Clinical trial results:
Phase-IIb-Study to Evaluate the Effect of a Neoadjuvant Chemotherapy with Docetaxel, Epirubicine and Cyclphosphamide (TEC) in Patients with primary HER-2 neu Negative Mammacarcinoma

Summary

EudraCT number	2008-003064-19
Trial protocol	DE
Global end of trial date	07 July 2016

Results information

Result version number	v1 (current)
This version publication date	02 August 2020
First version publication date	02 August 2020
Summary attachment (see zip file)	Study report (NeoTEC_Ergebnisbericht_Behörde_final_2.0_2020-03-

Trial information

Trial identification

Sponsor protocol code	NeoTEC

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	DRKS: DRKS00000162

Notes:

Sponsors

Sponsor organisation name	University of Leipzig
Sponsor organisation address	Ritterstr. 26, Leipzig, Germany, 04109
Public contact	Coordinating Investigator, Coordinating Investigator, St. Elisabeth-Krankenhaus Leipzig, Brustzentrum, Leipzig, 0049 341 39 59 493, Dagmar.Langanke@ek-leipzig.de
Scientific contact	Coordinating Investigator, St. Elisabeth-Krankenhaus Leipzig, Brustzentrum, Leipzig, 0049 341 39 59 493, Dagmar.Langanke@ek-leipzig.de

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 December 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 July 2016
Global end of trial reached?	Yes
Global end of trial date	07 July 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Estimation of the complete remission rate of invasive tumor cells in the breast confirmed by histological examinations, at surgery.

The treatment of the mammacarcinoma consists in this study normally on 6 chemotherapy cycles of the combination Docetaxel, Epirubicine and Cyclophosphamide (TEC-therapy). Followed by the surgery of the carcinoma, which takes place on day 28 after the last chemotherapy application, at the latest. An evaluation of the response of the treatment is performed after 2 and 4 cycles by use of palpation and mamma sonography. In case of complete remission, partial remission and no change the patient receives further two TEC cycles. In case of progress under therapy the surgery is immediately performed.

Protection of trial subjects:

During the course of the trial, every patient was monitored closely concerning the described safety parameters. Besides the documentation of adverse events , this encompasses the following parmeters:
- physical examinations
- Performancestatus (ECOG, Karnofsky Index)
- Labory parameters

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 March 2009
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 152
Worldwide total number of subjects	152
EEA total number of subjects	152

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	124
From 65 to 84 years	28
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between March 2009 and February 2011, 152 patients were recruited to the NeoTEC study in 15 Trial sites in Germany. The trial containted one arm only.

Pre-assignment

Screening details:

Eligibility for the study if:
- Women with histologically verified mamma carcinoma (assessment of estrogen and progesterone receptors, grading, negative HER-2/neu status)
- All receptor-negative mamma carcinoma starting from cT1c, all receptor-positive mamma carcinoma starting from cT3, cT4 includes inflammatory mamma carcinoma

Period 1

Period 1 title	treatment period
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Study arm

Arm description:

Chemotherapy combination of Docetaxel, Epirubicine and Cyclophosphamide with breast preserving surgery

Arm type	Experimental
Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Docetaxel 75 mg/m2 every 3 weeks for 6 cycles

Investigational medicinal product name	Epirubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Epirubicin 75 mg/m2 every 3 weeks for 6 cycles

Investigational medicinal product name	Cyclophosphamid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

500 mg/m2 every 3 weeks for 6 cycles

Number of subjects in period 1	Study arm
Started	152
Completed	148
Not completed	4
Adverse event, serious fatal	2
Consent withdrawn by subject	1
Adverse event, non-fatal	1

Period 2	
Period 2 title	Follow-up
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Follow-up

Arm description:

5 years Follow-up after study treatment

Arm type	Follow-up

No investigational medicinal product assigned in this arm

Number of subjects in period 2	Follow-up
Started	148
Completed	126
Not completed	22
change to another treating institution	4
removal to another city/contry	2
Lost to follow-up	15
termination due to psychosocial problems	1

Baseline characteristics

Reporting groups	
Reporting group title	treatment period

Reporting group description: -

Reporting group values	treatment period	Total	
Number of subjects	152	152	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	52.7		
standard deviation	± 11.2	-	
Gender categorical Units: Subjects			
Female	152	152	
Male	0	0	
ECOG Units: Subjects			
full activity	125	125	
restricted activity	23	23	
self-supply possible	3	3	
no data	1	1	
concomitant disease/s Units: Subjects			
yes	79	79	
no	73	73	
type of tumor Units: Subjects			
invasive-ductal	134	134	
invasice-lobular	12	12	
other	5	5	
no data	1	1	
receptor status Units: Subjects			
ER and PR-positive	55	55	
one of both positive	96	96	

no data	1	1	
TNM stage (sono) Units: Subjects			
T1N0M0	4	4	
T1N1M0	9	9	
T2N0M0	28	28	
T2N1M0	68	68	
T2N2M0	2	2	
T2N3M0	2	2	
T3N0M0	5	5	
T3N1M0	9	9	
T4N0M0	11	11	
T4N1M0	12	12	
T4N2M0	1	1	
no data	1	1	
menopause Units: Subjects			
yes	85	85	
no	66	66	
not available	1	1	
Body Surface Area Units: m²			
arithmetic mean	1.81		
standard deviation	± 0.19	-	
BMI Units: kg/m²			
arithmetic mean	28.3		
standard deviation	± 6.0	-	
tumor size (sono) Units: mm²			
arithmetic mean	1459		
standard deviation	± 6837	-	

Subject analysis sets

Subject analysis set title	FAS
Subject analysis set type	Full analysis

Subject analysis set description:

Since this study was one-armed, the overall description of all patients is the only useful information

Reporting group values	FAS		
Number of subjects	152		
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			

Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	52.7		
standard deviation	± 11.2		
Gender categorical Units: Subjects			
Female	152		
Male	0		
ECOG Units: Subjects			
full activity	125		
restricted activity	23		
self-supply possible	3		
no data	1		
concomitant disease/s Units: Subjects			
yes	79		
no	73		
type of tumor Units: Subjects			
invasive-ductal	134		
invasice-lobular	12		
other	5		
no data	1		
receptor status Units: Subjects			
ER and PR-positive	55		
one of both positive	96		
no data	1		
TNM stage (sono) Units: Subjects			
T1N0M0	4		
T1N1M0	9		
T2N0M0	28		
T2N1M0	68		
T2N2M0	2		
T2N3M0	2		
T3N0M0	5		
T3N1M0	9		
T4N0M0	11		
T4N1M0	12		
T4N2M0	1		
no data	1		
menopause Units: Subjects			
yes	85		
no	66		
not available	1		

Body Surface Area Units: m² arithmetic mean standard deviation	 1.81 ± 0.19		
BMI Units: kg/m² arithmetic mean standard deviation	 28.3 ± 6.0		
tumor size (sono) Units: mm² arithmetic mean standard deviation	 1459 ± 6837		

End points

End points reporting groups

Reporting group title	Study arm

Reporting group description:

Chemotherapy combination of Docetaxel, Epirubicine and Cyclophosphamide with breast preserving surgery

Reporting group title	Follow-up

Reporting group description:

5 years Follow-up after study treatment

Subject analysis set title	FAS
Subject analysis set type	Full analysis

Subject analysis set description:

Since this study was one-armed, the overall description of all patients is the only useful information

Primary: pCR b inv

End point title	pCR b inv[1]

End point description:

no mircoscopic findings of vital invasive tumor cells in resected tissues post surgery; in breast only, lymph nodes not considered

End point type	Primary

End point timeframe:

assessed after all cycles of TEC regimen applied and the following surgery

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the single-armed design no statistical analysis but the interval estimate of the end points (primary and secondary) are provided.

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	152			
Units: subjects				
complete remission	49			
incomplete remission	103			

Attachments (see zip file)	DRKS-Meldg_NeoTEC-1armig.pdf

Statistical analyses

No statistical analyses for this end point

Secondary: pCR inv

End point title	pCR inv

End point description:

neither in breast nor in axillary lymphnodes invasive rests of tumor; results of pathology; patients with premature EoT did not reach CR

End point type	Secondary

End point timeframe:
after all cycles of TEC and surgery (if applicable) = end of treatment

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	152			
Units: subjects				
premature EoT	4			
no rests	40			
rests	108			

Statistical analyses

No statistical analyses for this end point

Secondary: pCR

End point title	pCR

End point description:
neither invasive nor noninvasie rests of tumor (results of pathology)

End point type	Secondary

End point timeframe:
after EoT

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	152			
Units: subjects				
premature EoT	4			
no rests	34			
rests	114			

Statistical analyses

No statistical analyses for this end point

Secondary: cCR

End point title	cCR

End point description:
clinical response

End point type	Secondary

End point timeframe:
after EoT

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	150[2]			
Units: subjects				
complete remission	25			
partial remission	99			
minimal response	9			
no change	7			
progressive disease	5			
premature EoT	5			

Notes:
[2] - no data in 2 patients

Statistical analyses

No statistical analyses for this end point

Secondary: Regression grade (Sinn 1994)

End point title	Regression grade (Sinn 1994)

End point description:
acc. to Sinn HP et al. Geburtshilfe und Frauenheilkunde 1994:54; 552-558.

End point type	Secondary

End point timeframe:
after EoT

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	148			
Units: subjects				
grade 3/4	43			
grade<3	105			

Statistical analyses

No statistical analyses for this end point

Secondary: EFS

End point title	EFS

End point description:

End point type	Secondary

End point timeframe:
until the end of Study (60 months of FUP)

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	152			
Units: subjects				
no event	110			
relapse/ metastasis/ death	42			

Statistical analyses

No statistical analyses for this end point

Secondary: OS

End point title	OS

End point description:

End point type	Secondary

End point timeframe:
until EoS (60 months of FUP)

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	152			
Units: subjects				
survived	125			
deceased	27			

Statistical analyses

No statistical analyses for this end point

Secondary: breast-preserving surgery

End point title	breast-preserving surgery

End point description:

End point type	Secondary

End point timeframe:
after EoT

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	152			
Units: subjects				
yes	107			
no	41			
premature EoT w/o surgery	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment-associated toxicity of WHO grade >2

End point title	Treatment-associated toxicity of WHO grade >2

End point description:

End point type	Secondary

End point timeframe:
until the end of (S)AE reporting period

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	152			
Units: subjects				
Yes	110			
No	42			

Statistical analyses

No statistical analyses for this end point

Secondary: SAE occurred

End point title	SAE occurred

End point description:

End point type	Secondary

End point timeframe:
until the end of (S)AE reporting period

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	152			
Units: subjects				
yes	28			
no	124			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: tox-associated premature EoT

End point title	tox-associated premature EoT

End point description:

End point type	Other pre-specified

End point timeframe:
during chemotherapy (max. 6 cycles)

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	152			
Units: subjects				
Yes	6			
no	146			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first chemotherapy cycle up to 8 weeks after Administration of the last neoadjuvant chemotherapy cycle

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Safety

Reporting group description:

This set of patients is identical to the FAS.
The number of death refers to the entire period of observation (see sEP overall survival).

Serious adverse events	Safety		
Total subjects affected by serious adverse events			
subjects affected / exposed	28 / 152 (18.42%)		
number of deaths (all causes)	27		
number of deaths resulting from adverse events	2		
Vascular disorders			
Subclavian vein thrombosis			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Venous thrombosis limb			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haematoma			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			

subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Device dislocation			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fatigue			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General physical health deterioration			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	5 / 5		
deaths causally related to treatment / all	0 / 0		
Mucosal inflammation			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Multi-organ failure			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Pyrexia			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	2 / 152 (1.32%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	2 / 152 (1.32%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Investigations			
Haemoglobin decreased			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Craniocerebral injury			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiomyopathy			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Agranulocytosis			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Anaemia			
subjects affected / exposed	5 / 152 (3.29%)		
occurrences causally related to treatment / all	6 / 6		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			

subjects affected / exposed	3 / 152 (1.97%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
Granulocytopenia				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Leukopenia				
subjects affected / exposed	11 / 152 (7.24%)			
occurrences causally related to treatment / all	20 / 20			
deaths causally related to treatment / all	0 / 0			
Neutropenia				
subjects affected / exposed	7 / 152 (4.61%)			
occurrences causally related to treatment / all	10 / 10			
deaths causally related to treatment / all	0 / 0			
Pancytopenia				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				
subjects affected / exposed	4 / 152 (2.63%)			
occurrences causally related to treatment / all	4 / 4			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Diarrhoea				
subjects affected / exposed	4 / 152 (2.63%)			
occurrences causally related to treatment / all	4 / 4			
deaths causally related to treatment / all	0 / 0			
Enteritis				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Nausea				

subjects affected / exposed	6 / 152 (3.95%)		
occurrences causally related to treatment / all	6 / 6		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	4 / 152 (2.63%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Bone pain			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Abdominal wall abscess			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abscess			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infection			
subjects affected / exposed	3 / 152 (1.97%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		

Influenza				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Localised infection				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Mastitis				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	2 / 152 (1.32%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	1 / 1			
Metabolism and nutrition disorders				
Dehydration				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hypocalcaemia				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hypokalaemia				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Frequency threshold for reporting non-serious adverse events: 4 %

Non-serious adverse events	Safety		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	110 / 152 (72.37%)		
Vascular disorders			
Hot flush			
subjects affected / exposed	6 / 152 (3.95%)		
occurrences (all)	12		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	7 / 152 (4.61%)		
occurrences (all)	9		
Granulocytopenia			
subjects affected / exposed	40 / 152 (26.32%)		
occurrences (all)	113		
Leukopenia			
subjects affected / exposed	64 / 152 (42.11%)		
occurrences (all)	202		
Thrombocytopenia			
subjects affected / exposed	8 / 152 (5.26%)		
occurrences (all)	15		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	11 / 152 (7.24%)		
occurrences (all)	20		
Mucosal inflammation			
subjects affected / exposed	7 / 152 (4.61%)		
occurrences (all)	15		
Gastrointestinal disorders			
Intestinal obstruction			
subjects affected / exposed	4 / 152 (2.63%)		
occurrences (all)	9		
Nausea			
subjects affected / exposed	7 / 152 (4.61%)		
occurrences (all)	9		

Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all)	 35 / 152 (23.03%) 114		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported