

BUILDING TO THE PINNACLE OF PRECISION MEDICINE:

Translating the MMRF CoMMpassSM Study
into Actionable Insights and Clinical Trials

A White Paper for the Multiple Myeloma Research Foundation



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General Overview

The multiple myeloma community has seen unprecedented progress in terms of new drug approvals and survival gains over the past 15 years, more than almost any other cancer. Despite these enormous treatment advances, this hematologic malignancy of plasma cells in the bone marrow remains an incurable disease and most patients will eventually relapse.

Multiple myeloma poses unique treatment challenges to clinicians and patients. With at least eight subtypes identified to date and multiple clones possible per individual patient, it is a highly heterogeneous disease, necessitating a patient-specific, tailored treatment approach. The relative rarity of the condition presents additional hurdles, such as difficulties reaching adequate numbers of enrolled patients in clinical trials and securing sources of funding. In rare and complex cancers such as multiple myeloma, collaboration and data sharing are particularly essential in order to make meaningful progress.

THE MULTIPLE MYELOMA RESEARCH FOUNDATION (MMRF) HAS BEEN WORKING TIRELESSLY TO ACCELERATE THE PACE OF MULTIPLE MYELOMA RESEARCH AND ACHIEVE ITS MISSION OF DELIVERING A CURE TO EVERY PATIENT.

Over the last 20 years the Multiple Myeloma Research Foundation (MMRF) has worked tirelessly to accelerate the pace of multiple myeloma research and achieve its mission of delivering a cure to every patient, bringing together a diverse group of stakeholders to innovate and maximize resources. Using a comprehensive end-to-end model, the MMRF is facilitating precision medicine, beginning with generating genomic and clinical data and leading to the advancement and delivery of targeted therapies to patients with multiple myeloma.

The current white paper, which follows the original white paper published in 2016, provides new insights gleaned from the MMRF's cornerstone CoMMpassSM Study, a large-scale, longitudinal clinical study in multiple myeloma that represents the largest genomics data set of any cancer.

New insights from CoMMpass, which aims to identify genomic drivers of disease, include:

- Unique genomic subtypes of multiple myeloma, defined by specific DNA mutations and other abnormalities that can affect how each patient's disease responds to different treatments
- New genetic markers that identify those patients at highest risk of progression
- Genetic mechanisms that start to explain response in different patients
- Genetic profiles that may play a role in racial differences

This white paper also describes other MMRF-initiated genomic profiling efforts, which along with CoMMpass have led to the identification of actionable DNA mutations that can be targeted with precision treatments. We also review the MyDRUG™ platform trial, which is testing several precision treatment approaches based on genomic subtypes, as well as novel findings related to the expression of specific immune markers using samples from patients enrolled in CoMMpass that led to the creation of the MMRF MyCheckpoint™ clinical trial.

Precision Medicine

Challenges such as those faced in multiple myeloma have led to the emergence of precision medicine, an approach to disease management that takes into account an individual's genetics, environment, and lifestyle so that doctors and researchers can more accurately match patients with effective treatments. Given the complexity and heterogeneity of multiple myeloma, treatment success is dependent on a patient-specific approach.

The emergence of precision medicine coincides with a strong trend toward patients being active participants in the clinical decision-making process. Increasing patients' understanding of their unique disease characteristics and disease journey will empower them with knowledge to positively impact their outcome and further strengthen the role of precision medicine in the future.

The MMRF CoMMpassSM Study

The MMRF launched the CoMMpass Study ([Relating] Clinical Outcomes in Multiple Myeloma to Personal Assessment of Genetic Profiles) in 2011. CoMMpass is the first large-scale, longitudinal study in multiple myeloma focused on disease progression and response to treatment based on patients' genomic or molecular profiles (Clinicaltrials.gov identification number: NCT01454297). The CoMMpass data set represents the largest genomic data set of any cancer type.

Study design and implementation

CoMMpass is a prospective, longitudinal, observational study in newly diagnosed symptomatic patients with multiple myeloma. Now closed to enrollment, subjects were 18 years or older and were candidates for an immunomodulatory drug (e.g., Revlimid® [lenalidomide], Pomalyst® [pomalidomide], or Thalomid® [thalidomide]) and/or a proteasome inhibitor (e.g., Velcade® [bortezomib] or Kyprolis® [carfilzomib]) as part of their initial treatment regimen. In addition to therapy with an immunomodulatory drug and/or proteasome inhibitor, most patients received a corticosteroid such as dexamethasone (dex) and, in some cases, a chemotherapy agent such as cyclophosphamide. Initial therapy could be administered in doublet combinations such as Revlimid®-dex or Velcade®-dex; or triplet combinations such as Revlimid®-Velcade®-dex or Velcade®-cyclophosphamide-dex.

In 2015, CoMMpass reached its target enrollment of 1,000 multiple myeloma patients, a remarkable achievement in a relatively rare disease and a testament to the commitment of patients to help advance the field of multiple myeloma. CoMMpass involves an active assessment schedule, including bone marrow samples at baseline, at response to treatment, and at relapse. Each patient is followed for up to eight years. Preplanned interim analyses occur every six months.



“CoMMpass is the single most important effort in the MM community. The integration of genomics, epigenomics, and immune phenotyping with clinical outcomes will be the guide to the cure of multiple myeloma and the blueprint for the management of many other cancers.”

*David Siegel, MD, PhD
Division Chief, Myeloma
John Theurer Cancer Center*

Executing such an ambitious initiative requires collaborators. CoMMpass is a multinational study involving nonprofit, industry, and academic partners. Seventy-six community and academic cancer centers from across North America and Europe enrolled patients in the study. Industry

partners providing financial and scientific support include Takeda Pharmaceuticals Co. Ltd; Amgen, Inc.; Janssen Pharmaceuticals, Inc.; and Bristol-Myers Squibb Co. Other collaborators include The Translational Genomics Research Institute (TGen), GNS Healthcare, Spectrum Health Hospitals, the Department of Veterans Affairs, the US Oncology Network, and the Van Andel Research Institute. The MMRF designed CoMMpass to promote collaboration and data sharing to drive hypothesis generation, working to break down data silos that impede research while accelerating the pace of research in order to bring new treatments to patients as quickly as possible.

CoMMpass Patient Population

Baseline demographics

As the data mature, important findings have emerged from CoMMpass. Baseline characteristics of the CoMMpass population show broad representation and are consistent with characteristics of multiple myeloma patients in the general population. As of the most recent interim analysis (interim analysis 15), a total of 1,143 patients have enrolled, with 60% of these patients ongoing. 25% of patients have died; 58% of the deaths were due to disease progression versus 42% due to other

Table 1. Baseline Demographics

BASELINE CHARACTERISTIC		N=1,143
Age (yrs), median (min, max)		63 (27, 93)
Gender – Female, n (%)		453 (40)
Ethnicity*, n (%)		
Hispanic/Latino		76 (8)
Non-Hispanic/Non-Latino		861 (89)
Other		34 (3)
Race*, n (%)		
White		742 (76)
Black/African American		161 (17)
Asian		18 (2)
American Indian/Alaskan Native		1 (<1)
Other		49 (5)

**Ethnicity and race data are not available for a subset of Italian patients.*

causes. Nearly 700 patients continue to be followed in the study. At enrollment, patients had a median age of 63 years, and the majority were males of non-Hispanic/non-Latino descent (Table 1). Approximately 17% of CoMMpass patients self-reported as African American, an important feature, given the higher incidence of persons of African descent in the multiple myeloma population compared to the general population.¹

Most common lines of therapy

For the first line of therapy, the most common starting regimen was the triplet combination of Velcade®-Revlimid®-Dex (Table 2). Note that while two doublet combinations, Velcade®-Dex and Revlimid®-Dex were among the most commonly prescribed for first line treatment, triplet combinations are considered the standard of care regimen for this indication.

*Table 2. Most Common Treatment Regimens by Line of Therapy**

TREATMENT REGIMEN	First Line of Therapy	Second Line of Therapy	Third Line of Therapy
	[971 PATIENTS] #PTS. (% PTS)	[390 PATIENTS] #PTS. (% PTS)	[189 PATIENTS] #PTS. (% PTS)
Velcade® - Revlimid®- Dex	368 (37.9)	145 (37.2)	82 (43.4)
Velcade® - Cyclophosphamide - Dex	191 (19.7)	83 (21.3)	34 (18.0)
Velcade® - Dex	88 (9.1)	26 (6.7)	11 (5.8)
Kyprolis® - Revlimid® - Dex	28 (2.9)	8 (2.1)	6 (3.2)
Other Treatment	260 (26.7)	103 (26.4)	43 (22.7)

Dex = dexamethasone; PI (proteasome inhibitor) = Kyprolis®(carfilzomib) or Velcade® (bortezomib).

*IMiD (immunomodulator)=Revlimid® (lenalidomide); *Not included: 61 patients with fourth line and 23 with fifth line therapy.*

The most recent interim analysis of CoMMpass shows median progression-free survival – the time from enrollment to disease progression or death from any cause – was 35.8 months.

Genomic subtypes in myeloma

Genomic alterations that were first observed in previous MMRF-led genetics initiatives have been confirmed in the CoMMpass Study. Through CoMMpass, the MMRF has identified 12 different genomic subgroups of multiple myeloma using RNA sequencing including high risk subtypes and those with actionable genomic mutations. (Table 3)² including high risk subtypes and those with actionable genomic mutations.

CoMMpass Findings Around Genomic Risk in Multiple Myeloma

Risk assessment by Next Generation Sequencing (NGS) is vital to achieve the most accurate results for optimal risk-adjusted therapy

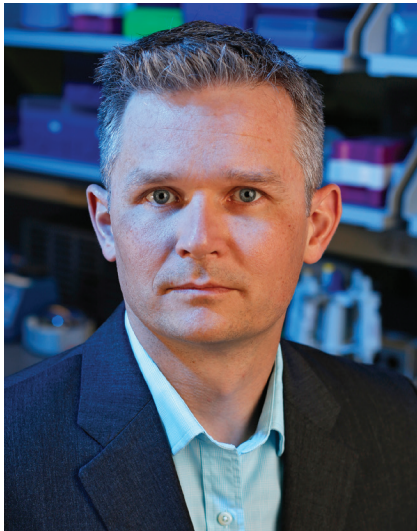
Traditionally, risk assessment for myeloma patients has been accomplished using fluorescence in situ hybridization (FISH), a cell staining technique that can detect genomic abnormalities such as increased or decreased numbers of chromosomes, deletion of parts of chromosomes, and DNA translocations. Risk in CoMMpass patients has been examined using FISH and next generation sequencing (NGS), whereby chromosomal abnormalities are very accurately determined by DNA sequencing. CoMMpass data has shown that using FISH alone is inadequate for accurate assessment of risk. Considering this finding, patients are encouraged to have NGS done when possible.

Discovery of a new high-risk translocation in patients who formerly were considered standard risk

A new higher-risk group of patients with certain genetic aberrations has been identified through the CoMMpass Study. These genetic changes include hyperdiploidy (having more than the usual number of chromosomes), as well as translocations (rearrangements) of parts of the chromosome involving the immunoglobulin light chain (IgL) locus. IgL translocations, also known as t(IgL), have been identified in approximately 10% of multiple myeloma patients and are a marker of poor prognosis independent of disease stage and age. Barwick and colleagues have found that patients with IgL-translocated myeloma — 70% of whom have hyperdiploid disease — do not benefit from immunomodulatory drugs.^{4,5} Hyperdiploid disease as defined by FISH has in the past been associated with standard risk as opposed to high risk; these new findings show that hyperdiploid patients with t(IgL) have a higher risk status than previously thought. This is a clinically relevant finding, as a new molecular test is being developed to detect t(IgL) in myeloma patients.

Discovery of the “highest risk” subtype of newly diagnosed myeloma, known as “double-hit”

Analysis of CoMMpass Study genetic data has revealed a small, previously unknown subset of newly diagnosed myeloma patients (6.1%) who have the poorest prognosis of any group. Their myeloma belongs to a type of myeloma referred to as double-hit myeloma, characterized by bi-allelic, complete inactivation of the TP53 tumor suppressor gene in combination with 1q amplification, which can only be detected using NGS.³



“As one of the only public datasets with regular updates to clinical outcome and genetic phenotype, the long-term value of CoMMpass is immense. We already have signals of events associated with drug resistance; with time, CoMMpass will define mechanisms of resistance and novel changes associated with disease progression that will open up new therapeutic opportunities.”

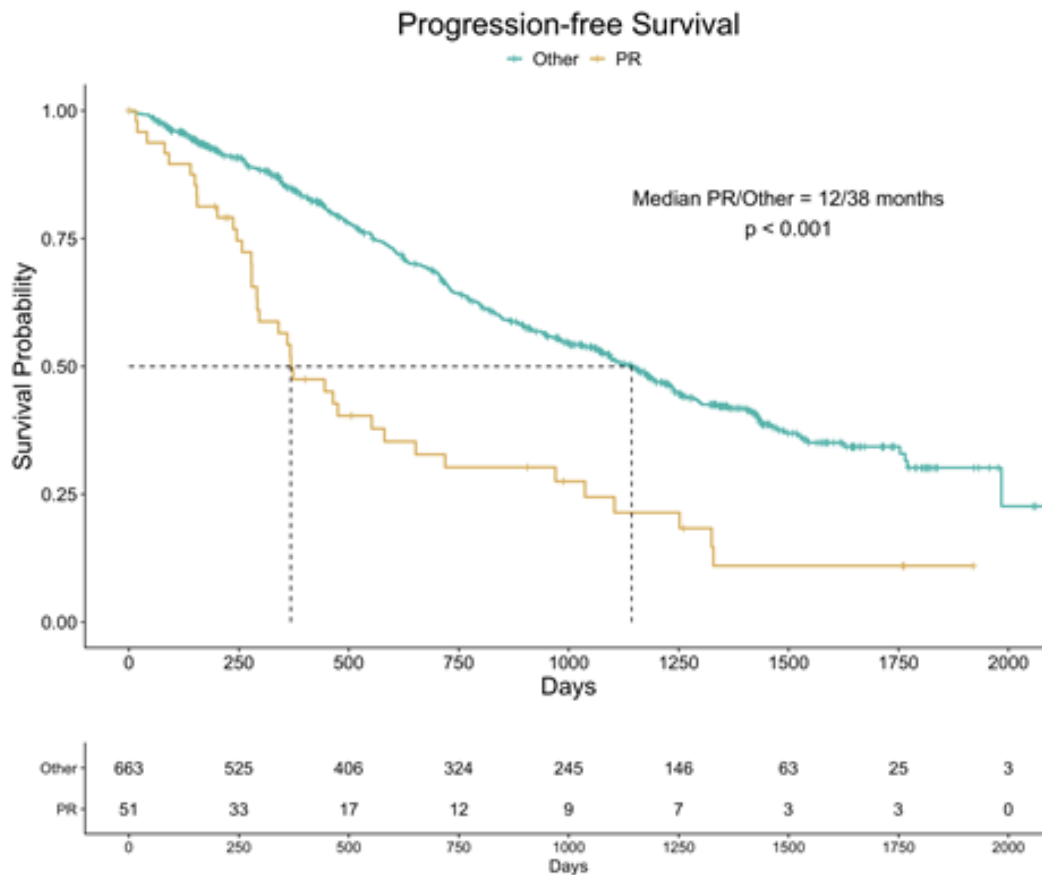
Jonathan Keats, PhD

*Assistant Professor & Director of Bioinformatics
Translational Genomics Research Institute (TGen)*

Discovery of new markers of transition to high-risk disease at relapse

Analysis of sequential patient samples from CoMMpass has identified a high-risk progression phenotype (PR). Work by Skerget et al. has shown very poor outcomes for this high-risk group, with PR patients progressing almost three times as fast as all other groups together (Figure 1).⁶ Approximately 25% of multiple myeloma patients transition to the PR group at relapse, which is mostly characterized by RAS/RAF and CDK pathway-activating alterations. The MMRF is currently testing targeted treatments for these specific alterations in the MyDRUG trial, which is discussed in detail later in this paper.

Figure 1. Progression-Free Survival of Patients in the High-risk PR Group vs Non-PR Group

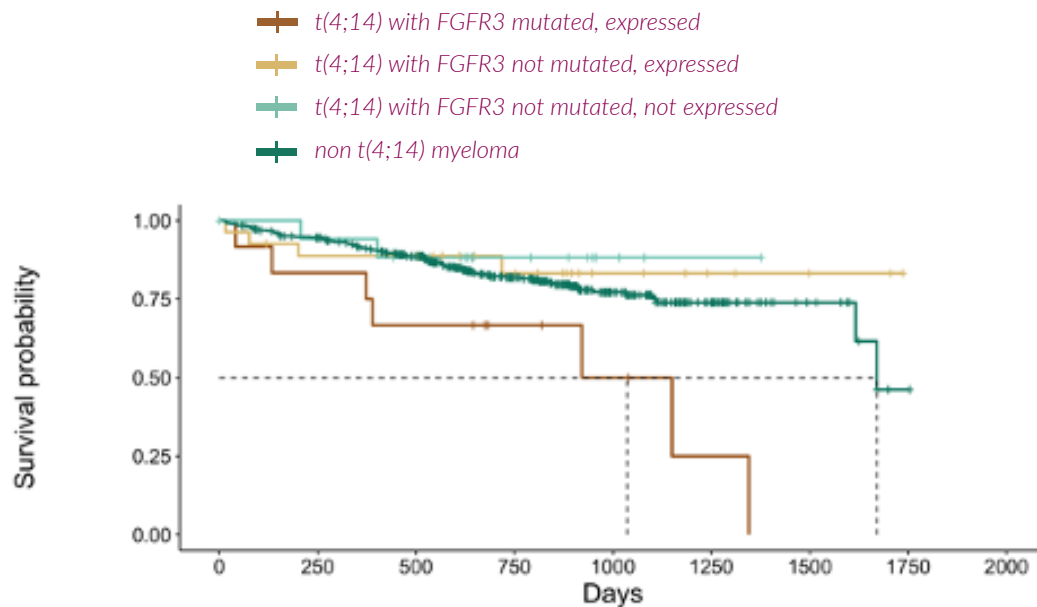


*PR group of patients **progress** almost 3x as fast
as all other groups combined*

Discovery that increased risk in t(4;14) patients may be due to concomitant FGFR3 mutation

The t(4;14) translocation is relatively common in myeloma (13% of CoMMpass patients) and has been associated with increased risk of progression. An analysis of CoMMpass data has revealed that those t(4;14) patients who also have a mutation in the FGFR3 gene (about 1/3 of t(4;14) patients) have a more high-risk prognosis, while those that do not, have a more standard risk prognosis (Figure 2). A targeted therapy that acts against the FGFR3 mutation is included in the MMRC MyDRUG trial, discussed later in this paper.

Figure 2: Decreased Overall Survival in t(4;14) Patients With FGFR3 Mutation



CoMMpass Findings Around Drug Response Mechanisms in Myeloma

The role of clonal hematopoiesis of indeterminate potential (CHIP) in myeloma

CHIP (clonal hematopoiesis of indeterminate potential) is a newly discovered process whereby typical cancer mutations can be detected in the blood starting at age 40. These mutations, detected by genomic sequencing of cells in the peripheral blood, can signal an increased risk of blood cancer, including myeloma.⁷ Work from Mouhieddine et al. showed that in multiple myeloma, CHIP is seen in up to 25% of newly diagnosed patients and appears to be linked to a worse outcome. However, the prognosis of these patients can significantly improve when they receive maintenance therapy with IMiDs (immunomodulatory drugs).⁸

Racial differences in myeloma

The CoMMpass Study has found significant differences between African American and Caucasian multiple myeloma patients with respect to mutation frequencies of key cancer genes. In an analysis by Manojlovic et al., which utilized CoMMpass data, African American patients had a lower incidence of high-risk features, such as mutations in TP53, compared to Caucasian patients (Table 4).⁹

Table 3. TP53 Mutation Profile in African American vs. Caucasian Myeloma Patients

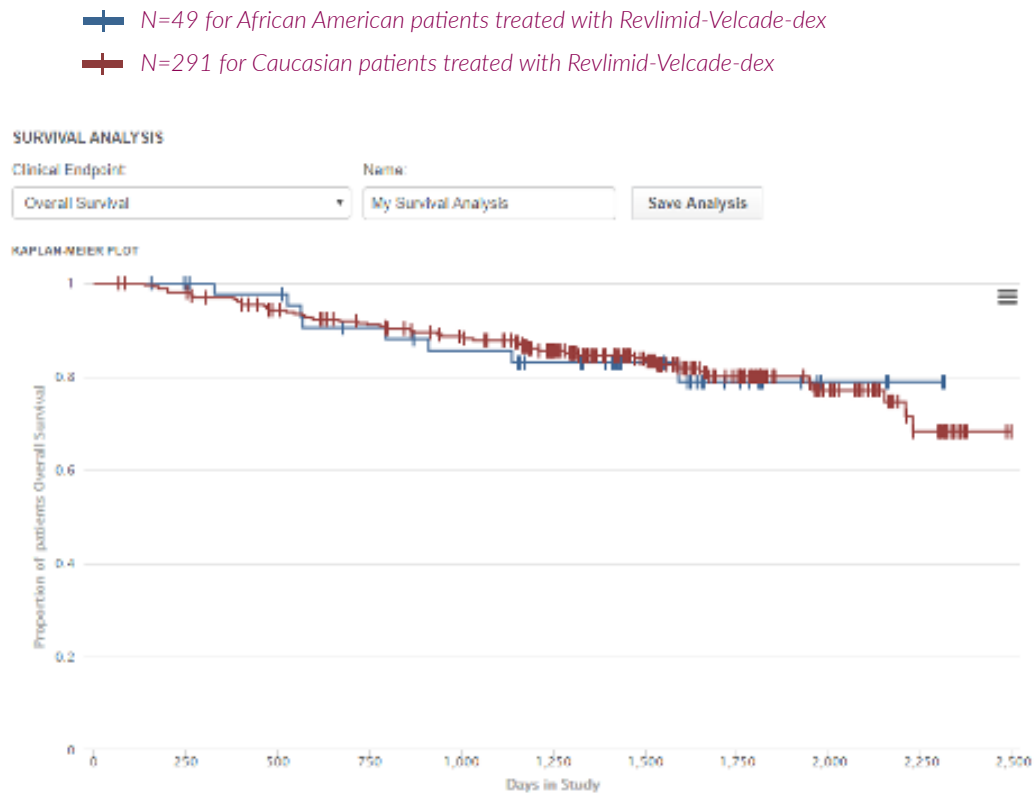
TP53 ABERRATION	AFRICAN-AMERICAN	CAUCASION	P-VALUE (FISHER'S)
Wild Type	84.3%	83.1%	0.75
Mono-Alleic	9.4%	9.1%	0.91
Bi-Alleic	0.8%	4.1%	0.07
LOH	6.3%	8.6%	0.39
Mutation	1.6%	6.6%	0.03
LOH+Mutation	7.9%	15.2%	0.03

Wildtype (both alleles are normal); Mono-Alleic (somatic mutation or copy loss event); Bi-Alleic (somatic TP53 event in both alleles); LOH (loss of heterozygosity only), Mutation (somatic mutation only); LOH+Mutation (combined loss of heterozygosity and mutations)

In addition, analysis of demographics data stratified by race has confirmed an earlier age of onset of multiple myeloma in African American compared to Caucasian patients, demonstrated by a significant, two-fold increase in the proportion of African American patients with disease onset in the 40- to 49-year-old age group compared to Caucasian patients.⁹

An analysis of CoMMpass data shows no significant difference in overall survival between African American and Caucasian myeloma patients based on race or age of onset in this cohort of similarly treated multiple myeloma patients (Figure 3).

Figure 3: Survival Analysis of African American and Caucasian patients in the CoMMpass Study



These findings are in contrast to data reported by the Surveillance, Epidemiology, and End Results (SEER) program, which show that overall in the US, the mortality rate for African American patients is higher compared to that of other races/ethnicities.¹ The reasons for this discrepancy in the findings of the CoMMpass Study compared to the SEER database are not fully understood and might be due to a variety of factors, including the possibility that in the real-world setting, treatment options – and access to treatment – are not equal across all racial/ethnic groups. More work is needed to understand the reasons behind racial disparities and to ensure that all patients, regardless of race/ethnicity, have the same treatment options.

What We Expect to Learn from CoMMpass

As the CoMMpass data continue to mature, answers to some of the questions most important to patients are beginning to be answered, such as: Is my genomic profile predictive of my risk or response to treatment? How is my disease doing? Am I a candidate for immunomodulatory drugs? Similarly, for clinicians, CoMMpass is beginning to answer questions such as: Which clinical and genomic variables predict treatment response? What genomic subtype is my patient? Does my patient have high-risk disease or other genomic markers that could inform treatment decisions?

