Neutrophil-guided dosing of anthracycline/cyclophosphamide chemotherapy in patients with breast cancer: a feasibility study

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Breast neoplasms malignant and unspecified (incl nipple)
Study type	Interventional

Summary

ID

NL-OMON34109

Source
ToetsingOnline

Brief title
ANC-guided dosing of cHemOtheRapy: The ANCHOR-study.

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
breast cancer, neutrophil count

Research involving
Human

Sponsors and support

Primary sponsor: Ikazia Ziekenhuis

Source(s) of monetary or material Support: Ikazia Ziekenhuis Rotterdam

Intervention

Keyword: Breast cancer, Chemotherapy, Neutrophil

Outcome measures

Primary outcome

Rather arbitrarily, neutrophil-guided dose escalation will be considered

potentially useful if a >=15% dose escalation is feasible in at least three out

of thirty patients.

Secondary outcome

Assessment of interindividual variability (IIV) in neutrophil counts after a

first cycle of anthracyclin/cyclophosphamide chemotherapy (ACC).

Study description

Background summary

Cytotoxic anticancer treatments have narrow therapeutic margins and huge inter-individual variability (IIV) in treatment effects (anticancer efficacy, toxicity) that is not sufficiently reduced by standard body surface area (BSA)-based dosing. Neutropenia is a major side-effect, and often the dose-limiting factor which also applies for anthracycline/cyclophosphamide-based chemotherapy (ACC). Furthermore, there is evidence of an association between chemotherapy-induced neutropenia and treatment efficacy. In clinical practice, treatment overdose (e.g. manifested by febrile neutropenia) is managed by dose reduction and/or addition of granulocyte colony-stimulating factor (G-CSF) and/or prophylactic antibiotic treatment whereas an inappropriate low dose of chemotherapy is not routinely detected and therefore will not be corrected for during subsequent treatment cycles. This could result in sub-therapeutic dosing in a substantial number of cancer patients.

Study objective

We estimate that the anthracycline and cyclophosphamide dose could be

significantly (>=15%) increased in at least 15% of ACC-treated patients. Therefore, in order to diminish the risk of under-dosing ACC, we aim to develop a neutrophil-guided dosing algorithm. Furthermore, IIV for chemotherapy-related neutropenia will be assessed.

Study design

Non-blinded, intra-patient stepwise chemotherapy dose escalation pilot study guided by absolute neutrophil counts (ANC) during the first two cycles of ACC.

Intervention

Patients with clinically non-significant (grade 0-2) neutropenia and no other dose-limiting toxicity after the first cycle of chemotherapy will undergo a 10-25% (depending on the course of ANC) dose escalation during the second cycle. If possible, in the same manner, a further 10-25% dose escalation will be undertaken for the third treatment cycle. Patients that continue treatment for a total of >3 cycles will receive subsequent cycles according to standard BSA-based dosing. Patients with nadir grade 3-4 neutropenia will not undergo dose escalation during subsequent treatment cycles, and patients with febrile neutropenia will be treated according to the usual standard of care.

Study burden and risks

The main risk of participation in this study consists of excessive toxicity after dose escalation of chemotherapy. Therefore, the amount of dose escalation has been chosen rather cautious when compared to the large IIV in drug exposure. Furthermore, subjects will be thoroughly assessed for toxicity, especially after dose escalation. During the first cycle of treatment, and during the second and third treatment cycle in patients undergoing dose escalation, extra blood counts will be obtained on days 8, 11 and 15 along with scoring of non-hematologic toxicity using the Common Cytotoxicity Criteria (CTC) version 3.0. Finally, for safety reasons, a maximum of three patients will be allowed on study treatment simultaneously.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

(1) breast cancer patients aged >=18 years planned for treatment with at least three cycles of one of the above-mentioned ACC-regimens (AC, FAC, or FEC) at the Department of Medical Oncology, Ikazia Hospital, Rotterdam, The Netherlands
(2) WHO performance status 0-1
(3) Life expectancy >3 months
(4) Adequate peripheral blood counts: leukocytes >=4.0x109/L and ANC >=2.0x109/L and platelet count >=150x109/L
(5) Adequate renal function defined as normal serum creatinine concentration and/or estimated creatinine clearance >=60 mL/min (by Cockroft-Gault formula: [140 - age (years)] x 1.05 x body weight (kg)] : serum creatinine concentration (µmol/L))
(6) Adequate liver function defined as normal serum bilirubin concentration (<=17 µmol/L) and serum ASAT and ALAT <=3 times the upper limit of normal (<=5 times the upper limit of normal in case of hepatic metastases)
(7) Normal serum albumin concentration (35-50 g/L)
(8) Written informed consent

Exclusion criteria

(1) Previous treatment with chemotherapy
(2) Unable to consent with weekly follow-up for blood counts and toxicity assessment
(3) Symptomatic brain metastasis

(4) History of cardiac dysfunction
(5) Uncontrolled arterial hypertension (blood pressure systolic >=180 mmHg and/or diastolic >=110 mmHg) and/or unstable angina pectoris

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-11-2010
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Adriamycin
Generic name:	Doxorubicin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Endoxan
Generic name:	Cyclophosfamid
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Epirubicin
Generic name:	Epirubicin
Registration:	Yes - NL intended use
Product type:	Medicine

Brand name:	Fluorouracil
Generic name:	Fluorouracil
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	04-10-2010
Application type:	First submission
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)

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
EudraCT	EUCTR2010-020309-33-NL
CCMO	NL32077.101.10

Study results

Date completed:	25-02-2014
Actual enrolment:	30