The BEACON Study (BrEAst Cancer Outcomes with NKTR-102): A Phase 3 Open-Label, Randomized, Multicenter Study of NKTR-102 versus Treatment of Physician*s Choice (TPC) in Patients with Locally Recurrent or Metastatic Breast Cancer Previously Treated with an Anthracycline, a Taxane, and Capecitabine

Published: 04-05-2012
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Primary Objectives:* To compare overall survival (OS) of patients who receive NKTR-102given once every 21 days (q21d) to patients who receive Treatment ofPhysician*s Choice (TPC) selected from the following list of seven singleagentintravenous...

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

Summary

ID

NL-OMON41606

Source
ToetsingOnline

Brief title
BEACON

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
Metastatic Breast Cancer

Research involving
Human

Sponsors and support

Primary sponsor: Nektar Therapeutics
Source(s) of monetary or material Support: the pharmaceutical industry

Intervention

Keyword: Breast Cancer, NKTR-102, previously treated

Outcome measures

Primary outcome

Primary Endpoint is Overall Survival

Secondary outcome

secondary endpoint is

objective response rate,

progression free survival,

clinical benefit rate,

Duration of Response,

Incidence and severity of treatment-emergent adverse events (TEAEs), laboratory

abnormalities, targeted symptoms (including diarrhea and neuropathy); incidence

of dose reductions; dose intensity

QLQ-C30 individual scale, overall score and BR23 score value and change over

the time of study participation

Derived PK parameters, including Cmax, AUC, time to Cmax (Tmax), V, elimination

t* and CL, with an exploratory analysis regarding possible correlation to

various baseline characteristics (eg, age and UGT1A1 status)

Selected measures of health care utilization

Quantification of CTCs and assessment of various biomarkers (eg, topoisomerase

1 and 2 expression, DNA damage and apoptosis at baseline); change from baseline

Study description

Background summary

NKTR-102 is a prodrug, that provides slow release of irinotecan, which is in turn coverted to SN-38, a topoisomerase 1 inhibitor.The apparent elimination T* for SN38 after NKTR-102 administration is approximately 50 days. This greatly increased SN38 T* results in plasma SN38 concentrations that are significantly more sustained between doses than are possible with irinotecan.

Study objective

Primary Objectives:
* To compare overall survival (OS) of patients who receive NKTR-102 given once every 21 days (q21d) to patients who receive Treatment of Physician*s Choice (TPC) selected from the following list of seven singleagent intravenous therapies: eribulin, ixabepilone, vinorelbine, gemcitabine, paclitaxel, docetaxel or nab-paclitaxel
Secondary Objectives:
* To compare the objective response rate (ORR) per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 (hereafter referred to as RECIST)
* To compare progression-free survival (PFS)
* To compare the clinical benefit rate (CBR, the proportion of patients having complete response (CR), partial response (PR), or stable disease (SD) for at least 6 months)
* To compare duration of response (DoR)
* To determine the safety profiles of NKTR-102 and TPC (including Grade 3 and higher toxicities, incidence of dose reductions and dose intensity)
* To compare health-related Quality of Life (QoL), using the QLQ-C30 questionnaire with the BR23 subscale
* To obtain pharmacokinetic (PK) data (in selected patients randomized to

NKTR-102 only)
* To evaluate the pharmacoeconomic implications of NKTR-102 therapy using selected measures of health care utilization
Exploratory Objective
* To correlate specific biomarker data with response, PFS, survival, selected toxicities and possibly PK parameters (in patients who consent)

Study design

This is an open-label, randomized, parallel, two arm, multicenter, international Phase 3 study of NKTR-102 versus TPC in patients with locally recurrent or metastatic breast cancer (MBC) previously treated with at least two and a maximum of five prior cytotoxic chemotherapy regimens including an anthracycline, a taxane, and capecitabine. In Arm A, NKTR-102 will be administered at a dose level of 145 mg/m2 on a q21d schedule as a 90-minute intravenous (IV) infusion on Day 1 of each treatment cycle.
In Arm B, TPC will be administered per standard of care. TPC must be commercially available in the medical center for treatment of patients with cancer. Patients randomized to TPC will receive single agent chemotherapy, limited to choice of one of the following seven agents: eribulin, ixabepilone, vinorelbine, gemcitabine, or a taxane (paclitaxel, docetaxel or nabpaclitaxel). TPC must consist of single-agent IV therapy (not combination therapy).
This study will randomize approximately 840 patients using a 1:1 randomization ratio. Prior to randomization of a patient, the Investigator must determine which TPC will be offered to the patient as part of the informed consent process and must enter the chosen agent into the medical chart and the central randomization system. Randomization will be stratified by geographic region (North America/Western Europe/Australia versus Eastern Europe versus Asia/Latin America/South Africa), prior use of eribulin (Yes versus No), and receptor status (Triple Negative Breast Cancer [TNBC] versus HER2+ versus Other).
Data will be collected on subsequent anticancer therapies in both treatment arms from the time patients come off the study treatment until the time of primary data analysis for OS.
An independent data monitoring committee (DMC) will review the safety of NKTR-102 treatment in the study and will assess interim efficacy data.

Intervention

In Arm A, NKTR-102 will be administered at a dose level of 145 mg/m2 on a q21d schedule as a 90-minute intravenous (IV) infusion on Day 1 of each treatment cycle. In Arm B, TPC will be administered per standard of care.

Study burden and risks

Common side effects Severe diarrhea & decreased number of

white blood cells dehydratation, fever, Nausea, vomiting,
fatigue,
abdominal pain, lack of appetite, blurred vision
Less common side effects Black or bloody stools, lightheadedness, dizziness,
faintness, constipation, loss of weight, loss of hair
Chest pain; shortness of
breath; or swelling in one of your limbs (signs of blood clots)
Uncommon/Rare side effects Kidney failure
leading to death Severe blood infections that may be life threatening and
thrombocytopenia (very low number of platelets)

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

*An eligible patient is an adult female with histologically or cytologically confirmed carcinoma of the breast. Patients may have either measurable by RECIST v1.1 or non-measurable disease, locally recurrent or metastatic disease that is not resectable or amenable to curative treatment.
Prior therapy (administered in the neoadjuvant, adjuvant and/or metastatic setting) must include an anthracycline (unless not medically appropriate or contraindicated for the patient), a taxane, and Xeloda® (capecitabine). Patients must have received a minimum of two and a maximum of five prior cytotoxic chemotherapy regimens for the treatment of breast cancer, with the last dose administered within 6 months of the date of consent for this trial. Patients must have Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 with adequate organ function. Patients with brain metastases may be eligible, provided local therapy was completed and use of corticosteroids for this indication discontinued for at least 3 weeks prior to randomization with stable brain metastases (by symptoms and imaging).
The complete list of inclusion and exclusion criteria is provided in Section 5.0 .

Exclusion criteria

*Patient who have had a last dose of IV chemotherapy within 21 days, last dose of oral chemotherapy, radiotherapy within 14 days, biological therapy with 14 days or hormonal therapy within 7 days prior to randomization. Patients who have undergone high-dose chemotherapy followed by stem cell transplantation (autologous or allogeneic). Refer to Study Reference Manual for categories of anticancer therapies;*Patient with any major surgery within 28 days prior to randomization.;*Patient with concurrent use of biologic agents for the treatment of cancer including antibodies or any investigational agent(s).;*Patient with prior treatment for cancer with a camptothecin derivative.;*Patient with chronic or acute GI disorders resulting in diarrhea of any severity grade; patients who are using chronic anti-diarrheal supportive care to control diarrhea in the 28 days prior to randomization.;*Patient received pharmacotherapy for hepatitis B or C, tuberculosis or HIV.;*Patient with known cirrhosis diagnosed with Child-PUGH Class A or higher liver disease.;*Patient with prior malignancy (other than breast cancer) except for non-melanoma skin cancer and carcinoma in situ (of the cervix or bladder), unless diagnosed and definitively treated more than 5 years prior to randomization.;*Patient requiring daily use of oxygen supplementation in the 28 days prior to randomization.;*Patients with significant cardiovascular impairment.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-07-2012
Enrollment:	10
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Abraxane
Generic name:	Paclitaxel albumin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	etirinotecan pegol
Generic name:	NKTR-102
Product type:	Medicine
Brand name:	Gemzar
Generic name:	Gemcitabine,
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Halaven
Generic name:	eribulin
Product type:	Medicine
Brand name:	Navelbine
Generic name:	Vinorelbine

Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	04-05-2012
Application type:	First submission
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	09-07-2012
Application type:	First submission
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	17-09-2012
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	23-08-2013
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	10-04-2014
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	24-10-2014
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	31-12-2014
Application type:	Amendment

Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	26-11-2015
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	22-03-2016
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)

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
EudraCT	EUCTR2011-003832-30-NL
ClinicalTrials.gov	NCT01492101
CCMO	NL40386.072.12