FUnctional selection of advanced breast cancer patients for Talazoparib treatment Using the REpair Capacity (RECAP) test:The FUTURE trial

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON26112

Source
Nationaal Trial Register

Brief title
FUTURE

Health condition

Breast cancer

Sponsors and support

Primary sponsor: Erasmus Medical Center
Source(s) of monetary or material Support: Pfizer

Intervention

Outcome measures

Primary outcome

To test if the RECAP test has the potential of selecting patients who are sensitive to

treatment with the PARP inhibitor talazoparib.

Secondary outcome

- To determine overall response rate and overall survival among patients with HRD tumors treated with talazoparib.

Study description

Background summary

Optimal patient selection for poly (adenosine diphosphate [ADP]-ribose) polymerase (PARP) inhibitors (PARPi) and double strand break (DSB) inducing chemotherapy is of great clinical importance. Although evidence is emerging that the use of these therapies can be extended beyond germline BRCA1/2 mutated cancers, a gold standard test for predicting response to treatments targeting homologous recombination (HR) is not yet available. Recently, we have developed the REpair CAPacity (RECAP) test. This is a functional assay exploiting RAD51 (a DSB repair protein) focus formation after ex vivo irradiation of fresh breast cancer tissue [1]. This allows testing of the HR status on a real-time basis. Based on the HR phenotype rather than BRCA germline or somatic status, more patients can be identified who are likely to benefit from PARPi treatment. Furthermore, the RECAP test can also detect reversion of the HRD phenotype in BRCA deficient tumors and thereby prevent unnecessary treatment.
It is of the utmost importance to determine the predictive value of the RECAP test for the in vivo response to PARPi. Talazoparib is one of the most promising PARPi, given its significant potency and superior PARP-trapping properties compared to other PARPi.

Our trial will select patients for treatment with talazoparib using the RECAP test.

Study objective

This study will investigate wheter the RECAP test has the potential of selecting patients who are sensitive to treatment with the PARP inhibitor talazoparib as measured by the PFS rate at 4 months.

Study design

NA

Intervention

Talazoparib

Contacts

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Eligibility criteria

Inclusion criteria

• Age ≥18 years
• WHO performance status 0-2
• Locally advanced breast cancer without options for treatment with curative intent or metastatic breast cancer
• Objective progressive disease (PD) according to RECIST within 4 months prior to study entry
• The breast cancer must be high grade (Bloom & Richardson grade 3) ER positive (>10%) and HER2 negative primary breast cancer or triple negative (ER<10%, PR<10% and HER2 negative). The Bloom & Richardson grading is always based on the primary tumor. The receptor status can be based on the primary tumor or a metastatic lesion whichever comes latest. Patients with breast cancer and a known BRCA1 and/or BRCA2 germline or somatic mutation are eligible independent of the Bloom & Richardson grading and receptor status.
• The site of the metastatic lesion (or primary tumor in case it is still in situ) should be easily amendable for biopsy. NB lung metastases (high risk of hemato/pneumo-thorax) and bone metastases (not suitable for RECAP test because calcifications interfere with experimental procedures) are excluded. The local guidelines will be used for stopping and restarting of anticoagulation. Bilirubin <1.5 ULN (except elevated bilirubin due to Gilbert's disease or a similar syndrome involving slow conjugation of bilirubin) and both AST and ALT <5x ULN in case a liver biopsy is planned.
• The tumor must be HRD, defined as HRD identified by the RECAP test determined just before the start of potential Talazoparib treatment within this study (also in case a proven germline BRCA1/2 mutation is present).
• Maximum of four prior lines of chemotherapy for advanced disease; Patients who received platinum compounds are eligible if they have had at least a progression free interval of four months.
• Measureable or evaluable disease according to RECIST 1.1 criteria (appendix 2)

• Life expectancy ≥ 3 months
• Hemoglobin ≥ 10 g/dL (6,2 mmol/L) and ANC of ≥ 1.5 x 109 /L
• Platelets >100 x 10e9/L
• Hepatic function as defined by total serum bilirubin ≤ 1. 5 x ULN (except elevated bilirubin due to Gilbert's disease or a similar syndrome involving slow conjugation of bilirubin), ASAT and ALAT < 3 x ULN or <5 x ULN in case of liver metastasis
• Adequate renal function as defined by either serum creatinine ≤ 1.5 x ULN or creatinine clearance ≥ 50 mL/min (by Cockcroft-Gault formula)
• Negative pregnancy test (urine/serum) for female patients with childbearing potential
• Written informed consent

Exclusion criteria

• Any psychological condition potentially hampering compliance with the study protocol
• Any treatment with investigational antitumor drugs within 28 days prior to receiving the first dose of investigational treatment; or within 21 days for standard chemotherapy; or within 14 days for weekly scheduled chemotherapeutic regimens or endocrine therapy
• Radiotherapy within the last four weeks prior to receiving the first dose of investigational treatment; except 1 or 2 x 8 Gy for pain palliation, then seven days interval after the last radiation should be maintained
• Known persistent (>4 weeks) ≥ Grade 2 toxicity from prior cancer therapy (except for alopecia grade 2)
• Symptomatic brain or leptomeningeal metastases. Patients completely free of symptoms and without corticosteroids for at least four weeks after adequate treatment by resection and/or irradiation could be eligible (consult PI).
• Women who have a positive pregnancy test (urine/serum) and/or who are breastfeeding;
• Unreliable contraceptive methods. Women and men enrolled in this trial must agree to use a reliable contraceptive method throughout the study (adequate contraceptive methods are: intra-uterine devices or systems, condom or other barrier contraceptive measures, sterilization and true abstinence)
• Concomitant use of P-gp inhibitors or inducers or BCRP inhibitors (see Appendix A)
• Any known history of myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML)
• Uncontrolled infectious disease (such as Human Immunodeficiency Virus HIV-1 or HIV-2 infection) or known active hepatitis B or C
• Recent myocardial infarction (< six months) or unstable angina

Study design

Design

Study type: Interventional

Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	19-09-2019
Enrollment:	67
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	26-09-2019
Application type:	First submission

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
NTR-new	NL8099

Register	ID
Other	METC EMC : MEC 2019-0070

Study results