

CLL SOCIETY

Smart Patients Get Smart Care™

6th Annual Patient & Caregiver Ed Forum

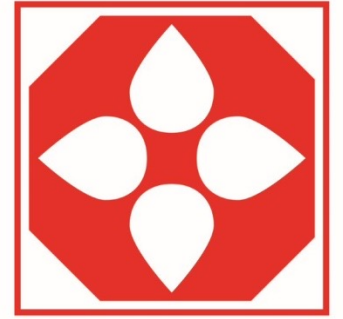
November 16, 2022

9:30 AM PT, 10:30 AM MT,
11:30 AM CT, 12:30 AM ET

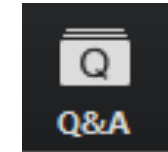


Pre-Event Notes

- The audience is muted
- Please direct your questions to CLL Society staff and speakers using the Q&A function (located at the bottom of your screen) at any time throughout the presentation
- Questions can only be seen by staff and speakers. We will do our best to answer as many questions as possible
- Please complete the short survey emailed after the event. Your response will help CLL Society plan future events
- The virtual event is being recorded and will be available on our website
- Closed captions are available. If you want to turn them on or off, go to Live Transcript and Show Subtitle or Hide Subtitle



CLL SOCIETY



Show Subtitle

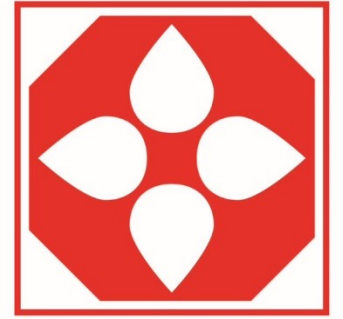
View Full Transcript

Subtitle Settings...



Live Transcript

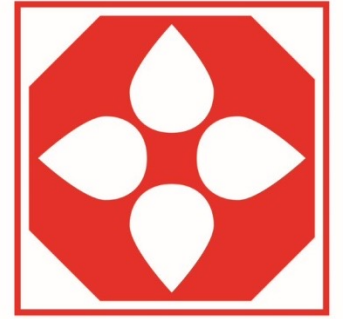
This program was made possible by grant support from



CLL SOCIETY



CLL Society Programs and Resources

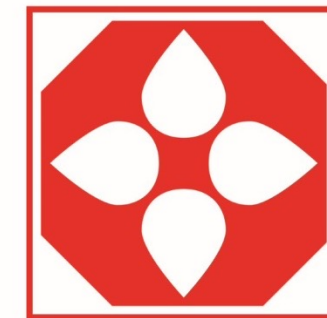


CLL SOCIETY

- CLL Society Patient & Caregiver Support Groups
- Expert Access™ Program – Free, online, 2nd opinion from a CLL expert physician
- Webinars / Virtual Community Meetings
- Weekly Email Newsletter
- COVID-19 & CLL-specific Updates, Expert Interviews & Conference News
- Ask the Expert
- Patient Centric Research
- Test Before Treat™ Campaign

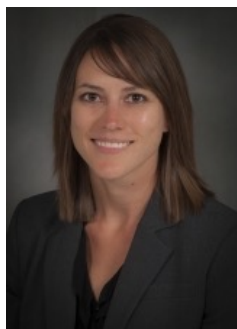
Contact us at Support@cllsociety.org

Huntsman CLL Team: Providers

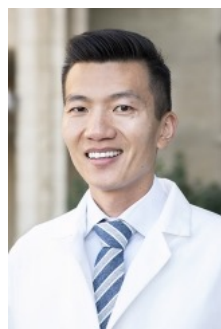


CLL SOCIETY

Doctors



Deborah Stephens



Boyu Hu



Harsh Shah



Lindsey Fitzgerald

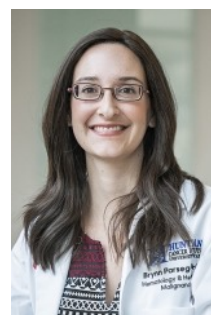


Ahmad Halwani

Advanced Care Practitioners



Renée Vadeboncouer



Brynn Parsegov

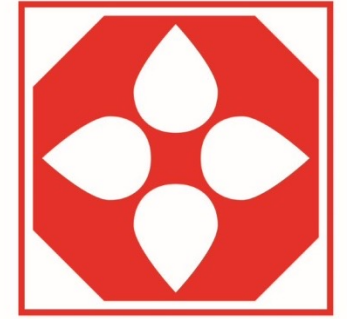


Clayton Savage

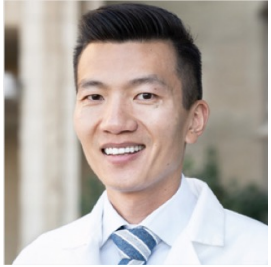


Tara Greenley

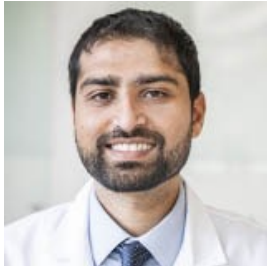
Agenda, Speakers, and Moderator



CLL SOCIETY



Boyu Hu, MD



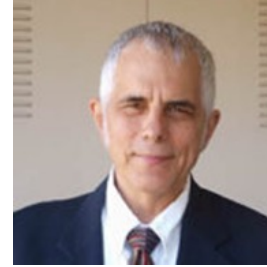
Harsh, Shah,
DO



Deborah
Stephens, DO



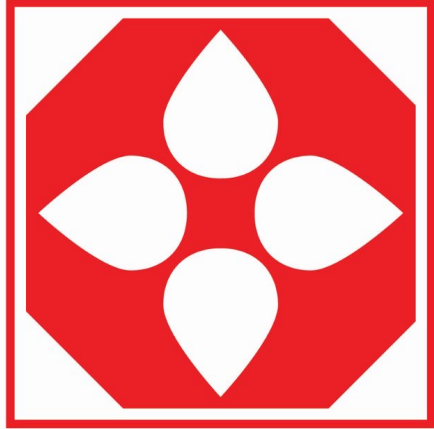
Stephen
Feldman



Brian Koffman, MDCM
(retired), MS Ed

Agenda

10:30 AM MT	Program Welcome and Overview	Drs. Koffman and Stephens
10:35 AM	Patient Self-Advocacy, Support, and Education	Stephen Feldman
10:45 AM	CLL Basics	Dr. Boyu Hu
11:00 AM	What to Watch While You Wait	Dr. Harsh Shah
11:15 AM	CLL Treatments and Clinical Trials	Dr. Deborah Stephens
11:30 AM	Huntsman Foundation	Brandon Plewe
11:32 AM	Audience Q&A	All Speakers
12:00 PM	Program Close	Dr. Brian Koffman



CLL SOCIETY

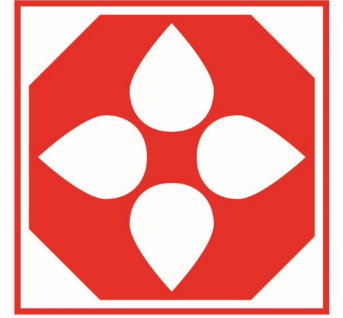
Smart Patients Get Smart Care™

Stephen Feldman

- CLL Patient
- Senior Support Group Facilitator
- Member: CLL Society Patient Advisory Board



The Patient Experience: Taking the Lead in Learning from Experts



CLL SOCIETY

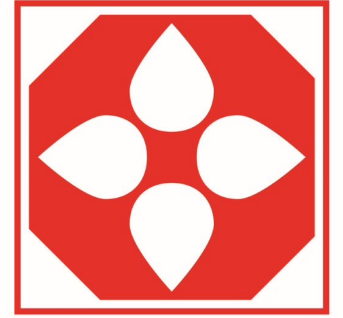


Why Advocate?

"Unless someone like you cares
a whole awful lot, Nothing is
going to get better. It's not."
- Dr. Seuss, The Lorax



Lead and Follow, Follow and Lead: Sharing Knowledge & Experience



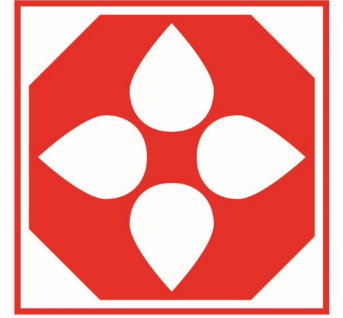
CLL SOCIETY



CHARTING THE COURSE

- You charted a course to this education forum.
- You're listening to and learning from *experts* in the field.
- You're listening to and learning from *patients* and *caregivers*.
- Smart patients learn from and pass along knowledge to smart patients.

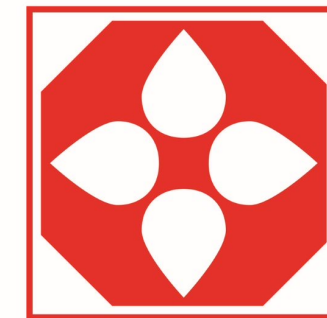
The CLL Society Experience



CLL SOCIETY

- Community: We're in this together, patients and physicians
- Premier resource for reliable, current, physician-curated information
- Stay connected
 - Join one of our patient-led support groups
 - Stay current: register to receive our weekly newsletter
- Explore our website and resources

CLL Society Resources: the clickables



CLL SOCIETY



QUICK LINKS

UPCOMING
EVENTS

LIST OF
CLL HEALTHCARE PROVIDERS

CLL GLOSSARY

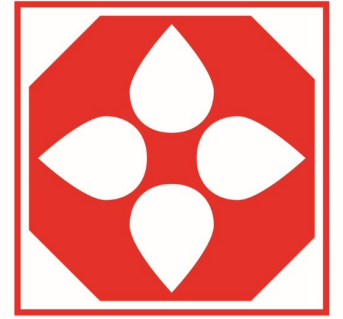
CLL SOCIETY
SUPPORT GROUPS

OFFICIAL STATEMENTS AND GUIDELINES

CLL SOCIETY
IN THE NEWS

ADVOCACY

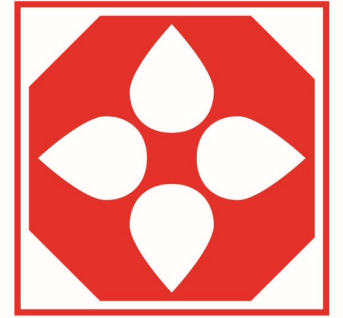
Important Takeaways from CLL Society



CLL SOCIETY

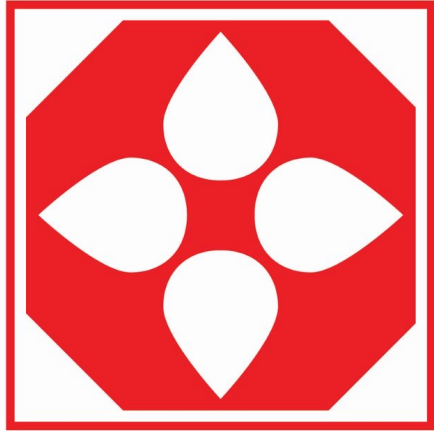
- Watch & Wait is your friend – Time to get up to speed
- Wisdom and advice from those who traveled the path
- Clinical trials
- CLL Society's "Prime Directive":
 - **Have a CLL specialist on your team, accept no substitutions!**
- CLL Society's Expert Access™ Program can help with 2nd opinions

Last Thoughts



CLL SOCIETY

- This is also not your father's CLL
- You can (and will likely) live a LONG (and healthy) time with bad news
- Major paradigm shift: Growing arsenal of powerfully effective targeted, non-chemo treatment options

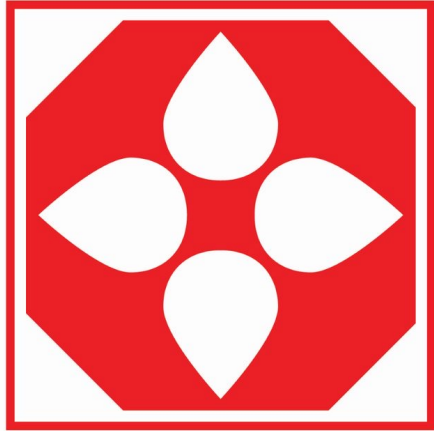


CLL SOCIETY

Smart Patients Get Smart Care™

Thank you!

<http://cllsociety.org>



CLL SOCIETY

Smart Patients Get Smart Care™

CLL Basics

Boyu Hu, MD

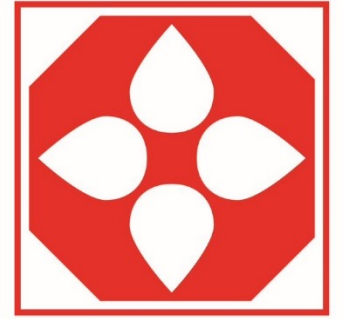
Assistant Professor, Division of
Hematology and Hematologic
Malignancies, Department of
Internal Medicine

Huntsman Cancer Institute /
University of Utah

November 16, 2022

What is CLL?

(Usually) slow growing blood cancer

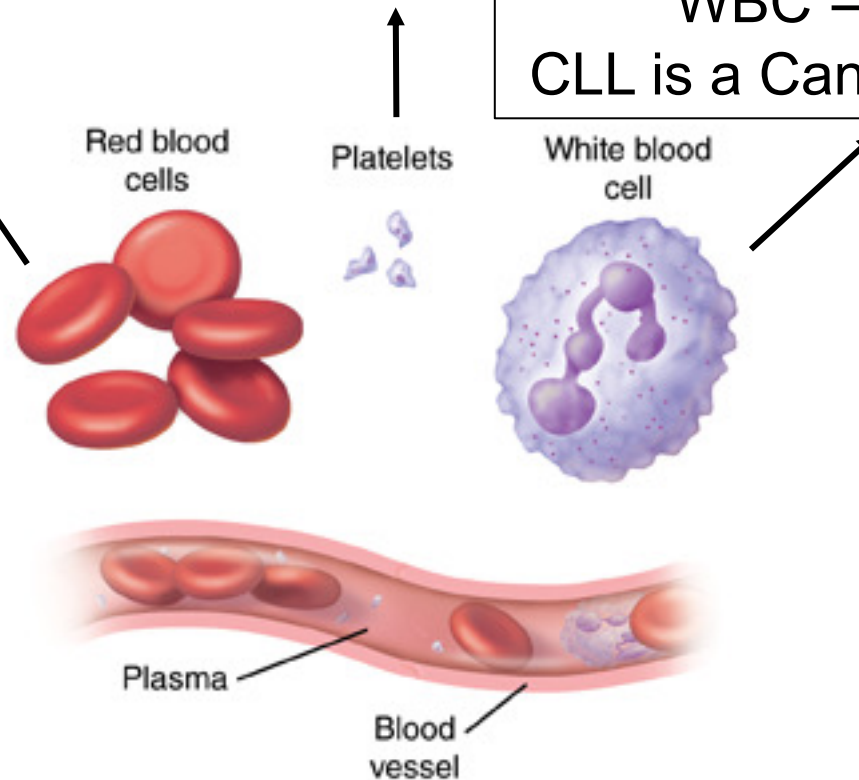


CLL SOCIETY

Platelets = Make Blood Clots
Low platelets = Thrombocytopenia

RBC = Carry Oxygen
Low RBC = Anemia

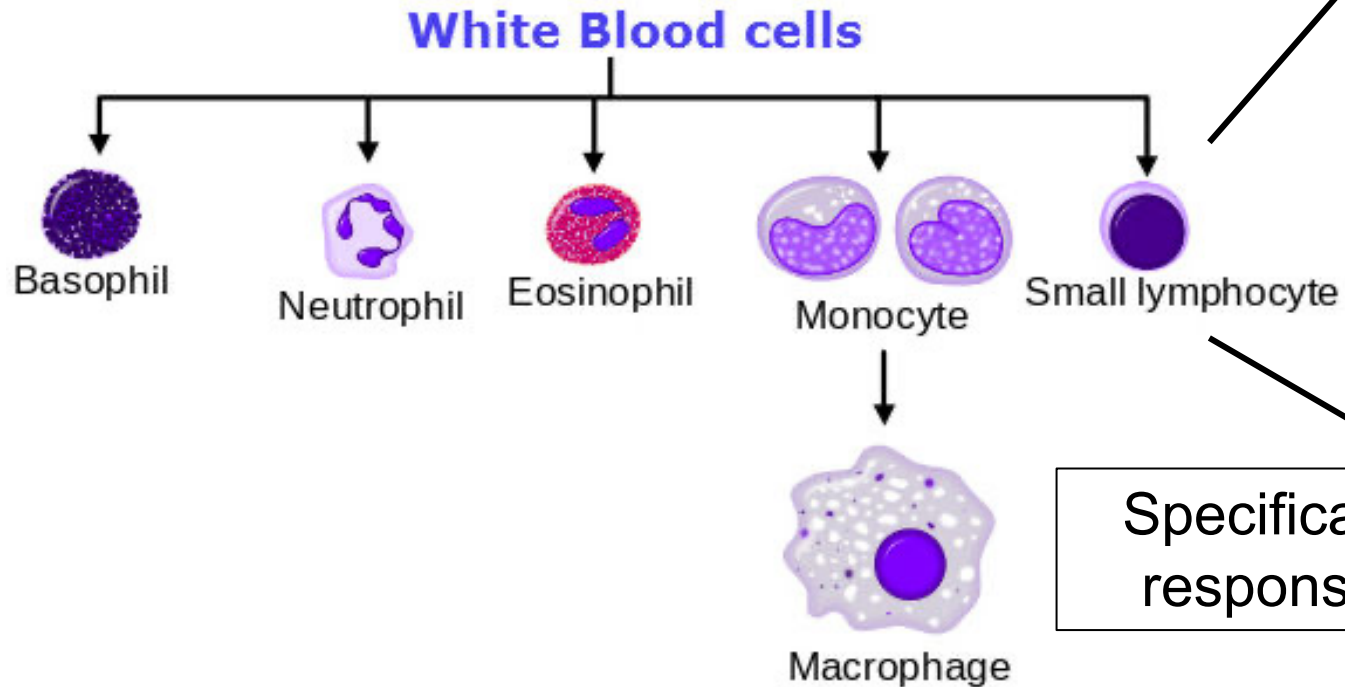
WBC = Fight Infections
CLL is a Cancer of a Type of WBC



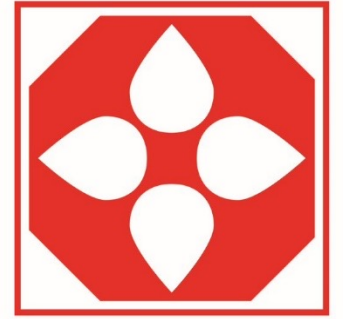
What is CLL?

CLL is a cancer of lymphocytes

Lymphocytes Normally Help Fight Infections – Especially Viruses

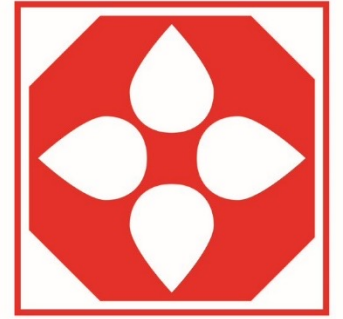


Specifically B lymphocytes responsible for “memory”



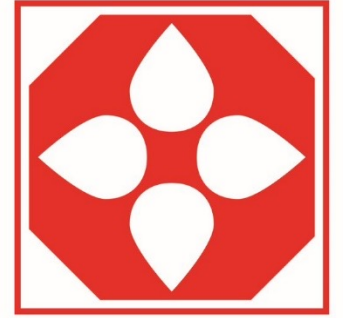
CLL SOCIETY

CLL Epidemiology



CLL SOCIETY

- CLL is the most common adult leukemia
 - One third of new leukemia cases
- In 2019, American Cancer Society estimates:
 - 20,940 new cases of CLL
 - 4,510 deaths from CLL
- Average person's lifetime risk of getting CLL is 1:175
- Average age at diagnosis is 70
- More common in men (2:1)



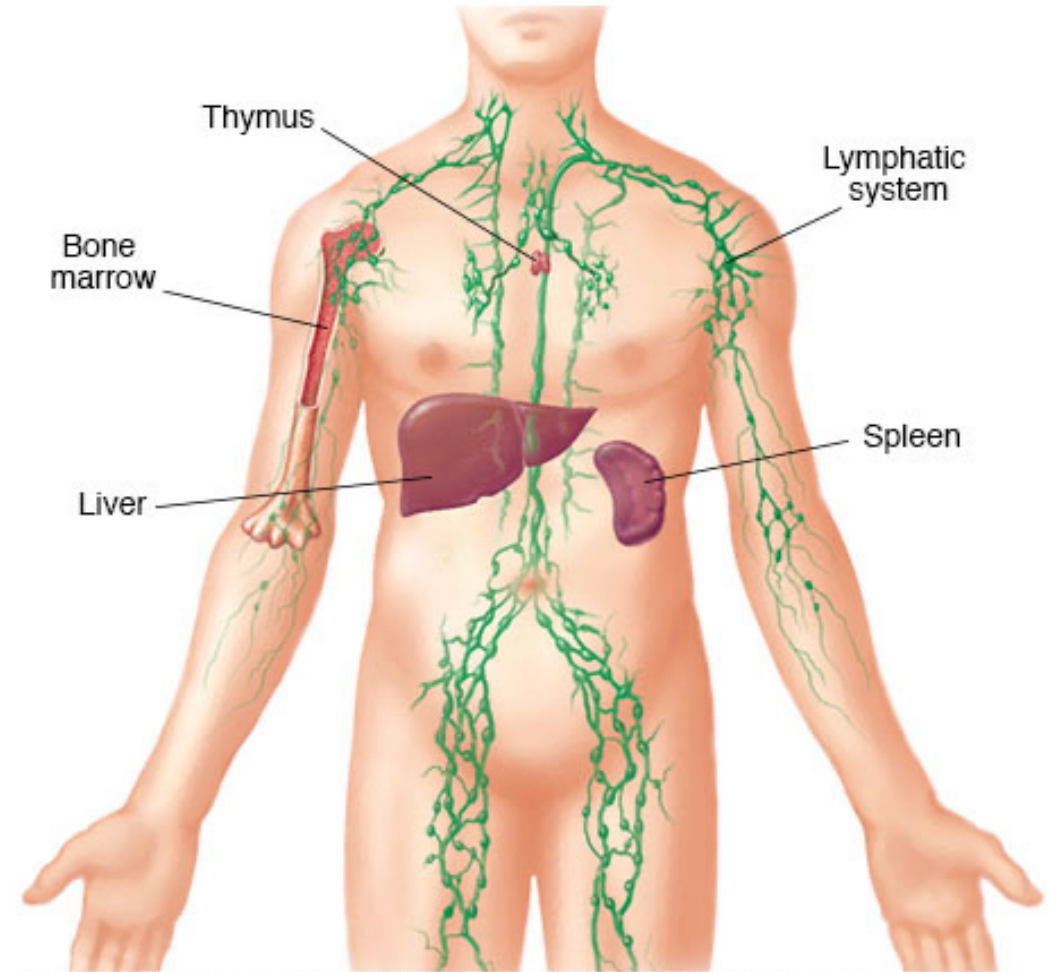
CLL SOCIETY

Typical Clinical Course

- Prolonged periods with no symptoms
 - 40% of patients are diagnosed because of an unexpected finding on routine blood work
- Initial Symptoms
 - Lymph node swelling
 - Fatigue
 - “B” symptoms (fevers, drenching night sweats, weight loss)
- Findings on exam
 - Enlarged lymph nodes
 - Enlarged liver and/or spleen

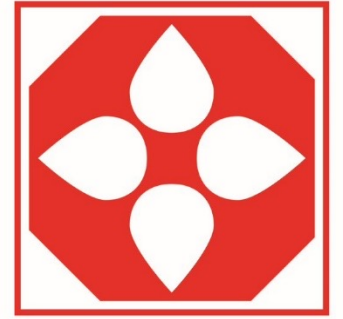
What Are Lymph Nodes?

- Part of the **lymphatic system**
- Vital part of the immune system
- Contains WBCs
- Transports infection-fighting WBC to site of infections
- Contains 500-700 lymph nodes

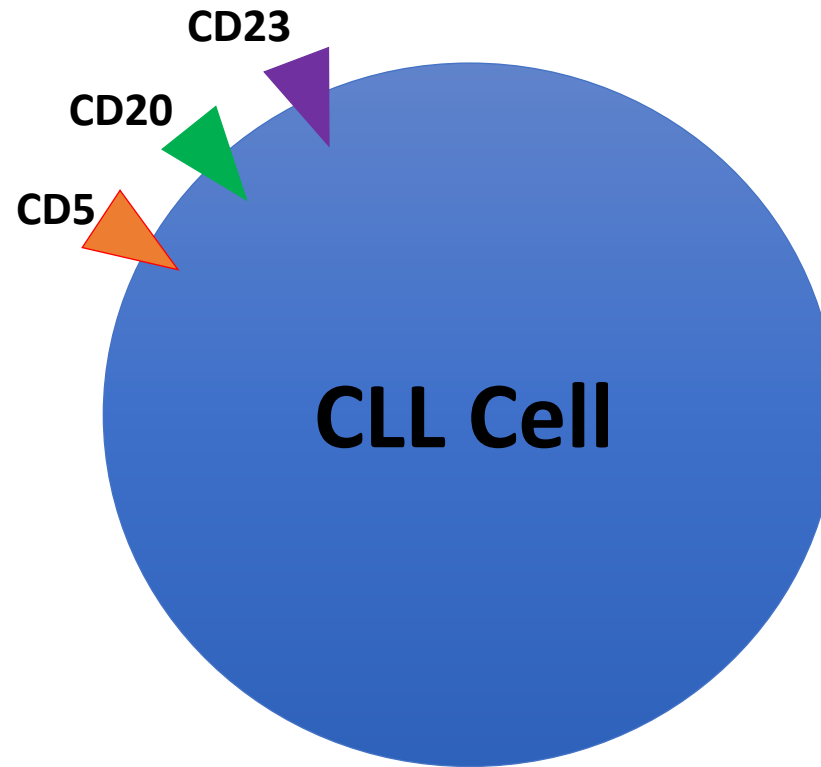


© MAYO FOUNDATION FOR MEDICAL EDUCATION AND RESEARCH. ALL RIGHTS RESERVED.

Cell Surface Protein Expression for Diagnosis



CLL SOCIETY



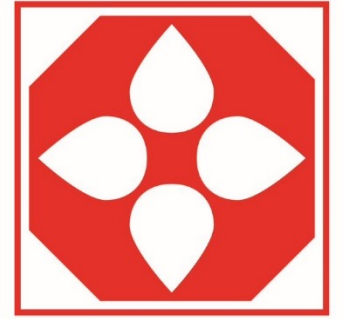
Must also be negative for:

- CD10
- Cyclin D1

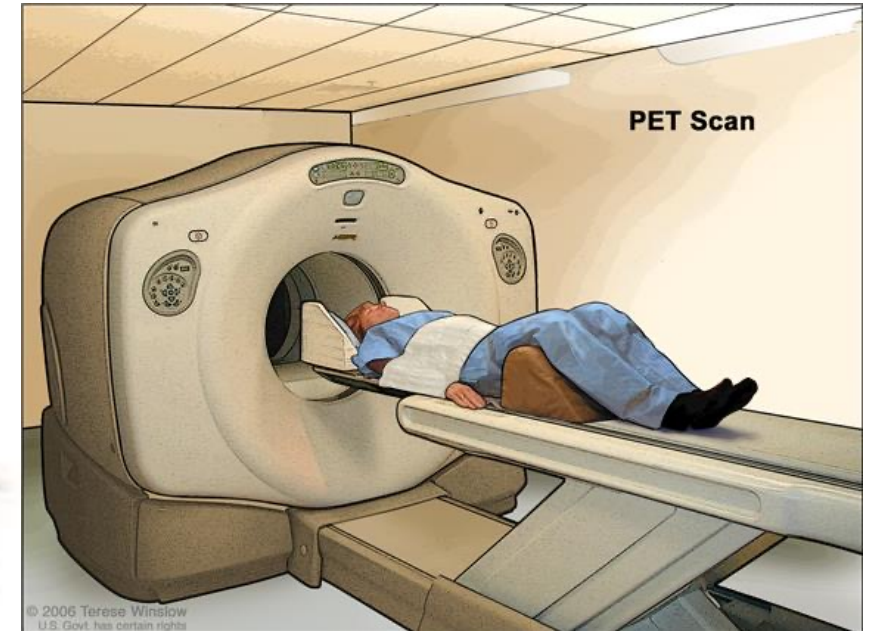
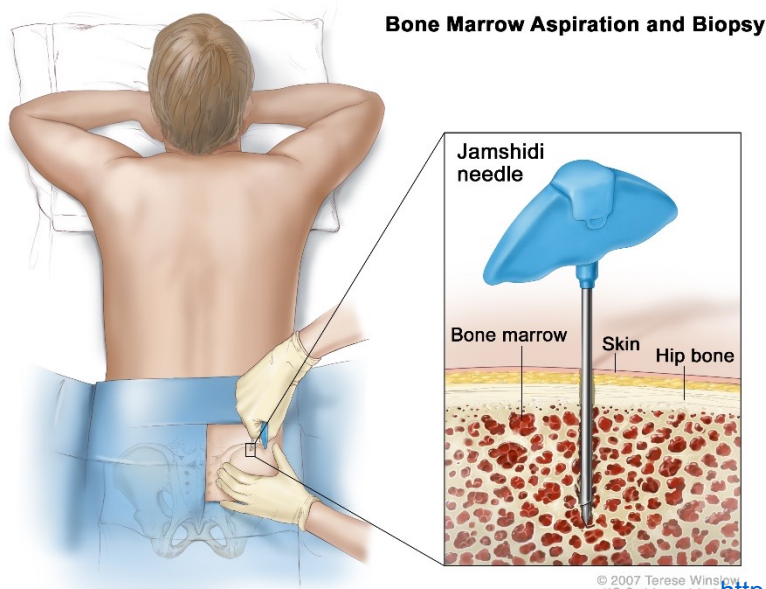
The number of these CLL cells in the blood must be ≥ 5000

Further Work Up

- Not required (but may be indicated):
 - Bone marrow Biopsy
 - CT Scan
 - PET Scan



CLL SOCIETY



© 2007 Terese Winslow
U.S. Govt. has certain rights

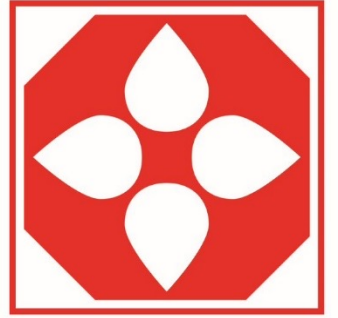
<http://mashingmyeloma.blogspot.com/2012/12/bone-marrow-biopsy-aspiration-ouch.html>;

<http://my.clevelandclinic.org/services/imaging-institute/imaging-services/hic-computed-tomography-ct-scan>;

<http://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=46140>

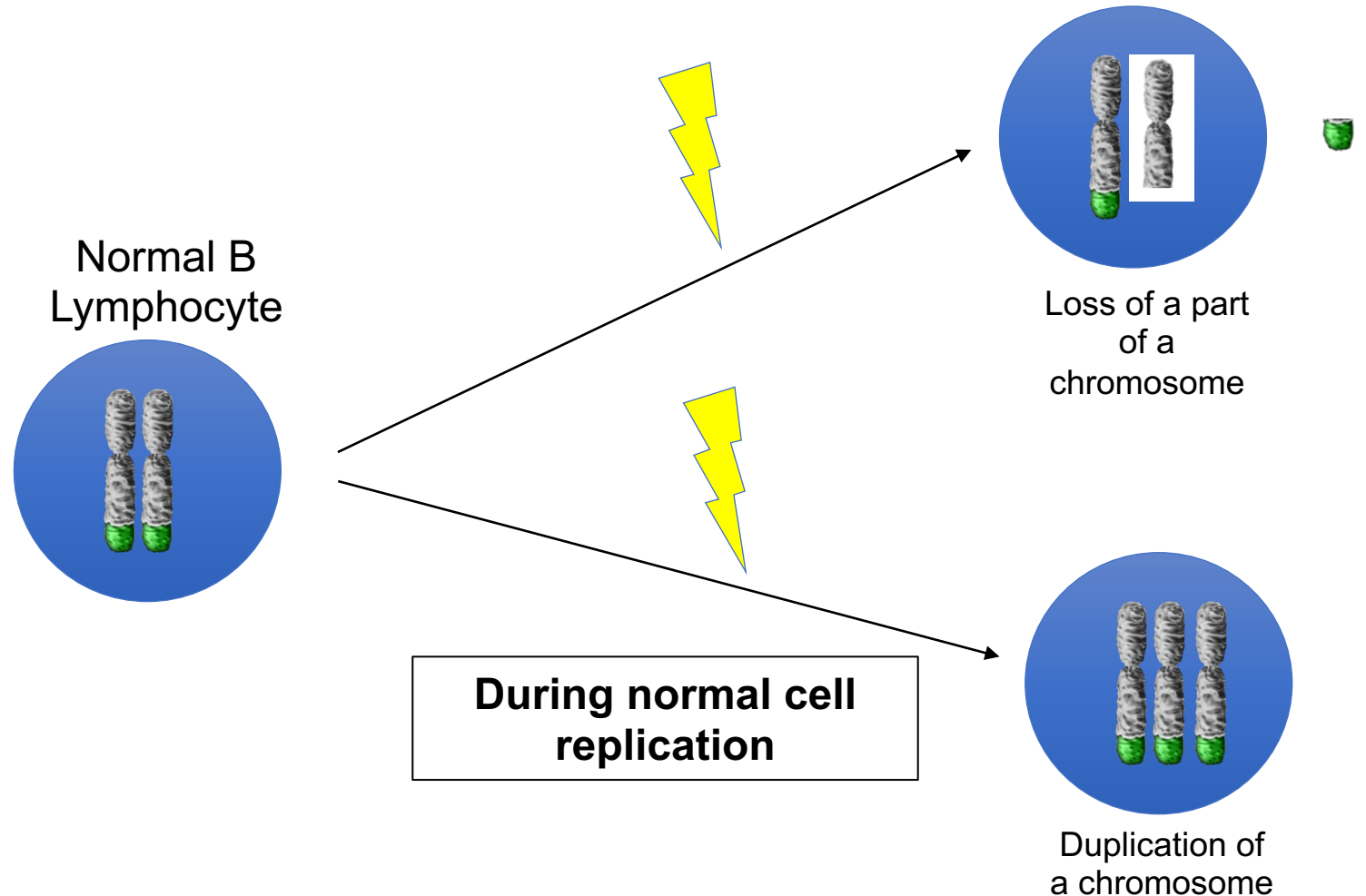
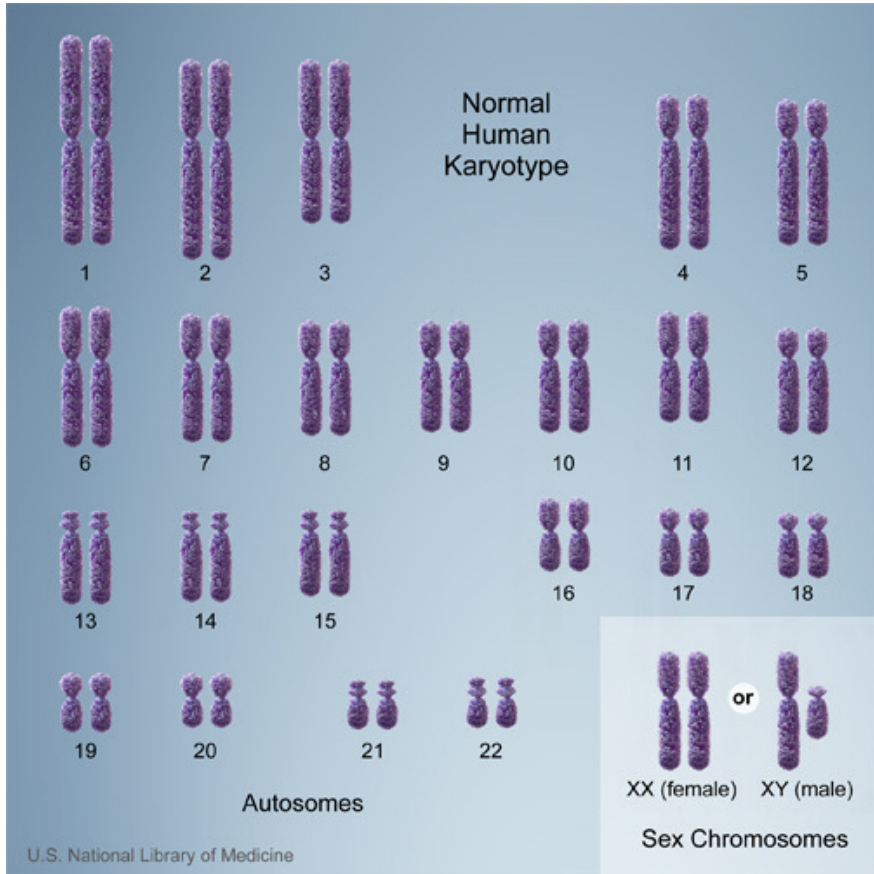
CLL Prognostic Factors

- Usually changes in DNA or genes that are only found in the CLL cells
- Most Prognostic
 - FISH
 - Immunoglobulin Heavy Chain Variable (*IGHV* or *IGVH*) Region mutational status
 - Karyotype
 - CLL gene mutations



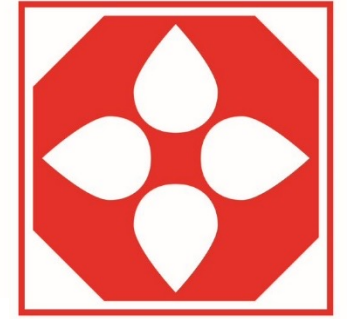
CLL SOCIETY

CLL FISH – What does it mean?



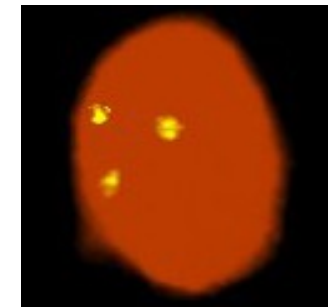
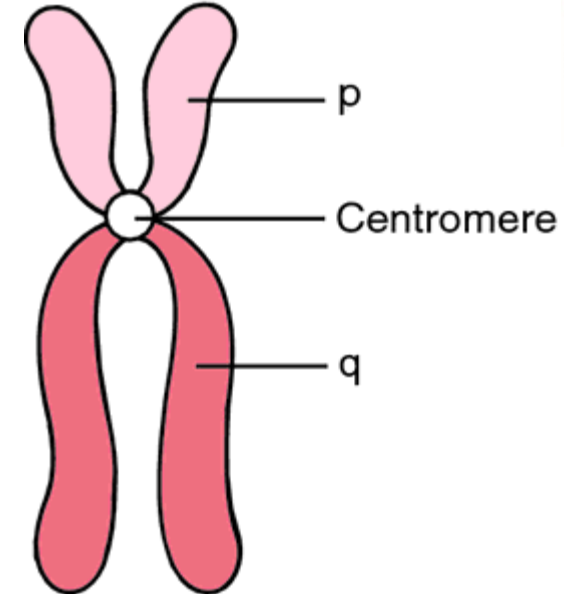
FISH Panel

FISH used to probe for common/significant chromosome changes found in CLL cancer cells (not all of your cells).



CLL SOCIETY

Mutation	%	Good or Bad
Del(13q)	30-45	Good
Trisomy 12	~20	In between
Del(11q)	17-20	Bad
Del(17p)	7-10	Bad

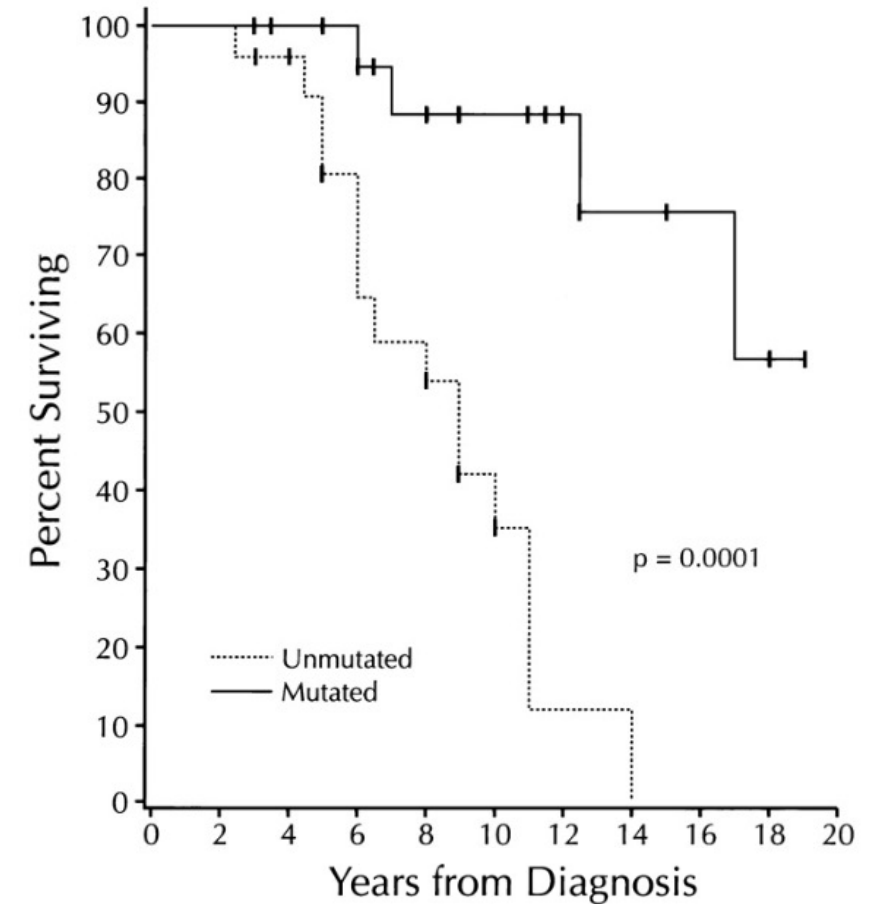


Trisomy 12

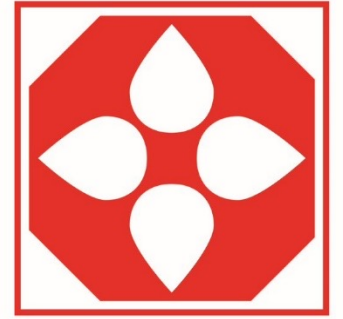
IGHV Mutational Status

- Tests for a gene that is normally mutated to produce immune cells
- ~60% of CLL considered unmutated
- Does not change over time
- Mutated = OS ~ 25 years
 - ~80% No therapy
- Unmutated = OS ~9 years
 - ~20% No therapy

Survival outcomes for *IGHV* mutated and unmutated patients are now about the same in the era of targeted therapies.



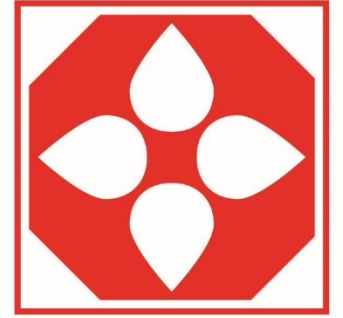
CLL Gene Mutations



CLL SOCIETY

- Most common: *TP53, ATM, SF3B1, NOTCH1*
- Less common: *BTK, PLCG2, BCL2, XPO1, POT1*
- HCl has a 27 gene mutation panel specific to CLL that we will send out (takes 2-3 weeks to result)

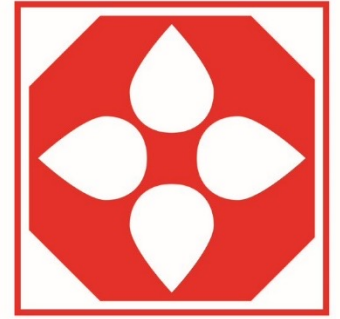
When Do We Send These Tests?



CLL SOCIETY

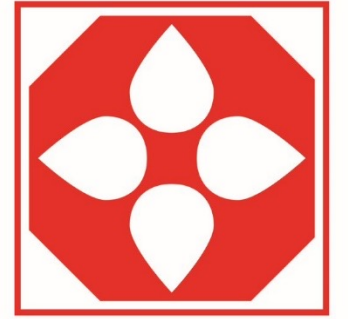
- Most of the time at diagnosis
- After some treatment and before the next line of treatment
 - *IGHV* mutational status is “static” – does not change with time or treatment
 - FISH (i.e. deletion 13q, trisomy 12, deletion 11q and deletion 17p), karyotype and mutations can change over time with treatment

CLL Basic Takeaways



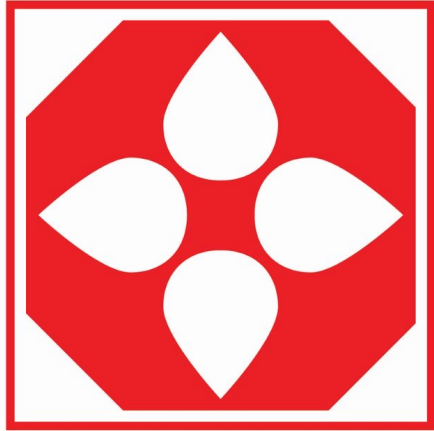
CLL SOCIETY

- CLL is the most common adult leukemia that affects mainly the blood, bone marrow and lymph nodes.
 - Monoclonal B lymphocytosis is a pre-cursor state to CLL and is when the number of CLL cells in the blood are <5000 .
- There are many imaging and genetic tests we may choose to perform at diagnosis and relapse.
 - Gives us both prognostic data and also may guide treatment selection.



CLL SOCIETY

Thank You and Questions at the End



CLL SOCIETY

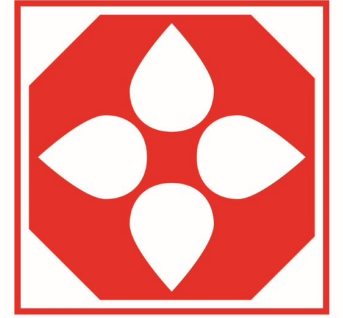
Smart Patients Get Smart Care™

Watch & Wait in
CLL

Harsh Shah, DO

November 16, 2022

When Do We Treat CLL

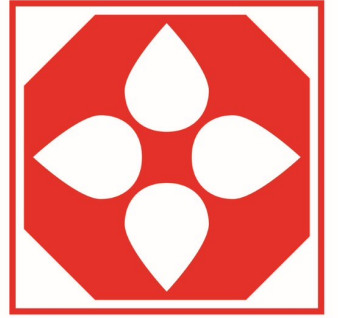


CLL SOCIETY

- Evidence of progressive marrow failure (“low counts”)
- Constitutional symptoms (fever, night sweats or weight loss)
- Massive lymph nodes
- Symptomatic enlarged spleen (splenomegaly)

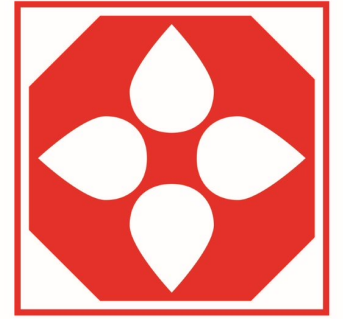
Vaccinations

- Avoid Live Vaccines
- TdAP every 10 years
- Pneumonia series (Two options)
 - **PCV15** followed by **PPSV23** (8 weeks later)
 - Single dose of **PCV20******
 - **PROTECT CLL trial at HCI** (NCT05183854)
- Shingrix after age 50
- Annual flu vaccine



CLL SOCIETY

Cancer Screening with CLL

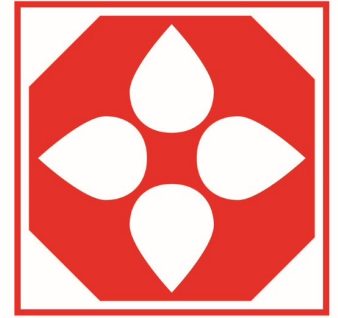


CLL SOCIETY

- Age/sex appropriate cancer screenings
 - Colon cancer screening starting at 45 years old
 - Yearly mammograms for females 40 and older
 - Pap smears for women (usually every 3-5 years)
- Annual skin exams
 - Increased risk of Melanoma (3-5%) and Non-Melanoma Skin Cancers (10-15%)
 - **Nicotinamide study at HCl in patients with history of Non-Melanoma Skin Cancer within last 5 years**
 - **Sunscreen (SPF15 or higher)**

Diet and Lifestyle

- Stay healthy!
 - Most patients with CLL die from something else
 - Heart disease, stroke, kidney disease, obesity, diabetes are still more likely to occur in patients who live in the Western World
 - Sunscreen and skin protection
- Follow the AHA guidelines for diet and exercise
 - Diet and lifestyle:
 - [The American Heart Association Diet and Lifestyle Recommendations | American Heart Association](#)



CLL SOCIETY



How much **physical activity** do you need?

Here are the American Heart Association recommendations for adults.



Fit in 150+

Get at least 150 minutes per week of moderate-intensity aerobic activity or 75 minutes per week of vigorous aerobic activity (or a combination of both), preferably spread throughout the week.



Move More, Sit Less

Get up and move throughout the day. Any activity is better than none. Even light-intensity activity can offset the serious health risks of being sedentary.



Add Intensity

Moderate to vigorous aerobic exercise is best. Your heart will beat faster, and you'll breathe harder than normal. As you get used to being more active, increase your time and/or intensity to get more benefits.



Add Muscle

Include moderate- to high-intensity muscle-strengthening activity (like resistance or weight training) at least twice a week.



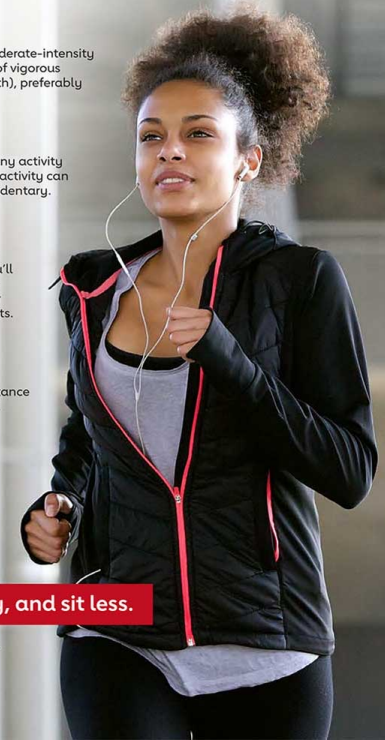
Feel Better

Physical activity is one of the best ways to keep your body and brain healthy. It relieves stress, improves mood, gives you energy, helps with sleep and can lower your risk of chronic disease, including dementia and depression.

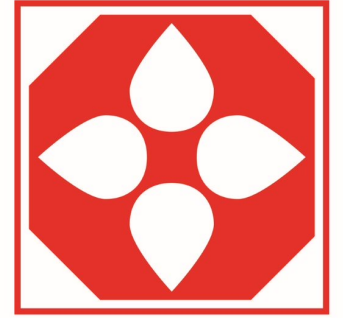
Move more, with more intensity, and sit less.

Find out how at heart.org/movemore.

© Copyright 2021 American Heart Association, Inc., a 501(c)(3) not-for-profit. All rights reserved. Healthy for Good is a trademark. Unauthorized use prohibited. 3/21 1517388



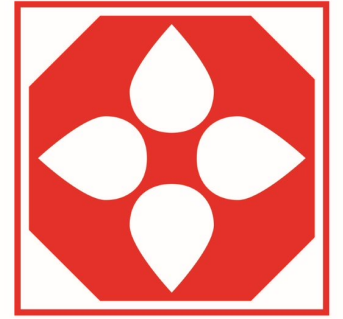
COVID-19 Prevention



CLL SOCIETY

- **Bivalent COVID-19 Booster**
 - Protects against original strains of virus (beta and delta)
 - **Additional protection against Omicron variant (BA.4 and BA.5)**
- Approved for individuals 6 years of age and older as a single booster dose administered **at least 2 months after either:**
 - Completion of primary vaccination with any authorized or approved monovalent COVID-19 vaccine, or
 - Receipt of the most recent booster dose with any authorized or approved monovalent COVID-19 vaccine

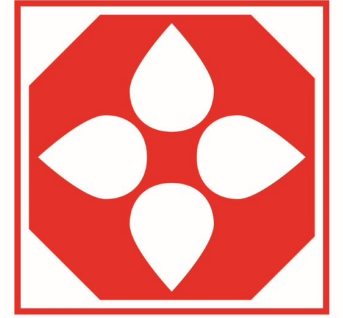
Evusheld (Pre-Exposure Prophylaxis)



CLL SOCIETY

- Cocktail of two COVID-19 monoclonal antibodies, tixagevimab and cilgavimab
- Recommended at the dose of 300mg every six months
- Provides protection against BA.5 (~50% of COVID-19 variants in the USA and the number is falling)
- All CLL patients qualify as they are immunocompromised

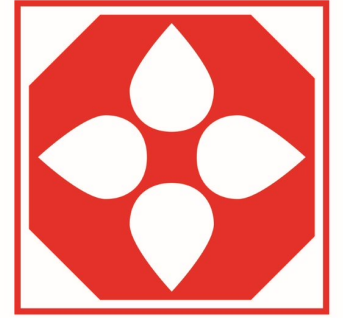
Outpatient Treatment of COVID-19



CLL SOCIETY

- Antivirals (target specific parts of the virus to stop it from multiplying in the body, helping to prevent severe illness and death)
 - Paxlovid (nirmatrelvir co-packaged with ritonavir) (**Pill**)
 - Approved for mild to moderate COVID-19
 - Reduces hospitalization by 90%
 - Interaction with CLL medications, so they should be held during treatment
 - Veklury (remdesivir) (**IV**)
 - **3 days of IV infusion outpatient**
 - Lagevrio (molnupiravir) (**Pill**)
 - Alternate oral option when Paxlovid is not available
- Monoclonal antibody (help the immune system recognize and respond more effectively to the virus)
 - Bebtelovimab (**IV**) – may not be effective against new strains
 - **Single infusion**

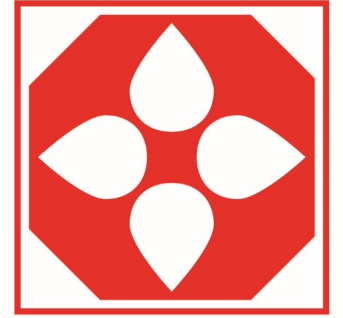
General Criteria for Outpatient COVID-19 Treatment



CLL SOCIETY

- You test positive for SARS-CoV-2 (virus that causes COVID-19)
- You currently have [COVID-19 symptoms](#) that began within the last 5-7 days
- You are not newly on oxygen or on an increased oxygen supply
- You are not hospitalized
- You are at high risk for severe illness from COVID-19 due to your age and certain medical conditions, including being severely immunocompromised (**all CLL patients meet this criteria**)

Conclusions



CLL SOCIETY

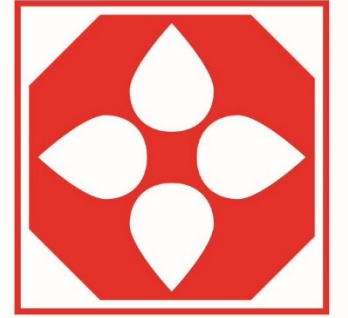
- Work with your health care team in making sure that watch and wait does not lead to increased anxiety and stay informed about your disease
- Get up-to-date on routine vaccines
- Yearly skin exam is essential
- Eat healthy and exercise
- Get COVID-19 bivalent booster
- Evusheld every six months (at least for now)

CLL Treatments and Clinical Trials

Deborah Stephens, DO

November 16, 2022

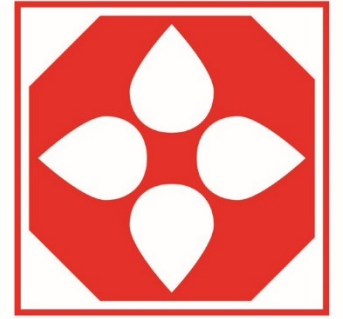




CLL SOCIETY

Current Treatment Options

General Cancer Treatment Options



CLL SOCIETY

- Surgery:
 - No
- Radiation:
 - Rarely
 - Palliation
- Chemotherapy:
 - Usual choice
 - Blood cancer = treat all blood
 - Classic, Immunotherapy, Targeted



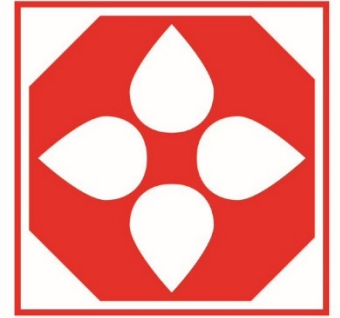
Classic Chemotherapy

- Non-specific killing of growing cells
- Fludarabine
- Cyclophosphamide
- Bendamustine
- Pentostatin
- Chlorambucil
- Short-term: Nausea, hair loss, fatigue, low blood counts, infection, nerve pain, rash, blood in urine
- Long-term: Bone marrow damage

RARELY RECOMMENDED DUE TO SIDE EFFECTS AND NEW OPTIONS



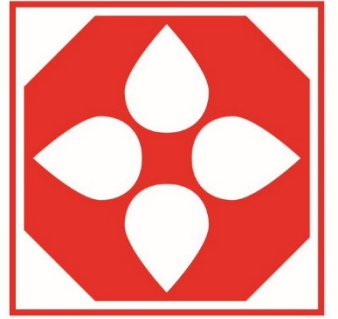
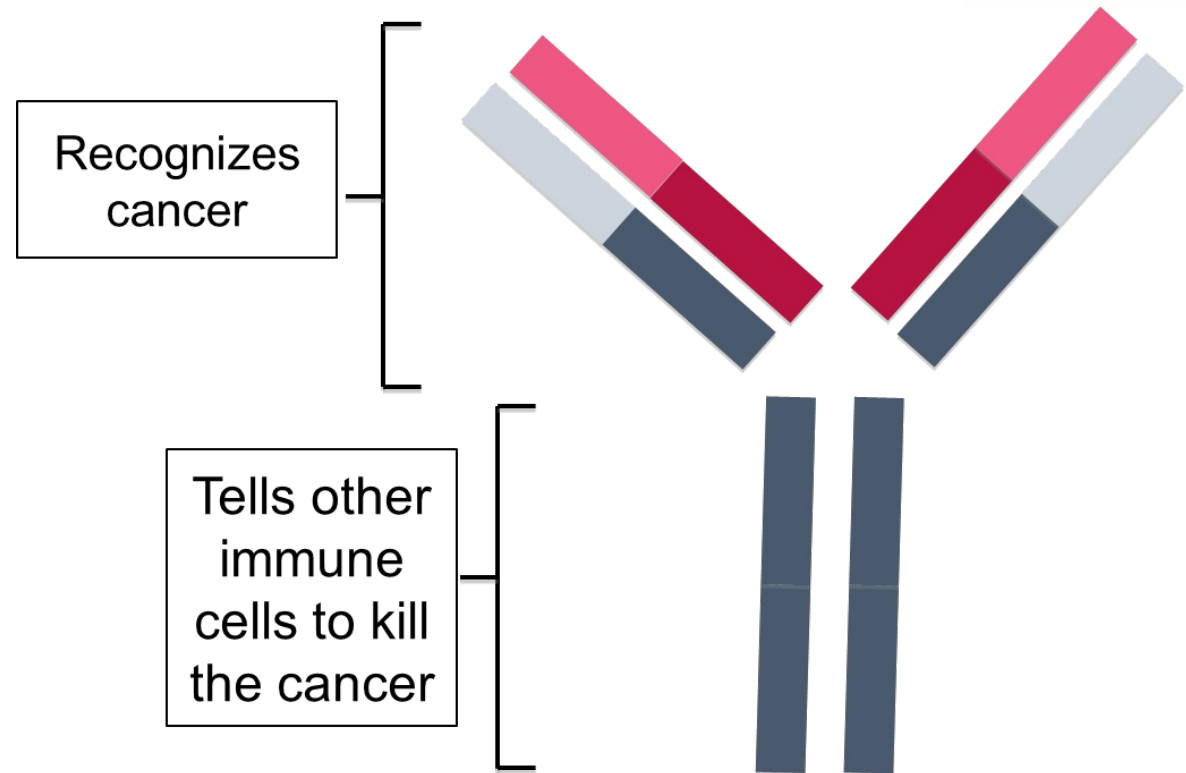
“At least yours will
grow back.”



CLL SOCIETY

Immunotherapy

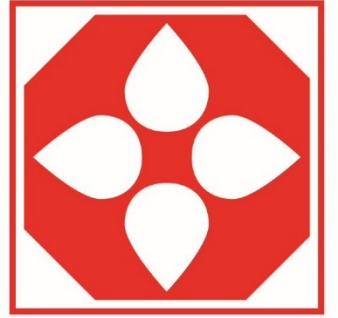
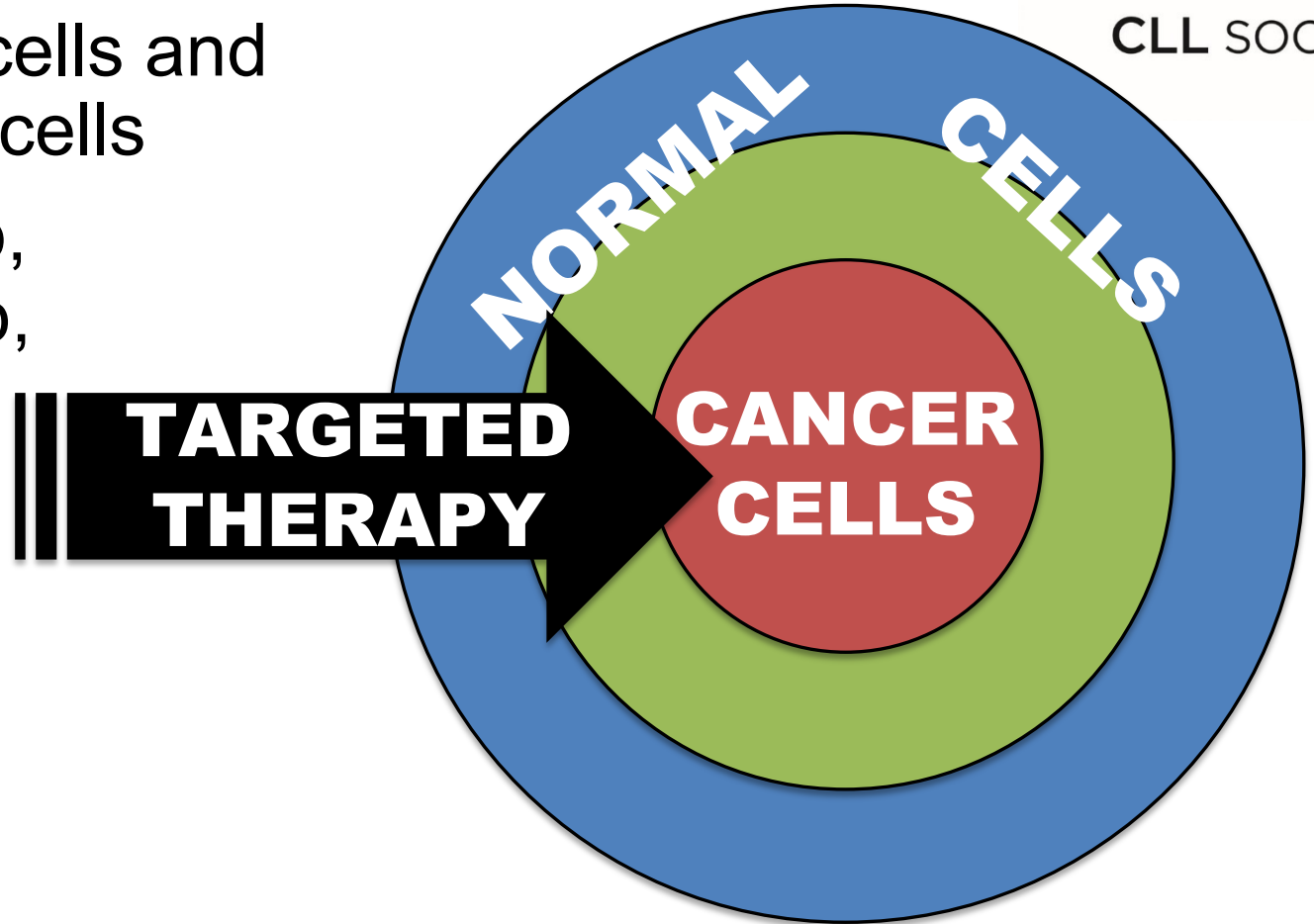
- Specifically targeting something that lives on the outside of a CLL cell
- **Antibodies (CD20):**
 - Rituximab
 - Ofatumumab
 - Obinutuzumab



CLL SOCIETY

Targeted Therapy

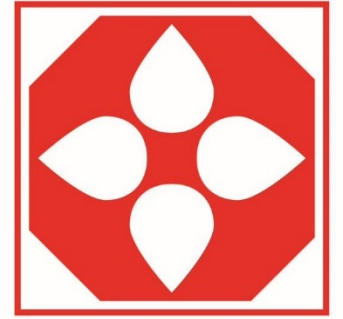
- Avoids killing normal cells and goes after the cancer cells
- Ibrutinib, acalabrutinib, zanubrutinib, idelalisib, venetoclax....



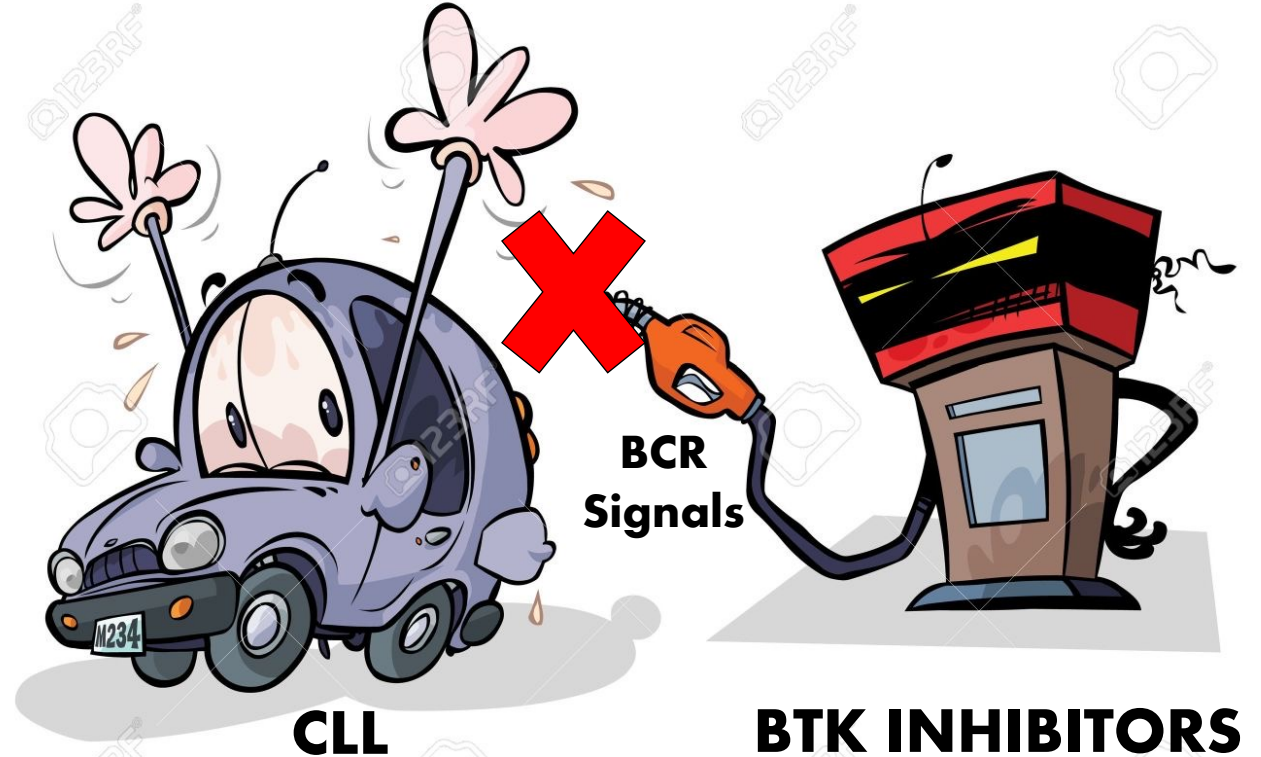
CLL SOCIETY

Bruton's Tyrosine Kinase (BTK) Inhibitors

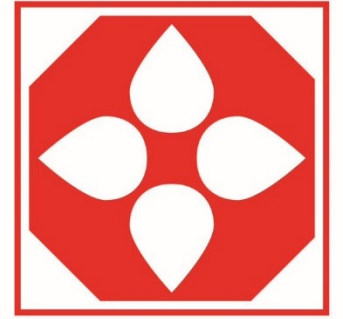
- Block cancer survival signals (B-cell receptor pathway)
- Like taking gas out of your car
- **Ibrutinib**: Approved all CLL patients
- **Acalabrutinib**: Approved all CL patients
- **Zanubrutinib**: Coming soon...



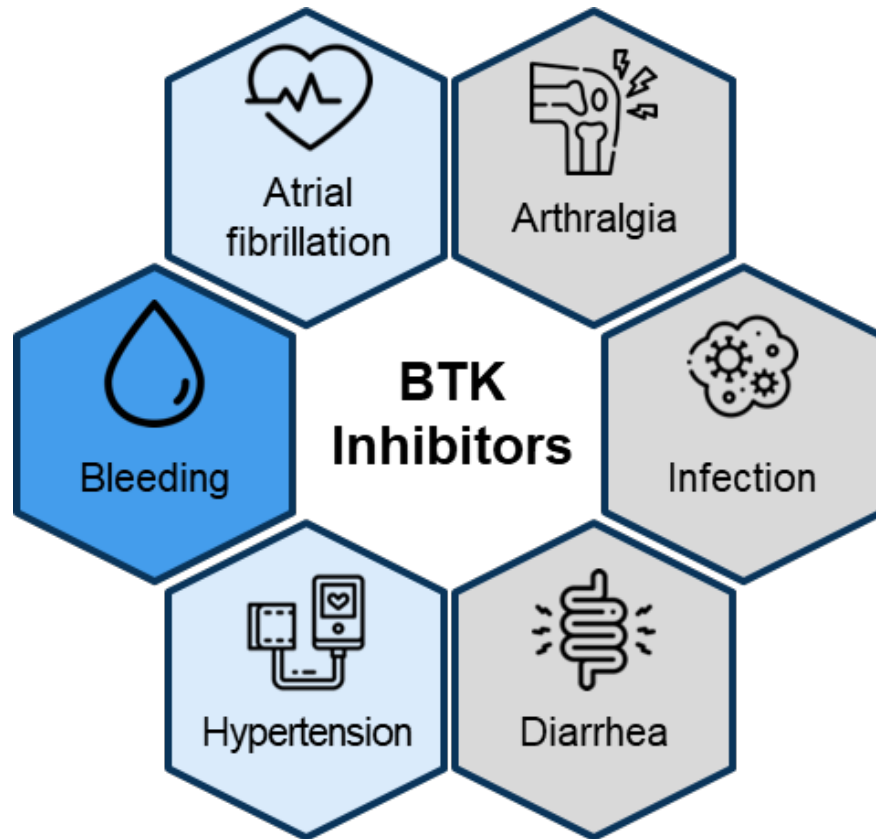
CLL SOCIETY



Common Toxicities with BTK Inhibitors



CLL SOCIETY



Early: Goes Away with Time

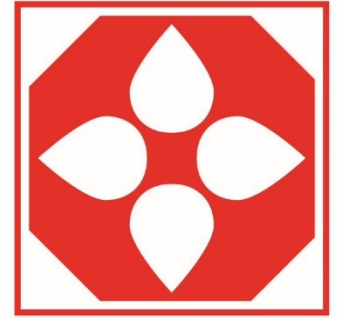
Later: Risk Increases with Time

Any Time: Always a Risk

NOTE: Less toxicity with
Acalabrutinib or Zanubrutinib

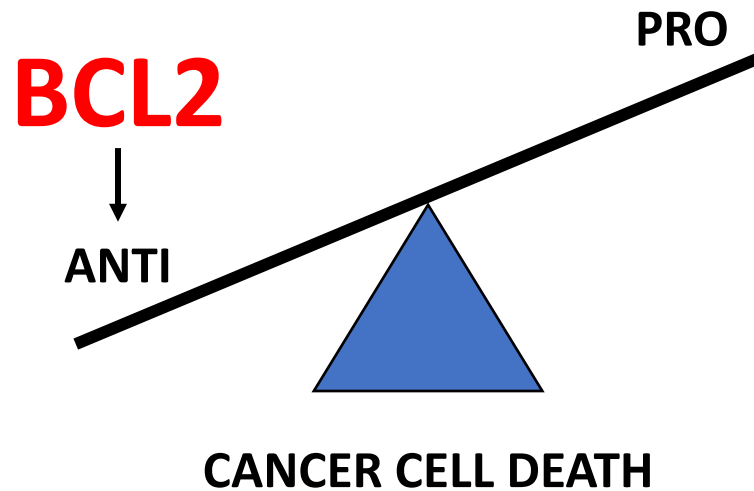
Venetoclax

Venetoclax = Approved for
all CLL patients in
combination with anti-CD20

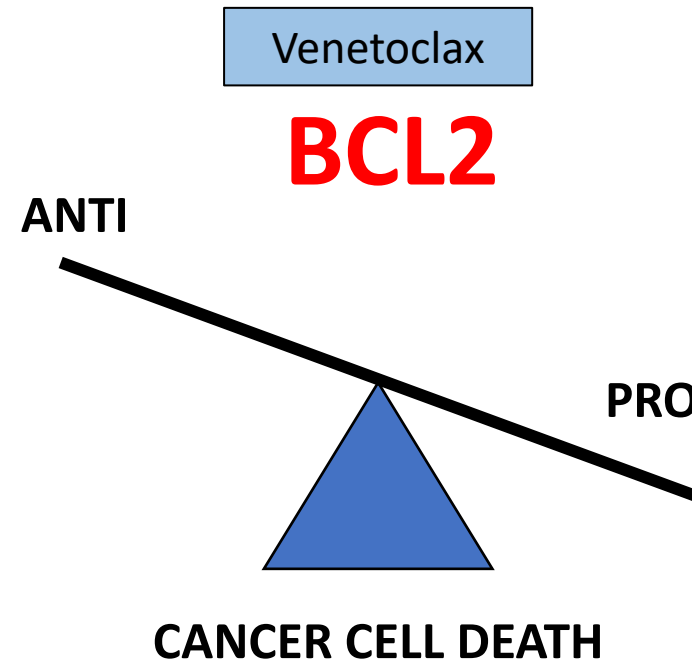


CLL SOCIETY

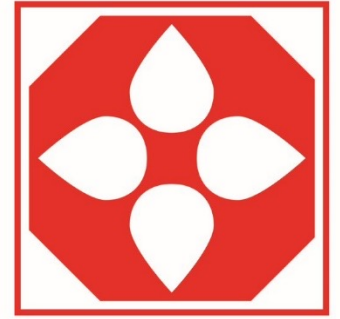
CLL Cells Increase BCL2 to Live Longer



Venetoclax Blocks BCL2 and Promotes Cell Death



Venetoclax: Toxicities and Management



CLL SOCIETY



Tumor Lysis Syndrome:

-Hydration, drugs to prevent uric acid build-up, hospitalization?



Diarrhea and Nausea:

-Antidiarrhea and nausea medications, taking dose at night



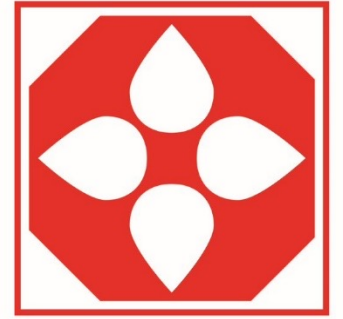
Low infection fighting WBC (neutrophils) or platelets:

-Doctor to monitor, growth factor injections



Infections/Lack of Vaccine Response:

-Vaccines before starting treatment, antibiotics, monitor for fever

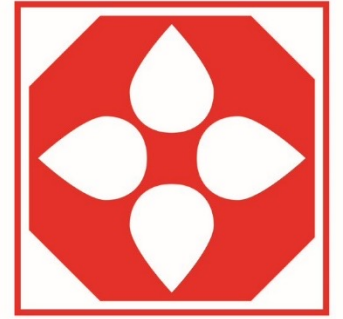


CLL SOCIETY

New Treatment Approaches

Currently available on clinical trials

Combinations of New Drugs



CLL SOCIETY

- Pick 2 or 3 good drugs and combine them

Bruton's Tyrosine Kinase (BTK) Inhibitor

Ibrutinib

Acalabrutinib

Zanubrutinib



BCL2 Inhibitor

Venetoclax

? Other new drug ?



Anti-CD20 Antibody Treatment

Obinutuzumab

Rituximab

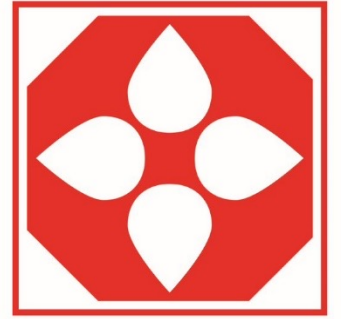
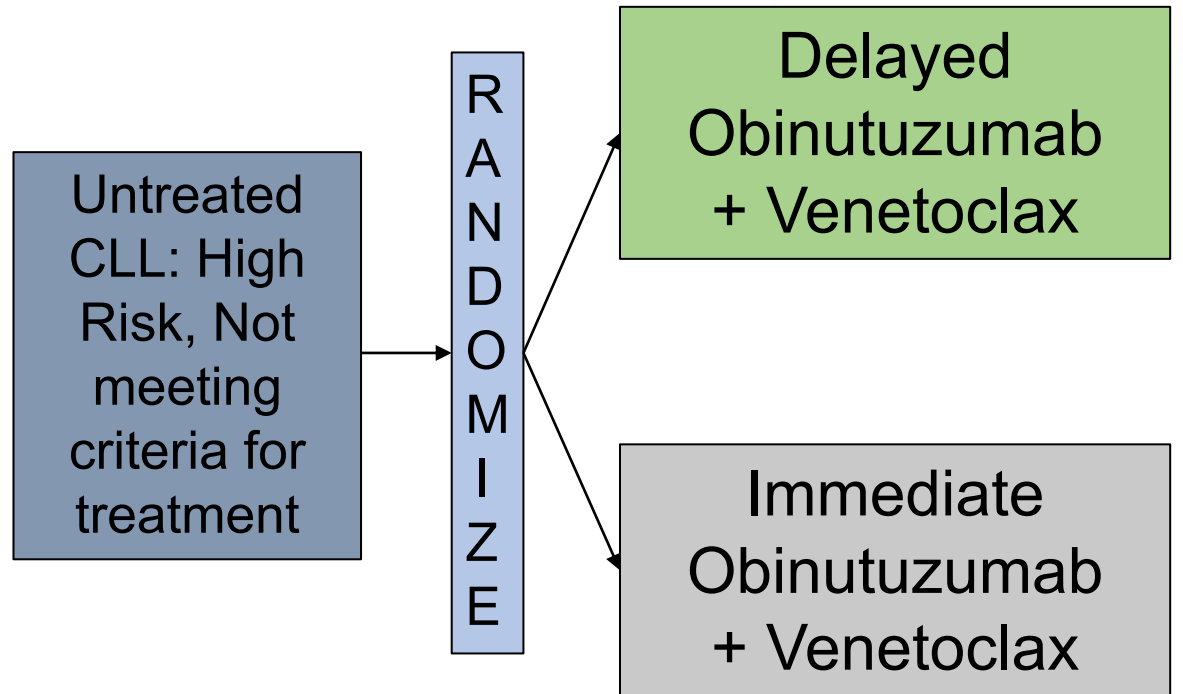
Ublituximab

- Advantages: Deeper or Longer Lasting Responses, Shorten Treatment Length

Early Treatment

- S1925 EVOLVE CLL Study
- High risk: Del(17p) or combination of clinical and genetic risks
- Must have new diagnosis of CLL within the last year

Accrual
Ongoing



CLL SOCIETY

When a BTKi Doesn't Work Anymore....

- ▲ BTK (C481S)

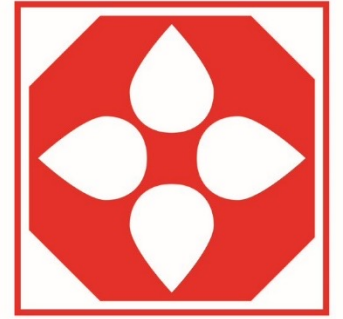
- ▲ Still fits, but doesn't block well
- ▲ Rapid progression after BTKi d/c

- ▲ **DO NOT D/C BTKi without another plan!**

- ▲ Applies to ibrutinib, acalabrutinib, and zanubrutinib



BTKi



CLL SOCIETY

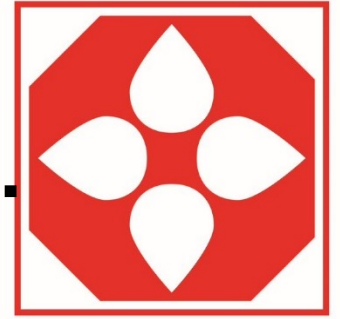
KEYHOLE: SPOT ON CLL WHERE
BTKi BINDS



BTKi

KEYHOLE: CHANGES AND BTKi
DOESN'T FIT WELL

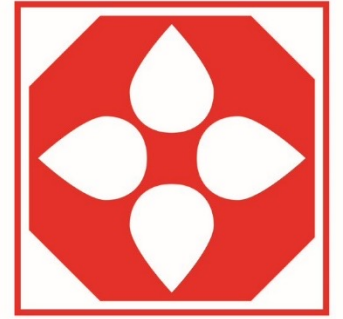
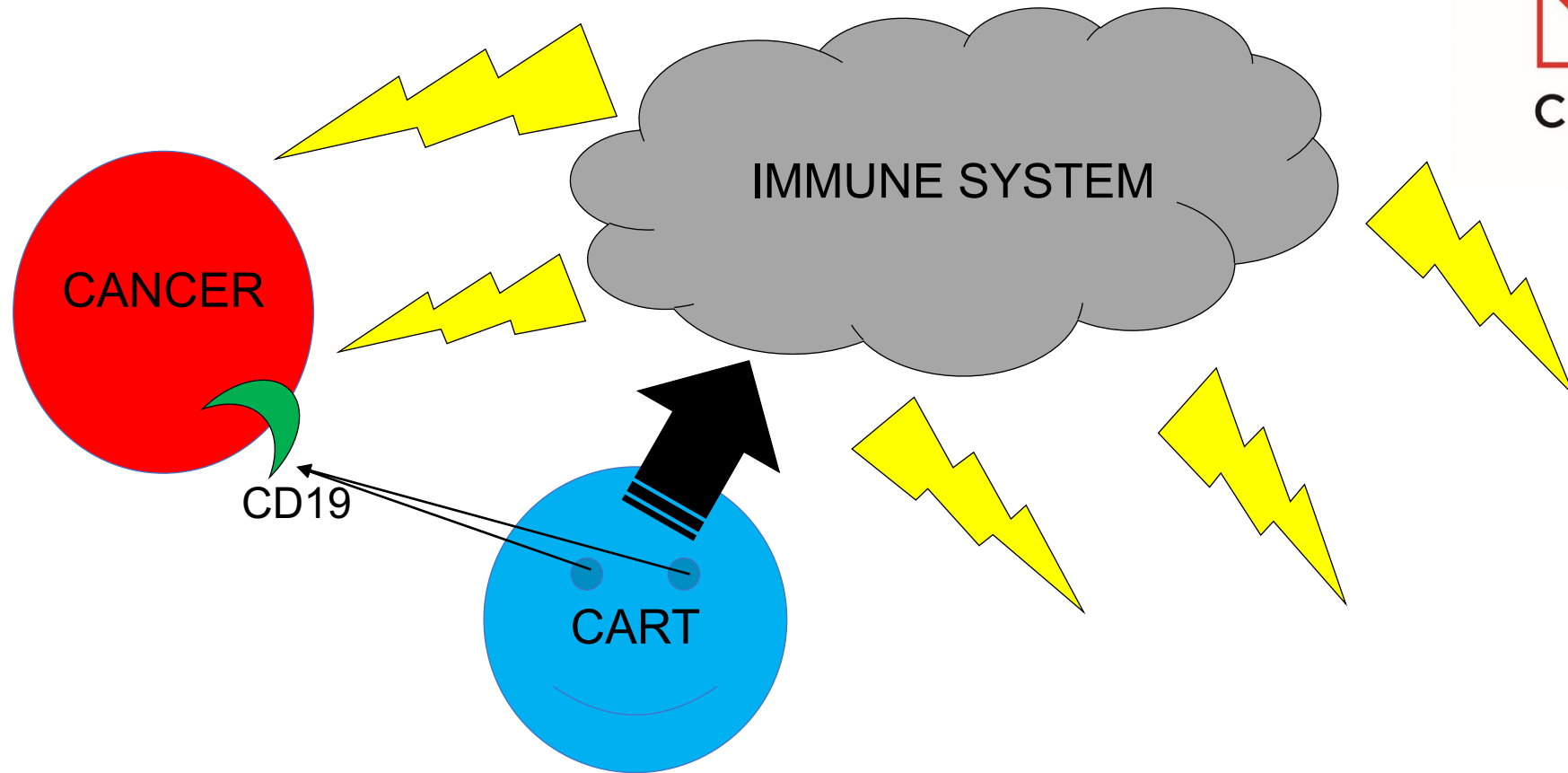
When Ibrutinib Doesn't Work Anymore...



CLL SOCIETY

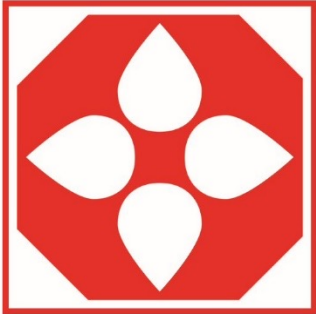
Bruton's Tyrosine Kinase (BTK) Inhibitor		
Generation 1/2	Next Generation	Status
Ibrutinib	Pirtobrutinib (LOXO-305)	Open clinical trials showing response in CLL after generation 1 & 2 BTKi with less side effects
Acalabrutinib	ARQ-531	
Zanubrutinib	LP-168	Clinical trial open! Now enrolling in Utah!

CAR-T Cell Therapy

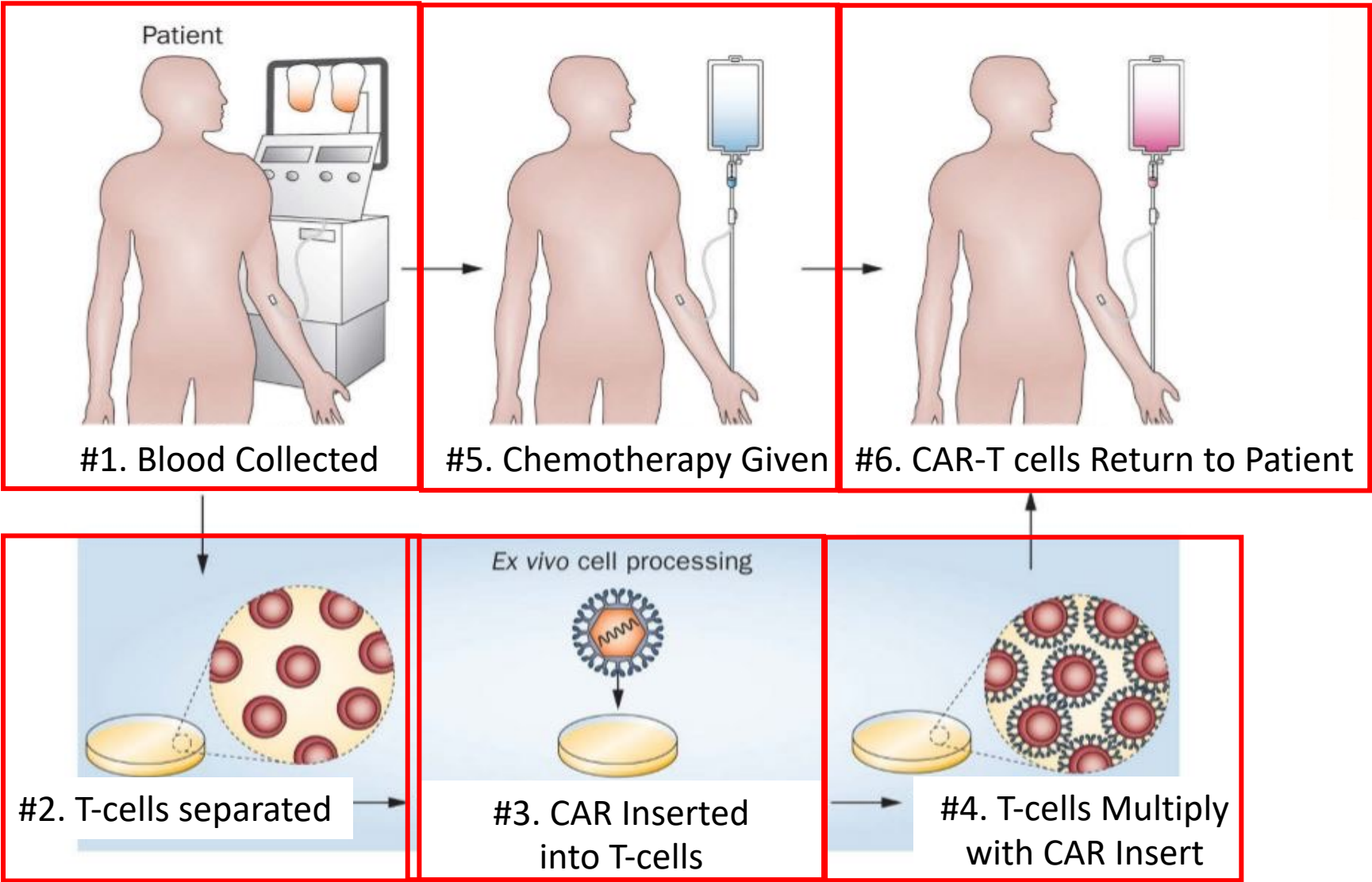


CLL SOCIETY

CAR-T Cell Therapy

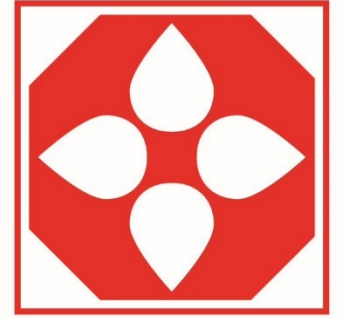


CLL SOCIETY



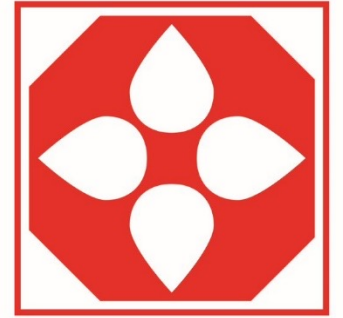
Review

- Current Treatment Options
 - Classic Chemotherapy
 - Immunotherapy
 - Targeted Agents
- New Treatment Approaches
 - Combinations of New Drugs
 - Early Treatment
 - New Targeted Agents
 - CART Therapy



CLL SOCIETY

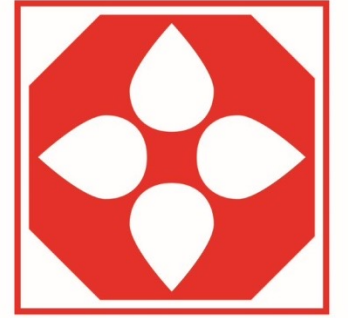
**ASK YOUR DOCTOR IF YOU
QUALIFY FOR A CLINICAL
TRIAL TODAY!**



CLL SOCIETY

Questions?

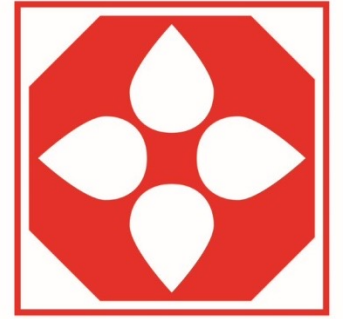
Twitter: @Debbiemstephens



CLL SOCIETY

Audience Questions & Answers

This program was made possible by grant support from

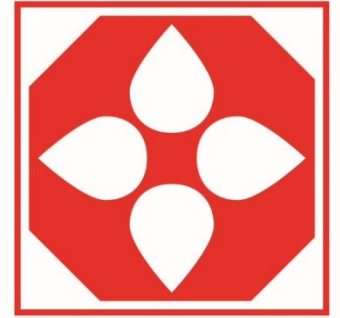


CLL SOCIETY



Thank You for Attending!

Please take a moment to complete our **post-event survey**, your feedback is important to us



CLL SOCIETY

Join us on December 5th for our **Facebook Live Event**
“Ask Me Anything” Featuring Dr. Nicole Lamanna and
Doreen Zetterlund

If your question was not answered, please feel free to
email asktheexpert@cllsociety.org

CLL Society is invested in your long life. Please invest in
the long life of the CLL Society by supporting our work

cllsociety.org/donate-to-cll-society/