

THE PATH TO

PRECISION MEDICINE

IN MULTIPLE MYELOMA



MULTIPLE MYELOMA
Research Foundation

themmrf.org

ABOUT THE MULTIPLE MYELOMA RESEARCH FOUNDATION

The Multiple Myeloma Research Foundation (MMRF) was established in 1998 by identical twin sisters Kathy Giusti and Karen Andrews shortly after Kathy's diagnosis with multiple myeloma. Kathy and Karen soon learned that little progress against this disease had been made in decades, and that myeloma patients had few treatment options. They decided that it was time to accelerate change.

Working with its partners in industry, research, government agencies, and academia, the MMRF has helped launch ten new treatments in the past decade, an achievement that has almost tripled the life expectancy for myeloma patients. As a patient-founded organization, the MMRF stands with those who are battling multiple myeloma—patients, families, caregivers, doctors, and researchers—and is focused squarely on speeding the discovery of a cure. We see a world where every person has precisely what he or she needs to prevent or defeat multiple myeloma.

As the multiple myeloma community's most trusted source of information, the MMRF supports patients from the time of diagnosis throughout the course of the disease. All information on the MMRF website (www.themmr.org) is organized by disease stage, so patients can get the information they need, when they need it.

To learn more about the MMRF, visit www.themmr.org or call (203) 229-0464.

To speak to a Nurse Patient Navigator at the Patient Support Center, call 1-866-603-MMCT (6628) or email patientnavigator@themmr.org.

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INTRODUCTION

Recent research has shown that **multiple myeloma** is a highly variable disease, meaning that it is different in every patient. For this reason, myeloma treatment cannot be applied in a one-size-fits-all fashion. A number of treatments are currently available for the different forms of myeloma—and more are in development.

Currently, myeloma treatments are tailored to the characteristics of an individual patient's myeloma with an emphasis on making sure he or she gets the right treatment at the right time, minimizing treatment side effects, and avoiding under- or over-treating.

Increasingly, research into myeloma therapy is focusing on **precision medicine**, a specific type of treatment that uses genetic tests to more specifically identify a patient's myeloma genetic **subtype** and **immune profile**. This better enables the health care team to choose (and adjust as needed) the myeloma drug regimen(s) that will be most effective for that patient. Precision medicine is an active area of research, and clinical trials in myeloma are ongoing.

This booklet is designed to help patients with multiple myeloma—as well as their friends, families, and caregivers—better understand the concept and the promise of precision medicine. Words that may be unfamiliar are **bolded** and defined in the Glossary (page 10).

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

For more information about multiple myeloma and its treatment, please refer to the companion brochures (*Multiple Myeloma Disease Overview* and *Multiple Myeloma Treatment Overview*) and the MMRF website (www.themmrf.org).

PRECISION MEDICINE: THE RIGHT TREATMENT AT THE RIGHT TIME FOR THE RIGHT PATIENT

Many of the drugs used to treat myeloma have been shown in clinical trials to work in most patients. That is, drugs are chosen for use in a given patient because studies have shown these drugs to be effective in other patients whose myeloma is at a similar stage or has a similar level of risk. Precision medicine is changing that model. By focusing on finding the drugs that work best for each individual patient—based on his or her specific genetic makeup and immune profile—precision medicine emphasizes a more personalized treatment approach.

Precision medicine shifts the focus of myeloma treatment from what works best for most patients to what works best for you.

MMRF CoMMpass STUDYSM: ADVANCING PRECISION MEDICINE

There are at least 12 different forms, or subtypes, of myeloma. Each subtype differs in terms of its genomic features, clinical features (that is, its symptoms and disease course), and **prognosis**. Further complicating the diagnostic picture is that each myeloma patient can have several different myeloma cell populations, or **clones**, within a subtype. Myeloma cell clones differ from one another genetically. Each clone can evolve and change with each disease stage and in response to treatment. The number of clones can rise and fall in response to treatment; this is referred to as **clonal tides**.

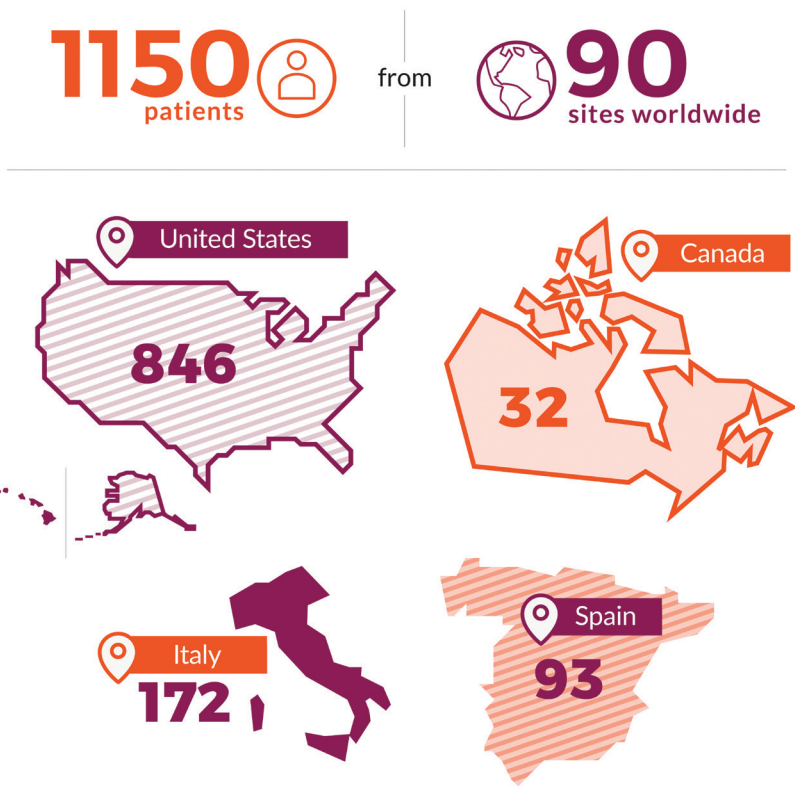
In the future, identifying a patient's subtype could be extremely useful in determining which treatment is most likely to yield a **complete response**, a primary goal of myeloma treatment. Consequently, some current efforts to develop new myeloma treatments focus on finding drugs that are well matched against the specific myeloma subtypes. To that end, the MMRF in 2011 initiated the **CoMMpass StudySM**, a landmark, large-scale, **longitudinal study** of patients with newly diagnosed active multiple myeloma. In this study, extensive data about myeloma patients is collected: clinical, genetic, and **demographic** information; what treatments each patient receives and how well they work; whether the patients receive a stem cell transplant; and much more.

At the core of the CoMMpass StudySM is collecting genetic information and putting together a complete, comprehensive genetic record (known as a **genomic profile**) for each patient. The level of detailed information in these genomic profiles—which has never before been available—is providing insight into myeloma, how it changes over time, and how it can be treated most effectively. Importantly, the CoMMpass StudySM includes information from a large (and growing) number of myeloma patients—far more than could be collected at a single myeloma center—and thus offers the opportunity for researchers, health care providers, and patients to benefit from a body of information that is unprecedented and that represents the dawning of an exciting new era in myeloma care.

Every myeloma patient in the **CoMMpass StudySM** has his or her genome sequenced at diagnosis and at each relapse so that changes in myeloma genomic makeup can be recorded and potentially related back to treatment response.

The goals of the CoMMpass StudySM are to learn which myeloma subtypes respond best to which therapies and to use this information to better target treatments to each patient's biological makeup. As of 2015, 1,150 patients have been enrolled in the CoMMpass StudySM. Initial **bone marrow** samples of these patients have been collected, their genomic information has been analyzed, and their treatment and disease course will be followed for at least 8 years.

MMRF CoMMpass StudySM

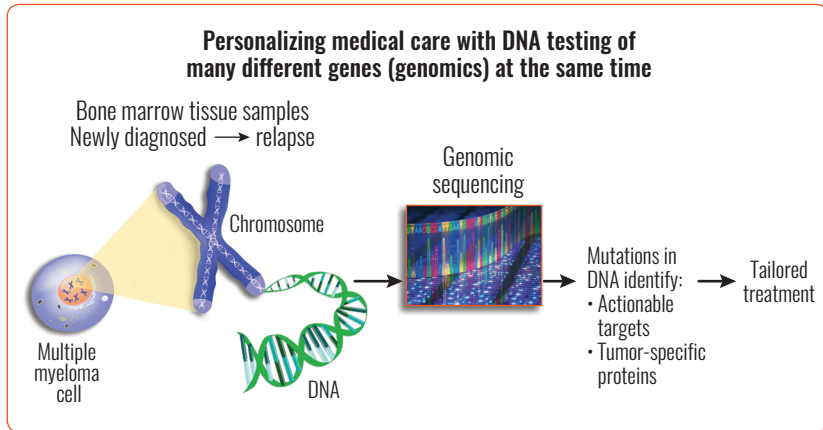


Through the **CoMMpass StudySM**, the MMRF is able to track patients with multiple myeloma and see what treatment they received, how long they received it, and how well it worked. Ultimately, all these myeloma patients' treatments and results will be used to guide decisions for other newly diagnosed patients. To learn more about **genomics** research and the **MMRF CoMMpass StudySM**, speak to an MMRF Nurse Patient Navigator at 866.603.6628 or visit www.themmrf.org/CoMMpass.

GENOMIC SEQUENCING AND TISSUE BANKING

Putting together a genomic profile begins with obtaining myeloma cells from **tissue** samples taken from the patient's bone marrow. Once the myeloma cells have been collected, their **DNA** and **RNA**—the most basic genetic material and the building blocks of life—are examined using highly sophisticated and precise tests. The structure of the DNA is analyzed (using a test called **sequencing**) to determine whether any defects (errors) are present. These errors, called **mutations**, are detected by comparing the sequencing results of the myeloma cells to the results from normal cells. Some mutations can cause cancer to develop, and some drugs are available that can block the cancer-causing activity of these mutations. Mutations that can be targeted in this way are called **actionable targets** (examples include *BRAF*, *NRAS*, *KRAS*, and *FGFR3*). Other mutations can cause changes in myeloma cells such that the body's **immune system** can recognize and attack them.

Precision medicine



The Multiple Myeloma Research Consortium (MMRC), a unique collaboration of 25 centers in the United States and Canada conducting clinical research, has several trials under way to assess the activity of drugs that block the actionable targets in myeloma patients, as well as drugs known to stimulate an **immune response**. The MMRC has three precision medicine trials under way that involve the actionable targets of MDM2, BRAF, and FGFR3. More such trials against other targets and new combinations are planned.

MMRF CoMMpass RESULTS: WHAT HAVE WE LEARNED?

Data from the CoMMpass StudySM has revealed that myeloma patients can have the same mutations that are present in patients with other types of cancer. This information is highly significant and may be used to assess patient prognosis and response to treatment.

Further data from the CoMMpass StudySM and other trials is expected to provide additional insight into new ways to better personalize therapy and offer more precise options to patients.

Some CoMMpass StudySM findings

- Patients who received a three-drug regimen as frontline treatment lived longer without disease recurrence than did those who received a two-drug regimen
- Patients who received a three-drug regimen and a frontline autologous stem cell transplant lived longer without disease recurrence than did those that did not receive a transplant
- DNA from myeloma cells reveals that some patients have more mutations, which can cause high production of **tumor-specific proteins** and may decrease survival in patients receiving currently available therapies
- Twelve different subtypes of multiple myeloma have been identified. With subtypes identified, researchers can investigate whether treatments that target those genetic changes help to improve prognosis



12 Subtypes of multiple myeloma	
MyD88	CDKN2C
IDH1/2	CCND1
IGF1R	BRAF
ALK	KRAS
FGFR3	NRAS
PI3K-AKT	Others

MMRF PATIENT SUPPORT AND RESOURCES

The MMRF is dedicated to supporting 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

Speak to an MMRF Nurse Patient Navigator at the Patient Support Center for answers to your questions about disease management, treatments, clinical trials, and assistance with finding financial and other available resources.

Telephone: 1.866.603.6628

Monday–Friday, 9:00 a.m. to 7:00 p.m. ET

Email: patientnavigator@themmrf.org

FIND AND PARTICIPATE IN A CLINICAL TRIAL

Search for a clinical trial in your area or let MMRF Nurse Patient Navigators help guide you through the process.

Clinical Trial Search: themmrf.org/trialfinder

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:

Visit www.themmrf.org

The MMRF would like to thank Faith E. Davies, MBBCh, MRCP, MD, FRCPPath, Professor of Medicine and Medical Director of the Myeloma Institute Little Rock at the University of Arkansas for Medical Sciences in Little Rock, Arkansas, and our patient advocates Allan and Deb Osborne of Millis, Massachusetts and Cindy Chmielewski of Lawrenceville, New Jersey for their contributions to this brochure.

GLOSSARY

actionable target A genetic mutation that can be a specific site of action for a drug or treatment

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

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

clonal tide Increase and/or decrease in the number of myeloma clonal cells in response to treatment

clone A specific kind of myeloma cell within a subtype

CoMMpass StudySM Clinical Outcomes in Multiple Myeloma to Personal Assessment of Genetic Profiles study; a large-scale, longitudinal study initiated in 2011 to better understand the molecular and genetic components of multiple myeloma at diagnosis and at other key time points

complete response (CR) A treatment outcome in which the level of plasma cells in the bone marrow is no more than 5%, there is no evidence of myeloma proteins in the serum or urine as measured by standard laboratory techniques, and all signs and symptoms of cancer have disappeared (though cancer still may be in the body); also called *complete remission*

demographic A particular group within a population

DNA Genetic material of the cell located in the chromosomes

genomic profile The complete set of genetic material within an individual

genomics Study of DNA sequences to detect errors or mutations and to see how DNA changes over time

immune profile The inherent activity of a patient's immune system toward cancer cells

immune response Reaction of the cells and fluids of the body against a substance or agent (for example, bacteria, a virus, or a foreign cell) that is not recognized as a part the body

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

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

longitudinal study Repeated observations over a long time with a large number of patients

multiple myeloma A blood cancer that develops in the bone marrow, the soft, spongy tissue found in the center of many bones and the location where blood cells are produced. In myeloma, plasma cells, which are normal cells that produce antibodies (or *immunoglobulins*), transform into cancerous myeloma cells

mutation A defect or error in a gene

precision medicine Highly specialized approach to myeloma therapy in which DNA test results are used to guide treatment

prognosis Prediction of the course and outcome of a disease

RNA Genetic material of the cell that codes for proteins

sequencing The process of analyzing and identifying the structure of the genetic code (for example, DNA and RNA)

subtype Molecularly defined type of myeloma characterized by distinct and unique clinical features and disease outcomes

tissue A group of structurally and functionally similar cells

tumor-specific protein Molecule from a tumor cell that can be recognized by the immune system



MMRF RESOURCES IN PERSON OR ONLINE



Attend a Multiple Myeloma Patient Summit

Learn about standard and emerging therapies including stem cell transplants, promising clinical trials, and more for optimal disease management. Attend a complimentary symposium for all the information you need to make well-informed decisions about your treatment and care.

To register, view past summits and the complete calendar, visit:

themmrf.org/patient



View Past Programs on Demand

Access our archive of recorded Patient Summit symposia and webcasts. Hear expert perspectives on key clinical research and the rapidly evolving myeloma treatment landscape.

All available online, and free, at:

themmrf.org/education



Find a Clinical Trial Near You

Clinical trials are critically important in order to develop new myeloma treatments and better understand the biology of the disease. The more people who enroll, the faster we can find answers. Patients who enroll in clinical trials have the opportunity to be among the first to receive the newest drugs or drug combinations in development and receive close monitoring.

To find a clinical trial near you, visit:

themmrf.org/trialfinder

Don't miss out on the latest myeloma updates! Sign up today to receive all of our educational programming and myeloma news!

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Contact one of our
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Hours: *Mon-Fri, 9am-7pm ET*

Email: *patientnavigator@themmrf.org*



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