Clinical trial results:
Tocotrienol as a nutritional supplement in patients with advanced pulmonal cancer

Summary

EudraCT number	2015-002742-32
Trial protocol	DK
Global end of trial date	09 May 2019

Results information

Result version number	v1 (current)
This version publication date	10 April 2021
First version publication date	10 April 2021

Trial information

Trial identification

Sponsor protocol code	Toco-Pulm

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02644252
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Vejle Hospital
Sponsor organisation address	Beriderbakken 4, Vejle, Denmark,
Public contact	Clinical Trial Unit, Vejle Hospital, kfe.onko@rsyd.dk
Scientific contact	Clinical Trial Unit, 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	01 May 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 May 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective is to investigate the effect of tocotrienol as a nutritional supplement in combination with first-line chemotherapy on progression free survival (PFS) in patients with advanced NSCLC

Protection of trial subjects:

Anti-emetics and analgesics administered as needed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 February 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: 78
Worldwide total number of subjects	78
EEA total number of subjects	78

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)	27
From 65 to 84 years	51
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Danish patients with advanced non-small cell lung cancer recruited in the outpatient setting.

Pre-assignment

Screening details:

Patients with locally advanced non-small cell lung cancer were screened on an outpatient basis.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Standard treatment + placebo

Arm description:

Combination chemotherapy with platinum

Arm type	Placebo
Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Day 1: Cisplatin 75 mg/m2 plus vinorelbine 25 mg/m2

Arm title	Standard treatment + tocotrienol

Arm description:

Combination chemotherapy with platinum + tocotrienol

Arm type	Experimental
Investigational medicinal product name	Tocotrienol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Daily: Tocotrienol 300 mg x 3

Number of subjects in period 1	Standard treatment + placebo	Standard treatment + tocotrienol
Started	40	38
Completed	30	30
Not completed	10	8
Consent withdrawn by subject	3	-
Adverse event, non-fatal	7	8

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial
Reporting group description: -	

Reporting group values	Overall trial	Total	
Number of subjects	78	78	
Age categorical 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)	27	27	
From 65-84 years	51	51	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	40	40	
Male	38	38	

Subject analysis sets	
Subject analysis set title	Arm A, standard + placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description: Patients with advanced lung cancer receiving standard chemotherapy + placebo	
Subject analysis set title	Arm B, standard + tocotrienol
Subject analysis set type	Intention-to-treat
Subject analysis set description: Patients with advanced lung cancer receiving standard chemotherapy + tocotrienol	

Reporting group values	Arm A, standard + placebo	Arm B, standard + tocotrienol	
Number of subjects	40	38	
Age categorical 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)	13	14	

From 65-84 years	25	26	
85 years and over	0	0	

Gender categorical Units: Subjects			
Female	18	20	
Male	20	20	

End points

End points reporting groups

Reporting group title	Standard treatment + placebo
Reporting group description: Combination chemotherapy with platinum	
Reporting group title	Standard treatment + tocotrienol
Reporting group description: Combination chemotherapy with platinum + tocotrienol	
Subject analysis set title	Arm A, standard + placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description: Patients with advanced lung cancer receiving standard chemotherapy + placebo	
Subject analysis set title	Arm B, standard + tocotrienol
Subject analysis set type	Intention-to-treat
Subject analysis set description: Patients with advanced lung cancer receiving standard chemotherapy + tocotrienol	

Primary: Progression free survival

End point title	Progression free survival[1]
End point description:	
End point type	Primary
End point timeframe: From date of randomization to progression	

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 trial was ended prematurely because of a poor accrual rate

End point values	Arm A, standard + placebo	Arm B, standard + tocotrienol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	40	38		
Units: Months				
number (not applicable)	40	38		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Before start of each treatment cycle, i.e. every three weeks.

Adverse event reporting additional description:

AEs graded according to CTCAE version 4.0

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4

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: The frequency of each non-serious event was below the 5% cut-off.

Serious adverse events	Toxicity		
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 78 (21.79%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events	0		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	5 / 78 (6.41%)		
occurrences causally related to treatment / all	5 / 5		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Infection			
subjects affected / exposed	5 / 78 (6.41%)		
occurrences causally related to treatment / all	8 / 8		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	7 / 78 (8.97%)		
occurrences causally related to treatment / all	10 / 10		
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 / 78 (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

None reported