Clinical trial results:
An open label continuation study of oral AKT inhibitor GSK2110183 in subjects with solid
tumors and hematologic malignancies.

Summary

EudraCT number	2014-002041-22
Trial protocol	IE
Global end of trial date	20 June 2018

Results information

Result version number	v1 (current)
This version publication date	06 July 2019
First version publication date	06 July 2019

Trial information

Trial identification

Sponsor protocol code	115131 (CASB183X2X01B)

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01531894
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma, AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma, AG, +41 316241111, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma, AG, +41 316241111, novartis.email@novartis.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 June 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 June 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to provide treatment with afuresertib for subjects who had previously participated in an afuresertib study sponsored previously by GlaxoSmithKline (GSK) or Novartis or another research organization working on behalf of Novartis.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 February 2012
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	Australia: 4
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Ireland: 2
Country: Number of subjects enrolled	Korea, Republic of: 2
Country: Number of subjects enrolled	United States: 1
Worldwide total number of subjects	11
EEA total number of subjects	2

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)	6
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

As this was a rollover study, there was no planned number of subjects. Eleven subjects were enrolled and analyzed in the study.

Pre-assignment

Screening details:

There was no planned duration of treatment as this was a rollover study. The subjects could permanently discontinue the study treatment due to protocol deviation, adverse event, disease progression, withdrawal of consent, Investigator's discretion, lost to follow-up, termination of study or death.

Period 1

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

Arms

Arm title	GSK2110183 (afuresertib)

Arm description:

All patients received the GSK2110183 (afuresertib) treatment

Arm type	Experimental
Investigational medicinal product name	GSK2110183 (afuresertib)
Investigational medicinal product code	afuresertib
Other name	ASB183
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Afuresertib is an oral, low nanomolar pan-AKT kinase inhibitor immediate release (IR) 50 mg or 75 mg tablets was to be taken orally with at least 200 mL of water, with or without food, in the morning.

Number of subjects in period 1	GSK2110183 (afuresertib)
Started	11
Completed	2
Not completed	9
Adverse event, serious fatal	1
Physician decision	8

Baseline characteristics

Reporting groups	
Reporting group title	GSK2110183 (afuresertib)
Reporting group description:	
All patients received the GSK2110183 (afuresertib) treatment	

Reporting group values	GSK2110183 (afuresertib)	Total	
Number of subjects	11	11	
Age categorical Units: Subjects			
Adults (18-64 years)	6	6	
From 65-84 years	5	5	
Age Continuous Units: Years			
arithmetic mean	60.1		
standard deviation	± 14.00	-	
Sex: Female, Male Units: Subjects			
Female	8	8	
Male	3	3	
Race/Ethnicity, Customized Units: Subjects			
Asian - East Asian heritage	2	2	
White - White/Caucasian/European heritage	9	9	

End points

End points reporting groups

Reporting group title	GSK2110183 (afuresertib)

Reporting group description:

All patients received the GSK2110183 (afuresertib) treatment

Primary: Number of participants with at least one Adverse Events (AEs)

End point title	Number of participants with at least one Adverse Events

End point description:

Adverse Events (AEs) includes Summary of adverse events, drug related AEs, Serious adverse events, adverse events leading to study treatment discontinuation and death.

End point type	Primary

End point timeframe:

from the time of consent until the final study visit up to approx. 76 months

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: No statistical analysis was planned for this endpoint.

End point values	GSK2110183 (afuresertib)			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: Participants	11			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events and serious adverse events were collected for the maximum actual duration of treatment exposure and follow up for a participant per the protocol for approximately 2239 days.

Adverse event reporting additional description:

All cause mortality (deaths) was collected for as long as participants could be contacted from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV) up to a maximum of about 76 months.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	All Patients

Reporting group description:

All Patients

Serious adverse events	All Patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 11 (18.18%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 1		

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

Non-serious adverse events	All Patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 11 (100.00%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Raynaud's phenomenon			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Chest discomfort			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	2		
Fatigue			
subjects affected / exposed	5 / 11 (45.45%)		
occurrences (all)	5		
Oedema			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Oedema peripheral			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Peripheral swelling			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 11 (27.27%)		
occurrences (all)	4		
Dyspnoea			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		

Epistaxis subjects affected / exposed occurrences (all) Nasal congestion subjects affected / exposed occurrences (all)	 2 / 11 (18.18%) 2 2 / 11 (18.18%) 2		
Cardiac disorders Palpitations subjects affected / exposed occurrences (all)	 1 / 11 (9.09%) 1		
Nervous system disorders Ageusia subjects affected / exposed occurrences (all) Anosmia subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Paraesthesia subjects affected / exposed occurrences (all)	 1 / 11 (9.09%) 1 1 / 11 (9.09%) 1 1 / 11 (9.09%) 1 1 / 11 (9.09%) 2		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Lymphopenia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all)	 1 / 11 (9.09%) 1 1 / 11 (9.09%) 1 2 / 11 (18.18%) 2		
Ear and labyrinth disorders Ear discomfort subjects affected / exposed occurrences (all)	 1 / 11 (9.09%) 1		

Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Abdominal distension			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	7 / 11 (63.64%)		
occurrences (all)	18		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Large intestine polyp			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	4		
Oesophageal discomfort			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Oesophageal pain			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Tooth disorder			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	4		
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Pruritus			

subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	2		
Pruritus generalised			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Skin ulcer			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Renal and urinary disorders			
Micturition urgency			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Nephrolithiasis			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Foot deformity			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Muscle spasms			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Temporomandibular joint syndrome			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Infections and infestations			
Chronic sinusitis			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Conjunctivitis			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Helicobacter infection			

subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Respiratory tract infection			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Tooth infection			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	9		
Urinary tract infection			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	5		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	2		
Hyperglycaemia			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 November 2011	Added disease assessments to the section 'Transition Visit'; Removed central lab wording from 'Clinical Laboratory Assessments' because central labs were not used; Incorporated liver function tests into the clinical chemistries table to insure that liver function tests were to be administered whenever clinical chemistries were due; Updated the AE monitoring language to mention that the AEs will be monitored till the final study visit.; Updated to mention that the subject must be withdrawn from the study if there was a third dose reduction or reduction of dose below 75 mg; Added standard acetaminophen protein adduct testing to liver event follow-up assessments; Updated the list of prohibited and cautionary medications; Updated the section for non-drug therapies to mention that the administration of herbal medication (which was prohibited during study) was to be recorded in the eCRF; Added definition of disease state, response criteria and response definition for Langerhans cell histocytosis (LCH)
30 September 2014	IR tablet description was added because the formulation was changed to tablet from capsule. The protocol description, synopsis, study treatments and dosage/administration sections were all updated to reflect this change; The introduction, summary of risk management, supportive measures for hyperglycemia, management of diarrhea, rash, dyspepsia, mucositis, liver chemistry stopping criteria, drug restart/rechallenge, con meds and non-drug therapies, meals and dietary restrictions and liver safety drug restart guidelines sections have all been updated with the latest information; Multiple myeloma specific disease assessments were added; AE follow-up was shortened to 30 days.
31 March 2016	After the acquisition of GSK compound GSK2110183 (afuresertib), the purpose of this protocol Amendment 03 was to: Delete or replace references to GSK or its staff with that of Novartis and its authorized agents to align with the change of sponsorship; Make administrative changes to align with Novartis processes and procedures.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported