TransBioLine
Translational Safety Biomarker Pipeline

821283 – TransBioLine

Translational Safety Biomarker Pipeline

WP9 – Overall project governance and project management

D9.15 Templates of the informed consent form and information sheets finalized

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Document History

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V1.0	18/10/2019	First Draft
V2.0	30/10/2019	Comments
V3.0	30/10/2019	Final Version

Definitions

Participants of the TransBioLine Consortium are referred to herein according to the following codes:

UZH. University of Zurich, Switzerland
UMA-IBIMA. Universidad de Málaga, Spain
ITTM. Information Technology for Translational Medicine, Luxembourg
Landspitali. Landspitali University Hospital. Iceland
KUM. Klinikum der Universität München. Germany
UNOTT. The University of Nottingham. United Kingdom
USAL. Universidad de Salamanca. Spain
IR-HSCSP-ICCC. Fundació Privada Institut de Recerca de l'Hospital de la Santa Creu i Sant Pau. Spain
TAM. TAmiRNA GmbH. Austria
SIGNATOPE. SIGNATOPE GmbH. Germany
ABX-CRO. ABX-CRO Advanced Pharmaceutical Services Forschungsgesellschaft mbH. Germany
MetaHeps. MetaHeps GmbH. Germany
APHP. Assistance Publique - Hopitaux de Paris. France
SYNAPSE. Synapse Research Management Partners S.L. Spain
Charité. Charité - Universitätsmedizin Berlin. Germany
UNEW. University of Newcastle Upon Tyne. United Kingdom
ULIV. The University of Liverpool. United Kingdom
MLM. MLM Medical Labs GmbH. Germany
UL. University of Leiden. Netherlands
SAS. Servicio Andaluz de Salud. Spain
PFIZER. LTD PFIZER UK
MSD. Merck Sharp & Dohme Corp. USA & France
LLY. Eli Lilly. USA & UK
NOVARTIS. NOVARTIS Pharma AG. Switzerland
ROCHE. F. Hoffman-La Roche Ltd. Switzerland
Janssen. JANSSEN Pharmaceutica NV. Belgium; U.S.A.
SARD. SANOFI-AVENTIS RECHERCHE & DEVELOPPEMENT. France

Grant Agreement. The agreement signed between the beneficiaries and the IMI JU for the undertaking of the TransBioLine project (No 821283).
Project. The sum of all activities carried out in the framework of the Grant Agreement.
Consortium. The TransBioLine Consortium, comprising the above-mentioned legal entities.
Consortium Agreement. Agreement concluded amongst TransBioLine participants for the implementation of the Grant Agreement. Such an agreement shall not affect the parties' obligations to the Community and/or to one another arising from the Grant Agreement.

Publishable Summary

This deliverable provides the template for the Inform Consent Form (ICF) and Patient Information Sheet (PIS) of TransBioLine.

This template shall be used by the different DILI, DIKI, DIPI, DIVI and DINI studies, ensuring that their local ICF and PIS, as adapted to the local ethics standards and requirements, are aligned within TransBioLine and meet the standards detailed herein.

Beneficiary 11. ABX-CRO and/or the consortium's independent Ethical Advisory Board (EAB) may be requested to ensure alignment of ICFs with current ethical and regulatory standards and guidance.

Studies conducted by the consortium should be built on ICFs allowing samples and data use outside and beyond the TransBioLine project, in order to enable sustainability of the value of remaining sample material and of the data generated here after the end of the project.

Template of the Inform Consent Form and Patient Information Leaflet

Instructions to site: This template is available to use for the TransBioLine study. Update all blue text and delete all red help text before submitting / using.

WP1-DIKI / WP2-DILI / WP3-DIPI / WP4-DIVI / WP5-DINI

TransBioLine Patient Information Leaflet

For informed consent concerning the donation, storage, and utilization of biological materials and supporting data as well as the collecting, processing and usage for scientific research purposes

Dear patient,

You are currently being treated as a patient at the_____ *clinic/hospital or participate* in the_____ *study* and therefore are invited to take part in this 'Translational Safety Biomarker Pipeline (TransBioLine)' study.

This research study as well as the present patient information and Informed Consent Form (ICF) have received a favourable opinion from the independent Ethics Committee.

The study is funded by the Innovative Medicines Initiative (IMI). IMI is the world's biggest public-private partnership (PPP) in life sciences. It is a partnership between the European Union (represented by the European Commission) and the European pharmaceutical industry.

Your participation in this study is voluntary. You can decide anytime to withdraw your consent to the study without indicating any reasons. The decision not to participate or the premature withdrawal of your consent will not have any negative impact on your further medical care.

Please read the following information carefully as an addition to the oral consultation with your study doctor. Please do not hesitate to ask questions. In addition, please feel free to discuss the information given to you with your family or family doctor before making any decision.

Please sign this consent only:

- If you fully understand the course of this research study,
- If you are willing to give your consent to participate,
- If you are fully aware of your rights as a patient before, during and following a study as a participant.

1. Introduction

Below you will find information on the aims and scope of the kidney (WP1-DIKI), liver (WP2-DILI), pancreas (WP3-DIPI), vascupar system (WP4-DIVI), nervous system (WP5-DINI) or body fluids (WP6-liquid Biopsies) TransBioLine study (referred to as "TransBioLine study") and the measures that are being taken to protect your privacy that will enable you to form your own opinion before making a decision.

We are working with a central biobank at Charité Hospital Berlin. This biobank stores human biological materials such as blood, urine or tissues linked to selected medical information.
The human biological materials and supporting data collected for this study will be made accessible for medical research in an effort to improve the prevention, diagnosis and treatment of human diseases. Only projects with a positive ethics vote will receive samples and data in a pseudonymous or anonymised form.

If any points regarding the collected samples and data remain unclear, please ask your attending physician or your study physician before giving your consent. If you have any further questions at a later stage, you may also contact your study doctor who can provide you a list of study contact details.

2. Aim of this study

The TransBioLine study will focus on the development of protein biomarkers of drug-induced injury to liver, kidney, pancreas, vasculature, and central nervous system (CNS) and the development of novel techniques based on microRNAs. The analysis of microRNAs in liquid biopsies is a minimal-invasive alternative to a surgical biopsy. In this case, it is a blood sample, which is specially treated to quantify very small RNA molecules.

When your body is affected by a particular disease, tissue injury occurs, which in turn causes certain molecules to be released into the blood. These molecules are called biomarkers.

The TransBioLine study aims to study these biomarkers and make the data from this study available to academic centers and private scientific-related institutions to aid further research.

The biomarkers are expected to improve safety of new drugs and to contribute to better diagnosis and management of acute and chronic diseases.

3. How is the study conducted?

This clinical study will be conducted at several sites across Europe, United Kingdom as well as in the United States of America.
In total, xxx patients are planned to be included.

Your doctor has identified you for the TransBioLine study, because your disease condition indicates Kidney Injury / Liver Injury / Pancreas Injury / Vascular Injury / Central Nervous System (CNS) Injury, or as a healthy volunteer.

If you agree to take part in this study, we will ask you questions about your general health, conduct a general examination, and measure your weight, height, blood pressure, heart rate and temperature. The aim of this screening is to confirm that all inclusion criteria are met and no exclusion criteria are applicable to your medical data and findings.

4. What type of biomaterials and data are collected?

(Note : Delete the case which is not applicable)
The biological materials which we would like to use for research are body fluids (blood, urine or CSF) that:
Case 1 have been collected for diagnostic/therapeutic purposes in the course of your present hospital stay, but which are no longer required for such purposes and would, therefore, be destroyed otherwise.
Case 2. will be drawn / collected by qualified health professionals.

Blood volumes collected will correspond to those used in clinical routine. Total volume of samples will not exceed **5** mL (**1** teaspoon).

The information collected for the TransBioLine study will include information about your person (e.g. age, ethnic origin, gender, body weight and height); past and present medical history, in addition to information about your health and test results from examinations and procedures done during this study. You doctor will ask you about your current medication too.

The biobank only stores a minimal dataset with the sample such as the patient ID (pseudonym), age, gender and sample information (date and time of sampling and freezing).

5. What personal benefit do I have from study participation?

You will not directly benefit by taking part in this study, because the most important health benefits will be realized many years from now. Rather, your participation will contribute to the advancement of scientific knowledge and help future patients by improving our understanding of factors that affect the health of the population.

6. Do any costs arise from my study participation? Do I receive any compensation or payments?

There is no charge to you for taking part in this study.
You will not receive any remuneration for donating your biomaterials and/or data for medical research purposes. Should such research result in commercially exploitable results, any profits will not be shared with you.

7. What are the risks associated with your donation?

a. Health risks:

(Note : Delete the case which is not applicable)

Case 1: *Only residual material will be used.*

As we intend to use only biomaterials that will be collected in the context of your diagnosis or treatment and that, otherwise, would be destroyed as residual material, the donation does not entail any additional health risk for you.

Case 2: We would like to draw xx ml of blood (corresponding to approximately xx teaspoons). Mild bruising around the area where the needle went into the vein is fairly common after a blood test. However, in some rare cases, transient inflammation may develop and the skin gets red and swollen. You may experience dizziness during or after a blood test; this is very common in people who have a fear of needles and injections. It is fairly common to have a haematoma but the bruising should heal independently over the course of time.

b. Further risks:

Any collection, storage and transfer of data related to your biomaterials in the context of (medical) research projects entails the risk of breaches of confidentiality (e.g. the possibility of identifying you). These risks cannot be completely excluded, Charité – Universitätsmedizin Berlin biobank will take all appropriate measures according to the current state of technology to protect your privacy and will transfer samples and/or data only to researchers/projects who can demonstrate appropriate data protection and confidentiality safeguards (*see* Item 8: “Who has access to your biomaterials and data?”).

8. Who has access to your biomaterials and/or data and how are they protected?

The object for the TransBioLine study is to make medical data available to academic centers and private scientific-related to aid further research, therefore your biomarker results will be used for a wide range of medical research. At present, it is not possible to describe all future medical research objectives. These can either refer to the above defined disease areas or to diseases that at present are still partially unknown (e.g. cancer, cardiovascular diseases, brain disorders). Thus it is possible that your biomaterials and data may also be used for research purposes which, at this stage, are unknown.

All personal data will only be gathered, processed and used in accordance with current applicable privacy protection acts. Personal data are information that can be used to determine your identity. Your study doctor and his study team will maintain a patient file. The patient file contains personal data such

as age, gender, etc. as well as medical results of prior and/or current treatments and further medical information regarding your study participation.

The funding body (IMI) of this trial and its representatives as well as authorised persons from regulatory authorities or independent Ethics Committees must be allowed access to your patient file for inspection and supervision purposes. In case of premature withdrawal of your consent to study participation, your personal data including health data which has been stored up to that point, might be used for future evaluations of study treatment or compilation of application documentation.

Some study data will need further analysis. For this reason, the transfer of data to third parties will only be made in pseudonymised form.

We also expect to receive access requests from overseas researchers and international collaborators. These researchers must follow the same procedures as all other researchers. All access is subject to the strictest scientific and ethical scrutiny, as described above.

a. Any data that directly identifies you (name, date of birth, address, etc.) will not be collected and will be replaced by a code (pseudonymized, encoded). Following this, the encoded data set is re-coded again before it is stored. Based on current knowledge, this double encoding/pseudonymization procedure minimizes the possibility that you may be re-identified by unauthorized parties. The bio-materials and/or data will only be made available for research purposes in this form (i.e. double pseudonymized).

All biomaterial samples will be pseudonymised and cannot be linked to you in any way.

b. Data that directly identifies you (personal identifying data) remain at the hospital in which the biomaterials and data have been obtained and will be stored separately from the biomaterials and related clinical data. Access to personal identifying data is necessary only in case additional or missing medical data is needed from your medical records, or in case of a need to re-contact you personally. In no case will personal identifying data be transferred to scientists and/or other unauthorized third parties, such as insurance companies or employers.

A list that links the coded information with your identity will be kept secure by the study doctor, to allow for your re-identification in certain circumstances. Your unique code will enable us to link the information from different data sets to you, but at the same time, will enable us to keep your identity confidential when we give your data to other researchers to use.

c. Based on pre-defined criteria and following a request/application, the double-encoded biomaterials and medical data may be transferred to other universities, research institutes and research companies, including those in foreign countries, for medical research. Under certain circumstances these data may be linked to medical data from other databases, provided that all legal and regulatory requirements are met.

d. Biomaterials and/or data that are transferred to third parties may only be used for the research purpose indicated in the application and must not be passed on by the recipient for other purposes. Material that has not been utilized will be returned to the biobank or destroyed.

e. Research results for scientific publication will be anonymized, i.e. data will be published only in a form that does not allow re-identification.

While study information could be printed in journals or shared with other people at scientific meetings or for teaching purposes, it will not be possible to identify you. Your identity will be kept confidential. All data will be presented as group data, rather than individual data. Also, specific rules regulate access to your data and samples by researchers.

You can soon find out more about how we use your information at www.TransBioLine.com

9. What are the constraints and safeguards for the use of your biomaterials and data?

Your biomaterials that have been stored in the TransBioLine biobank (or Charite) would be used exclusively for the research aims of the TransBioLine. Only approved research institutions can gain access to your coded data and samples, in order to protect your privacy.

a. A mandatory pre-requisite for the acquisition and use of your biomaterials and related personal data for research purposes is your written consent. Your consent is voluntary and can be withdrawn at any time (see also Item 10 "What does your right of withdrawal include?").

By giving TransBioLine permission to use your biomaterials and/or data, you also transfer ownership of the biomaterials to TransBioLine. You retain the right to correct any data that might have been incorrectly stored or processed at any time.

b. Your biomaterials will be stored in Central Biomaterial Bank (ZeBanC), Berlin under standardized quality and security conditions and are available for (medical) research purposes on request only. They are protected against unauthorized access according to the current state of technology. Your supporting health data will be stored at ITTM Luxembourg under standardized security conditions and are available for (medical) research purposes on request only. They are protected against unauthorized access according to the current state of technology.

c. *If applicable and required by your ethics:* A mandatory pre-requisite for the use of the biomaterials and data for a specific medical research project is a review by an ethics committee. The ethics committee assesses/evaluates the ethical and legal aspects of the respective research project.

The biomaterial samples are intended to be stored and made available for medical research for 10 years after TransBioLine project termination (i.e. 31/01/2024). The pseudonymised biomarker results and supporting data will be stored for at least 25 years after TransBioLine project termination (i.e. 31/01/2024). Further use or deletion of data beyond 25 years will have to be decided upon at that time.

10. What does your right of withdrawal include?

You are free to withdraw your consent for the use of your biomaterials and/or data at any time without giving a reason and without any fear of detriment. In case of withdrawal it is up to you to decide whether your biomaterials are to be destroyed and the corresponding data to be deleted, or whether they may be used in an anonymized form (that is, without any link to your person, *see* Item 8e) for further medical research projects. However, as soon as the link between the biomaterials and data and your person has been removed, previously donated biomaterials can no longer be destroyed. In addition, data cannot be removed from already completed studies/scientific analyses.

For withdrawal, please contact your local doctor.

11. Who can I contact for further information or in case of questions?

The present clinical study has received favourable opinion from the independent Ethics Committee.
If you have questions about this study, you should first discuss them with the clinic staff (contact details on the front page), study leaders or the ethics committee (details below):

For any questions about your rights as a study participant please contact:

Add details of responsible institution/contact person, e.g. complaints officer within the hospital or Patient Advice and Liaison Service (PALS)<address>

Telephone:

Email:

Or

[Research ethics committee name & contact details].

Additional Information on the New European Union General Data Protection Regulation (GDPR)

If you wish to raise a complaint on how we have handled your personal data, you can contact our Data Protection Officer who will investigate the matter. If you are not satisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO).

Our Data Protection Officer is _____ and you can contact them at _____.

Consent Form

I have read this document/had its contents explained to me. I have been given the opportunity to ask questions about the research study procedures and the potential risks have been explained to me. I have been given time to discuss with others to decide whether to agree to take part in this study.

I, hereby, agree that *[provide name of institution (clinic)/location of record]*
- **collects and stores my personal identifying data**
- **collects/extracts additional information on my health from my health records,**
- **and makes the data together with my biomaterials available in pseudonymized (that is, encoded) form for medical research projects.**

My biomaterials and data may be used for medical research projects for up to 10 years (biomaterial) / at least 25 years (Data) after TransBioLine project termination (31/01/2024).

1. It has been explained to me that I am free to leave the study at any time, without any disadvantage to my future care. I do freely give my consent to join this study, as described to me in this document. I understand that I will receive a copy of this document as signed below.

2. By signing this consent form, I give permission for **my biomaterials and data to be transferred in a pseudonymized form to universities, research institutions and research companies for medical research purposes.**

This may include transfer of double-encoded biomaterials and/or data for research projects involving foreign countries with a lower level of data protection

3. At the end of the study unused blood samples will be stored and, if you agree, may be used in future investigations to contribute to better diagnosis and management of acute and chronic diseases.

You can still be part of this study, even if you choose for your unused samples to be destroyed after the study has ended. Approval from the relevant ethics committees will be sought before the stored blood samples are used for any such future investigations. Samples from those who do not give consent for use of their blood samples after the study has ended will be destroyed.

Please let us know what you would like us to do with any samples left over at the end of the study (tick one only):

☐ Destroy all left over blood/urine/csf samples

☐ Keep samples for use in future research to understanding and identifying biomarkers that provide insights into mechanisms of tissue injury

I have received one copy each of the patient information sheet and the Informed Consent Form. The original remains my study doctor.

_____

Patient's/Participant's name (in printed letters):

_____ _____

Date (to be completed by patient/participant) Signature of the patient/participant

I conducted the patient/study participant consultation and have obtained the patient's/ participant's consent.

_____

Physician name (in printed letters):

_____ _____

Date (to be completed by physician) Signature of the physician