



Clinical trial results:

Dose Finding and Randomized, Multicenter, Placebo- Controlled, Phase 2 Study of Enzastaurin and Sunitinib versus Placebo and Sunitinib in Patients with Metastatic Renal Cell Carcinoma

Summary

EudraCT number	2007-003847-66
Trial protocol	FR AT PL IT ES
Global end of trial date	05 September 2018

Results information

Result version number	v1 (current)
This version publication date	21 September 2019
First version publication date	21 September 2019

Trial information

Trial identification

Sponsor protocol code	H6Q-MC-S061
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00709995
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 11531

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 877CTLilly,
Scientific contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 8772854559,

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	05 September 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	05 September 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This study will compare the effects of Enzastaurin plus Sunitinib versus Sunitinib alone in metastatic Renal Cell Cancer.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 June 2008
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	Austria: 2
Country: Number of subjects enrolled	Poland: 10
Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	France: 2
Worldwide total number of subjects	17
EEA total number of subjects	17

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)	12
From 65 to 84 years	5

85 years and over	0
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Subject disposition

Recruitment

Recruitment details:

No Text Available

Pre-assignment

Screening details:

Part 1 completers finished 3 or more cycles and included those with progressive disease. Part 2 was not performed and was not activated due to sponsor broad decision to not pursue enzastaurin in solid tumors.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer

Blinding implementation details:

Part 2 was to be a randomized, double-blind treatment phase.

Arms

Are arms mutually exclusive?	Yes
Arm title	Modified Regimen A (Cohort 1)

Arm description:

On cycle 1, day 1 a loading dose 125 milligram (mg) of Enzastaurin was administered by mouth orally, (BID) twice a day, followed by Enzastaurin 125 mg administered, twice a day, Days 2 through 42 of a 6-week cycle.

Sunitinib 50 mg was administered orally, (QD) once daily, Days 1-28, then rest (no drug given) Days 29-42.

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

Dosage and administration details:

On cycle 1, day 1 a loading dose 125 milligram (mg) of Enzastaurin was administered by mouth orally, (BID) twice a day, followed by Enzastaurin 125 mg administered, twice a day, Days 2 through 42 of a 6-week cycle.

Investigational medicinal product name	Sunitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Sunitinib 50 mg was administered orally, (QD) once daily, Days 1-28, then rest (no drug given) Days 29-42.

Arm title	Regimen A (Cohort 2)
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Arm description:

Enzastaurin was given on Day 1 of Cycle 1 as a loading dose of 1125 mg (3 tablets of 125 mg each, taken 3 times a day with at least 4 hours between doses), followed by daily total dose of 500 mg (2 tablets of 125 mg each, BID) continuously until disease progression, unacceptable toxicity, death, or discontinuation from the study for any other reason.

Sunitinib 50 mg was administered orally, once daily, Days 1-28, then rest (no drug given) Days 29-42.

Arm type	Placebo
Investigational medicinal product name	Enzastaurin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Enzastaurin was given on Day 1 of Cycle 1 as a loading dose of 1125 mg (3 tablets of 125 mg each, taken 3 times a day with at least 4 hours between doses), followed by daily total dose of 500 mg (2 tablets of 125 mg each, BID) continuously until disease progression, unacceptable toxicity, death, or discontinuation from the study for any other reason.

Investigational medicinal product name	Sunitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Sunitinib 50 mg was administered orally, once daily, Days 1-28, then rest (no drug given) Days 29-42.

Number of subjects in period 1	Modified Regimen A (Cohort 1)	Regimen A (Cohort 2)
Started	11	6
Progressive Disease	6	1
Completed	6	1
Not completed	5	5
Consent withdrawn by subject	1	3
Adverse event, non-fatal	4	2

Baseline characteristics

Reporting groups

Reporting group title	Modified Regimen A (Cohort 1)
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Reporting group description:

On cycle 1, day 1 a loading dose 125 milligram (mg) of Enzastaurin was administered by mouth orally, (BID) twice a day, followed by Enzastaurin 125 mg administered, twice a day, Days 2 through 42 of a 6-week cycle.

Sunitinib 50 mg was administered orally, (QD) once daily, Days 1-28, then rest (no drug given) Days 29-42.

Reporting group title	Regimen A (Cohort 2)
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Reporting group description:

Enzastaurin was given on Day 1 of Cycle 1 as a loading dose of 1125 mg (3 tablets of 125 mg each, taken 3 times a day with at least 4 hours between doses), followed by daily total dose of 500 mg (2 tablets of 125 mg each, BID) continuously until disease progression, unacceptable toxicity, death, or discontinuation from the study for any other reason.

Sunitinib 50 mg was administered orally, once daily, Days 1-28, then rest (no drug given) Days 29-42.

Reporting group values	Modified Regimen A (Cohort 1)	Regimen A (Cohort 2)	Total
Number of subjects	11	6	17
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
arithmetic mean	60.1	58.5	
standard deviation	± 5.44	± 8.42	-
Gender categorical			
Units: Subjects			
Female	5	1	6
Male	6	5	11
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	11	6	17
Unknown or Not Reported	0	0	0
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0

Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	11	6	17
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Region of Enrollment			
Units: Subjects			
Austria	1	1	2
Poland	6	4	10
Italy	3	0	3
France	1	1	2

End points

End points reporting groups

Reporting group title	Modified Regimen A (Cohort 1)
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Reporting group description:

On cycle 1, day 1 a loading dose 125 milligram (mg) of Enzastaurin was administered by mouth orally, (BID) twice a day, followed by Enzastaurin 125 mg administered, twice a day, Days 2 through 42 of a 6-week cycle.

Sunitinib 50 mg was administered orally, (QD) once daily, Days 1-28, then rest (no drug given) Days 29-42.

Reporting group title	Regimen A (Cohort 2)
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Reporting group description:

Enzastaurin was given on Day 1 of Cycle 1 as a loading dose of 1125 mg (3 tablets of 125 mg each, taken 3 times a day with at least 4 hours between doses), followed by daily total dose of 500 mg (2 tablets of 125 mg each, BID) continuously until disease progression, unacceptable toxicity, death, or discontinuation from the study for any other reason.

Sunitinib 50 mg was administered orally, once daily, Days 1-28, then rest (no drug given) Days 29-42.

Subject analysis set title	Sunitinib + Placebo
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Subject analysis set type	Per protocol
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Subject analysis set description:

Sunitinib: 50 mg administered orally, once daily, Day 1-28, then rest Days 29-42.

Placebo: Cycle 1 Day 1 loading dose 3 tablets on Day 1, then 2 tablets daily, Days 2-42.

Subject analysis set title	Enzastaurin + Sunitinib
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Subject analysis set type	Per protocol
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Subject analysis set description:

Enzastaurin: Cycle 1, Day 1 loading dose 375 mg administered orally, three times a day, followed by Part 1 dose twice a day on Days 2-42 of 6-week cycle.

Sunitinib: 50 mg administered orally, once daily, on Days 1-28, then rest Days 29-42.

Primary: Progression Free Survival (PFS) in Part 2

End point title	Progression Free Survival (PFS) in Part 2 ^[1]
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End point description:

Progression-free survival (PFS) was defined as the number of months between the date of randomization and the date of first documented disease progression or the date of death due to any cause, whichever came first.

End point type	Primary
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End point timeframe:

Randomization to Measured Progressive Disease (PD) (Up to 24 Months)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Zero participants were analyzed in the primary endpoint and therefore a statistical analysis was not done.

End point values	Sunitinib + Placebo	Enzastaurin + Sunitinib		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0 ^[2]	0 ^[3]		
Units: Number of Months				

Notes:

[2] - Zero participants data were collected. Part 2 was not activated due to sponsor broad decision.

[3] - Zero participants data were collected. Part 2 was not activated due to sponsor broad decision.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) in Part 2

End point title	Overall Survival (OS) in Part 2
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End point description:

OS time was defined as the number of months between the date of randomization and the date of death due to any cause.

End point type	Secondary
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End point timeframe:

Randomization to Death from Any Cause (Up to 24 Months)

End point values	Sunitinib + Placebo	Enzastaurin + Sunitinib		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0 ^[4]	0 ^[5]		
Units: Number of Months				

Notes:

[4] - Zero participants data were collected. Part 2 was not activated due to sponsor broad decision.

[5] - Zero participants data were collected. Part 2 was not activated due to sponsor broad decision.

Statistical analyses

No statistical analyses for this end point

Secondary: Time-To-Tumor Progression in Part 2

End point title	Time-To-Tumor Progression in Part 2
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End point description:

Time to tumor progression (TTP) at initial treatment was defined as the number of months between date of randomization and the date of first documented disease progression or the date of death due to disease under study, whichever came first.

End point type	Secondary
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End point timeframe:

Randomization to the Date of Objective Progressive Disease or Date of Death due to Study Disease, whichever came first (Up to 24 Months)

End point values	Sunitinib + Placebo	Enzastaurin + Sunitinib		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0 ^[6]	0 ^[7]		
Units: Number of Months				

Notes:

[6] - Zero participants data were collected. Part 2 was not activated due to sponsor broad decision.

[7] - Zero participants data were collected. Part 2 was not activated due to sponsor broad decision.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Adverse Events (AEs) or Serious AEs (SAEs) in Part 1

End point title	Number of Participants with Adverse Events (AEs) or Serious AEs (SAEs) in Part 1
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End point description:

Clinically significant events were defined as serious adverse events, regardless of causality. A summary of serious and other non-serious adverse events regardless of causality is located in the Reported Adverse Event module.

End point type	Secondary
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End point timeframe:

Randomization to Study Completion (Up to 6 Cycles)

End point values	Modified Regimen A (Cohort 1)	Regimen A (Cohort 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11 ^[8]	6 ^[9]		
Units: participants				
AEs	11	6		
SAEs	3	1		

Notes:

[8] - All randomized participants who received at least one dose of study drug.

[9] - All randomized participants who received at least one dose of study drug.

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK): Area Under Concentration Time Curve during One Dosing Interval at Steady State (AUC_{τ,ss}) of Enzastaurin + Metabolite (LSN326020) + Total Analytes in Part 1

End point title	Pharmacokinetics (PK): Area Under Concentration Time Curve during One Dosing Interval at Steady State (AUC _{τ,ss}) of Enzastaurin + Metabolite (LSN326020) + Total Analytes in Part 1
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End point description:

Pharmacokinetics (PK) was assessed in participants to determine the area under the concentration time curve during one dosing interval at steady state (AUC_{τ,ss}) of Enzastaurin, LSN326020 and total Analytes. τ equals 12 hours for Enzastaurin, LSN326020 and total Analytes.

End point type	Secondary
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End point timeframe:

Cycle 1 Day 15: Predose, 2, 4, and 6 - 8 hours, Up to 12 Hours Post dose

End point values	Modified Regimen A (Cohort 1)	Regimen A (Cohort 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11 ^[10]	5 ^[11]		
Units: nanomole*hour/liter (nmol*hr/L)				
geometric mean (geometric coefficient of variation)				
Enzastaurin	12000 (± 144)	22600 (± 91)		
LSN326020	8820 (± 76)	12200 (± 73)		
Total Analytes	21400 (± 101)	35200 (± 82)		

Notes:

[10] - All randomized participants who received at least one dose of study drug had evaluable PK data.

[11] - All randomized participants who received at least one dose of study drug had evaluable PK data.

Statistical analyses

No statistical analyses for this end point

Secondary: PK: Maximum Concentration at Steady State (C_{max,ss}) of Enzastaurin + LSN326020 + Total Analytes in Part 1

End point title	PK: Maximum Concentration at Steady State (C _{max,ss}) of Enzastaurin + LSN326020 + Total Analytes in Part 1
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End point description:

PK was assessed in participants to determine the maximum concentration at steady state (C_{max, ss}) of Enzastaurin + LSN326020 + total analytes.

End point type	Secondary
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End point timeframe:

Cycle 1 Day 15: Predose, 2, 4, and 6 - 8 hours, Up to 12 Hours Post dose

End point values	Modified Regimen A (Cohort 1)	Regimen A (Cohort 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11 ^[12]	5 ^[13]		
Units: nanomole/liter (nmol/L)				
geometric mean (geometric coefficient of variation)				
Enzastaurin	1310 (± 109)	2650 (± 71)		
LSN326020	816 (± 72)	1140 (± 64)		
Total Analytes	2130 (± 88)	3740 (± 65)		

Notes:

[12] - All randomized participants who received at least one dose of study drug had evaluable PK data.

[13] - All randomized participants who received at least one dose of study drug had evaluable PK data.

Statistical analyses

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Baseline to Study Completion (Up to 123 Months)

Adverse event reporting additional description:

All participants who received at least one dose of study drug in Part 1.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	12.0
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Reporting groups

Reporting group title	Modified Regimen A (Cohort 1)
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Reporting group description: -

Reporting group title	Regimen A (Cohort 2)
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Reporting group description: -

Serious adverse events	Modified Regimen A (Cohort 1)	Regimen A (Cohort 2)	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 11 (27.27%)	1 / 6 (16.67%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
thrombosis			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
general physical health deterioration			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
abdominal pain			
alternative dictionary used: MedDRA 12.0			

subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastrointestinal obstruction			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
dyspnoea			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hydrothorax			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pulmonary embolism			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Modified Regimen A (Cohort 1)	Regimen A (Cohort 2)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 11 (100.00%)	6 / 6 (100.00%)	
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 12.0			

subjects affected / exposed	4 / 11 (36.36%)	0 / 6 (0.00%)	
occurrences (all)	4	0	
hypotension			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	3 / 11 (27.27%)	1 / 6 (16.67%)	
occurrences (all)	5	1	
chest pain			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
chills			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	2 / 11 (18.18%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
face oedema			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	1 / 11 (9.09%)	1 / 6 (16.67%)	
occurrences (all)	1	5	
fatigue			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	5 / 11 (45.45%)	3 / 6 (50.00%)	
occurrences (all)	5	9	
general physical health deterioration			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	2 / 11 (18.18%)	1 / 6 (16.67%)	
occurrences (all)	2	2	
influenza like illness			
alternative dictionary used: MedDRA 12.0			

subjects affected / exposed	2 / 11 (18.18%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
malaise			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
mucosal inflammation			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
oedema			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	2 / 11 (18.18%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
oedema peripheral			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	4 / 11 (36.36%)	1 / 6 (16.67%)	
occurrences (all)	7	1	
pyrexia			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
dyspnoea			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
epistaxis			
alternative dictionary used: MedDRA 12.0			

<p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 11 (9.09%)</p> <p>1</p>	<p>0 / 6 (0.00%)</p> <p>0</p>	
<p>haemoptysis</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 11 (9.09%)</p> <p>1</p>	<p>0 / 6 (0.00%)</p> <p>0</p>	
<p>hydrothorax</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 11 (9.09%)</p> <p>1</p>	<p>0 / 6 (0.00%)</p> <p>0</p>	
<p>nasal congestion</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 11 (9.09%)</p> <p>1</p>	<p>0 / 6 (0.00%)</p> <p>0</p>	
<p>pharyngolaryngeal pain</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 11 (9.09%)</p> <p>1</p>	<p>0 / 6 (0.00%)</p> <p>0</p>	
<p>rhinorrhoea</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 11 (0.00%)</p> <p>0</p>	<p>1 / 6 (16.67%)</p> <p>1</p>	
<p>Psychiatric disorders</p> <p>depression</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 11 (9.09%)</p> <p>1</p>	<p>1 / 6 (16.67%)</p> <p>1</p>	
<p>insomnia</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>3 / 11 (27.27%)</p> <p>3</p>	<p>0 / 6 (0.00%)</p> <p>0</p>	
<p>Investigations</p> <p>alanine aminotransferase increased</p> <p>alternative dictionary used: MedDRA 12.0</p>			

subjects affected / exposed	1 / 11 (9.09%)	1 / 6 (16.67%)
occurrences (all)	1	13
aspartate aminotransferase increased		
alternative dictionary used: MedDRA 12.0		
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	60
blood amylase increased		
alternative dictionary used: MedDRA 12.0		
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	1
blood bilirubin decreased		
alternative dictionary used: MedDRA 12.0		
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)
occurrences (all)	1	0
blood cholesterol increased		
alternative dictionary used: MedDRA 12.0		
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	1
blood creatinine increased		
alternative dictionary used: MedDRA 12.0		
subjects affected / exposed	0 / 11 (0.00%)	3 / 6 (50.00%)
occurrences (all)	0	22
blood lactate dehydrogenase increased		
alternative dictionary used: MedDRA 12.0		
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)
occurrences (all)	2	0
blood sodium increased		
alternative dictionary used: MedDRA 12.0		
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)
occurrences (all)	1	0
blood triglycerides increased		
alternative dictionary used: MedDRA 12.0		

<p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 11 (0.00%)</p> <p>0</p>	<p>1 / 6 (16.67%)</p> <p>31</p>	
<p>blood urea increased</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 11 (9.09%)</p> <p>1</p>	<p>0 / 6 (0.00%)</p> <p>0</p>	
<p>c-reactive protein increased</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 11 (9.09%)</p> <p>2</p>	<p>0 / 6 (0.00%)</p> <p>0</p>	
<p>vitamin b12 decreased</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 11 (9.09%)</p> <p>1</p>	<p>0 / 6 (0.00%)</p> <p>0</p>	
<p>weight decreased</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>4 / 11 (36.36%)</p> <p>4</p>	<p>0 / 6 (0.00%)</p> <p>0</p>	
<p>weight increased</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 11 (9.09%)</p> <p>1</p>	<p>0 / 6 (0.00%)</p> <p>0</p>	
<p>Injury, poisoning and procedural complications</p> <p>skin laceration</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 11 (18.18%)</p> <p>2</p>	<p>1 / 6 (16.67%)</p> <p>1</p>	
<p>wound</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 11 (9.09%)</p> <p>1</p>	<p>0 / 6 (0.00%)</p> <p>0</p>	
<p>Cardiac disorders</p> <p>bradycardia</p> <p>alternative dictionary used: MedDRA 12.0</p>			

subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 6 (0.00%) 0	
Nervous system disorders			
dysgeusia alternative dictionary used: MedDRA 12.0 subjects affected / exposed occurrences (all)	4 / 11 (36.36%) 4	0 / 6 (0.00%) 0	
headache alternative dictionary used: MedDRA 12.0 subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 6 (0.00%) 0	
hypoesthesia alternative dictionary used: MedDRA 12.0 subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 6 (16.67%) 1	
paraesthesia alternative dictionary used: MedDRA 12.0 subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 6 (0.00%) 0	
Blood and lymphatic system disorders			
anaemia alternative dictionary used: MedDRA 12.0 subjects affected / exposed occurrences (all)	8 / 11 (72.73%) 33	4 / 6 (66.67%) 10	
leukopenia alternative dictionary used: MedDRA 12.0 subjects affected / exposed occurrences (all)	3 / 11 (27.27%) 4	0 / 6 (0.00%) 0	
lymphopenia alternative dictionary used: MedDRA 12.0 subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 2	0 / 6 (0.00%) 0	
neutropenia alternative dictionary used: MedDRA 12.0			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>thrombocytopenia</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>5 / 11 (45.45%)</p> <p>7</p> <p>9 / 11 (81.82%)</p> <p>20</p>	<p>1 / 6 (16.67%)</p> <p>87</p> <p>2 / 6 (33.33%)</p> <p>32</p>	
<p>Ear and labyrinth disorders</p> <p>vertigo</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 11 (0.00%)</p> <p>0</p>	<p>1 / 6 (16.67%)</p> <p>1</p>	
<p>Eye disorders</p> <p>eyelid oedema</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>lacrimation increased</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 11 (18.18%)</p> <p>2</p> <p>2 / 11 (18.18%)</p> <p>5</p>	<p>0 / 6 (0.00%)</p> <p>0</p> <p>0 / 6 (0.00%)</p> <p>0</p>	
<p>Gastrointestinal disorders</p> <p>abdominal discomfort</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>abdominal pain</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>abdominal pain upper</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>anal discomfort</p> <p>alternative dictionary used: MedDRA 12.0</p>	<p>1 / 11 (9.09%)</p> <p>1</p> <p>2 / 11 (18.18%)</p> <p>2</p> <p>1 / 11 (9.09%)</p> <p>1</p>	<p>0 / 6 (0.00%)</p> <p>0</p> <p>4 / 6 (66.67%)</p> <p>5</p> <p>0 / 6 (0.00%)</p> <p>0</p>	

subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	1
anal inflammation		
alternative dictionary used: MedDRA 12.0		
subjects affected / exposed	3 / 11 (27.27%)	1 / 6 (16.67%)
occurrences (all)	3	1
constipation		
alternative dictionary used: MedDRA 12.0		
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)
occurrences (all)	2	0
dental discomfort		
alternative dictionary used: MedDRA 12.0		
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)
occurrences (all)	1	0
diarrhoea		
alternative dictionary used: MedDRA 12.0		
subjects affected / exposed	7 / 11 (63.64%)	5 / 6 (83.33%)
occurrences (all)	14	5
dry mouth		
alternative dictionary used: MedDRA 12.0		
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	1
dyspepsia		
alternative dictionary used: MedDRA 12.0		
subjects affected / exposed	3 / 11 (27.27%)	0 / 6 (0.00%)
occurrences (all)	3	0
dysphagia		
alternative dictionary used: MedDRA 12.0		
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)
occurrences (all)	1	0
flatulence		
alternative dictionary used: MedDRA 12.0		
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	2

gastrointestinal pain		
alternative dictionary used: MedDRA 12.0		
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)
occurrences (all)	1	0
gingivitis		
alternative dictionary used: MedDRA 12.0		
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	1
haematochezia		
alternative dictionary used: MedDRA 12.0		
subjects affected / exposed	1 / 11 (9.09%)	1 / 6 (16.67%)
occurrences (all)	1	1
haemorrhoids		
alternative dictionary used: MedDRA 12.0		
subjects affected / exposed	0 / 11 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	2
mouth haemorrhage		
alternative dictionary used: MedDRA 12.0		
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)
occurrences (all)	1	0
nausea		
alternative dictionary used: MedDRA 12.0		
subjects affected / exposed	4 / 11 (36.36%)	2 / 6 (33.33%)
occurrences (all)	7	3
oesophagitis		
alternative dictionary used: MedDRA 12.0		
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	1
proctalgia		
alternative dictionary used: MedDRA 12.0		
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)
occurrences (all)	1	0
stomatitis		
alternative dictionary used: MedDRA 12.0		

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>vomiting</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>6 / 11 (54.55%)</p> <p>9</p> <p>3 / 11 (27.27%)</p> <p>3</p>	<p>1 / 6 (16.67%)</p> <p>4</p> <p>4 / 6 (66.67%)</p> <p>8</p>	
<p>Skin and subcutaneous tissue disorders</p> <p>alopecia</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>dry skin</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>hair colour changes</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>nail disorder</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>palmar-plantar erythrodysaesthesia syndrome</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>petechiae</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>rash papular</p> <p>alternative dictionary used: MedDRA 12.0</p>	<p>1 / 11 (9.09%)</p> <p>1</p> <p>1 / 11 (9.09%)</p> <p>1</p> <p>1 / 11 (9.09%)</p> <p>1</p> <p>1 / 11 (9.09%)</p> <p>1</p> <p>2 / 11 (18.18%)</p> <p>5</p> <p>1 / 11 (9.09%)</p> <p>1</p>	<p>0 / 6 (0.00%)</p> <p>0</p> <p>0 / 6 (0.00%)</p> <p>0</p> <p>0 / 6 (0.00%)</p> <p>1 / 6 (16.67%)</p> <p>1</p> <p>0 / 6 (0.00%)</p> <p>0</p> <p>0 / 6 (0.00%)</p> <p>0</p>	

<p>subjects affected / exposed</p> <p>1 / 11 (9.09%)</p> <p>0 / 6 (0.00%)</p> <p>occurrences (all)</p> <p>1</p> <p>0</p>			
<p>skin exfoliation</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>5 / 11 (45.45%)</p> <p>2 / 6 (33.33%)</p> <p>occurrences (all)</p> <p>7</p> <p>3</p>			
<p>skin ulcer</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>1 / 11 (9.09%)</p> <p>0 / 6 (0.00%)</p> <p>occurrences (all)</p> <p>1</p> <p>0</p>			
<p>urticaria localised</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>1 / 11 (9.09%)</p> <p>0 / 6 (0.00%)</p> <p>occurrences (all)</p> <p>1</p> <p>0</p>			
<p>yellow skin</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>2 / 11 (18.18%)</p> <p>1 / 6 (16.67%)</p> <p>occurrences (all)</p> <p>4</p> <p>1</p>			
<p>Renal and urinary disorders</p> <p>haematuria</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>2 / 11 (18.18%)</p> <p>0 / 6 (0.00%)</p> <p>occurrences (all)</p> <p>3</p> <p>0</p>			
<p>Endocrine disorders</p> <p>hyperthyroidism</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>1 / 11 (9.09%)</p> <p>0 / 6 (0.00%)</p> <p>occurrences (all)</p> <p>1</p> <p>0</p> <p>hypothyroidism</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>3 / 11 (27.27%)</p> <p>1 / 6 (16.67%)</p> <p>occurrences (all)</p> <p>3</p> <p>1</p>			
<p>Musculoskeletal and connective tissue disorders</p>			

<p>arthralgia</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 11 (9.09%)</p> <p>1</p>	<p>0 / 6 (0.00%)</p> <p>0</p>	
<p>bone pain</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 11 (9.09%)</p> <p>1</p>	<p>0 / 6 (0.00%)</p> <p>0</p>	
<p>musculoskeletal chest pain</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 11 (0.00%)</p> <p>0</p>	<p>1 / 6 (16.67%)</p> <p>1</p>	
<p>musculoskeletal pain</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 11 (9.09%)</p> <p>1</p>	<p>0 / 6 (0.00%)</p> <p>0</p>	
<p>pain in extremity</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 11 (18.18%)</p> <p>3</p>	<p>1 / 6 (16.67%)</p> <p>1</p>	
<p>Infections and infestations</p> <p>bronchitis</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>cystitis</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>herpes zoster</p> <p>alternative dictionary used: MedDRA 12.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>laryngitis</p> <p>alternative dictionary used: MedDRA 12.0</p>	<p>1 / 11 (9.09%)</p> <p>1</p> <p>1 / 11 (9.09%)</p> <p>1</p> <p>0 / 11 (0.00%)</p> <p>0</p>	<p>0 / 6 (0.00%)</p> <p>0</p> <p>0 / 6 (0.00%)</p> <p>0</p> <p>1 / 6 (16.67%)</p> <p>1</p>	

subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
pharyngitis			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
tooth infection			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
upper respiratory tract infection			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	2 / 11 (18.18%)	1 / 6 (16.67%)	
occurrences (all)	3	1	
Metabolism and nutrition disorders			
anorexia			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	4 / 11 (36.36%)	0 / 6 (0.00%)	
occurrences (all)	5	0	
hypercalcaemia			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
hypercholesterolaemia			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	1 / 11 (9.09%)	1 / 6 (16.67%)	
occurrences (all)	1	8	
hyperkalaemia			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	3 / 11 (27.27%)	2 / 6 (33.33%)	
occurrences (all)	7	2	
hyperuricaemia			
alternative dictionary used: MedDRA 12.0			

subjects affected / exposed	2 / 11 (18.18%)	1 / 6 (16.67%)	
occurrences (all)	2	1	
hypoalbuminaemia			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
hypocalcaemia			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	1 / 11 (9.09%)	1 / 6 (16.67%)	
occurrences (all)	2	1	
hypokalaemia			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	2 / 11 (18.18%)	0 / 6 (0.00%)	
occurrences (all)	3	0	
hypomagnesaemia			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
hyponatraemia			
alternative dictionary used: MedDRA 12.0			
subjects affected / exposed	0 / 11 (0.00%)	2 / 6 (33.33%)	
occurrences (all)	0	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 January 2010	The protocol has been amended to modify ECG monitoring in response to US FDA's recommendation on associated QTc prolongation for enzastaurin. Part 2 of the study, sponsor decided to not activate the randomized phase 2 portion of the study (Part 2). The study will end after all participants have discontinued from Part 1 of the study. Assessments in the participants on long-term study therapy, for those participants who continue enzastaurin treatment for extended durations, assessments for efficacy and safety will be performed at the investigator's discretion based on local practice standards.

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.

Part 1 completers finished 3 or more cycles and included those with progressive disease. Part 2 was not performed and was not activated due to sponsor broad decision to not pursue enzastaurin in solid tumors

Notes: