Clinical trial results:
Phase II study of cabazitaxel as 2nd-line treatment in patients with HER-2 negative metastatic breast cancer previously treated with taxanes.

Summary

EudraCT number	2011-003625-97
Trial protocol	GR
Global end of trial date	20 July 2017

Results information

Result version number	v1 (current)
This version publication date	04 October 2019
First version publication date	04 October 2019

Trial information

Trial identification

Sponsor protocol code	HE11B11

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01693549
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Hellenic Cooperative Oncology Group
Sponsor organisation address	Hatzikostanti 18, Athens, Greece, 11524
Public contact	Clinical Trials, Hellenic Cooperative Oncology Group, hecogoff@otenet.gr
Scientific contact	Clinical Trials, Hellenic Cooperative Oncology Group, hecogoff@otenet.gr

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	27 November 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 July 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to assess the clinical activity of cabazitaxel regarding the objective response rate (ORR).

Protection of trial subjects:

The study was conducted in accordance with the ethical principles of the Declaration of Helsinki, the Good Clinical Practice guidelines and the local regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 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	Greece: 84
Worldwide total number of subjects	84
EEA total number of subjects	84

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)	63
From 65 to 84 years	21
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled in the study from 3 October 2012 until 11 November 2016 from 15 sites in Greece.

Pre-assignment

Screening details:

Patients were screened for eligibility before entering the study and signed the informed consent form which was obtained before any study procedure.

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	Cabazitaxel
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Cabazitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cabazitaxel was administered on day 1 of each cycle, at a dose of 25 mg/m2 intravenously in 1 hour, every 21 days.

Number of subjects in period 1	Cabazitaxel
Started	84
Completed	25
Not completed	59
Adverse event, serious fatal	2
Physician decision	2
Consent withdrawn by subject	3
Adverse event, non-fatal	4
Death	1
Other	3
Progression	44

Baseline characteristics

Reporting groups

Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	84	84	
Age categorical Units: Subjects			
Adults (18-64 years)	63	63	
From 65-84 years	21	21	
85 years and over	0	0	
Age continuous Units: years			
median	57.5		
full range (min-max)	33.5 to 74.9	-	
Gender categorical Units: Subjects			
Female	84	84	
Male	0	0	

Subject analysis sets

Subject analysis set title	Response evaluable population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Analysis of response was additionally conducted in the subgroup of patients with measurable disease who received at least 2 cycles of cabazitaxel. In addition, cases with early disease progression (prior to cycle 2) were not excluded from this subgroup of patients.

Reporting group values	Response evaluable population		
Number of subjects	78		
Age categorical Units: Subjects			
Adults (18-64 years)	59		
From 65-84 years	19		
85 years and over			
Age continuous Units: years			
median	57.5		
full range (min-max)	33.5 to 74.9		
Gender categorical Units: Subjects			
Female	78		
Male	0		

End points

End points reporting groups

Reporting group title	Cabazitaxel
Reporting group description: -	
Subject analysis set title	Response evaluable population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Analysis of response was additionally conducted in the subgroup of patients with measurable disease who received at least 2 cycles of cabazitaxel. In addition, cases with early disease progression (prior to cycle 2) were not excluded from this subgroup of patients.

Primary: Objective response rate

End point title	Objective response rate[1]

End point description:

The primary endpoint of the clinical study was to evaluate the activity of cabazitaxel as 2nd line treatment in HER2-negative metastatic breast cancer patients.The objective response rate (ORR) was assessed according to response evaluation criteria in solid tumours (RECIST) guidelines.

End point type	Primary

End point timeframe:

Tumor response was assessed every 8 weeks through week 24 and every 3 months thereafter, until treatment completion

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: Since this was a single arm study and all patients received the same treatment, no comparisons between groups were applicable. The percentage of patients
with a confirmed complete or partial response was estimated using descriptive statistics in the entire study cohort and in the response evaluable population.

End point values	Cabazitaxel	Response evaluable population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	84	78		
Units: percentage of patients with CR or PR				
Objective response rate (%)	23	24		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival

End point description:

Overall survival was calculated from the date of patient's entry into the study to the date of death. Alive patients were censored at the date of their last contact.

End point type	Secondary

End point timeframe:

Patients were followed-up for a median of 32.2 months (95% CI 21.02-40.07).

End point values	Cabazitaxel			
Subject group type	Reporting group			
Number of subjects analysed	84			
Units: months				
median (confidence interval 95%)	15.2 (11.21 to 21.54)			

Attachments (see zip file)	Kaplan-Meier with respect to OS/KM_OS.tif

Statistical analyses

No statistical analyses for this end point

Secondary: Safety profile

End point title	Safety profile

End point description:

The safety profile was assessed in the safety population consisting of all enrolled patients that received at least one dose of the study drug.

End point type	Secondary

End point timeframe:

All AEs were followed until resolution or until 30 days after the last dose of study treatment.

End point values	Cabazitaxel			
Subject group type	Reporting group			
Number of subjects analysed	84			
Units: number of patients				
Any adverse event	72			
Adverse events ≥ grade 3	36			
Adverse events ≥ grade 4	17			
Fatal adverse events	2			
Serious adverse events	20			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival

End point title	Progression Free Survival

End point description:

Progression free survival (PFS) was calculated from the date of study entry to the date of first documented progression, death from any cause or last contact.

End point type	Secondary

End point timeframe:

Patients were followed up for a median of 32.2 months (95% CI 21.02-40.07).

End point values	Cabazitaxel			
Subject group type	Reporting group			
Number of subjects analysed	84			
Units: months				
median (confidence interval 95%)	3.7 (2.23 to 4.36)			

Attachments (see zip file)	Kaplan-Meier curve with respect to PFS./KM_PFS.tiff

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response

End point title	Duration of response

End point description:

Duration of response (DOR) was measured as the time interval between the date of onset of a complete or partial response and the date of progression, death from any cause or last contact, whichever occurred first.

End point type	Secondary

End point timeframe:

Tumor response was assessed every 8 weeks though week 24 and every 3 months thereafter, until treatment completion.

End point values	Cabazitaxel			
Subject group type	Reporting group			
Number of subjects analysed	19[2]			
Units: months				
median (full range (min-max))	5.6 (0.7 to 51.3)			

Notes:

[2] - DOR was only analysed for patients that achieved a complete or partial response.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

pEvaluation of Adverse Events will be performed every 21 days (per cycle) during treatment assessed up to 30 months.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Cabazitaxel

Reporting group description:

Cabazitaxel (XRP6258) will be administered on day 1 each cycle, every 21 days, at a dose of 25 mg/m^2 by i.v. route in 1 hour. Treatment could be continued until patient's consent withdrawal, intolerable toxicity or documented disease progression.

Serious adverse events	Cabazitaxel		
Total subjects affected by serious adverse events			
subjects affected / exposed	20 / 84 (23.81%)		
number of deaths (all causes)	55		
number of deaths resulting from adverse events	2		
Investigations			
Neutrophil count decreased			
subjects affected / exposed	3 / 84 (3.57%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Thrombosis			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebral disorder			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Headache			

subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	6 / 84 (7.14%)		
occurrences causally related to treatment / all	8 / 8		
deaths causally related to treatment / all	0 / 1		
Anaemia			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Epigastric pain			

subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abdominal pain				
subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neutropenic enterocolitis				
subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Dyspnoea exacerbated				
subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	2 / 84 (2.38%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Hematuria				
subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Acute kidney injury				
subjects affected / exposed	1 / 84 (1.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Impaired renal function			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Skin infection			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Cabazitaxel		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	69 / 84 (82.14%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	6 / 84 (7.14%)		
occurrences (all)	8		
General disorders and administration site conditions			
Edema limbs			
subjects affected / exposed	2 / 84 (2.38%)		
occurrences (all)	2		
Fatigue			
subjects affected / exposed	26 / 84 (30.95%)		
occurrences (all)	35		
Fever			

subjects affected / exposed	5 / 84 (5.95%)		
occurrences (all)	11		
Flu like symptoms			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences (all)	1		
Gait disturbance			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences (all)	1		
Pain - other	Additional description: due to right ureteral dilatation		
subjects affected / exposed	1 / 84 (1.19%)		
occurrences (all)	1		
Axillary pain			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences (all)	1		
Pain	Additional description: other - In right and left supraclavicular area		
subjects affected / exposed	1 / 84 (1.19%)		
occurrences (all)	1		
Immune system disorders			
Allergic reaction			
subjects affected / exposed	2 / 84 (2.38%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences (all)	1		
Epistaxis			
subjects affected / exposed	3 / 84 (3.57%)		
occurrences (all)	3		
Nasal congestion			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences (all)	1		
Voice alteration			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences (all)	1		
Psychiatric disorders			

Personality disorder			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences (all)	1		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	5 / 84 (5.95%)		
occurrences (all)	5		
Alkaline phosphatase increased			
subjects affected / exposed	9 / 84 (10.71%)		
occurrences (all)	9		
Aspartate aminotransferase increased			
subjects affected / exposed	12 / 84 (14.29%)		
occurrences (all)	14		
Blood bilirubin increased			
subjects affected / exposed	6 / 84 (7.14%)		
occurrences (all)	6		
Cholesterol high			
subjects affected / exposed	9 / 84 (10.71%)		
occurrences (all)	11		
CPK increased			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences (all)	1		
Creatinine increased			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences (all)	1		
GGT increased			
subjects affected / exposed	15 / 84 (17.86%)		
occurrences (all)	23		
LDH increased			
subjects affected / exposed	5 / 84 (5.95%)		
occurrences (all)	9		
Lymphocyte count decreased			
subjects affected / exposed	8 / 84 (9.52%)		
occurrences (all)	17		
Neutrophil count decreased			

subjects affected / exposed	24 / 84 (28.57%)		
occurrences (all)	44		
Platelet count decreased			
subjects affected / exposed	19 / 84 (22.62%)		
occurrences (all)	48		
White blood cell count decreased			
subjects affected / exposed	27 / 84 (32.14%)		
occurrences (all)	62		
Lymphocyte count increased			
subjects affected / exposed	2 / 84 (2.38%)		
occurrences (all)	5		
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 84 (2.38%)		
occurrences (all)	2		
Headache			
subjects affected / exposed	4 / 84 (4.76%)		
occurrences (all)	13		
Loss of consciousness			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences (all)	1		
Peripheral motor neuropathy			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences (all)	1		
Peripheral sensory neuropathy			
subjects affected / exposed	10 / 84 (11.90%)		
occurrences (all)	13		
Somnolence			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	36 / 84 (42.86%)		
occurrences (all)	68		
Lymphopenia			

subjects affected / exposed	2 / 84 (2.38%)		
occurrences (all)	2		
Leukocytosis			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences (all)	1		
Eye disorders			
Blurred vision			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences (all)	1		
Eye pain			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences (all)	1		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	4 / 84 (4.76%)		
occurrences (all)	10		
Diarrhoea			
subjects affected / exposed	15 / 84 (17.86%)		
occurrences (all)	19		
Flatulence			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences (all)	1		
Gastrointestinal pain			
subjects affected / exposed	7 / 84 (8.33%)		
occurrences (all)	11		
Mucositis oral			
subjects affected / exposed	3 / 84 (3.57%)		
occurrences (all)	3		
Nausea			
subjects affected / exposed	10 / 84 (11.90%)		
occurrences (all)	13		
Vomiting			
subjects affected / exposed	7 / 84 (8.33%)		
occurrences (all)	8		
Skin and subcutaneous tissue disorders			

Alopecia subjects affected / exposed occurrences (all)	8 / 84 (9.52%) 8		
Nail discoloration subjects affected / exposed occurrences (all)	1 / 84 (1.19%) 1		
Nail loss subjects affected / exposed occurrences (all)	1 / 84 (1.19%) 1		
Palmar-plantar erythrodysaesthesia syndrome subjects affected / exposed occurrences (all)	2 / 84 (2.38%) 2		
Pruritus subjects affected / exposed occurrences (all)	1 / 84 (1.19%) 1		
Redness subjects affected / exposed occurrences (all)	1 / 84 (1.19%) 1		
Onycholysis subjects affected / exposed occurrences (all)	1 / 84 (1.19%) 1		
Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all)	4 / 84 (4.76%) 6		
Proteinuria subjects affected / exposed occurrences (all)	3 / 84 (3.57%) 3		
Renal colic subjects affected / exposed occurrences (all)	1 / 84 (1.19%) 1		
Musculoskeletal and connective tissue disorders Low back pain subjects affected / exposed occurrences (all)	1 / 84 (1.19%) 1		
Psoriatic arthritis			

subjects affected / exposed	1 / 84 (1.19%)		
occurrences (all)	1		
Arthralgia			
subjects affected / exposed	3 / 84 (3.57%)		
occurrences (all)	3		
Bone pain			
subjects affected / exposed	9 / 84 (10.71%)		
occurrences (all)	17		
Buttock pain			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences (all)	1		
Muscle weakness	Additional description: Lower limb		
subjects affected / exposed	1 / 84 (1.19%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	2 / 84 (2.38%)		
occurrences (all)	2		
Infections and infestations			
Bladder infection			
subjects affected / exposed	2 / 84 (2.38%)		
occurrences (all)	3		
Flu			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences (all)	4		
Viral infection			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences (all)	3		
Laryngitis			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	4 / 84 (4.76%)		
occurrences (all)	5		
Urinary tract infection			
subjects affected / exposed	2 / 84 (2.38%)		
occurrences (all)	2		

Pyuria			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Polydipsia			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences (all)	1		
Anorexia			
subjects affected / exposed	4 / 84 (4.76%)		
occurrences (all)	4		
Hypercalcaemia			
subjects affected / exposed	3 / 84 (3.57%)		
occurrences (all)	3		
Hyperglycaemia			
subjects affected / exposed	10 / 84 (11.90%)		
occurrences (all)	14		
Hyperkalaemia			
subjects affected / exposed	2 / 84 (2.38%)		
occurrences (all)	8		
Hypermagnesaemia			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences (all)	2		
Hypernatraemia			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences (all)	1		
Hypertriglyceridaemia			
subjects affected / exposed	9 / 84 (10.71%)		
occurrences (all)	11		
Hyperuricaemia			
subjects affected / exposed	8 / 84 (9.52%)		
occurrences (all)	9		
Hypoalbuminaemia			
subjects affected / exposed	3 / 84 (3.57%)		
occurrences (all)	3		
Hypocalcaemia			

subjects affected / exposed	4 / 84 (4.76%)		
occurrences (all)	8		
Hypoglycaemia			
subjects affected / exposed	3 / 84 (3.57%)		
occurrences (all)	5		
Hypokalaemia			
subjects affected / exposed	4 / 84 (4.76%)		
occurrences (all)	5		
Hypomagnesaemia			
subjects affected / exposed	1 / 84 (1.19%)		
occurrences (all)	2		
Hyponatraemia			
subjects affected / exposed	3 / 84 (3.57%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 July 2013	Primary prophylaxis with Pegfilgrastim was recommended in all patients, due to the high incidence of Cabazitaxel-associated neutropenia.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported