Trial Comparing Irradiation Plus Long Term Adjuvant Androgen Deprivation With GnRH Antagonist Versus GnRH Agonist Plus Flare Protection in Patients With Very High Risk Localized or Locally Advanced Prostate Cancer (PEGASUS)

ClinicalTrials.gov Identifier:
NCT02799706

Recruitment Status: Recruiting
First Posted: June 15, 2016
Last Update Posted: June 19, 2018

See **Contacts and Locations**

Sponsor:
European Organisation for Research and Treatment of Cancer - **EORTC**

Information provided by (Responsible Party):
European Organisation for Research and Treatment of Cancer - EORTC

Study Description

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Brief Summary:

The primary objective of the trial is to assess if GnRH antagonists in combination with external beam radiation therapy improve progression free survival (progression that can be biological, clinical, or death) compared to GnRH agonists in combination with external beam radiation therapy.

Secondary objectives include:

- documentation of effect of GnRH antagonists on clinically significant cardiovascular events in the subgroup of patients at high risk of such events at baseline;
- documentation of side effects and quality of life, I-PSS and urinary tract infections;
- assessment of relative treatment effect on secondary efficacy endpoints (clinical progression, time to next line of systemic therapy, time on therapy, overall and cancer specific survival) and on PSA at 6 months after end of RT.

Condition or disease	Intervention/treatment	Phase
Prostate Cancer	Drug: Degarelix Drug: approved GnRH agonist Radiation: Radiotherapy	Phase 3

Detailed Description:

Phase IIIb randomized stratified open-label comparative 2-arm superiority study with a pre-set non-inferiority boundary.

Registered GnRH antagonists, degarelix, will be given at the dose of 240 mg given as two subcutaneous injections of 120 mg at a concentration of 40 mg/mL on day 1, followed by 80 mg given as one subcutaneous injection at a concentration of 20 mg/mL every 28 days (±2 days).

External beam radiotherapy (EBRT) to a total dose of 78-80 Gy, delivered as one daily fraction, five days a week, started between d1 and months 6 of the androgen deprivation therapy as per institution policy. The irradiation is the same as in the reference therapy arm.

The minimum duration of androgen deprivation with GnRH agonist or antagonist therapy is 18 months.

For each patient, the duration of therapy must be elected upfront by the treating physician among three possible options: 18, 24 or 36 months. The institution shall also declare upfront the duration of the neoadjuvant treatment they intend to deliver to each patient (between 0 and 6 months).

The primary endpoint is progression-free survival defined as the time in days from randomization to death, clinical or biochemical progression, whichever comes first.

Where

- PSA progression based on Phoenix definition, i.e. a rise by 2 ng/mL or more above the nadir PSA (Ref. 17) confirmed by a second value measured minimum 3 months later
- Clinical progression is defined as onset of obstructive symptoms requiring local treatment and demonstrated to be caused by cancer progression or evidence of metastases detected by clinical symptoms and confirmed by imaging
- Start of another line of systemic therapy in absence of progression
- Death due to any cause

Secondary endpoints:

- Clinical progression-free survival
- Time to next systemic anticancer therapy (including secondary hormonal manipulation)
- Proportion of patients switching from GnRH antagonists to GnRH agonists and total effective duration of treatment with the originally allocated drug.
- Overall survival
- Cancer specific survival
- PSA at six months after completion of RT Safety will be scored by the CTCAE version 4.0. The major safety endpoints in this study are
- the incidence of clinical cardiovascular events - CCE (i.e. arterial embolic or thrombotic events, hemorrhagic or ischemic cerebrovascular conditions, myocardial infarction, and other ischemic heart disease) in patients who had cardiovascular events before entering the trial and in those without such events.
- Incidence of urinary tract infection

Study Design Go to

Study Type:	Interventional (Clinical Trial)
Estimated Enrollment:	885 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	Phase IIIb Randomized Trial Comparing Irradiation Plus Long Term Adjuvant Androgen Deprivation With GnRH Antagonist Versus GnRH Agonist Plus Flare Protection in Patients With Very High Risk Localized or Locally Advanced Prostate Cancer. A Joint Study of the **EORTC** ROG and GUCG
Actual Study Start Date:	September 25, 2017
Estimated Primary Completion Date:	June 2024
Estimated Study Completion Date:	June 2024

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: Deslorelin Deslorelin acetate

U.S. FDA Resources

Arms and Interventions

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Arm	Intervention/treatment
Active Comparator: GnRH agonist + radiation therapy (RT) As the study investigates the effect of a drug given concomitantly to radiotherapy, all patients will be treated with the same treatment technique and target dose. The preferred treatment technique is intensity modulated radiotherapy (IMRT) + A GnRH-agonist will be given for the duration selected for each patient. A non-steroidal anti-androgen (e. g. flutamide, bicalutamide) will be given orally one week before the first injection of the GnRH agonist and will be continued for no longer than 8 weeks to protect against flare. Dose may vary due to availability of different brand names and pharmaceutical forms The start of antiandrogen must be registered as day 1 of treatment in the GnRH agonist arm.	Drug: approved GnRH agonist A non-steroidal anti-androgen (e. g. flutamide, bicalutamide) will be given orally one week before the first injection of the GnRH agonist and will be continued for no longer than 8 weeks to protect against flare.Dose may vary due to availability of different brand names and pharmaceutical forms The start of antiandrogen must be registered as day 1 of treatment in the GnRH agonist arm. Radiation: Radiotherapy .As the study investigates the effect of two drugs given concomitantly to radiotherapy, all patients will be treated with the same treatment technique and target dose. The preferred treatment technique is intensity modulated radiotherapy (IMRT)
Experimental: GnRH antagonist + radiation therapy (RT) As the study investigates the effect of two drugs	Drug: Degarelix a GnRH antagonist will be given for a predefined duration of 18, 24, or 36 months as per institution policy

given concomitantly to radiotherapy, all patients will be treated with the same treatment technique and target dose. The preferred treatment technique is intensity modulated radiotherapy (IMRT) +a GnRH antagonist will be given for a predefined duration of 18, 24, or 36 months as per institution policy. Each institution has to adhere to the chosen duration of treatment for all patients throughout the study	Radiation: Radiotherapy .As the study investigates the effect of two drugs given concomitantly to radiotherapy, all patients will be treated with the same treatment technique and target dose. The preferred treatment technique is intensity modulated radiotherapy (IMRT)

Outcome Measures

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Primary Outcome Measures:

1. Progression free survival [Time Frame: through study completion, an average of 1 year]

   The primary endpoint is progression-free survival defined as the time in days from randomization to death, clinical or biochemical progression, whichever comes first.

   Where

   - PSA progression based on Phoenix definition, i.e. a rise by 2 ng/mL or more above the nadir PSA (Ref. 17) confirmed by a second value measured minimum 3 months later
   - Clinical progression is defined as onset of obstructive symptoms requiring local treatment and demonstrated to be caused by cancer progression or evidence of metastases detected by clinical symptoms and confirmed by imaging
   - Start of another line of systemic therapy in absence of progression
   - Death due to any cause

Secondary Outcome Measures:

1. Clinical progression-free survival [Time Frame: through study completion, an average of 1 year]
2. Time to next systemic anticancer therapy (including secondary hormonal manipulation)
   [Time Frame: through study completion, an average of 1 year]
3. ♦ Proportion of patients switching from GnRH antagonists to GnRH agonists [Time Frame: through study completion, an average of 1 year]
4. ♦ Overall survival [Time Frame: through study completion, an average of 1 year]
5. Incidence of clinical cardiovascular events [Time Frame: through study completion, an average of 1 year]

   ♦ the incidence of clinical cardiovascular events - CCE (i.e. arterial embolic or thrombotic events, hemorrhagic or ischemic cerebrovascular conditions, myocardial infarction, and other ischemic heart disease) in patients who had cardiovascular events before entering the trial and in those without such events.

6. ♦ Incidence of urinary tract infection [Time Frame: through study completion, an average of 1 year]

Eligibility Criteria

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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 80 Years (Adult, Older Adult)
Sexes Eligible for Study:	Male
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

- Histologically confirmed diagnosis of prostate adenocarcinoma
- PSA ≥ 10 ng/ml and two of the following 4 criteria:
- PSA ≥ 20 ng/ml,
- Gleason sum ≥ 8,
- cN1 (regional LN with a short axis length >10mm by CT scan or MRI) or pathologically confirmed lymph nodes (pN1),
- cT3-T4 (by MRI or core biopsy) (i.e. If PSA≥ 20 ng/ml then only one of the other 3 risk factors is needed)
- M0 by standard imaging work-up (see chapter 6.1.1.1)
- Testosterone ≥ 200 ng/dl
- Adequate renal function: calculated creatinine clearance ≥ 50 mL/min (Appendix D) Magnesium and potassium within normal limits of the institution or corrected to within normal limits prior to the first dose of treatment.
- Patients with prolonged QT-intervals due to prescribed Class IA (quinidine, procainamide) or Class III (amiodarone, sotalol) antiarrhythmic medication must be carefully evaluated for GnRH-agonist or GnRH antagonist use, because these drugs may prolong the QT-interval.
- WHO Performance status 0-1
- Age ≥ 18 and ≤ 80 years
- Participants who have partners of childbearing potential must use adequate birth control measures, as defined by the investigator, during the study treatment period and for at least 3 months after last dose of study treatment. A highly effective method of birth control is defined as those which result in low failure rate (i.e. less than 1% per year) when used consistently and correctly
- Before patient registration/randomization, written informed consent must be given according to ICH/GCP, and national/local regulations.

Exclusion Criteria:

- Previous use of androgen deprivation therapy (ADT), antiandrogens. 5-alpha reductase inhibitors are allowed if interrupted for more than 6 months prior to entering the study
- History of severe untreated asthma, anaphylactic reactions or severe urticaria and/or angioedema.
- Hypersensitivity towards the investigational drug
- The following biological parameters :AST, ALT, total bilirubin, prothrombin time, serum albumin above upper level of normal range No severe hepatic impairment (Child Pugh C)
- History of gastro-intestinal disorders (medical disorder or extensive surgery) that may interfere with the

absorption of the protocol treatment.

- History of pituitary or adrenal dysfunction
- Uncontrolled diabetes mellitus
- History of ulcerative colitis, Crohn's Disease, ataxia, telangiectasia, systemic lupus erythematous, or Fanconi anemia.
- Clinically significant heart disease as evidence myocardial infarction, or arterial thrombotic events in the past 6 months, severe or unstable angina, or New York Heart Association (NYHA) class III or IV heart disease or cardiac ejection fraction measurement of < 50 % at baseline
- Coronary revascularization (PCI or multivessel CABG), carotid artery or iliofemoral artery revascularization (percutaneous or surgical procedure) within the last 30 days prior to entering the trial
- Certain risk factors for abnormal heart rhythms/QT prolongation: torsade de pointes ventricular arrhythmias (e.g, heart failure, hypokalemia, or a family history of a long QT syndrome), a QT or corrected QT (QTc) interval >450 ms at baseline, or intake of medications that prolong the QT/QTc interval
- Uncontrolled hypertension (systolic BP ≥ 160 mmHg or diastolic BP ≥ 95 mmHg); patients with a history of hypertension are allowed provided blood pressure is controlled by anti-hypertensive treatment.
- Prior history of malignancies other than prostate adenocarcinoma (except patients with basal cell, squamous cell carcinoma of the skin), or the patient has been free of malignancy for a period of 3 years prior to first dose of study drug(s). Prior history of bladder cancer excludes the patient.
- Prior radical prostatectomy (TURP or suprapubic adenomectomy for benign prostatic hyperplasia is allowed)
- Prior brachytherapy or other radiotherapy that would result in an overlap of radiotherapy fields
- Any contraindication to external beam radiotherapy
- Patients with significantly altered mental status prohibiting the understanding of the study or with psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule or any condition which, in the opinion of the investigator, would preclude participation in this trial

Contacts and Locations

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Information from the National Library of Medicine NIH NLM

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): ***NCT02799706***

Contacts

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Locations

Belgium

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Principal Investigator: Thomas Zilli

Sponsors and Collaborators

European Organisation for Research and Treatment of Cancer - **EORTC**

Investigators

Principal Investigator:	Dirk Boehmer, MD, PhD	Charite - Universitaetsmedizin Berlin - Campus Benjamin Franklin
Principal Investigator:	Pedro Lara, MD, PhD	Hospital Universitario de Gran Canaria Doctor Negrin

More Information

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Responsible Party:	European Organisation for Research and Treatment of Cancer - EORTC
ClinicalTrials.gov Identifier:	NCT02799706 History of Changes
Other Study ID Numbers:	**EORTC-1414**
First Posted:	June 15, 2016 Key Record Dates
Last Update Posted:	June 19, 2018
Last Verified:	June 2018

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

Keywords provided by European Organisation for Research and Treatment of Cancer - EORTC:

Prostate cancer	radiation therapy
GnRH antagonist	very high risk localized prostate cancer
GnRH agonist	locally advanced prostate cancer

Additional relevant MeSH terms:

Prostatic Neoplasms	Hormones, Hormone Substitutes, and Hormone
Genital Neoplasms, Male	Antagonists
Urogenital Neoplasms	Physiological Effects of Drugs
Neoplasms by Site	Enzyme Inhibitors
Neoplasms	Molecular Mechanisms of Pharmacological Action
Genital Diseases, Male	Luteolytic Agents
Prostatic Diseases	Contraceptive Agents, Female
Androgens	Contraceptive Agents
Prolactin Release-Inhibiting Factors	Reproductive Control Agents
Deslorelin	Antineoplastic Agents, Hormonal
Triptorelin Pamoate	Antineoplastic Agents
Nonsteroidal Anti-Androgens	Androgen Antagonists
Hormones	Hormone Antagonists