

CLL SOCIETY

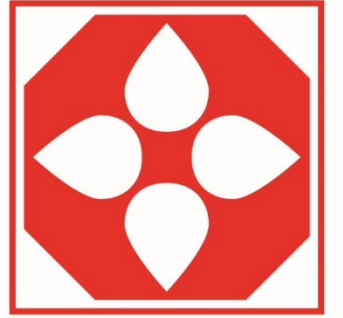
Smart Patients Get Smart Care™

The CLL/SLL Medicine Cabinet: Understanding Your Available Treatment Options

October 23, 2023

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

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Speakers



Speaker

Christina Russomanno, MSN, RN, ANP-C, AOCN

Nurse Practitioner, Leukemia Service
Herbert Irving Comprehensive Cancer Center
Columbia University Irving Medical Center



Welcome and Speaker

Robyn Brumble, MSN, RN

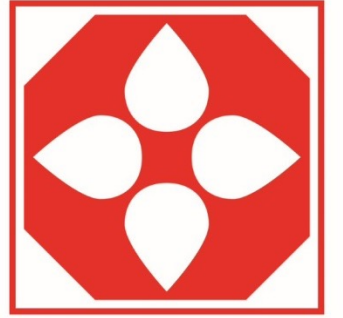
Director of Scientific Affairs and Research
CLL Society



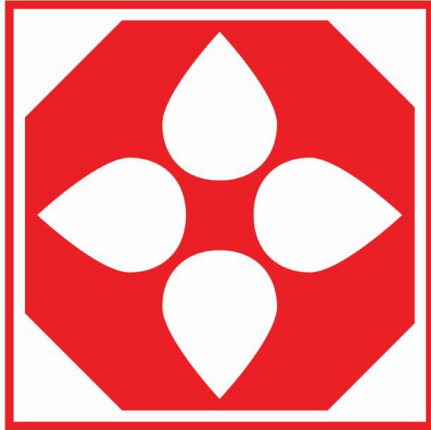
Moderator

Brian Koffman, MDCM (retired), MS Ed

Executive Vice President and Chief Medical Officer
CLL Society



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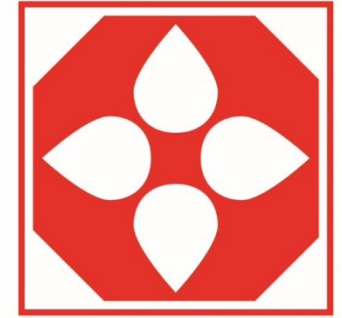
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The CLL Medicine Cabinet

Robyn Brumble, RN, MSN
Director of Scientific Affairs
CLL Society

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CLL 101 for the newly diagnosed

Welcome.

Let's get you started in the right direction

LEARN MORE

CLL Society is the world's leading authority for chronic lymphocytic leukemia and small lymphocytic lymphoma cancer patients.

We are devoted to serving our community through CLL and SLL education, support, advocacy and research.

Actively Enrolling Clinical Trials in CLL. To access additional clinical trials please search: clinicaltrials.gov

DO YOU HAVE AN IMPAIRED IMMUNE SYSTEM?
New clinical research study to protect people from COVID-19
Find out more to participate.
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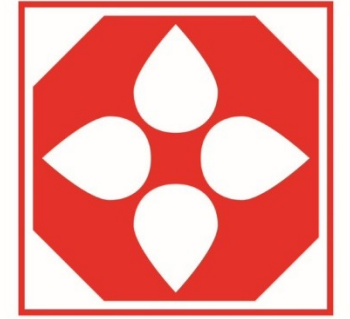
STUDY FOR IMMUNOCOMPROMISED PEOPLE WITH COVID-19
Study for people with weakened immune systems or other risk factors
Recently diagnosed with COVID-19
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NX-5948: a new oral BTK protein degrader
A novel drug designed to overcome resistance to BTK Inhibitors
View our open trials for patients with CLL/ SLL
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- FREE CLL EXPERT OPINION

Navigating Through The Medicine Cabinet



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The CLL Medicine Cabinet

Choosing the Right Treatment for You

There are several factors your healthcare provider will take into consideration when discussing what treatment options might be the best for you. These factors may include:

- Your **biomarker test results** (which help determine staging, disease aggressiveness, and prognosis)
- Your comorbidities (other conditions that you already have in addition to cancer, such as heart or kidney disease)
- Your age
- Whether this is the first time you need treatment (first-line), or if this is a subsequent treatment (second-line and beyond)
- What the expected benefit will be from a treatment
- What the common side effects might be
- How the treatment is administered (oral, intravenously)
- Where the treatment will need to be administered (home, an infusion center, or a hospital)
- How long the treatment must be taken (for a limited duration of time, or continuously until the medication no longer controls the disease)
- Your financial considerations (will the medication be covered by your insurance and if not are there any ways to obtain the treatment through other means, such as medication assistance programs)
- Whether the treatment is already FDA-approved or if it only accessible through a clinical trial

Click on the individual bottles below to view the available medication sheet and access links to other available medication information.



acalabrutinib
duvelisib
ibrutinib

idelalisib
obinutuzumab
pirtobrutinib

rituximab
venetoclax
zanabrutinib

Generic Name: **Ibrutinib**

Brand Name: **Imbruvica**

Drug Classification: Covalent Bruton Tyrosine Kinase (BTK) Inhibitor

INDICATIONS FOR USE

- **For CLL and SLL without 17p deletion or TP53 mutation:** Ibrutinib may be taken alone or in combination with another medication as an initial (first-line) treatment. When used as a combination therapy for front-line treatment, it is usually combined with either rituximab, obinutuzumab, or venetoclax. Ibrutinib may be taken alone as a second-line or subsequent treatment in those without 17p deletion or TP53 mutation.
- **For CLL and SLL with 17p deletion or TP53 mutation:** Ibrutinib may be taken alone or in combination with venetoclax as an initial (first-line) treatment, or alone as a second-line or subsequent treatment.

ADMINISTRATION ROUTE

Taken orally by mouth (available as a capsule, tablet, or liquid suspension).

LENGTH OF TIME ADMINISTERED

This medication should be taken indefinitely until either the disease progresses while on the medication (which would require switching to a medication to treat the CLL or SLL), or until certain unacceptable side effects occur requiring discontinuation of the drug.

DOSING

420 mg taken once per day, at the same time each day.

MISSED DOSE

If a dose is missed by more than three hours, it should be skipped. Then take the next dose at the regularly scheduled time. Do not take an extra dose to make up for the missed dose.

HOW TO TAKE THIS MEDICATION

- Swallow the medication with a full glass of water. Do not chew, break, open, or crush.
- If taking the liquid suspension form of this medication, shake well before use and measure the liquid dose carefully using the measuring device that is provided by your pharmacy.
- Drink lots of noncaffeinated liquids unless you are told otherwise by your healthcare provider.

- Do not ingest any starfruit, grapefruit juice, grapefruit, bitter orange/marmalade products, Seville oranges or pomegranate juice. Certain citrus foods are known to interfere with the metabolism of this medication and can potentially cause toxic levels of the drug to build up in the blood.

COMBINATION THERAPIES

Can be used in combination with other medications (i.e., obinutuzumab, rituximab, venetoclax).

COMMON SIDE EFFECTS

Side effects can occur as a result of any medication, some of which may go away with time as your body adjusts to the new medication. Please notify your healthcare provider right away if any of the following side effects occur:

- Low red blood cell count, low white blood cell count, or low platelet count
- Irregular heartbeat (heart palpitations or racing heartbeat)
- Respiratory infection
- Shortness of breath
- Diarrhea
- Constipation
- Nausea and vomiting
- Stomach pain
- Decreased appetite
- Mouth sores
- Fatigue or tiredness
- Muscle, joint, or bone pain
- Bruising or bleeding
- Rash
- Swelling of the legs and feet

Side effects not mentioned above may also occur. Notify your healthcare provider of any other unusual symptoms, as they may be able to tell you about ways to prevent or reduce certain side effects.

MANAGING COMMON SIDE EFFECTS

Some side effects are more common than others, many of which will go away after a short period of time after staying on the medication. It is important to talk to your healthcare provider to discuss if you might be able to manage side effects in the short term in order to stay on the therapy until your body has time to adjust to the new medication. Here are some possible ways to help manage some of the most common side effects of ibrutinib in consultation with your healthcare provider.

Generic Name: **Ibrutinib**

Brand Name: **Imbruvica**

Drug Classification: Covalent Bruton Tyrosine Kinase (BTK) Inhibitor

Diarrhea

- Increase your fluid intake.
- Take anti-diarrheal medications (such as Imodium) per package instructions.
- Eat a bland diet (such as bananas, rice, apples/ applesauce, toast, or plain pasta).

Constipation

- Increase your fluid intake.
- Consume more foods that are high in fiber (such as vegetables and whole grain bread).
- Consider over-the-counter fiber supplements (such as Fibercon, Miralax, or Metamucil).
- Move around more, as walking and other forms of light exercise can help.
- Take over-the-counter stool softeners (such as Colace) to help soften bowel movements.

Fatigue or Tiredness

- Ensure you are eating a well-rounded diet that includes a balance of lean meats, fruits, vegetables, whole grains, and limited amounts of processed foods.
- Incorporate light types of exercise (such as walking).
- If you are able, take one short twenty-minute nap during the day. Frequent or longer naps during the day can affect the amount of sleep you are getting during the night and increase fatigue/tiredness.

Muscle, Joint, or Bone Pain

- Take acetaminophen (such as Tylenol) per package instructions.
- It is important to avoid taking anti-inflammatories (such as ibuprofen) for mild pain while taking ibrutinib due to the slightly increased risk of bleeding.
- Antihistamines (such as Allegra, Zyrtec, or Claritin) may help slightly with bone pain.
- Magnesium supplements may help muscle cramping.
- Gentle stretching and application of heat or ice to the affected area(s) can provide temporary relief.
- If you are experiencing more severe joint pain, your healthcare provider may prescribe a short course of steroids.

REASONS TO TALK TO YOUR HEALTHCARE PROVIDER

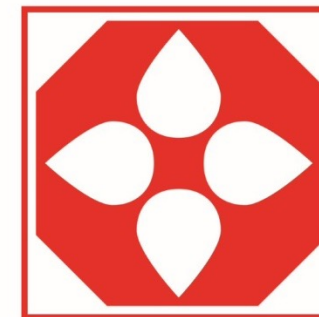
The presence of other medical problems may affect the use of ibrutinib. Make sure you share with your healthcare provider if you have any of the following conditions:

- Liver disease (ibrutinib should be avoided with severe liver impairment)

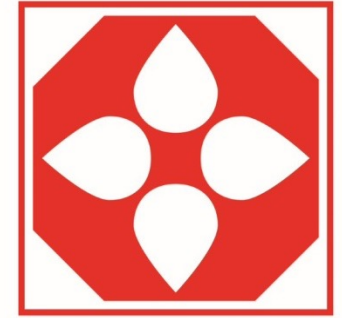
- Heart problems (including palpitations, fast or irregular heartbeat, dizziness, fainting, chest discomfort, or shortness of breath)
- High blood pressure (this medication may raise blood pressure)
- Recent or current infection
- Bleeding problems, or if you are on any blood thinning medication
- If you are pregnant or breastfeeding (or if you plan to become pregnant or breastfeed)

SPECIAL CONSIDERATIONS

- Ibrutinib can have a mild blood-thinning effect, so aspirin and other anti-inflammatory pain medications (such as ibuprofen/Advil) may need to be avoided. Stay away from rough sports or other situations where you could be bruised, cut, or injured. Brush and floss your teeth gently, be careful when using sharp objects, including razors and fingernail clippers.
- Serious bacterial, viral, or fungal infections can occur while taking ibrutinib. But this can also occur in part from being immunocompromised due to having CLL or SLL. Avoid being near people who are sick and wash your hands often.
- If you have had hepatitis B before or carry the virus, talk with your doctor. This drug can cause the dormant virus to become reactivated and protective medication may be needed.
- There are several medications that interfere with the metabolism of ibrutinib and can cause toxic levels of the drug to build up in the blood, or that increase the breakdown of ibrutinib which can decrease the drug's effectiveness. It is very important to tell your healthcare provider about all the medications you take, including prescription and over the counter medicines, vitamins, and herbal supplements (particularly in the case of ibrutinib you should not be on St. John's Wort).
- Secondary cancers have been reported while taking the medication, but this is also a common finding associated with having CLL or SLL. Please be diligent about annual cancer screenings and wearing sun protection when outside in sunlight.
- You may be advised to briefly stop taking ibrutinib for dental or surgical procedures for several days before and after the procedure to minimize the risk of bleeding. Please let your CLL/SLL healthcare provider know about any planned procedures. Never hold or stop taking this medication without the supervision of your healthcare provider.



How to Print the Medication Sheet



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Ibrutinib

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CLL SOCIETY **MEDICINE CABINET: IBRUTINIB**

Generic Name: **Ibrutinib** Brand Name: **Imbruvica**

Drug Classification: Covalent Bruton Tyrosine Kinase (BTK) Inhibitor

INDICATIONS FOR USE

- For CLL and SLL without 17p deletion or TP53 mutation:** Ibrutinib may be taken alone or in combination with another medication as an initial (first-line) treatment. When used as a combination therapy for front-line treatment, it is usually combined with either rituximab, obinutuzumab, or venetoclax. Ibrutinib may be taken alone as a second-line or subsequent treatment in those without 17p deletion or TP53 mutation.
- For CLL and SLL with 17p deletion or TP53 mutation:** Ibrutinib may be taken alone or in combination with venetoclax as an initial (first-line) treatment, or alone as a second-line or subsequent treatment.

ADMINISTRATION ROUTE

Taken orally by mouth (available as a capsule, tablet, or liquid suspension).

LENGTH OF TIME ADMINISTERED

This medication should be taken indefinitely until either the disease progresses while on the medication (which would require switching to a medication to treat the CLL or SLL), or until certain unacceptable side effects occur requiring discontinuation of the drug.

DOSING

420 mg taken once per day, at the same time each day.

MISSED DOSE

If a dose is missed by more than three hours, it should be skipped. Then take the next dose at the regularly scheduled time. Do not take an extra dose to make up for the missed dose.

HOW TO TAKE THIS MEDICATION

- Swallow the medication with a full glass of water. Do not chew, break, open, or crush.
- If taking the liquid suspension form of this medication, shake well before use and measure the liquid dose carefully using the measuring device that is provided by your pharmacy.
- Drink lots of noncaffeinated liquids unless you are told otherwise by your healthcare provider.

COMBINATION THERAPIES

Can be used in combination with other medications (i.e., obinutuzumab, rituximab, venetoclax).

COMMON SIDE EFFECTS

Side effects can occur as a result of any medication, some of which may go away with time as your body adjusts to the new medication. Please notify your healthcare provider right away if any of the following side effects occur:

- Low red blood cell count, low white blood cell count, or low platelet count
- Irregular heartbeat (heart palpitations or racing heartbeat)
- Respiratory infection
- Shortness of breath
- Diarrhea
- Constipation
- Nausea and vomiting
- Stomach pain
- Decreased appetite
- Mouth sores
- Fatigue or tiredness
- Muscle, joint, or bone pain
- Bruising or bleeding
- Rash
- Swelling of the legs and feet

Side effects not mentioned above may also occur. Notify your healthcare provider of any other unusual symptoms, as they may be able to tell you about ways to prevent or reduce certain side effects.

MANAGING COMMON SIDE EFFECTS

Some side effects are more common than others, many of which will go away after a short period of time after staying on the medication. It is important to talk to your healthcare provider to discuss if you might be able to manage side effects in the short term in order to stay on the therapy until your body has time to adjust to the new medication. Here are some possible ways to help manage some of the most common side effects of ibrutinib in consultation with your healthcare provider.

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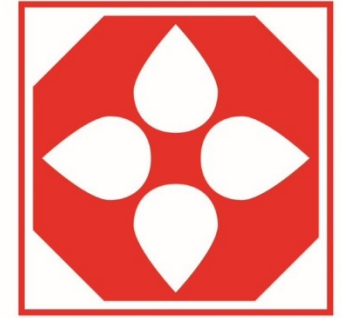
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Drug Classification: Covalent Bruton Tyrosine Kinase (BTK) Inhibitor

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- **For CLL and SLL with 17p deletion or TP53 mutation:** Ibrutinib may be taken alone or in combination with venetoclax as an initial (first-line) treatment, or alone as a second-line or subsequent treatment.

ADMINISTRATION ROUTE

Taken orally by mouth (available as a capsule, tablet, or liquid suspension).

LENGTH OF TIME ADMINISTERED

This medication should be taken indefinitely until either the disease progresses while on the medication (which would require switching to a medication to treat the CLL or SLL), or until certain unacceptable side effects occur requiring discontinuation of the drug.

DOSING

420 mg taken once per day, at the same time each day.

MISSED DOSE

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HOW TO TAKE THIS MEDICATION

- Swallow the medication with a full glass of water. Do not chew, break, open, or crush.
- If taking the liquid suspension form of this medication, shake well before use and measure the liquid dose carefully using the measuring device that is provided by your pharmacy.
- Drink lots of noncaffeinated liquids unless you are told otherwise by your healthcare provider.

COMBINATION THERAPIES

Can be used in combination with other medications (i.e., obinutuzumab, rituximab, venetoclax).

COMMON SIDE EFFECTS

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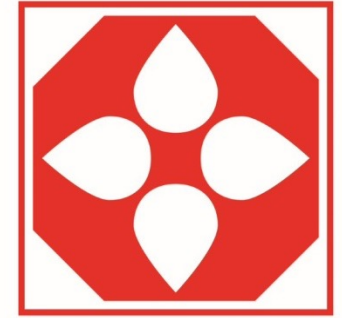
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CLL SOCIETY MEDICINE CABINET: **IBRUTINIB**

Generic Name: **Ibrutinib** Brand Name: **Imbruvica**

Drug Classification: Covalent Bruton Tyrosine Kinase (BTK) Inhibitor

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ADMINISTRATION ROUTE

Taken orally by mouth (available as a capsule, tablet, or liquid suspension).

LENGTH OF TIME ADMINISTERED

This medication should be taken indefinitely until either the disease progresses while on the medication (which would require switching to a medication to treat the CLL or SLL), or until certain unacceptable side effects occur requiring discontinuation of the drug.

DOSING

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- Drink lots of noncaffeinated liquids unless you are told otherwise by your healthcare provider.

COMBINATION THERAPIES

Can be used in combination with other medications (i.e., obinutuzumab, rituximab, venetoclax).

COMMON SIDE EFFECTS

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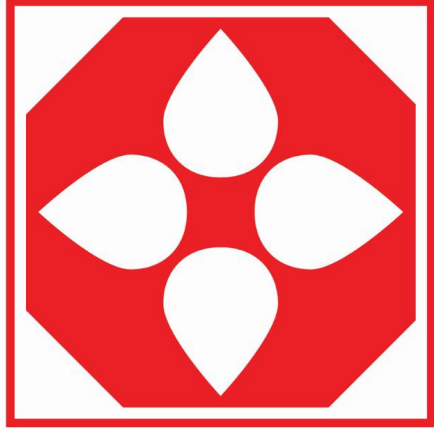
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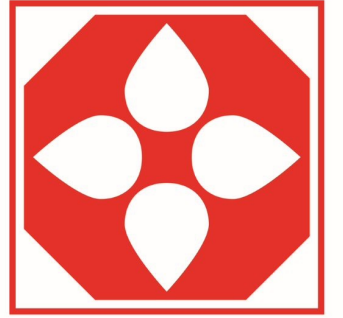
The CLL/SLL Medicine Cabinet: Understanding Your Available Treatment Options

**Christina Russomanno, MS,
RN, ANP-C, AOCN**

10/23/2023

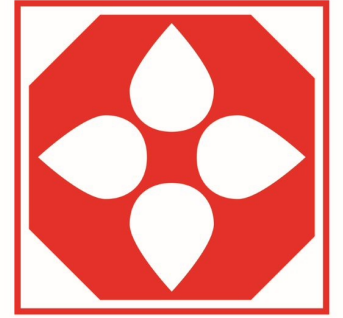
I Need Therapy, How Did I Get Here?

- Diagnosed and already need treatment
 - Rare, but possible
 - You may not have any symptoms
- Watch and Wait, Active Surveillance, Active Monitoring...
 - Educate
 - Support system (family, friends, a support group)
 - Health care maintenance
 - Meet with a CLL expert for a second opinion



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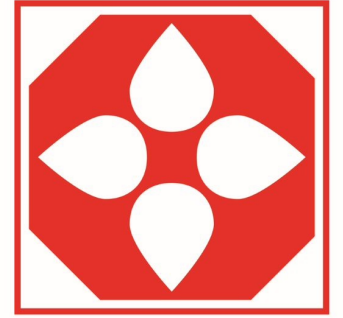
When is it Time to Start Therapy?



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- Progressive bone marrow failure with worsening anemia (hemoglobin < 10) and/or platelet count $< 100,000$
- Massive or progressive splenomegaly or lymphadenopathy
- Progressive lymphocytosis with an increase of $> 50\%$ over a two-month period or lymphocyte doubling time of < 6 months
- Symptomatic or functional extranodal involvement (i.e. skin, kidney, lung)
- Symptoms: significant fatigue limiting activity, night sweats (> 1 month without infection), weight loss ($> 10\%$ body weight in past 6 months), fevers for at least 2 weeks without infection
- Autoimmune Hemolytic Anemia (AIHA where the body attacks its own red cells) and/or Immune Thrombocytopenic Purpura (ITP where the body attacks its own platelets) that is poorly responsive to steroids or other standard therapy

Considerations Prior to Treatment



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Anemia or thrombocytopenia

- Exclude GI blood loss
- Assess for AIHA/ITP

Symptomatic disease

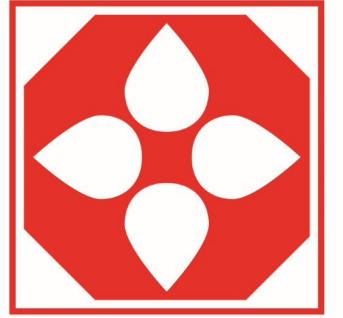
- Assess for possible lymphoma transformation

Rapidly progressive disease

- Assess for possible lymphoma transformation

AIHA = autoimmune hemolytic anemia; GI = gastrointestinal; ITP = immune thrombocytopenic purpura.

Factors To Consider When Choosing a New Therapy

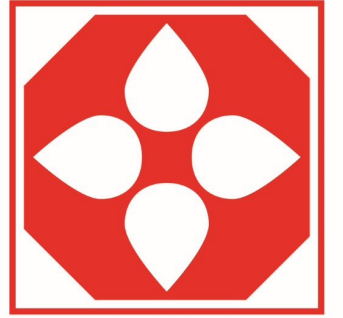


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- Age
- Specific disease markers – if not done at diagnosis, should be done prior to treatment
 - FISH, IGHV mutation status
- Performance status
- Comorbidities
- Your goals
- Your lifestyle
- Your support system

Current Treatment Options

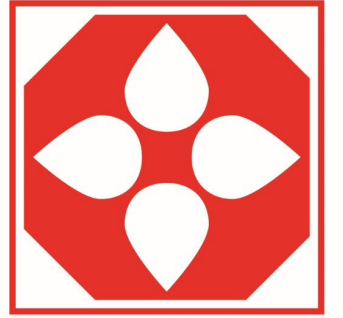
- Targeted Therapies
 - BTK inhibitors
 - BCL2 inhibitors
 - PI3K inhibitors
- Monoclonal Antibodies
 - Rituximab
 - Obinutuzumab
- Chemotherapy or Chemoimmunotherapy
 - Fludarabine, Cyclophosphamide, Rituximab (FCR)
 - Bendamustine + Rituximab (BR)
- CAR-T cell Therapy
- Stem cell/Bone marrow transplant
- Clinical Trials



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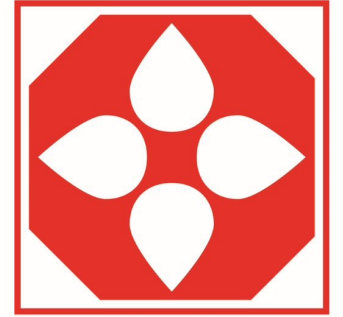
Targeted Therapy - What Does That Mean?

- Cancer treatments that target a particular area, protein, receptor, pathway in CLL cells
- They do not target healthy cells, limiting side effects
- But what do they do?
 - Block or turn off chemical signals that tell the cancer cell to grow and divide
 - Change proteins within the cancer cells so the cells die
 - Stop making new blood vessels to feed the cancer cells
 - Trigger your immune system to kill the cancer cells
 - Carry toxins to the cancer cells to kill them, but not normal cells



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Bruton's Tyrosine Kinase (BTK) Inhibitors



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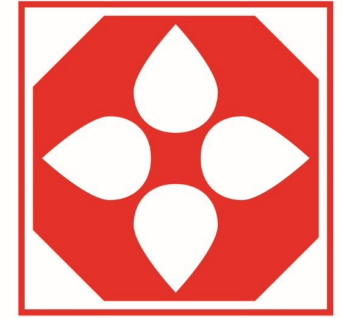
- Inhibit BTK by interfering with signaling, preventing growth/survival
- Continuous therapy taken every day
- Can be given alone or in combination with a monoclonal antibody
- Less office visits, less monitoring
- Fast improvement in lymph node size and liver/spleen size
- Work well in those with high-risk genomic features (ie del 17p)

- Examples of covalent BTKIs
 - Ibrutinib (Imbruvica) – 1st generation
 - Acalabrutinib (Calquence) – 2nd generation
 - Zanubrutinib (Brukinsa) – 2nd generation

- Examples of noncovalent BTKIs
 - Pirtobrutinib (Jaypirca)*
 - Nemtabrutinib*

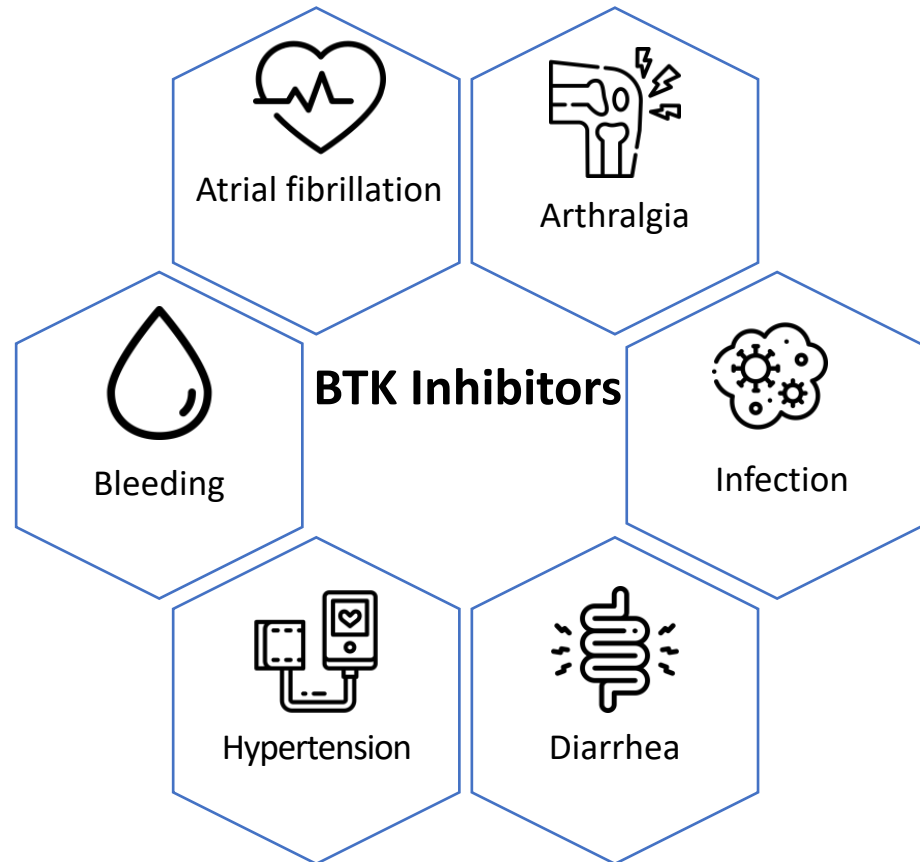
*Not yet approved in CLL, in clinical trials

