



CLL SOCIETY

Smart Patients Get Smart Care™

A GUIDE TO CLL / SLL TREATMENT SELECTION AND SEQUENCING

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SPEAKERS



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(SPEAKER)**

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(MODERATOR)

CLL Patient Advocate
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Smart Patients Get Smart Care™

A GUIDE TO CLL / SLL TREATMENT SELECTION AND SEQUENCING

Jennifer Woyach, MD

Director, Division of Hematology
The Ohio State University

OBJECTIVES

- **To introduce:**
 - Frontline treatment choices and testing/evaluation needed prior to frontline treatment
 - Treatment sequencing
 - Shared decision making
 - Clinical trials
 - Treatments on the horizon
- **To encourage questions!**



FRONTLINE THERAPY FOR CLL



WHAT INFORMATION IS NEEDED PRIOR TO TREATMENT?

- **Genetic risk of the CLL**
 - IGHV mutation status
 - FISH/cytogenetics
 - TP53 mutations
- **Other medical problems and medications**
- **Patient goals and preferences of treatment**
 - Shared decision making



INITIAL TREATMENT REGIMENS FOR CLL

- Targeted agents replaced chemoimmunotherapy for the treatment of CLL
- **BTK inhibitors** block B-cell receptor signaling resulting in long remissions but do not eliminate residual disease therefore are given continuously
- **BCL2 inhibitors** block an antiapoptotic protein resulting in rapid cell death and deep remissions allowing for fixed-duration treatment
- **Anti-CD20 antibodies** target a surface protein and engage the immune system



MECHANISM COVALENT BTK INHIBITORS (cBTKi)

- Binds to the **cysteine-481** residue on BTK
- Potent and irreversible inhibition of BTK
- All approved cBTKi bind at C481
 - Selectivity varies between drugs
 - Share resistance mechanisms

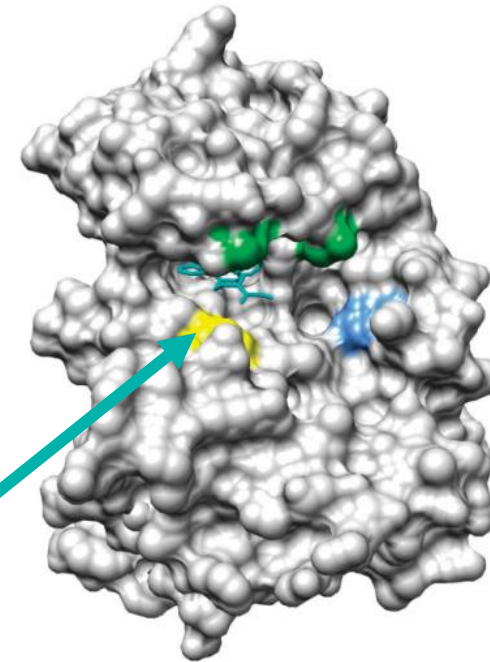
Covalent (cBTKi)

Ibrutinib

Acalabrutinib

Zanubrutinib

Cysteine 481



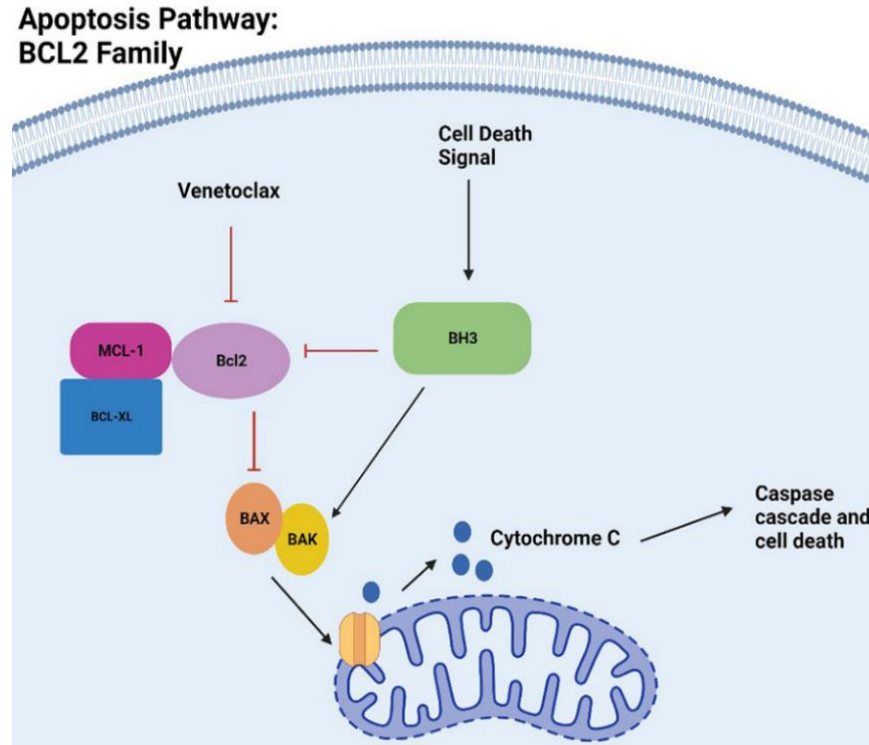
Modified from Hamasy et al., Leukemia 2017



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MECHANISM OF BCL2 INHIBITORS (VENETOCLAX)

- Binds to and inhibits the anti-apoptotic protein, BCL2
- CLL cells need this to survive
- Blocking BCL2 results in rapid cell death
- CLL cells are eliminated rapidly
- Risk for hyperacute tumor lysis syndrome (TLS)

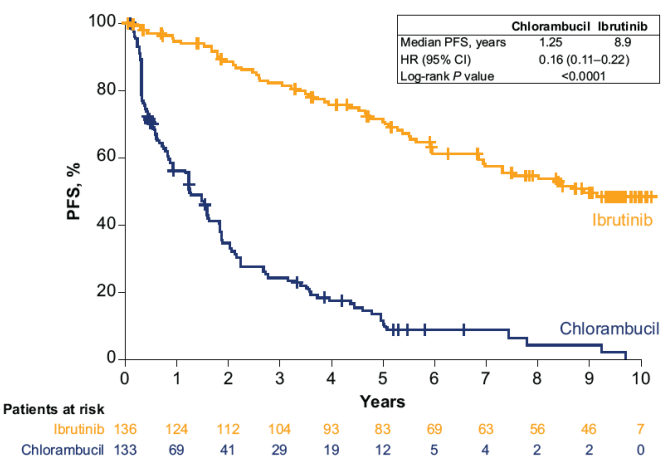


Reyes et al., Cancer Drug Resist 2023

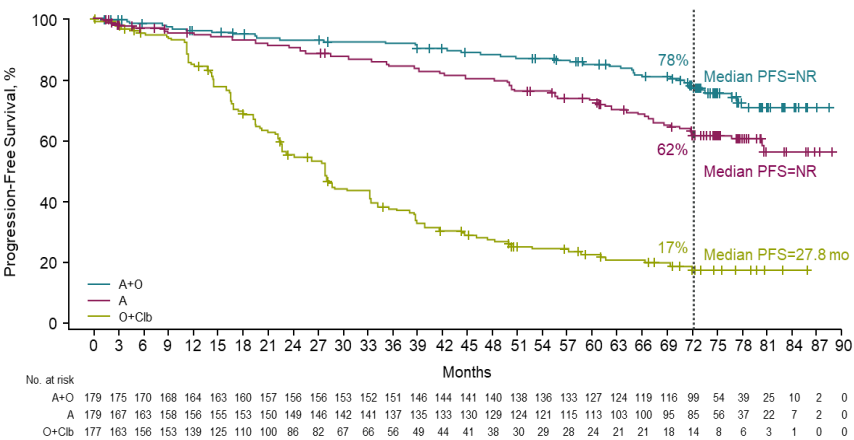
Reyes et al., Cancer Drug Resist 2023

BTKi ARE EFFECTIVE IN FRONTLINE CLL

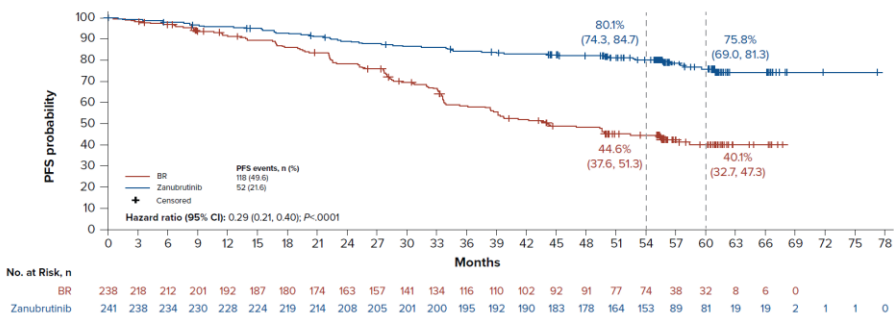
Ibrutinib median PFS 8.9 years



Acalabrutinib 6-year PFS 62%



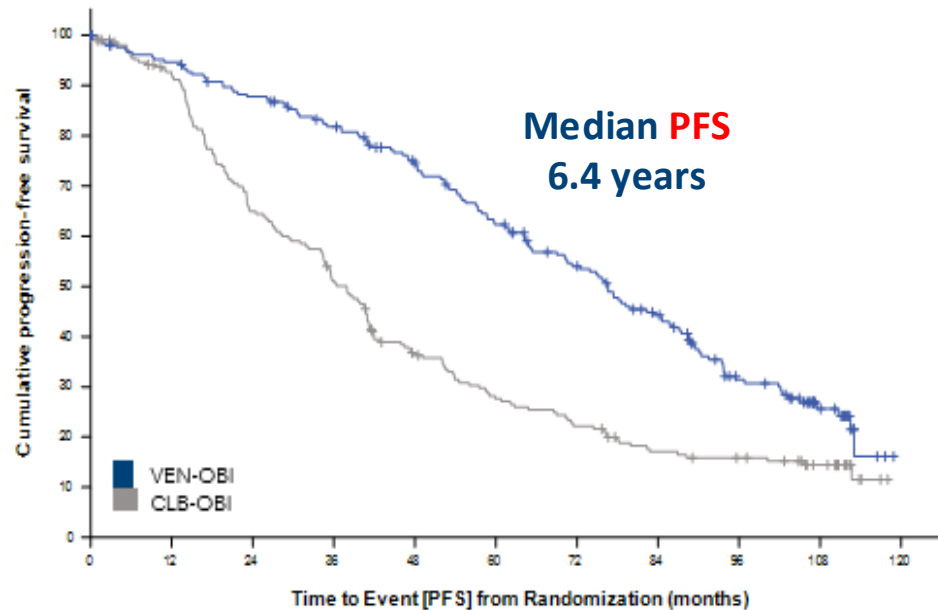
Zanubrutinib 5-year PFS 78%



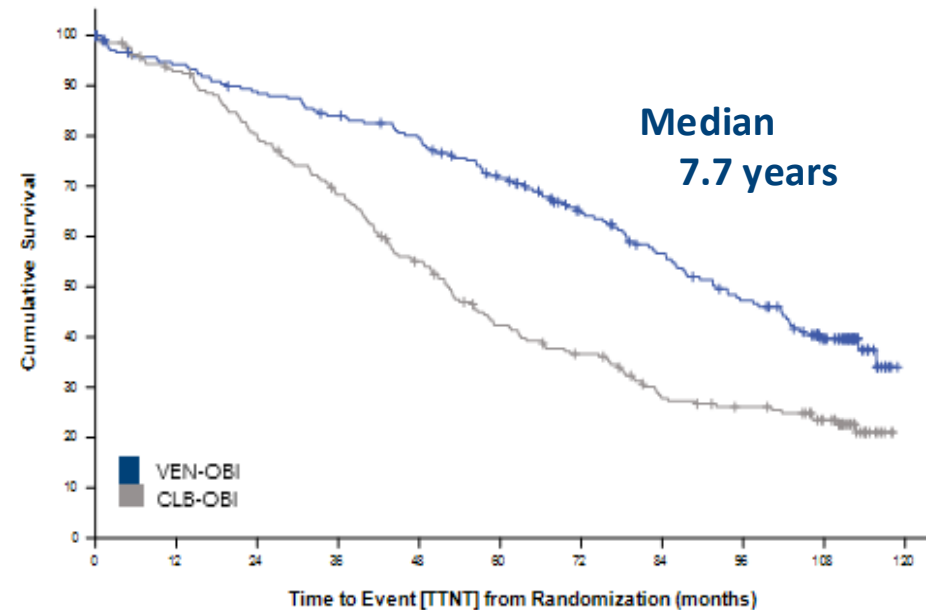
Burger EHA 2024, Sharman, ASH 2023, Shadman ASH 2024

VENETOCLAX PLUS OBINUTUZUMAB IS EFFECTIVE IN FRONTLINE CLL

Progression-Free Survival (PFS)



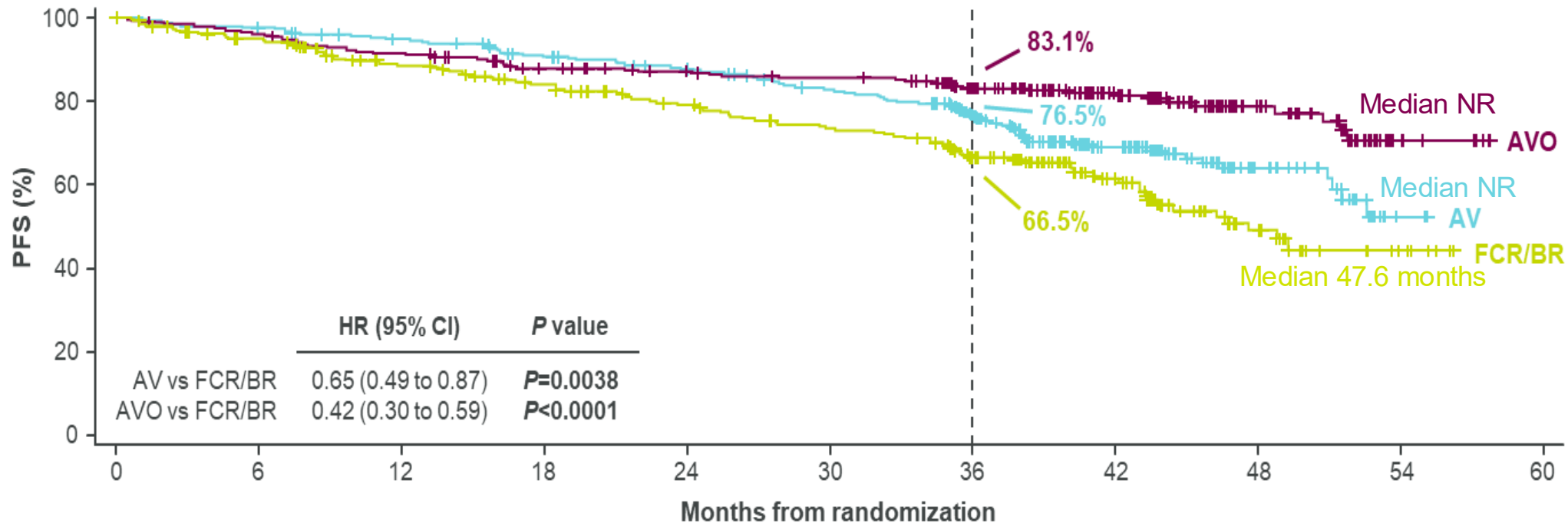
Time to Next Treatment (TTNT)



Fischer et al., EHA 2026

VENETOCLAX PLUS ACALABRUTINIB +/- OBINUTUZUMAB IS EFFECTIVE IN FRONTLINE CLL

Progression-Free Survival



Brown et al., NEJM 2025

SELECTION OF INITIAL CLL TREATMENT

	BTKi	BCL2i/Anti-CD20	BTKi/BCL2i
Pros	• Easy to start and use • All oral therapy	• Limits toxicity, cost, and drug resistance • No exposure to BTKi risks	• Limits toxicity, cost, and drug resistance • All oral therapy
Cons	• Continuous treatment • BTKi CV risks (hypertension, arrhythmias, and bleeding)	• 8-week start up (Obin+Ven) • Risk for TLS • Risk for infusion reactions	• 5-week ramp-up (Ven) • Risk for TLS • BTKi CV risks
CLL Feature Considerations	• Mitigates high-risk features: • del(17p)/TP53 mutations • IGHV unmutated status	• Long remissions for those with IGHV mutated CLL	• Long remissions for those with IGHV mutated CLL

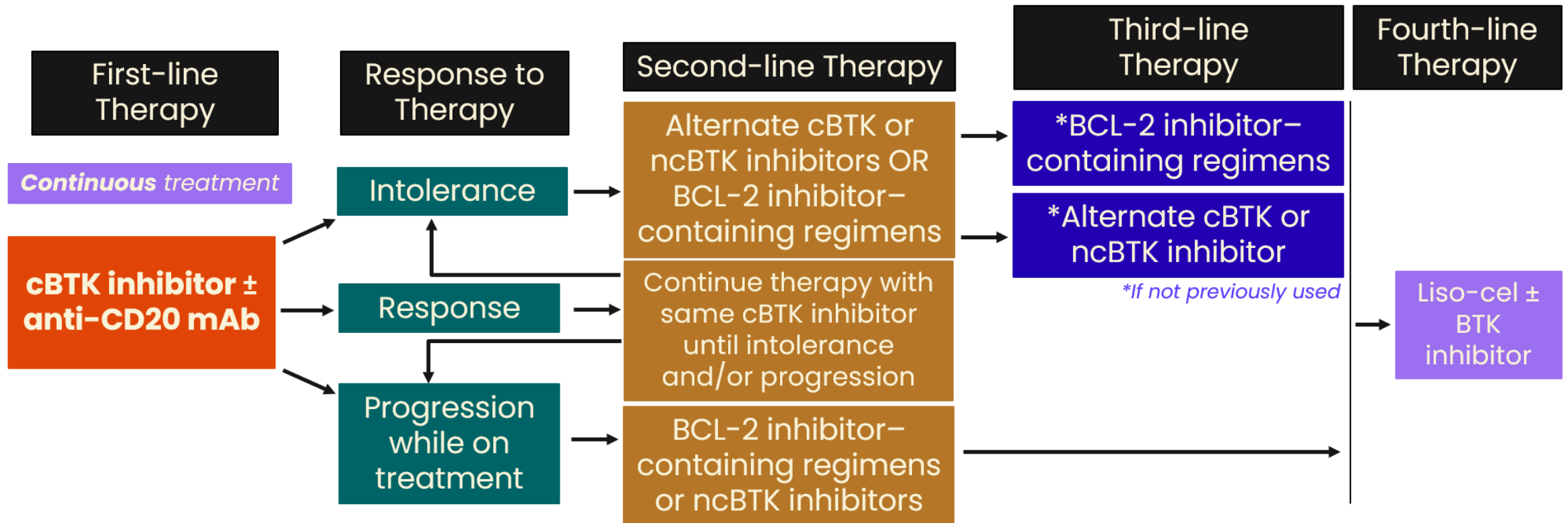
CV = Cardiovascular
TLS = Tumor Lysis Syndrome

WHAT'S NEXT?



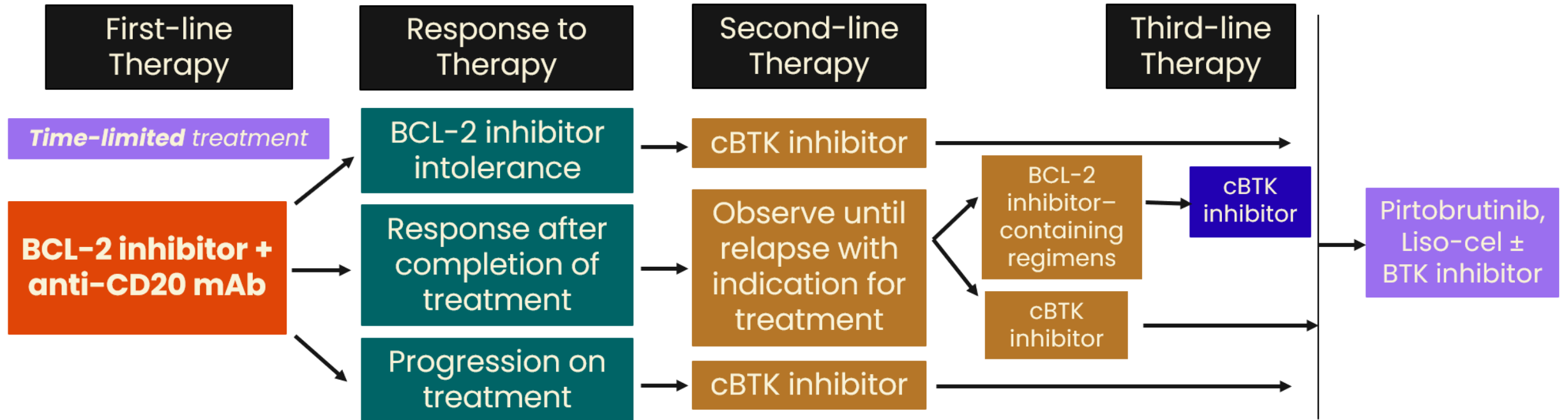
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IF FIRST TREATMENT IS COVALENT BTKi



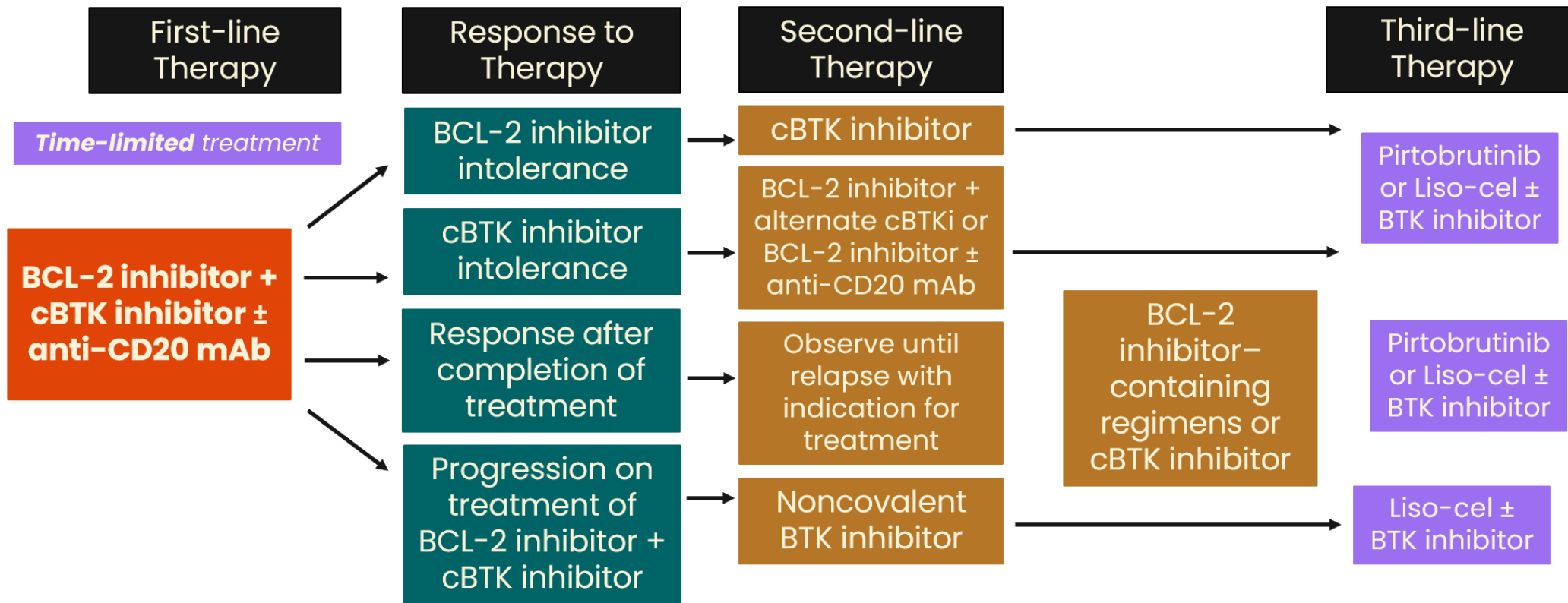
Adapted from NCCN guidelines 2026

IF FIRST TREATMENT IS VENETOCLAX PLUS OBINUTUZUMAB



Adapted from NCCN guidelines 2026

IF FIRST TREATMENT IS VENETOCLAX PLUS ACALABRUTINIB +/- ANTI-CD20 ANTIBODY

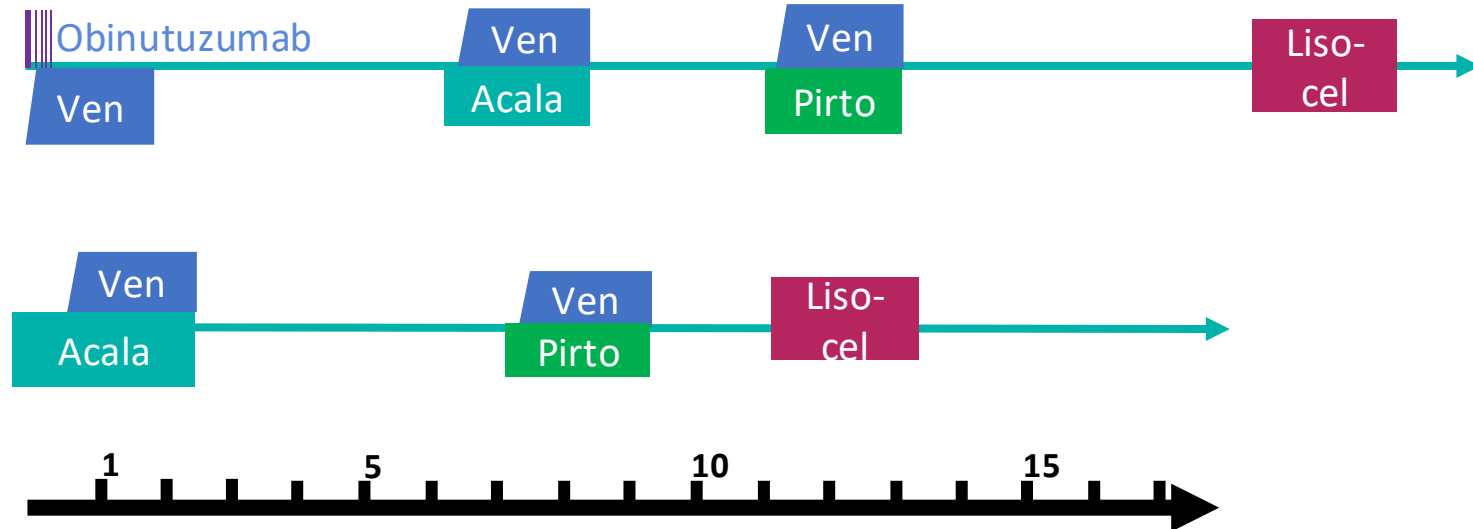


Adapted from NCCN guidelines 2026

PREFERENCES AND GOALS OF TREATMENT MAY SHAPE TREATMENT DECISIONS

If Goal Is TIME OFF TREATMENT

Most applicable for patients with low genetic risk disease

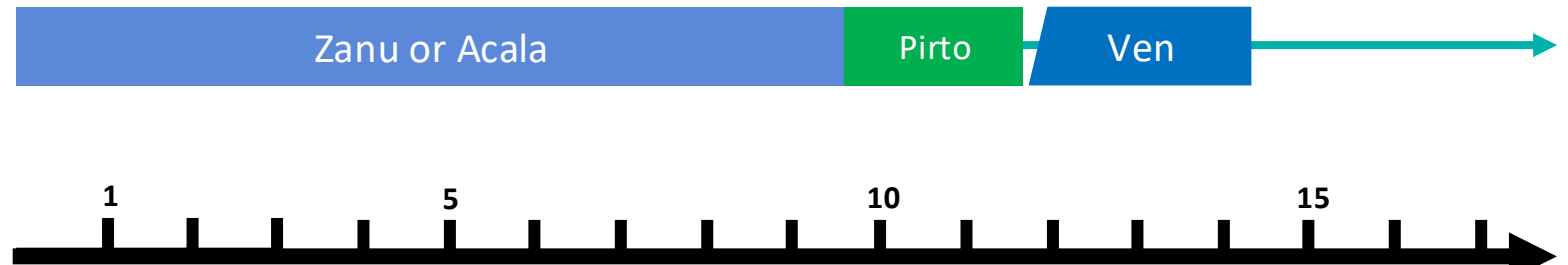


PREFERENCES AND GOALS OF TREATMENT MAY SHAPE TREATMENT DECISIONS

If Goal Is DECREASED VISITS TO CLINIC

Patients with

- Decreased mobility
- Child or elder care responsibilities; or
- Who live very far from clinic



SHARED DECISION MAKING

Medicine is best when patients and families are active partners—not passive recipients

- You are the expert on your own life, values, and what matters most to you.
- Your healthcare team is the expert on medical options, evidence, and outcomes.
- Shared decision making brings both kinds of expertise together.



WHAT SHARED DECISION MAKING MEANS

- A collaborative process in which patients and clinicians work together to make healthcare decisions informed by evidence, the care team's knowledge and experience, and the patient's values, goals, preferences, and circumstances.
- It is a deliberate departure from the old model where the doctor decided and the patient simply complied.
- Both the patient's lived experience and the clinician's medical knowledge are essential — neither alone is enough.
- Family members and caregivers are also an important part of this process.



WHAT SHARED DECISION MAKING IS AND ISN'T

× NOT Shared Decision Making

- × A pamphlet handed to you on your way out
- × The doctor telling you what to do
- × You deciding alone without guidance

✓ Shared Decision Making IS

- ✓ A two-way conversation where you play an active role
- ✓ Your provider sharing options and trade-offs
- ✓ You sharing what matters most to you
- ✓ Together arriving at the best choice for your situation



HOW TO PARTICIPATE MOST EFFECTIVELY



Before Your Appointment

Write down your questions, concerns, and what matters most to you



During Your Appointment

Ask *"What are my options?"* and *"What are the trade-offs?"*



Share What Matters to You

Tell your provider your goals, fears, and daily life priorities



Bring Support

Bring a family member or trusted person to help you listen and remember



Confirm Understanding

Ask your provider to use plain language and check that you understood



Take Your Time

It is always okay to say *"I need more time to decide"*



CLINICAL TRIALS

A clinical trial is a carefully designed research study that tests whether a new treatment is safe and helpful — not a last resort, but a genuine care option.

- A clinical trial may test new treatments, drug combinations, or approaches in real patients
- Every treatment used in CLL today — targeted therapies, combination regimens — was first proven in a clinical trial

WHY MIGHT YOU SEEK OUT A CLINICAL TRIAL?



Cutting-Edge Therapies

Access to targeted therapies not yet widely available outside of a trial setting.



Expert, Dedicated Monitoring

Close monitoring and expert attention from a specialized care team throughout the entire study.



Study Drug Often Covered

The cost of the study drug is typically covered by the trial, reducing your financial burden.

Clinical trials can offer access to promising new treatments and give you a meaningful role in advancing care for others with CLL.



Trials Actively Enrolling Worldwide

331+

active CLL clinical trials enrolling patients worldwide as of 2026.



Advancing Care for Future Patients

Your participation helps researchers discover what works best — directly benefiting future patients with CLL.



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THE FOUR PHASES OF A CLINICAL TRIAL

Each phase answers a different question, moving step by step from "is it safe?" to "is it better than what we already have?"

1

Phase 1 Safety

20-80 people

Finds safe dosages and identifies side effects and early signs of effectiveness in a small initial group.

2

Phase 2 Effectiveness

30-100 people

Tests whether the treatment actually works for the condition.

3

Phase 3 Comparison

200-1000 people

New treatment vs. current standard of care — the basis for FDA approval.

4

Phase 4 Post-Approval

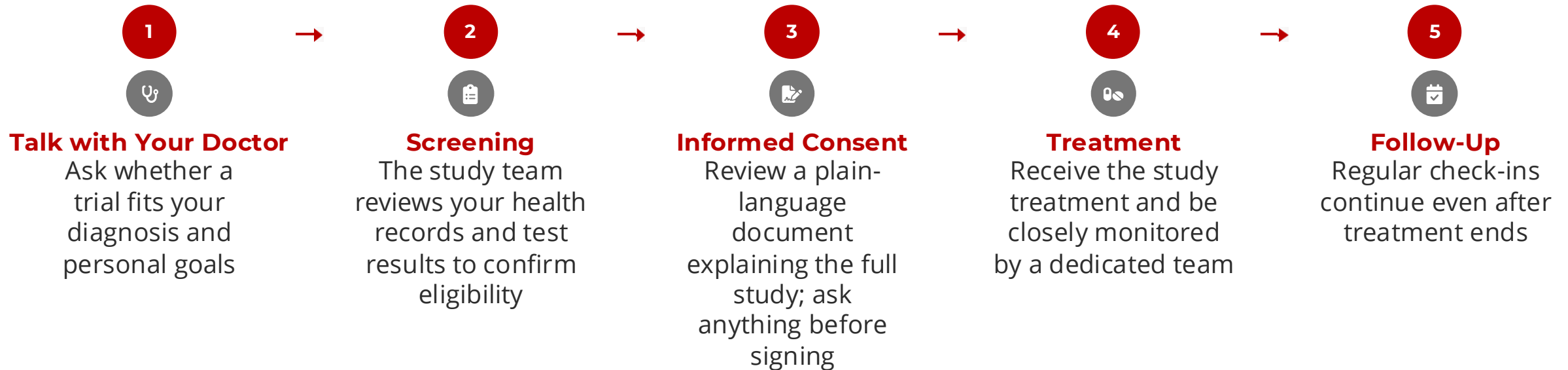
Ongoing

Ongoing monitoring of long-term safety and effectiveness in real-world use.



WHAT HAPPENS WHEN YOU JOIN A TRIAL?

Joining a trial is a step-by-step process with you in control at every stage — nothing happens without your full understanding and agreement.



RIGHTS OF A CLINICAL TRIAL PARTICIPANT

- **Right to full information:** every risk, benefit, and alternative must be explained clearly before you agree
- **Right to say no or stop:** your decision to join — or leave — never affects the quality of your other medical care
- A study coordinator is available to answer your questions at any point — you are never without support



QUESTIONS TO ASK YOUR CARE TEAM

- ❓ *"Is there a clinical trial that fits my stage and type of CLL?"*
- ❓ *"What phase is this trial and what is it designed to learn?"*
- ❓ *"What are the possible benefits and risks for my specific situation?"*
- ❓ *"Is this trial available here, or will I need to travel?"*
- ❓ *"What happens to my care if I decide to leave the trial or if it ends early?"*
- ❓ *"Are there costs I should plan for — travel, time off work, childcare?"*

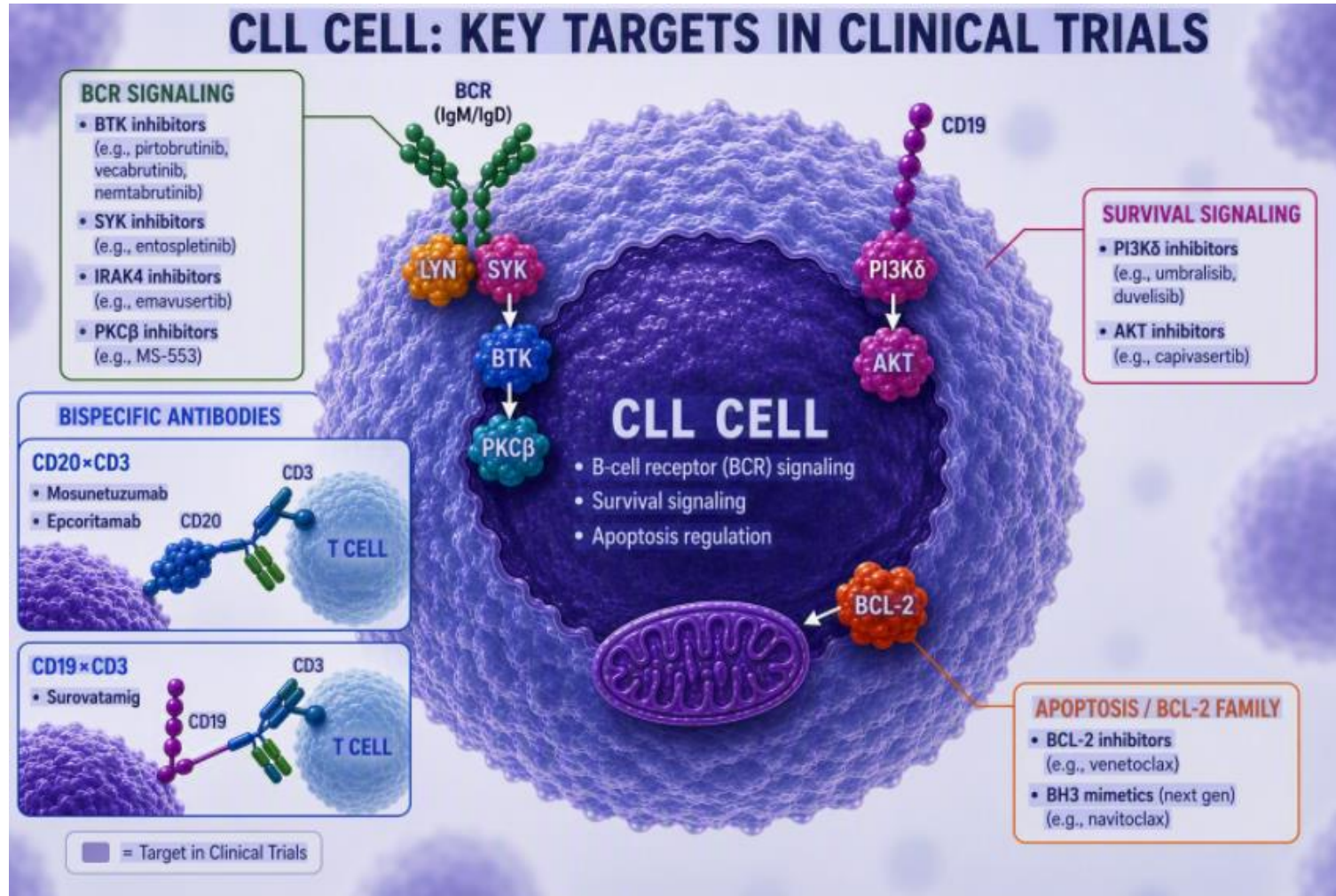


WHY MIGHT YOU SEEK OUT A CLINICAL TRIAL?

- Interest in receiving novel treatments that may become standard treatments in the future
- Available treatments do not have the desired outcomes, or have side effects that are not desirable
- Current cancer stage does not have a standard treatment or does not require treatment
- Interest in participating in a study that may have benefit to other patients in the future



SOME TARGETS OF INTEREST IN CURRENT AND FUTURE TRIALS



THANK YOU!



The James



THE OHIO STATE UNIVERSITY
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