



Clinical trial results:

CMML201: A phase 2 study of azacitidine in chronic myelomonocytic leukaemia (CMML)

Summary

EudraCT number	2008-006349-23
Trial protocol	GB
Global end of trial date	21 November 2014

Results information

Result version number	v1 (current)
This version publication date	29 March 2020
First version publication date	29 March 2020
Summary attachment (see zip file)	CMML201 End of Trial Report (End of Trial Report.pdf)

Trial information

Trial identification

Sponsor protocol code	HM08/8540
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Additional study identifiers

ISRCTN number	ISRCTN21428905
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Leeds
Sponsor organisation address	34 Hyde Terrace , Leeds , United Kingdom, LS2 9JT
Public contact	Quality Assurance Department , Leeds Institute of Clinical Trials Research University of Leeds LS2 9JT, medctrug@leeds.ac.uk
Scientific contact	Quality Assurance Department , Leeds Institute of Clinical Trials Research University of Leeds LS2 9JT , medctrug@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	21 May 2012
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 May 2012
Global end of trial reached?	Yes
Global end of trial date	21 November 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the safety, tolerability and efficacy of azacitidine in patients with CMML.

Protection of trial subjects:

Eligibility criteria were designed with patient safety as a primary concern and therefore none is unfairly excluded from or included in the trial.

Consent:

Informed consent will be taken by an authorised clinically trained member of staff who will ensure that the person will understand the purpose and nature of the study and what it involves, the benefits, risks and burdens and the alternative treatments to the study. They will also ensure the patient is able to retain the information long enough to make an effective decision with free choice. Patients will be allowed a minimum of 24 hours to decide if they would like to take part.

Risks, burdens and benefits:

The possible side effects of azacitidine are detailed in the patient information sheet. The side effects will be monitored closely and the dose adjusted to minimise these. If a patient experiences a severe reaction, then the study treatment may be discontinued and alternative treatment will be recommended. The trial is a 2 stage design to ensure regular safety checks are carried out during the study by the DMEC. The DMEC will review any treatment related deaths on a continuous basis.

Confidentiality:

All information collected during the course of the trial will be kept strictly confidential. Information will be held securely on paper and electronically at the Clinical Trials Research Unit (CTRU). The CTRU will comply with all aspects of the 1998 Data Protection Act.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 January 2010
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: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

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)	7
From 65 to 84 years	22
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

N=74 patients assessed for eligibility.

N=42 were excluded. Of these N=26 did not meet the inclusion criteria, N=9 declined to participate and N=7 were for another reason.

Period 1

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

Arms

Arm title	Azacitidine
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Arm description:

Azacitidine 75mg/m²/sc days 1-5 & 8-9

Patients to receive a minimum of 6x28 - day cycles

Arm type	Experimental
Investigational medicinal product name	Azacitidine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

The dose of azacitidine administered must be based on body surface area (BSA) and is to be calculated based on actual body weight using a standard nomogram.

The dose should be calculated on Day 1 of each cycle; the dose should remain the same throughout a treatment cycle but should be recalculated at the start of the next cycle. If a patient's body weight changes by more than 10% compared with baseline body weight, or compared with a previous body weight that required a dose adjustment, then the patient's dose should be recalculated.

Azacitidine for subcutaneous injection (sc) should be aseptically reconstituted in 4ml of sterile water for injection

under conditions approved by the hospital pharmacy. The diluent will contain 25mg/ml (100mg/4ml).

Doses

greater than 4ml should be divided equally and injected in two separate sites.

Number of subjects in period 1	Azacitidine
Started	30
Completed	16
Not completed	14
Adverse event, serious fatal	2

Consent withdrawn by subject	1
Lack of improvement in transfusion	1
Adverse event, non-fatal	2
AML transformation to CMML	1
Lack of efficacy	7

Baseline characteristics

Reporting groups

Reporting group title	Overall trial
Reporting group description: -	

Reporting group values	Overall trial	Total	
Number of subjects	30	30	
Age categorical			
Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Units: years			
arithmetic mean	70.1		
standard deviation	± 7.56	-	
Gender categorical			
Units: Subjects			
Female	10	10	
Male	20	20	

End points

End points reporting groups

Reporting group title	Azacitidine
Reporting group description: Azacitidine 75mg/m2/sc days 1-5 & 8-9 Patients to receive a minimum of 6x28 - day cycles	

Primary: Safety and tolerability

End point title	Safety and tolerability ^[1]
End point description: Safety and tolerability are as defined by frequency of: a) azacitidine-related death b) any grade 3/4 non haematological adverse reaction. Adverse reaction is defined as adverse event judged by either the Principal Investigator or the Chief Investigator (or his delegate) as having a reasonable suspected causal relationship to azacitidine. Haematological is defined as relating to haemoglobin, leukocytes (total white blood cells), lymphocytes, neutrophils/granulocytes (ANC/AGC) and platelets, non-haematological is defined as other adverse reactions.	
End point type	Primary
End point timeframe: From Registration	

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: This is a single arm trial and hence there is no comparative statistical analysis and merely an estimate of the proportion of the primary endpoints with a 95% confidence interval.

End point values	Azacitidine			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: 30	1			

Statistical analyses

No statistical analyses for this end point

Primary: Overall response rate

End point title	Overall response rate ^[2]
End point description: Overall response rate is defined as the sum of clinical remission, good response and minor response determined according to Wattel et al (16) at day 28 of the sixth or last cycle of azacitidine (whichever is the earliest)	
End point type	Primary
End point timeframe: From first treatment to day 28 of the sixth or last cycle of azacitidine	

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: This is a single arm trial and hence there is no comparative statistical analysis and merely an estimate of the proportion of the primary endpoints with a 95% confidence interval.

End point values	Azacitidine			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: 30	13			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

AEs, ARs, SAEs collected for all patients from the time of start of protocol treatment until 30 days after the last dose of treatment with azacitidine. SARs and SUSARs reported until end of trial

Assessment type	Systematic
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Dictionary used

Dictionary name	body system coding
Dictionary version	1

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: It is not our standard practice to code adverse events according to the full MEDRA system.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 September 2009	Requirement for a buccal swab at registration added to the protocol Clarification that recruitment will be continuous between the two stages and response rates at day 28 of Cycle 3 will be used as early indicator of response.
30 September 2009	Carton and vial label added to the trial specific Azacitidine prior to dispatch. This differed from the label text submitted and approved as part of the Clinical Trial Authorisation.
17 December 2009	Celgene (supplier of the pre-labelled trial specific azacitidine) informed the CTRU of a typographical error in the labels which required regulatory approval before the product can be QP released.
06 April 2010	Update to the Azacitidine Investigator Brochure v6 05/09/2008 by Addendum 1, 27th August 2009, and Addendum 2, 17 September 2009. The addendums did not alter the safety profile for the study.
01 November 2010	Change for Principal Investigator at an existing Site.
03 December 2010	Clarification of haematological toxicity in the protocol.
02 February 2012	Amendments made to the protocol include: Clarification of how long patients will be followed up for. Removal of the requirement for a bone marrow aspirate to be taken every 6 months.
08 July 2013	The requirement for central collection of serum, bone marrow and buccal swab samples as analysis was removed. End of Trial Definition updated. Reporting time for SARs and SUSARs amended from 30 days post treatment to end of trial.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported