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MyeChild 01: Treating children with acute myeloid leukaemia

Submission date 03/02/2016	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 03/02/2016	**Overall study status** Ongoing	
Last Edited 10/06/2025	**Condition category** Cancer	

Plain English summary of protocol
A trial looking at improving chemotherapy for children with acute myeloid leukaemia (MyeChild01)
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-using-gsk2857916-for-people-with-myeloma

A study of gemtuzumab ozogamicin with chemotherapy for children with AML (MyeChild01)
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-of-gemtuzumab-ozogamicin-with-chemotherapy-for-children-with-aml-myechild01

A trial looking at chemotherapy before a stem cell transplant for children with acute myeloid leukaemia (MyeChild01)
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-chemotherapy-before-a-stem-cell-transplant-for-children-with-acute-myeloid

Study website
http://www.birmingham.ac.uk/research/activity/mds/trials/crctu/trials/myechild01/index.aspx

Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
2014-005066-30

IRAS number

ClinicalTrials.gov number
NCT02724163

Secondary identifying numbers
19700

Study information

Scientific Title
International Randomised Phase III Clinical Trial in Children with Acute Myeloid Leukaemia - Incorporating an Embedded Dose Finding Study for Gemtuzumab Ozogamicin in Combination with Induction Chemotherapy

Acronym
MyeChild 01

Study objectives
Study aims:
1. To establish which number of doses of gemtuzumab ozogamicin (up to a maximum of 3 doses) is tolerated and can be safety delivered in combination with cytarabine plus mitoxantrone or liposomal daunorubicin in induction
2. To compare mitoxantrone (anthracenedione) and cytarabine with liposomal daunorubicin (anthracycline) & cytarabine as induction therapy
3. To compare a single dose of gemtuzumab ozogamicin with the optimum tolerated number of doses of gemtuzumab ozogamicin (identified by the dose-finding study) when combined with induction chemotherapy
4. To compare two consolidation regimens: high dose cytarabine (HD Ara-C) and fludarabine & cytarabine (FLA) in standard risk patients
5. To compare the toxicity and effectiveness of two haemopoietic stem cell transplant (HSCT) conditioning regimens of different intensity: conventional myeloablative conditioning (MAC) with busulfan/cyclophosphamide and reduced intensity conditioning (RIC) with fludarabine /busulfan

Ethics approval required
Old ethics approval format

Ethics approval(s)

Wales REC 3, 27/10/2015, ref: 15/WA/0316

Study design
Randomised; Interventional; Design type: Treatment

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

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
Acute myeloid leukaemia

Interventions
Current interventions as of 02/09/2021:
Trial Entry
Arm A Induction. Active Comparator: mitoxantrone (mitoxantrone & cytarabine)

Gemtuzumab Ozogamicin Dose Finding Study
Experimental: gemtuzumab ozogamicin (other names: Mylotarg)

Randomisation 3
Arm C Consolidation. Active Comparator: high dose cytarabine.
Arm D Consolidation. Experimental: fludarabine & cytarabine

Randomisation 4
Arm E HSCT. Active Comparator: Myeloablative conditioning (busulfan & cyclophosphamide)
Arm F HSCT. Experimental: Reduced intensity conditioning (busulfan & fludarabine)

The Arm B Induction (Experimental: liposomal daunorubicin) closed to recruitment early on 8th September 2017, due to manufacturing issues with liposomal daunorubicin experienced by the marketing authorisation holder, which could not be rectified.

Previous interventions:
Randomisation 1
Arm A Induction. Active Comparator: mitoxantrone (mitoxantrone & cytarabine)
Arm B Induction. Experimental: liposomal daunorubicin (liposomal daunorubicin & cytarabine)

Gemtuzumab Ozogamicin Dose Finding Study
Experimental: gemtuzumab ozogamicin (other names: Mylotarg)

Randomisation 3
Arm C Consolidation. Active Comparator: high dose cytarabine.
Arm D Consolidation. Experimental: fludarabine & cytarabine

Randomisation 4
Arm E HSCT. Active Comparator: Myeloablative conditioning (busulfan & cyclophosphamide)
Arm F HSCT. Experimental: Reduced intensity conditioning (busulfan & fludarabine)

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Gemtuzumab ozogamicin (Mylotarg), liposomal daunorubicin, mitoxantrone, fludarabine, cytarabine, busulfan, cyclophosphamide

Primary outcome measure
Gemtuzumab ozogamicin dose finding study:
Incidence of dose limiting toxicities (DLTs) are evaluated up to day 45 post course 1 and course 2 of induction chemotherapy.

Secondary outcome measures
1. Complete remission (R1 and R2) is evaluated and presented after course 1 and 2 or treatment
2. Relapse Free Survival (R3) is determined as time from randomisation 3 to first relapse or death
3. Cumulative Incidence of Relapse (all randomisations) is evaluated as time from randomisation to the relevant question of relapse
4. Days in hospital after each course of treatment (all randomisations) is evaluated once all patients have completed treatment
5. Death in complete remission (R1, R2 and R3) is evaluated as the time from randomisation to date of death from any cause in patients who achieved CR
6. Event Free Survival (R1, R2 and R3) is determined as time from randomisation to the first event
7. Nature, incidence and severity of adverse events (Gemtuzumab ozogamicin dose finding study) are evaluated by day 45 post course 1 and course 2
8. Responses measured by bone marrow assessment (Gemtuzumab ozogamicin dose finding study) on day 21-45 post day 1 of study drugs
9. Event Free Survival (R2) is determined as time from randomisation 2 to the 1st event
10. Gonadal function (R4) is evaluated at 1 year post-transplant and at the end of follow-up
11. Early Treatment Related Adverse Reactions (R4) is measured as incidence by day 100 post-transplant of grade 3-5 toxicity
12. (R4) Relapse Free Survival (R4) is determined as time from Randomisation 4 to the first relapse or death
13. Incidence of bilirubin of grade 3 of higher (R2 and R4) is evaluated 30 days after end of trial treatment
14. Incidence of cardiotoxicity (R1, R2 and R3) is evaluated 30 days after end of trial treatment
15. Incidence of mixed chimerism at day 100 post-transplant (R4) is evaluated at day 100 post-transplant
16. Incidence of toxicities (all randomisations) is evaluated 30 days after end of trial treatment
17. Incidence of Veno-Occlusive Disease(R2 and R4) is evaluated 30 days after end of trial treatment

18. Event Free Survival (R1) is determined as time from randomisation one to the first event
19. Minimal Residual Disease (MRD) clearance after course 1 and 2 (R1 and R2) is evaluated after course 1 and 2 of treatment
20. Overall survival (all randomisations) is determined as time from randomisation to death from any cause or date last seen for patients alive at end of trial
21. Reasons for failure to achieve complete remission (R1 and R2) is evaluated after course 1 and 2 of treatment
22. Clearance and Volume of Distribution (Serum pharmacokinetic parameters of gemtuzumab ozogamicin) at multiple sample time points during course 1
23. Time to haematological recovery (all randomisations) is evaluated by day 45 post course 1 and course 2.;
24. Treatment Related Mortality (R4) is evaluated as time in days between randomisation and death (considered related to the transplant)

Overall study start date
16/03/2016

Completion date
31/05/2032

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 02/09/2021:
Inclusion criteria for trial entry:
1. A diagnosis of AML/high risk myelodysplastic syndrome (MDS)/isolated myeloid sarcoma (either de novo or secondary)
2. Aged <18 years
3. No prior chemotherapy or biological therapy for AML other than that permitted in the protocol
4. Normal cardiac function (fractional shortening ≥28% or ejection fraction of 55%)
5. Fit for protocol chemotherapy
6. Documented negative pregnancy test for patients of childbearing potential
7. Patient agrees to use effective contraception (patients of childbearing potential)
8. Written informed consent from the patient and/or parent/legal guardian

Inclusion criteria for participation in the gemtuzumab ozogamicin dose finding study:
Centres must be formally activated in order to take part in the embedded dose escalation study (please contact the trial office for further information).
1. Patient meets the inclusion criteria for trial entry
2. Aged either:
2.1. ≥12 months for the major dose finding study
2.2. ≥12 weeks and <12 months
3. Normal renal function defined as calculated creatinine clearance ≥90 ml/min/1.73m² (calculated using the BNFc formula, or that in use locally)
4. Normal hepatic function defined as total bilirubin ≤2.5 x upper limit of normal (ULN) for age unless it is caused by leukaemic involvement, Gilbert's syndrome, or a similar disorder
5. ALT or AST ≤10 x ULN for age
6. Written informed consent from the patient and/or parent/legal guardian

Inclusion criteria for treatment with gemtuzumab ozogamicin for patients not participating in the gemtuzumab ozogamicin dose finding study or R2:
Centres must be formally activated to be able to deliver treatment with gemtuzumab ozogamicin (please contact the trial office for further information).
1. Patient meets the inclusion criteria for trial entry
2. Aged either:
2.1. ≥12 months
2.2. ≥12 weeks and <12 months
2.3. ≥28 days and and <12 weeks
3. Normal renal function defined as calculated creatinine clearance ≥90 ml/min/1.73m² (calculated using the BNFc formula, or that in use locally)
4. Normal hepatic function defined as total bilirubin ≤2.5 x upper limit of normal (ULN) for age unless it is caused by leukaemic involvement, Gilbert's syndrome, or a similar disorder
5. ALT or AST ≤10 x ULN for age
6. Written informed consent from the patient and/or parent/legal guardian

Inclusion criteria for participation in R2 (once open to randomisation in the applicable age group):
1. Patient meets the inclusion criteria for trial entry
2. Aged either:
2.1. ≥12 months
2.2. ≥12 weeks and <12 months (once R2 open in patients aged ≥12 weeks and <12 months)
3. Normal renal function defined as calculated creatinine clearance ≥90 ml/min/1.73m² (calculated using the BNFc formula, or that in use locally)
4. Normal hepatic function defined as total bilirubin ≤2.5 x upper limit of normal (ULN) for age unless it is caused by leukaemic involvement, Gilbert's syndrome, or a similar disorder
5. ALT or AST ≤10 x ULN for age
6. Written informed consent from the patient and/or parent/legal guardian

Inclusion criteria for participation in R4:
1. Patient meets the inclusion criteria for trial entry
2. Induction treatment as per MyeChild 01 protocol or treated with 1 or 2 courses of mitoxantrone & cytarabine ± treatment intensification with FLA-Ida off trial
3. Patient is in CR or CRi defined as <5% blasts confirmed by flow cytometry//molecular/FISH in a bone marrow aspirate taken within 6 weeks prior to randomisation to R4
4. Patient meets one of the following criteria and is a candidate for HSCT as per the protocol:
4.1. High risk after course 1 (all patients with poor risk cytogenetics and patients with intermediate risk cytogenetics who fail to achieve CR/CRi)
4.2. Intermediate risk cytogenetics with MRD >0.1% after courses 1 and 2 measured by flow. If no flow MRD marker of sufficient sensitivity is identified, a molecular MRD marker with a sensitivity of >0.1% may be used
4.3. Good risk cytogenetics with flow MRD >0.1% confirmed by a decrease in molecular MRD of <3 logs or rising transcript levels after course 3 despite treatment intensification (FLAIda) and after discussion with the Clinical Coordinators
5. Availability of a 9-10/10 HLA matched family or unrelated donor or 5-8/8 matched cord blood unit with an adequate cell dose as defined by the protocol section 17.1
6. Written informed consent from the patient and/or parent/legal guardian

Previous participant inclusion criteria:
Inclusion criteria for trial entry and Randomisation 1 (induction chemotherapy randomisation):
1. A diagnosis of AML/high risk myelodysplastic syndrome (MDS)/isolated myeloid sarcoma (either de novo or secondary)
2. Aged less than 18 years

3. No prior chemotherapy or biological therapy for AML other than that permitted in the protocol
4. Normal cardiac function (fractional shortening ≥28% or ejection fraction =55%)
5. Fit for protocol chemotherapy
6. Documented negative pregnancy test for female patients of childbearing potential
7. Patient agrees to use effective contraception (patients of childbearing potential)
8. Written informed consent from the patient and/or parent/legal guardian

Inclusion criteria for participation in the gemtuzumab ozogamicin dose finding study:
1. Patients meets the inclusion criteria for trial entry
2. Aged ≥12 months for the major dose finding study
3. Aged ≥12 weeks and 12 months for the minor dose finding study
4. Karnofsky or Lansky performance score of =50
5. Normal renal function defined as calculated creatinine clearance =90ml/min/1.73m2
6. Normal hepatic function defined as total bilirubin =2.5 upper limit of normal (ULN) for age unless it is caused by leukaemic involvement or Gilbert's syndrome or similar disorder
7. ALT or AST =10 x ULN for age
8. Written informed consent from the patient or parent/legal guardian

Inclusion criteria for participation in R3:
1. Patient meets the inclusion criteria for trial entry
2. Induction treatment as per MyeChild 01 protocol or treated with 2 courses of mitoxantrone & cytarabine off trial
3. Minimal residual disease (MRD) response (performed in MyeChild 01 centralised laboratories):
3.1. Patients with good risk cytogenetics/molecular genetics and a MRD level <0.1% by flow after course 2, or a decrease in transcript levels of >3 logs after course 2 for those with an informative molecular marker but without an informative marker of sufficient sensitivity for flow MRD monitoring
Or
3.2. Patients with intermediate risk cytogenetics/molecular genetics with a MRD level <0.1% by flow after course 1 and course 2, or a decrease in transcript levels of >3 logs after course 1 and course 2 for those with an informative molecular marker, but without an informative marker of sufficient sensitivity for flow MRD monitoring
4. Written informed consent from the patient and/or parent/legal guardian

Inclusion criteria for participation in R4:
1. Patient meets the eligibility criteria for trial entry
2. Induction treatment as per MyeChild 01 protocol or treated with 1 or 2 courses of mitoxantrone & cytarabine ± treatment intensification with FLA-Ida off trial
3. Patient is in CR or CRi defined as <5% blasts confirmed by flow cytometry//molecular/FISH in a bone marrow aspirate taken within 6 weeks prior to randomisation to R4.
4. Patient meets one of the following criteria and is a candidate for haemopoeitic stem cell transplant (HSCT) as per the protocol:
4.1. High risk after course 1 (all patients with poor risk cytogenetics and patients with intermediate risk cytogenetics who fail to achieve CR/CRi)
4.2. Intermediate risk cytogenetics with MRD >0.1% after course 1 and 2 measured by flow. If no flow MRD marker of sufficient sensitivity is identified, a molecular MRD marker with a sensitivity of >0.1% may be used
4.3. Good risk cytogenetics with flow MRD >0.1% confirmed by a decrease in molecular MRD of <3 logs or rising transcript levels after course 3 despite treatment intensification (FLAIda) and after discussion with the Clinical Coordinators
5. Availability of a 9-10/10 human leukocyte antigen (HLA) matched family or unrelated donor or

5-8/8 matched cord blood unit with an adequate cell dose as defined by the protocol section 17.1
6. Written informed consent from the patient or parent/legal guardian

Participant type(s)
Patient

Age group
Child

Upper age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 700; UK Sample Size: 350

Key exclusion criteria
Current participant exclusion criteria as of 02/09/2021:
1. Acute promyelocytic leukaemia (APL)
2. Myeloid leukaemia of Down Syndrome (ML DS)
3. Blast crisis of chronic myeloid leukaemia
4. Relapsed or refractory AML
5. Bone marrow failure syndromes
6. Prior anthracycline exposure which would inhibit the delivery of study anthracyclines
7. Concurrent treatment or administration of any other experimental drug or with any other biological therapy for AML/high risk MDS/isolated MS
8. Pregnant or lactating

Previous participant exclusion criteria:
1. Acute promyelocytic leukaemia (APL)
2. Myeloid leukaemia of Down Syndrome (ML DS)
3. Blast crisis of chronic myeloid leukaemia
4. Relapsed or refractory AML
5. Bone marrow failure syndromes
6. Prior anthracycline exposure which would inhibit the delivery of study anthracyclines
7. Concurrent treatment or administration of any other experimental drug or with any other biological therapy for AML
8. Pregnant or lactating females

Date of first enrolment
29/04/2016

Date of final enrolment
31/03/2025

Locations

Countries of recruitment

Australia

England

France

Ireland

New Zealand

Switzerland

United Kingdom

Study participating centre
University of Birmingham
Clinical Trials Unit
Edgbaston
Birmingham
United Kingdom
B15 2TT

Sponsor information

Organisation
University of Birmingham

Sponsor details
School of Medical Sciences
Edgbaston
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United Kingdom
B15 2TT

Sponsor type
University/education

Website
https://www.birmingham.ac.uk/

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK

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
Results of this trial will be submitted for publication in peer reviewed journals.

Intention to publish date
31/05/2033

Individual participant data (IPD) sharing plan
Access to this data is controlled through application to the CRCTU New Business Committee and is granted in accordance with the CRCTU Data Sharing Policy.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			26/07/2023	No	No