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Ethics policy report of U-PGx

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Policy regarding ethical approvals to conduct the clinical study in U-PGx

The clinical study PREPARE (Preemptive Pharmacogenomic Testing for Preventive Adverse Drug Reactions) is an international prospective, multi-center, open, block-randomized study. It investigates the impact of pre-emptive genotyping of a panel of clinically relevant pharmacogenomic-markers on patient outcomes. Pre-emptive pharmacogenomic (PGx) tests are implemented in seven European countries' clinical sites. For this purpose, patients' materials, i.e. DNA samples, are collected at recruitment for genotyping.

For the recruitment of patients and collection of clinical data and samples, U-PGx complies with ethical standards and European regulations.

Policy:

All research conducted for U-PGx has to comply with high ethical standards, including those of Horizon 2020, and all relevant European requirements.

The ethical approval of the local and/or national ethics committee is required.

All participants must be informed about the relevance and the content of the study, the biological samples and DNA procurement, storage and analysis plans, as well as all the relevant procedures to be followed. Consent and personal rights must be protected.

Policy regarding the principle of confidentiality in U-PGx

Confidentiality is one of the major principles to be enforced in the U-PGx project.

In the clinical study PREPARE information on personal and clinical data will be extracted from DNA and medical records. These sources are used for research only and governed by strict regulations.

Policy:

Research must guarantee confidentiality of data and privacy of participants.

Provisions will be made to ensure respect for the privacy of participants and for the confidentiality of records in which participants are identified. Confidentiality will be ensured thanks to internal procedures, authorized and secured facilities.

According to the methodology of the main PREPARE clinical study and of the PGx tests to be provided in the course of the project anonymization is not relevant. Thus, pseudonymization will be provided and will comply with European regulation. European legal requirements about personal data must be respected.

Policy regarding data storage and exchange

The work with the data is subject to the approval of the relevant local and/or national ethics committee for each study implementation country: Austria, Greece, Italy, The Netherlands, Slovenia, Spain and The United Kingdom. Personal data will be stored in accordance with relevant national and international legislation and good practices. Data may only be transferred to non-European countries with an adequate data protection policy. Only relevant data for U-PGx research will be collected and no excess data will be stored. Data and samples will be stored by each partner centre under their own responsibility and according to the respect of informed consent.

Policy:

Any partner who wishes to process personal data must request for authorisation in accordance with national and international data protection laws and recommendations. Confidentiality and privacy of patients shall be especially respected.

Policy regarding feedback of information to participants

In the genetic test group of the study, tests results and individual genotypes will be recorded in the patient's medical (electronic) record and printed on an individual card. These results will be used by their doctors and pharmacists during the study to personalize prescriptions. Patients in the standard of care group will receive their test results once the study will be completed.

In the main U-PGx project, incidental findings should be avoided because DNA capture is targeted only to specific variants in genes encoding drug metabolic enzymes. However, only patients who have agreed to be informed of the incidental findings will be recruited. Decisions about the clinical relevance of incidental findings will be discussed in the Executive Board and, if necessary, with the help of external experts.

All patients included in the study will be asked to provide informed consent for additional NGS analysis. The aim of this sub-study is to identify a possible genetic origin of the extreme phenotype. These data will only be used for exploratory analysis and will not be implemented in clinical care. As these data will be anonymised, results will not be returned to patients.

Policy:

Individual PGx-results will be communicated to individual participants by their health care provider enabling PGx informed decision making. Results of the NGS of the sub-study will not be returned to patients. Patients can refuse to provide consent for the sub-study and

will still be able to participate in the main study. This will be clearly explained during the process of consent collection.

Policy regarding withdrawal

In U-PGx, several types of withdrawals are possible depending on participants' choices about the future of their data.

- In case of withdrawal from the main study, data are lost for the study and can no longer be used. The patient may request that his/her data be destroyed.
- In case of withdrawal from the follow-up process, the patient declines to continue to be followed-up. But he/she consents that previously collected data can be used for the study.
- In case of a partial withdrawal, the patient withdraws from using the patient-reported online monitoring system but agrees to be contacted and to be kept informed by the research team.

Policy:

In U-PGx, options for withdrawal from the study should be explained to the patient during the information process and mentioned in the informed consent form. They should be precisely aware of how to discontinue their participation to the study

Patient involvement is voluntary; patients can leave the study and withdraw their participation at any time. No justification may be required.

Formal procedures to stop their participation to the automatic survey are already in place. This policy is also applying for the removal of samples.

Policy regarding public communication

Project results and newly generated knowledge dissemination to the public is one of the main goals of U-PGx program. To this end, the overall results and outcomes of the project will be published in international scientific papers and medical journals. All necessary information will also be provided through the website of the project.

To inform about U-PGx implications for society, press releases and media events will be planned.

Policy:

Feedback about the research activity provided in U-PGx will be reported to all relevant public. These general results will be published on the project's website and/or in scientific

publications, and at large through more general media.

Internal ethical oversight mechanisms

The U-PGx project deals with several ethical issues (e.g. biological samples, clinical research, informed consent, ethical approval, data storage and exchange), framed according to different standards and requirements in the European countries involved. These ethical issues are a continuous part of the agenda of the project. Hence, a work-package (WP8) is fully dedicated to the ELSI oversight. This work-package ensures that relevant ethical and legal issues are taken into account in the work performed in U-PGx and in the guidelines to be delivered by the project.

This work-package is acting in a proactive way and will manage the ethical issues prospectively. If a potential problem would appear, it will be discussed within the consortium and if necessary with the help of external advice. Furthermore, changes in ELSI European and Member States regulations may occur during the project, thus policies will be adapted accordingly.

Policy:

The ethical responsibility of U-PGx should not be limited to what was originally foreseen in the project. If new ethical issues arise during the project activities, all consortium members must be proactive and respond quickly. Some of these issues could be discussed at consortium meetings.