A Randomized, Double-blind, Placebo-controlled Study to Evaluate the Long-term Safety and Efficacy of Darbepoetin Alfa Administered at 500 µg Once-Every-3-Weeks (Q3W) in Anemic Subjects With Advanced Stage Non-small Cell Lung Cancer Receiving Multi-cycle Chemotherapy.

Published: 03-08-2009
Last updated: 06-05-2024

The purpose of this study is to evaluate the safety of darbepoetin alfa, inclusive of the effects on survival and cancer progression, and the necessity of blood transfusions.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Red blood cell disorders
Study type	Interventional

Summary

ID

NL-OMON40053

Source
ToetsingOnline

Brief title
Evaluate Safety of Darbepoetin Alfa in Subjects With NSCLC

Condition

- Red blood cell disorders
- Miscellaneous and site unspecified neoplasms benign

Synonym
Anemic, exsanguinity

Research involving
Human

Sponsors and support

Primary sponsor: Amgen
Source(s) of monetary or material Support: Amgen

Intervention

Keyword: Advanced Stage Non-small Cell Lung Cancer, Anemic, Darbepoetin Alfa

Outcome measures

Primary outcome

To demonstrate non-inferiority of overall survival (OS) when comparing subjects

on

darbepoetin alfa treated to a hemoglobin ceiling of 12.0 g/dL to subjects

treated with

placebo

Secondary outcome

To demonstrate non-inferiority of progression free survival (PFS) when comparing

subjects on darbepoetin alfa treated to a hemoglobin ceiling of 12.0 g/dL to

subjects

treated with placebo

• To demonstrate superiority in reducing the incidence of red blood cell (RBC)

transfusions when comparing subjects on darbepoetin alfa treated to a hemoglobin

ceiling of 12.0 g/dL to subjects treated with placebo

• To assess other safety and efficacy parameters in subjects on darbepoetin alfa

treated to a hemoglobin ceiling of 12.0 g/dL compared to subjects treated with

placebo

Study description

Background summary

In this study, the study medication darbepoetin alfa is evaluated for the treatment of patients with non-small cell lung cancer. Darbepoetin alfa is approved for the treatment of anaemia in chronic renal failure in the United States, Canada, Australia, the European Union, Israel and many other countries worldwide. It is also approved for the treatment of anaemia caused by chemotherapy, in patients with non-¬myeloid, malignant tumours (cancer that does not originate in the bone marrow).
Approximately 3000 subjects are to be recruited for this study, at about 500 study sites in North-America, Europe, Latin-America, Australia, Asia and Africa.

Red blood cells are important because they contain haemoglobin, which transports oxygen in the body to the tissues and organs. Chemotherapy, which is used for the treatment of cancer, often causes anaemia. Severe anaemia can cause physical weakness (fatigue), shortness of breath, pale skin and rapid heartbeat. The treatment of severe anaemia by increasing the number of red blood cells in your body, may lead to reducing these symptoms or make them disappear. Darbepoetin alfa is a medicine from the group of erythropoietic stimulating agents (ESA); they increase the production of red blood cells. The other ESAs include the medicines epoetin beta and epoetin alfa

Study objective

The purpose of this study is to evaluate the safety of darbepoetin alfa, inclusive of the effects on survival and cancer progression, and the necessity of blood transfusions.

Study design

The study consists of a screening period, a treatment period, a follow-up visit to evaluate the safety and a long-term follow-up period.

During this study, darbepoetin alfa or placebo will be injected under the skin (subcutaneously) once every 3 weeks, in a dosage of 500 microgram (µg).

The patient has a 2 in 3 chance (67%) that he/she will receive darbepoetin alfa once every 3 weeks and a 1 in 3 chance (33%) that he/she will receive a placebo

once every 3 weeks.

The treatment with the study medicine will be started in the event that the haemoglobin level in the patients blood is less than or equal to 6.8 mmol/L and will be withheld in the event that this level exceeds 7.4 mmol/L.

The patient needs to come every three weeks to the clinic till disease progression.

After progression of the disease has occurred, the patient will start with the part of the study in which the long-term follow-up will take place. The patient will visit the clinic once every three months and the study staff will collect only a limited amount of information about the treatment and about any medications the patient uses until the end of the study. In the event that the patient is unable to come for these visits, the doctor may call to obtain this information from the patient.

Intervention

The Change of 2 out of 3 (67%) of receiving 1 x every 3 weeks darbepoëtine alfa, and the change of 1 out of 3 (33%) receiving placebo every 3 weeks.

Study burden and risks

During screening the following tests will be done: bloodsamples, CT scan or MRI, physical examination.
During the treatment phase; expected duration is 12 weeks (4 cycli), the patient will visit the clinic once every three weeks to receive medication and to collect bloodsamples. Imaging scans will be carried out once every 9 weeks until progression of the disease occurs
De risks for the patient are limited.

If the patient experiences no profit of the treatment and if there is an unacceptable situation (for patient or research worker) it can be decided to stop the research at any time.

Contacts

Public
Amgen

Minervum 7061
Breda 4817 ZK
NL

Scientific
Amgen

Minervum 7061
Breda 4817 ZK
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Disease Related;• Subjects with stage IV NSCLC (not recurrent or re-staged);• Expected to receive at least 2 additional cycles (at least 6 total weeks) of first line myelosuppressive cyclic chemotherapy after randomization. Subjects should not be expected to receive only maintenance chemotherapy.;Demographic;• Eastern Cooperative Oncology Group performance status of 0 or 1 as assessed within 21 days prior to randomization;• 18 years of age or older at screening.;• Life expectancy > 6 months based on the judgment of the investigator and documented during screening.;Laboratory;• Hemoglobin level <= 11.0 g/dL as assessed by the local laboratory; ;sample obtained within 7 days prior to randomization (retest in screening is acceptable).;• Adequate serum folate (>= 2 ng/mL) and vitamin B12 (>= 200 pg/mL) levels assessed by central laboratory (supplementation and retest acceptable) during screening.;Imaging;• Subjects must have had a baseline scan (CT, MRI, or PET/CT) of the chest to assess disease burden before starting on first line chemotherapy for NSCLC and those images must have been reviewed;by the investigator prior to randomization. If the scan was performed more than 28 days prior to randomization, an additional scan must be performed and reviewed by the investigator to confirm that the patient has not progressed before randomization.;Ethical;• Before any study-specific procedure, the appropriate written informed consent must be obtained from the subject or a legally accepted representative.

Exclusion criteria

Disease Related;• Known primary benign or malignant hematologic disorder which can cause anemia.;• History of, or current active cancer other than NSCLC, with the exception of curatively resected non-melanomatous skin cancer, curatively treated cervical carcinoma in situ, or other primary solid tumors curatively treated with no known active disease present and no curative treatment administered for the last 3 years.;• Received any prior adjuvant or neoadjuvant therapy for NSCLC;• Subjects with a history of brain metastasis.;• Uncontrolled hypertension (systolic BP > 160 mmHg or diastolic BP > 100 mmHg), or as determined by the investigator during screening.;• History of neutralizing antibody activity to rHuEPO or darbepoetin alfa.;• Uncontrolled angina, uncontrolled heart failure, or uncontrolled cardiac arrhythmia as determined by the investigator at screening. Subjects with known myocardial infarction within 6 months prior to randomization.;• Subjects with a history of seizure disorder taking anti-seizure medication within 30 days prior to randomization.;• Clinically significant systemic infection or uncontrolled chronic inflammatory disease (eg, rheumatoid arthritis, inflammatory bowel disease) as determined by the investigator during screening.;• Known seropositivity for HIV or diagnosis of AIDS, positive for hepatitis B surface antigen, or seropositive for hepatitis C virus.;• History of pure red cell aplasia.;• History of deep venous thrombosis or embolic event (eg, pulmonary ;embolism) within 6 months prior to randomization.;Laboratory;• Transferrin saturation < 20% and ferritin < 50 ng/mL as assessed by the ;central laboratory during screening. Subjects must have both to be ;excluded supplementation and retest acceptable).;• Abnormal renal function (serum creatinine level > 2X ULN) as assessed by ;the central laboratory during screening.;• Abnormal liver function (total bilirubin > 2X ULN or liver enzymes ALT or AST > 2.5X ULN for subjects without liver metastasis or >= 5X ULN for subjects with liver metastasis) as assessed by the central laboratory during screening. ;Subjects with documented Gilbert*s Disease may be eligible.;Medications;• Received any RBC transfusion within 28 days prior to randomization.;• Plan to receive any RBC transfusion between randomization and study day 1.;• Known previous treatment failure to ESAs (eg, rHuEPO, darbepoetin alfa).;• ESA therapy within the 28 days prior to randomization.;• Known hypersensitivity to recombinant ESAs or the excipients contained within the investigational product.;General;• Less than 30 days since receipt of any investigational product or device.;Investigational use/receipt of a medicinal product or device that has been approved by the country*s local regulatory authority for any indication is permitted.;• Subjects of reproductive potential who are pregnant, breast feeding or not willing to use effective contraceptive precautions during the study and for at least one month after the last dose of investigational product in the judgment of the investigator (including females of childbearing potential who are partners of male subjects).;• Previously randomized to this study.;• Investigator has concerns regarding the ability of the subject to give written informed consent and/or to comply with study procedures (including availability for follow-up visits).

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	06-01-2011
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Aranesp
Generic name:	Darbepoetin Alfa
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	03-08-2009
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	26-11-2009
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO

Date:	22-02-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-02-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-08-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-09-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-06-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	30-10-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-11-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-02-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United

	(Nieuwegein)
Approved WMO Date:	28-02-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	26-09-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	03-10-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-02-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-02-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-09-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-09-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-03-2016

Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-04-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-03-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-03-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	27-03-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2007-005792-34-NL
ClinicalTrials.gov	NCT00858364
CCMO	NL28191.060.09