QT-Cab: An Open-Label Study to Investigate the Effect of Cabazitaxel on the QTc Interval in Cancer Patients

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Primary objective: To assess the potential effect on QTcF interval (QTc Fridericia) of cabazitaxel in cancer patientsSecondary objectives:• To assess the effects of cabazitaxel on heart rate (HR), QT, QTcB (Bazett*s correction), and QTcN (population...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Miscellaneous and site unspecified neoplasms benign
Study type	Interventional

Summary

ID

NL-OMON34078

Source
ToetsingOnline

Brief title
QT-Cab

Condition

- Miscellaneous and site unspecified neoplasms benign

Synonym
Cancer, oncology

Research involving
Human

Sponsors and support

Primary sponsor: Sanofi-aventis
Source(s) of monetary or material Support: sanofi-aventis

Intervention

Keyword: Advanced, Cancer, solid tumors

Outcome measures

Primary outcome

Primary end-point:

• QTcF, change from baseline, derived from core lab reading of QT interval (baseline will be taken on Day 1 of Cycle 1, within 15 min prior to the first cabazitaxel infusion)

Secondary outcome

Secondary end-points:

• Change from baseline in HR, QT, QTcB and QTcN intervals (same baseline as above)

• Other ECG parameters: PR, QRS intervals, ECG morphology

• Clinical safety: adverse events and serious adverse events

• Pharmacokinetics: cabazitaxel plasma concentrations, Cmax and partial AUC

Study description

Background summary

Cabazitaxel is a new anticancer research drug that is not yet marketed in your country. The U.S. Food and Drug Administration (FDA) has recently granted marketing authorization for Jevtana (cabazitaxel) for the treatment of patients with metastatic hormone-refractory prostate cancer previously treated with a docetaxel-containing treatment regimen. To date, cabazitaxel has been administered to more than 500 patients with various cancers, including breast cancer.

Current regulations require that, for all potential new drugs, a specific clinical study be conducted to assess its effects on the electrocardiogram (the

electrocardiogram or ECG measures the electrical activity of the heart). The purpose of QT-Cab is to meet this mandatory requirement.
The QT-Cab study will therefore assess the effects of cabazitaxel on the electrocardiogram and relate these effects with the cabazitaxel blood levels.

Study objective

Primary objective: To assess the potential effect on QTcF interval (QTc Fridericia) of cabazitaxel in cancer patients

Secondary objectives:
• To assess the effects of cabazitaxel on heart rate (HR), QT, QTcB (Bazett*s correction), and QTcN (population specific correction formulae) intervals
• To assess the clinical safety of cabazitaxel
• To assess cabazitaxel plasma concentrations at Cycle 1 at early timepoints (during 1h infusion and up to 23h post end of infusion)

Study design

This is a prospective multicenter, multinational, open-label study. Patients enrolled must have a solid malignancy (confirmed by a cytology or pathologic report) for which standard curative treatment does not exist and a treatment with a novel taxane agent is considered.
The study will include 2 treatment periods (after an initial screening and registration):
• A main period (2 cycles) which will be the basis for the study analysis: including ECG, PK, adverse events (AEs), and serious adverse event (SAEs).
• The main period will be followed by an optional, extension period (Cycle 3 and beyond), during which patients will have the option to continue to receive cabazitaxel treatment as long as they are benefiting from it, and provided there is no unacceptable toxicity, or need to use anti-cancer treatment other than cabazitaxel. During the extension period, there will be a reduced data collection (will include SAE, related AE). During the entire treatment period, cabazitaxel is administered every 3 weeks (preceded by an IV pre-medication regimen). Cycle 1, Day 1 and 2 is the main visit for QT assessment:
• QTc and other ECG intervals will be assessed at Cycle 1, using a 12-lead Holter ECG monitor. The ECG Holter recording will last 26 hours (with recording starting before the IV pre-medication regimen, continuing through the IV pre-medication regimen and the IV cabazitaxel infusion, and ending 23 hours after the end of the cabazitaxel infusion).
• At Cycle 1, the IV pre-medication regimen should be administered during the time interval ranging from 90 to 60 min before the start of cabazitaxel infusion. Other medications could be administered on that day only if clinically required.
• Concomitant serial PK blood sampling will also be performed on Cycle 1, Day 1 and 2. In addition, the use of concomitant medications known to significantly

prolong QT interval will be forbidden from screening until Cycle 1, Day 1 and 2. In particular, use of anti-emetics of the 5 HT-3 receptor antagonist class (or setron class) will be strictly controlled, and restricted to palonosetron during the last week in screening and Cycle 1, Day 1 and 2. Use of strong CYP 3A4/5 inhibitors is not authorized throughout the study (main and extension period).

Intervention

At every cycle (every 3 weeks), on Day 1, patients will receive cabazitaxel, administered by IV infusion over 1 hour, at 25 mg/m2.

An IV premedication regimen composed of up to 4 treatments (antihistamine, corticosteroids, H2 antagonist other than cimetidine at all cycles, plus palonosetron at cycle 1) will be administered before cabazitaxel infusion.

Study burden and risks

Risk associated with cabazitaxel:
Not all side effects of cabazitaxel are known yet. The more known significant side effects include abnormalities in the blood (anemia, thrombocytopenia and leucopenia). Lowering of your white blood cell count may occur, which could increase your risk of infection. Other possible effects on your blood system include a decrease in your red blood cells, which can lead to shortness of breath and fatigue; and a decrease in platelets, which can lead to bleeding.

Procedure-Related Risks:
Blood drawn can cause bruising at or near the site of puncture or blood collection. Setting up the Holter ECG with the patches can cause itching.

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

- Histologically or cytologically confirmed solid malignancy that is metastatic or unresectable, and for which standard curative measures do not exist, and a treatment with a novel taxane agent is considered.
-Written informed consent
- 18 years or older

Exclusion criteria

• Conditions with screening ECG repolarization difficult to interpret, or showing significant abnormalities. This includes, but is not limited to: high degree AV block, pace-maker, atrial fibrillation or flutter
• QTcF >480 msec on screening ECG
• Significant hypokalemia at screening (K+ <3.5 mMol/L)
• Significant hypomagnesemia at screening (Mg++ <0.7 mMol/L)
(Note: Patient may be enrolled after correction of these laboratory abnormalities)
• Patient receives (and cannot discontinue), or is scheduled to receive a QT-prolonging drug (see Appendix B)
• Known allergy or intolerance to palonosetron
* Patients less than 18 years old

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-10-2010
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Jevtana
Generic name:	Cabazitaxel

Ethics review

Approved WMO

Date:	09-08-2010
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	20-09-2010
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	10-01-2011
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	24-01-2011
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	EUCTR2009-016864-35-NL
ClinicalTrials.gov	NCT01087021
CCMO	NL32199.068.10