Side Effects of BTK Inhibitors

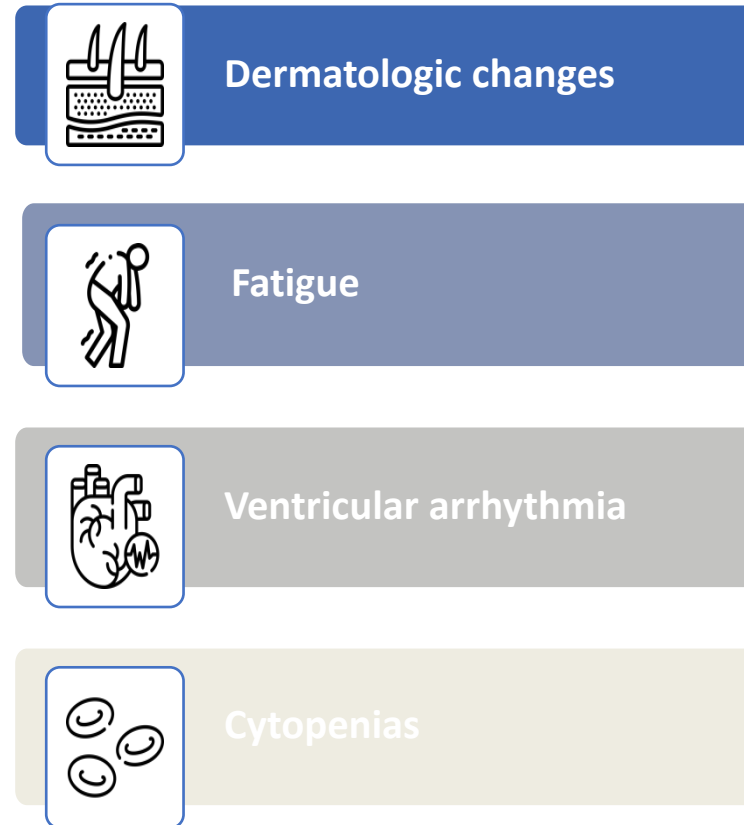


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Common Side Effects

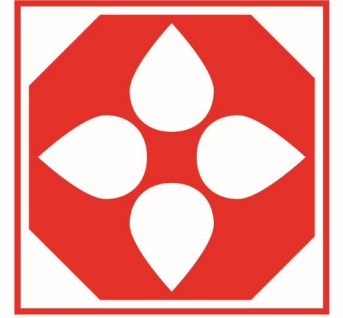


Other Important Side Effects



Zanubrutinib – neutropenia; Acalabrutinib - headaches

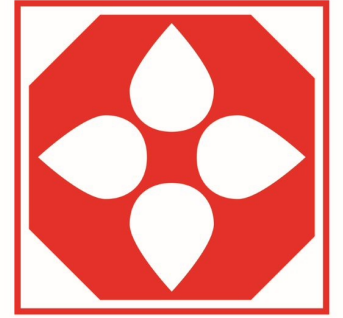
BCL-2 Inhibitors



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- Venetoclax (Venclexta)
 - Inhibits BCL-2, which normally protects cancer cells from dying
 - Time-limited therapy
 - In combo with Obinutuzumab in upfront therapy (total of 12 months)
 - In combo with Rituximab in relapsed setting (total of 24 months)
 - Drug ramp up over 5 weeks with close monitoring
 - Risk of tumor lysis syndrome, low blood counts, GI symptoms, infections
 - More daunting schedule early on
 - Possibility of uMRD (undetectable measurable residual disease)
 - Possibility of retreatment if relapse \geq 24-36 months from initial therapy

PI3K Inhibitors

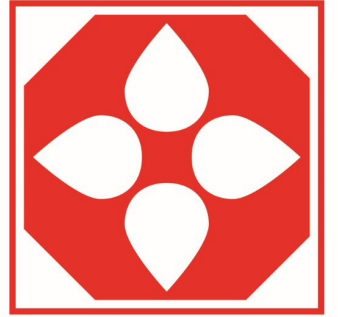


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- Idelalisib (Zydelig)
 - FDA approved in relapsed CLL in combination with Rituximab
 - Oral medication
 - High risk of infection (48%), hepatotoxicity (16%), diarrhea or colitis (20%), pneumonitis (4%), intestinal perforation
- Duvelisib (Copiktra)
 - FDA approved in relapsed or refractory CLL after at least two prior therapies
 - Oral medication
 - High risk of infection (31%), diarrhea or colitis (18%), cutaneous reactions (5%), pneumonitis (5%)

Monoclonal Antibodies

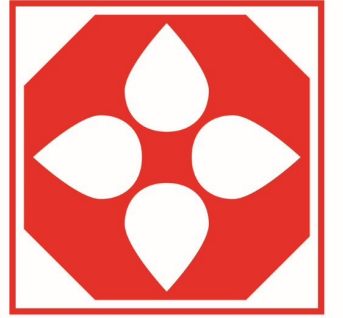
- Type of immunotherapy, but also a targeted therapy
- Man-made versions of immune system proteins (antibodies)
- Attach to a specific target. In CLL, this protein is CD20 which is found on the surface of B-lymphocytes.
- Help your immune system react to and destroy the cancer cells
- Given via an infusion or under the skin (subcutaneous)
- Can be used alone or in combination with other drugs
- Common side effects: Infusion reactions, fevers, chills, low blood counts, infections
- Impair antibody response to vaccines
- Commonly used in CLL: Rituximab (Rituxin) and Obinutuzumab (Gazyva)



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Combinations

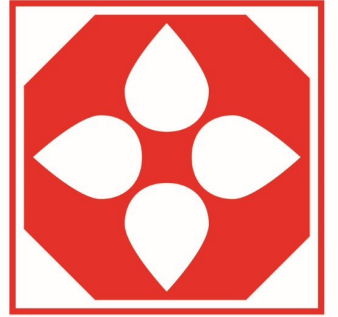
- Targeted therapy + monoclonal antibody
 - Common
 - Continuous + time limited therapy
- 2 novel agents – BTKi + Venetoclax (doublets)
 - Time-limited
 - Approved in Europe, not in the US
 - Not commonly given outside of a clinical trial
- 2 novel agents + monoclonal antibody (triplet)
 - Available in clinical trials, some combinations have not shown benefit over doublet therapy



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Traditional Chemoimmunotherapy in CLL

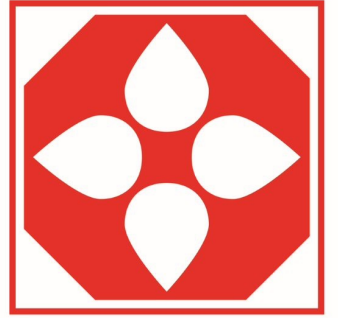
- Given via intravenous infusion in cycles
- Target all quickly dividing cells, not just cancer cells
- Side effects are your cancer treatment stereotypes – nausea/vomiting, hair loss, low blood counts, fatigue, infections, loss of appetite, etc.
- Less to no role in CLL these days, and not recommended for those with del 17p or TP53 aberration or those with unmutated IGHV (must check first before starting therapy)
 - BR
 - Bendamustine & Rituximab
 - FCR
 - Fludarabine, Cyclophosphamide, Rituximab



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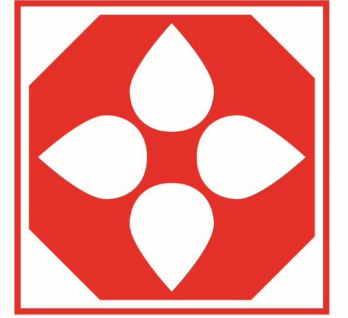
Bone Marrow Transplant in CLL

- IV infusion of **blood forming stem cells** collected from bone marrow, peripheral blood, or umbilical cord blood with the goal of cure
- Allogeneic meaning donated by another person
- Involves rigorous testing, finding a compatible donor, conditioning chemotherapy, hospital stay and close monitoring
- Lots of possible side effects (infection, low blood counts, bleeding, graft v. host disease) and even death
- Considered in relapsed/refractory disease, especially those running out of options or Richter's Syndrome (when CLL transforms into an aggressive lymphoma)



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Chimeric Antigen Receptor (CAR) T-Cell Therapy

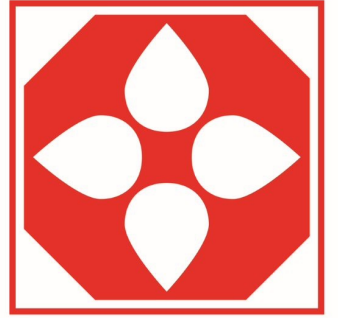


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- Immunotherapy that uses cells instead of drugs to fight CLL
- Patients' own T-lymphocytes are harvested, trained to attack the CLL, grown, and then re-infused
- Risk of cytokine release syndrome (CRS), neurotoxicity
- Not currently approved in CLL, clinical trial only

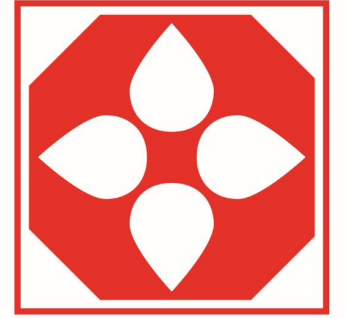
Clinical Trials

- Access to the newest and most advanced treatments, before they are widely available.
- Important drugs currently being used in trials
 - BTK degraders – degrade BTK instead of just inhibiting it
 - Overcomes some mutations that develop on BTK inhibitors
 - BITES (bispecifics)
 - work by attaching to two different antigens on separate cells—1 on the CLL cell and 1 on a T-lymphocyte, leading to destruction of the CLL
 - **NEW TARGETS and COMBINATIONS**



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Conclusion

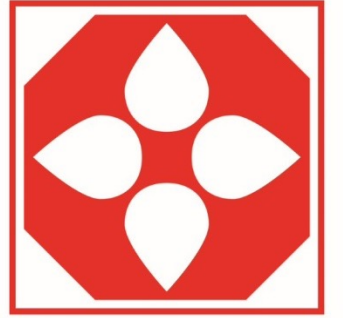


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- Be an advocate for yourself when it comes to treatment
- Consider a 2nd opinion if you feel unsure or need more information
- Very little – no role for chemoimmunotherapy in CLL these days
- Novel agents are the mainstay of therapy
- Most patients will see more than one therapy in their lives
- Rely on your care team when you have questions/concerns – they are there to help!

Thank you!

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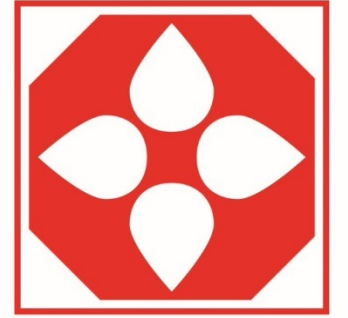


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Please take a moment to complete our **post-event survey**, your feedback is important to us



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

Join us on Thursday, November 16th for our next event, “Ask Me Anything” a Facebook Live event featuring Dr. Sameer Parikh

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