Clinical trial results:
Multicenter study of a single arm to evaluate the safety of eribulin in 3rd line chemotherapy for patients with HER2-negative metastatic or locally advanced previously treated with anthracyclines and taxanes: Onsite Study"

Summary

EudraCT number	2013-001416-30
Trial protocol	ES
Global end of trial date	31 January 2016

Results information

Result version number	v1 (current)
This version publication date	10 December 2017
First version publication date	10 December 2017
Summary attachment (see zip file)	CSR ONSITE (20170125_Informe_Final_ONSITE_v1.0_ENG.pdf) Summary of results and conclussions (20171124_Resumen Resultados_ONSITE_FINAL.pdf)

Trial information

Trial identification

Sponsor protocol code	ONCOSUR-2012-02

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	ONCOSUR 2012-02: OnSITE Study

Notes:

Sponsors

Sponsor organisation name	Fundación ONCOSUR
Sponsor organisation address	Gran Via del Marqués del Túria, 65, Valencia, Spain, 46005
Public contact	Dr. D. Luis Manuel Manso Sánchez lmanso.hdoc@salud.madrid.org, Fundación ONCOSUR, 0034 913908003, lmanso.hdoc@salud.madrid.org
Scientific contact	Dr. D. Luis Manuel Manso Sánchez , Fundación ONCOSUR, 0034 913908003, lmanso.hdoc@salud.madrid.org

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	25 January 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 January 2016
Global end of trial reached?	Yes
Global end of trial date	31 January 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety of eribulin as single agent in third-line therapy in patients with locally advanced or metastatic HER2-negative breast cancer previously treated with taxanes and anthracyclines in terms of adverse reactions.

Protection of trial subjects:

This clinical trial was approved by an Ethics Committee

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 July 2013
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	Spain: 66
Worldwide total number of subjects	66
EEA total number of subjects	66

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)	48
From 65 to 84 years	16

85 years and over	2

Subject disposition

Recruitment

Recruitment details:

The first patient was included on 17/Dic/2013.
End of patient enrollment was December 2014, but it was increased to March of 2015.

Pre-assignment

Screening details:

The total number of patients enrolled was 66, 7 out of which were screening failures.
59 patients received monotherapy with eribulin (1.23 mg/m2 in IV bolus) on Day 1 and Day 8 of each 21-day cycle. Treatment was administered until disease progression.

Pre-assignment period milestones

Number of subjects started	66
Number of subjects completed	59

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Protocol deviation: 7

Period 1

Period 1 title	Treatment and follow up (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Treatment Arm

Arm description:

All patients enrolled in the study received the same treatment, there was only a treatment arm.

Arm type	Experimental
Investigational medicinal product name	Halaven
Investigational medicinal product code	nd
Other name	eribulin mesilate, eribulin
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

All patients enrolled in the study received the same treatment, there were no different treatment groups.

The study dose of eribulin as a ready-to-take solution is 1.23 mg/m2 (equivalent to 1.4 mg/m2 of eribulin mesylate), which is administered intravenously over 2 to 5 minutes on Days 1 and 8 of each 21-day cycle.

Number of subjects in period 1[1]	Treatment Arm
Started	59
Completed	51
Not completed	8
Physician decision	1
Consent withdrawn by subject	5
Trial was closed out	1
Lack of efficacy	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 66 patients were recruited but only 59 met eligibility criteria

Baseline characteristics

Reporting groups	
Reporting group title	Treatment and follow up
Reporting group description:	
Patients meeting selection criteria which have received at least a dose of the study drug.	

Reporting group values	Treatment and follow up	Total	
Number of subjects	59	59	
Age categorical Units: Subjects			
Adults (18-64 years)	41	41	
From 65-84 years	16	16	
85 years and over	2	2	
Age continuous			
Age at treatment start			
Units: years arithmetic mean standard deviation	 57.71 ± 12.81	 -	
Gender categorical Units: Subjects			
Female	59	59	
Male	0	0	

End points

End points reporting groups

Reporting group title	Treatment Arm

Reporting group description:

All patients enrolled in the study received the same treatment, there was only a treatment arm.

Primary: Treatment duration

End point title	Treatment duration[1]

End point description:

End point type	Primary

End point timeframe:

From first to last dose 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: This is a single arm study and the application requires at least two arms for statistical analysis.

End point values	Treatment Arm			
Subject group type	Reporting group			
Number of subjects analysed	59			
Units: months				
number (not applicable)	59			

Statistical analyses

No statistical analyses for this end point

Primary: Number of patients treated

End point title	Number of patients treated[2]

End point description:

End point type	Primary

End point timeframe:

From start to end of trial

Notes:

[2] - 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: This is a single arm study and the application requires at least two arms for statistical analysis.
Moreover, this endpoint was aimed at counting the number of patients receiving the study treatment.
No other statistical analyses were specified regarding this endpoint.

End point values	Treatment Arm			
Subject group type	Reporting group			
Number of subjects analysed	59			
Units: Count				
Patients treated	59			
Patients not treated	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of patients who complied with the regimen

End point title	Number of patients who complied with the regimen[3]

End point description:

Dose delays and adjustments were allowed during the study. This endpoint focuses on patients without dose delay or adjustment.

End point type	Primary

End point timeframe:

From start to end of trial

Notes:

[3] - 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: This is a single arm study and the application requires at least two arms for statistical analysis.

End point values	Treatment Arm			
Subject group type	Reporting group			
Number of subjects analysed	59			
Units: Count				
Regime compliance	28			
Regime non-compliance	31			

Statistical analyses

No statistical analyses for this end point

Primary: Drug dose strength

End point title	Drug dose strength[4]

End point description:

Total actual dose / Total target dose where total target dose hase been defined as full dose*total number of administered cycles*2
Full dose was 1.23 mg/m2

End point type	Primary

End point timeframe:

From first to last dose of treatment

Notes:

[4] - 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: This is a single arm study and the application requires at least two arms for statistical analysis.

End point values	Treatment Arm			
Subject group type	Reporting group			
Number of subjects analysed	59			
Units: mg/m2				
number (not applicable)	59			

Statistical analyses

No statistical analyses for this end point

Primary: Starting dose

End point title	Starting dose[5]

End point description:

Starting dose should be 1.23 mg/m2 for every patient. But other doses may be 0.97 mg/m2 or 0.62 mg/m2

End point type	Primary

End point timeframe:

Time of first dose of treatment

Notes:

[5] - 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: This is a single arm study and the application requires at least two arms for statistical analysis.

End point values	Treatment Arm			
Subject group type	Reporting group			
Number of subjects analysed	59			
Units: Count				
1.23 mg/m2	59			
0.97 mg/m2	0			
0.62 mg/m2	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Since the signature of the patient information sheet and informed consent until the end of study and follow-up period.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	Safety set

Reporting group description:

Eligible patients which received at least a treatment dose.

Serious adverse events	Safety set		
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 59 (28.81%)		
number of deaths (all causes)	15		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Spinal cord compression			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Hemiparesis			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ischaemic stroke			

subjects affected / exposed	1 / 59 (1.69%)		
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	2 / 59 (3.39%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 1		
Febrile neutropenia			
subjects affected / exposed	3 / 59 (5.08%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 1		
Pancytopenia			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 59 (3.39%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 1		
Pain			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	2 / 59 (3.39%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			

subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Cough			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

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

Non-serious adverse events	Safety set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	57 / 59 (96.61%)		
Vascular disorders			
Hypertension			

subjects affected / exposed	4 / 59 (6.78%)		
occurrences (all)	4		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	32 / 59 (54.24%)		
occurrences (all)	58		
Pyrexia			
subjects affected / exposed	6 / 59 (10.17%)		
occurrences (all)	20		
Mucosal inflammation			
subjects affected / exposed	10 / 59 (16.95%)		
occurrences (all)	13		
Chest pain			
subjects affected / exposed	4 / 59 (6.78%)		
occurrences (all)	6		
Oedema peripheral			
subjects affected / exposed	4 / 59 (6.78%)		
occurrences (all)	4		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	9 / 59 (15.25%)		
occurrences (all)	15		
Catarrh			
subjects affected / exposed	6 / 59 (10.17%)		
occurrences (all)	8		
Pleural effusion			
subjects affected / exposed	4 / 59 (6.78%)		
occurrences (all)	4		
Cough			
subjects affected / exposed	4 / 59 (6.78%)		
occurrences (all)	4		
Psychiatric disorders			
Depression			
subjects affected / exposed	4 / 59 (6.78%)		
occurrences (all)	4		
Investigations			

Blood lactate dehydrogenase increased			
subjects affected / exposed	8 / 59 (13.56%)		
occurrences (all)	9		
Gamma-glutamyltransferase increased			
subjects affected / exposed	5 / 59 (8.47%)		
occurrences (all)	7		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	5		
Alanine aminotransferase increased			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	5		
Nervous system disorders			
Neuropathy peripheral			
subjects affected / exposed	15 / 59 (25.42%)		
occurrences (all)	23		
Headache			
subjects affected / exposed	9 / 59 (15.25%)		
occurrences (all)	12		
Paraesthesia			
subjects affected / exposed	8 / 59 (13.56%)		
occurrences (all)	11		
Dysgeusia			
subjects affected / exposed	6 / 59 (10.17%)		
occurrences (all)	7		
Polyneuropathy			
subjects affected / exposed	4 / 59 (6.78%)		
occurrences (all)	6		
Neurotoxicity			
subjects affected / exposed	5 / 59 (8.47%)		
occurrences (all)	5		
Dizziness			
subjects affected / exposed	2 / 59 (3.39%)		
occurrences (all)	3		
Blood and lymphatic system disorders			

Neutropenia subjects affected / exposed occurrences (all)	13 / 59 (22.03%) 20		
Leukopenia subjects affected / exposed occurrences (all)	9 / 59 (15.25%) 16		
Anaemia subjects affected / exposed occurrences (all)	9 / 59 (15.25%) 13		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	2 / 59 (3.39%) 3		
Eye disorders Lacrimation increased subjects affected / exposed occurrences (all)	3 / 59 (5.08%) 3		
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all)	20 / 59 (33.90%) 24		
Diarrhoea subjects affected / exposed occurrences (all)	9 / 59 (15.25%) 14		
Nausea subjects affected / exposed occurrences (all)	12 / 59 (20.34%) 14		
Vomiting subjects affected / exposed occurrences (all)	8 / 59 (13.56%) 10		
Abdominal pain subjects affected / exposed occurrences (all)	5 / 59 (8.47%) 5		
Dyspepsia subjects affected / exposed occurrences (all)	3 / 59 (5.08%) 4		
Abdominal pain upper			

subjects affected / exposed	3 / 59 (5.08%)		
occurrences (all)	3		
Hepatobiliary disorders			
Hypertransaminasaemia			
subjects affected / exposed	3 / 59 (5.08%)		
occurrences (all)	3		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	24 / 59 (40.68%)		
occurrences (all)	27		
Onycholysis			
subjects affected / exposed	3 / 59 (5.08%)		
occurrences (all)	6		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	9 / 59 (15.25%)		
occurrences (all)	10		
Arthralgia			
subjects affected / exposed	8 / 59 (13.56%)		
occurrences (all)	10		
Bone pain			
subjects affected / exposed	6 / 59 (10.17%)		
occurrences (all)	6		
Pain in extremity			
subjects affected / exposed	6 / 59 (10.17%)		
occurrences (all)	6		
Musculoskeletal chest pain			
subjects affected / exposed	3 / 59 (5.08%)		
occurrences (all)	5		
Neck pain			
subjects affected / exposed	3 / 59 (5.08%)		
occurrences (all)	3		
Myalgia			
subjects affected / exposed	3 / 59 (5.08%)		
occurrences (all)	3		
Muscular weakness			

subjects affected / exposed occurrences (all)	2 / 59 (3.39%) 3		
Infections and infestations Respiratory tract infection subjects affected / exposed occurrences (all) Influenza subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	 5 / 59 (8.47%) 5 3 / 59 (5.08%) 5 3 / 59 (5.08%) 3		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) Hyperglycaemia subjects affected / exposed occurrences (all) Hypercholesterolaemia subjects affected / exposed occurrences (all)	 12 / 59 (20.34%) 15 5 / 59 (8.47%) 6 3 / 59 (5.08%) 3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 February 2014	Clarify inclusion and exclusion criteria
02 March 2015	New data to be recorded during the follow-up visit.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported