

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

<b>Submission date</b> 15/07/2020	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 17/07/2020	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 29/01/2025	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data <input type="checkbox"/> 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  
papchris10@gmail.com

## Contact information

**Type(s)**  
Scientific

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## Additional identifiers

**Clinical Trials Information System (CTIS)**  
Nil known

**ClinicalTrials.gov (NCT)**  
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 (<sup>1</sup>H 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 <sup>1</sup>H 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**

Av/del Dr. Josep Laporte, 2

Reus

Spain

43204

**Study participating centre**

**Institute of Health Pere Virgili**

Av/del Dr. Josep Laporte, 2

Reus

Spain

43204

**Study participating centre**

**Universitat Rovira i Virgili**  
Carrer de l'Escorxador, s/n  
Tarragona  
Spain  
43003

## 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)

SaludISCI, Instituto de Salud Carlos III, 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 (ISCI), ISCI

### 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](mailto:papchris10@gmail.com)).

**IPD sharing plan summary**  
Available on request

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes