Testosterone based dosing regimen of goserelin in patients with prostate cancer

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The primary objective is to determine in which percentage of patients with prostate cancer with an indication for ADT, it is safe to extend the dosing interval of goserelin 10,8 mg by four weeks, before the 4th injection, using a testosterone based...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Reproductive and genitourinary neoplasms gender unspecified NEC
Study type	Interventional

Summary

ID

NL-OMON54398

Source
ToetsingOnline

Brief title
TEST-TOSTERON

Condition

- Reproductive and genitourinary neoplasms gender unspecified NEC
- Prostatic disorders (excl infections and inflammations)

Synonym
Prostate cancer, prostate tumour

Research involving
Human

Sponsors and support

Primary sponsor: Franciscus Gasthuis & Vlietland
Source(s) of monetary or material Support: geen financiering beschikbaar;het wordt

verricht onder het reguliere arbeidscontract met het ziekenhuis

Intervention

Keyword: ADT, LHRH-agonists, Prostatic Neoplasms, testosterone-based dosing

Outcome measures

Primary outcome

The primary endpoint of this study is the percentage (%) of patients for whom the dosing interval before the fourth goserelin 10.8 mg injection can safely be extended with 4 weeks using a testosterone based dosing regimen.

Secondary outcome

The percentage (%) of patients, that can safely extend the dosing interval of the 4th goserelin injection with 8 or 12 weeks, using a testosterone based dosing regimen.

The percentage (%) of patients, for whom the dosing interval of the fourth injection was extended with maximum 12 weeks, that can safely extend the dosing interval of the 5th goserelin 10,8 mg injection with 4, 8 or 12 weeks, using a testosterone level-based dosing regimen

The percentage of patients indicating an overall preference for testosterone-based dosing regimen or regular treatment with a 12-weekly based dosing regimen. Patient is its own control.

Difference in treatment costs per patient in the testosterone based regimen compared to regular treatment with a 12-weekly based goserelin 10.8 mg injection, including:

- Depot injections of goserelin 10.8 mg

- Laboratory tests

- Outpatient monitoring

- Other medication and surgical interventions related to the disease

- Complications after a surgery related to the disease

- Our data will be compared to data published in previous studies.

Overview of the metabolome of testosterone.

Study description

Background summary

Rationale: Chemical or surgical castration is a key strategy in patients with locally advanced or metastatic prostate cancer. Chemical castration is achieved by administering Luteinizing Hormone Releasing Hormone (LHRH) agonists on a regular basis. Successful castration is internationally characterized by prolonged serum testosterone levels <= 1.7nmol/L. Currently, the dosing regimen for LHRH agonist goserelin is a manufacturer recommended fixed dose (10.8 mg) in a fixed interval of 12 weeks. Also, during this fixed dose goserelin LHRH-therapy, testosterone levels are not routinely monitored.
Several studies have also shown that serum testosterone levels remain suppressed below the 1.7 nmol/L level for more than three months after administration of a single dose or after cessation of LHRH therapy. These results suggest that a more personalized way of dosing LHRH agonists, namely dosing based on a patient*s testosterone level, could be equally effective in achieving chemical castration compared to 12-weekly based dosing of LHRH agonists.
In a recent study, researchers investigated the possibility of extending the dosing interval of goserelin, straight from the onset of treatment, with a testosterone level-based dosing regimen. The median time to the next goserelin injection in the study group was 22.8 weeks, versus the current fixed dosing interval of 12 weeks in the control group. In two patients, an unpredicted rapid rise of the testosterone level above the castrate level (>1.7 nmol/L) occurred [6]. Possible explanations for the rapid rise of testosterone levels are reactivation of the available LHRH-receptors, a fast upregulation of LHRH-receptors or a combinations of both mechanisms. These effects might be stronger in patients that only have a limited number of injections of LHRH. Prolonging the dosing interval in patients who have been treated with androgen deprivation therapy ADT for a longer period of time seems promising. The hypothesis in this study, is that in patients who have been treated with ADT

for a longer period of time, the testis are less active and are less likely to produce testosterone to the extent of rising above 1.7 nmol/L. So prolonging the dosing interval in patients who have been treated with ADT for a longer period of time seems promising.

Study objective

The primary objective is to determine in which percentage of patients with prostate cancer with an indication for ADT, it is safe to extend the dosing interval of goserelin 10,8 mg by four weeks, before the 4th injection, using a testosterone based dosing regimen.

Secundairy objectives:
• to determine the percentage of the included patients, that can safely extend the dosing interval of the 4th goserelin 10,8 mg injection with 8 or 12 or weeks, before the 4th injection, using a testosterone based dosing regimen.
• to determine the percentage of the included patients, for whom the dosing interval of the fourth injection was extended with maximum 12 weeks, that can safely extend the dosing interval of the 5th goserelin 10,8 mg injection with 4, 8 or 12 weeks, using a testosterone based dosing regimen.
• Time to castrate refractory disease
• to establish the patient preference for either testosterone-based dosing regimen of goserelin 10.8 mg injection or regular treatment with a 12-weekly based goserelin 10.8 mg injection.
• to perform a pharmaco-economic analysis. To determine whether a testosterone-based dosing regimen of goserelin 10.8 mg is cost-saving compared to regular treatment with a 12-weekly based goserelin 10.8 mg injection.
• To explore the metabolites of testosterone.

Study design

Study design: This study is a non-randomized prospective interventional study. Patients will be included after they have been treated with 3 goserelin 10.8 mg injections according to standard of care, being 12-weekly depot injections of goserelin 10.8 mg (see Figure 1). During the study patients will be treated with 1 or 2 goserelin 10.8 mg injections (dependent on the dosing regimen of the 4th goserelin injection) following a testosterone-based dosing regimen, according to the defined algorithm.

Intervention

A conservative algorithm will be applied to ensure that testosterone will remain at castrate level (below 1.7 nmol/L). Approximately 11 weeks after the third depot injection of goserelin 10.8 mg, blood levels of

testosterone will be measured. When one of the following rule does not apply, a depot injection of goserelin 10.8 mg is injected subcutaneously administer at 12 weeks:

A. The testosterone level <= 1.2 nmol/L.
B. An increase of < 0.5 nmol/L from the nadir

When the testosterone level does meet both of the above mentioned requirements, goserelin treatment will be postponed, blood levels of testosterone will be measured again after 3 weeks and according to the described algorithm the next injection of goserelin is given or again postponed for 3 weeks, with a maximum of 12 weeks.

Study burden and risks

If a patient participates in the study, there is no therapeutic benefit in the treatment of prostate cancer. But it helps the researchers gain more insight into the treatment of prostate cancer with goserelin. Participation in this studies might lead to patients receiving fewer injections of goserelin in the future. This ultimately leads to patient convenience and savings costs for society.

Participating in the study may have these drawbacks:
- blood sampling may hurt, bruising may occur.
- Participating in the study takes extra time, blood is taken every month, this takes about 15 minutes at a time.

The risk of getting side effects in this study is the same as with regular treatment.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Informed consent
- >= 18 years
- Diagnosed with prostate cancer with an indication for Androgen Deprivation Therapy (>= 2 years or permanently)

Exclusion criteria

- Patients with a history of hypersensitivity to LHRH agonists
- Patients not able to visit hospital*s laboratory for blood sampling
- Patients with a serum testosterone > 1.2 nmol/L while treated with LHRH therapy (patients who fail on LHRH therapy, in the first half year of treatment)
- Concurrent systemic anti- cancertherapy other than goserelin

Study design

Design

Study phase:	4
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-07-2022
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Zoladex
Generic name:	Goserelin
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	28-12-2021
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-08-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2021-004646-38-NL
CCMO	NL78358.100.21