NEO-ALTTO

Neo-**A**djuvant **L**apatinib and/or **T**rastuzumab **T**reatment **O**ptimisation

CASE REPORT FORM

Protocol number BIG 1-06 / EGF 106903

Centre No.							Subject No.						

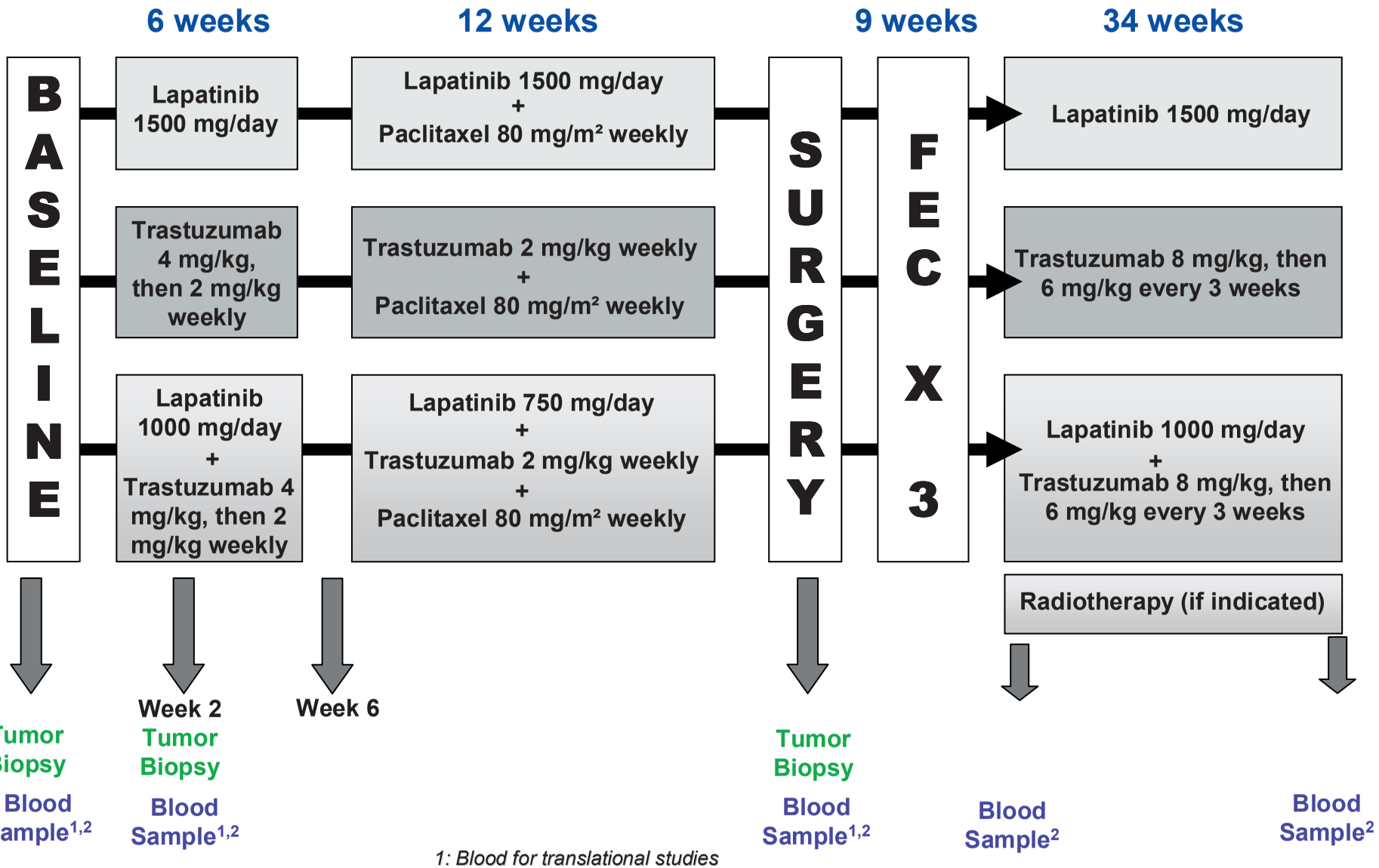
Study: Neo-ALTTO v. 6.0 (19Mar09)

Case Report Form (CRF) index and timelines for completion and faxing

Case Report Form (CRF) index and timelines for completion and faxing (Cont.)

Form	*Page*	Completion and faxing timelines
Hormonotherapy	*110*	Within 2 weeks from treatment start
Radiotherapy	*111*	Within 2 weeks from radiotherapy treatment completion
Concomitant treatments	*112-114*	Any time a new treatment is started
Administration of study drug: Paclitaxel	*115-116*	Within 2 weeks from start and within 2 weeks from treatment completion
FEC adjuvant treatment	*117-118*	Within 2 weeks from start and within 2 weeks from treatment completion
Administration of study drug: Lapatinib	*119*	Within 2 weeks from starting lapatinib and each time there is change in dose or an interruption and within 1 week of treatment completion
Investigational product compliance	*120*	Within 2 weeks from treatment completion
Administration of study drug: Trastuzumab	*121-125*	Within 2 weeks from starting treatment, then every 12 weeks and within 1 week of treatment completion
Adverse event	*126-132*	Within 1 week from each AE start
Unscheduled EKG	*133-134*	Within 2 weeks of each assessment
Unscheduled LVEF	*135-137*	Within 2 weeks of each assessment
Unscheduled radiological exams	*138-142*	Within 2 weeks of each assessment
Adjuvant Treatment completion	*143*	Within 1 week from study treatment completion
Adjuvant Treatment completion *(comments and signature page)*	*144*	Every time a new comment is reported. NOTE: the date and signature should be added only after request from data management
Recurrence of disease: local/regional	*145*	Within 1 week from occurrence
Recurrence of disease: distant	*146*	Within 1 week from occurrence
Second primary malignancy and CBC	*147*	Within 1 week from occurrence
Post event treatments	*148-149*	Within 2 weeks from start and within 2 weeks from completion
Additional comments	*150*	Every time a new comment is reported after the collection of page 144
Survival follow up	*151-165*	Yearly starting from 1 year after recurrence of disease. Within 2 weeks from visit
Death	*166*	Within 1 week from occurrence
Additional signature page	*167-169*	Upon request from data management
Liver function tests (scheduled visits)	*170-198*	Within 2 weeks from visit
Unscheduled liver function tests	*199-204*	Within 2 weeks of each assessment

Study design: treatment schedule



1: Blood for translational studies
2: Blood for CTC analysis selected centres only
3: In selected sites only

CTC analysis to be also performed at start of adjuvant therapy and 6 months after completion of adjuvant therapy (W1 and Month15 FU), and at relapse

Advice to the investigator on the completion of a Case Report Form (CRF)

Month #	Abb
1	JAN
2	FEB
3	MAR
4	APR
5	MAY
6	JUN
7	JUL
8	AUG
9	SEP
10	OCT
11	NOV
12	DEC

Completion of questions

- Please write legibly, only use **black** ink.
- All text and explanatory comments should be brief, in English and, if possible in CAPITAL letters.
- All dates should be in the format dd/mmm/yyyy, example: 12FEB2008 (see the list of month abbreviations on the right)
- Answer every question clearly, do not use ditto marks/commas (“).
- Only enter results in the fields provided.
- If the answer is zero, do not leave the field blank; write ‘**0**’.
- If the answer to a question is unknown, or not available, write ‘not known’ or ‘**NK**’.
- If a requested test has not been done, write ‘not done’ or ‘**ND**’.
- If a question is not applicable, write ‘not applicable’ or ‘**NA**’.
- Avoid abbreviations other than the above

Additional pages

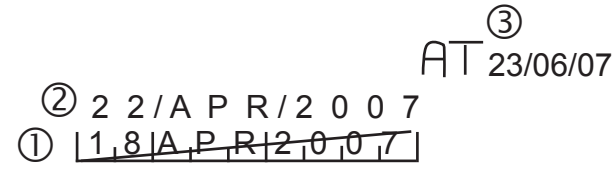
An additional page is a copy of a numbered CRF page which is used to carry over data that cannot be entered on the original page, for example due to lack of space.

To create an additional page photocopy the relevant page that requires more data from the unbarcoded CRF in the Investigator File, write the Centre no. and Subject no. on the top of the page and please, be careful to number such pages correctly with a “-” and a sequential number after the printed page number, as shown in the examples on the right.

112-1
112-2

Correction of errors

If an error occurs please correct in the following way:



① Cross through with a single straight line

② Write the correct value above or to the side

③ Initial and date the correction. In case of error in a date, please make sure that we can clearly distinguish the date of correction from the corrected date

Please do not use White-out.

Completion and sign-off of a CRF

A CRF should be completed for every randomised patient participating in the trial, including those who do not complete the trial.

A CRF should not be completed for screen failures.

Completion and sign off of a CRF should only be done after request from data management.

Only authorized investigators can sign a CRF.

For reasons of patient confidentiality, names or initials of patients must not appear on a CRF or on any other document.

Schedule of assessments

Follow-up starting point is day 1 of adjuvant biological targeted therapy or date of surgery for patients who don't receive biological therapy for any reason.

	Within 2 weeks prior to rando-misation	PRIOR TO SURGERY															ADJUVANT TREATMENT FOLLOW-UP PERIOD									
		WEEKS																								
		NEO-ADJUVANT TREATMENT															SURGERY	FEC			TARGETED THERAPY						
		2 Day 14	4 Day 28	6 Day 42	7	8	9	10	11	12	13	14	15	16	17	18	20-22	1 C1	4 C2	7 C3	10 W1	16 W7	22 W13 FU M3	28 W19	34 W25 FU M6	40 W31	43 W34 FU M9^^
Informed consent	X																										
Physical examination†† - Weight - Menstrual status/Pregn. Test**	 X X	X	X	X				X			X			X			X	X	X	X	X		X		X		X
Medical History	X																										
Vital signs	X	X	X	X				X			X			X			X	X	X	X	X		X		X		X
Performance Status	X	X	X	X				X			X			X			X	X	X	X	X		X		X		X
ErbB2 status	X																										
ER/PgR expression	X																										
Breast palpation with tumor measurements and nodal status	X	X	X	X*				X			X			X			X										
Prior/Concomitant medication	X	X	X	X				X			X			X			X	X	X	X	X		X		X		X
Bilateral Mammography	X			X*^													X										
Bilateral breast echography	X#			X*#													X#										
Chest X-ray or CT scan	X																										
Haematology	X		X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X		X		X
Blood chemistry	X		X	X				X			X			X			X	X	X	X	X	X	X	X	X	X	X
Cardiac Monitoring - LVEF - ECG - Signs and symptoms	 X X X			X													X				X		X		X		X
Tumor biopsy for translational studies	X***	X†															X										
PET (selected centres)	Xs	X‡		X‡‡																							
Blood collection for translational study	Xs	X															X										
Blood PGx	Xs																										
Blood sample for CTC (selected centres)	Xs	X															X				X						
Feasibility / type of surgery planned	X																										
Type of surgery performed																	X										
AE and SAE (NCI-CTCAE)	X	X																									

† On day 14 ± 2 after treatment start; †† After surgery physical examination includes thorax wall and axilla assessment * Within 3 days prior to the first infusion of paclitaxel; ** Only for women of childbearing potential; *** tumor biopsy for translational studies can be up to 4 weeks prior to randomisation; ^ Of the breast containing tumor only; ^^Please note that the 9 months FU visit will be done at week 34 of targeted therapy; # If applicable only; s To be performed after randomisation only; ‡ Prior to 2 weeks biopsy; ‡‡ Prior to paclitaxel administration

Schedule of assessments (Continued)

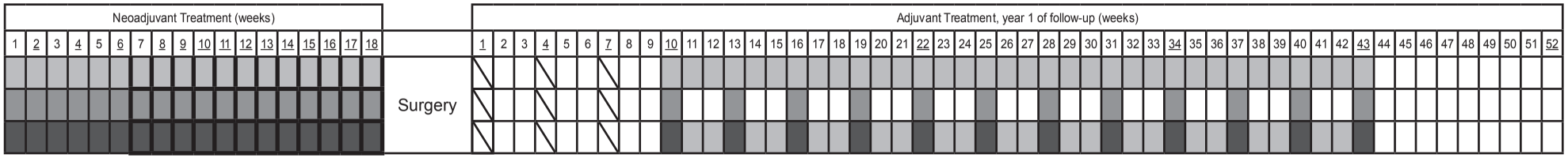
Follow-up starting point is day 1 of adjuvant biological targeted therapy or date of surgery for patients who don't receive biological therapy for any reason.

	FOLLOW-UP											
	MONTHS											YEARS
	12	15	18	21	24	30	36	42	48	54	60	6 to 10
Physical examination - Vital signs - Weight - Performance Status	X	X	X	X	X	X	X	X	X	X	X	X
Haematology	X		X		X		X		X		X	X
Blood chemistry	X	X	X		X		X		X		X	X
Radiologic Exam: Chest X-ray/CT Scan Bone scan / X-ray [a] Bilateral Mammography [b] Liver imaging	 (X) (X) X (X)				 (X) (X) X (X)		 (X) (X) X (X)		 (X) (X) X (X)		 (X) (X) X (X)	 (X) (X) X (X)
Concomitant medication	X	X	X	X	X	X	X	X	X	X	X	
Cardiac Monitoring - LVEF - EKG[c] - Signs and symptoms	 X X X		 X X X		 X X X		 X X X		 X X X		 X X X	 X X X
Blood sample for CTC (selected centres)		X										
AE and SAE (NCI-CTCAE)[d]	X											

[a] Plain films (CT scan or MRI in case of vertebral abnormalities) are required to exclude metastatic disease if a bone scan is positive
[b] Unilateral for patients with mastectomy
[c] To be performed at any time if symptoms or clinical suspicion are present
[d] See section 9.1.2 for requirements and timeframes on AE and SAEs reporting

Study design: treatment schedule

Treatment schedule



Lapatinib

Trastuzumab

Lapatinib + Trastuzumab

As above color indication + weekly Paclitaxel

FEC

2 Visit weeks

Centre No. | | | | | | |

Subject No. | | | | | | |

YES NO

Eligibility screening form

Inclusion criteria *(Note that if any box is marked "NO", the patient is not eligible for enrollment.)*

1. Female gender ☐ ☐
2. Age ≥ 18 years ☐ ☐
3. Eastern Cooperative Oncology Group (ECOG) performance status ≤ 1; ☐ ☐
4. Histologically confirmed invasive breast cancer: ☐ ☐
   - Primary tumor greater than 2 cm diameter, measured by clinical examination and mammography or echography;
   - Any N,
   - No evidence of metastasis (M0) (isolated supraclavicular node involvement allowed);
5. Overexpression and/or amplification of HER2 in the invasive component of the primary tumor according to one of the following definitions and confirmed by certified laboratory before randomisation: ☐ ☐
   – 3+ over expression by IHC (> 30% of invasive tumor cells);
   – 2+ or 3+ (in 30% or less neoplastic cells) over expression by IHC AND in situ hybridization (FISH/CISH) test demonstrating HER2 gene amplification;
   – HER2 gene amplification by FISH/CISH (> 6 HER2 gene copies per nucleus, or a FISH ratio [HER2 gene copies to chromosome 17 signals] of > than 2.2.).

   Equivocal local results may be submitted for a final determination by the certified laboratory
6. Hormone receptor (HR) status:
   - Oestrogen Receptor (ER) status must be known ☐ ☐
   - Progesterone (PR) status must be known ☐ ☐
7. Haematopoietic status:
   - Absolute Neutrophil count ≥ 1.5 x 10^9/L, ☐ ☐
   - Platelet count ≥ 100 x 10^9/L, ☐ ☐
   - Hemoglobin at least 9 g/dL ☐ ☐
8. Hepatic status:
   - Bilirubin ≤ 1.5 x upper limit of normal (ULN). In the case of known Gilbert's syndrome, a higher serum total bilirubin (< 2 X ULN) is allowed, ☐ ☐
   - AST and ALT ≤ 2.5 times ULN, ☐ ☐
   - Alkaline phosphatase ≤ 2.5 times ULN, ☐ ☐
9. Renal Status:
   - Creatinine ≤ 2.0 mg/dL, ☐ ☐
10. Baseline LVEF ≥ 50% measured by echocardiography (ECHO) or Multiple Gate Acquisition (MUGA) scan, ☐ ☐
11. Negative serum pregnancy test, within 2-weeks (preferably 7 days) prior to randomisation (For women of childbearing potential); ☐ ☐ NA ☐

*Note: Patients with a prior malignancy diagnosed more than 10 years prior to randomisation may enter the study. Patients must have been curatively treated with surgery alone. Radiation therapy or systemic therapy (chemotherapy or endocrine) are NOT permitted. Prior diagnoses of breast cancer or melanoma are excluded.

	YES	NO	NA
12. Fertile patients must use effective contraception (barrier method - condoms, diaphragm - also in conjunction with spermicidal jelly, or total abstinence. Oral, injectable, or implant hormonal contraceptives are not allowed) ;	☐	☐	☐
13. Signed written informed consent (approved by an Independent Ethics Committee [IEC] and obtained prior to any study specific screening procedures);	☐	☐	
14. Patient accepts to make available tumors samples for submission to central laboratory to conduct translational studies as part of this protocol	☐	☐	

Exclusion criteria *(Note that if any box is marked "YES", the patient is not eligible for enrollment.)*

1. Received any prior treatment for primary invasive breast cancer;	☐	☐
2. Previous (less than 10 years) or current history of malignant neoplasms. However, subjects with a past or current history of completely resected basal and squamous cell carcinoma of the skin or successfully treated in situ carcinoma of the cervix are eligible*;	☐	☐
3. Diagnosis of inflammatory breast cancer;	☐	☐
4. Bilateral cancer;	☐	☐
5. This exclusion criterion has been removed as of protocol amendment 1;	☐	☐
6. Known history of uncontrolled or symptomatic angina, clinically significant arrhythmias, congestive heart failure, transmural myocardial infarction, uncontrolled hypertension (≥ 180/110), unstable diabetes mellitus, dyspnoea at rest, or chronic therapy with oxygen;	☐	☐
7. Concurrent disease or condition that would make the subject inappropriate for study participation or any serious medical disorder that would interfere with the subject's safety;	☐	☐
8. Unresolved or unstable, serious adverse events from prior administration of another investigational drug;	☐	☐
9. Active or uncontrolled infection;	☐	☐
10. Dementia, altered mental status, or any psychiatric condition that would prevent the understanding or rendering of ICF;	☐	☐
11. Malabsorption syndrome, disease significantly affecting gastrointestinal function, or resection of the stomach or small bowel. Subjects with ulcerative colitis are also excluded;	☐	☐
12. Concurrent neoadjuvant cancer therapy (chemotherapy, radiation therapy, immunotherapy, biologic therapy other than the trial therapies);	☐	☐
13. Concurrent treatment with an investigational agent or participation in another therapeutic clinical trial;	☐	☐
14. Known immediate or delayed hypersensitivity reaction or idiosyncrasy or contraindication to drugs chemically related to any of the study treatment or their excipients;	☐	☐
15. Pregnant or lactating women;	☐	☐
16. Concomitant use of CYP3A4 inhibitors or inducers (see protocol section 7.2 for list of prohibited medications).	☐	☐

Centre No. | | | | | | |

Subject No. | | | | | | |

Randomisation

Date of randomisation ___ ___ ___ (DD MMM YYYY)

Assigned treatment arm
- ☐ Lapatinib alone
- ☐ Trastuzumab alone
- ☐ Lapatinib in combination with Trastuzumab

Informed consents

Date informed consent signed ___ ___ ___ (DD MMM YYYY)

Did the patient consent to:	No	Yes
Participate in PET/CT Scan imaging study (in selected sites only)	☐	☐
Participate in CTC analysis	☐	☐
Participate in Pharmacogenetic research	☐	☐

Date of birth

___ ___ ___ (DD MMM YYYY)

Race

- ☐ **American Indian or Alaska Native**: a person having origins in any of the original peoples of North and South America (including Central America) and who maintains tribal affiliation or community attachment
- ☐ **Asian**: Central/South Asian Heritage - a person having origins in Central Asia (Kazakstan, Kyrgystan, Tajikstan, Turkmenistan and Uzbekistan) and Indian Subcontinent (India, Pakistan, Bangladesh and Sri Lanka)
- ☐ **Asian**: East Asian Heritage - a person having origins in China, Korea
- ☐ **Asian**: Japanese Heritage - a person having origins in Japan
- ☐ **Asian**: South East Asia Heritage - a person having origins in Malaysia, the Philippines, Indonesia, Thailand, Vietnam, Laos, Burma or Cambodia
- ☐ **Black or African American/African Heritage**: a person having origins in any of the black racial group of Africa.
- ☐ **Native Hawaiian or other Pacific Islander**: a person having origins in any of the original peoples of Hawaii, Guam, Samoa or other Pacific Islands, Australia (Aborigines), Papua New Guinea, New Zealand, Marshalls and other island groups west and south of Japan
- ☐ **White**: Arabic/North African Heritage - a person having origins in any of the original peoples of Middle East or North Africa .
- ☐ **White**: White/Caucasian European Heritage - a person having origins in any of the original peoples of Europe
- ☐ **Other**, specify: _____

Ethnicity (only for North American sites)

- ☐ Hispanic or Latino
- ☐ Not Hispanic or Latino

Centre No. | | | | | | |

Subject No. | | | | | | |

Menopausal Status *(check one)*

- ☐ Premenopausal (<6 months since last menstrual period AND no prior bilateral ovariectomy AND not on oestrogen replacement; OR biochemical evidence of premenopausal status, according to local policies)
- ☐ Postmenopausal (prior bilateral ovariectomy/oopherectomy OR >12 months since last menstrual period with no prior hysterectomy; OR biochemical evidence of postmenopausal status, according to local policies)
- ☐ Above categories not applicable AND age < 50
- ☐ Above categories not applicable AND age >= 50

Date of last menstrual period DD MMM YYYY

Please report at least Month and Year. If LMP was more than 2 years prior to randomisation, report at least Year.

Pregnancy test

Date of pregnancy test DD MMM YYYY

- ☐ Positive → *Patient is not eligible*
- ☐ Negative
- ☐ Not applicable (not of chilbearing potential)

Has the patient had:

Hysterectomy ☐ No ☐ Yes → ☐ Total or ☐ Partial DD MMM YYYY

Unilateral* ovariectomy/oophorectomy, specify side: ☐ No ☐ Yes → ☐ Left or ☐ Right DD MMM YYYY

** Bilateral ovariectomy/oophorectomy should not be recorded here but in the section: "Hormone therapy for primary breast cancer", page 110, even if performed before diagnosis of breast cancer.*

ECOG performance status

ECOG	Performance status	Approximate Karnofsky
0	Fully active, able to carry on all pre-disease performance without restriction.	90 - 100
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.	70 - 80
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.	50 - 60
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.	30 - 40
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	10 - 20

New York Heart Association (NYHA) Functional Classification
NOTE: If the patient does not have congestive heart failure (CHF), leave this field blank.

Class I. Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain.

Class II. Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.

Class III. Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.

Class IV. Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

Vital signs and physical measurements

Date of physical exam ___ ___ ___ (DD MMM YYYY)

☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant → *Specify abnormality in "Previous or current diseases" page 13*

Height (cm) ___

Weight (Kg) ___.___

Blood pressure ___ / ___ mmHg (systolic / diastolic)

Heart rate (beats/min) ___

ECOG performance status ___

EKG

Date of EKG ___ ___ ___ (DD MMM YYYY)

Result
☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant → *Specify in "Previous or current cardiovascular diseases" page 12*

LVEF

Date of LVEF ___ ___ ___ (DD MMM YYYY)

LVEF (patient value) ___.___ % → *if LVEF < 50%, patient is not eligible*

Method of Evaluation ☐ Echocardiogram ☐ MUGA scan

☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant → *Specify in "Previous or current cardiovascular diseases" page 12*

Symptomatic CHF
☐ No
☐ Yes → *Specify below*

NYHA classification **(complete only in case of CHF)**
☐ Class I *(in case of asymptomatic CHF, tick No for the question above)*
☐ Class II
☐ Class III
☐ Class IV

Centre No. ☐☐☐☐☐☐ Subject No. ☐☐☐☐☐☐

HER2/neu status

Was local laboratory certified according to Neo-ALTTO Pathologist Board criteria?

For IHC ☐ No ☐ Yes
For FISH ☐ No ☐ Yes
For CISH ☐ No ☐ Yes

Results from Certified Local Lab or Central Lab only

(Please transcribe the data analysed by the local certified lab or report the data as reported on the "Central Lab requisition form")

Material ID number: _____

Certified Immunohistochemistry (IHC) result Sample test date ☐☐ ☐☐☐ ☐☐☐☐ (DD MMM YYYY) ☐ Not done

Antibody used: DAKO Herceptest ☐ No ☐ Yes

Result ☐ Positive ☐ Equivocal ☐ Negative ☐ Not interpretable

Percentage of invasive tumor cells with complete membrane staining (3+) ☐☐

Certified FISH result Sample test date ☐☐ ☐☐☐ ☐☐☐☐ (DD MMM YYYY) ☐ Not done

Kit or Test Type: ☐ Vysis/PathVysion ☐ Dako Probe ☐ Ventana/Oncorprobe
☐ Other: _____

Fish Result ☐ Amplified (>2.2) ☐ Equivocal (≥1.8; ≤ 2.2) ☐ Not amplified (<1.8) ☐ Not interpretable

FISH Her2/neu Chromosome 17 ratio ☐☐.☐☐

Chromosome 17 copy number
☐ Not evaluated
☐ Polysomy (3 or more signals in ≥ 30% of cells)
☐ Monosomy (60% of cells with 1 or no signals)
☐ Normal

Certified CISH result Sample test date ☐☐ ☐☐☐ ☐☐☐☐ (DD MMM YYYY) ☐ Not done

Kit or Test Type: ☐ Ventana INFORM ☐ Zymed ☐ Other: _____

CISH Result ☐ Amplified (>6 gene copies/nucleus) ☐ Equivocal (4-6 copies) ☐ Not amplified (<4 copies) ☐ Not interpretable

Chromosome 17 copy number
☐ Not evaluated
☐ Polysomy (3 or more signals in ≥ 30% of cells)
☐ Monosomy (60% of cells with 1 or no signals)
☐ Normal

Centre No. | | | | | | |

Subject No. | | | | | | |

HER2/neu status (Continued)

Results from Non Certified Local Labs only

If your lab was not certified, please provide below the local IHC assessment ☐ Not done

Staining antibody ☐ DAKO A0485l ☐ NCL-c-erbB2-316

☐ CB-11/Ventana Kit ☐ Other, specify: _____

☐ TAB-250

IHC Result ☐ Positive ☐ Equivocal ☐ Negative

Percentage of invasive tumor cells with complete membrane staining (3+) |__|__|

If your lab was not certified, please provide below the local FISH assessment ☐ Not done

Kit or Test Type: ☐ Vysis/PathVysion ☐ Dako Probe ☐ Ventana/Oncorprobe

☐ Other: _____

Fish Result ☐ Amplified (>2.2) ☐ Equivocal (≥1.8; ≤ 2.2) ☐ Not amplified (<1.8) ☐ Not interpretable

FISH Her2/neu Chromosome 17 ratio |__|__|.|__|__|

Chromosome 17 copy number

☐ Not evaluated
☐ Polysomy (3 or more signals in ≥ 30% of cells)
☐ Monosomy (60% of cells with 1 or no signals)
☐ Normal

If your lab was not certified, please provide below the local CISH assessment ☐ Not done

Kit or Test Type: ☐ Ventana INFORM ☐ Zymed ☐ Other: _____

CISH Result ☐ Amplified (>6 gene copies/nucleus) ☐ Equivocal (4-6 copies) ☐ Not amplified (<4 copies) ☐ Not interpretable

Chromosome 17 copy number

☐ Not evaluated
☐ Polysomy (3 or more signals in ≥ 30% of cells)
☐ Monosomy (60% of cells with 1 or no signals)
☐ Normal

Centre No. | | | | | | Subject No. | | | | | | |

History of primary breast cancer

Date of initial pathological diagnosis* ___ ___ ___ (DD MMM YYYY)

Method of evaluation
- ☐ Fine Needle Aspiration
- ☐ Core biopsy

Tumor laterality ☐ Left ☐ Right

Clinical tumor size by calliper: MD (mm) X LPD (mm)** ___.__ x ___.__

Clinical N stage
- ☐ N0 (no regional lymph nodes metastasis)
- ☐ N1 (metastasis to movable ipsilateral axillary lymph nodes)
- ☐ N2a (metastasis in ipsilateral axillary lymph nodes fixed to one another (matted) or to other structures)
- ☐ N2b (metastasis only in clinically apparent ipsilateral internal mammary nodes and in the absence of clinically evident axillary lymph node metastasis
- ☐ N3a (metastasis in ipsilateral infraclavicular lymph nodes)
- ☐ N3b (metastasis in ipsilateral internal mammary lymph nodes and axillary lymph node)
- ☐ N3c (metastasis in ipsilateral subclavicular lymph nodes)
- ☐ Nx (not assessed)

Method of evaluation (N status)
- ☐ Clinical
- ☐ Radiological, specify type of test: _____

Invasive histologic type *(tick all that apply)*

- ☐ Ductal NOS
- ☐ Lobular
- ☐ Mixed ductal and lobular
- ☐ Tubular
- ☐ Apocrine
- ☐ Tubulolobular
- ☐ Micropapillary
- ☐ Cribriform
- ☐ Mucinous
- ☐ Invasive NOS
- ☐ Medullary
- ☐ Other, specify: _____

* date when a sample allowing conclusive diagnosis of invasive carcinoma is taken, and this may only be a biopsy (tru-cut or core biopsy or mammotome biopsy)

** MD: maximal diameter, LPD: largest perpendicular diameter

Centre No. | | | | | | |

Subject No. | | | | | | |

History of primary breast cancer (Continued)

Is carcinoma in situ present?
- ☐ No
- ☐ Yes → ☐ DCIS
  - ☐ LCIS
  - ☐ Mixed DCIS and LCIS

Is there lymphovascular invasion?
- ☐ No
- ☐ Yes
- ☐ Unknown

Is Paget's disease of the nipple present?
- ☐ No
- ☐ Yes

Histologic Grade

- Gx ☐ Differentiation cannot be assessed
- G1 ☐ Well differentiated
- G2 ☐ Moderately differentiated
- G3 ☐ Poorly differentiated / Undifferentiated

Is the tumor multifocal/multicentric?
- ☐ No
- ☐ Yes → Are the different lesions showing *(tick all that apply)*
  - ☐ Same HER2 and ER/PgR status
  - ☐ Different HER2 status
  - ☐ Different ER status
  - ☐ Different PgR status
  - ☐ Other lesions were not assessed

Centre No. | | | | | | |

Subject No. | | | | | | |

History of primary breast cancer (continued)

Local Lab hormonal receptor status

Every effort should be made to obtain the detailed result of the hormonal receptors, even if done in another hospital.

Laboratory Name _____

City _____ Postal Code _____

ER status

- ☐ Positive
- ☐ Negative
- ☐ Unknown

Is oestrogen receptor analysis result available?

- ☐ No
- ☐ Yes → Specify below

fmol/mg protein ☐☐☐☐☐

ER % cells stained positive ☐☐☐

H-score (0-300) ☐☐☐

Allred score (0-8) ☐☐

Remmele score (0-12) ☐☐

Other ☐☐☐ specify _____ (_____)
Method Range

PgR status

- ☐ Positive
- ☐ Negative
- ☐ Unknown

Is progesterone receptor analysis result available?

- ☐ No
- ☐ Yes → Specify below

fmol/mg protein ☐☐☐☐☐

PgR % cells stained positive ☐☐☐

H-score (0-300) ☐☐☐

Allred score (0-8) ☐☐

Remmele score (0-12) ☐☐

Other ☐☐☐ specify _____ (_____)
Method Range

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Neutrophils	<LLN – 1500/mm³ <LLN – 1.5 x 10^9/L	<1500 – 1000/mm³ <1.5 – 1.0 x 10^9/L	<1000 – 500/mm³ <1.0 – 0.5 x 10^9/L	<500/mm³ <0.5 x 10^9/L	Death
WBC	<LLN – 3000/mm³ <LLN – 3.0 x 10^9/L	<3000 – 2000/mm³ <3.0 – 2.0 x 10^9/L	<2000 – 1000/mm³ <2.0 – 1.0 x 10^9/L	<1000/mm³ <1.0 x 10^9/L	Death
Haemoglobin	<LLN - 10.0 g/dL <LLN - 6.2 mmol/L <LLN - 100 g/L	<10.0 – 8.0 g/dL <6.2 – 4.9 mmol/L <100 – 80 g/L	<8.0 – 6.5 g/dL <4.9 – 4.0 mmol/L <80-65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
Platelets	<LLN -75,000/mm³ <LLN-75.0 x 10^9/L	<75,000-50,000/mm³ <75.0-50.0 x 10^9/L	<50,000-25,000/mm³ <50.0-25.0 x 10^9/L	<25,000/mm³ <25.0 x 10^9/L	Death
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	
Serum creatinine	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 6.0 x ULN	>6.0 x ULN	Death

Centre No. | | | | | | |

Subject No. | | | | | | |

Feasibility of surgery and type of <u>planned</u> breast cancer surgery at the time of initial diagnosis *(check one)*

☐ Not operable → *Specify below*

- ☐ Locally advanced
- ☐ T4a-c
- ☐ T4d → *Patient is not eligible*

☐ Lumpectomy

☐ Quadrantectomy / Segmentectomy

☐ Partial mastectomy

☐ Modified radical mastectomy

☐ Radical mastectomy (Halsted)

☐ Other, specify: _____

Haematology and biochemistry

Please check the blood tests that should be done within 14 days prior to randomisation, as per protocol, and report any <u>G3-4 or significant abnormality</u> in the "**Previous or current diseases**" page.

Date blood drawn DD MMM YYYY

Result

- ☐ Normal
- ☐ Abnormal - Not clinically significant
- ☐ Abnormal - <u>Clinically significant</u> → *Specify abnormality in "Previous or current diseases" page 13*

Centre No. | | | | | | |

Subject No. | | | | | | |

Previous or current cardiovascular diseases

Does the patient have a history of cardiovascular disease?

☐ No ☐ Yes → Specify below

Medical condition (record only one per line)	**Resolved** ✓	**Current*** ✓ →	**CTCAE Grade** →	**Treat. required?**** No	Yes
Hypertension	☐	☐		☐	☐
Hypotension	☐	☐		☐	☐
Sinus tachycardia	☐	☐		☐	☐
Atrial tachycardia	☐	☐		☐	☐
Palpitation	☐	☐		☐	☐
Arrhythmia	☐	☐		☐	☐
Atrial fibrillation	☐	☐		☐	☐
Valvular heart disease	☐	☐		☐	☐
Restrictive cardiomyopathy	☐	☐		☐	☐
Cardiac ischemia	☐	☐		☐	☐
Thrombosis/thrombus/embolism	☐	☐		☐	☐
Cardiac infarction	☐	☐		☐	☐
	☐	☐		☐	☐
	☐	☐		☐	☐
	☐	☐		☐	☐
	☐	☐		☐	☐
	☐	☐		☐	☐
	☐	☐		☐	☐
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	☐	☐		☐	☐
	☐	☐		☐	☐
	☐	☐		☐	☐
	☐	☐		☐	☐
	☐	☐		☐	☐
	☐	☐		☐	☐
	☐	☐		☐	☐
	☐	☐		☐	☐

* Report grade and treatments only for diseases current at time of randomisation. Grade using NCI CTCAE v.3

**Report all ongoing treatments on the "Concomitant treatment" pages 112-114

Previous or current diseases other than primary breast cancer and cardiovascular diseases

Any clinically significant diseases currently or at any time previously?

☐ No ☐ Yes → Specify below

Medical condition (record only one per line)	**Resolved** ✓	**Current*** ✓ →	**CTCAE Grade** →	**Treat. required?**** **No**	**Yes**
Osteoporosis	☐	☐	☐	☐	☐
Hot flashes/flushes	☐	☐	☐	☐	☐
Thyroid function, low (hypothyroidism)	☐	☐	☐	☐	☐
Thyroid function, high (hyperthyroidism)	☐	☐	☐	☐	☐
Insomnia	☐	☐	☐	☐	☐
Mood alteration - Anxiety	☐	☐	☐	☐	☐
Mood alteration - Depression	☐	☐	☐	☐	☐
Bronchospasm, wheezing	☐	☐	☐	☐	☐
Pain - Back	☐	☐	☐	☐	☐
Arthritis (non-septic)	☐	☐	☐	☐	☐
Cholesterol, serum-high (hypercholesteremia)	☐	☐	☐	☐	☐
Fatigue	☐	☐	☐	☐	☐
Diabetes	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐

* Report grade and treatments only for diseases current at time of randomisation. Grade using NCI CTCAE v.3 **Report all ongoing treatments on the "Concomitant treatment" pages 112-114

Centre No. ☐☐☐☐☐☐ Subject No. ☐☐☐☐☐☐

Type of radiological examination

	Not done	Date of test (DD/MMM/YYYY)	Are there any <u>clinically significant</u> abnormalities? *(Please report a short description)*
Abdominal CT-scan	☐	__/___/____	☐ No ☐ Yes → Specify ________
Chest X-ray*	☐	__/___/____	☐ No ☐ Yes → Specify ________
Chest CT-scan*	☐	__/___/____	☐ No ☐ Yes → Specify ________
Bone scan (scintigraphy)	☐	__/___/____	☐ No ☐ Yes → Specify ________
Bone X-ray	☐	__/___/____	☐ No ☐ Yes → Specify ________
Bone CT-scan	☐	__/___/____	☐ No ☐ Yes → Specify ________

* *Mandatory tests*

Anatomical site	Description
AB	Abdomen/abdominal wall
AD	Adrenals
BE	Bone
BR	Bladder
BT	Breast
CL	Colon
CR	Colorectal
CS	CNS (brain)
CW	Chest
CX	Cervix
EO	Esophagus/Oesophagus
HN	Head and neck
HT	Heart
K	Kidney
LG	Lung
LN	Lymph nodes

Anatomical site	Description
LV	Liver
OC	Oral cavity
OT	Other
OV	Ovary
PA	Pleura
PM	Peritoneum
PR	Prostate
PS	Pancreas
PV	Pelvis
RC	Rectum
SH	Stomach
SI	Small intestine
SK	Skin
SP	Spleen
TD	Thyroid
WB	Whole body

Type of radiological examination *(continued)*

	Not done	Date of test (DD/MMM/YYYY)	tumor measurement	Are there any clinically significant abnormalities? (Please report a short description)
Left breast mammogram*	☐		X mm	☐ No ☐ Yes →
Right breast mammogram*	☐		X mm	☐ No ☐ Yes →
Left breast echography	☐		X mm	☐ No ☐ Yes →
Right breast echography	☐		X mm	☐ No ☐ Yes →
MRI	☐		X mm	☐ No ☐ Yes →

Type of radiological examination**	Anatomical site***	Side (L or R)	Date of test (DD/MMM/YYYY)	Are there any clinically significant abnormalities?
				☐ No ☐ Yes → Specify
				☐ No ☐ Yes → Specify

*Mandatory tests

**BS=Bone scan (scintigraphy); C=CT scan; E=Endoscopy; L=Lymphangiogram; M=MRI; MA=Mammography; NS=Nuclear scan; PC=PET/CT Scan; PT=PET scan; TU=Transvaginal ultrasound; UL=Ultrasound (echography); XR=X-ray

*** See facing page for anatomical site codes

Centre No. Subject No.

PET/CT scan (only in selected sites)

Date of assessment DD MMM YYYY ☐ Not done

Subject preparation

Weight (Kg) ___.___

Injection site _____

Pre-injection blood glucose (mg/dL) ___ Time (hh:mm) __:__

Amount of FDG in syringe pre-injection (mCi) __.__ Time (hh:mm) __:__

Amount of FDG injected (mCi) __.__ Time (hh:mm) __:__

Amount of FDG in syringe post-injection (mCi) __.__ Time (hh:mm) __:__

→ *Please describe any clinically significant problem which occured during injection on "Adverse event" page*

Data acquisition protocol

Start Time (hh:mm) __:__

End Time (hh:mm) __:__

FOV Time (mm) __

Number of FOVS __

Technical CT parameter (kV) ___

Technical CT parameter (mA) ___

PET ☐ 2D ☐ 3D

Please describe any problem which occurred during data acquisition protocol (delay, etc.)

_____

_____

_____

Centre No. ☐☐☐☐☐☐ Subject No. ☐☐☐☐☐☐

PET/CT scan *(cont.)*

Description of lesions

Targeted lesion number	Site (organ)	Side: Left	Side: Right	Localization within this organ (quadrant, lymphatic region, etc.)	CT Largest bidimensional measurement of lesion (2 major axis) (mm) *	Metabolic volume (cc)	Uptake: No	Uptake: Yes	SUV_{max} (g/ml)	SUV_{mean} (g/ml)
⌴	Breast	☐	☐	____	⌴⌴⌴ X ⌴⌴⌴	⌴⌴⌴	☐	☐	⌴⌴.⌴	⌴⌴.⌴
⌴	Breast	☐	☐	____	⌴⌴⌴ X ⌴⌴⌴	⌴⌴⌴	☐	☐	⌴⌴.⌴	⌴⌴.⌴
⌴	Breast	☐	☐	____	⌴⌴⌴ X ⌴⌴⌴	⌴⌴⌴	☐	☐	⌴⌴.⌴	⌴⌴.⌴
⌴	Lymphnode	☐	☐	____	⌴⌴⌴ X ⌴⌴⌴	⌴⌴⌴	☐	☐	⌴⌴.⌴	⌴⌴.⌴
⌴	Lymphnode	☐	☐	____	⌴⌴⌴ X ⌴⌴⌴	⌴⌴⌴	☐	☐	⌴⌴.⌴	⌴⌴.⌴
⌴	Lymphnode	☐	☐	____	⌴⌴⌴ X ⌴⌴⌴	⌴⌴⌴	☐	☐	⌴⌴.⌴	⌴⌴.⌴
⌴	Lymphnode	☐	☐	____	⌴⌴⌴ X ⌴⌴⌴	⌴⌴⌴	☐	☐	⌴⌴.⌴	⌴⌴.⌴
	Specify:									
⌴	____	☐	☐	____	⌴⌴⌴ X ⌴⌴⌴	⌴⌴⌴	☐	☐	⌴⌴.⌴	⌴⌴.⌴

* Report the structural measurement of the lesion, not the measurement showing metabolic activity

Biological samples

Type of tissue	**Was sample obtained?** **No Yes →**	**Date of specimen collection** **(dd/mmm/yyyy)**
FFPE* tumor core biopsy	☐ ☐	
Blood sample for PGx**	☐ ☐	
Blood sample for proteomics: - serum	☐ ☐	
Blood sample for proteomics: - plasma	☐ ☐	
Additional blood sample for CTC*** *(only in selected centres)*	☐ ☐	
Snap frozen tumor sample (2 cores)	☐ ☐	

* Formalin Fixed Paraffin Embedded.
** PGx: Pharmacogenetics
*** CTC: Circulating tumor cells

ECOG performance status

ECOG	Performance status	Approximate Karnofsky
0	Fully active, able to carry on all pre-disease performance without restriction.	90 - 100
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.	70 - 80
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.	50 - 60
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.	30 - 40
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	10 - 20

WHO Criteria

Response	**Measurable disease**
Complete response	The disappearance of all known disease.
Partial response	50% or more decrease in total tumor size, i.e. the sum of the products of the maximal diameter (MD) and the corresponding largest perpendicular diameter (LPD) of the lesions which have been measured to determine the effect of therapy. In addition, there can be no appearance of new lesions or progression of any lesion.
Progressive disease	At least a 25% increase in total tumor size, i.e. the sum of the products MD*LPD of lesions, and/or the appearance of one or more new lesion/s.
No change	A 50% decrease in total tumor size, i.e. the sum of the products MD*LPD of lesions cannot be established nor a 25% increase in the size of one or more measurable lesions has been determined.

Patient status

Date of physical exam ☐ Not done
DD MMM YYYY

☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant → *Specify abnormality on "Adverse event" page*

Vital signs and physical measurements

Weight (Kg) ___.__

Blood pressure ___ / ___ mmHg
systolic diastolic

Heart rate (beats/min) ___

ECOG performance status ___

Breast palpation with tumor measurements and nodal status

Clinical tumor size by calliper: MD (mm) X LPD (mm)* ___.__ X ___.__

New lesion(s) ☐ No ☐ Yes

Clinical N stage
☐ N0 (no regional lymph nodes metastasis)
☐ N1 (metastasis to movable ipsilateral axillary lymph nodes)
☐ N2a (metastasis in ipsilateral axillary lymph nodes fixed to one another (matted) or to other structures)
☐ N2b (metastasis only in clinically apparent ipsilateral internal mammary nodes and in the absence of clinically evident axillary lymph node metastasis
☐ N3a (metastasis in ipsilateral infraclavicular lymph nodes)
☐ N3b (metastasis in ipsilateral internal mammary lymph nodes and axillary lymph node)
☐ N3c (metastasis in ipsilateral subclavicular lymph nodes)
☐ Nx (not assessed)

Overall clinical tumor response (WHO criteria) using physical measurements

☐ Complete response
☐ Partial response
☐ Progressive disease
☐ No change
☐ Not evaluated

* MD: maximal diameter, LPD: largest perpendicular diameter

Centre No. Subject No.

PET/CT scan (only in selected sites)

Date of assessment DD MMM YYYY ☐ Not done

Subject preparation

Weight (Kg) ___.___

Injection site _____

Pre-injection blood glucose (mg/dL) ___ Time (hh:mm) __:__

Amount of FDG in syringe pre-injection (mCi) __.__ Time (hh:mm) __:__

Amount of FDG injected (mCi) __.__ Time (hh:mm) __:__

Amount of FDG in syringe post-injection (mCi) __.__ Time (hh:mm) __:__

→ *Please describe any clinically significant problem which occured during injection on "Adverse event" page*

Data acquisition protocol

Start Time (hh:mm) __:__

End Time (hh:mm) __:__

FOV Time (mm) __

Number of FOVS __

Technical CT parameter (kV) ___

Technical CT parameter (mA) ___

PET ☐ 2D ☐ 3D

Please describe any problem which occurred during data acquisition protocol (delay, etc.)

_____

_____

_____

mCR: complete metabolic response would be complete resolution of [^{18}F]-FDG uptake within the tumor volume so that it was indistinguishable from surrounding normal tissue.

mPR: partial metabolic response would be classified as a reduction greater than 25% of [^{18}F]-FDG uptake. Reporting would need to be accompanied by adequate and disclosed reproducibility measurements from each centre. An empirical 25% was found to be a useful cut-off point, but there is a need for a reproducibility analysis to determine the appropriate cutt-offs for statistical significance. A reduction in th extent of the tumor [^{18}F]-FDG uptake is not a requirement for partial metabolic response.

mSD: stable metabolic disease would be classified as an increase in tumor [^{18}F]-FDG SUV of less than 25% or a decrease of less than 15% and no visible increase in extent of [^{18}F]-FDG tumor uptake (>20% in the longest dimension).

mPD: progressive metabolic disease would be classified as an increase in [^{18}F]-FDG tumor SUV of greater than 25% within the tumor region defined on the baseline scan, visible increase in the extent of [^{18}F]-FDG tumor uptake (>20% in the longest dimension) or the appearance of new [^{18}F]-FDG uptake in metastatic lesions.

Centre No. | Subject No.

PET/CT scan *(cont.)*

Description of lesions

Targeted lesion number*	Site (organ)	Side: Left	Side: Right	Localization (within this organ)	CT Largest bidimensional measurement of lesion (2 major axis) (mm)**	Metabolic volume (cc)	Uptake: No	Uptake: Yes	SUV_{max} (g/ml)	SUV_{mean} (g/ml)	Lesion Metabolic response***
	Breast	☐	☐		X		☐	☐	.	.	m
	Breast	☐	☐		X		☐	☐	.	.	m
	Breast	☐	☐		X		☐	☐	.	.	m
	Lymphnode	☐	☐		X		☐	☐	.	.	m
	Lymphnode	☐	☐		X		☐	☐	.	.	m
	Lymphnode	☐	☐		X		☐	☐	.	.	m
	Lymphnode	☐	☐		X		☐	☐	.	.	m

* The same lesion should carry the same lesion number throughout the 3 PET/CT scan assessments (see page 17)
** Report the structural measurement of the lesion, not the measurement showing metabolic activity
*** See facing page for metabolic response definitions

mCR: complete metabolic response would be complete resolution of [^{18}F]-FDG uptake within the tumor volume so that it was indistinguishable from surrounding normal tissue.

mPR: partial metabolic response would be classified as a reduction greater than 25% of [^{18}F]-FDG uptake. Reporting would need to be accompanied by adequate and disclosed reproducibility measurements from each centre. An empirical 25% was found to be a useful cut-off point, but there is a need for a reproducibility analysis to determine the appropriate cutt-offs for statistical significance. A reduction in th extent of the tumor [^{18}F]-FDG uptake is not a requirement for partial metabolic response.

mSD: stable metabolic disease would be classified as an increase in tumor [^{18}F]-FDG SUV of less than 25% or a decrease of less than 15% and no visible increase in extent of [^{18}F]-FDG tumor uptake (>20% in the longest dimension).

mPD: progressive metabolic disease would be classified as an increase in [^{18}F]-FDG tumor SUV of greater than 25% within the tumor region defined on the baseline scan, visible increase in the extent of [^{18}F]-FDG tumor uptake (>20% in the longest dimension) or the appearance of new [^{18}F]-FDG uptake in metastatic lesions.

Centre No. Subject No.

PET/CT scan *(cont.)*

Description of distant lesions

Targeted lesion number*	Site (organ)	Side: Left	Side: Right	Localization within this organ (quadrant, lymphatic region, etc.)	CT Largest bidimensional measurement of lesion (2 major axis) (mm)**	Metabolic volume (cc)	Uptake: No	Uptake: Yes	SUV_{max} (g/ml)	SUV_{mean} (g/ml)	Lesion Metabolic response***
		☐	☐		X		☐	☐	.	.	m
		☐	☐		X		☐	☐	.	.	m
		☐	☐		X		☐	☐	.	.	m
		☐	☐		X		☐	☐	.	.	m
		☐	☐		X		☐	☐	.	.	m

* The same lesion should carry the same lesion number throughout the 3 PET/CT scan assessments (see page 17)
** See facing page for metabolic response definitions

Translational research

Type of tissue	**Was sample obtained?** **No Yes →**	**Date of specimen collection** **(dd/mmm/yyyy)**
FFPE* tumor core biopsy	☐ ☐	
Blood sample for proteomics: - serum	☐ ☐	
Blood sample for proteomics: - plasma	☐ ☐	
Additional blood sample for CTC** *(only in selected centres)*	☐ ☐	
Snap frozen tumor sample (2 cores)	☐ ☐	

* Formalin Fixed Paraffin Embedded.
** CTC: Circulating tumor cells

ECOG performance status

ECOG	Performance status	Approximate Karnofsky
0	Fully active, able to carry on all pre-disease performance without restriction.	90 - 100
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.	70 - 80
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.	50 - 60
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.	30 - 40
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	10 - 20

WHO Criteria

Response	**Measurable disease**
Complete response	The disappearance of all known disease.
Partial response	50% or more decrease in total tumor size, i.e. the sum of the products of the maximal diameter (MD) and the corresponding largest perpendicular diameter (LPD) of the lesions which have been measured to determine the effect of therapy. In addition, there can be no appearance of new lesions or progression of any lesion.
Progressive disease	At least a 25% increase in total tumor size, i.e. the sum of the products MD*LPD of lesions, and/or the appearance of one or more new lesion/s.
No change	A 50% decrease in total tumor size, i.e. the sum of the products MD*LPD of lesions cannot be established nor a 25% increase in the size of one or more measurable lesions has been determined.

Centre No. Subject No.

Patient status

Date of physical exam ☐ Not done

DD MMM YYYY

☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant → *Specify abnormality on "Adverse event" page*

Vital signs and physical measurements

Weight (Kg) ___.__

Blood pressure ___ / ___ mmHg

systolic diastolic

Heart rate (beats/min) ___

ECOG performance status ___

Breast palpation with tumor measurements and nodal status

Clinical tumor size by calliper: MD (mm) X LPD (mm)* ___.__ X ___.__

New lesion(s) ☐ No ☐ Yes

Clinical N stage
- ☐ N0 (no regional lymph nodes metastasis)
- ☐ N1 (metastasis to movable ipsilateral axillary lymph nodes)
- ☐ N2a (metastasis in ipsilateral axillary lymph nodes fixed to one another (matted) or to other structures)
- ☐ N2b (metastasis only in clinically apparent ipsilateral internal mammary nodes and in the absence of clinically evident axillary lymph node metastasis
- ☐ N3a (metastasis in ipsilateral infraclavicular lymph nodes)
- ☐ N3b (metastasis in ipsilateral internal mammary lymph nodes and axillary lymph node)
- ☐ N3c (metastasis in ipsilateral subclavicular lymph nodes)
- ☐ Nx (not assessed)

Overall clinical tumor response (WHO criteria) using physical measurements

- ☐ Complete response
- ☐ Partial response
- ☐ Progressive disease
- ☐ No change
- ☐ Not evaluated

* MD: maximal diameter, LPD: largest perpendicular diameter

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Neutrophils	<LLN – 1500/mm³ <LLN – 1.5 x 10^9/L	<1500 – 1000/mm³ <1.5 – 1.0 x 10^9/L	<1000 – 500/mm³ <1.0 – 0.5 x 10^9/L	<500/mm³ <0.5 x 10^9/L	Death
WBC	<LLN – 3000/mm³ <LLN – 3.0 x 10^9/L	<3000 – 2000/mm³ <3.0 – 2.0 x 10^9/L	<2000 – 1000/mm³ <2.0 – 1.0 x 10^9/L	<1000/mm³ <1.0 x 10^9/L	Death
Haemoglobin	<LLN - 10.0 g/dL <LLN - 6.2 mmol/L <LLN - 100 g/L	<10.0 – 8.0 g/dL <6.2 – 4.9 mmol/L <100 – 80 g/L	<8.0 – 6.5 g/dL <4.9 – 4.0 mmol/L <80-65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
Platelets	<LLN -75,000/mm³ <LLN-75.0 x 10^9/L	<75,000-50,000/mm³ <75.0-50.0 x 10^9/L	<50,000-25,000/mm³ <50.0-25.0 x 10^9/L	<25,000/mm³ <25.0 x 10^9/L	Death
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	
Serum creatinine	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 6.0 x ULN	>6.0 x ULN	Death

Centre No. | | | | | | |

Subject No. | | | | | | |

Haematology and biochemistry

Please check the blood tests that should be done at this visit, as per protocol, and report any clinically significant (NCI CTCAE G3-4) abnormality on the "**Adverse event**" page.

Date blood drawn ____ ____ ____
DD MMM YYYY

Result
- ☐ Normal
- ☐ Abnormal - Not clinically significant
- ☐ Abnormal - Clinically significant (G3-4) → *Report on Adverse Event page*

ECOG performance status

ECOG	Performance status	Approximate Karnofsky
0	Fully active, able to carry on all pre-disease performance without restriction.	90 - 100
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.	70 - 80
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.	50 - 60
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.	30 - 40
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	10 - 20

WHO Criteria

Response	**Measurable disease**
Complete response	The disappearance of all known disease.
Partial response	50% or more decrease in total tumor size, i.e. the sum of the products of the maximal diameter (MD) and the corresponding largest perpendicular diameter (LPD) of the lesions which have been measured to determine the effect of therapy. In addition, there can be no appearance of new lesions or progression of any lesion.
Progressive disease	At least a 25% increase in total tumor size, i.e. the sum of the products MD*LPD of lesions, and/or the appearance of one or more new lesion/s.
No change	A 50% decrease in total tumor size, i.e. the sum of the products MD*LPD of lesions cannot be established nor a 25% increase in the size of one or more measurable lesions has been determined.

Centre No. Subject No.

Patient status

Date of physical exam DD MMM YYYY ☐ Not done

☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant → *Specify abnormality on "Adverse event" page*

Vital signs and physical measurements

Weight (Kg) ___.__

Blood pressure ___ / ___ mmHg (systolic / diastolic)

Heart rate (beats/min) ___

ECOG performance status ___

Breast palpation with tumor measurements and nodal status

Clinical tumor size by calliper: MD (mm) X LPD (mm)* ___.__ X ___.__

New lesion(s) ☐ No ☐ Yes

Clinical N stage
- ☐ N0 (no regional lymph nodes metastasis)
- ☐ N1 (metastasis to movable ipsilateral axillary lymph nodes)
- ☐ N2a (metastasis in ipsilateral axillary lymph nodes fixed to one another (matted) or to other structures)
- ☐ N2b (metastasis only in clinically apparent ipsilateral internal mammary nodes and in the absence of clinically evident axillary lymph node metastasis
- ☐ N3a (metastasis in ipsilateral infraclavicular lymph nodes)
- ☐ N3b (metastasis in ipsilateral internal mammary lymph nodes and axillary lymph node)
- ☐ N3c (metastasis in ipsilateral subclavicular lymph nodes)
- ☐ Nx (not assessed)

Overall clinical tumor response (WHO criteria) using physical measurements

- ☐ Complete response
- ☐ Partial response
- ☐ Progressive disease
- ☐ No change
- ☐ Not evaluated

* MD: maximal diameter, LPD: largest perpendicular diameter

New York Heart Association (NYHA) Functional Classification
NOTE: If the patient does not have congestive heart failure (CHF), leave this field blank.

Class I. Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain.

Class II. Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.

Class III. Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.

Class IV. Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Neutrophils	<LLN – 1500/mm³ <LLN – 1.5 x 10^9/L	<1500 – 1000/mm³ <1.5 – 1.0 x 10^9/L	<1000 – 500/mm³ <1.0 – 0.5 x 10^9/L	<500/mm³ <0.5 x 10^9/L	Death
WBC	<LLN – 3000/mm³ <LLN – 3.0 x 10^9/L	<3000 – 2000/mm³ <3.0 – 2.0 x 10^9/L	<2000 – 1000/mm³ <2.0 – 1.0 x 10^9/L	<1000/mm³ <1.0 x 10^9/L	Death
Haemoglobin	<LLN - 10.0 g/dL <LLN - 6.2 mmol/L <LLN - 100 g/L	<10.0 – 8.0 g/dL <6.2 – 4.9 mmol/L <100 – 80 g/L	<8.0 – 6.5 g/dL <4.9 – 4.0 mmol/L <80-65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
Platelets	<LLN -75,000/mm³ <LLN-75.0 x 10^9/L	<75,000-50,000/mm³ <75.0-50.0 x 10^9/L	<50,000-25,000/mm³ <50.0-25.0 x 10^9/L	<25,000/mm³ <25.0 x 10^9/L	Death
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	
Serum creatinine	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 6.0 x ULN	>6.0 x ULN	Death

Cardiac monitoring

LVEF

Date of LVEF ___ ___ ___ (DD MMM YYYY)

LVEF (patient value) ___.___ % Method of Evaluation ☐ Echocardiogram ☐ MUGA scan

☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant → *Please complete the "Adverse event" page.*

Symptomatic CHF ☐ No ☐ Yes → *Specify below*

NYHA classification **(complete only in case of CHF)**
☐ Class I *(in case of asymptomatic CHF, tick No for the question above)*
☐ Class II
☐ Class III (*study treatment should be interrupted)*
☐ Class IV (*study treatment should be interrupted)*

EKG should be performed at any time if symptoms or clinical suspicion are present and reported on the "Unscheduled EKG" page

Haematology and biochemistry

Please check the blood tests that should be done at this visit, as per protocol, and report any clinically significant (NCI CTCAE G3-4) abnormality on the "**Adverse event**" page.

Date blood drawn ___ ___ ___ (DD MMM YYYY)

Result
☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant (G3-4) → *Report on Adverse Event page*

Type of radiological examination

	Not done	Date of test (DD/MMM/YYYY)	tumor measurement	Are there any clinically significant abnormalities? *(Please report a short description)*
Left breast mammogram	☐	___	___ X ___ mm	☐ No ☐ Yes → ___
Right breast mammogram	☐	___	___ X ___ mm	☐ No ☐ Yes → ___
Left breast echography	☐	___	___ X ___ mm	☐ No ☐ Yes → ___
Right breast echography	☐	___	___ X ___ mm	☐ No ☐ Yes → ___
MRI	☐	___	___ X ___ mm	☐ No ☐ Yes → ___

Centre No. Subject No.

PET/CT scan (only in selected sites)

Date of assessment DD MMM YYYY ☐ Not done

Subject preparation

Weight (Kg) ___.___

Injection site _____

Pre-injection blood glucose (mg/dL) ___ Time (hh:mm) __:__

Amount of FDG in syringe pre-injection (mCi) __.__ Time (hh:mm) __:__

Amount of FDG injected (mCi) __.__ Time (hh:mm) __:__

Amount of FDG in syringe post-injection (mCi) __.__ Time (hh:mm) __:__

→ *Please describe any clinically significant problem which occured during injection on "Adverse event" page*

Data acquisition protocol

Start Time (hh:mm) __:__

End Time (hh:mm) __:__

FOV Time (mm) __

Number of FOVS __

Technical CT parameter (kV) ___

Technical CT parameter (mA) ___

PET ☐ 2D ☐ 3D

Please describe any problem which occurred during data acquisition protocol (delay, etc.)

_____

_____

_____

mCR: complete metabolic response would be complete resolution of [^{18}F]-FDG uptake within the tumor volume so that it was indistinguishable from surrounding normal tissue.

mPR: partial metabolic response would be classified as a reduction greater than 25% of [^{18}F]-FDG uptake. Reporting would need to be accompanied by adequate and disclosed reproducibility measurements from each centre. An empirical 25% was found to be a useful cut-off point, but there is a need for a reproducibility analysis to determine the appropriate cutt-offs for statistical significance. A reduction in th extent of the tumor [^{18}F]-FDG uptake is not a requirement for partial metabolic response.

mSD: stable metabolic disease would be classified as an increase in tumor [^{18}F]-FDG SUV of less than 25% or a decrease of less than 15% and no visible increase in extent of [^{18}F]-FDG tumor uptake (>20% in the longest dimension).

mPD: progressive metabolic disease would be classified as an increase in [^{18}F]-FDG tumor SUV of greater than 25% within the tumor region defined on the baseline scan, visible increase in the extent of [^{18}F]-FDG tumor uptake (>20% in the longest dimension) or the appearance of new [^{18}F]-FDG uptake in metastatic lesions.

Centre No. ☐☐☐☐☐☐ Subject No. ☐☐☐☐☐☐

PET/CT scan *(cont.)*

Description of lesions

Targeted lesion number*	Site (organ)	Side Left	Side Right	Localization within this organ (quadrant, lymphatic region, etc.)	CT Largest bidimensional measurement of lesion (2 major axis) (mm)**	Metabolic volume (cc)	Uptake No	Uptake Yes	SUV_{max} (g/ml)	SUV_{mean} (g/ml)	Lesion Metabolic response***
	Breast	☐	☐		X		☐	☐	.	.	m
	Breast	☐	☐		X		☐	☐	.	.	m
	Breast	☐	☐		X		☐	☐	.	.	m
	Lymphnode	☐	☐		X		☐	☐	.	.	m
	Lymphnode	☐	☐		X		☐	☐	.	.	m
	Lymphnode	☐	☐		X		☐	☐	.	.	m
	Lymphnode	☐	☐		X		☐	☐	.	.	m

* The same lesion should carry the same lesion number throughout the 3 PET/CT scan assessments (see pages 17, 21 and 22)
** Report the structural measurement of the lesion, not the measurement showing metabolic activity
*** See facing page for metabolic response definitions

mCR: complete metabolic response would be complete resolution of [^{18}F]-FDG uptake within the tumor volume so that it was indistinguishable from surrounding normal tissue.

mPR: partial metabolic response would be classified as a reduction greater than 25% of [^{18}F]-FDG uptake. Reporting would need to be accompanied by adequate and disclosed reproducibility measurements from each centre. An empirical 25% was found to be a useful cut-off point, but there is a need for a reproducibility analysis to determine the appropriate cutt-offs for statistical significance. A reduction in th extent of the tumor [^{18}F]-FDG uptake is not a requirement for partial metabolic response.

mSD: stable metabolic disease would be classified as an increase in tumor [^{18}F]-FDG SUV of less than 25% or a decrease of less than 15% and no visible increase in extent of [^{18}F]-FDG tumor uptake (>20% in the longest dimension).

mPD: progressive metabolic disease would be classified as an increase in [^{18}F]-FDG tumor SUV of greater than 25% within the tumor region defined on the baseline scan, visible increase in the extent of [^{18}F]-FDG tumor uptake (>20% in the longest dimension) or the appearance of new [^{18}F]-FDG uptake in metastatic lesions.

Centre No.	Subject No.
☐☐☐☐☐☐	☐☐☐☐☐☐

PET/CT scan *(cont.)*

Description of distant lesions

Targeted lesion number	Site (organ)	Side: Left	Side: Right	Localization (within this organ)	CT Largest bidimensional measurement of lesion (2 major axis) (mm)	PET volume (cc)	Uptake: No	Uptake: Yes	SUV_{max} (g/ml)	SUV_{mean} (g/ml)	Lesion Metabolic response**
☐	____	☐	☐	____	☐☐☐ X ☐☐☐	☐☐☐	☐	☐	☐☐.☐	☐☐.☐	m☐☐
☐	____	☐	☐	____	☐☐☐ X ☐☐☐	☐☐☐	☐	☐	☐☐.☐	☐☐.☐	m☐☐
☐	____	☐	☐	____	☐☐☐ X ☐☐☐	☐☐☐	☐	☐	☐☐.☐	☐☐.☐	m☐☐
☐	____	☐	☐	____	☐☐☐ X ☐☐☐	☐☐☐	☐	☐	☐☐.☐	☐☐.☐	m☐☐
☐	____	☐	☐	____	☐☐☐ X ☐☐☐	☐☐☐	☐	☐	☐☐.☐	☐☐.☐	m☐☐

* The same lesion should carry the same lesion number throughout the 3 PET/CT scan assessments (see pages 17, 21 and 22)
** See facing page for metabolic response definitions

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Neutrophils	<LLN – 1500/mm³ <LLN – 1.5 x 10^9/L	<1500 – 1000/mm³ <1.5 – 1.0 x 10^9/L	<1000 – 500/mm³ <1.0 – 0.5 x 10^9/L	<500/mm³ <0.5 x 10^9/L	Death
WBC	<LLN – 3000/mm³ <LLN – 3.0 x 10^9/L	<3000 – 2000/mm³ <3.0 – 2.0 x 10^9/L	<2000 – 1000/mm³ <2.0 – 1.0 x 10^9/L	<1000/mm³ <1.0 x 10^9/L	Death
Haemoglobin	<LLN - 10.0 g/dL <LLN - 6.2 mmol/L <LLN - 100 g/L	<10.0 – 8.0 g/dL <6.2 – 4.9 mmol/L <100 – 80 g/L	<8.0 – 6.5 g/dL <4.9 – 4.0 mmol/L <80-65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
Platelets	<LLN -75,000/mm³ <LLN-75.0 x 10^9/L	<75,000-50,000/mm³ <75.0-50.0 x 10^9/L	<50,000-25,000/mm³ <50.0-25.0 x 10^9/L	<25,000/mm³ <25.0 x 10^9/L	Death
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	
Serum creatinine	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 6.0 x ULN	>6.0 x ULN	Death

Haematology

Please check the blood tests that should be done at these visits, as per protocol, and report any clinically significant (NCI CTCAE G3-4) abnormality on the "**Adverse event**" page.

Date blood drawn week 8 DD MMM YYYY

Result
- ☐ Normal
- ☐ Abnormal - Not clinically significant
- ☐ Abnormal - Clinically significant (G3-4) → *Report on Adverse Event page*

Date blood drawn week 9 DD MMM YYYY

Result
- ☐ Normal
- ☐ Abnormal - Not clinically significant
- ☐ Abnormal - Clinically significant (G3-4) → *Report on Adverse Event page*

ECOG performance status

ECOG	Performance status	Approximate Karnofsky
0	Fully active, able to carry on all pre-disease performance without restriction.	90 - 100
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.	70 - 80
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.	50 - 60
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.	30 - 40
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	10 - 20

WHO Criteria

Response	**Measurable disease**
Complete response	The disappearance of all known disease.
Partial response	50% or more decrease in total tumor size, i.e. the sum of the products of the maximal diameter (MD) and the corresponding largest perpendicular diameter (LPD) of the lesions which have been measured to determine the effect of therapy. In addition, there can be no appearance of new lesions or progression of any lesion.
Progressive disease	At least a 25% increase in total tumor size, i.e. the sum of the products MD*LPD of lesions, and/or the appearance of one or more new lesion/s.
No change	A 50% decrease in total tumor size, i.e. the sum of the products MD*LPD of lesions cannot be established nor a 25% increase in the size of one or more measurable lesions has been determined.

Centre No. Subject No.

Patient status

Date of physical exam DD MMM YYYY ☐ Not done

☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant → *Specify abnormality on "Adverse event" page*

Vital signs and physical measurements

Weight (Kg) ___.__

Blood pressure ___ (systolic) / ___ (diastolic) mmHg

Heart rate (beats/min) ___

ECOG performance status ___

Breast palpation with tumor measurements and nodal status

Clinical tumor size by calliper: MD (mm) X LPD (mm)* ___.__ X ___.__

New lesion(s) ☐ No ☐ Yes

Clinical N stage
- ☐ N0 (no regional lymph nodes metastasis)
- ☐ N1 (metastasis to movable ipsilateral axillary lymph nodes)
- ☐ N2a (metastasis in ipsilateral axillary lymph nodes fixed to one another (matted) or to other structures)
- ☐ N2b (metastasis only in clinically apparent ipsilateral internal mammary nodes and in the absence of clinically evident axillary lymph node metastasis
- ☐ N3a (metastasis in ipsilateral infraclavicular lymph nodes)
- ☐ N3b (metastasis in ipsilateral internal mammary lymph nodes and axillary lymph node)
- ☐ N3c (metastasis in ipsilateral subclavicular lymph nodes)
- ☐ Nx (not assessed)

Overall clinical tumor response (WHO criteria) using physical measurements

- ☐ Complete response
- ☐ Partial response
- ☐ Progressive disease
- ☐ No change
- ☐ Not evaluated

* MD: maximal diameter, LPD: largest perpendicular diameter

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Neutrophils	<LLN – 1500/mm³ <LLN – 1.5 x 10^9/L	<1500 – 1000/mm³ <1.5 – 1.0 x 10^9/L	<1000 – 500/mm³ <1.0 – 0.5 x 10^9/L	<500/mm³ <0.5 x 10^9/L	Death
WBC	<LLN – 3000/mm³ <LLN – 3.0 x 10^9/L	<3000 – 2000/mm³ <3.0 – 2.0 x 10^9/L	<2000 – 1000/mm³ <2.0 – 1.0 x 10^9/L	<1000/mm³ <1.0 x 10^9/L	Death
Haemoglobin	<LLN - 10.0 g/dL <LLN - 6.2 mmol/L <LLN - 100 g/L	<10.0 – 8.0 g/dL <6.2 – 4.9 mmol/L <100 – 80 g/L	<8.0 – 6.5 g/dL <4.9 – 4.0 mmol/L <80-65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
Platelets	<LLN -75,000/mm³ <LLN-75.0 x 10^9/L	<75,000-50,000/mm³ <75.0-50.0 x 10^9/L	<50,000-25,000/mm³ <50.0-25.0 x 10^9/L	<25,000/mm³ <25.0 x 10^9/L	Death
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	
Serum creatinine	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 6.0 x ULN	>6.0 x ULN	Death

Centre No. | | | | | | |

Subject No. | | | | | | |

Haematology and biochemistry

Please check the blood tests that should be done at this visit, as per protocol, and report any clinically significant (NCI CTCAE G3-4) abnormality on the "**Adverse event**" page.

Date blood drawn _ _ DD _ _ _ MMM _ _ _ _ YYYY

Result

- ☐ Normal
- ☐ Abnormal - Not clinically significant
- ☐ Abnormal - Clinically significant (G3-4) ⟶ *Report on Adverse Event page*

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Neutrophils	<LLN – 1500/mm³ <LLN – 1.5 x 10^9/L	<1500 – 1000/mm³ <1.5 – 1.0 x 10^9/L	<1000 – 500/mm³ <1.0 – 0.5 x 10^9/L	<500/mm³ <0.5 x 10^9/L	Death
WBC	<LLN – 3000/mm³ <LLN – 3.0 x 10^9/L	<3000 – 2000/mm³ <3.0 – 2.0 x 10^9/L	<2000 – 1000/mm³ <2.0 – 1.0 x 10^9/L	<1000/mm³ <1.0 x 10^9/L	Death
Haemoglobin	<LLN - 10.0 g/dL <LLN - 6.2 mmol/L <LLN - 100 g/L	<10.0 – 8.0 g/dL <6.2 – 4.9 mmol/L <100 – 80 g/L	<8.0 – 6.5 g/dL <4.9 – 4.0 mmol/L <80-65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
Platelets	<LLN -75,000/mm³ <LLN-75.0 x 10^9/L	<75,000-50,000/mm³ <75.0-50.0 x 10^9/L	<50,000-25,000/mm³ <50.0-25.0 x 10^9/L	<25,000/mm³ <25.0 x 10^9/L	Death
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	
Serum creatinine	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 6.0 x ULN	>6.0 x ULN	Death

Haematology

Please check the blood tests that should be done at these visits, as per protocol, and report any clinically significant (NCI CTCAE G3-4) abnormality on the "**Adverse event**" page.

Date blood drawn week 11 DD MMM YYYY

Result
- ☐ Normal
- ☐ Abnormal - Not clinically significant
- ☐ Abnormal - Clinically significant (G3-4) ⟶ *Report on Adverse Event page*

Date blood drawn week 12 DD MMM YYYY

Result
- ☐ Normal
- ☐ Abnormal - Not clinically significant
- ☐ Abnormal - Clinically significant (G3-4) ⟶ *Report on Adverse Event page*

ECOG performance status

ECOG	Performance status	Approximate Karnofsky
0	Fully active, able to carry on all pre-disease performance without restriction.	90 - 100
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.	70 - 80
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.	50 - 60
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.	30 - 40
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	10 - 20

WHO Criteria

Response	**Measurable disease**
Complete response	The disappearance of all known disease.
Partial response	50% or more decrease in total tumor size, i.e. the sum of the products of the maximal diameter (MD) and the corresponding largest perpendicular diameter (LPD) of the lesions which have been measured to determine the effect of therapy. In addition, there can be no appearance of new lesions or progression of any lesion.
Progressive disease	At least a 25% increase in total tumor size, i.e. the sum of the products MD*LPD of lesions, and/or the appearance of one or more new lesion/s.
No change	A 50% decrease in total tumor size, i.e. the sum of the products MD*LPD of lesions cannot be established nor a 25% increase in the size of one or more measurable lesions has been determined.

Centre No. Subject No.

Patient status

Date of physical exam DD MMM YYYY ☐ Not done

☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant → *Specify abnormality on "Adverse event" page*

Vital signs and physical measurements

Weight (Kg) ___.__

Blood pressure ___ / ___ mmHg (systolic / diastolic)

Heart rate (beats/min) ___

ECOG performance status ___

Breast palpation with tumor measurements and nodal status

Clinical tumor size by calliper: MD (mm) X LPD (mm)* ___.__ X ___.__

New lesion(s) ☐ No ☐ Yes

Clinical N stage
- ☐ N0 (no regional lymph nodes metastasis)
- ☐ N1 (metastasis to movable ipsilateral axillary lymph nodes)
- ☐ N2a (metastasis in ipsilateral axillary lymph nodes fixed to one another (matted) or to other structures)
- ☐ N2b (metastasis only in clinically apparent ipsilateral internal mammary nodes and in the absence of clinically evident axillary lymph node metastasis
- ☐ N3a (metastasis in ipsilateral infraclavicular lymph nodes)
- ☐ N3b (metastasis in ipsilateral internal mammary lymph nodes and axillary lymph node)
- ☐ N3c (metastasis in ipsilateral subclavicular lymph nodes)
- ☐ Nx (not assessed)

Overall clinical tumor response (WHO criteria) using physical measurements

- ☐ Complete response
- ☐ Partial response
- ☐ Progressive disease
- ☐ No change
- ☐ Not evaluated

* MD: maximal diameter, LPD: largest perpendicular diameter

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Neutrophils	<LLN – 1500/mm³ <LLN – 1.5 x 10^9/L	<1500 – 1000/mm³ <1.5 – 1.0 x 10^9/L	<1000 – 500/mm³ <1.0 – 0.5 x 10^9/L	<500/mm³ <0.5 x 10^9/L	Death
WBC	<LLN – 3000/mm³ <LLN – 3.0 x 10^9/L	<3000 – 2000/mm³ <3.0 – 2.0 x 10^9/L	<2000 – 1000/mm³ <2.0 – 1.0 x 10^9/L	<1000/mm³ <1.0 x 10^9/L	Death
Haemoglobin	<LLN - 10.0 g/dL <LLN - 6.2 mmol/L <LLN - 100 g/L	<10.0 – 8.0 g/dL <6.2 – 4.9 mmol/L <100 – 80 g/L	<8.0 – 6.5 g/dL <4.9 – 4.0 mmol/L <80-65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
Platelets	<LLN -75,000/mm³ <LLN-75.0 x 10^9/L	<75,000-50,000/mm³ <75.0-50.0 x 10^9/L	<50,000-25,000/mm³ <50.0-25.0 x 10^9/L	<25,000/mm³ <25.0 x 10^9/L	Death
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	
Serum creatinine	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 6.0 x ULN	>6.0 x ULN	Death

Centre No. | | | | | | |

Subject No. | | | | | | |

Haematology and biochemistry

Please check the blood tests that should be done at this visit, as per protocol, and report any clinically significant (NCI CTCAE G3-4) abnormality on the "**Adverse event**" page.

Date blood drawn ___ ___ ___
DD MMM YYYY

Result
- ☐ Normal
- ☐ Abnormal - Not clinically significant
- ☐ Abnormal - Clinically significant (G3-4) ⟶ *Report on Adverse Event page*

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Neutrophils	<LLN – 1500/mm³ <LLN – 1.5 x 10^9/L	<1500 – 1000/mm³ <1.5 – 1.0 x 10^9/L	<1000 – 500/mm³ <1.0 – 0.5 x 10^9/L	<500/mm³ <0.5 x 10^9/L	Death
WBC	<LLN – 3000/mm³ <LLN – 3.0 x 10^9/L	<3000 – 2000/mm³ <3.0 – 2.0 x 10^9/L	<2000 – 1000/mm³ <2.0 – 1.0 x 10^9/L	<1000/mm³ <1.0 x 10^9/L	Death
Haemoglobin	<LLN - 10.0 g/dL <LLN - 6.2 mmol/L <LLN - 100 g/L	<10.0 – 8.0 g/dL <6.2 – 4.9 mmol/L <100 – 80 g/L	<8.0 – 6.5 g/dL <4.9 – 4.0 mmol/L <80-65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
Platelets	<LLN -75,000/mm³ <LLN-75.0 x 10^9/L	<75,000-50,000/mm³ <75.0-50.0 x 10^9/L	<50,000-25,000/mm³ <50.0-25.0 x 10^9/L	<25,000/mm³ <25.0 x 10^9/L	Death
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	
Serum creatinine	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 6.0 x ULN	>6.0 x ULN	Death

Haematology

Please check the blood tests that should be done at these visits, as per protocol, and report any clinically significant (NCI CTCAE G3-4) abnormality on the "**Adverse event**" page.

Date blood drawn week 14 DD MMM YYYY

Result
- ☐ Normal
- ☐ Abnormal - Not clinically significant
- ☐ Abnormal - Clinically significant (G3-4) ⟶ *Report on Adverse Event page*

Date blood drawn week 15 DD MMM YYYY

Result
- ☐ Normal
- ☐ Abnormal - Not clinically significant
- ☐ Abnormal - Clinically significant (G3-4) ⟶ *Report on Adverse Event page*

ECOG performance status

ECOG	Performance status	Approximate Karnofsky
0	Fully active, able to carry on all pre-disease performance without restriction.	90 - 100
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.	70 - 80
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.	50 - 60
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.	30 - 40
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	10 - 20

WHO Criteria

Response	**Measurable disease**
Complete response	The disappearance of all known disease.
Partial response	50% or more decrease in total tumor size, i.e. the sum of the products of the maximal diameter (MD) and the corresponding largest perpendicular diameter (LPD) of the lesions which have been measured to determine the effect of therapy. In addition, there can be no appearance of new lesions or progression of any lesion.
Progressive disease	At least a 25% increase in total tumor size, i.e. the sum of the products MD*LPD of lesions, and/or the appearance of one or more new lesion/s.
No change	A 50% decrease in total tumor size, i.e. the sum of the products MD*LPD of lesions cannot be established nor a 25% increase in the size of one or more measurable lesions has been determined.

Centre No. Subject No.

Patient status

Date of physical exam DD MMM YYYY ☐ Not done

☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant → *Specify abnormality on "Adverse event" page*

Vital signs and physical measurements

Weight (Kg) ___.__

Blood pressure ___ / ___ mmHg (systolic / diastolic)

Heart rate (beats/min) ___

ECOG performance status ___

Breast palpation with tumor measurements and nodal status

Clinical tumor size by calliper: MD (mm) X LPD (mm)* ___.__ X ___.__

New lesion(s) ☐ No ☐ Yes

Clinical N stage
- ☐ N0 (no regional lymph nodes metastasis)
- ☐ N1 (metastasis to movable ipsilateral axillary lymph nodes)
- ☐ N2a (metastasis in ipsilateral axillary lymph nodes fixed to one another (matted) or to other structures)
- ☐ N2b (metastasis only in clinically apparent ipsilateral internal mammary nodes and in the absence of clinically evident axillary lymph node metastasis
- ☐ N3a (metastasis in ipsilateral infraclavicular lymph nodes)
- ☐ N3b (metastasis in ipsilateral internal mammary lymph nodes and axillary lymph node)
- ☐ N3c (metastasis in ipsilateral subclavicular lymph nodes)
- ☐ Nx (not assessed)

Overall clinical tumor response (WHO criteria) using physical measurements

- ☐ Complete response
- ☐ Partial response
- ☐ Progressive disease
- ☐ No change
- ☐ Not evaluated

* MD: maximal diameter, LPD: largest perpendicular diameter

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Neutrophils	<LLN – 1500/mm³ <LLN – 1.5 x 10^9/L	<1500 – 1000/mm³ <1.5 – 1.0 x 10^9/L	<1000 – 500/mm³ <1.0 – 0.5 x 10^9/L	<500/mm³ <0.5 x 10^9/L	Death
WBC	<LLN – 3000/mm³ <LLN – 3.0 x 10^9/L	<3000 – 2000/mm³ <3.0 – 2.0 x 10^9/L	<2000 – 1000/mm³ <2.0 – 1.0 x 10^9/L	<1000/mm³ <1.0 x 10^9/L	Death
Haemoglobin	<LLN - 10.0 g/dL <LLN - 6.2 mmol/L <LLN - 100 g/L	<10.0 – 8.0 g/dL <6.2 – 4.9 mmol/L <100 – 80 g/L	<8.0 – 6.5 g/dL <4.9 – 4.0 mmol/L <80-65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
Platelets	<LLN -75,000/mm³ <LLN-75.0 x 10^9/L	<75,000-50,000/mm³ <75.0-50.0 x 10^9/L	<50,000-25,000/mm³ <50.0-25.0 x 10^9/L	<25,000/mm³ <25.0 x 10^9/L	Death
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	
Serum creatinine	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 6.0 x ULN	>6.0 x ULN	Death

Centre No. | | | | | | |

Subject No. | | | | | | |

Haematology and biochemistry

Please check the blood tests that should be done at this visit, as per protocol, and report any clinically significant (NCI CTCAE G3-4) abnormality on the "**Adverse event**" page.

Date blood drawn ____ ____ ____
DD MMM YYYY

Result
- ☐ Normal
- ☐ Abnormal - Not clinically significant
- ☐ Abnormal - Clinically significant (G3-4) ⟶ *Report on Adverse Event page*

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Neutrophils	<LLN – 1500/mm³ <LLN – 1.5 x 10^9/L	<1500 – 1000/mm³ <1.5 – 1.0 x 10^9/L	<1000 – 500/mm³ <1.0 – 0.5 x 10^9/L	<500/mm³ <0.5 x 10^9/L	Death
WBC	<LLN – 3000/mm³ <LLN – 3.0 x 10^9/L	<3000 – 2000/mm³ <3.0 – 2.0 x 10^9/L	<2000 – 1000/mm³ <2.0 – 1.0 x 10^9/L	<1000/mm³ <1.0 x 10^9/L	Death
Haemoglobin	<LLN - 10.0 g/dL <LLN - 6.2 mmol/L <LLN - 100 g/L	<10.0 – 8.0 g/dL <6.2 – 4.9 mmol/L <100 – 80 g/L	<8.0 – 6.5 g/dL <4.9 – 4.0 mmol/L <80-65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
Platelets	<LLN -75,000/mm³ <LLN-75.0 x 10^9/L	<75,000-50,000/mm³ <75.0-50.0 x 10^9/L	<50,000-25,000/mm³ <50.0-25.0 x 10^9/L	<25,000/mm³ <25.0 x 10^9/L	Death
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	
Serum creatinine	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 6.0 x ULN	>6.0 x ULN	Death

Haematology

Please check the blood tests that should be done at these visits, as per protocol, and report any clinically significant (NCI CTCAE G3-4) abnormality on the "**Adverse event**" page.

Date blood drawn week 17 DD MMM YYYY

Result
- ☐ Normal
- ☐ Abnormal - Not clinically significant
- ☐ Abnormal - Clinically significant (G3-4) → *Report on Adverse Event page*

Date blood drawn week 18 DD MMM YYYY

Result
- ☐ Normal
- ☐ Abnormal - Not clinically significant
- ☐ Abnormal - Clinically significant (G3-4) → *Report on Adverse Event page*

Note: The pre-surgery visit should take place within a few days prior to surgery. Surgery will take place at 2-4 weeks after the last dose of paclitaxel.

ECOG performance status

ECOG	Performance status	Approximate Karnofsky
0	Fully active, able to carry on all pre-disease performance without restriction.	90 - 100
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.	70 - 80
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.	50 - 60
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.	30 - 40
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	10 - 20

WHO Criteria

Response	**Measurable disease**
Complete response	The disappearance of all known disease.
Partial response	50% or more decrease in total tumor size, i.e. the sum of the products of the maximal diameter (MD) and the corresponding largest perpendicular diameter (LPD) of the lesions which have been measured to determine the effect of therapy. In addition, there can be no appearance of new lesions or progression of any lesion.
Progressive disease	At least a 25% increase in total tumor size, i.e. the sum of the products MD*LPD of lesions, and/or the appearance of one or more new lesion/s.
No change	A 50% decrease in total tumor size, i.e. the sum of the products MD*LPD of lesions cannot be established nor a 25% increase in the size of one or more measurable lesions has been determined.

Centre No. Subject No.

Patient status

Date of physical exam DD MMM YYYY ☐ Not done

☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant → *Specify abnormality on "Adverse event" page*

Vital signs and physical measurements

Weight (Kg) ___.__

Blood pressure ___ (systolic) / ___ (diastolic) mmHg

Heart rate (beats/min) ___

ECOG performance status ___

Breast palpation with tumor measurements and nodal status

Clinical tumor size by calliper: MD (mm) X LPD (mm)* ___.__ X ___.__

New lesion(s) ☐ No ☐ Yes

Clinical N stage
☐ N0 (no regional lymph nodes metastasis)
☐ N1 (metastasis to movable ipsilateral axillary lymph nodes)
☐ N2a (metastasis in ipsilateral axillary lymph nodes fixed to one another (matted) or to other structures)
☐ N2b (metastasis only in clinically apparent ipsilateral internal mammary nodes and in the absence of clinically evident axillary lymph node metastasis
☐ N3a (metastasis in ipsilateral infraclavicular lymph nodes)
☐ N3b (metastasis in ipsilateral internal mammary lymph nodes and axillary lymph node)
☐ N3c (metastasis in ipsilateral subclavicular lymph nodes)
☐ Nx (not assessed)

Overall clinical tumor response (WHO criteria) using physical measurements

☐ Complete response
☐ Partial response
☐ Progressive disease
☐ No change
☐ Not evaluated

* MD: maximal diameter, LPD: largest perpendicular diameter

New York Heart Association (NYHA) Functional Classification
NOTE: If the patient does not have congestive heart failure (CHF), leave this field blank.

Class I. Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain.

Class II. Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.

Class III. Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.

Class IV. Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Neutrophils	<LLN – 1500/mm³ <LLN – 1.5 x 10^9/L	<1500 – 1000/mm³ <1.5 – 1.0 x 10^9/L	<1000 – 500/mm³ <1.0 – 0.5 x 10^9/L	<500/mm³ <0.5 x 10^9/L	Death
WBC	<LLN – 3000/mm³ <LLN – 3.0 x 10^9/L	<3000 – 2000/mm³ <3.0 – 2.0 x 10^9/L	<2000 – 1000/mm³ <2.0 – 1.0 x 10^9/L	<1000/mm³ <1.0 x 10^9/L	Death
Haemoglobin	<LLN - 10.0 g/dL <LLN - 6.2 mmol/L <LLN - 100 g/L	<10.0 – 8.0 g/dL <6.2 – 4.9 mmol/L <100 – 80 g/L	<8.0 – 6.5 g/dL <4.9 – 4.0 mmol/L <80-65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
Platelets	<LLN -75,000/mm³ <LLN-75.0 x 10^9/L	<75,000-50,000/mm³ <75.0-50.0 x 10^9/L	<50,000-25,000/mm³ <50.0-25.0 x 10^9/L	<25,000/mm³ <25.0 x 10^9/L	Death
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	
Serum creatinine	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 6.0 x ULN	>6.0 x ULN	Death

Cardiac monitoring

LVEF

Date of LVEF ___ ___ ___ (DD MMM YYYY)

LVEF (patient value) ___.___ % Method of Evaluation ☐ Echocardiogram ☐ MUGA scan

☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant ⟶ *Please complete the "Adverse event" page.*

Symptomatic CHF ☐ No ☐ Yes ⟶ *Specify below*

NYHA classification **(complete only in case of CHF)**
☐ Class I *(in case of asymptomatic CHF, tick No for the question above)*
☐ Class II
☐ Class III (*study treatment should be interrupted)*
☐ Class IV (*study treatment should be interrupted)*

EKG should be performed at any time if symptoms or clinical suspicion are present and reported on the "Unscheduled EKG" page

Haematology and biochemistry

Please check the blood tests that should be done at this visit, as per protocol, and report any clinically significant (NCI CTCAE G3-4) abnormality on the "**Adverse event**" page.

Date blood drawn ___ ___ ___ (DD MMM YYYY)

Result
☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant (G3-4) ⟶ *Report on Adverse Event page*

Type of radiological examination

	Not done	Date of test (DD/MMM/YYYY)	tumor measurement	Are there any clinically significant abnormalities? *(Please report a short description)*
Bilateral mammogram*	☐	___	___ X ___ mm	☐ No ☐ Yes →
Left breast echography	☐	___	___ X ___ mm	☐ No ☐ Yes →
Right breast echography	☐	___	___ X ___ mm	☐ No ☐ Yes →
MRI	☐	___	___ X ___ mm	☐ No ☐ Yes →

* Mandatory test

Centre No. Subject No.

Sentinel node(s) sampling

Was sentinel node sampling performed? ☐ No ☐ Yes

Sentinel node biopsy date DD MMM YYYY ☐ Left ☐ Right

Axillary sentinel node biopsy ☐ Not done

☐ Negative

☐ Positive → Total sampled

Total positive

Internal sentinel mammary nodes biopsy → ☐ Negative ☐ Positive ☐ Not done

Pathological N status

☐ pNX (Regional lymph nodes cannot be assessed)

☐ pN0 (i**-**): (No regional lymph node metastasis histologically, negative IHC)

☐ pN0 (i**+**): (No regional lymph node metastasis histologically, positive IHC, no IHC cluster greater than 0.2mm)

☐ pN0 (mol**-**): (No regional lymph node metastasis histologically, negative molecular findings (RT-PCR))

☐ pN0 (mol**+**): (No regional lymph node metastasis histologically, positive molecular findings (RT-PCR))

☐ pN1mi: Micrometastasis (larger than 0.2 mm but not larger than 2.0 mm)

☐ pN1a: Metastasis in one to three axillary lymph nodes

☐ pN1b: Metastasis in internal mammary nodes with microscopic disease detected by SLN dissection but not clinically apparent

☐ pN1c: Metastasis in one to three axillary lymph nodes and in internal mammary lymph nodes with microscopic disease detected by SLN dissection but not clinically apparent

☐ pN2a: Metastasis in four to nine axillary lymph nodes (at least one tumor deposit larger than 2.0 mm)

☐ pN2b: Metastasis in clinically apparent internal mammary lymph nodes in the absence of axillary lymph node metastasis

☐ pN3a: Metastasis in 10 or more axillary lymph nodes (at least 1 tumor deposit larger than 2.0 mm); or, metastasis to the infraclavicular lymph nodes

☐ pN3b: Metastasis in clinically apparent ipsilateral internal mammary lymph nodes in the presence of one or more positive axillary lymph node(s); or, in more than three axillary lymph nodes and in internal mammary lymph nodes with microscopic disease detected by sentinel lymph node dissection but not clinically apparent

☐ pN3c: Metastasis in ipsilateral supraclavicular lymph nodes

Pathological measurement of largest lymph node (mm) ____.__

Centre No. ☐☐☐☐☐☐ Subject No. ☐☐☐☐☐☐

Axillary node dissection

Date of axillary dissection ☐☐-☐☐☐-☐☐☐☐ (DD MMM YYYY) ☐ Left ☐ Right ☐ Not done

Number of lymph nodes <u>examined</u> ☐☐

Number of <u>positive</u> lymph nodes ☐☐

Primary breast cancer surgery

Was surgery done? ☐ No ☐ Yes

Type of surgery *(check all that apply)*	Laterality		Date *(DD/MMM/YYYY)*
Lumpectomy	☐ Left	☐ Right	☐☐-☐☐☐-☐☐☐☐
Quadrantectomy / Segmentectomy	☐ Left	☐ Right	☐☐-☐☐☐-☐☐☐☐
Partial mastectomy	☐ Left	☐ Right	☐☐-☐☐☐-☐☐☐☐
Modified radical mastectomy	☐ Left	☐ Right	☐☐-☐☐☐-☐☐☐☐
Radical mastectomy (Halsted)	☐ Left	☐ Right	☐☐-☐☐☐-☐☐☐☐
Other, specify: _____	☐ Left	☐ Right	☐☐-☐☐☐-☐☐☐☐

Centre No. | | | | | | |

Subject No. | | | | | | |

Tumor characteristics

Largest bidimensional measurement of invasive lesion (mm) ___.___ x ___.___

Invasive histologic type *(tick all that apply)*

- ☐ Ductal Not Otherwise Specified (NOS)
- ☐ Lobular
- ☐ Mixed ductal and lobular
- ☐ Tubular
- ☐ Apocrine
- ☐ Tubulolobular
- ☐ Micropapillary
- ☐ Cribriform
- ☐ Mucinous
- ☐ Invasive Not Otherwise Specified (NOS)
- ☐ Medullary
- ☐ Other, specify: _____

Is carcinoma in situ present?

- ☐ No
- ☐ Yes → ☐ DCIS, ☐ LCIS, ☐ Mixed

Is Paget's disease present?

- ☐ No
- ☐ Yes

Margin involvement?

- ☐ No
- ☐ Yes → ☐ Involved with invasive disease, ☐ Involved with DCIS only, ☐ Non-resectable deep margins

Histologic Grade

- Gx ☐ Differentiation cannot be assessed
- G1 ☐ Well differentiated
- G2 ☐ Moderately differentiated
- G3 ☐ Poorly differentiated / Undifferentiated

Breast pathological response (pathological complete response (pT0 or pTIS))

- ☐ No
- ☐ Yes → ☐ pT0, ☐ pTIS

Centre No. | | | | | | |

Subject No. | | | | | | |

Translational research

Type of tissue	**Was sample obtained?** **No** ☐ **Yes** ☐ →	**Date of specimen collection** **(dd/mmm/yyyy)**
FFPE* tumor core biopsy	☐ ☐	
Blood sample for proteomics: - serum	☐ ☐	
Blood sample for proteomics: - plasma	☐ ☐	
Additional blood sample for CTC** *(only in selected centres)*	☐ ☐	
Snap frozen tumor sample (2 cores)	☐ ☐	

* Formalin Fixed Paraffin Embedded.

** CTC: Circulating tumor cells

Centre No. | | | | | | |

Subject No. | | | | | | |

Neo-adjuvant treatment completion*

Reasons for treatment discontinuation

Did the patient complete the planned preoperative Lapatinib (**L**)?

☐ Yes
☐ No → Specify below
☐ NA

Did the patient complete the planned preoperative Trastuzumab (**T**)?

☐ Yes
☐ No → Specify below
☐ NA

Did the patient complete the planned preoperative Paclitaxel (**P**)?

☐ Yes
☐ No → Specify below

	L	**T**	**P****	
Adverse event	☐	☐	☐	→ *Complete "Adverse event" page*
Protocol violation	☐	☐	☐	→ Specify: _____
Subject decided to withdraw from investigational product but is continuing to be followed per protocol	☐	☐	☐	
Subject decided to withdraw from the study	☐	☐	☐	
Progression of disease or second primary malignancy (SPM) or contalateral breast cancer (CBC)	☐	☐	☐	
Death	☐	☐	☐	→ *Complete "Death" page*
Lost to follow-up	☐	☐	☐	
Other	☐	☐	☐	→ Specify: _____

Date of last study drug administration: DD MMM YYYY

*"No" should only be ticked for 'Did the patient complete the planned preoperative [therapy]?', if the study drug was permanently discontinued earlier than the protocol specified treatment duration.

**L=Lapatinib; T=Trastuzumab; P=Paclitaxel

Additional comments and Investigator's signature

(Please add here any comment you might have regarding the data up to the neo-adjuvant treatment completion)

CRF page number	Comments

All data entered in this case report form have been entered under my authority and to the best of my knowledge are accurate and complete.

Investigator's signature _____ *(A medically qualified sub-investigator is allowed to sign the CRF if he/she is listed on the form FDA 1572)*

Date ___ ___ ___
DD MMM YYYY

Please date and sign <u>ONLY</u> after request from data management

ECOG performance status

ECOG	Performance status	Approximate Karnofsky
0	Fully active, able to carry on all pre-disease performance without restriction.	90 - 100
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.	70 - 80
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.	50 - 60
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.	30 - 40
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	10 - 20

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Neutrophils	<LLN – 1500/mm³ <LLN – 1.5 x 10^9/L	<1500 – 1000/mm³ <1.5 – 1.0 x 10^9/L	<1000 – 500/mm³ <1.0 – 0.5 x 10^9/L	<500/mm³ <0.5 x 10^9/L	Death
WBC	<LLN – 3000/mm³ <LLN – 3.0 x 10^9/L	<3000 – 2000/mm³ <3.0 – 2.0 x 10^9/L	<2000 – 1000/mm³ <2.0 – 1.0 x 10^9/L	<1000/mm³ <1.0 x 10^9/L	Death
Haemoglobin	<LLN - 10.0 g/dL <LLN - 6.2 mmol/L <LLN - 100 g/L	<10.0 – 8.0 g/dL <6.2 – 4.9 mmol/L <100 – 80 g/L	<8.0 – 6.5 g/dL <4.9 – 4.0 mmol/L <80-65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
Platelets	<LLN -75,000/mm³ <LLN-75.0 x 10^9/L	<75,000-50,000/mm³ <75.0-50.0 x 10^9/L	<50,000-25,000/mm³ <50.0-25.0 x 10^9/L	<25,000/mm³ <25.0 x 10^9/L	Death
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	
Serum creatinine	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 6.0 x ULN	>6.0 x ULN	Death

Centre No. | Subject No.

Patient status

Date of physical exam ☐ Not done

DD MMM YYYY

Vital signs and physical measurements

Weight (Kg) ___.__

BSA (m^2) _.__

Blood pressure ___ / ___ mmHg

systolic diastolic

Heart rate (beats/min) ___

ECOG performance status _

Haematology and biochemistry

Please check the blood tests that should be done at this visit, as per protocol, and report any clinically significant (NCI CTCAE G3-4) abnormality on the "**Adverse event**" page.

Date blood drawn

DD MMM YYYY

Result

☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant (G3-4) ⟶ *Report on Adverse Event page*

ECOG performance status

ECOG	Performance status	Approximate Karnofsky
0	Fully active, able to carry on all pre-disease performance without restriction.	90 - 100
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.	70 - 80
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.	50 - 60
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.	30 - 40
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	10 - 20

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Neutrophils	<LLN – 1500/mm³ <LLN – 1.5 x 10^9/L	<1500 – 1000/mm³ <1.5 – 1.0 x 10^9/L	<1000 – 500/mm³ <1.0 – 0.5 x 10^9/L	<500/mm³ <0.5 x 10^9/L	Death
WBC	<LLN – 3000/mm³ <LLN – 3.0 x 10^9/L	<3000 – 2000/mm³ <3.0 – 2.0 x 10^9/L	<2000 – 1000/mm³ <2.0 – 1.0 x 10^9/L	<1000/mm³ <1.0 x 10^9/L	Death
Haemoglobin	<LLN - 10.0 g/dL <LLN - 6.2 mmol/L <LLN - 100 g/L	<10.0 – 8.0 g/dL <6.2 – 4.9 mmol/L <100 – 80 g/L	<8.0 – 6.5 g/dL <4.9 – 4.0 mmol/L <80-65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
Platelets	<LLN -75,000/mm³ <LLN-75.0 x 10^9/L	<75,000-50,000/mm³ <75.0-50.0 x 10^9/L	<50,000-25,000/mm³ <50.0-25.0 x 10^9/L	<25,000/mm³ <25.0 x 10^9/L	Death
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	
Serum creatinine	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 6.0 x ULN	>6.0 x ULN	Death

Centre No. | | | | | |

Subject No. | | | | | |

Patient status

Date of physical exam ⌊⌊⌊⌊⌊⌊⌊⌊ DD MMM YYYY ☐ Not done

Vital signs and physical measurements

Weight (Kg) ⌊⌊⌊.⌊

BSA (m^2) ⌊.⌊⌊

Blood pressure ⌊⌊⌊ / ⌊⌊⌊ mmHg (systolic / diastolic)

Heart rate (beats/min) ⌊⌊⌊

ECOG performance status ⌊

Haematology and biochemistry

Please check the blood tests that should be done at this visit, as per protocol, and report any clinically significant (NCI CTCAE G3-4) abnormality on the "**Adverse event**" page.

Date blood drawn ⌊⌊⌊⌊⌊⌊⌊⌊ DD MMM YYYY

Result
- ☐ Normal
- ☐ Abnormal - Not clinically significant
- ☐ Abnormal - Clinically significant (G3-4) → *Report on Adverse Event page*

ECOG performance status

ECOG	Performance status	Approximate Karnofsky
0	Fully active, able to carry on all pre-disease performance without restriction.	90 - 100
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.	70 - 80
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.	50 - 60
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.	30 - 40
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	10 - 20

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Neutrophils	<LLN – 1500/mm³ <LLN – 1.5 x 10^9/L	<1500 – 1000/mm³ <1.5 – 1.0 x 10^9/L	<1000 – 500/mm³ <1.0 – 0.5 x 10^9/L	<500/mm³ <0.5 x 10^9/L	Death
WBC	<LLN – 3000/mm³ <LLN – 3.0 x 10^9/L	<3000 – 2000/mm³ <3.0 – 2.0 x 10^9/L	<2000 – 1000/mm³ <2.0 – 1.0 x 10^9/L	<1000/mm³ <1.0 x 10^9/L	Death
Haemoglobin	<LLN - 10.0 g/dL <LLN - 6.2 mmol/L <LLN - 100 g/L	<10.0 – 8.0 g/dL <6.2 – 4.9 mmol/L <100 – 80 g/L	<8.0 – 6.5 g/dL <4.9 – 4.0 mmol/L <80-65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
Platelets	<LLN -75,000/mm³ <LLN-75.0 x 10^9/L	<75,000-50,000/mm³ <75.0-50.0 x 10^9/L	<50,000-25,000/mm³ <50.0-25.0 x 10^9/L	<25,000/mm³ <25.0 x 10^9/L	Death
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	
Serum creatinine	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 6.0 x ULN	>6.0 x ULN	Death

Centre No. | Subject No.

Patient status

Date of physical exam DD MMM YYYY ☐ Not done

Vital signs and physical measurements

Weight (Kg) ___.__

BSA (m^2) _.___

Blood pressure ___ (systolic) / ___ (diastolic) mmHg

Heart rate (beats/min) ___

ECOG performance status _

Haematology and biochemistry

Please check the blood tests that should be done at this visit, as per protocol, and report any clinically significant (NCI CTCAE G3-4) abnormality on the "**Adverse event**" page.

Date blood drawn DD MMM YYYY

Result
- ☐ Normal
- ☐ Abnormal - Not clinically significant
- ☐ Abnormal - Clinically significant (G3-4) ⟶ *Report on Adverse Event page*

ECOG performance status

ECOG	Performance status	Approximate Karnofsky
0	Fully active, able to carry on all pre-disease performance without restriction.	90 - 100
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.	70 - 80
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.	50 - 60
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.	30 - 40
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	10 - 20

Patient status

Date of physical exam ☐ Not done
DD MMM YYYY

Vital signs and physical measurements

Weight (Kg) ___.__

Blood pressure ___ / ___
systolic diastolic

Heart rate (beats/min) ___

ECOG performance status ___

Translational research

Type of tissue	Was sample obtained? No Yes	Date of specimen collection (dd/mmm/yyyy)
Additional blood sample for CTC* *(only in selected centres)*	☐ ☐	

*Circulating tumor cells

New York Heart Association (NYHA) Functional Classification
NOTE: If the patient does not have congestive heart failure (CHF), leave this field blank.

Class I. Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain.

Class II. Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.

Class III. Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.

Class IV. Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Neutrophils	<LLN – 1500/mm³ <LLN – 1.5 x 10^9/L	<1500 – 1000/mm³ <1.5 – 1.0 x 10^9/L	<1000 – 500/mm³ <1.0 – 0.5 x 10^9/L	<500/mm³ <0.5 x 10^9/L	Death
WBC	<LLN – 3000/mm³ <LLN – 3.0 x 10^9/L	<3000 – 2000/mm³ <3.0 – 2.0 x 10^9/L	<2000 – 1000/mm³ <2.0 – 1.0 x 10^9/L	<1000/mm³ <1.0 x 10^9/L	Death
Haemoglobin	<LLN - 10.0 g/dL <LLN - 6.2 mmol/L <LLN - 100 g/L	<10.0 – 8.0 g/dL <6.2 – 4.9 mmol/L <100 – 80 g/L	<8.0 – 6.5 g/dL <4.9 – 4.0 mmol/L <80-65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
Platelets	<LLN -75,000/mm³ <LLN-75.0 x 10^9/L	<75,000-50,000/mm³ <75.0-50.0 x 10^9/L	<50,000-25,000/mm³ <50.0-25.0 x 10^9/L	<25,000/mm³ <25.0 x 10^9/L	Death
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	
Serum creatinine	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 6.0 x ULN	>6.0 x ULN	Death

Cardiac monitoring

LVEF

Date of LVEF ☐☐ ☐☐☐ ☐☐☐☐ (DD MMM YYYY)

LVEF (patient value) ☐☐.☐ % Method of Evaluation ☐ Echocardiogram ☐ MUGA scan

☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant → *Please complete the "Adverse event" page.*

Symptomatic CHF ☐ No ☐ Yes → *Specify below*

NYHA classification **(complete only in case of CHF)**
☐ Class I *(in case of asymptomatic CHF, tick No for the question above)*
☐ Class II
☐ Class III
☐ Class IV

EKG should be performed at any time if symptoms or clinical suspicion are present and reported on the "Unscheduled EKG" page

Haematology and biochemistry

Please check the blood tests that should be done at this visit, as per protocol, and report any clinically significant (NCI CTCAE G3-4) abnormality on the "**Adverse event**" page.

Date blood drawn ☐☐ ☐☐☐ ☐☐☐☐ (DD MMM YYYY)

Result
☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant (G3-4) → *Report on Adverse Event page*

ECOG performance status

ECOG	Performance status	Approximate Karnofsky
0	Fully active, able to carry on all pre-disease performance without restriction.	90 - 100
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.	70 - 80
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.	50 - 60
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.	30 - 40
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	10 - 20

Patient status

Date of physical exam ☐ Not done

DD MMM YYYY

Vital signs and physical measurements

Weight (Kg) ___.__

Blood pressure ___ / ___

systolic diastolic

Heart rate (beats/min) ___

ECOG performance status ___

Are there any changes since the previous assessment?

☐ No
☐ Yes → *Specify below*

☐ Recurrence of disease *(complete the "Recurrence of disease" page)*

☐ Second primary malignancy or contralateral breast cancer *(complete the "Second primary malignancy and contralateral BC" page)*

☐ Significant cardiac disease *(complete the "Adverse event" page)*

☐ Adverse event *(complete the "Adverse event" page)*

☐ Death *(complete the "Death" page)*

☐ Lost to follow-up
☐ Patient withdrew study consent → Date of last contact (*or date study consent withdrawn*)

DD MMM YYYY

☐ Patient withdrew treatment but remains on follow-up

(For patients "Lost to Follow-up", the date of last contact should be the last date the patient was known to be alive.
The last date the patient was known to be alive could either be the same as the previous reported visit date or any date between the previous visit and this one.)

New York Heart Association (NYHA) Functional Classification
NOTE: If the patient does not have congestive heart failure (CHF), leave this field blank.

Class I. Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain.

Class II. Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.

Class III. Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.

Class IV. Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Neutrophils	<LLN – 1500/mm³ <LLN – 1.5 x 10^9/L	<1500 – 1000/mm³ <1.5 – 1.0 x 10^9/L	<1000 – 500/mm³ <1.0 – 0.5 x 10^9/L	<500/mm³ <0.5 x 10^9/L	Death
WBC	<LLN – 3000/mm³ <LLN – 3.0 x 10^9/L	<3000 – 2000/mm³ <3.0 – 2.0 x 10^9/L	<2000 – 1000/mm³ <2.0 – 1.0 x 10^9/L	<1000/mm³ <1.0 x 10^9/L	Death
Haemoglobin	<LLN - 10.0 g/dL <LLN - 6.2 mmol/L <LLN - 100 g/L	<10.0 – 8.0 g/dL <6.2 – 4.9 mmol/L <100 – 80 g/L	<8.0 – 6.5 g/dL <4.9 – 4.0 mmol/L <80-65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
Platelets	<LLN -75,000/mm³ <LLN-75.0 x 10^9/L	<75,000-50,000/mm³ <75.0-50.0 x 10^9/L	<50,000-25,000/mm³ <50.0-25.0 x 10^9/L	<25,000/mm³ <25.0 x 10^9/L	Death
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	
Serum creatinine	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 6.0 x ULN	>6.0 x ULN	Death

Cardiac monitoring

LVEF

Date of LVEF ☐☐ ☐☐☐ ☐☐☐☐ (DD MMM YYYY)

LVEF (patient value) ☐☐.☐ % Method of Evaluation ☐ Echocardiogram ☐ MUGA scan

☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant → *Please complete the "Adverse event" page.*

Symptomatic CHF ☐ No ☐ Yes → *Specify below*

NYHA classification **(complete only in case of CHF)**
☐ Class I *(in case of asymptomatic CHF, tick No for the question above)*
☐ Class II
☐ Class III
☐ Class IV

EKG should be performed at any time if symptoms or clinical suspicion are present and reported on the "Unscheduled EKG" page

Haematology and biochemistry

Please check the blood tests that should be done at this visit, as per protocol, and report any clinically significant (NCI CTCAE G3-4) abnormality on the "**Adverse event**" page.

Date blood drawn ☐☐ ☐☐☐ ☐☐☐☐ (DD MMM YYYY)

Result
☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant (G3-4) → *Report on Adverse Event page*

ECOG performance status

ECOG	Performance status	Approximate Karnofsky
0	Fully active, able to carry on all pre-disease performance without restriction.	90 - 100
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.	70 - 80
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.	50 - 60
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.	30 - 40
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	10 - 20

Patient status

Date of physical exam DD MMM YYYY ☐ Not done

Vital signs and physical measurements

Weight (Kg) ___.__

Blood pressure ___ / ___ (systolic / diastolic)

Heart rate (beats/min) ___

ECOG performance status ___

Are there any changes since the previous assessment?

☐ No
☐ Yes → *Specify below*

☐ Recurrence of disease *(complete the "Recurrence of disease" page)*

☐ Second primary malignancy or contralateral breast cancer *(complete the "Second primary malignancy and contralateral BC" page)*

☐ Significant cardiac disease *(complete the "Adverse event" page)*

☐ Adverse event *(complete the "Adverse event" page)*

☐ Death *(complete the "Death" page)*

☐ Lost to follow-up
☐ Patient withdrew study consent → Date of last contact (*or date study consent withdrawn*) DD MMM YYYY

☐ Patient withdrew treatment but remains on follow-up

(For patients "Lost to Follow-up", the date of last contact should be the last date the patient was known to be alive.
The last date the patient was known to be alive could either be the same as the previous reported visit date or any date between the previous visit and this one.)

New York Heart Association (NYHA) Functional Classification
NOTE: If the patient does not have congestive heart failure (CHF), leave this field blank.

Class I. Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain.

Class II. Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.

Class III. Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.

Class IV. Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Neutrophils	<LLN – 1500/mm³ <LLN – 1.5 x 10^9/L	<1500 – 1000/mm³ <1.5 – 1.0 x 10^9/L	<1000 – 500/mm³ <1.0 – 0.5 x 10^9/L	<500/mm³ <0.5 x 10^9/L	Death
WBC	<LLN – 3000/mm³ <LLN – 3.0 x 10^9/L	<3000 – 2000/mm³ <3.0 – 2.0 x 10^9/L	<2000 – 1000/mm³ <2.0 – 1.0 x 10^9/L	<1000/mm³ <1.0 x 10^9/L	Death
Haemoglobin	<LLN - 10.0 g/dL <LLN - 6.2 mmol/L <LLN - 100 g/L	<10.0 – 8.0 g/dL <6.2 – 4.9 mmol/L <100 – 80 g/L	<8.0 – 6.5 g/dL <4.9 – 4.0 mmol/L <80-65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
Platelets	<LLN -75,000/mm³ <LLN-75.0 x 10^9/L	<75,000-50,000/mm³ <75.0-50.0 x 10^9/L	<50,000-25,000/mm³ <50.0-25.0 x 10^9/L	<25,000/mm³ <25.0 x 10^9/L	Death
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	
Serum creatinine	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 6.0 x ULN	>6.0 x ULN	Death

Cardiac monitoring

LVEF

Date of LVEF ☐☐ ☐☐☐ ☐☐☐☐ (DD MMM YYYY)

LVEF (patient value) ☐☐.☐ % Method of Evaluation ☐ Echocardiogram ☐ MUGA scan

☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant → *Please complete the "Adverse event" page.*

Symptomatic CHF ☐ No ☐ Yes → *Specify below*

NYHA classification **(complete only in case of CHF)**
☐ Class I *(in case of asymptomatic CHF, tick No for the question above)*
☐ Class II
☐ Class III
☐ Class IV

EKG should be performed at any time if symptoms or clinical suspicion are present and reported on the "Unscheduled EKG" page

Haematology and biochemistry

Please check the blood tests that should be done at this visit, as per protocol, and report any clinically significant (NCI CTCAE G3-4) abnormality on the "**Adverse event**" page.

Date blood drawn ☐☐ ☐☐☐ ☐☐☐☐ (DD MMM YYYY)

Result
☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant (G3-4) → *Report on Adverse Event page*

ECOG performance status

ECOG	Performance status	Approximate Karnofsky
0	Fully active, able to carry on all pre-disease performance without restriction.	90 - 100
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.	70 - 80
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.	50 - 60
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.	30 - 40
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	10 - 20

Patient status

Date of physical exam ☐ Not done
DD MMM YYYY

Vital signs and physical measurements

Weight (Kg) ___.__

Blood pressure ___ / ___
systolic diastolic

Heart rate (beats/min) ___

ECOG performance status ___

Are there any changes since the previous assessment?

☐ No
☐ Yes → *Specify below*

☐ Recurrence of disease *(complete the "Recurrence of disease" page)*

☐ Second primary malignancy or contralateral breast cancer *(complete the "Second primary malignancy and contralateral BC" page)*

☐ Significant cardiac disease *(complete the "Adverse event" page)*

☐ Adverse event *(complete the "Adverse event" page)*

☐ Death *(complete the "Death" page)*

☐ Lost to follow-up
☐ Patient withdrew study consent
→ Date of last contact (*or date study consent withdrawn*)
DD MMM YYYY

☐ Patient withdrew treatment but remains on follow-up

(For patients "Lost to Follow-up", the date of last contact should be the last date the patient was known to be alive.
The last date the patient was known to be alive could either be the same as the previous reported visit date or any date between the previous visit and this one.)

New York Heart Association (NYHA) Functional Classification
NOTE: If the patient does not have congestive heart failure (CHF), leave this field blank.

Class I. Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain.

Class II. Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.

Class III. Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.

Class IV. Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Neutrophils	<LLN – 1500/mm³ <LLN – 1.5 x 10^9/L	<1500 – 1000/mm³ <1.5 – 1.0 x 10^9/L	<1000 – 500/mm³ <1.0 – 0.5 x 10^9/L	<500/mm³ <0.5 x 10^9/L	Death
WBC	<LLN – 3000/mm³ <LLN – 3.0 x 10^9/L	<3000 – 2000/mm³ <3.0 – 2.0 x 10^9/L	<2000 – 1000/mm³ <2.0 – 1.0 x 10^9/L	<1000/mm³ <1.0 x 10^9/L	Death
Haemoglobin	<LLN - 10.0 g/dL <LLN - 6.2 mmol/L <LLN - 100 g/L	<10.0 – 8.0 g/dL <6.2 – 4.9 mmol/L <100 – 80 g/L	<8.0 – 6.5 g/dL <4.9 – 4.0 mmol/L <80-65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
Platelets	<LLN -75,000/mm³ <LLN-75.0 x 10^9/L	<75,000-50,000/mm³ <75.0-50.0 x 10^9/L	<50,000-25,000/mm³ <50.0-25.0 x 10^9/L	<25,000/mm³ <25.0 x 10^9/L	Death
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	
Serum creatinine	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 6.0 x ULN	>6.0 x ULN	Death

Cardiac monitoring

LVEF

Date of LVEF ☐☐ ☐☐☐ ☐☐☐☐ (DD MMM YYYY)

LVEF (patient value) ☐☐.☐ % Method of Evaluation ☐ Echocardiogram ☐ MUGA scan

☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant → *Please complete the "Adverse event" page.*

Symptomatic CHF ☐ No ☐ Yes → *Specify below*

NYHA classification **(complete only in case of CHF)**
☐ Class I *(in case of asymptomatic CHF, tick No for the question above)*
☐ Class II
☐ Class III
☐ Class IV

EKG should be performed at any time if symptoms or clinical suspicion are present and reported on the "Unscheduled EKG" page

Haematology and biochemistry

Please check the blood tests that should be done at this visit, as per protocol, and report any clinically significant (NCI CTCAE G3-4) abnormality on the "**Adverse event**" page.

Date blood drawn ☐☐ ☐☐☐ ☐☐☐☐ (DD MMM YYYY)

Result
☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant (G3-4) → *Report on Adverse Event page*

This page has been deleted from CRF version 4.0 due to changed timelines for CTC blood collection

ECOG performance status

ECOG	Performance status	Approximate Karnofsky
0	Fully active, able to carry on all pre-disease performance without restriction.	90 - 100
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.	70 - 80
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.	50 - 60
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.	30 - 40
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	10 - 20

Patient status

Date of physical exam ☐ Not done

DD MMM YYYY

Vital signs and physical measurements

Weight (Kg) ___.__

Blood pressure ___ / ___

systolic diastolic

Heart rate (beats/min) ___

ECOG performance status ___

Are there any changes since the previous assessment?

☐ No
☐ Yes → *Specify below*

☐ Recurrence of disease *(complete the "Recurrence of disease" page)*

☐ Second primary malignancy or contralateral breast cancer *(complete the "Second primary malignancy and contralateral BC" page)*

☐ Significant cardiac disease *(complete the "Adverse event" page)*

☐ Adverse event *(complete the "Adverse event" page)*

☐ Death *(complete the "Death" page)*

☐ Lost to follow-up
☐ Patient withdrew study consent → Date of last contact (*or date study consent withdrawn*)

DD MMM YYYY

(For patients "Lost to Follow-up", the date of last contact should be the last date the patient was known to be alive.
The last date the patient was known to be alive could either be the same as the previous reported visit date or any date between the previous visit and this one.)

New York Heart Association (NYHA) Functional Classification
NOTE: If the patient does not have congestive heart failure (CHF), leave this field blank.

Class I. Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain.

Class II. Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.

Class III. Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.

Class IV. Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Neutrophils	<LLN – 1500/mm³ <LLN – 1.5 x 10^9/L	<1500 – 1000/mm³ <1.5 – 1.0 x 10^9/L	<1000 – 500/mm³ <1.0 – 0.5 x 10^9/L	<500/mm³ <0.5 x 10^9/L	Death
WBC	<LLN – 3000/mm³ <LLN – 3.0 x 10^9/L	<3000 – 2000/mm³ <3.0 – 2.0 x 10^9/L	<2000 – 1000/mm³ <2.0 – 1.0 x 10^9/L	<1000/mm³ <1.0 x 10^9/L	Death
Haemoglobin	<LLN - 10.0 g/dL <LLN - 6.2 mmol/L <LLN - 100 g/L	<10.0 – 8.0 g/dL <6.2 – 4.9 mmol/L <100 – 80 g/L	<8.0 – 6.5 g/dL <4.9 – 4.0 mmol/L <80-65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
Platelets	<LLN -75,000/mm³ <LLN-75.0 x 10^9/L	<75,000-50,000/mm³ <75.0-50.0 x 10^9/L	<50,000-25,000/mm³ <50.0-25.0 x 10^9/L	<25,000/mm³ <25.0 x 10^9/L	Death
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	
Serum creatinine	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 6.0 x ULN	>6.0 x ULN	Death

Cardiac monitoring

LVEF

Date of LVEF ☐☐ ☐☐☐ ☐☐☐☐ (DD MMM YYYY)

LVEF (patient value) ☐☐.☐ % Method of Evaluation ☐ Echocardiogram ☐ MUGA scan

☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant → *Please complete the "Adverse event" page.*

Symptomatic CHF ☐ No ☐ Yes → *Specify below*

NYHA classification **(complete only in case of CHF)**
☐ Class I *(in case of asymptomatic CHF, tick No for the question above)*
☐ Class II
☐ Class III
☐ Class IV

EKG should be performed at any time if symptoms or clinical suspicion are present and reported on the "Unscheduled EKG" page

Haematology and biochemistry

Please check the blood tests that should be done at this visit, as per protocol, and report any clinically significant (NCI CTCAE G3-4) abnormality on the "**Adverse event**" page.

Date blood drawn ☐☐ ☐☐☐ ☐☐☐☐ (DD MMM YYYY)

Result
☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant (G3-4) → *Report on Adverse Event page, if related to study drug*

Type of radiological examination

	Not done	Date of test (DD/MMM/YYYY)	Are there any clinically significant abnormalities? *(Please report a short description)*
Abdominal CT-scan	☐		☐ No ☐ Yes → Specify
Chest X-ray	☐		☐ No ☐ Yes → Specify
Chest CT-scan	☐		☐ No ☐ Yes → Specify
Bone scan (scintigraphy)	☐		☐ No ☐ Yes → Specify
Bone X-ray	☐		☐ No ☐ Yes → Specify
Bone CT-scan	☐		☐ No ☐ Yes → Specify
Bilateral mammography	☐		☐ No ☐ Yes → Specify
Left mammography, only	☐		☐ No ☐ Yes → Specify
Right mammography, only	☐		☐ No ☐ Yes → Specify

Anatomical site	Description
AB	Abdomen/abdominal wall
AD	Adrenals
BE	Bone
BR	Bladder
BT	Breast
CL	Colon
CR	Colorectal
CS	CNS (brain)
CW	Chest
CX	Cervix
EO	Esophagus/Oesophagus
HN	Head and neck
HT	Heart
K	Kidney
LG	Lung
LN	Lymph nodes

Anatomical site	Description
LV	Liver
OC	Oral cavity
OT	Other
OV	Ovary
PA	Pleura
PM	Peritoneum
PR	Prostate
PS	Pancreas
PV	Pelvis
RC	Rectum
SH	Stomach
SI	Small intestine
SK	Skin
SP	Spleen
TD	Thyroid
WB	Whole body

Type of radiological examination *(continued)*

Type of radiological examination*	Anatomical site**	Side (L or R)	Date of test	Are there any clinically significant abnormalities? *(Please report a short description)*
			DD MMM YYYY	☐ No ☐ Yes → Specify _____
			DD MMM YYYY	☐ No ☐ Yes → Specify _____

* BS=Bone scan (scintigraphy); C=CT scan; E=Endoscopy; L=Lymphangiogram; M=MRI; MA=Mammography; NS=Nuclear scan; PC=PET/CT Scan; PT=PET scan; TU=Transvaginal ultrasound; UL=Ultrasound (echography); XR=X-ray

** See facing page for anatomical site codes

ECOG performance status

ECOG	Performance status	Approximate Karnofsky
0	Fully active, able to carry on all pre-disease performance without restriction.	90 - 100
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.	70 - 80
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.	50 - 60
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.	30 - 40
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	10 - 20

Centre No. | Subject No.

Patient status

Date of physical exam ☐ DD ☐ MMM ☐ YYYY ☐ Not done

Vital signs and physical measurements

Weight (Kg) ☐☐☐.☐

Blood pressure ☐☐☐ / ☐☐☐ (systolic / diastolic)

Heart rate (beats/min) ☐☐☐

ECOG performance status ☐

Are there any changes since the previous assessment?

☐ No
☐ Yes → *Specify below*

☐ Recurrence of disease *(complete the "Recurrence of disease" page)*

☐ Second primary malignancy or contralateral breast cancer *(complete the "Second primary malignancy and contralateral BC" page)*

☐ Significant cardiac disease *(complete the "Adverse event" page)*

☐ Adverse event *(complete the "Adverse event" page)*

☐ Death *(complete the "Death" page)*

☐ Lost to follow-up
☐ Patient withdrew study consent
→ Date of last contact (*or date study consent withdrawn*) ☐ DD ☐ MMM ☐ YYYY

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3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.	30 - 40
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	10 - 20

Centre No. | Subject No.

Patient status

Date of physical exam DD MMM YYYY ☐ Not done

Vital signs and physical measurements

Weight (Kg) ___.__

Blood pressure ___ / ___ (systolic / diastolic)

Heart rate (beats/min) ___

ECOG performance status ___

Are there any changes since the previous assessment?

☐ No
☐ Yes → *Specify below*

☐ Recurrence of disease *(complete the "Recurrence of disease" page)*

☐ Second primary malignancy or contralateral breast cancer *(complete the "Second primary malignancy and contralateral BC" page)*

☐ Significant cardiac disease *(complete the "Adverse event" page)*

☐ Adverse event *(complete the "Adverse event" page)*

☐ Death *(complete the "Death" page)*

☐ Lost to follow-up
☐ Patient withdrew study consent
→ Date of last contact (*or date study consent withdrawn*) DD MMM YYYY

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WBC	<LLN – 3000/mm³ <LLN – 3.0 x 10^9/L	<3000 – 2000/mm³ <3.0 – 2.0 x 10^9/L	<2000 – 1000/mm³ <2.0 – 1.0 x 10^9/L	<1000/mm³ <1.0 x 10^9/L	Death
Haemoglobin	<LLN - 10.0 g/dL <LLN - 6.2 mmol/L <LLN - 100 g/L	<10.0 – 8.0 g/dL <6.2 – 4.9 mmol/L <100 – 80 g/L	<8.0 – 6.5 g/dL <4.9 – 4.0 mmol/L <80-65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
Platelets	<LLN -75,000/mm³ <LLN-75.0 x 10^9/L	<75,000-50,000/mm³ <75.0-50.0 x 10^9/L	<50,000-25,000/mm³ <50.0-25.0 x 10^9/L	<25,000/mm³ <25.0 x 10^9/L	Death
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	
Serum creatinine	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 6.0 x ULN	>6.0 x ULN	Death

Cardiac monitoring

LVEF

Date of LVEF ⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋ (DD MMM YYYY)

LVEF (patient value) ⌊ ⌋⌊ ⌋.⌊ ⌋ % Method of Evaluation ☐ Echocardiogram ☐ MUGA scan

☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant ⟶ *Please complete the "Adverse event" page.*

Symptomatic CHF ☐ No ☐ Yes ⟶ *Specify below*

NYHA classification **(complete only in case of CHF)**
☐ Class I *(in case of asymptomatic CHF, tick No for the question above)*
☐ Class II
☐ Class III
☐ Class IV

EKG should be performed at any time if symptoms or clinical suspicion are present and reported on the "Unscheduled EKG" page

Haematology and biochemistry

Please check the blood tests that should be done at this visit, as per protocol, and report any clinically significant (NCI CTCAE G3-4) abnormality on the "**Adverse event**" page.

Date blood drawn ⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋⌊ ⌋ (DD MMM YYYY)

Result
☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant (G3-4) ⟶ *Report on Adverse Event page, if related to study drug*

ECOG performance status

ECOG	Performance status	Approximate Karnofsky
0	Fully active, able to carry on all pre-disease performance without restriction.	90 - 100
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.	70 - 80
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.	50 - 60
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.	30 - 40
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	10 - 20

Centre No. | Subject No.

Patient status

Date of physical exam DD MMM YYYY ☐ Not done

Vital signs and physical measurements

Weight (Kg) ___.__

Blood pressure ___ / ___ (systolic / diastolic)

Heart rate (beats/min) ___

ECOG performance status ___

Are there any changes since the previous assessment?

☐ No
☐ Yes → *Specify below*

☐ Recurrence of disease *(complete the "Recurrence of disease" page)*

☐ Second primary malignancy or contralateral breast cancer *(complete the "Second primary malignancy and contralateral BC" page)*

☐ Significant cardiac disease *(complete the "Adverse event" page)*

☐ Adverse event *(complete the "Adverse event" page)*

☐ Death *(complete the "Death" page)*

☐ Lost to follow-up
☐ Patient withdrew study consent
→ Date of last contact (*or date study consent withdrawn*) DD MMM YYYY

(For patients "Lost to Follow-up", the date of last contact should be the last date the patient was known to be alive.
The last date the patient was known to be alive could either be the same as the previous reported visit date or any date between the previous visit and this one.)

ECOG performance status

ECOG	Performance status	Approximate Karnofsky
0	Fully active, able to carry on all pre-disease performance without restriction.	90 - 100
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.	70 - 80
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.	50 - 60
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.	30 - 40
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	10 - 20

New York Heart Association (NYHA) Functional Classification
NOTE: If the patient does not have congestive heart failure (CHF), leave this field blank.

Class I. Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain.

Class II. Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.

Class III. Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.

Class IV. Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

Centre No. | Subject No.

Patient status

Date of physical exam ☐ Not done
DD MMM YYYY

Vital signs and physical measurements

Weight (Kg) ___.__

Blood pressure ___ / ___
systolic diastolic

Heart rate (beats/min) ___

ECOG performance status ___

Cardiac monitoring

LVEF

Date of LVEF
DD MMM YYYY

LVEF (patient value) ___.__ % Method of Evaluation ☐ Echocardiogram ☐ MUGA scan

☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant → *Please complete the "Adverse event" page.*

Symptomatic CHF ☐ No ☐ Yes → *Specify below*

NYHA classification **(complete only in case of CHF)**
☐ Class I *(in case of asymptomatic CHF, tick No for the question above)*
☐ Class II
☐ Class III
☐ Class IV

EKG should be performed at any time if symptoms or clinical suspicion are present and reported on the "Unscheduled EKG" page

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Neutrophils	<LLN – 1500/mm³ <LLN – 1.5 x 10^9/L	<1500 – 1000/mm³ <1.5 – 1.0 x 10^9/L	<1000 – 500/mm³ <1.0 – 0.5 x 10^9/L	<500/mm³ <0.5 x 10^9/L	Death
WBC	<LLN – 3000/mm³ <LLN – 3.0 x 10^9/L	<3000 – 2000/mm³ <3.0 – 2.0 x 10^9/L	<2000 – 1000/mm³ <2.0 – 1.0 x 10^9/L	<1000/mm³ <1.0 x 10^9/L	Death
Haemoglobin	<LLN - 10.0 g/dL <LLN - 6.2 mmol/L <LLN - 100 g/L	<10.0 – 8.0 g/dL <6.2 – 4.9 mmol/L <100 – 80 g/L	<8.0 – 6.5 g/dL <4.9 – 4.0 mmol/L <80-65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
Platelets	<LLN -75,000/mm³ <LLN-75.0 x 10^9/L	<75,000-50,000/mm³ <75.0-50.0 x 10^9/L	<50,000-25,000/mm³ <50.0-25.0 x 10^9/L	<25,000/mm³ <25.0 x 10^9/L	Death
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	
Serum creatinine	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 6.0 x ULN	>6.0 x ULN	Death

Haematology and biochemistry

Please check the blood tests that should be done at this visit, as per protocol, and report any clinically significant (NCI CTCAE G3-4) abnormality on the "**Adverse event**" page.

Date blood drawn DD MMM YYYY

Result
- ☐ Normal
- ☐ Abnormal - Not clinically significant
- ☐ Abnormal - Clinically significant (G3-4) → *Report on Adverse Event page, if related to study drug*

Translational research

Type of tissue	**Was sample obtained?** **No Yes**	**Date of specimen collection** **(dd/mmm/yyyy)**
Additional blood sample for CTC* *(only in selected centres)*	☐ ☐	

*Circulating tumor cells

Type of radiological examination

	Not done	Date of test (DD/MMM/YYYY)	Are there any clinically significant abnormalities? *(Please report a short description)*
Abdominal CT-scan	☐		☐ No ☐ Yes → Specify
Chest X-ray	☐		☐ No ☐ Yes → Specify
Chest CT-scan	☐		☐ No ☐ Yes → Specify
Bone scan (scintigraphy)	☐		☐ No ☐ Yes → Specify
Bone X-ray	☐		☐ No ☐ Yes → Specify
Bone CT-scan	☐		☐ No ☐ Yes → Specify
Bilateral mammography	☐		☐ No ☐ Yes → Specify
Left mammography, only	☐		☐ No ☐ Yes → Specify
Right mammography, only	☐		☐ No ☐ Yes → Specify

Anatomical site	Description
AB	Abdomen/abdominal wall
AD	Adrenals
BE	Bone
BR	Bladder
BT	Breast
CL	Colon
CR	Colorectal
CS	CNS (brain)
CW	Chest
CX	Cervix
EO	Esophagus/Oesophagus
HN	Head and neck
HT	Heart
K	Kidney
LG	Lung
LN	Lymph nodes

Anatomical site	Description
LV	Liver
OC	Oral cavity
OT	Other
OV	Ovary
PA	Pleura
PM	Peritoneum
PR	Prostate
PS	Pancreas
PV	Pelvis
RC	Rectum
SH	Stomach
SI	Small intestine
SK	Skin
SP	Spleen
TD	Thyroid
WB	Whole body

Type of radiological examination *(continued)*

Type of radiological examination*	Anatomical site**	Side (L or R)	Date of test	Are there any clinically significant abnormalities? *(Please report a short description)*
			DD MMM YYYY	☐ No ☐ Yes → Specify _____
			DD MMM YYYY	☐ No ☐ Yes → Specify _____

* BS=Bone scan (scintigraphy); C=CT scan; E=Endoscopy; L=Lymphangiogram; M=MRI; MA=Mammography; NS=Nuclear scan; PC=PET/CT Scan; PT=PET scan; TU=Transvaginal ultrasound; UL=Ultrasound (echography); XR=X-ray

** See facing page for anatomical site codes

ECOG performance status

ECOG	Performance status	Approximate Karnofsky
0	Fully active, able to carry on all pre-disease performance without restriction.	90 - 100
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.	70 - 80
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.	50 - 60
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.	30 - 40
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	10 - 20

Patient status

Date of physical exam |_|_|_|_|_|_|_|_|_| DD MMM YYYY ☐ Not done

Vital signs and physical measurements

Weight (Kg) |_|_|_|.|_|

Blood pressure |_|_|_| / |_|_|_| systolic diastolic

Heart rate (beats/min) |_|_|_|

ECOG performance status |_|

Are there any changes since the previous assessment?

☐ No
☐ Yes → *Specify below*

☐ Recurrence of disease *(complete the "Recurrence of disease" page)*

☐ Second primary malignancy or contralateral breast cancer *(complete the "Second primary malignancy and contralateral BC" page)*

☐ Significant cardiac disease *(complete the "Adverse event" page)*

☐ Adverse event *(complete the "Adverse event" page)*

☐ Death *(complete the "Death" page)*

☐ Lost to follow-up

☐ Patient withdrew study consent

→ Date of last contact (*or date study consent withdrawn*) |_|_|_|_|_|_|_|_|_| DD MMM YYYY

(For patients "Lost to Follow-up", the date of last contact should be the last date the patient was known to be alive.
The last date the patient was known to be alive could either be the same as the previous reported visit date or any date between the previous visit and this one.)

ECOG performance status

ECOG	Performance status	Approximate Karnofsky
0	Fully active, able to carry on all pre-disease performance without restriction.	90 - 100
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.	70 - 80
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.	50 - 60
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.	30 - 40
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	10 - 20

Centre No. | Subject No.

Patient status

Date of physical exam ☐ DD ☐ MMM ☐ YYYY ☐ Not done

Vital signs and physical measurements

Weight (Kg) ☐☐☐.☐

Blood pressure ☐☐☐ / ☐☐☐ (systolic / diastolic)

Heart rate (beats/min) ☐☐☐

ECOG performance status ☐

Are there any changes since the previous assessment?

☐ No
☐ Yes → *Specify below*

☐ Recurrence of disease *(complete the "Recurrence of disease" page)*

☐ Second primary malignancy or contralateral breast cancer *(complete the "Second primary malignancy and contralateral BC" page)*

☐ Significant cardiac disease *(complete the "Adverse event" page)*

☐ Adverse event *(complete the "Adverse event" page)*

☐ Death *(complete the "Death" page)*

☐ Lost to follow-up
☐ Patient withdrew study consent
→ Date of last contact (*or date study consent withdrawn*) ☐ DD ☐ MMM ☐ YYYY

(For patients "Lost to Follow-up", the date of last contact should be the last date the patient was known to be alive.
The last date the patient was known to be alive could either be the same as the previous reported visit date or any date between the previous visit and this one.)

New York Heart Association (NYHA) Functional Classification
NOTE: If the patient does not have congestive heart failure (CHF), leave this field blank.

Class I. Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain.

Class II. Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.

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NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Neutrophils	<LLN – 1500/mm³ <LLN – 1.5 x 10^9/L	<1500 – 1000/mm³ <1.5 – 1.0 x 10^9/L	<1000 – 500/mm³ <1.0 – 0.5 x 10^9/L	<500/mm³ <0.5 x 10^9/L	Death
WBC	<LLN – 3000/mm³ <LLN – 3.0 x 10^9/L	<3000 – 2000/mm³ <3.0 – 2.0 x 10^9/L	<2000 – 1000/mm³ <2.0 – 1.0 x 10^9/L	<1000/mm³ <1.0 x 10^9/L	Death
Haemoglobin	<LLN - 10.0 g/dL <LLN - 6.2 mmol/L <LLN - 100 g/L	<10.0 – 8.0 g/dL <6.2 – 4.9 mmol/L <100 – 80 g/L	<8.0 – 6.5 g/dL <4.9 – 4.0 mmol/L <80-65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
Platelets	<LLN -75,000/mm³ <LLN-75.0 x 10^9/L	<75,000-50,000/mm³ <75.0-50.0 x 10^9/L	<50,000-25,000/mm³ <50.0-25.0 x 10^9/L	<25,000/mm³ <25.0 x 10^9/L	Death
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	
Serum creatinine	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 6.0 x ULN	>6.0 x ULN	Death

Cardiac monitoring

LVEF

Date of LVEF ☐☐ ☐☐☐ ☐☐☐☐ (DD MMM YYYY)

LVEF (patient value) ☐☐.☐ % Method of Evaluation ☐ Echocardiogram ☐ MUGA scan

☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant → *Please complete the "Adverse event" page.*

Symptomatic CHF ☐ No ☐ Yes → *Specify below*

NYHA classification **(complete only in case of CHF)**
☐ Class I *(in case of asymptomatic CHF, tick No for the question above)*
☐ Class II
☐ Class III
☐ Class IV

EKG should be performed at any time if symptoms or clinical suspicion are present and reported on the "Unscheduled EKG" page

Haematology and biochemistry

Please check the blood tests that should be done at this visit, as per protocol, and report any clinically significant (NCI CTCAE G3-4) abnormality on the "**Adverse event**" page.

Date blood drawn ☐☐ ☐☐☐ ☐☐☐☐ (DD MMM YYYY)

Result
☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant (G3-4) → *Report on Adverse Event page, if related to study drug*

Type of radiological examination

	Not done	Date of test (DD/MMM/YYYY)	Are there any clinically significant abnormalities? *(Please report a short description)*
Abdominal CT-scan	☐		☐ No ☐ Yes → Specify
Chest X-ray	☐		☐ No ☐ Yes → Specify
Chest CT-scan	☐		☐ No ☐ Yes → Specify
Bone scan (scintigraphy)	☐		☐ No ☐ Yes → Specify
Bone X-ray	☐		☐ No ☐ Yes → Specify
Bone CT-scan	☐		☐ No ☐ Yes → Specify
Bilateral mammography	☐		☐ No ☐ Yes → Specify
Left mammography, only	☐		☐ No ☐ Yes → Specify
Right mammography, only	☐		☐ No ☐ Yes → Specify

Anatomical site	Description
AB	Abdomen/abdominal wall
AD	Adrenals
BE	Bone
BR	Bladder
BT	Breast
CL	Colon
CR	Colorectal
CS	CNS (brain)
CW	Chest
CX	Cervix
EO	Esophagus/Oesophagus
HN	Head and neck
HT	Heart
K	Kidney
LG	Lung
LN	Lymph nodes

Anatomical site	Description
LV	Liver
OC	Oral cavity
OT	Other
OV	Ovary
PA	Pleura
PM	Peritoneum
PR	Prostate
PS	Pancreas
PV	Pelvis
RC	Rectum
SH	Stomach
SI	Small intestine
SK	Skin
SP	Spleen
TD	Thyroid
WB	Whole body

Type of radiological examination *(continued)*

Type of radiological examination*	Anatomical site**	Side (L or R)	Date of test	Are there any clinically significant abnormalities? *(Please report a short description)*
			DD MMM YYYY	☐ No ☐ Yes → Specify _____
			DD MMM YYYY	☐ No ☐ Yes → Specify _____

* BS=Bone scan (scintigraphy); C=CT scan; E=Endoscopy; L=Lymphangiogram; M=MRI; MA=Mammography; NS=Nuclear scan; PC=PET/CT Scan; PT=PET scan; TU=Transvaginal ultrasound; UL=Ultrasound (echography); XR=X-ray

** See facing page for anatomical site codes

ECOG performance status

ECOG	Performance status	Approximate Karnofsky
0	Fully active, able to carry on all pre-disease performance without restriction.	90 - 100
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4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	10 - 20

Centre No. | Subject No.

Patient status

Date of physical exam ☐ DD ☐ MMM ☐ YYYY ☐ Not done

Vital signs and physical measurements

Weight (Kg) ☐☐☐.☐

Blood pressure ☐☐☐ / ☐☐☐ (systolic / diastolic)

Heart rate (beats/min) ☐☐☐

ECOG performance status ☐

Are there any changes since the previous assessment?

☐ No
☐ Yes → *Specify below*

☐ Recurrence of disease *(complete the "Recurrence of disease" page)*

☐ Second primary malignancy or contralateral breast cancer *(complete the "Second primary malignancy and contralateral BC" page)*

☐ Significant cardiac disease *(complete the "Adverse event" page)*

☐ Adverse event *(complete the "Adverse event" page)*

☐ Death *(complete the "Death" page)*

☐ Lost to follow-up
☐ Patient withdrew study consent
→ Date of last contact (*or date study consent withdrawn*) ☐ DD ☐ MMM ☐ YYYY

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4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	10 - 20

Centre No. | Subject No.

Patient status

Date of physical exam ☐ DD ☐ MMM ☐ YYYY ☐ Not done

Vital signs and physical measurements

Weight (Kg) ☐☐☐.☐

Blood pressure ☐☐☐ / ☐☐☐ (systolic / diastolic)

Heart rate (beats/min) ☐☐☐

ECOG performance status ☐

Are there any changes since the previous assessment?

☐ No
☐ Yes → *Specify below*

☐ Recurrence of disease *(complete the "Recurrence of disease" page)*

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☐ Death *(complete the "Death" page)*

☐ Lost to follow-up
☐ Patient withdrew study consent
→ Date of last contact (*or date study consent withdrawn*) ☐ DD ☐ MMM ☐ YYYY

(For patients "Lost to Follow-up", the date of last contact should be the last date the patient was known to be alive.
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WBC	<LLN – 3000/mm³ <LLN – 3.0 x 10^9/L	<3000 – 2000/mm³ <3.0 – 2.0 x 10^9/L	<2000 – 1000/mm³ <2.0 – 1.0 x 10^9/L	<1000/mm³ <1.0 x 10^9/L	Death
Haemoglobin	<LLN - 10.0 g/dL <LLN - 6.2 mmol/L <LLN - 100 g/L	<10.0 – 8.0 g/dL <6.2 – 4.9 mmol/L <100 – 80 g/L	<8.0 – 6.5 g/dL <4.9 – 4.0 mmol/L <80-65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
Platelets	<LLN -75,000/mm³ <LLN-75.0 x 10^9/L	<75,000-50,000/mm³ <75.0-50.0 x 10^9/L	<50,000-25,000/mm³ <50.0-25.0 x 10^9/L	<25,000/mm³ <25.0 x 10^9/L	Death
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	
Serum creatinine	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 6.0 x ULN	>6.0 x ULN	Death

Cardiac monitoring

LVEF

Date of LVEF ☐☐ ☐☐☐ ☐☐☐☐ (DD MMM YYYY)

LVEF (patient value) ☐☐.☐ % Method of Evaluation ☐ Echocardiogram ☐ MUGA scan

☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant → *Please complete the "Adverse event" page.*

Symptomatic CHF ☐ No ☐ Yes → *Specify below*

NYHA classification **(complete only in case of CHF)**
☐ Class I *(in case of asymptomatic CHF, tick No for the question above)*
☐ Class II
☐ Class III
☐ Class IV

EKG should be performed at any time if symptoms or clinical suspicion are present and reported on the "Unscheduled EKG" page

Haematology and biochemistry

Please check the blood tests that should be done at this visit, as per protocol, and report any clinically significant (NCI CTCAE G3-4) abnormality on the "**Adverse event**" page.

Date blood drawn ☐☐ ☐☐☐ ☐☐☐☐ (DD MMM YYYY)

Result
☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant (G3-4) → *Report on Adverse Event page, if related to study drug*

Type of radiological examination

	Not done	Date of test (DD/MMM/YYYY)	Are there any clinically significant abnormalities? *(Please report a short description)*
Abdominal CT-scan	☐		☐ No ☐ Yes → Specify
Chest X-ray	☐		☐ No ☐ Yes → Specify
Chest CT-scan	☐		☐ No ☐ Yes → Specify
Bone scan (scintigraphy)	☐		☐ No ☐ Yes → Specify
Bone X-ray	☐		☐ No ☐ Yes → Specify
Bone CT-scan	☐		☐ No ☐ Yes → Specify
Bilateral mammography	☐		☐ No ☐ Yes → Specify
Left mammography, only	☐		☐ No ☐ Yes → Specify
Right mammography, only	☐		☐ No ☐ Yes → Specify

Anatomical site	Description
AB	Abdomen/abdominal wall
AD	Adrenals
BE	Bone
BR	Bladder
BT	Breast
CL	Colon
CR	Colorectal
CS	CNS (brain)
CW	Chest
CX	Cervix
EO	Esophagus/Oesophagus
HN	Head and neck
HT	Heart
K	Kidney
LG	Lung
LN	Lymph nodes

Anatomical site	Description
LV	Liver
OC	Oral cavity
OT	Other
OV	Ovary
PA	Pleura
PM	Peritoneum
PR	Prostate
PS	Pancreas
PV	Pelvis
RC	Rectum
SH	Stomach
SI	Small intestine
SK	Skin
SP	Spleen
TD	Thyroid
WB	Whole body

Type of radiological examination *(continued)*

Type of radiological examination*	Anatomical site**	Side (L or R)	Date of test	Are there any clinically significant abnormalities? *(Please report a short description)*
			DD MMM YYYY	☐ No ☐ Yes → Specify _____
			DD MMM YYYY	☐ No ☐ Yes → Specify _____

* BS=Bone scan (scintigraphy); C=CT scan; E=Endoscopy; L=Lymphangiogram; M=MRI; MA=Mammography; NS=Nuclear scan; PC=PET/CT Scan; PT=PET scan; TU=Transvaginal ultrasound; UL=Ultrasound (echography); XR=X-ray

** See facing page for anatomical site codes

ECOG performance status

ECOG	Performance status	Approximate Karnofsky
0	Fully active, able to carry on all pre-disease performance without restriction.	90 - 100
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.	70 - 80
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.	50 - 60
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.	30 - 40
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	10 - 20

Centre No. | | | | | | |

Subject No. | | | | | | |

Patient status

Date of physical exam ☐ DD ☐ MMM ☐ YYYY ☐ Not done

Vital signs and physical measurements

Weight (Kg) ☐☐☐.☐

Blood pressure ☐☐☐ / ☐☐☐ (systolic / diastolic)

Heart rate (beats/min) ☐☐☐

ECOG performance status ☐

Are there any changes since the previous assessment?

☐ No
☐ Yes → *Specify below*

☐ Recurrence of disease *(complete the "Recurrence of disease" page)*

☐ Second primary malignancy or contralateral breast cancer *(complete the "Second primary malignancy and contralateral BC" page)*

☐ Significant cardiac disease *(complete the "Adverse event" page)*

☐ Adverse event *(complete the "Adverse event" page)*

☐ Death *(complete the "Death" page)*

☐ Lost to follow-up
☐ Patient withdrew study consent
→ Date of last contact (*or date study consent withdrawn*) ☐ DD ☐ MMM ☐ YYYY

(For patients "Lost to Follow-up", the date of last contact should be the last date the patient was known to be alive.
The last date the patient was known to be alive could either be the same as the previous reported visit date or any date between the previous visit and this one.)

ECOG performance status

ECOG	Performance status	Approximate Karnofsky
0	Fully active, able to carry on all pre-disease performance without restriction.	90 - 100
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.	70 - 80
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.	50 - 60
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.	30 - 40
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	10 - 20

New York Heart Association (NYHA) Functional Classification
NOTE: If the patient does not have congestive heart failure (CHF), leave this field blank.

Class I. Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain.

Class II. Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.

Class III. Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.

Class IV. Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

Patient status

Date of physical exam ☐ Not done

DD MMM YYYY

Vital signs and physical measurements

Weight (Kg) ___.__

Blood pressure ___/___

systolic diastolic

Heart rate (beats/min) ___

ECOG performance status ___

Cardiac monitoring

LVEF

Date of LVEF

DD MMM YYYY

LVEF (patient value) ___.__ % Method of Evaluation ☐ Echocardiogram ☐ MUGA scan

☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant → *Please complete the "Adverse event" page.*

Symptomatic CHF ☐ No ☐ Yes → *Specify below*

NYHA classification **(complete only in case of CHF)**
☐ Class I *(in case of asymptomatic CHF, tick No for the question above)*
☐ Class II
☐ Class III
☐ Class IV

EKG should be performed at any time if symptoms or clinical suspicion are present and reported on the "Unscheduled EKG" page

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Neutrophils	<LLN – 1500/mm³ <LLN – 1.5 x 10^9/L	<1500 – 1000/mm³ <1.5 – 1.0 x 10^9/L	<1000 – 500/mm³ <1.0 – 0.5 x 10^9/L	<500/mm³ <0.5 x 10^9/L	Death
WBC	<LLN – 3000/mm³ <LLN – 3.0 x 10^9/L	<3000 – 2000/mm³ <3.0 – 2.0 x 10^9/L	<2000 – 1000/mm³ <2.0 – 1.0 x 10^9/L	<1000/mm³ <1.0 x 10^9/L	Death
Haemoglobin	<LLN - 10.0 g/dL <LLN - 6.2 mmol/L <LLN - 100 g/L	<10.0 – 8.0 g/dL <6.2 – 4.9 mmol/L <100 – 80 g/L	<8.0 – 6.5 g/dL <4.9 – 4.0 mmol/L <80-65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
Platelets	<LLN -75,000/mm³ <LLN-75.0 x 10^9/L	<75,000-50,000/mm³ <75.0-50.0 x 10^9/L	<50,000-25,000/mm³ <50.0-25.0 x 10^9/L	<25,000/mm³ <25.0 x 10^9/L	Death
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	
Serum creatinine	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 6.0 x ULN	>6.0 x ULN	Death

Haematology and biochemistry

Please check the blood tests that should be done at this visit, as per protocol, and report any clinically significant (NCI CTCAE G3-4) abnormality on the "**Adverse event**" page.

Date blood drawn DD MMM YYYY

Result
- ☐ Normal
- ☐ Abnormal - Not clinically significant
- ☐ Abnormal - Clinically significant (G3-4) → *Report on Adverse Event page, if related to study drug*

Type of radiological examination

	Not done	Date of test (DD/MMM/YYYY)	Are there any clinically significant abnormalities? *(Please report a short description)*
Abdominal CT-scan	☐		☐ No ☐ Yes → Specify
Chest X-ray	☐		☐ No ☐ Yes → Specify
Chest CT-scan	☐		☐ No ☐ Yes → Specify
Bone scan (scintigraphy)	☐		☐ No ☐ Yes → Specify
Bone X-ray	☐		☐ No ☐ Yes → Specify
Bone CT-scan	☐		☐ No ☐ Yes → Specify
Bilateral mammography	☐		☐ No ☐ Yes → Specify
Left mammography, only	☐		☐ No ☐ Yes → Specify
Right mammography, only	☐		☐ No ☐ Yes → Specify

Anatomical site	Description
AB	Abdomen/abdominal wall
AD	Adrenals
BE	Bone
BR	Bladder
BT	Breast
CL	Colon
CR	Colorectal
CS	CNS (brain)
CW	Chest
CX	Cervix
EO	Esophagus/Oesophagus
HN	Head and neck
HT	Heart
K	Kidney
LG	Lung
LN	Lymph nodes

Anatomical site	Description
LV	Liver
OC	Oral cavity
OT	Other
OV	Ovary
PA	Pleura
PM	Peritoneum
PR	Prostate
PS	Pancreas
PV	Pelvis
RC	Rectum
SH	Stomach
SI	Small intestine
SK	Skin
SP	Spleen
TD	Thyroid
WB	Whole body

Type of radiological examination *(continued)*

Type of radiological examination*	Anatomical site**	Side (L or R)	Date of test	Are there any clinically significant abnormalities? *(Please report a short description)*
			DD MMM YYYY	☐ No ☐ Yes → Specify _____
			DD MMM YYYY	☐ No ☐ Yes → Specify _____

* BS=Bone scan (scintigraphy); C=CT scan; E=Endoscopy; L=Lymphangiogram; M=MRI; MA=Mammography; NS=Nuclear scan; PC=PET/CT Scan; PT=PET scan; TU=Transvaginal ultrasound; UL=Ultrasound (echography); XR=X-ray

** See facing page for anatomical site codes

ECOG performance status

ECOG	Performance status	Approximate Karnofsky
0	Fully active, able to carry on all pre-disease performance without restriction.	90 - 100
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.	70 - 80
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.	50 - 60
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.	30 - 40
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	10 - 20

Centre No. | Subject No.

Patient status

Date of physical exam DD MMM YYYY ☐ Not done

Vital signs and physical measurements

Weight (Kg) ___.__

Blood pressure ___ / ___ (systolic / diastolic)

Heart rate (beats/min) ___

ECOG performance status ___

Are there any changes since the previous assessment?

☐ No
☐ Yes → *Specify below*

☐ Recurrence of disease *(complete the "Recurrence of disease" page)*

☐ Second primary malignancy or contralateral breast cancer *(complete the "Second primary malignancy and contralateral BC" page)*

☐ Significant cardiac disease *(complete the "Adverse event" page)*

☐ Adverse event *(complete the "Adverse event" page)*

☐ Death *(complete the "Death" page)*

☐ Lost to follow-up
☐ Patient withdrew study consent
→ Date of last contact (*or date study consent withdrawn*) DD MMM YYYY

(For patients "Lost to Follow-up", the date of last contact should be the last date the patient was known to be alive.
The last date the patient was known to be alive could either be the same as the previous reported visit date or any date between the previous visit and this one.)

New York Heart Association (NYHA) Functional Classification
NOTE: If the patient does not have congestive heart failure (CHF), leave this field blank.

Class I. Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain.

Class II. Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.

Class III. Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.

Class IV. Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Neutrophils	<LLN – 1500/mm³ <LLN – 1.5 x 10^9/L	<1500 – 1000/mm³ <1.5 – 1.0 x 10^9/L	<1000 – 500/mm³ <1.0 – 0.5 x 10^9/L	<500/mm³ <0.5 x 10^9/L	Death
WBC	<LLN – 3000/mm³ <LLN – 3.0 x 10^9/L	<3000 – 2000/mm³ <3.0 – 2.0 x 10^9/L	<2000 – 1000/mm³ <2.0 – 1.0 x 10^9/L	<1000/mm³ <1.0 x 10^9/L	Death
Haemoglobin	<LLN - 10.0 g/dL <LLN - 6.2 mmol/L <LLN - 100 g/L	<10.0 – 8.0 g/dL <6.2 – 4.9 mmol/L <100 – 80 g/L	<8.0 – 6.5 g/dL <4.9 – 4.0 mmol/L <80-65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
Platelets	<LLN -75,000/mm³ <LLN-75.0 x 10^9/L	<75,000-50,000/mm³ <75.0-50.0 x 10^9/L	<50,000-25,000/mm³ <50.0-25.0 x 10^9/L	<25,000/mm³ <25.0 x 10^9/L	Death
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	
Serum creatinine	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 6.0 x ULN	>6.0 x ULN	Death

Centre No. Subject No.

Cardiac monitoring

LVEF

Date of LVEF |_|_|_|_|_|_|_|_|_| DD MMM YYYY

LVEF (patient value) |_|_|_|.|_| % Method of Evaluation ☐ Echocardiogram ☐ MUGA scan

☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant ⟶ *Please complete the "Adverse event" page.*

Symptomatic CHF ☐ No
☐ Yes ⟶ *Specify below*

NYHA classification **(complete only in case of CHF)**
☐ Class I *(in case of asymptomatic CHF, tick No for the question above)*
☐ Class II
☐ Class III
☐ Class IV

EKG should be performed at any time if symptoms or clinical suspicion are present and reported on the "Unscheduled EKG" page

Haematology and biochemistry

Please check the blood tests that should be done at this visit, as per protocol, and report any clinically significant (NCI CTCAE G3-4) abnormality on the "**Adverse event**" page.

Date blood drawn |_|_|_|_|_|_|_|_|_| DD MMM YYYY

Result
☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant (G3-4) ⟶ *Report on Adverse Event page, if related to study drug*

Type of radiological examination

	Not done	Date of test (DD/MMM/YYYY)	Are there any clinically significant abnormalities? *(Please report a short description)*
Abdominal CT-scan	☐		☐ No ☐ Yes → Specify
Chest X-ray	☐		☐ No ☐ Yes → Specify
Chest CT-scan	☐		☐ No ☐ Yes → Specify
Bone scan (scintigraphy)	☐		☐ No ☐ Yes → Specify
Bone X-ray	☐		☐ No ☐ Yes → Specify
Bone CT-scan	☐		☐ No ☐ Yes → Specify
Bilateral mammography	☐		☐ No ☐ Yes → Specify
Left mammography, only	☐		☐ No ☐ Yes → Specify
Right mammography, only	☐		☐ No ☐ Yes → Specify

Anatomical site	Description
AB	Abdomen/abdominal wall
AD	Adrenals
BE	Bone
BR	Bladder
BT	Breast
CL	Colon
CR	Colorectal
CS	CNS (brain)
CW	Chest
CX	Cervix
EO	Esophagus/Oesophagus
HN	Head and neck
HT	Heart
K	Kidney
LG	Lung
LN	Lymph nodes

Anatomical site	Description
LV	Liver
OC	Oral cavity
OT	Other
OV	Ovary
PA	Pleura
PM	Peritoneum
PR	Prostate
PS	Pancreas
PV	Pelvis
RC	Rectum
SH	Stomach
SI	Small intestine
SK	Skin
SP	Spleen
TD	Thyroid
WB	Whole body

Type of radiological examination *(continued)*

Type of radiological examination*	Anatomical site**	Side (L or R)	Date of test	Are there any clinically significant abnormalities? *(Please report a short description)*
			DD MMM YYYY	☐ No ☐ Yes → Specify _____
			DD MMM YYYY	☐ No ☐ Yes → Specify _____

* BS=Bone scan (scintigraphy); C=CT scan; E=Endoscopy; L=Lymphangiogram; M=MRI; MA=Mammography; NS=Nuclear scan; PC=PET/CT Scan; PT=PET scan; TU=Transvaginal ultrasound; UL=Ultrasound (echography); XR=X-ray

** See facing page for anatomical site codes

ECOG performance status

ECOG	Performance status	Approximate Karnofsky
0	Fully active, able to carry on all pre-disease performance without restriction.	90 - 100
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.	70 - 80
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.	50 - 60
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.	30 - 40
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	10 - 20

Centre No. | Subject No.

Patient status

Date of physical exam DD MMM YYYY ☐ Not done

Vital signs and physical measurements

Weight (Kg) ___.__

Blood pressure ___ / ___ (systolic / diastolic)

Heart rate (beats/min) ___

ECOG performance status ___

Are there any changes since the previous assessment?

☐ No
☐ Yes → *Specify below*

☐ Recurrence of disease *(complete the "Recurrence of disease" page)*

☐ Second primary malignancy or contralateral breast cancer *(complete the "Second primary malignancy and contralateral BC" page)*

☐ Significant cardiac disease *(complete the "Adverse event" page)*

☐ Adverse event *(complete the "Adverse event" page)*

☐ Death *(complete the "Death" page)*

☐ Lost to follow-up
☐ Patient withdrew study consent
→ Date of last contact (*or date study consent withdrawn*) DD MMM YYYY

(For patients "Lost to Follow-up", the date of last contact should be the last date the patient was known to be alive.
The last date the patient was known to be alive could either be the same as the previous reported visit date or any date between the previous visit and this one.)

New York Heart Association (NYHA) Functional Classification
NOTE: If the patient does not have congestive heart failure (CHF), leave this field blank.

Class I. Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain.

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Class IV. Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Neutrophils	<LLN – 1500/mm³ <LLN – 1.5 x 10^9/L	<1500 – 1000/mm³ <1.5 – 1.0 x 10^9/L	<1000 – 500/mm³ <1.0 – 0.5 x 10^9/L	<500/mm³ <0.5 x 10^9/L	Death
WBC	<LLN – 3000/mm³ <LLN – 3.0 x 10^9/L	<3000 – 2000/mm³ <3.0 – 2.0 x 10^9/L	<2000 – 1000/mm³ <2.0 – 1.0 x 10^9/L	<1000/mm³ <1.0 x 10^9/L	Death
Haemoglobin	<LLN - 10.0 g/dL <LLN - 6.2 mmol/L <LLN - 100 g/L	<10.0 – 8.0 g/dL <6.2 – 4.9 mmol/L <100 – 80 g/L	<8.0 – 6.5 g/dL <4.9 – 4.0 mmol/L <80-65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
Platelets	<LLN -75,000/mm³ <LLN-75.0 x 10^9/L	<75,000-50,000/mm³ <75.0-50.0 x 10^9/L	<50,000-25,000/mm³ <50.0-25.0 x 10^9/L	<25,000/mm³ <25.0 x 10^9/L	Death
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	
Serum creatinine	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 6.0 x ULN	>6.0 x ULN	Death

Centre No. | Subject No.

Cardiac monitoring

LVEF

Date of LVEF ☐☐ ☐☐☐ ☐☐☐☐ (DD MMM YYYY)

LVEF (patient value) ☐☐.☐ % Method of Evaluation ☐ Echocardiogram ☐ MUGA scan

☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant → *Please complete the "Adverse event" page.*

Symptomatic CHF ☐ No ☐ Yes → *Specify below*

NYHA classification **(complete only in case of CHF)**
☐ Class I *(in case of asymptomatic CHF, tick No for the question above)*
☐ Class II
☐ Class III
☐ Class IV

EKG should be performed at any time if symptoms or clinical suspicion are present and reported on the "Unscheduled EKG" page

Haematology and biochemistry

Please check the blood tests that should be done at this visit, as per protocol, and report any clinically significant (NCI CTCAE G3-4) abnormality on the "**Adverse event**" page.

Date blood drawn ☐☐ ☐☐☐ ☐☐☐☐ (DD MMM YYYY)

Result
☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant (G3-4) → *Report on Adverse Event page, if related to study drug*

Type of radiological examination

	Not done	Date of test (DD/MMM/YYYY)	Are there any clinically significant abnormalities? *(Please report a short description)*
Abdominal CT-scan	☐		☐ No ☐ Yes → Specify
Chest X-ray	☐		☐ No ☐ Yes → Specify
Chest CT-scan	☐		☐ No ☐ Yes → Specify
Bone scan (scintigraphy)	☐		☐ No ☐ Yes → Specify
Bone X-ray	☐		☐ No ☐ Yes → Specify
Bone CT-scan	☐		☐ No ☐ Yes → Specify
Bilateral mammography	☐		☐ No ☐ Yes → Specify
Left mammography, only	☐		☐ No ☐ Yes → Specify
Right mammography, only	☐		☐ No ☐ Yes → Specify

Anatomical site	Description
AB	Abdomen/abdominal wall
AD	Adrenals
BE	Bone
BR	Bladder
BT	Breast
CL	Colon
CR	Colorectal
CS	CNS (brain)
CW	Chest
CX	Cervix
EO	Esophagus/Oesophagus
HN	Head and neck
HT	Heart
K	Kidney
LG	Lung
LN	Lymph nodes

Anatomical site	Description
LV	Liver
OC	Oral cavity
OT	Other
OV	Ovary
PA	Pleura
PM	Peritoneum
PR	Prostate
PS	Pancreas
PV	Pelvis
RC	Rectum
SH	Stomach
SI	Small intestine
SK	Skin
SP	Spleen
TD	Thyroid
WB	Whole body

Type of radiological examination *(continued)*

Type of radiological examination*	Anatomical site**	Side (L or R)	Date of test	Are there any clinically significant abnormalities? *(Please report a short description)*
			DD MMM YYYY	☐ No ☐ Yes → Specify _____
			DD MMM YYYY	☐ No ☐ Yes → Specify _____

* BS=Bone scan (scintigraphy); C=CT scan; E=Endoscopy; L=Lymphangiogram; M=MRI; MA=Mammography; NS=Nuclear scan; PC=PET/CT Scan; PT=PET scan; TU=Transvaginal ultrasound; UL=Ultrasound (echography); XR=X-ray

** See facing page for anatomical site codes

ECOG performance status

ECOG	Performance status	Approximate Karnofsky
0	Fully active, able to carry on all pre-disease performance without restriction.	90 - 100
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.	70 - 80
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.	50 - 60
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.	30 - 40
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	10 - 20

Centre No. | Subject No.

Patient status

Date of physical exam DD MMM YYYY ☐ Not done

Vital signs and physical measurements

Weight (Kg) ___.__

Blood pressure ___ / ___ (systolic / diastolic)

Heart rate (beats/min) ___

ECOG performance status ___

Are there any changes since the previous assessment?

☐ No
☐ Yes → *Specify below*

☐ Recurrence of disease *(complete the "Recurrence of disease" page)*

☐ Second primary malignancy or contralateral breast cancer *(complete the "Second primary malignancy and contralateral BC" page)*

☐ Significant cardiac disease *(complete the "Adverse event" page)*

☐ Adverse event *(complete the "Adverse event" page)*

☐ Death *(complete the "Death" page)*

☐ Lost to follow-up
☐ Patient withdrew study consent
→ Date of last contact (*or date study consent withdrawn*) DD MMM YYYY

(For patients "Lost to Follow-up", the date of last contact should be the last date the patient was known to be alive.
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NOTE: If the patient does not have congestive heart failure (CHF), leave this field blank.

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Class II. Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.

Class III. Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.

Class IV. Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Neutrophils	<LLN – 1500/mm³ <LLN – 1.5 x 10^9/L	<1500 – 1000/mm³ <1.5 – 1.0 x 10^9/L	<1000 – 500/mm³ <1.0 – 0.5 x 10^9/L	<500/mm³ <0.5 x 10^9/L	Death
WBC	<LLN – 3000/mm³ <LLN – 3.0 x 10^9/L	<3000 – 2000/mm³ <3.0 – 2.0 x 10^9/L	<2000 – 1000/mm³ <2.0 – 1.0 x 10^9/L	<1000/mm³ <1.0 x 10^9/L	Death
Haemoglobin	<LLN - 10.0 g/dL <LLN - 6.2 mmol/L <LLN - 100 g/L	<10.0 – 8.0 g/dL <6.2 – 4.9 mmol/L <100 – 80 g/L	<8.0 – 6.5 g/dL <4.9 – 4.0 mmol/L <80-65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
Platelets	<LLN -75,000/mm³ <LLN-75.0 x 10^9/L	<75,000-50,000/mm³ <75.0-50.0 x 10^9/L	<50,000-25,000/mm³ <50.0-25.0 x 10^9/L	<25,000/mm³ <25.0 x 10^9/L	Death
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	
Serum creatinine	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 6.0 x ULN	>6.0 x ULN	Death

Cardiac monitoring

LVEF

Date of LVEF ⌊__|__|__⌋ (DD MMM YYYY)

LVEF (patient value) ⌊__|__.__⌋ % Method of Evaluation ☐ Echocardiogram ☐ MUGA scan

☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant → *Please complete the "Adverse event" page.*

Symptomatic CHF ☐ No ☐ Yes → *Specify below*

NYHA classification **(complete only in case of CHF)**
☐ Class I *(in case of asymptomatic CHF, tick No for the question above)*
☐ Class II
☐ Class III
☐ Class IV

EKG should be performed at any time if symptoms or clinical suspicion are present and reported on the "Unscheduled EKG" page

Haematology and biochemistry

Please check the blood tests that should be done at this visit, as per protocol, and report any clinically significant (NCI CTCAE G3-4) abnormality on the "**Adverse event**" page.

Date blood drawn ⌊__|__|__⌋ (DD MMM YYYY)

Result
☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant (G3-4) → *Report on Adverse Event page, if related to study drug*

Type of radiological examination

	Not done	Date of test (DD/MMM/YYYY)	Are there any clinically significant abnormalities? *(Please report a short description)*
Abdominal CT-scan	☐	_____	☐ No ☐ Yes → Specify _____
Chest X-ray	☐	_____	☐ No ☐ Yes → Specify _____
Chest CT-scan	☐	_____	☐ No ☐ Yes → Specify _____
Bone scan (scintigraphy)	☐	_____	☐ No ☐ Yes → Specify _____
Bone X-ray	☐	_____	☐ No ☐ Yes → Specify _____
Bone CT-scan	☐	_____	☐ No ☐ Yes → Specify _____
Bilateral mammography	☐	_____	☐ No ☐ Yes → Specify _____
Left mammography, only	☐	_____	☐ No ☐ Yes → Specify _____
Right mammography, only	☐	_____	☐ No ☐ Yes → Specify _____

Anatomical site	Description
AB	Abdomen/abdominal wall
AD	Adrenals
BE	Bone
BR	Bladder
BT	Breast
CL	Colon
CR	Colorectal
CS	CNS (brain)
CW	Chest
CX	Cervix
EO	Esophagus/Oesophagus
HN	Head and neck
HT	Heart
K	Kidney
LG	Lung
LN	Lymph nodes

Anatomical site	Description
LV	Liver
OC	Oral cavity
OT	Other
OV	Ovary
PA	Pleura
PM	Peritoneum
PR	Prostate
PS	Pancreas
PV	Pelvis
RC	Rectum
SH	Stomach
SI	Small intestine
SK	Skin
SP	Spleen
TD	Thyroid
WB	Whole body

Type of radiological examination *(continued)*

Type of radiological examination*	**Anatomical site****	**Side (L or R)**	**Date of test**	**Are there any clinically significant abnormalities?** *(Please report a short description)*
			DD MMM YYYY	☐ No ☐ Yes → Specify _____
			DD MMM YYYY	☐ No ☐ Yes → Specify _____

* BS=Bone scan (scintigraphy); C=CT scan; E=Endoscopy; L=Lymphangiogram; M=MRI; MA=Mammography; NS=Nuclear scan; PC=PET/CT Scan; PT=PET scan; TU=Transvaginal ultrasound; UL=Ultrasound (echography); XR=X-ray

** See facing page for anatomical site codes

ECOG performance status

ECOG	Performance status	Approximate Karnofsky
0	Fully active, able to carry on all pre-disease performance without restriction.	90 - 100
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.	70 - 80
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.	50 - 60
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.	30 - 40
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	10 - 20

Patient status

Date of physical exam DD MMM YYYY ☐ Not done

Vital signs and physical measurements

Weight (Kg) ___.__

Blood pressure ___ / ___ (systolic / diastolic)

Heart rate (beats/min) ___

ECOG performance status ___

Are there any changes since the previous assessment?

☐ No
☐ Yes → *Specify below*

☐ Recurrence of disease *(complete the "Recurrence of disease" page)*

☐ Second primary malignancy or contralateral breast cancer *(complete the "Second primary malignancy and contralateral BC" page)*

☐ Significant cardiac disease *(complete the "Adverse event" page)*

☐ Adverse event *(complete the "Adverse event" page)*

☐ Death *(complete the "Death" page)*

☐ Lost to follow-up
☐ Patient withdrew study consent
→ Date of last contact (*or date study consent withdrawn*) DD MMM YYYY

(For patients "Lost to Follow-up", the date of last contact should be the last date the patient was known to be alive.
The last date the patient was known to be alive could either be the same as the previous reported visit date or any date between the previous visit and this one.)

New York Heart Association (NYHA) Functional Classification
NOTE: If the patient does not have congestive heart failure (CHF), leave this field blank.

Class I. Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain.

Class II. Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.

Class III. Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.

Class IV. Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Neutrophils	<LLN – 1500/mm³ <LLN – 1.5 x 10^9/L	<1500 – 1000/mm³ <1.5 – 1.0 x 10^9/L	<1000 – 500/mm³ <1.0 – 0.5 x 10^9/L	<500/mm³ <0.5 x 10^9/L	Death
WBC	<LLN – 3000/mm³ <LLN – 3.0 x 10^9/L	<3000 – 2000/mm³ <3.0 – 2.0 x 10^9/L	<2000 – 1000/mm³ <2.0 – 1.0 x 10^9/L	<1000/mm³ <1.0 x 10^9/L	Death
Haemoglobin	<LLN - 10.0 g/dL <LLN - 6.2 mmol/L <LLN - 100 g/L	<10.0 – 8.0 g/dL <6.2 – 4.9 mmol/L <100 – 80 g/L	<8.0 – 6.5 g/dL <4.9 – 4.0 mmol/L <80-65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
Platelets	<LLN -75,000/mm³ <LLN-75.0 x 10^9/L	<75,000-50,000/mm³ <75.0-50.0 x 10^9/L	<50,000-25,000/mm³ <50.0-25.0 x 10^9/L	<25,000/mm³ <25.0 x 10^9/L	Death
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	
Serum creatinine	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 6.0 x ULN	>6.0 x ULN	Death

Centre No. | | | | | |

Subject No. | | | | | |

Cardiac monitoring

LVEF

Date of LVEF |__|__|__|__|__|__|__|__|__| DD MMM YYYY

LVEF (patient value) |__|__|.|__| % Method of Evaluation ☐ Echocardiogram ☐ MUGA scan

☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant → *Please complete the "Adverse event" page.*

Symptomatic CHF ☐ No
☐ Yes → *Specify below*

NYHA classification **(complete only in case of CHF)**

☐ Class I *(in case of asymptomatic CHF, tick No for the question above)*
☐ Class II
☐ Class III
☐ Class IV

EKG should be performed at any time if symptoms or clinical suspicion are present and reported on the "Unscheduled EKG" page

Haematology and biochemistry

Please check the blood tests that should be done at this visit, as per protocol, and report any clinically significant (NCI CTCAE G3-4) abnormality on the "**Adverse event**" page.

Date blood drawn |__|__|__|__|__|__|__|__|__| DD MMM YYYY

Result
☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant (G3-4) → *Report on Adverse Event page, if related to study drug*

Type of radiological examination

	Not done	Date of test (DD/MMM/YYYY)	Are there any clinically significant abnormalities? *(Please report a short description)*
Abdominal CT-scan	☐		☐ No ☐ Yes → Specify
Chest X-ray	☐		☐ No ☐ Yes → Specify
Chest CT-scan	☐		☐ No ☐ Yes → Specify
Bone scan (scintigraphy)	☐		☐ No ☐ Yes → Specify
Bone X-ray	☐		☐ No ☐ Yes → Specify
Bone CT-scan	☐		☐ No ☐ Yes → Specify
Bilateral mammography	☐		☐ No ☐ Yes → Specify
Left mammography, only	☐		☐ No ☐ Yes → Specify
Right mammography, only	☐		☐ No ☐ Yes → Specify

Anatomical site	Description
AB	Abdomen/abdominal wall
AD	Adrenals
BE	Bone
BR	Bladder
BT	Breast
CL	Colon
CR	Colorectal
CS	CNS (brain)
CW	Chest
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EO	Esophagus/Oesophagus
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LG	Lung
LN	Lymph nodes

Anatomical site	Description
LV	Liver
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PS	Pancreas
PV	Pelvis
RC	Rectum
SH	Stomach
SI	Small intestine
SK	Skin
SP	Spleen
TD	Thyroid
WB	Whole body

Type of radiological examination *(continued)*

Type of radiological examination*	Anatomical site**	Side (L or R)	Date of test	Are there any clinically significant abnormalities? *(Please report a short description)*
			DD MMM YYYY	☐ No ☐ Yes → Specify _____
			DD MMM YYYY	☐ No ☐ Yes → Specify _____

* BS=Bone scan (scintigraphy); C=CT scan; E=Endoscopy; L=Lymphangiogram; M=MRI; MA=Mammography; NS=Nuclear scan; PC=PET/CT Scan; PT=PET scan; TU=Transvaginal ultrasound; UL=Ultrasound (echography); XR=X-ray

** See facing page for anatomical site codes

ECOG performance status

ECOG	Performance status	Approximate Karnofsky
0	Fully active, able to carry on all pre-disease performance without restriction.	90 - 100
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.	70 - 80
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.	50 - 60
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.	30 - 40
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.	10 - 20

Centre No. | Subject No.

Patient status

Date of physical exam DD MMM YYYY ☐ Not done

Vital signs and physical measurements

Weight (Kg) ___.__

Blood pressure ___ / ___ (systolic / diastolic)

Heart rate (beats/min) ___

ECOG performance status ___

Are there any changes since the previous assessment?

☐ No
☐ Yes → *Specify below*

☐ Recurrence of disease *(complete the "Recurrence of disease" page)*

☐ Second primary malignancy or contralateral breast cancer *(complete the "Second primary malignancy and contralateral BC" page)*

☐ Significant cardiac disease *(complete the "Adverse event" page)*

☐ Adverse event *(complete the "Adverse event" page)*

☐ Death *(complete the "Death" page)*

☐ Lost to follow-up
☐ Patient withdrew study consent
→ Date of last contact (*or date study consent withdrawn*) DD MMM YYYY

(For patients "Lost to Follow-up", the date of last contact should be the last date the patient was known to be alive.
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NOTE: If the patient does not have congestive heart failure (CHF), leave this field blank.

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Neutrophils	<LLN – 1500/mm³ <LLN – 1.5 x 10^9/L	<1500 – 1000/mm³ <1.5 – 1.0 x 10^9/L	<1000 – 500/mm³ <1.0 – 0.5 x 10^9/L	<500/mm³ <0.5 x 10^9/L	Death
WBC	<LLN – 3000/mm³ <LLN – 3.0 x 10^9/L	<3000 – 2000/mm³ <3.0 – 2.0 x 10^9/L	<2000 – 1000/mm³ <2.0 – 1.0 x 10^9/L	<1000/mm³ <1.0 x 10^9/L	Death
Haemoglobin	<LLN - 10.0 g/dL <LLN - 6.2 mmol/L <LLN - 100 g/L	<10.0 – 8.0 g/dL <6.2 – 4.9 mmol/L <100 – 80 g/L	<8.0 – 6.5 g/dL <4.9 – 4.0 mmol/L <80-65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
Platelets	<LLN -75,000/mm³ <LLN-75.0 x 10^9/L	<75,000-50,000/mm³ <75.0-50.0 x 10^9/L	<50,000-25,000/mm³ <50.0-25.0 x 10^9/L	<25,000/mm³ <25.0 x 10^9/L	Death
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	
Serum creatinine	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 6.0 x ULN	>6.0 x ULN	Death

Centre No. | Subject No.

Cardiac monitoring

LVEF

Date of LVEF: DD MMM YYYY

LVEF (patient value): ☐☐.☐ % Method of Evaluation ☐ Echocardiogram ☐ MUGA scan

☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant → *Please complete the "Adverse event" page.*

Symptomatic CHF
☐ No
☐ Yes → *Specify below*

NYHA classification **(complete only in case of CHF)**
☐ Class I *(in case of asymptomatic CHF, tick No for the question above)*
☐ Class II
☐ Class III
☐ Class IV

EKG should be performed at any time if symptoms or clinical suspicion are present and reported on the "Unscheduled EKG" page

Haematology and biochemistry

Please check the blood tests that should be done at this visit, as per protocol, and report any clinically significant (NCI CTCAE G3-4) abnormality on the "**Adverse event**" page.

Date blood drawn: DD MMM YYYY

Result
☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant (G3-4) → *Report on Adverse Event page, if related to study drug*

Type of radiological examination

	Not done	Date of test (DD/MMM/YYYY)	Are there any clinically significant abnormalities? *(Please report a short description)*
Abdominal CT-scan	☐		☐ No ☐ Yes → Specify
Chest X-ray	☐		☐ No ☐ Yes → Specify
Chest CT-scan	☐		☐ No ☐ Yes → Specify
Bone scan (scintigraphy)	☐		☐ No ☐ Yes → Specify
Bone X-ray	☐		☐ No ☐ Yes → Specify
Bone CT-scan	☐		☐ No ☐ Yes → Specify
Bilateral mammography	☐		☐ No ☐ Yes → Specify
Left mammography, only	☐		☐ No ☐ Yes → Specify
Right mammography, only	☐		☐ No ☐ Yes → Specify

Anatomical site	Description
AB	Abdomen/abdominal wall
AD	Adrenals
BE	Bone
BR	Bladder
BT	Breast
CL	Colon
CR	Colorectal
CS	CNS (brain)
CW	Chest
CX	Cervix
EO	Esophagus/Oesophagus
HN	Head and neck
HT	Heart
K	Kidney
LG	Lung
LN	Lymph nodes

Anatomical site	Description
LV	Liver
OC	Oral cavity
OT	Other
OV	Ovary
PA	Pleura
PM	Peritoneum
PR	Prostate
PS	Pancreas
PV	Pelvis
RC	Rectum
SH	Stomach
SI	Small intestine
SK	Skin
SP	Spleen
TD	Thyroid
WB	Whole body

Type of radiological examination *(continued)*

Type of radiological examination*	Anatomical site**	Side (L or R)	Date of test	Are there any clinically significant abnormalities? *(Please report a short description)*
			DD MMM YYYY	☐ No ☐ Yes → Specify _____
			DD MMM YYYY	☐ No ☐ Yes → Specify _____

* BS=Bone scan (scintigraphy); C=CT scan; E=Endoscopy; L=Lymphangiogram; M=MRI; MA=Mammography; NS=Nuclear scan; PC=PET/CT Scan; PT=PET scan; TU=Transvaginal ultrasound; UL=Ultrasound (echography); XR=X-ray

** See facing page for anatomical site codes

Hormone therapy for primary breast cancer

Has the patient received hormone therapy before or during the trial? ☐ No ☐ Yes → Specify below

Name of treatment* or surgical procedure	Dose	Units	Adjuvant hormonal therapy start date (dd/mmm/yyyy)	Adjuvant hormonal therapy end date (dd/mmm/yyyy)	Ongoing at time of study completion ✓
Tamoxifen		mg			☐
Anastrozole		mg			☐
Letrozole		mg			☐
Exemestane		mg			☐
Goserelin		mg			☐
Other LH-RH analogue: _____		mg			☐
Bilateral ovariectomy/oophorectomy	NA	NA		NA	NA
					☐
					☐
					☐
					☐

* generic name whenever possible, record only one per line

Adjuvant radiotherapy for primary breast cancer

Radiation therapy ☐ No ☐ Yes → Specify below

Radiation therapy site	Side left	Side right	Total dose of radiation therapy	Units 1=Gy (100rads) 2=cGy 3=Rads	Radiation therapy start date (dd/mmm/yyyy)	Radiation therapy end date (dd/mmm/yyyy)
Breast	☐	☐				
Chest wall	☐	☐				
Axilla	☐	☐				
Supraclavicular area	☐	☐				
Internal mammary nodes	☐	☐				
Tumor bed, boost	☐	☐				
	☐	☐				
	☐	☐				

Note: in case of mastectomy, please report the site as chest wall instead of breast

In case of treatment given as study treatment pre-medication or any prophylaxis treatment given intermittently, please report only one line with start date of first administration and end date of last administration.

Concomitant treatments

Centre No. ☐☐☐☐☐☐ Subject No. ☐☐☐☐☐☐

Concomitant relevant treatments and/or surgical procedures
(Please report here also significant treatments ongoing from screening or surgical procedures performed before screening)

Name of treatment *(generic name whenever possible, record only one per line)*	**Indication for use** 5=Prophylactic 9=Curative	**Date started (dd/mmm/yyyy)**	**Date stopped (dd/mmm/yyyy)**	**Ongoing (at time of study completion)** ✓
Bisphosphonate, specify: ____	☐	__/___/____	__/___/____	☐
Oestrogen replacement, specify: ____	☐	__/___/____	__/___/____	☐
Prophylactic mastectomy ☐ Left or ☐ Right	☐	__/___/____	NA	NA
Breast reconstruction ☐ Left or ☐ Right	☐	__/___/____	NA	NA
	☐	__/___/____	__/___/____	☐
	☐	__/___/____	__/___/____	☐
	☐	__/___/____	__/___/____	☐
	☐	__/___/____	__/___/____	☐
	☐	__/___/____	__/___/____	☐
	☐	__/___/____	__/___/____	☐
	☐	__/___/____	__/___/____	☐
	☐	__/___/____	__/___/____	☐

In case of treatment given as study treatment pre-medication or any prophylaxis treatment given intermittently, please report only one line with start date of first administration and end date of last administration.

Concomitant relevant treatments and/or surgical procedures

(Please report here also significant treatments ongoing from screening or surgical procedures performed before screening)

Name of treatment *(generic name whenever possible, record only one per line)*	**Indication for use** 5=Prophylactic 9=Curative	**Date started (dd/mmm/yyyy)**	**Date stopped (dd/mmm/yyyy)**	**Ongoing (at time of study completion)** ✓
				☐
				☐
				☐
				☐
				☐
				☐
				☐
				☐
				☐
				☐
				☐
				☐

In case of treatment given as study treatment pre-medication or any prophylaxis treatment given intermittently, please report only one line with start date of first administration and end date of last administration.

Concomitant relevant treatments and/or surgical procedures

(Please report here also significant treatments ongoing from screening or surgical procedures performed before screening)

Name of treatment *(generic name whenever possible, record only one per line)*	**Indication for use** 5=Prophylactic 9=Curative	**Date started (dd/mmm/yyyy)**	**Date stopped (dd/mmm/yyyy)**	**Ongoing (at time of study completion)** ✓
				☐
				☐
				☐
				☐
				☐
				☐
				☐
				☐
				☐
				☐
				☐
				☐

Dose delay: please note that the delay of +/- 1 day from the planned cycle date is not considered as a delay

Primary reason for dose delay or reduction

Code	Description	Examples
1	Haematologic adverse event *(Report Adverse Event)*	
2	Cardiac adverse event *(Report Adverse Event)*	
3	Adverse event other than haematologic or cardiac *(Report Adverse Event)*	
4	Dosing error	
7	Subject non-compliance	- Patient's holiday - Patient's request - Personal reasons
9	Administrative reasons	- Public holiday - Investigator or study staff error - Delivery of study medication delayed
OT	Other	None of the above

Centre No. ☐☐☐☐☐☐ Subject No. ☐☐☐☐☐☐

Administration of Paclitaxel

Date agent administered (dd/mmm/yyyy)	Dose (mg/m²)	Total dose (mg)	Was treatment delayed? No / Yes, specify code*	Was dose reduced? No / Yes, specify code*
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify

**See adjacent table for coding of primary reason for delay of treatment or dose reduction*

Dose delay: please note that the delay of +/- 1 day from the planned cycle date is not considered as a delay

Primary reason for dose delay or reduction

Code	Description	Examples
1	Haematologic adverse event *(Report Adverse Event)*	
2	Cardiac adverse event *(Report Adverse Event)*	
3	Adverse event other than haematologic or cardiac *(Report Adverse Event)*	
4	Dosing error	
7	Subject non-compliance	- Patient's holiday - Patient's request - Personal reasons
9	Administrative reasons	- Public holiday - Investigator or study staff error - Delivery of study medication delayed
OT	Other	None of the above

Centre No. ☐☐☐☐☐☐ Subject No. ☐☐☐☐☐☐

Administration of Paclitaxel

Date agent administered (dd/mmm/yyyy)	Dose (mg/m²)	Total dose (mg)	Was treatment delayed? No / Yes, specify code*	Was dose reduced? No / Yes, specify code*
__ __/__ __ __/__ __ __ __			☐ ☐ __ __ if OT, specify ______	☐ ☐ __ __ if OT, specify ______
__ __/__ __ __/__ __ __ __			☐ ☐ __ __ if OT, specify ______	☐ ☐ __ __ if OT, specify ______
__ __/__ __ __/__ __ __ __			☐ ☐ __ __ if OT, specify ______	☐ ☐ __ __ if OT, specify ______
__ __/__ __ __/__ __ __ __			☐ ☐ __ __ if OT, specify ______	☐ ☐ __ __ if OT, specify ______
__ __/__ __ __/__ __ __ __			☐ ☐ __ __ if OT, specify ______	☐ ☐ __ __ if OT, specify ______
__ __/__ __ __/__ __ __ __			☐ ☐ __ __ if OT, specify ______	☐ ☐ __ __ if OT, specify ______
__ __/__ __ __/__ __ __ __			☐ ☐ __ __ if OT, specify ______	☐ ☐ __ __ if OT, specify ______

**See adjacent table for coding of primary reason for delay of treatment or dose reduction*

Primary reason for dose delay or reduction

Code	Description	Examples
1	Haematologic adverse event *(Report Adverse Event)*	
2	Cardiac adverse event *(Report Adverse Event)*	
3	Adverse event other than haematologic or cardiac *(Report Adverse Event)*	
4	Dosing error	
7	Subject non-compliance	- Patient's holiday - Patient's request - Personal reasons
9	Administrative reasons	- Public holiday - Investigator or study staff error - Delivery of study medication delayed
OT	Other	None of the above

FEC adjuvant treatment

Name of treatment	Date agent administered (dd/mmm/yyyy)	Dose (mg/m^2)	Total dose (mg)	Was treatment delayed? No / Yes, specify code*	Was dose reduced? No / Yes, specify code*
Fluorouracil				☐ ☐ ☐☐ if OT, specify _____	☐ ☐ ☐☐ if OT, specify _____
Epirubicin				☐ ☐ ☐☐ if OT, specify _____	☐ ☐ ☐☐ if OT, specify _____
Cyclophosphamide				☐ ☐ ☐☐ if OT, specify _____	☐ ☐ ☐☐ if OT, specify _____
Fluorouracil				☐ ☐ ☐☐ if OT, specify _____	☐ ☐ ☐☐ if OT, specify _____
Epirubicin				☐ ☐ ☐☐ if OT, specify _____	☐ ☐ ☐☐ if OT, specify _____
Cyclophosphamide				☐ ☐ ☐☐ if OT, specify _____	☐ ☐ ☐☐ if OT, specify _____

**See adjacent table for coding of primary reason for delay of treatment or dose reduction*

Primary reason for dose delay or reduction

Code	Description	Examples
1	Haematologic adverse event *(Report Adverse Event)*	
2	Cardiac adverse event *(Report Adverse Event)*	
3	Adverse event other than haematologic or cardiac *(Report Adverse Event)*	
4	Dosing error	
7	Subject non-compliance	- Patient's holiday - Patient's request - Personal reasons
9	Administrative reasons	- Public holiday - Investigator or study staff error - Delivery of study medication delayed
OT	Other	None of the above

FEC adjuvant treatment

Name of treatment	Date agent administered (dd/mmm/yyyy)	Dose (mg/m^2)	Total dose (mg)	Was treatment delayed? No ☐ Yes, specify code* ☐☐ if OT, specify _____	Was dose reduced? No ☐ Yes, specify code* ☐☐ if OT, specify _____
Fluorouracil	☐☐☐☐☐☐☐☐☐				
Epirubicin	☐☐☐☐☐☐☐☐☐				
Cyclophosphamide	☐☐☐☐☐☐☐☐☐				

**See adjacent table for coding of primary reason for delay of treatment or dose reduction*

Completion instruction in case of Lapatinib interruption or dose reduction:

In case of interruption, please tick the checkbox “Yes” for “Was treatment interrupted?”, report the stop date (last date of administration before interruption) and start a new line with the first day the treatment is restarted as the start date.

If the dose is reduced, please enter the last date of administration (before the dose reduction) as the “Date stopped”. In the next row, enter the reduced dose, the date treatment is restarted at the reduced dose and tick the checkbox “Yes” for “Was dose reduced?”.the reduced dose.

Primary reason for dose reduction or treatment interruption

Code	Description	Examples
1	Haematologic adverse event *(Report Adverse Event)*	
2	Cardiac adverse event *(Report Adverse Event)*	
3	Adverse event other than haematologic or cardiac *(Report Adverse Event)*	
4	Dosing error	
7	Subject non-compliance	- Patient’s holiday - Patient’s request - Personal reasons
9	Administrative reasons	- Public holiday - Investigator or study staff error - Delivery of study medication delayed
OT	Other	None of the above

Administration of study drug

Centre No. ☐☐☐☐☐☐ Subject No. ☐☐☐☐☐☐

Administration of Lapatinib

Date started (dd/mmm/yyyy)	Date stopped (dd/mmm/yyyy)	Total daily dose of agent (or drug) (mg)	Was treatment interrupted? No / Yes, specify code*	Was dose reduced? No / Yes, specify code*
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify

**See adjacent table for coding of primary reason for interruption of treatment or dose reduction*

Investigational product compliance

Please record the data from the Lapatinib Dispensing Log on this form.

Agent Name	Date tablets dispensed (dd/mmm/yyyy)	Number of tablets dispensed	Date tablets returned (dd/mmm/yyyy)	Number of tablets returned
Lapatinib				
Lapatinib				
Lapatinib				
Lapatinib				
Lapatinib				
Lapatinib				
Lapatinib				

Dose delay: please note that the delays within the limits reported below are not considered as a delay
- 3 weekly schedule: +/- 3 days from the planned cycle date
- weekly schedule: +/- 1 day from the planned cycle date

Total dose received: if weight changes more than 10% from screening, it is recommended to recalculate the dose

If the trastuzumab infusion is interrupted and re-started on the same day, please enter the the total of all trastuzumab doses given in the same day in one row of the table.

Primary reason for treatment delay or dose interrupted

Code	Description	Examples
1	Haematologic adverse event *(Report Adverse Event)*	
2	Cardiac adverse event *(Report Adverse Event)*	
3	Adverse event other than haematologic or cardiac *(Report Adverse Event)*	
4	Dosing error	
7	Subject non-compliance	- Patient's holiday - Patient's request - Personal reasons
9	Administrative reasons	- Public holiday - Investigator or study staff error - Delivery of study medication delayed
OT	Other	None of the above

Administration of study drug

Centre No. ☐☐☐☐☐☐ Subject No. ☐☐☐☐☐☐

Administration of Trastuzumab

Date agent administered (dd/mmm/yyyy)	Dose (mg/kg)	Total dose (mg)	Was treatment delayed? No / Yes, specify code*	Was dose interrupted? No / Yes, specify code*
__/___/____			☐ ☐ __ if OT, specify ____	☐ ☐ __ if OT, specify ____
__/___/____			☐ ☐ __ if OT, specify ____	☐ ☐ __ if OT, specify ____
__/___/____			☐ ☐ __ if OT, specify ____	☐ ☐ __ if OT, specify ____
__/___/____			☐ ☐ __ if OT, specify ____	☐ ☐ __ if OT, specify ____
__/___/____			☐ ☐ __ if OT, specify ____	☐ ☐ __ if OT, specify ____
__/___/____			☐ ☐ __ if OT, specify ____	☐ ☐ __ if OT, specify ____
__/___/____			☐ ☐ __ if OT, specify ____	☐ ☐ __ if OT, specify ____

**See adjacent table for coding of primary reason for delay of treatment or dose interruption*

Dose delay: please note that the delays within the limits reported below are not considered as a delay
- 3 weekly schedule: +/- 3 days from the planned cycle date
- weekly schedule: +/- 1 day from the planned cycle date

Total dose received: if weight changes more than 10% from screening, it is recommended to recalculate the dose

If the trastuzumab infusion is interrupted and re-started on the same day, please enter the the total of all trastuzumab doses given in the same day in one row of the table.

Primary reason for treatment delay or dose interrupted

Code	Description	Examples
1	Haematologic adverse event *(Report Adverse Event)*	
2	Cardiac adverse event *(Report Adverse Event)*	
3	Adverse event other than haematologic or cardiac *(Report Adverse Event)*	
4	Dosing error	
7	Subject non-compliance	- Patient's holiday - Patient's request - Personal reasons
9	Administrative reasons	- Public holiday - Investigator or study staff error - Delivery of study medication delayed
OT	Other	None of the above

Centre No. | | | | | | |

Subject No. | | | | | | |

Administration of Trastuzumab (cont.)

Date agent administered (dd/mmm/yyyy)	Dose (mg/kg)	Total dose (mg)	Was treatment delayed? No / Yes, specify code*	Was dose interrupted? No / Yes, specify code*
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify

**See adjacent table for coding of primary reason for delay of treatment or dose interruption*

Dose delay: please note that the delays within the limits reported below are not considered as a delay
- 3 weekly schedule: +/- 3 days from the planned cycle date
- weekly schedule: +/- 1 day from the planned cycle date

Total dose received: if weight changes more than 10% from screening, it is recommended to recalculate the dose

If the trastuzumab infusion is interrupted and re-started on the same day, please enter the the total of all trastuzumab doses given in the same day in one row of the table.

Primary reason for treatment delay or dose interrupted

Code	Description	Examples
1	Haematologic adverse event *(Report Adverse Event)*	
2	Cardiac adverse event *(Report Adverse Event)*	
3	Adverse event other than haematologic or cardiac *(Report Adverse Event)*	
4	Dosing error	
7	Subject non-compliance	- Patient's holiday - Patient's request - Personal reasons
9	Administrative reasons	- Public holiday - Investigator or study staff error - Delivery of study medication delayed
OT	Other	None of the above

Centre No. ☐☐☐☐☐☐ Subject No. ☐☐☐☐☐☐

Administration of Trastuzumab (cont.)

Date agent administered (dd/mmm/yyyy)	Dose (mg/kg)	Total dose (mg)	Was treatment delayed? No / Yes, specify code*	Was dose interrupted? No / Yes, specify code*
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify

**See adjacent table for coding of primary reason for delay of treatment or dose interruption*

Dose delay: please note that the delays within the limits reported below are not considered as a delay
- 3 weekly schedule: +/- 3 days from the planned cycle date
- weekly schedule: +/- 1 day from the planned cycle date

Total dose received: if weight changes more than 10% from screening, it is recommended to recalculate the dose

If the trastuzumab infusion is interrupted and re-started on the same day, please enter the the total of all trastuzumab doses given in the same day in one row of the table.

Primary reason for treatment delay or dose interrupted

Code	Description	Examples
1	Haematologic adverse event *(Report Adverse Event)*	
2	Cardiac adverse event *(Report Adverse Event)*	
3	Adverse event other than haematologic or cardiac *(Report Adverse Event)*	
4	Dosing error	
7	Subject non-compliance	- Patient's holiday - Patient's request - Personal reasons
9	Administrative reasons	- Public holiday - Investigator or study staff error - Delivery of study medication delayed
OT	Other	None of the above

Centre No. ☐☐☐☐☐☐ Subject No. ☐☐☐☐☐☐

Administration of Trastuzumab (cont.)

Date agent administered (dd/mmm/yyyy)	Dose (mg/kg)	Total dose (mg)	Was treatment delayed? No / Yes, specify code*	Was dose interrupted? No / Yes, specify code*
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify

**See adjacent table for coding of primary reason for delay of treatment or dose interruption*

Dose delay: please note that the delays within the limits reported below are not considered as a delay
- 3 weekly schedule: +/- 3 days from the planned cycle date
- weekly schedule: +/- 1 day from the planned cycle date

Total dose received: if weight changes more than 10% from screening, it is recommended to recalculate the dose

If the trastuzumab infusion is interrupted and re-started on the same day, please enter the the total of all trastuzumab doses given in the same day in one row of the table.

Primary reason for dose delay or reduction

Code	Description	Examples
1	Haematologic adverse event *(Report Adverse Event)*	
2	Cardiac adverse event *(Report Adverse Event)*	
3	Adverse event other than haematologic or cardiac *(Report Adverse Event)*	
4	Dosing error	
7	Subject non-compliance	- Patient's holiday - Patient's request - Personal reasons
9	Administrative reasons	- Public holiday - Investigator or study staff error - Delivery of study medication delayed
OT	Other	None of the above

Administration of Trastuzumab (cont.)

Date agent administered (dd/mmm/yyyy)	Dose (mg/kg)	Total dose (mg)	Was treatment delayed? No Yes, specify code*	Was dose interrupted? No Yes, specify code*
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify
			☐ ☐ if OT, specify	☐ ☐ if OT, specify

**See adjacent table for coding of primary reason for delay of treatment or dose interruption*

AE name	• Enter only the diagnosis (if known); otherwise enter sign or symptom. If a diagnosis subsequently becomes available then this must be entered instead. • Pre-exisiting conditions, which worsen during the study are to be reported as Adverse Events • Use medical terminology in English. Do not use abbreviations. • Include the anatomical site. • Recurrence of breast cancer must not be recorded as an Adverse Event. Second Primary Malignancy (SPM) must be reported as a Serious Adverse Event
Serious	• Refer to Protocol 'Definition of a Serious Adverse Event' • All deaths thought to be related to the study drug(s) at any time must be reported as an SAE • All primary cardiac endpoints (symptomatic CHF and cardiac death) must be reported as an SAE • All Grade 4 laboratory abnormalities must be reported as SAEs • If the event meets the definition of 'serious', sites must submit the Serious Adverse Event Report to GSK with the exception of sites participating with the CTSU in the United States and Canada which must file an electronic report via the NCI Adverse Event Electronic Reporting System (AdEERS).
CTCAE begin date	• Events that occur in intermittent episodes must be reported on one line. The start date will be the date of the first episode and the end date will be the date of resolution. • If the exact Begin Date is not known, at a minimum record the month and year.
CTCAE end date	• Complete the end date when the AE becomes 'Resolved' or 'Resolved with sequelae' • Leave blank if the AE is 'Resolving' or 'Unresolved'
Grade (maximum)	• Record the maximum grade that occurred over the duration of the event. Refer to the SPAM for more detail. • National Cancer Institute (NCI) Common Toxicity Criteria (CTC) Version 3.0 will be used for grading of events with the exception of congestive heart failure where the NYHA classification system; NYHA classes I, II, III, and IV replaces NCI-CTCAE v3.0 Grades 1, 2, 3, and 4 respectively.
Outcome of the adverse event	Leave blank if the adverse event is not resolved. Tick 'Unresolved' or 'Resolving' only if the AE is still ongoing at time of: • Death, withdrawal of consent, recurrence of disease, lost to follow-up, or the end of the 10 year follow-up period. • EXCEPTION: where possible, cardiac, cardio-vascular or study drug-related AEs must be followed until resolution.
Action taken at time of adverse event	1) Protocol treatment(s) discontinued: Administration of investigational product(s) was permanently discontinued 2) Study Dose Reduced: Dose is reduced for one or more investigational product(s) 4) None: Investigational product(s) continues even though an adverse event has occurred 5) Protocol treatment(s) delayed (or interrupted): Administration of one or more investigational products was stopped temporarily but then restarted X) Not applicable: Subject was not receiving investigational product(s) when the event occurred. (e.g. pre- or post-dosing)
relation to study drug(s)	It is a regulatory requirement for investigators to assess relationships to investigational products based on information available. The assessment should be reviewed on receipt of any new information and amended if necessary. Indicate if there was a reasonable possibility that the event was caused by an investigational product. 'A reasonable possibility' is meant to convey that there are facts/evidence or arguments to suggest a causal relationship. Facts/evidence or arguments that may support a reasonable possibility include e.g. a temporal relationship, a pharmacologically predicted event or positive dechallenge or rechallenge. Confounding factors, such as concomitant medication, a concurrent illness or relevant medical history, should also be considered.

Adverse event (AE)

Centre No. ☐☐☐☐☐☐ Subject No. ☐☐☐☐☐☐

Adverse events (AE)

AE Name	Serious No Yes	CTCAE begin date (dd/mmm/yyyy)	CTCAE end date (dd/mmm/yyyy)	Grade (maximum) 1=Mild 2=Moderate 3=Severe 4=Life threatening 5=Death	Outcome of adverse event 1=Resolved 2=Resolving 3=Unresolved 4=Resolved with sequelae 5=Death	Action taken at time of adverse event 1=protocol treatment discontinued 2=Study dose reduced 4=None 5=protocol treatment delayed (or interrupted) X=Not applicable	Relation to study drug No Yes
	☐ ☐						☐ ☐
	☐ ☐						☐ ☐
	☐ ☐						☐ ☐
	☐ ☐						☐ ☐
	☐ ☐						☐ ☐
	☐ ☐						☐ ☐
	☐ ☐						☐ ☐
	☐ ☐						☐ ☐
	☐ ☐						☐ ☐
	☐ ☐						☐ ☐

In case of intermittent episodes, please report on one line with the start date of the first episode and the end date of the last

AE name	• Enter only the diagnosis (if known); otherwise enter sign or symptom. If a diagnosis subsequently becomes available then this must be entered instead. • Pre-exisiting conditions, which worsen during the study are to be reported as Adverse Events • Use medical terminology in English. Do not use abbreviations. • Include the anatomical site. • Recurrence of breast cancer must not be recorded as an Adverse Event. Second Primary Malignancy (SPM) must be reported as a Serious Adverse Event
Serious	• Refer to Protocol 'Definition of a Serious Adverse Event' • All deaths thought to be related to the study drug(s) at any time must be reported as an SAE • All primary cardiac endpoints (symptomatic CHF and cardiac death) must be reported as an SAE • All Grade 4 laboratory abnormalities must be reported as SAEs • If the event meets the definition of 'serious', sites must submit the Serious Adverse Event Report to GSK with the exception of sites participating with the CTSU in the United States and Canada which must file an electronic report via the NCI Adverse Event Electronic Reporting System (AdEERS).
CTCAE begin date	• Events that occur in intermittent episodes must be reported on one line. The start date will be the date of the first episode and the end date will be the date of resolution. • If the exact Begin Date is not known, at a minimum record the month and year.
CTCAE end date	• Complete the end date when the AE becomes 'Resolved' or 'Resolved with sequelae' • Leave blank if the AE is 'Resolving' or 'Unresolved'
Grade (maximum)	• Record the maximum grade that occurred over the duration of the event. Refer to the SPAM for more detail. • National Cancer Institute (NCI) Common Toxicity Criteria (CTC) Version 3.0 will be used for grading of events with the exception of congestive heart failure where the NYHA classification system; NYHA classes I, II, III, and IV replaces NCI-CTCAE v3.0 Grades 1, 2, 3, and 4 respectively.
Outcome of the adverse event	Leave blank if the adverse event is not resolved. Tick 'Unresolved' or 'Resolving' only if the AE is still ongoing at time of: • Death, withdrawal of consent, recurrence of disease, lost to follow-up, or the end of the 10 year follow-up period. • EXCEPTION: where possible, cardiac, cardio-vascular or study drug-related AEs must be followed until resolution.
Action taken at time of adverse event	1) Protocol treatment(s) discontinued: Administration of investigational product(s) was permanently discontinued 2) Study Dose Reduced: Dose is reduced for one or more investigational product(s) 4) None: Investigational product(s) continues even though an adverse event has occurred 5) Protocol treatment(s) delayed (or interrupted): Administration of one or more investigational products was stopped temporarily but then restarted X) Not applicable: Subject was not receiving investigational product(s) when the event occurred. (e.g. pre- or post-dosing)
relation to study drug(s)	It is a regulatory requirement for investigators to assess relationships to investigational products based on information available. The assessment should be reviewed on receipt of any new information and amended if necessary. Indicate if there was a reasonable possibility that the event was caused by an investigational product. 'A reasonable possibility' is meant to convey that there are facts/evidence or arguments to suggest a causal relationship. Facts/evidence or arguments that may support a reasonable possibility include e.g. a temporal relationship, a pharmacologically predicted event or positive dechallenge or rechallenge. Confounding factors, such as concomitant medication, a concurrent illness or relevant medical history, should also be considered.

Adverse event (AE)

Centre No. | | | | | | |

Subject No. | | | | | | |

Adverse events (AE)

AE Name	Serious No Yes	CTCAE begin date (dd/mmm/yyyy)	CTCAE end date (dd/mmm/yyyy)	Grade (maximum) 1=Mild 2=Moderate 3=Severe 4=Life threatening 5=Death	Outcome of adverse event 1=Resolved 2=Resolving 3=Unresolved 4=Resolved with sequelae 5=Death	Action taken at time of adverse event 1=protocol treatment discontinued 2=Study dose reduced 4=None 5=protocol treatment delayed (or interrupted) X=Not applicable	Relation to study drug No Yes
	☐ ☐						☐ ☐
	☐ ☐						☐ ☐
	☐ ☐						☐ ☐
	☐ ☐						☐ ☐
	☐ ☐						☐ ☐
	☐ ☐						☐ ☐
	☐ ☐						☐ ☐
	☐ ☐						☐ ☐
	☐ ☐						☐ ☐
	☐ ☐						☐ ☐

In case of intermittent episodes, please report on one line with the start date of the first episode and the end date of the last

AE name	• Enter only the diagnosis (if known); otherwise enter sign or symptom. If a diagnosis subsequently becomes available then this must be entered instead. • Pre-exisiting conditions, which worsen during the study are to be reported as Adverse Events • Use medical terminology in English. Do not use abbreviations. • Include the anatomical site. • Recurrence of breast cancer must not be recorded as an Adverse Event. Second Primary Malignancy (SPM) must be reported as a Serious Adverse Event
Serious	• Refer to Protocol 'Definition of a Serious Adverse Event' • All deaths thought to be related to the study drug(s) at any time must be reported as an SAE • All primary cardiac endpoints (symptomatic CHF and cardiac death) must be reported as an SAE • All Grade 4 laboratory abnormalities must be reported as SAEs • If the event meets the definition of 'serious', sites must submit the Serious Adverse Event Report to GSK with the exception of sites participating with the CTSU in the United States and Canada which must file an electronic report via the NCI Adverse Event Electronic Reporting System (AdEERS).
CTCAE begin date	• Events that occur in intermittent episodes must be reported on one line. The start date will be the date of the first episode and the end date will be the date of resolution. • If the exact Begin Date is not known, at a minimum record the month and year.
CTCAE end date	• Complete the end date when the AE becomes 'Resolved' or 'Resolved with sequelae' • Leave blank if the AE is 'Resolving' or 'Unresolved'
Grade (maximum)	• Record the maximum grade that occurred over the duration of the event. Refer to the SPAM for more detail. • National Cancer Institute (NCI) Common Toxicity Criteria (CTC) Version 3.0 will be used for grading of events with the exception of congestive heart failure where the NYHA classification system; NYHA classes I, II, III, and IV replaces NCI-CTCAE v3.0 Grades 1, 2, 3, and 4 respectively.
Outcome of the adverse event	Leave blank if the adverse event is not resolved. Tick 'Unresolved' or 'Resolving' only if the AE is still ongoing at time of: • Death, withdrawal of consent, recurrence of disease, lost to follow-up, or the end of the 10 year follow-up period. • EXCEPTION: where possible, cardiac, cardio-vascular or study drug-related AEs must be followed until resolution.
Action taken at time of adverse event	1) Protocol treatment(s) discontinued: Administration of investigational product(s) was permanently discontinued 2) Study Dose Reduced: Dose is reduced for one or more investigational product(s) 4) None: Investigational product(s) continues even though an adverse event has occurred 5) Protocol treatment(s) delayed (or interrupted): Administration of one or more investigational products was stopped temporarily but then restarted X) Not applicable: Subject was not receiving investigational product(s) when the event occurred. (e.g. pre- or post-dosing)
relation to study drug(s)	It is a regulatory requirement for investigators to assess relationships to investigational products based on information available. The assessment should be reviewed on receipt of any new information and amended if necessary. Indicate if there was a reasonable possibility that the event was caused by an investigational product. 'A reasonable possibility' is meant to convey that there are facts/evidence or arguments to suggest a causal relationship. Facts/evidence or arguments that may support a reasonable possibility include e.g. a temporal relationship, a pharmacologically predicted event or positive dechallenge or rechallenge. Confounding factors, such as concomitant medication, a concurrent illness or relevant medical history, should also be considered.

Centre No. Subject No.

Adverse events (AE)

AE Name	Serious No Yes	CTCAE begin date (dd/mmm/yyyy)	CTCAE end date (dd/mmm/yyyy)	Grade (maximum) 1=Mild 2=Moderate 3=Severe 4=Life threatening 5=Death	Outcome of adverse event 1=Resolved 2=Resolving 3=Unresolved 4=Resolved with sequelae 5=Death	Action taken at time of adverse event 1=protocol treatment discontinued 2=Study dose reduced 4=None 5=protocol treatment delayed (or interrupted) X=Not applicable	Relation to study drug No Yes
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	☐ ☐						☐ ☐

In case of intermittent episodes, please report on one line with the start date of the first episode and the end date of the last

AE name	• Enter only the diagnosis (if known); otherwise enter sign or symptom. If a diagnosis subsequently becomes available then this must be entered instead. • Pre-exisiting conditions, which worsen during the study are to be reported as Adverse Events • Use medical terminology in English. Do not use abbreviations. • Include the anatomical site. • Recurrence of breast cancer must not be recorded as an Adverse Event. Second Primary Malignancy (SPM) must be reported as a Serious Adverse Event
Serious	• Refer to Protocol 'Definition of a Serious Adverse Event' • All deaths thought to be related to the study drug(s) at any time must be reported as an SAE • All primary cardiac endpoints (symptomatic CHF and cardiac death) must be reported as an SAE • All Grade 4 laboratory abnormalities must be reported as SAEs • If the event meets the definition of 'serious', sites must submit the Serious Adverse Event Report to GSK with the exception of sites participating with the CTSU in the United States and Canada which must file an electronic report via the NCI Adverse Event Electronic Reporting System (AdEERS).
CTCAE begin date	• Events that occur in intermittent episodes must be reported on one line. The start date will be the date of the first episode and the end date will be the date of resolution. • If the exact Begin Date is not known, at a minimum record the month and year.
CTCAE end date	• Complete the end date when the AE becomes 'Resolved' or 'Resolved with sequelae' • Leave blank if the AE is 'Resolving' or 'Unresolved'
Grade (maximum)	• Record the maximum grade that occurred over the duration of the event. Refer to the SPAM for more detail. • National Cancer Institute (NCI) Common Toxicity Criteria (CTC) Version 3.0 will be used for grading of events with the exception of congestive heart failure where the NYHA classification system; NYHA classes I, II, III, and IV replaces NCI-CTCAE v3.0 Grades 1, 2, 3, and 4 respectively.
Outcome of the adverse event	Leave blank if the adverse event is not resolved. Tick 'Unresolved' or 'Resolving' only if the AE is still ongoing at time of: • Death, withdrawal of consent, recurrence of disease, lost to follow-up, or the end of the 10 year follow-up period. • EXCEPTION: where possible, cardiac, cardio-vascular or study drug-related AEs must be followed until resolution.
Action taken at time of adverse event	1) Protocol treatment(s) discontinued: Administration of investigational product(s) was permanently discontinued 2) Study Dose Reduced: Dose is reduced for one or more investigational product(s) 4) None: Investigational product(s) continues even though an adverse event has occurred 5) Protocol treatment(s) delayed (or interrupted): Administration of one or more investigational products was stopped temporarily but then restarted X) Not applicable: Subject was not receiving investigational product(s) when the event occurred. (e.g. pre- or post-dosing)
relation to study drug(s)	It is a regulatory requirement for investigators to assess relationships to investigational products based on information available. The assessment should be reviewed on receipt of any new information and amended if necessary. Indicate if there was a reasonable possibility that the event was caused by an investigational product. 'A reasonable possibility' is meant to convey that there are facts/evidence or arguments to suggest a causal relationship. Facts/evidence or arguments that may support a reasonable possibility include e.g. a temporal relationship, a pharmacologically predicted event or positive dechallenge or rechallenge. Confounding factors, such as concomitant medication, a concurrent illness or relevant medical history, should also be considered.

Centre No. | | | | | | | Subject No. | | | | | | |

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Centre No. ☐☐☐☐☐☐ Subject No. ☐☐☐☐☐☐

Adverse events (AE)

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Adverse event (AE)

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	☐ ☐						☐ ☐

In case of intermittent episodes, please report on one line with the start date of the first episode and the end date of the last

Centre No. | | | | | | |

Subject No. | | | | | | |

EKG

Date of EKG DD MMM YYYY

Result

☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant → *Please complete the "Adverse event" page*

EKG

Date of EKG DD MMM YYYY

Result

☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant → *Please complete the "Adverse event" page*

EKG

Date of EKG DD MMM YYYY

Result

☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant → *Please complete the "Adverse event" page*

Centre No. | | | | | | |

Subject No. | | | | | | |

EKG

Date of EKG DD MMM YYYY

Result

- ☐ Normal
- ☐ Abnormal - Not clinically significant
- ☐ Abnormal - Clinically significant → *Please complete the "Adverse event" page*

EKG

Date of EKG DD MMM YYYY

Result

- ☐ Normal
- ☐ Abnormal - Not clinically significant
- ☐ Abnormal - Clinically significant → *Please complete the "Adverse event" page*

EKG

Date of EKG DD MMM YYYY

Result

- ☐ Normal
- ☐ Abnormal - Not clinically significant
- ☐ Abnormal - Clinically significant → *Please complete the "Adverse event" page*

New York Heart Association (NYHA) Functional Classification
NOTE: If the patient does not have congestive heart failure (CHF), leave this field blank.

Class I. Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain.

Class II. Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.

Class III. Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.

Class IV. Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

Centre No. | | | | | | |

Subject No. | | | | | | |

LVEF

Date of LVEF ☐☐ ☐☐☐ ☐☐☐☐
DD MMM YYYY

LVEF (patient value) ☐☐.☐ % Method of Evaluation ☐ Echocardiogram ☐ MUGA scan

☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant → *Please complete the "Adverse event" page.*

Symptomatic CHF ☐ No ☐ Yes → *Specify below*

NYHA classification **(complete only in case of CHF)** ☐ Class I *(in case of asymptomatic CHF, tick No for the question above)* ☐ Class II ☐ Class III ☐ Class IV

LVEF

Date of LVEF ☐☐ ☐☐☐ ☐☐☐☐
DD MMM YYYY

LVEF (patient value) ☐☐.☐ % Method of Evaluation ☐ Echocardiogram ☐ MUGA scan

☐ Normal
☐ Abnormal - Not clinically significant
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Symptomatic CHF ☐ No ☐ Yes → *Specify below*

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LVEF

Date of LVEF ☐☐ ☐☐☐ ☐☐☐☐ (DD MMM YYYY)

LVEF (patient value) ☐☐.☐ % Method of Evaluation ☐ Echocardiogram ☐ MUGA scan

☐ Normal
☐ Abnormal - Not clinically significant
☐ Abnormal - Clinically significant → *Please complete the "Adverse event" page.*

Symptomatic CHF ☐ No ☐ Yes → *Specify below*

NYHA classification **(complete only in case of CHF)** ☐ Class I *(in case of asymptomatic CHF, tick No for the question above)* ☐ Class II ☐ Class III ☐ Class IV

LVEF

Date of LVEF ☐☐ ☐☐☐ ☐☐☐☐ (DD MMM YYYY)

LVEF (patient value) ☐☐.☐ % Method of Evaluation ☐ Echocardiogram ☐ MUGA scan

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☐ Abnormal - Not clinically significant
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Symptomatic CHF ☐ No ☐ Yes → *Specify below*

NYHA classification **(complete only in case of CHF)** ☐ Class I *(in case of asymptomatic CHF, tick No for the question above)* ☐ Class II ☐ Class III ☐ Class IV

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☐ Normal
☐ Abnormal - Not clinically significant
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Symptomatic CHF ☐ No ☐ Yes → *Specify below*

NYHA classification **(complete only in case of CHF)** ☐ Class I *(in case of asymptomatic CHF, tick No for the question above)* ☐ Class II ☐ Class III ☐ Class IV

LVEF

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Symptomatic CHF ☐ No ☐ Yes → *Specify below*

NYHA classification **(complete only in case of CHF)** ☐ Class I *(in case of asymptomatic CHF, tick No for the question above)* ☐ Class II ☐ Class III ☐ Class IV

Anatomical site	Description
AB	Abdomen/abdominal wall
AD	Adrenals
BE	Bone
BR	Bladder
BT	Breast
CL	Colon
CR	Colorectal
CS	CNS (brain)
CW	Chest
CX	Cervix
EO	Esophagus/Oesophagus
HN	Head and neck
HT	Heart
K	Kidney
LG	Lung
LN	Lymph nodes

Anatomical site	Description
LV	Liver
OC	Oral cavity
OT	Other
OV	Ovary
PA	Pleura
PM	Peritoneum
PR	Prostate
PS	Pancreas
PV	Pelvis
RC	Rectum
SH	Stomach
SI	Small intestine
SK	Skin
SP	Spleen
TD	Thyroid
WB	Whole body

Unscheduled radiological exams

Centre No. ☐☐☐☐☐☐ Subject No. ☐☐☐☐☐☐

Type of radiological examination*	Anatomical site**	Side (L or R)	Date of test	Are there any **clinically significant** abnormalities? *(Please report a short description)*
__|__	__|__	__	DD MMM YYYY	☐ No ☐ Yes → Specify ________
__|__	__|__	__	DD MMM YYYY	☐ No ☐ Yes → Specify ________
__|__	__|__	__	DD MMM YYYY	☐ No ☐ Yes → Specify ________
__|__	__|__	__	DD MMM YYYY	☐ No ☐ Yes → Specify ________
__|__	__|__	__	DD MMM YYYY	☐ No ☐ Yes → Specify ________
__|__	__|__	__	DD MMM YYYY	☐ No ☐ Yes → Specify ________

* BS=Bone scan (scintigraphy); C=CT scan; E=Endoscopy; L=Lymphangiogram; M=MRI; MA=Mammography; NS=Nuclear scan; PC=PET/CT Scan; PT=PET scan; TU=Transvaginal ultrasound; UL=Ultrasound (echography); XR=X-ray

** See facing page for anatomical site codes

Anatomical site	Description
AB	Abdomen/abdominal wall
AD	Adrenals
BE	Bone
BR	Bladder
BT	Breast
CL	Colon
CR	Colorectal
CS	CNS (brain)
CW	Chest
CX	Cervix
EO	Esophagus/Oesophagus
HN	Head and neck
HT	Heart
K	Kidney
LG	Lung
LN	Lymph nodes

Anatomical site	Description
LV	Liver
OC	Oral cavity
OT	Other
OV	Ovary
PA	Pleura
PM	Peritoneum
PR	Prostate
PS	Pancreas
PV	Pelvis
RC	Rectum
SH	Stomach
SI	Small intestine
SK	Skin
SP	Spleen
TD	Thyroid
WB	Whole body

Unscheduled radiological exams

Centre No. Subject No.

Type of radiological examination*	Anatomical site**	Side (L or R)	Date of test	Are there any clinically significant abnormalities? *(Please report a short description)*
			DD MMM YYYY	☐ No ☐ Yes → Specify ______
			DD MMM YYYY	☐ No ☐ Yes → Specify ______
			DD MMM YYYY	☐ No ☐ Yes → Specify ______
			DD MMM YYYY	☐ No ☐ Yes → Specify ______
			DD MMM YYYY	☐ No ☐ Yes → Specify ______
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** See facing page for anatomical site codes

Anatomical site	Description
AB	Abdomen/abdominal wall
AD	Adrenals
BE	Bone
BR	Bladder
BT	Breast
CL	Colon
CR	Colorectal
CS	CNS (brain)
CW	Chest
CX	Cervix
EO	Esophagus/Oesophagus
HN	Head and neck
HT	Heart
K	Kidney
LG	Lung
LN	Lymph nodes

Anatomical site	Description
LV	Liver
OC	Oral cavity
OT	Other
OV	Ovary
PA	Pleura
PM	Peritoneum
PR	Prostate
PS	Pancreas
PV	Pelvis
RC	Rectum
SH	Stomach
SI	Small intestine
SK	Skin
SP	Spleen
TD	Thyroid
WB	Whole body

Unscheduled radiological exams

Centre No. | | | | | |

Subject No. | | | | | |

Type of radiological examination*	Anatomical site**	Side (L or R)	Date of test	Are there any <u>clinically significant</u> abnormalities? *(Please report a short description)*
|_|_|	|_|_|	|_|	DD MMM YYYY	☐ No ☐ Yes → Specify ________
|_|_|	|_|_|	|_|	DD MMM YYYY	☐ No ☐ Yes → Specify ________
|_|_|	|_|_|	|_|	DD MMM YYYY	☐ No ☐ Yes → Specify ________
|_|_|	|_|_|	|_|	DD MMM YYYY	☐ No ☐ Yes → Specify ________
|_|_|	|_|_|	|_|	DD MMM YYYY	☐ No ☐ Yes → Specify ________
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Unscheduled radiological exams

Centre No. | | | | | |

Subject No. | | | | | |

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__|__	__|__	__	DD MMM YYYY	☐ No ☐ Yes → Specify ________
__|__	__|__	__	DD MMM YYYY	☐ No ☐ Yes → Specify ________
__|__	__|__	__	DD MMM YYYY	☐ No ☐ Yes → Specify ________
__|__	__|__	__	DD MMM YYYY	☐ No ☐ Yes → Specify ________
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Unscheduled radiological exams

Centre No. ☐☐☐☐☐☐ Subject No. ☐☐☐☐☐☐

Type of radiological examination*	Anatomical site**	Side (L or R)	Date of test	Are there any <u>clinically significant</u> abnormalities? *(Please report a short description)*
☐☐	☐☐	☐	DD MMM YYYY	☐ No ☐ Yes → Specify ____
☐☐	☐☐	☐	DD MMM YYYY	☐ No ☐ Yes → Specify ____
☐☐	☐☐	☐	DD MMM YYYY	☐ No ☐ Yes → Specify ____
☐☐	☐☐	☐	DD MMM YYYY	☐ No ☐ Yes → Specify ____
☐☐	☐☐	☐	DD MMM YYYY	☐ No ☐ Yes → Specify ____
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** See facing page for anatomical site codes

Centre No. | | | | | | |

Subject No. | | | | | | |

Adjuvant Treatment completion*

Did the patient complete Lapatinib (**L**) as per protocol?

☐ Yes
☐ No → Specify below
☐ NA

Did the patient complete Trastuzumab (**T**) as per protocol?

☐ Yes
☐ No → Specify below
☐ NA

Did the patient complete FEC as per protocol?

☐ Yes
☐ No → Specify below
☐ NA

Reasons for treatment discontinuation	L	T	FEC**	
Adverse event	☐	☐	☐ →	*Complete "Adverse event" page*
Protocol violation	☐	☐	☐	
Subject decided to withdraw from investigational product but is continuing to be followed per protocol	☐	☐	☐	
Subject decided to withdraw from the study	☐	☐	☐	
Recurrence of disease or second primary malignancy (SPM) or contalateral breast cancer (CBC)	☐	☐	☐ →	*Complete "Recurrence of disease" or "SPM"-"CBC" page*
Death	☐	☐	☐ →	*Complete "Death" page*
Lost to follow-up	☐	☐	☐	

Date of last study drug administration: DD MMM YYYY

*"No" should only be ticked for 'Did the patient complete [therapy] as per protocol?', if the study drug was permanently discontinued earlier than the protocol specified treatment duration.

**L= Lapatinib; T=Trastuzumab; FEC

Centre No. | | | | | | |

Subject No. | | | | | | |

Additional comments and Investigator's signature

(Please add here any comment you might have regarding the data up to the treatment completion)

CRF page number	Comments

All data entered in this case report form have been entered under my authority and to the best of my knowledge are accurate and complete.

Investigator's signature _____ *(Medically-qualified sub-investigator is allowed to sign the CRF, as long as he/she is listed on the form 1572)*

Date _____
DD MMM YYYY

Please date and sign <u>ONLY</u> after request from data management

Guidelines for reporting of recurrence, second primary malignancy and contralateral breast cancer. Record the following:

1. the first event defining disease-free survival (local, regional or distant recurrence of invasive breast cancer, contralateral breast cancer, second non-breast malignancy, or death without prior cancer event),
2. the first distant breast cancer recurrence occurring at any time,
3. the first central nervous system (CNS) breast cancer recurrence occurring at any time,
4. the second primary malignancies occurring at any time and complete the adverse event form.

NOTE: Ductal carcinoma in situ (DCIS), lobular carcinoma in situ of the breast (LCIS) and myelodisplastic syndrome (MDS) are not considered recurrence events.

Recurrence of disease

Type of recurrence	Recurrence date (dd/mmm/yyyy)	Method of evaluation* C	Method of evaluation* R	Biopsy No	Biopsy Yes	Biopsy date	Histology type
Local recurrence							
Breast surgical scar		☐	☐	☐	☐		
Ipsilateral breast		☐	☐	☐	☐		
Ipsilateral anterior chest wall		☐	☐	☐	☐		
Skin or soft tissue within the local area		☐	☐	☐	☐		
Regional recurrence							
Ipsilateral axillary		☐	☐	☐	☐		
Infraclavicular		☐	☐	☐	☐		
Internal mammary		☐	☐	☐	☐		
Skin or soft tissue within the regional area		☐	☐	☐	☐		

*Method: C=clinical; R=radiological (please report the radiological test in appropriate “Radiological examination” page, either the applicable visit page or the “Unscheduled radiological exams” page)

Guidelines for reporting of recurrence, second primary malignancy and contralateral breast cancer. Record the following:

1. the first event defining disease-free survival (local, regional or distant recurrence of invasive breast cancer, contralateral breast cancer, second non-breast malignancy, or death without prior cancer event),
2. the first distant breast cancer recurrence occurring at any time,
3. the first central nervous system (CNS) breast cancer recurrence occurring at any time,
4. the second primary malignancies occurring at any time and complete the adverse event form.

NOTE: Ductal carcinoma in situ (DCIS), lobular carcinoma in situ of the breast (LCIS) and myelodisplastic syndrome (MDS) are not considered recurrence events.

Recurrence of disease

Type of recurrence	Recurrence date (dd/mmm/yyyy)	Method of evaluation* C	Method of evaluation* R	Biopsy No	Biopsy Yes	Biopsy date	Histology type
Distant recurrence *(Report the first distant recurrence at any time)*							
Skin or lymph nodes other than specified on local / regional recurrence page		☐	☐	☐	☐		
Bone		☐	☐	☐	☐		
Lung		☐	☐	☐	☐		
Liver		☐	☐	☐	☐		
Pleural effusion		☐	☐	☐	☐		
Other distant site, specify _____		☐	☐	☐	☐		
Other distant site, specify _____		☐	☐	☐	☐		
Central nervous system *(report at any time)*		☐	☐	☐	☐		
Brain metastasis ☐							
Meningitis carcinomatosa ☐							

*Method: C=clinical; R=radiological (please report the radiological test in appropriate “Radiological examination” page, either the applicable visit page or the “Unscheduled radiological exams” page)

Guidelines for reporting of recurrence, second primary malignancy and contralateral breast cancer. Record the following:

1. the first event defining disease-free survival (local, regional or distant recurrence of invasive breast cancer, contralateral breast cancer, second non-breast malignancy, or death without prior cancer event),
2. the first distant breast cancer recurrence occurring at any time,
3. the first central nervous system (CNS) breast cancer recurrence occurring at any time,
4. the second primary malignancies occurring at any time and complete the adverse event form.

NOTE: Ductal carcinoma in situ (DCIS), lobular carcinoma in situ of the breast (LCIS) and myelodisplastic syndrome (MDS) are not considered recurrence events.

Second primary malignancy *(Report <u>all</u> second primary malignancies at any time they occur)* **and contralateral breast cancer**

Type of recurrence	Recurrence date (dd/mmm/yyyy)	Method of evaluation* C	R	Biopsy No	Yes	Biopsy date	Histology type
<u>Contralateral breast cancer</u>		☐	☐	☐	☐		
<u>Second primary malignancy</u> *(with the exception of contralateral breast cancer which should always be reported above) (report at any time)*							
		☐	☐	☐	☐		
		☐	☐	☐	☐		
		☐	☐	☐	☐		

*Method: C=clinical; R=radiological (please report the radiological test in appropriate “Radiological examination” page, either the applicable visit page or the “Unscheduled radiological exams” page)

Centre No. | | | | | | |

Subject No. | | | | | | |

Additional therapy for breast cancer recurrence or second primary or contralateral BC malignancy *(Please report only the first line of treatment, except for additional targeted therapies that should be reported at any time.)*

Chemotherapy

Did the patient receive additional chemotherapy after recurrence of breast cancer or second primary malignacy or contralateral BC?

☐ No ☐ Yes → *Specify below*

Agent name	Total no. of cycles	Initial dose	Units	Date started (dd/mmm/yyyy)	Date stopped (dd/mmm/yyyy)
Doxorubicin			mg/m²		
Epirubicin			mg/m²		
Paclitaxel			mg/m²		
Docetaxel			mg/m²		
Capecitabine			mg/m²		

Targeted therapy *(report at any time)*

Did the patient receive additional targeted therapy after recurrence of breast cancer or second primary malignancy or contralateral BC?

☐ No ☐ Yes → *Specify below*

Agent name	Total no. of cycles	Dose	Units	Date started (dd/mmm/yyyy)	Date stopped (dd/mmm/yyyy)
Lapatinib	NA		mg/24Hr		
Trastuzumab*			mg/kg		

** Report maintenance dose (2 mg/kg or 6 mg/kg)*

Centre No. | | | | | | |

Subject No. | | | | | | |

Additional therapy for breast cancer relapse or second primary malignancy *(cont.)*

Hormone therapy Did the patient receive additional hormone therapy after recurrence of breast cancer or second primary malignancy or contralateral BC?

☐ No ☐ Yes → *Specify below*

Agent name	Dose	Units	Date started (dd/mmm/yyyy)	Date stopped (dd/mmm/yyyy)
Tamoxifen		mg		
Anastrozole		mg		
Letrozole		mg		
Exemestane		mg		
Goserelin		mg		
Other LH-RH analogue: _____		mg		NA
Bilateral ovariectomy/oopherectomy	NA	NA		NA

Radiotherapy Did the patient receive additional radiotherapy after recurrence of breast cancer or second primary malignancy or contralateral BC?

☐ No ☐ Yes → *Specify below*

Radiotherapy site	Side left	Side right	Total dose	Units 1=Gy 2=cGy 3=Rads	Radiation Therapy Start Date (dd/mmm/yyyy)	Radiation Therapy End Date (dd/mmm/yyyy)
	☐	☐				
	☐	☐				
	☐	☐				
	☐	☐				

Surgery Did the patient receive additional cancer related surgery after recurrence of breast cancer or second primary malignancy or contralateral BC?

☐ No ☐ Yes → *Specify below*

Surgery site	Surgery date (dd/mmm/yyyy)

Centre No. | | | | | | |

Subject No. | | | | | | |

Additional comments

(Please add here any comment you might have regarding the data reported after treatment completion)

CRF page number	Comments

Centre No. | | | | | | |

Subject No. | | | | | | |

Patient status

To be completed on a yearly basis, starting one year after the first recurrence of disease.

☐ Alive → *If the patient has developed the first distant recurrence, a CNS recurrence or a new primary malignancy, please update the "Recurrence of disease" or the "Second primary malignancy and contralateral BC" page.*

☐ Death → *Please complete "Death" page.*

☐ Lost to Follow-up

☐ Subject decided to withdraw study consent.

Date of last contact or death DD MMM YYYY

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Investigator's signature _____ *(A medically qualified sub-investigator is allowed to sign the CRF if he/she is listed on the form FDA 1572)*

Date DD MMM YYYY

(Please sign and date only after request from data management)

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- ☐ Lost to Follow-up
- ☐ Subject decided to withdraw study consent.

Date of last contact or death |__|__|__|__|__|__|__|__|__|
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Date of last contact or death |_|_|_|_|_|_|_|_|_| DD MMM YYYY

(For patients "Lost to Follow-up" or that "withdrew study consent", the date of last contact should also be the last date the patient was known to be alive.
The last date the patient was known to be alive could either be the same as the previous reported visit date or any date between the previous visit and this one.)

All data entered in this case report form have been entered under my authority and to the best of my knowledge are accurate and complete.

Investigator's signature ________________________________ *(A medically qualified sub-investigator is allowed to sign the CRF if he/she is listed on the form FDA 1572)*

Date |_|_|_|_|_|_|_|_|_| DD MMM YYYY

(Please sign and date only after request from data management)

Centre No. | | | | | |

Subject No. | | | | | |

Patient status

To be completed on a yearly basis, starting one year after the first recurrence of disease.

- ☐ Alive → *If the patient has developed the first distant recurrence, a CNS recurrence or a new primary malignancy since the last "Survival follow-up" page was completed, please update the "Recurrence of disease" or the "Second primary malignancy and contralateral BC" page.*
- ☐ Death → *Please complete "Death" page.*
- ☐ Lost to Follow-up
- ☐ Subject decided to withdraw study consent.

Date of last contact or death |__|__|__|__|__|__|__|__|__|
DD MMM YYYY

(For patients "Lost to Follow-up" or that "withdrew study consent", the date of last contact should also be the last date the patient was known to be alive.
The last date the patient was known to be alive could either be the same as the previous reported visit date or any date between the previous visit and this one.)

All data entered in this case report form have been entered under my authority and to the best of my knowledge are accurate and complete.

Investigator's signature ______________________________ *(A medically qualified sub-investigator is allowed to sign the CRF if he/she is listed on the form FDA 1572)*

Date |__|__|__|__|__|__|__|__|__|
DD MMM YYYY

(Please sign and date only after request from data management)

Centre No. | | | | | |

Subject No. | | | | | |

Patient status

To be completed on a yearly basis, starting one year after the first recurrence of disease.

☐ Alive → *If the patient has developed the first distant recurrence, a CNS recurrence or a new primary malignancy since the last "Survival follow-up" page was completed, please update the "Recurrence of disease" or the "Second primary malignancy and contralateral BC" page.*

☐ Death → *Please complete "Death" page.*

☐ Lost to Follow-up

☐ Subject decided to withdraw study consent.

Date of last contact or death |_|_|_|_|_|_|_|_|_|
DD MMM YYYY

*(For patients "Lost to Follow-up" or that "withdrew study consent", the date of last contact should also be the last date the patient was known to be alive.
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Date |_|_|_|_|_|_|_|_|_|
DD MMM YYYY

(Please sign and date only after request from data management)

Centre No. | | | | | | |

Subject No. | | | | | | |

Patient status

To be completed on a yearly basis, starting one year after the first recurrence of disease.

☐ Alive → *If the patient has developed the first distant recurrence, a CNS recurrence or a new primary malignancy since the last "Survival follow-up" page was completed, please update the "Recurrence of disease" or the "Second primary malignancy and contralateral BC" page.*

☐ Death → *Please complete "Death" page.*

☐ Lost to Follow-up

☐ Subject decided to withdraw study consent.

Date of last contact or death ___ ___ ___
DD MMM YYYY

(For patients "Lost to Follow-up" or that "withdrew study consent", the date of last contact should also be the last date the patient was known to be alive.
The last date the patient was known to be alive could either be the same as the previous reported visit date or any date between the previous visit and this one.)

All data entered in this case report form have been entered under my authority and to the best of my knowledge are accurate and complete.

Investigator's signature _____ *(A medically qualified sub-investigator is allowed to sign the CRF if he/she is listed on the form FDA 1572)*

Date ___ ___ ___
DD MMM YYYY

(Please sign and date only after request from data management)

Centre No. | | | | | | Subject No. | | | | | |

Patient status

To be completed on a yearly basis, starting one year after the first recurrence of disease.

☐ Alive → *If the patient has developed the first distant recurrence, a CNS recurrence or a new primary malignancy since the last "Survival follow-up" page was completed, please update the "Recurrence of disease" or the "Second primary malignancy and contralateral BC" page.*

☐ Death → *Please complete "Death" page.*

☐ Lost to Follow-up

☐ Subject decided to withdraw study consent.

Date of last contact or death |_|_|_|_|_|_|_|_|_|
DD MMM YYYY

(For patients "Lost to Follow-up" or that "withdrew study consent", the date of last contact should also be the last date the patient was known to be alive.
The last date the patient was known to be alive could either be the same as the previous reported visit date or any date between the previous visit and this one.)

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Investigator's signature ______________________________ *(A medically qualified sub-investigator is allowed to sign the CRF if he/she is listed on the form FDA 1572)*

Date |_|_|_|_|_|_|_|_|_|
DD MMM YYYY

(Please sign and date only after request from data management)

Centre No. | | | | | | |

Subject No. | | | | | | |

Death

Date of death ____ ____ ____
DD MMM YYYY

Every effort should be made to exercise diligence in reporting the complete date of death. Overall survival is an important study endpoint.

Primary cause of death *(check one)*

- ☐ Breast cancer progression
- ☐ Adverse event during study
- ☐ Adverse event during treatment given after recurrence
- ☐ Malignant disease other than breast cancer
- ☐ Other, specify: _____

Was autopsy performed?
- ☐ Unknown
- ☐ No
- ☐ Yes → *Please summarize findings:*

_____

_____

_____

_____

Centre No. | | | | | | |

Subject No. | | | | | | |

Additional signature page

Please complete this page only when instructed by data management

All data entered in the case report form pages listed below have been entered under my authority and to the best of my knowledge are accurate and complete.

Visit up to and including: Week _____ or Month _____ or Year _____

(Please complete only the applicable)

Non-visit forms	*Pages (tick all used pages)*
Hormonotherapy	*110* ☐
Radiotherapy	*111* ☐
Concomitant treatments	*112* ☐ *113* ☐ *114* ☐
Administration of study drug: Paclitaxel	*115* ☐ *116* ☐
Administration of FEC adjuvant treatment	*117* ☐ *118* ☐
Administration of study drug: Lapatinib	*119* ☐
Investigational product compliance	*120* ☐
Administration of study drug: Trastuzumab	*121* ☐ *122* ☐ *123* ☐ *124* ☐ *125* ☐
Adverse event	*126* ☐ *127* ☐ *128* ☐ *129* ☐ *130* ☐ *131* ☐ *132* ☐
Unscheduled EKG	*133* ☐ *134* ☐
Unscheduled LVEF	*135* ☐ *136* ☐ *137* ☐
Unscheduled radiological exams	*138* ☐ *139* ☐ *140* ☐ *141* ☐ *142* ☐
Adjuvant treatment completion	*143* ☐
Adjuvant treatment completion	*144* ☐
Recurrence of disease: local/regional	*145* ☐
Recurrence of disease: distant	*146* ☐
Second primary malignancy and CBC	*147* ☐
Post event treatments	*148* ☐ *149* ☐
Additional comments	*150* ☐
Death	*166* ☐
Liver function tests	*170* ☐ *171* ☐ 172 ☐ 173 ☐ 174 ☐ 175 ☐ 176 ☐
Liver function tests	*177* ☐ *178* ☐ 179 ☐ 180 ☐ 181 ☐ 182 ☐ 183 ☐
Liver function tests	*184* ☐ *185* ☐ 186 ☐ 187 ☐ 188 ☐ 189 ☐ 190 ☐
Liver function tests	*191* ☐ *192* ☐ 193 ☐ 194 ☐ 195 ☐ 196 ☐ 197 ☐
Liver function tests	*198* ☐
Unscheduled liver function tests	*199* ☐ *200* ☐ 201 ☐ 202 ☐ 203 ☐ 204 ☐
Additional pages, if any:	

Investigator's signature _____ Date DD MMM YYYY

(A medically qualified sub-investigator is allowed to sign the CRF if he/she is listed on the form FDA 1572)

Centre No. | | | | | | |

Subject No. | | | | | | |

Additional signature page

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(Please complete only the applicable)

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Concomitant treatments	*112* ☐ *113* ☐ *114* ☐
Administration of study drug: Paclitaxel	*115* ☐ *116* ☐
Administration of FEC adjuvant treatment	*117* ☐ *118* ☐
Administration of study drug: Lapatinib	*119* ☐
Investigational product compliance	*120* ☐
Administration of study drug: Trastuzumab	*121* ☐ *122* ☐ *123* ☐ *124* ☐ *125* ☐
Adverse event	*126* ☐ *127* ☐ *128* ☐ *129* ☐ *130* ☐ *131* ☐ *132* ☐
Unscheduled EKG	*133* ☐ *134* ☐
Unscheduled LVEF	*135* ☐ *136* ☐ *137* ☐
Unscheduled radiological exams	*138* ☐ *139* ☐ *140* ☐ *141* ☐ *142* ☐
Adjuvant treatment completion	*143* ☐
Adjuvant treatment completion	*144* ☐
Recurrence of disease: local/regional	*145* ☐
Recurrence of disease: distant	*146* ☐
Second primary malignancy and CBC	*147* ☐
Post event treatments	*148* ☐ *149* ☐
Additional comments	*150* ☐
Death	*166* ☐
Liver function tests	*170* ☐ *171* ☐ 172 ☐ 173 ☐ 174 ☐ 175 ☐ 176 ☐
Liver function tests	*177* ☐ *178* ☐ 179 ☐ 180 ☐ 181 ☐ 182 ☐ 183 ☐
Liver function tests	*184* ☐ *185* ☐ 186 ☐ 187 ☐ 188 ☐ 189 ☐ 190 ☐
Liver function tests	*191* ☐ *192* ☐ 193 ☐ 194 ☐ 195 ☐ 196 ☐ 197 ☐
Liver function tests	*198* ☐
Unscheduled liver function tests	*199* ☐ *200* ☐ 201 ☐ 202 ☐ 203 ☐ 204 ☐
Additional pages, if any:	

Investigator's signature _____ Date DD MMM YYYY

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Centre No. | | | | | | |

Subject No. | | | | | | |

Additional signature page

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All data entered in the case report form pages listed below have been entered under my authority and to the best of my knowledge are accurate and complete.

Visit up to and including: Week _____ or Month _____ or Year _____

(Please complete only the applicable)

Non-visit forms	*Pages (tick all used pages)*
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Administration of study drug: Paclitaxel	*115* ☐ *116* ☐
Administration of FEC adjuvant treatment	*117* ☐ *118* ☐
Administration of study drug: Lapatinib	*119* ☐
Investigational product compliance	*120* ☐
Administration of study drug: Trastuzumab	*121* ☐ *122* ☐ *123* ☐ *124* ☐ *125* ☐
Adverse event	*126* ☐ *127* ☐ *128* ☐ *129* ☐ *130* ☐ *131* ☐ *132* ☐
Unscheduled EKG	*133* ☐ *134* ☐
Unscheduled LVEF	*135* ☐ *136* ☐ *137* ☐
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Post event treatments	*148* ☐ *149* ☐
Additional comments	*150* ☐
Death	*166* ☐
Liver function tests	*170* ☐ *171* ☐ 172 ☐ 173 ☐ 174 ☐ 175 ☐ 176 ☐
Liver function tests	*177* ☐ *178* ☐ 179 ☐ 180 ☐ 181 ☐ 182 ☐ 183 ☐
Liver function tests	*184* ☐ *185* ☐ 186 ☐ 187 ☐ 188 ☐ 189 ☐ 190 ☐
Liver function tests	*191* ☐ *192* ☐ 193 ☐ 194 ☐ 195 ☐ 196 ☐ 197 ☐
Liver function tests	*198* ☐
Unscheduled liver function tests	*199* ☐ *200* ☐ 201 ☐ 202 ☐ 203 ☐ 204 ☐
Additional pages, if any:	

Investigator's signature _____ Date | | | | | | | | |

DD MMM YYYY

(A medically qualified sub-investigator is allowed to sign the CRF if he/she is listed on the form FDA 1572)

Centre No. | | | | | | |

Subject No. | | | | | | |

Screening Sample collection date ___ ___ ___ (DD MMM YYYY)

	Result (use dot "." as decimal separator)	**Unit**	**Unit if other unit used**	**Normal range*** Min	Max
SGOT (ASAT)		U/l			
SGPT (ALAT)		U/l			
Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

** Please report the normal range as listed on the laboratory results*

Please check the blood tests and report any clinically significant abnormality on the "**Previous or current diseases other than primary breast cancer and cardiovascular diseases** " page 13.

Centre No. | | | | | | |

Subject No. | | | | | | |

Week 4 Sample collection date ___ ___ ___ (DD MMM YYYY)

	Result (use dot "." as decimal separator)	**Unit**	**Unit if other unit used**	**Normal range*** Min	Max
SGOT (ASAT)		U/l			
SGPT (ALAT)		U/l			
Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

** Please report the normal range as listed on the laboratory results*

Please check the blood tests and report any clinically significant abnormality on the "**Adverse event**" page.

Centre No. | | | | | | |

Subject No. | | | | | | |

Week 6 Sample collection date ___ ___ ___ (DD MMM YYYY)

	Result (use dot "." as decimal separator)	**Unit**	**Unit if other unit used**	**Normal range*** Min	Max
SGOT (ASAT)		U/l			
SGPT (ALAT)		U/l			
Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

** Please report the normal range as listed on the laboratory results*

Please check the blood tests and report any clinically significant abnormality on the "**Adverse event**" page.

Centre No. | | | | | | |

Subject No. | | | | | | |

Week 10 Sample collection date ___ ___ ___ (DD MMM YYYY)

	Result (use dot "." as decimal separator)	**Unit**	**Unit if other unit used**	**Normal range*** Min	Max
SGOT (ASAT)		U/l			
SGPT (ALAT)		U/l			
Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

** Please report the normal range as listed on the laboratory results*

Please check the blood tests and report any clinically significant abnormality on the "**Adverse event**" page.

Centre No. | | | | | | |

Subject No. | | | | | | |

Week 13 Sample collection date ___ ___ ___ (DD MMM YYYY)

	Result (use dot "." as decimal separator)	**Unit**	**Unit if other unit used**	**Normal range*** Min	Max
SGOT (ASAT)		U/l			
SGPT (ALAT)		U/l			
Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

** Please report the normal range as listed on the laboratory results*

Please check the blood tests and report any clinically significant abnormality on the "**Adverse event**" page.

Centre No. | | | | | | |

Subject No. | | | | | | |

Week 16 Sample collection date ___ ___ ___ (DD MMM YYYY)

	Result (use dot "." as decimal separator)	**Unit**	**Unit if other unit used**	**Normal range*** Min	Max
SGOT (ASAT)		U/l			
SGPT (ALAT)		U/l			
Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

** Please report the normal range as listed on the laboratory results*

Please check the blood tests and report any clinically significant abnormality on the "**Adverse event**" page.

Centre No. | | | | | | |

Subject No. | | | | | | |

Pre-surgery visit

Sample collection date ___ ___ / ___ ___ ___ / ___ ___ ___ ___
DD MMM YYYY

	Result (use dot "." as decimal separator)	Unit	Unit if other unit used	Normal range* Min	Max
SGOT (ASAT)		U/l			
SGPT (ALAT)		U/l			
Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

** Please report the normal range as listed on the laboratory results*

Please check the blood tests and report any clinically significant abnormality on the "**Adverse event**" page.

Centre No. | | | | | | |

Subject No. | | | | | | |

Week 1 FEC Sample collection date ___ ___ ___ (DD MMM YYYY)

	Result (use dot "." as decimal separator)	**Unit**	**Unit if other unit used**	**Normal range*** Min	Max
SGOT (ASAT)		U/l			
SGPT (ALAT)		U/l			
Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

** Please report the normal range as listed on the laboratory results*

Please check the blood tests and report any clinically significant abnormality on the "**Adverse event**" page.

Centre No. | | | | | | |

Subject No. | | | | | | |

Week 4 FEC Sample collection date ⌊__⌋⌊__⌋ ⌊__⌋⌊__⌋⌊__⌋⌊__⌋

DD MMM YYYY

	Result (use dot "." as decimal separator)	**Unit**	**Unit if other unit used**	**Normal range*** Min	Max
SGOT (ASAT)	⌊_____⌋	U/l	_____	_____	_____
SGPT (ALAT)	⌊_____⌋	U/l	_____	_____	_____
Alk. phosphatase	⌊_____⌋	U/l	_____	_____	_____
Bilirubin total	⌊_____⌋	mg/dl	_____	_____	_____

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

** Please report the normal range as listed on the laboratory results*

Please check the blood tests and report any clinically significant abnormality on the "**Adverse event**" page.

Centre No. | | | | | | |

Subject No. | | | | | | |

Week 7 FEC Sample collection date DD MMM YYYY

	Result (use dot "." as decimal separator)	**Unit**	**Unit if other unit used**	**Normal range*** Min	Max
SGOT (ASAT)		U/l			
SGPT (ALAT)		U/l			
Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

** Please report the normal range as listed on the laboratory results*

Please check the blood tests and report any clinically significant abnormality on the "**Adverse event**" page.

Centre No. | | | | | | |

Subject No. | | | | | | |

Week 10 (Week 1 targeted therapy)

Sample collection date ⌊__⌋⌊__⌋ ⌊__⌋⌊__⌋⌊__⌋⌊__⌋

DD MMM YYYY

	Result (use dot "." as decimal separator)	Unit	Unit if other unit used	Normal range* Min	Max
SGOT (ASAT)	⌊_____⌋	U/l	_____	_____	_____
SGPT (ALAT)	⌊_____⌋	U/l	_____	_____	_____
Alk. phosphatase	⌊_____⌋	U/l	_____	_____	_____
Bilirubin total	⌊_____⌋	mg/dl	_____	_____	_____

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

** Please report the normal range as listed on the laboratory results*

Please check the blood tests and report any clinically significant abnormality on the "**Adverse event**" page.

Centre No. | | | | | | |

Subject No. | | | | | | |

Week 16 (Week 7 targeted therapy)

Sample collection date ___ ___ ___ (DD MMM YYYY)

	Result (use dot "." as decimal separator)	Unit	Unit if other unit used	Normal range* Min	Max
SGOT (ASAT)		U/l			
SGPT (ALAT)		U/l			
Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

** Please report the normal range as listed on the laboratory results*

Please check the blood tests and report any clinically significant abnormality on the "**Adverse event**" page.

Centre No. | | | | | | |

Subject No. | | | | | | |

Week 22 (Week 13 targeted therapy)

Sample collection date ⌊__⌋⌊__⌋ ⌊__⌋⌊__⌋⌊__⌋⌊__⌋

DD MMM YYYY

	Result (use dot "." as decimal separator)	Unit	Unit if other unit used	Normal range* Min	Max
SGOT (ASAT)	⌊_____⌋	U/l	_____	_____	_____
SGPT (ALAT)	⌊_____⌋	U/l	_____	_____	_____
Alk. phosphatase	⌊_____⌋	U/l	_____	_____	_____
Bilirubin total	⌊_____⌋	mg/dl	_____	_____	_____

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

** Please report the normal range as listed on the laboratory results*

Please check the blood tests and report any clinically significant abnormality on the "**Adverse event**" page.

Centre No. | | | | | | |

Subject No. | | | | | | |

Week 28 (Week 19 targeted therapy)

Sample collection date ⌊__⌋⌊__⌋ ⌊__⌋⌊__⌋⌊__⌋⌊__⌋

DD MMM YYYY

	Result (use dot "." as decimal separator)	Unit	Unit if other unit used	Normal range* Min	Max
SGOT (ASAT)	⌊_____⌋	U/l	_____	_____	_____
SGPT (ALAT)	⌊_____⌋	U/l	_____	_____	_____
Alk. phosphatase	⌊_____⌋	U/l	_____	_____	_____
Bilirubin total	⌊_____⌋	mg/dl	_____	_____	_____

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

** Please report the normal range as listed on the laboratory results*

Please check the blood tests and report any clinically significant abnormality on the "**Adverse event**" page.

Centre No. | | | | | | |

Subject No. | | | | | | |

Week 34 (Week 25 targeted therapy)

Sample collection date ⌊__⌋⌊__⌋ ⌊__⌋⌊__⌋⌊__⌋⌊__⌋

DD MMM YYYY

	Result (use dot "." as decimal separator)	Unit	Unit if other unit used	Normal range* Min	Max
SGOT (ASAT)	⌊_____⌋	U/l	_____	_____	_____
SGPT (ALAT)	⌊_____⌋	U/l	_____	_____	_____
Alk. phosphatase	⌊_____⌋	U/l	_____	_____	_____
Bilirubin total	⌊_____⌋	mg/dl	_____	_____	_____

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

** Please report the normal range as listed on the laboratory results*

Please check the blood tests and report any clinically significant abnormality on the "**Adverse event**" page.

Centre No. | | | | | | |

Subject No. | | | | | | |

Week 40 (Week 31 targeted therapy)

Sample collection date ⌊__⌋⌊__⌋ ⌊__⌋⌊__⌋⌊__⌋⌊__⌋

DD MMM YYYY

	Result (use dot "." as decimal separator)	Unit	Unit if other unit used	Normal range* Min	Max
SGOT (ASAT)	⌊_____⌋	U/l	_____	_____	_____
SGPT (ALAT)	⌊_____⌋	U/l	_____	_____	_____
Alk. phosphatase	⌊_____⌋	U/l	_____	_____	_____
Bilirubin total	⌊_____⌋	mg/dl	_____	_____	_____

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

** Please report the normal range as listed on the laboratory results*

Please check the blood tests and report any clinically significant abnormality on the "**Adverse event**" page.

Centre No. | | | | | | |

Subject No. | | | | | | |

Week 43 (Week 34 targeted therapy)

Sample collection date ⌊__⌋⌊__⌋ ⌊__⌋⌊__⌋⌊__⌋⌊__⌋

DD MMM YYYY

	Result (use dot "." as decimal separator)	Unit	Unit if other unit used	Normal range* Min	Max
SGOT (ASAT)	⌊_____⌋	U/l	_____	_____	_____
SGPT (ALAT)	⌊_____⌋	U/l	_____	_____	_____
Alk. phosphatase	⌊_____⌋	U/l	_____	_____	_____
Bilirubin total	⌊_____⌋	mg/dl	_____	_____	_____

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

** Please report the normal range as listed on the laboratory results*

Please check the blood tests and report any clinically significant abnormality on the "**Adverse event**" page.

Centre No. | | | | | | |

Subject No. | | | | | | |

Month 12 Sample collection date DD MMM YYYY

	Result (use dot "." as decimal separator)	**Unit**	**Unit if other unit used**	**Normal range*** Min	Max
SGOT (ASAT)		U/l			
SGPT (ALAT)		U/l			
Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

** Please report the normal range as listed on the laboratory results*

Please check the blood tests and report any clinically significant abnormality on the "**Adverse event**" page.

Centre No. | | | | | | |

Subject No. | | | | | | |

Month 15 Sample collection date DD MMM YYYY

	Result (use dot "." as decimal separator)	**Unit**	**Unit if other unit used**	**Normal range*** Min	Max
SGOT (ASAT)		U/l			
SGPT (ALAT)		U/l			
Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

** Please report the normal range as listed on the laboratory results*

Please check the blood tests and report any clinically significant abnormality on the "**Adverse event**" page.

Centre No. | | | | | | |

Subject No. | | | | | | |

Month 18 Sample collection date ___ ___ ___ (DD MMM YYYY)

	Result (use dot "." as decimal separator)	**Unit**	**Unit if other unit used**	**Normal range*** Min	Max
SGOT (ASAT)		U/l			
SGPT (ALAT)		U/l			
Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

** Please report the normal range as listed on the laboratory results*

Please check the blood tests and report any clinically significant abnormality on the "**Adverse event**" page.

Centre No. | | | | | | |

Subject No. | | | | | | |

Month 24 Sample collection date DD MMM YYYY

	Result (use dot "." as decimal separator)	**Unit**	**Unit if other unit used**	**Normal range*** Min	Max
SGOT (ASAT)		U/l			
SGPT (ALAT)		U/l			
Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

** Please report the normal range as listed on the laboratory results*

Please check the blood tests and report any clinically significant abnormality on the "**Adverse event**" page.

Centre No. | | | | | | |

Subject No. | | | | | | |

Month 36 Sample collection date ___ ___ ___ (DD MMM YYYY)

	Result (use dot "." as decimal separator)	**Unit**	**Unit if other unit used**	**Normal range*** Min	Max
SGOT (ASAT)		U/l			
SGPT (ALAT)		U/l			
Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

** Please report the normal range as listed on the laboratory results*

Please check the blood tests and report any clinically significant abnormality on the "**Adverse event**" page.

Centre No. | | | | | | |

Subject No. | | | | | | |

Month 48 Sample collection date DD MMM YYYY

	Result (use dot "." as decimal separator)	**Unit**	**Unit if other unit used**	**Normal range*** Min	Max
SGOT (ASAT)		U/l			
SGPT (ALAT)		U/l			
Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

** Please report the normal range as listed on the laboratory results*

Please check the blood tests and report any clinically significant abnormality on the "**Adverse event**" page.

Centre No. | | | | | | |

Subject No. | | | | | | |

Month 60 Sample collection date DD MMM YYYY

	Result (use dot "." as decimal separator)	**Unit**	**Unit if other unit used**	**Normal range*** Min	Max
SGOT (ASAT)		U/l			
SGPT (ALAT)		U/l			
Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

** Please report the normal range as listed on the laboratory results*

Please check the blood tests and report any clinically significant abnormality on the "**Adverse event**" page.

Centre No. | | | | | | |

Subject No. | | | | | | |

Year 6 Sample collection date DD MMM YYYY

	Result (use dot "." as decimal separator)	**Unit**	**Unit if other unit used**	**Normal range*** Min	Max
SGOT (ASAT)		U/l			
SGPT (ALAT)		U/l			
Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

** Please report the normal range as listed on the laboratory results*

Please check the blood tests and report any clinically significant abnormality on the "**Adverse event**" page.

Centre No. | | | | | | |

Subject No. | | | | | | |

Year 7 Sample collection date DD MMM YYYY

	Result (use dot "." as decimal separator)	**Unit**	**Unit if other unit used**	**Normal range*** Min	Max
SGOT (ASAT)		U/l			
SGPT (ALAT)		U/l			
Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

** Please report the normal range as listed on the laboratory results*

Please check the blood tests and report any clinically significant abnormality on the "**Adverse event**" page.

Centre No. | | | | | | |

Subject No. | | | | | | |

Year 8 Sample collection date DD MMM YYYY

	Result (use dot "." as decimal separator)	**Unit**	**Unit if other unit used**	**Normal range*** Min	Max
SGOT (ASAT)		U/l			
SGPT (ALAT)		U/l			
Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

** Please report the normal range as listed on the laboratory results*

Please check the blood tests and report any clinically significant abnormality on the "**Adverse event**" page.

Centre No. | | | | | | |

Subject No. | | | | | | |

Year 9 Sample collection date ___ ___ ___ (DD MMM YYYY)

	Result (use dot "." as decimal separator)	**Unit**	**Unit if other unit used**	**Normal range*** Min	Max
SGOT (ASAT)		U/l			
SGPT (ALAT)		U/l			
Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

** Please report the normal range as listed on the laboratory results*

Please check the blood tests and report any clinically significant abnormality on the "**Adverse event**" page.

Centre No. | | | | | | |

Subject No. | | | | | | |

Year 10 Sample collection date ___ ___ ___ (DD MMM YYYY)

	Result (use dot "." as decimal separator)	**Unit**	**Unit if other unit used**	**Normal range*** Min	Max
SGOT (ASAT)		U/l			
SGPT (ALAT)		U/l			
Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

** Please report the normal range as listed on the laboratory results*

Please check the blood tests and report any clinically significant abnormality on the "**Adverse event**" page.

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

Unscheduled liver function tests

Centre No. Subject No.

Sample collection date DD MMM YYYY

	Result (use dot "." as decimal separator)	Unit	Unit if other unit used	Normal range* Min	Max
SGOT (ASAT)		U/l			
SGPT (ALAT)		U/l			
Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

Sample collection date DD MMM YYYY

	Result (use dot "." as decimal separator)	Unit	Unit if other unit used	Normal range* Min	Max
SGOT (ASAT)		U/l			
SGPT (ALAT)		U/l			
Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

Sample collection date DD MMM YYYY

	Result (use dot "." as decimal separator)	Unit	Unit if other unit used	Normal range* Min	Max
SGOT (ASAT)		U/l			
SGPT (ALAT)		U/l			
Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

** Please report the normal range as listed on the laboratory results*

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

Unscheduled liver function tests

Centre No. | | | | | |

Subject No. | | | | | |

Sample collection date |__|__| |__|__|__| |__|__|__|__|
DD MMM YYYY

	Result (use dot "." as decimal separator)	Unit	Unit if other unit used	Normal range* Min	Max
SGOT (ASAT)		U/l			
SGPT (ALAT)		U/l			
Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

Sample collection date |__|__| |__|__|__| |__|__|__|__|
DD MMM YYYY

	Result (use dot "." as decimal separator)	Unit	Unit if other unit used	Normal range* Min	Max
SGOT (ASAT)		U/l			
SGPT (ALAT)		U/l			
Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

Sample collection date |__|__| |__|__|__| |__|__|__|__|
DD MMM YYYY

	Result (use dot "." as decimal separator)	Unit	Unit if other unit used	Normal range* Min	Max
SGOT (ASAT)		U/l			
SGPT (ALAT)		U/l			
Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

** Please report the normal range as listed on the laboratory results*

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

Unscheduled liver function tests

Centre No. | | | | | |

Subject No. | | | | | |

Sample collection date __ __ / __ __ __ / __ __ __ __ (DD MMM YYYY)

	Result (use dot "." as decimal separator)	Unit	Unit if other unit used	Normal range* Min	Normal range* Max
SGOT (ASAT)		U/l			
SGPT (ALAT)		U/l			
Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

Sample collection date __ __ / __ __ __ / __ __ __ __ (DD MMM YYYY)

	Result (use dot "." as decimal separator)	Unit	Unit if other unit used	Normal range* Min	Normal range* Max
SGOT (ASAT)		U/l			
SGPT (ALAT)		U/l			
Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

Sample collection date __ __ / __ __ __ / __ __ __ __ (DD MMM YYYY)

	Result (use dot "." as decimal separator)	Unit	Unit if other unit used	Normal range* Min	Normal range* Max
SGOT (ASAT)		U/l			
SGPT (ALAT)		U/l			
Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

** Please report the normal range as listed on the laboratory results*

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

Unscheduled liver function tests

Centre No. | | | | | | Subject No. | | | | | |

Sample collection date |_|_|_|_|_|_|_|_|_| DD MMM YYYY

	Result (use dot "." as decimal separator)	Unit	Unit if other unit used	Normal range* Min	Max
SGOT (ASAT)		U/l			
SGPT (ALAT)		U/l			
Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

Sample collection date |_|_|_|_|_|_|_|_|_| DD MMM YYYY

	Result (use dot "." as decimal separator)	Unit	Unit if other unit used	Normal range* Min	Max
SGOT (ASAT)		U/l			
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Bilirubin total		mg/dl			

Sample collection date |_|_|_|_|_|_|_|_|_| DD MMM YYYY

	Result (use dot "." as decimal separator)	Unit	Unit if other unit used	Normal range* Min	Max
SGOT (ASAT)		U/l			
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Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

** Please report the normal range as listed on the laboratory results*

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

Unscheduled liver function tests

Centre No. | | | | | | |

Subject No. | | | | | | |

Sample collection date |__|__|__|__|__|__|__|__|__| DD MMM YYYY

	Result (use dot "." as decimal separator)	Unit	Unit if other unit used	Normal range* Min	Max
SGOT (ASAT)		U/l			
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Bilirubin total		mg/dl			

Sample collection date |__|__|__|__|__|__|__|__|__| DD MMM YYYY

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SGOT (ASAT)		U/l			
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Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

Sample collection date |__|__|__|__|__|__|__|__|__| DD MMM YYYY

	Result (use dot "." as decimal separator)	Unit	Unit if other unit used	Normal range* Min	Max
SGOT (ASAT)		U/l			
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Alk. phosphatase		U/l			
Bilirubin total		mg/dl			

** Please report the normal range as listed on the laboratory results*

NCI CTCAE v. 3: haematology and biochemistry toxicity scale

Test	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
SGOT (ALAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
SGPT (ASAT)	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Alkaline Phosphatase	>ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN	
Bilirubin total	>ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN	

Centre No. | | | | | | |

Subject No. | | | | | | |

Sample collection date ___ ___ ___ (DD MMM YYYY)

	Result (use dot "." as decimal separator)	**Unit**	**Unit if other unit used**	**Normal range*** Min	Max
SGOT (ASAT)		U/l			
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** Please report the normal range as listed on the laboratory results*