

**Clinical trial results:****Pilot study of 5 Azacitidine in the treatment of MDS/AML with high risk (chromosome 7 and/or complex cytogenetic abnormality)****Summary**

EudraCT number	2005-003732-22
Trial protocol	GB
Global end of trial date	01 December 2013

Results information

Result version number	v1 (current)
This version publication date	27 July 2019
First version publication date	27 July 2019
Summary attachment (see zip file)	FINAL STUDY REPORT (End of study report Monosomy 7.pdf)

Trial information**Trial identification**

Sponsor protocol code	M7-1, Version 1, 03/08/05
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00915785
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	King's College London
Sponsor organisation address	The Strand, London, United Kingdom, WC2R 2LS
Public contact	Professor Ghulam Mufti, King's College London, 44 020 3299 3080, ghulam.mufti@kcl.ac.uk
Scientific contact	Professor Ghulam Mufti, King's College London, 44 020 3299 3080, ghulam.mufti@kcl.ac.uk
Sponsor organisation name	King's College Hospital
Sponsor organisation address	Denmark Hill, London, United Kingdom, SE59RS
Public contact	Professor Ghulam Mufti, King's College Hospital, 44 203 299 3080, ghulam.mufti@kcl.ac.uk
Scientific contact	Professor Ghulam Mufti, King's College Hospital, 44 203 299 3080, ghulam.mufti@kcl.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	01 December 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 December 2013
Global end of trial reached?	Yes
Global end of trial date	01 December 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Assess complete/cytogenetic remission in patients with chromosome 7 abnormalities .

All participants will be followed up every 3 months until death due to disease progression.

Protection of trial subjects:

Any patient who experiences a nonhematological adverse event with NCI CTC toxicity Grade 3 or 4 that is an escalation from his or her status at Baseline (prior to the first dose) will have azacitidine temporarily discontinued until the toxicity grade returns to the Baseline value. Azacitidine should be permanently discontinued if the nonhematological toxicity persists for more than 21 days, despite the temporary interruption of study drug, or if the toxicity is life threatening.

Background therapy:

n/a

Evidence for comparator:

n/a

Actual start date of recruitment	31 May 2006
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 43
Worldwide total number of subjects	43
EEA total number of subjects	43

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)	9
From 65 to 84 years	34
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was an open-label, single centre pilot study to investigate azacitidine as first-line therapy in patients with MDS/AML with chromosome 7 abnormalities. Participants were recruited from one centre within the UK from 2006 until 2013

Pre-assignment

Screening details:

Screening/baseline procedures to be performed prior to the first day of treatment.

Period 1

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

Blinding implementation details:

Open label trial

Arms

Arm title	Full study
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Arm description:

Participants receive azacitidine (75 mg/m²/day SC for 7 days every 28 days). Patients will continue to receive Azacitidine until i) bone marrow disease progression or ii) relapse following documented erythroid haematologic improvement (CR, PR) or iii) unless there is unacceptable non-haematological toxicity

Arm type	Experimental
Investigational medicinal product name	azacitidine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants receive azacitidine (75 mg/m²/day SC for 7 days every 28 days). Patients will continue to receive Azacitidine until i) bone marrow disease progression or ii) relapse following documented erythroid haematologic improvement (CR, PR) or iii) unless there is unacceptable non-haematological toxicity

Number of subjects in period 1	Full study
Started	43
Completed	40
Not completed	3
Adverse event, serious fatal	2
Adverse event, non-fatal	1

Baseline characteristics

Reporting groups

Reporting group title	Overall Trial
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Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	43	43	
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)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
17 to 59 years	9	9	
60 to 85 years	34	34	
Gender categorical			
Units: Subjects			
Female	15	15	
Male	28	28	

End points

End points reporting groups

Reporting group title	Full study
Reporting group description: Participants receive azacitidine (75 mg/m ² /day SC for 7 days every 28 days). Patients will continue to receive Azacitidine until i) bone marrow disease progression or ii) relapse following documented erythroid haematologic improvement (CR, PR) or iii) unless there is unacceptable non-haematological toxicity	

Primary: Primary Endpoint

End point title	Primary Endpoint ^[1]
End point description: To assess the rate of haematological and cytogenetic response in patients with MDS/AML with a chromosome 7 abnormality either alone or as part of a complex clone.	
End point type	Primary
End point timeframe: Duration of participation in trial	
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: Please see attached Final Study report for results data.	

End point values	Full study			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: whole	43			

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary Endpoint

End point title	Secondary Endpoint
End point description: <ul style="list-style-type: none">• Time to Relapse after complete remission (CR) or partial remission (PR), or Disease Progression (per IWG criteria), censored at death;• Duration of response and duration of improvement;• Time to AML transformation or death from any cause;	
End point type	Secondary
End point timeframe: Duration of participation in trial.	

End point values	Full study			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: whole	43			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

30 days +/-2 days after the administration of the last dose of study drug

Adverse event reporting additional description:

Adverse Events that do not require Reporting:-

Progression of disease or relapse during the course of treatment.

Hospital admissions for the treatment of progressive or relapsed disease.

Death due to disease or disease progression

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.1
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Reporting groups

Reporting group title	Whole Trial
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Reporting group description: -

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: Adverse Events that do not require Reporting:- Progression of disease or relapse during the course of treatment.

Hospital admissions for the treatment of progressive or relapsed disease.

Death due to disease or disease progression

Serious adverse events	Whole Trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 43 (30.23%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	2		
Vascular disorders			
Subdural haematoma			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Epistaxis			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Generally unwell			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Shortness of breath			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hickman line infection			
subjects affected / exposed	2 / 43 (4.65%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cellulitis abdomen at administration site			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile Neutropenia			
subjects affected / exposed	2 / 43 (4.65%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Anaemia			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Low HB & Platelet Possibly 7039 Count (anaemia)			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Respiratory, thoracic and mediastinal disorders			
Right sided pleural effusion			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal Impairment			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Perianal abscess			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neutropenic Sepsis			
subjects affected / exposed	7 / 43 (16.28%)		
occurrences causally related to treatment / all	2 / 7		
deaths causally related to treatment / all	1 / 2		
Sepsis			
subjects affected / exposed	2 / 43 (4.65%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Chest Infection			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Buccal abscess and right thigh skin infection			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infected abscess in right arm			

subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Whole Trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 43 (0.00%)		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 September 2010	<p>The main changes are as follow:</p> <ol style="list-style-type: none">1) The sample size has been changed from 40 to 50 patients. This is to enable 40 efficacy evaluable patients to be analysed.2) The investigational medicinal product, Azacitidine, will now be supplied beyond the 6 cycles study phase until patients show bone marrow disease progression, pr progression/relapse following documented erythroid haematologic improvement (CR,PR) or unless there is unacceptable toxicity. In addition, follow up procedures have been added to include an end of study visit and three-monthly follow up after the discontinuation of study treatment.3) Celgene Europe Limited (Celgene Corporation acquired Pharmion) gained marketing authorisation in 2008 for Vidaza (trade name for Azacitidine), however clinical trial supply will continue to be provided for this trial. The formulation for the clinical trial supply is the same as the commercial supply, but with different packaging and labelling. The SmPC is submitted for information. Handling of the trial medication has been added to the protocol.4) The label has been updated by Celgene and submitted for approval.5) King's College Hospital NHS Foundation Trust and King's College London will co-sponsor the study.6) Secondary objective for the study has been removed.7) Laboratory parameters and time points when the assessments are completed have been updated. The inclusion criteria on laboratory parameters have been updated.8) Pharmacovigilance reporting section is significantly updated to include reporting of pregnancies and reporting to Joint Clinical Trials Office acting on behalf of the trial sponsors.9) Further sections have been added to specify the following aspects of trial conduct: direct access to source data and documents, EC and Regulatory approvals, Quality assurance, data handling, publication policy and financial aspects.10) The importer information is updated on the CTA as Cardinal Health Clinical Supply Services was acquired by Catalent Phar

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

This trial is an open label intention to treat trial and as such is not statistically powered.

Notes: