cec ONCOLOGY

Guiding Light

Oncology Nurses' Vital Role in Supporting Patients through CLL Therapy

This activity is supported by educational grants from BeiGene USA Inc.; Janssen Biotech Inc., administered by Janssen Scientific Affairs LLC (both are Johnson & Johnson companies); and Lilly.

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To Ask a Question

Use the **Q&A feature** at the bottom of the screen.

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Clinical Trial and Real-world Evidence Supporting the Use of Targeted Therapies in CLL

Differentiate patient- and disease-specific variables that inform CLL treatment selection.

LEARNING OBJECTIVE 1

Etiology, Pathophysiology, and Risk Factors

- CLL is the most common type of leukemia in adults the United States (25% of cases), but it is rare when considering all types of cancer
- The average age of diagnosis is 70; it is rare under age 40 and is extremely rare in children
- CLL is a disorder of lymphocytes that are morphologically mature but immunologically less mature
- It is incurable with standard treatment, and risk score is tied to prognosis
    - Historical overall survival at 5 years ranges from 20% (very high risk) to more than 90% (low risk)

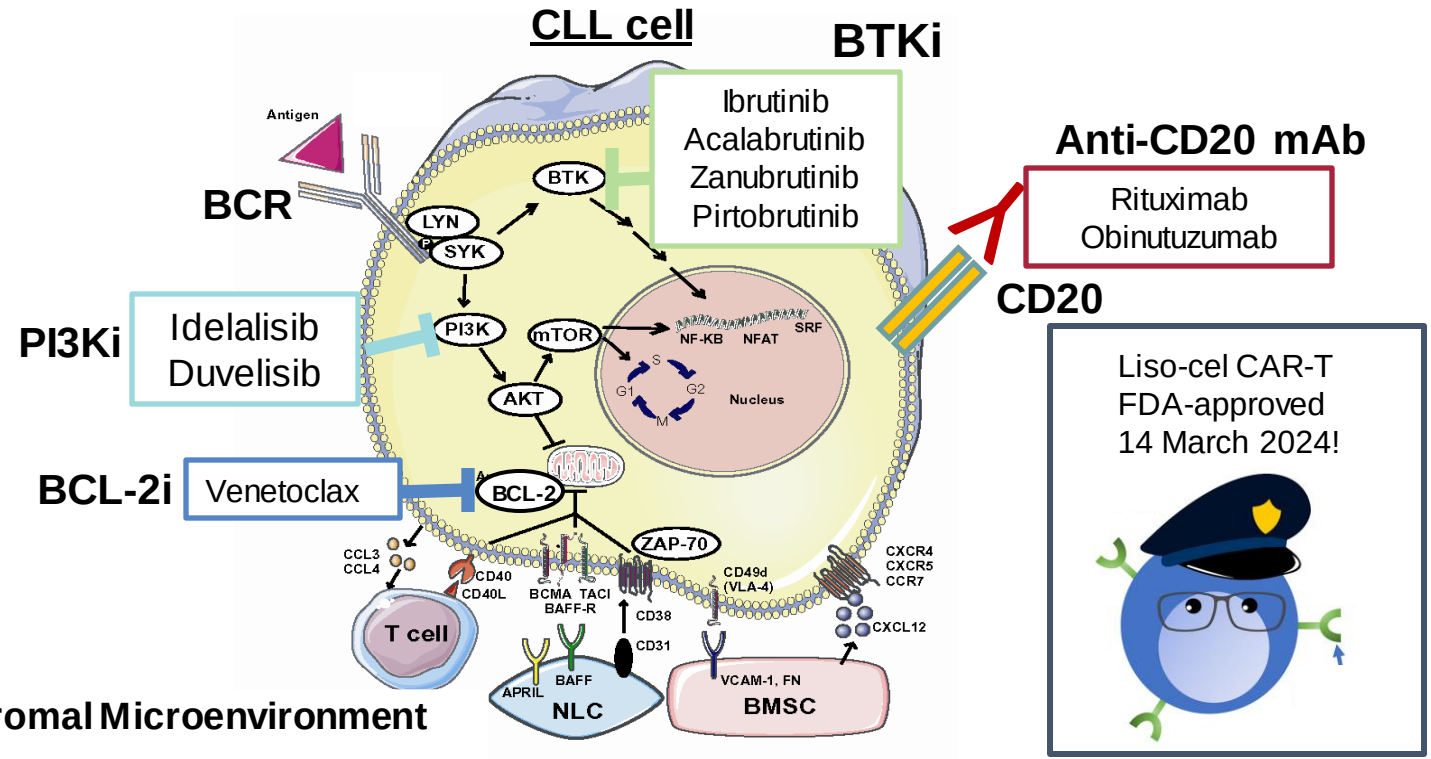
American Cancer Society [ACS]. Key statistics for chronic lymphocytic leukemia. 2024. https://www.cancer.org/cancer/types/chronic-lymphocytic-leukemia/about/key-statistics.html.
ACS. What are the risk factors for chronic lymphocytic leukemia?. Https://www.cancer.org/cancer/chronic-lymphocytic-leukemia/causes-risks-prevention/risk-factors.html.
Wierda WG, et al. *J Natl Compr Canc Netw.* 2024;22(3):175–204.

Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

- Monoclonal mature B lymphocytes expressing CD5 in the blood, bone marrow, and secondary lymphatic organs
- B-cell receptor (BCR) and its downstream signaling cascade is a main driver of proliferation and survival
- CLL cells depend on B-cell lymphoma 2 (BCL-2) proteins for survival
- Biomarker testing can predict time to first treatment, treatment outcomes, and survival
  - IGHV mutational status (higher-risk: unmutated)
  - FISH testing (high-risk: del17p)
  - Karyotype (high-risk: complex)
  - Mutation testing (high-risk: TP53 mutations)

FISH = fluorescence in situ hybridization; IGVH = immunoglobulin variable heavy chain.
Koehrer S, Burger JA. *Acta Haematologica*. 2023:1-14.

A Diverse Array of Novel Agents are Highly Active in CLL



Adapted from Davids MS, et al. *Leuk Lymph.* 2012;120(17):3501-3509. Lokaj R. Cancer Network. FDA approves Liso-cel for relapsed/refractory CLL/SLL. 2024. https://www.cancernetwork.com/view/fda-approves-liso-cel-for-relapsed-refractory-cll-sll.

Clinical Presentation

- Some patients have “B symptoms”
  - Severe fatigue
  - Drenching night sweats
  - Unintentional weight loss*
  - Fever without infection
- Most patients have no symptoms but an abnormal CBC is noted on routine blood work
- Liver and spleen may be enlarged and can cause early satiety
- Lymphadenopathy can be present
- Recurrent infections can be a problem due to immunologically immature lymphocytes and hypogammaglobulinemia

Variable	Acute Leukemia	Chronic Leukemia
Age	All ages	Adults
Clinical onset	Sudden	Slow growing
Lymphocytes	Immature	Mature
Anemia	Mild to severe	Mild
Thrombocytopenia	Mild to severe	Mild
White blood cells	Variable (high or low)	Elevated
Organomegaly	Mild	Prominent (especially spleen and liver)

*(≥ 10% in the previous 6 months)

Bispo JAB, et al. *Cold Spring Harb Perspect Med*. 2020;10(6):a034819. Wierda WG, et al. *J Natl Compr Canc Netw*. 2024;22(3):175–204.

Audience Response

How often do you consider biomarker testing to inform treatment decisions for your patients with CLL?

A. I do not use biomarker testing
B. Only at initial diagnosis
C. Only at first progression
D. At initial diagnosis and first progression
E. Prior to any new treatment

Recommended Testing

- For diagnosis
  - Flow cytometry analysis of the blood; could also use lymph node biopsy
  - Immunophenotyping for kappa/lambda, CD19, CD20, CD5, CD23, CD10, CD200; also recommended to include cytospin for cyclin D1 or FISH for t(11;14), t(11q;v)
- Biomarker testing
  - Minimum testing should include fluorescence in situ hybridization (FISH), *TP53*, and immunoglobulin heavy chain variable region (IGHV) mutation
  - Retest FISH and TP53 before each line of treatment if not high risk on prior testing
  - Access to testing varies by location
    - Resource-limited settings pose greater challenges

Wierda G, et al. *J Natl Compr Canc Netw.* 2024;22(3):175–204.

Risk Stratification and Prognosis

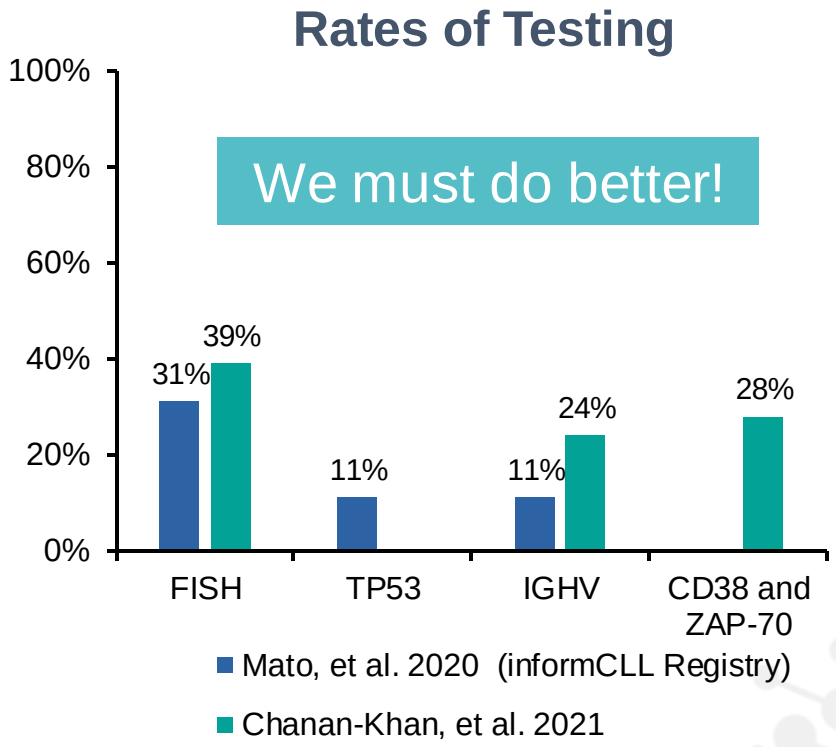
Method of Detection	Prognostic Variable	Risk Category
Interphase cytogenetics (FISH)	Del(17p)	Unfavorable
	Del(11q)	Intermediate
	Trisomy 12	Intermediate
	Normal	Intermediate
	Del(13q) (as a sole abnormality)	Favorable
DNA sequencing	TP53	Wild-type: favorable Mutated: unfavorable
	IGHV	> 2% Mutation: favorable* ≤ 2% Mutation: unfavorable
CpG-stimulated metaphase karyotype	Complex karyotype (≥ 5 abnormalities)	Unfavorable

- Del(17p) reflects the loss of the *TP53* gene and is frequently associated with mutations in the remaining *TP53* allele
- *TP53* mutations can happen without del(17p)
- Independent of 17p status, *TP53* mutations are predictors of resistance fludarabine- or bendamustine-based regimens and poor survival

Wierda G, et al. *J Natl Compr Canc Netw.* 2024;22(3):175–204.

Real-world Data: Testing for Prognostic Factors

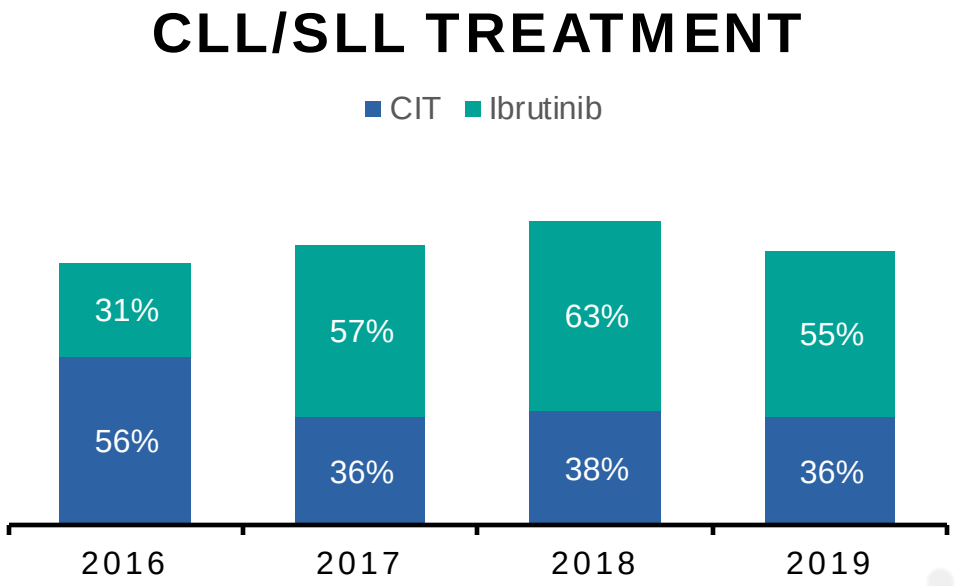
- **informCLL** showed prognostic testing rates were poor among community-based providers
  - Low rates of testing led to treatment decisions that contradicted consensus guidelines
- Lack of testing in the community was confirmed by another study that identified newly diagnosed CLL patients via the **Flatiron Health EHR database**
  - Found that patients who were 65 and older, female, or lived in the western United States were significantly less likely to receive recommended prognostic testing



Mato AR, et al. *Clin Lymphoma Myeloma Leuk*. 2020;20(3):174-183.e3.; Chanan-Khan A, et al. *Blood.* 2021;142(1):5144.

Prognostic Testing and Treatment Patterns in Black Patients

- Compared to the overall population, Black patients:
  - Younger
  - Worse ECOG status
  - More advanced disease
  - Shorter time to 1L therapy
- Persistent CIT use
- Similar rate of FISH testing (25%)



CIT = chemoimmunotherapy.

Barrientos JC, et al. *J Clin Oncol*. 2022;40:e18559.

Indications for Treatment

Active disease should be clearly documented. At least 1 of these criteria should be met:

- Progressive marrow failure, Hgb < 10 gm/dL, or PLT < 100 × 10^9/L
- Massive (≥ 6 cm below left costal margin) or progressive or symptomatic splenomegaly
- Massive (≥ 10 cm in longest diameter) or progressive or symptomatic lymphadenopathy
- Progressive lymphocytosis + increase of ≥ 50% over a 2-month period or lymphocyte doubling time of < 6 months
- Autoimmune complications of CLL that are poorly responsive to corticosteroids
- Symptomatic extranodal involvement (e.g., skin, kidney, lung, and spine)
- Disease-related symptoms (unintended weigh-loss ≥ 10%, significant fatigue, persistent fevers with no infection, persistent nigh sweats with no infection)

Hallek M, et al. *Blood*. 2018;131:2745-2760.

1L Therapy for CLL/SLL – NCCN Guidelines

Preferred regimens	Other recommended regimens	Useful in certain circumstances
Without del(17)p/TP53 mutation		

• Acalabrutinib ± obinutuzumab
• Venetoclax + obinutuzumab
• Zanubrutinib
	• Ibrutinib
	• Ibrutinib + obinutuzumab
	• Ibrutinib + rituximab
	• Ibrutinib + venetoclax
		• Consider for IGHV-mutated CLL in patients aged < 65 w/o significant comorbidities
		  • FCR
		• Consider when BTKi and venetoclax are not available or contraindicated or rapid disease debulking needed
		  • Bendamustine + anti-CD20 mAb
		  • Chlorambucil ± obinutuzumab
		  • HDMP + anti-CD20 mAb

With del(17)p/TP53 mutation		

• Acalabrutinib ± obinutuzumab
• Venetoclax + obinutuzumab
• Zanubrutinib
	• Ibrutinib
	• Ibrutinib + venetoclax
		• Consider when BTKi and venetoclax are not available or contraindicated or rapid disease debulking needed
		  • HDMP + anti-CD20 mAb
		  • Obinutuzumab

mAb = monoclonal antibody; HDMP = high dose methylprednisolone; FCR = fludarabine, cyclophosphamide, rituximab.

Wierda WG, et al. *J Natl Compr Canc Netw.* 2024;22(3):175–204.

CIT for 1L Therapy for CLL/SLL

- Chemoimmunotherapy (CIT) used to be standard of care
  - No longer a category 1 recommendation
  - Not recommended for patients with del(17p)/*TP53* Mutation given low response rates
- Now, only *considered* for patients who are:
  - Young
  - Fit
  - *IGHV* mutated

Yet, in the inform CLL registry, 40% of patients with unmutated *IGHV* received CIT, despite decreased efficacy

Mato A et al. *Clin Lymphoma Myeloma Leuk*. 2020;20:174-183.

Current NCCN Guidelines for CLL/SLL: Second- or Third-line Therapy

Second- or Third-line Therapy	Without (del)17p/TP53 Mutation	With (del)17p/TP53 Mutation
Preferred	**Acalabrutinib** **Venetoclax +rituximab** **Zanubrutinib**	**Acalabrutinib** **Venetoclax + rituximab** **Zanubrutinib** Venetoclax
Other Recommended	**Ibrutinib** Venetoclax Ibrutinib + Venetoclax	**Ibrutinib** Ibrutinib + Venetoclax
Useful in Certain Circumstances	Resistance or intolerance to prior covalent BTKi therapy: Pirtobrutinib For relapse after a period of remission (if previously used): Venetoclax ± anti-CD20 mAb*	
CAR-T (3rd line and beyond, must have received prior BTKi and BCL2 inhibitor)	Lisocabtagene maraleucel	

Category 1 Recommendation

*(venetoclax + obinutuzumab preferred)
BTKi = Bruton's tyrosine kinase inhibitor; CLL = chronic lymphocytic leukemia; NCCN = National Comprehensive Cancer Network; mAb = monoclonal antibody; CAR-T = chimeric antigen receptor T-cell therapy..
Wierda G, et al. *J Natl Compr Canc Netw.* 2024;22(3):175–204.

Long-term Evidence Supporting Continuous BTKi Therapy – RESONATE-2

- Ibrutinib versus chlorambucil in treatment-naïve CLL
  - 8 years of follow-up
- PFS benefit with ibrutinib
  - 59% vs 9% at 7 years
  - Benefit in del(11q) and unmutated *IGVH* patients
  - OS at 7 years was 78% with ibrutinib

Sustained benefit with 1L ibrutinib including patients with high-risk genomic features

PFS = progression-free survival; OS = overall survival; 1L = first line.

Barr PM, et al. *Blood Adv*. 2022;6:3440-3450.

Long-term Evidence Supporting Continuous BTKi Therapy – ELEVATE-TN

- Acalabrutinib versus acalabrutinib + obinutuzumab versus obinutuzumab + chlorambucil (O-Clb)
  - 6 years of follow-up
- PFS benefit with acalabrutinib regimens sustained at median follow-up of 74.5 months
  - PFS *not reached* for for A+O and A vs 27.8 mo for O+Clb
- A+O reduced the risk for death by 38% compared with O+Clb

Sustained benefit with acalabrutinib regimens compared to O-Clb in treatment-naïve CLL

Sharman JP, et al. *Blood.* 2023;142(Suppl1):636.

Long-term Evidence Supporting Continuous BTKi Therapy – SEQUOIA

- Zanubrutinib versus bendamustine + rituximab (BR)
  - 42-month follow-up
- PFS benefit with zanubrutinib sustained at median follow-up of 43.7 months
  - PFS was not reached for zanubrutinib versus 42.2 mo for BR
  - 42-month PFS rates were 82.4% for zanubrutinib
  - OS NR in either arm
- With long-term follow-up, benefit demonstrated in patients with mutated IGHV in addition to the previously reported benefit in those with unmutated IGHV
- Patients with del(17p) continue to demonstrate PFS benefits consistent with the randomized cohort

Sustained benefit with zanubrutinib compared to BR in treatment-naïve CLL

Munir T, et al. *Hemasphere*. 2023;7(Suppl):e15364af.

CLL14 Trial Design

Previously untreated patients with CLL and coexisting medical conditions

CIRS > 6 and/or CrCl < 70mL/min

Enrollment from 2015 to 2016

1:1 randomization

Venetoclax–Obinutuzumab 6 cycles → **Venetoclax** 6 cycles

Chlorambucil–Obinutuzumab 6 cycles → **Chlorambucil** 6 cycles

Follow-up Phase

Primary endpoint:
Progression-free survival

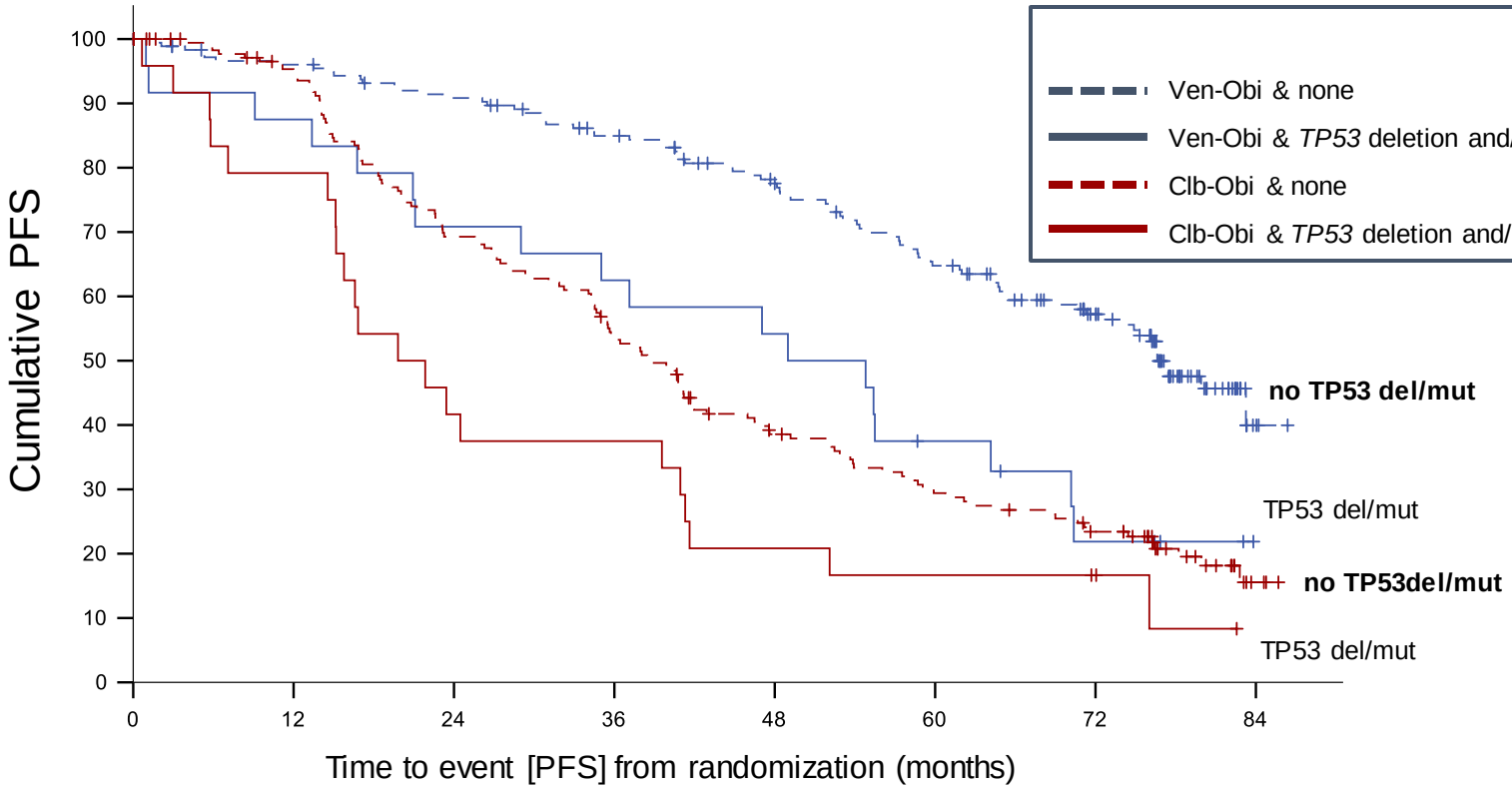
Key secondary endpoints:
Response
Minimal residual disease
Overall survival

Current median observation time: 76.4 months

CIRS = cumulative illness rating scale; CrCl = creatinine clearance.

Fischer K, et al. *N Engl J Med.* 2019;380(23):2225-2236.

CLL14: PFS by TP53 Status



Al-Sawaf O, et al. *Hematol Oncol*. 2023;41(S2):58–60.

Efficacy of Fixed-duration Regimens: Undetectable MRD

Agents	1y uMRD	2y uMRD	PFS & DFS
Obinutuzumab + venetoclax[1,2]	57% BM 76% PB	26.9% PB	Estimated 4-year PFS 74%
Ibrutinib + venetoclax CAPTIVATE[3,4]	68% BM 74% PB		Fixed-duration: 4 y PFS 79% MRD-directed continuation of therapy: 3 y PFS ≥ 95%
Ibrutinib + venetoclax MD Anderson[5]	56% BM	66% BM	
Ibrutinib + venetoclax GLOW[6,7]	40.6% BM 80.4% PB		4-year PFS: 75%

- Combination associated with higher incidence of GI events and neutropenia than single-agent ibrutinib
- Toxicities tend to occur early and decrease over time

PB = peripheral blood; BM = bone marrow; DFS = disease-free survival; uMRD =undetectable minimal/measurable residual disease.

1. Fischer K, et al. *NEJM*. 2019;380:2225-2236; 2. Al-Saw af O, et al. *JCO*. 2021;39:4049-4061; 3. Wierda WG, et al. *JCO*. 2021;39:3853-3865; 4. Barr PM, et al. *JCO*. 2023; 41: 7535-75355; Jain N, et al. *JAMA Oncol*. 2021;7:1213-1219; 6. Munir T, et al. *Clin Lymphoma Myeloma Leuk*. 2022;22:S264-S265; 7. Niemann CU, et al. *Lancet Oncol*. 2023;24(12):1423-1433.

Goals of Continuous- vs. Fixed-duration Therapy in CLL/SLL

Be prepared to review goals of care with patients and empower their decision-making

Goals of continuous therapy

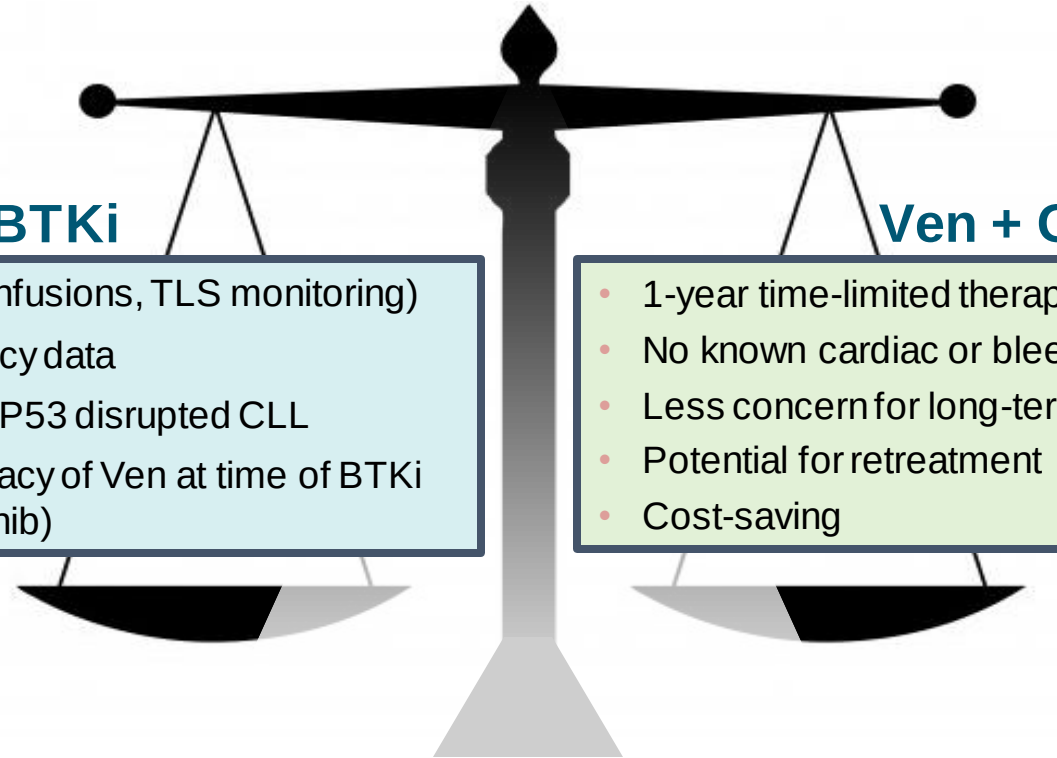
- ☑ Disease control
- ☑ Prolonged PFS
- ☑ Independent from response, MRD

Goals of fixed-duration therapy

- ☑ Disease eradication
- ☑ Prolonged PFS
- ☑ Undetectable MRD

MRD = minimal/measurable residual disease.

Front-Line BTKi vs. Ven + Obi: Factors to Consider



BTKi

- Convenience (no infusions, TLS monitoring)
- Longer-term efficacy data
- More effective in TP53 disrupted CLL
- More data for efficacy of Ven at time of BTKi progression (ibrutinib)

Ven + Obi

- 1-year time-limited therapy
- No known cardiac or bleeding risks
- Less concern for long-term adherence
- Potential for retreatment
- Cost-saving

BTKi Resistance

16%–23% of patients on continuous BTKi therapy develop BTKi resistance

- Most information comes from studies with ibrutinib
  - However, similar mechanisms were reported for acalabrutinib
- The two most common alterations are C481S in the ATP binding site of BTK
  - The mutations prevent attachment of covalent BTKis

Resistance typically arises with indefinite treatment

- More common in previously treated patients and patients with TP53 abnormalities

Munir T, et al. *Am J Hematol.* 2019;94(12):1353–1363. Hampel PJ, et al. *Blood Cancer J.* 2022;12(9):124.
Barr PM, et al. *Blood Adv.* 2022;6(11):3440–3450. Frustaci AM, et al. *Cancers (Basel)*. 2023;15(5). Kaptein A et al. *Blood*. 2018;132(Suppl 1):1871.

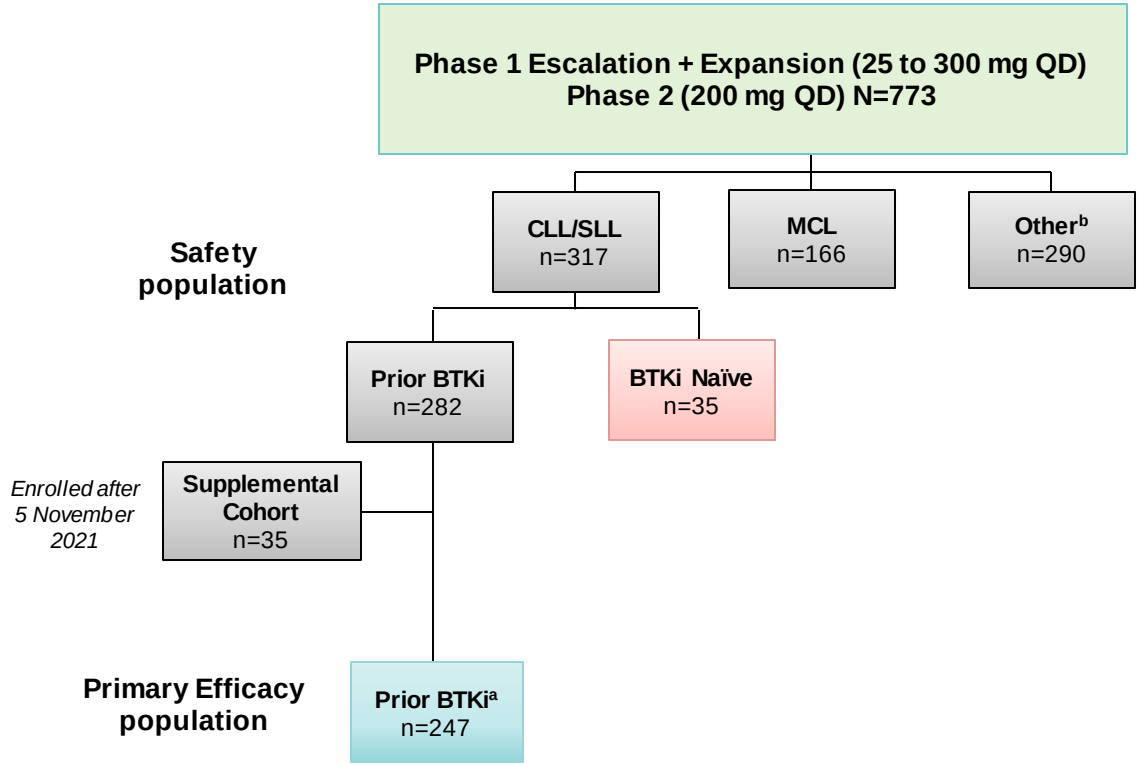
Covalent vs. Noncovalent BTKis

Covalent BTKi	Noncovalent BTKi
Ibrutinib Acalabrutinib Zanubrutinib	Pirtobrutinib Nemtabrutinib*
Inhibited	No inhibition
Both wild type and mutant BTK inhibited	

* Nemtabrutinib is not FDA-approved for the treatment of CLL

Tambaro FP, et al. *J Exp Pharmacol.* 2021;13:923-935.

Pirtobrutinib in Covalent BTK-Inhibitor Pre-Treated R/R CLL/SLL and MCL Phase 1/2 BRUIN Study: Design, Eligibility, and Enrollment



Phase 1 3+3 design

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

Eligibility

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

Key endpoints

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

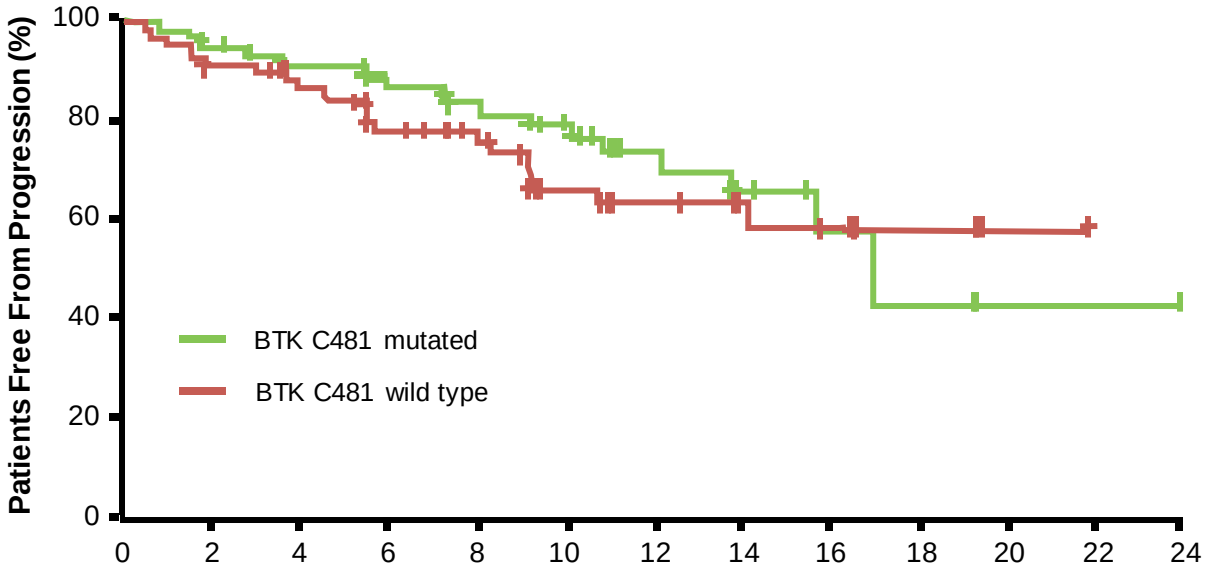
Primary efficacy population[a]

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

DOR = duration of response; MCL = mantle cell lymphoma; MTD = maximum tolerated dose; ORR = overall response rate.

Mato AR, et al. *Blood*. 2022;140(suppl 1):2316-2320.

BRUIN:
PFS in High-Risk CLL Subgroups

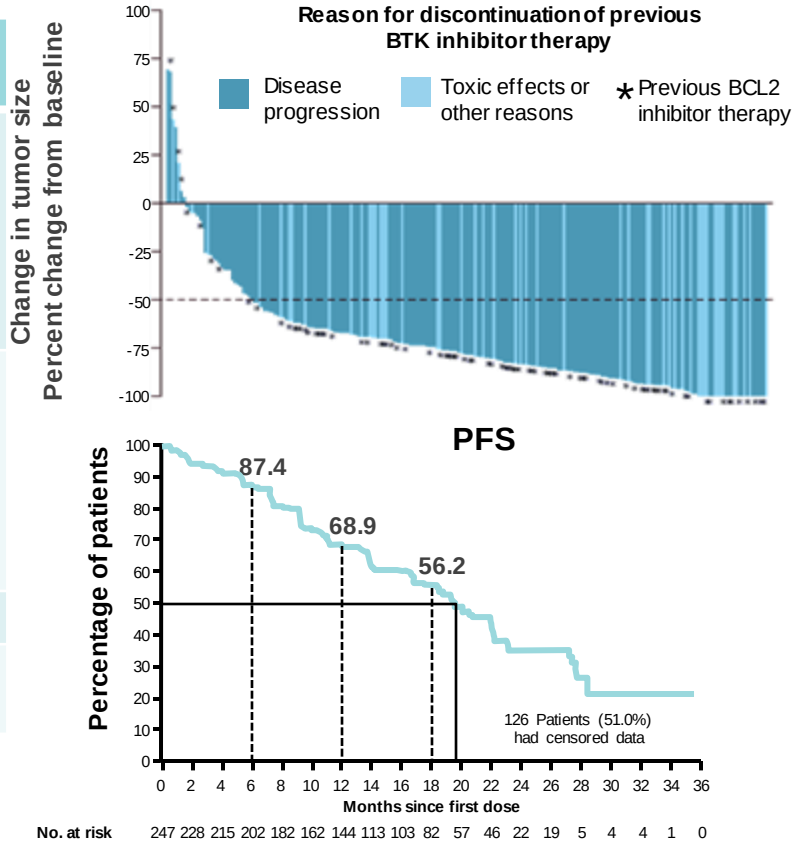


Patients at Risk, n													
***BTK* C481 mutated**	84	68	54	49	40	33	18	10	7	3	1	1	0
***BTK* C481 wild type**	74	62	52	40	35	23	19	13	11	5	1	0	

Mato AR, et al. European Hematology Association Annual Congress; Vienna, Austria; June 9-17, 2022. Abstract S147.

BRUIN Phase I/II Trial: Efficacy of Pirtobrutinib in R/R CLL/SLL

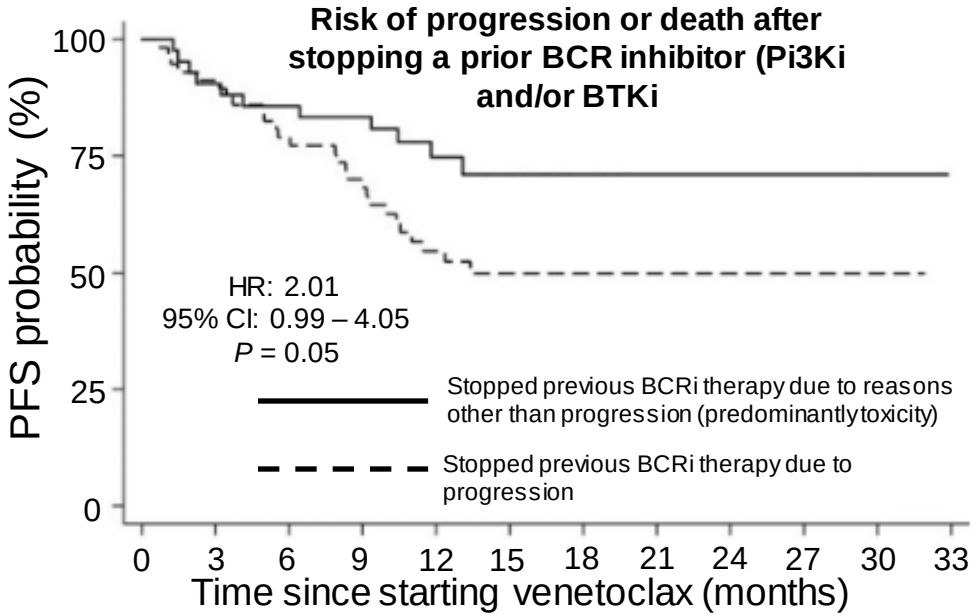
Variable	Previous BTKi (n = 247)	Previous BTKi + BCL2i (n = 100)
ORR, % (95% CI)		
• Including CR, nodular PR, or PR	73.3 (67.3–78.7)	70.0 (60.0–78.8)
• Including CR, nodular PR, PR, or PR with lymphocytosis	82.2 (76.8–86.7)	79.0 (69.7–86.5)
Best response, %		
• CR	1.6	0
• Nodular PR	0.4	0
• PR	71.3	70.0
• PR with lymphocytosis	8.9	9.0
• SD	10.5	11.0
mPFS, months (95% CI)	19.6 (16.9–22.1)	16.8 (13.2–18.7)
Median follow-up, months	19.4	18.2



BCL2i = B-cell lymphoma 2 inhibitor.

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

Venetoclax after BTK Inhibitor



Takeaway: Reason(s) for stopping BCR inhibitor (Pi3Ki and/or BTKi) influences venetoclax outcomes

Multicenter retrospective: 98 patients with R/R CLL who received venetoclax after BCR inhibitor (Pi3Ki and/or BTKi). At ≥ 2 lines:

- 60% previously received a BTKi
- 25% previously received a Pi3Ki
- 10% previously received both

Challenges to utilizing venetoclax include complexity of the ramp-up and caution in patients with significant renal dysfunction

BCRi = B cell receptor inhibitor; BTKi = Bruton Tyrosine Kinase inhibitor; Pi3Ki = phosphoinositide 3-kinase inhibitor;. R/R = relapsed/refractory.

Eyre TA, et al. *Br J Haematol.* 2019;185:656-669.

Liso-cel anti-CD19 CAR-T: TRANSCEND CLL 004 – Efficacy outcomes (DL2 only)

	Full study population at DL2 (n = 88)	BTKi progression/venetoclax failure subset at DL2 (n = 50)
Primary endpoint: IRC-assessed CR/CRi rate per iwCLL 2018, n (%) [95% CI]	17 (19) [12—29]	10 (20) [10—34]
Key secondary endpoints		
IRC-assessed ORR, n (%) [95% CI]	42 (48) [37—59]	22 (44) [30—59]
uMRD rate in blood, n (%) [95% CI]	58 (66) [55—76]	32 (64) [49—77]
Exploratory endpoint: uMRD rate in marrow, n (%) [95% CI]	53 (60) [49—71]	30 (60) [45—74]
Other secondary endpoints		
Best overall response, n (%)		
CR/CRi	17 (19)	10 (20)
PR/nPR	25 (28)	12 (24)
SD	34 (39)	21 (42)
PD	6 (7)	4 (8)
Not evaluable	6 (7)	3 (6)
Time to first response, months, median (range)	1.3 (0.8—17.4)	1.1 (0.8—17.4)
Time to first CR/CRi, months, median (range)	5.5 (0.8—18.0)	2.1 (0.8—18.0)

- uMRD was achieved in MRD-evaluable patients in the full population at DL2 by:
  - 15/15 (100%) patients with CR/CRi in blood and 15[a]/16 (94%) in marrow
  - 24/24 (100%) patients with PR/nPR in blood and 23/23 (100%) in marrow
  - 19/32 (59%) patients with SD in blood and 15/32 (47%) in marrow

[a]One patient had an indeterminate status for MRD, which was considered positive as per FDA guidelines. SD = stable disease.

Siddiqi T, et al. 65th American Society of Hematology [ASH®] Meeting and Exposition. 2023. [Presentation #330].

Differentiating Common and Serious Adverse Effects with CLL Treatments

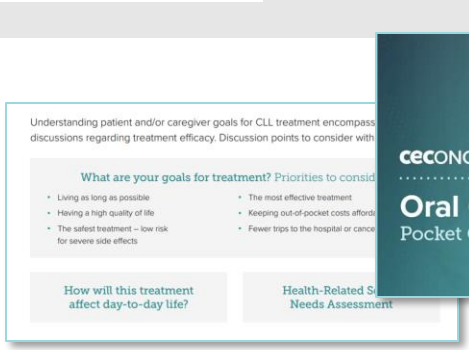
Develop plans for managing AEs arising from new and emerging CLL treatment approaches, as well as long-term and late effects of treatments

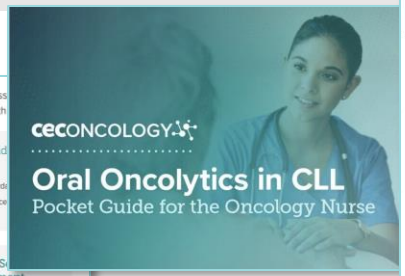
LEARNING OBJECTIVE 2

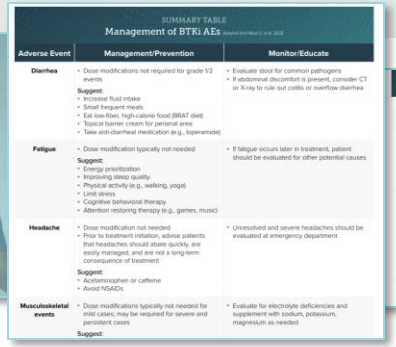
Resource

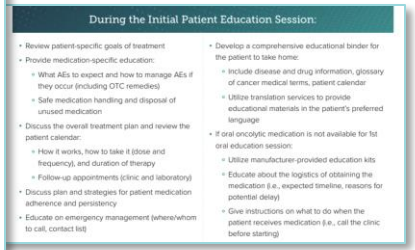
Scan the QR Code or click resources tab during the program

Access a digital online pocket guide for oncology nurses on oral Oncolytics that includes information on assessing patient goals for therapy and quick references for adverse event counseling and management

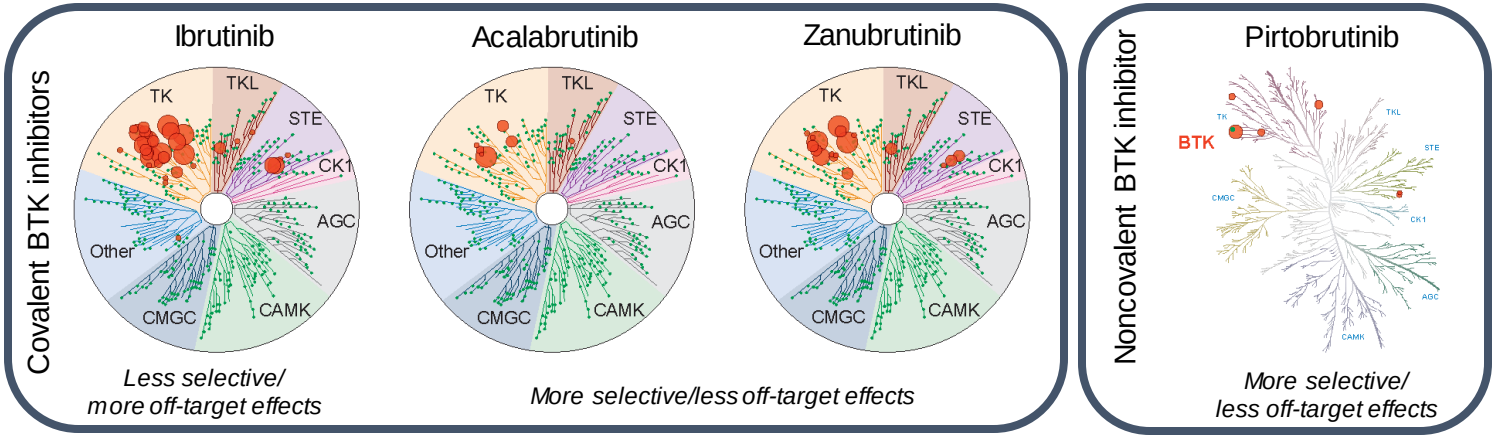








What Are the Implications of Covalent and Noncovalent BTKi Selectivity for Off-Target Effects



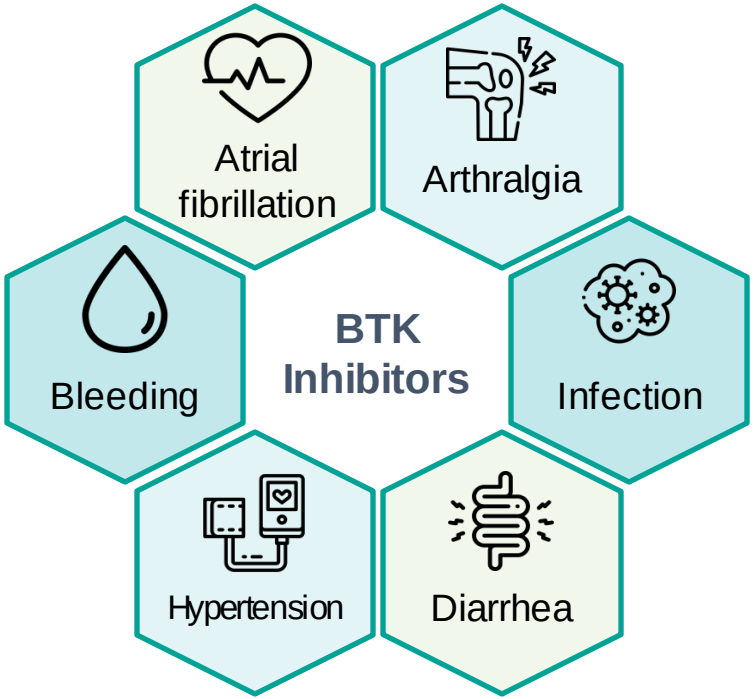
Less selective BTK inhibitors (e.g., ibrutinib) have more off-target effects, which contribute to more toxicity compared with more selective agents

Potential off-target effects include:

AGC = containing PKA, PKG, PKC families; BTK = Bruton's tyrosine kinase; BTKi = Bruton's tyrosine kinase inhibitor; CAMK = calcium/calmodulin-dependent protein kinase; CK1 = casein kinase 1; CMGC = containing CDK, MAPK, GSK3, CLK families; EGFR = epidermal grow th factor receptor; STE = homologs of yeast Sterile 7, Sterile 11, Sterile 20 kinases; TEC = tyrosine kinase expressed in hepatocellular carcinoma; TK = tyrosine kinase; TKL = tyrosine kinase-like. Gaballa S, et al. *Curr Hematol Malig Rep*. 2021;16(5):422-432. Kaptein A, et al. *Blood*. 2018;132(Suppl 1):1871. Thompson PA, Tam CS. *Blood*.2023;141(26):3137-3142.

Overview of BTK Inhibitor Toxicities in CLL

Common Toxicities



Additional Important Toxicities

- Dermatologic changes
- Fatigue
- Ventricular arrhythmia
- Cytopenias

Nixon S, et al. *Curr Oncol*. 2023;30(4):4222-4245.

Common Adverse Events (AEs) of BTK Inhibitors in CLL (≥ 25%)

Adverse Event	Ibrutinib	Acalabrutinib	Zanubrutinib	Pirtobrutinib
Cytopenias (neutropenia, anemia, thrombocytopenia)	✓	✓	✓	✓
Diarrhea	✓	✓	✓	✓
Myalgia, arthralgia, or musculoskeletal pain	✓	✓	✓	✓
Rash	✓	✓	✓	
Fatigue	✓	✓	✓	✓
Upper respiratory tract infection	✓	✓	✓	
Bruising	✓	✓		✓
Headache	✓	✓		
Pyrexia and general infections	✓	✓		
Peripheral edema	✓			
Nausea	✓			
Cough				✓

BRUKINSA® (zanubrutinib) [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/213217s011lbl.pdf.
CALQUENCE® (acalabrutinib capsules) [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/210259s009lbl.pdf.
CALQUENCE® (acalabrutinib maleate tablets) [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/216387Orig2s000Correctedlbl.pdf.
IMBRUVICA® (ibrutinib) [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/217003s002lbl.pdf.
JAYPIRCA® (pirtobrutinib) [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/216059s001lbl.pdf.

Serious AEs of BTK Inhibitors

- Hemorrhage
- Atrial fibrillation and flutter; risk factors include:
  - Age ≥ 65, male, history of Afib, hypertension, hyperlipidemia, or pre-existing cardiac disease
- Grade ≥ 3 infections, including opportunistic infections
- Grade 3-4 cytopenias
- Secondary primary malignancies

BTKi	Secondary Primary Malignancies
Ibrutinib	10% total, most common was non-melanoma skin cancer 4%
Acalabrutinib	12% total, most common was skin cancer 6%
Zanubrutinib	14% total, most common is non-melanoma skin cancer 8%, solid tumors 4%
Pirtobrutinib	9% total, most common was non-melanoma skin cancer 4%

Afib = atrial fibrillation.

Lipsky A, Lamanna N. *Am Soc Hematol Educ Program*. 2020;(1):336-345. Mato AR, et al. *N Engl J Med*. 2023;389:33-44. Nixon S, et al. *Curr Oncol*. 2023;30(4):4222-4245.

Management of BTKi AEs Summary Table

Adverse Event	Management Strategy
Atrial fibrillation	Monitor for Afib during treatment, administer DOACs, discontinue BTKi if Afib is not medically controllable
Bleeding events	Monitor for signs of bleeding, hold BTKi for 3–7 days before and after surgery, depending on the type of surgery and bleeding risk
Diarrhea	Use antidiarrheal medication (e.g., loperamide) as needed
Headache	Prior to treatment initiation, advise patients that headaches should abate quickly, are easily managed, and are not a long-term consequence of treatment; after treatment initiation, use acetaminophen or caffeine and avoid NSAIDS
Hypertension	Monitor for treatment-emergent HTN, manage with anti-HTN medication, reduce anti-HTN medication dose once BTKis are discontinued

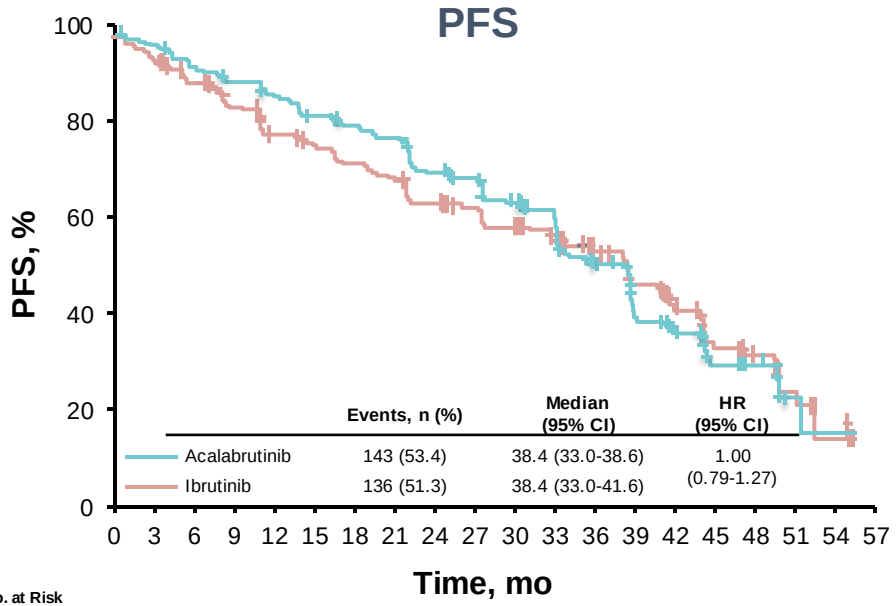
O'Brien SM, et al. *Front Oncol*. 2021;11:720704. Nixon S, et al. *Curr Oncol*. 2023;30(4):4222-4245.

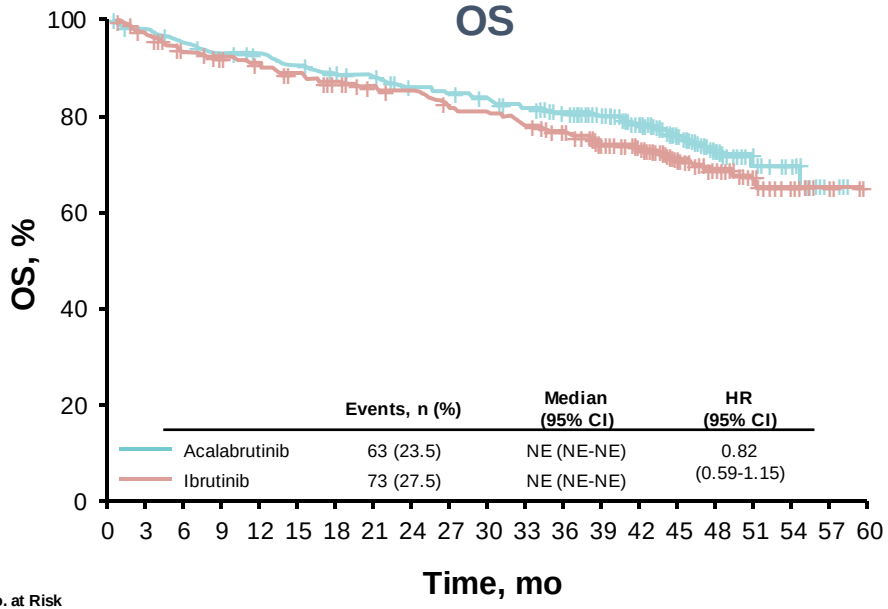
Management of BTKi AEs Summary Table (cont.)

Adverse Event	Management Strategy
Infection	Consider prophylaxis for patients at an increased risk of opportunistic infection, monitor for signs/symptoms of infection and treat as needed (consider drug-drug interactions with BTKi)
Myalgia/arthralgia	Grade 1 myalgias/arthralgias may not need intervention, use dose reduction or dose interruption as appropriate
Nausea	BTKis can be taken at night, but also utilize antinausea therapies to manage
Neutropenia	• 1st–3rd occurrences of grade 3–4: growth factor support is recommended, and dose interruptions can be considered • 4th occurrence: discontinuation of the BTKi should be considered
Rash	Topical steroids and/or oral antihistamines
Thrombocytopenia	• 1st–3rd occurrences of grade 3–4: dose interruptions should be considered • 4th occurrence: discontinuation of the BTKi is recommended (unless thrombocytopenia is related to CLL infiltration in the bone marrow)

O'Brien SM, et al. *Front Oncol*. 2021;11:720704. Nixon S, et al. *Curr Oncol*. 2023;30(4):4222-4245.

ELEVATE-RR (Acalabrutinib vs. Ibrutinib): PFS and OS





No. at Risk																				
Acalabrutinib	268	250	235	227	219	207	200	193	173	163	148	110	84	59	31	21	13	3	1	0
Ibrutinib	265	240	221	205	186	178	168	160	148	142	130	108	81	66	41	26	15	8	2	0

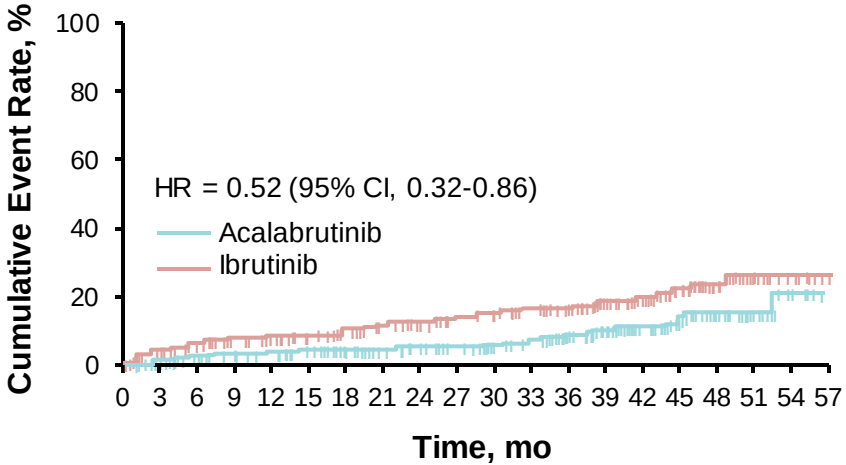
No. at Risk																							
Acalabrutinib	268	259	247	242	236	231	223	218	210	207	201	196	183	155	127	95	59	32	18	4	0		
Ibrutinib	265	252	241	233	227	220	212	205	203	194	191	186	173	143	121	88	60	28	15	2	0		

OS = overall survival; PFS = progression free survival.

Byrd JC, et al. *J Clin Oncol*. 2021;39(31):3441-3452.

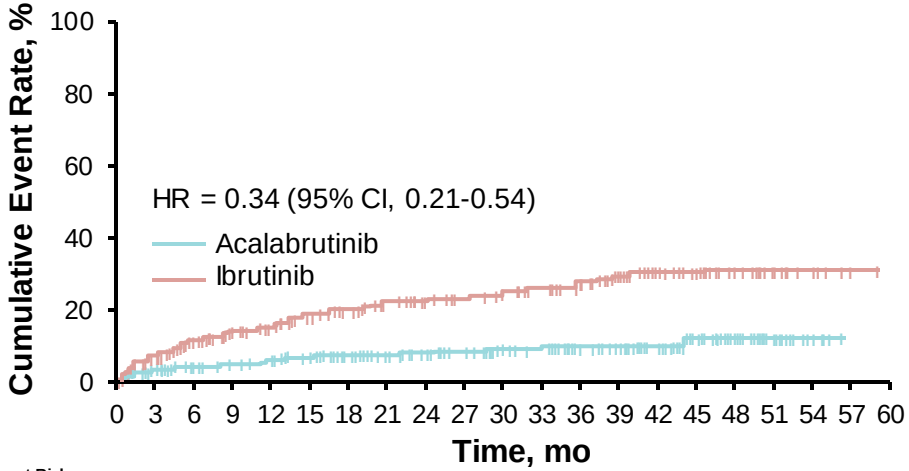
ELEVATE-RR: Cardiac AEs of Interest

Atrial Fibrillation



No. at Risk																				
Acalabrutinib	268	255	240	231	228	218	206	197	188	183	172	167	142	115	89	58	35	19	8	0
Ibrutinib	263	241	224	208	199	185	176	166	156	143	136	128	117	96	73	56	26	18	8	0

Hypertension

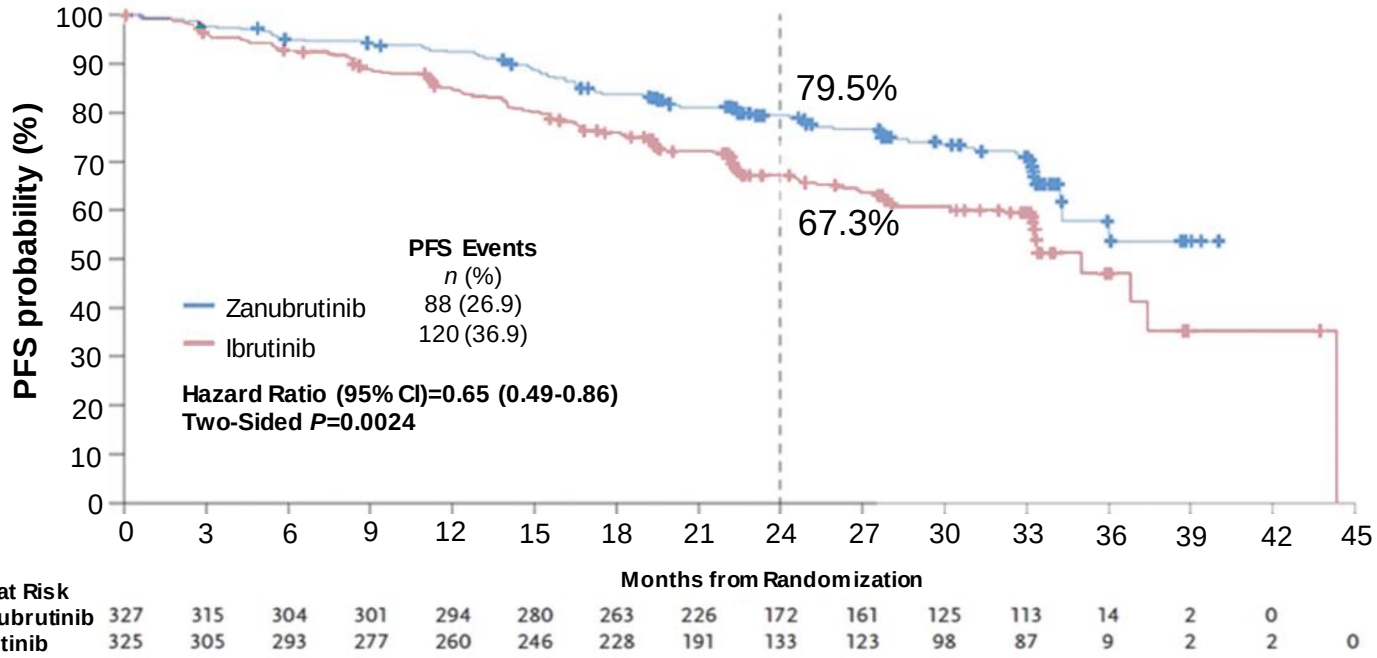


No. at Risk																					
Acalabrutinib	266	246	229	220	216	205	193	184	176	169	157	153	136	114	89	60	34	17	5	0	0
Ibrutinib	263	230	203	183	170	153	141	130	120	111	104	98	85	69	48	40	27	15	7	1	0

Byrd JC, et al. *J Clin Oncol*. 2021;39(31):3441-3452.

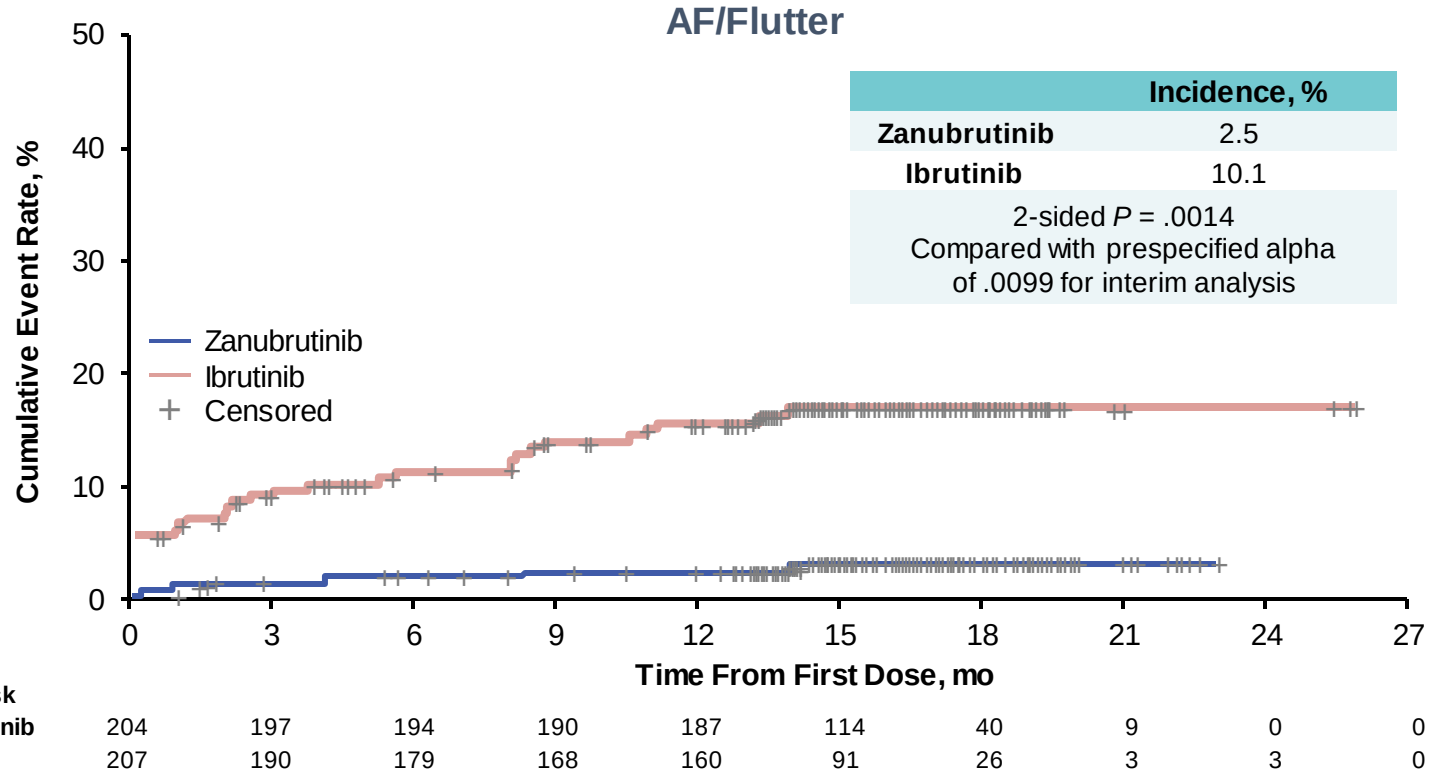
ALPINE: Improved ORR and PFS With Zanubrutinib vs. Ibrutinib in R/R CLL/SLL

After a median follow-up of 29.6 months, improved PFS with zanubrutinib intent-to-treat population



Brown JR, et al. 64th American Society of Hematology Annual Meeting: New Orleans, LA;2022. Abstract LBA-6.

ALPINE: Safety Analysis Showed Lower Rates of AF/Flutter With Zanubrutinib



	Incidence, %
Zanubrutinib	2.5
Ibrutinib	10.1

2-sided *P* = .0014
Compared with prespecified alpha of .0099 for interim analysis

No. at Risk										
Zanubrutinib	204	197	194	190	187	114	40	9	0	0
Ibrutinib	207	190	179	168	160	91	26	3	3	0

Hillmen P, et al. European Hematology Association Annual Congress; 2021. Abstract LB1900.

Sequential Use of Acalabrutinib in Patients with Ibrutinib Intolerance Is an Effective and Safe Option

AE	No. of Patients With Ibrutinib Intolerance[a]	Acalabrutinib Experience for Same Patients, n			
		Total	Lower Grade	Same Grade	Higher Grade
Atrial fibrillation	16[b]	2	2	0	0
Diarrhea	7	5	3	2	0
Rash	7	3	3	0	0
Bleeding[c,d]	6	5	3	2	0
Arthralgia	7[e]	2	1	1	0
Total	41	24	18	6	1

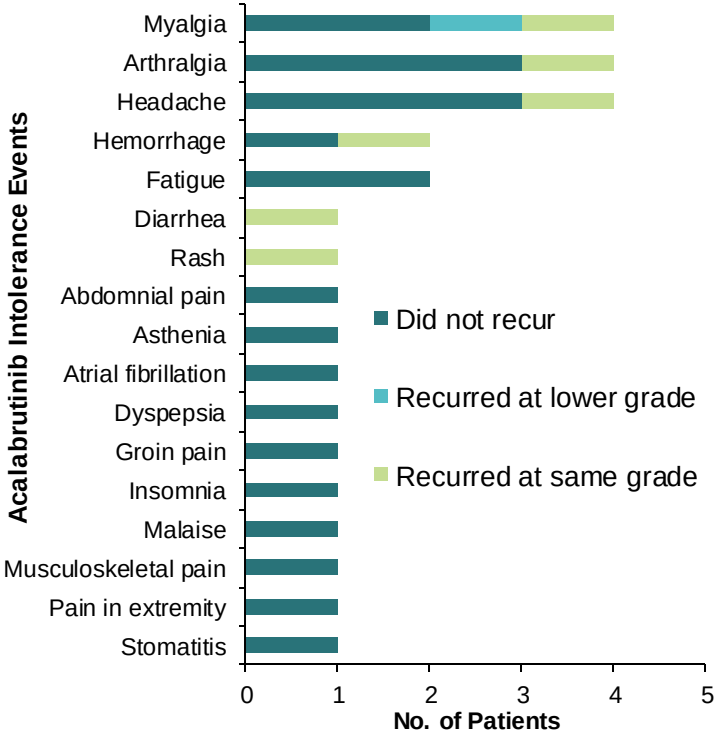
[a]Among 60 patients meeting the study enrollment criteria, 41 patients had a medical history of ≥ 1 (43 events in total) of the following categories of ibrutinib-intolerance events: AF, diarrhea, rash, bleeding, or arthralgia. [b] Includes patients with atrial flutter (n = 2). [c] Events categorized as bleeding included ecchymosis, hemorrhage, epistaxis, contusion, hematuria, and subdural hematoma. [d] All but 1 patient experienced a different type of bleeding event with acalabrutinib compared with ibrutinib treatment. [e] Includes 1 patient with arthritis.

Rogers KA, et al. *Haematologica*. 2021;106(9):2364-2373.

Zanubrutinib: BTK Inhibitor Intolerance

- Prior evidence has shown that zanubrutinib was effective in B-cell cancer patients intolerant of ibrutinib or acalabrutinib[1]
- For example, of 87 ibrutinib-intolerant events, 72 intolerant events (83%) did not recur
- Disease was controlled in 13 (93%) of 14 efficacy-evaluable patients treated with zanubrutinib, and 11 (65%) did not experience any recurrence of prior intolerance events

ASH 2022: zanubrutinib in acalabrutinib-intolerant patients with B-cell malignancies[2]



[a]No intolerance AEs recurred at a higher grade. ASH, American Society of Hematology;

1. Shadman M, et al. ASCO 2021. Abstract e19506. 2. Shadman M, et al. ASH 2022. Abstract 1587.

Audience Response

Ms. Y started acalabrutinib 5 months ago for CLL and has had persistent arthralgia. Despite following your suggestions to alleviate the pain, the arthralgia persists, significantly impacting her daily life. What other options would be appropriate given her intolerance to acalabrutinib?

A. Zanubrutinib
B. Zanubrutinib or pirtobrutinib
C. Zanubrutinib or ibrutinib
D. Pirtobrutinib

Important Drug Interactions with BTK Inhibitors

	Ibrutinib	Acalabrutinib	Zanubrutinib	Pirtobrutinib
Strong CYP3A Inhibitors	Avoid	Avoid	Reduce dose	Avoid
Moderate CYP3A Inhibitors	Reduce dose	Reduce dose	Reduce dose	
CYP3A Inducers	Avoid	Avoid	Avoid	Avoid
Warfarin/Vitamin K antagonists	Avoid			
Proton pump inhibitors	Avoid only with capsule formulation			
Renal impairment	Mild/moderate: no dose adjustment needed	Mild/moderate: no dose adjustment needed		Severe: Reduce dose
Hepatic Impairment	Mild/moderate: reduce dose Severe: avoid	Severe: avoid	Severe: reduce dose	
Administer with caution	• Drugs that prolong the PR interval • Anticoagulants/antiplatelets • BCRP and P-gp substrates	BCRP and MATE1 substrates		Sensitive CYP2C8, CYP2C19, CYP3A, P-gp, or BCRP Substrates
		Consider the risk/benefit of anticoagulants or antiplatelets		

Nixon S, et al. Curr Oncol. 2023;30(4):4222-4245. Nixon S, et al. *Curr Oncol*. 2023;30(4):4222-4245. BRUKINSA® (zanubrutinib) [package inserthttps://www.accessdata.fda.gov/drugsatfda_docs/label/2024/213217s011lbl.pdf.
CALQUENCE® (acalabrutinib capsules) [package inserthttps://www.accessdata.fda.gov/drugsatfda_docs/label/2022/210259s009lbl.pdf. CALQUENCE® (acalabrutinib maleate tablets) [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/216387Orig2s000Correctedlbl.pdf. IMBRUVICA® (ibrutinib) [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/217003s002lbl.pdf.
JAYPIRCA® (pirtobrutinib) [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/216059s001lbl.pdf.

BTKi Therapy Sequencing

Covalent BTKi Resistance

- Ibrutinib → Noncovalent (pirtobrutinib)
- Acalabrutinib → Noncovalent (pirtobrutinib)
- Zanubrutinib → Noncovalent (pirtobrutinib)

Covalent BTKi Intolerance

- Ibrutinib → Acalabrutinib or zanubrutinib or noncovalent (pirtobrutinib)
- Acalabrutinib → Zanubrutinib or noncovalent (pirtobrutinib)
- Zanubrutinib → Acalabrutinib or noncovalent (pirtobrutinib)

Shadman M, et al. Blood. 2023;142(suppl 1):3279. Mato AR, et al. *N Engl J Med.* 2023;389:33-44. Wierda G, et al. *J Natl Compr Canc Netw.* 2024;22(3):175–204.

Differentiating Factors BTK Inhibitors (BTKi)

	Ibrutinib	Acalabrutinib	Zanubrutinib	Pirtobrutinib
Dose	420 mg PO daily	100 mg PO Q12H	160 mg PO BID or 320 mg PO daily	200 mg PO daily
Dose modifications needed when	Used with CYP3A inhibitors; mild-moderate hepatic impairment	Used with CYP3A inhibitors or inducers	Used with CYP3A inhibitors; severe hepatic impairment	Used with CYP3A inhibitors or inducers; severe renal impairment.
Administration	Take with or without food at approximately the same time(s) each day			
Dosage forms	Capsules: 70 mg, 140 mg Tablets: 140 mg, 280 mg, 420 mg Oral Suspension: 70 mg/ml	Capsules: 100 mg Tablets: 100 mg	Capsules: 80 mg	Tablets: 50 mg, 100 mg
Drug interactions	Avoid P-gp substrates	Capsules: avoid PPIs; take acala at least 2 hours before H2RAs or antacids Tablets: no issues using concurrent acid reducing agents		Sensitive CYP2C8, CYP2C19, CYP3A, P-gp, or BCRP Substrates
	Avoid concomitant use of CYP3A inhibitors and inducers			
Food interactions	Avoid grapefruit/grapefruit juice, Seville oranges (often in orange marmalade), and starfruit			
BTK C481S mutation associated resistance	Yes	Yes	Yes	No

Nixon S, et al. *Curr Oncol*. 2023;30(4):4222-4245. BRUKINSA® (zanubrutinib) [package inserthttps://www.accessdata.fda.gov/drugsatfda_docs/label/2024/213217s011lbl.pdf. CALQUENCE® (acalabrutinib capsules) [package inserthttps://www.accessdata.fda.gov/drugsatfda_docs/label/2022/210259s009lbl.pdf. CALQUENCE® (acalabrutinib maleate tablets) [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/216387Orig2s000Correctedlbl.pdf. IMBRUVICA® (ibrutinib) [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/217003s002lbl.pdf.
JAYPIRCA® (pirtobrutinib) [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/216059s001lbl.pdf.

Audience Response

Mr. J has been on initial therapy with ibrutinib for over 7 years for CLL. He is now progressing, and molecular analysis finds a BTK C481S mutation. He asks if he is still able to remain on a Bruton tyrosine kinase inhibitor (BTKi). What are his options?

A. He must discontinue treatment with a BTKi
B. Zanubrutinib
C. Pirtobrutinib
D. Acalabrutinib

Using Venetoclax in CLL

Dose modifications are needed when…	Used with CYP3A or P-glycoprotein inhibitors, or in patients with severe hepatic impairment
Administration	Take with food around the same time each day

Dosage forms	• Tablets: 10 mg, 50 mg, 100 mg; starter pack as well as 100 mg tablets, which are used for weeks 5 and beyond (28, 120, 180 count/bottle)
	• Each starter pack contains four weekly wallet blister packs
	  • Week 1 (14 × 10 mg tablets)
	  • Week 2 (7 × 50 mg tablets)
	  • Week 3 (7 × 100 mg tablets)
	  • Week 4 (14 × 100 mg tablets)

Drug interactions	CYP3A inhibitors, P-gp inhibitors
Food interactions	Avoid grapefruit/grapefruit juice, Seville oranges (often in marmalade), and starfruit

VENCLEXTA® (venetoclax tablets) [package insert]. North Chicago, IL: AbbVie Inc.; Revised 2022. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/208573s027lbl.pdf.

Common AEs with Venetoclax in CLL (≥ 20%)

When used in combination with obinutuzumab or rituximab or alone:

- Cytopenias (neutropenia, thrombocytopenia, anemia)
- Diarrhea
- Nausea
- Upper respiratory tract infection and cough
- Myalgia
- Pain
- Fatigue
- Edema

- Grade 3–4 neutropenia occurs in about 40% of patients on single-agent venetoclax
  - Increases to about 60% with the addition of anti-CD20 monoclonal antibodies
  - Increases to about 70% when used with BTKi
- Rates of febrile neutropenia are typically low, 3%–5%

VENCLEXTA® (venetoclax tablets) [package insert]. North Chicago, IL: AbbVie Inc.; Revised 2022. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/208573s027lbl.pdf. Fischer K, et al. *Hematology Am Soc Hemaol Educ Program*. 2020(1):357-362.

Serious AEs with Venetoclax in CLL

- Tumor lysis syndrome (TLS)
  - TLS is when a large number of cancer cells die within a short period of time, releasing their contents into the blood
  - For patients with CLL who followed the 5-week dose ramp up and TLS prophylaxis and monitoring measures, rates of TLS = 2%
  - Co-administration of venetoclax with strong CYP3A inhibitors at initiation and during the 5-week ramp-up phase is contraindicated
- Fatal and serious infections, such as pneumonia and sepsis, have occurred; monitor for signs and symptoms of infections and treat source of infection promptly, should they occur

Gupta A, Moore JA. *JAMA Oncol*. 2018; 4(6):895. VENCLEXTA® (venetoclax tablets) [package insert]. North Chicago, IL: AbbVie Inc.; Revised 2022. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/208573s027lbl.pdf.

Tumor Lysis Risk Factors

- Increased risk of TLS
  - When starting venetoclax therapy and during any dose increases (includes the ramp-up period)
  - High tumor burden
  - Decreased renal function
  - Splenomegaly
  - Concomitant use of venetoclax with P-gp inhibitors or strong/moderate CYP3A inhibitors
- Lab abnormalities
  - Increased potassium, uric acid, LDH, phosphorus
  - Decreased calcium
- Requires measure of absolute lymphocyte count (ALC) and imaging to determine disease burden and risk of TLS
- Pre-treatment labs to include TLS panel:
  - CBC, diff, platelets
  - CMPNL
  - Phosphorus
  - Uric Acid
  - Lactate dehydrogenase

Gupta A, Moore JA. *JAMA Oncol*. 2018; 4(6):895. VENCLEXTA® (venetoclax tablets) [package insert]. North Chicago, IL: AbbVie Inc.; Revised 2022. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/208573s027lbl.pdf.

Key Questions to Ask When Considering Fixed-duration Regimens

There is an increased risk for tumor lysis with venetoclax/obinutuzumab	• Can the patient stay adequately hydrated (1.2-2 L daily)?
Ramp-up dosing with venetoclax	• Can the patient be compliant with medications?
Frequent, long clinic visits are required for multiple labs and IV hydration	• Does the patient have transportation to and from the clinic?

IV = intravenous

When Administering Obinutuzumab Monitor for Infusion-related Reactions

Definition: any sign or symptom experienced by a patient, during or after the infusion of a pharmacologic or biologic agent

- Immediate = during or within 1 hour of infusion
- Delayed = 1 hour to 1 week after infusion

- Infusion reactions always involve the immune system
- May range from mild cutaneous symptoms to death
- Clinical manifestations are similar and require prompt assessment and management

Pre-medicate before each infusion

Have an established protocol for management

Pagani M, et al. *Allergy*. 2022;77:388-403. GAZYVA® (obinutuzumab) [package insert]. South San Francisco, CA: Genentech, Inc.; Revised 2022. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/125486s034lbl.pdf.

Audience Response

Mr. B is starting venetoclax + obinutuzumab as initial therapy for his CLL. You explain the need for frequent blood testing in the first two months to monitor for:

A. Electrolyte abnormalities
B. Tumor lysis syndrome
C. Hyperlipidemia
D. Transaminitis

Key Takeaways

- BTK and BCL2 inhibitors are widely utilized in CLL
- Covalent BTKIs are safe and effective
- Noncovalent BTKis can overcome resistance to covalent BTKis
- Combination regimens being used
- First CAR-T recently approved (2024)
- Shared decision making is needed due to multiple options
- Comprehensive and ongoing patient education and diligent monitoring is critical to optimizing patient outcomes

Patient-tethered Treatment Approaches

Incorporate strategies to address patient-related treatment barriers to improve adherence to CLL therapy.

LEARNING OBJECTIVE 3

Patient Engagement – Considerations Among a "Menu" of Treatment Options for CLL/SLL

Agent

- Oral – novel agents
- Infusion
- Combination of oral/IV therapies

Duration

- Fixed vs continuous duration therapies
- Time to achieve undetectable measurable residual disease (uMRD)

Outcome

- Disease control vs. deep remission

Toxicity profile & patient comorbidities

Cost

Key Components of Patient Counseling

Dosing

- Administration and dosing schedule
- Missed dose management
- Storage and disposal of unused medication

Drug-drug and drug-food interactions

Common and rare, but serious AEs

- Signs/symptoms and self-monitoring at home
- When to call the clinic and when to seek immediate medical attention

Shared Decision-making Tools

S	Seek your patient's participation
H	Help your patient explore and compare treatment options
A	Assess your patient's values and preferences
R	Reach a decision with your patient
E	Evaluate your patient's decision

Assess

- Patient's beliefs, behavior, knowledge

Advise

- Provide specific information about health risks and benefits of change

Agree

- Collaboratively set goals based on patient's interest and confidence in ability to change behavior

Assist

- Identify personal barriers, strategies, problem-solving techniques, and social support

Arrange

- Specify a plan for follow-up

Agency for Healthcare Research and Quality [AHRQ]. The SHARE Approach. 2014. http:// www.ahrq.gov/professionals/education/curriculum-tools/shareddecisionmaking/index.html. Sheridan SL, et al. *Am J Prev Med*. 2004;26(1):56-66.

Keys for Discussing CLL Treatment Options with Your Patients

- Informed decision making ≠ shared decision making (SDM)
- SDM is a back-and-forth flow of information
  - Provider shares information and recommendations with their patient
  - Patient shares their values and preferences with their provider
- The goal is to create alignment with the patient at every juncture (treatment naïve and R/R settings)
- It is important to meet the patient where they are and work with your team to overcome any challenges (i.e., social needs, financial barriers, language barriers, etc.)

Schrager SB, et al. *Fam Pract Manag*. 2017;24(3):5-10. Sanders JJ, et al. *J Palliat Med*. 2018;21(S2):S17-S27.

Keys for Discussing CLL Treatment Options with Your Patients (cont.)

- Considerations when recommending treatment to your patients

Patient-centric Approach

- Patient factors: comorbidities and past medical history
- Therapy factors: adverse events and intangible things (logistics), such as distance of travel to the clinic, ability to pay for medications, insurance coverage

Goal Concordant Care

- Understanding patient goals
- Setting expectations together
- Realigning expectations as needed
- Measuring success

Schrager SB, et al. *Fam Pract Manag*. 2017;24(3):5-10. Sanders JJ, et al. *J Palliat Med*. 2018;21(S2):S17-S27.

Optimizing Care for Patients on Oral Therapies

- Education by an oncology pharmacist or advanced practice provider or oncology nurse with planned follow-up
- Many specialty pharmacies conduct refill outreach, adherence assessments, quality of life, and clinical assessments at several timepoints during the patient's care
- Team approach to prevent or promptly manage adverse events is critical
  - Goal: prolong time on each treatment before needing to move to the next
  - Poorly managed AEs can compromise adherence and quality of life
  - Adherence impacts outcomes
    - Poor adherence to ibrutinib (missing 8 or more doses) was related to worse progression-free survival and this may also be applicable to other oral CLL therapies

Association of Community Cancer Centers (ACCC). STEPS TO SUCCESS: Implementing Oral Oncolytics. 2016. https://www.accc-cancer.org/docs/projects/pdf/implementing-oral-oncolytics-final.pdf?sfvrsn=274a112_0.

Oral Antineoplastics Program

Goal of Oral Antineoplastics Program:

- Reduce severity of side effects
- Reduce ER visits
- Reduce hospitalizations
- Reduce cost
- Increase adherence to treatment plan
- Increase patient satisfaction
- Meet OCM Requirements

Key Components:

- Oral Antineoplastics Nurse Navigator (OANN)
- Oral Antineoplastics Patient Pharmacy Advocate (PT)
- Oral Antineoplastics Pharmacist (Pharm)
- Interdisciplinary team
  - Provider
  - Nurse Coordinator (NC)
  - Clinical Pharmacists (PharmD)
  - Medical Assistant

Association of Community Cancer Centers (ACCC). STEPS TO SUCCESS: Implementing Oral Oncolytics. 2016. https://www.accc-cancer.org/docs/projects/pdf/implementing-oral-oncolytics-final.pdf?sfvrsn=274a112_0.

Oral Antineoplastics Program

Oral Antineoplastics Patient Pharmacy Advocate	Oral Antineoplastics Nurse Navigator	Oral Antineoplastics Pharmacist
Processes all Rxs for oral antineoplastic medications	Ensures chemotherapy consent completed and signed	Evaluates for on-label or off-label indication
Submits prior authorization request to insurance	Meets with or calls pt to provide tailored antineoplastic education	Evaluates for potential drug-drug interactions, drug-specific pre-treatment requirements
Determines need for Specialty Pharmacy	Updates medication list to include new oral antineoplastic med	
Applies for financial assistance(co-pay card, free drug, grant) when needed	Implements follow-up call algorithm	
Notifies OANN and Provider Team when Rx ready to be filled		

Association of Community Cancer Centers (ACCC). STEPS TO SUCCESS: Implementing Oral Oncolytics. 2016. https://www.accc-cancer.org/docs/projects/pdf/implementing-oral-oncolytics-final.pdf?sfvrsn=274a112_0.

Oral Antineoplastics Program

Oral Antineoplastics Nurse Navigator	
Initial Tailored Antineoplastic Education	**Tailored Antineoplastic Adherence and AE Management**
Diagnosis, goal, and duration of treatment	Follow-up calls weekly x 2, then every 2 weeks x 3 and prn
Dose and schedule	Taking medication as prescribed
What to do if dose missed	• If not, assess for barriers
Drug-food interactions	AEs
Safe storage and handling	• CTCAE grade of AE
Expected AEs and management strategies, including Rxs and OTCs	• Controlled with home medications
Symptoms that require emergent management	• Need same day clinic visit for symptom management
How to obtain refills	Review next OANN follow-up call
Disposal of unused medication	
How to take supplements	
Follow-up phone calls	
Follow-up appointments	

CTCAE = The Common Terminology Criteria for Adverse Events; OTC = over the counter. Association of Community Cancer Centers (ACCC). STEPS TO SUCCESS: Implementing Oral Oncolytics. 2016. https://www.accc-cancer.org/docs/projects/pdf/implementing-oral-oncolytics-final.pdf?sfvrsn=274a112_0.

SMART Goals

Specific, Measurable, Attainable, Relevant, Timely

- Take proactive measures to manage adverse events associated with CLL treatments and educate patients on self-monitoring for early and late treatment effects.
- Address common barriers to CLL therapy adherence with your multidisciplinary team and utilize a team-based approach to increase treatment adherence rates for patients on oral oncolytics.
- Implement a structured patient counseling program to educate patients with CLL on key variables influencing treatment selection, including risk category, genetic markers, and treatment goals, with the aim of increasing patient understanding and empowerment in decision-making.

QUESTIONS & ANSWERS

Thank you for joining us.
Don’t forget to collect your credit.

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cec ONCOLOGY

Guiding Light

Oncology Nurses' Vital Role in Supporting Patients through CLL Therapy

This activity is supported by educational grants from BeiGene USA Inc.; Janssen Biotech Inc., administered by Janssen Scientific Affairs LLC (both are Johnson & Johnson companies); and Lilly.