Clinical trial results:
A Phase III randomised trial of Peri-Operative chemotherapy versus sUrveillance in upper Tract urothelial cancer

Summary

EudraCT number	2011-002577-33
Trial protocol	GB
Global end of trial date	21 October 2025

Results information

Result version number	v1 (current)
This version publication date	01 November 2026
First version publication date	01 November 2026

Trial information

Trial identification

Sponsor protocol code	ICR-CTSU/2011/10031

Additional study identifiers

ISRCTN number	ISRCTN98387754
ClinicalTrials.gov id (NCT number)	NCT01993979
WHO universal trial number (UTN)	-
Other trial identifiers	Sponsor Identification Number: CCR3675, ICR-CTSU Protocol Number:: ICR-CTSU/2011/10031

Notes:

Sponsors

Sponsor organisation name	The Institute of Cancer Research Clinical Trials and Statistics Unit
Sponsor organisation address	32 Oakleaf Avenue, Sutton, United Kingdom, SM25GP
Public contact	Rebecca Lewis, Institute of Cancer Research, ctsu@icr.ac.uk
Scientific contact	Rebecca Lewis, Institute of Cancer Research, ctsu@icr.ac.uk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 February 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 February 2022
Global end of trial reached?	Yes
Global end of trial date	21 October 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine whether adjuvant combination chemotherapy improves disease-free survival for patients with resected histologically confirmed muscle invasive (pT2-T4, N0-3) or node positive upper tract urothelial carcinoma.

Protection of trial subjects:

Detailed participant information materials and the opportunity to ask questions prior to enrolment; close monitoring and management of toxicities, particularly during the treatment phase; adherence to relevant data protection regulations; oversight of emerging data by an Independent Data Monitoring Committee (IDMC).

Background therapy:

None

Evidence for comparator:

Prior to this trial, there was some evidence for a benefit of chemotherapy in this setting from non-randomised studies.

Actual start date of recruitment	19 June 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 260
Worldwide total number of subjects	260
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	100

From 65 to 84 years	156
85 years and over	4

Subject disposition

Recruitment

Recruitment details:

Recruitment took place from June 2012 to November 2017 at 57 UK centres

Pre-assignment

Screening details:

Screening information is not available

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Not applicable - open-label trial

Arms

Are arms mutually exclusive?	Yes
Arm title	Surveillance

Arm description:

Participants have post-surgery monitoring according to standard practice

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Chemotherapy

Arm description:

Participants receive four 21-day cycles of Gemcitabine-Cisplatin or, if GFR 30-49 ml/min, gemcitabine-carboplatin chemotherapy will be given.

Arm type	Experimental
Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1000mg/m2 day 1 and day 8 as 30 minute intravenous infusion

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin given instead of cisplatin only for participants with a creatinine clearance of 30-49ml/min. AUC 4.5 or AUC 5 (according to local practice) calculated according to the Calvert formula.

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

70mg/m2 day 1 as a 4 hour intravenous infusion.

If the patient’s calculated or measured GFR was 50-70 mls/min then it was recommended that the cisplatin dose is split over 2 days (35mg/m2 /day) and given on day 1 and 2 if this was standard practice locally.

Number of subjects in period 1	Surveillance	Chemotherapy
Started	129	131
Completed	129	131

Baseline characteristics

Reporting groups	
Reporting group title	Surveillance
Reporting group description:	
Participants have post-surgery monitoring according to standard practice	
Reporting group title	Chemotherapy
Reporting group description:	
Participants receive four 21-day cycles of Gemcitabine-Cisplatin or, if GFR 30-49 ml/min, gemcitabine-carboplatin chemotherapy will be given.	

Reporting group values	Surveillance	Chemotherapy	Total
Number of subjects	129	131	260
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	57	43	100
From 65-84 years	69	87	156
85 years and over	3	1	4
Age continuous			
Units: years			
median	66	69	
full range (min-max)	43 to 88	36 to 85	-
Gender categorical			
Units: Subjects			
Female	46	38	84
Male	83	93	176
Not reported	0	0	0

End points

End points reporting groups

Reporting group title	Surveillance
Reporting group description:	
Participants have post-surgery monitoring according to standard practice	
Reporting group title	Chemotherapy
Reporting group description:	
Participants receive four 21-day cycles of Gemcitabine-Cisplatin or, if GFR 30-49 ml/min, gemcitabine-carboplatin chemotherapy will be given.	
Subject analysis set title	Allocated surveillance
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Intention-to-treat	
Subject analysis set title	Allocated chemotherapy
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Intention-to-treat	
Subject analysis set title	Received surveillance
Subject analysis set type	Safety analysis
Subject analysis set description:	
Underwent surveillance and did not receive any study drug	
Subject analysis set title	Received chemotherapy
Subject analysis set type	Safety analysis
Subject analysis set description:	
Received at least one dose of study drug	

Primary: Disease-free survival

End point title	Disease-free survival
End point description:	
Time from randomisation to either first recurrence in the tumour bed, first metastasis, or death from any cause.	
End point type	Primary
End point timeframe:	
Up to 5 years post-randomisation	

End point values	Surveillance	Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	131		
Units: Proportion event-free at 5 years				
number (confidence interval 95%)	0.45 (0.36 to 0.55)	0.62 (0.53 to 0.71)		

Statistical analyses

Statistical analysis title	Comparison of disease-free survival (ITT)
Comparison groups	Surveillance v Chemotherapy
Number of subjects included in analysis	260
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.38
upper limit	0.8

Secondary: Overall survival	
End point title	Overall survival
End point description:	
Time from random assignment to death from any cause (observations censored at date last known to be alive)	
End point type	Secondary
End point timeframe:	
Up to 5 years post-randomisation	

End point values	Surveillance	Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	131		
Units: Proportion surviving at 5 years				
number (confidence interval 95%)	0.57 (0.48 to 0.66)	0.66 (0.57 to 0.74)		

Statistical analyses

Statistical analysis title	Comparison of overall survival (ITT)
Comparison groups	Surveillance v Chemotherapy
Number of subjects included in analysis	260
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.68

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.46
upper limit	1

Secondary: Metastasis-free survival

End point title	Metastasis-free survival

End point description:

Time from randomisation to the first event of distant recurrence or death from any cause

End point type	Secondary

End point timeframe:

Up to 5 years post-randomisation

End point values	Surveillance	Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	131		
Units: Proportion event-free at 5 years				
number (confidence interval 95%)	0.46 (0.37 to 0.55)	0.64 (0.55 to 0.73)		

Statistical analyses

Statistical analysis title	Comparison of metastasis-free survival (ITT)
Comparison groups	Surveillance v Chemotherapy
Number of subjects included in analysis	260
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.38
upper limit	0.79

Secondary: Time to bladder second primary tumours

End point title	Time to bladder second primary tumours

End point description:

Time from randomisation to the first event of non-muscle invasive bladder cancer or muscle invasive bladder cancer

End point type	Secondary

End point timeframe:

Up to 5 years post-randomisation

End point values	Surveillance	Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	131		
Units: Proportion event-free at 5 years				
number (confidence interval 95%)	0.66 (0.56 to 0.75)	0.66 (0.57 to 0.75)		

Statistical analyses

Statistical analysis title	Comparison of second primary in the bladder (ITT)
Comparison groups	Chemotherapy v Surveillance
Number of subjects included in analysis	260
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.75
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	1.46

Secondary: Late toxicity

End point title	Late toxicity

End point description:

Adverse events graded according to Common Terminology Criteria for Adverse Events (CTCAE) v4, experienced between 6 months and 2 years post-randomisation

End point type	Secondary

End point timeframe:

From 6 months to 2 years post-randomisation

End point values	Received surveillance	Received chemotherapy		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	117	123		
Units: Participants				
Grade 0	22	9		
Grade 1	38	57		
Grade 2	33	32		
Grade 3	21	21		
Grade 4	1	3		
Grade 5	0	1		
Grade not specified	2	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AE reporting throughout treatment up to 13 weeks post-randomisation (end of treatment); SAE reporting in patients receiving chemotherapy up to 30 days after last drug administration.

Adverse event reporting additional description:

Routine AE data collection at fixed time points after each cycle (or equivalent time points in surveillance group); SAE reporting in chemotherapy group only. Data on late effects reported between 6 and 24 months are included in Endpoints section.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	11.9

Reporting groups

Reporting group title	Received surveillance

Reporting group description:

Participants who underwent surveillance and did not receive any study drug

Reporting group title	Received chemotherapy

Reporting group description:

Received at least one dose of study drug

Serious adverse events	Received surveillance	Received chemotherapy	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 133 (0.75%)	46 / 126 (36.51%)	
number of deaths (all causes)	62	44	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Arterial thrombosis			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest discomfort			

subjects affected / exposed	0 / 133 (0.00%)	2 / 126 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
chill			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extravasation			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 133 (0.00%)	5 / 126 (3.97%)	
occurrences causally related to treatment / all	0 / 0	4 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	0 / 133 (0.00%)	2 / 126 (1.59%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised oedema			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral swelling			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			

subjects affected / exposed	0 / 133 (0.00%)	2 / 126 (1.59%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 133 (0.00%)	6 / 126 (4.76%)	
occurrences causally related to treatment / all	0 / 0	6 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood urea increased			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil count decreased			
subjects affected / exposed	0 / 133 (0.00%)	9 / 126 (7.14%)	
occurrences causally related to treatment / all	0 / 0	8 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	

Platelet count decreased			
subjects affected / exposed	0 / 133 (0.00%)	5 / 126 (3.97%)	
occurrences causally related to treatment / all	0 / 0	5 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoglobin decreased			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Transfusion reaction			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palpitations			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 133 (0.00%)	2 / 126 (1.59%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lethargy			
subjects affected / exposed	0 / 133 (0.00%)	2 / 126 (1.59%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia			

subjects affected / exposed	0 / 133 (0.00%)	4 / 126 (3.17%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Haemorrhoids			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 133 (0.00%)	3 / 126 (2.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 133 (0.00%)	4 / 126 (3.17%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			

subjects affected / exposed	1 / 133 (0.75%)	6 / 126 (4.76%)	
occurrences causally related to treatment / all	1 / 1	6 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 133 (0.00%)	6 / 126 (4.76%)	
occurrences causally related to treatment / all	0 / 0	6 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash macular			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal pain			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			

Cystitis			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periodontitis			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinitis			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 133 (0.00%)	6 / 126 (4.76%)	
occurrences causally related to treatment / all	0 / 0	4 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orchitis			

subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 133 (0.00%)	3 / 126 (2.38%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 133 (0.00%)	1 / 126 (0.79%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Received surveillance	Received chemotherapy	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	108 / 133 (81.20%)	126 / 126 (100.00%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	8 / 133 (6.02%)	29 / 126 (23.02%)	
occurrences (all)	8	29	
Blood creatinine increased			
subjects affected / exposed	11 / 133 (8.27%)	20 / 126 (15.87%)	
occurrences (all)	11	20	
Neutrophil count decreased			
subjects affected / exposed	1 / 133 (0.75%)	79 / 126 (62.70%)	
occurrences (all)	1	79	
Platelet count decreased			

subjects affected / exposed	4 / 133 (3.01%)	50 / 126 (39.68%)	
occurrences (all)	4	50	
White blood cell count decreased			
subjects affected / exposed	0 / 133 (0.00%)	8 / 126 (6.35%)	
occurrences (all)	0	8	
Vascular disorders			
Hypertension			
subjects affected / exposed	26 / 133 (19.55%)	32 / 126 (25.40%)	
occurrences (all)	26	32	
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	1 / 133 (0.75%)	10 / 126 (7.94%)	
occurrences (all)	1	10	
Headache			
subjects affected / exposed	1 / 133 (0.75%)	7 / 126 (5.56%)	
occurrences (all)	1	7	
Lethargy			
subjects affected / exposed	48 / 133 (36.09%)	97 / 126 (76.98%)	
occurrences (all)	48	97	
Peripheral sensory neuropathy			
subjects affected / exposed	4 / 133 (3.01%)	22 / 126 (17.46%)	
occurrences (all)	4	22	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	4 / 133 (3.01%)	15 / 126 (11.90%)	
occurrences (all)	4	15	
Localised oedema			
subjects affected / exposed	8 / 133 (6.02%)	21 / 126 (16.67%)	
occurrences (all)	8	21	
Mucosal inflammation			
subjects affected / exposed	0 / 133 (0.00%)	7 / 126 (5.56%)	
occurrences (all)	0	7	
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	9 / 133 (6.77%)	20 / 126 (15.87%)	
occurrences (all)	9	20	

Tinnitus			
subjects affected / exposed	7 / 133 (5.26%)	20 / 126 (15.87%)	
occurrences (all)	7	20	
Gastrointestinal disorders			
Anaemia			
subjects affected / exposed	3 / 133 (2.26%)	34 / 126 (26.98%)	
occurrences (all)	3	34	
Constipation			
subjects affected / exposed	2 / 133 (1.50%)	35 / 126 (27.78%)	
occurrences (all)	2	35	
Diarrhoea			
subjects affected / exposed	2 / 133 (1.50%)	20 / 126 (15.87%)	
occurrences (all)	2	20	
Dyspepsia			
subjects affected / exposed	2 / 133 (1.50%)	11 / 126 (8.73%)	
occurrences (all)	2	11	
Nausea			
subjects affected / exposed	13 / 133 (9.77%)	70 / 126 (55.56%)	
occurrences (all)	13	70	
Vomiting			
subjects affected / exposed	5 / 133 (3.76%)	24 / 126 (19.05%)	
occurrences (all)	5	24	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 133 (1.50%)	9 / 126 (7.14%)	
occurrences (all)	2	9	
Dyspnoea			
subjects affected / exposed	6 / 133 (4.51%)	20 / 126 (15.87%)	
occurrences (all)	6	20	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 133 (0.00%)	18 / 126 (14.29%)	
occurrences (all)	0	18	
Pruritus			
subjects affected / exposed	8 / 133 (6.02%)	23 / 126 (18.25%)	
occurrences (all)	8	23	

Rash			
subjects affected / exposed	1 / 133 (0.75%)	11 / 126 (8.73%)	
occurrences (all)	1	11	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	12 / 133 (9.02%)	10 / 126 (7.94%)	
occurrences (all)	12	10	
Proteinuria			
subjects affected / exposed	5 / 133 (3.76%)	9 / 126 (7.14%)	
occurrences (all)	5	9	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	10 / 133 (7.52%)	6 / 126 (4.76%)	
occurrences (all)	10	6	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	5 / 133 (3.76%)	10 / 126 (7.94%)	
occurrences (all)	5	10	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 133 (0.75%)	10 / 126 (7.94%)	
occurrences (all)	1	10	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 February 2012	Addition of mandatory post-operative CT scans of the abdomen and pelvis prior to trial entry for patients whose pre-operative CT scan showed nodal disease. Additional guidance/clarification around chemotherapy dosing.
07 September 2012	Clarification of the endpoint 'Invasive recurrence/second primary in the bladder', split into two separate items: Progression to muscle invasive disease in the bladder; second primary in the bladder. Addition of 3 month abdomen and pelvis CT scan.
21 January 2014	Addition of translational sample collection, POUT-T. Lowering of age limit in inclusion criteria to ≥16 years of age. Addition of cystoscopy prior to trial entry if not conducted prior to nephro-ureterectomy.
25 June 2015	Closure of qualitative recruitment sub-study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Recruitment closed early (of target n=345) on recommendation from the IDMC, since the early stopping rule for the primary endpoint had been met. This was not due to any safety concern.
1 participant who withdrew consent for data use is not reported.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/32145825

http://www.ncbi.nlm.nih.gov/pubmed/38350047