



Clinical trial results:

A Phase II, Double-blind, Placebo-controlled, Randomized Study of GDC-0941 (Pictilisib) or GDC-0980 (Apitolisib) with Fulvestrant versus Fulvestrant in Advanced or Metastatic Breast Cancer in Patients Resistant to Aromatase Inhibitor Therapy

Summary

EudraCT number	2010-023763-17
Trial protocol	BE CZ GB DK HU DE IT
Global end of trial date	07 April 2016

Results information

Result version number	v1 (current)
This version publication date	21 April 2017
First version publication date	21 April 2017

Trial information

Trial identification

Sponsor protocol code	GDC4950g
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01437566
WHO universal trial number (UTN)	-
Other trial identifiers	Secondary ID: GO00769

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.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	15 June 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 April 2016
Global end of trial reached?	Yes
Global end of trial date	07 April 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objectives were to evaluate the efficacy and safety of fulvestrant + pictilisib in all treated subjects and subjects with PIK3CA-mutant tumors and mutations; and to evaluate the safety of fulvestrant + apitolisib all treated subjects.

Protection of trial subjects:

Each subject, or the subject's representative, signed an informed consent form prior to study participation.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 August 2011
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	Australia: 21
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	Chile: 8
Country: Number of subjects enrolled	Czech Republic: 14
Country: Number of subjects enrolled	Denmark: 16
Country: Number of subjects enrolled	Spain: 18
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	United Kingdom: 33
Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	Hong Kong: 4
Country: Number of subjects enrolled	Israel: 12
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	Korea, Republic of: 2
Country: Number of subjects enrolled	Malaysia: 3
Country: Number of subjects enrolled	Mexico: 1
Country: Number of subjects enrolled	New Zealand: 5
Country: Number of subjects enrolled	Peru: 2
Country: Number of subjects enrolled	Russian Federation: 2
Country: Number of subjects enrolled	Singapore: 6
Country: Number of subjects enrolled	Thailand: 5

Country: Number of subjects enrolled	United States: 87
Worldwide total number of subjects	261
EEA total number of subjects	103

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)	170
From 65 to 84 years	90
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

A total of 261 subjects were enrolled in the study.

Pre-assignment

Screening details:

Subjects with estrogen receptor (ER)-positive locally advanced breast cancer or metastatic breast cancer (MBC) were screened for study; Part 1: recurrent or progressive disease while receiving treatment with an aromatase inhibitor (AI) as the most recent treatment; Part 2: PIK3CA mutant tumor progression during or after treatment with an AI.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	GDC-0941 (340 mg) + Fulvestrant

Arm description: -

Arm type	Experimental
Investigational medicinal product name	GDC-0941
Investigational medicinal product code	
Other name	Pictilisib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

GDC-0941, 340 mg, once daily, starting on Day 15 of Cycle 1 (28-day cycle), after the fulvestrant "run-in" period (Cycle 1, Day 1 to Cycle 1, Day 14)

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

Dosage and administration details:

Fulvestrant, 500 mg, on Day 1 and Day 15 of Cycle 1 and Day 1 of each subsequent 28-day cycle.

Arm title	GDC-0941-Matching Placebo (340 mg) + Fulvestrant
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Arm description: -

Arm type	Placebo
Investigational medicinal product name	GDC-0941-Matching Placebo (340 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo was administered similarly to GDC-0941 (340 mg) treatment.

Investigational medicinal product name	Fulvestrant
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Fulvestrant, 500 mg, on Day 1 and Day 15 of Cycle 1 and Day 1 of each subsequent 28-day cycle.

Arm title	GDC-0980 + Fulvestrant
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	GDC-0980
Investigational medicinal product code	
Other name	Apitolisib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

GDC-0980, 30 mg, once daily, starting on Day 15 of Cycle 1 (28-day cycle), after the fulvestrant "run-in" period (Cycle 1, Day 1 to Cycle 1, Day 14)

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

Dosage and administration details:

Fulvestrant, 500 mg, on Day 1 and Day 15 of Cycle 1 and Day 1 of each subsequent 28-day cycle.

Arm title	GDC-0980-Matching Placebo + Fulvestrant
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Arm description: -

Arm type	Placebo
Investigational medicinal product name	GDC-0980-Matching Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo was administered similarly to GDC-0980 treatment.

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

Dosage and administration details:

Fulvestrant, 500 mg, on Day 1 and Day 15 of Cycle 1 and Day 1 of each subsequent 28-day cycle.

Arm title	GDC-0941 (260 mg) + Fulvestrant
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	GDC-0941
Investigational medicinal product code	
Other name	Pictilisib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

GDC-0941, 260 mg, once daily, starting on Day 15 of Cycle 1 (28-day cycle), after the fulvestrant "run-in" period (Cycle 1, Day 1 to Cycle 1, Day 14)

Investigational medicinal product name	Fulvestrant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Fulvestrant, 500 mg, on Day 1 and Day 15 of Cycle 1 and Day 1 of each subsequent 28-day cycle.	
Arm title	GDC-0941-Matching Placebo (260 mg) + Fulvestrant
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	GDC-0941-Matching Placebo (260 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Placebo was administered similarly to GDC-0941 (260 mg) treatment.	
Investigational medicinal product name	Fulvestrant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Fulvestrant, 500 mg, on Day 1 and Day 15 of Cycle 1 and Day 1 of each subsequent 28-day cycle.	

Number of subjects in period 1	GDC-0941 (340 mg) + Fulvestrant	GDC-0941-Matching Placebo (340 mg) + Fulvestrant	GDC-0980 + Fulvestrant
Started	89	79	21
Completed	0	0	0
Not completed	89	79	21
Physician decision	-	1	-
Withdrawal By Subject	4	6	3
Study Terminated By Sponsor	35	30	5
Adverse event, non-fatal	-	-	1
Death	47	39	12
Reason Not Specified	-	1	-
Progressive Disease	1	-	-
Lost to follow-up	2	2	-

Number of subjects in period 1	GDC-0980-Matching Placebo + Fulvestrant	GDC-0941 (260 mg) + Fulvestrant	GDC-0941-Matching Placebo (260 mg) + Fulvestrant
Started	11	41	20
Completed	0	0	0
Not completed	11	41	20

Physician decision	-	-	-
Withdrawal By Subject	1	5	3
Study Terminated By Sponsor	6	23	10
Adverse event, non-fatal	-	1	-
Death	3	11	5
Reason Not Specified	-	-	-
Progressive Disease	-	1	1
Lost to follow-up	1	-	1

Baseline characteristics

Reporting groups

Reporting group title	GDC-0941 (340 mg) + Fulvestrant
Reporting group description: -	
Reporting group title	GDC-0941-Matching Placebo (340 mg) + Fulvestrant
Reporting group description: -	
Reporting group title	GDC-0980 + Fulvestrant
Reporting group description: -	
Reporting group title	GDC-0980-Matching Placebo + Fulvestrant
Reporting group description: -	
Reporting group title	GDC-0941 (260 mg) + Fulvestrant
Reporting group description: -	
Reporting group title	GDC-0941-Matching Placebo (260 mg) + Fulvestrant
Reporting group description: -	

Reporting group values	GDC-0941 (340 mg) + Fulvestrant	GDC-0941-Matching Placebo (340 mg) + Fulvestrant	GDC-0980 + Fulvestrant
Number of subjects	89	79	21
Age Categorical Units: Subjects			
Adults (18-64 years)	60	50	14
Elderly (From 65-84 years)	28	29	7
Elderly 85 years and over	1	0	0
Age Continuous Units: years			
arithmetic mean	60	61.1	61.2
standard deviation	± 10.9	± 10.1	± 10.5
Gender Categorical Units: Subjects			
Female	89	79	21
Male	0	0	0

Reporting group values	GDC-0980-Matching Placebo + Fulvestrant	GDC-0941 (260 mg) + Fulvestrant	GDC-0941-Matching Placebo (260 mg) + Fulvestrant
Number of subjects	11	41	20
Age Categorical Units: Subjects			
Adults (18-64 years)	7	28	11
Elderly (From 65-84 years)	4	13	9
Elderly 85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	60.3	58.3	62.7
standard deviation	± 10.3	± 10.2	± 11.3
Gender Categorical Units: Subjects			
Female	11	41	20

Male	0	0	0
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Reporting group values	Total		
Number of subjects	261		
Age Categorical Units: Subjects			
Adults (18-64 years)	170		
Elderly (From 65-84 years)	90		
Elderly 85 years and over	1		
Age Continuous Units: years arithmetic mean standard deviation	-		
Gender Categorical Units: Subjects			
Female	261		
Male	0		

End points

End points reporting groups

Reporting group title	GDC-0941 (340 mg) + Fulvestrant
Reporting group description: -	
Reporting group title	GDC-0941-Matching Placebo (340 mg) + Fulvestrant
Reporting group description: -	
Reporting group title	GDC-0980 + Fulvestrant
Reporting group description: -	
Reporting group title	GDC-0980-Matching Placebo + Fulvestrant
Reporting group description: -	
Reporting group title	GDC-0941 (260 mg) + Fulvestrant
Reporting group description: -	
Reporting group title	GDC-0941-Matching Placebo (260 mg) + Fulvestrant
Reporting group description: -	
Subject analysis set title	GDC-0941 (340 mg) + Fulvestrant
Subject analysis set type	Safety analysis
Subject analysis set description:	
Safety analysis	
Subject analysis set title	GDC-0941-Matching Placebo (340 mg) + Fulvestrant
Subject analysis set type	Safety analysis
Subject analysis set description:	
Safety analysis	
Subject analysis set title	GDC-0980 + Fulvestrant
Subject analysis set type	Safety analysis
Subject analysis set description:	
Safety analysis	
Subject analysis set title	GDC-0980-Matching Placebo + Fulvestrant
Subject analysis set type	Safety analysis
Subject analysis set description:	
Safety analysis	
Subject analysis set title	GDC-0941 (260 mg) + Fulvestrant
Subject analysis set type	Safety analysis
Subject analysis set description:	
Safety analysis. This analysis set includes one subject who crossed over from placebo treatment.	
Subject analysis set title	GDC-0941-Matching Placebo (260 mg) + Fulvestrant
Subject analysis set type	Safety analysis
Subject analysis set description:	
Safety analysis	

Primary: Progression Free Survival (PFS, 10 April 2013 Data Cut-Off)

End point title	Progression Free Survival (PFS, 10 April 2013 Data Cut-Off) ^[1]
End point description:	
PFS was assessed by the investigator, per Modified Response Evaluation Criteria In Solid Tumors (RECIST), v 1.1, criteria, and defined as the start date of any treatment to first disease progression or death from any cause within 30 days after the last dose of any study treatment. The intent-to-treat (ITT) population included all randomized subjects according to their randomized treatment.	
End point type	Primary
End point timeframe:	
Up to approximately 1 year, 8 months	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was analyzed in the reported arms only.

End point values	GDC-0941 (340 mg) + Fulvestrant	GDC-0941- Matching Placebo (340 mg) + Fulvestrant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	79		
Units: months				
median (confidence interval 95%)	6.5 (3.9 to 8.2)	3.8 (3.6 to 6)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	GDC-0941 (340 mg) + Fulvestrant v GDC-0941-Matching Placebo (340 mg) + Fulvestrant
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.2505
Method	Logrank

Primary: Progression Free Survival (PFS, 12 September 2014 Data Cut-Off)

End point title	Progression Free Survival (PFS, 12 September 2014 Data Cut-Off) ^[2]
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End point description:

PFS was assessed by the investigator, per Modified Response Evaluation Criteria In Solid Tumors (RECIST), v 1.1, criteria, and defined as the start date of any treatment to first disease progression or death from any cause within 30 days after the last dose of any study treatment. The intent-to-treat (ITT) population included all randomized subjects according to their randomized treatment.

End point type	Primary
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End point timeframe:

Up to approximately 2 years, 11 months

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was analyzed in the reported arms only.

End point values	GDC-0941 (260 mg) + Fulvestrant	GDC-0941- Matching Placebo (260 mg) + Fulvestrant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	20		
Units: months				
median (confidence interval 95%)	5.4 (3.8 to 8.3)	10 (3.6 to		

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Comparison groups	GDC-0941 (260 mg) + Fulvestrant v GDC-0941-Matching Placebo (260 mg) + Fulvestrant
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.842
Method	Logrank

Primary: Percentage of Subjects with Adverse Events (AEs)

End point title	Percentage of Subjects with Adverse Events (AEs) ^[3]
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End point description:

An adverse event can be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of study drug, whether or not considered related to the study drug. The safety-evaluable population included all subjects who were randomized and received at least one dose of fulvestrant, pictilisib, apitolisib, or placebo, with subjects allocated to the treatment arm associated with the regimen actually received.

End point type	Primary
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End point timeframe:

4 years, 8 months

Notes:

[3] - 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: Descriptive analysis only.

End point values	GDC-0941 (340 mg) + Fulvestrant	GDC-0941-Matching Placebo (340 mg) + Fulvestrant	GDC-0980 + Fulvestrant	GDC-0980-Matching Placebo + Fulvestrant
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	89	79	21	11
Units: percentage of subjects				
number (not applicable)	98.9	93.7	100	90.9

End point values	GDC-0941 (260 mg) + Fulvestrant	GDC-0941-Matching Placebo (260 mg) + Fulvestrant		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	42	19		

Units: percentage of subjects				
number (not applicable)	97.6	100		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

4 years, 8 months

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.0
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Reporting groups

Reporting group title	GDC-0941 (340 mg) + Fulvestrant
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Reporting group description: -

Reporting group title	GDC-0941-Matching Placebo (340 mg) + Fulvestrant
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Reporting group description: -

Reporting group title	GDC-0980 + Fulvestrant
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Reporting group description: -

Reporting group title	GDC-0980-Matching Placebo + Fulvestrant
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Reporting group description: -

Reporting group title	GDC-0941 (260 mg) + Fulvestrant
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Reporting group description: -

Reporting group title	GDC-0941-Matching Placebo (260 mg) + Fulvestrant
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Reporting group description: -

Serious adverse events	GDC-0941 (340 mg) + Fulvestrant	GDC-0941-Matching Placebo (340 mg) + Fulvestrant	GDC-0980 + Fulvestrant
Total subjects affected by serious adverse events			
subjects affected / exposed	27 / 89 (30.34%)	11 / 79 (13.92%)	5 / 21 (23.81%)
number of deaths (all causes)	3	1	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 89 (0.00%)	1 / 79 (1.27%)	0 / 21 (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
Meningioma			
subjects affected / exposed	1 / 89 (1.12%)	0 / 79 (0.00%)	0 / 21 (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
Tumour pain			

subjects affected / exposed	1 / 89 (1.12%)	0 / 79 (0.00%)	0 / 21 (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
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 89 (1.12%)	0 / 79 (0.00%)	0 / 21 (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
Surgical and medical procedures			
Transcatheter aortic valve implantation			
subjects affected / exposed	0 / 89 (0.00%)	1 / 79 (1.27%)	0 / 21 (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			
Disease progression			
subjects affected / exposed	2 / 89 (2.25%)	1 / 79 (1.27%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 0
Asthenia			
subjects affected / exposed	1 / 89 (1.12%)	0 / 79 (0.00%)	0 / 21 (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
Chest pain			
subjects affected / exposed	0 / 89 (0.00%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 89 (0.00%)	1 / 79 (1.27%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucosal inflammation			

subjects affected / exposed	0 / 89 (0.00%)	0 / 79 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 89 (0.00%)	2 / 79 (2.53%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	2 / 89 (2.25%)	0 / 79 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 89 (1.12%)	1 / 79 (1.27%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	1 / 89 (1.12%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 89 (1.12%)	0 / 79 (0.00%)	0 / 21 (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
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 89 (1.12%)	0 / 79 (0.00%)	0 / 21 (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
Femur fracture			

subjects affected / exposed	1 / 89 (1.12%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac tamponade			
subjects affected / exposed	1 / 89 (1.12%)	0 / 79 (0.00%)	0 / 21 (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
Mitral valve disease			
subjects affected / exposed	0 / 89 (0.00%)	1 / 79 (1.27%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Palpitations			
subjects affected / exposed	0 / 89 (0.00%)	1 / 79 (1.27%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 89 (0.00%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dystonia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	1 / 89 (1.12%)	0 / 79 (0.00%)	0 / 21 (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
Syncope			
subjects affected / exposed	0 / 89 (0.00%)	1 / 79 (1.27%)	0 / 21 (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
Blood and lymphatic system disorders			

Haemolytic anaemia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	1 / 89 (1.12%)	0 / 79 (0.00%)	0 / 21 (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
Ear and labyrinth disorders			
Deafness unilateral			
subjects affected / exposed	0 / 89 (0.00%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tinnitus			
subjects affected / exposed	0 / 89 (0.00%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Eye pain			
subjects affected / exposed	0 / 89 (0.00%)	1 / 79 (1.27%)	0 / 21 (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
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	2 / 89 (2.25%)	1 / 79 (1.27%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	2 / 89 (2.25%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			

subjects affected / exposed	1 / 89 (1.12%)	0 / 79 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	1 / 89 (1.12%)	0 / 79 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	2 / 89 (2.25%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 89 (0.00%)	1 / 79 (1.27%)	0 / 21 (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
Diarrhoea haemorrhagic			
subjects affected / exposed	1 / 89 (1.12%)	0 / 79 (0.00%)	0 / 21 (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
Dysphagia			
subjects affected / exposed	1 / 89 (1.12%)	0 / 79 (0.00%)	0 / 21 (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
Pancreatitis			
subjects affected / exposed	0 / 89 (0.00%)	1 / 79 (1.27%)	0 / 21 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 89 (0.00%)	1 / 79 (1.27%)	0 / 21 (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
Skin and subcutaneous tissue disorders			
Rash			

subjects affected / exposed	3 / 89 (3.37%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash generalised			
subjects affected / exposed	1 / 89 (1.12%)	0 / 79 (0.00%)	0 / 21 (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
Rash maculo–papular			
subjects affected / exposed	1 / 89 (1.12%)	0 / 79 (0.00%)	0 / 21 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 89 (0.00%)	0 / 79 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	0 / 89 (0.00%)	1 / 79 (1.27%)	0 / 21 (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
Osteoarthritis			
subjects affected / exposed	1 / 89 (1.12%)	0 / 79 (0.00%)	0 / 21 (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
Infections and infestations			
Device related infection			
subjects affected / exposed	0 / 89 (0.00%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious colitis			
subjects affected / exposed	1 / 89 (1.12%)	0 / 79 (0.00%)	0 / 21 (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

Paratyphoid fever			
subjects affected / exposed	1 / 89 (1.12%)	0 / 79 (0.00%)	0 / 21 (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
Pneumonia			
subjects affected / exposed	1 / 89 (1.12%)	0 / 79 (0.00%)	0 / 21 (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
Sepsis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 79 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 89 (0.00%)	1 / 79 (1.27%)	0 / 21 (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
Viral infection			
subjects affected / exposed	0 / 89 (0.00%)	1 / 79 (1.27%)	0 / 21 (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
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	2 / 89 (2.25%)	0 / 79 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 89 (0.00%)	0 / 79 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	1 / 89 (1.12%)	0 / 79 (0.00%)	0 / 21 (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
Hyponatraemia			

subjects affected / exposed	1 / 89 (1.12%)	0 / 79 (0.00%)	0 / 21 (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
Hypophagia			
subjects affected / exposed	1 / 89 (1.12%)	0 / 79 (0.00%)	0 / 21 (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

Serious adverse events	GDC-0980-Matching Placebo + Fulvestrant	GDC-0941 (260 mg) + Fulvestrant	GDC-0941-Matching Placebo (260 mg) + Fulvestrant
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 11 (9.09%)	5 / 42 (11.90%)	3 / 19 (15.79%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningioma			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Transcatheter aortic valve implantation			

subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	0 / 11 (0.00%)	1 / 42 (2.38%)	0 / 19 (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
Asthenia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucosal inflammation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 11 (0.00%)	1 / 42 (2.38%)	0 / 19 (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
Pneumonitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pulmonary embolism			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac tamponade			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mitral valve disease			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Palpitations			

subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 11 (9.09%)	0 / 42 (0.00%)	0 / 19 (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
Dystonia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Haemolytic anaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Deafness unilateral			
subjects affected / exposed	1 / 11 (9.09%)	0 / 42 (0.00%)	0 / 19 (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

Tinnitus			
subjects affected / exposed	1 / 11 (9.09%)	0 / 42 (0.00%)	0 / 19 (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
Eye disorders			
Eye pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 11 (0.00%)	1 / 42 (2.38%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 42 (2.38%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 11 (0.00%)	1 / 42 (2.38%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 11 (0.00%)	1 / 42 (2.38%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Diarrhoea haemorrhagic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash generalised			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 42 (2.38%)	0 / 19 (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
Osteoarthritis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Device related infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious colitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paratyphoid fever			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Viral infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophagia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
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	GDC-0941 (340 mg) + Fulvestrant	GDC-0941-Matching Placebo (340 mg) + Fulvestrant	GDC-0980 + Fulvestrant
Total subjects affected by non-serious adverse events			
subjects affected / exposed	88 / 89 (98.88%)	72 / 79 (91.14%)	21 / 21 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Cancer pain subjects affected / exposed occurrences (all)	0 / 89 (0.00%) 0	0 / 79 (0.00%) 0	0 / 21 (0.00%) 0
Vascular disorders			
Hot flush subjects affected / exposed occurrences (all)	11 / 89 (12.36%) 14	11 / 79 (13.92%) 14	3 / 21 (14.29%) 4
Hypertension subjects affected / exposed occurrences (all)	6 / 89 (6.74%) 8	3 / 79 (3.80%) 3	1 / 21 (4.76%) 1
Lymphoedema subjects affected / exposed occurrences (all)	3 / 89 (3.37%) 5	1 / 79 (1.27%) 3	0 / 21 (0.00%) 0
Peripheral coldness subjects affected / exposed occurrences (all)	0 / 89 (0.00%) 0	0 / 79 (0.00%) 0	0 / 21 (0.00%) 0
Poor peripheral circulation subjects affected / exposed occurrences (all)	0 / 89 (0.00%) 0	0 / 79 (0.00%) 0	0 / 21 (0.00%) 0
Surgical and medical procedures			
Knee arthroplasty subjects affected / exposed occurrences (all)	0 / 89 (0.00%) 0	0 / 79 (0.00%) 0	0 / 21 (0.00%) 0
General disorders and administration site conditions			
Fatigue subjects affected / exposed occurrences (all)	37 / 89 (41.57%) 69	25 / 79 (31.65%) 36	10 / 21 (47.62%) 20
Injection site pain subjects affected / exposed occurrences (all)	10 / 89 (11.24%) 10	10 / 79 (12.66%) 11	3 / 21 (14.29%) 3
Pyrexia subjects affected / exposed occurrences (all)	13 / 89 (14.61%) 18	2 / 79 (2.53%) 3	4 / 21 (19.05%) 4
Mucosal inflammation subjects affected / exposed occurrences (all)	9 / 89 (10.11%) 14	2 / 79 (2.53%) 2	4 / 21 (19.05%) 6

Oedema peripheral subjects affected / exposed occurrences (all)	5 / 89 (5.62%) 7	4 / 79 (5.06%) 5	6 / 21 (28.57%) 7
Chest pain subjects affected / exposed occurrences (all)	2 / 89 (2.25%) 2	7 / 79 (8.86%) 8	0 / 21 (0.00%) 0
Asthenia subjects affected / exposed occurrences (all)	4 / 89 (4.49%) 4	4 / 79 (5.06%) 5	1 / 21 (4.76%) 1
Pain subjects affected / exposed occurrences (all)	4 / 89 (4.49%) 4	4 / 79 (5.06%) 4	2 / 21 (9.52%) 2
Chills subjects affected / exposed occurrences (all)	3 / 89 (3.37%) 3	1 / 79 (1.27%) 1	3 / 21 (14.29%) 4
Injection site bruising subjects affected / exposed occurrences (all)	0 / 89 (0.00%) 0	1 / 79 (1.27%) 1	0 / 21 (0.00%) 0
Cyst subjects affected / exposed occurrences (all)	0 / 89 (0.00%) 0	0 / 79 (0.00%) 0	0 / 21 (0.00%) 0
Reproductive system and breast disorders Breast pain subjects affected / exposed occurrences (all)	2 / 89 (2.25%) 2	4 / 79 (5.06%) 4	1 / 21 (4.76%) 1
Breast discomfort subjects affected / exposed occurrences (all)	1 / 89 (1.12%) 1	0 / 79 (0.00%) 0	0 / 21 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	15 / 89 (16.85%) 20	12 / 79 (15.19%) 18	4 / 21 (19.05%) 5
Dyspnoea subjects affected / exposed occurrences (all)	9 / 89 (10.11%) 18	8 / 79 (10.13%) 10	4 / 21 (19.05%) 5
Oropharyngeal pain			

subjects affected / exposed	8 / 89 (8.99%)	4 / 79 (5.06%)	3 / 21 (14.29%)
occurrences (all)	11	4	3
Dyspnoea exertional			
subjects affected / exposed	5 / 89 (5.62%)	3 / 79 (3.80%)	0 / 21 (0.00%)
occurrences (all)	6	4	0
Pneumonitis			
subjects affected / exposed	5 / 89 (5.62%)	2 / 79 (2.53%)	0 / 21 (0.00%)
occurrences (all)	6	2	0
Epistaxis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 79 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	2
Hypoxia			
subjects affected / exposed	1 / 89 (1.12%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	0 / 89 (0.00%)	0 / 79 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	8 / 89 (8.99%)	7 / 79 (8.86%)	1 / 21 (4.76%)
occurrences (all)	16	9	1
Anxiety			
subjects affected / exposed	3 / 89 (3.37%)	4 / 79 (5.06%)	1 / 21 (4.76%)
occurrences (all)	4	5	1
Depression			
subjects affected / exposed	6 / 89 (6.74%)	2 / 79 (2.53%)	1 / 21 (4.76%)
occurrences (all)	6	2	1
Depressed mood			
subjects affected / exposed	1 / 89 (1.12%)	1 / 79 (1.27%)	0 / 21 (0.00%)
occurrences (all)	2	1	0
Mood swings			
subjects affected / exposed	0 / 89 (0.00%)	1 / 79 (1.27%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
Investigations			
Aspartate aminotransferase increased			

subjects affected / exposed	11 / 89 (12.36%)	11 / 79 (13.92%)	1 / 21 (4.76%)
occurrences (all)	16	15	1
Alanine aminotransferase increased			
subjects affected / exposed	8 / 89 (8.99%)	6 / 79 (7.59%)	1 / 21 (4.76%)
occurrences (all)	18	8	1
Blood alkaline phosphatase increased			
subjects affected / exposed	6 / 89 (6.74%)	8 / 79 (10.13%)	0 / 21 (0.00%)
occurrences (all)	9	16	0
Weight decreased			
subjects affected / exposed	7 / 89 (7.87%)	3 / 79 (3.80%)	3 / 21 (14.29%)
occurrences (all)	8	6	4
Blood cholesterol increased			
subjects affected / exposed	1 / 89 (1.12%)	4 / 79 (5.06%)	0 / 21 (0.00%)
occurrences (all)	2	5	0
Lipase increased			
subjects affected / exposed	3 / 89 (3.37%)	3 / 79 (3.80%)	0 / 21 (0.00%)
occurrences (all)	3	4	0
Blood bilirubin increased			
subjects affected / exposed	3 / 89 (3.37%)	0 / 79 (0.00%)	1 / 21 (4.76%)
occurrences (all)	5	0	2
Blood creatinine increased			
subjects affected / exposed	2 / 89 (2.25%)	1 / 79 (1.27%)	2 / 21 (9.52%)
occurrences (all)	2	1	2
Neutrophil count decreased			
subjects affected / exposed	2 / 89 (2.25%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences (all)	5	0	0
Weight increased			
subjects affected / exposed	1 / 89 (1.12%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Blood potassium decreased			
subjects affected / exposed	0 / 89 (0.00%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 89 (0.00%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Blood triglycerides increased			

subjects affected / exposed occurrences (all)	0 / 89 (0.00%) 0	0 / 79 (0.00%) 0	0 / 21 (0.00%) 0
White blood cell count decreased subjects affected / exposed occurrences (all)	1 / 89 (1.12%) 5	0 / 79 (0.00%) 0	0 / 21 (0.00%) 0
Blood alkaline phosphatase subjects affected / exposed occurrences (all)	0 / 89 (0.00%) 0	0 / 79 (0.00%) 0	0 / 21 (0.00%) 0
Blood magnesium decreased subjects affected / exposed occurrences (all)	0 / 89 (0.00%) 0	0 / 79 (0.00%) 0	0 / 21 (0.00%) 0
Injury, poisoning and procedural complications			
Contusion subjects affected / exposed occurrences (all)	2 / 89 (2.25%) 4	3 / 79 (3.80%) 3	0 / 21 (0.00%) 0
Tooth fracture subjects affected / exposed occurrences (all)	0 / 89 (0.00%) 0	0 / 79 (0.00%) 0	0 / 21 (0.00%) 0
Excoriation subjects affected / exposed occurrences (all)	0 / 89 (0.00%) 0	0 / 79 (0.00%) 0	0 / 21 (0.00%) 0
Procedural pain subjects affected / exposed occurrences (all)	0 / 89 (0.00%) 0	0 / 79 (0.00%) 0	0 / 21 (0.00%) 0
Nervous system disorders			
Dysgeusia subjects affected / exposed occurrences (all)	36 / 89 (40.45%) 46	3 / 79 (3.80%) 6	3 / 21 (14.29%) 4
Headache subjects affected / exposed occurrences (all)	16 / 89 (17.98%) 21	10 / 79 (12.66%) 13	7 / 21 (33.33%) 12
Dizziness subjects affected / exposed occurrences (all)	8 / 89 (8.99%) 10	7 / 79 (8.86%) 10	1 / 21 (4.76%) 1
Paraesthesia			

subjects affected / exposed	3 / 89 (3.37%)	3 / 79 (3.80%)	2 / 21 (9.52%)
occurrences (all)	4	4	2
Neuropathy peripheral			
subjects affected / exposed	1 / 89 (1.12%)	2 / 79 (2.53%)	0 / 21 (0.00%)
occurrences (all)	1	3	0
Hypoaesthesia			
subjects affected / exposed	1 / 89 (1.12%)	1 / 79 (1.27%)	0 / 21 (0.00%)
occurrences (all)	1	1	0
Lethargy			
subjects affected / exposed	1 / 89 (1.12%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Memory impairment			
subjects affected / exposed	1 / 89 (1.12%)	1 / 79 (1.27%)	0 / 21 (0.00%)
occurrences (all)	1	1	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 89 (0.00%)	2 / 79 (2.53%)	0 / 21 (0.00%)
occurrences (all)	0	2	0
Hyperaesthesia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Hypokinesia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	6 / 89 (6.74%)	7 / 79 (8.86%)	1 / 21 (4.76%)
occurrences (all)	8	10	1
Thrombocytopenia			
subjects affected / exposed	0 / 89 (0.00%)	2 / 79 (2.53%)	0 / 21 (0.00%)
occurrences (all)	0	4	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 89 (0.00%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Eye disorders			

Dry eye			
subjects affected / exposed	1 / 89 (1.12%)	5 / 79 (6.33%)	0 / 21 (0.00%)
occurrences (all)	2	7	0
Lacrimation increased			
subjects affected / exposed	1 / 89 (1.12%)	3 / 79 (3.80%)	0 / 21 (0.00%)
occurrences (all)	1	5	0
Vision blurred			
subjects affected / exposed	0 / 89 (0.00%)	1 / 79 (1.27%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
Visual acuity reduced			
subjects affected / exposed	0 / 89 (0.00%)	4 / 79 (5.06%)	0 / 21 (0.00%)
occurrences (all)	0	4	0
Eye pain			
subjects affected / exposed	0 / 89 (0.00%)	2 / 79 (2.53%)	0 / 21 (0.00%)
occurrences (all)	0	3	0
Eye irritation			
subjects affected / exposed	0 / 89 (0.00%)	0 / 79 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Periorbital oedema			
subjects affected / exposed	0 / 89 (0.00%)	0 / 79 (0.00%)	2 / 21 (9.52%)
occurrences (all)	0	0	4
Eye disorder			
subjects affected / exposed	0 / 89 (0.00%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	59 / 89 (66.29%)	12 / 79 (15.19%)	14 / 21 (66.67%)
occurrences (all)	119	17	23
Nausea			
subjects affected / exposed	50 / 89 (56.18%)	23 / 79 (29.11%)	17 / 21 (80.95%)
occurrences (all)	87	27	23
Vomiting			
subjects affected / exposed	25 / 89 (28.09%)	11 / 79 (13.92%)	6 / 21 (28.57%)
occurrences (all)	34	15	8
Constipation			

subjects affected / exposed	14 / 89 (15.73%)	12 / 79 (15.19%)	6 / 21 (28.57%)
occurrences (all)	18	14	7
Stomatitis			
subjects affected / exposed	17 / 89 (19.10%)	2 / 79 (2.53%)	2 / 21 (9.52%)
occurrences (all)	22	2	2
Abdominal pain			
subjects affected / exposed	10 / 89 (11.24%)	6 / 79 (7.59%)	2 / 21 (9.52%)
occurrences (all)	13	6	2
Dyspepsia			
subjects affected / exposed	11 / 89 (12.36%)	2 / 79 (2.53%)	1 / 21 (4.76%)
occurrences (all)	14	4	1
Dry mouth			
subjects affected / exposed	8 / 89 (8.99%)	6 / 79 (7.59%)	3 / 21 (14.29%)
occurrences (all)	8	6	4
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 89 (3.37%)	6 / 79 (7.59%)	3 / 21 (14.29%)
occurrences (all)	5	7	5
Abdominal pain upper			
subjects affected / exposed	7 / 89 (7.87%)	5 / 79 (6.33%)	0 / 21 (0.00%)
occurrences (all)	8	6	0
Mouth ulceration			
subjects affected / exposed	6 / 89 (6.74%)	1 / 79 (1.27%)	1 / 21 (4.76%)
occurrences (all)	6	1	1
Abdominal distension			
subjects affected / exposed	4 / 89 (4.49%)	3 / 79 (3.80%)	0 / 21 (0.00%)
occurrences (all)	5	3	0
Flatulence			
subjects affected / exposed	2 / 89 (2.25%)	3 / 79 (3.80%)	1 / 21 (4.76%)
occurrences (all)	3	3	1
Gingival pain			
subjects affected / exposed	2 / 89 (2.25%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences (all)	2	0	0
Oral pain			
subjects affected / exposed	1 / 89 (1.12%)	1 / 79 (1.27%)	2 / 21 (9.52%)
occurrences (all)	1	1	2
Ascites			

subjects affected / exposed	2 / 89 (2.25%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences (all)	2	0	0
Rectal haemorrhage			
subjects affected / exposed	1 / 89 (1.12%)	1 / 79 (1.27%)	0 / 21 (0.00%)
occurrences (all)	1	1	0
Abdominal pain lower			
subjects affected / exposed	1 / 89 (1.12%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Eructation			
subjects affected / exposed	1 / 89 (1.12%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Gingival bleeding			
subjects affected / exposed	0 / 89 (0.00%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Tongue ulceration			
subjects affected / exposed	0 / 89 (0.00%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	22 / 89 (24.72%)	8 / 79 (10.13%)	14 / 21 (66.67%)
occurrences (all)	68	8	29
Pruritus			
subjects affected / exposed	9 / 89 (10.11%)	8 / 79 (10.13%)	7 / 21 (33.33%)
occurrences (all)	22	12	13
Rash maculo–papular			
subjects affected / exposed	14 / 89 (15.73%)	2 / 79 (2.53%)	4 / 21 (19.05%)
occurrences (all)	24	2	13
Dry skin			
subjects affected / exposed	9 / 89 (10.11%)	3 / 79 (3.80%)	4 / 21 (19.05%)
occurrences (all)	11	4	4
Alopecia			
subjects affected / exposed	10 / 89 (11.24%)	3 / 79 (3.80%)	0 / 21 (0.00%)
occurrences (all)	12	3	0
Erythema			
subjects affected / exposed	3 / 89 (3.37%)	2 / 79 (2.53%)	2 / 21 (9.52%)
occurrences (all)	3	2	2

Night sweats			
subjects affected / exposed	5 / 89 (5.62%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences (all)	7	0	0
Hyperhidrosis			
subjects affected / exposed	2 / 89 (2.25%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences (all)	2	0	0
Pain of skin			
subjects affected / exposed	1 / 89 (1.12%)	1 / 79 (1.27%)	0 / 21 (0.00%)
occurrences (all)	1	1	0
Pruritus generalised			
subjects affected / exposed	1 / 89 (1.12%)	0 / 79 (0.00%)	2 / 21 (9.52%)
occurrences (all)	2	0	3
Skin mass			
subjects affected / exposed	0 / 89 (0.00%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Trichorrhexis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	12 / 89 (13.48%)	22 / 79 (27.85%)	3 / 21 (14.29%)
occurrences (all)	13	28	5
Back pain			
subjects affected / exposed	10 / 89 (11.24%)	15 / 79 (18.99%)	2 / 21 (9.52%)
occurrences (all)	18	18	2
Pain in extremity			
subjects affected / exposed	6 / 89 (6.74%)	16 / 79 (20.25%)	2 / 21 (9.52%)
occurrences (all)	8	21	2
Bone pain			
subjects affected / exposed	12 / 89 (13.48%)	10 / 79 (12.66%)	1 / 21 (4.76%)
occurrences (all)	15	14	1
Myalgia			
subjects affected / exposed	8 / 89 (8.99%)	7 / 79 (8.86%)	3 / 21 (14.29%)
occurrences (all)	12	8	3
Muscle spasms			

subjects affected / exposed	12 / 89 (13.48%)	4 / 79 (5.06%)	0 / 21 (0.00%)
occurrences (all)	17	4	0
Musculoskeletal pain			
subjects affected / exposed	3 / 89 (3.37%)	8 / 79 (10.13%)	0 / 21 (0.00%)
occurrences (all)	3	10	0
Musculoskeletal chest pain			
subjects affected / exposed	5 / 89 (5.62%)	5 / 79 (6.33%)	0 / 21 (0.00%)
occurrences (all)	6	7	0
Neck pain			
subjects affected / exposed	4 / 89 (4.49%)	1 / 79 (1.27%)	1 / 21 (4.76%)
occurrences (all)	5	1	1
Muscular weakness			
subjects affected / exposed	2 / 89 (2.25%)	2 / 79 (2.53%)	0 / 21 (0.00%)
occurrences (all)	2	2	0
Flank pain			
subjects affected / exposed	2 / 89 (2.25%)	1 / 79 (1.27%)	0 / 21 (0.00%)
occurrences (all)	8	1	0
Arthritis			
subjects affected / exposed	0 / 89 (0.00%)	1 / 79 (1.27%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
Osteoarthritis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Muscle twitching			
subjects affected / exposed	0 / 89 (0.00%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	11 / 89 (12.36%)	5 / 79 (6.33%)	3 / 21 (14.29%)
occurrences (all)	13	6	3
Upper respiratory tract infection			
subjects affected / exposed	3 / 89 (3.37%)	5 / 79 (6.33%)	2 / 21 (9.52%)
occurrences (all)	3	6	7
Nasopharyngitis			
subjects affected / exposed	4 / 89 (4.49%)	5 / 79 (6.33%)	0 / 21 (0.00%)
occurrences (all)	5	7	0

Sinusitis			
subjects affected / exposed	2 / 89 (2.25%)	4 / 79 (5.06%)	0 / 21 (0.00%)
occurrences (all)	2	8	0
Bronchitis			
subjects affected / exposed	1 / 89 (1.12%)	2 / 79 (2.53%)	2 / 21 (9.52%)
occurrences (all)	1	2	2
Conjunctivitis			
subjects affected / exposed	2 / 89 (2.25%)	1 / 79 (1.27%)	1 / 21 (4.76%)
occurrences (all)	4	2	1
Herpes zoster			
subjects affected / exposed	2 / 89 (2.25%)	1 / 79 (1.27%)	0 / 21 (0.00%)
occurrences (all)	2	1	0
Localised infection			
subjects affected / exposed	1 / 89 (1.12%)	0 / 79 (0.00%)	1 / 21 (4.76%)
occurrences (all)	1	0	1
Rhinitis			
subjects affected / exposed	2 / 89 (2.25%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences (all)	2	0	0
Lower respiratory tract infection			
subjects affected / exposed	1 / 89 (1.12%)	1 / 79 (1.27%)	0 / 21 (0.00%)
occurrences (all)	1	1	0
Respiratory tract infection			
subjects affected / exposed	0 / 89 (0.00%)	1 / 79 (1.27%)	1 / 21 (4.76%)
occurrences (all)	0	1	1
Eye infection			
subjects affected / exposed	0 / 89 (0.00%)	1 / 79 (1.27%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
Folliculitis			
subjects affected / exposed	0 / 89 (0.00%)	1 / 79 (1.27%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	23 / 89 (25.84%)	11 / 79 (13.92%)	7 / 21 (33.33%)
occurrences (all)	33	12	12
Hyperglycaemia			

subjects affected / exposed	15 / 89 (16.85%)	6 / 79 (7.59%)	3 / 21 (14.29%)
occurrences (all)	33	17	3
Hypokalaemia			
subjects affected / exposed	5 / 89 (5.62%)	4 / 79 (5.06%)	3 / 21 (14.29%)
occurrences (all)	5	5	3
Dehydration			
subjects affected / exposed	3 / 89 (3.37%)	1 / 79 (1.27%)	2 / 21 (9.52%)
occurrences (all)	5	1	2
Hypomagnesaemia			
subjects affected / exposed	0 / 89 (0.00%)	4 / 79 (5.06%)	1 / 21 (4.76%)
occurrences (all)	0	8	1
Hypercalcaemia			
subjects affected / exposed	0 / 89 (0.00%)	3 / 79 (3.80%)	0 / 21 (0.00%)
occurrences (all)	0	3	0
Hypocalcaemia			
subjects affected / exposed	2 / 89 (2.25%)	0 / 79 (0.00%)	1 / 21 (4.76%)
occurrences (all)	4	0	1
Hyponatraemia			
subjects affected / exposed	0 / 89 (0.00%)	2 / 79 (2.53%)	0 / 21 (0.00%)
occurrences (all)	0	5	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 89 (0.00%)	2 / 79 (2.53%)	0 / 21 (0.00%)
occurrences (all)	0	2	0
Hypoglycaemia			
subjects affected / exposed	1 / 89 (1.12%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Hypermagnesaemia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 79 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	GDC-0980- Matching Placebo + Fulvestrant	GDC-0941 (260 mg) + Fulvestrant	GDC-0941- Matching Placebo (260 mg) + Fulvestrant
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 11 (90.91%)	40 / 42 (95.24%)	19 / 19 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Cancer pain subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 42 (0.00%) 0	0 / 19 (0.00%) 0
Vascular disorders			
Hot flush subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 3	4 / 42 (9.52%) 4	2 / 19 (10.53%) 2
Hypertension subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 42 (0.00%) 0	1 / 19 (5.26%) 1
Lymphoedema subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 42 (2.38%) 1	1 / 19 (5.26%) 2
Peripheral coldness subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 42 (0.00%) 0	1 / 19 (5.26%) 1
Poor peripheral circulation subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 42 (0.00%) 0	1 / 19 (5.26%) 2
Surgical and medical procedures			
Knee arthroplasty subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 42 (0.00%) 0	1 / 19 (5.26%) 1
General disorders and administration site conditions			
Fatigue subjects affected / exposed occurrences (all)	6 / 11 (54.55%) 7	12 / 42 (28.57%) 21	6 / 19 (31.58%) 6
Injection site pain subjects affected / exposed occurrences (all)	3 / 11 (27.27%) 6	4 / 42 (9.52%) 4	2 / 19 (10.53%) 3
Pyrexia subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	5 / 42 (11.90%) 6	1 / 19 (5.26%) 2
Mucosal inflammation subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	6 / 42 (14.29%) 9	1 / 19 (5.26%) 1

Oedema peripheral subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	3 / 42 (7.14%) 3	0 / 19 (0.00%) 0
Chest pain subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	2 / 42 (4.76%) 2	3 / 19 (15.79%) 3
Asthenia subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	2 / 42 (4.76%) 2	2 / 19 (10.53%) 2
Pain subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 2	2 / 42 (4.76%) 3	0 / 19 (0.00%) 0
Chills subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	2 / 42 (4.76%) 2	0 / 19 (0.00%) 0
Injection site bruising subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 42 (0.00%) 0	0 / 19 (0.00%) 0
Cyst subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 42 (0.00%) 0	0 / 19 (0.00%) 0
Reproductive system and breast disorders Breast pain subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 42 (0.00%) 0	0 / 19 (0.00%) 0
Breast discomfort subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 42 (0.00%) 0	1 / 19 (5.26%) 1
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	3 / 11 (27.27%) 3	6 / 42 (14.29%) 6	2 / 19 (10.53%) 2
Dyspnoea subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 2	6 / 42 (14.29%) 7	2 / 19 (10.53%) 5
Oropharyngeal pain			

subjects affected / exposed	0 / 11 (0.00%)	1 / 42 (2.38%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Dyspnoea exertional			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Pneumonitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 42 (2.38%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 42 (2.38%)	2 / 19 (10.53%)
occurrences (all)	0	1	3
Hypoxia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed	1 / 11 (9.09%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 11 (9.09%)	2 / 42 (4.76%)	2 / 19 (10.53%)
occurrences (all)	1	2	4
Anxiety			
subjects affected / exposed	2 / 11 (18.18%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences (all)	2	0	2
Depression			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Depressed mood			
subjects affected / exposed	1 / 11 (9.09%)	1 / 42 (2.38%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
Mood swings			
subjects affected / exposed	1 / 11 (9.09%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Investigations			
Aspartate aminotransferase increased			

subjects affected / exposed	2 / 11 (18.18%)	10 / 42 (23.81%)	3 / 19 (15.79%)
occurrences (all)	2	12	4
Alanine aminotransferase increased			
subjects affected / exposed	1 / 11 (9.09%)	8 / 42 (19.05%)	2 / 19 (10.53%)
occurrences (all)	1	9	5
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 11 (0.00%)	3 / 42 (7.14%)	0 / 19 (0.00%)
occurrences (all)	0	3	0
Weight decreased			
subjects affected / exposed	0 / 11 (0.00%)	2 / 42 (4.76%)	1 / 19 (5.26%)
occurrences (all)	0	3	1
Blood cholesterol increased			
subjects affected / exposed	2 / 11 (18.18%)	2 / 42 (4.76%)	1 / 19 (5.26%)
occurrences (all)	3	2	1
Lipase increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 42 (2.38%)	1 / 19 (5.26%)
occurrences (all)	0	1	2
Blood creatinine increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 42 (2.38%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Weight increased			
subjects affected / exposed	0 / 11 (0.00%)	2 / 42 (4.76%)	1 / 19 (5.26%)
occurrences (all)	0	2	1
Blood potassium decreased			
subjects affected / exposed	0 / 11 (0.00%)	2 / 42 (4.76%)	1 / 19 (5.26%)
occurrences (all)	0	2	1
Lymphocyte count decreased			
subjects affected / exposed	0 / 11 (0.00%)	2 / 42 (4.76%)	1 / 19 (5.26%)
occurrences (all)	0	3	3
Blood triglycerides increased			

subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	1 / 42 (2.38%) 1	0 / 19 (0.00%) 0
White blood cell count decreased subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 42 (0.00%) 0	1 / 19 (5.26%) 1
Blood alkaline phosphatase subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 42 (0.00%) 0	1 / 19 (5.26%) 1
Blood magnesium decreased subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 42 (0.00%) 0	1 / 19 (5.26%) 1
Injury, poisoning and procedural complications			
Contusion subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 42 (2.38%) 2	1 / 19 (5.26%) 1
Tooth fracture subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	2 / 42 (4.76%) 2	1 / 19 (5.26%) 1
Excoriation subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 42 (0.00%) 0	1 / 19 (5.26%) 1
Procedural pain subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 42 (0.00%) 0	1 / 19 (5.26%) 1
Nervous system disorders			
Dysgeusia subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 2	13 / 42 (30.95%) 13	3 / 19 (15.79%) 3
Headache subjects affected / exposed occurrences (all)	5 / 11 (45.45%) 6	9 / 42 (21.43%) 12	3 / 19 (15.79%) 4
Dizziness subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 2	5 / 42 (11.90%) 6	1 / 19 (5.26%) 1
Paraesthesia			

subjects affected / exposed	1 / 11 (9.09%)	4 / 42 (9.52%)	1 / 19 (5.26%)
occurrences (all)	1	5	1
Neuropathy peripheral			
subjects affected / exposed	0 / 11 (0.00%)	1 / 42 (2.38%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Hypoaesthesia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 42 (2.38%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Lethargy			
subjects affected / exposed	0 / 11 (0.00%)	1 / 42 (2.38%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Memory impairment			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Hyperaesthesia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Hypokinesia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 11 (18.18%)	1 / 42 (2.38%)	2 / 19 (10.53%)
occurrences (all)	5	3	3
Thrombocytopenia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 11 (9.09%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Eye disorders			

Dry eye			
subjects affected / exposed	0 / 11 (0.00%)	1 / 42 (2.38%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Lacrimation increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Vision blurred			
subjects affected / exposed	1 / 11 (9.09%)	1 / 42 (2.38%)	1 / 19 (5.26%)
occurrences (all)	1	1	1
Visual acuity reduced			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Eye irritation			
subjects affected / exposed	1 / 11 (9.09%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Periorbital oedema			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Eye disorder			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 11 (18.18%)	29 / 42 (69.05%)	8 / 19 (42.11%)
occurrences (all)	3	104	9
Nausea			
subjects affected / exposed	4 / 11 (36.36%)	19 / 42 (45.24%)	6 / 19 (31.58%)
occurrences (all)	6	26	11
Vomiting			
subjects affected / exposed	1 / 11 (9.09%)	10 / 42 (23.81%)	2 / 19 (10.53%)
occurrences (all)	1	13	8
Constipation			

subjects affected / exposed	2 / 11 (18.18%)	3 / 42 (7.14%)	6 / 19 (31.58%)
occurrences (all)	2	3	7
Stomatitis			
subjects affected / exposed	1 / 11 (9.09%)	5 / 42 (11.90%)	0 / 19 (0.00%)
occurrences (all)	1	7	0
Abdominal pain			
subjects affected / exposed	1 / 11 (9.09%)	4 / 42 (9.52%)	3 / 19 (15.79%)
occurrences (all)	1	5	6
Dyspepsia			
subjects affected / exposed	1 / 11 (9.09%)	4 / 42 (9.52%)	2 / 19 (10.53%)
occurrences (all)	1	4	2
Dry mouth			
subjects affected / exposed	0 / 11 (0.00%)	2 / 42 (4.76%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Gastroesophageal reflux disease			
subjects affected / exposed	0 / 11 (0.00%)	3 / 42 (7.14%)	1 / 19 (5.26%)
occurrences (all)	0	3	2
Abdominal pain upper			
subjects affected / exposed	0 / 11 (0.00%)	2 / 42 (4.76%)	1 / 19 (5.26%)
occurrences (all)	0	3	1
Mouth ulceration			
subjects affected / exposed	0 / 11 (0.00%)	4 / 42 (9.52%)	1 / 19 (5.26%)
occurrences (all)	0	4	1
Abdominal distension			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	4
Flatulence			
subjects affected / exposed	0 / 11 (0.00%)	1 / 42 (2.38%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Gingival pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 42 (2.38%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Oral pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Ascites			

subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Rectal haemorrhage			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Abdominal pain lower			
subjects affected / exposed	1 / 11 (9.09%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Eructation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
Gingival bleeding			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Tongue ulceration			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 11 (9.09%)	16 / 42 (38.10%)	1 / 19 (5.26%)
occurrences (all)	1	31	1
Pruritus			
subjects affected / exposed	0 / 11 (0.00%)	7 / 42 (16.67%)	3 / 19 (15.79%)
occurrences (all)	0	9	3
Rash maculo–papular			
subjects affected / exposed	0 / 11 (0.00%)	6 / 42 (14.29%)	0 / 19 (0.00%)
occurrences (all)	0	19	0
Dry skin			
subjects affected / exposed	0 / 11 (0.00%)	6 / 42 (14.29%)	0 / 19 (0.00%)
occurrences (all)	0	6	0
Alopecia			
subjects affected / exposed	0 / 11 (0.00%)	4 / 42 (9.52%)	0 / 19 (0.00%)
occurrences (all)	0	4	0
Erythema			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0

Night sweats			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Hyperhidrosis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 42 (2.38%)	1 / 19 (5.26%)
occurrences (all)	0	1	2
Pain of skin			
subjects affected / exposed	1 / 11 (9.09%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Pruritus generalised			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Skin mass			
subjects affected / exposed	0 / 11 (0.00%)	1 / 42 (2.38%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Trichorrhexis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 11 (18.18%)	9 / 42 (21.43%)	4 / 19 (21.05%)
occurrences (all)	2	12	7
Back pain			
subjects affected / exposed	2 / 11 (18.18%)	7 / 42 (16.67%)	3 / 19 (15.79%)
occurrences (all)	3	11	4
Pain in extremity			
subjects affected / exposed	1 / 11 (9.09%)	3 / 42 (7.14%)	4 / 19 (21.05%)
occurrences (all)	2	5	6
Bone pain			
subjects affected / exposed	2 / 11 (18.18%)	2 / 42 (4.76%)	4 / 19 (21.05%)
occurrences (all)	3	3	4
Myalgia			
subjects affected / exposed	1 / 11 (9.09%)	4 / 42 (9.52%)	2 / 19 (10.53%)
occurrences (all)	1	4	2
Muscle spasms			

subjects affected / exposed	1 / 11 (9.09%)	4 / 42 (9.52%)	1 / 19 (5.26%)
occurrences (all)	1	6	3
Musculoskeletal pain			
subjects affected / exposed	2 / 11 (18.18%)	3 / 42 (7.14%)	3 / 19 (15.79%)
occurrences (all)	2	3	4
Musculoskeletal chest pain			
subjects affected / exposed	1 / 11 (9.09%)	1 / 42 (2.38%)	1 / 19 (5.26%)
occurrences (all)	1	1	1
Neck pain			
subjects affected / exposed	1 / 11 (9.09%)	1 / 42 (2.38%)	2 / 19 (10.53%)
occurrences (all)	1	2	3
Muscular weakness			
subjects affected / exposed	1 / 11 (9.09%)	1 / 42 (2.38%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
Flank pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Arthritis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Osteoarthritis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
Muscle twitching			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	2 / 11 (18.18%)	3 / 42 (7.14%)	1 / 19 (5.26%)
occurrences (all)	2	3	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 11 (9.09%)	1 / 42 (2.38%)	3 / 19 (15.79%)
occurrences (all)	2	2	4
Nasopharyngitis			
subjects affected / exposed	0 / 11 (0.00%)	5 / 42 (11.90%)	0 / 19 (0.00%)
occurrences (all)	0	5	0

Sinusitis			
subjects affected / exposed	0 / 11 (0.00%)	2 / 42 (4.76%)	1 / 19 (5.26%)
occurrences (all)	0	3	1
Bronchitis			
subjects affected / exposed	1 / 11 (9.09%)	2 / 42 (4.76%)	0 / 19 (0.00%)
occurrences (all)	1	2	0
Conjunctivitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Herpes zoster			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Localised infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 42 (2.38%)	1 / 19 (5.26%)
occurrences (all)	0	2	1
Rhinitis			
subjects affected / exposed	1 / 11 (9.09%)	1 / 42 (2.38%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Eye infection			
subjects affected / exposed	1 / 11 (9.09%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Folliculitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 11 (18.18%)	11 / 42 (26.19%)	4 / 19 (21.05%)
occurrences (all)	2	12	4
Hyperglycaemia			

subjects affected / exposed	0 / 11 (0.00%)	12 / 42 (28.57%)	0 / 19 (0.00%)
occurrences (all)	0	25	0
Hypokalaemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 42 (2.38%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Dehydration			
subjects affected / exposed	0 / 11 (0.00%)	1 / 42 (2.38%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Hypomagnesaemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 42 (2.38%)	1 / 19 (5.26%)
occurrences (all)	0	1	2
Hypercalcaemia			
subjects affected / exposed	0 / 11 (0.00%)	2 / 42 (4.76%)	1 / 19 (5.26%)
occurrences (all)	0	2	3
Hypocalcaemia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Hyponatraemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 42 (2.38%)	2 / 19 (10.53%)
occurrences (all)	0	2	3
Hypercholesterolaemia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Hypoglycaemia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 42 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Hypermagnesaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 42 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 October 2012	Protocol Amendment 2 included the following changes: halted enrollment in the apitolisib /matching placebo arm of the study due to an unacceptably high rate of Grade 3 rash; added two additional study arms to examine the safety and tolerability and to estimate the effect of pictilisib at a dose of 260 mg, once daily, in combination with fulvestrant versus fulvestrant + placebo in subjects who received prior treatment with an aromatase inhibitor and whose tumors had a PIK3CA mutation.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported