Randomisation Form for International Sites

Version 5.0—24 Jan 2023

Form #2(i)

Participant Trial Number: ☐☐☐☐

To randomise, please enter the below details onto the online Randomisation system

2.1 SITE DETAILS *(Refer to completion guidance for this section)*

Country:

Site:

Randomising investigator: (individual who obtained consent)

2.2 CONTACT'S DETAILS *(Refer to completion guidance for this section)*

Name:

Telephone:

2.3 PARTICIPANT DETAILS *(Refer to completion guidance for this section)*

1. Participant initials: ☐☐☐

2. Gender: Female ☐ Male ☐

3. Date of birth: ☐☐-☐☐☐-☐☐☐☐ (d d - m m m - y y y y)

4. Has the patient been treated with pre-surgical endocrine therapy? Yes ☐ No ☐

*If **YES** a pre-treatment core biopsy must be sent to the Central Laboratory.*

2.4 STRATIFICATION (please select one answer for each question)

1. Invasive tumour size: < 30mm ☐ ≥ 30mm ☐

2. Histological grade: Grade 1 ☐ Grade 2 ☐ Grade 3 ☐

For questions 1 and 2: If the participant has multiple tumours, please see form completion guidance for information on which tumour the patient should be stratified by.

For question 3: Please refer to the completion guidance.

3. Number of involved nodes:

Node negative (includes Isolated Tumour Cells only) ..... ☐

Positive sentinel node biopsy with micrometastases only and no axillary clearance ..... ☐

Positive sentinel node biopsy with macrometastases and no axillary clearance ..... ☐

1-3 involved nodes with axillary clearance (count both micrometastases and macrometastases) ... ☐

4-9 involved nodes with axillary clearance (count both micrometastases and macrometastases) ... ☐

4. Intended chemotherapy regimen:

FEC75-80 ☐ FEC90-100 ☐ TC ☐ (F)EC-T ☐ (F)EC-P ☐ dd AC/EC-P ☐

E-CMF ☐ EC90-100 ☐ AC-T ☐ AC-P ☐

TAC ☐

5. Are you intending to treat this patient with abemaciclib?:

Yes ☐ No ☐

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2.4 STRATIFICATION continued. (please select one answer for each question)

6. Menopausal status:

Male ☐

Postmenopausal ☐

Premenopausal ☐ → **If premenopausal, state intended endocrine therapy:**

Tamoxifen + ovarian suppression ☐

Aromatase inhibitor + ovarian suppression ☐

2.5 PARTICIPANT ELIGIBILITY (answers must fall in unshaded boxes)	**No**	**Yes**
1. Has a suitably delegated individual completed and signed an Eligibility Form?	☐	☐
2. Does the participant meet all of the eligibility criteria?	☐	☐

2.6 PARTICIPANT CONSENT FOR OPTIMA (answers must fall in unshaded boxes)	**No**	**Yes**
1. Has the participant given informed consent to be randomised?	☐	☐

2. Please confirm type of consent received prior to randomisation:

☐ Full written consent

	No	**Yes**
Have all the fields on the consent form been completed correctly?	☐	☐
Has the participant consented to share their anonymised data for future studies?	☐	☐
Has the participant consented to donate their tumour sample to future research?	☐	☐
Has the participant consented to be contacted regarding future studies?	☐	☐

Date consent form signed by participant: ☐☐-☐☐☐-☐☐☐☐ (d d - m m m - y y y y)

OR ☐ Remote Verbal consent*

(*Remember to complete CRF2a once written consent is completed)

Date of Remote Verbal Consent: ☐☐-☐☐☐-☐☐☐☐ (d d - m m m - y y y y)

Form completed by

Printed name: _____ Signature: _____ Date signed: ☐☐-☐☐☐-☐☐☐☐ (d d - m m m - y y y y)

N.B. The individual named must be on the delegation log with the assigned responsibility to perform randomisation.

TO BE COMPLETED BY SITE AFTER RANDOMISATION

(please also record the Participant Trial Number in the form header on Page 1)

PARTICIPANT TRIAL NUMBER: ☐☐☐☐

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Completion Guidelines for CRF 2i - Randomisation Form

2.1. SITE DETAILS

Randomising investigator

This is the trial investigator who counter-signed the participant's consent form. This individual's name must be on the Site Signature and Delegation Log with the assigned responsibility to obtain informed consent.

2.2. CONTACT'S DETAILS

Contact's name

This will be the person the randomisation confirmation fax and email will be sent to and to whom queries regarding the randomisation will be directed. This individual's name must be on the Site Signature and Delegation Log with the assigned responsibility to perform randomisation.

2.3. PARTICIPANT DETAILS

Participant initials

Write the initials of the participant's first/given name, middle name and surname/family name. If no middle name place dash ("-") in middle box.

Date of birth: Please use the following format for dates: 06-Jun-1956.

Has the patient been treated with pre-surgical endocrine therapy?

If yes, a pre-treatment core biopsy **must** be sent to the Central Laboratory for processing; a sample from a surgical excision or other on-treatment biopsy is not acceptable. Refer to the Protocol / Site Sample Collection SOP for further guidance.

2.4. STRATIFICATION

Questions 1 and 2: Invasive tumour size and histological grade

If the participant has multiple ipsilateral tumours which meet the inclusion criteria please record details of the tumour with the highest Nottingham Prognostic Index (NPI) score. NPI score is calculated using the following formula:

NPI Score = (0.2 x Invasive tumour size) + Grade + Nodal status

Where:

- Invasive tumour size (*not total tumour size*) is measured in cm
- Grade is the histological grade: Grade 1 = Score 1 | Grade 2 = Score 2 | Grade 3 = Score 3
- Nodal status: 0 positive nodes = Score 1 | 1-3 positive nodes = Score 2 | ≥4 positive nodes = Score 3

In practice, nodal status can be ignored for comparing tumours as this is the same for all tumours in the breast.

Example (*nodal status is included here for completeness*):
For a 30mm Grade 2 carcinoma with 2 nodes positive the NPI = 4.6 (Derived from [0.2 x 3.0] + 2 + 2)
For an 8mm Grade 3 carcinoma with 2 nodes positive the NPI = 5.16 (Derived from [0.2 x 0.8] + 3 + 2)
Record the details of the 8mm Grade 3 carcinoma as this has the higher score.

Question 3: Number of involved nodes

The number of nodes is the total from all surgical procedures and includes both micro– and macro-metastasis.

Question 6: Menopausal status

Women who fulfil the following criteria at trial entry will be considered postmenopausal:

- Age >45 and natural amenorrhoea of at least 1 year's duration
- Bilateral surgical oophorectomy
- For amenorrhoea not fulfilling the above criteria including women who have undergone hysterectomy without bilateral surgical oophorectomy and are age <60, the diagnosis of postmenopausal status should be supported by hormone measurement. Please refer to the protocol for additional detail including on interpreting hormone results.

Please note: caution is needed for women with amenorrhoea who are using hormonal contraception, particularly injectable contraception such as Depo-Provera and implants including Nexplanon® (etonogestrel). These last for many months so all such women should be considered premenopausal.

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