



Understanding
**Thalidomide
Therapy**



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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**®

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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 Thalidomide Therapy focuses on a drug that was approved by the US Food and Drug Administration (FDA) only for the treatment of newly diagnosed myeloma, but is widely in the **frontline, consolidation, and relapsed** disease settings. You will learn how thalidomide works to treat myeloma, how to use it safely, what **side effects** might be expected and how doctors can minimize side effects, and how thalidomide may be used in combination with other therapies.

What is thalidomide?

Thalidomide is an oral, small-molecule **immunomodulatory drug**, an agent that can modify or regulate the **immune system**. It has both **anti-inflammatory** and anti-cancer activities. Immunomodulatory drugs induce immune responses, enhance the activity of immune **cells**, and inhibit inflammation by altering the levels of **growth factors** called **cytokines** and **interleukins**. Immunomodulatory drugs kill cancer cells by enhancing the activation of specialized **T cells (T lymphocytes)** called **natural killer (NK) cells** – and by inhibiting the growth of blood vessels upon which cancer cells depend for sustenance and growth.

The emergence of thalidomide as a treatment for myeloma

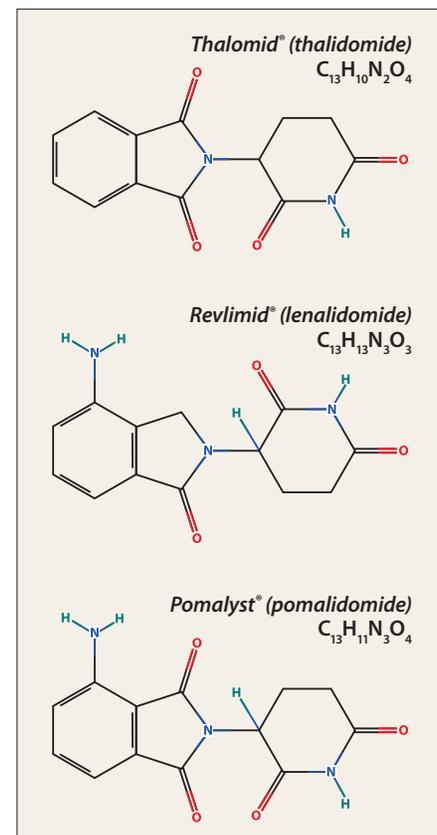
Using thalidomide to treat myeloma is an idea that emerged in the 1990s, but thalidomide itself has been studied for many decades. Much is known about how thalidomide works in the treatment of different diseases and how its side effects can be managed.

From 1957 to 1966, thalidomide was manufactured by a German company and was prescribed to pregnant women outside the US to combat symptoms associated with morning sickness. When taken during the first trimester of pregnancy, thalidomide prevented the proper growth of the fetus, resulting in severe birth defects. Only 50% of the affected children survived. It is now understood how important it is to prevent women who may be pregnant from being exposed to thalidomide. Because of the risk to fetal development, the FDA required Celgene Corporation, the company that manufactures Thalomid, to establish an oversight system for education and prescribing safety.

Thalidomide was first approved in the US for the treatment of *erythema nodosum leprosum*, an inflammatory condition seen in some patients with leprosy. Thalidomide was first used to treat myeloma in 1997, when Dr. Bart Barlogie conducted a small **clinical trial** for patients with advanced disease. The research was published in 1999, ushering in a new age in the treatment of myeloma.

In 2006, thalidomide was approved by the FDA for the treatment of patients with newly diagnosed myeloma in combination with dexamethasone, a powerful corticosteroid, and many myeloma patients around the globe have benefited from this therapy. Thalidomide is also used in combination with other agents for the treatment of myeloma.

Thalidomide was the first effective new drug for myeloma in decades, and it launched the era of "novel therapies" that has defined the last 15 years in myeloma treatment. It gave rise to a next generation of immune modulators with increased **efficacy** and reduced side effects, the drugs Revlimid® (lenalidomide) and Pomalyst® (pomalidomide).



Is thalidomide the same as chemotherapy?

Chemotherapy works by killing cells that are dividing rapidly. These cells include cancer cells as well as some normal cells in the body, such as hair cells and the cells of the mucosa lining the mouth and digestive tract. Hair loss, nausea and vomiting, and gastric upset are common side effects that occur with chemotherapy. Thalidomide and other immune modulators are not considered chemotherapy because they work very differently than chemotherapy agents.

Who can benefit from thalidomide therapy?

Thalidomide is active against myeloma and can produce lasting complete or partial **responses**, as well as disease stabilization. Over the past 15 years, thalidomide has been found to be effective in patients with different **stages** of myeloma, including:

- Patients with newly diagnosed myeloma.
- Patients who have not responded to other treatments.
- Patients in whom myeloma has returned after initial successful treatment.

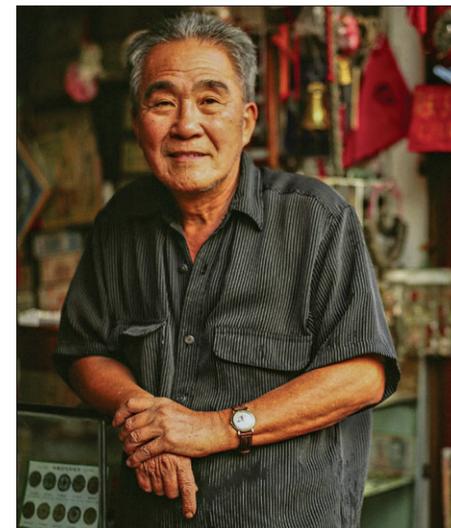
What is the dose and schedule of thalidomide + dexamethasone combination therapy?

Over the years, with the data gathered from clinical trials, doctors have learned to tailor the dose and schedule of thalidomide + dexamethasone combination therapy to improve patients' quality of life. When quality of life improves, patients can adhere better to a treatment protocol, and in turn respond better to the treatment.

A study of low-dose versus high-dose thalidomide for advanced myeloma was published in 2012 in the *European Journal of Hematology* by Inter-groupe Francophone du Myélome (IFM), the French myeloma research group. The study concluded that "low-dose thalidomide



100 mg/day has significant activity in advanced myeloma with an improved safety profile." Selection of the appropriate treatment and dosage is made on a case-by-case basis. In general, thalidomide is rarely prescribed at over 100 mg/day, while once-weekly dexamethasone at a dose of 40 mg has all but replaced the repeated four-day "pulses." These lower doses have been found to be as effective as higher doses, not least because they are far better tolerated.



How long does it take to respond to thalidomide?

Response to thalidomide therapy takes time. Generally, improvement in the disease is seen after about 3 months of treatment; however, improvements have been noted as early as 2 weeks and as late as 8 months after initiating treatment. Once a response is achieved, the physician will determine if ongoing **maintenance therapy** is appropriate, usually at a dose of 50 mg/day. The presence or absence of side effects will influence the decision to continue therapy or not and will help determine the dose. It is important to note that not everyone who takes thalidomide will have a response, and other therapies may be considered.

Current uses of thalidomide

In the US, thalidomide is less commonly prescribed than its successor, Revlimid, because of Revlimid's increased efficacy and reduced side effects. However, Revlimid can cause low blood counts. For patients with low blood counts, thalidomide may be a good alternative because it has a more minor impact on the **bone marrow's** ability to make new blood cells. Moreover, thalidomide may be a more affordable option for patients whose insurers cover the cost of Revlimid inadequately or not at all.

Soon after **oncologists** had proof of thalidomide's value in treating myeloma, Dr. Brian G.M. Durie noticed that his patients who were concurrently taking the antibiotic clarithromycin while being treated with thalidomide had markedly improved responses. A clinical trial of thalidomide + dexamethasone + clarithromycin revealed that clarithromycin

does increase the efficacy of thalidomide. It has since been verified that clarithromycin also enhances the activity of the other immunomodulatory drugs. Patients who are not responding well or quickly enough to thalidomide + dexamethasone may benefit from the addition of clarithromycin to the regimen.



Thalidomide is more commonly prescribed outside the US, particularly in such **induction** and consolidation regimens as Velcade® (bortezomib) + thalidomide + dexamethasone (VTD) and cyclophosphamide + thalidomide + dexamethasone (CTD).

Thalidomide in the maintenance setting

Thalidomide has been tested extensively in the maintenance setting. In the British MRC IX study in 2012, thalidomide was demonstrated to improve **progression-free survival (PFS)**, but not **overall survival (OS)** in newly diagnosed patients who had received a wide variety of prior therapies. In that study, maintenance thalidomide was given at 50 mg/day, increasing to 100 mg/day after 4 weeks, if tolerated, and continuing until progression. Thalidomide at the low 50–100 mg/day dose level remains an option for maintenance therapy.

In 2017, a study published in the journal *Leukemia* compared maintenance therapy with thalidomide + Velcade to either thalidomide alone or recombinant interferon alpha-2b (Intron A®) alone in newly diagnosed myeloma patients after their induction therapy. Recombinant interferon alpha-2b is an antiviral and anticancer drug with immune-modulating effects. After a median follow-up of 58.6 months, median PFS was significantly longer with thalidomide + Velcade than with either of the other two therapies alone. There was no significant difference in overall survival between the three maintenance therapy arms.

Thalidomide in current clinical trials

Thalidomide is currently in clinical trials in Europe and Asia as a component of new triplet therapy combinations for relapsed and **refractory** myeloma. Clinical trials that are recruiting patients as of this writing are:

- Study of bendamustine + thalidomide + dexamethasone that is being conducted in Italy.
- Study of Kyprolis® (carfilzomib) + thalidomide + dexamethasone vs Kyprolis + Revlimid + dexamethasone that is being conducted in Austria.
- Study of Ninlaro® (ixazomib) + thalidomide + dexamethasone that is being conducted in Austria, the Czech Republic (Czechia), and Germany.
- Study of Darzalex® (daratumumab) + thalidomide + dexamethasone that is being conducted by the Asian Myeloma Network (AMN).

What are the possible side effects of thalidomide?

The most common side effects associated with thalidomide are:

- Drowsiness – feelings of sleepiness or fatigue.
- Peripheral neuropathy – tingling, numbness, or pain in the arms, hands, legs, or feet.
- Dizziness – sensation of unsteadiness.
- Constipation – delayed or infrequent passage of hardened feces.
- Rash – an eruption on the skin.
- Leukopenia – a low level of **white blood cells (WBC)**.

Other side effects have been reported, although infrequently. Any side effect a patient experiences while receiving treatment should be discussed with a doctor or nurse as soon as possible. In addition, any changes in overall health or well-being should also be reported to a healthcare professional. Also report all prescription medications and over-the-counter products you are taking.

Drowsiness

Thalidomide often causes feelings of drowsiness. These methods may help relieve this side effect:

- Taking thalidomide at bedtime.
- Avoiding use of other drugs that may cause drowsiness while taking thalidomide.
- At the discretion of a doctor or nurse, taking other drugs to help alleviate drowsiness.
- Avoiding alcohol.



Avoid situations in which drowsiness may be a problem. Mental and physical abilities needed to perform dangerous tasks may be impaired (e.g., driving a car).

Peripheral neuropathy

Impairment of the nerves in the extremities (hands, arms, legs, feet) is known as peripheral neuropathy. This side effect can be mild, causing tingling in the hands and feet; more rarely, it can be severe and painful. Peripheral neuropathy typically occurs after

a long period of taking thalidomide, but it can sometimes occur sooner. These strategies may help alleviate symptoms of peripheral neuropathy:

- Walking and other forms of exercising.
- Avoiding tight shoes and socks with elastic.
- At the discretion of a doctor, reducing the dose of thalidomide.
- At the discretion of a doctor, taking additional medications.

A physician should be notified if any symptoms of peripheral neuropathy occur. If side effects are severe, thalidomide therapy may need to be discontinued.

Dizziness

Dizziness may occur during treatment with thalidomide. Sitting up and waiting a few minutes before standing or getting out of bed may help reduce dizziness.

Constipation

Constipation may occur during treatment with thalidomide; however, constipation is rarely severe. Prevention is the key to management. These strategies may help alleviate constipation:

- Drinking at least 8 glasses of fluid daily.
- Consuming dietary fiber every morning (e.g., prune juice, apple juice, bran).
- Exercising.
- At the recommendation of a doctor or nurse, taking stool softeners and laxatives.

If constipation becomes severe, the dose of thalidomide may be lowered or temporarily discontinued.

Rash

In some cases, a rash may develop while taking thalidomide. A mild rash (red or discolored skin, with or without raised bumps) usually begins on the body and spreads to the arms and legs. Mild rashes may be relieved in the following ways:

- At the recommendation of a doctor or nurse, taking antihistamines and topical corticosteroids.
- To alleviate dry skin, use oatmeal soap, calendula cream, cocoa butter cream, Eucerin® cream, or Acid Mantle® cream.

Rashes often resolve spontaneously after 10 to 14 days of treatment. Some rashes are a potentially serious reaction to thalidomide treatment. Rare reactions include Stevens-Johnson syndrome and toxic epidermal necrolysis (TEN). Symptoms of Stevens-Johnson syndrome include persistent fever, rash, blisters, or red splotches on the skin and blisters in the mouth, eyes, ears, nose, and genital area. TEN is characterized by blistering and peeling of large sections of skin.

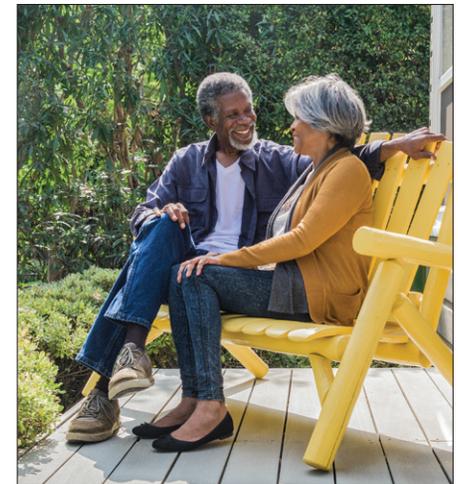
A doctor should be contacted immediately if a fever and/or drop in blood pressure occur.

Leukopenia

Thalidomide can sometimes cause a decrease in white blood cells. This condition is called leukopenia. Because of this possibility, blood tests need to be done regularly. If the white blood cell count becomes too low, the dose of thalidomide may have to be changed or the treatment may need to be interrupted.

The Thalomid® REMS™ program

If thalidomide is taken during pregnancy, it can cause severe birth defects or death to an unborn baby. Thalidomide should never be used by women who are pregnant or



who could become pregnant while taking the drug. Thalidomide may be detected in male sperm. Therefore, both men and women are required to follow strict rules for birth control while taking thalidomide.

Only physicians and pharmacists who are registered with the Thalomid® Risk Evaluation and Mitigation Strategy (REMS)™ program (as it is known in the US and in some other countries) can prescribe or dispense thalidomide. In the US, physicians and pharmacists may register with the Thalomid® REMS™ program by visiting thalomidrems.com or by calling Celgene Corporation at 888-423-5436. Both men and women must agree to follow this program before receiving thalidomide. To minimize the risk of exposing an unborn child to thalidomide, the Thalomid® REMS™ program includes the following elements:

- Patients must provide **informed consent**, complete confidential enrollment, and complete follow-up surveys throughout treatment.
- Women of childbearing age must have pregnancy tests every week during the first month of thalidomide therapy and monthly afterwards (every 2 weeks for women with irregular menstrual cycles).
- Women of childbearing age must receive contraceptive counseling and use 2 methods of birth control 4 weeks before, during, and at least 4 weeks after completing therapy.
- Men who are sexually involved with women of childbearing age must use a latex condom during and until at least 4 weeks after completing thalidomide therapy.

How is thalidomide given?

Thalidomide is available as a capsule. The dose, or number of capsules to be taken every day, will be determined by whether thalidomide is being given alone or in combination with other drugs. How the drug is tolerated by the body will also determine the dose. The dose may be gradually increased over time. A gradual increase ensures the most effective dose is given as safely as possible.



If side effects occur, immediately notify your doctor or nurse. The dose may need to be lowered, or even discontinued, if the side effects are severe. The dose should only be changed under the direction of a doctor.

Can thalidomide be taken with other cancer treatments?

Yes, thalidomide can be taken alone or in combination with chemotherapy, **radiation therapy**, or biologic treatments. A doctor experienced with myeloma should be able to give advice on the appropriate treatment for each individual. As already mentioned, thalidomide is used in combination with other anti-myeloma agents, most commonly with Velcade (with and without dexamethasone) and with melphalan + prednisone. For more information, read the IMF's booklets *Understanding Velcade® (bortezomib) for Injection* and *Understanding Dexamethasone and Other Steroids*.

Patient resources

In the US, the Celgene Patient Support program 800-931-8691 offers therapy assistance.

If you no longer respond to thalidomide

A phase I/II trial with the combination therapy Revlimid + thalidomide + dexamethasone conducted at MD Anderson Cancer Center in Texas for patients with relapsed or refractory myeloma demonstrated not only that it is possible to combine these drugs effectively, but that patients who were refractory to thalidomide can still respond to the combination of thalidomide + Revlimid + dexamethasone. Further studies were not conducted with this combination.

From the MD Anderson study, and many others, we know that patients who are refractory to thalidomide can still respond to Revlimid. It is generally not good treatment strategy, however, to give a second immunomodulatory drug to a patient who has just become refractory to a prior immunomodulator. Instead, it is preferable to switch to another class of therapy, such as a proteasome inhibitor, to enhance the chances for a good response, before trying another immunomodulator.

Important note

Thalidomide is a valuable option as a treatment for myeloma. However, like any drug, it can cause harm if misused. When taking thalidomide, it is important that you follow the advice given by your healthcare professionals. Questions or concerns regarding treatment may arise once it is started. Some of these may be about the drug itself. Others may be about treatment outcome or side effects. Still others may be emotional, and even

financial, in nature. Any questions should be promptly addressed with a doctor or nurse.

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

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

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.

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.

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



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, and in addition, they 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.

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.

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. They are normally released in response to infection.

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

Frontline: 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**.”

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

Immune system: The body's defense system from pathogens and foreign substances which 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**.”

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.

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**.”

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

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.

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

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.

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 progression-free survival is one way to see 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.

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).

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 $\leq 5\%$ 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).

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

Stage: The extent of a cancer in the 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).

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.



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's library of educational publications will help arm you with one of the most important weapons in the fight against myeloma: INFORMATION. The IMF publications listed below are available in English, and selected titles are also available in other languages. All IMF publications are free of charge and can be viewed, downloaded, or ordered at publications.myeloma.org

- *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*

In addition, the IMF produces an array of **Tip Cards**, concise reference tools on a variety of topics of interest, as well as periodicals such as the quarterly journal **Myeloma Today**, the weekly e-newsletter **Myeloma Minute**. Subscriptions to all IMF periodicals are free of charge at subscribe.myeloma.org

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.

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