

CTC sensitivity profile to Cisplatin chemotherapy

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON24910

Source

NTR

Brief title

CTC-cDDP

Health condition

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

Sponsors and support

Primary sponsor: Erasmus MC Cancer Center, Department of Medical Oncology

Source(s) of monetary or material Support: Stichting A Sisters Hope

Intervention

Outcome measures

Primary outcome

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).

Secondary outcome

- Time to treatment switch
- Overall survival
- cDDP toxicity
- Retrospective comparison of CTC expression profiles between cDDP responders and non-responders (regardless of the patients' cDDP sensitivity profile)
- Association between a functional assay for predicting homologous recombination deficiency in metastatic tissue and clinical outcome
- Accordance between the CTC cDDP-sensitivity profile and a metastatic tissue cDDP-profile.

Study description

Background summary

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 (\pm 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.

Study objective

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

Study design

- 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.

Intervention

- 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.

Contacts

Public

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Eligibility criteria

Inclusion criteria

- 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 \geq 18 years
- WHO performance status \leq 2 (see Appendix C)
- Adequate haematological functions defined as ANC \geq $1.0 \times 10^9/L$, platelets \geq $100 \times 10^9/L$
- Adequate renal function defined as creatinin clearance \geq 60 mL/min (Cockcroft Gault)
- Patients with reproductive potential must use a reliable method of contraception
- Written informed consent

Exclusion criteria

- 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.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL	
Recruitment status:	Recruitment stopped
Start date (anticipated):	07-06-2013
Enrollment:	100
Type:	Actual

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date: 26-06-2013

Application type: First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 44123

Bron: ToetsingOnline

Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

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

Study results

Summary results

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)