ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
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A Study of Subcutaneous Mircera in Patients With Chronic Kidney Disease, Not on Dialysis.

This study has been completed.

Sponsor:	Hoffmann-La Roche
Collaborators:	
Information provided by (Responsible Party):	Hoffmann-La Roche
ClinicalTrials.gov Identifier:	NCT00442702

Purpose

This 2 arm study will compare the efficacy and safety of Mircera and darbepoetin alfa in the treatment of anemia in patients with chronic kidney disease who are not on dialysis and who are receiving subcutaneous darbepoetin alfa maintenance therapy. Patients will be randomized either to remain on darbepoetin alfa therapy as per local label, or to switch to monthly subcutaneous Mircera, at a starting dose of 120, 200 or 360 micrograms, depending on the weekly dose of darbepoetin alfa administered prior to the first dose of Mircera. The anticipated time on study treatment is 3-12 months, and the target sample size is 100-500 individuals.

Condition	Intervention	Phase
Anemia	Drug: Mircera Drug: Darbepoetin alfa	Phase 3

Study Type: Interventional
Study Design: Treatment, Parallel Assignment, Open Label, Randomized, Safety/Efficacy Study
Official Title: An Open-label, Randomized, Multi-center, Parallel Group Non-inferiority Study of Subcutaneous Injections of RO0503821 Given Once Monthly vs. Darbepoetin Alfa Given According to Local Label in Patients With Chronic Kidney Disease Who Are Not on Dialysis.

Further study details as provided by Hoffmann-La Roche:

Primary Outcome Measure:

- Change in Hemoglobin (Hb) Concentration From Baseline to the Evaluation Period [Time Frame: Baseline (measurements at Week -4, Week -2 and Day 1) and Evaluation Period (Months 8 and 9; measurements twice a month and at the final visit).] [Designated as safety issue: No]
  A time adjusted average baseline hemoglobin (Hb) concentration was calculated using the trapezoid rule from all available Hb measurements taken during the baseline period. The average evaluation period Hb concentration for each individual was calculated using the same method, from all their available measurements taken during the two month evaluation period. The change in Hb concentration between the baseline and evaluation periods was calculated by subtracting the baseline Hb from the evaluation period Hb. All blood samples for Hb measurements were taken prior to study drug administration.

Secondary Outcome Measures:

- Change in Hemoglobin Concentration From Baseline Over Time [Time Frame: From Baseline to 9 months; blood samples for hemoglobin measurements were taken twice a month, at each study visit.] [Designated as safety issue: No]
- Number of Participants With Red Blood Cell (RBC) Transfusions [Time Frame: From randomization to Month 9] [Designated as safety issue: No]
  Red blood cell (RBC) transfusions could be given during the treatment period in case of medical need, i.e., in severely anemic patients with recognized symptoms or signs of anemia (e.g., in patients with acute blood loss, with severe angina, or whose Hemoglobin decreased to critical levels). The number of participants who had at least one red blood cell transfusion during the entire study, during the Titration Period and during the Evaluation Period is presented. Participants who received more than one transfusion within a defined period are only counted once.
- Participants With Adverse Events [Time Frame: Randomization to Month 10 (final visit)] [Designated as safety issue: No]
  Adverse events were collected during the treatment period (from the first treatment dose) up to 30 days after last dose or at least until the date of last contact if the date of last contact occurred after the specified 30 day period.

Enrollment: 228
Study Start Date: September 2007
Primary Completion Date: August 2010
Study Completion Date: August 2010

Arms	Assigned Interventions
Experimental: Mircera Participants received Mircera by subcutaneous injection once every month during the dose titration (7 months) and evaluation period (2 months). The starting dose was based on the weekly dose of darbepoetin alfa administered prior to the switch to Mircera, and was either 120, 200 or 360 µg Mircera per month. The dose was then adjusted to maintain Hemoglobin levels within the defined target range and also according to the need for red blood cell transfusions (due to worsening anemia), or for toxicity related to Mircera.	Drug: Mircera Starting dose of 120, 200 and 360 micrograms administered by subcutaneous injection once a month. Other Names: RO0503821 Methoxy polyethylene glycol-epoetin beta
Active Comparator: Darbepoetin alfa	Drug: Darbepoetin alfa

Arms	Assigned Interventions
Participants continued to receive the same dose of darbepoetin alfa as before screening by subcutaneous injection once every week, once every 2 weeks or once every month as per local labeling during the dose titration (7 months) and the evaluation period (2 months).	As prescribed, subcutaneous injection once every week, once every 2 weeks or once every month as per local labeling specifications. Other Names: Aranesp®

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- adult patients, >=18 years of age;
- chronic kidney disease, not requiring dialysis;
- receiving darbepoetin alfa maintenance therapy for >=8 weeks before screening, and during screening/baseline period.

Exclusion Criteria:

- overt gastrointestinal bleeding within 8 weeks before screening, or during screening/baseline period;
- transfusion of red blood cells within 8 weeks before screening, or during screening/baseline period;
- active malignant disease;
- previous treatment with Mircera.

Contacts and Locations

Locations

United States, California
Granada Hills, California, United States, 91344
United States, Florida
Lauderdale Lakes, Florida, United States, 33313
United States, Georgia
Augusta, Georgia, United States, 30309
United States, New York
Mineola, New York, United States, 11501
Orchard Park, New York, United States, 14127
United States, North Carolina
Raleigh, North Carolina, United States, 27609
United States, Oregon

Oregon City, Oregon, United States, 97045
United States, Rhode Island
Providence, Rhode Island, United States, 02903
United States, Tennessee
Chattanooga, Tennessee, United States, 37404
United States, Virginia
Salem, Virginia, United States, 24153
United States, West Virginia
Morgantown, West Virginia, United States, 26506
Australia
Adelaide, Australia, SA 5000
Gosford, Australia, 2250
Lismore, Australia, 2480
Reservoir, Australia, 3073
Richmond, Australia, 3121
Belgium
Aalst, Belgium, 9300
Roeselare, Belgium, 8800
Canada, Alberta
Calgary, Alberta, Canada, T2N 2T9
Canada, Newfoundland and Labrador
St John's, Newfoundland and Labrador, Canada, A1B 3V6
Canada, Ontario
Kingston, Ontario, Canada, K7L 3N6
Mississauga, Ontario, Canada, L5M 2V8
Toronto, Ontario, Canada, M9N 1N8
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Strasbourg, France, 67091
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Coburg, Germany, 96450
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Dortmund, Germany, 44263
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Szigetvar, Hungary, 7390
VAC, Hungary, 2600

Israel

Hadera, Israel, 38100
Jerusalem, Israel, 91031
Kfar Saba, Israel, 44281
Nahariya, Israel, 22100
Rehovot, Israel, 76100

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Chieti, Italy, 66013
Ferrara, Italy, 44100
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La Spezia, Italy, 19124
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Lodz, Poland, 90-153
Radom, Poland, 20-610
Rzeszow, Poland, 35-055
Rzeszow, Poland, 35-055
Sieradz, Poland, 98-200
Szczecin, Poland, 70-111
Warszawa, Poland, 02-006

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Barcelona, Spain, 08025
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Investigators

Study Director:	Clinical Trials	Hoffmann-La Roche

More Information

Responsible Party:	Hoffmann-La Roche
Study ID Numbers:	BH20051
Health Authority:	United States: Food and Drug Administration

Study Results

Participant Flow

Reporting Groups

	Description
Mircera	Participants received Mircera by subcutaneous injection once every month during the dose titration (7 months) and evaluation period (2 months). The starting dose was based on the weekly dose of darbepoetin alfa administered prior to the switch to Mircera, and was either 120, 200 or 360 µg Mircera per month. The dose was then adjusted to maintain Hemoglobin levels within the defined target range and also according to the need for red blood cell transfusions (due to worsening anemia), or for toxicity related to Mircera.
Darbepoetin Alfa	Participants continued to receive the same dose of darbepoetin alfa by subcutaneous injection once every week, once every 2 weeks or once every month as per local labeling during the dose titration (7 months) and the evaluation period (2 months).

Titration Period

	Mircera	Darbepoetin Alfa
Started	114	114
Safety Population	115 [1]	113
Completed	102	111
Not Completed	12	3
Adverse Event	2	0
Death	3	2
Insufficient Therapeutic Response	1	0
Refused Treatment	4	1
Failure to return	1	0
Hospitalized in another hospital	1	0

[1] One patient was randomized to darbepoetin alfa but treated by mistake with Mircera

Evaluation Period

	Mircera	Darbepoetin Alfa
Started	102	111
Completed	97	107
Not Completed	5	4
Adverse Event	1	0
Death	1	1
Insufficient Therapeutic Response	1	0
Refused treatment	1	1
Renal transplant	0	1
Failure to return	1	0
Site closure	0	1

Baseline Characteristics

Reporting Groups

	Description
Mircera	Participants received Mircera by subcutaneous injection once every month during the dose titration (7 months) and evaluation period (2 months). The starting dose was based on the weekly dose of darbepoetin alfa administered prior to the switch to Mircera, and was either 120, 200 or 360 µg Mircera per month. The dose was then adjusted to maintain Hemoglobin levels within the defined target range and also according to the need for red blood cell transfusions (due to worsening anemia), or for toxicity related to Mircera.
Darbepoetin Alfa	Participants continued to receive the same dose of darbepoetin alfa by subcutaneous injection once every week, once every 2 weeks or once every month as per local labeling during the dose titration (7 months) and the evaluation period (2 months).

Baseline Measures

	Mircera	Darbepoetin Alfa	Total
Number of Participants	114	114	228
Age, Continuous [units: years] Mean (Standard Deviation)	71.3 (11.03)	69.6 (14.02)	70.4 (12.62)
Gender, Male/Female [units: participants]			
Female	66	66	132
Male	48	48	96

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Change in Hemoglobin (Hb) Concentration From Baseline to the Evaluation Period
Measure Description	A time adjusted average baseline hemoglobin (Hb) concentration was calculated using the trapezoid rule from all available Hb measurements taken during the baseline period. The average evaluation period Hb concentration for each individual was calculated using the same method, from all their available measurements taken during the two month evaluation period. The change in Hb concentration between the baseline and evaluation periods was calculated by subtracting the baseline Hb from the evaluation period Hb. All blood samples for Hb measurements were taken prior to study drug administration.
Time Frame	Baseline (measurements at Week -4, Week -2 and Day 1) and Evaluation Period (Months 8 and 9; measurements twice a month and at the final visit).

Safety Issue?	No

Analysis Population Description

Per Protocol population consisted of all randomized patients who had received at least one dose of trial medication and who have no major protocol violation. Data missing at the end of the evaluation period were handled using the last observation carried forward method (LOCF).

Reporting Groups

	Description
Mircera	Participants received Mircera by subcutaneous injection once every month during the dose titration (7 months) and evaluation period (2 months). The starting dose was based on the weekly dose of darbepoetin alfa administered prior to the switch to Mircera, and was either 120, 200 or 360 µg Mircera per month. The dose was then adjusted to maintain Hemoglobin levels within the defined target range and also according to the need for red blood cell transfusions (due to worsening anemia), or for toxicity related to Mircera.
Darbepoetin Alfa	Participants continued to receive the same dose of darbepoetin alfa by subcutaneous injection once every week, once every 2 weeks or once every month as per local labeling during the dose titration (7 months) and the evaluation period (2 months).

Measured Values

	Mircera	Darbepoetin Alfa
Number of Participants Analyzed	91	99
Change in Hemoglobin (Hb) Concentration From Baseline to the Evaluation Period [units: g/dL] Mean (Standard Deviation)		
Baseline Hb	11.29 (0.382)	11.33 (0.397)
Change from baseline	0.15 (0.899)	-0.03 (0.693)

2. Secondary Outcome Measure:

Measure Title	Change in Hemoglobin Concentration From Baseline Over Time
Measure Description	
Time Frame	From Baseline to 9 months; blood samples for hemoglobin measurements were taken twice a month, at each study visit.
Safety Issue?	No

Analysis Population Description

Intent-to-treat population, including all randomized patients. "n" refers to the number of patients for whom data was available at each time point.

Reporting Groups

	Description
Mircera	Participants received Mircera by subcutaneous injection once every month during the dose titration (7 months) and evaluation period (2 months). The starting dose was based on the weekly dose of darbepoetin alfa administered prior to the switch to Mircera, and was either 120, 200 or 360 µg Mircera per month. The dose was then adjusted to maintain Hemoglobin levels within the defined target range and also according to the need for red blood cell transfusions (due to worsening anemia), or for toxicity related to Mircera.
Darbepoetin Alfa	Participants continued to receive the same dose of darbepoetin alfa by subcutaneous injection once every week, once every 2 weeks or once every month as per local labeling during the dose titration (7 months) and the evaluation period (2 months).

Measured Values

	Mircera	Darbepoetin Alfa
Number of Participants Analyzed	114	114
Change in Hemoglobin Concentration From Baseline Over Time [units: g/dL] Mean (Standard Deviation)		
Baseline [n=114, 114]	11.27 (0.390)	11.31 (0.393)
Change at 0.5 Months [n=113, 114]	0.29 (0.737)	0.03 (0.490)
Change at 1 Month [n=114, 113]	0.34 (0.813)	0.06 (0.575)
Change at 1.5 Months [n=111, 113]	0.45 (0.866)	0.11 (0.599)
Change at 2 Months [n=112, 112]	0.27 (0.897)	0.02 (0.716)
Change at 2.5 Months [n=110, 112]	0.45 (0.924)	0.16 (0.673)
Change at 3 Months [n=111, 112]	0.23 (1.010)	0.10 (0.602)
Change at 3.5 Months [n=108, 108]	0.18 (1.095)	0.05 (0.675)
Change at 4 Months [n=109, 110]	0.05 (0.893)	0.00 (0.681)
Change at 4.5 Months [n=104, 108]	0.18 (0.940)	0.13 (0.699)
Change at 5 Months [n=108, 111]	-0.03 (0.897)	-0.07 (0.757)
Change at 5.5 Months [n=105, 110]	0.15 (0.922)	-0.03 (0.729)
Change at 6 Months [n=103, 111]	-0.05 (0.988)	-0.06 (0.820)

	Mircera	Darbepoetin Alfa
Change at 6.5 Months [n=100, 110]	0.06 (1.087)	0.04 (0.817)
Change at 7 Months [n=102, 111]	0.03 (1.008)	-0.00 (0.842)
Change at 7.5 Months [n=99, 110]	0.12 (1.166)	-0.00 (0.873)
Change at 8 Months [n=100, 108]	-0.04 (1.198)	-0.12 (0.905)
Change at 8.5 Months [n=97, 107]	0.14 (1.256)	0.02 (0.766)
Change at 9 Months [n=94, 101]	0.07 (1.045)	-0.06 (0.956)

3. Secondary Outcome Measure:

Measure Title	Number of Participants With Red Blood Cell (RBC) Transfusions
Measure Description	Red blood cell (RBC) transfusions could be given during the treatment period in case of medical need, i.e., in severely anemic patients with recognized symptoms or signs of anemia (e.g., in patients with acute blood loss, with severe angina, or whose Hemoglobin decreased to critical levels). The number of participants who had at least one red blood cell transfusion during the entire study, during the Titration Period and during the Evaluation Period is presented. Participants who received more than one transfusion within a defined period are only counted once.
Time Frame	From randomization to Month 9
Safety Issue?	No

Analysis Population Description

Safety population included all randomized patients who received at least one dose of trial medication and a safety follow-up, according to the treatment received.

Reporting Groups

	Description
Mircera	Participants received Mircera by subcutaneous injection once every month during the dose titration (7 months) and evaluation period (2 months). The starting dose was based on the weekly dose of darbepoetin alfa administered prior to the switch to Mircera, and was either 120, 200 or 360 µg Mircera per month. The dose was then adjusted to maintain Hemoglobin levels within the defined target range and also according to the need for red blood cell transfusions (due to worsening anemia), or for toxicity related to Mircera.
Darbepoetin Alfa	Participants continued to receive the same dose of darbepoetin alfa by subcutaneous injection once every week, once every 2 weeks or once every month as per local labeling during the dose titration (7 months) and the evaluation period (2 months).

Measured Values

	Mircera	Darbepoetin Alfa
Number of Participants Analyzed	115	113
Number of Participants With Red Blood Cell (RBC) Transfusions [units: participants]		
Entire Study	9	3
Titration Period	5	1
Evaluation Period	5	2

4. Secondary Outcome Measure:

Measure Title	Participants With Adverse Events
Measure Description	Adverse events were collected during the treatment period (from the first treatment dose) up to 30 days after last dose or at least until the date of last contact if the date of last contact occurred after the specified 30 day period.
Time Frame	Randomization to Month 10 (final visit)
Safety Issue?	No

Analysis Population Description

Safety population

Reporting Groups

	Description
Mircera	Participants received Mircera by subcutaneous injection once every month during the dose titration (7 months) and evaluation period (2 months). The starting dose was based on the weekly dose of darbepoetin alfa administered prior to the switch to Mircera, and was either 120, 200 or 360 µg Mircera per month. The dose was then adjusted to maintain Hemoglobin levels within the defined target range and also according to the need for red blood cell transfusions (due to worsening anemia), or for toxicity related to Mircera.
Darbepoetin Alfa	Participants continued to receive the same dose of darbepoetin alfa by subcutaneous injection once every week, once every 2 weeks or once every month as per local labeling during the dose titration (7 months) and the evaluation period (2 months).

Measured Values

	Mircera	Darbepoetin Alfa
Number of Participants Analyzed	115	113

	Mircera	Darbepoetin Alfa
Participants With Adverse Events [units: participants]		
Any adverse event	102	88
Fatal Adverse event	4	3
Serious adverse event	41	23
Adverse event leading to withdrawal	3	0

Reported Adverse Events

Time Frame	All adverse events that occurred from the first treatment dose were summarized. Adverse events were included up to 30 days after last dose or at least until the date of last contact if the date of last contact occurred after the specified 30 day period.
Additional Description	Safety population was used for analysis.

Reporting Groups

	Description
Mircera	Participants received Mircera by subcutaneous injection once every month during the dose titration (7 months) and evaluation period (2 months). The starting dose was based on the weekly dose of darbepoetin alfa administered prior to the switch to Mircera, and was either 120, 200 or 360 µg Mircera per month. The dose was then adjusted to maintain Hemoglobin levels within the defined target range and also according to the need for red blood cell transfusions (due to worsening anemia), or for toxicity related to Mircera.
Darbepoetin Alfa	Participants continued to receive the same dose of darbepoetin alfa by subcutaneous injection once every week, once every 2 weeks or once every month as per local labeling during the dose titration (7 months) and the evaluation period (2 months).

Serious Adverse Events

	Mircera	Darbepoetin Alfa
	Affected/At Risk (%)	Affected/At Risk (%)
Total	41/115 (35.65%)	23/113 (20.35%)
Blood and lymphatic system disorders		

	Mircera	Darbepoetin Alfa
	Affected/At Risk (%)	Affected/At Risk (%)
NEPHROGENIC ANAEMIA [A] †	1/115 (0.87%)	0/113 (0%)
Cardiac disorders		
ACUTE MYOCARDIAL INFARCTION [A] †	1/115 (0.87%)	0/113 (0%)
AORTIC VALVE DISEASE MIXED [A] †	1/115 (0.87%)	0/113 (0%)
ARRHYTHMIA [A] †	1/115 (0.87%)	0/113 (0%)
ATRIAL FIBRILLATION [A] †	1/115 (0.87%)	1/113 (0.88%)
ATRIAL FLUTTER [A] †	1/115 (0.87%)	0/113 (0%)
BRADYCARDIA [A] †	0/115 (0%)	1/113 (0.88%)
CARDIAC FAILURE [A] †	0/115 (0%)	1/113 (0.88%)
CARDIAC FAILURE CONGESTIVE [A] †	2/115 (1.74%)	1/113 (0.88%)
CARDIOGENIC SHOCK [A] †	1/115 (0.87%)	0/113 (0%)
CORONARY ARTERY DISEASE [A] †	1/115 (0.87%)	0/113 (0%)
MYOCARDIAL INFARCTION [A] †	1/115 (0.87%)	0/113 (0%)
MYOCARDIAL ISCHAEMIA [A] †	1/115 (0.87%)	0/113 (0%)
SICK SINUS SYNDROME [A] †	1/115 (0.87%)	0/113 (0%)
SILENT MYOCARDIAL INFARCTION [A] †	1/115 (0.87%)	0/113 (0%)
Ear and labyrinth disorders		
VERTIGO [A] †	1/115 (0.87%)	2/113 (1.77%)
Eye disorders		
CATARACT [A] †	0/115 (0%)	1/113 (0.88%)
Gastrointestinal disorders		
COLITIS ISCHAEMIC [A] †	1/115 (0.87%)	0/113 (0%)
DIARRHOEA [A] †	1/115 (0.87%)	0/113 (0%)

	Mircera	Darbepoetin Alfa
	Affected/At Risk (%)	Affected/At Risk (%)
GASTROINTESTINAL HAEMORRHAGE [A] †	0/115 (0%)	1/113 (0.88%)
HIATUS HERNIA [A] †	1/115 (0.87%)	0/113 (0%)
PANCREATITIS ACUTE [A] †	2/115 (1.74%)	0/113 (0%)
RECTAL POLYP [A] †	1/115 (0.87%)	0/113 (0%)
General disorders		
NON-CARDIAC CHEST PAIN [A] †	0/115 (0%)	1/113 (0.88%)
OEDEMA PERIPHERAL [A] †	1/115 (0.87%)	0/113 (0%)
Hepatobiliary disorders		
CHOLECYSTITIS [A] †	1/115 (0.87%)	0/113 (0%)
CHOLELITHIASIS [A] †	1/115 (0.87%)	0/113 (0%)
Infections and infestations		
BRONCHOPNEUMONIA [A] †	1/115 (0.87%)	0/113 (0%)
CORYNEBACTERIUM SEPSIS [A] †	0/115 (0%)	1/113 (0.88%)
GASTROENTERITIS [A] †	1/115 (0.87%)	0/113 (0%)
INFECTED SKIN ULCER [A] †	1/115 (0.87%)	0/113 (0%)
NEUROLOGICAL INFECTION [A] †	1/115 (0.87%)	0/113 (0%)
OSTEOMYELITIS [A] †	1/115 (0.87%)	0/113 (0%)
PNEUMONIA [A] †	2/115 (1.74%)	1/113 (0.88%)
POST PROCEDURAL INFECTION [A] †	1/115 (0.87%)	0/113 (0%)
RESPIRATORY TRACT INFECTION [A] †	2/115 (1.74%)	0/113 (0%)
URINARY TRACT INFECTION [A] †	0/115 (0%)	1/113 (0.88%)
Injury, poisoning and procedural complications		

	Mircera	Darbepoetin Alfa
	Affected/At Risk (%)	Affected/At Risk (%)
FEMORAL NECK FRACTURE [A] †	1/115 (0.87%)	0/113 (0%)
LOWER LIMB FRACTURE [A] †	2/115 (1.74%)	0/113 (0%)
PELVIC FRACTURE [A] †	1/115 (0.87%)	0/113 (0%)
Metabolism and nutrition disorders		
DEHYDRATION [A] †	1/115 (0.87%)	0/113 (0%)
DIABETES MELLITUS INADEQUATE CONTROL [A] †	0/115 (0%)	1/113 (0.88%)
FLUID OVERLOAD [A] †	1/115 (0.87%)	1/113 (0.88%)
FLUID RETENTION [A] †	1/115 (0.87%)	0/113 (0%)
HYPERKALAEMIA [A] †	0/115 (0%)	2/113 (1.77%)
HYPOGLYCAEMIA [A] †	1/115 (0.87%)	0/113 (0%)
HYPONATRAEMIA [A] †	1/115 (0.87%)	0/113 (0%)
Musculoskeletal and connective tissue disorders		
ARTHRALGIA [A] †	1/115 (0.87%)	0/113 (0%)
PATHOLOGICAL FRACTURE [A] †	1/115 (0.87%)	0/113 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
ANGIOSARCOMA [A] †	1/115 (0.87%)	0/113 (0%)
BASAL CELL CARCINOMA [A] †	0/115 (0%)	1/113 (0.88%)
COLON CANCER METASTATIC [A] †	1/115 (0.87%)	0/113 (0%)
Nervous system disorders		
ATAXIA [A] †	1/115 (0.87%)	0/113 (0%)
CEREBROVASCULAR ACCIDENT [A] †	1/115 (0.87%)	1/113 (0.88%)
HEADACHE [A] †	1/115 (0.87%)	0/113 (0%)

	Mircera	Darbepoetin Alfa
	Affected/At Risk (%)	Affected/At Risk (%)
NERVE ROOT COMPRESSION [A] †	0/115 (0%)	1/113 (0.88%)
PARTIAL SEIZURES [A] †	1/115 (0.87%)	0/113 (0%)
SCIATICA [A] †	1/115 (0.87%)	0/113 (0%)
TRANSIENT ISCHAEMIC ATTACK [A] †	0/115 (0%)	1/113 (0.88%)
VERTEBROBASILAR INSUFFICIENCY [A] †	0/115 (0%)	1/113 (0.88%)
Renal and urinary disorders		
CALCULUS URETERIC [A] †	0/115 (0%)	1/113 (0.88%)
RENAL FAILURE CHRONIC [A] †	2/115 (1.74%)	1/113 (0.88%)
RENAL IMPAIRMENT [A] †	5/115 (4.35%)	0/113 (0%)
Reproductive system and breast disorders		
BENIGN PROSTATIC HYPERPLASIA [A] †	0/115 (0%)	1/113 (0.88%)
Respiratory, thoracic and mediastinal disorders		
ASTHMA [A] †	1/115 (0.87%)	0/113 (0%)
CHRONIC OBSTRUCTIVE PULMONARY DISEASE [A] †	0/115 (0%)	1/113 (0.88%)
Skin and subcutaneous tissue disorders		
SKIN ULCER [A] †	2/115 (1.74%)	0/113 (0%)
Vascular disorders		
ARTERIOSCLEROSIS [A] †	0/115 (0%)	1/113 (0.88%)
EXTREMITY NECROSIS [A] †	1/115 (0.87%)	0/113 (0%)
HYPERTENSION [A] †	0/115 (0%)	1/113 (0.88%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (13.0)

Other Adverse Events

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

	Mircera	Darbepoetin Alfa
	Affected/At Risk (%)	Affected/At Risk (%)
Total	59/115 (51.3%)	49/113 (43.36%)
Endocrine disorders		
HYPERPARATHYROIDISM SECONDARY [A] †	8/115 (6.96%)	1/113 (0.88%)
Gastrointestinal disorders		
CONSTIPATION [A] †	6/115 (5.22%)	3/113 (2.65%)
DIARRHOEA [A] †	5/115 (4.35%)	8/113 (7.08%)
General disorders		
OEDEMA DUE TO RENAL DISEASE [A] †	6/115 (5.22%)	7/113 (6.19%)
Infections and infestations		
NASOPHARYNGITIS [A] †	7/115 (6.09%)	13/113 (11.5%)
URINARY TRACT INFECTION [A] †	10/115 (8.7%)	4/113 (3.54%)
Musculoskeletal and connective tissue disorders		
BACK PAIN [A] †	6/115 (5.22%)	3/113 (2.65%)
Renal and urinary disorders		
RENAL IMPAIRMENT [A] †	13/115 (11.3%)	12/113 (10.62%)
Vascular disorders		
HYPERTENSION [A] †	30/115 (26.09%)	20/113 (17.7%)

† Indicates events were collected by systematic assessment.

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.

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