A pharmacokinetic study of edoxaban in patients with breast cancer using the P-glycoprotein inhibitor tamoxifen

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To compare the plasma concentration of edoxaban in women with breast cancer before and during treatment with tamoxifen.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Breast neoplasms malignant and unspecified (incl nipple)
Study type	Interventional

Summary

ID

NL-OMON49411

Source
ToetsingOnline

Brief title
PHIX-IT study

Condition

- Breast neoplasms malignant and unspecified (incl nipple)
- Embolism and thrombosis

Synonym
trombosis, venous thromboembolism

Research involving
Human

Sponsors and support

Primary sponsor: Tergooiziekenhuizen
Source(s) of monetary or material Support: Daiichi Pharmaceutical,Daiichi Sankyo

Intervention

Keyword: Edoxaban, Interaction, P-glycoprotein, Tamoxifen

Outcome measures

Primary outcome

a comparison between day 4 and 36 of edoxaban area under the plasma

concenctration curve (AUC),maximum concentration (Cmax and several other

coagulation, pharmacokinetic and pharmacodynamic parameters.

Secondary outcome

NVT

Study description

Background summary

Edoxaban is an oral direct factor Xa inhibitor which is widely used in patients with venous thromboembolism (VTE) or non-valvular atrial fibrillation. Recently, this agent has been shown to be non-inferior to low-molecular-weight heparin (LMWH) to prevent recurrent VTE in cancer patients. Edoxaban is also a substrate for P-glycoprotein (P-gp), a protein that excretes certain xenobiotics into the urine, faeces, and bile. Tamoxifen, an anti-estrogen drug used as adjuvant treatment in breast cancer patients, is a known P- gp inhibitor. Therefore, concomitant use of tamoxifen can potentially increase plasma levels of edoxaban and thereby increase the risk of bleeding. In this study, the effect of tamoxifen on the pharmacokinetics of edoxaban will be evaluated.

Study objective

To compare the plasma concentration of edoxaban in women with breast cancer before and during treatment with tamoxifen.

Study design

An open-label, single-sequence crossover study

Intervention

Twenty-six breast cancer patients who are scheduled for adjuvant or palliative treatment with tamoxifen, will be given edoxaban 60 mg once daily for 4 days. On day 5, edoxaban will be stopped and tamoxifen therapy started. When steady-state of tamoxifen is reached after 28 days, edoxaban 60 mg once daily is given for 4 days concomitantly with ongoing tamoxifen therapy. At the fourth day of both edoxaban treatment periods, 4 blood samples (at 0, 1, 2, and 3 hours after ingestion) and one blood sample randomly taken in the time period 4 * 8 hours after ingestion will be collected.

Study burden and risks

Patients will be seen in the hospital for inclusion and two times for a series of blood withdrawal on day 4 and 36. On days 4 and 36, patients have to be in the hospital for 3 hours. During these days, patients will get a venous cannula from which 4 blood samples will be taken per day over a time period of 3 hours. One sample will be obtained 4 to 8 hours aftere ingestion of edoxaban. Total volume of blood withdrawn is maximum 50.7 ml. In this study, patients will use edoxaban, an anticoagulant drug. Patients may experience side effects of medication, such as hematomas. Based on previous studies with edoxaban, it is estimated that there is an individual risk of bleeding of 0.06% during this study. There is no individual benefit from participating in this study.
However, the results may have clinical impact, because in patients with breast cancer, tamoxifen is the mainstay of adjuvant treatment, often for a period of 5 years, where patients may suffer from VTE. Therefore, information on the safety of this combination is important.

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

-Women with breast cancer who will start with tamoxifen
-Age >18

Exclusion criteria

- Inability to provide informed consent
- Inherited bleeding disorder (e.g. von Willebrand disease)
- Major bleeding16 or clinically relevant non-major bleeding17 in the past 3 months
- History of intracranial bleeding
- Gastric or duodenal ulcer in the past 5 years
- Uncontrolled blood pressure with systolic pressure >180 mmHg
- Use of antiplatelet or anticoagulant therapy
- Chronic NSAID use
- Major surgery in the past 3 weeks (surgery which penetrates and exposes a body cavity or
produces substantial impairment of physical function)
- Pregnancy, puerperium, or current breast feeding
- Use of strong P-gp inhibitors or inducers (see appendix B)
- Brain metastases
- Use of chemotherapy in the past 7 days or in the upcoming 32 days
- AST or ALT >3x of the upper limit in the past 7 days
- Liver cirrhosis Child Pugh A, B, or C
- Creatinine clearance of <50mL/min calculated with the Cockcroft and Gault formula in the past
7 days
- Body weight <60kg

- Platelet count <50,000/mL in the past 7 days

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):	05-12-2019
Enrollment:	26
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Lixiana
Generic name:	edoxaban
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	tamoxifen
Generic name:	tamoxifen
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	28-03-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO Date:	01-08-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-09-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-11-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2018-004450-24-NL
CCMO	NL68239.018.18