Clinical trial results:
Prospective evaluation of the predictive value of a circulating tumor cell (CTC) sensitivity profile to Cisplatin chemotherapy in metastatic breast cancer patients

Summary

EudraCT number	2012-005395-34
Trial protocol	NL
Global end of trial date	20 September 2019

Results information

Result version number	v2 (current)
This version publication date	23 March 2021
First version publication date	25 February 2021
Version creation reason	• Changes to summary attachments Amendment to protocol added

Trial information

Trial identification

Sponsor protocol code	CTC-cDDP

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	tiralregister.nl: NTR4046

Notes:

Sponsors

Sponsor organisation name	Erasmus MC Cancer Institute
Sponsor organisation address	Doctor Molewaterplein 40, Rotterdam, Netherlands,
Public contact	Trial Office Daniel den Hoed, Erasmus MC, +31 107041301, trialbureau@erasmusmc.nl
Scientific contact	Trial Office Daniel den Hoed, Erasmus MC, +31 107041301, trialbureau@erasmusmc.nl

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	05 May 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 February 2019
Global end of trial reached?	Yes
Global end of trial date	20 September 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To establish whether single-agent cDDP yields a response rate considered worthwhile to be further explored in metastatic breast cancer patients with more than 5 CTCs/7.5 mL of blood harboring a favorable CTC cDDP-sensitivity profile.

Protection of trial subjects:

Subjects can leave the study at any time for any reason if they wish to do so without any consequences. The local investigator can decide to withdraw a subject from the study for urgent medical reasons. Also all medication needed to prevent or diminish side effects can be used. Furthermore, (serious) adverse events are collected and frequently evaluated.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 June 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	Belgium: 5
Country: Number of subjects enrolled	Netherlands: 67
Worldwide total number of subjects	72
EEA total number of subjects	72

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)	53
From 65 to 84 years	19

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

first inclusion 07-06-2013, last inclusion 28-09-2018

Pre-assignment

Screening details:

Female patients with metastatic breast cancer who have been pretreated with at least anthracycline- and taxane-based chemotherapy

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	Complete set
Arm description: -	
Arm type	cDDP
Investigational medicinal product name	cisplatin
Investigational medicinal product code	ATC L01XA01
Other name	cDDP
Pharmaceutical forms	Suspension for injection
Routes of administration	Intravenous use

Dosage and administration details:

all patients will receive 3-weekly cDDP at 70 mg/m2 for a maximum of 6 cycles.

Number of subjects in period 1	Complete set
Started	72
Completed	65
Not completed	7
did not receive cDDP therapy	2
Protocol deviation	5

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	72	72	
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)	53	53	
From 65-84 years	19	19	
85 years and over	0	0	
Age continuous Units: years			
median	56		
full range (min-max)	34 to 76	-	
Gender categorical Units: Subjects			
Female	72	72	
Male	0	0	

End points

End points reporting groups	
Reporting group title	Complete set
Reporting group description: -	
Subject analysis set title	CTC-cDDP sensitive patients
Subject analysis set type	Per protocol
Subject analysis set description: CTC-cDDP sensitive patients	
Subject analysis set title	CTC-cDDP non sensitive patients
Subject analysis set type	Per protocol
Subject analysis set description: CTC-cDDP non sensitive patients (resistant patients)	

Primary: Response rate	
End point title	Response rate
End point description: Number of patients with response after 4 cycles of cDDP	
End point type	Primary
End point timeframe: From start of cDDP therapy till progression	

End point values	CTC-cDDP sensitive patients	CTC-cDDP non sensitive patients		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	48		
Units: response				
number (not applicable)	0	3		

Statistical analyses

Statistical analysis title	Response rate
Comparison groups	CTC-cDDP non sensitive patients v CTC-cDDP sensitive patients
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.561 [1]
Method	Chi-squared

Notes:

[1] - fisher exact since 2 cells have count less than 5

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

From first inclusion till finishing follow up of last inclusion (07-06-2013 till 28-02-2019)

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4

Reporting groups

Reporting group title	All patients

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: as mentioned in the patient section, non-serious adverse events are not collected and therefore, not displayed here

Serious adverse events	All patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	38 / 72 (52.78%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
tumor pain			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypotension			
subjects affected / exposed	2 / 72 (2.78%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
thromboembolic event			
subjects affected / exposed	3 / 72 (4.17%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
fever			

subjects affected / exposed	3 / 72 (4.17%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Fatigue				
subjects affected / exposed	2 / 72 (2.78%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Dyspnoea				
subjects affected / exposed	5 / 72 (6.94%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	3 / 72 (4.17%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Cough				
subjects affected / exposed	2 / 72 (2.78%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	2 / 72 (2.78%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pleuritic pain				
subjects affected / exposed	1 / 72 (1.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
hoarseness				
subjects affected / exposed	1 / 72 (1.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				

Agitation			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Congestive cardiomyopathy			
subjects affected / exposed	2 / 72 (2.78%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Palpitations			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
reversible posterior leukoencephalopathy syndrome			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	5 / 72 (6.94%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			

subjects affected / exposed	3 / 72 (4.17%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypomagnesaemia			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hypocalcaemia			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
hearing loss			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			

posterior vitreous detachment				
subjects affected / exposed	1 / 72 (1.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	3 / 72 (4.17%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
nausea				
subjects affected / exposed	12 / 72 (16.67%)			
occurrences causally related to treatment / all	5 / 15			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	3 / 72 (4.17%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Ascites				
subjects affected / exposed	2 / 72 (2.78%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
bleeding lower tr. dig.				
subjects affected / exposed	1 / 72 (1.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
mucositis				
subjects affected / exposed	1 / 72 (1.39%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatic failure				
subjects affected / exposed	1 / 72 (1.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Constipation				

subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Incontinence			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
acute kidney failure			
subjects affected / exposed	9 / 72 (12.50%)		
occurrences causally related to treatment / all	4 / 10		
deaths causally related to treatment / all	0 / 0		
Haematuria			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Incontinence			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	4 / 72 (5.56%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
leg pain			
subjects affected / exposed	2 / 72 (2.78%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

thorax pain				
subjects affected / exposed	1 / 72 (1.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
implending femur fracture				
subjects affected / exposed	1 / 72 (1.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
muscle weakness right arm				
subjects affected / exposed	1 / 72 (1.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Urinary tract infection				
subjects affected / exposed	2 / 72 (2.78%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	1 / 72 (1.39%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Hypercalcaemia				
subjects affected / exposed	3 / 72 (4.17%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Hyponatraemia				
subjects affected / exposed	3 / 72 (4.17%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Hypokalaemia				
subjects affected / exposed	4 / 72 (5.56%)			
occurrences causally related to treatment / all	2 / 4			
deaths causally related to treatment / all	0 / 0			

anorexia			
subjects affected / exposed	2 / 72 (2.78%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Dehydration			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Weight decreased			
subjects affected / exposed	1 / 72 (1.39%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	All patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 72 (0.00%)		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 March 2014	Adding new centers to the study and therefore changing the EudraCT form and ABR form
11 July 2014	Adding new center to the study
11 October 2016	Change local researcher of one of the participating hospitals

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported