



Clinical trial results:

Enzastaurin Before and Concomitant With Radiation Therapy, Followed by Enzastaurin Maintenance Therapy in Patients With Newly Diagnosed Glioblastoma Without Methylation of the Promoter Gene of MGMT Enzyme - a Phase II Study

Summary

EudraCT number	2007-000281-21
Trial protocol	DE
Global end of trial date	04 July 2008

Results information

Result version number	v1 (current)
This version publication date	15 June 2018
First version publication date	15 June 2018

Trial information

Trial identification

Sponsor protocol code	H6Q-MC-S039
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00509821
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 11491

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, 1 877-CTLilly,
Scientific contact	Available Mon-Fri 9 AM-5 PM EST, Eli Lilly and Company, 1 877-285-4559,

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	04 July 2008
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 July 2008
Global end of trial reached?	Yes
Global end of trial date	04 July 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of the protocol was to induce a novel radiochemotherapy with enzastaurin as first-line treatment regimen in glioblastoma: Participants with active, unmethylated MGMT promoter were treated with enzastaurin before, concomitant, and after radiotherapy to determine safety and PFS at 6 months (PFS-6) in phase II.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonisation (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	12 August 2004
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 60
Worldwide total number of subjects	60
EEA total number of subjects	60

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)	48
From 65 to 84 years	12

85 years and over	0
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Subject disposition

Recruitment

Recruitment details:

No text entered

Pre-assignment

Screening details:

Completers are participants who had failure event (progressive disease, death), or off treatment or censored. Participants completed follow-up after receiving 1 dose of study drug and a post dose efficacy evaluation. 3 participants received 1125 mg loading dose then 500 mg PO once daily but were not included or analyzed, but AEs are reported.

Period 1

Period 1 title	Overall Ezastaurin BID (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Enzastaurin Twice a Day (BID)
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Arm description:

Enzastaurin 1125 mg loading dose D(-)7 then 250 mg twice daily (BID) PO.

Arm type	Experimental
Investigational medicinal product name	Enzastaurin
Investigational medicinal product code	
Other name	LY317615
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1125 mg loading dose D(-)7 then 250 mg Twice Daily BID.

Number of subjects in period 1 ^[1]	Enzastaurin Twice a Day (BID)
Started	57
Induction	57
Radiation	53
Maintenance	49 ^[2]
Follow UP	50
Completed	50
Not completed	7
Adverse event, serious fatal	5
Progressive disease	2

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 3 participants received Enzastaurin given orally (PO) once daily (QD). 1125 mg loading dose D(-)7 then 500 mg PO,QD with concomitant radiotherapy. These 3 were not analyzed for any endpoints, but Adverse Events and Serious Adverse Events were reported.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Participants did not have to enter into every milestone in the study to proceed to a different milestone and receive study drug.

Baseline characteristics

Reporting groups

Reporting group title	Enzastaurin Twice a Day (BID)
Reporting group description:	
Enzastaurin 1125 mg loading dose D(-)7 then 250 mg twice daily (BID) PO.	

Reporting group values	Enzastaurin Twice a Day (BID)	Total	
Number of subjects	57	57	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	45	45	
From 65-84 years	12	12	
85 years and over	0	0	
Age Continuous			
Units: years			
arithmetic mean	55.6		
standard deviation	± 11.29	-	
Gender categorical			
Units: Subjects			
Female	21	21	
Male	36	36	
Sex: Female, Male			
Units: Subjects			
Female	21	21	
Male	36	36	
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	57	57	
Unknown or Not Reported	0	0	
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	57	57	
More than one race	0	0	
Unknown or Not Reported	0	0	

Region of Enrollment			
Units: Subjects			
Germany	57	57	

End points

End points reporting groups

Reporting group title	Enzastaurin Twice a Day (BID)
Reporting group description: Enzastaurin 1125 mg loading dose D(-)7 then 250 mg twice daily (BID) PO.	
Subject analysis set title	Mini Mental Questionnaire Set
Subject analysis set type	Sub-group analysis
Subject analysis set description: All participants who received at least 1 dose of study drug and had evaluable data .	

Primary: Progression Free Survival Rate 6 Months (PFS-6)

End point title	Progression Free Survival Rate 6 Months (PFS-6) ^[1]
End point description: PFS-6 is defined as the rate of PFS at 6 months from the date of diagnosis to the first date of objectively determined progressive disease (based on radiological assessment) or death from any cause. It is assumed that PFS follows an exponential distribution.	
End point type	Primary
End point timeframe: Baseline to 6 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: This is a single arm study with no comparison groups.	

End point values	Enzastaurin Twice a Day (BID)			
Subject group type	Reporting group			
Number of subjects analysed	57			
Units: Months				
number (confidence interval 95%)	53.6 (39.8 to 65.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival at 1 and 2 Years After Surgery

End point title	Overall Survival at 1 and 2 Years After Surgery
End point description: Overall survival (OS) time is defined as the time from the date of diagnosis to the date of death from any cause. For participants who are still alive at the time of analysis, survival time will be censored at the last contact date. OS rate at 1 year (respectively 2 years) is determined using the OS times.	
End point type	Secondary
End point timeframe: Baseline to 1 and 2 year	

End point values	Enzastaurin Twice a Day (BID)			
Subject group type	Reporting group			
Number of subjects analysed	57			
Units: percent				
number (confidence interval 95%)				
1 year	63.0 (49.1 to 74.1)			
2 year	27.0 (16.2 to 39.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Response Rate

End point title	Response Rate
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End point description:

Response rate is calculated as the number of participants with best response: complete response (CR: disappearance of all enhancing tumor on consecutive CT or magnetic resonance imaging (MRI) scans at least 1 month apart, off steroids, and neurologically stable or improved) or partial response (PR: -50% reduction in size of enhancing tumor on consecutive CT or MRI scans at least 1 month apart, steroids stable or reduced, and neurologically stable or improved), divided by the number of participants treated, multiplied by 100. CR and PR were assessed according to the criteria defined by MacDonald et al. 1990. A CR or PR must be confirmed by a second assessment, performed ≥ 28 days after the first evidence of response.

End point type	Secondary
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End point timeframe:

Baseline to 30 months

End point values	Enzastaurin Twice a Day (BID)			
Subject group type	Reporting group			
Number of subjects analysed	57			
Units: percent				
number (confidence interval 95%)	7.0 (2.0 to 17.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Neurologic Status as Measured by Mini Mental Status Questionnaire, Total Score

End point title	Change in Neurologic Status as Measured by Mini Mental Status Questionnaire, Total Score
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End point description:

Mini Mental State Status questionnaire is 11 questions, total score can range from 0 to 30, with a higher score indicating better function and a negative change in baseline indicating decrease in cognitive function.

End point type	Secondary
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End point timeframe:

Baseline through Week 12 .

End point values	Mini Mental Questionnaire Set			
Subject group type	Subject analysis set			
Number of subjects analysed	56 ^[2]			
Units: units on a scale				
arithmetic mean (standard deviation)	28.3 (± 4.86)			

Notes:

[2] - Participants had to have completed the evaluation form.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Entire Study

Adverse event reporting additional description:

H6Q-MC-S039

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.0
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Reporting groups

Reporting group title	ENZASTAURIN QD Induction
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Reporting group description: -

Reporting group title	ENZASTAURIN BID Induction
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Reporting group description: -

Reporting group title	ENZASTAURIN QD Radiation
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Reporting group description: -

Reporting group title	ENZASTAURIN BID Radiation
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Reporting group description: -

Reporting group title	ENZASTAURIN QD Maintenance
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Reporting group description: -

Reporting group title	ENZASTAURIN BID Maintenance
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Reporting group description: -

Reporting group title	ENZASTAURIN QD Overall
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Reporting group description: -

Reporting group title	ENZASTAURIN BID Overall
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Reporting group description: -

Serious adverse events	ENZASTAURIN QD Induction	ENZASTAURIN BID Induction	ENZASTAURIN QD Radiation
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	5 / 57 (8.77%)	0 / 3 (0.00%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
intracranial tumour haemorrhage			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Vascular disorders			

deep vein thrombosis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
haemorrhage			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
thrombosis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
fatigue			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
general physical health deterioration			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
impaired healing			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
soft tissue inflammation			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
pneumonia aspiration			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pulmonary embolism			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
hepatic enzyme increased			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
ventricular fibrillation			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
brain oedema			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cerebrospinal fluid leakage			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
dizziness			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
epilepsy			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
generalised tonic-clonic seizure			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hemiparesis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
intracranial pressure increased			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
partial seizures			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

seizure			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
leukopenia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
thrombocytopenia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
vertigo			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
diarrhoea			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
nausea			

alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pancreatitis necrotising			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
vomiting			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
renal failure			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
neck pain			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pain in extremity			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
bronchopulmonary aspergillosis			

alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
cerebral aspergillosis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
cystitis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
empyema				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
erysipelas				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
pneumocystis jirovecii infection				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
pneumonia				
alternative dictionary used: MedDRA 19.0				

subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
sepsis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
sinusitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
wound infection			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
hyperkalaemia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	ENZASTAURIN BID Radiation	ENZASTAURIN QD Maintenance	ENZASTAURIN BID Maintenance
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 53 (30.19%)	0 / 3 (0.00%)	8 / 49 (16.33%)
number of deaths (all causes)	5	0	0
number of deaths resulting from adverse events	2	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
intracranial tumour haemorrhage			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 53 (0.00%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
deep vein thrombosis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 53 (5.66%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
haemorrhage			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 53 (0.00%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
thrombosis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 53 (1.89%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
fatigue			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 53 (3.77%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
general physical health deterioration			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 53 (1.89%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
impaired healing			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 53 (1.89%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
soft tissue inflammation			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 53 (0.00%)	0 / 3 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
pneumonia aspiration			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 53 (1.89%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pulmonary embolism			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 53 (1.89%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
hepatic enzyme increased			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 53 (1.89%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
ventricular fibrillation			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 53 (1.89%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Nervous system disorders			
brain oedema			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 53 (1.89%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cerebrospinal fluid leakage alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 53 (0.00%)	0 / 3 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
dizziness alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 53 (1.89%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
epilepsy alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 53 (1.89%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
generalised tonic-clonic seizure alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 53 (1.89%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hemiparesis alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 53 (1.89%)	0 / 3 (0.00%)	2 / 49 (4.08%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
intracranial pressure increased alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 53 (1.89%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

partial seizures			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 53 (1.89%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
seizure			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 53 (3.77%)	0 / 3 (0.00%)	4 / 49 (8.16%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 53 (1.89%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
leukopenia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 53 (1.89%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
thrombocytopenia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 53 (1.89%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
vertigo			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 53 (0.00%)	0 / 3 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
diarrhoea			

alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 53 (0.00%)	0 / 3 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
nausea			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 53 (1.89%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pancreatitis necrotising			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 53 (0.00%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
vomiting			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 53 (0.00%)	0 / 3 (0.00%)	2 / 49 (4.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
renal failure			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 53 (1.89%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
neck pain			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 53 (1.89%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pain in extremity			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 53 (1.89%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
bronchopulmonary aspergillosis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 53 (1.89%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cerebral aspergillosis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 53 (1.89%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
cystitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 53 (1.89%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
empyema			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 53 (1.89%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
erysipelas			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 53 (1.89%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumocystis jirovecii infection			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 53 (1.89%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 53 (5.66%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
sepsis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 53 (3.77%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
sinusitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 53 (0.00%)	0 / 3 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
wound infection			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 53 (1.89%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
hyperkalaemia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 53 (1.89%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	ENZASTAURIN QD Overall	ENZASTAURIN BID Overall	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	27 / 57 (47.37%)	
number of deaths (all causes)	0	7	

number of deaths resulting from adverse events	0	3	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
intracranial tumour haemorrhage			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Vascular disorders			
deep vein thrombosis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	3 / 57 (5.26%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
haemorrhage			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
thrombosis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
fatigue			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	2 / 57 (3.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
general physical health deterioration			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
impaired healing			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
soft tissue inflammation			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
pneumonia aspiration			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pulmonary embolism			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	2 / 57 (3.51%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
hepatic enzyme increased			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
ventricular fibrillation			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
brain oedema			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
cerebrospinal fluid leakage			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
dizziness			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
epilepsy			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
generalised tonic-clonic seizure			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hemiparesis			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 3 (0.00%)	4 / 57 (7.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
intracranial pressure increased			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
partial seizures			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
seizure			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	6 / 57 (10.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
leukopenia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
thrombocytopenia			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 3 (0.00%)	2 / 57 (3.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
vertigo			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
diarrhoea			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
nausea			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	2 / 57 (3.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
pancreatitis necrotising			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
vomiting			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	3 / 57 (5.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
renal failure			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
neck pain			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pain in extremity			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
bronchopulmonary aspergillosis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cerebral aspergillosis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
cystitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
empyema			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
erysipelas			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumocystis jirovecii infection			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	4 / 57 (7.02%)	
occurrences causally related to treatment / all	0 / 0	2 / 4	
deaths causally related to treatment / all	0 / 0	1 / 1	
sepsis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	3 / 57 (5.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
sinusitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
wound infection			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Metabolism and nutrition disorders			
hyperkalaemia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	1 / 57 (1.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	ENZASTAURIN QD Induction	ENZASTAURIN BID Induction	ENZASTAURIN QD Radiation
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	22 / 57 (38.60%)	3 / 3 (100.00%)
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 3 (33.33%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
fatigue			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	4 / 57 (7.02%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
oedema peripheral			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
pyrexia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

epistaxis alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 57 (0.00%) 0	1 / 3 (33.33%) 1
Psychiatric disorders agitation alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) confusional state alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) depression alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) irritability alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0	0 / 57 (0.00%) 0 0 / 57 (0.00%) 0 0 / 57 (0.00%) 0 0 / 57 (0.00%) 0	0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 1 / 3 (33.33%) 1
Investigations alanine aminotransferase increased alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) blood creatinine increased alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) electrocardiogram qt prolonged alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) haemoglobin decreased	0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0	0 / 57 (0.00%) 0 0 / 57 (0.00%) 0 0 / 57 (0.00%) 0	0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0

alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 57 (0.00%) 0	0 / 3 (0.00%) 0
weight increased alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 57 (0.00%) 0	0 / 3 (0.00%) 0
Nervous system disorders			
aphasia alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 57 (0.00%) 0	1 / 3 (33.33%) 1
dizziness alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	2 / 57 (3.51%) 2	1 / 3 (33.33%) 1
head discomfort alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 57 (0.00%) 0	1 / 3 (33.33%) 1
headache alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 57 (0.00%) 0	2 / 3 (66.67%) 2
peripheral motor neuropathy alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 57 (0.00%) 0	0 / 3 (0.00%) 0
seizure alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 57 (0.00%) 0	0 / 3 (0.00%) 0
somnolence alternative dictionary used: MedDRA 19.0			

subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 57 (0.00%) 0	0 / 3 (0.00%) 0
Blood and lymphatic system disorders leukopenia alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 57 (0.00%) 0	0 / 3 (0.00%) 0
lymphopenia alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 57 (0.00%) 0	0 / 3 (0.00%) 0
Gastrointestinal disorders abdominal discomfort alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 57 (0.00%) 0	0 / 3 (0.00%) 0
constipation alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 57 (0.00%) 0	0 / 3 (0.00%) 0
diarrhoea alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 57 (0.00%) 0	0 / 3 (0.00%) 0
nausea alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 57 (0.00%) 0	1 / 3 (33.33%) 1
vomiting alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 57 (0.00%) 0	0 / 3 (0.00%) 0
Skin and subcutaneous tissue disorders alopecia alternative dictionary used: MedDRA 19.0			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>dermatitis</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>pruritus</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>rash</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>rash erythematous</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 3 (0.00%)</p> <p>0</p> <p>0 / 3 (0.00%)</p> <p>0</p> <p>0 / 3 (0.00%)</p> <p>0</p> <p>0 / 3 (0.00%)</p> <p>0</p> <p>0 / 3 (0.00%)</p> <p>0</p> <p>0 / 3 (0.00%)</p> <p>0</p>	<p>0 / 57 (0.00%)</p> <p>0</p> <p>0 / 57 (0.00%)</p> <p>0</p> <p>0 / 57 (0.00%)</p> <p>0</p> <p>0 / 57 (0.00%)</p> <p>0</p> <p>0 / 57 (0.00%)</p> <p>0</p> <p>0 / 57 (0.00%)</p> <p>0</p>	<p>3 / 3 (100.00%)</p> <p>3</p> <p>1 / 3 (33.33%)</p> <p>1</p> <p>1 / 3 (33.33%)</p> <p>2</p> <p>0 / 3 (0.00%)</p> <p>0</p> <p>1 / 3 (33.33%)</p> <p>1</p>
<p>Renal and urinary disorders</p> <p>chromaturia</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>3 / 3 (100.00%)</p> <p>3</p>	<p>9 / 57 (15.79%)</p> <p>9</p>	<p>0 / 3 (0.00%)</p> <p>0</p>
<p>Musculoskeletal and connective tissue disorders</p> <p>back pain</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 3 (0.00%)</p> <p>0</p>	<p>0 / 57 (0.00%)</p> <p>0</p>	<p>0 / 3 (0.00%)</p> <p>0</p>
<p>Infections and infestations</p> <p>cystitis</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>gingivitis</p> <p>alternative dictionary used: MedDRA 19.0</p>	<p>0 / 3 (0.00%)</p> <p>0</p>	<p>0 / 57 (0.00%)</p> <p>0</p>	<p>0 / 3 (0.00%)</p> <p>0</p>

subjects affected / exposed	1 / 3 (33.33%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
nasopharyngitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 3 (33.33%)	0 / 57 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
sinusitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
tinea pedis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 3 (0.00%)	0 / 57 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	ENZASTAURIN BID Radiation	ENZASTAURIN QD Maintenance	ENZASTAURIN BID Maintenance
Total subjects affected by non-serious adverse events			
subjects affected / exposed	43 / 53 (81.13%)	3 / 3 (100.00%)	28 / 49 (57.14%)
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 53 (0.00%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
fatigue			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	5 / 53 (9.43%)	0 / 3 (0.00%)	3 / 49 (6.12%)
occurrences (all)	5	0	3
oedema peripheral			
alternative dictionary used: MedDRA 19.0			

<p>subjects affected / exposed</p> <p>0 / 53 (0.00%)</p> <p>0</p>	<p>0 / 3 (0.00%)</p> <p>0</p>	<p>0 / 49 (0.00%)</p> <p>0</p>
<p>pyrexia</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>0 / 53 (0.00%)</p> <p>0</p>	<p>1 / 3 (33.33%)</p> <p>1</p>	<p>2 / 49 (4.08%)</p> <p>2</p>
<p>Respiratory, thoracic and mediastinal disorders</p> <p>cough</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>0 / 53 (0.00%)</p> <p>0</p>	<p>0 / 3 (0.00%)</p> <p>0</p>	<p>0 / 49 (0.00%)</p> <p>0</p>
<p>epistaxis</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>0 / 53 (0.00%)</p> <p>0</p>	<p>0 / 3 (0.00%)</p> <p>0</p>	<p>0 / 49 (0.00%)</p> <p>0</p>
<p>Psychiatric disorders</p> <p>agitation</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>0 / 53 (0.00%)</p> <p>0</p>	<p>0 / 3 (0.00%)</p> <p>0</p>	<p>0 / 49 (0.00%)</p> <p>0</p>
<p>confusional state</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>0 / 53 (0.00%)</p> <p>0</p>	<p>0 / 3 (0.00%)</p> <p>0</p>	<p>0 / 49 (0.00%)</p> <p>0</p>
<p>depression</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>0 / 53 (0.00%)</p> <p>0</p>	<p>0 / 3 (0.00%)</p> <p>0</p>	<p>3 / 49 (6.12%)</p> <p>3</p>
<p>irritability</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>0 / 53 (0.00%)</p> <p>0</p>	<p>0 / 3 (0.00%)</p> <p>0</p>	<p>0 / 49 (0.00%)</p> <p>0</p>
Investigations		

alanine aminotransferase increased alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	4 / 53 (7.55%) 4	0 / 3 (0.00%) 0	0 / 49 (0.00%) 0
blood creatinine increased alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 53 (0.00%) 0	0 / 3 (0.00%) 0	0 / 49 (0.00%) 0
electrocardiogram qt prolonged alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 53 (0.00%) 0	0 / 3 (0.00%) 0	0 / 49 (0.00%) 0
haemoglobin decreased alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 53 (0.00%) 0	0 / 3 (0.00%) 0	0 / 49 (0.00%) 0
weight increased alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 53 (0.00%) 0	0 / 3 (0.00%) 0	0 / 49 (0.00%) 0
Nervous system disorders aphasia alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	1 / 53 (1.89%) 1	0 / 3 (0.00%) 0	0 / 49 (0.00%) 0
dizziness alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	3 / 53 (5.66%) 3	0 / 3 (0.00%) 0	0 / 49 (0.00%) 0
head discomfort alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 53 (0.00%) 0	0 / 3 (0.00%) 0	0 / 49 (0.00%) 0
headache alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	10 / 53 (18.87%)	0 / 3 (0.00%)	3 / 49 (6.12%)
occurrences (all)	12	0	3
peripheral motor neuropathy alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 53 (0.00%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
seizure alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 53 (0.00%)	0 / 3 (0.00%)	6 / 49 (12.24%)
occurrences (all)	0	0	6
somnolence alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 53 (0.00%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
leukopenia alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 53 (0.00%)	1 / 3 (33.33%)	0 / 49 (0.00%)
occurrences (all)	0	1	0
lymphopenia alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	4 / 53 (7.55%)	1 / 3 (33.33%)	1 / 49 (2.04%)
occurrences (all)	4	1	1
Gastrointestinal disorders			
abdominal discomfort alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 53 (5.66%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences (all)	3	0	0
constipation alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 53 (0.00%)	0 / 3 (0.00%)	0 / 49 (0.00%)
occurrences (all)	0	0	0
diarrhoea alternative dictionary used: MedDRA 19.0			

<p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>3 / 53 (5.66%)</p> <p>3</p>	<p>0 / 3 (0.00%)</p> <p>0</p>	<p>4 / 49 (8.16%)</p> <p>4</p>
<p>nausea</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>5 / 53 (9.43%)</p> <p>5</p>	<p>0 / 3 (0.00%)</p> <p>0</p>	<p>4 / 49 (8.16%)</p> <p>4</p>
<p>vomiting</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 53 (0.00%)</p> <p>0</p>	<p>0 / 3 (0.00%)</p> <p>0</p>	<p>7 / 49 (14.29%)</p> <p>7</p>
<p>Skin and subcutaneous tissue disorders</p> <p>alopecia</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>12 / 53 (22.64%)</p> <p>12</p>	<p>0 / 3 (0.00%)</p> <p>0</p>	<p>0 / 49 (0.00%)</p> <p>0</p>
<p>dermatitis</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>3 / 53 (5.66%)</p> <p>3</p>	<p>0 / 3 (0.00%)</p> <p>0</p>	<p>0 / 49 (0.00%)</p> <p>0</p>
<p>pruritus</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 53 (0.00%)</p> <p>0</p>	<p>0 / 3 (0.00%)</p> <p>0</p>	<p>0 / 49 (0.00%)</p> <p>0</p>
<p>rash</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 53 (0.00%)</p> <p>0</p>	<p>1 / 3 (33.33%)</p> <p>1</p>	<p>1 / 49 (2.04%)</p> <p>1</p>
<p>rash erythematous</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 53 (1.89%)</p> <p>1</p>	<p>0 / 3 (0.00%)</p> <p>0</p>	<p>0 / 49 (0.00%)</p> <p>0</p>
<p>Renal and urinary disorders</p> <p>chromaturia</p> <p>alternative dictionary used: MedDRA 19.0</p>			

subjects affected / exposed occurrences (all)	0 / 53 (0.00%) 0	0 / 3 (0.00%) 0	0 / 49 (0.00%) 0
Musculoskeletal and connective tissue disorders back pain alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 53 (0.00%) 0	1 / 3 (33.33%) 1	2 / 49 (4.08%) 3
Infections and infestations cystitis alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) gingivitis alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) nasopharyngitis alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) sinusitis alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) tinea pedis alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 53 (0.00%) 0 0 / 53 (0.00%) 0 2 / 53 (3.77%) 2 0 / 53 (0.00%) 0 0 / 53 (0.00%) 0	1 / 3 (33.33%) 1 0 / 3 (0.00%) 0 1 / 3 (33.33%) 1 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0	1 / 49 (2.04%) 1 0 / 49 (0.00%) 0 4 / 49 (8.16%) 10 0 / 49 (0.00%) 0 0 / 49 (0.00%) 0
Metabolism and nutrition disorders decreased appetite alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 53 (0.00%) 0	0 / 3 (0.00%) 0	0 / 49 (0.00%) 0

Non-serious adverse events	ENZASTAURIN QD Overall	ENZASTAURIN BID Overall	
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Total subjects affected by non-serious adverse events subjects affected / exposed	3 / 3 (100.00%)	50 / 57 (87.72%)	
Vascular disorders hypertension alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	1 / 57 (1.75%) 1	
General disorders and administration site conditions fatigue alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) oedema peripheral alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) pyrexia alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 1 / 3 (33.33%) 1	13 / 57 (22.81%) 13 3 / 57 (5.26%) 5 3 / 57 (5.26%) 3	
Respiratory, thoracic and mediastinal disorders cough alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) epistaxis alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0 1 / 3 (33.33%) 1	4 / 57 (7.02%) 4 0 / 57 (0.00%) 0	
Psychiatric disorders agitation alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all) confusional state	1 / 3 (33.33%) 1	0 / 57 (0.00%) 0	

<p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 3 (0.00%)</p> <p>0</p>	<p>3 / 57 (5.26%)</p> <p>3</p>	
<p>depression</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 3 (0.00%)</p> <p>0</p>	<p>3 / 57 (5.26%)</p> <p>3</p>	
<p>irritability</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 3 (33.33%)</p> <p>1</p>	<p>0 / 57 (0.00%)</p> <p>0</p>	
Investigations			
<p>alanine aminotransferase increased</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 3 (0.00%)</p> <p>0</p>	<p>5 / 57 (8.77%)</p> <p>5</p>	
<p>blood creatinine increased</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 3 (0.00%)</p> <p>0</p>	<p>3 / 57 (5.26%)</p> <p>3</p>	
<p>electrocardiogram qt prolonged</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 3 (0.00%)</p> <p>0</p>	<p>4 / 57 (7.02%)</p> <p>6</p>	
<p>haemoglobin decreased</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 3 (0.00%)</p> <p>0</p>	<p>4 / 57 (7.02%)</p> <p>4</p>	
<p>weight increased</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 3 (33.33%)</p> <p>1</p>	<p>2 / 57 (3.51%)</p> <p>2</p>	
Nervous system disorders			

<p>aphasia</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 3 (33.33%)</p> <p>1</p>	<p>2 / 57 (3.51%)</p> <p>2</p>	
<p>dizziness</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 3 (66.67%)</p> <p>2</p>	<p>6 / 57 (10.53%)</p> <p>7</p>	
<p>head discomfort</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 3 (33.33%)</p> <p>1</p>	<p>0 / 57 (0.00%)</p> <p>0</p>	
<p>headache</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 3 (66.67%)</p> <p>2</p>	<p>14 / 57 (24.56%)</p> <p>20</p>	
<p>peripheral motor neuropathy</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 3 (0.00%)</p> <p>0</p>	<p>3 / 57 (5.26%)</p> <p>3</p>	
<p>seizure</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 3 (0.00%)</p> <p>0</p>	<p>9 / 57 (15.79%)</p> <p>9</p>	
<p>somnolence</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 3 (33.33%)</p> <p>1</p>	<p>2 / 57 (3.51%)</p> <p>2</p>	
<p>Blood and lymphatic system disorders</p> <p>leukopenia</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>lymphopenia</p> <p>alternative dictionary used: MedDRA 19.0</p>	<p>1 / 3 (33.33%)</p> <p>1</p>	<p>1 / 57 (1.75%)</p> <p>1</p>	

subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	7 / 57 (12.28%) 9	
Gastrointestinal disorders			
abdominal discomfort alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	4 / 57 (7.02%) 4	
constipation alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	3 / 57 (5.26%) 3	
diarrhoea alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	8 / 57 (14.04%) 8	
nausea alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	9 / 57 (15.79%) 11	
vomiting alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	9 / 57 (15.79%) 9	
Skin and subcutaneous tissue disorders			
alopecia alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	3 / 3 (100.00%) 3	13 / 57 (22.81%) 13	
dermatitis alternative dictionary used: MedDRA 19.0 subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	3 / 57 (5.26%) 3	
pruritus alternative dictionary used: MedDRA 19.0			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>rash</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>rash erythematous</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 3 (33.33%)</p> <p>2</p> <p>1 / 3 (33.33%)</p> <p>1</p> <p>1 / 3 (33.33%)</p> <p>1</p>	<p>0 / 57 (0.00%)</p> <p>0</p> <p>2 / 57 (3.51%)</p> <p>2</p> <p>1 / 57 (1.75%)</p> <p>1</p>	
<p>Renal and urinary disorders</p> <p>chromaturia</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>3 / 3 (100.00%)</p> <p>3</p>	<p>11 / 57 (19.30%)</p> <p>11</p>	
<p>Musculoskeletal and connective tissue disorders</p> <p>back pain</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 3 (33.33%)</p> <p>1</p>	<p>4 / 57 (7.02%)</p> <p>5</p>	
<p>Infections and infestations</p> <p>cystitis</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>gingivitis</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>nasopharyngitis</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>sinusitis</p> <p>alternative dictionary used: MedDRA 19.0</p>	<p>1 / 3 (33.33%)</p> <p>1</p> <p>1 / 3 (33.33%)</p> <p>1</p> <p>3 / 3 (100.00%)</p> <p>3</p>	<p>1 / 57 (1.75%)</p> <p>1</p> <p>1 / 57 (1.75%)</p> <p>1</p> <p>6 / 57 (10.53%)</p> <p>13</p>	

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>tinea pedis</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 3 (0.00%)</p> <p>0</p> <p>1 / 3 (33.33%)</p> <p>1</p>	<p>3 / 57 (5.26%)</p> <p>4</p> <p>0 / 57 (0.00%)</p> <p>0</p>	
<p>Metabolism and nutrition disorders</p> <p>decreased appetite</p> <p>alternative dictionary used: MedDRA 19.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 3 (0.00%)</p> <p>0</p>	<p>3 / 57 (5.26%)</p> <p>3</p>	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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.

3 participants receiving 500 mg enzastaurin QD were not included in analysis for outcome measures per protocol but had AE/SAEs reported.
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Notes: