Clinical trial results:
A Phase I, Open-Label, Multi-Centre Study to Assess the Safety, Tolerability, Pharmacokinetics, and Preliminary Efficacy of the JAK2 Inhibitor, AZD1480, Administered Orally to Patients with Primary Myelofibrosis (PMF) and Post-Polycythaemia Vera/Essential Thrombocythaemia Myelofibrosis (Post-PV/ET MF)

Summary

EudraCT number	2007-006647-45
Trial protocol	FR
Global end of trial date	25 August 2014

Results information

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

Trial information

Trial identification

Sponsor protocol code	D1060C00001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	Room C2B-424 A, 1800 Concord Pike, Wilmington, United States, DE 19850-5437
Public contact	Srdan Verstovsek, MD PhD, University of Texas MD Anderson Cancer Center, 001 +1 713-792-2121,
Scientific contact	Dr Gregory Curt, MD, AstraZeneca, Gregory.Curt@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	06 February 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 April 2012
Global end of trial reached?	Yes
Global end of trial date	25 August 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Primary objectives of the trial are as follows:
To assess the safety and tolerability of AZD1480 in patients with PMF and post-PV/ET MF.
To determine the PK of AZD1480 following both single and multiple oral dosing of AZD1480 (QD dosing and/or BID dosing).
To evaluate the extent of inhibition of phosphorylation of STAT3 following treatment with AZD1480.

Secondary objectives are:
To explore the role of JAK2 V617F mutation load in patient response.
To provide information on preliminary signs of efficacy.

Part A of the study had the main aim of determining the maximum tolerated dose (MTD) of AZD1480 with Part B designed to further assess the safety profile and preliminary signs of efficacy information on AZD1480.

Protection of trial subjects:

Data protection for patients - The Master Informed Consent Form explained that study data will be stored in a computer database, maintaining confidentiality in accordance with national data legislation. All data computer processed by AstraZeneca will be identified by e - code/study number/initials.
A study Safery Review Committee met during Part A following each dose step (i.e., following the first cycle of treatment for each dose level).
Before the first patient is enrolled into the study, a representative of AstraZeneca visited the investigational study site (as determined necessary by AstraZeneca) and had regular contacts with the study site, including visits.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 May 2009
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	1 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 16
Country: Number of subjects enrolled	United States: 19
Worldwide total number of subjects	35
EEA total number of subjects	16

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)	15
From 65 to 84 years	20
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

65 enrolled. 35 dosed with AZD1480. 33 discontinued.

At DCO 2 patients ongoing. 1 patient in the 50 mg QD group and 1 patient in the 15 mg BID group with status (at July 2015):
Patient in 15 mg BID group: Stable disease, no SAE.
Patient in 50 mg QD group: Stable disease, no SAE, dose currently reduced to 40 mg QD.

Pre-assignment

Screening details:

There is a 28 day screening period prior to Cycle 1 Day 1.

Pre-assignment period milestones

Number of subjects started	35
Number of subjects completed	35

Period 1

Period 1 title	Baseline (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Not applicable since this is an open-label trial

Arms

Are arms mutually exclusive?	Yes
Arm title	2.5 mg QD AZD1480

Arm description: -

Arm type	Experimental
Investigational medicinal product name	AZD1480
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

2.5 mg QD

Arm title	5.0 mg QD AZD1480

Arm description: -

Arm type	Experimental
Investigational medicinal product name	AZD1480
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

5.0 mg QD

Arm title	10 mg QD AZD1480

Arm description: -	
Arm type	Experimental
Investigational medicinal product name	AZD1480
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 10 mg QD	
Arm title	20 mg QD AZD1480
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	AZD1480
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 20 mg QD	
Arm title	30 mg QD AZD1480
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	AZD1480
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: AZD1480	
Arm title	50 mg QD AZD1480
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	AZD1480
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 50 mg QD	
Arm title	70 mg QD AZD1480
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	AZD1480
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 70 mg QD	
Arm title	10 mg BID AZD1480

Arm description: -	
Arm type	Experimental
Investigational medicinal product name	AZD1480
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:
10 mg BID

Arm title	15 mg BID AZD1480
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	AZD1480
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:
15 mg BID

Number of subjects in period 1	2.5 mg QD AZD1480	5.0 mg QD AZD1480	10 mg QD AZD1480
Started	6	3	3
Completed	0	0	0
Not completed	6	3	3
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	4	3	2
As per eCRF	2	-	1

Number of subjects in period 1	20 mg QD AZD1480	30 mg QD AZD1480	50 mg QD AZD1480
Started	3	3	6
Completed	0	0	1
Not completed	3	3	5
Consent withdrawn by subject	-	-	3
Adverse event, non-fatal	3	3	1
As per eCRF	-	-	1

Number of subjects in period 1	70 mg QD AZD1480	10 mg BID AZD1480	15 mg BID AZD1480
Started	1	6	4
Completed	0	0	1
Not completed	1	6	3
Consent withdrawn by subject	1	2	-
Adverse event, non-fatal	-	4	3
As per eCRF	-	-	-

Baseline characteristics

Reporting groups	
Reporting group title	2.5 mg QD AZD1480
Reporting group description: -	
Reporting group title	5.0 mg QD AZD1480
Reporting group description: -	
Reporting group title	10 mg QD AZD1480
Reporting group description: -	
Reporting group title	20 mg QD AZD1480
Reporting group description: -	
Reporting group title	30 mg QD AZD1480
Reporting group description: -	
Reporting group title	50 mg QD AZD1480
Reporting group description: -	
Reporting group title	70 mg QD AZD1480
Reporting group description: -	
Reporting group title	10 mg BID AZD1480
Reporting group description: -	
Reporting group title	15 mg BID AZD1480
Reporting group description: -	

Reporting group values	2.5 mg QD AZD1480	5.0 mg QD AZD1480	10 mg QD AZD1480
Number of subjects	6	3	3
Age Categorical			
Age group (years) of subjects eligible are 25+ and have been classified in the demography table according to the following standard classes:>=18-<65>=65 - <74>=75			
Units: Subjects			
Adults (>=18 - <65 years)	5	1	0
From >=65 - < 74	1	1	1
>= 75	0	1	2
Age Continuous			
Units: years			
arithmetic mean	57.5	66.3	76.7
standard deviation	± 7.7	± 9.6	± 10.5
Gender Categorical			
Units: Subjects			
Female	1	1	1
Male	5	2	2

Reporting group values	20 mg QD AZD1480	30 mg QD AZD1480	50 mg QD AZD1480
Number of subjects	3	3	6
Age Categorical			
Age group (years) of subjects eligible are 25+ and have been classified in the demography table according to the following standard classes:>=18-<65>=65 - <74>=75			
Units: Subjects			
Adults (>=18 - <65 years)	0	3	1
From >=65 - < 74	2	0	5
>= 75	1	0	0

Age Continuous			
Units: years			
arithmetic mean	75.7	49.3	69.3
standard deviation	± 3.8	± 4.2	± 3.8
Gender Categorical			
Units: Subjects			
Female	2	1	5
Male	1	2	1

Reporting group values	70 mg QD AZD1480	10 mg BID AZD1480	15 mg BID AZD1480
Number of subjects	1	6	4
Age Categorical			
Age group (years) of subjects eligible are 25+ and have been classified in the demography table according to the following standard classes:>=18-<65>=65 - <74>=75			
Units: Subjects			
Adults (>=18 - <65 years)	1	2	2
From >=65 - < 74	0	2	1
>= 75	0	2	1
Age Continuous			
Units: years			
arithmetic mean	56	65.3	66.5
standard deviation	± 0	± 11.3	± 10.3
Gender Categorical			
Units: Subjects			
Female	1	2	0
Male	0	4	4

Reporting group values	Total		
Number of subjects	35		
Age Categorical			
Age group (years) of subjects eligible are 25+ and have been classified in the demography table according to the following standard classes:>=18-<65>=65 - <74>=75			
Units: Subjects			
Adults (>=18 - <65 years)	15		
From >=65 - < 74	13		
>= 75	7		
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender Categorical			
Units: Subjects			
Female	14		
Male	21		

Subject analysis sets	
Subject analysis set title	Full Analysis Set
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All patients who recieved treatment.	
Subject analysis set title	PK Analysis set

Subject analysis set type	Sub-group analysis

Subject analysis set description:

All patients who receive at least 1 dose of AZD1480 per the protocol, for whom any post-dose data are available and do not violate or deviate from the protocol in ways that would significantly affect the PK analyses will be included in the PK analysis set. The population will be defined by the Study Team Physician, Pharmacokineticist and Statistician prior to any analyses being performed.

Subject analysis set title	Evaluable for Clinical Improvement (CI) set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

A subset of the FAS. These patients are evaluable, defined as either:
a) reached day 28 visit and received at least 18 of the planned 26 doses in Cycle 1 and has sufficient safety evaluations as judged by SRC performed during Cycle 1, or
b) experienced DLT

Subject analysis set title	Safety Analysis Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects who recieved at least one dose of AZD1480, according to the treatment recieved.

Reporting group values	Full Analysis Set	PK Analysis set	Evaluable for Clinical Improvement (CI) set
Number of subjects	35	35	33
Age Categorical			
Age group (years) of subjects eligible are 25+ and have been classified in the demography table according to the following standard classes:>=18-<65>=65 - <74>=75			
Units: Subjects			
Adults (>=18 - <65 years)	15	15	15
From >=65 - < 74	13	13	13
>= 75	7	7	7
Age Continuous			
Units: years			
arithmetic mean	65.1	65.1	65.5
standard deviation	± 10.6	± 10.6	± 10.8
Gender Categorical			
Units: Subjects			
Female	14	14	13
Male	21	21	20

Reporting group values	Safety Analysis Set		
Number of subjects	35		
Age Categorical			
Age group (years) of subjects eligible are 25+ and have been classified in the demography table according to the following standard classes:>=18-<65>=65 - <74>=75			
Units: Subjects			
Adults (>=18 - <65 years)	15		
From >=65 - < 74	13		
>= 75	7		
Age Continuous			
Units: years			
arithmetic mean	65.1		
standard deviation	± 10.6		
Gender Categorical			
Units: Subjects			
Female	14		
Male	21		

End points

End points reporting groups

Reporting group title	2.5 mg QD AZD1480
Reporting group description: -	
Reporting group title	5.0 mg QD AZD1480
Reporting group description: -	
Reporting group title	10 mg QD AZD1480
Reporting group description: -	
Reporting group title	20 mg QD AZD1480
Reporting group description: -	
Reporting group title	30 mg QD AZD1480
Reporting group description: -	
Reporting group title	50 mg QD AZD1480
Reporting group description: -	
Reporting group title	70 mg QD AZD1480
Reporting group description: -	
Reporting group title	10 mg BID AZD1480
Reporting group description: -	
Reporting group title	15 mg BID AZD1480
Reporting group description: -	
Subject analysis set title	Full Analysis Set
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All patients who recieved treatment.	
Subject analysis set title	PK Analysis set
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All patients who receive at least 1 dose of AZD1480 per the protocol, for whom any post-dose data are available and do not violate or deviate from the protocol in ways that would significantly affect the PK analyses will be included in the PK analysis set. The population will be defined by the Study Team Physician, Pharmacokineticist and Statistician prior to any analyses being performed.	
Subject analysis set title	Evaluable for Clinical Improvement (CI) set
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
A subset of the FAS. These patients are evaluable, defined as either: a) reached day 28 visit and received at least 18 of the planned 26 doses in Cycle 1 and has sufficient safety evaluations as judged by SRC performed during Cycle 1, or b) experienced DLT	
Subject analysis set title	Safety Analysis Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects who recieved at least one dose of AZD1480, according to the treatment recieved.	

Primary: Pharamcokinetic parameters following single dosing

End point title	Pharamcokinetic parameters following single dosing[1]
End point description:	
Single dose: AUC(0-inf),AUC(0-24)	
End point type	Primary
End point timeframe:	
0 to 24 hour sampling (Day 1: 0, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 24 hrs post dose)	

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: There are 12 warnings which are due to no statstical analysis being posted. There are no statistical analysis to post for this study

End point values	2.5 mg QD AZD1480	5.0 mg QD AZD1480	10 mg QD AZD1480	20 mg QD AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	3	3	3
Units: ug.h/L				
geometric mean (standard deviation)				
AUC (ug.h/L)	83.5 (± 36.6)	312 (± 79.5)	378 (± 290)	517 (± 294)
AUC0-24 (ug.h/L)	70.2 (± 28.7)	308 (± 76)	285 (± 252)	508 (± 280)

End point values	30 mg QD AZD1480	50 mg QD AZD1480	70 mg QD AZD1480	10 mg BID AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	1	0[2]
Units: ug.h/L				
geometric mean (standard deviation)				
AUC (ug.h/L)	2040 (± 657)	3650 (± 2980)	6300 (± 0)	()
AUC0-24 (ug.h/L)	2000 (± 624)	3540 (± 2570)	6260 (± 0)	()

Notes:

[2] - NA

End point values	15 mg BID AZD1480			
Subject group type	Reporting group			
Number of subjects analysed	0[3]			
Units: ug.h/L				
geometric mean (standard deviation)				
AUC (ug.h/L)	()			
AUC0-24 (ug.h/L)	()			

Notes:

[3] - NA

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetic parameters following single dosing (2)

End point title	Pharmacokinetic parameters following single dosing (2)[4]
End point description:	
Single dose Tmax	
End point type	Primary
End point timeframe:	
0 to 24 hour sampling (Day 1: 0, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 24 hrs post dose)	

Notes:

[4] - 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: There are 12 warnings which are due to no statstical analysis being posted. There are no statistical analysis to post for this study

End point values	2.5 mg QD AZD1480	5.0 mg QD AZD1480	10 mg QD AZD1480	20 mg QD AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	3	3	3
Units: hr				
median (full range (min-max))				
tmax(h)	0.625 (0.5 to 1.5)	0.75 (0.5 to 2)	0.75 (0.5 to 0.75)	0.75 (0.5 to 1.03)

End point values	30 mg QD AZD1480	50 mg QD AZD1480	70 mg QD AZD1480	10 mg BID AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	1	6
Units: hr				
median (full range (min-max))				
tmax(h)	1 (1 to 1.5)	0.89 (0.75 to 1.5)	0.75 (0.75 to 0.75)	0.625 (0.5 to 1)

End point values	15 mg BID AZD1480			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: hr				
median (full range (min-max))				
tmax(h)	0.875 (0.5 to 1)			

Statistical analyses

No statistical analyses for this end point

Primary: PK parameters following multiple dosing (3)

End point title	PK parameters following multiple dosing (3)[5]

End point description:

Multiple dose Cmax,ss and Cmin,ss

End point type	Primary

End point timeframe:

On Days 1 and 28 at 0, 1, 2, 3, 6, 8, 12 and 24 hrs post dose and 0, 2, 4 hrs post-dose on Days 4 and 10.

Notes:

[5] - 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: There are 12 warnings which are due to no statstical analysis being posted. There are no statistical analysis to post for this study

End point values	2.5 mg QD AZD1480	5.0 mg QD AZD1480	10 mg QD AZD1480	20 mg QD AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	3	3	3
Units: ug/L				
geometric mean (standard deviation)				
Cmax,ss (ug/L)	51.3 (± 18)	134 (± 36.3)	176 (± 179)	241 (± 346)
Cmin,ss (ug/L)	0.177 (± 0.05)	1.47 (± 0.32)	1.2 (± 0.75)	7 (± 12.4)

End point values	30 mg QD AZD1480	50 mg QD AZD1480	70 mg QD AZD1480	10 mg BID AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	5	1	5
Units: ug/L				
geometric mean (standard deviation)				
Cmax,ss (ug/L)	658 (± 265)	924 (± 461)	1500 (± 0)	218 (± 72.3)
Cmin,ss (ug/L)	19.4 (± 6.56)	56.2 (± 280)	26.4 (± 0)	7.37 (± 4.77)

End point values	15 mg BID AZD1480			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: ug/L				
geometric mean (standard deviation)				
Cmax,ss (ug/L)	334 (± 68.2)			
Cmin,ss (ug/L)	7.69 (± 35.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetic parameters following multiple dose (4)

End point title	Pharmacokinetic parameters following multiple dose (4)[6]
End point description:	
Multiple Dose Tmax,ss	
End point type	Primary
End point timeframe:	
On days 1 and 28 at 0, 1, 2, 3, 4, 6, 8,, 12, 24 hrs post-dose, and at 0, 2, 4 hrs post-dose on days 4 and 10	

Notes:

[6] - 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: There are 12 warnings which are due to no statstical analysis being posted. There are no statistical analysis to post for this study

End point values	2.5 mg QD AZD1480	5.0 mg QD AZD1480	10 mg QD AZD1480	20 mg QD AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	3	3	3
Units: hr				
median (full range (min-max))				
tmax,ss (h)	0.5 (0.5 to 1)	0.78 (0.75 to 1)	0.77 (0.75 to 1)	1 (0.75 to 3)

End point values	30 mg QD AZD1480	50 mg QD AZD1480	70 mg QD AZD1480	10 mg BID AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	1	6
Units: hr				
median (full range (min-max))				
tmax,ss (h)	0.75 (0.52 to 1)	0.78 (0.25 to 2.25)	1.5 (1.5 to 1.5)	1 (0.5 to 1.5)

End point values	15 mg BID AZD1480			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: hr				
median (full range (min-max))				
tmax,ss (h)	0.875 (0.75 to 1.5)			

Statistical analyses

No statistical analyses for this end point

Primary: Inhibition of phosphorylation of STAT3 (count)

End point title	Inhibition of phosphorylation of STAT3 (count)[7]

End point description:

Number of patient with a 50% reduction in PSTAT3 levels

End point type	Primary

End point timeframe:

Visits 2 and 6 (2 and 4 hours post dose)

Notes:

[7] - 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: There are 12 warnings which are due to no statstical analysis being posted. There are no statistical analysis to post for this study

End point values	2.5 mg QD AZD1480	5.0 mg QD AZD1480	10 mg QD AZD1480	20 mg QD AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	3	3	3
Units: Percent of patients with a 50% reduction				
2 Hour Post dose (count)	0	0	0	0
4 Hour Post dose (count)	0	0	0	0

End point values	30 mg QD AZD1480	50 mg QD AZD1480	70 mg QD AZD1480	10 mg BID AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	1	6
Units: Percent of patients with a 50% reduction				
2 Hour Post dose (count)	1	3	0	0
4 Hour Post dose (count)	0	0	0	1

End point values	15 mg BID AZD1480			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Percent of patients with a 50% reduction				
2 Hour Post dose (count)	0			
4 Hour Post dose (count)	0			

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetic parameters following single dosing (1a)

End point title	Pharmacokinetic parameters following single dosing (1a)[8]
End point description:	
Single dose CL/F	
End point type	Primary
End point timeframe:	
0 to 24 hour sampling (Dat 1: 0, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 24hrs post dose)	

Notes:

[8] - 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: There are 12 warnings which are due to no statstical analysis being posted. There are no statistical analysis to post for this study

End point values	2.5 mg QD AZD1480	5.0 mg QD AZD1480	10 mg QD AZD1480	20 mg QD AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	3	3	3
Units: L/h				
geometric mean (standard deviation)				
CL/F (L/h)	35.2 (± 13.9)	16 (± 4.25)	34.8 (± 22.5)	38.7 (± 16.7)

End point values	30 mg QD AZD1480	50 mg QD AZD1480	70 mg QD AZD1480	10 mg BID AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	1	6
Units: L/h				
geometric mean (standard deviation)				
CL/F (L/h)	14.7 (± 5.52)	13.8 (± 8.5)	11.1 (± 0)	22.6 (± 9.05)

End point values	15 mg BID AZD1480			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: L/h				
geometric mean (standard deviation)				
CL/F (L/h)	29.7 (± 13)			

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetic parameters following single dosing (1b)

End point title	Pharmacokinetic parameters following single dosing (1b)[9]

End point description:

Single Dose Vz/F

End point type	Primary

End point timeframe:

0 to 24 hour sampling (Day 1: 0, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 24 hrs post dose)

Notes:

[9] - 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: There are 12 warnings which are due to no statstical analysis being posted. There are no statistical analysis to post for this study

End point values	2.5 mg QD AZD1480	5.0 mg QD AZD1480	10 mg QD AZD1480	20 mg QD AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	3	3	3
Units: Litres				
geometric mean (standard deviation)				
Vz/F (L)	222 (± 125)	108 (± 28.1)	138 (± 161)	284 (± 92.3)

End point values	30 mg QD AZD1480	50 mg QD AZD1480	70 mg QD AZD1480	10 mg BID AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	1	0[10]
Units: Litres				
geometric mean (standard deviation)				
Vz/F (L)	97 (± 15)	105 (± 82.2)	57.9 (± 0)	()

Notes:

[10] - NA

End point values	15 mg BID AZD1480			
Subject group type	Reporting group			
Number of subjects analysed	0[11]			
Units: Litres				
geometric mean (standard deviation)				
Vz/F (L)	()			

Notes:

[11] - NA

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetic parameters following single dose (1c)

End point title	Pharmacokinetic parameters following single dose (1c)[12]

End point description:

Single dose Cmax

End point type	Primary

End point timeframe:

0 to 24 hour sampling (Day 1: 0, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 24 hrs post-dose)

Notes:

[12] - 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: There are 12 warnings which are due to no statstical analysis being posted. There are no statistical analysis to post for this study

End point values	2.5 mg QD AZD1480	5.0 mg QD AZD1480	10 mg QD AZD1480	20 mg QD AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	3	3	3
Units: ug/L				
geometric mean (standard deviation)				
Cmax (ug/L)	69.9 (± 32.7)	133 (± 54.7)	157 (± 145)	268 (± 227)

End point values	30 mg QD AZD1480	50 mg QD AZD1480	70 mg QD AZD1480	10 mg BID AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	1	6
Units: ug/L				
geometric mean (standard deviation)				
Cmax (ug/L)	739 (± 307)	1320 (± 379)	2600 (± 0)	273 (± 62.2)

End point values	15 mg BID AZD1480			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: ug/L				
geometric mean (standard deviation)				
Cmax (ug/L)	324 (± 79.5)			

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetic parameters following multiple dose(3a)

End point title	Pharmacokinetic parameters following multiple dose(3a)[13]

End point description:

CLss/F following multiple dose

End point type	Primary

End point timeframe:

On Days 1 and 28 at 0, 1, 2, 3, 4, 6, 8, 12, 24 hrs post-dose and at 0, 2, 4 hours post dose on Days 4 and 10.

Notes:

[13] - 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: There are 12 warnings which are due to no statstical analysis being posted. There are no statistical analysis to post for this study

End point values	2.5 mg QD AZD1480	5.0 mg QD AZD1480	10 mg QD AZD1480	20 mg QD AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	3	3	3
Units: L/h				
geometric mean (standard deviation)				
CLss/F (L/h)	37.8 (± 6)	15.8 (± 4.4)	30.1 (± 21.7)	20.8 (± 21)

End point values	30 mg QD AZD1480	50 mg QD AZD1480	70 mg QD AZD1480	10 mg BID AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	1	6
Units: L/h				
geometric mean (standard deviation)				
CLss/F (L/h)	17 (± 5.26)	16 (± 8.94)	9.75 (± 0)	20 (± 6.91)

End point values	15 mg BID AZD1480			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: L/h				
geometric mean (standard deviation)				
CLss/F (L/h)	20.4 (± 13.8)			

Statistical analyses

No statistical analyses for this end point

Primary: Inhibition of PSTAT3 - number with >=50% reduction

End point title	Inhibition of PSTAT3 - number with >=50% reduction[14]

End point description:

50% reduction in PSTAT3

End point type	Primary

End point timeframe:

Visits 2 and 6 (2 and 4 hours post dose)

Notes:

[14] - 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: There are 12 warnings which are due to no statstical analysis being posted. There are no statistical analysis to post for this study

End point values	2.5 mg QD AZD1480	5.0 mg QD AZD1480	10 mg QD AZD1480	20 mg QD AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	3	3	3
Units: percent				
2 Hour Post Dose	0	0	0	0
4 Hour Pose Dose	0	0	0	0

End point values	30 mg QD AZD1480	50 mg QD AZD1480	70 mg QD AZD1480	10 mg BID AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	1	6
Units: percent				
2 Hour Post Dose	33	50	0	0
4 Hour Pose Dose	0	0	0	17

End point values	15 mg BID AZD1480			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: percent				
2 Hour Post Dose	0			
4 Hour Pose Dose	0			

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetic parameters following single dosing (1d)

End point title	Pharmacokinetic parameters following single dosing (1d)[15]

End point description:

Single Dose AUC0-12

End point type	Primary

End point timeframe:

0-12 hour sampling (Day 1:0, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12 hrs post dose)

Notes:

[15] - 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: There are 12 warnings which are due to no statstical analysis being posted. There are no statistical analysis to post for this study

End point values	2.5 mg QD AZD1480	5.0 mg QD AZD1480	10 mg QD AZD1480	20 mg QD AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	3	3	3
Units: ug.h/L				
geometric mean (standard deviation)				
AUC0-12 (ug.h/L)	69.2 (± 27.5)	295 (± 68.2)	278 (± 257)	472 (± 257)

End point values	30 mg QD AZD1480	50 mg QD AZD1480	70 mg QD AZD1480	10 mg BID AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	1	6
Units: ug.h/L				
geometric mean (standard deviation)				
AUC0-12 (ug.h/L)	1860 (± 546)	3090 (± 2060)	5800 (± 0)	425 (± 190)

End point values	15 mg BID AZD1480			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: ug.h/L				
geometric mean (standard deviation)				
AUC0-12 (ug.h/L)	497 (± 191)			

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetic parameters following single dosing (2a)

End point title	Pharmacokinetic parameters following single dosing (2a)[16]

End point description:

Single dose T1/2

End point type	Primary

End point timeframe:

24 hours (Day 1: 0, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 6, 8, 12, 24 hrs post dose)

Notes:

[16] - 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: There are 12 warnings which are due to no statstical analysis being posted. There are no statistical analysis to post for this study

End point values	2.5 mg QD AZD1480	5.0 mg QD AZD1480	10 mg QD AZD1480	20 mg QD AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	3	3	3
Units: hr				
arithmetic mean (standard deviation)				
T1/2 (h)	8.06 (± 2.26)	4.76 (± 1.15)	2.45 (± 1.35)	5.46 (± 2.37)

End point values	30 mg QD AZD1480	50 mg QD AZD1480	70 mg QD AZD1480	10 mg BID AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	1	0[17]
Units: hr				
arithmetic mean (standard deviation)				
T1/2 (h)	4.62 (± 0.87)	5.81 (± 0.899)	3.61 (± 0)	()

Notes:

[17] - NA

End point values	15 mg BID AZD1480			
Subject group type	Reporting group			
Number of subjects analysed	0[18]			
Units: hr				
arithmetic mean (standard deviation)				
T1/2 (h)	()			

Notes:

[18] - NA

Statistical analyses

No statistical analyses for this end point

Secondary: JAK2 V617 mutation status

End point title	JAK2 V617 mutation status

End point description:

JAK2 V617F Mutation status (mutation detected/not detected) in patients

End point type	Secondary

End point timeframe:

Determined locally during the screening period

End point values	2.5 mg QD AZD1480	5.0 mg QD AZD1480	10 mg QD AZD1480	20 mg QD AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	3	3	3
Units: count (%)				
Unknown (count)	0	0	0	0
JAK2 V617F Mutation Detected (count)	4	2	2	1
JAK2 V617F Mutation Not Detected (count)	2	1	1	2
Unknown (%)	0	0	0	0
JAK2 V617F Mutation Detected (%)	67	67	67	33
JAK2 V617F Mutation Not Detected (%)	33	33	33	67

End point values	30 mg QD AZD1480	50 mg QD AZD1480	70 mg QD AZD1480	10 mg BID AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	1	6
Units: count (%)				
Unknown (count)	0	0	0	3
JAK2 V617F Mutation Detected (count)	2	5	1	1
JAK2 V617F Mutation Not Detected (count)	1	1	0	2
Unknown (%)	0	0	0	50
JAK2 V617F Mutation Detected (%)	67	83	100	17
JAK2 V617F Mutation Not Detected (%)	33	17	0	33

End point values	15 mg BID AZD1480			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: count (%)				
Unknown (count)	4			
JAK2 V617F Mutation Detected (count)	0			
JAK2 V617F Mutation Not Detected (count)	0			
Unknown (%)	100			
JAK2 V617F Mutation Detected (%)	0			
JAK2 V617F Mutation Not Detected (%)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Efficacy: Clinical Improvement (CI) overall

End point title	Efficacy: Clinical Improvement (CI) overall

End point description:

To be evaluble for clinical improvement, patients must be evaluable for improvement in hemoglobin, spleen size, transfusionrequirements, platelet count, or ANC*Clinical improvement by IWG criteria in hemoglobin, spleen size, transfusion requirements, platelet count, or ANC

End point type	Secondary

End point timeframe:

This single summary is formed form emerging data gathered during the course of the study

End point values	2.5 mg QD AZD1480	5.0 mg QD AZD1480	10 mg QD AZD1480	20 mg QD AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	3	3
Units: count (%)				
Clinical Improvement (count)	0	2	0	0
Clinical Improvement (%)	0	67	0	0
No Clinical Improvement (count)	4	1	3	3
No Clinical Improvement (%)	100	33	100	100

End point values	30 mg QD AZD1480	50 mg QD AZD1480	70 mg QD AZD1480	10 mg BID AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	1	6
Units: count (%)				
Clinical Improvement (count)	0	2	0	1
Clinical Improvement (%)	0	33	0	17
No Clinical Improvement (count)	3	4	1	5
No Clinical Improvement (%)	100	67	100	83

End point values	15 mg BID AZD1480			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: count (%)				
Clinical Improvement (count)	0			
Clinical Improvement (%)	0			
No Clinical Improvement (count)	4			
No Clinical Improvement (%)	100			

Statistical analyses

No statistical analyses for this end point

Secondary: 50% Clinical Improvement in spleen size from baseline

End point title	50% Clinical Improvement in spleen size from baseline

End point description:

To be evaluable for improvement in spleen size, spleen size by palpatation needs to be >= 5cm at baseline. Spleen size reduction needs to be maintained for a minimum of 8 weeks (56 days) from baseline.

End point type	Secondary

End point timeframe:

8 weeks

End point values	2.5 mg QD AZD1480	5.0 mg QD AZD1480	10 mg QD AZD1480	20 mg QD AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	1	2	3
Units: cm				
Clinical Improvement (count)	0	0	0	0
Clinical Improvement (%)	0	0	0	0
No Clinical Improvement (ount)	4	1	2	3
No clinical Improvement (%)	100	100	100	100

End point values	30 mg QD AZD1480	50 mg QD AZD1480	70 mg QD AZD1480	10 mg BID AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	5	1	3
Units: cm				
Clinical Improvement (count)	0	0	0	1
Clinical Improvement (%)	0	0	0	33
No Clinical Improvement (ount)	3	5	1	2
No clinical Improvement (%)	100	100	100	67

End point values	15 mg BID AZD1480			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: cm				
Clinical Improvement (count)	0			
Clinical Improvement (%)	0			
No Clinical Improvement (ount)	3			
No clinical Improvement (%)	100			

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Improvement: haemoglobin

End point title	Clinical Improvement: haemoglobin

End point description:

To be evaluable for improvement in haemoglobin, patients had to have haemoglobin levels of <10g/L at baseline. The increase in haemoglobin has to be maintained for at least 56 days (8 weeks).

End point type	Secondary

End point timeframe:

8 weeks (56 days)

End point values	2.5 mg QD AZD1480	5.0 mg QD AZD1480	10 mg QD AZD1480	20 mg QD AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	1	2
Units: g/L				
Clinical Improvement (count)	0	0	0	0
Clinical Improvement (%)	0	0	0	0
No Clinical improvement (count)	3	3	1	2
no clinical improvement (%)	100	100	100	100

End point values	30 mg QD AZD1480	50 mg QD AZD1480	70 mg QD AZD1480	10 mg BID AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	5	1	4
Units: g/L				
Clinical Improvement (count)	0	1	0	0
Clinical Improvement (%)	0	20	0	0
No Clinical improvement (count)	1	4	1	4
no clinical improvement (%)	100	80	100	100

End point values	15 mg BID AZD1480			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: g/L				
Clinical Improvement (count)	0			
Clinical Improvement (%)	0			
No Clinical improvement (count)	1			
no clinical improvement (%)	100			

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical improvement: transfusion requirements

End point title	Clinical improvement: transfusion requirements

End point description:

To be evaluable for improvement in transfusion requirements, patients must have required at least one transfusion of packed RBCs or whole blood one month prior to first dose of AZD1480.

End point type	Secondary

End point timeframe:

56 days (8 weeks)

End point values	2.5 mg QD AZD1480	5.0 mg QD AZD1480	10 mg QD AZD1480	20 mg QD AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	3	0[19]	1
Units: counts				
Clinical Improvement (count)	0	2		0
Clinical improvement (%)	0	67		0
No Clinical Improvement (count)	1	1		1
No clinical Improvement (%)	100	33		100

Notes:

[19] - non evaluable

End point values	30 mg QD AZD1480	50 mg QD AZD1480	70 mg QD AZD1480	10 mg BID AZD1480
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[20]	1	1	2
Units: counts				
Clinical Improvement (count)		1	0	0
Clinical improvement (%)		100	0	0
No Clinical Improvement (count)		0	1	2
No clinical Improvement (%)		0	100	100

Notes:

[20] - Non evaluable

End point values	15 mg BID AZD1480			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: counts				
Clinical Improvement (count)	0			
Clinical improvement (%)	0			
No Clinical Improvement (count)	1			
No clinical Improvement (%)	100			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs (SAEs and non-serious AEs) will be collected throughout the study, from informed consent until 30 days after study treatment is discontinued.

Adverse event reporting additional description:

The death wasn't deemed causally related.

Dose: 15 mg BID
Time from start of treatment to death (days): 129
Primary cause of death : ACCIDENT
Secondary cause of death: HEMORRHAGHE: ANEMIA AGGRAVATION (GRADE 4)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups

Reporting group title	2.5 mg QD AZD1480
Reporting group description:	
2.5 mg QD AZD1480	
Reporting group title	5.0 mg QD AZD1480
Reporting group description:	
5.0 mg QD AZD1480	
Reporting group title	20 mg QD AZD1480
Reporting group description:	
20 mg QD AZD1480	
Reporting group title	10 mg QD AZD1480
Reporting group description:	
10 mg QD AZD1480	
Reporting group title	30 mg QD AZD1480
Reporting group description:	
30 mg QD AZD1480	
Reporting group title	50 mg QD AZD1480
Reporting group description:	
50 mg QD AZD1480	
Reporting group title	70 mg QD AZD1480
Reporting group description:	
70 mg QD AZD1480	
Reporting group title	10 mg BID AZD1480
Reporting group description:	
10 mg BID AZD1480	
Reporting group title	15 mg BID AZD1480
Reporting group description:	
15 mg BID AZD1480	

Serious adverse events	2.5 mg QD AZD1480	5.0 mg QD AZD1480	20 mg QD AZD1480
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 6 (33.33%)	2 / 3 (66.67%)	3 / 3 (100.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
HAEMOGLOBIN DECREASED			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BASAL CELL CARINOMA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
CRANIOCEREBRAL INJURY			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
UPPER LIMB FRACTUR			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial flutter/ fibrillation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC FAILURE CHRONIC			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (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
CORONARY ARTERY DISEASE			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
TACHYCARDIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
APHASIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
AMNESIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 disorder, central	Additional description: ATAXIA		
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSARTHRIA	Additional description: DYSARTHRIA		
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
ANAEMI			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPENIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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

SPLENIC INFARCTION			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
PYREXIA			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (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
Psychiatric disorders			
Confusional State	Additional description: Confusional State		
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
PNEUMONIA			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (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
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GOUT			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (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

Serious adverse events	10 mg QD AZD1480	30 mg QD AZD1480	50 mg QD AZD1480
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	4 / 6 (66.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			

HAEMOGLOBIN DECREASED			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (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
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BASAL CELL CARINOMA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
CRANIOCEREBRAL INJURY			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (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
UPPER LIMB FRACTUR			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial flutter/ fibrillation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC FAILURE CHRONIC			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (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
CORONARY ARTERY DISEASE			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (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
TACHYCARDIA			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (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			
APHASIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
AMNESIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorder, central	Additional description: ATAXIA		
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (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
DYSARTHRIA	Additional description: DYSARTHRIA		
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMI			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPENIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (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
SPLENIC INFARCTION			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (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			
PYREXIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional State	Additional description: Confusional State		
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
PNEUMONIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (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
GOUT			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (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

Serious adverse events	70 mg QD AZD1480	10 mg BID AZD1480	15 mg BID AZD1480
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	3 / 6 (50.00%)	1 / 4 (25.00%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Investigations			
HAEMOGLOBIN DECREASED			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (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
Neoplasms benign, malignant and			

unspecified (incl cysts and polyps)			
BASAL CELL CARINOMA			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	0 / 4 (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
Injury, poisoning and procedural complications			
CRANIOCEREBRAL INJURY			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (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
UPPER LIMB FRACTUR			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (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
Cardiac disorders			
Atrial flutter/ fibrillation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (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
CARDIAC FAILURE CHRONIC			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (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
CORONARY ARTERY DISEASE			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	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
TACHYCARDIA			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	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
Nervous system disorders			
APHASIA			

subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (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
AMNESIA			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (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 disorder, central	Additional description: ATAXIA		
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (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
DYSARTHRIA	Additional description: DYSARTHRIA		
alternative dictionary used: MedDRA 14.1			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (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			
ANAEMI			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
NEUTROPENIA			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	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
SPLENIC INFARCTION			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	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
General disorders and administration site conditions			
PYREXIA			

subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	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
Psychiatric disorders			
Confusional State	Additional description: Confusional State		
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (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
Infections and infestations			
PNEUMONIA			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (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
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (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
GOUT			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (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: 5 %

Non-serious adverse events	2.5 mg QD AZD1480	5.0 mg QD AZD1480	20 mg QD AZD1480
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	3 / 3 (100.00%)	3 / 3 (100.00%)
General disorders and administration site conditions			
FATIGUE	Additional description: FATIGUE		
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
ASTHENIA	Additional description: ASTHENIA		
subjects affected / exposed	2 / 6 (33.33%)	1 / 3 (33.33%)	2 / 3 (66.67%)
occurrences (all)	2	1	2

Mucosal inflammation NOS	Additional description: MUCOSAL INFLAMMATION		
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PYREXIA			
subjects affected / exposed	2 / 6 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
HYPERTHERMIA			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
OEDEMA PERIPHERAL			
subjects affected / exposed	1 / 6 (16.67%)	1 / 3 (33.33%)	2 / 3 (66.67%)
occurrences (all)	1	1	2
OEDEMA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
DYSPNOEA	Additional description: DYSPNOEA		
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
EPITAXIS	Additional description: EPITAXIS		
alternative dictionary used: CTCAE 3.0			
subjects affected / exposed	1 / 6 (16.67%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Psychiatric disorders			
CONFUSIONAL STATE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
INSOMNIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Investigations			
Weight increase			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
CARDIAC MURMUR	Additional description: CARDIAC MURMUR		
alternative dictionary used: CTCAE 3.0			

subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Injury, poisoning and procedural complications			
EXCORIATION	Additional description: EXCORIATION		
alternative dictionary used: CTCAE 3.0			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
HEADACHE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PARAESTHES			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	1 / 6 (16.67%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
NEUTROPENIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia, unspecified			
subjects affected / exposed	1 / 6 (16.67%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Eye disorders			
RETINAL HAEMORRHAGE	Additional description: RETINAL HAEMORRHAGE		
alternative dictionary used: CTCAE 3.0			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
CATARAC			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
CONJUNCTIVAL HAEMORRHAG			

subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
DRY EYE			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
HAEMORRHAGE			
alternative dictionary used: CTCAE 3.0			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
KERATITI			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Diarrhoea NOS			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Vomiting alone			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
ASCITES	Additional description: ASCITES		
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Abdominal wall disorder	Additional description: ABDOMINAL DISTENSION		
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
ABDOMINAL PAIN	Additional description: ABDOMINAL PAIN		
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
CONSTIPATION	Additional description: CONSTIPATION		
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
GASTROOESOPHAGEAL REFLUX DISEASE	Additional description: GASTROOESOPHAGEAL REFLUX DISEASE		

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
NAUSEA	Additional description: NAUSEA		
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
HYPERBILIRUBINAEMIA	Additional description: HYPERBILIRUBINAEMIA		
alternative dictionary used: CTCAE 3.0			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
ECCHYMOSI			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
PETECHIAE	Additional description: PETECHIAE		
alternative dictionary used: CTCAE 3.0			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pruritis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
RASH	Additional description: RASH		
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
PROTEINURIA			
subjects affected / exposed	3 / 6 (50.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	3	1	1
HAEMATURIA	Additional description: HAEMATURIA		
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			

MUSCLE SPASMS	Additional description: MUSCLE SPASMS		
alternative dictionary used: CTCAE 3.0			
subjects affected / exposed	1 / 6 (16.67%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
BONE PAIN	Additional description: BONE PAIN		
alternative dictionary used: CTCAE 3.0			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
MUSCULOSKELETAL PAIN	Additional description: MUSCULOSKELETAL PAIN		
alternative dictionary used: CTCAE 3.0			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Myalgia aggravated	Additional description: MYALGIA		
alternative dictionary used: CTCAE 3.0			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain	Additional description: PAIN IN EXTREMITY		
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
FOLLICULITIS			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	10 mg QD AZD1480	30 mg QD AZD1480	50 mg QD AZD1480
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	6 / 6 (100.00%)
General disorders and administration site conditions			
FATIGUE	Additional description: FATIGUE		
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
ASTHENIA	Additional description: ASTHENIA		
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	1 / 6 (16.67%)
occurrences (all)	1	1	1
Mucosal inflammation NOS	Additional description: MUCOSAL INFLAMMATION		

subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	1 / 6 (16.67%)
occurrences (all)	1	1	1
PYREXIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
HYPERTHERMIA			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
OEDEMA PERIPHERAL			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
OEDEMA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
DYSPNOEA	Additional description: DYSPNOEA		
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	1 / 6 (16.67%)
occurrences (all)	1	1	1
EPITAXIS	Additional description: EPITAXIS		
alternative dictionary used: CTCAE 3.0			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
CONFUSIONAL STATE			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
INSOMNIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Investigations			
Weight increase			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
CARDIAC MURMUR	Additional description: CARDIAC MURMUR		
alternative dictionary used: CTCAE 3.0			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
EXCORIATION	Additional description: EXCORIATION		
alternative dictionary used: CTCAE 3.0			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	3 / 6 (50.00%)
occurrences (all)	0	2	3
HEADACHE			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
PARAESTHES			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	1 / 6 (16.67%)
occurrences (all)	1	1	1
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	4 / 6 (66.67%)
occurrences (all)	1	0	4
NEUTROPENIA			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Thrombocytopenia, unspecified			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	3 / 6 (50.00%)
occurrences (all)	0	0	3
Eye disorders			
RETINAL HAEMORRHAGE	Additional description: RETINAL HAEMORRHAGE		
alternative dictionary used: CTCAE 3.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
CATARAC			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
CONJUNCTIVAL HAEMORRHAG			

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
DRY EYE			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	3 / 6 (50.00%)
occurrences (all)	0	0	3
HAEMORRHAGE			
alternative dictionary used: CTCAE 3.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
KERATITI			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	2 / 6 (33.33%)
occurrences (all)	1	0	2
Gastrointestinal disorders			
Diarrhoea NOS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Vomiting alone			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
ASCITES	Additional description: ASCITES		
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal wall disorder	Additional description: ABDOMINAL DISTENSION		
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
ABDOMINAL PAIN	Additional description: ABDOMINAL PAIN		
subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	2 / 6 (33.33%)
occurrences (all)	0	2	2
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	2 / 6 (33.33%)
occurrences (all)	0	1	2
CONSTIPATION	Additional description: CONSTIPATION		
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
GASTROOESOPHAGEAL REFLUX DISEASE	Additional description: GASTROOESOPHAGEAL REFLUX DISEASE		

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Haemorrhoids			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
NAUSEA	Additional description: NAUSEA		
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Hepatobiliary disorders			
HYPERBILIRUBINAEMIA	Additional description: HYPERBILIRUBINAEMIA		
alternative dictionary used: CTCAE 3.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
ECCHYMOSI			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
PETECHIAE	Additional description: PETECHIAE		
alternative dictionary used: CTCAE 3.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pruritis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
RASH	Additional description: RASH		
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Renal and urinary disorders			
PROTEINURIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
HAEMATURIA	Additional description: HAEMATURIA		
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			

MUSCLE SPASMS	Additional description: MUSCLE SPASMS		
alternative dictionary used: CTCAE 3.0			
subjects affected / exposed	2 / 3 (66.67%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
BONE PAIN	Additional description: BONE PAIN		
alternative dictionary used: CTCAE 3.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
MUSCULOSKELETAL PAIN	Additional description: MUSCULOSKELETAL PAIN		
alternative dictionary used: CTCAE 3.0			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Myalgia aggravated	Additional description: MYALGIA		
alternative dictionary used: CTCAE 3.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pain	Additional description: PAIN IN EXTREMITY		
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
FOLLICULITIS			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	70 mg QD AZD1480	10 mg BID AZD1480	15 mg BID AZD1480
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)	6 / 6 (100.00%)	4 / 4 (100.00%)
General disorders and administration site conditions			
FATIGUE	Additional description: FATIGUE		
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
ASTHENIA	Additional description: ASTHENIA		
subjects affected / exposed	0 / 1 (0.00%)	4 / 6 (66.67%)	0 / 4 (0.00%)
occurrences (all)	0	4	0
Mucosal inflammation NOS	Additional description: MUCOSAL INFLAMMATION		

subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
PYREXIA			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
HYPERTHERMIA			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
OEDEMA PERIPHERAL			
subjects affected / exposed	1 / 1 (100.00%)	3 / 6 (50.00%)	2 / 4 (50.00%)
occurrences (all)	1	3	2
OEDEMA			
subjects affected / exposed	1 / 1 (100.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
DYSPNOEA	Additional description: DYSPNOEA		
subjects affected / exposed	0 / 1 (0.00%)	2 / 6 (33.33%)	1 / 4 (25.00%)
occurrences (all)	0	2	1
EPITAXIS	Additional description: EPITAXIS		
alternative dictionary used: CTCAE 3.0			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
CONFUSIONAL STATE			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
INSOMNIA			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Investigations			
Weight increase			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
CARDIAC MURMUR	Additional description: CARDIAC MURMUR		
alternative dictionary used: CTCAE 3.0			

subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
EXCORIATION	Additional description: EXCORIATION		
alternative dictionary used: CTCAE 3.0			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	1 / 1 (100.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
HEADACHE			
subjects affected / exposed	1 / 1 (100.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
PARAESTHES			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
NEUTROPENIA			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Thrombocytopenia, unspecified			
subjects affected / exposed	0 / 1 (0.00%)	2 / 6 (33.33%)	1 / 4 (25.00%)
occurrences (all)	0	2	1
Eye disorders			
RETINAL HAEMORRHAGE	Additional description: RETINAL HAEMORRHAGE		
alternative dictionary used: CTCAE 3.0			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
CATARAC			
subjects affected / exposed	0 / 1 (0.00%)	2 / 6 (33.33%)	1 / 4 (25.00%)
occurrences (all)	0	2	1
CONJUNCTIVAL HAEMORRHAG			

subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
DRY EYE			
subjects affected / exposed	0 / 1 (0.00%)	3 / 6 (50.00%)	0 / 4 (0.00%)
occurrences (all)	0	3	0
HAEMORRHAGE			
alternative dictionary used: CTCAE 3.0			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
KERATITI			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Diarrhoea NOS			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Vomiting alone			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
ASCITES	Additional description: ASCITES		
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Abdominal wall disorder	Additional description: ABDOMINAL DISTENSION		
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
ABDOMINAL PAIN	Additional description: ABDOMINAL PAIN		
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
CONSTIPATION	Additional description: CONSTIPATION		
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
GASTROOESOPHAGEAL REFLUX DISEASE	Additional description: GASTROOESOPHAGEAL REFLUX DISEASE		

subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Haemorrhoids			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
NAUSEA	Additional description: NAUSEA		
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			
HYPERBILIRUBINAEMIA	Additional description: HYPERBILIRUBINAEMIA		
alternative dictionary used: CTCAE 3.0			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Skin and subcutaneous tissue disorders			
ECCHYMOSI			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
PETECHIAE	Additional description: PETECHIAE		
alternative dictionary used: CTCAE 3.0			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Pruritis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
RASH	Additional description: RASH		
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Renal and urinary disorders			
PROTEINURIA			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
HAEMATURIA	Additional description: HAEMATURIA		
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			

MUSCLE SPASMS	Additional description: MUSCLE SPASMS		
alternative dictionary used: CTCAE 3.0			
subjects affected / exposed	0 / 1 (0.00%)	2 / 6 (33.33%)	1 / 4 (25.00%)
occurrences (all)	0	2	1
BONE PAIN	Additional description: BONE PAIN		
alternative dictionary used: CTCAE 3.0			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
MUSCULOSKELETAL PAIN	Additional description: MUSCULOSKELETAL PAIN		
alternative dictionary used: CTCAE 3.0			
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Myalgia aggravated	Additional description: MYALGIA		
alternative dictionary used: CTCAE 3.0			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Pain	Additional description: PAIN IN EXTREMITY		
subjects affected / exposed	0 / 1 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
FOLLICULITIS			
subjects affected / exposed	0 / 1 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 March 2009	This is to simplify the assessment of response in this study by using the most commonly used
01 June 2009	To provide a more accurate time frame for screening eye exams.
07 October 2009	To clarify that patients cannot be dosed on Day 4 and Day 10 if there are significant eye,
04 March 2010	To remove the drug washout on Days 2 and 3. Patients will now dose continuously from Day
03 June 2010	To correct the pulmonary toxicity DLT definition in the protocol. A decrease in FVC or DLco
30 September 2010	To add clarification regarding the definition of DLT, and to ensure consistency across other
15 February 2011	To ensure the exploratory objectives in the synopsis are consistent with the those in the body
30 June 2011	This is an administrative change whereby the update AZ template does not allow for all

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.

All patients were enrolled into Part A only.

The study was planned as 2 parts (A and B); however, all patients were enrolled into Part A.

No formal statistical analysis was performed.

Notes: