Clinical trial results:
Immediate or early salvage post-operative external radiotherapy combined with concomitant and adjuvant hormonal treatment versus immediate or early salvage post-operative external radiotherapy alone in pT3a-b R0-1 cNOMO/pT2R1 cN0M0, Gleason score 5-10 prostatic carcinoma. A phase III study.

Summary

EudraCT number	2006-002772-17
Trial protocol	NL BE FR ES
Global end of trial date	05 January 2014

Results information

Result version number	v1 (current)
This version publication date	09 July 2020
First version publication date	09 July 2020
Summary attachment (see zip file)	Short report (22043-30041ShortReportAuthoritiez_20141218.pdf)

Trial information

Trial identification

Sponsor protocol code	22043-30041

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00949962
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	European Organisation for Research and Treatment of Cancer
Sponsor organisation address	Avenue E. Mounier 83/11, Brussels, Belgium, 1200
Public contact	Project, Budget and Regulatory Dept, European Organisation for Research and Treatment of Cancer, +32 27441062, regulatory@eortc.be
Scientific contact	Project, Budget and Regulatory Dept, European Organisation for Research and Treatment of Cancer, +32 27441062, regulatory@eortc.be

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	18 December 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 January 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To investigate the potential benefit, in terms of biochemical progression free survival, of a combined adjuvant treatment consisting of short term androgen suppression in addition to postoperative RT in comparison to post-operative RT alone.

Due to the small number of patients, no formal analysis of the trial endpoints can be performed as stand alone.

Protection of trial subjects:

The responsible investigator ensured that this study was conducted in agreement with either the Declaration of Helsinki (available on the World Medical Association web site (http://www.wma.net)) and/or the laws and regulations of the country, whichever provides the greatest protection of the patient.
The protocol had been written, and the study was conducted according to the ICH Harmonized Tripartite Guideline on Good Clinical Practice (ICH-GCP, available online at http://www.ema.europa.eu/pdfs/human/ich/013595en.pdf). The protocol was approved by the competent ethics committee(s) as required by the applicable national legislation.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 October 2009
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	Netherlands: 3
Country: Number of subjects enrolled	Spain: 19
Country: Number of subjects enrolled	Belgium: 13
Country: Number of subjects enrolled	France: 42
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Switzerland: 8
Worldwide total number of subjects	86
EEA total number of subjects	78

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)	51
From 65 to 84 years	35
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Trial opened to recruitment on 06/10/2009 and was prematurely closed on 12/08/2013, due to lack of recruitment, with only 86 randomised patients (out of 600 planned to be recruited) from 19 sites in 6 countries.

Pre-assignment

Screening details:

Before Surgery:
- cT1-2-3a, cN0M0
- PSA <= 30 ng/ml
- WHO 0-1
- Age <= 80 years

Pre-assignment period milestones

Number of subjects started	86
Number of subjects completed	86

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm I

Arm description:

Patients undergo post-operative conformal external beam irradiation (immediate post-operative or salvage) for approximately 6.5 to 8 weeks.

Arm type	Comparator

No investigational medicinal product assigned in this arm

Arm title	Arm II

Arm description:

Patients undergo post-operative conformal external beam irradiation (immediate post-operative or salvage) for approximately 6.5 to 8 weeks, plus one injection of ELIGARD 45 mg 6-month depot and the required pretreatment with anti-androgens.

Arm type	Experimental
Investigational medicinal product name	ELIGARD® 45mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Dose: ELIGARD® 45 mg delivers 45 mg of leuprorelin acetate over a 6-month period.
Route of administration: subcutaneous injection.

Number of subjects in period 1	Arm I	Arm II
Started	44	42
Completed	35	31
Not completed	9	11
Patient stopped without giving any reasons	1	-
Serious adverse event before receiving ELIGARD.	-	1
Anti-androgen not given.	-	2
Radiation therapy not documented.	-	8
Radiation therapy not documented	8	-

Baseline characteristics

Reporting groups	
Reporting group title	Arm I
Reporting group description:	
Patients undergo post-operative conformal external beam irradiation (immediate post-operative or salvage) for approximately 6.5 to 8 weeks.	
Reporting group title	Arm II
Reporting group description:	
Patients undergo post-operative conformal external beam irradiation (immediate post-operative or salvage) for approximately 6.5 to 8 weeks, plus one injection of ELIGARD 45 mg 6-month depot and the required pretreatment with anti-androgens.	

Reporting group values	Arm I	Arm II	Total
Number of subjects	44	42	86
Age categorical Units: Subjects			
< 65 years	23	28	51
>= 65 years	21	14	35
Gender categorical Units: Subjects			
Male	44	42	86
WHO Performance status Units: Subjects			
WHO: 0	39	37	76
WHO: 1	5	5	10
Clinical stage - T Units: Subjects			
cT1c	21	19	40
cT2a	7	11	18
cT2b	8	4	12
cT2c	5	6	11
cT3a	3	2	5
Gleason Sum			
Sum of Gleason Pattern 1 and Gleason Pattern 2.			
Units: Subjects			
<=6	8	7	15
3+4	18	18	36
4+3	9	10	19
>7	9	7	16
Pre-operative PSA level			
PSA level measured as "ng/ml" (i.e. nanograms of PSA per milliliter (ng/mL) of blood).			
Units: ng/ml			
median	7.0	8.6	
full range (min-max)	4.3 to 22.0	2.4 to 30.0	-

End points

End points reporting groups

Reporting group title	Arm I

Reporting group description:

Patients undergo post-operative conformal external beam irradiation (immediate post-operative or salvage) for approximately 6.5 to 8 weeks.

Reporting group title	Arm II

Reporting group description:

Patients undergo post-operative conformal external beam irradiation (immediate post-operative or salvage) for approximately 6.5 to 8 weeks, plus one injection of ELIGARD 45 mg 6-month depot and the required pretreatment with anti-androgens.

Primary: Biochemical progression free survival

End point title	Biochemical progression free survival[1]

End point description:

Biochemical failure (or PSA progression) is defined by a post-treatment PSA measurement that is ≥ 0.4 ng/ml and is confirmed by a second increasing measurement at least 4 weeks later. For patients in the early salvage setting, post-treatment PSA failure will be declared as above but patients in whom the PSA remains ≥ 0.4 ng/ml at the 6 month follow-up visit (approximately 4.5 months after end of RT) will be considered having had a PSA failure at that visit.

End point type	Primary

End point timeframe:

Biochemical progression free survival is counted from the day of randomization to the day of first record of either biochemical failure, clinical progression, administration of a new (systemic) treatment for prostate cancer or death due to any cause.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses was done for the primary endpoint because the trial was prematurely ended.

End point values	Arm I	Arm II		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: % at 5 year				
number (confidence interval 95%)	(to)	(to)		

Notes:

[2] - No statistical analyses was done for the primary endpoint because the trial was prematurely ended.

[3] - No statistical analyses was done for the primary endpoint because the trial was prematurely ended.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected at baseline, during radiotherapy, at month 3 (approximately 6 weeks after end of radiotherapy) and during follow-up (6 months after randomization, then 6 months for the first 5 years and yearly thereafter).

Adverse event reporting additional description:

CRF for AEs contains pre-specified items. (1.2% AEs are reported as "other" and are not reported as not available from the list of SOC).
Note that AEs related to hematology and biochemistry lab values were not specifically collected and are not included in the table below.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	3

Reporting groups

Reporting group title	Arm I
Reporting group description: -	
Reporting group title	Arm II

Reporting group description: -

Serious adverse events	Arm I	Arm II	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 44 (2.27%)	2 / 42 (4.76%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
ANASTOMOTIC STENOSIS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
HAEMATURIA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
URETHRAL MEATUS STENOSIS			
alternative dictionary used: CTCAE			

3			
subjects affected / exposed	1 / 44 (2.27%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY RETENTION			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	
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: 0 %

Non-serious adverse events	Arm I	Arm II	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 44 (95.45%)	42 / 42 (100.00%)	
Vascular disorders			
THROMBOSIS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 44 (2.27%)	1 / 42 (2.38%)	
occurrences (all)	1	1	
Surgical and medical procedures			
MOTOR NERVE LESION POSTSURGERY			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
ABDOMEN NOS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 44 (2.27%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
FATIGUE			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	13 / 44 (29.55%)	11 / 42 (26.19%)	
occurrences (all)	27	16	

INSOMNIA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 44 (0.00%)	3 / 42 (7.14%)	
occurrences (all)	0	4	
OBESITY			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
PELVIS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	3 / 44 (6.82%)	3 / 42 (7.14%)	
occurrences (all)	3	3	
SWEATING			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
WEIGHT GAIN			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	2	
Reproductive system and breast disorders			
EJACULATORY DYSFUNCTION			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 44 (2.27%)	0 / 42 (0.00%)	
occurrences (all)	2	0	
ERECTILE DYSFUNCTION			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	39 / 44 (88.64%)	36 / 42 (85.71%)	
occurrences (all)	209	203	
GYNECOMASTIA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	2 / 44 (4.55%)	4 / 42 (9.52%)	
occurrences (all)	2	5	
LIBIDO			
alternative dictionary used: CTCAE			

3			
subjects affected / exposed	7 / 44 (15.91%)	18 / 42 (42.86%)	
occurrences (all)	15	65	
TESTICLE			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 44 (2.27%)	1 / 42 (2.38%)	
occurrences (all)	1	1	
Investigations			
WEIGHT LOSS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Cardiac disorders			
HYPERTENSION			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
MYOCARDIAL ISCHEMIA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 44 (0.00%)	4 / 42 (9.52%)	
occurrences (all)	0	4	
Nervous system disorders			
DEPRESSION			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 44 (0.00%)	2 / 42 (4.76%)	
occurrences (all)	0	3	
DIZZINESS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 44 (2.27%)	2 / 42 (4.76%)	
occurrences (all)	1	2	
NEURALGIA/PERIPHERAL NERVE			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 44 (2.27%)	1 / 42 (2.38%)	
occurrences (all)	1	1	
NEUROPATHY MOTOR			
alternative dictionary used: CTCAE			

3			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	3	
NEUROPATHY MOTOR PERIPHERAL POST SURGERY			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
NEUROPATHY SENSORY			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
NEUROPATIC PAIN			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 44 (2.27%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
EDEMA LIMB			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 44 (2.27%)	0 / 42 (0.00%)	
occurrences (all)	6	0	
LYMPHEDEMA-RELATED FIBROSIS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 44 (2.27%)	1 / 42 (2.38%)	
occurrences (all)	1	3	
LYMPHOCELE			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
MALLEOLAR OEDEMA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 44 (2.27%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			

ANAL FISSURE			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
COLITIS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
CONSTIPATION			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 44 (0.00%)	2 / 42 (4.76%)	
occurrences (all)	0	2	
DIARRHEA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	17 / 44 (38.64%)	18 / 42 (42.86%)	
occurrences (all)	25	28	
ESOPHAGITIS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
FLATULENCE			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	4 / 44 (9.09%)	0 / 42 (0.00%)	
occurrences (all)	7	0	
GASTROINTESTINAL COMPLAINTS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 44 (2.27%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
HEMORRHAGE GI RECTUM			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	7 / 44 (15.91%)	9 / 42 (21.43%)	
occurrences (all)	8	11	
HEMORRHOIDS			
alternative dictionary used: CTCAE 3			

subjects affected / exposed	2 / 44 (4.55%)	1 / 42 (2.38%)	
occurrences (all)	2	1	
PROCTITIS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	16 / 44 (36.36%)	11 / 42 (26.19%)	
occurrences (all)	26	19	
RECTAL IRRITATION			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
TENESMUS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 44 (0.00%)	2 / 42 (4.76%)	
occurrences (all)	0	2	
Hepatobiliary disorders			
HEPATOBILIARY/PANCREAS GALBLADDER			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
FLUSHING			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	2	
PRURITUS/ITCHING			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 44 (0.00%)	2 / 42 (4.76%)	
occurrences (all)	0	2	
SKIN BREAKDOWN			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
Renal and urinary disorders			

CYSTITIS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 44 (2.27%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
INCONTINENCE URINARY			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	27 / 44 (61.36%)	34 / 42 (80.95%)	
occurrences (all)	100	118	
OBSTRUCTION GU URETER			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 44 (2.27%)	1 / 42 (2.38%)	
occurrences (all)	1	3	
RENAL OTHER DYSURIA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	11 / 44 (25.00%)	9 / 42 (21.43%)	
occurrences (all)	19	12	
RENAL OTHER HEMATURIA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	5 / 44 (11.36%)	5 / 42 (11.90%)	
occurrences (all)	7	7	
STRICTURE/STENOSIS (INCLUDING ANASTOMOTIC) GU BLA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
STRICTURE/STENOSIS (INCLUDING ANASTOMOTIC) GU URE			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 44 (2.27%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
URINARY FREQUENCY/URGENCY			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	32 / 44 (72.73%)	22 / 42 (52.38%)	
occurrences (all)	75	74	
URINARY RETENTION			
alternative dictionary used: CTCAE 3			

subjects affected / exposed	8 / 44 (18.18%)	6 / 42 (14.29%)	
occurrences (all)	15	15	
Endocrine disorders			
HOT FLASHES/FLUSHES			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 44 (2.27%)	26 / 42 (61.90%)	
occurrences (all)	2	50	
Musculoskeletal and connective tissue disorders			
ARTHRITIS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 44 (2.27%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
FRACTURE			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 44 (2.27%)	1 / 42 (2.38%)	
occurrences (all)	1	1	
MUSCLE WEAKNESS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	2 / 44 (4.55%)	0 / 42 (0.00%)	
occurrences (all)	2	0	
OSTEOPOROSIS			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 44 (2.27%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
HERPES ZOSTER			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
PULMONARY INFECTION			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 44 (2.27%)	0 / 42 (0.00%)	
occurrences (all)	1	0	
URINARY TRACT NOS			
alternative dictionary used: CTCAE 3			

subjects affected / exposed	1 / 44 (2.27%)	1 / 42 (2.38%)	
occurrences (all)	2	1	
Metabolism and nutrition disorders			
ANOREXIA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	0 / 44 (0.00%)	1 / 42 (2.38%)	
occurrences (all)	0	1	
HYPERCHOLESTEREMIA			
alternative dictionary used: CTCAE 3			
subjects affected / exposed	1 / 44 (2.27%)	1 / 42 (2.38%)	
occurrences (all)	1	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 August 2011	The study was extremely poorly recruiting due to several reasons, which include delayed referral of patients to RT after surgery and different practices regarding adjuvant treatment of high risk prostate cancer patients. Among these recent developments of prostate cancer treatment the most important are considered utilization of early salvage treatment concept, increased utilization of sensitive PSA tests and higher RT doses and modern RT technologies. The changes proposed in the amendment are expected to enhance recruitment and enable the combined analysis with the ongoing RADICALS study. This was considered a scientific amendement (the proposed changes add a new stratum in the study and enlarge the patient eligibility criteria). The major scientific changes proposed: •Increase the time interval between surgery and the start of RT to maximum 26 weeks for the stratum "immediate post-operative adjuvant setting". •Add a new stratum for patients treated in the "early post-operative salvage setting" i.e. upon post-operative PSA failure. Post-operative PSA failure was defined as either 2 consecutive increases of the PSA level and final PSA value >0.1 ng/ml and ≤0.5ng/ml or, in the case where the third PSA value is not >0.1ng/ml, by 3 consecutive rises of the PSA and a final PSA value ≤0.5ng/ml. •Allow cN0 patients with negative staging examinations (either CT or MRI of pelvis and abdomen) to be included in the protocol. •Increase pre-operative PSA upper limit from 20ng/ml (5xULN) to 30ng/ml. •Relax the requirements on the radiotherapy dose schedule. The sites will opt for their preferred RT regimen for each setting in a range of doses specified for each setting (between 64-70 Gy). Higher doses may also be acceptable pending feasibility, upfront dummy run and QART approval. •To better capture biochemical failure after protocol treatment, intermediate PSA values will be recorde between the visits (PSA to be taken every 3 months for up to 5 years and then every 6 months).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
12 August 2013	Trial was prematurely closed on 12/08/2013, due to lack of recruitment, with only 86 randomised patients (out of 600 planned to be recruited) from 19 sites in 6 countries.	-

Notes:

Limitations and caveats

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

Decision to end the trial prematurely due to poor recruitment.

Notes: