ERGO No: 45724
IRAS No: 217804, 265580

Information for Clinicians

The PURA Global Network. Understanding PURA Syndrome.

PURA Syndrome Longitudinal Natural History Study.

We would like to invite you to take part in this research study. We hope that you find the below information helpful. Please contact the study administrative team at PURA@soton.ac.uk, if there is anything that is not clear or if you would like more information.

What is the purpose of the study?

The aim of this study is to improve our understanding of the PURA syndrome phenotype and understand how it affects patients over time. We have written a series of medical questionnaires that will ask you and the patient's parent/guardian/relative/personal consultee questions about different medical problems. We intend to increase the number of questionnaires over time and repeat collection of this information at annual intervals. This represents the first ever long-term study of PURA syndrome.

Which patients are eligible for the study?

Any patient who has had genetic testing that confirms PURA syndrome, 5q31.3 deletion including the PURA gene, or a 5q31.3 duplication including the PURA gene. Study participants that live in a Country subject to UK sanctions, a Country on the USA State Sponsors of Terrorism list, or are 16 years and over and live in Northern Ireland, are not eligible for inclusion. If you are unsure if your patient resides in one of these Countries, a list is available by emailing the study administrative team at PURA@soton.ac.uk or on the Study protocol which is available on the PURA Syndrome Foundation website, https://www.purasyndrome.org.

Can I get involved?

You can enter details about your patient provided they fulfill inclusion criteria, the patient's parents/guardians/relative/personal consultee have given consent/personal consultee declaration and you have appropriate ethical and institutional approval. To access the study questionnaires, you will need to agree to the Clinician Study Terms. These terms can be accessed and electronically signed after you have received login details to the study site.

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How do I get involved in the study?

Clinicians can enter the study by two routes.

1. The patient recommends clinician.

   This is when your patient's parent/guardian/relative/personal consultee have accessed the study and have recommended you to enter information about their child/ward/relative/person with PURA Syndrome. The study administrative team will contact you from the PURA@soton.ac.uk email account with the patient name, date of birth, address and information about the study, using the contact details supplied by your patient's parent/guardian/relative/personal consultee. Hopefully the patient's parent/guardian/relative/personal consultee will have told you of their recommendation and supplied you with the study participants pseudonymised ID number. To ensure you are entering information on your patient, we ask that you confirm this recommendation with the patient's parent/guardian/relative/personal consultee using the contact details stored by your institution, or face-to-face. It is also sufficient if the patient's parent/guardian/personal consultee has notified you of their recommendation using the contact details stored by your institution, or face-to-face. We ask for this validation process, to ensure that we are linking your account with your "real" patient.

   If you wanted to proceed with the study, you would need to reply to the study administrative team email account (PURA@soton.ac.uk); confirming the patient details and pseudonymised ID. We will then generate a study account for you to use and send access details to your email. The patient's parent/guardian/relative/personal consultee will have already provided online consent/personal consultee declaration for you to enter information and once you have access to the study, you will be able to view this consent/personal consultee declaration form.

2. Clinician self-referral to the study.

   This is when you have a patient who fulfills inclusion criteria but their parent/guardian/relative/personal consultee haven't accessed the study. You can still enter information about your patient, but you will need to gain consent/personal consultee declaration to do this. There are clinic consent/personal consultee declaration forms available for this purpose on the PURA Syndrome Foundation website (https://www.purasyndrome.org) or by contacting the study administrative team at PURA@soton.ac.uk. To gain study access, you need to email the study administrative team at PURA@soton.ac.uk from your professional/institutional verifiable email address**.** This email needs to include your patients name, date of birth, current Country of residence, confirmation of PURA syndrome/PURA gene deletion/PURA gene duplication, if you

already have an account and your own professional contact details. Prior to sending this email, you need to have consented the patient's parent/guardian/relative or gained personal consultee declaration. The email that you send this information from, is the email the study administrative team will use to contact you. The study administrative team will then confirm that that the patient meets inclusion criteria and there is no duplicate record. If a duplicate record exists, the clinician will be asked to contact the family and ask if they can be added as a clinician to the patient's account. If there is no duplicate record and the patient meets inclusion criteria, we will generate a study account for you to use and send access details to your email. We ask that if you are recruiting in this way that you explain to the parent/guardian/relative/personal consultee that they can also access and upload information into the study.

Who will give consent for patients with PURA Syndrome to be involved in the study?

From our understanding of PURA Syndrome, children and adults with PURA Syndrome do not have the capacity to consent for involvement in this research study. If during the process of this study you identify a patient with PURA Syndrome who you believe has capacity to consent then please let the study administrative team know. If the patient's parent/guardian/relative/personal consultee have recommended you, consent for you to enter information will already have been given through the study platform.

If you are self-referring, then you will need to gain consent/personal consultee declaration. If the study participant is a child (under 16 years of age), consent will need to be sought from one of the parents or legal guardians/custodians of the study participant. If the study participant is aged 16 years or over and lives in England or Wales, a "personal consultee" opinion should be sought. A personal consultee is someone who cares for, and is interested in the welfare of the study participant other than in a professional capacity. If the study participant is aged 16 or over and lives in any Country other than England or Wales, consent will need to be sought from the study participants legal representative. If a legal representative has not been appointed, then consent should be given by their nearest relative (as defined by the Mental Health (Scotland) Act 1984 relationship hierarchy).

To allow ongoing study access for study participants that turn 16 during the study, we require that the appropriate consent/personal consultee opinion (as detailed above) is sought when your patient turns 16 years. Please note that we are currently unable to continue access for study participants in Northern Ireland once they turn 16 years of age. If you have any questions regarding this, please contact the study administrative team.

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What if I look after multiple patients with PURA Syndrome?

You will be able to see all of your patients' study accounts and add information on each of your patients from your one account. It is very important to ensure that you confirm that you are entering the correct information on the correct patients account and patient demographic details will be available for you to see for this purpose. If you need to add a new patient to your account, then you need to follow the above 'How do I get involved in the study?' steps. During this correspondence, you should notify us that you already have an account.

Do I have to take part?

No. Participation is entirely optional.

Do I need ethical approval?

Yes. To access the study, you will need to have received appropriate national or institutional ethical approval. The study has UK Research Ethics Committee (REC) approval (IRAS No: 217804 & 265580), University of Southampton approval (ERGO 457241), and is a Musketeers Memorandum (MM) study. This approval allows clinicians based at a regional genetics centre in the United Kingdom to enter data. University Hospital Southampton NHS Foundation Trust is acting as the lead Research and Development (R&D) office for MM. If you are not based at one of these centres, we will aim to help in your attainment of ethical approval, but will not be held responsible for applying for each application process. To aid in this, we can provide you with the protocol, sample forms and UK ethical proposals. International ethical regulations are variable and you will need to ensure that you comply with institutional and national ethical regulations.

How do I withdraw from the study?

You can withdraw from the study or unlink with a patient's accounts at any time, without providing a reason. If you withdraw, you will not be able to add any further information into the study. Data that has been submitted up to that point will be included in the research study, however we will not request any further information. You can withdraw by emailing the study administrative team at PURA@soton.ac.uk or by accessing the study withdrawal document on the study site. If you have multiple patients, you will need to confirm in the email whether you want your whole account closed or just to be unlinked to a certain patient account. If you are doing this by the study withdrawal

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document then you will need to be complete this for each of the patients accounts that you wish to withdraw from.

If your patient's parent/guardian/relative/personal consultee withdraws consent where there is a corresponding clinician entry, the parent/guardian/relative/personal consultee and clinician will not be able to add information to that account.

In these circumstances, your account will remain active so that you can still access your other patient accounts, but will no longer be able to access the "withdrawn" patient account.

What information will be collected?

We will ask you to provide us with your name, institution/professional work place and contact details. The questionnaires will cover your patient's past medical history, development and medical history. This may include clinical information attained from medical records, outcomes of clinical examination, investigation reports, investigation images, radiological images and reports from surgical procedures. In time, we may ask you to upload photographs. You should only upload photographs if the patient's parent/guardian/relative/personal consultee have specifically opted in on the consent/personal consultee declaration form. You do not have to fill out all of the questionnaires, although the information you provide should be as complete and accurate as possible.

Patient's parent/guardian/ relative/personal consultee will be able to view the information you have entered on their child/ward/relative and you will be able to see the information that they have entered.

We are collecting information that is considered 'sensitive data' or 'special category data'. This type of data requires researchers to take additional care in its collection, storage and use. In addition, this data includes the collection of personal information. This essentially means that the information collected is capable of either directly or indirectly identifying your patient. All research where someone can be identified will be conducted in accordance with data protection laws. We aim to protect study participants identity and will not provide researchers with patient names, date of birth, address or contact details.

What are the possible benefits of taking part?

We hope to gain a better understanding of PURA syndrome and its course. It is hoped that an improved understanding of PURA syndrome will help in establishing effective management guidelines for clinicians, provide information to families and guide further research.

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What are the possible disadvantages and risks of taking part?

The study does not come at any physical risk to your patient, although there may be no direct benefit to your patient. Because PURA syndrome is so rare, there is a risk that a small amount of information may allow people who know your patient well to identify them from research papers, information on the Foundation website or PURA Syndrome Foundation conference lectures. Every effort will be made to keep this information as private as possible. This has also been explained in the Study Information document.

Will my entry be acknowledged?

One of the main aims of the study is to promote further research and publication. Researchers can apply to access pseudonymised datasets from the study. If this dataset includes data that you have submitted, they will be provided with your contact details. We ask that researchers contact you to offer appropriate acknowledgment such as collaborator recognition or co-authorship. We will only be able to give your contact details, if you have opted-in for this on the Clinician Study Terms document. Acknowledgments should be decided based on the International Committee of Medical Journal Editors acknowledgment recommendations (http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html). Researchers should make appropriate efforts to make this contact via the contact details provided, although in the absence of a response in an appropriate time frame, they can proceed in submission for publication. Researchers will not be provided with information that links you to your record and you should not try to link information to identify your patients from the study cohort. Sharing of additional information is not covered in the PURA Syndrome Natural History study consent/personal consultee declaration or study protocol.

How will the information be kept confidential and safe?

All participant details will remain confidential and protected, in compliance with General Data Protection Regulation 2016/679, Data Protection Act 2018 and the University of Southampton data management policy. The University of Southampton is the data controller, and is responsible for safely collecting the information, looking after it and using it properly. All personal information is handled according to the University's policies and legal and regulatory requirements. Data protection laws require that personal data is; used lawfully, fairly and in a transparent way, collected only for valid purposes that have clearly been explained, proportionate and relevant to the purposes told about, accurate and up to date, kept only as long as necessary and kept securely.

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The questionnaires are held on a secure website and the data stored on a secure server, currently in the Netherlands. When an account is created, your patient is given a pseudonymised patient ID. All of the information entered into the questionnaires is entered under this patient ID and stored separately to your patient's name, genetic report and contact details.

Who will have access to the study information?

The study administrative team will have access to all the information that you enter. Responsible members of the University of Southampton, the data system staff (currently FormsVision) or individuals from regulatory authorities may be given access to monitor and uphold data management regulations. International researchers can apply for pseudonymised datasets from the study. Data will only be exported to researchers after successful application to, and authorization from, the PURA Syndrome Study Advisory Steering Committee. Clinicians who have entered data onto the system and would like further access for research, need to apply in this way. Researchers from both inside and outside of the European Economic Area (EEA) will need to manage data in accordance with the study Data Sharing Agreement and General Data Protection Regulation (GDPR). Outcomes of this research may be shared in reports, publications and conferences. As the data controller, the University of Southampton, may also have to disclose information if required so by law in order to comply with legal obligation, to protect University rights, interests or property, to act in urgent circumstances to protect the personal safety of University staff, students and public, or protect the University against any legal liability.

What happens when the research study finishes?

The length of the study will be regularly reviewed and the end date decided by the PURA Syndrome Foundation. There is currently no definite end date for this study, although you or your patients' parent/guardian/relative/personal consultee can withdraw at any time. The length that data is kept after the study is closed will be in accordance with General Data Protection Regulation 2016/679, Data Protection Act 2018 and the University of Southampton data management policy.

Who is running the study?

The study administrative team are based at the University of Southampton. University of Southampton are sponsoring the study. Professor Diana Baralle is the Chief Investigator of the study and data custodian.

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Who is funding the study?

The PURA Syndrome Foundation - https://www.purasyndrome.org/

What is the legal basis for this study?

The legal basis for the collecting and processing of this information is to perform a task in the public interest. The University of Southampton endeavour to maintain the highest of standards in the research they conduct. Researchers affiliated to the University of Southampton must comply with the University codes of conduct, policies and procedures to ensure the research complies with University and national regulations and legislation.

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