



## Clinical trial results:

**Multicentric, open-label, phase II clinical trial with pegylated liposomal doxorubicin (Caelyx®) as primary treatment in patients with breast cancer and a history of heart disease or over 65 years (CAPRICE).**

### Summary

EudraCT number	2007-001428-11
Trial protocol	ES
Global end of trial date	27 April 2016

### Results information

Result version number	v1 (current)
This version publication date	25 May 2022
First version publication date	25 May 2022

### Trial information

#### Trial identification

Sponsor protocol code	50SOLTI-0702
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00563953
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	SOLTI
Sponsor organisation address	C/ Balmes 89 3-7, Barcelona, Spain, 08008
Public contact	INVESTIGACION CLINICA, SOLTI, +34 933436302, regsolti@gruposolti.org
Scientific contact	INVESTIGACION CLINICA, SOLTI, +34 933436302, regsolti@gruposolti.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 September 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	27 April 2016
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

- To assess the frequency of complete pathological response (CRp) at the time of surgery in patients at risk of developing anthracycline cardiotoxicity and who started a primary chemotherapy regimen with pegylated liposomal doxorubicin and cyclophosphamide followed by paclitaxel.

Protection of trial subjects:

The investigator provided all details of the study verbally, in writing, or both, and obtained the written informed consent of each subject before participating in the study. Patients (or their legal representative and / or witness, as applicable) personally signed and dated the informed consent form; also signed by the person who provided the information to the patients. In providing this information, it was emphasized that participation in the study was voluntary and that the patient could withdraw from it at any time and for any reason. All patients were given the opportunity to ask questions about the study and were given sufficient time to decide whether they wanted to participate in it.

All patients and / or legal representative were given a copy of the informed consent.

The consent included information that the data were registered, collected and processed in accordance with Organic Law 15/1999, of December 13, on the protection of personal data. According to this law, the data was treated in such a way that the information that had been obtained could not be associated with an identified or identifiable person.

Background therapy:

Anthracyclines and taxanes are the most effective drugs against non-hormone-dependent breast cancer. Due to its toxicity, its use is limited in elderly patients or patients with a history of heart disease. DLP has shown similar efficacy to doxorubicin in metastatic breast cancer with less cardiotoxicity. The combination of DLP and CFM in QTP has shown promising results in a phase II study. The most effective regimen in primary chemotherapy is the sequential administration of anthracyclines and taxanes. Doxorubicin administration is contraindicated in cardiac or elderly patients. This study aims to demonstrate that the administration of DLP, in a scheme with CFM followed by paclitaxel in QTP, maintains the efficacy of conventional anthracyclines, in terms of pCR, without increasing cardiotoxicity, in a sample of patients that otherwise would not be known. You may benefit from anthracycline treatment.

Evidence for comparator: -

Actual start date of recruitment	10 October 2007
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 50
Worldwide total number of subjects	50
EEA total number of subjects	50

Notes:

<b>Subjects enrolled per age group</b>	
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)	6
From 65 to 84 years	34
85 years and over	10

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details: -

### Pre-assignment period milestones

Number of subjects started	50
Number of subjects completed	50

### Period 1

Period 1 title	Baseline (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	surgeried

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Caelyx pegylated liposoma
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

35 mg/m2

Investigational medicinal product name	cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for concentrate for solution for infusion
Routes of administration	Concentrate for solution for infusion

Dosage and administration details:

600 mg/m2

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

Dosage and administration details:

80 mg/m2 por 12

<b>Arm title</b>	non surgied
Arm description: -	
Arm type	Active comparator

Investigational medicinal product name	Caelyx pegylated liposoma
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for concentrate for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
35 mg/m2	
Investigational medicinal product name	cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for concentrate for solution for infusion
Routes of administration	Concentrate for solution for infusion
Dosage and administration details:	
600 mg/m2	
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for concentrate for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
80 mg/m2 por 12	

<b>Number of subjects in period 1</b>	surgeried	non surgied
Started	46	4
Completed	46	4

## Baseline characteristics

### Reporting groups

Reporting group title	Baseline
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Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	50	50	
Age categorical			
Units: Subjects			
<60 years	6	6	
60-64 years	2	2	
65-69 years	11	11	
70-74 years	11	11	
75-79 years	14	14	
>79 years	6	6	
Age continuous			
Units: years			
geometric mean	73		
full range (min-max)	35 to 84	-	
Gender categorical			
Units: Subjects			
Female	0	0	
Male	50	50	
ECOG			
Units: Subjects			
zero	43	43	
one	7	7	
Menopausal status			
Units: Subjects			
Premenopausal	4	4	
Postmenopausal	46	46	
Tumor Grading			
Units: Subjects			
G1	4	4	
G2	10	10	
G3	36	36	
Tumor stadium			
Units: Subjects			
II	24	24	
III	26	26	
Her2/neu			
Units: Subjects			
Negative	49	49	
Positive	1	1	
Stadium			
Units: Subjects			
II	24	24	

III	26	26	
Clinic T			
Units: Subjects			
T2-3	29	29	
T4a-c	14	14	
T4d	7	7	
Clinic N			
Units: Subjects			
N0	23	23	
N1	14	14	
N2	11	11	
N3	2	2	
Type of surgery			
Units: Subjects			
Mastectomy	37	37	
Conservative surgery	13	13	
Tumor size			
Units: millimeter(s)			
geometric mean	33.7		
full range (min-max)	5 to 123	-	

## End points

### End points reporting groups

Reporting group title	surgeried
Reporting group description: -	
Reporting group title	non surgied
Reporting group description: -	
Subject analysis set title	Surgied
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Patients Surgied	
Subject analysis set title	Total
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
total	
Subject analysis set title	PCR breast
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Pathologic Complete Response in Surgical Breast Specimens	
Subject analysis set title	CPR breast and armpit
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Pathologic Complete Response in Breast and Axillary Surgical Specimens	

### Primary: Complete pathological response

End point title	Complete pathological response
End point description:	
Breast surgical specimens were evaluated for evaluation according to the NSABP guidelines. Patients were considered to have CRp if there was no evidence of invasive breast cancer or there was only non-invasive cancer in situ in the breast specimen. The NSABP guidelines do not take into account the histological status of the nodes to define CRP. The CRp rate is summarized as the percentage (%) of patients meeting the criterion, with the exact 95% confidence interval.	
End point type	Primary
End point timeframe:	
until progression	

End point values	PCR breast	CPR breast and armpit		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50	50		
Units: percent				
geometric mean (confidence interval 95%)	32 (19.5 to 46.7)	24 (12.1 to 35.8)		

## Statistical analyses



<b>Statistical analysis title</b>	ITT RCp
Comparison groups	PCR breast v CPR breast and armpit
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	≥ 0.05
Method	t-test, 2-sided
Parameter estimate	Hazard ratio (HR)
Point estimate	32
Confidence interval	
level	95 %
sides	2-sided
lower limit	19.5
upper limit	46.7
Variability estimate	Standard deviation
Dispersion value	18

### Secondary: Radiological Response Rate

End point title	Radiological Response Rate
End point description:	
End point type	Secondary
End point timeframe:	
Until progression	

End point values	Total			
Subject group type	Subject analysis set			
Number of subjects analysed	50			
Units: percent				
geometric mean (confidence interval 95%)				
PLD- cyclofosfamide	2 (0.05 to 10.6)			
PLD- cyclofosfamide-paclitaxel	6 (1.25 to 16.5)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Relapse-free survival at 5 years

End point title	Relapse-free survival at 5 years
End point description:	

End point type	Secondary
End point timeframe:	
Until death	

End point values	Total			
Subject group type	Subject analysis set			
Number of subjects analysed	50			
Units: percent				
geometric mean (confidence interval 95%)				
RFS 5 years	54.4 (38.3 to 67.9)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Overall survival -5 years

End point title	Overall survival -5 years
End point description:	
End point type	Secondary
End point timeframe:	
Until death	

End point values	Surgied			
Subject group type	Subject analysis set			
Number of subjects analysed	46			
Units: percent				
geometric mean (confidence interval 95%)	56 (41.2 to 68.4)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Conservative surgery rate

End point title	Conservative surgery rate
End point description:	
End point type	Secondary

End point timeframe:

NA

<b>End point values</b>	Surgied			
Subject group type	Subject analysis set			
Number of subjects analysed	46			
Units: percent				
number (not applicable)				
conservative surgery	58.7			
mastectomy	41.3			
axillary lymphadenectomy	84			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Complete response at the level of axillary nodes

End point title	Complete response at the level of axillary nodes
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End point description:

End point type	Secondary
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End point timeframe:

NA

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Until close study

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	13.0
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### Reporting groups

Reporting group title	Safety population
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Reporting group description: -

Serious adverse events	Safety population		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 50 (16.00%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events	3		
Vascular disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haematoma			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Angina pectoris			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			

Amyotrophic lateral sclerosis subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Partial seizures subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Syncope subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Convulsions local subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders Diarrhoea subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders Pneumonia aspiration subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Pneumonia			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Skin and subcutaneous tissue disorders			
Skin toxicity			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Infections and infestations			
Neutropenia			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infection			
subjects affected / exposed	1 / 50 (2.00%)		
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 %

<b>Non-serious adverse events</b>	Safety population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 50 (76.00%)		
General disorders and administration site conditions			
Alopecia			
subjects affected / exposed	37 / 50 (74.00%)		
occurrences (all)	37		
Mucositis management			

subjects affected / exposed occurrences (all)	30 / 50 (60.00%) 30		
Oedema peripheral subjects affected / exposed occurrences (all)	6 / 50 (12.00%) 6		
Fever subjects affected / exposed occurrences (all)	6 / 50 (12.00%) 6		
Seroma subjects affected / exposed occurrences (all)	4 / 50 (8.00%) 4		
Immune system disorders Neutropenia subjects affected / exposed occurrences (all)	12 / 50 (24.00%) 12		
Reproductive system and breast disorders Mastalgia subjects affected / exposed occurrences (all)	3 / 50 (6.00%) 3		
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all)	4 / 50 (8.00%) 4		
Cough subjects affected / exposed occurrences (all)	4 / 50 (8.00%) 4		
Catarrh subjects affected / exposed occurrences (all)	3 / 50 (6.00%) 3		
Hyporexia subjects affected / exposed occurrences (all)	3 / 50 (6.00%) 3		
Rhinorea subjects affected / exposed occurrences (all)	3 / 50 (6.00%) 3		
Nervous system disorders			

Neuropathy peripheral subjects affected / exposed occurrences (all)	14 / 50 (28.00%) 14		
Neurotoxicity subjects affected / exposed occurrences (all)	13 / 50 (26.00%) 13		
Dysgeusia subjects affected / exposed occurrences (all)	9 / 50 (18.00%) 9		
Dizziness subjects affected / exposed occurrences (all)	6 / 50 (12.00%) 6		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	8 / 50 (16.00%) 8		
Leukopenia subjects affected / exposed occurrences (all)	4 / 50 (8.00%) 4		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	3 / 50 (6.00%) 3		
Eye disorders Abdominal pain subjects affected / exposed occurrences (all)	4 / 50 (8.00%) 4		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	18 / 50 (36.00%) 18		
Diarrhoea subjects affected / exposed occurrences (all)	17 / 50 (34.00%) 17		
Constipation subjects affected / exposed occurrences (all)	10 / 50 (20.00%) 10		



Vomiting			
subjects affected / exposed	9 / 50 (18.00%)		
occurrences (all)	9		
Epigastric discomfort			
subjects affected / exposed	4 / 50 (8.00%)		
occurrences (all)	4		
Skin and subcutaneous tissue disorders			
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	14 / 50 (28.00%)		
occurrences (all)	14		
Skin toxicity			
subjects affected / exposed	11 / 50 (22.00%)		
occurrences (all)	11		
Rash			
subjects affected / exposed	9 / 50 (18.00%)		
occurrences (all)	9		
Nail toxicity			
subjects affected / exposed	8 / 50 (16.00%)		
occurrences (all)	8		
Redness facial			
subjects affected / exposed	6 / 50 (12.00%)		
occurrences (all)	6		
Erythema			
subjects affected / exposed	4 / 50 (8.00%)		
occurrences (all)	4		
Onychodystrophy			
subjects affected / exposed	4 / 50 (8.00%)		
occurrences (all)	4		
Nail disorder			
subjects affected / exposed	3 / 50 (6.00%)		
occurrences (all)	3		
Pruritus			
subjects affected / exposed	3 / 50 (6.00%)		
occurrences (all)	3		
Dry skin			

subjects affected / exposed occurrences (all)	3 / 50 (6.00%) 3		
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all)	3 / 50 (6.00%) 3		
Musculoskeletal and connective tissue disorders Artralxia subjects affected / exposed occurrences (all)  Lumbar pain subjects affected / exposed occurrences (all)	10 / 50 (20.00%) 10  7 / 50 (14.00%) 7		
Infections and infestations Conjunctivitis subjects affected / exposed occurrences (all)  Urinary tract infection subjects affected / exposed occurrences (all)	4 / 50 (8.00%) 4  3 / 50 (6.00%) 3		
Metabolism and nutrition disorders Anorexia nervosa subjects affected / exposed occurrences (all)	19 / 50 (38.00%) 19		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

NA
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Notes: