

**Clinical trial results:****A Randomised Double-Blind Phase IIa Study (with Combination Safety Run-in) to Assess the Safety and Efficacy of AZD4547 in Combination with Fulvestrant vs. Fulvestrant Alone in ER+ Breast Cancer Patients with FGFR1 Polysomy or Gene Amplification who have Progressed Following Treatment with Prior Endocrine Therapy (Adjuvant or First-line Metastatic) (GLOW)****Summary**

EudraCT number	2010-021220-10
Trial protocol	GB FR DE HU CZ IT
Global end of trial date	21 October 2014

**Results information**

Result version number	v1 (current)
This version publication date	12 May 2016
First version publication date	12 May 2016

**Trial information****Trial identification**

Sponsor protocol code	D2610C00003
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**Additional study identifiers**

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

Notes:

**Sponsors**

Sponsor organisation name	Astrazeneca
Sponsor organisation address	Alderley Park, Macclesfield, United Kingdom, SK10 4TG
Public contact	Richard Mather, AstraZeneca, 44 01763263593, ClinicalTrialTransparency@astrazeneca.com
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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:

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## Results analysis stage

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Analysis stage	Final
Date of interim/final analysis	18 February 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 October 2014
Global end of trial reached?	Yes
Global end of trial date	21 October 2014
Was the trial ended prematurely?	Yes

Notes:

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## General information about the trial

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Main objective of the trial:

Safety run-in

To assess the safety and tolerability and to determine the dose and schedule of AZD4547 to be used in combination with an endocrine therapy. Initially, exemestane, then changed by protocol amendment to fulvestrant.

Randomised Phase IIa

To assess the relative efficacy of AZD4547 in combination with fulvestrant compared with fulvestrant+placebo by assessment of progression free survival (PFS) in all randomised patients and also in patients with tumours that had FGFR1 gene amplification (fluorescence in situ hybridisation [FISH] score 6).

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Protection of trial subjects:

Ongoing safety monitoring and dose adjustment and discontinuation guidance for trial drugs was provided to protect subjects from side effects.

A safety review committee (SRC) consisting of a sponsor physician and a physician investigator and representatives from each study site met regularly to review safety during the safety run-in phase of the trial. Additional independent experts were consulted as appropriate.

An independent safety review committee (SRC) was used to support the randomised phase II section of the trial, consisting of an independent sponsor physician, a sponsor safety physician and two non-study independent physician investigators.

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Background therapy: -

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Evidence for comparator: -

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Actual start date of recruitment	08 December 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	10 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

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## Population of trial subjects

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### Subjects enrolled per country

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Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	Czech Republic: 1
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	Hungary: 3
Country: Number of subjects enrolled	United Kingdom: 19

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Worldwide total number of subjects	40
EEA total number of subjects	40

Notes:

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**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)	17
From 65 to 84 years	23
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

First patient was enrolled on 8 Dec 2010 and Last patient last visit was on 21 Oct 2014. Recruitment was slow, leading to concerns about the feasibility of completing enrolment. Moreover, the limited evidence of clinical activity of AZD4547 monotherapy in FGFR gastric cancer and NSCLC has resulted in a business decision to terminate enrolment.

### Pre-assignment

Screening details:

Part A: 38 patients enrolled, 31 patients received AZD4547+exemestane; 7 patients did not receive (5 patients were not eligible, 1 patient due to patient decision, 1 patient due to "Other") Part B: 89 patients enrolled; 80 were not eligible, 9 patients received the treatment

### Period 1

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

Blinding implementation details:

The safety run-in was not blinded.

### Arms

Are arms mutually exclusive?	Yes
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<b>Arm title</b>	AZD4547 80mg bd cont + Exemestane 25mg
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Arm description:

80 mg AZD4547 BD continuous + 25 mg exemestane

Arm type	Experimental
Investigational medicinal product name	AZD4547
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

80mg bd continuous

<b>Arm title</b>	AZD4547 40mg cont + Exemestane 25mg
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Arm description:

40 mg AZD4547 BD continuous + 25 mg exemestane

Arm type	Experimental
Investigational medicinal product name	AZD4547
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

40mg bd continuous

<b>Arm title</b>	AZD4547 80mg bd 1w/1w + Exemestane 25mg
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Arm description:

80 mg AZD4547 bd one week on/one week off + 25 mg exemestane

Arm type	Experimental
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Investigational medicinal product name	AZD4547
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

80mg bd 1w/1w intermittant

<b>Arm title</b>	AZD4547 80mg bd 2w/1w + Exemestane
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Arm description:

80 mg AZD4547 BD two week on/one week off + 25 mg exemestane

Arm type	Experimental
Investigational medicinal product name	AZD4547
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

80mg bd 2w/1w intermittant

<b>Arm title</b>	Part B: AZD4547 + Fulvestrant
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Arm description:

80 mg AZD4547 BD + 500 mg Fulvestrant

Arm type	Experimental
Investigational medicinal product name	AZD4547
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

80mg bd continuous

<b>Arm title</b>	Part B: Placebo + Fulvestrant
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Arm description:

80mg Placebo BD + 500 mg Fulvestrant

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

Dosage and administration details:

80mg bd

<b>Number of subjects in period 1</b>	AZD4547 80mg bd cont + Exemestane 25mg	AZD4547 40mg cont + Exemestane 25mg	AZD4547 80mg bd 1w/1w + Exemestane 25mg
Started	5	5	12
Completed	0	0	1
Not completed	5	5	11
Consent withdrawn by subject	-	-	-

Objective Disease Progression	3	1	-
Adverse event, non-fatal	2	1	4
Other reason as per investigator	-	3	7

<b>Number of subjects in period 1</b>	AZD4547 80mg bd 2w/1w + Exemestane	Part B: AZD4547 + Fulvestrant	Part B: Placebo + Fulvestrant
Started	9	5	4
Completed	2	0	0
Not completed	7	5	4
Consent withdrawn by subject	-	2	1
Objective Disease Progression	-	2	-
Adverse event, non-fatal	4	-	-
Other reason as per investigator	3	1	3

## Baseline characteristics

<b>Reporting groups</b>	
Reporting group title	AZD4547 80mg bd cont + Exemestane 25mg
Reporting group description: 80 mg AZD4547 BD continuous + 25 mg exemestane	
Reporting group title	AZD4547 40mg cont + Exemestane 25mg
Reporting group description: 40 mg AZD4547 BD continuous + 25 mg exemestane	
Reporting group title	AZD4547 80mg bd 1w/1w + Exemestane 25mg
Reporting group description: 80 mg AZD4547 bd one week on/one week off + 25 mg exemestane	
Reporting group title	AZD4547 80mg bd 2w/1w + Exemestane
Reporting group description: 80 mg AZD4547 BD two week on/one week off + 25 mg exemestane	
Reporting group title	Part B: AZD4547 + Fulvestrant
Reporting group description: 80 mg AZD4547 BD + 500 mg Fulvestrant	
Reporting group title	Part B: Placebo + Fulvestrant
Reporting group description: 80mg Placebo BD + 500 mg Fulvestrant	

<b>Reporting group values</b>	AZD4547 80mg bd cont + Exemestane 25mg	AZD4547 40mg cont + Exemestane 25mg	AZD4547 80mg bd 1w/1w + Exemestane 25mg
Number of subjects	5	5	12
Age categorical Units: Subjects			
In Utero Preterm newborn-gestational age < 37 wk	0	0	0
Newborns (0-27days)	0	0	0
Infants and toddlers (28days – 23months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 year)	0	0	0
From 18 - 64 years	3	3	4
From 65 – 84 years	2	2	8
Over 85 years	0	0	0
Age Continuous   Units: Years			
arithmetic mean	58.4	61.2	66.5
standard deviation	± 16.7	± 9.36	± 8.46
Gender categorical Units: Subjects			
Female	5	5	12
Male	0	0	0
Age, Customized Units: Subjects			
Total Age Category	5	5	12
Gender, Customized			

Units: Subjects			
Total Gender Category	5	5	12

<b>Reporting group values</b>	AZD4547 80mg bd 2w/1w + Exemestane	Part B: AZD4547 + Fulvestrant	Part B: Placebo + Fulvestrant
Number of subjects	9	5	4
Age categorical Units: Subjects			
In Utero Preterm newborn- gestational age < 37 wk	0	0	0
Newborns (0-27days)	0	0	0
Infants and toddlers (28days - 23months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 year)	0	0	0
From 18 - 64 years	3	3	1
From 65 - 84 years	6	2	3
Over 85 years	0	0	0
Age Continuous   Units: Years			
arithmetic mean	67.3	61	67.3
standard deviation	± 9.66	± 6.82	± 9.46
Gender categorical Units: Subjects			
Female	9	5	4
Male	0	0	0
Age, Customized Units: Subjects			
Total Age Category	9	5	4
Gender, Customized Units: Subjects			
Total Gender Category	9	5	4

<b>Reporting group values</b>	Total		
Number of subjects	40		
Age categorical Units: Subjects			
In Utero Preterm newborn- gestational age < 37 wk	0		
Newborns (0-27days)	0		
Infants and toddlers (28days - 23months)	0		
Children (2-11 years)	0		
Adolescents (12-17 year)	0		
From 18 - 64 years	17		
From 65 - 84 years	23		
Over 85 years	0		
Age Continuous   Units: Years			
arithmetic mean	-		
standard deviation	-		

Gender categorical Units: Subjects			
Female	40		
Male	0		
Age, Customized Units: Subjects			
Total Age Category	40		
Gender, Customized Units: Subjects			
Total Gender Category	40		

## End points

### End points reporting groups

Reporting group title	AZD4547 80mg bd cont + Exemestane 25mg
Reporting group description:	80 mg AZD4547 BD continuous + 25 mg exemestane
Reporting group title	AZD4547 40mg cont + Exemestane 25mg
Reporting group description:	40 mg AZD4547 BD continuous + 25 mg exemestane
Reporting group title	AZD4547 80mg bd 1w/1w + Exemestane 25mg
Reporting group description:	80 mg AZD4547 bd one week on/one week off + 25 mg exemestane
Reporting group title	AZD4547 80mg bd 2w/1w + Exemestane
Reporting group description:	80 mg AZD4547 BD two week on/one week off + 25 mg exemestane
Reporting group title	Part B: AZD4547 + Fulvestrant
Reporting group description:	80 mg AZD4547 BD + 500 mg Fulvestrant
Reporting group title	Part B: Placebo + Fulvestrant
Reporting group description:	80mg Placebo BD + 500 mg Fulvestrant

### Primary: Safety and tolerability in terms of number of patients with Adverse events (serious and non-serious)

End point title	Safety and tolerability in terms of number of patients with Adverse events (serious and non-serious) <sup>[1]</sup>
End point description:	
End point type	Primary
End point timeframe:	3 years, 10 months (Adverse events recorded from patient screening to discontinuation plus 28 days safety follow-up).

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis was planned for the primary endpoint.

End point values	AZD4547 80mg bd cont + Exemestane 25mg	AZD4547 40mg cont + Exemestane 25mg	AZD4547 80mg bd 1w/1w + Exemestane 25mg	AZD4547 80mg bd 2w/1w + Exemestane
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	12	9
Units: Participants	5	5	12	9

End point values	Part B: AZD4547 + Fulvestrant	Part B: Placebo + Fulvestrant		

Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	4		
Units: Participants	5	2		

### **Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

3 years, 10 months (Adverse events recorded from patient screening to discontinuation plus 28 days safety follow-up).

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

### Reporting groups

Reporting group title	AZD4547 80mg bd cont + Ex 25mg
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Reporting group description:

80 mg AZD4547 bd continuous + 25 mg exemestane

Reporting group title	AZD4547 40mg bd cont + Ex 25mg
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Reporting group description:

40 mg AZD4547 BD continuous + 25 mg exemestane

Reporting group title	AZD4547 80mg bd 1w/1w + Ex 25mg
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Reporting group description:

80 mg AZD4547 BD one week on/one week off + 25 mg exemestane

Reporting group title	AZD4547 80mg bd 2w/1w + Ex 25mg
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Reporting group description:

80 mg AZD4547 bd two week on/one week off + 25 mg exemestane

Reporting group title	Part B: AZD4547 + Fulvestrant
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Reporting group description:

80 mg AZD4547 BD + 500 mg Fulvestrant

Reporting group title	Part B: Placebo + Fulvestrant
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Reporting group description:

80 mg Placebo BD + 500 mg Fulvestrant

<b>Serious adverse events</b>	AZD4547 80mg bd cont + Ex 25mg	AZD4547 40mg bd cont + Ex 25mg	AZD4547 80mg bd 1w/1w + Ex 25mg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 5 (40.00%)	2 / 5 (40.00%)	5 / 12 (41.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
TROPONIN INCREASED			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
JUGULAR VEIN THROMBOSIS			

subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Nervous system disorders</b>			
<b>DIZZINESS</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>VIITH NERVE PARALYSIS</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Blood and lymphatic system disorders</b>			
<b>ANAEMIA</b>			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>General disorders and administration site conditions</b>			
<b>DEVICE DEPOSIT ISSUE</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>INFLAMMATION</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (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
<b>GAIT DISTURBANCE</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (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
<b>Gastrointestinal disorders</b>			
<b>DIARRHOEA</b>			

subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (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
<b>OESOPHAGEAL ACHALASIA</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>STOMATITIS</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Respiratory, thoracic and mediastinal disorders</b>			
<b>ASTHMA</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>DYSPNOEA</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>PLEURAL EFFUSION</b>			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (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
<b>Renal and urinary disorders</b>			
<b>RENAL FAILURE</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Musculoskeletal and connective tissue disorders</b>			
<b>ACUTE CRISIS OF PSORIASIC OLIGOARTHRITIS</b>			

subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (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
<b>Infections and infestations</b>			
<b>LOWER RESPIRATORY TRACT INFECTION VIRAL</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>NEUTROPENIC SEPSIS</b>			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (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
<b>PLEURAL INFECTION</b>			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (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
<b>PYELONEPHRITIS</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

<b>Serious adverse events</b>	<b>AZD4547 80mg bd 2w/1w + Ex 25mg</b>	<b>Part B: AZD4547 + Fulvestrant</b>	<b>Part B: Placebo + Fulvestrant</b>
<b>Total subjects affected by serious adverse events</b>			
subjects affected / exposed	1 / 9 (11.11%)	1 / 5 (20.00%)	1 / 4 (25.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
<b>Investigations</b>			
<b>TROPONIN INCREASED</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (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
<b>Vascular disorders</b>			
<b>JUGULAR VEIN THROMBOSIS</b>			

subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (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
<b>Nervous system disorders</b>			
<b>DIZZINESS</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>VIITH NERVE PARALYSIS</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (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
<b>Blood and lymphatic system disorders</b>			
<b>ANAEMIA</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (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
<b>General disorders and administration site conditions</b>			
<b>DEVICE DEPOSIT ISSUE</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (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
<b>INFLAMMATION</b>			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (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
<b>GAIT DISTURBANCE</b>			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (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
<b>Gastrointestinal disorders</b>			
<b>DIARRHOEA</b>			

subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (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
<b>OESOPHAGEAL ACHALASIA</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (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
<b>STOMATITIS</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (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
<b>Respiratory, thoracic and mediastinal disorders</b>			
<b>ASTHMA</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (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
<b>DYSPNOEA</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (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
<b>PLEURAL EFFUSION</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (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
<b>Renal and urinary disorders</b>			
<b>RENAL FAILURE</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (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
<b>Musculoskeletal and connective tissue disorders</b>			
<b>ACUTE CRISIS OF PSORIASIC OLIGOARTHRITIS</b>			

subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (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
<b>Infections and infestations</b>			
<b>LOWER RESPIRATORY TRACT INFECTION VIRAL</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (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
<b>NEUTROPENIC SEPSIS</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (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
<b>PLEURAL INFECTION</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (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
<b>PYELONEPHRITIS</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (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: 0 %

<b>Non-serious adverse events</b>	AZD4547 80mg bd cont + Ex 25mg	AZD4547 40mg bd cont + Ex 25mg	AZD4547 80mg bd 1w/1w + Ex 25mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)	5 / 5 (100.00%)	12 / 12 (100.00%)
<b>Neoplasms benign, malignant and unspecified (incl cysts and polyps)</b>			
<b>BREAST CANCER METASTATIC</b>			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
<b>METASTATIC PAIN</b>			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
<b>NEURILEMMOMA BENIGN</b>			

subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
TUMOUR PAIN			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
HOT FLUSH			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
HYPERTENSION			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
HYPOTENSION			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
LYMPHOEDEMA			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
PALLOR			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Phlebitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
CRYING			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
DEVICE BREAKAGE			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
FATIGUE			

subjects affected / exposed	3 / 5 (60.00%)	2 / 5 (40.00%)	4 / 12 (33.33%)
occurrences (all)	3	2	4
<b>FIBROSIS</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
<b>GENERAL PHYSICAL HEALTH DETERIORATION</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
<b>INFLUENZA LIKE ILLNESS</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
<b>INJURY ASSOCIATED WITH DEVICE</b>			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
<b>LOCAL SWELLING</b>			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
<b>OEDEMA</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
<b>OEDEMA PERIPHERAL</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
<b>PYREXIA</b>			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
<b>Gait disturbance</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
<b>Induration</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
<b>Inflammation</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Injection site rash subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 12 (0.00%) 0
Mucosal inflammation subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 12 (0.00%) 0
Feeling hot subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 12 (0.00%) 0
Immune system disorders SEASONAL ALLERGY subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 5 (20.00%) 1	0 / 12 (0.00%) 0
Reproductive system and breast disorders BREAST DISORDER subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	1 / 12 (8.33%) 1
BREAST PAIN subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 5 (0.00%) 0	1 / 12 (8.33%) 1
VULVOVAGINAL DRYNESS subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	1 / 12 (8.33%) 1
Respiratory, thoracic and mediastinal disorders ASTHMA subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	1 / 12 (8.33%) 1
COUGH subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	1 / 5 (20.00%) 1	1 / 12 (8.33%) 1
DRY THROAT subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	1 / 5 (20.00%) 1	1 / 12 (8.33%) 1
DYSPHONIA subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	1 / 12 (8.33%) 1

DYSпноEA			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	2 / 12 (16.67%)
occurrences (all)	0	1	2
EPISTAXIS			
subjects affected / exposed	3 / 5 (60.00%)	2 / 5 (40.00%)	2 / 12 (16.67%)
occurrences (all)	3	2	2
LUNG CONSOLIDATION			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
NASAL DISCOMFORT			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
NASAL DRYNESS			
subjects affected / exposed	1 / 5 (20.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
NASAL INFLAMMATION			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
OROPHARYNGEAL PAIN			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
PLEURAL EFFUSION			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
PLEURITIC PAIN			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
PRODUCTIVE COUGH			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
RALES			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
RHINALGIA			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0

RHINORRHOEA subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 12 (0.00%) 0
Psychiatric disorders			
DEPRESSED MOOD subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	1 / 12 (8.33%) 1
DEPRESSION subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	1 / 5 (20.00%) 1	0 / 12 (0.00%) 0
DEREALISATION subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 12 (0.00%) 0
INSOMNIA subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 5 (20.00%) 1	2 / 12 (16.67%) 2
SLEEP DISORDER subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	1 / 12 (8.33%) 1
Investigations			
ALANINE AMINOTRANSFERASE INCREASED subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 5 (0.00%) 0	0 / 12 (0.00%) 0
ASPARTATE AMINOTRANSFERASE INCREASED subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	1 / 5 (20.00%) 1	0 / 12 (0.00%) 0
BLOOD ALKALINE PHOSPHATASE INCREASED subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 5 (0.00%) 0	0 / 12 (0.00%) 0
BLOOD CREATININE INCREASED subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	1 / 12 (8.33%) 1
BLOOD GLUCOSE INCREASED subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	1 / 12 (8.33%) 1

BLOOD IRON DECREASED			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
BLOOD PHOSPHORUS INCREASED			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	3 / 12 (25.00%)
occurrences (all)	1	0	3
BODY TEMPERATURE INCREASED			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
C-REACTIVE PROTEIN INCREASED			
subjects affected / exposed	1 / 5 (20.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
CARDIAC ENZYMES INCREASED			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
COLD AGGLUTININS POSITIVE			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
ELECTROCARDIOGRAM T WAVE ABNORMAL			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
INSPIRATORY CAPACITY DECREASED			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
NEUTROPHIL COUNT INCREASED			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
OXYGEN SATURATION DECREASED			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
TROPONIN T INCREASED			

subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 5 (0.00%) 0	0 / 12 (0.00%) 0
WEIGHT DECREASED subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 5 (0.00%) 0	0 / 12 (0.00%) 0
Ejection fraction decreased subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 12 (0.00%) 0
Injury, poisoning and procedural complications			
ARTHROPOD BITE subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	1 / 12 (8.33%) 1
CONTUSION subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	1 / 5 (20.00%) 1	0 / 12 (0.00%) 0
FALL subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 5 (20.00%) 1	0 / 12 (0.00%) 0
JOINT INJURY subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 5 (20.00%) 1	0 / 12 (0.00%) 0
LACERATION subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 5 (20.00%) 1	0 / 12 (0.00%) 0
TRAUMATIC HAEMATOMA subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 12 (0.00%) 0
Arthropod sting subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 12 (0.00%) 0
Cardiac disorders			
PERICARDIAL EFFUSION subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	1 / 12 (8.33%) 1
TACHYCARDIA			

subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Palpitations			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
AGEUSIA			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
APHASIA			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
DYSGEUSIA			
subjects affected / exposed	2 / 5 (40.00%)	2 / 5 (40.00%)	6 / 12 (50.00%)
occurrences (all)	2	2	6
HEADACHE			
subjects affected / exposed	1 / 5 (20.00%)	1 / 5 (20.00%)	3 / 12 (25.00%)
occurrences (all)	1	1	3
HYPOAESTHESIA			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
HYPOKINESIA			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
LETHARGY			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
MYOCLONUS			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
NEURALGIA			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
NEUROPATHY PERIPHERAL			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1

PARAESTHESIA			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	3 / 12 (25.00%)
occurrences (all)	0	1	3
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
SCIATICA			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
TREMOR			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Burning sensation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	2 / 12 (16.67%)
occurrences (all)	0	1	2
LYMPHADENOPATHY			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
NEUTROPENIA			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
VERTIGO			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
CHORIORETINOPATHY			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
DETACHMENT OF RETINAL PIGMENT			

<b>EPITHELIUM</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	3 / 12 (25.00%)
occurrences (all)	0	0	3
<b>DRY EYE</b>			
subjects affected / exposed	2 / 5 (40.00%)	1 / 5 (20.00%)	1 / 12 (8.33%)
occurrences (all)	2	1	1
<b>EYE DISCHARGE</b>			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
<b>EYE DISORDER</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
<b>EYE IRRITATION</b>			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
<b>EYE PAIN</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
<b>EYELID PAIN</b>			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
<b>GROWTH OF EYELASHES</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
<b>KERATITIS</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
<b>LACRIMATION INCREASED</b>			
subjects affected / exposed	1 / 5 (20.00%)	1 / 5 (20.00%)	1 / 12 (8.33%)
occurrences (all)	1	1	1
<b>MACULOPATHY</b>			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
<b>OCULAR DISCOMFORT</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1

SUBRETINAL FLUID			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
ULCERATIVE KERATITIS			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
VISION BLURRED			
subjects affected / exposed	2 / 5 (40.00%)	1 / 5 (20.00%)	1 / 12 (8.33%)
occurrences (all)	2	1	1
VISUAL IMPAIRMENT			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
VITREOUS FLOATERS			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Cataract			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Corneal epithelium defect			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Photophobia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
ABDOMINAL DISTENSION			
subjects affected / exposed	0 / 5 (0.00%)	2 / 5 (40.00%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
ABDOMINAL MASS			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
ABDOMINAL PAIN			

subjects affected / exposed	1 / 5 (20.00%)	1 / 5 (20.00%)	2 / 12 (16.67%)
occurrences (all)	1	1	2
<b>ABDOMINAL PAIN UPPER</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
<b>ABDOMINAL TENDERNESS</b>			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
<b>APHTHOUS STOMATITIS</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
<b>ASCITES</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
<b>CONSTIPATION</b>			
subjects affected / exposed	1 / 5 (20.00%)	4 / 5 (80.00%)	4 / 12 (33.33%)
occurrences (all)	1	4	4
<b>DIARRHOEA</b>			
subjects affected / exposed	3 / 5 (60.00%)	2 / 5 (40.00%)	3 / 12 (25.00%)
occurrences (all)	3	2	3
<b>DRY MOUTH</b>			
subjects affected / exposed	4 / 5 (80.00%)	3 / 5 (60.00%)	7 / 12 (58.33%)
occurrences (all)	4	3	7
<b>DYSPEPSIA</b>			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
<b>DYSPHAGIA</b>			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
<b>FAECAL INCONTINENCE</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
<b>GASTRITIS</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
<b>GASTROESOPHAGEAL REFLUX</b>			

<b>DISEASE</b>			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
<b>GLOSSODYNIA</b>			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
<b>LIP DRY</b>			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
<b>MELAENA</b>			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
<b>MOUTH ULCERATION</b>			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
<b>NAUSEA</b>			
subjects affected / exposed	1 / 5 (20.00%)	2 / 5 (40.00%)	3 / 12 (25.00%)
occurrences (all)	1	2	3
<b>OESOPHAGEAL SPASM</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
<b>ORAL PAIN</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
<b>PARAESTHESIA ORAL</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
<b>STOMATITIS</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	4 / 12 (33.33%)
occurrences (all)	0	0	4
<b>TONGUE DISCOLOURATION</b>			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
<b>VOMITING</b>			
subjects affected / exposed	1 / 5 (20.00%)	1 / 5 (20.00%)	1 / 12 (8.33%)
occurrences (all)	1	1	1

Hepatobiliary disorders			
<b>CHOLELITHIASIS</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
<b>ALOPECIA</b>			
subjects affected / exposed	5 / 5 (100.00%)	3 / 5 (60.00%)	6 / 12 (50.00%)
occurrences (all)	5	3	6
<b>BLISTER</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
<b>DRY SKIN</b>			
subjects affected / exposed	2 / 5 (40.00%)	1 / 5 (20.00%)	5 / 12 (41.67%)
occurrences (all)	2	1	5
<b>ERYTHEMA</b>			
subjects affected / exposed	2 / 5 (40.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
<b>MADAROSIS</b>			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
<b>NAIL BED BLEEDING</b>			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
<b>NAIL DISCOLOURATION</b>			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
<b>NAIL DISORDER</b>			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	4 / 12 (33.33%)
occurrences (all)	1	0	4
<b>NAIL DYSTROPHY</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
<b>NIGHT SWEATS</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
<b>ONYCHALGIA</b>			

subjects affected / exposed	2 / 5 (40.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
ONYCHOLYSIS			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
PAIN OF SKIN			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
PALMAR-PLANTAR ERYTHRODYSAESTHESIA SYNDROME			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
PAPULE			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
RASH			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
RASH ERYTHEMATOUS			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	2 / 12 (16.67%)
occurrences (all)	1	0	2
RASH MACULAR			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
RASH PRURITIC			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
SKIN DISCOLOURATION			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
SKIN FISSURES			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
SKIN HAEMORRHAGE			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

SKIN ULCER			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
SWELLING FACE			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Dermatitis contact			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
HYDRONEPHROSIS			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
NEPHROLITHIASIS			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
PROTEINURIA			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
URINARY RETENTION			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
URINARY TRACT OBSTRUCTION			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	2 / 5 (40.00%)	1 / 5 (20.00%)	3 / 12 (25.00%)
occurrences (all)	2	1	3
ARTHRITIS			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
JOINT EFFUSION			

subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
<b>JOINT SWELLING</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
<b>MUSCLE SPASMS</b>			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
<b>MUSCULOSKELETAL CHEST PAIN</b>			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
<b>MUSCULOSKELETAL PAIN</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
<b>MYALGIA</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	3 / 12 (25.00%)
occurrences (all)	0	0	3
<b>NECK PAIN</b>			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	2 / 12 (16.67%)
occurrences (all)	0	1	2
<b>PAIN IN EXTREMITY</b>			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	2 / 12 (16.67%)
occurrences (all)	0	1	2
<b>PAIN IN JAW</b>			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
<b>Back pain</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
<b>Bursitis</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
<b>Joint stiffness</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
<b>Psoriatic arthropathy</b>			

subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 12 (0.00%) 0
<b>Infections and infestations</b>			
<b>CELLULITIS</b>			
subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	1 / 12 (8.33%) 1
<b>CONJUNCTIVITIS</b>			
subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 5 (0.00%) 0	0 / 12 (0.00%) 0
<b>CYSTITIS</b>			
subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	1 / 12 (8.33%) 1
<b>GINGIVITIS</b>			
subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	1 / 12 (8.33%) 1
<b>INFLUENZA</b>			
subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 5 (0.00%) 0	0 / 12 (0.00%) 0
<b>LARYNGITIS</b>			
subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	2 / 12 (16.67%) 2
<b>LOCALISED INFECTION</b>			
subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 5 (0.00%) 0	0 / 12 (0.00%) 0
<b>LOWER RESPIRATORY TRACT INFECTION</b>			
subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	0 / 12 (0.00%) 0
<b>LOWER RESPIRATORY TRACT INFECTION VIRAL</b>			
subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	1 / 5 (20.00%) 1	2 / 12 (16.67%) 2
<b>LYMPHANGITIS</b>			
subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 5 (0.00%) 0	1 / 12 (8.33%) 1
<b>MASTITIS</b>			

subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
<b>NAIL INFECTION</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
<b>OESOPHAGEAL CANDIDIASIS</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
<b>ORAL CANDIDIASIS</b>			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
<b>PARONYCHIA</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
<b>PHARYNGITIS</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
<b>SINUSITIS</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
<b>URINARY TRACT INFECTION</b>			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	3 / 12 (25.00%)
occurrences (all)	0	1	3
<b>URINARY TRACT INFECTION BACTERIAL</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
<b>URINARY TRACT INFECTION FUNGAL</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
<b>VARICELLA</b>			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
<b>VIRAL UPPER RESPIRATORY TRACT INFECTION</b>			

subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
<b>VULVOVAGINAL CANDIDIASIS</b>			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
<b>Herpes zoster</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
<b>Nasopharyngitis</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
<b>Oropharyngeal candidiasis</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
<b>Post viral fatigue syndrome</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
<b>Rash pustular</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
<b>Metabolism and nutrition disorders</b>			
<b>DECREASED APPETITE</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
<b>DEHYDRATION</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
<b>HYPERCALCAEMIA</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
<b>HYPERGLYCAEMIA</b>			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
<b>HYPERPHOSPHATAEMIA</b>			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1

HYPONATRAEMIA			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1

<b>Non-serious adverse events</b>	AZD4547 80mg bd 2w/1w + Ex 25mg	Part B: AZD4547 + Fulvestrant	Part B: Placebo + Fulvestrant
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 9 (100.00%)	5 / 5 (100.00%)	2 / 4 (50.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BREAST CANCER METASTATIC			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
METASTATIC PAIN			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
NEURILEMMOMA BENIGN			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
TUMOUR PAIN			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
HOT FLUSH			
subjects affected / exposed	2 / 9 (22.22%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	2	1	0
HYPERTENSION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
HYPOTENSION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
LYMPHOEDEMA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
PALLOR			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Phlebitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 9 (0.00%)	2 / 5 (40.00%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
CRYING			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
DEVICE BREAKAGE			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
FATIGUE			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
FIBROSIS			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
INJURY ASSOCIATED WITH DEVICE			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
LOCAL SWELLING			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
OEDEMA			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
OEDEMA PERIPHERAL			

subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
<b>PYREXIA</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>Gait disturbance</b>			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
<b>Induration</b>			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
<b>Inflammation</b>			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
<b>Injection site rash</b>			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
<b>Mucosal inflammation</b>			
subjects affected / exposed	0 / 9 (0.00%)	2 / 5 (40.00%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
<b>Feeling hot</b>			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
<b>Immune system disorders</b>			
<b>SEASONAL ALLERGY</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>Reproductive system and breast disorders</b>			
<b>BREAST DISORDER</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>BREAST PAIN</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>VULVOVAGINAL DRYNESS</b>			

subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>Respiratory, thoracic and mediastinal disorders</b>			
<b>ASTHMA</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>COUGH</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>DRY THROAT</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>DYSPHONIA</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>DYSPNOEA</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>EPISTAXIS</b>			
subjects affected / exposed	2 / 9 (22.22%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
<b>LUNG CONSOLIDATION</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>NASAL DISCOMFORT</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>NASAL DRYNESS</b>			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
<b>NASAL INFLAMMATION</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>OROPHARYNGEAL PAIN</b>			

subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	1
<b>PLEURAL EFFUSION</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>PLEURITIC PAIN</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>PRODUCTIVE COUGH</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>RALES</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>RHINALGIA</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>RHINORRHOEA</b>			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
<b>Psychiatric disorders</b>			
<b>DEPRESSED MOOD</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>DEPRESSION</b>			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
<b>DEREALISATION</b>			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
<b>INSOMNIA</b>			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
<b>SLEEP DISORDER</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
BLOOD CREATININE INCREASED			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	1
BLOOD GLUCOSE INCREASED			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
BLOOD IRON DECREASED			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
BLOOD PHOSPHORUS INCREASED			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
BODY TEMPERATURE INCREASED			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
C-REACTIVE PROTEIN INCREASED			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
CARDIAC ENZYMES INCREASED			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
COLD AGGLUTININS POSITIVE			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
ELECTROCARDIOGRAM T WAVE			

ABNORMAL			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
INSPIRATORY CAPACITY DECREASED			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
NEUTROPHIL COUNT INCREASED			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
OXYGEN SATURATION DECREASED			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
TROPONIN T INCREASED			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
WEIGHT DECREASED			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Ejection fraction decreased			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
ARTHROPOD BITE			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
CONTUSION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
FALL			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
JOINT INJURY			

subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>LACERATION</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>TRAUMATIC HAEMATOMA</b>			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
<b>Arthropod sting</b>			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
<b>Cardiac disorders</b>			
<b>PERICARDIAL EFFUSION</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>TACHYCARDIA</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>Palpitations</b>			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
<b>Nervous system disorders</b>			
<b>AGEUSIA</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>APHASIA</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>DYSGEUSIA</b>			
subjects affected / exposed	6 / 9 (66.67%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	6	0	0
<b>HEADACHE</b>			
subjects affected / exposed	2 / 9 (22.22%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	2	1	0
<b>HYPOAESTHESIA</b>			

subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
<b>HYPOKINESIA</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>LETHARGY</b>			
subjects affected / exposed	2 / 9 (22.22%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
<b>MYOCLONUS</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>NEURALGIA</b>			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
<b>NEUROPATHY PERIPHERAL</b>			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
<b>PARAESTHESIA</b>			
subjects affected / exposed	1 / 9 (11.11%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
<b>PERIPHERAL SENSORY NEUROPATHY</b>			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
<b>SCIATICA</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>TREMOR</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>Burning sensation</b>			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
<b>Dizziness</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
<b>Blood and lymphatic system disorders</b>			

ANAEMIA			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
LYMPHADENOPATHY			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
NEUTROPENIA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
VERTIGO			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
CHORIORETINOPATHY			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
DETACHMENT OF RETINAL PIGMENT EPITHELIUM			
subjects affected / exposed	3 / 9 (33.33%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	3	0	0
DRY EYE			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
EYE DISCHARGE			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
EYE DISORDER			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
EYE IRRITATION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
EYE PAIN			
subjects affected / exposed	1 / 9 (11.11%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
EYELID PAIN			

subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>GROWTH OF EYELASHES</b>			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
<b>KERATITIS</b>			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
<b>LACRIMATION INCREASED</b>			
subjects affected / exposed	1 / 9 (11.11%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
<b>MACULOPATHY</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>OCULAR DISCOMFORT</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>SUBRETINAL FLUID</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>ULCERATIVE KERATITIS</b>			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
<b>VISION BLURRED</b>			
subjects affected / exposed	1 / 9 (11.11%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
<b>VISUAL IMPAIRMENT</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>VITREOUS FLOATERS</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>Cataract</b>			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
<b>Corneal epithelium defect</b>			

subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Ocular hyperaemia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Photophobia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
<b>Gastrointestinal disorders</b>			
<b>ABDOMINAL DISTENSION</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>ABDOMINAL MASS</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>ABDOMINAL PAIN</b>			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
<b>ABDOMINAL PAIN UPPER</b>			
subjects affected / exposed	2 / 9 (22.22%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	2	1	0
<b>ABDOMINAL TENDERNESS</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>APHTHOUS STOMATITIS</b>			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
<b>ASCITES</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>CONSTIPATION</b>			
subjects affected / exposed	3 / 9 (33.33%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	3	1	0
<b>DIARRHOEA</b>			
subjects affected / exposed	3 / 9 (33.33%)	2 / 5 (40.00%)	0 / 4 (0.00%)
occurrences (all)	3	2	0

DRY MOUTH			
subjects affected / exposed	5 / 9 (55.56%)	4 / 5 (80.00%)	0 / 4 (0.00%)
occurrences (all)	5	4	0
DYSPEPSIA			
subjects affected / exposed	1 / 9 (11.11%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
DYSPHAGIA			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
FAECAL INCONTINENCE			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
GASTRITIS			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
GASTROESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
GLOSSODYNIA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
LIP DRY			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
MELAENA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
MOUTH ULCERATION			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
NAUSEA			
subjects affected / exposed	5 / 9 (55.56%)	2 / 5 (40.00%)	1 / 4 (25.00%)
occurrences (all)	5	2	1
OESOPHAGEAL SPASM			

subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>ORAL PAIN</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>PARAESTHESIA ORAL</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>STOMATITIS</b>			
subjects affected / exposed	3 / 9 (33.33%)	2 / 5 (40.00%)	0 / 4 (0.00%)
occurrences (all)	3	2	0
<b>TONGUE DISCOLOURATION</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>VOMITING</b>			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
<b>Hepatobiliary disorders</b>			
<b>CHOLELITHIASIS</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>Skin and subcutaneous tissue disorders</b>			
<b>ALOPECIA</b>			
subjects affected / exposed	5 / 9 (55.56%)	2 / 5 (40.00%)	0 / 4 (0.00%)
occurrences (all)	5	2	0
<b>BLISTER</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>DRY SKIN</b>			
subjects affected / exposed	3 / 9 (33.33%)	2 / 5 (40.00%)	0 / 4 (0.00%)
occurrences (all)	3	2	0
<b>ERYTHEMA</b>			
subjects affected / exposed	1 / 9 (11.11%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
<b>MADAROSIS</b>			

subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
<b>NAIL BED BLEEDING</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>NAIL DISCOLOURATION</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>NAIL DISORDER</b>			
subjects affected / exposed	4 / 9 (44.44%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	4	1	0
<b>NAIL DYSTROPHY</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>NIGHT SWEATS</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>ONYCHALGIA</b>			
subjects affected / exposed	2 / 9 (22.22%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
<b>ONYCHOLYSIS</b>			
subjects affected / exposed	1 / 9 (11.11%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
<b>PAIN OF SKIN</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>PALMAR-PLANTAR ERYTHRODYSAESTHESIA SYNDROME</b>			
subjects affected / exposed	3 / 9 (33.33%)	2 / 5 (40.00%)	0 / 4 (0.00%)
occurrences (all)	3	2	0
<b>PAPULE</b>			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
<b>RASH</b>			
subjects affected / exposed	2 / 9 (22.22%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0

RASH ERYTHEMATOUS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
RASH MACULAR			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
RASH PRURITIC			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
SKIN DISCOLOURATION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
SKIN FISSURES			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
SKIN HAEMORRHAGE			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
SKIN ULCER			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
SWELLING FACE			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
HYDRONEPHROSIS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
NEPHROLITHIASIS			

subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>PROTEINURIA</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>URINARY RETENTION</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>URINARY TRACT OBSTRUCTION</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>Musculoskeletal and connective tissue disorders</b>			
<b>ARTHRALGIA</b>			
subjects affected / exposed	1 / 9 (11.11%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
<b>ARTHRITIS</b>			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
<b>JOINT EFFUSION</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>JOINT SWELLING</b>			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
<b>MUSCLE SPASMS</b>			
subjects affected / exposed	1 / 9 (11.11%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
<b>MUSCULOSKELETAL CHEST PAIN</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>MUSCULOSKELETAL PAIN</b>			
subjects affected / exposed	1 / 9 (11.11%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
<b>MYALGIA</b>			

subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
<b>NECK PAIN</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>PAIN IN EXTREMITY</b>			
subjects affected / exposed	2 / 9 (22.22%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	2	1	0
<b>PAIN IN JAW</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>Back pain</b>			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
<b>Bursitis</b>			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
<b>Joint stiffness</b>			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
<b>Psoriatic arthropathy</b>			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
<b>Infections and infestations</b>			
<b>CELLULITIS</b>			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
<b>CONJUNCTIVITIS</b>			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
<b>CYSTITIS</b>			
subjects affected / exposed	1 / 9 (11.11%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
<b>GINGIVITIS</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

<b>INFLUENZA</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>LARYNGITIS</b>			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
<b>LOCALISED INFECTION</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>LOWER RESPIRATORY TRACT INFECTION</b>			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
<b>LOWER RESPIRATORY TRACT INFECTION VIRAL</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>LYMPHANGITIS</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>MASTITIS</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>NAIL INFECTION</b>			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
<b>OESOPHAGEAL CANDIDIASIS</b>			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
<b>ORAL CANDIDIASIS</b>			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
<b>PARONYCHIA</b>			
subjects affected / exposed	1 / 9 (11.11%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
<b>PHARYNGITIS</b>			

subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
<b>SINUSITIS</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>URINARY TRACT INFECTION</b>			
subjects affected / exposed	1 / 9 (11.11%)	2 / 5 (40.00%)	0 / 4 (0.00%)
occurrences (all)	1	2	0
<b>URINARY TRACT INFECTION BACTERIAL</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>URINARY TRACT INFECTION FUNGAL</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>VARICELLA</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>VIRAL UPPER RESPIRATORY TRACT INFECTION</b>			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
<b>VULVOVAGINAL CANDIDIASIS</b>			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
<b>Herpes zoster</b>			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
<b>Nasopharyngitis</b>			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
<b>Oropharyngeal candidiasis</b>			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
<b>Post viral fatigue syndrome</b>			

subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	1 / 5 (20.00%) 1	0 / 4 (0.00%) 0
Rash pustular subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	1 / 5 (20.00%) 1	0 / 4 (0.00%) 0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed occurrences (all)	4 / 9 (44.44%) 4	1 / 5 (20.00%) 1	0 / 4 (0.00%) 0
DEHYDRATION			
subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	0 / 5 (0.00%) 0	0 / 4 (0.00%) 0
HYPERCALCAEMIA			
subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	0 / 5 (0.00%) 0	1 / 4 (25.00%) 1
HYPERGLYCAEMIA			
subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	0 / 5 (0.00%) 0	0 / 4 (0.00%) 0
HYPERPHOSPHATAEMIA			
subjects affected / exposed occurrences (all)	3 / 9 (33.33%) 3	0 / 5 (0.00%) 0	0 / 4 (0.00%) 0
HYPONATRAEMIA			
subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1	0 / 5 (0.00%) 0	0 / 4 (0.00%) 0

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 December 2010	Exclusion criterion 1 was modified to reflect the timing of radiotherapy for palliation with respect to first dose of AZD4547/placebo. Exclusion criterion relating to total bilirubin amended to >1.5 times ULN as a marker for inadequate bone marrow reserve or organ function. Additional restriction added: Patients to avoid excessive sun exposure and use adequate screening protection. The use of sunbeds and tanning booths should be avoided. The precaution relating to exposure to sunlight added following non-clinical studies which indicated potential for phototoxicity. Additional option added to the decisions available to the Safety Review Committee to allow recommendation for an intermittent dosing schedule for the toxicity management algorithm. Section 5.1.6 of the Clinical Study Protocol "Dose modifications" amended to include a table of dose interventions, which also resulted in amendments to the associated flowchart figure. An additional optional tumour biopsy sample during Screening was added (Table 2.). Text relating to the time period for recording of AEs was updated. "SAEs will be collected after stage 1 informed consent (see section 6.3), only for patients who provide fresh tumour tissue sample for determination of FGFR1 FISH score. AEs will not be collected for patients who provide stage 1 consent, who provide an archival tumour tissue sample only, prior to signing of stage 2 consent. AEs will be collected throughout the study, from Stage 2 informed consent....." (Section 5.7.1.12). Amendment to the efficacy assessments text relating to the timing of baseline assessments, which were now to be no more than 28 before docing with AZD4547. Changes to the statistical model to be used to analyse PFS and changes in tumour size in FGFR1 amplified patients, and information on the non parametric sensitivity analysis for the change in tumour size added. Additional minor protocol clarifications were made.
06 May 2011	Addition of the option to test an intermittent dosing schedule. Cohorts were added to test a different dose and/or schedule of AZD4547. (Sections 4.1, 5.1, 5.2.3, 5.4.2.1 and Figure 1.). As a result of the addition of the intermittent dosing schedule(s) the planned number of patients to be included in the safety run in phase (Part A) was increased overall from 12 to 28 patients. In addition, the required number of evaluable patients in an intermittent dosing cohort was stated to be 9 rather than 3 to 6 as required for cohorts testing a continuous dosing schedule. The assessment period for the intermittent dosing schedule was stipulated as 28-days rather than 21 days as protocolled for the continuous dosing cohorts. (Sections 5.1.1, 5.2.3 and 5.7.3.). Throughout the wording "dose escalation was removed. The wording 'optimum dose' was amended to 'recommended dose'. In addition, the wording was further amended to "recommended dose and schedule". (Section 5.1.). Amendment of the exemestane run-in period (7 days to ≥7 days) (Sections 5.1 and 5.4.2.1 and Figure 1.). Wording changed to allow collection of serial biopsies. Requirement to avoid exposure to sunlight removed.
14 June 2011	Patients with increased risk for Retinal Pigment Epithelium Detachment (RPED) excluded. Inclusion of a phosphate management algorithm. Revised management of ophthalmological toxicity. Change in the frequency of ophthalmological monitoring and details around ophthalmological examinations were revised.
08 August 2011	Revisions to the exclusion of patients with increased risk of developing or re occurrence of RPED or with conditions that could confound the ophthalmological assessment. Increased frequency of mandatory ophthalmologic examinations.

20 December 2012	The combination agent for Part B of the study was changed from exemestane to fulvestrant and changes made throughout consistent with this. The protocol was updated to reflect the risks and precautions associated with the use of fulvestrant. Progression-Free Survival (PFS) promoted from a secondary to primary objective for part B. Tumour size analysis demoted from a primary to a secondary objective in Part B. Samples for determination of lipid profile would only be collected in Part A as lipid profiling was only relevant for patients taking exemestane. Duration of response added as a secondary objective and the statistical sections were updated to reflect this. Information was collected on quality of life and health utility. Secondary objective regarding the percentage of patients with progressive disease at 12 weeks amended and Overall Survival added as an exploratory objective for Part B. Exploratory objective relating to the association between FGFR1 FISH score, FGFR1 removed from parts A and B, and a modified objective included in part B. Exploratory endpoint of assessing changes in tumour burden was removed. FGFR1 gene amplification and FISH scoring criteria revised and indicated as subject to change. The Extension Phase cross over to AZD4547 was removed. The inclusion/exclusion criteria were updated to bring them in line with indications for treatment with fulvestrant. Updated description of tablet strengths from 20 mg to 100 mg. Planned dose reductions updated. Details included about blinding and unblinding individual patients. Eye toxicity management information updated. Sample size and details in Section 7 regarding the timing of the PFS and change in tumour size analyses revised. Section 7 updated to reflect changes made to efficacy endpoints and to specify an Intention To Treat population. Appendix G updated.
10 June 2014	This amendment described the decision to terminate the study early. Recruitment into the study was much slower than predicted, leading to concerns about the feasibility of completing enrolment in a realistic timeframe. This resulted in a business decision to terminate enrolment to the study.

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Part B enrolment was terminated on 27Mar14. Slow recruitment led to concerns that enrolment would not be completed in a realistic timeframe and a business decision to terminate enrolment. No statistical analysis was planned for the primary endpoint.

Notes: