CLINICAL RESEARCH IN INFECTIOUS DISEASES

STATISTICAL ANALYSIS PLAN

for

DMID Protocol: 16-0098

Study Title:

A MULTI-SITE, RANDOMIZED TRIAL OF SUBJECT-COLLECTED DRIED BLOOD SPOT CMV TESTING WITH MOBILE TECHNOLOGY SUPPORT TO OPTIMIZE PREEMPTIVE THERAPY LATER AFTER ALLOGENEIC HCT

NCT03910478

Version 1.0

DATE: December 11, 2024

A MULTI-SITE, RANDOMIZED TRIAL OF SUBJECT-COLLECTED CMV DRIED BLOOD SPOT TESTING WITH MOBILE TECHNOLOGY SUPPORT TO OPTIMIZE PREEMPTIVE THERAPY LATE AFTER ALLOGENEIC HCT

Protocol Number Code:	**DMID Protocol: 16-0098**
Products:	CMV polymerase chain reaction (PCR) testing of a Dried Blood Spot (DBS) Sample
Form/Route:	Not applicable
Indication Studied:	Late cytomegalovirus (CMV) disease post allogeneic hematopoietic cell transplantation (HCT)
Sponsor:	Division of Microbiology and Infectious Diseases National Institute of Allergy and Infectious Diseases National Institutes of Health
Clinical Trial Initiation Date:	03 May 2019
Clinical Trial Completion Date:	16 January 2024
Date of the Analysis Plan:	11 December 2024
Version Number:	1.0

This study was performed in compliance with Good Clinical Practice.

TABLE OF CONTENTS

LIST OF ABBREVIATIONS

AE	Adverse event
ATG	Anti-thymocyte globulin
CMV	Cytomegalovirus
CRF	Case report form
CSR	Clinical Study Report
CTR	CMV Test Results
DBS	Dried blood spot
DHHS	Department of Health and Human Services
DMID	Division of Microbiology and Infectious Diseases, NIAID, NIH, DHHS
DSMB	Data and Safety Monitoring Board
eCRF	Electronic Case Report Form
EDC	Electronic data capture
FDA	(U.S.) Food and Drug Administration
GI	Gastrointestinal
GVHD	Graft versus host disease
HCT	Hematopoietic cell transplantation
HLA	Human leukocyte antigen
ICH	International Conference on Harmonisation
IRB	Institutional Review Board
ITT	Intent-to-treat
MedDRA	Medical Dictionary for Regulatory Activities
mITT	Modified intent-to-treat
MOP	Manual of Procedures
N	Number (typically refers to participants)
N/A	Not applicable
NIAID	National Institute of Allergy and Infectious Diseases, NIH, DHHS
NIH	National Institutes of Health
NPV	Negative Predictive Value
ORA	Office of Regulatory Affairs, DMID, NIAID, NIH, DHHS
PCR	Polymerase chain reaction

PI	Principal Investigator
PPV	Positive Predictive Value
PT	Preferred Term
SAE	Serious adverse event
SAESI	Serious adverse event of special interest
SOC	Standard of Care
SOC MedDRA	System Organ Class MedDRA
UADE	Unanticipated adverse device effect
USPS	United States Postal Services
WB	Whole blood
WHO	World Health Organization

1. PREFACE

The Statistical Analysis Plan (SAP) for "A Multi-Site, Randomized Trial of Subject-Collected Dried Blood Spot CMV Testing with Mobile Technology Support to Optimize Preemptive Therapy Later After Allogeneic HCT" (DMID protocol 16-0098) describes and expands upon the statistical information presented in the protocol. This document describes all planned analyses and provides reasons and justifications for these analyses. It also includes sample tables, listings, and figures planned for the final analyses. Regarding the final analyses and Clinical Study Report (CSR), this SAP follows the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Guidelines, as indicated in Topic E3 (Structure and Content of Clinical Study Reports), and more generally is consistent with Topic E8 (General Considerations for Clinical Trials) and Topic E9 (Statistical Principles for Clinical Trials). The structure and content of the SAP provides sufficient detail to meet the requirements identified by the FDA and ICH, while all work planned and reported for this SAP will follow internationally accepted guidelines published by the American Statistical Association and the Royal Statistical Society for statistical practice.

This document contains four sections: (1) a review of the study design, (2) general statistical considerations, (3) comprehensive statistical analysis methods for efficacy and safety outcomes, and (4) a list of proposed tables and figures. Within the table and figure mock-ups (Appendices 1 and 2), references to CSR sections are included. Changes to the planned analyses described in this SAP would be included in amendment(s) to the SAP or described and justified in the CSR, as appropriate. The reader of this SAP is encouraged to also review the study protocol for details on conduct of the study and the operational aspects of clinical assessments.

2. INTRODUCTION

Despite strong evidence that preemptive therapy is highly effective in preventing cytomegalovirus (CMV) end organ disease after hematopoietic cell transplant (HCT), CMV monitoring adherence decreases significantly after day 100, when patients typically leave the care of the transplant team. Outside of the clinical trial setting, the requirement for weekly blood draws is burdensome for patients late after HCT. Finger-stick collected DBS CMV testing would allow participants to collect their samples at home and mail the cards directly to the laboratory. In addition, mobile technology can be used to automate simple reminder and notification systems and to facilitate ongoing communication among the patient, their primary oncologist, and the transplant center.

This study is a multi-site randomized trial where participants are randomized to either participant-collected DBS CMV testing with mobile technology support or standard of care to optimize preemptive therapy late after allogeneic HCT. 150 allogeneic HCT recipients ≥15 years of age, who are considered by their transplant team to be at risk for late CMV disease and are recommended to continue CMV monitoring after day 100 post-transplant will be randomized and will be followed from discharge to 365 days post-transplant. The primary aim of the study is to evaluate adherence to recommended CMV monitoring during the first year after transplant upon enrollment.

2.1. Purpose of the Analyses

This Statistical Analysis Plan describes the data and analyses that will be included in the final clinical study report. Analyses planned for presentation to the Data and Safety Monitoring Board (DSMB) meetings are described in a separate DSMB report shell document.

3. STUDY OBJECTIVES AND ENDPOINTS

3.1. Study Objectives

3.1.1. Primary Objective

To evaluate adherence to recommended CMV monitoring duration and interval during the first year after HCT upon enrollment using participant collected dried blood spot testing.

3.1.2. Secondary Objectives

1. Evaluate the mean difference between the recommended monitoring that each participant completes between the DBS and the control arm
2. Compare the incidence of CMV disease between the DBS monitoring and standard of care arms
3. Evaluate the safety of DBS monitoring

3.1.3. Exploratory Objectives

1. Evaluate the transit time from self-collection to arrival in the laboratory
2. Assess the mechanism for non-compliance as defined by a missing DBS sample PCR result (e.g. mobile technology failure, sample collection failure, sample delivery failure, sample viability failure)
3. Compare the performance characteristics of concurrently drawn DBS with plasma CMV PCR (e.g., sensitivity and specificity concordance)
4. Determine if the randomized study population is representative of the population as a whole
5. Obtain a population-based estimate of late CMV disease in observational and randomized cohorts
6. Describe local provider CMV treatment algorithms
7. Assess participant and provider satisfaction of DBS testing

3.2. Outcome Measures

3.2.1. Primary Outcome Measures

The number of participants who have completed >90% of their recommended CMV monitoring tests at one year after HCT in the DBS and control arms

3.2.2. Secondary Outcome Measures

1. The total number of recommended CMV monitoring tests that were completed per participant by 1 year after HCT
2. Number of participants in DBS and standard of care arms with end-organ CMV disease, possible and proven/probable by 1 year after HCT; CMV syndrome will not be used to define CMV disease
3. Number of participants with finger-stick procedure-related Grade 3 AEs at 1 year after HCT

3.2.3. Exploratory Outcome Measures

1. Mean time from scheduled pick-up at participant residence (DBS tests) or blood draw facility (plasma sample) to arrival at the laboratory (hours) at all applicable test points throughout the study period
2. Number of mobile technology failures, sample collection failures, sample delivery failures, and sample viability failures.
3. Sensitivity, specificity and predictive values of CMV detection in DBS versus plasma testing
4. Number and type of key transplant characteristics in randomized participants and observational participants
5. Describe the baseline participant demographics of randomized cohort and observational cohort.
6. Number of participants with end-organ CMV disease (possible and proven/possible) at 1 year after HCT in randomized participants and observational participants
7. Describe local provider CMV treatment viral load treatment thresholds
8. Describe local provider CMV monitoring interval recommendations
9. Report composite scores of different variables of participant and provider satisfactions according to the 5-point Likert scale questionnaires.

3.3. Study Definitions and Derived Variables

3.3.1. End of Follow-up

End of follow-up is defined as the day of protocol completion for those who completed the protocol or the day of early termination for those who have withdrawn from the study. If participants withdrew from DBS collection but agreed to have their medical charts reviewed, end of follow-up will still be considered as the date of withdrawal for adherence and DBS collection compliance analyses because they didn't receive intended intervention after withdrawal. The end of follow-up for these participants for safety analyses will be the date of last medical chart review.

3.3.2. Study Period

The study period for all safety analyses is defined as the time from enrollment to End of Follow-up.

The study period for all adherence analyses and DBS collection compliance analyses is the time from discharge to End of Follow-up. For participants in the DBS arm who were hospitalized during the follow-up, the duration of hospitalization will be subtracted from the study period for assessment of compliance with DBS collection.

3.3.3. Maximal Possible Study Period

The maximal possible study period is defined as the time from enrollment to end of maximal possible follow-up time, which is 1 year after HCT, or the date of death if a participant died during the follow-up. If a participant completed the study, the maximal possible study period will be the same as the study period defined in Section 3.3.2.

Sensitivity analyses for the primary outcomes will be conducted with ITT and mITT populations in the follow-up time between discharge and the end of the maximal possible study period.

If a participants withdrew from the DBS collection but agreed to have their medical chart reviewed, the clinician recommended monitoring interval after withdrawal will be used to calculate the number of recommended monitoring tests, until the end of maximal possible study period.

If a participant withdrew from the study and didn't agree to have their medical chart reviewed, the last-observed clinician-recommended interval prior to withdrawal of consent will be carried over to the remainder of the maximal possible study period and number of clinician-recommended monitoring test will be calculated with the method described in Section 3.3.4 and Appendix 4.

3.3.4. Number of Clinician-Recommended CMV Monitoring Tests Expected

At discharge, the clinician-recommended CMV monitoring schedule is anticipated to be weekly, however during the course of the study the participant's clinical team may recommend that monitoring become less frequent, for example at bi-weekly, monthly, quarterly or other schedules. The recommended monitoring schedules and the dates on which they come into effect are entered into the data system on the Visit Documentation electronic Case Report Form (eCRF) at discharge, each quarterly contact, or as needed between quarterly contacts, during medical chart abstraction. Letting d represent the number of days between clinician recommended CMV monitoring tests in the new schedule, the number of expected tests will be calculated using the following assumptions:

1. The first expected test occurs d days after discharge.
2. If the monitoring frequency is reduced, then the first test for the next schedule is expected d days after the last expected test in the previous interval.
3. If the monitoring frequency is increased, then the first test for the new schedule is expected d days after the date that the recommended interval was changed.

The number of expected tests during the study period for a given participant is the sum of the number of expected tests during each monitoring schedule over the course of the study period (defined in Section 3.3.2). Detailed information for the calculations of the number of expected tests can be found in Appendix 4.

At the University of Minnesota, the clinician recommended CMV monitoring schedule was not recorded, so this site entered the actual number of monitoring tests instead. These data will be used for the primary adherence analysis in the ITT population. A sensitivity analysis will be conducted to exclude all participants from the University of Minnesota for the primary and secondary adherence measures along with the local provider CMV monitoring interval recommendations summary (See Section 6.4, Section 8, and Section 14 for further details).

3.3.5. Number of Clinician-Recommended CMV Monitoring Tests Completed

The clinician-recommended CMV monitoring tests actually completed are entered into the data system on the CMV Test Results (CTR) – Chart Review eCRF. The number of tests completed will be the number of records entered on this eCRF that were collected on or prior to the end of follow up date or, as a sensitivity analysis, the maximal possible study period end date.

3.3.6. Quarterly Contact Target Dates

The targets dates for the quarterly contacts are 90 days after HCT (Quarterly Contact 1), 180 days after HCT (Quarterly Contact 2), 270 days after HCT (Quarterly Contact 3), and 365 days after HCT (Final Study Visit).

3.3.7. Least-Frequent Clinician-Recommended Monitoring Interval Category

The least-frequent clinician-recommended monitoring interval category summarizes the least-frequent monitoring interval category between discharge from transplant center and each quarterly contact. This is defined from least frequent to most frequent on the Visit Documentation eCRF as "No Further Monitoring Required" < "Quarterly" < "Monthly" < "Bi-weekly" < "Weekly" and participants will be categorized as such. Clinician-recommended CMV monitoring intervals of "Other" will not be considered for determining the least-frequent clinician-recommended monitoring interval category but will be included in Listing 14.

If a participant withdraws consent or dies prior to a quarterly contact or the final study visit, then their last-observed clinician-recommended prior to withdrawal of consent or death will be used to categorize their least-frequent clinician -recommended monitoring interval which will be carried forward for the remainder of the study.

3.3.8. Scheduled DBS Tests

Participants in the DBS arm were instructed to collect DBS on the same day and at approximately the same time each week (Sunday through Wednesday to avoid delays due to weekend shipping). If a DBS sample PCR result is missing, it is considered as noncompliant to the scheduled DBS test, i.e. missed recommended DBS tests.

3.3.9. Confirmatory Whole Blood (WB) Tests

If positive CMV result was detected from a DBS test in participants in the DBS arm and recorded on the CMV Laboratory Data Upload eCRF, a confirmatory whole blood (WB) test will be performed by the study laboratory and recorded on the CMV Laboratory Data Upload eCRF. The confirmatory WB sample was collected within 3 days of the positive DBS sample.

3.3.10. Confirmatory DBS Tests

Participants that were required to undergo confirmatory WB testing were also required to produce an additional confirmatory DBS sample to provide additional virologic data to assess the performance of the DBS assay. Confirmatory DBS tests are DBS tests entered on the CMV Laboratory Data Upload eCRF with the same collection date as the WB samples recorded on the CMV Laboratory Data Upload eCRF. Note that Confirmatory DBS Tests will not be used to assess any outcome measures related to adherence to the weekly DBS collection schedule but will be used to assess Unanticipated Adverse Device Effects (Section 3.3.14).

3.3.11. Mobile Technology Reminder Failure

A Mobile Technology Reminder or Device Failure will be analyzed as one of the possible mechanisms for participants in the DBS arm to have non-compliance to the weekly DBS collection schedule. This failure will be defined as the occurrence of a failure to deliver the weekly DBS monitoring reminder message which may have prevented the scheduled monitoring test from being performed. The record of whether the weekly DBS monitoring reminder was sent is automatically generated by the Electronic Data Capture (EDC) system and stored in the Sent Notification eCRF.

For participants receiving both email and text message reminders, a failure is deemed to occur if either the email or text message was not sent. If the participant did not select a standard service provider, then only email notifications could be sent. The type of notification, i.e. whether it is the first or second reminder for an expected DBS test, is also saved. A second DBS reminder should be sent to a participant if a DBS test result record has not been uploaded within 4 days of their scheduled DBS test reminder. Because the second DBS

reminder could not be sent if the initial notification failed, descriptive analyses of device failures will be restricted to the status of the initial notification.

Failures will be identified by determining whether there are any days when a notification should have been sent, for which there is no record in the Sent Notification eCRF indicating that an initial reminder was sent. Participants in the DBS arm recorded their preferred day of the week for receiving the reminder on the DBS Testing Reminder eCRF. Participants were able to update the preferred day by submitting additional eCRFs. A failure is represented when there is no record in the Sent Notification eCRF where the recorded reminder date is the expected reminder date, and the reminder sequence number for the week is the first reminder.

3.3.12. Sample Failures

DBS or WB sample collection failure will be identified when a participant in the DBS arm reports that the DBS or WB sample collection kit was not used due to a problem with the kit. DBS or WB kit problems were recorded by study staff in the Sample Collection Kit Problem eCRF. Frequencies of failures will be reported, and descriptions of the kit problems listed in detail.

Sample delivery failure is defined as any instance where a participant entered DBS or WB shipment data but there is no lab record entered for the expected DBS or WB test. Shipment data were entered by participants on the CMV Dried Blood Spot Shipment and CMV Whole Blood Shipment eCRFs.

Sample viability failure is defined as any instance where a participant entered DBS or WB shipment data and there is lab record entered for the expected DBS or WB test, but the DBS test result shows that the specimen is unevaluable. Results of the DBS or WB tests are entered into the CMV Laboratory Data Upload eCRF.

3.3.13. DBS Participant and Provider Satisfaction Measures

Participant questionnaires will be administered in the DBS arm after the third training visit, at one month post discharge, and at study completion. The provider questionnaire will be administered at study completion.

Questions on the questionnaires are measured on the Likert scale, on the binary scale (No or Yes), or measure the best response to each question. Regardless of measurement scale, all questions include a "Prefer not to answer" option. Questions asked on the Likert scale are for agreement (1-Strongly Disagree, 2-Disagree, 3-Neither Agree nor Disagree, 4-Agree, 5-Strongly Agree) or frequency (1-Never, 2- Very Rarely, 3-Rarely, 4-Occasionally. 5-Very Frequently). Answers to questions asked on the Likert scale will be converted to numbers ranging from 1-5 or missing if Prefer Not to Answer was selected. Answers to questions on the binary scale will be converted to 0 for No, 1 for Yes or missing for Prefer Not to Answer. Questions for which participants were to select the best response will be analyzed as categorical variables, where Prefer Not to Answer will be included as one of the levels of the variable.

For the questions asked on the Likert scale, a composite score will be calculated over all related questions at 1-month after discharge and end of study for participant satisfaction measures and at end of study for provider satisfaction measures (detail in Section 12.2).

3.3.14. Unanticipated Adverse Device Effects or Device Failures

False positive results and false negative results from the testing conducted at the University of Washington Laboratory on DBS samples are Unanticipated Adverse Device Effects (UADEs) and are considered Device Failures and will be reported as an Unanticipated Problem.

The following rules will be used to identify possible false positive or false negative results:

False Positive is reported in either of the following cases:

- A DBS sample is positive at a viral load above the treatment threshold at the respective site and a confirmatory WB sample is negative and collected within 3 days of the DBS sample.
- A confirmatory DBS is positive at a viral load above the treatment threshold at the respective site and a confirmatory WB sample is negative and collected on the same day.

False Negative is reported in either of the following cases:

- A CMV PCR result identified in the quarterly chart review is positive at a viral load above the treatment threshold at the respective site and a DBS sample is negative and collected within 3 days of the clinical plasma sample.
- A confirmatory DBS sample is negative and a confirmatory WB sample is positive at a viral load above the treatment threshold at the respective site collected on the same day.

Both DBS and WB results for UADE monitoring are obtained from the laboratory data uploaded by the University of Washington Laboratory (See Section 3.3.8 and Section 3.3.9 for further details).

4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

This is a randomized clinical trial to assess whether self-collection of samples (DBS) that are mailed for testing to a central laboratory will improve the compliance with the clinical recommendation CMV testing of HCT recipients. 150 allogeneic HCT recipients ≥15 years of age, who are considered by their transplant teams to be at risk for late CMV disease and who are clinically recommended to continue CMV monitoring after day 100 post-transplant, will be randomized (2:1) to participant self-collected DBS CMV monitoring with mobile technology support or standard of care with office-based testing. Randomization will occur when discharge from the transplant service is imminent, generally near day 100 post-transplant (enrollment window day 60-180 post-transplant). DBS self-collections will start the week after discharge. More than 85% of late CMV disease occurs within the first year after HCT [1]. While most patients are discharged to long-term primary care providers approximately 100 days after HCT, some may be discharged earlier, and some may stay longer with the transplant team due to complications. These latter patients are often at particularly high risk for late CMV complications and thus are important candidates for participation in this trial. For this reason, study entry is allowed up to 180 days (~6 months) after HCT and the duration of study participation is anticipated to be within a range of 26 weeks to 43 weeks. The transplant centers participating in this study have either a standard process where transplant recipients are offered to sign a consent to allow data from their charts to be accessed for retrospective trials or a waiver of additional consents for accessing charts for retrospective trials. This offers an opportunity to assess whether the study sample is representative of HCT population as a whole and to obtain a population-based estimate of later CMV disease. Therefore, clinical charts from an additional 450 HCT recipients (Observational Cohort) who meet eligibility criteria and have already consented for retrospective studies at the enrolling sites but are not participating in the DBS testing for CMV will be reviewed for the incidence and timing of CMV disease, morphologic relapse of the underlying disease, and death. Data from these participants will be used to assess whether the randomized study sample is representative of the DBS study population and to obtain a population-based estimate of late CMV disease participants.

The Schematic of the study design is also shown in Figure 1. The DSMB committee will be convened for an organizational meeting, ad hoc meetings to review safety data while the study is ongoing, and for a final meeting once the study has been completed after database lock. If the lower one-sided 90% confidence interval for the percent of participants experiencing CMV disease by one-year exceeds 8% (operationally 7 out of 50), a DSMB meeting will be convened. The DSMB will be charged with determining whether this exceptionally high rate of CMV disease has plausible clinical explanations related to the participant characteristics, or if it is the result of a failure in the monitoring system, and if so, what the source of the failure is (lack of compliance, failure of the system). Ultimately, they will make a recommendation to the PI as to whether any aspect of the study should be modified or terminated.

All enrolled participants will be followed for one year (365 days) post-HCT. Table 1 contains the schedule of events.

4.2. Discussion of Study Design, Including the Choice of Control Groups

The study is designed to compare adherence to clinician-recommended CMV-monitoring after discharge from HCT in participants simultaneously collecting DBS with mobile or web-based reminders compared with the current standard of care. An observational cohort of participants that were eligible for the randomized portion of the study, but were unable to participate in the randomized cohort, will also be followed to determine whether the participants in the randomized portion are representative of the general patient population meeting the inclusion criteria for the study.

4.3. Selection of Study Population

4.3.1. Inclusion Criteria

4.3.1.1. Randomized Cohort

- Must be ≥15 years of age at the time of enrollment
- Must be able to provide written consent and complete the informed consent
- Must have received allogeneic hematopoietic cell transplantation within 60-180 days prior to randomization
- CMV seropositive or had a donor who was CMV positive
- One or both of the following:
  - CMV event[1] within the first 100 days post-transplant requiring anti-viral treatment.
  - Receipt of CMV prophylaxis[2] prior to randomization. Continuation of letermovir or acyclovir/valacyclovir (high and low dose) prophylaxis after day 100 per institutional standard of care is permitted.
    [1] CMV event defined as DNA detection or disease
    [2] Anti-viral treatment or prophylaxis includes ganciclovir, valganciclovir, foscarnet, letermovir, maribabir or acyclovir/valaclycovir (high and low dose)
- Direct availability to the internet either by a computer in the residence or a smart phone
- Had at least one or more of these conditions:
  - HLA mismatch[3]
  - Umbilical cord blood source[4]
  - Graft versus host disease (GVHD)[5]
  - T-cell depletion[6]
    [3] Human leukocyte antigen (HLA)-related(sibling) donor with at least one mismatch at one of the following three HLA-gene loci: HLA-A, -B or -DR, Haploidentical donor, Unrelated donor with at least one mismatch at one of the following four HLA-gene loci: HLA-A, -B, -C and -DRB1
    [4] Use of umbilical cord blood as stem cell source
    [5] Acute or chronic GVHD requiring topical steroid for gastrointestinal (GI) GVHD and/or systemic steroid treatment (>1mg/kg/day of prednisone or equivalent dose of another corticosteroid) within 6 weeks prior to enrollment

[6] Participants who have received partial or full T-cell depletion (with or without GVHD). T-cell depletion can be given as either ex-vivo or in-vivo for GVHD prophylaxis. T-cell depleting agents include, but are not limited to, ATG and alemtuzumab.

4.3.1.2. Observational Cohort

- Must be ≥15 years of age at the time of enrollment
- Must have one of the following:
  - Consented for retrospective studies at their transplant center, or
  - Be included under the auspices of the site's IRB approved waiver of additional consent for retrospective studies
- Must have received allogeneic hematopoietic cell transplantation during or within 1 year prior to the conduct of the randomized trial (defined as time during which randomization is done).
- CMV seropositive or had a donor who was CMV positive
- One or both of the following:
  - CMV event[1] within the first 100 days post-transplant requiring anti-viral treatment.
  - Receipt of CMV prophylaxis[2] (for at least 30 days) prior to registration. Continuation of letermovir prophylaxis or acyclovir/valacyclovir (high and low dose) after day 100 per institutional standard of care is permitted.

  [1] CMV event defined as DNA detection or disease
  [2] Anti-viral treatment or prophylaxis includes ganciclovir, valganciclovir, foscarnet, letermovir, maribavir or acyclovir/valacyclovir (high and low dose)
- Meet one or more criteria of the following:
  - HLA mismatch[3]
  - Umbilical cord blood source[4]
  - GVHD[5]
  - T-cell depletion[6]

  [3] Human leukocyte antigen (HLA)-related(sibling) donor with at least one mismatch at one of the following three HLA-gene loci: HLA-A, -B or -DR, Haploidentical donor, Unrelated donor with at least one mismatch at one of the following four HLA-gene loci: HLA-A, -B, -C and -DRB1
  [4] Use of umbilical cord blood as stem cell source

  [5] Acute or chronic GVHD requiring topical steroid for GI GVHD and/or systemic steroid treatment (>1mg/kg/day of prednisone or equivalent dose of another corticosteroid) within 6 weeks prior to enrollment

  [6] Participants who have received partial or full T-cell depletion (with or without GVHD). T-cell depletion can be given as either ex-vivo or in-vivo for GVHD prophylaxis. T-cell depleting agents include, but are not limited to, anti-thymocyte globulin (ATG) and alemtuzumab.

4.3.2. Exclusion Criteria

4.3.2.1. Randomized Study

- Inability to fully comprehend the study website and study procedures
- Any other condition which in the opinion of the investigator would interfere with successful completion of this clinical trial
- Morphological relapse (bone marrow or peripheral blood blast) prior to registration.

4.3.2.2. Observational Cohort

- Did not meet all inclusion criteria
- Morphological relapse (bone marrow or peripheral blood blast) prior to registration

4.4. Interventions

4.4.1. Intervention Administered

In the randomized cohort, participants will be randomized to weekly participant collection of DBS samples with mobile technology support or to no intervention (standard of care, SOC). Participants randomized to both the DBS arm and the SOC arm completed standard of care CMV monitoring at the clinician-recommended interval with samples collected and tested by the clinical care team, the results of which are recorded in the medical chart.

Participants randomized to the DBS arm conducted weekly DBS testing. They received weekly text message or email reminders to complete the DBS testing. Participants in the DBS arm were also be notified by text message or email if a positive result for a DBS sample was entered into the data system by the study laboratory. If a positive result was reported, the participant was required to have a confirmatory whole blood sample collected by their clinical team, as well as a confirmatory DBS sample, which were both mailed to the study lab for testing.

There were no interventions in the observational cohort. The results of clinician-recommended monitoring were not collected in the observational cohort. This cohort was included to assess the incidence of late CMV disease in the population.

4.4.2. Identity of Investigational Product(s)

The study intervention is the combination of weekly DBS monitoring along with text or email DBS monitoring reminders and text or email notifications of positive DBS test results.

Participants in the DBS arm will receive DBS self-collection and WB collection kits. The DBS self-collection kits will be assembled, packaged and distributed to each enrolling site by Fred Hutchinson Cancer Research Center; the kit will be stored and shipped at room temperature. Participants are responsible for ordering additional self-collection kits.

4.4.3. Method of Assigning Participants to Intervention Groups (Randomized or Observational Cohort)

Participants will be randomized in an approximate 2:1 ratio to participant-collected DBS CMV monitoring with mobile technology support (n=100) or no intervention (n=50). Treatment allocation follows a Block Urn

Design [13] within each stratum. The Block Urn Design treatment allocation method prevents prediction of future treatment allocations and is suitable for unblinded studies. Randomization will be stratified by transplant site and participant's perceived ease of access to blood draw facility (easy or difficult). Randomized participants may withdraw from the study for any reason. If participants withdraw prior to their first scheduled monitoring test, they are eligible for replacement.

Additional participants will be enrolled as retrospective observational controls and will not be randomized (n=450).

Participants in both the randomized and observational cohorts will be entered into the data system after the required demographic and eligibility information were entered.

4.4.4. Replacement of Withdrawals

Participants in the randomized cohort who withdraw prior to their first scheduled monitoring test are eligible for replacement, with the replacement participant receiving a randomized treatment allocation (as opposed to being assigned the same treatment as the participant being replaced).

4.4.5. Selection of DBS Monitoring Interval

Participants in the DBS arm should have conducted DBS monitoring weekly after discharge from transplant center through one-year post-transplant as HCT patients remain at a high risk for late-CMV disease but are no longer in the care of their transplant team.

4.4.6. Blinding

This is an unblinded study.

4.4.7. Prior and Concomitant Therapy

At time of randomization, any of the following medications, if applicable, that were administered within 14 days prior to or ongoing at the time of randomization will be recorded:

- Steroids, topical only for GI GVHD and systemic (within 6 weeks prior to randomization)
- PUVA (combination treatment which consists of Psoralens (P) and then exposing the skin to UVA (long wave ultraviolet radiation)
- Immunosuppressant for acute or chronic GVHD (within 14 days prior to randomization, collecting only the start and stop dates)
- Preemptive or prophylaxis antivirals (i.e. dosing of foscarnet, ganciclovir, valganciclovir, cidofovir, brincidofovir, letermovir, acyclovir/valacyclovir [high and low dose], or any other investigational anti-CMV agent) (within 14 days prior to randomization)
- T-cell depleting agents including, but not limited to, ATG, alemtuzumab, etc. (any time after conditioning)

Use of antivirals for CMV treatment, topical steroids for GI GVHD, and systemic steroids during the study period will be recorded during medical chart review at quarterly follow-ups. Participants are expected to continue with their recommended monitoring if they initiate pre-emptive treatment for CMV during the study period.

4.4.8. Intervention Compliance

Participants randomized to the DBS arm will receive training on DBS self-collection prior to discharge from the transplant center. Since the primary objective is to compare monitoring compliance between intervention and standard of care, the study procedures have been designed to limit contact between study staff and participants during the study period.

4.5. Adherence and Safety Variables

4.5.1. Primary Outcome Measures

- The primary outcome is the number of participants in each intervention group who complete >90% of their clinician-recommended CMV monitoring tests in the study period (Section 3.3.2), by 1-year post-transplant.

The proportion of clinician-recommended CMV monitoring tests completed will be defined for each participant as the number of clinician-recommended CMV monitoring tests completed divided by the number of recommended clinician-recommended CMV monitoring tests, where the number of clinician-recommended CMV monitoring tests completed and the number of recommended clinician-recommended CMV monitoring tests are defined as in Section 3.3.

The primary outcome measure will be considered a binary variable based on each participant's observed proportion of clinician recommended CMV monitoring tests completed:

- Met > 90% threshold: the participant completed > 90% of their clinician recommended CMV monitoring tests (Success)
- Did not meet > 90% threshold: the participant completed $\leq$ 90% of their clinician recommended CMV monitoring tests (Fail)

Participants who withdraw prior to discharge will be considered as fail, i.e. not meeting the >90% threshold. Participants who didn't have recommended monitoring test scheduled will also be considered as fail.

The primary and secondary adherence outcomes will be analyzed with ITT, mITT and completer populations during the Study Period defined in Section 3.3.2. A sensitivity analysis will be conducted to exclude all participants from the University of Minnesota for the primary and secondary adherence measures.

In addition, sensitivity analyses with Maximal Study Period defined in Section 3.3.3 will be performed with ITT, mITT and completer populations with and without the participants from the University of Minnesota.

4.5.2. Secondary Outcome Measures

- The total number of recommended clinician recommended CMV monitoring tests that were completed per participant in the study period by 1 year after HCT will be defined as in Section 3.3.

The primary and secondary adherence outcomes will be analyzed with ITT, mITT and completer populations during the Study Period defined in Section 3.3.2. A sensitivity analysis will be conducted to exclude all participants from the University of Minnesota for the primary and secondary adherence measures.

In addition, sensitivity analyses with Maximal Study Period defined in Section 3.3.3 will be performed with ITT, mITT and completer populations with and without the participants from the University of Minnesota.

- The number of participants in the DBS and standard of care arms with possible, probable or proven end-organ CMV disease in the study period by 1 year after HCT will be measured from data entered by clinic staff during medical chart abstraction. Chart abstraction will occur at enrollment, quarterly contacts and at the study close-out visit. Proven/probably breakthrough CMV disease will be considered as a Serious Adverse Event of Special Interest (SAESI).
- Finger-stick procedure-related Grade 3 AEs will be abstracted through medical chart review at quarterly contacts and at the final close-out contact as described in the Manual of Procedures (MOP). Participants will be considered as meeting the outcome measure if they have at least one finger-stick procedure-related Grade 3 AE during the study period.

4.5.3. Exploratory Outcome Measures

- The time between scheduled pick-up of the sample and arrival at the laboratory will be calculated as follows:
  - Scheduled Pick-up: Participants in the DBS arm will enter the scheduled date and time of pick-up for each of their DBS samples into the data system on the CMV Dried Blood Spot Shipment form. WB samples will be entered on the CMV Whole Blood Shipment form.
  - Receipt at the Laboratory: For each DBS or WB sample received, the study laboratory will enter the date and time of arrival on the CMV Laboratory Data Upload form.
  - For each study sample received, the time between scheduled pick-up and receipt will be calculated as the time between scheduled pick-up and receipt at the laboratory. The mean time between scheduled pick-up and receipt at the laboratory across all participants and samples will be reported separately for DBS and WB samples.
- The number of participants in the DBS arm for whom a Mobile Technology Reminder or Device Failure occurred during the study period will be reported. Mobile Technology Reminder or Device Failures are defined in Section 3.3.10.
- The number of sample failures, including collection failures, delivery failures, and viability failures will be identified and reported as described in Section 3.3.11.
- The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for initial DBS when compared to confirmatory WB tests (Section 3.3.8) will be calculated as follows:
  - $Sensitivity = 100\% * \frac{\#\ of\ True\ Positives}{(\#\ of\ True\ Positives + \#\ of\ False\ Negatives + \#\ Unevaluable)}$
  - $Specificity = 100\% * \frac{\#\ of\ True\ Negatives}{(\#\ of\ True\ Negatives + \#\ of\ False\ Positives + \#\ Unevaluable)}$
  - $PPV = 100\% * \frac{\#\ of\ True\ Positives}{(\#\ of\ True\ Positive + \#\ of\ False\ Positives + \#\ Unevaluable)}$
  - $NPV = 100\% * \frac{\#\ of\ True\ Negatives}{(\#\ of\ True\ Negatives + \#\ of\ False\ Negatives + \#\ Unevaluable)}$

Where the number of true positives is reported in either of the following cases:

- A DBS sample is positive at a viral load above the treatment threshold at the respective site and a confirmatory WB sample is positive and collected within 3 days of the DBS sample.
- A confirmatory DBS is positive at a viral load above the treatment threshold at the respective site and a confirmatory WB sample is positive and collected on the same day.

The number of true negative is reported in either of the following cases:

- A CMV PCR result identified in the quarterly chart review is negative at a viral load above the treatment threshold at the respective site and a DBS sample is negative and collected within 3 days of the clinical plasma sample.
- A confirmatory DBS sample is negative and a confirmatory WB sample is negative at a viral load above the treatment threshold at the respective site collected on the same day.

The number of unevaluable samples reported in either of the following cases:

- A confirmatory DBS sample that is unevaluable.
- A scheduled DBS that is unevaluable and was collected within 3 days of the WB sample.

The number of samples unevaluable is the number of samples where either the DBS sample and/or the WB sample is recorded as unevaluable on the laboratory data upload, and the number of false positives and false negatives are calculated as described in Section 3.3.13. The sensitivity, specificity, PPV, and NPV will be calculated analogously for the confirmatory DBS (Section 3.3.9), by comparing the confirmatory DBS to the confirmatory WB tests.

The number of participants in the randomized and observational cohorts with the key transplant characteristics will be reported, where each key transplant characteristic is defined to align with the inclusion criteria described in Section 4.3.1. Key transplant characteristics were assessed as part of the process of determining eligibility prior to enrollment. In addition, data were collected on the following key characteristics at enrollment on the CMV Infection or Disease eCRF:

  - Whether transplant was an HLA mismatch.
  - Umbilical cord blood source
  - GVHD
  - CMV event within the first 100 days post-transplant requiring anti-viral treatment
  - CMV prophylaxis for at least 30 days from the day of transplant to 100 days post-transplant

- Participant baseline demographics will be presented for the randomized and observational cohorts. Stratification variables will be presented for the randomized cohort as these were not collected in the observational cohort.
- The number of participants in the randomized and observational cohorts with possible, probable or proven end-organ CMV disease by 1 year after HCT will be reported. These data were collected on the CMV Infection or Disease eCRF at each follow-up.
- The local provider CMV viral load treatment threshold will be reported. These data were entered on the CMV Viral Treatment Threshold eCRF at enrollment or when new thresholds became effective.
- The local provider CMV clinician recommended CMV monitoring intervals will be reported as described (Section 3.3.4, 3.3.5, and 3.3.7).

- The composite scores of different variables of participant and provider satisfactions according to the 5-point Likert scale questionnaires will be reported as described. (Section 3.3.12, 12.2).

5. SAMPLE SIZE CONSIDERATIONS

Power calculations used a binomial distribution to ascertain the number of participants needed to detect a clinically meaningful difference in proportions of participants meeting the primary endpoint [10]. Based on preliminary data, the assumed proportion of individuals completing >90% of their recommended surveillance tests in the standard office-based testing arm would be in the range of 50-55%. In a previously reported clinical trial, high proportions of CMV monitoring completion resulted in the clinically relevant outcome of a low incidence of late CMV disease [1]. To be successful, this proof-of-concept trial needs to demonstrate that similarly high proportions of monitoring can be achieved with participant collected DBS monitoring. With 150 participants, randomized 2:1, there will be 90-96% power to detect an absolute difference in testing proportions of 25-30% between participants in the intervention (80% with >90% adherence rate) and control arms (50% with >90% adherence rate) (Table 2. Although the 2:1 randomization does not result in increased statistical power, randomizations that favor the experimental arm (2:1 or 3:1) appear to increase the appeal to the potential study participant and have been used successfully in several recent multicenter CMV randomized trials [4, 2, 12].

6. GENERAL STATISTICAL CONSIDERATIONS

6.1. General Principles

Continuous variables will be summarized using the following descriptive statistics unless otherwise noted: n (non-missing sample size), mean, standard deviation, median, maximum and minimum. The frequency and percentages (based on the non-missing sample size) of observed levels will be reported for categorical measures unless otherwise noted. In general, all data will be listed, sorted by site, treatment, and participant ID, and when appropriate by visit number within participant. Tables presenting data from more than one intervention arm in the randomized cohort will be structured with a column for each intervention in the order DBS, SOC, All Randomized and will be annotated with the total population size relevant to that table/treatment. Tables presenting data from all enrolled participants will be structured with columns for each intervention group in the order DBS, SOC, All Randomized, Observational.

6.2. Timing of Analyses

6.2.1. Interim Analyses

The following interim analyses may be conducted prior to the database lock. No additional interim analyses are planned.

- Among the first 50 participants enrolled on the DBS intervention arm, if the lower one-sided 90% confidence interval for the percent of participants experiencing CMV disease by one-year exceeds 8% (operationally 7 out of 50), a DSMB meeting will be convened. The DSMB will be charged with determining whether this exceptionally high rate of CMV disease has plausible clinical explanations related to the participant characteristics, or if it is the result of a failure in the monitoring system, and if so, what the source of the failure is (lack of compliance, failure of the system).
- Additional ad hoc DSMB meetings to review safety events such as UADEs or SAESIs may also be held.

6.2.2. Final Analysis

The final analysis will be performed after database lock.

6.3. Analysis Populations

6.3.1. Intention-to-Treat Analysis (ITT) Population

The Intention-to-Treat population includes all participants in the randomized cohort in the intervention group to which they were randomly assigned, regardless of their monitoring compliance and regardless of subsequent withdrawal or deviation from the protocol. Participants who withdraw before discharge and participants that withdraw after discharge but before their first scheduled in-office CMV monitoring test will be considered as fail, which is not meeting the >90% threshold for the primary adherence analyses.

6.3.2. Modified Intention-to-Treat (mITT) Population

The mITT population will include all participants in the ITT who have at least one result for the number of clinician-recommended CMV monitoring tests and remained enrolled through their first scheduled clinician-recommended CMV monitoring test (e.g., a participant assigned weekly clinician-recommended CMV monitoring at discharge must remain enrolled for at least 1 week after discharge to be included in the mITT

population). Participants will be grouped based on the intervention received, where participants that complete at least one self-collected DBS sample will be grouped in the DBS arm and all other participants will be grouped in the SOC arm. This population will be used as a supplemental analysis for all adherence outcome measures.

6.3.3. Completer Population

The completer population will include all participants in mITT who were not found ineligible after enrollment, remained enrolled at discharge, have clinician recommended CMV monitoring test interval(s) available and completed the study close-out visit which is scheduled to occur 365 days post-transplant. This population is only being used for sensitivity analyses.

6.3.4. All Enrolled Participants

Some analyses will be completed among all enrolled participants. This includes all randomized participants, if in the randomized cohort, or enrolled, if in the observational cohort.

6.3.5. Safety Population

The safety population will consist of all enrolled participants that had any safety data collected after randomization. Most of the safety data will be collected at the quarterly contact.

6.4. Covariates and Subgroups

As randomization was stratified by transplant site and participant's perceived ease of access to blood draw facility, transplant site and participant's perceived ease of access to blood draw facility are included as covariates in the logistic regression used to conduct the primary analysis.

The protocol does not define any formal subgroup analyses and the study is not adequately powered to perform subgroup analyses. However, a sensitivity analysis will be conducted for the adherence outcome measures to exclude all participants from the University of Minnesota, as this site entered actual number of monitoring tests into the recommended monitoring schedule.

6.5. Missing Data

6.5.1. Withdrawal Prior to First Recommended Monitoring Test

If participants withdraw prior to their first scheduled clinician-recommended CMV monitoring test, the number of recommended clinician-recommended CMV monitoring tests will be zero, monitoring compliance cannot be calculated. These participants will be included in the ITT analyses and considered as fail, not meeting the >90% threshold for the primary endpoint. They will not be included in the mITT or Completer analyses.

If the clinician recommended monitoring test interval is "No further monitoring required" at discharge and not changed until withdrawal or 1 year after HCT, then these participants will be included in the ITT analyses and considered as fail, not meeting the >90% threshold.

6.5.2. Withdrawal After First Recommended Monitoring Test

If participants withdraw after their first scheduled clinician recommended CMV monitoring test the number of clinician recommended CMV monitoring test will not be zero. Therefore, the monitoring compliance can be calculated with the actual number of clinician-recommended CMV monitoring tests completed prior to

withdrawal divided by the number of recommended clinician-recommended CMV monitoring tests before withdrawal.

6.5.3. Missing Participant Questionnaires

In the DBS arm participants were asked to complete satisfaction questionnaires. Since participants have the option to respond "Prefer Not to Answer" for any given question, this answer will be considered as missing for analysis. The number of missing responses will be reported. Composite scores combining responses to multiple survey questions are defined in Section 12.2. For a given composite score, only observations where responses are available for all component survey questions of the score will be used to compute the composite and the number of participants excluded for this descriptive analysis will be reported. Because the composite scores will not be used in analyses of hypothesis tests, advanced methods of imputing missing responses based on assumed data distributions will not be attempted, and descriptive results will be presented with a discussion of the frequency of missing responses for each item.

6.6. Interim Analyses and Data Monitoring

See Section 6.2.1 for a description of interim analyses and interim monitoring.

6.7. Multicenter Studies

Randomization is stratified by transplant site. Transplant site will be included as a covariate in the logistic regression used to conduct the primary analysis.

6.8. Multiple Comparisons/Multiplicity

There is only one primary outcome measure. No adjustments for multiple testing are planned.

7. STUDY PARTICIPANTS

7.1. Disposition of Participants

The disposition of participants in the study will be tabulated by intervention group (Table 5). The table shows the total number of participants screened, enrolled/randomized, early terminated (including those who consented and did not consent to data collection from medical records), remained enrolled at discharge, remained enrolled through the date of the first scheduled clinician-recommended CMV monitoring test, completed at least one scheduled clinician-recommended CMV monitoring test, completed at least one self-collected DBS sample with laboratory results, and completed the study close-out visit. Table 7 will summarize the dates of first enrollment by site and intervention group. Table 8 will present a summary of the reasons that participants were screened but not enrolled into the randomized cohort.

The composition of participant analysis populations, including reasons for participant exclusion, by intervention group, is presented in Table 6. Individuals excluded from analysis populations are presented in Listing 4.

A flowchart showing the disposition of study participants, adapted from the Consort Statement will be included (Figure 2). This figure will present the number of participants screened, enrolled, lost to follow-up, and analyzed, by intervention group.

A listing of participants who terminated from study follow-up and the reason will be included in Listing 1.

7.2. Protocol Deviations

A summary of participant-specific protocol deviations will be presented by the reason for the deviation, the deviation category, and intervention group for all participants (Table 3). Deviations will be reviewed by the Sponsor and classified as either major or minor. All participant-specific protocol deviations and non-participant specific protocol deviations will be included in Appendix 3 as data listings (Listing 2 and Listing 3, respectively).

8. ADHERENCE EVALUATION

Descriptive statistics will be reported by intervention group and overall, for the adherence outcomes. N, Mean, Standard Deviation, Minimum and Maximum will be reported for continuous adherence variables and number and percent for categorical adherence variables.

Primary and secondary analyses of adherence outcomes will be performed using logistic regression models. Separate models will be fit to the binary outcome of whether or not individual participants completed >90% of their clinician recommended CMV monitoring, and to the proportion of completed clinician recommended CMV monitoring tests per participant. All models will include intervention and the categorical stratification variables transplant site and participant's perceived ease of access to blood draw facility as independent variables.

Model assumptions will be checked by viewing plots of the residual distribution, and the model will be adjusted accordingly based on the assumption check. Listings of CMV monitoring results (including clinician-recommended and self-collected) and clinician-recommended monitoring intervals will be presented in Listing 9 and Listing 13, respectively.

8.1. Primary Adherence Analysis

A traditional logistic regression model will be fit to the ITT population where the outcome is whether or not the participants completed > 90% of their clinician-recommended CMV monitoring tests in the study period by 1-year after HCT. A two-sided Wald-test for evidence of a non-zero coefficient for intervention group in the regression will be conducted at the 5% significance level. This analysis will be repeated in the mITT population and the Completer population. The summary of the primary adherence analysis results will be presented in Table 14.

A sensitivity analysis, logistic regression will be fit in the ITT and mITT populations with the maximal possible study period, where the outcome is whether or not the participant completed > 90% of their recommended monitoring tests by the end of maximal possible study period. These results will be presented in Table 15.

In addition, as a sensitivity analysis, logistic regression will be fit in the ITT and mITT populations excluding all participants from the University of Minnesota (See Section 6.4), where the outcome is whether or not the participant completed > 90% of their recommended monitoring tests by 1-year after HCT. These results will be presented in Table 16. Example SAS code for this analysis is included below and specifies the INFLUENCE option to display regression diagnostics and the PARAM=REF option to obtain parameter estimates appropriate to the reference coding where the regression coefficient and odds ratio are estimated for the effect of the intervention compared to the standard of care.

```
ODS GRAPHICS ON;

PROC LOGISTIC DATA=DSN;

  CLASS TRT SITE EASE / PARAM=REF;

  MODEL SUCCESS = TRT SITE EASE /INFLUENCE IPLOTS;

RUN;

ODS GRAPHICS OFF;
```

8.2. Secondary Adherence Analyses

A fractional logistic regression model will be fit with quasi-maximum likelihood estimates in the ITT population where the outcome will be the proportion of recommended monitoring tests completed per participant, and the covariates will be randomized intervention group and the stratification variables. This fractional response model was introduced by Papke and Wooldridge (1996) in their frequently cited extension of the generalized linear model to analyze proportion data that are bounded by 0 and 1. Although commonly applied to these outcome data for simplicity, ordinary least squares regression assumes that the predictor variables and continuous outcome variable are linearly related and that the variance is independent of the mean, the violations of which in models of fractional outcomes result in biased estimates and potentially misleading inference. The marginal effects of predictor variables on the mean proportion response can be estimated using the binominal likelihood framework with robust standard errors. Appropriate to the proportion outcome data, the model allows for responses at the 0 and 1 boundaries, in contrast to the beta regression approach that has been described for proportion data that do not include extremes (zero or one).

To estimate the treatment effect of the DBS intervention on the proportion of recommended tests completed by individuals in the DBS vs SOC group, we will fit the fractional logistic model using SAS PROC GLIMMIX with logit link function and the random residual option to estimate model parameters using a quasi-likelihood function. A two-sided Wald-test for evidence of association between intervention group and proportion of recommended monitoring tests completed will be conducted at the 5% significance level. This analysis will be repeated in the mITT population and the Completer population. The results from the models of the proportion of recommended tests completed will be presented in Table 17. Table 18 presents the results from the sensitivity analysis conducted on the ITT and mITT populations with the maximal possible study period. Table 19 presents the results from the sensitivity analysis conducted on the ITT and mITT populations excluding participants from the University of Minnesota. Example SAS code for this analysis is shown below and specifies the S or SOLUTION option to report the fixed effects parameter estimates, and ILINK option to report estimates on the mean (probability) scale. Variables for transplant site and the participants' perceived ease of access to the blood draw facility will be included as covariates as described in Section 8 for all adherence models.

```
PROC GLIMMIX DATA=DSN;
  MODEL PCT=TRT  SITE EASE/ DIST=BINOMIAL LINK=LOGIT S;
  RANDOM _RESIDUAL_;
  OUTPUT OUT=FRACOUT PRED(ILINK)=PRED LCL(ILINK)=LOWER UCL(ILINK)=UPPER;
  RUN;
```

8.3. Exploratory Adherence Analyses

No exploratory adherence analyses are planned.

9. SAFETY EVALUATION

9.1. Demographic and Other Baseline Characteristics

Summaries of age, sex, ethnicity, race, transplant site, participants' perceived ease of access to blood draw facility, and days from HCT (calculated as the time from enrollment – HCT date + 1) will be presented by intervention group in Table 11 and Table 12. Similar summaries of categorical and continuous demographic and baseline characteristics will also be presented by site for the randomized cohort (Table 9 and Table 10). Ethnicity is categorized as Hispanic or Latino, or not Hispanic and not Latino. In accordance with NIH reporting policy, participants may self-designate as belonging to more than one race or may refuse to identify a race, the latter reflected in the CRF as "No" to each racial option.

Individual participant listings (Appendix 3) will be presented for all demographics (Listing 5) sorted by intervention group, and Participant ID.

9.1.1. Prior and Concurrent Medical Conditions

A summary of transplant and neoplastic disease characteristics is presented by intervention group in Table 13. Listings of participants' transplant information, GVHD status, and CMV reactivation or disease will be presented (Listing 6, Listing 7, and Listing 8). Proven/Probable CMV disease is considered a Serious Adverse Event of Special Interest and is summarized as described in Section 9.4.

9.1.2. Prior and Concomitant Medications

Concomitant medications will be coded to the Anatomical Therapeutic Classification using the WHO Drug Dictionary. The use of prior and concomitant medications taken during the study will be recorded on the CRFs. A by-participant listing of concomitant medication use will be presented. The use of concomitant medications during the study will be summarized by ATC1, ATC2 code and intervention group for the Safety population (Table 30).

9.2. Adverse Events

When calculating the incidence of adverse events (i.e., on a per participant basis), each participant will only be counted once and any repetitions of adverse events within a participant will be ignored; the denominator will be the total population size. All adverse events reported will be included in the summaries and analyses. Overall summary of adverse events (Table 20) and adverse events occurring in more than 5% of participants in any intervention group (Table 21) are summarized. Table 21 presents data by MedDRA system organ class, preferred term, and intervention group.

9.2.1. Elicited Events

The number and proportion of participants in the DBS arm experiencing Finger-Stick Procedure-Related Severe Adverse Events will be presented (Table 24). The exact 95% binomial CI for the proportion of participants and the total number of events will also be presented.

9.3. Deaths, Serious Adverse Events and other Significant Adverse Events

Proven or probable CMV disease is a serious adverse event of special interest. The number of participants, proportion of participants and Clopper-Pearson Exact 95% confidence interval for all enrolled participants experiencing proven or probable CMV disease between discharge and 365 days after HCT will be

summarized in the randomized groups (Table 22). The same quantities will be summarized between HCT and 365 days after HCT in the randomized groups (Table 23).

To assess whether incidence of possible, probable or proven CMV disease at 1 year differed between intervention groups, the proportional hazards model for the sub distribution of CMV (ShafeFine and Gray, 1999) with death as a competing risk will be fit in the safety population. Example SAS code for this analysis is included below and specifies the EVENTCODE=1 indicate the event of interest is relapse of CMV (status =1), death is the competing risk (status =2), and censored observations are those with Status = 0. The PLOTS =CIF option to obtain cumulative incidence function of each intervention group.

```
DATA RISK;
TRT=1; OUTPUT;
TRT=2; OUTPUT;
FORMAT  TRT TRTGRP;
PROC PHREG DATA=DATA  PLOTS (OVERLAY=STRATUM)=CIF;
CLASS  TRT (ORDER=INTERNAL REF=FIRST);
MODEL T*STATUS(0)= TRT  / EVENTCODE=1;
HAZARDRATIO  TRT/DIFF ;
BASELINE COVARIATES=RISK OUT=OUT1 CIF=_ALL_ / SEED=SEED;
RUN;
```

The outcome of the regression will be the occurrence of possible, probable or proven CMV disease. End of follow-up will be defined as the earliest of death date, date of withdrawal, or 365 days post HCT. Gray's test will be used to test for differences in the sub distribution hazard of CMV disease between intervention groups at the 5% significance level, the cumulative incidence function of CMV diseases presented (Figure 3).

Similarly, for another analysis with all enrolled participants, the proportional hazards model for the sub distribution of CMV disease, with death as a competing risk, will be fit. Gray's test will be used to test for differences in the sub distribution hazard of CMV disease between the All Randomized and Observational groups at the 5% significance level, the cumulative incidence function of CMV diseases presented (Figure 4).

The following listings describing deaths, SAEs, or other significant AEs will be presented:

- Serious Adverse Events of Special Interest (Table 25);
- Finger-Stick Procedure-Related Severe Adverse Events (Table 26);
- Unanticipated Adverse Device Effects (Table 27);
- Deaths (Table 28);
- Hospitalizations (Table 29).

9.4. Pregnancies

Pregnancy data will not be collected in this study.

9.5. Clinical Laboratory Evaluations

Listing 9 presents results of all clinical laboratory testing of dried blood spot and whole blood samples. Investigations into the concordance between positive dried blood spot and confirmatory whole blood samples are described in Section 13.

9.6. Vital Signs and Physical Evaluations

No vital signs or physical exams will be conducted for this study.

10. PHARMACOKINETICS

No pharmacokinetic analyses will be conducted.

11. IMMUNOGENICITY

No immunogenicity analyses will be conducted.

12. PARTICIPANT AND PROVIDER SATISFACTION EVALUATION

12.1. Participant and Provider Satisfaction Responses

Summaries of responses to questionnaires from participant and provider satisfaction questionnaires will be presented by time point of questionnaire: after training, one month post discharge, and after study completion. Questionnaire responses will be converted to numeric values as described in Section 3.3.13. The responses to questions asked on the Likert Scale will be converted to numbers from 1-5 and the number of non-missing responses, as well as the mean, standard deviation, median, minimum and maximum responses will be summarized. For Yes/No questions, the number of non-missing responses as well as the number and proportion of "Yes" responses will be summarized. For questions asking for the best reason, out of those who answered "Yes" to the preceding question, the number and proportion of participants who picked each option will be summarized.

For summaries of the participant and provider satisfaction data, data will be presented in the DBS group from the ITT population for each time point of interest.

The tables will present data from the participants in the DBS group corresponding to each questionnaire time point (Table 31, Table 33, and Table 34). All provider satisfaction responses will be summarized in Table 35.

Individual participant and provider satisfaction responses are listed in Listing 15, Listing 16, Listing 17, and Listing 18.

12.2. Participant and Provider Satisfaction Composite Scores

Composite scores for overall participant satisfaction with email and mobile technology and overall satisfaction with kit contents and testing and shipping procedures will be presented for the one month post-discharge and after study completions surveys (Table 32). Composite scores for overall provider satisfaction with CMV DBS self-collection results will be presented for the after-study completion survey (Table 35).

For each survey timepoint, the composite scores will be defined as the mean of Likert scale responses converted to the numeric scale to the questions defined below.

	Composite Score	**Component Survey Questions**
Participant	Overall satisfaction with email and mobile technology	The self-collection teaching videos are helpful and easy to follow.
		The web and mobile phone site is easy to use and provides me with the information I need to do the testing at home.
		The web or mobile phone options give me the choices I want for how and when I received the reminders.
		The email or mobile phone messages remind me to do the self-collection.
	Overall satisfaction with kit content, and testing and shipping procedures	The self-collection kit had everything I needed to do the testing.
		The CMV dried blood spot self-collection is easy.
		Scheduling USPS to pick up my sample is easy.

	Composite Score	**Component Survey Questions**
Provider	Overall satisfaction with CMV dried blood spot self-collection results	DBS testing will increase adherence to CMV surveillance late after HCT.
		The results of the finger stick CMV self-collection were available to me in an easy and timely fashion.
		I was confident with the results of the CMV dried blood spot self-collection results
		If I have the results of the CMV self-collection, I do not feel I need an additional plasma blood draw to decide on treatment for my patient
		I would participate in another study with use of this type of blood self-collection

13. MOBILE TECHNOLOGY, DEVICE AND SHIPMENT EVALUATION

Mobile technology, device and shipment evaluation will include summaries of time from scheduled pick-up at participant residence to arrival at lab, the number of samples unevaluable due to lack of amplification or inhibition, and number of mobile technology failures.

The number of DBS testing reminder failures will be summarized (Table 39). The number of failed reminders overall, number of participants who had failed reminders, and the number of failed reminders per participant will be presented. In addition, the number of participants who missed a recommended DBS test following a failed reminder and the number of tests missed following failed reminders will be summarized. A listing presenting the DBS testing reminder configuration data is presented in Listing 10.

The number of samples with collection time, shipment time and arrival time entered, as well as the mean, standard deviation, minimum, maximum and median hours from scheduled pick-up to arrival at study laboratory will be summarized by transplant site and participants' perceived ease of access to blood draw facility for the participants in DBS arm (Table 36).

The number and proportion of unevaluable samples, and the number and proportion of participants with unevaluable samples, will be summarized by transplant site. (Table 37).

The Lin's concordance correlation coefficient will be calculated (Table 38). Sensitivity, specificity and predictive values of CMV detection in confirmatory DBS versus confirmatory WB testing will be reported. In addition, a correlation between the confirmatory DBS result and the confirmatory WB result will be visualized in Figure 5. A Bland-Altman plot of difference between the confirmatory DBS result and the confirmatory WB result will be presented in Figure 6.

For sample collection and sample delivery failures, the total number of failures, the number of participants with failures and the median, minimum and maximum number of failures per participant will be summarized by sample type, i.e. DBS, WB or any sample, in Table 40.

14. LOCAL PROVIDER CARE EVALUATION

The number of participants in each intervention group receiving pre-emptive therapy for CMV disease, as well as the mean and standard deviation of viral load at time of the decision to initiate pre-emptive therapy, by transplant site and participants' perceived ease of access to blood draw facility, as well as overall, will be summarized (Table 41).

At each quarterly contact, the least-frequent clinician-recommended monitoring interval recorded for each participant up until 90 days post-HCT (first contact), 180 days post-HCT (second contact), 270 days post-HCT (third contact) and 365 days post-HCT (final contact) will be categorized as described in Section 3.3.7.

The number and proportion of participants in each of the groups between enrollment and the first, second, third and final contacts will be summarized by intervention group, as well as by stratification variables and overall (Table 42, Table 43, Table 44, and Table 45). Note that University of Minnesota results will be excluded from the perceived ease of access stratification as this site recorded actual number of clinician-recommended CMV monitoring tests completed instead of the clinician-recommended CMV monitoring intervals.

15. REPORTING CONVENTIONS

P-values ≥0.001 and ≤0.999 will be reported to 3 decimal places; p-values less than 0.001 will be reported as "<0.001" The mean, standard deviation, and other statistics will be reported to one decimal place greater than the original data. The minimum and maximum will use the same number of decimal places as the original data. Proportions will be presented as two decimal places; values greater than zero but <0.01 will be presented as "<0.01". Percentages will be reported to the nearest whole number; values greater than zero but < 1% will be presented as "<1"; values greater than 99% but less than 100% will be reported as >99%. Estimated parameters, not on the same scale as raw observations (e.g. regression coefficients) will be reported to 3 significant figures.

16. TECHNICAL DETAILS

SAS version 9.4 or above will be used to generate all tables and listings. Figures will be generated in either R 3.2.5 or SAS version 9.4.

17. SUMMARY OF CHANGES IN THE CONDUCT OF THE STUDY OR PLANNED ANALYSES

A sensitivity analysis excluding University of Minnesota participants for whom the site entered the actual number of monitoring tests instead of clinician-recommended tests was requested by the study team. The analysis is added in this SAP.

18. REFERENCES

1. Boekh, M., Nichols, W. G., Chemaly, R. F., et. al. (2015). Valganciclovir for the prevention of complications of late cytomegalovirus infection after allogeneic hematopoietic cell transplantation: a randomized trial, *Annals of Internal Medicine, 162*(1), 1–10.
2. Chemaly, R.F. Ullmann, A. J., Stoelben, S. et. al. (2014). Letermovir for Cytomegalovirus Prophylaxis in Hematopoietic-Cell Transplantation, *New England Journal of Medicine, 370*(19), 1781–1789.
3. Fine, J. P. & Gray, R. J. (1999). A Proportional Hazards Model for the Subdistribution of a Competing Risk, *Journal of the American Statistical Association, 94*, 496–509.
4. Marty, F. M., Winston, D. J., Rowley, S.D. et. al. (2013). CMX001 to Prevent Cytomegalovirus Disease in Hematopoietic-Cell Transplantation, *New England Journal of Medicine, 369*(26), 1227–1236.
5. Papke, L. E.., & Woodcock, J. M. (1996). Econometric Methods for Fractional Response Variables with an Application to 401 (K) Plan Participation Rates, *Journal of Applied Econometrics, 11*(6), 619-632.
6. Rubin, D. B. (1987). Multiple Imputation for Nonresponse in Surveys, New York: John Wiley & Sons.
7. SAS Institute Inc. (2007). SAS Note 56992. Modeling continuous proportions: Fractional and 4- (or 5-) parameter logit models. Available http://www.support.sas.com
8. Schafer, J. L. (1997). Analysis of incomplete multivariate data, London: Chapman & Hall.
9. Shulz, L., Altman, D. & Moher, D. (2010). CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMC medicine, 8*(1), 18.
10. Ury, H. K., & Fleiss, J. L. (1980). On approximate sample sizes for comparing two independent proportions with the use of Yates' correction, *Biometrics, 36*(2), 347-351.
11. van Buuren, S., and Groothuis-Oudshoorn, K. (2011) mice: Multivariate Imputation by Chained Equations in R, *Journal of Statistical Software, 45*(3), 1-67.
12. Winston, D. J., Young, J-A. H., Pullarkat, V. et. al. (2008). Maribavir prophylaxis for prevention of cytomegalovirus infection in allogeneic stem cell transplant recipients: a multicenter, randomized, double-blind, placebo-controlled, dose-ranging study, *Blood, 111*(11),5403-5410.
13. Zhao, W., Weng, Y. (2011). Block urn design - a new randomization algorithm for sequential trials with two or more treatments and balanced or unbalanced allocation, Contemp Clin Trials, 32(6), 953-961.
14. Boeckh M, Marr KA. Infection in Hematopoietic Stem Cell Transplantation. In: *Clinical Approach to Infection in the Compromised Host*. Boston, MA: Springer US; 2002:527-571. doi:10.1007/0-306-47527-8_16.

19. LISTING OF TABLES, FIGURES, AND LISTINGS

Table, figure, and listing shells are presented in Appendices 1, 2, and 3.

APPENDICES

APPENDIX 1. TABLE MOCK-UPS

LIST OF TABLES

9.5.1 Adherence and Safety Measurements Assessed and Flow Chart

Table 1: Schedule of Study Procedures

Visit/Contact	Screening[1]	Enrollment[2]	Initial Study Visit	DBS self-collection	Plasma Collection[3]	Quarterly Contact 1	Quarterly Contact 2	Quarterly Contact 3	Final Study Visit
Days after HCT	60-180			60-365	60-365	90	180	270	365
Window (days)	N/A					±14	±14	±14	(+120)
Confirm informed consent		X							
Eligibility assessment	X, Z								
Randomization		X							
Confirm CMV monitoring interval			X, Z			X	X	X	
Adherence counseling			Y						
DBS collection and website training[4]			Y						
Participant questionnaire[5]			Y	Y					Y
Provider questionnaire[6]									Y
Safety monitoring						X	X	X	X
Obtain interim medical records[7]						X	X	X	X, Z

X = performed for all randomized participants
Y = performed for DBS arm participants only
Z = performed for observational cohort only

GRAY columns may not be required. Depending on when a participant enrolls in the study, the duration of participation will be between 26 and 44 weeks. Columns marked in GRAY apply to those participants whose participation includes these time points. If the participant is randomized within 10 days of scheduled quarterly visit, the first quarterly follow-up visit will be waived.

[1] Screening will be done approximately one month prior to planned discharge from the primary transplant clinic
[2] Screening, enrollment, and initial study visit may occur on the same day
[3] Confirmatory plasma sample will be collected from DBS arm participants if they had a CMV positive DBS
[4] After the initial DBS collection and website training, two additional trainings are to be scheduled each one week apart
[5] Patient questionnaire will be given after 2nd training session, 1 month after discharge, and at the end of study;
[6] Primary care providers will be given a questionnaire at the time of last quarterly contact for medical records review
[7] Obtain CMV testing frequency and results, presence of CMV disease, use of antivirals of CMV treatment, and use of steroids for GVHD

9.7.1 Sample Size

Table 2: Sample Size/Probability Estimates

Sample size Total	Sample size DBS group	Sample size Control	Proportion of participants with >90% Adherence rate DBS arm	Proportion of participants with >90% Adherence rate Control arm	Sig. level Two-sided	Power
150	100	50	0.8	0.5	0.05	**96%**
150	100	50	0.8	0.55	0.05	**89%**
150	100	50	0.8	0.58	0.05	**80%**

10.2 Protocol Deviations

Table 3: Distribution of Protocol Deviations by Category, Type, and Intervention Group

Category	Deviation Type	DBS (N=X)		SOC (N=X)		All Randomized (N=X)		Observational (N=X)	
		# Part.	# Dev.	# Part.	# Dev.	# Part.	# Dev.	# Part.	# Dev.
Major Deviations									
Eligibility/enrollment	Any type	x	x	x	x	x	x	x	x
	Did not meet inclusion criterion	x	x	x	x	x	x	x	x
	Met exclusion criterion	x	x	x	x	x	x	x	x
	Incorrect version of ICF signed	x	x	x	x	x	x	x	x
	ICF not signed prior to study procedures	x	x	x	x	x	x	x	x
	Required procedure not conducted	x	x	x	x	x	x	N/A	N/A
	Required procedure done incorrectly	x	x	x	x	x	x	N/A	N/A
	Missed visit/visit not conducted	x	x	x	x	x	x	N/A	N/A
	Out of window visit	x	x	x	x	x	x	N/A	N/A
	Other	x	x	x	x	x	x	x	x
Follow-up visit schedule	Any type	x	x	x	x	x	x	N/A	N/A
	Out of window visit	x	x	x	x	x	x	N/A	N/A
	Missed visit/visit not conducted	x	x	x	x	x	x	N/A	N/A
	Other	x	x	x	x	x	x	N/A	N/A
Protocol procedure/assessment	Any type	x	x	x	x	x	x	x	x
	Incorrect version of ICF signed	x	x	x	x	x	x	x	x
	Required procedure not conducted	x	x	x	x	x	x	N/A	N/A
	Required procedure done incorrectly	x	x	x	x	x	x	N/A	N/A
	CMV test result not obtained	x	x	N/A	N/A	N/A	N/A	N/A	N/A
	Other	x	x	x	x	x	x	x	x
[Repeat for Minor Deviations]									
[Repeat for All Deviations]									
N=Number of participants enrolled.									

12.2.2 Displays of Adverse Events

Only those events that are considered "Severe" and "Related" to the DBS collection and finger stick procedure will be reported. See below for definition of "Severe" and "Related".

Table 4: Elicited Adverse Event Grading Scale

Severe	Events interrupt a participant's usual daily activity and require systemic drug therapy or other medically administered treatment.
Related	There is a reasonable possibility that the study product caused the adverse event. Reasonable possibility means that there is evidence to suggest a causal relationship between the study product and the adverse event.

14.1 Description of Study Participants

14.1.1 Disposition of Participants

Table 5: Participant Disposition by Treatment Group

Participant Disposition	DBS (N=X)		SOC (N=X)		All Randomized (N=X)		Observational (N=X)	
	n	%	n	%	n	%	n	%
Screened	x	--	X	--	x	--	x	--
Enrolled/Randomized	x	100	xx	100	x	100	x	100
Completed ≥ 1 Training DBS Collection	x	100	N/A	N/A	N/A	N/A	N/A	N/A
Remained Enrolled at Discharge	x	xx	x	xx	x	xx	N/A	N/A
Remained Enrolled through First Scheduled Clinician-Recommended CMV Monitoring Test	x	xx	x	xx	x	xx	N/A	N/A
Completed ≥ 1 Scheduled Clinician-Recommended CMV Monitoring Test[a]	x	xx	x	xx	x	xx	N/A	N/A
Completed ≥ 1 Self-Collected DBS Sample[b]	x	xx	N/A	N/A	N/A	N/A	N/A	N/A
Completed Study Close-out Visit[c]	x	xx	x	xx	x	xx	x	xx
Early Terminated	x	xx	x	xx	x	xx	N/A	N/A
Did not consent to data collection from medical chart review	x	xx	x	xx	x	xx	N/A	N/A
Consented to data collection from medical chart review	x	xx	x	xx	x	xx	N/A	N/A

N=Number of participants enrolled.
[a] Based on the number of clinician recommended CMV monitoring tests entered on the CMV Chart Review form.
[b] Based on the number of self-collected DBS samples with laboratory results (including unevaluable) entered on the CMV Laboratory Data Upload form.
[c] Refer to the "Early Terminations" listing for reasons participants terminated early.

Table 6: Analysis Populations by Intervention Group

[Implementation Note: The reasons listed here should match the SAP text that describes who will be excluded from analyses.]

Analysis Populations	Reason Participants Excluded	DBS (N=X)		SOC (N=X)		All Randomized (N=X)		Observational (N=X)	
		n	%	n	%	n	%	n	%
Safety	Any Reasons	x	xx	x	xx	x	xx	x	xx
	Not in the randomized cohort	x	xx	x	xx	x	xx	x	xx
	No safety data collected	x	xx	x	xx	x	xx	x	xx
ITT	Not in the randomized cohort	x	xx	x	xx	x	xx	x	xx
mITT	Any Reason	x	xx	x	xx	x	xx	x	xx
	Excluded from ITT	x	xx	x	xx	x	xx	x	xx
	No recommended monitoring schedule available	x	xx	x	xx	x	xx	N/A	N/A
	Withdrew prior to first scheduled clinician recommended CMV monitoring test	x	xx	x	xx	x	xx	N/A	N/A
Completer	Any Reason	x	xx	x	xx	x	xx	x	xx
	Excluded from mITT	x	xx	x	xx	x	xx	x	xx
	Found ineligible at baseline							x	xx
	No recommended monitoring schedule available	x	xx	x	xx	x	xx	x	xx
	Withdrew prior to the study close-out visit	x	xx	x	xx	x	xx	x	xx

N=Number of enrolled participants.
N/A = Not Applicable.

Table 7: Dates of First Enrollment by Site and Intervention Group

[Implementation Note: If the number of sites and/or groups causes this table to be too wide (wider than the page), then break into 2 tables: one by site and one by treatment group, similar to the demographics tables.

Monthly intervals will be used for the enrollment time.]

	Fred Hutchinson Cancer Research Center			Memorial Sloan Kettering Cancer Center			University of Minnesota			MD Anderson Cancer Center			All Sites		
Dates of Enrollment	**DBS (N=X)**	**SOC (N=X)**	**Observational (N=X)**	**DBS (N=X)**	**SOC (N=X)**	**Observational (N=X)**	**DBS (N=X)**	**SOC (N=X)**	**Observational (N=X)**	**DBS (N=X)**	**SOC (N=X)**	**Observational (N=X)**	**DBS (N=X)**	**SOC (N=X)**	**Observational (N=X)**
Total (Entire period of enrollment)															
May 2019	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
June 2019															
…															
N= Number of enrolled participants.															

Table 8: Ineligibility Summary of Screen Failures

Inclusion/Exclusion Category	Inclusion/Exclusion Criterion	n[a]	%[b]
Inclusion and Exclusion	Number of participants failing any eligibility criterion	x	100
Inclusion	Any inclusion criterion	x	xx
	[inclusion criterion 1]	x	xx
	[inclusion criterion 2]	x	xx
	[inclusion criterion 3]	x	xx
Exclusion	Any exclusion criterion	x	xx
	[exclusion criterion 1]	x	xx
	[exclusion criterion 2]	x	xx
	[exclusion criterion 3]	x	xx
Eligible but not enrolled	Any eligible but not enrolled reason	x	xx
	[Eligible but not enrolled reason 1]	x	xx
	[Eligible but not enrolled reason 2]	x	xx
	[Eligible but not enrolled reason 3]	x	xx

[a] More than one criterion may be marked per participant.
[b] Denominator for percentages is the total number of screen failures.

14.1.2 Demographic Data

Table 9: Summary of Categorical Demographic and Baseline Characteristics by Site, All Randomized Participants

Variable	Characteristic	Fred Hutchinson Cancer Research Center (N=X)		Memorial Sloan Kettering Cancer Center (N=X)		University of Minnesota (N=X)		MD Anderson Cancer Center (N=X)		All Sites (N=X)	
		n	%	n	%	n	%	n	%	n	%
Perceived Ease of Access to Blood Draw Facility	Easy										
	Difficult										
Sex	Male	x	xx	x	xx	x	xx	x	xx	x	xx
	Female										
Ethnicity	Not Hispanic or Latino	x	xx	x	xx	x	xx	x	xx	x	xx
	Hispanic or Latino										
	Not Reported										
	Unknown										
Race	American Indian or Alaska Native	x	xx	x	xx	x	xx	x	xx	x	xx
	Asian										
	Native Hawaiian or Other Pacific Islander										
	Black or African American										
	White										
	Multi-Racial										
	Unknown										

N=Number of randomized participants.

Table 10: Summary of Continuous Demographic and Baseline Characteristics by Site, All Randomized Participants

[Implementation note: Days from HCT is calculated as Enrollment Date – HCT Date + 1. Age at enrollment is SDTM age variable, calculated as years on date of enrollment.]

Variable	Statistic	Fred Hutchinson Cancer Research Center (N=X)	Memorial Sloan Kettering Cancer Center (N=X)	University of Minnesota (N=X)	MD Anderson Cancer Center (N=X)	All Sites (N=X)
Days from HCT	Mean	xx	xx	xx	xx	xx
	Standard Deviation	xx	xx	xx	xx	xx
	Median	xx	xx	xx	xx	xx
	Minimum	x	x	x	x	x
	Maximum	x	x	x	x	x
Age (years)	Mean	xx	xx	xx	xx	xx
	Standard Deviation	xx	xx	xx	xx	xx
	Median	xx	xx	xx	xx	xx
	Minimum	x	x	x	x	x
	Maximum	x	x	x	x	x
N=Number of randomized participants.						

Table 11: Summary of Categorical Demographic and Baseline Characteristics by Intervention Group, All Enrolled Participants

Variable	Characteristic	DBS (N=X)		SOC (N=X)		All Randomized (N=X)		Observational (N=X)	
		n	%	n	%	n	%	n	%
Transplant Site	Fred Hutchinson Cancer Research Center								
	Memorial Sloan Kettering Cancer Center								
	University of Minnesota								
	MD Anderson Cancer Center								
Perceived Ease of Access to Blood Draw Facility	Easy							N/A	N/A
	Difficult							N/A	N/A
Sex	Male	x	xx	x	xx	x	xx	x	xx
	Female								
Ethnicity	Not Hispanic or Latino	x	xx	x	xx	x	xx	x	xx
	Hispanic or Latino								
	Not Reported								
	Unknown								
Race	American Indian or Alaska Native	x	xx	x	xx	x	xx	x	xx
	Asian								
	Native Hawaiian or Other Pacific Islander								
	Black or African American								
	White								
	Multi-Racial								
	Unknown								

N=Number of enrolled participants.

Table 12: Summary of Continuous Demographic and Baseline Characteristics by Intervention group, All Enrolled Participants

Variable	Statistic	DBS (N=X)	SOC (N=X)	All Randomized (N=X)	Observational (N=X)
Days from HCT	Mean	xx	xx	xx	xx
	Standard Deviation	xx	xx	xx	xx
	Median	x	x	x	x
	Minimum	x	x	x	x
	Maximum	x	x	x	x
Age (years)	Mean	xx	xx	xx	xx
	Standard Deviation	xx	xx	xx	xx
	Median	x	x	x	x
	Minimum	x	x	x	x
	Maximum	x	x	x	x
N=Number of participants enrolled.					

14.1.3 Prior and Concurrent Medical Conditions

Table 13: Summary of Transplant and Neoplastic Disease Characteristics by Intervention Group

Variable	Characteristic	DBS (N=X)		SOC (N=X)		All Randomized (N=X)		Observational (N=X)	
		n	%	n	%	n	%	n	%
Donor source	Related	x	xx	x	xx	x	xx	x	xx
	Unrelated								
Cell source	Marrow								
	PBSC								
	Cord blood[a]								
Conditioning regimen	Myeloablative								
	Non-myeloablative								
	Reduced intensity								
Underlying Disease	ALL								
	AML								
	CLL								
	CML								
	Aplastic anemia								
	MDS								
	Multiple myeloma								
	NHL								
	Hodgkin's								
	MPD								
	Other								
HLA match	Matched								
	Mismatched								
GVHD at baseline	Present								
	Absent								
GVHD maximal grade	Grade I								
	Grade II								
	Grade III								
	Grade IV								
	Unknown								
GVHD requiring treatment?	Yes[b]								
	No								
GVHD primary site	Gastrointestinal tract								

Variable	Characteristic	DBS (N=X)		SOC (N=X)		All Randomized (N=X)		Observational (N=X)	
		n	%	n	%	n	%	n	%
	Skin								
	Liver								
	Other								
Neoplastic disease status	Complete remission								
	Subsequent remission								
	Partial remission								
	Refractory								
	Relapse								
	Newly diagnosed								
	N/A								
	Other								

N=Number of participants enrolled.
Note: T-cell depletion was not collected in the clinical database. If the data entered indicated the participant did not have HLA mismatch or umbilical cord blood source or GVHD, the site was asked to confirm the participant's eligibility for the trial. Protocol deviations were submitted for participants that did not meet eligibility criteria.
[a] Umbilical cord blood as stem cell source.
[b] Acute or chronic GVHD requiring topical steroid for GI GVHD and/or systemic steroid treatment (> 1mg/kg/day of prednisone or equivalent dose of another corticosteroid) within 14 days prior to enrollment.

14.2 Adherence Data

Table 14: Proportion of Participants Completing >90% Recommended Monitoring Tests During Study Period[a] by 1- Year after HCT, by Intervention Group

Analysis Population	Statistic	DBS	SOC
ITT	Number of participants in analysis population	X	X
	Number of recommended monitoring tests per participant: Median [Min, Max]	xx (xx, xx)	xx (xx, xx)
	Completed >90% recommended monitoring: n	x	x
	Completed >90% recommended monitoring: Proportion [95% CI][a]	xx% (x.x%, x.x%)	xx% (x.x%, x.x%)
	p-value[b]	--	0.xxxx
mITT	Number of participants in analysis population	X	X
	Number of recommended monitoring tests per participant: Median [Min, Max]	xx (xx, xx)	xx (xx, xx)
	Completed >90% recommended monitoring: n	x	x
	Completed >90% recommended monitoring: Proportion [95% CI][a]	xx% (x.x%, x.x%)	xx% (x.x%, x.x%)
	p-value[c]	--	0.xxxx
Completer	Number of participants in analysis population	X	X
	Number of recommended monitoring tests per participant: Median [Min, Max]	xx (xx, xx)	xx (xx, xx)
	Completed >90% recommended monitoring: n	x	x
	Completed >90% recommended monitoring: Proportion [95% CI][a]	xx% (x.x%, x.x%)	xx% (x.x%, x.x%)
	p-value[b]	--	0.xxxx

[a]The study period for all safety analyses is defined as the time from enrollment to End of Follow-up.
[b]95% CI = 95% Wilson Confidence Interval.
[c]p-value from two-sided Wald test for association between intervention group and completion of >90% of recommended monitoring, as modeled from a logistic regression adjusted for transplant site and participants' perceived ease of access to blood draw facility.

Table 15: Sensitivity Analysis with the Maximal Possible Study Period: Proportion of Participants Completing >90% Recommended Monitoring Tests by 1- Year after HCT, by Intervention Group

Analysis Population	Statistic	DBS	SOC
ITT	Number of participants in analysis population	X	X
	Number of recommended monitoring tests per participant: Median [Min, Max]	xx (xx, xx)	xx (xx, xx)
	Completed >90% recommended monitoring: n	x	x
	Completed >90% recommended monitoring: Proportion [95% CI][a]	xx% (x.x%, x.x%)	xx% (x.x%, x.x%)
	p-value[b]	--	0.xxxx
mITT	Number of participants in analysis population	X	X
	Number of recommended monitoring tests per participant: Median [Min, Max]	xx (xx, xx)	xx (xx, xx)
	Completed >90% recommended monitoring: n	x	x
	Completed >90% recommended monitoring: Proportion [95% CI][a]	xx% (x.x%, x.x%)	xx% (x.x%, x.x%)
	p-value[b]	--	0.xxxx

[a] 95% CI = 95% Wilson Confidence Interval
[b] p-value from two-sided Wald test for association between intervention group and completion of >90% of recommended monitoring, as modeled from a logistic regression adjusted for transplant site and participants' perceived ease of access to blood draw facility.

Table 16: Sensitivity Analysis Excluding University of Minnesota Participants: Proportion of Participants Completing >90% Clinician-Recommended Monitoring by 1- Year after HCT, by Intervention Group

Analysis Population	Statistic	DBS	SOC
ITT	Number of participants in analysis population	X	X
	Number of recommended monitoring tests per participant: Median [Min, Max]	xx (xx, xx)	xx (xx, xx)
	Completed >90% recommended monitoring: n	x	x
	Completed >90% recommended monitoring: Proportion [95% CI][b]	xx% (x.x%, x.x%)	xx% (x.x%, x.x%)
	p-value[c]	--	0.xxxx
mITT	Number of participants in analysis population	X	X
	Number of recommended monitoring tests per participant: Median [Min, Max]	xx (xx, xx)	xx (xx, xx)
	Completed >90% recommended monitoring: n	x	x
	Completed >90% recommended monitoring: Proportion [95% CI][b]	xx% (x.x%, x.x%)	xx% (x.x%, x.x%)
	p-value[c]	--	0.xxxx

[a]95% CI = 95% Wilson Confidence Interval
[b]p-value from two-sided Wald test for association between intervention group and completion of >90% of recommended monitoring, as estimated from traditional logistic regression adjusted for transplant site and participants' perceived ease of access to blood draw facility.

Table 17: Number of Clinician-Recommended Monitoring Tests Completed by 1-Year after HCT, by Intervention Group

Analysis Population	Statistic	DBS	SOC
ITT	Number of participants in analysis population	X	X
	Number of recommended monitoring tests by participant, Median [Min, Max]	xx [xx, xx]	xx [xx, xx]
	Number of recommended monitoring tests completed by participant, Median [Min, Max]	xx [xx, xx]	xx [xx, xx]
	Proportion of completed recommended monitoring, Mean [95% CI][a]	xx% (xx.x%, xx.x%)	xx% (xx.x%, xx.x%)
	p-value[b]	--	0.xxxx
mITT	Number of participants in analysis population	X	X
	Number of recommended monitoring tests by participant, Median [Min, Max]	xx [xx, xx]	xx [xx, xx]
	Number of recommended monitoring tests completed by participant, Median [Min, Max]	xx [xx, xx]	xx [xx, xx]
	Proportion of completed recommended monitoring, Mean [95% CI][a]	xx% (xx.x%, xx.x%)	xx% (xx.x%, xx.x%)
	p-value[b]	--	0.xxxx
Completer	Number of participants in analysis population	X	X
	Number of recommended monitoring tests by participant, Median [Min, Max]	xx [xx, xx]	xx [xx, xx]
	Number of recommended monitoring tests completed by participant, Median [Min, Max]	xx [xx, xx]	xx [xx, xx]
	Proportion of completed recommended monitoring, Mean [95% CI][a]	xx% (xx.x%, xx.x%)	xx% (xx.x%, xx.x%)
	p-value[b]	--	0.xxxx

[a]95% CI = Mean ±1.96*se.
[b]p-value from two-sided Wald test for association between intervention group and proportion of recommended monitoring, as estimated from fractional logistic regression adjusted for transplant site and participant's perceived ease of access to blood draw facility.

Table 18: Sensitivity Analysis with the Maximal Possible Study Period: Number of Clinician-Recommended Monitoring Tests Completed by 1-Year after HCT During, by Intervention Group

Analysis Population	Statistic	DBS	SOC
ITT	Number of participants in analysis population	X	X
	Number of recommended monitoring tests by participant, Median [Min, Max]	xx [xx, xx]	xx [xx, xx]
	Number of recommended monitoring tests completed by participant, Median [Min, Max]	xx [xx, xx]	xx [xx, xx]
	Proportion of completed recommended monitoring, Mean [95% CI][a]	xx% (xx.x%, xx.x%)	xx% (xx.x%, xx.x%)
	p-value[b]	--	0.xxxx
mITT	Number of participants in analysis population	X	X
	Number of recommended monitoring tests by participant, Median [Min, Max]	xx [xx, xx]	xx [xx, xx]
	Number of recommended monitoring tests completed by participant, Median [Min, Max]	xx [xx, xx]	xx [xx, xx]
	Proportion of completed recommended monitoring, Mean [95% CI][a]	xx% (xx.x%, xx.x%)	xx% (xx.x%, xx.x%)
	p-value[b]	--	0.xxxx

[a]95% CI = Mean ±1.96*se.
[b]p-value from two-sided Wald test for association between intervention group and proportion of recommended monitoring, as estimated from fractional logistic regression adjusted for transplant site and participant's perceived ease of access to blood draw facility.

Table 19: Sensitivity Analysis Excluding University of Minnesota Participants: Number of Clinician-Recommended Monitoring Tests Completed by 1-Year after HCT, by Intervention Group

Analysis Population	Statistic	DBS	SOC
ITT	Number of participants in analysis population	X	X
	Number of recommended monitoring tests by participant, Median [Min, Max]	xx [xx, xx]	xx [xx, xx]
	Number of recommended monitoring tests completed by participant, Median [Min, Max]	xx [xx, xx]	xx [xx, xx]
	Proportion of completed recommended monitoring, Mean [95% CI][a]	xx% (xx.x%, xx.x%)	xx% (xx.x%, xx.x%)
	p-value[b]	--	0.xxxx
mITT	Number of participants in analysis population	X	X
	Number of recommended monitoring tests by participant, Median [Min, Max]	xx [xx, xx]	xx [xx, xx]
	Number of recommended monitoring tests completed by participant, Median [Min, Max]	xx [xx, xx]	xx [xx, xx]
	Proportion of completed recommended monitoring, Mean [95% CI][a]	xx% (xx.x%, xx.x%)	xx% (xx.x%, xx.x%)
	p-value[b]	--	0.xxxx

[a]95% CI = Mean ±1.96*se.
[b]p-value from two-sided Wald test for association between intervention group and proportion of recommended monitoring, as estimated from fractional logistic regression adjusted for transplant site and participant's perceived ease of access to blood draw facility.

14.3 Safety Data

14.3.1 Displays of Adverse Events

Table 20: Overall Summary of Adverse Events, Safety Population

	DBS (N = xx)		SOC (N = xx)		All Randomized (N = xx)	
Participants[a] with	**n**	**%**	**n**	**%**	**n**	**%**
At least one finger-stick procedure-related, severe (Grade 3) adverse event	x	x	N/A	N/A	N/A	N/A
At least one serious adverse event of special interest[b]	x	x	x	x	x	x
At least one adverse event leading to early termination[c]	x	x	x	x	x	x

N=Number of participants in the Safety Population
[a] Participants are counted once for each category regardless of the number of events.
[b] A listing of Serious Adverse Events of Special Interest is included in the "Listing of Serious Adverse Events of Special Interest".
[c] As reported on the Adverse Event eCRF.

Table 21: Adverse Events Occurring in 5% of Participants in Any Intervention group by MedDRA System Organ Class, Preferred Term, and Intervention Group, Safety Population

[Implementation Note: If neither type of event occurs in at least 5% of participants in any intervention group then keep table but fill each cell with "-" and add the following footnote: "Neither SAESIs nor Finger-Stick Procedure-Related Severe AEs occurred in 5% of participants in any intervention group."]

MedDRA System Organ Class	Preferred Term	DBS (N=X)			SOC (N=X)			All Randomized (N=X)		
		n	%	Events	n	%	Events	n	%	Events
Serious Adverse Events of Special Interest										
All	All	x	x	x	x	x	x	x	x	x
SOC MedDRA1	PT1	x	x	x	x	x	x	x	x	x
Etc.	Etc.	x	x	x	x	x	x	x	x	x
Finger-Stick Procedure-Related Severe AE										
All	All	x	x	x	N/A	N/A	N/A	N/A	N/A	N/A
SOC MedDRA1	PT1	x	x	x	x	x	x	x	x	x
Etc.	Etc.	x	x	x	x	x	x	x	x	x

N=Number of participants in the Safety Population.
n=Number of participants reporting event.
Events=Total frequency of events reported.

14.3.1.1 Adverse Events

Table 22: Number of Participants with CMV Disease Between Discharge and End of Follow-up, by Intervention Group

	DBS (N=X)			SOC (N=X)			All Randomized (N=X)			Observational (N=X)		
	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
Diagnosis Type												
Possible	x	x	(x.x%, x.x%)	x	x	(x.x%, x.x%)	x	x	(x.x%, x.x%)	x	x	(x.x%, x.x%)
Probable	x	x	(x.x%, x.x%)	x	x	(x.x%, x.x%)	x	x	(x.x%, x.x%)	x	x	(x.x%, x.x%)
Proven	x	x	(x.x%, x.x%)	x	x	(x.x%, x.x%)	x	x	(x.x%, x.x%)	x	x	(x.x%, x.x%)
Probable/Proven[a]	x	x	(x.x%, x.x%)	x	x	(x.x%, x.x%)	x	x	(x.x%, x.x%)	x	x	(x.x%, x.x%)
Any Diagnosis	x	x	(x.x%, x.x%)	x	x	(x.x%, x.x%)	x	x	(x.x%, x.x%)	x	x	(x.x%, x.x%)

N=Number of participants enrolled.
n=Number of participants reporting event.
95% CI = Clopper-Pearson Exact 95% Confidence Interval.
[a] Proven/Probable CMV Diagnoses are SAEs of Special Interest.

Table 23: Number of Participants with CMV Disease Between HCT and End of Follow-up, by Intervention Group

	DBS (N=X)			SOC (N=X)			All Randomized (N=X)			Observational[b] (N=X)		
	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
Diagnosis Type												
Possible	x	x	(x.x%, x.x%)	x	x	(x.x%, x.x%)	x	x	(x.x%, x.x%)	x	x	(x.x%, x.x%)
Probable	x	x	(x.x%, x.x%)	x	x	(x.x%, x.x%)	x	x	(x.x%, x.x%)	x	x	(x.x%, x.x%)
Proven	x	x	(x.x%, x.x%)	x	x	(x.x%, x.x%)	x	x	(x.x%, x.x%)	x	x	(x.x%, x.x%)
Probable/Proven[a]	x	x	(x.x%, x.x%)	x	x	(x.x%, x.x%)	x	x	(x.x%, x.x%)	x	x	(x.x%, x.x%)
Any Diagnosis	x	x	(x.x%, x.x%)	x	x	(x.x%, x.x%)	x	x	(x.x%, x.x%)	x	x	(x.x%, x.x%)

N=Number of participants enrolled.
n=Number of participants reporting event.
95% CI = Clopper-Pearson Exact 95% Confidence Interval.
[a] Proven/Probable CMV Diagnoses are SAEs of Special Interest.

Table 24: Finger-Stick Procedure-Related Severe Adverse Events

	DBS (N = xxx)			
	n	**%**	**95% CI**	**Events**
Finger-Stick Procedure-Related Severe Adverse Events	x	x	(x.x%, x.x%)	x

N=Number of participants in the Safety Population
n=Number of participants reporting event.
95% CI = Exact 95% binomial Confidence Interval.
Events=Total frequency of events reported.

14.3.2 Listing of Deaths, Other Serious and Significant Adverse Events

Table 25: Listing of Serious Adverse Events of Special Interest

[Implementation Note: This listing is included in the table shells document, as it is included in the body of the CSR. If the event is ongoing (no stop date), indicate "Ongoing" for the "Duration" column. In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. If "Other" is selected for Primary Site of CMV infection, display "Other: [SPECIFY]" where [SPECIFY] is the response entered in the "If Other, specify" field. Listing should be sorted by Intervention Group, Participant ID, and Date of CMV Disease Diagnosis.]

Intervention Group	Participant ID	Days from Transplantation	Study Day	Duration	Diagnosis Proven or Probable	Primary Site of CMV Infection	Outcome of Disease
[e.g. DBS, SOC]		xxx	xxx		[e.g. Proven, Probable]	[e.g. Central nervous system, Gastrointestinal tract, Respiratory tract, Blood, Other: [SPECIFY]]	[e.g. Recovered/resolved, Recovering/resolving]

Table 26: Listing of Finger-Stick Procedure-Related Severe Adverse Events

[Implementation Note: This listing is included in the table shells document, as it is included in the body of the CSR. If the event is ongoing (no stop date), indicate "ongoing" for the "Duration". In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Listing should be sorted by Intervention Group, Participant ID and Date of Onset.]

Intervention Group	Participant ID	Days from Transplantation	Study Day	Duration	Severity	Relationship to Study Treatment	Did AE Result in Study Discontinuation?	Outcome
DBS		xxx	xxx		Severe	Related	[e.g. No,Yes]	[e.g. Recovered/ resolved, Recovered/ resolved with sequelae, Recovering/resolving, Not recovered/not resolved, Fatal]

Table 27: Listing of Unanticipated Adverse Device Effects

[Implementation Note: This listing is included in the table shells document, as it is included in the body of the CSR. In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Listing should be sorted by Intervention Group, Participant ID , Date of DBS Test, and Date of Non-DBS Test Result.]

Intervention Group	Participant ID	Type of Adverse Device Effect	Quarterly Contact	Study Day of DBS Test	DBS Test Result (IU/mL)	Study Day of Non-DBS Test Result	Non-DBS Test Result
DBS		[e.g. False Positive, False Negative]	[e.g. 1, 2, 3, 4]				xxxx.xxxx [units]

Table 28: Listing of Deaths

Intervention Group	Participant ID	Study Day	Cause of Death
DBS, SOC, Observational			[e.g. CMV infection, Organ failure, Relapse of underlying disease i.e. neoplasm recurrence), Graft-versus-host disease, Other: SPECIFY]

Table 29: Listing of Hospitalizations

Intervention Group	Participant ID	Study Day of Admission	Study Day of Discharge	Reason for Hospitalization
DBS, SOC, Observational				
Hospitalizations in the Observational Intervention Group were recorded only for participants enrolled in version 2.0 of the protocol.				

14.3.3 Narratives of Deaths, Other Serious and Significant Adverse Events

(not included in SAP, but this is a placeholder for the CSR)

14.4 Summary of Concomitant Medications

Table 30: Number and Percentage of Participants with Prior and Concurrent Medications by WHO Drug Classification and Treatment Group

WHO Drug Code Level 1, Anatomic Group	WHO Drug Code Level 2, Therapeutic Subgroup	DBS (N=X)		SOC (N=X)		All Randomized (N=X)		Observational (N=X)	
		n	%	n	%	n	%	n	%
Any Level 1 Codes	Any Level 2 Codes	x	xx	x	xx	x	xx	x	xx
[ATC Level 1 - 1]	Any [ATC 1 – 1]								
	[ATC 2 - 1]								
	[ATC 2 - 2]								
	[ATC 2 - 3]								
[ATC Level 1 – 2]	[ATC 2 - 1]								
	[ATC 2 - 2]								
	[ATC 2 - 3]								

N=Number of participants in the Safety Population
n=Number of participants reporting taking at least one medication in the specific WHO Drug Class.

14.5 Participant and Provider Satisfaction Data

Table 31: Participant Questionnaire, After Third Training

[Implementation Note: Questions with responses on the Likert scale are converted to numeric as described in Section 3.3.12. For each question, the number of participants who selected a response other than "Prefer not to Answer" are summarized in the "Responses, n" row. For Yes/No questions, the number in the "Responses, n" row is the denominator for the "Yes, n (%)" row. The denominator for the rows under "If yes, describe" is the count from the number of participants who responded "Yes" to the previous question.]

Question	Statistic	After Second Training (N=X)
The self-collection teaching videos are helpful and easy to follow.	Responses, n	X
	Mean (SD)	x.x (x.x)
	Median [Min, Max]	x [x, x]
The CMV dried blood spot self-collection is easy.	Responses, n	n=X
	Mean (SD)	x.x (x.x)
	Median [Min, Max]	x [x, x]
After the training sessions, I feel confident collecting my own CMV dried blood spot samples.	Responses, n	n=X
	Mean (SD)	x.x (x.x)
	Median [Min, Max]	x [x, x]
After the training sessions, I feel confident about scheduling USPS pick-up for my sample.	Responses, n	n=X
	Mean (SD)	x.x (x.x)
	Median [Min, Max]	x [x, x]
Do you foresee any problems with collecting dried blood spot samples when you are back at home?	Responses, n	n=X
	Yes, n (%)	xxx (xx%)
If yes, describe:		
Unable to reach caregiver	n (%)	xxx (xx%)
Inadequate supplies	n (%)	xxx (xx%)
Do not feel comfortable performing procedure	n (%)	xxx (xx%)
Technical difficulties	n (%)	xxx (xx%)
N=Number of participants in the DBS arm with questionnaire data available Questions asked on the Likert scale are for agreement (1-Strongly Disagree, 2-Disagree, 3-Neither Agree nor Disagree, 4-Agree, 5-Strongly Agree) or frequency (1-Never, 2- Very Rarely, 3-Rarely, 4-Occasionally. 5-Very Frequently). Answers to questions asked on the Likert scale will be converted to numbers ranging from 1-5, or missing if Prefer Not To Answer was selected.		

Table 32: Composite Scores of Participant Satisfaction, One Month Post-Discharge and After Study Completion

[Implementation note: Composite scoring definitions are provided in Section 12.2. Responses on the Likert scale are converted to numeric as described in Section 3.3.12]

Composite Score	Statistic	One Month Post-Discharge (N=X)	After Study Completion (N=X)
Overall satisfaction with email and mobile technology	Responses, n	X	X
	Mean (SD)	x.x (x.x)	x.x (x.x)
	Median [Min, Max]	x [x, x]	x [x, x]
Overall satisfaction with kit contents, testing and shipping procedures	Responses, n	n=X	n=X
	Mean (SD)	x.x (x.x)	x.x (x.x)
	Median [Min, Max]	x [x, x]	x [x, x]
N=Number of participants in the DBS arm with questionnaire data available Questions asked on the Likert scale are for agreement (1-Strongly Disagree, 2-Disagree, 3-Neither Agree nor Disagree, 4-Agree, 5-Strongly Agree) or frequency (1-Never, 2- Very Rarely, 3-Rarely, 4-Occasionally. 5-Very Frequently). Answers to questions asked on the Likert scale will be converted to numbers ranging from 1-5, or missing if Prefer Not To Answer was selected.			

Table 33: Participant Questionnaire, One Month Post-Discharge

[Implementation Note: Questions with responses on the Likert scale are converted to numeric as described in Section 3.3.12. For each question, the number of participants who selected a response other than "Prefer not to Answer" are summarized in the "Responses, n" row. For Yes/No questions, the number in the "Responses, n" row is the denominator for the "Yes, n (%)" row. The denominator for the rows under "If yes, describe" is the count from the number of participants who responded "Yes" to the previous question.]

Question	Statistic	One Month Post-Discharge (N=X)
The self-collection teaching videos are helpful and easy to follow.	Responses, n	X
	Mean (SD)	x.x (x.x)
	Median [Min, Max]	x [x, x]
The web or mobile phone site is easy to use and provides me with the information I need to do the testing at home.	Responses, n	n=X
	Mean (SD)	x.x (x.x)
	Median [Min, Max]	x [x, x]
The web or mobile phone options give me the choices I want for how and when I receive the reminders.	Responses, n	n=X
	Mean (SD)	x.x (x.x)
	Median [Min, Max]	x [x, x]
The email or mobile phone messages remind me to do the self-collection.	Responses, n	n=X
	Mean (SD)	x.x (x.x)
	Median [Min, Max]	x [x, x]
The self-collection kit had everything I needed to do the testing.	Responses, n	n=X
	Mean (SD)	x.x (x.x)
	Median [Min, Max]	x [x, x]
The CMV dried blood spot self-collection is easy.	Responses, n	n=X
	Mean (SD)	x.x (x.x)
	Median [Min, Max]	x [x, x]
Did you need any help from another person to collect your dried blood spot?	Responses, n	n=X
	Yes, n (%)	xxx (xx%)
Scheduling USPS to pick up my sample is easy.	Responses, n	n=X
	Mean (SD)	x.x (x.x)
	Median [Min, Max]	x [x, x]
Did you have any trouble scheduling USPS mail pick up?	Responses, n	n=X
	Yes, n (%)	xxx (xx%)
If yes, select best response:		
Application failed and could not schedule	n (%)	xxx (xx%)
Difficulty navigating portal to schedule	n (%)	xxx (xx%)
Forgot to schedule pick up	n (%)	xxx (xx%)
Pick up did not occur	n (%)	xxx (xx%)
Pick up occurred but was more than 4 hours after the scheduled time	n (%)	xxx (xx%)

Question	Statistic	One Month Post-Discharge (N=X)
Unable to connect to USPS website	n (%)	xxx (xx%)
Unable to call USPS to schedule the pick-up	n (%)	xxx (xx%)
Did you miss any DBS collections thus far?	Responses, n	n=X
	Yes, n (%)	xxx (xx%)
Reasons for not collecting DBS at any time during the study	Responses, n	n = X
I was too busy to do the self collection	Mean (SD)	x.x (x.x)
	Median [Min, Max]	x [x, x]
I did not feel well enough	Mean (SD)	x.x (x.x)
	Median [Min, Max]	x [x, x]
I forgot or collection reminder failed	Mean (SD)	x.x (x.x)
	Median [Min, Max]	x [x, x]
I was hospitalized or had health complications	Mean (SD)	x.x (x.x)
	Median [Min, Max]	x [x, x]
I was on holiday or vacation	Mean (SD)	x.x (x.x)
	Median [Min, Max]	x [x, x]
I did not have caregiver's help	Mean (SD)	x.x (x.x)
	Median [Min, Max]	x [x, x]
I lost interest in the study	Mean (SD)	x.x (x.x)
	Median [Min, Max]	x [x, x]
What would make the dried blood spot testing work better for you?	Responses, n	n = X
More frequent testing	n (%)	xxx (xx%)
Less frequent testing	n (%)	xxx (xx%)
Clearer written instructions	n (%)	xxx (xx%)
More training sessions with coordinator	n (%)	xxx (xx%)
No changes are needed	n (%)	xxx (xx%)
What would make the videos work better for you?	Responses, n	n = X
Structure or content	n (%)	xxx (xx%)
Shorter length	n (%)	xxx (xx%)
Effective DBS demonstration	n (%)	xxx (xx%)
Pace of instruction	n (%)	xxx (xx%)
No changes are needed	n (%)	xxx (xx%)
What would make the reminders work better for you?	Responses, n	n = X
Phone call reminders	n (%)	xxx (xx%)
Content of the reminder	n (%)	xxx (xx%)
More frequent reminders	n (%)	xxx (xx%)
Flexibility in reminder day	n (%)	xxx (xx%)
No changes are needed	n (%)	xxx (xx%)

Question	Statistic	One Month Post-Discharge (N=X)
What can we improve?	Responses, n	n = X
Training	n (%)	xxx (xx%)
DBS Test kit supplies	n (%)	xxx (xx%)
Data entry	n (%)	xxx (xx%)
DBS testing Reminders	n (%)	xxx (xx%)
No changes are needed	n (%)	xxx (xx%)

N=Number of participants in the DBS arm with questionnaire data available.
Questions asked on the Likert scale are for agreement (1-Strongly Disagree, 2-Disagree, 3-Neither Agree nor Disagree, 4-Agree, 5-Strongly Agree) or frequency (1-Never, 2- Very Rarely, 3-Rarely, 4-Occasionally. 5-Very Frequently). Answers to questions asked on the Likert scale will be converted to numbers ranging from 1-5, or missing if Prefer Not To Answer was selected.

Table 34: Participant Questionnaire, After Study Completion

[Implementation Note: Questions with responses on the Likert scale are converted to numeric as described in Section 3.3.12. For each question, the number of participants who selected a response other than "Prefer not to Answer" are summarized in the "Responses, n" row. For Yes/No questions, the number in the "Responses, n" row is the denominator for the "Yes, n (%)" row. The denominator for the rows under "If yes, describe" is the count from the number of participants who responded "Yes" to the previous question.]

Question	Statistic	After Study Completion (N=X)
[Question on the Likert Scale]	Responses, n	X
	Mean (SD)	x.x (x.x)
	Median [Min, Max]	x [x, x]
What can we improve?	Responses, n	n = X
Training	n (%)	xxx (xx%)
DBS Test kit supplies	n (%)	xxx (xx%)
Data entry	n (%)	xxx (xx%)
DBS testing Reminders	n (%)	xxx (xx%)
No changes are needed	n (%)	xxx (xx%)

N=Number of participants in the DBS arm with questionnaire data available
Questions asked on the Likert scale are for agreement (1-Strongly Disagree, 2-Disagree, 3-Neither Agree nor Disagree, 4-Agree, 5-Strongly Agree) or frequency (1-Never, 2- Very Rarely, 3-Rarely, 4-Occasionally. 5-Very Frequently). Answers to questions asked on the Likert scale will be converted to numbers ranging from 1-5, or missing if Prefer Not To Answer was selected.

Table 35: Provider Questionnaire, After Study Completion

[Implementation Note: Questions with responses on the Likert scale are converted to numeric as described in Section 3.3.12. For each question, the number of participants who selected a response other than "Prefer not to Answer" are summarized in the "Responses, n" row. For Yes/No questions, the number in the "Responses, n" row is the denominator for the "Yes, n (%)" row. The denominator for the rows under "If yes, describe" is the count from the number of participants who responded "Yes" to the previous question.]

Question	Statistic	After Study Completion (N=X)
Overall satisfaction with CMV dried blood spot self-collection results[a]	Responses, n	X
	Mean (SD)	x.x (x.x)
	Median [Min, Max]	x [x, x]
DBS testing will increase adherence to CMV surveillance late after HCT.	Responses, n	X
	Mean (SD)	x.x (x.x)
	Median [Min, Max]	x [x, x]
The results of the finger stick CMV self-collection were available to me in an easy and timely fashion.	Responses, n	n=X
	Mean (SD)	x.x (x.x)
	Median [Min, Max]	x [x, x]
I was confident with the results of the CMV dried blood spot self-collection results	Responses, n	n=X
	Mean (SD)	x.x (x.x)
	Median [Min, Max]	x [x, x]
If I have the results of the CMV self-collection, I do not feel I need an additional plasma blood draw to decide on treatment for my patient	Responses, n	n=X
	Mean (SD)	x.x (x.x)
	Median [Min, Max]	x [x, x]
I would participate in another study with use of this type of blood self-collection	Responses, n	n=X
	Mean (SD)	x.x (x.x)
	Median [Min, Max]	x [x, x]

N=Number of Participants in the DBS arm with questionnaire data available
The primary care providers of each participant should have been sent a provider questionnaire at the time of the participant's last quarterly follow-up records request.
Questions asked on the Likert scale are for agreement (1-Strongly Disagree, 2-Disagree, 3-Neither Agree nor Disagree, 4-Agree, 5-Strongly Agree) or frequency (1-Never, 2- Very Rarely, 3-Rarely, 4-Occasionally. 5-Very Frequently). Answers to questions asked on the Likert scale will be converted to numbers ranging from 1-5, or missing if Prefer Not To Answer was selected.
[a] The composite score is calculated from the Likert scale values.

14.6 Testing and Technology Data

Table 36: Time Between Scheduled Sample Pick-Up and Arrival at Study Laboratory, by Site and Perceived Ease of Access to Blood Draw Facility

Perceived Ease of Access to Blood Draw Facility	Variable	Statistic	Fred Hutchinson Cancer Research Center (N=X)	Memorial Sloan Kettering Cancer Center (N=X)	University of Minnesota (N=X)	MD Anderson Cancer Center (N=X)	All Sites (N=X)
Easy	Samples with shipment time and arrival time entered	n	X	X	X	X	X
	Hours from scheduled pick-up to arrival	Mean (SD)					
		Median [Min, Max]					
Difficult	Samples with shipment time and arrival time entered	Number					
	Hours from scheduled pick-up to arrival	Mean (SD)					
		Median [Min, Max]					
Any Difficulty	Samples with shipment time and arrival time entered	Number					
	Hours from scheduled pick-up to arrival	Mean (SD)					
		Median [Min, Max]					

N= Number of participants with available shipment data.
Specimen shipment information is participant-entered data and may possess inaccurate shipment times or not have been entered for specimens. Any specimens received by the lab lacking shipment information or with a shipment time less than or equal to arrival time are excluded from this analysis.

Table 37: Number of Scheduled DBS Unevaluable Due to Lack of Amplification or Inhibition, by Site

Statistic	Fred Hutchinson Cancer Research Center (N=X)	Memorial Sloan Kettering Cancer Center (N=X)	University of Minnesota (N=X)	MD Anderson Cancer Center (N=X)	All Sites (N=X)
Sample pick-ups scheduled[a], n	XXX	XXX	XXX	XXX	XXX
Samples received, n	XXX	XXX	XXX	XXX	XXX
Number of participants with unevaluable samples, n (%[c])	XXX (xx%)	XXX (xx%)	XXX (xx%)	XXX (xx%)	XXX (xx%)
Number unevaluable samples, n (%[b])	XXX (xx%)	XXX (xx%)	XXX (xx%)	XXX (xx%)	XXX (xx%)

N=Number of participants in the DBS arm in the ITT Population.
[a] Specimen shipment information is participant-entered data and may not have been entered for specimens, resulting in the number of specimens shipped being less than the number of specimens received and entered into the data system by the testing lab.
[b] Relative to number of samples received.
[c]An unevaluable sample is the equivalent of sample viability failure.

Table 38: Concordance between Confirmatory WB and Confirmatory DBS Testing

Statistic	DBS Participants with Concordance Samples (N=X)
Number of positive DBS tests, n	xxx
Number of confirmatory DBS samples received, n	xxx
Number of positive confirmatory DBS tests, n	xxx
Number of confirmatory WB samples received, n	xxx
Number of positive confirmatory WB tests, n (%)	xxx (xx%)
Sensitivity	xx.x
Specificity	xx.x
Positive predictive value	xx.x
Negative predictive value	xx.x
Lin's Concordance Correlation Coefficient[a] between Confirmatory WB and Confirmatory DBS Testing	x.xxx

N= Number of participants in DBS arm with available samples for the Concordance analysis.
Positive predictive value=Number of positive confirmatory whole blood tests / Number of positive DBS tests.
[a] Lin's Correlation between the Confirmatory WB and Confirmatory DBS Testing results (IU/mL).

Table 39: Mechanism of Non-Compliance - Mobile Technology DBS Testing Reminder Failures

Statistic	DBS (N=X)
Failed notifications, n	xxx
Participants with failed notification, n	xxx
Failed notification per participant for those with failed notifications, Median [Min, Max]	xxx [xxx, xxx]
Missed recommended tests, n	xxx
Participants with missed recommended tests, n	xxx
Missed recommended tests, with failed notifications within 7 days, n	xxx
Participants with missed recommended tests, with failed notification within 7 days, n	xxx
Number of Missed recommended tests per participant, Median [Min, Max]	xxx [xxx, xxx]
Number of missed recommended tests with failed notification within 7 days per participant, Median [Min, Max]	xxx [xxx, xxx]
N=Number of participants in the DBS arm in the ITT population.	

Table 40: Mechanism of Non-Compliance to DBS Collection- Sample Failures

Statistic	DBS (N=X)
Missed recommended tests, n	xxx
Participants with missed recommended tests, n	xxx
Missed recommended tests, with failed sample collection, n	xxx
Participants with missed recommended tests, with failed sample collection, n	xxx
Missed recommended tests, with failed sample delivery, n	xxx
Participants with missed recommended tests, with failed sample delivery, n	xxx
Unevaluable samples, n	xxx
Participants with unevaluable samples, n	xxx

Note: N=Number of participants in the DBS arm in the ITT population.
[a]An unevaluable sample is the equivalent of sample viability failure.

14.6 Local Provider Care Data

Table 41: Primary Care Physician Viral Load Treatment Thresholds, by Intervention Group, Transplant Site and Perceived Ease of Access to Blood Draw Facility

Variable Category	DBS (N=X)		SOC (N=X)		All Randomized (N=X)	
	Num. Treated Part.	Treatment Threshold (IU/mL)	Num. Treated Part.	Treatment Threshold (IU/mL)	Num. Treated Part.	Treatment Threshold (IU/mL)
	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)
Transplant Site						
Fred Hutchinson Cancer Research Center	xxx	xx.x (xx.x)	xxx	xx.x (xx.x)	xxx	xx.x (xx.x)
Memorial Sloan Kettering Cancer Center	xxx	xx.x (xx.x)	xxx	xx.x (xx.x)	xxx	xx.x (xx.x)
University of Minnesota	xxx	xx.x (xx.x)	xxx	xx.x (xx.x)	xxx	xx.x (xx.x)
MD Anderson Cancer Center	xxx	xx.x (xx.x)	xxx	xx.x (xx.x)	xxx	xx.x (xx.x)
Perceived Ease of Access to Blood Draw Facility						
Easy	xxx	xx.x (xx.x)	xxx	xx.x (xx.x)	xxx	xx.x (xx.x)
Difficult	xxx	xx.x (xx.x)	xxx	xx.x (xx.x)	xxx	xx.x (xx.x)
Overall	xxx	xx.x (xx.x)	xxx	xx.x (xx.x)	xxx	xx.x (xx.x)

N=Number of participants in the Safety Population

Table 42: Least-Frequent Clinician-Recommended Monitoring Interval Categories by 90 Days Post-HCT, by Intervention Group and Stratification Variables

[Implementation note: Within each variable and category, the percentages should be row percentages within each intervention group.]

Treatment Arm	Least-Frequent Clinician-Recommended Monitoring Interval	Transplant Site								Perceived Ease of Access to Blood Draw Facility (Excluding University of Minnesota[a])					
		Fred Hutchinson Cancer Research Center		Memorial Sloan Kettering Cancer Center		University of Minnesota[a]		MD Anderson Cancer Center		Easy		Difficult		Overall	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%
DBS (N = X)	No Further Monitoring Required	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x
	Weekly	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x
	Bi-Weekly	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x
	Monthly	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x
	Quarterly	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x
SOC (N = X)	No Further Monitoring Required	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x
	Weekly	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x
	Bi-Weekly	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x
	Monthly	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x
	Quarterly	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x
All Randomized (N = X)	No Further Monitoring Required	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x
	Weekly	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x

Treatment Arm	Least-Frequent Clinician-Recommended Monitoring Interval	Transplant Site								Perceived Ease of Access to Blood Draw Facility (Excluding University of Minnesota[a])					
		Fred Hutchinson Cancer Research Center		Memorial Sloan Kettering Cancer Center		University of Minnesota[a]		MD Anderson Cancer Center		Easy		Difficult		Overall	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Bi-Weekly	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x
	Monthly	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x
	Quarterly	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x	xxx	xx.x

N=Number of participants in the ITT Population with recommended in-office CMV monitoring intervals recorded.
n = Number of participants with results reported for the clinician-recommended CMV monitoring intervals, excluding monitoring intervals of "Other".
[a]The University of Minnesota entered the actual number of clinician-recommended CMV monitoring tests instead of the expected number of clinician-recommended CMV monitoring tests.

Tables with similar format:

Table 43: Least Frequent Clinician-Recommended Interval Categories by 180 Days Post-HCT, by Intervention Group and Stratification Variables

Table 44: Least Frequent Clinician-Recommended Interval Categories by 270 Days Post HCT, by Intervention Group and Stratification Variables

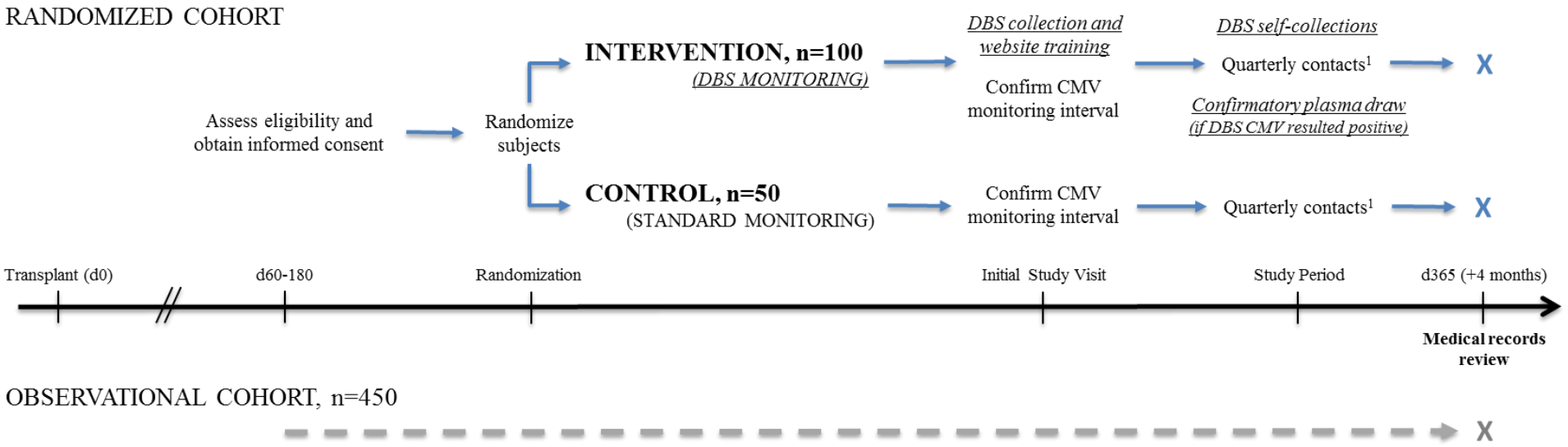
Table 45: Least Frequent Clinician-Recommended Interval Categories by 365 Days Post-HCT, by Intervention Group and Stratification Variables

APPENDIX 2. FIGURE MOCK-UPS

LIST OF FIGURES

9.1 Overall Study Design and Plan Description

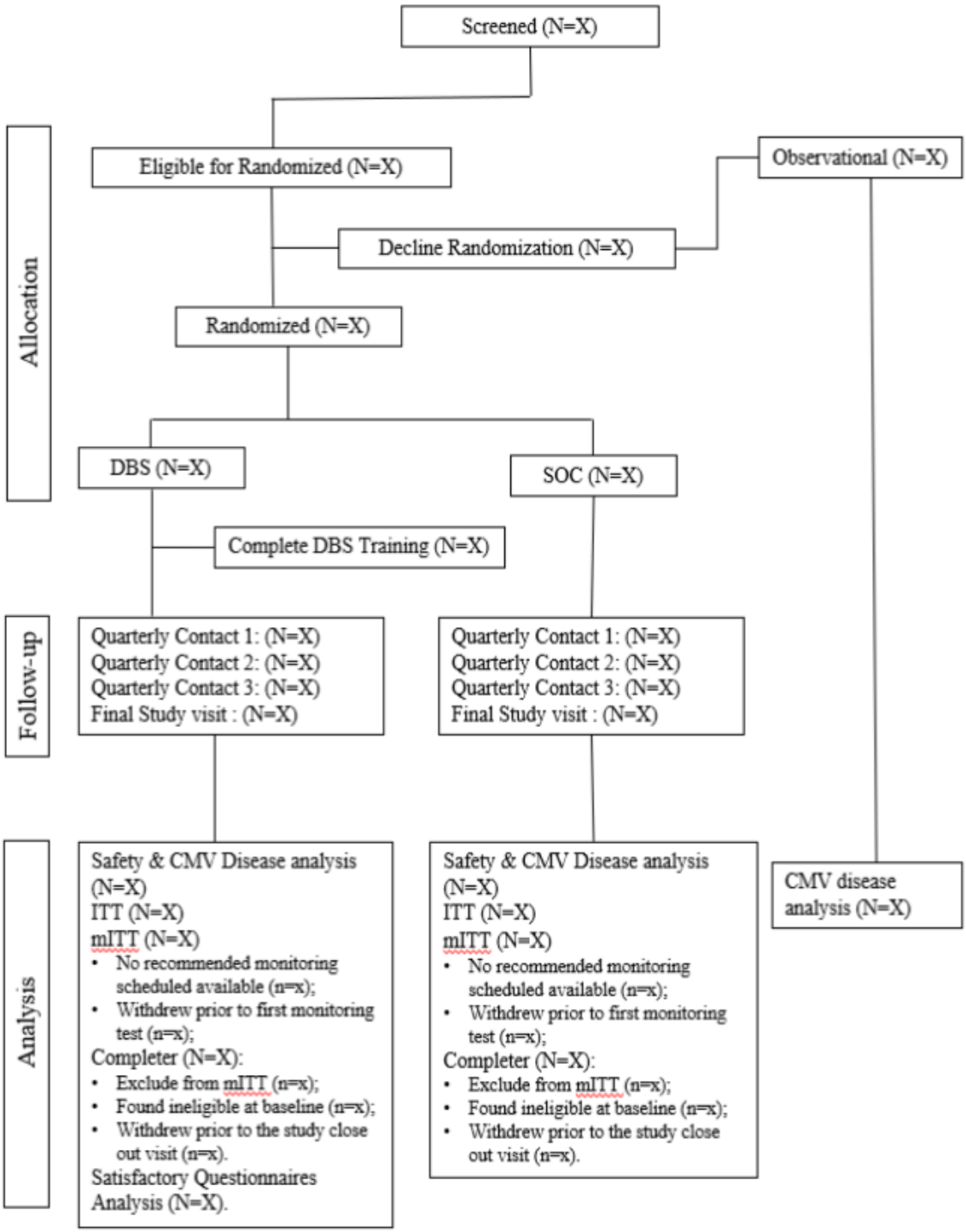
Figure 1: Study Schedule



[1] Quarterly contacts will be scheduled from the date of transplant, not based on the date of enrollment.

10.1 Disposition of Participants

Figure 2: CONSORT Flow Diagram



14.3.1.1 Solicited Adverse Events

Figure 3: Cumulative Incidence of CMV Disease in All Randomized Participants, by Intervention Group

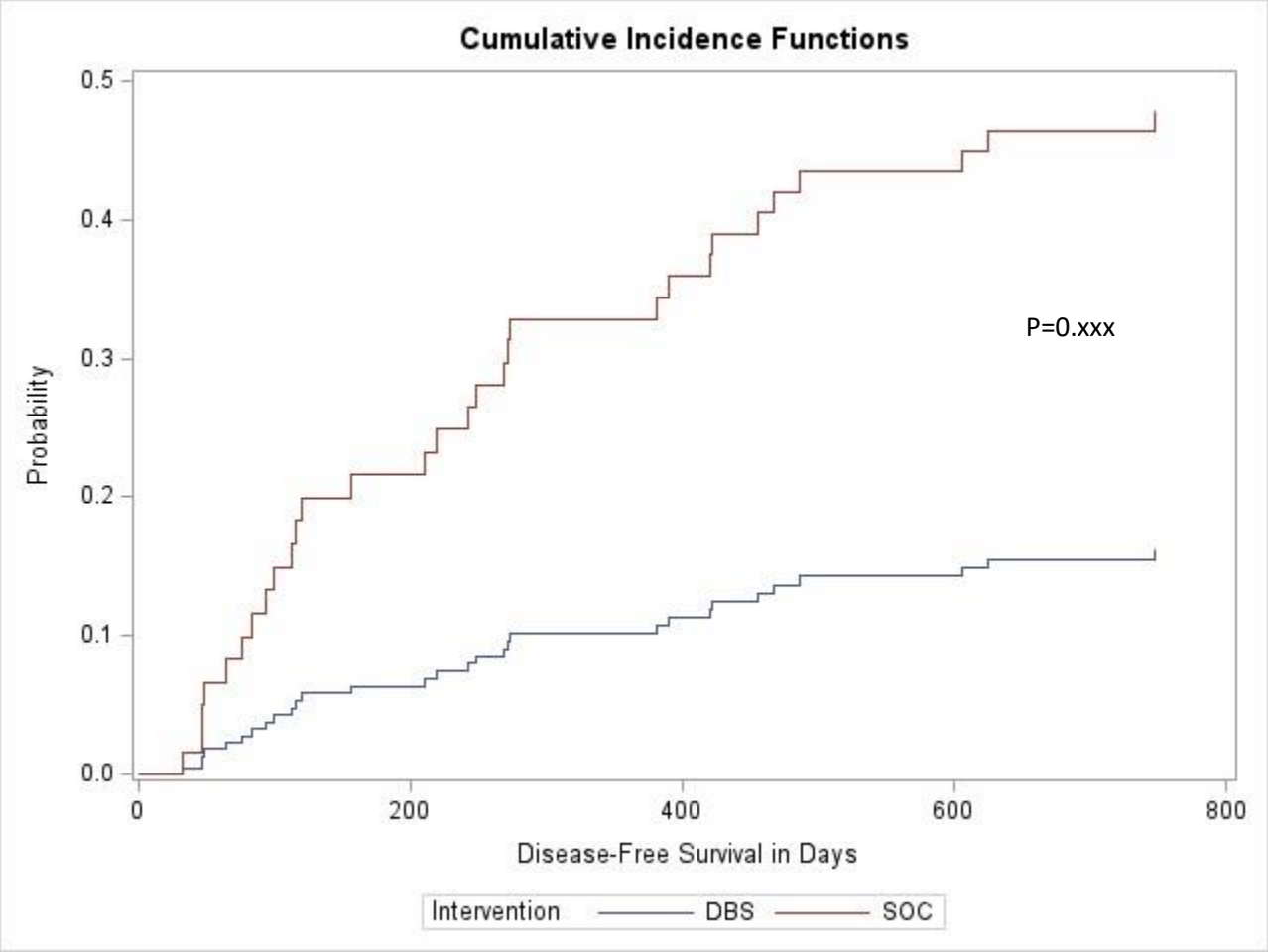
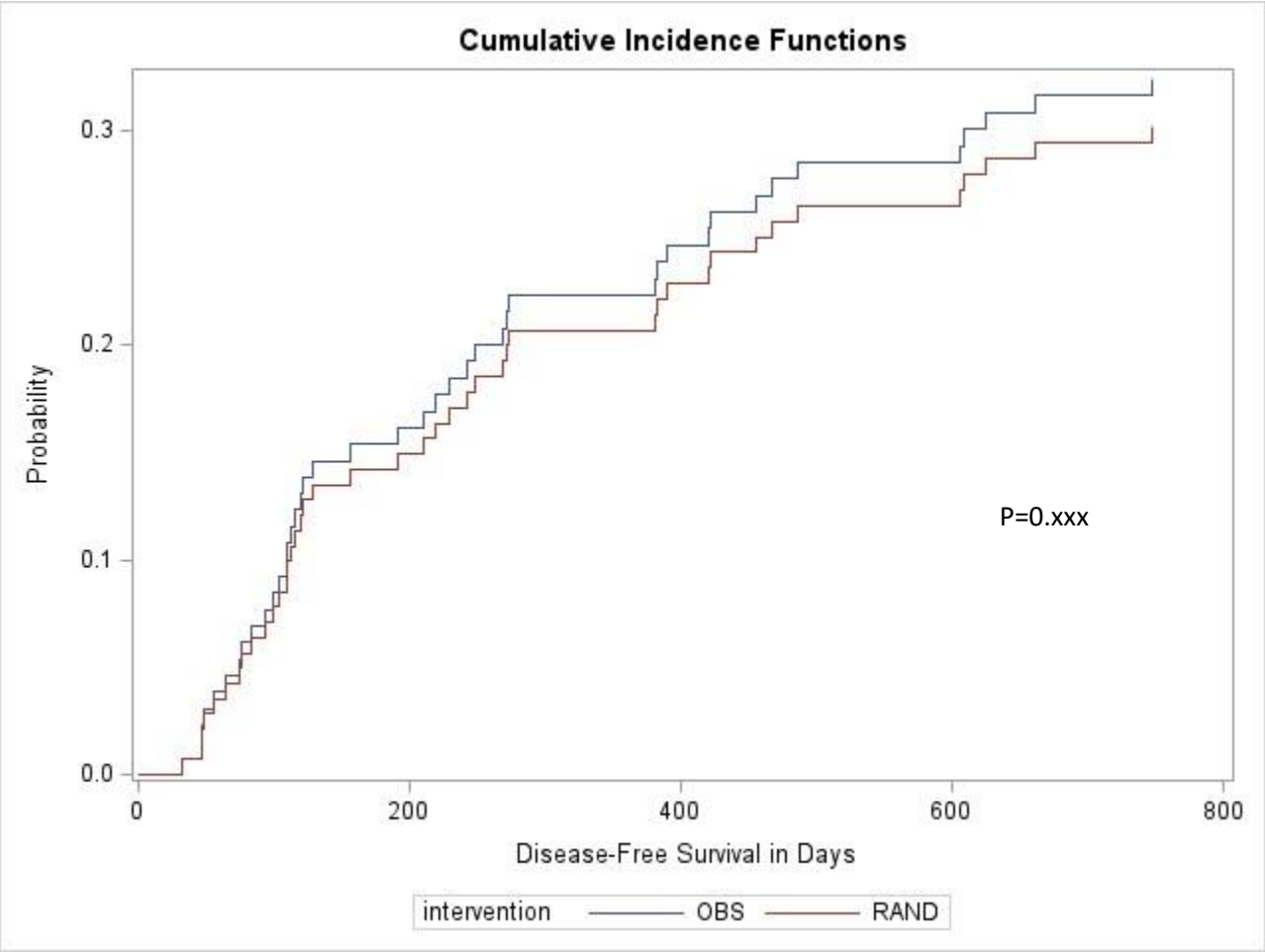


Figure 4: Cumulative Incidence of CMV Disease in All Enrolled Participants, by Intervention Group



14.6 Testing and Technology Data

Figure 5: Association Between Confirmatory Whole Blood Test Results and Confirmatory DBS Test Results

[Implementation note: 1. plot the scatter plot, add Lin's Concordance correlation coefficient instead of R^2.

2. the x-axis should be "Confirmatory DBS Result (IU/mL)"

3. the data will be plot in log10 scale]

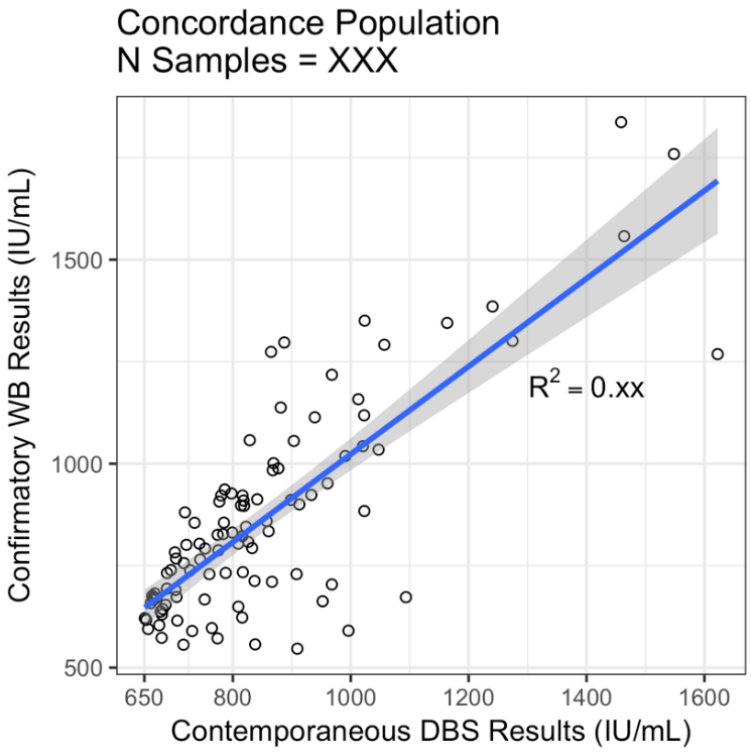
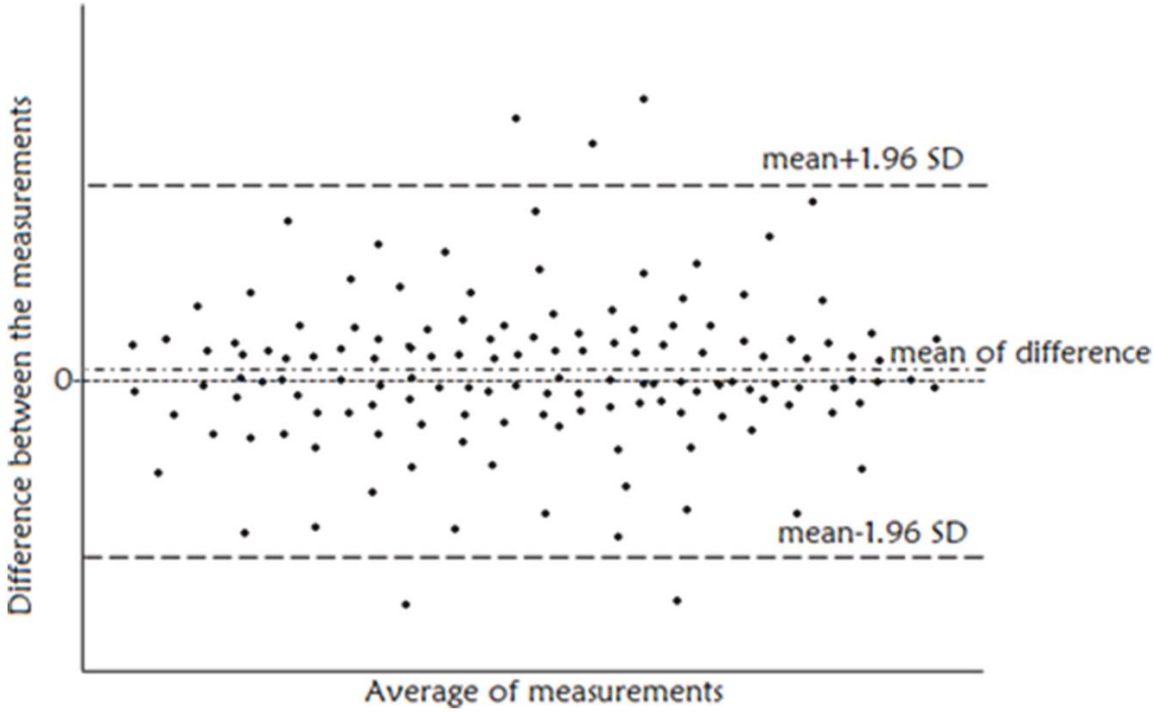


Figure 6: Differences Between Confirmatory Whole Blood Test Results and Confirmatory DBS Test Results

[Implementation note: 1. Bland-Altman plot of differences if plotted here

1. The x-axis should be "Average of the test results (IU/mL)"
2. The data will be plot in log10 scale]



APPENDIX 3. LISTINGS MOCK-UPS

LISTINGS

16.1.6 Listing of Participants Receiving Investigational Product

(not included in SAP, but this is a placeholder for the CSR)

16.2 Database Listings by Participant

16.2.1 Discontinued Participants

Listing 1: 16.2.1 Early Terminations

[Implementation Note: In the "Reason" column, concatenate any "specify" fields, including AE number and DV number. In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Intervention Group, Participant ID.]

Intervention group	Participant ID	Reason for Early Termination	Study Day	Consent to Data Collection from Medical Records?
[e.g. DBS, SOC, Observational]				Yes/No

16.2.2 Protocol Deviations

Listing 2: 16.2.2.1: Participant-Specific Protocol Deviations

[Implementation Note: Deviations will be classified as either major or minor by the Sponsor. In the "Deviation" column, concatenate any and all "specify" fields (including visit number, etc.). If "Reason for Deviation" is "Other," concatenate "specify" field, separate by a colon, e.g., "Other: Participant refusal." If Intervention group is SOC or Observational, then the "Deviation Affected Kit Stability" column has "N/A". In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Intervention group, Participant ID, DV Number.]

Study Group	Participant ID	DV Number	Deviation	Deviation Category	Study Day	Reason for Deviation	Deviation Resulted in AE?	Deviation Resulted in Participant Termination?	Deviation Affected Kit Stability?	Deviation Classification	Deviation Resolution	Comments
[e.g. DBS, SOC, Observational]												

Listing 3: 16.2.2.2: Non-Participant-Specific Protocol Deviations

[Implementation Note: In the "Deviation" column, concatenate any and all "specify" fields (including visit number, etc.). If "Reason for Deviation" is "Other," concatenate "specify" field, separate by a colon, e.g., "Other: Subject refusal." Sort order: Site, Start Date.]

Site	Start Date	Deviation	End Date	Reason for Deviation	Deviation Resulted in Participant Termination?	Deviation Affected Kit Stability?	Deviation Category	Deviation Classification	Deviation Resolution	Comments

16.2.3 Participants and Samples Excluded from the Analysis Populations

Listing 4: 16.2.3.1: Participants Excluded from Analysis Populations

[Implementation Note: This data in this listing should be congruent with the "Participant Analysis Populations by Intervention Group" table. The reasons included here should match the SAP text that describes who will be excluded from analyses. In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Intervention Group, Participant ID.]

Intervention Group	Participant ID	Analyses in which Participant is Included	Analyses from which Participant is Excluded	Results Available?	Reason Participant Excluded
[e.g. DBS, SOC]		[e.g., Safety, ITT, mITT,completer]	[e.g., Safety, ITT, mITT, completer, Day x]		
"Yes" in the "Results available" column indicates that available data were removed from the analysis. "No" indicates that no data were available for inclusion in the analysis.					

16.2.4 Demographic Data

Listing 5: 16.2.4 Demographic Data

[Implementation Note: If a participant is multi-racial, in "Race" column, note "Multiple: (list races, separated by a comma)."

In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification.] Sort order: Intervention Group, Participant ID.]

Intervention Group	Participant ID	Sex	Age at Enrollment (years)	Ethnicity	Race

16.2.5 Transplant, CMV Disease and Graft-Versus Host Disease Data

Listing 6: 16.2.5.1Transplant Information

[Implementation Note: In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Intervention Group, Participant ID.]

Intervention Group	Participant ID	Donor Source	Cell Source	Conditioning Regimen	HLA match	Neoplastic Disease Status	Study Day Most Recent Chemotherapy
[e.g. DBS, SOC, Observational]		[e.g. Related, Unrelated]	[e.g. Marrow, PBSC, Cord blood]	[e.g. Myeloablative, Non-myeloablative, Reduced intensity]	[e.g. Matched, Mismatched]	[e.g. Complete remission, Subsequent remission, Partial remission, Refractory, Relapse, Newly Diagnosed, Other: [SPECIFY]]	

Listing 7: 16.2.5.2: Graft-Versus Host Disease

[Implementation Note: In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Listing should be sorted by Intervention Group, Participant ID, Visit, Disease Site, Category, and Date of Onset. At each visit, if record is for the primary site of the GVHD, then Disease Site Category is "Primary". Disease Site Category is "Secondary" for all additional instance of GVHD at additional sites reported for the visit. If "Other" cause of death indicated, include in CSR as "Other: [Cause Specified]" where Cause Specified is the information entered in the "If Other, specify" field.]

Intervention Group	Participant ID	Visit	Disease Site Category	Study Day of Onset	Days from Transplantation	Disease Site	Maximum Grade
DBS		[e.g. Enrollment, Week 13, Week 26, Week 39, Week 52]	[e.g. Primary, Secondary]		xxx	[e.g. Gastrointestinal tract, Skin, Liver, Other: [SPECIFY]]	[e.g. Grade I, Grade II, Grade III, Grade IV, Unknown]

Listing 8: 16.2.5.3: CMV Disease Information

[Implementation Note: In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Listing should be sorted by Intervention Group, Participant ID and Date of Diagnosis. If Outcome is "Recovering/resolving" then put "Recovering/Resolving" in the "Date of Resolution" column, otherwise put the date of resolution if outcome is "Recovered/Resolved". If participant is not receiving pre-emptive therapy for CMV disease, then enter "-" in the "Viral Load at Initiation of Pre-Emptive Therapy (IU/mL)" and "Date of Viral Load Measurement" columns.]

Intervention Group	Participant ID	Recipient CMV Status	Donor CMV Status	Study Day of Diagnosis	Proof Category	Site of Primary CMV Infection	Study Day of Resolution	Receiving Pre-Emptive Therapy	Viral Load at Initiation of Pre-Emptive Therapy (IU/mL)	Date of Viral Load Measurement
[e.g. DBS, SOC, Observational]		[e.g. Negative, Positive, Unknown]	[e.g. Negative, Positive, Unknown]		[e.g. Proven, Probable, Possible]	[e.g. Central nervous system, Gastrointestinal tract, Respiratory tract, Blood, Other: [SPECIFY]]	[e.g. 3, Recovering/Resolving]	[e.g. Yes, No]	[e.g. xxx, -]	[e.g. DDMMMYYYY, -]

16.2.6 Individual CMV Monitoring Data

Listing 9: 16.2.6.1 Individual CMV Monitoring Data

[Implementation Note: In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Hour in date-time fields will be from the 24-hour clock. Listing should be sorted by Intervention Group, Participant ID, Collection or Test Date, and Sample Type. The order of Sample Type is DBS, Confirmatory DBS, and Confirmatory WB. Results in copy/mL will be converted to IU/mL at a rate of 4 copies per 1 IU. (Ref: https://depts.washington.edu/labweb/referencelab/clinical/TestForms/CMV_IU-ml_Conversion.pdf).

Test Result Source is "Central Laboratory Data Upload" if the result is from a sample sent to the central laboratory and entered on the Central Data Upload form. If the result was abstracted through medical chart review and entered on the CMV form, then Test Result Source is "Chart Review".]

Intervention Group	Participant ID	Study Day of Collection or Test[a]	Study Day	Test Result Source	Days from Scheduled Pick-Up to Arrival at Study Laboratory	Sample Type	Result (IU/mL)	Result Within Limits of Detection?
[e.g. DBS, SOC]			xxx	[e.g. Central Laboratory Data Upload, Chart Review]	[e.g. xx.x, NA (if Test Result Source is Chart Review]	[e.g. DBS, Confirmatory WB, Confirmatory DBS, Plasma, Serum, Whole blood]	[e.g. xx.x, Unevaluable]	[e.g. Yes, No, Above Standard Curve, Less than 1 copy/mL, NA (if unevaluable)]
[a]Collection or test date contains the collection date if the sample was collected using a study-provided kit and sent to the study laboratory for testing (DBS, Confirmatory WB, Confirmatory DBS). If the sample was collected as part of a participant's clinical care and the test results were obtained by medical chart review, then the column contains the test date								

.

Listing 10: 16.2.7 DBS Testing Reminder Listing

[Implementation Note: In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. The listing should be sorted by Participant ID and Sequence Number.]

Participant ID	Enrollment (Study Day)	Expected Date of Notification	Sequence Number	Preferred Notification Method	Reminder Time	Reminder Sent?
			[e.g. 001, 002, etc.]	[e.g. Email, Text message, Both email and text message]	Day HH:MM AM/PM	Yes/No

Listing 11: 16.2.8 Listing of Shipment Information

[Implementation Note: In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. The listing should be sorted by Participant ID and Sequence Number.]

Participant ID	Enrollment (Study Day)	Sequence Number	Kit Number	Sample Type	Study Day of Collection	Study Day of Scheduled Pick-Up	Study Day of Sample Received
		[e.g. 001, 002, etc.]		[e.g. DBS, WB]			
Study Day of Collection and Scheduled Pick-Up are participant-entered data. Study Day of Sample Received is entered by the study laboratory.							

Listing 12: 16.2.9 Listing of Sample Collection Kit Problems

[Implementation Note: In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. The listing should be sorted by Participant ID and Sequence Number.]

Participant ID	Enrollment (Study Day)	Kit Number	Sample Type	Study Day of Problem Reported	Description of Problem	Was Kit Used by Participant?
	XXX		[e.g. DBS, WB]	XXX	Description of problem	Yes, No

16.3.1 Physician Recommended Monitoring Interval Data

Listing 13: 16.3.1 Primary Physician Recommended CMV Monitoring Intervals

[Implementation Note: In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Listing should be sorted by Intervention Group, Participant ID, Visit and Date CMV Monitoring Interval Defined. If "Other" is specified for the recommended monitoring interval, then display "Other: [SPECIFY]" where [SPECIFY] is the text entered in the "If Other, specify:" field.]

Intervention Group	Participant ID	Transplant (Study Day)	Enrollment (Study Day)	Visit (Study Day)	CMV Monitoring Interval Defined (Study Day)	Recommended Monitoring Interval
[e.g. DBS, SOC]		XXX	XXX	XXX	XXX	[e.g. Weekly, Biweekly, Monthly, Quarterly, Other:[SPECIFY]]

16.4.1 Concomitant Medications

Listing 14: 16.2.9 Concomitant Medications

[Implementation Note: "Medication Start Day" and "Medication End Day" are relative to enrollment (which is Day 1, day before enrollment is Day -1).

If ongoing, display "Ongoing" in the "Medication End Day" column. In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Intervention group, Participant ID, and CM Number.]

Intervention group	Participant ID	CM Number	Medication	Medication Start Day	Medication End Day	Indication	ATC Level 1 (ATC Level 2)
[e.g. DBS, SOC, Observational]		xxx		xxx	xxx		

16.5.1 Questionnaire Data

Listing 15: 16.5.1 Participant Questionnaire After Training

[Implementation Note: In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Question (in the order of the questionnaire), Participant ID.

Response will be formatted value of the questionnaire question. For questions where participants are asked to describe their result, format as "Yes: [REASON]".]

Question	Participant ID	Study Day	Response
			[e.g. Strongly Disagree, Disagree, etc.]

Listing 16: 16.5.2 Participant Questionnaire 1-Month Post Discharge

[Implementation Note: In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Question (in the order of the questionnaire), Participant ID.

Response will be formatted value of the questionnaire question. For questions where participants are asked to describe their result, format as "Yes: [REASON]".]

Question	Participant ID	Study Day	Response
			[e.g. Strongly Disagree, Disagree, etc.]

Listing 17: 16.5.3 Participant Questionnaire After Study Completion

[Implementation Note: In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Question (in the order of the questionnaire), Participant ID.

Question	Participant ID	Study Day	Response
			[e.g. Strongly Disagree, Disagree, etc.]

Listing 18: 16.5.4 Provider End-of-Study Questionnaire

[Implementation Note: In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Question (in the order of the questionnaire), Participant ID.

Question	Participant ID	Study Day	Response
			[e.g. Strongly Disagree, Disagree, etc.]

APPENDIX 4. WORKED EXAMPLES OF NUMBER OF EXPECTED TESTS

For a given participant, the number of expected tests is derived based on the start dates of the intervals as follows:

Notation:

1. Let $t_{i,0}$ denote the date of discharge for participant i
2. Let $c_i \in \{0,1, \dots\}$ denote the number of times participant i's recommended monitoring interval was changed by their primary care physician during the study period, defined for each participant as the time from enrollment to the earlier of Protocol Completion and Early Termination.
3. Let $t_{i,1}, \dots, t_{i,c_i}$ denote the times at which the recommended monitoring interval was changed for participant i. $t_{i,1}$ is the end date of the initial interval for participant i.
4. Let t_{i,c_i+1} denote the end of the monitoring period for participant i. This is the earlier of the end of the study period or the date after which recommended monitoring is no longer required.
5. Let $d_{i,1}, \dots, d_{i,c_i}$ denote the corresponding number of days between recommended monitoring tests when the recommended frequency is changed at times $t_{i,1}, \dots, t_{i,c_i}$. The days $d_{i,j}$ take the value 7 if recommended frequency is weekly, 14 if the frequency is bi-weekly, 30 if the frequency is monthly and 90 if the frequency is quarterly, 3.5 if the frequency is twice a week, and 17.5 if the frequency is every 2-3 weeks. The initial recommended monitoring frequency should be weekly so the number of days between tests, $d_{i,o}$, should be 7.
6. Let $I_{i,j}$ denote the recommended monitoring interval for the j^{th} change to the recommended frequency for participant i. The recommended monitoring interval(s) for participant i are therefore

$$I_{i,0} = [t_{i,0}, t_{i,1}], I_{i,1} = (t_{i,1}, t_{i,2}], \dots, I_{i,c_i} = (t_{i,c_i}, t_{i,c_i+1}]$$

The number of expected tests in the first interval is calculated as follows. It is assumed that the first expected test is $d_{i,o}$ days after $t_{i,0}$. Let $n_{i,0}$ denote the number of expected tests during $I_{i,0}$. Then,

$n_{i,0} = floor\left(\frac{t_{i,1} - t_{i,0}+1}{d_{i,0}}\right)$.

Let $m_{i,0}$ denote the date of the last expected recommended monitoring test for participant i during interval I_{i0}. Then,

$m_{i,0} = t_{i,0} + d_{i,0}n_{i,0}$.

There are two possibilities for changes in the monitoring frequency:

1. Frequency in interval $I_{i,j}$ is less frequent than in $I_{i,j-1}$, i.e. $d_{i,j} > d_{i,j-1}$

If the frequency in interval $I_{i,j}$ is less frequent than in $I_{i,j-1}$, i.e. $d_{i,j} > d_{i,j-1}$, then the first test in interval $I_{i,j}$ should occur $d_{i,j}$ days after the last expected test in interval $I_{i,j-1}$. The number of expected tests in interval $I_{i,j}$ is calculated from the last expected test in interval $I_{i,j-1}$:

$$n_{i,j} = floor\left(\frac{t_{i,j+1} - m_{i,j-1}}{d_{i,j}}\right), \text{ and}$$

$$m_{i,j} = m_{i,j-1} + d_{i,j}n_{i,j}.$$

2. Frequency in interval $I_{i,j}$ is more frequent than in j-1, i.e. $d_{i,j} < d_{i,j-1}$

If the frequency in interval $I_{i,j}$ is more frequent than in $I_{i,j-1}$, i.e. $d_{i,j} < d_{i,j-1}$, then the number of expected tests will be calculated from the date that the recommended interval was changed.

The number of expected tests in interval $I_{i,j}$ is

$$n_{i,j} = floor\left(\frac{t_{i,j+1} - t_{i,j}}{d_{i,j}}\right),$$

and the last expected test during the interval is

$$m_{i,j} = t_{i,j} + d_{i,j}n_{i,j}.$$

The number of expected tests during the study period for participant i, N_i, is therefore the sum of the number of expected tests during each monitoring interval, i.e.

$$N_i = \sum_{j=0}^{c_i} n_{i,j}.$$

Example 1

Participant A has their HCT on March 1, 2020 and is discharged on May 1, 2020 ($t_{A,0}$). Their primary care physician would like them to continue CMV monitoring until 365 days post-HCT. Their recommended monitoring interval does not change during the study, i.e. c_A = 0. Their end of study date is $t_{A,1}$ = March 1, 2020 + 365 = March 1, 2021.

Their recommended monitoring interval is $I_{A,0} = [t_{A,0}, t_{A,1}]$ = [May 1, 2020, March 1, 2021]. The number of days between recommended monitoring tests is $d_{A,0} = 7$ in interval $I_{A,0}$.

The number of recommended tests in interval $I_{A,0}$, $n_{A,0}$, is

$$N_A = n_{A,0} = floor\left(\frac{March\ 1,2021 - \text{May } 1,2020 + 1}{d_{A,0}}\right)$$

$$= floor\left(\frac{305}{7}\right)$$

= 43

Example 2

Participant B has their HCT on March 1, 2020 and is discharged on May 1, 2020 ($t_{B,0}$). Their primary care physician would like them to continue CMV monitoring until 365 days post-HCT but recommends that they perform bi-weekly testing on $t_{B,1}$ = November 1, 2020. For participant B, the number of times

that their recommended monitoring interval is changed is c_B = 1. Their end of study date is $t_{B,2}$ = March 1, 2020 + 365 = March 1, 2021.

Their recommended monitoring intervals are

$I_{B,0} = [t_{B,0}, t_{B,1}]$ = [May 1, 2020, November 1, 2020] and

$I_{B,1} = (t_{B,1}, t_{B,2}]$ = (November 1, 2020, March 1, 2021].

The number of days between recommended monitoring tests is $d_{B,0} = 7$ in interval $I_{B,0}$ and $d_{B,1} = 14$ in interval $I_{B,1}$.

The number of recommended tests in interval $I_{B,0}$, $n_{B,0}$, is

$$n_{B,0} = floor\left(\frac{November\ 1,\ 2020 - \text{May } 1,2020+1}{d_{B,0}}\right)$$

$$= floor\left(\frac{185}{7}\right)$$

= 26

The last recommended test during interval $I_{B,0}$ occurs on

$m_{B,0} = May\ 1, 2020 + 7 * 26 =$ October 30, 2020.

The number of recommended tests in interval $I_{B,1}$, $n_{B,1}$, is

$$n_{B,1} = floor\left(\frac{\text{March } 1,2021 - \text{October } 30,2020}{d_{B,1}}\right)$$

$$= floor\left(\frac{120}{14}\right)$$

= 8

Therefore, the number of expected tests during the study period for participant B is

$N_B = \sum_{j=0}^{1} n_{B,j}$ = 26 + 8 = 34.

Example 3

Participant C has their HCT on March 1, 2020 and is discharged on May 1, 2020 ($t_{C,0}$). Their primary care physician would like them to continue CMV monitoring until 365 days post-HCT however recommends that they perform bi-weekly testing on $t_{C,1}$ = November 1, 2020. Their physician recommends that they resume weekly testing for the remainder of the study period on January 20, 2021. For participant C, the number of times that their recommended monitoring interval is changed is c_C = 2. Their end of study date is $t_{C,3}$ = March 1, 2020 + 365 = March 1, 2021.

Their recommended monitoring intervals are

$I_{C,0} = [t_{C,0}, t_{C,1}]$ = [May 1, 2020, November 1, 2020] and

$I_{C,1} = (t_{C,1}, t_{C,2}]$ = (November 1, 2020, January 20, 2021], and

$I_{C,2} = (t_{C,2}, t_{C,3}]$ = (January 20, 2021, March 1, 2021].

The number of days between recommended monitoring tests is $d_{C,0} = 7$ in interval $I_{C,0}$, $d_{C,1} = 14$ in interval $I_{C,1}$ and $d_{C,2} = 7$ in interval $I_{C,2}$.

Interval $I_{C,0}$:

The number of recommended tests in interval $I_{C,0}$, $n_{C,0}$, is

$$n_{C,0} = floor\left(\frac{November\ 1,\ 2020 - \text{May } 1,2020+1}{d_{C,0}}\right)$$

$$= floor\left(\frac{185}{7}\right)$$

= 26

The last recommended test during interval $I_{C,0}$ occurs on

$m_{C,0} = May\ 1, 2020 + 7 * 26 =$ October 30, 2020.

Interval $I_{C,1}$:

The number of recommended tests in interval $I_{C,1}$, $n_{C,1}$, is

$$n_{C,1} = floor\left(\frac{\text{January } 20,2021 - \text{October } 30,2020}{d_{C,1}}\right)$$

$$= floor\left(\frac{80}{14}\right)$$

= 5

The last recommended test during interval $I_{C,1}$ occurs on

$m_{C,1} = October\ 30, 2020 + 14 * 5 =$ January 8, 2021.

Interval $I_{C,2}$:

The number of recommended tests in $I_{C,2}$, $n_{C,2}$, is

$$n_{C,2} = floor\left(\frac{t_{C,3} - t_{C,2}}{d_{C,2}}\right)$$

$$= floor\left(\frac{March\ 1, 2021 - January\ 20,\ 2021}{7}\right)$$

$$= floor\left(\frac{40}{7}\right)$$

= 5

Therefore, the number of expected tests during the study period for participant C is

$N_C = \sum_{j=0}^{2} n_{C,j}$ = 26 + 5 + 5 = 36.