Clinical trial results:
Essai multicentrique de phase II évaluant l'efficacité et la tolérance de l'association de bevacizumab, paclitaxel et capecitabine en première ligne chez des patientes atteintes de cancer du sein métastatique ou localement avancé récepteurs triples negatifs .

Summary

EudraCT number	2009-016708-21
Trial protocol	FR
Global end of trial date	03 February 2016

Results information

Result version number	v1 (current)
This version publication date	09 July 2022
First version publication date	09 July 2022

Trial information

Trial identification

Sponsor protocol code	GINECO-BR108

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	ARCAGY-GYNECO
Sponsor organisation address	HOPITAL HOTEL DIEU-B2 5eme étage 1 Place du Parvis de Notre Dame, PARIS, France, 75181 cedex 4
Public contact	S. Armanet, ARCAGY, reglementaire@arcagy.org
Scientific contact	Dr Rémy LARGILLIER , Centre Azuréen de Cancérologie 1 Place du Dr Jean-Luc Broquerie 06250 Mougins, +33 492923739, rlargillier@wanadoo.fr

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	17 May 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 May 2013
Global end of trial reached?	Yes
Global end of trial date	03 February 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Le recours à l'association de paclitaxel en administration hebdomadaire à 80 mg par mètre carré trois semaines sur quatre et de la capécitabine cinq jours sur sept à la dose de 1600 mg par mètre carré par jour avec une thérapeutique anti-angiogénique telle que le bevacizumab pourrait permettre d'optimiser le schéma thérapeutique aussi bien en terme de réponse que de survie sans rechute avec un profil de tolérance acceptable dans la population des patientes atteintes d'un cancer du sein métastatique « triple négatif ».
Objectif Primaire : Taux de réponse

Protection of trial subjects:

Cette étude a été menée selon les recommandations :
- de la loi Huriet (n°88-1138) du 20 décembre 1988 relative à la Protection des Personnes se prêtant à la Recherche Biomédicale et modifiée par la loi de santé publique (n°2004-806) du 9 août 2004,
- de la loi Informatique et Libertés n°78-17 modifiée par la loi n° 2004-801 du 6 août 2004 relative à la protection des personnes physiques à l'égard des traitements de données à caractère personnel,
- de la loi Bioéthique n° 2004-800 du 6 août 2004,
- des bonnes pratiques cliniques de la conférence internationale d'harmonisation (ICH-E6 du 17/07/1996),
- de la direction européenne (2001/20/CE) sur la conduite des essais cliniques.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 April 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Scientific research
Long term follow-up duration	24 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 62
Worldwide total number of subjects	62
EEA total number of subjects	62

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)	46
From 65 to 84 years	16
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Eligible patients were aged 18 years with an Eastern Cooperative Oncology Group performance status of 0 or 1 and measurable triple-negative LA/MBC (negative estrogen receptor, progesterone receptor, and HER2 status).

Period 1

Period 1 title	OVERALL TRIAL (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Paclitaxel/Capecitabine/Bevacizumab

Arm description:

Combination of bevacizumab with weekly paclitaxel and capecitabine

Arm type	Experimental
Investigational medicinal product name	Bevacizumab
Investigational medicinal product code	R04876646
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

10 mg/kg at Day 1 and Day 15 (on 28 days cycle)

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

80 mg/m2 at Day 1, Day 8 and Day 15 (on 28 days cycle)

Investigational medicinal product name	Capecitabine Xeloda
Investigational medicinal product code	3657456
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

1600 mg/m2/day from Day 1 to Day 5, weeks 1, 2 and 3 (on 28 days cycle)

Number of subjects in period 1	Paclitaxel/Capecitabine/Bevacizumab
Started	62
Completed	62

Baseline characteristics

Reporting groups

Reporting group title	OVERALL TRIAL (overall period)

Reporting group description: -

Reporting group values	OVERALL TRIAL (overall period)	Total	
Number of subjects	62	62	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	55.7		
standard deviation	± 13.7	-	
Gender categorical Units: Subjects			
Female	62	62	
Male	0	0	

End points

End points reporting groups

Reporting group title	Paclitaxel/Capecitabine/Bevacizumab
Reporting group description: Combination of bevacizumab with weekly paclitaxel and capecitabine	
Subject analysis set title	Response analysis
Subject analysis set type	Per protocol
Subject analysis set description: Efficacy analyis for objective response rate (ORR). 5 patients non analysable for ORR because of absence of mesurable lesion at inclusion	
Subject analysis set title	Survival analysis
Subject analysis set type	Intention-to-treat
Subject analysis set description: Population for survival analysis	

Primary: Ojective response rate (ORR)

End point title	Ojective response rate (ORR)[1]
End point description:	
End point type	Primary
End point timeframe: during the study	

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: Only descriptive statistics

End point values	Response analysis			
Subject group type	Subject analysis set			
Number of subjects analysed	57			
Units: number				
Response (CR or PR)	44			
No response (SD or PD)	13			

Statistical analyses

No statistical analyses for this end point

Primary: Response duration

End point title	Response duration[2]
End point description:	
End point type	Primary
End point timeframe: During the study	

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: Only descriptive statistics

End point values	Response analysis			
Subject group type	Subject analysis set			
Number of subjects analysed	57			
Units: month				
median (full range (min-max))	5.6 (1.3 to 27.6)			

Statistical analyses

No statistical analyses for this end point

Primary: Response

End point title	Response[3]

End point description:

End point type	Primary

End point timeframe:

During the study

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: Only descriptive statistics

End point values	Response analysis			
Subject group type	Subject analysis set			
Number of subjects analysed	57			
Units: number				
Complete response (CR)	11			
Partial response (PR)	33			
Stable disease (SD)	8			
Progressive disease (PD)	5			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival (PFS)

End point title	Progression free survival (PFS)

End point description:

End point type	Secondary

End point timeframe:
During the study

End point values	Survival analysis			
Subject group type	Subject analysis set			
Number of subjects analysed	62			
Units: month				
median (confidence interval 95%)	7.6 (6.3 to 9.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS)

End point title	Overall survival (OS)

End point description:

End point type	Secondary

End point timeframe:
During the study

End point values	Survival analysis			
Subject group type	Subject analysis set			
Number of subjects analysed	62			
Units: month				
median (confidence interval 95%)	19.2 (17.4 to 20.9)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Until the end of the treatment period

Adverse event reporting additional description:

"Subjects affected number" is also reported in "occurences all number" as thi"occurences all number" is not calculated

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.03

Reporting groups

Reporting group title	Paclitaxel/Capecitabine/Bevacizumab

Reporting group description:

Combination of bevacizumab with weekly paclitaxel and capecitabine

Serious adverse events	Paclitaxel/Capecitabine/Bevacizumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	32 / 62 (51.61%)		
number of deaths (all causes)	43		
number of deaths resulting from adverse events	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to meninges			
subjects affected / exposed	2 / 62 (3.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Aneurysm			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Epistaxis			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			

subjects affected / exposed	1 / 62 (1.61%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Retinal artery occlusion				
subjects affected / exposed	1 / 62 (1.61%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Thrombosis				
subjects affected / exposed	3 / 62 (4.84%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
Surgical and medical procedures				
Cementoplasty				
subjects affected / exposed	1 / 62 (1.61%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Death				
subjects affected / exposed	1 / 62 (1.61%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 1			
Disease progression				
subjects affected / exposed	1 / 62 (1.61%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Mucosal inflammation				
subjects affected / exposed	2 / 62 (3.23%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	1 / 1			
Multi-organ failure				
subjects affected / exposed	1 / 62 (1.61%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			

Pain				
subjects affected / exposed	1 / 62 (1.61%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Performance status decreased				
subjects affected / exposed	1 / 62 (1.61%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Hypersensitivity				
subjects affected / exposed	1 / 62 (1.61%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Transaminases increased				
subjects affected / exposed	1 / 62 (1.61%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Fall				
subjects affected / exposed	1 / 62 (1.61%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Implant site infection				
subjects affected / exposed	1 / 62 (1.61%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injection site infection				
subjects affected / exposed	1 / 62 (1.61%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal fracture				

subjects affected / exposed	1 / 62 (1.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	2 / 62 (3.23%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Cardio-respiratory arrest			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Neuropathy peripheral			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Disseminated intravascular coagulation			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	2 / 62 (3.23%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Anal fistula			

subjects affected / exposed	1 / 62 (1.61%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	1 / 62 (1.61%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	1 / 62 (1.61%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastritis				
subjects affected / exposed	1 / 62 (1.61%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Hepatocellular injury				
subjects affected / exposed	2 / 62 (3.23%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Nail disorder				
subjects affected / exposed	1 / 62 (1.61%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Onycholysis				
subjects affected / exposed	3 / 62 (4.84%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
Palmar-plantar erythrodysaesthesia syndrome				
subjects affected / exposed	2 / 62 (3.23%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			

Infections and infestations			
Abscess			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infection			
subjects affected / exposed	3 / 62 (4.84%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Meningitis viral			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Food intolerance			
subjects affected / exposed	1 / 62 (1.61%)		
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	Paclitaxel/Capecitabine/Bevacizumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	62 / 62 (100.00%)		
Vascular disorders			
lymphedema			
subjects affected / exposed	14 / 62 (22.58%)		
occurrences (all)	14		
Thrombosis			
subjects affected / exposed	5 / 62 (8.06%)		
occurrences (all)	5		
Hypertension			
subjects affected / exposed	49 / 62 (79.03%)		
occurrences (all)	49		
Hot flush			

subjects affected / exposed	5 / 62 (8.06%)		
occurrences (all)	5		
Epistaxis			
subjects affected / exposed	32 / 62 (51.61%)		
occurrences (all)	32		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	56 / 62 (90.32%)		
occurrences (all)	56		
fever			
subjects affected / exposed	15 / 62 (24.19%)		
occurrences (all)	15		
weight loss			
subjects affected / exposed	8 / 62 (12.90%)		
occurrences (all)	8		
Pain			
subjects affected / exposed	52 / 62 (83.87%)		
occurrences (all)	52		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	11 / 62 (17.74%)		
occurrences (all)	11		
Dyspnoea			
subjects affected / exposed	15 / 62 (24.19%)		
occurrences (all)	15		
Psychiatric disorders			
Mood altered			
subjects affected / exposed	14 / 62 (22.58%)		
occurrences (all)	14		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	4 / 62 (6.45%)		
occurrences (all)	3		
Nervous system disorders			
Paresthesia / Dysesthesia			

subjects affected / exposed	36 / 62 (58.06%)		
occurrences (all)	36		
Peripheral motor			
subjects affected / exposed	5 / 62 (8.06%)		
occurrences (all)	5		
Dizziness			
subjects affected / exposed	9 / 62 (14.52%)		
occurrences (all)	9		
Dysgeusia			
subjects affected / exposed	10 / 62 (16.13%)		
occurrences (all)	10		
Dysphonia			
subjects affected / exposed	4 / 62 (6.45%)		
occurrences (all)	4		
Headache			
subjects affected / exposed	18 / 62 (29.03%)		
occurrences (all)	18		
Eye disorders			
Conjunctivitis			
subjects affected / exposed	6 / 62 (9.68%)		
occurrences (all)	6		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	31 / 62 (50.00%)		
occurrences (all)	31		
Vomiting			
subjects affected / exposed	16 / 62 (25.81%)		
occurrences (all)	16		
Constipation			
subjects affected / exposed	18 / 62 (29.03%)		
occurrences (all)	18		
Diarrhoea			
subjects affected / exposed	24 / 62 (38.71%)		
occurrences (all)	24		
Mucositis			

subjects affected / exposed occurrences (all) Gastrooesophageal reflux subjects affected / exposed occurrences (all)	33 / 62 (53.23%) 33 5 / 62 (8.06%) 5		
Hepatobiliary disorders Hepatic failure subjects affected / exposed occurrences (all)	 6 / 62 (9.68%) 6		
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all) Nail toxicity subjects affected / exposed occurrences (all) Hand and foot syndrome subjects affected / exposed occurrences (all) Dry skin subjects affected / exposed occurrences (all) Erythema subjects affected / exposed occurrences (all) rash acneiform subjects affected / exposed occurrences (all)	 41 / 62 (66.13%) 41 33 / 62 (53.23%) 33 34 / 62 (54.84%) 34 7 / 62 (11.29%) 7 6 / 62 (9.68%) 6 6 / 62 (9.68%) 6		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all)	 14 / 62 (22.58%) 14 11 / 62 (17.74%) 11		
Infections and infestations			

Bronchitis subjects affected / exposed occurrences (all)	5 / 62 (8.06%) 5		
Catheter site infection subjects affected / exposed occurrences (all)	4 / 62 (6.45%) 4		
Infection subjects affected / exposed occurrences (all)	15 / 62 (24.19%) 15		
Rhinitis subjects affected / exposed occurrences (all)	12 / 62 (19.35%) 12		
urinary infection subjects affected / exposed occurrences (all)	9 / 62 (14.52%) 9		
Laryngitis subjects affected / exposed occurrences (all)	4 / 62 (6.45%) 4		
Metabolism and nutrition disorders weight gain subjects affected / exposed occurrences (all)	5 / 62 (8.06%) 5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 October 2010	Version 3.0 du 26 Avril 2010 approuvée par le CPP ile de France 1 en date du 18/05/2010 et autorisée par l'AFSSAPS le 12/05/2010

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported