



# Let's Talk CLL!

Patients & Doctors  
Discuss the Latest-  
LIVE



The Patient Story



• CHRONIC LYMPHOCYTIC LEUKEMIA •

# MEET THE EXPERT PANEL



**DR.  
WILLIAM  
WIERDA**

**THE UNIVERSITY OF  
TEXAS MD  
ANDERSON CANCER  
CENTER**

At MD Anderson Cancer Center, Dr. Wierda occupies several roles, including the holder of the Jane and John Justin Distinguished Chair in Leukemia Research, CLL Section Chief, Center Medical Director of the Department of Leukemia, and Executive Medical Director of Inpatient Medical Services. In these capacities, he actively shapes clinical and research priorities, manages research personnel, and oversees infrastructure vital to the CLL program's success. Collaborating with fellow faculty members, he plays a crucial role in developing CLL clinical trials and research endeavors. Additionally, Dr. Wierda serves as the co-principal Investigator for the CLL Moon Shot Program at MDACC, a program dedicated to groundbreaking research aimed at curing the disease.



**DR.  
NICOLE  
LAMANNA**

**COLUMBIA  
UNIVERSITY  
COMPREHENSIVE  
CANCER CENTER**

Dr. Nicole Lamanna serves as Professor of Medicine and Director of the Chronic Lymphocytic Leukemia (CLL) Program on the Leukemia Service for the Hematologic Malignancies Section in the Hematology/Oncology Division at Columbia University Medical Center. Dr. Lamanna specializes in the treatment of adult patients with acute and chronic leukemias with a focus on chronic lymphocytic leukemia (CLL). Her clinical research focus has been the development of novel combination therapies that include immune-modulatory drugs, kinase inhibitors, bcl-2 inhibitors, monoclonal antibodies as well new agents in development for this disease. She is a staunch patient advocate and participates regularly in CLL patient advocacy groups with the goal of educating patients about their disease and treatment options. She has lectured and chaired CLL sessions at international and national meetings.



## **DR. ADAM KITTAI**

**THE OHIO STATE  
UNIVERSITY  
COMPREHENSIVE  
CANCER CENTER**

Dr. Kittai is a clinical assistant professor in the Division of Hematology at The Ohio State University (OSU) in Columbus, Ohio. His clinical and research focus is on Chronic Lymphocytic Leukemia, Richter's syndrome and related disorders. He attained his medical degree from Tel Aviv University, went on to train in Internal Medicine at the George Washington University where he was also chief resident, and completed his fellowship training in Hematology/Oncology at the Oregon Health & Science University. He joined the faculty at OSU in 2019. He is the primary investigator of multiple investigator-initiated trials exploring the use of small molecule inhibitors with novel designs and deploying cellular therapies for CLL and Richter's syndrome. Dr. Kittai is also interested in re-defining prognostic features for patients with CLL in the era of targeted therapies, as well as defining and mitigating racial disparities that exist in CLL. Lastly, Dr. Kittai has a keen interest in drug development, the regulatory pathway, and governmental oversight.



## **DR. JACKIE BROADWAY- DUREN**

**THE UNIVERSITY OF  
TEXAS MD  
ANDERSON CANCER  
CENTER**

Dr. Jackie Broadway-Duren joined the Leukemia team at UT MD Anderson Cancer Center in February 2001 and has since remained in the Department of Leukemia as a Nurse Practitioner, mentor, and educator. Dr. Broadway-Duren completed her Doctor of Nursing Practice (DNP) at the University of Texas Health Science Center in Houston in 2014 and PhD in 2020 at Texas Woman's University. She is an active member of the American Association of Nurse Practitioners and Texas Nurse Practitioners, and other organizations. She has served as adjunct faculty at the University of Texas Health Science Cizik School of Nursing for several years. She has had numerous publications since 2014 and her current focus is education, clinical research, and survivorship for Leukemia patients. In addition, she has received several awards for excellence in patient care.



## **JEFF FOLLODER**

**CLL ADVOCATE &  
EVENT HOST**

Although Jeff is currently relapsed with CLL, he is living his life to the maximum! Jeff is a devoted husband, loving father, and passionate patient advocate. He is devoted to fitness and is training daily for the upcoming Bataan Memorial Marathon to be held in the high desert of New Mexico in March. "I am living my life to the fullest. I enjoy great food, good whiskey and wine, sharing time with my friends, and being focused on figuring out a way to smile more often. I want others to learn that it is possible to live a great life with a cancer diagnosis." Jeff credits his extensive support group with providing a firm foundation for all he wants to accomplish. Family, friends, his medical team, and the online communities he helps manage are all a wonderful part of his world.



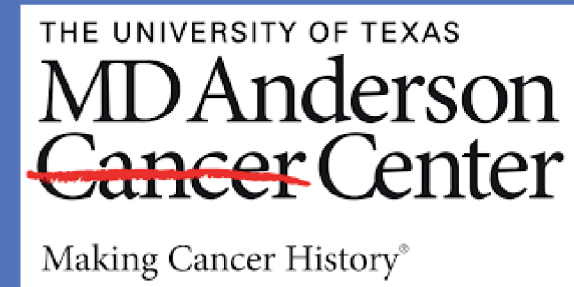
## **THE PATIENT STORY**

**EVENT ORGANIZER**

Whether you're contemplating your next big treatment decision, preparing for an upcoming appointment, or researching the best way to support a loved one who's just been diagnosed -**The Patient Story is here for you with human answers to your cancer questions.**

Founded by Stephanie Chuang, a stage 3 non-Hodgkin's lymphoma survivor, The Patient Story's mission is to humanize cancer through rich storytelling.

At ThePatientStory.com, you'll find a network of hundreds of voices - patients, survivors, caregivers, and top medical experts - with insights into areas like how to navigate life after a diagnosis, the latest on promising treatments, and most importantly, connection to others who've been through what you're going through now.



***LET'S TALK CLL!***

**PATIENTS & DOCTORS  
DISCUSS THE LATEST**



This educational forum is presented

**In Collaboration with:**

CLL Global Research Foundation and  
The University of Texas MD Anderson Cancer Center

**Produced by:**

The Patient Story

Special thanks to AbbVie, Inc. and BeiGene, Inc. for supporting this independent education program!



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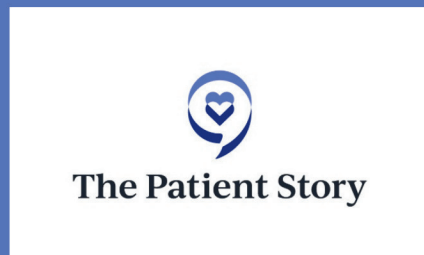
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[community@thepatientstory.com](mailto:community@thepatientstory.com)**





# INTRODUCTIONS



**DR. WILLIAM WIERDA**  
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**DR. ADAM KITTAI**  
THE OHIO STATE  
UNIVERSITY  
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**DR. NICOLE LAMANNA**  
COLUMBIA UNIVERSITY  
IRVING MEDICAL  
CENTER



**DR. JACKIE  
BROADWAY-DUREN**  
MD ANDERSON  
CANCER CENTER

# Program Schedule

Time	Session
10:00 AM	Welcome & Introductions
10:15 – 12:00 PM	Discussion of CLL Treatments, Research and Monitoring
12:00 – 12:30 PM	Lunch Break
12:30 – 1:00 PM	Receiving Optimized Care / Limiting Side Effects
1:00 – 1:30 PM	Strategies for Living Well with CLL
1:30 – 1:45 PM	Break
1:45 – 2:15 PM	Q&A Session
2:15 – 2:30 PM	Final Guidance

# CURRENT TREATMENT OPTIONS

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- **Common Chemotherapy Agents**
  - Fludara (“F” Fludarabine)
  - Cytoxan (“C” Cyclophosphamide)
  - Bendeka or Treanda (“B” Bendamustine)
  - Leukeran (Chlorambucil)

# CURRENT TREATMENT OPTIONS

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- **Immunotherapy / Monoclonal Antibodies**
  - Campath (alemtuzumab)
  - Gazyva (obinutuzumab)
  - Arzerra (ofatumumab)
  - Rituxan (rituximab)
  - Rituxan Hycela (rituximab and hyaluronidase human)

# CURRENT TREATMENT OPTIONS

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## Targeted Therapies

- **Bruton's tyrosine kinase (BTK) inhibitors**
  - Imbruvica (ibrutinib)
  - Calquence (acalabrutinib)
  - Brukinsa (zanubrutinib)
- **BCL-2 Inhibitors**
  - Venclexta (venetoclax)
- **PI3K inhibitor**
  - Zydelig (idealisib)

# DEVELOPING RESEARCH & CLINICAL TRIALS

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- **Second Generation vs. First Generation BTK Inhibitors**
  - ALPINE Trial (zanubrutinib vs. ibrutinib)
  - ELEVATE-RR Trial (acalabrutinib vs. ibrutinib)
- **Long Term Results**
  - CLL14 Trial (venetoclax + obinutuzumab)



# DEVELOPING RESEARCH & CLINICAL TRIALS

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## Updates on Clinical Trials

- **CLL 17 Trial**
  - Ibrutinib vs. venetoclax + obinutuzumab vs ibrutinib + venetoclax
- **ALLIANCE Trial**
  - ibrutinib + obinutuzumab vs. the combo + venetoclax

## Pirtobrutinib trials

- **BRUIN CLL-314 Trial:**
  - Pirtobrutinib vs. ibrutinib
- **BRUIN CLL-322 Trial:**
  - Pirtobrutinib + venetoclax + rituximab vs. venetoclax + rituximab

# DEVELOPING RESEARCH & CLINICAL TRIALS

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## Updates on Clinical Trials



### CAR T-CELL THERAPY

- **TRANSCEND CLL 004 Trial:**
  - LISO-CEL for R/R CLL

### BISPECIFIC ANTIBODIES

- **EPCORE CLL-1 Trial:**
  - Epcoritamab for R/R CLL



# DEVELOPING RESEARCH & CLINICAL TRIALS

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## Updates on Clinical Trials

- What's next? After BTKi, BCL2i, Pirtobrutinib and CAR T
- BTK Degraders in Development
  - Richter Transformation
    - Zanubrutinib + liso-cel
    - Ibrutinib + liso-cel
    - MOLTO Trial: Venetoclax, atezolizumab + obinutuzumab

# Monitoring and Treatment Planning

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## Watch and Wait (*Active Surveillance*)



- What is *watch and wait*
- When to start treatment
- Communicating with your medical team
- Quality of life



# Lunch Break

***Online Audience:  
We will return at 12:30 pm CST***

# Optimized Care & Limiting Side Effects

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- **Treatment Side Effects**
  - How and when to communicate with your healthcare team
- **Secondary cancers or associated conditions to watch out for**
- **Finding a CLL Specialist**
- **Drug costs and access to medication assistance programs**

# Strategies for Coping & Living Well with CLL

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- **Emotional and Mental Health Aspects of Living with CLL**
  - Dealing with anxiety and depression
- **Coping with Treatment:**
  - How do I cope during *“Watch and Wait”*
- **How Diet and Lifestyle Can Make a Difference**



# Break

***Online Audience:  
We will return at 1:45 pm CST***

# Q&A Session

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**ONLINE AUDIENCE:  
TO SUBMIT A QUESTION, PLEASE EMAIL:**

**[community@thepatientstory.com](mailto:community@thepatientstory.com)**

# Final Guidance and Takeaways

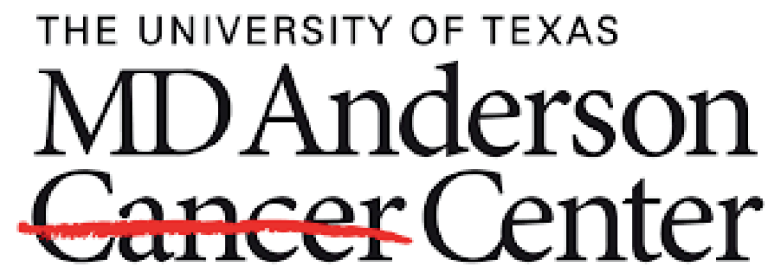


# SPECIAL THANK YOU

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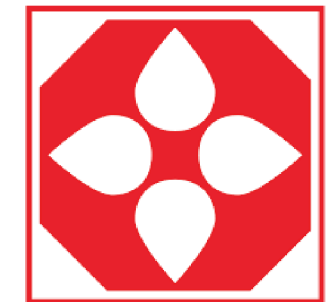


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# NOTES

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# NOTES

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## Glossary of Terms

### Blood Components

**Albumin:** A protein made by your liver that helps keep fluid in your bloodstream, so it does not leak into other tissues. It also carries various substances throughout your body, including hormones, vitamins, and enzymes.

**Basophil:** A type of white blood cell that is involved in allergic and inflammatory reactions.

**Blast Cell:** A young white blood cell or leukocyte seen more often in acute leukemia.

**Blood Cells:** There are three main types of cells found in the blood. Red cells carry oxygen to the tissues in the body. White cells fight infection. Platelets help prevent bleeding.

**B-Lymphocyte:** This is a type of white blood cell that is involved in the production of antibodies to fight infections caused by bacteria or viruses.

**Cord Blood Stem Cells:** Stem cells extracted from blood within the umbilical cord of a newborn baby. The blood from the umbilical cord has a high concentration of stem cells, which are the cells from which all types of blood cells develop.

**Eosinophil:** This is a type of white blood cell that kills parasites and is involved in inflammatory and allergic responses.

**Erythrocyte:** Another term for a red blood cell.

**Granulocyte:** White blood cells with granules that contain enzymes to help fight infection. Neutrophils, eosinophils, and basophils are types of granulocytes.

**Immunoglobulins:** These are proteins found in the liquid part of the blood (plasma). They work as antibodies and help to control infections. Patients with CLL frequently have low levels of immunoglobulins and recurrent infection. One type of immunoglobulin, IGG, may be replaced with a pooled blood product, IVIG (intravenous immunoglobulin) that may reduce the risk of infections.

**Leukocytes:** An overall term for white blood cells (WBC) that fight disease and infection. Specific types of WBCs include granulocytes, lymphocytes, and monocytes.

