Clinical trial results:
A Phase II, single-arm study of orally administered BKM120 as second-line therapy in patients with advanced endometrial carcinoma

Summary

EudraCT number	2010-022015-19
Trial protocol	ES BE DE IT
Global end of trial date	20 March 2014

Results information

Result version number	v1 (current)
This version publication date	27 May 2016
First version publication date	27 May 2016

Trial information

Trial identification

Sponsor protocol code	CBKM120C2201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01289041
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 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	20 March 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 March 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the efficacy of BKM120 as measured by Objective Response Rate (ORR) per RECIST in patients with advanced endometrial carcinoma who exhibit PI3K pathway activation.
To demonstrate the efficacy of BKM120 as measured by ORR per RECIST in all patients enrolled in the study

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.

Local radiotherapy for analgesic purposes or for lytic lesions at risk of fracture was to be carried out if required. The trial could be stopped early due to futility. In such case patients receiving study treatment at that time continued to receive BKM120 for as long as they continue to receive benefit in the opinion of the Investigator.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 February 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	Belgium: 7
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Brazil: 3
Country: Number of subjects enrolled	Canada: 11
Country: Number of subjects enrolled	Japan: 4
Country: Number of subjects enrolled	United States: 19
Country: Number of subjects enrolled	Russian Federation: 4
Country: Number of subjects enrolled	Singapore: 3
Country: Number of subjects enrolled	Australia: 3

Worldwide total number of subjects	70
EEA total number of subjects	23

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)	40
From 65 to 84 years	30
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

One hundred fourteen patients were screened and 70 patients were enrolled at 42 centers in 14 countries. Forty-nine patients had activated P13K pathway status and 21 with non-activated status. Forty patients screen failed for not meeting entry criteria and 4 patients were patient/investigator decision.

Period 1

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

Arms

Arm title	All patients

Arm description: -

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

Dosage and administration details:

BKM120 was administered on a continuous once daily dosing schedule at a dose of 100 mg (po). The patients were dosed on a flat scale of mg/day and the dose of the drug was not to be adjusted to body weight or body surface area.
Patients were instructed to take the dose of BKM120 daily in the morning, at approximately the same time each day, except on the days of the fasting plasma glucose and c-peptide sampling and pharmacokinetic sampling when the patients were to take their dose in the clinic.
On days with a pre-dose fasting glucose sample M120 was to be taken 1 hour after a light breakfast and on days with a PK blood sampling BKM120 was to be taken 1 hour after a light breakfast. Patients were instructed to avoid consumption of Seville oranges, grapefruit and hybrids and other exotic fruits during the course of the study.

Number of subjects in period 1	All patients
Started	70
Completed	0
Not completed	70
Physician decision	1
Consent withdrawn by subject	3
Adverse event, non-fatal	24
Death	1
Progressive disease	41

Baseline characteristics

Reporting groups	
Reporting group title	Treatment

Reporting group description: -

Reporting group values	Treatment	Total	
Number of subjects	70	70	
Age categorical Units: Subjects			
Adults (18-64 years)	40	40	
From 65-84 years	30	30	
Gender categorical Units: Subjects			
Female	70	70	

End points

End points reporting groups

Reporting group title	All patients
Reporting group description: -	
Subject analysis set title	P13K Activated
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects who exhibit PI3K pathway activation defined as the presence of a PIK3CA and/or PTEN mutation and/or PTEN negative by IHC (less than 10% staining).	

Subject analysis set title	P13K Non- Activated
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects who did not exhibit activation of P13K pathway	
Subject analysis set title	All patients
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All patients	

Primary: Overall Response Rate (ORR) According to PI3K Activation Pathway Status

End point title	Overall Response Rate (ORR) According to PI3K Activation Pathway Status[1]

End point description:

ORR was based on investigator assessment of overall lesion response using RECIST criteria guidelines.

Overall response rate (ORR) = Complete Response (CR) + Partial Response (PR)
Complete Response (CR): 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 1
Partial Response (PR): At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters.

Interim analysis was performed when 24 patients with activated PI3K pathway were observed for at least 4 months. The following hypothesis was tested:
H0: ORR ≤ 10%
In favor of the alternative
H1: ORR >10%
Rejection of the null hypotheses was based on the computation of the probability to obtained observed ORR under a binomial distribution with parameter p0 = 0.10.
Full analysis set includes all patients who received at least one dose of study medication.

End point type	Primary

End point timeframe:

24 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: There was no available method in this system to describe the statistical analysis provided for Overall Response Rate (ORR). A more detailed description of this endpoint can be found in the endpoint description.

End point values	P13K Activated	P13K Non-Activated	All patients	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	49	21	70	
Units: Response Rate				
number (confidence interval 95%)				
Overall Reponse Rate (Complete + Partial Response	1 (0.1 to 10.9)	1 (0.1 to 23.8)	2 (0.3 to 9.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) According to PI3K Activation Pathway Status

End point title	Progression Free Survival (PFS) According to PI3K Activation Pathway Status

End point description:

PFS is defined as the time from start of treatment to the date of first documented progression or death due to any cause. If a patient has not had an event, PFS will be censored at the date of last adequate tumor assessment. Full analysis set includes all patients who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

24 months

End point values	P13K Activated	P13K Non-Activated		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	49	21		
Units: Participants				
median (confidence interval 95%)	1.9 (1.8 to 3.2)	1.9 (1.6 to 3.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) According to PI3K Activation Pathway Status

End point title	Overall Survival (OS) According to PI3K Activation Pathway Status

End point description:

Overall survival (OS) was defined as the time from start of treatment to the date of death due to any cause. If a patient is not known to have died, survival was censored at the last date of contact. OS was to be reported at extension and after 3-year follow-up. The Kaplan-Meier median was used to analyze the OS.

End point type	Secondary

End point timeframe:

Overall Survival (OS) According to PI3K Activation Pathway Status

End point values	P13K Activated	P13K Non-Activated		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	49	21		
Units: months				
median (confidence interval 95%)	8.9 (6.3 to 16.2)	14.2 (8.6 to 24)		

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 are reported in this record from 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	16.1

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	33 / 70 (47.14%)		
number of deaths (all causes)	7		
number of deaths resulting from adverse events	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	1 / 70 (1.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 70 (1.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	2 / 70 (2.86%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Face oedema			
subjects affected / exposed	1 / 70 (1.43%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	3 / 70 (4.29%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	1 / 70 (1.43%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	2 / 70 (2.86%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 70 (1.43%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Confusional state			
subjects affected / exposed	1 / 70 (1.43%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Delirium			
subjects affected / exposed	2 / 70 (2.86%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		

Mental status changes				
subjects affected / exposed	2 / 70 (2.86%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Investigations				
International normalised ratio increased				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Transaminases increased				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Acute myocardial infarction				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cardio-respiratory arrest				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Nervous system disorders				
Cerebrovascular accident				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Convulsion				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Encephalopathy				

subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Leukoencephalopathy				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	2 / 70 (2.86%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Ascites				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Colonic obstruction				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Erosive oesophagitis				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal obstruction				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Nausea				

subjects affected / exposed	2 / 70 (2.86%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Stomatitis				
subjects affected / exposed	2 / 70 (2.86%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	3 / 70 (4.29%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Drug reaction with eosinophilia and systemic symptoms				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Rash				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Hydronephrosis				
subjects affected / exposed	3 / 70 (4.29%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Renal failure				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal failure acute				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			

Urinary incontinence				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Myalgia				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Bacteraemia				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lung infection				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	2 / 70 (2.86%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	1 / 1			
Uterine infection				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Urosepsis				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vulval abscess				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Decreased appetite				
subjects affected / exposed	2 / 70 (2.86%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Hypercreatininaemia				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dehydration				
subjects affected / exposed	4 / 70 (5.71%)			
occurrences causally related to treatment / all	2 / 5			
deaths causally related to treatment / all	0 / 1			
Hyperglycaemia				
subjects affected / exposed	4 / 70 (5.71%)			
occurrences causally related to treatment / all	4 / 4			
deaths causally related to treatment / all	0 / 0			
Hypoalbuminaemia				
subjects affected / exposed	1 / 70 (1.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

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	67 / 70 (95.71%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	17 / 70 (24.29%)		
occurrences (all)	20		
Aspartate aminotransferase increased			
subjects affected / exposed	18 / 70 (25.71%)		
occurrences (all)	20		
Blood alkaline phosphatase increased			
subjects affected / exposed	4 / 70 (5.71%)		
occurrences (all)	4		
Blood creatinine increased			
subjects affected / exposed	6 / 70 (8.57%)		
occurrences (all)	6		
Gamma-glutamyltransferase increased			
subjects affected / exposed	11 / 70 (15.71%)		
occurrences (all)	12		
Weight decreased			
subjects affected / exposed	14 / 70 (20.00%)		
occurrences (all)	14		
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 70 (7.14%)		
occurrences (all)	5		
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	10 / 70 (14.29%)		
occurrences (all)	11		
Dizziness			
subjects affected / exposed	11 / 70 (15.71%)		
occurrences (all)	11		
Memory impairment			
subjects affected / exposed	5 / 70 (7.14%)		
occurrences (all)	5		

Headache			
subjects affected / exposed	8 / 70 (11.43%)		
occurrences (all)	10		
Tremor			
subjects affected / exposed	7 / 70 (10.00%)		
occurrences (all)	7		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	13 / 70 (18.57%)		
occurrences (all)	14		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	6 / 70 (8.57%)		
occurrences (all)	7		
Fatigue			
subjects affected / exposed	24 / 70 (34.29%)		
occurrences (all)	28		
Oedema peripheral			
subjects affected / exposed	9 / 70 (12.86%)		
occurrences (all)	9		
Pain			
subjects affected / exposed	4 / 70 (5.71%)		
occurrences (all)	4		
Pyrexia			
subjects affected / exposed	6 / 70 (8.57%)		
occurrences (all)	8		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	15 / 70 (21.43%)		
occurrences (all)	16		
Constipation			
subjects affected / exposed	12 / 70 (17.14%)		
occurrences (all)	13		
Diarrhoea			
subjects affected / exposed	17 / 70 (24.29%)		
occurrences (all)	28		

Dyspepsia subjects affected / exposed occurrences (all)	9 / 70 (12.86%) 9		
Dysphagia subjects affected / exposed occurrences (all)	4 / 70 (5.71%) 4		
Vomiting subjects affected / exposed occurrences (all)	14 / 70 (20.00%) 27		
Stomatitis subjects affected / exposed occurrences (all)	10 / 70 (14.29%) 11		
Nausea subjects affected / exposed occurrences (all)	31 / 70 (44.29%) 36		
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all)	8 / 70 (11.43%) 9		
Skin and subcutaneous tissue disorders Dry skin subjects affected / exposed occurrences (all)	8 / 70 (11.43%) 9		
Erythema subjects affected / exposed occurrences (all)	6 / 70 (8.57%) 7		
Rash subjects affected / exposed occurrences (all)	21 / 70 (30.00%) 22		
Pruritus subjects affected / exposed occurrences (all)	10 / 70 (14.29%) 11		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	17 / 70 (24.29%) 17		

Depression subjects affected / exposed occurrences (all)	16 / 70 (22.86%) 17		
Confusional state subjects affected / exposed occurrences (all)	9 / 70 (12.86%) 9		
Insomnia subjects affected / exposed occurrences (all)	8 / 70 (11.43%) 8		
Mood altered subjects affected / exposed occurrences (all)	6 / 70 (8.57%) 7		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	6 / 70 (8.57%) 6		
Musculoskeletal pain subjects affected / exposed occurrences (all)	4 / 70 (5.71%) 4		
Pain in extremity subjects affected / exposed occurrences (all)	4 / 70 (5.71%) 4		
Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all)	10 / 70 (14.29%) 10		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	28 / 70 (40.00%) 31		
Hyperglycaemia subjects affected / exposed occurrences (all)	37 / 70 (52.86%) 54		
Hypoalbuminaemia subjects affected / exposed occurrences (all)	4 / 70 (5.71%) 5		

Hypokalaemia subjects affected / exposed occurrences (all)	12 / 70 (17.14%) 21		
Hypomagnesaemia subjects affected / exposed occurrences (all)	5 / 70 (7.14%) 6		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 April 2011	Amendment 1 Due to safety findings, modifications were made to the protocol including: stringent liver specific inclusion/exclusion criteria, follow-up assessments in case of LFT elevations, and a standardized follow up was introduced in case of pneumonitis. Clarifications have been introduced regarding the storage of samples collected and the amount of archival tissue material required for biomarker evaluations. Specific corrective measures including procedures for monitoring liver function during the study, dose modification and follow-up guidelines in case of development of liver toxicity, monitoring of mood alternations. The exclusion criterion #3 on Corticosteroids was updated to clarify that patients with controlled and asymptomatic CNS metastases could receive stable low dose corticosteroid treatment at study entry and continue on unmodified low dose corticosteroids therapy. Treatment compliance was consolidated by including guidelines for definition and treatment of overdose. Clarifications were made regarding the assessment of patients with unknown PI3K status at the time of the interim analyses. Guidance on treatment options for patients requiring anticoagulant treatment during the study was added, as treatment with warfarin sodium (Coumadin®) or any other coumarin-derivative anticoagulants were not permitted during the study.

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.

The interim analysis provided limited evidence for the efficacy of single agent buparlisib in patients with endometrial cancer, and the observed number of responders did not allow crossing futility boundary and the enrollment was stopped.

Notes: