

CML Glossary (and abbreviations)

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INTRODUCTION:

Included here are terms specifically related to the disease of CML, as well as some other terms which have been used at one time among fellow CMLers – but which may not be so central to understanding CML the disease. CML terms are asterisked (**d).

We wish to thank Dr. Richard Rockefeller for allowing us to update and use this CML Glossary, which he originally prepared for us in, May of 2001. (Dr. Rockefeller, himself a CML patient, supported CML research and did much to further the understanding of CML. He died tragically in 2014 in an unrelated accident.)

Glossary and abbreviations

***a-INT=** alpha Interferon.

The preferred abbreviation is IFN-a

***ABL =** a gene (named for a researcher whose last name was Abelson) on human chromosome # 9, involved in normal white blood cell replication. Abl only causes trouble when it leaves to join chromosome #22, creating the bcr-abl gene. (See bcr-abl)

***Absolute neutrophil count =** the total number of neutrophil cells per microliter of blood. It is calculated by using the total white blood count (WBC) and the percentage of neutrophils shown on the laboratory “differential.”

***Accelerated phase =** a phase of CML between chronic and blast phase. The actual definition of accelerated phase is somewhat variable and depends on whom you

ask. Evidence of acceleration includes: recurrence of certain clinical findings such as night sweats, fatigue and an enlarged spleen; increased difficulty in controlling the blood cell counts; increases in certain cell types such as basophils, eosinophils, and especially blasts; and the appearance of new chromosomal abnormalities on cytogenetic analysis. Any one of these may (or may not) be cause for concern, but the appearance of two or more in combination makes the diagnosis of accelerated phase more likely. Untreated, the accelerated phase progresses to blast phase within a few months.

Additive = often used in discussion of combined drug efficacy: when the effect of two drugs is additive it means that their effect together is only equivalent to the sum of their

individual effects. Compare this to a “synergistic” effect, where the result is greater than the sum of the parts.

* **aGVHD** = Acute Graft vs. Host Disease

ALL = Acute lymphocytic leukemia (not covered in this primer)

* **ALLO-BMT** = Allogeneic Bone Marrow Transplant

* **Allogeneic (as in allogeneic stem cell transplant)** = with respect to CML, this term is usually used in reference to stem cell or bone marrow transplantation. Allogeneic stem cells mean that they come from another person. “Allo” means other – as in another person. Compare to Autologous (see below).

ALT = alanine aminotransferase: a blood test used to detect liver inflammation (see AST)

AML = Acute myelocytic (or myelogenous, or myeloid) leukemia (not covered in this primer)

* **ANC** = absolute neutrophil count

* **Angiogenesis** = creation or promotion of new blood vessels. Tumor angiogenesis is an abnormal type of new blood vessel production stimulated by chemicals produced by cancer cells, which need extra supplies of oxygen and nutrients in order to keep growing. Angiogenesis inhibitor drugs are a new class of drugs targeted against this abnormal

process, which block or slow tumor growth.

Antigen = a substance (often a protein) that induces an immune response (usually an antibody, or cell-mediated response).

Apoptosis = programmed cell death. Normal cells are programmed to die after a certain amount of time or a certain number of cell divisions. Cancerous cells lose this characteristic and go on living and dividing as long as they get the nutrition they need. Certain anti-leukemia drugs (in particular **Gleevec, Sprycel, Tasigna, Bosulif, iClusig and interferon – with more drugs in trial**) inhibit the cancer’s anti-apoptotic mechanisms – that is, they restore the cells’ ability to die and, therefore, help to eliminate the disease.

* **Ara-C** = Cytarabine (cytosine arabinoside) - a chemotherapy agent sometimes used in the treatment of CML.

ASH = American Society of Hematologists

Aspirate = to draw in by suction

AST = aspartate aminotransferase: a blood test used to detect liver inflammation (see ALT).

* **Autologous** = refers to getting tissue back from yourself (auto = self). In an autologous stem cell transplant, for example, one’s own marrow cells are harvested and the “good” ones separated from the “bad.” One’s own

marrow is then destroyed (usually but not always – see non-myeloablative, below) with radiation and chemotherapy. Then the autologous cells are re-transfused. Neither graft rejection **nor** graft vs. host disease (see GVHD) is a significant problem with autologous transplants. The reason they are not done routinely is that 1) it is currently not possible to **insure** that ALL the leukemic cells have been eliminated from the autologous marrow, so there is a significant chance **that leukemic cells are reintroduced**; and 2) one's own immune cells are not as effective as donor immune cells at suppressing the leukemic cells that might have been reinfused.

Avascular Necrosis (AVN) = pathological bone death; a rare complication of interferon therapy, seen almost exclusively in patients whose platelet counts remain abnormally high despite treatment.

AVN = avascular necrosis.

***Basophil** = a type of myeloid white blood cell which is often elevated in CML.

***bcr** = breakpoint cluster region – a gene on human chromosome # 22 which is involved in the pathophysiology (abnormal functioning) of CML.

***bcr-abl** = the abnormal gene that characterizes the leukemic stem cells of most people with CML. For CML to occur, the “abl” gene (named after the researcher Abelson) must come

unglued from its usual location on chromosome # 9, and become attached to the “bcr” (breakpoint cluster region) of chromosome #22, thus creating the bcr-abl hybrid, or “chimera” which has a number of nasty properties. It appears that the genetic “mistake” producing bcr-abl is quite common and may occur several times during the lives of normal people; however, their immune systems recognize and kill the abnormal cells. This fails to happen in people who develop CML, but it is not known why.

Bioethics = the application of ethics to the science and practice of biology including medicine, especially as applied to human and animal life

Biopsy = see bone marrow biopsy

***Blast (or blastic) phase** = the third phase of CML after chronic and accelerated phases, characterized by the presence of increasing numbers of highly immature blood cells (“myeloblasts,” or “blasts”) in the blood, bone marrow and other organs. Blast phase is often, but not always, fatal within months, though new treatments show promise in prolonging survival. It is believed that blast phase is reached when the CML cells have reached a critical mass of mutations which put them beyond all the body's control mechanisms.

***BMA** = bone marrow aspiration

***BMB** = bone marrow biopsy

BMT = bone marrow transplant

***Bone marrow** = the central portion of our bones, where the majority of blood cells types are made and stored. Bone marrow contains many other types of tissue besides blood cells, including a fine meshwork of bone (“spicules”), connective tissue, and blood vessels.

***Bone marrow aspiration (BMA)** = a procedure in which liquid contents of a patient’s bone marrow are withdrawn (aspirated) through a needle. This procedure is used to make the diagnosis of CML and, now, sometimes used to follow the progress of treatment of CML.

***Bone marrow biopsy (BMB)** = similar to a bone marrow aspiration, but used less frequently and performed with slightly different equipment. It is used when a larger or different kind of sample of marrow is needed, or when a BMA is unsuccessful because the marrow is too fibrous to permit aspiration through the BMA needle.

***Bone marrow transplant (BMT)** = a procedure in which bone marrow is taken from one person and given to another, for therapeutic purposes. In fact, this procedure is rarely used in CML nowadays, having been largely replaced by stem cell transplants (SCT’s); however, many people still use the term BMT even when they’re referring to an SCT.

Bosulif = branded name of bosutinib, a TKI from Pfizer.

Bosutinib = the generic name of a second generation tyrosine kinase inhibitor. In Canada, this TKI can only be prescribed after failure to respond appropriately to first-line TKIs.

BUN = Blood Urea Nitrogen (a measure of kidney function).

CADTH = Canadian Agency for Drugs and Technology in Health. Provides the health care divisions of Canada’s federal, provincial and territorial governments with credible, impartial and evidence based information about the effectiveness and cost effectiveness of drugs and other health technologies (www.cadth.ca)

***CBC** = complete blood count.

***CCR** = complete cytogenetic response.

CSF = cerebrospinal fluid – a specialized bodily fluid that bathes the central nervous system.

Chemotherapy = the treatment or control of cancer using drugs which interfere with cancerous (and, unfortunately, normal) cells’ ability to grow and multiply. Most chemo drugs are targeted to a specific phase of the cell cycle, and kill only cells which are both multiplying and in that particular phase. Tyrosine kinase inhibitors are not chemotherapy drug, rather, they are anti-leukemic drugs and work in a different way.

CHF = Congestive heart failure

Chimera = a fusion of unrelated species or types. Bcr-abl is considered a chimeric gene because it results from the abnormal fusion of the “abl” gene on chromosome #9 with the “bcr” portion of chromosome #22. Classically, a chimera is a mythical monster with a lion’s head, a goat’s body and a serpent’s tail. Bcr-abl is equally monstrous in its effects!

Chromosome = in a cell nucleus, a structure containing a molecule of DNA that transmits genetic information. Each organism of a species normally has a characteristic number of chromosomes in its somatic cells; the normal number for humans is 46. The chromosomal mutation leading to CML involves chromosomes number 9 and 22 - though if the disease is untreated, other chromosomal abnormalities accumulate as well. This process is called clonal evolution.

***Chronic myelogenous (or myeloid) leukemia (CML)** = a disease involving the overproduction of certain types of white (“myeloid”) blood cells. Untreated, CML progresses through three phases – chronic, accelerated, and acute or blastic phase – each phase is shorter and harder to treat than the previous phase. Also called chronic “myeloid” or “myleocytic,” or “granulocytic” leukemia

*** Chronic phase** = in the context here, the earliest (and generally longest) phase of CML. It is characterized by a single abnormality of marrow stem cells, which grow too fast and don’t die soon enough. During the chronic phase, CML is relatively easy to

control because it does not really behave like a cancer.

Clinical trial = Trials to evaluate the safety and effectiveness of medication (in particular) using a predetermined design or protocol. Numerous clinical trials are necessary to obtain the right (given by a specific government agency) to market a drug.

CLL = chronic lymphocytic leukemia - not covered in this primer.

***Clonal evolution** = the accumulation of DNA (chromosome) mutation which occurs in untreated CML, and which leads to progression of the disease.

Clone = a colony or group of organisms, or a colony of cells derived from a single organism or cell by asexual reproduction, having identical genetic constitution.

***CML** = chronic myelogenous (or myeloid) leukemia - the subject of this Primer!

CO₂ = carbon dioxide

Comparative Genomic

Hybridization = a highly specialized test performed on the DNA of stem cells to see whether they have mutated over time.

Complete blood count (CBC) = a blood test that measures the proportions and total number of white blood cells, red blood cells, and platelets. It also gives information concerning the shape, size and variation of these cells. In CML, a

“white cell differential” is usually performed along with the CBC. This tells which of several kinds of white cells are present, and in what proportions.

***Complete cytogenetic response = CCR;** absence of leukemic (Ph+) cells in the bone marrow by either conventional or FISH cytogenetic testing.

***Constitutive** = the property of being continuously switched on. Normal marrow stem cell growth is controlled by signals from surrounding cells, but bcr-abl, the chimeric enzyme that causes CML, is “CONSTITUTIVELY active” - that is, it keeps commanding the Ph+ cells to grow and not to die, despite negative feedback from the local environment.

***Cytogenetics. = Cyto** = cell; genetics refers to looking at the **cells'** chromosomes, their genetic material. Two types of cytogenetics, “conventional” and FISH, are used to diagnose and follow the course of CML. Conventional cytogenetics (so called because it's been around a long time) is a microscopic exam of up to 25 marrow cells in a phase of cell division when their chromosomes can be clearly seen and differentiated.

***Cytogenetic response (CR)** = is a response to treatment of CML that occurs in the marrow, rather than just in the blood..... There are 3 levels of cytogenetic response: 1) just plain cytogenetic response (CR); 2) Major cytogenetic response (MCR); and 3) complete cytogenetic response

(CCR). A plain cytogenetic response means any Ph+ cells less than what you began with; major means 35% or less, but more than 0; and complete cytogenetic response means NO Ph+ cells as measured by either conventional or FISH cytogenetic testing (though the PCR test may still be positive).

Cytopenia = a reduction in the number of blood cells

Dasatinib = generic name for the **SRC kinase inhibitor** marketed under the brand name of Sprycel from Bristol Myers Squibb. Dasatinib is indicated for patients who develop resistance with Gleevec or are intolerant of Gleevec. It is 300 times more potent than Gleevec.

***Deep Molecular Response = 4.5** reduction of bcr-abl transcript level as measured by PCR

Diff = differential white blood count = a relative count of the different white blood cells types in a blood sample. A “normal” diff might be 60% neutrophils (or “poly's”); 35% lymphocytes (lymphs); 2% monocytes (monos); 1% basophils (basos); 1% eosinophils (eos).

***DLI** = Donor Leukocyte Infusion.

DNA = Molecule that carries genetic information. The DNA is assembled into discrete packets called chromosomes. Humans have 23 pairs of chromosomes, or 46 of them, total, in each cell.

***Donor Leukocyte Infusion** = a procedure done for relapsed SCTs. Immune system cells are taken from the original donor and transfused to the CML patient. See also <http://www.haem.net/clinical/clinical012.asp>

***Durable** = long lasting; the term is used in qualifying response to therapy: a durable response to Gleevec, for example, is one that lasts.

***Dx** = abbreviation for “diagnosis”

***ELN = European LeukemiaNet:** this European group has prepared guidelines in CML management to direct physician care with respect to CML; along with NCCN guidelines, ELN guidelines are considered to be the minimum standard of care for CML patients.

*** Enzyme** = a protein that catalyzes changes in other biological substances. Too many white cells are produced in CML because of an abnormal tyrosine kinase enzyme - whose sole activity is sticking phosphate molecules onto tyrosine molecules. It's hard to imagine that so much mischief could be caused by such a simple act!

EPO = a brand name for artificially produced Erythropoietin, a hormone that stimulates red blood cell production, for example, Procrit or Eprex.

***Erythrocyte** = red blood cell (erythro = red; cyte = cell)

***Erythropoietin** = a hormone that stimulates red blood cell production (see Procrit, EPO or Eprex).

FISH = Fluorescence In Situ Hybridization

***Fluorescence In Situ Hybridization (FISH)** = a cytogenetic test that is used to reveal the presence of the “bcr-abl” gene. The abl DNA shows up as a red dot in the microscope slide and bcr DNA shows as a green dot (see <http://path.upmc.edu/cases/case171/mole.html> for a nice picture). In the nuclei of normal cells, where abl and bcr are on different chromosomes, these dots appear separately. But in Ph+ leukemic cells where bcr and abl are fused, the dots appear together. If you see RedGreen the cell is Ph+, while Red-----Green (that is, they're far apart) is Ph-, normal.

***G-CSF** = granulocyte colony stimulating factor (brand name Neupogen) = a naturally occurring hormone that stimulates white blood cell production

Generic imatinib = a formulation of imatinib (Gleevec); in Canada this is made with the original alpha crystal formulation of imatinib (not tested in clinical trials) for which the patent expired in 2013 (in Canada) allowing for a generic version. In Canada both Teva and Apotex manufacture a generic imatinib which has been approved by Health Canada.

***GEP** = Gene Expression Profiling: an experimental technique for determining which genes in a tissue sample are being over or under expressed. Patterns of over and under expression can help predict whether a cancer will or won't spread, and what drugs will work best against it.

***Gleevec** = branded name for Novartis' anti-CML drug. Gleevec works by binding to and inhibiting the bcr-abl enzyme that is the hallmark of this disease. Gleevec's generic name is imatinib mesylate, so it's also referred to as IM.

***Glivec** = the spelling used for Gleevec in some other countries other than the US and Canada.

***GM-CSF** = Granulocyte-monocyte colony stimulating factor = a naturally occurring hormone that stimulates white blood cell production (in a different way than G-CSF does)

***Graft vs. host disease (GVHD)** = a collection of ailments that complicate stem cell (bone marrow) transplantation. In GVHD, the donor's immune system (the "graft") attacks various parts of the patient's (the host's) tissues.

***Granulocyte** = another name for a white blood cell

***GVHD** = graft vs. host disease

***Functional cure** = continued long term therapy that prevents progression of CML and the emergence of resistance is

currently considered a functional or "operational" cure

***Hct** = Hematocrit

***Hematologic response** = normalization of the white blood cell counts in the blood, though not necessarily in the bone marrow. The response can be partial (reduction in white cells, but not down to normal range) or complete (white blood count at or below approximately 12,000 white cells/microliter).

Hematologist = a physician who specializes in disorders of the blood, including blood cancers such as leukemia. (heme = blood in Greek)

Heme-onc = hematologist-oncologist: a doctor specialist who treats both blood diseases and solid cancers

***Hematopoietic** = pertaining to hematopoiesis, the production of all blood cells

***Hematopoietic Growth Factor** = any group of glycoproteins that promote the proliferation and maturation of blood cells.

***Hemoglobin** = the molecule in red blood cells which carries oxygen

***Hgb** = Hemoglobin

HLA = Human Leukocyte Antigen

HMO = Health Maintenance Organization

***HR** = hematologic response

Human Leukocyte Antigen (HLA) = an antigen (molecule recognized by the immune system) used to determine compatibility of tissue types between one person and another. Nowadays compatibility is more often determined using MHC, or major histocompatibility complex.

***Hydrea (hydroxyurea, HU)** = a chemotherapy drug which is often used first in the treatment of CML. Lethal to mature leukemic cells Hydrea can bring elevated white blood counts (WBCs) back to normal; however, it does not kill many leukemic stem cells in the bone marrow, and therefore does not effectively slow the progression of the disease.

iClusig = branded name for ponatinib from Ariad (marketed by Paladin in Canada); a TKI that is used to treat CML patients who are either refractory to all other CML treatments or who have a T315I mutation.

***IFN** = interferon

IFN-a = interferon-alpha, specifically, interferon-alpha 2a, the type of interferon used to treat some patients with CML.

***IM** = imatinib mesylate, the brand name for Gleevec (Glivec, outside the US and Canada)

INESSS = institut national d'excellence en sante et en services sociaux. Its mission is to promote

clinical excellence and efficient use of resources in Quebec's health and social sectors. (www.inesss.qc.ca)

INT = interferon
(the official abbreviation is IFN)

***Interferon** = a chemical which is produced normally by mammalian cells in order to fight infection and cancer. It is now produced by recombinant DNA techniques, and used as a therapeutic drug for a number of diseases, including CML.

Intravenous = IV = within a vein

***IS** = International Scale – PCR standardization protocols that will ensure that all laboratories that process PCR's are held to the same standards throughout the world. PCR results that have been processed using the IS will be reported as a percentage rather than a log reduction.

LAP = leukocyte alkaline phosphatase: a chemical produced in high quantities in certain leukemias, but always low in chronic phase CML. A low serum LAP is thus used to support the diagnosis of CML.

LD (or LDH) = Lactate dehydrogenase = an enzyme produced by certain cell and tissue types. It is used to help diagnose CML "blast" phase, since blasts produce LDH in abnormally high quantities.

***Leukemia** = cancer of the white blood cells. Leukemia literally means "white blood" (leukos = white).

***Leukocyte** = white blood cell (leukos = white; cytos = cell in Greek). The main types of leukocytes are neutrophils, lymphocytes, monocytes, basophils, and eosinophils.

Lymph = abbreviation for lymphocyte

Lymphocyte = a type of white blood cell generally not involved in CML. Two main types of lymphocytes are **B-cells** and **T-cells**.

Major histocompatibility complex (MHC) = a group of 3 linked genes (MHC I, II and III) that code for cell surface antigens. The MHC antigens are used to determine compatibility of donors and recipient stem cells.

***Matched Related Donor (MRD)** = in the setting of CML, a stem cell donor whose stem cells match those of the related patient on six out of six (6/6) different antigens.

***MCR** = major cytogenetic response (see cytogenetic response).

Mcg (or µg) = microgram (1/1,000,000th of a gram) - a measurement of quantity of, say, drug dose.

MCH = Mean Corpuscular Hemoglobin or Mean Cell Hemoglobin (MCH = Hemoglobin x 10/RBC)

MCHC = Mean Corpuscular Hemoglobin Concentration (MCHC = Hemoglobin x 100/Hematocrit)

Mcl = microliter (or µL)

MCV = Mean Corpuscular Volume or Mean Cell Volume (MCV = Hematocrit x 10/RBC) - a measure of red blood cell volume.

Mg = milligram - 1/1000th of a gram

***Milestones** = the time point at which it is considered optimal to reach cytogenetic and molecular parameters during therapy (e.g. CCyR, MMR and CMR based on ELN and NCCN guidelines).

***Mini-transplant** = non-myeloablative stem cell transplant (mini-transplant) - a type of stem cell transplant in which the patient's marrow (myelo-) is not destroyed (ablated) prior to the transplant procedure.

***Minimal residual disease** = a term used mainly in the setting of stem cell transplantation for CML, where bcr-abl is still detectable by PCR, but cytogenetics are negative, or nearly so.

MIU, or MU = million units (in CML treatment, for example, dosages of interferon-alpha are measured in MU).

***Molecular remission (or response)** = defined as a negative PCR or other negative molecular test. Dr. Druker prefers to call this "PCR undetectable, or PCRU"

Mono = monocyte; a type of white blood cell.

***MPD** = myeloproliferative disorder

***MR** = molecular response, or molecular remission

***MMR** = major molecular response, or major molecular remission – defined as 0.01 on the IS or as a -3 log reduction.

***MRD** = Matched Related Donor or Minimum Residual Disease.

MU = Million units.

***MUD** = Matched Unrelated Donor (see matched related donor).

Mutation = in the context of CML, it means that there are additional changes in the genes creating additional mutations, not just the bcr-abl mutation.

***Myelofibrosis** = replacement of blood stem cells in the bone marrow with fibrous tissue. Myelofibrosis occurs as a complication of CML and of its treatments, especially interferon.

***Myeloid** = of or related to the bone marrow

***Myeloproliferative disorder (MPD)** = a family of diseases involving the over production of one or another marrow cell types. CML is a myeloproliferative disorder.

***NCCN = National Comprehensive Cancer Network; this American group has prepared guidelines in CML management to direct physician care with respect to CML; along with ELN guidelines, NCCN guidelines are considered to**

be the minimum standard of care for CML patients.

Neutrophils = the type of myeloid white blood cell which is most increased in CML. Also referred to as polys (polymorphonuclear leukocytes); granulocytes (though this term also includes other types of white cells, such as basophils and eosinophils); and neutrophils.

Nilotinib = generic name for the oral tyrosine kinase cancer inhibitor that targets bcr-abl, KIT, and platelet derived growth factor receptor (PDGFR). It is 80 times more potent than Gleevec.

NMDP = National Marrow Donor Program

***NMSCT** = non-myeloablative stem cell transplant (“mini-transplant”). Also called NST

***Non-myeloablative (as in non-myeloablative stem cell transplant): myelo** = marrow; ablative = destructive. So non-myeloablative stem cell transplant is one in which the patient’s marrow is not totally destroyed prior to receiving the donors stem cells.

NSAID = nonsteroidal anti inflammatory drugs - such as ibuprofen, naproxen, etc.

Neutropenia = an unusually low number of neutrophils

***NST** = another acronym for non-myeloablative stem cell transplant.

ONC = Oncologist

Oncologist = cancer specialist
(Oncos = cancer in Greek)

Oncogene = Any of a family of genes that normally encode proteins involved in cell growth or regulation (e.g., protein kinases, GTPases, nuclear proteins, growth factors) but that may foster malignant processes if mutated or activated by contact with retroviruses.

PAPs = Patient Assistance Programs

Patient Assistance Programs = programs created by pharmaceutical and medical supply manufacturers to help financially needy patients purchase their necessary medications and supplies.

***PB** = Peripheral (circulating) Blood

***PBPC** = Peripheral Blood Progenitor Cells

pCODR = pan Canadian Oncology Drug review; now falls under the auspices of CADTH.

***PCR** = polymerase chain reaction

***PCR test** = polymerase chain reaction test

***PCRU** = PCR Undetectable – a recent (and perhaps more accurate) term for molecular remission.

***PEG-IFN** = **pegylated** interferon: interferon (IFN) that has PEG

(PolyEthylene Glycol) molecules attached to it. PEG gives IFN a longer half-life in the body, and may reduce the drug's toxicity and increase its effectiveness.

***Ph** = Philadelphia Chromosome.

***Ph+ and Ph-** = refers to the presence and absence, respectively, of the Philadelphia chromosome in white blood cells of CML patients. The proportion of Ph+ to Ph- cells is used to track progress in treating the disease: anything less than you started with is called a Cytogenetic Response (CR); 35% or less Ph+ is a Major Cytogenetic Response (MCR), and 0% Ph+ is a Complete Cytogenetic Response (CCR).

***Philadelphia chromosome (Ph)** = is a term used to describe the abnormal appearance certain chromosomes (chromosome #22), in dividing white blood cells found in 95% of people who have CML. The Philadelphia chromosome results from a mutation that involves the swapping of genetic material between chromosome # 9 and chromosome #22 (see bcr-abl)

***Phillies** = abbreviation for philadelphia chromosome positive (Ph+) cells, coined by members of the YahooGroups CML list.

Pleural Effusion = abnormal amount of fluid around the lung

***Plts** = platelets

***Polys** = polymorphonuclear leukocytes (neutrophils)

***Polymerase Chain Reaction (PCR) test** = a very sensitive test which can be used to detect the presence of very low levels of specific genetic material (DNA). It is used to detect, and sometimes to quantify, bcr-abl in bone marrow cells of patients with CML. The most sensitive PCR tests can detect as few as one in 100,000,000 cells. PCR can use blood or bone marrow. For an explanation of how PCR works, see <http://www.scientific.org/tutorials/articles/riley/riley.html>

Prognosis = the likely course of a disease

Prognostic Factors = a clinical or biological factor that can be objectively measured. In the context of CML this relates to SOKAL score.

PROT = abbreviation for total protein in a blood sample

Protocol = a set of rules or guidelines to follow a particular treatment path. In the context of CML this can pertain to whether you take your TKI on a full or empty stomach

PT = Physical Therapy or Physical Therapist

***RBC** = red blood cells

RA = Rheumatoid Arthritis

***RAS Oncogene** = a mutated version of a gene on chromosome 17 that has been shown to be involved in more than half of all human cancers. It

works its mischief by inhibiting apoptosis, or normal programmed cell death.

RBCs = Blood Cells or Red blood cell count

RDW = Red cell distribution width (variation in red blood cell size; a high RDW is associated with a number of conditions including alcoholism and a disturbed bone marrow)

***Remission** = abatement or lessening in severity of the symptoms, signs and laboratory abnormalities of a disease. A not-very-specific term, especially as applied to CML. The term "response" is often preferred. Hematologic remission (response) means that the white cells in your blood are back within the normal range. HR says nothing about the proportion of phillies to normal cells. A cytogenetic remission (CR) means that you're getting some normal cells back. There are 3 levels of cytogenetic response: just plain cytogenetic response (CR); Major cytogenetic response (MCR); and complete cytogenetic response (CCR). A CR means a Ph+ less than you began with but more than 35%; major response means between 0% and 35% Phillies; and complete cytogenetic response means zero Phillies as measured by either conventional cytogenetics or FISH. Conventional cytogenetics looks at only 20-25 cells, whereas FISH looks at 400 to 500 cells, so FISH is theoretically more accurate. However, some labs have a problem with false positives with FISH, that is, they can read a cell as a Philly when it's really

not. FISH can be done on blood or bone marrow, while conventional cyto can be done only from bone marrow only.

***Molecular response (remission) (MR)** = Using the conventional qualitative PCR test, there's only one level of molecular response, that is, you either have it or you don't. This test is very sensitive, so if you're told you have a MR, it means you have less than 1 in 1,000,000 leukemic cells left in your marrow. Quantitative PCR can give an estimate of how many cells are left, but is not quite as sensitive; it can detect down to about one in 100,000 cells.

RN = registered nurse

Rx = prescription

***SCT** = stem cell transplant

Sib = sibling

Sx = symptoms

***Signal transduction inhibitor (STI)** = one of the most exciting types of molecules in cancer research, STIs inhibit enzymes that carry out the actions which make cancer cells behave as they do: multiplying too fast, living too long, invading other tissues, etc. Gleevec is an STI and was long known as STI 571.

***Sokal Score** = a prognostic score used in CML that calculates variable risks based on platelets and blasts percentage, age of patient and spleen size at diagnosis

***Sprycel** = The branded name of dasatinib, a TKI from Bristol Myers Squibb.

***Stem cell** = a progenitor, or "primitive" cell. Stem cells are ancestors of all the cell types in the body, including blood cell types. It is more accurate to speak of "hematopoietic (of blood origin) stem cells" when referring to the progenitor cells involved in leukemia.

***Stem Cell Transplant (SCT)** = previously known as bone marrow transplant or **BMT** (these terms and abbreviations are used interchangeably, but SCT is technically more correct) = a procedure in which the patient's bone marrow cells are replaced with a donor's marrow cells in hopes of curing a disease. There are two different types of SCT: conventional and non-myeloablative.

***STI** = signal transduction inhibitor

***STI-571** = chemical name for Gleevec (the generic name is imatinib).

Synergistic = refers to the general condition where the whole is greater than the sum of the parts. When two drugs work together synergistically, it means they have more of an effect than one could predict merely by adding their two effects together; compare to additive.

***T153I** = a particular mutation which, when present in cells carrying the bcr-abl oncogene in

sufficient proportions, renders CML resistant to first and second generation TKIs.

***Tasigna** = the branded name of nilotinib, a TKI from Novartis.

TP = total protein (a measure of the amount of protein in the serum; used to assess nutritional status and the functioning of various organs, especially of the digestive system).

***Translocation** = where a bit of genetic material from one chromosome (humans have a total of 46 chromosomes) is swapped with a bit from another chromosome. In CML, a piece (called “abl”) from chromosome # 9 is swapped onto a segment (called “bcr”) on chromosome #22 to create the “bcr-abl oncogene” that causes this disease.

***TFR** = treatment free remission pertains to CML patients who continue to have a complete molecular response after treatment discontinuance. Patients in TFR are followed very closely with monthly PCR tests at the beginning. Patients in TFR must be followed up in a clinical setting.

TSH = Thyroid Stimulating Hormone - a measure of thyroid function (when the TSH is high, thyroid function is generally low, and vice versa)

***Tyrosine Kinase** = enzymes involved in many kinds of communication within cells. The bcr-abl gene codes for an abnormal tyrosine kinase that causes much of the mischief in CML.

ul = microliter (should be written μ l, but sometimes the μ symbol gets translated to an “m” by e-mail programs)

***WBC** = white blood count – the number of white blood cells in a sample of blood.

XX = traditionally used to designate to Female chromosome complement

XY = traditionally used to designate the Male chromosome complement