ISRCTN96020335 https://doi.org/10.1186/ISRCTN96020335

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

Registration date
22/11/2023

Overall study status
Completed

Last Edited
21/11/2023

Condition category
Haematological Disorders

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] 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 brushing 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

Type(s)
Public, Scientific, Principal Investigator

Contact name
Prof Bak Leong Goh

ORCID ID
http://orcid.org/0000-0002-4644-7743

Contact details
Nephrology Department Hospital Serdang, Jalan Puchong
Kajang
Malaysia
43000
+60 389475467
drgohbakleong@moh.gov.my

Type(s)
Public, Scientific

Contact name
Mr Kim Liong Ang

ORCID ID
http://orcid.org/0000-0001-5699-3935

Contact details
Clinical Research Centre Hospital Serdang, Jalan Puchong
Kajang
Malaysia
43000
+60 389475467
angkl@crc.gov.my

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
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
Ethics approval required

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

Study design
Open label randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet.

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

Pharmaceutical study type(s)
Not Applicable

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Darbepoetin alpha, erythropoietin beta or alpha

Primary outcome measure
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)

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

Overall study start date
21/06/2016

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

Age group
Adult

Lower age limit
18 Years

Upper age limit
80 Years

Sex
Both

Target number of participants
236

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

Sponsor details
Persiaran Setia Murni
Setia Alam
Malaysia
43000
+60 333628888
mrecsec@moh.gov.my

Sponsor type
Government

Website
https://nih.gov.my/

Organisation
Kyowa Hakko Kirin Malaysia

Sponsor details
Wisma Cosplant 2, Jalan SS 16/1
Subang Jaya
Malaysia
47500
+60 122913740
enquiry.kkmy@kyowakirin.com

Sponsor type
Industry

Website
https://www.kyowakirin.com/malaysia/index.html

Funder(s)

Funder type
Government

Funder Name
National Institute of Health (NIH) Malaysia

Funder Name
Kyowa Hakko Kirin Malaysia

Results and Publications

Publication and dissemination plan
Final manuscript is ready and has been submitted to BMC Nephrology journal recently pending review outcome.

Intention to publish date
31/12/2023

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