Clinical trial results:
A Phase Ib/II, open-label, multi-center study of INC280 in combination with buparlisib in adult patients with recurrent glioblastoma

Summary

EudraCT number	2013-000699-14
Trial protocol	NL ES
Global end of trial date	23 December 2016

Results information

Result version number	v1 (current)
This version publication date	24 December 2017
First version publication date	24 December 2017

Trial information

Trial identification

Sponsor protocol code	CINC280X2204

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01870726
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, Novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	23 December 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 December 2016
Global end of trial reached?	Yes
Global end of trial date	23 December 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the Phase Ib part was to estimate the maximum tolerated dose (MTD) and/or to identify the recommended Phase II dose (RP2D) for the combination of INC280 and buparlisib.
The primary objective of the Phase II part of the study w as to estimate the clinical efficacy and safety of INC280 as a single agent and in combination with buparlisib. The primary objective of the surgical arm was to determine the PK/PD profile of the study treatment.

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	09 January 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	Switzerland: 2
Country: Number of subjects enrolled	Netherlands: 13
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Spain: 11
Country: Number of subjects enrolled	United States: 9
Worldwide total number of subjects	43
EEA total number of subjects	32

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)	35
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 33 patients were enrolled into the Phase Ib part of the study. Patients were assigned to 6 dose combinations of INC280 with buparlisib. In the Phase II part of the study, 10 patients were enrolled.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	200 mg BID Cap+50 mg QD

Arm description:

Phase Ib: The combination of 200mg INC280 (BID) capsule and 50 mg Buparlisib (QD) once daily for Phase Ib.

Arm type	Experimental
Investigational medicinal product name	INC280 and Buparlisib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

The combination of 200mg INC280 capsule and 50 mg Buparlisib once daily for Phase Ib.

Arm title	400 mg BID Cap+50 mg QD

Arm description:

Phase Ib: The combination of 400 mg INC280 (BID) capsule and 50mg Buparlisib (QD) once daily for Phase Ib.

Arm type	Experimental
Investigational medicinal product name	INC280 and Buparlisib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

The combination of 400mg INC280 capsule and 50 mg Buparlisib once daily for Phase Ib.

Arm title	500 mg BID Cap+50 mg QD

Arm description:

Phase Ib: The combination of 500 mg INC280 (BID) capsule and 50mg Buparlisib (QD) once daily for Phase Ib.

Arm type	Experimental

Investigational medicinal product name	INC280 and Buparlisib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

The combination of 500mg INC280 capsule and 50 mg Buparlisib once daily for Phase Ib.

Arm title	500 mg BID Cap+80 mg QD

Arm description:

Phase Ib: The combination of 500 mg INC280 (BID) capsule and 80mg Buparlisib (QD) once daily for Phase Ib.

Arm type	Experimental
Investigational medicinal product name	INC280 and Buparlisib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

The combination of 500mg INC280 capsule and 80 mg Buparlisib once daily for Phase Ib.

Arm title	300 mg BID Tab +80 mg QD

Arm description:

Phase Ib: The combination of 300 mg INC280 (BID) tablet and 80mg Buparlisib (QD) once daily for Phase Ib.

Arm type	Experimental
Investigational medicinal product name	INC280 and Buparlisib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

The combination of 300mg INC280 tablet and 80 mg Buparlisib once daily for Phase Ib.

Arm title	400 mg BID Tab +80 mg QD

Arm description:

Phase Ib: The combination of 400 mg INC280 (BID) tablet and 80mg Buparlisib (QD) once daily for Phase Ib.

Arm type	Experimental
Investigational medicinal product name	INC280 and Buparlisib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The combination of 400mg INC280 tablet and 80 mg Buparlisib once daily for Phase Ib.

Arm title	400 mg BID Tab

Arm description:

Phase II: 400 mg INC280 (BID) tablet

Arm type	Experimental

Investigational medicinal product name	INC280
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

400mg INC280 tablet

Number of subjects in period 1	200 mg BID Cap+50 mg QD	400 mg BID Cap+50 mg QD	500 mg BID Cap+50 mg QD
Started	5	6	4
Completed	0	0	0
Not completed	5	6	4
Consent withdrawn by subject	-	1	-
Adverse event, non-fatal	-	-	-
Progressive disease	5	5	4
Withdrawal of informed consent	-	-	-

Number of subjects in period 1	500 mg BID Cap+80 mg QD	300 mg BID Tab +80 mg QD	400 mg BID Tab +80 mg QD
Started	6	7	5
Completed	0	0	0
Not completed	6	7	5
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	-	1	1
Progressive disease	5	6	4
Withdrawal of informed consent	1	-	-

Number of subjects in period 1	400 mg BID Tab
Started	10
Completed	0
Not completed	10
Consent withdrawn by subject	-
Adverse event, non-fatal	-
Progressive disease	10
Withdrawal of informed consent	-

Baseline characteristics

Reporting groups	
Reporting group title	200 mg BID Cap+50 mg QD
Reporting group description:	
Phase Ib: The combination of 200mg INC280 (BID) capsule and 50 mg Buparlisib (QD) once daily for Phase Ib.	
Reporting group title	400 mg BID Cap+50 mg QD
Reporting group description:	
Phase Ib: The combination of 400 mg INC280 (BID) capsule and 50mg Buparlisib (QD) once daily for Phase Ib.	
Reporting group title	500 mg BID Cap+50 mg QD
Reporting group description:	
Phase Ib: The combination of 500 mg INC280 (BID) capsule and 50mg Buparlisib (QD) once daily for Phase Ib.	
Reporting group title	500 mg BID Cap+80 mg QD
Reporting group description:	
Phase Ib: The combination of 500 mg INC280 (BID) capsule and 80mg Buparlisib (QD) once daily for Phase Ib.	
Reporting group title	300 mg BID Tab +80 mg QD
Reporting group description:	
Phase Ib: The combination of 300 mg INC280 (BID) tablet and 80mg Buparlisib (QD) once daily for Phase Ib.	
Reporting group title	400 mg BID Tab +80 mg QD
Reporting group description:	
Phase Ib: The combination of 400 mg INC280 (BID) tablet and 80mg Buparlisib (QD) once daily for Phase Ib.	
Reporting group title	400 mg BID Tab
Reporting group description:	
Phase II: 400 mg INC280 (BID) tablet	

Reporting group values	200 mg BID Cap+50 mg QD	400 mg BID Cap+50 mg QD	500 mg BID Cap+50 mg QD
Number of subjects	5	6	4
Age Categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	2	6	4
>=65 years	3	0	0
Age continuous Units: years			
arithmetic mean	59.2	48.0	56.0
standard deviation	± 10.03	± 12.43	± 3.56
Gender, Male/Female Units: Subjects			
Female	0	2	2
Male	5	4	2

Reporting group values	500 mg BID Cap+80 mg QD	300 mg BID Tab +80 mg QD	400 mg BID Tab +80 mg QD
Number of subjects	6	7	5

Age Categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	5	4	4
>=65 years	1	3	1
Age continuous Units: years			
arithmetic mean	52.0	63.0	60.4
standard deviation	± 13.48	± 10.08	± 5.50
Gender, Male/Female Units: Subjects			
Female	3	0	2
Male	3	7	3

Reporting group values	400 mg BID Tab	Total	
Number of subjects	10	43	
Age Categorical Units: Subjects			
<=18 years	0	0	
Between 18 and 65 years	10	35	
>=65 years	0	8	
Age continuous Units: years			
arithmetic mean	47.6		
standard deviation	± 11.06	-	
Gender, Male/Female Units: Subjects			
Female	7	16	
Male	3	27	

End points reporting groups

Reporting group title	200 mg BID Cap+50 mg QD
Reporting group description:	
Phase Ib: The combination of 200mg INC280 (BID) capsule and 50 mg Buparlisib (QD) once daily for Phase Ib.	
Reporting group title	400 mg BID Cap+50 mg QD
Reporting group description:	
Phase Ib: The combination of 400 mg INC280 (BID) capsule and 50mg Buparlisib (QD) once daily for Phase Ib.	
Reporting group title	500 mg BID Cap+50 mg QD
Reporting group description:	
Phase Ib: The combination of 500 mg INC280 (BID) capsule and 50mg Buparlisib (QD) once daily for Phase Ib.	
Reporting group title	500 mg BID Cap+80 mg QD
Reporting group description:	
Phase Ib: The combination of 500 mg INC280 (BID) capsule and 80mg Buparlisib (QD) once daily for Phase Ib.	
Reporting group title	300 mg BID Tab +80 mg QD
Reporting group description:	
Phase Ib: The combination of 300 mg INC280 (BID) tablet and 80mg Buparlisib (QD) once daily for Phase Ib.	
Reporting group title	400 mg BID Tab +80 mg QD
Reporting group description:	
Phase Ib: The combination of 400 mg INC280 (BID) tablet and 80mg Buparlisib (QD) once daily for Phase Ib.	
Reporting group title	400 mg BID Tab
Reporting group description:	
Phase II: 400 mg INC280 (BID) tablet	
Subject analysis set title	400 mg BID Tab+80 mg QD
Subject analysis set type	Full analysis
Subject analysis set description:	
Phase Ib: The combination of 400 mg INC280 (BID) tablet and 80mg Buparlisib (QD) once daily for Phase Ib.	
Subject analysis set title	BID Tab+Buparlisib
Subject analysis set type	Full analysis
Subject analysis set description:	
Phase II: INC280 (BID) as a single agent and in combination with buparlisib	
Subject analysis set title	BID + QD
Subject analysis set type	Full analysis
Subject analysis set description:	
The combination of INC280 (BID) and Buparlisib (QD).	
Subject analysis set title	300 mg BID Tab + 80 mg QD
Subject analysis set type	Full analysis
Subject analysis set description:	
Phase Ib: The combination of 300 mg INC280 (BID) tablet and 80mg Buparlisib (QD) once daily for Phase Ib.	
Subject analysis set title	400 mg BID Tab + 80 mg QD
Subject analysis set type	Full analysis
Subject analysis set description:	
Phase Ib: the combination of 400 mg INC280 (BID) tablet and 80 mg Buparlisib (QD) once daily	
Subject analysis set title	400 mg BID Tab+80 mg QD

Subject analysis set type	Full analysis

Subject analysis set description:

Phase Ib: The combination of 400 mg INC280 (BID) tablet and 80mg Buparlisib (QD) once daily for Phase Ib.

Subject analysis set title	400 mg BID Tab+80 mg QD
Subject analysis set type	Full analysis

Subject analysis set description:

Phase Ib: The combination of 400 mg INC280 (BID) capsule and 80mg Buparlisib (QD) once daily for Phase Ib.

Subject analysis set title	All Patients
Subject analysis set type	Full analysis

Subject analysis set description:

The combination of INC280 (BID) and Buparlisib (QD).

Primary: Incidence of dose limiting toxicities (DLTs) in Cycle 1

End point title	Incidence of dose limiting toxicities (DLTs) in Cycle 1[1][2]

End point description:

A DLT is defined as an adverse event or abnormal laboratory value where the relationship to study treatment cannot be ruled out, and is not primarily related to disease, disease progression, inter-current illness, or concomitant medications that occurs within the first cycle of treatment (28 days) with INC280 in combination with buparlisib and meets any of the pre-defined criteria.
Analysis was done in the dose-determining set (DDS). The DDS consisted of all patients from the SAS who either met the following minimum exposure criterion and had sufficient safety evaluations during cycle 1, or discontinued earlier due to DLT during Cycle 1: A patient was considered to have met the minimum exposure criterion if they had received at least 21 out of the 28 planned daily combo doses of INC280 and buparlisib (once daily) in the first 28 days of dosing.

End point type	Primary

End point timeframe:

Cycle 1

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No comparative statistical analysis was conducted for this endpoint. The relationship between dose and the probability of DLT was modeled using adaptive Bayesian logistic regression model with overdose control principle. MTD was declared at INC280 300mg bid + BKM120 80mg qd. RP2D was not be declared.
[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only treatment groups which are part of dose determining set are included.

End point values	200 mg BID Cap+50 mg QD	400 mg BID Cap+50 mg QD	500 mg BID Cap+50 mg QD	500 mg BID Cap+80 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	5	3	4
Units: Number of Patients				
Personality Change	0	1	0	0
Nausea	0	0	0	0
Aspartate Aminotransferase Increased	0	0	0	0

End point values	300 mg BID Tab +80 mg QD	400 mg BID Tab +80 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	4		
Units: Number of Patients				

Personality Change	0	0		
Nausea	1	0		
Aspartate Aminotransferase Increased	0	2		

Statistical analyses

No statistical analyses for this end point

Primary: Phase II: Progression free survival rate (PFSR)

End point title	Phase II: Progression free survival rate (PFSR)[3]

End point description:

Estimated rate of patients treated during 6 months without experiencing disease progression.

End point type	Primary

End point timeframe:

6 months

Notes:

[3] - 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: Due to early termination, no statistical analysis was planned for this endpoint.

End point values	BID Tab+Buparlisib			
Subject group type	Subject analysis set			
Number of subjects analysed	0[4]			
Units: Percentages of participants				

Notes:

[4] - PFS was not performed due to an insufficient number of patients enrolled.

Statistical analyses

No statistical analyses for this end point

Primary: Phase II Surgical arm: Concentrations of INC280 and buparlisib in tumor

End point title	Phase II Surgical arm: Concentrations of INC280 and buparlisib in tumor[5]

End point description:

Concentrations of INC280 and buparlisib in tumor tissue.

End point type	Primary

End point timeframe:

7 days

Notes:

[5] - 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: Due to early termination, no statistical analysis was planned for this endpoint.

End point values	BID + QD			
Subject group type	Subject analysis set			
Number of subjects analysed	0[6]			
Units: mmol/L				

Notes:

[6] - A RP2D was not determined and phase II combination arms were not opened.

Statistical analyses

No statistical analyses for this end point

Secondary: Overview of Adverse Events

End point title	Overview of Adverse Events

End point description:

To characterize the safety of INC280 single agent and in combination with buparlisib including type, frequency, severity of adverse events, serious adverse events, and dose interruptions and adjustments. Analysis was done in the safety analysis set (SAS).
The SAS comprised all patients who received at least one full or partial dose of study treatment. Patients were analyzed according to the treatment actually received. The SAS was used for all safety analyses.

End point type	Secondary

End point timeframe:

Throughout the duration of the trial, approximately 3 years from FPFV to LPLV.

End point values	200 mg BID Cap+50 mg QD	400 mg BID Cap+50 mg QD	500 mg BID Cap+50 mg QD	500 mg BID Cap+80 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	6	4	6
Units: Participants				
Adverse events	5	6	4	6
Treatment-related AEs	4	4	4	4
AEs with grade ≥ 3	5	4	4	2
SAEs	3	2	3	3
AEs leading to discontinuation	0	0	0	0
AEs leading to dose adjustment/interruption	2	3	2	4
AEs requiring additional therapy	4	5	3	5

End point values	300 mg BID Tab +80 mg QD	400 mg BID Tab +80 mg QD	400 mg BID Tab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	5	9	
Units: Participants				
Adverse events	7	5	9	
Treatment-related AEs	7	5	6	
AEs with grade ≥ 3	5	4	8	
SAEs	3	4	2	
AEs leading to discontinuation	1	1	0	

AEs leading to dose adjustment/interruption	4	4	5	
AEs requiring additional therapy	7	5	7	

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic profile of INC280 - AUCtau

End point title	Pharmacokinetic profile of INC280 - AUCtau[7]

End point description:

Plasma concentration profile of INC280 in combination with Buparlisib. AUCtau is the AUC from time zero to the end of dosing interval. Analysis was done in the pharmacokinetic analysis set (PAS). The PAS consisted of all patients who provided an evaluable PK profile. A profile was considered evaluable if all of the following conditions were satisfied:
1) Patient received one of the planned treatments of both study drugs
2) For PK samples taken on Cycle 1 Day 15 and Cycle 2 Day 1, patient took the same dose of INC280 for at least three consecutive days and the same dose of buparlisib for at least seven consecutive days prior to sampling
3) Patients provided at least one primary PK parameter of either INC280 or buparlisib
4) Patient did not vomit within four hours after the dosing of INC280 and/or buparlisib
The respective PAS was used for the analysis and listings of the PK derived parameters.

End point type	Secondary

End point timeframe:

Cycle 1 to cycle 6, approximately 6 months

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only treatment groups which are part of Pharmacokinetic analysis set are included.

End point values	200 mg BID Cap+50 mg QD	400 mg BID Cap+50 mg QD	500 mg BID Cap+50 mg QD	500 mg BID Cap+80 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	4	6
Units: hr*ng/ml				
median (full range (min-max))				
Cycle 1 Day 1	2435.6 (1870.1 to 4978.4)	3005.9 (1010.1 to 5581.5)	4789.7 (1716.5 to 8086.8)	5071.7 (2463.8 to 8018.8)
Cycle 1 Day 15	5749.3 (4045.6 to 10405.8)	11261.7 (3069.8 to 13946.9)	10581.0 (6276.0 to 31532.5)	2779.4 (1940.8 to 3618.0)
Cycle 2 Day 1	4894.6 (3880.4 to 7192.8)	2655.6 (2655.6 to 2655.6)	23498.3 (19903.7 to 27092.8)	10554.3 (4793.3 to 14289.7)

End point values	300 mg BID Tab +80 mg QD	400 mg BID Tab +80 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	5		
Units: hr*ng/ml				

median (full range (min-max))				
Cycle 1 Day 1	5732.2 (1657.2 to 8924.7)	11127.7 (2978.35 to 13776.6)		
Cycle 1 Day 15	12801.3 (8606.0 to 16381.0)	16590.6 (11576.1 to 17422.8)		
Cycle 2 Day 1	9593.5 (7002.3 to 12184.7)	13051.1 (13051.1 to 13051.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic profile of INC280 - Cmax

End point title	Pharmacokinetic profile of INC280 - Cmax[8]

End point description:

Plasma concentration profile of INC280 in combination with Buparlisib. Cmax is the Maximum (peak) observed drug concentration after dose administration.
Analysis was done in the pharmacokinetic analysis set (PAS).

End point type	Secondary

End point timeframe:

Cycle 1 to cycle 6, approximately 6 months

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only treatment groups which are part of Pharmacokinetic analysis set are included.

End point values	200 mg BID Cap+50 mg QD	400 mg BID Cap+50 mg QD	500 mg BID Cap+50 mg QD	500 mg BID Cap+80 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	4	6
Units: ng/ml				
median (full range (min-max))				
Cycle 1 Day 1	618.0 (406.0 to 1680.0)	880.0 (219.0 to 1410.0)	960.5 (434.0 to 2510.0)	860.0 (195.0 to 2770.0)
Cycle 1 Day 15	1560.0 (745.0 to 2610.0)	2005.0 (763.0 to 3930.0)	3480.0 (1350.0 to 8350.0)	545.5 (315.0 to 776.0)
Cycle 2 Day 1	1200.0 (578.0 to 1540.0)	2142.5 (675.0 to 3610.0)	5010.0 (4230.0 to 5790.0)	2254.5 (479.0 to 3740.0)

End point values	300 mg BID Tab +80 mg QD	400 mg BID Tab +80 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	5		
Units: ng/ml				
median (full range (min-max))				

Cycle 1 Day 1	1990.0 (423.0 to 2510.0)	3635.0 (1210.0 to 4640.0)		
Cycle 1 Day 15	3610.0 (2320.0 to 4940.0)	4850.0 (1800.0 to 5350.0)		
Cycle 2 Day 1	3080.0 (2720.0 to 3440.0)	3220.0 (3220.0 to 3220.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic profile of INC280 - Tmax

End point title	Pharmacokinetic profile of INC280 - Tmax[9]

End point description:

Plasma concentration profile of INC280 in combination with Buparlisib. Tmax is the time to reach maximum (peak) observed concentration (Cmax) after dose administration.
Analysis was done in the pharmacokinetic analysis set (PAS).

End point type	Secondary

End point timeframe:

Cycle 1 to cycle 6, approximately 6 months

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only treatment groups which are part of Pharmacokinetic analysis set are included.

End point values	200 mg BID Cap+50 mg QD	400 mg BID Cap+50 mg QD	500 mg BID Cap+50 mg QD	500 mg BID Cap+80 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	4	6
Units: hr				
median (full range (min-max))				
Cycle 1 Day 1	1.1 (1.0 to 2.0)	2.0 (2.0 to 4.0)	1.5 (1.0 to 2.2)	1.3 (1.1 to 4.0)
Cycle 1 Day 15	1.9 (0.9 to 2.0)	2.0 (1.0 to 2.1)	2.0 (1.0 to 2.1)	2.6 (1.2 to 4.0)
Cycle 2 Day 1	2.0 (1.0 to 4.0)	2.0 (2.0 to 2.0)	1.5 (1.0 to 2.1)	2.1 (1.5 to 4.0)

End point values	300 mg BID Tab +80 mg QD	400 mg BID Tab +80 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	5		
Units: hr				
median (full range (min-max))				
Cycle 1 Day 1	1.6 (1.0 to 2.2)	2.0 (0.9 to 2.0)		
Cycle 1 Day 15	1.0 (1.0 to 1.0)	1.5 (1.0 to 2.1)		
Cycle 2 Day 1	1.5 (1.0 to 2.0)	1.0 (1.0 to 1.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic profile of INC280 - T1/2

End point title	Pharmacokinetic profile of INC280 - T1/2[10]

End point description:

Plasma concentration profile of INC280 in combination with Buparlisib. T1/2 is the terminal half life. Analysis was done in the pharmacokinetic analysis set (PAS).

End point type	Secondary

End point timeframe:

Cycle 1 to cycle 6, approximately 6 months

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only treatment groups which are part of Pharmacokinetic analysis set are included.

End point values	200 mg BID Cap+50 mg QD	400 mg BID Cap+50 mg QD	500 mg BID Cap+50 mg QD	500 mg BID Cap+80 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	4	6
Units: hr				
median (full range (min-max))				
Cycle 1 Day 15	13.4 (4.1 to 31.2)	20.8 (16.3 to 28.6)	26.0 (13.2 to 28.1)	7.3 (7.3 to 7.3)
Cycle 2 Day 1	9.9 (3.8 to 20.1)	17.4 (17.4 to 17.4)	26.3 (23.5 to 29.1)	8.7 (5.8 to 11.5)

End point values	300 mg BID Tab +80 mg QD	400 mg BID Tab +80 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	5		
Units: hr				
median (full range (min-max))				
Cycle 1 Day 15	13.1 (7.0 to 19.3)	8.0 (4.2 to 28.0)		
Cycle 2 Day 1	6.3 (6.3 to 6.3)	4.3 (4.3 to 4.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic profile of Buparlisib - AUCtau

End point title	Pharmacokinetic profile of Buparlisib - AUCtau[11]

End point description:

Plasma concentration profile of INC280 in combination with Buparlisib. AUCtau is the AUC from time zero to the end of dosing interval.
Analysis was done in the pharmacokinetic analysis set (PAS).

End point type	Secondary

End point timeframe:

Cycle 1 to cycle 6, approximately 6 months

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only treatment groups which are part of Pharmacokinetic analysis set are included.

End point values	200 mg BID Cap+50 mg QD	400 mg BID Cap+50 mg QD	500 mg BID Cap+50 mg QD	500 mg BID Cap+80 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	4	6
Units: hr*ng/ml				
median (full range (min-max))				
Cycle 1 Day 1	3072.0 (2119.7 to 3448.0)	1865.0 (1383.2 to 3840.8)	3328.2 (2830.2 to 4104.1)	3825.8 (2784.0 to 5201.4)
Cycle 1 Day 15	8728.5 (4874.3 to 10962.7)	4591.9 (3167.1 to 10562.3)	6108.4 (5300.5 to 7605.5)	10844.6 (6761.7 to 14927.4)
Cycle 2 Day 1	7930.8 (3563.5 to 9712.2)	3776.7 (3477.6 to 4075.7)	6976.0 (3436.1 to 10515.9)	5903.0 (4850.4 to 12072.9)

End point values	300 mg BID Tab +80 mg QD	400 mg BID Tab +80 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	5		
Units: hr*ng/ml				
median (full range (min-max))				
Cycle 1 Day 1	4425.3 (3109.8 to 5238.2)	3658.8 (3347.7 to 5509.4)		
Cycle 1 Day 15	10366.5 (8257.8 to 11052.6)	8535.1 (4102.2 to 8908.3)		
Cycle 2 Day 1	7857.2 (7757.7 to 9361.9)	7344.3 (7344.3 to 7344.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic profile of Buparlisib - Cmax

End point title	Pharmacokinetic profile of Buparlisib - Cmax[12]

End point description:

Plasma concentration profile of INC280 in combination with Buparlisib. Cmax is the Maximum (peak) observed drug concentration after dose administration.
Analysis was done in the pharmacokinetic analysis set (PAS).

End point type	Secondary

End point timeframe:

Cycle 1 to cycle 6, approximately 6 months

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only treatment groups which are part of Pharmacokinetic analysis set are included.

End point values	200 mg BID Cap+50 mg QD	400 mg BID Cap+50 mg QD	500 mg BID Cap+50 mg QD	500 mg BID Cap+80 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	4	6
Units: ng/ml				
median (full range (min-max))				
Cycle 1 Day 1	484.0 (234.0 to 590.0)	351.0 (162.0 to 488.0)	399.0 (347.0 to 469.0)	522.0 (333.0 to 776.0)
Cycle 1 Day 15	664.0 (568.0 to 791.0)	459.0 (294.0 to 623.0)	542.0 (456.0 to 791.0)	785.0 (684.0 to 886.0)
Cycle 2 Day 1	560.0 (290.0 to 813.0)	377.5 (285.0 to 470.0)	611.0 (409.0 to 813.0)	529.5 (383.0 to 865.0)

End point values	300 mg BID Tab +80 mg QD	400 mg BID Tab +80 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	5		
Units: ng/ml				
median (full range (min-max))				
Cycle 1 Day 1	508.0 (373.0 to 711.0)	475.0 (361.0 to 542.0)		
Cycle 1 Day 15	814.0 (628.0 to 1330.0)	788.5 (390.0 to 1700.0)		
Cycle 2 Day 1	735.0 (558.0 to 890.0)	600.0 (600.0 to 600.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic profile of Buparlisib - Tmax

End point title	Pharmacokinetic profile of Buparlisib - Tmax[13]

End point description:

Plasma concentration profile of INC280 in combination with Buparlisib. Tmax is the time to reach maximum (peak) observed concentration (Cmax) after dose administration.
Analysis was done in the pharmacokinetic analysis set (PAS).

End point type	Secondary

End point timeframe:

Cycle 1 to cycle 6, approximately 6 months

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only treatment groups which are part of Pharmacokinetic analysis set are included.

End point values	200 mg BID Cap+50 mg QD	400 mg BID Cap+50 mg QD	500 mg BID Cap+50 mg QD	500 mg BID Cap+80 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	4	6
Units: hr				
median (full range (min-max))				
Cycle 1 Day 1	1.0 (0.6 to 1.2)	1.0 (0.6 to 2.0)	1.0 (0.5 to 1.2)	0.6 (0.5 to 2.0)
Cycle 1 Day 15	0.9 (0.9 to 1.0)	2.0 (1.0 to 2.1)	1.0 (1.0 to 2.0)	1.6 (1.2 to 2.0)
Cycle 2 Day 1	1.0 (0.5 to 2.0)	1.5 (1.0 to 2.0)	1.0 (1.0 to 1.0)	1.8 (1.0 to 2.1)

End point values	300 mg BID Tab +80 mg QD	400 mg BID Tab +80 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	5		
Units: hr				
median (full range (min-max))				
Cycle 1 Day 1	1.2 (0.5 to 2.0)	1.0 (0.9 to 2.0)		
Cycle 1 Day 15	1.0 (0.5 to 1.0)	1.3 (0.5 to 2.1)		
Cycle 2 Day 1	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic profile of Buparlisib - T1/2

End point title	Pharmacokinetic profile of Buparlisib - T1/2[14]

End point description:

Plasma concentration profile of INC280 in combination with Buparlisib. T1/2 is the terminal half life.
Analysis was done in the pharmacokinetic analysis set (PAS).

End point type	Secondary

End point timeframe:

Cycle 1 to cycle 6, approximately 6 months

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only treatment groups which are part of Pharmacokinetic analysis set are included.

End point values	200 mg BID Cap+50 mg QD	400 mg BID Cap+50 mg QD	500 mg BID Cap+50 mg QD	500 mg BID Cap+80 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	4	6
Units: hr				
median (full range (min-max))				
Cycle 1 Day 15	37.3 (29.1 to 52.4)	31.1 (18.7 to 46.4)	21.8 (20.8 to 29.4)	30.9 (19.9 to 41.8)
Cycle 2 Day 1	34.0 (10.4 to 37.9)	21.3 (16.4 to 26.1)	27.0 (9.6 to 44.3)	17.2 (16.8 to 31.9)

End point values	300 mg BID Tab +80 mg QD	400 mg BID Tab +80 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	5		
Units: hr				
median (full range (min-max))				
Cycle 1 Day 15	38.0 (21.3 to 44.9)	22.8 (5.8 to 31.5)		
Cycle 2 Day 1	20.1 (19.4 to 41.2)	12.0 (12.0 to 12.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Best Overall Response (BOR)

End point title	Best Overall Response (BOR)

End point description:

Best Overall Response (BOR) observed in the study population of INC280 Single Agent and in Combination with Buparlisib

End point type	Secondary

End point timeframe:

throughout the duration of the trial - approximately 3 years (from FPFV to LPLV)

End point values	200 mg BID Cap+50 mg QD	400 mg BID Cap+50 mg QD	500 mg BID Cap+50 mg QD	500 mg BID Cap+80 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	6	4	6
Units: Percentages of participants				
Complete Response (CR)	0	0	0	0
Partial Response (PR)	0	0	0	0
Stable Disease (SD)	0	0	0	1
Progressive Disease (PD)	5	5	4	4
Unknown (UNK)	0	0	0	0
Not Assessed	0	1	0	1

End point values	300 mg BID Tab +80 mg QD	400 mg BID Tab +80 mg QD	400 mg BID Tab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	5	10	
Units: Percentages of participants				
Complete Response (CR)	0	0	0	
Partial Response (PR)	0	0	0	
Stable Disease (SD)	0	0	3	
Progressive Disease (PD)	7	4	6	
Unknown (UNK)	0	0	0	
Not Assessed	0	1	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS)

End point title	Overall survival (OS)

End point description:

Survival rate of patients from start of treatment to date of death due to any cause

End point type	Secondary

End point timeframe:

throughout the duration of the trial - approximately 3 years (FPFV to LPLV)

End point values	All Patients			
Subject group type	Subject analysis set			
Number of subjects analysed	0[15]			
Units: Percentages of participants				

Notes:

[15] - OS was not performed as there were an insufficient number of patients enrolled for the analysis.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment Emergent Adverse Events (AEs) are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All AEs 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	19.1

Reporting groups

Reporting group title	INC280 200 mg BID Tab
Reporting group description:	
INC280 200 mg BID Tab	
Reporting group title	INC280 200 mg BID Cap + Buparlisib 50 mg QD
Reporting group description:	
INC280 200 mg BID Cap + Buparlisib 50 mg QD	
Reporting group title	INC280 400 mg BID Cap + Buparlisib 50 mg QD
Reporting group description:	
INC280 400 mg BID Cap + Buparlisib 50 mg QD	
Reporting group title	INC280 500 mg BID Cap + Buparlisib 50 mg QD
Reporting group description:	
INC280 500 mg BID Cap + Buparlisib 50 mg QD	
Reporting group title	INC280 500 mg BID Cap + Buparlisib 80 mg QD
Reporting group description:	
INC280 500 mg BID Cap + Buparlisib 80 mg QD	
Reporting group title	INC280 300 mg BID Tab + Buparlisib 80 mg QD
Reporting group description:	
INC280 300 mg BID Tab + Buparlisib 80 mg QD	
Reporting group title	INC280 400 mg BID Tab + Buparlisib 80 mg QD
Reporting group description:	
INC280 400 mg BID Tab + Buparlisib 80 mg QD	
Reporting group title	Phase Ib All@Patients
Reporting group description:	
Phase Ib All@Patients	
Reporting group title	INC280 400 mg BID Tab
Reporting group description:	
INC280 400 mg BID Tab	
Reporting group title	Phase II All Patients
Reporting group description:	
Phase II All@Patients	

Serious adverse events	INC280 200 mg BID Tab	INC280 200 mg BID Cap + Buparlisib 50 mg QD	INC280 400 mg BID Cap + Buparlisib 50 mg QD
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)	3 / 5 (60.00%)	2 / 6 (33.33%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
FALL			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
EMBOLISM			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERTENSION			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
APHASIA			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATAXIA			

subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRAIN OEDEMA			
subjects affected / exposed	1 / 1 (100.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMORRHAGE INTRACRANIAL			
subjects affected / exposed	0 / 1 (0.00%)	2 / 5 (40.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEMIPARESIS			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LETHARGY			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUROLOGICAL DECOMPENSATION			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PARAPARESIS			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PARTIAL SEIZURES			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEIZURE			

subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
PYREXIA			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIARRHOEA			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRIC ULCER			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NAUSEA			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
DERMATITIS ALLERGIC			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RASH			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Psychiatric disorders			
APATHY			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
FEBRILE INFECTION			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFLUENZA			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERITONITIS			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMOCYSTIS JIROVECII PNEUMONIA			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
HYPONATRAEMIA			

subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	INC280 500 mg BID Cap + Buparlisib 50 mg QD	INC280 500 mg BID Cap + Buparlisib 80 mg QD	INC280 300 mg BID Tab + Buparlisib 80 mg QD
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 4 (75.00%)	3 / 6 (50.00%)	3 / 7 (42.86%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
FALL			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
EMBOLISM			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERTENSION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			

APHASIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATAXIA			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRAIN OEDEMA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMORRHAGE INTRACRANIAL			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEMIPARESIS			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LETHARGY			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUROLOGICAL DECOMPENSATION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PARAPARESIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PARTIAL SEIZURES			

subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEIZURE			
subjects affected / exposed	2 / 4 (50.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
PYREXIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIARRHOEA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRIC ULCER			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NAUSEA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
DERMATITIS ALLERGIC			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

RASH			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
APATHY			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
FEBRILE INFECTION			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFLUENZA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERITONITIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMOCYSTIS JIROVECII PNEUMONIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Metabolism and nutrition disorders			
HYPONATRAEMIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	INC280 400 mg BID Tab + Buparlisib 80 mg QD	Phase Ib All@Patients	INC280 400 mg BID Tab
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 5 (80.00%)	18 / 33 (54.55%)	2 / 9 (22.22%)
number of deaths (all causes)	0	1	1
number of deaths resulting from adverse events	0	0	0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	3 / 5 (60.00%)	4 / 33 (12.12%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	3 / 3	4 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	3 / 5 (60.00%)	3 / 33 (9.09%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	3 / 3	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
FALL			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
EMBOLISM			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERTENSION			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Nervous system disorders			
APHASIA			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATAXIA			
subjects affected / exposed	1 / 5 (20.00%)	3 / 33 (9.09%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRAIN OEDEMA			
subjects affected / exposed	0 / 5 (0.00%)	0 / 33 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMORRHAGE INTRACRANIAL			
subjects affected / exposed	0 / 5 (0.00%)	3 / 33 (9.09%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEMIPARESIS			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LETHARGY			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUROLOGICAL DECOMPENSATION			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PARAPARESIS			
subjects affected / exposed	1 / 5 (20.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PARTIAL SEIZURES			

subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEIZURE			
subjects affected / exposed	0 / 5 (0.00%)	3 / 33 (9.09%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
PYREXIA			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIARRHOEA			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRIC ULCER			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NAUSEA			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
DERMATITIS ALLERGIC			
subjects affected / exposed	1 / 5 (20.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

RASH			
subjects affected / exposed	1 / 5 (20.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
APATHY			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
FEBRILE INFECTION			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFLUENZA			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERITONITIS			
subjects affected / exposed	0 / 5 (0.00%)	0 / 33 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMOCYSTIS JIROVECII PNEUMONIA			
subjects affected / exposed	1 / 5 (20.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Metabolism and nutrition disorders			
HYPONATRAEMIA			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Phase II All Patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 10 (30.00%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
FALL			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
EMBOLISM			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HYPERTENSION			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			

APHASIA				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ATAXIA				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
BRAIN OEDEMA				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
HAEMORRHAGE INTRACRANIAL				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
HEMIPARESIS				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
LETHARGY				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
NEUROLOGICAL DECOMPENSATION				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PARAPARESIS				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PARTIAL SEIZURES				

subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SEIZURE				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
PYREXIA				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
ABDOMINAL PAIN				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
DIARRHOEA				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
GASTRIC ULCER				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
NAUSEA				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
DERMATITIS ALLERGIC				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

RASH				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
APATHY				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
FEBRILE INFECTION				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
INFLUENZA				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PERITONITIS				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PNEUMOCYSTIS JIROVECII PNEUMONIA				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PNEUMONIA				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
URINARY TRACT INFECTION				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Metabolism and nutrition disorders			
HYPONATRAEMIA			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	INC280 200 mg BID Tab	INC280 200 mg BID Cap + Buparlisib 50 mg QD	INC280 400 mg BID Cap + Buparlisib 50 mg QD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	5 / 5 (100.00%)	6 / 6 (100.00%)
Vascular disorders			
EMBOLISM			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
HAEMATOMA			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
HOT FLUSH			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
HYPERTENSION			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
HYPOTENSION			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
CHILLS			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
FATIGUE			

subjects affected / exposed	0 / 1 (0.00%)	2 / 5 (40.00%)	3 / 6 (50.00%)
occurrences (all)	0	2	3
GAIT DISTURBANCE			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
OEDEMA PERIPHERAL			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
PYREXIA			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
TESTICULAR PAIN			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
BRONCHOSPASM			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
COUGH			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
HICCUPS			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
PRODUCTIVE COUGH			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
RHINORRHOEA			

subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
AGITATION			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
ANXIETY			
subjects affected / exposed	0 / 1 (0.00%)	2 / 5 (40.00%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
APATHY			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
BRADYPHRENIA			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
CONFUSIONAL STATE			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
DEPRESSED MOOD			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
DEPRESSION			
subjects affected / exposed	0 / 1 (0.00%)	2 / 5 (40.00%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
DISORIENTATION			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	1 / 6 (16.67%)
occurrences (all)	0	2	1
INSOMNIA			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
IRRITABILITY			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
MOOD ALTERED			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	1 / 6 (16.67%)
occurrences (all)	0	1	2

PERSONALITY CHANGE			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
SLEEP DISORDER			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
AMYLASE INCREASED			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
BLOOD ALBUMIN DECREASED			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
BLOOD CREATININE INCREASED			
subjects affected / exposed	0 / 1 (0.00%)	2 / 5 (40.00%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
BLOOD GLUCOSE INCREASED			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
BLOOD POTASSIUM INCREASED			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
BLOOD TRIGLYCERIDES INCREASED			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
GLOMERULAR FILTRATION RATE DECREASED			

subjects affected / exposed	0 / 1 (0.00%)	2 / 5 (40.00%)	0 / 6 (0.00%)
occurrences (all)	0	5	0
INSULIN C-PEPTIDE INCREASED			
subjects affected / exposed	0 / 1 (0.00%)	2 / 5 (40.00%)	1 / 6 (16.67%)
occurrences (all)	0	2	1
LIPASE INCREASED			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
LYMPHOCYTE COUNT DECREASED			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
PLATELET COUNT DECREASED			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
PROTEIN TOTAL DECREASED			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
PROTHROMBIN TIME PROLONGED			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
WEIGHT DECREASED			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
WEIGHT INCREASED			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
FALL			

subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
LACERATION			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
LEFT VENTRICULAR DYSFUNCTION			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
SINUS BRADYCARDIA			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
AMNESIA			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
APHASIA			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
ATAXIA			
subjects affected / exposed	0 / 1 (0.00%)	2 / 5 (40.00%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
BRAIN OEDEMA			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
COGNITIVE DISORDER			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
DISTURBANCE IN ATTENTION			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
DIZZINESS			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
DYSARTHRIA			

subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
DYSKINESIA			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
DYSMETRIA			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
EPILEPSY			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
FACIAL PARALYSIS			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
FACIAL PARESIS			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
HEADACHE			
subjects affected / exposed	0 / 1 (0.00%)	2 / 5 (40.00%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
HEMIANOPIA			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
HEMIANOPIA HOMONYMOUS			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
HEMIPARESIS			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
HEMIPLEGIA			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
LETHARGY			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
MEMORY IMPAIRMENT			

subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
NEUROLOGIC NEGLECT SYNDROME			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
NEUROLOGICAL SYMPTOM			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
PARAESTHESIA			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
PARALYSIS			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
PARAPARESIS			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
PARESIS			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
PERIPHERAL MOTOR NEUROPATHY			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
PYRAMIDAL TRACT SYNDROME			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
RESTLESS LEGS SYNDROME			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
SEIZURE			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
SOMNOLENCE			

subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
TREMOR			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
VITH NERVE PARALYSIS			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
LEUKOPENIA			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
NEUTROPENIA			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
THROMBOCYTOPENIA			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	1 / 6 (16.67%)
occurrences (all)	0	2	1
Eye disorders			
DIPLOPIA			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
VISION BLURRED			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
CONSTIPATION			

subjects affected / exposed	0 / 1 (0.00%)	2 / 5 (40.00%)	1 / 6 (16.67%)
occurrences (all)	0	2	1
DIARRHOEA			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	1 / 6 (16.67%)
occurrences (all)	0	2	1
DYSPEPSIA			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
DYSPHAGIA			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
HAEMORRHOIDS			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
NAUSEA			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	2 / 6 (33.33%)
occurrences (all)	0	2	2
RECTAL ULCER HAEMORRHAGE			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
STOMATITIS			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
VOMITING			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	1 / 6 (16.67%)
occurrences (all)	0	3	1
Hepatobiliary disorders			
HEPATIC STEATOSIS			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
HYPERBILIRUBINAEMIA			

subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
ALOPECIA			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
DERMATITIS ACNEIFORM			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
DRY SKIN			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
PRURITUS			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
RASH			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
RASH MACULAR			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
SKIN ATROPHY			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
CHRONIC KIDNEY DISEASE			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
CYSTITIS NONINFECTIVE			

subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
HAEMATURIA			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
MICTURITION URGENCY			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
URINARY INCONTINENCE			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
URINARY RETENTION			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
MUSCLE SPASMS			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
MUSCULAR WEAKNESS			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
MUSCULOSKELETAL PAIN			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
MYALGIA			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			

ORAL HERPES			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
ORCHITIS			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	0 / 1 (0.00%)	2 / 5 (40.00%)	1 / 6 (16.67%)
occurrences (all)	0	2	1
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 1 (0.00%)	2 / 5 (40.00%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
HYPERURICAEMIA			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
HYPOALBUMINAEMIA			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
HYPOGLYCAEMIA			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
HYPOKALAEMIA			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
HYPONATRAEMIA			
subjects affected / exposed	0 / 1 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
HYPOPHOSPHATAEMIA			
subjects affected / exposed	0 / 1 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	INC280 500 mg BID Cap + Buparlisib 50 mg QD	INC280 500 mg BID Cap + Buparlisib 80 mg QD	INC280 300 mg BID Tab + Buparlisib 80 mg QD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	6 / 6 (100.00%)	7 / 7 (100.00%)

Vascular disorders			
EMBOLISM			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
HAEMATOMA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
HOT FLUSH			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
HYPERTENSION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
HYPOTENSION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
CHILLS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
FATIGUE			
subjects affected / exposed	1 / 4 (25.00%)	2 / 6 (33.33%)	2 / 7 (28.57%)
occurrences (all)	1	2	3
GAIT DISTURBANCE			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
OEDEMA PERIPHERAL			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	1	2	0
PYREXIA			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
TESTICULAR PAIN			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
BRONCHOSPASM			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
COUGH			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
HICCUPS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
PRODUCTIVE COUGH			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
RHINORRHOEA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
AGITATION			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
ANXIETY			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	2 / 7 (28.57%)
occurrences (all)	0	1	2
APATHY			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
BRADYPHRENIA			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
CONFUSIONAL STATE			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
DEPRESSED MOOD			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
DEPRESSION			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	3 / 7 (42.86%)
occurrences (all)	1	0	3
DISORIENTATION			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
INSOMNIA			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
IRRITABILITY			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
MOOD ALTERED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
PERSONALITY CHANGE			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
SLEEP DISORDER			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	2 / 7 (28.57%)
occurrences (all)	1	0	2
AMYLASE INCREASED			

subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	2 / 7 (28.57%)
occurrences (all)	1	0	3
BLOOD ALBUMIN DECREASED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	2 / 4 (50.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	2	0	1
BLOOD CREATININE INCREASED			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
BLOOD GLUCOSE INCREASED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
BLOOD POTASSIUM INCREASED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
BLOOD TRIGLYCERIDES INCREASED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
GLOMERULAR FILTRATION RATE DECREASED			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
INSULIN C-PEPTIDE INCREASED			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	2 / 7 (28.57%)
occurrences (all)	1	0	2
LIPASE INCREASED			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
LYMPHOCYTE COUNT DECREASED			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	2 / 7 (28.57%)
occurrences (all)	0	0	3
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
PLATELET COUNT DECREASED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	2
PROTEIN TOTAL DECREASED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
PROTHROMBIN TIME PROLONGED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
WEIGHT DECREASED			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
WEIGHT INCREASED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
FALL			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
LACERATION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
LEFT VENTRICULAR DYSFUNCTION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
SINUS BRADYCARDIA			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
AMNESIA			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
APHASIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	2 / 7 (28.57%)
occurrences (all)	0	0	2
ATAXIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
BRAIN OEDEMA			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
COGNITIVE DISORDER			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
DISTURBANCE IN ATTENTION			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	1 / 7 (14.29%)
occurrences (all)	1	1	1
DIZZINESS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
DYSARTHRIA			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
DYSKINESIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
DYSMETRIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
EPILEPSY			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

FACIAL PARALYSIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
FACIAL PARESIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
HEADACHE			
subjects affected / exposed	1 / 4 (25.00%)	2 / 6 (33.33%)	2 / 7 (28.57%)
occurrences (all)	1	2	2
HEMIANOPIA			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
HEMIANOPIA HOMONYMOUS			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
HEMIPARESIS			
subjects affected / exposed	2 / 4 (50.00%)	1 / 6 (16.67%)	1 / 7 (14.29%)
occurrences (all)	2	1	1
HEMIPLEGIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
LETHARGY			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
MEMORY IMPAIRMENT			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	2 / 7 (28.57%)
occurrences (all)	1	0	2
NEUROLOGIC NEGLECT SYNDROME			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
NEUROLOGICAL SYMPTOM			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
PARAESTHESIA			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0

PARALYSIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
PARAPARESIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
PARESIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
PERIPHERAL MOTOR NEUROPATHY			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
PYRAMIDAL TRACT SYNDROME			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
RESTLESS LEGS SYNDROME			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
SEIZURE			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
SOMNOLENCE			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
TREMOR			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
VITH NERVE PARALYSIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
ANAEMIA			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
LEUKOPENIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
NEUTROPENIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
THROMBOCYTOPENIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
DIPLOPIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
VISION BLURRED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
CONSTIPATION			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
DIARRHOEA			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	2 / 7 (28.57%)
occurrences (all)	1	1	3
DYSPEPSIA			
subjects affected / exposed	0 / 4 (0.00%)	2 / 6 (33.33%)	2 / 7 (28.57%)
occurrences (all)	0	2	2
DYSPHAGIA			

subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
HAEMORRHOIDS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
NAUSEA			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	3 / 7 (42.86%)
occurrences (all)	1	1	4
RECTAL ULCER HAEMORRHAGE			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
STOMATITIS			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
VOMITING			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Hepatobiliary disorders			
HEPATIC STEATOSIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
HYPERBILIRUBINAEMIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
ALOPECIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
DERMATITIS ACNEIFORM			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
DRY SKIN			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
PRURITUS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
RASH			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
RASH MACULAR			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
SKIN ATROPHY			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
CHRONIC KIDNEY DISEASE			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
CYSTITIS NONINFECTIVE			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
HAEMATURIA			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
MICTURITION URGENCY			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
URINARY INCONTINENCE			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1

URINARY RETENTION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
MUSCLE SPASMS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
MUSCULAR WEAKNESS			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
MUSCULOSKELETAL PAIN			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
MYALGIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	2 / 7 (28.57%)
occurrences (all)	0	0	2
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
ORAL HERPES			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
ORCHITIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	1 / 7 (14.29%)
occurrences (all)	1	1	1
HYPERGLYCAEMIA			
subjects affected / exposed	2 / 4 (50.00%)	1 / 6 (16.67%)	2 / 7 (28.57%)
occurrences (all)	3	1	2

HYPERURICAEMIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
HYPOALBUMINAEMIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
HYPOGLYCAEMIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
HYPOKALAEMIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
HYPONATRAEMIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
HYPOPHOSPHATAEMIA			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	2 / 7 (28.57%)
occurrences (all)	1	0	2

Non-serious adverse events	INC280 400 mg BID Tab + Buparlisib 80 mg QD	Phase Ib All@Patients	INC280 400 mg BID Tab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)	33 / 33 (100.00%)	9 / 9 (100.00%)
Vascular disorders			
EMBOLISM			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
HAEMATOMA			
subjects affected / exposed	1 / 5 (20.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
HOT FLUSH			
subjects affected / exposed	0 / 5 (0.00%)	0 / 33 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
HYPERTENSION			
subjects affected / exposed	1 / 5 (20.00%)	2 / 33 (6.06%)	1 / 9 (11.11%)
occurrences (all)	1	2	1
HYPOTENSION			

subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 5 (0.00%)	2 / 33 (6.06%)	1 / 9 (11.11%)
occurrences (all)	0	2	1
CHILLS			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
FATIGUE			
subjects affected / exposed	2 / 5 (40.00%)	12 / 33 (36.36%)	3 / 9 (33.33%)
occurrences (all)	2	13	5
GAIT DISTURBANCE			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	0 / 5 (0.00%)	0 / 33 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
OEDEMA PERIPHERAL			
subjects affected / exposed	2 / 5 (40.00%)	4 / 33 (12.12%)	1 / 9 (11.11%)
occurrences (all)	2	5	3
PYREXIA			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
TESTICULAR PAIN			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
BRONCHOSPASM			
subjects affected / exposed	0 / 5 (0.00%)	0 / 33 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
COUGH			

subjects affected / exposed	1 / 5 (20.00%)	3 / 33 (9.09%)	2 / 9 (22.22%)
occurrences (all)	1	3	2
HICCUPS			
subjects affected / exposed	1 / 5 (20.00%)	2 / 33 (6.06%)	0 / 9 (0.00%)
occurrences (all)	1	3	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
PRODUCTIVE COUGH			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
RHINORRHOEA			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
AGITATION			
subjects affected / exposed	0 / 5 (0.00%)	2 / 33 (6.06%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
ANXIETY			
subjects affected / exposed	1 / 5 (20.00%)	6 / 33 (18.18%)	1 / 9 (11.11%)
occurrences (all)	1	6	1
APATHY			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
BRADYPHRENIA			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
CONFUSIONAL STATE			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
DEPRESSED MOOD			
subjects affected / exposed	0 / 5 (0.00%)	0 / 33 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
DEPRESSION			
subjects affected / exposed	2 / 5 (40.00%)	8 / 33 (24.24%)	1 / 9 (11.11%)
occurrences (all)	2	8	1

DISORIENTATION			
subjects affected / exposed	0 / 5 (0.00%)	3 / 33 (9.09%)	0 / 9 (0.00%)
occurrences (all)	0	4	0
INSOMNIA			
subjects affected / exposed	0 / 5 (0.00%)	3 / 33 (9.09%)	1 / 9 (11.11%)
occurrences (all)	0	3	1
IRRITABILITY			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
MOOD ALTERED			
subjects affected / exposed	0 / 5 (0.00%)	2 / 33 (6.06%)	0 / 9 (0.00%)
occurrences (all)	0	3	0
PERSONALITY CHANGE			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
SLEEP DISORDER			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	4 / 5 (80.00%)	9 / 33 (27.27%)	0 / 9 (0.00%)
occurrences (all)	4	9	0
AMYLASE INCREASED			
subjects affected / exposed	0 / 5 (0.00%)	2 / 33 (6.06%)	2 / 9 (22.22%)
occurrences (all)	0	3	2
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	3 / 5 (60.00%)	8 / 33 (24.24%)	0 / 9 (0.00%)
occurrences (all)	3	9	0
BLOOD ALBUMIN DECREASED			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	1 / 5 (20.00%)	5 / 33 (15.15%)	1 / 9 (11.11%)
occurrences (all)	2	7	2
BLOOD CREATININE INCREASED			

subjects affected / exposed	2 / 5 (40.00%)	5 / 33 (15.15%)	1 / 9 (11.11%)
occurrences (all)	2	5	1
BLOOD GLUCOSE INCREASED			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
BLOOD POTASSIUM INCREASED			
subjects affected / exposed	1 / 5 (20.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
BLOOD TRIGLYCERIDES INCREASED			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
GLOMERULAR FILTRATION RATE DECREASED			
subjects affected / exposed	0 / 5 (0.00%)	4 / 33 (12.12%)	0 / 9 (0.00%)
occurrences (all)	0	7	0
INSULIN C-PEPTIDE INCREASED			
subjects affected / exposed	0 / 5 (0.00%)	6 / 33 (18.18%)	0 / 9 (0.00%)
occurrences (all)	0	6	0
LIPASE INCREASED			
subjects affected / exposed	1 / 5 (20.00%)	4 / 33 (12.12%)	3 / 9 (33.33%)
occurrences (all)	2	5	3
LYMPHOCYTE COUNT DECREASED			
subjects affected / exposed	0 / 5 (0.00%)	3 / 33 (9.09%)	1 / 9 (11.11%)
occurrences (all)	0	5	3
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
PLATELET COUNT DECREASED			
subjects affected / exposed	2 / 5 (40.00%)	3 / 33 (9.09%)	0 / 9 (0.00%)
occurrences (all)	2	4	0
PROTEIN TOTAL DECREASED			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
PROTHROMBIN TIME PROLONGED			
subjects affected / exposed	1 / 5 (20.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	1	1	0

WEIGHT DECREASED			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
WEIGHT INCREASED			
subjects affected / exposed	0 / 5 (0.00%)	0 / 33 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
FALL			
subjects affected / exposed	2 / 5 (40.00%)	3 / 33 (9.09%)	2 / 9 (22.22%)
occurrences (all)	2	3	2
LACERATION			
subjects affected / exposed	0 / 5 (0.00%)	0 / 33 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Cardiac disorders			
LEFT VENTRICULAR DYSFUNCTION			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
SINUS BRADYCARDIA			
subjects affected / exposed	1 / 5 (20.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
Nervous system disorders			
AMNESIA			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
APHASIA			
subjects affected / exposed	1 / 5 (20.00%)	4 / 33 (12.12%)	0 / 9 (0.00%)
occurrences (all)	1	4	0
ATAXIA			
subjects affected / exposed	1 / 5 (20.00%)	3 / 33 (9.09%)	0 / 9 (0.00%)
occurrences (all)	1	3	0
BRAIN OEDEMA			
subjects affected / exposed	0 / 5 (0.00%)	2 / 33 (6.06%)	0 / 9 (0.00%)
occurrences (all)	0	2	0

COGNITIVE DISORDER			
subjects affected / exposed	1 / 5 (20.00%)	2 / 33 (6.06%)	0 / 9 (0.00%)
occurrences (all)	1	2	0
DISTURBANCE IN ATTENTION			
subjects affected / exposed	2 / 5 (40.00%)	7 / 33 (21.21%)	0 / 9 (0.00%)
occurrences (all)	2	7	0
DIZZINESS			
subjects affected / exposed	0 / 5 (0.00%)	2 / 33 (6.06%)	1 / 9 (11.11%)
occurrences (all)	0	2	1
DYSARTHRIA			
subjects affected / exposed	1 / 5 (20.00%)	3 / 33 (9.09%)	0 / 9 (0.00%)
occurrences (all)	1	3	0
DYSKINESIA			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
DYSMETRIA			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
EPILEPSY			
subjects affected / exposed	0 / 5 (0.00%)	0 / 33 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
FACIAL PARALYSIS			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
FACIAL PARESIS			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
HEADACHE			
subjects affected / exposed	2 / 5 (40.00%)	9 / 33 (27.27%)	4 / 9 (44.44%)
occurrences (all)	2	10	5
HEMIANOPIA			
subjects affected / exposed	0 / 5 (0.00%)	2 / 33 (6.06%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
HEMIANOPIA HOMONYMOUS			
subjects affected / exposed	0 / 5 (0.00%)	2 / 33 (6.06%)	0 / 9 (0.00%)
occurrences (all)	0	2	0

HEMIPARESIS			
subjects affected / exposed	1 / 5 (20.00%)	5 / 33 (15.15%)	1 / 9 (11.11%)
occurrences (all)	1	5	1
HEMIPLEGIA			
subjects affected / exposed	0 / 5 (0.00%)	0 / 33 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
LETHARGY			
subjects affected / exposed	0 / 5 (0.00%)	2 / 33 (6.06%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
MEMORY IMPAIRMENT			
subjects affected / exposed	2 / 5 (40.00%)	7 / 33 (21.21%)	0 / 9 (0.00%)
occurrences (all)	2	7	0
NEUROLOGIC NEGLECT SYNDROME			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
NEUROLOGICAL SYMPTOM			
subjects affected / exposed	0 / 5 (0.00%)	0 / 33 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
PARAESTHESIA			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
PARALYSIS			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
PARAPARESIS			
subjects affected / exposed	1 / 5 (20.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
PARESIS			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
PERIPHERAL MOTOR NEUROPATHY			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	1 / 5 (20.00%)	2 / 33 (6.06%)	1 / 9 (11.11%)
occurrences (all)	1	2	1

PYRAMIDAL TRACT SYNDROME			
subjects affected / exposed	1 / 5 (20.00%)	2 / 33 (6.06%)	0 / 9 (0.00%)
occurrences (all)	1	2	0
RESTLESS LEGS SYNDROME			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
SEIZURE			
subjects affected / exposed	0 / 5 (0.00%)	3 / 33 (9.09%)	1 / 9 (11.11%)
occurrences (all)	0	3	1
SOMNOLENCE			
subjects affected / exposed	0 / 5 (0.00%)	4 / 33 (12.12%)	1 / 9 (11.11%)
occurrences (all)	0	4	1
TREMOR			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
VITH NERVE PARALYSIS			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
LEUKOPENIA			
subjects affected / exposed	0 / 5 (0.00%)	2 / 33 (6.06%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
NEUTROPENIA			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
THROMBOCYTOPENIA			
subjects affected / exposed	0 / 5 (0.00%)	2 / 33 (6.06%)	0 / 9 (0.00%)
occurrences (all)	0	3	0
Eye disorders			
DIPLOPIA			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
VISION BLURRED			

subjects affected / exposed	0 / 5 (0.00%)	0 / 33 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	1 / 5 (20.00%)	2 / 33 (6.06%)	1 / 9 (11.11%)
occurrences (all)	1	2	1
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
CONSTIPATION			
subjects affected / exposed	1 / 5 (20.00%)	5 / 33 (15.15%)	3 / 9 (33.33%)
occurrences (all)	1	5	3
DIARRHOEA			
subjects affected / exposed	1 / 5 (20.00%)	7 / 33 (21.21%)	1 / 9 (11.11%)
occurrences (all)	1	9	2
DYSPEPSIA			
subjects affected / exposed	1 / 5 (20.00%)	6 / 33 (18.18%)	1 / 9 (11.11%)
occurrences (all)	1	6	1
DYSPHAGIA			
subjects affected / exposed	0 / 5 (0.00%)	2 / 33 (6.06%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	1 / 5 (20.00%)	1 / 33 (3.03%)	1 / 9 (11.11%)
occurrences (all)	1	1	1
HAEMORRHOIDS			
subjects affected / exposed	1 / 5 (20.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
NAUSEA			
subjects affected / exposed	2 / 5 (40.00%)	10 / 33 (30.30%)	2 / 9 (22.22%)
occurrences (all)	2	12	2
RECTAL ULCER HAEMORRHAGE			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
STOMATITIS			

subjects affected / exposed	1 / 5 (20.00%)	2 / 33 (6.06%)	1 / 9 (11.11%)
occurrences (all)	1	2	1
VOMITING			
subjects affected / exposed	2 / 5 (40.00%)	5 / 33 (15.15%)	1 / 9 (11.11%)
occurrences (all)	2	7	1
Hepatobiliary disorders			
HEPATIC STEATOSIS			
subjects affected / exposed	1 / 5 (20.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
HYPERBILIRUBINAEMIA			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
ALOPECIA			
subjects affected / exposed	0 / 5 (0.00%)	0 / 33 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
DERMATITIS ACNEIFORM			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
DRY SKIN			
subjects affected / exposed	2 / 5 (40.00%)	2 / 33 (6.06%)	1 / 9 (11.11%)
occurrences (all)	2	2	1
PRURITUS			
subjects affected / exposed	1 / 5 (20.00%)	3 / 33 (9.09%)	0 / 9 (0.00%)
occurrences (all)	1	3	0
RASH			
subjects affected / exposed	1 / 5 (20.00%)	1 / 33 (3.03%)	1 / 9 (11.11%)
occurrences (all)	2	2	1
RASH MACULAR			
subjects affected / exposed	1 / 5 (20.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
RASH MACULO-PAPULAR			
subjects affected / exposed	1 / 5 (20.00%)	2 / 33 (6.06%)	0 / 9 (0.00%)
occurrences (all)	1	2	0
SKIN ATROPHY			

subjects affected / exposed	1 / 5 (20.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 5 (0.00%)	0 / 33 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
CHRONIC KIDNEY DISEASE			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
CYSTITIS NONINFECTIVE			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
HAEMATURIA			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
MICTURITION URGENCY			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
URINARY INCONTINENCE			
subjects affected / exposed	1 / 5 (20.00%)	4 / 33 (12.12%)	0 / 9 (0.00%)
occurrences (all)	1	4	0
URINARY RETENTION			
subjects affected / exposed	1 / 5 (20.00%)	2 / 33 (6.06%)	0 / 9 (0.00%)
occurrences (all)	1	2	0
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
MUSCLE SPASMS			
subjects affected / exposed	1 / 5 (20.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
MUSCULAR WEAKNESS			
subjects affected / exposed	1 / 5 (20.00%)	3 / 33 (9.09%)	0 / 9 (0.00%)
occurrences (all)	1	3	0
MUSCULOSKELETAL PAIN			

subjects affected / exposed	0 / 5 (0.00%)	0 / 33 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
MYALGIA			
subjects affected / exposed	0 / 5 (0.00%)	2 / 33 (6.06%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
PAIN IN EXTREMITY			
subjects affected / exposed	1 / 5 (20.00%)	1 / 33 (3.03%)	1 / 9 (11.11%)
occurrences (all)	1	1	1
Infections and infestations			
ORAL HERPES			
subjects affected / exposed	1 / 5 (20.00%)	1 / 33 (3.03%)	1 / 9 (11.11%)
occurrences (all)	1	1	1
ORCHITIS			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	0 / 5 (0.00%)	6 / 33 (18.18%)	0 / 9 (0.00%)
occurrences (all)	0	6	0
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 5 (0.00%)	7 / 33 (21.21%)	1 / 9 (11.11%)
occurrences (all)	0	9	1
HYPERURICAEMIA			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
HYPOALBUMINAEMIA			
subjects affected / exposed	1 / 5 (20.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
HYPOGLYCAEMIA			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
HYPOKALAEMIA			
subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
HYPONATRAEMIA			

subjects affected / exposed	0 / 5 (0.00%)	1 / 33 (3.03%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
HYPOPHOSPHATAEMIA			
subjects affected / exposed	0 / 5 (0.00%)	4 / 33 (12.12%)	0 / 9 (0.00%)
occurrences (all)	0	4	0

Non-serious adverse events	Phase II All Patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 10 (90.00%)		
Vascular disorders			
EMBOLISM			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
HAEMATOMA			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
HOT FLUSH			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
HYPERTENSION			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
HYPOTENSION			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
CHILLS			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
FATIGUE			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	5		
GAIT DISTURBANCE			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
OEDEMA PERIPHERAL			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	3		
PYREXIA			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
TESTICULAR PAIN			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
BRONCHOSPASM			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
COUGH			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
HICCUPS			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
OROPHARYNGEAL PAIN			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
PRODUCTIVE COUGH			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
RHINORRHOEA			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			

AGITATION				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
ANXIETY				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
APATHY				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
BRADYPHRENIA				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
CONFUSIONAL STATE				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
DEPRESSED MOOD				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
DEPRESSION				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
DISORIENTATION				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
INSOMNIA				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
IRRITABILITY				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
MOOD ALTERED				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
PERSONALITY CHANGE				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			

SLEEP DISORDER			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
AMYLASE INCREASED			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
BLOOD ALBUMIN DECREASED			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	2		
BLOOD CREATININE INCREASED			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
BLOOD GLUCOSE INCREASED			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
BLOOD POTASSIUM INCREASED			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
BLOOD TRIGLYCERIDES INCREASED			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
GLOMERULAR FILTRATION RATE DECREASED			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
INSULIN C-PEPTIDE INCREASED			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
LIPASE INCREASED			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	3		
LYMPHOCYTE COUNT DECREASED			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	3		
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
PLATELET COUNT DECREASED			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
PROTEIN TOTAL DECREASED			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
PROTHROMBIN TIME PROLONGED			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
WEIGHT DECREASED			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
WEIGHT INCREASED			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
FALL			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
LACERATION			

subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Cardiac disorders			
LEFT VENTRICULAR DYSFUNCTION			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
SINUS BRADYCARDIA			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
AMNESIA			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
APHASIA			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
ATAXIA			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
BRAIN OEDEMA			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
COGNITIVE DISORDER			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
DISTURBANCE IN ATTENTION			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
DIZZINESS			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
DYSARTHRIA			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
DYSKINESIA			

subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
DYSMETRIA				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
EPILEPSY				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
FACIAL PARALYSIS				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
FACIAL PARESIS				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
HEADACHE				
subjects affected / exposed	4 / 10 (40.00%)			
occurrences (all)	5			
HEMIANOPIA				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
HEMIANOPIA HOMONYMOUS				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
HEMIPARESIS				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
HEMIPLEGIA				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
LETHARGY				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
MEMORY IMPAIRMENT				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
NEUROLOGIC NEGLECT SYNDROME				

subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
NEUROLOGICAL SYMPTOM				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
PARAESTHESIA				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
PARALYSIS				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
PARAPARESIS				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
PARESIS				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
PERIPHERAL MOTOR NEUROPATHY				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
PERIPHERAL SENSORY NEUROPATHY				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
PYRAMIDAL TRACT SYNDROME				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
RESTLESS LEGS SYNDROME				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
SEIZURE				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
SOMNOLENCE				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
TREMOR				

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
VITH NERVE PARALYSIS			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
LEUKOPENIA			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
NEUTROPENIA			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
THROMBOCYTOPENIA			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Eye disorders			
DIPLOPIA			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
VISION BLURRED			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
CONSTIPATION			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	3		
DIARRHOEA			

subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 2		
DYSPEPSIA subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
DYSPHAGIA subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
GASTROOESOPHAGEAL REFLUX DISEASE subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
HAEMORRHOIDS subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
NAUSEA subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 2		
RECTAL ULCER HAEMORRHAGE subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
STOMATITIS subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
VOMITING subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Hepatobiliary disorders HEPATIC STEATOSIS subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
HYPERBILIRUBINAEMIA subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Skin and subcutaneous tissue disorders			

ALOPECIA			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
DERMATITIS ACNEIFORM			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
DRY SKIN			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
PRURITUS			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
RASH			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
RASH MACULAR			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
SKIN ATROPHY			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
CHRONIC KIDNEY DISEASE			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
CYSTITIS NONINFECTIVE			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
HAEMATURIA			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
MICTURITION URGENCY			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
URINARY INCONTINENCE			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
URINARY RETENTION			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
MUSCLE SPASMS			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
MUSCULAR WEAKNESS			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
MUSCULOSKELETAL PAIN			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
MYALGIA			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
PAIN IN EXTREMITY			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Infections and infestations			
ORAL HERPES			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
ORCHITIS			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
HYPERGLYCAEMIA			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
HYPERURICAEMIA			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
HYPOALBUMINAEMIA			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
HYPOGLYCAEMIA			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
HYPOKALAEMIA			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
HYPONATRAEMIA			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
HYPOPHOSPHATAEMIA			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 August 2013	Added clarification to the collection and analysis of the pre-screening tumor samples, as requested from regulatory health authorities. In addition, guidelines for clarification in the completion of psychiatric questionnaires GAD-7 and PHQ-9 were added.
07 July 2014	1) Tablet formulation was developed with higher dosage strengths. 2) For local pre-screening performed during dose escalation, a threshold for PTEN negativity was introduced. 3) For the Phase II part of the study, no local pre-screening was allowed. PTEN pre-screening was to be done centrally for all patients in order to achieve comparable results and to allow testing for other molecular markers for those patients who had given their consent. 4) Clarification was added regarding the use of corticosteroids for the treatment arms as well as the surgical arm. 5) For patients in Phase II, who consented to additional biomarker assessments, HGF mRNA expression in tumor samples was to be measured.
02 March 2015	To introduce a second arm with INC280 monotherapy into the Phase II part, in order to investigate single agent INC280 in c-MET altered GBM patients (c-MET amplified GCN >5), fusion or mutant).
03 August 2015	To provide additional information and guidance to Investigators for the management of liver toxicities.
30 March 2016	This amendment provided additional guidance to Investigators for the management of liver toxicities and specifically work-up guidelines for potential Drug Induced Liver Injury (DILI) cases. Specific guidance for actions to be taken on the study treatment (e.g. discontinuation) and for monitoring of liver function tests was implemented and clarified.

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.

At the end of Phase Ib, it was decided not to enroll patients in the two Phase II arms evaluating INC280 with buparlisib. The phase II INC280 single agent arm was halted before it reached target enrollment due to lack of objective clinical response.

Notes: