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Anti-CD47 antibody therapy in relapsed /refractory Haematological Malignancies

Submission date 14/05/2015	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 14/05/2015	**Overall study status** Completed	
Last Edited 25/06/2024	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-of-magrolimab-for-acute-myeloid-leukaemia-and-myelodysplastic-syndrome-camellia

Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
2015-000720-29

ClinicalTrials.gov (NCT)
NCT02678338

Protocol serial number
CPMS 18953

Study information

Scientific Title
A Phase I dose escalation trial of the Humanized Anti-CD47 Monoclonal Antibody Hu5F9-G4 in Haematological Malignancies

Acronym
CAMELLIA

Study objectives
Current study hypothesis:
The aim of this study is to determine whether a new drug, called Hu5F9-G4, is a safe and well tolerated treatment for patients with Acute Myeloid Leukaemia (AML) or Myelodysplastic Syndrome (MDS), whose disease has either not responded to standard treatments or has relapsed following an initial response. There is an urgent need for new treatments for these patients, who currently only receive supportive care and have a median survival of only 2 months.

Previous study hypothesis:
The aim of this study is to determine whether a new drug, called Hu5F9-G4, is a safe and well tolerated treatment for patients with Acute Myeloid Leukaemia (AML), whose disease has either not responded to standard treatments or has relapsed following an initial response. There is an urgent need for new treatments for these patients, who currently only receive supportive care and have a median survival of only 2 months.

Ethics approval required
Old ethics approval format

Ethics approval(s)
South Central- Oxford C', 14/05/2015, ref: 15/SC/0215

Study design
Non-randomized; Interventional; Design type: Treatment

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: Cancer; Subtopic: Haematological Oncology; Disease: Leukaemia (acute myeloid) and Myelodysplastic syndrome (MDS)

Interventions
All patients will receive the trial drug Hu5F9-G4, there is no control arm. Hu5F9-G4 is given as an intravenous infusion once or twice a week. The trial is of a dose escalation design. Patients who respond to the first 4 weeks of treatment will have the option of continuing treatment for a further 8 weeks i.e. up to 12 weeks in total.

There is also allowance for patients to continue on treatment for a further 40 weeks (i.e. up to 1 year in total). (added 16/08/2016)

Added 26/10/2017:
If patients are still benefiting from treatment, they may have the option to continue on trial treatment until 52 weeks after the last patient has been recruited.

Intervention Type
Biological/Vaccine

Phase
Phase I

Drug/device/biological/vaccine name(s)
Hu5F9-G4

Primary outcome(s)
Maximum tolerated dosing regimen of Hu5F9-G4; Timepoint(s): Over 4 weeks of treatment

Key secondary outcome(s))
Current as of 26/10/2017:
1. CD47 receptor occupancy; Timepoint(s): Days 1, 8, 11, 15, 18, 25, 36, 53, 64, 81 and weeks 16, 28, 40, 52 and every 12 weeks beyond week 52, 30-35 days post end of treatment, and disease progression
2. Immunogenicity of Hu5F9-G4; Timepoint(s): Days 1, 29, 53 and 81, and weeks 16, 20, 24, 28, 32, 36, 40, 44, 48, and 52 every 4 weeks beyond week 52 and at 30-35 days post end of treatment.
3. Impact of blood transfusion on Hu5F9-G4 pharmacokinetics; Timepoint(s): Timings as per PK sampling.
4. Pharmacokinetic profile of Hu5F9-G4; Timepoint(s): Days 1,4, 8, 11, 15, 22, 25, 36, 50, 64, 78, and Weeks 16, 20, 24, 28, 32, 36, 40, 44, 48 & 52 and every 4 weeks beyond week 52.
5. Preliminary evidence of anti-leukaemic/myelodysplastic activity of Hu5F9-G4; Timepoint(s): Days 25, 53, 81, and weeks 16, 28, 40 and 52 and every 12 weeks beyond week 52.
6. Safety of extending treatment duration: From week 5 until 30-35 day post end of treatment.

As of 02/08/2017:
1. CD47 receptor occupancy; Timepoint(s): Days 1, 8, 11, 15, 18, 25, 36, 53, 64, 81 and weeks 16, 28, 40, 52 and disease progression
2. Immunogenicity of Hu5F9-G4; Timepoint(s): Days 1, 29, 53 and 81, and weeks 16, 20, 24, 28, 32, 36, 40, 44, 48, and 52
3. Impact of blood transfusion on Hu5F9-G4 pharmacokinetics; Timepoint(s): Days 1,4, 8, 11, 15, 22, 25, 36, 50, 64, 78, and Weeks 16, 20, 24, 28, 32, 36, 40, 44, 48 & 52
4. Pharmacokinetic profile of Hu5F9-G4; Timepoint(s): Days 1,4, 8, 11, 15, 22, 25, 36, 50, 64, 78, and Weeks 16, 20, 24, 28, 32, 36, 40, 44, 48 & 52
5. Preliminary evidence of anti-leukaemic/myelodysplastic activity of Hu5F9-G4; Timepoint(s): Days 25, 53, 81, and weeks 16, 28, 40 and 52
6. Safety of extending treatment duration to 1 year; Timepoint(s): Weeks 5- 52 of treatment

As of 16/08/2016:
1. CD47 receptor occupancy; Timepoint(s): Days 1, 8, 15, 22, 36, 53, 64, 81 and weeks 16, 28, 40, 52 and disease progression
2. Immunogenicity of Hu5F9-G4; Timepoint(s): Days 1, 29, 53 and 81, and weeks 16, 20, 24, 28, 32,

36, 40, 44, 48, and 52
3. Impact of blood transfusion on Hu5F9-G4 pharmacokinetics; Timepoint(s): Days 1,4, 8, 15, 22, 25, 36, 50, 64, 78, and Weeks 16, 20, 24, 28, 32, 36, 40, 44, 48 & 52
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5. Preliminary evidence of anti-leukaemic activity of Hu5F9-G4; Timepoint(s): Days 25, 53, 81, and weeks 16, 28, 40 and 52
6. Safety of extending treatment duration to 1 year; Timepoint(s): Weeks 5- 52 of treatment

Initial:
1. CD47 receptor occupancy; Timepoint(s): Days 1, 8, 15, 22, 36, 53, 64, 81 and at disease progression
2. Immunogenicity of Hu5F9-G4; Timepoint(s): Days 1, 29, 53 & 81 (if positive repeat assay every 4 weeks until no longer positive)
3. Impact of blood transfusion on Hu5F9-G4 pharmacokinetics; Timepoint(s): Days 1, 4, 8, 15, 22, 25, 36, 50, 64 & 78
4. Pharmacokinetic profile of Hu5F9-G4; Timepoint(s): Days 1,4, 8, 15, 22, 25, 36, 50, 64 & 78
5. Preliminary evidence of anti-leukaemic activity of Hu5F9-G4; Timepoint(s): Days 25, 53 & 81 (per International Working Group AML response criteria (2003))
6. Safety of extending treatment duration to 12 weeks; Timepoint(s): Weeks 5-12 of treatment

Completion date
07/06/2019

Eligibility

Key inclusion criteria
Current inclusion criteria as of 26/10/2017:
1. Pathologically confirmed relapsed or refractory (primary refractory and relapsed refractory) AML (defined by WHO criteria) for which no further conventional therapy is suitable for the patient; or confirmed myelodysplastic syndrome defined according to WHO classification, with an International Prognostic Scoring System (IPSS) risk category of intermediate-2 or high risk, that is relapsed, refractory or intolerant to conventional therapy within 3 weeks of registration.
2. Peripheral white blood cell (WBC) count ≤20x109/L within 1 week of registration (Day -7 to Day 1). Patients with WBC >20x109/L can be treated with hydroxyurea (up to 4 g/day) throughout the trial to reduce the WBC to ≤20x109/L prior to each dose of IMP. The white count must also be measured on the day of the first dose and be ≤20x109/L. Oral etoposide (up to 200mg PO/ day) may be given as an alternative to hydroxyurea for patients who are intolerant to hydroxyurea or cannot achieve sufficient white count lowering on hydroxyurea.
3. Male or female, Age >= 18 years
4. ECOG performance score of 01
5. Willing and able to comply with the protocol for the duration of the study, and scheduled followup visits and examinations
6. Willing to undergo blood transfusions as deemed clinically necessary
7. Pretreatment blood cross match completed
8. Written (signed and dated) informed consent and be capable of cooperating with protocol
9. Biochemical indices within the ranges shown below:
9.1. AST/SGOT or ALT/SGPT = 3 x ULN
9.2. Alkaline phosphatase = 2 x ULN

9.3. Bilirubin = 2x ULN (except for patients with a known or suspected history of Gilbert's Syndrome)
9.4. eGFR >35 mls/min (Cockcroft and Galton method)

Current inclusion criteria as of 02/08/2017:
1. Pathologically confirmed relapsed or refractory (primary refractory and relapsed refractory) AML (defined by WHO criteria) for which no further conventional therapy is suitable for the patient; or confirmed myelodysplastic syndrome defined according to WHO classification, with an International Prognostic Scoring System (IPSS) risk category of intermediate-2 or high risk, that is relapsed, refractory or intolerant to conventional therapy within 3 weeks of registration.
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3. Male or female, Age >= 18 years
4. ECOG performance score of 01
5. Willing and able to comply with the protocol for the duration of the study, and scheduled followup visits and examinations
6. Willing to undergo blood transfusions as deemed clinically necessary
7. Pretreatment blood cross match completed
8. Written (signed and dated) informed consent and be capable of cooperating with protocol
9. Haematological and biochemical indices within the ranges shown below:
9.1. AST/SGOT or ALT/SGPT = 3 x ULN
9.2. Alkaline phosphatase = 2 x ULN
9.3. Bilirubin = 2x ULN (except for patients with a known or suspected history of Gilbert's Syndrome)
9.4. eGFR >35 mls/min (Cockcroft and Galton method)

Previous inclusion criteria:
1. Pathologically confirmed relapsed or refractory (primary refractory and relapsed refractory) AML (defined by WHO criteria) for which no further conventional therapy is suitable for the patient within 3 weeks of registration
2. Peripheral white blood cell (WBC) count =10x10*9/L within 1 week of registration (Day 7 to Day 1). Patients with WBC >10x10*9/L can be treated with hydroxycarbamide (up to 4 g/day) throughout the trial to reduce the WBC to =10x10*9/L prior to each dose of IMP. The white count must also be measured on the day of the first dose and be =10x10*9/L prior to each dose of IMP. The white count must also be measured on the day of the first dose and be =10x10*9/L
3. Male or female, Age >= 18 years
4. ECOG performance score of 01
5. Willing and able to comply with the protocol for the duration of the study, and scheduled followup visits and examinations
6. Willing to undergo blood transfusions as deemed clinically necessary
7. Pretreatment blood cross match completed
8. Written (signed and dated) informed consent and be capable of cooperating with protocol
9. Haematological and biochemical indices within the ranges shown below:
9.1. AST/SGOT or ALT/SGPT = 3 x ULN
9.2. Alkaline phosphatase = 2 x ULN
9.3. Bilirubin = 2x ULN (except for patients with a known or suspected history of Gilbert's Syndrome)
9.4. eGFR >35 mls/min (Cockcroft and Galton method)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
19

Key exclusion criteria
Current exclusion criteria as of 26/10/2017:
1. Females: Pregnant or breastfeeding women, or women of childbearing potential unless effective method of contraception is used during and for 3 months after the trial. Males: unless an effective method of contraception is used during and for 3 months after the trial
2. Any prior exposure to Hu5F9G4 or other CD47 targeting agent
3. Treatment with any other investigational agent within 28 days prior to enrolment
4. Prior cytotoxic chemotherapy (with the exception of hydroxycarbamide), immunotherapy, or radiotherapy within 4 weeks prior to Day 1
5. Acute Promyelocytic Leukaemia
6. Patients with known inherited or acquired bleeding disorders
7. Previous allogeneic haematopoietic stem cell transplant within 6 months prior to enrollment, active graft versus host disease (GVHD), or requiring transplant-related immunosuppression
8. Evidence for active CNS involvement by leukaemia
9. Clinical evidence or known history of cardiopulmonary disease defined as follows:
9.1. Acute myocardial infarction within the last 12 months
9.2. Requirement for treatment of angina or existence of unstable angina
9.3. Congestive heart failure NYHA Class II–IV
9.4. Uncontrolled hypertension despite adequate treatmen
10. Symptomatic intrinsic lung disease (chronic obstructive pulmonary disease, pulmonary fibrosis)
11. Other psychological, social or medical condition (e.g. active severe sepsis) physical examination finding or a laboratory abnormality that the Investigator considers would make the patient a poor trial candidate or could interfere with protocol compliance or the interpretation of trial results
12. Any other malignancy within the previous 24 months, with the exception of adequately treated cone biopsied in situ carcinoma of the cervix uteri and basal or squamous cell carcinoma of the skin
13. Patients who are known to be serologically positive for Hepatitis B, Hepatitis C or HIV

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9.1. Acute myocardial infarction within the last 12 months
9.2. Requirement for treatment of angina or existence of unstable angina
9.3. Congestive heart failure NYHA Class II–IV
9.4. Uncontrolled hypertension despite adequate treatment (sustained systolic BP > 150 or diastolic BP > 100)
10. Symptomatic intrinsic lung disease (chronic obstructive pulmonary disease, pulmonary fibrosis)
11. Other psychological, social or medical condition (e.g. active severe sepsis) physical examination finding or a laboratory abnormality that the Investigator considers would make the patient a poor trial candidate or could interfere with protocol compliance or the interpretation of trial results
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Date of first enrolment
27/11/2015

Date of final enrolment
07/06/2018

Locations

Countries of recruitment
United Kingdom

England

Wales

Study participating centre
Churchill Hospital (lead site)
Oxford
United Kingdom
OX3 7LJ

Study participating centre
Christie Hospital
Manchester
United Kingdom
M20 4BX

Study participating centre
Royal Liverpool Hospital
Liverpool
United Kingdom
L7 8XP

Study participating centre
St James Hospital
Leeds
United Kingdom
LS9 7TF

Study participating centre
University Hospital of Wales
Cardiff
United Kingdom
CF14 4XW

Sponsor information

Organisation
Forty Seven, Inc.

Funder(s)

Funder type
Charity

Funder Name
Bloodwise

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Funder Name
Medical Research Council

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

Funder Name
NIHR Oxford Biomedical Research Centre (BRC)

Funder Name
CRUK Cancer Centre

Funder Name
California Institute for Regenerative Medicine

Alternative Name(s)
California Institute for Regenerative Med, CA Institute for Regenerative Med, CIRM, California's Stem Cell Agency, The California Institute for Regenerative Medicine, Instituto de Medicina Regenerativa de California, Institut californien de médecine régénérative, , , CIRM

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/07/2019	09/08/2019	Yes	No
HRA research summary			28/06/2023	No	No
Plain English results			25/06/2024	No	Yes