

Accrual: The process of enrolling patients in a clinical trial (research study), or the number of patients already enrolled in a trial or anticipated to enroll in a trial.

Acute: In reference to disease, of sudden onset or of short duration, rapidly progressive, and in need of immediate care.

Acute tubular necrosis (ATN): The death of tubular epithelial cells that form the renal tubules of the kidneys. ATN is a form of acute renal failure. Kidney function can be recovered when not all tubular cells are affected.

Adrenal glands: Glands located at the top of the kidneys that are chiefly responsible for releasing sex hormones and cortisol, a hormone that helps human beings respond to stress.

Adrenocortical steroid: Any of the steroidal hormones produced by the adrenal cortex (the outer part of the adrenal gland) or their synthetic (man-made) equivalents. Also known as adrenocorticoids, glucocorticosteroids, or corticosteroids.

Adverse event (AE): Also known as “adverse reaction” or “side effect.” See “**Side effects.**”

Aggresome: A collection (aggregation) of misfolded proteins in the cell, formed when the protein-degradation system of the cell is overwhelmed. Protein folding occurs when a chain of randomly coiled polypeptides (amino acids that are bonded together) folds into a characteristic three-dimensional structure. The sequence of amino acids in the peptide chain determines its final structure. Unchecked misfolding of proteins results in such diseases as Alzheimer’s, Parkinson’s, and amyloidosis.

Albumin (ALB): Simple water-soluble protein found in blood serum. Production of albumin is inhibited by interleukin-6 when myeloma is very active.

Albuminuria: The presence of an excess of serum albumin in the urine.

Alkylating agent: A chemotherapeutic agent such as melphalan or cyclophosphamide. Alkylating refers to the way in which these agents cross-link the DNA of myeloma cells and block cell division.

Allergen: A substance that causes an allergic reaction.

Allogeneic: See “**Transplant.**”

Amyloid light-chain amyloidosis (AL amyloidosis): AL amyloidosis is a condition in which myeloma light chains crosslink with each other in a beta-pleated fashion and then are deposited in tissues and organs throughout the body, such as the heart, nerves, and kidneys, rather than being excreted by the kidneys. This condition is also known as primary amyloidosis.

Amyloidosis: A group of systemic diseases characterized by the deposition of amyloid protein in various organs and/or tissues. One type (AL amyloidosis) is related to multiple myeloma; other types include hereditary amyloidosis, AA amyloidosis, wild-type ATTR amyloidosis, ALECT2 amyloidosis, and AB2M amyloidosis. See “**Amyloid light-chain amyloidosis (AL amyloidosis).**”

Analgesic: Any drug that relieves pain. Aspirin and acetaminophen are mild analgesics.

Analog: A chemical compound that is structurally similar to another but differs slightly in composition.

Anemia: A decrease in hemoglobin, a protein which is contained in red blood cells and carries oxygen to the body's tissues and organs. Anemia is usually defined as hemoglobin below 10 g/dL, and/or as a decrease of ≥ 2 g/dL from the normal level for an individual. Over 13–14 g/dL is considered normal.

Anesthesia: Loss of feeling or awareness. Local anesthesia causes loss of feeling in a part of the body. General anesthesia induces loss of sensation in the entire body that can cause loss of consciousness.

Angiogenesis: Blood vessel formation, which usually accompanies the growth of malignant tissue, including myeloma.

Angiogenesis inhibitors: Compounds that reduce new blood vessel formation associated with cancer cell growth.

Ankylosing spondylitis: A form of chronic inflammation of the spine and the sacroiliac joints.

Anti-emetic agent: A drug that prevents or controls nausea and vomiting.

Anti-inflammatory: A substance or treatment that reduces inflammation or swelling.

Antibiotics: Drugs used to treat bacterial infections.

Antibody: A protein produced by white blood cells called plasma cells in response to an antigen that enters the body. The medical term for antibody is "immunoglobulin."

Antifungal agent: A drug used to treat fungal infections.

Antigen: Any foreign substance (such as bacteria, a virus, toxin, or tumor) that causes the immune system to produce natural antibodies.

Antihistamine: A drug that acts against histamine, a powerful and highly irritant agent released in the body after contact with certain allergens.

Antineoplastic agent: A drug that prevents, kills, or blocks the growth and spread of cancer cells.

Apheresis: Sometimes called leukapheresis, apheresis is a procedure in which blood is taken from a patient or donor and the portion of the blood containing plasma, white blood cells, and platelets is separated from red blood cells. The red blood cells are transfused back into the patient or donor. The portion containing white blood cells includes the rare blood cell-making (hematopoietic) stem cells.

Appendicular skeleton: The part of the skeleton consisting of the appendages: the bones of the arms and legs.

Apoptosis: A normal cellular process leading to the death of a cell.

Arrhythmia: An arrhythmia is a problem with the rate or rhythm of the heartbeat. It means that the heart beats too quickly, too slowly, or with an irregular pattern. Arrhythmias are caused by problems with the heart's electrical conduction system.

Aspiration: The process of removing fluid or tissue, or both, from a specific area such as the bone marrow.

Asthenia: A condition in which the body lacks or has lost strength either as a whole or in any of its parts.

Asymptomatic myeloma: Myeloma that presents no signs or symptoms of disease; early-stage myeloma. Also called “**Smoldering multiple myeloma (SMM).**”

Autocrine: The process whereby a growth factor is produced by a cell, such as a myeloma cell, while also stimulating the cell to grow, creating a positive feedback loop. Also see “**Paracrine.**”

Autoimmune disease: A condition that occurs when the immune system abnormally creates antibodies to a normal body part. Common autoimmune diseases include type 1 diabetes, celiac disease, inflammatory bowel disease, multiple sclerosis, psoriasis, and rheumatoid arthritis.

Autologous: See “**Transplant.**”

Axial skeleton: Consists of spine, pelvis, ribs, and skull. The axial skeleton is most commonly affected by myeloma, along with the upper ends of the long bones of the arms and legs.

B cells (B lymphocytes): White blood cells that are part of the natural immune system. Some B cells develop into plasma cells in the bone marrow and are the source of antibodies.

Bacteria: Single-celled microorganisms that can exist either as independent (free-living) organisms or as parasites (dependent on another organism for life). The plural of bacterium.

Basophil: A type of white blood cell. Basophils help prevent blood from clotting and release histamine during allergic reactions. Neutrophils, basophils, and eosinophils are all types of white blood cells known as granulocytes.

Bence-Jones myeloma: Myeloma characterized by the presence of Bence-Jones protein, an abnormal protein in urine made up of free kappa or lambda light chains.

Bence-Jones protein: A myeloma monoclonal protein. The protein is composed of either free kappa or free lambda light chains. Because of their small size, Bence-Jones light chains can be filtered through the kidneys and pass into the urine. The amount of Bence-Jones protein in the urine is expressed in terms of grams per 24 hours. Normally, a very small amount of protein (< 0.1 g/24 h) can be present in the urine, but this is albumin rather than Bence-Jones protein. The presence of any Bence-Jones protein in the urine is abnormal. Myeloma protein heavy chains are too large to be filtered through the kidneys.

Benign: Not cancerous; does not invade nearby tissue or spread to other parts of the body.

Beta-2 microglobulin (also called β 2-microglobulin, β ₂M, or β 2M): A small protein found in the blood. High levels occur in patients with active myeloma. Low or normal levels occur in patients with early myeloma and/or inactive disease. Approximately 10% of patients have myeloma that does not produce β 2M. At the time of relapse, β 2M can increase before there is any change in the myeloma protein level. Factors such as viral infection can sometimes produce elevated serum β 2M levels.

Biopsy: The removal of a sample of tissue for microscopic examination to aid in diagnosis.

Bisphosphonate: A type of drug that protects against osteoclast activity (bone breakdown) and binds to the surface of bone where it is being resorbed or destroyed.

Blood cells: Minute structures produced in the bone marrow; they include red blood cells, white blood cells, and platelets.

Blood count: The number of red blood cells, white blood cells, and platelets in a sample of blood.

Blood glucose: A type of blood sugar that the body produces from the food in our diet. Glucose is transported via the bloodstream to all the cells in our body. It is our primary source of energy. Certain medications can affect our blood glucose levels. There are tests that measure and monitor blood glucose.

Blood stem cells: Stem cells in the bone marrow that are responsible for making all the blood cells. The medical term is “hematopoietic” stem cells.

Blood urea nitrogen (BUN): A measure of the urea level in the blood. Urea is excreted by the kidneys. BUN is a laboratory blood test to assess kidney function. Diseases such as myeloma, which can compromise kidney function, frequently lead to increased levels of BUN in the bloodstream.

Bone marrow: The soft, spongy tissue in the center of bones that produces white blood cells, red blood cells, and platelets. This is the tissue within which abnormal plasma cells build up when myeloma is growing.

Bone marrow aspiration: The removal, by a needle, of a sample of fluid and cells from the bone marrow for examination under a microscope.

Bone marrow biopsy: The removal, by a hollow-bore needle, of a sample of tissue from the bone. The cells are checked to see whether they are cancerous. If cancerous plasma cells are found,

the pathologist estimates how much of the bone marrow is affected. Bone marrow biopsy is usually done at the same time as bone marrow aspiration.

Bone marrow transplant: See “**Transplant.**”

Bone-modifying agent: The group of drugs that includes denosumab (Xgeva®), zoledronic acid (Zometa®), and pamidronate (Aredia®). These agents are used to prevent bone breakdown in myeloma and some other cancers.

Bone remodeling: The normal coordination (coupling) between osteoclast cells (which resorb or destroy bone) and osteoblast cells (which create new bone matrix) to maintain a balanced state of bone production and destruction.

C-reactive protein (CRP): A protein made in the liver that increases in amount when there is inflammation throughout the body.

Calcium: A mineral found mainly in the hard part of bone matrix (hydroxyapatite). If produced or released in excess, it can build up in the bloodstream. See “**Hypercalcemia.**”

Cancer: A term for diseases in which malignant cells divide without control. Cancer cells can invade nearby tissues and spread through the bloodstream and lymphatic system to other parts of the body.

Carcinogen: Any substance or agent that produces or stimulates cancer growth.

CAR T cell (Chimeric Antigen Receptor T cell) therapy: An experimental immunologic treatment approach for hematologic cancers through which patients’ own immune cells are engineered

to recognize and attack their tumors. Clinical trial results have been mixed, with deep and prolonged responses in some patients with low disease burden, but at the risk of serious immune system side effects. See “**Cytokine storm**” and “**Response or remission.**”

Catheter: A tube that is placed in a blood vessel to provide a pathway for drugs or nutrients. A central venous catheter (CVC) is special tubing that is surgically inserted into a large vein near the heart and exits from the chest or abdomen. The catheter allows medications, fluids, or blood products to be given and blood samples to be taken.

CD34+: The CD34-positive laboratory marker on the surface of hematopoietic stem cells is used to select and to quantify the stem cells. A specified minimum number of CD34+ stem cells is required to safely support a transplant procedure.

Cell: The basic unit of any living organism. Millions of microscopic cells comprise each organ and tissue in the body.

Cell differentiation: The process during which young, immature (unspecialized) cells develop individual characteristics and reach their mature (specialized) form and function.

Cell proliferation: An increase in the number of cells as a result of cell growth and cell division.

Chemotherapy: Any drugs used to kill cancer cells. “Combination chemotherapy” uses more than one drug in a cancer treatment regimen.

Chromatid: One of two identical chromosomal strands into which a chromosome splits longitudinally before cell division.

Chromosome: A strand of DNA and proteins in the nucleus of a cell. Chromosomes contain genes and function in the transmission of genetic information. Normally, human cells contain 46 chromosomes (23 pairs).

Chronic: Persisting over a long period of time.

Clinical: Involving direct observation or examination of a patient.

Clinical trial: A research study of new treatment that involves patients. Each study is designed to find better ways to prevent, detect, diagnose, or treat cancer and to answer scientific questions.

- *Control group* – The arm of a randomized clinical trial that receives the standard treatment or placebo (no treatment).
- *Experimental group* – The arm of a randomized trial that gets the new treatment.
- *Randomized clinical trial* – A research study in which subjects are randomly assigned to receive a particular treatment or not.
- *Arm* – One of the treatment groups of a randomized trial. The majority of randomized trials have two, but some have more.
- *End point* – The goal of the trial; what a clinical trial is trying to measure or find out. Typical end points include measurements of toxicity, response rate, and survival.
- *Double blind* – Aspect of a randomized trial in which neither the participant nor the investigator knows the arm of the trial to which the patient is assigned. The purpose is to eliminate any bias in the reporting of results.

- *Phase I trial* – A trial designed to determine the maximum-tolerated dose (MTD) of a new drug or a new combination of drugs. It is usually the first human testing of a new treatment, although in phase I trials of combination therapies, the individual elements may already have been well tested. Patients in phase I trials generally have advanced cancer that is refractory to all standard treatment. In a typical phase I trial, successive groups (“cohorts”) of 3 to 6 patients are given the treatment. All patients in a cohort get the same dose. The first cohort typically gets a very low dose, and the dose is raised in each subsequent cohort until a set number of patients experience dose-limiting toxicity (DLT). The dose level used for the previous cohort is then taken to be the MTD. This dose is then used in a phase II trial.

- *Phase II trial* – A trial designed to determine the response rate of a new therapy that has already been tested in phase I trials. Typically, 14 to 50 patients with one type of cancer are treated to see how many have a response. Patients are usually required to have advanced cancer that is refractory to any standard treatment. In addition, patients must have measurable disease. If results from a phase II trial are promising enough, the treatment may then be tested in a phase III trial. If the results are obviously much better than the standard treatment, then it may not be necessary to do a phase III trial, and the treatment may be approved based on phase II trial results.

- *Phase III trial* – A trial designed to compare two or more treatments for a given type and stage of cancer. The end point of a phase III trial is usually survival or disease-free survival. Phase III trials are usually randomized, so patients don’t choose which treatment they receive. A typical phase III trial has 50 to thousands of patients. Some phase III trials compare a new treatment that has had good results in phase II trials with an

older, well known, standard treatment. Other phase III trials compare treatments that are already in common use. Some treatments in phase III trials may be available outside the clinical trial setting.

- *Phase IV trial* – Even after a drug has been approved by the United States Food and Drug Administration (FDA) for use in a particular indication, there may be need for additional studies. Phase IV clinical trials may be required by regulatory authorities or may be undertaken by the sponsoring company for a variety of reasons. For example, safety surveillance is designed to detect any rare or long-term side effects over a larger patient population and longer time period than was possible during the phase I-III clinical trials.

Colony-stimulating factor (CSF): Proteins that stimulate the development and growth of blood cells. Neupogen® (filgrastim), Neulasta® (pegfilgrastim), and Leukine® (sargramostim) are colony-stimulating factors that are used to mobilize stem cells from the bone marrow into the bloodstream prior to apheresis. These may also be used after the transplant to hasten blood count recovery, or to treat low white cell count caused by therapy.

Complement proteins: A complex system of more than 30 proteins that act in concert to help eliminate infectious microorganisms. The complement system causes the lysis (bursting) of foreign and infected cells, the phagocytosis (ingestion) of foreign particles and cell debris, and the inflammation of surrounding tissue.

Complete response: See “Response or remission.”

Computerized axial tomography (CAT or CT) scan: A test using computerized X-rays to create three-dimensional images of organs

and structures inside the body. In myeloma, used to detect small areas of bone damage or soft tissue involvement.

Conditioning: A treatment regimen given to a patient to destroy cancer cells prior to stem cell transplant. The most common conditioning regimen given to myeloma patients is 200 mg of melphalan per square meter of body mass.

Congestive heart failure: A condition that occurs when the heart's pumping function is weakened, causing a series of events that result in the body retaining fluid and salt. If fluid builds up in the arms, legs, feet, ankles, lungs, or other organs, the body becomes congested.

Consolidation therapy: Treatment given for a short duration (i.e., 2 to 4 cycles), usually with the same regimen used for induction therapy, following high-dose therapy with autologous stem cell rescue.

Corticosteroid: A group of natural and synthetic analogues of the hormones secreted by the pituitary gland. These include the glucocorticoids used in the treatment of myeloma such as dexamethasone, prednisone, and methylprednisolone. Glucocorticoids have multiple effects and are used for a large number of conditions.

CRAB criteria: An elevated level of **C**alcium in the blood, **R**enal damage, **A**nemia or low red blood cell count, and **B**one damage are criteria used to diagnose myeloma along with "**Myeloma-defining event (MDE).**"

Creatinine: A small chemical compound normally excreted by the kidneys into the urine. If the kidneys are damaged, the serum level

of creatinine builds up, resulting in an elevated serum creatinine. The serum creatinine test is used to measure kidney function.

CT scan: See "**Computerized axial tomography.**"

Cyst: An accumulation of fluid or semi-solid material within a sac. A cyst can occur in any organ or tissue.

Cytokine: Cytokines are proteins secreted by cells which can stimulate or inhibit growth/activity in other cells. Cytokines are produced locally (for myeloma, in the bone marrow) and circulate in the bloodstream. Cytokines are normally released in response to infection.

Cytokine storm: A potentially fatal, uncontrolled immune reaction in which chemical messengers called cytokines become highly elevated and trigger an overwhelming immune system response. A cytokine storm can seriously damage body tissues and organs. See "**Cytokine.**"

Cytoplasm: The jellylike material inside the membrane of a human cell, excluding the cell's nucleus.

Deep vein thrombosis (DVT): A condition that occurs when a blood clot (thrombus) forms in one or more of the deep veins in the body, usually in the legs. DVT can cause leg pain or swelling, but can occur without any symptoms.

Deoxyribonucleic acid (DNA): The substance of heredity; a large molecule that carries the genetic information that cells need to replicate and to produce all components of the body.

Dexamethasone: A powerful corticosteroid given alone or with other drugs.

Diagnosis: The process of identifying a disease by its signs, symptoms, and test results.

Dialysis: The process of removing water, excess salt, and toxins from the blood when a person's kidneys are no longer capable of doing so. The two types of dialysis are hemodialysis, which uses a machine, and peritoneal dialysis, which uses the lining of the abdomen (the peritoneum), to filter the blood.

Disease-free survival: The length of time the patient survives after treatment without any detectable cancer. This is also called "**Progression-free survival (PFS).**"

Disease progression: See "**Progressive disease.**"

Disease stabilization: When cancer stops growing and remains stable.

Dose-limiting toxicity (DLT): Side effects severe enough to prevent giving more of the treatment.

Down-regulation: The process by which a cell decreases the quantity of a cellular component, such as RNA or protein, in response to an external variable.

Drug resistance: When a drug becomes less effective at curing a disease or condition. In treating cancer, the cancer cells may become resistant to therapy via a number of tools involving genes, proteins, and altered pathways to ensure their survival.

Dual-energy X-ray absorptiometry (DXA, previously DEXA) study: An enhanced form of X-ray technology used to measure bone loss.

Eastern Cooperative Oncology Group (ECOG) status: See "**Performance Status.**"

Edema: Swelling; an abnormal accumulation of fluid in part of the body.

Efficacy: In cancer research, "efficacy" refers to whether the treatment is effective.

Electrolytes: Minerals in your blood and other body fluids that carry an electrical charge and are essential for life. Electrolytes include sodium, potassium, calcium, magnesium, chloride, phosphate, and bicarbonate. They affect the amount of water in the body, the acidity of the blood (pH), nerve and muscle function (including the heart), and other important processes.

Electrophoresis: A laboratory test in which a patient's serum (blood) or urine proteins are subjected to separation according to their size and electrical charge. For myeloma patients, electrophoresis of the blood or urine allows both the calculation of the amount of myeloma protein via serum or urine electrophoresis (SPEP or UPEP), as well as the identification of the type of M-spike for each patient (immunoelectrophoresis, IFE). Electrophoresis is used as a tool both for diagnosis and for monitoring.

Engraftment: The process by which stem cells in the transplanted bone marrow or peripheral blood migrate to the patient's bone marrow and begin to grow and produce new white blood cells, red blood cells, and platelets.

Enzyme: A protein molecule manufactured by a cell. An enzyme acts as a catalyst that increases the rate of a specific biochemical reaction in the body.

Erythrocytes: Red blood cells (RBCs). RBCs carry oxygen to body cells and carbon dioxide away from body cells.

Erythropoiesis: The formation of new red blood cells.

Erythropoietin: A hormone produced by the kidneys that stimulates the production of red blood cells. Myeloma patients with damaged kidneys don't produce enough erythropoietin and can become anemic. Injections with synthetic erythropoietin can be helpful. Blood transfusion is another alternative treatment for anemia, especially in an emergency. Synthetic erythropoietin can be used as a supportive therapy during anti-myeloma treatment to avoid anemia.

Esophagitis: Inflammation of the esophagus, which is the tube that transports food from the mouth to the stomach.

Extramedullary plasmacytoma: A tumor made up of monoclonal plasma cells that is found in soft tissue outside of the bone marrow and separate from bone.

Extravasation: Passage or escape of a drug (such as intravenous chemotherapy) or bone cement (during vertebroplasty or kyphoplasty) into surrounding tissue.

Facet joint: The connection between the bones of the spine.

Fluorescence in situ hybridization (FISH): A procedure that allows researchers to locate the positions of specific DNA sequences on chromosomes.

Flow cytometry: A technology used in cell counting, cell sorting, and biomarker detection by suspending cells in a stream of fluid and passing them through a laser.

Focal lesion: An area of irregular cells seen in the bone marrow on MRI (magnetic resonance imaging) study. In order to be considered diagnostic of myeloma, there must be at least two focal lesions that are at least 5 mm in size.

Free light chain: An immunoglobulin (antibody) light chain is the smaller of two units that make up an antibody. There are two types of light chain: kappa and lambda. A light chain may be bound to a heavy chain or it may be unbound, or free. Free light chains circulate in the blood and are small enough to pass into the kidneys, where they may be filtered out into the urine or may stick together and block up the kidney's tubules.

Frontline therapy: A general term for the initial treatment used in an effort to achieve response in a newly diagnosed myeloma patient. Also see "**Induction therapy**" and "**Response.**"

Gastrointestinal (GI) side effects: Side effects of medication that affect the digestive tract, such as nausea, vomiting, diarrhea, and constipation.

Gene: A specific sequence of DNA coding for a particular protein.

Gene therapy: Treatment that alters the activity of genes. This usually implies adding or removing a gene or genes.

Generic drug name: A generic drug name refers to the chemical makeup of a drug rather than its brand name. A generic name is given to a drug before it is approved and given a brand name. After a drug goes off patent, other manufacturers may make generic versions of the drug. For example: ibuprofen is the generic name for drugs brand-named Advil® and Motrin®.

Genetic: Relating to genes or heredity in all living organisms. The biological process by which characteristics are passed from parent to offspring through DNA in the genes.

Glaucoma: A disease associated with the build-up of pressure inside the eye that, if untreated, can result in vision loss and blindness.

Glycoproteins: Proteins on the outer surface of cells that have sugars (carbohydrates) attached to them. They function as receptor sites where other molecules may attach to the cell.

Graft-versus-host disease (GVHD): An immune-related reaction of donated tissue against the recipient's own tissue.

Granulocyte: A type of white blood cell that kills bacteria. Neutrophils, eosinophils, and basophils are all types of granulocytes.

Growth factors: Drugs that stimulate blood stem cells to both grow and be released into the bloodstream.

Heavy chain: An immunoglobulin heavy chain is the larger of two units of an antibody (immunoglobulin). There are five types of heavy chains: G, A, D, E, and M. The heavy chains most commonly made by myeloma cells are G and A.

Hematocrit (Hct): The percentage of red blood cells in the blood. A low hematocrit measurement indicates anemia.

Hematologic: Relating to the blood, originating in the blood, disseminated through the bloodstream.

Hematologic malignancy: A cancer of the bone marrow or blood cells.

Hematologist: A doctor who specializes in the problems of blood and bone marrow.

Hemoglobin: A protein in red blood cells that carries oxygen.

Herpes simplex: A common virus that causes sores, often seen around the mouth, commonly called cold sores.

Herpes zoster: The virus that causes chicken pox. When reactivated, the herpes zoster infection frequently affects nerves. This condition is also called "Shingles."

High-risk myeloma: According to the International Myeloma Working Group (IMWG) consensus on risk stratification in myeloma, markers have been identified that can be applied to more than 90% of all myeloma patients to define high-risk myeloma: ISS stage II/III and the presence of either the t(4;14) or 17p13 genetic mutations by FISH testing.

Hormones: Chemicals produced by various glands that regulate the actions of certain cells or organs in the body.

Human leukocyte antigen (HLA) test: A blood test used to match a blood, bone marrow, or organ donor to a recipient for transfusion or transplant.

Hydroxyapatite: A compound that helps form bones and gives them rigidity and strength.

Hypercalcemia: A higher than normal level of calcium in the blood. In myeloma patients, it usually results from bone breakdown with release of calcium from the bone into the bloodstream. This condition can cause a number of symptoms, including loss of

appetite, nausea, thirst, fatigue, muscle weakness, restlessness, and confusion. See “**Calcium.**”

Hypersensitivity reaction: Undesirable reactions, sometimes in response to a medication, produced by the normal immune system, including allergies and autoimmunity. These reactions may be damaging, uncomfortable, or fatal.

Hypertension: A chronic medical condition in which the blood pressure in the arteries is elevated. Also known as high blood pressure.

Hyposecretory: Low- or non-secreting disease. Also known as oligosecretory.

IgG, IgA: The two most common types of myeloma. The G and the A refer to the type of heavy chain protein produced by the myeloma cells. The myeloma protein, which is an immunoglobulin, consists of two heavy chains, (for example, of a G type) combined with two light chains, which are either kappa or lambda. The terms “heavy” and “light” refer to the size or molecular weight of the protein, with the heavy chains being larger than the light chains.

IgD, IgE: Two types of myeloma that occur less frequently. See “**IgG, IgA.**”

IgM: Usually associated with Waldenström’s macroglobulinemia. In rare cases, IgM can be a type of myeloma.

Immune system: The body’s defense system from pathogens and foreign substances destroys infected and malignant cells, and removes cellular debris. The immune system includes white blood cells and organs and tissues of the lymphatic system.

Immunoassay: Test used in the study of biological systems by tracking different proteins, hormones, and antibodies.

Immunoassays rely on the inherent ability of an antibody to bind to the specific structure of a molecule. Because antibodies are developed to the specific three-dimensional structure of an antigen, they are highly specific and will bind only to that structure. ELISA (enzyme-linked immunosorbent assay) is a commonly used test to detect antibodies in the blood.

Immunodeficiency: A lowering of the body’s ability to fight off infection and disease.

Immunofixation electrophoresis (IFE): An immunologic test of the serum or urine used to identify proteins. For myeloma patients, it enables the doctor to identify the M-protein type (IgG, IgA, kappa, or lambda). The most sensitive routine immunostaining technique, it identifies the exact heavy- and light-chain type of M-protein.

Immunofluorescence: This test uses the specificity of antibodies to their antigen to direct fluorescent dyes (fluorophores) to specific targets within a cell, and therefore allows visualization of the distribution of the target molecule through the sample.

Immunoglobulin (Ig): A protein produced by plasma cells; an essential part of the body’s immune system. Immunoglobulins attach to foreign substances (antigens) and assist in destroying them. The classes (also called isotypes) of immunoglobulins are IgG, IgA, IgD, IgE, and IgM. The non-medical word for immunoglobulin is “antibody.”

Immunohistochemistry (IHC): Immunohistochemistry refers to the process of detecting antigens in cells of a tissue section by exploiting the principle of antibodies binding specifically to antigens.

Immunohistochemical staining is widely used in the diagnosis of abnormal cells, such as those found in cancerous tumors.

Immunomodulatory drug: An agent that affects, enhances, or suppresses the immune system. Sometimes called an IMiD[®] compound.

Immunosuppression: Weakening of the immune system that causes a lowered ability to fight infection and disease. Immunosuppression may occur both from the effect of myeloma on the immune system and from treatments for myeloma.

Immunotherapy: Treatment that enhances the body's natural defenses to fight cancer. Also called biological therapy.

Incidence: The number of new cases of a disease diagnosed each year.

Induction therapy: A specific term used for the initial treatment given to a patient in preparation for an autologous stem cell transplant (ASCT). Also see “**Frontline therapy**” and “**Line of therapy.**”

Inflammatory: Relating to inflammation, a protective response of the body against injury or disease.

Informed consent: The process that requires a doctor to give a patient enough information about a proposed procedure for the patient to make an informed decision about whether or not to undergo the procedure or planned strategy. The doctor must, in addition to explaining all procedures, address the issues of risks, benefits, alternatives, and potential costs.

Infusion: Delivering fluids or medications into the bloodstream over a period of time.

Infusion pump: A device that delivers measured amounts of fluids or medications into the bloodstream over a period of time.

Infusion reaction: An allergic or cytokine-related response to an intravenously administered cancer treatment.

Inhibit: To stop something or hold it in check.

Injection: The use of a syringe and needle to introduce a medication into the body.

Interferon: A naturally produced hormone (cytokine) released by the body in response to infection or disease that stimulates the growth of certain disease-fighting blood cells in the immune system. Interferon can be artificially produced by genetic engineering techniques and used as a form of immunotherapy.

Interleukin: A naturally produced chemical released by the body, or a substance used in biological therapy. Interleukins stimulate the growth and activities of certain kinds of white blood cells. Interleukin-2 (IL-2) is a type of biological response modifier that stimulates the growth of certain blood cells in the immune system that can fight some types of cancer. Interleukin-6 (IL-6) is a cytokine that is a potent stimulus to osteoclast and plasma cell growth.

Interventional radiology: The branch of radiology concerned with providing diagnosis and treatment of disease by a variety of procedures performed through the skin under the guidance of radiologic imaging.

Intravenous (IV): Administered into a vein.

Ischemic events: An event caused by an inadequate supply of blood to an organ or tissues, such as from an obstructed blood flow. Myocardial ischemia occurs when blood supply to the heart is reduced, preventing it from receiving enough oxygen. This can cause damage to the heart muscle.

Kyphoplasty: The injection of liquid cement into damaged bone using a balloon technique. This procedure may provide acute pain relief and improvement in structural integrity of collapsed vertebrae or other damaged bones.

Kyphosis: An exaggeration of the normal curve of the spine, sometimes referred to as a “hunchback” or “dowager’s hump.”

Lactate dehydrogenase (LDH): An energy-producing enzyme that is present in almost all of the tissues in the body. LDH levels in the bloodstream rise in response to cell damage. LDH may be used to monitor myeloma activity.

Lesion: An area of abnormal tissue; a lump or abscess that may be caused by injury or disease, such as cancer. In myeloma, “lesion” can refer to a plasmacytoma or a hole in the bone.

Leukocytes: Cells that help the body fight infections and other diseases. Also called white blood cells (WBCs).

Leukopenia: A low number of white blood cells.

Light chain: An immunoglobulin light chain is the smaller of two units of an antibody (immunoglobulin). The light chains are bound by chemical bonds to the ends of the heavy chains, but we make extra light chains that enter the bloodstream. These are called “free light chains.” There are two types of light chains: kappa and lambda.

Light chain deposition disease: A type of monoclonal gammopathy that is characterized by deposition of immunoglobulin light chains in various organs, most frequently in the kidneys.

Light Chain Escape: An increase of free light chains at the time of relapse without corresponding increase of the intact monoclonal immunoglobulin.

Line of therapy: A term used to calculate the number of therapies a patient has received. Induction therapy + an autologous stem cell transplant (ASCT) is considered a single line of therapy. See “**Induction therapy.**”

Lupus: Systemic lupus erythematosus (SLE) is a chronic inflammatory autoimmune disorder that can affect the skin, joints, kidneys, and other organs.

Lymphocytes: B cells, T cells, and natural killer (NK) cells, which together constitute 30% of white blood cells. B lymphocytes and T lymphocytes are responsible for the adaptive immune response, which enables immune system cells to attach to specific antigens on the cell surfaces of infectious organisms, tumors, and other foreign substances.

Lymphocytopenia: Low levels of B cells, T cells, and natural killer (NK) cells.

Lymphopenia: Low levels of B cells, T cells, and natural killer (NK) cells.

Lytic (lysis): Dissolution or destruction of cells or tissues.

Lytic lesion: The damaged area of a bone that shows up as a dark spot on an X-ray when at least 30% of the healthy bone in any one

area is eaten away. Lytic lesions look like holes in the bone and are evidence that the bone is being weakened.

Macrophage: A macrophage is an immune system cell whose job it is to engulf and devour any cell (including a cancer cell) that does not have proteins on its surface that identify it as a healthy body cell.

Magnetic resonance imaging (MRI): A diagnostic imaging test that uses magnetic fields and radio waves, not ionizing radiation, to produce detailed two- or three-dimensional images of organs and structures inside the body. MRI gives very fine resolution of soft tissues, especially encroachments on the spinal cord, but is less accurate for bone lesions.

Maintenance therapy: Drugs given to patients in remission to delay or prevent a relapse.

Malignant: Cancerous; capable of invading nearby tissue and spreading to other parts of the body.

Matched unrelated donor (MUD) transplant: See “Transplant.”

Maximum-tolerated dose (MTD): The highest dose of a treatment that most people can safely withstand.

Median: The middle number or the mean of the two central numbers in a series of numbers. For example, “median progression-free survival (PFS)” means that half the patients had remissions that were shorter than the median PFS, and half the patients had remissions that were longer than the median PFS.

Melanoma: A cancer of the pigment-forming cells of the skin or the retina of the eye. Not associated with myeloma despite the similar-sounding name.

Meta-analysis: An analysis that combines, or pools, the data from multiple scientific studies.

Metastasize: To spread from one part of the body to another. When cancer cells metastasize and form secondary tumors, the cells in the metastatic tumor are like those in the original (primary) tumor. This term is commonly used to describe a disease process in solid tumors (e.g., breast, prostate) and not in myeloma, which is a blood-related cancer.

Minimal residual disease (MRD): The presence of residual tumor cells after treatment has been completed and complete remission (CR) has been attained. Even patients who have attained a stringent complete response (sCR) may have MRD. Very sensitive new testing methods are now able to detect 1 myeloma cell among 1,000,000 sampled cells in blood or bone marrow.

Mobilizing agent: An agent injected into a patient or donor to trigger the release of bone marrow stem cells into the bloodstream.

Molecule: The smallest particle of a substance that retains all the properties of the substance. A molecule is an electrically neutral group composed of two or more atoms held together by chemical bonds.

Monoclonal: A clone or duplicate of a single cell. Myeloma cells are derived from a “monoclonal,” a single malignant plasma cell in the bone marrow. The type of myeloma protein produced is also monoclonal, a single form rather than many forms (polyclonal). The

important practical aspect of a monoclonal protein is that it shows up as a sharp spike (M-spike) on the protein electrophoresis test.

Monoclonal antibody: An antibody manufactured in a lab rather than produced in the human body. Monoclonal antibodies are specifically designed to find and bind to cancer cells and/or immune system cells for diagnostic or treatment purposes. Monoclonal antibodies can be used alone, or they can be used to deliver drugs, toxins, or radioactive material directly to tumor cells.

Monoclonal gammopathy of undetermined significance (MGUS): A category of plasma cell disorder characterized by comparatively low levels of monoclonal protein in the blood and/or urine. Bone marrow plasma cell levels are low (<10%). Myeloma-related symptoms (i.e., anemia, renal failure, hypercalcemia, and lytic lesions) are absent.

Monoclonal protein (myeloma protein, M-protein, M-spike): An abnormal protein produced by myeloma cells that accumulates in and damages bone and bone marrow. Antibodies or parts of antibodies found in unusually large amounts in the blood or urine of myeloma patients. A monoclonal spike (M-Spike), the sharp pattern that occurs on protein electrophoresis, is the telltale indicator of M-protein in the blood, a marker for the activity of myeloma cells. See “**Monoclonal.**”

Monocyte: A type of white blood cell found in the circulation. Also called a macrophage when present in tissues.

Multi-drug resistance (MDR): A resistance to standard treatment. The resistance is caused by a buildup of P-glycoprotein in the outer cell membrane of the myeloma cells. This results in drugs being kicked back out of the myeloma cell instead of building up and eventually killing it.

Multiple myeloma: A cancer of the bone marrow plasma cells, white blood cells that make antibodies. The cancerous plasma cells are called myeloma cells.

Myeloablation: The killing of bone marrow by radiation or chemotherapy. This term usually refers to the complete or near-complete destruction of the bone marrow.

Myelodysplastic syndrome (MDS): A condition in which the bone marrow does not function normally and does not produce enough blood cells. This condition can occasionally progress and become acute leukemia.

Myeloid: Referring to myelocytes, a type of white blood cell. Also called myelogenous. Myeloma is a lymphoid cancer, not a myeloid cancer.

Myeloma-defining event (MDE): One of three biologic markers that indicate progression to symptomatic myeloma within 18 months to 2 years. One or more of these markers indicates the need for treatment of asymptomatic (smoldering) myeloma. The MDEs are (1) the presence of 60% or more clonal plasma cells in the bone marrow, (2) more than one focal lesion at least 5 millimeters in size, and (3) a Freelite ratio greater than or equal to 100.

Myelosuppression: A decrease in the production of red blood cells, platelets, and some white blood cells by the bone marrow.

Natural killer (NK) cell: A lymphocyte (type of white blood cell) that is a component of the innate immune system. NK cells are responsible for tumor surveillance and are able to induce strong responses against tumors through the release of cytokines.

Neoplasia: Abnormal new growth of cells; cancer.

Neoplasm: Abnormal new growth of tissue or cells creating a malignant tumor.

Nephrotic syndrome: A group of diseases characterized by excretion of large amounts of protein (mostly albumin) into urine. Nephrotic syndrome frequently produces edema.

Nephrotoxicity: The quality of being toxic or destructive to kidney cells.

Neurosurgeon: A doctor who performs surgery on any part of the nervous system, including the back and the spinal cord.

Neutropenia: A reduced level of neutrophils, a type of white blood cell necessary to combat bacterial infection.

Neutrophil: A type of white blood cell necessary to combat bacterial infection.

Non-secretory myeloma: Approximately 1% of myeloma patients do not have detectable M-protein in the blood (serum) and urine. Some of these patients can be successfully monitored using the serum free light chain assay; others may be monitored with bone marrow biopsy and/or PET/CT scan. Patients with non-secretory myeloma are treated in the same fashion as those with M-protein-secreting disease.

Nonsteroidal anti-inflammatory drug (NSAID): A drug used to reduce fever, swelling, and pain.

Nucleus: The nucleus of the cell in advanced organisms is the control center of the cell. It serves two functions: it stores all the genetic material (DNA) of the cell, and it coordinates the cell's

activities, which include growth, intermediary metabolism, protein synthesis, and reproduction (cell division).

Oligosecretory myeloma: Low-secreting disease. See also “Hyposecretory.”

Oncogene: A gene or DNA sequence that normally directs cell growth, but which can also promote or allow the uncontrolled growth of cancer if it is damaged (mutated) by environmental exposure to carcinogens, or if the oncogene is damaged or missing because of an inherited defect. An oncogene has the potential to cause a normal cell to become cancerous.

Oncologist: A doctor who specializes in treating cancer. Some oncologists specialize in a particular type of cancer.

Orphan drug: The orphan drug designation is granted by the US Food and Drug Administration to provide incentives such as tax credits, user fee waivers, and eligibility for orphan drug exclusivity to assist and encourage the development of drugs for rare diseases.

Orthopedic surgeon: Orthopedic surgeons use both surgical and nonsurgical means to treat musculoskeletal trauma, sports injuries, degenerative diseases, infections, tumors, and congenital disorders.

Osteoblast: A bone cell associated with production of bone tissue. Osteoblasts produce osteoid, which then becomes mineralized with calcium to form new hard bone.

Osteoclast: A cell found at the junction between the bone marrow and the bone. It is responsible for breaking down or remodeling old bone tissue. In myeloma, the osteoclasts are overstimulated, while osteoblast activity is blocked. The combination of accelerated bone resorption and blocked new bone formation results in lytic lesions.

Osteoid: The protein produced by osteoblasts which becomes mineralized with calcium to form hard bones.

Osteonecrosis of the jaw (ONJ): A jaw problem observed in a small percentage of patients taking bisphosphonates. The condition can cause pain, swelling, and bone damage around the tooth sockets in the jaws. Bone necrosis, or death of bone, occurs and can lead to loose teeth, sharp edges of exposed bone, bone spurs, and the breaking loose of small bone spicules or dead bone. It is defined as \geq 3 months with non-healing exposed bone. Symptoms may not be obvious at first, or may include pain, swelling, numbness or a “heavy jaw” feeling, or loosening of a tooth.

Osteopenia: A condition in which bone mineral density is lower than normal, but not low enough to be classified as osteoporosis.

Osteoporosis: A progressive bone disease that is characterized by a decrease in bone mass and density, leading to an increased risk of fracture. Diffuse involvement of bones with myeloma produces what looks like osteoporosis on X-ray and bone density measurement.

Overall response rate (ORR): The percentage of patients in a clinical trial whose monoclonal protein decreased by at least 50% in response to treatment.

Overall survival (OS): The median number of individuals in a group who are alive after a particular duration of time. OS is often used as a measure of treatment efficacy in clinical trials. The lengthening duration of OS in myeloma trials makes it a difficult endpoint to use, leading to the effort to validate minimal residual disease status as a new endpoint.

Palliative treatment: A treatment designed to improve the quality of life by relieving pain and symptoms of disease but not intended to alter its course.

Paracrine: In a paracrine loop, factors produced by the microenvironment surrounding myeloma cells can stimulate these cells. Stimulated myeloma cells produce factors that can in turn stimulate microenvironmental cells. Also see “**Autocrine.**”

Partial response: See “**Response or remission.**”

Pathogen: An infectious agent such as a virus, bacterium, prion, fungus, viroid, or parasite that causes disease in its host.

Pathologic fracture: A break in a bone usually caused by cancer or some disease condition. Occurs in myeloma-weakened bones, which can’t bear normal weight or stress.

Pathology: The study of disease by the examination of tissues and body fluids under the microscope. A doctor who specializes in pathology is called a pathologist.

Performance status: A measure of the level of activity of which a patient is capable. By implication, a measure of the severity of disease. Developed by the Eastern Cooperative Oncology Group (ECOG), the ECOG scale runs from 0 to 5, with 0 being “fully active, able to carry on all pre-disease activities without restriction,” and 5 being “death.” Also called ECOG status. Many clinical trials require ECOG status of 0 or 1; trials enrolling patients with a status of 3 or 4 are rare.

Peripheral blood stem cells (PBSC): Stem cells collected from the circulating blood. These cells are similar to stem cells found in the

bone marrow. The term “peripheral” means that the cells come from blood outside of the marrow.

Peripheral blood stem cell transplant: See “Transplant.”

Peripheral neuropathy (PN): Numbness, tingling, and/or pain in the hands, feet, legs, and/or arms.

PET scan: See “Positron emission tomography.”

Pharmacodynamics: The study of the action or effects drugs have on human cells.

Pharmacogenetics or pharmacogenomics: Interchangeable terms that refer to the study of specific changes in genes that result in various responses to treatments.

Pharmacokinetics: The study of the processes by which a drug is absorbed, distributed, metabolized, and eliminated by the body.

Phlebitis: Inflammation of a vein.

Placebo: An inert (inactive) substance often used in clinical trials for comparison with an experimental drug. No clinical trial for cancer patients in the United States can ethically or legally randomize patients to receive a placebo alone when they require treatment. In the placebo arm of a cancer treatment trial, patients receive treatment with approved therapy *plus* a placebo.

Plasma: The liquid part of the blood in which red blood cells, white blood cells, and platelets are suspended.

Plasma cells: Special white blood cells that produce antibodies (immunoglobulins). Myeloma is a cancer of the plasma cells. Malignant plasma cells are called myeloma cells. In myeloma, malignant plasma cells produce abnormal antibodies that lack the ability to fight infection. These abnormal antibodies are the monoclonal protein, or M-protein, that functions as a tumor marker for myeloma. The presence of malignant plasma cells in the bone marrow can lead to organ and tissue damage (anemia, kidney damage, bone disease, and nerve damage).

Plasmacytoma: See "Extramedullary plasmacytoma" and "Solitary plasmacytoma of bone (SPB)."

Plasmapheresis: The process of removing certain proteins from the blood. Plasmapheresis can be used to remove high levels of monoclonal myeloma protein from the blood of myeloma patients.

Platelets: One of the three major types of blood cells, the others being red blood cells and white blood cells. Platelets plug up breaks in the blood vessel walls and release substances that stimulate blood clot formation. Platelets are the major defense against bleeding. Also called thrombocytes.

Positron emission tomography (PET): A diagnostic test that uses a sophisticated camera and computer to produce images of the body. PET scans show the difference between healthy and abnormally functioning tissues based upon the uptake of radiolabeled sugar by active cancer cells.

Port (implanted): A catheter connected to a quarter-sized disc that is surgically placed just below the skin in the chest or abdomen. The catheter is inserted through a large vein or artery directly into the bloodstream. Fluids, drugs, or blood products can be infused, and blood can be drawn through a needle that is inserted into the disc.

Precancerous: A term used to describe a condition that may or may not become cancer. See **MGUS**.

Prognosis: The projected outcome or course of a disease; the chance of recovery; life expectancy.

Progression-free survival (PFS): The length of time during and after the treatment of a disease, such as cancer, that a patient lives with the disease but it does not get worse. In a clinical trial, measuring the PFS is one way to determine how well a new treatment works. Also called PFS. See “**Progressive disease**.”

Progressive disease: Myeloma that is becoming worse or relapsing, as documented by tests. Defined as an increase of $\geq 25\%$ from lowest confirmed response value in the myeloma protein level and/or new evidence of disease.

Proteasome: A joined group (or complex) of enzymes that destroy damaged or unwanted proteins and undamaged proteins that require degradation in the cell. This turnover or “recycling” of proteins is important to maintain balance within the cell and helps to regulate several functions including cell growth.

Proteasome inhibitor: Any drug that interferes with the normal function of the proteasome, an enzyme complex responsible for breaking down and recycling unwanted proteins in both normal cells and cancer cells.

Proteins: Substances composed of amino acids. Proteins are an essential part of all living organisms, especially as structural components of body tissues such as muscle, hair, collagen, etc., as well as enzymes and antibodies.

Protocol: A detailed treatment plan, which includes the dose and schedule of any drugs used.

Pulmonary embolism (PE): A condition that occurs when a blood clot in the vein (deep vein thrombosis, or DVT) breaks loose, travels through the bloodstream, and lodges in a lung, blocking blood flow.

Radiation therapy: Treatment with X-rays, gamma rays, or electrons to damage or kill malignant cells. The radiation may come from outside the body (external radiation) or from radioactive materials placed directly in the tumor (implant radiation).

Radiologist: A doctor who specializes in creating and interpreting images of areas inside the body. The images are produced with X-rays, sound waves, magnetic fields, or other types of energy.

Recurrence: The reappearance of a disease after a period of remission.

Red blood cells (RBC, erythrocytes): Cells in the blood that contain hemoglobin, deliver oxygen to all parts of the body, and take away carbon dioxide. Red cell production is stimulated by a hormone (erythropoietin) produced by the kidneys. Myeloma patients with damaged kidneys don’t produce enough erythropoietin and can become anemic. Myeloma patients can also become anemic because of myeloma cells’ effect on the ability of bone marrow to make new red blood cells.

Refractory: Disease that is no longer responsive to standard treatments. Patients with refractory myeloma have had progressive disease either during treatment or within 60 days following treatment. Most clinical trials for advanced disease are for patients with relapsed and/or refractory myeloma.

Regression: The shrinkage in size of a cancer or tumor.

Relapse: The reappearance of signs and symptoms of a disease after a period of improvement. Patients with relapsed disease have been treated, then developed signs and symptoms of myeloma at least 60 days after treatment ended. Most clinical trials for advanced disease are for patients with relapsed and/or refractory myeloma.

Research Study: See “Clinical Trial.”

Response or remission: Complete or partial disappearance of the signs and symptoms of cancer. Remission and response are interchangeable terms.

- *Stringent complete response (sCR)* – sCR is CR (as defined below) plus normal FLC ratio and absence of clonal cells in bone marrow by immunohistochemistry or immunofluorescence.
- *Complete response (CR)* – For myeloma, CR is negative immunofixation on serum (blood) and urine, and disappearance of any soft tissue plasmacytomas, and ≤ 5% plasma cells in bone marrow. CR is not the same as a cure.
- *Very good partial response (VGPR)* – VGPR is less than CR. VGPR is serum M-protein and urine M-protein detectable by immunofixation but not on electrophoresis, or 90% or greater reduction in serum M-protein, plus urine M-protein less than 100 mg per 24 hours.
- *Partial response (PR)* – PR is a level of response in which there is at least a 50% reduction in M-protein, and reduction in 24-hour urinary M-protein by at least 90% (or to less than 200 mg per 24 hours).

Ribonucleic acid (RNA): Any of various nucleic acids that are associated with the control of cellular chemical activities. RNA is one of the two nucleic acids found in all cells – the other is DNA (deoxyribonucleic acid). RNA transfers genetic information from DNA to proteins produced by the cell.

Sacrum: Below the lumbar spine is the sacrum, a triangular-shaped bone comprised of 5 fused segments, S1 through S5. The sacrum is inserted like a wedge between the hip bones, with its bottom part connecting with the coccyx (tailbone).

Salvage therapy: A treatment regimen that is given after the patient’s disease does not respond to preferred therapies or the patient cannot tolerate other available therapies.

Scleroderma: A connective tissue disorder characterized by tightening of the skin of the arms, face, or hands; puffy hands and feet; and joint stiffness. It can affect the entire body or just one part.

Second primary malignancy (SPM): A second, unrelated primary cancer that is diagnosed after a person has been treated for cancer. Certain types of treatment may increase the risk of a second primary malignancy.

Serum: The colorless, liquid part of blood in which the blood cells are suspended.

Serum osteocalcin: A protein produced and secreted by osteoblasts when they are making osteoid. A low level reflects active myeloma. A higher than normal level reflects more stable myeloma.

Serum sickness: A hypersensitivity reaction caused by the administration of a foreign serum; it causes fever, swelling, skin rash, and enlargement of the lymph nodes.

Shingles: See “Herpes zoster.”

Side effect: Unwanted effect caused by a drug. Also known as adverse reaction or adverse event (AE).

Skeletal-related event (SRE): Bone damage or fracture.

Skeletal survey (metastatic survey): A series of plain X-rays of the skull, spine, ribs, pelvis, and long bones to look for lytic lesions and/or osteoporosis.

Smoldering multiple myeloma (SMM): SMM is a higher level of disease than MGUS, but is still not active myeloma with CRAB features indicating organ damage. Patients with standard-risk SMM do not require treatment, but should be observed at regular intervals by a hematologist-oncologist. Patients with high-risk SMM may choose to participate in a clinical trial.

Solitary plasmacytoma of bone (SPB): A discreet, single mass of monoclonal plasma cells in a bone. The diagnosis of SPB requires a solitary bone lesion, a biopsy of which shows infiltration by plasma cells; negative imaging results for other bone lesions; absence of clonal plasma cells in a random sample of bone marrow; and no evidence of anemia, hypercalcemia, or renal involvement suggesting systemic myeloma.

Spinal cord: A long, thin, tubular bundle of nervous tissue and support cells that extends from the brain. The brain and spinal cord together make up the central nervous system. The spinal cord

begins at the occipital bone and extends down to the space between the first and second lumbar vertebrae.

Spine: The spine is divided into four main regions. The neck region is known as the cervical spine, comprised of 7 vertebrae, abbreviated as C1 through C7 (top to bottom). The chest region is known as the thoracic spine, consisting of 12 vertebrae, T1 through T12. The lumbar spine in the lower back is comprised of 5 vertebrae, L1 through L5. Below the lumbar spine is the sacrum, a triangular-shaped bone comprised of 5 fused segments, S1 through S5. The sacrum is inserted like a wedge between the hip bones, with its bottom part connecting with the coccyx (tailbone).

Stable disease: This describes patients who have some response to treatment but with < 25% improvement or progression in protein level. With slow-moving myeloma, stabilization can last for many years.

Stage: The extent of a cancer in the body.

Staging: Doing exams and tests to learn the extent of the cancer in the body.

Stem cells (hematopoietic stem cells): The immature cells from which all blood cells develop. Normal stem cells give rise to normal blood components, including red cells, white cells, and platelets. Stem cells are normally located in the bone marrow and can be harvested for transplant.

Stem cell selection: A cell processing technology that is used to obtain a stem cell-enriched product and thereby reduce cancer cells in the transplant. Not used successfully for myeloma patients.

Steroid: A type of hormone. Synthetic steroids are often given to myeloma patients along with one or more anticancer drugs and typically enhance the anti-myeloma treatment benefit.

Substrate: A molecule upon which an enzyme acts.

Supportive care: Treatment given to prevent, control, or relieve complications and side effects and to improve the patient's comfort and quality of life.

Syngeneic: See "Transplant."

Systemic lupus erythematosus (SLE): See "Lupus."

Systemic treatment: Treatment using substances that travel through the bloodstream to reach and affect cells in the entire body.

T cells (T lymphocytes): A type of white blood cell that plays a central role in the immune system. T cells can be distinguished from other lymphocytes, such as B-cells and natural killer (NK) cells, by the presence of a T-cell receptor (TCR) on the cell surface. They are called T cells because they mature in the thymus (although some also mature in the tonsils).

Thrombocytes: See "Platelets."

Thrombocytopenia: A low number of platelets in the blood. "Normal" levels vary from laboratory to laboratory. The normal level at the Mayo Clinic is 150,000–450,000. If the platelet count is less than 50,000, bleeding problems could occur. Major bleeding is usually associated with a reduction to less than 10,000.

Toxins: Poisons produced by certain animals, plants, or bacteria.

Trabecular bone: Also known as cancellous bone; the light, porous bone enclosing numerous large spaces that give it a sponge-like appearance. Trabecular bone contains marrow and blood vessels.

Transfusion: The transfer of blood or blood products.

Transplant (transplantation): There are several different types of transplantation.

- *Peripheral blood stem cell (PBSC) transplant* – Doctors remove healthy blood-making stem cells from a patient's circulating blood (not from the bone marrow), which are then frozen and stored. The patient receives high-dose chemotherapy to destroy the cancer cells, but healthy blood cells are also destroyed. The frozen stem cells are then defrosted and returned to the patient, where they can produce new blood cells to replace cells destroyed by the treatment.

- *Autologous transplant* – A procedure in which stem cells are removed from a patient's blood and then are given back to the patient following intensive treatment.

- *Bone marrow transplant* – This term refers to the process of collecting stem cells from the bone marrow and infusing them into a patient. This term is used less frequently today in myeloma as stem cells are now collected from the peripheral (circulating) blood.

- *Allogeneic (allograft) transplant* – The infusion of bone marrow or stem cells from one individual (donor) to another (recipient). A patient receives bone marrow or stem cells from a compatible, though not genetically identical, donor. An HLA blood test is done to determine if a patient has a potential donor match. A donor may be a family member or may be

obtained through a donor registry such as the National Marrow Donor Program (NMDP). Rarely, donor cells may be obtained from an umbilical cord blood bank. The donor's immune system cells recognize the recipient's myeloma cells as foreign, and attack them. Unfortunately, the donated cells also attack other tissues in the recipient's body, causing graft-versus-host disease (GVHD), which may be fatal.

- *Reduced-intensity conditioning (RIC) allo transplant* – A newer and, for myeloma, safer technique than an allogeneic transplant. RIC is a non-myeloablative, reduced-intensity “mini-allo” transplant performed within 180 days after a standard autologous transplant.

- *Tandem transplant* – A term used to indicate two autologous transplants done in succession. Tandem transplants are usually planned with 3-month to 6-month intervals between transplants. Tandem transplantation has become less common in the US in the era of effective novel therapies.

- *Matched unrelated donor (MUD) transplant* – Refers to a stem cell transplantation procedure in which the patient and the stem cells are genetically matched but are not from family members. This procedure is not recommended for myeloma patients because it carries an unacceptably high mortality rate from graft-versus-host disease (GVHD).

- *Syngeneic transplant* – The infusion of bone marrow or stem cells from one identical twin into another.

- *Umbilical cord blood transplant* – Stem cells obtained from the umbilical cords of newborns. These are frozen and stored in cord blood banks. Because multiple cords are needed to provide enough stem cells for an adult transplant, the risk of graft-

versus-host disease is increased with this type of transplant, making it even riskier for myeloma patients.

Tumor: An abnormal mass of tissue that results from excessive cell division. In myeloma, a tumor is referred to as a plasmacytoma.

Tumor lysis syndrome (TLS): A disorder caused by the break-down products of dying cancer cells, which can overwhelm the kidneys and lead to kidney failure. TLS can occur when a patient responds very quickly and deeply to therapy. TLS is usually treated with allopurinol, a treatment for gout.

Tumor marker: A substance in blood or other body fluids that may suggest that a person has cancer. In myeloma, the tumor marker is monoclonal protein found in the blood and/or urine.

Tumor necrosis factor (TNF): A cell signaling protein (cytokine) involved in systemic inflammation and bone resorption. TNF alpha is elevated in myeloma patients.

Tumor suppressor gene: Also called an anti-oncogene. A gene that protects a cell from one step on the path to cancer. When this gene mutates to cause a loss or reduction in its function, the cell can progress to cancer, usually in combination with other genetic changes.

Umbilical cord blood transplant: See “Transplant.”

Vaccine: A preparation of killed microorganisms, living attenuated organisms, or living fully virulent organisms that is administered to produce or artificially increase immunity to a particular disease.

Vascular endothelial growth factor (VEGF): A growth factor that promotes the growth of new blood vessels (angiogenesis).

Venous thromboembolism (VTE): A condition that includes both deep vein thrombosis (DVT) and pulmonary embolism (PE). Risk factors include infection, age >75, cancer, and a history of VTE. See "**Deep vein thrombosis (DVT)**" and "**Pulmonary embolism (PE)**."

Vertebra: Any one of the 33 bony segments of the spinal column.

Vertebral body: The round bony area of a vertebra.

Vertebroplasty: A minimally invasive surgical procedure in which polymethyl methacrylate (PMMA) cement is injected into collapsed vertebrae to reduce pain and stabilize the spine after vertebral compression fracture.

Virus: A small living particle that can infect cells and change how the cells function. The disease and the symptoms caused by a viral infection vary based on the type of virus and the type of cells that are infected.

Waldenström's macroglobulinemia (WM): A rare type of indolent lymphoma that affects plasma cells. Excessive amounts of IgM protein are produced. Not a type of myeloma.

White blood cells (WBC): General term for a variety of cells responsible for fighting invading germs, infection, and allergy-causing agents. These cells begin their development in bone marrow and then travel to other parts of the body. Specific white blood cells include neutrophils, basophils, eosinophils, lymphocytes, and monocytes.

X-ray: A form of electromagnetic radiation that can penetrate the human body. Used in low doses, X-rays produce images of body structures and tissues that can reveal signs of disease or injury. Used in fluoroscopy for diagnosis or treatment, as well as in

computed tomography for detailed still images. High-dose radiation therapy is used to stop the multiplication of cancer cells.

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