Clinical trial results:
A Randomised Open-Label Phase II Study to Assess the Efficacy and Safety of AZD4547 Monotherapy versus Paclitaxel in Patients with Advanced Gastric Adenocarcinoma (including Adenocarcinoma of the Lower-Third of the Oesophagus or the Gastro-Oesophageal Junction) with FGFR2 Polysomy or Gene Amplification (Shine study)

Summary

EudraCT number	2010-023377-19
Trial protocol	GB DE CZ ES BE IT HU BG
Global end of trial date	27 June 2013

Results information

Result version number	v1 (current)
This version publication date	04 November 2016
First version publication date	04 November 2016

Trial information

Trial identification

Sponsor protocol code	D2610C00004

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, Cheshire, United Kingdom, SK10 4TG
Public contact	Prof Eric Van Cutsem, MD, PhD, University Hospital Gasthuisberg, eric.vancutsem@med.kuleuven.be
Scientific contact	Donal Landers, Astra Zeneca, Donal.Landers@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	17 December 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 June 2013
Global end of trial reached?	Yes
Global end of trial date	27 June 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Prompted by slow recruitment and concerns about the feasibility of completing enrolment in a realistic timeframe, AstraZeneca and the Safety Review Committee (SRC) for the study agreed that it would be appropriate to conduct an unscheduled analysis of the efficacy (based on average change in tumour size) and tolerability data.
The results of this unscheduled analysis did not show superiority of AZD4547 over paclitaxel in patients with advanced gastric cancer tumours that have FGFR2 amplification. Thus, it was concluded that the study was unlikely to meet its primary objective of demonstrating superiority of AZD4547 monotherapy over paclitaxel, based on PFS, and a decision was made to cease enrolment and close the study.

Protection of trial subjects:

An SRC was appointed to review all available safety data at approximately 2-month intervals.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 November 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Korea, Republic of: 17
Country: Number of subjects enrolled	United Kingdom: 15
Country: Number of subjects enrolled	Czech Republic: 8
Country: Number of subjects enrolled	Taiwan: 6
Country: Number of subjects enrolled	Japan: 5
Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	India: 1
Country: Number of subjects enrolled	Spain: 13
Worldwide total number of subjects	71
EEA total number of subjects	42

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)	44
From 65 to 84 years	27
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted in 11 countries. Enrolment started in November 2011 and last patient visit was in August 2013. In total, 960 patients were enrolled out of which 71 were randomised. A total of 67 patients received treatment , 40 of these patients received AZD4547 and 27 received Paclitaxel.

Pre-assignment

Screening details:

Patients ≥ 25 years with locally advanced or metastatic gastric adenocarcinoma that had FGFR2 polysomy or FGFR2 gene amplification and whose disease had progressed during or after 1st line therapy. Patients whose disease had progressed within 6 months following adjuvant or neo-adjuvant therapy could be included at the discretion of the investigator

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	AZD4547

Arm description:

80mg BD 2 weeks on/1 week off

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 2 weeks on/1 week off

Arm title	Paclitaxel

Arm description:

80mg / m**2

Arm type	Active comparator
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion in pre-filled syringe
Routes of administration	Intravenous use

Dosage and administration details:

80mg / m**2

Number of subjects in period 1	AZD4547	Paclitaxel
Started	41	30
Received treatment	40	27
Did not receive treatment	1	3
Ongoing treatment at data cut-off	1	1
Completed	0	0
Not completed	41	30
Adverse event, serious fatal	27	16
Consent withdrawn by subject	1	1
Death before treatment	1	2
Lost to follow-up	1	-
Did not receive treatment	-	1
Unclassified reason for not completed	11	10

Baseline characteristics

Reporting groups	
Reporting group title	AZD4547
Reporting group description: 80mg BD 2 weeks on/1 week off	
Reporting group title	Paclitaxel
Reporting group description: 80mg / m**2	

Reporting group values	AZD4547	Paclitaxel	Total
Number of subjects	41	30	71
Age categorical Units: Subjects			
Adults (18-64 years)	27	17	44
From 65-84 years	14	13	27
Age Continuous | Units: years			
arithmetic mean	60.6	61.9	
standard deviation	± 11.38	± 10.65	-
Gender, Male/Female			
Gender			
Units: Participants			
Female	12	8	20
Male	29	22	51
Age, Customized			
Age by category			
Units: Subjects			
<50 years	7	4	11
>=50 - < 65 years	20	13	33
>= 65 years	14	13	27

End points

End points reporting groups	
Reporting group title	AZD4547
Reporting group description:	
80mg BD 2 weeks on/1 week off	
Reporting group title	Paclitaxel
Reporting group description:	
80mg / m**2	

Primary: Progression Free Survival	
End point title	Progression Free Survival
End point description:	
PFS is the time from randomisation until the date of objective disease progression as defined by Response Evaluation Criteria In Solid Tumours (RECIST version 1.1) or death (by any cause in the absence of progression).	
End point type	Primary
End point timeframe:	
Week 8 (±1 week) and then every 8 weeks (±1 week)	

End point values	AZD4547	Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	30		
Units: Patients	36	26		

Statistical analyses

Statistical analysis title	Progression free survival (Full analysis set)
Statistical analysis description:	
The analysis was performed using a Cox proportional hazards model with factors for treatment and FGFR2 FISH score (4/5 versus 6).	
Comparison groups	AZD4547 v Paclitaxel
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.9581 [2]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.57
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	1.12
upper limit	2.21

Notes:

[1] - The 3 patients from the Full analysis set with an FGFR FISH score of 2 or 3 were not included in the analysis.A hazard ratio < 1 favours AZD4547 80mg BD 2 weeks on/1 week off.CI calculated using Profile Likelihood.

[2] - 1-sided

Secondary: Overall Survival

End point title	Overall Survival

End point description:

End point type	Secondary

End point timeframe:

Week 8 (±1 week) and then every 8 weeks (±1 week)

End point values	AZD4547	Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	30		
Units: Patients	27	18		

Statistical analyses

Statistical analysis title	Overall Survival
Comparison groups	AZD4547 v Paclitaxel
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.8156 [3]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.31
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.89
upper limit	1.95

Notes:

[3] - 1-sided

Secondary: Objective Response Rate

End point title	Objective Response Rate

End point description:

End point type	Secondary

End point timeframe:

Week 8 (±1 week) and then every 8 weeks (±1 week)

End point values	AZD4547	Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	30		
Units: Patients	1	7		

Statistical analyses

Statistical analysis title	Objective response Rate
Comparison groups	AZD4547 v Paclitaxel
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.997 [4]
Method	Regression, Logistic
Parameter estimate	Hazard ratio (HR)
Point estimate	0.09
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.02
upper limit	0.35

Notes:

[4] - 1-sided

Secondary: Change in tumour size at 8 weeks

End point title	Change in tumour size at 8 weeks

End point description:

End point type	Secondary

End point timeframe:

Week 8 (±1 week)

End point values	AZD4547	Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	26		
Units: patients				
geometric mean (geometric coefficient of variation)	27.5 (± 26.9)	-7 (± 37.3)		

Statistical analyses

Statistical analysis title	Change in tumour size at 8 wks
Comparison groups	AZD4547 v Paclitaxel
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.99 [5]
Method	ANCOVA
Parameter estimate	Hazard ratio (HR)
Point estimate	39.44
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	25.18
upper limit	55.33

Notes:
[5] - 1-sided

Secondary: Mean change in tumour size

End point title	Mean change in tumour size

End point description:

End point type	Secondary

End point timeframe:
Week 8 (±1 week)

End point values	AZD4547	Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	26		
Units: Patients				
number (not applicable)	28.4	-1.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of patients without progressive disease at 8 weeks

End point title	Percentage of patients without progressive disease at 8 weeks

End point description:

End point type	Secondary

End point timeframe:
Week 8 (±1 week)

End point values	AZD4547	Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	30		
Units: Patients				
number (not applicable)				
Number of patients	10	16		
Percentage of patients	24.4	53.3		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs will be collected throughout the study, from randomisation until the end of the follow-up period. The follow-up period is defined as 28 days after study treatment (AZD4547 or paclitaxel) is discontinued.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16

Reporting groups

Reporting group title	Paclitaxel
Reporting group description:	
80mg / m**2	
Reporting group title	AZD4547
Reporting group description:	
80mg BD 2 weeks on/1 week off	

Serious adverse events	Paclitaxel	AZD4547	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 27 (22.22%)	8 / 40 (20.00%)	
number of deaths (all causes)	16	27	
number of deaths resulting from adverse events	0	0	
Investigations			
Blood bilirubin indirect increased			
subjects affected / exposed	0 / 27 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases increased			
alternative dictionary used: MedDRA 16			
subjects affected / exposed	0 / 27 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Arterial disorder			
subjects affected / exposed	0 / 27 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 27 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 27 (3.70%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Dyspepsia			
subjects affected / exposed	0 / 27 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal haemorrhage			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 27 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyphagia			
subjects affected / exposed	1 / 27 (3.70%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstruction gastric			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 27 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 27 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Vomiting alone			
subjects affected / exposed	2 / 27 (7.41%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 27 (3.70%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Obstruction of bile duct			
alternative dictionary used: MedDRA 16			
subjects affected / exposed	0 / 27 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Biliary tract infection			
subjects affected / exposed	1 / 27 (3.70%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	0 / 27 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infectio			
subjects affected / exposed	1 / 27 (3.70%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 27 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Paclitaxel	AZD4547	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 27 (96.30%)	39 / 40 (97.50%)	
General disorders and administration site conditions			
Asthenia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	5 / 27 (18.52%)	11 / 40 (27.50%)	
occurrences (all)	5	11	
fatigue			
subjects affected / exposed	8 / 27 (29.63%)	6 / 40 (15.00%)	
occurrences (all)	8	6	
Oedema of extremities	Additional description: Oedema peripheral		
subjects affected / exposed	2 / 27 (7.41%)	4 / 40 (10.00%)	
occurrences (all)	2	4	
Pyrexia			
subjects affected / exposed	2 / 27 (7.41%)	4 / 40 (10.00%)	
occurrences (all)	2	4	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 27 (3.70%)	3 / 40 (7.50%)	
occurrences (all)	1	3	
Epistaxis	Additional description: Epistaxis		
subjects affected / exposed	1 / 27 (3.70%)	3 / 40 (7.50%)	
occurrences (all)	1	3	
Dysphonia	Additional description: Dysphonia		
subjects affected / exposed	1 / 27 (3.70%)	2 / 40 (5.00%)	
occurrences (all)	1	2	
productiveCough			
subjects affected / exposed	2 / 27 (7.41%)	0 / 40 (0.00%)	
occurrences (all)	2	0	
Psychiatric disorders			
Insomnia			

subjects affected / exposed	3 / 27 (11.11%)	2 / 40 (5.00%)	
occurrences (all)	3	2	
Peripheral neuropathy hereditary	Additional description: Neuropathy periheral		
subjects affected / exposed	4 / 27 (14.81%)	1 / 40 (2.50%)	
occurrences (all)	4	1	
Investigations			
aspartate	Additional description: Aspartate aminotransferase increased		
subjects affected / exposed	5 / 27 (18.52%)	7 / 40 (17.50%)	
occurrences (all)	0	7	
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 27 (3.70%)	4 / 40 (10.00%)	
occurrences (all)	1	4	
Bilirubin value increased			
subjects affected / exposed	0 / 27 (0.00%)	5 / 40 (12.50%)	
occurrences (all)	0	5	
Alanine amonitransferase increased	Additional description: Alanine amonitransferase increased		
subjects affected / exposed	1 / 27 (3.70%)	4 / 40 (10.00%)	
occurrences (all)	1	4	
Blood phosphorus increase			
subjects affected / exposed	0 / 27 (0.00%)	3 / 40 (7.50%)	
occurrences (all)	0	3	
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	4 / 27 (14.81%)	6 / 40 (15.00%)	
occurrences (all)	4	6	
Headache			
subjects affected / exposed	1 / 27 (3.70%)	4 / 40 (10.00%)	
occurrences (all)	1	4	
Dizziness			
subjects affected / exposed	1 / 27 (3.70%)	3 / 40 (7.50%)	
occurrences (all)	1	3	
Lethargy			
subjects affected / exposed	2 / 27 (7.41%)	1 / 40 (2.50%)	
occurrences (all)	2	1	
Peripheral sensory neuropathy	Additional description: Peripheral sensory neuropathy		

subjects affected / exposed	3 / 27 (11.11%)	0 / 40 (0.00%)	
occurrences (all)	3	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	6 / 27 (22.22%)	7 / 40 (17.50%)	
occurrences (all)	6	7	
Neutropenia			
subjects affected / exposed	9 / 27 (33.33%)	2 / 40 (5.00%)	
occurrences (all)	9	2	
Eye disorders			
Detachment of macular retinal pigment epithelium			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 27 (0.00%)	6 / 40 (15.00%)	
occurrences (all)	0	6	
Dryness of eyes			
subjects affected / exposed	0 / 27 (0.00%)	4 / 40 (10.00%)	
occurrences (all)	0	4	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	6 / 27 (22.22%)	10 / 40 (25.00%)	
occurrences (all)	6	10	
Constipation			
subjects affected / exposed	5 / 27 (18.52%)	10 / 40 (25.00%)	
occurrences (all)	5	10	
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	5 / 27 (18.52%)	9 / 40 (22.50%)	
occurrences (all)	5	9	
Vomiting alone			
subjects affected / exposed	5 / 27 (18.52%)	8 / 40 (20.00%)	
occurrences (all)	5	8	
Stomatitis ulcerative	Additional description: Stomatitis		
subjects affected / exposed	2 / 27 (7.41%)	10 / 40 (25.00%)	
occurrences (all)	2	10	
Abdominal pain upper			
subjects affected / exposed	0 / 27 (0.00%)	9 / 40 (22.50%)	
occurrences (all)	0	9	

Hepatobiliary disorders			
Diarrhoea			
subjects affected / exposed	6 / 27 (22.22%)	6 / 40 (15.00%)	
occurrences (all)	6	6	
Skin and subcutaneous tissue disorders			
Alopecia mucinosa	Additional description: Alopecia		
subjects affected / exposed	13 / 27 (48.15%)	2 / 40 (5.00%)	
occurrences (all)	13	2	
Dry skin			
subjects affected / exposed	1 / 27 (3.70%)	3 / 40 (7.50%)	
occurrences (all)	1	3	
Onychomadesis	Additional description: Onychomadesis		
subjects affected / exposed	0 / 27 (0.00%)	3 / 40 (7.50%)	
occurrences (all)	0	3	
Nail discolouration	Additional description: Nail discolouration		
subjects affected / exposed	1 / 27 (3.70%)	2 / 40 (5.00%)	
occurrences (all)	1	2	
Pruritus	Additional description: Pruritus		
subjects affected / exposed	1 / 27 (3.70%)	2 / 40 (5.00%)	
occurrences (all)	1	2	
onycholysis	Additional description: onycholysis		
subjects affected / exposed	0 / 27 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	6 / 27 (22.22%)	1 / 40 (2.50%)	
occurrences (all)	6	1	
Arthralgia			
subjects affected / exposed	0 / 27 (0.00%)	3 / 40 (7.50%)	
occurrences (all)	0	3	
Myalgia	Additional description: Myalgia		
subjects affected / exposed	3 / 27 (11.11%)	0 / 40 (0.00%)	
occurrences (all)	3	0	
Infections and infestations			
Urinary tract infectio			

subjects affected / exposed	2 / 27 (7.41%)	2 / 40 (5.00%)	
occurrences (all)	2	2	
Lower respiratory tract infection	Additional description: Lower respiratory tract infection		
subjects affected / exposed	3 / 27 (11.11%)	0 / 40 (0.00%)	
occurrences (all)	3	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	8 / 27 (29.63%)	16 / 40 (40.00%)	
occurrences (all)	8	16	
Hyperkalaemia	Additional description: Hyperkalaemia		
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 27 (7.41%)	2 / 40 (5.00%)	
occurrences (all)	2	2	
Hypokalaemia	Additional description: Hypokalaemia		
subjects affected / exposed	2 / 27 (7.41%)	1 / 40 (2.50%)	
occurrences (all)	2	1	
Dry mouth			
subjects affected / exposed	0 / 27 (0.00%)	9 / 40 (22.50%)	
occurrences (all)	0	9	
Hyperphosphataemia	Additional description: Hyperphosphataemia		
subjects affected / exposed	0 / 27 (0.00%)	3 / 40 (7.50%)	
occurrences (all)	0	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 May 2012	Patients with gastric adenocarcinoma of lower-third of the oesophagus or the Gastro-oesophageal junction were to be included in the study. The phase of the study was modified to Phase II due to increased sample size. Clarification of patient population and re-labelling of the study as Phase II to reflect the increase in study size. Sample size of randomised patients was increased to 160 patients.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
27 June 2013	It was concluded that the study was unlikely to meet its primary objective of demonstrating superiority of AZD4547 monotherapy over paclitaxel, based on PFS, and a decision was made to cease enrolment and close the study.	-

Notes:

Limitations and caveats

None reported