Clinical Performance Study Plan for Ki-67 IHC MIB-1 pharmDx (Dako Omnis) on Early Breast Cancer Specimens used to identify subjects for enrolment in AstraZeneca*s Phase III CAMBRIA-1 trial (D8531C00002)

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Ethical review	Not approved
Status	Will not start
Health condition type	Breast disorders
Study type	Interventional

Summary

ID

NL-OMON56528

Source
ToetsingOnline

Brief title
CPSP for Ki-67 IHC MIB-1 pharmDx (Dako Omnis)

Condition

- Breast disorders

Synonym
Breast cancer, ER+/HER2- early breast cancer

Research involving

Human

Sponsors and support

Primary sponsor: Astra Zeneca
Source(s) of monetary or material Support: AstraZeneca

Intervention

Keyword: Breast cancer, estrogen receptor, FFPE tumour, Ki-67 expression

Outcome measures

Primary outcome

The clinical utility of the Ki-67 IHC MIB-1 pharmDx (Dako Omnis) will be evaluated if the D8530C0002 clinical study confirms clinically relevant efficacy and meets its primary endpoint (outlined in the D8531C00002 CSP, Section 9.4.2). Clinical evidence for the Ki-67 assay will be evaluated through subgroup analysis of the primary endpoint based on tumour expression of Ki-67 as measured by Ki-67 IHC MIB-1 pharmDx (Dako Omnis) in all tested samples. Clinical performance of the device will be established if patients with tumours that have Ki-67 > 20% have at least similar efficacy profiles as compared to the overall study population.

Secondary outcome

N/A

Study description

Background summary

Ki-67 IHC MIB-1 pharmDx (Dako Omnis) is a qualitative immunohistochemical (IHC) assay using Monoclonal Mouse Anti-Ki-67, Clone MIB-1 intended for use in the detection of Ki-67 protein in formalin-fixed, paraffin-embedded (FFPE) breast

carcinoma using the EnVision FLEX visualization system on Dako Omnis.
Ki-67 IHC MIB-1 pharmDx (Dako Omnis) will be used as an aid in identifying patients with early-stage breast cancer at intermediate or high risk of disease recurrence for recruitment into the CAMBRIA-1 study.
Ki-67 IHC MIB-1 pharmDx (Dako Omnis) is designed to be run on the Dako Omnis automated staining system (Dako Omnis) with Dako Omnis Software and the Dako Link Omnis Workstation and Server software. Instruments and software are not specific to the Ki-67 assay and will not be evaluated as part of the clinical performance study.

Study objective

This clinical performance study will evaluate the effectiveness of the Ki 67 IHC MIB-1 pharmDx (Dako Omnis) to identify estrogen receptor (ER)+/human epidermal growth factor receptor 2 (HER2)- early breast cancer patients whose tumours score Ki-67 >= 20%, using archival FFPE tumour tissue.
The objective of this study is to support the AstraZeneca CAMBRIA-1 clinical trial (D8531C00002) by testing for Ki-67 expression in FFPE tumour specimens from patients with ER+/HER2- early breast cancer in order to identify patients with an intermediate or high risk of recurrence following standard of care therapy.
This clinical performance study is intended to obtain clinical evidence for use of this device as a (potential) companion diagnostic (CDx) to assess Ki-67 expression as one of the components to classify patients with ER+/HER2- early breast cancer in order to identify patients with an intermediate or high risk of recurrence that are eligible for treatment with camizestrant.

Study design

This interventional clinical performance study conducted as part of the CAMBRIA-1 clinical study protocol (CSP), D8531C00002, therefore represents a combined study, in which the diagnostic will be used for the selection of specific patients (Section 15). CAMBRIA-1 is a prospective, 2-arm, international, multicentre, randomised, open-label, Phase III study to evaluate the effect of extended therapy with camizestrant with or without luteinising hormone-releasing hormone (LHRH) agonist(s) compared to standard ET. Approximately 5375 patients will be screened to randomise approximately 4300 patients with ER+/HER2- early breast cancer with intermediate or high risk of recurrence, who have completed definitive locoregional therapy and at least 2 years and up to 5 years (+3 months) of standard adjuvant ET with or without a CDK4/6 inhibitor, with no disease recurrence, in a 1:1 ratio to one of the following arms: • Arm A: Continue the standard ET of investigator*s choice (aromatase inhibitors [exemestane, letrozole, anastrozole] or tamoxifen, standard dose per investigator, once daily) with or without LHRH agonist(s) • Arm B: Camizestrant (150 mg, once daily) with or without LHRH agonist(s) • Among other criteria defined in Section 5.1 of the CAMBRIA 1 CSP (D8531C00002),

patient eligibility will be determined based on tumour size, lymph node status, grade of tumour, genomic signature assessment, Ki-67 testing, and use of prior chemotherapy. Eligible patients will be pre-, peri-, or post-menopausal women, or men, with at least one of the following: (a) T4 tumours (tumour of any size with direct extension to the chest wall and/or the skin - ulceration or macroscopic nodules), regardless of nodal status. (b) Pathological primary invasive tumour size >5 cm regardless of nodal status. For patients who received neoadjuvant systemic therapy (chemotherapy and/or ET), primary tumour size >5 cm on breast imaging is allowed. (c) Pathological tumour of any size with involvement in >=2 ipsilateral lymph nodes. Note: for patients who have suspected involvement of locoregional lymph nodes, confirmation of nodal disease by pathology, cytology, immunohistochemistry, and/or one-step nucleic acid amplification is required. Patients with lymph nodes assessed by imaging only are not eligible. For this study, locoregional lymph nodes include ipsilateral lymph nodes (axillary, infraclavicular, supraclavicular, and internal mammary), but exclude intramammary lymph nodes. Patients with involvement of contralateral lymph nodes are not allowed. (d) Pathological primary invasive tumour size >1 cm and <=5 cm with involvement of 1 positive lymph node (or only micrometastatic disease) if at least one of the following features is present: (i) Pathological grade 3 (ii) Pre-existing high risk of recurrence per genomic signature assessment from medical record if in compliance with local regulations and conducted in accordance with intended use (see CAMBRIA-I CSP [D8531C00002] Section 4.1) (iii) Centrally assessed Ki-67 >20% via an AstraZeneca-provided laboratory test using archival sample where country-specific IVD approvals are available, as required. (e) Pathological primary invasive tumour size >1 cm and <=5 cm without involvement of any ipsilateral lymph nodes if at least one of the following features is present: (i) Pathological grade 3 (ii) Pre-existing high risk of recurrence per genomic signature assessment from medical record if in compliance with local regulations and conducted in accordance with intended use (see CAMBRIA-I CSP [D8531C00002] Section 4.1) (iii) Centrally assessed Ki-67 >20% via an AstraZeneca-provided laboratory test using archival sample where country-specific IVD approvals are available, as required. (iv) Prior cytotoxic chemotherapy for the current diagnosis of breast cancer. All patients, regardless of qualifying criteria, will provide archival tissue for central testing with Ki-67 IHC MIB-1 pharmDx (Dako Omnis).

Intervention

NA

Study burden and risks

NA

Contacts

Public
Astra Zeneca

/ /
Södertalje SE 151 85
SE
Scientific
Astra Zeneca

/ /
Södertalje SE 151 85
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Sample requirements for testing from patients with ER+/HER2- early breast cancer and who have completed definitive locoregional therapy and at least 2 years of standard adjuvant endocrine-based therapy without disease recurrence.
Please note, overall patient inclusion/exclusion criteria for this study are documented in Section 5.1 of the CAMBRIA-I CSP (D8531C00002) and summarised below.
Specimen Inclusion criteria:
All patients in this study must provide an archival FFPE tumour tissue sample. If the patient has not received any neoadjuvant treatment, a tumour sample collected during definitive surgery is preferable (although tumour sample collected during initial diagnostic workup will be accepted). If the patient has received neoadjuvant treatment, then a tumour sample collected during

initial diagnostic workup is required.
At least 200 viable tumour cells in invasive tumour component of the FFPE sample.
FFPE tissue specimen cut into sections of 4-5 µm and stained within 4 months of sectioning and stored at room temperature.

Exclusion criteria

Specimen Exclusion criteria: Bone biopsies, fine needle aspirates, cell pellets, or cytology samples. Specimens prepared using fixatives and/or fixation times other than 6 to 72 hours in 10% Neutral Buffered Formalin.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	42
Type:	Anticipated

Medical products/devices used

Generic name:	Ki-67 MIB-1 IHC pharmDx (Dako Omnis)
Registration:	No

Ethics review

Not approved

Date:	16-02-2024
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
Other	2022-501024-20-00
CCMO	NL84406.000.23