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REGiM: Prolonged treatment with darbepoetin alpha (EPO), with/without recombinant human granulocyte colony stimulating factor (G-CSF), versus best supportive care in patients with low-risk myelodysplastic syndromes (MDS)

Submission date 24/06/2010	**Recruitment status** No longer recruiting	[ ] Prospectively registered [ ] Protocol
Registration date 24/06/2010	**Overall study status** Completed	[ ] Statistical analysis plan [ ] Results
Last Edited 28/02/2019	**Condition category** Cancer	[ ] Individual participant data [ ] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2004-002862-39

ClinicalTrials.gov (NCT)
NCT00234143

Protocol serial number
4658

Study information

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

Acronym
REGiM

Study objectives
Myelodysplastic syndromes (MDS) are acquired clonal disorders of the bone marrow. The clinical consequences of MDS are bone marrow failure and a predisposition to develop acute myeloid leukaemia (AML). Patients with 'low risk MDS' have less than 10% myeloblasts in the marrow and include the World Health Organization (WHO) subtypes refractory anaemia (RA), refractory anaemia with ring sideroblasts (RARS) and refractory anaemia with excess blasts-I (RAEB-I). This group of patients have a relatively low risk of leukaemic transformation and the major clinical problem is the manifestations of bone marrow failure. Up to 80% of these patients become red cell transfusion dependent.

To date the only curative therapy is allogeneic stem cell transplantation. Unfortunately, a median age at diagnosis of more than 65 years excludes this type of therapy for most patients with MDS. The aim of treatment is, therefore, supportive therapy (long term red cell transfusions).

In this clinical study we are investigating if treatment with an erythropoiesis stimulating agent (darbepoetin alpha) with or without G-CSF therapy can increase haemoglobin concentration and reduce/eliminate red cell transfusion in selected patients with MDS. Our primary endpoints include a measure of erythroid response and quality of life to see if treatment with darbepoetin alpha with/without G-CSF is more effective than best supportive care (long term red cell transfusions).

The trial is a multi-centre, randomised, triple arm, open-label study. We aim to open 40 sites in the UK in the first instance recruiting 360 patients in total. When the eligibility is confirmed, patients will be randomised within 42 days into a 1:1:1 ratio to either:
1. Arm A: Darbepoetin alpha and best supportive care
2. Arm B: Darbepoetin alpha with G-CSF and best supportive care
3. Arm C: Best supportive care only

Ethics approval required
Old ethics approval format

Ethics approval(s)
Brighton East Research Ethics Committee approved on the 8th November 2004 (ref: 04/Q1907 /94)

Study design
Multicentre randomised interventional treatment trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: National Cancer Research Network; Subtopic: Haematological Oncology; Disease: Leukaemia (acute myeloid)

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.

Arm A: Darbepoetin Alpha (Aranesp®) 500 mcg subcutaneously (s.c.) once every 2 weeks
Arm B: Aranesp® and G-CSF (Neupogen®) 300 mcg s.c. twice a week, 3 - 4 days apart
Arm C: Best supportive care; patients randomised to no growth factor treatment

Study entry: registration and one or more randomisations

Intervention Type
Drug

Phase
Phase III

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

Primary outcome(s)
Quality of life at 24 weeks

Key secondary outcome(s))
1. Quality of life at 12, 36 and 52 weeks
2. Overall erythroid response (major and minor) at 24 weeks (main analysis point) and also at 12 and 52 weeks, as defined by the International Working Group criteria
3. Incidence of disease progression
4. Overall survival
5. Economic costs of managing anaemia in each arm of the study

Completion date
11/12/2009

Eligibility

Key inclusion criteria
1. A confirmed diagnosis of MDS - WHO type:
1.1. Refractory anaemia (RA)
1.2. Hypoplastic RA ineligible for or failed immunosuppressive therapy (ALG, cyclosporine)
1.3. Refractory anaemia with ring sideroblasts (RARS)
1.4. Refractory cytopenia with multilineage dysplasia
1.5. Myelodysplastic syndrome unclassifiable
2. IPSS low or Int-1, but with BM blasts less than 5%
3. A haemoglobin concentration of less than 10 g/dl and/or red cell transfusion dependence
4. Written informed consent
5. Aged more than 18 years old, no upper limit, either sex

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. MDS with bone marrow blasts greater than or equal to 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 than or equal to 5 cm from left costal margin
6. Platelets less than 30 x 10^9/l
7. Uncorrected haematinic deficiency
8. Age less than 18 years
9. Woman who are pregnant or lactating
10. Women of child bearing age unless using reliable contraception
11. Life expectancy less than 6 months
12. Uncontrolled hypertension, previous venous thromboembolism, or uncontrolled cardiac or pulmonary disease
13. Previous adverse events to the study medications or its components
14. Patients who have had previous therapy with EPO ± G-CSF within 4 weeks of study entry
15. Patients currently receiving experimental therapy, e.g. with thalidomide, or who are participating in another clinical trial
16. Medical or psychiatric illness, which makes the patient unsuitable or unable to give, informed consent

Date of first enrolment

13/07/2005

Date of final enrolment
11/12/2009

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Institute of Cancer
London
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Sponsor information

Organisation
Barts and The London NHS Trust (UK)

ROR
https://ror.org/00b31g692

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK (CRUK) (UK) (ref: C4047)

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

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary