Pharmacokinetic Interaction between Antiretroviral and Cytotoxic therapy in HIV-infected patients - a pilot study

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1º Is there a significant difference of more than 10% in the pharmacokinetic parameter AUC of the investigated antineoplastic drugs (as a surrogate parameter for the efficacy) in the presence and absence of NNRTIs and/or PIs?2º Are there clinically...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Lymphomas Hodgkin's disease
Study type	Observational invasive

Summary

ID

NL-OMON37346

Source
ToetsingOnline

Brief title
Phineac-study

Condition

- Lymphomas Hodgkin's disease
- Viral infectious disorders

Synonym
Human Immunodeficiency Virus (HIV), lymphoma

Research involving
Human

Sponsors and support

Primary sponsor: Onze Lieve Vrouwe Gasthuis
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: antiretroviral drug, chemotherapy, drug-drug interaction, pharmacokinetics

Outcome measures

Primary outcome

Serum levels of the antineoplastic and antiretroviral agents will be measured.

Pharmacokinetic parameters will be calculated and compared to individual and

population parameters. Clinical parameters, adverse events and if possible

clinical outcome will be collected by laboratory values and EORTC-QLQ C30

questionnaires and related to the collected pharmacokinetic parameters.

Secondary outcome

n/a

Study description

Background summary

Due to an increased number of treatments with antineoplastic agents in HIV-infected patients over the past decade, the urge to investigate drug-drug interactions between cytotoxic and antiretroviral agents has become relevant. As yet, there is little knowledge about the effects of NNRTIs and PIs on the pharmacokinetics of the antineoplastic therapy and visa versa. The proposed mechanism of such interactions is that NNTRIs and PIs induce or inhibit respectively the CYP-enzymes and P-pg transporters, which results in altered pharmacokinetics of the antineoplastic agents. This may lead to an altered exposure and/or altered toxicity of the antineoplastic drug, which could be clinical relevant because PK/PD correlations are found between antineoplastic levels and the efficacy and toxicity. Thus far, no dose or HAART adjustments are described for HIV-infected patients treated with antineoplastic agents and HAART. Therefore, measuring serum levels of possibly affected drugs (cyclophosphamide, etoposide, vinblastine and vincristine and their metabolites) seems to be a fair surrogate parameter to monitor the efficacy and/or toxicity of the antineoplastic therapy in the presence and absence of NNRTIs and/or PIs.

Study objective

1º Is there a significant difference of more than 10% in the pharmacokinetic parameter AUC of the investigated antineoplastic drugs (as a surrogate parameter for the efficacy) in the presence and absence of NNRTIs and/or PIs?
2º Are there clinically significant differences in toxicity of the investigated antineoplastic drugs (measured by questionnaires and laboratory values) due to drug-drug interactions between antineoplastic drugs, PIs and NNRTIs? Are dose adjustments necessary for investigated antineoplastic drugs used in patients co-treated with PI- or NNTRI-based HAART? And/or, is it necessary to avoid PIs and NNTRIs when patients are treated with antineoplastic drugs?

Study design

A randomized, observational, crossover controlled clinical pilot study.

Study burden and risks

Patients will not have advantages of participation at this study. Patients will temporarily switch of their regular HAART to II-based HAART. Theoretically, II-based HAART has no interaction with antineoplastic agents and therefore the chemotherapy will be the most optimal therapy, but it will be a switch of their patient-tailored anti-HIV therapy. II-based HAART is generally well tolerated. Switching or not-switching may either benefit or harm for this patient group. A disadvantage of participation will be the extra blood drawing, which will be per occurrence 6 extra tubes (approx. 40ml) and filling in the questionnaires. The antineoplastic treatment of the patient shall not be changed by inclusion in this study.

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

Biopsy proven lymphoma
Treated with cyclophosphamide, doxorubicin, vinblastine and/or vincristine
proven HIV positive on HAART

Exclusion criteria

Seriously compromised peripheral venous vasculature complicating venous blood sampling
No written informed consent obtained

Study design

Design

Study type:	Observational invasive
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-03-2013
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO

Date:	26-03-2012
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	NL39601.100.12