



Clinical trial results:

A multicenter phase II clinical trial assessing the efficacy of the combination of lapatinib and capecitabine in patients with non pretreated brain metastasis from HER2 positive breast cancer.

Summary

EudraCT number	2008-001084-10
Trial protocol	FR
Global end of trial date	01 June 2014

Results information

Result version number	v1 (current)
This version publication date	23 October 2025
First version publication date	23 October 2025

Trial information

Trial identification

Sponsor protocol code	GEP 02/0801
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00967031
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UNICANCER
Sponsor organisation address	101 rue de Tolbiac, Paris, France, 75015
Public contact	Nourredine AIT RAHMOUNE, UNICANCER, 33 0171936704, n.ait-rahmoune@unicancer.fr
Scientific contact	Nourredine AIT RAHMOUNE, UNICANCER, 33 0171936704, n.ait-rahmoune@unicancer.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	01 July 2012
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 February 2012
Global end of trial reached?	Yes
Global end of trial date	01 June 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the objective response rate by volumetric analysis of the combination lapatinib and capecitabine on brain metastasis as assessed by MRI, in metastatic HER2 positive breast cancer patients, prior to any brain radiotherapy.

Protection of trial subjects:

The clinical trial was conducted in accordance with:

- The principles of ethics as stated in the last version in use of the Declaration of Helsinki,
- The Good Clinical Practices defined by the International Conference on Harmonization (ICH-E6, 17 July 96),
- The European directive 2001/20/CE on the conduct of clinical trials,
- The Huriet's law (n° 88-1138) of 20 December 1988, relative to the protection of persons participating in biomedical research and modified by the Public Health Law n°2004-806 of 9 August 2004,
- The law on " " (Informatique et Libertés n° 78-17) of 6 January 1978 modified by the law n° 2004-801 of 6 August 2004 relative to the protection of persons with regard to the computerized processing of personal data,
- The bioethics law n° 2004-800 of 6 August 2004.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 April 2009
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 45
Worldwide total number of subjects	45
EEA total number of subjects	45

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)	33
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Overall, 45 patients were included in the study from 14 April 2009 to 2 August 2010, in 11 sites in France; all patients received at least 1 dose of the study drug.

Pre-assignment

Screening details:

Patients with Histologically confirmed invasive, HER2 positive breast cancer with stage IV disease and radiographically confirmed brain metastasis (excepted single BM) were included. Patients were to receive lapatinib and capecitabine as 21-day cycles.

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	Lapatinib + Capecitabine
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Arm description:

Patients were to receive lapatinib and capecitabine as 21-day cycles:

- Lapatinib 1250 mg was administered once daily
- Capecitabine was administered from Day 1 to Day 14 of each cycle.

Patients were to receive the study treatments as long as they could benefit from it, according to the investigator's judgment.

Arm type	Experimental
Investigational medicinal product name	Lapatinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Patients were to receive Lapatinib: 1250 mg/day once a day one hour after lunch.

Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Patients were to receive capecitabine: 1000 mg/m²/day (2000 mg/m²/day) during breakfast and dinner.

Capecitabine was administered from Day 1 to Day 14 of each cycle.

Number of subjects in period 1	Lapatinib + Capecitabine
Started	45
Completed	1
Not completed	44
Tumoral progression	37
Other	1
Deaths	1
Unacceptable toxicity	4
Refusal to receive treatment	1

Baseline characteristics

Reporting groups

Reporting group title	Overall trial (overall period)
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Reporting group description: -

Reporting group values	Overall trial (overall period)	Total	
Number of subjects	45	45	
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)	33	33	
From 65-84 years	12	12	
85 years and over	0	0	
Age continuous Units: years			
median	56		
full range (min-max)	35 to 79	-	
Gender categorical Units: Subjects			
Female	45	45	
Male	0	0	
ECOG status Units: Subjects			
ECOG 0	17	17	
ECOG 1	25	25	
ECOG 2	2	2	
Missing data	1	1	
Hormonal status of the tumor Units: Subjects			
ER+/PR+	11	11	
ER+/PR-	10	10	
ER-/PR+	1	1	
ER-/PR-	22	22	
Missing data	1	1	
Stage at time of diagnosis Units: Subjects			
Stage I	3	3	
Stage IIa	13	13	
Stage IIb	8	8	
Stage IIIa	5	5	
Stage IIIb	5	5	

Stage IIIC	3	3	
Stage IV	8	8	
Location of primary tumor site Units: Subjects			
Unilateral	45	45	
Breast metastatic site at time of diagnosis Units: Subjects			
No	37	37	
Yes	8	8	
Lung metastatic site at time of diagnosis Units: Subjects			
No	41	41	
Yes	4	4	
Bone metastatic site at time of diagnosis Units: Subjects			
No	37	37	
Yes	8	8	
Liver metastatic site at time of diagnosis Units: Subjects			
No	40	40	
Yes	5	5	
Brain metastatic site at time of diagnosis Units: Subjects			
No	44	44	
Yes	1	1	
Lymphatic system metastatic site at time of diagnosis Units: Subjects			
No	39	39	
Yes	6	6	
Other metastatic site at time of diagnosis Units: Subjects			
No	45	45	

End points

End points reporting groups

Reporting group title	Lapatinib + Capecitabine
Reporting group description:	
Patients were to receive lapatinib and capecitabine as 21-day cycles:	
- Lapatinib 1250 mg was administered once daily	
- Capecitabine was administered from Day 1 to Day 14 of each cycle.	
Patients were to receive the study treatments as long as they could benefit from it, according to the investigator's judgment.	

Primary: CNS objective response (CNS-OR rate)

End point title	CNS objective response (CNS-OR rate) ^[1]
End point description:	
The primary endpoint was the proportion of patients with a centrally assessed CNS objective response (CNS-OR rate).	
CNS-OR was defined as either a complete response (complete resolution of all BM) or a partial response ($\geq 50\%$ reduction in the volumetric sum of all evaluable [≥ 1 cm diameter] lesions without progression of non-measurable lesions) provided all the following criteria were also satisfied: no new brain lesion, no progressive extra-CNS disease, no worsening of neurologic symptoms and no corticosteroid use increase.	
End point type	Primary
End point timeframe:	
february 2012	
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 analysis to report for this end point.	

End point values	Lapatinib + Capecitabine			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: percent				
number (confidence interval 95%)				
Number of patients with CNS-OR	65.9 (50.1 to 79.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to progression in Central Nervous System (TTP)

End point title	Time to progression in Central Nervous System (TTP)
End point description:	
We measured time to CNS progression from the date of inclusion to the date of event defined as first documented CNS progression assessed by volumetric analysis.	
End point type	Secondary

End point timeframe:

From the date of inclusion to the date of event defined as first documented CNS progression

End point values	Lapatinib + Capecitabine			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: Months				
median (confidence interval 95%)				
Median TTP [IC 95%]	5.5 (4.3 to 6)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events occurred during all the course of study treatment

Adverse event reporting additional description:

or non serious adverse events only treatment-related adverse events (TRAEs) were available. The number of occurrence are not available and will be always noted "1".

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	NA
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Reporting groups

Reporting group title	Lapatinib + Capecitabine
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Reporting group description: -

Serious adverse events	Lapatinib + Capecitabine		
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 45 (31.11%)		
number of deaths (all causes)	26		
number of deaths resulting from adverse events	0		
Vascular disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vena cava thrombosis			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Coma			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Confusion			

subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertension intracranial			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fever chills			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General physical health deterioration			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Shivers			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhea			
subjects affected / exposed	3 / 45 (6.67%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	0 / 0		
Hypochondrium pain right			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Mucositis oral			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Vomiting			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Erysipelas			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Pyelonephritis			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dehydration			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypocalcemia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Lapatinib + Capecitabine		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	45 / 45 (100.00%)		
Vascular disorders			

Left ventricular ejection fraction subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1		
Nervous system disorders Insomnia subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1		
Headaches subjects affected / exposed occurrences (all)	11 / 45 (24.44%) 1		
Neurosensitivity disorder subjects affected / exposed occurrences (all)	6 / 45 (13.33%) 1		
General disorders and administration site conditions Pain subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1		
Asthenia subjects affected / exposed occurrences (all)	22 / 45 (48.89%) 1		
Gastrointestinal disorders Anorexia subjects affected / exposed occurrences (all)	13 / 45 (28.89%) 1		
Constipation subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1		
Diarrhoea subjects affected / exposed occurrences (all)	38 / 45 (84.44%) 1		
Abdominal pain subjects affected / exposed occurrences (all)	7 / 45 (15.56%) 1		
Mucositis subjects affected / exposed occurrences (all)	13 / 45 (28.89%) 1		

Nausea subjects affected / exposed occurrences (all)	23 / 45 (51.11%) 1		
Gastroesophageal reflux subjects affected / exposed occurrences (all)	4 / 45 (8.89%) 1		
Vomiting subjects affected / exposed occurrences (all)	16 / 45 (35.56%) 1		
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1		
Hepatobiliary disorders Aminotransferases elevation subjects affected / exposed occurrences (all) Bilirubine elevation subjects affected / exposed occurrences (all) Alcaline phosphatase elevation subjects affected / exposed occurrences (all)	26 / 45 (57.78%) 1 21 / 45 (46.67%) 1 21 / 45 (46.67%) 1		
Skin and subcutaneous tissue disorders Hand-foot syndrome subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all) Dry skin subjects affected / exposed occurrences (all)	34 / 45 (75.56%) 1 21 / 45 (46.67%) 1 14 / 45 (31.11%) 1		
Musculoskeletal and connective tissue disorders Arthralgia			

subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	1		
Extremities pain			
subjects affected / exposed	3 / 45 (6.67%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Mucosal inflammation			
subjects affected / exposed	9 / 45 (20.00%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 February 2010	Update the list of investigators and co-investigators.
26 January 2012	Change in sponsor, from "Fédération Nationale des Centres de Lutte Contre le Cancer" to "UNICANCER".

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported