ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 03/08/2016

ClinicalTrials.gov ID: NCT00699348

Study Identification

Unique Protocol ID:	ML21438
Brief Title:	A Study of Monthly Intravenous C.E.R.A. (Mircera) in Hemodialysis Participants With Chronic Renal Anemia (CARISMA)
Official Title:	A Single Arm, Open Label Study to Assess the Efficacy, Safety and Tolerability of Once-monthly Administration of Intravenous C.E.R.A. for the Maintenance of Haemoglobin Levels in Hemodialysis Patients With Chronic Renal Anaemia
Secondary IDs:	2007-005799-15 [EudraCT Number]

Study Status

Record Verification:	March 2016
Overall Status:	Completed
Study Start:	July 2008
Primary Completion:	July 2010 [Actual]
Study Completion:	July 2010 [Actual]

Sponsor/Collaborators

Sponsor:	Hoffmann-La Roche
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	No
IND/IDE Protocol?:	No

Review Board:	Approval Status: Approved Approval Number: 0010343/08 U Board Name: Comitato Etico Azienda Ospedaliera Ospedale di Lecco Board Affiliation: Presidi Ospedalieri di Lecco - Merate - Bellano Phone: +39 0341 489580 489590 Email: com.etico@ospedale.lecco.it
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	Italy: Ministry of Health

Study Description

Brief Summary:	This single arm study will assess the efficacy, safety and tolerability of once-monthly administration of intravenous methoxy polyethylene glycolepoetin beta (Mircera) for the maintenance of hemoglobin levels in hemodialysis participants with chronic renal anemia. Participants currently receiving intravenous epoetin alfa or beta or darbepoetin alfa will receive intravenous Mircera at a starting dose of 120, 200 or 360 micrograms/month (based on the erythropoietin stimulating agent [ESA] dose administered on week -1). Subsequent doses will be adjusted to maintain hemoglobin levels within the target range of 10 to12 gram per deciliter (g/dL). The anticipated time on study treatment is 1-2 years, and the target sample size is 100-500 individuals.
Detailed Description:	

Conditions

Conditions:	Anemia
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 3
Intervention Model:	Single Group Assignment
Number of Arms:	1
Masking:	Open Label
Allocation:	N/A
Endpoint Classification:	Safety/Efficacy Study

Enrollment: 351 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: C.E.R.A.	Drug: Methoxy polyethylene glycol-epoetin beta (C.E.R.A.) Intravenous methoxy polyethylene glycol-epoetin beta (C.E.R.A.) at starting dose of 120, 200, or 360 micrograms every 4 weeks for 24 weeks. Other Names: • Mircera

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Chronic renal anemia;
- Continuous intravenous maintenance erythropoietin stimulating agent (ESA) treatment during previous month;
- Regular long term hemodialysis therapy with the same mode of dialysis for >=3 months.

Exclusion Criteria:

- Transfusion of red blood cells during previous 2 months;
- Significant acute or chronic bleeding, such as overt gastrointestinal bleeding;
- Active malignant disease (except non-melanoma skin cancer).

Contacts/Locations

Study Officials: Clinical Trials
Study Director
Hoffmann-La Roche

Locations: Italy

Palermo, Italy, 90127

Catania, Italy, 95126

Ancona, Italy, 60121

Milano, Italy, 20142

Pisa, Italy, 56100

San Miniato, Italy, 56028

Torino, Italy, 10126

Roma, Italy, 00161

Firenze, Italy, 50100

Benevento, Italy, 82100

Reggio Emilia, Italy, 42100

Napoli, Italy, 80131

Roma, Italy, 00189

Taranto, Italy, 74100

Milazzo, Italy, 98057

Napoli, Italy, 80131

Napoli, Italy, 80137

Sassari, Italy, 07100

Roma, Italy, 00133

Mantova, Italy, 46100

Chieti, Italy, 66013

Legnano, Italy, 20025

Ascoli Piceno, Italy, 63100

Lecco, Italy, 23900

Ravenna, Italy, 48100

Catania, Italy, 95124

San Daniele Del Friuli, Italy, 33038

La Spezia, Italy, 19124

Lodi, Italy, 26900

Udine, Italy, 33100

Cagliari, Italy, 09100

Cernusco Sul Naviglio, Italy, 20063

Cosenza, Italy, 87100

Matera, Italy, 75100

Novara, Italy, 28100

Lucera, Italy, 71036

Nuoro, Italy, 08100

Nocera Inferiore, Italy, 84014

Borgomanero, Italy, 28021

Brescia, Italy, 25123

Arenzano, Italy, 16011

Foggia, Italy, 71100

Acireale, Italy, 95024

Chieri, Italy, 10023

Ostia Lido, Italy, 00121

Perugia, Italy, 06126

Verona, Italy, 37126

Brindisi, Italy, 72100

Castellammare, Italy, 80053

Anzio, Italy, 00042

Piacenza, Italy, 29100

Firenze, Italy, 50011

Montevarchi, Italy, 52025

Pavia, Italy, 27100

Genova, Italy, 16132

Civitavecchia, Italy, 00053

Vicenza, Italy, 36100

Roma, Italy, 00149

Genova, Italy, 16132

Bollate, Italy, 20021

Avellino, Italy, 83100

Ferrara, Italy, 44100

Pavia, Italy, 27100

Arenzano, Italy, 16011

References

Citations:

Links:

Study Data/Documents:

Participant Flow

Reporting Groups

	Description
C.E.R.A.	Adult participants with chronic renal disease and who had received intravenous epoetin (epoetin alfa, epoetin beta or darbepoetin alfa) maintenance treatment, received (after fulfilling all inclusion/exclusion criteria and 4 weeks stability verification period [Week -4 to Week 0]) intravenous methoxy polyethylene glycolepoetin beta (C.E.R.A.) at starting dose of 120, 200, or 360 microgram (mcg) every 4 weeks for 24 weeks.

Overall Study

	C.E.R.A.
Started	351
Completed	261
Not Completed	90
Death	6
Adverse Event	15
Withdrawal by Subject	11
Protocol Violation	10
Lack of Efficacy	8
Failure to return	1
Blood transfusion	24
Renal transplantation	10
Unspecified	5

Baseline Characteristics

Analysis Population Description

The safety population included all participants who were treated with at least 1 dose of C.E.R.A. and had a safety follow-up, whether withdrawn prematurely or not.

Reporting Groups

	Description
C.E.R.A.	Adult participants with chronic renal disease and who had received intravenous epoetin (epoetin alfa, epoetin beta or darbepoetin alfa) maintenance treatment, received (after fulfilling all inclusion/exclusion criteria and 4 weeks stability verification period) intravenous C.E.R.A. at starting dose of 120, 200, or 360 mcg every 4 weeks for 24 weeks.

Baseline Measures

	C.E.R.A.
Number of Participants	351
Age, Continuous [units: years] Mean (Standard Deviation)	65.7 (13.32)
Gender, Male/Female [units: participants]	
Female	149
Male	202

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants Maintaining Mean Hemoglobin Concentration Within Plus or Minus (+/-) 1 Gram Per Deciliter (g/dL) of Reference and Within the Target Range
Measure Description	Percentage of participants maintaining the mean hemoglobin concentration within +/- 1.0 g/dL of their reference hemoglobin value and within the target range of 10.0 to 12.0 g/dL during the efficacy evaluation period (EEP) was assessed. The reference hemoglobin value was defined on the basis of the 5 assessments recorded during the stability verification period (SVP) at Weeks -4, -3, -2, -1 and 0. The mean hemoglobin concentration for each individual participant during the EEP (Week 17 to Week 24) was estimated as a time adjusted average.
Time Frame	Week 17 up to Week 24
Safety Issue?	No

Analysis Population Description

Per protocol (PP) population included all participants who received at least 1 dose of C.E.R.A. and for whom data for at least 1 follow-up variable was available with the exception of participants who did not fulfill the protocol specified inclusion criteria for this analysis set.

Reporting Groups

	Description
C.E.R.A.	Adult participants with chronic renal disease and who had received intravenous epoetin (epoetin alfa, epoetin beta or darbepoetin alfa) maintenance treatment, received (after fulfilling all inclusion/exclusion criteria and 4 weeks stability verification period) intravenous C.E.R.A. at starting dose of 120, 200, or 360 mcg every 4 weeks for 24 weeks.

Measured Values

	C.E.R.A.
Number of Participants Analyzed	165
Percentage of Participants Maintaining Mean Hemoglobin Concentration Within Plus or Minus (+/-) 1 Gram Per Deciliter (g/dL) of Reference and Within the Target Range [units: percentage of participants] Number (95% Confidence Interval)	60.00 (52.10 to 67.54)

2. Secondary Outcome Measure:

Measure Title	Change in Hemoglobin Concentration Between Reference SVP and EEP
Measure Description	The mean change of the time adjusted average of hemoglobin from reference value obtained during the SVP (Week -4 up to Week 0) and the value during EEP (Week 17 up to Week 24) was assessed.
Time Frame	Week -4 up to Week 0 and Week 17 up to Week 24
Safety Issue?	No

Analysis Population Description

PP Population.

Reporting Groups

	Description
C.E.R.A.	Adult participants with chronic renal disease and who had received intravenous epoetin (epoetin alfa, epoetin beta or darbepoetin alfa) maintenance treatment, received (after fulfilling all inclusion/exclusion criteria and 4 weeks stability verification period) intravenous C.E.R.A. at starting dose of 120, 200, or 360 mcg every 4 weeks for 24 weeks.

Measured Values

	C.E.R.A.
Number of Participants Analyzed	165
Change in Hemoglobin Concentration Between Reference SVP and EEP [units: g/dL] Mean (Standard Deviation)	-0.10 (0.98)

3. Secondary Outcome Measure:

Measure Title	Percentage of Participants Maintaining Hemoglobin Concentration Within the Target Range
Measure Description	Percentage of participants maintaining hemoglobin concentration within the target range of 10.0 to 12.0 g/dL during EEP (Week 17 to Week 24) was assessed.
Time Frame	Week 17 up to Week 24
Safety Issue?	No

Analysis Population Description
PP population.

Reporting Groups

	Description
C.E.R.A.	Adult participants with chronic renal disease and who had received intravenous epoetin (epoetin alfa, epoetin beta or darbepoetin alfa) maintenance treatment, received (after fulfilling all inclusion/exclusion criteria and 4 weeks stability verification period) intravenous C.E.R.A. at starting dose of 120, 200, or 360 mcg every 4 weeks for 24 weeks.

Measured Values

	C.E.R.A.
Number of Participants Analyzed	165
Percentage of Participants Maintaining Hemoglobin Concentration Within the Target Range [units: percentage of participants] Number (95% Confidence Interval)	73.94 (66.54 to 80.45)

4. Secondary Outcome Measure:

Measure Title	Median Time Spent by Participants With Hemoglobin Concentration in the Target Range During the EEP
Measure Description	Median time spent by participants with hemoglobin concentration within the target range of 10.0 to 12.0 g/dL during the EEP (Week 17 to Week 24) was assessed.
Time Frame	Week 17 up to Week 24
Safety Issue?	No

Analysis Population Description
PP population.

Reporting Groups

	Description
C.E.R.A.	Adult participants with chronic renal disease and who had received intravenous epoetin (epoetin alfa, epoetin beta or darbepoetin alfa) maintenance treatment, received (after fulfilling all inclusion/exclusion criteria and 4 weeks stability verification period) intravenous C.E.R.A. at starting dose of 120, 200, or 360 mcg every 4 weeks for 24 weeks.

Measured Values

	C.E.R.A.
Number of Participants Analyzed	165
Median Time Spent by Participants With Hemoglobin Concentration in the Target Range During the EEP [units: days] Median (Full Range)	44.0 (0.0 to 56.0)

5. Secondary Outcome Measure:

Measure Title	Percentage of Participants Requiring Any Dose Adjustment
Measure Description	Percentage of participants requiring any adjustment in the dose of study drug during the dose titration period (DTP: Week 1 to Week 16) and EEP (Week 17 to Week 24) was reported.
Time Frame	Week 1 up to Week 16 and Week 17 up to Week 24
Safety Issue?	No

Analysis Population Description
PP population.

Reporting Groups

	Description
C.E.R.A.	Adult participants with chronic renal disease and who had received intravenous epoetin (epoetin alfa, epoetin beta or darbepoetin alfa) maintenance treatment, received (after fulfilling all inclusion/exclusion criteria and 4 weeks stability verification period) intravenous C.E.R.A. at starting dose of 120, 200, or 360 mcg every 4 weeks for 24 weeks.

Measured Values

	C.E.R.A.
Number of Participants Analyzed	165
Percentage of Participants Requiring Any Dose Adjustment [units: percentage of participants]	
DTP	70.3
EEP	50.9

6. Secondary Outcome Measure:

Measure Title	Number of Participants With Red Blood Cell Transfusion During the Study
Measure Description	Number of participant who underwent red blood cell transfusion during the study was reported.
Time Frame	Week -4 up to Week 52
Safety Issue?	No

Analysis Population Description

Safety population.

Reporting Groups

	Description
C.E.R.A.	Adult participants with chronic renal disease and who had received intravenous epoetin (epoetin alfa, epoetin beta or darbepoetin alfa) maintenance treatment, received (after fulfilling all inclusion/exclusion criteria and 4 weeks stability verification period) intravenous C.E.R.A. at starting dose of 120, 200, or 360 mcg every 4 weeks for 24 weeks.

Measured Values

	C.E.R.A.
Number of Participants Analyzed	351
Number of Participants With Red Blood Cell Transfusion During the Study [units: participants]	38

Reported Adverse Events

Time Frame	Up to 52 weeks
Additional Description	Only adverse events with an onset date after the start of medication were included.

Reporting Groups

	Description
C.E.R.A.	Adult participants with chronic renal disease and who had received intravenous epoetin (epoetin alfa, epoetin beta or darbepoetin alfa) maintenance treatment, received (after fulfilling all inclusion/exclusion criteria and 4 weeks stability verification period) intravenous C.E.R.A. at starting dose of 120, 200, or 360 mcg every 4 weeks for 24 weeks.

Serious Adverse Events

	C.E.R.A.
	Affected/At Risk (%)
Total	98/351 (27.92%)
Blood and lymphatic system disorders	
Anaemia [A] *	7/351 (1.99%)
Cardiac disorders	
Acute coronary syndrome [A] *	1/351 (0.28%)
Acute myocardial infarction [A] *	2/351 (0.57%)
Angina pectoris [A] *	1/351 (0.28%)
Angina unstable [A] *	1/351 (0.28%)

	C.E.R.A.
	Affected/At Risk (%)
Atrial fibrillation [A] *	2/351 (0.57%)
Bradycardia [A] *	1/351 (0.28%)
Cardiac disorder [A] *	1/351 (0.28%)
Cardiac failure [A] *	2/351 (0.57%)
Myocardial infarction [A] *	3/351 (0.85%)
Myocardial ischaemia [A] *	2/351 (0.57%)
Congenital, familial and genetic disorders	
Gastrointestinal angiodysplasia [A] *	1/351 (0.28%)
Eye disorders	
Retinal detachment [A] *	2/351 (0.57%)
Gastrointestinal disorders	
Abdominal pain [A] *	1/351 (0.28%)
Gastritis erosive [A] *	1/351 (0.28%)
Gastrointestinal haemorrhage [A] *	2/351 (0.57%)
Haemorrhoidal haemorrhage [A] *	1/351 (0.28%)
Intestinal ischaemia [A] *	1/351 (0.28%)
Large intestinal haemorrhage [A] *	1/351 (0.28%)
Melaena [A] *	1/351 (0.28%)
Rectal haemorrhage [A] *	2/351 (0.57%)
General disorders	
Catheter site haemorrhage [A] *	1/351 (0.28%)
Device malfunction [A] *	1/351 (0.28%)
Pyrexia [A] *	3/351 (0.85%)

	C.E.R.A.
	Affected/At Risk (%)
Vessel puncture site haemorrhage [A] *	1/351 (0.28%)
Hepatobiliary disorders	
Cholecystitis [A] *	1/351 (0.28%)
Cholelithiasis [A] *	2/351 (0.57%)
Infections and infestations	
Bronchopneumonia [A] *	2/351 (0.57%)
Campylobacter intestinal infection [A] *	1/351 (0.28%)
Device related infection [A] *	2/351 (0.57%)
Influenza [A] *	2/351 (0.57%)
Lung infection [A] *	1/351 (0.28%)
Oropharyngitis fungal [A] *	1/351 (0.28%)
Osteomyelitis [A] *	1/351 (0.28%)
Pneumonia [A] *	3/351 (0.85%)
Sepsis [A] *	1/351 (0.28%)
Staphylococcal sepsis [A] *	1/351 (0.28%)
Injury, poisoning and procedural complications	
Arteriovenous fistula aneurysm [A] *	1/351 (0.28%)
Arteriovenous fistula thrombosis [A] *	9/351 (2.56%)
Fall [A] *	1/351 (0.28%)
Femur fracture [A] *	2/351 (0.57%)
Head injury [A] *	1/351 (0.28%)
Operative haemorrhage [A] *	1/351 (0.28%)

	C.E.R.A.
	Affected/At Risk (%)
Post procedural haematoma [A] *	1/351 (0.28%)
Skin laceration [A] *	1/351 (0.28%)
Traumatic haemorrhage [A] *	1/351 (0.28%)
Vascular access complication [A] *	3/351 (0.85%)
Investigations	
Haemoglobin decreased [A] *	3/351 (0.85%)
Metabolism and nutrition disorders	
Cachexia [A] *	2/351 (0.57%)
Diabetic foot [A] *	1/351 (0.28%)
Hyperkalaemia [A] *	1/351 (0.28%)
Musculoskeletal and connective tissue disorders	
Foot deformity [A] *	1/351 (0.28%)
Intervertebral disc protrusion [A] *	1/351 (0.28%)
Musculoskeletal chest pain [A] *	1/351 (0.28%)
Musculoskeletal pain [A] *	1/351 (0.28%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	
Colon cancer [A] *	1/351 (0.28%)
Gallbladder cancer [A] *	1/351 (0.28%)
Lung carcinoma cell type unspecified recurrent [A] *	1/351 (0.28%)
Prostate cancer [A] *	1/351 (0.28%)
Squamous cell carcinoma [A] *	1/351 (0.28%)
Nervous system disorders	

	C.E.R.A.
	Affected/At Risk (%)
Cerebrovascular disorder [A] *	1/351 (0.28%)
Nervous system disorder [A] *	1/351 (0.28%)
Paraesthesia [A] *	1/351 (0.28%)
Syncope [A] *	1/351 (0.28%)
Transient ischaemic attack [A] *	4/351 (1.14%)
Psychiatric disorders	
Depression [A] *	1/351 (0.28%)
Renal and urinary disorders	
Haematuria [A] *	1/351 (0.28%)
Respiratory, thoracic and mediastinal disorders	
Acute pulmonary oedema [A] *	4/351 (1.14%)
Dyspnoea [A] *	2/351 (0.57%)
Epistaxis [A] *	1/351 (0.28%)
Pulmonary embolism [A] *	1/351 (0.28%)
Pulmonary oedema [A] *	2/351 (0.57%)
Skin and subcutaneous tissue disorders	
Skin ulcer [A] *	1/351 (0.28%)
Surgical and medical procedures	
Arteriovenous fistula operation [A] *	1/351 (0.28%)
Implantable defibrillator insertion [A] *	1/351 (0.28%)
Knee arthroplasty [A] *	1/351 (0.28%)
Vascular disorders	
Angiopathy [A] *	3/351 (0.85%)

	C.E.R.A.
	Affected/At Risk (%)
Deep vein thrombosis [A] *	1/351 (0.28%)
Haemorrhage [A] *	1/351 (0.28%)
Hypotension [A] *	1/351 (0.28%)
Necrosis ischaemic [A] *	1/351 (0.28%)
Peripheral arterial occlusive disease [A] *	2/351 (0.57%)
Peripheral ischaemia [A] *	4/351 (1.14%)
Thrombosis [A] *	1/351 (0.28%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (13.0)

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	C.E.R.A.
	Affected/At Risk (%)
Total	23/351 (6.55%)
Vascular disorders	
Hypertension [A] *	23/351 (6.55%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (13.0)

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The Study being conducted under this Agreement is part of the Overall Study. Investigator is free to publish in reputable journals or to present at professional conferences the results of the Study, but only after the first publication or presentation that involves the Overall Study. The Sponsor may request that Confidential Information be deleted and/or the publication be postponed in order to protect the Sponsor's intellectual property rights.

Results Point of Contact:

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