



Clinical trial results:

A Randomised, Double-blind, Parallel-group, Multicentre, Phase III Study to Compare the Efficacy and Tolerability of Fulvestrant (FASLODEX™) 500 mg with Anastrozole (ARIMIDEX™) 1 mg as Hormonal Treatment for Postmenopausal Women with Hormone Receptor-Positive Locally Advanced or Metastatic Breast Cancer Who Have Not Previously Been Treated with Any Hormonal Therapy (FALCON)

Summary

EudraCT number	2011-006326-24
Trial protocol	GB ES CZ SK IT PL
Global end of trial date	16 January 2026

Results information

Result version number	v1 (current)
This version publication date	30 April 2026
First version publication date	30 April 2026

Trial information

Trial identification

Sponsor protocol code	D699BC00001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01602380
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca AB
Sponsor organisation address	Karlebyhusentren, B674 Astraallen, Södertälje, Sweden, 151 85
Public contact	Global Clinical Lead, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca, +1 877-240-9479, information.center@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	16 January 2026
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 January 2026
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to demonstrate the superior progression-free survival (PFS) of patients treated with fulvestrant 500 milligram (mg) versus patients treated with anastrozole 1 mg.

Protection of trial subjects:

This study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with International Council for Harmonisation/Good Clinical Practice, applicable regulatory requirements, and the AstraZeneca policy on Bioethics.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 October 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 12
Country: Number of subjects enrolled	Brazil: 7
Country: Number of subjects enrolled	Canada: 29
Country: Number of subjects enrolled	China: 25
Country: Number of subjects enrolled	Czechia: 7
Country: Number of subjects enrolled	Italy: 15
Country: Number of subjects enrolled	Japan: 31
Country: Number of subjects enrolled	Mexico: 19
Country: Number of subjects enrolled	Peru: 23
Country: Number of subjects enrolled	Poland: 9
Country: Number of subjects enrolled	Romania: 8
Country: Number of subjects enrolled	Russian Federation: 102
Country: Number of subjects enrolled	Slovakia: 6
Country: Number of subjects enrolled	South Africa: 16
Country: Number of subjects enrolled	Spain: 19
Country: Number of subjects enrolled	Taiwan: 11
Country: Number of subjects enrolled	Türkiye: 1
Country: Number of subjects enrolled	Ukraine: 85
Country: Number of subjects enrolled	United Kingdom: 17
Country: Number of subjects enrolled	United States: 20

Worldwide total number of subjects	462
EEA total number of subjects	64

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)	263
From 65 to 84 years	189
85 years and over	10

Subject disposition

Recruitment

Recruitment details:

First patient enrolled: 17 October 2012.

Pre-assignment

Screening details:

524 patients were enrolled (signed informed consent). Patients were assigned to treatment if they met all inclusion and none of the exclusion criteria. 62 patients were not randomised, mainly due to eligibility criteria not being fulfilled (44/62 patients) or patient decision (13/62 patients). 462 patients were randomised to receive treatment.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Fulvestrant 500 mg

Arm description:

Patients received fulvestrant (Faslodex™) 500 mg, administered as two 5 milliliters (mL) intramuscular injections, 1 in each buttock, at each visit on Days 0, 14 (± 3), 28 (± 3) and every 28 (± 3) days thereafter. In order to support the double-blind, double-dummy design of the trial, each patient randomised to receive fulvestrant, also received placebo to match the anastrozole schedule (tablets, once daily).

Arm type	Experimental
Investigational medicinal product name	Placebo to match anastrozole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Matching placebo was administered orally as a single daily tablet at a dose of 1 mg/day from randomisation on Day 0 until the patient permanently discontinued the treatment.

Investigational medicinal product name	Fulvestrant
Investigational medicinal product code	
Other name	Faslodex
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Fulvestrant 500 mg was administered as two 5 ml intramuscular injections, one in each buttock, on Days 0, 14 (± 3), 28 (± 3) and every 28 (± 3) days thereafter until the patient permanently discontinued the treatment.

Arm title	Anastrozole 1 mg
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Arm description:

Patients received anastrozole (Arimidex™), administered orally as a single tablet at a dose of 1 mg/day from randomisation on Day 0 and once daily thereafter. In order to support the double-blind, double-dummy design of the trial, each patient randomised to receive anastrozole also received placebo to match the fulvestrant schedule (injections on Days 0, 14 [± 3], 28 [± 3] and every 28 [± 3] days thereafter).

Arm type	Active comparator
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Investigational medicinal product name	Placebo to match fulvestrant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Matching placebo was administered as two 5 mL intramuscular injections, one in each buttock, at each visit on Days 0, 14 (± 3), 28 (± 3) and every 28 (± 3) days thereafter until the patient permanently discontinued the treatment.

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

Dosage and administration details:

Anastrozole was administered as a 1 mg oral tablet from randomisation on Day 0 until the patient permanently discontinued the treatment.

Number of subjects in period 1	Fulvestrant 500 mg	Anastrozole 1 mg
Started	230	232
Completed	25	31
Not completed	205	201
Consent withdrawn by subject	39	41
Eligibility criteria not fulfilled	2	3
Death	147	145
Unspecified	2	-
Lost to follow-up	15	12

Baseline characteristics

Reporting groups

Reporting group title	Fulvestrant 500 mg
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Reporting group description:

Patients received fulvestrant (Faslodex™) 500 mg, administered as two 5 milliliters (mL) intramuscular injections, 1 in each buttock, at each visit on Days 0, 14 (± 3), 28 (± 3) and every 28 (± 3) days thereafter. In order to support the double-blind, double-dummy design of the trial, each patient randomised to receive fulvestrant, also received placebo to match the anastrozole schedule (tablets, once daily).

Reporting group title	Anastrozole 1 mg
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Reporting group description:

Patients received anastrozole (Arimidex™), administered orally as a single tablet at a dose of 1 mg/day from randomisation on Day 0 and once daily thereafter. In order to support the double-blind, double-dummy design of the trial, each patient randomised to receive anastrozole also received placebo to match the fulvestrant schedule (injections on Days 0, 14 [± 3], 28 [± 3] and every 28 [± 3] days thereafter).

Reporting group values	Fulvestrant 500 mg	Anastrozole 1 mg	Total
Number of subjects	230	232	462
Age categorical			
Units: Subjects			

Age Continuous			
Units: years			
arithmetic mean	63.8	63.3	
standard deviation	± 9.86	± 10.38	-
Sex: Female, Male			
Units:			
Female	230	232	462
Male	0	0	0
Race/Ethnicity, Customized			
Units: Subjects			
American Indian or Alaska Native	1	5	6
Asian	36	34	70
Black or African American	4	4	8
White	175	174	349
Other	14	15	29

End points

End points reporting groups

Reporting group title	Fulvestrant 500 mg
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Reporting group description:

Patients received fulvestrant (Faslodex™) 500 mg, administered as two 5 milliliters (mL) intramuscular injections, 1 in each buttock, at each visit on Days 0, 14 (± 3), 28 (± 3) and every 28 (± 3) days thereafter. In order to support the double-blind, double-dummy design of the trial, each patient randomised to receive fulvestrant, also received placebo to match the anastrozole schedule (tablets, once daily).

Reporting group title	Anastrozole 1 mg
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Reporting group description:

Patients received anastrozole (Arimidex™), administered orally as a single tablet at a dose of 1 mg/day from randomisation on Day 0 and once daily thereafter. In order to support the double-blind, double-dummy design of the trial, each patient randomised to receive anastrozole also received placebo to match the fulvestrant schedule (injections on Days 0, 14 [± 3], 28 [± 3] and every 28 [± 3] days thereafter).

Primary: Comparison of PFS in Patients Treated With Fulvestrant With Those Treated With Anastrozole

End point title	Comparison of PFS in Patients Treated With Fulvestrant With Those Treated With Anastrozole
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End point description:

PFS was defined as the time from randomisation until objective disease progression according to Response Evaluation Criteria in Solid Tumours version 1.1 (RECIST 1.1), surgery or radiotherapy to manage worsening of disease or death by any cause (in the absence of progression). Outcome measure is reported as median time from randomisation to PFS, calculated using the Kaplan-Meier technique. The intention to treat (ITT) analysis set included all randomised patients.

End point type	Primary
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End point timeframe:

Baseline RECIST 1.1 assessments (Day 0) and then every 12 weeks until the earliest of disease progression evident, patient dies or has surgery/radiotherapy for their disease (up to approximately 38 months)

End point values	Fulvestrant 500 mg	Anastrozole 1 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	230	232		
Units: Months				
median (confidence interval 95%)	16.6 (13.83 to 20.99)	13.8 (11.99 to 16.59)		

Statistical analyses

Statistical analysis title	Comparison of PFS
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Statistical analysis description:

If the true PFS hazard ratio (HR) for comparison of fulvestrant vs. anastrozole was 0.69 (likely to correspond to a 45% prolongation of PFS) the study had 90% power to demonstrate a statistically significant difference for PFS with a one-sided type 1 error of 2.5% (two-sided 5%).

Comparison groups	Anastrozole 1 mg v Fulvestrant 500 mg
Number of subjects included in analysis	462
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
P-value	= 0.0486 ^[2]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.797
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.637
upper limit	0.999

Notes:

[1] - Stratified log-rank test with factors for prior chemotherapy for locally advanced or metastatic disease and measurable disease at baseline. A hazard ratio < 1 favours fulvestrant.

[2] - 2-sided p-value

Secondary: Comparison of Overall Survival (OS) in Patients Treated With Fulvestrant With Those Treated With Anastrozole; Percentage of Patients With Events

End point title	Comparison of Overall Survival (OS) in Patients Treated With Fulvestrant With Those Treated With Anastrozole; Percentage of Patients With Events
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End point description:

OS was defined as the time from randomisation until death by any cause. The current OS data correspond to that of the final analysis and the outcome measure is reported as percentage of patients with events. The ITT analysis set included all randomised patients. Date of death of 2 patients were unknown in the Anastrozole 1 mg arm, hence they were censored for OS analysis.

End point type	Secondary
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End point timeframe:

Baseline (Day 0) up to data cut-off for final analysis (up to approximately 116 months). Following disease progression, patients were to be contacted at 12 weekly intervals to determine survival status

End point values	Fulvestrant 500 mg	Anastrozole 1 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	230	232		
Units: Percentage of patients				
number (not applicable)	68.3	67.7		

Statistical analyses

Statistical analysis title	Comparison of OS
Statistical analysis description:	
65% OS maturity	
Comparison groups	Fulvestrant 500 mg v Anastrozole 1 mg

Number of subjects included in analysis	462
Analysis specification	Pre-specified
Analysis type	superiority ^[3]
P-value	= 0.7579 ^[4]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.966
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.773
upper limit	1.206

Notes:

[3] - Stratified log-rank test with factors for prior chemotherapy for locally advanced or metastatic disease and measurable disease at baseline. A HR of <1 favours fulvestrant.

[4] - 2-sided p-value

Secondary: Objective Response Rate (ORR) for Fulvestrant Treatment Versus Anastrozole Treatment

End point title	Objective Response Rate (ORR) for Fulvestrant Treatment Versus Anastrozole Treatment
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End point description:

ORR was defined as the percentage of patients with an objective response (those recording a partial response [PR] or complete response [CR]) at some point during the study, prior to disease progression. ORR was assessed in patients with measurable disease at baseline only. The determination of measurable disease at baseline was done using baseline RECIST data. CR was disappearance of all target lesions since baseline; was any pathological lymph nodes selected as target lesions (TL) to have a reduction in short axis to <10 millimeter. PR was at least a 30% decrease in the sum of the diameters of TL, taking as reference the baseline sum of diameters. Percentages for ORR were calculated based on the number of patients in the ITT analysis set (which included all randomised patients) who had measurable disease at baseline (n=193 for Fulvestrant arm and n=196 for Anastrozole arm).

End point type	Secondary
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End point timeframe:

Baseline RECIST 1.1 assessments (Day 0) and then every 12 weeks until disease progression or treatment discontinuation (up to approximately 38 months)

End point values	Fulvestrant 500 mg	Anastrozole 1 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	193	196		
Units: Percentage of patients				
number (not applicable)	46.1	44.9		

Statistical analyses

Statistical analysis title	ORR
Comparison groups	Fulvestrant 500 mg v Anastrozole 1 mg

Number of subjects included in analysis	389
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.729 ^[5]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.074
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.716
upper limit	1.614

Notes:

[5] - 2-sided p-value

Secondary: Duration of Response (DoR) for Fulvestrant Treatment Versus Anastrozole Treatment

End point title	Duration of Response (DoR) for Fulvestrant Treatment Versus Anastrozole Treatment
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End point description:

DoR was defined only for patients who had an objective response, as the time in days from date of first documentation of response (CR/PR) until date of disease progression. CR was disappearance of all target lesions since baseline; any pathological lymph nodes selected as TL to have a reduction in short axis to <10 mm. At least a 30% decrease in the sum of the diameters of TL, taking as reference the baseline sum of diameters. Only patients in the ITT analysis set (which included all randomised patients), who also had an objective response and had measurable disease at baseline were included in the DoR analysis (n=89 for Fulvestrant arm and n=88 for Anastrozole arm). 99999=75th percentile value not calculable due to insufficient data.

End point type	Secondary
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End point timeframe:

Baseline RECIST 1.1 assessments (Day 0) and then every 12 weeks until disease progression or treatment discontinuation (up to approximately 38 months)

End point values	Fulvestrant 500 mg	Anastrozole 1 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	88		
Units: Months				
median (inter-quartile range (Q1-Q3))	20.0 (10.6 to 99999)	13.2 (8.3 to 24.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Expected Duration of Response (EDoR) for Fulvestrant Treatment Versus Anastrozole Treatment

End point title	Expected Duration of Response (EDoR) for Fulvestrant Treatment Versus Anastrozole Treatment
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End point description:

EDoR was estimated using the formula $EDoR = p \cdot Efp(x)$, where $x = DoR$, p = proportion of responders, and $Efp(x)$ = mean duration of response for responders. The estimation was completed by using the maximum likelihood estimates of p and $Efp(x)$, as described by Ellis (Ellis S et al. Analysis of duration of response in oncology trials, Contemp Clin Trials 2008; 29:456–65). EDoR analysis was based on the number of patients in the ITT analysis set (which included all randomised patients) who had measurable disease at baseline ($n=193$ for Fulvestrant arm and $n=196$ for Anastrozole arm).

End point type	Secondary
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End point timeframe:

Baseline RECIST 1.1 assessments and then every 12 weeks until disease progression or treatment discontinuation (up to approximately 38 months)

End point values	Fulvestrant 500 mg	Anastrozole 1 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	193	196		
Units: Days				
number (not applicable)	346.84	227.58		

Statistical analyses

Statistical analysis title	EDoR
Comparison groups	Fulvestrant 500 mg v Anastrozole 1 mg
Number of subjects included in analysis	389
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0367 ^[6]
Method	Method of Ellis et al
Parameter estimate	Rato of EDoR
Point estimate	1.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	2.26

Notes:

[6] - 2-sided p-value

Secondary: Clinical Benefit Rate (CBR) for Fulvestrant Treatment Versus Anastrozole Treatment

End point title	Clinical Benefit Rate (CBR) for Fulvestrant Treatment Versus Anastrozole Treatment
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End point description:

CBR was defined as the percentage of patients who had a clinical benefit (i.e. best objective response of CR, PR or stable disease), that was maintained for at least 24 weeks, prior to any evidence of progression. Note that a minimum duration of 22 weeks for CBR was applicable in the analysis (rather than 24 weeks) to allow for the protocolled window of +/-2 weeks. The ITT analysis set included all randomised patients.

End point type	Secondary
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End point timeframe:

Baseline RECIST 1.1 assessments (Day 0) and then every 12 weeks until disease progression or treatment discontinuation (up to approximately 38 months)

End point values	Fulvestrant 500 mg	Anastrozole 1 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	230	232		
Units: Percentage of patients				
number (not applicable)	78.3	74.1		

Statistical analyses

Statistical analysis title	CBR
Comparison groups	Fulvestrant 500 mg v Anastrozole 1 mg
Number of subjects included in analysis	462
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3045 [7]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.253
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.815
upper limit	1.932

Notes:

[7] - 2-sided p-value

Secondary: Duration of Clinical Benefit (DoCB) for Fulvestrant Treatment Versus Anastrozole Treatment

End point title	Duration of Clinical Benefit (DoCB) for Fulvestrant Treatment Versus Anastrozole Treatment
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End point description:

DoCB was defined only for patients who had clinical benefit, as the time in days from date of randomisation until the date of disease progression. Only patients in the ITT analysis set (which included all randomised patients) who also had a clinical benefit were included in the DoCB analysis (n=180 for Fulvestrant arm and n=172 for Anastrozole arm). 99999=75th percentile value not calculable due to insufficient data.

End point type	Secondary
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End point timeframe:

Baseline RECIST 1.1 assessments (Day 0) and then every 12 weeks until disease progression or treatment discontinuation (up to approximately 38 months)

End point values	Fulvestrant 500 mg	Anastrozole 1 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	180	172		
Units: Months				
median (inter-quartile range (Q1-Q3))	22.1 (11.2 to 99999)	19.1 (11.3 to 30.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Expected Duration of Clinical Benefit (EDoCB) for Fulvestrant Treatment Versus Anastrozole Treatment

End point title	Expected Duration of Clinical Benefit (EDoCB) for Fulvestrant Treatment Versus Anastrozole Treatment
End point description:	
EDoCB was estimated using the formula $EDoCB = p \cdot Efp(x)$, where $x = EDoCB$, p = proportion of responders, and $Efp(x)$ = mean duration of response for responders. The estimation was completed by using the maximum likelihood estimates of p and $Efp(x)$, as described by Ellis (Ellis S et al. Analysis of duration of response in oncology trials, Contemp Clin Trials 2008; 29:456–65). The ITT analysis set included all randomised patients.	
End point type	Secondary
End point timeframe:	
Baseline RECIST 1.1 assessments (Day 0) and then every 12 weeks until disease progression or treatment discontinuation (up to approximately 38 months)	

End point values	Fulvestrant 500 mg	Anastrozole 1 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	230	232		
Units: Days				
number (not applicable)	667.94	532.04		

Statistical analyses

Statistical analysis title	EDoCB
Comparison groups	Fulvestrant 500 mg v Anastrozole 1 mg
Number of subjects included in analysis	462
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0561 [8]
Method	Method of Ellis et al
Parameter estimate	Ratio of EDoCB
Point estimate	1.26

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	1.59

Notes:

[8] - 2-sided p-value

Secondary: Comparison of the Effect of Fulvestrant Treatment Versus Anastrozole Treatment on Time to Deterioration of Health-Related Quality of Life (HRQoL)

End point title	Comparison of the Effect of Fulvestrant Treatment Versus Anastrozole Treatment on Time to Deterioration of Health-Related Quality of Life (HRQoL)
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End point description:

The Functional Assessment of Cancer Therapy - Breast (FACT-B) questionnaire was the instrument selected to assess HRQoL and comprised of following subscales: physical well-being (PWB), functional well-being (FWB), social well-being, emotional well-being, and breast cancer subscale (BCS). The main outcome measure from the FACT-B questionnaire was the Trial Outcome Index (TOI), which was a summary of the following subscales: PWB, FWB, and BCS. Outcome measure is reported as median time to deterioration, defined as the interval from the date of baseline of final analysis to the first assessment of worsened without an improvement in the next 12 weeks in FACT-B TOI, or the date of death (by any cause in the absence of symptom deterioration). Time to deterioration as measured by FACT-B total score was derived similarly and is also reported. The ITT analysis set included all randomised patients.

End point type	Secondary
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End point timeframe:

Quality of life questionnaires administered at 3 months post objective disease progression, then at 6-monthly intervals (approximately 75 months)

End point values	Fulvestrant 500 mg	Anastrozole 1 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	230	232		
Units: months				
median (inter-quartile range (Q1-Q3))				
Time to TOI deterioration	14.1 (5.5 to 44.1)	11.1 (5.5 to 38.3)		
Time to FACT-B total score deterioration	13.8 (5.5 to 38.7)	11.1 (4.8 to 33.6)		

Statistical analyses

Statistical analysis title	Comparison of the effect on HRQoL
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Statistical analysis description:

Comparative statistical analysis for time to deterioration of FACT-B total score is presented (fulvestrant versus anastrozole).

Comparison groups	Fulvestrant 500 mg v Anastrozole 1 mg
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Number of subjects included in analysis	462
Analysis specification	Pre-specified
Analysis type	superiority ^[9]
P-value	= 0.0844 ^[10]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	1.03

Notes:

[9] - Stratified log-rank test with factors for prior chemotherapy for locally advanced/metastatic disease and measurable/non-measurable disease at baseline. A hazard ratio < 1 favours fulvestrant.

[10] - 2-sided p-value

Statistical analysis title	Comparison of the effect on HRQoL
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Statistical analysis description:

Comparative statistical analysis for time to deterioration of TOI score is presented (fulvestrant versus anastrozole).

Comparison groups	Fulvestrant 500 mg v Anastrozole 1 mg
Number of subjects included in analysis	462
Analysis specification	Pre-specified
Analysis type	superiority ^[11]
P-value	= 0.2846 ^[12]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.11

Notes:

[11] - Stratified log-rank test with factors for prior chemotherapy for locally advanced/metastatic disease and measurable/non-measurable disease at baseline. A hazard ratio < 1 favours fulvestrant.

[12] - 2-sided p-value

Adverse events

Adverse events information

Timeframe for reporting adverse events:

116 months (duration from first patient enrolled to data cut-off date for the final analysis)

Adverse event reporting additional description:

All-Cause Mortality: The ITT analysis set: All randomised patients. Serious adverse events and other (non-serious) adverse events: Safety population was defined as all patients who received at least 1 dose of randomised study medication. 2 patients in the Fulvestrant 500 mg arm did not receive treatment and were not included in safety population.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.0
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Reporting groups

Reporting group title	Fulvestrant 500 mg
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Reporting group description:

Patients received fulvestrant (Faslodex™) 500 mg, administered as two 5 mL intramuscular injections, 1 in each buttock, at each visit on Days 0, 14 (± 3), 28 (± 3) and every 28 (± 3) days thereafter. In order to support the double-blind, double-dummy design of the trial, each patient randomised to receive fulvestrant, also received placebo to match the anastrozole schedule (tablets, once daily).

Reporting group title	Anastrozole 1 mg
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Reporting group description:

Patients received anastrozole (Arimidex™), administered orally as a single tablet at a dose of 1 mg/day from randomisation on Day 0 and once daily thereafter. In order to support the double-blind, double-dummy design of the trial, each patient randomised to receive anastrozole also received placebo to match the fulvestrant schedule (injections on Days 0, 14 [± 3], 28 [± 3] and every 28 [± 3] days thereafter).

Serious adverse events	Fulvestrant 500 mg	Anastrozole 1 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	39 / 228 (17.11%)	36 / 232 (15.52%)	
number of deaths (all causes)	157	159	
number of deaths resulting from adverse events	7	9	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colorectal cancer			
subjects affected / exposed	1 / 228 (0.44%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	1 / 228 (0.44%)	3 / 232 (1.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			

subjects affected / exposed	0 / 228 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma of colon			
subjects affected / exposed	1 / 228 (0.44%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acoustic neuroma			
subjects affected / exposed	0 / 228 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphoma			
subjects affected / exposed	1 / 228 (0.44%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of the oral cavity			
subjects affected / exposed	1 / 228 (0.44%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	2 / 228 (0.88%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	0 / 228 (0.00%)	2 / 232 (0.86%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circulatory collapse			
subjects affected / exposed	0 / 228 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			

Drug hypersensitivity			
subjects affected / exposed	1 / 228 (0.44%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Bronchiectasis			
subjects affected / exposed	0 / 228 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	3 / 228 (1.32%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	2 / 4	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pleural effusion			
subjects affected / exposed	7 / 228 (3.07%)	2 / 232 (0.86%)	
occurrences causally related to treatment / all	0 / 10	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 228 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	2 / 228 (0.88%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute respiratory failure			
subjects affected / exposed	0 / 228 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Psychiatric disorders			
Anxiety			

subjects affected / exposed	0 / 228 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 228 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alanine aminotransferase increased			
subjects affected / exposed	0 / 228 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			
subjects affected / exposed	0 / 228 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Skin abrasion			
subjects affected / exposed	1 / 228 (0.44%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	0 / 228 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 228 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	1 / 228 (0.44%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Radius fracture			
subjects affected / exposed	2 / 228 (0.88%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	1 / 228 (0.44%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic spinal cord compression			
subjects affected / exposed	1 / 228 (0.44%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure acute			
subjects affected / exposed	0 / 228 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Atrial flutter			
subjects affected / exposed	0 / 228 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute coronary syndrome			
subjects affected / exposed	0 / 228 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	0 / 228 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Angina pectoris			
subjects affected / exposed	1 / 228 (0.44%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			

subjects affected / exposed	1 / 228 (0.44%)	2 / 232 (0.86%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 228 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure			
subjects affected / exposed	0 / 228 (0.00%)	3 / 232 (1.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardio-respiratory arrest			
subjects affected / exposed	0 / 228 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Palpitations			
subjects affected / exposed	1 / 228 (0.44%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Haemorrhagic stroke			
subjects affected / exposed	1 / 228 (0.44%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	2 / 228 (0.88%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cerebral infarction			
subjects affected / exposed	0 / 228 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cerebral haemorrhage			

subjects affected / exposed	0 / 228 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain oedema			
subjects affected / exposed	1 / 228 (0.44%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	1 / 228 (0.44%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 228 (0.44%)	2 / 232 (0.86%)	
occurrences causally related to treatment / all	0 / 1	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 228 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia macrocytic			
subjects affected / exposed	1 / 228 (0.44%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	1 / 228 (0.44%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal dilatation			
subjects affected / exposed	0 / 228 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			

subjects affected / exposed	1 / 228 (0.44%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 228 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal stenosis			
subjects affected / exposed	1 / 228 (0.44%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	1 / 228 (0.44%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	0 / 228 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice cholestatic			
subjects affected / exposed	0 / 228 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	1 / 228 (0.44%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 228 (0.00%)	2 / 232 (0.86%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Musculoskeletal and connective tissue			

disorders			
Neck pain			
subjects affected / exposed	0 / 228 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 228 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 228 (0.44%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 228 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	0 / 228 (0.00%)	2 / 232 (0.86%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Device related sepsis			
subjects affected / exposed	1 / 228 (0.44%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 228 (0.44%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 228 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Lower respiratory tract infection subjects affected / exposed	1 / 228 (0.44%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis subjects affected / exposed	2 / 228 (0.88%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia subjects affected / exposed	3 / 228 (1.32%)	4 / 232 (1.72%)	
occurrences causally related to treatment / all	0 / 3	0 / 7	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pyelonephritis subjects affected / exposed	0 / 228 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection subjects affected / exposed	2 / 228 (0.88%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock subjects affected / exposed	1 / 228 (0.44%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metabolism and nutrition disorders Dehydration subjects affected / exposed	0 / 228 (0.00%)	2 / 232 (0.86%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Fulvestrant 500 mg	Anastrozole 1 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	166 / 228 (72.81%)	171 / 232 (73.71%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	16 / 228 (7.02%)	8 / 232 (3.45%)	
occurrences (all)	18	8	
Aspartate aminotransferase increased			
subjects affected / exposed	12 / 228 (5.26%)	9 / 232 (3.88%)	
occurrences (all)	13	9	
Vascular disorders			
Hypertension			
subjects affected / exposed	18 / 228 (7.89%)	22 / 232 (9.48%)	
occurrences (all)	19	25	
Hot flush			
subjects affected / exposed	26 / 228 (11.40%)	24 / 232 (10.34%)	
occurrences (all)	35	32	
Nervous system disorders			
Headache			
subjects affected / exposed	12 / 228 (5.26%)	12 / 232 (5.17%)	
occurrences (all)	13	12	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	9 / 228 (3.95%)	20 / 232 (8.62%)	
occurrences (all)	10	21	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	29 / 228 (12.72%)	18 / 232 (7.76%)	
occurrences (all)	35	20	
Injection site pain			
subjects affected / exposed	12 / 228 (5.26%)	10 / 232 (4.31%)	
occurrences (all)	15	23	
Oedema peripheral			
subjects affected / exposed	11 / 228 (4.82%)	14 / 232 (6.03%)	
occurrences (all)	11	15	
Gastrointestinal disorders			

Constipation subjects affected / exposed occurrences (all)	16 / 228 (7.02%) 16	11 / 232 (4.74%) 13	
Diarrhoea subjects affected / exposed occurrences (all)	15 / 228 (6.58%) 20	15 / 232 (6.47%) 17	
Nausea subjects affected / exposed occurrences (all)	25 / 228 (10.96%) 29	25 / 232 (10.78%) 27	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	12 / 228 (5.26%) 15	9 / 232 (3.88%) 12	
Dyspnoea subjects affected / exposed occurrences (all)	10 / 228 (4.39%) 10	15 / 232 (6.47%) 17	
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	18 / 228 (7.89%) 19	15 / 232 (6.47%) 16	
Anxiety subjects affected / exposed occurrences (all)	12 / 228 (5.26%) 13	4 / 232 (1.72%) 4	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	42 / 228 (18.42%) 65	31 / 232 (13.36%) 40	
Back pain subjects affected / exposed occurrences (all)	22 / 228 (9.65%) 25	18 / 232 (7.76%) 19	
Myalgia subjects affected / exposed occurrences (all)	16 / 228 (7.02%) 19	8 / 232 (3.45%) 11	
Pain in extremity subjects affected / exposed occurrences (all)	17 / 228 (7.46%) 22	11 / 232 (4.74%) 15	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 December 2012	Clarified that patients who continued to receive open-label study treatment beyond the closure of the database were no longer required to continue with the placebo treatment. Editorial corrections included. Eligibility criteria updated. The methods for unblinding the study were updated. Updates and clarifications were made to the concomitant and post-study treatment. Clarified that the statistical analysis was to be performed on the oestrogen containing hormone replacement therapy data.
01 December 2017	Clarified that the delay of final OS analysis would be to 75% maturity. Updated to describe the investigational product supply in the post OS analysis phase. Updated to explain that serious adverse events (SAEs) were to be recorded on a paper-based SAE report form in the post-OS analysis period.
17 December 2021	Change of final OS analysis trigger from when 75% of patients died to: when at least 65% of patients died and at least 8 years passed since the last patient was enrolled. Updated with details of provision of fulvestrant and anastrozole being supplied as a continued access phase after final database lock. Clarified that Coronavirus Disease-2019 (COVID-19) vaccination with authorised vaccines was permitted at the discretion of the investigator. Change in the wording of SAE reporting as opposed to SAE recorded. Updated the study timetable details. Change of contract research organization name from Quintiles to IQVIA. Other minor corrections/updates were made throughout the document.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported