Assessment and optimisation of carboplatin exposure in pediatric oncology patients using different markers of kidney function

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Primary:- Can carboplatin exposure in children be predicted by taking the plasma concentrations of creatinine of cystatine C into account?Secundary:- Which is the effective carboplatin exposure in the current pediatric treatment protocols?- Is there…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Observational non invasive

Summary

ID

NL-OMON37073

Source
ToetsingOnline

Brief title
Carboplatin pharmacokinetics

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified
- Nephropathies

Synonym
cancer, Malignancy

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Marlene Schickedanz Kinderkrebsstiftung;VUmc Onderzoek naar Kinderkanker

Intervention

Keyword: carboplatin, cystatin C, kidney function, pharmacokinetics

Outcome measures

Primary outcome

Using the NONMEM software (version VI level 1.1, GloboMax LLC, Hanover, MD) a on-linear mixed-effect population pharmacokinetic model will be calculated [10]. In this model the concentration of free platina in plasma will be used as a measure of the plasma carboplatin concentration. Both interindividual (IIV) and interoccasion variability (IOV) will be modelled.

At least three different models for the description of the relationship between carboplatin clearance, plasma creatinine and cystatine C will be tested:

The hypothesis that there is not relationship between carboplatin clearance and the concentration of the kidney function paramers will be used as reference.

This will be compared with models including plasma cystatine C or creatinine or both. The area-under-the-concentration-time-curve (AUC) as a measure of effective carboplatin exposure will be calculated from carboplatin clearance and dose.

Secondary outcome

- Assessment of effective carboplatin exposure in current pediatric treatment protocols.

- Relationship between effective carboplatin exposure and therapy-related

complications, which will be assessed using the standard procedures of the

individual treatment protocol (blood count, plasma creatinine and cystatin C,

audiometry)

- Relationship between effective carboplatin exposure and DNA-adducts as

measure of carboplatin action on a cellular level.

Study description

Background summary

Carboplatin is a toxic cytostatic drug which is mainly excreted by the kidneys. Previous studies have shown that carboplatin dosage can be optimized if kidney function is taken into account. In these studies, renal function was measured using 51Cr-EDTA clearance, which is invasive (radiation risk), costly, time consuming and not available in many institutions. Recently, endogenous markers of kidney function (creatinine en cystatin C) have been shown to be useful for carboplatin dose adjustment in adults.

Study objective

Primary:
- Can carboplatin exposure in children be predicted by taking the plasma concentrations of creatinine of cystatine C into account?

Secundary:
- Which is the effective carboplatin exposure in the current pediatric treatment protocols?
- Is there a relationship between effective carboplatin exposure and side effects?
- Is there a relationship between effective carboplatin exposure and the amount of DNA-adducts as a measure of carboplatin action on a cellular level?

Study design

Longitudinal observational study as a pilot study.
Measurement of carboplatin concentrations for the calculation of carboplatin clearance. Analysis of factors which affect carboplatin clearance, namely endogenous markers of renal function (creatinine and cystatin C).

Study burden and risks

This is an observational study incorporating a low to negligible risk.
Blood will be taken from a central venous line using a Bionecteur® system, which will further decrease the risk of infectious complications. The amout of blood taken is minimal and will be limited to 9 ml with a minimum patient weight of 2.5 kg (i.e. maximum loss of 4.5% of effective blood volume).
As pharmacokinetic data from adults cannot be extrapolated to children, this study can only be performed in a pediatric population. We expect that the safety of carboplatin therapy can be improved based on the findings obtained in this pilot study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

Carboplatin therapy, weight above 2.5 kg, central venous line for bloodsampling

Exclusion criteria

Weight below 2.5 kg, no central venous access for bloodsampling

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-01-2009
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO Date:	14-07-2008
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-02-2010
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO Date:	22-03-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
CCMO	NL23370.029.08