

Darbepoetin (synthetic version of erythropoietin) vs erythropoietin to stimulate red blood cell production in dialysis patients

Submission date 16/11/2023	Recruitment status No longer recruiting	☐ Prospectively registered
		☐ Protocol
Registration date 22/11/2023	Overall study status Completed	☐ Statistical analysis plan
		☐ Results
Last Edited 21/11/2023	Condition category Haematological Disorders	☐ Individual participant data
		☐ Record updated in last year

Plain English summary of protocol

Background and study aims

Darbepoetin is used to treat anemia (low red blood cells in your blood). This medication works in exactly the same way as the natural hormone erythropoietin. Erythropoietin is produced in your kidneys and encourages your bone marrow to produce more red blood cells. In kidney failure, the kidney does not produce enough of the natural hormone erythropoietin which can often cause low red blood cells, and the symptoms may be tiredness, weakness and difficulty in breathing. This study will determine the effects of darbepoetin.

Who can participate?

You have been invited to take part in this study because you have been diagnosed with kidney failure with low red blood cells (anemia), and you have been undergoing dialysis. Participation in this study is voluntary. It is up to you to decide whether or not to take part. Even if you decide to take part, you are still free to withdraw at any time and without giving any reason. This will not affect the standard of care you receive.

What does the study involve?

If you agree to take part in this study, you will have to do the following:

- a) You will be asked to sign an informed consent form and a copy of the form will be given to you.
- b) You will be required to come to clinic to undergo a screening assessment to determine if you are suitable to enter the study. The screening assessment includes a complete medical history and physical examinations, blood test and urine test. Urine pregnancy test will also be done for female patient.
- c) If you are suitable to enter this study, your study doctor will enroll you and schedule your visits for the full duration of the study period.
- d) You will be asked to come one week before the scheduled study visit to do your blood test. Approximately 20 ml of blood will be taken for blood tests during each visit.
- e) Each study visit has been designed to closely monitor you for any side effect. It is very important for all blood tests to be performed regularly at each visit because blood test results may be the only signs of any adverse effect.

f) If you are on recombinant human erythropoietin, you will be asked to stop the medication for 2 weeks before allocating you to one of the study medications. Stopping the medication will cause your hemoglobin level to become lower than normal. However, the drop in hemoglobin is not expected to be drastic to cause immediate complications in short period of time (less than 3 months). Unlike low potassium and low calcium levels that need to be treated immediately, low hemoglobin levels are relatively harmless as you may remain asymptomatic. You will not be given any medication for low hemoglobin levels in these 2 weeks.

g) You will then be randomly allocated to 1 of the 2 groups of treatments which means you will be assigned to a group by chance, like flipping a coin. One group will receive darbepoetin injection and the other group will receive recombinant human erythropoietin injections for treatment period of 20 weeks. Your chances of being in either group are 50:50. You will be given appointment to see the doctor during the study period.

h) You must report to your study doctor all medications that you are presently taking including those that are not prescribed like over the counter medications, traditional or herbal remedy. You must inform your study doctor if you receive additional medications from other doctors for the treatment of any disease at any time during the study.

i) If you experience any side effects or anything unusual you must report to your study doctor immediately. Your study doctor may decide to stop your participation in the study if he/she considers it to be in your best interest.

j) You are advised to stick to your dietary regime and the usual medications as prescribed by your doctor. If you are a female, you are advised not to become pregnant during your participation in this study and in case, you become pregnant, you should immediately inform your doctor.

What are the possible benefits and risks of taking part?

Various studies have shown that darbepoetin is effective in treating anemia. Moreover, darbepoetin has been shown to increase hemoglobin levels within a shorter period of time as compared to erythropoietin. Unlike erythropoietin, darbepoetin does not require injections 2 to 3 times per week as it is administered once a week or once in 2 weeks.

The side effects of darbepoetin are listed including hypertension, allergic reactions, pain around the injected area, rash or redness of the skin, convulsions or stroke. However, if you experience any side effects during the treatment period, you should inform your study doctor as soon as possible. You may also experience brief and minor discomfort such as pain or bruising at the area where blood is drawn from a vein.

Where is the study run from?

Nephrology Clinic Hospital Serdang (Malaysia)

When is the study starting and how long is it expected to run for?

June 2016 to September 2019

Who is funding the study?

This study is funded by the National Institute of Health (NIH) Malaysia and Kyowa Hakko Kirin Co. Ltd. (Kyowa Kirin), which included the procurement of investigational products, logistic support and patient reimbursement during the study. The NIH and Kyowa Kirin are not involved in the design and conduct of the study.

Who is the main contact?

Primary Investigator: Prof. Dr. Goh Bak Leong, bak.leong@gmail.com

Study Coordinator: Mr. Ang Kim Liong, angkl@crc.gov.my

Contact information

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Additional identifiers

Protocol serial number

CT88-01

Study information

Scientific Title

A randomized, open-label trial to establish the therapeutic equivalence between Darbepoetin Alpha and Erythropoietin Beta or Alpha in patients on dialysis.

Study objectives

The primary benefit of darbepoetin is the correction of anemia, including the relief of associated signs and symptoms and an increased quality of life. It is expected to be at least as safe as erythropoietin. Current data suggests that darbepoetin can be administered less frequently as compared to erythropoietin, to achieve and maintain optimal Hb levels. This can improve compliance and may pave the way for cost effective treatment of anemia amongst dialysis patients. It is anticipated that less frequent darbepoetin injections as compared to erythropoietin will be comparable in efficacy in the treatment of anemia in dialysis patients, with an acceptable safety profile. Darbepoetin may offer a valuable alternative to the current treatment options in the management of anemia in dialysis patients.

Ethics approval required

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Ethics approval(s)

Approved 21/06/2016, Medical Research Ethics Committee (MREC), Ministry of Health Malaysia (National Institute of Health (NIH), Persiaran Setia Murni, Setia Alam, 40170, Malaysia; +60 333628205; mrecsec@moh.gov.my), ref: NMRR-15-2120-26431

Primary study design

Interventional

Study design

Open label randomized controlled trial

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Anaemia in dialysis patients

Interventions

Patients on regular dialysis are randomized to darbepoetin or erythropoietin group and monitored for a treatment period of 20 weeks.

The investigator will randomise the patient by using the permuted block method of randomisation. A random number sequence is generated from a computer. Each possible permuted block is assigned a number. Using each number in the random number sequence in turn selects the next block, determining the next four patient allocations. Numbers in the random number sequence greater than the number of permuted block combinations are not used to select blocks. Upon successful randomisation, the subject will be assigned a subject ID number.

Intervention Type

Drug

Phase

Phase IV

Drug/device/biological/vaccine name(s)

Darbepoetin alpha, erythropoietin beta or alpha

Primary outcome(s)

Hb levels measured using blood sample at screening and baseline (day 0), randomization (week 2), week 6, week 10, week 14, week 18, and follow up end of study (week 22)

Key secondary outcome(s)

Safety parameters (vital signs, adverse events, and laboratory values) measured using patient records throughout the study

Completion date

12/09/2019

Eligibility

Key inclusion criteria

1. Written informed consent obtained.
2. Patients aged between 18 and 80 years.
3. Patients who are medically stable on dialysis for a minimum of 3 months.
4. Patients on erythropoietin treatment for ESKD related anemia and maintaining Hb level at or above 9 g/dL while on a stable dose (no change in dose) of erythropoietin within 6 weeks prior to the screening phase of this study.

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 Years

Upper age limit

80 Years

Sex

All

Total final enrolment

50

Key exclusion criteria

1. Pregnant or nursing women, or women of childbearing potential without an effective method of birth control. Effective birth control methods are oral contraception, Norplant, surgical sterilization, IUD or diaphragms in conjunction with spermicidal foam and condom on the male partner.
2. Participation in any drug trial in which the patient received an epoetin investigational drug within 30 days preceding the screening phase of this study.

3. Those persons directly involved in the conduct of the study.
4. History of seizure disorder.
5. Active acute or chronic infection or inflammatory disease.
6. Any illness that required hospitalization within the last one month.
7. Any medical or social reasons which in the investigator's judgment may interfere with patient's ability to participate in the study, or interfere with the study assessments or interpretation of the results.

Date of first enrolment

03/07/2016

Date of final enrolment

28/02/2019

Locations

Countries of recruitment

Malaysia

Study participating centre

Nephrology Department Hospital Serdang

Jalan Puchong

Kajang

Malaysia

43000

Sponsor information

Organisation

National Institute of Health (NIH) Malaysia

Organisation

Kyowa Hakko Kirin Malaysia

Funder(s)

Funder type

Government

Funder Name

National Institute of Health (NIH) Malaysia

Funder Name

Kyowa Hakko Kirin Malaysia

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated and analyzed for the study are available on reasonable request from the corresponding author: Prof. Dr. Bak-Leong Goh at email: bak.leong@gmail.com

IPD sharing plan summary

Available on request