What I Tell My Patients:
Integrating New Research Information into Current Clinical Care

A Complimentary NCPD Hybrid Symposium Series Held During the 49th Annual ONS Congress

Chronic Lymphocytic Leukemia and Bispecific Antibodies in the Management of Lymphoma

Thursday, April 25, 2024

6:00 PM – 8:00 PM

Faculty

John N Allan, MD
Brad S Kahl, MD
Robin Klebig, MSN, APRN, CNP, AOCNP
Mollie Moran, APRN-CNP, AOCNP

Moderator

Neil Love, MD

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Faculty

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Moderator

Neil Love, MD
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Dr Allan — Disclosures

Advisory Committee	NeoGenomics
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Dr Kahl — Disclosures

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Ms Klebig — Disclosures

No relevant conflicts of interest to disclose

Ms Moran — Disclosures

No relevant conflicts of interest to disclose

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This educational activity contains discussion of non-FDA-approved uses of agents and regimens. Please refer to official prescribing information for each product for approved indications.

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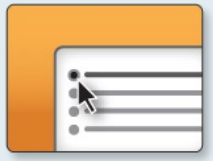
Clinicians in the Meeting Room

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.

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

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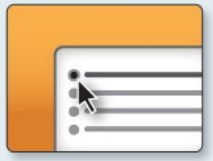
Clinicians Attending via Zoom

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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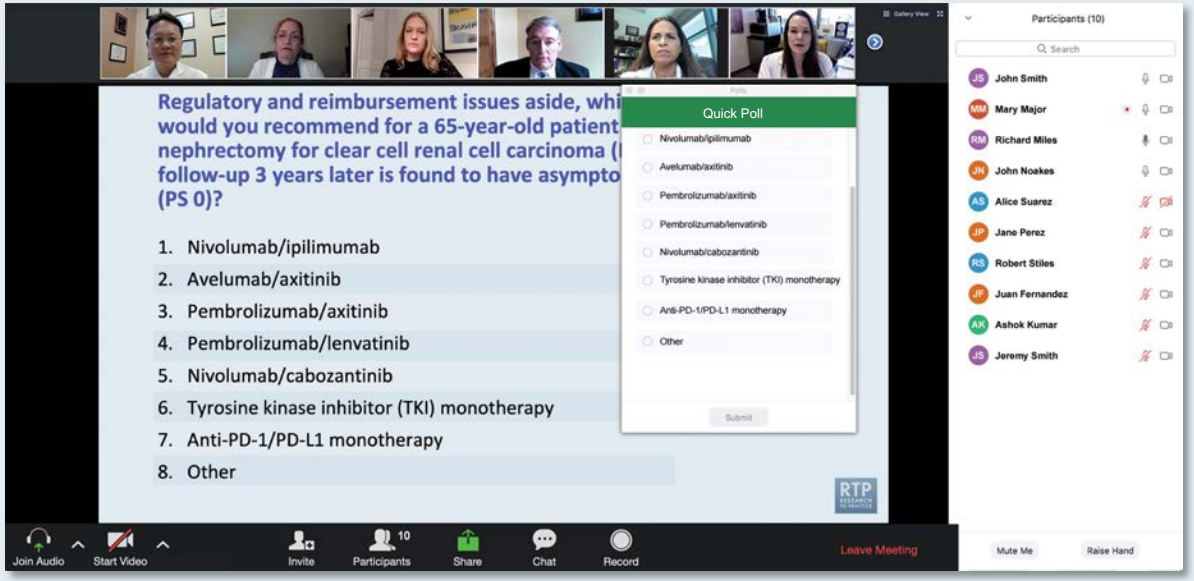
Clinicians, Please Complete the Pre- and Postmeeting Surveys



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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”
Sixteenth Annual RTP-ONS NCPD Symposium Series

Wednesday April 24	**Hormone Receptor–Positive Breast Cancer** 6:00 PM – 8:00 PM ET
Thursday April 25	**Endometrial Cancer** 6:00 AM – 7:30 AM ET
	Antibody–Drug Conjugates 12:15 PM – 1:45 PM ET
	Chronic Lymphocytic Leukemia and Bispecific Antibodies in Lymphoma 6:00 PM – 8:00 PM ET
Friday April 26	**Head and Neck Cancer** 6:00 AM – 7:30 AM ET
	Non–Small Cell Lung Cancer with an EGFR Mutation 12:15 PM – 1:45 PM ET
	Ovarian Cancer 6:00 PM – 7:30 PM ET
Saturday April 27	**Hepatobiliary Cancers** 6:00 AM – 7:30 AM ET
	Myelofibrosis 12:15 PM – 1:45 PM ET
	Gastroesophageal and Colorectal Cancers 6:00 PM – 8:00 PM ET
Wednesday, May 1	**LIVE WEBINAR — Prostate Cancer** 7:00 PM – 8:00 PM ET

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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?

Consulting Nurse Faculty

Jacqueline Broadway-Duren, PhD, DNP, APRN, FNP-BC
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Little Rock, Arkansas

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Los Angeles, California

https://www.ResearchToPractice.com/ONS2024Clips

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Oncology clinical trial terminology

- Waterfall plot
- Kaplan-Meier curve
- Overall survival
- Progression-free survival
- Disease-free survival
- Objective response rate
- Hazard ratio
- Phase I/II/III
- Minimal residual disease
- Circulating tumor DNA

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Agenda

Introduction

Module 1: Biology of Chronic Lymphocytic Leukemia (CLL)

Module 2: Venetoclax-Based Up-Front Treatment for CLL

Module 3: BTK Inhibition Alone or in Combination with Venetoclax for CLL

Module 4: Bispecific Antibodies as a Treatment Option for Non-Hodgkin Lymphoma

Module 5: Bispecific Antibodies in the Management of Follicular Lymphoma

Module 6: Bispecific Antibodies for the Treatment of Diffuse Large B-Cell Lymphoma

Module 7: Practical Considerations and Tolerability of Bispecific Antibodies

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Consulting Nursing Faculty Comments

Patient self-advocacy and treatment decision-making

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

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Biology of CLL

Dr Allan
New York, New York

Dr Kahl
St Louis, Missouri

- **Implications of various biomarkers, such as IGHV mutation, deletion 17p and TP53 mutation, for prognosis and therapeutic selection**
- **Indications for initiating active therapy for patients with previously untreated CLL**
- **Relevant comorbidities, such as hypertension, preexisting cardiac arrhythmias and chronic kidney disease, that can influence clinical decision-making for patients with CLL**
- **Risk of infection and timing of vaccinations for patients with CLL**

Robin Klebig, MSN, APRN, CNP, AOCNP

What I tell my patients with newly diagnosed CLL who are going to be observed rather than starting active therapy

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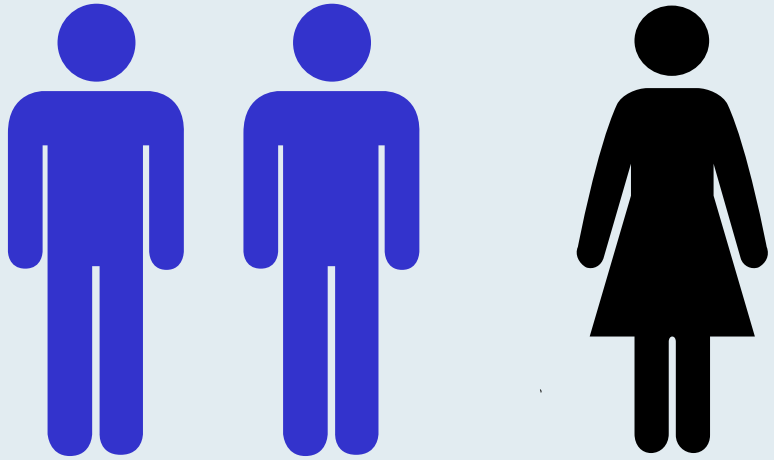
CLL Affects a Significant Number of Patients Worldwide, and Predominantly Older Patients

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. 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. 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 be 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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Venetoclax-Based Up-Front Treatment

Dr Allan
New York, New York

Dr Kahl
St Louis, Missouri

- **Outcomes observed with venetoclax-based up-front treatment for patients with CLL**
- **Key factors placing patients at risk for tumor lysis syndrome (TLS) with venetoclax; approaches to monitoring for and management of laboratory and clinical TLS**
- **Spectrum, incidence, severity and management of other toxicities reported with venetoclax, such as neutropenia, infections and gastrointestinal disorders**
- **Definition and clinical significance of minimal residual disease (MRD)**
- **Current role, if any, of MRD assessment in the management of CLL; implications for the duration of venetoclax-based treatment**

Mollie Moran, APRN-CNP, AOCNP

What I tell my patients about to begin treatment with venetoclax/obinutuzumab

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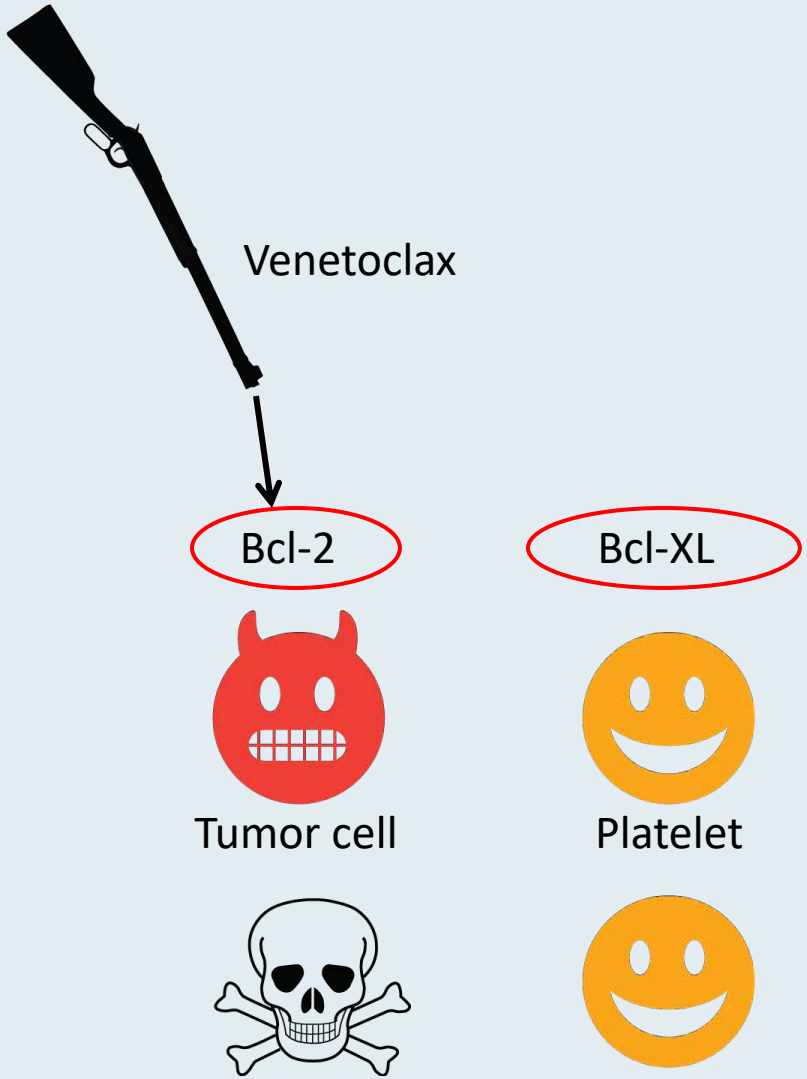
Mechanism of Action of Venetoclax



- **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.

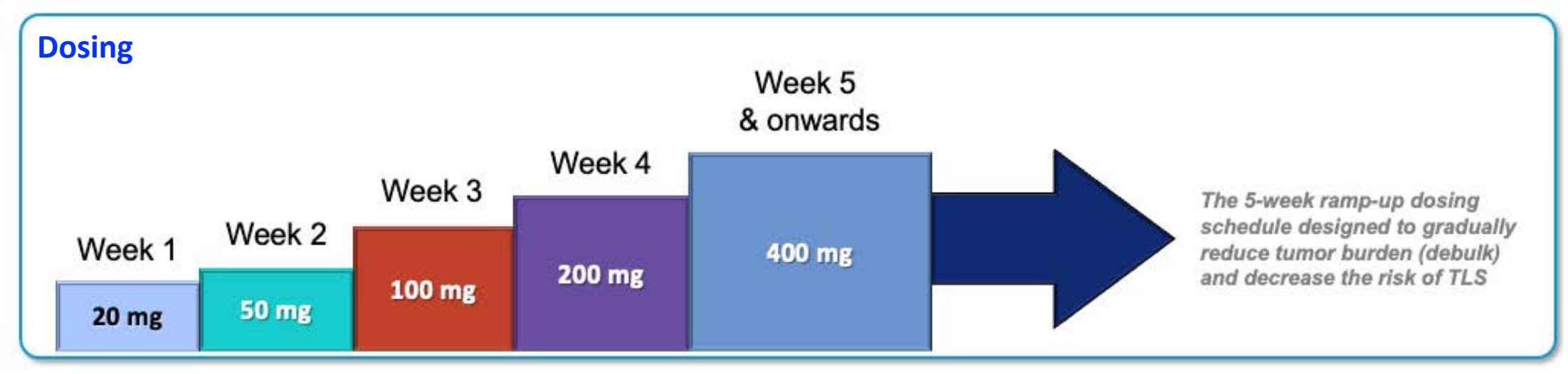
Venetoclax

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

Courtesy of Robin Klebig, MSN, APRN, CNP, AOCNP

Patient Education: Venetoclax (Continued)

Potential for tumor lysis syndrome (TLS)

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

Nausea

- Antiemetic as needed

Diarrhea

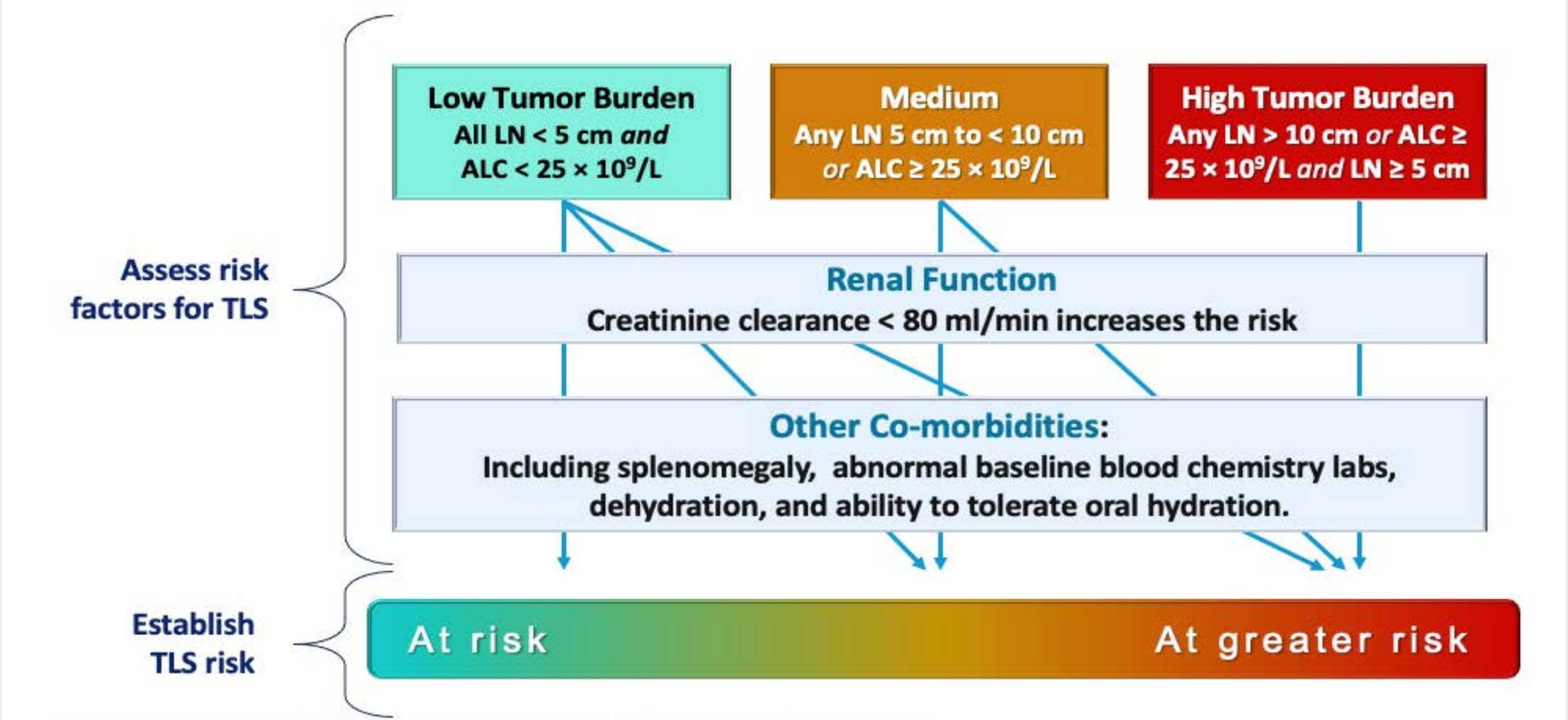
- Loperamide as needed
- Record # stools per day at baseline

Cytopenias

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

Courtesy of Robin Klebig, MSN, APRN, CNP, AOCNP

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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Available Bruton Tyrosine Kinase (BTK) Inhibitors

Dr Allan
New York, New York

Dr Kahl
St Louis, Missouri

- **Long-term findings from Phase III studies assessing ibrutinib-, acalabrutinib- and zanubrutinib-based therapy for patients with treatment-naïve CLL**
- **Incidence and severity of cardiac arrhythmias, including atrial fibrillation or flutter, documented with approved BTK inhibitors**
- **Probability of other cardiovascular toxicities, such as stroke, hypertension and bruising or bleeding**
- **Spectrum and frequency of clinically relevant noncardiovascular toxicities, including cytopenias, infections, headache, dermatologic symptoms, arthralgias or myalgia and gastrointestinal-related events**
- **Appropriate monitoring for and management of treatment-related cardiovascular and noncardiovascular events in patients receiving BTK inhibitors**

Robin Klebig, MSN, APRN, CNP, AOCNP

What I tell my patients about to begin treatment with a BTK inhibitor

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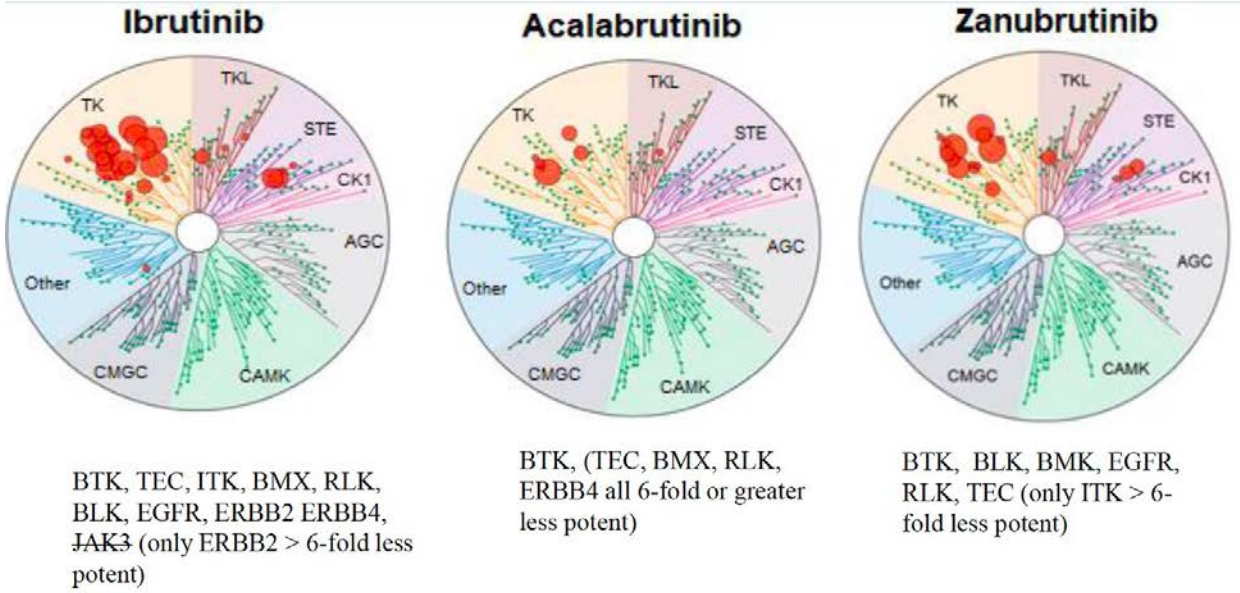
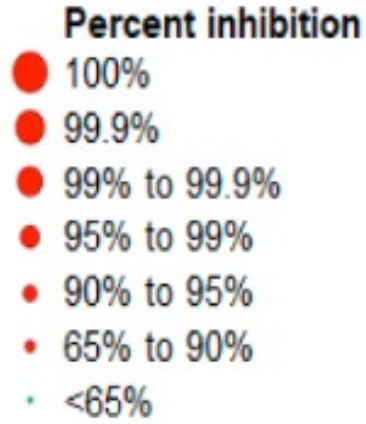
Irreversible and Reversible BTK Inhibitors for CLL

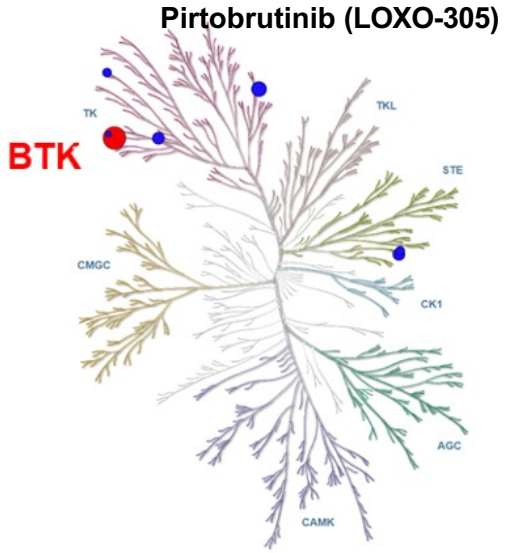
BTK inhibitor	Binding	T1/2 (hours)	IC50 (nM)	Dosing
Ibrutinib	Covalent irreversible C481	4-8	0.5	420 mg
Acalabrutinib	Covalent irreversible C481	0.9	5.1	100 mg BID
Zanubrutinib	Covalent irreversible C481	2-4	0.5	160 or 320 mg BID
Pirtobrutinib	Noncovalent reversible	Not available	0.85	200 mg

Irreversible





Reversible



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

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.

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, with or without food**

Key issues

- **Dose reduction guidelines**

Acalabrutinib package insert, 8/2022.

Zanubrutinib

Mechanism of action

- **BTK inhibitor**

Indication

- **For patients with CLL or SLL**

Recommended dose

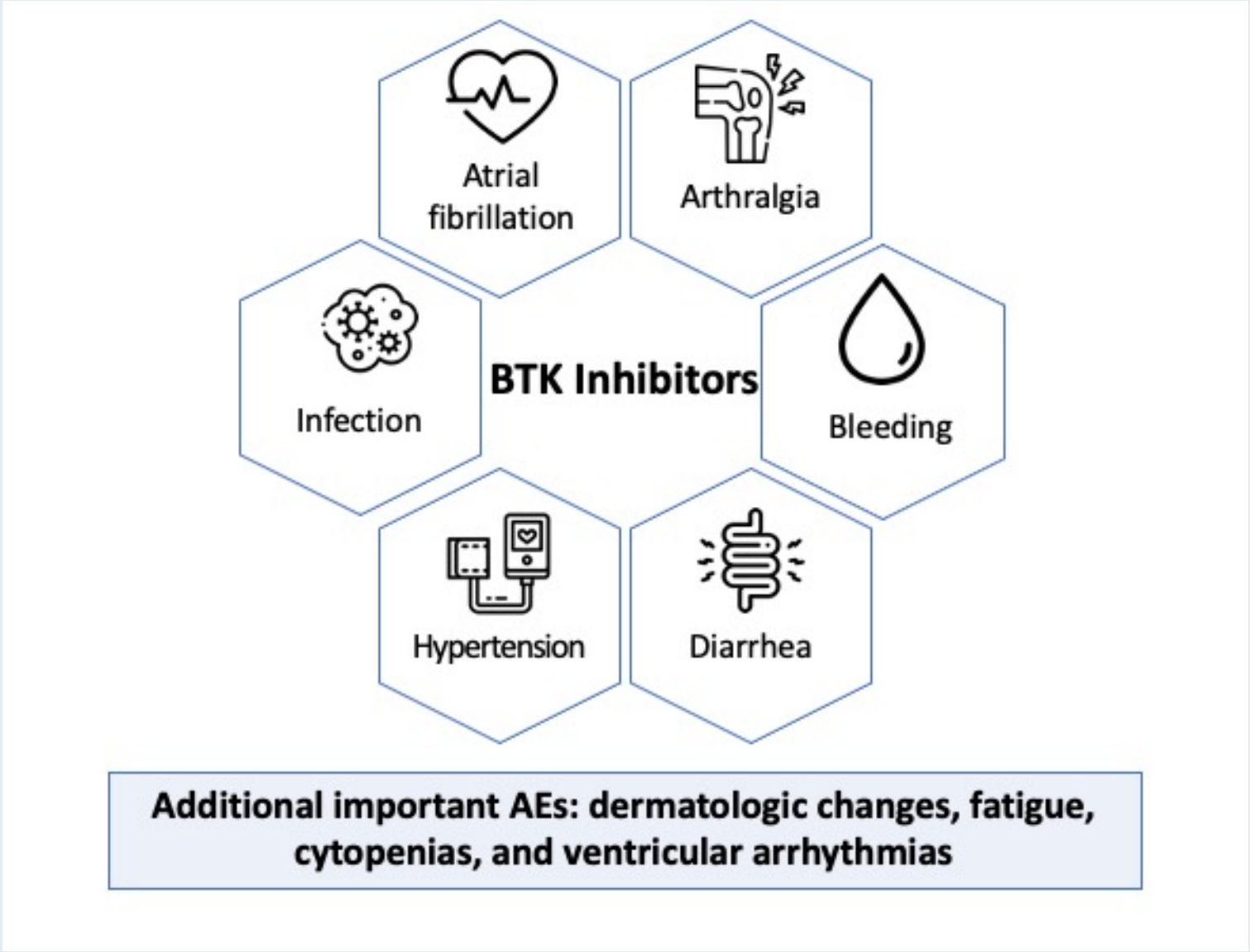
- **160 mg po twice daily or 320 mg po once daily, swallowed whole with water, with or without food**

Key issues

- **Dose reduction guidelines**

Zanubrutinib package insert, 3/2024.

Summary of Adverse Events with BTK Inhibitors



Courtesy of Matthew S Davids, MD, MMSc

Potential Role of BTK Inhibitors with Venetoclax

Dr Allan
New York, New York

Dr Kahl
St Louis, Missouri

- **Mechanistic rationale for combining BTK inhibitors and venetoclax with and without CD20 antibodies for CLL**
- **Published data sets evaluating ibrutinib/venetoclax for newly diagnosed and relapsed/refractory (R/R) CLL**
- **Available data with acalabrutinib or zanubrutinib in combination with venetoclax with or without an anti-CD20 antibody**
- **Ongoing Phase III studies assessing novel doublet and triplet combinations for previously untreated and R/R disease; potential clinical role of this strategy**
- **Incidence and severity of clinically relevant toxicities encountered when combining BTK inhibitors and venetoclax**

Mollie Moran, APRN-CNP, AOCNP

What I tell my patients about to begin treatment with a BTK inhibitor in combination with venetoclax

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Selection and Sequencing of Therapies for R/R CLL

Dr Allan
New York, New York

Dr Kahl
St Louis, Missouri

- **Long-term follow-up from Phase III trials evaluating BTK inhibitors and venetoclax for R/R CLL**
- **Role of rechallenging with agents used in a prior line of treatment**
- **Antitumor activity documented with pirtobrutinib in patients with R/R CLL; current clinical role**
- **Biological rationale for and available data with CD19-directed chimeric antigen receptor (CAR) T-cell therapy for CLL; recent FDA approval**

Pirtobrutinib

Mechanism of action

- **BTK inhibitor**

Indication

- **For patients with CLL or SLL who have received at least 2 prior lines of therapy, including a BTK inhibitor and a Bcl-2 inhibitor**

Recommended dose

- **200 mg orally once daily; swallow whole with water, with or without food. Do not cut, crush or chew tablets**

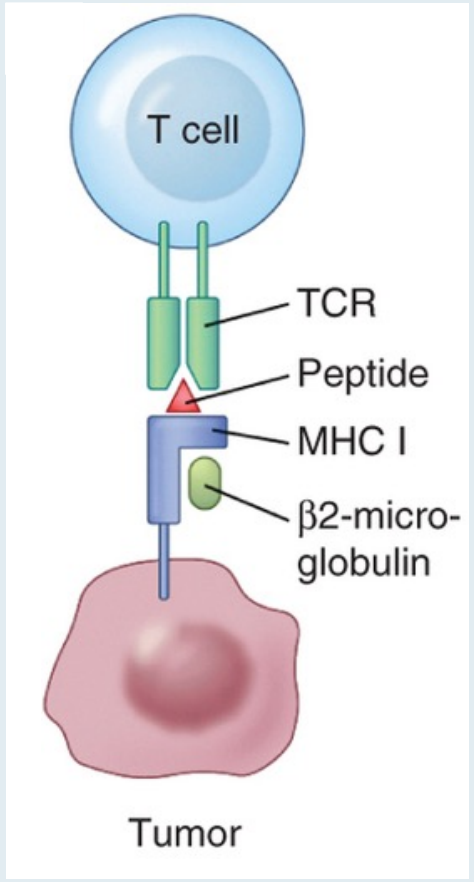
Key issues

- **Dose reduction guidelines**

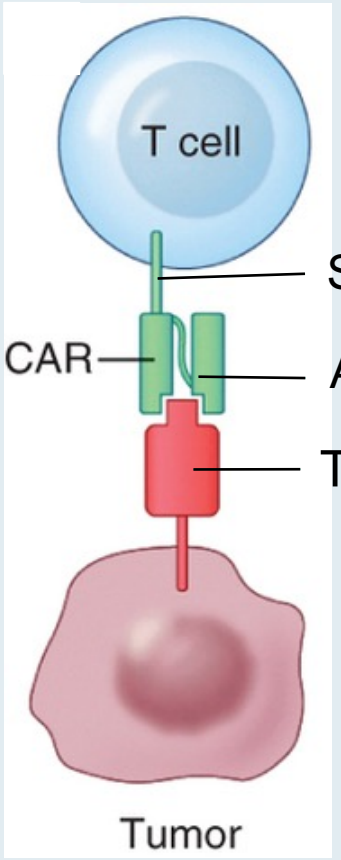
Pirtobrutinib package insert, 12/2023.

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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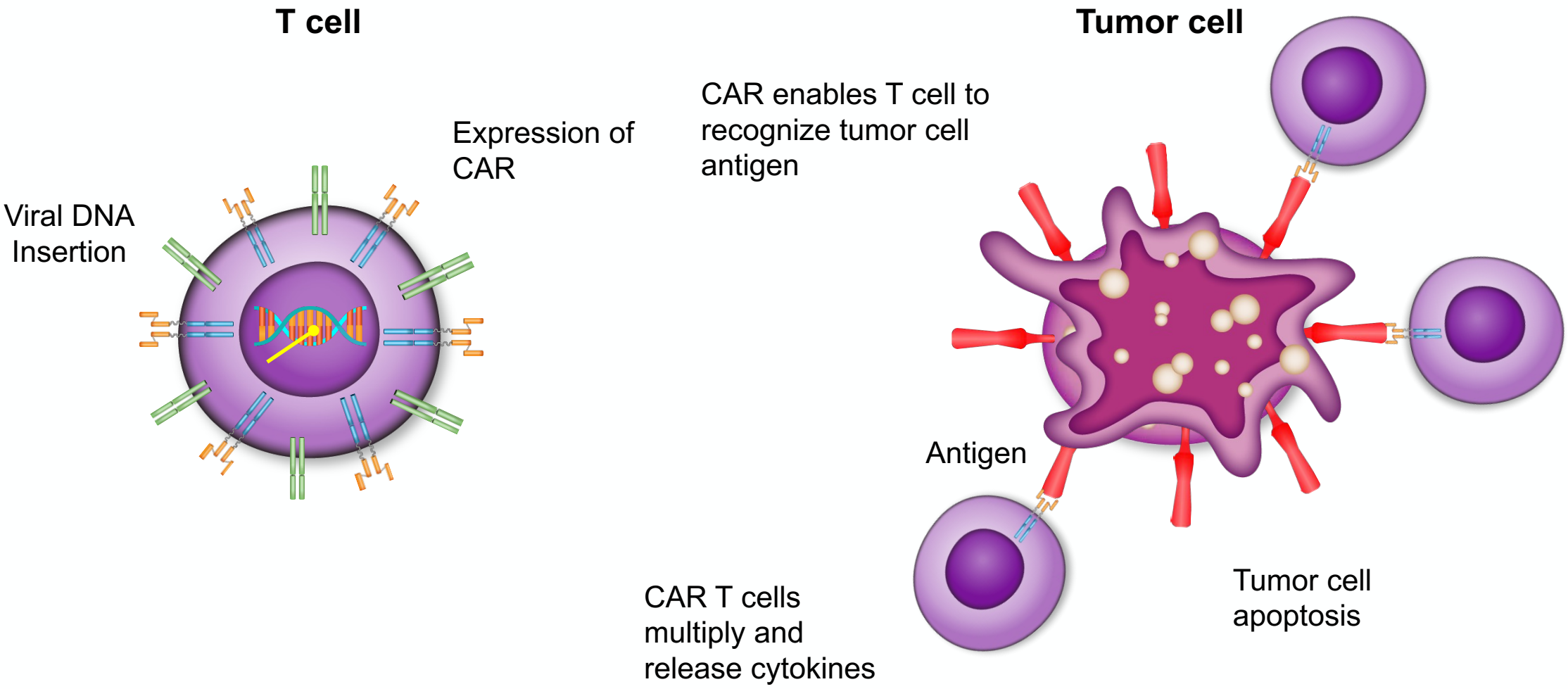
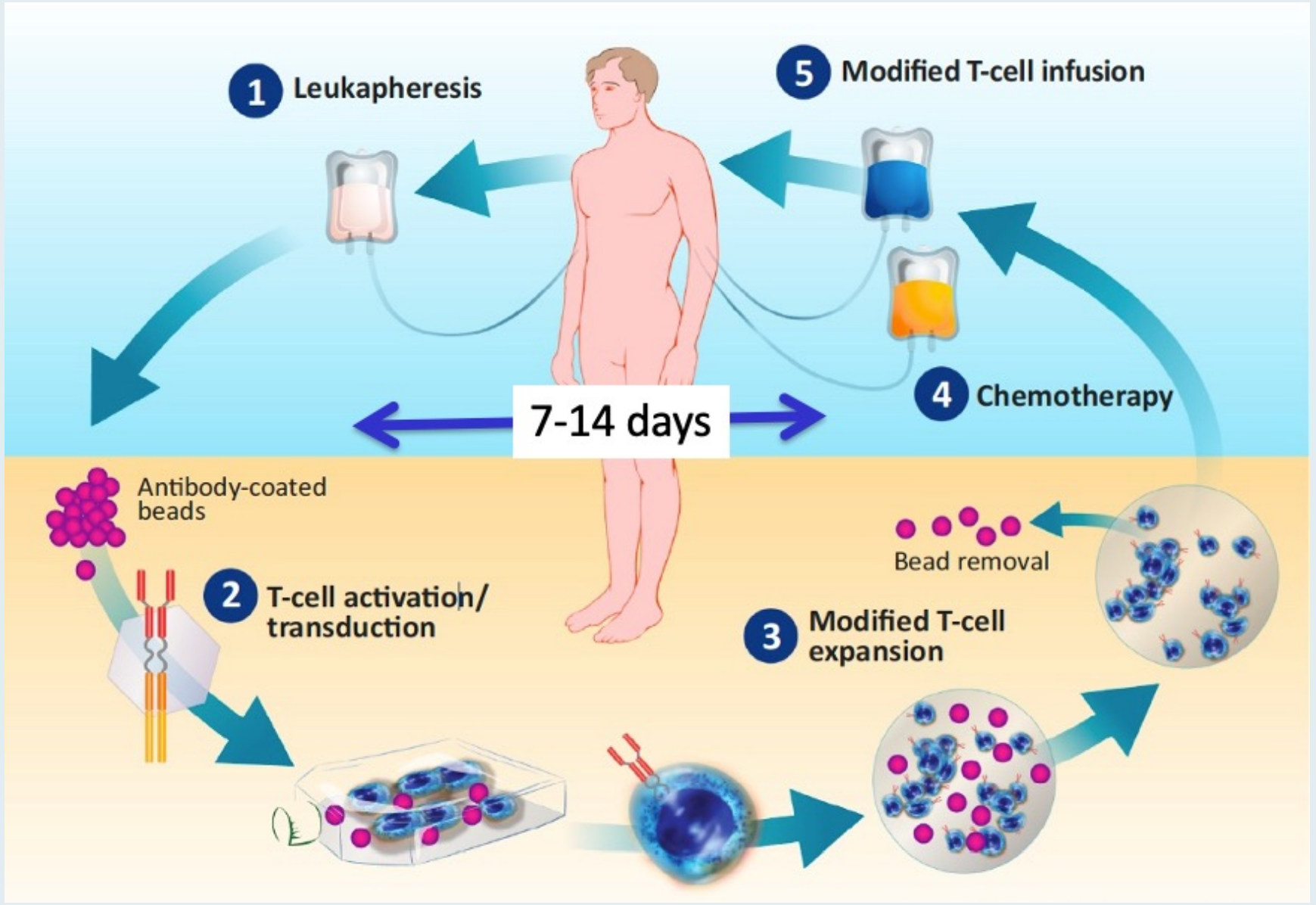
CAR T Cells: Mechanism of Action



Overview of CAR T-Cell Therapy



Modification, Courtesy of David Porter, MD

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U.S. FDA Approves Liso-Cel as the First and Only CAR T Cell Therapy for Adults with Relapsed or Refractory Chronic Lymphocytic Leukemia (CLL) or Small Lymphocytic Lymphoma (SLL)
Press Release: March 14, 2024

"…the U.S. Food and Drug Administration (FDA) has granted accelerated approval of lisocabtagene maraleucel (liso-cel), a CD19-directed chimeric antigen receptor (CAR) T cell therapy, for the treatment of adult patients with relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) who have received at least two prior lines of therapy, including a Bruton tyrosine kinase (BTK) inhibitor and a B-cell lymphoma 2 (BCL-2) inhibitor. This indication is approved under accelerated approval based on response rate and duration of response.

TRANSCEND CLL 004 (NCT03331198) is a Phase 1/2 open-label, single-arm, multicenter study evaluating liso-cel in patients with relapsed or refractory chronic lymphocytic leukemia or small lymphocytic lymphoma. The Phase 1 dose escalation portion of the study assessed the safety and recommended dose for the subsequent Phase 2 expansion cohort. The Phase 2 portion of the study is evaluating liso-cel at the recommended dose from the Phase 1 monotherapy arm. The primary endpoint of the Phase 2 portion of the study is complete response rate, including complete remission with incomplete bone marrow recovery, based on independent review committee according to the International Workshop on Chronic Lymphocytic Leukemia (iwCLL) 2018 guidelines.."

https://news.bms.com/news/corporate-financial/2024/U.S.-FDA-Approves-Bristol-Myers-Squibbs-Breyanzi--as-the-First-and-Only-CAR-T-Cell-Therapy-for-Adults-with-Relapsed-or-Refractory-Chronic-Lymphocytic-Leukemia-CLL-or-Small-Lymphocytic-Lymphoma-SLL/default.aspx

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Approved CAR T Cell Therapies in Lymphoma

Agent	Approved Indications
Axicabtagene Ciloleucel	• Large B-Cell Lymphoma refractory to 1L chemoimmunotherapy or relapsed within 12 months of 1L chemoimmunotherapy • R/R Large B-Cell Lymphoma after 2+ lines of systemic therapy • R/R FL after 2+ lines of systemic therapy
Brexucabtagene Autoleucel	• R/R MCL after prior chemotherapy, anti-CD20 therapy, and a BTK inhibitor
Lisocabtagene Maraleucel	• Large B-Cell Lymphoma refractory to 1L chemoimmunotherapy or relapsed within 12 months of 1L chemoimmunotherapy • R/R Large B-Cell Lymphoma after 2+ lines of systemic therapy • R/R CLL or SLL after 2+ lines of therapy, including a BTKi and a BCL-2 inhibitor
Tisagenlecleucel	• R/R Large B-Cell Lymphoma after 2+ lines of systemic therapy • R/R FL after 2+ lines of systemic therapy

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Consulting Nursing Faculty Comments

Interactions between community oncologists and tertiary care centers

Amy Goodrich, CRNP

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Consulting Nursing Faculty Comments

Bispecific immunotherapy and risk for infection

Amy Goodrich, CRNP

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Module 1: Biology of Chronic Lymphocytic Leukemia (CLL)

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Module 6: Bispecific Antibodies for the Treatment of Diffuse Large B-Cell Lymphoma

Module 7: Practical Considerations and Tolerability of Bispecific Antibodies

Bispecific Antibodies as a Treatment Option for Non-Hodgkin Lymphoma (NHL)

Dr Allan
New York, New York

Dr Kahl
St Louis, Missouri

- **Potential therapeutic advantages over traditional monoclonal antibodies of using bispecific antibodies to engage 2 disease targets with 1 molecule**
- **Scientific rationale for the selection of CD20 and CD3 as targets for bispecific antibodies in NHL**
- **Mechanistic similarities and differences among the various approved and investigational CD20 x CD3 bispecific antibodies, such as epcoritamab, glofitamab, mosunetuzumab and odronextamab**
- **Potential practical advantages of the “off-the-shelf” nature of bispecific antibodies relative to CAR T-cell therapy**

Robin Klebig, MSN, APRN, CNP, AOCNP

What I tell my patients about what bispecific antibodies are and how they work

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Approved and Investigational Bispecific Antibodies for NHL

Drug Name	Route of Administration	Investigational Status
Mosunetuzumab	Intravenous	Approved (R/R FL)
Glofitamab	Intravenous	Approved (R/R DLBCL)
Epcoritamab	Subcutaneous	Approved (R/R DLBCL)
Odronextamab	Intravenous	Investigational (R/R FL, DLBCL)* **03/2024: FDA issued CRLs*

Radhakrishnan VS, Davies AJ. *Front Immunol* 2024 January 11:14:1295599.

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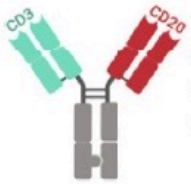
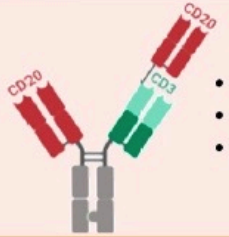
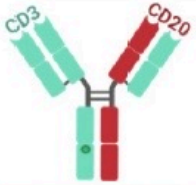
Structure of Select Bispecific Antibodies

Bi-Specific Antibody	Targets	Design	Ig Fragment Formats
blinatumomab	CD19 x CD3		• two murine scFv joined by a glycine-serine linker • monovalent CD19 and monovalent CD3 binding • cloned from anti-CD19 (clone HD37) and anti-CD3 (clone L2K-07) murine mAbs
mosunetuzumab	CD20 x CD3		• humanized mouse heterodimeric IgG1-based antibody • monovalent CD20 and monovalent CD3ε binding • modified Fc devoid of FcγR and complement binding
glofitamab	$(CD20)_2$ x CD3		• humanized mouse IgG1-based antibody • bivalent CD20 and monovalent CD3ε binding • modified Fc devoid of FcγR and complement binding
odronextamab	CD20 x CD3		• fully human IgG4-based heterodimeric antibody • monovalent CD20 and monovalent CD3ε binding • Fc-dependent effector function-minimized antibody with Fc of the anti-CD3ε heavy chain modified to reduce Protein A binding • common κ light chain from anti-CD3ε mAb
epcoritamab	CD20 x CD3		• humanized mouse IgG1-based heterodimeric antibody • monovalent CD20 and monovalent CD3 binding • IgG1 Fc modified to minimize Fc-dependent effector functions and to control Fab-arm exchange of mAb half-molecules, resulting in high bispecific product yield

Ig, immunoglobulin; scFv, single-chain variable fragment; mAb, monoclonal antibody; Fc, fragment crystallizable; FcγR, Fc gamma receptor

Schuster SJ. *Hematol Oncol* 2021;39(S1):113-16.

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Module 7: Practical Considerations and Tolerability of Bispecific Antibodies

Bispecific Antibodies in the Management of Follicular Lymphoma (FL)

Dr Allan
New York, New York

Dr Kahl
St Louis, Missouri

- **Frequency, depth and durability of responses to mosunetuzumab in patients with R/R FL**
- **Recent FDA approval of mosunetuzumab for patients with FL after 2 or more lines of systemic therapy**
- **Optimal integration of mosunetuzumab into FL treatment algorithms**
- **Available data and ongoing research with other CD20 x CD3 bispecific antibodies for FL, such as epcoritamab, glofitamab and odronextamab**

Mosunetuzumab

Mechanism of action

- **Bispecific CD20-directed CD3 T-cell engager**

Indication

- **For patients with relapsed or refractory FL after 2 or more lines of systemic therapy**

Recommended administration

- **Intravenous infusion**

Key issues

- **Boxed warning for serious or life-threatening CRS; warnings and precautions include neurologic toxicity, infections, cytopenias and tumor flare**

Mosunetuzumab package insert, 12/2022.

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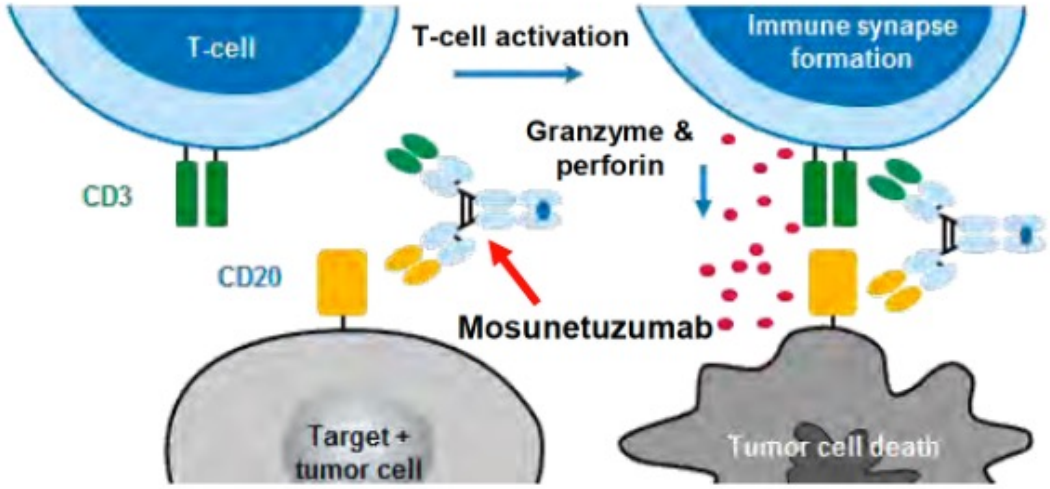
Mosunetuzumab: Mechanism of Action

- Mosunetuzumab **(first-in-class)** is approved in the EU and is under Priority Review by the FDA, for the treatment of **relapsed/refractory follicular lymphoma (R/R FL)** after ≥2 prior systemic therapies[1,2]
  - **ORR 80%, CR 60%,** majority maintaining response after 18 months[3]
  - Consistent benefit in patients with double-refractory disease and POD24[3]
  - **Off-the-shelf, fixed-duration** treatment that can be administered in the **outpatient** setting[3]

Mosunetuzumab: CD20xCD3 T-cell-engaging bispecific antibody that redirects T cells to engage and eliminate malignant B cells[4,5]



Bartlett NL et al. ASH 2022;Abstract 610.

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Module 7: Practical Considerations and Tolerability of Bispecific Antibodies

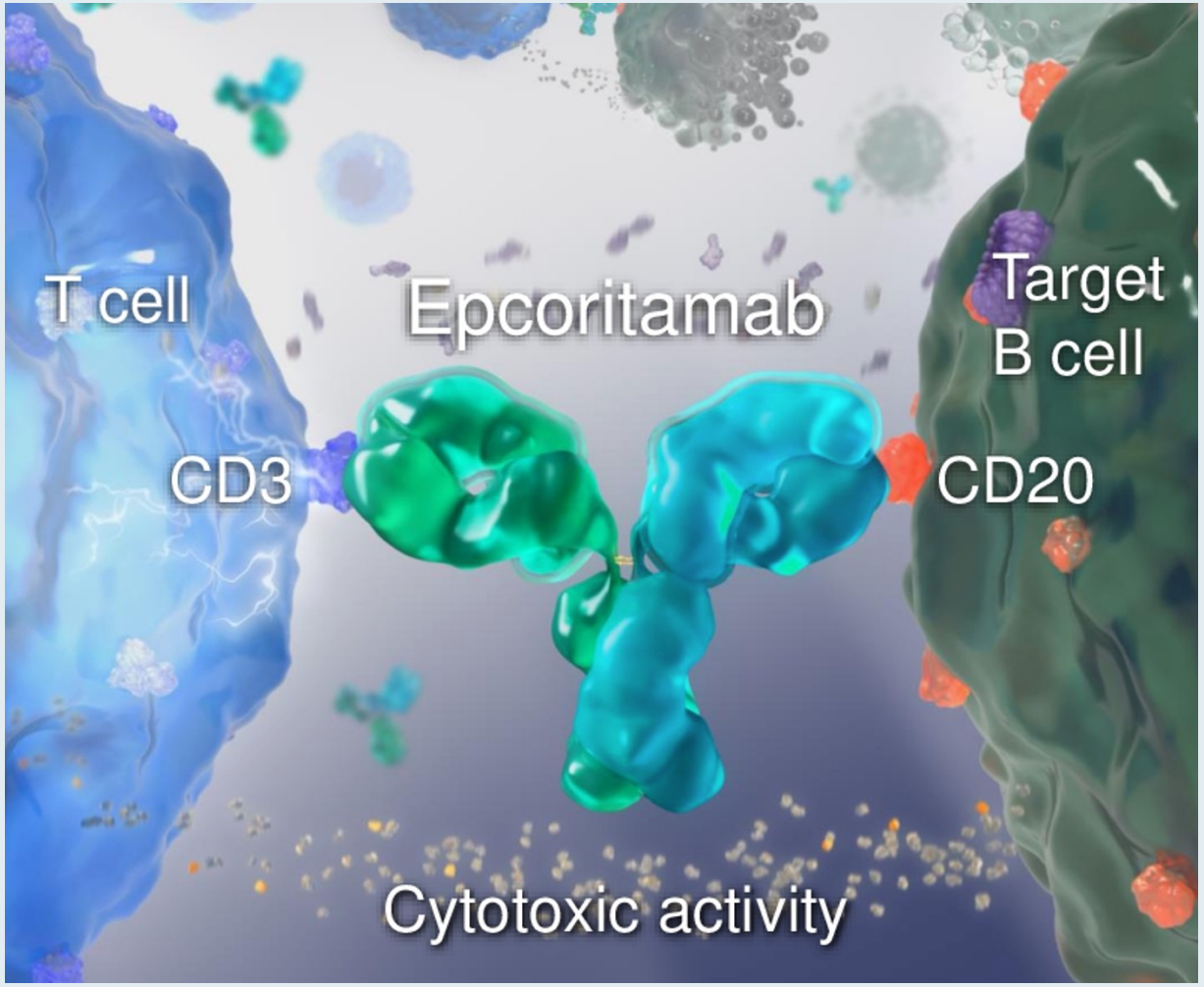
Bispecific Antibodies in the Management of Diffuse Large B-Cell Lymphoma (DLBCL)

Dr Allan
New York, New York

Dr Kahl
St Louis, Missouri

- **Pivotal clinical trial results with glofitamab and with epcoritamab for multiregimen-relapsed DLBCL**
- **FDA-approved indications for glofitamab and epcoritamab in patients with DLBCL**
- **Optimal sequencing of bispecific antibodies relative to other available therapies for DLBCL; patient and disease-related factors**

Epcoritamab: Mechanism of Action of Subcutaneous Bispecific Antibody



Falchi L et al. ASCO 2022;Abstract 7524.

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Epcoritamab

Mechanism of action

- **Bispecific CD20-directed CD3 T-cell engager**

Indication

- **For patients with relapsed or refractory DLBCL not otherwise specified, including DLBCL arising from indolent lymphoma, and high-grade B-cell lymphoma after 2 or more lines of systemic therapy**

Recommended administration

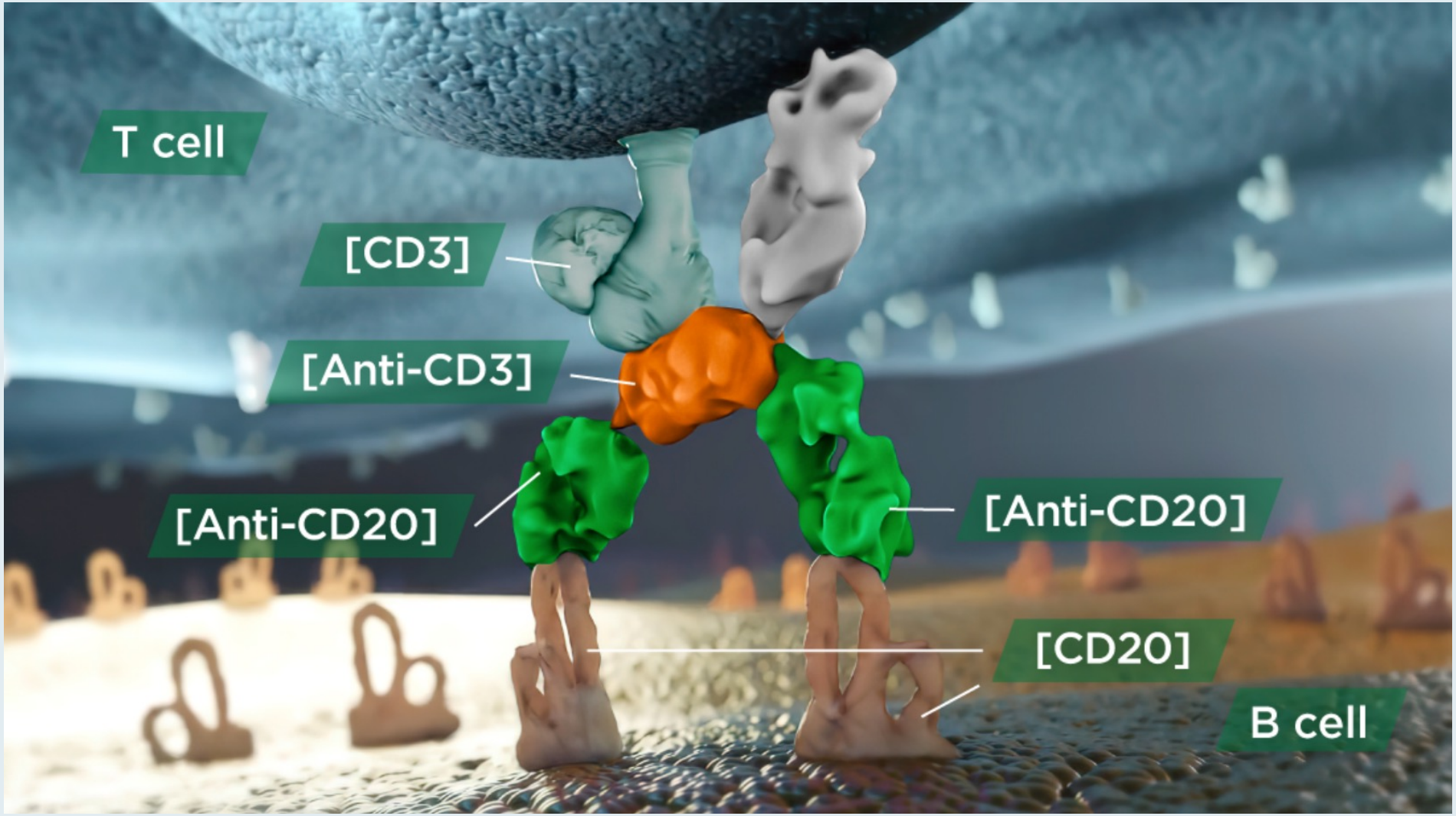
- **Subcutaneous injection**

Key issues

- **Boxed warning for serious or life-threatening CRS and ICANS (immune effector cell-associated neurotoxicity syndrome); warnings and precautions include infections, cytopenias and embryo-fetal toxicity**

Epcoritamab package insert, 5/2023.

Glofitamab: Mechanism of Action



https://www.columvi-hcp.com/about/how-columvi-works.html.

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Glofitamab

Mechanism of action

- **Bispecific CD20-directed CD3 T-cell engager**

Indication

- **For patients with relapsed or refractory DLBCL not otherwise specified or large B-cell lymphoma arising from FL, after 2 or more lines of systemic therapy**

Recommended administration

- **Intravenous infusion**

Key issues

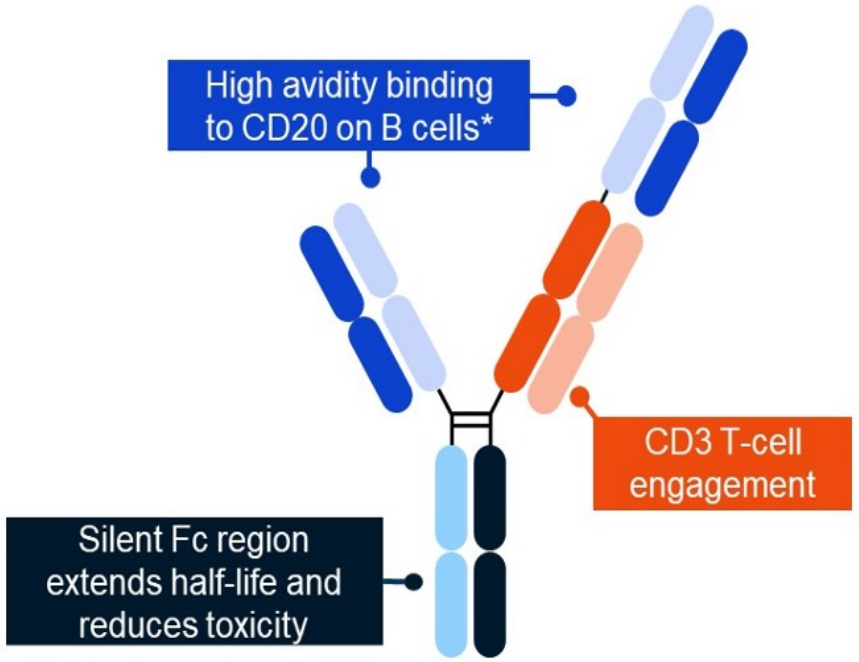
- **Boxed warning for serious or fatal CRS; warnings and precautions include neurologic toxicity, serious infections, tumor flare and embryo-fetal toxicity**

Glofitamab package insert, 6/2023.

Glofitamab: Background and Mechanism of Action

- **Patients with R/R DLBCL (≥2 prior therapies) have a poor prognosis[1,2]**
  - poor outcomes are reported in patients with treatment failure after R-CHOP, particularly in those with refractory disease[3]
  - CAR T-cell therapy is an option for patients with R/R DLBCL but its use may be limited by logistical challenges[4,5]
- **Glofitamab**
  - off-the-shelf and fixed duration treatment[6,7]
- **Phase I experience (NCT03075696)[7]**
  - encouraging efficacy and manageable safety with glofitamab monotherapy in patients with R/R B-cell NHL[6,7]
  - established a step-up dosing schedule and target dose (30mg) in patients with B-cell NHL in multiple cohorts[8]

Glofitamab: *CD20xCD3 bispecific monoclonal antibody with 2:1 format for increased potency vs 1:1 format[6]*



Dickinson M et al. ASCO 2022;Abstract 7500; EHA 2022;Abstract S220.

Glofitamab Meets Primary Endpoint of Overall Survival for Relapsed or Refractory DLBCL in Phase III STARGLO Study

Press Release: April 14, 2024

“The Phase III STARGLO study met its primary endpoint of overall survival.

The study demonstrated that people with relapsed or refractory (R/R) diffuse large B-cell lymphoma (DLBCL), who have received at least one prior line of therapy and are not candidates for autologous stem cell transplant, lived longer when treated with glofitamab-gxbm in combination with gemcitabine and oxaliplatin (GemOx) versus rituximab in combination with GemOx.

Safety of the combination appeared consistent with the known safety profiles of the individual medicines. The data will be submitted to health authorities and shared at an upcoming medical meeting.”

https://www.gene.com/media/press-releases/15021/2024-04-14/genentechs-columvi-meets-primary-endpoin

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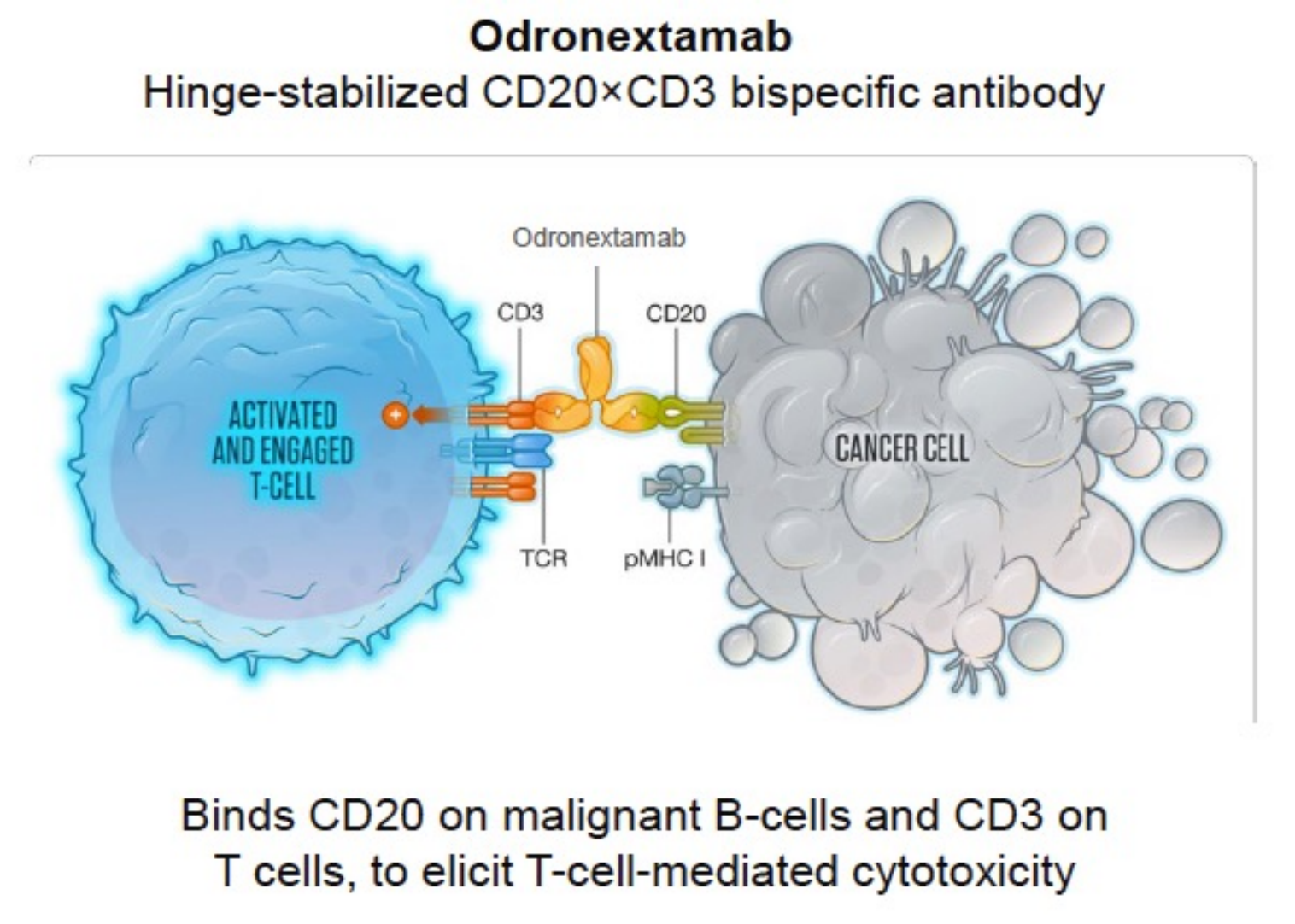
Odronextamab: Mechanism of Action



Kim TM et al. ASH 2022;Abstract 949.

