Understanding the Current Paradigm and New Approaches in the Care of Patients with Cancer

A Complimentary NCPD Hybrid Symposium Series Held During the 50th Annual ONS Congress

Chronic Lymphocytic Leukemia

Thursday, April 10, 2025

6:00 PM – 7:30 PM

Faculty

Jacqueline Broadway-Duren, PhD, DNP, APRN, FNP-BC
Bita Fakhri, MD, MPH
Corinne Hoffman, MS, APRN-CNP, AOCNP
Jeff Sharman, MD

Moderator

Neil Love, MD

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Faculty

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Family Nurse Practitioner
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MD Anderson Cancer Center
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Sarah Cannon Research Institute
at Willamette Valley Cancer Center
Eugene, Oregon

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Dr Broadway-Duren — Disclosures

Advisory Committees	AbbVie Inc, BeiGene Ltd

Dr Fakhri — Disclosures

Advisory Committees	AbbVie Inc, AstraZeneca Pharmaceuticals LP, BeiGene Ltd, Bristol Myers Squibb, Genentech, a member of the Roche Group, Janssen Biotech Inc, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Pharmacyclics LLC, an AbbVie Company
Contracted Research	AbbVie Inc, BeiGene Ltd, Genmab US Inc, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company
Speakers Bureaus	AbbVie Inc, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company

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Ms Hoffman — Disclosures

No relevant conflicts of interest to disclose.

Dr Sharman — Disclosures

Consulting Agreements and Contracted Research	AbbVie Inc, AstraZeneca Pharmaceuticals LP, BeiGene Ltd, Bristol Myers Squibb, Genentech, a member of the Roche Group, Lilly, Merck

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Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP and Lilly.

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

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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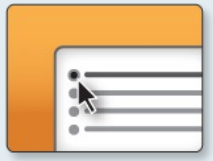
Clinicians in the Meeting Room

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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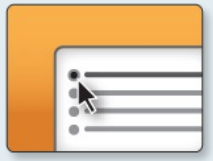
Clinicians Attending via Zoom

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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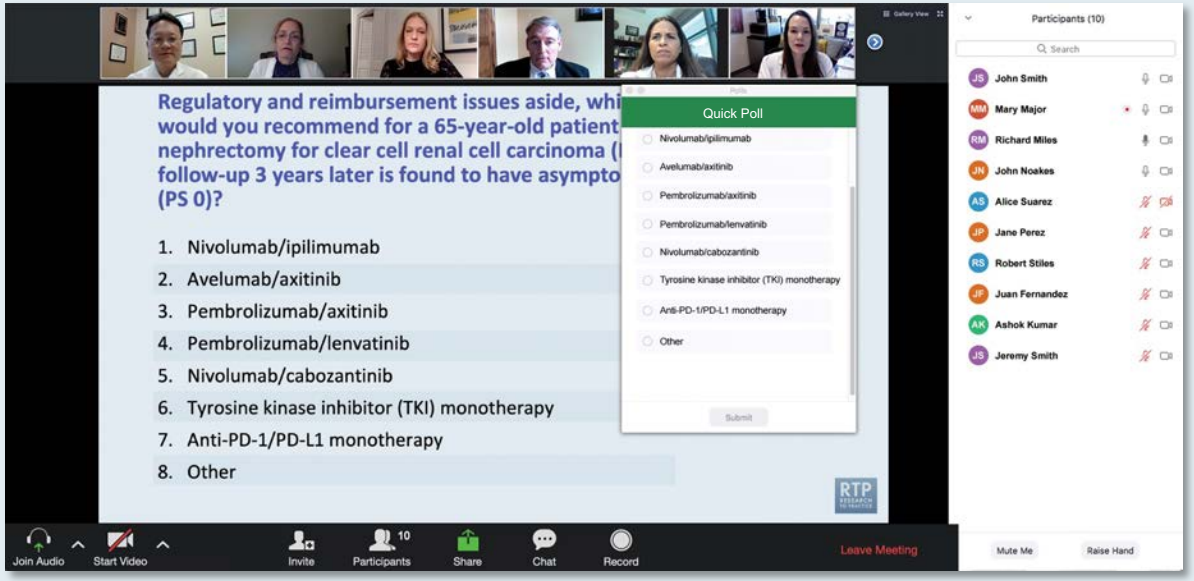
Clinicians, Please Complete the Pre- and Postmeeting Surveys



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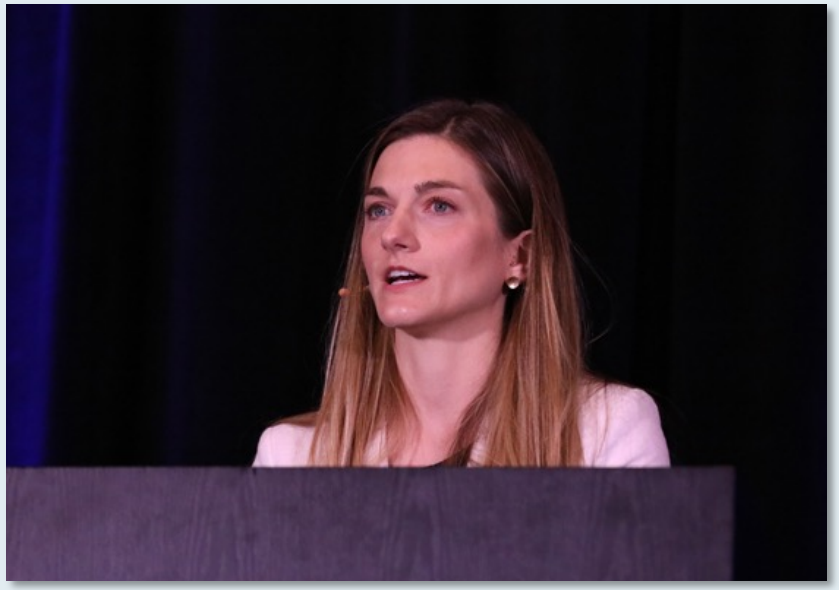
About the Enduring Program



- The live meeting is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based 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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ONCOLOGY NURSING UPDATE WITH DR NEIL LOVE

Bispecific Antibodies in Lymphoma Part 1 — An Interview with Ms Robin Klebig for Oncology Nurses

MS ROBIN KLEBIG
MAYO CLINIC

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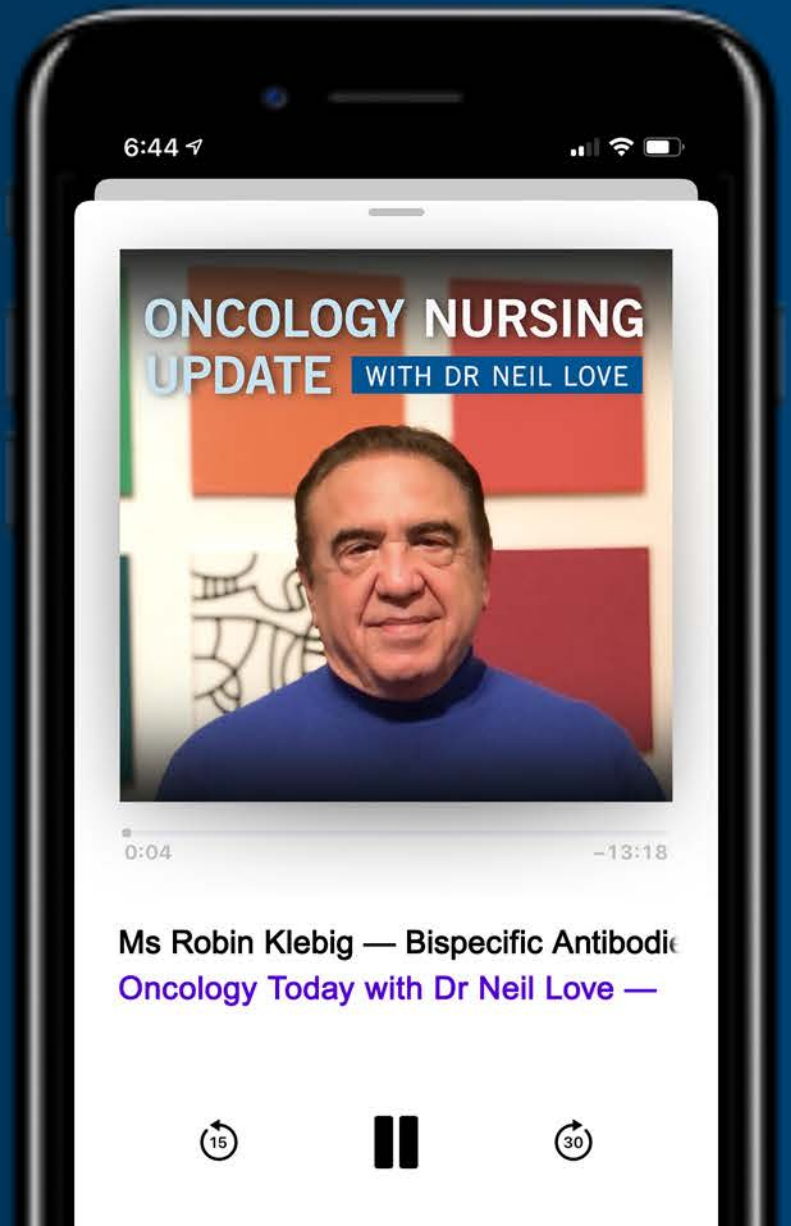
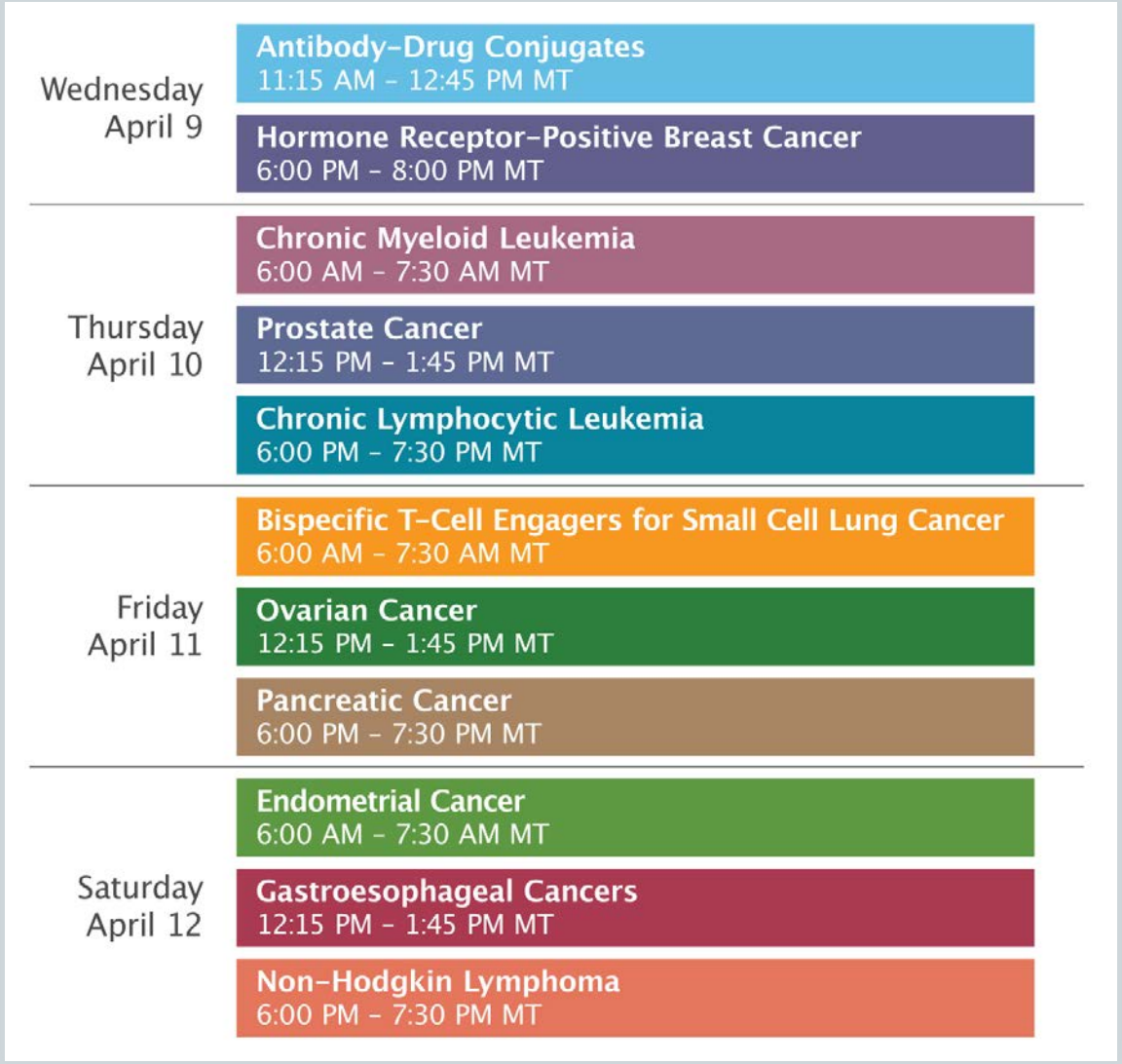
Spotify

Listen on Google Podcasts



“Understanding the Current Paradigm and New Approaches”
Seventeenth Annual RTP-ONS NCPD Symposium Series



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Understanding the Current Paradigm and New Approaches
RTP Faculty at ONS 2025

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Introduction: Key Factors in the Management Patients with Chronic Lymphocytic Leukemia (CLL)

Module 1: Role of Covalent Bruton Tyrosine Kinase (BTK) Inhibitors for Newly Diagnosed CLL

Module 2: Role of Time-Limited Up-Front Treatment, Including Therapy Combining BTK Inhibitors and Venetoclax, for Newly Diagnosed CLL

Module 3: Role of Pirtobrutinib for Relapsed/Refractory (R/R) CLL

Module 4: CAR (Chimeric Antigen Receptor) T-Cell Therapy for R/R CLL

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Key Factors in Managing Patients With CLL

Timing of Therapy

- Deciding when to start therapy
  - Many patients discovered incidentally; how to handle the "worried well"
  - Comorbidities and fitness; where the patient is in their life cycle
- Deciding when to stop therapy

Key Prognostic Factors

- The importance of FISH, *TP53*, and mutational status of immunoglobulin genes
- How to test for MRD (ie, flow cytometry or molecular methods) and how to use it to guide clinical decision-making

Key Classes of Drugs

- BTKi (eg, acalabrutinib, zanubrutinib, ibrutinib)
- BCL2i (eg, venetoclax)
- Anti-CD20 antibodies (eg, rituximab, obinutuzumab)
- Chemotherapy/ chemoimmunotherapy (eg, chlorambucil, FCR, BR)

Courtesy of Bita Fakhri, MD, MPH

Agenda

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Clinical Scenario

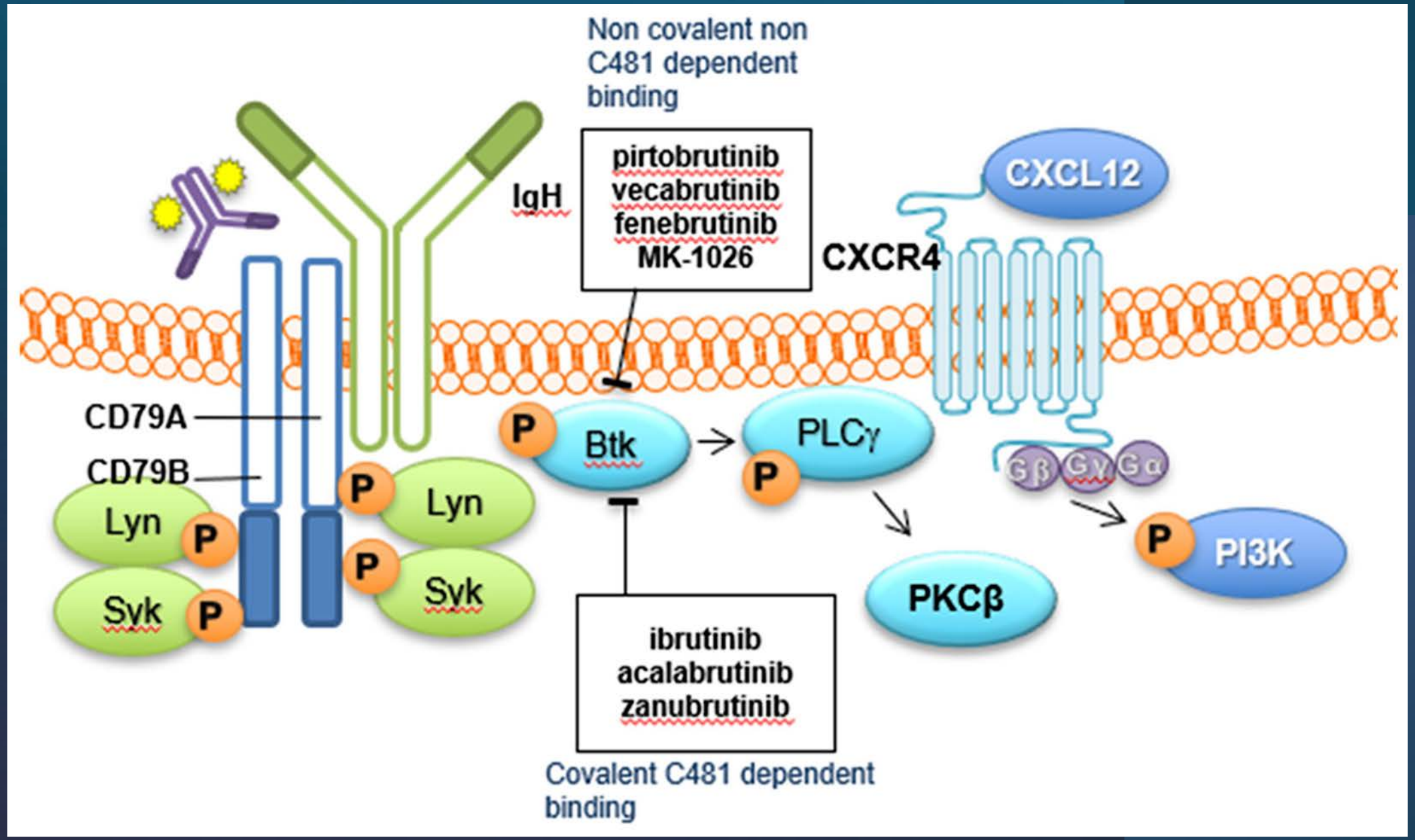
A patient with newly diagnosed CLL is about to start treatment with acalabrutinib or zanubrutinib

Considerations in CLL Treatment Choices

Jeff Sharman M.D.

