ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 04/08/2016

ClinicalTrials.gov ID: NCT00605293

Study Identification

Unique Protocol ID:	ML21060
Brief Title:	A Study of Intravenous Mircera (C.E.R.A or Methoxy Polyethylene Glycol-epoetin Beta) for the Maintenance Treatment of Hemodialysis Participants With Chronic Renal Anemia
Official Title:	An Open Label Randomised Controlled Study to Compare the Efficacy, Safety and Tolerability of Once-monthly Administration of Intravenous C.E.R.A. Versus Epoetin Alfa for the Maintenance of Haemoglobin Levels in Hemodialysis Patients With Chronic Renal Anaemia
Secondary IDs:	2007-002065-12 [EudraCT Number]

Study Status

Record Verification:	October 2013
Overall Status:	Completed
Study Start:	January 2008
Primary Completion:	January 2010 [Actual]
Study Completion:	January 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: 2 Board Name: Secretaria del Comite Etico de Investigacion Clinica Board Affiliation: Hospital Universitari Vall d'Hebron Phone: 93 489 4010 Email: mirenavarro@ir.vhebron.net
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	Spain: Sanitarios

Study Description

Brief Summary:	This 2 arm study will compare the efficacy and safety of monthly administration of intravenous (IV) Mircera versus epoetin alfa for the maintenance of hemoglobin levels in hemodialysis patients with chronic renal anemia. Participants currently receiving maintenance treatment with epoetin alfa will be randomized either to receive monthly injections of 120, 200 or 360 micrograms Mircera, with the starting dose derived from the dose of epoetin alfa they were receiving in the week preceding study start, or to continue on epoetin alfa treatment. The anticipated duration of study is 32 weeks, and the target sample size is 146 participants.
Detailed Description:	

Conditions

Conditions:	Anemia
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 3
Intervention Model:	Parallel Assignment
Number of Arms:	2

Masking:	Open Label
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	101 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: C.E.R.A Participants received starting dose of 120, 200 or 360 mcg of C.E.R.A IV once monthly for 6 months. The starting dose was based on the dose of epoetin alfa administered in Week -1.	Drug: methoxy polyethylene glycol-epoetin beta 120, 200 or 360 micrograms iv/month (starting dose) Other Names: • Mircera; C.E.R.A
Active Comparator: Epoetin Alfa Participants received IV injection of 6000 International Units (IU) of epoetin alfa every 3 weeks (q3wk) during the Stability Verification Period (SVP; Week -4 to -1), and 7443 IU of epoetin alfa q3wk during Dose Titration Period (DTP; Week 0 to 15), 7363 IU of epoetin alfa q3wk during Efficacy Evaluation Period (EEP; Week 16 to 23) up to 23 weeks.	Drug: Epoetin alfa As prescribed

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 iv maintenance epoetin alfa therapy, with the same dosing interval during the previous month to and during SVP;
- regular hemodialysis for greater than or equal to (>=) 3 months

Exclusion Criteria:

- transfusion of red blood cells during previous 2 months
- poorly controlled hypertension requiring interruption of epoetin alfa treatment in previous 6 months;

Contacts/Locations

Study Officials: Clinical Trials
Study Director
Hoffmann-La Roche

Locations: Spain

Barcelona, Barcelona, Spain, 08035

Castellon, Castellon, Spain, 12004

Zamora, Zamora, Spain, 49022

Valencia, Valencia, Spain, 46009

Huelva, Huelva, Spain, 21005

Cádizv, Cadiz, Spain, 11008

Salamanca, Salamanca, Spain, 37008

Madrid, Madrid, Spain, 28905

Tudela, Navarra, Spain, 46010

Madrid, Madrid, Spain, 28041

Caceres, Caceres, Spain, 10310

Marbella, Malaga, Spain, 29603

Teruel, Teruel, Spain, 44003

Valencia, Valencia, Spain, 46010

Badajoz, Badajoz, Spain, 06300

Pontevedra, Pontevedra, Spain, 36071

Zaragoza, Zaragoza, Spain, 50009

Zaragoza, Zaragoza, Spain, 50009

Ciudad Real, Ciudad Real, Spain, 13005

Madrid, Madrid, Spain, 28034

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Reporting Groups

	Description
C.E.R.A	Participants received starting dose of 120, 200 or 360 micrograms (mcg) of C.E.R.A intravenously (IV) once monthly for 6 months. The starting dose was based on the dose of epoetin alfa administered in Week -1.
Epoetin Alfa	Participants received IV injection of 6000 International Units (IU) of epoetin alfa every 3 weeks (q3wk) during the Stability Verification Period (SVP; Week -4 to -1), 7443 IU of epoetin alfa q3wk during Dose Titration Period (DTP; Week 0 to 15), and 7363 IU of epoetin alfa q3wk during Efficacy Evaluation Period (EEP; Week 16 to 23) up to 23 weeks.

Overall Study

	C.E.R.A	Epoetin Alfa
Started	65	36
Completed	48	31
Not Completed	17	5
Death	2	1
Insufficient Therapeutic Response	2	0
Adverse Event	1	0
Holidays Dialysis Out	1	0
Blood Transfusion	7	1
Renal Transplantation	3	1

	C.E.R.A	Epoetin Alfa
Incorrect Epoetin Beta Administration	1	0
Dialysis Out of Centre for 3 Months	0	1
Principal Investigator Decision	0	1

Baseline Characteristics

Analysis Population Description

Intent-to-treat (ITT) population included all participants who received at least one dose of C.E.R.A. or epoetin alfa after Week 0, and for whom, data for at least one follow-up variable was available.

Reporting Groups

	Description
C.E.R.A	Participants received starting dose of 120, 200 or 360 mcg of C.E.R.A IV once monthly for 6 months. The starting dose was based on the dose of epoetin alfa administered in Week -1.
Epoetin Alfa	Participants received IV injection of 6000 IU of epoetin alfa q3wk during the SVP (Week -4 to -1), 7443 IU of epoetin alfa q3wk during DTP (Week 0 to 15), and 7363 IU of epoetin alfa q3wk during EEP (Week 16 to 23) up to 23 weeks.

Baseline Measures

	C.E.R.A	Epoetin Alfa	Total
Number of Participants	65	36	101
Age, Continuous [units: years] Mean (Standard Deviation)	65.2 (14.93)	64.5 (16.62)	64.9 (15.47)
Gender, Male/Female [units: participants]			
Female	29	17	46
Male	36	19	55

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants Who Maintained Average Hemoglobin (Hb) Concentration Within Plus Minus (+/-) 1 Grams Per Deciliter (g/dL) of Their Reference Hb and Between 10 and 12 g/dL During the EEP

Measure Description	Participants who maintained average Hb concentration within +/-1 g/dL of their reference Hb and between 10 to 12 g/dL during EEP are reported. The reference Hb value was defined on the basis of all assessments at Weeks -4, -3, -2, -1 and 0.
Time Frame	EEP (Week 16 to 23)
Safety Issue?	No

Analysis Population Description

Per Protocol (PP) population was as a subset of the ITT population who completed the study without any major protocol deviations.

Reporting Groups

	Description
C.E.R.A	Participants received starting dose of 120, 200 or 360 mcg of C.E.R.A IV once monthly for 6 months. The starting dose was based on the dose of epoetin alfa administered in Week -1.
Epoetin Alfa	Participants received IV injection of 6000 IU of epoetin alfa q3wk during the SVP (Week -4 to -1), 7443 IU of epoetin alfa q3wk during DTP (Week 0 to 15), and 7363 IU of epoetin alfa q3wk during EEP (Week 16 to 23) up to 23 weeks.

Measured Values

	C.E.R.A	Epoetin Alfa
Number of Participants Analyzed	44	29
Percentage of Participants Who Maintained Average Hemoglobin (Hb) Concentration Within Plus Minus (+/-) 1 Grams Per Deciliter (g/dL) of Their Reference Hb and Between 10 and 12 g/dL During the EEP [units: percentage of participants] Number (95% Confidence Interval)	45.45 (30.39 to 61.15)	55.17 (35.69 to 73.55)

Statistical Analysis 1 for Percentage of Participants Who Maintained Average Hemoglobin (Hb) Concentration Within Plus Minus (+/-) 1 Grams Per Deciliter (g/dL) of Their Reference Hb and Between 10 and 12 g/dL During the EEP

Statistical Analysis Overview	Comparison Groups	C.E.R.A, Epoetin Alfa
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.4778
	Comments	[Not specified]
	Method	Fisher Exact
	Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Change in Hb Concentrations Between Baseline SVP and the EEP
Measure Description	Change in Hb concentration between baseline SVP and the EEP was evaluated by subtracting the mean of Hb concentration during the SVP (Weeks -4 to -1) with the mean of Hb concentration during the EEP (Weeks 16 to 23).
Time Frame	SVP (Week -4 to -1), EEP (Week 16 to 23)
Safety Issue?	No

Analysis Population Description
ITT population.

Reporting Groups

	Description
C.E.R.A	Participants received starting dose of 120, 200 or 360 mcg of C.E.R.A IV once monthly for 6 months. The starting dose was based on the dose of epoetin alfa administered in Week -1.
Epoetin Alfa	Participants received IV injection of 6000 IU of epoetin alfa q3wk during the SVP (Week -4 to -1), 7443 IU of epoetin alfa q3wk during DTP (Week 0 to 15), and 7363 IU of epoetin alfa q3wk during EEP (Week 16 to 23) up to 23 weeks.

Measured Values

	C.E.R.A	Epoetin Alfa
Number of Participants Analyzed	65	36
Change in Hb Concentrations Between Baseline SVP and the EEP [units: g/dL] Mean (Standard Deviation)	-0.35 (1.32)	0.32 (1.06)

3. Secondary Outcome Measure:

Measure Title	Percentage of Participants Who Maintained Hb Concentration Between 10 and 12 g/dL Throughout the EEP

Measure Description	Participants who maintained Hb concentration between 10 to 12 g/dL throughout the EEP are reported.
Time Frame	EEP (Week 16 to 23)
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
C.E.R.A	Participants received starting dose of 120, 200 or 360 mcg of C.E.R.A IV once monthly for 6 months. The starting dose was based on the dose of epoetin alfa administered in Week -1.
Epoetin Alfa	Participants received IV injection of 6000 IU of epoetin alfa q3wk during the SVP (Week -4 to -1), 7443 IU of epoetin alfa q3wk during DTP (Week 0 to 15), and 7363 IU of epoetin alfa q3wk during EEP (Week 16 to 23) up to 23 weeks.

Measured Values

	C.E.R.A	Epoetin Alfa
Number of Participants Analyzed	65	36
Percentage of Participants Who Maintained Hb Concentration Between 10 and 12 g/dL Throughout the EEP [units: percentage of participants]	32.7	40.6

4. Secondary Outcome Measure:

Measure Title	Mean Time Spent in Hb Range 10-12 g/dL
Measure Description	
Time Frame	SVP (Week -4 to -1), DTP (Week 0 to 15), and EEP (Week 16 to 23)
Safety Issue?	No

Analysis Population Description

ITT population. Here, n = participants who were evaluable for each category, for respective arm groups.

Reporting Groups

	Description
C.E.R.A	Participants received starting dose of 120, 200 or 360 mcg of C.E.R.A IV once monthly for 6 months. The starting dose was based on the dose of epoetin alfa administered in Week -1.
Epoetin Alfa	Participants received IV injection of 6000 IU of epoetin alfa q3wk during the SVP (Week -4 to -1), 7443 IU of epoetin alfa q3wk during DTP (Week 0 to 15), and 7363 IU of epoetin alfa q3wk during EEP (Week 16 to 23) up to 23 weeks.

Measured Values

	C.E.R.A	Epoetin Alfa
Number of Participants Analyzed	65	36
Mean Time Spent in Hb Range 10-12 g/dL [units: days] Mean (Standard Deviation)		
SVP (Week -4 to -1) (n=65, 36)	26.7 (4.46)	27.1 (4.74)
DTP (Week 0 to 15) (n=65, 36)	67.5 (33.92)	72.9 (37.03)
EEP (Week 16 to 23) (n=55, 32)	32.2 (18.25)	28.9 (21.53)

5. Secondary Outcome Measure:

Measure Title	Percentage of Participants Who Required Dose Adjustments During the DTP and EEP
Measure Description	
Time Frame	DTP (Week 0 to 15) and EEP (Week 16 to 23)
Safety Issue?	No

Analysis Population Description

Safety population included all those participants who were treated with at least one dose of the trial medication and had a safety follow-up, whether withdrawn prematurely or not. Here, "n" = participants who were evaluable for each category, for respective arm groups.

Reporting Groups

	Description
C.E.R.A	Participants received starting dose of 120, 200 or 360 mcg of C.E.R.A IV once monthly for 6 months. The starting dose was based on the dose of epoetin alfa administered in Week -1.

	Description
Epoetin Alfa	Participants received IV injection of 6000 IU of epoetin alfa q3wk during the SVP (Week -4 to -1), 7443 IU of epoetin alfa q3wk during DTP (Week 0 to 15), and 7363 IU of epoetin alfa q3wk during EEP (Week 16 to 23) up to 23 weeks.

Measured Values

	C.E.R.A	Epoetin Alfa
Number of Participants Analyzed	65	36
Percentage of Participants Who Required Dose Adjustments During the DTP and EEP [units: percentage of participants]		
DTP: No dose change (n=65, 36)	30.8	44.4
DTP: Any dose change (n=65, 36)	67.7	55.6
DTP: Dose increased (n=65, 36)	18.5	19.4
DTP: Dose decreased (n=65, 36)	24.6	25.0
DTP: Dose decreased and increased (n=65, 36)	24.6	11.1
DTP:Only one dose changed (n=65,36)	1.5	0.0
EEP: No dose change (n=55, 32)	60.0	65.6
EEP: Any dose change (n=55, 32)	30.9	34.4
EEP: Dose increased (n=55, 32)	20.0	12.5
EEP: Dose decreased (n=55, 32)	10.9	18.8
EEP: Dose decreased and increased (n=55, 32)	0.0	3.1
EEP: Only one dose changed (n=55, 32)	9.1	0.0

6. Secondary Outcome Measure:

Measure Title	Percentage of Participants Who Received Red Blood Cell (RBC) Transfusions During DTP and EEP
Measure Description	RBC transfusions could be given during the study in case of medical need, i.e., in severely anemic participants with recognized symptoms or signs of anemia (e.g., in participants with acute blood loss, with severe angina, or whose hemoglobin decreased to critical levels).
Time Frame	DTP (Week 0 to 15) up to EEP (Week 16 to 23)

Safety Issue?	No

Analysis Population Description
ITT population

Reporting Groups

	Description
C.E.R.A	Participants received starting dose of 120, 200 or 360 mcg of C.E.R.A IV once monthly for 6 months. The starting dose was based on the dose of epoetin alfa administered in Week -1.
Epoetin Alfa	Participants received IV injection of 6000 IU of epoetin alfa q3wk during the SVP (Week -4 to -1), 7443 IU of epoetin alfa q3wk during DTP (Week 0 to 15), and 7363 IU of epoetin alfa q3wk during EEP (Week 16 to 23) up to 23 weeks.

Measured Values

	C.E.R.A	Epoetin Alfa
Number of Participants Analyzed	65	36
Percentage of Participants Who Received Red Blood Cell (RBC) Transfusions During DTP and EEP [units: percentage of participants]	12.3	2.8

Reported Adverse Events

Time Frame	Week 0 to Week 28
Additional Description	[Not specified]

Reporting Groups

	Description
C.E.R.A	Participants received starting dose of 120, 200 or 360 mcg of C.E.R.A IV once monthly for 6 months. The starting dose was based on the dose of epoetin alfa administered in Week -1.
Epoetin Alfa	Participants received IV injection of 6000 IU of epoetin alfa q3wk during the SVP (Week -4 to -1), 7443 IU of epoetin alfa q3wk during DTP (Week 0 to 15), and 7363 IU of epoetin alfa q3wk during EEP (Week 16 to 23) up to 23 weeks.

Serious Adverse Events

	C.E.R.A	Epoetin Alfa
	Affected/At Risk (%)	Affected/At Risk (%)
Total	16/65 (24.62%)	4/36 (11.11%)
Blood and lymphatic system disorders		
Anaemia [A] *	1/65 (1.54%)	0/36 (0%)
Cardiac disorders		
Acute myocardial infarction [A] *	1/65 (1.54%)	0/36 (0%)
Angina pectoris [A] *	1/65 (1.54%)	0/36 (0%)
Cardiac arrest [A] *	1/65 (1.54%)	0/36 (0%)
Cardiac failure congestive [A] *	1/65 (1.54%)	0/36 (0%)
Myocardial infarction [A] *	1/65 (1.54%)	0/36 (0%)
Gastrointestinal disorders		
Intestinal obstruction [A] *	1/65 (1.54%)	0/36 (0%)
General disorders		
Death [A] *	0/65 (0%)	1/36 (2.78%)
Pyrexia [A] *	1/65 (1.54%)	0/36 (0%)
Hepatobiliary disorders		
Cholecystitis acute [A] *	1/65 (1.54%)	0/36 (0%)
Infections and infestations		
Bronchiectasis [A] *	1/65 (1.54%)	0/36 (0%)
Cellulitis [A] *	1/65 (1.54%)	0/36 (0%)
Lung infection pseudomonal [A] *	1/65 (1.54%)	0/36 (0%)
Pneumonia [A] *	2/65 (3.08%)	0/36 (0%)
Pyelonephritis [A] *	0/65 (0%)	1/36 (2.78%)

	C.E.R.A	Epoetin Alfa
	Affected/At Risk (%)	Affected/At Risk (%)
Respiratory tract infection [A] *	1/65 (1.54%)	1/36 (2.78%)
Sepsis [A] *	1/65 (1.54%)	0/36 (0%)
Urinary tract infection [A] *	0/65 (0%)	1/36 (2.78%)
Injury, poisoning and procedural complications		
Hip fracture [A] *	1/65 (1.54%)	0/36 (0%)
Musculoskeletal and connective tissue disorders		
Back pain [A] *	1/65 (1.54%)	0/36 (0%)
Nervous system disorders		
Ischaemic neuropathy [A] *	1/65 (1.54%)	0/36 (0%)
Psychiatric disorders		
Confusional state [A] *	1/65 (1.54%)	0/36 (0%)
Respiratory, thoracic and mediastinal disorders		
Asthma [A] *	1/65 (1.54%)	0/36 (0%)
Vascular disorders		
Peripheral ischaemia [A] *	1/65 (1.54%)	0/36 (0%)
Shock [A] *	1/65 (1.54%)	0/36 (0%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (12.0)

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

	C.E.R.A	Epoetin Alfa
	Affected/At Risk (%)	Affected/At Risk (%)
Total	11/65 (16.92%)	9/36 (25%)
Cardiac disorders		

	C.E.R.A	Epoetin Alfa
	Affected/At Risk (%)	Affected/At Risk (%)
Atrial fibrillation [A] *	5/65 (7.69%)	0/36 (0%)
Infections and infestations		
Nasopharyngitis [A] *	1/65 (1.54%)	2/36 (5.56%)
Metabolism and nutrition disorders		
Hyperlipidaemia [A] *	0/65 (0%)	2/36 (5.56%)
Hyperphosphataemia [A] *	0/65 (0%)	2/36 (5.56%)
Vascular disorders		
Hypertension [A] *	6/65 (9.23%)	4/36 (11.11%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (12.0)

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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