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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; 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

 Patients with active acute or chronic extensive graft-versus-host-disease (GvHD), or a history of grade 3 or 4 GvHD
 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
 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
 Patients with active symptomatic fungal, bacterial, and/or viral infection
 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 Plain English results	Details	Date created	Date added	Реег reviewed? No	Patient-facing? 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
<u>HRA research summary</u>			28/06/2023	NO	NO