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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

Submission date 18/06/2008	**Recruitment status** No longer recruiting	[X] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [X] Results [ ] Individual participant data
Registration date 11/07/2008	**Overall study status** Completed	
Last Edited 25/10/2022	**Condition category** Cancer	

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
Prof David Bowen

Contact details
Consultant Haematologist
Bexley Wing 3rd Floor
St James's Institute of Oncology
Beckett Street
Leeds
United Kingdom
LS9 7DF

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
HM08/8451

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

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

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^2 twice daily by intravenous push for 10 days
2. Daunorubicin 50 mg/m^2 days 1, 3, 5 by intravenous infusion
3. Etoposide 100 mg/m^2 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 x 10^9/l and platelets greater than 80 x 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^2 twice daily by intravenous push for 8 days
2. Daunorubicin 50 mg/m^2 days 1, 3, 5 by intravenous infusion
3. Etoposide 100 mg/m^2 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 x 10^9/l and neutrophils greater than 1 x 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 measure
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.

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

Overall study start date
01/01/2009

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

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
39

Total final enrolment
14

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 (Cockroft) 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
England

United Kingdom

Study participating centre
St James's Institute of Oncology
Leeds
United Kingdom
LS9 7DF

Sponsor information

Organisation
Leeds Teaching Hospitals NHS Trust (UK)

Sponsor details
c/o Dr Derek Norfolk
Associate Director of R&D
Department of Research & Development
A/B Floor, Old Site Worsley Building
Leeds General Infirmary
Great George Street
Leeds
England
United Kingdom
LS1 3EX

Sponsor type
Hospital/treatment centre

Website
http://www.leedsth.nhs.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, 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

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	28/08/2013		Yes	No
Plain English results			25/10/2022	No	Yes