



Clinical trial results:

A multicentre, phase II randomised controlled trial evaluating cabazitaxel versus docetaxel re-challenge for the treatment of metastatic Castrate Refractory Prostate Cancer, previously treated with docetaxel at inception of primary hormone therapy

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2012-003835-40 |
| Trial protocol | GB |
| Global end of trial date | 29 April 2016 |

Results information

| | |
|--------------------------------|-------------|
| Result version number | v1 |
| This version publication date | 14 May 2017 |
| First version publication date | 14 May 2017 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | RG12-024 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|---|
| ISRCTN number | ISRCTN16465571 |
| ClinicalTrials.gov id (NCT number) | - |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | CRCTU reference number: PR2103, Sanofi study number: Cabaz_L_05879, Cancer Research UK number: A15721 |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | University of Birmingham |
| Sponsor organisation address | Room 119, Aston Webb Building, Birmingham, United Kingdom, B15 2TT |
| Public contact | Mr Nick Martin, Cancer Research UK Clinical Trials Unit, University of Birmingham, +44 01214145102, cantata@trials.bham.ac.uk |
| Scientific contact | Mr Nick Martin, Cancer Research UK Clinical Trials Unit, University of Birmingham, +44 01214145102, cantata@trials.bham.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 April 2017 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 13 April 2016 |
| Global end of trial reached? | Yes |
| Global end of trial date | 29 April 2016 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this phase II study are to determine the tolerability and activity of cabazitaxel compared with docetaxel re-challenge as second-line chemotherapy treatment in metastatic patients who received primary therapy with docetaxel.

Protection of trial subjects:

What are the key risks related to therapeutic interventions you plan to monitor in this trial? How will these risks be minimised?

For the following, clinical assessment 3 weekly will be carried out during treatment.

*CARDIAC DISORDERS. *EAR & LABYRINTH DISORDER *EYE DISORDERS *GASTROINTESTINAL DISORDERS*GENERAL DISORDERS & ADMINISTRATION SITE CONDITIONS *IMMUNE SYSTEM DISORDERS *BLOOD & LYMPHATIC SYSTEM DISORDERS *INFECTIONS & INFESTATIONS *METABOLISM & NUTRITION DISORDERS *RENAL & URINARY DISORDERS *MUSCULOSKELETAL & CONNECTIVE TISSUE DISORDERS *SKIN & SUBCUTANEOUS TISSUE DISORDERS *VASCULAR DISORDERS *RESPIRATORY, THORACIC & MEDIASTINAL DISORDERS *NERVOUS SYSTEM DISORDERS *PSYCHIATRIC DISORDERS *REPRODUCTIVE SYSTEM & BREAST DISORDERS *INVESTIGATIONS (WEIGHT LOSS & RAISED LFTs)

Patients may be required to undergo 1 additional CT or MRI scan in order to verify progression at trial entry.

Data Protection:

In routine correspondence between the CRCTU and the site patients will be referred to by their unique Trial Number, initials and date of birth. The patient's consent will be obtained for this.

All patient data (both paper and electronic) is securely stored and will only be accessible by authorised personnel in accordance with the CRCTU Quality Management System (QMS).

In addition, patients who are participating in the STAMPEDE trial will be asked to consent to the sharing of some data between the CRCTU and the MRC CTU. This is to minimise the duplication of data taken from the same patient.

Background therapy:

Premedication Regimen: Administer intravenously 30 minutes before each dose of cabazitaxel:

* Antihistamine (chlorpheniramine 5 mg or equivalent antihistamine)

*Dexamethasone 8 mg or equivalent steroid

*H2 antagonist (ranitidine 50 mg or equivalent H2 antagonist)

*Antiemetic prophylaxis (oral or intravenous) is recommended as needed, and should follow local policy.

*Variations based on local practice can be considered after discussion with the Trial Office

G-CSF: Patients experiencing severe neutropenia or neutropenic sepsis should be considered for G-CSF prophylaxis with subsequent cycles.

The recommended anti-emetic regimen is:

30 minutes prior to docetaxel administration:

* Ondansetron 8mg IV stat or equivalent

* Dexamethasone 8mg IV stat or equivalent steroid

Followed by:

* Ondansetron 8mg BD/PRN for 3 days
* Domperidone 20mg PO QDS/PRN

Evidence for comparator:

Until recently there was a need for new treatments in advanced prostate cancer, but in 2010 de Bono and colleagues published the results of the TROPIC trial(10). TROPIC was a randomised phase III trial in men with mCRPC who had previously been treated with hormone therapy, but whose disease had progressed during or after treatment with docetaxel.

Based on the results of the TROPIC trial, cabazitaxel, in combination with prednisone or prednisolone, was approved by the US Food and Drug Administration (June 2010) and the European Medicines Agency (March 2011), for the treatment of patients with mCRPC who have previously been treated with docetaxel. There are also four clinical trials currently recruiting which are assessing cabazitaxel safety and efficacy in this group of patients (NCT00417079, NCT01308580, NCT01308567, NCT01324583).

In conclusion, treatment with cabazitaxel is a potential therapeutic option for patients with mCRPC whose disease has progressed during or after docetaxel-based therapy. Caution, however, must be employed due to its significant haematological toxicities.

| | |
|---|------------------|
| Actual start date of recruitment | 10 December 2012 |
| 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: 15 |
| Worldwide total number of subjects | 15 |
| EEA total number of subjects | 15 |

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) | 3 |
| From 65 to 84 years | 12 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

15 patients randomised in total; 7 to Cabazitaxel and 8 to Docetaxel. 1 patient in the Docetaxel group was found to be ineligible post-randomisation but remain in analysis since protocol states that on an intention to treat basis, all ineligible patients will be included.

First patient randomised= 09-May-2013

Last patient randomised= 04-Jan-2016

Pre-assignment

Screening details:

Eligible: prostate CA, previously treated with 6 cycles of Docetaxel, confirmed progression, metastatic disease, ≥ 18 , performance status 0-2, adequate blood results

Exclusion criteria: prior chemotherapy other than docetaxel, progressive disease on docetaxel, active infection, malignant disease in last 5 years, active peripheral neuropathy

Period 1

| | |
|------------------------------|-------------------------|
| Period 1 title | Baseline |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Blinding implementation details:

na

Arms

| | |
|------------------------------|-------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Cabazitaxel |

Arm description:

Cabazitaxel 25mg/m²
3 weekly plus
prednisolone for up to
10 cycles

| | |
|--|---------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Cabazitaxel |
| Investigational medicinal product code | XRP6258/RPR116258 |
| Other name | Jevtana |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous drip use |

Dosage and administration details:

Cabazitaxel will be administered at a dose of 25 mg/m² (in either 0.9% sodium chloride solution or 5% dextrose solution) as 1 hour intravenous infusion every three weeks, in combination with oral prednisolone 10 mg administered daily, throughout treatment.

| | |
|------------------|-----------|
| Arm title | Docetaxel |
|------------------|-----------|

Arm description:

Docetaxel 75mg/m²
3 weekly plus
prednisolone for up to
10 cycles

| | |
|--|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Docetaxel |
| Investigational medicinal product code | |
| Other name | Taxotere |
| Pharmaceutical forms | Concentrate and solvent for solution for infusion |
| Routes of administration | Intravenous drip use |

Dosage and administration details:

Docetaxel will be administered at a dose of 75 mg/m² (in either 0.9% sodium chloride solution or 5% dextrose solution) as 1 hour intravenous infusion every three weeks, in combination with oral prednisolone 10 mg administered daily, throughout treatment.

| Number of subjects in period 1 | Cabazitaxel | Docetaxel |
|---------------------------------------|-------------|-----------|
| Started | 7 | 8 |
| Completed | 7 | 8 |

Period 2

| | |
|------------------------------|-------------------------|
| Period 2 title | End of trial |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Blinding implementation details:

na

Arms

| | |
|------------------------------|-------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Cabazitaxel |

Arm description:

Cabazitaxel 25mg/m²
3 weekly plus
prednisolone for up to
10 cycles

| | |
|--|---------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Cabazitaxel |
| Investigational medicinal product code | XRP6258/RPR116258 |
| Other name | Jevtana |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous drip use |

Dosage and administration details:

Cabazitaxel will be administered at a dose of 25 mg/m² (in either 0.9% sodium chloride solution or 5% dextrose solution) as 1 hour intravenous infusion every three weeks, in combination with oral prednisolone 10 mg administered daily, throughout treatment.

| | |
|------------------|-----------|
| Arm title | Docetaxel |
|------------------|-----------|

Arm description:

Docetaxel 75mg/m²
3 weekly plus
prednisolone for up to
10 cycles

| | |
|--|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Docetaxel |
| Investigational medicinal product code | |
| Other name | Taxotere |
| Pharmaceutical forms | Concentrate and solvent for solution for infusion |
| Routes of administration | Intravenous drip use |

Dosage and administration details:

Docetaxel will be administered at a dose of 75 mg/m² (in either 0.9% sodium chloride solution or 5% dextrose solution) as 1 hour intravenous infusion every three weeks, in combination with oral prednisolone 10 mg administered daily, throughout treatment.

| Number of subjects in period 2 | Cabazitaxel | Docetaxel |
|---------------------------------------|-------------|-----------|
| Started | 7 | 8 |
| Completed | 7 | 8 |

Baseline characteristics

Reporting groups

| | |
|---|-------------|
| Reporting group title | Cabazitaxel |
| Reporting group description: Cabazitaxel 25mg/m2 3 weekly plus prednisolone for up to 10 cycles | |
| Reporting group title | Docetaxel |
| Reporting group description: Docetaxel 75mg/m2 3 weekly plus prednisolone for up to 10 cycles | |

| Reporting group values | Cabazitaxel | Docetaxel | Total |
|--|--------------|--------------|-------|
| Number of subjects | 7 | 8 | 15 |
| Age categorical | | | |
| Date of birth is collected at randomisation. All subjects are required to be over 18. | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 4 | 1 | 5 |
| From 65-84 years | 3 | 7 | 10 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous | | | |
| Units: years | | | |
| median | 62.7 | 69.9 | |
| inter-quartile range (Q1-Q3) | 57.5 to 75.2 | 66.1 to 72.5 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 0 | 0 | 0 |
| Male | 7 | 8 | 15 |
| Experiencing disease related pain | | | |
| Stratification variable of whether a patient has disease related pain at randomisation | | | |
| Units: Subjects | | | |
| Disease related pain | 4 | 5 | 9 |
| No disease related pain | 3 | 3 | 6 |
| Prior exposure to a new generation hormone therapy | | | |
| Stratification variable of prior exposure to a new generation hormone therapy | | | |
| Units: Subjects | | | |
| Prior exposure to a new gen hormone therapy | 1 | 2 | 3 |

| | | | |
|---|---|---|----|
| No prior exposure to a new gen hormone therapy | 6 | 6 | 12 |
| Prior hormone used | | | |
| For those who used a prior new generation hormone | | | |
| Units: Subjects | | | |
| No prior hormone | 6 | 6 | 12 |
| Abiraterone | 1 | 0 | 1 |
| Enzalutamide | 0 | 2 | 2 |
| Other hormone | 0 | 0 | 0 |

End points

End points reporting groups

| | |
|---|-------------|
| Reporting group title | Cabazitaxel |
| Reporting group description: Cabazitaxel 25mg/m2 3 weekly plus prednisolone for up to 10 cycles | |
| Reporting group title | Docetaxel |
| Reporting group description: Docetaxel 75mg/m2 3 weekly plus prednisolone for up to 10 cycles | |
| Reporting group title | Cabazitaxel |
| Reporting group description: Cabazitaxel 25mg/m2 3 weekly plus prednisolone for up to 10 cycles | |
| Reporting group title | Docetaxel |
| Reporting group description: Docetaxel 75mg/m2 3 weekly plus prednisolone for up to 10 cycles | |

Primary: Clinical Progression Free Survival (CPFS)

| | |
|--|---|
| End point title | Clinical Progression Free Survival (CPFS) |
| End point description: Clinical progression is defined as the earliest time between date of randomisation and either date of occurrence of pain progression (date patient is seen in clinic and pain progression identified), date of occurrence of a cancer-related skeletal-related event or date of death from any cause. Patients who do not suffer one of the specified events are censored at the date they were last known to be event free. | |
| End point type | Primary |
| End point timeframe: The time between the date of randomisation and the date of clinical progression. 'Clinical progression' is an event defined as the clinician being of the opinion that disease has progressed. | |

| End point values | Cabazitaxel | Docetaxel | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7 | 8 | | |
| Units: Number of events (as defined below) | | | | |
| Clinically Progressed | 2 | 4 | | |
| Hasn't clinically progressed | 5 | 4 | | |

Statistical analyses

| | |
|-----------------------------------|----------------------------------|
| Statistical analysis title | Not enough patients for analysis |
|-----------------------------------|----------------------------------|

Statistical analysis description:

There are not enough patients to justify any form of formal statistical analysis since the trial stopped very short of numbers intended. One patient on the Docetaxel arm was ineligible but has been included due the protocol stating 'Intention to treat'. 2 out of 7 Cabazitaxel patients progressed (either had pain progression or died) and 4 out of 8 Docetaxel patients (either had pain progression or died) Therefore, it can only be a very descriptive statement

| | |
|---|-------------------------|
| Comparison groups | Cabazitaxel v Docetaxel |
| Number of subjects included in analysis | 15 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[1] |
| P-value | = 1 ^[2] |
| Method | Not done |
| Parameter estimate | 40 |

Notes:

[1] - Not enough patients to justify any form of formal statistical analysis since trial stopped very short of numbers intended. 1 patient on the Docetaxel arm was ineligible but has been included due to the protocol stating 'Intention to treat'. For patients who received trial treatment (including ineligible patient) 2 out of 7 Cabazitaxel patients progressed and 4 out of 8 Docetaxel patients progressed. Therefore, it can only be descriptive.

[2] - There are not enough patients to justify any form of formal statistical analysis since the trial stopped very short of numbers intended. The p-value of 1 has been input by default to fill in the box. Also for parameter value.

Secondary: Skeletal-related-event-free-survival

| | |
|-----------------|--------------------------------------|
| End point title | Skeletal-related-event-free-survival |
|-----------------|--------------------------------------|

End point description:

No skeletal-related events have occurred

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

The time between the date of randomisation and the date of a skeletal-related event. Those who have no skeletal-related event are censored at last date of follow-up.

| End point values | Cabazitaxel | Docetaxel | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7 | 8 | | |
| Units: Number of events (as defined below) | | | | |
| Skeletal-related event | 0 | 0 | | |
| No skeletal-related event | 7 | 8 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Pain progression-free survival

| | |
|-----------------|--------------------------------|
| End point title | Pain progression-free survival |
|-----------------|--------------------------------|

End point description:

The number of patients who had pain progression following randomisation was extremely small (two on the Docetaxel arm and one on the Cabazitaxel arm). This is not enough patients to carry out any formal statistical testing.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Time from date of randomisation to date of pain progression. Patients who are pain free are censored at the date of last follow-up visit.

| End point values | Cabazitaxel | Docetaxel | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7 | 8 | | |
| Units: Number of events (as defined below) | | | | |
| Pain progression | 1 | 2 | | |
| No pain progression | 6 | 6 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Toxicity (National Cancer Institute CTC V4)

| | |
|-----------------|---|
| End point title | Toxicity (National Cancer Institute CTC V4) |
|-----------------|---|

End point description:

Treatment safety is assessed by the number of patients developing adverse events (AE's) during treatment (acute toxicities) and after trial therapy has been completed (late toxicities). Late toxicity is defined as 30 days after the last injection of cabazitaxel or docetaxel. AE's will be classified by causality, grade, type, duration and system involved.

This information will be recorded in the Adverse events section.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Adverse events are recorded both during treatment and after trial therapy has been completed

| End point values | Cabazitaxel | Docetaxel | | |
|---|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7 | 7 | | |
| Units: Number of patients developing AE's | 7 | 8 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

| | |
|--|------------------|
| End point title | Overall Survival |
| End point description: There have been only 4 deaths in total; 1 on the Cabazitaxel arm and 3 on the Docetaxel arm. All 4 deaths were disease related. There are not enough events to carry out any formal statistical testing. | |
| End point type | Secondary |
| End point timeframe: Time between date of randomisation and the date of death from any cause. Patients who do not die will be censored at the date of last follow-up or date last known to be alive. | |

| End point values | Cabazitaxel | Docetaxel | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7 | 8 | | |
| Units: Number of events (as defined below) | | | | |
| Alive | 6 | 6 | | |
| Died | 1 | 2 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: PSA-progression free survival

| | |
|---|-------------------------------|
| End point title | PSA-progression free survival |
| End point description: Nine patients had a least one raised PSA at a follow-up visit (5 Cabazitaxel and 4 Docetaxel). There are therefore not enough events to carry out any formal statistical testing. | |
| End point type | Secondary |
| End point timeframe: Time between date of randomisation and the date a biochemical failure (PSA progression). Patients who do not progress are censored at time of last follow up visit. | |

| End point values | Cabazitaxel | Docetaxel | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7 | 8 | | |
| Units: Number of events (as defined below) | | | | |
| PSA progression | 5 | 4 | | |
| No PSA progression | 2 | 4 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events will be documented and reported from date of commencement of treatment until 30 days after treatment finishes.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|--------------------|-------|
| Dictionary name | CTCAE |
| Dictionary version | 4 |

Reporting groups

| | |
|-----------------------|-------------|
| Reporting group title | Cabazitaxel |
|-----------------------|-------------|

Reporting group description: -

| | |
|-----------------------|-----------|
| Reporting group title | Docetaxel |
|-----------------------|-----------|

Reporting group description:

One patient did not receive any treatment at all so will not be counted as being exposed.

| Serious adverse events | Cabazitaxel | Docetaxel | |
|--|----------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 7 (71.43%) | 2 / 7 (28.57%) | |
| number of deaths (all causes) | 1 | 3 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Investigations | | | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 7 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 7 (14.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Fever | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 0 / 7 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fatigue | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 7 (14.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 7 (14.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 7 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 7 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 7 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 7 (14.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Lung infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 7 (14.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Hyperglycaemia | | | |

| | | | |
|---|---------------|----------------|--|
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 7 (14.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Cabazitaxel | Docetaxel | |
|--|---------------------------------------|-----------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 7 / 7 (100.00%) | 7 / 7 (100.00%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Tumor pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 7 (14.29%) | |
| occurrences (all) | 0 | 1 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) - Other, specify | Additional description: Cyst on groin | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 7 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Vascular disorders | | | |
| Hot flashes | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 7 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Phlebitis | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 7 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 4 / 7 (57.14%) | 4 / 7 (57.14%) | |
| occurrences (all) | 25 | 21 | |
| Fever | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 1 / 7 (14.29%) | |
| occurrences (all) | 2 | 1 | |
| Malaise | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 7 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pain | | | |

| | | | |
|--|-------------------------------------|----------------|--|
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 7 (14.29%) | |
| occurrences (all) | 1 | 1 | |
| General disorders and administration site conditions- Other, specify | Additional description: Common cold | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 7 (14.29%) | |
| occurrences (all) | 1 | 1 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 7 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dyspnea | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 1 / 7 (14.29%) | |
| occurrences (all) | 8 | 2 | |
| Epistaxis | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 0 / 7 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| Sore throat | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 7 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Respiratory, thoracic and mediastinal disorders - Other, specify | Additional description: Watery nose | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 7 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Psychiatric disorders | | | |
| depression | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 7 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 0 / 7 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Alkaline phosphatase increased | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 7 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Creatinine increased | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 7 (0.00%) | |
| occurrences (all) | 1 | 0 | |

| | | | |
|--|--|---------------------|--|
| Neutrophil count decreased subjects affected / exposed occurrences (all) | 2 / 7 (28.57%) 2 | 1 / 7 (14.29%) 1 | |
| Platelet count decreased subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 2 | 0 / 7 (0.00%) 0 | |
| Weight loss subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 1 / 7 (14.29%) 1 | |
| Investigations - Other, specify subjects affected / exposed occurrences (all) | Additional description: White blood cell count increased | | |
| | 1 / 7 (14.29%) 2 | 0 / 7 (0.00%) 0 | |
| Injury, poisoning and procedural complications Bruising subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 6 | 0 / 7 (0.00%) 0 | |
| Cardiac disorders Atrial fibrillation subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 7 (0.00%) 0 | |
| Nervous system disorders dysgeusia subjects affected / exposed occurrences (all) | 3 / 7 (42.86%) 9 | 1 / 7 (14.29%) 2 | |
| Headache subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 7 (0.00%) 0 | |
| Lethargy subjects affected / exposed occurrences (all) | 3 / 7 (42.86%) 5 | 2 / 7 (28.57%) 5 | |
| Peripheral sensory neuropathy subjects affected / exposed occurrences (all) | 2 / 7 (28.57%) 4 | 2 / 7 (28.57%) 3 | |
| Nervous system disorders - Other, specify subjects affected / exposed occurrences (all) | Additional description: Neurotoxicity fingers | | |
| | 0 / 7 (0.00%) 0 | 1 / 7 (14.29%) 2 | |

| | | | |
|--------------------------------------|-----------------------------|----------------|----------------|
| Blood and lymphatic system disorders | | | |
| | Anaemia | | |
| | subjects affected / exposed | 5 / 7 (71.43%) | 2 / 7 (28.57%) |
| | occurrences (all) | 21 | 6 |
| | | | |
| | Febrile Neutropenia | | |
| | subjects affected / exposed | 1 / 7 (14.29%) | 1 / 7 (14.29%) |
| | occurrences (all) | 1 | 1 |
| Ear and labyrinth disorders | | | |
| | Ear pain | | |
| | subjects affected / exposed | 1 / 7 (14.29%) | 1 / 7 (14.29%) |
| | occurrences (all) | 1 | 1 |
| Eye disorders | | | |
| | Blurred Vision | | |
| | subjects affected / exposed | 2 / 7 (28.57%) | 0 / 7 (0.00%) |
| | occurrences (all) | 2 | 0 |
| | Watering eyes | | |
| | subjects affected / exposed | 1 / 7 (14.29%) | 1 / 7 (14.29%) |
| Gastrointestinal disorders | | | |
| | Constipation | | |
| | subjects affected / exposed | 1 / 7 (14.29%) | 2 / 7 (28.57%) |
| | occurrences (all) | 1 | 5 |
| | Diarrhoea | | |
| | subjects affected / exposed | 6 / 7 (85.71%) | 3 / 7 (42.86%) |
| | occurrences (all) | 8 | 16 |
| | Dry mouth | | |
| | subjects affected / exposed | 2 / 7 (28.57%) | 0 / 7 (0.00%) |
| | occurrences (all) | 2 | 0 |
| | Mucositis oral | | |
| | subjects affected / exposed | 1 / 7 (14.29%) | 0 / 7 (0.00%) |
| | occurrences (all) | 2 | 0 |
| | Nausea | | |
| | subjects affected / exposed | 3 / 7 (42.86%) | 2 / 7 (28.57%) |
| | occurrences (all) | 3 | 5 |
| | Vomiting | | |
| | subjects affected / exposed | 3 / 7 (42.86%) | 2 / 7 (28.57%) |
| | occurrences (all) | 3 | 2 |

| | | | |
|--|---------------------|----------------------|--|
| Gastrointestinal disorders- Other, specify subjects affected / exposed occurrences (all) | 3 / 7 (42.86%) 3 | 2 / 7 (28.57%) 3 | |
| Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 3 / 7 (42.86%) 13 | |
| Dry Skin subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 1 / 7 (14.29%) 1 | |
| Nail ridging subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 2 / 7 (28.57%) 4 | |
| Skin and subcutaneous tissue disorders - Other, specify subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 1 / 7 (14.29%) 1 | |
| Additional description: Rash on Hand | | | |
| Renal and urinary disorders Acute kidney injury subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 7 (0.00%) 0 | |
| Urinary frequency subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 7 (0.00%) 0 | |
| Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 2 | 2 / 7 (28.57%) 7 | |
| Bone pain subjects affected / exposed occurrences (all) | 2 / 7 (28.57%) 2 | 0 / 7 (0.00%) 0 | |
| Arthralgia subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 4 / 7 (57.14%) 7 | |
| Muscle weakness lower limb | | | |

| | | | |
|--|----------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 1 / 7 (14.29%) 1 | |
| Muscle weakness upper limb subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 1 / 7 (14.29%) 1 | |
| Myalgia subjects affected / exposed occurrences (all) | 2 / 7 (28.57%) 3 | 0 / 7 (0.00%) 0 | |
| Infections and infestations | | | |
| Gum Infection subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 1 / 7 (14.29%) 1 | |
| Lung infection subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 7 (0.00%) 0 | |
| Sinusitis subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 7 (0.00%) 0 | |
| Skin infection subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 2 / 7 (28.57%) 2 | |
| Urinary tract infection subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 1 / 7 (14.29%) 1 | |
| Metabolism and nutrition disorders | | | |
| Anorexia subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 3 | 1 / 7 (14.29%) 3 | |
| Hyperkalaemia subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 7 (0.00%) 0 | |
| Hypoalbuminemia subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 10 | 0 / 7 (0.00%) 0 | |
| Hypokalaemia | | | |

| | | | |
|-----------------------------|----------------|---------------|--|
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 7 (0.00%) | |
| occurrences (all) | 3 | 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 16 November 2012 | <p>Amendment number 1</p> <p>Protocol v 2.0. Update to comply with MHRA request re original submission on 26-Oct-2012. Update inclusion/exclusion criteria: patients with bilirubin equal or larger than ULN must be excluded; ANC notation made consistent throughout protocol.</p> <p>New wording: The radiation dose received from an additional set of scans is equivalent to less than 10 years of background radiation. The risk to you from this extra radiation will be negligible.</p> <p>Comments/ explanation/ reasons for substantial amendment: Two sentences have been added to the original paragraph (PIS, page 7) in order to explain the risk of an additional set of scans to the patient. The addition of these sentences to the Patient Information Sheet was requested during the NHS R&D approval process so that the Patient Information Sheet would match the wording supplied by the Medical Physics Expert in the original ethics application (submitted 24 October 2012). (</p> |

| | |
|--------------|---|
| 27 June 2014 | <p>Amendment number 4</p> <p>Substantial Amendment Inclusion of text regarding optional tissue collection sub-study; change to haemoglobin notation.</p> <p>Changes to protocol text include:</p> <ol style="list-style-type: none"> 1. Change to version no and date on page 1 and page 2, and in header/footer 2. Addition of the ISRCTN on the cover page this had not been received when the protocol was first submitted. 3. Clarification of wording in screening section (Schedule of Assessments, page 10) patients should receive "up to" not "at least" 6 cycles of docetaxel in their prior treatment. 4. Addition of section 3.3 on page 21 regarding the optional future Tissue Collection Substudy. This substudy is mentioned in the Patient Information Sheet and included on the Informed Consent Form, but had been removed from the protocol at a draft stage and not reinstated. 5. Change to notation for haemoglobin: from 10g/dL to 100g/L. Most laboratories use the 100g/L notation now. 6. Before a new treatment cycle begins, the patient's platelet count must be greater than or equal to 100×10^9 L. This has been corrected on pages 25 and 27. 7. On page 24, addition of information regarding the use of prednisolone as a NIMP. 8. On page 25, clarification that sites may be able to adhere to local practice if the site's premedication regimen is different to that currently listed in the protocol, but only after agreeing this regimen with the Trial Office. 9. Change to definition of end date for the purposes of the main REC approval on in section 11, page 39 (removing the reference to "latest data capture" as this phrase is unclear). 10. Change to section 12.4 to update the statistical information. The incorrect numbers were retained from an earlier draft of the protocol. 11. Corrections of several minor misspellings (on page 25). |
|--------------|---|

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.

Early termination of trial occurred leading to a small number of subjects analysed. MHRA and ethics informed on 29-Apr-2016.

Notes: