ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 08/17/2016

ClinicalTrials.gov ID: NCT00605345

Study Identification

Unique Protocol ID:	ML21058
Brief Title:	A Study Comparing Subcutaneous Mircera and Darbepoetin Alfa for Maintenance Treatment of Anemia in Kidney Transplant Recipients.
Official Title:	An Open Label Randomised Controlled Study to Compare the Efficacy, Safety and Tolerability of Once-monthly Administration of Subcutaneous Mircera Versus Darbepoetin Alfa for the Maintenance of Haemoglobin Levels in Renal Transplant Recipients With Chronic Renal Anaemia.
Secondary IDs:	

Study Status

Record Verification:	April 2016
Overall Status:	Completed
Study Start:	December 2007
Primary Completion:	July 2009 [Actual]
Study Completion:	July 2009 [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: unknown Board Name: Comite Etico de Investigacion Clinica del Hospital Clinic I Provincial de Barcelona Board Affiliation: Unknown Phone: 0034 93 227 5400 Email: bgomez@clinic.ub.es
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	Spain: AEMPS

Study Description

Brief Summary:	This two arm study will compare the efficacy and safety of subcutaneous Mircera versus darbepoetin alfa for the maintenance of hemoglobin levels in kidney transplant recipients with chronic renal anemia. Patients currently receiving maintenance treatment with darbepoetin alfa will be randomized either to receive 4-weekly injections of Mircera with a starting dose (120, 200 or 360 micrograms subcutaneously) derived from the dose of darbepoetin alfa they were receiving in the 2 weeks preceding study start, or to stay on 2-weekly darbepoetin alfa therapy. 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
Intervention Model:	Parallel Assignment

Number of Arms:	2
Masking:	Open Label
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	71 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: CERA Treatment Once Monthly	Drug: methoxy polyethylene glycol-epoetin beta [Mircera] 120, 200 or 360 micrograms sc 4-weekly (starting dose)
Active Comparator: Darbepoetin Alfa Once Biweekly	Drug: Darbepoetin alfa As prescribed

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age:	18 Years
Maximum Age:	
Gender:	Both
Accepts Healthy Volunteers?:	No
Criteria:	Inclusion Criteria:

- adult patients, > or = 18 years of age;
- kidney transplant recipients with stage 3 or stage 4 chronic kidney disease;
- functioning graft of > 6 months and < 10 years after kidney transplantation, with no signs of acute rejection;
- stable maintenance subcutaneous darbepoetin alfa therapy every 2 weeks.

Exclusion Criteria:

- transfusion of red blood cells during previous 2 months;
- poorly controlled hypertension;
- significant acute or chronic bleeding;
- need for dialysis therapy expected in next 6 months.

Contacts/Locations

Study Officials: Clinical Trials
Study Director
Hoffmann-La Roche

Locations: Spain

Santander, Cantabria, Spain, 39008

La Coruna, La Coruña, Spain, 15006

Santiago de Compostela, La Coruña, Spain, 15706

Barcelona, Barcelona, Spain, 08003

Alicante, Alicante, Spain, 03010

Madrid, Madrid, Spain, 28040

Madrid, Madrid, Spain, 28222

Valencia, Valencia, Spain, 46017

Granada, Granada, Spain, 18014

Barakaldo, Vizcaya, Spain, 48903

Hospitalet de Llobregat, Barcelona, Spain, 08907

Madrid, Madrid, Spain, 28041

Barcelona, Barcelona, Spain, 08036

Madrid, Madrid, Spain, 28007

Barcelona, Barcelona, Spain, 08025

Córdoba, Cordoba, Spain, 14004

Badajoz, Badajoz, Spain, 06080

Ciudad Real, Ciudad Real, Spain, 13005

Badalona, Barcelona, Spain, 08915

Galdakao, Vizcaya, Spain, 48960

Valladolid, Valladolid, Spain, 47005

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Reporting Groups

	Description
CERA Treatment Once Monthly	CERA 120, 200 or 360 micrograms subcutaneously
Darbepoetin Alfa Once Biweekly	Darbepoetin Alfa as prescribed

Overall Study

	CERA Treatment Once Monthly	Darbepoetin Alfa Once Biweekly
Started	46	25
Completed	45	22
Not Completed	1	3
Withdrawal by Subject	1	0
Adverse Event	0	1
Protocol Violation	0	2

Baseline Characteristics

Reporting Groups

	Description
CERA Treatment Once Monthly	CERA 120, 200 or 360 micrograms subcutaneously

	Description
Darbepoetin Alfa Once Biweekly	Darbepoetin Alfa as prescribed

Baseline Measures

	CERA Treatment Once Monthly	Darbepoetin Alfa Once Biweekly	Total
Number of Participants	46	25	71
Age, Continuous [units: years] Mean (Standard Deviation)	54.6 (11.04)	56.7 (10.49)	55.3 (10.82)
Gender, Male/Female [units: participants]			
Female	27	8	35
Male	19	17	36
Region of Enrollment Spain [units: participants]	46	25	71

Outcome Measures

1. Primary Outcome Measure:

Measure Title	The Percentage of Participants Maintaining Average Haemoglobin (Hb) Concentration During the Efficacy Evaluation Period (EEP) Within the Target Range
Measure Description	Key outcomes will be assessed during the first 12 weeks following the 16 weeks dose titration period, i.e. during the Efficacy Evaluation Period (EEP). Assessments performed every four weeks, beginning at week 16 up to week 28. The reference haemoglobin is defined as the mean of the two assessments recorded during the SVP (weeks -4 and -2). For the purposes of efficacy assessment the target haemoglobin concentration range will be defined as ± 1 g/dL of the reference haemoglobin concentration AND within the range 10 – 12 g/dL.
Time Frame	Weeks 16-28
Safety Issue?	No

Analysis Population Description

Analysis was performed in the per protocol (PP) population.

Reporting Groups

	Description
CERA Treatment Once Monthly	CERA 120, 200 or 360 micrograms subcutaneously
Darbepoetin Alfa Once Biweekly	Darbepoetin Alfa as prescribed

Measured Values

	CERA Treatment Once Monthly	Darbepoetin Alfa Once Biweekly
Number of Participants Analyzed	42	21
The Percentage of Participants Maintaining Average Haemoglobin (Hb) Concentration During the Efficacy Evaluation Period (EEP) Within the Target Range [units: percentage of participants] Number (95% Confidence Interval)	64.29 (48.03 to 78.45)	57.14 (34.02 to 78.18)

Statistical Analysis 1 for The Percentage of Participants Maintaining Average Haemoglobin (Hb) Concentration During the Efficacy Evaluation Period (EEP) Within the Target Range

Statistical Analysis Overview	Comparison Groups	CERA Treatment Once Monthly, Darbepoetin Alfa Once Biweekly
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	Yes
	Comments	Non-inferiority was met if the lower limit of the confidence interval for the response rate of the CERA group was greater than the observed response rate of the darbepoetin group minus 15%. The calculated lower limit of an acceptable difference in response rates thus, was based on the actual percentage of “responders“ in the darbepoetin group and this percentage minus 15% had to be excluded.

Statistical Test of Hypothesis	P-Value	0.5947
	Comments	[Not specified]
	Method	Fisher Exact
	Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Mean Change in Hb Concentration From Baseline to Efficacy Evaluation Period (EEP)
Measure Description	Reference haemoglobin at baseline is defined as the mean of the two assessments recorded at weeks -4 and -2. Additional assessments were then performed every 4 weeks at week 0 through week 28. Mean change was calculated as value at 28 weeks minus baseline.
Time Frame	Baseline to 28 weeks
Safety Issue?	No

Analysis Population Description

Analysis performed in the Intent toTreat (ITT) population, which includes all participants receiving at least one dose of the study drug.

Reporting Groups

	Description
CERA Treatment Once Monthly	CERA 120, 200 or 360 micrograms subcutaneously
Darbepoetin Alfa Once Biweekly	Darbepoetin Alfa as prescribed

Measured Values

	CERA Treatment Once Monthly	Darbepoetin Alfa Once Biweekly
Number of Participants Analyzed	46	25
Mean Change in Hb Concentration From Baseline to Efficacy Evaluation Period (EEP) [units: g/dL] Mean (Standard Deviation)	0.08 (0.85)	0.05 (1.06)

3. Secondary Outcome Measure:

Measure Title	Percentage of Participants Maintaining Hb Concentration in 10-12 g/dL Range Throughout the Efficacy Evaluation Period (EEP)
Measure Description	
Time Frame	Weeks 16-28
Safety Issue?	No

Analysis Population Description

Analysis performed with intent to treat (ITT) population, which includes all participants receiving at least one dose of the study drug.

Reporting Groups

	Description
CERA Treatment Once Monthly	CERA 120, 200 or 360 micrograms subcutaneously
Darbepoetin Alfa Once Biweekly	Darbepoetin Alfa as prescribed

Measured Values

	CERA Treatment Once Monthly	Darbepoetin Alfa Once Biweekly
Number of Participants Analyzed	46	25

	CERA Treatment Once Monthly	Darbepoetin Alfa Once Biweekly
Percentage of Participants Maintaining Hb Concentration in 10-12 g/dL Range Throughout the Efficacy Evaluation Period (EEP) [units: percentage of participants]	71.7	64.0

4. Secondary Outcome Measure:

Measure Title	Mean Time Spent in 10-12g/dL Range During the Efficacy Evaluation Period (EEP)
Measure Description	Efficacy Evaluation Period was the 12 weeks following 16 weeks of treatment in the Dose Titration Period.
Time Frame	Weeks 16-28
Safety Issue?	No

Analysis Population Description

Analysis was performed using the intent to treat (ITT) population, which includes all participants receiving at least one dose of the study drug.

Reporting Groups

	Description
CERA Treatment Once Monthly	CERA 120, 200 or 360 micrograms subcutaneously
Darbepoetin Alfa Once Biweekly	Darbepoetin Alfa as prescribed

Measured Values

	CERA Treatment Once Monthly	Darbepoetin Alfa Once Biweekly
Number of Participants Analyzed	46	25
Mean Time Spent in 10-12g/dL Range During the Efficacy Evaluation Period (EEP) [units: days] Mean (Standard Deviation)	57.0 (23.98)	50.5 (27.7)

5. Secondary Outcome Measure:

Measure Title	Percentage of Participants Needing Dose Adjustments
Measure Description	Assessment of the Dose Titration Period of 16 weeks of treatment and following 12 weeks, known as the Efficacy Evaluation Period (EEP).

Time Frame	Up to 28 weeks
Safety Issue?	No

Analysis Population Description

Analysis was performed on the safety population.

Reporting Groups

	Description
CERA Treatment Once Monthly	CERA 120, 200 or 360 micrograms subcutaneously
Darbepoetin Alfa Once Biweekly	Darbepoetin Alfa as prescribed

Measured Values

	CERA Treatment Once Monthly	Darbepoetin Alfa Once Biweekly
Number of Participants Analyzed	46	25
Percentage of Participants Needing Dose Adjustments [units: percentage of participants]		
Dose Titration Period	73.9	56.0
Efficacy Evaluation Period (n=45,23)	33.3	20.8

6. Secondary Outcome Measure:

Measure Title	Incidence of RBC Transfusions
Measure Description	Assessment of the Dose Titration Period of 16 weeks of treatment and following 12 weeks, known as the Efficacy Evaluation Period (EEP).
Time Frame	Up to 28 weeks
Safety Issue?	No

Analysis Population Description

Analysis performed with the intent to treat (ITT) population, which includes all participants receiving at least one dose of the study drug.

Reporting Groups

	Description
CERA Treatment Once Monthly	CERA 120, 200 or 360 micrograms subcutaneously

	Description
Darbepoetin Alfa Once Biweekly	Darbepoetin Alfa as prescribed

Measured Values

	CERA Treatment Once Monthly	Darbepoetin Alfa Once Biweekly
Number of Participants Analyzed	46	25
Incidence of RBC Transfusions [units: participants]	1	2

Reported Adverse Events

Time Frame	Up to 28 weeks
Additional Description	The intent to treat (ITT) population included all participants receiving at least one dose of the study drug. This population was primarily used for the reporting of safety information.

Reporting Groups

	Description
CERA Treatment Once Monthly	CERA 120, 200 or 360 micrograms subcutaneously
Darbepoetin Alfa Once Biweekly	Darbepoetin Alfa as prescribed

Serious Adverse Events

	CERA Treatment Once Monthly		Darbepoetin Alfa Once Biweekly	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Total	9/46 (19.57%)		3/25 (12%)	
Blood and lymphatic system disorders				
Lymphadenopathy [A] †	1/46 (2.17%)	1	0/25 (0%)	0
Cardiac disorders				
Arrhythmia [A] †	1/46 (2.17%)	1	0/25 (0%)	0
Cardiac Failure Congestive [A] †	0/46 (0%)	0	1/25 (4%)	1

	CERA Treatment Once Monthly		Darbepoetin Alfa Once Biweekly	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Infections and infestations				
Gastroenteritis [A] †	1/46 (2.17%)	1	0/25 (0%)	0
Pyelonephritis [A] †	2/46 (4.35%)	3	1/25 (4%)	1
Respiratory Tract Infection [A] †	2/46 (4.35%)	2	0/25 (0%)	0
Urinary Tract Infection [A] †	1/46 (2.17%)	1	0/25 (0%)	0
Injury, poisoning and procedural complications				
Device Breakage [A] †	1/46 (2.17%)	1	0/25 (0%)	0
Metabolism and nutrition disorders				
Hypocalcaemia [A] †	0/46 (0%)	0	2/25 (8%)	2
Nervous system disorders				
Sciatica [A] †	1/46 (2.17%)	1	0/25 (0%)	0
Renal and urinary disorders				
Proteinuria [A] †	1/46 (2.17%)	1	0/25 (0%)	0
Respiratory, thoracic and mediastinal disorders				
Laryngeal Granuloma [A] †	1/46 (2.17%)	1	0/25 (0%)	0
Vascular disorders				
Aneurysm [A] †	1/46 (2.17%)	1	0/25 (0%)	0

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 12.0

Other Adverse Events

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

	CERA Treatment Once Monthly		Darbepoetin Alfa Once Biweekly	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Total	27/46 (58.7%)		16/25 (64%)	
Gastrointestinal disorders				

	CERA Treatment Once Monthly		Darbepoetin Alfa Once Biweekly	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Diarrhoea [A] †	4/46 (8.7%)	4	2/25 (8%)	2
General disorders				
Asthenia [A] †	0/46 (0%)	0	2/25 (8%)	2
Fatigue [A] †	0/46 (0%)	0	3/25 (12%)	3
Oedema [A] †	2/46 (4.35%)	2	2/25 (8%)	2
Oedema Peripheral [A] †	3/46 (6.52%)	3	3/25 (12%)	3
Infections and infestations				
Escherichia Urinary Tract Infection [A] †	5/46 (10.87%)	5	0/25 (0%)	0
Influenza [A] †	3/46 (6.52%)	4	1/25 (4%)	1
Nasopharyngitis [A] †	2/46 (4.35%)	2	4/25 (16%)	4
Upper Respiratory Tract Infection [A] †	6/46 (13.04%)	6	0/25 (0%)	0
Urinary Tract Infection [A] †	4/46 (8.7%)	4	2/25 (8%)	2
Metabolism and nutrition disorders				
Hypocalcaemia [A] †	0/46 (0%)	0	2/25 (8%)	3
Musculoskeletal and connective tissue disorders				
Arthralgia [A] †	0/46 (0%)	0	2/25 (8%)	2
Respiratory, thoracic and mediastinal disorders				
Dyspnoea [A] †	1/46 (2.17%)	1	2/25 (8%)	2
Vascular disorders				
Hypertension [A] †	9/46 (19.57%)	9	3/25 (12%)	3

† Indicates events were collected by systematic assessment.
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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