Clinical trial results:
Phase II study of irinotecan weekly in patients with locally advanced or metastatic HER2-negative breast cancer and increased cancer cell copy number of the topoisomerase 1 gene (TOP1)"

Summary

EudraCT number	2012-002348-26
Trial protocol	DK
Global end of trial date	05 July 2016

Results information

Result version number	v1 (current)
This version publication date	27 November 2019
First version publication date	27 November 2019

Trial information

Trial identification

Sponsor protocol code	MA1214

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Danish Breast Cancer Group (DBCG)
Sponsor organisation address	Blegdamsvej 9, Copenhagen, Denmark, 2100
Public contact	Department of Oncology, Herlev Hospital, 0045 38686472, iben.kumler@regionh.dk
Scientific contact	Department of Oncology, Herlev Hospital, 0045 38686472, iben.kumler@regionh.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	12 August 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 July 2016
Global end of trial reached?	Yes
Global end of trial date	05 July 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Clinical benefit rate defined as the fraction of patients with stable disease >= 4 months, complete or partial response according to RECIST 1.1

Protection of trial subjects:

Eligibility criteria, standard safety monitoring

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 2012
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: 9
Worldwide total number of subjects	9
EEA total number of subjects	9

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)	5
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment was open at 6 sites in Denmark from October 2012 til July 2016. Patient were recruited from the pool of patients participating in a pre-screening protocol (not part of this trial) that analyses the copy number of topoisomerase 1 gene in patients with metastatic breast cancer.

Pre-assignment

Screening details:

Patients with metastatic breast cancer, negative for Her2 and increased copy number of topoisomerase 1 gene. Measurable disease according to RECIST 1.1, Max 3 or 4 (after an amendment) lines of chemotherapy for advanced or metastatic disease

Period 1

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

Arms

Arm title	Study treatment

Arm description:

Irinotecan

Arm type	Experimental
Investigational medicinal product name	Irinotecan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

75 mg/m2 given weekly for 4 weeks followed by 2 weeks without administration. In case of non-PD this treatment was repeated every 6 weeks.

Number of subjects in period 1	Study treatment
Started	9
Completed	6
Not completed	3
Adverse event, non-fatal	2
Patient wish	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	9	9	
Age categorical Units: Subjects			
Adults (18-64 years)	5	5	
From 65-84 years	4	4	
Age continuous Units: years			
median	62		
full range (min-max)	50 to 74	-	
Gender categorical Units: Subjects			
Female	9	9	
Male	0	0	

End points

End points reporting groups

Reporting group title	Study treatment
Reporting group description:	
Irinotecan	

Primary: Clinical Benefit Rate

End point title	Clinical Benefit Rate[1]
End point description:	
Patients with SD >= 4 months, PR or CR	
End point type	Primary
End point timeframe:	
Tumor assessments were done every 6th week	

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: No statistical analyses performed due to low number of patients

End point values	Study treatment			
Subject group type	Reporting group			
Number of subjects analysed	7[2]			
Units: number of patients				
Clinical Benefit	3			

Notes:

[2] - 2 patients were not evaluable

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From treatment start to 28 days after last treatment	
Assessment type	Systematic

Dictionary used	
Dictionary name	NCI-CTCAE
Dictionary version	4.0

Reporting groups	
Reporting group title	Study treatment
Reporting group description: Irinotecan	

Serious adverse events	Study treatment		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 9 (55.56%)		
number of deaths (all causes)	9		
number of deaths resulting from adverse events	0		
Vascular disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary oedema			

subjects affected / exposed	1 / 9 (11.11%)		
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	Study treatment		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 9 (100.00%)		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 9 (33.33%)		
occurrences (all)	4		
Weight loss			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	4 / 9 (44.44%)		
occurrences (all)	5		
Vomiting			
subjects affected / exposed	4 / 9 (44.44%)		
occurrences (all)	5		
Diarrhoea			
subjects affected / exposed	4 / 9 (44.44%)		
occurrences (all)	13		
Mucositis			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	3		
Constipation			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Dyspepsia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	2		
Infections and infestations			

Pneumonia subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 August 2013	Inclusion criteria amendment from maximum of previously 3 lines of treatment for advanced of metastatic disease allowed to maximum of previously 4 lines of treatment for advanced of metastatic disease allowed
03 March 2014	Starting dose of Irinotecan reduced from 100 mg/m2 to 75 mg/m2

Notes:

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.

slow recruitment, Adequate patient number not reached at premature end of trial

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/31196001