Clinical trial results:
Use of Decitabine in Myelodysplastic Syndrome (MDS) Following Azacitidine (AZA) Failure (DEC-MDS)

Summary

EudraCT number	2009-017098-40
Trial protocol	GB
Global end of trial date	14 August 2014

Results information

Result version number	v1 (current)
This version publication date	20 October 2018
First version publication date	20 October 2018
Summary attachment (see zip file)	FINAL STUDY REPORT (EoS Report signed.pdf)

Trial information

Trial identification

Sponsor protocol code	DEC-MDS

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01133886
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	Department of Haematology, King's College Hospital, +44 0203299 1183, Lorraine.Catt@kch.nhs.uk
Scientific contact	Department of Haematology, King's College Hospital, +44 0203299 1183, Lorraine.Catt@kch.nhs.uk
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Public contact	Department of Haematology, King's College Hospital, +44 0203299 1183, lorraine.catt@nhs.net
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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	14 August 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 August 2014
Global end of trial reached?	Yes
Global end of trial date	14 August 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the overall response rate (CR+PR as per IWG 2006) at 6 months in MDS patients, CMML-2 patients, and AML patients with up to 30% bone marrow blasts (previously classified as RAEB-t by the FAB MDS classification), treated with low-dose decitabine who have previously failed therapy with 5-azacitidine.

Protection of trial subjects:

Patients are free to withdraw consent for study treatment and/or consent to participate in the study at any time and without the prejudice to further treatment. Patients who withdraw from study treatment, but are willing to continue to participate in the follow-up visits should be followed according to the procedures outlined in the protocol.

Background therapy:

None

Evidence for comparator:

n/a as this is a single arm trial.

Actual start date of recruitment	15 December 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: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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	11
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

Participants were recruited from 5 centers in the United Kingdom between 2010 and 2014.

Pre-assignment

Screening details:

Inclusion Criteria
18 yrs or more, 3. diagnosed MOS with 5% or more marrow blasts & IPSS risk, intermediate 2 or high risk; or chronic myelomonocytic leukemia (CMML-2); or AML with 20-30% bone marrow blasts (previously defined as RAEB-t by the FAB
MOS classification). Failed therapy with azacitidine. Adequate hepatic & renal function.

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	Full study

Arm description:

Patients will receive decitabine as a 20mg/m2 1-hour intravenous infusion once daily on
Days 1-5 of a 4-week cycle. The initial phase of the study will comprise of 6 cycles of treatment of decitabine

Arm type	Experimental
Investigational medicinal product name	Decitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients will receive decitabine as a 20mg/m2 1-hour intravenous infusion once daily on Days 1-5 of a 4-week cycle.
The initial phase of the study will comprise of 6 cycles of treatment of decitabine.

Number of subjects in period 1	Full study
Started	20
Completed	5
Not completed	15
Physician decision	8
Consent withdrawn by subject	1
Adverse event, non-fatal	6

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial

Reporting group description:

At the time the trial was terminated (MHRA notification 02/Sept/2014), a total of 25 patients across all sites had consented onto the study. Only 20 patients actually received 1 or more cycles of Decitabine. Only 5 patients had 6 cycles or more and no patients met primary end point (CR or PR as per IWG 2006).

Reporting group values	Overall Trial	Total	
Number of subjects	20	20	
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 60-69 years	6	6	
Adults 70 - 79 years	11	11	
Adults 80 - 89 years	3	3	
Gender categorical Units: Subjects			
Female	7	7	
Male	13	13	

End points

End points reporting groups

Reporting group title	Full study

Reporting group description:

Patients will receive decitabine as a 20mg/m2 1-hour intravenous infusion once daily on Days 1-5 of a 4-week cycle. The initial phase of the study will comprise of 6 cycles of treatment of decitabine

Primary: Primary Objective

End point title	Primary Objective[1]

End point description:

To assess the overall response rate (CR+PR as per IWG 2006) at 6 months in MOS patients, CMML-2 patients, and AML patients with up to 30% bone marrow blasts (previously classified as RAEB-t by the FAB MOS classification), treated with low-dose decitabine who have previously failed therapy with 5-azacitidine.

End point type	Primary

End point timeframe:

6 cycles of decitabine - 6months.

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: 5 patients had 6 cycles or more and no patients met primary end point (CR or PR as per IWG 2006. Please see attached summary document for more information.

End point values	Full study			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: whole				

Notes:

[2] - 5 patients had 6 cycles or more and no patients met primary end point (CR or PR as per IWG 2006.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Whole trial

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Whole Trial

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: SAEs were experienced by the study patients; there were no unexpected SAEs related to trial medication nor were than any significant AEs to report.

Serious adverse events	Whole Trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 20 (65.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Suspected Heart abnormality			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	9 / 20 (45.00%)		
occurrences causally related to treatment / all	7 / 9		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Gastrointestinal Bleed			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Epistaxis			

subjects affected / exposed	1 / 20 (5.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Extramedullary Haemopoiesis				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Pneumonia - Grade 3				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oedema & shortness of breath.				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Neutropenic Sepsis				
subjects affected / exposed	12 / 20 (60.00%)			
occurrences causally related to treatment / all	10 / 12			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	2 / 20 (10.00%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	2 / 20 (10.00%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Bacterial Infection				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

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

Non-serious adverse events	Whole Trial		
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 20 (0.00%)		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 December 2010	Secondary objective changed to look at grade 3 and 4 treatment related toxicity only. Assessment for: Survival, Relapse, Subsequent treatment removed from end of treatment visit. Text added to clarify that grade 1 and 2 haematological and organ toxicities do not need to be recorded. Information on BSA capping included. Text changed so that decitabine will only be delayed due to myelosuppression after 3 cycles of treatment. Text added to define women of child bearing potential.
09 May 2011	hanges to the protocol are as follows: 1) Demographics will be recorded at the screening visit. 2) ECOG performance score will be assessed at the end of treatment visit. 3) A bone marrow sample will be performed and exploratory samples taken at the end (day 21+) of the 3rd and 6th cycle instead of after day 28. 4) Patients will be recommenced on a lower dose of decitabine following a dose delay of at least 14 days. 5) All concomitant medications will be recorded from day 1 until the end of treatment visit. 6) Other administrative changes In addition, Nottingham and Cardiff added as sites.
18 July 2011	Protocol changed to allow dose delays due to scheduling issues. Clarification that patients are only excluded if they have received prior intensive chemotherapy or high-dose cytarabine for the treatment of MDS or AML. Non-Substantial amendments 3 & 4 have been incorporated into documentation
17 October 2011	Protocol updated to protocol v6.0 Changes in patient eligibility criteria. Changes in labelling and labelling site.
20 December 2011	Protocol updated to protocol v7.0, the following sections have been updated with new information from IB Edition 5 • Recognised Adverse Drug Reactions section • Cardiovascular/Pulmonary Section • CNS Effects • Concomitant Medication New edition of Investigator Brochure (Edition 5, 17-Aug-11)

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.

At the interim analysis, a review of the current subjects recruited up to that point took place, as was the rate of recruitment. Based on this primary information it was decided by the TSC to close the study.

Notes: