Understanding POMALYST® (pomalidomide) capsules
Founded in 1990, the International Myeloma Foundation (IMF) is the first and largest organization focusing specifically on multiple myeloma. The IMF’s reach extends to more than 525,000 members in 140 countries worldwide. The IMF is dedicated to improving the quality of life of myeloma patients while working toward prevention and a cure through our four founding principles: Research, Education, Support, and Advocacy.

RESEARCH The signature project of the IMF’s Research division is the Black Swan Research Initiative®, a groundbreaking and collaborative effort to develop the first definitive cure for myeloma. Each year, the IMF also awards Brian D. Novis Grants, which promote research for better myeloma treatments, management, and practices in the field. In addition, more than 200 leading myeloma researchers comprise the IMF’s International Myeloma Working Group (IMWG), a research body that has developed myeloma guidelines that are followed around the world. Finally, the IMF’s Nurse Leadership Board (NLB), comprised of nurses from leading myeloma treatment centers, develops recommendations for the nursing care of myeloma patients.

EDUCATION The IMF Patient & Family Seminars and Regional Community Workshops are held around the world to provide up-to-date information presented by leading myeloma specialists and researchers directly to patients and their families. The IMF’s library of more than 100 publications, for patients and caregivers as well as for healthcare professionals, is updated annually and available free of charge. Publications are available in more than 20 languages.

SUPPORT The IMF’s InfoLine is staffed by information specialists who answer myeloma-related questions and provide support via phone and email to thousands of families each year. In addition, the IMF sustains a network of more than 150 myeloma support groups and offers training for the hundreds of dedicated patients, caregivers, and nurses who volunteer to lead these groups in their communities.

ADVOCACY The IMF’s Advocacy team has educated and empowered thousands of individuals who make a positive impact each year on issues critical to the myeloma community. Working in the US at both federal and state levels, we lead coalitions to advocate for parity in insurance coverage. We also represent the myeloma community’s interests before the US Congress and agencies such as the National Institutes of Health, the Food and Drug Administration, the Centers for Medicare and Medicaid Services, and the Veterans Administration. Outside the US, the IMF’s Global Myeloma Action Network (GMAN) works to help patients gain access to treatment.

Learn more about the ways the IMF is helping to improve the quality of life of myeloma patients while working toward prevention and a cure. Contact us at 818.487.7455 or 800.452.CURE, or visit myeloma.org.

Improving Lives Finding the Cure®
What you will learn from this booklet

The IMF’s Understanding series of booklets is designed to acquaint you with treatments and supportive care measures for multiple myeloma (which we refer to simply as “myeloma”). Words in bold-blue type are explained in the “Terms and definitions” section at the end of this booklet, as well as in a more complete compendium of myeloma-related vocabulary, the IMF’s Glossary of Myeloma Terms and Definitions, located at glossary.myeloma.org.

Myeloma is a cancer that is not known to most patients at the time of diagnosis. To be empowered to play an active role in your own medical care and to make good decisions about your care with your doctor, it is vital for you to learn as much as possible about myeloma and its treatments. The information in this booklet will help you in discussions with your healthcare team. The more information you have about resources that are available to you, the better and more fruitful that discussion will be.

Understanding POMALYST® (pomalidomide) capsules focuses on a drug that is approved only for patients with relapsed and refractory myeloma. This booklet presents information on pomalidomide and how it works, the results of clinical trials and ongoing research with pomalidomide, how and when to take pomalidomide, its possible side effects, and how to manage them.

What is Pomalyst?

Pomalyst is a medication in capsule form that is taken by mouth. Pomalyst in combination with dexamethasone was approved by the US Food and Drug Administration (FDA) in February 2013, by the European Medicines Agency (EMA) in August 2013, and by Health Canada in February 2014. Pomalyst + dexamethasone is indicated for patients with myeloma who have received at least two prior therapies, including Revlimid® (lenalidomide) and Velcade® (bortezomib), and have demonstrated disease progression on or within 60 days of completion of the last therapy. In June 2018, the Darzalex® + Pomalyst + dexamethasone regimen was approved by the FDA for the treatment of patients with myeloma who have received at least two prior therapies including Revlimid and a proteasome inhibitor (Velcade, Ninlaro®, or Kyprolis®).

Pomalidomide is the newest in the line of anti-myeloma agents called immunomodulatory drugs, also known as IMiD® compounds. These agents can modify or regulate the functioning of the immune system. Since myeloma is a cancer of certain cells in the immune system, immunomodulators are particularly effective anti-myeloma agents. Thalomid® (thalidomide), an immune modulator, was approved by the FDA for the treatment of myeloma in 2003. Revlimid® (lenalidomide) was approved by the FDA in June 2006.

The National Comprehensive Cancer Network (NCCN) has included Pomalyst + dexamethasone as one of the “Other Recommended Regimens” in category 1, “highest level of evidence.” It has also included Darzalex® (daratumumab) + Pomalyst + dexamethasone, Pomalyst + Velcade + dexamethasone, Pomalyst + cyclophosphamide + dexamethasone, and Pomalyst + Kyprolis + dexamethasone among the “Other Recommended Regimens” in category 2A, “based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.”

How does Pomalyst work?

Immunomodulatory drugs have multiple actions. They have both anti-cancer and anti-inflammatory effects. They are vascular endothelial growth factor (VEGF) inhibitors, drugs that prevent the formation of blood vessels necessary to sustain tumor cells. Immunomodulatory drugs are also able to reduce the levels of various cellular growth factors, called cytokines and interleukins, which promote the growth of cancer cells. Interleukin-6 (IL-6), for example, is known to stimulate and support the growth of myeloma cells, and it has been reported that pomalidomide “down-regulates,” or reduces the amount, of IL-6. In addition, immunomodulatory compounds enhance the activation of specialized white blood cells (WBC), both the T cell lymphocytes and T cells known as “natural killer” (NK) cells, which kill cancer cells.

Lab tests have shown that pomalidomide is more potent in stimulating T cell proliferation than thalidomide.

What are the results with Pomalyst in clinical trials?

Data from the large, randomized, international phase III MM-003 clinical trial for 455 patients with relapsed/refractory myeloma was presented at the 2012 annual meeting of the American Society of Hematology (ASH)
and was the basis for the FDA approval of Pomalyst. Follow-up data from the Pomalyst + dexamethasone study presented at ASH 2015 firmly established the efficacy of Pomalyst in the relapsed/refractory setting.

A French study published in January 2016 showed that patients with relapsed/refractory myeloma who had longer exposure (≥1 year) to Pomalyst + dexamethasone had an overall response rate (ORR) of 83%, with median overall survival (OS) of 91% at 18 months, both of which far exceed the response rate, progression-free survival (PFS), and OS of patients treated for <1 year.

Data presented at ASH 2016 included two important clinical trial updates of the FDA-approved combination of pomalidomide + dexamethasone.

- MM-014: Pomalyst + low-dose dexamethasone (Pd) was demonstrated to be effective in relapsed/refractory myeloma irrespective of the number of prior therapies. Patients refractory to lenalidomide can be successfully treated with Pd. However, patients may achieve longer PFS and OS if Pd is used 18 months or more after the last dose of lenalidomide. Further investigation is needed to identify optimal treatment strategy.
- MM-010: Approximately 6% of newly diagnosed myeloma patients present with renal failure severe enough to require dialysis. Half of these patients can become dialysis-independent after Velcade-based therapy, especially if they achieve a rapid myeloma response. Pomalyst + Velcade + dexamethasone (PVd) therapy increases the probability of renal response when compared to Velcade + dexamethasone alone. Independence from dialysis is associated with longer survival.

PFS data for the phase III OPTIMISMM clinical trial comparing PVd to Vd were presented by Dr. Paul Richardson at the June 2018 meeting of the European Hematology Association (EHA). The 559 myeloma patients in this study have relapsed and/or refractory disease previously treated with at least one but not more than three prior regimens, including a Revlimid-containing regimen. Significantly, with a median follow-up of 16 months, PVd reduced the risk of progression or death by 39% and resulted in deeper responses. Median PFS was 11.2 vs. 7.1 months. Data for the overall survival analysis are not yet mature.

### How is Pomalyst taken?

- Pomalyst is taken in capsule form by mouth.
- On the days that Pomalyst is taken, it should be taken at the same time of the day.
- Swallow Pomalyst with water. Pomalyst may be taken with or without food.
- Do not break, chew, or open the capsules.
- Do not handle the capsules more than needed.
- If you touch a broken Pomalyst capsule, wash the area of your body that came in contact with the medicine immediately and thoroughly with soap and water.
- If you miss a dose of Pomalyst, and it has been less than 12 hours since your regular time to take it, you should take it as soon as possible. If it has been more than 12 hours since your regular time, just skip your missed dose. Do NOT take two doses at the same time.
- If you take too much Pomalyst or overdose, call your healthcare provider or poison control center right away.
- Store Pomalyst at room temperature.
- Keep Pomalyst and all medications out of the reach of children.

### What are the dose and schedule of Pomalyst?

Pomalyst capsules are given orally at 4 mg per day on days 1 to 21 of repeated 28-day cycles until disease progression. Pomalyst was approved in combination with dexamethasone, an adrenocortical steroid. The recommended dose of dexamethasone is 40 mg per day on days 1, 8, 15, and 22 of each 28-day cycle, but your doctor can adjust the dose if you are experiencing intolerable side effects. You must report any and all new problems when you visit the oncologist’s office. Pomalyst capsules are manufactured in 4 mg, 3 mg, 2 mg, and 1 mg strengths. Your doctor will determine if it is necessary and/or appropriate to treat you with less than the recommended 4 mg dose and, as above, you must report any side effects to the members of your healthcare team.

<table>
<thead>
<tr>
<th>STRENGTH</th>
<th>COLOR</th>
<th>COLOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 mg</td>
<td>blue</td>
<td>blue</td>
</tr>
<tr>
<td>3 mg</td>
<td>blue</td>
<td>green</td>
</tr>
<tr>
<td>2 mg</td>
<td>blue</td>
<td>orange</td>
</tr>
<tr>
<td>1 mg</td>
<td>blue</td>
<td>yellow</td>
</tr>
</tbody>
</table>
Warnings and precautions
While most of the side effects associated with Pomalyst are manageable and predictable, there are certain potential side effects that are serious enough to require an FDA-mandated “Boxed Warning” on the package insert. A Boxed Warning is the strictest warning put in the labeling of prescription drugs when there is reasonable evidence of an association with a serious hazard from the drug. In the prescribing information for Pomalyst, the Boxed Warnings include the risk of embryo-fetal toxicity (birth defects or death of a developing fetus) and an increased risk of venous and arterial thromboembolism (blood clot, pulmonary embolism, heart attack, and stroke).

Female patients of childbearing potential and all male patients are required to complete a monthly phone survey. Doctors must check monthly pregnancy tests, limit prescriptions to a 28-day supply, and report any pregnancies to the FDA.

Pomalyst REMS
Because of the embryo-fetal risk, Pomalyst is available only through a restricted program under a Risk Evaluation and Mitigation Strategy called “Pomalyst REMS®.” Prescribers and pharmacists must be certified with the program. Patients must sign an agreement form and comply with the requirements. Patients or their physicians must report any suspected fetal exposure to Pomalyst to the FDA via the MedWatch program at 800-332-1088, and also to Celgene Corporation at 888-423-5436.

Women of childbearing potential
One of the most important discoveries about Pomalyst during lab studies is that it harms the developing fetuses of laboratory animals. Because Pomalyst is a chemical analog of thalidomide, which is known to harm human fetuses, Pomalyst should never be taken by pregnant women and women who are capable of becoming pregnant.

Male patients
Pomalyst is present in the semen of male patients who take it, so they must also comply with mandatory contraceptive measures.

Nursing mothers
Because many drugs are excreted in human milk and because of the potential for adverse events in nursing infants from Pomalyst, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Drug interactions
No formal drug interaction studies have been conducted with Pomalyst, which is primarily metabolized by CYP1A2 and CYP3A enzyme systems. Pomalyst is also a substrate of P-glycoprotein (P-gp). Patients should not take Pomalyst with drugs that are strong inhibitors of CYP1A2, CYP3A, or P-gp. Patients should be aware that cigarette smoking may reduce the efficacy of Pomalyst due to CYP1A2 activation. Any concerns and questions about possible drug interactions or smoking should be discussed with your doctor and pharmacist.

Age
Safety and effectiveness of Pomalyst in patients under the age of 18 have not been established. No dosage adjustment is required for Pomalyst based on age. In clinical trials, however, patients aged 65 years or older were more likely to experience pneumonia than patients less than 65 years of age.

Second primary malignancy
Cases of acute myelogenous leukemia (AML) have been reported in patients receiving Pomalyst in clinical trials, although none of these were patients in myeloma trials.

Use in renal and hepatic impairment
Pomalyst is metabolized in the liver. Pomalyst and its metabolites are excreted by the kidneys. The influence of renal (kidney) and hepatic (liver) impairment on the safety, efficacy, and pharmacokinetics of Pomalyst has not been evaluated. Pomalyst should not be taken by the following patients:

- Patients whose serum creatinine is > 3.0 mg/dL.
- Patients whose serum bilirubin is > 2.0 mg/dL.
- Patients whose AST/ALT is > 3.0 x ULN (upper limit of normal).
Patients must be aware of these and other warnings and precautions before taking Pomalyst. Speak with your doctor or nurse if you notice any changes in your health. Being a “good patient” doesn’t mean suffering in silence; it means accurately and promptly reporting any problems or changes in your health to your healthcare providers so that they can take appropriate steps. No problem is too small to report. Be proactive.

**Adverse events**

In the clinical trial of 219 patients who received Pomalyst alone or Pomalyst + low-dose dexamethasone, all patients had at least one adverse event (side effect). The most common adverse events, occurring in 30% or more of patients, included fatigue and weakness (asthenia), low white blood cell count (neutropenia), low red blood cell count (anemia), constipation, nausea, diarrhea, difficulty breathing, upper respiratory tract infection, back pain, and fever. The most common serious adverse events were low blood counts and pneumonia. For serious adverse events, treatment with Pomalyst should be held, and then when the side effect resolves, restarted at 1 mg less than the previous dose.

**Hypersensitivity reactions**

Patients with a prior history of serious sensitivity to Thalomid or Revlimid were excluded from studies with Pomalyst and may be at higher risk of allergic reactions to Pomalyst. Drug hypersensitivity results from the interaction of a drug and the immune system. Risk factors for drug hypersensitivity reactions include age, female gender, concurrent illnesses, and previous hypersensitivity to related drugs. Symptoms may include difficulty breathing, rash, hives, fever, swelling, vomiting, or diarrhea.

**Prevention and treatment of hypersensitivity reactions**

Treatment is largely supportive and includes discontinuation of the medication and treatment of the symptoms. Contact your healthcare provider immediately if you experience any symptoms after taking Pomalyst.

**Neutropenia**

Neutropenia (decreased white blood cell count) of any grade was reported in 50% of patients and was the most frequently reported serious adverse event, followed by anemia (low red blood cell count) and thrombocytopenia (low platelet count). Since your white blood cells make up your immune system, which is your defense against viral and bacterial illnesses, having too few of these cells can lead to infection. Fever is the most common sign of having too few neutrophils and is a sign that you need immediate medical attention. Other common symptoms associated with a low neutrophil count include sore throat and mouth sores.

When patients with relapsed myeloma begin therapy with Pomalyst, neutropenia is often a problem that results from the combined effects of myeloma infiltration of the bone marrow, the impact of prior therapy, and the impact of the Pomalyst.

**Prevention and treatment of neutropenia**

In the first 2–3 months of therapy, it is especially important to try to maintain the full dose of Pomalyst as much as possible and, if need be, to support the white blood cells with a drug such as Neupogen® (G-CSF, colony-stimulating factor), a growth factor to stimulate neutrophil production. As the myeloma cells are cleared out of the bone marrow, the neutrophils recover, and tolerance for the full dose of pomalidomide improves.

Patients should be monitored with weekly complete blood counts for the first eight weeks of treatment, and monthly thereafter. Treatment can be modified if blood counts are too low. You should inform your doctor if you have any cold or flu symptoms. Neutropenia accompanying viral infections (such as the flu) may be short-term and may resolve quickly after the infection has cleared.

With ongoing Pomalyst therapy beyond the initial cycles, support for white blood cell production may be an ongoing concern. Mild neutropenia generally has no symptoms and may not need treatment. In severe cases of neutropenia, the doctor may prescribe a white blood cell...
growth factor to achieve a safe level of neutrophils. If the white blood cell count remains low, dose reduction of Pomalyst may also be required once response has been achieved.

**Deep vein thrombosis (DVT)**

Patients receiving Pomalyst have developed venous thromboembolisms (VTE, blood clots) reported as serious adverse reactions. In the clinical trial data submitted to the FDA for approval of Pomalyst, all study patients were required to receive treatment to prevent blood clots. The rate of deep vein thrombosis (DVT) or pulmonary embolism (PE) was 3%.

DVT is a serious condition and is potentially life-threatening. DVT is a blood clot in a deep vein of the lower extremities (usually occurring in the leg or thigh, and very occasionally in the neck or upper arm). A blood clot from a DVT can break loose (embolize) and travel to the heart or lungs. An embolus is very dangerous. If you are taking Pomalyst and you experience warmth, swelling, redness, difficulty breathing, and/or pain in an extremity, notify your doctor immediately.

**Prevention and treatment of DVT**

Although relatively few patients who have taken Pomalyst have had venous thromboembolic events, anticoagulation (blood thinner) therapy is recommended. Your physician will evaluate your individual risk factors and determine which type of anticoagulation agent is appropriate for you.

**Dizziness and confusion**

Eighteen percent of patients in the clinical trial leading to FDA approval of Pomalyst experienced dizziness and 12% of patients experienced some mental confusion.

**Prevention of dizziness and confusion**

Patients should be aware that dizziness and confusion are potential side effects and should avoid situations where this would pose a risk to, or problem for, themselves or others. You may need to avoid taking other medications if they cause dizziness or confusion. You should discuss your other medications with your physician and/or pharmacist.

**Neuropathy**

Eighteen percent of patients experienced neuropathy (toxicity to nerve tissue), approximately half of which was peripheral neuropathy (PN). There were no cases of serious neuropathic adverse events. Symptoms of neuropathy include dizziness and fainting; symptoms of peripheral neuropathy include numbness, tingling, and pain in the hands and/or feet.

**Prevention and treatment of neuropathy**

We strongly urge you to contact your physician if you experience new or worsening symptoms of this condition. Early detection and dose modification can prevent progression of neuropathy.

**Fatigue**

Feeling unusually tired is a common side effect of treatment for myeloma (and other cancers). Although many of the patients in clinical trials with Pomalyst felt fatigued, very few had severe fatigue that prevented them from performing the activities of daily living. As a general rule, any patient suffering from fatigue should exercise caution if operating machinery, including automobiles. The IMF has a publication called *Understanding Fatigue* that will be useful if you or someone you care for experiences this side effect.

**Prevention and treatment of fatigue**

If your fatigue is severe, your doctor may have to intervene with appropriate supportive care measures. There are drugs, such as Provigil® (modafinil), to treat this problem. The effects of fatigue may be minimized by maintaining:

- A moderate level of activity (because inactivity breeds greater fatigue).
- A healthy diet and proper fluid intake.
- A consistent sleeping schedule with enough rest.
- Regularly scheduled visits with your healthcare providers to discuss your fatigue issues.

**Asthenia**

Asthenia is a medical term for physical weakness and loss of strength. It is a common complication of a number of drugs that are used to treat myeloma, and of cancer treatments in general.

**Prevention and treatment of asthenia**

In cases of severe asthenia, there are several things that can be done to help. First and easiest, try taking your Pomalyst at night before you go to sleep. This will help limit the drug’s effects to the hours when you’re asleep in bed. If you are
still experiencing significant physical weakness during your waking hours, your doctor may reduce the dosage of Pomalyst. Asthenia may also improve by itself with prolonged therapy. Doctors have reported that asthenia and fatigue often improve as the myeloma disease burden decreases, usually after the first two cycles of therapy. Finally, in cases of severe asthenia, the doctor can prescribe drugs that are given at low doses early in the morning (for example, Ritalin® or Adderall®) to ensure that patients are able to be more active during the day.

Thrombocytopenia
Patients taking Pomalyst may experience a decrease in the level of blood cells called thrombocytes, or platelets, which are responsible for clotting the blood. Low levels of platelets can result in bruising, bleeding, and slower healing.

Prevention and treatment of thrombocytopenia
You should inform your physician if you experience excessive bruising or bleeding. Management may include platelet transfusions at the discretion of your physician.

Anemia
Red blood cells contain hemoglobin, a protein that contains iron and transports oxygen from the lungs to the body’s organs and tissues. When a patient has anemia, the result is low levels of oxygen in the body, which may cause shortness of breath and feelings of exhaustion.

Prevention and treatment of anemia
Your healthcare providers will determine which treatment regimen for anemia is best suited to and safest for you.

The following are options for treatment of anemia:

- Adjusting medications.
- Blood transfusions.
- Erythropoietic (red blood cell-making) agents.

Looking forward
In addition to clinical trials that combine Pomalyst with new experimental agents in phase I trials, currently recruiting clinical trials with Pomalyst include many phase III triplet combination therapies, including Pomalyst + Kyprolis + dexamethasone, Pomalyst + cyclophosphamide + dexamethasone, isatuximab + Pomalyst + dexamethasone, and Ninlaro + Pomalyst + dexamethasone. Four-drug combination trials in progress are evaluating the combination of Empliciti® + Pomalyst + Velcade + dexamethasone and Ninlaro + Pomalyst + Biaxin® + dexamethasone.

In closing
While a diagnosis of cancer is something you cannot control, gaining knowledge that will improve your interaction with your doctors and nurses is something you can control, and it will have a significant impact on how well you do throughout the disease course.

This booklet is not meant to replace the advice of your doctors and nurses who are best able to answer questions about your specific healthcare management plan. The IMF intends only to provide you with information that will guide you in discussions with your healthcare team. To help ensure effective treatment with good quality of life, you must play an active role in your own medical care.

We encourage you to visit myeloma.org for more information about myeloma and to contact the IMF InfoLine with your myeloma-related questions and concerns. The IMF InfoLine consistently provides callers with the most up-to-date and accurate information about myeloma in a caring and compassionate manner. IMF InfoLine specialists can be reached at InfoLine@myeloma.org or 818.487.7455 or 800.452.CURE.

Terms and definitions

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.”

Anemia: A decrease in hemoglobin, 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.

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

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

**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.

**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.

**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.

**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.

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

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

**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.

**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.

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

**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.

**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 (MRD) status as a new endpoint.

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

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

**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.

**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 see how well a new treatment works. See “Progressive disease.”

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

**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.

**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.
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.

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.

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

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.

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).

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.

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

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).”

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, basophils, eosinophils, lymphocytes, and monocytes.