The TOTAM study

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON23682

Source
NTR

Health condition

Adjuvante behandeling van oestrogeenreceptor positieve (HR+) borstkanker.

Sponsors and support

Primary sponsor: Erasmus Medical Center, Rotterdam
Source(s) of monetary or material Support: n.a.

Intervention

Outcome measures

Primary outcome

To prove that TDM of tamoxifen is feasible in clinical practice.

Secondary outcome

-Toxicity
-Dose related adverse events
-Compliance
-Cost effectiveness
-Incidence of tamoxifen induced non-alcoholic fatty liver disease

Study description

Background summary

As a prodrug, tamoxifen is susceptible to metabolism by the cytochrome P450 enzyme system. The most active metabolite created in this process is endoxifen. Adjuvant treatment with tamoxifen significantly reduces the chance of recurrence. Nevertheless, the five year recurrence rate in the adjuvant setting after 5-years of tamoxifen treatment is 11-23%, depending on nodal status and prior chemotherapy. The literature indicates that a minimal endoxifen concentration of 16 nmol/L is needed to produce a therapeutic effect. This implies that the endoxifen levels in individual patients must stay above this threshold throughout the entire treatment period. Factors that could contribute to endoxifen levels include: non-compliance with treatment regime, co-medication, advanced age, low BMI, genotype and phenotype. Several studies have demonstrated that the endoxifen levels of tamoxifen varied greatly in patients administrated with the same daily dose tamoxifen. Because of the wide intra-patient variability in drug exposure due to differences in pharmacokinetics of tamoxifen, optimal dose seems to be a problem in 20-30% of the patients. Therapeutic Drug Monitoring can in those cases be a useful tool for physicians managing patients with tamoxifen treatment.The aim of this process is to individualize therapeutic regimens for optimal patient benefit. The important question is whether TDM guided dose individualization is also feasible in large patient groups. In this exploratory study we will therefore evaluate the impact of TDM guided dosing on endoxifen levels in patients with breast cancer, treated with tamoxifen.

Study objective

The literature indicates that a minimal endoxifen concentration of 16 nmol/L is needed to produce a therapeutic effect. This implies that the endoxifen levels in individual patients must stay above this threshold throughout the entire treatment period. Factors that could contribute to endoxifen levels include: non-compliance with treatment regime, co-medication, advanced age, low BMI, genotype and phenotype. Several studies have demonstrated that the endoxifen levels of tamoxifen varied greatly in patients administrated with the same daily dose tamoxifen. Because of the wide intra-patient variability in drug exposure due to differences in pharmacokinetics of tamoxifen, optimal dose seems to be a problem in 20-30% of the patients. Therapeutic Drug Monitoring can in those cases be a useful tool for physicians managing patients with tamoxifen treatment. The aim of this process is to individualize therapeutic regimens for optimal patient benefit.

Study design

Patients will be seen in the outpatient clinic for pharmacokinetic blood sampling (Therapeutic Drug Monitoring of tamoxifen) on months 3, 6, 12, 18 and 24 after start with tamoxifen treatment.

Intervention

TDM guided dosage modifications are allowed during the study period. Start dosing tamoxifen 20 mg once daily, thereafter dosing advices based on blood concentration endoxifen.

Contacts

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Eligibility criteria

Inclusion criteria

1. Adult women (≥ 18 years of age) who are planned to start adjuvant tamoxifen therapy.

2. WHO Performance Status ≤ 1

3. Able and willing to sign the Informed Consent Form prior to screening evaluations

4. Able and willing to undergo blood sampling for PK analysis.

Exclusion criteria

1. Woman who are pregnant or breast feeding;

2. Endometrial cancer (diagnosis < 3 years ago)

3. Symptomatic CNS metastases or history of psychiatric disorder that would prohibit the understanding and giving of informed consent.

4. Patients with known alcoholism, drug addiction and/or psychiatric of physiological condition which in the opinion of the investigator would impair treatment compliance.

5. Evidence of any other disease, neurological or metabolic dysfunction, physical examination finding or laboratory finding giving reasonable suspicion of a disease or condition that contraindicates the use of tamoxifen or puts the patient at high risk for treatment related complications.

6. 3 months tamoxifen treatment

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-01-2018
Enrollment:	0
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	07-02-2018

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	NL6918
NTR-old	NTR7113
Other	METC Erasmus MC : MEC 17-548 // NL.63787.078.17

Study results