ISRCTN84681538 https://doi.org/10.1186/ISRCTN84681538

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

Registration date
23/02/2006

Last Edited
27/11/2025

Recruitment status
No longer recruiting

Overall study status
Completed

Condition category
Cancer

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] 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
Prof John Kelly

Contact details
Room 447, Department of Oncology
UCL (Division Of Surgery & Interventional Science) 4th Floor
74 Huntley Street
London
United Kingdom
WC1E 6AU
+44 (0)20 7679 6490
j.d.kelly@ucl.ac.uk

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 ≥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 ≥10 g/dl;
5.2 neutrophil count ≥ 1.5 x 109/l;
5.3 platelets ≥ 100 x 109/l;
5.4 WBC ≥ 3.0 x 109/l or ANC ≥ 1.5 x 109/l;
5.5 Serum creatinine < 1.5 x 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 (≤ 150mg 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 ≥1.5 x 10^9/l
c. Platelets ≥100 x 10^9/l
d. White blood cell count (WBC) ≥3.0 x 10^9/l or absolute neutrophil count (ANC) ≥1.5 x 10^9/l
e. Serum creatinine <1.5 x 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. ≥T2 TCC or previous history of ≥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 ≤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
United Kingdom

England

Study participating centre
University College London
-
London
England
WC1E 6AU

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?
Results article	results	01/12/2014		Yes	No
Results article	results	01/04/2019	14/08/2019	Yes	No
Plain English results				No	Yes