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Glossary of Terms

Adjuvant chemotherapy – Treatment given in addition to the primary treatment to enhance the effectiveness of the primary treatment, usually after all detectable tumor is surgically removed.

Angiogenesis inhibitors: Compounds that attempt to cut off the blood supply to tumors.

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

Antibody: A protein substance produced by the immune system and found in the blood or tissues in response to a specific antigen, such as a bacterium or toxin

Antigen: Any material that causes the immune system to react when it comes into contact with human or animal tissues.

Approval: Data are analyzed and submitted for regulatory review. The U.S. submission to the FDA is called an NDA (New Drug Application) or BLA (Biologic License Application); in Europe, data are submitted to the EMEA (European Medicines Evaluation Agency) in a submission called an MAA (Marketing Authorization Application). After stringent analysis and review of the submission, the regulatory agency provides final approval.

Apoptosis: Programmed cell death, a natural process that the body uses to dispose of old, damaged or unwanted cells.

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

Bone marrow: The soft, spongy tissue in the center of bones that produces white blood cells, red blood cells, and platelets.

Cell: A mass of protoplasm containing a nucleus or nuclear material. It is the unit of structure of all animals and plants.

Cell differentiation: The process during which young, immature (unspecialized) cells take on 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: The treatment of cancer with drugs.

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.

Clinical Evaluation

Phase I: Human trials conducted to demonstrate the safety and effectiveness or (efficacy) of an experimental drug or procedure. Tests are conducted with paid volunteers to establish dosage, side effects and pharmacokinetics.

Clinical Phase II: Trials with small numbers of patients conducted to identify drug performance characteristics (optimal dosing, administration, key indication).

Clinical Phase III: Pivotal trials conducted with larger patient populations to establish efficacy and provide additional safety information.

Discovery: Identification of a biological, genetic or protein target linked to a particular disease, and subsequent lead identification of a potential drug that interacts with the target to help cure the disease or halt its progression.

Combination chemotherapy – The use of more than one drug given in a chemotherapy regimen during cancer treatment.

Complete Remission (CR) – CR is the absence of myeloma protein from the serum and/or urine by standard testing; absence of myeloma cells from the bone marrow and/or other areas of myeloma involvement; clinical remission and improvement of other laboratory parameters to normal. CR is not the same thing as a cure. Sensitive testing methods can detect minute levels of myeloma. Relapse occurs. The time to relapse is influenced by the type of initial treatment as well as the maintenance used.

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

Disease free survival: The length of time the patient survives without any detectable cancer.

Drug development process:

Efficacy: The power to produce an effect; in cancer research ‘efficacy’ refers to whether the treatment is effective.

Fast Track Status: The Food and Drug Administration Modernization Act of 1997 (FDAMA) includes Section 112, “Expediting study and approval of fast track drugs.” This section mandates the Agency to facilitate the development and expedite review of drugs and biologics intended to treat serious or life-threatening conditions and that demonstrate the potential to address unmet medical needs. *Fast track* adds to existing programs, such as accelerated approval, the possibility of a “rolling submission” for a marketing application. An important feature of *fast track* is that it emphasizes the critical nature of close early communication between the FDA and sponsor to improve the efficiency of product development.

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

Immune system: The complex group of organs and cells that produces antibodies to defend the body against foreign substances such as bacteria, viruses, toxins, and cancers.

Inhibit: To prohibit from doing something, to hold in check.

Injection: Pushing a medication into the body with the use of a syringe and needle.

Metastasize: In cancer, to spread, by transferring a malignancy (out-of-control growth) from the site of disease to another part of the body.

Multiple myeloma: Multiple myeloma (also known as myeloma or plasma cell myeloma) is a cancer of the blood in which malignant plasma cells are overproduced in the bone marrow. Plasma cells are white blood cells that help produce antibodies called immunoglobulins that fight infection and disease. However, most patients with multiple myeloma have cells that produce a form of immunoglobulin called paraprotein (or M protein) that does not benefit the body. In addition, the malignant plasma cells replace normal plasma cells and other white blood cells important to the immune system. Multiple myeloma cells can also attach to other tissues of the body, such as bone, and produce tumors. The cause of the disease is unknown. Multiple myeloma is the second most common cancer of the blood, representing approximately one percent of all cancers and two percent of all cancer deaths with a worldwide prevalence of approximately 200,000 cases. In the year 2002, there were an estimated 74,000 new cases of multiple myeloma worldwide. The estimated number of deaths from multiple myeloma in 2002 was 57,370 worldwide.

Myelodysplastic Syndromes: Myelodysplastic syndromes (MDS) are a group of hematologic conditions that affect approximately 300,000 people worldwide. The five types of MDS are refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, refractory anemia with excess blasts in formation, and chronic myelomonocytic leukemia. Myelodysplastic syndromes occur when blood cells remain in an immature or "blast" stage within the bone marrow and never develop into mature cells capable of performing their necessary functions. Eventually, the bone marrow becomes filled with blast cells until there is no room for normal cells to develop. According to the American Cancer Society 14,000 new cases of MDS are diagnosed each year in the United States (approximately 87,000 worldwide), with survival rates ranging from six months to five years for the different types of MDS. MDS patients must now often rely on blood transfusions to manage symptoms of anemia and fatigue until they develop life-threatening iron overload and or toxicity, thus underscoring the critical need for new effective therapies targeting the cause of the condition rather than simply managing its symptoms.

New Drug Application: For decades, the regulation and control of new drugs in the United States has been based on the New Drug Application (NDA). Since 1938, every new drug has been the subject of an approved NDA before U.S. commercialization. The NDA application is the vehicle through which drug sponsors formally propose that the FDA approve a new pharmaceutical for sale and marketing in the U.S. The data gathered during the animal studies and human clinical trials of an [Investigational New Drug \(IND\)](#) become part of the NDA.

Oncogene: The part of the cell that normally directs cell growth, but which can also promote or allow the uncontrolled growth of cancer if damaged (mutated) by an environmental exposure to carcinogens, or if damaged or missing because of an inherited defect. A gene that 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 treatment.

Orphan Drug Designation: there are many diseases and conditions, such as Huntington's disease, ALS (Lou Gehrig's disease), Tourette syndrome, and muscular dystrophy which affect such small numbers of individuals (<200,000) residing in the United States that the diseases and conditions are considered rare in the United States. Adequate drugs for many of such diseases and conditions have not been developed. Drugs for these diseases and conditions are commonly referred to as "orphan drugs" because so few individuals are affected by any one rare disease or condition. Pharmaceutical or biotech companies developing an orphan drug may reasonably expect the drug to generate relatively small sales in comparison to the cost of developing the drug and consequently to incur a financial loss. The FDA believes that some promising orphan drugs will not be developed unless drug developers are properly

incentivized. Orphan designation qualifies the sponsor of the drug for the tax credit and marketing exclusivity incentives of the ODA.

Partial Remission (PR) – PR is a level of response less than CR. In SWOG studies, it has meant >50%<75% response. In other studies it has meant >50% response. RNA (ribonucleic acid): 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.

Patent: A grant made by the government giving the creator of an invention the sole right to make, use and sell the invention for a set period of time.

Pathway profiling: The process of mapping and identifying additional proteins along a pathway

Pathway: A series of related steps or events along a defined route. In metabolism, the term refers to a sequence of reactions which change one substance into another.

Personalized medicine: The core philosophy of Millennium of delivering the right drugs, directed toward the right molecular targets, to the right patients, at the right time.

Pre-clinical: Comprehensive in vitro (lab dish) and animal testing of the drug candidate to establish its target [specificity](#), toxicity in various doses and [pharmacokinetics](#) .

Progression-free survival: The time period during which the patient survives and the cancer does not become worse. The improved survival of a patient that can be directly attributed to the treatment given for the myeloma. This term identifies myeloma patients who are in complete remission versus those who have had an episode of relapse or progression.

Progressive disease: Disease that is becoming worse, as documented by tests.

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).

Red blood cells (Erythrocytes): Cells in the blood that contain hemoglobin and deliver oxygen to all parts of the body and take carbon dioxide from them. 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. Injections with synthetic erythropoietin can be helpful. Blood transfusion is another alternative, especially in an emergency. Synthetic erythropoietin is being used prophylactically before chemotherapy and as supportive therapy after chemotherapy to avoid anemia.

Refractory: Disease that is unresponsive to standard treatments.

Relapse: The reappearance of signs and symptoms of a disease after a period of improvement.

Remission or Response: Complete or partial disappearance of the signs and symptoms of cancer. Remission and response are used interchangeably.

Responders:

Complete

Partial

Minimal

Side effects: Problems that occur due to drugs used for disease treatment. Common side effects of cancer treatment are fatigue, nausea, vomiting, decreased blood cell counts, hair loss, and mouth sores.

Virus: A small living particle that can infect cells and change how the cells function. Infection with a virus can cause a person to develop symptoms. The disease and symptoms that are caused depend on the type of virus and the type of cells that are infected.

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 the bone marrow and then travel to other parts of the body. Specific white blood cells include neutrophils, granulocytes, lymphocytes, and monocytes.

Adapted from the International Myeloma Foundation and Celgene glossary.



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Resource List

American Association for Cancer Research (AACR)

615 Chestnut St., 17th Floor
Philadelphia, PA 19106-4404
Phone: 215-440-9300
Web site: www.aacr.org

American Cancer Society (ACS)

1599 Clifton Road NE
Atlanta, GA 30329
Phone: 800-227-2345
Web site: www.cancer.org

American Society of Clinical Oncology (ASCO)

1900 Duke Street, Suite 200
Alexandria, VA 22314
Phone: 703-299-0150
Web site: www.asco.org

International Myeloma Foundation (IMF)

12650 Riverside Drive, Suite 206
North Hollywood, CA 91607
Phone: 818-487-7455
Web site: www.myeloma.org

Multiple Myeloma Research Foundation (MMRF)

3 Forest Street
New Canaan, CT 06840
Phone: 203-972-1250
Web site: www.multiplemyeloma.org

National Cancer Institute (NCI)

Suite 3036A
6116 Executive Boulevard, MSC8322
Bethesda, MD 20892-8322
Phone: 800-422-6237
Web site: www.nci.nih.gov

National Comprehensive Cancer Network (NCCN)

50 Huntingdon Pike, Suite 200
Rockledge, PA 19046
Phone: 215-728-4788
Web site: www.nccn.org

National Organization for Rare Disorders (NORD)

55 Kenosia Avenue
PO Box 1968
Danbury, CT 06813-1968
Phone: 203-744-0100
Web site: www.rarediseases.org

U. S. Food and Drug Administration (FDA)

5600 Fishers Lane
Rockville MD 20857-0001
Phone: 301-827-6242
Web site: www.fda.gov