# S1803 – Multiple Myeloma

PHASE III STUDY OF DARATUMUMAB/rHuPH20 (NSC- 810307) + LENALIDOMIDE OR LENALIDOMIDE AS POST AUTOLOGOUS STEM CELL TRANSPLANT MAINTENANCE THERAPY IN PATIENTS WITH MULTIPLE MYELOMA (MM) USING MINIMAL RESIDUAL DISEASE TO DIRECT THERAPY DURATION (**DRAMMATIC** STUDY)

## Things to remember

- Baseline Tumor Assessment (BTA) must be completed with initial diagnosis disease assessment
- Step 1 Source Documents are to be from initial diagnosis
    - Each document must be uploaded separately to resolve expectations
    - Required documents are diagnostic pathology, radiology and FISH reports
    - If one of the required documents are not available due to not being completed at time of diagnosis, notify SDMC to have expectation manually resolved.
- All patients require a 24-hour UPEP at these timepoints:
    - Within 60 days prior to Registration to Step 2
    - 12 months after registration to Step 2
    - 24 months after registration to Step 2
    - 36 months after registration to Step 2
    - 48 months after registration to Step 2
    - To confirm a complete response as defined per section 10 of the protocol
- Archival slides, or linkable commercial sequencing is required for all patients registered after 9/15/2022
    - Without a successful archival slide or linkable sequencing, MRD results cannot be provided.
    - SWOG SDMC will reach out to sites for patients who have a failed or polyclonal archival result to ask if additional sample may be submitted. Sites will be reimbursed for the additional submission if required.
- 24-month MRD results **MUST** come from Adaptive and the SDMC. Local MRD results are not allowed to determine Step 3 eligibility.
- Sites **MUST** wait for the completion of the 24-month MRD and Response eCRF in Rave before registering patients to Step 3.
- Any specimen not collected must be noted as such in the Specimen Tracking System (STS). Help document is available on CTSU to detail this process.
- Updated CRF Guidelines will be uploaded to CTSU

## Helpful Contacts

- myelomaquestion@crab.org
    - Reach out to this email first for all study related questions. If we can't help you, we will loop in the appropriate contacts
- ctsucontact@westat.com
    - CTSU grants access to Rave. The SDMC cannot provide this access and will refer you to this distribution list.
- Clinicaltrials-diagnostics@adaptivebiotech.com
    - Adaptive can help link commercial sequencing if archival slides are not available
        - Will assist with the Adaptive Portal to log specimens being shipped to Adaptive.

# S1803 Data Submission Guidelines

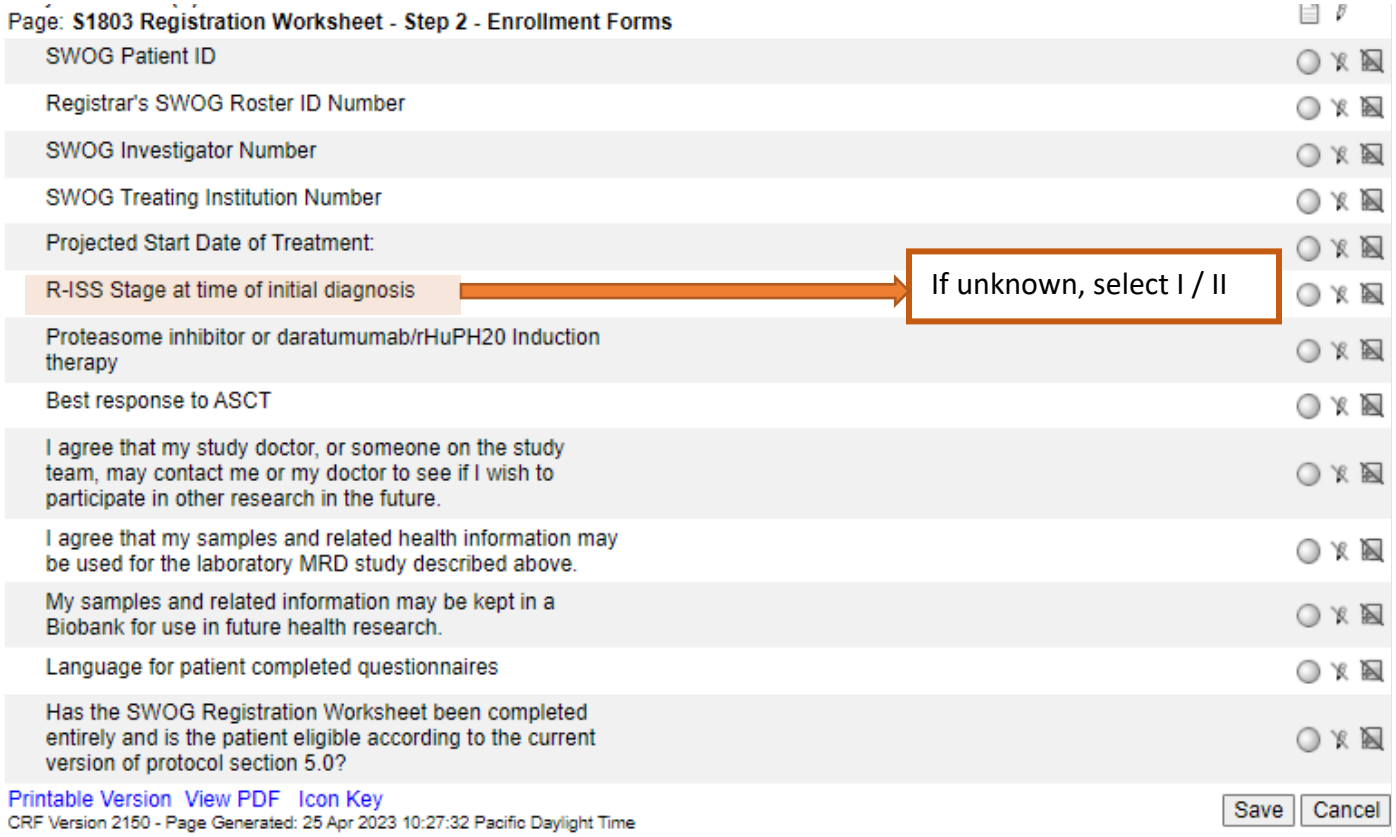
These guidelines were developed to address frequently asked questions and common errors. Not all forms available are included in this guideline; if there are not frequently asked questions about a form, it may not have been included in this document. This guide is not a replacement for form instructions. Please carefully read all form instructions before submitting data.

**If you have further questions about data entry or eligibility, please email MyelomaQuestion@crab.org.**

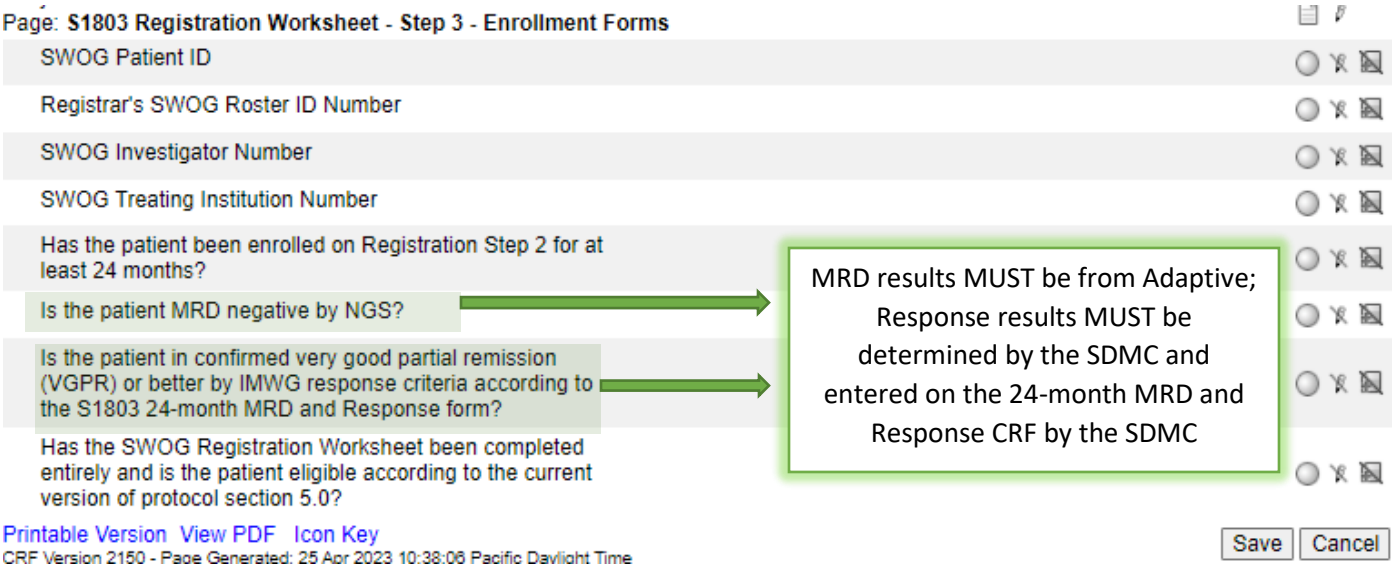
For other questions, please refer to the S1803 Protocol Contact Information page in the S1803 protocol.

## Contents

## Step 2 Registration Worksheet




## Step 3 Registration Worksheet



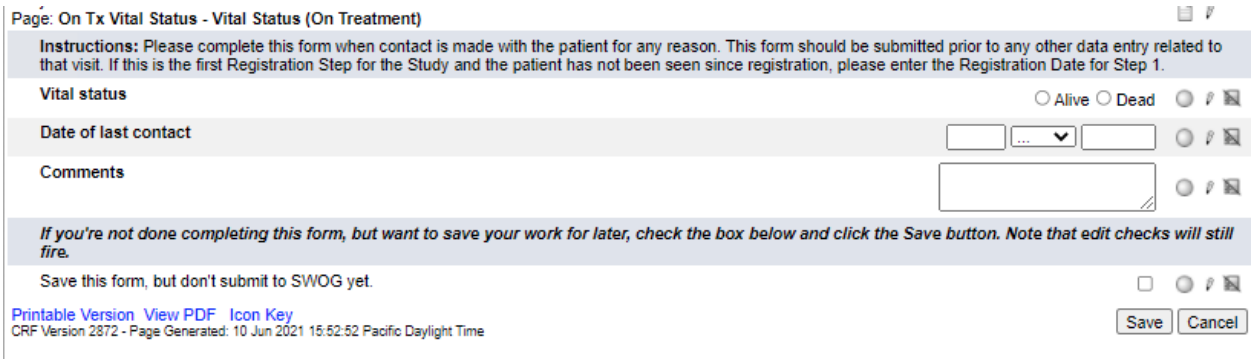

**Step 3 Registration information**

- Patients are not to be registered until the 24-month MRD and Response form has been completed by SWOG.
    - Results for the MRD assessment, and patients' current response will be entered to determine patient eligibility.
        - All disease assessment data MUST be up to date before response is able to be determined

    - This includes completion of 24 hour UPEP assessment and results of the 24 month bone marrow biopsy
- Site's MRD assessments CAN NOT to be used to determine 24-month MRD results.
    - Only results provided by SWOG SDMC are to be used.
    - MRD results must be by Next Gen Sequencing (NGS) provided by Adaptive
- See Step 3 Registration and Procedures document for additional information

## Vital Status Form

Fill out the Vital Status form any time you enter data, **PRIOR to submitting any other data**. Otherwise, you will get system queries on other forms. See protocol section 14.4 for required timepoints for completion.


Page: **On Tx Vital Status - Vital Status (On Treatment)**

**Instructions:** Please complete this form when contact is made with the patient for any reason. This form should be submitted prior to any other data entry related to that visit. If this is the first Registration Step for the Study and the patient has not been seen since registration, please enter the Registration Date for Step 1.

**Vital status** ○ Alive ○ Dead

**Date of last contact** ... 

**Comments**

***If you're not done completing this form, but want to save your work for later, check the box below and click the Save button. Note that edit checks will still fire.***

Save this form, but don't submit to SWOG yet.

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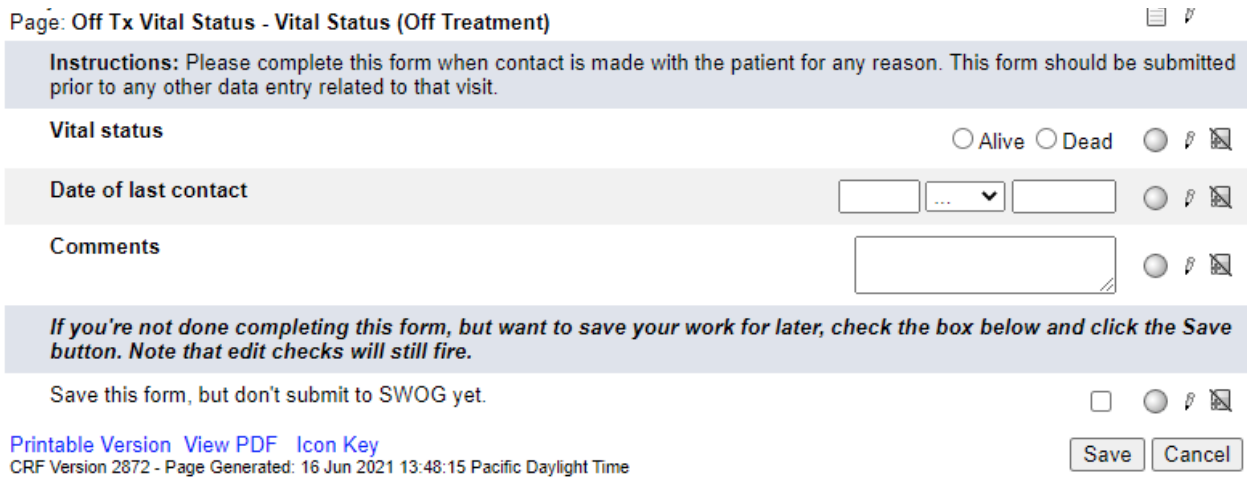
CRF Version 2872 - Page Generated: 10 Jun 2021 15:52:52 Pacific Daylight Time

Save Cancel


Page: **Off Tx Vital Status - Vital Status (Off Treatment)**

**Instructions:** Please complete this form when contact is made with the patient for any reason. This form should be submitted prior to any other data entry related to that visit.

**Vital status** ○ Alive ○ Dead

**Date of last contact** ... 

**Comments**

***If you're not done completing this form, but want to save your work for later, check the box below and click the Save button. Note that edit checks will still fire.***

Save this form, but don't submit to SWOG yet.

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Save Cancel

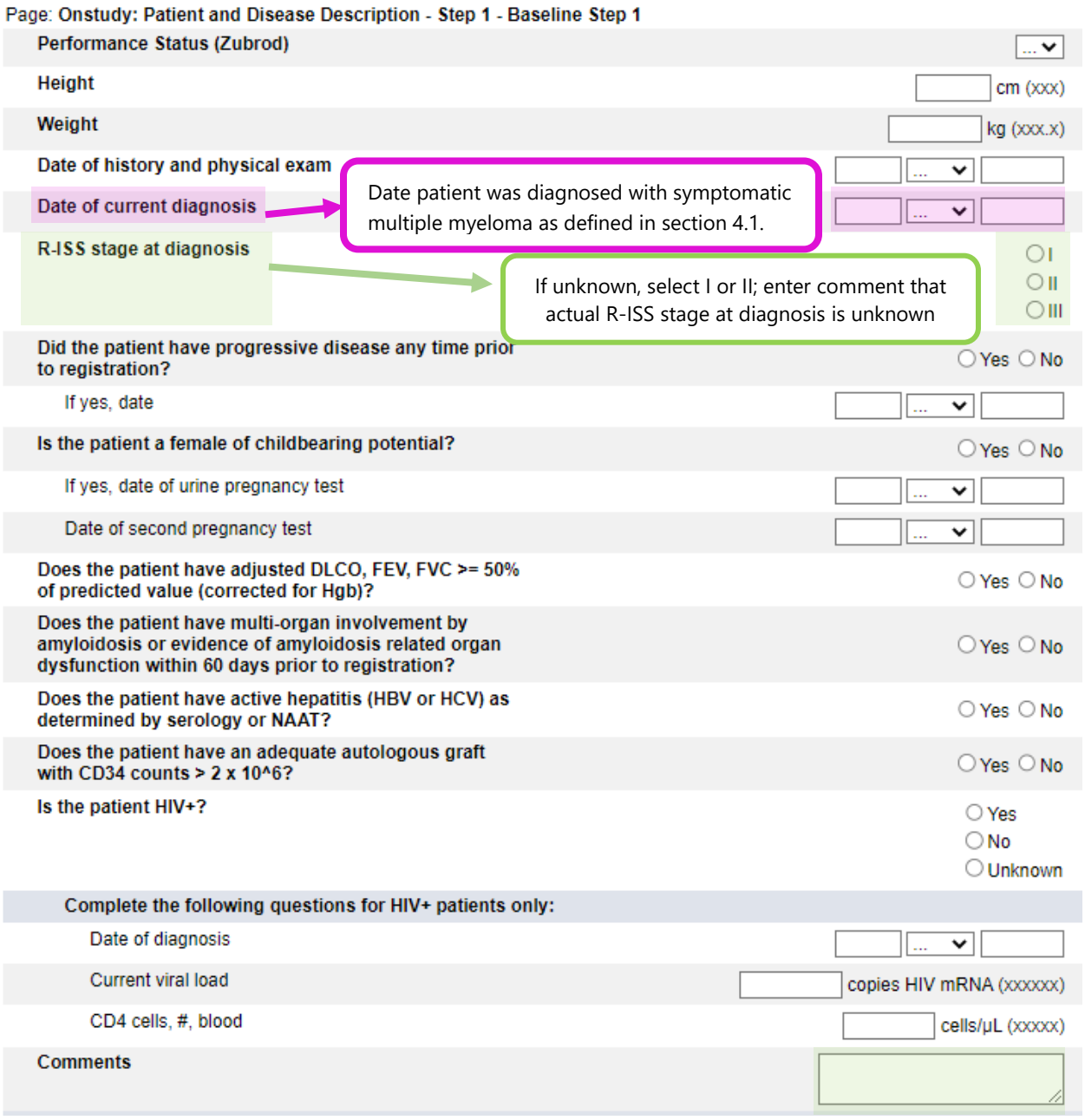
Confirmation of vital status can be obtained through phone call, EMR records, tele-health visits, etc.

# Step 1 Onstudy Forms

- The Onstudy forms should use the screening information from prior to Step 1 Registration

**Patient and Disease Description – Step 1**

- History and Physical must be performed within 28 days prior to registration to Step 1
- Date of current diagnosis is asking for the date the patient was diagnosed with symptomatic multiple myeloma as defined in section 4.1
- If R-ISS Stage at diagnosis is not known, or was not done, please select stage I or II and enter a comment at the bottom of the form stating the test was not performed at time of diagnosis.



**Laboratory Values – Step 1**

- Labs should be entered to match the Lab test units to the left of the lab value
  - Platelets: XXX,XXX (100000)
  - ANC: X,XXX (2000)
  - No commas should be entered
- If LLN or ULN boxes are listed, values are required for that lab assessment
- Section 5.1 of the protocol specifies the timeframes that labs must be collected within. There are some labs that do not have a window and, if available, may be entered from any time after diagnosis from any time can be entered (LVEF, LDH, Beta-2 Microglobulin and C Reactive Protein)
  - Log lines 1-8 should be collected as close to registration as possible
  - Log lines 9-14 can be from any time after diagnosis, if collected.

Page: **Onstudy: Laboratory Values - Step 1 - Baseline Step 1**

Confirm values are entered in the correct units

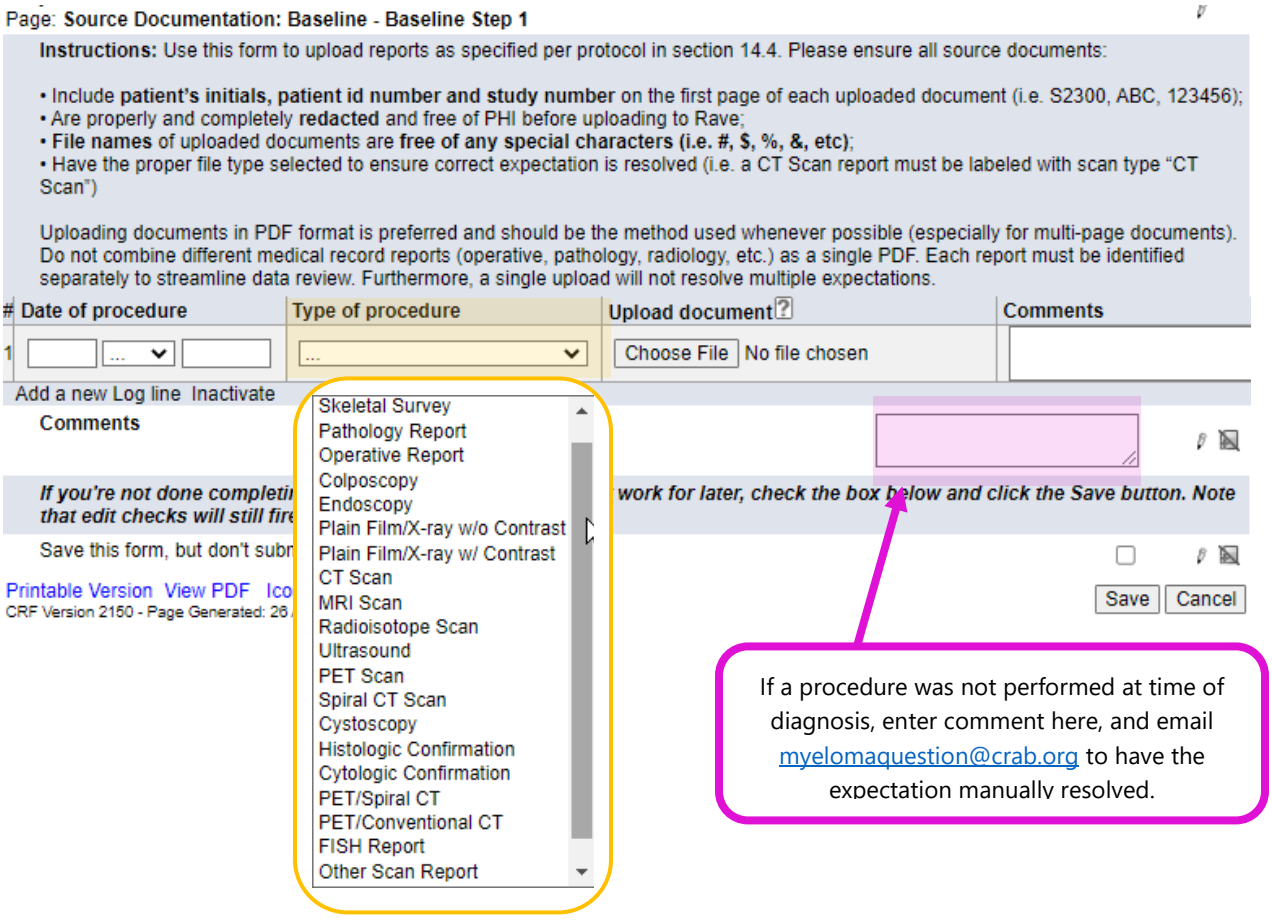
| # | Lab test | Lab test units | Lab value | LLN | ULN | Sample collection date |
|---|---|---|---|---|---|---|
| 1 | Absolute Neutrophil Count (ANC), Blood | /uL (x,xxx) | | | | ... |
| 2 | Platelets, Blood | /uL (xxx,xxx) | | | | ... |
| 3 | Hemoglobin, Blood | g/dL (xx.x) | | | | ... |
| 4 | Creatinine, Serum | mg/dL (xx.xx) | | | | ... |
| 5 | Creatinine Clearance (CrCl), Cockcroft-Gault, Serum | mL/min | | | | |
| 6 | Aspartate Aminotransferase (AST or SGOT), Serum | U/L (xxx) | | | | ... |
| 7 | Alanine Aminotransferase (ALT or SGPT), Serum | U/L (xxx) | | | | ... |
| 8 | Bilirubin, Total, Serum | mg/dL (xxx.x) | | | | ... |
| 9 | ECHO | % (xxx) | | | | ... |
| 10 | LVEF | % (xxx) | | | | ... |
| 11 | Lactate Dehydrogenase (LDH), Serum | U/L (xxxx) | | | | ... |
| 12 | Beta-2 Microglobulin, Serum | ug/mL (xx.x) | | | | ... |
| 13 | C Reactive Protein, Serum | ug/dL (xxx.x) | | | | ... |
| 14 | Albumin, Serum | g/dL (xx.x | | | | ... |

These labs are not required per protocol. If they were completed at time of diagnosis, please enter this data.

**Comments**

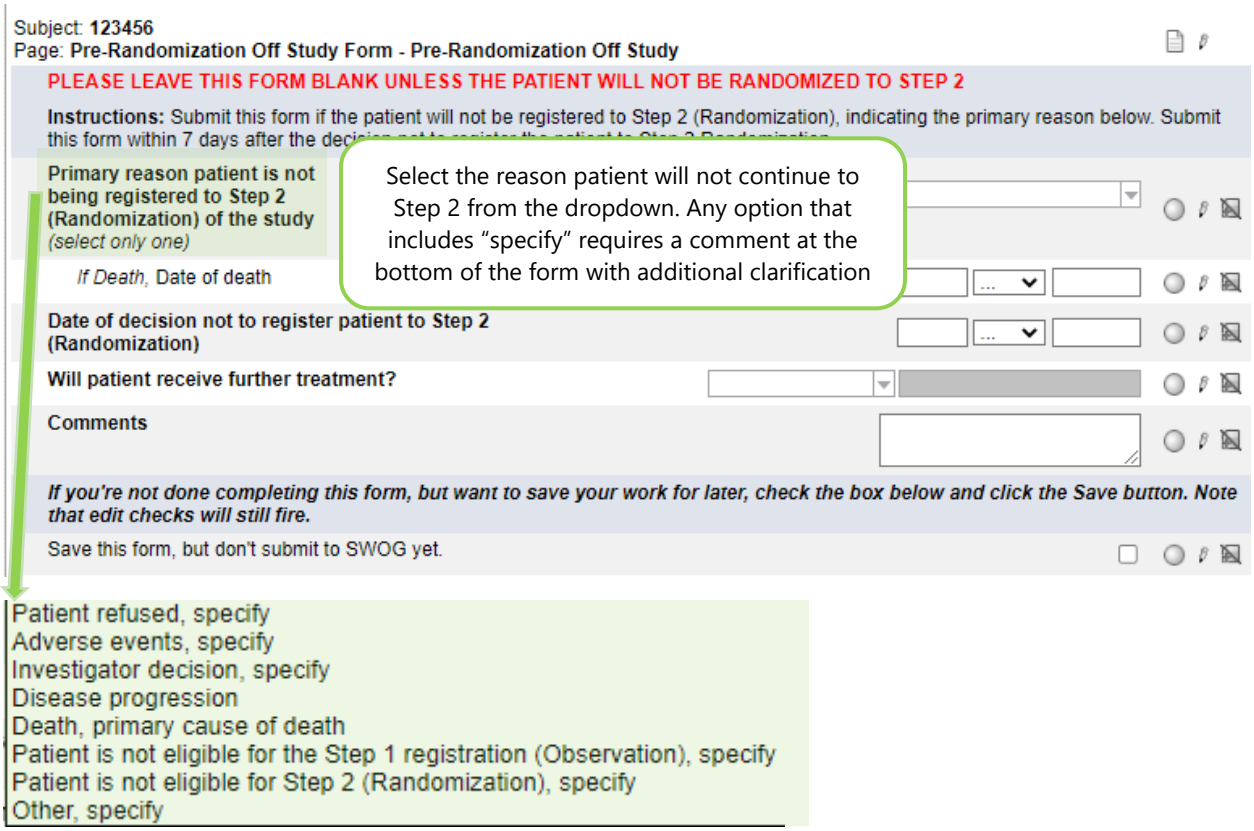
**Baseline Source Documentation – Step 1**

- Please upload **only diagnostic reports** here
  - Include diagnostic radiology and pathology reports
  - Include diagnostic FISH/CYTO reports separately – Indicate the "Type of scan" for these reports as "Cytologic Confirmation" or "FISH Report"
    - The full FISH report is preferred as it provides more information for the study chairs
  - Additional labs and physicals are not required documents and **should not be uploaded**
- All uploaded source documentation must contain the patient's initials and patient ID number on at least one page of each uploaded document
- Use the drop down to select the correct Type of Procedure
  - Expectations will not resolve unless the correct type of scan/document is selected. See protocol section 14.4 for required documents
- Avoid using "Other Scan Type" whenever possible
- Date of procedure is to be the date the scan/biopsy was performed, not the date the results were provided/received



## Pre-Randomization Off Study

Patients not continuing to randomization (Step 2 registration) will have this form completed. DO NOT COMPLETE THIS FORM IF PATIENT WILL BE REGISTERED TO STEP 2




All patients registered to Step 1 must complete **ALL** Baseline Step-1 Onstudy forms and Baseline Tumor Assessment form.

## Baseline Tumor Assessment (BTA)

**Completing the BTA**

- Unlike most studies, S1803 requires the Baseline Tumor Assessment (BTA) to be completed using INITIAL DIAGNOSIS disease assessment rather than the screening assessment.
    - Patient must have measurable disease by either SPEP, UPEP or FLC as defined in protocol criteria 5.1.a.
    - Information should be around the date of initial diagnosis entered on the Baseline Step 1 Onstudy form.
    - This form must be completed with an assessment from prior to any induction-treatment
- Date of diagnosis and start date of induction therapy will be compared to the dates of assessments entered on the BTA to ensure the data is from initial diagnosis.
- All patients registered to Step 1 must have this form completed.

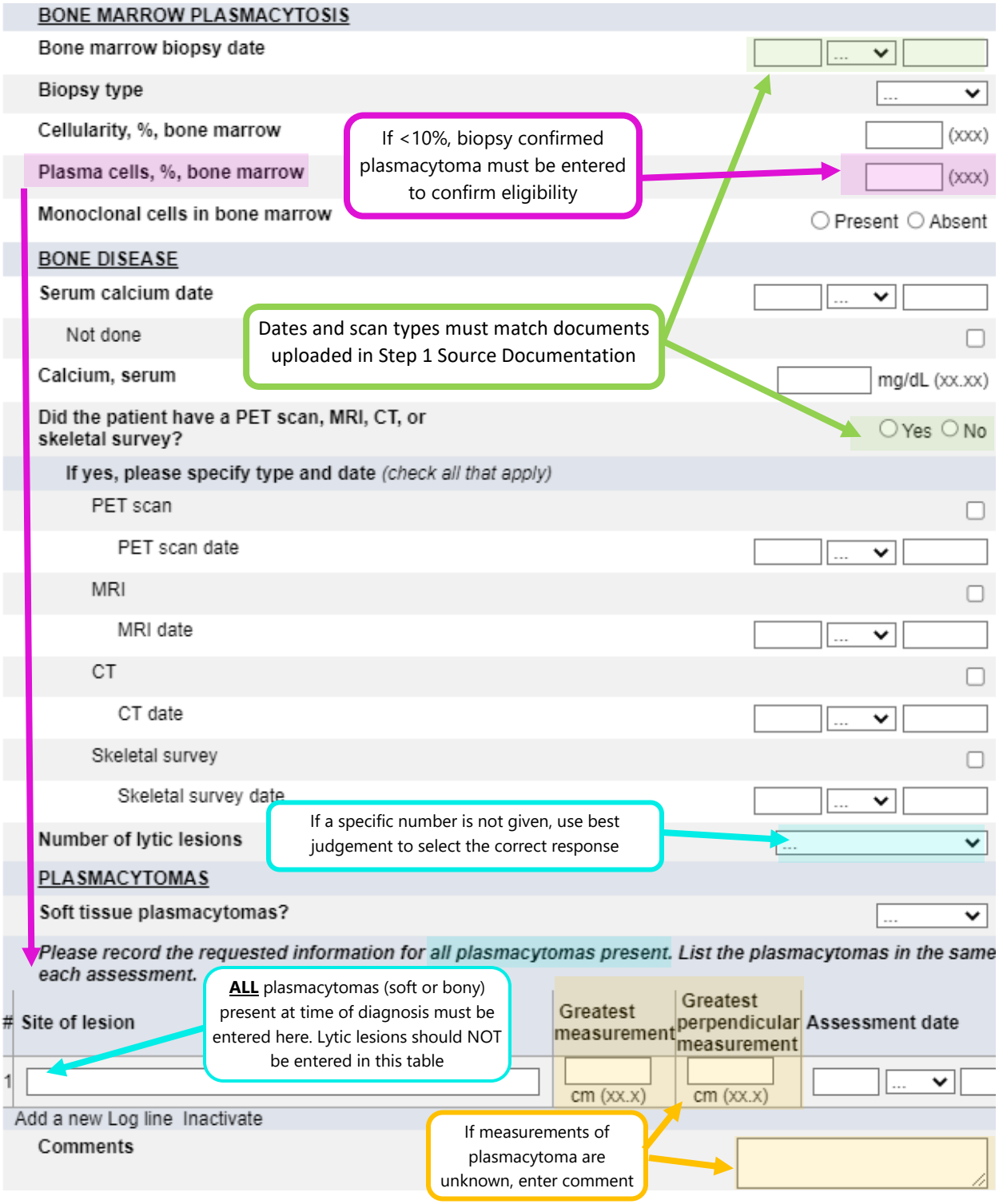
Page: **Baseline Tumor Assessment for Multiple Myeloma - Disease Assessment**

| | |
|---|---|
| **SERUM M-PROTEIN** | |
| **Date of SPEP** | ... |
| SPEP not done | ☐ |
| **Monoclonal protein, electrophoresis, serum** | g/dL (xx.x) |
| Too small to quantify | ☐ |
| **Date of immunofixation** | ... |
| Immunofixation not done | ☐ |
| **Monoclonal protein, immunofixation electrophoresis, serum** | ○ Negative ○ Positive |
| **Free light chains, freelite assay, serum** | |
| Kappa free light chain | mg/dL (xxxxx.xx) |
| Lambda free light chain | mg/dL (xxxxx.xx) |
| Kappa/lambda ratio *(derived)* | (xxxxxx.xx) |
| Kappa/lambda difference (dFLC) | mg/dL (xxxxx.xx) |
| **Quantitative immunoglobulins** | |
| Immunoglobulin G (IgG), serum | mg/dL (xxxxx) |
| Immunoglobulin A (IgA), serum | mg/dL (xxxxx) |
| Immunoglobulin M (IgM), serum | mg/dL (xxxxx) |
| Immunoglobulin D (IgD), serum | mg/dL (xxxxx) |
| Immunoglobulin E (IgE), serum | mg/dL (xxxxx) |
| **Light chain serum** | ... |
| **Heavy chain, serum** | ... |
| **URINE M-PROTEIN** | |
| **Date of 24-hour UPEP** | ... |
| 24-hour UPEP not done | ☐ |
| **Monoclonal protein, electrophoresis, urine** | mg/24.h (xxxxx) |
| Too small to quantify | ☐ |
| **Date of immunofixation** | ... |
| Not done | ☐ |
| **Monoclonal protein, immunofixation eletrophoresis, urine** | ○ Negative ○ Positive |
| **Urine volume** | ml/24.h (xxxx) |
| **Urine total protein** | mg/24.h (xxxx) |
| **Urine light chain** | ... |

Confirm value is entered in mg/dL rather than mg/L. If your site reports in mg/L, convert value by dividing by 10

Derived by Rave

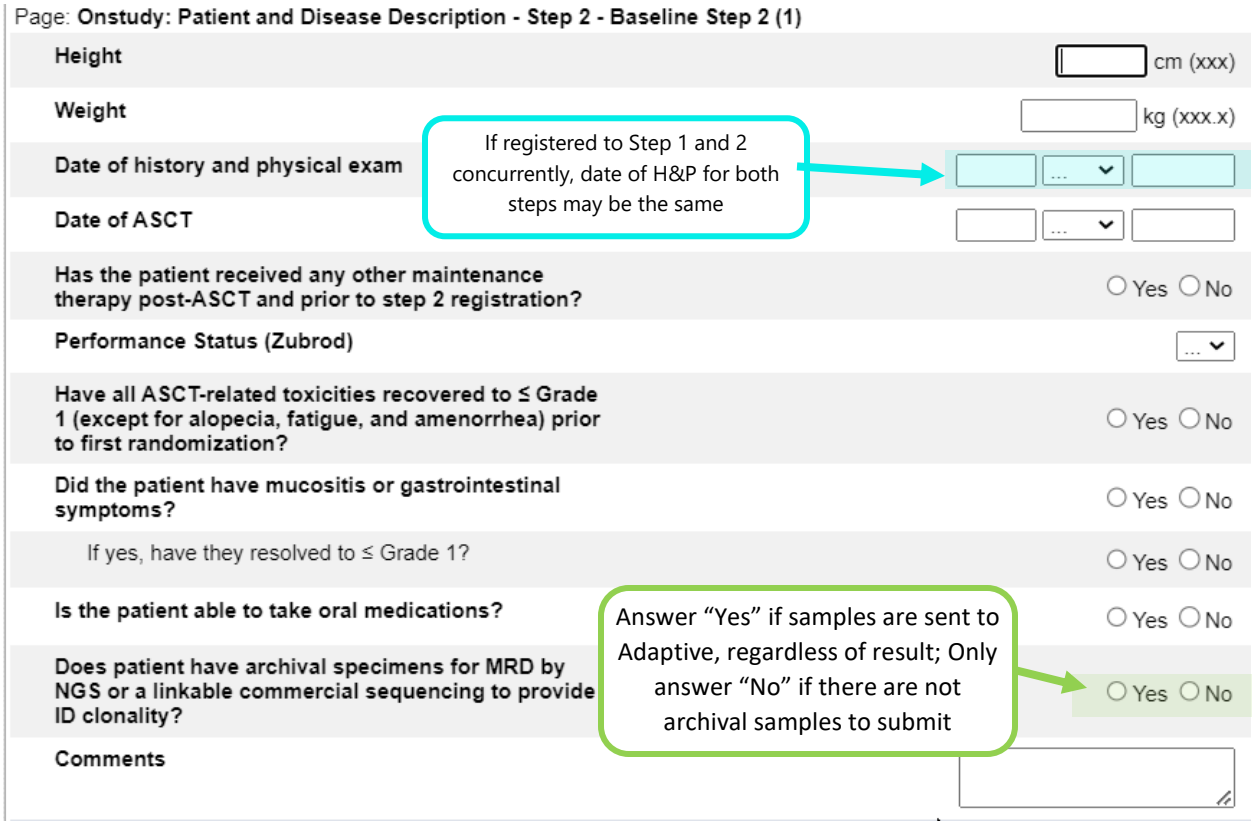
Ensure this is the monoclonal protein, not total protein


BONE MARROW PLASMACYTOSIS
Bone marrow biopsy date
Biopsy type
Cellularity, %, bone marrow
(xxx)
Plasma cells, %, bone marrow
(xxx)
Monoclonal cells in bone marrow
Present Absent
If <10%, biopsy confirmed plasmacytoma must be entered to confirm eligibility
BONE DISEASE
Serum calcium date
Not done
Calcium, serum
mg/dL (xx.xx)
Dates and scan types must match documents uploaded in Step 1 Source Documentation
Did the patient have a PET scan, MRI, CT, or skeletal survey?
Yes No
If yes, please specify type and date (check all that apply)
PET scan
PET scan date
MRI
MRI date
CT
CT date
Skeletal survey
Skeletal survey date
Number of lytic lesions
If a specific number is not given, use best judgement to select the correct response
PLASMACYTOMAS
Soft tissue plasmacytomas?
Please record the requested information for all plasmacytomas present. List the plasmacytomas in the same each assessment.
# Site of lesion
ALL plasmacytomas (soft or bony) present at time of diagnosis must be entered here. Lytic lesions should NOT be entered in this table
Greatest measurement
Greatest perpendicular measurement
Assessment date
1
cm (xx.x)
cm (xx.x)
Add a new Log line Inactivate
Comments
If measurements of plasmacytoma are unknown, enter comment

# Step 2 Onstudy Forms

**Patient and Disease Description – Step 2**

- Complete with data from as close to registration to Step 2 as possible.
  - Unless otherwise specified that assessment must be done sooner, all assessments must be completed within 60 days prior to registration to Step 2
  - Patients registered to Steps 1 and 2 concurrently may use a lot of the same screening information



## Laboratory Values – Step 2

- All Step 2 labs must be completed within 28 days prior to registration to Step 2
- Patients registered to Steps 1 and 2 concurrently may use the same labs for both steps, but they must be entered on each form
- LLN and ULN are required if able to enter a value. If your institution does not have these values, please use the standard LLN and ULN that can be found online

Page: **Onstudy: Laboratory Values - Step 2 - Baseline Step 2 (1)**

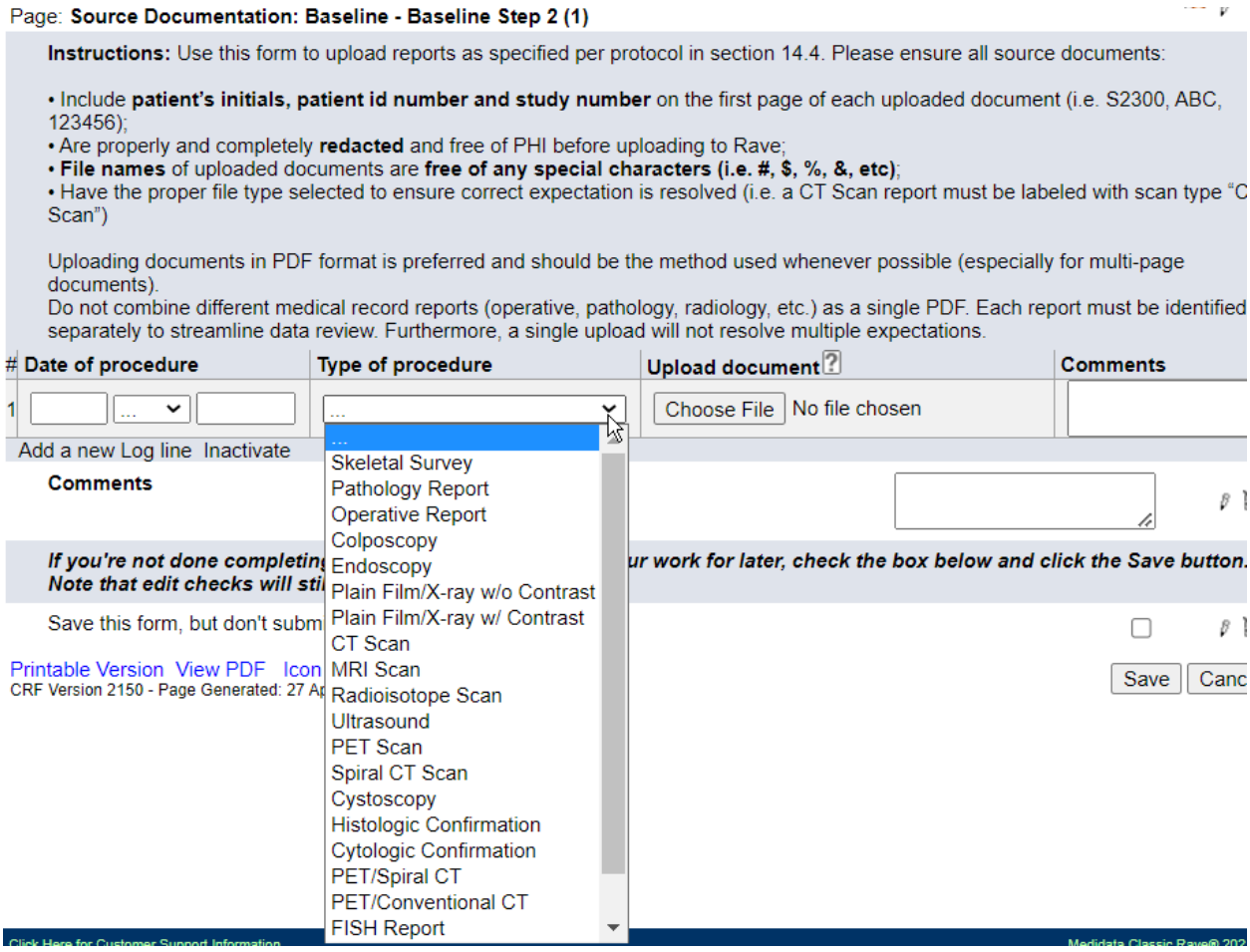
| # | Lab test | Lab test units | Lab value | LLN | ULN | Sample collection date |
|---|---|---|---|---|---|---|
| 1 | Absolute Neutrophil Count (ANC), Blood | /uL (x,xxx) | | | | ... |
| 2 | Platelets, Blood | /uL (xxx,xxx) | | | | ... |
| 3 | Hemoglobin, Blood | g/dL (xx.x) | | | | ... |
| 4 | Creatinine, Serum | mg/dL (xx.xx) | | | | ... |
| 5 | Creatinine Clearance (CrCl), Cockcroft-Gault, Serum | mL/min | | | | |
| 6 | Aspartate Aminotransferase (AST or SGOT), Serum | U/L (xxx) | | | | ... |
| 7 | Alanine Aminotransferase (ALT or SGPT), Serum | U/L (xxx) | | | | ... |
| 8 | Bilirubin, Total, Serum | mg/dL (xxx.x) | | | | ... |

Value derived by Rave

**Comments**

## Source Documentation – Step 2

- Upload Pre-Registration Step 2 pathology and radiology reports
  - If FISH/CYTO was completed, upload as a separate document
  - All reports should be within 60 days prior to registration to Step 2
- Only the above reports are required
  - Please do not upload additional reports
  - Other screening lab reports should not be uploaded
- Ensure patient number and initials are present on at least one page of each uploaded document
- Do not use special characters (#, &, $, %, etc.) when naming document to be uploaded
  - The SDMC cannot open documents that contain special characters in the title. You will be queried to rename and reupload
- Use the dropdown to select the appropriate type of procedure.
  - "Other Scan Type" should not be needed or used here.




## PRO-CTCAE

- Complete within ±7 days of registration to Step 2, but PRIOR to C1D1
- Following PRO-CTCAE forms will be completed at the end of the cycle with patient's AE assessment
- This form is not used as a replacement for AE assessment. A full toxicity assessment is to be completed at the end of each cycle.

# Patient Reported Outcomes

- Questionnaires/QOL have been added to Revision 5 (PVD 3/10/2022) and are required to be completed by all patients registered to this protocol version or later.
    - Patients registered prior to version 5, WILL NOT complete the questionnaires.
    - The documents may be printed from the CTSU website for patients to complete; results are entered into respective eCRFs in Rave.
    - Training for administration of the questionnaires can be found here: https://www.swog.org/clinical-trials/protocol-workbench
- Due:
    - Registration to Step 2
    - 12 months after registration to Step 2
    - 24 months after registration to Step 2
    - 36 months after registration to Step 2
    - 48 months after registration to Step 2

**PROMIS-29 Profile**

- Complete within ±7 days of registration to Step 2, but PRIOR to C1D1
- Use drop down options to select patient's response
- Required for patients who speak English or Spanish (if initially registered to protocol revision 5-revision 9)
    - Also available for patients who speak French (if initially registered to Protocol revision 5-revision 9)
    - Language is selected during registration

**Intolerance of Uncertainty Scale (IUS) Short Form**

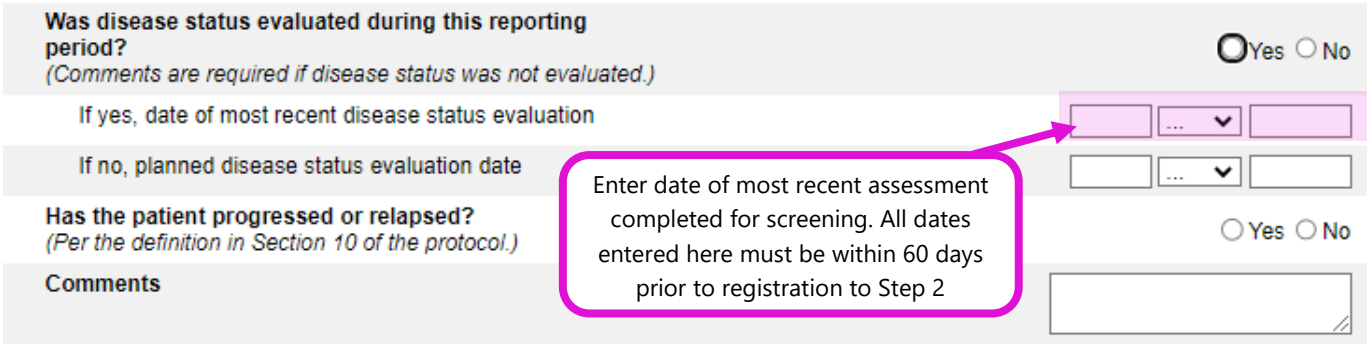
- Complete within ±7 days of registration to Step 2, but PRIOR to C1D1
- Use drop down options to select patient's response
- Required for patients who speak English or Spanish (if initially registered to protocol revision 5-revision 9)
    - Also available for patients who speak French (if initially registered to Protocol revision 5-revision 9)
    - Language is selected during registration
- To determine the patient's Score, add the values of the answers:
    - 1 Point = Not at all characteristic of me
    - 2 Points = A little characteristic of me
    - 3 Points = Somewhat characteristic of me
    - 4 Points = Very characteristic of me
    - 5 Points = Entirely characteristic of me
    - 0 Points = Not answered by patient

Page: **Intolerance of Uncertainty Scale Short Form - .Questionnaires: Registration**

| | |
|---|---|
| **Date Questionnaire Completed** | ... |
| **Please circle the number that best corresponds to how much you agree with each item.** | |
| 1 Unforeseen events upset me greatly. | ... |
| 2 It frustrates me not having all the information I need. | ... |
| 3 Uncertainty keeps me from living a full life. | ... |
| 4 One should always look ahead so as to avoid surprises. | ... |
| 5 A small unforeseen event can spoil everything, even with the best of planning. | ... |
| 6 When it's time to act, uncertainty paralyses me. | ... |
| 7 When I am uncertain I can't function very well. | ... |
| 8 I always want to know what the future has in store for me. | ... |
| 9 I can't stand being taken by surprise. | ... |
| 10 The smallest doubt can stop me from acting. | ... |
| 11 I should be able to organize everything in advance. | ... |
| 12 I must get away from all uncertain situations. | ... |
| **Score:** Use points detailed above (and on Master Forms Set) to get the sum of the patient's score and enter that value here | (xx) |
| **Comments** | |

# First Follow-up Tumor Assessment (FUTA)

Page: **Follow-Up Tumor Assessment for Multiple Myeloma: Assessment - Follow-up Tumor: Assessment**




**General notes for completing first Follow-up Tumor Assessment**

- Complete the first FUTA using patient's post-transplant, pre-registration step 2 information
    - Using this data allows us to see the patient's response to induction/transplant therapies which is a stratification factor per protocol.
        - All assessments are required to be completed prior to Registration Step 2, **including 24-hour UPEP**, regardless of how the patient had measurable disease at diagnosis.
        - All assessments must be from within 60 days prior to registration per eligibility criterion 5.2.e.
    - If the patient had measurable disease by UPEP at diagnosis, the patient MUST be followed by UPEP for the duration of the study per section 10.2.e.
- Only numeric values can be entered on this form
    - If a result is provided with "<", please enter the whole number in the field, and enter a comment at the bottom of the field stating "Resulted as <5"
- Upload bone marrow pathology report and imaging report to the Source Documentation folder
    - Must be uploaded to BOTH Step 2 Source Documentation, and this Source Documentation folders to ease the study chairs' review process
    - Please do not upload other lab results; they are not required
    - Ensure all documents are fully redacted and labeled per form instructions (patient number, patient initials and study number

**Follow-up Tumor Assessment: Report**

- Enter patient's screening (Pre-registration Step 2) disease assessment here
  - All assessments entered must be from within **60 days prior to registration to Step 2**
  - Bone marrow biopsy, imaging and 24-hour UPEP are required for ALL patients, in addition to SPEP, free light chain assessment and serum calcium assessment

Page: **Follow-Up Tumor Assessment for Multiple Myeloma: Report - Follow-up Tumor: Assessment (new)**

| | |
|---|---|
| **SERUM M-PROTEIN** | |
| Date of SPEP | ... |
| SPEP not done | ☐ |
| **Monoclonal protein, electrophoresis, serum** | g/dL (xx.x) |
| Too small to quantify | ☐ |
| **Date of immunofixation** | ... |
| Immunofixation not done | ☐ |
| **Monoclonal protein, immunofixation electrophoresis, serum** | ○ Negative ○ Positive |
| **Free light chains, Freelite assay, serum** | |
| Kappa free light chain | mg/dL (xxxxx.xx) |
| Lambda free light chain | mg/dL (xxxxx.xx) |
| Kappa/lambda ratio *(derived)* | (xxxxx.xx) |
| Kappa/lambda difference (dFLC) | mg/dL (xxxxx.xx) |
| **Quantitative Immunoglobulins** | |
| Immunoglobulin G (IgG), serum | mg/dL (xxxxx) |
| Immunoglobulin A (IgA), serum | mg/dL (xxxxx) |
| Immunoglobulin M (IgM), serum | mg/dL (xxxxx) |
| Immunoglobulin D (IgD), serum | mg/dL (xxxxx) |
| Immunoglobulin E (IgE), serum | mg/dL (xxxxx) |
| **Light chain, serum** | ... |
| **Heavy chain, serum** | ... |
| **URINE M-PROTEIN** | |
| Date of 24-hour UPEP | ... |
| 24-hour UPEP not done | ☐ |
| **Monoclonal protein, electrophoresis, urine** | mg/24.h (xxxxx) |
| Too small to quantify | ☐ |
| **Date of immunofixation** | ... |
| Not done | ☐ |
| **Monoclonal protein, immunofixation electrophoresis, urine** | ○ Negative ○ Positive |
| **Urine volume** | ml/24.h (xxxx) |
| **Urine total protein** | mg/24.h (xxxx) |
| **Urine light chain** | ... |

Required for all eligible patients; date must be within 60 days prior to registration to Step 2

Confirm value is entered in mg/dL rather than mg/L. If your site reports in mg/L, convert value by dividing by 10

Derived by Rave

Required for all eligible patients. Date must be within 60 days prior to Step 2 registration

**BONE MARROW PLASMACYTOSIS**

Bone Marrow Biopsy Date ... (Required for all eligible patients. Date must be within 60 days prior to Step 2 registration)

Biopsy type ...

Cellularity, %, bone marrow (xxx)

Plasma cells, %, bone marrow (xxx)

Monoclonal cells in bone marrow ○ Present ○ Absent

**BONE DISEASE**

Serum calcium date ...

Not done ☐

Calcium, serum mg/dL (xx.xx)

Did the patient have a PET scan, MRI, CT, or skeletal survey? ○ Yes ○ No

If yes, please specify type and date *(check all that apply)*

PET scan ☐ (Required for all eligible patients. Date must be within 60 days prior to registration to Step 2)

PET scan date ...

MRI ☐

MRI date ...

CT ☐

CT date ...

Skeletal survey ☐

Skeletal survey date ...

Number of lytic lesions ...

Compared to last survey, bone health is ...

**PLASMACYTOMAS**

Soft tissue plasmacytomas? ...

*Please record the requested information for all plasmacytomas present. List the plasmacytomas in the same o each assessment.*

| # | Site of lesion | Greatest measurement | Greatest perpendicular measurement | Assessment date |
|---|---|---|---|---|
| 1 | | cm (xx.x) | cm (xx.x) | ... |

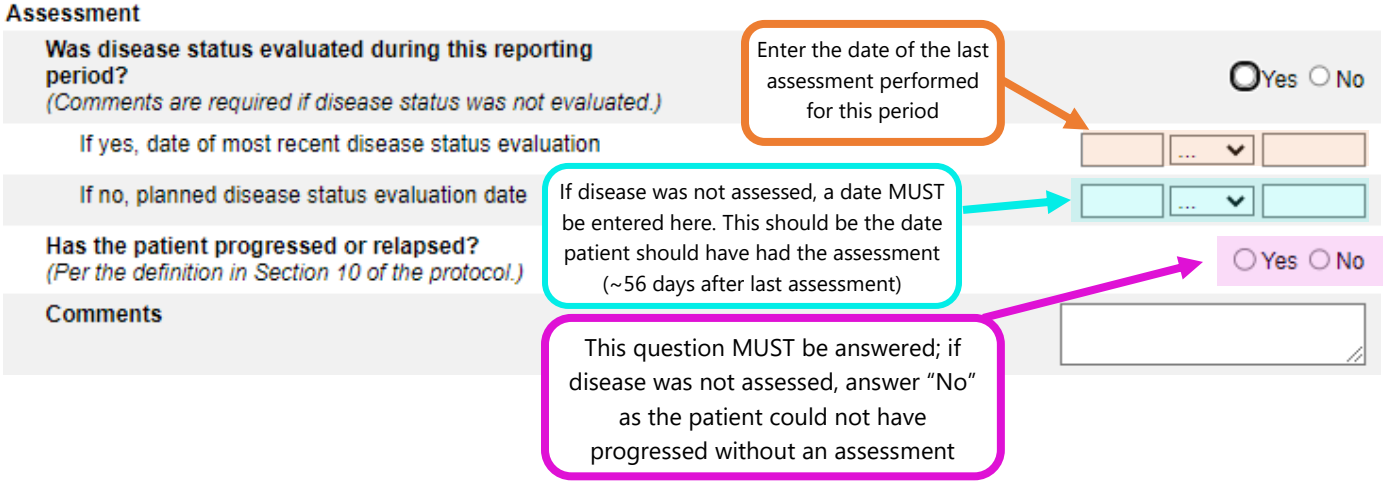
Add a new Log line Inactivate

Has the patient had a confirmed progression per the definition in Section 10.0 of the protocol? ○ Yes ○ No

Comments (If patient had plasmacytoma (soft or bony) at time of diagnosis, please enter comment if it has fully resolved. If it has not fully resolved, please enter the lesion site and measurements (if available))

# Ongoing Follow-up Tumor Assessments (FUTA)

Page: **Follow-Up Tumor Assessment for Multiple Myeloma: Assessment - Follow-up Tumor: Assessment**




**General notes for follow-up tumor assessments:**

- Only numeric values can be entered on this form
  - If a result is provided with "<", please enter the whole number in the field, and enter a comment at the bottom of the field stating "Resulted as <5"
- Disease assessments are due every other cycle (approximately every 56 days)
- Assessments only documenting the IgG value are not to be entered in Rave as a separate follow-up tumor assessment. Only enter the IgG value with a complete disease assessment
- It is site's discretion whether to follow at odd or even cycles
  - If pre-registration step 2 assessment was completed within 30 days of registration, it is advised that patient be followed at the end of cycle 1 (prior to cycle 2) and at the end of odd cycles going forward.
  - If pre-registration step 2 assessment utilized the full 60-day window, it is advised that patient have disease assessed prior to C1D1 and prior at the end of each even cycle going forward.
- If a patient's IFE (immunofixation) result is negative, we expect the monoclonal protein value to be "0"
  - Immunofixation is a more sensitive test that confirms or rules out the presence of monoclonal protein.
  - If SPEP or UPEP result states "trace amounts" or "possible monoclonal protein" etc., but the IFE result is negative, the monoclonal protein value should be entered as "0" rather than "too small to quantify"
- Patients with measurable disease at diagnosis by UPEP (≥200 mg/24hr) **MUST** be followed by 24-hour UPEP at EACH disease assessment for the duration of the study
- All patients are to complete 24-hour UPEP performed at the protocol defined bone marrow biopsy time points (12, 24, 36, 48 months after registration to Step 2).
  - If complete response (as defined by section 10 of the protocol) is seen, a second 24-hour UPEP should be completed to confirm the patient's response
- Only radiology reports and pathology reports completed at the disease assessment are to be uploaded to Source Documentation. It is not necessary to upload other assessment results.

Page: **Follow-Up Tumor Assessment for Multiple Myeloma: Report - Follow-up Tumor: Assessment (new)**

| | |
|---|---|
| **SERUM M-PROTEIN** | |
| **Date of SPEP** | ... |
| SPEP not done | ☐ |
| **Monoclonal protein, electrophoresis, serum** | g/dL (xx.x) |
| Too small to quantify | ☐ |
| **Date of immunofixation** | ... |
| Immunofixation not done | ☐ |
| **Monoclonal protein, immunofixation electrophoresis, serum** | ○ Negative ○ Positive |
| **Free light chains, Freelite assay, serum** | |
| Kappa free light chain | mg/dL (xxxxx.xx) |
| Lambda free light chain | mg/dL (xxxxx.xx) |
| Kappa/lambda ratio *(derived)* | (xxxxx.xx) |
| Kappa/lambda difference (dFLC) | mg/dL (xxxxx.xx) |
| **Quantitative Immunoglobulins** | |
| Immunoglobulin G (IgG), serum | mg/dL (xxxxx) |
| Immunoglobulin A (IgA), serum | mg/dL (xxxxx) |
| Immunoglobulin M (IgM), serum | mg/dL (xxxxx) |
| Immunoglobulin D (IgD), serum | mg/dL (xxxxx) |
| Immunoglobulin E (IgE), serum | mg/dL (xxxxx) |
| **Light chain, serum** | ... |
| **Heavy chain, serum** | ... |
| **URINE M-PROTEIN** | |
| **Date of 24-hour UPEP** | ... |
| 24-hour UPEP not done | ☐ |
| **Monoclonal protein, electrophoresis, urine** | mg/24.h (xxxxx) |
| Too small to quantify | ☐ |
| **Date of immunofixation** | ... |
| Not done | ☐ |
| **Monoclonal protein, immunofixation electrophoresis, urine** | ○ Negative ○ Positive |
| **Urine volume** | ml/24.h (xxxx) |
| **Urine total protein** | mg/24.h (xxxx) |
| **Urine light chain** | ... |

Confirm value is entered in mg/dL rather than mg/L. If your site reports in mg/L, convert value by dividing by 10

Derived by Rave

**BONE MARROW PLASMACYTOSIS**

Bone Marrow Biopsy Date [ ] [...] [ ]

Biopsy type [...]

Cellularity, %, bone marrow [ ] (xxx)

Plasma cells, %, bone marrow [ ] (xxx)

Monoclonal cells in bone marrow ○ Present ○ Absent

Required for ALL patients at 12, 24, 36 and 48 months after registration to Step 2

**BONE DISEASE**

Serum calcium date [ ] [...] [ ]

Not done ☐

Calcium, serum [ ] mg/dL (xx.xx)

Did the patient have a PET scan, MRI, CT, or skeletal survey? ○ Yes ○ No

If yes, please specify type and date *(check all that apply)*

PET scan ☐

PET scan date [ ] [...] [ ]

MRI ☐

MRI date [ ] [...] [ ]

CT ☐

CT date [ ] [...] [ ]

Skeletal survey ☐

Skeletal survey date [ ] [...] [ ]

If radiology was performed as clinically indicated, complete this section and upload source documentation

Number of lytic lesions [...]

Compared to last survey, bone health is [...]

**PLASMACYTOMAS**

Soft tissue plasmacytomas? [...]

*Please record the requested information for all plasmacytomas present. List the plasmacytomas in the same o each assessment.*

| # | Site of lesion | Greatest measurement | Greatest perpendicular measurement | Assessment date |
|---|---|---|---|---|
| 1 | | cm (xx.x) | cm (xx.x) | [ ] [...] |

Add a new Log line Inactivate

Has the patient had a confirmed progression per the definition in Section 10.0 of the protocol? ○ Yes ○ No

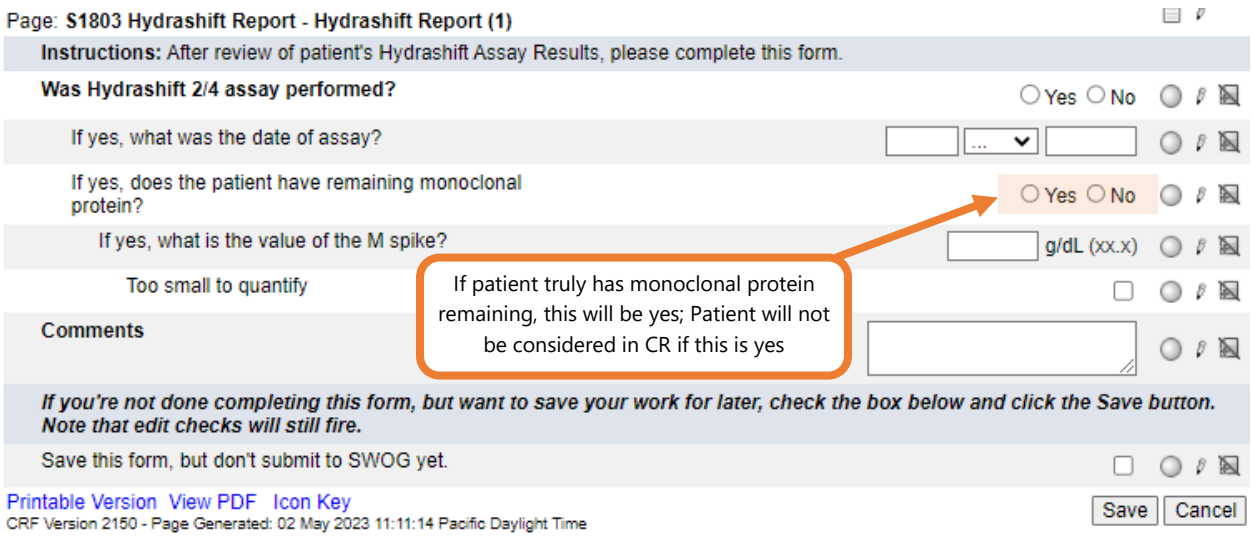
Comments

Use the comments field to enter any additional information not captured or explained in the form above

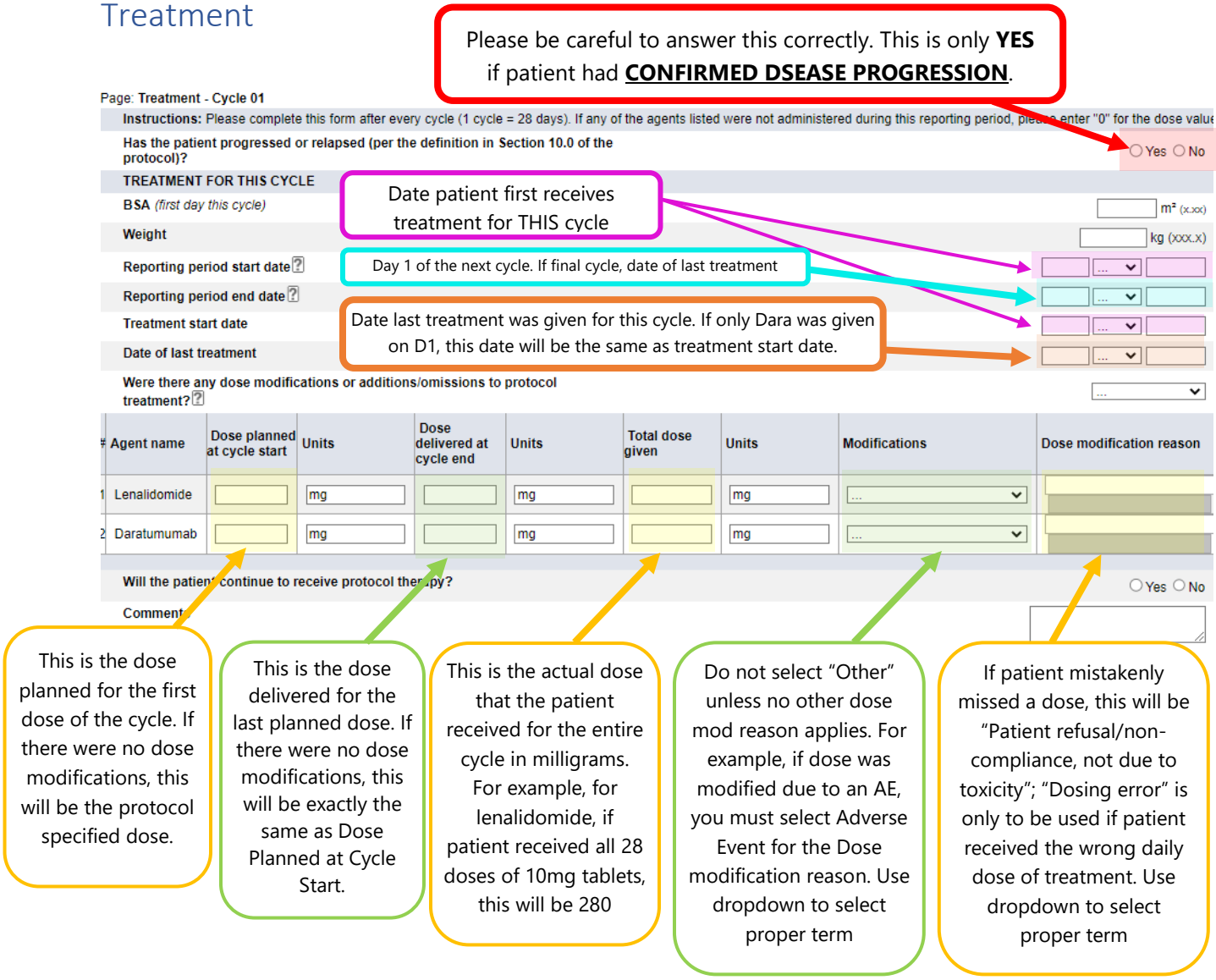
# Hydrashift Report

**Instructions**

- Patients registered to Arm 1 or Arm 1b with IgG Kappa Myeloma may experience daratumumab interference on immunofixation which may provide a false VGPR response when patient is actually in CR
- To rule this out, these patients will have a hydrashift assay performed at the timepoints of bone marrow biopsies (prior to starting C1D1 for the pre-registration to Step 2 timepoint), 12 months, 24 months, 36 months and 48 months after registration to Step 2.
    - Results will be entered in Rave by using the Add Event function to add the Hydrashift Report
- The assay may be known as a few different names:
    - Hydrashift 2/4 Assay
    - Immunofixation, Daratumumab-Specific, Serum
    - Daratumumab specific IFE reflex assay
    - Daratumumab – specific immunofixation electrophoresis reflex assay
    - Daratumumab interference reflex assay
- Assay is to be completed locally; sites will be reimbursed for protocol specified timepoints
- If patient had the assessment completed at a different timepoint that is not specified per protocol, please enter results on the form.



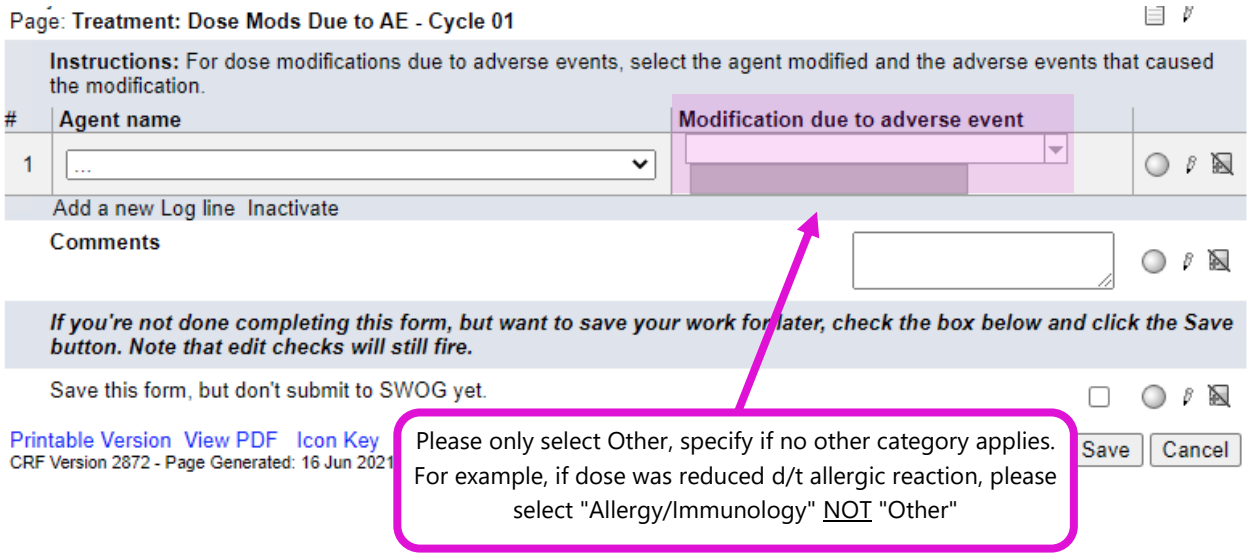
# Treatment


Please be careful to answer this correctly. This is only **YES** if patient had **CONFIRMED DSEASE PROGRESSION**.
Page: Treatment - Cycle 01
Instructions: Please complete this form after every cycle (1 cycle = 28 days). If any of the agents listed were not administered during this reporting period, please enter "0" for the dose value
Has the patient progressed or relapsed (per the definition in Section 10.0 of the protocol)?
Yes No
TREATMENT FOR THIS CYCLE
BSA (first day this cycle)
m² (x.xx)
Weight
kg (xxx.x)
Reporting period start date
Reporting period end date
Treatment start date
Date of last treatment
Date patient first receives treatment for THIS cycle
Day 1 of the next cycle. If final cycle, date of last treatment
Date last treatment was given for this cycle. If only Dara was given on D1, this date will be the same as treatment start date.
Were there any dose modifications or additions/omissions to protocol treatment?
# Agent name
Dose planned at cycle start
Units
Dose delivered at cycle end
Units
Total dose given
Units
Modifications
Dose modification reason
1 Lenalidomide
mg
mg
mg
2 Daratumumab
mg
mg
mg
Will the patient continue to receive protocol therapy?
Yes No
Comment
This is the dose planned for the first dose of the cycle. If there were no dose modifications, this will be the protocol specified dose.
This is the dose delivered for the last planned dose. If there were no dose modifications, this will be exactly the same as Dose Planned at Cycle Start.
This is the actual dose that the patient received for the entire cycle in milligrams. For example, for lenalidomide, if patient received all 28 doses of 10mg tablets, this will be 280
Do not select "Other" unless no other dose mod reason applies. For example, if dose was modified due to an AE, you must select Adverse Event for the Dose modification reason. Use dropdown to select proper term
If patient mistakenly missed a dose, this will be "Patient refusal/non-compliance, not due to toxicity"; "Dosing error" is only to be used if patient received the wrong daily dose of treatment. Use dropdown to select proper term

**Treatment notes**

- Reporting period end date should always be Day 1 of the next cycle Reporting this way ensures the patient's treatment is reported completely through this cycle and into the next
    - One way to think about this is we follow the patient on C1 until 12:00, and begin following for C2 at 12:01.
        - The next cycle reporting period start date should be the same as the reporting period end date of the previous cycle.
        - Usually the day after date of last treatment
- Treatment start date: Date patient first takes treatment for the cycle
- Treatment end date: Date patient takes last dose of treatment (in most cases for this study, the last dose date of Lenalidomide) in the cycle.
    - If patient is only on Dara, may be the same date as treatment start date
- Dose planned at cycle start
    - Daily dose planned at start of cycle
    - If patient did not receive an agent, enter "0"
- Dose delivered at cycle end
    - Daily dose that was given at the end of the cycle
        - This allows us to document if a patient down-dosed in the middle of a cycle due to AE or other reason
    - If patient did not receive an agent, enter "0"
- Total dose given
    - Sum of the daily doses received.
        - If a cycle is extended or shortened for some reason, please be sure to account for this in the total dose given
            - For example, if a cycle was 26 days rather than 28 days due to scheduling, the patient Lenalidomide total dose would be 260 rather than 280 (if dosing 10mg/day every day)
            - If a patient missed 2 doses due to accidentally forgetting, this would also be 260 rather than 280 (if dosing 10mg/day)
            - If a cycle was extended for some reason and patient continued to dose, ALL doses must be included in the total dose given. If a patient dosed for 30 days, the total dose given would be 300 (if dosing 10mg/day and did not miss any doses)
        - The dates of treatment (Treatment start date and date of last treatment) are used by the SDMC to calculate the expected total dose given. If this does not add up, a dose modification must be entered and a comment given as to why the totals do not match.
    - Daratumumab total dose given changes depending on the cycle and how many doses were received within the cycle.
    - If patient did not receive an agent, enter "0"
- Modification
    - If a patient accidentally skips a dose, the dose modification should be "Patient refusal/non-compliance (not due to toxicity)"
    - If a patient did not take a dose due to an AE (related to treatment or not) the dose modification should be "Adverse Event"
    - Doses missed should not be made up, per protocol
- Will the patient continue to receive protocol therapy?
    - Answering "yes" to this question is the only way to get the next cycle to roll out.
    - When answered "no", the off-treatment form will populate instead of the next treatment cycle.

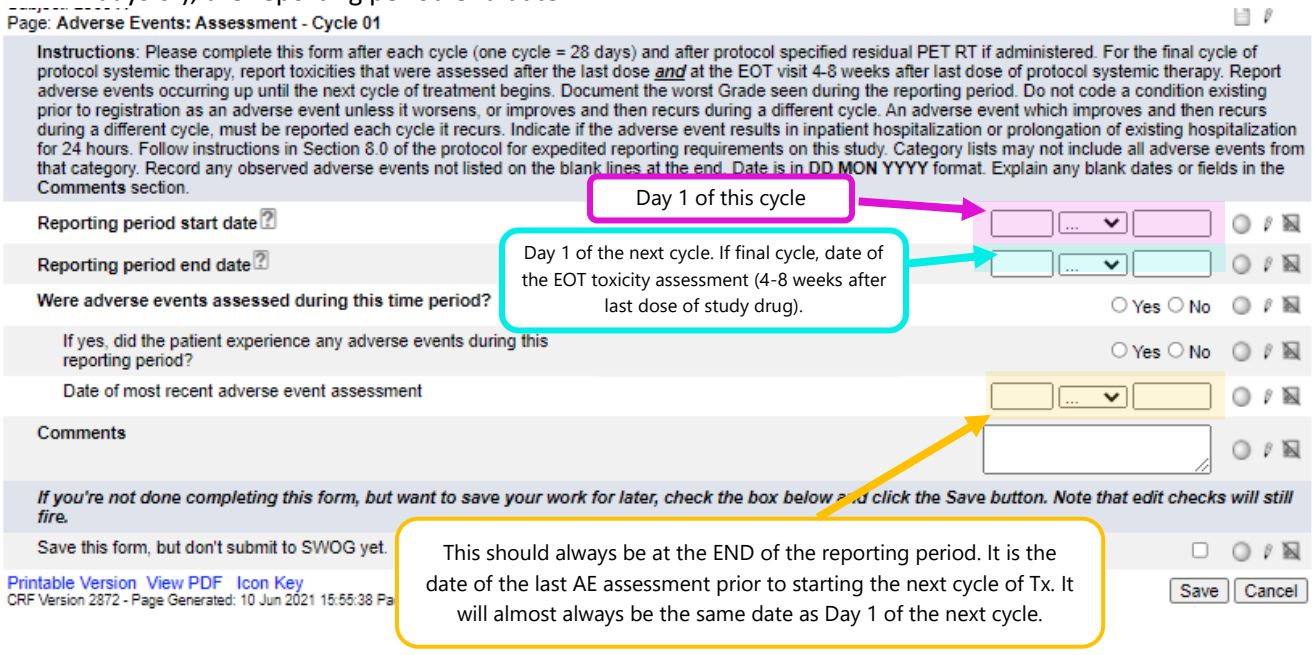
# Dose Mods due to AE




# Adverse Events

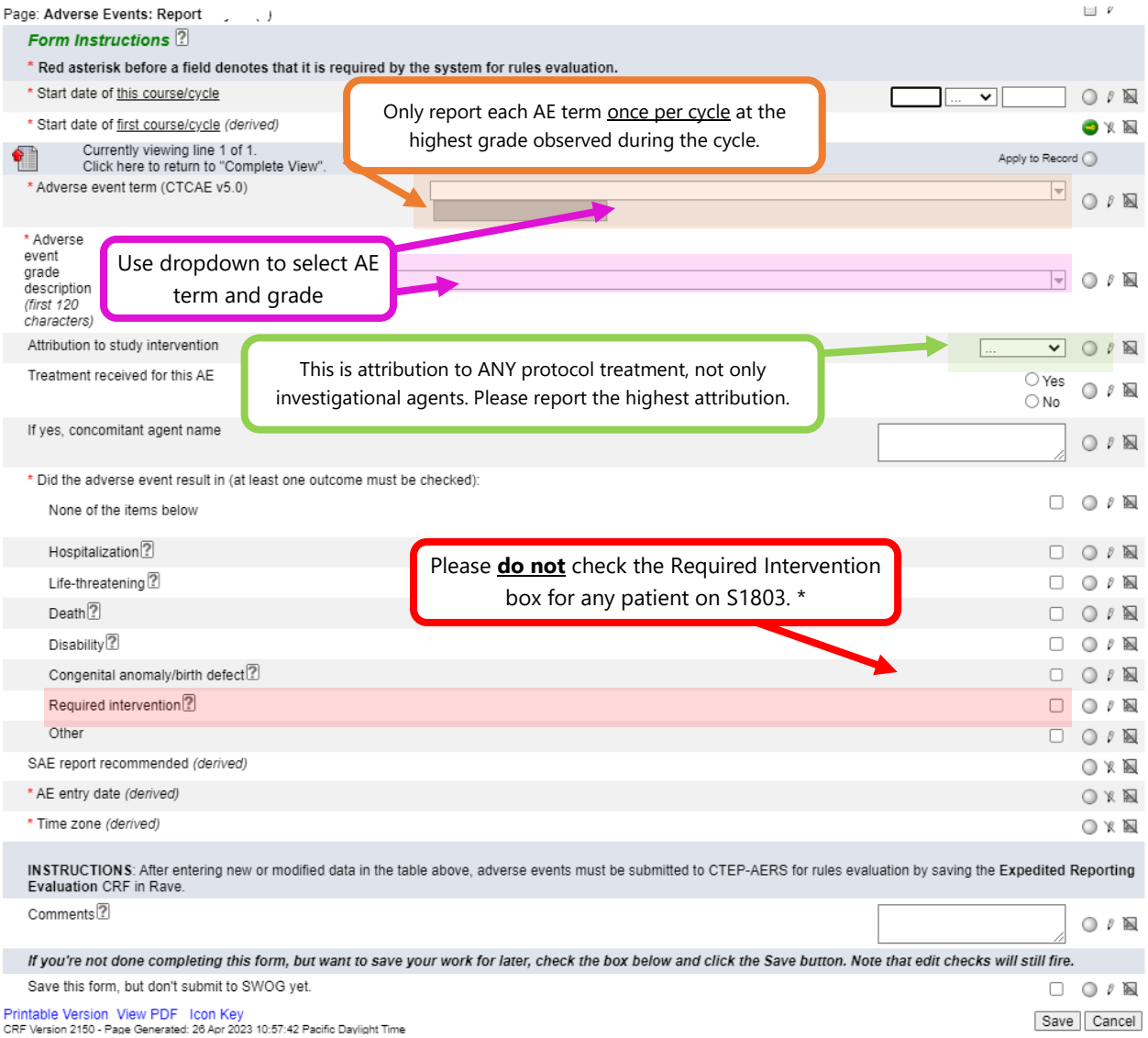
**Adverse Events: Assessment**

- Reporting period start and end date should match the dates entered on the treatment form.
- Date of most recent adverse event assessment should be the same, or very close to (within 5 days of), the reporting period end date.

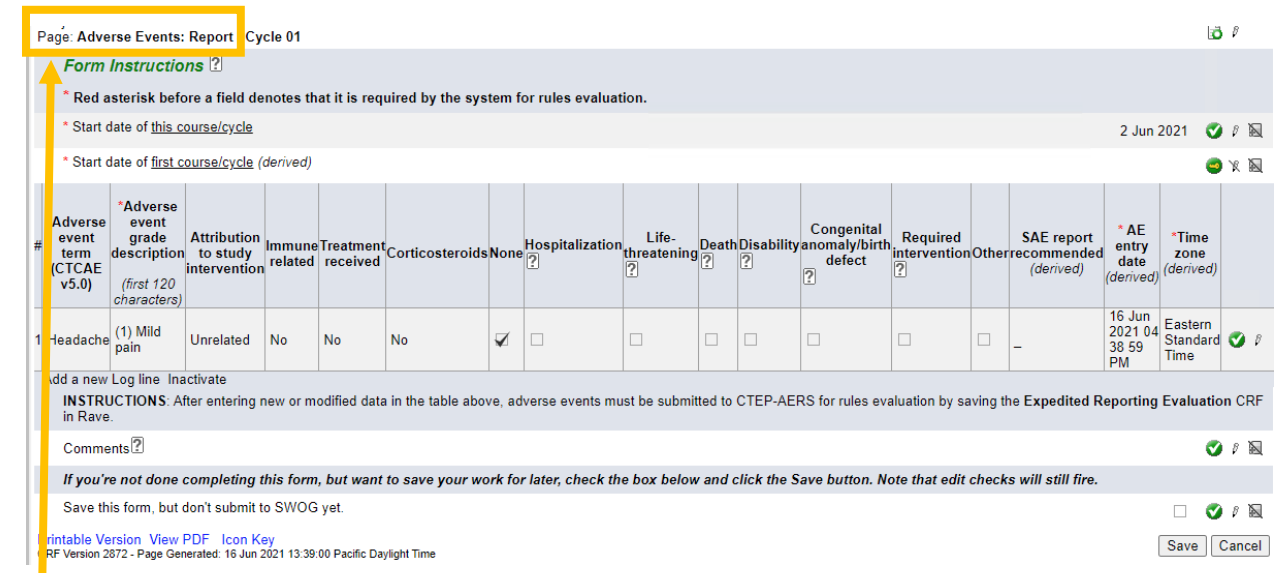


**Adverse Events: Report**

- All AEs should match a dropdown that matches a CTCAE V5 term. Beginning to type the event name should bring up options to select
    - Typing in the name of an AE without selecting from the drop down will result in "non-conformant data"
    - The grade should also be selected with the dropdown.
    - The "other, specify" option should *only* be used if there is no other CTCAE term applicable to the AE
- Only the highest grade seen in a cycle should be reported
    - If a patient experienced fatigue grade 2 that resolved and then re appeared later in the cycle at grade 1, only the grade 2 instance would be reported
- All AEs seen in a cycle should be reported in that cycle regardless of when the AE began (with the exception of AEs present at baseline prior to starting treatment that remain unchanged).
    - Ongoing AEs should be reported in each cycle that they are seen.




***The AE form above is a standard form for studies with CTEP-AERS integration. The "Required Intervention" checkbox is only for device trials. S1803 is not a device trial, so it should never be checked for patients on S1803.***



Page: **Adverse Events: Report** Cycle 01

***Form Instructions***

* **Red asterisk before a field denotes that it is required by the system for rules evaluation.**

* Start date of this course/cycle 2 Jun 2021

* Start date of first course/cycle *(derived)*

| # | Adverse event term (CTCAE v5.0) | *Adverse event grade description *(first 120 characters)* | Attribution to study intervention | Immune related | Treatment received | Corticosteroids | None | Hospitalization | Life-threatening | Death | Disability | Congenital anomaly/birth defect | Required intervention | Other | SAE report recommended *(derived)* | * AE entry date *(derived)* | *Time zone *(derived)* | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Headache | (1) Mild pain | Unrelated | No | No | No | ☑ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | – | 16 Jun 2021 04 38 59 PM | Eastern Standard Time | |

Add a new Log line Inactivate

**INSTRUCTIONS**: After entering new or modified data in the table above, adverse events must be submitted to CTEP-AERS for rules evaluation by saving the **Expedited Reporting Evaluation** CRF in Rave.

Comments

***If you're not done completing this form, but want to save your work for later, check the box below and click the Save button. Note that edit checks will still fire.***

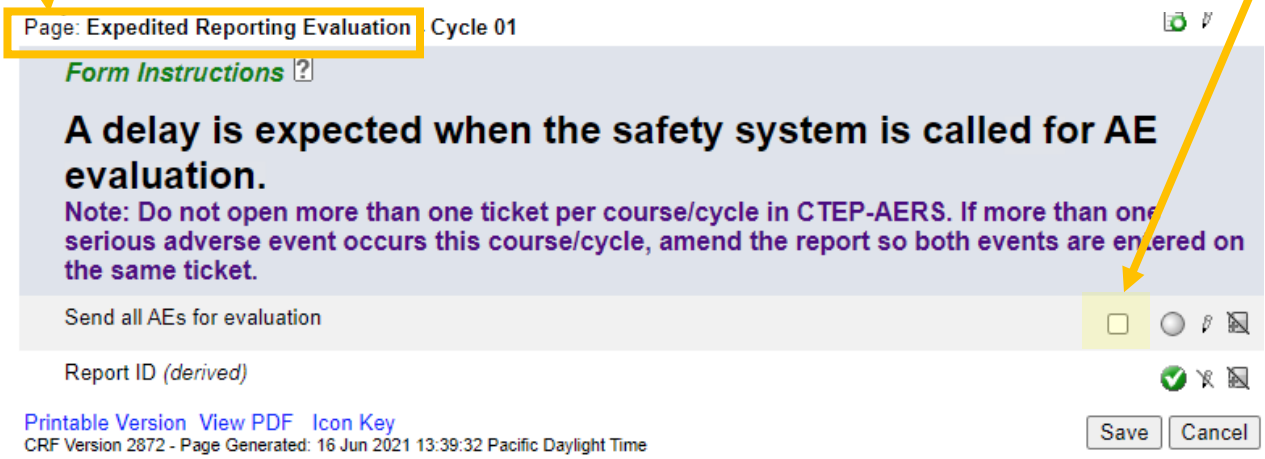
Save this form, but don't submit to SWOG yet. ☐

Printable Version View PDF Icon Key

CRF Version 2872 - Page Generated: 16 Jun 2021 13:39:00 Pacific Daylight Time

Save Cancel

**These two forms are linked to each other. Any time you enter or amend data on the *Adverse Events: Report (top)* form, you must run the *Expedited Reporting Evaluation (bottom)* form by checking the "Send all AEs for evaluation" checkbox and saving the form.**



Page: **Expedited Reporting Evaluation** Cycle 01

***Form Instructions***

**A delay is expected when the safety system is called for AE evaluation.**

**Note: Do not open more than one ticket per course/cycle in CTEP-AERS. If more than one serious adverse event occurs this course/cycle, amend the report so both events are entered on the same ticket.**

Send all AEs for evaluation ☐

Report ID *(derived)*

Printable Version View PDF Icon Key

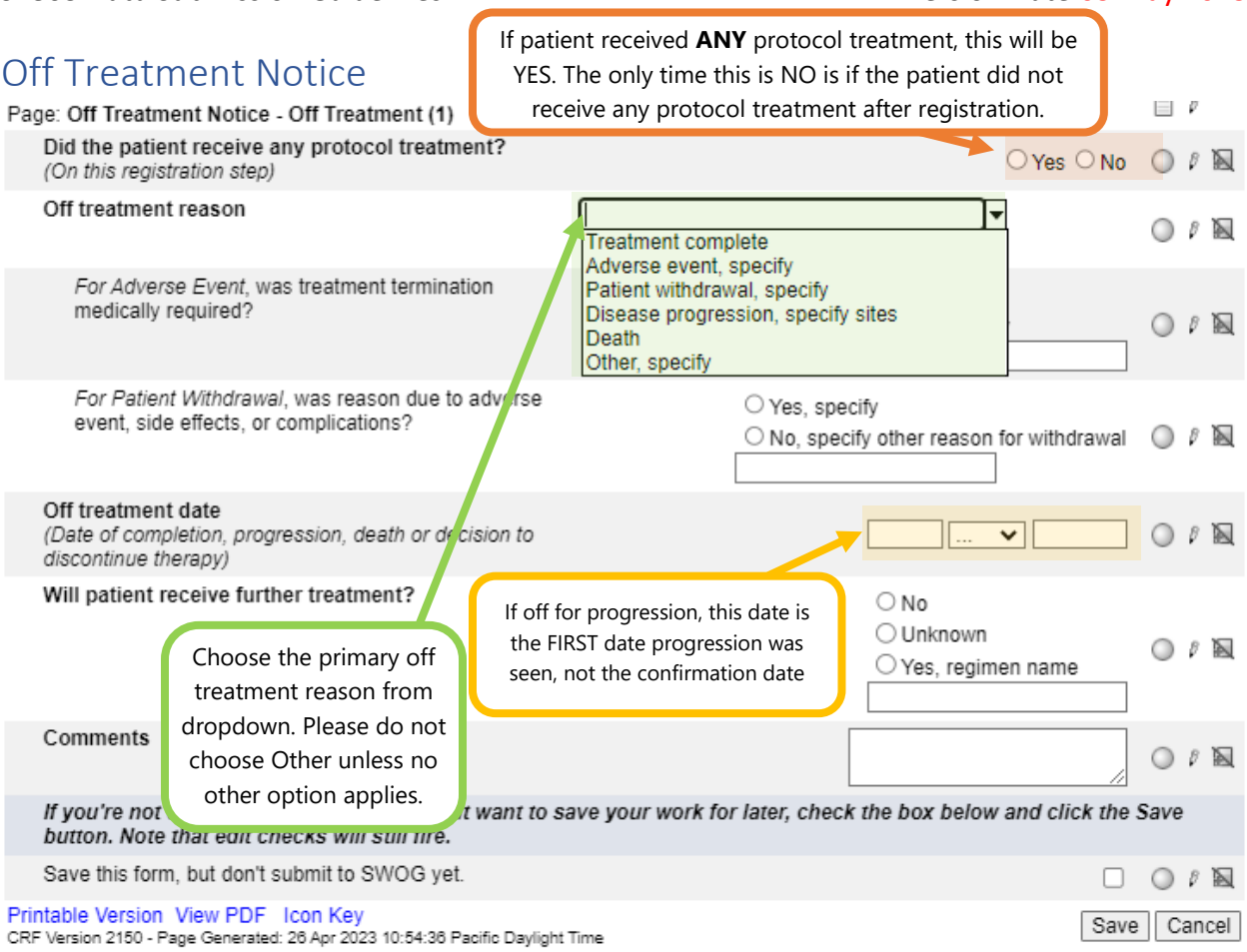
CRF Version 2872 - Page Generated: 16 Jun 2021 13:39:32 Pacific Daylight Time

Save Cancel

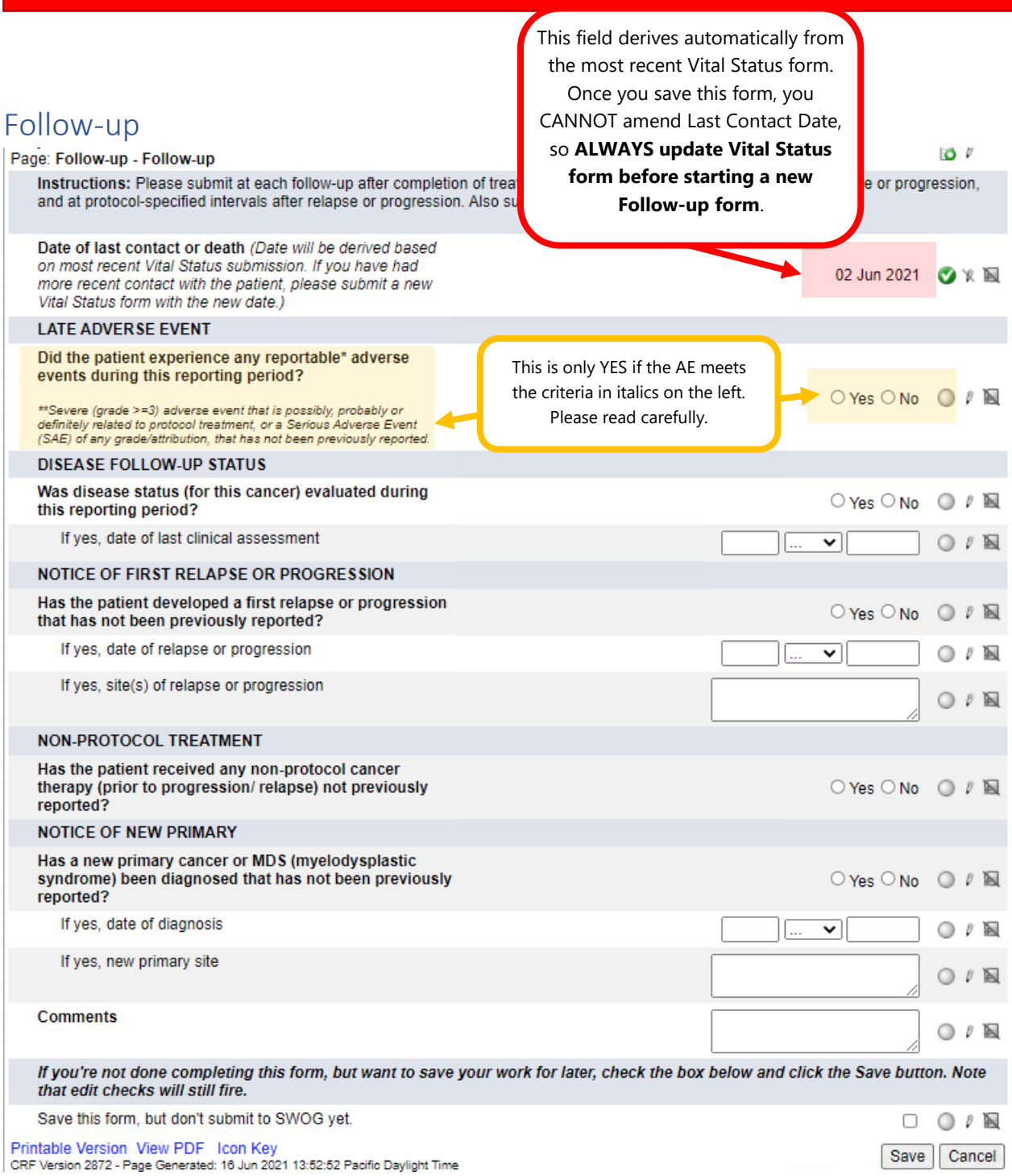
In the event your PI disagrees with the suggestion for an expedited report, you can amend the answer to the Recommended action for report field to "NONE" rather than "CREATE"

If there is any question about the reportability of an SAE, please refer to protocol section 16, or contact the SAE Program Manager at the Operations Office, 210/614-8808 or adr@swog.org, before preparing the report.

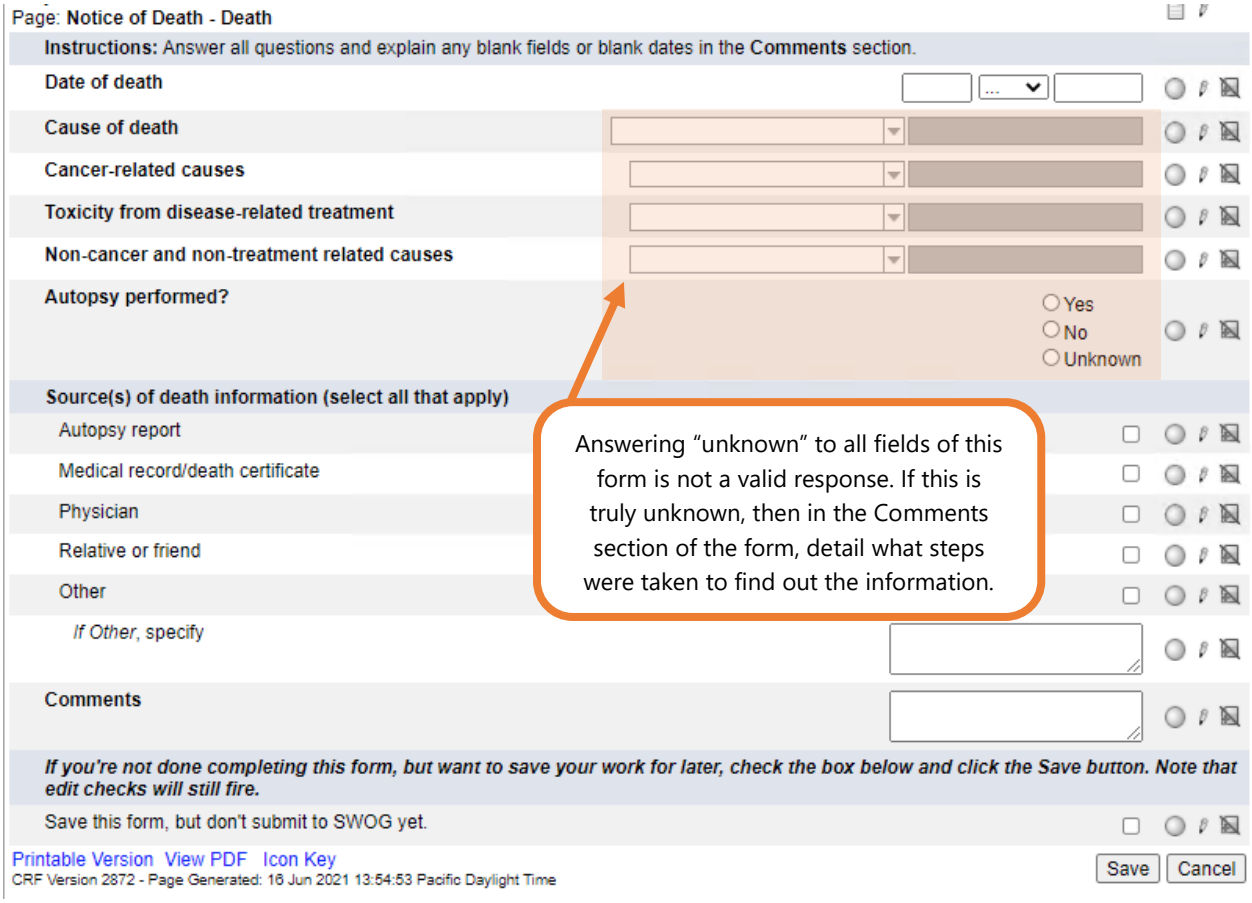
# Off Treatment Notice



**DO NOT MAKE ANY ENTRIES ON THE FOLLOW-UP FORM UNTIL YOU HAVE UPDATED THE VITAL STATUS FORM.**

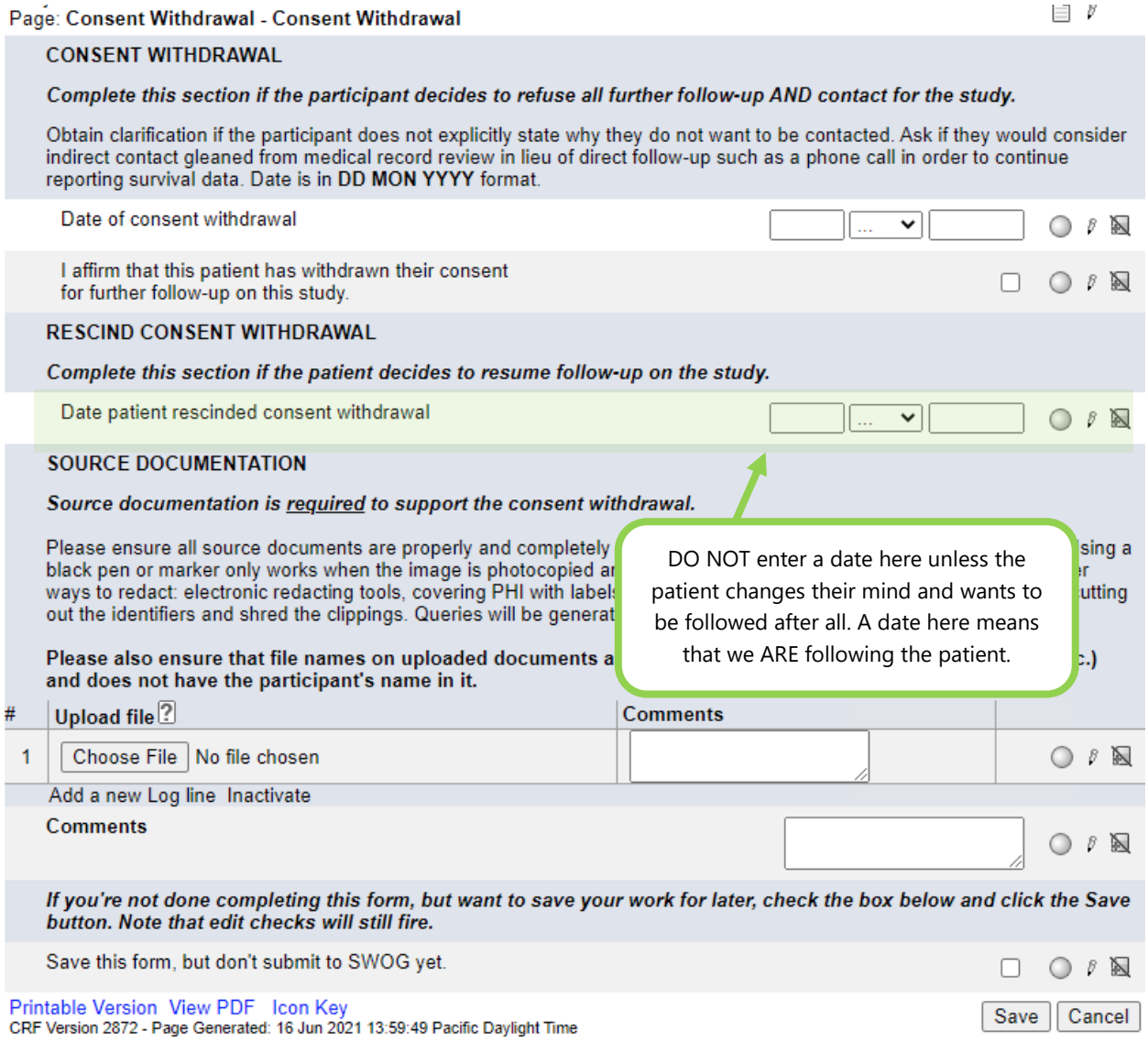


# Notice of Death



# Consent Withdrawal

This form can only be populated by the SWOG Data Coordinators. If the patient has withdrawn **all** consent **including follow-up and survival**, then please email MyelomaQuestion@crab.org.



# Specimen Submission Tips


If a specimen cannot be submitted (and will never be submitted), use this link to document that the specimen will not be submitted.

**If you have questions about how to log and ship specimens in the Specimen Tracking System, there are written instructions and a training video linked on the home page in STS (you may need to scroll down a bit to find them). If this resource does not answer your question, please reach out to MyelomaQuestion@crab.org.**

**Bone marrow biopsy/aspirate details**

- Specimens are to be collected and sent until patient progression.
- Step 1 Pre-Reg refers to the patient's initial diagnostic bone marrow sample
    - Archival slides or a commercially completed NGS report must be sent to Adaptive for ID clonality testing for future MRD tests
        - If Archival slides or commercially completed report fail testing or result in polyclonal results, future MRD samples should not be submitted to Adaptive as they cannot run these samples without the archival analysis.
        - Archival samples should be from prior to any treatment to allow the study team to assess patients' initial disease status and to confirm the patient meets diagnostic criteria from section 4.1
        - Slides should contain disease burden of 5% or greater
        - 3-5 Bone Marrow Aspirate smear slides OR 5-10 FFPE slides from bone marrow clot (target 40 microns of material; decalcified bone marrow core is not

acceptable). The slides must be of the same type (all BMA smears or all FFPE slides, not a mix of both types)
        - The sample may be exhausted in testing, meaning no material will remain to return
        - If contacted by the SDMC that results of the archival test failed or have a polyclonal result, sites will be asked to resubmit slides if available.
            - Use the Specimen Tracking System to create a new shipment for the slides and use the Baseline: Resubmission timepoint
            - Sites will be reimbursed for additional submissions
    - Results of the diagnostic biopsy (cellularity and plasma cell percentages) are entered on the Baseline tumor assessment eCRF.
    - Upload the pathology report to the Baseline Step 1: Source Documentation folder.
- Step 2 Pre-Reg refers to patient's post-transplant, pre-registration Step 2. This must be collected within 60 days prior to registration to Step 2 per eligibility criterion 5.2.e
    - Fresh aspirate should be shipped to Adaptive day of collection for MRD testing.
        - Results from this test are not required to register and begin treatment.
            - MRD results are blinded to the site until the 24-month timepoint at which point that result will be uploaded by the SWOG SDMC to the 24 Month MRD and Response form in Rave.
        - If the patient consented to optional biobanking, an additional sample must also be sent to Nationwide
        - Patients do not need to be registered to the study to send specimens. Please refer to the "Creating a patient ID through Spec Track" document for further instruction
    - Results from this biopsy must be entered on the first Follow-Up tumor assessment folder
        - This allows us to see the patient's response to induction/transplant therapies
        - Also allows us to see patient's status prior to beginning protocol therapy
    - Please upload this pathology report in the Baseline Step 2: Source documentation folder **and** the Source documentation folder for the first follow-up tumor assessment for ease of review of data for the study chair
    - Patients may have this specimen submitted prior to registration
        - Follow instructions from this document to obtain patient number prior to registration
- Other biopsy time points
    - 12 months post-registration to Step 2
        - **Biopsy must be done regardless of optional specimen consent. We want to see patients' disease response after 12 months of treatment**
            - Only the specimen submission to Adaptive is optional, **all** patients are to complete the 12-month bone marrow biopsy procedure to assess disease status after 12 months on protocol
            - Submission to Adaptive only occurs when patient has consented to optional biobanking
    - 24, 36, and 48 months post-registration to Step 2
        - Submit fresh aspirate to Adaptive on same day as collection
        - 24-month biopsy should be planned to allow time for sites to receive MRD results
            - MRD results are entered on the 24 Month MRD and Response Assessment eCRF by SDMC Staff. Sites will also receive an email indicating the results are ready for review on the SWOG Reports page.

- If patient is MRD-negative and in VGPR or better, patient will be re-randomized to Step 3 to either continue treatment, or stop treatment
- If patient is MRD-positive, patient will remain on assigned study treatment
- If Archival specimens were not available or did not provide an ID clone, patient will be considered MRD-positive and remain on assigned treatment
- See "Step 3 Registration Overview and Procedures" document for additional Step 3 registration information

## Other helpful tips

- The "Best Practices" document on the CRA workbench is a very valuable tool recommended for printing, or keeping handy.
- For study related questions, use the distribution list myelomaquestion@crab.org to ensure a data manager receives your questions. You may also call 206-652-2267.
- An Intake calendar/ pill tracker is available in the appendix of the protocol. Sites using the CIRB are required to use the provided intake calendar.
- The CRA workbench is a very helpful resource in general; please review for beneficial information.
- If something on a form was not completed and a system query generates, enter a comment at the bottom of the form to avoid additional queries from the SDMC