CTC sensitivity profile to Cisplatin chemotherapy

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A Cisplatin(cDDP)-sensitivity profile determined in circulating tumor cells (CTC) of heavily pretreated metastatic BC patients will be able to identify a subgroup of patients who will benefit from cDDP therapy

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

Samenvatting

ID

NL-OMON24910

Bron
Nationaal Trial Register

Verkorte titel
CTC-cDDP

Aandoening

Gemetastaseerd mammacarcinoom, metastatic breast cancer, cisplatin, cDDP, circulerende tumorcellen, circulating tumor cells, moleculaire karakterisatie, molecular characterization

Ondersteuning

Primaire sponsor: Erasmus MC Cancer Center, Department of Medical Oncology
Overige ondersteuning: Stichting A Sisters Hope

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Response rate (RR) (complete response (CR) and partial response (PR)) according to RECIST

version 1.1 following 4 cycles of cDDP in three groups of patients (5 or more CTCs/7.5 mL of blood and a favorable cDDP-sensitivity profile, >=5 CTCs/7.5 ml and an unfavorable CTC cDDP-sensitivity profile and <5 CTCs/7.5 mL of blood).

Toelichting onderzoek

Achtergrond van het onderzoek

Despite significant progress, there is a high need for new effective systemic treatments for advanced/metastatic breast cancer (BC) patients. Cisplatin (cDDP) is used in many tumor types but not in unselected BC patients. In old studies (± 1980s), cDDP monotherapy, given to highly pretreated patients, yielded response rates (RR) of maximum 21% and PFS of 3–4 months. Also, cDDP-containing combination regimens given to pretreated metastatic BC patients have not greatly improved outcomes. In addition, cDDP is associated with relevant toxicity, consisting of nausea and vomiting, nephrotoxicity and neurotoxicity. Fortunately, due to decades of acquired experience with cDDP and improved anti-emetics, cDDP associated toxicity is nowadays more manageable. However, due to the availability of effective and less toxic newer chemotherapeutical and targeted agents, cDDP is not considered standard therapy in unselected BC patients.
Recently, the use of cDDP in BC has regained interest. Several attempts have been made to identify patients who are likely to benefit from cDDP-based treatment based on primary tumor characteristics such as mutations, overexpression and promotor hypermethylation of BRCA1, p53 mutations, so-called triple-negative disease and expression of specific microRNAs. Since data from prospective clinical trials exploring the use of the previously mentioned factors is lacking, there is still an unmet need for factors identifying BC patients likely to benefit from cDDP. If available, cDDP could add an extra available anti-tumor agent for a particular subgroup of BC patients.

One potential pitfall that may cause the previously mentioned factors to be less reliable is the fact that they all have been determined on primary tumor tissue. It is becoming increasingly clear that the characteristics of the primary tumor and metastases may differ, while systemic treatment and genomic instability further augments these differences over time. As a result, primary tumor material obtained at diagnosis is unlikely to reliably represent characteristics of metastases. Unfortunately, tumor tissues of metastatic lesions are hard to obtain, as taking biopsies is often a painful and cumbersome procedure.

Circulating tumor cells (CTCs) are tumor cells that circulate in the peripheral blood of cancer patients and are thought to represent features of metastases better than the primary tumor does. In addition, CTC counts have been correlated with clinical outcome in metastatic BC. Besides that, molecular characterization of CTCs holds great promise as a tool to personalize medicine. We have recently developed a panel of 96 genes, of which 55 mRNAs and 10 miRNAs are CTC-specific, which can be reliably measured in CTCs enabling detailed CTC characterization. From these 96 genes, we identified 23 genes that predict cDDP sensitivity and resistance. Potentially, determination of this gene expression profile in CTCs of BC

patients will enable the identification of BC patients responding to cDDP.

The aim of this study is to prospectively explore the predictive value of a cDDP-sensitivity profile determined in CTCs of metastatic BC patients previously treated with at least anthracycline- and taxane-based chemotherapy.

Doel van het onderzoek

A Cisplatin(cDDP)-sensitivity profile determined in circulating tumor cells (CTC) of heavily pretreated metastatic BC patients will be able to identify a subgroup of patients who will benefit from cDDP therapy

Onderzoeksopzet

- Baseline: CT Thorax/abdomen, CTC enumeration and characterization and, if applicable, metastatic tissue biopsy

- Following the second cDDP cycle and in case of acceptable toxicity and non-progressive disease, if applicable, the fourth and sixth cDDP cycle: CT Thorax/Abdomen for response evaluation

- Following each cycle: cDDP toxicity assessment

- 6 months follow-up after the initial administration of cDDP: monitoring of survival and treatment switch.

Onderzoeksproduct en/of interventie

1) blood collection for CTC enumeration and characterization

2) administration of cDDP (though cDDP is also given to this patient category in daily clinical practice)

3) if applicable, a metastatic tissue biopsy.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

- Female patient with metastatic breast cancer who has been pretreated with at least anthracycline and taxane-based chemotherapy in the adjuvant and/or metastatic setting

- Measurable disease according to RECIST 1.1, i.e. at least one measurable lesion on CT-scan where the longest diameter in the plane of measurement is a minimum size of 10mm

- Age >= 18 years

- WHO performance status ¡Ü2 (see Appendix C)

- Adequate haematological functions defined as ANC >= 1.0 x 109/L, platelets ¡Ý 100 x 109/L

- Adequate renal function defined as creatinin clearance >= 60 mL/min (Cockcroft Gault)

- Patients with reproductive potential must use a reliable method of contraception

- Written informed consent

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

- Other anticancer chemotherapy, use of biological response modifiers, or immunotherapy within two weeks prior to treatment start. Hormonal antitumor treatment within one week prior to treatment start.

- Hearing loss of at least Common Terminology Criteria for Adverse Events (CTCAE) grade 2

- Neuropathy of at least CTCAE grade 2

- Pregnant or lactating patients

- Serious illness or medical unstable condition prohibiting adequate treatment and follow-up

- Symptomatic CNS metastases (the presence of at least one key symptom in combination with radiologic evidence (positive contrast-enhanced CT or MRI of the brain))

- History of psychiatric disorder that would prohibit the understanding and giving of informed consent or that would prohibit adequate follow-up.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Niet-gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Actieve controle groep

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	07-06-2013
Aantal proefpersonen:	100
Type:	Werkelijke startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Positief advies

Datum:	26-06-2013
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 44123
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL3885
NTR-old	NTR4046
CCMO	NL42824.078.12
ISRCTN	ISRCTN wordt niet meer aangevraagd.
OMON	NL-OMON44123

Resultaten

Samenvatting resultaten
de Kruijff et al. Prospective Evaluation of a Circulating Tumor Cell Sensitivity Profile to Predict Response to Cisplatin Chemotherapy in Metastatic Breast Cancer Patients. Frontiers in Oncology (2021)