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Myelomatosis therapy trial for patients of all age groups

Submission date 21/09/2000	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 21/09/2000	**Overall study status** Completed	
Last Edited 19/10/2018	**Condition category** Cancer	

Plain English summary of protocol
http://cancerhelp.cancerresearchuk.org/trials/a-trial-comparing-treatments-for-myeloma

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
G0100132

Study information

Scientific Title
Myelomatosis therapy trial for patients of all age groups

Acronym

MRC Myeloma IX

Study objectives

1. Therapeutic questions within the intensive pathway:
1. 1. To compare an oral induction regimen containing thalidomide with a standard infusional induction chemotherapy, CTD versus CVAD, with respect to overall/progression-free survival and response.
1.2. To investigate the effects of giving additional consolidation therapy in the form of a low intensity conditioning allogeneic stem cell transplantation on survival.

2. Therapeutic questions within the non-intensive pathway:
2.1. To compare attenuated C-Thal-Dex (CTDa) with standard MP with respect to overall /progression-free survival and response.

3. Therapeutic questions across both pathways:
3.1. To assess the value of low dose thalidomide in maintenance in improving overall and progression-free survival.
3.2. To compare an aminobisphosphonate, zoledronic acid, with standard clodronate on the severity of bone disease and in improving survival.
3.3. To investigate quality of life in the short-term (during induction chemotherapy /bisphosphonate treatment) and in the long-term (during maintenance therapy).
3.4. To investigate prognostic factors for outcome.

4. Biological objectives:
4.1. To determine the clinical relevance of genetic/cytogenetic changes present at presentation in the definition of prognostic groups.
4.2. To determine the relevance of cellular phenotypes at presentation and to subsequently use these data to monitor residual disease.
4.3. To evaluate serum free light chain (flc) measurement as a prognostic factor and in monitoring disease.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Not provided at time of registration

Primary study design

Interventional

Study design

Randomised controlled trial

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Multiple Myeloma

Interventions

There are two main pathways:
1. Intensive for 'younger/fitter' patients
2. Non-intensive for 'older/less fit' patients
There are three randomised comparisons within each pathway.

1. Intensive pathway
At diagnosis:
1.1. Cyclophosphamide, vincristine, adriamycin, dexamethasone (CVAD) versus cyclophosphamide, thalidomide, dexamethasone (CTD)
1.2. Clodronate versus Zoledronic acid
After high dose consolidation therapy (HDT):
1.3. Thalidomide versus no maintenance therapy
In addition, following standard high dose melphalan with autograft, patients with an available tissue-compatible sibling donor may be offered a reduced intensity conditioning allograft, if appropriate.

2. Non-intensive pathway
At diagnosis:
2.1. Melphalan, prednisolone (MP) versus cyclophosphamide, thalidomide, dexamethasone (attenuated) (CTDa)
2.2. Clodronate versus Zoledronic acid
After achievement of plateau state:
2.3. Thalidomide versus no maintenance therapy

Intervention Type
Other

Phase
Not Specified

Primary outcome(s)
1. Overall survival
2. Progression-free survival
3. Response

Key secondary outcome(s)
1. Quality of Life
2. Skeletal related events
3. Toxicity
4. Thromboembolic events
5. Renal toxicity
6. Haematologic toxicity
7. Graft versus Host Disease (GvHD)

Completion date
31/07/2014

Eligibility

Key inclusion criteria

1. Aged 18 years or greater
2. Newly diagnosed as having symptomatic multiple myeloma or non secretory multiple myeloma based on:
2.1. Paraprotein (M-protein) in serum and/or urine
2.2. Bone marrow clonal plasma cells or plasmacytoma
2.3. Related organ or tissue impairment
3. Written informed consent
4. Prepared to use contraception
5. Negative pregnancy test

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. Asymptomatic myeloma
2. Solitary plasmacytoma of bone
3. Extramedullary plasmacytoma (without evidence of myeloma)
4. Previous or concurrent active malignancies, except surgically removed basal cell carcinoma of the skin or other in situ carcinomas
5. Previous treatment for myeloma, except the following:
5.1. local radiotherapy to relieve bone pain or spinal cord compression
5.2. prior bisphosphonate treatment
5.3. low-dose corticosteroids (up to 12 mg/day dexamethasone or 80 mg/day prednisolone, for 14 days)
5.4. up to four single doses of corticosteroids (total dose 1 g methylperdnisolone, 200 mg dexamethasone, or 1.25 g prenisolone)
Caution is advised in patients with a past history of ischaemic heart disease or psychiatric disorders, but exclusion is essentially to be at the discretion of the treating clinician.
6. Acute renal failure (unresponsive to up to 72 h of rehydration characterised by creatine >500 µmol/l or urine output <400 ml/day or requirement for dialysis). These patients are not eligible for this study but may be eligible for inclusion in MERIT (Myeloma Renal Impairment Trial). NB Patients with serum creatinine >2 x upper limit or normal (or creatinine clearance <20 ml/min) are eligible for Myeloma IX, but bisphosphonates should not be administered until serum creatinine has decreased to <2 x upper limit of normal (or creatinine clearance >30 ml/min)

Date of first enrolment
14/05/2003

Date of final enrolment
31/07/2014

Locations

Countries of recruitment
United Kingdom

England

New Zealand

South Africa

Study participating centre
Clinical Trials Research Unit
Leeds
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Sponsor information

Organisation
University of Leeds (UK)

ROR
https://ror.org/024mrxd33

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council (MRC) (UK)

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results on homozygous deletion mapping in myeloma samples	15/03/2010		Yes	No
Results article	results on XBP1s levels in multiple myeloma	15/07/2010		Yes	No
Results article	results on genomic profiling of multiple myeloma	14/10/2010		Yes	No
Results article	results on secondary outcomes	01/08/2011		Yes	No
Results article	results on CTD initial therapy	04/08/2011		Yes	No
Results article	results	01/10/2011		Yes	No
Results article	results and meta-analysis	05/01/2012		Yes	No
Results article	results	01/03/2012		Yes	No
Results article	results	02/08/2012		Yes	No
Results article	results	24/10/2013		Yes	No
Results article	results	01/11/2013		Yes	No
Results article	results	29/05/2014		Yes	No
Results article	results	19/03/2015		Yes	No
Interim results article	interim results	01/02/2005		Yes	No
Plain English results				No	Yes