Plan Overview

A Data Management Plan created using DMPonline

Title: Utilising Physiologically Based Pharmacokinetic Modelling and Simulation for Precision Dosing in Cirrhotic Patients

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Affiliation: University of Manchester

Template: University of Manchester Generic Template

Project abstract:

A sizable population suffers from liver cirrhosis worldwide. The purpose of this work is to investigate the impact of the most prominent changes in physiology on pharmacokinetics. With the high number of drugs on the market that have been approved without confirmative pharmacokinetic studies on hepatic impairment patients, clinicians face a huge obstacle in treating those patients without appropriate labelling guidelines or dosage recommendations. There is an increasing trend towards incorporating hepatically impaired patients into early phases of clinical trials as they are a part of the likely patient population who are going to receive this medication after approval. Thus, specifying the most convenient dose for hepatically impaired patients, prior to clinical trials, has become a necessity. The prediction of drug exposure utilising physiological information as well as the drug exposure through physiologically-based pharmacokinetic (PBPK) modelling and simulation may reduce suboptimal dosing, aid clinical study design, and subsequently lower adverse effects in special patient populations. In order to properly understand the physiology of the disease and its effect on pharmacokinetics, determining the absolute abundances and activities of different drug metabolising enzymes (DME) and transporters in the liver of cirrhotic patients and how these differ from healthy subjects is necessary. Data from this study will be to help develop mechanistic models for different drugs that are administered for this group of hepatically impaired patients.

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Utilising Physiologically Based Pharmacokinetic Modelling and Simulation for Precision Dosing in Cirrhotic Patients

Manchester Data Management Outline

1. Is this project already funded?

- Yes

Will you be applying for funding from any of the following sources? If your funder isn't listed, please enter in the free text box provided.

N/A

3. Is The University of Manchester the lead institution for this project?

- Yes - only institution involved

4. What data will you use in this project (please select all that apply)?

- Acquire new data

5. Where will the data be stored and backed-up during the project lifetime?

- University of Manchester Research Data Storage Service (Isilon)

research team's Shared drive on the University secured system

6. If you will be using Research Data Storage, how much storage will you require?

- < 1 TB

7. If you have a contractual agreement with a 3rd party data provider will any of the data associated with this project be sourced from, processed or stored outside of the

institutions and groups stated on your agreement?

- No

8. How long do you intend to keep your data for after the end of your project (in years)?

- 10 - 20 years

Questions about personal information

Personal information or personal data, the two terms are often used interchangeably, relates to identifiable living individuals. Special category personal data is more sensitive information such as medical records, ethnic background, religious beliefs, political opinions, sexual orientation and criminal convictions or offences information. If you are not using personal data then you can skip the rest of this section.

Please note that in line with data protection law (the General Data Protection Regulation and Data Protection Act 2018), personal information should only be stored in an identifiable form for as long as is necessary for the project; it should be pseudonymised (partially de-identified) and/or anonymised (completely de—identified) as soon as practically possible. You must obtain the appropriate ethical approval in order to use identifiable personal data.

- Pseudonymised personal data

cambridge University hospitals will create IDs for patient's samples and their matched clinical data. No personal/identifiable data will be available for the research team.

10. Please provide details of how you plan to store, protect and ensure confidentiality of the participants' information as stated in the question above.

The pseudonymised personal data of the patients (e.g demographics and clinical data) will be kept with participants ID in a passport protected excel sheet on the shared drive between the research team only. The research team will not have access to the key which can identify the participants, only the healthcare team in the NHS hospital (Cambridge University hospitals and their tissue banks) will have this access and deliver the records to the research team in a pseudonymised form with an ID number relevant to each patient.

Data will be archived in a durable form that is immune to subsequent tampering and falsification for a minimum period of 10 years in the research team shared drive with username and password.
University staff and students are not permitted to remove such records when leaving the University without obtaining permission from their head of school in writing.
Lab books and documents will be stored in a secure locker in the lab with an access only with the research team's university cards.

Study data and material may be looked at by the University of Manchester, from regulatory authorities or from the NHS Trust for monitoring and auditing purposes, and this may well include access to personal data. The University has an SOP to cover handling and storage of confidentiality. This outlines

the controls that should be in place when processing different types of confidential information.

11. If you are storing personal information will you need to keep it beyond the end of the project?

- Yes – the project relies on identifiable personal data in order to be understood

In a pseudonymised form, the clinical data will be linked to the samples without any identifiable data.

12. Sharing person identifiable information can present risks to participants' privacy, researchers and the institution. Will the participants' information (personal and/or sensitive) be shared with or accessed by anyone outside of the University of Manchester? This includes using 3rd party service providers such as cloud storage providers or survey platforms.

- No

13. If you will be sharing personal information outside of the University of Manchester will the individual or organisation you are sharing with be outside the EEA?

- Not applicable

14. Are you planning to use the personal information for future purposes such as research?

- Yes

the pseudonymised data may be used for future research. No identifiable data are included in this research.

15. Who will act as the data custodian or information asset owner for this study?

Amin Rostami-Hodjegan (the PI)

16. Please provide the date on which this plan was last reviewed (dd/mm/yyyy).

31/08/2018

Project details

What is the purpose of your research project?

- Using PBPK as a tool to predict the precise dose of different drugs in cirrhosis disease population.
- Quantitative determination of the absolute abundances of hepatic microsomal DMEs contents (specifically CYP2B6, CYP3A5, UGT2B17, and UGT1A1), as well as hepatic transporters in cirrhotic patients with different disease severities, identifying how they are different from healthy individuals, and incorporating these levels into mathematical models to evaluate their impact on drug exposure.

What policies and guidelines on data management, data sharing, and data security are relevant to your research project?

The University of Manchester's research data Management Policy
The University of Manchester Records Management Policy
http://documents.manchester.ac.uk/display.aspx?DocID=14916
The University of Manchester Data Protection Policy
http://documents.manchester.ac.uk/display.aspx?DocID=14914
The University of Manchester Intellectual Property Policy
http://documents.manchester.ac.uk/display.aspx?DocID=24420
The University of Manchester IT policies and guidelines
http://www.itservices.manchester.ac.uk/aboutus/policy/

Responsibilities and Resources

Who will be responsible for data management?

The PI

What resources will you require to deliver your plan?

1- The project fund
2- CAPKR training (how to use lab instruments, software tools for data analysis, Simcyp simulation software tool training)
3- Access to the research team's shared drive

Data Collection

What data will you collect or create?

1- Demographic data (administered drugs, disease cause, age, sex, weight, ethnicity, alcohol intake, and smoking), and Clinical data (Child-Pugh score, liver function tests (AST, ALT, bilirubin), prothrombin time or INR, serum albumin level, encephalopathy and ascites scores) will be obtained in a pseudonymised form from the tissue bank in a tabular form linked to an ID number for each patient.

2- this data will help in dividing the samples based on Child-Pugh classification into 3 classes mild, moderate, and severe cirrhotic samples (20 samples/ group = 60 samples + 20 healthy tissue)

2- The LC/MS/MS sheets to be analysed using different software tools (Maxquant, Progenesis, Mascot, excel) to determine the enzymes and transporters abundances in the samples.

3- Modeling and simulation data obtained using Simcyp simulation software.

4- collected or created data will be kept in the research team's shared drive that can be only accessed by them.

How will the data be collected or created?

1- The clinical and demographic data will be collected from the tissue bank in a pseudonomysied form linked to an ID number for each patient in a tabular spreadsheet form.

2- Samples will be analysed in the LC/MS/MS in duplicates and the data created after analysis will be collected in mgf files to be processed further into spreadsheets, mascot, progenesis and maxquant.

3- Simcyp creates excel sheets as outputs.

Documentation and Metadata

What documentation and metadata will accompany the data?

Along with each data sheet another sheet in the same workbook will include what have been done with this data in details (who created the sheet, the conditions of the analytical procedures; sample type, size, date of analysis, fixed and variable modification done in the sample preparation, method used for sample preparation, units of measurements, version of software used, the date on which each modification are made, the type of modification or data processing if any).

Data will be used in this research to help in the interpretation of the proteomic results after samples analysis. For examples the proteins that are either higher or lower at each stage of liver cirrhosis relative to other stages and to healthy tissue. The demographic data as well might help in improving the population data set on Simcyp software tool used for modeling and simulation of drug's pharmacokinetic profile. The cause of cirrhotic disease will help also in comparing the metabolic enzymes affected by each cause and how this will consequently affect the drug pharmacokinetics.

The size of the samples and how much has been used for analysis will allow the future researchers to define the remaining amount for other projects with the same type of samples

Ethics and Legal Compliance

How will you manage any ethical issues?

Data will be kept in the university secured shared drive among the research team in a password

protected spreadsheets. The clinical data of sample sources will be pseudonymised by the source tissue bank and no identifiable personal data will be available for the research team and for publication. The tissue bank responsible for supplying the samples has its own NHS license for use of samples for researches.

How will you manage copyright and Intellectual Property Rights (IPR) issues?

Copyright and intellectual property rights will be managed as per University's Intellectual Property Policy.
Samples that will be brought from Cambridge tissue bank will follow terms and conditions in the agreement that will be set before their transfer.

Storage and backup

How will the data be stored and backed up?

The pseudonymised personal data of the patients (e.g demographics and clinical data) will be kept with participants ID in a passport protected excel sheet on the shared drive between the research team only. The research team will not have access to the key which can identify the participants, only the healthcare team in the NHS hospital (Cambridge University hospitals and their tissue banks) will have this access and deliver the records to the research team in a pseudonymised form with an ID number relevant to each patient.
Data will be archived in a durable form that is immune to subsequent tampering and falsification for a minimum period of 10 years in the research team shared drive with username and password.
University staff and students are not permitted to remove such records when leaving the University without obtaining permission from their head of school in writing.
Lab books and documents will be stored in a secure locker in the lab with an access only with the research team's university cards. Computers and laptops are serviced by university IT for automatic backup services
Study data and material may be looked at by the University of Manchester, from regulatory authorities or from the NHS Trust for monitoring and auditing purposes, and this may well include access to personal data. The University has an SOP to cover handling and storage of confidentiality. This outlines the controls that should be in place when processing different types of confidential information.

How will you manage access and security?

The use of RDM service, encrypting devices, password protected spreadsheets. All computers and laptops will be serviced by the IT department with global protection, antiviral system, and encryption.

Selection and Preservation

Which data should be retained, shared, and/or preserved?

Clinical data and samples ID will be transferred from the tissue bank to the research team through MTA.
These data will be saved in the research team shared drive and will be retained after the study for future researches that are linked to the same samples and might help in the interpretation of the research outcome.
Information and analysis results will be kept in a separate folder in the shared drive. University staff and students are not permitted to remove such records when leaving the University without obtaining permission from their head of school in writing.

What is the long-term preservation plan for the dataset?

For 10 years with the PI and the plan will be renewed with new projects.

Data Sharing

How will you share the data?

Data will be shared within the research team through files in the shared drive. For less sensitive data like already published articles, it can be shared via institutional e-mail using protected devices.

Are any restrictions on data sharing required?

Clinical data from samples donors will be pseudonymised before being handled by the research team. Copyright permissions will be gained before using original work.