Trial record **1 of 3** for: AZD9496

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Study to Compare the Effects of AZD9496 vs Fulvestrant in Breast Cancer. (D6090C00002)

ClinicalTrials.gov Identifier: NCT03236974

Recruitment Status: Recruiting
First Posted: August 2, 2017
Last Update Posted: June 25, 2018

See **Contacts and Locations**

Sponsor:
AstraZeneca

Information provided by (Responsible Party):
AstraZeneca

Study Details | **Tabular View** | **No Results Posted** | Disclaimer | How to Read a Study Record

Study Description

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Brief Summary:

This is an open label randomised multicentre pre-surgical pharmacodynamics study to compare and assess the biological effects of **AZD9496** and fulvestrant in postmenopausal women with estrogen receptor (ER) positive (ER+), human epidermal growth factor receptor 2 (HER-2) negative (HER2-) primary breast cancer.

Patients will receive **AZD9496** or fulvestrant and will have an on-treatment image

-guided core biopsy after 5-14 days of commencing treatment.

Condition or disease	Intervention/treatment	Phase
Postmenopausal Women With ER+ HER2- Primary Breast Cancer	Drug: Standard Arm - Fulvestrant Drug: **AZD9496**	Phase 1

Detailed Description:

This is an open label, randomized, multi-centre study in postmenopausal women with primary ER+ HER2- breast cancer. Patients will be randomised to an oral dose of 250 mg bd AZD9496 or 500mg fulvestrant i.m. administered on one occasion. Patients diagnosed with primary breast cancer who are scheduled for surgery with curative intent will be consented to the study including consent to use the formalin fixed paraffin embedded (FFPE) diagnostic tumor biopsy sample and fresh frozen tumor biopsy sample (if available) for research purposes. Patients may also consent to provide an optional pretreatment fresh frozen tumor biopsy sample if this was not obtained at the time of initial diagnostic biopsy. If the diagnostic biopsy was taken ≥ 6 weeks prior to starting treatment or was not of sufficient quality, new tumor core biopsies (FFPE and fresh frozen) must be taken. Following the screening visit, eligible patients will be randomised to receive one of the following study treatments:

- AZD9496 administered at 250 mg bd orally for 5-14 days commencing on Day 1, and continuing up to the day of biopsy OR
- fulvestrant 500 mg administered as two consecutive 5 ml intramuscular injections on Day 1, one in each buttock.

After the morning dose of AZD9496 on the day of biopsy dosing will be stopped. If following initiation of AZD9496 treatment, dosing will be stopped if biopsy is postponed beyond Day 14. Patients will be considered not evaluable for the study if biopsy is postponed beyond day 14 of AZD9496/fulvestrant treatment initiation. Core tumor biopsies will be taken at either the time of definitive surgery or at a separate visit prior to surgery in the period between (and including) day 5 and day 14. Subjects who are scheduled to start a subsequent neoadjuvant therapy must have their core tumor biopsies performed before commencing neoadjuvant treatment.

Study Design

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Study Type:	Interventional (Clinical Trial)
Estimated Enrollment:	48 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Masking:	None (Open Label)
Masking Description:	Not applicable, thisis an open-label study.
Primary Purpose:	Treatment
Official Title:	An Open Label, Randomised, Pre-surgical, Pharmacodynamics Study to Compare the Biological Effects of **AZD9496** Versus Fulvestrant in Postmenopausal Women With ER Positive HER-2 Negative Primary Breast Cancer
Actual Study Start Date:	October 5, 2017
Estimated Primary Completion Date:	February 8, 2019
Estimated Study Completion Date:	February 8, 2019

Arms and Interventions

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Arm	Intervention/treatment
Active Comparator: Standard arm Fulvestrant, 500 mg	Drug: Standard Arm - Fulvestrant 500 mg Fulvestrant administered as two consecutive 5 ml intramuscular injections on Day 1, one in each buttock Other Name: Fulvestrant
Experimental: **AZD9496** 250 mg bd taken orally for 5-14 days	Drug: **AZD9496** Administered at 250 mg bd orally for 5-14 days commencing on Day 1, and continuing up to the day of biopsy Other Name: Study drug

Outcome Measures

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Primary Outcome Measures:

1. Pharmacodynamics changes to estrogen receptor (ER) expression following treatment with **AZD9496** or fulvestrant [Time Frame: Tumour biopsy taken at baseline within 6 weeks of planned start of study treatment; on-treatment tumour biopsy taken following 5-14 day on study treatment]

   Evaluation of **AZD9496** and fulvestrant activity in the tumour by assessment of pharmacodynamics biomarker changes i.e. ER expression

Secondary Outcome Measures:

1. Pharmacodynamics changes to progesterone receptor (PgR) expression following treatment with **AZD9496** or fulvestrant [Time Frame: Tumour biopsy taken at baseline within 6 weeks of planned start of study treatment; on-treatment tumour biopsy taken following 5-14 day on study treatment]

   Evaluation of **AZD9496** and fulvestrant activity in the tumour by assessment of pharmacodynamics biomarker changes i.e. PgR expression

2. Pharmacodynamics changes to Ki67 protein biomarker expression following treatment with **AZD9496** or fulvestrant [Time Frame: Tumour biopsy taken at baseline within 6 weeks of planned start of study treatment; on-treatment tumour biopsy taken following 5-14 day on study treatment]

   Evaluation of **AZD9496** and fulvestrant activity in the tumour by assessment of pharmacodynamics biomarker changes i.e. Ki67 protein biomarker expression

3. Safety and tolerability of **AZD9496** [Time Frame: From first dose until 28 days after last dose of AZD9496]

   Safety and tolerability will be assessed in terms of adverse events (AEs), laboratory data, vital signs and ECG changes.

4. Safety and tolerability of fulvestrant [Time Frame: From first dose until 28 days after fulvestrant]

   Safety and tolerability will be assessed in terms of adverse events (AEs), laboratory data and vital signs

5. Plasma concentration of **AZD9496** - stand alone biopsy visit option [Time Frame: Blood samples collected close as possible to time of biopsy, 1-2 hours after biopsy and optional 3-4 hours after biopsy]

Determination of **AZD9496** concentrations in plasma

6. Plasma concentration of fulvestrant [Time Frame: A blood sample will be collected anytime before biopsy.]

   Determination of fulvestrant concentration in plasma

7. Plasma concentration of **AZD9496** - on the table biopsy option [Time Frame: Blood samples collected close as possible to time of biopsy, at least 2 hours after biopsy and 8-12 hours after last dose or at discharge which is defined as up to 12 hours after last dose]

   Determination of **AZD9496** concentration in plasma

Eligibility Criteria

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Information from the National Library of Medicine

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, Learn About Clinical Studies.

Ages Eligible for Study:	18 Years to 120 Years (Adult, Older Adult)
Sexes Eligible for Study:	Female
Accepts Healthy Volunteers:	No

Criteria

Inclusion criteria:

1. Signed and dated informed consent form (ICF)
2. Women >=18 years
3. Patients with newly diagnosed resectable primary breast cancer scheduled to undergo treatment with curative intent by surgery
4. Histologically confirmed invasive breast cancer involving a palpable tumor of any size, or a tumor with an ultrasound assessed diameter of ≥ 1.0 cm
5. Any clinical nodal status
6. ER+breast cancer
7. HER2- breast cancer defined as a negative in situ hybridization test or an immno-histochemistry (IHC) status of 0 or 1+
8. Eastern Co-operative Oncology group (ECOG) performance status 0-1
9. Post-menopausal status defined as meeting at least one of the following criteria: Have undergone a bilateral oophorectomy; Age ≥60 years; Age ≥50 years and with cessation of regular menses ≥12 months and with an intact uterus in the absence of oral contraception or hormone-replacement therapy (HRT) prior to the diagnosis of breast cancer; Age <60 years and with cessation of regular menses ≥12 months and follicle stimulating hormone (FSH) and oestradiol levels in the postmenopausal range

Exclusion criteria:

1. Pre-treatment biopsy sample not likely to provide adequate tissue sections for the biomarker assays

2. Previous systemic or local treatment for the new primary breast cancer currently under investigation (including surgery, radiotherapy, cytotoxic and endocrine treatments)
3. Inflammatory breast cancer
4. Evidence of metastases
5. Patients currently receiving medications or herbal supplements known to be strong inhibitors/inducers of CYP3A4/5 or strong inhibitors of CYP2C8 or that are sensitive substrates of CYP2C8 inhibition
6. Concurrent treatment with other experimental drugs within 4 weeks prior to receiving study treatment
7. Use of hormone-replacement therapy from <4 weeks of the diagnostic/baseline core biopsy to the start of trial treatment
8. Patients with second primary cancer. Any endocrine therapies or other anti-cancer therapies must have been ceased at least 12 months prior to enrollment.
9. Any of the following cardiac criteria:
    - Mean resting QT interval corrected for heart rate (QTc) > 470 msec obtained from 3 ECGs using Fridericia's formula
    - Any clinically important abnormalities in rhythm, conduction or morphology of resting ECG
    - Any factors that increase the risk of QTc prolongation or risk of arrhythmic events
10. Experience of any of the following in the preceding 6 months: coronary artery bypass graft (CABG), angioplasty, vascular stent, myocardial infarction (MI), angina pectoris, congestive heart failure New York Heart Association (NYHA) Grade ≥2, cerebrovascular accident (CVA), transient ischaemic attack (TIA), deep venous or arterial thrombosis, pulmonary embolism, bleeding diathesis (i.e., disseminated intravascular coagulation, clotting factor deficiency) or requirement of anticoagulant therapy
11. As judged by the Investigator, any evidence of severe or uncontrolled systemic diseases,
12. Uncontrolled symptomatic thyroid dysfunction (hyperthyroidism or hypothyroidism).
13. Unexplained symptomatic endometrial disorders.
14. Refractory nausea and vomiting, uncontrolled chronic GI diseases, inability to swallow the formulated product or previous significant bowel resection that would preclude adequate absorption of AZD9496.
15. Inadequate bone marrow reserve or organ function as demonstrated by any of the following laboratory values: absolute neutrophil count < 1.5 x 109/L, Platelet count < 100 x 109/L, Haemoglobin < 90 g/L, alanine aminotransferase (ALT) > 2.5x upper limit of normal (ULN), aspartate aminotransferase (AST) > 2.5 x ULN, Total bilirubin > 1.5 x ULN or > 3 x in case of Gilbert's Syndrome, glomerular filtration rate < 50 mL/min
16. Direct involvement in the planning and conduct of the study
17. History of hypersensitivity to AZD9496
18. History of hypersensitivity to fulvestrant and/or castor oil
19. Judgment by the investigator that the patient should not participate in the study if unlikely to comply with study procedures, restrictions and requirements In addition, the following is considered a criterion for exclusion from the exploratory genetic research: Previous allogeneic bone marrow transplant; Non-leukocyte depleted whole blood transfusion within 120 days of the date of the genetic sample collection

Contacts and Locations

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Please refer to this study by its ClinicalTrials.gov identifier (NCT number): ***NCT03236974***

Contacts

Contact: AstraZeneca Clinical Study Information Center 1-877-240-9479 information.center@astrazeneca.com

Locations

Germany

Research Site **Not yet recruiting**
Berlin, Germany, 10117

Research Site **Recruiting**
Erlangen, Germany, 91054

Research Site **Recruiting**
Kiel, Germany, 24105

Research Site **Recruiting**
Köln, Germany, 50935

Research Site **Recruiting**
Minden, Germany, 32429

Research Site **Not yet recruiting**
Mönchengladbach, Germany, 41061

Research Site **Not yet recruiting**
München, Germany, 81377

Research Site **Recruiting**
Schwerin, Germany, 19049

United Kingdom

Research Site **Not yet recruiting**
Birmingham, United Kingdom, B15 2TG

Research Site **Withdrawn**
Bournemouth, United Kingdom, BH7 7DW

Research Site **Recruiting**
Derby, United Kingdom, DE22 3DT

Research Site **Recruiting**
Edinburgh, United Kingdom, EH4 2XU

Research Site **Recruiting**
London, United Kingdom, EC1M 6BQ

Research Site **Recruiting**
London, United Kingdom, SE1 9RT

Research Site **Recruiting**
London, United Kingdom, W12 0NN

Research Site **Recruiting**
Manchester, United Kingdom, M23 9LT

Research Site **Recruiting**
Poole, United Kingdom, BH15 2JB

Research Site **Not yet recruiting**

Sutton In Ashfield, United Kingdom, NG17 4JL

Sponsors and Collaborators

AstraZeneca

More Information

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Responsible Party:	AstraZeneca	
ClinicalTrials.gov Identifier:	NCT03236974	History of Changes
Other Study ID Numbers:	D6090C00002	
First Posted:	August 2, 2017	Key Record Dates
Last Update Posted:	June 25, 2018	
Last Verified:	June 2018	

Individual Participant Data (IPD) Sharing Statement:

Plan to Share IPD: Undecided

Studies a U.S. FDA-regulated Drug Product:	No
Studies a U.S. FDA-regulated Device Product:	No

Additional relevant MeSH terms:

Breast Neoplasms
Neoplasms by Site
Neoplasms
Breast Diseases
Skin Diseases
Fulvestrant
Estradiol
Antineoplastic Agents, Hormonal
Antineoplastic Agents
Estrogen Receptor Antagonists
Estrogen Antagonists
Hormone Antagonists
Hormones, Hormone Substitutes, and Hormone Antagonists
Physiological Effects of Drugs
Estrogens
Hormones