Clinical trial results:
A comparison of plerixafor/G-CSF with chemotherapy/G-CSF for stem cell transplantation

Summary

EudraCT number	2009-013798-16
Trial protocol	GB
Global end of trial date	12 September 2013

Results information

Result version number	v1 (current)
This version publication date	25 July 2020
First version publication date	25 July 2020
Summary attachment (see zip file)	phantastic publication (bcj201479a.pdf)

Trial information

Trial identification

Sponsor protocol code	3809

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Royal Liverpool & Broadgreen University Hospitals NHS Trust
Sponsor organisation address	Prescot St, Liverpool, United Kingdom, L7 8XP
Public contact	Research Governance Manager, RD&I Royal Liverpool Hospital Prescot St Liverpool, 044 151 706 3702, RGT@rlbuht.nhs.uk
Scientific contact	Research Governance Manager, RD&I Royal Liverpool Hospital Prescot St Liverpool, 044 151 706 3702, RGT@rlbuht.nhs.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	12 September 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 September 2013
Global end of trial reached?	Yes
Global end of trial date	12 September 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Using plerixafor plus granulocyte-colony stimulating factor (G-CSF), is the yield of stem (CD34+) cells at least as good as can be obtained with conventional chemotherapy plus G-CSF?, and can this be accomplished in the same or fewer stem cell collections (known as aphereses)?

Stated more formally, the primary study endpoint is a composite of BOTH an adequate stem cell harvest (at least 4 x 10 E6 CD34+ cells per kg body weight in no more than 2 aphereses) AND a neutrophil count that never falls below 1.0 x 10 E9 / Litre in the 3 weeks following initiation of mobilisation.

Protection of trial subjects:

This study was a reduction in SoC medication. Patients were reviewed regularly for remission.

Background therapy:

The daily dose of G-CSF is the same as used at the Royal Liverpool University Hospital (RLUH) for some years in chemotherapy containing stem cell mobilisation; 300 ug for patients weighing 60kg or less; 480 ug for patients over 60 kg but under 96 kg, and 600 ug for patients weighing 96 kg or more. This equates to a dose of at least 5 ug/kg (maximum 8 mg/kg) for all patients up to 120 kg. The daily dose of plerixafor is 240 ug/kg if the creatinine clearance is equal to or greater than 50mls/minute; if less than this then the dose is 160 ug/kg daily.

Evidence for comparator:

Comparison will be made to an immediately preceding cohort of 200 eligible patients who were mobilised with chemotherapy plus G-CSF. This comparator population is suitable, since the case mix, G-CSF dose for harvesting and the transplant conditioning have not changed during the past few years nor are seen as likely to change during the course of the study

Actual start date of recruitment	01 May 2010
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: 249
Worldwide total number of subjects	249
EEA total number of subjects	249

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	240
From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

patients recruited between 01/05/2010-01/05/2012
plerixafor plus G-CSF as a mobilisation regime in 100 consecutive myeloma and lymphoma patients undergoing stem cell harvesting. Comparison will be made to an immediately preceding consecutive cohort of 200 myeloma and lymphoma patients mobilised with chemotherapy plus G-CSF.

Pre-assignment

Screening details:

101 participants, 98 completed, 1 screen failure and 2 not made to mobilisation

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	interventional arm

Arm description:

100 patients treated with plerixafor and G-CSF

Arm type	Experimental
Investigational medicinal product name	Plerixafor
Investigational medicinal product code	L 03 AX 16
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

The dose of plerixafor is 240 ug/kg daily if the creatinine clearance is equal to or greater than 50mls/minute; if less than this then the dose is 160 ug/kg daily.

Arm title	retrospective standard of care

Arm description:

patients treated with standard of care chemotherapy G-CSF

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	interventional arm	retrospective standard of care
Started	98	151
Completed	98	151

Baseline characteristics

Reporting groups	
Reporting group title	overall trial
Reporting group description:	
interventional	

Reporting group values	overall trial	Total	
Number of subjects	249	249	
Age categorical			
98 interventional and 151 retrospective comparrators			
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)	240	240	
From 65-84 years	9	9	
85 years and over	0	0	
Age continuous			
Units: years			
median	56		
full range (min-max)	20 to 68	-	
Gender categorical			
Units: Subjects			
Female	97	97	
Male	152	152	

Subject analysis sets	
Subject analysis set title	Full set
Subject analysis set type	Per protocol
Subject analysis set description:	
achieved primary endpoint	

Reporting group values	Full set		
Number of subjects	249		
Age categorical			
98 interventional and 151 retrospective comparrators			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			

Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years median full range (min-max)			
Gender categorical Units: Subjects			
Female	151		
Male	152		

End points

End points reporting groups

Reporting group title	interventional arm
Reporting group description:	
100 patients treated with plerixafor and G-CSF	
Reporting group title	retrospective standard of care
Reporting group description:	
patients treated with standard of care chemotherapy G-CSF	
Subject analysis set title	Full set
Subject analysis set type	Per protocol
Subject analysis set description:	
achieved primary endpoint	

Primary: composite primary end point

End point title	composite primary end point
End point description:	
composite of BOTH an adequate stem cell harvest (at least 4 x 106 CD34+ cells per kg body weight in no more than 2 aphereses) AND a neutrophil count that never falls below 1.0 x 109 / Litre in the 3 weeks following initiation of mobilisation.	
End point type	Primary
End point timeframe:	
during 3 weeks post mobilisation	

End point values	interventional arm	retrospective standard of care	Full set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	98	151	249	
Units: cells				
number (not applicable)				
adequate stem cell harvest	70	111	181	
neutrophil count does not fall below 1.0x109/litre	98	84	182	

Statistical analyses

Statistical analysis title	descriptive
Statistical analysis description:	
descriptive stats	
Comparison groups	retrospective standard of care v interventional arm

Number of subjects included in analysis	249
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	> 0.05 [2]
Method	Wilcoxon (Mann-Whitney)

Notes:

[1] - descriptive sats

[2] - descriptive stats

Adverse events

Adverse events information

Timeframe for reporting adverse events:

3 months post mobilisation

Adverse event reporting additional description:

assessed daily during in patient phase then at 3 month follow-up or unscheduled admission

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	intervention

Reporting group description: -

Reporting group title	retrospective standard of care

Reporting group description: -

Serious adverse events	intervention	retrospective standard of care	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 98 (1.02%)	18 / 151 (11.92%)	
number of deaths (all causes)	1	3	
number of deaths resulting from adverse events	1	3	
Blood and lymphatic system disorders			
Neutropenic sepsis			
subjects affected / exposed	0 / 98 (0.00%)	10 / 151 (6.62%)	
occurrences causally related to treatment / all	0 / 0	10 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vena cava embolism			
subjects affected / exposed	0 / 98 (0.00%)	1 / 151 (0.66%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage	Additional description: femoral vein		
subjects affected / exposed	0 / 98 (0.00%)	1 / 151 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphoma	Additional description: progressive lymphoma - disease progression not related to imp		

subjects affected / exposed	1 / 98 (1.02%)	3 / 151 (1.99%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	1 / 1	3 / 3	
Infections and infestations			
Sepsis	Additional description: non neutropenic		
subjects affected / exposed	0 / 98 (0.00%)	3 / 151 (1.99%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	intervention	retrospective standard of care	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 98 (11.22%)	11 / 151 (7.28%)	
Gastrointestinal disorders			
Gastrointestinal disorder	Additional description: These are associated with citrate anticoagulant used in Leukopharesis		
subjects affected / exposed	11 / 98 (11.22%)	11 / 151 (7.28%)	
occurrences (all)	11	11	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 November 2011	increase in sample size

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.

Assessment of non serious adverse events is complicated by the fact that many patients undergoing leukapheresis report symptoms attributable to the toxicity of the citrate anticoagulant 11 had gastro intestinal symptoms, headache and insomnia

Notes: