

A randomised phase III placebo-controlled trial evaluating the addition of celecoxib to standard treatment of transitional cell carcinoma of the bladder

Submission date 12/01/2006	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 23/02/2006	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 18/09/2019	Condition category Cancer	<input type="checkbox"/> Individual participant data

Plain English summary of protocol

<https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-standard-treatment-with-or-without-celecoxib-for-transitional-cell-bladder-cancer>

Contact information

Type(s)

Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

UR0601

Study information

Scientific Title

A randomised phase III placebo-controlled trial evaluating the addition of celecoxib to standard treatment of transitional cell carcinoma of the bladder

Acronym

BOXIT (Bladder COX-2 Inhibition Trial)

Study objectives

1. To determine if the addition of the oral cyclooxygenase-2(COX-2) inhibitor celecoxib to standard therapy is more effective in terms of recurrence-free survival at three years than standard therapy alone towards the treatment of superficial transitional cell carcinoma (TCC) of the bladder at high risk of recurrence
2. To determine if the addition of the oral COX-2 inhibitor celecoxib to standard therapy is more effective in terms of recurrence-free survival at three years than standard therapy alone for the treatment of superficial TCC of the bladder at intermediate risk of recurrence.

Please note, as of 15/02/2011 the anticipated end date and target participant number for this trial have been updated. The initial anticipated end date of 15/05/2010 has been extended to 01/11/2011 and the original target number of participants reduced from 900 to 412.

As of 10/01/2012, the target number of participants has been updated from 412 (900 at time of registration) to 475. The overall trial end date has been further extended to 01/04/2012.

Ethics approval required

Old ethics approval format

Ethics approval(s)

NRES Committee East of England - Cambridge East, 20/11/2006, ref: 06/Q0104/57

Study design

Randomised phase III parallel-group multi-centre double-blind placebo-controlled clinical trial

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

Health condition(s) or problem(s) studied

Transitional Cell Carcinoma (TCC) of the bladder

Interventions

Celecoxib: 400 mg daily (200 mg twice a day [bid]) for two years or placebo.

Intervention Type

Drug

Phase

Phase III

Drug/device/biological/vaccine name(s)

Celecoxib

Primary outcome measure

Recurrence-free survival of TCC of the bladder at three years

Secondary outcome measures

1. Recurrence rate (overall and at three months)
2. Progression to invasive disease (high-risk patients)
3. Safety and tolerability of celecoxib
4. Disease-free survival
5. Overall survival
6. Quality of life
7. Cost effectiveness
8. Reduction in recurrence within the first two years compared with that observed beyond two years

Overall study start date

15/05/2006

Completion date

01/04/2012

Eligibility

Key inclusion criteria

Current inclusion criteria as of 27/09/2011:

1. Primary or recurrent non-muscle invasive TCC of the bladder of high or intermediate risk of recurrence:
High risk cases are those patients who are scheduled to receive BCG. Intermediate risk includes all other Ta, T1 cases excluding low risk disease.
Full definitions of the risk groups based on EAU guidelines are given in appendix 4:
2. Age ≥ 18 .
3. WHO performance status 0, 1 or 2.
4. No evidence of upper tract TCC on imaging studies within the past 36 months or before randomisation.

5. Pre-treatment haematology and biochemistry values within acceptable limits:
 - 5.1 haemoglobin ≥ 10 g/dl;
 - 5.2 neutrophil count $\geq 1.5 \times 10^9/l$;
 - 5.3 platelets $\geq 100 \times 10^9/l$;
 - 5.4 WBC $\geq 3.0 \times 10^9/l$ or ANC $\geq 1.5 \times 10^9/l$;
 - 5.5 Serum creatinine $< 1.5 \times$ UNL.
6. Negative pregnancy test for women of child-bearing potential.
7. At least 2 months since prior celecoxib or NSAIDs (other than low dose aspirin (≤ 150 mg daily)).
8. Baseline ECG showing no evidence of established or acute ischaemic heart disease (e.g. left bundle branch block, pathological q waves, ST elevation or ST-segment depression) and normal clinical cardiovascular assessment.
9. Written informed consent and available for long-term follow-up.

Previous inclusion criteria:

1. Primary or recurrent superficial TCC of the bladder of intermediate or high risk of recurrence. High-risk patients are defined as:
 - a. Any Grade 3
 - b. Tis (i.e. carcinoma in situ)
 - c. T1 Grade 2 and multiple tumours (≥ 3)
 - d. T1 Grade 2 and highly recurrent (≥ 3 per year)
 - e. T1 Grade 2 and diameter ≥ 3 cm
 Intermediate-risk patients are defined as:
 - a. T1 Grade 2 (other than high risk)
 - b. Ta Grade 2 and multiple (≥ 3)
 - c. Ta Grade 2 and diameter ≥ 3 cm
 - d. Ta Grade 2 and ≥ 2 recurrences in past year
 - e. Ta Grade 1 and multiple (≥ 3)
 - f. Ta Grade 1 and diameter ≥ 3 cm
 - g. Ta Grade 1 and highly recurrent (≥ 3 in past year)
 - h. T1 Grade 1
2. Age > 18
3. World Health Organisation (WHO) performance status 0, 1 or 2
4. Normal kidneys and urethras on imaging study within the past 36 months or before randomisation
5. Pre-treatment haematology and biochemistry values within acceptable limits:
 - a. Haemoglobin ≥ 10 g/dl
 - b. Neutrophil count $\geq 1.5 \times 10^9/l$
 - c. Platelets $\geq 100 \times 10^9/l$
 - d. White blood cell count (WBC) $\geq 3.0 \times 10^9/l$ or absolute neutrophil count (ANC) $\geq 1.5 \times 10^9/l$
 - e. Serum creatinine $< 1.5 \times$ upper normal limit (UNL)
6. Negative pregnancy test for women of childbearing potential
7. At least two months since prior taking of celecoxib or other non-steroidal anti-inflammatory drugs (NSAIDs) other than low dose aspirin (150 mg daily)
8. Normal baseline electrocardiogram (ECG) and normal clinical cardiovascular assessment
9. Written informed consent and availability for long-term follow-up

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Both

Target number of participants

475

Total final enrolment

472

Key exclusion criteria

Current exclusion criteria as of 27/09/2011:

1. Low risk of recurrence TCC of the bladder (i.e. stage Ta, G1, solitary (<3), <3cm and <3 occurrences in the past 12 months; stage Ta, G2, solitary (<3), <3cm and <2 recurrences in past 12 months).
2. Carcinoma involving the prostatic urethra or upper urinary tract.
3. \geq T2 TCC or previous history of \geq T2.
4. Significant bleeding disorder, such as familial/genetic pre-disposition to clotting disorder e.g. haemophilia and Von Willebrand disease.
5. Chronic or acute renal disorder.
6. Oesophageal gastric, pyloric channel, or duodenal ulceration diagnosed or treated within the past 30 days.
7. Active or previous peptic ulceration or gastrointestinal bleeding in the last year.
8. Inflammatory bowel disease (e.g. Crohn's disease or ulcerative colitis).
9. Pancreatitis.
10. Pregnant or lactating women or women of childbearing potential unwilling or unable to use adequate non-hormonal contraception.
11. Hypersensitivity or adverse reactions to sulfonamides, COX-2 inhibitors, salicylates, or other NSAIDs.
12. On current or planned chronic NSAIDs therapy (except low dose aspirin \leq 150 mg once daily). Chronic use of NSAIDs is defined as a frequency of 1 or more a day for more than 50 consecutive days in a year.
13. Regular use of celecoxib within the previous 8 weeks.
14. Current or long-term use of oral corticosteroids.
15. Known or suspected congestive heart failure (II-IV NYHA defined in appendix 10) and/or coronary heart disease, previous history of myocardial infarction, coronary artery bypass graft, invasive coronary revascularization or angina, uncontrolled arterial hypertension (ie BP >160 /100mmHg).
16. Patients with diabetes controlled by diet and oral medication are eligible for the study; however patients treated with insulin will be excluded.
17. Past history of stroke/TIA, symptomatic peripheral vascular disease, or documented abdominal aortic aneurysm.
18. Other malignancy within the past 2 years, except: non-melanomatous skin cancer cured by excision, adequately treated carcinoma in situ of the cervix, DCIS/LCIS of the breast or prostate cancer in patients who have a life expectancy of over 5 years upon trial entry.
19. Concurrent chemotherapy other than intravesical MMC.
20. Psychiatric or addictive disorders which could preclude obtaining informed consent.

Previous exclusion criteria:

1. Low risk of recurrence TCC of the bladder (i.e. stage Ta, G1, solitary [<3], <3 cm and <3 recurrences in past 12 months; stage Ta, G2, solitary [<3], <3 cm and <3 recurrences in past 12 months)
2. Carcinoma involving the prostatic urethra or upper urinary tract
3. T2 or $>$ T2 TCC
4. Significant bleeding disorder
5. Chronic or acute renal disorder
6. Oesophageal gastric, pyloric channel, or duodenal ulceration diagnosed or treated within the past 30 days
7. Active or previous peptic ulceration or gastrointestinal bleeding in the last year
8. Inflammatory bowel disease (e.g. Crohns disease or ulcerative colitis)
9. Pancreatitis
10. Pregnant or lactating women or women of childbearing potential unwilling or unable to use adequate non-hormonal contraception
11. Hypersensitivity or adverse reactions to sulfonamides, COX-2 inhibitors, salicylates, or other NSAIDs
12. On current or planned chronic NSAIDs therapy (except low-dose aspirin ≤ 150 mg once daily). Chronic use of NSAIDs is defined as a frequency of one or more a day, for more than a total of 50 days per year.
13. Regular use of low-dose celecoxib within the previous eight weeks
14. Current or long-term use of corticosteroids
15. Known or suspected congestive heart failure ($>$ New York Heart Association [NYHA] I) and/or coronary heart disease, previous history of myocardial infarction, uncontrolled arterial hypertension (i.e. blood pressure $>160/90$ mmHg under treatment with two anti-hypertensive drugs), rhythm abnormalities requiring permanent treatment. ECG should be within limits prior to starting trial therapy. Echocardiogram although not essential can be carried out if the investigator judges it to be necessary.
16. Patients with diabetes controlled by diet and oral medication are eligible for the study; however patients with insulin dependent diabetes are excluded
17. Past history of stroke/transient ischemic attack (TIA), symptomatic peripheral vascular disease
18. Other malignancy within the past five years, except: non-melanomatous skin cancer cured by excision, adequately treated carcinoma in situ of the cervix or ductal carcinoma in situ (DCIS) /lobular carcinoma in situ (LCIS) of the breast
19. Concurrent chemotherapy other than intravesical mitomycin C (MMC)
20. Psychiatric or addictive disorders which could preclude obtaining informed consent

Date of first enrolment

15/05/2006

Date of final enrolment

01/04/2012

Locations

Countries of recruitment

England

United Kingdom

Study participating centre
University College London
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Sponsor information

Organisation

The Institute of Cancer Research (UK)

Sponsor details

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Sponsor type

Research organisation

ROR

<https://ror.org/043jzw605>

Funder(s)

Funder type

Charity

Funder Name

Cancer Research UK - C8262/A5669

Alternative Name(s)

CR_UK, Cancer Research UK - London, CRUK

Funding Body Type

Private sector organisation

Funding Body Subtype

Other non-profit organizations

Location

United Kingdom

Results and Publications

Publication and dissemination plan

Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Plain English results				No	Yes
Results article	results	01/12/2014		Yes	No
Results article	results	01/04/2019	14/08/2019	Yes	No