ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 02/16/2016

ClinicalTrials.gov ID: NCT00660023

Study Identification

Unique Protocol ID:	ML20752
Brief Title:	A Study of Intravenous Mircera in Participants With Chronic Renal Anemia Who Are on Dialysis
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 Dialysis Patients With Chronic Renal Anaemia
Secondary IDs:	2006-005621-28

Study Status

Record Verification:	February 2016
Overall Status:	Completed
Study Start:	August 2008
Primary Completion:	November 2010 [Actual]
Study Completion:	November 2010 [Actual]

Sponsor/Collaborators

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

Oversight

FDA Regulated?:	Yes
Applicable Trial?:	Section 801 Clinical Trial? No

	Delayed Posting?
IND/IDE Protocol?:	No
Review Board:	Approval Status: Approved Approval Number: Unknown Board Name: Medical Research Council Ethics Committee for Clinical Pharmacology Board Affiliation: Indpendent Ethics Committee Phone: +36 1 301 7871 Email:
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	Hungary: National Institute of Pharmacy, Central Ethics Committee

Study Description

Brief Summary:	This single-arm study will assess the efficacy and safety of monthly administration of intravenous methoxy polyethylene glycol-epoetin beta (CERA/Mircera) for the maintenance of hemoglobin (Hb) levels in participants on dialysis with chronic renal anemia in routine clinical practice in Hungary. Participants currently receiving maintenance treatment with intravenous epoetin or darbepoetin will receive monthly injections of Mircera, with the starting dose derived from the erythropoiesis-stimulating agent (ESA) dose they had been receiving.
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: 124 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Mircera in Renal Anemia Participants with chronic renal anemia previously treated with ESA therapy will receive intravenous Mircera, also known as continuous erythropoietin receptor activator (CERA), every 4 weeks for a total of 52 weeks in this single-arm study. The first dose will be determined by the dose of ESA received prior to administration of study treatment, and subsequent doses will be adjusted to achieve target Hb concentrations.	Drug: Methoxy polyethylene glycol-epoetin beta Participants will receive intravenous CERA/Mircera every month, with starting dose based on previous ESA therapy. Treatment will continue for 52 weeks. Other Names: • CERA/Mircera

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Adults greater than or equal to (≥) 18 years of age
- Chronic renal anemia
- Continuous stable intravenous or subcutaneous maintenance epoetin or darbepoetin therapy during previous month
- Regular long-term hemodialysis therapy with the same mode of dialysis for the previous 3 months

Exclusion Criteria:

- Transfusion of red blood cells during previous 2 months
- Poorly controlled hypertension
- Significant acute or chronic bleeding

Contacts/Locations

Study Officials: Clinical Trials

Study Director
Hoffmann-La Roche

Locations: Hungary
Baja, Hungary, 6500

Szolnok, Hungary, 5000

Debrecen, Hungary, 4032

Miskolc, Hungary, 3526

Budapest, Hungary, 1062

Esztergom, Hungary, 2500

VAC, Hungary, 2600

Zalaegerszeg, Hungary, 8900

Keszthely, Hungary, 8360

Salgótarján, Hungary, 3100

References

Citations:

Links:

Study Data/Documents:

Participant Flow

Reporting Groups

	Description
Mircera in Renal Anemia	Participants with chronic renal anemia who were previously treated with erythropoiesis-stimulating agent (ESA) therapy received intravenous methoxy polyethylene glycol-epoetin beta (Mircera), also known as continuous erythropoietin receptor activator (CERA), every 4 weeks for a total of 52 weeks in this single-arm study. The first dose of 120, 200, or 360 micrograms (mcg) was based upon the dose of ESA received in the week preceding the switch to Mircera/CERA, while subsequent doses were adjusted to maintain hemoglobin (Hb) concentrations within target of 10.0 and 12.0 grams per deciliter (g/dL).

Overall Study

	Mircera in Renal Anemia
Started	124
Treated	114
Completed	95
Not Completed	29
Adverse Event	2
Death	8
Blood Transfusion	5
Renal Transplantation	3
Withdrawal by Subject	1
Missed Pregnancy Test	1
Other Screening Failure	9

Baseline Characteristics

Analysis Population Description

Intent-to-Treat (ITT) Population: All participants who received at least one dose of Mircera/CERA and for whom data from at least one follow-up assessment were available.

Reporting Groups

	Description
Mircera in Renal Anemia	Participants with chronic renal anemia who were previously treated with ESA therapy received intravenous Mircera/CERA, every 4 weeks for a total of 52 weeks in this single-arm study. The first dose of 120, 200, or 360 mcg was based upon the dose of ESA received in the week preceding the switch to Mircera/CERA, while subsequent doses were adjusted to maintain Hb concentrations within target of 10.0 and 12.0 g/dL.

Baseline Measures

	Mircera in Renal Anemia
Number of Participants	114
Age, Continuous [units: years] Median (Full Range)	63.5 (22 to 88)
Gender, Male/Female [units: participants]	
Female	66
Male	48

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants Who Maintained Average Hb Within Plus/Minus (±) 1 g/dL of Reference Hb and Within Target Range During the Efficacy Evaluation Period (EEP)
Measure Description	Reference Hb was determined individually per participant as the average of all Hb values during a pre-treatment stability assessment (Weeks -4 to -1). During the EEP (Weeks 18 to 24), participants provided a total of four blood samples for Hb monitoring while on treatment with CERA/Mircera. The average Hb during the EEP was calculated per participant and assessed against the reference value. The percentage of participants who had average Hb during the EEP in the target range of 10.0 to 12.0 g/dL and within ±1 g/dL of their individual reference Hb was determined as the primary endpoint. The 95 percent (%) confidence interval (CI) was calculated using the Pearson-Clopper method for exact confidence bounds.
Time Frame	Weeks -4, -3, -2, and -1; pre-dose (0 hours) during Weeks 18, 20, 22, and 24
Safety Issue?	No

Analysis Population Description

Per Protocol (PP) Population: All participants from the ITT Population who fulfill inclusion/exclusion criteria per study protocol.

Reporting Groups

	Description
Mircera in Renal Anemia	Participants with chronic renal anemia who were previously treated with ESA therapy received intravenous Mircera/CERA, every 4 weeks for a total of 52 weeks in this single-arm study. The first dose of 120, 200, or 360 mcg was based upon the dose of ESA received in the week preceding the switch to Mircera/CERA, while subsequent doses were adjusted to maintain Hb concentrations within target of 10.0 and 12.0 g/dL.

Measured Values

	Mircera in Renal Anemia
Number of Participants Analyzed	88
Percentage of Participants Who Maintained Average Hb Within Plus/Minus (±) 1 g/dL of Reference Hb and Within Target Range During the Efficacy Evaluation Period (EEP) [units: percentage of participants] Number (95% Confidence Interval)	72.7 (62.2 to 81.7)

2. Secondary Outcome Measure:

Measure Title	Mean Change in Time-Adjusted Hb From Baseline to EEP
Measure Description	Reference Hb was determined individually per participant as the average of all Hb values during a pre-treatment stability assessment (Weeks -4 to -1). During the EEP (Weeks 18 to 24), participants provided a total of four blood samples for Hb monitoring while on treatment with CERA/Mircera. The average Hb during the EEP was calculated per participant and assessed against the reference value. The mean change in Hb value between reference (i.e., "Baseline") Hb and the EEP average Hb was calculated and expressed in g/dL.
Time Frame	At Weeks -4, -3, -2, and -1; pre-dose (0 hours) during Weeks 18, 20, 22, and 24
Safety Issue?	No

Analysis Population Description
ITT Population.

Reporting Groups

	Description
Mircera in Renal Anemia	Participants with chronic renal anemia who were previously treated with ESA therapy received intravenous Mircera/CERA, every 4 weeks for a total of 52 weeks in this single-arm study. The first dose of 120, 200, or 360 mcg was based upon the dose of ESA received in the week preceding the switch to Mircera/CERA, while subsequent doses were adjusted to maintain Hb concentrations within target of 10.0 and 12.0 g/dL.

Measured Values

	Mircera in Renal Anemia
Number of Participants Analyzed	114
Mean Change in Time-Adjusted Hb From Baseline to EEP [units: g/dL] Mean (Standard Deviation)	-0.06 (1.04)

3. Secondary Outcome Measure:

Measure Title	Percentage of Participants Whose Hb Remained Within Target Range Throughout the EEP
Measure Description	During the EEP (Weeks 18 to 24), participants provided a total of four blood samples for Hb monitoring while on treatment with CERA/Mircera. The percentage of participants who maintained each single Hb measurement in the target range of 10.0 to 12.0 g/dL was determined. The 95% CI was calculated using the Pearson-Clopper method for exact confidence bounds.
Time Frame	Pre-dose (0 hours) during Weeks 18, 20, 22, and 24
Safety Issue?	No

Analysis Population Description

ITT Population.

Reporting Groups

	Description
Mircera in Renal Anemia	Participants with chronic renal anemia who were previously treated with ESA therapy received intravenous Mircera/CERA, every 4 weeks for a total of 52 weeks in this single-arm study. The first dose of 120, 200, or 360 mcg was based upon the dose of ESA received in the week preceding the switch to Mircera/CERA, while subsequent doses were adjusted to maintain Hb concentrations within target of 10.0 and 12.0 g/dL.

Measured Values

	Mircera in Renal Anemia
Number of Participants Analyzed	114
Percentage of Participants Whose Hb Remained Within Target Range Throughout the EEP [units: percentage of participants] Number (95% Confidence Interval)	79.0 (70.3 to 86.0)

4. Secondary Outcome Measure:

Measure Title	Mean Time Spent in the Target Range for Hb During the EEP
Measure Description	During the EEP (Weeks 18 to 24), participants provided a total of four blood samples for Hb monitoring while on treatment with CERA/Mircera. Time spent in the target range of 10.0 to 12.0 g/dL was defined as time from first on-target Hb to time of last known on-target Hb, as collected during the EEP. Time spent in the target range was averaged among all participants and expressed in days.
Time Frame	Pre-dose (0 hours) during Weeks 18, 20, 22, and 24
Safety Issue?	No

Analysis Population Description

ITT Population.

Reporting Groups

	Description
Mircera in Renal Anemia	Participants with chronic renal anemia who were previously treated with ESA therapy received intravenous Mircera/CERA, every 4 weeks for a total of 52 weeks in this single-arm study. The first dose of 120, 200, or 360 mcg was based upon the dose of ESA received in the week preceding the switch to Mircera/CERA, while subsequent doses were adjusted to maintain Hb concentrations within target of 10.0 and 12.0 g/dL.

Measured Values

	Mircera in Renal Anemia
Number of Participants Analyzed	114
Mean Time Spent in the Target Range for Hb During the EEP [units: days] Mean (Standard Deviation)	43.5 (15.64)

5. Secondary Outcome Measure:

Measure Title	Mean Dose of Mircera/CERA During the Dose Titration Period (DTP) and EEP
Measure Description	Study drug administration occurred monthly during the DTP (Weeks 0 to 16), which began with a pre-specified dose of Mircera/CERA according to the dose of ESA administered during Week -1. Subsequent doses could be adjusted throughout the study including during the EEP (Weeks 18 to 24) on the basis of Hb levels or other modification criteria. The dose received at each administration visit was averaged among all participants during the DTP and EEP and expressed in mcg.

Time Frame	Weeks 0, 4, 8, 12, 16, 20, and 24
Safety Issue?	No

Analysis Population Description

ITT Population; the number (n) of participants who received at least one dose during the specific period was used for analysis.

Reporting Groups

	Description
Mircera in Renal Anemia	Participants with chronic renal anemia who were previously treated with ESA therapy received intravenous Mircera/CERA, every 4 weeks for a total of 52 weeks in this single-arm study. The first dose of 120, 200, or 360 mcg was based upon the dose of ESA received in the week preceding the switch to Mircera/CERA, while subsequent doses were adjusted to maintain Hb concentrations within target of 10.0 and 12.0 g/dL.

Measured Values

	Mircera in Renal Anemia
Number of Participants Analyzed	114
Mean Dose of Mircera/CERA During the Dose Titration Period (DTP) and EEP [units: mcg] Mean (Standard Deviation)	
DTP (n=114)	113 (39.4)
EEP (n=110)	100.3 (69.43)

6. Secondary Outcome Measure:

Measure Title	Percentage of Participants Who Required Any Dose Adjustment of Mircera/CERA During the DTP and EEP
Measure Description	Study drug administration occurred monthly during the DTP (Weeks 0 to 16), which began with a pre-specified dose of Mircera/CERA according to the dose of ESA administered during Week -1. Subsequent doses could be adjusted throughout the study including during the EEP (Weeks 18 to 24) on the basis of Hb levels or other modification criteria. The percentage of participants who required a dose adjustment for any reason was calculated during the DTP and EEP.
Time Frame	Weeks 0, 4, 8, 12, 16, 20, and 24
Safety Issue?	No

Analysis Population Description

ITT Population; the number (n) of participants who received at least one dose during the specific period was used for analysis.

Reporting Groups

	Description
Mircera in Renal Anemia	Participants with chronic renal anemia who were previously treated with ESA therapy received intravenous Mircera/CERA, every 4 weeks for a total of 52 weeks in this single-arm study. The first dose of 120, 200, or 360 mcg was based upon the dose of ESA received in the week preceding the switch to Mircera/CERA, while subsequent doses were adjusted to maintain Hb concentrations within target of 10.0 and 12.0 g/dL.

Measured Values

	Mircera in Renal Anemia
Number of Participants Analyzed	114
Percentage of Participants Who Required Any Dose Adjustment of Mircera/CERA During the DTP and EEP [units: percentage of participants]	
DTP (n=114)	79.8
EEP (n=110)	48.2

7. Secondary Outcome Measure:

Measure Title	Number of Participants Receiving Blood Transfusion During the DTP and EEP
Measure Description	The number of participants who received blood transfusion during the DTP (Weeks 0 and 16) and EEP (Weeks 18 to 24) was reported.
Time Frame	Continuously and at every visit from Week 0 (every week until Week 2, thereafter every 2 weeks) through Week 24
Safety Issue?	No

Analysis Population Description

ITT Population; the number (n) of participants who received at least one dose during the specific period was used for analysis.

Reporting Groups

	Description
Mircera in Renal Anemia	Participants with chronic renal anemia who were previously treated with ESA therapy received intravenous Mircera/CERA, every 4 weeks for a total of 52 weeks in this single-arm study. The first dose of 120, 200, or 360 mcg was based upon the dose of ESA received in the week preceding the switch to Mircera/CERA, while subsequent doses were adjusted to maintain Hb concentrations within target of 10.0 and 12.0 g/dL.

Measured Values

	Mircera in Renal Anemia
Number of Participants Analyzed	114
Number of Participants Receiving Blood Transfusion During the DTP and EEP [units: participants]	
DTP (n=114)	3
EEP (n=110)	0

8. Secondary Outcome Measure:

Measure Title	Number of Blood Transfusions During the DTP and EEP
Measure Description	The number of blood transfusion during the DTP (Weeks 0 and 16) and EEP (Weeks 18 to 24) was reported.
Time Frame	Continuously and at every visit from Week 0 (every week until Week 2, thereafter every 2 weeks) through Week 24
Safety Issue?	No

Analysis Population Description

ITT Population; the number (n) of participants who received at least one dose during the specific period was used for analysis.

Reporting Groups

	Description
Mircera in Renal Anemia	Participants with chronic renal anemia who were previously treated with ESA therapy received intravenous Mircera/CERA, every 4 weeks for a total of 52 weeks in this single-arm study. The first dose of 120, 200, or 360 mcg was based upon the dose of ESA received in the week preceding the switch to Mircera/CERA, while subsequent doses were adjusted to maintain Hb concentrations within target of 10.0 and 12.0 g/dL.

Measured Values

	Mircera in Renal Anemia
Number of Participants Analyzed	114
Number of Blood Transfusions During the DTP and EEP [units: blood transfusions]	
DTP (n=114)	4
EEP (n=110)	0

Reported Adverse Events

Time Frame	Continuously and at every visit from Week -3 (every week until Week 2, every 2 weeks until Week 48) through the final visit at Week 52
Additional Description	Safety Population: All participants who received at least one dose of trial medication and at least one safety follow-up assessment, whether prematurely withdrawn or not.

Reporting Groups

	Description
Mircera in Renal Anemia	Participants with chronic renal anemia who were previously treated with ESA therapy received intravenous Mircera/CERA, every 4 weeks for a total of 52 weeks in this single-arm study. The first dose of 120, 200, or 360 mcg was based upon the dose of ESA in the week preceding the switch to Mircera/CERA, while subsequent doses were adjusted to maintain Hb concentrations within target of 10.0 and 12.0 g/dL.

Serious Adverse Events

	Mircera in Renal Anemia
	Affected/At Risk (%)
Total	45/114 (39.47%)
Blood and lymphatic system disorders	
Haemolysis [A] *	1/114 (0.88%)
Cardiac disorders	
Cardiac asthma [A] *	1/114 (0.88%)
Cardiac failure [A] *	4/114 (3.51%)
Cardiovascular disorder [A] *	1/114 (0.88%)
Mitral valve incompetence [A] *	1/114 (0.88%)
Myocardial infarction [A] *	1/114 (0.88%)
Supraventricular tachycardia [A] *	1/114 (0.88%)
Eye disorders	

	Mircera in Renal Anemia
	Affected/At Risk (%)
Cataract [A] *	1/114 (0.88%)
Gastrointestinal disorders	
Abdominal pain [A] *	1/114 (0.88%)
Gastrointestinal haemorrhage [A] *	2/114 (1.75%)
Pancreatitis acute [A] *	1/114 (0.88%)
General disorders	
Medical device complication [A] *	2/114 (1.75%)
Pyrexia [A] *	3/114 (2.63%)
Infections and infestations	
Bronchitis [A] *	1/114 (0.88%)
Cellulitis [A] *	1/114 (0.88%)
Device related infection [A] *	1/114 (0.88%)
Gangrene [A] *	1/114 (0.88%)
Pneumonia [A] *	2/114 (1.75%)
Renal cyst infection [A] *	1/114 (0.88%)
Sepsis [A] *	1/114 (0.88%)
Injury, poisoning and procedural complications	
Arteriovenous fistula site complication [A] *	1/114 (0.88%)
Arteriovenous fistula thrombosis [A] *	2/114 (1.75%)
Femoral neck fracture [A] *	1/114 (0.88%)
Femur fracture [A] *	1/114 (0.88%)
Shunt thrombosis [A] *	1/114 (0.88%)
Investigations	

	Mircera in Renal Anemia
	Affected/At Risk (%)
Haemoglobin decreased [A] *	1/114 (0.88%)
Metabolism and nutrition disorders	
Fluid overload [A] *	1/114 (0.88%)
Malnutrition [A] *	1/114 (0.88%)
Musculoskeletal and connective tissue disorders	
Intervertebral disc protrusion [A] *	1/114 (0.88%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	
Multiple myeloma [A] *	1/114 (0.88%)
Renal neoplasm [A] *	1/114 (0.88%)
Nervous system disorders	
Cerebral haemorrhage [A] *	2/114 (1.75%)
Cerebrovascular disorder [A] *	1/114 (0.88%)
Headache [A] *	1/114 (0.88%)
Paraparesis [A] *	1/114 (0.88%)
Subarachnoid haemorrhage [A] *	1/114 (0.88%)
Transient ischaemic attack [A] *	1/114 (0.88%)
Respiratory, thoracic and mediastinal disorders	
Pleural effusion [A] *	1/114 (0.88%)
Respiratory failure [A] *	1/114 (0.88%)
Respiratory tract inflammation [A] *	1/114 (0.88%)
Surgical and medical procedures	
Cataract operation [A] *	1/114 (0.88%)
Cholecystectomy [A] *	1/114 (0.88%)

	Mircera in Renal Anemia
	Affected/At Risk (%)
Vascular disorders	
Hypertension [A] *	2/114 (1.75%)
Hypertensive crisis [A] *	1/114 (0.88%)
Intermittent claudication [A] *	1/114 (0.88%)
Peripheral arterial occlusive disease [A] *	1/114 (0.88%)
Thrombosis [A] *	1/114 (0.88%)
Venous thrombosis [A] *	1/114 (0.88%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (13.1)

Other Adverse Events

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

	Mircera in Renal Anemia
	Affected/At Risk (%)
Total	40/114 (35.09%)
Infections and infestations	
Bronchitis [A] *	8/114 (7.02%)
Musculoskeletal and connective tissue disorders	
Muscle spasm [A] *	9/114 (7.89%)
Vascular disorders	
Hypertension [A] *	29/114 (25.44%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (13.1)

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:

Name/Official Title: Medical Communications
Organization: Hoffmann-LaRoche
Phone: 800-821-8590
Email: genentech@druginfo.com