Randomized multicenter, phase III trial evaluating the safety of 2 schedules of cabazitaxel (bi-weekly versus tri-weekly) plus prednisone in elderly men (* 65 years) with metastatic castration-resistant prostate cancer (mCRPC) previously treated with a docetaxel-containing regimen (CABASTY).

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To evaluate the incidence of grade * 3 neutropenia (measured at Day 7 and Day 14) and/or neutropenic complications (febrile neutropenia, neutropenic infection) with two schedules of cabazitaxel (bi-weekly versus tri-weekly) plus prednisone in…

Ethical review	Approved WMO
Status	Will not start
Health condition type	Reproductive neoplasms male malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON48773

Source
ToetsingOnline

Brief title
CABASTY

Condition

- Reproductive neoplasms male malignant and unspecified

Synonym
Prostate cancer

Research involving
Human

Sponsors and support

Primary sponsor: ARTIC
Source(s) of monetary or material Support: ARTIC

Intervention

Keyword: cabazitaxel, elderly population, metastatic, Prostate

Outcome measures

Primary outcome

Grade *3 neutropenia (measured at D7 and D14 of each cycle) and/or neutropenic complications (febrile neutropenia, neutropenic infection or sepsis) during the overall treatment period

Secondary outcome

The following parameters will be evaluated in each arm:

*Dose reductions and dose delays

*Radiological progression-free survival (rPFS)

*Time to PSA progression

*Time to first symptomatic Skeletal-Related Event (SRE) and incidence of SREs

*Time to opioid treatment (if relevant)

*Prostate-specific antigen (PSA) response rate

*Quality of Life (FACT-P)

*Objective response rate (ORR) in measurable lesions (RECIST criteria 1.1 * Appendix G)

*Overall Survival (OS)

*Factors influencing survival (duration of response to first androgen deprivation therapy (ADT), serum testosterone, cumulative dose of cabazitaxel, neutrophils/lymphocytes ratio, Gleason score, geriatric assessment G8, grade *3 neutropenia).

*Time to onset of grade *3 neutropenia

*Grade *3 neutropenia duration (from date of onset of grade * 3 until grade * 2)

*Analysis of grade *3 neutropenia and/or neutropenia by cycle

*Adverse events

Study description

Background summary

There is growing evidence that the older men have more aggressive prostate carcinomas. If elderly patients with localized prostate carcinoma are more likely to receive a curative treatment than their younger counterparts, the trend is in inverse proportion for older patients with metastatic disease who receive less frequently chemotherapy probably due to concerns about tolerability.
At present, physicians are tempted to treat elderly metastatic castration-resistant prostate cancer (mCRPC) patients with new androgen receptor (AR)-targeted agents, such as abiraterone acetate or enzalutamide, since they have proven to prolong overall survival (OS), are orally delivered, and well tolerated. However, because prostate cancer is a heterogeneous disease, all of the patients will not respond to AR-targeted agents. Indeed, some of them present a primary resistance to these agents, and others will develop an acquired resistance in course of time. Moreover, retrospective studies, involving a small number of patients, suggest that once a patient has progressed with an AR-targeted agent, he will poorly respond to another AR-targeted agent. Finally, the place of first-line androgen deprivation therapy (ADT) for advanced prostate cancer is now strongly challenged. Systematic review and meta-analysis of randomized studies in hormone-sensitive prostate cancer also confirms that ADT plus 6 cycles docetaxel significantly

prolongs survival in hormone-sensitive metastatic prostate cancer and this regimen is now recommended as standard of care by ESMO guidelines
The purpose of this phase III international, Randomized, open-label, is to compared cabazitaxel 25 mg/m2 on Day 1 of a 3-week cycle plus daily prednisone versus cabazitaxel 16 mg/m2 on Day 1 and Day 15 of a 4-week cycle in mCRPC patients aged * 65 years.
We would like to confirm the improved safety profile of cabazitaxel bi-weekly regimen in this study comparing cabazitaxel 25mg/m2 every 3 weeks versus cabazitaxel 16 mg/m2 every 2 weeks until disease progression or unacceptable toxicity. G-CSF will be given systematically according to European Organization for Research and Treatment of Cancer (EORTC) recommendations

Study objective

To evaluate the incidence of grade * 3 neutropenia (measured at Day 7 and Day 14) and/or neutropenic complications (febrile neutropenia, neutropenic infection) with two schedules of cabazitaxel (bi-weekly versus tri-weekly) plus prednisone in elderly men (* 65 years) with mCRPC previously treated with a docetaxel-containing regimen.

Study design

Randomized, open-label, phase 3 trial comparing cabazitaxel 25mg/m2 every 3 weeks versus cabazitaxel 16mg/m2 every 2 weeks in mCRPC patients aged * 65 years.

Intervention

Not applicable

Study burden and risks

The risks associated with this study are:
adverse effects due to study drugs
risks related with the study procedures

Contacts

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Patient aged * 65 years with mCRPC previously treated with docetaxel
2. Medical or surgical castration with castrate level of testosterone (< 50 ng/dl) based on the EAU definition of castrate level of testosterone
3. Progressive disease according to PCWG2 (Appendix H)
4. Histologically proven prostate carcinoma
5. Health status allowing use of chemotherapy: G8 > 14; or G8 score * 14 with geriatric assessment concluding to reversible impairment allowing use of chemotherapy
6. ECOG-PS 0, 1 or 2(ECOG-PS 2 should be related to prostate cancer)
7. Adequate hematologic, liver and renal functions:
a) Neutrophil count *1.5 109/L
b) Haemoglobin *10 g/ dL
c) Platelet count *100.109/L
d) Total bilirubin * 1 the upper limit of normal (ULN)
e) Transaminases * 1.5 ULN
f) Serum creatinine * 2.0 ULN
8. Ongoing LHRH therapy at study entry
9. Signed informed consent

Exclusion criteria

1.History of severe hypersensitivity reaction (.grade 3) to docetaxel
2.History of severe hypersensitivity reaction (.grade 3) to polysorbate 80 containing drugs
3.Uncontrolled severe illness or medical condition (including uncontrolled diabetes mellitus)
4.Concurrent or planned treatment with strong inhibitors or strong inducers of cytochrome P450 3A4/5 (a one week wash-out period is necessary for patients who are already on these treatments) (see Appendix E)
5.ECOG-PS >2 not related to prostate cancer disease
6.G8 . 14 with geriatric assessment contra-indicating standard cabazitaxel regimen
7.Concomitant vaccination with yellow fever vaccine
8.Patient who cannot be regularly followed or cannot answer to quality of life questionnaires because of psychological, social, familial or geographic reasons
9.Participation in another clinical trial with any investigational drug within 30 days prior to study enrolment

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	20
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	JEVTANA

Generic name:	NA
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	25-06-2018
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-10-2019
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-12-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-12-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR201600117960-NL
CCMO	NL65862.091.18