Clinical trial results:
A Phase 2 Study of SGI-110 in the Treatment of Advanced Hepatocellular Carcinoma (HCC) Subjects Who Failed Prior Treatment with Sorafenib

Summary

EudraCT number	2012-003977-24
Trial protocol	GB
Global end of trial date	20 August 2015

Results information

Result version number	v1 (current)
This version publication date	20 April 2018
First version publication date	20 April 2018

Trial information

Trial identification

Sponsor protocol code	SGI-110-03

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01752933
WHO universal trial number (UTN)	-
Other trial identifiers	IND: 116144

Notes:

Sponsors

Sponsor organisation name	Astex Pharmaceuticals Inc.
Sponsor organisation address	4420 Rosewood Drive, Suite 200, Pleasanton, California, United States, 94588
Public contact	Dr Harold Keer, Astex Pharmaceuticals Inc., 001 9257190741, Harold.Keer@astx.com
Scientific contact	Dr Harold Keer, Astex Pharmaceuticals Inc., 001 9257190741, Harold.Keer@astx.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	20 August 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 August 2015
Global end of trial reached?	Yes
Global end of trial date	20 August 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary:
*To assess the disease control rate (DCR) at 16 weeks for subjects treated with guadecitabine after failure of sorafenib.

Secondary:
*To assess the safety and tolerability of guadecitabine treatment as well as to determine the progressive-free survival (PFS) and overall survival (OS) of guadecitabine treatment.

*To determine alpha fetoprotein (AFP) response to guadecitabine treatment; the biological effect of guadecitabine on methylation of long interspersed nucleotide elements-1 (LINE-1) in blood and tumour tissue; the pharmacokinetics (PK) of guadecitabine and decitabine in subjects with HCC; and the methylation status, and re-expression of silenced genes, in particular tumour suppressor genes (TSGS) such as RASSF1A, SFRP, MZB1, P16 and others, after guadecitabine treatment.

*To explore baseline mutations status of certain genes such as p53, or the methylation status of selected genes in tumour tissue before & after treatment as predictive of response to therapy.

Protection of trial subjects:

The study was conducted in accordance with the International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) guidelines; the US 21 Code of Federal Regulations (CFR) Parts 50, 54, 56 and 312; local regulatory requirements; and the principles enunciated in the Declaration of Helsinki.

The Informed Consent Forms (ICFs) used for each study centre complied with ICH, the principles enunciated in the Declaration of Helsinki, local regulatory requirements and ICH GCP guidelines, and was approved by the sponsor and the investigator's Institutional Review Board (IRB)/Independent Ethics Committee (IEC). The investigator, or a person delegated by the investigator, explained the medical aspects of the study, including the nature and purpose of the study and treatment, the procedures involved and the potential benefits and risks. Other tasks in the informed consent process was delegated by the investigator. After having been informed that participation was voluntary and that subjects may withdraw from the study at any time, without prejudice, each subject signed the IRB/IEC-approved ICF prior to undergoing any study-specific procedures and enrolment in the study.

Background therapy:

In general, concomitant medications and therapies deemed necessary for the supportive care and safety of the subject were allowed, provided their use was documented in the subject records and on the appropriate case report form (CRF). If toxicity occurs, the appropriate treatment was used to ameliorate signs and symptoms. All supportive measures for optimal medical care were to be provided during the period of study.

Antibiotics could be utilised to prevent or manage febrile neutropenia based on institutional standard practice. Febrile neutropenia was defined as temperature at least 38.5ºC when the absolute neutrophil count (ANC) was < 1000 µL. Febrile subjects were to be evaluated by physical examination, complete blood count (CBC) with differential, and blood culture. Subjects with febrile neutropenia or suspected sepsis on the basis of the physical examination were to be hospitalised for appropriate broad spectrum antibiotic coverage, consistent with local pathogen sensitivities.

Granulocyte-colony stimulating factor (GCSF) and other white blood cell stimulating factors could be administered during Cycle 1 and onwards according to American Society for Clinical Oncology (ASCO) guidelines (Smith et al 2006), accepted practice or institutional guidelines, at the discretion of the treating physician. Red blood cell (RBC) transfusions could be administered at the discretion of the treating physician.

The administration of any other anticancer agents including chemotherapy and biologic agents was NOT permitted. Similarly, the use of other concurrent investigational drugs was not allowed. Locoregional therapies for treatment of hepatocellular carcinoma (HCC) were not permitted during the period of study.

Evidence for comparator:

Not applicable.

Actual start date of recruitment	15 April 2013
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	Canada: 7
Country: Number of subjects enrolled	United States: 45
Worldwide total number of subjects	52
EEA total number of subjects	0

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)	38
From 65 to 84 years	14
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 17 principal investigators at 17 study centres (15 in the US and 2 in Canada) enroled subjects in this study. The first subject was dosed with guadecitabine on 15 April 2013 and the last subject completed observation on 20 August 2015.

Pre-assignment

Screening details:

A total of 68 subjects were screened for enrolment in the study. Of these, 16 were screen failures and 52 were enroled. For 14 subjects, the reason for screen failure was that they did not meet all eligibility criteria; 2 subjects withdrew consent. Of the 52 subjects who were enroled, 50 received study drug.

Period 1

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

Arms

Arm title	Regimen

Arm description:

Guadecitabine administered by subcutaneous (SC) injection at a dose of 60 or 45 mg/m2/day on days 1 to 5 (daily x5) of every 28-day cycle.

Arm type	Experimental
Investigational medicinal product name	Guadecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Starting dose of 60 or 45 mg/m2 on day 1 to 5 daily of every 28-day cycle, administered subcutaneously by injection.

Number of subjects in period 1	Regimen
Started	52
Completed	50
Not completed	2
Subject died prior to being treated	1
Subject no longer met eligibility criteria	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial period
Reporting group description: -	

Reporting group values	Overall trial period	Total	
Number of subjects	52	52	
Age categorical 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)	38	38	
From 65-84 years	14	14	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	7	7	
Male	45	45	

Subject analysis sets	
Subject analysis set title	Guadecitabine, 60 mg/m2
Subject analysis set type	Full analysis
Subject analysis set description: Guadecitabine, 60 mg/m2 SC once daily on days 1 to 5 every 28-day cycle	
Subject analysis set title	Guadecitabine, 45 mg/m2
Subject analysis set type	Full analysis
Subject analysis set description: Guadecitabine, 45 mg/m2 SC once daily on days 1 to 5 every 28-day cycle	

Reporting group values	Guadecitabine, 60 mg/m2	Guadecitabine, 45 mg/m2	
Number of subjects	4	46	
Age categorical 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	33	

From 65-84 years	0	13	
85 years and over	0	0	

Gender categorical Units: Subjects			
Female	0	7	
Male	4	39	

End points

End points reporting groups

Reporting group title	Regimen
Reporting group description:	
Guadecitabine administered by subcutaneous (SC) injection at a dose of 60 or 45 mg/m2/day on days 1 to 5 (daily x5) of every 28-day cycle.	
Subject analysis set title	Guadecitabine, 60 mg/m2
Subject analysis set type	Full analysis
Subject analysis set description:	
Guadecitabine, 60 mg/m2 SC once daily on days 1 to 5 every 28-day cycle	
Subject analysis set title	Guadecitabine, 45 mg/m2
Subject analysis set type	Full analysis
Subject analysis set description:	
Guadecitabine, 45 mg/m2 SC once daily on days 1 to 5 every 28-day cycle	

Primary: Disease Control Rate (DCR)

End point title	Disease Control Rate (DCR)[1]
End point description:	
DCR at 16 weeks, defined as percentage of subjects who achieved a best clinical response of complete response (CR) or partial response (PR), plus subjects who had stable disease at 16 weeks using RECIST v1.1 criteria.	
End point type	Primary
End point timeframe:	
Subjects were encouraged to remain on treatment for at least 16 weeks, unless they developed unacceptable toxicity or unequivocal and symptomatic clinical progression that required the use of another anticancer treatment.	

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: Only the descriptive statistics are reported here.

End point values	Regimen	Guadecitabine, 60 mg/m2	Guadecitabine, 45 mg/m2	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	45	4	41	
Units: percent				
number (confidence interval 95%)				
DCR	24.4 (12.9 to 39.5)	25 (0.6 to 80.6)	24.4 (12.4 to 40.3)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
All adverse events and serious adverse events mentioned in the safety section of this report are treatment-emergent adverse events.	
Adverse event reporting additional description:	
NOTE: Only one occurrence per preferred term is reported in the tables below.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	14

Reporting groups	
Reporting group title	60 mg/m2
Reporting group description:	
Guadecitabine, 60 mg/m2 SC once daily on days 1 to 5 every 28-day cycle	
Reporting group title	45 mg/m2
Reporting group description:	
Guadecitabine, 60 mg/m2 SC once daily on days 1 to 5 every 28-day cycle	

Serious adverse events	60 mg/m2	45 mg/m2	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)	21 / 46 (45.65%)	
number of deaths (all causes)	4	34	
number of deaths resulting from adverse events	0	2	
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 4 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Scrotal pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Hypoxia			

subjects affected / exposed	0 / 4 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 4 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Road traffic accident			
subjects affected / exposed	0 / 4 (0.00%)	2 / 46 (4.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 4 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Hepatic encephalopathy			
subjects affected / exposed	0 / 4 (0.00%)	1 / 46 (2.17%)	
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			
Febrile neutropenia			
subjects affected / exposed	1 / 4 (25.00%)	5 / 46 (10.87%)	
occurrences causally related to treatment / all	1 / 1	5 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			

subjects affected / exposed	0 / 4 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)	2 / 46 (4.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	0 / 4 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 4 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 4 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	0 / 4 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Portal vein thrombosis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	0 / 4 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Endocrine disorders			
Adrenal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 4 (0.00%)	2 / 46 (4.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			

subjects affected / exposed	0 / 4 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 46 (2.17%)	
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	60 mg/m2	45 mg/m2	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	46 / 46 (100.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 4 (0.00%)	8 / 46 (17.39%)	
occurrences (all)	0	8	
Hypotension			
subjects affected / exposed	0 / 4 (0.00%)	5 / 46 (10.87%)	
occurrences (all)	0	5	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 4 (75.00%)	24 / 46 (52.17%)	
occurrences (all)	3	24	
Oedema peripheral			
subjects affected / exposed	1 / 4 (25.00%)	9 / 46 (19.57%)	
occurrences (all)	1	9	
Pyrexia			
subjects affected / exposed	1 / 4 (25.00%)	9 / 46 (19.57%)	
occurrences (all)	1	9	

Chills			
subjects affected / exposed	0 / 4 (0.00%)	5 / 46 (10.87%)	
occurrences (all)	0	5	
Early satiety			
subjects affected / exposed	0 / 4 (0.00%)	3 / 46 (6.52%)	
occurrences (all)	0	3	
Injection site erythema			
subjects affected / exposed	2 / 4 (50.00%)	3 / 46 (6.52%)	
occurrences (all)	2	3	
Injection site haematoma			
subjects affected / exposed	1 / 4 (25.00%)	3 / 46 (6.52%)	
occurrences (all)	1	3	
Mucosal inflammation			
subjects affected / exposed	1 / 4 (25.00%)	2 / 46 (4.35%)	
occurrences (all)	1	2	
Injection site pain			
subjects affected / exposed	2 / 4 (50.00%)	21 / 46 (45.65%)	
occurrences (all)	2	21	
Injection site reaction			
subjects affected / exposed	0 / 4 (0.00%)	6 / 46 (13.04%)	
occurrences (all)	0	6	
Non-cardiac chest pain			
subjects affected / exposed	1 / 4 (25.00%)	2 / 46 (4.35%)	
occurrences (all)	1	2	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 4 (25.00%)	12 / 46 (26.09%)	
occurrences (all)	1	12	
Dyspnoea			
subjects affected / exposed	1 / 4 (25.00%)	6 / 46 (13.04%)	
occurrences (all)	1	6	
Oropharyngeal pain			
subjects affected / exposed	0 / 4 (0.00%)	3 / 46 (6.52%)	
occurrences (all)	0	3	
Psychiatric disorders			

Insomnia			
subjects affected / exposed	1 / 4 (25.00%)	4 / 46 (8.70%)	
occurrences (all)	1	4	
Mental status changes			
subjects affected / exposed	0 / 4 (0.00%)	3 / 46 (6.52%)	
occurrences (all)	0	3	
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 4 (25.00%)	14 / 46 (30.43%)	
occurrences (all)	1	14	
Alanine aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	8 / 46 (17.39%)	
occurrences (all)	0	8	
Hypoalbuminaemia			
subjects affected / exposed	0 / 4 (0.00%)	3 / 46 (6.52%)	
occurrences (all)	0	3	
Weight decreased			
subjects affected / exposed	0 / 4 (0.00%)	4 / 46 (8.70%)	
occurrences (all)	0	4	
Weight increased			
subjects affected / exposed	0 / 4 (0.00%)	3 / 46 (6.52%)	
occurrences (all)	0	3	
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 4 (25.00%)	10 / 46 (21.74%)	
occurrences (all)	1	10	
Blood bilirubin increased			
subjects affected / exposed	0 / 4 (0.00%)	4 / 46 (8.70%)	
occurrences (all)	0	4	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 4 (0.00%)	3 / 46 (6.52%)	
occurrences (all)	0	3	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 4 (50.00%)	6 / 46 (13.04%)	
occurrences (all)	2	6	

Dizziness			
subjects affected / exposed	1 / 4 (25.00%)	6 / 46 (13.04%)	
occurrences (all)	1	6	
Neuropathy peripheral			
subjects affected / exposed	0 / 4 (0.00%)	3 / 46 (6.52%)	
occurrences (all)	0	3	
Dysgeusia			
subjects affected / exposed	2 / 4 (50.00%)	1 / 46 (2.17%)	
occurrences (all)	2	1	
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	1 / 4 (25.00%)	21 / 46 (45.65%)	
occurrences (all)	1	21	
Anaemia			
subjects affected / exposed	1 / 4 (25.00%)	11 / 46 (23.91%)	
occurrences (all)	1	11	
Lymphopenia			
subjects affected / exposed	0 / 4 (0.00%)	10 / 46 (21.74%)	
occurrences (all)	0	10	
Thrombocytopenia			
subjects affected / exposed	4 / 4 (100.00%)	20 / 46 (43.48%)	
occurrences (all)	4	20	
Neutropenia			
subjects affected / exposed	4 / 4 (100.00%)	39 / 46 (84.78%)	
occurrences (all)	4	39	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 4 (50.00%)	11 / 46 (23.91%)	
occurrences (all)	2	11	
Nausea			
subjects affected / exposed	2 / 4 (50.00%)	11 / 46 (23.91%)	
occurrences (all)	2	11	
Abdominal pain			
subjects affected / exposed	1 / 4 (25.00%)	8 / 46 (17.39%)	
occurrences (all)	1	8	
Constipation			

subjects affected / exposed	0 / 4 (0.00%)	11 / 46 (23.91%)	
occurrences (all)	0	11	
Vomiting			
subjects affected / exposed	1 / 4 (25.00%)	9 / 46 (19.57%)	
occurrences (all)	1	9	
Abdominal distension			
subjects affected / exposed	0 / 4 (0.00%)	7 / 46 (15.22%)	
occurrences (all)	0	7	
Abdominal pain upper			
subjects affected / exposed	1 / 4 (25.00%)	4 / 46 (8.70%)	
occurrences (all)	1	4	
Ascites			
subjects affected / exposed	0 / 4 (0.00%)	3 / 46 (6.52%)	
occurrences (all)	0	3	
Stomatitis			
subjects affected / exposed	1 / 4 (25.00%)	3 / 46 (6.52%)	
occurrences (all)	1	3	
Abdominal discomfort			
subjects affected / exposed	1 / 4 (25.00%)	2 / 46 (4.35%)	
occurrences (all)	1	2	
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 4 (0.00%)	5 / 46 (10.87%)	
occurrences (all)	0	5	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 4 (0.00%)	5 / 46 (10.87%)	
occurrences (all)	0	5	
Pruritus			
subjects affected / exposed	0 / 4 (0.00%)	3 / 46 (6.52%)	
occurrences (all)	0	3	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 4 (25.00%)	10 / 46 (21.74%)	
occurrences (all)	1	10	
Pain in extremity			

subjects affected / exposed	1 / 4 (25.00%)	5 / 46 (10.87%)	
occurrences (all)	1	5	
Arthralgia			
subjects affected / exposed	1 / 4 (25.00%)	5 / 46 (10.87%)	
occurrences (all)	1	5	
Neck pain			
subjects affected / exposed	0 / 4 (0.00%)	3 / 46 (6.52%)	
occurrences (all)	0	3	
Bone pain			
subjects affected / exposed	2 / 4 (50.00%)	2 / 46 (4.35%)	
occurrences (all)	2	2	
Myalgia			
subjects affected / exposed	1 / 4 (25.00%)	2 / 46 (4.35%)	
occurrences (all)	1	2	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	4 / 46 (8.70%)	
occurrences (all)	0	4	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 4 (25.00%)	9 / 46 (19.57%)	
occurrences (all)	1	9	
Hyperglycaemia			
subjects affected / exposed	0 / 4 (0.00%)	7 / 46 (15.22%)	
occurrences (all)	0	7	
Hyponatraemia			
subjects affected / exposed	0 / 4 (0.00%)	6 / 46 (13.04%)	
occurrences (all)	0	6	
Hyperkalaemia			
subjects affected / exposed	0 / 4 (0.00%)	3 / 46 (6.52%)	
occurrences (all)	0	3	
Hypocalcaemia			
subjects affected / exposed	0 / 4 (0.00%)	3 / 46 (6.52%)	
occurrences (all)	0	3	
Hypoglycaemia			

subjects affected / exposed	0 / 4 (0.00%)	3 / 46 (6.52%)	
occurrences (all)	0	3	
Hypokalaemia			
subjects affected / exposed	0 / 4 (0.00%)	3 / 46 (6.52%)	
occurrences (all)	0	3	
Hypomagnesaemia			
subjects affected / exposed	0 / 4 (0.00%)	3 / 46 (6.52%)	
occurrences (all)	0	3	
Hypophosphataemia			
subjects affected / exposed	0 / 4 (0.00%)	4 / 46 (8.70%)	
occurrences (all)	0	4	
Hyperalbuminaemia			
subjects affected / exposed	0 / 4 (0.00%)	5 / 46 (10.87%)	
occurrences (all)	0	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 August 2013	Amendment 1: The main changes in Amendment 1 were: 1. To add pharmacokinetic blood sampling in a target of 16 subjects in total from both Stages 1 and 2 in Cycle 1, Day 1 in order to determine the PK of SGI-110 and decitabine in subjects with HCC, and 2. To have a lower starting dose of SGI-110 of 45 mg/m2 from 60 mg/m2 originally based on findings from the Data and Safety Review Committee after review of safety data from the first 4 subjects treated.

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.

None reported.

Notes: