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Niraparib Efficacy in patients with unresectable Mesothelioma: A randomised phase II trial of Niraparib versus active symptom control in patients with previously treated mesothelioma

eCRF Completion Guidelines

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Role	Name	Signature	Date
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For technical problems relating to Medidata Rave, please contact the Medidata help desk via email at: helpdesk@mdsol.com or by telephone on 0800 001 5212.



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1. DOCUMENT HISTORY

Version number	Effective date	Summary of changes	Author
1	30-JUN-2022	New Document	Lucy Johnson

2. GENERAL INSTRUCTIONS

Once logged on via www.imedidata.com, using your unique username and password, you will be directed to the Rave EDC home page where you will have access to the NERO study once all pre-requisite e-learning has been completed.

2.1 Navigation

Once you click into the NERO study you will see the Subject list for your site. The navigation bar at the top of the screen allows you to navigate between different studies (if you have access to more than one).



2.2 Icon Keys

Icon keys will appear at site, subject, form and question level. A table of common icons is shown below. Some icons can be used to show the current status of an entry (e.g. the “Complete” icon), or to show that corrective action is required on an entry (e.g. the “Query Open” icon), or to use as an “Action” button to make entries (e.g. the “Edit” icon).

Importance (1 = Highest, 10 = Least)	Icon	Description
1		Open Query
2		Answered Query
3		Read Only Opened Query
4		Non-Conformant Data
5		Requires Review
6		Requires Translation
7		Requires Verification
9		Overdue
10		Requires Coding
11		Requires Signature
12		Entered
13		Entering
14		Unsubmitted Form
15		Requires Data Freeze
16		Requires Data Lock
17		Data entry complete Locked

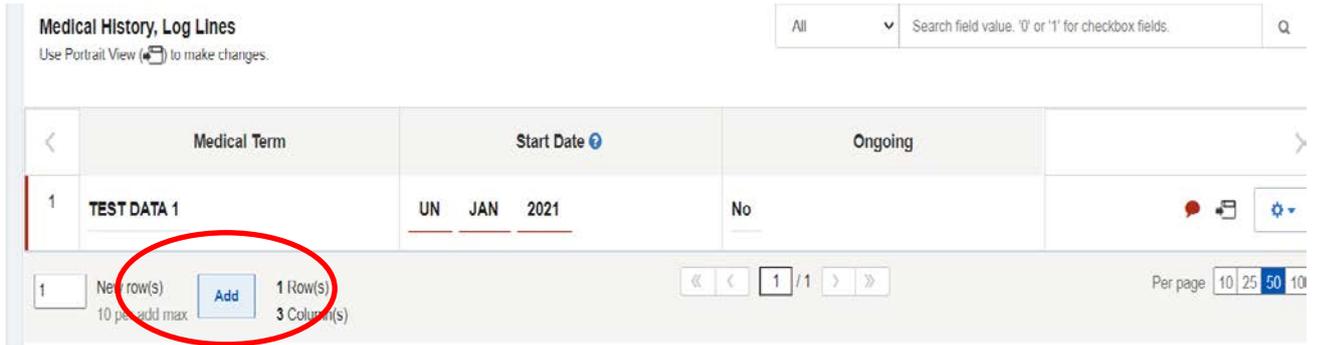
Important Note: Only some of these icon keys will be visible depending on your role.

2.3 Log Forms

The log form allows users to add additional entries to a single form. Each entry is a log line. By default, log forms display 20 log lines per page. This can be changed in the ‘My Profile’ section of Medidata. Log lines can be added, inactivated, and reactivated as described below.

Addition of a New Log Line

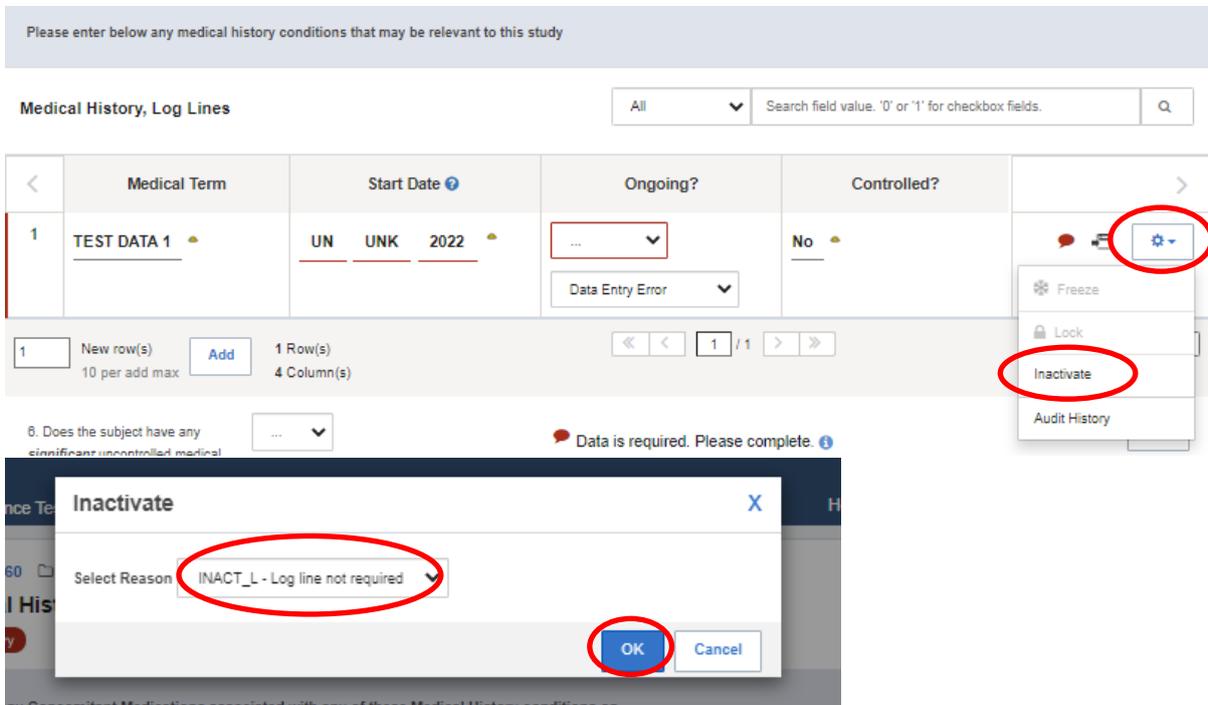
To add additional log lines within a log form, click on ‘Add’ (repeat process to add multiple records).



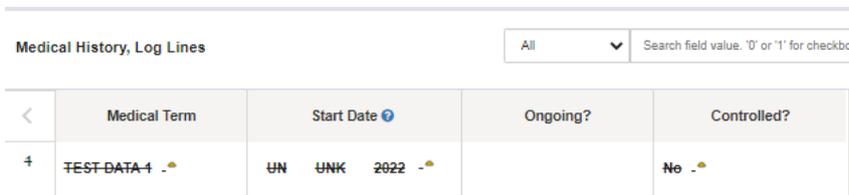
Inactivate/Activate Records

Records in a log form or an add entry table can be inactivated. This will not delete data or remove it from the form. It will always remain visible but will appear scored through.

To do this, select 'Inactivate' from the actions button (the cog wheel) on the right of the log line.



Select the reason for inactivating and click 'OK.' The record will appear scored through as below:



To reactivate a log line, select 'Reactivate' from the same cog wheel icon, enter the reason, and select 'OK.'

2.4 Answering Queries

You can respond to queries in two ways:

1. Modify the data in the data entry field and click save. No additional response is required.

2. Include an additional response in the user response field. Once an answer is entered click the 'Reply' button underneath the response field and this will then appear below the query.

2.5 Task Summary

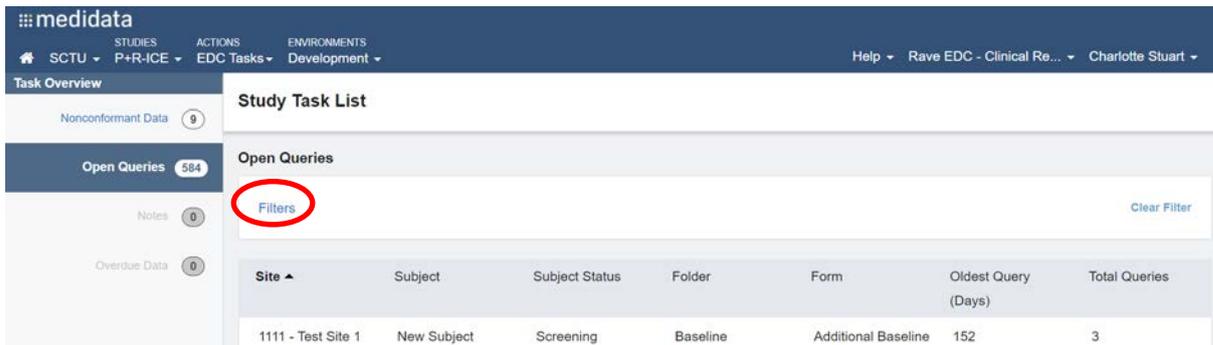
After entering data, it is a good idea to go into the "Task Summary" to see if any "Open Queries" can be resolved. The "Task Summary" can be accessed in two ways:

1. Via the actions tab at the top of the screen.
2. Via the patient overview page

1. Click on the 'Actions' tab at the top of the screen and select 'EDC Tasks'

You will then be able to see the options on the left to select tasks such as 'Nonconformant data' By clicking on this you will be able to see all the non-conformant data at your site.

These results can be narrowed down by patient, form, visit, etc by clicking on the 'Filters' button and selecting the result you want to look at.



- On the individual patient overview form, you will be able to see what actions need to be taken for the patient record you are viewing. The three circled examples below would show that this patient has not had their Physical Examination form entered at Cycle 2, that there are open queries on the LB Chemistry form at the Screening visit and that the LB Chemistry form at Cycle 1 has only partially been completed.

	Subject	AE/CM	Screening	Cycle 1	Cycle 2	End of Study
Subject Characteristics						
Medical History						
Treatment History			<input type="radio"/>			
Disease Characteristics			<input type="radio"/>			
Physical Examination			<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
Performance Status			<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	
Vital Signs			<input checked="" type="radio"/>			
LB Serology						
LB Chemistry				<input checked="" type="radio"/>	<input type="radio"/>	
LB Haematology			<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	

2.6 Changing Previously Entered and Saved Data

In case of data entry error or new data becoming available, it is possible to change entered and saved data by simply clicking into the field you wish to edit.

Important Note: Please do not record any subject-identifiable information in the eCRF pages, item comments or query responses, as it will be permanently stored in the audit trail. Please refer to a person's role or group if necessary, e.g. Research Nurse, Investigator, etc. Clinical Research Coordinator etc.

2.7 Audit History

The Audit history page can be utilised to see previous responses to queries, who entered or amended data and to add comments. To access the Audit history, click on the actions button (the cog wheel) on the right of the data point and click on 'Audit History' and you will see how the data point has changed, along with any queries/query responses and when these changes were made.



AU2-2222001 Screening

Date of Visit

Please ensure to record ALL new adverse events or concomitant medications for the participant at this visit

1. Did the visit take place? **Yes**

1.1. If "Yes", what is the visit date? dd / ... / yyyy

Save Cancel

Settings menu: Freeze Field, Lock Field, Audit History

DataPoint - 1. Did the visit take place?

Parent [Record - Date of Visit](#)

Siblings [DataPoint - 1. Did the visit take place?](#)

Audit	User	Time
User entered 'Yes (1)'	Charlotte Stuart (2513 - C_Stuart1)	02 Nov 2021 08:55:03

Comment

Submit

Cancel

While on the Audit trail page there is sometimes a choice of data points, so ensure the correct one is selected from the drop-down list before entering the comments e.g.:

Record - Medical History (1)

Parent [DataPage - Medical History](#)

Children [DataPoint - 1. Did the visit take place?](#)

Audit	User	Time
Record activated with code reason code Log line required.	Alex Allen (813 - apa1f131)	15 Nov 2021 15:13:10
Record inactivated with code reason code Log line not required.	Alex Allen (813 - apa1f131)	15 Nov 2021 15:12:18
Record created.	Charlotte Stuart (2513 - C_Stuart1)	02 Nov 2021 08:55:49

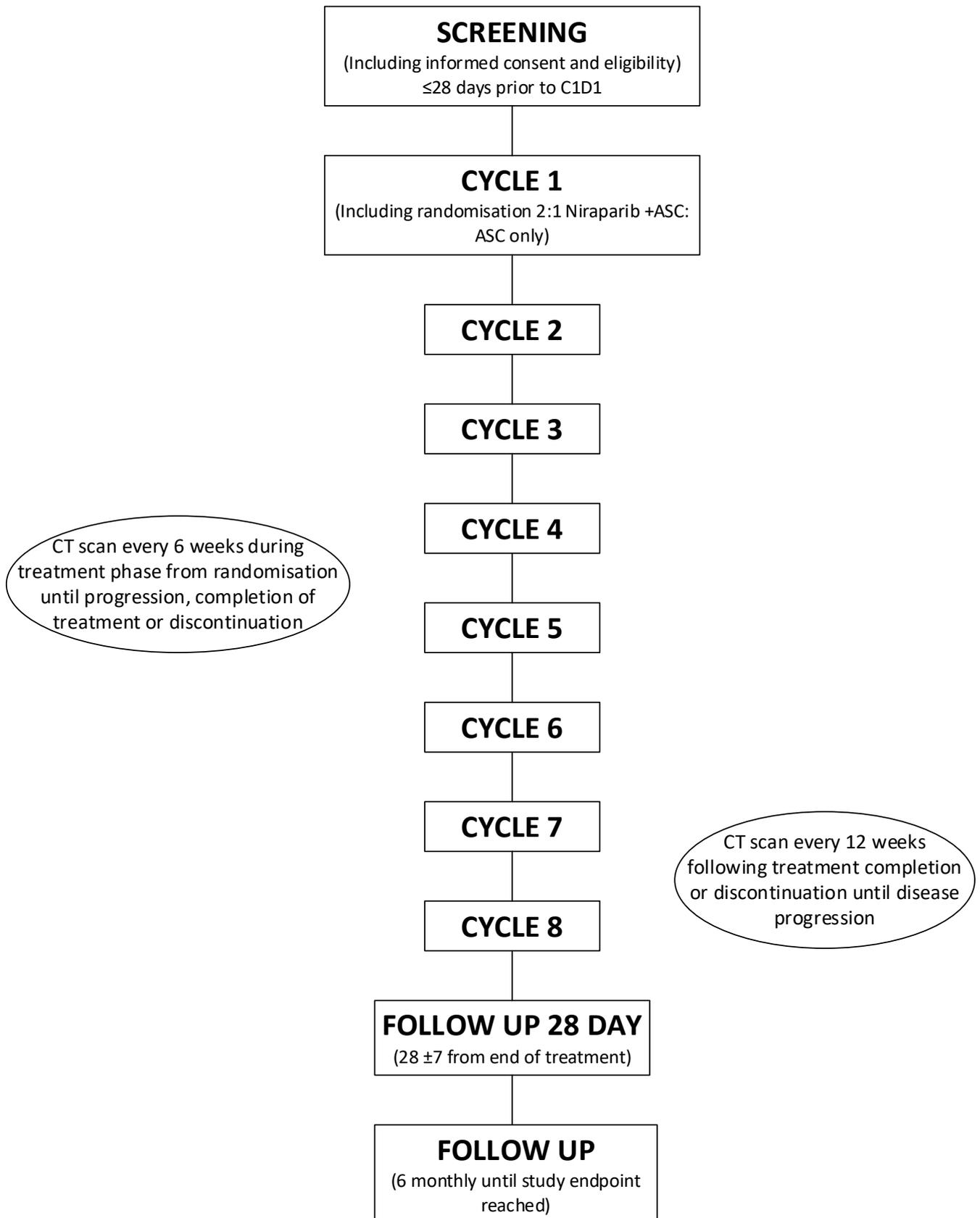
Drop-down menu options:

- ...
- DataPoint - 3. What is the start date of the medical history condition/event?
- DataPoint - 2. What is the term for the medical history condition/event?
- DataPoint - 4. Is the condition/event ongoing?

Cancel



3. OVERVIEW OF TRIAL VISITS





4. NERO SPECIFIC FORMS

Not all forms available within the database have been explained here, only those which have specific data requirements or a high likelihood of non-conformant data.

Please note that except for unknown concomitant medication start dates and previous treatment dates, exact dates for all other data items should be entered. Dates should be entered in the format DD MMM YYYY unless specified otherwise. If the day and month are not known, enter UN and UNK, e.g. 'UN UNK 2013'. Unknown years should be entered in the format '0001'.

When an assessment/procedure is recorded as being 'Not Done' a reason is requested. The reason(s) for it not being done e.g. 'Subject refused' should be supplied, rather than a duplicated statement 'not done'.

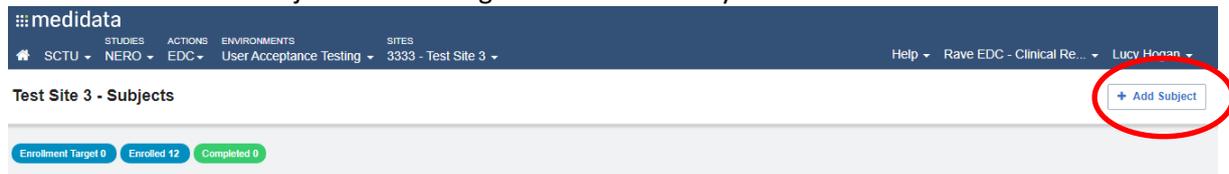
Help boxes are denoted by the  icon. These support data entry by indicating what data format certain data items should be in or they provide guidance on how to complete log lines where applicable. To view the help text, click on the icon.

Forms can be accessed using the overview panel in the centre of the subject screen or via the folder/form visit pane on the left-hand side of the subject screen.

At each visit, please ensure the Adverse Event form and the Concomitant Medications form are updated as applicable.

4.1 Adding a New Subject

Please click on 'Add Subject' which will generate the Primary Record Form.



If the subject initials are not available, please click 'save' which will generate the patient ID in a ten-digit format. The first 3 letters represent the study, the next four numbers represent the site number, and the last three numbers represent the unique subject identity number e.g. NE2-8778123 where NE2 represents NERO and 2 represents a phase 2 trial, 8778 is the site number and 123 is the subject identity number.

Subject initials should be entered in the format XXX or X-X where there is no middle initial. All other combinations will cause a non-conformance query to fire.

4.2 Eligibility Form

Please ensure that for any ineligible patients that the failed inclusion/exclusion criteria are accurately recorded using the relevant code(s) and description(s) from the screening log. The End of Study form should also be completed.

4.3 Subject Characteristics

If Q2. 'What is the sex of the subject?' is answered 'Female' two additional questions will become visible. If Q2.1. 'If 'Female', is the subject of childbearing potential?' is answered 'Yes' then a Pregnancy Test form will become visible at all time-points as indicated by the schedule of events in the protocol.

Please note if data has been entered on the pregnancy test form and the patient is not of childbearing potential, this form will remain visible even when Q2.1. 'If 'Female', is the subject of childbearing potential?' is amended to 'No'.

If Q4. 'Is the subject willing to use acceptable contraception as defined in the study protocol?' is answered 'No', the participant is ineligible and data queries will fire prompting the Eligibility and End of Study forms to be updated/completed to reflect this.

Q6. 'Date of consent form signed?' must be ≤ 28 days prior to day 1 cycle 1. If treatment is delayed the participant may need to be reconsented.

4.4 Medical History

Any medically significant pre-existing condition prior to informed consent must be recorded. Add conditions to the log table.

If any question relating to eligibility identifies the patient is ineligible, data queries will fire prompting the Eligibility and End of Study forms to be updated/completed to reflect this.

4.5 Previous Treatment

If either Q1. or Q12. are answered 'No' or any of Q2.-Q4. are answered 'Yes' the participant is ineligible and data queries will fire prompting the Eligibility and End of Study forms to be updated/completed to reflect this.

Q5. And Q6. Must be accurately recorded as these are stratification factors for the trial. This should match the data recorded on the randomisation notification .pdf.

4.6 Disease Characteristics

Q3. 'Mesothelioma cell type' must be accurately recorded as this is a stratification factor for the trial. This should match the data recorded on the randomisation notification .pdf.

Q4. 'Date of the most recent CT scan of chest and upper abdomen' should match Q2. 'Date of CT scan' on the Screening Disease Assessment Target form in the CT Scan folder.

4.7 Vital Signs

All questions which require a measurement to be entered have the help  icon. These indicate the data formats that can be used in these fields.

Please note the participants weight at screening must be entered to allow SCTU staff to check the correct dose of Niraparib has been dispensed to the participant.

4.8 LB Chemistry and LB Haematology

At the Screening visit, some of the laboratory tests require the upper limit of normal (ULN) to be entered for eligibility requirements.

Please note that platelet count at screening must be entered to allow SCTU staff to check the correct dose of Niraparib has been dispensed to the participant.

Result fields are entered in the format xxxxxx.xxxx, with a maximum of 6 before and 4 after the decimal point. Anything outside of this range will flag as 'non-conformant'.

If a result is 'significant' clinician opinion must be sought to determine whether it represents an AE. If the result is outside the reference range and clinically significant an AE must be recorded.

4.9 Performance Status

If Q1.1. 'If 'Yes', what is the ECOG performance status?' is answered '5 = Dead', please complete the End of Study form and where applicable please update the Adverse Event form and/or submit an SAE form.

4.10 Translational Tissue Sample

If Q1. 'Is a tissue sample available?' is answered 'No', the participant is ineligible and data queries will fire prompting the Eligibility and End of Study forms to be updated/completed to reflect this.

4.11 Pregnancy Test and 6 Month Pregnancy Test

This form is visible if Q2.1. 'If 'Female', is the subject of childbearing potential?' is answered 'Yes' on the Subject Characteristics form. Ensure the patient status is captured correctly on the Subject Characteristics form for the appropriate Pregnancy Test form visibility.

If Q1.2. 'If 'Yes' what is the result of pregnancy test?' is answered 'Positive' at the Screening visit, the participant is ineligible and data queries will fire prompting the Eligibility and End of Study forms to be updated/completed to reflect this.

Pregnancy Test forms will be visible at the appropriate time-points as indicated by the schedule of events. If a Subject has a positive pregnancy test result from Cycle 1 onwards, please add and complete a Pregnancy Notification form. Refer to section 4.26 for guidance.

4.12 Randomisation

Randomisation is carried out by delegated site staff on the Alea system, **not** in Rave. Website at: <https://prod.tenalea.net/ciru/DM/DELogin.aspx> Once completed, a pdf will be emailed to you and should be used to add the information to the Randomisation form in the Cycle 1 folder.

Separate guidance will be provided for the Alea randomisation system.

4.13 Subject Continuing, Subject Continuing ASC, Subject Continuing Compassionate Use

Participants in the experimental arm will have Subject Continuing and/or Subject Continuing Compassionate Use (Cycle 8 only) forms available. When Q1. 'Is the subject continuing treatment?' on the Subject Continuing form is answered 'No' or either option is selected on the Subject Continuing Compassionate Use is selected, please ensure the newly visible End of Treatment form is completed.

Participants in the control arm will have Subject Continuing ASC form available. If Q1. 'Is the subject continuing active symptom control (ASC)?' is answered 'No', additional questions become visible. Select the applicable answer and complete additional forms as appropriate e.g. Disease Assessment Target or End of Study.

If Q4. 'Is the subject continuing in follow up?' is answered 'Yes' then Survival Data, Post Study Therapy and 28 Day Follow Up forms will become visible on the subject homepage. Please note for participants in the control arm, there is no End of Treatment form available.

4.14 Niraparib Drug Administration

This form is only visible for patients in the experimental arm. Please use the patient diary card to support data entry on this form.

Q4. 'Total number of capsules dispensed by pharmacy:' is automatically completed and is non-editable, when Q1. 'Was Niraparib dispensed?' is answered 'Yes'.



Q6. 'Expected (total) number of capsules to be returned (derived) will auto-populate and is non-editable by site. It is calculated dependant on responses to other questions on this form.

4.15 End of Treatment

This form is only visible for patients in the experimental arm. Please note this visit is not a physical patient visit.

Q3. 'What is the primary reason for ending treatment?' Select the applicable answer and complete additional forms as appropriate e.g. Disease Assessment Target or End of Study.

If Q4. 'Is the subject continuing in follow up?' is answered 'Yes' then Survival Data, Post Study Therapy and 28 Day Follow Up forms will become visible on the subject homepage.

4.16 Screening Disease Assessment Target and Disease Assessment Target

Once Q4. 'Was modified RECIST (mRECIST) or RECIST 1.1 used to assess the target lesions?' is answered from the drop-down list, the applicable measurement fields for that method of assessment will become visible.

Provided that the method of assessment is the same for subsequent scans as for screening and measurements are reported in the same order, text fields (i.e. lesion names) will be auto populated from the Screening scan data. It is important that the same method of reporting is used for all CT scans.

If Q1. 'Were any non-target lesions assessed?' in the non-target lesions section is answered 'Yes', then a Non-Target Lesions form is visible in the CT scan folder for that visit.

From Week 6 onwards and for all additional scans If Q1. 'Were any new lesions identified?' in the new lesions section is answered 'Yes', then a New Lesions form is visible in the CT scan folder for that visit.

4.17 Screening Disease Assessment Non-Target and Disease Assessment Non-Target

Once Q2. 'How many non-target lesions were assessed?' is answered, the applicable number of measurement fields will become visible. Please note that at screening the 'lesion status' field is auto-populated with 'Present'

Once Q1. And Q2. have been completed for subsequent scans (Week 6 onwards), text fields for 'anatomic site' will be auto populated from the Screening scan data.

4.18 New Lesions

If Q3. 'New lesion site' is answered 'Other site' please complete Q3.1., which should be used to enter the name (anatomic site) of the 'Other site' new lesion.

Q4. 'New lesion description' is where details of the new lesion should be entered e.g. lesion size/dimensions.

4.19 Inpatient Hospital Visits

If a patient is hospitalised as a result of an AE, please ensure the data in Q3. 'Reason for Admission?' accurately reflects the AE term.

If Q8. 'Was this admission planned (elective) or not planned (non-elective)?' Is answered 'non-elective', please ensure an SAE report is submitted.



4.20 Survival Status

If Q2. 'What is the subject status?' is answered 'Deceased', please ensure that the End of Study form has been completed and if applicable please submit an SAE.

4.21 Adverse Event (AE)

Please enter each AE on a new log line, including AE grade changes.

If Q6.3 'Change in concomitant medication' is answered 'Yes' please ensure the Concomitant Medication form (section 4.22) is completed.

If Q6.5. 'Hospitalisation or prolonged hospitalisation for this event' is answered 'Yes' please ensure the SAE is reported to the SCTU within 24 hours of site becoming aware. Ensure the Inpatient Hospital Visits form (section 4.19) is also completed.

Please complete all questions on the adverse event form. Non-completion of data will prompt SCTU staff to contact site as this may represent a potentially unreported SAE.

4.22 Concomitant Medications

Please enter each concomitant medication on a separate log line. Concomitant medications should be recorded from 14 days prior to informed consent and up to 30 days after treatment.

If Q4. 'Please select the primary indication that the medication/therapy was taken for' is answered 'Medical History' or 'Adverse Event', please ensure the relevant details are recorded on the Medical History and/or Adverse Event forms.

4.23 End of Study

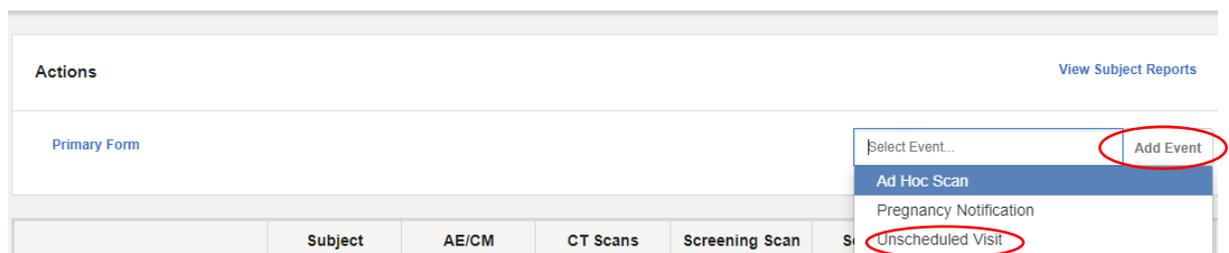
An 'End of Study' form must be completed for each subject once their trial involvement has ended.

If Q2. 'What is the primary reason for end of study?' is answered 'Death', please ensure Q2.1 'Cause of Death' is completed. If this field is left blank or answered with 'unknown' this will prompt SCTU staff to contact site for completion of an SAE.

4.24 Unscheduled visits

An unscheduled visit is any visit that takes place outside of those mandated by the protocol. To add an Unscheduled Visit, select 'Unscheduled Visit' from the Add Event function. The folder name will update with the date once Q1. Has been completed.

👤 NE2-3333090



Select 'Yes' in the appropriate fields to select the form(s) that apply to the data that was collected at the unscheduled visit. When the form is saved, any form that has been selected from this list will be available within the Unscheduled Visit folder.

4.25 Ad Hoc Scan

Please complete the data in these forms as per section 4.16 to 4.18 for any scans that occur outside of those mandated by the protocol. To add an Ad Hoc CT Scan, select 'Ad Hoc Scan' from the Add Event function (see screenshot in 4.24).

4.26 Pregnancy Notification

Complete this form if the subject is confirmed to be pregnant during the trial or if a partner of the subject is confirmed to be pregnant within 24 hours of site becoming aware of the pregnancy. To add a Pregnancy Notification form, select 'Pregnancy Notification' from the Add Event function (see screenshot in 4.24).

5. DATA ENTRY GUIDELINES

The following table contains guidance on entering data that will be coded, such as adverse event descriptions. This will help to reduce queries raised during the coding process. It will also contain any data entry guidelines created in response to future protocol amendments or data input issues identified on the eCRF.

Guidance on data entered by sites that will be coded – Adverse Events, Medical History, End of Study forms		
Coding Guidance	Issue	Example (if applicable)
A	Input a medical term	'Study disease area' whilst is obvious in context it is not a medical term.
B	Avoid using '/' as the terms used will often not be considered synonymous in the coding dictionary	'Shivering/shaking' is two terms
C	Only enter a single term	Fever and chills are two different medical concepts so cannot be coded as one individual event
D	Avoid 'describing' an event	'Subject attended visit with a runny nose, cough, aching limbs and sore throat.' This contains four different medical events and each should be entered separately
E	Avoid uncommon acronyms or acronyms that could mean different things in different contexts	'PE' for pulmonary embolism or pleural effusion, or pre-eclampsia for example
F	Surgery in medical history can contain two separate events	'Surgery on foot due to broken foot' contains two events, 'Broken foot' and 'Foot surgery'
G	Queries raised by the coder are an open dialogue and sites should respond accordingly	'Would >>TERM<< accurately reflect the Medical History as entered in this field?' – sites can respond to this with 'no' and/or provide further information that may help with finding an appropriate medical term. Clinician decision should be sought
H	Clarify any potentially ambiguous term	'Canal stenosis' could be 'ear canal' or 'spinal canal'. 'Cold' could refer to a common cold or feeling cold
I	Ensure drug-related reactions are stated explicitly	'Subject took paracetamol and developed a headache' does not confirm that this was a 'drug-induced headache'



6. eCRF SIGN-OFF

Once all required data has been entered, cleaned, and the database has reached the 'Database Freeze' milestone, the eCRF is ready for sign-off by the PI. SCTU will advise when this should take place and provide instructions at the same time.