Clinical trial results:
Response to Neoadjuvant Treatment With Anti-aromatase Anastrozole and Anti-estrogen Fulvestrant: a Randomized Phase II Study in Postmenopausal Patients With Hormone-sensitive Non-metastatic Breast Cancer and an Exploratory Study of Molecular Signatures of Response.

Summary

EudraCT number	2007-004216-31
Trial protocol	FR
Global end of trial date	28 March 2017

Results information

Result version number	v1 (current)
This version publication date	05 February 2022
First version publication date	05 February 2022

Trial information

Trial identification

Sponsor protocol code	IB 2007-26

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00871858
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Institut Bergonié
Sponsor organisation address	229 cours de l'Argonne, Bordeaux, France, 33076
Public contact	Regulatory Affairs Management Desk, Institut Bergonié, drci@bordeaux.unicancer.fr
Scientific contact	Regulatory Affairs Management Desk, Institut Bergonié, drci@bordeaux.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	02 July 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 March 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate clinical tumor response at 6 months in patients with hormone-sensitive non-metastatic breast cancer treated with neoadjuvant anastrozole and fulvestrant.

Protection of trial subjects:

A supervisory committee is constitued to evaluate the benefit/risk ratio along the study period.
A serious adverse event committee is constitued to review the safety cases

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 March 2008
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	France: 120
Worldwide total number of subjects	120
EEA total number of subjects	120

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)	29
From 65 to 84 years	84
85 years and over	7

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

•Histologically confirmed invasive breast cancer, meeting 1 of the following criteria:
◦SBR grade I-II disease (patients < 65 years of age)
◦SBR grade I-III disease (patients > 65 years of age)
•T2 (2-5 cm), T3, or T4B, and N0-1 disease
•No metastatic disease
•Breast lesion not amenable to breast-conserving resection
•No inflammatory brea

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A (ANA)

Arm description:

Patients receive oral anastrozole as 1 mg film-coated tablets, once daily for 6 months

Arm type	Experimental
Investigational medicinal product name	Anastrozole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients receive oral anastrozole as 1 mg film-coated tablets, once daily for 6 months.

Arm title	Arm B (FULV)

Arm description:

Patients received fulvestrant intramuscularly (250 mg/5 ml solution) on days 1, 14, and 28 and then once a month thereafter until 6 months.

Arm type	control
Investigational medicinal product name	Fulvestrant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Patients received fulvestrant intramuscularly (250 mg/5 ml solution) on days 1, 14, and 28 and then once a month thereafter until 6 months. fu

Number of subjects in period 1	Arm A (ANA)	Arm B (FULV)
Started	61	59
Completed	56	52
Not completed	5	7
Consent withdrawn by subject	1	1
Adverse event, non-fatal	1	1
Lost to follow-up	-	1
Protocol deviation	3	4

Baseline characteristics

Reporting groups	
Reporting group title	Arm A (ANA)
Reporting group description:	
Patients receive oral anastrozole as 1 mg film-coated tablets, once daily for 6 months	
Reporting group title	Arm B (FULV)
Reporting group description:	
Patients received fulvestrant intramuscularly (250 mg/5 ml solution) on days 1, 14, and 28 and then once a month thereafter until 6 months.	

Reporting group values	Arm A (ANA)	Arm B (FULV)	Total
Number of subjects	61	59	120
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			
median	69.1	70.5	
inter-quartile range (Q1-Q3)	64.1 to 77.5	64.0 to 77.8	-
Gender categorical			
Units: Subjects			
Female	61	59	120
Male	0	0	0

End points

End points reporting groups

Reporting group title	Arm A (ANA)
Reporting group description:	
Patients receive oral anastrozole as 1 mg film-coated tablets, once daily for 6 months	
Reporting group title	Arm B (FULV)
Reporting group description:	
Patients received fulvestrant intramuscularly (250 mg/5 ml solution) on days 1, 14, and 28 and then once a month thereafter until 6 months.	

Primary: Objective Response Rate (ORR) Determined by Clinical Palpation

End point title	Objective Response Rate (ORR) Determined by Clinical Palpation[1]
End point description:	
Objective response rate is defined as the rate of participants with partial or complete responses according to RECIST V1.0. Complete response is defined as the disappearance of all target lesions and partial response is defined as at least a 30% decrease in the sum of the longest diameters (SLD) of target lesions, taking as reference the baseline SLD (RECIST V1.0.).	
End point type	Primary
End point timeframe:	
6 months	

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 test has been performed as it is a non-comparative clinical trial. Calculation of confidence interval.

End point values	Arm A (ANA)	Arm B (FULV)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	52		
Units: percentage of participants				
number (confidence interval 95%)	58.9 (45 to 71.9)	53.8 (39.5 to 67.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Objective response rate (ORR) determined by ultrasound

End point title	Objective response rate (ORR) determined by ultrasound
End point description:	
Objective response rate is defined as the rate of participants with partial or complete responses according to RECIST V1.0. Complete response is defined as the disappearance of all target lesions and partial response is defined as at least a 30% decrease in the sum of the longest diameters (SLD) of target lesions, taking as reference the baseline SLD (RECIST V1.0.).	
End point type	Secondary

End point timeframe:

6 months

End point values	Arm A (ANA)	Arm B (FULV)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	21		
Units: percentage of participants				
number (confidence interval 95%)	35.1 (20.2 to 52.5)	52.4 (29.8 to 74.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Objective response rate (ORR) determined by mammography

End point title	Objective response rate (ORR) determined by mammography

End point description:

Objective response rate is defined as the rate of participants with partial or complete responses according to RECIST V1.0.
Complete response is defined as the disappearance of all target lesions and partial response is defined as at least a 30% decrease in the sum of the longest diameters (SLD) of target lesions, taking as reference the baseline SLD (RECIST V1.0.).

End point type	Secondary

End point timeframe:

6 months

End point values	Arm A (ANA)	Arm B (FULV)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	18		
Units: percentage of participants				
number (confidence interval 95%)	26.1 (10.4 to 48.4)	27.8 (9.7 to 53.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of breast-conserving surgery

End point title	Rate of breast-conserving surgery

End point description:

End point type	Secondary

End point timeframe:

6 months

End point values	Arm A (ANA)	Arm B (FULV)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	52		
Units: percentage of participants				
number (confidence interval 95%)	60.7 (46.8 to 73.5)	50.0 (35.8 to 64.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with 5-year Relapse-Free Survival

End point title	Percentage of Participants with 5-year Relapse-Free Survival

End point description:

Relapse-Free survival (RFS) is measured from the date of randomization to the date of the following events, whichever occurs first according to the DATECAN recommendations for breast cancer:
- Invasive ipsilateral breast tumor recurrence/ progression ;
- Local invasive recurrence/progression ;
- Regional invasive recurrence/progression (N+: regional progression) ;
- Appearance/Occurrence of Metastatic recurrence;
- Death whatever the cause.

Participants who did not experience events were censored at the date of last follow-up. RFS was estimated using the Kaplan-Meier method. No comparison test was performed between the two arms as this study is non-comparative.

End point type	Secondary

End point timeframe:

5 years

End point values	Arm A (ANA)	Arm B (FULV)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	52		
Units: Percentage of participants				
number (confidence interval 95%)	82.8 (69.6 to 90.7)	74.7 (60.4 to 84.5)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The adverse event are reported from the signature of the informed consent form to the study end participation of the patient

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	3.0

Reporting groups

Reporting group title	Arm A (ANA)

Reporting group description:

Experimental arm

Reporting group title	Arm B (FULV)

Reporting group description:

Control arm

Serious adverse events	Arm A (ANA)	Arm B (FULV)	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 60 (3.33%)	3 / 58 (5.17%)	
number of deaths (all causes)	6	6	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Clear cell kidney cancer			
subjects affected / exposed	0 / 60 (0.00%)	1 / 58 (1.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 60 (1.67%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Endometrial atrophy			
subjects affected / exposed	0 / 60 (0.00%)	1 / 58 (1.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Renal and urinary disorders			
Programmed peritoneal dialysis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchial infection			
subjects affected / exposed	0 / 60 (0.00%)	1 / 58 (1.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Arm A (ANA)	Arm B (FULV)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 60 (80.00%)	43 / 58 (74.14%)	
Investigations			
Weight gain			
subjects affected / exposed	3 / 60 (5.00%)	2 / 58 (3.45%)	
occurrences (all)	3	2	
Vascular disorders			
Hot flashes			
subjects affected / exposed	13 / 60 (21.67%)	14 / 58 (24.14%)	
occurrences (all)	13	14	
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 60 (5.00%)	2 / 58 (3.45%)	
occurrences (all)	3	2	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	7 / 60 (11.67%)	19 / 58 (32.76%)	
occurrences (all)	7	20	
Injection site reaction			
subjects affected / exposed	0 / 60 (0.00%)	9 / 58 (15.52%)	
occurrences (all)	0	9	
Gastrointestinal disorders			

Nausea subjects affected / exposed occurrences (all)	4 / 60 (6.67%) 4	2 / 58 (3.45%) 2	
Psychiatric disorders Agitation subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 3	4 / 58 (6.90%) 4	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	20 / 60 (33.33%) 20	11 / 58 (18.97%) 11	
MYALGIA subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 2	3 / 58 (5.17%) 3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 July 2009	Protocol V3 dated 22-jun-2009
07 March 2012	Protocol V4 dated 22-feb-2012
04 April 2014	Protocol V5 dated 18-feb-2014

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/26171933