The TOTAM study

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Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON23682

Bron
NTR

Aandoening

Adjuvante behandeling van oestrogeenreceptor positieve (HR+) borstkanker.

Ondersteuning

Primaire sponsor: Erasmus Medical Center, Rotterdam
Overige ondersteuning: n.a.

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

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.

Onderzoeksproduct en/of interventie

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.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Anders
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	01-01-2018
Aantal proefpersonen:	0
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Positief advies

Datum:	07-02-2018
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL6918
NTR-old	NTR7113
Ander register	METC Erasmus MC : MEC 17-548 // NL.63787.078.17

Resultaten