Clinical trial results:
Phase I/II study of oral MEK inhibitor Selumetinib (AZD6244 Hyd-Sulphate) in Combination with Highly Active Anti-Retroviral Therapy (HAART) in AIDS-associated Kaposi's sarcoma (KS)

Summary

EudraCT number	2011-003099-35
Trial protocol	GB
Global end of trial date	20 December 2017

Results information

Result version number	v1 (current)
This version publication date	04 February 2026
First version publication date	04 February 2026

Trial information

Trial identification

Sponsor protocol code	STH16059

Additional study identifiers

ISRCTN number	ISRCTN24921472
ClinicalTrials.gov id (NCT number)	NCT01752569
WHO universal trial number (UTN)	-
Other trial identifiers	Cancer Research UK Trial Number: CRUKD/11/005

Notes:

Sponsors

Sponsor organisation name	Sheffield Teaching Hospitals NHS Foundation Trust
Sponsor organisation address	D Floor, Royal Hallamshire Hospital, Glossop Road, Sheffield, United Kingdom, S10 2JF
Public contact	SCART Trial Office, Cancer Research UK Clinical Trials Unit (CRCTU), University of Birmingham, 44 01214146788, scart@contacts.bham.ac.uk
Scientific contact	SCART Trial Office, Cancer Research UK Clinical Trials Unit (CRCTU), University of Birmingham, 44 01214146788, scart@contacts.bham.ac.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	01 April 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 September 2015
Global end of trial reached?	Yes
Global end of trial date	20 December 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To establish the safety and dose of selumetinib in combination with HAART and to establish evidence of whether AIDS-associated KS lesions respond to (i.e. get smaller with) selumetinib in combination with HAART.

Protection of trial subjects:

A data monitoring committee was involved to protect SCART trial participants (especially in relation to safety) and to assist and advise the Chief Investigator and other members of the Trial Management Group (TMG) to ensure the validity and credibility of the trial. This was to safeguard the interests of participants, assess the safety and efficacy of the interventions, and monitor the overall conduct of the clinical trial. A risk assessment was also in place to document any potential risks of the trial and how these would be minimised.

Background therapy:

HAART remains fundamental to the treatment of AIDS-associated KS. The commonest HAART regimen currently used in the UK is Atripla (Gilead Sciences Ltd), a combination of Efavirenz, Emtricitabine and Tenofovir. Patients were required to have been established on a HAART regimen for at least 3 months prior to study entry.

Evidence for comparator: -

Actual start date of recruitment	15 June 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 19
Worldwide total number of subjects	19
EEA total number of subjects	19

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)	19
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

12 patients to Phase I and 25 patients to Phase II were to be recruited over a 3 year period.

Pre-assignment

Screening details:

Potentially eligible HIV positive patients with confirmed progressive KS on an established HAART regimen (≥ 3 months) could be screened for entry into this trial. A patient who gave written informed consent and who satisfied all the inclusion and exclusion criteria could be entered into the trial.

Period 1

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

Arms

Arm title	Selumetinib

Arm description:

Phase I was a dose-finding study to discover the maximum tolerated dose of selumetinib in combination with HAART. Phase II was to consider the efficacy of selumetinib for treating Kaposi's sarcoma at the recommended phase II dose discovered in phase I.

Arm type	Experimental
Investigational medicinal product name	selumetinib
Investigational medicinal product code	AZD6244
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

The treatment schedule required selumetinib to be taken either once daily at the same time each day or twice daily approximately 12 hours apart. Selumetinib should be taken with water at least 2 hours after a meal and 1 hour before the next meal. Selumetinib capsules were to be administered in a continuous 21 day cycle (6 cycles), unless disease progression occured.

Number of subjects in period 1[1]	Selumetinib
Started	16
Completed	6
Not completed	10
Consent withdrawn by subject	2
Adverse event, non-fatal	4
Progression	4

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: There were 19 patients recruited to the SCART Trial, however only 16 started trial treatment; 3 did not receive any trial treatment for the following reasons:
1 patient on 50mg dose allocation was not consented after non-permitted treatment was given

1 patient on 75mg dose allocation was found to be ineligible post-registration
1 patient on 75mg dose allocation withdrew consent as couldn’t commit to trial requirements due to personal circumstances

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	16	16	
Age categorical			
Patients needed to be 18 years or older to enter the trial			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	16	16	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Patients needed to be 18 years or older to enter the trial			
Units: years			
arithmetic mean	45.6		
full range (min-max)	33.7 to 63.7	-	
Gender categorical			
Units: Subjects			
Female	1	1	
Male	15	15	
Ethnicity			
Units: Subjects			
Caucasian	12	12	
Black - African	3	3	
Mixed	1	1	
WHO Performance Status			
Units: Subjects			
Zero	13	13	
One	2	2	
Two	1	1	
Photographic Assessment Lesion Grade			
Units: Subjects			
More Than 0 Less Or Equal To 10 Lesions	3	3	
More Than 10 Less Or Equal To 50 Lesions	9	9	
More Than 50 Lesions	3	3	
Missing Data	1	1	

Height Units: cm arithmetic mean full range (min-max)	 173.1 154.0 to 190.0	 -	
Weight Units: kg arithmetic mean full range (min-max)	 80.1 55.7 to 124.0	 -	

Subject analysis sets

Subject analysis set title	50mg dose allocation
Subject analysis set type	Full analysis
Subject analysis set description: Patients recruited to 50mg dose allocation of selumetinib	
Subject analysis set title	75mg dose allocation
Subject analysis set type	Full analysis
Subject analysis set description: Patients recruited to 75mg dose allocation of selumetinib	

Reporting group values	50mg dose allocation	75mg dose allocation	
Number of subjects	4	12	
Age categorical			
Patients needed to be 18 years or older to enter the trial			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	4	12	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Patients needed to be 18 years or older to enter the trial			
Units: years			
arithmetic mean	50.3	44.0	
full range (min-max)	39.9 to 63.7	33.7 to 56.4	
Gender categorical Units: Subjects			
Female	0	1	
Male	4	11	
Ethnicity Units: Subjects			
Caucasian	3	9	
Black - African	1	2	
Mixed	0	1	
WHO Performance Status Units: Subjects			

Zero	3	10	
One	1	1	
Two	0	1	
Photographic Assessment Lesion Grade Units: Subjects			
More Than 0 Less Or Equal To 10 Lesions	1	2	
More Than 10 Less Or Equal To 50 Lesions	2	7	
More Than 50 Lesions	1	2	
Missing Data	0	1	
Height Units: cm			
arithmetic mean	172.8	173.2	
full range (min-max)	165.0 to 190.0	154.0 to 184.0	
Weight Units: kg			
arithmetic mean	87.3	77.7	
full range (min-max)	71.5 to 124.0	55.7 to 100.4	

End points

End points reporting groups

Reporting group title	Selumetinib
Reporting group description:	
Phase I was a dose-finding study to discover the maximum tolerated dose of selumetinib in combination with HAART. Phase II was to consider the efficacy of selumetinib for treating Kaposi's sarcoma at the recommended phase II dose discovered in phase I.	
Subject analysis set title	50mg dose allocation
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients recruited to 50mg dose allocation of selumetinib	
Subject analysis set title	75mg dose allocation
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients recruited to 75mg dose allocation of selumetinib	

Primary: Phase I Determination of the Maximum Tolerated Dose (MTD)

End point title	Phase I Determination of the Maximum Tolerated Dose (MTD)[1]
End point description:	
To identify a safe dose for selumetinib in combination with HAART	
End point type	Primary
End point timeframe:	
21 day (1 cycle)	

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: Determination of the Maximum Tolerated Dose (MTD) was made using dose decision rules based on dose limiting toxicities (DLTs) experienced by patients each each cohort. Therefore no statistical analysis was performed.

End point values	Selumetinib	50mg dose allocation	75mg dose allocation	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	13	5	8	
Units: Patients				
Eligible for dose decision	10	4	6	
Ineligible for dose decision	3	1	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Objective response rates assessed using ACTG criteria

End point title	Objective response rates assessed using ACTG criteria
End point description:	
Best responses recorded during the first 6 treatment cycles for each separately defined patient population for analyses	
End point type	Secondary

End point timeframe:

6 treatment cycles (21 day cycle)

End point values	Selumetinib			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: Patients				
complete response (CR)	0			
partial response (PR)	1			
stable disease (SD)	11			
progressive disease (PD)	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival rate 6 months from the start of study treatment assessed using ACTG criteria

End point title	Progression free survival rate 6 months from the start of study treatment assessed using ACTG criteria

End point description:

The any dose population (n=16) is defined as the patients from both Phase I and II that received at least one dose of selumetinib at any level.

End point type	Secondary

End point timeframe:

6 months from the start of study treatment

End point values	Selumetinib			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Probability				
number (confidence interval 90%)				
3 months	0.6185 (0.3876 to 0.7843)			
6 months	0.4123 (0.2080 to 0.6069)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Details of all adverse events were documented and reported from the date of commencement of protocol defined treatment until 30 days after the last administration of selumetinib

Adverse event reporting additional description:

Adverse events were reported on an adverse event form completed by the research team at each visit.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.0

Reporting groups

Reporting group title	Selumetinib

Reporting group description:

Phase I was a dose-finding study to discover the maximum tolerated dose of selumetinib in combination with HAART. Phase II was to consider the efficacy of selumetinib for treating Kaposi's sarcoma at the recommended phase II dose discovered in phase I.

Serious adverse events	Selumetinib		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 16 (12.50%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Spinal cord compression			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Skin infection			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infection			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Selumetinib		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 16 (100.00%)		
Vascular disorders			
Lymphedema			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	9 / 16 (56.25%)		
occurrences (all)	10		
Edema limbs			
subjects affected / exposed	6 / 16 (37.50%)		
occurrences (all)	7		
Flu like symptoms			
subjects affected / exposed	4 / 16 (25.00%)		
occurrences (all)	5		
Pain			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Chills			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Puffiness			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Suprapubic Oedema			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Fever			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
General Oedema All Over Body			

subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Puffiness On Left Cheek			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Fluid Retention			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Oedema			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
2X Nodes Right Groin			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Wooded Thickened Groins			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Tumour Pain (Pain In Sacrum, Anal Area And Lower Abdomen)			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Swollen Ankles			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	5		
Sore throat			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	3		
Pneumonitis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Bronchospasm			

subjects affected / exposed occurrences (all) Dyspnea subjects affected / exposed occurrences (all) Inflamed Throat subjects affected / exposed occurrences (all) Abnormal Respiratory Sounds subjects affected / exposed occurrences (all) Tonsillitis subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1 1 / 16 (6.25%) 1 1 / 16 (6.25%) 1 1 / 16 (6.25%) 1 1 / 16 (6.25%) 1		
Psychiatric disorders Delusions subjects affected / exposed occurrences (all) Personality change subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all)	 1 / 16 (6.25%) 1 1 / 16 (6.25%) 1 1 / 16 (6.25%) 1		
Investigations Red Blood Cell Decreased subjects affected / exposed occurrences (all) Creatine Phosphokinase Increased subjects affected / exposed occurrences (all) Alanine aminotransferase increased subjects affected / exposed occurrences (all) Albumin Decreased	 7 / 16 (43.75%) 22 10 / 16 (62.50%) 15 5 / 16 (31.25%) 13		

subjects affected / exposed	3 / 16 (18.75%)			
occurrences (all)	12			
Aspartate aminotransferase increased				
subjects affected / exposed	7 / 16 (43.75%)			
occurrences (all)	11			
Alkaline phosphatase increased				
subjects affected / exposed	6 / 16 (37.50%)			
occurrences (all)	8			
Phosphate Increased				
subjects affected / exposed	8 / 16 (50.00%)			
occurrences (all)	8			
Haemoglobin Decreased				
subjects affected / exposed	5 / 16 (31.25%)			
occurrences (all)	5			
Lymphocyte Decreased				
subjects affected / exposed	2 / 16 (12.50%)			
occurrences (all)	4			
Monocyte count increased				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	3			
Urea Increased				
subjects affected / exposed	2 / 16 (12.50%)			
occurrences (all)	3			
Weight gain				
subjects affected / exposed	3 / 16 (18.75%)			
occurrences (all)	3			
Bilirubin increased				
subjects affected / exposed	2 / 16 (12.50%)			
occurrences (all)	3			
Creatinine increased				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	2			
Basophil count increased				
subjects affected / exposed	2 / 16 (12.50%)			
occurrences (all)	2			

Eosinophil count decreased				
subjects affected / exposed	2 / 16 (12.50%)			
occurrences (all)	2			
Platelets Increased				
subjects affected / exposed	2 / 16 (12.50%)			
occurrences (all)	2			
Weight loss				
subjects affected / exposed	2 / 16 (12.50%)			
occurrences (all)	2			
Creatine Phosphokinase Decreased				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	2			
Fibrinogen Increased				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Decreased Phosphate				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Total Protein Outside Normal Range				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
MCV Decreased				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Calcium Decreased				
subjects affected / exposed	2 / 16 (12.50%)			
occurrences (all)	2			
Gamma-Glutamyl Transferase Increased				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Total Protein Increased				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Creatinine Reactive Protein Increased				

subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
MCHC Decreased				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Sodium Decreased				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Creatinine Decrease				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	2			
Lymphocyte count increased				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Eosinophils Increased				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
White blood cell decreased				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Globulin Increased				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Protein Increased				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Hypophosphatemia				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Investigations - Other, not specified				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	3			
Neutrophil count decreased				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Monocytes Out Of Range				

subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Bruising			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	3		
Burn			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Fall			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Graze On Cheek 1.5M X7Mm			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Paresthesia			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Headache			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
Lethargy			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Tingling In Hands			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Neurotoxicity In Feet			

subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Shotty Lymph Nodes			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
Anemia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Palpable Lymph Node Right Axilla			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Leukocytosis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
V. Small Lymph Node Posterior Triangle R Side Neck			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Eye disorders			
Blurred vision			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	6		
Floaters			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Eye pain			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Occassional Visual Disturbance-Focussing			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Watering eyes			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Gastrointestinal disorders			

Nausea				
subjects affected / exposed	7 / 16 (43.75%)			
occurrences (all)	11			
Vomiting				
subjects affected / exposed	3 / 16 (18.75%)			
occurrences (all)	11			
Diarrhea				
subjects affected / exposed	6 / 16 (37.50%)			
occurrences (all)	8			
Constipation				
subjects affected / exposed	6 / 16 (37.50%)			
occurrences (all)	6			
Mucositis oral				
subjects affected / exposed	4 / 16 (25.00%)			
occurrences (all)	4			
Dyspepsia				
subjects affected / exposed	3 / 16 (18.75%)			
occurrences (all)	3			
Abdominal Cramp				
subjects affected / exposed	2 / 16 (12.50%)			
occurrences (all)	2			
Intermittent Diarrhea				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Oral hemorrhage				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Toothache				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Dry Mouth				
subjects affected / exposed	2 / 16 (12.50%)			
occurrences (all)	2			
Indigestion				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	2			

Fecal incontinence subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1			
Dental Extraction subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1			
Abdominal pain subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1			
Bloating subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1			
Rectal hemorrhage subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1			
Skin and subcutaneous tissue disorders Rash acneiform subjects affected / exposed occurrences (all)	8 / 16 (50.00%) 11			
Dry skin subjects affected / exposed occurrences (all)	7 / 16 (43.75%) 7			
Alopecia subjects affected / exposed occurrences (all)	5 / 16 (31.25%) 5			
Erythema multiforme subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 3			
Rash subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 3			
Folliculitis subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 2			
Cellulitis				

subjects affected / exposed	2 / 16 (12.50%)			
occurrences (all)	2			
Brittle Nails				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	2			
Rash maculo-papular				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	2			
Peeling Skin On Finger Tips				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Seborrheic Dermatitis Forehead				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Eczema				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Rash Legs And Face				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Pruritus				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Periorbital edema				
subjects affected / exposed	3 / 16 (18.75%)			
occurrences (all)	3			
Itchy Rash				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Itchy Skin				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Skin Rash Chest				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Rash On Chest And Back				

subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Leg Skin Erythema			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Spot or Rash On Chest And Back			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Renal and urinary disorders			
Pain When Urinating			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Muscle Pain			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Bone pain			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Infections and infestations			
Skin infection			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	3		
Chest Infection			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
Viral Load Detectable			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Upper respiratory infection			

subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Gum infection			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Eye infection			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Hyponatremia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
Hyperkalemia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Appetite Increased			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Hypocalcemia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Hypercalcemia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 December 2011	Rewording or amendment of text for clarification in the Treatment Details and Translational Research sections of the protocol.
30 March 2012	Trial Monitor contact details removed. Trials in the QA team are dealt with by various personnel within the team. Wording of exclusion criteria changed with reference to hepatitis B and C Clotting Studies clarified in text and assessment table Instructions for sites to send clinical photographs to the trial office mailbox Statistical section was redrafted for clarity.
11 October 2012	Updated Contact Details Clarified dose cohort safety teleconference Updated information regarding the continuation of patients on treatment past 12 months Amended Inclusion criterion to provide clarity Updated the Informed Consent Procedure. Updated link for HAART drug interactions Additional text added regarding HAART regimen and interactions with CYP3A Clarified the histology assessment ECHO/MUGA, Ophthalmology assessment and tumour biopsy moved from within 2 weeks of treatment to within 4 weeks of treatment). Corrected error in Phase II assessment table Clarified abnormal laboratory findings as adverse events Updated Case Report Form table Inserted the NHYA classification
26 February 2013	Alter eligibility criteria to include patients on Atazanavir, who have asymptomatic elevated levels of bilirubin, but normal liver function Clarify procedure for gaining approval from AstraZeneca for patient continuation past the standard 6 cycles of treatment Additional instructions added requesting that patients do not change HAART medication unless clinically necessary.
02 October 2013	Updated Contact Details; Dr Young and Professor Dockrell named as Clinical Coordinator and Deputy Clinical Coordinator, respectively. Trial Coordinator and Trial Administrator updated accordingly. Addition to/amendment of text regarding the expedited reporting of DLTs. Additional text added regarding the prompt return of Cycle 1 CRF copies. Corrected a minor error regarding the PBMC sample collection to match the Laboratory Manual. Minor formatting of reference section
09 December 2013	Altered eligibility criteria to exclude patients of Japanese ethnicity Metabolic side effects updated to include hypoalbuminaemia Date of Amendment 6 added to table Updated contact details for Registration of patients

10 December 2014	Updated Trial Contact and Registration details. Amended page numbering. Clarified that progression free survival data will be collected for each patient for 6 months from commencing treatment for analysis and for 12 months from completing treatment as supportive data Removed Japanese ethnicity from exclusion criteria Amended trial duration Rearranged a sentence to clarify the conditions required to raise the dose to level 3 during phase I Additional text added to phase I section to include DLT recording window and reflect that the MTD for selumetinib has been found as part of the completion of phase I Amended exclusion criteria as per AstraZeneca's guidance Added a section on the eligibility of Asian patients Added a section on Asian Pharmacokinetic Data Associated with Selumetinib. Amended text regarding vitamin E exposure Removed phase I assessments list and schedule table and amended text to reflect the successful completion of phase I Added windows for visits in phase II Clarified assessments patients should undergo when discontinuing selumetinib treatment Clarified definition of the follow-up period. Clarified reporting requirements for adverse events for conditions which change CTCAE grade since the previous visit Added ad hoc Haematology/ Clinical Chemistry Assessments Form and Post Treatment Adverse Event Follow-Up Form to CRF table). Clarified end of trial definition Changed Trial Steering Committee to Safety Review Committee. Added Frequency of DMC meetings and amended a spelling mistake. Correction of grammatical, formatting/ spelling errors. Added AEs of interstitial lung disease-like events and updated information regarding visual events Updated guidance for management of LVEF, dyspnoea, vision disorders, CK, diarrhoea and rashes Changed ECOG to WHO in line with IRAS form Added note to check Appendix 10 after Non-Haematologic Adverse Events section regarding elevated CK
29 June 2015	Added bullet point to 7.9.6 Post-Treatment Follow-Up: CT scans every 12 weeks for 12 months post end of treatment if visceral or extensive disease identified on baseline CT. Added sentence to 7.11 Patient Follow Up: plus additional CT scans if visceral or extensive disease identified on baseline CT.
01 December 2015	Removal of Co-Investigator from Trial Contacts and addition of Senior Trial Manager Removal of HIV physician from trial management team Added note clarifying reasons for discontinuation of treatment after one year: if disease progression and in opinion of Chief Investigator Added point to Concomitant medication section regarding interaction of grapefruit juice and St John's wort with HAART and selumetinib
10 March 2016	Change of Chief Investigator
03 February 2017	Change of End of Trial definition

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.

Trial closed due to poor recruitment a factor of which was the improvement in HIV treatment and fewer cases of Kaposi's Sarcoma.
Number of samples for translational research low and poor quality which limited analyses that could be performed.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/40108492