A phase 2 study of trifluridine/tipiracil in patients with ER-positive, HER2-negative advanced breast cancer that previously received chemotherapy

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This study has been transitioned to CTIS with ID 2024-519204-27-00 check the CTIS register for the current data. To evaluate the efficacy of trifluridine/tipiracil by determination of the percentage of patients being progression free at 8 weeks on...

Ethical review	Approved WMO
Status	Completed
Health condition type	Breast neoplasms malignant and unspecified (incl nipple)
Study type	Interventional

Summary

ID

NL-OMON52884

Source
ToetsingOnline

Brief title
TIBET

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
ER-positive breast cancer;, Metastatic breast cancer; Her2 negative

Research involving
Human

Sponsors and support

Primary sponsor: BOOG Study Center

Source(s) of monetary or material Support: BOOG,Servier

Intervention

Keyword: Breast Cancer, Efficacy, metastatic, trifluridine/tipiracil

Outcome measures

Primary outcome

Percentage of patients being progression free at 8 weeks on

trifluridine/tipiracil prescribed for ER-positive, HER2-negative advanced

breast cancer patients previously treated with a taxane and capecitabine

Secondary outcome

• Progression-free survival

• Response rate CR/PR at 16 weeks

• Adverse events

• QoL

Study description

Background summary

Treatment goals for metastatic breast cancer (MBC) are palliative in nature, primarily focused on decreasing tumor size, reducing tumor-related complaints and extending survival with preservation of quality of life. In patients with ER-positive, HER2-negativeadvanced disease without rapidly progressive visceral metastases, deprivation of estrogen signaling is first choice. In the case of endocrine resistance or rapidly progressive disease chemotherapy is required.

Preclinical studies with trifluridine/tipiracil have demonstrated that colorectal cancer patients that were pretreated with a fluoropyrimidine (among others) show an overall survival benefit from trifluridine/tipiracil as compared to placebo. Trifluridine/tipiracil appears to be tolerated well and does not cause hand-foot syndrome HFS of importance. It may be anticipated that patients with ER-positive, HER2-negative advanced breast cancer refractory to capecitabine may have benefit from trifluridine/tipiracil. Therefore, it is

proposed to study the efficacy and the safety of trifluridine/tipiracil in disease pretreated with a taxane and capecitabine.

Study objective

This study has been transitioned to CTIS with ID 2024-519204-27-00 check the CTIS register for the current data.

To evaluate the efficacy of trifluridine/tipiracil by determination of the percentage of patients being progression free at 8 weeks on trifluridine/tipiracil prescribed for ER-positive, HER2-negative advanced breast cancer patients previously treated with an anthracycline, a taxane and capecitabine

Study design

This is a multicenter phase 2 study evaluating the efficacy and safety of trifluridine/tipiracil in women with metastatic or locally advanced breast cancer not amenable to curative treatment by surgery or radiotherapy. This study will be conducted under the sponsorship of BOOG, Amsterdam, NL.
Study medication should be started within 3 days after completion of screening and continue until a
study treatment discontinuation criterion is met.
Trifluridine/tipiracil will be administered orally BID on days 1 through 5, with the first dose administered in the morning of day 1 of each cycle and the last dose administered in the evening of day 5, followed by a recovery period from day 6 through day 7. Trifluridine/tipiracil will be administered orally BID on days 8 through 12, with the first dose administered in the morning of day 8 of each cycle and the last dose administered in the evening of day 12, followed by a recovery period from day 13 through day 28. Each cycle will be 28 days.
Patients will be evaluated for PFS and ORR. Tumor assessments will be performed throughout the study based on Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1) as described in Section 9.0. Computed tomography (CT) scans will be performed in week 8 and then 16 weeks. CT scan should be repeated at 20 weeks to confirm CR/PR at 16 weeks. Safety will be assessed by AEs and laboratory evaluations according to the Common Terminology Criteria for Adverse Events (CTC-AE version 4.03).

Intervention

trifluridine/tipiracil 35mg/m2, twice daily, p.o. day 1-2-3-4-5 & 8-9-10-11-12
Repeat every 28 days

Study burden and risks

Physical examination before treatment, before cycle 2 and 30 days after stopping.

Quality of life questionnaires prior to the study and after 8, 16, 24 and 32 weeks

In addition to the standard treatment:
pregnancy test (urine dipstick)
1x ECG
maximum 2 CT scans
maximum 1 bone scan

Like all medications, the medications that patients receive during this study can have side effects. Most of the side effects disappear once the study drug is stopped. Sometimes the side effects can be serious. They can remain present for a long time or possibly be fatal. Furthermore, some measurements can cause inconveniences or complications. Side effects, discomforts or complications can also occur that are still unknown.

The use of this medications may have a beneficial effect on the disease. Previous research in patients with colon cancer shows that, despite earlier use of 5-FU / capecitabine, they may have a survival advantage of the research drug trifluridine / tipiracil (TAS102, LONSURF®). It is expected that this beneficial effect can also be seen in metastatic ER positive, Her-2 negative breast cancer.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Adult women(>= 18 years of age) with proven diagnosis of metastatic or locally advanced breast cancer not amenable to curative treatment by surgery or radiotherapy
2. Documented ER positive (10%) / PR positive (10%) and HER2 negative metastatic breast cancer
3. Progressive disease based on imaging
4. Women previously treated with capecitabine (in metastatic setting), and a maximum of two other lines of chemotherapy including a taxane either in the (neo)adjuvant or metastatic setting.
5. Evaluable disease as defined per RECIST v.1.1 (see Appendix A). Tumor lesions previously irradiated or subjected to other locoregional therapy will only be deemed measurable if disease progression at the treated site after completion of therapy is clearly documented.
6. Eastern Cooperative Oncology Group (ECOG) performance status<= 1
7. Life expectancy of >= 12 weeks
8. Willing and able to comply with scheduled visits and study procedures
9. Adequate organ, bone marrow and coagulation function as shown by:
• Absolute neutrophil count (ANC) >= 1.5 ×109/L
• Platelets >= 75 ×109/L
• Hemoglobin (Hgb) >= 5.6 mmol/L
• Serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) <= 2.5 ULN (or <= 5 if hepatic metastases are present)
• Total serum bilirubin <= 1.5 × ULN (<= 3 × ULN for patients known to have Gilbert Syndrome)
• Creatinine clearance >=60 ml/min
10. Written informed consent obtained before any screening procedure and according to local guidelines.
11. Resolution of all acute toxic effects of prior anti-cancer therapy or

surgical procedures to NCI CTCAE version 4.0 Grade <=1, except alopecia or other toxicities not considered a safety risk for the patient at investigator's discretion.

Exclusion criteria

1. HER2-overexpressing patients by local laboratory testing (IHC 3+ staining or in situ hybridization positive) and ER-negative patients are not eligible
2. No more than two lines of chemotherapy for advanced disease
3. Remaining of side-effects from previous chemotherapy > grade 1 (except for alopecia)
4. Radiotherapy within four weeks prior to enrollment is not allowed except in case of localized radiotherapy for analgesic purpose or for lytic lesions at risk of fracture which can then be completed within two weeks prior to enrollment. Patients must have recovered from radiotherapy toxicities prior to enrollment.
5. 30% or more marrow-bearing bone being irradiated. Other primary tumors within the last 5 years before study entry are not allowed, except for adequately controlled basal cell carcinoma of the skin, or carcinoma in situ of the cervix.
6. Previous or current CNS metastases, carcinomatous meningitis, are not allowed. A CT or MRI of the brain must be performed within 4 weeks prior to registration if the presence of metastases at this site is suspected.
7. Evidence of clinically significant cardiovascular or pulmonary disease or any other disease, metabolic or psychological dysfunction, physical examination finding, or clinical laboratory finding giving reasonable suspicion of a disease or condition that contraindicates the use of an investigational drug, or that may affect patient compliance with study routines, or places the patient at high risk from treatment related complications. (e.g lactose intolerance)
8. Previously received trifluridine/tipiracil
9. Since trifluridine/tipiracil contains lactose, patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine (see section 4.4 of the SmPC). (APPENDIX B)
10. Diagnosis of any other malignancy prior to registration, except those that are not believed to influence the patient*s prognosis and do not require any further treatment.
11. Other severe acute or chronic medical or psychiatric condition or laboratory abnormality that may increase the risk associated with study participation or investigational product administration or may interfere with the interpretation of study results and, in the judgment of the investigator, would make the patient inappropriate for entry into this study.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	25-09-2020
Enrollment:	50
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Lonsurf
Generic name:	trifluridine (FTD) / tipiracil hydrochloride (TPI)
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	24-07-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	22-01-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	22-02-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-05-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-06-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-11-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-11-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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
EU-CTR	CTIS2024-519204-27-00
EudraCT	EUCTR2019-001706-15-NL
ClinicalTrials.gov	NCT04489173
CCMO	NL69646.078.19