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Sunitinib in advanced urothelial cancer in combination with standard cisplatin /gemcitabine chemotherapy treatment

Submission date 11/03/2008	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 25/04/2008	**Overall study status** Completed	
Last Edited 25/10/2022	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/trial-cisplatin-gemcitabine-sunitinib-advanced-transitional-cell-cancer-urinary-sytem-SUCCINCT

Contact information

Type(s)
Scientific

Contact name
Dr Tom Geldart

Contact details
Department of Oncology and Haematology
Royal Bournemouth Hospital
Castle Lane East
Bournemouth
United Kingdom
BH7 7DW
+44 (0)1202 726088
tom.geldart@rbch.nhs.uk

Additional identifiers

EudraCT/CTIS number
2007-007591-42

IRAS number

ClinicalTrials.gov number

NCT01089088

Secondary identifying numbers
SPON 416-07; C9325/A9347

Study information

Scientific Title
A phase II single-arm trial to evaluate cisplatin and gemcitabine chemotherapy in combination with sunitinib for first-line treatment of patients with advanced transitional carcinoma of the urothelium

Acronym
SUCCINCT

Study objectives
The prognosis for patients with advanced urothelial cancer (predominantly bladder) is poor and approximately 4,700 patients in the United Kingdom (UK) die each year from the disease. Approximately 50% of patients who are fit enough to undergo cisplatin-based chemotherapy will respond to treatment. Median progression-free survival for such patients is approximately 8 months and median overall survival 14 months. Despite a recent increase in our understanding of the molecular basis of bladder cancer, there have been few clinical studies using molecularly-targeted compounds in advanced urothelial cancer.

Sunitinib (Sutent®) is an oral drug that slows down tumour growth and prevents the formation of new blood vessels associated with cancer growth. Clinical trial data has recently demonstrated sunitinib to be highly active in some cancers, including advanced kidney cancer and rare types of stomach cancer. Early phase clinical trial data confirms that sunitinib is active in urothelial cancer. Additional data also demonstrates that sunitinib can be safely combined with standard cisplatin based chemotherapy. This trial will assess whether the addition of sunitinib to standard cisplatin/gemcitibine cancer chemotherapy improves outcome for patients with advanced urothelial disease.

On 24/02/2011 the overall trial end date was changed from 01/12/2010 to 01/10/2011.

Ethics approval required
Old ethics approval format

Ethics approval(s)
West of Scotland Research Ethics Committee on 03/12/2008 (ref: 08/S0703/123).
Each participating centre will be approved through a Regional Ethics Committee (REC) prior to patient recruitment.

Study design
A late phase II single-arm non-randomised open-label multicentre trial

Primary study design
Interventional

Secondary study design

Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

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
Locally advanced and/or metastatic transitional cell carcinoma of the urothelium

Interventions
Patients will be recruited over approximately 18 months. All patients will receive a maximum of six, 21 day cycles of cisplatin and gemcitabine chemotherapy in combination with sunitinib. Each treatment cycle will consist of:
1. Cisplatin 70 mg/m^2 intravenously on day one
2. Gemcitabine 1000 mg/m^2 intravenously on days one and eight
3. Sunitinib 37.5 mg once daily orally on days 2 - 15

Dose modifications or discontinuation of treatment due to toxicity will be implemented according to specific criteria. Assessments will be performed at baseline, at specified times during trial treatment, and at 6 and 12 months from date of enrolment, as per timelines specified in the trial protocol, and including:
1. Diagnostic biopsy and cystoscopy (where appropriate)
2. Cross-sectional imaging (chest, abdomen and pelvis)
3. Physical exam (including height, weight and blood pressure)
4. WHO performance status
5. Haematology
6. Serum biochemistry
7. Thyroid function test
8. Isotopic GFR
9. Isotope bone scintigram (if clinically relevant)
10. Electrocardiogram
11. Plain film chest x-ray
12. Toxicity and late toxicity
13. Pregnancy test (females of childbearing potential)

Additional blood samples will be requested at baseline, and at 6 and 12 months after date of enrolment, for patients participating in an optional translational/pharmacodynamic sub-study. Permission will also be sought to analyse sections of previous histological specimens. These additional samples will be analysed as part of a translational sub-study that will be submitted for separate funding and addressed by separate questions on patient consent form.

Disease response/progression and performance status will be assessed by cross-sectional imaging at baseline, after cycle three of treatment (week 9) and 6 and 12 months after date of enrolment.

If results confirm sufficient activity of the three-drug chemotherapy, the combination treatment will be taken forward into a randomised phase III setting.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Sunitinib (Sutent®), cisplatin, gemcitabine

Primary outcome measure
Activity assessed as progression-free survival at 6 months

Secondary outcome measures
1. Toxicity, during and after treatment: measured at baseline (less than or equal to one week before treatment) and every 21 days whilst on treatment to coincide with the beginning of each new treatment cycle. Late toxicity will be measured at the end of treatment, and at 6 and 12 months from date of enrolment. Serious adverse events (SAEs) will be collected in real time.
2. Tolerability and feasibility of use: determined as the number of patients requiring dose delays or reduction and/or treatment withdrawal and will be determined after all patients have completed treatment
3. Overall survival: calculated at the end of the study duration (2.5 years) based on the time of enrolment to date of death or date censored (date last known to be alive)
4. Progression-free survival (time-to-event): calculated as the time from enrolment to any disease progression and/or death. Those progression-free and alive will be censored at time last seen.
5. Objective response rate: determined relative to baseline prior to treatment cycle four (week nine) and at 6 and 12 months from date of completion of treatment

Overall study start date
01/04/2008

Completion date
18/07/2013

Eligibility

Key inclusion criteria
1. Aged greater than or equal to 18 years, either sex
2. Histologically confirmed transitional cell carcinoma (pure or mixed histology) of urothelium (upper or lower urinary tract)
3. Radiologically measurable locally advanced and/or metastatic disease (T4b Nany Many, Tany N2-3 Many or Tany Nany M1) not amenable to curative treatment with surgery or radiotherapy
4. Estimated life expectancy greater than three months
5. World Health Organization (WHO) performance status 0 - 2
6. Fit to receive cisplatin-containing combination chemotherapy
7. No prior systemic therapy for locally advanced or metastatic disease - patients who have received prior neoadjuvant or adjuvant chemotherapy for urothelial cancer (up to four cycles),

completed at least six months prior to first documented disease progression will remain eligible
8. No prior radiotherapy within one month prior to registration or involving more than 30% of total bone marrow volume
9. No investigational drug within one month prior to registration
10. Adequate renal function (glomerular filtration rate [GFR] greater than 60 ml/min, uncorrected for surface area and measured by isotopic means
11. Adequate bone marrow function (absolute neutrophil count greater than or equal to 1.5 x 10^9/l; platelets greater than or equal to 100 x 10^9/l at baseline)
12. Adequate liver function (bilirubin less than or equal to 1.5 x upper limit of normal [ULN]; alanine aminotransferase [ALT] and alkaline phosphatase [ALP] less than or equal to 2.5 ULN at baseline)
13. Prothrombin time (PT) or International normalised ratio (INR) less than or equal to 1.5 x ULN
14. Written informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
63

Total final enrolment
63

Key exclusion criteria
1. Patients with transitional cell cancer in whom subsequent radical treatment is being considered with a view to possible cure
2. Previous malignancy other than non-melanoma skin cancer, cervical carcinoma in situ or incidental localised prostate cancer
3. Previously-identified central nervous system (CNS) metastases - routine baseline computed tomography (CT) scanning of the head is not a requirement for trial entry and should only be performed if clinically indicated
4. Women who are pregnant or breast feeding. Woman of childbearing potential must have a negative pregnancy test performed within seven days prior to the start of trial therapy.
5. Men and women not prepared to practice method(s) of birth control of established efficacy
6. Known infection with human immunodeficiency virus (HIV) or chronic hepatitis B or C
7. Uncontrolled hypertension
8. Symptomatic coronary artery disease, myocardial infarction within the last six months, congestive cardiac failure greater than New York Heart Association [NYHA] class II, uncontrolled or symptomatic cardiac arrhythmia
9. Clinically significant bacterial or fungal infection
10. Concurrent anticoagulant therapy with warfarin or un-fractionated heparin - patients requiring anti-coagulation may be entered after successful conversion to low molecular weight

heparin (LMWH)
11. Concomitant medication which have adverse interactions with sunitinib

Date of first enrolment
20/07/2009

Date of final enrolment
01/02/2013

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Royal Bournemouth Hospital
Bournemouth
United Kingdom
BH7 7DW

Sponsor information

Organisation
Cardiff University (UK)

Sponsor details
Research and Commercial Division (RACD)
7th Floor
30 - 36 Newport Road
Cardiff
Wales
United Kingdom
CF24 ODE

Sponsor type
University/education

Website
http://www.cf.ac.uk/racdv/index.html

ROR
https://ror.org/03kk7td41

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK (CRUK) (UK) (ref: C9325/A9347) - grant funded by the Feasibility Study Committee (FSC)

Funder Name
Pfizer (UK) - provided sunitinib and its distribution costs free-of-charge (subject to contract)

Funder Name
The Wales Cancer Trials Unit (WCTU) is core funded by CRUK and WCTU core resources will be used to support this trial.

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/04/2015		Yes	No
Plain English results			25/10/2022	No	Yes
HRA research summary			28/06/2023	No	No