Clinical trial results:
A phase II study of Cabazitaxel chemotherapy in relapsed locally advanced and/or metastatic carcinoma of the penis.

Summary

EudraCT number	2014-002336-14
Trial protocol	GB
Global end of trial date	14 August 2017

Results information

Result version number	v1 (current)
This version publication date	26 September 2018
First version publication date	26 September 2018
Summary attachment (see zip file)	PFS and OS Curves (PFS and OS curves.pdf)

Trial information

Trial identification

Sponsor protocol code	ON/2012/4233

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03114254
WHO universal trial number (UTN)	-
Other trial identifiers	JAVA-P: ON/2012/4233

Notes:

Sponsors

Sponsor organisation name	University Hospitals Bristol NHS Foundation Trust, Trust HQ, Marlborough Street, Bristol, bs3 1ta, United Kingdom
Sponsor organisation address	Trust HQ, Marlborough Street, Bristol, Bristol, United Kingdom, bs3 1ta
Public contact	JAVA P Study Manager, University Hospitals Bristol NHS Foundation trust, +44 1173427860, javap@uhbristol.nhs.uk
Scientific contact	JAVA P Study Manager/Chief Investigator - Prof Amit Bahl, University Hospitals Bristol NHS Foundation trust, +44 1173427860, javap@uhbristol.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	27 July 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 August 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the activity of Cabazitaxel chemotherapy in relapsed cancer of the penis as assessed by objective response rate.
The primary endpoint is objective response rate defined as complete response and partial response recorded from the start of the treatment to completion of 6 cycles of treatment determined by radiological response assessment

Protection of trial subjects:

Full trial sample size was calculated to be 17 patients, with a stopping rule at 9 patients. The protocol stated that recruitment would be stopped at the point at which 'there is a 99% chance that the response rate is less than 60%. If no patients are seen to respond to treatment, the study will stop at the point at which 9 patients results are known'. Of the first 9 patients recruited 0 patients responded to treatment. The IDMC met on 06/01/2017 and recommended no further recruitment into the trial in adherence to the stopping rule. According to the protocol 'the study is deemed to have ended 5 years after the last patient has undergone chemotherapy'. The trial therefore ended having recruited 9 patients with the end of trial being the date of the last patient last visit which was 14/08/2017 (the date the last patient died).

Background therapy:

Docetaxel, Cisplatin, 5FU triplet combination therapy is the standard of care for specific penile cancer patients in several UK cancer centres, However, on relapse there is no UK standard secondary chemotherapy treatment available.

Therefore this study presented a second line treatment option for these subset of patients, which these patients would not otherwise receive.

Evidence for comparator:

This study had no comparator as per above, this treatment was in addition to first line treatment.

Actual start date of recruitment	01 October 2014
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: 9
Worldwide total number of subjects	9
EEA total number of subjects	9

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)	7
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Cancer of the penis is a rare disease. Discussion within the supra-network MDT of all eligible patients is encouraged/ To enable recruitment, this study has been supported by the NCRI Penile Cancer Clinical Studies Subgroup, recognizing that there are no available treatment options in this setting.

Pre-assignment

Screening details:

Patients must be adult males with histologically-proven SCC of the penis. SCC of the penile urethra is also allowed. Patients must be stage M1 or; M0TxN3; M0TxN2; M0TxN1, M0T4. Patients must have received first line treatment previously and have an ECOG status 0-2. They must not have had previous cabazitaxel treatment.

Period 1

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

Arms

Arm title	Cabazitaxel

Arm description:

Platinum based combination chemotherapy is the standard of care for patients with symptomatic advanced/metastatic penile cancer. However, on relapse there is no standardised second line treatment in the UK. This trial aimed to evaluate the activity, safety and tolerability of cabazitaxel as second line treatment in relapsed penile cancer.

A phase II single arm trial was designed to recruit 17 patients with the primary endpoint being objective response rate – ORR (complete response plus partial response).

Arm type	Non RCT
Investigational medicinal product name	Cabazitaxel
Investigational medicinal product code	
Other name	Jevtana
Pharmaceutical forms	Solution for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dose: 25mg/m2 capped at BSA 2.25
Formulation: 60 mg concentrate and solvent for solution for IV infusion

Number of subjects in period 1	Cabazitaxel
Started	9
Completed	9

Baseline characteristics

Reporting groups

Reporting group title	Overall trial - baseline

Reporting group description: -

Reporting group values	Overall trial - baseline	Total	
Number of subjects	9	9	
Age categorical			
Age of subjects Median (Range) 61 (27-73)			
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)	7	7	
From 65-84 years	2	2	
85 years and over	0	0	
Adults registered	0	0	
Age continuous			
Age of subjects Median (Range) 61 (27-73)			
Units: years			
median	61		
full range (min-max)	27 to 73	-	
Gender categorical			
All participants were male.			
Units: Subjects			
Female	0	0	
Male	9	9	
M Stage			
M stage			
Units: Subjects			
M0 loco regional	2	2	
M1 metastatic	7	7	
Previous treatments			
Number of lines of treatments the patients have received prior to registration onto the trial.			
Units: Subjects			
One line	7	7	
Two lines	1	1	
Three lines	1	1	

End points

End points reporting groups

Reporting group title	Cabazitaxel

Reporting group description:

Platinum based combination chemotherapy is the standard of care for patients with symptomatic advanced/metastatic penile cancer. However, on relapse there is no standardised second line treatment in the UK. This trial aimed to evaluate the activity, safety and tolerability of cabazitaxel as second line treatment in relapsed penile cancer.

A phase II single arm trial was designed to recruit 17 patients with the primary endpoint being objective response rate – ORR (complete response plus partial response).

Primary: Overall response rate (ORR)

End point title	Overall response rate (ORR)[1]

End point description:

The primary endpoint is objective response rate defined as complete response and partial response recorded from the start of the treatment to completion of 6 cycles of treatment determined by radiological response assessment

End point type	Primary

End point timeframe:

Within 6 cycles 3 weekly chemotherapy (18 weeks)

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: None of the patients recruited achieved the primary endpoint of objective response rate (ORR), after 6 cycles of cabazitaxel, therefore the null hypothesis was accepted. An interim analysis was planned based on the premise that if no patient achieved ORR among the first 9 patients treated, then the null hypothesis that the ORR is <10% (based on a response rate of 0.25) would be accepted, and the trial would be stopped (α = 0.05, Simon's 2 stage design).

End point values	Cabazitaxel			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Subjects				
Non responders	9			
Responders	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival

End point title	Progression Free Survival

End point description:

Progression-free survival (defined as the time from date of consent to the first of one of the following: development of radiological disease progression (RECIST 1.1) or death from any cause, whichever comes first).;

End point type	Secondary

End point timeframe:

With 4 months of the patients consenting onto the clinical trial.

End point values	Cabazitaxel			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: months				
median (full range (min-max))	1.3 (1 to 3.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Overall Survival defined as the time from date of consent to death from any cause.

End point type	Secondary

End point timeframe:

Within 15 months of the patients being consented for the clinical trial.

End point values	Cabazitaxel			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: months				
median (full range (min-max))	5.6 (1.9 to 13)			

Attachments (see zip file)	PFS and OS curves.docx

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were recorded from cycle 1 day 1 of chemotherapy until 6 months post the last date of treatment.

Adverse event reporting additional description:

AEs were reported and graded according to CTCAE v4.03. Causality was assigned by the PI or Co-I at site referring to the RSI.

There were 6 SAEs reported.

Overall there were 59 adverse events reported.

The adverse events reported below are only adverse events that are deemed related to the IMP (25 events)

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.03

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	4 / 9 (44.44%)		
number of deaths (all causes)	9		
number of deaths resulting from adverse events	2		
Injury, poisoning and procedural complications			
Wound complication	Additional description: Bleeding from penile wound		
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Vascular disorders			
Thromboembolic event			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Blood and lymphatic system disorders			
Febrile neutropenia			

subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fever			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Sepsis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypercalcemia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	All patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 9 (100.00%)		
Injury, poisoning and procedural complications			
Infusion reaction			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Nervous system disorders			
Peripheral neuropathy			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
General disorders and administration site conditions			

Fever	Additional description: These are adverse reactions (deemed related to the IMP)		
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	4 / 9 (44.44%)		
occurrences (all)	4		
Blood and lymphatic system disorders			
Neutropenic sepsis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Anaemia			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Gastrointestinal disorders			
Mucositis oral			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Diarrhoea			
subjects affected / exposed	5 / 9 (55.56%)		
occurrences (all)	5		
Constipation			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Infections and infestations			
Sepsis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hypocalcemia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		

Anorexia subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 May 2015	• Amendment 1 - addition of Clatterbridge Cancer Centre as a site; administration of pegylated GCSF allowed; avoidance of grapefruit juice; clarification of restrictions for use of CYP3A inhibitors and inducers.
18 December 2015	• Amendment 2 – addition of Treliske Hospital as a site; confirmation that prior chemotherapy except cabazitaxel is allowed; clarification of the trial second line status in the title; removal of the TSC.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported