ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: May 17, 2016

ClinicalTrials.gov ID: NCT00642850

Study Identification

Unique Protocol ID:	ML21040
Brief Title:	STABIL Study: National Study With Mircera for Maintenance of Hemoglobin Level in Dialysis Patients
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:	

Study Status

Record Verification:	May 2016
Overall Status:	Completed
Study Start:	November 2007 []
Primary Completion:	July 2009 [Actual]
Study Completion:	July 2009 [Actual]

Sponsor/Collaborators

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

Oversight

U.S. FDA-regulated Drug:	
U.S. FDA-regulated Device:	

Unapproved/Uncleared Device:	No
U.S. FDA IND/IDE:	No
Human Subjects Review:	Board Status: Approved Approval Number: 1555/07 (L07/70) Board Name: Ethics Committee of the Institute for Clin. and Exp. Medicine and Faculty Thomayer Hospital Board Affiliation: Unknown Phone: 420-261-083-481 Email: Address: Videnska 800, 140 59 Praha 4, Czech Republic
Data Monitoring:	
FDA Regulated Intervention:	No

Study Description

Brief Summary:	This single arm study will assess the efficacy, safety and tolerability of once-monthly administration of intravenous Mircera for the maintenance of hemoglobin levels in dialysis participants with chronic renal anemia. Participants will receive monthly intravenous injections of Mircera, at a starting dose of 120, 200 or 360 micrograms, according to the dose of epoetin administered in the week preceding first study drug administration. The anticipated time on study treatment is 3-12 months, 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
Interventional Study Model:	Single Group Assignment
Number of Arms:	1

Masking:	None (Open Label)
Allocation:	N/A
Enrollment:	188 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: 1	Drug: methoxy polyethylene glycol-epoetin beta [Mircera] 120, 200 or 360 micrograms iv monthly (starting dose)

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age:	18 Years
Maximum Age:	
Sex:	All
Gender Based:	
Accepts Healthy Volunteers:	No

Criteria: Inclusion Criteria:

- Chronic renal anemia;
- Continuous stable intravenous maintenance epoetin therapy during previous month;
- Regular long-term hemodialysis therapy with the same mode of dialysis for previous 3 months.

Exclusion Criteria:

- Transfusion of red blood cells during previous 2 months;
- Poorly controlled hypertension, that is, sitting blood pressure exceeding 170/100 millimeter of mercury (mmHg) despite medication;
- Significant acute or chronic bleeding.

Contacts/Locations

Central Contact Person: Reference Study ID Number: ML21040 www.roche.com/about_roche/roche_worldwide.htm
Telephone: 888-662-6728 (U.S. Only)
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Central Contact Backup:

Study Officials: Clinical Trials
Study Director
Hoffmann-La Roche

Locations: **Czechia**

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USTI NAD LABEM, Czechia, 401 13

LIBEREC, Czechia, 460 63

Kolin III, Czechia, 280 20

PRAHA 6, Czechia, 169 00

STRAKONICE, Czechia, 38629

SUMPERK, Czechia, 787 01

JIHLAVA, Czechia, 586 33

TABOR, Czechia, 390 03

HAVIROV, Czechia, 736 24

PRAHA, Czechia, 128 08

ZNOJMO, Czechia, 76275

KARLOVY VARY, Czechia, 360 73

DECIN, Czechia, 405 99

HRADEC KRALOVE, Czechia, 500 05

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TEPLICE, Czechia, 415 01

BRNO, Czechia, 656 91

OSTRAVA, Czechia, 708 52

TREBIC, Czechia, 674 01

OLOMOUC, Czechia, 775 20

PRAHA, Czechia, 14000

IPDSharing

Plan to Share IPD:

References

Citations:

Links:

Available IPD/Information:

Study Results

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) intravenous methoxy polyethylene glycol-epoetin 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	188
Completed	155
Not Completed	33
Death	7

	C.E.R.A.
Adverse Event	2
Lack of Efficacy	1
Protocol Violation	2
Kidney transplantation	8
Blood transfusion	6
Other reasons	7

Baseline Characteristics

Baseline Analysis Population Description

The safety population was defined as all participants enrolled into the study.

Reporting Groups

	Description
C.E.R.A.	Adult participants with chronic renal disease and who had received intravenous epoetin maintenance treatment, received 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.
Overall Number of Participants		188
Age, Continuous Mean (Standard Deviation) Unit of measure: years	Number Analyzed	188 participants
		64.9 (11.56)
Sex: Female, Male Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	188 participants
	Female	84 44.68%
	Male	104 55.32%

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants Maintaining Average Hemoglobin Concentration Within +/-1 Gram Per Deciliter (g/dL) of Reference and Within the Target Range
Measure Description	Percentage of participants maintaining their mean hemoglobin concentration in g/dL within plus or minus (+/-) 1 g/dL of their reference hemoglobin value, and between the target range of 10.0 and 12.0 g/dL during the efficacy evaluation period (EEP). 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 up to Week 24) was estimated as a time adjusted average.
Time Frame	Week 17 up to Week 24

Analysis Population Description

Per protocol (PP) population included all participants in the safety population with the exception of participants with less than 3 recorded hemoglobin values, missing administrations of C.E.R.A., withdrawal, inadequate iron status in Weeks 16-24.

Reporting Groups

	Description
C.E.R.A.	Adult participants with chronic renal disease and who had received intravenous epoetin maintenance treatment, received 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.
Overall Number of Participants Analyzed	154
Percentage of Participants Maintaining Average Hemoglobin Concentration Within +/-1 Gram Per Deciliter (g/dL) of Reference and Within the Target Range Number (95% Confidence Interval) Unit of measure: percentage of participants	53.3 (45.1 to 61.3)

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 -1) and the value during EEP (Week 17 up to Week 24) was assessed.

Time Frame	Week -4 up to Week -1 and Week 17 up to Week 24

Analysis Population Description

The Intention-to-treat (ITT) population included all participants who had received at least 1 dose of C.E.R.A. (Week 0) and for whom data for at least 1 follow-up variable had been available.

Reporting Groups

	Description
C.E.R.A.	Adult participants with chronic renal disease and who had received intravenous epoetin maintenance treatment, received 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.
Overall Number of Participants Analyzed	186
Change in Hemoglobin Concentration Between Reference (SVP) and EEP Mean (Standard Deviation) Unit of measure: g/dL	0.0 (1.21)

3. Secondary Outcome Measure:

Measure Title	Percentage of Participants Maintaining Hemoglobin Concentration Within the Target Range During EEP
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

Analysis Population Description

ITT Population.

Reporting Groups

	Description
C.E.R.A.	Adult participants with chronic renal disease and who had received intravenous epoetin maintenance treatment, received 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.
Overall Number of Participants Analyzed	186
Percentage of Participants Maintaining Hemoglobin Concentration Within the Target Range During EEP Number (95% Confidence Interval) Unit of measure: percentage of participants	57.0 (49.5 to 64.2)

4. Secondary Outcome Measure:

Measure Title	Mean Time Spent by Participants With Hemoglobin Concentration in the Target Range During the EEP
Measure Description	Mean time spent by participants with hemoglobin concentration in 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

Analysis Population Description
ITT Population.

Reporting Groups

	Description
C.E.R.A.	Adult participants with chronic renal disease and who had received intravenous epoetin maintenance treatment, received 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.
Overall Number of Participants Analyzed	186
Mean Time Spent by Participants With Hemoglobin Concentration in the Target Range During the EEP Mean (Standard Deviation) Unit of measure: days	32 (18.4)

5. Secondary Outcome Measure:

Measure Title	Percentage of Participants Requiring Any Dose Adjustment
Measure Description	Percentage of participants requiring 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 to Week 16 and Week 17 to Week 24

Analysis Population Description

ITT Population. Here, 'N' (number of participants analyzed) signifies the number of participants evaluable for this outcome measure and 'n' signifies the number of participants evaluable for specified category.

Reporting Groups

	Description
C.E.R.A.	Adult participants with chronic renal disease and who had received intravenous epoetin maintenance treatment, received 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.
Overall Number of Participants Analyzed	186
Percentage of Participants Requiring Any Dose Adjustment Measure Type: Number Unit of measure: percentage of participants	
DTP (n = 186)	75.0
EEP (n = 165)	32.0

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 28

Analysis Population Description

ITT Population.

Reporting Groups

	Description
C.E.R.A.	Adult participants with chronic renal disease and who had received intravenous epoetin maintenance treatment, received 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.
Overall Number of Participants Analyzed	186
Number of Participants With Red Blood Cell Transfusion During the Study Measure Type: Number Unit of measure: participants	9

7. Secondary Outcome Measure:

Measure Title	Number of Participants With Anti-epoetin Antibody
Measure Description	
Time Frame	Week -4 and at early withdrawal or Week 28

Analysis Population Description
ITT Population.

Reporting Groups

	Description
C.E.R.A.	Adult participants with chronic renal disease and who had received intravenous epoetin maintenance treatment, received 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.
Overall Number of Participants Analyzed	186
Number of Participants With Anti-epoetin Antibody Measure Type: Number Unit of measure: participants	
Week -4	0
Early Withdrawal or Week 28	0

Reported Adverse Events

Time Frame	Up to 28 weeks
Adverse Event Reporting Description	Only adverse events with an onset date after the start of medication included.

Reporting Groups

	Description
C.E.R.A.	Adult participants with chronic renal disease and who had received intravenous epoetin maintenance treatment, received intravenous C.E.R.A. at starting dose of 120, 200, or 360 mcg every 4 weeks for 24 weeks.

All-Cause Mortality

	C.E.R.A.
	Affected/At Risk (%)
Total All-Cause Mortality	/

Serious Adverse Events

	C.E.R.A.
	Affected/At Risk (%)
Total	41/188 (21.81%)
Cardiac disorders	
Angina pectoris [A] *	1/188 (0.53%)
Atrial fibrillation [A] *	2/188 (1.06%)
Atrioventricular block [A] *	1/188 (0.53%)
Cardiac arrest [A] *	1/188 (0.53%)
Cardiac failure [A] *	1/188 (0.53%)
Myocardial ischaemia [A] *	1/188 (0.53%)
Ventricular fibrillation [A] *	1/188 (0.53%)

	C.E.R.A.
	Affected/At Risk (%)
Gastrointestinal disorders	
Coeliac artery stenosis [A] *	1/188 (0.53%)
Dyspepsia [A] *	2/188 (1.06%)
Gastric ulcer haemorrhage [A] *	1/188 (0.53%)
Gastric ulcer perforation [A] *	1/188 (0.53%)
Haemorrhoidal haemorrhage [A] *	1/188 (0.53%)
Intestinal angina [A] *	1/188 (0.53%)
Intestinal haemorrhage [A] *	1/188 (0.53%)
General disorders	
Sudden death [A] *	1/188 (0.53%)
Infections and infestations	
Arteriovenous fistula site infection [A] *	1/188 (0.53%)
Bronchitis [A] *	2/188 (1.06%)
Catheter sepsis [A] *	2/188 (1.06%)
Chlamydial infection [A] *	1/188 (0.53%)
Gastroenteritis [A] *	1/188 (0.53%)
Haematoma infection [A] *	1/188 (0.53%)
Herpes zoster [A] *	1/188 (0.53%)
Sepsis [A] *	2/188 (1.06%)
Wound infection staphylococcal [A] *	1/188 (0.53%)
Injury, poisoning and procedural complications	
Accident [A] *	1/188 (0.53%)
Arteriovenous fistula site complication [A] *	1/188 (0.53%)

	C.E.R.A.
	Affected/At Risk (%)
Complications of transplanted kidney [A] *	1/188 (0.53%)
Concussion [A] *	1/188 (0.53%)
Femur fracture [A] *	1/188 (0.53%)
Graft complication [A] *	1/188 (0.53%)
Humerus fracture [A] *	1/188 (0.53%)
Post procedural haemorrhage [A] *	1/188 (0.53%)
Investigations	
Arteriogram [A] *	1/188 (0.53%)
Arteriogram coronary [A] *	2/188 (1.06%)
Metabolism and nutrition disorders	
Fluid retention [A] *	1/188 (0.53%)
Musculoskeletal and connective tissue disorders	
Polymyalgia rheumatica [A] *	1/188 (0.53%)
Spondylolisthesis [A] *	1/188 (0.53%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	
Benign pancreatic neoplasm [A] *	1/188 (0.53%)
Lung carcinoma cell type unspecified stage III [A] *	1/188 (0.53%)
Nervous system disorders	
Carotid artery stenosis [A] *	1/188 (0.53%)
Cerebral haemorrhage [A] *	2/188 (1.06%)
Cerebrovascular accident [A] *	1/188 (0.53%)
Subarachnoid haemorrhage [A] *	1/188 (0.53%)

	C.E.R.A.
	Affected/At Risk (%)
Transient ischaemic attack [A] *	1/188 (0.53%)
Reproductive system and breast disorders	
Breast dysplasia [A] *	1/188 (0.53%)
Respiratory, thoracic and mediastinal disorders	
Dyspnoea [A] *	1/188 (0.53%)
Hydrothorax [A] *	2/188 (1.06%)
Skin and subcutaneous tissue disorders	
Dry gangrene [A] *	1/188 (0.53%)
Surgical and medical procedures	
Arteriovenous fistula operation [A] *	1/188 (0.53%)
Coronary artery bypass [A] *	1/188 (0.53%)
Surgery [A] *	1/188 (0.53%)
Vascular disorders	
Aneurysm ruptured [A] *	1/188 (0.53%)
Hypertension [A] *	1/188 (0.53%)
Shock [A] *	1/188 (0.53%)

***** 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.
	Affected/At Risk (%)
Total	38/188 (20.21%)
Gastrointestinal disorders	
Diarrhoea [A] *	11/188 (5.85%)

	C.E.R.A.
	Affected/At Risk (%)
Infections and infestations	
Bronchitis [A] *	10/188 (5.32%)
Vascular disorders	
Hypertension [A] *	22/188 (11.7%)

* 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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