

TRANSCAN-3 JTC2021
International
Networking Event



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HOSPITAL UNIVERSITARIO PUERTA DE HIERRO- MAJADAHONDA (HUPHM)



- The hospital is part of the Puerta de Hierro Majadahonda Health Research Institute, a functional structure for biomedical and translational research oriented to basic, clinical, epidemiological and health services research.
- HUPHM Medical Oncology Department has 2 large areas of research.
 - Clinical Research Unit: Clinical trials (all stages)
 - Translational Research Unit, with a molecular biology approach
 - Lung Cancer:
 - ✓ Collection of series of patients/cases of different types of lung cancer, well characterized clinically and with quality biological material to be analyzed, with prognostic factors and treatment.
 - ✓ Identification of molecular signatures as a prognostic factor.
 - ✓ Genomic studies for routes and genes involved in resistance to chemotherapy treatment.
 - ✓ Exploitation of clinical data through big data tools to develop personalized medicine.
 - Lymphoma: analysis of existing molecular alterations in lymphomas using massive analysis techniques (massive sequencing, gene expression, etc.) combined with functional trial, with the ultimate aim of identifying essential genes/ pathways in the survival of lymphomas to contribute to the improvement of the diagnosis, prognosis and treatment of lymphomas.
 - Sarcoma
 - Therapeutic Targets:
 - ✓ Study of fibroblast activation processes associated with tumors
 - ✓ Mechanisms of release of pro-inflammatory cytokines with activating effect of fibroblasts
 - ✓ Study of resistance processes to chemotherapeutic treatments based on alkylating agents.





HUPHM Medical Oncology Liquid Biopsy Lab (LBL)



- The Liquid Biopsy Lab (LBL) of the Department of Medical Oncology at HUPHM provides diagnostic services and conducts research in the field of personalized medicine, specializing in patients with lung cancer.
- LBL is a reference lab for the study of biomarkers in liquid biopsy that allows the identification of somatic mutations of the tumor, therapeutic targets of certain targeted drugs, in the blood plasma, being a minimally invasive technique.
- LBL participates in several clinical trials of the Spanish Lung Cancer Group, analyzing plasma samples and receiving blood samples from inpatients, as well as from other hospitals for the diagnosis of hereditary cancer syndromes through mass sequencing techniques.
- LBL participates in various External Quality Assessment (EQA) schemes organized by the European Molecular Genetics Quality Network (EMQN) and has accredited most of its NGS tests in accordance with ISO15189.

Participation in International R&I projects



-  **iASiS** Integration and analysis of heterogeneous big data for precision medicine and suggested treatments for different type of patients (H2020)
Big Data for Precision Medicine
-  **BIG Medilotics** Big Data PPP project for the development of Big data-driven approaches for the improvement of healthcare systems and precision medicine (H2020)
-  **CLARIFY** Cancer Long Survivor Artificial Intelligence Follow-up
-  **P4 LUCAT** Personalized medicine for lung cancer treatment: using Big Data-driven approaches for decision support (ERA PerMED)

Project Idea



Aim 1: Identification and validation of tumour microenvironment (TME) subclasses and their contribution to the resistance mechanisms

- 1.2 Definition of the contribution of TME to resistance mechanisms and identification of new therapeutic targets through multiomics (epigenomic, transcriptomic, proteomic, metabolomics, study of the microbiome and virome, etc.) to assess functional characteristics of TME-tumour cell interplay within the primary tumour and/or metastases (e.g the underlying signaling, the transcriptional landscape, the cell-cell communication, the network regulation of immune cells, etc.), to identify candidate TME targets and to assess the activity of pathway-targeting agents.
- 1.3 Development of tools capable of predicting treatment efficacy and tumour recurrence using minimally- or noninvasive techniques (generation of algorithms modelling the network dynamics, predictive models based on artificial intelligence, integrating -omics data and network approaches). Development of robust noninvasive biomarkers of disease course (radiomics, cell-free circulating tumour DNA, miRNA signatures, circulating tumour cells, etc.). Sex/gender impact must be considered.

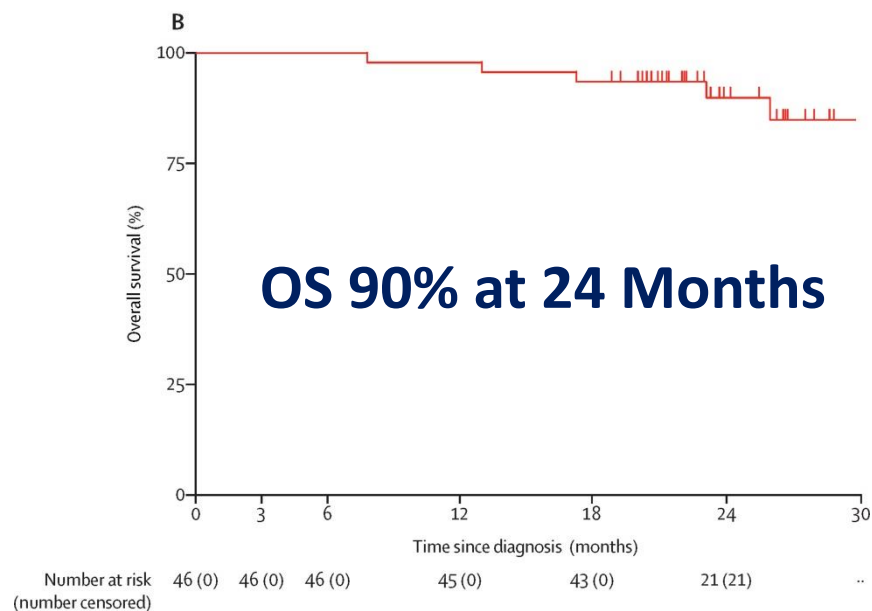
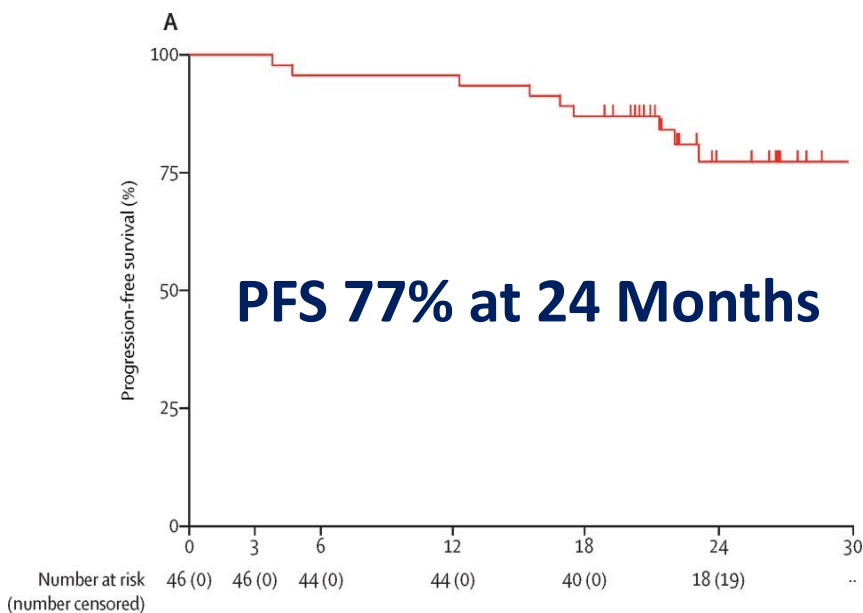
TENTATIVE PROJECT TITLE: PREDICTIVE BIOMARKERS FOR CHEMO-IMMUNOTHERAPY IN OPERABLE NSCLC

Project idea background: NADIM results clinics

Neoadjuvant Nivo+QT was well tolerated
No surgery delays
100% R0 resections

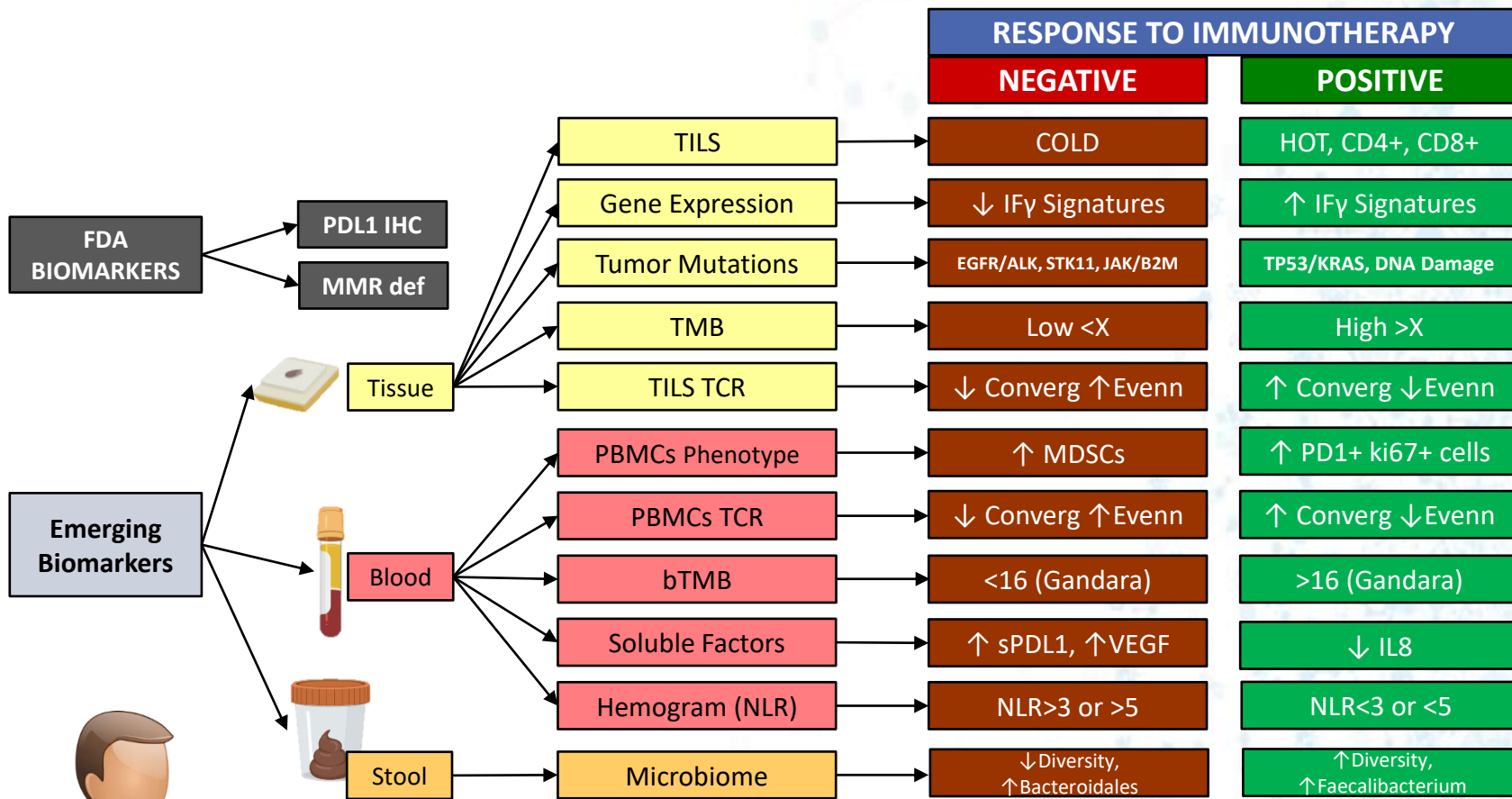
Neoadjuvant chemotherapy and nivolumab in resectable nonsmall-cell lung cancer (NADIM): an open-label, multicentre, single-arm, phase 2 trial

Mariano Provencio, Ernest Nadal, Amelia Insa, María Rosario García Campelo, Joaquín Casal-Rubio, Manuel Dómine, Margarita Majem, Delvys Rodríguez-Abreu, Alex Martínez-Martí, Javier De Castro Carpeño, Manuel Cobo, Guillermo López Vivanco, Edel Del Barco, Reyes Bernabé Caro, Nuria Viñolas, Isidoro Barneto Aranda, Santiago Viteri, Eva Pereira, Ana Royuela, Marta Casarrubios, Clara Salas Antón, Edwin R Parra, Ignacio Wistuba, Virginia Calvo, Raquel Laza-Briviesca, Atocha Romero, Bartomeu Massutí, Alberto Cruz-Bermúdez



Provencio et. al., *Lancet Oncol.* 2020
Nov;21(11):1413-1422.

Project idea background: NADIM results



Need for better **BIOMARKERS** and **PRECISION MEDICINE**.

Project Idea

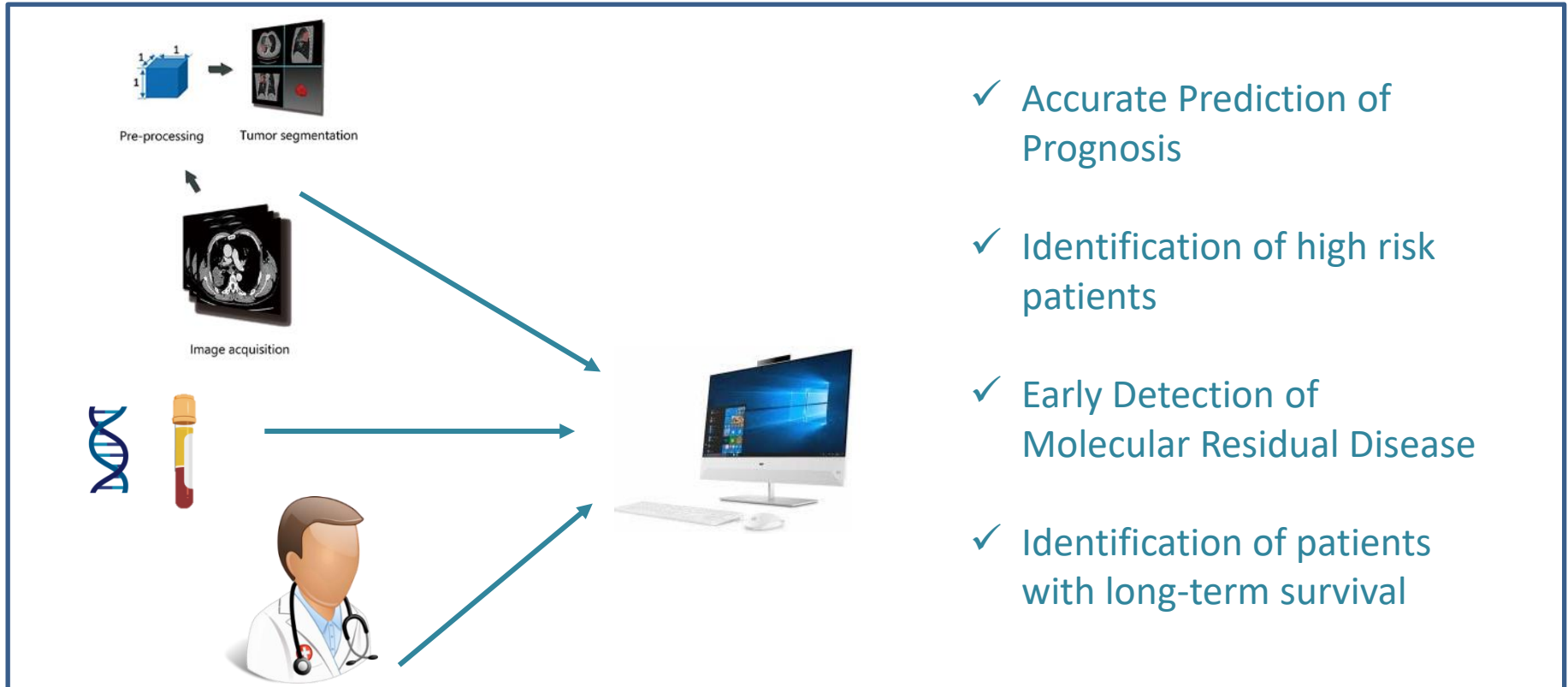


GENERAL OBJECTIVE: to develop a patient risk stratification tool for NSCLC patients under neoadjuvant CH-I treatment capable of identifying, from a simple blood test, patients who can be cured.

- **Objective 1.** To develop an optimized **assay** with exceptional sensitivity and specificity capable of reliably detecting **MRD** after CH-I treatment.
- **Objective 2.** To evaluate the **intratumoral heterogeneity** due to subclonal evolution during neoadjuvant CH-I. To analyse **temporally divergent mutational profiles in responder and resistant tumours**. Identify novel mutations/genes/pathways underlying tumour resistance to CH-I.
- **Objective 3.** To discover **T-cell biomarkers for immunotherapy by T-cell characterization**, obtained from of patients undergoing CH-I, BY tcr SEQUENCING
- **Objective 4.** To develop a **patient risk stratification tool** that allows clinicians to discern which patients have the highest probability of relapse and which patients can be cured, helping oncologist to tailor clinical management of stage III NSCLC patients.

Project Idea

PROJECT EXPECTED RESULTS



Consortium - required partners

No	Expertise	Country	Role in the project
01	Bioinformatics: <ul style="list-style-type: none">• Analysis of NGS data.• RNA seq analysis.• Discover mutational signatures that can predict the tumor response to treatment using unsupervised learning algorithms (hierarchical clustering on categorical variables) as well as supervised approaches.	EU/Turkey	COMPUTATIONAL ANALYSIS. We attempt to discover molecular signatures that can predict the CH-I response using unsupervised learning algorithms (hierarchical clustering on categorical variables) as well as supervised approaches. To this aim, several machine learning methods will be evaluated to determine the classifier that performs the best indicators in the prediction of survival.
02	Biostatistics <ul style="list-style-type: none">• Data analysis and statistical consulting in the context of clinical trials• Develop statistics model for risk stratification• Advance knowledge of R and STATA• Capacity to work with large data sets	EU/Turkey	STATISTICAL ANALYSIS. To develop a patient risk stratification tool, the prognostic value of different biomarkers in terms of overall survival (OS) and progression-free survival (PFS). Importantly data is mature enough for long-term survival analysis (maturity over 90% at 36 months).