

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

<b>Submission date</b> 25/02/2014	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 25/02/2014	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 09/08/2021	<b>Condition category</b> Cancer	<input type="checkbox"/> 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

### Contact name

Mrs Kathryn Wheeler

### Contact details

Cancer Research UK Clinical Trials Unit  
Institute for Cancer Studies  
Edgbaston  
Birmingham  
United Kingdom  
B15 2TT

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Viola@trials.bham.ac.uk

## Additional identifiers

Clinical Trials Information System (CTIS)

2013-002118-11

**Protocol serial number**

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

## **Study type(s)**

Treatment

## **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(s)**

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

**Key secondary outcome(s)**

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

**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

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 years

**Sex**

All

**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  $\geq 2.5$  x upper limit of normal (ULN)\*  
Aspartate aminotransferase (AST) or Alanine aminotransferase (ALT)  $\geq 3.0$  x ULN  
Estimated Glomerular Filtration Rate (eGFR)  $\leq 40$ mls/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**

United Kingdom

England

**Study participating centre**

Cancer Research UK Clinical Trials Unit

Birmingham

United Kingdom

B15 2TT

**Sponsor information**

## Organisation

University of Birmingham (UK)

## ROR

<https://ror.org/03angcq70>

## Funder(s)

### Funder type

Charity

### Funder Name

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

## Results and Publications

### 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?
<a href="#">Results article</a>		17/01/2019	09/08/2021	Yes	No
<a href="#">Funder report results</a>	version 1.0a	31/10/2016	09/08/2021	No	No
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Plain English results</a>				No	Yes