ISRCTN98011567 https://doi.org/10.1186/ISRCTN98011567

REGiME Trial: Prolonged treatment with darbepoetin alpha (DA) in patients with low-risk myelodysplastic syndromes

Submission date 16/06/2010	**Recruitment status** No longer recruiting	[X] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 12/10/2010	**Overall study status** Completed	
Last Edited 13/05/2019	**Condition category** Cancer	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT01196715

Secondary identifying numbers
version 1.1 dated 21 May 2010

Study information

Scientific Title
REGiME Trial: A randomised controlled trial of prolonged treatment with darbepoetin alpha (DA) with/without recombinant human granulocyte colony stimulating factor (G-CSF), versus best supportive care in patients with low-risk myelodysplastic syndromes

Acronym
REGiME

Study objectives
To compare the haemoglobin response and quality of life of low risk myelodysplastic syndrome (MDS) patients randomised to receive prolonged treatment with darbepoetin alpha (DA) alone, DA with recombinant human granulocyte colony stimulating factor (G-CSF) or best supportive care alone.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Randomised controlled triple-arm study

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
Low-risk myelodysplastic syndrome

Interventions
The treatment schedule uses the concept of 'frontloading' to give patients the highest doses of DA at the start of therapy in order to induce a response as quickly as possible. The long-acting

nature of darbepoetin alpha avoids excessive frequency of injections, but allows delivery of high doses of ESA. At week 24, if no response is achieved, the study treatment is deemed to have failed and is stopped and patients will receive 'best supportive care' only. Response assessment will follow IWG criteria.

Arm A:
Darbepoetin alpha (Aranesp®) and best supportive care if applicable:
1. Aranesp® 500 µg subcutaneous (s.c.) once every 2 weeks:
1.1. If a rapid response is obtained (haemoglobin [Hb] increase greater than or equal to 2 g/dl in any 4 week period), titrate down the dose frequency of Aranesp®
1.2. If major response, titrate Aranesp® to lowest dose frequency that maintains the response
2. At 24 weeks:
2.1. If no response, stop Aranesp® and give supportive therapy only
2.2. If minor response, continue Aranesp® 500 µg once every 2 weeks s.c.
2.3. If major response, titrate Aranesp® to lowest dose frequency that maintains the response
3. If patients present symptoms, they will receive red cell transfusion support to achieve a predicted posttransfusion haemoglobin of 11.0 to 12.0 g/dl at a quantity and frequency such that:
3.1. The minimum haemoglobin is never below 8.0 g/dl, or
3.2. The patient is never excessively symptomatic, according to local transfusion guidelines /policy

Arm B:
Darbepoetin alpha (Aranesp®) and recombinant human granulocyte colony stimulating factor (G-CSF) and best supportive care if applicable:
1. G-CSF (Neupogen®) 300 µg s.c. twice a week, 3 - 4 days apart
2. Aranesp® 500 µg s.c. once every 2 weeks:
2.1. If a rapid response is obtained (Hb increase greater than or equal to 2 g/dl in any 4 week period), titrate down the dose frequency of Aranesp®
2.2. If major response, titrate Aranesp® and G-CSF to lowest dose frequency that maintains the response
3. At 24 weeks:
3.1. If no response, stop Aranesp® and G-CSF and give supportive therapy only
3.2. If minor response, continue Aranesp® 500 µg every 2 weeks s.c. and G-CSF 300 µg s.c. twice a week, 3 - 4 days apart
3.3. If major response, titrate Aranesp® and G-CSF to lowest dose frequency that maintains the response
4. If patients present symptoms, they will receive red cell transfusion support to achieve a predicted post-transfusion haemoglobin of 11.0 to 12.0 g/dl at a quantity and frequency such that:
4.1. The minimum haemoglobin is never below 8.0 g/dl, or
4.2. The patient is never excessively symptomatic, according to local transfusion guidelines /policy

Arm C:
Best supportive care only:
Patients randomised to no growth factor treatment will receive best supportive care only, which is defined as red cell transfusion support to achieve a predicted post-transfusion haemoglobin of 11.0 to 12.0 g/dl at a quantity and frequency such that;
1. The minimum haemoglobin is never below 8.0 g/dl, or
2. The patient is never excessively symptomatic, according to local transfusion guidelines/policy

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Darbepoetin alpha, recombinant human granulocyte colony stimulating factor

Primary outcome measure
1. Quality of life, measured at weeks 0, 12, 24, 36 and 52
2. Haemoglobine response, measured every week until 24 weeks and then at weeks 36 and 52

Secondary outcome measures
1. Economic costs measured at baseline
2. Utility of prognostic factor and predictive factor assessment, measured weekly

Overall study start date
01/11/2010

Completion date
31/10/2015

Eligibility

Key inclusion criteria
1. Males and females aged over 18 years (no upper age limit)
2. Eastern Cooperative Oncology Group (ECOG) performance status 0 - 2
3. Life expectancy more than 6 months
4. A confirmed diagnosis of MDS - World Health Organization (WHO) type:
4.1. Refractory anaemia (RA)
4.2. Hypoplastic RA ineligible for or failed immunosuppressive therapy (antilymphocyte globulin [ALG], cyclosporine)
4.3. Refractory anaemia with ring sideroblasts (RARS)
4.4. Refractory cytopenia with multilineage dysplasia
4.5. Myelodysplastic syndrome unclassifiable
5. International Prognostic Scoring System (IPSS) low or Int-1, but with bone marrow (BM) blasts less than 5%
6. A haemoglobin concentration of less than 10 g/dl and/or red cell transfusion dependence
7. Able to understand the implications of participation in the trial and give written informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
360

Key exclusion criteria
1. MDS with bone marrow blasts greater or equal than 5%
2. Myelodysplastic syndrome associated with del (5q)(q31 - 33) syndrome
3. Chronic myelomonocytic leukaemia (monocytes greater than 1.0 x 10^9/l)
4. Therapy-related MDS
5. Splenomegaly, with spleen greater or equal than 5 cm from left costal margin
6. Platelets less than 30 x 10^9/l
7. Uncorrected haematinic deficiency. Patient deplete to iron, B12 and folate according to local lab ranges.
8. Women who are pregnant or lactating
9. Females of childbearing potential and all males must be willing to use an effective method of contraception (hormonal or barrier method of birth control; abstinence) for the duration of the study and for up to 3 months after the last dose of study medication. Note: Subjects are not considered of child bearing potential if they are surgically sterile (they have undergone a hysterectomy, bilateral tubal ligation, or bilateral oophorectomy) or they are post-menopausal.
10. Females of childbearing potential must have a negative pregnancy test prior to starting the study
11. Uncontrolled hypertension, previous venous thromboembolism, or uncontrolled cardiac or pulmonary disease
12. Previous serious adverse events to the study medications or its components
13. Patients who have had previous therapy with erythropoiesis-stimulating agents (ESAs) with /without G-CSF within 4 weeks of study entry
14. Patients currently receiving experimental therapy, e.g. with thalidomide, or who are participating in another clinical trial of investigational medicinal product (CTIMP)
15. Medical or psychiatric illness, which makes the patient unsuitable or unable to give informed consent

Date of first enrolment
01/11/2010

Date of final enrolment
31/10/2015

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
St Bartholomew's Hospital
London

United Kingdom
EC1A 7BE

Sponsor information

Organisation
Barts and The London NHS Trust (UK)

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England
United Kingdom
E1 2AN

Sponsor type
Hospital/treatment centre

Website
http://www.bartsandthelondon.nhs.uk/

ROR
https://ror.org/00b31g692

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK (CRUK) (UK) (ref: C17401/A9616)

Alternative Name(s)
CR_UK, Cancer Research UK - London, CRUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location

United Kingdom

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration