Monitoring SARS-CoV-2 Vaccines and COVID-19 Related Outcomes in Individuals with Multiple Myeloma

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Study Summary

Title	Monitoring SARS-CoV-2 Vaccines and COVID-19 Related Outcomes in Individuals with Multiple Myeloma
Short Title	**C**OVID19 **O**utcome**S** in **M**yeloma and the **I**mpact of Va**C**cines **(COSMIC)**
Keywords	Myeloma, COVID-19, Vaccine, COSMIC
Sample Size	200 subjects
Study Population	Individuals with multiple myeloma will be enrolled in the United States
Duration	Duration of participation in the study will be approximately six months
Enrollment Period	Up to two years
Study Design	Multicenter
Primary Objective	Establish feasibility of clinical and patient-reported data collection related to SARS-CoV-2 vaccines, COVID-19 related outcomes, and overall health status in a decentralized, real-world evidence study for patients with multiple myeloma currently undergoing therapy.
Secondary Objective	Monitor incidence of COVID-19 infection requiring hospitalization and related outcomes in participants using electronic patient reported outcomes and participant-permissioned electronic health record data capture.
Inclusion and Exclusion Criteria	**Inclusion Criteria** • Diagnosis of multiple myeloma per the International Myeloma Working Group and currently receiving active treatment for any phase of the disease, including initial therapy, maintenance, or relapsed disease. • Access to the internet • An active patient portal (or willingness to activate) • Willing to electronically sign the study-specific informed consent and authorization form **Exclusion Criteria** • Non-English speaking • Lack of internet access • Cognitive impairment precluding ability to provide informed consent

Contents

1 Introduction

1.1 Background and Study Rationale

The COVID-19 pandemic has had an outsized impact on individuals with underlying social and medical vulnerability, leading to increased rates of severe disease, hospitalization, and death in these groups. Participants with underlying immune compromise, such as those with multiple myeloma, represent one such group. The advent of vaccines against SARS-CoV-2 has significantly limited morbidity and mortality across all groups, but the effectiveness of vaccination in individuals who are less likely to mount sufficient antibody response is uncertain. For this reason, booster vaccines have been recommended for those with underlying immune compromise. However, several key gaps remain in our understanding of how to best protect these individuals.

There is a dearth of real-world evidence about the effectiveness of vaccination and boosters in patients who are immunocompromised, and very little information specifically about the recently approved mRNA boosters. Additionally, rates of vaccination and booster uptake in the United States remain low. A rapid, decentralized method of ascertaining information related to booster vaccine response and adverse events related to vaccines and COVID-19 infection is critical not only to answer questions about the booster vaccines, but to develop an infrastructure for answering similar questions about future vaccines or other diseases.

2 Study Objectives

- Establish feasibility of clinical and patient-reported data collection related to SARS-CoV-2 vaccines, COVID-19 related outcomes, and overall health status in a decentralized, real-world evidence study network for patients with multiple myeloma currently undergoing therapy.
- Monitor COVID-19 related outcomes in participants using electronic patient reported outcomes (PRO) and participant-permissioned EHR data capture.

2.1 Investigational Plan

The purpose of this project is to implement and establish the feasibility of a decentralized real-world evidence study network for patients with multiple myeloma and to monitor outcomes related to COVID-19 infection in this immunosuppressed population. Subjects with multiple myeloma will be invited to participate. The electronic portal will handle all consenting activities. Participants will be asked to complete specific study procedures electronically, including permission for EHR data transfer. Participants will be asked to complete electronic questionnaires periodically.

2.2 Study Endpoints

- **Primary endpoint:** Feasibility of obtaining baseline, 30-day, and 6-month clinical and PRO data capture from 200 consented patients.

- **Secondary endpoints:**
    - Percent of patients who enroll on the study platform who had previously received a SARS-CoV-2 booster.

- Percent of patients who enroll on the study platform who went on to receive a SARS-CoV-2 booster after enrollment.
- Percent of patients providing patient reported outcomes (PROs) at each timepoint.
- Among patients providing PROs, percentage for which PROs were viewed by site personnel.
- Percent of patients reporting COVID-19 infection confirmed by home-based or other testing.
- Patient-reported adverse outcomes related to confirmed COVID-19 infection *(as applicable).*
- Hospitalization or death related to COVID-19 as ascertained by full EHR data transmission provided by permission from the patient *(as applicable).*

3 Study Design

3.1 Study Population and Duration of Participation

Up to 200 participants will be enrolled at up to 10 sites in the United States. Duration of participation in the study will be approximately six months.

3.2 Inclusion Criteria

1. Diagnosis of multiple myeloma per the International Myeloma Working Group and currently receiving active treatment for any phase of the disease, including initial therapy, maintenance, or relapsed disease.
2. Access to the internet.
3. An active patient portal (or willingness to activate).
4. Willing to electronically sign the study-specific consent and authorization form.

3.3 Exclusion Criteria

1. Non-English speaking.
2. Lack of internet access.
3. Cognitive impairment precluding ability to provide informed consent.

3.4 Subject Recruitment

Participants will be informed of the study by site physicians, other site personnel, or ASH Research Collaborative recruitment materials. The importance of SARS-CoV-2 booster vaccination in patients with multiple myeloma will be discussed/presented. Potential participants will be directed to the study application to learn more and provide consent if interested. Information about the study may be shared with participants by their care team in-person or virtually, through patient advocacy groups, or other IRB approved advertising mechanisms. Participants may also be contacted by IRB approved letter, social media, email, patient portal, textbacks, or phone call.

4 Study Procedures and Schedule of Events

4.1 Informed Consent

Before initiating any study procedures, subjects will review an electronic version of the informed consent and authorization using the link and/or QR code provided. Upon reviewing the form, the subject

will provide his/her/their electronic signature. A signed copy of the consent will be available to the subject upon signing.

4.2 Electronic Health Record Data Transmission

The following variables to be obtained from the electronic health record, include elements that fall under the categories below, as available through routine clinical practice or obtained as part of this study:

- Diagnoses and disease status
- Pathology
- Laboratory results
- Clinical features
- Co-morbid conditions
- Multiple myeloma related treatments

4.3 Patient-Generated Health Data

Subjects will be asked to complete questions specific to their health as outlined below. All questions will be administered electronically through the study application. These measures will be obtained to establish health status and COVID-19 infection(s) acquired after study entry. These measures will be included at baseline and at specified timepoints, as outlined in the Schedule of Activities.

The following patient-generated health data (PGHD) will be collected directly from the participating patient and are specified in Appendix A:

- Study eligibility questions
- Contact information and socio-demographics
- Multiple myeloma diagnosis and disease status
- SARS-CoV-2 vaccination history
- Documented COVID-19 infections and treatments
- COVID-19 specific questions

Participants may request additional information about COVID-19 booster vaccinations. Sponsor will receive notification that a participant has requested additional information. Sponsor will also monitor participant requests.

4.4 Patient Reported Outcomes

Subjects will be asked to complete standardized PROs specific to their quality of life as outlined below. All questions will be administered electronically through the study application. These measures will be obtained to establish feasibility of routine PRO capture. These measures will be included at baseline and at specified timepoints, as outlined in the Schedule of Activities:

Quality of Life PROs

- European Organisation for Research and Treatment of Cancer (EORTC) QLQ-MY20
- European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30

Participants will be reminded electronically, if needed, to complete PROs and questionnaires at Day 0, Day 30, and Day 180 as scheduled. Reminders will be provided in advance of the window, and then weekly until completed.

Health care personnel at sites where participants receive care may be asked to review PROs as part of routine care. The number of unique health care personnel and the number of unique geographic sites from where the PRO portal is accessed will be recorded.

4.5 Schedule of Activities

	Time 0 Screening, Consent, and Baseline	**Time 1**	**Time 2**
Activity	**Day 0**	**Day 30** *+ 15 days*	**Day 180** *+ 30 days*
Study ICAF	X		
EHR Data Transmitted	X	X	X
PGHD	X	X	X
PROs	X	X	X

Time 0 (Screening, Enrollment, and Baseline)

The following procedures will be performed at the time of screening and enrollment and will be completed virtually:

- Study ICAF
- EHR data transmission
- PGHD
- PROs

Time 1

Time 1 will occur 30 days (+ 15 days) following baseline and the following will be completed virtually:

- EHR data transmission
- PGHD
- PROs

Time 2

Time 2 will occur 180 days (+ 30 days) following baseline and the following will be completed virtually:

- EHR data transmission
- PGHD
- PROs

4.6 Subject Withdrawal and Early Termination

Subjects may withdraw from the study at any time without impact to their care. It will be documented whether or not each subject completes the study.

5 Statistical Considerations

The accrual goal for this study is the enrollment of 200 participants, defined as eligible subjects who access the portal and consent to participate. The primary end point of this study is the proportion of consented participants who provide responses for the PRO instruments; we will separately track the proportion of consented participants who permission access to clinical data through the EHR. We will estimate the proportions and present them descriptively, with a point estimate and an exact binomial confidence interval at each of the PRO time points (Baseline, Day 30, and Day 180). We will also present descriptively the proportion of consented participants who permission EHR access.

We will also report descriptive statistics for each of the secondary objectives, including the proportion of participants who had received a SARS-CoV-2 booster prior to enrollment; the proportion who received a SARS-CoV-2 booster after enrollment; the incidence of patient-reported COVID-19 infection confirmed

by home-based or other testing (per patient report); and the incidence of patient-reported adverse outcomes related to confirmed COVID-19 infection, including long COVID.

Lastly, we will report descriptive statistics on the incidence of hospitalization (at the primary institution at which the patient received myeloma care) or death related to COVID-19 during the 6-month period of observation. We will report estimates for these metrics from two forms of ascertainment: patient-permissioned EHR data transmission and site-provided EHR data abstraction (received under the Data Hub's overarching umbrella protocol). We may perform exploratory analyses of clinical and laboratory correlates of severe adverse COVID-19 related outcomes, sample size permitting, based on site-provided EHR data abstraction (under the Data Hub's umbrella protocol).

6 Safety and Adverse Events

Given this study is observational in nature and COVID-19 vaccines are administered as part of standard of care, reactions to COVID-19 vaccines **are not** considered an AE. If a subject has a reaction to a vaccine, investigators are encouraged to report those events to the FDA through MedWatch as they would through normal standards of practice. Patients may also submit any vaccine-related adverse events to the Centers for Disease Control and Prevention's Vaccine Adverse Event Reporting System.

There are no study procedures that are expected to generate adverse events.

7 Study Administration, Data Handling, and Record Keeping

7.1 Confidentiality

Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). These regulations require a signed subject authorization informing the subject of the following:

- What protected health information (PHI) will be collected from subjects in this study.
- Who will have access to that information and why.
- Who will use or disclose that information.
- The rights of a research subject to revoke their authorization for use of their PHI.

In the event that a subject revokes authorization to collect or use PHI, the investigator, by regulation, retains the ability to use all information collected prior to the revocation of subject authorization. For subjects that have revoked authorization to collect or use PHI, attempts should be made to obtain permission to collect at least vital status (i.e., that the subject is alive) at the end of their scheduled study period.

7.2 Data Collection and Management

All data will be collected and stored in the Data Hub. Data collection will be done from subjects' existing medical records and/or manual data entry into the Data Hub's electronic data capture form via a website or mobile application.

7.3 Physical Security and Access Control

The Data Hub provides end-to-end protection for all data, both in transit and at rest. Data Hub application environments use GPG with AES 256 encryption; all end-user connections to Data Hub Portals are encrypted using SSL; file transfers are conducted over SFTP or HTTPS; and all received FHIR messages and data files are individually encrypted with GPG before archiving in an AES 256 encrypted environment. Data is also archived to the Data Hub's secure cloud backups service. Everything contained on the Data Hub server is encrypted (e.g., GPG, AES256), and all data sent to and from the server is encrypted. All backups are encrypted with GPG before transmission.

7.4 Study Monitoring

Study data entered in the Data Hub will be reviewed by the study sponsor or designee on a regular basis to ensure data quality and timely data entry.

8 Ethical Considerations

This study is to be conducted in accordance with applicable United States government regulations and international standards of Good Clinical Practice, and applicable institutional research policies and procedures.

This protocol and any amendments will be submitted to a properly constituted independent Ethics Committee (EC) or IRB, in agreement with local legal prescriptions, for formal approval of the study conduct. The decision of the EC/IRB concerning the conduct of the study will be made in writing to the investigator and a copy of this decision will be provided to the study sponsor before commencement of this study.

8.1 Vulnerable Populations

Investigators should exercise discretion in ensuring that human subjects that may be vulnerable (prisoners, educationally disadvantaged, economically disadvantaged, or individuals with impaired decision making) undergo appropriate enrollment procedures and are protected.

8.2 Risks

Risk of loss of confidentiality: There is small risk of loss of confidentiality if identifiable data were inadvertently accessed by someone outside the study team. This risk is minimized by the use of secure storage methods.

8.3 Benefits

Subjects are not expected to directly benefit from this study. Knowledge gained from this study may benefit subjects with multiple myeloma.

8.4 Risk-Benefit Assessment

The procedures in this protocol are of minimal risk. The benefit and relevance of the knowledge gained from this study offset the risks associated with participating.

9 Study Finances

9.1 Funding Source

ASH Research Collaborative is the sponsor of the study, with funding support from Moderna Therapeutics.

9.2 Subject Payments

Modest remuneration will be provided to participants in the study to help defray the cost of participation. The following represents the projected compensation scheme for each subject; however, payments may be made in installments that accommodate participant scheduling.

Subjects will receive up to a total of $400 for completing all study visits:

- **Time 0**: $200 upon completion of enrollment activities (study ICAF, EHR data transmitted, PGHD, and PROs)
- **Time 1**: $100 (EHR data transmitted, PGHD, and PROs)
- **Time 2**: $100 (EHR data transmitted, PGHD, and PROs)

10 Key Personnel

Key study personnel include:

- Co-investigators
- ASH RC staff
- Subcontractors (as outlined below)

ASH RC will subcontract with the following organizations for the conduct of this study:

Breakthrough Healthcare

Breakthrough Healthcare provides clinical registry services, clinical dataset and measures development, program and service design, and organizational strategy services. Our clients include nonprofit medical societies, healthcare membership associations, government agencies, and data-driven healthcare enterprises.

Eureka Research

The cloud-based healthcare platform designed to empower people with their digital health data. The company's platform offers secure acquisition, harmonization, and utilization of health-related data from electronic health record and billing systems, surveys, wearables, sensors, and medical devices, enabling

users to embrace the potential of their health information and gather all their data into one place to improve health for themselves, their family, and for society.

IQVIA

IQVIA, the Data Hub's technology vendor, brings together advances in data science, technology, and healthcare expertise to help customers make better decisions and ultimately improve patient outcomes.

Yale Center for Outcomes Research & Evaluation

Yale Center for Outcomes Research & Evaluation (Yale CORE) is a leading national outcomes research center working on select projects designed to assess healthcare quality and evaluate clinical decision making and comparative effectiveness of specific healthcare interventions. Yale CORE will leverage its' scientific expertise and infrastructure to provide comprehensive data analytic services for this project.

References

Chu, L., Vrbicky, K., Montefiori, D. *et al.* Immune response to SARS-CoV-2 after a booster of mRNA-1273: an open-label phase 2 trial. *Nat Med* **28**, 1042–1049 (2022). https://doi.org/10.1038/s41591-022-01739-w

Appendix A: Patient-Generated Health Data Elements

Time 0 (Baseline)

Registration Questions			
First Name		**Middle Name**	
Last Name		**Date of Birth (DOB)**	/ /
Email Address *Required for payment purposes.*		**Phone Number** (optional)	( ) ____-________ O Decline to Provide

Before Informed Consent

Eligibility Survey	
Do you have access to your online medical records (patient health portal) or would you be willing to activate it?	O Yes O No
Have you been diagnosed with multiple myeloma?	O Yes O No
Are you currently receiving treatment for multiple myeloma?	O Yes O No

After Informed Consent

Participant Information	
Socio-Demographics	
Birth sex	O Male O Female O Other O Decline to Answer
What race(s) do you identify as? *(Select all that apply)*	☐ American Indian or Alaskan Native ☐ Asian ☐ Black or African American ☐ White ☐ Native Hawaiian or Other Pacific Islander ☐ Other ☐ Decline to Answer
Hispanic ethnicity	O Hispanic or Latino/Latina O Not Hispanic or Latino/Latina O Decline to Answer

COVID-19 History		
List all COVID-19 vaccinations received.		
Have you received a COVID-19 Vaccination?	O Yes O No O I Don't Know	
Vaccination date	**Which vaccine dose(s) did you receive?**	**Which vaccine did you receive?**
/ (MM/YYYY) O I Don't Know	O First Dose O Second Dose O Booster(s) O I Don't Know	O Pfizer O Moderna O Johnson & Johnson O Novavax O I Don't Know
/ (MM/YYYY) O I Don't Know	O First Dose O Second Dose O Booster(s) O I Don't Know	O Pfizer O Moderna O Johnson & Johnson O Novavax O I Don't Know
/ (MM/YYYY) O I Don't Know	O First Dose O Second Dose O Booster(s) O I Don't Know	O Pfizer O Moderna O Johnson & Johnson O Novavax O I Don't Know
/ (MM/YYYY) O I Don't Know	O First Dose O Second Dose O Booster(s) O I Don't Know	O Pfizer O Moderna O Johnson & Johnson O Novavax O I Don't Know
/ (MM/YYYY) O I Don't Know	O First Dose O Second Dose O Booster(s) O I Don't Know	O Pfizer O Moderna O Johnson & Johnson O Novavax O I Don't Know
/ (MM/YYYY) O I Don't Know	O First Dose O Second Dose O Booster(s) O I Don't Know	O Pfizer O Moderna O Johnson & Johnson O Novavax O I Don't Know
If you have not received any COVID-19 booster vaccinations, would you be willing to be contacted to discuss the benefits and risks of obtaining one?		O Yes O No O I Don't Know
Would you be willing to receive a yearly COVID-19 vaccination if recommended by your physician?		O Yes O No O I Don't Know

COVID-19 Infections			
List all current and prior COVID-19 infections.			
Have you been diagnosed with COVID-19?	O Yes O No O I Don't Know		
When was your COVID-19 Infection Confirmed?	/ (MM/YYYY) O I Don't Know	**How was your COVID-19 Infection Confirmed?**	O Home Test Kit O Diagnosis by a Healthcare Professional O I Don't Know
Did This COVID-19 Infection Cause You to be Hospitalized?	O Yes O No O I Don't Know	**If Yes, About How Many Days Were You in the Hospital?**	____________ O I Don't Know

Time 1 (30 Days) and Time 2 (180 Days)

COVID-19 History		
List all COVID-19 vaccinations received since you completed the Baseline questionnaire.		
Have you received a COVID-19 vaccine since your last visit?		O Yes O No O I Don't Know
Vaccination Date	**Which Vaccine Dose Did You Receive?**	**Which Vaccine Did You Receive?**
/ (MM/YYYY) O I Don't Know	O First Dose O Second Dose O Booster(s) O I Don't Know	O Pfizer O Moderna O Johnson & Johnson O Novavax O I Don't Know
/ (MM/YYYY) O I Don't Know	O First Dose O Second Dose O Booster(s) O I Don't Know	O Pfizer O Moderna O Johnson & Johnson O Novavax O I Don't Know
/ (MM/YYYY) O I Don't Know	O First Dose O Second Dose O Booster(s) O I Don't Know	O Pfizer O Moderna O Johnson & Johnson O Novavax O I Don't Know
/ (MM/YYYY) O I Don't Know	O First Dose O Second Dose O Booster(s) O I Don't Know	O Pfizer O Moderna O Johnson & Johnson O Novavax O I Don't Know
/ (MM/YYYY) O I Don't Know	O First Dose O Second Dose O Booster(s) O I Don't Know	O Pfizer O Moderna O Johnson & Johnson O Novavax O I Don't Know
/ (MM/YYYY) O I Don't Know	O First Dose O Second Dose O Booster(s) O I Don't Know	O Pfizer O Moderna O Johnson & Johnson O Novavax O I Don't Know
If you have not received any COVID-19 booster vaccinations, would you be willing to be contacted to discuss the benefits and risks of obtaining one?		O Yes O No O I Don't Know
Would you be willing to receive a yearly COVID-19 vaccination if recommended by your physician?		O Yes O No O I Don't Know

COVID-19 Infections			
List all COVID-19 infections since you completed the Baseline questionnaire.			
Have you been diagnosed with COVID-19 since your last visit?		O Yes O No O I Don't Know	
When was your COVID-19 Infection Confirmed?	/ (MM/YYYY) O I Don't Know	**How was your COVID-19 Infection Confirmed?**	O Home Test Kit O Diagnosis by a Healthcare Professional O I Don't Know
Did This COVID-19 Infection Cause You to be Hospitalized?	O Yes O No O I Don't Know	**If Yes, About How Many Days Were You in the Hospital?**	__________ O I Don't Know