Clinical trial results:
Phase ll Study of the Adjunctive Use of Azacitidine in Patients Undergoing Reduced Intensity Allogeneic Transplantation for Acute Myeloid Leukaemia

Summary

EudraCT number	2007-006475-36
Trial protocol	GB
Global end of trial date	31 January 2014

Results information

Result version number	v1 (current)
This version publication date	19 February 2020
First version publication date	19 February 2020

Trial information

Trial identification

Sponsor protocol code	RG_07-187

Additional study identifiers

ISRCTN number	ISRCTN36825171
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Birmingham
Sponsor organisation address	Vincent Drive, Birmingham, United Kingdom, B15 2TT
Public contact	CRCTU general enquires, University of Birmingham, crctu-generalenqueries@bham.ac.uk
Scientific contact	CRCTU general enquires, University of Birmingham, crctu-generalenqueries@bham.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	22 January 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 January 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and tolerability of Azacitidine in patients following reduced intensity conditioned allogeneic transplantation for AML.

Protection of trial subjects:

Specific dose modifications were recommended to decrease the incidence and relieve the symptoms of:
Grade 3 and 4 haematological toxicities
Grade 3/ and 4 non-haematological toxicities

The following rules were put in place:
If 3 out of the first 5 patients experience Grade 4 haematological toxicities which are deemed related to Azacitidine then Azacitidine will be reduced to a dose of 24mg/m2 for all subsequent patients.

The trial will be stopped if 4 patients experience sustained Grade 4 haematological toxicities of more than 42 days or more than 4 recurring grade 3-4 non haematological toxicities deemed related to Azacitidine.

The trial will be stopped if more than 4 patients develop unexpected recurring non- haematological Grade 3-4 toxicities deemed related to Azacitidine

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 July 2008
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: 51
Worldwide total number of subjects	51
EEA total number of subjects	51

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)	39
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited form 8 UK sites between 24-Jul-2008 and 05-Oct-2011.

Pre-assignment

Screening details:

Screening commenced following consent and prior to patient registration in order to confirm eligibility. All patients had a full medical, disease and drug therapy history, pre-transplant bone marrow.
Patients who were unfit to receive Azacitadine following transplant did not begin trial treatment and so, did not reach the baseline period.

Pre-assignment period milestones

Number of subjects started	51
Number of subjects completed	37

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Consent withdrawn by subject: 3
Reason: Number of subjects	Ineligible: 2
Reason: Number of subjects	Suffered Acute GvHD: 1
Reason: Number of subjects	Infection: 8

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	Azacitadine treatment

Arm description: -

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

Dosage and administration details:

36 mg/m^2 sc x 5 days every 28 days commenced on week 6 post transplant for 10 cycles.

Number of subjects in period 1[1]	Azacitadine treatment
Started	37
Completed	16
Not completed	21
Relapse	9

Physician decision	1
Adverse event, non-fatal	9
Not reported	2

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: The protocol defines evaluable patients as those who commenced at least 1 cycle of Azacitidine. Not all of the patients that were registered to the trial started Azacitadine treatment, so only those that did are included in the baseline period.

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	37	37	
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)	30	30	
From 65-84 years	7	7	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	21	21	
Male	16	16	
Diagnosis Units: Subjects			
AML - de novo	24	24	
AML - secondary	13	13	
Karyotype Units: Subjects			
Intermediate	30	30	
Poor	7	7	
Disease status Units: Subjects			
First complete remission (CR1)	24	24	
Second Complete Remission (CR2)	8	8	
First relapse	3	3	
Primary refractory disease	2	2	
Conditioning Treatment Units: Subjects			
Fludarabine, Melphalan, Campath (FMC)	34	34	
Fludarabine, Cytarabine, Amsacrine (FLAMSA)	3	3	
Donor Type Units: Subjects			
Identical sibling	12	12	
Mismatched relative	1	1	
Mismatched unrelated donor	1	1	

Matched unrelated donor	23	23	
CMV status (patient/donor) Units: Subjects			
positive/positive	14	14	
positive/negative	6	6	
negative/positive	3	3	
negative/negative	14	14	
Stem cell source Units: Subjects			
Peripheral Blood	34	34	
Bone Marrow	3	3	

End points

End points reporting groups

Reporting group title	Azacitadine treatment

Reporting group description: -

Primary: Tolerability of Azacitidine post transplant

End point title	Tolerability of Azacitidine post transplant[1]

End point description:

Tolerability is defined as the number of patients completing treatment.

End point type	Primary

End point timeframe:

Post transplant

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 formal statistical analyses were performed. The protocol states that 'All analysis will be descriptive'.

End point values	Azacitadine treatment			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: Patients				
Tolerated treatment	30			
Did not tolerate treatment	7			

Statistical analyses

No statistical analyses for this end point

Secondary: Relapse Free Survival

End point title	Relapse Free Survival

End point description:

Relapse free survival at one year post-transplant and two years post-transplant

End point type	Secondary

End point timeframe:

One year, Two year

End point values	Azacitadine treatment			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: RFS				
number (confidence interval 95%)				
1 year RFS (%)	56.8 (42.8 to 75.2)			
2 year RFS (%)	48.6 (34.9 to 67.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival

End point description:

End point type	Secondary

End point timeframe:

One year, two year

End point values	Azacitadine treatment			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: OS				
number (confidence interval 95%)				
1 year OS (%)	80.6 (68.7 to 94.6)			
2 year OS (%)	49.6 (35.6 to 69.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Graft versus Host Disease (Acute)

End point title	Graft versus Host Disease (Acute)

End point description:

End point type	Secondary

End point timeframe:

Post transplant

End point values	Azacitadine treatment			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: Patients				
Did not experience acute GvHD	20			
Experienced grade 1 or 2 acute GvHD	17			
Experienced grade 3 or 4 acute GvHD	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Graft versus Host Disease (Chronic)

End point title	Graft versus Host Disease (Chronic)

End point description:

End point type	Secondary

End point timeframe:

Post-transplant

End point values	Azacitadine treatment			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: Patients				
Did not experience Chronic GvHD	30			
Experienced limited chronic GvHD	7			
Experienced extensive chronic GvHD	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Chimerism (Whole blood)

End point title	Chimerism (Whole blood)

End point description:

End point type	Secondary

End point timeframe:

90 days post-transplant

End point values	Azacitadine treatment			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: Patients				
Full	22			
Mixed	15			

Statistical analyses

No statistical analyses for this end point

Secondary: Chimerism (T-cell)

End point title	Chimerism (T-cell)

End point description:

End point type	Secondary

End point timeframe:

90 days post-transplant

End point values	Azacitadine treatment			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: Patients				
Full	7			
Mixed	30			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were recorded from the start of Azacitidine treatment until 28 days after the last dose of Azacitidine or until the start of other anti-cancer therapy – whichever occurs first

Assessment type	Non-systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4

Reporting groups

Reporting group title	Azacitadine treatment

Reporting group description:

All patients who received Azacitadine treatment

Serious adverse events	Azacitadine treatment		
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 37 (40.54%)		
number of deaths (all causes)	19		
number of deaths resulting from adverse events			
Investigations			
Creatinine increased			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations - Other, Abnormal ALT			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			

subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fever			
subjects affected / exposed	4 / 37 (10.81%)		
occurrences causally related to treatment / all	1 / 9		
deaths causally related to treatment / all	0 / 0		
Pain			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 37 (8.11%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Mucositis oral			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomitting			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Apnea			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonitis			

subjects affected / exposed	1 / 37 (2.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cough				
subjects affected / exposed	1 / 37 (2.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Skin and Subcutaneous tissue disorders - Other, Rash				
subjects affected / exposed	1 / 37 (2.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders - Other, Shingles				
subjects affected / exposed	1 / 37 (2.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Bladder infection				
subjects affected / exposed	1 / 37 (2.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Device related infection				
subjects affected / exposed	1 / 37 (2.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations - Other, Chest infection				
subjects affected / exposed	2 / 37 (5.41%)			
occurrences causally related to treatment / all	1 / 5			
deaths causally related to treatment / all	0 / 0			
Sepsis				

subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Lung infection			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pharyngitis			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin infection			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and Infestations - Other, CMV			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Infections and Infestations - Other, H. influezae			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and Infestations - Other, Para influenza			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and Infestations - Other, Shingles			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Infections and infestations - Other, Staphylococcus aureus			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 37 (2.70%)		
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	Azacitadine treatment		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 37 (100.00%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
General disorders and administration site conditions			
Edema limbs			
subjects affected / exposed	4 / 37 (10.81%)		
occurrences (all)	4		
Fatigue			
subjects affected / exposed	12 / 37 (32.43%)		
occurrences (all)	23		
Fever			
subjects affected / exposed	8 / 37 (21.62%)		
occurrences (all)	14		
Injection site reaction			
subjects affected / exposed	25 / 37 (67.57%)		
occurrences (all)	64		
Lethargy			
subjects affected / exposed	6 / 37 (16.22%)		
occurrences (all)	7		

Pain			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Dyspnea			
subjects affected / exposed	4 / 37 (10.81%)		
occurrences (all)	4		
Cough			
subjects affected / exposed	10 / 37 (27.03%)		
occurrences (all)	12		
Psychiatric disorders			
Depression			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Investigations			
Alkaline phosphatase increased			
subjects affected / exposed	4 / 37 (10.81%)		
occurrences (all)	12		
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 37 (8.11%)		
occurrences (all)	5		
Hemoglobin increased			
subjects affected / exposed	5 / 37 (13.51%)		
occurrences (all)	7		
Hyperkalemia			
subjects affected / exposed	6 / 37 (16.22%)		
occurrences (all)	18		
Hypermagnesemia			
subjects affected / exposed	3 / 37 (8.11%)		
occurrences (all)	3		
Investigations - Other, Decreased calcium			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	4		
Neutrophil count decreased			

subjects affected / exposed	14 / 37 (37.84%)			
occurrences (all)	52			
Platelet count decreased				
subjects affected / exposed	24 / 37 (64.86%)			
occurrences (all)	113			
White blood cell decreased				
subjects affected / exposed	13 / 37 (35.14%)			
occurrences (all)	119			
Creatinine increased				
subjects affected / exposed	15 / 37 (40.54%)			
occurrences (all)	36			
Investigations - Other, Decreased magnesium				
subjects affected / exposed	3 / 37 (8.11%)			
occurrences (all)	10			
Investigations - Other, Decreased sodium				
subjects affected / exposed	2 / 37 (5.41%)			
occurrences (all)	6			
Investigations - Other, Decreased urea				
subjects affected / exposed	2 / 37 (5.41%)			
occurrences (all)	5			
Investigations - Other, Increased CRP				
subjects affected / exposed	8 / 37 (21.62%)			
occurrences (all)	28			
Investigations - Other, Increased LDH				
subjects affected / exposed	7 / 37 (18.92%)			
occurrences (all)	19			
Investigations - Other, Increased urea				
subjects affected / exposed	9 / 37 (24.32%)			
occurrences (all)	41			
Investigations - Other, Increased WCC				
subjects affected / exposed	3 / 37 (8.11%)			
occurrences (all)	10			

Nervous system disorders			
Headache			
subjects affected / exposed	9 / 37 (24.32%)		
occurrences (all)	9		
Neuralgia			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Tremor			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	23 / 37 (62.16%)		
occurrences (all)	119		
Eye disorders			
Dry eye			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 37 (10.81%)		
occurrences (all)	5		
Diarrhoea			
subjects affected / exposed	21 / 37 (56.76%)		
occurrences (all)	36		
Mucositis oral			
subjects affected / exposed	4 / 37 (10.81%)		
occurrences (all)	5		
Nausea			
subjects affected / exposed	23 / 37 (62.16%)		
occurrences (all)	46		
Vomiting			
subjects affected / exposed	12 / 37 (32.43%)		
occurrences (all)	20		
Constipation			
subjects affected / exposed	4 / 37 (10.81%)		
occurrences (all)	5		

Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Skin infection			
subjects affected / exposed	3 / 37 (8.11%)		
occurrences (all)	3		
Rash maculo-papular			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders - Other, Rash			
subjects affected / exposed	7 / 37 (18.92%)		
occurrences (all)	13		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	3 / 37 (8.11%)		
occurrences (all)	3		
Neck pain			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Infections and infestations			
Mucosal infection			
subjects affected / exposed	3 / 37 (8.11%)		
occurrences (all)	3		
Upper respiratory infection			
subjects affected / exposed	3 / 37 (8.11%)		
occurrences (all)	3		
Skin infection			
subjects affected / exposed	3 / 37 (8.11%)		
occurrences (all)	3		
Urinary tract infection			
subjects affected / exposed	3 / 37 (8.11%)		
occurrences (all)	3		
Infections and infestations - other, Chest infection			

subjects affected / exposed	3 / 37 (8.11%)		
occurrences (all)	9		
Infections and infestations - Other, CMV			
subjects affected / exposed	5 / 37 (13.51%)		
occurrences (all)	10		
Infections and infestations - Other, HSV			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Infections and infestations - Other, Infection			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Infections and infestations - Other, Para influenza			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Infections and infestations - Other, Rhinovirus			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Infections and infestations - Other, Shingles			
subjects affected / exposed	3 / 37 (8.11%)		
occurrences (all)	3		
Lung infection			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	4 / 37 (10.81%)		
occurrences (all)	4		
Hypoalbuminemia			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
hypocalcemia			
subjects affected / exposed	6 / 37 (16.22%)		
occurrences (all)	19		

Hypokalemia subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2		
Hypomagnesemia subjects affected / exposed occurrences (all)	8 / 37 (21.62%) 19		
Hyponatremia subjects affected / exposed occurrences (all)	5 / 37 (13.51%) 27		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 June 2008	An inclusion criterion was amended to remove an upper age limit for patient entry to the study. • The timeframe for patients to consent to the trial was extended • The contact details of staff managing the trial was amended • The patient information sheet (PIS) was amended to show the different time frame for consenting to the trial. • Addition of two new participating sites
17 October 2008	The PIS was amended to clarify that patients may have anonymised data sent to Celgene Corporation (who manufacture and supply the IMP) as part of their ongoing monitoring of the safety and activity of their agent. A revised consent form was sent to the Ethics board on 23rd Feb 2009 as the reference to the patient information sheet was incorrect.
12 April 2009	• Addition of a participating site • Inclusion criteria amended to allow inclusion of patients who undergo reduced intensity conditioned transplantation using an alternative chemotherapy (FLAMSA) regimen • Patients who have not recovered sufficiently after transplant to receive azacitidine (the IMP) by 6 months to be withdrawn from the trial. • Protocol amended to allow patients who have active non-life-threatening infection can receive azacitidine provided the blood counts are stable and meet the entry criteria for commencing azacitidine
30 April 2009	Myelodysplasia (MDS) patients were removed from the eligibility criteria • Blood samples required for immune studies were reduced • Criteria to assess renal function were also added.
04 November 2009	Change of Principal Investigator at Christie Hospital Foundation NHS Trust, Manchester
11 January 2011	• Planned recruitment was clarified to include 40 evaluable patients which was defined as patients commencing with least 1 cycle of azacitidine • Single allele mismatches defined to include RICAZA_Final_Clinical_Study_Report Version 1.0_29-May-2015 HLA-A, HLA-B, HLA-C, HLA-DRB1 • Addition of wording: No dose interruptions will be performed for grades 1 and 2 nonheamtological toxicities • Further guidance given on dose modifications for grade 3 haematological toxcities • Storage conditions for azacitidine amended • Serious Adverse Event (SAE) definition updated • Wording added to reflect that SAE and Suspected Unexpected Serious Adverse Reaction (SUSAR) information will be sent to Celgene
14 March 2011	• IMP label updated with new storage conditions • PIS was updated so that patients were aware what patient related data is accessible to 3rd parties and what type of information is passed on. • Addition of a Release of Medical Information Form and Consent Form to be used in relation to pregnancy notifications during the trial
21 June 2011	Amendment submitted to request the use of commercial stock of azacitidine for one dose to be given to a trial patient
21 December 2011	Addition of a participating site

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/22234690

http://www.ncbi.nlm.nih.gov/pubmed/26363443