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A trial of combined azacitidine and lenalidomide salvage therapy in patients with acute myeloid leukaemia and myelodysplasia who relapse after allogeneic stem cell transplantation

Submission date 25/02/2014	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 25/02/2014	**Overall study status** Completed	[_] Statistical analysis plan [X] Results
Last Edited 09/08/2021	**Condition category** Cancer	[_] Individual participant data

Plain English summary of protocol
http://www.cancerresearchuk.org/cancer-help/trials/a-trial-azacitidine-and-lenalidomide-for-acute-myeloid-leukaemia-or-mds-come-back-after-stem-cell-transplant-viola

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2013-002118-11

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
15789

Study information

Scientific Title
A phase I trial of combined azacitidine and lenalidomide salvage therapy in patients with acute myeloid leukaemia and myelodysplasia who relapse after allogeneic stem cell transplantation.

Acronym
VIOLA

Study objectives
Current study hypothesis as of 10/05/2018:
Treatment options for patients with acute myeloid leukaemia (AML) or myelodysplasia (MDS) who relapse following an allogeneic stem cell transplant (SCT) are extremely limited and most will die of resistant leukaemia. Two drugs, azacitidine and lenalidomide, have both been shown to have marked clinical activity in patients with AML and MDS who have failed to respond to conventional chemotherapy. Of interest, combined treatment with both azacitidine and lenalidomide appears to increase the response rate in patients with AML and MDS. Importantly, a number of small studies have demonstrated that both azacitidine and lenalidomide when administered alone can also be clinically active in patients who relapse after a stem cell transplant. To date however, combined treatment with azacitidine and lenalidomide has never been examined in this important patient population. In this study, we plan to determine the best tolerated combined dose of azacitidine and lenalidomide in patients who have relapsed after an allogeneic stem cell transplant. The information produced will inform the design of future clinical trials in patients with AML and MDS whose disease has relapsed after an allogeneic transplant. The trial will run in approximately 6 hospitals in the UK. Approximately 27 patients will be recruited to this phase I trial.

Previous study hypothesis:
Treatment options for patients with acute myeloid leukaemia (AML) who relapse following an allogeneic stem cell transplant (SCT) are extremely limited and most will die of resistant leukaemia. Two drugs, azacitidine and lenalidomide, have both been shown to have marked clinical activity in patients with AML who have failed to respond to conventional chemotherapy. Of interest, combined treatment with both azacitidine and lenalidomide appears to increase the response rate in patients with AML. Importantly, a number of small studies have demonstrated that both azacitidine and lenalidomide when administered alone can also be clinically active in patients who relapse after a stem cell transplant. To date however, combined treatment with azacitidine and lenalidomide has never been examined in this important patient population. In this study, we plan to determine the best tolerated combined dose of azacitidine and lenalidomide in patients who have relapsed after an allogeneic stem cell transplant. The information produced will inform the design of future clinical trials in patients with AML whose disease has relapsed after an allogeneic transplant. The trial will run in approximately 6 hospitals in the UK. Approximately 27 patients will be recruited to this phase 1 trial.

More details can be found at: http://public.ukcrn.org.uk/search/StudyDetail.aspx?StudyID=15789

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee South Central - Oxford B, 21/01/2014, ref. 13/SC/0581

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

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please contact your consultant for a patient information sheet

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

Interventions
Adverse event discussion, Adverse event discussion 10 minutes. 10 minutes with the doctor (with research nurse if available) within the haematology department; Azacitidine administration, Azacitidine (IMP 1) administration - Azacitidine will be administered by a research nurse/chemotherapy nurse in the haematology department - 20 mins
Bone marrow, A trained doctor will perform bone marrow aspirations on the designated haematology ward/day unit/department - 45 mins.
Discussion and consent, Initial trial discussion and full written informed consent. 1 hour with the doctor (with research nurse if available) within the haematology department; Discussion of GVHD, Discussion of graft versus host disease symptoms 10 minutes with the doctor (with research nurse if available) within the haematology dept
Electrocardiogram (ECG), An ECG will be performed by a research nurse in the haematology /cardiology department - 15 mins

Lenalidomide administration, Lenalidomide (IMP 2) administration - Patients will receive oral capsule(s) of lenalidomide. They will take this medication themselves at home at their convenience; Lenalidomide Education, Lenalidomide Education and Guidance Counselling - 15 mins with the doctor (with research nurse if available) within the haematology department; Medical history, Medical history and demographic data discussion. 30 minutes with the doctor (with research nurse if available) within the haematology department; Patient Diary, Completion

of patient diary - Patients will be asked to keep a medication diary from day 10-day 42 of each cycle of therapy (to be completed at the patients convenience).; Physical examination, Physical examination and
vital signs. A doctor will perform a physical exam and a research nurse will
perform and assessment of vital signs in the haematology department - 15 mins; Pregnancy test, Up to 16 pregnancy tests will be required for women of childbearing potential depending on their menstrual pattern. The tests will be performed in the haematology department by a research nurse - 5 mins; Venepuncture, Venepuncture for haematology and biochemistry assessments. Blood samples will be collected either by a research nurse or
phlebotomist in the haematology department - 5 minutes.; Venepuncture for research, Venepuncture for research
samples - Blood samples for research will be collected by the research - nurse in the haematology department- 5 mins; Follow Up Length: 12 month(s)

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
azactidine, lenalidomide

Primary outcome measure
Maximum tolerated dose (MTD); Timepoint(s): Maximum tolerated dose (MTD) of lenalidomide in combination with azacitidine in patients with relaps

Secondary outcome measures
1. Best response rate after combined lenalidomide and azacitidine salvage therapy; Timepoint (s): After combined lenalidomide and azacitidine salvage therapy
2. Overall survival; Timepoint(s): Registration - 1yr post trial treatment
3. Tolerability and safety of lenalidomide in combination with azacitidine; Timepoint(s): Each cycle

Overall study start date
05/02/2014

Completion date
31/12/2018

Eligibility

Key inclusion criteria
Current inclusion criteria as of 10/05/2018:
1. Patients with relapsed AML or MDS following an alemtuzumab- or anti-thymocyte globulin (ATG)-based reduced intensity conditioned allogeneic stem cell transplant using a sibling or unrelated donor
2. Patients able to receive treatment as an outpatient

3. Patients must be willing to comply with the lenalidomide risk management programme
4. Patients must have given written informed consent
5. Patients willing and able to comply with scheduled study visits and laboratory tests

Previous inclusion criteria:
1. Patients with relapsed AML following an alemtuzumab or anti-thymocyte globulin (ATG)-based reduced intensity conditioned allogeneic stem cell transplant using a sibling or unrelated donor
2. Patients able to receive treatment as an outpatient
3. Patients must be willing to comply with the lenalidomide risk management programme
4. Patients must have given written informed consent
5. Patients willing and able to comply with scheduled study visits and laboratory tests

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 30; UK Sample Size: 30

Total final enrolment
31

Key exclusion criteria
1. Patients with active acute or chronic extensive graft-versus-host-disease (GvHD), or a history of grade 3 or 4 GvHD
2. Patients with hepatic or renal impairment defined as follows:
Total bilirubin ≥ 2.5 x upper limit of normal (ULN)*
Aspartate aminotransferase (AST) or Alanine aminotransferase (ALT) ≥ 3.0 x ULN
Estimated Glomerular Filtration Rate (eGFR) ≤ 40mls/min
*Patients with elevated bilirubin due to Gilbert's syndrome are eligible
3. Patients who have received anti-tumour therapies, including prior experimental agents or approved anti-tumour small molecules and biologics, within 28 days before the start of protocol treatment
4. Patients with active symptomatic fungal, bacterial, and/or viral infection
5. Patients with contraindications to receiving azacitidine or lenalidomide
6. Patients with any other condition that in the Investigators opinion would affect the patient's participation in the trial

Date of first enrolment
05/02/2014

Date of final enrolment

01/02/2017

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Cancer Research UK Clinical Trials Unit
Birmingham
United Kingdom
B15 2TT

Sponsor information

Organisation
University of Birmingham (UK)

Sponsor details
Edgbaston
Birmingham
England
United Kingdom
B15 2TT

Sponsor type
University/education

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Charity

Funder Name
Leukaemia & Lymphoma Research (UK); Grant Codes: 13019

Results and Publications

Publication and dissemination plan
A publication is in preparation with aims to submit by 01/03/2019.

Intention to publish date
01/03/2019

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Plain English results				No	Yes
Funder report results	version 1.0a	31/10/2016	09/08/2021	No	No
Results article		17/01/2019	09/08/2021	Yes	No
HRA research summary			28/06/2023	No	No