Clinical trial results:
A Randomised, Double-blind, Parallel-group, Multicentre, Phase II Study to Evaluate the Efficacy and Tolerability of Fulvestrant (FASLODEXTM) 250 mg, Fulvestrant (FASLODEXTM) 250 mg (plus 250 mg Loading Regimen) and Fulvestrant (FASLODEXTM) 500 mg in Postmenopausal Women with Oestrogen Receptor Positive Advanced Breast Cancer Progressing or Relapsing after Previous Endocrine Therapy

Summary

EudraCT number	2005-004247-54
Trial protocol	BE HU CZ
Global end of trial date	13 March 2018

Results information

Result version number	v1 (current)
This version publication date	29 March 2020
First version publication date	29 March 2020

Trial information

Trial identification

Sponsor protocol code	D6997C00006

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	Alderley Park, Macclesfield, United Kingdom, ST10 4TG
Public contact	Faslodex Medical science director, AstraZeneca, +1 877-400-4656, clinicaltrialtransparency@astrazeneca.com
Scientific contact	Faslodex Medical science director, AstraZeneca, +1 877-400-4656, clinicaltrialtransparency@astrazeneca.com

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	13 June 2008
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 June 2008
Global end of trial reached?	Yes
Global end of trial date	13 March 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the objective response rate (ORR) of patients treated with fulvestrant 250 mg, fulvestrant 250 mg (plus 250 mg loading regimen) and fulvestrant 500 mg.

Protection of trial subjects:

The final Clinical Study Protocol, including the final version of the Informed Consent Form had to be approved or given a favourable opinion in writing by an IEC as appropriate. The site investigators were required to submit written approval to AstraZeneca before they could enrol any patient into the study. The Principal Investigator at each site was responsible for informing the IEC of any amendment to the protocol in accordance with local requirements. In addition, all advertising used to recruit patients for the study had to be approved by the IEC. The protocol had to be re-approved by the IEC annually, as local regulations required.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 May 2006
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	10 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 30
Country: Number of subjects enrolled	Canada: 31
Country: Number of subjects enrolled	Czech Republic: 8
Country: Number of subjects enrolled	France: 9
Country: Number of subjects enrolled	Hungary: 24
Country: Number of subjects enrolled	Poland: 29
Country: Number of subjects enrolled	Romania: 10
Country: Number of subjects enrolled	Turkey: 3
Worldwide total number of subjects	144
EEA total number of subjects	110

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)	58
From 65 to 84 years	83
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

The planned population size was 135 recruited patients. In total 144 patients were randomised in the study from 34 centres in 8 countries. The first patient was randomised into the study on 30 May 2006 and the last patient was randomised on 30 November 2007.

Pre-assignment

Screening details:

In total 161 patients were enrolled and 17 of them were not randomised.

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Fulvestrant 250 mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Fulvestrant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

250 mg fulvestrant (1 fulvestrant injection and 1 placebo injection) was to be given on Days 0, 28 (±3) and every 28 (±3) days; 2 placebo injections were given on Day 14 (±3 days). Time windows extended to ±7 days after 24 weeks

Arm title	Fulvestrant 250 mg + Loading Dose

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Fulvestrant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

An initial dose of 500 mg (2 fulvestrant injections) was to be given on Day 0, followed by 250 mg (1 fulvestrant injection and 1 placebo injection) on Days 14 (±3), 28 (±3) and every 28 (±3) days. Time windows extended to ±7 days after 24 weeks

Arm title	Fulvestrant 500 mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Fulvestrant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

500 mg fulvestrant (2 fulvestrant injections) was to be given on Days 0, 14 (±3), 28 (±3) and every 28 (±3) days. Time windows extended to ±7 days after 24 weeks.

Number of subjects in period 1	Fulvestrant 250 mg	Fulvestrant 250 mg + Loading Dose	Fulvestrant 500 mg
Started	47	51	46
Completed	47	51	46

Period 2

Period 2 title	Treatment Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Fulvestrant 250 mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Fulvestrant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

250 mg fulvestrant (1 fulvestrant injection and 1 placebo injection) was to be given on Days 0, 28 (±3) and every 28 (±3) days; 2 placebo injections were given on Day 14 (±3 days). Time windows extended to ±7 days after 24 weeks

Arm title	Fulvestrant 250 mg + Loading Dose

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Fulvestrant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

An initial dose of 500 mg (2 fulvestrant injections) was to be given on Day 0, followed by

250 mg (1 fulvestrant injection and 1 placebo injection) on Days 14 (±3), 28 (±3) and every 28 (±3) days. Time windows extended to ±7 days after 24 weeks

Arm title	Fulvestrant 500 mg
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Fulvestrant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

500 mg fulvestrant (2 fulvestrant injections) was to be given on Days 0, 14 (±3), 28 (±3) and every 28 (±3) days. Time windows extended to ±7 days after 24 weeks.

Number of subjects in period 2	Fulvestrant 250 mg	Fulvestrant 250 mg + Loading Dose	Fulvestrant 500 mg
Started	47	51	46
Completed	11	17	14
Not completed	36	34	32
Consent withdrawn by subject	1	-	1
Disease progression	31	26	27
Death	2	4	2
Adverse event	1	2	-
Progression (investigators opinion)	1	-	-
Incorrect enrollment	-	2	1
Lost to follow-up	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Fulvestrant 250 mg
Reporting group description: -	
Reporting group title	Fulvestrant 250 mg + Loading Dose
Reporting group description: -	
Reporting group title	Fulvestrant 500 mg
Reporting group description: -	

Reporting group values	Fulvestrant 250 mg	Fulvestrant 250 mg + Loading Dose	Fulvestrant 500 mg
Number of subjects	47	51	46
Age Categorical			
Full analysis set			
Units: Subjects			
Adults (18-64 years)	24	14	20
From 65-74 years	16	21	20
75 years and over	7	16	6
Age Continuous			
Full analysis set			
Units: years			
median	63	69	67
full range (min-max)	42 to 88	38 to 85	49 to 85
Gender Categorical			
Full analysis set			
Units: Subjects			
Female	47	51	46
Race/Ethnicity			
Full analysis set			
Units: Subjects			
Caucasian	45	51	46
Oriental (Japanese)	1	0	0
Oriental (Asian other than Chinese or Japanese)	1	0	0
Age			
Full analysis set			
Units: Years			
arithmetic mean	63.7	68.1	65.5
standard deviation	± 9.9	± 9.9	± 9.0
Weight			
Full analysis set			
Units: kg			
arithmetic mean	71.6	71.7	70.8
standard deviation	± 17.2	± 13.4	± 12.9
BMI			
Full analysis set			
Units: kg/m2			
arithmetic mean	27.7	28.0	27.3
standard deviation	± 6.3	± 4.8	± 4.2

Reporting group values	Total		
Number of subjects	144		
Age Categorical			
Full analysis set			
Units: Subjects			
Adults (18-64 years)	58		
From 65-74 years	57		
75 years and over	29		
Age Continuous			
Full analysis set			
Units: years			
median			
full range (min-max)	-		
Gender Categorical			
Full analysis set			
Units: Subjects			
Female	144		
Race/Ethnicity			
Full analysis set			
Units: Subjects			
Caucasian	142		
Oriental (Japanese)	1		
Oriental (Asian other than Chinese or Japanese)	1		
Age			
Full analysis set			
Units: Years			
arithmetic mean			
standard deviation	-		
Weight			
Full analysis set			
Units: kg			
arithmetic mean			
standard deviation	-		
BMI			
Full analysis set			
Units: kg/m2			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

Reporting group title	Fulvestrant 250 mg
Reporting group description: -	
Reporting group title	Fulvestrant 250 mg + Loading Dose
Reporting group description: -	
Reporting group title	Fulvestrant 500 mg
Reporting group description: -	
Reporting group title	Fulvestrant 250 mg
Reporting group description: -	
Reporting group title	Fulvestrant 250 mg + Loading Dose
Reporting group description: -	
Reporting group title	Fulvestrant 500 mg
Reporting group description: -	
Subject analysis set title	PK analysis set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Includes all patients who consented to blood draws for the analysis of fulvestrant plasma concentrations and have at least one evaluable blood sample drawn after baseline for the purpose of measuring fulvestrant plasma levels.

Primary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)[1]

End point description:

Objective response rate was defined as percentage of patients with either complete response (CR - disappearance of all target lesions) or partial response (PR - at least 30% decrease in the sum of diameters of target lesions). All patients were to be followed up every 12 weeks for progression, defined by response evaluation criteria in solid tumors (RECIST v1.1).

End point type	Primary

End point timeframe:

The planned data cut-off for this study was when all patients, except withdrawals, had been followed up for at least 24 weeks. Patients received treatment up to approximately 2 years.

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: 95% CI are provided, there was no other analysis for the primary endpoint.

End point values	Fulvestrant 250 mg	Fulvestrant 250 mg + Loading Dose	Fulvestrant 500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	47	51	46	
Units: Percentage of patients				
number (confidence interval)				
Percentage (%)	8.5 (2.4 to 20.4)	5.9 (1.2 to 16.2)	15.2 (6.3 to 28.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Progression (TTP)

End point title	Time to Progression (TTP)

End point description:

Time from randomisation until objective disease progression or death (in the absence of objective progression) using the Kaplan-Meier method. RECIST tumor assessments were carried out every 12 weeks until progression.

End point type	Secondary

End point timeframe:

The planned data cut-off for this study was when all patients, except withdrawals, had been followed up for at least 24 weeks. Patients received treatment up to approximately 2 years.

End point values	Fulvestrant 250 mg	Fulvestrant 250 mg + Loading Dose	Fulvestrant 500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	47	51	46	
Units: Days				
median (inter-quartile range (Q1-Q3))	88 (79 to 260)	172 (80 to 339)	169 (82 to 477)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR)

End point title	Duration of Response (DoR)

End point description:

DoR was defined as the time from date of first documentation of the response (CR or PR) until the date of disease progression or death from any cause.

End point type	Secondary

End point timeframe:

The planned data cut-off for this study was when all patients, except withdrawals, had been followed up for at least 24 weeks. Patients received treatment up to approximately 2 years.

End point values	Fulvestrant 250 mg	Fulvestrant 250 mg + Loading Dose	Fulvestrant 500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4[2]	3[3]	7[4]	
Units: Days				
median (inter-quartile range (Q1-Q3))	9999999 (9999999 to 9999999)	9999999 (66 to 9999999)	539 (539 to 539)	

Notes:

[2] - Only patients with response are analysed

[3] - Only patients with response are analysed

[4] - Only patients with response are analysed

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Benefit Rate (CBR)

End point title	Clinical Benefit Rate (CBR)

End point description:

CBR was defined as the proportion of all randomised patients who had clinical benefit (response of CR, PR or SD>=24 weeks).

End point type	Secondary

End point timeframe:

The planned data cut-off for this study was when all patients, except withdrawals, had been followed up for at least 24 weeks. Patients received treatment up to approximately 2 years.

End point values	Fulvestrant 250 mg	Fulvestrant 250 mg + Loading Dose	Fulvestrant 500 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	47	51	46	
Units: Percentage of patients				
number (confidence interval)	31.9 (19.1 to 47.1)	47.1 (32.9 to 61.5)	47.8 (32.9 to 63.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic Parameter: Mean population clearance, a measure of the efficiency with which Fulvestrant is eliminated from the body

End point title	Pharmacokinetic Parameter: Mean population clearance, a measure of the efficiency with which Fulvestrant is eliminated from the body

End point description:

A 2-compartment model with a 1st order absorption and 1st order elimination process was fitted to the fulvestrant concentration-time data. Relative standard error is reported for the mean.

End point type	Secondary

End point timeframe:

Baseline to 12 weeks

End point values	PK analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	72			
Units: litres per hour				
least squares mean (standard error)	31 (± 3.29)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic Parameter: Mean volume of distribution at steady state, a measure of the apparent volume in the body into which Fulvestrant distributes

End point title	Pharmacokinetic Parameter: Mean volume of distribution at steady state, a measure of the apparent volume in the body into which Fulvestrant distributes

End point description:

A 2-compartment model with a 1st order absorption and 1st order elimination process was fitted to the fulvestrant concentration-time data. Relative standard error is reported for the mean. The mean estimate of volume of distribution at steady state was reported as the sum of V1/F and V2/F in the clinical study report.

End point type	Secondary

End point timeframe:

Baseline to 12 weeks

End point values	PK analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	72			
Units: litres				
least squares mean (standard error)				
V1/F	20600 (± 3.67)			
V2/F	35700 (± 27.8)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From randomisation to the point of data cut off for primary analysis

Adverse event reporting additional description:

1 patient randomized to 250mg + LD arm was excluded from safety due to no treatment received

All-Cause Mortality: patients who died whilst whilst on treatment or during 56 days following the last fulvestrant injection
Serious Adverse Events: SAEs and AEs leading to death
Deaths Resulting From AE = deaths causally related to AE per investiga

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	11.0

Reporting groups

Reporting group title	Fulvestrant 250 mg
Reporting group description: -	
Reporting group title	Fulvestrant 250 mg + Loading Dose
Reporting group description: -	
Reporting group title	Fulvestrant 500 mg
Reporting group description: -	

Serious adverse events	Fulvestrant 250 mg	Fulvestrant 250 mg + Loading Dose	Fulvestrant 500 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 47 (8.51%)	9 / 50 (18.00%)	4 / 46 (8.70%)
number of deaths (all causes)	2	4	2
number of deaths resulting from adverse events	1	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell lung cancer			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus lesion			

subjects affected / exposed	1 / 47 (2.13%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	1 / 47 (2.13%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pain			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Eye disorders			
Macular hole			

subjects affected / exposed	1 / 47 (2.13%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diverticulum intestinal hemorrhagic			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Melaena			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 47 (0.00%)	2 / 50 (4.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract inflammation			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 47 (2.13%)	1 / 50 (2.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Mental disorder			
subjects affected / exposed	1 / 47 (2.13%)	0 / 50 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Fulvestrant 250 mg	Fulvestrant 250 mg + Loading Dose	Fulvestrant 500 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 47 (76.60%)	35 / 50 (70.00%)	31 / 46 (67.39%)
Investigations			
Weight decreased			
subjects affected / exposed	1 / 47 (2.13%)	6 / 50 (12.00%)	0 / 46 (0.00%)
occurrences (all)	1	6	0
Vascular disorders			
Hot flush			
subjects affected / exposed	9 / 47 (19.15%)	5 / 50 (10.00%)	3 / 46 (6.52%)
occurrences (all)	12	5	5
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 47 (2.13%)	3 / 50 (6.00%)	0 / 46 (0.00%)
occurrences (all)	1	3	0
Headache			
subjects affected / exposed	5 / 47 (10.64%)	4 / 50 (8.00%)	3 / 46 (6.52%)
occurrences (all)	9	5	3
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	5 / 47 (10.64%)	4 / 50 (8.00%)	4 / 46 (8.70%)
occurrences (all)	5	4	4
Fatigue			
subjects affected / exposed	4 / 47 (8.51%)	11 / 50 (22.00%)	7 / 46 (15.22%)
occurrences (all)	7	12	7
Injection site pain			
subjects affected / exposed	6 / 47 (12.77%)	7 / 50 (14.00%)	6 / 46 (13.04%)
occurrences (all)	7	12	7
Oedema peripheral			
subjects affected / exposed	2 / 47 (4.26%)	3 / 50 (6.00%)	2 / 46 (4.35%)
occurrences (all)	3	3	2
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	3 / 47 (6.38%)	3 / 50 (6.00%)	2 / 46 (4.35%)
occurrences (all)	3	3	3
Abdominal pain			
subjects affected / exposed	0 / 47 (0.00%)	3 / 50 (6.00%)	1 / 46 (2.17%)
occurrences (all)	0	3	1
Diarrhoea			
subjects affected / exposed	3 / 47 (6.38%)	4 / 50 (8.00%)	6 / 46 (13.04%)
occurrences (all)	3	4	7
Nausea			
subjects affected / exposed	12 / 47 (25.53%)	9 / 50 (18.00%)	7 / 46 (15.22%)
occurrences (all)	13	9	9
Vomiting			
subjects affected / exposed	3 / 47 (6.38%)	4 / 50 (8.00%)	5 / 46 (10.87%)
occurrences (all)	3	7	5
Constipation			
subjects affected / exposed	3 / 47 (6.38%)	7 / 50 (14.00%)	1 / 46 (2.17%)
occurrences (all)	3	7	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 47 (12.77%)	6 / 50 (12.00%)	4 / 46 (8.70%)
occurrences (all)	6	6	4
Dysphonia			

subjects affected / exposed	0 / 47 (0.00%)	0 / 50 (0.00%)	3 / 46 (6.52%)
occurrences (all)	0	0	3
Dyspnoea			
subjects affected / exposed	6 / 47 (12.77%)	6 / 50 (12.00%)	5 / 46 (10.87%)
occurrences (all)	7	7	5
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	3 / 46 (6.52%)
occurrences (all)	0	1	3
Pruritus			
subjects affected / exposed	0 / 47 (0.00%)	1 / 50 (2.00%)	3 / 46 (6.52%)
occurrences (all)	0	1	3
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 47 (4.26%)	5 / 50 (10.00%)	2 / 46 (4.35%)
occurrences (all)	2	6	2
Depression			
subjects affected / exposed	3 / 47 (6.38%)	3 / 50 (6.00%)	1 / 46 (2.17%)
occurrences (all)	3	3	1
Renal and urinary disorders			
Urinary incontinence			
subjects affected / exposed	0 / 47 (0.00%)	3 / 50 (6.00%)	0 / 46 (0.00%)
occurrences (all)	0	3	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 47 (8.51%)	7 / 50 (14.00%)	4 / 46 (8.70%)
occurrences (all)	4	8	4
Back pain			
subjects affected / exposed	5 / 47 (10.64%)	8 / 50 (16.00%)	7 / 46 (15.22%)
occurrences (all)	8	8	8
Musculoskeletal chest pain			
subjects affected / exposed	4 / 47 (8.51%)	3 / 50 (6.00%)	0 / 46 (0.00%)
occurrences (all)	4	4	0
Musculoskeletal pain			
subjects affected / exposed	3 / 47 (6.38%)	2 / 50 (4.00%)	2 / 46 (4.35%)
occurrences (all)	3	2	2

Myalgia			
subjects affected / exposed	6 / 47 (12.77%)	1 / 50 (2.00%)	2 / 46 (4.35%)
occurrences (all)	6	2	2
Pain in extremity			
subjects affected / exposed	5 / 47 (10.64%)	5 / 50 (10.00%)	0 / 46 (0.00%)
occurrences (all)	10	6	0
Infections and infestations			
Herpes zoster			
subjects affected / exposed	2 / 47 (4.26%)	3 / 50 (6.00%)	0 / 46 (0.00%)
occurrences (all)	2	3	0
Urinary tract infection			
subjects affected / exposed	1 / 47 (2.13%)	3 / 50 (6.00%)	1 / 46 (2.17%)
occurrences (all)	1	3	2
Nasopharyngitis			
subjects affected / exposed	2 / 47 (4.26%)	3 / 50 (6.00%)	3 / 46 (6.52%)
occurrences (all)	4	3	3
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	2 / 47 (4.26%)	4 / 50 (8.00%)	3 / 46 (6.52%)
occurrences (all)	2	5	3

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 February 2008	The estimated date of last patient completed was corrected to account for the follow-up procedure for patients still receiving clinical benefit, in the opinion of the investigator, after the data cut-off for the primary analysis. Follow-up procedures post DCO for the primary analysis were clarified.
12 February 2010	The primary statistical analysis of the fulvestrant "CONFIRM" study (D6997C00002, CSR dated 09 July 2009), showed a clinically and statistically significant advantage for the 500 mg fulvestrant dose group compared to the 250 mg dose group with respect to the primary endpoint of time to progression (TTP), with no clinically significant differences in adverse events in the 500 mg dose group compared to the 250 mg group. The CONFIRM Independent Data Monitoring Committee (IDMC) reviewed these results and recommended that all patients who remain on fulvestrant 250 mg, be given the option to transfer to fulvestrant 500 mg. Dr. Angelo Di Leo, the CONFIRM International Coordinating Investigator, has endorsed this position and agreed that patients receiving fulvestrant 250mg should be assessed on an individual basis by their treating physician, and if both agree, the patient will be transferred to fulvestrant 500 mg. Ongoing patients on the FINDER2 trial are currently receiving open label supplies. Patients who are currently receiving the fulvestrant 250 mg will be given the option of transferring to fulvestrant 500 mg. Patients wishing to transfer to the higher dose will be asked to provide re-consent as required by the AstraZeneca Informed Consent Process. No further analysis will be performed for this study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported