Clinical trial results:
To assess the safety of continuous IV administration of the CXCR4 antagonist, plerixafor (Mozobil), at potentially active plasma concentrations and assess its impact on the immune microenvironment in patients with advanced pancreatic, high grade serous ovarian and colorectal adenocarcinomas

Summary

EudraCT number	2014-000117-31
Trial protocol	GB
Global end of trial date	12 December 2019

Results information

Result version number	v1 (current)
This version publication date	01 January 2020
First version publication date	01 January 2020

Trial information

Trial identification

Sponsor protocol code	CAM-PLEX (A093446)

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02179970
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Cambridge University Hospitals NHS Trust and the University of Cambridge
Sponsor organisation address	Hills Road, Cambridge, United Kingdom, CB2 0QQ
Public contact	Mrs Carrie Bayliss, Cambridge University Hospitals NHS Trust and the University of Cambridge, cctu@addenbrookes.nhs.uk
Scientific contact	Professor Duncan Jodrell, CRUK Cambridge Institute, University of Cambridge, duncan.jodrell@cruk.cam.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	12 December 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 December 2018
Global end of trial reached?	Yes
Global end of trial date	12 December 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Primary Objective
To assess safety of continuous IV administration of plerixafor in doses needed to achieve and maintain circulating levels similar to those active in a murine model of PDAC (2 µg/ml)

Secondary Objective
To explore objective anticancer clinical impact of this strategy.

Protection of trial subjects:

The study was approved by a Research Ethics Committee and received authorisation from the medicine and Healthcare Product Regulatory Authority. Patients received verbal and written information prior to consenting to the trial, and had time to consider their participation and opportunity to ask questions. Consenting patients had as series of screening test and to ensure they were suitable for the study and it was safe to proceed. On registration to the trial the participants were allocated a unique reference number that was to be used on all data and samples sent to the sponsor which allowed their personal data remain anonymous. Only the participants direct care team had access to their recruited participants personal data during the trial. Any patient information that was sent such a laboratory reports to confirm eligibility, which were sent to the coordinating center were anonymised and annotated with the trial reference number.

Background therapy: -

Evidence for comparator:

N/A

Actual start date of recruitment	05 January 2015
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 States: 2
Country: Number of subjects enrolled	United Kingdom: 24
Worldwide total number of subjects	26
EEA total number of subjects	24

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)	9
From 65 to 84 years	17
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The sample size for the trial was up to 28 patients who were to complete 7 days of treatment with Plerixafor. initially up to 18 patients were to be enrolled into the dose escalation phase, followed by a further 10 patients into the expansion phase of the trial. 26 participants were enrolled into the trial across 2 centres internationally.

Pre-assignment

Screening details:

34 patients were consented and assessed for eligibility. 18 patients were enrolled into the dose escalation phase of the trial and 8 enrolled into the treatment expansion phase. 8 patients were found not to meet the eligibility criteria, during the screening period.

Pre-assignment period milestones

Number of subjects started	34[1]
Number of subjects completed	26

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Non-eligibility: 8

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same. Justification: 34 patients were consented and assessed for eligibility, 8 patients were found not to meet the eligibility criteria, during the screening period.

Period 1

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

Blinding implementation details:

N/A

Arms

Are arms mutually exclusive?	Yes
Arm title	Dose level 20 ug/kg/hr

Arm description:

Patient with inoperable, histologically proven locally advanced or metastatic pancreatic, high grade serous ovarian or colorectal adenocarcinoma, refractory to conventional chemotherapy or a patient who has declined conventional chemotherapy were enrolled into the dose escalation phase. Three (3) patients were to be entered into the trial sequentially per dose level using the standard 3+3 phase l trial design. The dose levels for the dose escalation phase started at 20 ug/kg/hr. The dose was to be escalated to the next sequential dose level (40, 80 or 120 µg/kg/hr) only after 3 patients completed the previous dose level, in the absence of a dose limiting toxicity (DLT) and as long as the primary objective had not been reached. All 3 patients completed the Day 28 follow-up visit for the dose level and there were no safety issues

Arm type	Experimental
Investigational medicinal product name	plerixafor
Investigational medicinal product code	GZ316455
Other name	Mozobil (AMD3100)
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Plerixafor was to be given as a continuous 7 day IV infusion, starting at a dose of 20 ug/kg/hr. Plerixafor given as a continuous 7 day IV infusion, at a dose of 20 ug/kg/hr (as an inpatient for at least the initial

72 hours)..

Arm title	Dose level 40 ug/kg/hr

Arm description:

Dose escalation level 2.

Arm type	Experimental
Investigational medicinal product name	plerixafor
Investigational medicinal product code	GZ316455
Other name	Mozobil (AMD3100)
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Plerixafor was to be given as a continuous 7 day IV infusion, starting at a dose of 40 ug/kg/hr. Plerixafor given as a continuous 7 day IV infusion, at a dose of 40 ug/kg/hr (as an inpatient for at least the initial 72 hours).

Arm title	Dose level 80 ug/kg/hr

Arm description:

Dose escalation level 3

During the treatment expansion phase patients with inoperable, histologically proven locally advanced or metastatic pancreatic, refractory to conventional chemotherapy or a patient who has declined conventional chemotherapy were enrolled in the treatment expansion phase of the trial up to 10 patients in total at this dose level which was evaluated at the RP2D determined in the dose escalation phase.

Arm type	Experimental
Investigational medicinal product name	plerixafor
Investigational medicinal product code	GZ316455
Other name	Mozobil (AMD3100)
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Plerixafor was to be given as a continuous 7 day IV infusion, starting at a dose of 80 ug/kg/hr. Plerixafor given as a continuous 7 day IV infusion, at a dose of 80 ug/kg/hr (as an inpatient for at least the initial 72 hours).

Arm title	Dose level 120 ug/kg/hr

Arm description:

Dose escalation level 4

Arm type	Experimental
Investigational medicinal product name	plerixafor
Investigational medicinal product code	GZ316455
Other name	Mozobil (AMD3100)
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Plerixafor was to be given as a continuous 7 day IV infusion, starting at a dose of 120 ug/kg/hr. Plerixafor given as a continuous 7 day IV infusion, at a dose of 120 ug/kg/hr (as an inpatient for at least the initial 72 hours).

Number of subjects in period 1	Dose level 20 ug/kg/hr	Dose level 40 ug/kg/hr	Dose level 80 ug/kg/hr
Started	3	5	11
Completed	3	3	10
Not completed	0	2	1
Adverse event, non-fatal	-	2	1

Number of subjects in period 1	Dose level 120 ug/kg/hr
Started	7
Completed	6
Not completed	1
Adverse event, non-fatal	1

Baseline characteristics

Reporting groups	
Reporting group title	On Study

Reporting group description: -

Reporting group values	On Study	Total	
Number of subjects	26	26	
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)	9	9	
From 65-84 years	17	17	
85 years and over	0	0	
Age continuous Units: years			
median	66.2		
full range (min-max)	49.7 to 75.9	-	
Gender categorical Units: Subjects			
Female	9	9	
Male	17	17	
Site of Primary Cancer Units: Subjects			
Colorectal Adenocarcinoma	15	15	
Ovarian Adenocarcinoma	0	0	
Pancreatic Ductal Adenocarcinoma (PDAC)	11	11	

End points

End points reporting groups

Reporting group title	Dose level 20 ug/kg/hr

Reporting group description:

Patient with inoperable, histologically proven locally advanced or metastatic pancreatic, high grade serous ovarian or colorectal adenocarcinoma, refractory to conventional chemotherapy or a patient who has declined conventional chemotherapy were enrolled into the dose escalation phase. Three (3) patients were to be entered into the trial sequentially per dose level using the standard 3+3 phase l trial design. The dose levels for the dose escalation phase started at 20 ug/kg/hr. The dose was to be escalated to the next sequential dose level (40, 80 or 120 µg/kg/hr) only after 3 patients completed the previous dose level, in the absence of a dose limiting toxicity (DLT) and as long as the primary objective had not been reached. All 3 patients completed the Day 28 follow-up visit for the dose level and there were no safety issues

Reporting group title	Dose level 40 ug/kg/hr

Reporting group description:

Dose escalation level 2.

Reporting group title	Dose level 80 ug/kg/hr

Reporting group description:

Dose escalation level 3

During the treatment expansion phase patients with inoperable, histologically proven locally advanced or metastatic pancreatic, refractory to conventional chemotherapy or a patient who has declined conventional chemotherapy were enrolled in the treatment expansion phase of the trial up to 10 patients in total at this dose level which was evaluated at the RP2D determined in the dose escalation phase.

Reporting group title	Dose level 120 ug/kg/hr

Reporting group description:

Dose escalation level 4

Primary: Safety and tolerability

End point title	Safety and tolerability[1]

End point description:

Grading according to NCI CTCAE v. 4.03

End point type	Primary

End point timeframe:

Adverse events were reported from informed consent and throughout treatment and follow up to resolution.

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 statistical analyses to compare between the groups have been performed as this end point is not powered to compare the different dose levels. No DLTs were reported in the first 3 dose levels of the dose escalation phase. At the highest dose level (120µg/kg/hr), 2 DLTs were recorded. Therefore, the previous dose level (80µg/kg/hr) was selected for the expansion phase, recruiting patients with pancreatic adenocarcinomas only. Therefore, the first primary endpoint was achieved.

End point values	Dose level 20 ug/kg/hr	Dose level 40 ug/kg/hr	Dose level 80 ug/kg/hr	Dose level 120 ug/kg/hr
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[2]	4[3]	11[4]	7[5]
Units: total number				
number (not applicable)				
Number of grade 3 and above Adverse events	0	2	12	13

Number of grade 1-2 Adverse events reported	40	60	213	172

Notes:

[2] - Out of the Grade 1-2 Adverse Events reported, 3 events were adverse events of special interest

[3] - 1 patient did not receive IMP; 3 G+, and 5 G1-2 AEs reported; 3 events were AESIs

[4] - Out of the Grade 1-2 Adverse Events reported, 21 events were AESI

[5] - Out of the Grade 3 and above AEs reported, 2 events were DLTs and 13 of the grade 1-2 were AESIs

Statistical analyses

No statistical analyses for this end point

Primary: Css - PK concentration

End point title	Css - PK concentration[6]

End point description:

Measurement of plerixafor concentration in plasma at 3 time points (days 2, 4 and 8), during the continuous i.v. infusion.

End point type	Primary

End point timeframe:

The plasma pharmacokinetics of plerixafor in patients with cancer. Css ≥2 µg/ml should be achieved in ≥80% of patients treated at the RP2D. PKs assessed on research blood samples collected during treatment on day 2, day 4, day 8 and day 13-17.

Notes:

[6] - 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 statistical analyses for this end point as this was a laboratory analyses related endpoint that determined the concentration of the drug. This did not meet the second primary endpoint (≥80% of patients achieving a plasma concentration of >2µg/ml), but emerging pharmacodynamic data suggested no incremental dose response above 40µg/kg/hr.

End point values	Dose level 20 ug/kg/hr	Dose level 40 ug/kg/hr	Dose level 80 ug/kg/hr	Dose level 120 ug/kg/hr
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4[7]	10[8]	4[9]
Units: microgram(s)				
arithmetic mean (standard deviation)				
Concentration a Day 2	0.339 (± 0.0370)	0786 (± 0.176)	1.69 (± 0.507)	2.38 (± 0.364)
Concentration at Day 4	0.499 (± 0.0473)	0.940 (± 0.165)	2.21 (± 0.756)	3.54 (± 1.235)
Concentration at Day 8	0.584 (± 0.0194)	1.015 (± 0.291)	2.28 (± 0.886)	2.99 (± 0.804)

Notes:

[7] - 1 patient was withdrawn on day 7

[8] - 1 patient withdrawn by Day 7; 7/11 (64%) patients achieved a plasma concentration >2µg/ml

[9] - 3 patients withdrawn by day 7; 4 patients achieved a plasma Css >2µg/ml (range 2.38-4.16 µg/ml).

Statistical analyses

No statistical analyses for this end point

Secondary: Objective data on disease status to assess response at Day 28

End point title	Objective data on disease status to assess response at Day 28

End point description:

Contrast enhance CT scan and RECIST 1.1

End point type	Secondary

End point timeframe:

Assessed on day 20-24

End point values	Dose level 20 ug/kg/hr	Dose level 40 ug/kg/hr	Dose level 80 ug/kg/hr	Dose level 120 ug/kg/hr
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4[10]	11	6[11]
Units: Overall response				
number (not applicable)				
Complete reponse	0	0	0	0
Partial reponse	0	0	0	0
Stable disease	2	3	4	5
progressive disease	1	1	7	1

Notes:

[10] - 1 patient did not start treatment therefore not evaluable

[11] - 1 patient withdrawn therefore not evaluable

Statistical analyses

No statistical analyses for this end point

Secondary: Metabolic changes in tumour using FDG-PET

End point title	Metabolic changes in tumour using FDG-PET

End point description:

FDG-PET/CT scans were performed during the screening period and on Day 8, after the core tissue biopsy. Paired PET-CT scans were evaluable in 19 patients (12 escalation phase, 7 expansion phase). Of these, 11 patients had CRC and 8 PDAC). Clinically significant (defined as delta SUV MWA ≥ 30%) changes were seen in 2 patients. Two patients (CRC, 40 µg/kg/hr) had a ≥30% increase in SUV MWA (71% and 32%).

End point type	Secondary

End point timeframe:

Assessment of metabolic changes in tumour using non-invasive imaging (18FDG-PET). An FDG-PET/CT was assessed on day 8 and compare to pre-treatment to generate a delta SUVMWA value (%).

End point values	Dose level 20 ug/kg/hr	Dose level 40 ug/kg/hr	Dose level 80 ug/kg/hr	Dose level 120 ug/kg/hr
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2[12]	3[13]	5[14]	5[15]
Units: percent weight/weight				
number (not applicable)				
≥30% increase in SUVMWA	0	2	0	0
≥30% decrease in SUVMWA	0	0	0	0

Notes:

[12] - Mean Delta SUV -6.7%

[13] - MeanDelta SUVMWA +38.7%

[14] - MeanDelta SUVMWA -3.30%

[15] - MeanDelta SUVMWA -9.70%

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Timeframe for AE

Adverse event reporting additional description:

26 patients had adverse events reported, however 1 patient did not receive any IMP they had 8 events reported, one of which was a serious adverse event.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	All patients

Reporting group description: -

Serious adverse events	All patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 25 (48.00%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Vascular disorders			
Hypertension	Additional description: Hypertension		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thromboembolic event	Additional description: Thromboembolic event		
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Vasovagal reaction	Additional description: Vasovagal reaction		
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		

Blood and lymphatic system disorders			
Anemia	Additional description: Anemia		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain	Additional description: Abdominal pain		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Duodenal obstruction	Additional description: Duodenal obstruction		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastritis	Additional description: Gastritis		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatobiliary disorders - Other, biliary tract obstr	Additional description: Hepatobiliary disorders - Other, biliary tract obstr		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders - Other, obstruction of intr	Additional description: Hepatobiliary disorders - Other, obstruction of intr		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Psychiatric disorders			
Psychiatric disorders - Other, panic attack	Additional description: Psychiatric disorders - Other, panic attack		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Biliary tract infection	Additional description: Biliary tract infection		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection	Additional description: Urinary tract infection		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	All patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 25 (100.00%)		
Vascular disorders			
Flushing	Additional description: Flushing		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Hot flashes	Additional description: Hot flashes		
alternative assessment type: Non-systematic			
subjects affected / exposed	8 / 25 (32.00%)		
occurrences (all)	9		
Hypertension	Additional description: Hypertension		
alternative assessment type: Non-systematic			

subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	3		
Hypotension	Additional description: Hypotension		
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	3		
General disorders and administration site conditions			
Chills	Additional description: Chills		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	2		
Fatigue	Additional description: Fatigue		
alternative assessment type: Non-systematic			
subjects affected / exposed	10 / 25 (40.00%)		
occurrences (all)	14		
Fever	Additional description: Fever		
alternative assessment type: Non-systematic			
subjects affected / exposed	7 / 25 (28.00%)		
occurrences (all)	11		
Non-cardiac chest pain	Additional description: Non-cardiac chest pain		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Pelvic pain	Additional description: Pelvic pain		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough	Additional description: Cough		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Dyspnea	Additional description: Dyspnea		

alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Hiccups	Additional description: Hiccups		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Hoarseness	Additional description: Hoarseness		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Pleural effusion	Additional description: Pleural effusion		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders - Ot	Additional description: Respiratory, thoracic and mediastinal disorders - Ot		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Psychiatric disorders			
Anxiety	Additional description: Anxiety		
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	3		
Confusion	Additional description: Confusion		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Insomnia	Additional description: Insomnia		
alternative assessment type: Non-systematic			
subjects affected / exposed	18 / 25 (72.00%)		
occurrences (all)	22		
Psychiatric disorders - Other, claustrophobia	Additional description: Psychiatric disorders - Other, claustrophobia		
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Investigations			
Activated partial thromboplastin time prolonged	Additional description: Activated partial thromboplastin time prolonged		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Alanine aminotransferase increased	Additional description: Alanine aminotransferase increased		
alternative assessment type: Non-systematic			
subjects affected / exposed	10 / 25 (40.00%)		
occurrences (all)	14		
Alkaline phosphatase increased	Additional description: Alkaline phosphatase increased		
alternative assessment type: Non-systematic			
subjects affected / exposed	14 / 25 (56.00%)		
occurrences (all)	16		
Blood bilirubin increased	Additional description: Blood bilirubin increased		
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	4		
Creatinine increased	Additional description: Creatinine increased		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Electrocardiogram QT corrected interval prolonged	Additional description: Electrocardiogram QT corrected interval prolonged		
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	5		
INR increased	Additional description: INR increased		
alternative assessment type: Non-systematic			
subjects affected / exposed	5 / 25 (20.00%)		
occurrences (all)	5		
Investigations - Other, CRP increased	Additional description: Investigations - Other, CRP increased		
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Investigations - Other, eosinophil count increased	Additional description: Investigations - Other, eosinophil count increased		
alternative assessment type: Non-systematic			
subjects affected / exposed	15 / 25 (60.00%)		
occurrences (all)	18		
Investigations - Other, monocyte count increased	Additional description: Investigations - Other, monocyte count increased		
alternative assessment type: Non-systematic			
subjects affected / exposed	21 / 25 (84.00%)		
occurrences (all)	22		
Investigations - Other, neutrophil count increased	Additional description: Investigations - Other, neutrophil count increased		
alternative assessment type: Non-systematic			
subjects affected / exposed	22 / 25 (88.00%)		
occurrences (all)	26		
Investigations - Other, prothrombin time increased	Additional description: Investigations - Other, prothrombin time increased		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Investigations - Other, white blood cell count incre	Additional description: Investigations - Other, white blood cell count incre		
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	3		
Lymphocyte count decreased	Additional description: Lymphocyte count decreased		
alternative assessment type: Non-systematic			
subjects affected / exposed	4 / 25 (16.00%)		
occurrences (all)	7		
Lymphocyte count increased	Additional description: Lymphocyte count increased		
alternative assessment type: Non-systematic			
subjects affected / exposed	5 / 25 (20.00%)		
occurrences (all)	5		
Platelet count decreased	Additional description: Platelet count decreased		
alternative assessment type: Non-systematic			

subjects affected / exposed	5 / 25 (20.00%)		
occurrences (all)	6		
Injury, poisoning and procedural complications			
Bruising	Additional description: Bruising		
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	4		
Injury, poisoning and procedural complications - Oth	Additional description: Injury, poisoning and procedural complications - Oth		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Cardiac disorders			
Atrial fibrillation	Additional description: Atrial fibrillation		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Atrioventricular block first degree	Additional description: Atrioventricular block first degree		
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Cardiac disorders - Other, intraventricular conducti	Additional description: Cardiac disorders - Other, intraventricular conducti		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Cardiac disorders - Other, left axis deviation	Additional description: Cardiac disorders - Other, left axis deviation		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Cardiac disorders - Other, multifocal atrial tachyca	Additional description: Cardiac disorders - Other, multifocal atrial tachyca		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Cardiac disorders - Other, right	Additional description: Cardiac disorders - Other, right bundle branch block		

bundle branch block			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Cardiac disorders - Other, supraventricular arrhythm	Additional description: Cardiac disorders - Other, supraventricular arrhythm		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Cardiac disorders - Other, supraventricular ectopics	Additional description: Cardiac disorders - Other, supraventricular ectopics		
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Palpitations	Additional description: Palpitations		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Sinus bradycardia	Additional description: Sinus bradycardia		
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	3		
Sinus tachycardia	Additional description: Sinus tachycardia		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Supraventricular tachycardia	Additional description: Supraventricular tachycardia		
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	3		
Ventricular arrhythmia	Additional description: Ventricular arrhythmia		
alternative assessment type: Non-systematic			
subjects affected / exposed	4 / 25 (16.00%)		
occurrences (all)	4		
Nervous system disorders			

Dizziness	Additional description: Dizziness		
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Dysgeusia	Additional description: Dysgeusia		
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	3		
Headache	Additional description: Headache		
alternative assessment type: Non-systematic			
subjects affected / exposed	4 / 25 (16.00%)		
occurrences (all)	6		
Nervous system disorders - Other, abnormal dreams	Additional description: Nervous system disorders - Other, abnormal dreams		
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Nervous system disorders - Other, nightmare/ abnorma	Additional description: Nervous system disorders - Other, nightmare/ abnorma		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Nervous system disorders - Other, vivid dreams	Additional description: Nervous system disorders - Other, vivid dreams		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Nervous system disorders - Other, vivid dreams/flash	Additional description: Nervous system disorders - Other, vivid dreams/flash		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Paresthesia	Additional description: Paresthesia		
alternative assessment type: Non-systematic			
subjects affected / exposed	15 / 25 (60.00%)		
occurrences (all)	19		
Peripheral sensory neuropathy	Additional description: Peripheral sensory neuropathy		

alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	2		
Presyncope	Additional description: Presyncope		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Tremor	Additional description: Tremor		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anemia	Additional description: Anemia		
alternative assessment type: Non-systematic			
subjects affected / exposed	11 / 25 (44.00%)		
occurrences (all)	17		
Eye disorders			
Watering eyes	Additional description: Watering eyes		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal distension	Additional description: Abdominal distension		
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Abdominal pain	Additional description: Abdominal pain		
alternative assessment type: Non-systematic			
subjects affected / exposed	13 / 25 (52.00%)		
occurrences (all)	19		
Ascites	Additional description: Ascites		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Constipation	Additional description: Constipation		

alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Diarrhea	Additional description: Diarrhea		
alternative assessment type: Non-systematic			
subjects affected / exposed	15 / 25 (60.00%)		
occurrences (all)	18		
Dry mouth	Additional description: Dry mouth		
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Duodenal obstruction	Additional description: Duodenal obstruction		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Flatulence	Additional description: Flatulence		
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	3		
Gastrointestinal disorders - Other, aphthous ulcer	Additional description: Gastrointestinal disorders - Other, aphthous ulcer		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Mucositis oral	Additional description: Mucositis oral		
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		
Nausea	Additional description: Nausea		
alternative assessment type: Non-systematic			
subjects affected / exposed	10 / 25 (40.00%)		
occurrences (all)	15		
Vomiting	Additional description: Vomiting		
alternative assessment type: Non-systematic			

subjects affected / exposed	9 / 25 (36.00%)		
occurrences (all)	11		
Hepatobiliary disorders			
Hepatic pain	Additional description: Hepatic pain		
alternative assessment type: Non-systematic			
subjects affected / exposed	6 / 25 (24.00%)		
occurrences (all)	12		
Hepatobiliary disorders - Other, hyperbilirubinaemia	Additional description: Hepatobiliary disorders - Other, hyperbilirubinaemia		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Dry skin	Additional description: Dry skin		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Pruritus	Additional description: Pruritus		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Renal and urinary disorders			
Proteinuria	Additional description: Proteinuria		
alternative assessment type: Non-systematic			
subjects affected / exposed	14 / 25 (56.00%)		
occurrences (all)	24		
Musculoskeletal and connective tissue disorders			
Back pain	Additional description: Back pain		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorder - Oth	Additional description: Musculoskeletal and connective tissue disorder - Oth		
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 25 (12.00%)		
occurrences (all)	3		

Musculoskeletal and connective tissue disorders - Ot	Additional description: Musculoskeletal and connective tissue disorders - Ot		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Neck pain	Additional description: Neck pain		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Infections and infestations			
Biliary tract infection	Additional description: Biliary tract infection		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Infections and infestations - Other, gastroenteritis	Additional description: Infections and infestations - Other, gastroenteritis		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Infections and infestations - Other, oral candidiasi	Additional description: Infections and infestations - Other, oral candidiasi		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Mucosal infection	Additional description: Mucosal infection		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Upper respiratory infection	Additional description: Upper respiratory infection		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Urinary tract infection	Additional description: Urinary tract infection		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Metabolism and nutrition disorders			

Anorexia	Additional description: Anorexia		
alternative assessment type: Non-systematic			
subjects affected / exposed	5 / 25 (20.00%)		
occurrences (all)	7		
Hypercalcemia	Additional description: Hypercalcemia		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		
Hypoalbuminemia	Additional description: Hypoalbuminemia		
alternative assessment type: Non-systematic			
subjects affected / exposed	18 / 25 (72.00%)		
occurrences (all)	44		
Hypoglycemia	Additional description: Hypoglycemia		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	2		
Hypokalemia	Additional description: Hypokalemia		
alternative assessment type: Non-systematic			
subjects affected / exposed	7 / 25 (28.00%)		
occurrences (all)	8		
Hyponatremia	Additional description: Hyponatremia		
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	4		
Hypophosphatemia	Additional description: Hypophosphatemia		
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 December 2015	The United States sponsored participating site (Weill Cornell) was added to the study therefore the protocol was amended to reflect this. Other changes to the protocol and/or patient information sheet included; - Addition of routine blood sampling to the Day 13-17 and Day 20-24 visits for safety monitoring. - Clarification of CT scan type. - Clarification of patient discharge criteria. - Removal of ECOG on days 2, 3, 4, 5, 6 & 7. - Removal of urinalysis on days 3, 5, 6 & 7. - Clarification of cardiac events as an AE. - Updates to AESI terms. - Updates to SAE/AESI reporting guidelines. This amendment was submitted to both REC and MHRA.
03 February 2016	The protocol and patient information updated to increase duration of telemetry monitoring from 48 hours to 72 hours, this amendment also Incorporated increasing the time the patient was an in-patient for 48 hours to 72 hours to allow for the extended telemetry monitoring and vital signs. The protocol were also updated to include additional PK sample and blood volumes updated on the patient information sheet. This amendment submitted to REC.
29 November 2016	changes made to the protocol and/or patient information sheet to add or clarify the following: - Addition of saliva samples for cortisol measurement. - Screening lymphocyte count changed from 'normal level for institution' to '<1.0 x 10^9/L'. - Clarification of IMP interruption and stopping criteria. - Clarification of research sample types. - Informed consent timeframe of 21 days added. - Sanofi PV details removed from protocol as per Sanofi request. Information included in contract only. This amendment was submitted to both REC and MHRA
24 May 2017	The protocol Reference Safety Information section was amended to align with the MHRA process for reference safety information management, the added reference to the latest approved SmPC for Mozobil. The amendment includes changes to the CTA documentation, so therefore the amendment was also submitted to the MHRA. The MHRA werel also be notified of the new RSI for this trial as part of the amendment.
18 October 2017	Amendment submitted to notify the HRA and REC that the IMP supply arrangements had been modified. This amendment was also submitted to the MHRA for their approval. Penn Pharmaceuticals (PCI Pharma Services) were previously the importer of the finished product were also to be used for secondary packaging and labelling of the licenced IMP. Penn Pharmaceuticals (PCI Pharma Services were then responsible for QP certification. Genzyme CPRS no longer performed secondary packaging and labelling.
11 December 2017	plerixafor (Mozobil) SmPC text revised and the safety section updated, therefore changes made on the safety sections of the protocol and the side effects in the patient information sheet updated to reflect changes on the SmPC.

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.

Decision to close recruitment early was made as recruitment was slower than expected and although the recruitment target were not met, upon review of the data collected, it was determined that there was sufficient data to answer the trial objectives

Notes: