ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 06/06/2014

Dynepo Long-Term Safety Study

This study has been terminated.
(The termination of the study is not linked to a product recall or result of any safety signal. Rather it was sponsor's commercial decision to withdraw the MA)

Sponsor:	Shire
Collaborators:	
Information provided by:	Shire
ClinicalTrials.gov Identifier:	NCT00514813

Purpose

To assess the incidence rate of Treatment Emergent Adverse Events (TEAEs) over 2 years in patients treated with Dynepo.

Condition	Intervention	Phase
Anemia Kidney Failure, Chronic	Drug: Dynepo	Phase 4

Study Type: Interventional
Study Design: Single Group Assignment, Open Label, Randomized, Safety Study
Official Title: An Open-Label, Phase IV, Multi-Centre Study to Investigate the Long-Term Safety and Efficacy of Subcutaneous Dynepo in Adult Patients With Anaemia Associated With Chronic Kidney Disease

Further study details as provided by Shire:

Primary Outcome Measure:

- Rate of Emergence of Treatment Emergent Adverse Events (TEAEs) [Time Frame: Over the course of 2 Years] [Designated as safety issue: Yes]

Secondary Outcome Measures:

- Change From Baseline in Hemoglobin (Hb) Concentrations at 2 Years [Time Frame: Baseline and 2 years] [Designated as safety issue: Yes]

- Change From Baseline in Hematocrits at 2 Years [Time Frame: Baseline and 2 years] [Designated as safety issue: Yes]

Enrollment: 152
Study Start Date: June 2007
Primary Completion Date: July 2008
Study Completion Date: July 2008

Arms	Assigned Interventions
Experimental: Dynepo (Epoetin delta) Subjects received Dynepo (Epoetin delta) either twice weekly (BIW), once weekly (QW), once every 2 weeks (Q2W) or once every 4 weeks (Q4W) based on what is appropriate for the subject	Drug: Dynepo Subcutaneous injection either BIW, QW, Q2W or Q4W based on what is appropriate for the subject Other Names: Epoetin delta

Eligibility

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

Criteria

Inclusion Criteria:

1. Patients who complete Dynepo study SPD490-301.
2. Patients who continue to require epoetin (EPO) treatment and have had a Hb level of 10g/dL between Weeks 16 and 24 of study SPD490-301.

Exclusion Criteria:

1. Withdrawal, before Week 24, from study SPD490-301.
2. Pregnant or lactating women.
3. Uncontrolled hypertension.
4. Thrombocytopenia (platelet count <75,000/mm3).
5. Active bleeding disorder (diathesis) (for example, gastrointestinal bleeding or genitourinary tract bleeding).
6. Treatment with immunosuppressive drugs (other than corticosteroids for a chronic condition) in the 30 days immediately prior to enrolment in this study.
7. Androgen therapy in the 30 days immediately prior to enrolment in this study.
8. Known Human Immunodeficiency Virus (HIV) infection.
9. History of hypersensitivity to Dynepo.
10. Known to have Ab against EPO.

Contacts and Locations

Locations
Belgium

Department of Nephrology
Heilig Hartziekenhuis, Wilgenstraat 2, Belgium

Investigators
Principal Investigator: Iain C Macdougall, MD Kings College Hospital, London

More Information

Responsible Party: Shire (Timothy Whitaker, M.D.)
Study ID Numbers: SPD490-402
2007-000054-31 [EudraCT Number]
Health Authority: Belgium: The Federal Public Service (FPS) Health, Food Chain Safety and Environment

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Study Results

Participant Flow

Recruitment Details	This study was terminated on July 31, 2008 as a result of a decision by Shire Pharmaceutical to permanently cease marketing Dynepo and withdraw the Marketing Authorisation. The decision was for commercial reasons, it was not the result of any safety signal.
Pre-Assignment Details	Subjects received Dynepo (Epoetin delta) either twice weekly (BIW), once weekly (QW), once every 2 weeks (Q2W) or once every 4 weeks (Q4W) at a dose that is appropriate for them and not to exceed 20,000 IU at any one time.

Reporting Groups

	Description
Dynepo (Epoetin Delta) Twice Weekly (BIW)	Epoetin delta (Dynepo) dosed twice-a-week
Dynepo Once Weekly (QW)	Epoetin delta dosed once-a-week
Dynepo Once Every 2 Weeks (Q2W)	Epoetin delta dosed once every 2 weeks
Dynepo Once Every 4 Weeks (Q4W)	Epoetin delta dosed once every 4 weeks

Overall Study

	Dynepo (Epoetin Delta) Twice Weekly (BIW)	Dynepo Once Weekly (QW)	Dynepo Once Every 2 Weeks (Q2W)	Dynepo Once Every 4 Weeks (Q4W)
Started	15	86	47	4
Completed	0	0	0	0
Not Completed	15	86	47	4
Study terminated	14	74	40	2
Adverse Event	0	2	2	0
Protocol Violation	1	0	0	0
Withdrawal by Subject	0	1	0	0
Lack of Efficacy	0	1	0	0
Kidney transplant	0	6	2	0
Death	0	2	3	2

Baseline Characteristics

Reporting Groups

	Description
Dynepo (Epoetin Delta) Twice Weekly (BIW)	Epoetin delta (Dynepo) dosed twice-a-week
Dynepo Once Weekly (QW)	Epoetin delta dosed once-a-week
Dynepo Once Every 2 Weeks (Q2W)	Epoetin delta dosed once every 2 weeks
Dynepo Once Every 4 Weeks (Q4W)	Epoetin delta dosed once every 4 weeks

Baseline Measures

	Dynepo (Epoetin Delta) Twice Weekly (BIW)	Dynepo Once Weekly (QW)	Dynepo Once Every 2 Weeks (Q2W)	Dynepo Once Every 4 Weeks (Q4W)	Total
Number of Participants	15	86	47	4	152
Age, Categorical [units: participants]					
<=18 years	0	0	0	0	0

	Dynepo (Epoetin Delta) Twice Weekly (BIW)	Dynepo Once Weekly (QW)	Dynepo Once Every 2 Weeks (Q2W)	Dynepo Once Every 4 Weeks (Q4W)	Total
Between 18 and 65 years	7	31	22	1	61
>=65 years	8	55	25	3	91
Age, Continuous [units: years] Mean (Standard Deviation)	63.4 (12.93)	64.8 (13.7)	65.2 (14.03)	66.3 (21.39)	64.9 (13.8)
Gender, Male/Female [units: participants]					
Female	7	33	16	2	58
Male	8	53	31	2	94
Region of Enrollment [units: participants]					
Belgium	0	6	6	0	12
Austria	0	1	0	0	1
France	1	6	3	1	11
Germany	5	19	7	0	31
Italy	1	24	17	0	42
Latvia	3	7	3	0	13
Spain	0	8	8	3	19
United Kingdom	5	15	3	0	23

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Rate of Emergence of Treatment Emergent Adverse Events (TEAEs)
Measure Description	
Time Frame	Over the course of 2 Years
Safety Issue?	Yes

Analysis Population Description

This study was terminated on July 31, 2008 as a result of a decision by Shire Pharmaceutical to permanently cease marketing Dynepo and withdraw the Marketing Authorisation. The decision was for commercial reasons, it was not the result of any safety signal.

Reporting Groups

	Description
Dynepo (Epoetin Delta) Twice Weekly (BIW)	Epoetin delta (Dynepo) dosed twice-a-week
Dynepo Once Weekly (QW)	Epoetin delta dosed once-a-week
Dynepo Once Every 2 Weeks (Q2W)	Epoetin delta dosed once every 2 weeks
Dynepo Once Every 4 Weeks (Q4W)	Epoetin delta dosed once every 4 weeks

Measured Values

	Dynepo (Epoetin Delta) Twice Weekly (BIW)	Dynepo Once Weekly (QW)	Dynepo Once Every 2 Weeks (Q2W)	Dynepo Once Every 4 Weeks (Q4W)
Number of Participants Analyzed	0	0	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

2. Secondary Outcome Measure:

Measure Title	Change From Baseline in Hemoglobin (Hb) Concentrations at 2 Years
Measure Description	
Time Frame	Baseline and 2 years
Safety Issue?	Yes

Analysis Population Description

This study was terminated on July 31, 2008 as a result of a decision by Shire Pharmaceutical to permanently cease marketing Dynepo and withdraw the Marketing Authorisation. The decision was for commercial reasons, it was not the result of any safety signal.

Reporting Groups

	Description
Dynepo (Epoetin Delta) Twice Weekly (BIW)	Epoetin delta (Dynepo) dosed twice-a-week
Dynepo Once Weekly (QW)	Epoetin delta dosed once-a-week
Dynepo Once Every 2 Weeks (Q2W)	Epoetin delta dosed once every 2 weeks
Dynepo Once Every 4 Weeks (Q4W)	Epoetin delta dosed once every 4 weeks

Measured Values

	Dynepo (Epoetin Delta) Twice Weekly (BIW)	Dynepo Once Weekly (QW)	Dynepo Once Every 2 Weeks (Q2W)	Dynepo Once Every 4 Weeks (Q4W)
Number of Participants Analyzed	0	0	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

3. Secondary Outcome Measure:

Measure Title	Change From Baseline in Hematocrits at 2 Years
Measure Description	
Time Frame	Baseline and 2 years
Safety Issue?	Yes

Analysis Population Description

This study was terminated on July 31, 2008 as a result of a decision by Shire Pharmaceutical to permanently cease marketing Dynepo and withdraw the Marketing Authorisation. The decision was for commercial reasons, it was not the result of any safety signal.

Reporting Groups

	Description
Dynepo (Epoetin Delta) Twice Weekly (BIW)	Epoetin delta (Dynepo) dosed twice-a-week
Dynepo Once Weekly (QW)	Epoetin delta dosed once-a-week
Dynepo Once Every 2 Weeks (Q2W)	Epoetin delta dosed once every 2 weeks
Dynepo Once Every 4 Weeks (Q4W)	Epoetin delta dosed once every 4 weeks

Measured Values

	Dynepo (Epoetin Delta) Twice Weekly (BIW)	Dynepo Once Weekly (QW)	Dynepo Once Every 2 Weeks (Q2W)	Dynepo Once Every 4 Weeks (Q4W)
Number of Participants Analyzed	0	0	0	0

No data displayed because Outcome Measure has zero total participants analyzed.

Reported Adverse Events

Time Frame	[Not specified]

Additional Description	The adverse events were collected on the Safety Population defined as all subjects randomized who received at least one dose of Dynepo. Therefore, 150 of the 152 enrolled subjects constituted the Safety Population. Therefore, the second Arm has 84 subjects instead of 86 as shown in the participant flow.

Reporting Groups

	Description
Dynepo (Epoetin Delta) Twice Weekly (BIW)	Epoetin delta (Dynepo) dosed twice-a-week
Dynepo Once Weekly (QW)	Epoetin delta dosed once-a-week
Dynepo Once Every 2 Weeks (Q2W)	Epoetin delta dosed once every 2 weeks
Dynepo Once Every 4 Weeks (Q4W)	Epoetin delta dosed once every 4 weeks

Serious Adverse Events

	Dynepo (Epoetin Delta) Twice Weekly (BIW)	Dynepo Once Weekly (QW)	Dynepo Once Every 2 Weeks (Q2W)	Dynepo Once Every 4 Weeks (Q4W)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	1/15 (6.67%)	14/84 (16.67%)	6/47 (12.77%)	1/4 (25%)
Cardiac disorders				
Acute MI *	0/15 (0%)	1/84 (1.19%)	0/47 (0%)	0/4 (0%)
Angina pectoris *	0/15 (0%)	1/84 (1.19%)	0/47 (0%)	0/4 (0%)
Cardiac failure *	0/15 (0%)	1/84 (1.19%)	0/47 (0%)	0/4 (0%)
Coronary artery stenosis *	0/15 (0%)	1/84 (1.19%)	0/47 (0%)	0/4 (0%)
Tachycardia *	0/15 (0%)	1/84 (1.19%)	0/47 (0%)	0/4 (0%)
Gastrointestinal disorders				
Abdominal pain upper *	0/15 (0%)	0/84 (0%)	1/47 (2.13%)	0/4 (0%)
Fecaloma *	0/15 (0%)	1/84 (1.19%)	0/47 (0%)	0/4 (0%)
Hematemesis *	0/15 (0%)	0/84 (0%)	1/47 (2.13%)	0/4 (0%)
Peritonitis *	0/15 (0%)	0/84 (0%)	2/47 (4.26%)	0/4 (0%)
General disorders				
Catheter-related complication *	0/15 (0%)	1/84 (1.19%)	0/47 (0%)	0/4 (0%)
Sudden death *	0/15 (0%)	1/84 (1.19%)	0/47 (0%)	0/4 (0%)

	Dynepo (Epoetin Delta) Twice Weekly (BIW)	Dynepo Once Weekly (QW)	Dynepo Once Every 2 Weeks (Q2W)	Dynepo Once Every 4 Weeks (Q4W)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Infections and infestations				
Bronchitis *	0/15 (0%)	0/84 (0%)	0/47 (0%)	1/4 (25%)
Pneumonia *	0/15 (0%)	1/84 (1.19%)	0/47 (0%)	0/4 (0%)
Respiratory tract infection *	0/15 (0%)	0/84 (0%)	0/47 (0%)	1/4 (25%)
Injury, poisoning and procedural complications				
Arteriovenous fistula site complication *	1/15 (6.67%)	0/84 (0%)	1/47 (2.13%)	0/4 (0%)
Dialysis device complication *	1/15 (6.67%)	0/84 (0%)	0/47 (0%)	0/4 (0%)
Splenic rupture *	0/15 (0%)	1/84 (1.19%)	0/47 (0%)	0/4 (0%)
Traumatic fracture *	0/15 (0%)	0/84 (0%)	2/47 (4.26%)	0/4 (0%)
Metabolism and nutrition disorders				
Hyperglycemia *	0/15 (0%)	1/84 (1.19%)	0/47 (0%)	0/4 (0%)
Musculoskeletal and connective tissue disorders				
Bursitis *	0/15 (0%)	1/84 (1.19%)	0/47 (0%)	0/4 (0%)
Musculoskeletal chest pain *	0/15 (0%)	1/84 (1.19%)	0/47 (0%)	0/4 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Lung neoplasm malignant *	0/15 (0%)	1/84 (1.19%)	0/47 (0%)	0/4 (0%)

* Indicates events were collected by non-systematic methods.

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

	Dynepo (Epoetin Delta) Twice Weekly (BIW)	Dynepo Once Weekly (QW)	Dynepo Once Every 2 Weeks (Q2W)	Dynepo Once Every 4 Weeks (Q4W)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	7/15 (46.67%)	62/84 (73.81%)	32/47 (68.09%)	4/4 (100%)
Gastrointestinal disorders				
Constipation *	0/15 (0%)	5/84 (5.95%)	2/47 (4.26%)	0/4 (0%)
Diarrhea *	1/15 (6.67%)	4/84 (4.76%)	6/47 (12.77%)	1/4 (25%)
Nausea *	0/15 (0%)	5/84 (5.95%)	1/47 (2.13%)	0/4 (0%)

	Dynepo (Epoetin Delta) Twice Weekly (BIW)	Dynepo Once Weekly (QW)	Dynepo Once Every 2 Weeks (Q2W)	Dynepo Once Every 4 Weeks (Q4W)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Vomiting *	0/15 (0%)	6/84 (7.14%)	2/47 (4.26%)	0/4 (0%)
General disorders				
Edema peripheral *	1/15 (6.67%)	1/84 (1.19%)	1/47 (2.13%)	0/4 (0%)
Vessel puncture site hematoma *	1/15 (6.67%)	0/84 (0%)	0/47 (0%)	0/4 (0%)
Infections and infestations				
Catheter site infection *	1/15 (6.67%)	0/84 (0%)	0/47 (0%)	0/4 (0%)
Influenza *	1/15 (6.67%)	5/84 (5.95%)	4/47 (8.51%)	0/4 (0%)
Nasopharyngitis *	0/15 (0%)	6/84 (7.14%)	1/47 (2.13%)	0/4 (0%)
Oral herpes *	1/15 (6.67%)	0/84 (0%)	1/47 (2.13%)	0/4 (0%)
Pneumonia *	1/15 (6.67%)	2/84 (2.38%)	0/47 (0%)	0/4 (0%)
Injury, poisoning and procedural complications				
Arteriovenous fistula site complication *	1/15 (6.67%)	2/84 (2.38%)	3/47 (6.38%)	0/4 (0%)
Dialysis device complication *	1/15 (6.67%)	0/84 (0%)	0/47 (0%)	0/4 (0%)
Injury *	1/15 (6.67%)	0/84 (0%)	0/47 (0%)	0/4 (0%)
Investigations				
Hemaglobin decreased *	1/15 (6.67%)	0/84 (0%)	1/47 (2.13%)	0/4 (0%)
Metabolism and nutrition disorders				
Hyperphosphatemia *	1/15 (6.67%)	3/84 (3.57%)	2/47 (4.26%)	0/4 (0%)
Musculoskeletal and connective tissue disorders				
Arthralgia *	1/15 (6.67%)	3/84 (3.57%)	2/47 (4.26%)	0/4 (0%)
Pain in extremity *	0/15 (0%)	4/84 (4.76%)	1/47 (2.13%)	1/4 (25%)
Respiratory, thoracic and mediastinal disorders				
Bronchitis chronic *	1/15 (6.67%)	0/84 (0%)	0/47 (0%)	0/4 (0%)
Cough *	0/15 (0%)	5/84 (5.95%)	1/47 (2.13%)	0/4 (0%)
Dyspnea *	1/15 (6.67%)	3/84 (3.57%)	2/47 (4.26%)	0/4 (0%)
Hydrothorax *	1/15 (6.67%)	0/84 (0%)	0/47 (0%)	0/4 (0%)

	Dynepo (Epoetin Delta) Twice Weekly (BIW)	Dynepo Once Weekly (QW)	Dynepo Once Every 2 Weeks (Q2W)	Dynepo Once Every 4 Weeks (Q4W)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Skin and subcutaneous tissue disorders				
Alopecia *	1/15 (6.67%)	0/84 (0%)	0/47 (0%)	0/4 (0%)
Dermatitis allergic *	1/15 (6.67%)	0/84 (0%)	0/47 (0%)	0/4 (0%)
Pruritus *	0/15 (0%)	6/84 (7.14%)	0/47 (0%)	0/4 (0%)
Skin ulcer *	1/15 (6.67%)	1/84 (1.19%)	0/47 (0%)	0/4 (0%)
Vascular disorders				
Hypertension *	0/15 (0%)	6/84 (7.14%)	2/47 (4.26%)	1/4 (25%)
Hypotension *	0/15 (0%)	3/84 (3.57%)	3/47 (6.38%)	1/4 (25%)
Orthostatic hypertension *	1/15 (6.67%)	0/84 (0%)	0/47 (0%)	0/4 (0%)

* Indicates events were collected by non-systematic methods.

Limitations and Caveats

This study terminated early due to a decision by Shire Pharmaceuticals to permanently cease marketing Dynepo due to commercial reasons, it was not the result of any safety signal. Not enough subjects completed the study to do any efficacy analyses.

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.

If a multicenter publication is not submitted within twelve (12) months after conclusion, abandonment or termination of the Study at all sites, or after Sponsor confirms there shall be no multicenter Study publication, the Institution and/or such Principal Investigator may publish the results from the Institution site individually.

Results Point of Contact:

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