Clinical trial results:
A PHASE II STUDY EVALUATING INTRAVENOUS MELPHALAN WITH AUTOLOGOUS WHOLE BLOOD STEM CELL TRANSPLANTATION (PBSCT) OVER THREE CYCLES IN PATIENTS WITH CASTRATION-RESISTANT PROSTATE CANCER

Summary

EudraCT number	2012-000351-14
Trial protocol	GB
Global end of trial date	22 December 2016

Results information

Result version number	v1 (current)
This version publication date	20 December 2017
First version publication date	20 December 2017

Trial information

Trial identification

Sponsor protocol code	PR201206

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01907009
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Barts Health NHS Trust
Sponsor organisation address	5 Walden Street, London, United Kingdom, E1 2EF
Public contact	Jonathan Shamash, Barts Health NHS Trust, +44 0207 882 8761, bci-melcap@qmul.ac.uk
Scientific contact	Jonathan Shamash, Barts Health NHS Trust, +44 0207 882 8761, bci-melcap@qmul.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 December 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 December 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To determine the efficacy of intensified intravenous melphalan with autologous whole blood stem cell transplantation in patients with castration-resistant prostate cancer using Progression Free Survival rate

Protection of trial subjects:

Patients were closely monitored as part of the clinical trial. Side effects were closely measured, and blood tests were taken before any administration of melphalan to ensure patient suitability to continue on the trial. As neutropenia was a known risk, bloods were taken every 24-48 hours if neutrophils were low to ensure close monitoring.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2012
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: 29
Worldwide total number of subjects	29
EEA total number of subjects	29

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)	13
From 65 to 84 years	16
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between January 2013 and December 2016, 29 patients were recruited to the MELCAP trial. This was a single site study, being carried out at Barts Health NHS Trust.

Pre-assignment

Screening details:

No patients failed the screening period, with all 29 patients entering the trial.

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

Arm title	Lenograstim plus melphalan

Arm description:

intervention arm (single)

Arm type	Experimental
Investigational medicinal product name	Lenograstim
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Lenograstim will be administered over a period of 3 cycles (14 days per cycle).

Cycle 1:
Day -4 to -2 and Day 7-12: 10mcg/kg /day

Cycle 2:
Day 7-12 Lenograstim 10mcg/kg/day

Cycle 3:
Day 1-10 Lenograstim 263mcg/day

Investigational medicinal product name	Melphalan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for injection
Routes of administration	Intravenous use

Dosage and administration details:

Melphalan is given on Day-1 of each cycle for three cycles. Each cycle is 14 days.
The doses given were 60 mg/m2 over 15 minutes in cycle 1 and 40 mg/m2 over 15 minutes in cycle 2 and cycle 3.

Number of subjects in period 1	Lenograstim plus melphalan
Started	29
Completed	29

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	29	29	
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)	13	13	
From 65-84 years	16	16	
85 years and over	0	0	
Age continuous Units: years			
median	65		
full range (min-max)	50 to 81	-	
Gender categorical Units: Subjects			
Female	0	0	
Male	29	29	

End points

End points reporting groups

Reporting group title	Lenograstim plus melphalan
Reporting group description: intervention arm (single)	

Primary: Radiological and / symptomatic progression free survival (PFS) rate at 6-months

End point title	Radiological and / symptomatic progression free survival (PFS) rate at 6-months[1]
End point description: This analysis was not carried out due to early termination of the trial.	
End point type	Primary
End point timeframe: PFS rate at 6 months	

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: This trial terminated early prior to the full number of 39 patients being recruited. No statistical analysis has been carried out.

End point values	Lenograstim plus melphalan			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: months				
median (confidence interval 95%)	(to)			

Notes:

[2] - Primary endpoint analysis was not carried out as the trial was terminated early.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Entire trial	
Adverse event reporting additional description:	
Only treatment-related Grade 3 and above non serious AEs are reported here	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	CTC
Dictionary version	4.02

Reporting groups	
Reporting group title	Lenograstim plus melphalan
Reporting group description:	
intervention arm (single)	

Serious adverse events	Lenograstim plus melphalan		
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 29 (65.52%)		
number of deaths (all causes)	12		
number of deaths resulting from adverse events			
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebellar infarction			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	1 / 1		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	12 / 29 (41.38%)		
occurrences causally related to treatment / all	17 / 19		
deaths causally related to treatment / all	1 / 1		
Hypocalcaemia			

subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 29 (10.34%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
orbital cellulitis			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Rectal haemorrhage			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting	Additional description: Diarrhoea and fever also		
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Mucositis			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			

subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Lenograstim plus melphalan		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 29 (93.10%)		
Vascular disorders			
lymphedema			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
anemia			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	4		
Neutrophil count decreased			
subjects affected / exposed	21 / 29 (72.41%)		
occurrences (all)	45		
Febrile neutropenia			
subjects affected / exposed	3 / 29 (10.34%)		
occurrences (all)	4		
Hypokalaemia			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	2		
Hyperkalaemia			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Haematuria			

subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
White blood cell count abnormal			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Platelet count decreased			
subjects affected / exposed	22 / 29 (75.86%)		
occurrences (all)	49		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	5 / 29 (17.24%)		
occurrences (all)	7		
chest pain			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
hip pain			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	2		
oral mucositis			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences (all)	1		
Infections and infestations			
Infection toxicity			
subjects affected / exposed	12 / 29 (41.38%)		
occurrences (all)	17		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 August 2012	Responses to conditions listed in conditional approval from REC and changes following non-acceptance from MHRA. Includes separating the two PIS for patients who have received Docetaxel and those who are Docetaxel naive. Other administrative changes.
15 October 2012	Changes requested by MHRA to contraindications in exclusion criteria based on SmPCs.
29 January 2013	Change in eligibility criteria to allow patients who had been in a hormone or steroid clinical trials within previous 30 days to enter.
29 October 2013	Changes to dosing of lenograstim and introduction of dose rounding document to help pharmacists dispense correct dose; introduction of patient diary card.
26 October 2015	Clarification for the exempt concomitant medications and how to record them. Clarification on the end of trial definition. Name change of sponsor's representative to Barts Health NHS Trust. Clarification on exempt SAEs. The end of trial date has been extended 01/09/2019 to complete the overall accrual for the trial.
22 July 2016	Temporary halt to recruitment following licensing issue for autologous blood transfusions held by Barts Health NHS Trust.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
22 July 2016	A halt to recruitment was submitted on the 22nd July 2016 due to Barts Health NHS Trust not holding the correct license for autologous blood transfusions. This was followed with an early termination of the trial submitted on the 8th December 2016.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

No endpoint analyses are included in these results due to early termination of this trial. Adverse events are reported for data collected until the date of early termination.

Notes: