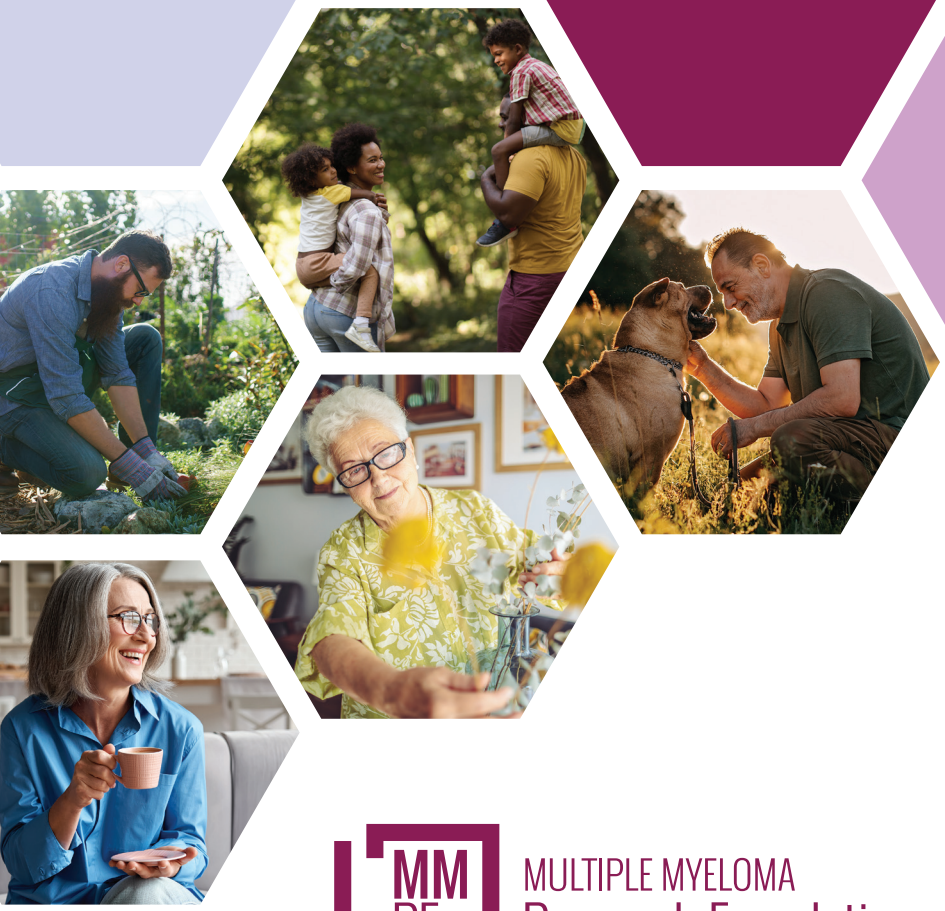


MULTIPLE MYELOMA
Research Foundation

MULTIPLE MYELOMA TREATMENT OVERVIEW

themmrf.org

MULTIPLE MYELOMA
Research Foundation

ABOUT THE **MMRF**

The Multiple Myeloma Research Foundation® (MMRF®) is the largest nonprofit in the world solely focused on accelerating a cure for each and every multiple myeloma patient. We drive the development and delivery of next-generation therapies, leverage data to identify optimal and more personalized treatment approaches, and empower myeloma patients and the broader community with information and resources to extend their lives.

Central to our mission is our commitment to advancing access for all so that every myeloma patient can benefit from the scientific and clinical advances we pursue. Since our inception, the MMRF has raised over $600 million for research, opened over 100 clinical trials, and helped bring more than 15 FDA-approved therapies to market, which have tripled the life expectancy of myeloma patients.

To learn more about the MMRF, visit **themmrf.org**.

To speak to a patient navigator at the Patient Navigation Center, call **1-888-841-6673** or email **patientnavigator@themmrf.org**.

Accredited by:

CONTENTS

INTRODUCTION

Patients with **multiple myeloma** have more treatment options than ever before. Over the last two decades, more than 15 treatments have been approved by the US Food and Drug Administration (FDA) for the treatment of myeloma, and many other therapies are under investigation.

This booklet is designed to help you better understand the current treatment options for multiple myeloma, as well as the emerging treatment options that are being tested in **clinical trials**. Words that may be unfamiliar are **bolded** and defined in the Glossary (page 30).

The information in this booklet is not intended to replace the services or advice of trained health care professionals. Please consult with your care provider regarding specific questions relating to your health, especially questions about myeloma diagnosis or treatment.

For more information about how myeloma develops, as well as its symptoms, diagnosis, and **prognosis**, refer to the companion booklet ***Multiple Myeloma Disease Overview*** and the MMRF website, **themmrf.org**.

WHAT FACTORS ARE CONSIDERED IN DEVELOPING A MYELOMA TREATMENT PLAN?

There's no single, standard approach to treating multiple myeloma. Every patient's treatment plan is unique and built around their medical factors and personal goals. Based on these considerations, your care team will work carefully to design a plan that's right for you.

After you receive a myeloma diagnosis, you'll partner with your doctor and care team to review the factors that define your disease and discuss what outcomes matter most to you. Your team will then design a plan tailored to your needs.

In the MMRF, you have an advocate by your side—one who is an expert on all things myeloma, who is committed to helping you get the care and support you need, and who understands what you're going through. The Patient Navigation Center is available to answer your questions about disease management, treatments, and clinical trials and to help you find financial and other available resources.

Telephone: **1-888-841-6673**
Monday–Friday, 9:00 AM to 7:00 PM ET
Email: **patientnavigator@themmrf.org**

GOALS OF MYELOMA THERAPY

Myeloma treatment focuses on reducing symptoms and achieving a response that helps stop disease progression while maintaining quality of life. This involves working with your care team to balance treatment effectiveness with managing side effects.

Goals and guiding principles of myeloma therapy.

Having different options can help you reach your treatment goals. If one regimen stops working, another can be used. There are many choices available today—and treatments continue to improve.

INDUCTION THERAPY

Most patients in the United States begin with a four-drug **(quadruplet) induction therapy** (also known as **frontline therapy**) regimen. This approach aims to reduce **malignant plasma cells** (that is, myeloma cells) and **M protein** (an abnormal **antibody** found in large quantities in the blood and urine of people with myeloma) levels as much as possible. Depending on their health and disease factors, patients sometimes receive a three-drug **(triplet)** combination.

After induction therapy, treatment may continue with:

- High-dose **chemotherapy** followed by an **autologous stem cell transplant (ASCT)**
- **Maintenance therapy**, which uses lower doses of the same or similar drugs to maintain response and prevent relapse.

The choice of what induction therapy to use depends on many factors, including the features of your myeloma, the risk of side effects, convenience, and your preferences.

Questions to ask your care team before induction therapy.

- What are my treatment choices?
- What are the risks and benefits of my treatment choices?
- What can I do to prepare for treatment?
- How will treatment affect my normal routine?
- What lab values and test results are important to track for a response or to monitor for side effects?
- What resources are available for me and my family?
- What is the best way to get in touch with you for questions or emergencies?
- Should I consider a clinical trial?

QUADRUPLETS AND TRIPLETS

For most patients, quadruplets are now considered the standard approach for induction therapy. These regimens combine four drugs that work together to attack myeloma cells in different ways.

Quadruplets commonly consist of the following:

- An anti-CD38 **monoclonal antibody;** for example, Darzalex (daratumumab) or Sarclisa (isatuximab)
- A **proteasome inhibitor**; for example, Kyprolis (carfilzomib) or Velcade (bortezomib)
- An **immunomodulatory drug**; for example, Revlimid (lenalidomide)
- A steroid; for example, dexamethasone

Triplets are still very effective and may be used for some patients—for example, older patients, patients with several other health concerns, or when side effects are a particular concern.

Effective induction regimens for multiple myeloma.

Regimen	Abbreviation
Quadruplets	
Darzalex, Velcade, Revlimid, dexamethasone	D-VRd
Darzalex, Kyprolis, Revlimid, dexamethasone	D-KRd
Sarclisa, Velcade, Revlimid, dexamethasone	Isa-VRd
Sarclisa, Kyprolis, Revlimid, dexamethasone	Isa-KRd
Triplets	
Velcade, Revlimid, dexamethasone*	VRd
Kyprolis, Revlimid, dexamethasone	KRd
Darzalex, Revlimid, dexamethasone	DRd

*For patients with poor kidney function, cyclophosphamide is sometimes used in place of Revlimid (CyBorD).

DARZALEX

Darzalex is an anti-CD38 monoclonal antibody used to treat patients with newly diagnosed myeloma and those with myeloma that has **relapsed** (recurred after initially responding to therapy) or is **refractory** (progressed during therapy).

Some patients in clinical trials had **infusion reactions** (chills and low-grade fever) while receiving Darzalex. You'll receive drugs before and after administration to reduce your risk of these reactions.

Darzalex.

When it's used	How it's given*	What to expect
• Newly diagnosed myeloma • Relapsed/refractory myeloma	• Injection under the skin (**subcutaneous**)† • Less commonly, given directly into a vein (**intravenous**) • Once a week for the first 8 weeks then every 2 weeks for 4 months, then monthly – The first prescribed dose may be split over 2 consecutive days	• Infusion reactions • Fatigue • Nausea • Fever • Cough • Upper respiratory tract infection • **Anemia** • Low **platelet** counts

*Dose schedule varies slightly depending on combination and **formulation**.
†Subcutaneous formulation is named Darzalex-Faspro.

SARCLISA

Sarclisa is an anti-CD38 antibody that is typically given with Pomalyst or Kyprolis and dexamethasone to patients with relapsed or refractory myeloma. It can also be given in different combinations to patients with newly diagnosed myeloma.

Sarclisa.

When it's used	How it's given	What to expect
• Newly diagnosed myeloma • Relapsed/refractory myeloma	• Intravenously • Once a week for the first 4 weeks then every 2 weeks thereafter • Premedication for infusion reactions	• Low numbers of **white blood cells** • Infusion-related reactions • Pneumonia • Upper respiratory tract infection • Anemia • Low platelet counts

VELCADE

Velcade was the first proteasome inhibitor to be approved by the FDA to treat patients with newly diagnosed myeloma and those with relapsed or refractory myeloma.

A common side effect of Velcade is **peripheral neuropathy**, which is damage to the nerves that can produce numbness, tingling, and, in some cases, pain. These symptoms typically start in the toes or fingertips. If you experience these symptoms, it's important to notify your doctor, as adjusting the dose can stop the neuropathy from getting worse. There are also treatments that can help reduce the discomfort or pain associated with neuropathy.

The FDA has approved a generic version of Velcade, known as bortezomib. It has the same active ingredient, dosage, and strength as Velcade, it works exactly as Velcade does, and it has the same benefits and risks.

Velcade.

When it's used*	How it's given	What to expect
• Newly diagnosed myeloma • Relapsed/refractory myeloma	• 1.3, 1.0, or 0.7 mg/m^2 once or twice a week: – Injection under the skin (subcutaneous) – Less commonly, given intravenously (for example, for patients who have a reaction to an injection)	• Peripheral neuropathy • Low platelet count • Gastrointestinal problems: nausea, diarrhea, vomiting, loss of appetite • Fatigue • Rash • Risk of shingles reactivation

*Generic version available.

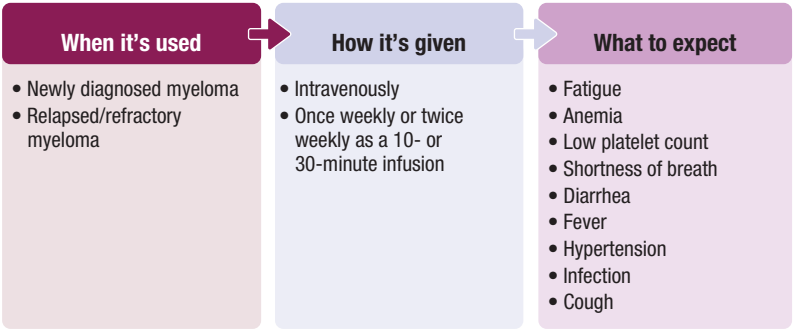
KYPROLIS

Kyprolis is another proteasome inhibitor used to treat patients with newly diagnosed myeloma and those with relapsed or refractory myeloma. Kyprolis is not typically used as first-line treatment.

Although uncommon, there's a risk of cardiovascular side effects with Kyprolis, including congestive heart failure. If you have a heart condition, you'll be evaluated to determine whether Kyprolis is an appropriate treatment. If you have heart problems, your doctor will monitor you closely while you take Kyprolis.

Peripheral neuropathy is rare and tends to be mild when it occurs.

Kyprolis.



REVLIMID

Revlimid is an immunomodulatory drug approved by the FDA for patients with multiple myeloma, whether their disease is newly diagnosed, relapsed, or refractory. Revlimid is also FDA-approved for use as maintenance therapy following ASCT.

Revlimid is given orally and usually taken once a day. The starting dose is typically 25 mg/day, but patients may move to a lower dose if they have a sustained response to treatment.

Fatigue is a common side effect of Revlimid that can sometimes be managed by adjusting the dose or changing the time of day that the pill is taken.

Revlimid can also decrease blood counts. When this occurs, **growth factors** are sometimes given to bring your blood counts up. You may develop a rash when taking Revlimid, sometimes (though not frequently) to an extent where it's necessary to stop taking the drug.

Revlimid can also increase the risk of blood clots. To reduce this risk, most patients take a low-dose (baby) aspirin every day. If you have additional risk factors, such as a prior blood clot or limited physical activity, your doctor may recommend a stronger blood thinner, such as Lovenox (injectable) or an oral drug like Eliquis or Xarelto.

The FDA has approved a generic version of Revlimid, known as lenalidomide. It has the same active ingredient, dosage, and strength as Revlimid, it works exactly as Revlimid does, and it has the same benefits and risks.

Revlimid.

When it's used*	How it's given	What to expect‡
• Newly diagnosed myeloma • Relapsed/refractory myeloma • Maintenance therapy following ASCT	• Oral capsule • For relapsed/refractory or newly diagnosed myeloma: 25 mg† once daily for 21 days out of a 28-day cycle (3 weeks on, 1 week off) • For myeloma maintenance therapy: 10 mg† once daily continuously for 28 days of repeated 28-day cycles	• Potential for blood clots • Reduced blood counts • Rash • Fatigue • Muscle pain or muscle cramping • Diarrhea • Small chance of new cancers§

*Generic version available.
†Dose may be adjusted as needed.
‡Black box warnings:
- Embryo-fetal toxicity; Revlimid is available only through a restricted distribution program
- Hematologic toxicity
- Venous and arterial thromboembolism

§In patients who receive high-dose melphalan and transplant

STEROIDS

Steroids such as dexamethasone or prednisone are a standard component of the quadruplets used in myeloma treatment. Steroids kill cancer cells, reduce swelling, and relieve symptoms like pain and pressure.

However, steroids can cause side effects, including sleep problems, mood changes, weight gain, high blood sugar, increased infection risk, and weakening of bones. To manage these side effects, doctors may lower the steroid dose, recommend taking the steroid early in the day, or add treatments to protect your stomach and bones. Monitoring blood sugar, using infection prevention measures, and promptly reporting new symptoms to your care team are also important to managing steroid side effects.

HIGH-DOSE CHEMOTHERAPY AND ASCT

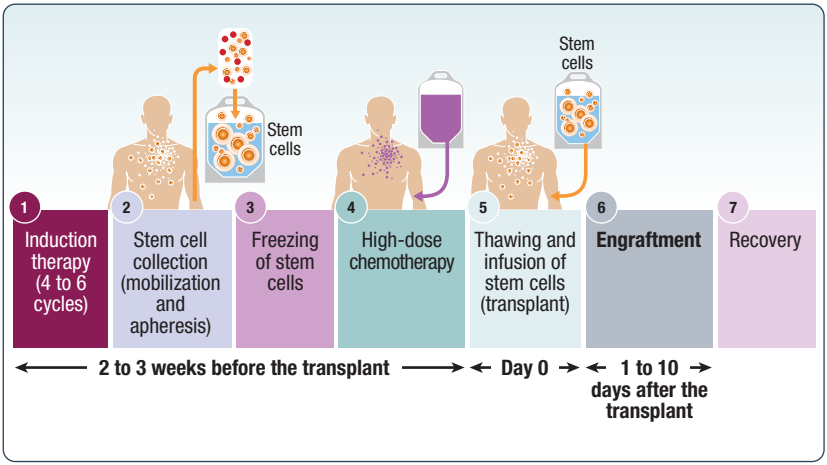
For many myeloma patients, high-dose chemotherapy (usually melphalan) with ASCT given as part of first-line treatment offers the best chance for long-lasting remission.

High-dose chemotherapy, though effective in killing myeloma cells, also destroys normal blood-forming cells (called **hematopoietic stem cells**) in the **bone marrow**. ASCT replaces these important cells. Results of this approach to myeloma therapy have improved with the release of several newer drugs.

Recovery after ASCT usually takes several months, starting with a hospital stay of about 2 to 3 weeks. However, some centers perform ASCT as an outpatient procedure, so a hospital stay may not be necessary or advised. You'll continue to heal at home for several weeks. During this time, your body uses the transplanted stem cells to rebuild healthy blood cells, which helps your **immune system** recover. Some days you may feel tired or weak, and others you may feel stronger as your blood counts improve.

Not all myeloma patients can receive high-dose chemotherapy and ASCT. It's important to discuss with your provider if you're a candidate for these procedures. If you are, you may choose to undergo the procedure after you receive four to six cycles of induction therapy. Or you may decide to complete induction therapy and consider transplant later, in which case your care team would collect stem cells and store them for future use.

ASCT.



MAINTENANCE THERAPY

Maintenance therapy is the prolonged use of treatment, often at a low dose, after induction therapy. The goal of maintenance therapy is to maintain your initial response to treatment for as long as possible and hopefully improve survival.

For an overview of maintenance therapy, see the ***Maintenance Therapy*** **High-Impact Topic** video.

bit.ly/MaintenanceTherapy_HIT

Revlimid is currently the only drug FDA-approved for maintenance therapy in myeloma. Treatment guidelines state that standard maintenance therapy should continue until your disease progresses, you have an unacceptable side effect, or you ask to stop. If you have difficulty tolerating maintenance therapy, your doctor may adjust the dose.

Clinical trials studying new potential options for myeloma maintenance therapy with agents such as Ninlaro, Velcade, Kyprolis, and Darzalex are also under way. Your doctor may suggest one of these agents if you can't tolerate Revlimid.

For high-risk patients (that is, patients whose myeloma has features that make it more aggressive and harder to treat), two-drug (**doublet**) maintenance therapy has been shown to improve survival. Typically, the doublets used combine Revlimid with Velcade, Kyprolis, or Darzalex. Alternatively, high-risk patients might be encouraged to enroll in a clinical trial.

As patients experience longer and deeper remissions with induction therapy followed by high-dose chemotherapy and ASCT and/or maintenance therapy, it may be appropriate to lower doses of treatment or stop treatment altogether after several years of remission. Clinical trials are investigating the risks and benefits of stopping maintenance therapy.

Maintenance therapy options.

Revlimid	• Reduction in myeloma progression • Improved survival (one of three studies, meta-analysis) • Increased risk of second cancers when used after melphalan • Approved for use as maintenance treatment after ASCT
Velcade	• Supported by several smaller studies • Combined with Revlimid recommended for high-risk myeloma
Ninlaro	• Oral proteasome inhibitor • Reduction in myeloma progression (one large study) • When other maintenance therapies aren't an option
Kyprolis + Revlimid	• Improved survival (one large study) compared with lenalidomide alone • Recommended for high-risk myeloma
Darzalex ± Revlimid	• Supported by two large studies • Combination recommended for high-risk myeloma

Additional agents under investigation: Empliciti and Tecvayli

HOW DO I KNOW IF A TREATMENT IS WORKING?

During and after treatment, doctors monitor your symptoms and may perform some of the same tests that were done when you were initially diagnosed with myeloma. These tests show how well the treatment is working and may detect side effects. They can also help determine if, after an initial response to treatment, your myeloma relapses.

Testing may include the following:

- Level of abnormal myeloma cells in the bone marrow
- Amount of M protein or free **light chains** in the blood
- Presence or absence of other symptoms, such as anemia or bone issues

For more information about how your care team knows if your treatment is working, refer to the ***Learn Your Labs*** booklet in our Patient Toolkit, as well as the MMRF website, **themmrf.org**.

WHAT IF I RELAPSE OR DON'T RESPOND TO THERAPY?

If you have relapsed or refractory myeloma, there are many effective options your doctor can use. These include targeted and immune-based therapies. Sometimes, older chemotherapy drugs can also help if newer treatments don't work as well. Your doctor may add on to previous regimens you have received, forming different combinations.

Additional myeloma drugs used if your myeloma returns.

CAR T-cell therapy	Abecma (idecabtagene vicleucel)*	Carvykti (ciltacabtagene autoleucel)†		
Bispecific antibodies	Elrexfio (elranatamab)*	Talvey (talquetamab)*	Tecvayli (teclistamab)*	Lynozyfic (linvoseltamab)*
Antibody-drug conjugates	Blenrep (belantamab mafodotin)‡			

*Used after 2 prior therapies.
†Used after 1 prior therapy.
‡Used after 4 or more prior therapies.

If your myeloma comes back or stops responding to treatment, your doctor will consider several factors to find a treatment that works well and keeps side effects as low as possible.

Factors to consider in choosing therapy for relapsed or refractory myeloma.

Treatment options for relapsed or refractory myeloma include:

- Any myeloma drug that has not been previously used
- A different combination of myeloma drugs (which can include a previously used drug)
- High-dose chemotherapy and stem cell transplant (if appropriate)

Some drugs for relapsed or refractory myeloma are used after only three or fewer treatments. This is because myeloma is still sensitive to most medicines at that stage, so options that are proven to work early are chosen for the best results. After four or more lines of therapy, myeloma often becomes resistant to many common drugs, so newer treatments or drugs with unique ways of working are used.

This stepwise approach helps doctors save the strongest or newest therapies for when they are truly needed—that is, when the myeloma becomes harder to control.

To accelerate development of new therapies for myeloma, all eligible patients should consider participating in a clinical trial.

PROTEASOME INHIBITORS

Proteasome inhibitors—including those used in induction therapy, like Kyprolis and Velcade—may be used to treat relapsed or refractory myeloma.

Ninlaro

Though not commonly used, Ninlaro may be used in combination with other myeloma drugs for patients who have received at least one therapy.

Ninlaro.

When it's used	How it's given	What to expect
• Relapsed/refractory myeloma	• Oral capsule	• Diarrhea • Constipation • Low platelet counts • Peripheral neuropathy • Nausea • Peripheral edema • Vomiting

IMMUNOMODULATORY DRUGS

Pomalyst

Pomalyst is used in combination with other treatments for some patients with relapsed or refractory myeloma.

Side effects vary by patient and are generally manageable. Similar to other immunomodulatory drugs, some patients who received Pomalyst in clinical trials developed blood clots. For this reason, aspirin or another blood thinner is given with Pomalyst.

Numerous clinical trials are studying the use of Pomalyst in other types of patients and in combination with other myeloma drugs.

Pomalyst.

When it's used	How it's given*	What to expect†
• Relapsed/refractory myeloma	• Oral capsule	• Fatigue and weakness • Low white blood cell counts • Anemia • Gastrointestinal effects (constipation, nausea, or diarrhea) • Shortness of breath • Upper respiratory infection • Fever • Blood clots

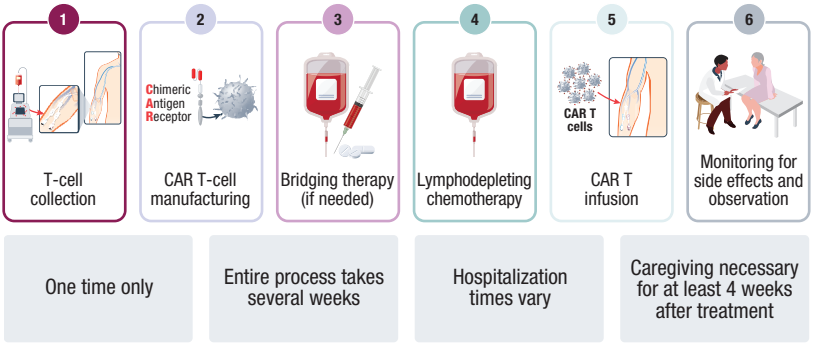
*Dosing can be adjusted if needed.
†Black box warnings:
- Embryo-fetal toxicity; Pomalyst is available only through a restricted distribution program.
- Venous and arterial thromboembolism

CAR T-CELL THERAPY

Chimeric antigen receptor (CAR) T-cell therapy uses **T cells** that have been collected from your blood. The T cells are modified in a lab to increase their ability to recognize myeloma cells and are then infused back into you—now with an enhanced ability to find and kill myeloma cells.

CAR T-cell therapy is given as a single one-time infusion and does not require additional maintenance therapy.

CAR T-cell therapy.



Abecma

Abecma is a BCMA-directed CAR T-cell therapy.

In a clinical trial of patients with relapsed or refractory myeloma who had received two to four previous therapies, Abecma increased survival and produced a response that lasted around 13 months.

Abecma is FDA-approved for patients who have received two or more previous therapies.

Abecma.

When it's used	How it's given	What to expect*
• Relapsed/refractory myeloma	• Intravenously • One-time infusion 2 days after completing lympho-depleting chemotherapy (cyclophosphamide IV and fludarabine) • Hospitalization required for treatment infusion	• Low blood counts • **Cytokine release syndrome** • **Neurotoxicity** • Infection • Fatigue • Musculoskeletal pain • **Hypogammaglobulinemia** • Diarrhea

*Black box warnings:
- Cytokine release syndrome
- Neurologic toxicities
- Hemophagocytic lymphohistiocytosis/ macrophage activation syndrome
- Prolonged cytopenia
- T-cell malignancies

Carvykti

Carvykti uses T cells that have been modified to recognize BCMA.

Carvykti was studied in a clinical trial of patients with relapsed or refractory myeloma who had received one to three previous therapies. Patients treated with Carvykti had improved survival, and this benefit was the same regardless of how many previous therapies they had received. Treatment response has been shown to last more than 5 years for some patients.

Carvykti is approved by the FDA for use in patients who have received at least one previous therapy, and are refractory to Revlimid.

Carvykti.

When it's used	How it's given	What to expect*
• Relapsed/refractory myeloma	• Intravenously • One-time infusion after completing lymphodepleting chemotherapy (cyclo-phosphamide IV and fludarabine IV daily for 3 days) • Hospitalization required after treatment infusion	• Low blood counts • Cytokine release syndrome • Neurotoxicity • Infection • Fever • Musculoskeletal pain • Fatigue • Hypogammaglobulinemia • Hypotension

*Black box warnings:
- Cytokine release syndrome
- **Immune effector cell-associated neurotoxicity syndrome (ICANS)**
- Parkinsonism and Guillain-Barré syndrome and associated complications
- Hemophagocytic lymphohistiocytosis/ macrophage activation syndrome
- Prolonged and/or recurrent cytopenias
- Secondary hematologic malignancies, including myelodysplastic syndrome and acute myeloid leukemia

BISPECIFIC ANTIBODIES

Bispecific antibodies are another type of antibody-based **immunotherapy** and are made by combining parts of two regular antibodies—like those normally produced by your immune system. One part attaches to myeloma cells (making them easier for your immune system to find). The other attaches to your immune cells—specifically, T cells—and helps these T cells find and fight the tagged myeloma cells.

Bispecific antibodies are used later in treatment, after you've received at least four therapies.

Bispecific antibodies target certain proteins that are found on the surface of myeloma—and, sometimes, healthy—cells.

- BCMA is a protein found on almost all myeloma cells. Bispecific antibodies that target BCMA include Lynozyfic, Tecvayli, and Elrexfio
- GPRC5D is a protein found on myeloma cells but also on some healthy cells, including cells in the skin and nails. Talvey is a bispecific antibody that targets GRPC5D
- FcRH5, another protein found on myeloma cells, is being studied in clinical trials as a possible target for bispecific antibodies

Because bispecific antibodies can cause serious side effects, their availability is restricted through what are called Risk Evaluation and Mitigation Strategy (REMS) programs. These programs ensure that these treatments are used safely.

To minimize side effects, bispecific antibodies are typically given in doses that start small and gradually ramp up to a full dose. This is referred to as **step-up dosing**. You'll be hospitalized for these step-up doses, and for your first full treatment dose, so that your care team can monitor for side effects.

Lynozyfic

Lynozyfic targets BCMA on the surface of myeloma cells and CD3 receptors on the surface of T cells.

Lynozyfic.

When it's used	How it's given	What to expect†
• Relapsed/refractory myeloma	• Intravenous injection with step-up dosing on days 1 and 8, followed by the first full dose on day 15 • Once weekly from week 4 to week 13. Starting on week 14, it's given every 2 weeks*	• Cytokine release syndrome • Neurotoxicity • Infection • Low blood counts • Musculoskeletal pain • Cough • Diarrhea • Fatigue

*For patients who achieve a **very good partial response** or better, dosing may be administered every 4 weeks. Hospitalization is required for 24 hours after the first and second step-up doses.
†Black box warnings:
- Cytokine release syndrome
- Neurologic toxicity
- Lynozyfic is available only through a restricted distribution program.

Tecvayli

Tecvayli targets BCMA on the surface of myeloma cells and CD3 receptors on the surface of T cells.

Tecvayli.

When it's used	How it's given	What to expect†
• Relapsed/refractory myeloma	• Subcutaneous injection with step-up dosing on days 1 and 4, followed by the first full dose on day 7; given once weekly thereafter*	• Cytokine release syndrome • Neurotoxicity • Infection • Low blood counts • Fever • Musculoskeletal pain • Injection site reaction • Fatigue

*Patients who have achieved and maintained a complete response or better for at least 6 months may have dosing frequency decreased to every 2 weeks until disease progression or unacceptable toxicity. Hospitalization is required for 48 hours after all doses in the step-up dosing schedule.

†Black box warnings:
- Cytokine release syndrome
- Neurologic toxicities
- Tecvayli is available only through a restricted distribution program.

Elrexfio

Elrexfio (elotuzumab) targets BCMA on the surface of myeloma cells and CD3 receptors on the surface of T cells.

Elrexfio.

When it's used	How it's given	What to expect†
• Relapsed/refractory myeloma	• Subcutaneous injection with step-up dosing on days 1 and 4, followed by the first full dose on day 8; given once weekly thereafter*	• Cytokine release syndrome • Neurotoxicity • Infection • Low blood counts • Musculoskeletal pain • Injection-site reaction • Fatigue

*After 24 weeks, patients who are responding to therapy may have dosing frequency decreased to every 2 weeks. Hospitalization is required for 48 hours after first step-up dose and 24 hours after second step-up dose.

†Black box warnings:
- Cytokine release syndrome
- Neurologic toxicity
- Elrexfio is available only through a restricted distribution program.

Talvey

Talvey targets GPRC5D on the surface of myeloma cells and CD3 receptors on the surface of T cells.

Talvey.

When it's used	How it's given	What to expect†
• Relapsed/refractory myeloma	• Subcutaneous injection with step-up dosing on days 1 and 4, followed by the first full dose on day 7; given once weekly thereafter*	• Cytokine release syndrome • Neurotoxicity • Infection • Altered or loss of sense of taste • Low blood counts • Musculoskeletal pain • Injection site reaction • Fatigue • Nail changes • Fever • Weight loss

*Alternative three-step step-up dosing is available. Hospitalization is required for 48 hours after first step-up dose and 24 hours after second step-up dose.
†Black box warnings:
- Cytokine release syndrome
- Neurologic toxicity
- Talvey is only available through a restricted distribution program.

ANTIBODY-DRUG CONJUGATES

Antibody–drug conjugates (ADCs) use a monoclonal antibody that is coupled to a cancer drug or a **toxin** to kill myeloma cells.

Blenrep

Blenrep is the first ADC to be approved by the FDA for multiple myeloma. It's currently approved to be given with Velcade and dexamethasone.

Blenrep.

When it's used*	How it's given	What to expect
• Relapsed/refractory myeloma	• Intravenously • Once every 3 weeks in a 30-minute infusion	• Corneal epithelium change on eye exam • Decreased visual acuity • Blurred vision • Fever • Fatigue • Low blood counts • Dry eye • Light sensitivity • Feeling like something is in your eye • Diarrhea • Infection

*Black box warnings:
- Changes in the corneal epithelium resulting in changes in vision
- Blenrep is available only through a restricted distribution program.

MONOCLONAL ANTIBODIES

Empliciti

Empliciti targets SLAMF7, a protein found on myeloma cells and immune cells, helping the immune cells detect and attack myeloma cells. Empliciti is not commonly used.

Empliciti.

When it's used	How it's given	What to expect
• Relapsed/refractory myeloma	• Intravenous injection • Once a week for the first 8 weeks then every 2 weeks	• Fatigue • Diarrhea • Fever • Constipation • Cough • Peripheral neuropathy • Infusion reactions • Nasopharyngitis • Upper respiratory tract infection • Decreased appetite • Pneumonia • Small chance of second new cancer

OTHER DRUGS

Drugs with other **mechanisms of action** work in different ways than drugs in the other classes. Myeloma drugs with novel mechanisms of action target proteins involved in cell growth and division. These drugs may target proteins that are specific to myeloma cells or common to all cells.

Xpovio

Xpovio (selinexor) is the first in a drug class called nuclear export inhibitors. Xpovio targets and disrupts the function of a protein called XPO1, which ultimately leads to myeloma cell death. Xpovio is not commonly used.

Xpovio.

When it's used	How it's given	What to expect
• Relapsed/refractory myeloma	• Oral tablet • Taken once or twice a week	• Low platelet count • Low white blood cell counts • Fatigue • Anemia • Decreased appetite • Decreased weight • Diarrhea • Vomiting • Low sodium levels • Constipation • Upper respiratory infection

CHEMOTHERAPY

Chemotherapy agents are still commonly used in relapsed or refractory myeloma when other treatments are no longer effective or when the myeloma is aggressive.

Chemotherapy agents used include cyclophosphamide, cisplatin, etoposide, doxorubicin, and bendamustine. These agents are often used in combination with other newer treatments, other chemotherapy agents, and a steroid. At higher doses, chemotherapy is typically administered in an inpatient setting.

BEYOND TREATMENT: MAINTAINING A HEALTHY LIFESTYLE

In addition to following the treatments you and your care team choose, there are things you can do to maintain your overall health and quality of life as you navigate living with myeloma.

NUTRITION

Maintaining good nutrition can have important benefits for myeloma patients. Eating a healthy diet can help keep your immune system in peak shape, which helps you avoid infections (or at least recover from them faster).

Some myeloma treatments can reduce your appetite, so it's important to make the most of what you eat. Eating small meals every few hours and keeping energy-dense high-protein snacks like nuts, eggs, and cheese handy are strategies that can help you maintain a healthy diet.

Your nutritional needs may have changed since your myeloma diagnosis, and they may continue to change throughout your treatment. Your care team may recommend that you meet with a nutritionist to review your diet plan and recommend supplements if needed.

EXERCISE

Getting regular exercise can improve your physical and mental health while you receive myeloma treatment, providing such benefits as maintaining fitness, strengthening bones, boosting your immune system, and reducing fatigue.

How much exercise is "enough" will depend on your fitness level and where you are in your myeloma journey. For example, weight-bearing exercise may not be an option if you are at high risk for bone fractures.

Before starting any kind of exercise, it's important to talk with your care team.

MENTAL HEALTH AND EMOTIONAL SUPPORT

Multiple myeloma often causes fear, anxiety, and distress. Many sources of support are available, including caregivers, mental health professionals, and myeloma support groups.

Stress-reducing activities can help reduce anxiety and improve your mental well-being. Some options include acupuncture, deep-breathing exercises, massage, meditation, mindfulness, and yoga.

As with physical exercise, it's important to keep a dialogue going with your care team about what strategies you use to manage the mental and emotional challenges of multiple myeloma.

SLEEP

For many myeloma patients, sleep disturbances are common and can result from a number of causes, including pain, drug, depression, and anxiety. Many myeloma drugs can cause insomnia, daytime sleepiness, fatigue, and/or side effects that are worse at night, which can make getting restful sleep more challenging.

Determining the cause of any sleep disturbances you experience can help your care team devise strategies for reducing them.

Fatigue—a feeling of persistent tiredness, weakness, and lack of energy—is another challenge that you may encounter, as it's a common effect of both multiple myeloma itself and many of the treatments used to treat it. If you're having difficulty sleeping, it's more likely that you'll feel fatigued.

IS A CLINICAL TRIAL RIGHT FOR ME?

Clinical trials are essential to the development of new myeloma treatments, providing new therapeutic options for myeloma patients at all stages of the disease. The greater the number of people there are enrolling in clinical trials, the faster new treatments can be made available to patients. It's only through patient participation in clinical trials that we've achieved the high number and various types of myeloma treatments available today.

To learn more about clinical trials, see the ***Clinical Trials*** **High-Impact Topic** video.

bit.ly/ClinicalTrial_HIT

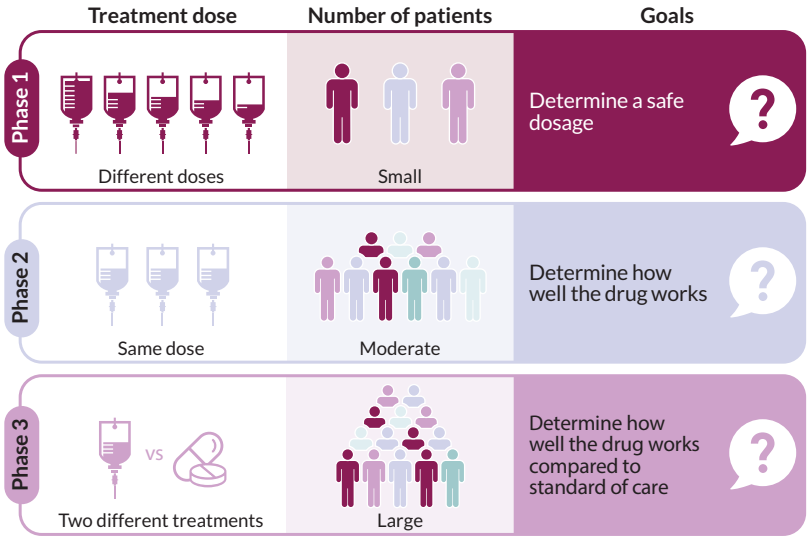
Clinical trials compare new treatments or combinations with current standards of care. If you enroll in a clinical trial, you have the opportunity to be among the first to receive the newest drugs and therapies in development, before they're available commercially.

However, it's important to understand that new treatments may be equivalent to, more effective than, or not as effective as standard treatment options. They may also have unexpected side effects.

In all myeloma clinical trials, participants receive either the experimental therapy being tested or the best available standard treatment. In other words, you'll never receive *no* treatment in a myeloma clinical trial.

Clinical trials take place in different stages, with each phase serving a distinct purpose.

Clinical trial stages.



Based on the results of clinical trials, the FDA approves treatments that are safe, effective, and shown to be better than the standard treatments available.

Clinical trials take place at cancer centers, hospitals, clinics, or doctors' offices. Before you enroll in a clinical trial, all details of the treatment are explained, and you must consent to participate. If you agree to participate in a clinical trial, you're free to withdraw at any time.

The MMRF would like to thank Joshua Richter, MD, Associate Professor of Medicine, Hematology and Oncology, in the Myeloma Division at the Tisch Cancer Institute at the Icahn School of Medicine at Mount Sinai and Director of Myeloma at the Blavatnik Family Chelsea Medical Center at Mount Sinai and our patient advocate, Kerri Hoffman of Carlsbad, California, for their contributions to this booklet.

REIMBURSEMENT-ASSISTANCE PROGRAMS

Many drug companies offer assistance programs to help patients cover the cost of treatment and copays. Other patient-assistance programs can provide free or discounted treatment for eligible patients.

Patient Access Network

Services: Help and hope to people with chronic or life-threatening illnesses for whom cost limits access to critical medical treatments
Phone: 1-866-316-PANF (1-866-316-7263)
Website: panfoundation.org/contact

Amgen Inc

Products: Neupogen/Neulasta/Kyprolis/Xgeva
Website: amgensupportplus.com/patient
Phone: 1-866-264-2778

Bristol-Myers Squibb

Products: Empliciti/Pomalyst/Revlimid/Thalomid/Abecma
Website: bmsaccesssupport.com/patient
Phone: 1-800-861-0048

GlaxoSmithKline

Product: Blenrep
Website: togetherwithgsk.com/blenrep/patient/
Phone: 1-844-4GSK-ONC (844-447-5662)

Janssen

Product: Darzalex
Website: jnjwithme.com/patient/darzalex/withme/cost-support/
Phone: 1-877-227-3728

Product: Carvykti
Website: carvykti.com/resources-and-support
Phone: 1-800-559-7875

Product: Talvey
Website: jnjwithme.com/patient/talvey/withme/cost-support/
Phone: 1-844-628-1234

Product: Tecvayli
Website: jnjwithme.com/patient/tecvayli/withme/cost-support/
Phone: 1-877-227-3728

Karyopharm

Product: XPOVIO
Website: karyforward.com
Phone: 1-877-KARY4WD (1-877-527-9493)

Pfizer

Product: Elrexfio
Website: elrexfio.com/financial-savings-and-support
Phone: 1-877-744-5675

Regeneron

Product: Lynozyfic
Website: lynozyfic.com/support-and-resources/patient-support
Phone: 1-844-RGN-HEME (1-844-746-4363)

Sanofi

Product: Sarclisa
Website: sanoficareassist.com
Phone: 1-833-WE+CARE (1-833-930-2273)

Takeda Oncology Company

Product: Velcade/Ninlaro
Website: here2assist.com/patient
Phone: 1-844-817-6486, Option 2

GLOSSARY

adaptive immunity Part of the immune system that is made up of specialized cells that recognize and attack foreign invaders

anemia Decrease in the number of *red blood cells* in the blood

antibody Protein produced by plasma cells that helps protect the body from infection and disease (also called *immunoglobulin*)

antibody-drug conjugates (ADCs) Monoclonal antibodies that are coupled to a cancer drug; an example is Blenrep

autologous stem cell transplant (ASCT) Procedure in which stem cells collected from a patient are transplanted back into that patient; the most common type of transplant performed in myeloma

bispecific antibodies Monoclonal antibodies that can bind to two different proteins at the same time

bone marrow Soft, spongy tissue found in the center of many bones and the site of blood cell production

chemotherapy Use of drugs to kill rapidly dividing cells, such as cancer cells

chimeric antigen receptor T (CAR-T)-cell therapy A form of immunotherapy in which a patient's immune cells (mostly T cells) are collected, engineered in a lab to be better able to identify and attack myeloma cells, and then returned to the patient; examples are Abecma and Carvykti

clinical trials Studies of the safety and effectiveness of a drug using consenting human participants

cytokine Protein produced and secreted by cells of the immune system

cytokine release syndrome Flu-like reaction that can develop as a result of treatment; it may cause fevers, chills, and low blood pressure

doublet Combination of two drugs used to treat a disease

engraftment Process by which stem cells that have been infused into the body start to grow and make new blood cells

formulation The preparation of a drug

frontline therapy Initial treatment given to a newly diagnosed patient (also known as *induction therapy* and *first-line therapy*)

growth factors Substances that stimulate cells to multiply

hematopoietic Related to the production of blood cells

hypogammaglobulinemia Condition in which the levels of serum immunoglobulin or antibodies in the body are reduced

immune effector cell–associated neurotoxicity syndrome (ICANS) Side effect of the nervous system seen after certain immunotherapies (such as CAR T-cell therapy and bispecific antibody therapy) that can include confusion or delirium, speech problems, motor weakness, tremor, headache, seizures, and reduced level of consciousness

immune system Network of cells that protect the body from foreign substances and destroy infected and cancerous cells

immunoglobulin Protein that helps protect the body from infection (also called *antibody*)

immunomodulatory drug Drug that fights cancer by boosting the immune system; examples include Thalomid, Revlimid, and Pomalyst

immunotherapy Prevention or treatment of disease with drugs that stimulate the immune system

induction therapy The first treatment a patient receives for myeloma after he or she is diagnosed; also refers to the use of anti-myeloma drugs prior to high-dose chemotherapy and stem cell transplant (see also *frontline therapy*)

infusion reactions Symptoms that sometimes develop after a patient receives intravenous drugs; commonly include chills, fever, nausea, weakness, headache, skin rash, and/or itching; although rare, severe reactions such as difficulty breathing or low blood pressure can occur

intravenous Into a vein

light chains The shorter of two protein chains that make up an antibody, characterized as either kappa or lambda type; when these proteins chains are not part of an antibody, they are called *free light chains*

M proteins Abnormal antibodies produced by myeloma cells that are found in large quantities in the blood and urine of people with myeloma

maintenance therapy Treatment given over a long period of time to patients in remission to reduce the risk of relapse

malignant Cancerous; able to grow and spread to other parts of the body

mechanisms of action Biochemical processes through which a drug produces an effect on the body

monoclonal antibody Antibody produced in a lab that is used to diagnose and treat some diseases

multiple myeloma Blood cancer that develops in the bone marrow as a result of plasma cells transforming into myeloma cells

neuropathy Disorder of the nerves that can disrupt sensation or cause burning/tingling; when the hands and feet are affected, it is referred to as *peripheral neuropathy*

neurotoxicity Damage to the nervous system, including the brain and/or nerves

peripheral neuropathy Disorder of the nerves that causes a burning/tingling sensation in the hands and feet

phase 1 The first round of a clinical trial, conducted with a small number of participants to assess a drug's safety and non-toxic dosage levels

phase 2 The second stage of a clinical trial, conducted with a larger number of participants to assess a drug's effectiveness and further evaluate its safety

phase 3 The most advanced stage of drug development, conducted with a large number of participants to confirm a drug's effectiveness, identify and monitor its side effects, compare it to commonly used treatments, and collect information that will allow the drug to be used safely; usually required for FDA approval of drugs

plasma cell Antibody-secreting immune cell that develops from a B cell; in myeloma, it is this cell that has become cancerous or abnormal

platelet Small cell fragment in the blood that helps it to clot

prognosis Prediction of the course and outcome of a disease

proteasome inhibitor Drug that slows myeloma cell growth and kills myeloma cells by disrupting cell function; examples include Velcade, Ninlaro, and Kyprolis

quadruplet Combination of four drugs used to treat a disease

red blood cell Blood cell that carries oxygen

refractory Not responding to therapy

relapsed Disease that progresses after initially responding to therapy

remission Period when the signs and symptoms of a disease lessen or disappear

stem cells Cells that grow and divide to produce *red blood cells*, white blood cells, and platelets; found in bone marrow and blood

step-up dosing Method of giving a drug in doses that start small and gradually increase to a full dose to minimize side effects

subcutaneous Under the skin

T cell Type of white blood cell that can be divided into two subgroups, helper and cytotoxic T cells; helper T cells are responsible for *adaptive immunity*; cytotoxic T cells kill cells that have been targeted for death

toxin A poisonous substance

triplet Combination of three drugs used to treat a disease

very good partial response Treatment outcome in which there is a greater than 90% decrease in M protein

white blood cells One of the major cell types in the blood; attacks infection and cancer cells as part of the immune system

MMRF PATIENT SUPPORT AND RESOURCES

The MMRF supports the myeloma community by providing a broad range of resources for myeloma patients and their family members and caregivers. The MMRF is available to help guide you through your multiple myeloma journey every step of the way.

YOUR QUESTIONS ANSWERED

The Patient Navigation Center is available to answer your questions about disease management and treatments, help you find clinical trials, and connect you with financial and other resources.

Telephone: 1-888-841-6673
Monday—Friday, 9:00 AM to 7:00 PM ET
Email: **patientnavigator@themmrf.org**

themmrf.org/support/patient-navigation-center

CONNECT WITH AN MMRF MYELOMA MENTOR

Connect one-on-one with a trained patient and/or caregiver mentor that can share their patient journeys and experiences.

themmrf.org/support/myeloma-mentors

FIND A CLINICAL TRIAL

The MMRF Clinical Trial Finder lets you search for a clinical trial in your area.

themmrf.org/diagnosis-and-treatment/clinical-trials-and-emerging-therapies/clinical-trial-finder/

VIEW PAST PROGRAMS ON DEMAND

Access our archive of recorded Patient Summits and webcasts. Hear expert perspectives on key clinical research and the rapidly evolving myeloma treatment landscape. All available online, and free.

themmrf.org/educational-resources

SUPPORT THE MMRF

Help support the MMRF's efforts to accelerate research and find a cure! Participate in an event or donate today.

Telephone: 1-203-229-0464
Donate now/Take action: **themmrf.org/get-involved**

ATTEND A MULTIPLE MYELOMA PATIENT SUMMIT

Available in-person and virtually, MMRF Patient Summits discuss new treatments, promising clinical trials, and all the information you need to make well-informed decisions about your treatment and care.

themmrf.org/educational-resources

Don’t miss out on the latest myeloma updates!
Sign up today to receive news updates and notice of educational programs.

Name:

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Or sign up at **themmrf.org**

I AM A:

- ☐ Myeloma Patient
- ☐ Myeloma Patient Caregiver
- ☐ Myeloma Patient Family Member (non-caregiver)
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- ☐ Healthcare Professional or Researcher
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