ISRCTN14475880 https://doi.org/10.1186/ISRCTN14475880

Central pain processing and modulation biomarkers profile in chronic pain prediction in patients with cancer

Submission date 28/03/2023	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol
Registration date 21/07/2023	**Overall study status** Ongoing	[_] Statistical analysis plan [_] Results
Last Edited 05/03/2026	**Condition category** Cancer	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims
Previous research on biomarkers of cancer pain has been focused on the study of blood samples and as a condition, chemotherapy-induced neuropathic pain. This study will extend the investigation of biomarkers (including biomarkers of central pain modulation) to the most common types of cancer pain (breast, lung, pancreas and colon cancer) and to the stage before the cancer treatment. Thus, in this study, the researchers will select a panel of biomarkers related to the central processing and modulation of pain, propose a bedside assessment protocol, and analyse their power to predict the appearance of pain. In addition, they will assess the most relevant clinical domains/outcomes (other illnesses, main symptoms, cancer characteristics, etc) and other moderator variables (age, sex, lifestyle). There are some previous positive results that support the use of quantitative sensory tests (QST) as predictors of chronic pain appearance or responsiveness to treatment. In some studies, dysfunctional conditioned pain modulation predicted future chronic pain development after various interventions and also analgesic effectiveness towards therapeutic interventions. Regarding cancer, QST data have also demonstrated that the presence of pre-existing sensory deficits before chemotherapy are a contributing factor to the onset of painful chemotherapy-induced peripheral neuropathy (CIPN). Moreover, it has been observed that that QST indices were predictors of response to therapy in cancer-induced bone pain. Nevertheless, no specific bedsite protocol assessment of central pain biomarkers nor specific tools for cancer pain prediction have been developed so far. Thus, the final goal of this study is to develop a prediction tool for cancer pain (including central pain biomarkers, clinical and sociodemographic variables) through artificial intelligence (AI) analysis.

Who can participate?
Patients aged 18 years and over who have had a recent diagnosis of cancer

What does the study involve?
Participants will complete an assessment that will include an initial interview and questionnaires /tests about their health condition. Also, there will be sensory testing and an electroencephalogram (EEG, a recording of brain activity). During the interview, the researchers will collect relevant sociodemographic data (e.g., sex, age, lifestyle) and clinical history (other

illnesses, type of tumor, extension, time since diagnosis, evolution, previous chronic diseases, risk factors for cancer, antecedents of cancer). The researchers will ask the patients for authorization to access data from their clinical records.

What are the possible benefits and risks of participating?
There are no direct benefits from participating in this study except perhaps the individual satisfaction in contributing to research that helps to improve the application of new predictive biomarkers in clinical settings.

Where is the study run from?
IPO Porto (Portugal)

When is the study starting and how long is it expected to run for?
June 2022 to January 2027

Who is funding the study?
Horizon Europe Framework Programme

Who is the main contact?
1. Maria Teresa Carrillo, mteresa.carrillo@usc.es
2. Rui Medeiros, ruimedei@ipoporto.min-saude.pt

Contact information

Type(s)
Scientific

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Study information

Scientific Title
Selection of a panel of biomarkers of central pain processing and modulation, and assessment of their validity to predict chronic pain in patients with cancer - WP1

Acronym
PAINLESS-PredictCANCERPAIN (WP1)

Study objectives
Poorer pain modulation mechanisms at pre-cancer treatment in the patients who will develop chronic pain at 6 and 12 months later.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 19/01/2023, Comissão de Ética para a Saúde - Instituto Português de Oncologia do Porto (R. Dr. António Bernardino de Almeida 865, Porto, 4200-072, Portugal; +351 (0)225 084 000; diripo@ipoporto.min-saude.pt), ref: CES.05/023

Primary study design
Observational

Study design
Multi-centre longitudinal cohort observational study

Study type(s)
Quality of life

Health condition(s) or problem(s) studied
Cancer

Interventions
After signing the informed consent, participants will complete an assessment protocol that will include an initial interview and questionnaires/tests about their health condition (in digital files). Also, the researchers will assess quantitative sensory testing (Temporal Summation of Pain [TSP], Conditioned Pain Modulation [CPM], Heat Pain Threshold [HPT], Cold Detection Threshold [CDT], Cold Pain Threshold [CPT], Offset Analgesia [OA], thermal stimulator [TCS], electroencephalography [EEG], contact heat evoked potentials [CHEPS]) using a TCS device and a cold plate, and EEG and CHEPs registry using an ambulatory EEG device. During the interview,

they will collect relevant sociodemographic data to characterize the sample (e.g., sex, age, lifestyle) and data from the clinical history (comorbidities, type of tumor, extension, time since diagnosis, evolution, previous chronic diseases, risk factors for cancer, antecedents of cancer). In the informed consent the researchers will ask the patients for authorization to access data from their clinical records.

Each assessment session will have an estimated duration of 2 hours and will take place at the hospitals at three timepoints: before the antineoplastic treatment, 6 months after Visit 1 (basal assessment) and 12 months after Visit 1 (basal assessment). The complete participation in the study will take around 6 hours.

Intervention Type
Device

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
-

Primary outcome(s)
Measured before the antineoplastic treatment, 6 months after Visit 1 (basal assessment) and 12 months after Visit 1 (basal assessment):
1. Pain intensity and distress measured using an 11-point (0-10) numerical rating scale (NRS) measure of pain intensity (in the last week) and an NRS for distress (unpleasantness) caused by pain
2. Functional impact of pain and quality of life (QoL) measured using the Brief Pain Inventory (BPI), the Short Form 36 Health Survey (SF-36) and EQ- 5D-3L (EuroQol)
3. Functionality or performance status measured using the Eastern Cooperative Oncology Group (ECOG) scale
4. Sleep quality measured using the Pittsburgh Sleep Quality Index (PSQI)
5. Fatigue measured using the Modified Fatigue Impact Scale (MFIS)
6. Emotional functioning measured using the Brief Measure for Assessing General Anxiety Disorder (GAD7) and the Patient Health Questionnaire (PHQ-9)
7. Catastrophizing measured using the Pain Catastrophism Scale (PCS)

Key secondary outcome(s)
There are no secondary outcome measures

Completion date
01/01/2027

Eligibility

Key inclusion criteria
Current inclusion criteria as of 05/03/2025:
1. Adult subjects ≥18 years old
2. Able to provide informed consent to participate in the study
3. Able to self-report pain
4. Recent diagnosis (less than 6 months) of cancer affecting the lung, breast, pancreas or colon (with metastases or not)

5. Not having started systemic cancer treatment
6. Have a life expectancy of at least 12 months
7. Ability to use the internet and WhatsApp or have a person (family member, caregiver) to help them

Previous inclusion criteria:
1. Adult subjects ≥18 years old
2. Able to provide informed consent to participate in the study
3. Able to self-report pain
4. Recent diagnosis (less than 6 months) of cancer affecting the lung, breast, pancreas or colon (with metastases or not)
5. Not having started cancer treatment (all treatments are included)
6. Have a life expectancy of at least 12 months
7. Ability to use the internet and WhatsApp or have a person (family member, caregiver) to help them

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
100 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Pregnant women or women of fertile age not having efficacious contraception during the whole period of the study
2. Neurological and psychiatric disease (except anxiety and depression)
3. Unstable medical conditions (e.g., uncontrolled diabetes, uncompensated cardiac issues, heart failure or chronic obstructive pulmonary disease)
4. History of neurosurgery, traumatic brain injury with loss of consciousness, and/or cortical lesions
5. History of non-malignant chronic pain

Date of first enrolment
01/04/2023

Date of final enrolment

Locations

Countries of recruitment
Denmark

Portugal

Romania

Spain

Study participating centre
IPO Porto
R António Bernardino de Almeida
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4200-072

Study participating centre
SERGAS - Galician Service of Health
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Santiago de Compostela
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15703

Study participating centre
FIDIS - Santiago de Compostela Health Institute Foundation
Travesa Da Choupana
Santiago De Compostela
Spain
15706

Study participating centre
FBGS - Galicia Sur Biomedical Foundation
Hospital Alvaro Cunqueiro, Bloque Tecni
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36312

Study participating centre
AAU - Aalborg University
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Study participating centre
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Sponsor information

Organisation
IPO Porto

ROR
https://ror.org/027ras364

Funder(s)

Funder type
Government

Funder Name
HORIZON EUROPE Framework Programme HORIZON-HLTH-2021-DISEASE-04 (2022-2027)

Alternative Name(s)
Horizon Europe, Horizon Europe Programme, Framework Programme, Horizon Europe, EU Framework Programme, Horizon, Horizonte Europa

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

Results and Publications

Individual participant data (IPD) sharing plan

Concerning data protection, the researchers will comply with the directives of the General Data Protection Regulation (GDPR), approved by the European Commission on April 27, 2016 (UE 2016 /679). They will be advised by the Data Protection Officer of each of the involved institutions. They assure the confidentiality of all the data generated from the project. All the information will be codified, and none of the digital files will contain personal identification data.

The datasets generated during and/or analysed during the current study are/will be available upon request from Rui Medeiros (ruimedei@ipoporto.min-saude.pt) and Maria Teresa Carillho de La Pena (mteresa.carrillo@usc.es). The type of data that will be shared: biomarkers output and clinical outcomes. Dates of availability: at the end of the project. Consent from participants was required and obtained at the recruitment stage. All data will undergo an anonymization procedure. All procedures were approved by the ethical authorities and Data Protection Officer (DPO).

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		08/06/2024	10/06/2024	Yes	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes