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Measuring small molecules (metabolites) in blood and urine that predict the response to immunotherapy in lung cancer patients

Submission date
15/07/2020

Recruitment status
No longer recruiting

Registration date
17/07/2020

Overall study status
Completed

Last Edited
29/01/2025

Condition category
Cancer

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

Plain English summary of protocol

Background and study aims
Immunotherapy is a cancer treatment that uses the body's immune system to fight cancer in advanced stages. Despite the success of immunotherapy, there are still several barriers to extending its clinical benefit to a greater number of patients. Although there are patients who respond well to immunotherapy, some patients do not respond to the same treatment. At present, it is not well understood how and why this occurs. The ability to predict the response to immunotherapy should allow the development of personalized treatments, improve survival rates and reduce unnecessary exposure of patients to toxic medications. To achieve this, this study will evaluate a wide range of small molecules (metabolites) in blood and urine using different techniques and try to identify which metabolites are useful for predicting the response to treatment.

Who can participate?
Patients aged over 18 with stage III and IV non-small cell lung cancer, who are candidates for immunotherapy treatment

What does the study involve?
This study involves first-line treatments with immunotherapy exclusively or immunotherapy combined with chemotherapy, and second-line immunotherapy treatments after a chemotherapy-based first-line treatment. Fasting morning blood and urine samples will be collected and metabolites will be measured before and after immunotherapy.

What are the possible benefits and risks of participating?
Potential benefits of participating are a good response to immunotherapy and improvement of survival rates. The possible risks of participating include treatment toxicities or deterioration of performance status and disease progression.

Where is the study run from?
University Hospital Sant Joan de Reus (Spain)

When is the study starting and how long is it expected to run for?
September 2020 to December 2022

Who is funding the study?
Instituto de Salud Carlos III (Spain)

Who is the main contact?
Dr Christopher Papandreou
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
Nil known

Study information

Scientific Title
Metabolomic profiles in blood and urine as predictors of response to immunotherapy in lung cancer patients

Acronym
MetLung

Study objectives
The hypothesis of this proposal is that specific metabolites in blood and urine predict the response to immunotherapy. The researchers also hypothesize that immunotherapy will modulate specific metabolites in blood and urine differently in responders than in non-responders.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 09/04/2020, Institut d'Investigació Sanitària Pere Virgili (IISPV) - Ethical Committee (Hospital Universitaria Sant Joan. Avda. Josep Laporte, 2. Planta 0 - E2 43204 Reus, Hospital Universitari de Tarragona Joan XXII. c/ Doctor Mallafrè, 4 Parc Sanitari Hosp.Joan XXIII, 43005 Tarragona; +34 (0)977 759 395; ceim@iispv.cat), ref: CEIm: 072/2020

Study design
Prospective observational single-centre study

Primary study design
Observational

Study type(s)
Other

Health condition(s) or problem(s) studied
Locally advanced or metastatic non-small cell lung cancer

Interventions
First-line treatments with immunotherapy exclusively (those whose tumours express more than 50% of PDL1) or immunotherapy combined with chemotherapy (expression of PDL1 between 1 and 49%), and second-line immunotherapy treatments after a chemotherapy-based first line.

For the metabolomic analysis in blood and urine samples, different analytic platforms will be used according to the sample. Three different metabolomics platforms will be used: proton nuclear magnetic resonance (1H NMR), liquid chromatography coupled to mass spectrometry (LC-MS) and gas chromatography coupled to mass spectrometry (GC-MS). Targeted and untargeted metabolomics will also be performed in blood and urine samples. The duration of follow-up will be 12 weeks.

Intervention Type
Other

Primary outcome(s)
Metabolites in blood and urine will be measured using targeted and untargeted approaches, and 1H NMR, LC-MS and GC-MS analytical techniques at baseline and 12 weeks

Added 12/08/2020:
The first evaluation of the response to immunotherapy will be carried out at 9-12 weeks of treatment with computed tomography scan and following the guidelines for the Immune Response Evaluation Criteria in Solid Tumours (iRECIST) and then every 3 months or at the time when there is suspicion of progression, and classified according to disease control (complete response, partial response, and stable disease) and progressive response (non-response).

Key secondary outcome(s))
1. Toxicity assessment reflected in the medical history, classifying it by affected organ and by degree of severity (1-4) based on ESMO clinical practice guidelines, performed at 12 weeks
2. Fecal gut microbiome measured using V2-V4 r16S RNA and/or next generation sequencing platform (NGS)
3. Fecal metabolome measured using NMR/LC-MS/GC-MS
4. Epigenetic tags (i.e. miRNAs, long ncRNA, telomeres, DNA methylation) measured using qPCR arrays for miRNAs and lncRNA, Luminex-based assay for telomere length, pyrosequencing for DNA methylation
5. Inflammation and oxidation parameters measured using commercial ELISA methods and/or multiplexing
6. Dietary intake measured using a validated food-frequency questionnaire
7. Antibiotic use measured using self-report
8. Probiotic exposure measured using self-report
Measured at baseline and 12 weeks

Completion date
31/12/2022

Eligibility

Key inclusion criteria
Patients older than 18 years with stage III and IV NSCLC candidates for immunotherapy treatment

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
131

Key exclusion criteria
1. Patients with another primary malignancy diagnosed in the previous 5 years (except for cervical carcinoma in situ and non-melanoma skin cancer)
2. Patients with tumours expressing actionable mutations in EGFR, ALK or ROS1
3. Patients with stage IV severe kidney disease (creatinine clearance < 30 ml/min)
4. Patients with severe liver disease (hepatitis, cirrhosis)
5. Patients with low Performance Status (ECOG 3-4)
6. Patients who refuse to sign the informed consent
7. Any previous systemic immunotherapeutic treatment will also make the patient ineligible for the study

Date of first enrolment
01/09/2020

Date of final enrolment
31/12/2022

Locations

Countries of recruitment
Spain

Study participating centre
Hospital Universitari Sant Joan
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Study participating centre
Institute of Health Pere Virgili
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Study participating centre
Universitat Rovira i Virgili
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Sponsor information

Organisation
Instituto de Salud Carlos III

ROR
https://ror.org/00ca2c886

Funder(s)

Funder type
Government

Funder Name
Instituto de Salud Carlos III

Alternative Name(s)
SaludISCIII, InstitutodeSaludCarlosIII, Instituto de Salud Carlos III | Madrid, Spain, Carlos III Institute of Health, Institute of Health Carlos III, Carlos III Health Institute, La misión del Instituto de Salud Carlos III (ISCIII), ISCIII

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Spain

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Dr Christopher Papandreou (papchris10@gmail.com).

IPD sharing plan summary
Available on request