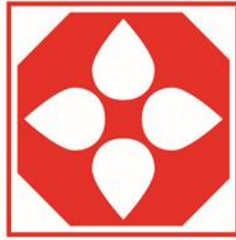
**Lymphocyte:** These white blood cells are part of the body's immune system. There are three types of lymphocytes: B-lymphocytes, t-lymphocytes, and natural killer (NK cells)

**Macrophage:** A type of white blood cell or monocyte which migrates from the bloodstream into infected tissues and acts as a scavenger ingesting particles such as bacteria and dead cells

**Megakaryocyte:** A large cell in the bone marrow that makes platelets, the cells responsible for normal blood clotting.

**Monoclonal:** Proteins made by cells which all belong to the same clone are identical and are called monoclonal.

**Monocyte:** A large white blood cell that can leave the bloodstream and enter infected tissues where it becomes a macrophage. A macrophage is a type of immune cell that surrounds and kills bacteria and viruses.



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**Natural Killer Cells:** A type of lymphocyte that attacks virus-infected cells or tumor cells. Neutrophil: This is the most common type of cell within the granulocyte group of white blood cells. They are important for helping the body fight infections, especially bacterial and fungal infections.

**Peripheral Blood Stem Cell:** Although present in only small quantities, stem cells are found in the circulation.

**Phagocyte:** This type of white blood cell helps protect the body from infection by surrounding and killing microorganisms, such as bacteria and fungi. They also remove dead cells. Monocytes, macrophages, and neutrophils are phagocytes.

**Plasma:** The fluid part of the blood. Plasma is mostly made of water with chemicals in it. These chemicals include clotting factors, proteins, hormones, minerals, and vitamins.

**Platelet:** This smallest type of blood cell originates from megakaryocytes in the bone marrow. The platelet's sticky surface helps the blood to clot and stop bleeding. They are also called thrombocytes.

**Progenitor Cell or Precursor Cell:** Immature cell in the bone marrow, which is responsible for producing mature blood cells.

**Red Blood Cell:** These are the most numerous types of blood cell in the circulation of healthy people. Red blood cells contain hemoglobin, a protein that carries oxygen from the lungs to all the tissues in the body. Reticulocytes: These are immature red blood cells that are normally found in the bone marrow. They should be present in the bloodstream only in very low numbers.

**Stem Cells:** Blood-forming or hematopoietic stem cells are the most primitive cells in the bone marrow. They make copies of themselves and develop into red cells, white cells, and platelets.

**Serum:** The part of the blood, which remains after cells, platelets, and fibrinogen (clotting factor) have been removed, usually by allowing the blood to clot.

**T-Lymphocyte:** A type of white blood cell that originates in the bone marrow and develops in the thymus (hence T cells). As we age, most of the T-cell development occurs in the circulating blood. These are immune cells that can directly kill infected cells or cancer cells, assist B-cell maturation, and control other immune cell activity.

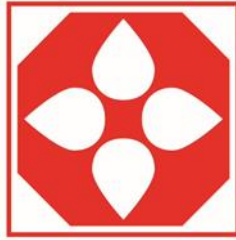
**White Blood Cell:** These are cells in the body that fight disease and infection by attacking and killing germs. There are several types of white blood cells including granulocytes (neutrophils, Eosinophils, basophils), lymphocytes, and monocytes. Each type of cell fights a different kind of germ. They are also called Leukocytes.

## Lab Tests

**Absolute Lymphocyte Count:** The number of cells is expressed as an absolute number, rather than as a percentage. Absolute lymphocyte count is calculated by multiplying the number of white blood cells against the percentage of lymphocytes.

**Absolute Neutrophil Count:** This is the actual number of white blood cells that are neutrophils. It is calculated by multiplying the white blood cell count by the percent of neutrophils. The percent of neutrophils includes both fully mature neutrophils and almost mature neutrophils, also called bands.





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**Blood Urea Nitrogen:** A blood test that measures the amount of nitrogen in your blood that comes from the waste product urea. Urea is made when protein is broken down in your body by the liver and passed out of your body in the urine. This test is done to see how well your kidneys are working.

**Complete Blood Count:** This is a routine test performed on a small amount of blood. This count measures the number of each blood cell type, the size of the red blood cells, the total amount of hemoglobin, and the fraction of the blood that is made of red blood cells. It may also be called a blood count.

**Creatinine:** This is a waste product made by your muscles as part of regular, everyday activity. Normally, your kidneys filter creatinine from your blood and send it out of the body in the urine. If there is a problem with your kidneys, creatinine can build up in the blood and less will be excreted.

**Hematocrit:** This is a blood test that is usually part of the complete blood count. It measures the proportion of the blood containing red blood cells. This measurement depends on the number of red blood cells and their size. It is also sometimes referred to as packed cell volume.

**Hemoglobin:** This is the iron-containing pigment in red blood cells. It carries oxygen from the lungs to the tissues in the body.

**Mean Corpuscular Volume:** This measures the volume or size of the red blood cells.

**Mean Corpuscular Hemoglobin Concentration:** A calculation of the average percentage of hemoglobin in each red blood cell.

**Mean Corpuscular Hemoglobin:** Measures the average amount of hemoglobin in a red blood cell.

**Mean Platelet Volume:** A measure of the average size of your platelets. This lab result is particularly important in determining the cause of thrombocytopenia (low platelet count) or thrombocytosis (high platelet count).

**Red Cell Distribution Width:** Measures the amount of red blood cell variation in volume and size.

**White Blood Cell Differential:** This is a group of tests that includes the following: absolute neutrophil count or % of neutrophils, absolute lymphocyte count or % of lymphocytes, absolute monocyte count or % of monocytes, absolute eosinophil count or % of eosinophils, and absolute basophil count or % of basophils.

## Lab Results

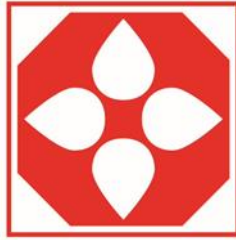
**Anemia:** A condition in which the blood does not have enough healthy red blood cells. Symptoms of anemia are fatigue and tiredness.

**Basophilia:** An increase in the number of basophils in the blood.

**Cytopenia:** A shortage of one or more blood cell types circulating in the blood. It is also called a low blood count.

**Essential Thrombocythemia:** This is a myeloproliferative disorder (blood cancer) where the bone marrow makes too many platelets. It is also called primary thrombocythemia. Complications include excessive bleeding and clotting.

**Leukopenia:** A condition in which the number of white blood cells or leukocytes circulating in the blood is reduced below normal. A low number of white blood cells leads to an increased risk of infections.



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**Lymphoproliferation:** An increase in the production of lymphocytes or white blood cells. This may occur as a normal response to infection.

**Neutropenia:** This is a condition in which there are too few neutrophils in the bloodstream. Neutrophils are a type of white blood cell. The reduction of white blood cells leads to an increased risk for infection.

**Pancytopenia:** This is a condition where there is a shortage of all types of blood cells, including red blood cells, white blood cells, and platelets.

**Thrombocytosis:** When an increased number of platelets (thrombocytes) is found in the blood from any cause, cancerous or non-cancerous.

**Thrombocytopenia:** A condition in which there is a shortage of platelets in the bloodstream. This results in a low platelet count and can result in problems with bleeding and bruising.

### Diagnostic Procedures

**Biopsy:** A small sample of tissue (from bone marrow or a lymph node) taken to establish or confirm a diagnosis.

**Bone Marrow Aspiration:** A procedure performed to acquire a small amount of liquid bone marrow. The sample is examined to find abnormal bone marrow cells (cell size, shape, or look). Additional testing may be done to identify genetic abnormalities. The area around the hip bone is numbed, and then a special needle is inserted so that a sample of (liquid) bone marrow is obtained.

**Bone Marrow Biopsy:** A medical procedure performed to remove a small piece of solid bone marrow. The solid bone marrow is examined for cell abnormalities, the number of different cells, and whether there is any scarring of the bone marrow. This test is usually done at the same time as a bone marrow aspiration.

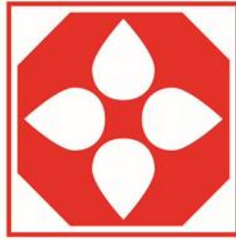
**CT Scan:** This is an imaging technique using computerized x-ray technology to create a three-dimensional internal image of a body part. It is often referred to as a CAT Scan or Computer Axial Tomography.

**Cytogenetics:** The study of the structure of chromosomes (DNA), which is the part of the cell that contains genetic information. Cytogenetic tests are carried out on samples of blood and bone marrow. It is used to detect any chromosomal abnormalities associated with chronic lymphocytic leukemia. This information helps in the diagnosis and selection of optimal treatment.

**Diagnostic Radiology:** Often simply referred to as radiology. X-rays are used to aid in the diagnosis of a disease.

**FISH (Fluorescence in Situ Hybridization):** This is a laboratory test that helps identify abnormalities in chromosomes and genetic mutations. Under a microscope, colored lights are directed at chromosomes and genes to see if any are missing or rearranged. This test can help to assess risk, identify treatment needs, and monitor treatment effectiveness.

**Flow Cytometry:** This is a test that is used to study blood cells or bone marrow cells, and provides information about surface markers on the cells. This is the cell's immune fingerprint. Doctors can use this test to see exactly what type of cells are in the specimen. Additionally, it can provide answers to



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questions such as is there evidence of a cancerous clone as found in CLL, or is there a mismatched ratio of immune cells as is found with AIDS.

**Immunophenotyping:** This is a process that is used to find specific types of cells within a blood sample. It looks at antigens or markers on the surface of the cell to identify antibodies.

**Magnetic Resonance Imaging:** This is a body scanning technique, which uses an intense magnetic field and computer processing to create images of internal organs. Because the properties of normal and cancerous tissue are different, malignant tumors can be visualized based on the signals detected. It is used less than CT scans in CLL, as it is usually less precise in measuring the size of lymph nodes.

**Next-Generation Sequencing:** Tests that look at the sequences of the four bases that make up DNA, thus search for mutated genes and DNA sequences that are unique to cancer.

**PET Scans:** Known as a positron emission tomography scan and is typically performed in conjunction with a CT scan. This is a nuclear imaging technique that in cancer produces a three-dimensional image of metabolic activity by measuring the uptake of a radioactive labeled sugar. In CLL, there is no role for this test, except to look for Richter's Transformation. Richter's Transformation sometimes can be diagnosed by increased metabolic activity on a PET scan.

**Polymerase Chain Reaction:** This test uses a technique to amplify trace amounts of DNA or RNA that is amplified to look for specific patterns.

**Staging:** Staging helps doctors assess how CLL is expected to progress over time and to develop a treatment plan. Staging takes many things into account including how elevated the number of leukemic lymphocytes are in the blood and bone marrow, the size and location of enlarged lymph nodes, the size of the spleen, if the patient has anemia (low red blood cell count), or if the patient has thrombocytopenia (low platelet count). The two systems that are used to stage CLL are the Rai System and the Binet System.

**Ultrasonography:** Typically referred to as just an ultrasound, this test uses reflected sound waves to create pictures of the body's internal organs.

**X-Rays:** A form of radiation used for both diagnosis and treatment.

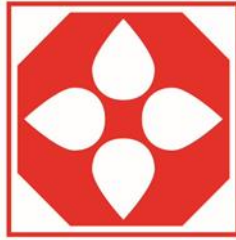
## Types of Therapy

**Anti-metabolites:** A group of anti-cancer or chemotherapy drugs that prevent cells from growing and dividing by blocking the actions in the cell required to produce DNA. Pentostatin and fludarabine are examples of anti-metabolites used in CLL.

**Anti-Emetic:** A drug used to prevent or alleviate nausea and vomiting, which is a common side effect of chemotherapy.

**Alkylating Agents:** This anti-leukemic drug interacts with the genetic material (DNA) to prevent the division of cells. Common alkylating agents used to treat CLL include bendamustine, cyclophosphamide, and chlorambucil.

**Antibiotics:** A drug used to kill or stop the growth of bacteria (penicillin for example). Some are used to treat cancer, but not usually in CLL.



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**BCL-2 (B-Cell Lymphoma 2) Inhibitors:** Medications that shift the cell towards apoptosis, or programmed cell death. Venetoclax is an example.

**Biologic Therapy:** A treatment that uses the patient's own immune system to fight cancer. These are substances (sometimes modified substances) that are made from living organisms to fight cancer. Monoclonal antibodies are an example of biologic therapy that are produced to target certain receptors on the cancerous cells (antigens) and to destroy the cancer cells. It may also be called biotherapy or immunotherapy.

**Blood Transfusion:** A procedure in which whole blood or one of its components (i.e., red blood cells or platelets) is infused into the bloodstream through an intravenous (IV) line. Transfusions of red blood cells or platelets can help some patients with low blood counts.

**Bruton Tyrosine Kinase Inhibitors:** Drugs that block the BTK pathway, thus blocking B-cell signaling through the B-cell receptor (BCR). Examples include ibrutinib, acalabrutinib, and zanubrutinib.

**CAR-T:** Chimeric antigen receptor T cells is an experimental cellular or cell-based therapy.

**Chemotherapy:** A type of medication that kills cells that are rapidly dividing. Chemotherapy affects rapidly dividing normal cells, such as in the hair and in the gut, as well as cancer cells. Therefore, hair loss and nausea often occur when receiving chemotherapy.

**Complementary and Alternative Medicine:** This includes medical approaches that are not currently part of standard practice. Complementary medicine is used along with standard medicine. Alternative medicine is used in place of standard medicine. Some examples include acupuncture, chiropractic, homeopathic, and herbal medicines. No complementary or alternative therapy has been proven to be effective in treating CLL. Though there is some evidence that one of the active components of green tea, EGCG (epigallocatechin gallate) may slow disease progression. Theoretically, some complementary and alternative medicine therapies can alter the effectiveness of standard medical care by interfering with the metabolism and activity of some cancer drugs.

**Corticosteroids:** Often referred to as just 'steroids', these are drugs that are similar to cortisol, which is a hormone that your body makes naturally. However, they are different from the male hormone-related steroids that are used by some athletes. For CLL, they are sometimes used to decrease side effects of chemotherapy, or to reduce strong reactions to monoclonal antibodies. In very high doses, they are used to destroy leukemia cells. Also, they are used to suppress graft rejection (aka, graft versus host disease) following bone marrow transplants. One of the many side effects of steroids is the increased risk of infection, which is already a problem in CLL. These medications include prednisone, prednisolone, methylprednisolone, and dexamethasone.

**Cyclosporine A:** This drug is used to suppress the immune system to prevent and treat rejection and graft versus host disease in bone marrow transplant patients. It is also used to control auto-immune complications of CLL, such as AIHA and ITP.

**Cytotoxic Drugs:** These are drugs that act by killing or preventing the division of cells, also known as chemotherapy.

**Diuretic:** A drug that may be used during chemotherapy to stimulate the kidneys to produce more urine, which helps excrete the anti-cancer drugs.



CLL SOCIETY

**Growth Factors:** These are substances made by the body to stimulate the bone marrow to produce blood cells. Some growth factors are man-made and used for treating low blood counts. Red blood cell growth factors are called erythropoietin-stimulating agents (ESA), and include epoetin alfa (Epogen and Procrit), as well as darbepoetin alfa (Aranesp). White blood cell growth factors are called granulocyte colony stimulating factors (GCSF) and granulocyte macrophage colony stimulating factors (GM-CSF). The newest compounds are smaller drugs that mimic platelet growth factors (thrombopoietin) so that they can pharmacologically stimulate platelet production. These drugs are therefore called thrombopoietin, or more commonly referred to as TPO mimetics.

**Immunotherapy:** Therapy that harnesses the body's immune system.

**Monoclonal Antibodies:** Identical clonal antibodies that have one target. In CLL, that is often a marker on the surface of the CLL cell called CD20, and the monoclonal antibodies are called anti-CD. Examples include rituximab and obinutuzumab.

**Off-Label Drug:** This is an approved drug that is prescribed by a licensed healthcare provider for a use other than that for which it was originally approved by the U.S. Food and Drug Administration.

**Orphan Drug:** These are drugs or biologic agents used to treat rare diseases or conditions. A disease is considered rare if fewer than 200,000 people in the United States have been diagnosed with it.

**Over The Counter Medication:** These are medicines that are available without a prescription from a healthcare provider. Often referred to as OTC medicines.

**Placebo:** A placebo is an inactive pill, liquid, or powder that has no treatment value.

**Platelet Transfusion:** An intravenous infusion of blood platelets into the bloodstream to increase blood counts and help control bruising and bleeding. Platelet transfusions may help some CLL patients.

**Prophylaxis:** A precautionary treatment that is given preventatively to avoid a disease or condition from occurring.

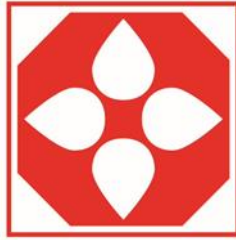
**Palliative Care:** A treatment used to relieve symptoms and pain. It does not contribute to curing the disease.

**Pharmacokinetics:** The study of the action of a drug in the body over a period of time, including the process of absorption, metabolism, and excretion.

**Phosphoinositide 3-Kinase Inhibitors:** More commonly referred to as PI3K inhibitors, this treatment blocks the signals that promote the growth of CLL cells by blocking the PI3K pathway. Examples of these drugs include idelalisib and duvelisib.

**Purine Analogues:** These are a type of anti-metabolite that is incorporated into a dividing cell's DNA, stopping cell growth and division. In CLL, fludarabine and pentostatin are used.

**Radiotherapy:** This type of therapy involves the use of x-rays and other forms of radiation to kill cancer cells. It is used in a specific area of the body and is an effective treatment for localized disease, such as an enlarged lymph node or spleen.



## CLL SOCIETY

**Red Blood Cell Transfusion:** This is an intravenous infusion of packed red blood cells into the bloodstream to increase blood counts and help improve the symptoms of anemia, such as fatigue. Donated blood must match the blood type and other factors of the recipient's blood.

**Signal Pathway Blockers:** CLL cells depend on signals that they receive through the BCR (B-cell receptor) for many vital activities and ultimately their survival. Targeted therapies such as ibrutinib and idelalisib can block this signaling at different steps along its pathway, often resulting in a profound therapeutic effect on the cancer.

**Splenectomy:** This is the surgical removal of the spleen and is sometimes performed for patients with CLL as part of their treatment when it becomes massive in size (splenomegaly) and is causing problems, such as low blood counts or abdominal symptoms.

**Supportive Care:** Another term for palliative care. It is provided to control symptoms and to improve the quality of life to the patient. This type of treatment does not contribute to curing the disease.

**Targeted Therapy:** This type of treatment involves drugs that attach one or more specific targets on (or inside of) cancer cells without harming normal cells. Some examples of targeted therapies include monoclonal antibody therapy and tyrosine kinase inhibitor therapy.

**Total Body Irradiation:** This is a type of radiotherapy that is given prior to a bone marrow transplant in an effort to kill leukemia cells that are still present in the patient.

**Tyrosine Kinase Inhibitors:** Often referred to as BTK inhibitors, this type of treatment blocks enzymes that promote the growth of CLL cells. These drugs target specific substances on the cancer cell. In most cases, these drugs are given as pills and are generally better tolerated than chemotherapy. Examples of these drugs include ibrutinib and other Bruton's Tyrosine Kinase (BTK) inhibitors. Other kinase inhibitors that are similar in action include idelalisib and other PI3K inhibitors.

**Vinca Alkaloids:** This is a type of chemotherapy drug that blocks cell division. It affects rapidly dividing cells, including normal cells and cancer cells. Drugs of this type include vincristine and vinblastine. These are used more in Richter's Transformation than CLL.

## Medication Administration

**Cannula:** This is a type of tube that is inserted into the body. Most often it is inserted into a vein via a sharp needle fitting. After insertion, the needle is withdrawn from the cannula to allow fluids to pass through the tube.

**Central Line:** Also referred to as an indwelling catheter or central venous catheter, it is a special tube put into a large vein in the upper chest. It is used to give medications, fluids, or blood products, as well as draw blood samples. It helps avoid repeated needle punctures into the veins.

**Intramuscular Injection:** This is when an injection is given into the muscle tissue.

**Intrathecal Injection:** This is when an injection is given into the spinal fluid.

**Intravenous Infusion:** When antibiotics, blood products, anti-cancer drugs, or nutrients flow into the vein through a tube over a prolonged period.

**Intravenous Injection:** When a medication is injected over a short period of time into the vein by a needle and syringe.



## CLL SOCIETY

**Portacath:** A form of a central venous line that is surgically implanted within the body. A membrane just below the skin provides access through a simple puncture to a line running straight into one of the main blood vessels. This provides a simple way to administer chemotherapy or obtain a blood sample, and avoids multiple needle sticks.

**Subcutaneous Injection:** A shallow injection into the tissue immediately under the skin.

### Diagnosis

**Chronic Lymphocytic Leukemia:** This form of leukemia progresses slowly and is characterized by an increased number of a type of white blood cells known as B-lymphocytes.

**Cytokine Release Syndrome:** A condition that may occur after treatment with some types of immunotherapy, such as monoclonal antibodies or CAR-T. It is a systemic inflammatory response that can be triggered by a variety of factors including infection, that causes a large release of cytokines into the blood. It is also sometimes referred to as a cytokine storm.

**Diffuse Large B-Cell Lymphoma:** This is an aggressive (fast-growing) cancer of the B lymphocytes. It is the most common type of non-Hodgkin's lymphomas that affects B-lymphocytes. It may be localized in one spot, or generalized throughout the body. Despite being an aggressive lymphoma, DLBCL is considered potentially curable.

**Leukemia:** A type of blood cancer is characterized by large numbers of abnormal blood cells, usually white blood cells, which take over the bone marrow and are often also found in the bloodstream. Other organs that may also be affected include lymph nodes, spleen, and liver.

**Lymphoma:** This type of cancer originates in the lymphoid tissue specifically, the lymph glands, liver, spleen, bowel, and bone marrow. It results from the uncontrolled production of lymphocytes. There are two main categories: Hodgkin's disease and non-Hodgkin's lymphoma.

**Richter's Transformation:** This condition is also referred to as Richter's Syndrome. It is the progression of CLL into an aggressive lymphoma. It occurs in a small number of CLL patients. This change is not a secondary cancer, but a transformation of the CLL cells.

**Secondary Myelodysplastic Syndrome:** This type of myelodysplastic syndrome arises from either previous chemotherapy or radiotherapy used to treat cancer. It is also called treatment-related, or therapy-related MDS.

**Small Lymphocytic Lymphoma:** This is a slow-growing type of lymphoma in which too many clonal white blood cells or lymphocytes are found in the lymph nodes, causing them to become enlarged. SLL most often occurs in people older than 50 years old. It is a type of non-Hodgkin's Lymphoma. When these clonal lymphocytes are found in the blood and bone marrow, the disease is called chronic lymphocytic leukemia as the cells involved are identical in CLL and SLL.

### Signs and Symptoms

**Alopecia:** This means the loss of hair. It can be a side effect of some forms of chemotherapy or radiotherapy used to treat leukemia. It is usually temporary.

**Anemia:** Describes low levels of hemoglobin in the blood, which is the part of the blood that carries oxygen throughout the body. Symptoms of anemia include pallor, tiredness, and breathlessness.



## CLL SOCIETY

**Anorexia:** When someone experiences an abnormal loss of appetite. Some cancer patients have anorexia and sometimes it occurs as a result of treatment for cancer.

**Autoimmune Hemolytic Anemia:** This is a rare autoimmune disorder that is seen more often in CLL. It is when the body's immune system attacks its own red blood cells, which results in anemia.

**Evan's Syndrome:** Fortunately, this is a very rare disorder that can be seen in CLL when the body's immune system attacks both the platelets and the red blood cells.

**Hemorrhage:** Bleeding either to the outside of the body through the skin, or internally.

**Idiopathic (Immune) Thrombocytopenic Purpura:** This is a rare autoimmune disorder that is seen more often in CLL in which the body's immune system attacks its own platelets, which results in bruising and/or bleeding.

**Immunocompromised (Immune) Deficiency:** A condition in which the immune system is not functioning properly, which makes the patient at risk for infection caused by a virus, bacteria, or fungi.

**Mucositis:** Inflammation of the mouth and throat, which may be caused by drugs used to treat leukemia.

**Neuropathy:** Damage to the nerves, which may occur as a complication of anti-leukemia treatment. It usually affects the peripheral nerves (nerves of the arms/legs) and may be reversible when treatment is stopped or reduced.

**Petechiae:** Small red or purple pinhead spots on the skin. They are caused by bleeding under the skin and are usually the result of a shortage of platelets. They are similar to purpura but are much smaller in size.

**Pruritus:** Acute or chronic condition of the skin that provokes the urge to scratch.

**Purpura:** These are purple spots on the skin that are a sign of bleeding under the skin. They occur because of low levels of platelets. They are similar to petechiae but are larger in size.

**Septicemia:** This is a general term used to describe a serious bacterial infection of the bloodstream, often associated with a high fever.

**Thrombosis:** The development of a clot in a blood vessel. They occur most often in a vein, but sometimes in an artery. When left untreated, this is a potentially life-threatening condition, depending on where the clot occurs.

**Tumor Lysis Syndrome:** A condition that occurs when a large number of cancer cells die within a short period and release their contents into the blood. When tumor cells are destroyed either spontaneously or in response to therapy, they suddenly release their contents into the bloodstream. When this happens, it can result in electrolyte and metabolic disturbances that can progress to kidney failure, cardiac arrhythmias, seizures, and sometimes even death due to multiorgan failure.

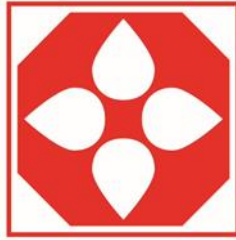
**Splenomegaly:** Enlargement of the spleen.

## Healthcare Personnel

**Cytogeneticist:** This is a health care expert who studies cells and chromosomes.

**Hematologist:** A physician who specializes in blood cell diseases and disorders that affect the blood-producing organs.





## CLL SOCIETY

**Hematopathologist:** This is a doctor or scientist who studies blood cells and blood tissues to identify and diagnose diseases.

**Oncologist:** A physician that specializes in the cause and diagnosis of disease by examining body tissues and fluids.

**Pharmacist:** Licensed professional whose job includes the preparation, distribution, and use of prescription drugs. They also advise patients, physicians, and other healthcare providers on the selection, dosages, interactions, and side effects of medications.

**Social Worker:** Licensed professional that is trained to help people manage their daily lives, understand, and adapt to necessary changes in their health and lifestyle. A social worker can also help people find community resources, healthcare, as well as legal and government assistance.

### Anatomy and Physiology

**Bone Marrow:** The soft, spongy tissue inside the hollow part of most bones where blood cells are formed. Once the blood cells have matured, they pass through the bone marrow and enter the bloodstream. Examining the bone marrow is an important part of diagnosing leukemia and monitoring the effectiveness of treatment.

**Hematopoiesis:** This is the process that describes the production and maturation of blood cells from stem cells inside the bone marrow.

**Lymphadenopathy:** Enlargement of the lymph nodes.

**Lymph Nodes:** These are small glandular structures found throughout the body (e.g., neck, groin, armpits, and abdomen). They contain both mature and immature lymphocytes. In patients with CLL, the cancerous lymphocytes are in excess, so the lymph nodes become enlarged.

**Lymphatic System:** This is a network of organs that include the spleen, lymph nodes, lymphatic channels, and areas of lymphoid tissue such as the tonsils. It helps to keep the body's fluids in balance, as well as fight infection by producing white blood cells.

**Lymphoid:** Referring to the lymphatic system, including lymphocytes and lymph nodes.

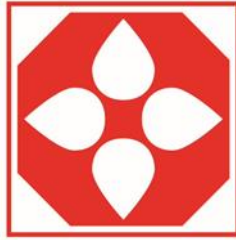
**Peripheral Blood:** The fluid that travels through your heart, arteries, capillaries, and veins. Its most important function is to transport oxygen and other nutrients to the body's cells and tissues. Additionally, it removes carbon dioxide and other waste products from the body.

**Spleen:** One of the spleen's main function is to act as a filter for the blood. It can selectively remove old red blood cells, bacteria, and other foreign bodies. The spleen produces lymphocytes and acts as a storehouse for platelets. It is often enlarged in leukemia.

### Disease State

**Minimal Residual Disease:** This describes the small amounts of cancer cells that may remain after treatment and when the patient is in remission. These cells are only identified by sensitive molecular techniques.

**Undetectable Minimal (Undetectable Measurable) Disease:** Often shortened to MRD negative status, this is considered to be a deep state of remission. Undetectable MRD is when no cancer cells can be found using the most sensitive molecular testing available.



## CLL SOCIETY

**Prognosis:** An assessment of the likely benefits of treatment for a patient, particularly concerning the chance of cure and complete recovery.

**Resistant to Treatment:** When cancer cells continue to grow even after treatment.

**Refractory Disease:** A type of cancer that does not go away or improve very much after initial treatment.

**Relapse/Recurrence:** When the cancer that had previously been in remission after treatment has recurred. In leukemia, this may be indicated by changes in the blood or bone marrow, even before the patient experiences any symptoms.

**Remission:** Occurs when the patient's blood, bone marrow, and general health has returned to normal after treatment. Complete remission means that all evidence of the disease is gone. Partial remission means that the disease has been markedly improved by treatment, but residual evidence of the disease is still present.

**Remission Induction:** The initial course of treatment given to patients on admission to the hospital to remove all clinically detectable cancer.

**Treatment Naïve:** A person who has never undergone a particular treatment for an illness.

## Research

**Clinical Trials:** A type of research study that studies how well a drug, medical device, or treatment approach works. There are several types including treatment, diagnostic, screening, quality of life, and preventative. Treatment trials test new treatment options. Diagnostic trials test new ways to diagnose a disease. Screening trials test the best ways to detect a disease or health problem. Quality of life (supportive care) trials study ways to improve the comfort of people with chronic illnesses. Preventative trials look for better ways to prevent disease in people who have never had the disease. Patients will always be informed when their treatment is part of a trial.

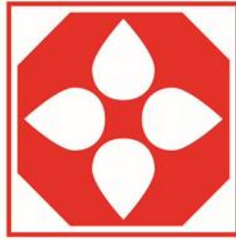
**Institutional Review Board:** Often referred to as an IRB, this is a committee located at each location doing a clinical trial. Under FDA regulations, an Institutional Review Board is a group that has been formally designated to review and monitor medical research involving human subjects. An IRB has the authority to approve, require modifications in (to secure approval), or disapprove research.

**Protocol:** This is the schedule of treatment planned in a clinical trial. It describes the number, frequency, and timing of administration of a course of anti-cancer drugs.

## Transplants

**Allogenic Stem Cell Transplant:** This is a procedure in which bone marrow stem cells are taken from a genetically matched donor and given to the patient through an intravenous line. If all goes as planned, after a period of time the donated stem cells will start making new and healthy blood cells in hopes of attacking any residual cancer cells.

**Apheresis:** This is a procedure in which blood is connected, part of the blood (such as platelets or white blood cells) is taken out, and the rest of the blood is returned to the donor. This process can also be done to collect stem cells from the blood, which can be immediately used for transplant or stored in frozen form until needed.



## CLL SOCIETY

**Autologous Stem Cell Transplantation:** A treatment that uses a patient's own stem cells to slow the growth of certain blood cancers. This is not used for patients with CLL, as cancerous cells are already typically present in the bone marrow at the time of diagnosis.

**Bone Marrow Transplant:** This is a procedure that is used in a variety of blood disorders including CLL. The patient receives very high doses of chemotherapy and/or radiotherapy, which damages the bone marrow and kills the cancerous cells. Replacement bone marrow is taken from a matched donor (allogeneic bone marrow transplant) or the patient themselves (autologous bone marrow transplant) and returned to the patient through an intravenous line. After time, the donated stem cells start to make new healthy blood cells.

**Consolidation Treatment:** To kill any remaining cancer cells, a course of chemotherapy and/or radiotherapy is given to the patient while in remission.

**Cord Blood Transplant:** The blood from the umbilical cord has a high concentration of stem cells, which are the cells from which all types of blood cells originally develop. Stem cells are extracted from the blood within the umbilical cord of a newborn baby at birth. They are then processed and given to the patient with cancer through an intravenous line. The donated stem cells will then begin making new, healthy blood cells in the recipient.

**Donor Lymphocyte Infusion:** If a patient who has had an allogeneic bone marrow transplant has a relapse with return of the original disease, they may be given lymphocytes from a donor to help eliminate leukemia cells.

**Engraftment:** This term refers to how well donor cells (a graft) are accepted by the recipient after a bone marrow or stem cell transplant. Factors such as the physical condition of the patient, severity of the disease, type of donor available, as well as age all contribute to better engraftment. Successful engraftment results in new bone marrow that produces healthy blood cells.

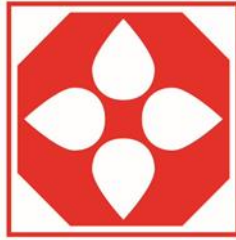
**Graft Rejection:** This is a rare occurrence in which the immune system rejects the donor cells received from an allogeneic bone marrow transplant. It may be possible to do a second transplant if this occurs.

**Graft-Versus-Host Disease:** This complication occurs after an allogeneic bone marrow/stem cell transplant when the donor's transplanted white blood cells see the cells of the patient as an enemy, so they attempt to destroy them. The severity can range from mild to very severe. It most commonly affects the patient's skin, intestines, or liver. This condition can be prevented and/or treated with immunosuppressive drugs.

**Human Leukocyte Antigens:** These are proteins found on the surface of white blood cells and other cells. They differ from person to person and determine if there is a match between a patient to be treated with a bone marrow transplant and a potential donor. Human leukocyte antigen factors are inherited from the mother and father, so the greatest chance of any sibling being a match is one out of four.

**Immunosuppression:** A deliberate treatment-induced reduction in the body's defense mechanisms or immune system. This is a necessary part of the bone marrow transplant procedure to prevent graft-versus-host disease and graft rejection.

**Matched Related Donor:** A donor that is a sibling or other relative of the patient.



## CLL SOCIETY

**Peripheral Blood Stem Cell Transplant:** This type of transplant uses stem cells obtained from a donor's peripheral blood. Donors are given growth factors to increase the number of stem cells in circulation so that they can then be harvested. The patient receives the cells through an intravenous infusion and the cells find their way to the bone marrow. The donor cells are called a graft.

**Reduced Intensity Transplant:** A procedure similar to the standard allogeneic bone marrow transplant. The patient receives lower doses of chemotherapy and/or radiation to prepare them for the transplant. This reduces side effects caused by chemotherapy, making it more tolerable for older adults. It does not reduce the risk of graft-versus-host disease. This is also sometimes called nonmyeloablative transplant, or a mini transplant.

**Stem Cell Transplant:** This is a procedure where blood-forming stem cells are taken from a healthy donor. The patient receives the cells through an intravenous infusion, and the cells then find their way to the bone marrow. The donor cells are called a graft. Stem cells can be obtained from bone marrow, cord blood, or the circulating peripheral blood.

**Unrelated Donor:** A donor that is not a sibling or other relative of the patient.

## Genetics

**Clone:** A group of cells that are genetically identical and originate from a single parent cell. Leukemia cells develop from one original abnormal cell. Leukemia is an example of a clonal cancer.

**Cluster of Differentiation:** This is a process of designating different protein molecules found on the surface of cells. Each unique surface molecule is assigned a different number which allows cell immunophenotypes to be identified, ultimately allowing for diagnosis.

**Complex Karyotype:** Defined as at least three distinct chromosomal abnormalities present in more than one phase of cell division. It is made up of a classification of cytogenetic risks for those with hematologic malignancies that have important applications in the diagnosis and prognosis of hematological malignancies.

**Cytogenetic Analysis:** This type of test examines the number and size of chromosomes in cells. It is often used in cancer treatment because it helps identify changes in cells before and after treatment.

**Chromosome:** These are long thread-like structures of DNA that are present in every single cell. Chromosomes are made up of many individual genes. Humans have 23 pairs of chromosomes in each cell. These chromosome pairs include 22 sets of non-sex chromosomes, and one set of sex chromosomes (XX for females and XY for males). Each chromosome has two arms, the shorter arm is called 'p' and the longer is called 'q'. Individual genes are identified by the number of the chromosome, a 'p' or 'q' to identify which arm, and then the number of the gene (1, 2, 3, etc.) on that arm.

**Deletion:** This is an abnormality of a chromosome where a part of a single chromosome has been lost.

**DNA:** Stands for deoxyribonucleic acid. It is the genetic material that makes up chromosomes and genes that essentially contains the instruction manual for how cells in the body should look and behave.



## CLL SOCIETY

**Epigenetics:** The study of how changes in gene activity (that are not directly caused by changes in the DNA sequence) influence the way a cell looks and behaves.

**Genes:** All living beings have genes. Genes determine everything about an organism, including appearance, how it lives, and how it behaves. Genes exist in long strands of DNA called chromosomes.

**Genetics:** The study of genes and how certain traits are passed down from generation to generation.

**Mutation:** When there is a change in the DNA that makes up a gene. Mutated DNA of cancer cells leads to increased cancer growth and resistance to chemotherapy cancer treatments.

**Synthetic Lethality:** Refers to when the death of cells takes place due to there being some sort of disruption in two genes (i.e., loss-of-function mutations, RNA interference, drug treatment, etc.), each of which would not be lethal if the disruption had occurred in only one gene alone.

**Translocation:** This is a chromosomal abnormality that occurs when a piece of one chromosome breaks off and attaches to the end of another chromosome. When a translocation takes place, the gene where the break occurred is altered or mutated. This type of gene mutation can cause cancer.

### Prognostic Indicators

**13q14 Deletion:** This is the deletion of region 14 on the long 'q' arm of chromosome 13.

**17p Deletion:** About 5% of patients with CLL at the time of diagnosis have deletions on the short arm of chromosome 17. The percentage with 17p deletion increases over time, and typically the TP53 gene is also deleted. People who have CLL with 17p deletion tend to have a higher risk disease and do not respond as well to standard chemotherapy.

**ATM:** This deletion is located on chromosome 11q. When a patient has the deletion of chromosome 11q, ATM is a part that is almost always missing. The mutation of ATM can occur with or without deletion of the other chromosome. Mutations of ATM rarely occur without the deletion of 11q. ATM is important because it is the damage response gene that senses DNA damage and stops cell division.

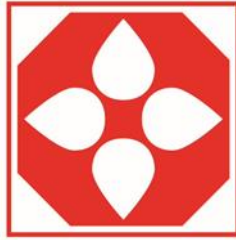
**BIRC3:** This is another marker that is located on the far end of the same 11q deletion that eliminates ATM. Some 11q deletions include BIRC3, so it is possible to have an 11q deletion and have either a normal or deleted BIRC3 depending on the size of the deletion. BIRC3 helps regulate cell death. CLL patients with a mutated BIRC3 are considered to be in a high-risk category. BIRC3 is another way cells can become resistant to fludarabine.

**Beta2-Microglobulin:** This is a protein that is shed from CLL cells. An elevated serum B2M level seems to correlate with unmutated IgHv gene status, and/or a high level of ZAP-70. This may indicate a more progressive form of CLL.

**CD38:** The level of this protein (or antigen) on CLL cells may be a marker to assist in predicting CLL disease progression.

**CD49d Gene Expression:** A surface protein on the outside of the CLL cell. Its presence is measured by FLOW cytometry. Recent studies have shown that CD49d can help in determining overall survival, as well as when to initiate treatment.

**Cluster Designation:** This is a term used with a number to identify a specific molecule on the surface of an immune cell. It is commonly used in an abbreviated form (for example, CD38).



## CLL SOCIETY

**Del(11q):** Describes a deletion on the long arm of chromosome 11. Up to 20% of patients with CLL have this chromosomal deletion. CLL patients with del11q tend to have a higher-risk of disease, are younger, and have enlarged lymph nodes.

**Del (13q):** A deletion on the long arm of chromosome 13. It is the most common chromosomal abnormality and is associated with more favorable outcomes.

**FBXW7:** The protein that turns off the NOTCH gene. The clinical significance of FBXW7 has not been evaluated closely. But with its association with NOTCH, it could be associated with high-risk disease similar to a NOTCH mutation.

**Immunoglobulin Heavy Chain Variable Region (IgHv) Gene Status:** This marker can distinguish between CLL subtypes (unmutated IgHv and mutated IgHv). Those diagnosed with CLL who have unmutated IgHv gene status may have a more progressive form of the disease.

**NOTCH1 Gene Mutation:** The NOTCH gene is involved in the development of different types of blood cells. Approximately 10-15% of CLL patients have mutations of this gene, causing it to be more active than it should be. Several studies have suggested that patients who have NOTCH1 gene mutations are considered high risk. They undergo transformation into Richter's Syndrome more frequently, and survival is shortened.

**SF3B1 Gene Mutation:** The SF3B1 gene is involved in the formation of select proteins in CLL as well as other blood cancers. Approximately 10-15% of patients have a mutation of this gene. Patients with SF3B1 mutations are resistant to fludarabine, and their CLL is considered high-risk. Other markers for fludarabine resistance include P53 and BIRC3.

**TP53 Gene Mutation:** Mutation of this gene is very commonly seen in patients who also have del(17p), but it can also occur independently without it. Patients with this mutation are considered high-risk disease. Newer therapies have been shown to be effective for patients who have del(17p) or TP53 gene mutations.

**Trisomy 12:** Chromosomes occur in pairs, which is also called a diploid. When there are instead three copies of a chromosome instead of two (a pair), it is called trisomy. About 10-20% of CLL patients have cells with three copies of chromosome number 12 instead of only two. This abnormality is associated with an intermediate risk of disease. If it occurs alongside additional chromosomal abnormalities, it is then associated with a higher-risk than trisomy 12 alone.

**ZAP-70:** this is an abbreviation for the cell protein called zeta-associated protein 70. A high level of ZAP-70 on the cells of patients with CLL is one factor that may predict more progressive disease.