Clinical trial results:
Radiotherapy and Androgen Deprivation in Combination After Local Surgery. A randomised controlled trial for patients with prostate cancer.

Summary

EudraCT number	2006-000205-34
Trial protocol	GB DK IE
Global end of trial date	31 December 2021

Results information

Result version number	v1 (current)
This version publication date	07 June 2023
First version publication date	07 June 2023

Trial information

Trial identification

Sponsor protocol code	PR10

Additional study identifiers

ISRCTN number	ISRCTN40814031
ClinicalTrials.gov id (NCT number)	NCT00541047
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University College London
Sponsor organisation address	Gower St, London, United Kingdom, WC1E 6BT
Public contact	UCL Research Limited, UCL Research Limited, f.gilani@ucl.ac.uk
Scientific contact	UCL Research Limited, UCL Research Limited, f.gilani@ucl.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	27 May 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 December 2021
Global end of trial reached?	Yes
Global end of trial date	31 December 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1. To test whether adjuvant treatment with radiotherapy following radical postatectomy leads to better outcomes than regular observation with early salvage treatment given at the tune of a rising PSA - Radiotherapy Timing Randomisation.

2. To test whether, in men receiving post-operative radiotherapy to the prostate bed, the addition of hormone therapy leads to better outcomes; and if so, whether two years of hormone therapy is better than six months - Hormone Therapy Duration Randomisation

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 November 2007
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: 2982
Country: Number of subjects enrolled	Denmark: 223
Country: Number of subjects enrolled	Ireland: 13
Country: Number of subjects enrolled	Canada: 747
Worldwide total number of subjects	3965
EEA total number of subjects	236

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)	1801
From 65 to 84 years	2164
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment between 30 January 2008 and 7 July 2015 for RADICALS-HD.
Recruitment between 30 January 2008 and 31 December 2016 for RADICALS-RT.

Pre-assignment

Screening details:

Prostate cancer patients post-surgery

Period 1

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

Blinding implementation details:

None

Arms

Are arms mutually exclusive?	No
Arm title	RADICALS-HD, 0 months

Arm description:

Hormone duration randomisation - no HT

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	RADICALS-HD, 6 months (0v6)

Arm description:

6 mths treatment, none vs short comparison

Arm type	Experimental
Investigational medicinal product name	zoladex
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Injection

Dosage and administration details:

Depot injection

Arm title	RADICALS-HD, 24 months

Arm description:

Hormone duration randomisation - 24 months HT

Arm type	Experimental
Investigational medicinal product name	zoladex
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Injection

Dosage and administration details:

Depot injection

Arm title	RADICALS-RT, Salvage

Arm description:

RT timing randomisation - salvage RT

Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	RADICALS-RT, Adjuvant
Arm description: RT timing randomisation - adjuvant RT	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	RADICALS-HD, 6 months (6v24)
Arm description: 6 mths treatment, short vs long comparison	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	RADICALS-HD, 0 months	RADICALS-HD, 6 months (0v6)	RADICALS-HD, 24 months
Started	737	743	762
Completed	737	743	762

Number of subjects in period 1	RADICALS-RT, Salvage	RADICALS-RT, Adjuvant	RADICALS-HD, 6 months (6v24)
Started	699	697	761
Completed	699	697	761

Baseline characteristics

Reporting groups	
Reporting group title	RADICALS-HD, 0 months
Reporting group description:	
Hormone duration randomisation - no HT	
Reporting group title	RADICALS-HD, 6 months (0v6)
Reporting group description:	
6 mths treatment, none vs short comparison	
Reporting group title	RADICALS-HD, 24 months
Reporting group description:	
Hormone duration randomisation - 24 months HT	
Reporting group title	RADICALS-RT, Salvage
Reporting group description:	
RT timing randomisation - salvage RT	
Reporting group title	RADICALS-RT, Adjuvant
Reporting group description:	
RT timing randomisation - adjuvant RT	
Reporting group title	RADICALS-HD, 6 months (6v24)
Reporting group description:	
6 mths treatment, short vs long comparison	

Reporting group values	RADICALS-HD, 0 months	RADICALS-HD, 6 months (0v6)	RADICALS-HD, 24 months
Number of subjects	737	743	762
Age categorical Units: Subjects			
Adults (18-64 years)	312	315	342
From 65-84 years	425	428	420
Age continuous Units: years			
median	66	65	65
inter-quartile range (Q1-Q3)	61 to 69	61 to 69	61 to 69
Gender categorical Units: Subjects			
Female	0	0	0
Male	737	743	762

Reporting group values	RADICALS-RT, Salvage	RADICALS-RT, Adjuvant	RADICALS-HD, 6 months (6v24)
Number of subjects	699	697	761
Age categorical Units: Subjects			
Adults (18-64 years)	332	343	352
From 65-84 years	367	354	409
Age continuous Units: years			
median	65	65	65
inter-quartile range (Q1-Q3)	60 to 68	60 to 68	60 to 69

Gender categorical Units: Subjects			
Female	0	0	0
Male	699	697	761

Reporting group values	Total		
Number of subjects	3965		
Age categorical Units: Subjects			
Adults (18-64 years)	1801		
From 65-84 years	2164		
Age continuous Units: years median inter-quartile range (Q1-Q3)	- -		
Gender categorical Units: Subjects			
Female	0		
Male	3965		

Subject analysis sets

Subject analysis set title	RADICALS-HD, 0months
Subject analysis set type	Intention-to-treat
Subject analysis set description: Hormone duration comparison - none vs 6 months	
Subject analysis set title	RADICALS-HD, 6 months (0v6)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Hormone duration - 0 months vs 6 months	
Subject analysis set title	RADICALS-HD, 24 months
Subject analysis set type	Intention-to-treat
Subject analysis set description: Hormone duration comparison, short vs long	
Subject analysis set title	RADICALS-RT, Salvage
Subject analysis set type	Intention-to-treat
Subject analysis set description: Radiotherapy timing comparison, salvage treatment	
Subject analysis set title	RADICALS-RT, Adjuvant
Subject analysis set type	Intention-to-treat
Subject analysis set description: Radiotherapy timing comparison, adjuvant treatment	
Subject analysis set title	RADICALS-HD, 6 months (6v24)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Hormone duration comparison, short vs long	

Reporting group values	RADICALS-HD, 0months	RADICALS-HD, 6 months (0v6)	RADICALS-HD, 24 months
Number of subjects	737	743	762

Age categorical Units: Subjects			
Adults (18-64 years)	312	315	342
From 65-84 years	425	428	420
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Gender categorical Units: Subjects			
Female	0	0	0
Male	737	743	762

Reporting group values	RADICALS-RT, Salvage	RADICALS-RT, Adjuvant	RADICALS-HD, 6 months (6v24)
Number of subjects	699	697	761
Age categorical Units: Subjects			
Adults (18-64 years)	332	343	352
From 65-84 years	367	354	409
Age continuous Units: years			
median	65	65	65
inter-quartile range (Q1-Q3)	60 to 68	60 to 68	60 to 69
Gender categorical Units: Subjects			
Female	0	0	0
Male	699	697	761

End points

End points reporting groups

Reporting group title	RADICALS-HD, 0 months
Reporting group description:	
Hormone duration randomisation - no HT	
Reporting group title	RADICALS-HD, 6 months (0v6)
Reporting group description:	
6 mths treatment, none vs short comparison	
Reporting group title	RADICALS-HD, 24 months
Reporting group description:	
Hormone duration randomisation - 24 months HT	
Reporting group title	RADICALS-RT, Salvage
Reporting group description:	
RT timing randomisation - salvage RT	
Reporting group title	RADICALS-RT, Adjuvant
Reporting group description:	
RT timing randomisation - adjuvant RT	
Reporting group title	RADICALS-HD, 6 months (6v24)
Reporting group description:	
6 mths treatment, short vs long comparison	
Subject analysis set title	RADICALS-HD, 0months
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Hormone duration comparison - none vs 6 months	
Subject analysis set title	RADICALS-HD, 6 months (0v6)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Hormone duration - 0 months vs 6 months	
Subject analysis set title	RADICALS-HD, 24 months
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Hormone duration comparison, short vs long	
Subject analysis set title	RADICALS-RT, Salvage
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Radiotherapy timing comparison, salvage treatment	
Subject analysis set title	RADICALS-RT, Adjuvant
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Radiotherapy timing comparison, adjuvant treatment	
Subject analysis set title	RADICALS-HD, 6 months (6v24)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Hormone duration comparison, short vs long	

Primary: Distant metastases

End point title	Distant metastases

End point description:

RADICALS-HD: Metastasis-free survival - new distant metastasis or death from any cause
RADICALS-RT: Freedom from distant metastasis - new distant metastasis or death from prostate cancer

End point type	Primary

End point timeframe:

Randomisation to end of follow-up

End point values	RADICALS-HD, 0months	RADICALS-HD, 6 months (0v6)	RADICALS-HD, 24 months	RADICALS-RT, Salvage
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	737	743	762	699
Units: patients	737	743	762	699

End point values	RADICALS-RT, Adjuvant	RADICALS-HD, 6 months (6v24)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	697	761		
Units: patients	697	761		

Statistical analyses

Statistical analysis title	Metastasis free survival - HD 0 vs 6mths

Statistical analysis description:

Primary outcome

Comparison groups	RADICALS-HD, 0months v RADICALS-HD, 6 months (0v6)
Number of subjects included in analysis	1480
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.346
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.886
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.688
upper limit	1.14

Statistical analysis title	Metastasis free survival - HD 6 vs 24mths

Statistical analysis description:	
Primary outcome	
Comparison groups	RADICALS-HD, 6 months (6v24) v RADICALS-HD, 24 months
Number of subjects included in analysis	1523
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.029
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.773
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.612
upper limit	0.975

Statistical analysis title	Freedom from distant metastasis - RT timing
Statistical analysis description:	
Adjuvant RT vs Salvage RT	
Comparison groups	RADICALS-RT, Salvage v RADICALS-RT, Adjuvant
Number of subjects included in analysis	1396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.095
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.681
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.432
upper limit	1.072

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Any time during follow-up	
Adverse event reporting additional description:	
RTOG graded toxicities, grade 3 or above	
Assessment type	Systematic

Dictionary used	
Dictionary name	RTOG
Dictionary version	1

Reporting groups	
Reporting group title	HD 0 months
Reporting group description:	
Hormone duration randomisation - no treatment	
Reporting group title	HD 6 months, (0v6)
Reporting group description:	
Hormone duration randomisation - 6 months treatment short vs long	
Reporting group title	HD 24 months
Reporting group description:	
Hormone duration randomisation - 2 years treatment	
Reporting group title	RT salvage
Reporting group description:	
Radiotherapy timing randomisation - salvage strategy	
Reporting group title	RT adjuvant
Reporting group description:	
Radiotherapy timing randomisation - adjuvant strategy	
Reporting group title	HD 6 months, (6v24)
Reporting group description:	
Hormone duration randomisation, 6 months treatment, short vs long	

Serious adverse events	HD 0 months	HD 6 months, (0v6)	HD 24 months
Total subjects affected by serious adverse events			
subjects affected / exposed	31 / 737 (4.21%)	30 / 743 (4.04%)	50 / 762 (6.56%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	0 / 737 (0.00%)	0 / 743 (0.00%)	0 / 762 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung cancer			

subjects affected / exposed	0 / 737 (0.00%)	1 / 743 (0.13%)	0 / 762 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pancreatic carcinoma			
subjects affected / exposed	0 / 737 (0.00%)	0 / 743 (0.00%)	0 / 762 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal cancer			
subjects affected / exposed	1 / 737 (0.14%)	0 / 743 (0.00%)	0 / 762 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal cancer			
subjects affected / exposed	1 / 737 (0.14%)	0 / 743 (0.00%)	0 / 762 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Melanoma			
subjects affected / exposed	0 / 737 (0.00%)	0 / 743 (0.00%)	0 / 762 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Thrombosis			
subjects affected / exposed	1 / 737 (0.14%)	0 / 743 (0.00%)	0 / 762 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Stroke			
subjects affected / exposed	0 / 737 (0.00%)	1 / 743 (0.13%)	3 / 762 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 1	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina			
subjects affected / exposed	1 / 737 (0.14%)	5 / 743 (0.67%)	1 / 762 (0.13%)
occurrences causally related to treatment / all	0 / 1	1 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			

subjects affected / exposed	0 / 737 (0.00%)	0 / 743 (0.00%)	0 / 762 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 737 (0.14%)	3 / 743 (0.40%)	4 / 762 (0.52%)
occurrences causally related to treatment / all	1 / 1	0 / 3	2 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Atrial fibrillation			
subjects affected / exposed	1 / 737 (0.14%)	0 / 743 (0.00%)	1 / 762 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 737 (0.00%)	1 / 743 (0.13%)	0 / 762 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute coronary syndrome			
subjects affected / exposed	0 / 737 (0.00%)	0 / 743 (0.00%)	3 / 762 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Other			
subjects affected / exposed	4 / 737 (0.54%)	2 / 743 (0.27%)	6 / 762 (0.79%)
occurrences causally related to treatment / all	0 / 4	0 / 2	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Collapse			
subjects affected / exposed	1 / 737 (0.14%)	0 / 743 (0.00%)	0 / 762 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 737 (0.00%)	0 / 743 (0.00%)	0 / 762 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma			

subjects affected / exposed	1 / 737 (0.14%)	0 / 743 (0.00%)	2 / 762 (0.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 737 (0.14%)	0 / 743 (0.00%)	0 / 762 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 737 (0.14%)	1 / 743 (0.13%)	1 / 762 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 737 (0.00%)	0 / 743 (0.00%)	0 / 762 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic cholecystitis			
subjects affected / exposed	0 / 737 (0.00%)	0 / 743 (0.00%)	0 / 762 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	1 / 737 (0.14%)	0 / 743 (0.00%)	0 / 762 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 737 (0.00%)	0 / 743 (0.00%)	0 / 762 (0.00%)
occurrences causally related to treatment / all	0 / 10	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small bowel obstruction			
subjects affected / exposed	1 / 737 (0.14%)	1 / 743 (0.13%)	0 / 762 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal ulcer			

subjects affected / exposed	0 / 737 (0.00%)	0 / 743 (0.00%)	0 / 762 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 737 (0.00%)	1 / 743 (0.13%)	1 / 762 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fistula			
subjects affected / exposed	0 / 737 (0.00%)	1 / 743 (0.13%)	1 / 762 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 737 (0.00%)	0 / 743 (0.00%)	1 / 762 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 737 (0.00%)	0 / 743 (0.00%)	0 / 762 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 737 (0.00%)	0 / 743 (0.00%)	1 / 762 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 737 (0.00%)	0 / 743 (0.00%)	1 / 762 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 737 (0.00%)	1 / 743 (0.13%)	0 / 762 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			

subjects affected / exposed	0 / 737 (0.00%)	0 / 743 (0.00%)	1 / 762 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 737 (0.00%)	0 / 743 (0.00%)	0 / 762 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	9 / 737 (1.22%)	4 / 743 (0.54%)	10 / 762 (1.31%)
occurrences causally related to treatment / all	0 / 11	0 / 4	0 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 737 (0.14%)	0 / 743 (0.00%)	0 / 762 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethral stricture			
subjects affected / exposed	3 / 737 (0.41%)	4 / 743 (0.54%)	5 / 762 (0.66%)
occurrences causally related to treatment / all	0 / 3	0 / 4	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	3 / 737 (0.41%)	0 / 743 (0.00%)	4 / 762 (0.52%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary sepsis			
subjects affected / exposed	1 / 737 (0.14%)	2 / 743 (0.27%)	0 / 762 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute renal failure			
subjects affected / exposed	1 / 737 (0.14%)	0 / 743 (0.00%)	0 / 762 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary incontinence			

subjects affected / exposed	0 / 737 (0.00%)	0 / 743 (0.00%)	2 / 762 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemolytic uraemic syndrome			
subjects affected / exposed	0 / 737 (0.00%)	0 / 743 (0.00%)	1 / 762 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 737 (0.00%)	0 / 743 (0.00%)	0 / 762 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Cystitis			
subjects affected / exposed	1 / 737 (0.14%)	2 / 743 (0.27%)	2 / 762 (0.26%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Crushed vertebra			
subjects affected / exposed	0 / 737 (0.00%)	0 / 743 (0.00%)	0 / 762 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoporosis			
subjects affected / exposed	0 / 737 (0.00%)	0 / 743 (0.00%)	1 / 762 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	RT salvage	RT adjuvant	HD 6 months, (6v24)
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 697 (2.15%)	32 / 699 (4.58%)	30 / 761 (3.94%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			

subjects affected / exposed	0 / 697 (0.00%)	1 / 699 (0.14%)	0 / 761 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung cancer			
subjects affected / exposed	0 / 697 (0.00%)	1 / 699 (0.14%)	0 / 761 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pancreatic carcinoma			
subjects affected / exposed	0 / 697 (0.00%)	1 / 699 (0.14%)	0 / 761 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal cancer			
subjects affected / exposed	0 / 697 (0.00%)	0 / 699 (0.00%)	0 / 761 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal cancer			
subjects affected / exposed	0 / 697 (0.00%)	0 / 699 (0.00%)	0 / 761 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Melanoma			
subjects affected / exposed	0 / 697 (0.00%)	0 / 699 (0.00%)	1 / 761 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Thrombosis			
subjects affected / exposed	0 / 697 (0.00%)	1 / 699 (0.14%)	0 / 761 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Stroke			
subjects affected / exposed	0 / 697 (0.00%)	0 / 699 (0.00%)	1 / 761 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

Angina			
subjects affected / exposed	1 / 697 (0.14%)	2 / 699 (0.29%)	1 / 761 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	1 / 697 (0.14%)	0 / 699 (0.00%)	0 / 761 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	2 / 697 (0.29%)	0 / 699 (0.00%)	1 / 761 (0.13%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 697 (0.00%)	0 / 699 (0.00%)	1 / 761 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 697 (0.00%)	0 / 699 (0.00%)	0 / 761 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute coronary syndrome			
subjects affected / exposed	0 / 697 (0.00%)	0 / 699 (0.00%)	0 / 761 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Other			
subjects affected / exposed	5 / 697 (0.72%)	5 / 699 (0.72%)	4 / 761 (0.53%)
occurrences causally related to treatment / all	0 / 5	0 / 5	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Collapse			
subjects affected / exposed	1 / 697 (0.14%)	0 / 699 (0.00%)	0 / 761 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Dehydration			
subjects affected / exposed	1 / 697 (0.14%)	0 / 699 (0.00%)	0 / 761 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma			
subjects affected / exposed	0 / 697 (0.00%)	0 / 699 (0.00%)	0 / 761 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 697 (0.00%)	0 / 699 (0.00%)	0 / 761 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 697 (0.14%)	0 / 699 (0.00%)	0 / 761 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 697 (0.00%)	1 / 699 (0.14%)	0 / 761 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic cholecystitis			
subjects affected / exposed	0 / 697 (0.00%)	1 / 699 (0.14%)	0 / 761 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 697 (0.00%)	1 / 699 (0.14%)	0 / 761 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	1 / 697 (0.14%)	1 / 699 (0.14%)	0 / 761 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small bowel obstruction			

subjects affected / exposed	0 / 697 (0.00%)	0 / 699 (0.00%)	1 / 761 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal ulcer			
subjects affected / exposed	0 / 697 (0.00%)	0 / 699 (0.00%)	1 / 761 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 697 (0.00%)	0 / 699 (0.00%)	2 / 761 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fistula			
subjects affected / exposed	0 / 697 (0.00%)	0 / 699 (0.00%)	2 / 761 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 697 (0.00%)	0 / 699 (0.00%)	0 / 761 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 697 (0.00%)	1 / 699 (0.14%)	0 / 761 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 697 (0.00%)	1 / 699 (0.14%)	1 / 761 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pneumonitis			
subjects affected / exposed	0 / 697 (0.00%)	1 / 699 (0.14%)	0 / 761 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			

subjects affected / exposed	0 / 697 (0.00%)	1 / 699 (0.14%)	0 / 761 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 697 (0.00%)	0 / 699 (0.00%)	0 / 761 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 697 (0.00%)	0 / 699 (0.00%)	1 / 761 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	2 / 697 (0.29%)	7 / 699 (1.00%)	3 / 761 (0.39%)
occurrences causally related to treatment / all	0 / 2	0 / 8	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 697 (0.14%)	0 / 699 (0.00%)	0 / 761 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethral stricture			
subjects affected / exposed	0 / 697 (0.00%)	5 / 699 (0.72%)	6 / 761 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	0 / 697 (0.00%)	3 / 699 (0.43%)	2 / 761 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary sepsis			
subjects affected / exposed	0 / 697 (0.00%)	0 / 699 (0.00%)	2 / 761 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute renal failure			

subjects affected / exposed	0 / 697 (0.00%)	0 / 699 (0.00%)	0 / 761 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary incontinence			
subjects affected / exposed	0 / 697 (0.00%)	0 / 699 (0.00%)	3 / 761 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemolytic uraemic syndrome			
subjects affected / exposed	0 / 697 (0.00%)	0 / 699 (0.00%)	0 / 761 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 697 (0.00%)	0 / 699 (0.00%)	1 / 761 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Cystitis			
subjects affected / exposed	0 / 697 (0.00%)	1 / 699 (0.14%)	0 / 761 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Crushed vertebra			
subjects affected / exposed	0 / 697 (0.00%)	1 / 699 (0.14%)	0 / 761 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoporosis			
subjects affected / exposed	0 / 697 (0.00%)	0 / 699 (0.00%)	0 / 761 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	HD 0 months	HD 6 months, (0v6)	HD 24 months
Total subjects affected by non-serious adverse events			
subjects affected / exposed	121 / 737 (16.42%)	100 / 743 (13.46%)	142 / 762 (18.64%)
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	13 / 737 (1.76%)	13 / 743 (1.75%)	13 / 762 (1.71%)
occurrences (all)	13	13	13
Proctitis			
subjects affected / exposed	23 / 737 (3.12%)	20 / 743 (2.69%)	25 / 762 (3.28%)
occurrences (all)	23	20	25
Renal and urinary disorders			
Cystitis			
subjects affected / exposed	17 / 737 (2.31%)	19 / 743 (2.56%)	23 / 762 (3.02%)
occurrences (all)	17	19	23
Haematuria			
subjects affected / exposed	53 / 737 (7.19%)	30 / 743 (4.04%)	53 / 762 (6.96%)
occurrences (all)	53	30	53
Urethral stricture			
subjects affected / exposed	52 / 737 (7.06%)	58 / 743 (7.81%)	75 / 762 (9.84%)
occurrences (all)	52	58	75

Non-serious adverse events	RT salvage	RT adjuvant	HD 6 months, (6v24)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	67 / 697 (9.61%)	116 / 699 (16.60%)	105 / 761 (13.80%)
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	6 / 697 (0.86%)	16 / 699 (2.29%)	10 / 761 (1.31%)
occurrences (all)	6	16	10
Proctitis			
subjects affected / exposed	5 / 697 (0.72%)	15 / 699 (2.15%)	16 / 761 (2.10%)
occurrences (all)	5	15	16
Renal and urinary disorders			
Cystitis			
subjects affected / exposed	10 / 697 (1.43%)	20 / 699 (2.86%)	13 / 761 (1.71%)
occurrences (all)	10	20	13
Haematuria			

subjects affected / exposed	10 / 697 (1.43%)	47 / 699 (6.72%)	41 / 761 (5.39%)
occurrences (all)	10	47	41
Urethral stricture			
subjects affected / exposed	46 / 697 (6.60%)	66 / 699 (9.44%)	57 / 761 (7.49%)
occurrences (all)	46	66	57

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported