Neo-ACT

eCRF Data Entry Instructions

v1.4

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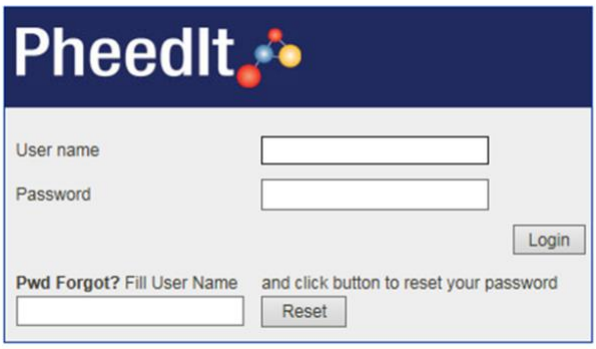
Log in

To enter the production environment (real patients), use the address (URL):

https://www.pheedit.sll.se/p303_prod

The following log-in window will appear:



- For new users: You will receive your login information via email from PheedIt Administration. At first login, you are prompted to change your password. New password must contain at least 6 characters including one number and one capital letter.
- For users who already have a Pheedit account: The login information (username and password) are the same as for the other studies. Log in as usual and select “Neo-ACT” from the study list.
- If you have forgotten your password, fill in your user name (normally name.surname) and click the Reset button. A new temporary password is sent to you.

General instructions

- Data should be entered as soon as possible and no more than one month after the patient visit.
- The first digit 0 (zero) never needs to be entered (except for dates!), nor zeroes after the decimal point, i.e. value 01.10 can be written 1.1. It saves data entry time!
- You can use either decimal comma ”,” or decimal point “.” as you prefer depending on keyboard. In most European countries the comma is easier to use.
- Ergonomics: Use the tab key to move between entry fields. In format lists, enter the first letter of the chosen alternativ and then the tab key, for instance “N” makes “No” highlighted, then the tab key to move to next entry field.

- **Data entry status symbols**

The data entry status icon changes colour depending on the entry status. In the table below the icon legend is outlined.

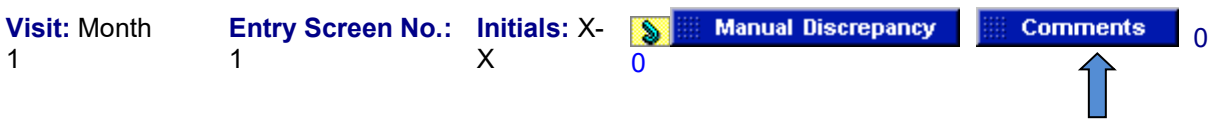
Data Entry Book Information	
Selected Study:	KPE_TEST
Selected Patient No.:	102 [Karolinska/Onkologen]
DEB Status Traffic Light Legend	
= No data has been entered...	= Data has been entered... = Partial entry...
= Data has been entered, but with discrepancies...	= Data has been entered, but with manual discrepancies...
= Data has been entered with DE comments...	= Monitor comments = SDV Done...

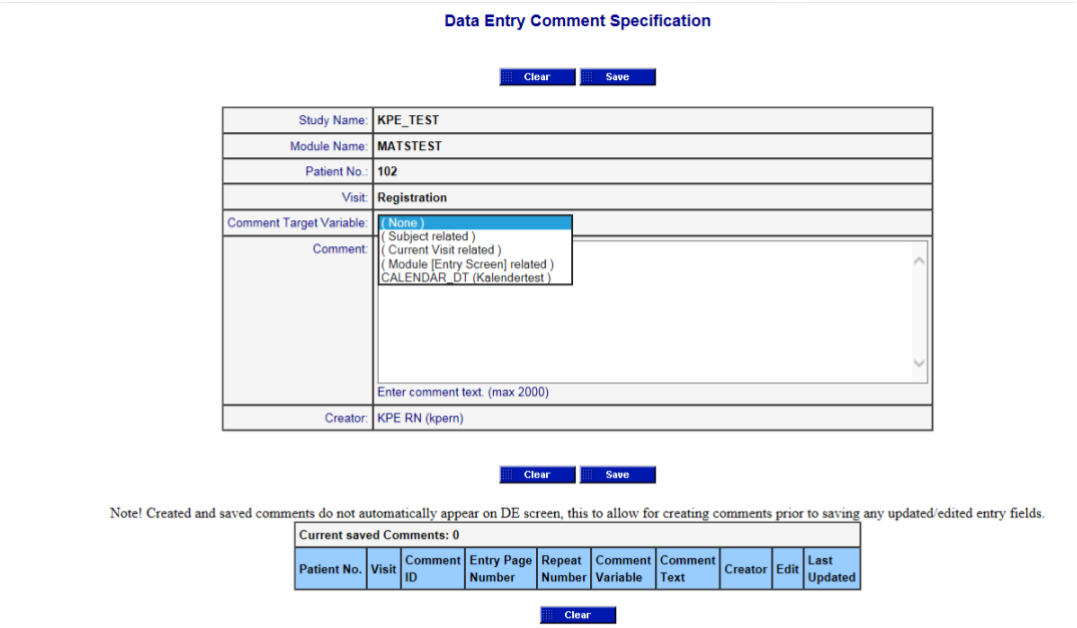
- **Browsing the system**
- 

”Back”: Takes you to the Data Entry Book Tree Overview, or the preselected visit.
-  ”Back to Subject selection screen”: Takes you to the “Data Entry Initiation” (“Select patient number”) screen.
-  Takes you to the previous data entry screen
-  Takes you to the next data entry screen
-  Takes you to the visit-overview
-  Some of the data entry screens can be duplicated by clicking this icon. An empty identical screen will appear, and data can be entered.

- **Comments**

Comments can be left on each data entry screen. Click on the “Comments”-button (see screenshot below). On the “Data Entry Comment Specification” screen that appears, select which data fields/variables the comment refers to. Comments can be made on several levels: variable, module, visit or patient. Several comments can be added on the same screen.





After a comment has been made and saved, the ”Comment”- button is highlighted in blue.

Note: The use of comments should be restricted and only be used if necessary, i.e. if no other options are available on the CRF. For example: no “not done” box is present to mark that a procedure was not performed.

- **Different data types**

The database contains different types of data fields. For example: text fields, numeric fields, format lists, dates, times, etc. All these fields have different characteristics.

Text fields

These fields can contain any type of character including text, letters, numbers and special characters.

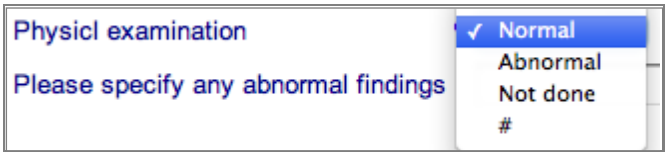
Numeric fields

Numeric fields can contain numbers only. Example: weight, length etc. Upon entering and saving other characters than number, a discrepancy will be generated.

Format lists

In format lists, the answers are predefined, and the correct answer is chosen by selecting the option(s) from a drop-down list, radio button or tick-box.

➔ Ergonomics: press the first letter of the chosen alternative, then the tab key to move to the next entry field. If there are multiple choices with the same letter, press several times on the same letter to jump between options. In the example on the picture below, press for example "n" twice to choose Not done.



- **Dates and times**

Enter dates without dots or hyphens in format DDMMYYYY, for example 24102022 for 24 October 2022. Leading zero's (0) should be entered for dates. If the date is 1 January 2023, the date should be entered as **0**1012023.

Time format is 00:00 - 23:59.

Note: Dates and times should always be entered as complete dates or times, unless otherwise specified. If dates or times are partial, please see section "Missing data" for instructions.

