Public Title	Darbepoetin Alfa in Anemic Low or Intermediate-1 Risk MDS
Scientific Title	A Multicenter, Randomised, Double-blind, Placebo-controlled Study of Darbepoetin Alfa for the Treatment of Anaemic Subjects With Low or Intermediate-1 Risk Myelodysplastic Syndrome (MDS)
Short Title	ARCADE
Id KN/ELN	LN_DEUTSC_2013_514
Trialgoup	Deutsche MDS
Type of Trial	multicentric, randomized, double-blind
Phase	Phase III
Disease	Myelodysplastic Syndrome(MDS) Low risk and intermedia I
Stage of Disease	.
Outcomes	- Achieving an International Working Group (IWG) erythroid response during the double-blind treatment period up to 24 weeks (Primary Outcome) - Adverse events, including treatment-emergent adverse events of interest (eg, pure red cell aplasia [PRCA]; thrombovascular events (TVE) [arterial thrombovascular events (ATE) and venous thrombovascular events (VTE)]) up to 73 weeks - Mortality through EOTP, EOATP, and LTFU up to 3 years - Disease progression to acute myeloid leukemia (AML) through EOTP, EOATP, and LTFU up to 3 years - At least one red blood cell (RBC) transfusion from week 5 to EOTP up to 20 weeks - Attaining a clinically meaningful change from baseline to EOTP in FACIT-F: improvement (at least a 3-point increase), deterioration (at least a 3-point decrease), unchanged (less than a 3-point in either direction) up to week 73 - Change in patient-reported fatigue and overall health status from baseline to week 13, EOTP, week 31, week 42/43, week 54/55, and week 72/73/ EOATP as measured by the Functional Assessment of Chronic Illness Therapy (FACIT-F) & EuroQOL-5D up to week 73 - Malignancies other than AML, basal cell carcinoma, or squamous cell carcinoma of the skin through EOTP up to 24 weeks - Neutralising antibody formation to darbepoetin alfa up to week 73
Inclusion Criteria	- Low or intermediate-1 risk MDS patients per IPSS at the time of randomisation, as determined by complete blood count (CBC) during screening and bone marrow examination and marrow cytogenetic analysis performed within 16 weeks prior to randomisation. Subject cannot have been rendered low or intermediate-1 risk by prior disease modifying therapy. Bone marrow slides must be available for centralised review at any time throughout the study - World Health Organization (WHO) classification of refractory anaemia (RA), refractory anaemia with ring sideroblasts (RARS), refractory cytopenias with multilineage dysplasia (RCMD), MDS-unclassified (MDSU), MDS with isolated del(5q) (5q- syndrome) or refractory anaemia with excess blasts-1 (RAEB-1) - Eastern Cooperative Oncology Group (ECOG) performance status score of 0 or 1 assessed during screening - Haemoglobin level <= 10.0 g/dL as assessed by the local laboratory; sample obtained within 7 days prior to randomisation (retest during screening is acceptable) - Adequate transferrin saturation (Tsat) (>= 15%) and serum ferritin (>= 10 ng/mL) as assessed by the central laboratory during screening (supplementation and retest during screening is acceptable) - Adequate serum folate (>= 4.5 nmol/L [>= 2.0 ng/mL]) or RBC folate (>= 317 nmol/L [>= 140 ng/mL]) as assessed by the local laboratory during screening (supplementation and retest during screening is acceptable)

- Adequate vitamin B12 (>= 148 pmol/L [>= 200 pg/mL]) as assessed by the local laboratory during screening (supplementation and retest during screening is acceptable)
- 18 years of age or older
- Subject or subject's legally acceptable representative has provided informed consent

Exclusion Criteria

- Previously diagnosed with intermediate-2 or high risk MDS per International Prognostic Scoring System (IPSS)
- Therapy-related or secondary MDS
- History of acute leukemia
- Evidence of bone marrow collagen fibrosis
- Inherited anaemia (eg, haemoglobinopathy, thalassemia, red cell membrane defect, red cell enzyme deficiency), active hemorrhage, red cell aplasia, haemolytic anaemia
- History of malignancies other than curatively treated non-melanoma skin or in situ carcinoma
- History of thrombosis within 6 months prior to randomisation
- Previous bone marrow or stem cell transplantation
- 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 randomisation
- Uncontrolled hypertension defined as systolic blood pressure >= 160 mmHg and/or diastolic blood pressure >= 100 mmHg at screening
- Clinically significant systemic infection or uncontrolled chronic inflammatory disease (ie, rheumatoid arthritis, inflammatory bowel disease) as determined by the investigator at screening
- History of seizure disorder (subject with previous history of seizure disorder will be eligible for the study if he/she had no evidence of seizure activity within 5 years of randomisation and is currently free of antiseizure medication)
- Previous or ongoing use of ESA therapy, eg, rHuEpo, darbepoetin alfa
- High transfusion demand: receiving a total of >= 4 units of RBC transfusion during either of 2 consecutive 8-week periods (ie, days -113 to -57 or days -56 to 0) prior to randomisation
- Received any RBC transfusion within 14 days prior to randomisation
- Received cytotoxic chemotherapy for any oncologic indication or planning to receive cytotoxic chemotherapy during the double-blind treatment period of the study
- Received biologic response modifiers (eg, thalidomide, lenalidomide, arsenic trioxide, azacitidine, decitabine) to treat MDS or planning to receive biologic response modifiers during the double-blind treatment period of the study
- Received myeloablative or craniospinal radiation or planning to receive myeloablative or craniospinal radiation during the double-blind treatment period of the study
- Received G-CSF therapy within 30 days prior to randomisation or planning to receive G-CSF therapy during the double-blind treatment period of the study (temporary use of G-CSF for neutropenia with fever and/or infection is acceptable)
- Abnormal renal function (serum creatinine level > 2 times the upper limit of the respective normal range [ULN]) as assessed by the central laboratory at screening
- Abnormal liver function (total bilirubin > 2 times, alanine aminotransferase [ALT] or aspartate aminotransferase [AST] > 3 times ULN) as assessed by the central laboratory at screening. (Subjects with abnormal bilirubin at screening due to documented Gilbert's Disease are eligible if all other criteria are met.)

- Serum endogenous erythropoetin (EPO) level > 500 mU/mL as assessed by the central laboratory at screening
- Known seropositivity for human immunodeficiency virus (HIV) or diagnosis of Acquired Immunodeficiency Syndrome (AIDS), positive for hepatitis B surface antigen, or seropositive for hepatitis C virus
- Subjects with active ethanol abuse, as judged by the investigator
- Currently enrolled in another investigational device or drug study, or less than 30 days since ending another investigational device or drug study(s), or receiving other investigational agent(s)
- Female subject is not willing to use highly effective contraception during treatment and for at least 1 month after the end of treatment
- Female subject is pregnant or planning to become pregnant within 1 month after the end of treatment
- Subject has known sensitivity to any of the products to be administered during dosing
- Subject has previously been randomised into this study
- Subject will not be available for protocol-required study visits, to the best of the subject and investigator's knowledge
- Subject has any kind of disorder that, in the opinion of the investigator, may compromise the ability of the subject to give written informed consent and/or to comply with all required study procedures
- Confirmed history of neutralising antibody activity to rHuEpo or darbepoetin alfa

Age >= 18 years

Status Closed

start of Recruitment 01.02.2013

Recruiting countries Germany
France
Czech Republic
Belgium
Spain
Italy
Greece

Target Sample Size 180

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Other Registers ClinicalTrials.govNCT01362140
European Clinical Trials Database - EUDRACT2009-016522-14