A PHASE II RANDOMIZED, OPEN-LABEL STUDY COMPARING SALVAGE RADIOTHERAPY IN COMBINATION WITH 6 MONTHS OF ANDROGEN-DEPRIVATION THERAPY WITH LHRH AGONIST OR ANTAGONIST VERSUS ANTI-ANDROGEN THERAPY WITH APALUTAMIDE IN PATIENTS WITH BIOCHEMICAL PROGRESSION AFTER RADICAL PROSTATECTOMY

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TRIAL IN PROGRESS (TiP)

BACKGROUND:

Salvage radiotherapy (SRT) is a potentially curative option for patients with rising PSA (biochemical recurrence) after radical prostatectomy. Recently, success rates of SRT were significantly improved through the use of concomitant anti-androgen (AAT) or androgen-deprivation (ADT) therapy. In RTOG 96-01, 2 years of bicalutamide 150 mg resulted in a 5% OS benefit at 12-years [ref 1]. In GETUG-AFU 16, 5-year progression-free survival was significantly improved when SRT was combined with 6 months of an LHRH agonist [ref 2].

Based on GETUG-AFU 16, most European urologists and (radiation) oncologists now combine SRT with at least 6 months of ADT. However, ADT comes with several serious side-effects, both physical (cardiovascular, metabolic, musculoskeletal) and psychological (sexual, emotional and cognitive).

Considering RTOG 96-01, and in view of new AAT options, it appears worthwhile to look for alternatives. In that respect, apalutamide (ERLEADA®), a next-generation anti-androgen, is an interesting candidate.

1. Shipley W.U. et al. Radiation with or without antiadrogen therapy in recurrent prostate cancer. N Engl J Med 2017.

2. Carrie C. et al. Salvage radiotherapy with or without short-term hormone therapy for rising prostate-specific antigen concentration after radical prostatectomy (GETUG-AFU 16): a randomised, multicentre, open-label phase 3 trial. Lancet Oncol 2016.

(CONTACT) DETAILS:

SAVE
A Clinical Trial for Prostate Cancer

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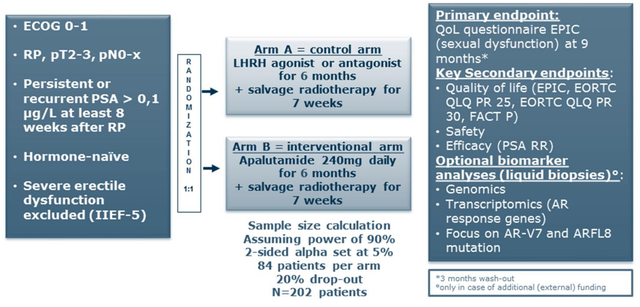
Eudract number: 2018-004365-13

www.clinicaltrials.gov: NCT03899077

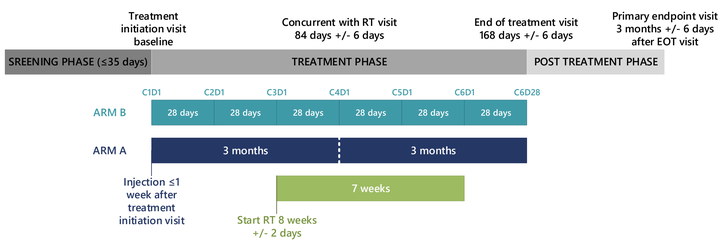
STUDY DESIGN:

This is a phase II randomized, open-label study comparing SRT in combination with 6 months of LHRH (ant)agonist (arm A) versus 6 cycles of apalutamide 240 mg daily (each cycle is 28 +/- 2 days) (arm B) in hormone-naïve patients with biochemical recurrence (PSA > 0.1 µg/L at least 8 weeks after radical prostatectomy).

All subjects will receive SRT to 70,0 Gy in 35 fractions as standard of care and will be randomly assigned in a 1:1 ratio to arm A or B.



SCHEMATIC STUDY OVERVIEW:



OUTCOME MEASURES:

1. EPIC-26 sexual domain score at 9 months after the start of hormonal treatment (0-100 scale, with higher scores representing better sexual function)
2. Quality of life: EPIC-26, EORTC QLQ C30 and PR25, FACT-P
   Toxicity: CTCAE version 5.0
   Efficacy: PSA (complete) response rates (i.e. decline from baseline in PSA level of 90% or greater)

PATIENT POPULATION:

Key inclusion criteria include:

1. Male, > 18 years old
2. ECOG 0-1
3. Histologically confirmed adenocarcinoma of the prostate
4. Previous radical prostatectomy (RP), pT2-3, pN0 or pNx
5. PSA > 0,1 µg/L at least 8 weeks after RP
6. Hormone-naive disease
7. Patients amendable to take oral medication
8. Patients must have clinical laboratory values at screening:
   a) Hemoglobin ≥9.0 g/dL, independent of transfusion and/or growth factors within 3 months prior to randomization
   b) Platelet count ≥100,000 x 109/µL independent of transfusion and/or growth factors within 3 months prior to randomization
   c) Serum albumin ≥3.0 g/dL
   d) Serum creatinine <2.0 × upper limit of normal (ULN)
   e) Serum potassium ≥3.5 mmol/L
   f) Serum total bilirubin ≤ 1.5 × ULN
   g) Aspartate aminotransferase or alanine aminotransferase <2.5 × ULN
9. Medications known to lower the seizure threshold must be discontinued or substituted at least 4 weeks prior to study entry.

Key exclusion criteria include:

1. Patients with severe erectile dysfunction according to international index of erectile function (IIEF-5) questionnaire (score 1-7)
2. Allergies, hypersensitivity or known intolerance to the study drugs or excipients.
3. History of any of the following:
   a) Seizure or known condition that may pre-dispose to seizure
   b) Severe or unstable angina, myocardial infarction, symptomatic congestive heart failure, arterial or venous thromboembolic events, or clinically significant ventricular arrhythmias within 6 months prior to randomization
4. Current evidence of any of the following:
   a) Uncontrolled hypertension
   b) Gastrointestinal disorder affecting absorption

ACCRUAL:

- Study approval local ethics committee: 16JAN2019
- Study approval Federal Agency for Medicine and Health Products: 04FEB2019
- Study activation (GZA only): 25MAR2019
- Anticipated study activation other centers: SEP-DEC2019
- Accrual as of 05APR2019: 4
- Anticipated accrual closure date: Q4 2021
- Anticipated final analysis: Q2 2023

PARTICIPATING CENTERS:

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Universiteit Antwerpen
az groeninge kortrijk
UZ GENT
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