- **Missing data**

A data field or variable should never be left empty, as it before database closure must be possible to distinguish between "real" missing data and missing data that study staff has failed to enter. In case data cannot be collected for any particular reason this should be reflected in the database. The handling of data is based on the data type. Therefore, enter the missing data according to the following instructions, unless other rules are agreed upon with the project team before the trial begins.

Text — If a value is missing, enter "ND" (Not done), "NA" (Not Applicable), "NK" (Unknown) or "NE" (Not evaluable/measurable). Enter a comment as well using the "Comments" button with a brief explanation why the value is missing.

Numeric — If a value is missing, enter "#ND" (Not done), "#NA" (Not Applicable), "#NK" (Unknown) or "NE" (Not evaluable/measurable), alternatively leave the field blank. Enter a comment as well using the "Comments" button with a brief explanation why the value is missing.

Format lists — Select "Not done", "Not applicable" or "Unknown" as an option. If the correct choice is not available as an option in the drop-down list/radio button, enter a comment using the "Comments" function explaining why the value is missing.

Date — The date field should always be entered with the full date (DDMMYYYY):

- If day part is unknown, enter "15", e.g., 15012014 instead of #012014.
- If day- and month-part are unknown enter "0107", e.g. 01072014 instead of ##2014.
- If date is fully unknown, year must be estimated, enter day and month as above i.e. "0107". If the year-part cannot be estimated for some reason, leave date field empty and clarify the reason why the date is missing by adding a comment. Note:

Time — The time field should always be entered as complete time in format (HH:MM):

- If the minutes-part is unknown enter "30", e.g., 10:30 instead of 10:##.
- If time is fully unknown, provide the estimated hour. Enter minutes as above i.e. "30". If the hour-part cannot be estimated for some reason, leave the time field empty and clarify the reason why the time is missing by adding a comment.

***Note**: A "missing" date or time field must never contain #. If # is entered, all data in that field will disappear during data export.*

Visit not performed

If an entire visit is not performed, mark the "Visit not done" box and leave the visit date blank. If no such box is available, add a comment "Visit not done" on the "Visit date" variable using the "Comments" function. Visit date and all other variables should be left completely empty for that visit.

The use of the hash tag #

The hash tag should not be used because as it will generate a discrepancy. If data is missing, leave the variable empty, follow the instructions above and, if not otherwise specified, add a comment explaining why the data is missing.

Exceptions:

- Some few entry fields are marked with a blue dot which indicates an "Enforced data entry"-field". This means tthis field can never be left blank, it must contain data in order to be able to save the eCRF. If data is missing for such an "Enforced data entry"- field enter # in the field and save the screen. An error message will appear. Provide a comment in the response of the discrepancy clarifying why the data is missing.
- If data is entered that is out of range for a field, an error message will appear stating that the data is not valid. If the value is correct, enter # and the out of range value and save the screen again. Now the system will allow moving on to the next screen.

Data entry start

Once logged in, choose Data Entry → **Data Entry Book**. Select the study and click "Next" → Choose the patient from the list and click "Start DEB…" (Data Entry Book).

- **New patient**

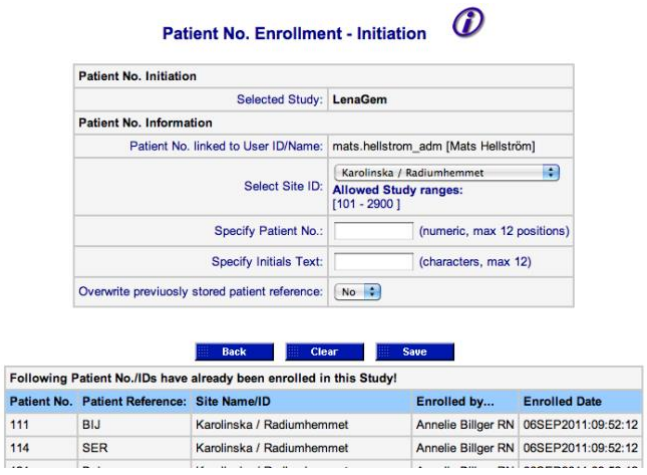
When the study starts, there are no patients present in the patient list yet. So, first of all, a new patient has to be created in the system before data entry can start.

Select "Data Entry" → "Patient Enrolment". Enter the patient number (Patient No) and the patient's initials or dummy initials in Initials Text. Select the correct study site (Site ID).

If a patient number already exists, the system will notify that the patient number is no longer available. At the bottom of the screen there is a list of all enrolled patients.

Click "Save" and data entry can begin.

Note that only the site's own patients are visible.



- **Save, edit and freeze entered data**

Every screen has to be ***saved*** before browsing to the next screen.  If not saved, the data will be lost.

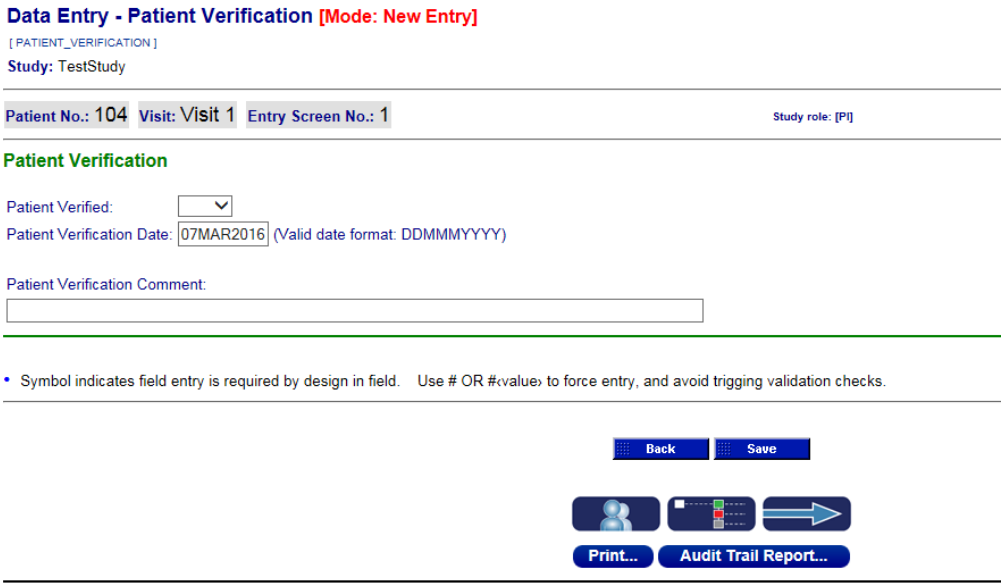
If ***changes*** are made to a screen after the page has been saved, a reason for change should be provided. Once the page is saved, a confirmation message appears.

When data entry is finalised for a module/screen and ready for monitoring, select the "***freeze*** button" at the bottom right of the screen. "Freeze button" must be clicked for all modules/screens **before monitoring can start.**

Patient verification

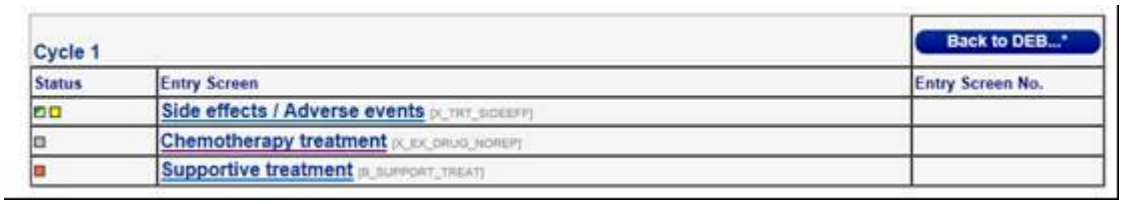
This screen corresponds to the paper CRF's "investigator signature". The patient verification module can only be completed by the site's Principle Investigator (PI). There is only one person per site with PI access rights. Once the PI confirms all data is complete and accurate, the patient can be "verified" by completing this eCRF. Once the patient is verified all eCRF's for this particular patient will be "locked" automatically and can no longer be modified by any other staff.

Choose the "Patient Verification" module, choose "Yes" and write a comment (if needed). The date is updated automatically and cannot be modified. Click "Save".

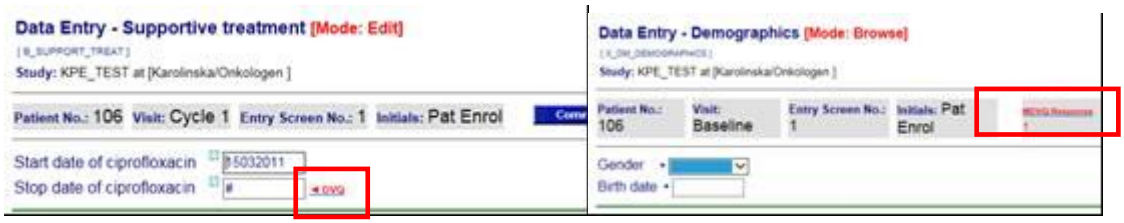


Discrepancies / Queries

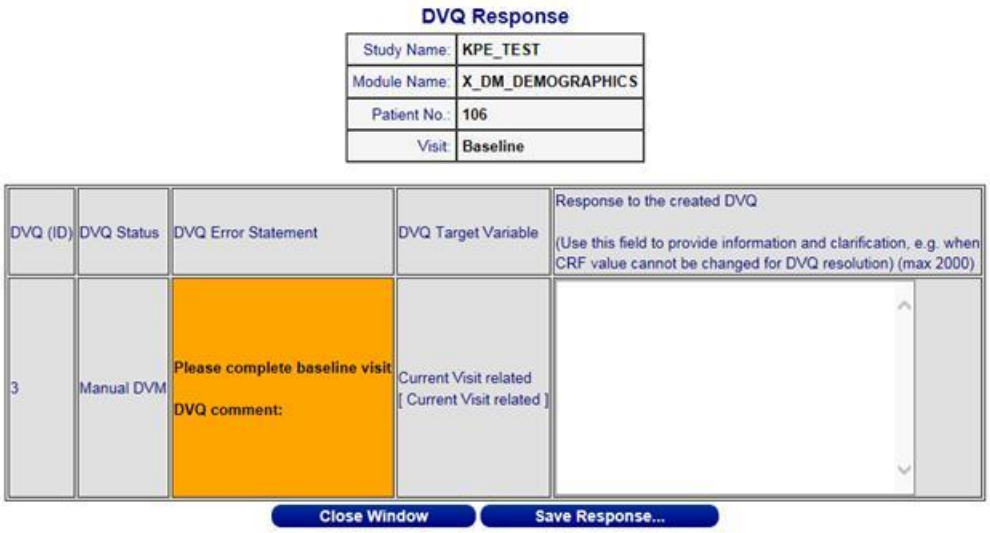
When data is incorrect or missing, an automatic discrepancy (DVQ – *Data Validation Query*) is generated (red square in the status column). Besides the system-generated discrepancies, queries can be created manually by the monitor or the data manager (yellow square in the status column). To get an overview of the queries for a certain patient, choose "Data Entry" → **Data entry book**. Select a patient number and (if needed) a visit.



Click on the "Entry Screen" name which has a DVQ associated to it (red or yellow square). If the query applies to a specific variable, that variable has a red "DVQ" mark next to it (see left screen shot below). If the DVQ refers to the entire module/screen or to the patient, "manual discrepancy" is present in red text on top of the page (see right screen shot below).

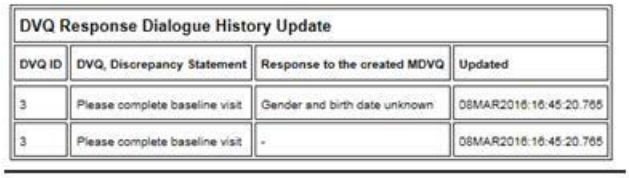


All DVQ's have to be answered and/or resolved, whether these are manually or systematically raised. Update the data if possible. In case data is correct, click on the red (manual) DVQ link and a response window appears (see below).



Confirm that the data is correct or provide a short explanation in the DVQ Response "Response to the created DVQ" window. Example: "Weight not done", "Data is correct", "Result not evaluable" etc. and save response.

At the bottom of the dialog window, the DVQ audit trail is tracked. The answer is also present there.



DVQ Response Dialogue History Update

DVQ ID	DVQ, Discrepancy Statement	Response to the created MDVQ	Updated
3	Please complete baseline visit	Gender and birth date unknown	08MAR2016:16:45:20.765
3	Please complete baseline visit	-	08MAR2016:16:45:20.765

Note: Systematic queries, for which data is updated, are resolved automatically upon saving the corrected data. However, all manual queries have to be resolved manually, whether data is updated or not. The monitor and/or data manager will close these queries.

Visits and modules/screens

The study is divided in visits following the study timeline. Each visit has one or more data entry screens, also called modules. The visits are similar to the visit schema in the study protocol.

The study's structure with visits and modules is shown in the table below:

Visit	Data Entry Screens/ Modules
Randomisation	Randomisation
Baseline	Diagnosis Tumour type Imaging Disease stage Axillary metastases Height Physical examination Heart investigations Research sample Quality of Life Questionnaires
Pre-surgery	Imaging Disease stage Physical examination Heart investigations Research samples Quality of Life Questionnaires Neoadjuvant treatment Chemotherapy summary Side effects
Post-surgery	Surgery and Histopathology
Follow up 1 year	Follow up status Adjuvant chemotherapy and targeted therapy

	Adjuvant endocrine therapy and radiotherapy [Quality of Life Questionnaires Cognitive test
Follow up 2 years	Follow up status Treatment during follow up Quality of Life Questionnaires
Recurrence	Recurrence
End of Study	End of study Patient verification

Note that some screens reappear in more than one visit.

Below is a review of all visits, entry screens and important CRF questions.

Visit Randomisation

One screen: **Randomisation**. All questions must be completed.

Please note: Even if a patient chooses to leave the trial directly after randomisation the following visits must be filled in:

- Registration
- Baseline
- End of study

Visit Baseline

- **Diagnosis**

Please enter basic information about the tumour. Multifocality is defined as more than one discernible tumour on diagnostic imaging.

- **Breast cancer hormone receptors".**

If "Tumour multifocality" is answered "No" section "Next largest tumor…" should be left empty. If Tumour multifocality" is answered "Yes, please complete both upper and lower part of the pageand register first the largest, then the next largest lesion.

Proliferative activity (Ki67 or similar), %: Register the global score, not values from hot spots. This is according to current international and national guidelines. If a score has a decimal value, round up if ,5 or more and round down if ,4 or less. For example, if the value is 13,6 round up to 14.

- **Imaging**

Size of the largest tumour is not to be confused with extent; first please register the largest size of the invasive tumour body (in case of multifocality, register both the largest and the next largest tumour size).

Ultrasound: Total number of suspectedly invasive tumours ("suspectedly" refers to amount of tumor foci according to ultrasound if multifocal tumor).

- **Disease stage**

Extraaxillary ipsilateral suspicious lymph nodes regard locations such as infra- or supraclavicular, interpectoral or internal mammary.

In case no ultrasound was performed, please register number of suspicious lymph nodes on e.g. MRI or PET-CT, if performed.

TNM classification is here used according to the following: Category cN1 disease encompasses metastases to movable ipsilateral level I and/or level II nodes. Category cN2 disease includes metastases to fixed or matted ipsilateral level I and/or level II nodes or to ipsilateral internal mammary (IM) nodes in the absence of axillary metastases. Category cN3 disease includes ipsilateral level III node metastases with or without level I or level II nodes, ipsilateral IM metastases with level I or level II metastases, or ipsilateral supraclavicular (SC) lymph node metastases. Metastatic intramammary lymph nodes are equivalent to level I for staging purposes.

Clinical tumour status: Palpable tumour size: In case different palpable size (For example palp by oncologist/palp by surgeon), enter the measurement that is closest to the inclusion date.

- **Axillary metastases**

For the definition of extraaxillary lymph nodes, see above.

- **Height**

Height in cm.

- **Physical examination**

Enter the data according to the "Testing recording sheet". If the Biometric Impedance Analysis was not performed mark these with N/A. Also, if the leg press was not performed at the site enter N/A.

- **Heart investigations**

Left ventricular ejection fraction is routinely only measured for HER2+ cases. Please enter if available/recorded.

- **Research sample**

Please observe that this page needs only to be completed for sites in the Stockholm region (Södersjukhuset, Karolinska Universitetssjukhuset, Capio S:t Görans Sjukhus) and Helsinki (partly).

Questions "Any use of antibiotic treatment in the last 6 months?" and "Does the participant medicate with proton pump inhibitors (PPIs)? only to be answered for patients taking faeces samples.

- **Quality of Life Questionnaires**

Please register in case the participant does not wish to receive questionnaires. Please note that the cognitive test is only performed twice, at baseline and at 1-year follow-up.

Visit Pre-surgery

Please enter the date for re-testing, i.e. the second physical exercise testing session.

- **Imaging**

Please complete this page in accordance with the identical screen at Baseline, registering the corresponding values from the post-neoadjuvant evaluation.

- **Disease stage**

Please complete this page in accordance with the identical screen at Baseline, registering the corresponding values from the post-neoadjuvant evaluation.

- **Physical examination**

Enter the data according to the "Testing recording sheet". If the Biometric Impedance Analysis was not performed mark these with N/A. Also, if the leg press was not performed at the site enter N/A.

Please note that in May 2025, three variables were added under Exercise Capacity Test: Hear rate 30W, Heart rate higher workload and Higher workload. Data should be filled in for new patients. Retrospective data will be completed centrally.

- **Heart investigations**

Left ventricular ejection fraction is routinely only measured for HER2+ cases. Please enter if available/recorded.

- **Research sample**

Please observe that this page needs only to be completed for sites in the Stockholm region (Södersjukhuset, Karolinska Universitetssjukhuset, Capio S:t Görans Sjukhus) and Helsinki (partly).

- **Quality of Life Questionnaires**

Please register in case the participant does not wish to receive questionnaires. Please note that the cognitive test is only performed twice, at baseline and at 1-year follow-up.

- **Neoadjuvant treatment**

Please report received systemic treatment per class of drug, including the generic name of the drug and the cumulative (total for all courses combined) dose per drug. The data of the last administered systemic is also reported here.

- **Chemotherapy summary**

Please report whether any dose reductions have been applied including the main reason for this. Possible premature treatment discontinuation and the main reason for this can be reported here. Also, hospitalizations due to toxicity of treatment is reported, including the number of unexpected/unplanned admissions and the total number of days with unexpected in-hospital care.

- **Side effects**

Any side effects from the neoadjuvant treatment yes/no/NK/ND .

Both : treatment-related and exercise-related events are reported here.

Note: There is a difference between reporting AEs and recording toxicity/side effects. We do not report AEs related to neoadjuvant chemotherapy, but we record side effects (=side effects, not adverse events) to estimate the burden on the patient and the effect of training on toxicity.

Please note, toxicities are to be reported for all regimens/cycles.

Visit Post-surgery

- **Surgery and Histopathology**

Reoperation due to surgical complications regards e.g. bleeding or infectious complications but does not include any surgery due to involved margins or completion axillary surgery. The latter are registered in the question "Total numbers of cancer-related surgeries performed" – please do not include reoperations due to surgical complications here.

The final type of axillary surgery is the last and largest intervention, e.g. axillary lymph node dissection in case of a sentinel lymph node biopsy or targeted axillary dissection that is then followed by an axillary lymph node dissection.

All lymph nodes with residual axillary metastases on histopathology need to be registered, even those that only contain isolated tumour cells.

Please enter Residual Cancer Burden in accordance to MD Anderson's definitions at http://www3.mdanderson.org/app/medcalc/index.cfm?pagename=jsconvert3.

Please note that the two last questions must be answered, else the screen cannot be saved.

Clavien-Dindo: Report whether the patient has experienced any surgical complication during the 30 postoperative days, pick a number on the Clavien-Dindo scale, see the exact definition of the different levels inserted on the page.

Visit Follow up 1 year

- **Follow up status**

Please note that it is crucial that in case of death, the End of Study screen **must** be completed immediately. The same applies to any case of recurrence, which mandates the completion of the Recurrence screen.

- **Adjuvant treatment during follow up**

Please enter given post-operative systemic therapies here, including chemotherapy, HER2-targeted therapies, CDK4/6-/PARP-/immune checkpoint inhibitors. Generic names of drugs are added as well as start date.

- **Treatment during follow up**

Please enter given post-operative systemic therapies here, including CDK4/6- inhibitors, antihormonal therapy, and bisphophonates here. Names of (combinations of) antihormonal agents are added as well as start date, whether the patient receives adjuvant bisphosphonates and start date, as well as sites and cumulative dose of post-operative radiotherapy .

Generic names of drugs are added as well as start date.

- **Research sample**

Please observe that this page needs only to be completed for sites in the Stockholm region (Södersjukhuset, Karolinska Universitetssjukhuset, Capio S:t Görans Sjukhus) and Helsinki (partly).

- **Quality of Life Questionnaires**

Please register in case the participant does not wish to receive questionnaires. Please note that the cognitive test is only performed twice, at baseline and at 1-year follow-up.

Visit Follow up 2 years

- **Follow up status**

Please note that it is crucial that in case of death, the End of Study screen **must** be completed immediately. The same applies to any case of recurrence, which mandates the completion of the Recurrence screen.

- **Treatment during follow up**

Please enter given post-operative systemic therapies here, including CDK4/6- inhibitors, antihormonal therapy, and bisphophonates here. Names of (combinations of) antihormonal agents are added as well as start date, whether the patient receives adjuvant bisphosphonates and start date, as well as sites and cumulative dose of post-operative radiotherapy .

Generic names of drugs are added as well as start date.

- **Quality of Life Questionnaires**

Please register in case the participant does not wish to receive questionnaires. Please note that the cognitive test is only performed twice, at baseline and at 1-year follow-up.

Visit Recurrence

- **Recurrence**

If a patient relapses during the study this **must** be entered here. Note: only the first recurrence should be entered! It is of major importance that the date of the respective recurrence is entered correctly.

Visit: End of study

- **End of Study**

The eCRF should be completed when the patient has followed the study for 2 years, or if the patient no longer wants to participate in the study and/or does not want to be followed any longer, or if the patient has died.

If the patient has died, it is **mandatory** to provide the date of death and cause of death.

- **Patient verification**

When all data is entered for a certain patient and all queries are solved, the Investigator must verify the data by answering Yes on the question Patient verified, and then save the screen. The patient's data is then locked.

If, by some reason, anything must be changed in the CRF, the Investigator can unlock the data by answering No and give a reason for change.

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Version Control log

Version	Date	Change	Reason for change
1.0	04NOV2022	Initial	N/A
1.1	24APR2023	Updates according to comments	Review of final CRF
1.2	01NOV2023	Visit Randomisation: Instruction regarding patient going off study directly after randomisation Visit Baseline: Instruction regarding Proliferative activity (Ki67 or similar), %: Visit Baseline and Follow up 1 Year: Screen Cognitive test removed.	Clarification
1.3	23FEB2025	?	?
1.4	15 May 2025	Added info about three new variables in Physical examination screen	Three new variables added