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SAKK 08/15 - PROMET - Salvage Radiotherapy +/- Metformin for Patients With Prostate Cancer After Prostatectomy

ClinicalTrials.gov Identifier: NCT02945813

Recruitment Status: Recruiting
First Posted: October 26, 2016
Last Update Posted: March 22, 2018

See Contacts and Locations

Sponsor:
Swiss Group for Clinical Cancer Research

Information provided by (Responsible Party):
Swiss Group for Clinical Cancer Research

Study Description

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Brief Summary:
The main objective of the trial is to explore the efficacy of salvage radiotherapy (SRT) plus metformin compared to SRT in the endpoint of time to progression after prostatectomy failure.

Condition or disease	Intervention/treatment	Phase
Prostate Cancer	Drug: Metformin Radiation: Salvage Radiotherapy SRT	Phase 2

Detailed Description:
Although the use of salvage radiotherapy (SRT) is the only potentially curative treatment after prostatectomy failure, it has provided suboptimal results over the years. Metformin may represent an effective and inexpensive means to improve SRT outcomes with a favorable therapeutic ratio. Taken pre-clinical and retrospective clinical data together, there is a compelling rationale for conducting a RCT with SRT and metformin. Herein we propose a multicenter, randomized, open-label, proof-of-concept phase II trial with the hypothesis that the addition of metformin to SRT can delay time to progression compared to the standard-of-care SRT. The study has 1:1 randomization and stratification variables include Gleason score, PSA at

SRT, surgical margin status and ADT use.

Study Design

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Study Type:	Interventional (Clinical Trial)
Estimated Enrollment:	170 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Masking:	Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)
Primary Purpose:	Treatment
Official Title:	**SAKK 08/15** - **PROMET** - Multicenter, Randomized Phase II Trial of Salvage Radiotherapy +/- Metformin for Patients With Prostate Cancer After Prostatectomy
Actual Study Start Date:	September 6, 2017
Estimated Primary Completion Date:	December 2019
Estimated Study Completion Date:	December 2030

Resource links provided by the National Library of Medicine

Genetics Home Reference related topics:
Prostate cancer

MedlinePlus related topics: Prostate Cancer

Drug Information available for: Metformin
Metformin hydrochloride

U.S. FDA Resources

Arms and Interventions

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Arm	Intervention/treatment
Experimental: Arm A: Metformin • Metformin - 850mg PO BID; 48 weeks • Salvage radiotherapy SRT - 35 x 2Gy; 7 weeks	Drug: Metformin 850mg PO BID; 48 weeks Radiation: Salvage Radiotherapy SRT SRT 35 x 2Gy; 7 weeks
Active Comparator: Arm B: Salvage Radiotherapy - Salvage radiotherapy SRT - 35 x 2Gy; 7 weeks	Radiation: Salvage Radiotherapy SRT SRT 35 x 2Gy; 7 weeks

Outcome Measures

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Primary Outcome Measures:

1. Time to progression (TTP) [Time Frame: within 18 months after randomization]

   The primary endpoint of the trial is time to progression (TTP), defined as time from randomization until one of the following events, whichever comes first:

   - Biochemical progression
   - Clinical progression
   - Death due to clinical progression

Secondary Outcome Measures :

1. Progression free survival (PFS) [Time Frame: within 18 months after randomization]

   PFS is defined as time from randomization until one of the following events, whichever comes first:

   - Biochemical progression
   - Clinical progression
   - Death from any cause

2. Undetectable Prostate Specific Antigen (PSA) under normal testosterone levels [Time Frame: up to 18 months after last radiotherapy fraction]

   Undetectable PSA is defined as a serum PSA value of ≤0.05 ng/mL for at least two consecutive measurements after the last radiotherapy fraction and up to 18 months thereafter. To count as undetectable PSA under normal testosterone levels, the testosterone level has to be ≥50 ng/dL (i.e. a non-castrate testosterone level).

3. 50% PSA response [Time Frame: at randomization up to 18 months after last radiotherapy fraction.]

   50% PSA response is defined as a ≥50% PSA decline after radiotherapy compared to the serum PSA level at randomization up to 18 months after last radiotherapy fraction.

4. Clinical progression-free survival [Time Frame: week 64 then every 6 months for the first year and every 12 months thereafter up to 10 years from last RT fraction.]

   Clinical progression-free survival will be calculated as the time from randomization until clinical progression or death due to any cause.

5. Time to further anti-cancer systemic therapy [Time Frame: week 64 then every 6 months for the first year and every 12 months thereafter up to 10 years from last RT fraction.]

   Time to further anti-cancer systemic therapy (e.g. hormonal treatment) is defined as the time from randomization to the start of any type of salvage systemic treatment.

6. Prostate cancer-specific survival (PCSS) [Time Frame: at week 64 then every 6 months for the first year and every 12 months thereafter up to 10 years from last RT fraction.]

   Prostate cancer-specific survival will be calculated as the time from randomization to the date of death due to prostate cancer.

7. Overall survival (OS) [Time Frame: at week 64 then every 6 months for the first year and every 12 months thereafter up to 10 years from last RT fraction.]

   Overall survival will be calculated as the time from randomization to the date of death from any cause.

8. Adverse Events (AE) [Time Frame: until 56 weeks (specific RT-related AEs : until 10 years)]

   AEs will be assessed according to NCI CTCAE v4.03.

Eligibility Criteria Go to

Information from the National Library of Medicine

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, Learn About Clinical Studies.

Ages Eligible for Study:	18 Years to 75 Years (Adult, Senior)
Sexes Eligible for Study:	Male
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

- Written informed consent according to ICH/GCP regulations before registration and prior to any trial specific procedures
- Histologically confirmed adenocarcinoma of the prostate without small cell features
- Tumor stage pT2a-3b, pN0 or cN0, M0, R0-1 resection margins, according to UICC TNM 2009, Gleason score available
- Radical prostatectomy (RP) at least 12 weeks before registration
- PSA progression after RP defined as two consecutive rises with the final PSA > 0.1 ng/mL or three consecutive rises. The first value must be measured earliest 4 weeks after RP
- PSA ≤ 2 ng/mL within 14 days prior to registration
- Age ≥ 18 years at time of registration
- WHO performance status 0-1
- Adequate hepatic function within 14 days prior to registration: bilirubin ≤ 1.5 x ULN (exception if Gilbert's syndrome ≤ 3 x ULN), AST and ALT ≤ 2.5 x ULN
- Adequate renal function within 14 days prior to registration: calculated corrected creatinine clearance ≥ 60 mL/min, according to the formula of corrected Cockcroft-Gault Patient agrees not to father a child and to use effective contraceptive methods during salvage radiotherapy and until 6 months after the last fraction of radiotherapy

Exclusion Criteria:

- Persistent PSA (> 0.4 ng/mL) 4 to 20 weeks after RP
- Pelvic lymph node enlargement > 0.8 cm in short axis diameter (cN positive) assessed by mpMRI within 12 weeks prior to registration, unless the enlarged lymph node is sampled and negative
- Evidence of macroscopic local recurrence assessed by mpMRI within 12 weeks prior to registration
- Palpable prostatic fossa mass suggestive of recurrence, unless an ultrasound guided biopsy is negative for malignancy
- Presence or history of prostate cancer metastases. In case of clinical suspicion (e.g. bone pain), imaging (e.g. bone scan, Choline-PET, PSMA-PET, whole body MRI) must be performed. The imaging method is at the discretion of the investigator.
- If PET/CT scan was performed, any metabolic uptake considered clinically suspicious for malignancy, unless biopsy proves to be negative.
- History of hematologic or primary solid tumor malignancy, unless in remission for at least 3 years from registration with the exception of curatively treated localized non-melanoma skin cancer

- Patients diagnosed with diabetes mellitus
- Treatment with metformin within the last 3 months prior to registration
- Prior pelvic radiotherapy
- Hormonal treatment as bilateral orchiectomy prior or following RP
- Usage of products known to affect PSA levels within 4 weeks prior to start of trial treatment
- Bilateral hip prosthesis
- Severe or active co-morbidity likely to impact on the advisability of salvage RT, e.g.:
  - History of inflammatory bowel disease or any malabsorption syndrome or conditions that would interfere with enteral absorption
  - Acute bacterial or fungal infection requiring intravenous antibiotics at the time of registration
  - Unstable angina and/or congestive heart failure requiring hospitalization within the last 6 months
  - Transmural myocardial infarction within the last 6 months
  - Chronic Obstructive Pulmonary Disease (COPD) exacerbation or other respiratory illness requiring hospitalization or precluding study therapy at the time of registration
- Any condition associated with increased risk of lactic acidosis (e.g. alcohol abuse, congestive heart failure NYHA III or IV
- Clinically significant history of liver disease consistent with Child-Pugh Class B or C, including viral or other hepatitis, current alcohol abuse, or cirrhosis
- Severe or uncontrolled kidney disease resulted in impaired kidney function (GFR <60ml/min)
- Any acute or chronic condition that could cause tissue hypoxia (e.g. cardiac or respiratory insufficiency, recent myocardial infarction, shock)
- Treatment with any experimental drug or participation within a clinical trial within 30 days prior to registration (exception: concurrent participation in the biobank project SAKK 63/12 is allowed)
- Any concomitant drug contraindicated for use with metformin according to the approved product information
- Known hypersensitivity to metformin/placebo or to any of its components
- Hereditary intolerance to fructose; known galactose-1-phosphate uridyl transferase deficiency, UDP galactose 4 epimerase deficiency, galactokinase deficiency, Fanconi-Bickel syndrome, congenital lactase deficiency, or glucose-galactose malabsorption (due to the lactose-containing placebo)
- Inability or unwillingness to swallow oral medication
- Any other serious underlying medical, psychiatric, psychological, familial or geographical condition, which in the judgment of the investigator may interfere with the planned staging, treatment and follow-up, affect patient compliance or place the patient at high risk from treatment-related complications

Contacts and Locations

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Information from the National Library of Medicine

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number): ***NCT02945813***

Contacts

Contact: Daniele Oberti, PhD +41 31 389 91 91 trials@sakk.ch

Locations

Germany

Universitätsmedizin Berlin — **Not yet recruiting**
Berlin, Germany, 13353
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Principal Investigator: Pirus Ghadjar, MD

Klinikum der Universität München — **Not yet recruiting**
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Principal Investigator: Claus Belka, Prof

Universitätsklinikum Rostock — **Not yet recruiting**
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Universitätsklinikum Würzburg — **Recruiting**
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Switzerland

Universitätsspital Basel — **Recruiting**
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Sponsors and Collaborators

Swiss Group for Clinical Cancer Research

Investigators

Study Chair:	Daniel M. Aebersold, Prof	Bern University Hospital - Radiation Oncology
Study Chair:	Alan Dal Pra, MD	Miller School of Medicine, University of Miami

More Information

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Responsible Party:	Swiss Group for Clinical Cancer Research
ClinicalTrials.gov Identifier:	NCT02945813 History of Changes
Other Study ID Numbers:	**SAKK 08/15** - **PROMET** 2016-003599-39 (EudraCT Number)
First Posted:	October 26, 2016 Key Record Dates
Last Update Posted:	March 22, 2018
Last Verified:	March 2018

Individual Participant Data (IPD) Sharing Statement:
Plan to Share IPD: No

Studies a U.S. FDA-regulated Drug Product: No
Studies a U.S. FDA-regulated Device Product: No

Keywords provided by Swiss Group for Clinical Cancer Research:
Prostate Cancer
Prostate Cancer after Prostatectomy
Phase II Trial
Salvage Radiotherapy
Metformin

Additional relevant MeSH terms:

Prostatic Neoplasms
Genital Neoplasms, Male
Urogenital Neoplasms
Neoplasms by Site
Neoplasms
Genital Diseases, Male
Prostatic Diseases
Metformin
Hypoglycemic Agents
Physiological Effects of Drugs