Odronextamab

Mechanism of action

- **Bispecific antibody directed against CD20 on B cells and CD3 on T cells**

Indication

- **Investigational**

Key trial data

- **Phase II ELM-2 study evaluating odronextamab for patients with relapsed or refractory DLBCL**

Kim WS et al. ASH 2022;Abstract 444.

FDA Issues Complete Response Letters for Odronextamab for R/R FL and R/R DLBCL

Press Release: March 25, 2024

"The US Food and Drug Administration (FDA) has issued Complete Response Letters (CRLs) for the Biologics License Application (BLA) for odronextamab in relapsed/refractory (R/R) follicular lymphoma (FL) and in R/R diffuse large B-cell lymphoma (DLBCL), each after two or more lines of systemic therapy. The only approvability issue is related to the enrollment status of the confirmatory trials. The CRLs – one for R/R FL and one for R/R DLBCL – did not identify any approvability issues with the odronextamab clinical efficacy or safety, trial design, labeling or manufacturing.

[The manufacturer] has been actively enrolling patients in multiple Phase 3 trials for odronextamab as part of the OLYMPIA program – one of the largest clinical programs in lymphoma. As the OLYMPIA program is intended to change the treatment paradigm of several B-cell non-Hodgkin lymphoma subtypes – including in earlier lines of therapy – in agreeing to the program, the FDA required that the trials include both dose-finding and confirmatory portions. Enrollment in the dose-finding portion has begun, but the CRLs indicate that the confirmatory portions of these trials should be underway and that the timelines to completion be agreed prior to resubmission. [The company] is committed to working closely with the FDA and investigators to bring odronextamab to patients with R/R FL and R/R DLBCL as quickly as possible. [The company] plans on sharing updates on enrollment and regulatory timelines later this year.

Regulatory review of odronextamab remains ongoing by the European Medicines Agency (EMA) for the treatment of R/R DLBCL and R/R FL. In the European Union, odronextamab was granted Orphan Drug Designation in DLBCL and FL."

https://investor.regeneron.com/news-releases/news-release-details/regeneron-provides-update-biologics-license-application

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Module 7: Practical Considerations and Tolerability of Bispecific Antibodies

Practical Considerations with the Use of Bispecific Antibodies

Dr Allan
New York, New York

Dr Kahl
St Louis, Missouri

- **Routes of administration and step-up dosing schedules of various bispecific antibodies**
- **Recommended premedication and prophylaxis for patients with NHL about to begin treatment with bispecific antibodies**
- **Educating patients about the need for hospitalization with specific bispecific antibody therapies; timing and duration of hospitalization**
- **Anticipated duration of treatment with bispecific antibody therapy**

Cytokine Release Syndrome (CRS) and Neurotoxicity with Bispecific Antibodies

Dr Allan
New York, New York

Dr Kahl
St Louis, Missouri

- **Incidence and severity of CRS and neurotoxicity with bispecific antibody therapy in patients with NHL**
- **Time course for and common signs and symptoms of CRS and neurotoxicity**
- **Optimal monitoring of patients for early detection of CRS and neurotoxicity**
- **Guideline-endorsed approaches to the mitigation and management of CRS and neurotoxicity**

Other Tolerability and Toxicity Issues with Bispecific Antibody Therapy

Dr Allan
New York, New York

Dr Kahl
St Louis, Missouri

- **Incidence of cytopenias, infections and tumor flare with bispecific antibody therapy in pivotal clinical trials**
- **Spectrum, frequency and severity of other common adverse events with bispecific antibodies among patients with NHL, such as fatigue, rash, musculoskeletal pain and laboratory anomalies**
- **Counseling patients about the importance of monitoring for and reporting symptoms of common and less common adverse events with bispecific antibodies**
- **Strategies to manage side effects of bispecific antibodies in routine practice; appropriate thresholds for dose modification and treatment discontinuation**

Mollie Moran, APRN-CNP, AOCNP

What I tell my patients about logistical considerations with bispecific antibodies, such as premedications/prophylaxis, the need for hospitalization, step-up dosing and duration of treatment

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Robin Klebig, MSN, APRN, CNP, AOCNP

What I tell my patients about CRS and neurotoxicity associated with bispecific antibodies

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Mollie Moran, APRN-CNP, AOCNP

What I tell my patients about other toxicities associated with bispecific antibodies, such as cytopenias and infections, tumor flare, fatigue, rash, musculoskeletal pain and laboratory anomalies

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Consulting Nursing Faculty Comments

Entering the oncology field and managing burnout

Sonia Glennie, ARNP, MSN, OCN

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Consulting Nursing Faculty Comments

Choosing oncology work over other clinical roles

Sonia Glennie, ARNP, MSN, OCN

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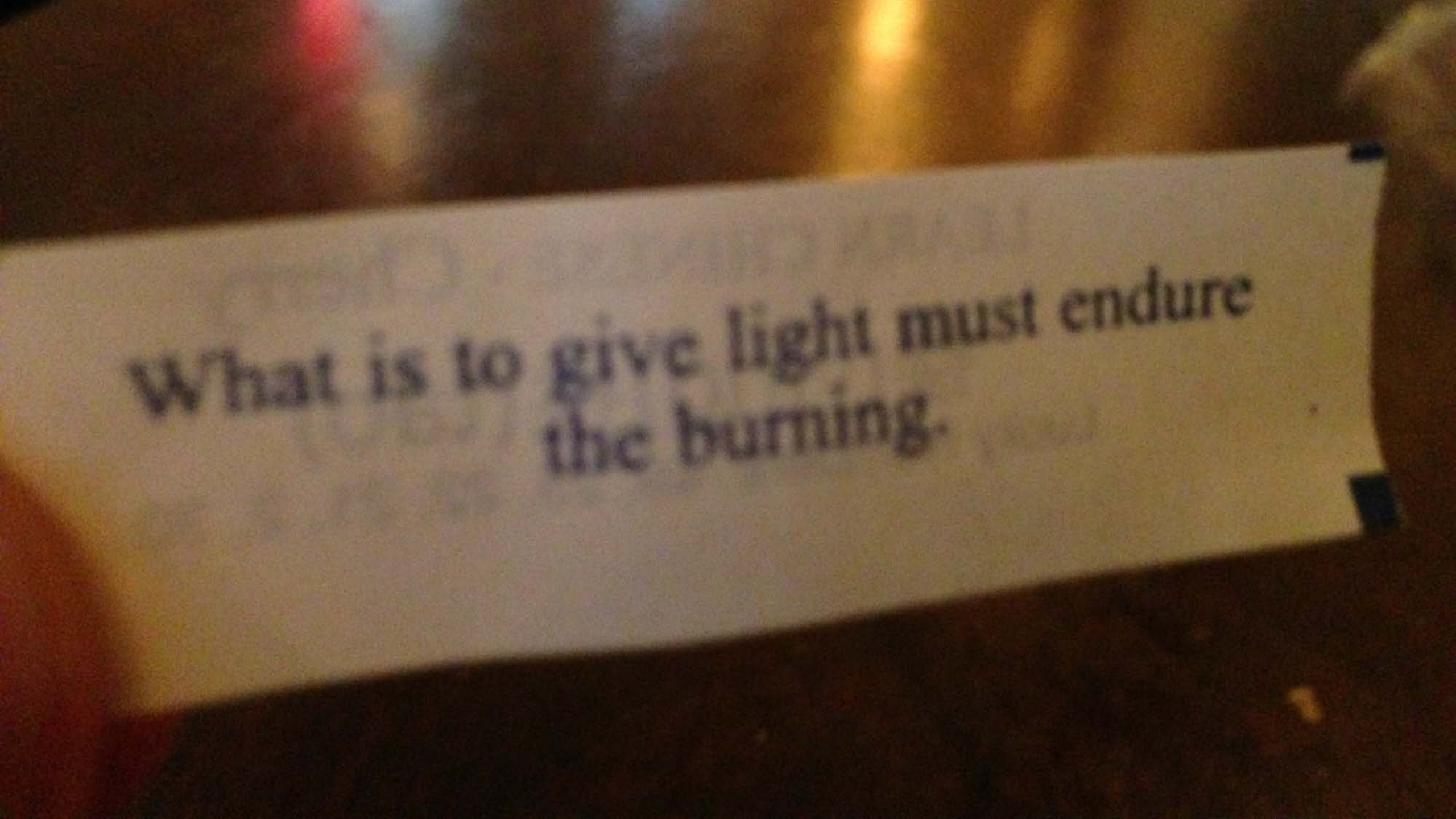
What is to give light must endure
the burning.

APPENDIX

CLL14 Trial: First-Line Venetoclax/Obinutuzumab

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

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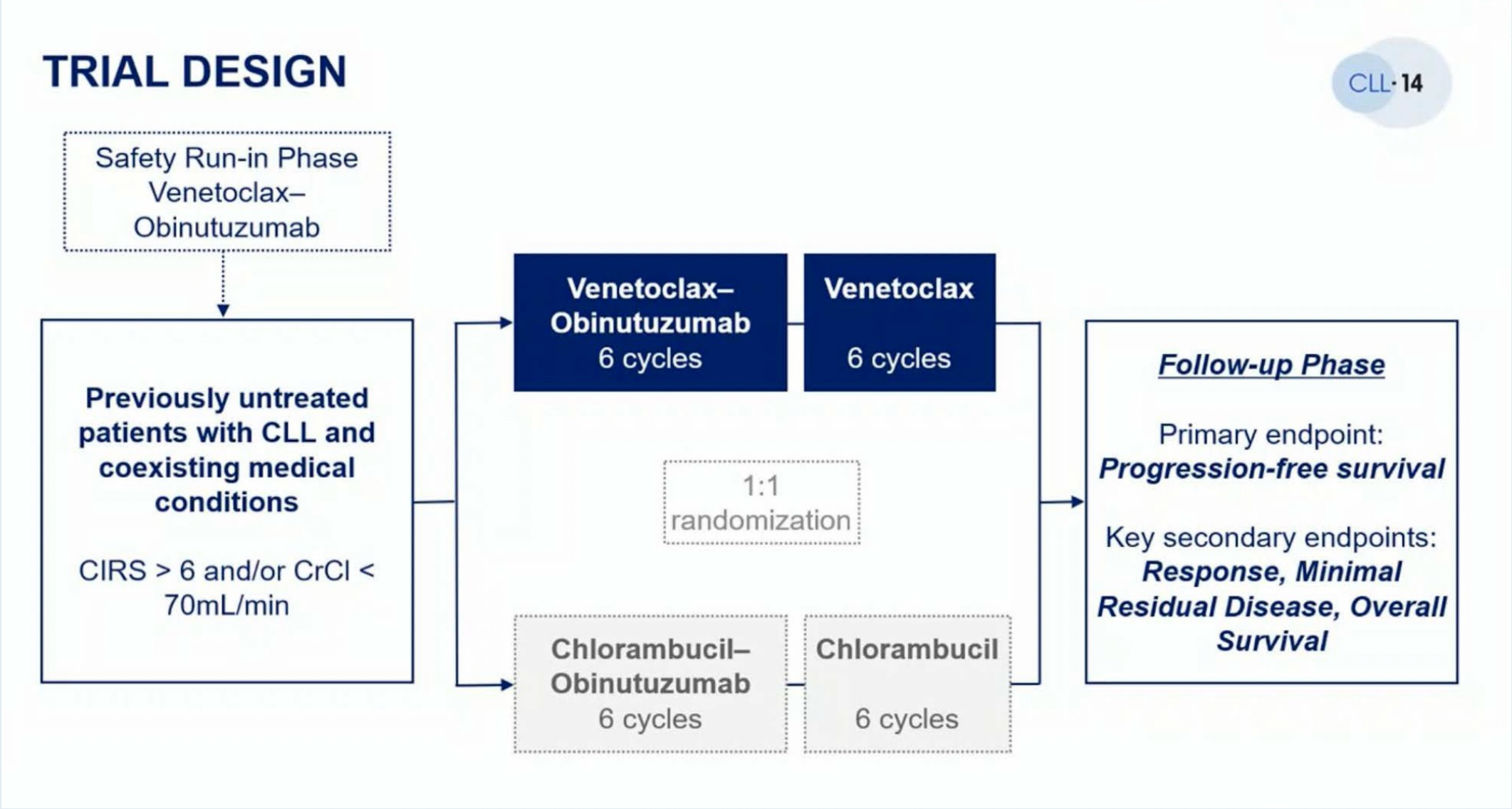
CLL14 Trial Design



