# THOMAS JEFFERSON UNIVERSITY
# Sidney Kimmel Cancer Center

## Open Label Single Arm Study to Assess the Implementation of Home Based Daratumumab Administration In Patients Being Treated for Multiple Myeloma


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## Signature Page

The signature below constitutes the approval of this protocol and the attachments, and provides the necessary assurances that this trial will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable US federal regulations and ICH guidelines.

Principal Investigator:

Signed: _____ Date: _____

Name: Adam Binder

Title: Assistant Professor

## Statement of Compliance

This study will be conducted in accordance with the International Conference on Harmonisation guidelines for Good Clinical Practice (ICH E6), the Code of Federal Regulations on the Protection of Human Subjects (45 CFR Part 46), and Thomas Jefferson University research policies

# List of Abbreviations

| | |
|---|---|
| AE | Adverse Event/Adverse Experience |
| CFR | Code of Federal Regulations |
| CIOMS | Council for International Organizations of Medical Sciences |
| CONSORT | Consolidated Standards of Reporting Trials |
| CRF | Case Report Form |
| CRO | Clinical Research Organization |
| CTCAE | Common Terminology Criteria for Adverse Events |
| CTSQ | Cancer Treatment Satisfaction Questionnaire |
| DSMC | Data and Safety Monitoring Committee |
| DSMP | Data and Safety Monitoring Plan |
| FDA | Food and Drug Administration |
| FWA | Federalwide Assurance |
| GCP | Good Clinical Practice |
| GWAS | Genome-Wide Association Studies |
| HIPAA | Health Insurance Portability and Accountability Act |
| IB | Investigator's Brochure |
| ICF | Informed Consent Form |
| ICH | International Conference on Harmonisation |
| IDE | Investigational Device Exemption |
| IND | Investigational New Drug Application |
| IRB | Institutional Review Board |
| MedDRA | Medical Dictionary for Regulatory Activities |
| MOP | Manual of Procedures |
| N | Number (typically refers to participants) |
| NCI | National Cancer Institute |
| NIH | National Institutes of Health |
| OHRP | Office for Human Research Protections |
| OOCAT | Oncology Opportunity Cost Assessment Tool |
| PHI | Protected Health Information |
| PI | Principal Investigator |
| PRC | Protocol Review Committee |
| QA | Quality Assurance |
| QC | Quality Control |

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|---|---|
| SAE | Serious Adverse Event/Serious Adverse Experience |
| SDS | Safety Data Sheet (formerly MSDS; Material Safety Data Sheet) |
| SKCC | Sidney Kimmel Cancer Center |
| SOP | Standard Operating Procedure |
| TJU | Thomas Jefferson University |
| UAP | Unanticipated Problem |

## Study Summary

**Title:** Open Label Single Arm Study to Assess the Implementation of Home based daratumumab administration.

**Précis:** This study will include all patients on the monthly phase of daratumumab. Patient reported outcome metrics as well as implantation metrics will be measured.

**Objectives:**

Primary: Evaluate treatment burden (using the CTSQ).

Secondary:

1. Determine adherence to home delivery of Darzalex-Faspro.
2. Evaluate quality of life (using EORTC QLQ-30) based on site of care (home vs. infusion center).
3. Evaluate financial burden (using the COST survey) based on site of care (home vs. infusion center).
4. Evaluate Safety of home administration of darzalex-faspro.
5. Evaluate barriers to home administration.

Exploratory:

1. Evaluate patient perceptions of home administration of anti-neoplastic therapy
2. Evaluate opportunity cost based on site of care (home vs. infusion center) using the Oncology Opportunity Cost Assessment Tool (OOCAT)

**Population:** The sample size will be 20 participants. All patients with a diagnosis of multiple myeloma who are receiving the monthly phase of daratumumab.

**Phase:** Pilot study

**Number of Sites:** 1- Sidney Kimmel Cancer Center
Thomas Jefferson University
925 Chestnut street, 4th floor
Philadelphia, PA 19107

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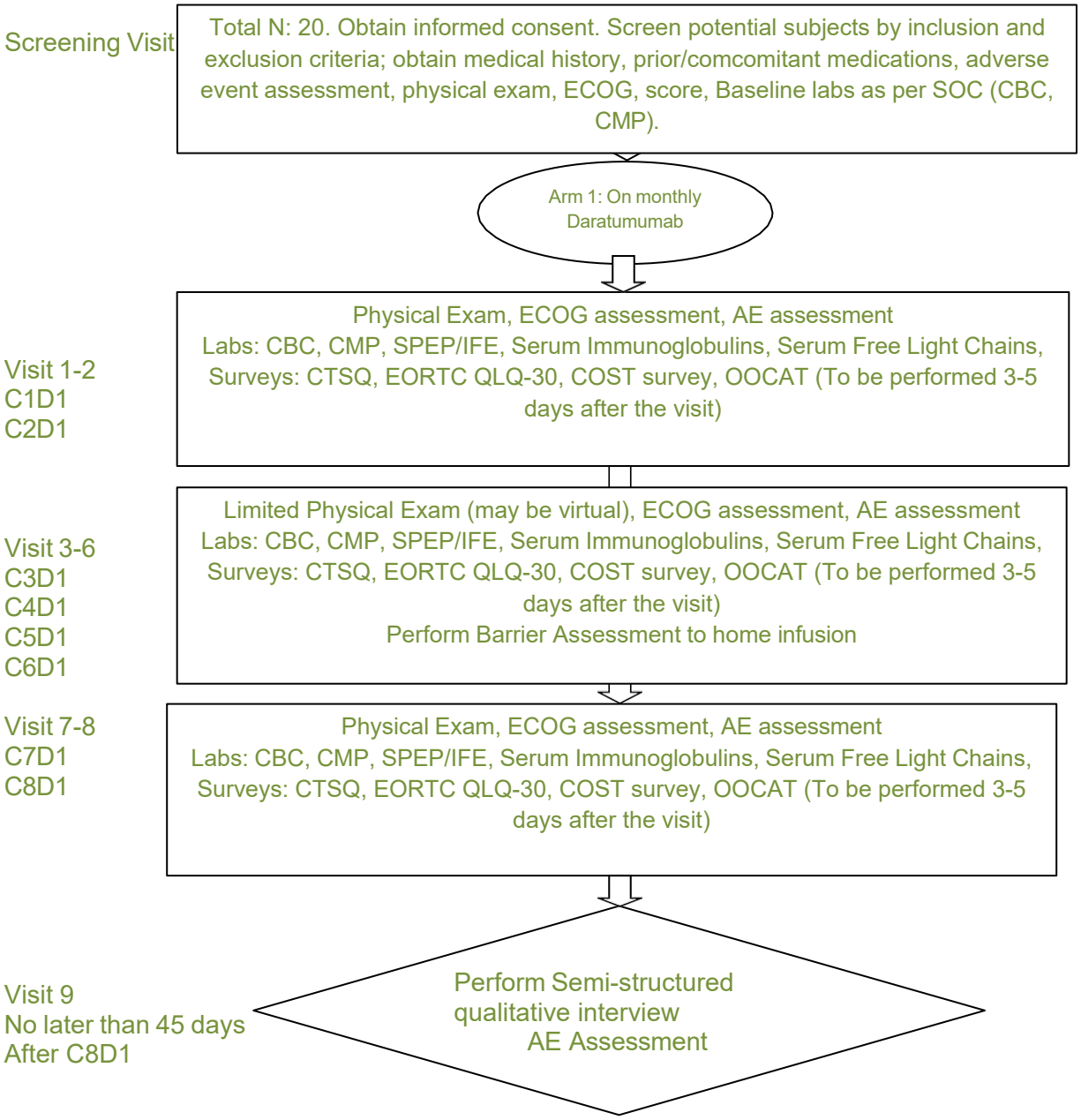
| **Description of Intervention:** | 1) All participants included in the study will receive daratumumab subcutaneous injection therapy (fixed dose 1800mg). On study, participants will receive 2 cycles of daratumumab in the infusion center, followed by 4 cycles at home followed by 2 more cycles at the infusion center. At the beginning of each cycle, patient reported outcome surveys and quality of life surveys will be collected (EORTC-QLQ-30, CTSQ, COST, and OOCAT). During the infusion center phase, administration will be given by an infusion center nurse. During the home infusion phase of the study a home infusion nurse will administer darzalex-faspro. During home administration, specific details on barriers to maintaining adherence will be collected and described with descriptive analysis (i.e. issues with storage, delivery, disposal of medication). |
| **Study Duration:** | 36 months |
| **Participant Participation Duration:** | 10 months |
| **Estimated Time to Complete Enrollment:** | 26 months |

**Schematic of Study Design:**




# 1 Introduction

## 1.1 Background Information

Multiple myeloma is an incurable cancer of the plasma cells that can be complicated by hypercalcemia, renal failure, anemia, bone lesions, and recurrent infections. Over the last two decades the treatment paradigm for multiple myeloma has changed dramatically[1]. With the evolution of more effective treatments, patients are living longer with a better quality of life. As

part of this evolution, especially within the US, continuous treatment approach as opposed to intermittent treatment approach has become the standard of care[2]. However, these improvements come with a cost. Not only is the total cost of care extraordinary[3-5], but the financial burden on the patient is also high[6]. In one study, 46% of patients with a diagnosis of multiple myeloma had to use their savings to help pay for their cost of care and 71% experienced financial burden with 20% of respondents reporting severe financial burden[6].

In addition, to financial cost of care, treatment burden and exposure to the healthcare system must be considered. For many patients receiving anti-myeloma therapy, treatments require weekly visits to the cancer center resulting in hours of time spent traveling to, waiting for, and receiving treatment. Time that could be spent in the comfort of their homes. This is particularly important in the current pandemic, in which patients are encouraged to shelter in place in order to minimize exposures to SARS–CoV-2. A recent study published revealed that patients with multiple myeloma, regardless of their disease status, have a high mortality rate if they contract SARS-CoV-2[7]. As a result of this publication and other data, the American Society of Hematology continues to recommend minimizing patient exposure to the health care system and to consider changing to all oral therapy when able[8]. While this recommendation balances efficacy of treatment with risk of COVID-19, treatment efficacy is compromised as it has been well established that triplet or quadruplet (if dara containing regimen) is superior to doublet therapies [9-11].

For these reasons mentioned above, home-based chemotherapy, administered by a trained team, should be considered. Chemotherapy at home remains uncommon in the US, though models for its use exist globally[12]. In these models, home-based chemotherapy is safe, preferred by patients, and can be administered at lower cost. Given that the healthcare economics within the United States is not comparable to other systems where a national healthcare system exists, research into the implementation of and barriers to home based chemotherapy within the US is vital. This need is reinforced by a recent position statement published by ASCO[13]. Herein, we propose to evaluate the implementation of a home based subcutaneous daratumumab program for patients with multiple myeloma. We hypothesize that this program will be feasible, reduce patient treatment and financial burden, improve quality of life and at the same time, minimize risk to the patient during the COVID-19 pandemic without sacrificing treatment efficacy.

## 1.2 **Rationale for the Proposed Study**

We propose to study the implementation of a home based anti-neoplastic therapy program with subcutaneous daratumumab and hyaluronidase-fihj (1800mg fixed dose). Home based chemotherapy has been well established in countries with national health care systems, but it has not been well studied within the US healthcare system. We plan to evaluate patient reported outcomes related to quality of life, treatment burden and cost burden of a home based anti-neoplastic therapy model. We will also evaluate the feasibility of delivering and administering anti-neoplastic therapy in the home. We

hypothesize that a home based anti-neoplastic therapy program will be feasible and improve quality of life while at the same time reduce treatment and cost burden.

## 1.3 Correlative Studies

N/A

## 1.4 Potential Risks and Benefits

### 1.4.1 Potential Risks

Potential risks associated with the administration of DARZALEX FASPRO in the home:

- Potential for delay in treatment due to medication not being delivered.
- Potential for missed doses or wasted doses of medication.

### 1.4.2 Benefits

Potential benefits of the study include:

- Improved quality of life while receiving medication in the home setting
- Decreased cost of care during the study period
- Decreased burden of care during the study period

# 2 Study Objectives

## 2.1 Objectives

### 2.1.1 Primary

1. Evaluate treatment burden (using the CTSQ).

### 2.1.2 Secondary

1. Determine adherence to home delivery of DARZALEX FASPRO.
2. Evaluate quality of life (using EORTC QLQ-30) based on site of care (home vs. infusion center).
3. Evaluate financial burden (using the COST survey) based on site of care (home vs. infusion center).
4. Evaluate Safety of home administration of darzalex-faspro.
5. Evaluate barriers to home administration.

### 2.1.3 **Exploratory**

1. Evaluate patient perceptions of home administration of anti-neoplastic therapy.
2. Evaluate opportunity cost based on site of care (home vs. infusion center) (using the OOCAT survey).

## 2.2 **Endpoints/Outcome Measures**

### 2.2.1 **Primary**

1. Treatment satisfaction will be measured using the Cancer Treatment Satisfaction Questionnaire (CTSQ).

### 2.2.2 **Secondary**

1. Adherence is defined as completing administration of medication in the home setting. Adherence will be measured for each dose given and failure would occur if the participant needs to go to the infusion center for administration for whatever reason. Based on previous studies of home based administration adherence rates over 75% would be needed to meet criteria for feasibility.
2. Measurement of quality of life will be measured using the EORTC QLQ-30.
3. Financial toxicity will be measured using the COST survey.
4. Safety will be evaluated through collection of adverse events, administration reactions related to Darzalex-Faspro.
5. Barriers to home administration will be measured through any delays in treatment related to delivery of medication, arrival time of the infusion nurse, issues related to storage of medication, issues related to administration of the medication.

### 2.2.3 **Exploratory**

1. Patient perceptions of home based anti-neoplastic therapy will be measured through semi-structured interviews.
2. Opportunity cost will be measured through the OOCAT survey.

# 3 **Study Design**

## 3.1 **Characteristics**

Open label, non-randomized trial in patients with multiple myeloma who are receiving DARZALEX FASPRO (daratumumab and hyaluronidase).

## 3.2 **Number of Participants**

20

## 3.3 Duration of Therapy

8 months

## 3.4 Duration of Follow Up

2 months

## 3.5 Treatment Assignment Procedures

### 3.5.1 Randomization Procedures (if applicable)

N/A

### 3.5.2 Masking Procedures (if applicable)

N/A

## 3.6 Study Timeline

### 3.6.1 Primary Completion

26 months to complete study enrollment.

### 3.6.2 Study Completion

36 months to study completion.

# 4 Study Enrollment and Withdrawal

## 4.1 Eligibility Criteria

### 4.1.1 Inclusion Criteria

Individuals must meet all of the following inclusion criteria in order to be eligible to participate in the study:

1. Able to provide signed and dated informed consent form
2. Willing to comply with all study procedures and be available for the duration of the study
3. Male or female, aged greater than 18 years of age
4. Has a diagnosis of Multiple Myeloma
5. Is on the monthly phase of daratumumab (either IV or SubQ) based regimen (every 4 weeks) (either monotherapy or in combination with oral agents)
6. Is willing to receive daratumumab subcutaneous injections
7. Lives within the range of Jefferson Home Infusion Services

8. Patients are willing to allow home infusion company visit them and administer Darzalex-Faspro in the home.
9. Women of reproductive potential must use highly effective contraception
10. Men of reproductive potential must use highly effective contraception
11. Adequate bone marrow function: ANC >1,000, Platelet Count > 50,000
12. Adequate liver function: AST/ALT < 2.5 times ULN, Bilirubin <2 times ULN
13. Adequate renal function: CrCl ≥ 20mL/min for single agent SC daratumumab. For combination studies: with lenalidomide ≥ 30mL/min
14. English Speaking

#### 4.1.2 **Exclusion Criteria**

An individual who meets any of the following criteria will be excluded from participation in this study:

1. Receiving daratumumab for an indication other than multiple myeloma
2. Receiving daratumumab in combination with other IV or subcutaneous therapy
3. Pregnancy or lactation
4. Known allergic reactions to components of the study product(s)
5. Uncontrolled human immunodeficiency virus (HIV)

6. Seropositive for hepatitis B (defined by a positive test for hepatitis B surface antigen [HBsAg]) who are not on hepatitis B prophylaxis. Subjects with resolved infection (ie, subjects who are HBsAg negative but positive for antibodies to hepatitis B core antigen [anti-HBc] and/or antibodies to hepatitis B surface antigen [anti-HBs]) must be screened using real-time polymerase chain reaction (PCR) measurement of hepatitis B virus (HBV) DNA levels. Those who are PCR positive and not on Hep B prophylaxis will be excluded. EXCEPTION: Subjects with serologic findings suggestive of HBV vaccination (anti-HBs positivity as the only serologic marker) AND a known history of prior HBV vaccination, do not need to be tested for HBV DNA by PCR.

7. Patients with reactivation of hepatitis B will be excluded.

8. Seropositive for hepatitis C (except in the setting of a sustained virologic response [SVR], defined as a viremia at least 12 weeks after completion of antiviral therapy).

9. Chronic obstructive pulmonary disease (COPD) with a forced expiratory volume in 1 second (FEV1) < 50% of predicted normal. Note that FEV1 testing is

required for participants suspected of having COPD and participants must be excluded if FEV1 is < 50% of predicted normal.

10. Moderate or severe persistent asthma within the past 2 years, or uncontrolled asthma of any classification. Note that participants who currently have controlled intermittent asthma or controlled mild persistent asthma are allowed to participate.

11. Clinically significant cardiac disease, including:
    a. Myocardial infarction within 6 months before randomization, or unstable or uncontrolled disease/condition related to or affection cardiac function (e.g., unstable angina, congestive heart failure, New York Heart Association Class III-IV)
    b. Uncontrolled cardiac arrhythmia
    c. Screening 12-lead ECG showing a baseline QT interval as corrected by Fridericia's formula >470 msec

- Non-English Speaking

## 4.2 Gender/Minority/Pediatric Inclusion for Research

Women and individuals of ethnic and racial minorities will be included in the study. Interval evaluations will occur to ensure women and individuals of ethnic and racial minorities are being enrolled onto the study. Processes to increase enrollment for this population will occur if they are found to be underrepresented. Pediatric patients will not be included in the study, but Multiple Myeloma is not a disease of individuals under the age of 18.

## 4.3 Strategies for Recruitment and Retention

Physicians, advanced practice practitioners or other supportive care staff will introduce the opportunity for clinical trial enrollment. We will collaborate with the SKCC's Recruitment Enhancement Service (RES), a dedicated recruitment resource nested within the SKCC's CRO that is available to all study teams. The goals of the RES are to reduce the burden of recruitment, to free up the time and resources of study teams, and to ensure teams meet recruitment goals on time. RES services include: (1) consulting with study teams to identify strategies for recruitment and retention of research participants; (2) searching the EHR to identify potential participants (e.g., searching by diagnostic labels and billing codes); (3) facilitating both paper and electronic contact of those individuals to invite their participation; and (4) enabling networking opportunities across Jefferson, its owned entities, and local community hospitals so that investigators can share recruitment resources. (5) Promoting studies via various mechanisms including social media. Overall, the RES model has successfully enrolled thousands of participants for studies, allowing them to meet their recruitment goals more quickly and easily. We will

collaborate with the SKCC's Recruitment Enhancement Service (RES) to query the EHR system to identify participants who are eligible for this study. We may also leverage their existing relationships with community organizations and local hospitals, expertise in traditional and social media, and in-house resources for promotion of studies. This will include individuals with an ICD-9-CM (or ICD-10-CM) diagnostic code at either an office visit or on their list of known chronic conditions.

Multiple contact methods will be obtained to maintain communication and follow up with participants. Extensive discussion of risks and possible benefits of study participation will be provided to participants and their families, if applicable. A consent form describing in detail the study procedures and risks will be given to the participant. Consent forms will be IRB-approved, and the participant is required to read and review the document or have the document read to him or her. The investigator or designee will explain the research study to the participant and answer any questions that may arise. The participant will sign the informed consent document prior to any study-related assessments or procedures. Participants will be given the opportunity to discuss the study with their surrogates or think about it prior to agreeing to participate. They may withdraw consent at any time throughout the course of the study. A copy of the signed informed consent document will be given to participants for their records. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their clinical care will not be adversely affected if they decline to participate in this study. The consent process will be documented in the clinical or research record.

## 4.4 Participant Withdrawal

### 4.4.1 Reasons for Withdrawal

Participants are free to withdraw from participation in the study at any time upon request.

An investigator may terminate a study participant's participation in the study if:

- Any clinical adverse event (AE), laboratory abnormality, or other medical condition or situation occurs such that continued participation in the study would not be in the best interest of the participant.
- The participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation.

### 4.4.2 Handling of Participant Withdrawals and Participant Discontinuation of Study Intervention

Participants who withdraw or discontinue the study intervention early will continue to receive their treatment in the infusion center as per the standard of care. If a patient withdraws from study early, end of study visit (semi-structured qualitative interviews) will

be offered. If a participant withdraws or discontinues the study early, they may be replaced at the discretion of the sponsor and Principal Investigator.

## 4.5 Premature Termination or Suspension of Study

This study may be suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to the investigator, Janssen Scientific Affairs, LLC, regulatory authorities. If the study is prematurely terminated or suspended, the principal investigator will promptly inform the IRB and will provide the reason(s) for the termination or suspension.

Circumstances that may warrant termination include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants.
- Insufficient adherence to protocol requirements.
- Data that is not sufficiently complete and/or evaluable.
- Determination of futility.

# 5 Study Intervention

## 5.1 Study Product

DARZALEX FASPRO (daratumumab and hyaluronidase-fihj) for subcutaneous (SC) administration

### 5.1.1 Daratumumab SC Dosing:

All daratumumab administrations will be in an outpatient or home setting. Subjects will receive pre-injection medications and post-injection medication as outlined in Sections 5.7.1 and 5.7.2, respectively.

Vital signs should be monitored extensively on Cycle 1 Day 1 before, and after the first administration of daratumumab. Patients will be monitored for 3 hours after the first subcutaneous injection as per institutional protocol. For all other administrations, vital signs should be measured before the start of injection and at the end of the injection. If the subject experiences any significant medical event, then the investigator should assess whether the subject should stay overnight for observation. If the subject has not experienced a significant medical event but is hospitalized overnight only for observation, then the hospitalization should not be reported as an SAE.

If an IRR develops, then the injection should be temporarily interrupted or slowed down. In the event of a life-threatening IRR (which may include pulmonary or cardiac events)

or anaphylactic reaction, daratumumab SC should be discontinued, and no additional daratumumab SC should be administered to the participant.

## 5.2 Study Product Description

### 5.2.1 Acquisition

The FDA approved product daratumumab and hyaluronidase-fihj will be supplied by the manufacturer during the home infusion phase of the study. During the infusion center phase of the study, the product will be acquired by the pharmacy.

### 5.2.2 Formulation, Packaging, and Labeling

Injection: 1,800 mg daratumumab and 30,000 units hyaluronidase per 15 mL (120 mg and 2,000 units/mL) solution in a single-dose vial.

DARZALEX FASPRO (daratumumab and hyaluronidase-fihj) injection is a sterile, preservative free, colorless to yellow, and clear to opalescent solution for subcutaneous use supplied as individually packaged single-dose vials providing 1,800 mg of daratumumab and 30,000 units of hyaluronidase per 15 mL (NDC 57894-503-01).

### 5.2.3 Product Storage and Stability

Store DARZALEX FASPRO vials in a refrigerator at 2ºC to 8ºC (36ºF to 46ºF) in the original carton to protect from light. Do not freeze or shake.

Once ready for use, it should be removed from refrigeration and equilibrate to ambient temperature [15°C to 30°C (59°F to 86°F)]. Store the unpunctured vial at ambient temperature and ambient light for a maximum of 24 hours. Keep out of direct sunlight.

If the syringe containing DARZALEX FASPRO is not used immediately, store refrigerated at 2°C to 8°C (36°F to 46°F) for up to 24 hours and/or at room temperature at 15°C to 25°C (59°F to 77°F) for up to 12 hours under ambient light.

Discard if storage time exceeds these limits.

## 5.3 If stored in the refrigerator, allow the solution to come to room temperature before administration.Dosage, Preparation, and Administration

**Daratumumab – Subcutaneous**

Daratumumab SC will be provided as a fixed-dose (1800 mg), combination drug product containing rHuPH20 drug substance (2000 U/mL) and daratumumab drug substance (120 mg/mL) in a single vial.

**Daratumumab Administration – Subcutaneous**

[Daratumumab should be given according to product information: http://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/DARZALEX+Faspro-pi.pdf]

Daratumumab (1800 mg) will be administered by SC injection by manual push over approximately 3 – 5 minutes in the abdominal subcutaneous tissues in the left/right locations, alternating between individual doses. The volume of the SC solution will be 15 mL for the 1800 mg dose. Reasons for continued observation on subsequent daratumumab injection may include but are not limited to the following: subjects with a higher risk of respiratory complications (e.g., subjects with mild asthma or subjects with COPD who have an FEV1 < 80% at screening or developed FEV1 < 80% during the study without any medical history), subjects with IRR with the first injection of study drug, subject with decreased condition on day of dosing compared to prior dosing day. The dose of daratumumab will remain constant throughout the study.

## 5.4 Dose Modifications and Dosing Delays

No dose reductions of DARZALEX FASPRO are recommended. Consider withholding DARZALEX FASPRO to allow recovery of blood cell counts in the event of myelosuppression.

Medication will be discontinued for life threatening hypersensitivity reactions.

## 5.5 Study Product Accountability

Records of study medication used, dosages administered, and intervals between visits and the completion of the study should be captured in the Drug Accountability Form. This information must be captured in the source document at each patient visit.

At the conclusion of the study, and, as appropriate during the course of the study, all unused drug will be properly destroyed and discarded.

## 5.6 Assessing Participant Compliance with Study Product Administration

Regular monitoring will take place to assess participant compliance with completion of the questionnaires. Research coordinators will review Redcap to ensure questionnaires are completed in a timely manner when these questionnaires are being completed electronically (during the home infusion phase of the study).

## 5.7 Concomitant Medications/Treatments

### 5.7.1 Pre-dose Medications for Prevention of Injection Reactions

All participants will receive the following medications 1 to 3 hours prior to each study drug administration:

- An antipyretic: paracetamol (acetaminophen) 650-1000 mg IV or PO
- An antihistamine: diphenhydramine 25-50 mg IV or PO or equivalent. Avoid IV use of promethazine.
    - After Cycle 6, if a participant has not developed an infusion-related reaction and is intolerant to antihistamines, modifications are acceptable as per investigator discretion.
- Corticosteroids (Long-acting or intermediate-acting):
    - Monotherapy: Methylprednisolone 100 mg, or equivalent, administered intravenously. Following the second infusion, the dose of corticosteroid may be reduced (oral or intravenous methylprednisolone 60 mg or equivalent).
    - Combination therapy:
        - Administer 20 mg dexamethasone (or equivalent) prior to every daratumumab infusion. When dexamethasone is the background regimen specific corticosteroid, the dexamethasone treatment dose will instead serve as pre-medication on daratumumab infusion days.
        - Dexamethasone is given orally or intravenously prior to the first daratumumab infusion and oral administration may be considered prior to subsequent infusions.
    - If the subject does not experience a major systemic administration-related reaction after the first 3 doses, consider discontinuing the administration of corticosteroids (excluding any background regimen-specific corticosteroid).
    - As per institutional guidelines, a leukotriene inhibitor (montelukast 10 mg PO or equivalent) is optional in Cycle 1 Day 1 and can be administered up to 24 hours before infusion as per investigator discretion.

If necessary, all PO pre-infusion medications may be administered out of the clinic on the day of the infusion, provided they are taken within 3 hours before administration. In the home setting, similarly, patients may take their premedication prior to the nurse arrival provided they are taken within 3 hours of Darzalex-Faspro administration.

### 5.7.2 **Post-dose Medication:**

Administer post-infusion medication to reduce the risk of delayed infusion related reactions as follows:

- *Monotherapy studies:*
    - In an effort to prevent delayed infusion-related reactions, all participants will receive long- or intermediate-acting corticosteroid orally (20 mg methylprednisolone or equivalent in accordance with local standards) on the 2 days following all daratumumab infusions (beginning the day after the infusion).
    - In the absence of infusion related AEs after the first 3 infusions, post-infusion corticosteroids should be administered per investigator discretion.
- *Combination therapy:*

- Consider administering low-dose methylprednisolone (≤ 20 mg) or equivalent, the day after the infusion. However, if a background regimen-specific corticosteroid (e.g. dexamethasone) is administered the day after the infusion, additional post-infusion steroids are not required, but may be considered by the investigator.

- **For all studies:**
  - For participants with a higher risk of respiratory complications (e.g. participants with mild asthma or participants with COPD who have an FEV1 < 80% at screening or developed FEV1 < 80% during the study without any medical history) the following post-infusion medication should be considered:
    - Antihistamine (diphenhydramine or equivalent)
    - Leukotriene inhibitor (montelukast or equivalent)
    - Short-acting β2 adrenergic receptor agonist such as salbutamol aerosol
    - Control medications for lung disease (e.g. inhaled corticosteroids ± long-acting β2 adrenergic receptor agonists with asthma; long-acting bronchodilators such as tiotropium or salmeterol ± inhaled corticosteroids for participants with COPD)
  - In addition, these at-risk participants may be hospitalized for monitoring for up to 2 nights after daratumumab administration. If participants are hospitalized, then an improvement in FEV1 should be performed and documented prior to discharge. If these participants are not hospitalized, then a follow-up telephone call should be made to monitor their condition within 48 hours after all infusions. If the participant has not experienced a significant medical event but is hospitalized overnight only for observation, then the hospitalization should not be reported as a serious adverse event. Investigators may prescribe bronchodilators, H1-antihistamines, and corticosteroids that are deemed necessary to provide adequate supportive care in the event a bronchospasm occurs after participants are released from the hospital/clinic. If an at-risk participant experiences no major infusion-related reactions, then these post-infusion medications may be waived after 4 doses at the investigator's discretion.
  - Any post-infusion medication will be administered after the infusion has completed.

### 5.7.3 **Prophylaxis for Herpes Zoster**

- Initiate antiviral prophylaxis to prevent herpes zoster reactivation within 1 week after starting DARZALEX FASPRO and continue for 3 months following the end of treatment

### 5.7.4 **Prophylaxis and Management of Hepatitis B Reactivation**

- Prophylaxis for Herpes Zoster Reactivation:
  - Prophylaxis for herpes zoster reactivation is recommended during the Treatment Phase, as per institutional guidelines. Initiate antiviral

prophylaxis to prevent herpes zoster reactivation within 1 week after starting study treatment and continue for 3 months following study treatment. Acceptable antiviral therapy includes acyclovir (eg 400 mg given orally 3 times a day, or 800 mg given orally 2 times a day or per institutional standards), famcyclovir (eg, 125 mg given orally, twice a day or per institutional standards), or valacyclovir (eg, 500 mg given orally, twice a day or per institutional standards), initiated within 1 week after the start of study drug.

- Management of Hepatitis B Virus Reactivation:
  - Primary antiviral prophylaxis is permitted as per local standard of care. Per protocol, HBV DNA testing by PCR is mandatory for participants at risk for HBV reactivation.
  - In patients who develop reactivation of HBV while on study treatment, suspend treatment with study treatment and any concomitant steroids, anti-neoplastic therapy, and institute appropriate treatment. Resumption of study treatment in patients whose HBV reactivation is adequately controlled should be discussed with physicians with expertise in managing HBV.

## 5.8 Dietary Restrictions

None

# 6 Study Schedule

## 6.1 Pretreatment Period/Screening

**Screening Visit (Day -30 to -1)**

- Obtain and document consent from potential participant on study consent form.
- Review medical history to determine eligibility based on inclusion/exclusion criteria.
- Review medications history to determine eligibility based on inclusion/exclusion criteria.
- Perform medical examinations needed to determine eligibility.
- Document ECOG performance status
- Collect screening labs: CBC, CMP, SPEP, sFLC, Serum Immunoglobulins, Pregnancy Test (serum or urine) for women of child bearing potential
- Document Current Multiple Myeloma Disease Status
- Schedule study visits for individuals who are eligible and available for the duration of the study.

## 6.2 Treatment Period

**Initial Visit (Visit 1, Day 1)**

- Verify inclusion/exclusion criteria.
- Document any changes in Medical History, Concomitant Medications
- Perform and record physical exam findings.
- Document ECOG performance status
- Collect labs: CBC, CMP, SPEP, sFLC, Serum Immunoglobulins
- Document Current Multiple Myeloma Disease Status
- Complete the following surveys electronically (Surveys will be completed 3-5 days after the treatment day):
    - Cancer Treatment Satisfaction Survey
    - EORTC QLQ-C30
    - COST Survey
    - OOCAT Survey
- Administer DARZALEX FASPRO in the infusion center. No observation period needed.

**Visit 2, Day 29 ± 3 days**

- Record adverse events as reported by participant or observed by investigator.
- Document any changes in Medical History, Concomitant Medications
- Perform and record physical exam findings.
- Document ECOG performance status
- Collect labs: CBC, CMP, SPEP, sFLC, Serum Immunoglobulins
- Document Current Multiple Myeloma Disease Status
- Complete the following surveys electronically (Surveys will be completed 3-5 days after the treatment day):
    - Cancer Treatment Satisfaction Survey
    - EORTC QLQ-C30
    - COST Survey
    - OOCAT Survey
- Administer DARZALEX FASPRO in the infusion center. No observation period needed.

**Visit 3 Day 57 ± 3 days**

- Record adverse events as reported by participant or observed by investigator (visit with provider may take place via telehealth).
- Document any changes in Medical History, Concomitant Medications
- Perform and record physical exam findings (may be limited if performed virtually) by APP or physician prior to home nursing visit.
- Document ECOG performance status
- Collect Cycle 3Day 1 labs: CBC, CMP, SPEP, sFLC, Serum Immunoglobulins, (Labs should be drawn 24-48 hours prior to injection date, can be collected in the patients home, local clinic, or at a local laboratory or at the main academic hospital)
- Document Current Multiple Myeloma Disease Status
- Complete the following surveys electronically (Surveys will be completed 3-5 days after the treatment day):
    - Cancer Treatment Satisfaction Survey
    - EORTC QLQ-C30
    - COST Survey
    - OOCAT Survey
- Barriers Assessment
    - Delay in anti-neoplastic therapy, delivery of medication, nurse arrival
    - Any wasted drug
    - Issues with storage or disposal of medication
    - Other issues that arise
- Patient to take Pre-meds prior to nurse arrival
- Administer DARZALEX FASPRO at home. No observation period needed.

**Visit 4 Day 85 ± 3 days**

- Record adverse events as reported by participant or observed by investigator (visit with provider may take place via telehealth).
- Document any changes in Medical History, Concomitant Medications
- Perform and record physical exam findings (may be limited if performed virtually).
- Document ECOG performance status

- Collect Cycle 4 Day 1 labs: CBC, CMP, SPEP, sFLC, Serum Immunoglobulins (Labs should be drawn 24-48 hours prior to injection date)
- Document Current Multiple Myeloma Disease Status
- Complete the following surveys electronically (Surveys will be completed 3-5 days after the treatment day):
    - Cancer Treatment Satisfaction Survey
    - EORTC QLQ-C30
    - COST Survey
    - OOCAT Survey
- Barriers Assessment
    - Delay in anti-neoplastic therapy, delivery of medication, nurse arrival
    - Any wasted drug
    - Issues with storage or disposal of medication
    - Other issues that arise
- Patient to take Pre-meds prior to nurse arrival
- Administer DARZALEX FASPRO at home. No observation period needed.

**Visit 5 Day 113 ± 3 days**

- Record adverse events as reported by participant or observed by investigator (visit with provider may take place via telehealth).
- Document any changes in Medical History, Concomitant Medications
- Perform and record physical exam findings (may be limited if performed virtually).
- Document ECOG performance status
- Collect Cycle 5 Day 1 labs: CBC, CMP, SPEP, sFLC, Serum Immunoglobulins (Labs should be drawn 24-48 hours prior to injection date)
- Document Current Multiple Myeloma Disease Status
- Complete the following surveys electronically (Surveys will be completed 3-5 days after the treatment day):
    - Cancer Treatment Satisfaction Survey
    - EORTC QLQ-C30
    - COST Survey
    - OOCAT Survey
- Barriers Assessment

  - Delay in anti-neoplastic therapy, delivery of medication, nurse arrival
  - Any wasted drug
  - Issues with storage or disposal of medication
  - Other issues that arise
- Patient to take Pre-meds prior to nurse arrival
- Administer DARZALEX FASPRO at home. No observation period needed.

**Visit 6 Day 141 ± 3 days**

- Record adverse events as reported by participant or observed by investigator (visit with provider may take place via telehealth).
- Document any changes in Medical History, Concomitant Medications
- Perform and record physical exam findings (may be limited if performed virtually).
- Document ECOG performance status
- Collect Cycle 6 Day 1 labs: CBC, CMP, SPEP, sFLC, Serum Immunoglobulins(Labs should be drawn 24-48 hours prior to injection date)
- Document Current Multiple Myeloma Disease Status
- Complete the following surveys electronically(Surveys will be completed 3-5 days after the treatment day):
  - Cancer Treatment Satisfaction Survey
  - EORTC QLQ-C30
  - COST Survey
  - OOCAT Survey
- Barriers Assessment
  - Delay in anti-neoplastic therapy, delivery of medication, nurse arrival
  - Any wasted drug
  - Issues with storage or disposal of medication
  - Other issues that arise
- Patient to take Pre-meds prior to nurse arrival
- Administer DARZALEX FASPRO at home. No observation period needed.

**Visit 7 Day 169 ± 3 days**

- Record adverse events as reported by participant or observed by investigator
- Document any changes in Medical History, Concomitant Medications

- Perform and record physical exam findings.
- Document ECOG performance status
- Collect Cycle 7 Day 1 labs: CBC, CMP, SPEP, sFLC, Serum Immunoglobulins
- Document Current Multiple Myeloma Disease Status
- Complete the following surveys electronically (Surveys will be completed 3-5 days after the treatment day):
    - Cancer Treatment Satisfaction Survey
    - EORTC QLQ-C30
    - COST Survey
    - OOCAT Survey
- Administer DARZALEX FASPRO in the infusion center. No observation period needed.

**Visit 8 Day 197 ± 3 days**

- Record adverse events as reported by participant or observed by investigator.
- Document any changes in Medical History, Concomitant Medications
- Perform and record physical exam findings.
- Document ECOG performance status
- Collect Cycle 8 Day 1 labs: CBC, CMP, SPEP, sFLC, Serum Immunoglobulins, LDH, Uric Acid
- Document Current Multiple Myeloma Disease Status
- Complete the following surveys electronically (Surveys will be completed 3-5 days after the treatment day):
    - Cancer Treatment Satisfaction Survey
    - EORTC QLQ-C30
    - COST Survey
    - OOCAT Survey
- Administer DARZALEX FASPRO in the infusion center. No observation period needed.

## 6.3 End of Treatment Study Procedures

**Final Study Visit (Visit 9, Day 198 + 45 days)**

- Record adverse events as reported by participant or observed by investigator (visit with provider may take place via telehealth).

- Perform and record physical exam findings.
- Document ECOG performance status
- Perform semi-structured qualitative interview with patient to evaluate perceptions of home vs. infusion center based administration of treatment.

## 6.4 Post-treatment/Follow-Up

N/A

## 6.5 Long Term/Survival Follow-up

N/A

# 7 Study Procedures and Evaluations

## 7.1 Study Procedures/Evaluations

- Medical History – Includes documentation of the patient's medical history at time of enrollment and any changes that occur during the duration of the study.
- Medication History – Includes documentation of the patient's medication list at time of enrollment and any changes that occur during the duration of the study. Includes both prescription and over the counter medications.
- The following Questionnaires will be administered either in person and completed on a tablet or remotely through a link that will be distributed via the participants email.
    - Cancer Treatment Satisfaction Survey
    - EORTC QLQ-C30
    - COST Survey
    - OOCAT Survey
- Semi Structures Qualitative Interview will be conducted. Interviews will be conducted by a member of the research team. All interviews will be recorded and transcribed.
- Barrier Assessment of home administration of anti-neoplastic therapy.
    - Delay in anti-neoplastic therapy, delivery of medication, nurse arrival
    - Any wasted drug
    - Issues with storage or disposal of medication

## 7.2 Laboratory Procedures/Evaluations

### 7.2.1 Clinical Laboratory Evaluations

HBV Serology: All subjects will be tested locally for hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (Anti-HBs), and hepatitis B core antibody (Anti-HBc) at Screening.

HBV DNA Tests: Subjects who are positive for Anti-HBc or Anti-HBs will undergo testing for hepatitis B DNA by PCR. Subjects with serologic findings suggestive of HBV vaccination (Anti-HBs positivity as the only serologic marker) and a known history of prior HBV vaccination do not need to be tested for HBV DNA by PCR. During and following study treatment, subjects who have history of HBV infection will be closely monitored for clinical and laboratory signs of reactivation of HBV as per institutional policy.

All other laboratory studies are per standard of care and per institutional guidelines for management and monitoring of patients with multiple myeloma.

### 7.2.2 Special Assays or Procedures

N/A

### 7.2.3 Specimen Preparation, Handling, and Storage

N/A

### 7.2.4 Specimen Shipment

N/A

# 8 Evaluation of Safety

## 8.1 Specification of Safety Parameters

### 8.1.1 Product Quality Complaints

A PQC may have an impact on the safety and efficacy of a Company product. Timely, accurate, and complete reporting and analysis of PQC information from studies are crucial for the protection of patients, investigators, and the Company, and are mandated by regulatory agencies worldwide. The Company has established procedures in conformity with regulatory requirements worldwide to ensure appropriate reporting of PQC information. The Institution agrees that Lot and/or Batch #s shall be collected, when available, for all PQC reports, including reports of failure of expected pharmacological action (i.e., lack of effect) of a Janssen Medicinal Product. A sample of the suspected product shall be maintained for further investigation if requested by the Company.

Any complaint that indicates a potential quality issue during manufacturing, packaging, release testing, stability monitoring, dose preparation, storage or distribution of the product or delivery system is considered a PQC. Not all PQCs involve a patient.

Examples of PQC include but are not limited to:

- Mislabelling or misbranding
- Information concerning microbial contamination, including a suspected transmission of any infectious agent by a product
- Any significant chemical, physical, or other changes that indicate deterioration in the distributed product
- Any foreign matter reported to be in the product
- Mixed product, e.g., two drugs are mixed-up in the packaging process
- Incorrect tablet sequence (e.g., oral contraceptive tablets)
- Insecure closure with serious medical consequences, e.g., cytotoxics, child-resistant containers, potent drugs
- Suspected counterfeit or tampered product

- Adverse Device Effects including any adverse event resulting from insufficiencies or inadequacies in the instructions for use, the deployment, implantation, installation, operation, or any malfunction of a medical device or combination product. This also includes any event that is a result of a use error or intentional misuse and dosing device malfunctions (e.g. auto-injector button not working, needle detaching from syringe, etc.)
- Physical defect (e.g. abnormal product odor, broken or crushed tablets, etc.)

### 8.1.2 **Unanticipated Problems**

Unanticipated problems (UAPs) include, in general, any incident, experience, or outcome that meets the following criteria:

- unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied;

UAPs are considered to pose risk to participants or others when they suggest that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

### 8.1.3 **Adverse Events**

An adverse event is any untoward or unfavorable medical occurrence in a human participant, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the participant's participation in the research, whether or not considered related to the participant's participation in the research.

### 8.1.4 **Adverse Events of Special Interest**

Adverse events of special interest are events that Janssen Scientific Affairs, LLC is actively monitoring as a result of a previously identified signal (even if non-serious). Adverse events of special interest of daratumumab will be reported to the Company as defined in the protocol. In case of any amendments to the AESI list, Company will notify the Institution/Investigator and the Institution/Investigator will inform sites. Institution/Investigator will ensure that these changes are updated in the protocol as soon as practical.

Adverse events of special interest are events that the COMPANY is actively monitoring as a result of a previously identified signal (even if non-serious).

These adverse events are:

- Infusion reactions: ≥ Grade 3
- Infections: ≥ Grade 4
- Cytopenias: ≥ Grade 4
- HBV Reactivation
- Other malignancies

### 8.1.5 **Serious Adverse Events**

A serious adverse event (SAE) is one that meets one or more of the following criteria:

- Results in death
- Is life-threatening (places the participant at immediate risk of death from the event as it occurred)
- Is disabling or incapacitating
- Results in inpatient hospitalization or prolongation of existing hospitalization
- Results in a persistent or significant disability or incapacity
- Results in a congenital anomaly or birth defect
- An important medical event that may not result in death, be life threatening, or require hospitalization may be considered an SAE when, based upon appropriate medical judgment, the event may jeopardize the participant or may require intervention to prevent one of the outcomes listed in this definition.
- Is considered medically significant*

*Any untoward medical occurrence that is considered medically significant. Medical and scientific judgment should be exercised in deciding whether expedited reporting is appropriate in other situations, such as important medical events that may not result in death, be life-

threatening or require hospitalization but may be considered a serious adverse drug experience when, based on appropriate medical judgement, that may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the other outcomes listed in the bulleted list above. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in hospitalization, or development of drug dependency or drug abuse or malignancy.

### 8.1.6 Hospitalizations

For reports of hospitalization, it is the sign, symptom or diagnosis which led to hospitalization that is the serious event for which details must be provided. Any event requiring hospitalization or prolongation of hospitalization that occurs during a study must be reported as a serious adverse event, except hospitalizations for the following:

- Hospitalizations not intended to treat an acute illness or adverse event (e.g., social reasons such as pending placement in long-term care facility)
- Surgery or procedure planned before entry into a study. [Note: Hospitalizations that were planned before the signing of ICF and where the underlying condition for which the hospitalization was planned has not worsened will not be considered serious adverse events. Any adverse event that results in a prolongation of the originally planned hospitalization is to be reported as a new serious adverse event.]

### 8.1.7 Life-threatening Conditions

Disease progression should not be recorded as an adverse event or serious adverse event term; instead, signs and symptoms of clinical sequelae resulting from disease progression/lack of efficacy will be reported if they fulfil the serious adverse event definition.

**If no SAE** is associated with the special situation, the special situation should be recorded in the CRF and sent annually to Janssen Scientific Affairs, LLC.

These safety events may not meet the definition of an adverse event; however, the Parties agree that for reporting purposes, they are deemed to be adverse events.

### 8.1.8 Special Situations

The following special situations must be reported to Company with or without an associated serious adverse event (SAE):

- Drug exposure during pregnancy (paternal, maternal)

- Suspected transmission of any infectious agent via administration of a Janssen Product(s) under study.

The following special situations must be reported to the Company when associated with a serious adverse event (SAE):

- Overdose of Janssen Product(s) under study
- Exposure to Janssen Product(s) under study from breastfeeding
- Suspected abuse/misuse of Janssen product(s) under study
- Inadvertent or accidental exposure to Janssen Product(s) under study
- Any failure of expected pharmacological action (i.e., lack of effect) of Janssen Product(s) under study
- Medication error (includes potential, intercepted or actual) involving a Janssen product (with or without patient exposure to the Janssen Product(s) under study, e.g., name confusion)
- Unexpected therapeutic or clinical benefit from use of Janssen Product(s) under study

## 8.2 "Extraordinary" correspondence

Correspondence with a regulatory authority or ethics committee regarding a safety issue that may impact the safety or benefit-risk balance of the Janssen Product(s) Under Study, and/or may impact patients or public health. Examples include:

- Safety issues relating to a quality defect
- Major safety issues identified with changes in the nature, severity or frequency of known serious adverse reactions which are medically significant or the detection of new risk factors for the development of a known adverse reaction or a new serious adverse reaction.
- Major safety issues identified in the context of ongoing or newly completed post-marketing studies e.g. an unexpected increased rate of fatal or life-threatening adverse events.

## 8.3 Safety Assessment and Follow-Up

The PI will follow adverse events with start dates occurring any time after informed consent is obtained until 7 (for non-serious AEs) or 30 days (for SAEs) after the last day of study participation. At each study visit, the investigator (or designee) will inquire about the occurrence of AE/SAEs since the last visit. Events will be followed for outcome information until resolution or stabilization.

## 8.4 Recording Adverse Events

**If no SAE** is associated with the special situation, the special situation should be recorded in the CRF and sent annually to the Company.

These safety events may not meet the definition of an adverse event; however, the Parties agree that for reporting purposes, they are deemed to be adverse events.

"Safety Assessment and Follow-Up

### 8.4.1 Relationship to Study Intervention

The relationship to study intervention or study participation must be assessed and documented for all adverse events. Evaluation of relatedness must consider etiologies such as natural history of the underlying disease, concurrent illness, concomitant therapy, study-related procedures, accidents, and other external factors.

The following guidelines are used to assess relationship of an event to study intervention:

1. Related (Possible, Probable, Definite)
    a. The event is known to occur with the study intervention.
    b. There is a temporal relationship between the intervention and event onset.
    c. The event abates when the intervention is discontinued.
    d. The event reappears upon a re-challenge with the intervention.
2. Not Related (Unlikely, Not Related)
    a. There is no temporal relationship between the intervention and event onset.
    b. An alternate etiology has been established.

### 8.4.2 Expectedness

The PI is responsible for determining whether an AE is expected or unexpected. An AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the intervention. Risk information to assess expectedness can be obtained from preclinical studies, the investigator's brochure, published medical literature, the protocol, or the informed consent document.

### 8.4.3 Severity of Event

Adverse events will be graded for severity according to the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0

### 8.4.4 Intervention

Any intervention implemented to treat the adverse event must be documented for all adverse events.

## 8.5 Safety Reporting

### 8.5.1 Reporting to IRB

### 8.5.2 Unanticipated Problems

All incidents or events that meet criteria for unanticipated problems (UAPs) as defined in Section 8.1.2 require the creation and completion of an unanticipated problem report form (OHR-20).

UAPs that pose risk to participants or others, and that are not AEs, will be submitted to the IRB on an OHR-20 form via the eazUP system within 10 working days of the investigator becoming aware of the event.

UAPs that do not pose risk to participants or others will be submitted to the IRB at the next continuing review.

#### 8.5.2.1 *Adverse Events*

Grade 1 AEs will be reported to the IRB at continuing review.

Grade 2 AEs will be reported to the IRB at the time of continuing review.

#### 8.5.2.2 *Serious Adverse Events*

SAEs will be reported to the IRB on OHR-10 forms via the electronic reporting system (eSAEy) according to the required time frames described below.

Grade 3-4 AEs that are unexpected and deemed to be at least possibly related to the study will be reported to the IRB within 2 working days of knowledge of the event.

Grade 3-4 AEs that are deemed unrelated to the study will be reported to the IRB within 5 working days.

Grade 5 AEs will be reported to the IRB within one working day of knowledge of the event.

All SAEs will be submitted to the IRB at continuing review, including those that were reported previously.

### 8.5.3 Reporting to SKCC DSMC

All AEs and SAEs, safety and toxicity data, and any corrective actions will be submitted to the DSMC per the frequency described in the SKCC DSMP. The report to the SKCC DSMC will also include any unanticipated problems that in the opinion of the PI should be reported to the DSMC.

For expedited reporting requirements, see table below:
DSMC AE/SAE Reporting Requirements

| | Grade 1 | Grade 2 | | Grade 3 | | | | Grades 4 and 5 |
|---|---|---|---|---|---|---|---|---|
| | | | | Unexpected | | Expected | | |
| | Unexpected and Expected | Unexpected | Expected | With Hospitalization | Without Hospitalization | With Hospitalization | Without Hospitalization | Unexpected and Expected |
| Unrelated Unlikely | Reviewed at Quarterly DSMC Meeting and IRB Annual Review | Reviewed at Quarterly DSMC Meeting and IRB Annual Review | Reviewed at Quarterly DSMC Meeting and IRB Annual Review | 5 Working Days | Reviewed at Quarterly DSMC Meeting and IRB Annual Review | 5 Working Days | Reviewed at Quarterly DSMC Meeting and IRB Annual Review | Phase I - 48 Hours<br>(Death: 24 Hours)<br>Phase II - 5 working days |
| Possible Probably Definite | Reviewed at Quarterly DSMC Meeting and IRB Annual Review | Reviewed at Quarterly DSMC Meeting and IRB Annual Review | Reviewed at Quarterly DSMC Meeting and IRB Annual Review | 48 Hours (Death: 24 Hours) | Phase I - 48 Hours<br>Phase II - 5 working days | 48 Hours (Death: 24 Hours) | Reviewed at Quarterly DSMC Meeting and IRB Annual Review | Phase I and Phase II - 48 Hours<br>(Death: 24 Hours) |

### 8.5.4 Reporting to Funding Company

#### 8.5.4.1 *Sponsor Responsibilities*

**8.5.4.1.1 Health Authority**

The Institution/Investigator shall be solely responsible for complying, within the required timelines, with any safety reporting obligation towards the competent health authorities, the Ethics Committees (EC) or Independent Review Board (IRB) and the participating (co- or sub-) investigators.

**8.5.4.1.2 General**

The Institution / Investigator shall notify Janssen immediately in case of a suspension of recruitment or premature stop of the concerned clinical study because of a safety concern; preferably by means of a telephone contact with the Company Representative, alternatively by email within twenty-four (24) hours of the decision.

Institution / Investigator shall provide to the Janssen copies of any and all relevant extraordinary (not including routine initial or follow-up ICSR submission) correspondences with health authorities and ethics committees regarding any and all serious adverse events (irrespective of the association with the Janssen Product(s) Under Study). Copies of such correspondence shall be provided within 24 hours of such report or correspondence being sent to applicable health authority.

Training: Institution of the Study shall be responsible for training the Study personnel (including the Investigator) on managing safety information arising from the Study according to agreed procedures and the requirements of this Agreement.

Management of Safety Data: The Institution and Investigator will provide safety information arising from the Study to the Company on adverse events, special situations including pregnancies and product quality complaints as defined within this exhibit. This safety information will be documented by the Investigator and reported as described in this exhibit from the time a subject has signed and dated an Informed Consent Form (ICF) until 30 days after the last dose of the Janssen Product(s) Under Study. All subsequent AEs and SAEs beyond 30 days after the last dose of the Janssen Product(s) under study shall be collected/reported if the investigator considers the AE/SAE to be causally related to the use of the Janssen Product(s) Under Study.

For the purposes of this Study, the Janssen Product(s) Under Study is (are):

DARZALEX FASPRO® (daratumumab hyaluronidase-fihj)

Maintenance of Safety Information: All safety data arising from the Study shall be maintained in a clinical database in a retrievable format. The Institution and Investigator shall provide a summary of all non-serious adverse events (NSAES) annually, and both serious and non-serious adverse events will be summarized in the final Study report (excluding those from subjects not exposed to a Janssen product). The summary shall include a listing of: Patient ID, adverse event term (uncoded), severity, relationship to Janssen Product(s) Under Study, and action taken with Janssen Product(s) Under Study. However, in certain circumstances more frequent provision of safety data may be

necessary, e.g. to fulfill a regulatory request, and as such the safety data shall be made available within a reasonable timeframe at the Company's request.

Follow-up: All (serious and non-serious) adverse events reported for a Janssen Product(s)Under Study shall be followed up in accordance with good clinical practice (GCP).

If batch/lot number is available, it must be reported. If batch/lot number is not available, it must be documented that it is not available. Without this documentation, Company is required to perform two follow-up attempts to obtain the batch/lot number.

#### 8.5.4.2 *Reporting of Safety data and Product Quality Complaints (PQCs) to Company*

All adverse events and special situations, whether serious or non-serious, related or not related, collected as per protocol design, following exposure to a Janssen Product(s) Under Study are to be documented by the investigator and recorded in the CRF and in the subject's source records. Investigators must record in the CRF their evaluation concerning the relationship of the adverse event to a Janssen Product(s) Under Study.

The Institution will submit (and procure that the Investigator submits), to the identified Company Representative in each Country/Territory the following safety information:

| Type of report | Timelines | How to report |
|---|---|---|
| **Serious Adverse Event,** | Within 3 business days of becoming aware of the event(s) | By a secure means, as agreed by the Parties, on a Serious Adverse Event Form. |
| **Adverse Events of Special Interest (AESI)** | Within 3 business days of becoming aware of the event(s) | By a secure means, as agreed by the Parties, on a Serious Adverse Event Form. |
| **Reports of drug exposure during pregnancy (maternal and paternal), with or without SAE.** | Within 3 business days of becoming aware of the event(s) | By a secure means, as agreed by the Parties, on a Pregnancy Notification Form/Serious Adverse Event Form. |
| **Reports of Suspected transmission of any infectious agent via administration of a Janssen Product, with or without an SAE** | Within 3 business days of becoming aware of the event(s) | By a secure means, as agreed by the Parties, on a Serious Adverse Event Form. |
| **Abnormal Pregnancy Outcomes (e.g. spontaneous abortion, fetal death, stillbirth, congenital anomaly, ectopic pregnancy)** | Within 3 business days of becoming aware of the event(s) | By a secure means, as agreed by the Parties, on a Serious Adverse Event Form. |
| **Special Situation (SS), if associated with an SAE** | Within 3 business days of becoming aware of the event(s) | By a secure means, as agreed by the Parties, on a Serious Adverse Event Form. |
| **Special Situation (not associated with an SAE)** | Annually and in final study report. | Recorded in CRF and reported annually and in final study report. |

| | | |
|---|---|---|
| **Product Quality Complaints** | Within 3 business days of becoming aware of the event(s) | By a secure means, as agreed by the Parties. |
| **Non-Serious Adverse Event* (*Not meeting other listed 3 business day reporting criteria e.g. AESI or SS)** | Annually and in final study report. | Recorded in CRF and reported annually and in final study report. |
| **Follow-up information** | Transmitted within the same timeframes as above i.e. if initial report was required to be submitted within 3 business days, follow-up information shall be submitted within the same timeframe. | Transmitted via same method as above i.e. if initial method of transmission was on an SAE form, follow-up information shall be transmitted in the same manner. |

The Institution and/or Investigator is responsible for ensuring that these cases are complete and if not, are promptly followed-up. A safety report is not considered complete until all clinical details needed to interpret the case are received.

Note: In the event the Study is blinded, the Investigator will submit an unblinded SAE or pregnancy exposure report to Company.

If the Investigator/agent of the Investigator receives safety information and is aware it involves a non-study J&J product, it will be reported to Company, indicating it is an incidental spontaneous report discovered during the course of the study.

#### 8.5.4.3 *Funder confirmation/review of SAEs*

Company Representative or designee will provide the Institution and Investigator with a list of the Study's SAEs (previously received by the Company from the Institution and the Investigator) on a semi-annual basis. Investigator will confirm to Company that all applicable SAEs related to Janssen Product(s) Under Study have been reported to Company. The principle investigator has the responsibility of reporting to the health authorities.

- Funder Responsibilities

Company Representative or designee will provide the Institution and Investigator with the following safety information:

- Refer to the Investigator's Brochure for the determination of expectedness.
  - http://www.darzalex.com/shared/product/darzalex/darzalex-prescribing-information.pdf
  - For DARZALEX® (daratumumab),the expectedness of an adverse event will be determined by whether or not it is listed in the Investigator's Brochure.

- any new information, which becomes available during the course of the Study, which may affect the overall safety profile of the Janssen Product(s) Under Study.
- ICF risk wording

#### 8.5.4.4 *Company Safety Contact Information*

Contact details for the Company representative for submission of information required under this exhibit.

Phone: contact the study assigned Janssen Trial Manager

| | |
|---|---|
| Janssen SAE/Pregnancy Notifications | TO: GMS_AE_Inbo@its.jnj.com<br><br>Please note the underscores (_) in the email name this is critical to highlight as if its missing then the SAE will fail to transmit.<br><br>CC: Marjohn Armoon (MArmoon@ITS.JNJ.com) & Annelore Cortoos (ACortoos@its.jnj.com) |
| Janssen PQC: | DL-DPYIE-Globalcontacts-NIS@its.jnj.com<br><br>CC: Marjohn Armoon (MArmoon@ITS.JNJ.com); Annelore Cortoos (ACortoos@its.jnj.com) & Salli Fennessey (SFenness@its.jnj.com) |
| Janssen Fax: | 1-215-293-9955 |

### 8.5.5 Reporting of Pregnancy

If a subject becomes pregnant during the study, in addition to reporting the pregnancy within 3 business days, a determination regarding Janssen Product(s) Under Study discontinuation and subject discontinuation must be made by the investigator in alignment with the protocol inclusion/exclusion criteria and in consultation with the reference safety information.

Because the effect of the Janssen Product(s) Under Study on sperm is unknown, pregnancies in partners of male subjects exposed to a Janssen Product(s) Under Study will be reported by the Investigator within 3 business days **of their knowledge of the event** using the Serious Adverse Event Form. Depending on local legislation this may require prior consent of the partner.

Follow-up information regarding the outcome of the pregnancy and any postnatal sequelae in the infant will be required.

## 8.6 Halting Rules

Temporary suspension of enrollment may occur for the following reasons:

- Significant delays in administration of daratumumab in the home due to logistical barriers.
- Infusion related reaction that occurs in the home that cannot be adequately managed.
- Recurrent lost medication.

# 9 Study Oversight

In addition to the PI's responsibility for oversight, study oversight will be under the direction of the SKCC's Data and Safety Monitoring Committee (DSMC). The SKCC DSMC operates in compliance with a Data and Safety Monitoring Plan (DSMP) that is approved by the NCI.

# 10 Clinical Site Monitoring and Auditing

Clinical site monitoring and auditing is conducted to ensure that the rights of human participants are protected, that the study is implemented in accordance with the protocol and/or other operating procedures, and that the quality and integrity of study data and data collection methods are maintained. Monitoring and auditing for this study will be performed in accordance with the SKCC's Data and Safety Monitoring Plan (DSMP) developed by the SKCC Data and Safety Monitoring Committee (DSMC). The DSMP specifies the frequency of monitoring, monitoring procedures, the level of clinical site monitoring activities (e.g., the percentage of participant data to be reviewed), and the distribution of monitoring reports. Some monitoring activities may be performed remotely, while others will take place at the study site(s). Appropriate staff will conduct monitoring activities and provide reports of the findings and associated action items in accordance with the details described in the SKCC DSMP.

# 11 Statistical Considerations

## 11.1 Study Hypotheses

The study hypothesis is that administration of daratumumab at home will improve patient satisfaction as compared administration of daratumumab in the infusion center.

## 11.2 Analysis Plans

For primary analysis, the SWT domain CTSQ scores after all cycles will be analyzed jointly in a linear mixed effects model with a random effect of patient and the fixed effect of the delivery mode (home vs. infusion center). Log or other transformation of CTSQ scores will be used, as appropriate, to satisfy the model assumptions, Possible time trends will be considered in the model and incorporated, if significant. The mean difference in CTSQ scores between home and infusion center will be computed with the corresponding 95% confidence interval and tested (null hypothesis of zero mean difference) using appropriate model-based contrast with alpha 0.05.

The same approach will be used for the secondary analysis of other CTSQ domains, EORTC QLQ-30, COST survey, and OOCAT survey scores.

The adherence at the home setting cycles will be analyzed in repeated measures logistic regression model with a random effect of patient and the fixed effect of the delivery mode (home vs. infusion center). The model will be used to compute the average rate of home setting adherence with the corresponding 95% confidence interval.

Secondary endpoints related to the barriers to home administration and exploratory endpoints related to the patient perceptions of home based anti-neoplastic therapy will summarized using descriptive statistics.

## 11.3 Interim Analyses and Stopping Rules

No interim analysis will occur.

### 11.3.1 Safety Review

N/A

### 11.3.2 Efficacy Review

N/A

## 11.4 Sample Size Considerations

The model-based contrast to be used for testing the primary null hypothesis is a generalization of the paired t-test to the case of more than one observation under each delivery mode (scores for 4 cycles at infusion center and 4 cycles at home). The proposed sample size of 20 patients provides 80% power to detect the minimally important difference of 5.9 points (Usmani et al, 2020) for CTSQ SWT domain score using the two-sided paired t-test with alpha 0.05 and assuming that the standard deviation of within patient differences is at most 8.92. Based on between-patient standard deviation of 13.76 for CTSQ SWT domain scores reported in Trask et al (2008), the standard deviation of within patient differences will be 8.92 or lower if the correlation between repeated score from the same patient is 0.79 or higher. The actual power will be higher since multiple observations per each delivery mode will be utilized in the linear mixed effects model.

### 11.4.1 Accrual Estimates

We estimate to enroll 20 patients in 26 months or 0.77 patients per month. We plan to complete enrollment after 26 months.

## 11.5 Exploratory Analysis

We will perform descriptive analysis as described above.

# 12 Source Documents and Access to Source Data/Documents

Study staff will maintain appropriate medical and research records for this study, in compliance with ICH E6, and regulatory and institutional requirements for the protection of confidentiality of participant information. Study staff will permit authorized representatives of SKCC and regulatory agencies to examine (and when required by

applicable law, to copy) research records for the purposes of quality assurance reviews, audits, and evaluation of the study safety, progress and data validity. Quality Control and Quality Assurance

13. Quality control and quality assurance of the data will follow the SOP that has been predetermined and agreed upon by the CRO at SKCC.

# 14. Ethics/Protection of Human Participants

## 14.1 Ethical Standard

The investigator will ensure that this study is conducted in full conformity with the principles set forth in The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research, as drafted by the US National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (April 18, 1979) and codified in 45 CFR Part 46 and/or the ICH E6.

## 14.2 Institutional Review Board

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the IRB for review and approval. Approval of both the protocol and the consent form must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented in the study.

## 14.3 Informed Consent Process

Informed consent is a process that is initiated prior to the individual agreeing to participate in the study and continues throughout study participation. Extensive discussion of risks and possible benefits of study participation will be provided to participants and their families, if applicable. A consent form describing in detail the study procedures and risks will be given to the participant. Consent forms will be IRB-approved, and the participant is required to read and review the document or have the document read to him or her. The investigator or designee will explain the research study to the participant and answer any questions that may arise. The participant will sign the informed consent document prior to any study-related assessments or procedures. Participants will be given the opportunity to discuss the study with their surrogates or think about it prior to agreeing to participate. They may withdraw consent at any time throughout the course of the study. A copy of the signed informed consent document will be given to participants for their records. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their clinical care will not be adversely affected if they decline to participate in this study. The consent process will be documented in the clinical or research record.

## 14.4 Exclusion of Women, Minorities, and Children (Special Populations)

Pediatric population will be excluded as multiple myeloma is not a disease that affects those under the age of 18.

### 14.5 Participant Confidentiality

Participant confidentiality is strictly held in trust by the investigators, study staff, and the sponsor(s) and their agents. This confidentiality is extended to cover testing of biological samples and genetic tests in addition to any study information relating to participants.

The study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party without prior written approval of the sponsor.

The study monitor or other authorized representatives of the sponsor may inspect all study documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) for the study participants. The clinical study site will permit access to such records.

### 14.6 Future Use of Stored Specimens and Other Identifiable Data

Specimens will not be stored for future use.

## 15 Data Handling and Record Keeping

The investigators are responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported. All source documents must be completed in a neat, legible manner to ensure accurate interpretation of data. The investigators will maintain adequate case histories of study participants, including accurate case report forms (CRFs), and source documentation.

### 15.1 Data Management Responsibilities

Data collection and accurate documentation are the responsibility of the study staff under the supervision of the investigator. All source documents and laboratory reports must be reviewed by the study team and data entry staff, who will ensure that they are accurate and complete. Unanticipated problems and adverse events must be reviewed by the investigator or designee.

### 15.2 Data Capture Methods

Data will be captured through RedCAP database. The data will be collection on an ongoing process.

REDCap is a secure, web-based platform designed for data capture and storage for research studies. The SKCC REDCap system is configured to be HIPAA compliant. The platform is housed on Jefferson IS&T managed servers and runs in two distinct environments: a webserver which allows access to the REDCap web application and a database server which houses data collected from all REDCap projects. The SKCC REDCap team keeps the REDCap software as

up to date as possible while conserving functionality of the platform and ensuring minimal interruptions. The REDCap database is backed up at regular intervals to a secondary location.

REDCap tracks all user activity to system logs which are available to project owners and other roles with the requisite permissions to view this information. Additional logging is available to the system administrators but is not routinely distributed without a significant reason for doing so. The REDCap systems are routinely scanned by Jefferson IS&T for potential problems and vulnerabilities. Any significant issues identified are remediated immediately.

Users are able to access the SKCC REDCap instance with a valid Jefferson campus key and password after agreeing to the terms and conditions for use. The REDCap support team automatically suspends users with long periods of inactivity for security reasons. At a project level, project owners are responsible for who has access to each project, as well as the level of access and permissions given to each project user. REDCap administrators will only over-ride this access in special circumstances and only with requisite approval.

## 15.3 Types of Data

Data that will be collected include laboratory data, medical history data, questionnaires, and logistical data.

Content reports will be performed quarterly.

## 15.4 Study Records Retention

Study records will be maintained for at least three years from the date that the grant federal financial report (FFR) is submitted to the NIH.

Study documents must be retained for a minimum of 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or until at least 2 years have elapsed since the formal discontinuation of clinical development of the investigational product. These documents will be retained for a longer period, however, if required by local regulations. No records will be destroyed without the written consent of the sponsor, if applicable. It is the responsibility of the sponsor to inform the investigator when these documents no longer need to be retained.

## 15.5 Protocol Deviations

A protocol deviation is any noncompliance with the clinical study protocol, Good Clinical Practice, or Manual of Procedures requirements. The noncompliance may be on the part of the participant, the investigator, or study staff. As a result of deviations, corrective actions are to be developed by the study staff and implemented promptly.

All deviations from the protocol must be addressed in study participant source documents and promptly reported to the IRB and other regulatory bodies according to their requirements.

# 16 Study Finances

## 16.1 Funding Source

The study is financed through Janssen IIT funding mechanism.

## 16.2 Conflict of Interest

Any investigator who has a conflict of interest with this study (patent ownership, royalties, or financial gain greater than the minimum allowable by their institution, etc.) must have the conflict reviewed by a properly constituted Conflict of Interest Committee with a Committee-sanctioned conflict management plan that has been reviewed and approved by the study sponsor prior to participation in this study. All Jefferson University Investigators will follow the TJU Conflicts of Interest Policy for Employees (107.03).

## 16.3 Participant Stipends or Payments

There will be compensation for study participation. Subjects will be awarded $50 per in clinic visit (a total of 6 visits). There will be no payment for at home infusions.

# 17 Publication and Data Sharing Policy

This study will comply with the NIH Public Access Policy, which ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central upon acceptance for publication.

The International Committee of Medical Journal Editors (ICMJE) member journals have adopted a clinical trials registration policy as a condition for publication. The ICMJE defines a clinical trial as any research project that prospectively assigns human participants to intervention or concurrent comparison or control groups to study the cause-and-effect relationship between a medical intervention and a health outcome. Medical interventions include drugs, surgical procedures, devices, behavioral treatments, process-of-care changes, and the like. Health outcomes include any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events. The ICMJE policy requires that all clinical trials be registered in a public trials registry such as ClinicalTrials.gov, which is sponsored by the National Library of Medicine. Other biomedical journals are considering adopting similar policies. The ICMJE does not review specific studies to determine whether registration is necessary; instead, the committee recommends that researchers who have questions about the need to register err on the side of registration or consult the editorial office of the journal in which they wish to publish.

U.S. Public Law 110-85 (Food and Drug Administration Amendments Act of 2007 or FDAAA), Title VIII, Section 801 mandates that a "responsible party" (i.e., the sponsor or designated principal investigator) register and report results of certain "applicable clinical trials:"

Trials of Drugs and Biologics: Controlled, clinical investigations, other than Phase I investigations, of a product subject to FDA regulation;

Trials of Devices: Controlled trials with health outcomes of a product subject to FDA regulation (other than small feasibility studies) and pediatric postmarket surveillance studies.

NIH grantees must take specific steps to ensure compliance with NIH implementation of FDAAA.

# 18 Literature References

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2. Palumbo, A., et al., *Continuous Therapy Versus Fixed Duration of Therapy in Patients With Newly Diagnosed Multiple Myeloma.* Journal of Clinical Oncology, 2015. **33**(30): p. 3459-3466.
3. Roy, A., et al., *Estimating the Costs of Therapy in Patients with Relapsed and/or Refractory Multiple Myeloma: A Model Framework.* American health & drug benefits, 2015. **8**(4): p. 204-215.
4. Fonseca, R. and J. Hinkel, *Value and Cost of Myeloma Therapy—We Can Afford It.* American Society of Clinical Oncology Educational Book, 2018(38): p. 647-655.
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8. Hematology, A.S.o., *COVID-19 and Multiple Myeloma*. Version 1.2; last updated July 21, 2020.
9. Durie, B.G.M., et al., *Longer term follow-up of the randomized phase III trial SWOG S0777: bortezomib, lenalidomide and dexamethasone vs. lenalidomide and dexamethasone in patients (Pts) with previously untreated multiple myeloma without an intent for immediate autologous stem cell transplant (ASCT).* Blood Cancer Journal, 2020. **10**(5): p. 53.
10. Mateos, M.-V., et al., *Daratumumab plus Bortezomib, Melphalan, and Prednisone for Untreated Myeloma.* New England Journal of Medicine, 2017. **378**(6): p. 518-528.
11. Facon, T., et al., *Daratumumab plus Lenalidomide and Dexamethasone for Untreated Myeloma.* New England Journal of Medicine, 2019. **380**(22): p. 2104-2115.
12. Evans, J.M., et al., *A multi-method review of home-based chemotherapy.* European Journal of Cancer Care, 2016. **25**(5): p. 883-902.
13. Directors, A.B.o., *American Society of Clinical Oncology Position Statement*

*Home Infusion of Anticancer Therapy*. 2020.

## SUPPLEMENTAL MATERIALS

These documents are relevant to the protocol, but they are not considered part of the protocol. They are stored and modified separately. As such, modifications to these documents do not require protocol amendments.

Appendix A: Schedule of Events

# Appendices

## Appendix A: Schedule of Events

### Events Schedule: Patients already on Monthly Daratumumab

| **Schedule of events** | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **For patients transitioning from IV to Subcutaneous therapy** | | | | | | | | | | | |
| **Events** | Screening | Infusion Center | | Home Infusion | | | | Infusion Center | | End of Study Assessment | Notes |
| | Day -30 to 0 | C1D1 (+/-3 days) | C2D1 (+/-3 days) | C3D1 (+/-3 days) | C4D1 (+/-3 days) | C5D1 (+/-3 days) | C6D1 (+/-3 days) | C7D1 (+/-3 days) | C8D1 (+/-3 days) | No later than 45 days after last treatment cycle | |
| **Administrative Procedures** | | | | | | | | | | | |
| **Informed consent** | X | | | | | | | | | | |
| **Inclusion/exclusion criteria** | X | | | | | | | | | | |
| **General medical history** | X | | | | | | | | | | |
| **Prior/Concomitant Medications** | X | | | | | | | | | | |
| **ECG** | X | | | | | | | | | | |
| **Current Myeloma Disease status** | X | | | | | | | | | | |
| **Schedule of events** | | | | | | | | | | | |
| **For patients transitioning from IV to Subcutaneous therapy** | | | | | | | | | | | |
| **Events** | Screening | Infusion Center | | Home Infusion | | | | Infusion Center | | End of Study Assessment | Notes |

| | Day -30 to 0 | C1D1 (+/-3 days) | C2D1 (+/-3 days) | C3D1 (+/-3 days) | C4D1 (+/-3 days) | C5D1 (+/-3 days) | C6D1 (+/-3 days) | C7D1 (+/-3 days) | C8D1 (+/-3 days) | No later than 45 days after last treatment cycle | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Pregnancy Test (WOCBP)** | X | | | | | | | | | | |
| **CBC** | X | X | X | X | X | X | X | X | X | | |
| **CMP** | X | X | X | X | X | X | X | X | X | | |
| **Serum Protein Electropheresis** | X | X | X | X | X | X | X | X | X | | |
| **Serum Free Light Chains** | X | X | X | X | X | X | X | X | X | | |
| **Serum Immunoglobulins** | X | X | X | X | X | X | X | X | X | | |
| **Hepatitis B (HBV) serology** | X | | | | | | | | | | If not previously tested, local testing for hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (Anti-HBs), and hepatitis B core antibody (Anti-HBc) should be sent. |
| **Schedule of events** | | | | | | | | | | | |
| **For patients transitioning from IV to Subcutaneous therapy** | | | | | | | | | | | |
| **Events** | Screening | Infusion Center | | Home Infusion | | | | Infusion Center | | End of Study Assessment | Notes |

| | Day -30 to 0 | C1D1 (+/-3 days) | C2D1 (+/-3 days) | C3D1 (+/-3 days) | C4D1 (+/-3 days) | C5D1 (+/-3 days) | C6D1 (+/-3 days) | C7D1 (+/-3 days) | C8D1 (+/-3 days) | No later than 45 days after last treatment cycle | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **HBV DNA testing** | X | | | | | | | | | | For subjects with serologic evidence of resolved HBV infection (i.e., positive Anti-HBs or positive Anti-HBc) at Screening, HBV DNA testing by PCR must be performed locally. |
| **Survey Assessments** | | | | | | | | | | | |
| **Treatment Burden Questionnaire** | | X | X | X | X | X | X | X | X | | |
| **COST Survey** | | X | X | X | X | X | X | X | X | | |
| **E-PRO survey tool** | | X | X | X | X | X | X | X | X | | |
| **Opportunity cost survey** | | X | X | X | X | X | X | X | X | | |
| **Safety Assessments** | | | | | | | | | | | |
| **AE assessment** | X | X | X | X | X | X | X | X | X | X | |
| **Schedule of events** | | | | | | | | | | | |
| **For patients transitioning from IV to Subcutaneous therapy** | | | | | | | | | | | |
| **Events** | Screening | Infusion Center | | Home Infusion | | | | Infusion Center | | End of Study Assessment | Notes |

| | Day -30 to 0 | C1D1 (+/-3 days) | C2D1 (+/-3 days) | C3D1 (+/-3 days) | C4D1 (+/-3 days) | C5D1 (+/-3 days) | C6D1 (+/-3 days) | C7D1 (+/-3 days) | C8D1 (+/-3 days) | No later than 45 days after last treatment cycle | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Physical Exam (can be virtual exam)** | X | X | X | X | X | X | X | X | X | X | |
| **ECOG assessment** | X | X | X | X | X | X | X | X | X | X | |
| **Barriers Assessment** | | | | | | | | | | | |
| **Delay in treatment** | | | | X | X | X | X | | | | |
| **Delay in medication delivery to home** | | | | X | X | X | X | | | | |
| **Delay in nurse arrival** | | | | X | X | X | X | | | | |
| **Wasted drug** | | | | X | X | X | X | | | | |
| **Issues with storage/disposal of drug** | | | | X | X | X | X | | | | |
| **Other supply chain issues** | | | | X | X | X | X | | | | |
| **Patient Interview** | | | | | | | | | | X | |