

# Pilot safety/tolerability study of Lenalidomide administered as monotherapy and in combination with standard chemotherapy for Acute Myeloid Leukaemia/high-risk myelodysplastic syndrome with structural abnormalities of chromosome 5

<b>Submission date</b> 18/06/2008	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 11/07/2008	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 25/10/2022	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

<https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/A-study-lenalidomide-acute-myeloid-leukaemia-high-risk-myelodysplastic-syndrome-abnormality-chromosome-5>

## Contact information

### Type(s)

Scientific

### Contact name

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## Additional identifiers

Protocol serial number

## Study information

### Scientific Title

Pilot safety/tolerability study of Lenalidomide administered as monotherapy and in combination with standard chemotherapy for Acute Myeloid Leukaemia/high-risk myelodysplastic syndrome with structural abnormalities of chromosome 5

### Acronym

AML Len5

### Study objectives

The primary objective is to assess safety and tolerability of the combination of oral lenalidomide administered as a single agent and simultaneously with induction chemotherapy using cytosine arabinoside, daunorubicin +/- etoposide (ADE) for patients with acute myeloid leukaemia/high-risk myelodysplastic syndrome (AML/MDS) and chromosome 5 cytogenetic abnormalities.

### Ethics approval required

Old ethics approval format

### Ethics approval(s)

Ethics approval to be submitted during summer 2008. The MREC committee will be assigned by NRES.

### Study design

Late phase II three-outcome non-randomised design

### Primary study design

Interventional

### Study type(s)

Treatment

### Health condition(s) or problem(s) studied

Acute myeloid leukaemia, high-risk myelodysplastic syndrome, chromosome 5 cytogenetic abnormalities

### Interventions

For patients with greater than 5% blasts at trial entry:

Lenalidomide monotherapy:

Lenalidomide will be administered orally at 10 mg daily for 21 days. Bone marrow examination will be performed at day 28. If complete remission (CR) has been achieved, consolidation with lenalidomide plus ADE 3+8+5 should follow. If less than 50% blast reduction (NR), proceed to induction with lenalidomide plus ADE 3+10+5. If no CR but blasts have reduced by greater than 50% from baseline (BMR), lenalidomide will be restarted as soon after day 28 as possible for a further 21 days. Bone marrow examination will then be performed at day 56 (or day 28 of cycle

2). If CR has been achieved, consolidation with lenalidomide plus ADE 3+8+5 will be given. If no CR, proceed to induction with lenalidomide plus ADE 3+10+5. Patients with progressive disease during monotherapy will proceed immediately to induction with lenalidomide plus ADE 3+10+5.

**Induction: lenalidomide plus ADE 3+10+5**

Lenalidomide will be administered orally at 10 mg daily for 10 days concurrently with ADE induction therapy (3+10+5) which comprises:

1. Cytosine arabinoside 100 mg/m<sup>2</sup> twice daily by intravenous push for 10 days
2. Daunorubicin 50 mg/m<sup>2</sup> days 1, 3, 5 by intravenous infusion
3. Etoposide 100 mg/m<sup>2</sup> daily days 1 - 5 by intravenous infusion

**Consolidation:**

Consolidation will be given after achievement of CR with either lenalidomide monotherapy or following induction with lenalidomide plus ADE. Consolidation will also be administered to patients achieving partial remission (PR) with lenalidomide plus ADE induction. Consolidation will comprise lenalidomide plus ADE 3+8+5. Consolidation should only be commenced after haematopoietic recovery, defined as neutrophils greater than  $1 \times 10^9/l$  and platelets greater than  $80 \times 10^9/l$ . Lenalidomide will be administered orally at 10 mg daily for 10 days concurrently with course 2 of ADE (3+8+5), which comprises:

1. Cytosine arabinoside 100 mg/m<sup>2</sup> twice daily by intravenous push for 8 days
2. Daunorubicin 50 mg/m<sup>2</sup> days 1, 3, 5 by intravenous infusion
3. Etoposide 100 mg/m<sup>2</sup> daily days 1 - 5 by intravenous infusion

For patients with less than 5% blasts at trial entry (Int-2 MDS):

**Lenalidomide monotherapy:**

Lenalidomide will be administered orally at 10 mg daily for 21 days. Bone marrow examination will be performed at day 28. If CR or PR has been achieved, a second course of oral lenalidomide 10 mg daily for a further 21 days will be administered. For patients in CR, await haematopoietic recovery before the second course of lenalidomide defined as platelets greater than  $80 \times 10^9/l$  and neutrophils greater than  $1 \times 10^9/l$ . For patients in PR recommence lenalidomide on day 28.

Patients in CR after course 1 or 2 should receive one additional course of lenalidomide 10 mg daily orally for 21 days after documentation of CR. Such patients are then eligible for allogeneic stem cell transplant subject to donor availability. If no transplant option, patients should commence maintenance lenalidomide for 12 months.

Post-remission therapy will be at the discretion of the investigator. All patients considered eligible for allogeneic stem cell transplantation and with a suitable donor should be offered a transplant.

**Maintenance:**

Lenalidomide after post-remission therapy for non-transplant candidates - 10 mg daily x 21 days repeated monthly for a maximum of 12 months (venous thromboembolism [VTE] prophylaxis will be considered on a case by case basis).

**Intervention Type**

Drug

**Phase**

Phase II

**Drug/device/biological/vaccine name(s)**

Lenalidomide, cytosine arabinoside, daunorubicin, etoposide

**Primary outcome(s)**

The primary endpoint of this study is safety and tolerability of the combination therapy, assessed by two outcomes: early death rate and the proportion of patients recovering their platelets and surviving by 42 days after chemotherapy. If the treatment is found to be safe and tolerable for BOTH of these endpoints, then we will consider the short term efficacy in terms of complete remission rate as a third primary endpoint and we will use this to determine whether or not to proceed to a phase III trial.

The early death rate and proportion of patients recovering platelets and surviving will be assessed at four points throughout the trial; after 10 patients, 19 patients, 30 patients, and 39 patients have been recruited.

**Key secondary outcome(s)**

1. Time to recovery of neutrophils
2. Blood product usage
3. Length of time spent in hospital

**Completion date**

31/12/2009

**Eligibility****Key inclusion criteria**

1. Patients diagnosed with primary/relapsed/refractory AML (as defined by World Health Organization [WHO]) or high risk MDS (defined as International Prognostic Scoring System [IPSS] Int-2/High) with chromosome 5 cytogenetic abnormalities
2. Aged 18 years old, either sex
3. Considered suitable for intensive chemotherapy
4. Capable of understanding and complying with protocol requirements
5. Written informed consent

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 years

**Sex**

All

**Total final enrolment**

**Key exclusion criteria**

1. Use of prior investigational agents within four weeks
2. The subject has received lenalidomide in a previous clinical study or as a therapeutic agent
3. The subject has a history or clinical manifestations of human immunodeficiency virus (HIV) or other active infection
4. The subject has a history of hypersensitivity or allergies to lactose
5. If female, the subject is pregnant or lactating
6. The subject has another active malignancy
7. The subject has other severe concurrent disease or mental illness
8. Eastern Cooperative Oncology Group (ECOG) performance status greater than 2
9. Myocardial dysfunction (as defined by left ventricular ejection fraction less than 50%)
10. Creatinine clearance (Cockcroft) less than 60 mls/min
11. Alanine aminotransferase (ALT)/aspartate aminotransferase (AST) greater than 3 x upper limit of normal (ULN)

**Date of first enrolment**

01/01/2009

**Date of final enrolment**

31/12/2009

**Locations****Countries of recruitment**

United Kingdom

England

**Study participating centre**

**St James's Institute of Oncology**

Leeds

United Kingdom

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**Sponsor information****Organisation**

Leeds Teaching Hospitals NHS Trust (UK)

**ROR**

<https://ror.org/00v4dac24>

# Funder(s)

## Funder type

Industry

## Funder Name

Cancer Research UK (CRUK) (UK) (ref: C24417/A10075) - funded by a grant from the Feasibility Study Committee (FSC)

## Alternative Name(s)

CR\_UK, Cancer Research UK - London, Cancer Research UK (CRUK), CRUK

## Funding Body Type

Private sector organisation

## Funding Body Subtype

Other non-profit organizations

## Location

United Kingdom

## Funder Name

Celgene Ltd (UK) (ref: RV-AML-NCRI-179)

# Results and Publications

## Individual participant data (IPD) sharing plan

Not provided at time of registration

## IPD sharing plan summary

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>	results	28/08/2013		Yes	No
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes
<a href="#">Plain English results</a>			25/10/2022	No	Yes