Medical Director of Hematology Research

Willamette Valley Cancer Institute & Sarah Cannon


Non covalent non C481 dependent binding
pirtobrutinib
vecabrutinib
fenebrutinib
MK-1026
IgH
CXCL12
CXCR4
CD79A
CD79B
P
Btk
PLCγ
Lyn
Lyn
Syk
Syk
Gβ
Gγ
Gα
PI3K
PKCβ
ibrutinib
acalabrutinib
zanubrutinib
Covalent C481 dependent binding

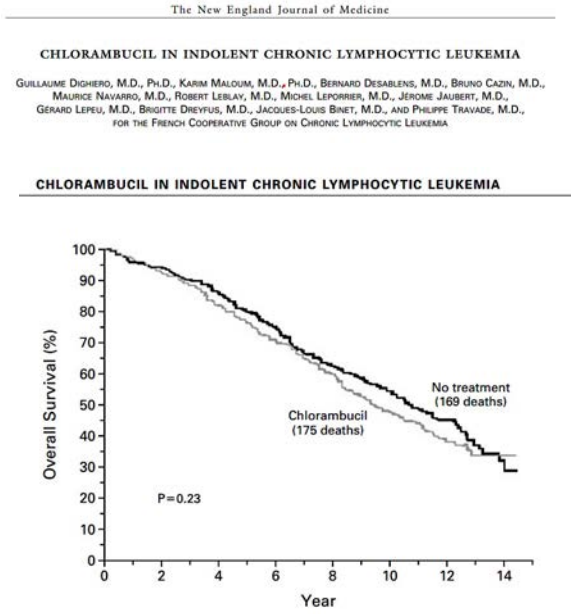
Treatment decisions in frontline CLL

- 78-year-old male
- Known coronary artery disease, s/p two stents, on chronic aspirin
- History of hypertension, well controlled on amlodipine, losartan, HCTZ
- No known history of a. fib, but reports “heart occasionally skips a beat” when asked about palpitations.
- Creatinine 1.5, GFR 50
- Lives 50 miles away from cancer center and his daughter takes off of work to drive him to appointments

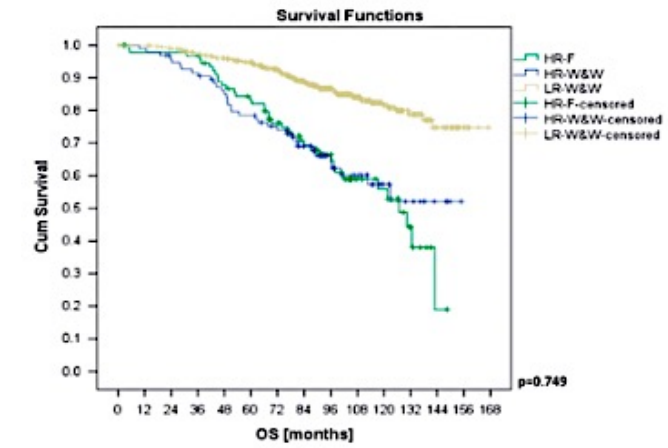
Treatment decisions in frontline CLL

- Initially diagnosed 18 months ago, but now WBC rising to 180K, Hgb 10, Platelets 110. Has developed moderate adenopathy
- IgHV unmutated, Trisomy 12, TP53 wild type
- How do each of the above influence treatment decisions????

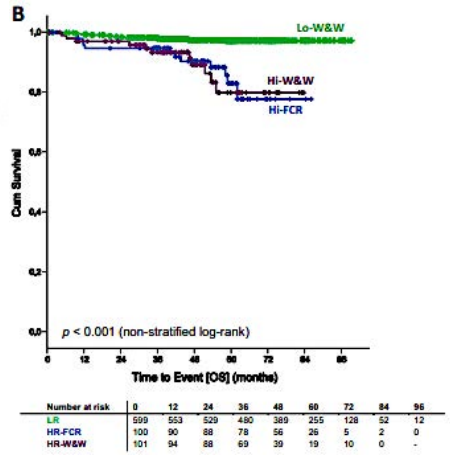
Watch and Wait… aka watch and freak out



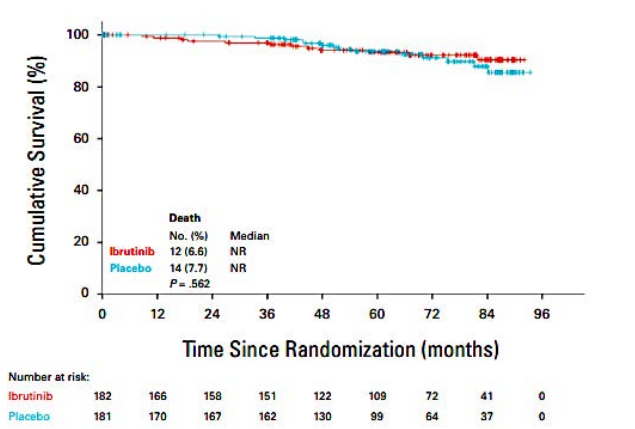
Chlorambucil



Fludarabine



FCR



Ibrutinib

IWCLL Criteria to Initiate Treatment

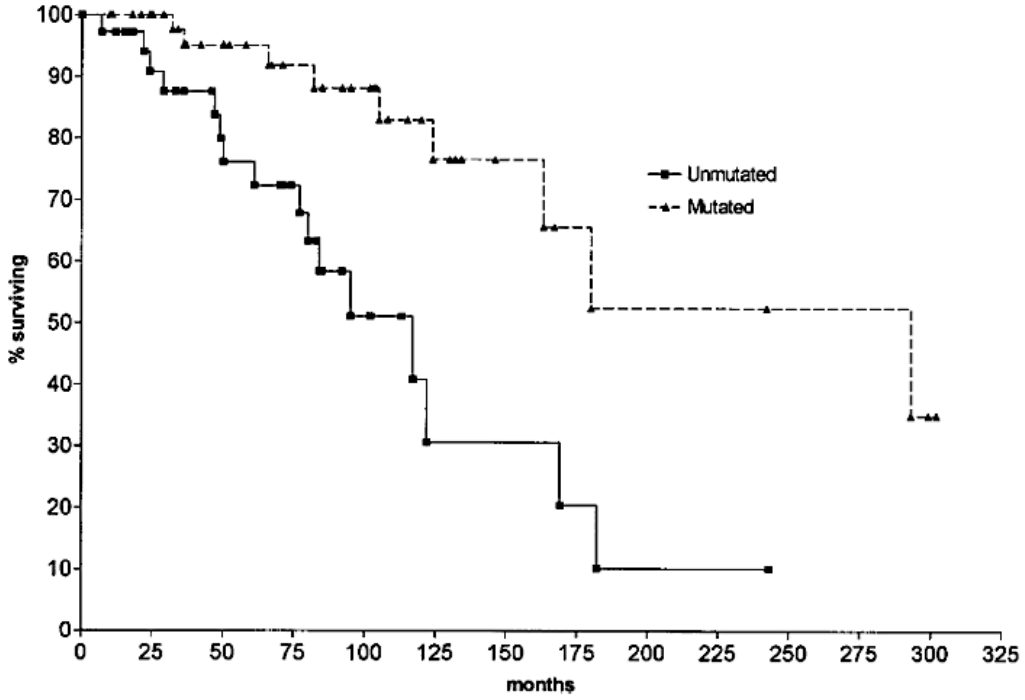
- Rapidly progressing ALC
- Emergence of bone marrow dysfunction
- Symptomatic adenopathy
- “Other”

Key Biomarkers

FOCUS ON HEMATOLOGY

Unmutated Ig V_H Genes Are Associated With a More Aggressive Form of Chronic Lymphocytic Leukemia

By Terry J. Hamblin, Zadie Davis, Anne Gardiner, David G. Oscier, and Freda K. Stevenson

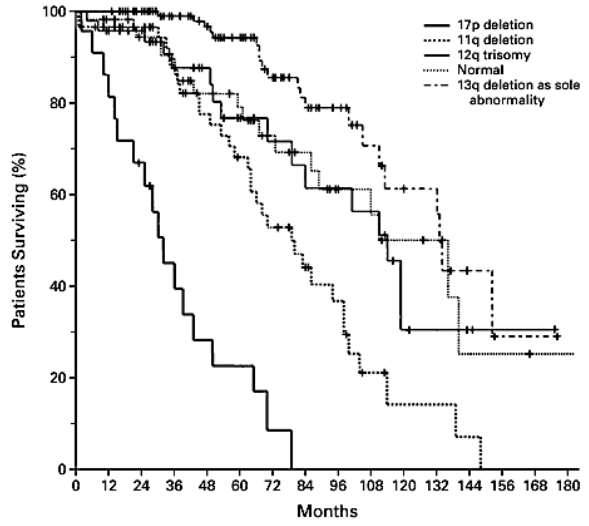


The New England Journal of Medicine

GENOMIC ABERRATIONS AND SURVIVAL IN CHRONIC LYMPHOCYTIC LEUKEMIA

HARTMUT DÖHNER, M.D., STEPHAN STILGENBAUER, M.D., AXEL BENNER, M.Sc., ELKE LEUPOLT, M.D., ALEXANDER KRÖBER, M.D., LARS BULLINGER, M.D., KONSTANZE DÖHNER, M.D., MARTIN BENTZ, M.D., AND PETER LICHTER, PH.D.

GENOMIC ABERRATIONS AND SURVIVAL IN CHRONIC LYMPHOCYTIC LEUKEMIA



No. at Risk															
17p deletion	23	18	13	8	5	4	1	0	0	0	0	0	0	0	0
11q deletion	56	53	47	43	33	27	20	15	10	4	2	2	1	0	0
12q trisomy	47	44	41	29	24	17	14	13	12	11	4	3	2	1	0
Normal	57	51	45	37	30	27	20	17	12	11	6	5	2	2	1	1
13q deletion as sole abnormality	117	117	106	91	80	63	45	36	24	16	12	11	3	1	1	0

Current NCCN Guidance

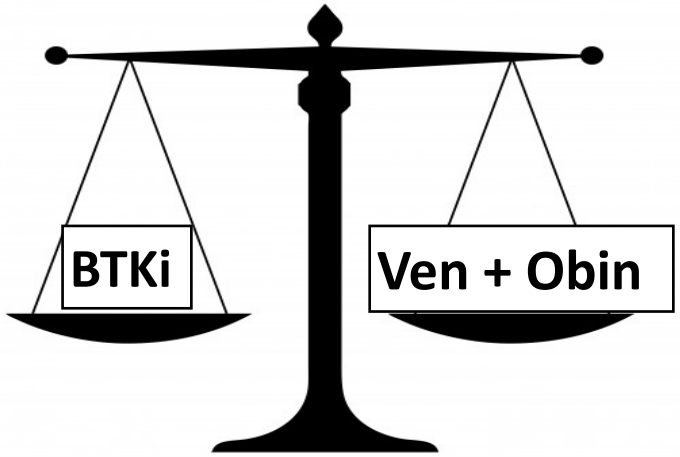
SUGGESTED TREATMENT REGIMENS[a,b]
CLL/SLL Without del(17p)*ITP53* Mutation
(alphabetical by category)

FIRST-LINE THERAPY[e]

Preferred Regimens	Other Recommended Regimens
• BCL2i-containing regimens ▸ Venetoclax[f,h] + obinutuzumab (category 1) ▸ Venetoclax[f,h] + acalabrutinib ± obinutuzumab (category 1) • cBTKi-based regimens ▸ Acalabrutinib[f,g] ± obinutuzumab (category 1) ▸ Zanubrutinib[f,g] (category 1)	• BCL2i-containing regimen ▸ Venetoclax[f,h] + ibrutinib[f,g] • cBTKi-based regimen ▸ Ibrutinib[f,g,i] (category 1)

NCCN Guidelines for CLL. V.3.2025.

Frontline BTKi vs. Ven + Obinutuzumab: Factors to Consider



- Convenience (no infusions, TLS monitoring)
- Long term efficacy data
- Phase 3 data compared to FCR and BR
- More data for efficacy of ven at time of BTKi progression

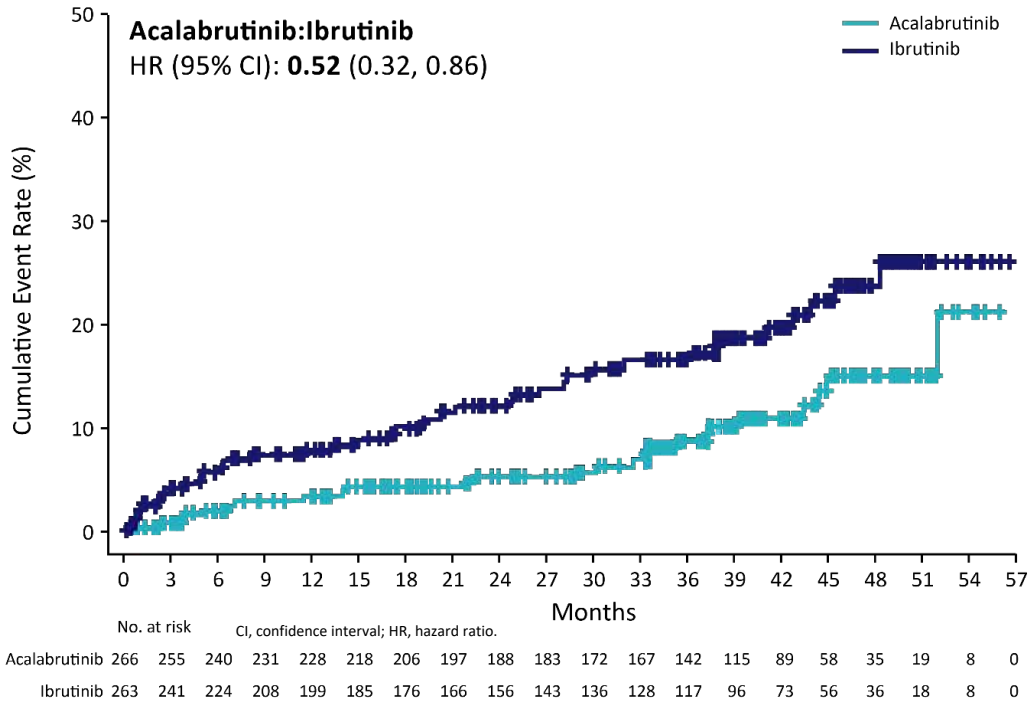
- Potential for 1-year time-limited therapy
- No known cardiac or bleeding risks
- Less concern for long term adherence
- Potential for cost-saving if 1-year of therapy is durable

BTK specific side effects

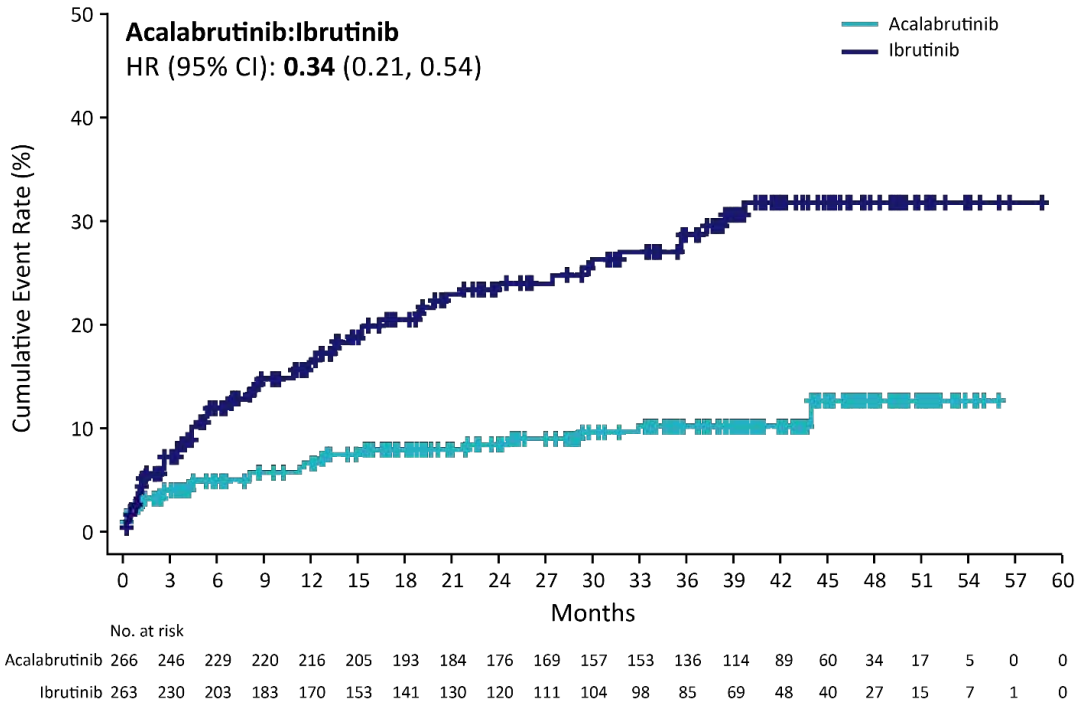
- Cardiac Side Effects
  - Atrial Fibrillation
  - Hypertension
  - Ventricular arrhythmias
- Bruising / Bleeding
- Arthralgias

Lower Cumulative Incidences of Any Grade Atrial Fibrillation/Flutter and Hypertension With Acalabrutinib

Afib/Flutter



Hypertension



Byrd et al J Clin Oncol 2021 Nov 1;39(31):3441-3452.

Returning to the case above

Older, “typical” CLL patient with existing cardiac risk factors (hypertension/aspirin), but also some chronic kidney disease who needs therapy

Lives some distance away and relies on transportation

Indication for therapy

Mixed molecular features

Roundtable Discussion

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BTK Inhibitors (Covalent)

Dr. Jackie Broadway-Duren

Nursing Considerations for Patients on BTKi

- Patient conversations
  - We discuss indications for the BTKi
  - Discuss how it works and what to expect while receiving it

Laboratory data

- WBC 52,000 with ALC 8.3
- Hbg – 11.0 gm/dL, Plts – 110,000
- Prognostic factors: mutated IgHV; FISH: 13q deletion; NGS: Negative
- Symptoms: night sweats, increased fatigue 7/10 (MDASI scale)

Side Effects for BTKi Therapy (Covalent)

- Cool, A., Nong, T., Montoya, S., & Taylor, J. (2024). BTK inhibitors: past, present, and future. *Science Direct, 45*(8), 691-707. https://doi.org/10.1016/j.tips.2024.06.006.

Ibrutinib (1st gen)	Acalabrutinib (2nd gen)	Zanubrutinib (2nd gen)
▪ Atrial fibrillation (16%) ▪ Ventricular arrythmias (~10%) ▪ Sudden cardiac death ▪ Hypertension (23%) ▪ Arthralgias (40%) ▪ Muscle spasms/cramps (25%) ▪ Bleeding/bruising (51.3%)	▪ Headache (~35%) ▪ Diarrhea (~35%) ▪ Cough/respiratory (~29%) ▪ Potential for bleeding/bruising ▪ arthralgias	▪ A. Fib (2%) ▪ Hypertension (~11%) ▪ Neutropenia (34%) ▪ Upper respiratory infections (~24%) ▪ Low potential for bleeding

Start BTKi

- 72 y/o female who was previously untreated who now presents for treatment recommendations due to progressing lymphadenopathy and WBC. PMH: hypertension, hypercholesterolemia
- After discussion of BTKi available, patient encouraged to start acalabrutinib
  - Discuss possibility of headaches (usually transient with early weeks on therapy)
  - Discussed minimal possibility of A. fib and management if occurs
- Patient developed a slight headache in 2nd week of therapy. HA resolved after a few days with a cup of coffee.
- Diarrhea – she developed "loose stools" for approximately 2-3 days of week 2, but symptoms resolved with loperamide.

***Patient continues on Acala with further complaints of symptoms**.

Advise on Toxicities with Initial Start of BTKi

- WBC will increase initially due to mechanism of the drug – **do not be alarmed with leukocytosis**
- Monitor blood pressure (keep log). Follow up with PCP or cardiologist
- Muscle or joint pain
- Be mindful of cardiac arrhythmias (A-fib)
  - Report any heart palpitations, flutters, etc
  - Report SOB

GI Toxicities with BTKis

- Diarrhea – may be self-limiting
- Loperamide – take as directed OTC
- Avoid high fat diet
- Avoid fruit and fruit juices
- Encourage BRAT diet (bananas, rice, applesauce, toast)
- Increase water intake to stay hydrated
- Contact provider if diarrhea persists > 3 days

Management of BTKi Toxicity

- Persistent, severe joint pains
  - Stretching exercises
  - Monitor and supplement potassium/magnesium (if indicated)
  - Warm compresses
  - Anecdotal: *Apple cider vinegar* (**not a medical recommendation**, but patients have had good results)
- Atrial fibrillation – obtain baseline cardiac evaluation
  - Beta blockers
  - Monitor and record occurrences
  - If A. fib persists despite β- blockers, **may switch to another agent**.

Neurological Toxicity

- Headaches – primarily seen with Acalabrutinib
  - **Caffeine** – coffee, coke, caffeine tablets (as indicated)
  - Rest as needed and stay hydrated
  - Cold compress to forehead
  - Rule out other causes i.e., allergy related, sinusitis, head trauma, etc.

Changing BTKi(s)

- Persistent A-fib (or other cardiac toxicity)
- Progressive disease on BTKi
- Persistent bleeding

Roundtable Discussion

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Clinical Scenario

A patient with newly diagnosed CLL is about to start treatment with a BTK inhibitor in combination with venetoclax

Considerations for the Treatment of Treatment-Naive CLL

Bita Fakhri, MD, MPH

Assistant Professor

Stanford University School of Medicine

Key Factors in Managing Patients With CLL

Timing of Therapy

- Deciding when to start therapy
  - Many patients discovered incidentally; how to handle the “worried well”
  - Comorbidities and fitness; where the patient is in their life cycle
- Deciding when to stop therapy

Key Prognostic Factors

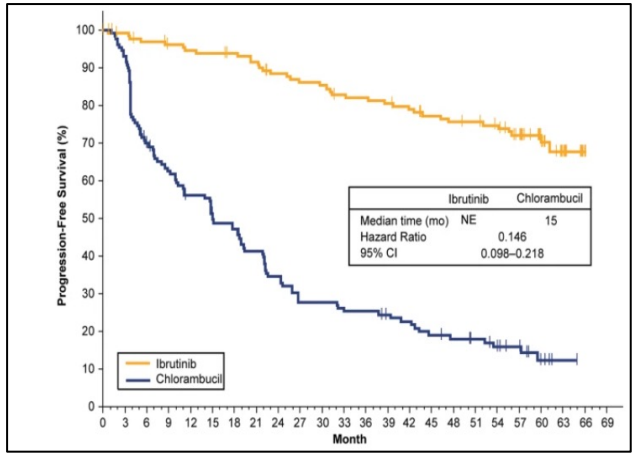
- The importance of FISH, *TP53*, and mutational status of immunoglobulin genes
- How to test for MRD (ie, flow cytometry or molecular methods) and how to use it to guide clinical decision-making

Key Classes of Drugs

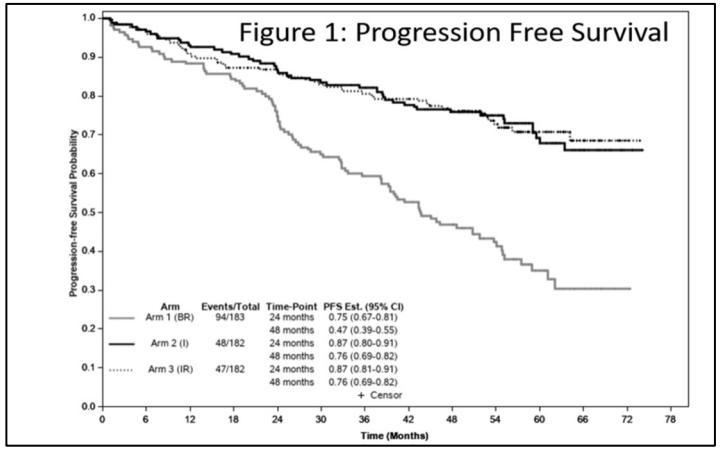
- BTKi (eg, acalabrutinib, zanubrutinib, ibrutinib)
- BCL2i (eg, venetoclax)
- Anti-CD20 antibodies (eg, rituximab, obinutuzumab)
- Chemotherapy/ chemoimmunotherapy (eg, chlorambucil, FCR, BR)

Background: Firstline chemotherapy is inferior to BTKis and Ven/Obi

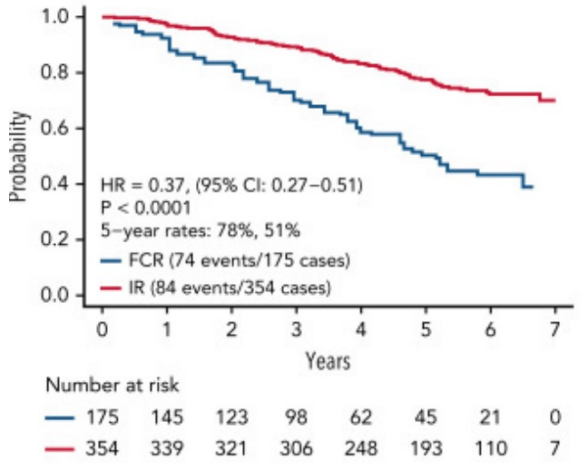
RESONATE 2 (Ibrutinib v Chl)



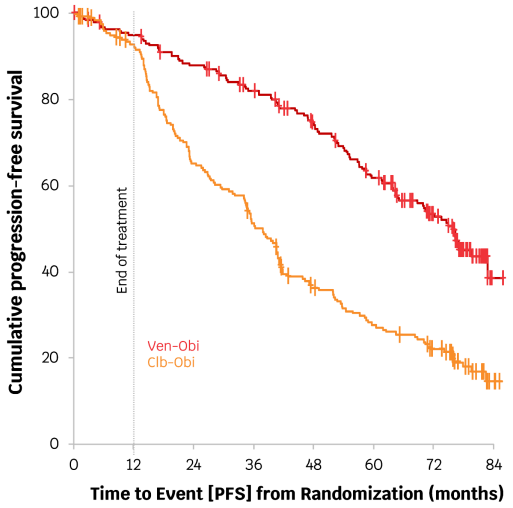
ALLIANCE (Ibrutinib vs Ibrutinib/rituximab v BR)



E1912 (Ibrutinib/Rituximab v FCR)



CLL 14 (Ven-Obi vs Clb-Obi)

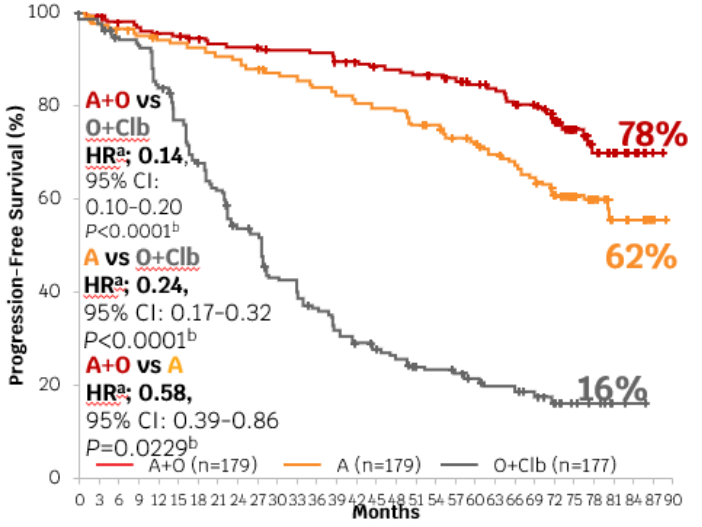


Median PFS
Ven-Obi: 76.2 months
Clb-Obi: 36.4 months

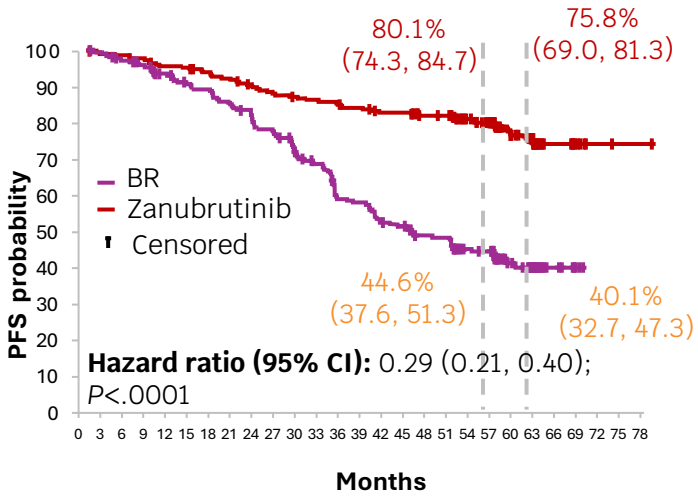
6-year PFS rate
Ven-Obi: 53.1%
Clb-Obi: 21.7%

HR 0.40, 95% CI [0.31-0.52]
P<0.0001

ELEVATE – TN (Acala v Chl-Obin)



SEQUOIA (Zanu v Benda-R)



1. Shanafelt. NEJM. 2019;381:432. 2. Woyach. NEJM. 2018;379:2517.
3. Burger. Leukemia. 2020 34:787

CLL14: 6-Year Follow-Up of Phase 3 Study of Venetoclax + Obinutuzumab vs Chlorambucil + Obinutuzumab – Study Design and Efficacy

Key Eligibility Criteria

- Patients with TN CLL and coexisting medical conditions
- CIRS >6 and/or CrCl <70 mL/min

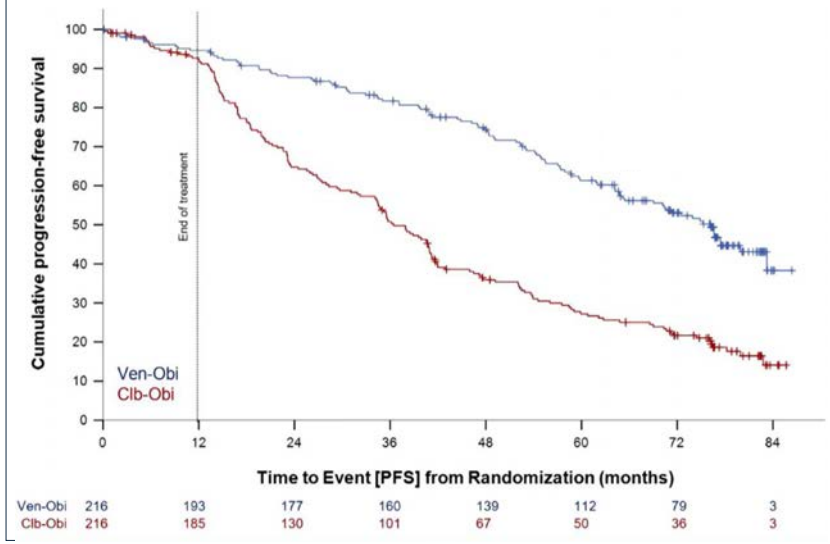
RANDOMIZED 1:1

- Venetoclax-Obinutuzumab (Ven-G) (6 cycles) followed by venetoclax (6 cycles)
- Chlorambucil-Obinutuzumab (Clb-G) (6 cycles) followed by chlorambucil (6 cycles)

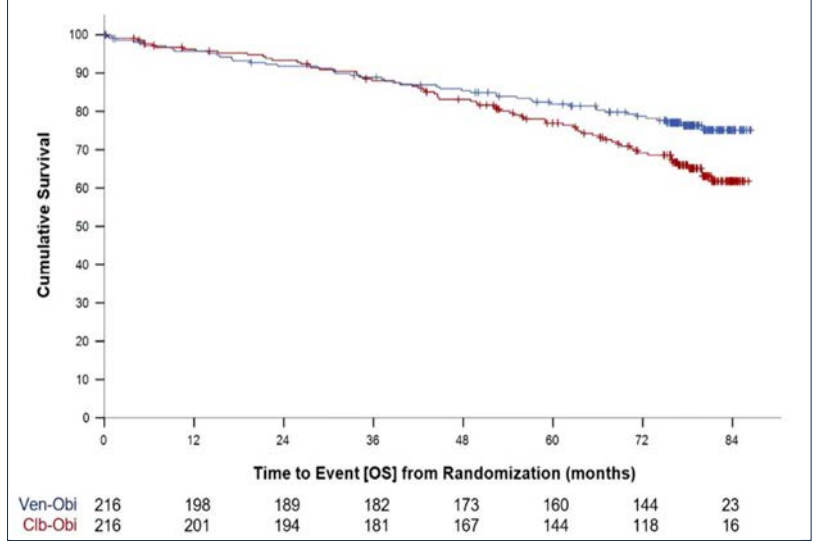
Primary endpoint
- PFS

Secondary endpoints
- Response
- MRD
- OS

PFS



OS



Median Follow-Up: 76.4 mo

Median PFS	6-year PFS rate	Median OS	5-year OS rate
Ven-G: 76.2 months Clb-G: 36.4 months	Ven-G: 53.1% Clb-G: 21.7%	Ven-G: not reached Clb-G: not reached	Ven-G: 78.7% Clb-G: 62.9%
HR 0.40 (95% CI: 0.31-0.52) *P*<0.0001		HR 0.69 (95% CI: 0.48-1.01) *P*=0.052	

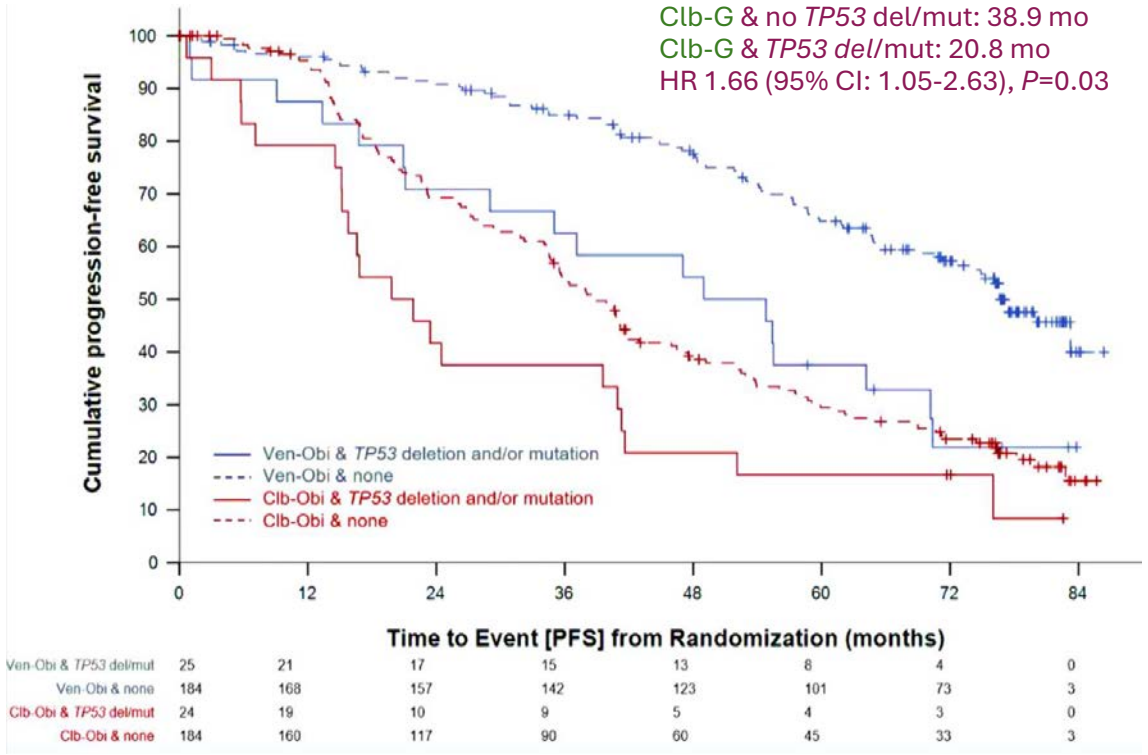
Al-Sawaf O, et al. EHA 2023. Abstract S145.

CLL14: 6-Year Follow-Up of Phase 3 Study of Venetoclax + Obinutuzumab vs Chlorambucil + Obinutuzumab – PFS by Mutational Status

PFS by *TP53* Status

Median PFS
Ven-G & no *TP53* del/mut: 76.6 mo
Ven-G & *TP53* del/mut: 51.9 mo
HR 2.29 (95% CI: 1.27-3.83), *P*=0.001

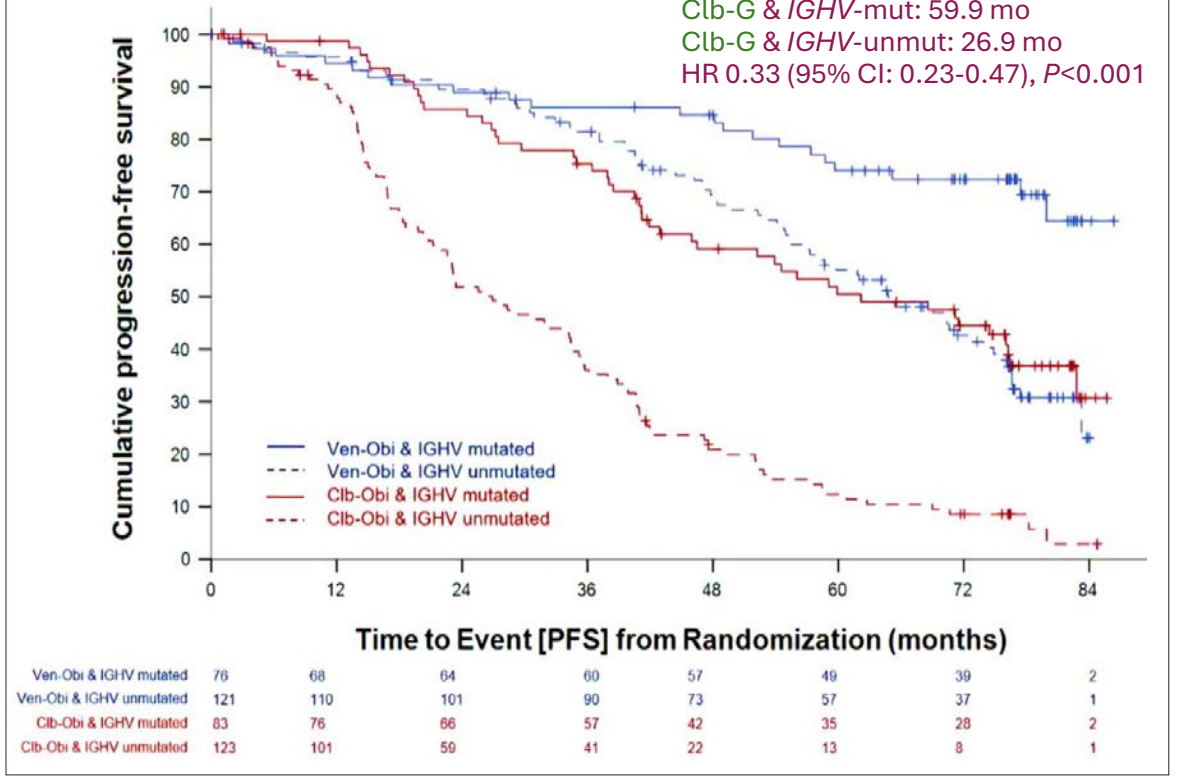
Clb-G & no *TP53* del/mut: 38.9 mo
Clb-G & *TP53 del*/mut: 20.8 mo
HR 1.66 (95% CI: 1.05-2.63), *P*=0.03



PFS by *IGHV* Status

Median PFS
Ven-G & *IGHV*-mut: NR
Ven-G & *IGHV*-unmut: 64.8 mo
HR 0.38 (95% CI: 0.23-0.61), *P*<0.001

Clb-G & *IGHV*-mut: 59.9 mo
Clb-G & *IGHV*-unmut: 26.9 mo
HR 0.33 (95% CI: 0.23-0.47), *P*<0.001



Al-Sawaf O, et al. EHA 2023. Abstract S145.

CLL14: 6-Year Follow-Up of Phase 3 Study of Venetoclax + Obinutuzumab vs Chlorambucil + Obinutuzumab – Safety

Most Frequent Grade ≥3 AEs,%	Ven-G (n=212)		Clb-G (n=214)	
	During treatment	After treatment	During treatment	After treatment
Neutropenia	51.9	3.8	47.2	1.9
Thrombocytopenia	14.2	0.5	15.0	0
Anemia	7.5	1.9	6.1	0.5
Febrile neutropenia	4.2	0.9	3.3	0.5
Leukopenia	2.4	0	4.7	0
Pneumonia	3.8	3.3	3.7	1.4
Infusion-related reaction	9.0	0	9.8	0.5
TLS	1.4	0	3.3	0

Secondary Primary Malignancies (SPM)	Ven-G (n=212)	Clb-G (n=214)
Overall total number of events,[a] n	31	20
Number of pts with ≥1 SPM, n (%)	30 (14.2)	18 (8.4)
Melanoma	8 (3.8)	4 (1.9)
Solid organ tumors	17 (8.0)	11 (5.1)
Hematological malignancies	3 (1.4)	2 (0.9)
Other	2 (0.9)	1 (0.5)

[a] Excluding non-melanoma skin cancers.

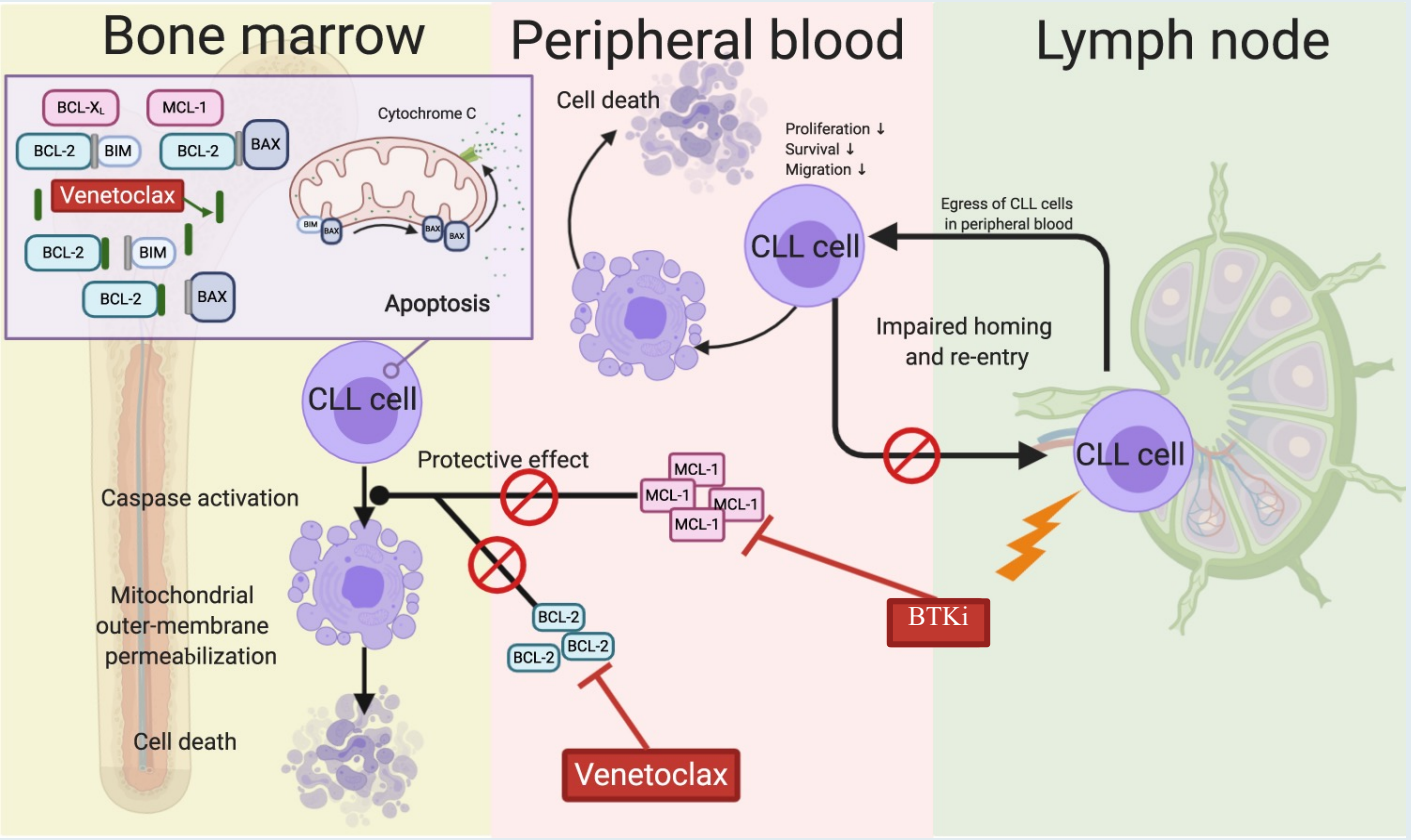
Al-Sawaf O, et al. EHA 2023. Abstract S145.

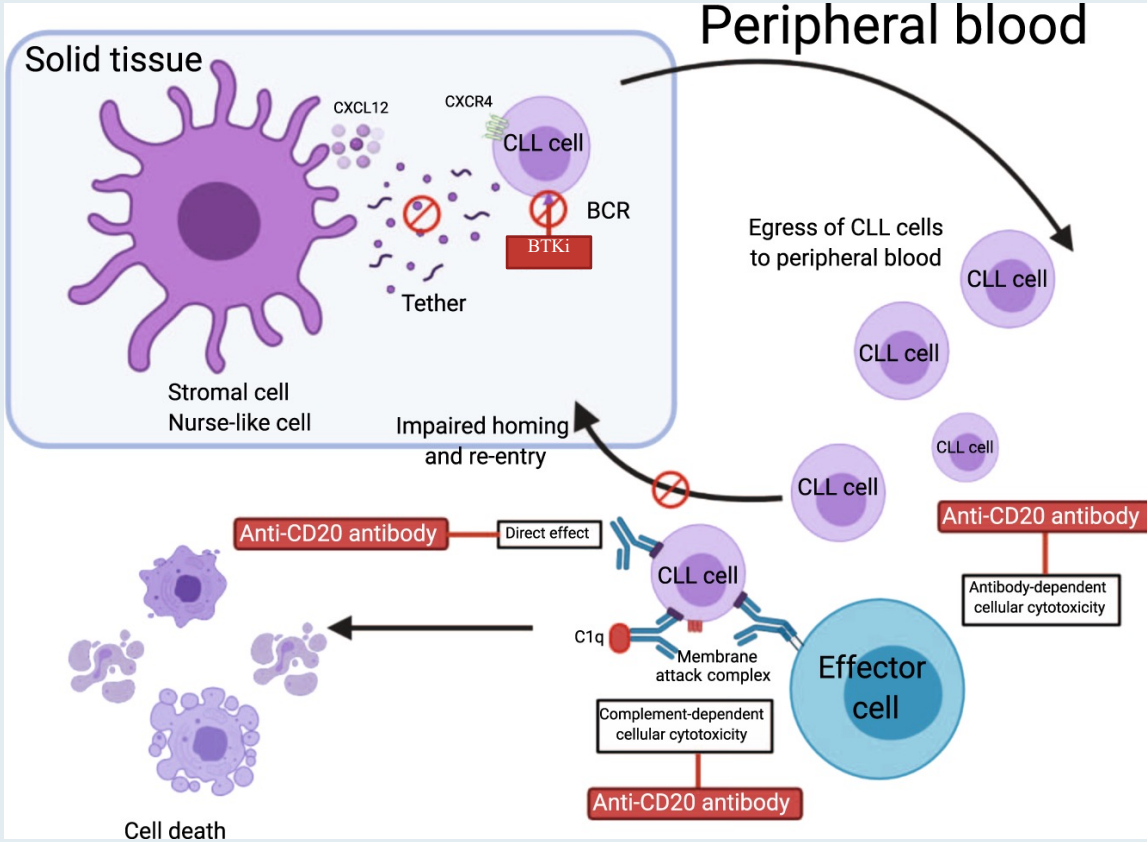
Patient Case 1: 56-year-old Male with CLL

- 56-year-old male with CLL diagnosed 2 years ago (trisomy 12, unmutated IGHV) presents with 10% weight loss in six months, drenching night sweats and CBC showing continued decline in hemoglobin (10.2 – hemolysis labs negative) and platelet count of 73K. He currently experiences excessive fatigue to a level that has interfered with his activities of daily living.

- No other comorbidities. He travels frequently and is interested in time-limited all-oral therapy.

Combining Therapies: Rationale for Bruton Tyrosine Kinase Inhibitor (BTKi) and Venetoclax with or without Anti-CD20 Therapy





Timofeeva N, Gandhi V. *Blood Cancer J* 2021 April 29;11(4):79.

Combination cBTKi and BCL2i therapy in 1L CLL? AMPLIFY

AMPLIFY

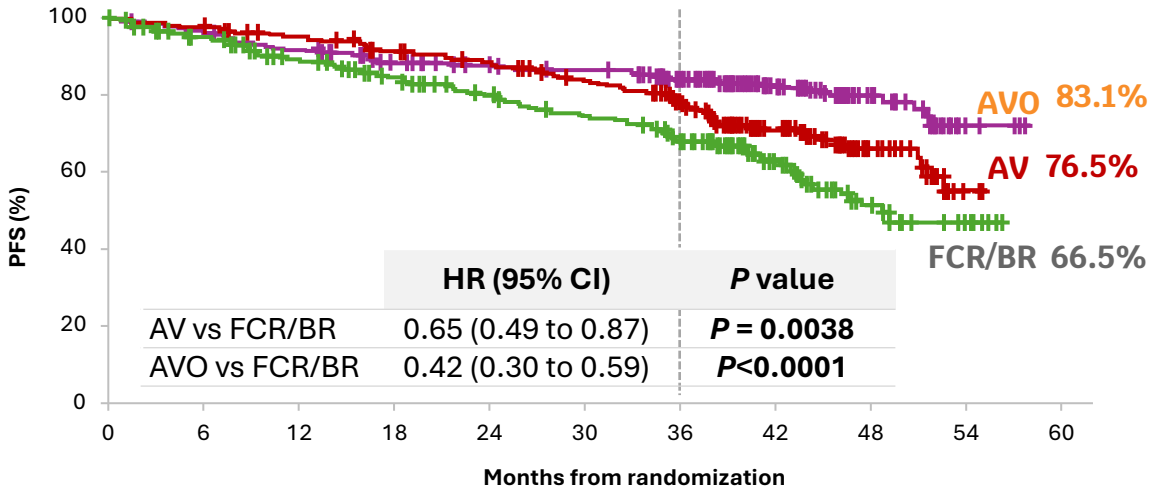
Treatment-naive CLL
- Age ≥ 18y/o
- ECOG: 0–2
- Active disease per IWCLL 2018 criteria

Exclusion
- del(17p), TP53

RANDOMIZE 1:1:1

- **Acalabrutinib + Venetoclax**
- **Acalabrutinib + Venetoclax + Obinutuzumab**
- **Chemo/IO (FCR or BR)**

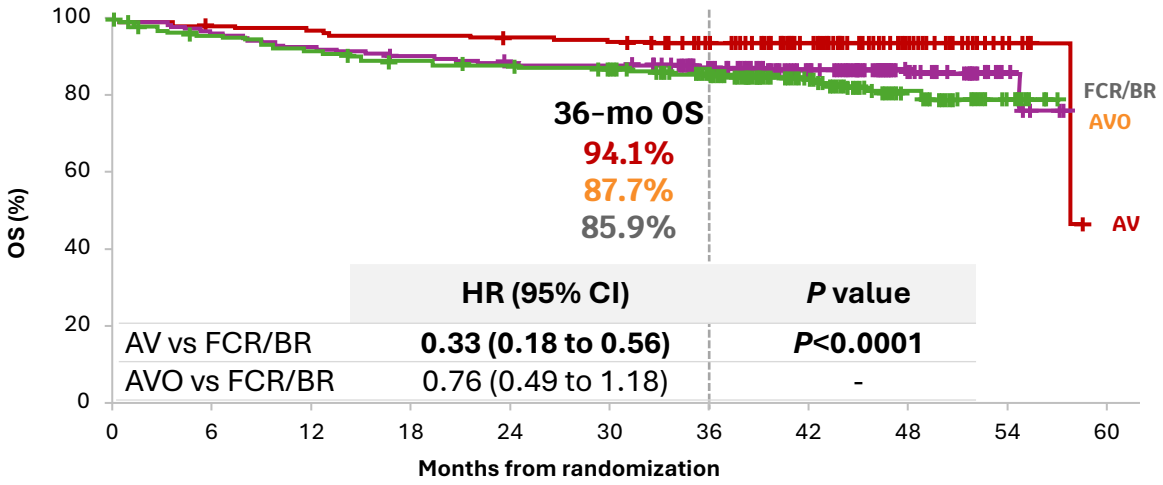
Primary endpoint: PFS (assessed by IRC)



	HR (95% CI)	*P* value
AV vs FCR/BR	0.65 (0.49 to 0.87)	***P* = 0.0038**
AVO vs FCR/BR	0.42 (0.30 to 0.59)	***P*<0.0001**

Patients at Risk

AV	291	282	269	251	237	219	177	102	35	3	0
AVO	286	272	258	237	225	219	191	116	51	7	0
FCR/BR	290	236	208	189	170	154	127	66	28	6	0



	HR (95% CI)	*P* value
AV vs FCR/BR	**0.33 (0.18 to 0.56)**	***P*<0.0001**
AVO vs FCR/BR	0.76 (0.49 to 1.18)	-

Patients at Risk

AV	291	286	281	277	275	270	233	142	58	10	0
AVO	286	276	265	257	252	250	223	143	64	10	0
FCR/BR	290	247	236	228	223	217	182	98	45	13	0

Median PFS was NR for AV and AVO, and was 47.6 mo for FCR/BR

Brown et. al. Fixed-Duration Acalabrutinib Plus Venetoclax with or without Obinutuzumab Versus Chemoimmunotherapy for First-Line Treatment of Chronic Lymphocytic Leukemia: Interim Analysis of the Multicenter, Open-Label, Randomized, Phase 3 AMPLIFY Trial. ASH 2024; abstract 1009.

AMPLIFY: AEs of Clinical Interest

	AV (n=291)		AVO (n=284)		FCR/BR (n=259)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any ECI	222 (76.3)	136 (46.7)	242 (85.2)	188 (66.2)	185 (71.4)	141 (54.4)
Cardiac events	27 (9.3)	5 (1.7)	34 (12.0)	7 (2.5)	9 (3.5)	3 (1.2)
Atrial fibrillation	2 (0.7)	1 (0.3)	6 (2.1)	2 (0.7)	2 (0.8)	2 (0.8)
Ventricular tachyarrhythmias[a]	2 (0.7)	0	3 (1.1)	0	0	0
Hypertension	12 (4.1)	8 (2.7)	11 (3.9)	6 (2.1)	7 (2.7)	2 (0.8)
Hemorrhage	94 (32.3)	3 (1.0)	86 (30.3)	6 (2.1)	11 (4.2)	1 (0.4)
Major hemorrhage	3 (1.0)	3 (1.0)	8 (2.8)	6 (2.1)	2 (0.8)	1 (0.4)
Neutropenia (any)[b]	108 (37.1)	94 (32.3)	143 (50.4)	131 (46.1)	132 (51.0)	112 (43.2)
Infections (any)	148 (50.9)	36 (12.4)	153 (53.9)	67 (23.6)	82 (31.7)	26 (10.0)
Second primary malignancies	15 (5.2)	5 (1.7)	12 (4.2)	5 (1.8)	2 (0.8)	0
Excl. non-melanoma skin	8 (2.7)	5 (1.7)	7 (2.5)	4 (1.4)	1 (0.4)	0
Tumor lysis syndrome	1 (0.3)	1 (0.3)	1 (0.4)	1 (0.4)	8 (3.1)	8 (3.1)

Brown et. al. Fixed-Duration Acalabrutinib Plus Venetoclax with or without Obinutuzumab Versus Chemoimmunotherapy for First-Line Treatment of Chronic Lymphocytic Leukemia: Interim Analysis of the Multicenter, Open-Label, Randomized, Phase 3 AMPLIFY Trial. ASH 2024; abstract 1009.

Comparison among Three Arms

	A+V	AVO	FCR/BR
3-year PFS	76%	83%	66%
ORR	93%	93%	75%
Covid-19 deaths	10	25	21
All deaths	18	37	42

Brown et. al. Fixed-Duration Acalabrutinib Plus Venetoclax with or without Obinutuzumab Versus Chemoimmunotherapy for First-Line Treatment of Chronic Lymphocytic Leukemia: Interim Analysis of the Multicenter, Open-Label, Randomized, Phase 3 AMPLIFY Trial. ASH 2024; abstract 1009.

Key Conclusions from Amplify

- Most likely AV will be FDA approved in the frontline setting.
- Will FDA approve AVO based on mortality data??
- Is AV better than OV? Majic trial will answer the question.

