



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 cNOM0, 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 (22043-30041ShortReportAutoritez_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 \leq 30 ng/ml
- WHO 0-1
- Age \leq 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 | |

| | | | |
|---|------------------|------------------|--|
| <p>INSOMNIA</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>OBESITY</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>PELVIS</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>SWEATING</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>WEIGHT GAIN</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | | | |
| | 0 / 44 (0.00%) | 3 / 42 (7.14%) | |
| | 0 | 4 | |
| | | | |
| | 0 / 44 (0.00%) | 1 / 42 (2.38%) | |
| | 0 | 1 | |
| | | | |
| | 3 / 44 (6.82%) | 3 / 42 (7.14%) | |
| | 3 | 3 | |
| | | | |
| | 0 / 44 (0.00%) | 1 / 42 (2.38%) | |
| | 0 | 1 | |
| | | | |
| | 0 / 44 (0.00%) | 1 / 42 (2.38%) | |
| | 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 | |
| DIRZINESS | | | |
| 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 | |
| NEUROPATHIC 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 | | |

| | | | |
|---|--|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>PROCTITIS</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>RECTAL IRRITATION</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>TENESMUS</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 44 (4.55%)</p> <p>2</p> <p>16 / 44 (36.36%)</p> <p>26</p> <p>0 / 44 (0.00%)</p> <p>0</p> <p>0 / 44 (0.00%)</p> <p>0</p> | <p>1 / 42 (2.38%)</p> <p>1</p> <p>11 / 42 (26.19%)</p> <p>19</p> <p>1 / 42 (2.38%)</p> <p>1</p> <p>2 / 42 (4.76%)</p> <p>2</p> | |
| <p>Hepatobiliary disorders</p> <p>HEPATOBIILIARY/PANCREAS GALBLADDER</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 44 (0.00%)</p> <p>0</p> | <p>1 / 42 (2.38%)</p> <p>1</p> | |
| <p>Skin and subcutaneous tissue disorders</p> <p>FLUSHING</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>PRURITUS/ITCHING</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>SKIN BREAKDOWN</p> <p>alternative dictionary used: CTCAE 3</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 44 (0.00%)</p> <p>0</p> <p>0 / 44 (0.00%)</p> <p>0</p> <p>0 / 44 (0.00%)</p> <p>0</p> | <p>1 / 42 (2.38%)</p> <p>2</p> <p>2 / 42 (4.76%)</p> <p>2</p> <p>1 / 42 (2.38%)</p> <p>1</p> | |
| 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 occurrences (all) | 8 / 44 (18.18%) 15 | 6 / 42 (14.29%) 15 | |
| Endocrine disorders HOT FLASHES/FLUSHES alternative dictionary used: CTCAE 3 subjects affected / exposed occurrences (all) | 1 / 44 (2.27%) 2 | 26 / 42 (61.90%) 50 | |
| Musculoskeletal and connective tissue disorders ARTHRITIS alternative dictionary used: CTCAE 3 subjects affected / exposed occurrences (all) FRACTURE alternative dictionary used: CTCAE 3 subjects affected / exposed occurrences (all) MUSCLE WEAKNESS alternative dictionary used: CTCAE 3 subjects affected / exposed occurrences (all) OSTEOPOROSIS alternative dictionary used: CTCAE 3 subjects affected / exposed occurrences (all) | 1 / 44 (2.27%) 1 1 / 44 (2.27%) 1 2 / 44 (4.55%) 2 1 / 44 (2.27%) 1 | 0 / 42 (0.00%) 0 1 / 42 (2.38%) 1 0 / 42 (0.00%) 0 0 / 42 (0.00%) 0 | |
| Infections and infestations HERPES ZOSTER alternative dictionary used: CTCAE 3 subjects affected / exposed occurrences (all) PULMONARY INFECTION alternative dictionary used: CTCAE 3 subjects affected / exposed occurrences (all) URINARY TRACT NOS alternative dictionary used: CTCAE 3 | 0 / 44 (0.00%) 0 1 / 44 (2.27%) 1 | 1 / 42 (2.38%) 1 0 / 42 (0.00%) 0 | |

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

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|----------------|---|
| 17 August 2011 | <p>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 amendment (the proposed changes add a new stratum in the study and enlarge the patient eligibility criteria). The major scientific changes proposed:</p> <ul style="list-style-type: none">•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 recorded 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: