Clinical trial results:
An open label two-stage study of orally administered BKM120 in patients with metastatic non-small cell lung cancer (NSCLC) with activated phosphatidylinositol 3-kinase (PI3K) pathway

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2010-024011-14
Trial protocol	GB BE HU DE NL IT ES
Global end of trial date	31 October 2014

Results information

Result version number	v1 (current)
This version publication date	05 May 2016
First version publication date	05 May 2016

Trial information

Trial identification

Sponsor protocol code	CBKM120D2201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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, 41 613241111,
Scientific contact	Study Director, Novartis Pharma AG, 41 613241000,
Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,

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	31 October 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 October 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Stage 1: To assess futility using progression free survival (PFS) rate at 12 weeks of buparlisib treatment within each histological group i.e. squamous and non-squamous
Stage 2: To evaluate the efficacy of buparlisib compared to chemotherapy based on PFS within each histological group as measured using response evaluation criteria in solid tumors
(RECIST 1.1) criteria

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	12 May 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	Argentina: 1
Country: Number of subjects enrolled	Belgium: 11
Country: Number of subjects enrolled	Brazil: 2
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	Hungary: 4
Country: Number of subjects enrolled	Italy: 11
Country: Number of subjects enrolled	Japan: 4
Country: Number of subjects enrolled	Singapore: 1
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	Taiwan: 2
Country: Number of subjects enrolled	United States: 8
Worldwide total number of subjects	63
EEA total number of subjects	44

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)	31
From 65 to 84 years	32
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

All patients were to receive buparlisib in Stage 1.

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

Are arms mutually exclusive?	Yes
Arm title	Squamous BKM120 100mg qd

Arm description:

Diagnosed patients with non-small cell lung cancer (NSCLC) that progressed after one prior, platinum-based chemotherapy line for metastatic disease.

Arm type	Experimental
Investigational medicinal product name	buparlisib
Investigational medicinal product code	BKM120
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Diagnosed patients with non-small cell lung cancer (NSCLC) that progressed after one prior, platinum-based chemotherapy line for metastatic disease.

Arm title	Non-Squamous BKM120 100mg qd

Arm description:

Diagnosed patients with non-squamous NSCLC that progressed after one or two prior antineoplastic therapy lines for metastatic disease.

Arm type	Experimental
Investigational medicinal product name	buparlisib
Investigational medicinal product code	BKM120
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Diagnosed patients with non-small cell lung cancer (NSCLC) that progressed after one prior, platinum-based chemotherapy line for metastatic disease.

Number of subjects in period 1	Squamous BKM120 100mg qd	Non-Squamous BKM120 100mg qd
Started	30	33
Completed	0	0
Not completed	30	33
Adverse event, serious fatal	2	1
Physician decision	3	2
Adverse event, non-fatal	11	6
Patient/Guardian decision	3	4
Progressive disease	11	20

Baseline characteristics

Reporting groups	
Reporting group title	Squamous BKM120 100mg qd
Reporting group description:	
Diagnosed patients with non-small cell lung cancer (NSCLC) that progressed after one prior, platinum-based chemotherapy line for metastatic disease.	
Reporting group title	Non-Squamous BKM120 100mg qd
Reporting group description:	
Diagnosed patients with non-squamous NSCLC that progressed after one or two prior antineoplastic therapy lines for metastatic disease.	

Reporting group values	Squamous BKM120 100mg qd	Non-Squamous BKM120 100mg qd	Total
Number of subjects	30	33	63
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	12	19	31
From 65-84 years	18	14	32
85 years and over	0	0	0
Age continuous Units: years			
median	65.1	61.2	
standard deviation	± 8.17	± 10.44	-
Gender, Male/Female Units: Participants			
Female	9	14	23
Male	21	19	40
Age, Customized Units: Subjects			
< 65 years	12	19	31
>= 65 years	18	14	32

End points

End points reporting groups

Reporting group title	Squamous BKM120 100mg qd
Reporting group description:	
Diagnosed patients with non-small cell lung cancer (NSCLC) that progressed after one prior, platinum-based chemotherapy line for metastatic disease.	
Reporting group title	Non-Squamous BKM120 100mg qd
Reporting group description:	
Diagnosed patients with non-squamous NSCLC that progressed after one or two prior antineoplastic therapy lines for metastatic disease.	

Primary: Progression Free Survival (PFS) rate as per Investigator local review measured using RECIST 1.1 of patients at week 12

End point title	Progression Free Survival (PFS) rate as per Investigator local review measured using RECIST 1.1 of patients at week 12[1]
End point description:	
PFS rate was defined as the percentage of participants who were progression free at 12 weeks. Participants were considered as a "success" for PFS rate evaluated at 12 weeks if they presented an overall response at their 2nd post-baseline tumor assessment.The enrollment into the study in either histology group would stop for futility if a PFS rate <50% at 12 weeks was observed. No statistical analysis was planned for this primary outcome. The results of the primary objective was based on the data from the interim analysis that took place at the cut off dates: 10-Apr-2013 for non-squamous and 08-Jan-2014 for squamous group.	
End point type	Primary
End point timeframe:	
Week 12	

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: There was no statistical analysis done for this study as it met futility at stage 1 and so stage 2 was not started.

End point values	Squamous BKM120 100mg qd	Non-Squamous BKM120 100mg qd		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	30		
Units: Percentage of participants				
number (confidence interval 95%)	23.3 (9.9 to 42.3)	20 (7.7 to 38.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) using Kaplan-Meier estimates

End point title	Overall Survival (OS) using Kaplan-Meier estimates
End point description:	
OS was defined as the time from start of study drug (Stage 1) until death from any cause. If a patient was not known to have died, survival was censored at the date of last contact.	

End point type	Secondary

End point timeframe:

Every 8 weeks up to 24 months

End point values	Squamous BKM120 100mg qd	Non-Squamous BKM120 100mg qd		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	33		
Units: Months				
median (confidence interval 95%)	7.98 (5.95 to 10.09)	7.2 (4.01 to 9.92)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate (ORR) based on Investigator assessment

End point title	Overall Response Rate (ORR) based on Investigator assessment

End point description:

ORR was defined as the percentage of participants with best overall response of complete response (CR) or partial response (PR). Complete response was defined as disappearance of all non-nodal target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to < 10 mm. Partial response was defined as at least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters. Analyses of response rates were performed based on investigators' assessments (as per RECIST 1.1 criteria). ORR included all patients with and without measurable disease at baseline.

End point type	Secondary

End point timeframe:

Every 6 weeks up to 24 months

End point values	Squamous BKM120 100mg qd	Non-Squamous BKM120 100mg qd		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	33		
Units: Percentage of participants				
number (not applicable)	3.3	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR)

End point title	Disease Control Rate (DCR)

End point description:

DCR defined as the percentage of participants with best overall response of CR or PR or stable disease (SD). Complete response was defined as disappearance of all non-nodal target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to < 10 mm. Partial response was defined as at least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters. Stable Disease (SD): Neither sufficient shrinkage to qualify for PR or CR nor an increase in lesions which would qualify for PD. Analyses of response rates were performed based on investigators' assessments (as per RECIST 1.1 criteria). DCR included all participants with and without measurable disease at baseline.

End point type	Secondary

End point timeframe:

Every 6 weeks up tp 24 months

End point values	Squamous BKM120 100mg qd	Non-Squamous BKM120 100mg qd		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	33		
Units: Percentage of participants				
number (not applicable)	46.7	45.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response (TTR)

End point title	Time to Response (TTR)

End point description:

TTR for a participant was defined as the time from the first treatment date to the date of first documented confirmed CR or PR evaluation. The date of event was defined as the date of response that was first determined and not using the date the response was confirmed.

End point type	Secondary

End point timeframe:

Every 6 weeks up to 24 months

End point values	Squamous BKM120 100mg qd	Non-Squamous BKM120 100mg qd		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	33		
Units: Days	41	42		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR)

End point title	Duration of Response (DoR)

End point description:

DoR was defined as the elapsed time between the date of first documented CR or PR response (not the date of confirmed response) and the following date of event defined as the first documented progression or death due to underlying cancer.

End point type	Secondary

End point timeframe:

Every 6 weeks up to 24 months

End point values	Squamous BKM120 100mg qd	Non-Squamous BKM120 100mg qd		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	33		
Units: Days	73	85		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit.

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Non-Squamous@BKM120@100 mg qd

Reporting group description:

Diagnosed patients with non-squamous NSCLC that progressed after one or two prior antineoplastic therapy lines for metastatic disease.

Reporting group title	Squamous@BKM120@100 mg qd

Reporting group description:

Diagnosed patients with non-small cell lung cancer (NSCLC) that progressed after one prior, platinum-based chemotherapy line for metastatic disease.

Serious adverse events	Non-Squamous@BKM120@100 mg qd	Squamous@BKM120@100 mg qd	
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 33 (45.45%)	16 / 30 (53.33%)	
number of deaths (all causes)	5	4	
number of deaths resulting from adverse events	0	2	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
TUMOUR PAIN			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vascular disorders			
THROMBOSIS			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			

FATIGUE			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ASTHENIA			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	0 / 33 (0.00%)	4 / 30 (13.33%)	
occurrences causally related to treatment / all	0 / 0	2 / 4	
deaths causally related to treatment / all	0 / 0	1 / 2	
PERIPHERAL SWELLING			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
ACUTE PULMONARY OEDEMA			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
EPISTAXIS			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSPNOEA			
subjects affected / exposed	3 / 33 (9.09%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	

HAEMOPTYSIS			
subjects affected / exposed	1 / 33 (3.03%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
HYPOXIA			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONITIS			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY FAILURE			
subjects affected / exposed	3 / 33 (9.09%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Investigations			
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
CARDIAC FAILURE			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIOGENIC SHOCK			

subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CEREBRAL ISCHAEMIA			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
BLEPHARITIS			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
ENTERITIS			

subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIARRHOEA			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ILEUS			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
HEPATITIS TOXIC			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
DERMATITIS ALLERGIC			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
RASH			
subjects affected / exposed	1 / 33 (3.03%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RASH MACULAR			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
MUSCULOSKELETAL PAIN			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

PAIN IN EXTREMITY			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ESCHERICHIA SEPSIS			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
LUNG ABSCESS			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY TRACT INFECTION			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEPSIS			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA			
subjects affected / exposed	1 / 33 (3.03%)	3 / 30 (10.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
LUNG INFECTION			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

URINARY TRACT INFECTION PSEUDOMONAL			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
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 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERGLYCAEMIA			
subjects affected / exposed	3 / 33 (9.09%)	2 / 30 (6.67%)	
occurrences causally related to treatment / all	3 / 3	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEHYDRATION			
subjects affected / exposed	0 / 33 (0.00%)	2 / 30 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Non-Squamous@BKM120 @100 mg qd	Squamous@BKM120 @100 mg qd	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 33 (96.97%)	29 / 30 (96.67%)	
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	2 / 33 (6.06%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
HYPOTENSION			
subjects affected / exposed	2 / 33 (6.06%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
General disorders and administration site conditions			
FATIGUE			
subjects affected / exposed	6 / 33 (18.18%)	11 / 30 (36.67%)	
occurrences (all)	6	12	

ASTHENIA			
subjects affected / exposed	12 / 33 (36.36%)	6 / 30 (20.00%)	
occurrences (all)	14	7	
HYPOTHERMIA			
subjects affected / exposed	2 / 33 (6.06%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
OEDEMA PERIPHERAL			
subjects affected / exposed	1 / 33 (3.03%)	3 / 30 (10.00%)	
occurrences (all)	1	3	
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	1 / 33 (3.03%)	3 / 30 (10.00%)	
occurrences (all)	1	3	
PAIN			
subjects affected / exposed	2 / 33 (6.06%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
PYREXIA			
subjects affected / exposed	4 / 33 (12.12%)	2 / 30 (6.67%)	
occurrences (all)	5	2	
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	7 / 33 (21.21%)	6 / 30 (20.00%)	
occurrences (all)	9	6	
DYSPNOEA			
subjects affected / exposed	7 / 33 (21.21%)	6 / 30 (20.00%)	
occurrences (all)	7	8	
HAEMOPTYSIS			
subjects affected / exposed	2 / 33 (6.06%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
PNEUMONITIS			
subjects affected / exposed	0 / 33 (0.00%)	3 / 30 (10.00%)	
occurrences (all)	0	3	
PRODUCTIVE COUGH			
subjects affected / exposed	2 / 33 (6.06%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
Psychiatric disorders			

CONFUSIONAL STATE			
subjects affected / exposed	1 / 33 (3.03%)	3 / 30 (10.00%)	
occurrences (all)	1	4	
ANXIETY			
subjects affected / exposed	8 / 33 (24.24%)	3 / 30 (10.00%)	
occurrences (all)	8	3	
DEPRESSION			
subjects affected / exposed	11 / 33 (33.33%)	4 / 30 (13.33%)	
occurrences (all)	11	4	
MOOD ALTERED			
subjects affected / exposed	4 / 33 (12.12%)	2 / 30 (6.67%)	
occurrences (all)	5	2	
INSOMNIA			
subjects affected / exposed	2 / 33 (6.06%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	6 / 33 (18.18%)	6 / 30 (20.00%)	
occurrences (all)	6	8	
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	6 / 33 (18.18%)	5 / 30 (16.67%)	
occurrences (all)	7	7	
BLOOD UREA INCREASED			
subjects affected / exposed	0 / 33 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
subjects affected / exposed	2 / 33 (6.06%)	3 / 30 (10.00%)	
occurrences (all)	3	3	
BLOOD LACTATE DEHYDROGENASE INCREASED			
subjects affected / exposed	2 / 33 (6.06%)	2 / 30 (6.67%)	
occurrences (all)	2	2	
BLOOD GLUCOSE INCREASED			
subjects affected / exposed	1 / 33 (3.03%)	2 / 30 (6.67%)	
occurrences (all)	1	2	

BLOOD CREATININE INCREASED			
subjects affected / exposed	1 / 33 (3.03%)	2 / 30 (6.67%)	
occurrences (all)	1	3	
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	1 / 33 (3.03%)	3 / 30 (10.00%)	
occurrences (all)	1	3	
INSULIN C-PEPTIDE INCREASED			
subjects affected / exposed	2 / 33 (6.06%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
TRANSAMINASES INCREASED			
subjects affected / exposed	2 / 33 (6.06%)	2 / 30 (6.67%)	
occurrences (all)	2	2	
WEIGHT DECREASED			
subjects affected / exposed	3 / 33 (9.09%)	8 / 30 (26.67%)	
occurrences (all)	3	8	
Cardiac disorders			
SINUS TACHYCARDIA			
subjects affected / exposed	0 / 33 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	1 / 33 (3.03%)	2 / 30 (6.67%)	
occurrences (all)	1	2	
SOMNOLENCE			
subjects affected / exposed	2 / 33 (6.06%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
NEUROPATHY PERIPHERAL			
subjects affected / exposed	2 / 33 (6.06%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
MYOCLONUS			
subjects affected / exposed	0 / 33 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
MEMORY IMPAIRMENT			
subjects affected / exposed	0 / 33 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	3	
HEADACHE			

subjects affected / exposed	0 / 33 (0.00%)	4 / 30 (13.33%)	
occurrences (all)	0	4	
DYSGEUSIA			
subjects affected / exposed	4 / 33 (12.12%)	4 / 30 (13.33%)	
occurrences (all)	4	4	
TREMOR			
subjects affected / exposed	1 / 33 (3.03%)	4 / 30 (13.33%)	
occurrences (all)	1	4	
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	2 / 33 (6.06%)	5 / 30 (16.67%)	
occurrences (all)	2	5	
THROMBOCYTOPENIA			
subjects affected / exposed	0 / 33 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	3	
Ear and labyrinth disorders			
TINNITUS			
subjects affected / exposed	2 / 33 (6.06%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Eye disorders			
LACRIMATION INCREASED			
subjects affected / exposed	1 / 33 (3.03%)	2 / 30 (6.67%)	
occurrences (all)	1	2	
VISION BLURRED			
subjects affected / exposed	2 / 33 (6.06%)	3 / 30 (10.00%)	
occurrences (all)	2	3	
Gastrointestinal disorders			
DYSPEPSIA			
subjects affected / exposed	0 / 33 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
DRY MOUTH			
subjects affected / exposed	1 / 33 (3.03%)	2 / 30 (6.67%)	
occurrences (all)	1	2	
DIARRHOEA			
subjects affected / exposed	11 / 33 (33.33%)	11 / 30 (36.67%)	
occurrences (all)	11	12	
CONSTIPATION			

subjects affected / exposed	3 / 33 (9.09%)	5 / 30 (16.67%)	
occurrences (all)	3	9	
ABDOMINAL PAIN UPPER			
subjects affected / exposed	1 / 33 (3.03%)	3 / 30 (10.00%)	
occurrences (all)	1	3	
DYSPHAGIA			
subjects affected / exposed	2 / 33 (6.06%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
VOMITING			
subjects affected / exposed	5 / 33 (15.15%)	6 / 30 (20.00%)	
occurrences (all)	6	6	
STOMATITIS			
subjects affected / exposed	4 / 33 (12.12%)	2 / 30 (6.67%)	
occurrences (all)	6	2	
NAUSEA			
subjects affected / exposed	9 / 33 (27.27%)	13 / 30 (43.33%)	
occurrences (all)	13	14	
Skin and subcutaneous tissue disorders			
ACNE			
subjects affected / exposed	2 / 33 (6.06%)	0 / 30 (0.00%)	
occurrences (all)	3	0	
ALOPECIA			
subjects affected / exposed	2 / 33 (6.06%)	1 / 30 (3.33%)	
occurrences (all)	3	1	
DRY SKIN			
subjects affected / exposed	5 / 33 (15.15%)	4 / 30 (13.33%)	
occurrences (all)	7	6	
ERYTHEMA			
subjects affected / exposed	3 / 33 (9.09%)	0 / 30 (0.00%)	
occurrences (all)	4	0	
NAIL DISORDER			
subjects affected / exposed	2 / 33 (6.06%)	1 / 30 (3.33%)	
occurrences (all)	3	1	
SKIN EXFOLIATION			
subjects affected / exposed	2 / 33 (6.06%)	1 / 30 (3.33%)	
occurrences (all)	2	1	

RASH			
subjects affected / exposed	6 / 33 (18.18%)	8 / 30 (26.67%)	
occurrences (all)	8	9	
PRURITUS			
subjects affected / exposed	4 / 33 (12.12%)	11 / 30 (36.67%)	
occurrences (all)	6	14	
Renal and urinary disorders			
RENAL FAILURE ACUTE			
subjects affected / exposed	0 / 33 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
Musculoskeletal and connective tissue disorders			
BONE PAIN			
subjects affected / exposed	0 / 33 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
BACK PAIN			
subjects affected / exposed	3 / 33 (9.09%)	3 / 30 (10.00%)	
occurrences (all)	5	3	
PAIN IN EXTREMITY			
subjects affected / exposed	3 / 33 (9.09%)	2 / 30 (6.67%)	
occurrences (all)	3	2	
NECK PAIN			
subjects affected / exposed	0 / 33 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
MUSCULOSKELETAL PAIN			
subjects affected / exposed	2 / 33 (6.06%)	2 / 30 (6.67%)	
occurrences (all)	2	2	
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	2 / 33 (6.06%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
MUSCULAR WEAKNESS			
subjects affected / exposed	1 / 33 (3.03%)	3 / 30 (10.00%)	
occurrences (all)	1	4	
MUSCLE SPASMS			
subjects affected / exposed	2 / 33 (6.06%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
Infections and infestations			

RHINITIS			
subjects affected / exposed	2 / 33 (6.06%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 33 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
CONJUNCTIVITIS			
subjects affected / exposed	3 / 33 (9.09%)	1 / 30 (3.33%)	
occurrences (all)	4	1	
CANDIDA INFECTION			
subjects affected / exposed	0 / 33 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	3	
BRONCHITIS			
subjects affected / exposed	0 / 33 (0.00%)	4 / 30 (13.33%)	
occurrences (all)	0	5	
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	12 / 33 (36.36%)	11 / 30 (36.67%)	
occurrences (all)	16	11	
DEHYDRATION			
subjects affected / exposed	0 / 33 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	3	
HYPERGLYCAEMIA			
subjects affected / exposed	11 / 33 (33.33%)	11 / 30 (36.67%)	
occurrences (all)	14	16	
HYPOKALAEMIA			
subjects affected / exposed	2 / 33 (6.06%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
HYPONATRAEMIA			
subjects affected / exposed	0 / 33 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 April 2012	The primary purpose of protocol amendment 1 is to update the biomarker objectives and the related biomarker procedures. Additionally, clarification is provided on the specific visit schedules for Stage 2 and the Cross-over parts of the trial. The provision for a potential expansion cohort is also introduced in Stage 1 and 2 of the study. Several inclusion and exclusion criteria are amended, and previous protocol inconsistencies are corrected. As of March 16, 2012, CBKM120D2201 has enrolled a total of 20 patients into Stage 1. Seven suspected serious study drug related toxicities have been reported for this trial.

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.

There was no statistical analysis done for this study as it met futility at stage 1 and so stage 2 was not started.

Notes: