Understanding

REVLIMID®
(lenalidomide)
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 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 those discussions will be.

Understanding REVLIMID® (lenalidomide) will familiarize you with a drug that is approved for treating myeloma in the newly diagnosed, relapsed and/or refractory, and maintenance therapy settings. It summarizes highlights of clinical trials with Revlimid® (generic drug name lenalidomide) and reviews potential side effects and how best to manage them.

What is Revlimid and how does it work?

Revlimid is the first oral medication developed for treatment of myeloma, and it is taken in capsule form. Because you do not need to be at the doctor’s office or in a clinic or hospital to receive Revlimid, the responsibility for taking this medication as directed by your doctor falls on you. It is crucial that you read and understand the information in this booklet and in any other materials your healthcare team provides you. Therefore, before you start taking Revlimid, we recommend that you also read a related IMF publication, Understanding Adherence to Oral Cancer Therapy.

Revlimid is an immunomodulatory drug. Revlimid has multiple actions, including both anti-cancer and anti-inflammatory activities. Immuno-modulatory drugs induce immune responses, enhance the activity of immune cells, and inhibit inflammation. They are able to alter the levels of various growth factors called cytokines and interleukins, and to affect cells of the immune system.

Immunomodulatory compounds enhance the activation of specialized white blood cells (WBC) of the immune system – both the T cell lymphocytes and T cells known as natural killer (NK) cells – which help kill cancer cells. Revlimid is also a vascular endothelial growth factor (VEGF) inhibitor. Revlimid belongs to a group of immunomodulatory drugs with the ability to inhibit formation of blood vessels, on which cancer cells depend for sustenance and growth.

What is the clinical trial experience with Revlimid?

Revlimid + dexamethasone was originally approved by the US Food and Drug Administration (FDA) in June 2006 for use in myeloma patients who have received at least one prior therapy.

Since then, clinical trials have demonstrated Revlimid’s efficacy throughout the disease course, not only as relapse therapy, but also as therapy for newly diagnosed myeloma and as maintenance therapy.

Clinical trials using Revlimid in the newly diagnosed setting

In September 2014, The New England Journal of Medicine published the results of a study of 1,623 patients from 18 countries who participated in the FIRST (Frontline Investigation of Revlimid + dexamethasone versus Standard Thalidomide) clinical trial. Newly diagnosed patients were either ≥ 65, or < 65 years of age and ineligible for stem cell transplant, and were randomized into three treatment arms:
1. Revlimid + low-dose dexamethasone (Rd) in 28-day cycles until disease progression (continuous Rd),
2. Revlimid + low-dose dexamethasone (Rd) for 72 weeks (18 cycles), or
3. Melphalan + prednisone + thalidomide (MPT) in 42-day cycles for 72 weeks (12 cycles).

The primary endpoint was a comparison of progression-free survival (PFS) for continuous Rd versus MPT. The results demonstrated the superiority of continuous Rd compared to MPT in newly diagnosed myeloma patients. These significant results prompted an expanded indication for the use of Revlimid in patients with newly diagnosed myeloma.

Clinical trials with Revlimid as a component of combination therapy in the frontline setting are an important part of ongoing research in myeloma. Data from the MAIA clinical trial of Darzalex® (daratumumab) + Revlimid + dexamethasone for the treatment of newly diagnosed myeloma patients who are not candidates for stem cell transplant were published in *The New England Journal of Medicine* in June 2019 and have been submitted to the FDA for consideration of approval.

**Clinical trials using Revlimid in the setting of smoldering myeloma**

Several clinical trials, including the so-called “Cure” trials in the US (“ASCENT”) and Spain (“CESAR”) and the ongoing Eastern Cooperative Oncology Group (ECOG) E3A06 clinical trial presented at the annual meeting of the American Society of Clinical Oncology (ASCO) in June 2019, are bringing Revlimid to an entirely new treatment setting in myeloma. In these studies, patients with high- and intermediate-risk smoldering multiple myeloma (SMM) are being treated with combination therapies that include Revlimid or, in the case of the E3A06 clinical trial, with Revlimid alone, to halt the progression of SMM to active disease. Data from these clinical trials are being gathered and analyzed to determine the possible benefits and risks of treating SMM with these different strategies.

**Maintenance therapy**

Two large clinical trials with more than 1,000 patients compared post-ASCT (autologous stem cell transplant) maintenance therapy with Revlimid given until disease progression or unacceptable side effects versus no maintenance therapy. The first study, CALGB 100104, was conducted in the US and demonstrated a median PFS of 5.7 years for patients who received Revlimid maintenance therapy, versus 1.9 years among patients who had no Revlimid maintenance therapy. Median overall survival (OS) in this trial was 9.3 years for patients who received Revlimid, versus 7 years for those who did not.

The second maintenance therapy clinical trial, IFM 2005-02, was conducted in Europe, and showed a median PFS of 3.9 years for patients who had Revlimid maintenance therapy versus 2 years for patients who had not. Median OS was 8.8 years for those who received Revlimid, versus 7.3 years for those who did not.

Another significant finding supporting Revlimid’s role as post-ASCT maintenance therapy was presented at the December 2016 meeting of the American Society of Hematology (ASH). Representing a group of investigators from centers across the US, Dr. Edward Stadtmauer (University of Pennsylvania) presented the data from the StaMINA trial, in which 758 transplant-eligible patients who were within 12 months of having started induction therapy and had no disease progression were randomized to one of three study arms: (1) single ASCT followed by 4 cycles of Revlimid + Velcade + dexamethasone (RVD) consolidation and Revlimid maintenance until disease progression; (2) tandem ASCT followed by Revlimid maintenance until disease progression; or (3) single ASCT followed by Revlimid maintenance until disease progression. The surprising preliminary results of the largest randomized US transplant clinical trial in myeloma demonstrated comparable PFS and OS in all three arms after 38 months of follow-up. The addition of RVD consolidation or a second ASCT was not superior to a single ASCT followed by Revlimid maintenance in the frontline therapy of myeloma.

The 2017 ASH meeting brought further confirmation of Revlimid’s role in maintenance therapy. Data from a large, randomized clinical trial in the UK (1,970 patients) demonstrated that Revlimid maintenance versus no maintenance significantly improves both PFS and OS regardless of the patient’s cytogenetic risk status. A smaller Spanish clinical trial examined the clinical and biological data, and the results of flow cytometry and PET-CT of patients treated with Revlimid maintenance therapy. The researchers concluded that Revlimid maintenance increases the proportion of patients who are MRD-negative by both flow cytometry and PET-CT, and that their prognosis is significantly superior to that of patients who do not receive Revlimid maintenance.

Revlimid maintenance therapy post-ASCT, however, can increase the risk of second primary malignancies (SPM), which arise among patients who have been exposed to both melphalan (which is used in ASCT) and Revlimid. Studies of early Revlimid maintenance trials revealed that
second hematologic (blood-related) cancers occurred in 7.5% of patients who received Revlimid maintenance compared to 3.3% of patients who received no maintenance. The incidence of hematologic plus solid tumor SPM was 14.9% compared to 8.8% over a follow-up period of almost ten years. Given the evident advantages but potential risks of post-transplant maintenance therapy with Revlimid, each patient must discuss the pros and cons of this course of treatment with their oncologist. Doctors must evaluate individual risk factors and the response to transplant before making a recommendation, and must monitor patients carefully when they are receiving Revlimid maintenance therapy.

**What are the approved indications for treatment with Revlimid?**

The initial FDA approval of Revlimid + dexamethasone in June 2006 for use in myeloma patients who have received at least one prior therapy has been followed over the years by expanded indications:

- In February 2015, based on the results of the FIRST clinical trial, the FDA updated the indication for use of Revlimid: “Revlimid in combination with dexamethasone is indicated for the treatment of patients with multiple myeloma.” This broad approval of Revlimid reflects its use throughout the disease course, from diagnosis through relapse.

- In February 2017, the FDA expanded the indication for Revlimid as a maintenance treatment for myeloma patients following ASCT. Revlimid is the first and only treatment approved for this indication in the US or elsewhere.

In Europe, the indication for the use of Revlimid in myeloma patients reads:

- For the treatment of adult patients with previously untreated (newly diagnosed) myeloma who are not eligible for transplant.

- In combination with dexamethasone for the treatment of myeloma in adult patients who have received at least one prior therapy.

- In February 2017, the European Commission expanded the indication for Revlimid to include Revlimid as monotherapy for the maintenance treatment of adult patients with newly diagnosed myeloma who have undergone ASCT.

In addition to approvals in the US and EU, Revlimid has been approved in Japan and in approximately 25 other countries for the treatment of adult patients with previously untreated myeloma who are ineligible for transplant.

Revlimid is also approved in nearly 70 countries for the treatment of myeloma patients who have received at least one prior therapy, and it is approved in Australia and New Zealand for the treatment of patients whose disease has progressed after one prior therapy.

In November 2015, the FDA approved two new drugs for the treatment of myeloma in combination with Revlimid + dexamethasone:

- Ninlaro® (ixazomib), an oral proteasome inhibitor. Patients must have had at least one prior therapy to receive treatment with Ninlaro + Revlimid + dexamethasone. For further information, please see the IMF publication *Understanding NINLARO® (ixazomib) capsules*.

- Empliciti® (elotuzumab), a monoclonal antibody. Patients must have had from one to three prior therapies in order to receive treatment with Empliciti + Revlimid + dexamethasone. For further information, please see the IMF publication *Understanding EMPLICITI® (elotuzumab)*.

In November 2016, based on the outstanding results of the POLLUX clinical trial of Darzalex® (daratumumab) + Revlimid + dexamethasone (Drd) versus Revlimid + dexamethasone alone, the FDA approved the Drd combination for myeloma patients who have received at least one prior therapy. For more information about Darzalex, read the IMF publication *Understanding Darzalex® (daratumumab) injection*.

**Possible side effects of Revlimid**

While most of the side effects associated with Revlimid are manageable and predictable, there are also potential side effects of Revlimid 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 current prescribing information for Revlimid, the Boxed Warnings include the risks of thrombocytopenia and neutropenia, and embryo-fetal toxicity.

For patients taking the combination of Revlimid + dexamethasone, the Boxed Warnings include an increased risk of arterial and venous thromboembolism (VTE, blood clots and pulmonary embolism, a blood clot that travels to the lung), myocardial infarction (heart attack), and stroke.

**Thrombocytopenia and neutropenia**

Patients taking Revlimid may experience thrombocytopenia, a lowered level of platelets in the blood. Platelets help blood to clot; fewer platelets can lead to bruising, bleeding, and slower healing.

Neutropenia, a lowered level of neutrophils, white blood cells that help to fight infection, may lead to infections.
Prevention and treatment
Inform your physician if you experience excessive bruising or bleeding. At the discretion of your physician, management of decreased platelet levels may include platelet transfusions.

The treatment of neutropenia depends on cause and severity. Contact your physician immediately if you experience fever, sore throat, or mouth sores. Because fever is a symptom indicating infection in someone with low neutrophil levels, immediate medical attention may be needed. The neutropenia accompanying viral infections may be transient and resolve after the infection has cleared. Mild neutropenia generally has no symptoms and may not need treatment.

Venous thromboembolism (VTE)
VTE is a condition that includes both deep vein thrombosis (DVT) and pulmonary embolism (PE).

DVT is a blood clot (thrombus) in a deep vein of the lower extremities, usually occurring in the leg or thigh, very occasionally occurring 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, potentially life-threatening.

PE is a condition that occurs when a blood clot in the vein breaks loose, travels through the bloodstream, and lodges in a lung, blocking blood flow.

Prevention and treatment
The Boxed Warning for Revlimid states that, “Anti-thrombotic prophylaxis [preventive therapy with a blood thinner] is recommended.” The type and dose of blood thinner will be tailored to your risk factors. You are strongly advised to notify your physician immediately if you experience difficulty breathing or warmth, swelling, redness, and/or pain in an extremity. Your physician will diagnose your condition and determine whether or not treatment is needed. Treatment depends upon both the location and the underlying cause.

Embryo-fetal toxicity
Animal studies have shown that Revlimid can cause severe birth defects or death of a developing fetus. The FDA therefore required that a risk management program be established. The goals of the Revlimid Risk Evaluation and Mitigation Strategy (known as REVLIMID REMS®) are as follows:

1. To prevent the risk of embryo-fetal exposure to Revlimid.
2. To inform prescribers, patients, and pharmacists about the serious risks and safe-use conditions for Revlimid.

Female patients of childbearing potential must undergo mandatory pregnancy testing and give informed consent before taking Revlimid. Female patients of childbearing potential and all male patients are also required to complete a monthly phone survey. Since most female myeloma patients are beyond the age of childbearing, they are enrolled in the REMS program by their physicians with a lower risk classification, and only have to do the phone survey once every six months. They will, however, have monthly counseling with the specialty pharmacy that dispenses their Revlimid.

Other side effects
In addition to the Boxed Warning side effects discussed above, the most common side effects to be aware of when taking Revlimid include diarrhea, fatigue, anemia, constipation, low white blood cell count, peripheral edema (swelling of the ankles and feet), insomnia, muscle cramp/spasms, abdominal pain, back pain, nausea, asthenia (a general feeling of weakness), fever, upper respiratory tract infection, bronchitis, gastroenteritis (upset stomach), cough, rash, dyspnea (difficulty breathing), dizziness, decreased appetite, and tremor.

The major studies that were the basis of Revlimid’s approval in the relapse setting used a combination of Revlimid + dexamethasone. It is important to be aware that additional toxicities can occur with this combination versus Revlimid alone. Side effects that may occur with Revlimid + dexamethasone include muscle weakness, anxiety, agitation, cardiac arrhythmias, nausea, increased blood sugar, elevated liver enzymes, and constipation and/or diarrhea. The use of dexamethasone in myeloma is discussed in a separate IMF booklet, Understanding Dexamethasone and Other Steroids.

Remember to discuss any changes in your health with a member of your healthcare team.

If you are planning to have a stem cell transplant
For newly diagnosed myeloma patients who plan to go on to ASCT, longer-term use of Revlimid can affect the blood-making stem cells. The prescribing information for Revlimid states: “For patients who are ASCT-eligible, hematopoietic stem cell mobilization [i.e. collection of
blood-making stem cells for use in autologous stem cell transplant should occur within 4 cycles of a Revlimid-containing therapy.”

**Caution regarding the combination of Revlimid and Keytruda® (pembrolizumab)**

The prescribing information for Revlimid cautions against the combination of “thalidomide analogs” (Revlimid and Pomalyst® [pomalidomide]) plus dexamethasone with the PD-1, PD-L1 blocking antibody Keytruda, which has been approved for melanoma and several other solid tumors, but is not approved in the setting of myeloma. This warning is based on two randomized trials for patients with myeloma in which pembrolizumab in combination with Revlimid or Pomalyst and dexamethasone led to increased mortality. The prescribing information reads: “Treatment of patients with multiple myeloma with a PD-1 or PD-L1 blocking antibody in combination with a thalidomide analogue plus dexamethasone is not recommended outside of controlled clinical trials.”

**Dose adjustments with Revlimid**

The standard dose for Revlimid is one 25-mg capsule each day for 21 days of a 28-day cycle. Your physician may consider reducing the dose because of lowered white and/or red blood cell counts. In addition, there may be cumulative side effects such as fatigue or slight neuropathy. Your physician may decide that dose reduction is appropriate, lowering first to 20 mg, then to 15 mg, then to 10 mg, and even to 7.5 mg, 5 mg, or 2.5 mg if necessary.

**Will a dose reduction in Revlimid change the effectiveness of treatment?**

Results from clinical trials show that with dose reductions after 12 months or longer of Revlimid therapy, treatment benefit is retained. Long remissions following dose reduction were reported in two clinical trials, MM009 and MM010, in which Revlimid + dexamethasone was compared to dexamethasone alone in myeloma patients who had relapsed after 1 to 3 prior lines of therapy. Patients who had dose reductions after 12 months or more of Revlimid had significantly longer PFS than those who had never had dose reductions at all.

It is important to communicate openly with your doctor or healthcare professional, follow your prescribed dose and schedule of medication, and keep regular appointments to maintain your Revlimid treatment schedule. Your doctor may choose to modify your dose of Revlimid as part of an overall plan to manage a particular side effect that you experience. Based on phase III clinical studies, the approved dose is 25 mg per day. If you experience a severe side effect, your doctor may modify your dose in either amount or schedule to reduce the severity of the side effect while maintaining treatment.

**How is Revlimid given?**

Revlimid is given as capsules that are swallowed with water. The most common dosing used in myeloma is 25 mg given orally daily on days 1–21 and repeated every 28 days (days 22–28 are rest days). Doses are then modified based on side effects.

**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**

**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.

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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.

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.”

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®.

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

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.

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.

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.

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.”

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.

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

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.

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

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.

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

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.

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 determine 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.
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.

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.

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.

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.

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).

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.

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

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.

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.

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.

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

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You are not alone. The IMF is here to help.

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 IMF produces and maintains a library of publications to help arm you with one of the most important weapons in the fight against myeloma: INFORMATION. The following is a partial list of publications available in English, and selected titles are also available in other languages.

- Patient Handbook
- Concise Review of the Disease and Treatment Options
- Understanding Clinical Trials
- Understanding Dexamethasone and Other Steroids
- Understanding DARZALEX® (daratumumab)
- Understanding EMPLICITI® (elotuzumab)
- Understanding Fatigue
- Understanding High-Dose Therapy with Stem Cell Rescue
- Understanding the Immune System in Myeloma
- Understanding KYPROLIS® (carfilzomib)
- Understanding MGUS and Smoldering Multiple Myeloma
- Understanding NINLARO® (ixazomib) capsules
- Understanding POMALYST® (pomalidomide)
- Understanding REVLIMID® (lenalidomide)
- Understanding Treatment of Myeloma Bone Disease
- Understanding Treatment of Myeloma-Induced Vertebral Compression Fractures
- Understanding VELCADE® (bortezomib)
- Understanding Your Test Results

All IMF publications and periodicals are always free of charge. Visit publications.myeloma.org to read, download, or order printed copies. Subscribe to IMF periodicals at subscribe.myeloma.org or by contacting the IMF.

As always, the IMF urges you to discuss all medical issues with your doctor, and to contact the IMF’s InfoLine specialists with your myeloma questions and concerns.