ISRCTN82499869 https://doi.org/10.1186/ISRCTN82499869

CTC-STOP Trial: A trial to determine if the use of Circulating Tumour Cell (CTC) counts can direct early discontinuation of docetaxel chemotherapy in patients with metastatic castration resistant prostate cancer (mCRPC), when compared with standard approaches to guide treatment switch decisions

Submission date
13/03/2017

Recruitment status
Stopped

Registration date
24/03/2017

Overall study status
Stopped

Last Edited
16/01/2020

Condition category
Cancer

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-looking-at-circulating-tumour-cells-in-men-having-treatment-for-advanced-prostate-cancer-ctc

Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
2015-001361-27

IRAS number

ClinicalTrials.gov number
NCT03327662

Secondary identifying numbers
34057

Study information

Scientific Title
CTC-STOP: Utilising Circulating Tumour Cell (CTC) Counts to Optimize Systemic Therapy of Metastatic Prostate Cancer

Acronym
CTC-STOP

Study objectives
The aim of this study is to determine whether a blood test which detects the number of circulating tumour cells (CTC's) could provide an earlier indicator for doctors to decide when to stop one chemotherapy treatment (docetaxel) and start another (cabazitaxel).

Ethics approval required
Old ethics approval format

Ethics approval(s)
London - Surrey Borders Research Ethics Committee, 21/09/2016, ref: 16/LO/1502

Study design
Randomised; Interventional; Design type: Treatment, Process of Care, Drug, Device, Active Monitoring

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet

Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Prostate cancer

Interventions
Patients with a Circulating Tumour Cell (CTC) count of over (and including) 5 cells at screening will be randomised 1:1 to either the control group (standard of care) or intervention group (CTC guided treatment). The trial has a two-stage entry process of registration and randomisation. Randomisation only occurs following confirmation of CTCs over (and including) 5 cells per 7.5 mL of blood and all other eligibility criteria. The Randomisation procedure will be performed via computer programme, centrally by the Institute of Cancer Research Clinical Trials Statistics Unit (ICR-CTSU). All patients regardless of group will commence first line chemotherapy with docetaxel 75mg/m2 three-weekly and will receive a minimum of 3 cycles of treatment before any recommendation to discontinue first-line docetaxel.

Control Group (standard of care): Participants will receive first line docetaxel until disease progression according to the treating doctor or completion of 10 cycles of treatment. Patients and treating doctors in the control group will not be disclosed to the results of CTC determinations (apart from the screening CTC value).

Intervention Group (CTC-guided treatment group): Participants will receive first line docetaxel until progression by CTCs, and/or disease progression according to the treating doctor or completion of 10 cycles of treatment. CTC results will be available to the treating doctor to guide decision-making. A progressing CTC count on Day 1 will require confirmation with a second CTC count performed on Day 15 of that cycle (except when the Cycle 2 Day 1 CTC count shows progression; needs to be subsequently confirmed by CTC progression on Cycle 3 Day 1 CTC count).If a patient is found to have two successive CTC determinations showing progression by CTCs, the doctor will receive a recommendation from the trial Chief Investigator to discontinue docetaxel on the following cycle.

The reasons of the treating doctor to discontinue docetaxel will be reported in both groups. Patients who discontinue first line docetaxel according to the criteria for each group will be switched to second line chemotherapy with cabazitaxel. After progression on cabazitaxel or completion of 10 cycles, patients will be followed up every three months until the end of study.

Intervention Type
Other

Phase
Phase III

Primary outcome measure
Overall survival is measured by the time from randomisation date to the date of death or last follow-up of the patient. After on-treatment visits, patient status and survival of patient are assessed every 12 weeks (patients' notes and/or interview) until death or loss to follow of the patient, or end of study. The time point of interest for the main analysis is the estimate of overall survival at 24 months.

Secondary outcome measures

1. Proportion of patients in the intervention group that undergo a chemotherapy switch guided by CTC results. This is assessed once 200 patients are recruited and have completed at least 24 weeks of docetaxel treatment
2. Number of cycles of docetaxel administered per patient (with a maximum of 10 cycles allowed) reviewed at 24 months post last patient first visit.
3. Safety is assessed by the rate of adverse events with first and second line chemotherapy; these are assessed at baseline, CxD1 for both treatments, Pre-cabazitaxel follow up visits (if patient receives 10 cycles of docetaxel), EOT and First Off Treatment Follow Up Visit
4. Quality of life is assessed using the FACT-P and EQ-5D questionnaires at baseline, CxD1 for both treatments, Pre-cabazitaxel follow up visits (if patient receives 10 cycles of docetaxel), EOT and First Off Treatment Follow Up Visit
5. Pain (progression and response) is measured by the Brief Pain Inventory Form and the Analgesic use at CxD1 for both treatments
6. Progression Free Survival is measured by the time from randomisation until disease progression, death or end of follow-up, whatever occurs first. Disease progression is defined per the PCWG2 criteria and includes: PSA progression, radiographic progression and clinical progression
6.1. PSA progression is assessed at baseline, CxD1 for both treatments, Pre-cabazitaxel follow up visits (if patient receives 10 cycles of docetaxel), EOT and First Off Treatment Follow Up Visit
6.2. Radiographic progression is assessed by CT/whole Body MRI and bone scans performed at baseline and as per clinical practice, every 2-3 months
6.3. Clinical progression is assessed by pain, analgesic use, patient reported symptoms and clinical assessment and is assessed at baseline and CxD1 for both treatments, Pre-cabazitaxel follow up visits (if patient receives 10 cycles of docetaxel), EOT and First Off Treatment Follow Up Visit
7. Radiographic Progression Free Survival is measured by the time from randomisation until radiographic progression, death or end of follow-up, whatever occurs first
8. Time to First Symptomatic Skeletal Related Event is measured form the date of randomisation to the date of the first documented symptomatic skeletal related event, defined by first occurrence of use of external beam radiation therapy, new symptomatic pathological fractures, spinal cord compression or tumour-related orthopaedic interventions. These events are assessed by imaging assessments at baseline and as per clinical practice, every 2-3 months; adverse events and clinical notes at baseline, CxD1 for both treatments, Pre-cabazitaxel follow up visits (if patient receives 10 cycles of docetaxel), EOT and First Off Treatment Follow Up Visit.
9. Time to CTC progression is measured from randomisation and assessed by CTC blood tests at CxD1 on docetaxel.
10. % Change from baseline values of CTC and PSA during first and second line therapy is assessed by CTC blood test and PSA blood test at CxD1 for both treatments
11. Proportion of patients with a stable CTC count by 12-weeks is assessed by CTC blood tests taken at C3D1 (or earlier if first line treatment discontinued)
12. Health economic assessments assessed by Health Economic Questionnaire Forms collected at CxD1 for both treatments (except C1D1 docetaxel), Pre-cabazitaxel follow up visits (if patient receives 10 cycles of docetaxel), EOT and First Off Treatment Follow Up Visit

Overall study start date
01/07/2014

Completion date
31/01/2022

Reason abandoned (if study stopped)

Participant recruitment issue

Eligibility

Key inclusion criteria
1. Written informed consent
2. Male patients over and including 18 years on the date of consent
3. Histologically confirmed diagnosis of adenocarcinoma of the prostate with availability of archival tumour tissue for molecular analyses (small cell prostate cancer is an exclusion); if no histological diagnosis has ever been acquired a fresh tumour biopsy confirming the presence of CRPC must be pursued
4. Metastatic castration-resistant disease with only bone metastases, confirmed by bone scan (within 4 weeks) or CT/ whole body MRI (within 6 weeks), of starting this trial (Cycle 1 Day 1). Patients with local recurrence, and bone metastases with an associated soft tissue component, will be allowed into the trial. Pelvic lymphadenopathy <2cm in size is not an exclusion.
5. Systemic chemotherapy indicated for disease progression, defined as:
5.1. Bone Scan Progression: Two or more documented new bone lesions over previous 6 months AND/OR
5.2. Increasing serum PSA level: Two consecutive increases in PSA levels documented over a previous reference value obtained at least one week apart are required. If the third PSA value is less than the second, an additional fourth test to confirm the rising PSA is required
6. Baseline laboratory values as stated below:
6.1. Creatinine ≤1.5 x upper limit of normal (ULN)
6.2. Bilirubin ≤1.0 x ULN
6.3. SGOT (AST) and SGPT (ALT) ≤2.5 x ULN
6.4. Castrate serum testosterone level (<50 ng/dL-or-<1.7 nmol/L)
6.5. ANC ≥1.5 x 109cells/L
6.6. Platelet count ≥100 x 109/L
6.7. PSA ≥ 5ng/mL
7. CTC levels ≥ 5 cells / 7.5 mL
8. Prior treatment with abiraterone and/or enzalutamide, discontinued due to disease progression
9. Patient willing to continue primary androgen suppression with gonadotropin-releasing hormone (GnRH) analogues (either agonists or antagonists) throughout the study, unless treated with bilateral orchiectomy
10. Eastern Cooperative Oncology Group (ECOG) performance status (PS) 0-2
11. At least 3 weeks should have elapsed since stopping any investigational agent at the time of randomisation. More than 4 weeks since completion of radiotherapy, other than when a single palliative fraction is administered when only a two week interval is required before trial treatment commencement.
12. Patient has recovered from any therapy-related toxicity to ≤ grade 2, (except alopecia, anaemia and any signs or symptoms of androgen deprivation therapy)
13. Patients willing to comply with the study protocol and follow-up schedule; these conditions should be discussed with the patient before registration in the trial
14. Patients must be surgically sterile or must agree to use effective contraception during the period of the therapy and for 12 months after the last dose of study treatment

Participant type(s)
Patient

Age group

Adult

Lower age limit
18 Years

Sex
Male

Target number of participants
Planned Sample Size: 1178; UK Sample Size: 833

Key exclusion criteria
1. Received any prior cytotoxic chemotherapy as treatment for castration-resistant prostate cancer. Patients that have received chemotherapy for hormone-sensitive metastatic prostate cancer will be allowed onto the trial, if the patient merits retreatment with docetaxel and at least 12 months has elapsed since the patient has completed that previous docetaxel therapy.
2. Measurable soft tissue or lymph node metastases or any metastatic disease outside the bone that is RECIST measurable will be an exclusion (unless it is pelvic nodal disease <2cm in size). Bone metastases with associated soft tissue components will also not be an exclusion.
3. Received any cycling, intermittent or continuous hormonal treatment 28 days prior to randomisation with the exception of the continuous LHRH analogues
4. History of or current documented brain metastasis or carcinomatous meningitis, treated or untreated. Brain imaging for asymptomatic patients is not required.
5. Current symptomatic cord compression requiring surgery or radiation therapy (once the patient is successfully treated the patient will be considered eligible for the study)
6. Active second malignancy (except non-melanoma skin or superficial bladder cancer) defined as requiring anticancer therapy or within the previous two years
7. Serious medical conditions such as heart failure, myocardial infarction, pulmonary thromboembolism within 12 months; stroke or treatment of a major active infection within 3 months of randomisation, as well as any significant medical illness that in the opinion of the Investigator would preclude protocol therapy
8. Planned concomitant participation in another clinical trial of an experimental agent, vaccine, or device. Concomitant participation in observational studies is acceptable.
9. Hypersensitivity to the active substance, to any of its excipients (including polysorbate 80) or to other taxanes
10. Concomitant vaccination with yellow fever vaccine
11. Concomitant use of medicinal products that are strong CYP3A inducers

Date of first enrolment
11/01/2017

Date of final enrolment
31/01/2020

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Royal Marsden Hospital
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Sponsor information

Organisation
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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/043jzw605

Funder(s)

Funder type
Charity

Funder Name
Prostate Cancer UK

Alternative Name(s)
Prostate Cancer, Prostate Action, ProstateUK, prostatecanceruk

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The main trial results will be published in a peer-reviewed journal, on behalf of all collaborators. The first planned publication will focus on the planned feasibility analysis to evaluate the feasibility of utilizing CTCs to inform early discontinuation of docetaxel and switch to cabazitaxel. This will occur after the first 200 patients have been randomised and followed for at least 24 weeks or until docetaxel discontinuation (whichever occurs first).

Intention to publish date
31/01/2023

Individual participant data (IPD) sharing plan
The current data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No