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Standard vs Modified Drug Therapy in Renal Cancer

Submission date 15/04/2011	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 15/04/2011	**Overall study status** Completed	
Last Edited 10/09/2024	**Condition category** Cancer	

Plain English summary of protocol
http://cancerhelp.cancerresearchuk.org/trials/trials-search/a-trial-comparing-2-ways-taking-sunitinib-for-advanced-kidney-cancer-star

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
HTA 09/91/21

Study information

Scientific Title
A randomised multi-stage, phase II/III trial of standard first-line therapy (sunitinib or pazopanib) comparing temporary cessation with allowing continuation in the treatment of locally advanced and/or metastatic renal cancer

Acronym
STAR

Study objectives
Current study hypothesis as of 15/05/2013:
The aim of the STAR trial is to evaluate the use of a modified sunitinib or pazopanib schedule compared to the standard sunitinib or pazopanib schedule, in patients with locally advanced and /or metastatic renal cancer.
The trial aims to determine whether a modified sunitinib or pazopanib schedule involving a drug-free interval is non-inferior in terms of 2 year overall survival (OS) and quality adjusted life year (QALY) (averaged over trial recruitment and follow-up) compared to sunitinib or pazopanib given according to the standard strategy.

Previous study hypothesis until 15/05/2013:
The aim of the STAR trial is to evaluate the use of a modified sunitinib schedule compared to the standard sunitinib schedule, in patients with locally advanced and/or metastatic renal cancer.
The trial aims to determine whether a modified sunitinib schedule involving a drug-free interval is non-inferior in terms of 2 year overall survival (OS) and quality adjusted life year (QALY) (averaged over trial recruitment and follow-up) compared to a sunitinib given according to the standard strategy.

On 15/05/2013 the following changes were made to the trial record:
1. The public title was previously "Standard vs Modified Sunitinib Treatment in Renal Cancer"
2. The scientific title was previously "A randomised multi stage, phase II/III trial of sunitinib. Comparing temporary cessation with allowing continuation, at the time of maximal radiological response, in the first-line treatment of locally advanced and/or metastatic renal cancer"

On 31/10/2014 the scientific title was changed from 'A randomised multi-stage, phase II/III trial of standard first-line therapy (sunitinib or pazopanib) comparing temporary cessation with allowing continuation, at the time of maximal radiological response, in the treatment of locally advanced and/or metastatic renal cancer' to 'A randomised multi-stage, phase II/III trial of standard first-line therapy (sunitinib or pazopanib) comparing temporary cessation with allowing continuation in the treatment of locally advanced and/or metastatic renal cancer'.

More details can be found at http://www.nets.nihr.ac.uk/projects/hta/099121
Protocol can be found at http://www.nets.nihr.ac.uk/__data/assets/pdf_file/0005/54761/PRO-09-91-21.pdf

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee North West Liverpool Central, 06/06/2011, REC ref: 11/NW/0246

Study design
Randomised controlled open-label multicentre three-stage 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 clear cell renal cancer

Interventions
Current interventions as of 31/10/2014:
Sunitinib: one cycle of treatment refers to 50mg (starting dose) od, days 1-28, repeated every 42 days.
Pazopanib: one cycle of treatment refers to 800mg (starting dose) od, days 1-42, repeated every 42 days.

All patients receive sunitinib or pazopanib and will be randomised to receive either drug according to either a Conventional continuation strategy (CCS) or drug-free interval strategy (DFIS)

Control arm: Conventional continuation strategy (CCS)
Patients continue sunitinib or pazopanib with regular radiological assessments every 12 weeks until protocol-defined progressive disease (PD) (RECIST), unacceptable cumulative toxicity or patient decision to stop treatment or withdraw from the study.

Research arm: Disease-free interval strategy (DFIS)
Patients stop treatment after 4 cycles of treatment (i.e. 6 months) and continue 6 weekly active surveillance (clinical assessment) and 12 weekly radiological assessment, with planned recommencement of sunitinib or pazopanib at the time of progressive disease (PD) (RECIST). Assuming further disease control, sunitinib or pazopanib is then continued again for a minimum of 4 cycles. At this point, assuming ongoing disease control, sunitinib or pazopanib can be again temporarily stopped at the discretion of the treating clinician until evidence of PD (RECIST) when again sunitinib or pazopanib is restarted. This DFIS is continued until PD occurs during sunitinib or paozpanib treatment, cumulative toxicity or patient decision to stop treatment or withdraw from the study.

Interventions from 15/05/2013 to 31/10/2014:
Sunitinib: one cycle of treatment refers to 50mg (starting dose) od, days 1-28, repeated every 42 days.
Pazopanib: one cycle of treatment refers to 800mg (starting dose) od, days 1-42, repeated every 42 days.

All patients receive sunitinib or pazopanib and will be randomised to receive either drug according to either a Conventional continuation strategy (CCS) or drug-free interval strategy (DFIS)

Control arm: Conventional continuation strategy (CCS)
Patients continue sunitinib or pazopanib with regular radiological assessments every 12 weeks until protocol-defined progressive disease (PD) (RECIST), unacceptable cumulative toxicity or patient decision to stop treatment or withdraw from the study.

Research arm: Disease-free interval strategy (DFIS)
Patients stop treatment and continue 6 weekly active surveillance (clinical assessment) and 12 weekly radiological assessment, with planned recommencement of sunitinib or pazopanib at the time of progressive disease (PD) (RECIST). Assuming further disease control, sunitinib or pazopanib is then continued again until the time of maximal radiological response and for a minimum of 4 cycles. At this point, assuming ongoing disease control, sunitinib or pazopanib can be again temporarily stopped until evidence of PD (RECIST) when again sunitinib or pazopanib is restarted. This DFIS is continued until PD occurs during sunitinib or paozpanib treatment, cumulative toxicity or patient decision to stop treatment or withdraw from the study.

Interventions from time of registration until 15/05/2013:
Sunitinib: one cycle of treatment refers to 50mg (starting dose) od, days 1-28, repeated every 42 days.

All patients receive sunitinib and will be randomised to receive it according to either a Conventional continuation strategy (CCS) or drug-free interval strategy (DFIS)

Control arm: Conventional continuation strategy (CCS)
Patients continue sunitinib with regular radiological assessments every 12 weeks until protocol-defined progressive disease (PD) (RECIST), unacceptable cumulative toxicity or patient decision to stop treatment or withdraw from the study.

Research arm: Disease-free interval strategy (DFIS)
Patients stop treatment and continue 6 weekly active surveillance (clinical assessment) and 12 weekly radiological assessment, with planned recommencement of sunitinib at the time of progressive disease (PD) (RECIST). Assuming further disease control, sunitinib is then continued again until the time of maximal radiological response and for a minimum of 4 cycles. At this point, assuming ongoing disease control, sunitinib can be again temporarily stopped until evidence of PD (RECIST) when again sunitinib is restarted. This DFIS is continued until PD occurs during sunitinib treatment, cumulative toxicity or patient decision to stop treatment or withdraw from the study.

Intervention Type
Other

Phase
Phase II/III

Primary outcome measure
1. Stage A: Recruitment rate/month
2. Stage B: Time to Strategy Failure (TSF)
3. Stage C/Overall: 2 year OS and averaged QALY (over recruitment and follow-up)

Secondary outcome measures
1. Time to strategy failure (TSF)
2. Summative progression free interval (SPFI)
3. Cost effectiveness (health economic endpoints)
4. Toxicity
5. Quality of Life (FACT-G, FSKI-15, EQ-5D and EQ-VAS)
6. Progression free survival (PFS)

Ancilliary study: Translational: tissue and imaging

Overall study start date
03/10/2011

Completion date
31/12/2020

Eligibility

Key inclusion criteria
Current inclusion criteria as of 31/10/2014:
1. Male or female aged ≥ 18 years old
2. Histological confirmation of a component of clear cell renal cell cancer
3. Inoperable loco-regional or metastatic disease
4. No prior systemic therapy for advanced disease (inoperable loco-regional and/or metastatic disease)
4.1 Allowed situation: previous treatment in the SORCE study providing on placebo arm and not active sorafenib arms
5. Eastern Cooperative Oncology Group (ECOG) performance status 0-1
6. Uni-dimensionally measurable disease (RECIST criteria
7. Full blood count:
7.1 Haemoglobin (Hb) ≥ 9 g/dl
7.2. Absolute Neutrophil Count (ANC) ≥ 1 x 10 9/l
7.3. Platelets ≥ 80 x 10 9/l
8. Renal biochemistry: measured or calculated GFR ≥ 30 ml/min
9. Hepatobiliary function
9.1. Aspartate transaminase (AST) or alanine transaminase (ALT) ≤ 2.5 x ULN
9.2. Bilirubin (BR) ≤ 1.5 x ULN, or in patients with Gilberts syndrome BR ≤ x3 x ULN and direct BR ≤ 35%
10. Provided written informed consent prior to any trial-specific procedures
11. Able and willing to comply with the terms of the protocol including:
11.1. Commencement of sunitinib or pazopanib within 5 (actual not working) days of randomisation
11.2. Temporarily stopping sunitinib or pazopanib if randomised to the DFIS arm
11.3. Capable of oral self-medication
11.4 randomisation within 42 days of the baseline CT scan
11.5. Capable of reporting toxicity and completing quality of life (QoL) and medical resource utilisation (MRU) / Health Economics questionnaires
12. If female and of child-bearing potential, must:
12.1. Have a negative pregnancy test within 72 hours prior to randomisation, and not be breast-feeding

12.2. Agree to use adequate, medically approved, contraceptive precautions (oral or barrier contraceptive under the supervision of a General Practitioner or Family Planning Clinic) during, and for 30 days after the last dose of sunitinib or pazopanib
13. If male with a partner of child bearing potential, must agree to use adequate, medically approved, contraceptive precautions (oral or barrier contraceptive under the supervision of a General Practitioner or Family Planning Clinic) during, and for 30 days after the last dose of sunitinib or pazopanib
14. Requirement to start first-line therapy with either sunitinib or pazopanib and decision already made as to which TKI to be used according to local standard practice
15. Allowed situations include:
15.1. Primary renal cancer in-situ or previous nephrectomy
15.2. Previous brain metastases treated with complete surgical resection, Stereotactic Brain Radiation Therapy (SBRT) or gamma knife with no subsequent evidence of progression (patients treated with whole brain radiotherapy are not eligible)
15.3. Previous radiotherapy and/or previous/ongoing bisphosphonates or bone anti-resorptive drugs for the treatment of symptomatic bony metastasis. Care should be taken to follow dental guidelines for the anti-bone resoptive drug.

Inclusion criteria from 15/05/2013 to 31/10/2014:
1. Male or female aged ≥ 18 years old
2. Histological confirmation of predominantly clear cell renal cell cancer
3. Inoperable loco-regional or metastatic disease
4. No prior systemic therapy for advanced disease (inoperable loco-regional and/or metastatic disease)
5. Eastern Cooperative Oncology Group (ECOG) performance status 0-1
6. Uni-dimensionally measurable disease (RECIST criteria, see Appendix 3)
7. Full blood count:
7.1 Haemoglobin (Hb) ≥ 9 g/dl
7.2. Absolute Neutrophil Count (ANC) ≥ 1 x 109/l
7.3. Platelets ≥ 80 x 109/l
8. Renal biochemistry: measured or calculated GFR ≥ 30 ml/min
9. Hepatobiliary function
9.1. Aspartate transaminase (AST) or alanine transaminase (ALT) ≤ 2.5 x ULN
9.2. Bilirubin (BR) ≤ 1.5 x ULN, or or in patients with Gilberts syndrome BR ≤ x3 x ULN and, direct BR ≤ 35%
10. Provided written informed consent prior to any trial-specific procedures
11. Able and willing to comply with the terms of the protocol including:
11.1. Commencement of sunitinib or pazopanib within 3 days of randomisation
11.2. Temporarily stopping sunitinib or pazopanibif randomised to the DFIS arm
11.3. Capable of oral self-medication
11.4. Capable of reporting toxicity and completing quality of life (QoL) and medical resource utilisation (MRU) questionnaires
12. If female and of child-bearing potential, must:
12.1. Have a negative pregnancy test within 72 hours prior to randomisation, and not be breast-feeding
12.2. Agree to use adequate, medically approved, contraceptive precautions (oral or barrier contraceptive under the supervision of a General Practitioner or Family Planning Clinic) during, and for 6 months after the last dose of sunitinib or pazopanib
13. If male with a partner of child bearing potential, must agree to use adequate, medically approved, contraceptive precautions (oral or barrier contraceptive under the supervision of a General Practitioner or Family Planning Clinic) during, and for 6 months after the last dose of sunitinib or pazopanib

14. Allowed situations include:
14.1. Primary renal cancer in-situ or previous nephrectomy
14.2. Previous brain metastases treated with complete surgical resection, Stereotactic Brain Radiation Therapy (SBRT) or gamma knife with no subsequent evidence of progression (patients treated with whole brain radiotherapy are not eligible)
14.3. Previous treatment in the SORCE study providing on placebo arm and not active sorafenib arms
14.4. Previous radiotherapy and/or previous/ongoing bisphosphonates or bone anti-resorptive drugs for the treatment of symptomatic bony metastasis

Inclusion criteria from time of registration until 15/05/2013:
1. Male or female aged ≥ 18 years old
2. Histological confirmation of predominantly clear cell renal cell cancer
3. Inoperable loco-regional or metastatic disease
4. No prior systemic therapy for advanced disease (inoperable loco-regional and/or metastatic disease)
5. Eastern Cooperative Oncology Group (ECOG) performance status 0-1
6. Uni-dimensionally measurable disease (RECIST criteria, see Appendix 3)
7. Full blood count:
7.1 Haemoglobin (Hb) ≥ 9 g/dl
7.2. Absolute Neutrophil Count (ANC) ≥ 1 x 109/l
7.3. Platelets ≥ 80 x 109/l
8. Renal biochemistry: measured or calculated GFR ≥ 30 ml/min
9. Hepatobiliary function
9.1. Aspartate transaminase (AST) or alanine transaminase (ALT) ≤ 2.5 x ULN
9.2. Bilirubin (BR) ≤ 1.5 x ULN, or or in patients with Gilberts syndrome BR ≤ x3 x ULN and, direct BR ≤ 35%
10. Provided written informed consent prior to any trial-specific procedures
11. Able and willing to comply with the terms of the protocol including:
11.1. Commencement of sunitinib within 3 days of randomisation
11.2. Temporarily stopping sunitinib if randomised to the DFIS arm
11.3. Capable of oral self-medication
11.4. Capable of reporting toxicity and completing quality of life (QoL) and medical resource utilisation (MRU) questionnaires
12. If female and of child-bearing potential, must:
12.1. Have a negative pregnancy test within 72 hours prior to randomisation, and not be breast-feeding
12.2. Agree to use adequate, medically approved, contraceptive precautions (oral or barrier contraceptive under the supervision of a General Practitioner or Family Planning Clinic) during, and for 6 months after the last dose of sunitinib
13. If male with a partner of child bearing potential, must agree to use adequate, medically approved, contraceptive precautions (oral or barrier contraceptive under the supervision of a General Practitioner or Family Planning Clinic) during, and for 6 months after the last dose of sunitinib
14. Allowed situations include:
14.1. Primary renal cancer in-situ or previous nephrectomy
14.2. Previous brain metastases treated with complete surgical resection or gamma knife with no subsequent evidence of progression (patients treated with whole brain radiotherapy are not eligible)
14.3. Previous treatment in the SORCE study providing on placebo arm and not active sorafenib

arms
14.4. Previous radiotherapy and/or previous/ongoing bisphosphonates or bone anti-resorptive drugs for the treatment of symptomatic bony metastasis

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
210 patients for phase II feasibility, continuing to 1000 patients in phase III trial

Total final enrolment
920

Key exclusion criteria
Current exclusion criteria as of 31/10/2014:
1. Pulmonary or mediastinal disease causing obstruction or clinically significant bleeding /haemoptysis
2. Patients with an estimated life expectancy of <6 months
3. Known contraindications to the particular TKI to be used (i.e. sunitinib or pazopanib)
4. Any previous treatment with sunitinib, pazopanib or other tyrosine kinase inhibitor (including in the adjuvant setting)
5. Untreated brain metastases
6. Any concurrent or previous other invasive cancer that could confuse diagnosis or endpoints
6.1. Allowed situations include (but not limited to): non-melanomatous skin cancer or superficial bladder cancer; for all other cases please discuss with Clinical Trials Research Unit (CTRU))
7. Hypersensitivity to the particular TKI to be used (i.e. sunitinib or pazopanib)
8. Any concomitant medication or substances forming part of local ongoing care known to significantly affect, or have the potential to significantly affect, the activity or pharmacokinetics of the particular TKI to be used (i.e. sunitinib or pazopanib)
9. Poorly controlled hypertension despite maximal medical therapy
10. Any other serious medical or psychiatric condition which in the opinion of the investigator could affect participation in the STAR trial, including gastro-intestinal abnormalities limiting effectiveness of orally administrated drugs, uncontrolled infections, current or recent history of clinically significant cardiovascular disease, significant haemorrhage or gastrointestinal perforation or fistula which, in the opinion of the local investigator, would render the patient unsuitable for standard sunitinib or pazopanib therapy

Exclusion criteria from 15/05/2013 to 31/10/2014:
1. Pulmonary or mediastinal disease causing obstruction or bleeding/haemoptysis
2. Patients with an estimated life expectancy of <6 months
3. Known contraindications to sunitinib or pazopanib
4. No previous treatment with sunitinib, pazopanib or other tyrosine kinase inhibitor (including

in the adjuvant setting)
5. Untreated brain metastases
6. Any concurrent or previous other invasive cancer that could confuse diagnosis (non-melanomatous skin cancer or superficial bladder cancer acceptable, for all other cases please discuss with Clinical Trials Research Unit (CTRU))
7. Hypersensitivity to sunitinib or pazopanib
8. Any concomitant medication or substances forming part of local ongoing care known to significantly affect, or have the potential to significantly affect, the activity or pharmacokinetics of sunitinib or pazopanib (see section 10.2 for further information on concomitant medications)
9. Poorly controlled hypertension despite maximal medical therapy
10. Any other serious medical or psychiatric condition which in the opinion of the investigator could affect participation in the STAR trial, including gastro-intestinal abnormalities limiting effectiveness of orally administrated drugs, uncontrolled infections, current or recent history of clinically significant cardiovascular disease, significant haemorrhage or gastrointestinal perforation or fistula which, in the opinion of the local investigator, would render the patient unsuitable for standard sunitinib or pazopanib therapy

Exclusion criteria from time of registration until 15/05/2013:
1. Pulmonary or mediastinal disease causing obstruction or bleeding/haemoptysis
2. Patients with an estimated life expectancy of <6 months
3. Known contraindications to sunitinib
4. No previous treatment with sunitinib or other tyrosine kinase inhibitor (including in the adjuvant setting)
5. Untreated brain metastases
6. Any concurrent or previous other invasive cancer that could confuse diagnosis (non-melanomatous skin cancer or superficial bladder cancer acceptable, for all other cases please discuss with Clinical Trials Research Unit (CTRU))
7. Hypersensitivity to sunitinib
8. Any concomitant medication or substances forming part of local ongoing care known to significantly affect, or have the potential to significantly affect, the activity or pharmacokinetics of sunitinib (see section 10.2 for further information on concomitant medications)
9. Poorly controlled hypertension despite maximal medical therapy
10. Any other serious medical or psychiatric condition which in the opinion of the investigator could affect participation in the STAR trial, including gastro-intestinal abnormalities limiting effectiveness of orally administrated drugs, uncontrolled infections, current or recent history of clinically significant cardiovascular disease which, in the opinion of the local investigator, would render the patient unsuitable for standard sunitinib therapy

Date of first enrolment
03/10/2011

Date of final enrolment
03/04/2018

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Unit of Clinical Oncology
Sheffield
United Kingdom
S10 2SJ

Sponsor information

Organisation
University of Leeds (UK)

Sponsor details
University of Leeds
Leeds
England
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LS2 9JT

Sponsor type
University/education

ROR
https://ror.org/024mrxd33

Funder(s)

Funder type
Government

Funder Name
NIHR Health Technology Assessment Programme - HTA (UK), Grant Ref: 09/91/21

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date
31/12/2022

Individual participant data (IPD) sharing plan

De-identified individual participant data datasets generated and/or analysed during the current study will be available upon request from the Clinical Trials Research Unit, University of Leeds (contact CTRU-DataAccess@leeds.ac.uk in the first instance). Data will be made available at the end of the trial, i.e. usually when all primary and secondary endpoints have been met and all key analyses are complete. Data will remain available from then on for as long as CTRU retains the data.

CTRU makes data available by a 'controlled access' approach. Data will only be released for legitimate secondary research purposes, where the Chief Investigator, Sponsor and CTRU agree that the proposed use has scientific value and will be carried out to a high standard (in terms of scientific rigour and information governance and security), and that there are resources available to satisfy the request. Data will only be released in line with participants' consent, all applicable laws relating to data protection and confidentiality, and any contractual obligations to which the CTRU is subject. No individual participant data will be released before an appropriate agreement is in place setting out the conditions of release. The agreement will govern data retention, usually stipulating that data recipients must delete their copy of the released data at the end of the planned project.

The CTRU encourages a collaborative approach to data sharing, and believe it is best practice for researchers who generated datasets to be involved in subsequent uses of those datasets. Recipients of trial data for secondary research will also receive data dictionaries, copies of key trial documents and any other information required to understand and reuse the released datasets.

The conditions of release for aggregate data may differ from those applying to individual participant data. Requests for aggregate data should also be sent to the above email address to discuss and agree suitable requirements for release.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	14/12/2012		Yes	No
Abstract results		19/09/2021	30/09/2021	No	No
Results article		13/02/2023	17/02/2023	Yes	No
HRA research summary			28/06/2023	No	No
Plain English results			09/02/2024	No	Yes
Results article	Temporary treatment cessation compared with continuation of tyrosine kinase inhibitors for adults with renal cancer: the STAR non-inferiority RCT	01/08/2024	10/09/2024	Yes	No