

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





This program was made possible by grant support from







Bristol Myers Squibb[™]





CLL Society Programs and Resources



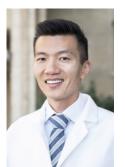
- Expert Access[™] Program Free, online, 2nd opinion from a CLL expert physician
- Webinars / Virtual Community Meetings
- Weekly Email Newsletter
- COVID-19 & CLL-specific Updates, Expert Interviews & Conference News
- Ask the Expert
- Patient Centric Research
- Test Before Treat[™] Campaign



Huntsman CLL Team: Providers

Doctors





Deborah Stephens Boyu Hu

yu Hu



Harsh Shah



Ahmad Halwani

CLL SOCIETY

Advanced Care Practitioners



Renée Vadeboncouer Brynn Parsegov

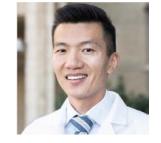


Clayton Savage



Tara Greenley

Agenda, Speakers, and Moderator





B



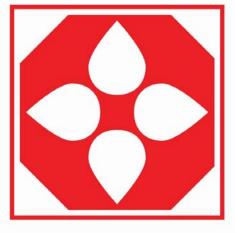






CLL SOCIETY

Boyu Hu, MD	Harsh, Shah, DO	Deborah Stephens, DO	Stephen Feldman	Brian Koffman, N (retired), MS Ed	
			Agenda		
10:30 AM MT Progra	am Welcome an	d Overview			Drs. Koffman and Stephens
10:35 AM Patien	nt Self-Advocacy	, Support, and E	ducation		Stephen Feldman
10:45 AM CLL B	asics				Dr. Boyu Hu
11:00 AM What to Watch While You Wait Dr. Harsh Shah					Dr. Harsh Shah
11:15 AM CLL Treatments and Clinical Trials					Dr. Deborah Stephens
11:30 AM Hunts	man Foundation	ı			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



Biography





- 62 years old
- Originally from New York City
- Los Angeles resident since 2014
- B.S. Biology, Hunter College
- M.S.Ed. Counseling, Fordham University
- Group Facilitator: City of Hope Support Group

Diagnosis: The Big One

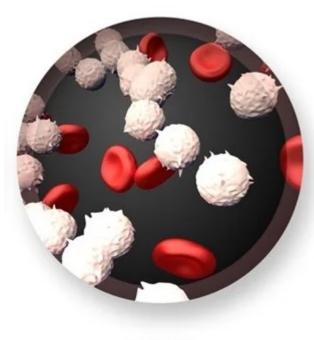




- 1983: Spinal Cord Injury (age 23)
- Cause: Arteriovenous Malformation (AVM)
 - "Spinal Stroke"
- Result: Paraplegia complete paralysis from midchest down

Diagnosis: The Less Big One





LEUKEMIA

- 2014: CLL Diagnosis (age 54)
- Genetics/Prognostics: 13q del; Trisomy 12; IgHV Mutated
- Watch & Wait (aka WaitWatchers™) 3 years
- Treatment: (2017) Combination of Ibrutinib + Obinutuzumab (Gazyva)
- Remission: uMRD, Flow Cytometry, ClonoSEQ

The Patient Experience: Taking the Lead in Learning from Experts







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





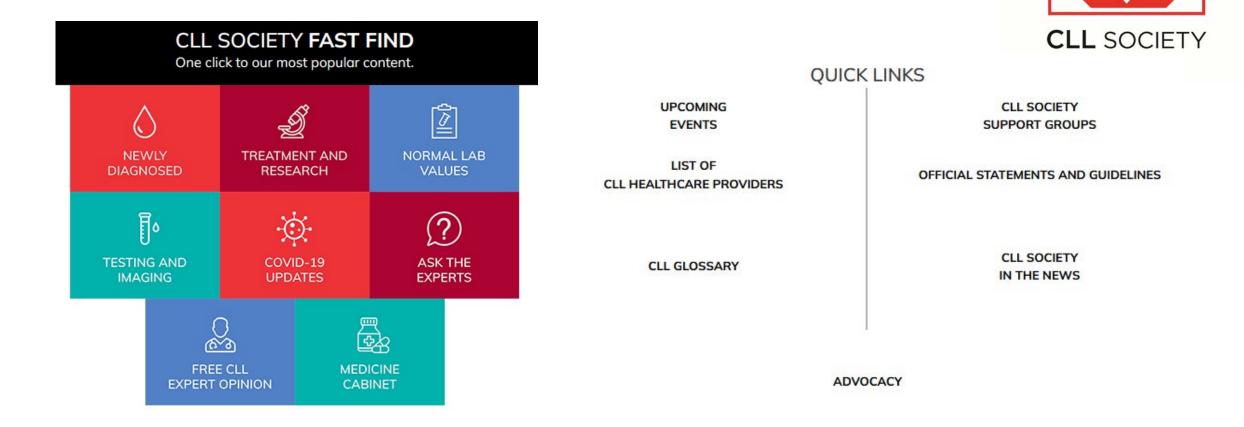
- You charted a course to this education forum.
- You're listening to and learning from *experts* in the field.
- You're listening to and learning from *patients* and *caregivers*.
- Smart patients learn from and pass along knowledge to smart patients.

The CLL Society Experience



- 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



Important Takeaways from 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":

oHave a CLL specialist on your team, accept no substitutions!

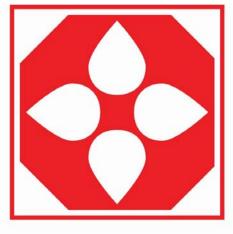
 CLL Society's Expert Access[™] Program can help with 2nd opinions

Last Thoughts





- 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

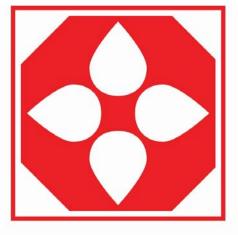


CLL SOCIETY

Smart Patients Get Smart Care™

Thank you!

http://cllsociety.org



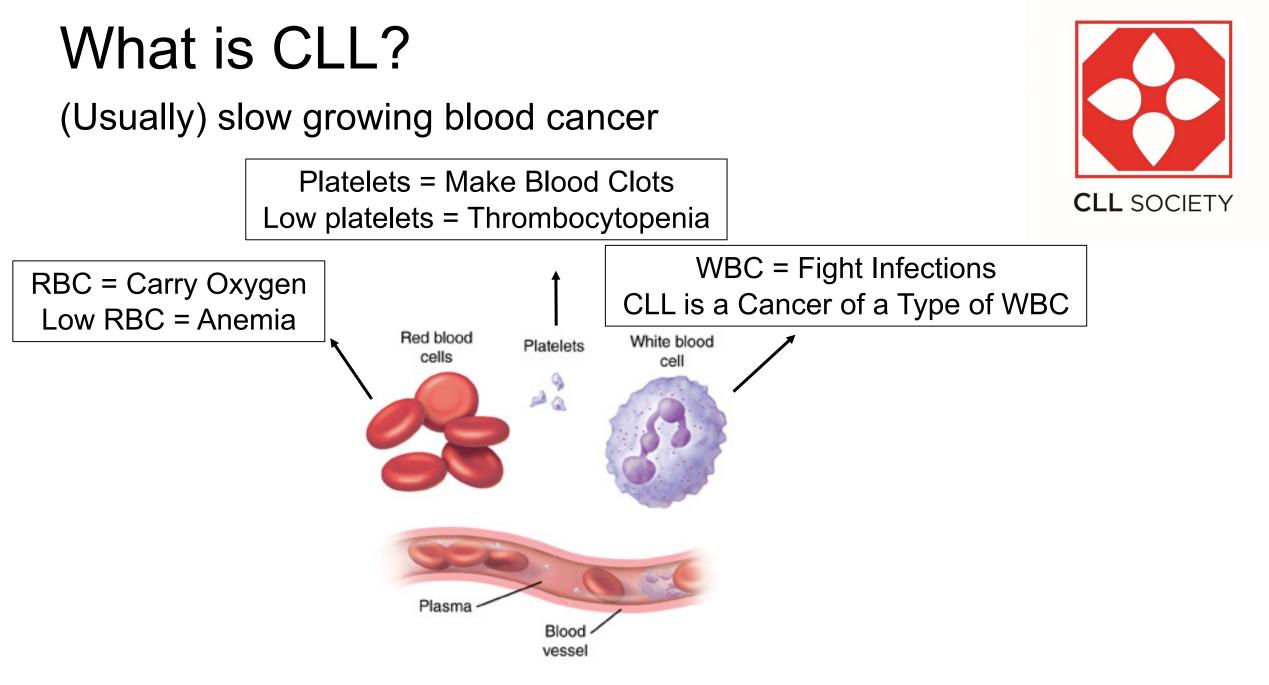
CLL SOCIETY

Smart Patients Get Smart Care™

CLL Basics

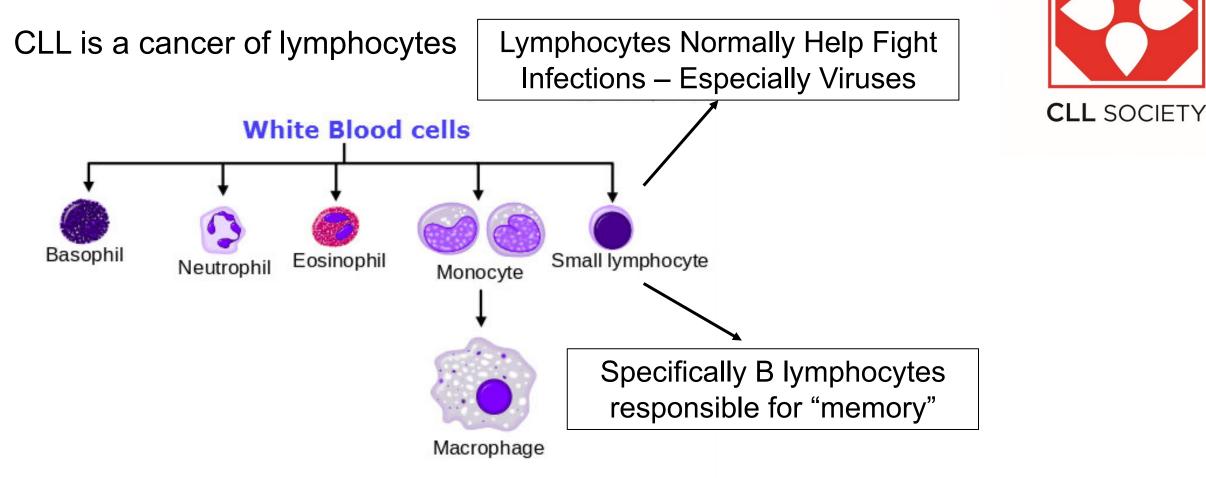
Boyu Hu, MD Assistant Professor, Division of Hematology and Hematologic Malignancies, Department of Internal Medicine Huntsman Cancer Institute / University of Utah

November 16, 2022



https://www.fairview.org/HealthLibrary/Article/40309

What is CLL?





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)

Risk Factors

- Male sex (incidence double that of females)
- White ancestry (4.14/100000 in 2004)
 - Asians, whether in US or Asia, are at lowest risk (0.84/100000) suggesting that genetics are more important than environment
- Family history of blood cancer
 - 5% of cases are familial, with at least 1 relative with CLL
 - Risk of CLL is higher in relatives of patients with any lymphoma or lymphoid leukemia



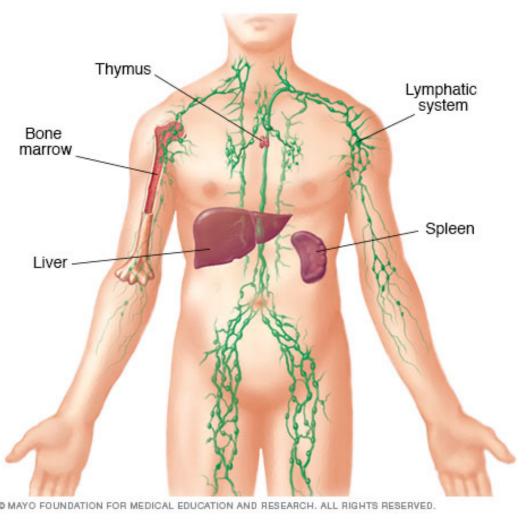
Typical Clinical Course



- 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



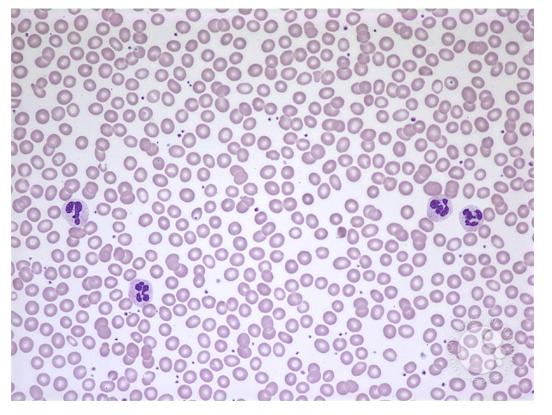
Clinical Case

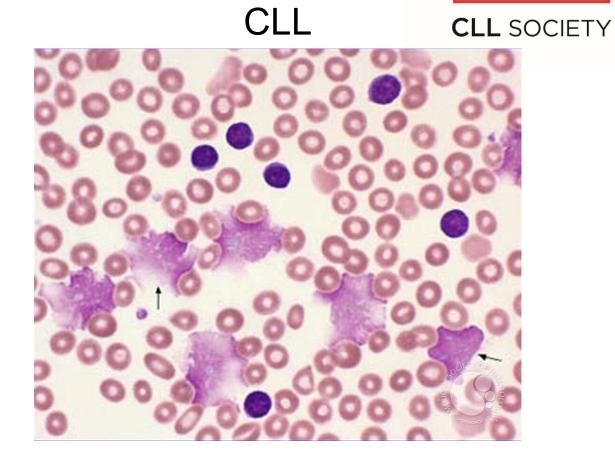


- 60-year-old male presented to doctor for yearly physical exam
- Routine labs showed WBC count of 40,000/uL (normal 4000-10,000/uL)
- Lab reports 88% of these as "abnormal lymphoid cells"
- Other blood counts are normal
- Doctor suspects CLL and patient is referred to Huntsman Cancer Institute
- What is necessary for diagnosis?

Blood Smear

Normal





Cell Surface Protein Expression for Diagnosis

CLL Cell



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



Bone Marrow Aspiration and Biopsy

Skin

Hip bone

Jamshidi needle

Bone marrow







2007 Terese Winstort Terese Winstort Physical Action Contract C



IN GENERAL: CLL staging is not that useful

CLL Staging

Back to Our Example Patient

- Flow cytometry confirmed CLL
- ↑ Lymphocytes (>5.0 k/uL)
- Enlarged lymph nodes
- Rai Stage I
- What other tests might be helpful?

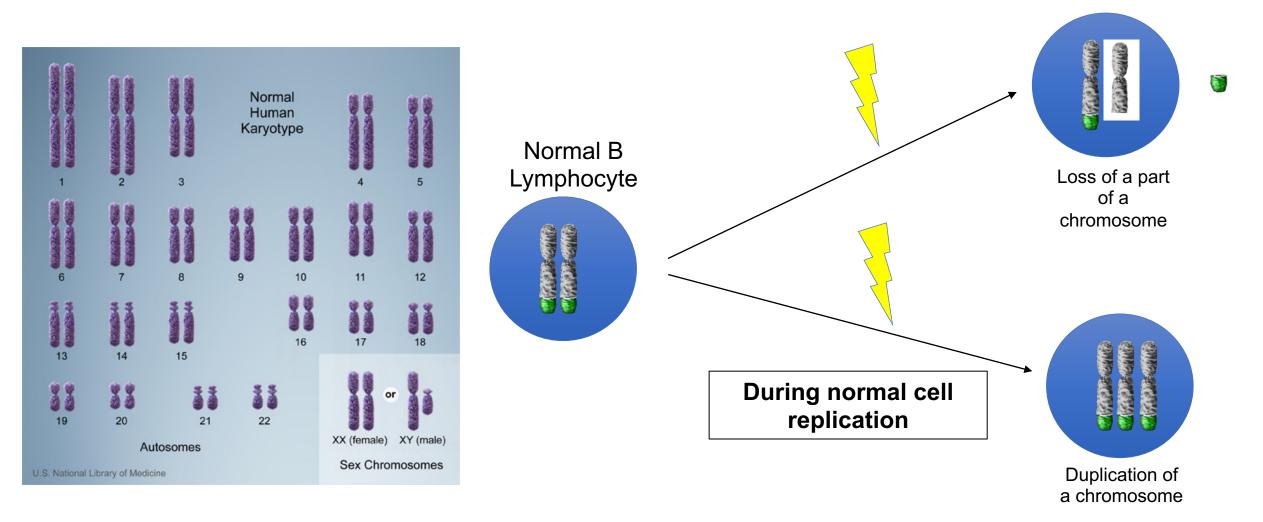


CLL Prognostic Factors



- 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

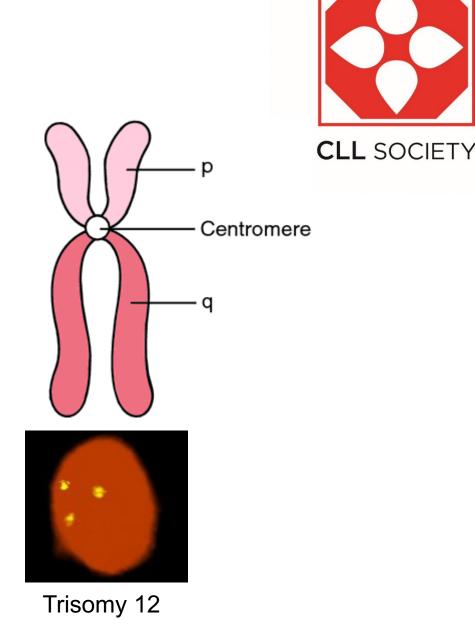
CLL FISH – What does it mean?



FISH Panel

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

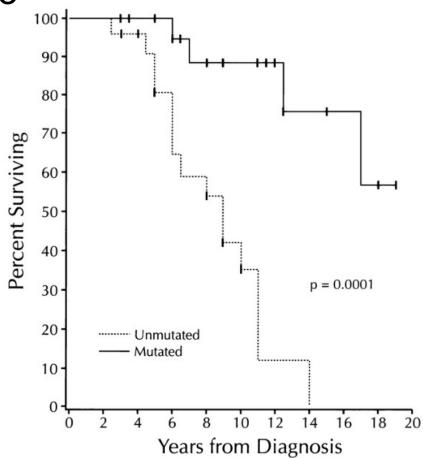
Mutation	%	Good or Bad
Del(13q)	30-45	Good
Trisomy 12	~20	In between
Del(11q)	17-20	Bad
Del(17p)	7-10	Bad



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



- Most common: TP53, ATM, SF3B1, NOTCH1
- Less common: *BTK, PLCG2, BCL2, XPO1, POT1*
- HCI 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?



- 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

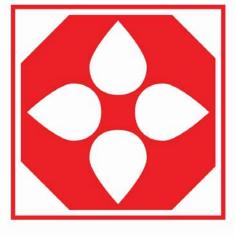
CLL Basic Takeaways



- CLL 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.



Thank You and Questions at the End



CLL SOCIETY

Smart Patients Get Smart Care™

Watch & Wait in CLL

Harsh Shah, DO

November 16, 2022

Learning Objectives

- Watch & Wait
- Vaccinations
- Secondary cancers/screenings
- Lifestyle diet and exercise
- COVID-19 updates



When Do We Treat CLL



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

Reasons for Watch & Wait in CLL

CLL SOCIETY

- CLL is still generally considered incurable
- Some patients may not need any treatment throughout their life
- Multiple studies have shown that treating asymptomatic CLL patients does not prolong life
 - Studies were done with traditional chemotherapy
 - With our current landscape of targeted therapies, it's unclear if some patients may have benefit with early treatment in absence of meeting criteria for treatment (**e.g. S1925**)

What Happens During Watch & Wait



- Most likely every 3 12 month visits with your doctor that will include lab work, history taking, and physical exam.
 - Patient symptoms are most important
 - Visits may be closer together or spaced further apart depending on what is happening with the patient and/or their "stability" (may depend on whether CLL is high vs low risk)
- Performing routine scans without new or worsening symptoms is generally not recommended
 - False positives leading to unnecessary biopsies or work up
 - You can't scan for ever!

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



Cancer Screening with CLL

- 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 HCI in patients with history of Non-Melanoma Skin Cancer within last 5 years
 - Sunscreen (SPF15 or higher)



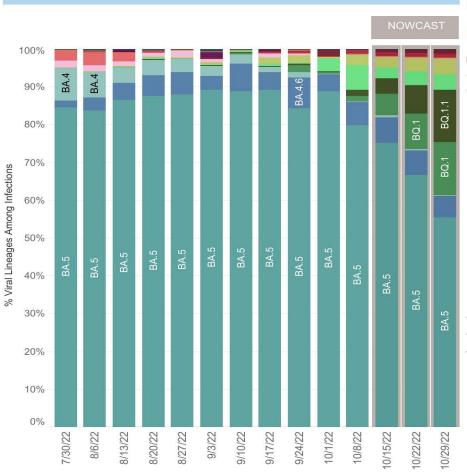
Diet and Lifestyle

- 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:
 - <u>The American Heart Association Diet and</u> <u>Lifestyle Recommendations | American Heart</u> <u>Association</u>



Copyright 2021 American Hinari Association, Inc., a 50(c)(3) not-far-peolit. All sights memorial estiling for Good is a trademark. Unauthorized use prohibited. 3/21 D517388

COVID-19 Variants in Mountain West



HHS Region 8: 7/24/2022 - 10/29/2022

Collection date, week ending

HHS Region 8: 10/23/2022 - 10/29/2022 NOWCAST

Region 8 - Colorado, Montana, North Dakota, South Dakota, Utah, and Wyoming

WHO label	Lineage #	US Class	%Total	95%PI	
Omicron	BA.5	VOC	55.4%	47.1-63.5%	
	BQ.1.1	VOC	13.9%	6.2-27.3%	
	BQ.1	VOC	13.9%	7.8-23.2%	
	BA.4.6	VOC	5.8%	4.4-7.5%	
	BF.7	VOC	4.4%	2.9-6.6%	
	BA.5.2.6	VOC	4.1%	2.4-7.0%	
	BA.2.75.2	VOC	1.1%	0.1-6.4%	
	BA.2.75	VOC	1.1%	0.3-3.1%	
	BA.4	VOC	0.2%	0.2-0.3%	
	BA.1.1	VOC	0.0%	0.0-0.0%	
	BA.2.12.1	VOC	0.0%	0.0-0.0%	
	BA.2	VOC	0.0%	0.0-0.0%	
	B.1.1.529	VOC	0.0%	0.0-0.0%	
Delta	B.1.617.2	VBM	0.0%	0.0-0.0%	
Other	Other*		0.0%	0.0-0.1%	

 Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all weeks displayed.
 These data include Nowcast estimates, which are modeled

projections that may differ from weighted estimates generated at later dates

BA.1, BA.3 and their sublineages (except BA.1.1 and its sublineages) are aggregated with B.1.1.529. Except BA.2.12.1, BA.2.75, BA.2.75.2 and their sublineages, BA.2 sublineages are aggregated with BA.2. Except BA.4.6, sublineages of BA.4 are aggregated to BA.4. Except BF.7, BA.5.2.6, BQ.1 and BQ.1.1, sublineages of BA.5 are aggregated to BA.5. For all the lineages listed in the above table, their sublineages are aggregated to the listed parental lineages respectively. Previously, BA.5.2.6 were aggregated with BA.5. Lineages BA.2.75.2, BA.4.6, BF.7, BA.5.2.6 and BQ.1.1 contain the spike substitution R346T.



BA.5 still the most common but BQ.1 and BA.4.6 are increasing

COVID-19 Prevention



- 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 <u>at least 2 months after either</u>:
 - 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)



- 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



 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



- You test positive for SARS-CoV-2 (virus that causes COVID-19)
- You currently have <u>COVID-19 symptoms</u> 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



- 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









Current Treatment Options



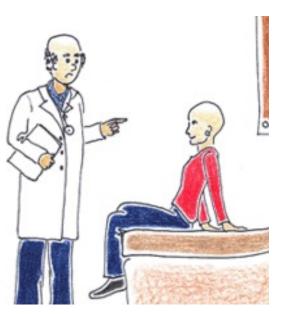
General Cancer Treatment Options

- 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



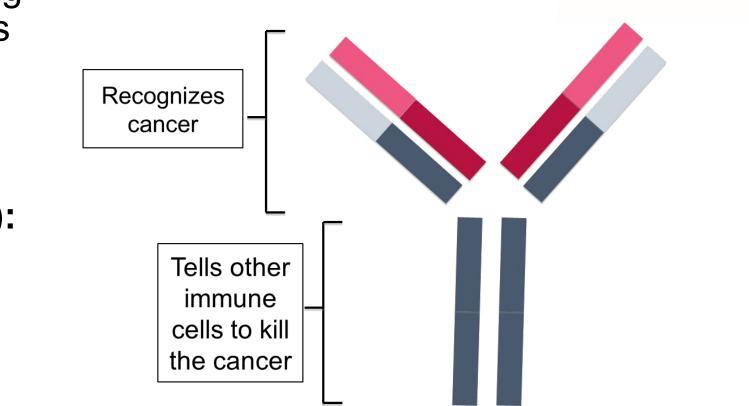


"At least yours will

- 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

Immunotherapy

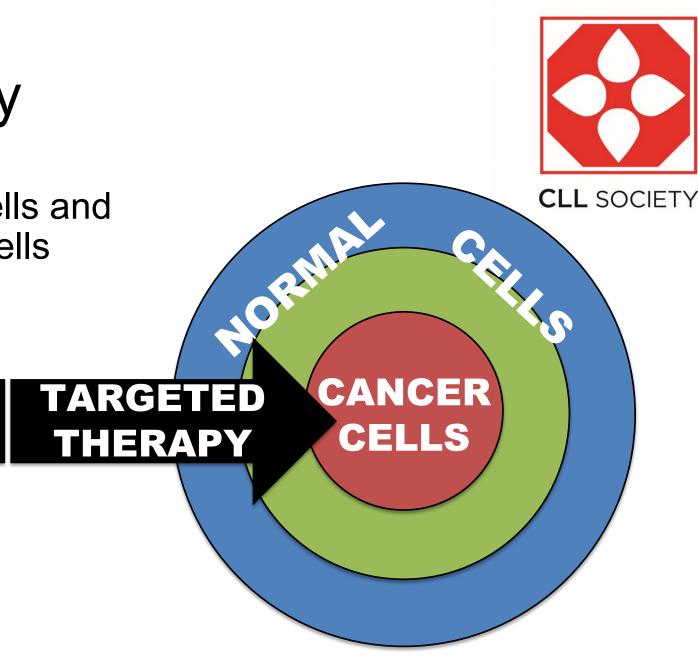
 Specifically targeting something that lives on the outside of a CLL cell CLL SOCIETY



- Antibodies (CD20):
 - Rituximab
 - Ofatumumab
 - Obinutuzumab

Targeted Therapy

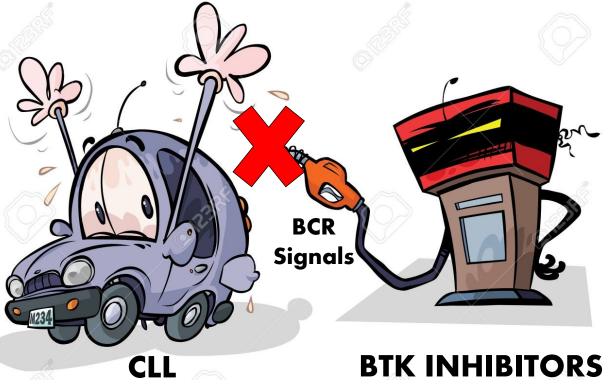
- Avoids killing normal cells and goes after the cancer cells
- Ibrutinib, acalabrutinib, zanubrutinib, idelalisib, venetoclax....



Bruton's Tyrosine Kinase (BTK) Inhibitors

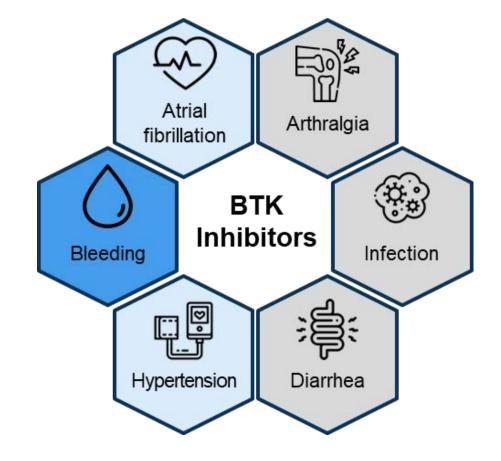
- Block cancer survival signals (Bcell receptor pathway)
- Like taking gas out of your car
- **Ibrutinib**: Approved all CLL patients
- Acalabrutinib: Approved all CL patients
- Zanubrutinib: Coming soon...





Common Toxicities with BTK Inhibitors





Early: Goes Away with Time

Later: Risk Increases with Time

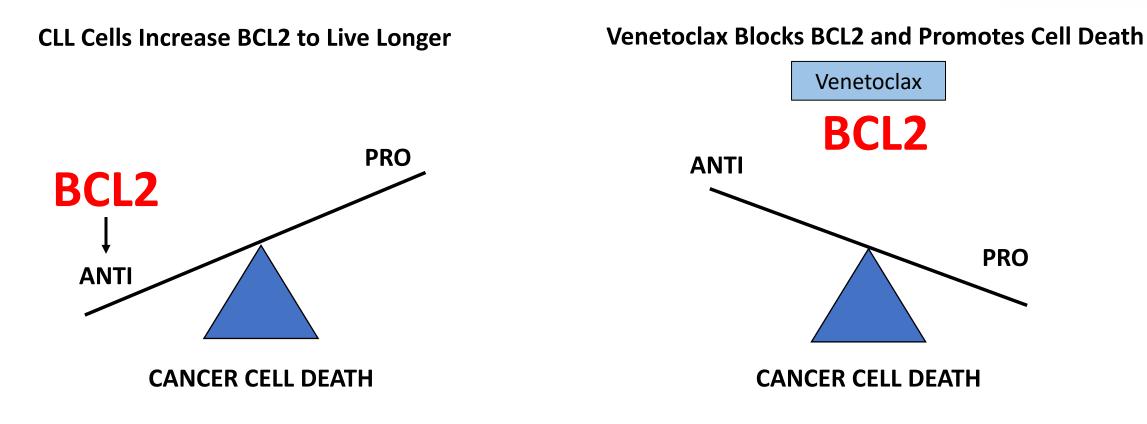
Any Time: Always a Risk

NOTE: Less toxicity with Acalabrutinib or Zanubrutinib

Venetoclax

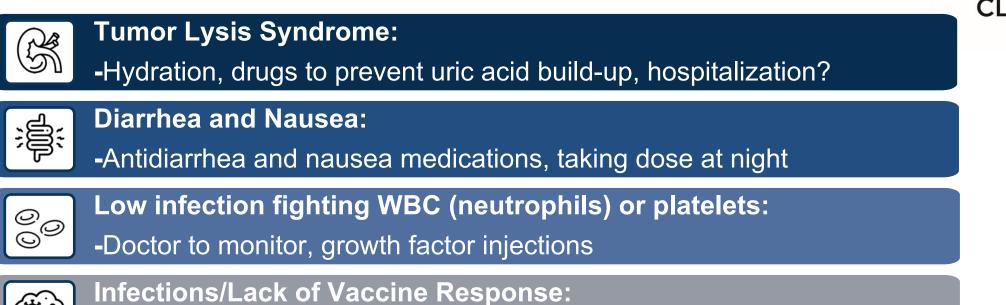
Venetoclax = Approved for all CLL patients in combination with anti-CD20







Venetoclax: Toxicities and Management



-Vaccines before starting treatment, antibiotics, monitor for fever

Strategies to Treat CLL



Continuous Therapy		Goal of Therapy	
 BTK inhibitors 		 Disease control Prolonged remission 	
Fixed Duration		Goal of Therapy	

Adapted from slide by C DeLucca



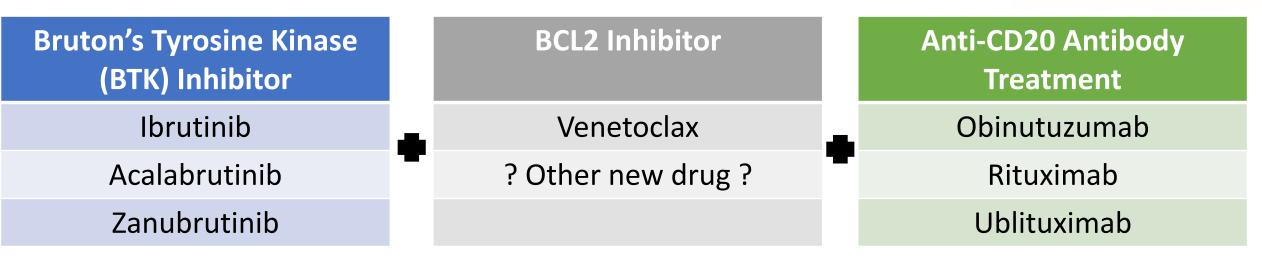
New Treatment Approaches

Currently available on clinical trials

Combinations of New Drugs



• Pick 2 or 3 good drugs and combine them

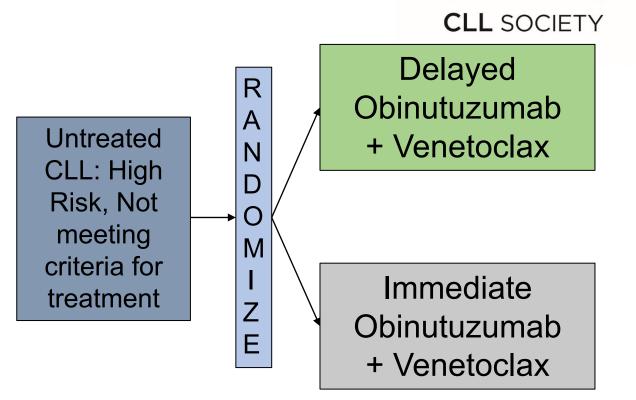


 Advantages: Deeper or Longer Lasting Responses, Shorten Treatment Length

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

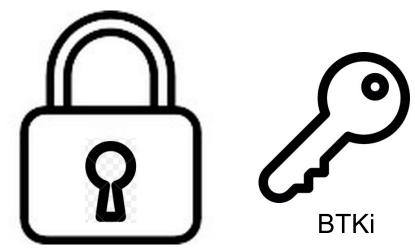


When a BTKi Doesn't Work Anymore....



▲ BTK (C481S)

- ▲ Still fits, but doesn't block well KEYHOLE: SPOT ON CLL WHERE
- ▲ Rapid progression after BTKi d/c
- ▲ DO NOT D/C BTKi without another plan!
- ▲ Applies to ibrutinib, acalabrutinib, and zanubrutinib



KEYHOLE: CHANGES AND BTKi DOESN'T FIT WELL

BTKi BINDS

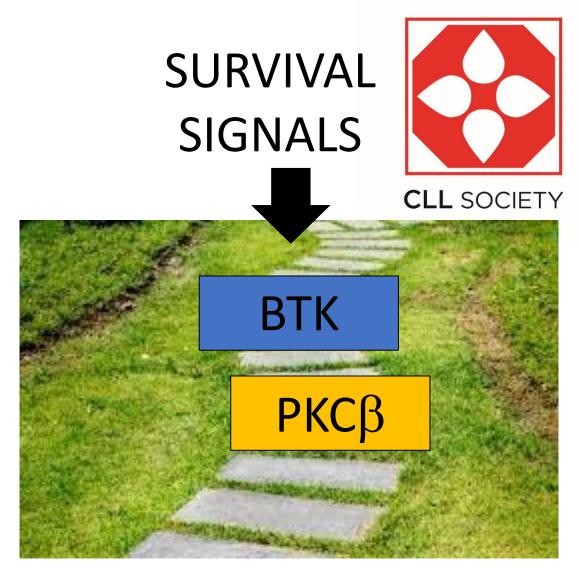


When Ibrutinib Doesn't Work Anymore...

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

MS-553

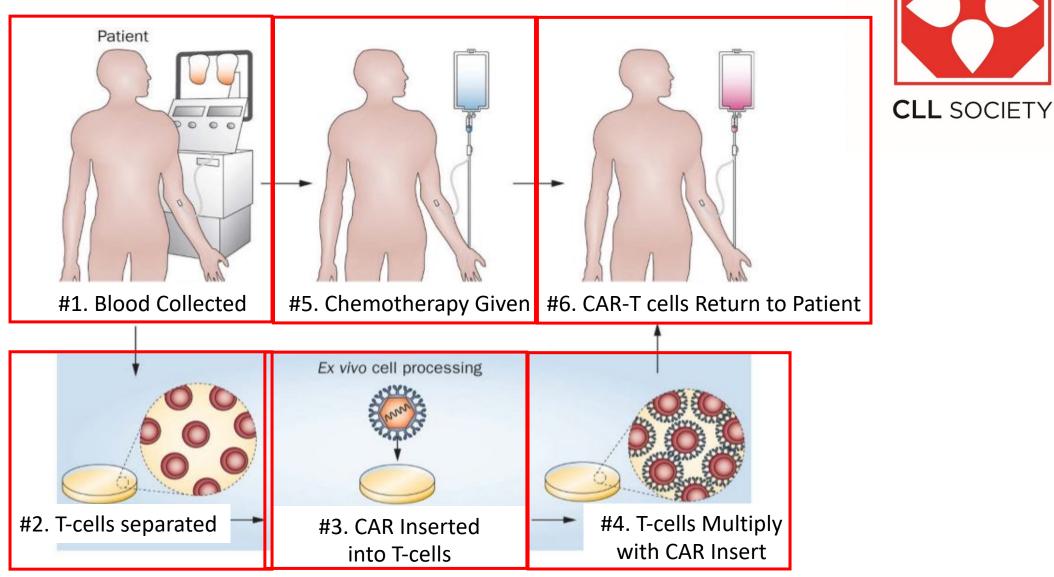
- BTK inhibitors block CLL survival signals
- PKC inhibitors block CLL survival signals in a different spot on the survival pathway
- Promising new pill that works when ibrutinib no longer works
- Clinical Trial Open at Utah!



CLL SURVIVAL

CAR-T Cell Therapy **CLL** SOCIETY **IMMUNE SYSTEM** CANCER CD19 CART

CAR-T Cell Therapy



Kochenderfer, Nat. Rev. Clin. Oncol. 2013

Review

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

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





Questions?

Twitter: @Debbiemstephens

Huntsman Cancer Foundation

- Brandon Plewe
- <u>bplewe@huntsmanfoundation.org</u>
- (801)584-5814
- Development Officer Fundraising







Audience Questions & Answers

This program was made possible by grant support from







Bristol Myers Squibb[™]





Thank You for Attending!

CLL SOCIETY

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

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

If you're 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/