Trial Description

Title

Multicenter randomized phase-III trial into adjuvant radiotherapy for prostate cancer patients with or without positive surgical margins post-prostatectomy and with low level lymph node involvement (mircrometastases, ≤2 lymph node macrometastases)

Trial Acronym

ART-2 Trial

URL of the trial

[---]*

Brief Summary in Lay Language

Prostate cancer patients who underwent surgical removal of the organ have a risk of recurrence of the disease that depends on the tumour's spatial extent. If the examination of the surgically resected tissue shows the cancer not to be restricted to the prostate gland, but also to involve single pelvic lymph nodes, then the risk of relapse rises.
One option to counter that risk is to irradiate the pelvis precautionary (adjuvant) soon after the relief of post-operative complaints. However, irradiation can cause side effects, which must be justified by significantly improved healing rates.
An alternative to adjuvant radiotherapy is the wait-and-see strategy: During scheduled follow-up, laboratory data (PSA measurements) can signal a relapse (biochemical recurrence). In that case, so-called salvage therapy still offers a good chance for cure, however, usually connected with stronger side effects than from adjuvant radiation.
The ART-2 trial is designed to test whether in patients with low-level lymph node involvement adjuvant radiotherapy can improve by 15% the post-operative 4-years rate of freedom from recurrence to 55%.

Brief Summary in Scientific Language

ART-2 is a prospectively randomized multicenter phase-III trial to compare the effect of adjuvant radiotherapy with a wait-and-see strategy in post prostatectomy patients with pathologically confirmed low-level lymph node involvement (micrometastases, 1-2 macrometastases). For pT3 N0 tumours with positive surgical margins, three randomized trials could show a benefit from adjuvant radiotherapy. For lymph node positive prostate cancer, such a benefit remains to be confirmed.

Organizational Data

- DRKS-ID: **DRKS00004733**

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- Date of Registration in DRKS: **2013/03/14**
- Date of Registration in Partner Registry or other Primary Registry: **[---]***
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **177/11 , Ethik-Kommission der Universität Ulm**

Secondary IDs

- Other Secondary-ID: **ARO 2010-2 (AG Radiologische Onkologie der DKG)**

Health condition or Problem studied

- ICD10: **C61 - Malignant neoplasm of prostate**

Interventions/Observational Groups

- Arm 1: **Wait-and-See (W+S) after radical prostatectomy.**
  Scheduled follow-up including PSA determination for early diagnosis of a potential (biochemical) relaps.
  In case of recurrence, antihormonal treatment with bicalutamid 150mg/day or salvage radiotherapy with individualized dose (at least 66 Gy to the prostate fossa) are offered.
- Arm 2: **Intensity modulated radiotherapy to the pelvic lymph nodes and the prostate bed with 2 Gy per fraction to a total dose of 50 Gy.**
  With negative surgical margins boost to 60 Gy to the prostate bed (pT2) and the seminal vesicles (≥pT3); with positive surgical margins boost to 64 Gy.
  (RapidArc, VMAT optional)

Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***
- Allocation: **Randomized controlled trial**
- Blinding: **[---]***
- Who is blinded: **[---]***
- Control: **Control group receives no treatment**
- Purpose: **Treatment**
- Assignment: **Parallel**

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Allocation: **Randomized controlled trial**

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Control: **Control group receives no treatment**

Purpose: **Treatment**

Assignment: **Parallel**

- Phase: **N/A**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **N/A**

Primary Outcome

Progression-free survival, maximum follow-up 9 years

Secondary Outcome

Overall survival (scheduled follow-up max. 9 years) ;
Distant metastases ;
Rate of acut side effects of radiotherapy ;
Rate of late side effects: Bladder/Urethra and intestine according to RTOG ;
Quality of life (EORTC query QLQ-C30 after 3-6-12-24-60 months) ;
Erectile dysfunction (International Index of Erectile Function, query form IIEF after 3-6-12-24-60 months)

Countries of recruitment

- DE **Germany**

Locations of Recruitment

- University Medical Center **Klinik für Urologie; Klinik für Strahlentherapie und Radioonkologie, Ulm**
- Medical Center **Urologische Klinik; Klinik für Strahlentherapie, Augsburg**
- University Medical Center **Urologische Klinik, Kliniken für Strahlentherapie und Radioonkologie , Berlin**
- Medical Center **Klinik für Strahlentherapie und Radioonkologie, Bochum**
- Medical Center **Klinik für Urologie; Klinik für Strahlentherapie, Tübingen**
- University Medical Center **Klinik für Urologie; Klinik für Strahlentherapie und Radioonkologie, Homburg/Saar**

- Medical Center **Evang. Huyssens-Stiftung/Knappschaft, Urologie , Essen**
- University Medical Center **Klinik für Strahlentherapie, Essen**
- University Medical Center **Martini-Klinik am UKE, Prostatakrebszentrum , Hamburg-Eppendorf**
- University Medical Center **Urologische Klinik; Klinik für Radioonkologie und Strahlentherapie, Heidelberg**
- University Medical Center **Urologische Klinik, Marienhospital, Bochum / Herne**
- University Medical Center **Klinik für Urologie und Kinderurologie; Klinik für Strahlentherapie und Radioonkologie, Homburg / Saar**
- University Medical Center **Klinik für Urologie; Klinik für Strahlentherapie, Münster**
- University Medical Center **Kliniken für Urologie; Kliniken für Radioonkologie; TU , München**
- University Medical Center **Universitätsklinik für Urologie, Oldenburg**
- University Medical Center **Klinik für Strahlentherapie und Radioonkologie, Dresden**
- University Medical Center **Klinik für Strahlentherapie, Klinik für Urologie; LMU, München**

Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2014/04/03**
- Target Sample Size: **298**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **National**

Inclusion Criteria

- Gender: **Male**
- Minimum Age: **40 Years**
- Maximum Age: **no maximum age**

Additional Inclusion Criteria

Status post radical prostatectomy (incl. nerve-sparing) with histologically confirmed stage pTx R0/R1 pN+ (micrometastases, 1-2 macrometastases with or without additional micrometastases);
extended lymphadenectomy (≥12 lymph nodes) ;
pre-OP PSA <50 ng/mL ;
negative pre-OP bone scintigram (obligatory for PSA >20 ng/mL or bioptic Gleason Score 8-10) ;
pre-OP abdominal and pelvic CT without pathological findings (obligatory for PSA >20 ng/mL or bioptic Gleason Score 8-10);
Consensus between local and central pathology on pT stage, surgical margin status, Gleason Score and lymph node status ;
Response to prostatectomy confirmed by achieving within 90 days post-OP a PSA

nadir <0.1 ng/mL (undetectable) ;
Age ≥40 years ;
Karnofsky Index > 80% ;
Capability and will to adhere to study conditions ;
Written informed consent to participate in the study

Exclusion criteria

Persisting complete incontinence (grade III) ;
Tumour stage pN0 ;
>2 lymph nodes involved macroscopically ;
distant metastases ;
Previous or actual inflammation of the large intestine ;
Previous radiotherapy to the true pelvis ;
Previous chemotherapy ;
Status post bilateral orchiectomy ;
Status after pre-OP neoadjuvant hormone therapy ;
Previous or actual post-OP medical hormone therapy ;
Presence of a second tumour except curatively treated basalioma ;
Previous or actual psychiatric disorder or addiction ;
Participation in another clinical study, concurrent or within the last three months before the start of ART-2 ;
Inability to understand the study purpose or to adhere to study conditions ;
Missing written informed consent

Addresses

- **Primary Sponsor**

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- **Contact for Scientific Queries**

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Sources of Monetary or Material Support

■ **Private sponsorship (foundations, study societies, etc.)**

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Private sponsorship (foundations, study societies, etc.)

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Status

- Recruitment Status: **Recruiting stopped after recruiting started**
- Study Closing (LPLV): **[---]***

Trial Publications, Results and other documents

Please note:
There are additional attributes available concerning this trial. To open an extended view please click here.