: Pirtobrutinib Safety Profile

	All Doses and Patients (N=773)			
	Treatment-Emergent AEs, (≥15%), %		Treatment-Related AEs, %	
Adverse Event (AEs)	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3
Fatigue	28.7%	2.1%	9.3%	0.8%
Diarrhea	24.2%	0.9%	9.3%	0.4%
Neutropenia[a]	24.2%	20.4%	14.7%	11.5%
Contusion	19.4%	0.0%	12.8%	0.0%
Cough	17.5%	0.1%	2.3%	0.0%
Covid-19	16.7%	2.7%	1.3%	0.0%
Nausea	16.2%	0.1%	4.7%	0.1%
Dyspnea	15.5%	1.0%	3.0%	0.1%
Anemia	15.4%	8.8%	5.2%	2.1%
AEs of Special Interest[b]	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3
Bruising[c]	23.7%	0.0%	15.1%	0.0%
Rash[d]	12.7%	0.5%	6.0%	0.4%
Arthralgia	14.4%	0.6%	3.5%	0.0%
Hemorrhage/Hematoma[e]	11.4%	1.8%	4.0%	0.6%
Hypertension	9.2%	2.3%	3.4%	0.6%
Atrial fibrillation/flutter[f,g]	2.8%	1.2%	0.8%	0.1%

Median time on treatment for the overall safety population was 9.6 months
Discontinuations due to treatment-related AEs occurred in 2.6% (n=20) of all patients
Dose reductions due to treatment-related AEs occurred in 4.5% (n=35) of all patients
Overall and CLL/SLL safety profiles are consistent[h]

Mato AR et al. ASH 2022;Abstract 961.

RTP RESEARCH TO PRACTICE

CAR T-Cell Therapy

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TO PRACTICE

Nature 2022;[Online ahead of print].

Article

Decade-long leukaemia remissions with persistence of CD4$^+$ CAR T cells

https://doi.org/10.1038/s41586-021-04390-6

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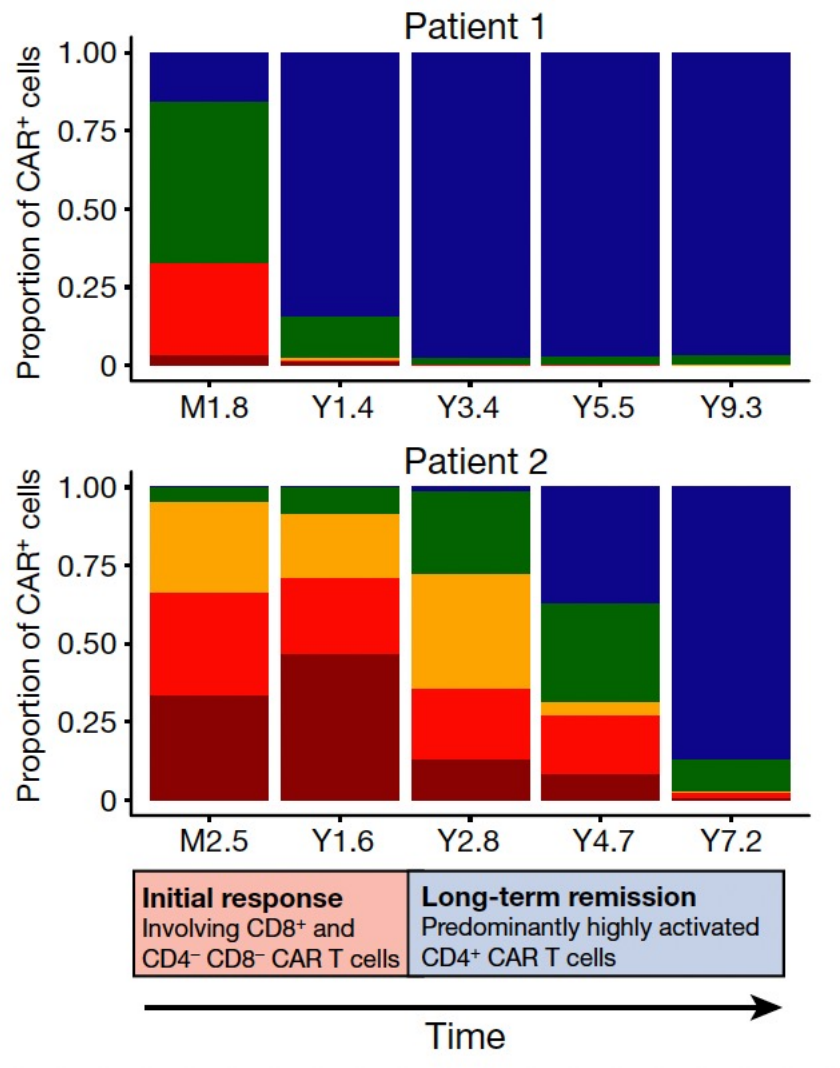
J. Joseph Melenhorst[1,2,3,4,5,15,16]✉, Gregory M. Chen[6,15], Meng Wang[1,2,3,14], David L. Porter[3,7,15], Changya Chen[8,9], McKensie A. Collins[1,2,3,10], Peng Gao[8,9], Shovik Bandyopadhyay[10], Hongxing Sun[1,2,3], Ziran Zhao[1,2,3], Stefan Lundh[1,2,3], Iulian Pruteanu-Malinici[11], Christopher L. Nobles[12], Sayantan Maji[1,2,3], Noelle V. Frey[3], Saar I. Gill[3], Lifeng Tian[1,3], Irina Kulikovskaya[1,2,3], Minnal Gupta[1,2,3], David E. Ambrose[1,2,3], Megan M. Davis[1,2,3], Joseph A. Fraietta[1,2,3,12], Jennifer L. Brogdon[11], Regina M. Young[1,2,3], Anne Chew[1,2,3], Bruce L. Levine[1,2,3], Donald L. Siegel[1,2,13], Cécile Alanio[4,5,14], E. John Wherry[4,5,14], Frederic D. Bushman[12], Simon F. Lacey[1,2,3], Kai Tan[2,4,6,9,10,16]✉ & Carl H. June[1,2,3,4,5,16]✉

RTP RESEARCH TO PRACTICE

Analysis of CD3+ CAR T Cells Using CyTOF Across Multiple Time Points



"Here we studied long-lasting CD19-redirected chimeric antigen receptor (CAR) T cells in two patients with chronic lymphocytic leukaemia who achieved a complete remission in 2010.
CAR T cells remained detectable more than ten years after infusion, with sustained remission in both patients. Notably, a highly activated CD4+ population emerged in both patients, dominating the CAR T cell population at the later time points…
…Our identification and characterization of these unexpected CAR T cell populations provide novel insight into the CAR T cell characteristics associated with anti-cancer response and long-term remission in leukaemia."

Melenhorst JJ et al. *Nature* 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

Blood 2022 March 24;139(12):1794-806.

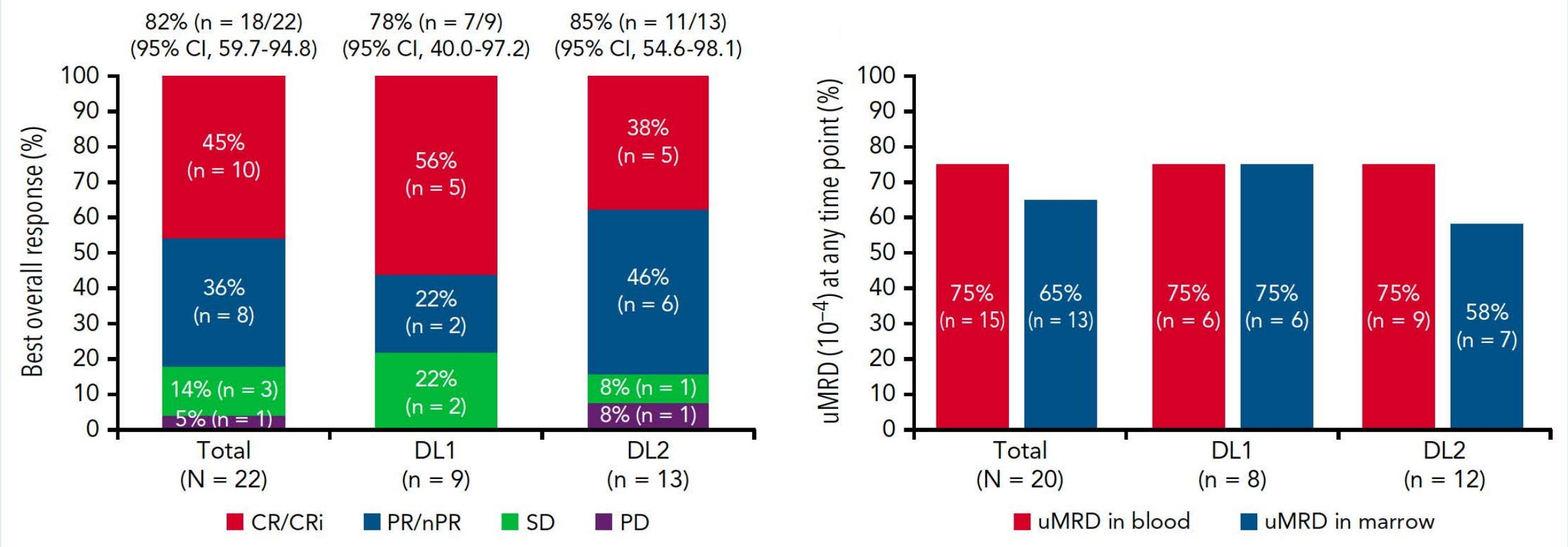
Regular Article

CLINICAL TRIALS AND OBSERVATIONS

Phase 1 TRANSCEND CLL 004 study of lisocabtagene maraleucel in patients with relapsed/refractory CLL or SLL

Tanya Siddiqi,[1] Jacob D. Soumerai,[2] Kathleen A. Dorritie,[3] Deborah M. Stephens,[4] Peter A. Riedell,[5] Jon Arnason,[6] Thomas J. Kipps,[7] Heidi H. Gillenwater,[8] Lucy Gong,[8] Lin Yang,[8] Ken Ogasawara,[9] Jerill Thorpe,[8] and William G. Wierda[10]

TRANSCEND CLL 004: Responses and uMRD



Siddiqi T et al. *Blood* 2022 March 24;139(12):1794-806.

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

Fifteenth Annual RTP Symposium Series Held During the Annual ONS Congress

Chronic Lymphocytic Leukemia

Thursday, April 27, 2023
12:15 PM – 1:45 PM

Faculty

John N Allan, MD
Jacqueline Broadway-Duren, PhD, DNP, APRN, FNP-BC
Corinne Hoffman, MS, APRN-CNP, AOCNP
Adam S Kittai, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

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

Fifteenth Annual RTP Symposium Series Held During the Annual ONS Congress

Management of HER2-Expressing Cancers Across the Oncology Spectrum: The Role of Antibody-Drug Conjugates

Thursday, April 27, 2023
6:00 PM – 7:30 PM

Faculty

Lyudmila A Bazhenova, MD
Kelly EH Goodwin, MSN, RN, ANP-BC
Virginia Kaklamani, MD, DSc
Caroline Kuhlman, MSN, APRN-BC
Alexis N McKinney, MSN, AGNP-BC
Zev Wainberg, MD, MSc

Moderator

Neil Love, MD

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Virtual attendees: The NCPD credit link is posted in the chat room.

NCPD/ONCC credit information will be emailed to each participant within 1 to 2 business days.

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