Future Directions in Upfront Therapy

- Celestial-TN: OV vs Zanubrutinib and sonrotoclax
- Majic trial: MRD-guided duration of therapy with OV vs AV

Roundtable Discussion

RTP
RESEARCH
TO PRACTICE

Nursing Considerations for Patients Receiving Time-Limited Up-Front Treatment

Corinne Hoffman, MS, APRN-CNP, AOCNP

Venetoclax + Obinutuzumab

- Venetoclax:
  - BCL-2 inhibitor
  - Oral tablet
- Obinutuzumab:
  - Anti-CD20 antibody
  - Intravenous infusion
- Duration of therapy: 1 year
  - Obinutuzumab, administered every 4 weeks, with the exception of the first cycle, for six cycles
  - Venetoclax, 5-week dose ramp up followed by 400 mg daily through cycle 12

Venetoclax package insert, 7/2024

Venetoclax Dose Escalation

Week	Venetoclax Daily Dose
1	20 mg
2	50 mg
3	100 mg
4	200 mg
5 and beyond	400 mg

Venetoclax package insert, 7/2024

Venetoclax: Preparing to Start

- Assess TLS risk
  - Determine if inpatient or outpatient escalation
- Hydration
- Allopurinol
- Consult with pharmacy, screen for medication interactions
  - CYP3A interactions – Avoid strong and moderate inhibitors and inducers and determine if dose adjustments are needed

Venetoclax package insert, 7/2024

Assessing TLS Risk

Low

Lymph Nodes < 5 cm

AND

ALC <25 x 10^9/L

Outpatient

Medium

Lymph Nodes 5 cm to < 10 cm

OR

ALC ≥ 25 x 10^9/L

Outpatient

High

Lymph Nodes ≥10 cm

OR

ALC ≥ 25 x 10^9/L and LN ≥ 5 cm

Inpatient for at least first two dose escalations

Venetoclax package insert, 7/2024

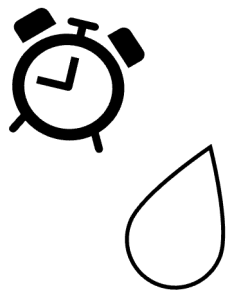
Venetoclax: Preparing to Start

- Other factors that may impact in what setting medication is initiated:
  - Tolerability of oral hydration
  - Baseline renal function
  - Baseline chemistry labs

Venetoclax package insert, 7/2024

Patient Education: Venetoclax + Obinutuzumab

- Risk for infusion reaction (obinutuzumab)
  - Pre-medications
- Tumor Lysis Syndrome
  - Explain rationale for 5-week dose ramp up
  - Pre-dose labs, 6-8 hour and 24-hour post dose labs
  - Stress importance of hydration
  - Confirm patient is taking allopurinol or other antihyperuricemic



Patient Education: Venetoclax + Obinutuzumab

- Diarrhea
  - Loperamide as needed
  - Grade severity, # stools/day
- Nausea
  - Antiemetic as needed
- Neutropenia
  - G-CSF support
  - Dose interruption or reduction needed?
- Fatigue
- Infection
- Thrombocytopenia

Venetoclax package insert, 7/2024

Patient Education: BTKi + Venetoclax

- Discuss with patient the common of side effects of both BTKis and venetoclax
- Potential for increased toxicities than with either agent alone but overall well tolerated
- Neutropenia/infections
  - Consider more frequent lab monitoring
  - Consider prophylaxis
- Potential for hold or dose reduction of one or both medications

Patient Case: BTKi + Venetoclax

- 58 year-old female
- Treatment is recommended for her CLL due to progressive anemia and thrombocytopenia
- Patient desires time-limited therapy
- Has not historically been on many prescription medications and is anxious about starting therapy
- Feels she can cope better knowing that treatment has an “end in sight”
- Chooses an all oral approach with acalabrutinib + venetoclax over venetoclax + obinutuzumab (IV)
- Patient is a caregiver for her mom who also has frequent medical appointments for a cancer diagnosis
- Outside of the venetoclax ramp-up period, likes how this regimen will allow for shorter visits and potentially some more scheduling flexibility

Roundtable Discussion

RTP
RESEARCH
TO PRACTICE

Agenda

Introduction: Key Factors in the Management Patients with Chronic Lymphocytic Leukemia (CLL)

Module 1: Role of Covalent Bruton Tyrosine Kinase (BTK) Inhibitors for Newly Diagnosed CLL

Module 2: Role of Time-Limited Up-Front Treatment, Including Therapy Combining BTK Inhibitors and Venetoclax, for Newly Diagnosed CLL

Module 3: Role of Pirtobrutinib for Relapsed/Refractory (R/R) CLL

Module 4: CAR (Chimeric Antigen Receptor) T-Cell Therapy for R/R CLL

Clinical Scenario

A patient with CLL has experienced disease progression on a covalent BTK inhibitor and venetoclax and is about to start treatment with pirtobrutinib

Pirtobrutinib Data Review

Bita Fakhri, MD, MPH

Assistant Professor

Stanford University School of Medicine

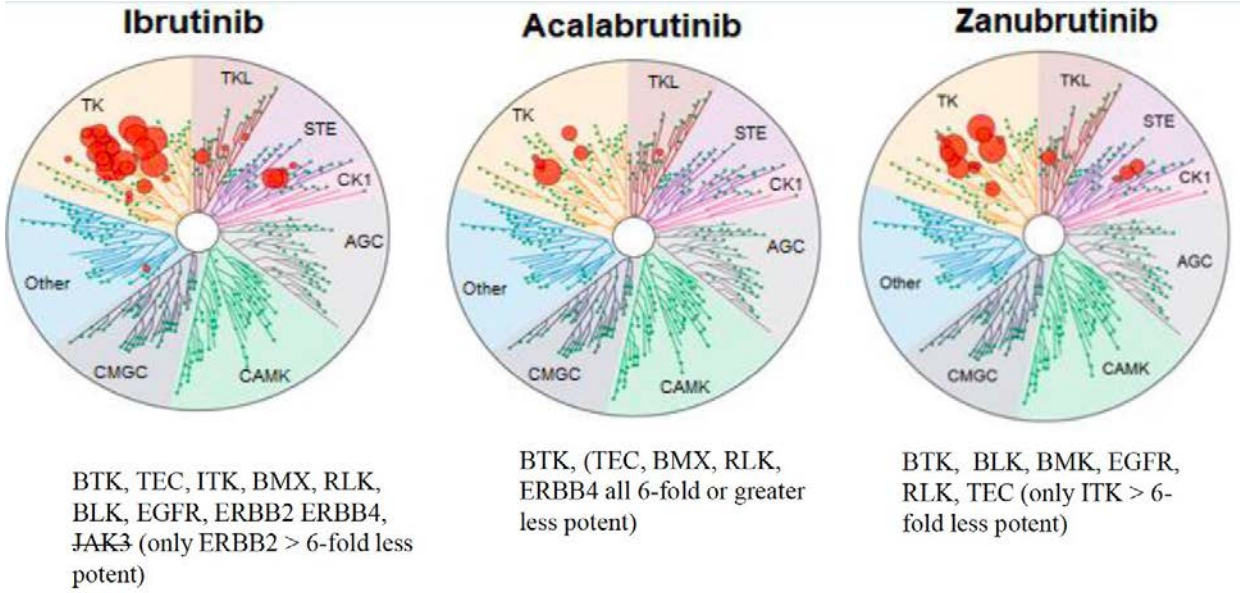
Patient Case 2: 66 year old Male with CLL

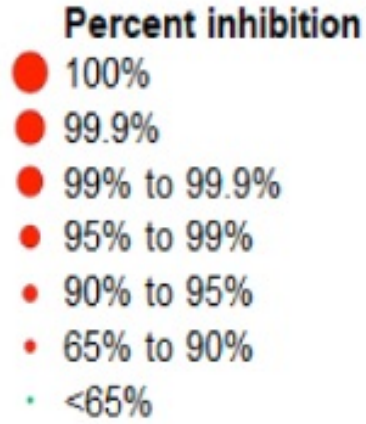
- 66 year old male diagnosed with CLL in 2019 after being admitted with significant abdominal pain due to retroperitoneal lymphadenopathy. FISH: del(17p) and mutated IGHV.
- 2019 OV → median PFS 3.5 years with rapidly progressive lymphadenopathy.
- 2022-2025 → acalabrutinib with recent cervical lymphadenopathy.
- Now at 72 years of age, he is interested in oral therapy.

Irreversible and Reversible BTK Inhibitors for CLL

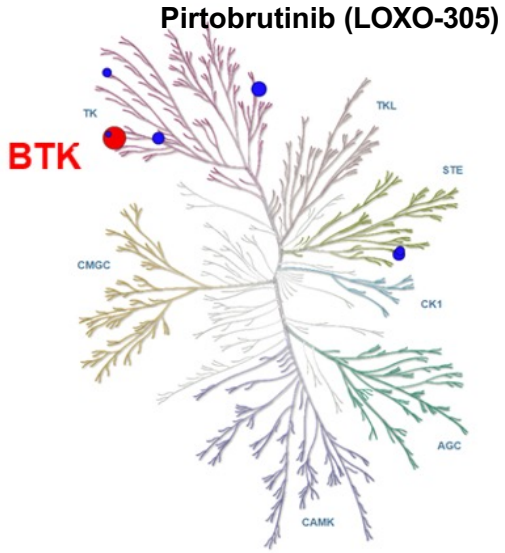
BTK inhibitor	Binding	T1/2 (hours)	IC50 (nM)	Dosing
Ibrutinib	Covalent irreversible C481	4-8	0.5	420 mg
Acalabrutinib	Covalent irreversible C481	0.9	5.1	100 mg BID
Zanubrutinib	Covalent irreversible C481	2-4	0.5	160 or 320 mg BID
Pirtobrutinib	Noncovalent reversible	Not available	0.85	200 mg

Irreversible





Reversible



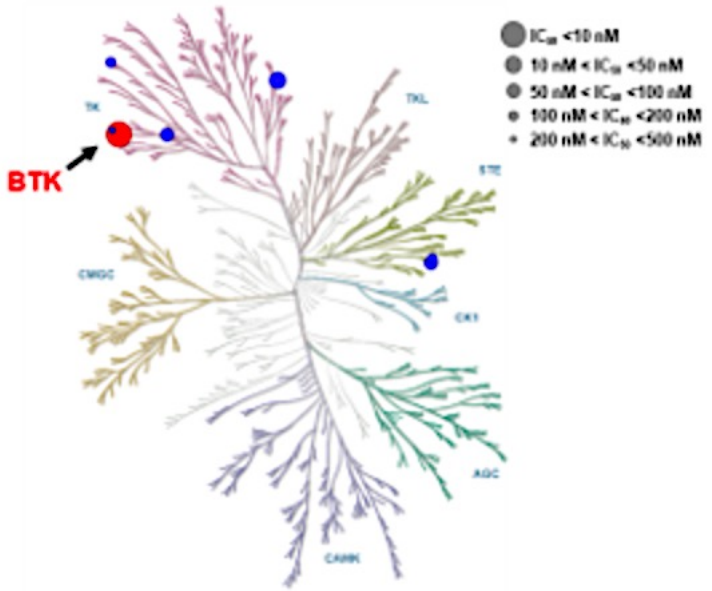
BID = twice a day

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

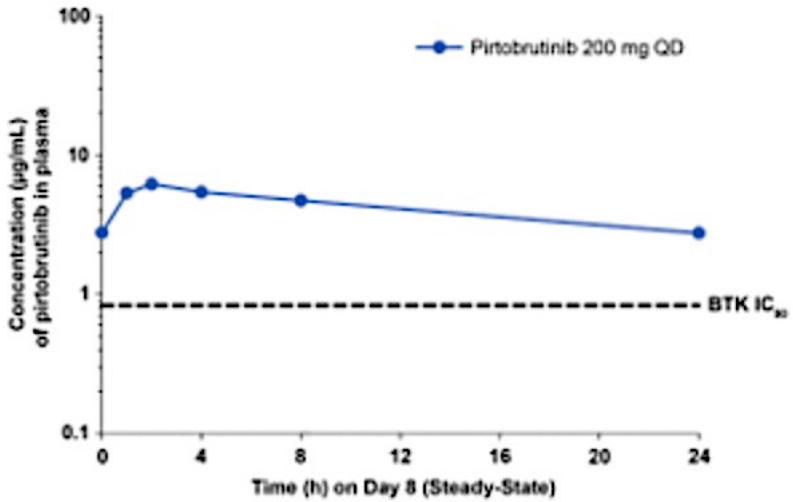
RTP RESEARCH TO PRACTICE

Pirtobrutinib is a Highly Selective, Non-Covalent (Reversible) BTK Inhibitor

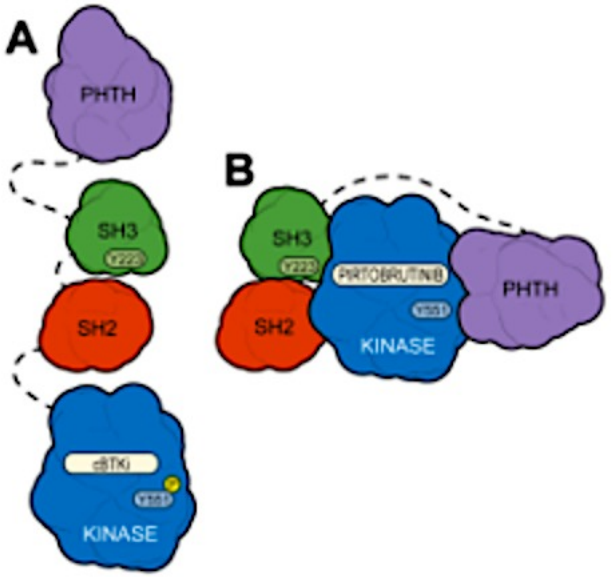
Highly selective for BTK[5,6]



Plasma exposures exceeded BTK IC_{90} throughout dosing interval



Pirtobrutinib may stabilize/maintain BTK in a closed inactive conformation[7]



- Inhibits both WT and C481-mutant BTK with equal low nM potency[7]
- Steady state plasma exposure corresponding to 96% BTK target inhibition and a half-life of about 20 hours[7]
- In contrast to cBTKi (A), pirtobrutinib (B) appears to stabilize BTK in a closed, inactive conformation, blocking access to upstream kinases and phosphorylation of Y551, thus inhibiting scaffolding interactions that support kinase-independent BTK signaling[7]

Woyach et al; ASH 2023

Pirtobrutinib currently approved post cBTKi and BCL2i based on BRUIN

BRUIN Phase 1/2 Study Design

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

Phase 1 Escalation + Expansion (25 to 300 mg QD) Phase 2 (200 mg QD)
N=778

- **MCL** n=166
- **CLL/SLL** n=317
- **Other[a]** n=295

Under CLL/SLL:

- **BTKi Naïve** n=35
- **Prior cBTKi** n=282

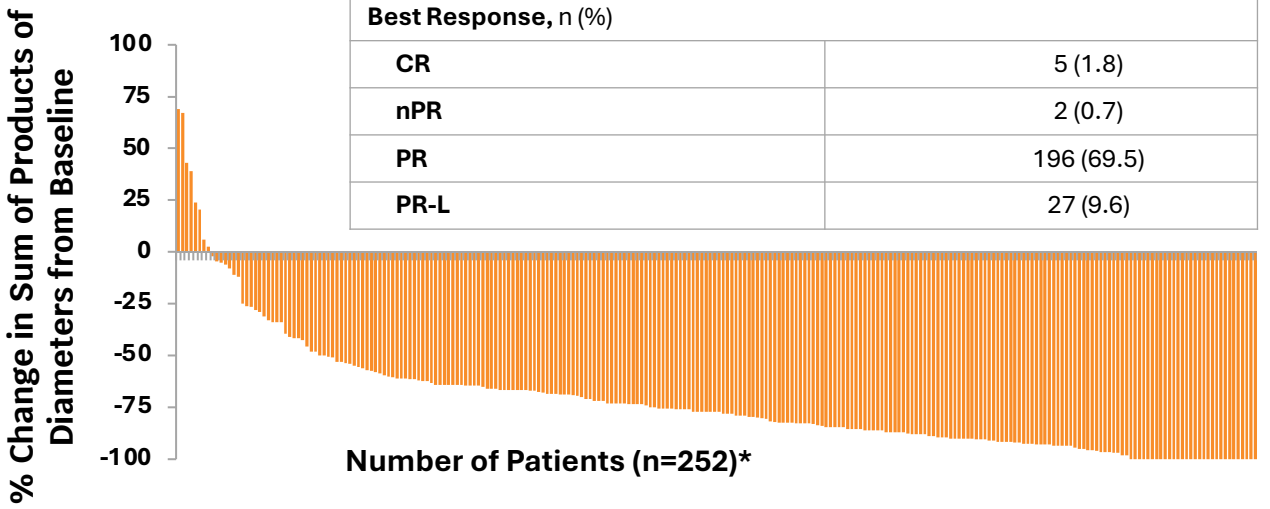
Under Prior cBTKi:

- **No Prior BCL2i (Naïve: BCL2i-N)** n=154
- **Prior BCL2i (Exposed: BCL2i-E)** n=128

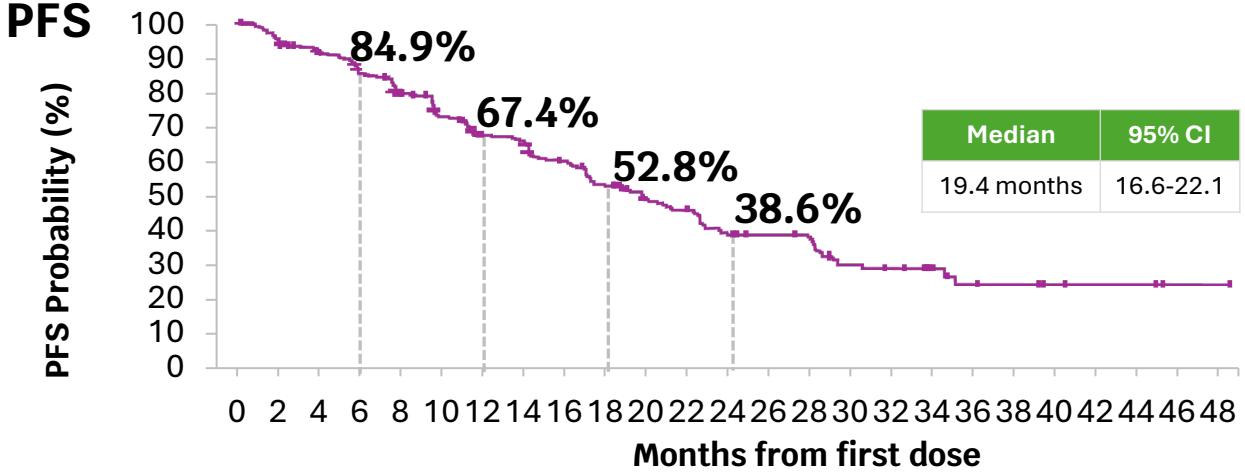
Key endpoints: Safety/tolerability, Determine MTD and RP2D, Pharmacokinetics, Efficacy (ORR according to iwCLL 2018 criteria, DoR, PFS, and OS)

ORR

Prior cBTKi	n=282[b]
ORR[a] incl. PR-L, %(95% CI)	81.6 (76.5-85.9)
Best Response, n (%)	
CR	5 (1.8)
nPR	2 (0.7)
PR	196 (69.5)
PR-L	27 (9.6)



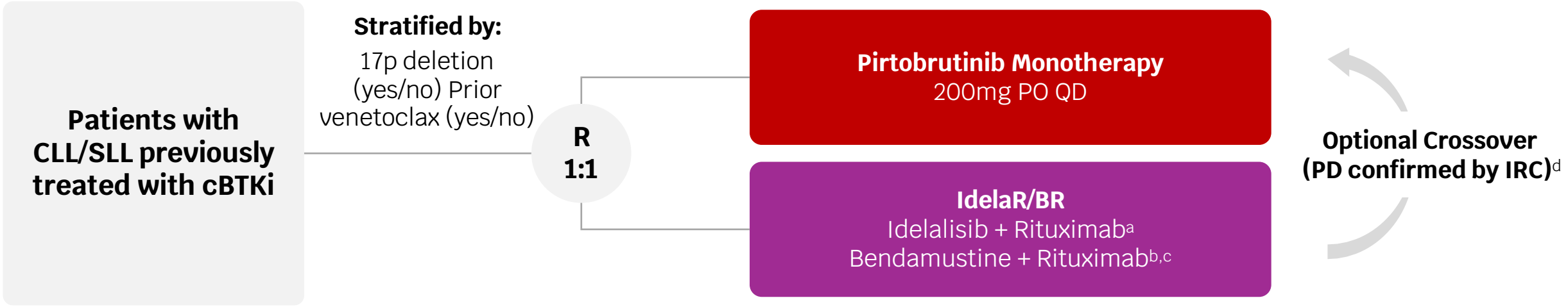
PFS



Median	95% CI
19.4 months	16.6-22.1

Woyach et. al., Pirtobrutinib in Post-cBTKi CLL/SLL: ~30 Months Follow-up and Subgroup Analysis With/Without Prior BCL2i from the Phase 1/2 BRUIN Study. ASH 2023 Oral Presentation

BRUIN CLL-321 Study Design



Key Eligibility

- Age ≥18
- ECOG PS 0–2
- Confirmed CLL/SLL requiring treatment per iwCLL 2018
- **Prior cBTKi required**
- **No limit on prior lines of therapy**
- **Prior history of atrial fibrillation allowed**

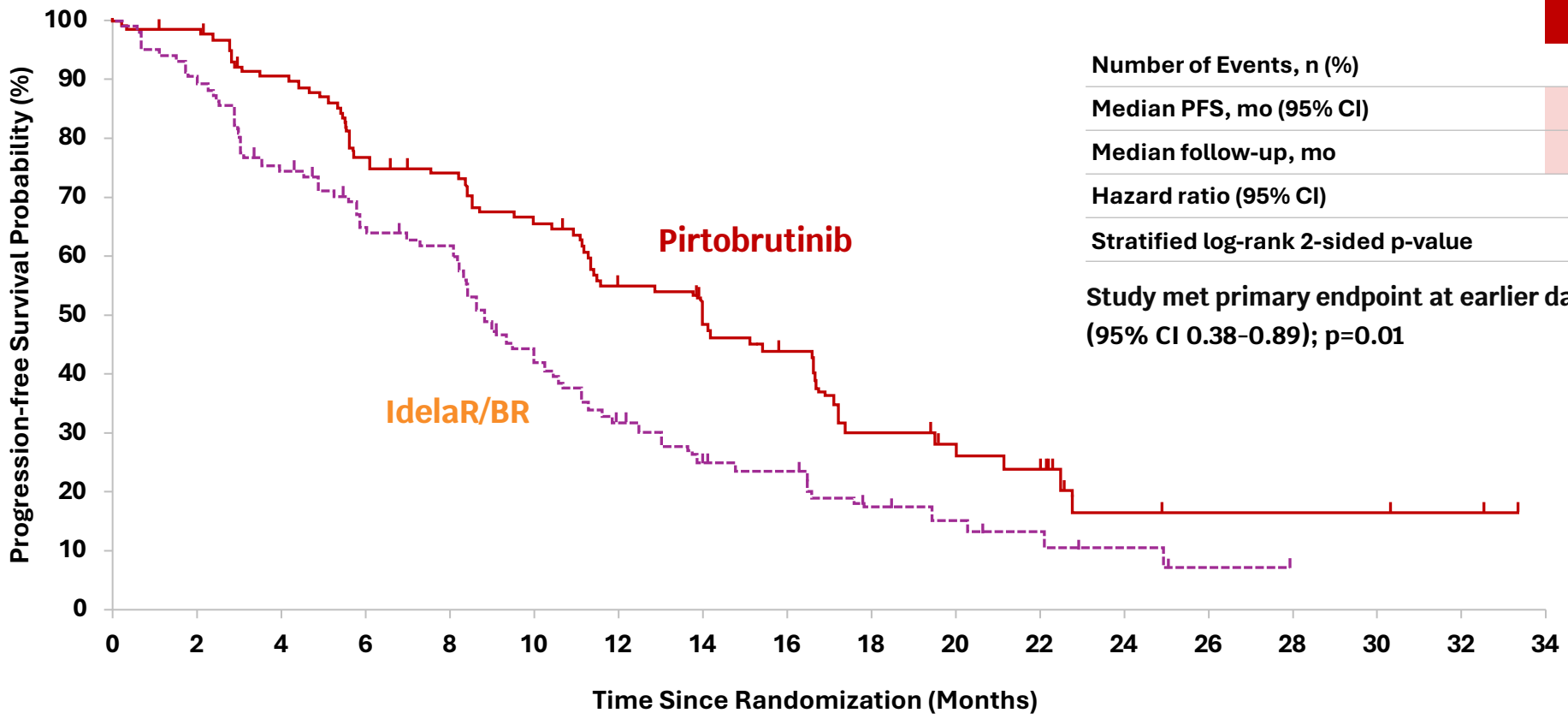
Key Endpoints

- **Primary Endpoint: PFS assessed by IRC**
- PFS assessed by investigator
- Event-Free Survival
- Time to Next Treatment
- Overall survival
- Safety

Treatment was given in 28-day cycles. PFS assessed based on iwCLL2018. [a]Idelalisib dosed at 150mg PO BID. Day 1 of cycle 1, first dose of rituximab at 375 mg/m^2, next 4 infusions at 500 mg/m^2 every 2 weeks, next 3 infusions at 500 mg/m^2 every 4 weeks. [b]Bendamustine (70 mg/m^2) administered IV D1, D2 of cycles 1–6. [c]Day 1 of cycle 1, first dose of rituximab at 375 mg/m^2, next 5 infusions day 1 of cycle 2 through cycle 6 at 500 mg/m^2. [d]Eligible patients receiving investigator's choice of IdelaR/BR could crossover to receive pirtobrutinib monotherapy upon confirmation of PD by IRC per protocol. Abbreviations: BID, twice daily; BR, bendamustine + rituximab; cBTKi, covalent Bruton tyrosine kinase inhibitor; CLL, chronic lymphocytic leukemia; ECOG PS, Eastern Cooperative Oncology Group Performance Status; IdelaR, idelalisib + rituximab; IRC, Independent Review Committee; iwCLL, international workshop on chronic lymphocytic leukemia; mg, milligram; PD, progressive disease; PFS, progression-free survival; PO, by mouth; QD, once daily; R, randomized; SLL, small lymphocytic lymphoma.

Sharman et. al. ASH 2024. Abstract 886.

BRUIN CLL-321: IRC-Assessed Progression-free Survival



	Pirtobrutinib n=119	IdelaR/BR n=119
Number of Events, n (%)	74 (62)	79 (66)
Median PFS, mo (95% CI)	**14.0** (11.2-16.6)	**8.7** (8.1-10.4)
Median follow-up, mo	19.4	17.7
Hazard ratio (95% CI)	**0.54 (0.39-0.75)**	
Stratified log-rank 2-sided p-value	0.0002*	

Study met primary endpoint at earlier data cut (Aug 2023) IRC HR=0.58 (95% CI 0.38-0.89); p=0.01

Pirtobrutinib reduced risk of progression or death by 46% according to IRC assessment

Number at risk

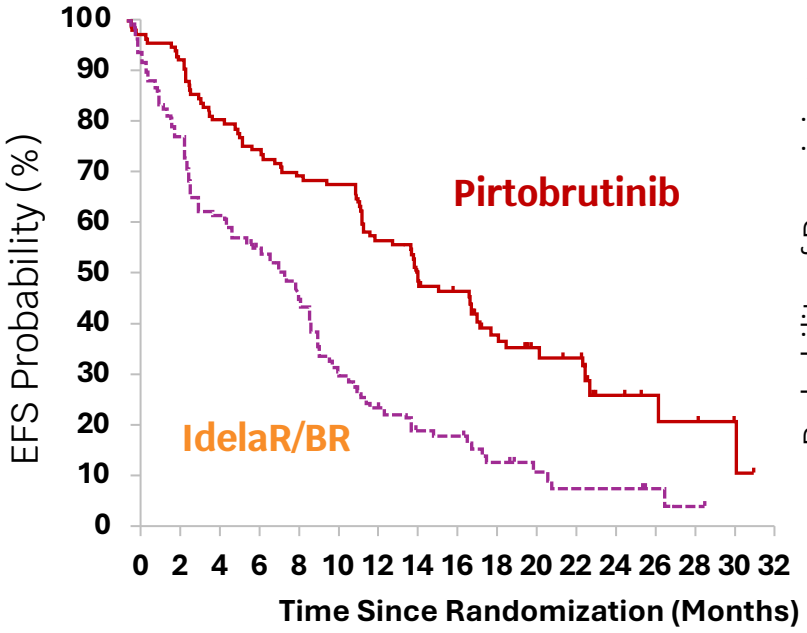
Pirtobrutinib	119	113	100	84	79	69	54	44	36	19	12	10	4	3	3	3	2	0
IdelaR/BR	119	92	73	60	57	37	25	18	16	10	7	5	3	1	0	0	0	0

*nominal p-value. Abbreviations: BR, bendamustine + rituximab; CI, confidence interval; HR, hazard ratio (pirtobrutinib vs. IdelaR/BR); IdelaR, idelalisib + rituximab; IRC, Independent Review Committee; mo, months; PFS, progression-free survival.

Sharman et. al. ASH 2024. Abstract 886.

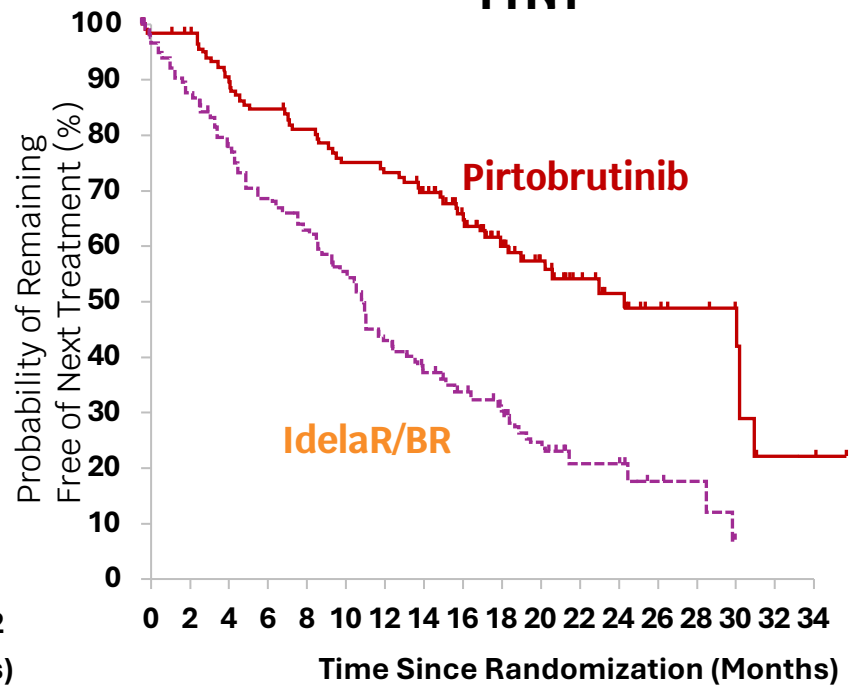
BRUIN CLL-321: Key Secondary Endpoints

EFS



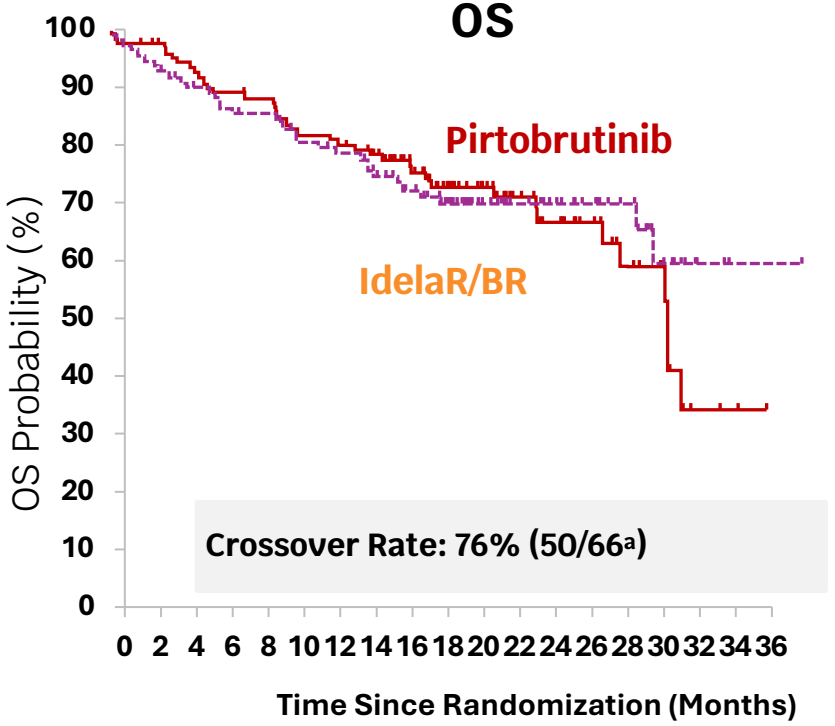
	Pirtobrutinib n=119	IdelaR/BR n=119
Number of Events, n (%)	77 (65)	94 (79)
m EFS, mo (95% CI)	**14.1** (11.4-17.0)	**7.6** (4.8-8.8)
mfollow-up, mo	19.4	18.7
Hazard ratio (95% CI)	**0.39 (0.28-0.53)**	
Stratified log-rank 2-sided p-value	<0.0001*	

TTNT



	Pirtobrutinib n=119	IdelaR/BR n=119
Number of Events, n (%)	54 (45)	82 (69)
mTTNT, mo (95% CI)	**24.0** (17.8-29.7)	**10.9** (8.7-12.5)
mfollow-up, mo	20.0	20.2
Hazard ratio (95% CI)	**0.37 (0.25-0.52)**	
Stratified log-rank 2-sided p-value	<0.0001*	

OS



	Pirtobrutinib n=119	IdelaR/BR n=119
Number of Events, n (%)	38 (32)	32 (27)
18-mo OS rate, % (95% CI)	**73.4** (63.9-80.7)	**70.8** (60.9-78.7)
mfollow-up, mo	20.4	19.2
Hazard ratio (95% CI)	**1.09 (0.68-1.75)**	
Stratified log-rank 2-sided p-value	0.7202	

Sharman et. al. ASH 2024. Abstract 886.

Adverse Events of Interest for Pirtobrutinib

Adverse Events of Interest[a] (AEI)	Pirtobrutinib (n=116)	
	Any grade n (%)	Grade 3+ n (%)
Bleeding	25 (21.6)	4 (3.4)
Bruising	9 (7.8)	1 (0.9)
Petechiae and purpura	6 (5.2)	1 (0.9)
Hemorrhage	18 (15.5)	3 (2.6)
Anemia	24 (20.7)	13 (11.2)
Neutropenia	31 (26.7)	24 (20.7)
Thrombocytopenia	11 (9.5)	9 (7.8)
Infection	74 (63.8)	34 (29.3)
Infection without Covid-19	67 (57.8)	30 (25.9)
Atrial fibrillation and atrial flutter	3 (2.6)[a]	2 (1.7)
Hypertension	8 (6.9)	3 (2.6)

[a]2 of 3 patients with atrial fibrillation had a past medical history of atrial fibrillation
[a]Treatment-emergent adverse events. [5]Mato et al.NEJM 2023;389:33-44.

Sharman et. al. ASH 2024. Abstract 886.

Pirtobrutinib Clinical Development Plan in CLL

Previously Treated CLL/SLL or NHL	Previously Treated CLL/SLL	BTKi-Naïve CLL/SLL
Phase 1/2: BRUIN **Previously Treated CLL/SLL or NHL** **Pirtobrutinib Monotherapy (Ph 1/2)** **Pirtobrutinib + Venetoclax +/- Rituximab (Ph 1b)** • Estimated Enrollment: 860 • Identifier: NCT03740529	**Phase 3: BRUIN CLL-321** **Previously Treated (must include BTKi) CLL/SLL** **Pirtobrutinib vs. Investigator's Choice of Idelalisib + Rituximab or Bendamustine + Rituximab (Optional Crossover)** • Estimated Enrollment: 250 • Identifier: NCT04666038	**Phase 3: BRUIN CLL-313** **Previously Untreated CLL/SLL** **Pirtobrutinib vs. Bendamustine + Rituximab (Optional Crossover)** • Estimated Enrollment: 250 • Identifier: NCT05023980
	Phase 3: BRUIN CLL-322 **Previously Treated (may include BTKi) CLL/SLL** **Fixed Duration Pirtobrutinib + Venetoclax + Rituximab vs. Venetoclax + Rituximab** • Estimated Enrollment: 600 • Identifier: NCT04965493	**Phase 3: BRUIN CLL-314** **Previously Untreated or Previously Treated (non-BTKi) CLL/SLL** **Pirtobrutinib vs. Ibrutinib** • Estimated Enrollment: 650 • Identifier: NCT05254743

BTKi=Bruton tyrosine kinase inhibitor; CLL=chronic lymphocytic leukemia; NHL=non-Hodgkin lymphoma; Ph=phase; SLL= small lymphocytic lymphoma.

1. ClinicalTrials.gov identifier: NCT03740529. https://www.clinicaltrials.gov/ct2/show/NCT03740529.
2. ClinicalTrials.gov identifier: NCT04666038. https://www.clinicaltrials.gov/ct2/show/NCT04666038.
3. ClinicalTrials.gov identifier: NCT04965493. https://www.clinicaltrials.gov/ct2/show/NCT04965493.
4. ClinicalTrials.gov identifier: NCT04662255. https://www.clinicaltrials.gov/ct2/show/NCT04662255.
5. ClinicalTrials.gov identifier: NCT05023980. https://www.clinicaltrials.gov/ct2/show/NCT05023980.
6. ClinicalTrials.gov identifier: NCT05254743. https://www.clinicaltrials.gov/ct2/show/NCT05254743.

Roundtable Discussion

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Nursing Considerations for Patients Receiving Pirtobrutinib

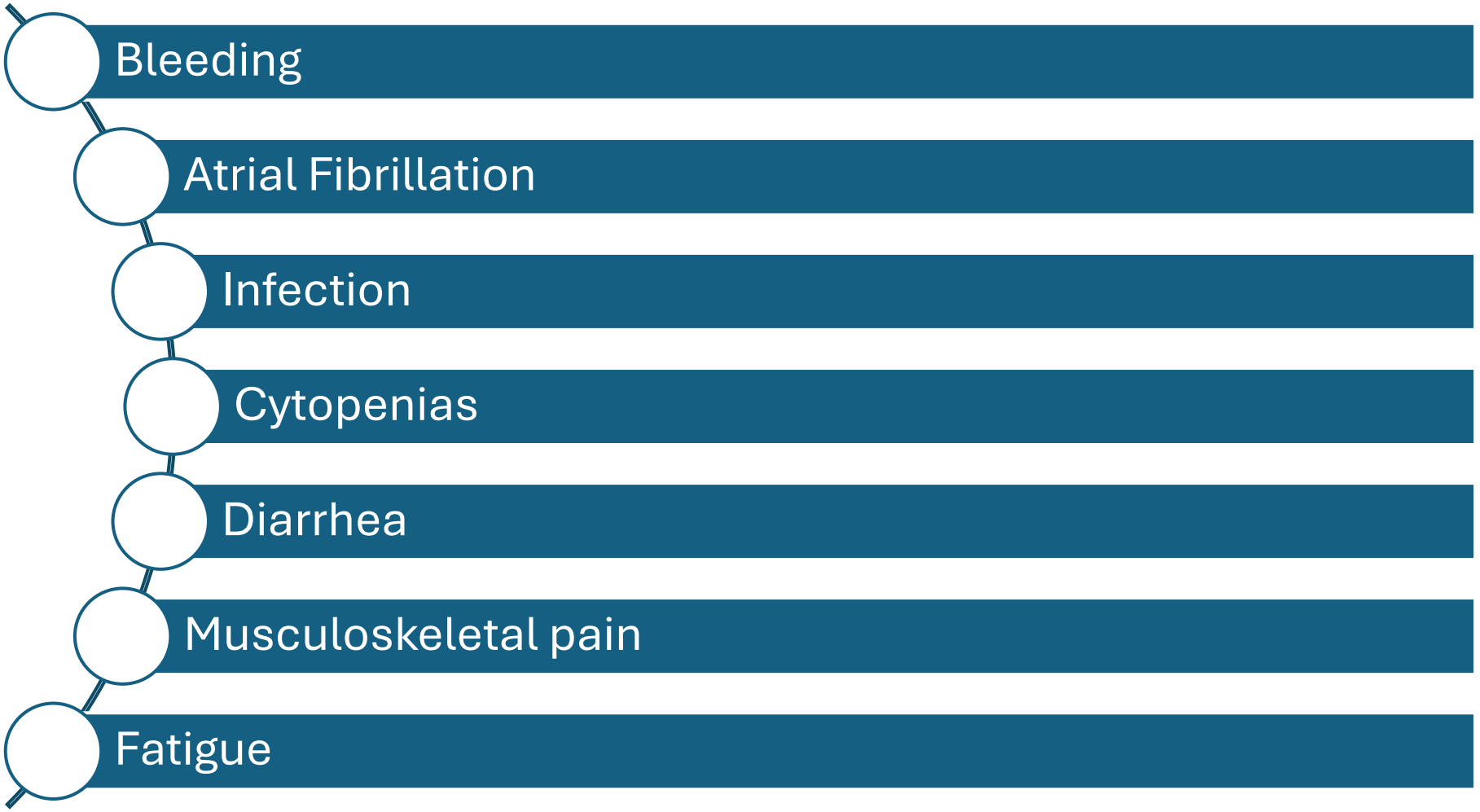
Corinne Hoffman, MS, APRN-CNP, AOCNP

Patient Education: Pirtobrutinib

- Noncovalent (reversible) BTKi
  - Explain that it binds BTK differently than the covalent BTKi they were previously taking, allowing it to have activity despite the presence of a known resistance mutation
- Approved for adults who have been on two prior lines of CLL therapy, including BTKi and BCL-2 inhibitor
- Overall similar side effect profile as BTKi they were previously taking but remind them of the most common adverse effects
- Once daily dosing

Pirtobrutinib package insert, 6/2024

Patient Education: Pirtobrutinib



Pirtobrutinib: Side Effects

- **Bleeding**
  - Monitor patient for signs of bleeding, especially if on concurrent anticoagulation
  - Instruct patient to inform provider about any upcoming procedures
  - Consider hold of 3 to 7 days depending upon type of surgery and bleeding risk
- **Atrial fibrillation**
  - Monitor for and educate patient on signs and symptoms of arrhythmia
  - 3.6% incidence (all grade)
  - New onset
    - Cardiology consult
    - Anticoagulation indicated?
    - Rate and/or rhythm control
      - Achieve prior to resuming treatment

Pirtobrutinib package insert, 6/2024

Pirtobrutinib: Side Effects

- **Infection**
  - Encourage patients to report fever and other signs and symptoms of infection promptly
  - Consider prophylaxis in high-risk individuals
  - Vaccination
- **Cytopenias**
  - Hold therapy or dose reduce depending on severity

Pirtobrutinib package insert, 6/2024

Pirtobrutinib: Side Effects

- **Diarrhea**
  - Usually self limited and manageable
  - Loperamide PRN
- **Musculoskeletal Pain**
  - Acetaminophen
  - Avoid NSAIDs when possible due to heightened bleeding risk

Roundtable Discussion

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Agenda

Introduction: Key Factors in the Management Patients with Chronic Lymphocytic Leukemia (CLL)

Module 1: Role of Covalent Bruton Tyrosine Kinase (BTK) Inhibitors for Newly Diagnosed CLL

Module 2: Role of Time-Limited Up-Front Treatment, Including Therapy Combining BTK Inhibitors and Venetoclax, for Newly Diagnosed CLL

Module 3: Role of Pirtobrutinib for Relapsed/Refractory (R/R) CLL

Module 4: CAR (Chimeric Antigen Receptor) T-Cell Therapy for R/R CLL

Clinical Scenario

A patient with CLL has experienced disease progression on a covalent BTK inhibitor, venetoclax and pirtobrutinib and has recently been referred for CAR T-cell therapy

CLL: Other Treatment Options

Jeff Sharman M.D.

Medical Director of Hematology Research

Willamette Valley Cancer Institute & Sarah Cannon

CLL – Therapies in heavily pre-treated

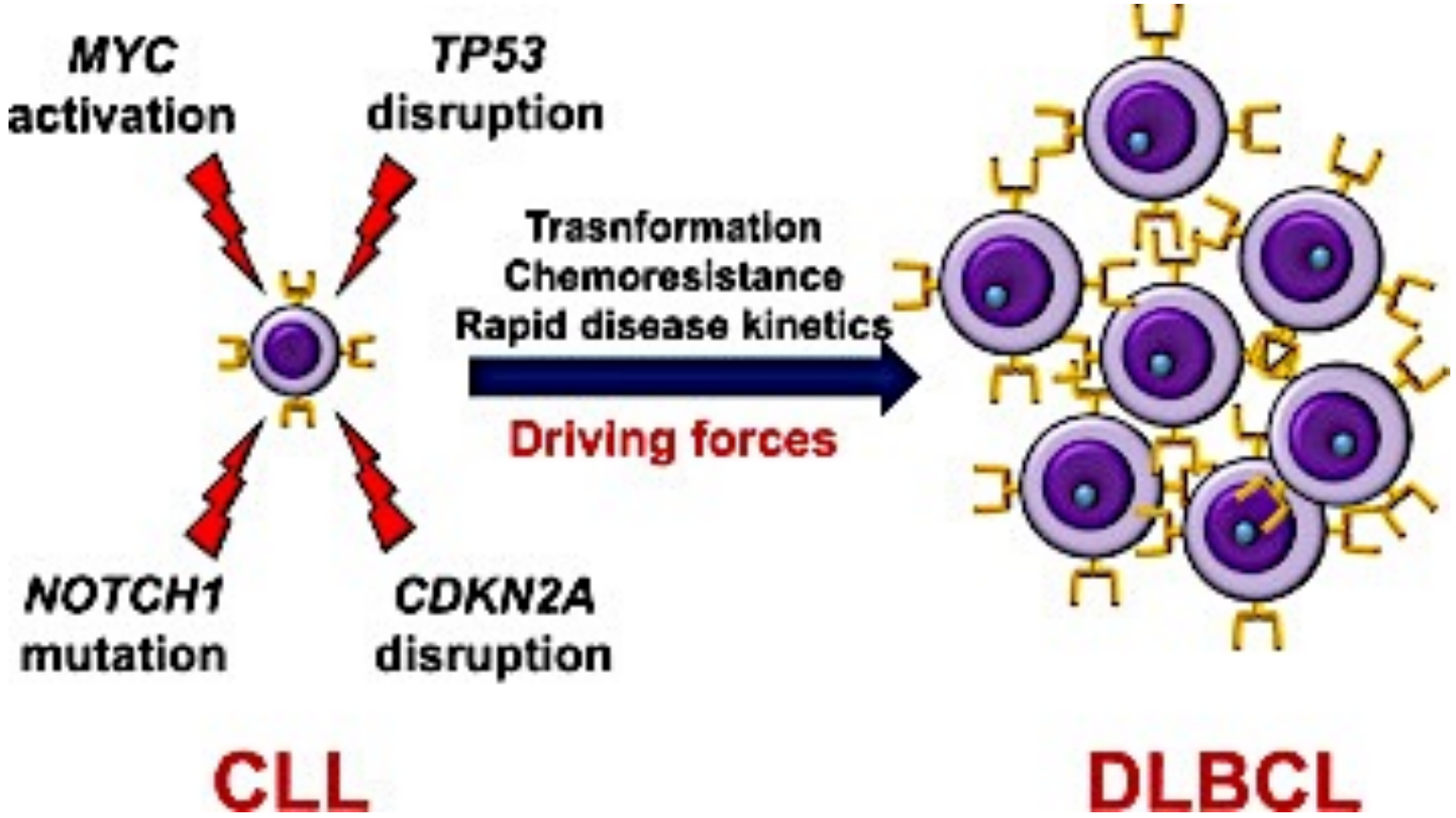
67-year-old, diagnosed at age 60 with high-risk disease (IgHV unmutated, Del17P). Bulky nodes, initial presentation meeting indication for therapy

Initially treated with ibrutinib, 3.5 years later had PD

Treated at that time with rituximab / venetoclax – responded to treatment but then PD at two years.

Enrolled on pirtobrutinib study with reasonably controlled disease, but now progressing – now what?

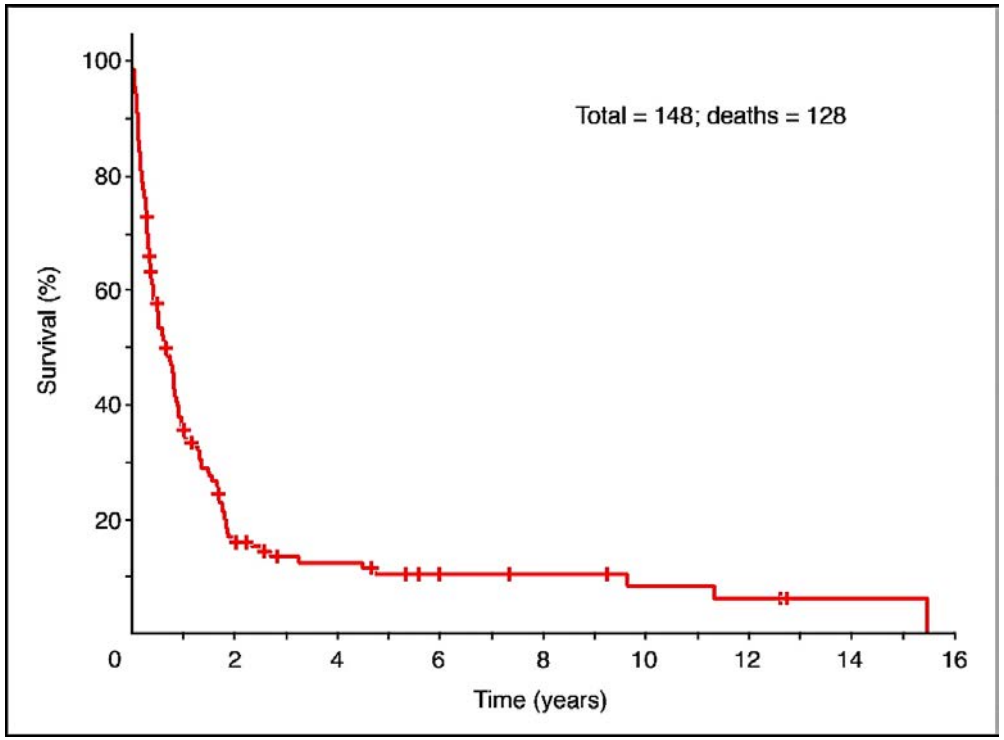
Richter's Syndrome: What is it?



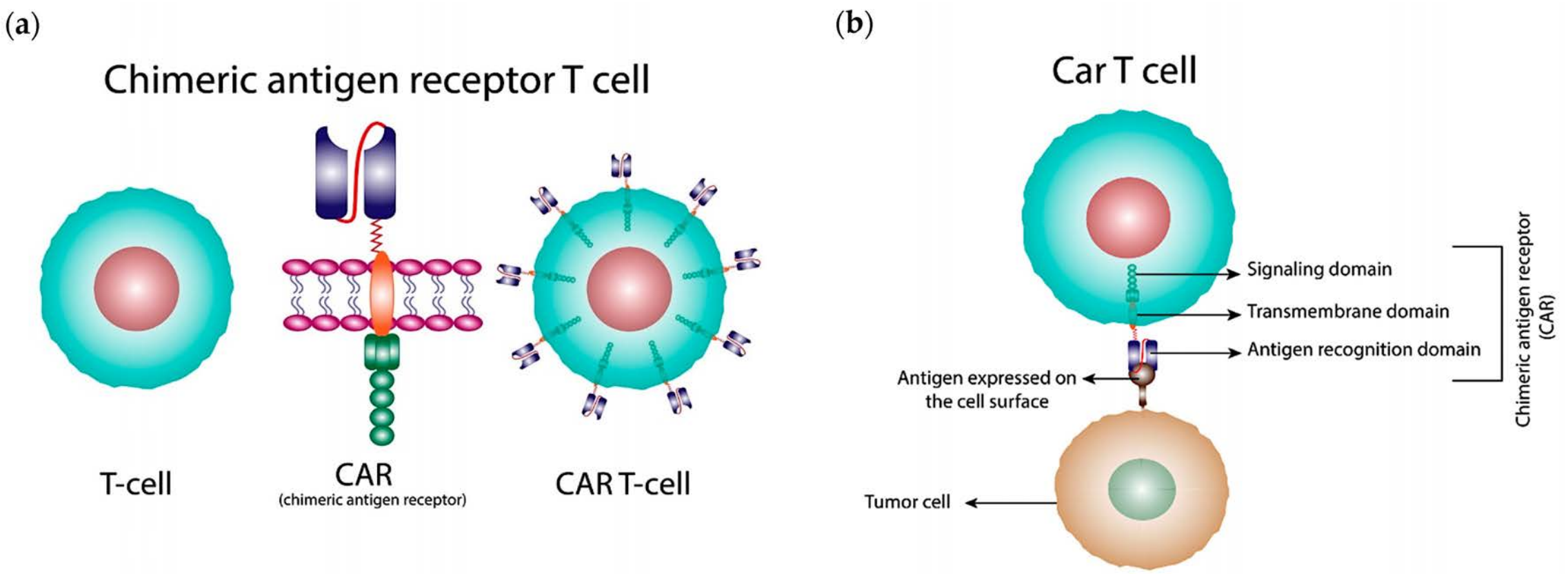
Richter’s Syndrome

- R-CHOP
- DA-R-EPOCH
- Transplant
- CAR-T

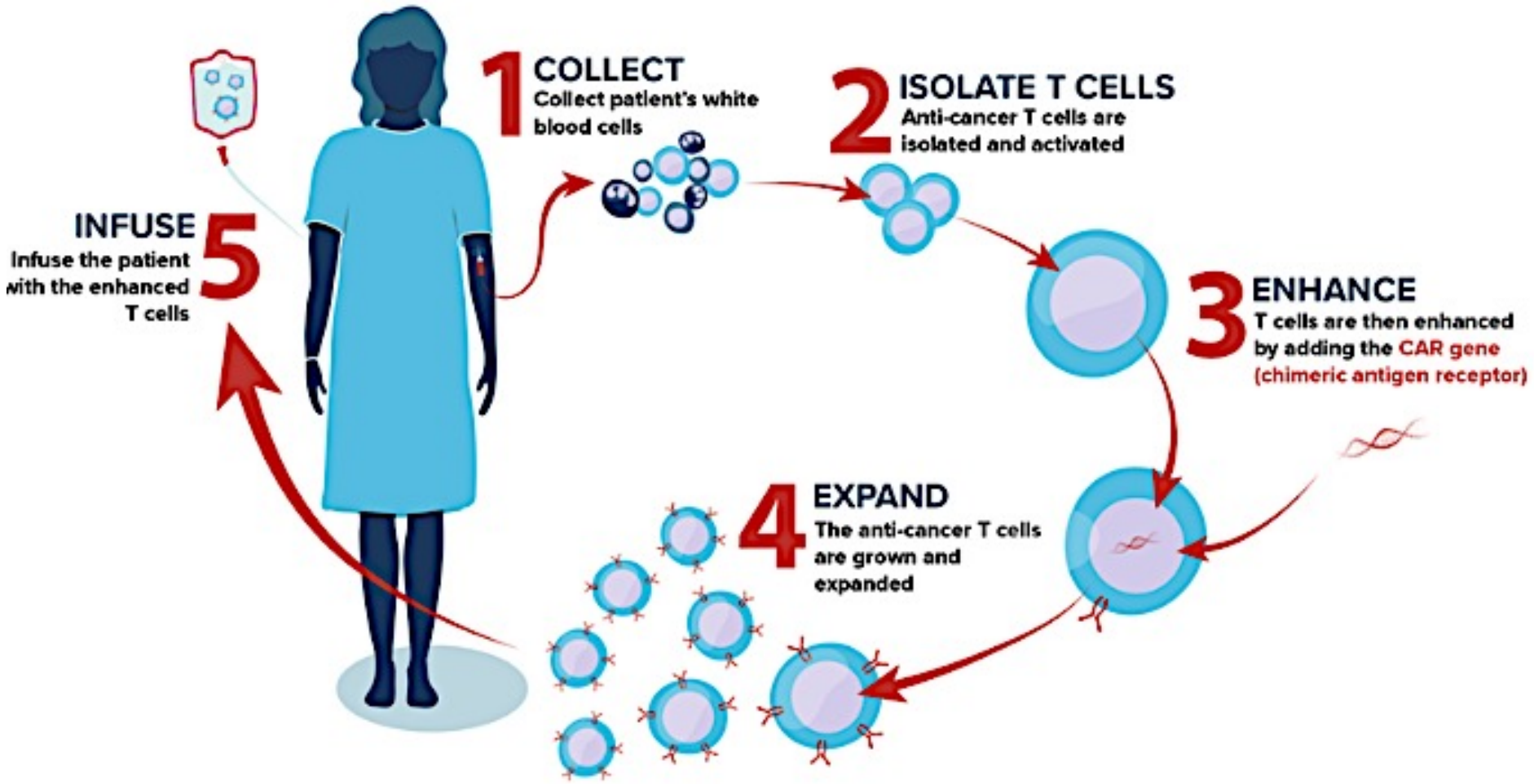
Clinical Outcomes and Prognostic Factors in Patients With Richter's Syndrome Treated With Chemotherapy or Chemoimmunotherapy With or Without Stem-Cell Transplantation



CAR-T: What is it?



CAR-T: How do we do it?



CAR-T in CLL

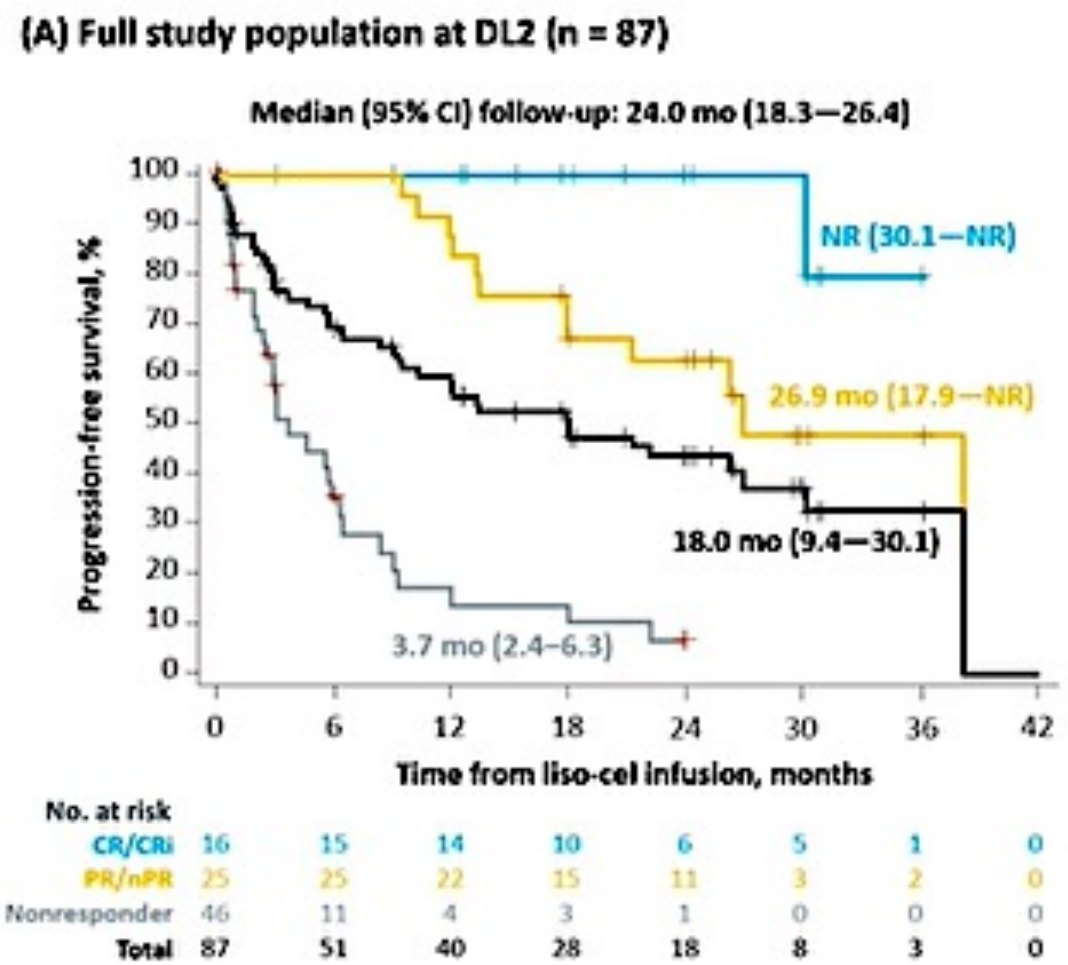
FDA Approves Liso-Cel for Relapsed/Refractory CLL/SLL
March 14, 2024

The 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.

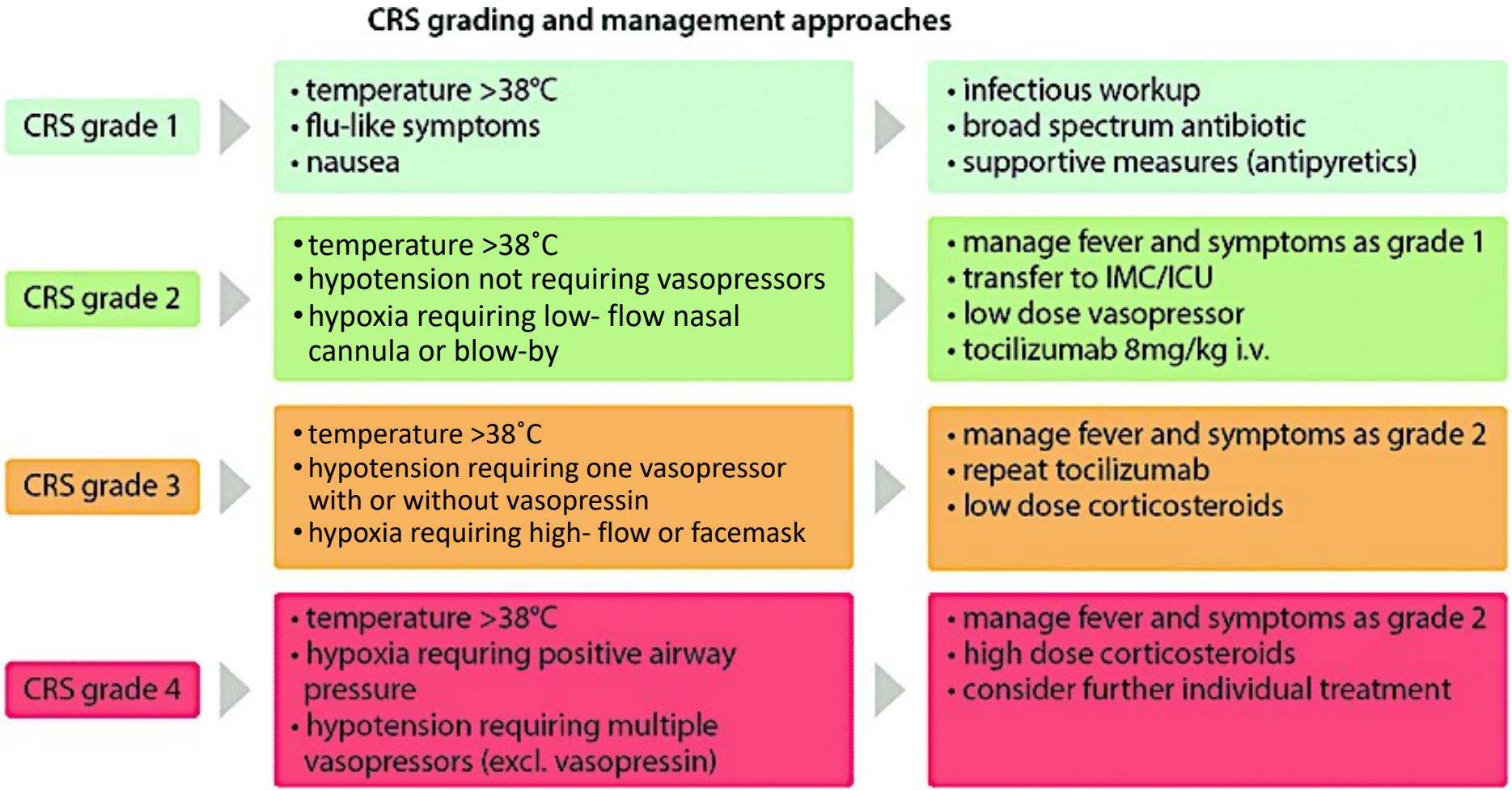
This indication is approved under accelerated approval based on response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

https://news.bms.com/news/details/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

CAR-T in CLL: How well it works

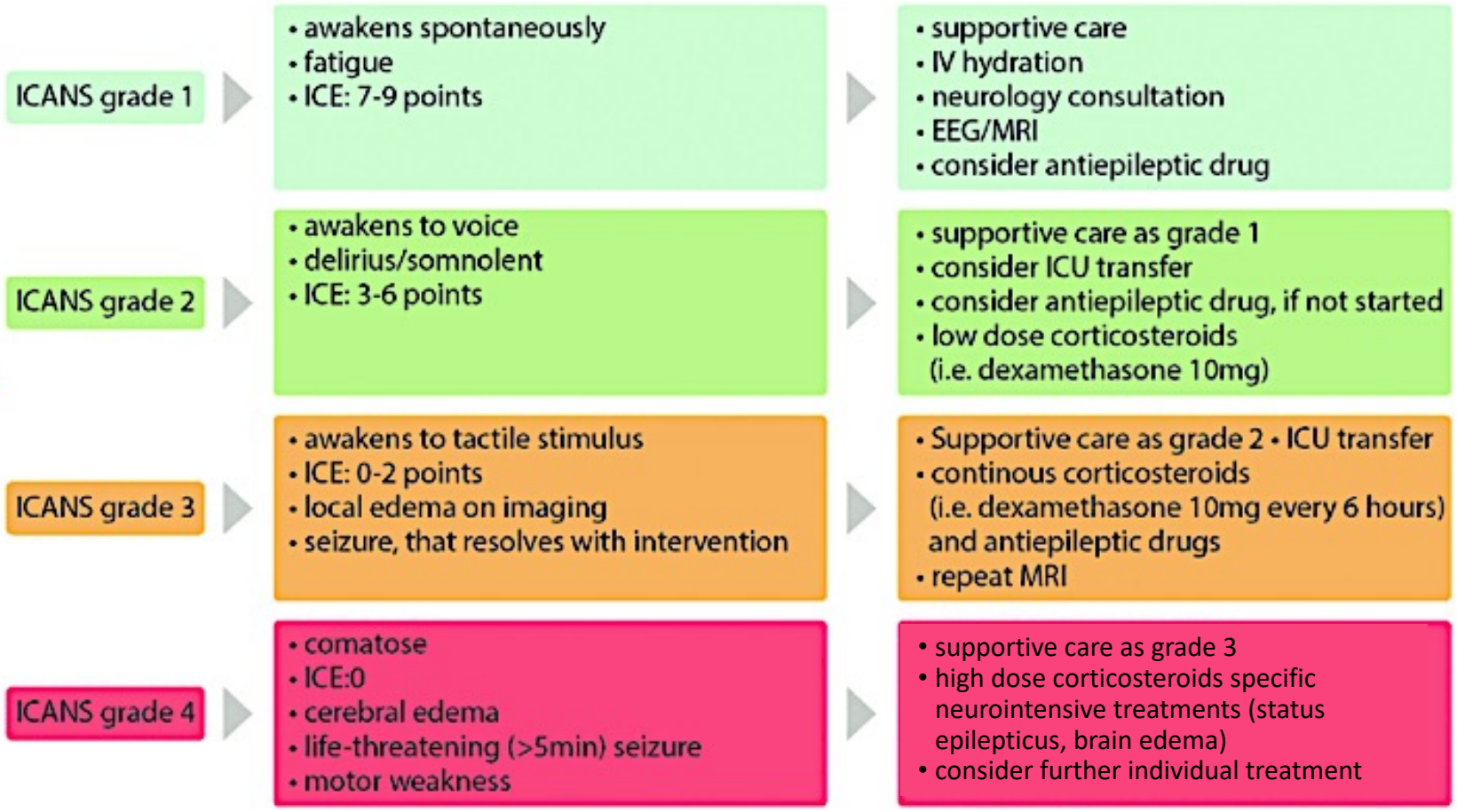


CRS

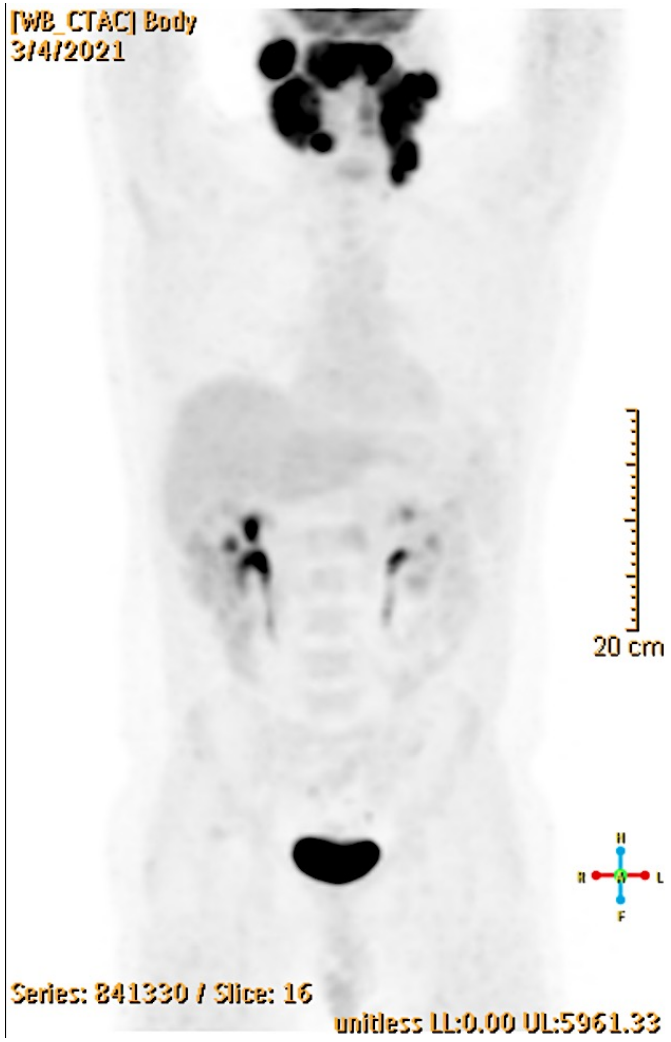

CRS grading and management approaches
CRS grade 1
• temperature >38°C
• flu-like symptoms
• nausea
• infectious workup
• broad spectrum antibiotic
• supportive measures (antipyretics)
CRS grade 2
• temperature >38˚C
• hypotension not requiring vasopressors
• hypoxia requiring low- flow nasal cannula or blow-by
• manage fever and symptoms as grade 1
• transfer to IMC/ICU
• low dose vasopressor
• tocilizumab 8mg/kg i.v.
CRS grade 3
• temperature >38˚C
• hypotension requiring one vasopressor with or without vasopressin
• hypoxia requiring high- flow or facemask
• manage fever and symptoms as grade 2
• repeat tocilizumab
• low dose corticosteroids
CRS grade 4
• temperature >38°C
• hypoxia requring positive airway pressure
• hypotension requiring multiple vasopressors (excl. vasopressin)
• manage fever and symptoms as grade 2
• high dose corticosteroids
• consider further individual treatment

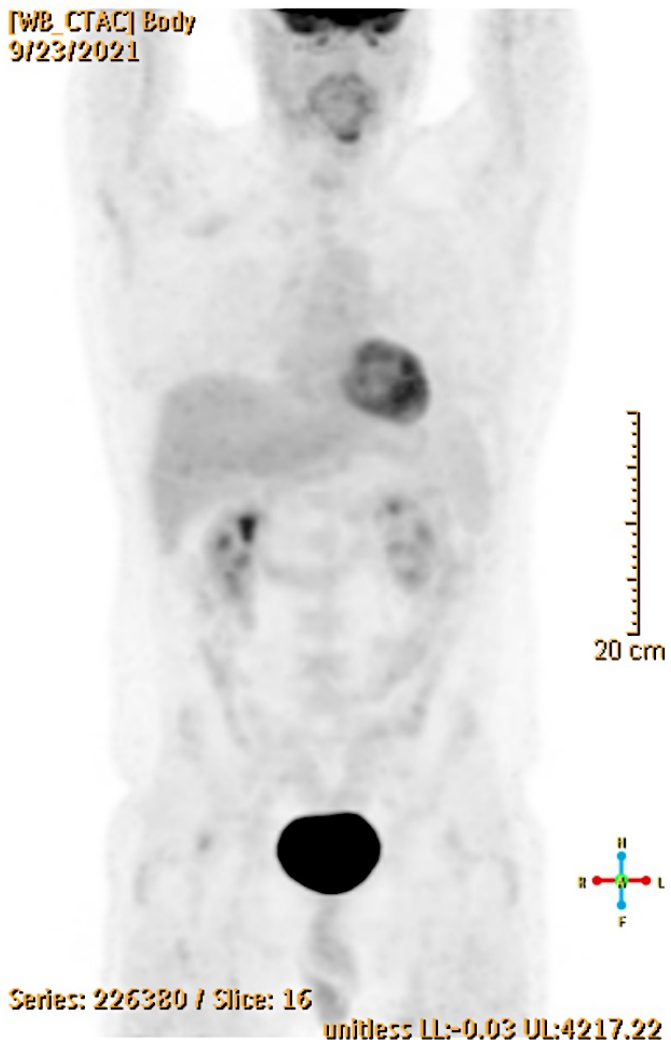
ICANS

ICANS grading and management approaches



CLL with Richters: treated with CAR-T





CAR-T

When to refer?

What are the barriers?

Who are the patients?

Roundtable Discussion

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CAR- T Cell Therapy in CLL

Dr. Jackie Broadway-Duren

Patient Education on CAR-T Cell Therapy

Discuss overview and mechanisms for CAR-T cell therapy

Process for CAR-T:

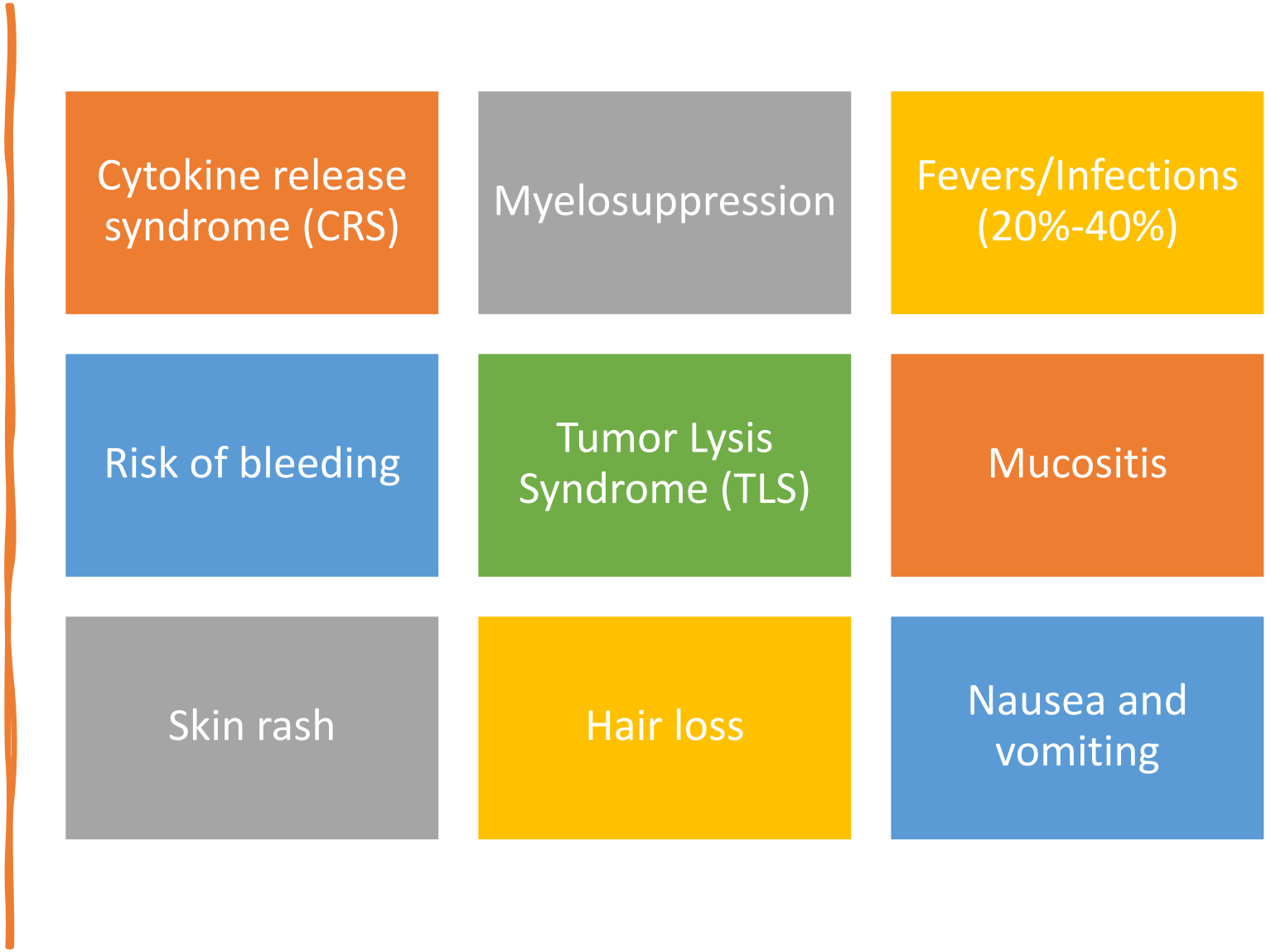
- Chimeric Antigen Receptor (CAR) Modified T cells
- Normal T cells are extracted from patients with indication for CART through process called leukopheresis.
- T cells are then genetically engineered (in laboratory)
- The altered T cells express an artificial receptor, CAR
- The CAR-T cells are expanded to increase number of cells *~15 days*
- The patient receives chemotherapy to deplete lymphocytes
- CAR-T cells are then infused into patient via IV infusion (inpt/outpt)

Patient Discussion

Patients are instructed on duration of hospitalization, usually 3-4 weeks

Patients instructed to plan to remain in close proximity to medical center for 2 weeks to 1 month

Adverse Effects with CAR-T cell Therapy



LLS, 2024

Neurotoxicity in CAR-T Cell Therapy

- Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) Language impairment (aphasia)
  - Confusion
  - Delirium
  - Involuntary muscle twitching
  - Hallucinations
  - Unresponsiveness
  - Seizures (cerebral edema)
  - Neuro toxicity in most cases is reversible

(LLS, 2024; Jain et al., 2023)

Management of CAR-T Cell Toxicities

- CRS – may occur within 5 days
  - Grade and manage accordingly
  - Treatments for CRS:
    - Toci – 80%
    - Steroids – 75%
    - Vasopressors – 40%
    - Monoclonal antibody infusion (in extreme CRS).

Patient Case of Neurotoxicity/CRS Post CART

- 64 y/o female with refractory CLL s/p multiple lines of therapy.
- Poor prognostic factors i.e, TP53
- PMH: HTN, sarcoidosis
- Admitted for CAR-T cell therapy
  - Received lymphodepletion therapy with Fludarabine and Cyclophosphamide
  - CAR-T cells infused on Day 1
    - Developed fever and CRS within 5 days
    - Treated for neutropenia
    - Admitted to ICU due to grade 3 CRS – treated with Toci and high dose steroids
    - Patient was hypotensive and received vasopressors
    - Received rituximab on Day 10 due to prolonged neurotoxicity, etc

Monitoring Patients after CAR-T Therapy

- In patient case, the CRS was reversed and the patient did well in the following weeks.
- Patient remained in the medical center for next month with weekly follow up in outpatient clinic
- Patient followed for 1-2 years depending on any neurological deficits.

Roundtable Discussion

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Understanding the Current Paradigm and New Approaches in the Care of Patients with Cancer

A Complimentary NCPD Hybrid Symposium Series Held During the 50th Annual ONS Congress

Bispecific T-Cell Engagers for Small Cell Lung Cancer

Friday, April 11, 2025

6:00 AM – 7:30 AM

Faculty

Anne Chiang, MD, PhD
Elizabeth Krueger, NP
Beth Sandy, MSN, CRNP, FAPO
Erin Schenk, MD, PhD

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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