Clinical trial results:
Elacestrant Monotherapy vs. Standard of Care for the Treatment of Patients with ER+/HER2- Advanced Breast Cancer Following CDK4/6 Inhibitor Therapy: A Phase 3 Randomized, Open-label, Active-controlled, Multicenter Trial

Summary

EudraCT number	2018-002990-24
Trial protocol	BE FR HU AT GR IE PT DK ES GB IT
Global end of trial date	22 August 2024

Results information

Result version number	v1 (current)
This version publication date	07 September 2025
First version publication date	07 September 2025

Trial information

Trial identification

Sponsor protocol code	RAD1901-308

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03778931
WHO universal trial number (UTN)	-
Other trial identifiers	Sponsor Acronym: EMERALD

Notes:

Sponsors

Sponsor organisation name	Menarini Ricerche S.p.A.
Sponsor organisation address	Via Tito Speri 10, Pomezia/Rome, Italy, 00071
Public contact	Clinical Operations, Radius Pharmaceuticals Inc., +1 617-551-4000, RAD1901-308@radiuspharm.com
Scientific contact	Clinical Operations, Radius Pharmaceuticals Inc., +1 617-551-4000, RAD1901-308@radiuspharm.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	22 August 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 August 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that elacestrant compared with the standard of care (SOC) options of either fulvestrant or an aromatase inhibitor is superior in prolonging progression-free survival based on a blinded imaging review committee (IRC) assessment in postmenopausal women and men with estrogen receptor positive/human epidermal growth factor receptor 2 negative (ER+/HER2-) advanced/metastatic breast cancer, either in participants with estrogen receptor 1 gene (ESR1) mutations (ESR1-mut participants) or in all participants, which includes participants without detectable ESR1 mutations (ESR1-wild-type [ESR1-wt]).

Protection of trial subjects:

All clinical trial information shall be recorded, processed, handled, and stored in such a way that it can be accurately reported, interpreted and verified; at the same time, the confidentiality of records and of the personal data of the participants shall remain protected in accordance with the Laws and Regulation on personal data protection from time to time applicable such as the EU General Data Protection Regulation 679/2016 and the EU Regulation on clinical trials on medicinal products for human use 536/2014 or the US Health Insurance Portability and Accountability Act regulations (HIPAA), the US Common Rule (45 CFR 46.116).

The study protocol defines the appropriate technical and organisational measures that shall be implemented to protect information and personal data processed against unauthorised or unlawful access, disclosure, dissemination, alteration, or destruction or accidental loss as well as to assure the fulfilment of participants' privacy rights.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 November 2018
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	Portugal: 12
Country: Number of subjects enrolled	Spain: 29
Country: Number of subjects enrolled	United Kingdom: 12
Country: Number of subjects enrolled	Austria: 7
Country: Number of subjects enrolled	Belgium: 70
Country: Number of subjects enrolled	Denmark: 9
Country: Number of subjects enrolled	France: 38
Country: Number of subjects enrolled	Greece: 10
Country: Number of subjects enrolled	Hungary: 29

Country: Number of subjects enrolled	Ireland: 7
Country: Number of subjects enrolled	Italy: 35
Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	United States: 136
Country: Number of subjects enrolled	Israel: 21
Country: Number of subjects enrolled	Korea, Republic of: 29
Country: Number of subjects enrolled	Argentina: 18
Country: Number of subjects enrolled	Australia: 11
Worldwide total number of subjects	478
EEA total number of subjects	246

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	213
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

All deaths regardless of causality are reported as 'number of deaths (all causes)' in the Serious Adverse Events table. Only deaths leading to study discontinuation are reported in the Subject Disposition.

Pre-assignment

Screening details:

This study screened 695 participants who granted informed consent for participation, and randomized 478 participants to treatment with either elacestrant or SOC.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Elacestrant

Arm description:

Participants in Arm 1 will receive elacestrant.

Elacestrant: 400 milligrams/day once daily oral dosing

Arm type	Experimental
Investigational medicinal product name	Elacestrant
Investigational medicinal product code	
Other name	RAD1901; ORSERDU
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Once per day

Arm title	Standard of Care (SoC)

Arm description:

Participants in Arm 2 will receive investigator’s choice of one of the SOC drugs (fulvestrant, anastrozole, letrozole, or exemestane).

SOC:
• Fulvestrant: 500 milligrams administered intramuscularly into the buttocks as two 5-millilitre injections on Cycle 1 Day 1, Cycle 1 Day 15, and Cycle 2 Day 1 and Day 1 of every subsequent 28-day cycle
• Anastrozole 1 milligram/day on a continuous dosing schedule
• Letrozole: 2.5 milligrams/day on a continuous dosing schedule
• Exemestane: 25 milligrams/day on a continuous dosing schedule

Arm type	Active comparator
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:

Cycle 1 Day 1, Cycle 1 Day 15, and Cycle 2 Day 1 and Day 1 of every subsequent 28-day cycle

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

Dosage and administration details:
Once per day

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

Dosage and administration details:
Once per day

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

Dosage and administration details:
Once per day

Number of subjects in period 1	Elacestrant	Standard of Care (SoC)
Started	239	239
Intent-to-Treat Population	239	239
Safety Population	237	230
Completed	152	130
Not completed	87	109
Physician decision	1	3
Consent withdrawn by subject	12	25
Participant Noncompliance	1	1
Death	69	79
Lost to follow-up	4	1

Baseline characteristics

Reporting groups

Reporting group title	Elacestrant

Reporting group description:

Participants in Arm 1 will receive elacestrant.

Elacestrant: 400 milligrams/day once daily oral dosing

Reporting group title	Standard of Care (SoC)

Reporting group description:

Participants in Arm 2 will receive investigator's choice of one of the SOC drugs (fulvestrant, anastrozole, letrozole, or exemestane).

SOC:
• Fulvestrant: 500 milligrams administered intramuscularly into the buttocks as two 5-millilitre injections on Cycle 1 Day 1, Cycle 1 Day 15, and Cycle 2 Day 1 and Day 1 of every subsequent 28-day cycle
• Anastrozole 1 milligram/day on a continuous dosing schedule
• Letrozole: 2.5 milligrams/day on a continuous dosing schedule
• Exemestane: 25 milligrams/day on a continuous dosing schedule

Reporting group values	Elacestrant	Standard of Care (SoC)	Total
Number of subjects	239	239	478
Age categorical Units: Subjects			
<18 years	0	0	0
Between 18 and 65 years	135	128	263
>65 years	104	111	215
Gender categorical Units: Subjects			
Female	233	238	471
Male	6	1	7
Ethnicity (NIH/OMB)			
NIH/OMB = National Institutes of Health/Office of Management and Budget			
Units: Subjects			
Hispanic or Latino	19	18	37
Not Hispanic or Latino	194	191	385
Unknown or Not Reported	26	30	56
Eastern Cooperative Oncology Group Performance Status			
Participants were graded on a scale from 0 to 5, where 5 was worst: 0. Normal activity. Fully active, able to carry on all pre-disease performance w/o restriction 1. Symptoms, but ambulatory. Restricted in strenuous activity, ambulatory and able to carry out light work 2. In bed <50% of time. Ambulatory, capable of all self-care, unable to carry out any work activities 3. In bed >50% of time. Capable of limited self-care 4. 100% bedridden. Completely disabled. Cannot carry out any self-care. Confined to bed or chair 5. Dead			
Units: Subjects			
0: Fully active, able to carry on all pre-disease	143	135	278
1: Restricted in physically strenuous activity	96	103	199
2: Ambulatory but unable to carry out any work	0	1	1

Height			
Data was not collected for five participants			
Units: centimetres arithmetic mean standard deviation	±	±	-
Weight Units: kilograms arithmetic mean standard deviation	72.70 ± 16.093	72.39 ± 16.390	-
Body Mass Index			
Data was not collected for five participants			
Units: kilograms/metre squared arithmetic mean standard deviation	±	±	-

Subject analysis sets	
Subject analysis set title	Elacestrant: Baseline Characteristics
Subject analysis set type	Intention-to-treat
Subject analysis set description: Participant data were missing for this baseline measurement.	
Subject analysis set title	Standard of Care (SoC): Baseline Characteristics
Subject analysis set type	Intention-to-treat
Subject analysis set description: Participant data were missing for this baseline measurement.	

Reporting group values	Elacestrant: Baseline Characteristics	Standard of Care (SoC): Baseline Characteristics	
Number of subjects	236	237	
Age categorical Units: Subjects			
<18 years Between 18 and 65 years >65 years			
Gender categorical Units: Subjects			
Female Male			
Ethnicity (NIH/OMB)			
NIH/OMB = National Institutes of Health/Office of Management and Budget			
Units: Subjects			
Hispanic or Latino Not Hispanic or Latino Unknown or Not Reported			
Eastern Cooperative Oncology Group Performance Status			
Participants were graded on a scale from 0 to 5, where 5 was worst: 0. Normal activity. Fully active, able to carry on all pre-disease performance w/o restriction 1. Symptoms, but ambulatory. Restricted in strenuous activity, ambulatory and able to carry out light work 2. In bed <50% of time. Ambulatory, capable of all self-care, unable to carry out any work activities 3. In bed >50% of time. Capable of limited self-care			

4. 100% bedridden. Completely disabled. Cannot carry out any self-care. Confined to bed or chair 5. Dead			
Units: Subjects			
0: Fully active, able to carry on all pre-disease 1: Restricted in physically strenuous activity 2: Ambulatory but unable to carry out any work			
Height			
Data was not collected for five participants			
Units: centimetres			
arithmetic mean	162.27	160.97	
standard deviation	± 7.860	± 7.149	
Weight			
Units: kilograms			
arithmetic mean			
standard deviation	±	±	
Body Mass Index			
Data was not collected for five participants			
Units: kilograms/metre squared			
arithmetic mean	27.58	27.92	
standard deviation	± 5.494	± 5.853	

End points

End points reporting groups

Reporting group title	Elacestrant

Reporting group description:

Participants in Arm 1 will receive elacestrant.

Elacestrant: 400 milligrams/day once daily oral dosing

Reporting group title	Standard of Care (SoC)

Reporting group description:

Participants in Arm 2 will receive investigator’s choice of one of the SOC drugs (fulvestrant, anastrozole, letrozole, or exemestane).

SOC:
• Fulvestrant: 500 milligrams administered intramuscularly into the buttocks as two 5-millilitre injections on Cycle 1 Day 1, Cycle 1 Day 15, and Cycle 2 Day 1 and Day 1 of every subsequent 28-day cycle
• Anastrozole 1 milligram/day on a continuous dosing schedule
• Letrozole: 2.5 milligrams/day on a continuous dosing schedule
• Exemestane: 25 milligrams/day on a continuous dosing schedule

Subject analysis set title	Elacestrant: Baseline Characteristics
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participant data were missing for this baseline measurement.

Subject analysis set title	Standard of Care (SoC): Baseline Characteristics
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participant data were missing for this baseline measurement.

Primary: Progression-free Survival in ESR1-mut Participants

End point title	Progression-free Survival in ESR1-mut Participants

End point description:

Progression-free survival based on blinded IRC assessment in ESR1-mut participants defined as the length of time from randomization until the date of objective disease progression per Response Evaluation Criteria In Solid Tumors Criteria (RECIST v1.1) as assessed by the blinded IRC or death from any cause. Progression is defined per RECIST v1.1 as a 20% increase in the sum of the longest diameter of target lesions, or a measurable increase in a non-target lesion, or the appearance of new lesions.

End point type	Primary

End point timeframe:

From Date of Randomization until Disease Progression or Death Due to Any Cause (up to 12 Months)

End point values	Elacestrant	Standard of Care (SoC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	113		
Units: months				
median (confidence interval 95%)	3.78 (2.17 to 7.26)	1.87 (1.87 to 2.14)		

Statistical analyses

Statistical analysis title	Progression-free Survival in ESR1-mut Participants

Statistical analysis description:

The analysis was performed using a stratified Cox Proportional Hazards model with ties=Efron and the stratification factors: prior treatment with fulvestrant (yes versus no) and presence of visceral metastases (yes versus no); the confidence interval calculated using a profile likelihood approach.

Comparison groups	Elacestrant v Standard of Care (SoC)
Number of subjects included in analysis	228
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0005 [1]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.546
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.387
upper limit	0.768

Notes:

[1] - The p-value was generated by using a two-sided stratified log-rank test.

Primary: Progression-free Survival in All Participants

End point title	Progression-free Survival in All Participants

End point description:

Progression-free survival based on blinded IRC assessment in all (ESR1-mut and ESR1-wt) participants.

End point type	Primary

End point timeframe:

From Date of Randomization until Disease Progression or Death Due to Any Cause (up to 12 Months)

End point values	Elacestrant	Standard of Care (SoC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	239		
Units: months				
median (confidence interval 95%)	2.79 (1.94 to 3.78)	1.91 (1.87 to 2.10)		

Statistical analyses

Statistical analysis title	Progression-free Survival in All Participants

Statistical analysis description:

The analysis was performed using a stratified Cox Proportional Hazards model with ties=Efron and the stratification factors: prior treatment with fulvestrant (yes versus no) and presence of visceral metastases (yes versus no); the confidence interval calculated using a profile likelihood approach.

Comparison groups	Elacestrant v Standard of Care (SoC)

Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0018 [2]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.697
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.552
upper limit	0.88

Notes:

[2] - The p-value was generated by using a two-sided stratified log-rank test.

Secondary: Overall Survival in ESR1-mut Participants

End point title	Overall Survival in ESR1-mut Participants

End point description:

Overall survival in ESR1-mut participants, where overall survival is defined as the length of time from randomization until the date of death from any cause. '9999' = not calculable (insufficient number of participants with events).

End point type	Secondary

End point timeframe:

From Date of Randomization until Death Due to Any Cause (Estimated up to 24 Months)

End point values	Elacestrant	Standard of Care (SoC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	113		
Units: months				
median (confidence interval 95%)	9999 (18.60 to 9999)	16.95 (14.00 to 9999)		

Statistical analyses

Statistical analysis title	Overall Survival in ESR1-mut Participants

Statistical analysis description:

The analysis was performed using a stratified Cox Proportional Hazards model with ties=Efron and the stratification factors: prior treatment with fulvestrant (yes versus no) and presence of visceral metastases (yes versus no); the confidence interval calculated using a profile likelihood approach.

Comparison groups	Elacestrant v Standard of Care (SoC)
Number of subjects included in analysis	228
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0325 [3]
Method	Logrank
Parameter estimate	Hazard Ratio
Point estimate	0.592

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.361
upper limit	0.958

Notes:

[3] - The p-value was generated by using a two-sided stratified log-rank test.

Secondary: Overall Survival in All Participants

End point title	Overall Survival in All Participants

End point description:

Overall survival in all (ESR1-mut and ESR1-wt) participants. '9999' = not calculable (insufficient number of participants with events).

End point type	Secondary

End point timeframe:

From Date of Randomization until Death Due to Any Cause (Estimated up to 24 Months)

End point values	Elacestrant	Standard of Care (SoC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	239		
Units: months				
median (confidence interval 95%)	9999 (19.29 to 9999)	9999 (15.80 to 9999)		

Statistical analyses

Statistical analysis title	Overall Survival in All Participants

Statistical analysis description:

Applied a stratified Cox Proportional Hazards model with ties=Efron and the stratification factors: ESR1-mutational status (ESR1-mut versus ESR1-wt), prior treatment with fulvestrant (yes versus no) and presence of visceral metastases (yes versus no).

Comparison groups	Elacestrant v Standard of Care (SoC)
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0697 [4]
Method	Logrank
Parameter estimate	Hazard Ratio
Point estimate	0.742
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.536
upper limit	1.025

Notes:
[4] - The p-value was generated by using a two-sided stratified log-rank test.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

24 months

Adverse event reporting additional description:

The 'number of deaths (all causes)', progression-free survival, and overall survival were assessed with the Intention-to-Treat Population, which consisted of all randomized participants. Adverse Events (Serious and Other) reporting reflects the Safety Population, which consisted of all participants who received at least 1 dose of study medication.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Elacestrant

Reporting group description:

Participants in Arm 1 will receive elacestrant.

Elacestrant: 400 milligrams/day once daily oral dosing

Reporting group title	Standard of Care (SoC)

Reporting group description:

Participants in Arm 2 will receive investigator’s choice of one of the SOC drugs (fulvestrant, anastrozole, letrozole, or exemestane).

SOC:
• Fulvestrant: 500 milligrams administered intramuscularly into the buttocks as two 5-millilitre injections on Cycle 1 Day 1, Cycle 1 Day 15, and Cycle 2 Day 1 and Day 1 of every subsequent 28-day cycle
• Anastrozole 1 milligram/day on a continuous dosing schedule
• Letrozole: 2.5 milligrams/day on a continuous dosing schedule
• Exemestane: 25 milligrams/day on a continuous dosing schedule

Serious adverse events	Elacestrant	Standard of Care (SoC)	
Total subjects affected by serious adverse events			
subjects affected / exposed	29 / 237 (12.24%)	25 / 230 (10.87%)	
number of deaths (all causes)	70	80	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm of pleura			
subjects affected / exposed	0 / 237 (0.00%)	1 / 230 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour pain			

subjects affected / exposed	0 / 237 (0.00%)	1 / 230 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 237 (0.42%)	0 / 230 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gait disturbance			
subjects affected / exposed	0 / 237 (0.00%)	1 / 230 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	1 / 237 (0.42%)	1 / 230 (0.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal inflammation			
subjects affected / exposed	1 / 237 (0.42%)	0 / 230 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 237 (0.42%)	0 / 230 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 237 (0.42%)	0 / 230 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung disorder			
subjects affected / exposed	1 / 237 (0.42%)	0 / 230 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pleural effusion			
subjects affected / exposed	1 / 237 (0.42%)	0 / 230 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 237 (0.42%)	1 / 230 (0.43%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood bilirubin increased			
subjects affected / exposed	1 / 237 (0.42%)	0 / 230 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil count decreased			
subjects affected / exposed	0 / 237 (0.00%)	1 / 230 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	0 / 237 (0.00%)	1 / 230 (0.43%)	
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			
Femoral neck fracture			
subjects affected / exposed	1 / 237 (0.42%)	0 / 230 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	1 / 237 (0.42%)	0 / 230 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			

subjects affected / exposed	0 / 237 (0.00%)	1 / 230 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	0 / 237 (0.00%)	1 / 230 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac arrest			
subjects affected / exposed	1 / 237 (0.42%)	0 / 230 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 237 (0.00%)	1 / 230 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 237 (0.00%)	1 / 230 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cranial nerve paralysis			
subjects affected / exposed	0 / 237 (0.00%)	1 / 230 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysarthria			
subjects affected / exposed	0 / 237 (0.00%)	1 / 230 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 237 (0.42%)	0 / 230 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			

subjects affected / exposed	0 / 237 (0.00%)	1 / 230 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Meningeal disorder			
subjects affected / exposed	0 / 237 (0.00%)	1 / 230 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorder			
subjects affected / exposed	1 / 237 (0.42%)	0 / 230 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 237 (0.00%)	1 / 230 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord compression			
subjects affected / exposed	2 / 237 (0.84%)	0 / 230 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Antiphospholipid syndrome			
subjects affected / exposed	1 / 237 (0.42%)	0 / 230 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 237 (0.00%)	2 / 230 (0.87%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 237 (0.00%)	1 / 230 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			

subjects affected / exposed	0 / 237 (0.00%)	1 / 230 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	0 / 237 (0.00%)	1 / 230 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 237 (0.00%)	1 / 230 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal ischaemia			
subjects affected / exposed	1 / 237 (0.42%)	0 / 230 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	3 / 237 (1.27%)	0 / 230 (0.00%)	
occurrences causally related to treatment / all	2 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	2 / 237 (0.84%)	0 / 230 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	2 / 237 (0.84%)	0 / 230 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 237 (0.42%)	0 / 230 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	1 / 237 (0.42%)	0 / 230 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 237 (0.00%)	1 / 230 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	2 / 237 (0.84%)	0 / 230 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone pain			
subjects affected / exposed	1 / 237 (0.42%)	0 / 230 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	1 / 237 (0.42%)	0 / 230 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathological fracture			
subjects affected / exposed	1 / 237 (0.42%)	1 / 230 (0.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 237 (0.00%)	1 / 230 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Device related sepsis			
subjects affected / exposed	0 / 237 (0.00%)	1 / 230 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Diverticulitis			
subjects affected / exposed	1 / 237 (0.42%)	1 / 230 (0.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 237 (0.42%)	3 / 230 (1.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sepsis			
subjects affected / exposed	0 / 237 (0.00%)	1 / 230 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	1 / 237 (0.42%)	0 / 230 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 237 (0.00%)	2 / 230 (0.87%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 237 (0.42%)	0 / 230 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	1 / 237 (0.42%)	0 / 230 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrolyte imbalance			
subjects affected / exposed	1 / 237 (0.42%)	0 / 230 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			

subjects affected / exposed	1 / 237 (0.42%)	1 / 230 (0.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 237 (0.00%)	1 / 230 (0.43%)	
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	Elacestrant	Standard of Care (SoC)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	215 / 237 (90.72%)	195 / 230 (84.78%)	
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	31 / 237 (13.08%)	29 / 230 (12.61%)	
occurrences (all)	40	33	
Alanine aminotransferase increased			
subjects affected / exposed	22 / 237 (9.28%)	24 / 230 (10.43%)	
occurrences (all)	29	29	
Blood alkaline phosphatase increased			
subjects affected / exposed	15 / 237 (6.33%)	17 / 230 (7.39%)	
occurrences (all)	18	19	
Vascular disorders			
Hot flush			
subjects affected / exposed	27 / 237 (11.39%)	19 / 230 (8.26%)	
occurrences (all)	30	27	
Hypertension			
subjects affected / exposed	9 / 237 (3.80%)	12 / 230 (5.22%)	
occurrences (all)	14	13	
Nervous system disorders			
Headache			
subjects affected / exposed	29 / 237 (12.24%)	26 / 230 (11.30%)	
occurrences (all)	39	34	
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	45 / 237 (18.99%)	44 / 230 (19.13%)	
occurrences (all)	50	54	
Injection site pain			
subjects affected / exposed	0 / 237 (0.00%)	14 / 230 (6.09%)	
occurrences (all)	0	16	
Asthenia			
subjects affected / exposed	21 / 237 (8.86%)	19 / 230 (8.26%)	
occurrences (all)	28	24	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	22 / 237 (9.28%)	17 / 230 (7.39%)	
occurrences (all)	35	36	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	83 / 237 (35.02%)	44 / 230 (19.13%)	
occurrences (all)	121	51	
Vomiting			
subjects affected / exposed	45 / 237 (18.99%)	20 / 230 (8.70%)	
occurrences (all)	60	27	
Diarrhoea			
subjects affected / exposed	33 / 237 (13.92%)	22 / 230 (9.57%)	
occurrences (all)	48	24	
Constipation			
subjects affected / exposed	29 / 237 (12.24%)	15 / 230 (6.52%)	
occurrences (all)	34	17	
Dyspepsia			
subjects affected / exposed	24 / 237 (10.13%)	6 / 230 (2.61%)	
occurrences (all)	25	9	
Abdominal pain			
subjects affected / exposed	15 / 237 (6.33%)	13 / 230 (5.65%)	
occurrences (all)	16	13	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	18 / 237 (7.59%)	16 / 230 (6.96%)	
occurrences (all)	18	17	

Cough			
subjects affected / exposed	15 / 237 (6.33%)	12 / 230 (5.22%)	
occurrences (all)	16	12	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	18 / 237 (7.59%)	11 / 230 (4.78%)	
occurrences (all)	19	14	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	34 / 237 (14.35%)	37 / 230 (16.09%)	
occurrences (all)	42	44	
Back pain			
subjects affected / exposed	32 / 237 (13.50%)	22 / 230 (9.57%)	
occurrences (all)	39	22	
Pain in extremity			
subjects affected / exposed	18 / 237 (7.59%)	14 / 230 (6.09%)	
occurrences (all)	21	16	
Bone pain			
subjects affected / exposed	14 / 237 (5.91%)	15 / 230 (6.52%)	
occurrences (all)	20	16	
Musculoskeletal chest pain			
subjects affected / exposed	14 / 237 (5.91%)	7 / 230 (3.04%)	
occurrences (all)	16	7	
Musculoskeletal pain			
subjects affected / exposed	11 / 237 (4.64%)	13 / 230 (5.65%)	
occurrences (all)	16	19	
Myalgia			
subjects affected / exposed	11 / 237 (4.64%)	17 / 230 (7.39%)	
occurrences (all)	15	19	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	16 / 237 (6.75%)	12 / 230 (5.22%)	
occurrences (all)	19	14	
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	35 / 237 (14.77%)	22 / 230 (9.57%)	
occurrences (all)	42	27	
Hyperglycaemia			
subjects affected / exposed	6 / 237 (2.53%)	12 / 230 (5.22%)	
occurrences (all)	8	12	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 March 2019	- Added an interim futility analysis at 70% enrollment - Added a study steering committee to provide guidance on protocol development, implementation, investigator selection, and recruitment strategies

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported