



Clinical trial results:

A Cancer Research UK Phase I/IIa trial of AT9283 (a selective inhibitor of aurora kinases) given over 72 hours every 21 days via intravenous infusion in children and adolescents aged 6 months to 18 years with relapsed and refractory acute leukaemia.

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

EudraCT number	2009-016952-36
Trial protocol	GB
Global end of trial date	01 July 2014

Results information

Result version number	v2 (current)
This version publication date	05 June 2016
First version publication date	24 July 2015
Version creation reason	<ul style="list-style-type: none">Correction of full data set Data reviewed and corrected following EudraCT system downtime (July 2015 to January 2016).

Trial information

Trial identification

Sponsor protocol code	CR0708-12
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01431664
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Cancer Research UK
Sponsor organisation address	407 St John Street, London, United Kingdom, EC1V 4AD
Public contact	Centre for Drug Development, Cancer Research UK, +44 02072420200, regquery@cancer.org.uk
Scientific contact	Centre for Drug Development, Cancer Research UK, +44 02072420200, regquery@cancer.org.uk

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	04 December 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 July 2014
Global end of trial reached?	Yes
Global end of trial date	01 July 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To recommend a dose of AT9283 for Phase II evaluation in paediatric patients with acute leukaemia.

Protection of trial subjects:

None

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 September 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 7
Worldwide total number of subjects	7
EEA total number of subjects	7

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)	2
Children (2-11 years)	3
Adolescents (12-17 years)	1
Adults (18-64 years)	1
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study participants were enrolled from 14 September 2011 to 01 July 2014 in 4 clinical study centres in the UK.

Pre-assignment

Screening details:

Patients were male or female aged 6 months to 18 years old, who had morphologically proven acute leukaemia (relapsed and refractory disease) with Karnofsky/Lansky play performance score of at least 50 and a life expectancy of at least 8 weeks.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1 (9.0 mg/m2/day)

Arm description:

AT9283 9.0 mg/m2/day dose level.

Arm type	Experimental
Investigational medicinal product name	AT9283
Investigational medicinal product code	AT9283
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered as a 72 hour intravenous infusion every 21 days (one treatment cycle).

Arm title	Cohort 2 (14.5 mg/m2/day)
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Arm description:

AT9283 14.5 mg/m2/day dose level.

Arm type	Experimental
Investigational medicinal product name	AT9283
Investigational medicinal product code	AT9283
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered as a 72 hour intravenous infusion every 21 days (one treatment cycle).

Arm title	Cohort 3 (23.0 mg/m2/day)
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Arm description:

AT9283 23.0 mg/m2/day dose level.

Arm type	Experimental
Investigational medicinal product name	AT9283
Investigational medicinal product code	AT9283
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered as a 72 hour intravenous infusion every 21 days (one treatment cycle).

Number of subjects in period 1	Cohort 1 (9.0 mg/m ² /day)	Cohort 2 (14.5 mg/m ² /day)	Cohort 3 (23.0 mg/m ² /day)
Started	3	3	1
Completed	3	3	1

Baseline characteristics

Reporting groups

Reporting group title	Cohort 1 (9.0 mg/m2/day)
Reporting group description: AT9283 9.0 mg/m2/day dose level.	
Reporting group title	Cohort 2 (14.5 mg/m2/day)
Reporting group description: AT9283 14.5 mg/m2/day dose level.	
Reporting group title	Cohort 3 (23.0 mg/m2/day)
Reporting group description: AT9283 23.0 mg/m2/day dose level.	

Reporting group values	Cohort 1 (9.0 mg/m2/day)	Cohort 2 (14.5 mg/m2/day)	Cohort 3 (23.0 mg/m2/day)
Number of subjects	3	3	1
Age categorical Units: Subjects			
Infants and toddlers (28 days-23 months)	1	1	0
Children (2-11 years)	1	1	1
Adolescents (12-17 years)	0	1	0
Adults (18-64 years)	1	0	0
Gender categorical Units: Subjects			
Female	1	0	1
Male	2	3	0

Reporting group values	Total		
Number of subjects	7		
Age categorical Units: Subjects			
Infants and toddlers (28 days-23 months)	2		
Children (2-11 years)	3		
Adolescents (12-17 years)	1		
Adults (18-64 years)	1		
Gender categorical Units: Subjects			
Female	2		
Male	5		

End points

End points reporting groups

Reporting group title	Cohort 1 (9.0 mg/m2/day)
Reporting group description: AT9283 9.0 mg/m2/day dose level.	
Reporting group title	Cohort 2 (14.5 mg/m2/day)
Reporting group description: AT9283 14.5 mg/m2/day dose level.	
Reporting group title	Cohort 3 (23.0 mg/m2/day)
Reporting group description: AT9283 23.0 mg/m2/day dose level.	
Subject analysis set title	All treated patients
Subject analysis set type	Full analysis
Subject analysis set description: All enrolled and eligible patients who received at least one dose of AT9283.	

Primary: Recommended Dose of AT9283 for Phase IIb Evaluation

End point title	Recommended Dose of AT9283 for Phase IIb Evaluation ^[1]
End point description: The biologically active dose of AT9283 and maximal dose of AT9283 at which no more than one out of up to six patients at that dose level experienced a probably or highly probably drug related dose limiting toxicity (DLT) during the first cycle of AT9283.	
End point type	Primary
End point timeframe: First cycle of AT9283 administration.	

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: All safety data were presented in a descriptive fashion, with adverse events reported for each dose level and presented by adverse event term by the worst grade observed.

End point values	All treated patients			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: mg/m2/day				
Maximum administered dose	23			

Statistical analyses

No statistical analyses for this end point

Secondary: Safety

End point title	Safety
End point description: The causality and severity grading of each adverse event (AE), according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE), Version 4.02. All AEs with a causality of possibly, probably or highly probably related to AT9283 were considered to indicate relatedness.	

End point type	Secondary
End point timeframe:	
From patient consent to 28 days post last dose of AT9283.	

End point values	All treated patients			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: No. of AEs				
All AEs	97			
Related AEs	29			
DLTs	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Response

End point title	Response
End point description:	
Patients' disease was measured and characterised according to the following disease response criteria: Complete remission (CR) - absolute neutrophil count (ANC) $\geq 1.0 \times 10^9/L$; platelet count $\geq 100 \times 10^9/L$; bone marrow <5% blasts. Complete remission with incomplete bone marrow recovery (CRi) - ANC $\geq 0.75 \times 10^9/L$; platelet count $\geq 75 \times 10^9/L$; bone marrow <5% blasts. Partial remission (PR) - ANC $\geq 0.75 \times 10^9/L$; platelet count $\geq 75 \times 10^9/L$; bone marrow <25% blasts. and disease progression (PD).	
End point type	Secondary
End point timeframe:	
From baseline until after 6 cycles.	

End point values	All treated patients			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: Number of subjects with a response				
CR	0			
CRi	0			
PR	0			
PD	7			

Statistical analyses

No statistical analyses for this end point

Secondary: AT9283 Pharmacokinetic Profile

End point title	AT9283 Pharmacokinetic Profile
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End point description:

Pharmacokinetic (PK) parameters: maximum concentration (C_{max}), area under the time-concentration curve (AUC), half-life, clearance (Cl) and steady state volume of distribution (V_{ss}).

End point type	Secondary
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End point timeframe:

Pre-treatment Day 1 through to Day 4 of Cycle 1.

End point values	Cohort 1 (9.0 mg/m2/day)	Cohort 2 (14.5 mg/m2/day)	Cohort 3 (23.0 mg/m2/day)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	1	
Units: ng/mL				
arithmetic mean (standard deviation)				
C _{max} (ng/mL)	21.9 (± 16.9)	37.5 (± 11.4)	46 (± 0)	
AUC (ng/mL. hr)	990 (± 514)	2268 (± 929)	2766 (± 0)	
Half-life (hr)	5.3 (± 0.9)	5.3 (± 1.1)	5.3 (± 0)	
Cl (L/hr)	25.7 (± 12.8)	23.1 (± 26)	18.4 (± 0)	
V _{ss} (L)	197 (± 125)	180 (± 215)	141.7 (± 0)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From patient consent to 28 days post last dose of AT9283.

Assessment type	Systematic
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Dictionary used

Dictionary name	NCI-CTCAE
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Dictionary version	4.02
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Reporting groups

Reporting group title	Cohort 1 (9.0 mg/m2/day)
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Reporting group description:

AT9283 9.0 mg/m2/day dose level.

Reporting group title	All treatment cohorts
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Reporting group description:

All patients treated at the range of AT9283 dose levels administered.

Reporting group title	Cohort 3 (23.0 mg/m2/day)
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Reporting group description:

AT9283 23.0 mg/m2/day dose level.

Reporting group title	Cohort 2 (14.5 mg/m2/day)
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Reporting group description:

AT9283 14.5 mg/m2/day dose level.

Serious adverse events	Cohort 1 (9.0 mg/m2/day)	All treatment cohorts	Cohort 3 (23.0 mg/m2/day)
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	5 / 7 (71.43%)	1 / 1 (100.00%)
number of deaths (all causes)	0	1	1
number of deaths resulting from adverse events	0	0	0
Investigations			
Neutrophil count decreased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 7 (14.29%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 3 (33.33%)	1 / 7 (14.29%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	2 / 2	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Sinus tachycardia			

subjects affected / exposed	1 / 3 (33.33%)	1 / 7 (14.29%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 3 (33.33%)	3 / 7 (42.86%)	1 / 1 (100.00%)
occurrences causally related to treatment / all	2 / 2	4 / 4	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders - other, specify			
subjects affected / exposed	1 / 3 (33.33%)	1 / 7 (14.29%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death NOS			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	1 / 1 (100.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pain			
subjects affected / exposed	1 / 3 (33.33%)	1 / 7 (14.29%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 3 (33.33%)	1 / 7 (14.29%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 3 (33.33%)	1 / 7 (14.29%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	2 / 2	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Bone pain			

subjects affected / exposed	1 / 3 (33.33%)	1 / 7 (14.29%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Sepsis			
subjects affected / exposed	1 / 3 (33.33%)	1 / 7 (14.29%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	2 / 2	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 2 (14.5 mg/m2/day)		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
Neutrophil count decreased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders - other, specify			

subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Death NOS			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Sepsis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Non-serious adverse events	Cohort 1 (9.0 mg/m2/day)	All treatment cohorts	Cohort 3 (23.0 mg/m2/day)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	7 / 7 (100.00%)	1 / 1 (100.00%)
General disorders and administration site conditions			
Facial oedema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Oedema limbs			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Fever			
subjects affected / exposed	1 / 3 (33.33%)	2 / 7 (28.57%)	0 / 1 (0.00%)
occurrences (all)	1	2	0
Flu like symptoms			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions - other, specify			
subjects affected / exposed	1 / 3 (33.33%)	1 / 7 (14.29%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Pain			
subjects affected / exposed	1 / 3 (33.33%)	2 / 7 (28.57%)	1 / 1 (100.00%)
occurrences (all)	2	3	1
Respiratory, thoracic and mediastinal disorders			
Nasal congestion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 3 (33.33%)	1 / 7 (14.29%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Confusion			
subjects affected / exposed	1 / 3 (33.33%)	1 / 7 (14.29%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Psychiatric disorders - other, specify			

subjects affected / exposed	1 / 3 (33.33%)	1 / 7 (14.29%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Restlessness			
subjects affected / exposed	1 / 3 (33.33%)	1 / 7 (14.29%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 7 (14.29%)	0 / 1 (0.00%)
occurrences (all)	3	3	0
Alkaline phosphatase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Blood bilirubin increased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 7 (14.29%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Investigations - other, specify			
subjects affected / exposed	1 / 3 (33.33%)	1 / 7 (14.29%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Neutrophil count decreased			
subjects affected / exposed	1 / 3 (33.33%)	2 / 7 (28.57%)	0 / 1 (0.00%)
occurrences (all)	1	2	0
Platelet count decreased			
subjects affected / exposed	1 / 3 (33.33%)	4 / 7 (57.14%)	0 / 1 (0.00%)
occurrences (all)	1	5	0
Weight gain			
subjects affected / exposed	1 / 3 (33.33%)	1 / 7 (14.29%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
White blood cell decreased			

subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 3	3 / 7 (42.86%) 4	0 / 1 (0.00%) 0
Injury, poisoning and procedural complications Injury, poisoning and procedural complications - other, specify subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	1 / 7 (14.29%) 1	0 / 1 (0.00%) 0
Nervous system disorders Lethargy subjects affected / exposed occurrences (all) Somnolence subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1 1 / 3 (33.33%) 1	1 / 7 (14.29%) 1 1 / 7 (14.29%) 1	0 / 1 (0.00%) 0 0 / 1 (0.00%) 0
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Blood and lymphatic system disorders - other, specify subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 3 1 / 3 (33.33%) 2	4 / 7 (57.14%) 7 1 / 7 (14.29%) 2	1 / 1 (100.00%) 1 0 / 1 (0.00%) 0
Eye disorders Conjunctivitis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 7 (14.29%) 1	0 / 1 (0.00%) 0
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Gastrointestinal disorders - other, specify	1 / 3 (33.33%) 1 1 / 3 (33.33%) 1 1 / 3 (33.33%) 1	1 / 7 (14.29%) 1 1 / 7 (14.29%) 1 1 / 7 (14.29%) 1	0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0

subjects affected / exposed	1 / 3 (33.33%)	2 / 7 (28.57%)	0 / 1 (0.00%)
occurrences (all)	1	2	0
Mucositis oral			
subjects affected / exposed	2 / 3 (66.67%)	2 / 7 (28.57%)	0 / 1 (0.00%)
occurrences (all)	2	2	0
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	1 / 1 (100.00%)
occurrences (all)	0	1	1
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	3 / 7 (42.86%)	1 / 1 (100.00%)
occurrences (all)	0	4	1
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	1 / 3 (33.33%)	1 / 7 (14.29%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Rash maculo-papular			
subjects affected / exposed	1 / 3 (33.33%)	1 / 7 (14.29%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	1 / 1 (100.00%)
occurrences (all)	0	1	1
Infections and infestations			
Infections and infestations - other, specify			
subjects affected / exposed	0 / 3 (0.00%)	2 / 7 (28.57%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Upper respiratory infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 7 (14.29%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	1 / 3 (33.33%)	1 / 7 (14.29%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Wound infection			

subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	1 / 7 (14.29%) 1	0 / 1 (0.00%) 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	1 / 7 (14.29%) 1	0 / 1 (0.00%) 0
Hypoalbuminaemia			
subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	2 / 7 (28.57%) 2	0 / 1 (0.00%) 0
Hypocalcaemia			
subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	2 / 7 (28.57%) 2	0 / 1 (0.00%) 0
Hypokalaemia			
subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	2 / 7 (28.57%) 2	0 / 1 (0.00%) 0
Hypomagnesaemia			
subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	1 / 7 (14.29%) 1	0 / 1 (0.00%) 0
Hypophosphataemia			
subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 4	2 / 7 (28.57%) 4	0 / 1 (0.00%) 0

Non-serious adverse events	Cohort 2 (14.5 mg/m2/day)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)		
General disorders and administration site conditions			
Facial oedema			
subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Oedema limbs			
subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Fever			
subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Flu like symptoms			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>General disorders and administration site conditions - other, specify</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 3 (33.33%)</p> <p>1</p> <p>0 / 3 (0.00%)</p> <p>0</p> <p>0 / 3 (0.00%)</p> <p>0</p>		
<p>Respiratory, thoracic and mediastinal disorders</p> <p>Nasal congestion</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 3 (33.33%)</p> <p>1</p>		
<p>Psychiatric disorders</p> <p>Anxiety</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Confusion</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Psychiatric disorders - other, specify</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Restlessness</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 3 (0.00%)</p> <p>0</p> <p>0 / 3 (0.00%)</p> <p>0</p> <p>0 / 3 (0.00%)</p> <p>0</p> <p>0 / 3 (0.00%)</p> <p>0</p>		
<p>Investigations</p> <p>Alanine aminotransferase increased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Alkaline phosphatase increased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Aspartate aminotransferase increased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 3 (0.00%)</p> <p>0</p> <p>1 / 3 (33.33%)</p> <p>1</p> <p>1 / 3 (33.33%)</p> <p>1</p>		

Blood bilirubin increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Investigations - other, specify subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Lymphocyte count decreased subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Neutrophil count decreased subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Platelet count decreased subjects affected / exposed occurrences (all)	3 / 3 (100.00%) 4		
Weight gain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
White blood cell decreased subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Injury, poisoning and procedural complications Injury, poisoning and procedural complications - other, specify subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Nervous system disorders Lethargy subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Somnolence subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 3		

Blood and lymphatic system disorders - other, specify subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Eye disorders Conjunctivitis subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Constipation subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Diarrhoea subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Gastrointestinal disorders - other, specify subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Mucositis oral subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Nausea subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Vomiting subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 3		
Skin and subcutaneous tissue disorders Dry skin subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Pruritus subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		

Rash maculo-papular subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Musculoskeletal and connective tissue disorders Bone pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
Infections and infestations Infections and infestations - other, specify subjects affected / exposed occurrences (all) Upper respiratory infection subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all) Wound infection subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 2 1 / 3 (33.33%) 1 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0		
Metabolism and nutrition disorders Dehydration subjects affected / exposed occurrences (all) Hypoalbuminaemia subjects affected / exposed occurrences (all) Hypocalcaemia subjects affected / exposed occurrences (all) Hypokalaemia subjects affected / exposed occurrences (all) Hypomagnesaemia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0 1 / 3 (33.33%) 1 1 / 3 (33.33%) 1 1 / 3 (33.33%) 1 0 / 3 (0.00%) 0		

Hypophosphataemia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0		
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More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 August 2011	Reduction in the starting and escalated doses of AT9283, addition of skin biopsy and notification of a change to the Sponsor's contact details.
20 June 2012	Change to the AT9283 dose levels explored in the study (starting dose and escalated dose).

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.

Early termination of the trial due to poor recruitment, attributed to a lack of patients and new competing studies meant that only a small number of patients were administered AT9283 (across a total of three dose levels).

Notes: