Clinical trial results:
Phase II Study of the Adjunctive Use of Lenalidomide in Patients Undergoing Reduced Intensity Conditioning Allogeneic Transplantation for Multiple Myeloma

Summary

EudraCT number	2009-012033-30
Trial protocol	GB
Global end of trial date	31 May 2018

Results information

Result version number	v1 (current)
This version publication date	28 December 2019
First version publication date	28 December 2019

Trial information

Trial identification

Sponsor protocol code	RRK3679

Additional study identifiers

ISRCTN number	ISRCTN16228367
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Birmingham
Sponsor organisation address	Edgbaston, Birmingham, Birmingham, United Kingdom, Birmingham, United Kingdom, B15 2TT
Public contact	LenaRIC trial coordinator, University of Birmingham, 0044 0121 371 4365, lenaric@trials.bham.ac.uk
Scientific contact	LenaRIC trial coordinator , University of Birmingham, 0044 0121 371 4365, lenaric@trials.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	31 May 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 May 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of Lenalidomide given after reduced intensity conditioned stem cell transplant on progression-free survival at 2 years in myeloma

Protection of trial subjects:

A detailed list of dose reduction/stopping criteria were described in the protocol to decrease the incidence and relieve the symptoms of:
Blood and lymphatic system - neutropenia and thrombocytopenia
Constitutional or general side effects
Deep vein thrombosis
Renal impairment

Background therapy:

None applicable

Evidence for comparator: -

Actual start date of recruitment	31 May 2011
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: 40
Worldwide total number of subjects	40
EEA total number of subjects	40

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	1

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

40 patients were registered over a 24 month period. Date the first patient allocated:17Aug2012

Pre-assignment

Screening details:

The following screening assessments included within 6 weeks of the patient being admitted for allogeneic stem cell transplant: Demographic data, Medical history, Haematology, Blood chemistry, Bone marrow aspirate, and trephine, cardiac and renal function test, Pregnancy tests, and standard transplant investigations.

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	Treatment Arm

Arm description:

This is an open label phase II study. Patients with multiple myeloma in first or second CR/VGPR within 180 days of autologous stem cell transplant who are not eligible for allogeneic transplantation using myeloablative conditioning will undergo a reduced intensity allograft in which Lenalidomide is administered until 12 months post-transplant. The role of Lenalidomide in this context is to control residual disease until it is safe to consider DLI in those patients who may require it.

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

Dosage and administration details:

Oral Lenalidomide will be started on Day 1 of Cycle 1 (day +35 [+/- 4 days] post-transplant) at a dose of 5mg daily and will be continued for 21 days of each 28 day cycle (day 1-21). This will be continued for a maximum of 12 cycles (given up to 12 months post-transplant) subject to toxicity and tolerability.

Number of subjects in period 1	Treatment Arm
Started	40
Completed	34
Not completed	6
Adverse event, serious fatal	3
Physician decision	3

Baseline characteristics

Reporting groups	
Reporting group title	overall trial

Reporting group description:

To evaluate the effect of Lenalidomide after reduced intensity conditioned (RIC) transplantation on progression free survival (PFS) at 2 years in myeloma.

Reporting group values	overall trial	Total	
Number of subjects	40	40	
Age categorical			
• Patients >18 years and ≤70 years in whom allogeneic transplantation using a reduced intensity conditioning regimen is not contra-indicated but who are not suitable for conventional allograft.			
Units: Subjects			
Adults (18-64 years)	39	39	
From 65-84 years	1	1	
Age continuous			
Units: years			
median	44		
full range (min-max)	18 to 70	-	
Gender categorical			
Units: Subjects			
Female	17	17	
Male	23	23	
Outcome of Autologous Stem Cell Transplant +120 days post transplant			
Units: Subjects			
CR1	8	8	
CR2	7	7	
VGPR1	16	16	
VGPR2	8	8	
transplant before 120 days	1	1	

End points

End points reporting groups

Reporting group title	Treatment Arm

Reporting group description:

This is an open label phase II study. Patients with multiple myeloma in first or second CR/VGPR within 180 days of autologous stem cell transplant who are not eligible for allogeneic transplantation using myeloablative conditioning will undergo a reduced intensity allograft in which Lenalidomide is administered until 12 months post-transplant. The role of Lenalidomide in this context is to control residual disease until it is safe to consider DLI in those patients who may require it.

Primary: Progression Free Survival

End point title	Progression Free Survival[1]

End point description:

End point type	Primary

End point timeframe:

Progression Free Survival at 2 years post entry into the 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: The statistical analysis is based on descriptive statistics

End point values	Treatment Arm			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: PFS				
number (confidence interval 95%)	43.33 (27.57 to 58.11)			

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:

Overall survival at 1, 2 and 3 years post-transplant.

End point values	Treatment Arm			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: OS				
number (confidence interval 95%)				
One year OS	84.27 (68.29 to 92.61)			
Two year OS	75.74 (58.47 to 86.60)			

Statistical analyses

No statistical analyses for this end point

Secondary: Disease free survival

End point title	Disease free survival

End point description:

End point type	Secondary

End point timeframe:

Disease free survival has been calculated from date attaining a CR to rst date of laboratory or biochemical relapse, clinical relapse, relapse from CR or date of death due to myeloma.

End point values	Treatment Arm			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: DFS				
number (confidence interval 95%)				
One year DFS %	72.73 (49.10 to 86.71)			
Two years DFS %	59.09 (32.88 to 77.97)			

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:

1 year non-relapse mortality rates.

End point values	Treatment Arm			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: RFS				
number (confidence interval 95%)				
One year RFS %	84.27 (68.29 to 92.61)			
Two year RFS %	74.51 (56.44 to 85.96)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events were reported at any time for the duration of the study, from the date of commencing Lenalidomide up to and including 3 years post-transplant.

Adverse event reporting additional description:

The reporting of adverse events (AEs) will be in accordance with the Medicines for Human Use Clinical Trials Regulations 2004 and its subsequent amendments. The Investigator should assess the seriousness and causality of all AEs experienced by the patient (this should be documented in the source data) with reference to the Investigator Brochure.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4

Reporting groups

Reporting group title	Treated patients

Reporting group description:

All 34 patients who received lenalidomide

Serious adverse events	Treated patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 34 (64.71%)		
number of deaths (all causes)	10		
number of deaths resulting from adverse events	2		
Investigations			
Creatinine increased			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Investigations - Other			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasms benign, malignant and unspecified (incl cysts and polyps) - Other			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Injury, poisoning and procedural complications			
Spinal fracture			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Blood and lymphatic system disorders - Other			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Unknown			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fever			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhea			
subjects affected / exposed	8 / 34 (23.53%)		
occurrences causally related to treatment / all	6 / 8		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders - Other			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Unknown			

subjects affected / exposed	1 / 34 (2.94%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Catheter related infection				
subjects affected / exposed	2 / 34 (5.88%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Device related infection				
subjects affected / exposed	3 / 34 (8.82%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Enterocolitis infectious				
subjects affected / exposed	1 / 34 (2.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations - Other				
subjects affected / exposed	1 / 34 (2.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lung infection				
subjects affected / exposed	1 / 34 (2.94%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Otitis media				
subjects affected / exposed	1 / 34 (2.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Sepsis				
subjects affected / exposed	2 / 34 (5.88%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 1			
Skin infection				

subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper respiratory infection			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Unknown			
subjects affected / exposed	1 / 34 (2.94%)		
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	Treated patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 34 (100.00%)		
Vascular disorders			
Hot flashes			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Hypertension			
subjects affected / exposed	9 / 34 (26.47%)		
occurrences (all)	12		
Hypotension			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
General disorders and administration site conditions			
Edema face			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	2		
Edema limbs			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	4		
Fatigue			

subjects affected / exposed	12 / 34 (35.29%)		
occurrences (all)	19		
Fever			
subjects affected / exposed	5 / 34 (14.71%)		
occurrences (all)	9		
Flu like symptoms			
subjects affected / exposed	4 / 34 (11.76%)		
occurrences (all)	5		
General disorders and administration site conditions			
subjects affected / exposed	4 / 34 (11.76%)		
occurrences (all)	4		
Localized edema			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
Malaise			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
Non-cardiac chest pain			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	3		
Pain			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	3		
Immune system disorders			
Allergic reaction			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	9 / 34 (26.47%)		
occurrences (all)	10		
Dyspnea			
subjects affected / exposed	6 / 34 (17.65%)		
occurrences (all)	6		
Hypoxia			

subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Nasal congestion			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Productive cough			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders - Other			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
Sore throat			
subjects affected / exposed	6 / 34 (17.65%)		
occurrences (all)	7		
Psychiatric disorders			
Depression			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
Insomnia			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	8 / 34 (23.53%)		
occurrences (all)	26		
Alkaline phosphatase increased			
subjects affected / exposed	9 / 34 (26.47%)		
occurrences (all)	18		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	7		
Blood bilirubin increased			
subjects affected / exposed	5 / 34 (14.71%)		
occurrences (all)	6		
Creatinine increased			

subjects affected / exposed	9 / 34 (26.47%)		
occurrences (all)	29		
Investigations - Other			
subjects affected / exposed	11 / 34 (32.35%)		
occurrences (all)	60		
Lymphocyte count decreased			
subjects affected / exposed	6 / 34 (17.65%)		
occurrences (all)	21		
Lymphocyte count increased			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Neutrophil count decreased			
subjects affected / exposed	21 / 34 (61.76%)		
occurrences (all)	63		
Platelet count decreased			
subjects affected / exposed	12 / 34 (35.29%)		
occurrences (all)	41		
Weight loss			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	3		
White blood cell decreased			
subjects affected / exposed	14 / 34 (41.18%)		
occurrences (all)	57		
Injury, poisoning and procedural complications			
Dermatitis radiation			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Spinal fracture			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Cardiac disorders			
Cardiac disorder			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Nervous system disorders			

Dizziness subjects affected / exposed occurrences (all)	1 / 34 (2.94%) 1		
Dysgeusia subjects affected / exposed occurrences (all)	2 / 34 (5.88%) 3		
Headache subjects affected / exposed occurrences (all)	3 / 34 (8.82%) 3		
Nervous system disorders - Other subjects affected / exposed occurrences (all)	1 / 34 (2.94%) 1		
Paresthesia subjects affected / exposed occurrences (all)	1 / 34 (2.94%) 1		
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	3 / 34 (8.82%) 4		
Tremor subjects affected / exposed occurrences (all)	3 / 34 (8.82%) 3		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	12 / 34 (35.29%) 30		
Febrile neutropenia subjects affected / exposed occurrences (all)	2 / 34 (5.88%) 2		
hemolysis subjects affected / exposed occurrences (all)	1 / 34 (2.94%) 1		
Eye disorders Conjunctivitis subjects affected / exposed occurrences (all)	2 / 34 (5.88%) 2		
Eye disorders			

subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
Watering eyes			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	7 / 34 (20.59%)		
occurrences (all)	11		
Bloating			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
Constipation			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	8		
Diarrhea			
subjects affected / exposed	15 / 34 (44.12%)		
occurrences (all)	28		
Dyspepsia			
subjects affected / exposed	5 / 34 (14.71%)		
occurrences (all)	5		
Dysphagia			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Flatulence			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Gastrointestinal disorder			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Mucositis oral			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	4		

Nausea			
subjects affected / exposed	12 / 34 (35.29%)		
occurrences (all)	19		
Oral pain			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	3		
Stomach pain			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	5 / 34 (14.71%)		
occurrences (all)	7		
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	12 / 34 (35.29%)		
occurrences (all)	13		
Erythema multiforme			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Periorbital edema			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
Pruritus			
subjects affected / exposed	4 / 34 (11.76%)		
occurrences (all)	4		
Rash acneiform			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Rash maculo-papular			
subjects affected / exposed	9 / 34 (26.47%)		
occurrences (all)	12		
Skin and subcutaneous tissue disorders - Other			
subjects affected / exposed	9 / 34 (26.47%)		
occurrences (all)	21		
Urticaria			

subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	2		
Renal and urinary disorders			
Cystitis noninfective			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Hematuria			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Renal and urinary disorders - Other			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Urinary frequency			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	2		
Urinary tract pain			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
Endocrine disorders			
Cushingoid			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	5 / 34 (14.71%)		
occurrences (all)	8		
Bone pain			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
Joint range of motion decreased			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorder - Other			

subjects affected / exposed	9 / 34 (26.47%)		
occurrences (all)	10		
Myalgia			
subjects affected / exposed	7 / 34 (20.59%)		
occurrences (all)	11		
Neck pain			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	4		
Osteonecrosis of jaw			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Osteoporosis			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Infections and infestations			
Bladder infection			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Bronchial infection			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Device related infection			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
Infections and infestation-Other			
subjects affected / exposed	11 / 34 (32.35%)		
occurrences (all)	18		
Papulopustular rash			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	2		
Rash pustular			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	2		

Skin infection			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	4		
Sepsis			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Upper respiratory infection			
subjects affected / exposed	14 / 34 (41.18%)		
occurrences (all)	21		
Urinary tract infection			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	4		
Hyperkalemia			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	3		
Hypermagnesemia			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	6		
Hypernatremia			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	3		
Hypoalbuminemia			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	8		
Hypocalcemia			
subjects affected / exposed	7 / 34 (20.59%)		
occurrences (all)	14		
Hypokalemia			
subjects affected / exposed	4 / 34 (11.76%)		
occurrences (all)	13		
Hypomagnesemia			

subjects affected / exposed	5 / 34 (14.71%)		
occurrences (all)	13		
Hyponatremia			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	5		
Metabolism and nutrition disorders - Other			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	7		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 April 2011	Updated Sponsor contact details; clarification of eligibility, screening, registration period and tests; sibling donor amended to related donor; clarification of use of dexamethasone and ciclosporin; sampling times for immune reconstitution amended; clarification of pregnancy risk management procedure; addition of consent procedure for donors; reclassification of transplant drugs to NIMPs and amendment to SAE reporting timeline and procedure; addition of current NIMP profiles; biochemistry requirements clarified; sample collection procedure for sub-study clarified; other minor corrections
01 March 2012	Updated contact details to include trial statistician; updated trial synopsis in line with the rest of the protocol such as included outcome measures, screening, consent and AE reporting requirements; clarification of secondary outcome measures; clarification of CR1/2 and VGPR1/2 in the inclusion criteria; clarification of pregnancy risk management procedure; clarification on screening procedure, specifically which tests are mandatory; amendment to the timings for obtaining informed consent and consent procedure; amended the Lenalidomide labelling section in line with new labelling; amended the side effects associated with Lenalidomide in line with the IB; amended the AE, GVHD and conmed monitoring period; included guidance on dose modifications in response to GVHD; added in pre-Lenalidomide assessments for consistency and modified follow-up assessments/efficacy assessments, specifically the frequency of blood tests and amended the schedule of events accordingly; amended the SAE reporting period and the requirement to report SPM as an SAE until 3 years post-transplant; modified the treatment discontinuation section to include guidance on GVHD; revised the statistics section following guidance from trial statistician; other minor corrections.
07 May 2013	Updated secondary outcome measures, addition of exploratory outcome measure, amendment to starting dose of lenalidomide, clarification of follow up schedule, clarification of trial entry criteria, clarification of dose modification criteria for episodes of GvHD
19 November 2013	Changes to reference safety information and clarification of the statistical analysis. Addition of eligibility and follow-up for non-secretory myeloma patients.

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.

None reported

Notes: