Clinical trial results:
Molecularly stratified parallel group phase II trial of the phosphoinositide 3-kinase (PI3K) inhibitor BKM120 in combination with tamoxifen in patients with hormone receptor-positive, HER2-negative inoperable (locally advanced or metastatic) breast cancer with prior exposure to antihormonal therapy

Summary

EudraCT number	2014-000599-24
Trial protocol	DE
Global end of trial date	18 October 2017

Results information

Result version number	v1 (current)
This version publication date	28 October 2018
First version publication date	28 October 2018
Summary attachment (see zip file)	PIKTAM_Synopsis_CSR_FINAL_V2.0_20181004 (PIKTAM_Synopsis_CSR_FINAL_V2.0_20181004.pdf)

Trial information

Trial identification

Sponsor protocol code	iOM-02282

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02404844
WHO universal trial number (UTN)	-
Other trial identifiers	Study Code Novartis - IMP supply : CBKM120ZDE02T, Code of AIO: AIO-MAM-0114/ass

Notes:

Sponsors

Sponsor organisation name	Universitätsklinikum Essen, Westdeutsches Tumorzentrum
Sponsor organisation address	Hufelandstr. 55, Essen, Germany, 45147
Public contact	Contract Research Organization, iOMEDICO AG, +49 761152420, info@iomedico.com
Scientific contact	Contract Research Organization, iOMEDICO AG, +49 761152420, info@iomedico.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	04 June 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 October 2017
Global end of trial reached?	Yes
Global end of trial date	18 October 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate efficacy of BKM120 in combination with tamoxifen in patients with ER/PR-positive, HER2-negative breast cancer stratified to PIK3CA mutation and preserved PTEN expression, loss of PTEN expression +/- PIK3CA mutation or PIK3CA wild type and preserved PTEN expression

Protection of trial subjects:

Safety and tolerability assessments: routine laboratory parameters, urinalysis and vital signs, ECOG, weight, pregnancy testing, collection of the adverse events, PHQ-9 and GAD-7 questionnaires to facilitate identification and severity assessment of potential mood alterations, ECG and cardiac imaging

Background therapy:

Tamoxifen: 20 mg/day, orally, on a continuous dosing schedule without interruption starting on day 1 in 28 day cycle

Evidence for comparator: -

Actual start date of recruitment	29 December 2014
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	Germany: 48
Worldwide total number of subjects	48
EEA total number of subjects	48

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)	27
From 65 to 84 years	21
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The investigator enrolled patients based on previously defined inclusion (IC) and exclusion criteriea (EC). Patients who fulfilled all of the IC and non of the EC were eligible to PIKTAM trial.

Pre-assignment

Screening details:

Pre-Screening: Biomarker analysis for PI3K pathway activation (PIK3CA and PTEN mutation status) performed centrally by the Laboratory of Molecular Pathology, Institute of Pathology, University Hospital of Essen, using archival tissue samples for molecular stratification. Screening: Check of further inclusion and exclusion criteria.

Pre-assignment period milestones

Number of subjects started	48
Number of subjects completed	25

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Study recruitment terminated by sponsor: 7
Reason: Number of subjects	Screening failure: 16

Period 1

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

Arms

Arm title	Total population

Arm description:

All patients received the investigational drug Buparlisib (BKM120) and in addition, daily tamoxifen as background treatment.

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

Dosage and administration details:

Dosing regimen:
- Buparlisib (BKM120): 100 mg/day, orally, on a continuous dosing schedule without interruption starting on day 1 in 28 day cycle
- Tamoxifen: 20 mg/day, orally, on a continuous dosing schedule without interruption starting on day 1 in 28 day cycle

Number of subjects in period 1[1]	Total population
Started	25
Completed	24
Not completed	1
Lost to follow-up	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 48 Patients were enrolled in pre-screening phase for analysis of biomarker status of PI3K pathway activation, 35 patients entered screening phase of the trial. Of those, only 25 patients were treated with buparlisib and are considered for data analysis.

Baseline characteristics

Reporting groups

Reporting group title	PIKTAM Overall trial

Reporting group description: -

Reporting group values	PIKTAM Overall trial	Total	
Number of subjects	25	25	
Age categorical Units: Subjects			
Adults (18-64 years)	16	16	
From 65-84 years	9	9	
85 years and over	0	0	
Age continuous Units: years			
median	62.9		
full range (min-max)	49.0 to 80.7	-	
Gender categorical Units: Subjects			
Female	25	25	
ECOG performance status Units: Subjects			
0 - fully functional, no symptoms	18	18	
1 - with symptoms, able to carry out light work	7	7	
Mutation status PTEN Units: Subjects			
PTEN preserved	22	22	
PTEN loss	3	3	
Mutation status PIK3CA (exon 10) Units: Subjects			
WT (exon 10)	21	21	
Mutant (exon 10)	4	4	
Mutation status PIK3CA (exon 21) Units: Subjects			
WT (exon 21)	20	20	
Mutant (exon 21)	5	5	
Tumor localization at primary diagnosis Units: Subjects			
left	17	17	
right	8	8	
Histology at primary diagnosis Units: Subjects			
invasive ductal	17	17	
invasive lobular	5	5	
other	3	3	
Tumor resections Units: Subjects			
Yes	23	23	

No	2	2	
Outcome of tumor resection Units: Subjects			
R0	16	16	
R1	4	4	
R2	1	1	
RX	2	2	
No resection	2	2	
Number of previous palliative treatment lines Units: Subjects			
No previous palliative treatment line	3	3	
1 previous palliative treatment line	13	13	
2 previous palliative treatment lines	6	6	
>/= 3 previous palliative teratment lines	3	3	
BMI Units: kg/m2			
median	24.2		
full range (min-max)	17.2 to 34.8	-	
PHQ-9 total score Units: total score			
median	2.0		
full range (min-max)	0.0 to 9.0	-	
GAD-7 total score Units: total score			
median	1.0		
full range (min-max)	0.0 to 6.0	-	
Time from primary diagnosis to date of first study treatment Units: years			
median	7.8		
full range (min-max)	0.9 to 26.9	-	
Time from first relapse/metastatic disease to date of first study treatment Units: years			
median	1.8		
full range (min-max)	0.1 to 11.8	-	
Disease-free interval Units: years			
median	10.6		
full range (min-max)	2.1 to 16.1	-	

Subject analysis sets

Subject analysis set title	mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The mITT population comprised all patients who qualified for analysis of the primary endpoint, i.e. all patients who received at least one dose of buparlisib and with tumor assessment performed at 6 months, unless patients progressed or died before completion of 6 months of treatment. Patient dropping out of the study before reaching the 6 months tumor assessment for reason other than progression were not evaluable for the primary endpoint.
The mITT was the relevant population for the efficacy evaluation including demographic and other

baseline characteristics as well as study treatment evaluations.

Subject analysis set title	PIK3CA mutation and preserved PTEN expression
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Subgroup of mITT population stratified according to biomarker status for PI3K pathway activation, as determined histologically using archival tumor tissue samples: PIK3CA mutation (exon 10 and/or exon21) and preserved PTEN expression.

Subject analysis set title	Loss of PTEN expression +/- PIK3CA mutation
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Subgroup of mITT population stratified according to biomarker status for PI3K pathway activation, as determined histologically using archival tumor tissue samples: Loss of PTEN expression +/- PIK3CA mutation (exon 10 and/or exon 21).

Subject analysis set title	PIK3CA wild type and preserved PTEN expression
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Subgroup of mITT population stratified according to biomarker status for PI3K pathway activation, as determined histologically using archival tumor tissue samples: PIK3CA wild type and preserved PTEN expression.

Reporting group values	mITT	PIK3CA mutation and preserved PTEN expression	Loss of PTEN expression +/- PIK3CA mutation
Number of subjects	21	8	2
Age categorical Units: Subjects			
Adults (18-64 years)	15	6	1
From 65-84 years	6	2	1
85 years and over	0	0	0
Age continuous Units: years			
median	62.8	63.2	65.7
full range (min-max)	49.0 to 80.7	57.8 to 80.7	62.5 to 69.0
Gender categorical Units: Subjects			
Female	21	8	2
ECOG performance status Units: Subjects			
0 - fully functional, no symptoms	15	6	0
1 - with symptoms, able to carry out light work	6	2	2
Mutation status PTEN Units: Subjects			
PTEN preserved	19	8	0
PTEN loss	2	0	2
Mutation status PIK3CA (exon 10) Units: Subjects			
WT (exon 10)	18	5	2
Mutant (exon 10)	3	3	0
Mutation status PIK3CA (exon 21) Units: Subjects			
WT (exon 21)	16	3	2
Mutant (exon 21)	5	5	0

Tumor localization at primary diagnosis Units: Subjects			
left	14	6	0
right	7	2	2
Histology at primary diagnosis Units: Subjects			
invasive ductal	15	6	1
invasive lobular	4	2	1
other	2	0	0
Tumor resections Units: Subjects			
Yes	20	8	2
No	1	0	0
Outcome of tumor resection Units: Subjects			
R0	14	6	1
R1	3	1	1
R2	1	0	0
RX	2	1	0
No resection	1	0	0
Number of previous palliative treatment lines Units: Subjects			
No previous palliative treatment line	3	0	1
1 previous palliative treatment line	11	5	0
2 previous palliative treatment lines	5	2	1
>/= 3 previous palliative teratment lines	2	1	0
BMI Units: kg/m2			
median	26.4	28.0	24.7
full range (min-max)	17.2 to 34.8	17.2 to 34.8	21.8 to 27.7
PHQ-9 total score Units: total score			
median	1.0	1.0	3.0
full range (min-max)	0.0 to 9.0	0.0 to 9.0	2.0 to 4.0
GAD-7 total score Units: total score			
median	1.0	0.0	1.0
full range (min-max)	0.0 to 6.0	0.0 to 6.0	0.0 to 2.0
Time from primary diagnosis to date of first study treatment Units: years			
median	4.9	9.4	2.9
full range (min-max)	0.9 to 26.9	1.6 to 26.9	0.9 to 4.9
Time from first relapse/metastatic disease to date of first study treatment Units: years			
median	1.6	1.7	2.0
full range (min-max)	0.1 to 11.8	0.1 to 11.8	1.0 to 3.0
Disease-free interval Units: years			
median	9.6	13.7	n.a.

full range (min-max)	2.1 to 15.1	2.4 to 15.1	n.a. to n.a.

Reporting group values	PIK3CA wild type and preserved PTEN expression		
Number of subjects	11		
Age categorical Units: Subjects			
Adults (18-64 years)	8		
From 65-84 years	3		
85 years and over	0		
Age continuous Units: years			
median	61.8		
full range (min-max)	49.0 to 73.7		
Gender categorical Units: Subjects			
Female	11		
ECOG performance status Units: Subjects			
0 - fully functional, no symptoms	9		
1 - with symptoms, able to carry out light work	2		
Mutation status PTEN Units: Subjects			
PTEN preserved	11		
PTEN loss	0		
Mutation status PIK3CA (exon 10) Units: Subjects			
WT (exon 10)	11		
Mutant (exon 10)	0		
Mutation status PIK3CA (exon 21) Units: Subjects			
WT (exon 21)	11		
Mutant (exon 21)	0		
Tumor localization at primary diagnosis Units: Subjects			
left	8		
right	3		
Histology at primary diagnosis Units: Subjects			
invasive ductal	8		
invasive lobular	1		
other	2		
Tumor resections Units: Subjects			
Yes	10		
No	1		
Outcome of tumor resection Units: Subjects			

R0	7		
R1	1		
R2	1		
RX	1		
No resection	1		
Number of previous palliative treatment lines Units: Subjects			
No previous palliative treatment line	2		
1 previous palliative treatment line	6		
2 previous palliative treatment lines	2		
>/= 3 previous palliative teratment lines	1		
BMI Units: kg/m2			
median	24.0		
full range (min-max)	19.7 to 32.8		
PHQ-9 total score Units: total score			
median	1.0		
full range (min-max)	0.0 to 6.0		
GAD-7 total score Units: total score			
median	1.0		
full range (min-max)	0.0 to 6.0		
Time from primary diagnosis to date of first study treatment Units: years			
median	8.8		
full range (min-max)	0.9 to 21.4		
Time from first relapse/metastatic disease to date of first study treatment Units: years			
median	1.2		
full range (min-max)	0.1 to 10.6		
Disease-free interval Units: years			
median	6.9		
full range (min-max)	2.1 to 13.3		

End points

End points reporting groups

Reporting group title	Total population

Reporting group description:

All patients received the investigational drug Buparlisib (BKM120) and in addition, daily tamoxifen as background treatment.

Subject analysis set title	mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The mITT population comprised all patients who qualified for analysis of the primary endpoint, i.e. all patients who received at least one dose of buparlisib and with tumor assessment performed at 6 months, unless patients progressed or died before completion of 6 months of treatment. Patient dropping out of the study before reaching the 6 months tumor assessment for reason other than progression were not evaluable for the primary endpoint.
The mITT was the relevant population for the efficacy evaluation including demographic and other baseline characteristics as well as study treatment evaluations.

Subject analysis set title	PIK3CA mutation and preserved PTEN expression
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Subgroup of mITT population stratified according to biomarker status for PI3K pathway activation, as determined histologically using archival tumor tissue samples: PIK3CA mutation (exon 10 and/or exon21) and preserved PTEN expression.

Subject analysis set title	Loss of PTEN expression +/- PIK3CA mutation
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Subgroup of mITT population stratified according to biomarker status for PI3K pathway activation, as determined histologically using archival tumor tissue samples: Loss of PTEN expression +/- PIK3CA mutation (exon 10 and/or exon 21).

Subject analysis set title	PIK3CA wild type and preserved PTEN expression
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Subgroup of mITT population stratified according to biomarker status for PI3K pathway activation, as determined histologically using archival tumor tissue samples: PIK3CA wild type and preserved PTEN expression.

Primary: 6-month PFS rate

End point title	6-month PFS rate[1]

End point description:

The primary endpoint is defined as the proportion of progression-free patients in the full population at month 6 (defined as 6-month tumor assessment: month 6 +/- 1 week). Patients discontinuing the study prior to the 6-month assessment for reasons other than progression or death are not evaluable for the analysis of the primary endpoint.

Null hypothesis: The 6-month progression-free survival (PFS) rate is less than or equal to p0 = 0.400. Alternative hypothesis: The 6-month PFS rate is greater than or equal to p1 = 0.540. The null hypothesis is accepted if the number of progression-free patients is equal to or less than a critical value r determined as follows: r is the smallest number of progression-free patients for which applies Σ [i=1, r] Bin(i|0.400,n) >0.95 (exact binomial test, n = number of patients in mITT population). If the number of progression-free patients is r+1 or greater the null hypothesis is rejected.

End point type	Primary

End point timeframe:

Time from first study drug administration to 6-month tumor assessment: month 6 +/- 1 week.

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: Statistical analysis of the primary endpoint has been performed as defined in the protocol:

Seven patients (33.3%) in the mITT population were progression-free at 6 months with a one-sided 95%-CI of 16.82 – 100 and a p-value of 0.800 (exact binominal test).

End point values	mITT			
Subject group type	Subject analysis set			
Number of subjects analysed	21			
Units: Percentage of patients				
number (confidence interval 95%)	33.33 (16.82 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: 6-month PFS rate in biomarker stratification groups

End point title	6-month PFS rate in biomarker stratification groups

End point description:

6-month PFS rate in the biomarker stratification groups.

End point type	Secondary

End point timeframe:

Time from first study drug administration to 6-month tumor assessment: month 6 +/- 1 week.

End point values	PIK3CA mutation and preserved PTEN expression	Loss of PTEN expression +/- PIK3CA mutation	PIK3CA wild type and preserved PTEN expression	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	8	2	11	
Units: Percentage of patients				
number (confidence interval 95%)	62.50 (28.92 to 100)	0.00 (0.00 to 100)	18.18 (3.33 to 100)	

Statistical analyses

No statistical analyses for this end point

Secondary: PFS

End point title	PFS

End point description:

Progression-free survival (PFS) is defined as the time from first study drug administration to tumor progression or death from any cause.

Patients without an event (progression or death) at the time of analysis or starting a subsequent antineoplastic therapy before propgression will be right-censored at the date of last adequate tumor assessment or at the start date of the subsequent therapy whichever comes first.

End point type	Secondary

End point timeframe:

Time from first study drug administration to tumor progression or death from any cause.

End point values	mITT	PIK3CA mutation and preserved PTEN expression	Loss of PTEN expression +/- PIK3CA mutation	PIK3CA wild type and preserved PTEN expression
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	21	8	2	11
Units: months				
median (confidence interval 95%)	4.8 (2.5 to 10.0)	8.7 (1.4 to 16.7)	2.1 (1.7 to 2.5)	4.8 (1.4 to 10.0)

Statistical analyses

No statistical analyses for this end point

Secondary: OS

End point title	OS

End point description:

Overall survival (OS) is defined as the time from first study drug administration to death from any cause. If a patient was not known to have died by the date of analysis, OS was censored at the date of last known date patient was alive.
Due to the low number of patients, the 95% confidence interval is not reached for OS of subgroups "PIK3CA mutation and preserved PTEN expression" and "PIK3CA wild type and preserved PTEN expression". "Not applicable" is shown as "999" in the OS results.

End point type	Secondary

End point timeframe:

Time from first study drug administration to death from any cause.

End point values	mITT	PIK3CA mutation and preserved PTEN expression	Loss of PTEN expression +/- PIK3CA mutation	PIK3CA wild type and preserved PTEN expression
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	21	8	2	11
Units: months				
median (confidence interval 95%)	23.8 (12.6 to 25.5)	20.1 (5.7 to 999)	12.8 (1.7 to 24.0)	23.8 (9.8 to 999)

Statistical analyses

No statistical analyses for this end point

Secondary: 1-year OS rate

End point title	1-year OS rate

End point description:

1-year overall survival (OS) rates, is defined as the proportion of patients alive after one year after first study drug administration.

End point type	Secondary

End point timeframe:

Time from first study drug administration until one year after.

End point values	mITT	PIK3CA mutation and preserved PTEN expression	Loss of PTEN expression +/- PIK3CA mutation	PIK3CA wild type and preserved PTEN expression
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	21	8	2	11
Units: Percentage of patients				
number (confidence interval 95%)	81.0 (56.9 to 92.4)	87.5 (38.7 to 98.1)	50.0 (0.6 to 91.0)	81.8 (44.7 to 95.1)

Statistical analyses

No statistical analyses for this end point

Secondary: 2-year OS rate

End point title	2-year OS rate

End point description:

2-year overall survival (OS) rates is defined as the proportion of patients alive after two years after first study drug administration.

End point type	Secondary

End point timeframe:

Time from first study drug administration until two years after.

End point values	mITT	PIK3CA mutation and preserved PTEN expression	Loss of PTEN expression +/- PIK3CA mutation	PIK3CA wild type and preserved PTEN expression
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	21	8	2	11
Units: Percentage of patients				
number (confidence interval 95%)	46.6 (24.4 to 66.1)	50.0 (15.2 to 77.5)	50.0 (0.6 to 91.0)	43.6 (14.7 to 69.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Best response - RECIST v1.1

End point title	Best response - RECIST v1.1

End point description:

Best response is shown as complete (CR), partial response (PR), stable disease (SD) or progressive disease (PD) as assessed during the first 6 months of treatment, including all response assessments up to the tumor assessment at 6 months (month 6 +/- 1 week), according to RECIST v1.1 criteria.
Only patients with measurable lesions at baseline were included in the analysis.
Relevant response evaluations were all evaluations from first study drug administration up to the 6 months tumor assessment irrespective whether they were performed at the pre-specified time point or not.

End point type	Secondary

End point timeframe:

Time from first study drug administration up to the 6 months tumor assessment (month 6 +/- 1 week).

End point values	mITT	PIK3CA mutation and preserved PTEN expression	Loss of PTEN expression +/- PIK3CA mutation	PIK3CA wild type and preserved PTEN expression
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	16	5	2	9
Units: Percentage of patients				
number (confidence interval 95%)				
CR	0.0 (0.0 to 20.6)	0.0 (0.0 to 52.2)	0.0 (0.0 to 84.2)	0.0 (0.0 to 33.6)
PR	12.5 (1.6 to 38.3)	40.0 (5.3 to 85.3)	0.0 (0.0 to 84.2)	0.0 (0.0 to 33.6)
SD	50.0 (24.7 to 75.3)	60.0 (14.7 to 94.7)	0.0 (0.0 to 84.2)	55.6 (21.2 to 86.3)
PD	31.3 (11.0 to 58.7)	0.0 (0.0 to 52.2)	50.0 (1.3 to 98.7)	44.4 (13.7 to 78.8)
Not done	6.3 (0.2 to 30.2)	0.0 (0.0 to 52.2)	50.0 (1.3 to 98.7)	0.0 (0.0 to 33.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Best response - clinically assessed

End point title	Best response - clinically assessed

End point description:

Best response according to clinical investigator assessment.
Relevant response evaluations were all evaluations from first study drug administration up to the 6 months tumor assessment irrespective whether they were performed at the pre-specified time point or not.

End point type	Secondary

End point timeframe:

Time from first study drug administration up to the 6 months tumor assessment (month 6 +/- 1 week).

End point values	mITT	PIK3CA mutation and preserved PTEN expression	Loss of PTEN expression +/- PIK3CA mutation	PIK3CA wild type and preserved PTEN expression
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	21	8	2	11
Units: Percentage of patients				
number (confidence interval 95%)				
CR	0.0 (0.0 to 16.1)	0.0 (0.0 to 36.9)	0.0 (0.0 to 84.2)	0.0 (0.0 to 28.5)
PR	14.3 (3.0 to 36.3)	25.0 (3.2 to 65.1)	0.0 (0.0 to 84.2)	9.1 (0.2 to 41.3)
SD	38.1 (18.1 to 61.6)	50.0 (15.7 to 84.3)	0.0 (0.0 to 84.2)	36.4 (10.9 to 69.2)
PD	42.9 (21.8 to 66.0)	25.0 (3.2 to 65.1)	50.0 (1.3 to 98.7)	54.5 (23.4 to 83.3)
Not done	4.8 (0.1 to 23.8)	0.0 (0.0 to 36.9)	50.0 (1.3 to 98.7)	0.0 (0.0 to 28.5)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall response rate - RECIST v1.1

End point title	Overall response rate - RECIST v1.1

End point description:

Overall response rate (ORR) is defined as the proportion of patients showing a best overall response of complete (CR) or partial response (PR) during the first 6 months of treatment including all response assessments up to the tumor assessment at 6 months (month 6 +/- 1 week) according to RECIST v1.1 criteria.
Only patients with measurable lesions at baseline were assessed for ORR.

End point type	Secondary

End point timeframe:

Time from first study drug administration to tumor assessment at 6 months (month 6 +/- 1 week).

End point values	mITT	PIK3CA mutation and preserved PTEN expression	Loss of PTEN expression +/- PIK3CA mutation	PIK3CA wild type and preserved PTEN expression
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	16	5	2	9
Units: Percentage of patients				
number (confidence interval 95%)	12.5 (1.6 to 38.3)	40.0 (5.3 to 85.3)	0.0 (0.0 to 84.2)	0.0 (0.0 to 33.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall response rate - clinically assessed

End point title	Overall response rate - clinically assessed

End point description:

Overall response rate (ORR) according to clinical investigator assessment.

End point type	Secondary

End point timeframe:

Time from first study drug administration to tumor assessment at 6 months (month 6 +/- 1 week).

End point values	mITT	PIK3CA mutation and preserved PTEN expression	Loss of PTEN expression +/- PIK3CA mutation	PIK3CA wild type and preserved PTEN expression
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	21	8	2	11
Units: Percentage of patients				
number (confidence interval 95%)	14.3 (3.0 to 36.3)	25.0 (3.2 to 65.1)	0.0 (0.0 to 84.2)	9.1 (0.2 to 41.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Disease control rate - RECIST v1.1

End point title	Disease control rate - RECIST v1.1

End point description:

Disease control rate (DCR) is defined as the proportion of patients showing a best overall response CR or PR or stable disease (SD) lasting more than 3 months according to RECIST v1.1.
Only patients with measurable lesions at baseline were assessed for DCR.
Relevant response evaluations were all evaluations from first study drug administration up to the 6 months tumor assessment.
A best response of stable disease (SD) was included in the DCR only if the respective tumor assessment was performed at least 12 weeks (minus 7 days) after treatment start.

End point type	Secondary

End point timeframe:

Time from first study drug administration to tumor assessment at 6 months (month 6 +/- 1 week).

End point values	mITT	PIK3CA mutation and preserved PTEN expression	Loss of PTEN expression +/- PIK3CA mutation	PIK3CA wild type and preserved PTEN expression
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	16	5	2	9
Units: Percentage of patients				
number (confidence interval 95%)	43.8 (19.8 to 70.1)	80.0 (28.4 to 99.5)	0.0 (0.0 to 84.2)	33.3 (7.5 to 70.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Disease control rate - clinically assessed

End point title	Disease control rate - clinically assessed

End point description:

Disease control rate (DCR), defined as the proportion of patients showing a best overall response CR or PR or stable disease (SD) lasting more than 3 months according to clinical investigator assessment. Relevant response evaluations were all evaluations from first study drug administration up to the 6 months tumor assessment.
A best response of stable disease (SD) was included in the DCR only if the respective tumor assessment was performed at least 12 weeks (minus 7 days) after treatment start.

End point type	Secondary

End point timeframe:

Time from first study drug administration to tumor assessment at 6 months (month 6 +/- 1 week).

End point values	mITT	PIK3CA mutation and preserved PTEN expression	Loss of PTEN expression +/- PIK3CA mutation	PIK3CA wild type and preserved PTEN expression
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	21	8	2	11
Units: Percentage of patients				
number (confidence interval 95%)	47.6 (25.7 to 70.2)	75.0 (34.9 to 96.8)	0.0 (0.0 to 84.2)	36.4 (10.9 to 69.2)

Statistical analyses

No statistical analyses for this end point

Secondary: PHQ-9 - total scores by visit

End point title	PHQ-9 - total scores by visit

End point description:

Change in depressive episodes assessed by Patient Health Questionnaire (PHQ)-9 questionnaire. The PHQ-9 questionnaire is a validated questionnaire for screening for the presence and severity of depression.
Total PHQ-9 scores can be categorized as follows regarding severity of symptoms of depression: 0-4 = none, 5-9 = mild, 10-19 = moderate, 20-27 = severe.
Patients with missing baseline or baseline assessment performed more than 8 days before treatment start were excluded from the analysis.
Numbers of patients in cycles might differ from exposure tables if a questionnaire was handed out although the patient did not receive any study medication in the respective cycle.

End point type	Secondary

End point timeframe:

Time from baseline until end of treatment visit.

End point values	Total population			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Total score				
median (full range (min-max))				
Baseline	1.0 (0.0 to 7.0)			
Cycle 1 Day 15	2.0 (0.0 to 15.0)			
Cycle 2 Day 1	2.0 (0.0 to 6.0)			
Cycle 2 Day 15	1.0 (0.0 to 9.0)			
Cycle 3 Day 1	2.5 (0.0 to 6.0)			
Cycle 4 Day 1	0.0 (0.0 to 6.0)			
Cycle 5 Day 1	0.0 (0.0 to 4.0)			
Cycle 6 Day 1	0.5 (0.0 to 5.0)			
End of treatment	2.0 (0.0 to 20.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: GAD-7 - total scores by visit

End point title	GAD-7 - total scores by visit

End point description:

Change in depressive episodes assessed by Generalized Anxiety Disorder (GAD)-7 questionnaire. The GAD-7 questionnaire is a validated questionnaire for screening and severity measuring of generalized anxiety disorder.
Total GAD-7 scores can be categorized as follows regarding severity of symptoms of general anxiety disorder: 0-4 = none, 5-9 = mild, 10-14 = moderate, 15-21 = severe.
Patients with missing baseline or baseline assessment performed more than 8 days before treatment start were excluded from the analysis.
Numbers of patients in cycles might differ from exposure tables if a questionnaire was handed out

although the patient did not receive any study medication in the respective cycle.

End point type	Secondary

End point timeframe:

Time from baseline until end of treatment visit.

End point values	Total population			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Total score				
median (full range (min-max))				
Baseline	0.0 (0.0 to 6.0)			
Cycle 1 Day 15	0.0 (0.0 to 7.0)			
Cycle 2 Day 1	0.0 (0.0 to 4.0)			
Cycle 2 Day 15	0.0 (0.0 to 5.0)			
Cycle 3 Day 1	1.0 (0.0 to 16.0)			
Cycle 4 Day 1	0.0 (0.0 to 9.0)			
Cycle 5 Day 1	0.0 (0.0 to 4.0)			
Cycle 6 Day 1	0.5 (0.0 to 3.0)			
End of treatment	0.5 (0.0 to 17.0)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From day of informed consent until 30 days after last dose of study medication.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Total population

Reporting group description:

All patients received the investigational drug BKM120/Buparlisib and in addition, daily tamoxifen as background treatment.

Dosing regimen:
- BKM120 (Buparlisib): 100 mg/day, orally, on a continuous dosing schedule without interruption starting on day 1 in 28 day cycle
- Tamoxifen: 20 mg/day, orally, on a continuous dosing schedule without interruption starting on day 1 in 28 day cycle

Serious adverse events	Total population		
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 25 (36.00%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Malignant neoplasm progression			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cognitive disorder			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
VIth nerve paresis			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Breast inflammation			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Photosensitivity reaction			

subjects affected / exposed	1 / 25 (4.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pruritus				
subjects affected / exposed	2 / 25 (8.00%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Skin induration				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Confusional state				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Mania				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Mood altered				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Hyperglycaemia				
subjects affected / exposed	1 / 25 (4.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Total population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 25 (96.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm progression			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Vascular disorders			
Flushing			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Hypertension			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Lymphoedema			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Disease progression			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	9 / 25 (36.00%)		
occurrences (all)	10		
General physical health deterioration			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Impaired healing			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Mucosal inflammation			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		

Oedema peripheral subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 2		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Dysphonia subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all)	 1 / 25 (4.00%) 1 1 / 25 (4.00%) 1 1 / 25 (4.00%) 1		
Psychiatric disorders Agitation subjects affected / exposed occurrences (all) Anxiety subjects affected / exposed occurrences (all) Confusional state subjects affected / exposed occurrences (all) Depression subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all) Mood altered subjects affected / exposed occurrences (all) Restlessness subjects affected / exposed occurrences (all) Suicidal ideation	 1 / 25 (4.00%) 1 5 / 25 (20.00%) 5 1 / 25 (4.00%) 1 6 / 25 (24.00%) 6 1 / 25 (4.00%) 1 2 / 25 (8.00%) 2 1 / 25 (4.00%) 1		

subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	5 / 25 (20.00%)		
occurrences (all)	6		
Aspartate aminotransferase increased			
subjects affected / exposed	5 / 25 (20.00%)		
occurrences (all)	8		
Blood calcium increased			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Blood creatinine increased			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Blood parathyroid hormone increased			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Blood pressure abnormal			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Blood pressure increased			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	3		
Blood thyroid stimulating hormone increased			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Electrocardiogram abnormal			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Gamma-glutamyltransferase increased			

subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Heart rate increased			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Platelet count decreased			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Cardiac disorders			
Cardiovascular disorder			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Silent myocardial infarction			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Tachycardia			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Nervous system disorders			
Aphasia			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Disturbance in attention			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	6 / 25 (24.00%)		
occurrences (all)	8		
Dysaesthesia			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Dysgeusia			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	3		
Facial nerve disorder			

subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1		
Headache subjects affected / exposed occurrences (all)	3 / 25 (12.00%) 3		
Memory impairment subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1		
Paraesthesia subjects affected / exposed occurrences (all)	3 / 25 (12.00%) 4		
Syncope subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1		
Tremor subjects affected / exposed occurrences (all)	2 / 25 (8.00%) 2		
Blood and lymphatic system disorders Leukopenia subjects affected / exposed occurrences (all)	2 / 25 (8.00%) 3		
Thrombocytopenia subjects affected / exposed occurrences (all)	2 / 25 (8.00%) 2		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	2 / 25 (8.00%) 2		
Eye disorders Cataract subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1		
Diplopia subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1		
Eye movement disorder			

subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Visual impairment			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Abdominal pain upper			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Aphthous ulcer			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	4 / 25 (16.00%)		
occurrences (all)	4		
Dry mouth			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Dyspepsia			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Dysphagia			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Gastric dilatation			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Gastric disorder			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		

Gastrointestinal disorder			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	7 / 25 (28.00%)		
occurrences (all)	9		
Oral disorder			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Retching			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Stomatitis			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Tongue erythema			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Tooth loss			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	2		
Toothache			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	5 / 25 (20.00%)		
occurrences (all)	6		
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Hyperbilirubinaemia			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Liver tenderness			

subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Dermatitis allergic			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Dry skin			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Erythema			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Onychoclasis			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Photodermatosis			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	2		
Photosensitivity reaction			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Pruritus			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Rash			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	3		
Rash maculo-papular			

subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Rash vesicular			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Renal and urinary disorders			
Bladder disorder			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Bone pain			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Flank pain			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Muscle spasms			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	3		
Muscular weakness			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Musculoskeletal pain			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Temporomandibular joint syndrome			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Infections and infestations			

Conjunctivitis			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Gastrointestinal infection			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Infection			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Ophthalmic herpes zoster			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Otitis externa			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Periodontitis			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Tonsillitis			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Viral upper respiratory tract infection			
subjects affected / exposed	4 / 25 (16.00%)		
occurrences (all)	4		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	4 / 25 (16.00%)		
occurrences (all)	4		
Dehydration			

subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Hyperglycaemia			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Underweight			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Vitamin D deficiency			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 October 2015	Protocol was amended to provide additional guidance to investigators regarding management of liver toxicities.
21 September 2016	Provide a clarification on the measures to follow when a patient exhibits suicidal ideation regardless of the response to question 9 of the PHQ-9 questionnaire (as has been described in the BKM120 Investigator's Brochure Ed. 9.0).

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.

Due to a re-evaluation of the risk-benefit profile of buparlisib, recruitment was stopped with 25 patients under buparlisib treatment (25% of the planned 99 patients) leading to a marked reduction of power and limitation of significance of the data.

Notes: