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Sponsor

Novartis

Generic Drug Name

Capmatinib

Trial Indication(s)

Solid Tumors

Protocol Number

CINC280A2105

Protocol Title

A phase I, multicenter, open-label, single-sequence drug-drug interaction study to assess the effect of INC280 on the pharmacokinetics of digoxin and rosuvastatin in patients with cMET-dysregulated advanced solid tumors

Clinical Trial Phase

Phase I

Phase of Drug Development

Phase II

Study Start/End Dates

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FRM-7043019 version 2.0

08-Dec-2015 to 28-Apr-2017

Reason for Termination (If applicable)

Not applicable

Study Design/Methodology

A multicenter, open-label, single-sequence study to assess the effect of capmatinib on the pharmacokinetics (PK) of digoxin (probe substrate for p-glycoprotein) and rosuvastatin (probe substrate for breast cancer resistant protein) administered as a two-drug cocktail in patients with advanced cMET-dysregulated solid tumors. This study consisted the following periods:

- A molecular pre-screening period for determining the tumor cMET dysregulation status (cMET mutations/amplifications or overexpression) determined by either local or central assessment
- A screening/baseline period of up to 28 days
- A drug-drug interaction (DDI) phase (Day 1 to Day 32) where the impact of DDI was evaluated after steady-state concentration was achieved for capmatinib (Day 22), to obtain the maximal inhibitory effect on p-glycoprotein. PK samples were collected for measurement of digoxin, rosuvastatin and capmatinib plasma concentrations at various time points during DDI phase.
- A post-DDI phase (Day 33 onward): after the completion of the DDI phase, the patients were allowed to continue treatment with capmatinib at 400 mg bid dose, administered orally on continuous 21-day cycles. All patients who entered the post-DDI phase were required to have an end of treatment visit at the time of discontinuation of study treatment.
- Follow-up (safety and efficacy): regardless of the reason for discontinuation from study treatment, patients were to be contacted for a safety follow-up 30 days after the last dose of study treatment. The Investigator was asked to record any adverse events (AEs)/ serious adverse events (SAEs) that could have occurred after discontinuation of study treatment and/or follow-up on resolution of ongoing AEs. If the study drug was discontinued for reasons other than documented disease progression or withdrawal of consent, patients were continued to be followed with tumor assessments until progression as per Investigator’s assessments, start of new anti-cancer therapy or death

Centers

Eight centers in five countries: Austria (1), Belgium (1), Italy (2), Spain (2) and United Kingdom (2)

Objectives

Primary objective

To evaluate the effect of multiple doses of capmatinib on the pharmacokinetics of a single oral dose of digoxin and rosuvastatin in patients with cMET-dysregulated advanced solid tumors

Key secondary objective

To assess safety and tolerability of capmatinib in patients with cMET-dysregulated advanced solid tumors

Other secondary objectives

- To evaluate the preliminary evidence of anti-tumor activity of capmatinib in patients with cMET-dysregulated advanced solid tumors
- To assess the PK of capmatinib in patients with cMET-dysregulated advanced solid tumors

Test Product (s), Dose(s), and Mode(s) of Administration

Study drug: Oral tablets of capmatinib (INC280) 400 mg bid from day 11 to 32 during DDI phase, afterwards 400 mg bid on continuous 21-day cycles
Probe drugs: Oral tablets of digoxin 0.25 mg and of rosuvastatin 10 mg, single dose each at Day 1 and Day 22 during DDI phase

Statistical Methods

Analysis sets

The Full Analysis Set (FAS) and Safety Set included all patients in the study who received at least one dose of any study treatment (probe drugs or capmatinib). Three separate Pharmacokinetics Analysis Sets (PAS) were considered for the evaluation of this study, one for each of the probe drugs (digoxin and rosuvastatin) and one for capmatinib.

- PAS for capmatinib included all patients who provided at least one evaluable PK concentration for capmatinib.

- In the following definition of PAS for digoxin and PAS for rosuvastatin “probe X” was replaced by digoxin and rosuvastatin, respectively.
  PAS for probe X included all patients who provided an evaluable PK profile for all periods (first period after the cocktail administration and second period after administration of cocktail + capmatinib).

Only PK parameters and concentrations from evaluable profiles were included in any analyses which used the PAS.

Pharmacokinetic

The respective PAS was used for statistical analyses of the primary endpoints. A formal statistical analysis was performed for the primary PK parameters (AUCinf, AUClast and Cmax). The comparison of interest was probe drug (digoxin or rosuvastatin) + capmatinib (test) vs. probe drug alone (reference).

A linear mixed model was fitted to the log-transformed PK parameters (AUCinf, AUClast and Cmax) to assess the effect of capmatinib on the PK of probe drug. The model included treatment as a fixed factor and patient as a random factor. For each of the comparisons, a point estimate and the corresponding 90% confidence interval (CI) for the difference between means of test and reference treatment (test – reference) was calculated. The point estimate and CI were anti-log transformed to obtain the point estimate and the 90% confidence interval for the geometric mean ratio on the original scale.

Efficacy

Anti-tumor activity of capmatinib was presented by listing of tumor assessment, overall response and Best Overall Rate (BOR) using FAS based on Investigator assessment (using RECIST v1.1). BOR was summarized using FAS; Overall response rate (ORR) and Disease control rate (DCR) were also be presented in the same table along with the exact 95% CI. BOR was calculated as per RECIST.

Safety

Safety assessments included AEs, laboratory data, vital signs, deaths and ECGs. The Safety set was used for all safety summaries. Safety summaries include only on treatment assessments; safety listings include all assessments with those not on treatment flagged (only AE listing had flags).

Study Population: Key Inclusion/Exclusion Criteria

Key Inclusion Criteria:

Patients must have:

- advanced solid tumors and have confirmed cMET dysregulation
- at least one measurable lesion as defined by RECIST 1.1.
- recovered from all toxicities related to prior anti-cancer therapies
- adequate organ function
- ECOG performance status (PS) of 0 or 1

Key Exclusion Criteria:

Patients must not have:

- known hypersensitivity to any of the excipients of INC280
- prior treatment with cMET or HGF-targeting inhibitor
- known hypersensitivity to digoxin or rosuvastatin or its excipients
- symptomatic central nervous system (CNS) metastases who are neurologically unstable
- presence or history of carcinomatous meningitis
- history of another primary malignancy that is currently clinically significant or currently requires active intervention
- Clinically significant, uncontrolled heart diseases, including QTcF ≥ 450 msec (male patients), ≥ 460 msec (female patients) on the screening ECG
- Thoracic radiotherapy to lung fields ≤ 4 weeks prior to starting INC280
- Major surgery within 4 weeks prior to starting INC280
- Patients receiving unstable or increasing doses of corticosteroids.
- Impairment of GI function or GI disease that may significantly alter the absorption of INC280
- Patients who have received, or are expected to receive digoxin or rosuvastatin within 21 days prior to the beginning of the DDI phase (Day 1) and for the duration of the DDI phase.

NOVARTIS

FRM-7043019 version 2.0

Participant Flow Table (full analysis set)

Disposition/Reason	All patients N=32 n (%)
DDI (Pharmacokinetic) phase	
Completed	26 (81.3)
Entered Post-DDI (treatment) phase	26 (81.3)
Discontinued from DDI (pharmacokinetic) phase	6 (18.8)
Entered Post-DDI (treatment) phase	1 (3.1)
Entered post-treatment follow-up	1 (3.1)
Primary reason for discontinuation from DDI (pharmacokinetic) phase	
Adverse event	2 (6.3)
Death	1 (3.1)
Physician decision	2 (6.3)
Progressive disease	1 (3.1)
Post-DDI (Treatment) Phase	
Discontinued from Post-DDI (treatment) phase	27 (84.4)
Primary reason for discontinuation from Post-DDI (treatment) phase	
Adverse event	1 (3.1)
Death	2 (6.3)
Lost to follow-up	1 (3.1)
Physician decision	3 (9.4)
Progressive disease	20 (62.5)
Post-treatment follow-up	
Discontinued from post-treatment follow-up	1 (3.1)
Primary reason for discontinuation from post-treatment follow-up	

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FRM-7043019 version 2.0

Disposition/Reason	All patients N=32 n (%)
Protocol deviation	1 (3.1)

Percentage is based on N

Reasons for discontinuation are from 'End of DDI (Pharmacokinetic) Phase Disposition', 'End of Post-DDI (Treatment) Phase Disposition' and 'End of Post Treatment Phase Disposition' CRF pages.

Baseline Characteristics (full analysis set)

Demographic Variable	All patients N=32
Age (years)	
n	32
Mean	61.1
SD	9.59
Median	61.5
Minimum	38
Maximum	81
Age category (years) - n (%)	
<65	20 (62.5)
≥ 65	12 (37.5)
Sex - n (%)	
Female	15 (46.9)
Male	17 (53.1)
Race - n (%)	
Unknown	2 (6.3)

Demographic Variable	All patients N=32
White	30 (93.8)
Ethnicity - n (%)	
Other	28 (87.5)
Unknown	4 (12.5)
Body mass index (Kg/m^2)	
n	31
Mean	24.82
SD	4.434
Median	23.95
Minimum	17.1
Maximum	35.7
ECOG performance status - n (%)	
0	8 (25.0)
1	24 (75.0)

BMI: body mass index; SD: standard deviation

Summary of Efficacy

Primary Outcome Result(s)

Summary of digoxin primary PK parameters by treatment (pharmacokinetics analysis set)

Parameter	Statistics	digoxin alone N=25	INC280 + digoxin N=25
AUCinf (ng*hr/mL)	n	9	12
	Mean (SD)	26.8 (10.1)	36.4 (14.5)
	CV%	37.6	39.9

Parameter	Statistics	digoxin alone N=25	INC280 + digoxin N=25
AUClast (ng*hr/mL)	Geo-mean	25.3	34.1
	Geo-CV%	36.3	37.9
	Median	25.2	34.6
	[Min; Max]	[15.3; 43.6]	[21.4; 69.8]
	n	25	25
	Mean (SD)	16.7 (8.89)	26.6 (13.0)
	CV%	53.3	49.0
Cmax (ng/mL)	Geo-mean	14.6	23.8
	Geo-CV%	58.0	50.5
	Median	14.8	24.1
	[Min; Max]	[5.03; 39.1]	[9.52; 59.1]
	n	25	25
	Mean (SD)	1.27 (0.649)	2.22 (1.09)
	CV%	50.9	49.3
	Geo-mean	1.12	1.95
	Geo-CV%	57.9	56.8
	Median	1.13	1.78
	[Min; Max]	[0.354; 2.94]	[0.620; 4.25]

n: number of patients with corresponding evaluable PK parameters.

CV% = coefficient of variation (%) = sd/mean*100, Geo-CV% = sqrt (exp (variance for log transformed data)-1)*100.

Summary of statistical analysis of primary PK parameters for digoxin (pharmacokinetics analysis set)

	Treatment comparison
	90% CI

PK parameter (unit)	Treatment group	n*	Adjusted geo-mean	Comparison(s)	Geo-mean ratio	Lower	Upper
AUCinf (ng*hr/mL)	digoxin alone	9	22.4				
	INC280 + digoxin	12	32.9	INC280 + digoxin/ digoxin alone	1.47	1.28	1.68
AUClast (ng*hr/mL)	digoxin alone	25	14.6				
	INC280 + digoxin	25	23.8	INC280 + digoxin/ digoxin alone	1.63	1.42	1.89
Cmax (ng/mL)	digoxin alone	25	1.12				
	INC280 + digoxin	25	1.95	INC280 + digoxin/ digoxin alone	1.74	1.43	2.13

Model is a linear mixed effects model of the log-transformed PK parameters. Included in the model were treatment as a fixed factor and patient as a random factor. The results were back transformed to get adjusted geometric mean, geometric mean ratio, and 90% CI.

n* = number of observations used for the analysis.

Summary of rosuvastatin primary PK parameters by treatment (pharmacokinetics analysis set)

Parameter	Statistics	rosuvastatin alone N=24	INC280 + rosuvastatin N=24
AUCinf (ng*hr/mL)	n	21	22
	Mean (SD)	96.0 (69.4)	235 (263)
	CV%	72.3	111.9
	Geo-mean	78.2	159
	Geo-CV%	73.4	99.8
	Median	86.4	125
	[Min; Max]	[21.3; 319]	[50.1; 1160]
AUClast (ng*hr/mL)	n	24	24
	Mean (SD)	87.3 (66.3)	216 (249)

Parameter	Statistics	rosuvastatin alone N=24	INC280 + rosuvastatin N=24
Cmax (ng/mL)	CV%	76.0	115.3
	Geo-mean	71.0	144
	Geo-CV%	71.3	102.6
	Median	73.8	118
	[Min; Max]	[20.4; 318]	[38.7; 1140]
	n	24	24
	Mean (SD)	9.43 (6.26)	30.8 (25.5)
	CV%	66.4	82.8
	Geo-mean	7.72	23.5
	Geo-CV%	73.4	85.5
	Median	8.51	21.2
	[Min; Max]	[2.24; 27.7]	[5.84; 89.9]

n: number of patients with corresponding evaluable PK parameters.

CV% = coefficient of variation (%) = sd/mean*100, Geo-CV% = sqrt (exp (variance for log transformed data)-1)*100.

Summary of statistical analysis of primary PK parameters for rosuvastatin (pharmacokinetics analysis set)

					Treatment comparison		
						90% CI	
PK parameter (unit)	Treatment group	n*	Adjusted geo-mean	Comparison(s)	Geo-mean ratio	Lower	Upper
AUCinf (ng*hr/mL)	rosuvastatin alone	21	75.2				
	INC280 + rosuvastatin	22	156	INC280 + rosuvastatin/ rosuvastatin alone	2.08	1.56	2.76
AUClast (ng*hr/mL)	rosuvastatin alone	24	71.0				

PK parameter (unit)	Treatment group	n*	Adjusted geo-mean	Comparison(s)	Treatment comparison: Geo-mean ratio	Treatment comparison: 90% CI Lower	Treatment comparison: 90% CI Upper
Cmax (ng/mL)	INC280 + rosuvastatin	24	144	INC280 + rosuvastatin/ rosuvastatin alone	2.03	1.61	2.56
	rosuvastatin alone	24	7.72				
	INC280 + rosuvastatin	24	23.5	INC280 + rosuvastatin/ rosuvastatin alone	3.04	2.36	3.92

Model is a linear mixed effects model of the log-transformed PK parameters. Included in the model were treatment as a fixed factor and patient as a random factor. The results were back transformed to get adjusted geometric mean, geometric mean ratio, and 90% CI.

n* = number of observations used for the analysis.

Secondary Outcome Result(s)

Key secondary objective: Refer to Summary of Safety Results section

Other Secondary Outcome Result(s)

Summary of digoxin secondary PK parameters by treatment (pharmacokinetics analysis set)

Parameter	Statistics	digoxin alone N=25	INC280 + digoxin N=25
Tmax (hr)	n	25	25
	Mean (SD)	N/A	N/A
	CV%	N/A	N/A
	Geo-mean	N/A	N/A
	Geo-CV%	N/A	N/A

Parameter	Statistics	digoxin alone N=25	INC280 + digoxin N=25
	Median	1.07	1.00
	[Min; Max]	[0.500; 6.00]	[0.417; 4.08]
T1/2 (hr)	n	9	12
	Mean (SD)	48.8 (14.3)	63.2 (16.4)
	CV%	29.2	25.9
	Geo-mean	47.0	61.4
	Geo-CV%	29.8	25.7
	Median	46.6	57.7
	[Min; Max]	[29.1; 76.5]	[42.0; 92.2]
Lambda_z (1/hr)	n	9	12
	Mean (SD)	0.0153 (0.0045)	0.0116 (0.00282)
	CV%	29.4	24.3
	Geo-mean	0.0147	0.0113
	Geo-CV%	29.8	25.7
	Median	0.0149	0.0121
	[Min; Max]	[0.00906; 0.0238]	[0.00751; 0.0165]
CL/F (L/hr)	n	9	12
	Mean (SD)	10.4 (3.41)	7.76 (2.60)
	CV%	32.7	33.5
	Geo-mean	9.89	7.33
	Geo-CV%	36.3	37.9
	Median	9.92	7.22
	[Min; Max]	[5.74; 16.3]	[3.58; 11.7]
Vz/F (L)	n	9	12
	Mean (SD)	679 (107)	663 (143)
	CV%	15.7	21.5

Parameter	Statistics	digoxin alone N=25	INC280 + digoxin N=25
	Geo-mean	671	649
	Geo-CV%	16.5	22.3
	Median	681	648
	[Min; Max]	[507; 805]	[424; 886]

n: number of patients with corresponding evaluable PK parameters.
CV% = coefficient of variation (%) = SD/mean*100, Geo-CV% = sqrt (exp (variance for log transformed data)-1)*100.

Summary of rosuvastatin secondary PK parameters by treatment (pharmacokinetics analysis set)

Parameter	Statistics	rosuvastatin alone N=24	INC280 + rosuvastatin N=24
Tmax (hr)	n	24	24
	Mean (SD)	N/A	N/A
	CV%	N/A	N/A
	Geo-mean	N/A	N/A
	Geo-CV%	N/A	N/A
	Median	2.04	1.55
	[Min; Max]	[0.500; 6.00]	[0.500; 9.93]
T1/2 (hr)	n	21	22
	Mean (SD)	27.5 (21.2)	24.7 (15.0)
	CV%	77.2	61.0
	Geo-mean	22.0	21.4
	Geo-CV%	73.8	56.6
	Median	21.8	21.0
	[Min; Max]	[7.87; 97.9]	[10.5; 73.9]
Lambda_z (1/hr)	n	21	22

Parameter	Statistics	rosuvastatin alone N=24	INC280 + rosuvastatin N=24
	Mean (SD)	0.0379 (0.0221)	0.0366 (0.0172)
	CV%	58.4	46.9
	Geo-mean	0.0315	0.0324
	Geo-CV%	73.8	56.6
	Median	0.0318	0.0333
	[Min; Max]	[0.00708; 0.0881]	[0.00938; 0.0661]
CL/F (L/hr)	n	21	22
	Mean (SD)	157 (109)	81.7 (52.6)
	CV%	69.5	64.3
	Geo-mean	128	62.8
	Geo-CV%	73.4	99.8
	Median	116	80.0
	[Min; Max]	[31.3; 469]	[8.62; 199]
Vz/F (L)	n	21	22
	Mean (SD)	5190 (4240)	2530 (1630)
	CV%	81.8	64.4
	Geo-mean	4060	1940
	Geo-CV%	80.2	105.1
	Median	3980	2140
	[Min; Max]	[998; 18900]	[135; 5480]

n: number of patients with corresponding evaluable PK parameters.

CV% = coefficient of variation (%) = SD/mean*100, Geo-CV% = sqrt (exp (variance for log transformed data)-1)*100.

NOVARTIS

FRM-7043019 version 2.0

Capmatinib PK results (pharmacokinetics analysis set)

Visit	Scheduled sampling timepoint	Statistics	INC280 Concentration (ng/mL)
Cycle 1 Day 22	0 hr (pre dose)	n	17
		m	17
		Mean (SD)	594 (505)
		CV%	85.0
		Geo-mean	407
		Geo-CV%	125.8
		Median	415
		[Min – Max]	[48.6; 1840]
Cycle 2 Day 1	0 hr (pre dose)	n	10
		m	10
		Mean (SD)	888 (1030)
		CV%	115.7
		Geo-mean	529
		Geo-CV%	135.2
		Median	360
		[Min – Max]	[189; 3060]

Visit	Scheduled sampling timepoint	Statistics	INC280 Concentration (ng/mL)
	2 hr	n	11
		m	11
		Mean (SD)	4280 (1640)
		CV%	38.3
		Geo-mean	3960
		Geo-CV%	45.5
		Median	4270
		[Min – Max]	[1640; 7300]

n: number of patients with evaluable values, m: number of non-zero concentrations.
Below the limit of quantitation (BLQ) values (< 1.0 ng/mL) have been set to zero.
Zero concentrations are considered as missing in Geo-mean and Geo-CV% calculations.
CV% = coefficient of variation (%) = SD/mean*100, Geo-CV% = sqrt (exp (variance for log transformed data)-1)*100.

Best overall response per Investigator assessment (full analysis set)

	All patients N=32 n (%)	95% CI [a]
Best overall response		
Stable Disease (SD)	8 (25.0)	
Progressive Disease (PD)	17 (53.1)	
Unknown (UNK)	7 (21.9)	
Disease Control Rate (DCR: CR+PR+SD)	8 (25.0)	(11.5, 43.4)

NOVARTIS

FRM-7043019 version 2.0

	All patients N=32 n (%) 95% CI [a]

N: The total number of patients in FAS. It is the denominator for percentage (%) calculation.

n: Number of patients who are at the corresponding category.

[a] Exact binomial 95% Confidence Interval.

Summary of Safety

Safety Results

All adverse events, regardless of study drug relationship by primary system organ class and maximum grade (Safety set)

Primary system organ class	All grades n (%)
Any primary system organ class	32 (100)
Gastrointestinal disorders	28 (87.5)
General disorders and administration site conditions	25 (78.1)
Investigations	16 (50.0)
Infections and infestations	12 (37.5)
Respiratory, thoracic and mediastinal disorders	11 (34.4)
Metabolism and nutrition disorders	10 (31.3)
Blood and lymphatic system disorders	8 (25.0)
Musculoskeletal and connective tissue disorders	7 (21.9)
Nervous system disorders	7 (21.9)
Psychiatric disorders	5 (15.6)
Vascular disorders	5 (15.6)
Cardiac disorders	4 (12.5)
Skin and subcutaneous tissue disorders	3 (9.4)
Ear and labyrinth disorders	2 (6.3)
Eye disorders	1 (3.1)
Injury, poisoning and procedural complications	1 (3.1)
Renal and urinary disorders	1 (3.1)

Primary system organ class	All grades n (%)
Primary system organ classes are sorted in descending frequency of 'All grades' column, as reported under 'All Patients', and then presented alphabetically.	
A patient with multiple occurrences of an AE under one treatment is counted only once in the AE category for that treatment.	
A patient with multiple adverse events within a primary system organ class is counted only once in the total row.	

On-treatment deaths, by primary system organ class, and preferred term (Safety set)

Primary system organ class Principal cause of death	All patients N=32 n (%)
Any primary system organ class	6 (18.8)
Cardiac disorders	1 (3.1)
Cardio-respiratory arrest	1 (3.1)
General disorders and administration site conditions	2 (6.3)
Disease progression	2 (6.3)
Infections and infestations	1 (3.1)
Respiratory tract infection	1 (3.1)
Neoplasms benign, malignant and unspecified (inclusive cysts and polyps)	1 (3.1)
Adenocarcinoma pancreas	1 (3.1)
Nervous system disorders	1 (3.1)
Depressed level of consciousness	1 (3.1)
Primary system organ classes are presented alphabetically; preferred terms are sorted within primary system organ class in descending frequency, as reported under 'All Patients'.	
Deaths up to 30 days after the last dose are all included.	

NOVARTIS

FRM-7043019 version 2.0

Serious adverse events, regardless of study drug relationship by preferred term, and maximum grade (Safety set)

	All patients N=32	
Preferred term	All grades n (%)	Grade 3/4 n (%)
Total	17 (53.1)	13 (40.6)
Pulmonary embolism	3 (9.4)	3 (9.4)
Vomiting	3 (9.4)	2 (6.3)
Dyspnoea	2 (6.3)	2 (6.3)
Abdominal pain	1 (3.1)	1 (3.1)
Anaemia	1 (3.1)	1 (3.1)
Asthenia	1 (3.1)	1 (3.1)
Atrial fibrillation	1 (3.1)	0
Bacterial infection	1 (3.1)	1 (3.1)
Biliary sepsis	1 (3.1)	1 (3.1)
Blood bilirubin increased	1 (3.1)	1 (3.1)
Brucellosis	1 (3.1)	0
Cardio-respiratory arrest	1 (3.1)	1 (3.1)
Depressed level of consciousness	1 (3.1)	1 (3.1)
Encephalopathy	1 (3.1)	1 (3.1)
Escherichia infection	1 (3.1)	0
Hypotension	1 (3.1)	0
Intestinal obstruction	1 (3.1)	1 (3.1)
Leukocytosis	1 (3.1)	1 (3.1)
Liver abscess	1 (3.1)	0
Malaise	1 (3.1)	1 (3.1)

Preferred term	All patients N=32 All grades n (%)	Grade 3/4 n (%)
Nausea	1 (3.1)	1 (3.1)
Oesophageal perforation	1 (3.1)	1 (3.1)
Pain	1 (3.1)	0
Photophobia	1 (3.1)	1 (3.1)
Pneumonia	1 (3.1)	0
Pyrexia	1 (3.1)	1 (3.1)
Raoultella ornithinolytica infection	1 (3.1)	0
Respiratory tract infection	1 (3.1)	1 (3.1)
Septic shock	1 (3.1)	0

Preferred terms are sorted in descending frequency of 'All Grades' column, as reported under 'All Patients'.
A patient with multiple occurrences of an AE under one treatment is counted only once in the AE Category for that treatment.
A patient with multiple adverse events is counted only once in the total row.
A patient with multiple severity grades for an AE while on treatment is only counted under the maximum grade.
Only AEs occurring during treatment or within 30 days of the last dose of study treatment are reported.
Missing grades are included under 'All grades' column.
AEs are graded according to the CTCAE V4.03; MedDRA version 20.0 is used.

Other Relevant Findings

None

Conclusion

The following conclusions can be drawn from this Phase I drug-drug interaction study to assess the effect of capmatinib on the Pharmacokinetics of digoxin and rosuvastatin in 32 patients with MET-dysregulated advanced solid tumors:

- Capmatinib is an inhibitor of p-glycoprotein as well as BCRP transporters, with clinically relevant drug-drug interaction potential
- Capmatinib was tolerated well by the study population with no major or new safety concerns.

Date of Clinical Trial Report

18-Dec-2017