De wisselwerking tussen edoxaban en tamoxifen behandeling bij vrouwen met borstkanker

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON23145

Source
Nationaal Trial Register

Brief title
PHIX-IT study

Health condition

Patients with oestrogen receptor positive breast cancer who are scheduled for adjuvant or palliative tamoxifen treatment

Sponsors and support

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

Intervention

Outcome measures

Primary outcome

Edoxaban plasma levels on day 4 (edoxaban alone) and day 36 (edoxaban + tamoxifen). The following pharmacokinetic parameters will be taken: the lowest plasma concentration

(Ctrough), the maximum plasma concentration (Cmax); time of maximum observed concentration (Tmax). The area under the curve (AUC) over 24 hours will be calculated by Byaesian analysis by the collected 5 samples.

Secondary outcome

Secondary parameters will include: anti-factor Xa activity calibrated for edoxaban, PT, aPTT and thrombin generation on day 4 and day 36.

Study description

Background summary

Rationale: 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.
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
Study population: Women with breast cancer and an indication for tamoxifen as adjuvant or palliative therapy.
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.
Main study parameters/endpoints: 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.
Nature and extent of the burden and risks associated with participation, benefit and group relatedness: 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 4 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 after ingestion of edoxaban. Total volume of blood withdrawn is 54.6 ml per day. 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.

Study objective

There is a minimal interaction between edoxaban and tamoxifen and it can safely be used concomitantly

Study design

Day 4: blood samples after four days of edoxaban use
Day 36: blood samples after four days of edoxaban use concomitantly with tamoxifen after steady state is reached

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.

Contacts

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Eligibility criteria

Inclusion criteria

- Age > 18 years
- Patients with oestrogen receptor positive breast cancer who are scheduled for adjuvant or palliative tamoxifen treatment

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 (see appendix A)
- 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 P-gp inhibitors or inducers and CYP3A4 inhibitors (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:	Observational non invasive
Intervention model:	Crossover
Allocation:	Non controlled trial

Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	30-09-2019
Enrollment:	26
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	30-09-2019
Application type:	First submission

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
NTR-new	NL8054
Other	METC AMC : METC 2018_328

Study results