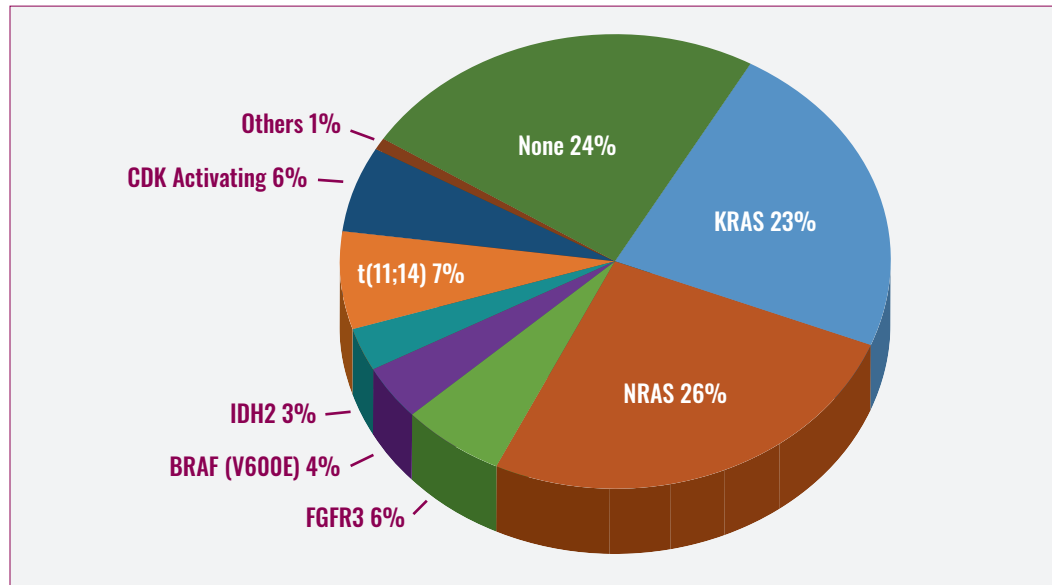
The MMRF Molecular Profiling Protocol

As the CoMMpass Study began to define myeloma subtypes based on genetic mutations in newly diagnosed patients, the MMRF developed the Molecular Profiling Protocol (NCT02884102) to screen high-risk relapsed myeloma patients for actionable genetic mutations (genetic mutations that

THE FINDINGS OF THE MOLECULAR PROFILING PROTOCOL HELPED TO SPUR THE LAUNCH OF THE MYDRUG TRIAL, WHICH IS AIMED AT TREATING HIGH-RISK MULTIPLE MYELOMA PATIENTS BASED ON EACH INDIVIDUAL'S ACTIONABLE MUTATIONS.

can be targeted by a specific drug or treatment) using a targeted panel of 1,700 genes thought to be important in myeloma. More than 500 patients were sequenced between 2016 and 2019; 76% of them had at least one actionable alteration (Figure 4), while 24% had no genetic mutations identified. It is important to note that in relapsed patients, new mutations may be found that were not present at the time of diagnosis, and some of these mutations can be treated with specific targeted therapies. The findings of the Molecular Profiling Protocol helped to spur the launch of the MyDRUG trial (discussed in the next section), which is aimed at treating high-risk multiple myeloma patients based on each individual's actionable mutations. In order to be eligible for the MyDRUG study, patients must consent to having their genome sequenced using the same targeted panel.

Figure 4. Actionable Genetic Mutations Identified in the MMRF Molecular Profiling Protocol



The MMRC MyDRUGSM Platform Trial

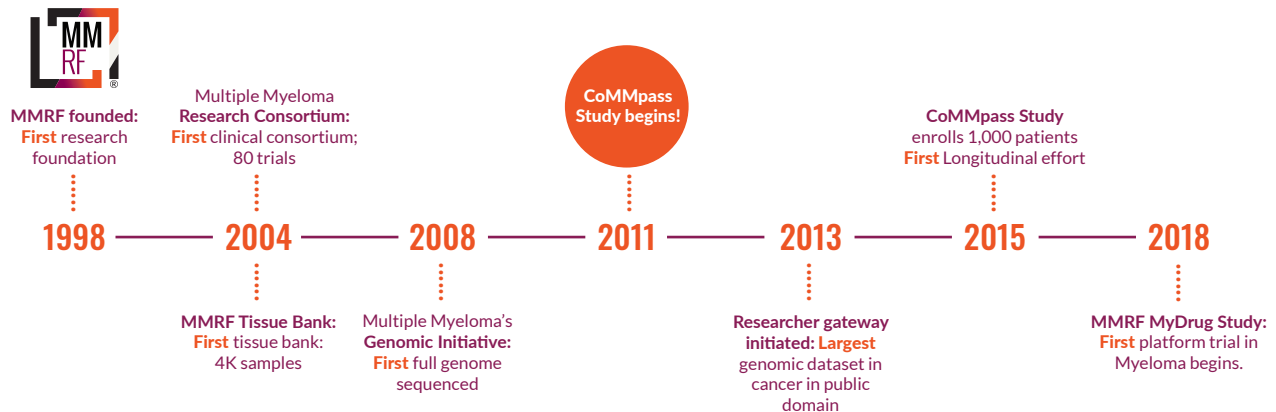
The MyDRUG (Myeloma – Developing Regimens Using Genomics) platform trial represents the pinnacle of precision medicine in multiple myeloma and the culmination of MMRF's precision medicine efforts. The MMRF began building the foundation for this effort through a number of initiatives, including:

- Forming the first tissue bank in multiple myeloma as a resource for researchers
- Sequencing the multiple myeloma genome, with the first actionable mutations found
- Launching the CoMMpass Study to confirm and/or identify new actionable mutations

MyDRUG evaluates therapies that target actionable subtypes individually, with the aim to improve overall treatment outcomes by taking into account the underlying genetic causes of multiple myeloma. The panel currently includes five targeted therapies (Table 5). In the future, as more targeted therapies are identified, more treatment arms may be added to the trial to target additional subtypes.

MyDRUG is the first-ever platform trial conducted in multiple myeloma and is made possible through the MMRF's investment (currently \$12 million) and through collaboration between MMRF and six

pharmaceutical companies, including: AbbVie, Inc.; Bristol-Myers Squibb Co.; Eli Lilly and Company; Genentech, Inc.; Janssen Pharmaceuticals, Inc.; and Takeda Oncology. Enrollment is ongoing at 17 leading academic centers across 13 states in the US. Although these treatments are being studied or are already approved in other cancers, they are being made available to myeloma patients for the first time only through MyDRUG. This provides a potential benefit not only to patients enrolled in the trial, but also to all patients, should any of these therapies be found effective and then approved for use in myeloma.



Study design

MyDRUG is an open-label Phase 1/2 platform trial, which will be conducted in high-risk patients with relapsed or refractory multiple myeloma who have received one to three prior treatment regimens, including a proteasome inhibitor and an immunomodulatory drug (NCT03732703). To be eligible for enrollment, patients must have had an early relapse following initial therapy or been primary refractory to initial therapy. Patients must consent to having their genomes sequenced via bone marrow biopsy.

Depending on their sequencing results, patients will enter one of six subprotocols/treatment arms (Table 5), including five gene-specific, precision medicine treatment groups and one non-targeted treatment arm. For all patients, the backbone of therapy will be an all-oral regimen of dex, Ninlaro® (ixazomib), and Pomalyst® (pomalidomide). Depending on the mutation, a targeted agent will also be administered. Targeted agents include the small molecule inhibitors Cotellic® (cobimetinib), IDHIFA® (enasidenib), Verzenio™ (abemaciclib), erdafitinib, and Venclexta® (venetoclax). If no actionable mutation is found, patients will receive an immune therapy (Darzalex® (daratumumab) or other

novel agent), plus backbone therapy. Additional therapy arms are being added in 2020, and more additions are planned into the future. Aside from Venclexta®, all of the targeted therapies in MyDRUG are new to multiple myeloma but have been identified as potentially effective treatments through genomic profiling efforts and other work by the MMRF. (It should be noted that on March 19, 2019, the FDA placed a partial clinical hold on all clinical trials evaluating Venclexta® for the investigational treatment of multiple myeloma following a review of data from the ongoing Phase 3 BELLINI trial. As such, enrollment in this arm of the MyDRUG trial will not proceed until the FDA completes the data review.)

The goal is to enroll 228 patients, with up to 38 patients in each of the six treatment arms. The primary endpoint will be overall response rate.

Table 4. MyDRUG Treatment Arms

SEQUENCING RESULT	TARGETED TREATMENT (+ SOC)	CURRENT FDA-APPROVED INDICATION FOR TARGETED TREATMENT
CDK pathway activating alteration	Verzenio™ (abemaciclib)	<ul style="list-style-type: none"> Hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer
IDH2 activating mutation	IDHIFA® (enasidenib)	<ul style="list-style-type: none"> Acute myeloid leukemia with an isocitrate dehydrogenase-2 (IDH2) mutation
RAF/RAS mutation	Cotellic® (cobimetinib)	<ul style="list-style-type: none"> Melanoma with a BRAF V600E or V600K mutation
FGFR3 activating alteration	Erdafitinib	<ul style="list-style-type: none"> Bladder Cancer
Translocation t(11;14)	Venclexta® (venetoclax)*	<ul style="list-style-type: none"> Chronic lymphocytic leukemia, with or without 17p deletion Acute myeloid leukemia
Non-actionable genetic alteration	Darzalex® (daratumumab) or other novel agent	<ul style="list-style-type: none"> Multiple myeloma

SOC = standard of care, defined as: dexamethasone + Ninlaro® (ixazomib) + Pomalyst® (pomalidomide).

*FDA = Food and Drug Administration. *On March 19, 2019, the FDA placed a partial clinical hold on all clinical trials evaluating Venclexta® for the investigational treatment of multiple myeloma following a review of data from the ongoing phase 3 BELLINI trial. No new patients are to be enrolled in any studies of Venclexta® for multiple myeloma until a further analysis of the data is completed.*

What we expect to learn from MyDRUG

The goal of MyDRUG is to improve treatment outcomes of high-risk multiple myeloma patients by advancing individualized treatment approaches. As a platform trial, MyDRUG will facilitate the rapid opening and closing of individual treatment arms as therapies show potential or fail, allowing investigators to focus on those regimens with the most promise. In addition, the MyDRUG study is designed to be as broad-reaching and inclusive as possible. Patients with both actionable and non-actionable genetic abnormalities will be included in the study and receive treatment; no patients will receive a placebo. Many of the targeted treatments used in MyDRUG, while FDA-approved in other disease states (Table 5), would not have been readily available to multiple myeloma patients in the absence of such a trial. MyDRUG will provide valuable information on the efficacy of various treatment approaches across the full spectrum of multiple myeloma and give essential insight on the impact of personalized medicine in this disease setting. All patients with multiple myeloma, not only those enrolled in MyDRUG, will benefit from the knowledge gleaned from the study, including potential new treatment options.

The MyCheckpointSM Immune Platform Trial

The introduction of immune checkpoint inhibitors was a critical development in cancer immunotherapy. These agents are engineered monoclonal antibodies that block cell surface molecules (immune checkpoints) that normally function to turn off T-cell immune responses. These agents do not attack the tumor directly; instead, they block inhibitory interactions of tumor-specific T-cells, which can then kill myeloma cells. The first checkpoint inhibitor, Yervoy[®] (ipilimumab), was approved by the FDA in 2011, and is directed against an immune checkpoint called cytotoxic T lymphocyte antigen (CTLA)-4. Analysis of CoMMpass specimens showed that T-cells from patients whose disease progressed after receiving Darzalex[®] expressed LAG-3 and TIGIT, two immune checkpoints that can turn off immune activity.

This critical information led to MyCheckpointSM, the first immune therapy platform trial in multiple myeloma. In this trial, myeloma patients who have received at least three prior lines of therapy, including at least one that includes Darzalex[®], will be treated with a checkpoint inhibitor directed against either LAG-3 or TIGIT, combined with Pomalyst[®] and dexamethasone. This project shows

how the precision medicine model developed with CoMMpass and the Molecular Profiling Protocol, and put into action with MyDRUG, can also be applied to groundbreaking immune therapy trials for multiple myeloma. MyCheckpoint is now open and will accrue 104 patients at ten MMRC sites.

Next Steps for Multiple Myeloma Research

The ongoing CoMMpass Study has already provided valuable insights into topics such as the diverse baseline characteristics of newly diagnosed multiple myeloma patients, high-risk signatures, drug resistance mechanisms, and racial differences. The genomic and clinical data generated from CoMMpass will continue to enhance our understanding of underlying disease mechanisms and how they change over time and will help to identify new drug targets. The MyDRUG platform trial will put these learnings into action by testing precision treatment approaches based on genomic

THE ULTIMATE GOAL IS FOR ALL PATIENTS WITH MULTIPLE MYELOMA TO HAVE GENOMIC AND IMMUNE PROFILING IN ORDER FOR THEM TO GET THE BEST POSSIBLE TREATMENT FOR THEIR PARTICULAR DISEASE.

subtypes. However, genomics is only part of the solution. To make precision medicine a reality, we must build upon our success and also harness the power of immunology. To this end, the MMRF kicked off a three-year strategic plan (2019-2021) designed to build upon the foundation of genomic data and apply the same model to gather and utilize precision immune data. CoMMpass samples are now being used to build the Immune Atlas, a comprehensive database that catalogs and links immune profile data from each patient to their disease status and treatment outcomes. The Atlas is envisioned as yet another way to delineate myeloma subtypes with the goal of helping predict patient response to immunotherapies.

Summary and Conclusions

Moving forward, combining immune and genomic data will provide the necessary tools and information to make precision medicine possible for all patients. The ultimate goal is for all patients

with multiple myeloma to have genomic and immune profiling in order for them to get the best possible treatment for their particular disease. The vision of the MMRF has always been one of patient-powered collaboration, where every patient has precisely what they need to prevent or defeat myeloma, and where the entire community collaborates seamlessly with ever-increasing momentum towards a cure. Together with their myeloma community partners and a large numbers of patient volunteers, the MMRF has been the leader in developing precision medicine models, which have uncovered new patient subpopulations and genomic targets in multiple myeloma. Building off these initiatives, the implementation of two major platform clinical trials, MyDRUG and MyCheckpoint, being wholly conducted by the MMRC, demonstrates the steadfast and unwavering commitment of the MMRF to accelerate the most promising new agents into the clinic to benefit patients. The ability of the MMRF to identify actionable insights and translate these insights into potentially ground-breaking clinical interventions sets it apart as an organization that is laser focused on finding a smarter, faster cure for every patient.



“CoMMpass will ultimately be remembered as one of the most impactful studies in cancer. CoMMpass has generated critical insights on high risk, disease subtypes, and genomic and immune determinants of response to treatment that have been translated to innovative trials like MyDRUG and MyCheckpoint to make precision medicine a reality for all myeloma patients.

*Daniel Auclair, PhD
Chief Scientific Officer
Multiple Myeloma Research Foundation*

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