March 2020

PERSEUS NEWSLETTER

Inside this Issue

Welcome to the 14th Edition of the Perseus Study Newsletter!

Please forward this Newsletter to all your study staff working on this trial.
Please also file this Newsletter in section 10.3 of your Investigator Site File.

COVID-19

First, the Perseus team would like to thank all of our site staff who during this challenging time, have continued to provide treatment to their patients and valuable feedback to the study team. The collaboration is truly amazing.

On 17 March 2020, a letter was distributed centrally to all Principal Investigators & Study Coordinators entitled "Guidance for Patient Management during Coronavirus Outbreak (COVID 19)". Please share with your site staff.

If you have not received it or have any questions, please contact your CSM

COVID-19 Questions & Answers

Question	Answer
Cycle 5 and Cycle 6 prior to ASCT due to COVID-19 outbreak ***(sponsor letter dated 17 March 2020 "Guidance for Patient Management during Coronavirus Outbreak (COVID 19)")***	
Stem Cell Collection	It is strongly recommended that stem cell collection is done after cycle 4 to ensure adequate mobilization and harvest. Sites are encouraged to proceed with mobilization using GCSF and plerixafor to avoid cytopenia caused by high dose cyclophosphamide. If absolutely not feasible due to local hospital restrictions, sites should proceed with cycle 5 and cycle 6, proceed to collect stem cells and then perform the ASCT after cycle 6.
If cycle 5 and cycle 6 are performed prior to ASCT, do subjects repeat consolidation after transplant?	If ASCT cannot be performed as per study protocol due to the coronavirus emergence and limited access to hospitalization then, C5 and C6 can be given immediately to maintain continuity of treatment as a bridge during this emergency time after stem cell collection. ASCT should be performed immediately following cycle 6. Following transplant, patients who received cycles 5 and 6 of treatment prior to transplant then proceed directly to maintenance therapy (C7) upon recovery from transplant. The pre-ASCT visit will be performed after cycle 6. The post-consolidation bone marrow should be performed prior to starting cycle 7 regardless of when cycles 5 & 6 are given.
Do sites need to enter a comment in RAVE for cases where ASCT is performed post cycle 5 & cycle 6?	Yes, the site should enter a comment to indicate that the delay was due to COVID-19 pandemic.
Covance ***(sponsor letter dated 17 March 2020 "Guidance for Patient Management during Coronavirus Outbreak (COVID 19)")***	
Supplies: Currently, Covance has essentially observed no impact on critical supply items at this time and only minor impact on specific supply items globally. Covance has partnered closely with key suppliers to maintain continuity of supplies and has	

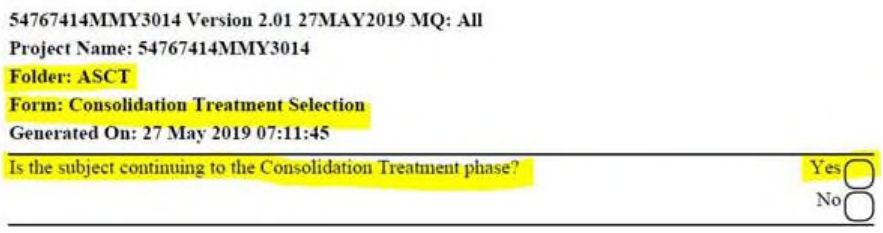
taken several actions to proactively address risks to our supply chain and to prevent the risks of supply outages. Their Kit Production capabilities are fully operational at this time.

Testing: Covance CLS is observing no material impact on their laboratory operations globally. Processes are established to utilize their global network of testing for contingencies, where applicable.

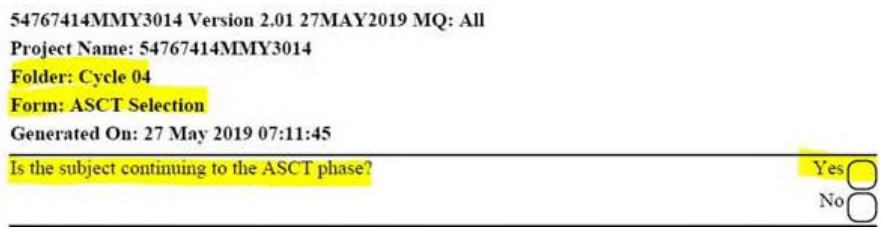
Are there currently interruptions of services to sites?	No
Should sites use local labs where possible if unable to ship required samples to Covance? Which tests should sites perform locally, and which samples can/should be stored at site for sending to Covance when possible?	Yes, sites should use local labs for Disease Evaluations (i.e., SPEP, UPEP, SIFE, UIFE, serum FLC, calcium and albumin), if they are unable to ship specimens to the Covance central lab. As bone marrow for MRD must be sent as fresh aspirate, please only collect bone marrow when you know it is possible to ship to the central lab. However, PK/immunogenicity samples should be collected using the central laboratory kits and kept frozen at -20°C or lower until such time as they can be shipped to the Covance central lab.
If C5 is prior to ASCT will an auto query fire in RAVE?	See below

An auto query will be posted if Stem Cell re-infusion start / end date is after C5D1 visit date.

Cycle 5 is triggered when site answers the question below as "yes"


54767414MMY3014 Version 2.01 27MAY2019 MQ: All
Project Name: 54767414MMY3014
Folder: ASCT
Form: Consolidation Treatment Selection
Generated On: 27 May 2019 07:11:45
Is the subject continuing to the Consolidation Treatment phase? Yes ☐ No ☐

If transplant is postponed and after C5, to trigger C5, site needs to trigger the ASCT folder, then complete this page. Pre-ASCT folder will trigger as well. Note: this method only applies to subjects who continued for ASCT phase.


54767414MMY3014 Version 2.01 27MAY2019 MQ: All
Project Name: 54767414MMY3014
Folder: Cycle 04
Form: ASCT Selection
Generated On: 27 May 2019 07:11:45
Is the subject continuing to the ASCT phase? Yes ☐ No ☐

Who should be informed in case sites plan to perform first cycle 5 and 6 and thereafter ASCT for patient?	**You should inform your CSM immediately as this must be tracked by him/her and must be discussed with the study team whether a manual (additional) drug shipment is required to ensure you have sufficient dug on site for cycle 5 and cycle 6.** The IWRS system was not set up in this way in the beginning. In case of specific patient-related questions, please contact the Medical Monitor team (details can be found at the end of this Newsletter).
How much time is permitted between end of cycle 6 and ASCT?	12 weeks is the interval between end of cycle 4 and ASCT with stem cell collection in between. If the patient has already collected stem cells, it is suggested to proceed with ASCT within a month, at maximum 2 months.
If the ASCT is between C6 and C7 do sites need to take another DE sample before C7D1 to see if post consolidation samples are needed?	Yes, this Disease Evaluation would be required as part of the Pre-ASCT visit to be performed after Cycle 6 and prior to ASCT
IWRS, Drug Shipments ***(sponsor letter dated 17 March 2020 "Guidance for Patient Management during Coronavirus Outbreak (COVID 19)")***	
Would it be acceptable/allowed to assign drug outside of the IWRS system to patients?	No, drug should always be assigned via IWRS system to ensure supply of drug at the site.
Is it allowed to assign 3 boxes Lena to patients in maintenance phase?	Yes, this can occur, however, if possible local labs should be performed and reviewed by site staff prior to patients continuing on to the next months' supply of drug.
Do we have a process for sending oral drug to patients for cases where patients will not attend visits at the hospital?	Only oral medications, i.e., Lenalidomide and Dexamethasone may be shipped from the study site direct to patients. **Any medications that must be administered by a trained healthcare profession (i.e., daratumumab and bortezomib) cannot be shipped direct to patients.** **If needed, patients can utilize local hospitals to receive commercial supply of drug then return to study site when possible (see below).** g. Putting patients' safety and benefit as the priority, investigators may make the decision to provide other available therapy to patients on the study. Please discuss any decision to provide other therapy outside of the protocol with the EMN Medical Monitor. Please ensure this is recorded on source document and the eCRF along with reason for administration.
Re-consenting remotely	
Would be possible to re-consent patient over the phone?	From our perspective, the re-consenting of subjects via telephone is acceptable under these COVID-19 circumstances. In fact, sharing the ICF updates with the subjects, at the first opportunity after IRB/IEC/other required approvals have been issued, is preferred so sites can discuss the new information with the subject via

	telephone, then obtain original signature once the subject is able to visit the site in person after the pandemic is behind us. Sites should confirm this to be acceptable per their local IRB/IEC/other guidance during this pandemic Process: Sites should proceed with reconsenting via phone if it´s allowed according local regulations and per their local IRB/IEC/other governing body: a. Study Coordinator sends the approved Informed Consent Form (ICF) to the patient via post. b. Investigator will contact the subject via phone to discuss the changes in the ICF and obtain subjects' agreement. Discussion and subject's agreement will be documented **in detail** in the source. c. At the next clinic visit, ICF version will be discussed again and signed off.
Subjects testing positive for COVID-19	
What if a subject develops COVID-19 and needs to be treated on a therapeutic clinical trial?	PERSEUS study treatment should be interrupted, so that the subject may be treated on the COVID-19 clinical trial. Once COVID-19 resolves and that treatment is completed, the investigator should discuss with EMN Medical Monitors whether re-starting PERSEUS study treatment is appropriate for the subject.
RAVE entries	
What happens if a patient is COVID-19 positive? Should such cases be entered as AEs in RAVE or reported as SAEs?	Inform your CSM immediately as these cases must be tracked and informed to Medical Monitors and Sponsor. Please enter these cases in RAVE as an AE/SAE**, as applicable as per protocol guidance. Please ensure to use the word "COVID-19" in your entry in RAVE and/or SAE notification so that these cases can be easily identified. Study treatment should be held until patient recovers. ****IMPORTANT:** • Please report all COVID-19 SAEs via EDC and on the paper SAE report form. Please include results of COVID-19 test in the section of Relevant test/laboratory data and signs, symptoms and other event details in the section of Description of event of the paper SAE report team. Please report non-serious COVID-19 AEs via EDC with AE term COVID-19 infection or infection caused by SARS-CoV-2.

The sponsor letter dated 16 March 2020 ""Guidance for Patient Management during Coronavirus Outbreak (COVID 19)", stated: g. Putting patients' safety and benefit as the priority, investigators may make the decision to provide other available therapy to patients on the study. Please discuss any decision to provide other therapy outside of the protocol with the EMN Medical Monitor. Please ensure this is recorded on source document and the eCRF along with reason for administration. What other treatment/therapy is being referred to here? Does it mean that sites should discontinue study treatment due to COVID-19, but patient should still be on the study (follow-up)?	No, this means that if necessary to allow for local treatment of a patient who cannot attend to the study hospital that the patient could receive commercial therapy with D-VRd or VRd. They should continue to remain with the same arm of study treatment as randomized in this study as the study has not yet met its primary endpoint. Please discuss any use of local commercial therapy with the CSM and ensure that this is well documented in the patient's source documents and documented in the CRF. Further when needed, a direct shipment of study medications can occur to maintain continuation of therapy particularly when in maintenance therapy. Patients receiving local therapy should continue to have local safety labs if possible, to ensure safe at home treatment for patients.
If another a local lab is used by patients, are reference ranges required to be collected & added in RAVE?	Yes

IDMC #2 – March 2020

- The 2nd regular IDMC meeting is planned after approximately 100 subjects have completed the consolidation phase (ie: Cycle 5 and Cycle 6).
- Data from all visits that occurred on or before **16 March 2020** will be included in this IDMC review.
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Preliminary Timelines are as follows

Cutoff Date:	**16 March 2020**
Last data entered in eCRF	**20 March 2020**
Last query issued	**23 April 2020**
Last query answered:	**28 April 2020**

With the evolving situation around the COVID-19, your CSM will provide feedback on how we will address our data cleaning moving forward. In the meantime, we ask for your continued support in entering missing visits, missing pages and to resolve open queries, including SAE queries.
THANK YOU!

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