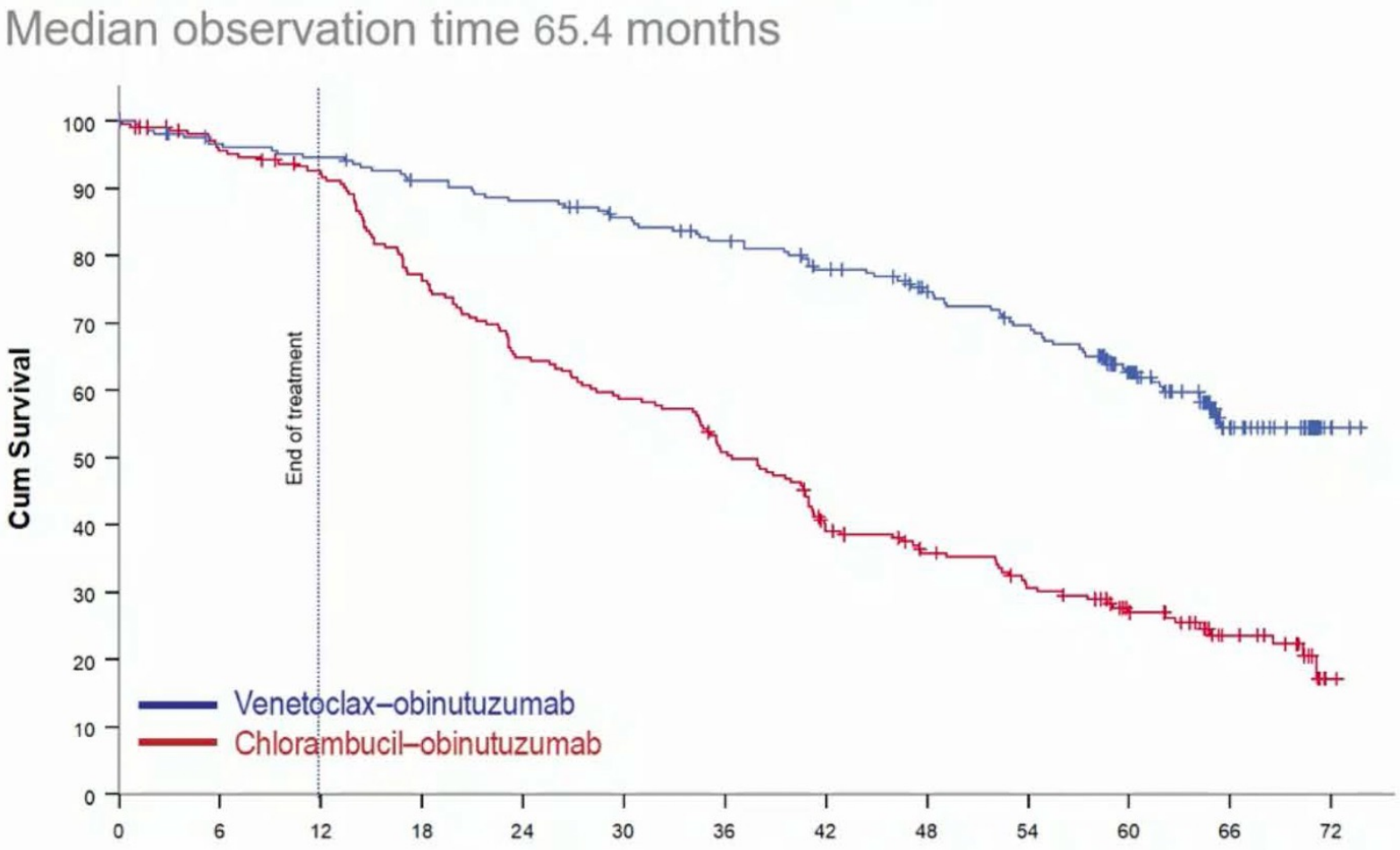
Al-Sawaf O et al. EHA 2022;Abstract S148.

CLL14: Most Frequent Grade ≥3 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.

CLL14: Progression-Free Survival (PFS)



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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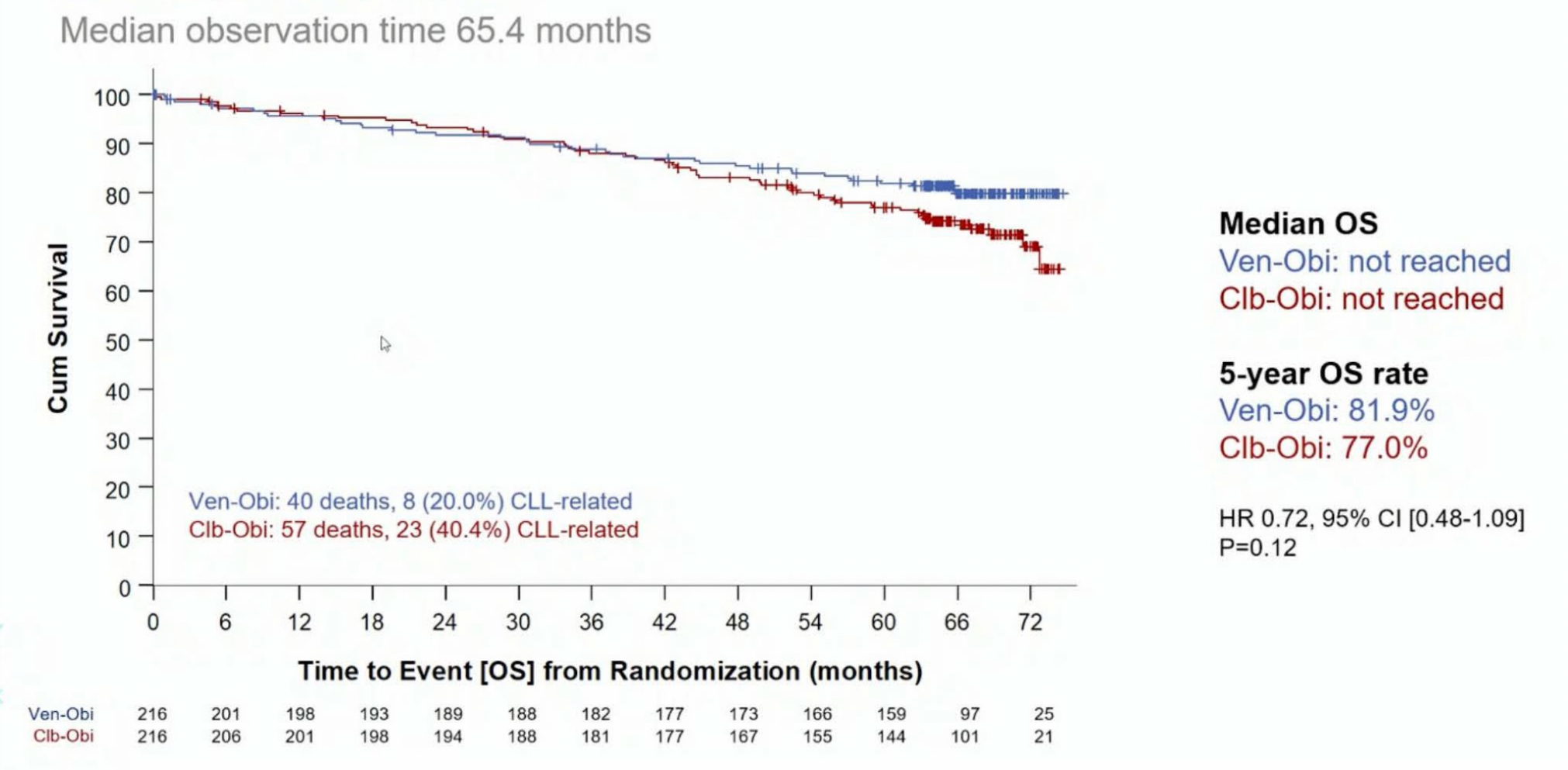
CLL14: Overall Survival (OS)



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

Mosunetuzumab

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Safety and efficacy of mosunetuzumab, a bispecific antibody, in patients with relapsed or refractory follicular lymphoma: a single-arm, multicentre, phase 2 study

Lihua E Budde, Laurie H Sehn, Matthew Matasar, Stephen J Schuster, Sarit Assouline, Pratyush Giri, John Kuruvilla, Miguel Canales, Sascha Dietrich, Keith Fay, Matthew Ku, Loretta Nastoupil, Chan Yoon Cheah, Michael C Wei, Shen Yin, Chi-Chung Li, Huang Huang, Antonia Kwan, Elicia Penuel, Nancy L Bartlett

Lancet Oncol 2022 August;23(8):1055-65.

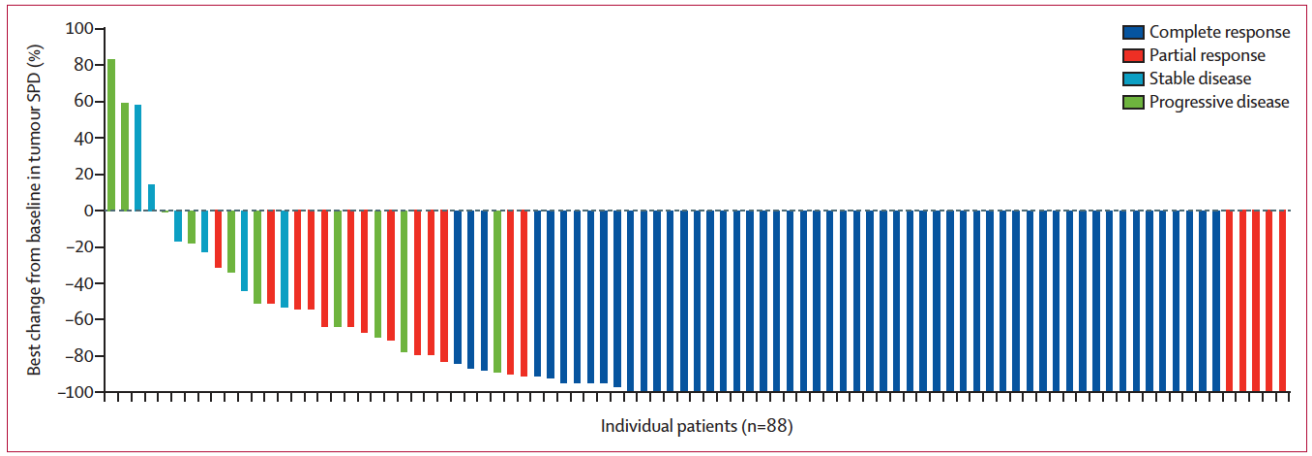
Mosunetuzumab Safety Profile in Patients With Relapsed/Refractory B-cell Non-Hodgkin Lymphoma: Clinical Management Experience From a Pivotal Phase I/II Trial

Matthew Matasar,[1] Nancy L. Bartlett,[2] Mazyar Shadman,[3] Lihua E. Budde,[4] Ian Flinn,[5] Gareth P. Gregory,[6] Won Seog Kim,[7] Georg Hess,[8] Dima El-Sharkawi,[9] Catherine S. Diefenbach,[10] Huang Huang,[11] Iris To,[12] Joana Parreira,[13] Mei Wu,[12] Antonia Kwan,[12] Sarit Assouline[14]

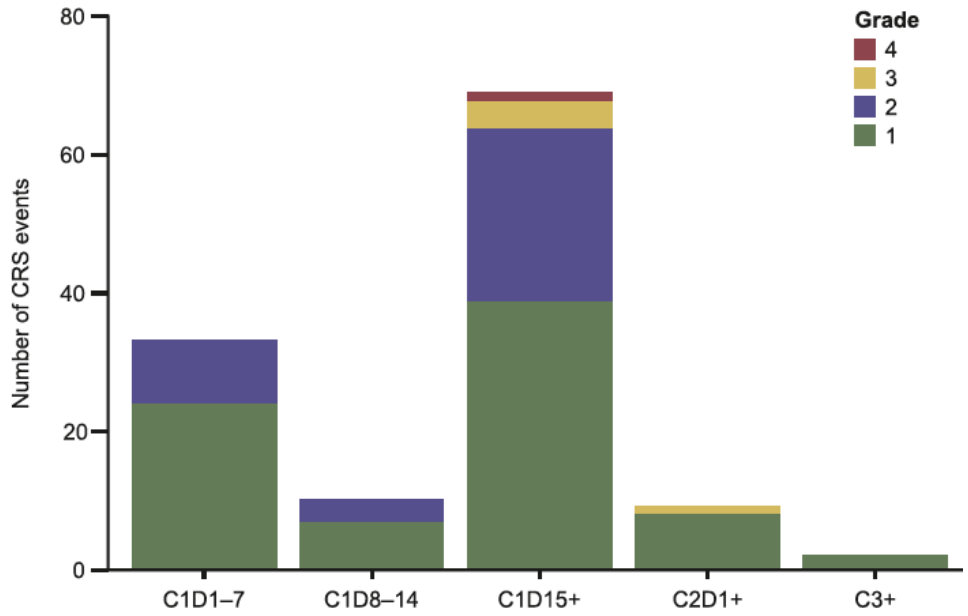
Clin Lymphoma Myeloma Leuk 2024 April;24(4):240-53.

Mosunetuzumab: Efficacy and CRS Events in R/R FL

Reduction in Tumor Size with Mosunetuzumab



CRS Events by Mosunetuzumab Dose Cycle



	Step-up doses		Loading doses		Target dose
	C1D1: 1 mg	C1D8: 2 mg	C1D15: 60 mg	C2D1: 60 mg	C3D1+: 30 mg
Median time to onset (hours)	5	28	25	46	–
Median duration (days)	1	3	3	5	–

Budde LE et al. *Lancet Oncol* 2022 August;23(8):1055-65; Matasar M et al. *Clin Lymphoma Myeloma Leuk* 2024 April;24(4):240-53.

RTP RESEARCH TO PRACTICE

Epcoritamab

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original reports

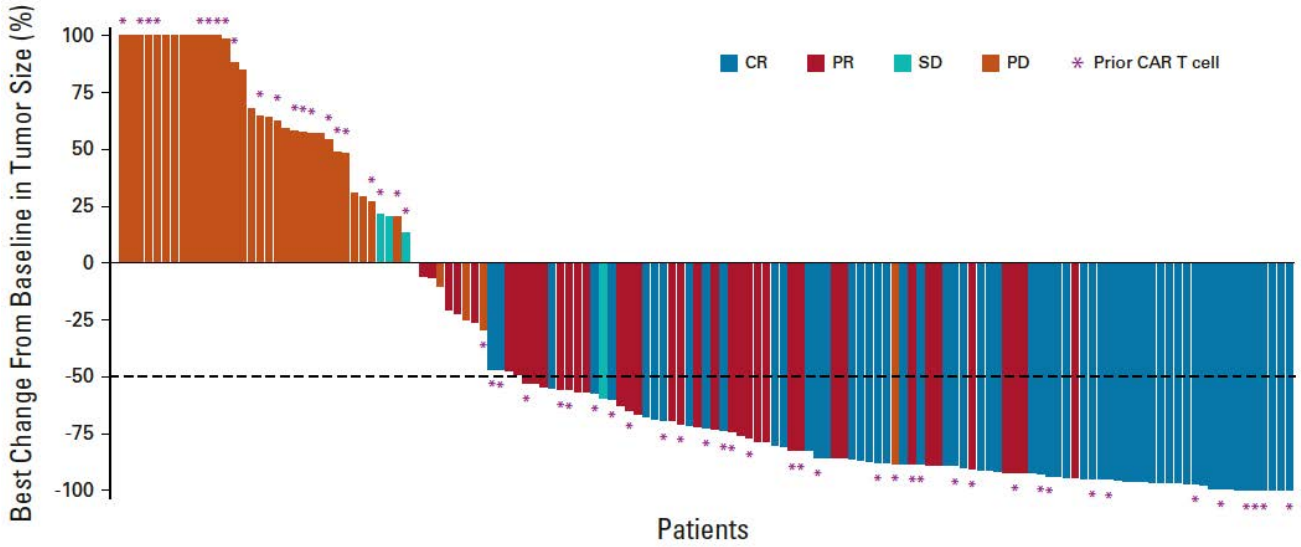
Epcoritamab, a Novel, Subcutaneous CD3xCD20 Bispecific T-Cell–Engaging Antibody, in Relapsed or Refractory Large B-Cell Lymphoma: Dose Expansion in a Phase I/II Trial

Catherine Thieblemont, MD, PhD[1]; Tycel Phillips, MD[2]; Herve Ghesquieres, MD, PhD[3]; Chan Y. Cheah, MBBS, DMSc[4,5]; Michael Roost Clausen, MD, PhD[6]; David Cunningham, MD[7]; Young Rok Do, MD, PhD[8]; Tatyana Feldman, MD[9]; Robin Gasiorowski, MBBS, PhD[10]; Wojciech Jurczak, MD, PhD[11]; Tae Min Kim, MD, PhD[12]; David John Lewis, MD[13]; Marjolein van der Poel, MD, PhD[14]; Michelle Limei Poon, MD[15]; Mariana Cota Stirner, MD, PhD[16]; Nurgul Kilavuz, MSc[17]; Christopher Chiu, PhD[17]; Menghui Chen, PhD[17]; Mariana Sacchi, MD[17]; Brian Elliott, MD[17]; Tahamtan Ahmadi, MD, PhD[17]; Martin Hutchings, MD, PhD[18]; and Pieternella J. Lugtenburg, MD, PhD[19]

J Clin Oncol 2023 April 20;41(12):2238-47.

Epcoritamab: Efficacy and Select Adverse Events in R/R DLBCL

Reduction in Tumor Size with Epcoritamab



Select Adverse Events

Patient	Any Grade (N = 157), No. (%)	Grade ≥ 3 (N = 157), No. (%)
Any AE	156 (99.4)	96 (61.1)
Any treatment-related AE	130 (82.8)	42 (26.8)
SAE	89 (56.7)	—
Serious treatment-related AE	55 (35.0)	—
Treatment-emergent AE leading to treatment discontinuation	12 (7.6)	11 (7.0)
Treatment-emergent AE in ≥ 10% of patients[a]		
CRS	78 (49.7)	4 (2.5)
Pyrexia[b]	37 (23.6)	0
Fatigue	36 (22.9)	3 (1.9)
AEs of special interest		
CRS[c]	78 (49.7)	4 (2.5)
ICANS[d]	10 (6.4)	1 (0.6)
Clinical tumor lysis syndrome	2 (1.3)	2 (1.3)

ICANS = immune effector cell-associated neurotoxicity syndrome

Thieblemont C et al. *J Clin Oncol* 2023 April 20;41(12):2238-47.

Glofitamab

ORIGINAL ARTICLE

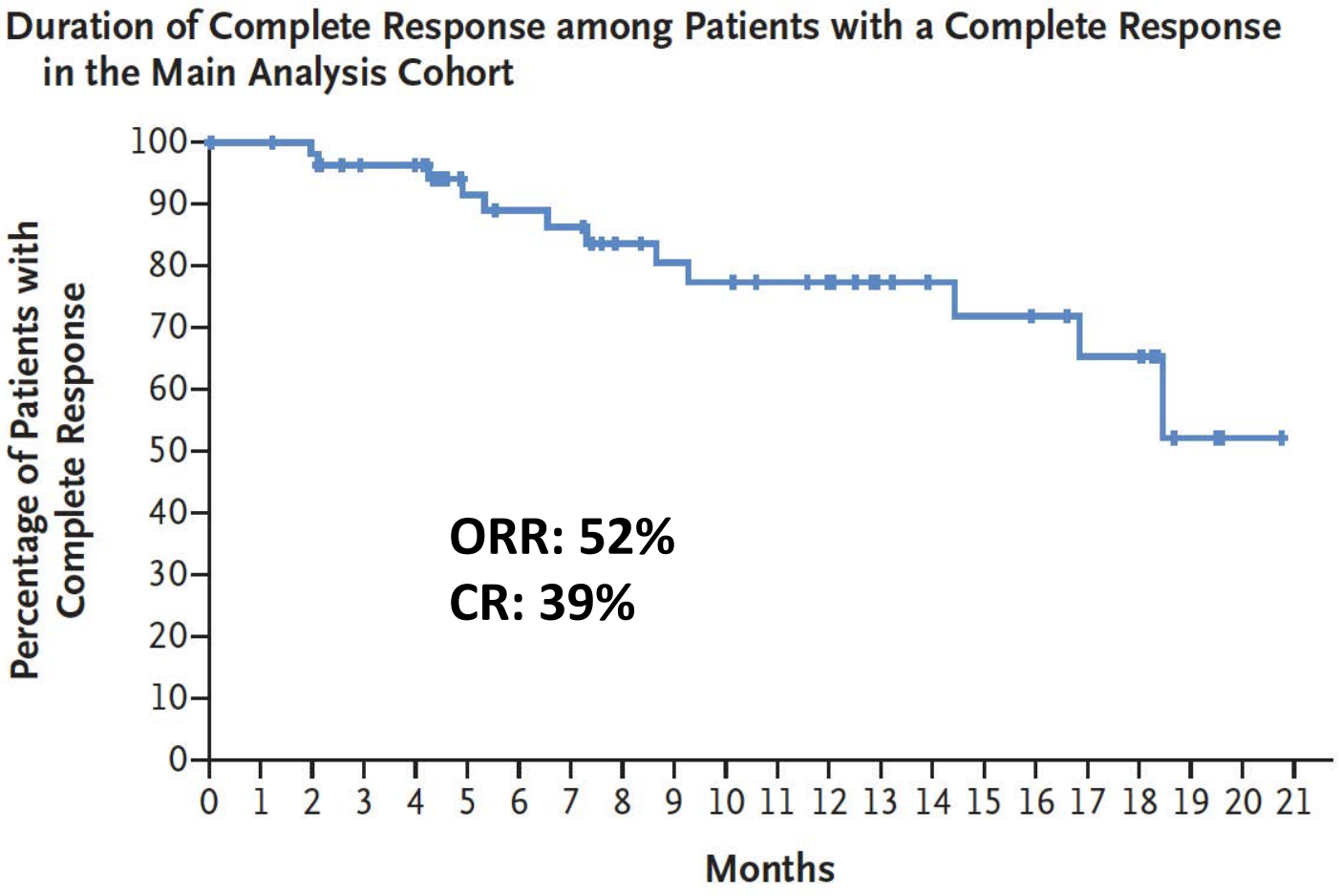
Glofitamab for Relapsed or Refractory Diffuse Large B-Cell Lymphoma

Michael J. Dickinson, M.B., B.S., D.Med.Sc., Carmelo Carlo-Stella, M.D., Franck Morschhauser, M.D., Ph.D., Emmanuel Bachy, M.D., Ph.D., Paolo Corradini, M.D., Gloria Iacoboni, M.D., Cyrus Khan, M.D., Tomasz Wróbel, M.D., Fritz Offner, M.D., Ph.D., Marek Trněný, M.D., Shang-Ju Wu, M.D., Ph.D., Guillaume Cartron, M.D., Ph.D., Mark Hertzberg, M.B., B.S., Ph.D., Anna Sureda, M.D., Ph.D., David Perez-Callejo, Ph.D., Linda Lundberg, Ph.D., James Relf, M.D., Mark Dixon, M.Sc., Emma Clark, M.Sc., Kathryn Humphrey, B.Sc., and Martin Hutchings, M.D., Ph.D.

N Engl J Med 2022 December 15;387(24):2220-31.

RTP RESEARCH TO PRACTICE

Glofitamab: Efficacy and Select Adverse Events in R/R DLBCL



Most common serious adverse events	
Cytokine release syndrome, per ASTCT	32 (21)
Sepsis	6 (4)
Tumor flare	5 (3)
Covid-19–related pneumonia	5 (3)
Covid-19	4 (3)
Adverse events of special interest	
Cytokine release syndrome, grade ≥2 per ASTCT	24 (16)
Cytokine release syndrome, grade ≥2 per Lee et al.	28 (18)
Infection, any grade	59 (38)
Neurologic event, grade ≥2	23 (15)
Event grade consistent with ICANS, any grade	12 (8)
Tumor flare, grade ≥2	11 (7)
AST, ALT, or total bilirubin elevation, grade ≥2	11 (7)
Febrile neutropenia, grade ≥3	4 (3)
Tumor lysis syndrome, grade ≥3	2 (1)

Dickinson MJ et al. *N Engl J Med* 2022 December 15;387(24):2220-31.

RTP RESEARCH TO PRACTICE

What I Tell My Patients:
Integrating New Research Information into Current Clinical Care

A Complimentary NCPD Hybrid Symposium Series Held During the 49th Annual ONS Congress

Chronic Lymphocytic Leukemia and Bispecific Antibodies in the Management of Lymphoma

Thursday, April 25, 2024

6:00 PM – 8:00 PM

Faculty

John N Allan, MD
Brad S Kahl, MD
Robin Klebig, MSN, APRN, CNP, AOCNP
Mollie Moran, APRN-CNP, AOCNP

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

What I Tell My Patients: Integrating New Research Information into Current Clinical Care

A Complimentary NCPD Hybrid Symposium Series Held During the 49th Annual ONS Congress

Head and Neck Cancer

Friday, April 26, 2024
6:00 AM – 7:30 AM

Faculty

Meetal Dharia, NP-C, AOCNP
Robert L Ferris, MD, PhD
Robert Haddad, MD
Lynsey P Teulings, APRN

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

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.

To Claim NCPD Credit

In-person attendees: Please refer to the program syllabus for the NCPD credit link or QR code.

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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