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Study investigating the impact, risk and mechanisms of neuropathic pain (nerve pain) associated with chemotherapy. Partnership for Assessment and Investigation of Neuropathic Pain (PAINSTORM)

Submission date
27/10/2022

Recruitment status
No longer recruiting

Registration date
15/11/2022

Overall study status
Completed

Last Edited
17/01/2025

Condition category
Nervous System Diseases

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Nerve or 'neuropathic' pain can occur when the nerves are damaged in some way. Unfortunately, many of the commonly used and effective chemotherapies for cancer treatment can damage nerves. People may develop Chemotherapy Induced Peripheral Neuropathy (CIPN) with pain and numbness, particularly in the hands and feet, during or after treatment.
CIPN can be so severe that the dose of chemotherapy needs to be reduced, or even stopped, during treatment. There are no effective preventive treatments, and limited treatment options available if CIPN does develop. We do not understand why some people get neuropathic pain from chemotherapy whilst others do not, nor why it gets better in some people but not in others. Research that we have done has found that sometimes factors such as a person's lifestyle, other diseases they have, past experiences they've had and family history (genetics), can make someone more likely to develop neuropathic pain. We want to understand what things make someone more or less likely to develop CIPN, and how it changes over time. This will then help us develop ways to reduce the risk of developing CIPN, as well as hopefully preventing or treating it.

Who can participate?
Patients 18 years or older with a planned course of potentially neurotoxic chemotherapy for the treatment of cancer.

What does the study involve?
If you decide to take part in the study, you will be asked to attend study visits before starting chemotherapy, half-way through your chemotherapy and at the end of your chemotherapy.

At the first study visit, you will be asked to complete a consent form to confirm that you want to take part in the study. You will also be asked about your health and any medication you take. The

following will also be recorded:
• Height and weight.
• Quantitative Sensory Testing (QST) – to examine nerve function. This includes checking how you feel different sensations such as temperature changes, light touch, and pin prick.
• Questionnaires – will be completed covering aspects of health, pain and quality of life. You will also be asked to complete questionnaires at home in between study visits, before each cycle of chemotherapy. Completed questionnaires can be sent in by email or completed online or sent by post.
The following activities are optional:
• Blood test
• Activity monitor – an activity monitor should be worn for 7 days to record steps per day and time spent sitting, standing and lying down.
• Brain MRI scan –100 participants will have a Magnetic Resonance Imaging (MRI) scan of their brain. The MRI will record any changes in nerves before and after chemotherapy.

Second and third visits
Activities:
• Quantitative Sensory Testing (QST) – as described for the first visit above
• Questionnaires
• Blood sample
• Activity monitor
• Brain MRI – on the third visit only.

After participants have finished their chemotherapy, they will be contacted again 3, 6, 9 and 12 months later to check their health and medication and complete a questionnaire. This follow-up contact will be by phone, online and/or by post.

What are the possible benefits and risks of participating?
Benefits:
The study might not bring benefit to participants personally, but the aim is to improve the treatment of people getting chemotherapy and to help to develop new ways to prevent or treat CIPN. Participants will be monitored closely for CIPN throughout their chemotherapy, with regular detailed assessments by an experienced research team. As participants are being monitored closely for CIPN, if they develop CIPN it might be picked it up more quickly than usual.
Risks:
It may be tiring for participants to have regular assessments throughout their chemotherapy. Quantitative Sensory Testing (QST) involves checking how well participants can feel skin temperature, touch and pressure changes. These tests may cause mild discomfort to the skin or be slightly painful.
Wearing an activity monitor can sometimes cause mild skin irritation.

Where is the study run from?
University of Dundee (UK)

When is the study starting and how long is it expected to run for?
July 2021 to June 2025

Who is funding the study?
1. UK Research and Innovation
2. Versus Arthritis (UK)
3. Eli Lilly and Company (USA)

Who is the main contact?
Prof. Lesley Colvin, l.a.colvin@dundee.ac.uk

Study website
https://www.dundee.ac.uk/projects/painstorm-dundee-chemotherapy-induced-peripheral-neuropathy-cipn-study

Contact information

Type(s)
Principal Investigator

Contact name
Prof Lesley Colvin

ORCID ID
https://orcid.org/0000-0002-1563-8600

Contact details
Division of Population Health and Genomics
University of Dundee
Mackenzie Building
Ninewells Hospital
Dundee
United Kingdom
DD1 9SY
+44 1382381880
l.a.colvin@dundee.ac.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
303039

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
2-016-22, IRAS 303039, CPMS 53404

Study information

Scientific Title
PAINSTORM: Partnership for Assessment and Investigation of NeuP: Studies Tracking Outcomes, Risks and Mechanisms

Acronym
PAINSTORM Dundee CIPN study

Study objectives
An individual's risk of developing acute or chronic CIPN can be predicted by specific psychosocial, genetic and clinical risk factors.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 05/09/2022, South Central - Hampshire A Research Ethics Committee (Temple Quay House, 2 The Square, Temple Quay, Bristol, BS1 6PN, UK; +44 2071048033/53; hampshirea.rec@hra.nhs.uk), ref: 22/SC/0233

Study design
Observational study of a longitudinal prospective cohort

Primary study design
Observational

Secondary study design
Longitudinal study

Study setting(s)
Hospital

Study type(s)
Quality of life

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied
Chemotherapy Induced Peripheral Neuropathy (CIPN)

Interventions
The ultimate aim of the PAINSTORM consortium is to reach a new understanding of NeuP, by combining molecular, physiological and psychological approaches to describe its development and progression. An inter-disciplinary approach will be used to determine the interaction of these different factors (with ‘biological’ and ‘psychosocial’ factors given equal weight) and develop innovative technologies and person-centred outcome measures to identify these pathophysiological processes in patients. PAINSTORM Dundee CIPIN Study will contribute to this, by generating a new, deeply phenotyped cohort of people undergoing potentially neurotoxic chemotherapy.

200 patients receiving potentially neurotoxic chemotherapy will be invited to take part. Participants will be seen pre-, mid- and after their chemotherapy where a full medical, concomitant medication and demographic history will be recorded. Nerve function will be examined using Quantitative Sensory Testing, checking sensations such as temperature changes, light touch and pinprick. Participants will complete questionnaires covering their health,

lifestyle, pain (characterisation, intensity and location) and quality of life including psychological and psychosocial aspects, these will also be completed before each cycle of chemotherapy. Optional activities will include blood tests for biomarker and genetic analysis and MRI will be offered to 100 participants to identify brain structural and functional changes associated with development of CIPN.

Intervention Type
Other

Primary outcome measure
1. Development (or persistence) of painless or painful CIPN measured:
1.1. Using change in chemotherapy/dose reduction due to neurotoxicity measured using EORTC-CIPN20 questionnaire at baseline, mid and end of chemotherapy 3, 6, 9 and 12 months after completion of chemotherapy.
1.2. By pain location using a list of body sites / Body map measured at baseline, mid and end of chemotherapy 3, 6, 9 and 12 months after completion of chemotherapy.
1.3. Using development (or persistence) of painless or painful CIPN measured by Total Neuropathy Score clinical (TNSc) questionnaire at baseline, mid and end of chemotherapy.
2. Pain severity change in Chronic Pain Grade and Brief Pain Inventory (BPI) Numeric Rating Scale (average in last 24 hours) at baseline mid and end of chemotherapy at 3, 6, 9 and 12 months after completion of chemotherapy.

Secondary outcome measures
1. Lifestyle factors affecting CIPN measured using:
1.1. Eastern Cooperative Oncology Group (ECOG) Performance Status Scale, any changes to planned oncological treatment, Step count (ActivPALTM accelerometer), Patterns of daily living (time spent sitting, standing, stepping and lying) using ActivPALTM accelerometer measured at baseline, mid and end of chemotherapy
1.2. Past medical History/ co-morbidities, Family History, Details of cancer type and stage, Oncological treatment including planned chemo protocol (and any changes to this with reasons, Duration of CIPN, Smoking questionnaire, Alcohol questionnaire, Illicit drugs measured at baseline.
1.3. Physical function, measured using Saltin-Grimby Physical Activity Level Scale, and concomitant medication and at Baseline, mid and end of chemotherapy at 3, 6, 9 and 12 months after completion of chemotherapy.
2. Demographic factors affecting CIPN: Age, Sex, Scottish Index of Multiple Deprivation (SIMD), Weight, Height, Years in full-time education, Working status, Household income measured at baseline
3. Clinical factors affecting CIPN: Blood/ serum biomarkers measured at baseline, mid and end of chemotherapy.
4. Type and quality of pain affecting CIPN measured using Douleur Neuropathique en 4 (DN4) and NeuP Symptom Inventory (12 items) at baseline, mid and end of chemotherapy at 3, 6, 9 and 12 months after completion of chemotherapy.
5. Quality of lif affecting CIPN measured using EQ-5D-5L21, Brief Pain Inventory (BPI) Pain interference and Core MD Anderson Symptom Inventory (MDASI) questionnaires at baseline, mid and end of chemotherapy at 3, 6, 9 and 12 months after completion of chemotherapy.
6. Psychological Health factors affecting CIPN measured using • Patient-Reported Outcomes Measurement Information System (PROMIS): Depression; Anxiety; Sleep; Support Trauma, Pain Catastrophizing Scale, Inventory of Depressive Symptomatology (IDS-SR), The 7-item State Optimism Measure (SOM-7) and Ten Item Personality Inventory (TIPI) questionnaires at baseline, mid and end of chemotherapy at 3, 6, 9 and 12 months after completion of chemotherapy.

Overall study start date
01/07/2021

Completion date
30/06/2025

Eligibility

Key inclusion criteria
1. 18 years or older
2. Planned course of potentially neurotoxic chemotherapy for the treatment of cancer. This includes the following:
2.1. Platinum drugs
2.2. Taxanes
2.3. Vinca alkaloids
2.4. Epothilones
2.5. Proteasome inhibitors
2.6. Thalidomide
2.7. Vedotin-based drugs
2.8. Checkpoint inhibitors

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
150

Key exclusion criteria
1. Incapacity to give consent or to complete the study questionnaires due to insufficient language command or mental deficiencies, in the opinion of the investigator.
2. Functional impairment - ECOG Performance Status Scale great than or equal to 3 at baseline.
3. Concurrent clinically defined severe physical or psychiatric disorders that would preclude accurate phenotyping.
4. Moderate to severe pain from other causes that may confound assessment or reporting of pain if unable to differentiate from CIPN.
5. Patients who are in the opinion of the investigator, or treating oncology team, unsuitable for participation in the study.

Date of first enrolment
01/12/2022

Date of final enrolment
30/06/2025

Locations

Countries of recruitment
England

Scotland

United Kingdom

Study participating centre
Ninewells Hospital and Medical School
NHS Tayside
Dundee
United Kingdom
DD1 9SY

Study participating centre
University Hospitals Bristol NHS Foundation Trust
Clinical Trials Unit
Bristol Haematology & Oncology Centre
Horfield Road
Bristol
United Kingdom
BS2 8ED

Sponsor information

Organisation
University of Dundee

Sponsor details
TASC
Level 3 Residency block
Ninewells Hospital, Dundee
Dundee
Scotland
United Kingdom
DD1 9SY
+44 1382383297
TASCgovernance@dundee.ac.uk

Sponsor type
University/education

Website
https://www.dundee.ac.uk/tasc/

ROR
https://ror.org/03h2bxq36

Funder(s)

Funder type
Government

Funder Name
UK Research and Innovation

Alternative Name(s)
UKRI

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Versus Arthritis

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Funder Name
Eli Lilly and Company

Alternative Name(s)
Lilly, Eli Lilly & Company, Eli Lilly & Co., Eli Lilly And Co

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Publication and dissemination plan
There will be a clear PAINSTORM strategy for reporting and dissemination of scientific output, overseen by a dissemination committee. Patient partners will be active members of the dissemination committee. Patient partners will lead the identification of ways of disseminating the results and review outputs aimed at patients and public. Results will be written up in high impact open access scientific papers and presented at scientific conferences internationally. A PAINSTORM website will be created, with public access, and papers will be shared there. Where results potentially affect patient care, e.g. through the identification of stratified approaches to risk management, these will be shared with stakeholders such as patient groups, national regulatory and professional bodies, health professionals and the general public, with a view of maximising overall impact. A Final Report will be prepared for the funding body and for the Ethics Committee.

Intention to publish date
01/01/2027

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available on request from Prof Lesley Colvin, l.a.colvin@dundee.ac.uk

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 1.0	25/05/2022	15/11/2022	No	No
HRA research summary			28/06/2023	No	No