Clinical trial results:
THE EFFICACY AND SAFETY OF LENALIDOMIDE (Revlimid®) MONOTHERAPY IN RED BLOOD CELL TRANSFUSION DEPENDENT SUBJECTS WITH MYELODYSPLASTIC SYNDROME ASSOCIATED WITH A DEL (5q) CYTOGENETIC ABNORMALITY

Summary

EudraCT number	2004-005101-29
Trial protocol	GB
Global end of trial date	23 May 2016

Results information

Result version number	v1 (current)
This version publication date	21 September 2019
First version publication date	21 September 2019
Summary attachment (see zip file)	RESULTS SUMMARY (revlimid results summary.pdf)

Trial information

Trial identification

Sponsor protocol code	KCH-MDS-04-1.0

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00874978
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	King's College Hospital
Sponsor organisation address	Denmark Hill , London, United Kingdom, SE5 9RS
Public contact	Professor Ghulam Mufti, King's College Hospital NHS Foundation Trust, 0044 0203299 3080, ghulam.mufti@kcl.ac.uk
Scientific contact	Professor Ghulam Mufti, King's College Hospital NHS Foundation Trust, 0044 0203299 3080, ghulam.mufti@kcl.ac.uk
Sponsor organisation name	King's College London
Sponsor organisation address	Strand, London, United Kingdom, WC2R 2LS
Public contact	Professor Ghulam Mufti, King's College London, 0044 02032993080, ghulam.mufti@kcl.ac.uk
Scientific contact	Professor Ghulam Mufti, King's College London, 0044 02032993080, 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	23 May 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 May 2016
Global end of trial reached?	Yes
Global end of trial date	23 May 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of lenalidomide treatments to achieve haematopoietic improvement in subjects with low- or intermediate-1 risk International Prognostic Scoring System1 (IPSS) myelodysplastic syndrome (MDS) associated with a del 5q cytogenetic abnormality
To evaluate the efficacy of lenalidomide to achieve haematopoietic improvement in patients with isolated del5q with blasts <20%

Protection of trial subjects:

Forty eight (48) subjects with a diagnosis of low- or intermediate-1 risk MDS associated with a del 5(q) cytogenetic abnormality or isolated del5(q) patients with up to 20% blasts, who are RBC transfusion-dependent and meet all the eligibility criteria will be enrolled into the study

Background therapy:

None

Evidence for comparator:

Not applicable

Actual start date of recruitment	03 January 2005
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: 44
Worldwide total number of subjects	44
EEA total number of subjects	44

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)	23
From 65 to 84 years	21
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited from one clinical site in the UK betweek 2005 and 2016

Pre-assignment

Screening details:

Aged 18 or over with diagnosis of low- or intermediate-1-risk (IPSS) MDS with a del(5q) cytogenetic abnormality which may be an isolated finding or may be associated with other cytogenetic abnormalities & if del5(q) is an isolated aberration the patient could have up to 20% blasts

Period 1

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

Blinding implementation details:

This study is a single centre, single-arm, open-label study of oral lenalidomide monotherapy administered to red blood cell (RBC) transfusion dependent subjects with IPSS low- or intermediate-1 risk MDS associated with a del5(q) cytogenetic abnormality and also in patients with isolated del5q with blasts <20%.

Arms

Arm title	Overall Trial

Arm description: -

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

Dosage and administration details:

Oral lenalidomide 10mg (two 5mg capsules) daily on Days 1-21 every 28 days for up to 12 cycles or until bone marrow disease progression or progression/relapse following erythroid haematologic improvement (Appendix 2). At the end of 12 cycles, if there is erythroid haematologic improvement, subjects will receive further cycles until bone marrow disease progression or progression/relapse.

Number of subjects in period 1	Overall Trial
Started	44
Completed	36
Not completed	8
Adverse event, serious fatal	8

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	44	44	
Age categorical Units: Subjects			
Adults (18-70 years)	25	25	
Adults (71-80years)	15	15	
81 years and over	4	4	
Gender categorical Units: Subjects			
Female	29	29	
Male	15	15	

End points

End points reporting groups

Reporting group title	Overall Trial

Reporting group description: -

Primary: Primary

End point title	Primary[1]

End point description:

To evaluate the efficacy of lenalidomide treatments to achieve haematopoietic improvement in subjects with low- or intermediate-1 risk International Prognostic Scoring System[1] (IPSS) myelodysplastic syndrome (MDS) associated with a del 5(q) cytogenetic abnormality.
To evaluate the efficacy of lenalidomide to achieve haematopoietic improvement in patients with isolated del5q with blasts <20%

End point type	Primary

End point timeframe:

During 12 cycles of treatment (12 months). Each cycle lasts 28 days.

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 document.

End point values	Overall Trial			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: Whole	36			

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary

End point title	Secondary

End point description:

End point type	Secondary

End point timeframe:

Through 12 cycles of treatment with Revlimid. (each cycle lasting 28 days).

End point values	Overall Trial			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: Whole	36			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

30 days + 2 days after last IMP dose

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Overall Trial

Reporting group description: -

Serious adverse events	Overall Trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 44 (40.91%)		
number of deaths (all causes)	8		
number of deaths resulting from adverse events	8		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma hand			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Irreguglar pulse requiring pacemaker			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Myopericarditis			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Neutropenia			
subjects affected / exposed	3 / 44 (6.82%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Neutropenic sepsis			
subjects affected / exposed	3 / 44 (6.82%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
MDS disease progression			
subjects affected / exposed	2 / 44 (4.55%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Anaemia			
subjects affected / exposed	2 / 44 (4.55%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fall			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lower back pain			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Loss of appetite			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Left knee pain			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Traumatic intracranial haemorrhage			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Gastrointestinal disorders			
Diverticulitis			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal Pain			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Peri-anal abcess			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary Embolis			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bilateral pleural effesions			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	3 / 44 (6.82%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 2		

Chest Infection				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	2 / 44 (4.55%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Infective exacerbation of COPD				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chest sepsis				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lung infection				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Skin rash				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Scrotal swelling				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Localised infection & disease progression				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Sepsis - (Stenotrophomonas maltropilila)			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Finger infetion			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Loclised infection of hand and elbow			
subjects affected / exposed	1 / 44 (2.27%)		
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	Overall Trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 44 (84.09%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 44 (4.55%)		
occurrences (all)	3		
Cardiac disorders			
Heart failure			
subjects affected / exposed	4 / 44 (9.09%)		
occurrences (all)	6		
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 44 (4.55%)		
occurrences (all)	6		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	13 / 44 (29.55%)		
occurrences (all)	15		
Headache			

subjects affected / exposed	2 / 44 (4.55%)		
occurrences (all)	6		
Eye disorders			
Eye infection			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences (all)	1		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	5 / 44 (11.36%)		
occurrences (all)	6		
Diarrhoea			
subjects affected / exposed	16 / 44 (36.36%)		
occurrences (all)	30		
Constipation			
subjects affected / exposed	8 / 44 (18.18%)		
occurrences (all)	11		
Abdominal pain			
subjects affected / exposed	6 / 44 (13.64%)		
occurrences (all)	7		
Vomiting			
subjects affected / exposed	5 / 44 (11.36%)		
occurrences (all)	5		
Dental Infection			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences (all)	1		
Mucositis oral			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Chest infection			
subjects affected / exposed	5 / 44 (11.36%)		
occurrences (all)	14		
Upper respiratory tract infection			
subjects affected / exposed	17 / 44 (38.64%)		
occurrences (all)	24		
Shortness of breath			

subjects affected / exposed	5 / 44 (11.36%)		
occurrences (all)	7		
Epistaxis			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences (all)	3		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	20 / 44 (45.45%)		
occurrences (all)	35		
Dry skin			
subjects affected / exposed	8 / 44 (18.18%)		
occurrences (all)	11		
Cellulitis			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences (all)	2		
Renal and urinary disorders			
Urine infection			
subjects affected / exposed	3 / 44 (6.82%)		
occurrences (all)	4		
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	2 / 44 (4.55%)		
occurrences (all)	5		
Neck pain			
subjects affected / exposed	3 / 44 (6.82%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 April 2010	1) Clarification of co-sponsor arrangements between King's College Hospital NHS Foundation Trust and King's College London . 2) The investigational medicinal product, lenalidomide, supply beyond the 12 month study phase until patients show disease progression, toxicity or a decline in response. 3) The sensitivity and time points for conducting the pregnancy tests and the birth control section altered in line with Celgene's most recent Pregnancy Prevention Programme for Investigator Initiated Trials in the European Union. 4) Follow up for patients who discontinue from study drug clarified in the protocol. 5) Change of Revlimid status from unlicensed product to confirmation of market authorisation.
19 September 2012	1) Change to the inclusion criteria to include patients with MDS and isolated del5q with blasts <20%. 2) Changes to the primary and secondary endpoints and study design in relation to the inclusion of patients with isolated del5q with blasts <20%. 3) Change in sample size from 36 to 48 patients The protocol has been updated to reflect the changes mentioned above with further administrative changes. The administrative changes include an update to the protocol appendix 4 Pregnancy Testing Guidelines and Acceptable Birth Control Methods, change in department name from Joint Clinical Trials Office to King's Health Partners Clinical Trials Office and change in the address for Celgene.
29 July 2013	1) Change in the packaging of the IMP from bottled supply to blister pack 2) Change in the site where QP certified batch release

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported