

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

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<b>Registration date</b> 23/02/2006	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 27/11/2025	<b>Condition category</b> 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

### Contact name

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## Additional identifiers

### Protocol serial number

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 3 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 3 years than standard therapy alone for the treatment of superficial TCC of the bladder at intermediate risk of recurrence.

## 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

## Study type(s)

Treatment

## 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 2 years or placebo.

Added 27/11/2025:

Additional Data Linkage Information:

Participants from this trial will also be included in the INTERACT project which will link to their data held by NHS England. For more information, please see the INTERACT website:

<https://www.icr.ac.uk/interact>.

## Intervention Type

Drug

## Phase

Phase III

## **Drug/device/biological/vaccine name(s)**

Celecoxib

## **Primary outcome(s)**

Recurrence-free survival of TCC of the bladder at 3 years

## **Key secondary outcome(s)**

1. Recurrence rate (overall and at 3 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 2 years compared with that observed beyond 2 years

## **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  $\geq 18$  years.
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  $\geq 10$  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 ( $\leq 150$ 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 ( $\geq 3$ )
  - d. T1 Grade 2 and highly recurrent ( $\geq 3$  per year)
  - e. T1 Grade 2 and diameter  $\geq 3$  cm
- Intermediate-risk patients are defined as:
- a. T1 Grade 2 (other than high risk)
  - b. Ta Grade 2 and multiple ( $\geq 3$ )
  - c. Ta Grade 2 and diameter  $\geq 3$  cm
  - d. Ta Grade 2 and  $\geq 2$  recurrences in past year
  - e. Ta Grade 1 and multiple ( $\geq 3$ )
  - f. Ta Grade 1 and diameter  $\geq 3$  cm
  - g. Ta Grade 1 and highly recurrent ( $\geq 3$  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  $\geq 10$  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

**Healthy volunteers allowed**

No

**Age group**

Mixed

**Lower age limit**

18 years

**Upper age limit**

100 years

**Sex**

All

**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  $>160/100$ mmHg).
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  $\leq 150$  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**

United Kingdom

England

**Study participating centre**

University College London

-

London

England

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## Sponsor information

**Organisation**

The Institute of Cancer Research (UK)

**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, Cancer Research UK (CRUK), CRUK

**Funding Body Type**

Private sector organisation

**Funding Body Subtype**

Other non-profit organizations

**Location**

United Kingdom

## Results and Publications

**Individual participant data (IPD) sharing plan**

**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?
<a href="#">Results article</a>	results	01/12/2014		Yes	No
<a href="#">Results article</a>	results	01/04/2019	14/08/2019	Yes	No
<a href="#">Plain English results</a>				No	Yes