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

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
Scientific contact	Richard Mather, AstraZeneca, 44 01763263593, ClinicalTrialTransparency@astrazeneca.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	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:

General information about the trial

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).

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.

Background therapy: -

Evidence for comparator: -

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:

Population of trial subjects

Subjects enrolled per country

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

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

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)	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
Arm title	AZD4547 80mg bd cont + Exemestane 25mg

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

Arm title	AZD4547 40mg cont + Exemestane 25mg

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

Arm title	AZD4547 80mg bd 1w/1w + Exemestane 25mg

Arm description:

80 mg AZD4547 bd one 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 1w/1w intermittant

Arm title	AZD4547 80mg bd 2w/1w + Exemestane

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

Arm title	Part B: AZD4547 + Fulvestrant

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

Arm title	Part B: Placebo + Fulvestrant

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

Number of subjects in period 1	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

Number of subjects in period 1	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

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	

Reporting group values	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

Reporting group values	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

Reporting group values	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)[1]
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

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

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	AZD4547 80mg bd cont + Ex 25mg
Reporting group description:	
80 mg AZD4547 bd continuous + 25 mg exemestane	
Reporting group title	AZD4547 40mg bd cont + Ex 25mg
Reporting group description:	
40 mg AZD4547 BD continuous + 25 mg exemestane	
Reporting group title	AZD4547 80mg bd 1w/1w + Ex 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 + Ex 25mg
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:	
80 mg Placebo BD + 500 mg Fulvestrant	

Serious adverse events	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
Nervous system disorders			
DIZZINESS			
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
VIITH NERVE PARALYSIS			
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
Blood and lymphatic system disorders			
ANAEMIA			
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
General disorders and administration site conditions			
DEVICE DEPOSIT ISSUE			
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
INFLAMMATION			
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
GAIT DISTURBANCE			
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
Gastrointestinal disorders			
DIARRHOEA			

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
OESOPHAGEAL ACHALASIA			
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
STOMATITIS			
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
Respiratory, thoracic and mediastinal disorders			
ASTHMA			
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
DYSPNOEA			
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
PLEURAL EFFUSION			
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
Renal and urinary disorders			
RENAL FAILURE			
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
Musculoskeletal and connective tissue disorders			
ACUTE CRISIS OF PSORIASIC OLIGOARTHRITIS			

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
Infections and infestations			
LOWER RESPIRATORY TRACT INFECTION VIRAL			
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
NEUTROPENIC SEPSIS			
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
PLEURAL INFECTION			
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
PYELONEPHRITIS			
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

Serious adverse events	AZD4547 80mg bd 2w/1w + Ex 25mg	Part B: AZD4547 + Fulvestrant	Part B: Placebo + Fulvestrant
Total subjects affected by serious adverse events			
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
Investigations			
TROPONIN INCREASED			
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
Vascular disorders			
JUGULAR VEIN THROMBOSIS			

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
Nervous system disorders			
DIZZINESS			
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
VIITH NERVE PARALYSIS			
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
Blood and lymphatic system disorders			
ANAEMIA			
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
General disorders and administration site conditions			
DEVICE DEPOSIT ISSUE			
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
INFLAMMATION			
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
GAIT DISTURBANCE			
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
Gastrointestinal disorders			
DIARRHOEA			

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
OESOPHAGEAL ACHALASIA			
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
STOMATITIS			
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
Respiratory, thoracic and mediastinal disorders			
ASTHMA			
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
DYSPNOEA			
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
PLEURAL EFFUSION			
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
Renal and urinary disorders			
RENAL FAILURE			
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
Musculoskeletal and connective tissue disorders			
ACUTE CRISIS OF PSORIASIC OLIGOARTHRITIS			

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
Infections and infestations			
LOWER RESPIRATORY TRACT INFECTION VIRAL			
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
NEUTROPENIC SEPSIS			
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
PLEURAL INFECTION			
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
PYELONEPHRITIS			
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 %

Non-serious adverse events	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%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BREAST CANCER METASTATIC			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
METASTATIC PAIN			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
NEURILEMMOMA BENIGN			

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
FIBROSIS			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
INJURY ASSOCIATED WITH DEVICE			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
LOCAL SWELLING			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
OEDEMA			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
OEDEMA PERIPHERAL			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
PYREXIA			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Gait disturbance			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Induration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Inflammation			
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	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Feeling hot			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
SEASONAL ALLERGY			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
BREAST DISORDER			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
BREAST PAIN			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
VULVOVAGINAL DRYNESS			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
ASTHMA			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
COUGH			
subjects affected / exposed	1 / 5 (20.00%)	1 / 5 (20.00%)	1 / 12 (8.33%)
occurrences (all)	1	1	1
DRY THROAT			
subjects affected / exposed	1 / 5 (20.00%)	1 / 5 (20.00%)	1 / 12 (8.33%)
occurrences (all)	1	1	1
DYSPHONIA			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1

DYSPNOEA			
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	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
DEPRESSED MOOD			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
DEPRESSION			
subjects affected / exposed	1 / 5 (20.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
DEREALISATION			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
INSOMNIA			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	2 / 12 (16.67%)
occurrences (all)	0	1	2
SLEEP DISORDER			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 5 (20.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
BLOOD CREATININE INCREASED			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
BLOOD GLUCOSE INCREASED			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	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	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
WEIGHT DECREASED			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Ejection fraction decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
ARTHROPOD BITE			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
CONTUSION			
subjects affected / exposed	1 / 5 (20.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
FALL			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
JOINT INJURY			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
LACERATION			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
TRAUMATIC HAEMATOMA			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Arthropod sting			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
PERICARDIAL EFFUSION			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	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			

EPITHELIUM			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	3 / 12 (25.00%)
occurrences (all)	0	0	3
DRY EYE			
subjects affected / exposed	2 / 5 (40.00%)	1 / 5 (20.00%)	1 / 12 (8.33%)
occurrences (all)	2	1	1
EYE DISCHARGE			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
EYE DISORDER			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
EYE IRRITATION			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
EYE PAIN			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
EYELID PAIN			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
GROWTH OF EYELASHES			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
KERATITIS			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
LACRIMATION INCREASED			
subjects affected / exposed	1 / 5 (20.00%)	1 / 5 (20.00%)	1 / 12 (8.33%)
occurrences (all)	1	1	1
MACULOPATHY			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
OCULAR DISCOMFORT			
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
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
ABDOMINAL TENDERNESS			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
APHTHOUS STOMATITIS			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
ASCITES			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
CONSTIPATION			
subjects affected / exposed	1 / 5 (20.00%)	4 / 5 (80.00%)	4 / 12 (33.33%)
occurrences (all)	1	4	4
DIARRHOEA			
subjects affected / exposed	3 / 5 (60.00%)	2 / 5 (40.00%)	3 / 12 (25.00%)
occurrences (all)	3	2	3
DRY MOUTH			
subjects affected / exposed	4 / 5 (80.00%)	3 / 5 (60.00%)	7 / 12 (58.33%)
occurrences (all)	4	3	7
DYSPEPSIA			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
DYSPHAGIA			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
FAECAL INCONTINENCE			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
GASTRITIS			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
GASTROOESOPHAGEAL REFLUX			

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

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

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

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

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

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

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

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

subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	1
PLEURAL EFFUSION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
PLEURITIC PAIN			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
PRODUCTIVE COUGH			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
RALES			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
RHINALGIA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
RHINORRHOEA			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
DEPRESSED MOOD			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
DEPRESSION			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
DEREALISATION			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
INSOMNIA			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
SLEEP DISORDER			
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
LACERATION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
TRAUMATIC HAEMATOMA			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Arthropod sting			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
PERICARDIAL EFFUSION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
TACHYCARDIA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
AGEUSIA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
APHASIA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
DYSGEUSIA			
subjects affected / exposed	6 / 9 (66.67%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	6	0	0
HEADACHE			
subjects affected / exposed	2 / 9 (22.22%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	2	1	0
HYPOAESTHESIA			

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

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

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
Gastrointestinal disorders			
ABDOMINAL DISTENSION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
ABDOMINAL MASS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
ABDOMINAL PAIN			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
ABDOMINAL PAIN UPPER			
subjects affected / exposed	2 / 9 (22.22%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	2	1	0
ABDOMINAL TENDERNESS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
APHTHOUS STOMATITIS			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
ASCITES			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
CONSTIPATION			
subjects affected / exposed	3 / 9 (33.33%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	3	1	0
DIARRHOEA			
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
GASTROOESOPHAGEAL 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
ORAL PAIN			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
PARAESTHESIA ORAL			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
STOMATITIS			
subjects affected / exposed	3 / 9 (33.33%)	2 / 5 (40.00%)	0 / 4 (0.00%)
occurrences (all)	3	2	0
TONGUE DISCOLOURATION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
VOMITING			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Hepatobiliary disorders			
CHOLELITHIASIS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
ALOPECIA			
subjects affected / exposed	5 / 9 (55.56%)	2 / 5 (40.00%)	0 / 4 (0.00%)
occurrences (all)	5	2	0
BLISTER			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
DRY SKIN			
subjects affected / exposed	3 / 9 (33.33%)	2 / 5 (40.00%)	0 / 4 (0.00%)
occurrences (all)	3	2	0
ERYTHEMA			
subjects affected / exposed	1 / 9 (11.11%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
MADAROSIS			

subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
NAIL BED BLEEDING			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
NAIL DISCOLOURATION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
NAIL DISORDER			
subjects affected / exposed	4 / 9 (44.44%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	4	1	0
NAIL DYSTROPHY			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
NIGHT SWEATS			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
ONYCHALGIA			
subjects affected / exposed	2 / 9 (22.22%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
ONYCHOLYSIS			
subjects affected / exposed	1 / 9 (11.11%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
PAIN OF SKIN			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
PALMAR-PLANTAR ERYTHRODYSAESTHESIA SYNDROME			
subjects affected / exposed	3 / 9 (33.33%)	2 / 5 (40.00%)	0 / 4 (0.00%)
occurrences (all)	3	2	0
PAPULE			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
RASH			
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
PROTEINURIA			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
URINARY RETENTION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
URINARY TRACT OBSTRUCTION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	1 / 9 (11.11%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
ARTHRITIS			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
JOINT EFFUSION			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
JOINT SWELLING			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
MUSCLE SPASMS			
subjects affected / exposed	1 / 9 (11.11%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
MUSCULOSKELETAL PAIN			
subjects affected / exposed	1 / 9 (11.11%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
MYALGIA			

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

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

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

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