Clinical trial results:
A Phase II, Open-label, Randomized Study of GDC-0980 versus Everolimus in Patients with Metastatic Renal Cell Carcinoma Who Have Progressed on or following VEGF-Targeted Therapy

Summary

EudraCT number	2011-000493-56
Trial protocol	ES DE GB
Global end of trial date	23 June 2015

Results information

Result version number	v1 (current)
This version publication date	08 July 2016
First version publication date	08 July 2016

Trial information

Trial identification

Sponsor protocol code	PIM4973g

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01442090
WHO universal trial number (UTN)	-
Other trial identifiers	Other Study Identifier : GO00885

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.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 June 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 June 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of GDC-0980 versus everolimus as measured by progression-free survival (PFS) defined as the time from randomization to disease progression.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 October 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 10
Country: Number of subjects enrolled	United Kingdom: 28
Country: Number of subjects enrolled	France: 20
Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	United States: 17
Worldwide total number of subjects	85
EEA total number of subjects	68

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)	59
From 65 to 84 years	25

85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 85 subjects were enrolled into the study from 5 countries.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	GDC-0980

Arm description:

Subjects with metastatic renal cell carcinoma (RCC) who have progressed on or after vascular endothelial growth factor (VEGF) targeted therapy received GDC0980 40 milligram (mg) orally, once daily up until disease progression, intolerable toxicity, elective withdrawal from the study, or study completion or termination.

Arm type	Experimental
Investigational medicinal product name	GDC-0980
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received GDC-0980 40 mg orally once daily.

Arm title	Everolimus

Arm description:

Subjects with metastatic renal cell carcinoma (RCC) who have progressed on or after vascular endothelial growth factor (VEGF) targeted therapy received everolimus 10 mg orally, once daily up until disease progression, intolerable toxicity, elective withdrawal from the study, or study completion or termination.

Arm type	Active comparator
Investigational medicinal product name	Everolimus
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received everolimus 10 mg orally once daily.

Number of subjects in period 1	GDC-0980	Everolimus
Started	42	43
Completed	0	0
Not completed	42	43
Death	28	23
Study terminated by sponsor	1	2
Reason not specified	12	15
Withdrawal by subject	1	3

Baseline characteristics

Reporting groups	
Reporting group title	GDC-0980
Reporting group description:	
Subjects with metastatic renal cell carcinoma (RCC) who have progressed on or after vascular endothelial growth factor (VEGF) targeted therapy received GDC0980 40 milligram (mg) orally, once daily up until disease progression, intolerable toxicity, elective withdrawal from the study, or study completion or termination.	
Reporting group title	Everolimus
Reporting group description:	
Subjects with metastatic renal cell carcinoma (RCC) who have progressed on or after vascular endothelial growth factor (VEGF) targeted therapy received everolimus 10 mg orally, once daily up until disease progression, intolerable toxicity, elective withdrawal from the study, or study completion or termination.	

Reporting group values	GDC-0980	Everolimus	Total
Number of subjects	42	43	85
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	28	31	59
From 65-84 years	14	11	25
85 years and over	0	1	1
Age continuous			
Units: years			
arithmetic mean	60.3	60.5	
standard deviation	± 8.1	± 9.9	-
Gender categorical			
Units: Subjects			
Female	9	12	21
Male	33	31	64

End points

End points reporting groups

Reporting group title	GDC-0980

Reporting group description:

Subjects with metastatic renal cell carcinoma (RCC) who have progressed on or after vascular endothelial growth factor (VEGF) targeted therapy received GDC0980 40 milligram (mg) orally, once daily up until disease progression, intolerable toxicity, elective withdrawal from the study, or study completion or termination.

Reporting group title	Everolimus

Reporting group description:

Subjects with metastatic renal cell carcinoma (RCC) who have progressed on or after vascular endothelial growth factor (VEGF) targeted therapy received everolimus 10 mg orally, once daily up until disease progression, intolerable toxicity, elective withdrawal from the study, or study completion or termination.

Primary: Duration of Progression-Free Survival (PFS)

End point title	Duration of Progression-Free Survival (PFS)[1]

End point description:

PFS was defined as the time from randomization to disease progression, as assessed by the investigator using Response Evaluation Criteria in Solid Tumors (RECIST) 1.1, or death from any cause. Progression was defined as a 20% increase in the sum of the longest diameter of target lesions, the appearance of new lesions and increase of at least 5 millimeters (mm) in the sum of diameters of target lesions. Kaplan-Meier was used to estimate the medians of each treatment arm. Analysis was performed on the safety evaluable population defined as all subjects who were treated with any amount of study drug.

End point type	Primary

End point timeframe:

Baseline until disease progression, or death, which occurred first (up to approximately 23 months)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be reported.

End point values	GDC-0980	Everolimus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	43		
Units: months				
median (confidence interval 95%)	3.7 (3.5 to 5.4)	6.1 (3.7 to 9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Plasma Concentration (Cmax) of GDC-0980

End point title	Maximum Plasma Concentration (Cmax) of GDC-0980[2]

End point description:

Pharmacokinetics (PK)-evaluable population was defined as all safety-evaluable subjects with any available PK data.

End point type	Secondary

End point timeframe:

Week 1 Day 1, Week 3 Day 1, Week 9 Day 1

Notes:

[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: No inter-group analysis was performed.

End point values	GDC-0980			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: nanogram per milliliter (ng/mL)				
geometric mean (standard deviation)				
Week 1 Day 1 (n=41)	210 (± 116)			
Week 3 Day 1 (n=33)	267 (± 155)			
Week 9 Day 1 (n=24)	266 (± 130)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax of Everolimus

End point title	Cmax of Everolimus[3]

End point description:

Week 1 Day 1 and Week 9 Day 1

End point type	Secondary

End point timeframe:

PK-evaluable population was defined as all safety-evaluable subjects with any available PK data.

Notes:

[3] - 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: No inter-group analysis was performed.

End point values	Everolimus			
Subject group type	Reporting group			
Number of subjects analysed	0[4]			
Units: (ng/mL)				
geometric mean (standard deviation)	()			

Notes:

[4] - Due to sampling error, no PK analyses were reported.

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Plasma Concentration (Cmin) of GDC-0980

End point title	Minimum Plasma Concentration (Cmin) of GDC-0980[5]

End point description:

PK-evaluable population was defined as all safety-evaluable subjects with any available PK data.

End point type	Secondary

End point timeframe:

Week 1 Day 1, Week 3 Day 1, Week 9 Day 1

Notes:

[5] - 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: No inter-group analysis was performed.

End point values	GDC-0980			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: ng/mL				
geometric mean (standard deviation)				
Week 1 Day 1 (n=41)	55.1 (± 52.1)			
Week 3 Day 1 (n=33)	57.5 (± 94.1)			
Week 9 Day 1 (n=24)	51.6 (± 74.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cmin of Everolimus

End point title	Cmin of Everolimus[6]

End point description:

PK-evaluable population was defined as all safety-evaluable subjects with any available PK data.

End point type	Secondary

End point timeframe:

Week 1 Day 1, Week 9 Day 1

Notes:

[6] - 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: No inter-group analysis was performed.

End point values	Everolimus			
Subject group type	Reporting group			
Number of subjects analysed	0[7]			
Units: ng/mL				
geometric mean (standard deviation)	()			

Notes:

[7] - Due to sampling error, no PK analyses were reported.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With an Adverse Event (AE)

End point title	Number of Subjects With an Adverse Event (AE)

End point description:

An AE was defined as any unfavorable or unintended sign, symptom, or disease temporally associated with the use of an investigational medicinal product or other protocol-imposed intervention, regardless

of attribution. Analysis was performed on the safety evaluable population defined as all subjects who were treated with any amount of study drug.

End point type	Secondary

End point timeframe:

Up to 30 days after end of treatment (approximately 23 months)

End point values	GDC-0980	Everolimus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	43		
Units: Subjects	42	41		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Objective Tumor Response

End point title	Number of Subjects With Objective Tumor Response

End point description:

Best objective response was assessed by RECIST 1.1 and defined as the best response recorded from the start of treatment until disease progression. Complete response (CR) was defined as the disappearance of all target lesions. Partial response (PR) was defined as at least a 30% decrease in the sum of diameters of target lesions. Progressive disease (PD) was defined as at least a 20% increase in the sum of diameters of target lesions. Stable disease (SD) was defined as neither sufficient shrinkage to qualify as PR nor sufficient increase to qualify as PD. Analysis was performed on the safety evaluable population defined as all subjects who were treated with any amount of study drug.

End point type	Secondary

End point timeframe:

Baseline until disease progression or death, whichever occurred first (up to approximately 23 months)

End point values	GDC-0980	Everolimus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	43		
Units: Subjects				
CR	1	1		
PR	3	6		
PD	8	11		
SD	27	25		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Objective Tumor Response

End point title	Duration of Objective Tumor Response

End point description:

Duration of objective tumor response was defined as the time from first observation of an objective tumor response until first observation of disease progression as assessed by the investigator using RECIST 1.1. Analysis was performed on the safety evaluable population defined as all subjects who were treated with any amount of study drug.

End point type	Secondary

End point timeframe:

Baseline until disease progression or death, whichever occurred first (up to approximately 23 months)

End point values	GDC-0980	Everolimus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[8]	0[9]		
Units: months				
median (confidence interval 95%)	(to)	(to)		

Notes:

[8] - Duration of response was not summarized due to limited number of responses.

[9] - Duration of response was not summarized due to limited number of responses.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Overall Survival (OS)

End point title	Duration of Overall Survival (OS)

End point description:

OS was defined as the time from treatment initiation until death from any cause. Analysis was performed on the safety evaluable population defined as all subjects who were treated with any amount of study drug. Here, '99999' represents that the confidence interval was not evaluable.

End point type	Secondary

End point timeframe:

Baseline until death (up to approximately 45 months)

End point values	GDC-0980	Everolimus		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	43		
Units: Months				
median (confidence interval 95%)	16.5 (10.8 to 21.4)	19.9 (12.4 to 99999)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From signing of the informed consent form up to 30 days after the last administration of study drug or until initiation of another anti-cancer therapy, whichever occurs first.

Adverse event reporting additional description:

An AE was defined as any unfavorable or unintended sign, symptom, or disease temporally associated with the use of an investigational medicinal product or other protocol-imposed intervention, regardless of attribution.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	GDC-0980

Reporting group description:

Subjects with metastatic renal cell carcinoma (RCC) who have progressed on or after vascular endothelial growth factor (VEGF) targeted therapy received GDC0980 40 milligram (mg) orally, once daily up until disease progression, intolerable toxicity, elective withdrawal from the study, or study completion or termination.

Reporting group title	Everolimus

Reporting group description:

Subjects with metastatic renal cell carcinoma (RCC) who have progressed on or after vascular endothelial growth factor (VEGF) targeted therapy received everolimus 10 mg orally, once daily up until disease progression, intolerable toxicity, elective withdrawal from the study, or study completion or termination.

Serious adverse events	GDC-0980	Everolimus	
Total subjects affected by serious adverse events			
subjects affected / exposed	28 / 42 (66.67%)	10 / 43 (23.26%)	
number of deaths (all causes)	28	23	
number of deaths resulting from adverse events	1	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Renal cell carcinoma			
subjects affected / exposed	2 / 42 (4.76%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration			

site conditions			
Chest pain			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal inflammation			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 42 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea exertional			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Pleural effusion			

subjects affected / exposed	2 / 42 (4.76%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 42 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Migraine			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fissure			

subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	0 / 42 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal angiodysplasia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Swollen tongue			
subjects affected / exposed	0 / 42 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			

Dermatitis exfoliative			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ichthyosis acquired			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash maculo-papular			
subjects affected / exposed	2 / 42 (4.76%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Anaemia			
subjects affected / exposed	1 / 42 (2.38%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteitis			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	0 / 42 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess			

subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eczema impetiginous			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 42 (2.38%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 42 (2.38%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	2 / 42 (4.76%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary sepsis			

subjects affected / exposed	0 / 42 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia haemophilus			
subjects affected / exposed	0 / 42 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	1 / 42 (2.38%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	4 / 42 (9.52%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	4 / 4	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	GDC-0980	Everolimus	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 42 (100.00%)	41 / 43 (95.35%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 42 (7.14%)	1 / 43 (2.33%)	
occurrences (all)	3	1	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	12 / 42 (28.57%)	16 / 43 (37.21%)	
occurrences (all)	19	32	
Mucosal inflammation			
subjects affected / exposed	10 / 42 (23.81%)	17 / 43 (39.53%)	
occurrences (all)	19	40	
Asthenia			

subjects affected / exposed	13 / 42 (30.95%)	10 / 43 (23.26%)	
occurrences (all)	36	26	
Pyrexia			
subjects affected / exposed	10 / 42 (23.81%)	5 / 43 (11.63%)	
occurrences (all)	10	6	
Oedema peripheral			
subjects affected / exposed	2 / 42 (4.76%)	8 / 43 (18.60%)	
occurrences (all)	3	15	
Pain			
subjects affected / exposed	2 / 42 (4.76%)	5 / 43 (11.63%)	
occurrences (all)	4	5	
Chest pain			
subjects affected / exposed	1 / 42 (2.38%)	4 / 43 (9.30%)	
occurrences (all)	1	4	
Chills			
subjects affected / exposed	3 / 42 (7.14%)	2 / 43 (4.65%)	
occurrences (all)	4	2	
Oedema			
subjects affected / exposed	0 / 42 (0.00%)	3 / 43 (6.98%)	
occurrences (all)	0	3	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	10 / 42 (23.81%)	19 / 43 (44.19%)	
occurrences (all)	14	32	
Dyspnoea			
subjects affected / exposed	5 / 42 (11.90%)	13 / 43 (30.23%)	
occurrences (all)	5	22	
Epistaxis			
subjects affected / exposed	3 / 42 (7.14%)	13 / 43 (30.23%)	
occurrences (all)	4	18	
Pneumonitis			
subjects affected / exposed	4 / 42 (9.52%)	7 / 43 (16.28%)	
occurrences (all)	4	11	
Dysphonia			

subjects affected / exposed	2 / 42 (4.76%)	3 / 43 (6.98%)	
occurrences (all)	2	4	
Productive cough			
subjects affected / exposed	1 / 42 (2.38%)	3 / 43 (6.98%)	
occurrences (all)	1	3	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	5 / 42 (11.90%)	6 / 43 (13.95%)	
occurrences (all)	5	7	
Investigations			
Weight decreased			
subjects affected / exposed	9 / 42 (21.43%)	4 / 43 (9.30%)	
occurrences (all)	12	4	
Blood creatine increased			
subjects affected / exposed	1 / 42 (2.38%)	7 / 43 (16.28%)	
occurrences (all)	1	11	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 42 (2.38%)	3 / 43 (6.98%)	
occurrences (all)	1	5	
Blood triglycerides increased			
subjects affected / exposed	0 / 42 (0.00%)	3 / 43 (6.98%)	
occurrences (all)	0	3	
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 42 (14.29%)	7 / 43 (16.28%)	
occurrences (all)	7	11	
Dysgeusia			
subjects affected / exposed	4 / 42 (9.52%)	6 / 43 (13.95%)	
occurrences (all)	6	8	
Lethargy			
subjects affected / exposed	4 / 42 (9.52%)	5 / 43 (11.63%)	
occurrences (all)	5	8	
Dizziness			
subjects affected / exposed	1 / 42 (2.38%)	4 / 43 (9.30%)	
occurrences (all)	1	7	
Paraesthesia			

subjects affected / exposed	3 / 42 (7.14%)	2 / 43 (4.65%)	
occurrences (all)	3	2	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 42 (11.90%)	13 / 43 (30.23%)	
occurrences (all)	9	33	
Thrombocytopenia			
subjects affected / exposed	1 / 42 (2.38%)	5 / 43 (11.63%)	
occurrences (all)	1	11	
Eye disorders			
Lacrimation increased			
subjects affected / exposed	3 / 42 (7.14%)	1 / 43 (2.33%)	
occurrences (all)	3	1	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	22 / 42 (52.38%)	23 / 43 (53.49%)	
occurrences (all)	44	44	
Nausea			
subjects affected / exposed	20 / 42 (47.62%)	14 / 43 (32.56%)	
occurrences (all)	26	16	
Vomiting			
subjects affected / exposed	16 / 42 (38.10%)	9 / 43 (20.93%)	
occurrences (all)	31	12	
Constipation			
subjects affected / exposed	8 / 42 (19.05%)	13 / 43 (30.23%)	
occurrences (all)	11	14	
Abdominal pain			
subjects affected / exposed	8 / 42 (19.05%)	9 / 43 (20.93%)	
occurrences (all)	10	15	
Stomatitis			
subjects affected / exposed	7 / 42 (16.67%)	9 / 43 (20.93%)	
occurrences (all)	17	14	
Dyspepsia			
subjects affected / exposed	5 / 42 (11.90%)	5 / 43 (11.63%)	
occurrences (all)	7	5	
Abdominal pain upper			

subjects affected / exposed	8 / 42 (19.05%)	1 / 43 (2.33%)	
occurrences (all)	8	1	
Dry mouth			
subjects affected / exposed	3 / 42 (7.14%)	5 / 43 (11.63%)	
occurrences (all)	4	6	
Mouth ulceration			
subjects affected / exposed	4 / 42 (9.52%)	2 / 43 (4.65%)	
occurrences (all)	6	2	
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 42 (7.14%)	1 / 43 (2.33%)	
occurrences (all)	3	1	
Haemorrhoids			
subjects affected / exposed	3 / 42 (7.14%)	0 / 43 (0.00%)	
occurrences (all)	5	0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	18 / 42 (42.86%)	22 / 43 (51.16%)	
occurrences (all)	36	37	
Pruritus			
subjects affected / exposed	10 / 42 (23.81%)	8 / 43 (18.60%)	
occurrences (all)	16	9	
Dry skin			
subjects affected / exposed	6 / 42 (14.29%)	10 / 43 (23.26%)	
occurrences (all)	8	13	
Rash maculo-papular			
subjects affected / exposed	8 / 42 (19.05%)	4 / 43 (9.30%)	
occurrences (all)	14	4	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	3 / 42 (7.14%)	5 / 43 (11.63%)	
occurrences (all)	5	6	
Onychoclasis			
subjects affected / exposed	1 / 42 (2.38%)	6 / 43 (13.95%)	
occurrences (all)	2	6	
Night sweats			

subjects affected / exposed	5 / 42 (11.90%)	1 / 43 (2.33%)	
occurrences (all)	7	1	
Rash pruritic			
subjects affected / exposed	0 / 42 (0.00%)	4 / 43 (9.30%)	
occurrences (all)	0	4	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 42 (0.00%)	3 / 43 (6.98%)	
occurrences (all)	0	4	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	3 / 42 (7.14%)	6 / 43 (13.95%)	
occurrences (all)	3	9	
Muscle spasms			
subjects affected / exposed	4 / 42 (9.52%)	4 / 43 (9.30%)	
occurrences (all)	10	4	
Arthralgia			
subjects affected / exposed	3 / 42 (7.14%)	3 / 43 (6.98%)	
occurrences (all)	3	5	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 42 (4.76%)	4 / 43 (9.30%)	
occurrences (all)	2	5	
Urinary tract infection			
subjects affected / exposed	3 / 42 (7.14%)	1 / 43 (2.33%)	
occurrences (all)	4	1	
Lung infection			
subjects affected / exposed	0 / 42 (0.00%)	3 / 43 (6.98%)	
occurrences (all)	0	3	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	24 / 42 (57.14%)	9 / 43 (20.93%)	
occurrences (all)	64	33	
Decreased appetite			
subjects affected / exposed	18 / 42 (42.86%)	10 / 43 (23.26%)	
occurrences (all)	30	15	

Dehydration			
subjects affected / exposed	3 / 42 (7.14%)	2 / 43 (4.65%)	
occurrences (all)	4	2	
Hypertriglyceridaemia			
subjects affected / exposed	1 / 42 (2.38%)	3 / 43 (6.98%)	
occurrences (all)	1	7	
Hypercholesterolaemia			
subjects affected / exposed	0 / 42 (0.00%)	3 / 43 (6.98%)	
occurrences (all)	0	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 August 2011	The eligibility criteria was updated to include an exclusion criteria of: hypersensitivity to any rapamycin derivatives or to any excipients of everolimus.
23 May 2012	The study was amended for updates to the management of hyperglycemia to reflect current best practices.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported