

# Standard vs Modified Drug Therapy in Renal Cancer

<b>Submission date</b> 15/04/2011	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 15/04/2011	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 10/09/2024	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data

## 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

### Contact name

Prof Janet Brown

### Contact details

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University of Sheffield  
Sheffield  
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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](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 pazopanib 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 pazopanib 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)

Ancillary 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  $\geq 18$  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)  $\geq 9$  g/dl
  - 7.2. Absolute Neutrophil Count (ANC)  $\geq 1 \times 10^9$ /l
  - 7.3. Platelets  $\geq 80 \times 10^9$ /l
8. Renal biochemistry: measured or calculated GFR  $\geq 30$  ml/min
9. Hepatobiliary function
  - 9.1. Aspartate transaminase (AST) or alanine transaminase (ALT)  $\leq 2.5 \times$  ULN
  - 9.2. Bilirubin (BR)  $\leq 1.5 \times$  ULN, or in patients with Gilberts syndrome BR  $\leq 3 \times$  ULN and direct BR  $\leq 35\%$
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 resorptive drug.

Inclusion criteria from 15/05/2013 to 31/10/2014:

1. Male or female aged  $\geq 18$  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)  $\geq 9$  g/dl
  - 7.2. Absolute Neutrophil Count (ANC)  $\geq 1 \times 10^9$ /l
  - 7.3. Platelets  $\geq 80 \times 10^9$ /l
8. Renal biochemistry: measured or calculated GFR  $\geq 30$  ml/min
9. Hepatobiliary function
  - 9.1. Aspartate transaminase (AST) or alanine transaminase (ALT)  $\leq 2.5 \times$  ULN
  - 9.2. Bilirubin (BR)  $\leq 1.5 \times$  ULN, or or in patients with Gilberts syndrome BR  $\leq 3 \times$  ULN and, direct BR  $\leq 35\%$
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 pazopanib 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 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  $\geq 18$  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)  $\geq 9$  g/dl
  - 7.2. Absolute Neutrophil Count (ANC)  $\geq 1 \times 10^9/\text{l}$
  - 7.3. Platelets  $\geq 80 \times 10^9/\text{l}$
- 8. Renal biochemistry: measured or calculated GFR  $\geq 30$  ml/min
- 9. Hepatobiliary function
  - 9.1. Aspartate transaminase (AST) or alanine transaminase (ALT)  $\leq 2.5 \times \text{ULN}$
  - 9.2. Bilirubin (BR)  $\leq 1.5 \times \text{ULN}$ , or or in patients with Gilberts syndrome BR  $\leq 3 \times \text{ULN}$  and, direct BR  $\leq 35\%$
- 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 administered 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 administered 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 administered 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  
United Kingdom  
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?
<a href="#">Protocol article</a>	protocol	14/12/2012		Yes	No
<a href="#">Abstract results</a>		19/09/2021	30/09/2021	No	No
<a href="#">Results article</a>		13/02/2023	17/02/2023	Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Plain English results</a>			09/02/2024	No	Yes
<a href="#">Results article</a>	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