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Checkpoint Inhibitor-Induced Liver Injury (ChILI)

Contents:

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1. What is the purpose of the study?

- Immune checkpoint inhibitors are proven cancer treatment drugs which have evolved over the last decade and improved outcomes in various cancers.
- They work to boost the normal immune system by restoring processes which get blocked when cancer develops.
- These drugs boost all the immune cells, not just the ones that can attack the cancer.
- The overactive immune system following this treatment can damage the **liver** and other organs which can be serious. These injuries are unpredictable and difficult to treat.
- Our aim is to develop new tests that can identify, predict and prevent checkpoint inhibitor-induced liver injury (ChILI) and identify the risk factors for developing this condition.

2. Why have I been invited?

You are being invited to take part because you are either about to start cancer treatment with immunotherapy (checkpoint inhibitors) or have developed liver injury secondary to treatment. We are inviting 160 participants in total to take part (40 patients who developed liver injury following checkpoint inhibitors (ChILI) and 120 who are starting treatment with checkpoint inhibitors)).

3a. Do I have to take part?

No. It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form (in paper form or electronically). If you decide to take part you are still free to withdraw at any time and without giving a reason. This will not affect your legal rights or care. Due to COVID-19, we also consider electronic consent (e-consent) through a secure website (REDCap) as a method of obtaining informed consent to reduce face to face contacts.

3b. What will happen to me if I take part?

If your specialist cancer doctor (oncologist) decided to start you on checkpoint inhibitors for your cancer or if you are already on the treatment and developed liver injury (ChILI), we will arrange to see you as soon as possible. We expect to see you 2-3 times over a month as shown in the diagram below.

Research Visits:

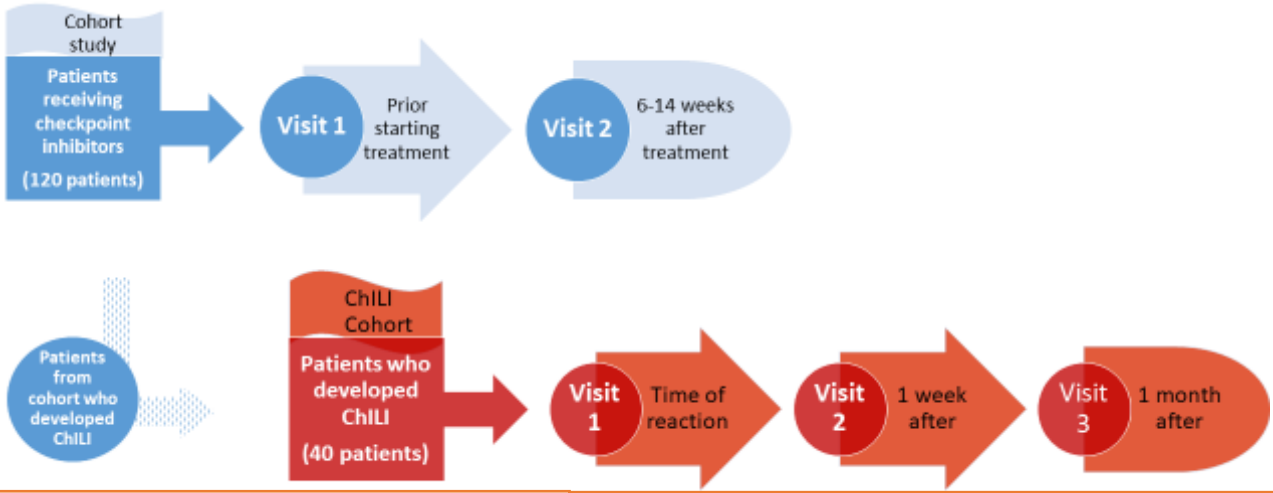
Duration: Each visit is expected to last about 30 minutes.

Location: [Insert location]

What happens during the visit:

- The research nurse will answer any questions you have and ask you about your health and medical history including your medications.
- We will collect up to 80 mls of blood (4½ tablespoons) for research and ask if you can provide a urine and/or stool ('poo') sample (urine and stool samples are optional).
- Samples for research will be collected alongside your clinical care blood tests.
- Visits will be adapted to coincide in with your routine hospital care and clinic visits whenever possible.

We will not change your cancer treatments or test any new drugs or treatment



4. Expenses and payments

Participants will not be paid to participate in the study. Travel expenses will be offered for any visits incurred as a result of participation.

5. What happens after the research study?

We will not alter your ongoing treatment or usual healthcare. We will analyse the samples and publish our findings in scientific journals and on our website.

6. What will happen to any samples I give?

Blood samples:

We expect to take 35mls (2 tablespoons) for research but at one or two visits we may request an additional 30mls of blood. Where possible we can take this extra blood at a separate time to suit you or at the same time as your clinical blood tests (maximum of 80 mls including clinical bloods, equivalent to 4½ tablespoons). Additional blood will enable us to carry out specialised antibody tests on particular immune cells which could help us to distinguish ChILI from other liver injuries.

Liver biopsy:

If you developed ChILI, the clinical team might consider liver biopsy to guide management. If you consent, we would request to use any surplus tissue for research. Samples (blood and tissue) might be sent to specialist centres for analysis, either in the UK or abroad (e.g.at Pfizer, USA).

What will be tested in these samples?

We will measure various constituents of your blood, urine and stool (e.g. the biochemical substances and types of cells present, the biological processes occurring and DNA features).

Retaining samples for future use:

We would like to ask your consent to store any samples leftover at the end of this study to use them in future research – it is optional. The samples will be stored with a code unique to you and securely at the University of Nottingham (Nottingham Digestive Diseases Centre) and made available for future studies by researchers here or at other institutions. Samples and data used will be anonymised and you will not be identified in anyway.

7. Will any genetic tests be done?

Your blood samples will be analysed to look at DNA & gene variations which may contribute to ChILI, if you agree.

We will run tests at specialist centres to identify immune cell types in your blood to determine how the immune system specifically responds to therapy and during drug-induced liver injury so we can understand how to prevent this.

We will not carry out clinical genetic testing of your samples to detect known inherited disorders.

8a. What are the possible disadvantages and risks of taking part?

We are not altering your treatment regime or testing new drugs. We will simply closely monitor your health and responses to your treatment requiring additional time at appointments. Blood sample collection may cause temporary discomfort and occasionally a bruise. It will be performed by trained personnel only and we don't expect any complications.

8b. What are the possible benefits?

This study will not help you but the information we get from this study may help future cancer patients receiving checkpoint inhibitors.

9. What will happen if I don't want to carry on with the study?

Your participation is voluntary and you are free to withdraw at any time, without giving any reason, and without your legal rights being affected. If you withdraw, we will no longer collect any information about you or from you but we will keep the information about you that we have already obtained as we are not allowed to tamper with study records and this information may have already been used in some analyses and may still be used in the final study analyses. To safeguard your rights, we will use the minimum personally-identifiable information possible.

10. Will my taking part in the study be kept confidential?

We will follow ethical and legal practice and all information about you will be handled in confidence.

If you join the study, we will use information collected from you and your medical records during the course of the research. This information will be kept **strictly confidential**, stored in a secure and locked office, and on a password protected database at the University of Nottingham. Under UK Data Protection laws the University is the Data Controller (legally responsible for the data security) and the Chief Investigator of this study (named above) is the Data Custodian (manages access to the data). This means we are responsible for looking after your information and using it properly. Your rights to access, change or move your information are limited as we need to manage your information in specific ways to comply with certain laws and for the research to be reliable and accurate. To safeguard your rights, we will use the minimum personally – identifiable information possible.

You can find out more about how we use your information and to read our privacy notice at: https://www.nottingham.ac.uk/utilities/privacy.aspx.

The data collected for the study will be looked at and stored by authorised persons from the University of Nottingham who are organising the research. They may also be looked at by authorised people from regulatory organisations to check that the study is being carried out correctly. All will have a duty of confidentiality to you as a research participant and we will do our best to meet this duty.

Your contact information including consent forms will be kept by the University of Nottingham for 12 months after the end of the study so that we are able to contact you about the findings of the study and possible follow-up studies (unless you advise us that you do not wish to be contacted). This information will be kept separately from the research data collected and only those who need to will have access to it. All other data (research data) will be kept securely for 7 years. After this time your data will be disposed of securely unless you consent to storage of your contact details for future contact about other projects. During this time all precautions will be taken by all those involved to maintain your confidentiality, only members of the research team given permission by the data custodian will have access to your personal data.

In accordance with the University of Nottingham's, the Government's and our funders' policies we may share our research data with researchers in other Universities and organisations, including those in other countries, for research in health and social care. Sharing research data is important to allow peer scrutiny, re-use (and therefore avoiding duplication of research) and to understand the bigger picture in particular areas of research. Data sharing in this way is usually anonymised (so that you could not be identified) but if we need to share identifiable information, we will seek your consent for this and ensure it is secure. Anonymised data may be shared with institutions in countries out of the European Economic Area (EEA) with different data protection regulation, only where contracts including adequate data security safeguards are in place. We will share study data with our collaborator Pfizer inc (USA) for analysis. We will follow University of Nottingham policies on data protection and all data will be anonymised to protect your confidentiality.

11. What will happen to the results?

- We will publish our findings in research journals and explain them at scientific meetings.
- We will provide a summary of our findings on our website: **https://nddcbru.org.uk/** after the end of the study.
- Participants will not be identified in any publication.
- The results will be written up as part of a PhD degree undertaken by Dr Edmond Atallah

12. Who is organising/funding the research?

The study is being organised by the University of Nottingham and is being funded by NIHR Nottingham Biomedical Research Centre and Pfizer Inc

13. Who has reviewed the study?

All research in healthcare is looked at by independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by North West - Haydock Research Ethics Committee and approved by Nottingham University Hospitals Trust and University of Nottingham.

14. What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions. If you remain unhappy and wish to complain formally, you can do this by contacting the National Health Service complaints procedure or NHS Patient Advice & Liaison Service (PALS): NUH NHS Trust, c/o PALS, Freepost, NEA 14614, Nottingham NG7 1BR. Tel 0800 183 0204, email: pals@nuh.nhs.uk

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against the University of Nottingham but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available.

15. Further information and contact details

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