Optimizing neoadjuvant systemic treatment in HER2 positive breast cancer - the TRAIN-2 study

Published: 17-05-2013
Last updated: 07-02-2025

To compare the efficacy of six cycles neoadjuvant PTC plus pertuzumab preceded by either three cycles of FEC-T plus pertuzumab or three cycles of PTC plus pertuzumab in HER2 positive breast cancerSecondary objectives• To describe the safety of the...

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

Summary

ID

NL-OMON45049

Source
ToetsingOnline

Brief title
TRAIN-2

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
breast cancer; HER2 positive breast cancer

Research involving
Human

Sponsors and support

Primary sponsor: BOOG Study Center (onderzoeksgroep zonder winstoogmerk)
Source(s) of monetary or material Support: Financiering door de BOOG;die unrestricted grants krijgt van farmaceuten.

Intervention

Keyword: breast cancer, HER2 positive, neoadjuvant, pertuzumab

Outcome measures

Primary outcome

Pathologic complete response (pCR) rate at surgery

Secondary outcome

• Recurrence-free, distant metastasis-free, breast cancer specific, and overall

survival (time from randomization to event)

• Percentage of conservative surgeries carried out

• Percentage of patients with grade >2 toxicity (CTCAE v4.03)

Study description

Background summary

Upfront trastuzumab treatment is beneficial to patients with HER2 positive breast cancer. The potential synergistic cardiotoxicity of trastuzumab and anthracyclines has lead to the development of non-anthracycline containing regimens, which have shown high pathologic complete response rates. Anthracyclines remain very active in HER2 positive breast cancer, however, and increasing evidence now supports safe combination of trastuzumab and epirubicin. Therefore, the addition of epirubicine to a non-anthracycline containing regimen may further improve outcome for patients with HER2 positive breast cancer.
Several reports confirmed benefit of dual HER2 blockade by adding pertuzumab to a trastuzumab containing neo-adjuvant regimen. The results of the combined treatment in the Neosphere study, however, are similar to what we found in a phase II trial using a weekly paclitaxel, trastuzumab, carboplatin combination with pCR rates of approximately 45%. Adding pertuzumab to this regimen is likely to also increase the high pCR rate and to add substantial benefit to patients.

Study objective

To compare the efficacy of six cycles neoadjuvant PTC plus pertuzumab preceded

by either three cycles of FEC-T plus pertuzumab or three cycles of PTC plus pertuzumab in HER2 positive breast cancer
Secondary objectives
• To describe the safety of the various regimens
• To identify prognostic and predictive biomarkers for pCR

Study design

Randomized multicenter national phase III study. Randomisation:
3 cycles PTC regimen (trastuzumab 6 mg/kg (loading dose 8 mg/kg) in 250 ml NaCl 0,0%; carboplatin AUC=6 in 250 ml NaCl 0,0%; paclitaxel 80 mg/m2 in 250 ml NaCl 0,0% or dextrose 5%). PTC day 1, P day 8 of each cycle.
Plus pertuzumab 420 mg (loading dose 840 mg) on day 1 of each cycle.
Or
3 cycles FEC-T regimen (5-FU 500 mg/kg in 100 ml NaCl 0,0%); epirubicine 90 mg/m2, i.v. bolus injection; cyclophosphamide 500 mg/m2 in 100 ml NaCl 0,0%); trastuzumab 6 mg/kg (loading dose 8 mg/kg) in 250 ml NaCl 0,0%. FEC-T all components only day 1 of each cycle..
Plus pertuzumab 420 mg (loading dose 840 mg) on day 1 of each course.

After these 3 randomized cycles 3 all participants will be treated with 6 PTC cycles plus pertuzumab.
The endpoint (pCR) will be assessed at surgery (<6 weeks after the last administration of chemotherapy).
Follow-up after surgery acc. to Dutch guidelines.
394 patients.
Independent DSMB.

Intervention

Treatment with 9 cycles PTC plus pertuzumab or 3 cycles FEC-T plus pertuzumab, followed by 6 cycles PTC plus pertuzumab

Study burden and risks

Risks: Adverse events of combination chemotherapy.
Burden:
There is no neo-adjuvant standard regimen for HER2 positive tumors. Most regimens are based on those that are used as standard in the adjuvant setting, such as 4x AC folowed by 12x paclitaxel + trastuzumab or 3x FEC followed by 3x docetaxel + trastuzumab. These regimen are comparable in terms of duration and burden with the regimens used in this study.
No extra visits.
Before the start of neoadjuvant systemic therapy a tumor biopsy is taken to determine the characteristics of the tumor. Based on these characteristics (and characteristics of the patiënt and his wishes) the choice for systemic therapy

is made.
3 additional tumor biopsies for translational research before the start of the study (optional)
10 ml blood at baseline, for translational research (optional).
Sentinel node procedure conform standard.
Hematology and biochemistry prior to every cycle, not different from standard.
Imaging conform standard.
Ejection fraction assessment every 3 months, not different from standard.

Contacts

Public
BOOG Study Center (onderzoeksgroep zonder winstoogmerk)

Plesmanlaan 125
Amsterdam 1066 CX
NL
Scientific
BOOG Study Center (onderzoeksgroep zonder winstoogmerk)

Plesmanlaan 125
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NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Histologically confirmed infiltrating breast cancer.
2. Stage II or III disease.

3. Overexpression and/or amplification of HER2 in an invasive component of the core biopsy. Definitions see protocol page 14.
4. Age >=18
5. ECOG Group performance status <=1
6. LVEF >=50% measured by echocardiography, MUGA or MRI
7. No evidence of a concurrent contralateral or ipsilateral second primary infiltrating breast cancer.

Exclusion criteria

1. Previous radiation therapy or chemotherapy
2. Pregnancy, breast feeding
3. Evidence of distant metastases
4. Evidence of bilateral infiltrating breast cancer
5. Concurrent anti-cancer treatment or another investigational drug.

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:	Recruiting
Start date (anticipated):	09-12-2013
Enrollment:	430
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	5-Fluorouracil
Generic name:	5-Fluorouracil
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Carboplatin
Generic name:	carbopletin
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Epirubicine
Generic name:	epirubicin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Herceptin
Generic name:	trastuzumab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Perjeta
Generic name:	pertuzumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	17-05-2013
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	04-09-2013
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	08-11-2013

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-11-2013
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-11-2013
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-02-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-02-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-03-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-03-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-04-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	22-04-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-05-2014

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-08-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-11-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	17-11-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	05-02-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	06-02-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	26-05-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	18-11-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-11-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-01-2016

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	29-01-2016
Application type:	Amendment
Review commission:	METC NedMec

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	Clinicaltrials.gov; registratienummer n.n.b.
EudraCT	EUCTR2013-001863-21-NL
CCMO	NL44736.031.13

Study results

Results posted:	22-01-2025
Actual enrolment:	438

First publication
22-01-2025