Clinical trial results:
Tocotrienol in combination with neoadjuvant chemotherapy for women with breast cancer

Summary

EudraCT number	2016-000080-16
Trial protocol	DK
Global end of trial date	14 January 2019

Results information

Result version number	v1 (current)
This version publication date	06 January 2021
First version publication date	06 January 2021

Trial information

Trial identification

Sponsor protocol code	NeoToc

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02909751
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Vejle Hospital
Sponsor organisation address	Beriderbakken 4, Vejle, Denmark,
Public contact	Clinical Trial Unit, Oncology, Vejle Hospital, kfe.onko@rsyd.dk
Scientific contact	Clinical Trial Unit, Oncology, Vejle Hospital, kfe.onko@rsyd.dk

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	09 December 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 January 2019
Global end of trial reached?	Yes
Global end of trial date	14 January 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluation of the frequency of pathologic complete response in breast cancer patients treated with neoadjuvant chemotherapy combined with tocotrienol.

Protection of trial subjects:

Infusion and monitoring were performed according to institutional guidelines

Anamnesis and clinical examination were performed at each cycle.

Background therapy:

Antiemetic prophylaxis was given according to institutional guidelines

Evidence for comparator: -

Actual start date of recruitment	01 April 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 80
Worldwide total number of subjects	80
EEA total number of subjects	80

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)	56
From 65 to 84 years	24
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Danish women with breast cancer
Enrollment from April 2016 until July 2018

Pre-assignment

Screening details:

Women with early breast cancer assigned to neoadjuvant chemotherapy according to institutional guidelines

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A Control

Arm description:

Neoadjuvant chemotherapy according to institutional guidelines

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Arm B Experimental

Arm description:

Neoadjjuvant chemotherapy according to institutional guidelines + Tocotrienol

Arm type	Experimental
Investigational medicinal product name	Tocotrienol
Investigational medicinal product code	
Other name	E-vitamin
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

200 mg x 3

Number of subjects in period 1	Arm A Control	Arm B Experimental
Started	41	39
Completed	41	39

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial (overall period)

Reporting group description: -

Reporting group values	Overall trial (overall period)	Total	
Number of subjects	80	80	
Age categorical			
Eraly breast cancer			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	56	56	
From 65-84 years	24	24	
85 years and over	0	0	
Age continuous			
Overall trial			
Units: years			
median	51.95		
full range (min-max)	28.5 to 82.8	-	
Gender categorical			
Overall trial			
Units: Subjects			
Female	80	80	
Male	0	0	

End points

End points reporting groups

Reporting group title	Arm A Control
Reporting group description:	
Neoadjuvant chemotherapy according to institutional guidelines	
Reporting group title	Arm B Experimental
Reporting group description:	
Neoadjjuvant chemotherapy according to institutional guidelines + Tocotrienol	

Primary: Rate of patological complete response to tocotrienol combined with neoadjuvant chemotherapy in women with breast cancer

End point title	Rate of patological complete response to tocotrienol combined with neoadjuvant chemotherapy in women with breast cancer[1]
End point description:	
End point type	Primary
End point timeframe:	
At the operation after 6 months of treatment	

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: The study was not designed to compare the two treatment arms. Randomization was conducted to avoid selection bias. The study was completed according to "Simon's two-stage minimax design".
The protocol dictates further studies only in case of more than 16 patients with pathological complete response in the experimental arm.

End point values	Arm A Control	Arm B Experimental		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	38		
Units: Number	18	15		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Toxicities were recorded at baseline, before every cycle and postoperative.

Adverse event reporting additional description:

Toxicities were graded using the National Cancer Institute's Common Toxicity Criteria (NCI-CTC) version 4.0, year 2010

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.0

Reporting groups

Reporting group title	Toxicity

Reporting group description: -

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Non-serious adverse events were not part of the primary endpoint.

Serious adverse events	Toxicity		
Total subjects affected by serious adverse events			
subjects affected / exposed	20 / 80 (25.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Vascular disorders			
Embolism venous			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	3 / 80 (3.75%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Mucositis management			

subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Skin necrosis			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Febrile neutropenia			
subjects affected / exposed	11 / 80 (13.75%)		
occurrences causally related to treatment / all	0 / 13		
deaths causally related to treatment / all	0 / 0		
Fever			
subjects affected / exposed	2 / 80 (2.50%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Toxicity		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 80 (0.00%)		

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was not designed to compare the two treatment arms (control and tocotrienol). Randomisation was conducted to avoid selection bias. The study was completed according to "Simon's two-stage minimax design".

Notes: