A CLL-Specific Glossary

Blood Cells

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 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.

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.

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.

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 which 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 blood stream and enter infected tissues where it becomes a macrophage. A macrophage is a type of immune cell that surrounds and kills bacteria and viruses.

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 (PBSC): 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. Platelets 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 type 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 are 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 cells' activity.

White blood cell (WBC): They 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.

Blood Lab Tests

Absolute neutrophil count (ANC): The absolute neutrophil count is the actual number of white blood cells (WBCs) that are neutrophils. It is calculated by multiplying the WBC count times the percent of neutrophils in the differential WBC count. The percent of neutrophils includes both fully mature neutrophils and almost mature neutrophils, also known as “bands”.

Complete blood count (CBC): This is a routine test performed on a small amount of blood. The CBC 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 made up of red blood cells. It may also be called a blood count.

Hematocrit: This is a blood test that is usually part of the CBC. It measures the proportion of the blood containing red blood cells. This measurement depends on the number of red blood cells and their size. Hematocrit is part of a complete blood count. Also called HCT, packed cell volume, PCV.

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 (MCV): This is the measure of the volume or size of the red blood cells.

Mean Corpuscular Hemoglobin Concentration (MCHC): This is a calculation of the average percentage of hemoglobin in each red blood cell.

Mean Corpuscular Hemoglobin (MCH): This is a measure of the average amount of hemoglobin in a red blood cell.

White blood cell differential: This is a group of tests that includes the following: absolute neutrophil count or % neutrophils, absolute lymphocyte count or % lymphocytes, absolute monocyte count or % monocytes, absolute eosinophil count or % esosinophils, and absolute basophil count or % basophils.

Lab Results

Anemia: A condition in which the in which the body 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: This is 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 or blood cancer where the bone marrow makes too many platelets. It is also called primary thrombocythemia. Complications including excessive bleeding and clotting.

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

Lymphoproliferation: This means 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 — red blood cells, white blood cells, and platelets.

Thrombocytosis: This means an increased number of platelets (thrombocytes) in the blood from any cause, cancerous or non-cancerous.

Thrombocytopenia: This is 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 Procedure Terminology

Biopsy: A small sample of tissue, for example from a lymph node or bone marrow, 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 and a sample of the marrow (liquid) is taken. This test is usually done at the same time as a bone marrow biopsy.

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 scaring 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. Also called 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 just 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 to help identify abnormalities in chromosomes or 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 and treatment needs, and to monitoring treatment effectiveness.

Flow cytometry: This is a test that is used to study blood cells, marrow cells or cells from a biopsy and provides information as to 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 and to answer questions such as, is there evidence of a cancerous clone, as in CLL or a mismatched ratio of immune cells, such as in 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 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.

PET Scans: Positron emission tomography scan is a nuclear medicine 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 the test except to look for Richter's Transformation (RT). RT sometimes can be diagnosed by increased metabolic activity on a PET scan. A PET scan is usually done in conjunction with a CT scan.

Polymerase Chain Reaction (PCR): This test uses a technique to amplify trace amounts of DNA or RNA so that the specific types can be studied and tested for.

Staging: Staging helps doctors assess how CLL is expected to progress over time and also to develop a treatment plan. Staging takes into account 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, and whether the patient has anemia (too few red blood cells) and/or thrombocytopenia (too few platelets). The 2 systems that are used are the Rai System and the Binet System.

Ultrasonography (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 which prevent cells 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, 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, for example penicillin. Some are used to treat cancer, but not usually in CLL.

Biologic therapy: Biologic therapy is a treatment that uses the patient's immune system to fight cancer.. These are substances or modified substances made from living organisms to fight cancer. Monoclonal antibodies are examples 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 (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.

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

Chemotherapy: This is a type of medicine 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. This explains why 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 effectively treat chronic lymphocytic leukemia, though there is some evidence that one of the active components of green tea, EGCG or epigallocatechin gallate may slow disease progression. Theoretically some CAM therapies can alter the effectiveness of standard medical care and interfere with the metabolism and activity of some cancer drugs.

Corticosteroids (steroids): These are drugs that are similar to cortisol, a hormone that your body makes naturally. They are sometimes referred to as "steroids", however they are different from the male hormone-related steroids that you may have heard about related to use by some athletes. For CLL, they are sometimes used to decrease some side effects of chemotherapy or to reduce strong reactions to monoclonal antibodies. In very high doses, they are also used to destroy the leukemia cells. Also, they are used to suppress graft rejection or graft versus host disease following bone marrow transplants. One of the many side effects of steroids is the increased risk of infection, 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 which act by killing or preventing the division of cells, also known as chemotherapy.

Diuretic: This is a drug that may be used during chemotherapy to stimulate the kidneys to produce more urine to help to excrete the anti-cancer drugs.

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 called erythropoietin-stimulating agents (ESA) and include Epoetin alfa (Epogen, Procrit) and darbepoetin alfa (Aranesp). White blood cell growth factors are called granulocyte colony stimulating factors (GCSF) and granulocyte macrophage colony stimulating factors (GMCSF). The newest compounds are smaller drugs that mimic platelet growth factors or thrombopoietin so that they can pharmacologically stimulate platelet production. These drugs are therefore called thrombopoietin or more commonly TPO mimetics.

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.

Monoclonal antibody: This is a type of targeted therapy in which a type of protein called an antibody is developed to attach to specific marker on CLL cells. This helps your body's immune system "see" the cancer cells so it can attack them. This type of medication does not affect the normal cells in a patient's body. There are many kinds of monoclonal antibodies. Each one looks for only one substance. Examples of monoclonal antibodies are rituximab, obinutuzumab, ofatumumab, and alemtuzumab. It may also be called Biologic Therapy.

Off label drug: This is an approved drug that is prescribed by a licensed doctor for a use other than that for which it was approved by the U.S. Food and Drug Administration (FDA).

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 it.

Over-the-counter medicine: These are medicines that are available without a prescription from the doctor. Also called OTC medicines.

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

Platelet Transfusion: This is 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: This is a precautionary treatment provided in order to prevent a disease from occurring.

Palliative Care: This kind of treatment is 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 processes of absorption, metabolism and excretion.

Purine Analogues: These are a type of anti-metabolite that is incorporated into a dividing cells 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 effective treatment for localized disease, such as an enlarged lymph node or spleen.

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 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 (splenomegaly) and is causing problems such as low blood counts or abdominal symptoms due to its size.

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

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

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

Tyrosine Kinase Inhibitors: This is a type of treatment that blocks the signals 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 BTK inhibitors. There are also other kinase inhibitors that are similar in their action and include idelalisib and other PI3K inhibitors.

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

Medication Administration

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

Central Line (Indwelling Catheter): A special tube put into a large vein in the patient's upper chest. It is used to give medications, fluids or blood products or to take blood samples. It helps to avoid repeated needle punctures of a vein. It is also known as a Central Venous Catheter.

Intramuscular Injection: This is an Injection into the muscle.

Intrathecal Injection: This is an Injection into the spinal fluid.

Intravenous Infusion: Over a prolonged period of time, antibiotics, blood products, anti-cancer drugs or nutrients flow into a patient's vein through a tube. The rate is often controlled through the use of a pump.

Intravenous Injection: A medication is injected into the vein through a syringe.

Portacath: A form of central venous line 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 to draw blood and avoids multiple needle sticks.

Subcutaneous Injection: An injection into tissue immediately under the skin.

Diagnosis

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

Leukemia: This type of blood cancer is characterized by large numbers of abnormal blood cells, usually white blood cell, which take over the bone marrow and often are also found in the blood stream. 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 describes the progression of CLL into an aggressive lymphoma. It occurs in a small number of CLL patients. This change is not a second cancer, but a transformation of the CLL cells. Also known as Richter's Syndrome.

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

Small Lymphocytic Lymphoma (SLL): 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 be enlarged. SLL most often occurs in people older than 50 years. It is a type of non-Hodgkin 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: This 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.

Anorexia: This means an abnormal loss of appetite. Some cancer patients have anorexia and sometimes it occurs as a result of treatment for cancer.

Autoimmune Hemolytic Anemia (AIHA): This is a rare autoimmune disorder that is seen more often in CLL where the body's immune system attacks its own red blood cells resulting in anemia.

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

Hemorrhage: This means bleeding either to the outside through the skin or internally.

Idiopathic (or Immune) Thrombocytopenic Purpura (ITP): 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 or Immune Deficiency: This means that the immune system is not functioning properly, which makes the patient at risk for infection caused by bacteria, viruses or fungi. This may be due to a low white blood cell count or due to some medicines.

Mucositis: This is an 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 to the arms and 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: This is another term for Itching.

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

Septicemia: This is a general term to describe serious bacterial infection of the blood stream often associated with high fever.

Thrombosis: The means the development of a clot in a blood vessel. They occur most often in a vein but sometimes in an artery. It is potentially life-threatening depending on where the clot occurs and if left untreated.

Personnel

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

Hematologist: This is a doctor who specializes in blood cell diseases and disorders that affect the blood-producing organs.

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

Oncologist: This is a type of physician that specializes in the diagnosis and treatment of cancer.

Pathologist: This is a doctor that specializes in the cause and diagnosis of disease by examining body tissues and fluids.

Pharmacist: A pharmacist is a licensed professional whose job includes the preparation, distribution, and use of prescription drugs. They also advise patients, as well as physicians and other health practitioners, on the selection, dosages, interactions, and side effects of medications.

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

Anatomy and Physiology

Bone marrow: The soft, spongy tissue inside most bones where blood cells are formed. Blood cells are formed in the bone marrow, which is located in the hollow central parts of the bones. 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 production and maturation of blood cells from stem cells. This takes place in the bone marrow.

Lymphadenopathy: Enlargement of lymph nodes.

Lymph Nodes or Glands: These are small structures found throughout the body, e.g. neck, groin, armpits, abdomen, which contains both mature and immature lymphocytes. In patients with chronic lymphocytic leukemia, the cancerous lymphocytes are excessive and the lymph nodes become enlarged.

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

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

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

Splenomegaly: Enlargement of the spleen.

Disease Status

Minimal Residual Disease (MRD): This describes the small amounts of cancer cells that may remain after treatment and when the patient is considered to be in remission. These cells are only identified by sensitive molecular techniques**. MRD negative refers to when no cancer cells can be found using the most sensitive molecular tests and is considered a deeper remission.**

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

Resistance to Treatment: This describes cancer cells that continue to grow even after treatment.

Refractory Disease: This describes a type of cancer that does not go away or improve much after initial treatment.

Relapse/Recurrence: This means that the cancer that had 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: Remission means that the patient's blood, bone marrow and general health of the patient to normal after treatment. Complete remission means that all evidence of the disease is gone. Partial remission means that the disease is markedly improved by treatment, but residual evidence of the disease is present.

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

Clinical Trials

Clinical trial: This is a type of research study that studies how well a drug, medical device, or treatment approach works in people. There are several types of clinical trials. Treatment trials

test new treatment options. Diagnostic trials test new ways to diagnose a disease. Screening trials test the best way to detect a disease or health problem. Quality of life (supportive care) trials study ways to improve the comfort of people with chronic illness. Prevention trials look for better ways to prevent disease in people who have never had the disease. A patient will always be informed when the treatment is part of a trial.

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. This plan is reviewed and approved by a committee at each place doing the clinical trial. This committee is known as the Institutional Review Board or IRB.

Transplants

Allogeneic stem cell transplant: This is a procedure in which bone marrow stem cells are taken from a genetically matched donor (a brother, sister, or unrelated 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, healthy blood cells and in CLL, attack the residual cancer cells.

Apheresis: This is a procedure in which blood is collected, 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 to be used for transplant or stored in frozen form until needed. Because stem cells are usually not seen in the blood stream and special drugs are used to mobilize the stem cells to move from their normal place in the bone marrow into the blood stream.

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

Consolidation Treatment: In order 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 develop. Stem cells extracted from blood within the umbilical cord of a newborn baby and are given to a patient through an intravenous (IV) line. The donated stem cells will begin making new, healthy blood cells.

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 the donor. This may eliminate the leukemia cells.

Engraftment: This term refers to how well donor cells (a graft) are accepted by the patient (recipient) after a bone marrow or stem cell transplant. Factors such as physical condition of

the patient, severity of the disease, type of donor available, and age 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 patient's immune system rejects the donor cells received from an allogeneic bone marrow transplant. It may be possible to do a second transplant.

Graft-Versus-Host Disease (GVHD): This complication occurs after an allogeneic bone marrow/stem cell transplant. It happens when the donor's transplanted white blood cells "think" the cells of the recipient (patient) are enemy cells and tries to fight and destroy them. The severity can range from mild to very severe. It most commonly affects the patient's skin, intestines or liver. It can be prevented or treated with immunosuppressive drugs.

Human leukocyte antigens (HLA): These are proteins found on the surface of white blood cells and other cells. They differ from person to person and determine the "match" between a patient to be treated with a bone marrow transplant and a potential donor. HLA factors are inherited from the mother and father so the greatest chance of sibling being a match is 1 in 4.

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: This is a donor that is a sibling or other relative of the patient.

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 the circulation so that they can 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: This is a procedure similar to the standard allogeneic bone marrow transplant. The patient receives lower doses of chemotherapy and/or radiation to prepare for the transplant. This reduces side effects caused by chemotherapy, making it more tolerable to older adults. It does not reduce the risk of graft-versus-host disease. Also called nonmyeloablative transplant or 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 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 circulating (peripheral) blood.

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

Prognostic Indicators

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

17P Deletion or Del (17p): About 5% of patients with CLL at time of diagnosis have deletions in the short arm of chromosome 17. The percent with (del)17p increases over time. Typically the TP53 gene is deleted. People who have CLL with del(17p) tend to have higher-risk disease and do not respond as well to standard chemotherapy.

ATM: ATM is located on chromosome 11q. If 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 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 the high-risk category. BIRC3 is another way cells can become resistant to fludarabine.

Beta2-microglobulin (B2M): 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: This level of this protein (or antigen) on CLL cells may be a marker to assist in predicting CLL progression.

CD49d gene expression: CD49d is 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 and when to initiate treatment.

Cluster Designation (CD): 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 its abbreviated form, for example, "CD38".

Del(11q): This describes a deletion on the long arm of chromosome 11. Up to 20% of patients with CLL have this chromosomal deletion. CLL patients with del 11q tend to be younger with enlarged lymph nodes and have high-risk disease.

Del(13q): This describes a deletion on the long arm of chromosome 13. It is the most common chromosomal abnormalities and is associated with more favorable outcomes.

FBXW7: This is 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). People with CLL with unmutated IgHv gene status may have a more progressive form of the disease.

NOTCH1 gene mutation: The Notch 1 gene is involved in the development of different type 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 to 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 mutations 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, BIRC3, and SF3B1.

TP53 gene mutations: Mutated DNA of cancer cells leads to increased cancer growth and resistance to chemotherapy cancer treatments. Mutation of the TP53 gene is very commonly seen in patients who also have del(17p) but can occur independently of (del)17p. Patients with mutation of the TP53 gene are considered high right. Certain newer therapies have been shown to be effective for patients who have del(17p) or the TP53 gene mutations.

Trisomy 12: Chromosomes occur in pairs which is called diploid. When there are 3 copies of a chromosome, it is called trisomy. About 10-20% of CLL patients have cells with three copies of chromosome 12 instead of two. This abnormality is associated with intermediate-risk. If it occurs with additional chromosomal abnormalities, it is associated with a higher risk than trisomy 12 alone.

ZAP-70: This is an abbreviation for the cell protein “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.

Genetics Terminology

Cytogenetic Analysis: This type of test examines the number and size of chromosomes in cells. It is often used in cancer treatment and to see changes in the cells before and after treatment.

Chromosome: These are long threadlike structures of DNA that are present in every cell. Chromosomes are made up of many individual genes. Humans have 23 pairs of chromosomes in each cell: chromosome pairs 1 to 22 and one pair 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 in which part of a single chromosome has been lost.

DNA: This is the genetic material that makes up chromosomes and genes. In simple terms, it is essentially the instruction manual for how cells in the body should look and behave.

Epigenetics: Epigenetics is the study of changes in gene activity which are not caused by changes in the DNA sequence. It is the study of gene expression, the way genes influence the way a cell looks and behaves.

Genes: All living beings have genes. Essentially genes determine everything about an organism: appearance, how it lives, and how it behaves. The genes exist in long strands of DNA (deoxyribonucleic acid) called chromosomes.

Genetics: Genetics is a term that refers to the study of genes and how certain traits are passed down from generation to generation.

Mutation: This means that there is a change in the DNA that makes up a gene.

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.