Clinical trial results:
An Open-Label Study to Investigate the Efficacy and Safety of Peginesatide in the Treatment of Anemia Caused by Antibody-Mediated Pure Red Cell Aplasia in Patients With Chronic Kidney Disease.

Summary

EudraCT number	2005-004944-30
Trial protocol	GB DE
Global end of trial date	31 October 2016

Results information

Result version number	v2 (current)
This version publication date	18 May 2019
First version publication date	08 November 2017
Version creation reason	• New data added to full data set Additional information.

Trial information

Trial identification

Sponsor protocol code	AFX01-06

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00314795
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Takeda Development Centre Europe Ltd
Sponsor organisation address	61 Aldwych, London, United Kingdom, WC2B 4AE
Public contact	Medical Director, Clinical Science, Takeda, +1 877-825-3327, clinicaltrialregistry@tpna.com
Scientific contact	Medical Director, Clinical Science, Takeda, +1 877-825-3327, clinicaltrialregistry@tpna.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	31 October 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 October 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate the ability of peginesatide (AF37702) to increase and maintain increased hemoglobin levels in participants with chronic kidney disease (CKD) (either not on dialysis, receiving regular hemodialysis or peritoneal dialysis, or following renal transplant) with confirmed antibody-mediated pure red cell aplasia (PRCA).

Protection of trial subjects:

All study participants were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 April 2006
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	6 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	United Kingdom: 8
Worldwide total number of subjects	22
EEA total number of subjects	22

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)	6

From 65 to 84 years	12
85 years and over	4

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at 5 investigative sites in Europe from 06-Apr-2006 to 31-Oct-2016.

Pre-assignment

Screening details:

Participants with a diagnosis of chronic renal failure (CRF) with confirmed antibody-mediated pure red cell aplasia (PRCA) were enrolled to receive peginesatide subcutaneous injection up to 0.3 mg/kg, once every 4 weeks for up to 60 months.

Period 1

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

Arms

Arm title	Peginesatide

Arm description:

Peginesatide 0.05 mg/kg injection, subcutaneously followed by peginesatide 0.1 mg/kg injection, subcutaneously once every 4 weeks for up to 60 months. Individual dose of peginesatide injection was modified based on hemoglobin levels. Dose adjustments were made in order to achieve and maintain hemoglobin in the target range of 10.0–12.0 g/dL.

Arm type	Experimental
Investigational medicinal product name	Peginesatide
Investigational medicinal product code	
Other name	AF37702
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular and intravenous use

Dosage and administration details:

Peginesatide injection

Number of subjects in period 1	Peginesatide
Started	22
Completed	2
Not completed	20
Adverse event, serious fatal	4
Renal Transplant	3
Adverse event, non-fatal	8
Participants Withdrew Consent	2
Reason not Specified	3

Baseline characteristics

Reporting groups	
Reporting group title	Peginesatide
Reporting group description:	
Peginesatide 0.05 mg/kg injection, subcutaneously followed by peginesatide 0.1 mg/kg injection, subcutaneously once every 4 weeks for up to 60 months. Individual dose of peginesatide injection was modified based on hemoglobin levels. Dose adjustments were made in order to achieve and maintain hemoglobin in the target range of 10.0–12.0 g/dL.	

Reporting group values	Peginesatide	Total	
Number of subjects	22	22	
Age categorical			
Units: Subjects			
Age Continuous			
Units: years			
arithmetic mean	73.3		
standard deviation	± 13.65	-	
Gender, Male/Female			
Units: Subjects			
Female	5	5	
Male	17	17	
Race/Ethnicity, Customized			
Units: Subjects			
Asian	4	4	
Caucasian	17	17	
Other	1	1	
Bone Marrow Evaluation			
Here Erythroblastopenia=EBP; Hypoplasia= HYP; Hypocellular=hpc; bone marrow=BM; Erythroid lineage-EL; diagnosis=dgn; reticulocyte=retic.			
Units: Subjects			
Aplasia of Erythropoese	1	1	
Erythroblastopenia (EBP)	1	1	
EBP 0% normal values for other cell lineages	1	1	
Erythroid series absent	1	1	
Erythroid severe HYP no decrease in other lineages	1	1	
Erythropoietic hypoplasia	1	1	
Hpc BM with reduced EL consistent with dgn of pure	1	1	
HYP of erythropoiesis staining of iron in BM retic	1	1	
Normal	1	1	
PRCA	8	8	
PRCA / Bone Marrow Trephine	1	1	
Pure Red Cell Aplasia	2	2	
Red cell aplasia	1	1	
Red cell hypoplasia	1	1	
Region of Enrollment			

Units: Subjects			
France	6	6	
Germany	8	8	
United Kingdom	8	8	
Study Specific Characteristic | Height			
Data was available for 21 participants.			
Units: cm			
arithmetic mean			
standard deviation	±	-	
Study Specific Characteristic | Weight			
Units: kg			
arithmetic mean	67.6		
standard deviation	± 12.31	-	
Study Specific Characteristic | Body Mass Index (BMI)			
Data was available for 21 participants.			
Units: kg/m^2			
arithmetic mean			
standard deviation	±	-	
Study Specific Characteristic | Baseline Hemoglobin (Hgb)			
Units: g/L			
arithmetic mean	96.5		
standard deviation	± 16.11	-	
Study Specific Characteristic | Baseline Ferritin			
Data was available for 21 participants.			
Units: ug/L			
arithmetic mean			
standard deviation	±	-	
Study Specific Characteristic | Baseline Transferrin Saturation			
Data was available for 19 participants.			
Units: % transferrin			
arithmetic mean			
standard deviation	±	-	
Study Specific Characteristic | Baseline Anti-erythropoietin (EPO) Antibody Titers			
Units: U/mL			
arithmetic mean	94.1		
standard deviation	± 217.08	-	

Subject analysis sets

Subject analysis set title	Peginesatide
Subject analysis set type	Full analysis

Subject analysis set description:

Peginesatide 0.05 mg/kg injection, subcutaneously followed by peginesatide 0.1 mg/kg injection, subcutaneously once every 4 weeks for up to 60 months. Individual dose of peginesatide injection was modified based on hemoglobin levels. Dose adjustments were made in order to achieve and maintain hemoglobin in the target range of 10.0–12.0 g/dL.

Subject analysis set title	Peginesatide
Subject analysis set type	Full analysis

Subject analysis set description:

Peginesatide 0.05 mg/kg injection, subcutaneously followed by peginesatide 0.1 mg/kg injection, subcutaneously once every 4 weeks for up to 60 months. Individual dose of peginesatide injection was modified based on hemoglobin levels. Dose adjustments were made in order to achieve and maintain hemoglobin in the target range of 10.0–12.0 g/dL.

Reporting group values	Peginesatide	Peginesatide	
Number of subjects	21	19	
Age categorical Units: Subjects			

Age Continuous Units: years arithmetic mean standard deviation	± 	± 	
Gender, Male/Female Units: Subjects			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
Asian Caucasian Other			
Bone Marrow Evaluation			
Here Erythroblastopenia=EBP; Hypoplasia= HYP; Hypocellular=hpc; bone marrow=BM; Erythroid lineage-EL; diagnosis=dgn; reticulocyte=retic.			
Units: Subjects			
Aplasia of Erythropoese Erythroblastopenia (EBP) EBP 0% normal values for other cell lineages Erythroid series absent Erythroid severe HYP no decrease in other lineages Erythropoietic hypoplasia Hpc BM with reduced EL consistent with dgn of pure HYP of erythropoiesis staining of iron in BM retic Normal PRCA PRCA / Bone Marrow Trephine Pure Red Cell Aplasia Red cell aplasia Red cell hypoplasia			
Region of Enrollment Units: Subjects			
France Germany United Kingdom			

Study Specific Characteristic | Height			
Data was available for 21 participants.			
Units: cm			
arithmetic mean	168.1		
standard deviation	± 9.66	±	
Study Specific Characteristic | Weight			
Units: kg			
arithmetic mean			
standard deviation	±	±	
Study Specific Characteristic | Body Mass Index (BMI)			
Data was available for 21 participants.			
Units: kg/m^2			
arithmetic mean	23.8		
standard deviation	± 2.41	±	
Study Specific Characteristic | Baseline Hemoglobin (Hgb)			
Units: g/L			
arithmetic mean			
standard deviation	±	±	
Study Specific Characteristic | Baseline Ferritin			
Data was available for 21 participants.			
Units: ug/L			
arithmetic mean	2332.0		
standard deviation	± 1695.02	±	
Study Specific Characteristic | Baseline Transferrin Saturation			
Data was available for 19 participants.			
Units: % transferrin			
arithmetic mean		79.2	
standard deviation	±	± 21.87	
Study Specific Characteristic | Baseline Anti-erythropoietin (EPO) Antibody Titers			
Units: U/mL			
arithmetic mean			
standard deviation	±	±	

End points

End points reporting groups

Reporting group title	Peginesatide

Reporting group description:

Peginesatide 0.05 mg/kg injection, subcutaneously followed by peginesatide 0.1 mg/kg injection, subcutaneously once every 4 weeks for up to 60 months. Individual dose of peginesatide injection was modified based on hemoglobin levels. Dose adjustments were made in order to achieve and maintain hemoglobin in the target range of 10.0–12.0 g/dL.

Subject analysis set title	Peginesatide
Subject analysis set type	Full analysis

Subject analysis set description:

Peginesatide 0.05 mg/kg injection, subcutaneously followed by peginesatide 0.1 mg/kg injection, subcutaneously once every 4 weeks for up to 60 months. Individual dose of peginesatide injection was modified based on hemoglobin levels. Dose adjustments were made in order to achieve and maintain hemoglobin in the target range of 10.0–12.0 g/dL.

Subject analysis set title	Peginesatide
Subject analysis set type	Full analysis

Subject analysis set description:

Peginesatide 0.05 mg/kg injection, subcutaneously followed by peginesatide 0.1 mg/kg injection, subcutaneously once every 4 weeks for up to 60 months. Individual dose of peginesatide injection was modified based on hemoglobin levels. Dose adjustments were made in order to achieve and maintain hemoglobin in the target range of 10.0–12.0 g/dL.

Primary: Percentage of Participants who Experienced Increase and Maintain Hemoglobin Levels (two consecutive values) Greater Than or Equal to the Lower Limit of the Target Range in the Absence of Red Blood Cell Transfusion in the Previous 28 days by Week 24

End point title	Percentage of Participants who Experienced Increase and Maintain Hemoglobin Levels (two consecutive values) Greater Than or Equal to the Lower Limit of the Target Range in the Absence of Red Blood Cell Transfusion in the Previous 28 days by Week 24[1]

End point description:

Percentage of participants who experienced increase and maintain hemoglobin levels (two consecutive values) greater than or equal to the lower limit (11 g/dL) in the absence of red blood cell transfusion in the previous 28 days by week 24 were reported.

End point type	Primary

End point timeframe:

Up to Week 24

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: Statistical analysis was not performed for this endpoint.

End point values	Peginesatide			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: percentage of participants				
number (confidence interval 95%)	(to)			

Notes:

[2] - Data was not collected due to low subject enrollment and the drug was withdrawn from the market.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Red Blood Cells (RBCs) Transfusions During the 26 Weeks Pre-treatment Period (prior to enrollment) and During 13- and 26 Weeks Intervals During the Study

End point title	Number of Red Blood Cells (RBCs) Transfusions During the 26 Weeks Pre-treatment Period (prior to enrollment) and During 13- and 26 Weeks Intervals During the Study

End point description:

End point type	Secondary

End point timeframe:

26 weeks prior to enrollment up to end of study (up to 60 months)

End point values	Peginesatide			
Subject group type	Reporting group			
Number of subjects analysed	0[3]			
Units: RBCs transfusion				

Notes:

[3] - Data was not collected due to low subject enrollment and the drug was withdrawn from the market.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with RBC Transfusions During the 26-week Pre-treatment Period and During 13- and 26-week Intervals During the Study

End point title	Percentage of Participants with RBC Transfusions During the 26-week Pre-treatment Period and During 13- and 26-week Intervals During the Study

End point description:

End point type	Secondary

End point timeframe:

26 weeks prior to enrollment up to end of study (up to 60 months)

End point values	Peginesatide			
Subject group type	Reporting group			
Number of subjects analysed	0[4]			
Units: percentage of participants				
number (confidence interval 95%)	(to)			

Notes:

[4] - Data was not collected due to low subject enrollment and the drug was withdrawn from the market.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Initial Achievement of Hemoglobin (Hgb) Greater Than or Equal to the Lower Limit of the Target Range in the Absence of Red Blood Cell Transfusions in the Previous 28 Days

End point title	Time to Initial Achievement of Hemoglobin (Hgb) Greater Than or Equal to the Lower Limit of the Target Range in the Absence of Red Blood Cell Transfusions in the Previous 28 Days

End point description:

The time between first dose administered and the initial achievement of a Hgb increase ≥11 g/dL for two consecutive visits was calculated for each participant as the number of days between the first dose administration date and the earlier of (1) the study termination date [i.e. censor date] and (2) the first date of an Hgb increase ≥ 11 g/dL for two consecutive visits without whole blood or RBC transfusion during the previous 28 days. Time to initial Hgb increase ≥ 11 g/dL will be calculated for each participant as the minimum of censor date and increase date minus the first dose date plus 1.

End point type	Secondary

End point timeframe:

Up to 60 months

End point values	Peginesatide			
Subject group type	Reporting group			
Number of subjects analysed	0[5]			
Units: days				
median (full range (min-max))	(to)			

Notes:

[5] - Data was not collected due to low subject enrollment and the drug was withdrawn from the market.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Adverse Events (AEs), Serious Adverse Events (SAEs), and AEs Leading to Treatment Discontinuation

End point title	Number of Participants with Adverse Events (AEs), Serious Adverse Events (SAEs), and AEs Leading to Treatment Discontinuation

End point description:

An Adverse Event (AE) is defined as any untoward medical occurrence in a clinical investigation participant administered a drug; it does not necessarily have to have a causal relationship with this treatment. A Serious Adverse Event (SAE) is any experience that suggests a significant hazard, contraindication, side effect or precaution that: results in death, is life-threatening, required in-patient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect or is medically significant. A treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset that occurs after receiving study drug. Safety analysis set included all participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

From signing of informed consent form up to Month 60

End point values	Peginesatide			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: participants				
AEs	22			
SAEs	17			
AEs Leading to Study Drug Discontinuation	3			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From signing of informed consent form up to Month 60

Adverse event reporting additional description:

At each visit the investigator had to document any occurrence of adverse events and abnormal laboratory findings. Any event spontaneously reported by the participant or observed by the investigator was recorded, irrespective of the relation to study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Peginesatide

Reporting group description:

Peginesatide 0.05 mg/kg injection, subcutaneously followed by peginesatide 0.1 mg/kg injection, subcutaneously once every 4 weeks for up to 60 months. Individual dose of peginesatide injection was modified based on hemoglobin levels. Dose adjustments were made in order to achieve and maintain hemoglobin in the target range of 10.0–12.0 g/dL.

Serious adverse events	Peginesatide		
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 22 (77.27%)		
number of deaths (all causes)	9		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gastrointestinal cancer metastatic	Additional description: One treatment emergent death occurred and is related to the study drug.		
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Metastases to bone			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Prostate cancer recurrent			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			

Aortic stenosis			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood pressure inadequately controlled			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Femoral artery aneurysm			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest Pain			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Death	Additional description: Treatment-emergent death is not related to the study drug.		
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Sudden death	Additional description: Treatment-emergent death is not related to the study drug.		
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Vascular stent restenosis			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			

subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pulmonary oedema				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Respiratory failure	Additional description: One treatment-emergent death occurred and is not related to the study drug.			
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Investigations				
C-reactive protein increased				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Drug specific antibody present				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Haematocrit decreased	Additional description: One treatment-emergent death occurred and is not related to the study drug.			
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Injury, poisoning and procedural complications				
Femur fracture				
subjects affected / exposed	2 / 22 (9.09%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Coronary artery restenosis				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Peritoneal dialysis complication				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Shunt occlusion				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular pseudoaneurysm				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Angina pectoris				
subjects affected / exposed	2 / 22 (9.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Acute myocardial infarction				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	3 / 22 (13.64%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Atrial flutter				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atrioventricular block				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atrioventricular block complete				

subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest	Additional description: One treatment-emergent death occurred and is not related to the study drug.		
subjects affected / exposed	2 / 22 (9.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Cardiac failure	Additional description: One treatment-emergent death occurred and is not related to the study drug.		
subjects affected / exposed	3 / 22 (13.64%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Cardiac failure acute			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Vascular dementia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Eye disorders			
Optic ischaemic neuropathy			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Anal prolapse			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage	Additional description: One treatment-emergent death occurred and is not related to the study drug.		
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Renal and urinary disorders			
Renal salt-wasting syndrome			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cytomegalovirus infection			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Endocarditis			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Disseminated tuberculosis			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gangrene			

subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Escherichia bacteraemia				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumocystis jirovecii pneumonia				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection	Additional description: One treatment-emergent death occurred and is not related to the study drug.			
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 1			
Urosepsis				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Fluid overload				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hyperkalaemia				

subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Peginesatide		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 22 (100.00%)		
Vascular disorders			
Haematoma			
subjects affected / exposed	3 / 22 (13.64%)		
occurrences (all)	3		
Hypertension			
subjects affected / exposed	6 / 22 (27.27%)		
occurrences (all)	14		
Hypotension			
subjects affected / exposed	3 / 22 (13.64%)		
occurrences (all)	3		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	5 / 22 (22.73%)		
occurrences (all)	9		
Oedema peripheral			
subjects affected / exposed	7 / 22 (31.82%)		
occurrences (all)	10		
Asthenia			
subjects affected / exposed	6 / 22 (27.27%)		
occurrences (all)	7		
Non-cardiac chest pain			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Pyrexia			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	3		
Immune system disorders			

Drug hypersensitivity subjects affected / exposed occurrences (all) Seasonal allergy subjects affected / exposed occurrences (all)	 3 / 22 (13.64%) 5 2 / 22 (9.09%) 3		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all) Rales subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all) Pleural effusion subjects affected / exposed occurrences (all)	 5 / 22 (22.73%) 7 3 / 22 (13.64%) 5 3 / 22 (13.64%) 5 2 / 22 (9.09%) 2 2 / 22 (9.09%) 2		
Investigations Haemoglobin decreased subjects affected / exposed occurrences (all) Weight decreased subjects affected / exposed occurrences (all) Blood pressure increased subjects affected / exposed occurrences (all) Blood phosphorus increased subjects affected / exposed occurrences (all) Blood potassium increased	 6 / 22 (27.27%) 11 4 / 22 (18.18%) 4 3 / 22 (13.64%) 5 2 / 22 (9.09%) 2		

subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Liver function test increased			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Platelet count decreased			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	3		
Reticulocyte count decreased			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	4		
Injury, poisoning and procedural complications			
Skin abrasion			
subjects affected / exposed	5 / 22 (22.73%)		
occurrences (all)	8		
Fall			
subjects affected / exposed	8 / 22 (36.36%)		
occurrences (all)	9		
Contusion			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	9		
Procedural hypotension			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	3		
Heat exhaustion			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Cardiac disorders			
Palpitations			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	4		
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 22 (13.64%)		
occurrences (all)	3		
Headache			

subjects affected / exposed occurrences (all) Restless legs syndrome subjects affected / exposed occurrences (all) Sciatica subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 5 2 / 22 (9.09%) 3 2 / 22 (9.09%) 2		
Ear and labyrinth disorders Tinnitus subjects affected / exposed occurrences (all)	 2 / 22 (9.09%) 2		
Eye disorders Cataract subjects affected / exposed occurrences (all)	 4 / 22 (18.18%) 4		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Toothache subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 10 / 22 (45.45%) 11 3 / 22 (13.64%) 5 3 / 22 (13.64%) 4 2 / 22 (9.09%) 3 3 / 22 (13.64%) 4		
Hepatobiliary disorders Hepatomegaly subjects affected / exposed occurrences (all)	 2 / 22 (9.09%) 2		
Skin and subcutaneous tissue disorders			

Eczema			
subjects affected / exposed	4 / 22 (18.18%)		
occurrences (all)	4		
Pruritus Generalised			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	3		
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	4 / 22 (18.18%)		
occurrences (all)	4		
Chronic kidney disease			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 22 (22.73%)		
occurrences (all)	6		
Muscle spasms			
subjects affected / exposed	5 / 22 (22.73%)		
occurrences (all)	5		
Back pain			
subjects affected / exposed	5 / 22 (22.73%)		
occurrences (all)	6		
Musculoskeletal pain			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Osteoarthritis			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Pain in extremity			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Infections and infestations			
Bronchitis			
subjects affected / exposed	6 / 22 (27.27%)		
occurrences (all)	9		

Nasopharyngitis subjects affected / exposed occurrences (all)	10 / 22 (45.45%) 20		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	3 / 22 (13.64%) 4		
Urinary tract infection subjects affected / exposed occurrences (all)	6 / 22 (27.27%) 14		
Cystitis subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2		
Cytomegalovirus infection subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 3		
Lower respiratory tract infection subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2		
Respiratory tract infection subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	4 / 22 (18.18%) 4		
Fluid overload subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 July 2006	Changed the study design for starting dose, dose escalation, maximum dose, and dose reduction criteria, extended dosing from 6 months to 24 months and updated inclusion criteria.
15 November 2007	Increased continuation of treatment duration to up to 60 months and revised individual patient peginesatide dose adjustment guidelines due to safety concerns associated with elevated haemoglobin (Hgb) values on erythropoiesis-stimulating agent use.
07 June 2010	Increased continuation of treatment duration to up to 70 months.
15 April 2011	Changed study design for starting dose, maximum dose, and Hgb target range, provided details for study endpoints and increased continuation of treatment duration to up to 108 months.
23 April 2013	Sponsor changed from Affymax to Takeda
04 April 2014	Extended continuation of treatment duration to 30 September 2015 and added vials with concentration of 6 mg/0.5 ml.
09 July 2014	Changed frequency of sample collection for peginesatide-specific and anti-erythropoietin antibodies.
16 June 2015	Extended continuation of treatment duration to approximately 30 September 2016.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
23 February 2013	Following post-marketing reports of serious hypersensitivity reactions, enrolment of new subjects into the study was halted (due to risk of hypersensitivity after first injection) and subjects already in the study were informed and reconsented, (ie, were given the option to stop or continue treatment), so study treatment was not halted (subjects with PRCA in the study had been receiving treatment for between approximately 1 and up to 7 years and their benefit:risk remained positive).	-

Notes:

Limitations and caveats

None reported