Right Dose, Right Now: Model Validation

Published: 15-06-2017
Last updated: 12-04-2024

To select the most appropriate pharmacometric models

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Hepatobiliary neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON45271

Source
ToetsingOnline

Brief title
Right Dose, Right Now: Model Validation

Condition

- Hepatobiliary neoplasms malignant and unspecified

Synonym
blood poisoning, infection, sepsis, Various infectious diseases

Research involving
Human

Sponsors and support

Primary sponsor: VUmc
Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: Antibiotics, Personalized medicine, Pharmacometrics, Prediction

Outcome measures

Primary outcome

- Agreement between predicted and observed relevant pharmcometric parameters

using Bland-Altman analysis

- Percentage of correct first predictions of each pharmacometric model.

- Extent in which all relevant pharmacometric goals are being met.

Secondary outcome

Not applicable

Study description

Background summary

(Of note: This study is a part of the Right dose, Right now project. For the full rationale of the project, a separate approved project request has been added to the appendix (gehonoreerde projectaanvraag). Also, additional information can be found on http://www.autokinetics.eu.)

Sepsis is a major and growing problem. In the Netherlands alone, around 15.000 patients are diagnosed with severe sepsis each year. Despite major scientific efforts, including many failed clinical trials mainly focusing on inflammatory mediators and the introduction of care bundles, the mortality rate for severe sepsis still remains unacceptably high at around 30%.
This is alarming, especially since the incidence of sepsis continues to increase and now exceeds that of colon cancer, breast cancer and AIDS combined.
Antibiotics are essential for treating sepsis. Their early and appropriate use has repetitively been shown to reduce mortality rates. However, achieving adequate antibiotic exposure in critically ill patients is a major challenge due to markedly different pharmacokinetic (PK) profiles in the critically ill. Nevertheless, doctors still rely on standard antibiotic dosing schemes, that were developed based on data from healthy volunteers and non-critically ill patients. Depending on patient characteristics, clinical course and therapy, this strategy may result in underdosing and/or drug-related toxicity during the

course of intensive care treatment.
Therefore, we developed AutoKinetics (AutoK) software. AutoK aims to make use of patient data that is available from the electronic patient records, for example about fluid balance and renal function. Using this data, AutoK is able to give fast and precise dosing advice, using published population pharmacokinetic models of any drug. AutoK runs on the computer at the bedside. Thus, advice is readily available, even before treatment is started, and is continuously updated as disease and therapy evolve: true personalised dosing. We believe that AutoK can improve antibiotic dosing, morbidity and mortality for severe sepsis.

Eventually, we will test AutoK in multicenter clinical trial. We will randomise patients with severe sepsis (n=42 per group, per antibiotic), for antibiotic dosing through AutoK or standard therapy. This will also concern a WMO request. We will file a separate request accordingly.

This request concerns the validation of pharmacometric models using prospectively collected data which is not being collected in the context of regular patient care and / or quality controls.

Study objective

To select the most appropriate pharmacometric models

Study design

This study concerns model validation based on prospectively gathered data that is not being collected in the context of regular patient care and / or quality controls.

We will validate existing pharmacometric models which are publically available from the international literature. We will select these models using a standardized search strategy. Examples of this strategy can be found in the attached approved project request (gehonoreerde projectaanvraag). We only intend to select pharmacometric models of common and relevant antibiotics and antimycotic agents used at the intensive care unit.
For the validation of the selected pharmacometric models, we aim to use both retrospectively available data and prospectively collected data. The exact content of data needed may vary and is dependent on the specific pharmacometric model used. A large part of the data will be routinely collected in the context of regular patient care and / or quality controls. In general, the data needed consists of demographic data like age and gender, data concerning time and quantity of medication administration and data generated by patient surveillance monitors and the laboratory. For the retrospective part of this research a separate non-WMO request has been filed, which has already been approved by the METc VUmc.

This specific request concerns model validation using data that has not or will not be collected in the context of regular patient care and / or quality controls. We aim to collect this data prospectively. The data needed mainly concerns serum concentrations at different time points of all relevant antibiotic and/or antimycotic agents commonly used at the intensive care unit.

If the selected pharmacometric models are not accurate enough according to Bland Altman anaylsis, as judged by > 20% error, we will attempt to either combine or calibrate the models. If this does not appear to be sufficient, we will develop new models using a part of the retrospectively and prospectively collected data. The remaining part of the data will subsequently be used to validate the newly developed models.

Study burden and risks

The blood samples are taken from existing lines. Therefore, the burden is minimal and the risk negligible.

This study is group related. The objective of this study is related to the prediction of antibiotic plasma concentrations among intensive care patients. By definition, this cannot be investigated other than within the group of intensive care patients.

Contacts

Public
VUmc

De Boelelaan 1117
Amsterdam 1081HV
NL
Scientific
VUmc

De Boelelaan 1117
Amsterdam 1081HV
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

The patient is hospitalized at the intensive care unit of the VUmc or OLVG and is being treated for infection with antimicrobial and/or antifungal agents.

Exclusion criteria

None

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	11-07-2017
Enrollment:	500
Type:	Actual

Ethics review

Approved WMO Date:	15-06-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-08-2017
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	NL60826.029.17