Improving bio-availability of the expensive oral oncolytic drug abiraterone by food intake

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Primary objective:To determine the equivalent dose of abiraterone when taken with a continental breakfast compared to 1000 mg in fasted stateSecondary objective:To evaluate the preference of the patients: intake of abiraterone with or without food

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Reproductive neoplasms male malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON45784

Source
ToetsingOnline

Brief title
SNACK

Condition

- Reproductive neoplasms male malignant and unspecified

Synonym
metastatic castration resistent prostate carinoma, prostate cancer

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: abiraterone, breakfast, pharmacokinetics

Outcome measures

Primary outcome

The aim of this part of the study is to determine the equivalent reduced dose

of abirateron when taken with a continental

breakfast compared to the registered intake of abirateron (e.g. 1000 mg OD

without food)

Secondary outcome

To explore, quantify and describe patients preference; abirateron intake with

or without food.

Study description

Background summary

Abiraterone is a selective inhibitor of androgen biosynthesis that potently and irreversibly blocks CYP17, a crucial enzyme in testosterone and oestrogen synthesis. A pro-drug of abiraterone, abiraterone acetate (Zytiga®), was developed to overcome its poor bio-availability and is fully converted to the active moiety abiraterone. Abiraterone acetate tablets are administered at a fixed oral dose of 1000mg QD in a fasted state in combination with 10mg prednisolon daily.
Abiraterone acetate has a low solubility in aqueous media and a low permeability. The bioavailability of abiraterone acetate is significantly influenced when ingested with food. Ingesting abiraterone acetate with a low fat or a high fat meal resulted respectively in a 5- or 10-fold increase in AUC0-*. The high and low fat FDA meals used in these food effect studies differ largely from breakfasts taken in everyday life(ca. 800-1000 cal). A continental breakfast contains 160 to 320 calories of which 25-50% is fat, is more compatible with a normal lifestyle and therefore easily sustainable in daily practice. However, the effect of a continental breakfast on the absorption of abiraterone is unknown yet. Furthermore, increasing healthcare costs are a growing concern in all developed countries. Therefore effort should be

invested to keep anticancer treatment affordable. A food intervention resulting in a better absorption and enhanced exposure to abiraterone, can lead to a reduced dose, which could significantly impact health care costs for a tumor which is so prevalent as metastatic prostate cancer.

Study objective

Primary objective:
To determine the equivalent dose of abiraterone when taken with a continental breakfast compared to 1000 mg in fasted state
Secondary objective:
To evaluate the preference of the patients: intake of abiraterone with or without food

Study design

Patients who use abiraterone are included.
A total of 24-27 patients will be included. Pharmacokinetic (PK) and safety evaluation will initially be performed in three patients treated with 1000 mg QD (100%) abiraterone in a fasted state for two weeks followed by two weeks of 500 mg QD (50%) abiraterone together with a standardized continental breakfast. PK assessment will be performed after 2 (1000mg QD without food) and 4 weeks (500mg QD with food) of abiraterone therapy. The results of these three patients will be analysed and discussed to determine a safe and feasible dose for the next patients in the study. The next 21-24 patienten will be randomized into to groups. One group will start with 1000mg abirateron taken in a fasted state, after two weeks of therapy they will switch to a reduced dose ingested with a continental breakfast. the second group starts with the reduced dose ingested with food and switches to 1000mg abirateron ingested fasted. The reduced dose for the next 21-24 patients will either be 750mg QD (75%), 500mg QD (50%) or 250mg QD (25%) based on the PK assessment and the safety profile observed in the initial three patients.

Study burden and risks

Participating patients will be asked for a hospital admission for two days to collect the blood samples. All blood samples will be drawn from a once placed intravenous cannula. A total of 11 blood samples will be taken per admission day. The burden for the participants of this part of the study is considered to be mild.
In general the risk for participation in this study is regarded moderate.
The risk of suboptimal dosing is minimized by the run in of three patients at 500 mg QD with food and the very limited period in which the dose is reduced (2 weeks in total). Furthermore previous studies showed a food effect of at least 200% when ingested with a meal. The risk of abiraterone related toxicity is very limited because previous studies showed no adverse events of >= grade 3

where seen when 1000mg abiraterone acetate was ingested with a high fat meal of a period of one week. Benefits associated with participating in this study are that patients and their treating physician get insight into their individual abiraterone exposure and the abiraterone exposure when taken with a continental breakfast.

Contacts

Public
Radboud Universitair Medisch Centrum

Geert Grooteplein zuid 10
Nijmegen 6525GA
NL
Scientific
Radboud Universitair Medisch Centrum

Geert Grooteplein zuid 10
Nijmegen 6525GA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

-Subjects must provide written informed consent prior to performance of study-specific procedures or assessments and must be willing to comply with treatment and follow-up.;->= 18 year old men who use abiraterone ;-Eastern Cooperative Oncology Group (ECOG) performance status of 0-2. ;-Feasible to collect blood samples from

Exclusion criteria

•Clinically significant gastrointestinal abnormalities that may affect absorption of investigational product ;•Malabsorption syndrome.;•Major resection of the stomach or small bowel.;•Any serious and/or unstable pre-existing medical, psychiatric, or other condition that could interfere with subject*s safety, provision of informed consent, or compliance to study procedures. ;•Unable or unwilling to discontinue use of prohibited medications listed in for at least 14 days or five half-lives of a drug (whichever is longer) prior to the first dose of day 1 and for the duration of the study.;•Concurrent use of other substances known or likely to interfere with the pharmacokinetics of abiraterone

Study design

Design

Study type:	Observational invasive
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	30-10-2016
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Zytiga
Generic name:	Abiraterone
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	13-07-2016
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	25-08-2016
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	02-03-2017
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	EUCTR2016-001943-37-NL
CCMO	NL57602.091.16