Clinical trial results:
A Phase 2 Study to Evaluate the Efficacy and Safety of Palifermin (Recombinant Human Keratinocyte Growth Factor) in the Reduction of Dysphagia in Patients Receiving Concurrent Chemoradiotherapy followed by Consolidation Chemotherapy for Locally Advanced Non-Small Cell Lung Cancer (NSCLC)

Summary

EudraCT number	2004-003116-33
Trial protocol	DE
Global end of trial date	29 January 2014

Results information

Result version number	v1 (current)
This version publication date	27 April 2016
First version publication date	27 April 2016

Trial information

Trial identification

Sponsor protocol code	20030185

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00094861
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Swedish Orphan Biovitrum AB
Sponsor organisation address	Tomtebodavägen 23A, Stockholm, Sweden, 112 76
Public contact	Medical Information, Swedish Orphan Biovitrum AB, +46 86972000, info@sobi.com
Scientific contact	Medical Information, Swedish Orphan Biovitrum AB, +46 86972000, info@sobi.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 January 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 January 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of palifermin administered at single weekly doses of 180 µg/kg in reducing the incidence of dysphagia (grade ≥ 2) induced by concurrent chemoradiotherapy (CT/RT) followed by consolidation chemotherapy in patients with unresectable stage III non-small cell lung cancer (NSCLC).

Protection of trial subjects:

This study was conducted in accordance with US Food and Drug Administration (FDA) and International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) regulations/guidelines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 January 2005
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Germany: 24
Country: Number of subjects enrolled	United States: 46
Country: Number of subjects enrolled	Spain: 12
Country: Number of subjects enrolled	Poland: 11
Worldwide total number of subjects	95
EEA total number of subjects	49

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)	53

From 65 to 84 years	42
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted in 42 sites globally with evaluable patients in 24 sites. 17 in the Unites States, 2 in Germany, 2 in Poland, 2 in Spain and 1 in France.

Pre-assignment

Screening details:

Study subjects were screened within a period up to 6 weeks before study randomization. Randomization to placebo or active treatment occured within 48 hours before the planned dose of investigational product.

Period 1

Period 1 title	Acute phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

A registration call was made to the IVRS 48 hours before the first dose of investigational product. At the completion of this call, a randomization number and a drug box number was assigned by the IVRD. From this point on, the subject was enrolled to the study and assignes to 1 of the 2 treatment groups.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo was given as subcutaneous bolus injections.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo was given as subcutaneous bolus injections. Placebo was presented as lyophilized white powder in 6.25 mg single-dose vials to be reconstituted with 1.2 ml of sterile water for injection. The reconstituted solution contained 10 mM histidin (pH6.5), 4 % mannitol, 2 % sucrose, 0.010 % polysorbate 20 and no preservatives.
Injections were to be given as single weekly doses before the initiation of concurrent chemoradiotherapy, and during weeks 1 through 6 after the last dose of radiation therapy of the week (a total of 7 doses).

Arm title	Palifermin

Arm description:

Kepivance was given as subcutaneous bolus injections.

Arm type	Experimental
Investigational medicinal product name	Palifermin
Investigational medicinal product code	
Other name	Kepivance
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Palifermin was given as subcutaneous bolus injections. Palifermin was presented as lyophilized white

powder in 6.25 mg single-dose vials to be reconstituted with 1.2 ml of sterile water for injection. The reconstituted solution contained 5 mg/mL (± 0.5 mg/mL) palifermin, 10 mM histidin (pH6.5), 4 % mannitol, 2 % sucrose, 0.010 % polysorbate 20 and no preservatives.
Injections were to be given as single weekly doses before the initiation of concurrent chemoradiotherapy, and during weeks 1 through 6 after the last dose of radiation therapy of the week (a total of 7 doses).

Number of subjects in period 1	Placebo	Palifermin
Started	46	49
Completed	28	40
Not completed	18	9
Adverse event, serious fatal	4	2
Consent withdrawn by subject	5	3
Adverse event, non-fatal	5	2
Other	3	-
Lost to follow-up	-	1
Administrative reason	1	1

Period 2	
Period 2 title	Long-term follow up
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms	
Are arms mutually exclusive?	Yes
Arm title	Placebo
Arm description:	
Subjects who received placebo during the active phase of the study.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Palifermin
Arm description:	
Subjects who received palifermin during the active phase of the study.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 2	Placebo	Palifermin
Started	28	40
Completed	12	8
Not completed	34	40
Adverse event, serious fatal	1	1
Death	32	37
Lost to follow-up	1	2
Joined	18	8
Subjects not completed Period1 counted in Period2	18	8

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo was given as subcutaneous bolus injections.	
Reporting group title	Palifermin
Reporting group description:	
Kepivance was given as subcutaneous bolus injections.	

Reporting group values	Placebo	Palifermin	Total
Number of subjects	46	49	95
Age categorical Units: Subjects			
Adults (18-64 years)	25	28	53
From 65-84 years	21	21	42
Gender categorical Units: Subjects			
Female	14	15	29
Male	32	34	66

Subject analysis sets	
Subject analysis set title	Placebo - safety subset
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects receiving at least one dose of IMP (placebo) in the in the active phase	
Subject analysis set title	Palifermin - safety analysis set
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects receiving at least one dose of IMP (palifermin) in the in the active phase	
Subject analysis set title	placebo - full analysis set
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects who received all 7 investigational product doses (placebo).	
Subject analysis set title	Palifermin - full analysis set
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects who received all 7 investigational product doses (palifermin).	
Subject analysis set title	Placebo - LTFU analysis set
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects who received placebo during the active phase of the study and were followed in the long term follow up phase.	
Subject analysis set title	Palifermin - LTFU analysis set
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects who received palifermin during the active phase of the study and were followed in the long term follow up phase.	

Reporting group values	Placebo - safety subset	Palifermin - safety analysis set	placebo - full analysis set
Number of subjects	46	48	46
Age categorical Units: Subjects			
Adults (18-64 years)	25	28	25
From 65-84 years	21	20	21
Gender categorical Units: Subjects			
Female	14	15	14
Male	32	33	32

Reporting group values	Palifermin - full analysis set	Placebo - LTFU analysis set	Palifermin - LTFU analysis set
Number of subjects	49	46	48
Age categorical Units: Subjects			
Adults (18-64 years)	28	25	28
From 65-84 years	21	21	20
Gender categorical Units: Subjects			
Female	15	14	15
Male	34	32	33

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Placebo was given as subcutaneous bolus injections.	
Reporting group title	Palifermin
Reporting group description:	
Kepivance was given as subcutaneous bolus injections.	
Reporting group title	Placebo
Reporting group description:	
Subjects who received placebo during the active phase of the study.	
Reporting group title	Palifermin
Reporting group description:	
Subjects who received palifermin during the active phase of the study.	
Subject analysis set title	Placebo - safety subset
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects receiving at least one dose of IMP (placebo) in the in the active phase	
Subject analysis set title	Palifermin - safety analysis set
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects receiving at least one dose of IMP (palifermin) in the in the active phase	
Subject analysis set title	placebo - full analysis set
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects who received all 7 investigational product doses (placebo).	
Subject analysis set title	Palifermin - full analysis set
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects who received all 7 investigational product doses (palifermin).	
Subject analysis set title	Placebo - LTFU analysis set
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects who received placebo during the active phase of the study and were followed in the long term follow up phase.	
Subject analysis set title	Palifermin - LTFU analysis set
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects who received palifermin during the active phase of the study and were followed in the long term follow up phase.	

Primary: Incidence of dysphagia (grade ≥ 2)

End point title	Incidence of dysphagia (grade ≥ 2)
End point description:	
Subjects underwent acute dysphagia assessments which were graded using the Common Terminology Criteria for Adverse Events, Version 3.0 (CTCAE v3.0) dysphagia scale twice weekly during weeks 1 through 7, and twice weekly thereafter (weeks 8 through 12) and once weekly after week 12 until dysphagia resolved to grade ≤ 1 but not beyond week 16.	
End point type	Primary
End point timeframe:	
Baseline until week 16	

End point values	placebo - full analysis set	Palifermin - full analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	46	49		
Units: Number of patients				
Yes	32	30		
No	13	18		
No assessment	1	1		

Statistical analyses

Statistical analysis title	Incidence of Grade 2 or Greater Dysphagia
Comparison groups	placebo - full analysis set v Palifermin - full analysis set
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.355
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	-0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.28
upper limit	0.1

Secondary: Duration (days) of grade ≥ 2 dysphagia

End point title	Duration (days) of grade ≥ 2 dysphagia

End point description:

End point type	Secondary

End point timeframe:

Duration of dysphagia was calculated from the onset of grade ≥ 2 dysphagia to resolution (toxicity grade reduced to 0 or 1) of this event.

End point values	placebo - full analysis set	Palifermin - full analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	46	49		
Units: days				
arithmetic mean (standard deviation)	32.4 (± 30.1)	25.3 (± 28)		

Statistical analyses

Statistical analysis title	Duration of Grade 2 or greater dysphagia
Comparison groups	placebo - full analysis set v Palifermin - full analysis set
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3189
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	-7.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.2
upper limit	4.5

Secondary: Maximum severity of dysphagia

End point title	Maximum severity of dysphagia

End point description:

Subjects underwent acute dysphagia assessments which were graded using the Common Terminology Criteria for Adverse Events, Version 3.0 (CTCAE v3.0) dysphagia scale twice weekly during weeks 1 through 7, and twice weekly thereafter (weeks 8 through 12) and once weekly after week 12 until dysphagia resolved to grade ≤ 1 but not beyond week 16.

End point type	Secondary

End point timeframe:

From baseline until week 16.

End point values	placebo - full analysis set	Palifermin - full analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	45	48		
Units: grade				
arithmetic mean (standard deviation)	1.9 (± 1)	1.8 (± 0.9)		

Statistical analyses

Statistical analysis title	Maximum severity of dysphagia
Comparison groups	placebo - full analysis set v Palifermin - full analysis set
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5086
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.3

Secondary: Maximal ECOG Status Increase From Baseline Through Week 12

End point title	Maximal ECOG Status Increase From Baseline Through Week 12
End point description:	
End point type	Secondary
End point timeframe:	
Twice weekly from baseline until week 12	

End point values	placebo - full analysis set	Palifermin - full analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44	46		
Units: ECOG status				
arithmetic mean (standard deviation)	1.5 (± 1.3)	0.9 (± 1.1)		

Statistical analyses

Statistical analysis title	Maximal ECOG status increase from baseline
Comparison groups	placebo - full analysis set v Palifermin - full analysis set
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0621
Method	Cochran-Mantel-Haenszel

Secondary: Maximal Weight Loss From Baseline Through Week 12

End point title	Maximal Weight Loss From Baseline Through Week 12

End point description:

End point type	Secondary

End point timeframe:

From baseline to week 12

End point values	placebo - full analysis set	Palifermin - full analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	42	45		
Units: kg				
arithmetic mean (standard deviation)	4.63 (± 4.13)	5.44 (± 4.33)		

Statistical analyses

Statistical analysis title	Maximal body weight loss
Comparison groups	placebo - full analysis set v Palifermin - full analysis set
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0763
Method	Cochran-Mantel-Haenszel

Secondary: Incidence of unplanned breaks in RT

End point title	Incidence of unplanned breaks in RT

End point description:

End point type	Secondary

End point timeframe:

From baseline to week 6 or 7

End point values	placebo - full analysis set	Palifermin - full analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	46	49		
Units: number				
Yes	15	9		
No	29	38		
Did not receive RT	2	2		

Statistical analyses

Statistical analysis title	Incidence of unplanned breaks in RT
Comparison groups	placebo - full analysis set v Palifermin - full analysis set
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1115
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	-0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.33
upper limit	0.03

Secondary: Incidence of hospitalization

End point title	Incidence of hospitalization

End point description:

End point type	Secondary

End point timeframe:

From baseline to week 16

End point values	placebo - full analysis set	Palifermin - full analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	46	49		
Units: incidence				
yes	31	34		
no	15	15		

Statistical analyses

Statistical analysis title	Incidence of hospitalization
Comparison groups	placebo - full analysis set v Palifermin - full analysis set
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8639
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0.2

Secondary: incidence of serum anti-palifermin antibody formation

End point title	incidence of serum anti-palifermin antibody formation
End point description:	
End point type	Secondary
End point timeframe:	
From baselinte to week 12	

End point values	Placebo - safety subset	Palifermin - safety analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	43		
Units: number of patients				
yes	0	0		
no	32	43		

Statistical analyses

No statistical analyses for this end point

Secondary: Tumor progression or Recurrence of Primary Disease

End point title	Tumor progression or Recurrence of Primary Disease
End point description:	
End point type	Secondary

End point timeframe:

From baseline until death, lost to follow up or study end

End point values	Placebo - LTFU analysis set	Palifermin - LTFU analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	46	48		
Units: number				
yes	29	33		

Statistical analyses

No statistical analyses for this end point

Secondary: Other malignancy

End point title	Other malignancy

End point description:

End point type	Secondary

End point timeframe:

From end of treatment until death, lost to follow up or study end.

End point values	Placebo - LTFU analysis set	Palifermin - LTFU analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	46	48		
Units: number				
yes	0	2		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Second primary tumors

End point title	Second primary tumors

End point description:

End point type	Other pre-specified

End point timeframe:

From end of treatment until death, lost to follow up or study end.

End point values	Placebo - LTFU analysis set	Palifermin - LTFU analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	46	48		
Units: number				
yes	2	2		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Death

End point title	Death

End point description:

End point type	Other pre-specified

End point timeframe:

From baseline until death, lost to follow up or study end.

End point values	Placebo - LTFU analysis set	Palifermin - LTFU analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	46	48		
Units: number				
yes	33	38		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline up to Week 12

Adverse event reporting additional description:

A Phase 2 Study to Evaluate the Efficacy and Safety of Palifermin in the Reduction of Dysphagia in Patients Receiving Concurrent Chemoradiotherapy followed by Consolidation Chemotherapy for Locally Advanced Non-Small Cell Lung Cancer

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10.0

Reporting groups

Reporting group title	palifermin
Reporting group description: -	
Reporting group title	placebo

Reporting group description: -

Serious adverse events	palifermin	placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 48 (43.75%)	30 / 46 (65.22%)	
number of deaths (all causes)	2	5	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm progression			
subjects affected / exposed	0 / 48 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Non-small cell lung cancer			
subjects affected / exposed	1 / 48 (2.08%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 48 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Deep vein thrombosis			

subjects affected / exposed	1 / 48 (2.08%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism			
subjects affected / exposed	0 / 48 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	0 / 48 (0.00%)	2 / 46 (4.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 48 (4.17%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest discomfort			
subjects affected / exposed	0 / 48 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	0 / 48 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Disease progression			
subjects affected / exposed	1 / 48 (2.08%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Mucosal inflammation			

subjects affected / exposed	1 / 48 (2.08%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	1 / 48 (2.08%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	1 / 48 (2.08%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Performance status decreased			
subjects affected / exposed	0 / 48 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 48 (2.08%)	2 / 46 (4.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Bronchial obstruction			
subjects affected / exposed	0 / 48 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 48 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	1 / 48 (2.08%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			

subjects affected / exposed	1 / 48 (2.08%)	2 / 46 (4.35%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	0 / 48 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	1 / 48 (2.08%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 48 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 48 (2.08%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 48 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Alcohol withdrawal syndrome			
subjects affected / exposed	0 / 48 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			

subjects affected / exposed	0 / 48 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Weight decreased			
subjects affected / exposed	1 / 48 (2.08%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Radiation oesophagitis			
subjects affected / exposed	1 / 48 (2.08%)	2 / 46 (4.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheal obstruction			
subjects affected / exposed	0 / 48 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular graft occlusion			
subjects affected / exposed	0 / 48 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 48 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	0 / 48 (0.00%)	2 / 46 (4.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 48 (2.08%)	2 / 46 (4.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Arrhythmia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	0 / 48 (0.00%)	2 / 46 (4.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	0 / 48 (0.00%)	2 / 46 (4.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 48 (2.08%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoaesthesia			
subjects affected / exposed	1 / 48 (2.08%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	1 / 48 (2.08%)	2 / 46 (4.35%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	1 / 48 (2.08%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	7 / 48 (14.58%)	5 / 46 (10.87%)	
occurrences causally related to treatment / all	1 / 7	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	

Neutropenia			
subjects affected / exposed	4 / 48 (8.33%)	3 / 46 (6.52%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	1 / 48 (2.08%)	2 / 46 (4.35%)	
occurrences causally related to treatment / all	0 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 48 (2.08%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 48 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 48 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colonic pseudo-obstruction			
subjects affected / exposed	0 / 48 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 48 (2.08%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	4 / 48 (8.33%)	2 / 46 (4.35%)	
occurrences causally related to treatment / all	0 / 8	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Odynophagia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	3 / 48 (6.25%)	3 / 46 (6.52%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal hypomotility			
subjects affected / exposed	1 / 48 (2.08%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	0 / 48 (0.00%)	4 / 46 (8.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 48 (2.08%)	2 / 46 (4.35%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute prerenal failure			
subjects affected / exposed	0 / 48 (0.00%)	1 / 46 (2.17%)	
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			
Arthralgia			
subjects affected / exposed	1 / 48 (2.08%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Myalgia			
subjects affected / exposed	1 / 48 (2.08%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 48 (2.08%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 48 (2.08%)	2 / 46 (4.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Respiratory moniliasis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 48 (2.08%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 48 (2.08%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	1 / 48 (2.08%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 48 (0.00%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			

Anorexia			
subjects affected / exposed	1 / 48 (2.08%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	1 / 48 (2.08%)	4 / 46 (8.70%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 48 (2.08%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypocalcaemia			
subjects affected / exposed	1 / 48 (2.08%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypomagnesaemia			
subjects affected / exposed	1 / 48 (2.08%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 2	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	palifermin	placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 48 (100.00%)	45 / 46 (97.83%)	
Vascular disorders			
Flushing			
subjects affected / exposed	5 / 48 (10.42%)	0 / 46 (0.00%)	
occurrences (all)	7	0	
Thrombophlebitis			
subjects affected / exposed	4 / 48 (8.33%)	0 / 46 (0.00%)	
occurrences (all)	4	0	
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	9 / 48 (18.75%)	5 / 46 (10.87%)	
occurrences (all)	12	9	
Chest pain			
subjects affected / exposed	7 / 48 (14.58%)	4 / 46 (8.70%)	
occurrences (all)	7	5	
Pyrexia			
subjects affected / exposed	8 / 48 (16.67%)	9 / 46 (19.57%)	
occurrences (all)	9	10	
Pain			
subjects affected / exposed	2 / 48 (4.17%)	3 / 46 (6.52%)	
occurrences (all)	2	4	
Oedema peripheral			
subjects affected / exposed	2 / 48 (4.17%)	4 / 46 (8.70%)	
occurrences (all)	4	4	
Non-cardiac chest pain			
subjects affected / exposed	3 / 48 (6.25%)	0 / 46 (0.00%)	
occurrences (all)	3	0	
Fatigue			
subjects affected / exposed	19 / 48 (39.58%)	14 / 46 (30.43%)	
occurrences (all)	34	21	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	19 / 48 (39.58%)	12 / 46 (26.09%)	
occurrences (all)	26	14	
Dysphonia			
subjects affected / exposed	9 / 48 (18.75%)	3 / 46 (6.52%)	
occurrences (all)	9	3	
Pharyngolaryngeal pain			
subjects affected / exposed	5 / 48 (10.42%)	11 / 46 (23.91%)	
occurrences (all)	7	12	
Hiccups			
subjects affected / exposed	3 / 48 (6.25%)	2 / 46 (4.35%)	
occurrences (all)	3	2	
Haemoptysis			

subjects affected / exposed	3 / 48 (6.25%)	0 / 46 (0.00%)	
occurrences (all)	3	0	
Epistaxis			
subjects affected / exposed	6 / 48 (12.50%)	4 / 46 (8.70%)	
occurrences (all)	6	4	
Dyspnoea			
subjects affected / exposed	12 / 48 (25.00%)	8 / 46 (17.39%)	
occurrences (all)	13	8	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	3 / 48 (6.25%)	6 / 46 (13.04%)	
occurrences (all)	3	6	
Depression			
subjects affected / exposed	2 / 48 (4.17%)	4 / 46 (8.70%)	
occurrences (all)	2	4	
Insomnia			
subjects affected / exposed	8 / 48 (16.67%)	9 / 46 (19.57%)	
occurrences (all)	8	9	
Investigations			
Weight decreased			
subjects affected / exposed	6 / 48 (12.50%)	7 / 46 (15.22%)	
occurrences (all)	8	8	
Injury, poisoning and procedural complications			
Radiation skin injury			
subjects affected / exposed	10 / 48 (20.83%)	6 / 46 (13.04%)	
occurrences (all)	17	10	
Nervous system disorders			
Dizziness			
subjects affected / exposed	6 / 48 (12.50%)	5 / 46 (10.87%)	
occurrences (all)	7	7	
Dysgeusia			
subjects affected / exposed	8 / 48 (16.67%)	3 / 46 (6.52%)	
occurrences (all)	8	3	
Headache			
subjects affected / exposed	4 / 48 (8.33%)	3 / 46 (6.52%)	
occurrences (all)	4	3	

Hypoaesthesia			
subjects affected / exposed	0 / 48 (0.00%)	3 / 46 (6.52%)	
occurrences (all)	0	4	
Neuropathy peripheral			
subjects affected / exposed	4 / 48 (8.33%)	0 / 46 (0.00%)	
occurrences (all)	5	0	
Paraesthesia			
subjects affected / exposed	3 / 48 (6.25%)	2 / 46 (4.35%)	
occurrences (all)	3	2	
Peripheral sensory neuropathy			
subjects affected / exposed	4 / 48 (8.33%)	3 / 46 (6.52%)	
occurrences (all)	7	4	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	27 / 48 (56.25%)	21 / 46 (45.65%)	
occurrences (all)	42	31	
Thrombocytopenia			
subjects affected / exposed	10 / 48 (20.83%)	5 / 46 (10.87%)	
occurrences (all)	23	11	
Neutropenia			
subjects affected / exposed	13 / 48 (27.08%)	11 / 46 (23.91%)	
occurrences (all)	26	27	
Leukopenia			
subjects affected / exposed	18 / 48 (37.50%)	8 / 46 (17.39%)	
occurrences (all)	39	22	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 48 (6.25%)	4 / 46 (8.70%)	
occurrences (all)	3	6	
Constipation			
subjects affected / exposed	14 / 48 (29.17%)	13 / 46 (28.26%)	
occurrences (all)	23	13	
Diarrhoea			
subjects affected / exposed	9 / 48 (18.75%)	9 / 46 (19.57%)	
occurrences (all)	12	10	
Dry mouth			

subjects affected / exposed	4 / 48 (8.33%)	1 / 46 (2.17%)	
occurrences (all)	4	1	
Vomiting			
subjects affected / exposed	10 / 48 (20.83%)	11 / 46 (23.91%)	
occurrences (all)	13	22	
Oesophagitis			
subjects affected / exposed	4 / 48 (8.33%)	1 / 46 (2.17%)	
occurrences (all)	9	1	
Nausea			
subjects affected / exposed	25 / 48 (52.08%)	23 / 46 (50.00%)	
occurrences (all)	34	27	
Dyspepsia			
subjects affected / exposed	8 / 48 (16.67%)	7 / 46 (15.22%)	
occurrences (all)	12	7	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	10 / 48 (20.83%)	6 / 46 (13.04%)	
occurrences (all)	13	6	
Hyperhidrosis			
subjects affected / exposed	2 / 48 (4.17%)	3 / 46 (6.52%)	
occurrences (all)	3	3	
Pruritus			
subjects affected / exposed	4 / 48 (8.33%)	1 / 46 (2.17%)	
occurrences (all)	4	1	
Rash			
subjects affected / exposed	4 / 48 (8.33%)	5 / 46 (10.87%)	
occurrences (all)	5	8	
Erythema			
subjects affected / exposed	8 / 48 (16.67%)	2 / 46 (4.35%)	
occurrences (all)	9	3	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 48 (6.25%)	3 / 46 (6.52%)	
occurrences (all)	8	3	
Myalgia			

subjects affected / exposed	6 / 48 (12.50%)	5 / 46 (10.87%)	
occurrences (all)	12	5	
Musculoskeletal pain			
subjects affected / exposed	3 / 48 (6.25%)	1 / 46 (2.17%)	
occurrences (all)	3	1	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 48 (2.08%)	3 / 46 (6.52%)	
occurrences (all)	1	5	
Back pain			
subjects affected / exposed	5 / 48 (10.42%)	5 / 46 (10.87%)	
occurrences (all)	5	5	
Neck pain			
subjects affected / exposed	1 / 48 (2.08%)	3 / 46 (6.52%)	
occurrences (all)	1	4	
Infections and infestations			
Pneumonia			
subjects affected / exposed	5 / 48 (10.42%)	1 / 46 (2.17%)	
occurrences (all)	5	1	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	8 / 48 (16.67%)	8 / 46 (17.39%)	
occurrences (all)	8	9	
Hypocalcaemia			
subjects affected / exposed	3 / 48 (6.25%)	3 / 46 (6.52%)	
occurrences (all)	3	3	
Dehydration			
subjects affected / exposed	10 / 48 (20.83%)	6 / 46 (13.04%)	
occurrences (all)	18	7	
Anorexia			
subjects affected / exposed	13 / 48 (27.08%)	8 / 46 (17.39%)	
occurrences (all)	20	10	
Hypomagnesaemia			
subjects affected / exposed	3 / 48 (6.25%)	1 / 46 (2.17%)	
occurrences (all)	3	2	
Hyponatraemia			

subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	3 / 46 (6.52%) 3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 June 2005	Patients with T3N1 and T4 disease are eligible to participate in the study. The Lung Cancer Symptom Scale (LCSS) has been removed from the PRO component of the study. The imaging requirements at screening to rule out metastatic disease in the chest and abdomen have been modified. Tumor response will no longer be evaluated using RECIST criteria. Beginning with week 8, PRO assessments can be discontinued if dysphagia resolves to CTCAE v3.0 grade ≤ 1. Consolidation chemotherapy (paclitaxel and carboplatin), which is given during weeks 7 and 10, may be administered any day of the week, at the discretion of the investigator. In order to standardize the administration of radiation therapy across multiple sites, RT guidelines are provided. Laboratory assessments (hematology and chemistry) required at baseline through week 12 have been modified to ensure consistency with other studies in the palifermin clinical development program. Pneumonitis assessments, which were previously required at month 6 only, will now be required at months 6, 9, and 12. Study conduct in the US will be expanded from 12 sites to approximately 20 sites and in the EU from 8 sites to approximately 10 sites.
03 March 2006	The exclusion criterion relating to the pleural or pericardial effusion was added in Amendment #1 with the intention of excluding stage IIIb subjects with malignant pleural effusion, who have poorer prognosis, has been clarified. The prescription dose of radiation therapy has been changed from a fixed dose of 60 Gy to a range of 60-66 Gy.
14 February 2008	Clarification of secondary objective 'To assess the effect of palifermin on treatmentrelated clinical sequelae' and the corresponding analyses. The planned analyses of treatment-related clinical sequelae have been reduced and no longer include: incidence and cumulative dose of opioid analgesics use (morphine equivalents); duration (days) of hospitalization; incidence of percutaneous endoscopic gastrostomy (PEG)/nasogastric (NG) tube, total parenteral nutrition (TPN), and IV hydration use; incidence of infections. Removal of secondary objective 'To assess the effect of palifermin on patient-reported outcomes (PRO)' and the corresponding analyses. No analyses based on a PRO efficacy evaluable subset are planned.
15 December 2008	The sponsorship was transferred from Amgen Inc to Biovitrum AB.
15 August 2013	The long term follow up period was limited to up to 5 years from the last subject randomized.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported