THE PATH TO

PRECISION MEDICINE

IN MULTIPLE MYELOMA

MULTIPLE MYELOMA
Research Foundation

themmrf.org

MULTIPLE MYELOMA
Research Foundation

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. Their mission was to ensure more access to better treatments and bring the promise of a cure for every myeloma patient.

Since its founding, the MMRF has remained steadfast in the pursuit of its mission. It is now the leading cancer research organization focused on the development and delivery of more precise therapies, and it is aggressively pursuing a world without myeloma. Working with its partners in industry, research, government, and academia, the MMRF has helped launch 15 new drugs in the past 18 years, an achievement that has almost tripled the life expectancy for myeloma patients. The MMRF is a patient-focused organization that stands with the entire myeloma community and is speeding the discovery of cures through precision medicine. Driven by data and innovative research, the MMRF is committed to empowering every patient with 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.themmrf.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.themmrf.org**.

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

Updates to and distribution of this booklet were supported by Adaptive Biotechnologies, Amgen, Bristol Myers Squibb, CURE Magazine, Genentech, GlaxoSmithKline, Karyopharm Therapeutics, Oncopeptides, and Takeda Oncology.

Accredited by:

INTRODUCTION

Recent research has shown that **multiple myeloma** is a highly diverse 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**, the treatment of each individual patient according to his or her specific or unique characteristics, such as myeloma genetic makeup and **immune profile**. The precision medicine approach better enables the patient and the health care team to choose (and adjust as needed) the myeloma drug regimen(s) that will be most effective. Precision medicine in myeloma is a major focus of current research, and many clinical trials 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 booklets *Multiple Myeloma Disease Overview, Multiple Myeloma Treatment Overview, Autologous Stem Cell Transplantation,* and *Multiple Myeloma Immunotherapy*—and also 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 or unique characteristics, such as 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.

ADVANCING PRECISION MEDICINE

There are at least eight 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

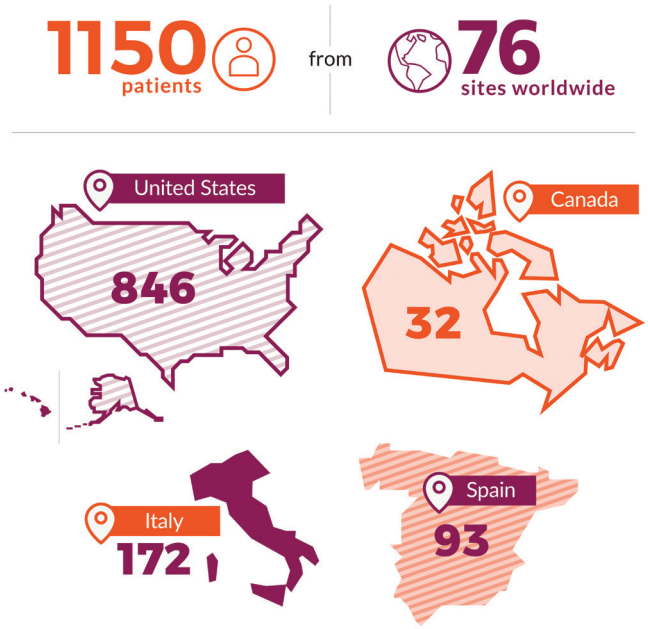
matched against the specific myeloma subtypes. To that end, the MMRF in 2011 initiated the **CoMMpass Study℠**, a landmark, large-scale, **longitudinal study** of patients with newly diagnosed active multiple myeloma. In this study, extensive data about myeloma patients is collected: clinical, genetic, 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 Study 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 Study includes information from a large 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 Study 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 Study 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. The CoMMpass Study encompasses 1,150 patients. 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 Study



Through the **CoMMpass Study**, 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 Study**, speak to an MMRF Patient Navigator at 888.841.6673 or visit **themmrf.org/finding-a-cure/our-work/the-mmrf-commpass-study**.

GENOMIC SEQUENCING AND TISSUE BANKING

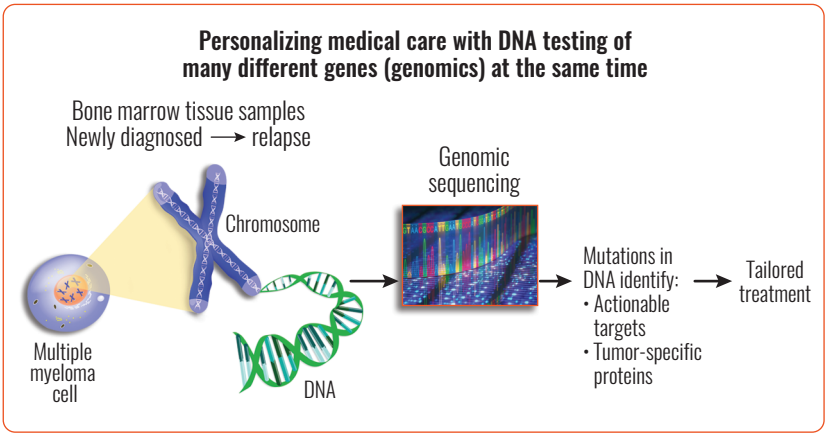
Putting together a genomic profile begins with obtaining myeloma cells from **tissue** samples taken from the patient's bone marrow. Once the myeloma cells have been collected, their **DNA** and **RNA**—the most basic genetic material and the building blocks of life—are examined using highly sophisticated 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.

CureCloud®

To accelerate research toward smarter multiple myeloma treatment options, the MMRF developed **CureCloud**, a study that includes the first at-home genomic testing program for multiple myeloma patients. For patients that participate in CureCloud, a detailed report showing the results of the genomic analysis is provided to both the patient and his or her physician. These reports include recommendations, based on any identified mutations, for clinical trials to consider. The MMRF CureCloud helps patients have more informed, substantive discussions with their care teams about their options. Additionally, the data collected through CureCloud is made available through the MMRF CureCloud database, a secure cloud-based platform that collects, organizes, and analyzes de-identified data from myeloma patients and helps scientists make use of this valuable information in their research. The data is also made available via a portal through which patients and their doctors can view their data, as well as aggregated data from other patients.

To accelerate the delivery of precision medicine to multiple myeloma patients, the MMRF created **CureCloud**, a centralized data hub that generates, aggregates, and visualizes data. To learn more about how you can contribute your data to the registry, please visit **www.mmrfcurecloud.org**.

Precision medicine



The Multiple Myeloma Research Consortium® (MMRC), a unique collaboration of 23 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**. More such trials against other targets and new combinations are planned.

MyDRUG℠

The CoMMpass Study and earlier MMRF efforts identified specific myeloma mutations. **MyDRUG** (**My**eloma – **D**eveloping **R**egimens **U**sing **G**enomics) is a study that is testing treatments for six of these mutations. Patients whose disease returned earlier than expected after undergoing autologous stem cell transplantation or maintenance therapy are eligible.

Patients enrolled in the MyDRUG trial undergo genomic sequencing and, based on the changes found, receive treatment that is matched to the drugs or therapies that target their specific myeloma subtype. The MyDRUG trial is testing different treatments that are known to specifically target genetic mutations in patients with high-risk myeloma. To learn more, please visit themmrf.org/finding-a-cure/our-work/my-drug.

Another unique feature of MyDRUG is that treatments that are shown not to work are removed from the study. Also, when additional information about genetic mutations and/or new drugs that target those mutations becomes available, the treatments can be added to the trial.

MyCheckpoint℠

Checkpoint inhibitors are a class of **monoclonal antibodies** that work slightly differently than traditional monoclonal antibodies, which attack myeloma cells directly. Instead, checkpoint inhibitors release the hold on myeloma-fighting **T cells** that have been "turned off" by myeloma cells. Checkpoint inhibitors interfere with cell surface proteins that enable a myeloma cell to avoid the immune system; by blocking these proteins, the "brakes" on the T cells are released, and the T cell is again able to kill myeloma cells. Checkpoint inhibitors have been used successfully in patients with solid tumors but are not approved for use in patients with multiple myeloma. Analysis of patient samples from the CoMMpass Study revealed that different immune checkpoints that turn off T-cell activity are expressed on the surface of myeloma cells in patients who have previously received treatment with Darzalex. This observation led to **MyCheckpoint**, a trial in which myeloma patients who have received previous therapy, including Darzalex, are treated with checkpoint inhibitor therapy.

The MMRF would like to thank Jesus G. Berdeja, MD, Director of Multiple Myeloma Research and Senior Investigator, Hematologic Malignancies at the Sarah Cannon Research Institute in Nashville, Tennessee, and Faith E. Davies, MBBCh, MRCP, MD, FRCPath, Director of the Clinical Myeloma Program at the Perlmutter Cancer Center at New York University Langone Health in New York, New York, and our patient advocates Allan and Deb Osborne of Millis, Massachusetts, and Cindy Chmielewski of Lawrenceville, New Jersey, for their contributions to this booklet.

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

Telephone: 1.888.841.6673
Monday–Friday, 9:00 AM to 7:00 PM ET
Email: patientnavigator@themmrf.org

Connect with an MMRF Myeloma Mentor™:
themmrf.org/resources/myeloma-mentors

This is a phone-based program offering the opportunity for patients and/or caregivers to connect one-on-one with a trained patient and/or caregiver mentor to share their patient journeys and experiences.

Join an MMRF Facebook Group focused on the various genetic alterations under investigation in the MyDRUG study. Go to www.facebook.com/theMMRF and select from several different patient groups dedicated to precision medicine.

FIND AND PARTICIPATE IN A CLINICAL TRIAL

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

Clinical Trial Search: themmrf.org/resources/clinical-trial-finder

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 themmrf.org/get-involved

GLOSSARY

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

adaptive immunity The part of the immune system that is composed of highly specialized cells designed to recognize foreign invaders and attack them any time they enter the body

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

checkpoint inhibitor A naked antibody that interferes with proteins that enable a cancer cell to hide from, overpower, or resist a patient's immune system; by blocking these proteins, the "brakes" on the immune system are released and immune cells are able to kill cancer cells

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 (Relating 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*

CureCloud A direct-to-patient research effort aimed at enrolling 5,000 individuals from whom comprehensive molecular and immune analyses will be generated from blood samples and the resulting data aggregated with the correlating clinical information

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

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

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

MyCheckpoint A clinical trial that is being conducted to evaluate two different checkpoint inhibitors for patients with relapsed refractory multiple myeloma who have relapsed after treatment with prior therapies, including Darzalex

MyDRUG (Myeloma – Developing Regimens Using Genomics) Trial that evaluates therapies targeting actionable subtypes in high-risk relapsed or refractory multiple myeloma patients using treatments that are being studied or are already approved in other cancers

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

T cell (or T lymphocyte) A type of white blood cell that can be subdivided into two groups called helper T cells and cytotoxic T cells; helper T cells are responsible for *adaptive immunity*; cytotoxic T cells kill cells that have been marked by the immune system as enemies, including cancer cells

tissue A group of structurally and functionally similar cells



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 or to view the complete calendar, visit:
themmrf.org/resources/education-programs

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/resources/education-programs

Find a Clinical Trial Near You

Clinical trials are critically important to developing new myeloma treatments and better understanding 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/resources/clinical-trial-finder

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

Name:

Address:

City: State: ZIP:

Telephone: Mobile:

Email:

Or sign up at themmrf.org

I AM A: (CHECK BOX)

- ☐ Patient
- ☐ Patient Spouse
- ☐ Patient Family
- ☐ Patient Friend
- ☐ Healthcare Professional
- ☐ MMRF Supporter

**Please tear off reply card and tape all three sides before mailing.*

Fold here

MULTIPLE MYELOMA Research Foundation

themmrf.org

MULTIPLE MYELOMA
Research Foundation

Place
stamp
here

Multiple Myeloma Research Foundation
383 Main Avenue, 5th Floor
Norwalk, CT 06851

Contact one of our Patient Navigators at the Patient Navigation Center

1-888-841-MMRF (6673)

Hours: *Mon–Fri, 9 AM–7 PM ET*

Email: *patientnavigator@themmrf.org*

MULTIPLE MYELOMA Research Foundation

383 Main Avenue, 5th Floor, Norwalk, CT 06851
Email: **info@themmrf.org**
www.themmrf.org

MM PM 04/2021