Clinical trial results:
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

Summary

EudraCT number	2008-004891-28
Trial protocol	GB
Global end of trial date	31 July 2013
Results information	
Result version number	v1 (current)
This version publication date	28 February 2016
First version publication date	28 February 2016
Summary attachment (see zip file)	End of Trial report (2008-004891-38_End_of_Trial_Report_v1.0_06.05.2014.pdf)

Trial information

Trial identification	
Sponsor protocol code	HM08 / 8451
Additional study identifiers	
ISRCTN number	ISRCTN58492795
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors	
Sponsor organisation name	Leeds Teaching Hospitals NHS Trust
Sponsor organisation address	34 Hyde Terrace, Leeds, United Kingdom, LS2 9LN
Public contact	CTRU QA department, Leeds Institute of Clinical Trials Research, 0113 34331477, medctruq@leeds.ac.uk
Scientific contact	CTRU QA department, Leeds Institute of Clinical Trials Research, 0113 34331477, medctruq@leeds.ac.uk

Notes:

Paediatric regulatory details	
Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 January 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 January 2011
Global end of trial reached?	Yes
Global end of trial date	31 July 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess safety, tolerability and efficacy 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 AML/MDS and chromosome 5 cytogenetic abnormalities.

Protection of trial subjects:

All chemotherapy treatment involves some side effects as well as potential benefits. The side effects will be monitored closely and the dose adjusted to minimise these. It is not expected that patients will have all these side effects and it is not possible to predict which ones patients will experience or how severe or serious they may be. If a patient experiences a severe reaction, then the study treatment may be discontinued and alternative treatment will be recommended.

Currently, all drugs used to treat AML/MDS have potential side effects. The possible side effects of the drugs used in this
study are detailed in the patient information sheet.

The potential for pain, discomfort or distress is no more than is usual for other patients receiving treatment for AML/MDS.

Patients may experience side effects from their treatment and will undergo blood tests and medical assessments.
However, these are all part of standard patient management.

Patients will need to attend hospital as an inpatient during the combination chemotherapy and allogeneic transplant
stages, but this would be required even if they were not taking part in the trial.

The bone marrow tests are potentially painful. This trial only requires samples to be taken at the same timepoints as
would be required for routine clinical management.

The CTRU will comply with all aspects of Data Protection Act 1998. All information collected during the course of the trial
will be kept strictly confidential.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 August 2009
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 14
Worldwide total number of subjects	14
EEA total number of subjects	14

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	6
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	14
Number of subjects completed	14

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Lenalidomide monotherapy

Arm description:

Lenalidomide monotherapy followed by a combination of Lenalidomide and intensive intravenous chemotherapy

Arm type	Experimental
Investigational medicinal product name	Lenalidomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Cycle 1:
Days 1 – 21 10mg Lenalidomide p.o / day.
Days 22-28 Rest Period

Number of subjects in period 1	Lenalidomide monotherapy
Started	14
Completed	14

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	14	14	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	6	6	
From 65-84 years	8	8	
85 years and over	0	0	
Age continuous Units: years			
median	65.5		
full range (min-max)	40 to 75	-	
Gender categorical Units: Subjects			
Female	7	7	
Male	7	7	

End points

End points reporting groups

Reporting group title	Lenalidomide monotherapy

Reporting group description:

Lenalidomide monotherapy followed by a combination of Lenalidomide and intensive intravenous chemotherapy

Primary: Early death rate

End point title	Early death rate[1]

End point description:

End point type	Primary

End point timeframe:

≤ 30 days since start of combination chemotherapy

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses have been specified for this primary endpoint due to the trial having one treatment group and therefore no comparator. The results from this primary end point have been entered into the 'end point values' section within 'end point definitions'.

End point values	Lenalidomide monotherapy			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Rate	0			

Statistical analyses

No statistical analyses for this end point

Primary: Platelet recovery and survival 42 days from last dose of the first course of the combination chemotherapy

End point title	Platelet recovery and survival 42 days from last dose of the first course of the combination chemotherapy[2]

End point description:

End point type	Primary

End point timeframe:

42 days from last dose of the first course of the combination chemotherapy

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses have been specified for this primary endpoint due to the trial having one treatment group and therefore no comparator. The results from this primary end point have been entered into the 'end point values' section within 'end point definitions'.

End point values	Lenalidomide monotherapy			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Number	2			

Statistical analyses

No statistical analyses for this end point

Primary: Complete remission rate

End point title	Complete remission rate[3]

End point description:

End point type	Primary

End point timeframe:

day 21 post the last cycle of lenalidomide plus intensive chemotherapy

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses have been specified for this primary endpoint due to the trial having one treatment group and therefore no comparator. The results from this primary end point have been entered into the 'end point values' section within 'end point definitions'.

End point values	Lenalidomide monotherapy			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Number	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Response rates for each cycle

End point title	Response rates for each cycle

End point description:

End point type	Secondary

End point timeframe:

Cycle 1

End point values	Lenalidomide monotherapy			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Number				
Complete Response (CR)	0			
CR with incomplete haematopoietic recovery (CRi)	0			
Partial Response (PR)	0			
No Response (NR)	5			
Progressive Disease (PD)	7			
HI-E	1			
Missing	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Neutrophil and platelet recovery

End point title	Neutrophil and platelet recovery

End point description:

End point type	Secondary

End point timeframe:

42 days post monotherapy

End point values	Lenalidomide monotherapy			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Number	5			

Statistical analyses

No statistical analyses for this end point

Secondary: Blood product usage (number of blood transfusions)

End point title	Blood product usage (number of blood transfusions)

End point description:

End point type	Secondary

End point timeframe:

cycle 1

End point values	Lenalidomide monotherapy			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Blood transfusion units				
arithmetic mean (standard deviation)	4.8 (± 4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Days in hospital

End point title	Days in hospital

End point description:

End point type	Secondary

End point timeframe:

cycle 1

End point values	Lenalidomide monotherapy			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Day visits to hospital				
arithmetic mean (standard deviation)	4.5 (± 2.85)			

Statistical analyses

No statistical analyses for this end point

Secondary: Days on antibiotics

End point title	Days on antibiotics

End point description:

End point type	Secondary

End point timeframe:

cycle 1

End point values	Lenalidomide monotherapy			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Days				
arithmetic mean (standard deviation)	7.1 (± 9.69)			

Statistical analyses

No statistical analyses for this end point

Secondary: Toxicity

End point title	Toxicity

End point description:

End point type	Secondary

End point timeframe:

in the trial

End point values	Lenalidomide monotherapy			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Number of participants reporting SAE	9			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients proceeding to allograft/DLI/maintenance therapy

End point title	Proportion of patients proceeding to allograft/DLI/maintenance therapy

End point description:

End point type	Secondary

End point timeframe:

in the trial

End point values	Lenalidomide monotherapy			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Number	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Survival

End point title	Survival

End point description:

End point type	Secondary

End point timeframe:

in the trial

End point values	Lenalidomide monotherapy			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Number of deaths				
Treatment-related	4			
Non-treatment-related	9			

Statistical analyses

No statistical analyses for this end point

Secondary: Relapse-free survival

End point title	Relapse-free survival

End point description:

End point type	Secondary

End point timeframe:

in the trial

End point values	Lenalidomide monotherapy			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Number relapsed	1			

Statistical analyses

No statistical analyses for this end point

Secondary: AML transformation of MDS

End point title	AML transformation of MDS

End point description:

End point type	Secondary

End point timeframe:

in the trial

End point values	Lenalidomide monotherapy			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Number	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Haematological improvement for each cycle in patients with MDS

End point title	Haematological improvement for each cycle in patients with MDS

End point description:

End point type	Secondary

End point timeframe:

Cycle 1

End point values	Lenalidomide monotherapy			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Number				
No	2			
Yes - HI-E	1			
Yes - HI-P	1			
Yes - HI-N	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Blood product usage (number of platelet transfusions)

End point title	Blood product usage (number of platelet transfusions)

End point description:

End point type	Secondary

End point timeframe:

cycle 1

End point values	Lenalidomide monotherapy			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Platelet transfusion units				
arithmetic mean (standard deviation)	5.3 (± 5.99)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

ARs- time of start of protocol treatment until 30 days post cessation of trial therapy for patients receiving chemotherapy / maintenance.

SAEs and SUSARS until 30 days post last trial treatment or 100 days post transplant

Adverse event reporting additional description:

For ARs only data relating to Neuropathy and Thromboembolic events will be collected following an allogeneic stem cell transplant/DLI and this will be collected until 100 days post transplant/DLI.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14

Frequency threshold for reporting non-serious adverse events: 0 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: See attached end of trial report submitted to the MHRA on 06/05/2014 for details of adverse events. Leeds Institute of Clinical Trials Research is an academic trials unit where full MedDRA coding is not the standard. It has therefore not been possible for adverse event data to be accurately entered into the full data view within EudraCT as all mandatory categories cannot be completed.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 June 2009	- Change in AE reporting definition -Change in exclusion criteria following on from DMEC advise
08 July 2010	- Study design amended to remove the monotherapy phase for patients with ≥5% blasts following on from the temporary halt of the trial. The trial was reopened with this amended design.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
28 May 2010	Halt due to the trigger of a protocol defined stopping rule for treatment-related deaths in the lenalidomide monotherapy phase for patients with ≥5% blasts.	28 July 2010

Notes:

Limitations and caveats

None reported