ESMO Translational Research Fellowship

(October 2021 – September 2023)

Pedro Filipe Simões da Rocha

FINAL REPORT

Host Institute: **Hospital del Mar Research Institute, Barcelona.**
Mentor: **Edurne Arriola Aperribay**
Project title: **Met inhibition in combination with anti-PD-1/PD-L1 as a new therapeutic approach in Small Cell Lung Cancer.**
Home Institute: **The University of Texas, MDAnderson Cancer Center**

Introduction

Small cell lung cancer (SCLC) is an aggressive and highly metastatic malignancy, leading to ~200.000 deaths each year worldwide[1]. Despite extensive research, only modest treatment advances have been achieved in this disease over the past 30 years, with the 5-year survival remaining less than 7%[2]. Recently, the addition of immune checkpoint inhibitors (ICI) to chemotherapy has become a new standard of care for extensive SCLC, although it confers a modest, 2-month improvement in median overall survival (from 10 to 12 months)[3,4] benefiting only a minority of patients with SCLC[5].

Patients that progress to the front-line chemoimmunotherapy have globally a dismal prognosis mostly due to the extremely aggressive nature of these tumors and the lack of therapeutic options in second and subsequent lines. In this setting, lurbinectedin (cytotoxic agent) in monotherapy or in combination (with doxorubicin, irinotecan) has shown clinical activity[6,7] granting accelerated approval by the regulatory agencies (FDA); however, the pivotal phase 3 trial comparing to standard topotecan has failed to demonstrate superiority of lurbinectedin limiting its use in our region.

In stark contrast with non-small cell lung cancer (particularly lung adenocarcinomas), SCLC subtypes are not defined by driver mutations, but instead, driven by dominant transcriptional programs[8]. Preclinical work suggests that transcriptomic subtyping (ASCL1, NEUROD1, POU2F3 and Inflamed)[9] can inform about different potential tumor vulnerabilities[9,10], and thus support therapeutic decisions. However, these results have not been yet translated to the clinic making the identification of SCLC subtypes in clinical practice and therefore targeting potential vulnerabilities still challenging.

Overall, these observations highlight major unmet needs for patients with SCLC: **1)** biomarkers to identify patients who benefit from chemo-ICI, **2)** to integrate new therapies in the SCLC patient's therapeutic armamentarium, and **3)** understanding resistance mechanisms and development of new strategies to overcome them.

In this setting, MET/HGF pathway stands out as a target that directly regulates key players in tumor aggressiveness and lack of response to approved treatments: **1)** Tumor cells through modulation of epithelial-mesenchymal transition (EMT) that characterize chemotherapy resistant SCLC tumors, and **2)** Immune cells fostering an increase in Met positive myeloid cells in the tumor immune microenvironment (TIME) that lead to a lack of efficacy of ICB agents.

Rationale and Aim

We hypothesize that inhibition of MET/HGF pathway might prevent and revert resistance to chemotherapy and ICB agents in SCLC through counteracting EMT and modifying immune infiltration within the tumor microenvironment, respectively.

Aim: To test the efficacy of Met inhibition in combination with anti-PD-1/PD-L1 agents in preclinical SCLC models and to evaluate potential biomarkers of benefit from this approach to be translated to clinical application

Experimental design

Mouse model:

A hybrid mouse model B6129SF1/J strain was generated in the PRBB animal facility (host institute) by crossing C57Bl/6 females with 129S1/SvlmJ males, this model represents a syngeneic immunocompetent recipient for the murine SCLC cell line KP1. Heterotopic tumors were induced by subcutaneous injection of KP1 cells in the flank. After confirmation of tumor growth, mice were randomized, to a single drug treatment (Chemotherapy, Savolitinib, anti-PD-1 (nivolumab) and anti-PD-L1 (durvalumab)) and all possible combinations.

Tumor Immune infiltrate phenotyping was assessed in tumor, peripheral blood, spleen, tumor-draining lymph node and bone marrow. Tumor immune infiltration will be isolated by mechanic disaggregation, enzymatic digestion and density gradient. Immune cells will be characterized and MET, and PD-1 expression determined in the myeloid subsets PMN-MDSC and M-MDSC by flow cytometry and immunofluorescence by using mouse specific antibodies.Tumor sections will be stained for molecular classification with ASCL1, NEUROD1 and POUF2F3 and with immunohistochemical markers for EMT (E-Cadherin, Snail, Vimentin and AXL), Met and immune infiltration (multiplex IHC/IF).

Human samples:

Obtained from patients included in the CANTABRICO study (*NCT04712903*). This was a Phase IIIb, interventional, single arm, multicentre study to evaluate safety, effectiveness, and patient reporting outcomes in patients with ES-SCLC treated with durvalumab in combination with platinum-etoposide as first-line treatment in Spain (Recruitment completed on May 5th, 2021).

Tumor biopsies were studied by IHC for the following markers: molecular classification (ASCL1, NEUROD1 and POU2F3) and EMT (E-Cadherin and Vimentin) and MET expression (cMET and pMET). IHC evaluation was performed using H-score. Cases expressing more than one marker were classified based on the predominant marker with the higher H-score (A, N, P and No A/N/P).

For blood samples the following studies were performed:

- Serum HGF, IL-2, IL-6 and TNFa levels by ELISA.
- Longitudinal plasma NGS.

Results

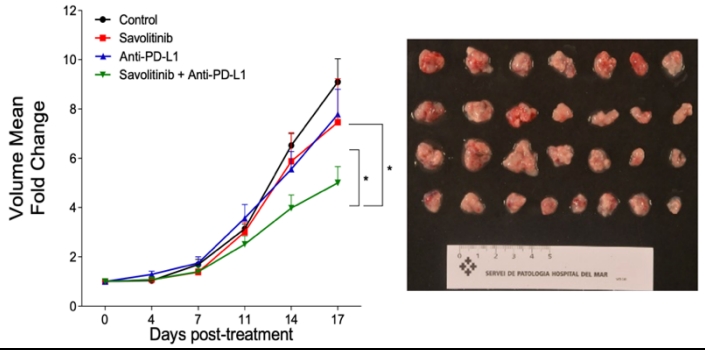
PROJECT 1: Met inhibition in combination with anti-PD-1/PD-L1 as a new therapeutic approach in Small Cell Lung Cancer. *This work is part of a PhD thesis R. Del Rey-Vergara member of Dr. Arriola's group. Manuscript in preparation.*

This project comprises two main parts: **1)** using a preclinical model, to evaluate the immune-modulatory effect of MET/HGT pathway inhibition, and **2)** analysis of human samples from patients included in the CANTABRICO study (Phase IIIb, single arm, multicenter study to evaluate safety, effectiveness, and patient reporting outcomes in patients with ES-SCLC treated with durvalumab in combination with platinum-etoposide as first-line treatment in Spain). Of note, during the fellowship, I assumed responsibility for coordinating samples, analyzing data, and interpreting results derived from patient samples.

1) Preclinical model (led by R. Del Rey-Vergara member of Dr. Arriola's group)**:**

Briefly, KP1 mouse SCLC cell line was subcutaneously injected in immunocompetent B6129SF1/J mice. Mice were allocated in four arms: control (isotype IgG), savolitinib (30 mg/kg daily PO), anti-mouse PD-L1 (10 mg/kg twice a week IP) and the combination of both compounds. Tumor growth was followed-up twice a week until day 18

Figure 1



post-treatment, when mice were sacrificed to obtain cellular suspensions from tumors. Tumor immune infiltrates were assessed by multiparametric spectral flow cytometry.

The addition of savolitinib to anti-PD-L1 reduced tumor growth (5 ±1.62-fold change) compared with control (9.1 ±1.87-fold change; p<0.05), savolitinib (7.46 ±3.54-fold change; p>0.05) and anti-PD-L1 (7.78 ±2.28-fold change; p<0.05) groups (**Figure 1**). Tumors treated with the combinatorial approach exhibited an increase of MHC-I expression on CD45- cells (39.22 ±22.09% vs 8.3 ±4.73%; p<0.05) and an increased infiltration of CD45+ cells (12.85 ±5.26% vs 5.48 ±5.12%; p=0.0667) compared with anti-PD-L1 treated tumors. In addition, tumors treated with the combination displayed a significant increased infiltration of effector memory (CD44+CD62L-) CD4+ T cells (14.53 ±4.05% vs 5.32 ±2.53%; p<0.01) and Granzyme B+CD8+ cytotoxic T cells (3.5 ±2.03% vs 0.77 ±1.09%; p<0.05) compared with control. A decreased infiltration of granulocytic-myeloid-derived suppressor cells (G-MDSC) was also observed in both combinatorial (1.68 ±1.33%) and savolitinib alone (2.92 ±4.34%) arms compared with control (4.39 ±3.92%) and anti-PD-L1 (3.69 ±1.95%) groups (p>0.05) (**Figure 2**).

Figure 2.

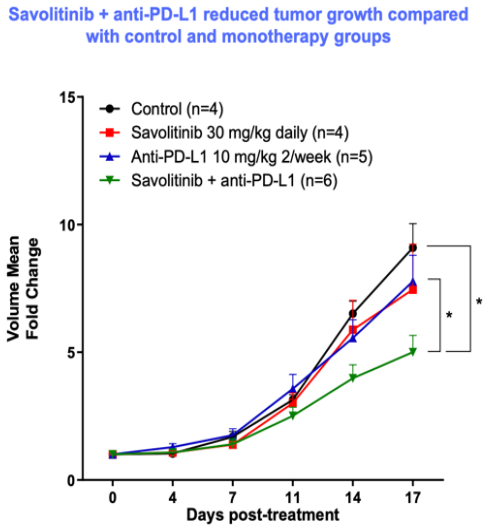


Figure 1. KP1 tumor growth in mice treated as indicated. Treatments were started at day 3 post-cell inoculation. Tumors were measured every 3-4 days. P-value: * (p<0.05).

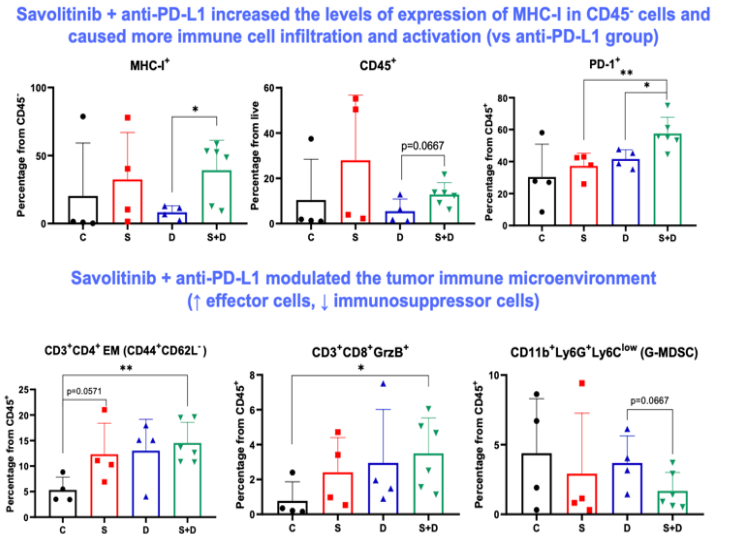


Figure 2. Flow cytometry analysis of CD45- and different immune cell subsets within KP1 tumors depending on the treatment. P-values: * (p<0.05); ** (p<0.01). C. control, S: savolitinib, D: anti-PD-L1. MHC-I: Major Histocompatibility Complex class I, EM: Effector Memory, GrzB: Granzyme B, G-MDSC: Granulocytic-Myeloid-Derived Suppressor Cells.

2) Results from patient samples analysis.

Evaluation of SCLC subtypes and EMT features using immunohistochemistry.

We performed IHC for ASCL1, NEUROD1, POU2F3, E-cadherin and Vimentin in 42 SCLC samples. IHC evaluation was performed using H-score. Cases expressing more than one marker were classified based on the predominant marker with the higher H-score.

Forty-four cases were evaluated, 21 classified as ASCL1 (47.7%), 10 as NEUROD1 (22.7%), 4 as POU2F3 (9.1%), and 9 as non-A/N/P (20.5%). Of note, consecutive staining of ASCL1, NEUROD1 and POU2F3 revealed that concomitant expression of these markers was observed in the same tumor in non-overlapping areas **Table 1** and **Figure 3**.

Characteristics	ASCL1 (n=21)	NEUROD1 (n=10)	POU2F3 (n=4)	No-A/N/P (n=9)
Age median (range)	64 (52-84)	64.5 (51-78)	65.5 (59-83)	64 (52-85)
Sex				
Male	14 (66.7%)	5 (50%)	3 (75%)	5 (55.6%)
Female	7 (33.3%)	5 (50%)	1 (25%)	4 (44.4%)
ECOG				
0	7 (33.3%)	2 (20%)	0 (0%)	2 (22.2%)
1	14 (66.7%)	8 (80%)	4 (100%)	4 (44.4%)
2	0 (0%)	0 (0%)	0 (0%)	3 (33.3%)
Smoking status				
Former	9 (42.9%)	6 (60%)	2 (50%)	4 (44.4%)
Current	12 (57.1%)	4 (40%)	1 (25%)	5 (55.6%)
NA	0 (0%)	0 (0%)	1 (25%)	
TNM Stage 8Ed				
IVa	9 (42.9%)	5 (50%)	0 (0%)	3 (33.3%)
IVb	11 (52.9%)	5 (50%)	4 (100%)	6 (66.7%)
NA	1 (4.8%)	0 (0%)	0 (0%)	0 (0%)
Liver M1				
Yes	5 (23.8%)	3 (30%)	4 (100%)	2 (22.2%)
No	16 (76.2%)	7 (70%)	0 (0%)	7 (77.8%)
Brain M1				
Yes	1 (4.8%)	2 (20%)	0 (0%)	0 (0%)
No	20 (95.2%)	8 (80%)	4 (100%)	9 (100%)
LDH median (range)	288 (144-697)	256 (152-1584)	580 (498-1102)	352,5 (213-501)
Treatment outcomes				
Partial Response	11 (52.4%)	8 (80%)	1 (25%)	6 (66.7%)
Stable Disease	5 (23.8)	1 (10%)	1 (25%)	1 (11.1%)
Progressive Disease	0 (0%)	0 (0%)	0 (0%)	1 (11.1%)
Not available	5 (23.8%)	1 (10%)	2 (50%)	1 (11.1%)
Survival				
Death	13 (61.9%)	7 (70%)	3 (75%)	3 (33.3%)
Alive	8 (38.1%)	3 (30%)	1 (25%)	6 (66.7%)

Table 1. Clinicopathological characteristics and treatment outcomes from the patients included in the CANTABRICO study by IHC subtype.

The 55.6% of tumors expressed E-cadherin and 26.1% vimentin. ASCL1 expression in tumor cells was positively correlated with tumoral E-cadherin expression (rho=0.47, p=0.0022). No correlation between subtypes and vimentin expression was observed **Figure 4A**.

Baseline lactate dehydrogenase (LDH) was higher in the POU2F3 positive tumors (median= 580 range (498-1102)) compared with the other subtypes (p=0.031) **Figure 4B**.
With a median follow-up of 12.4 months, median OS in all patients was 8.95 months. No survival differences were observed between SCLC subtypes. Of note, 6 out of 9 patients with No-A/N/P tumors are still alive **Figure 4C**.

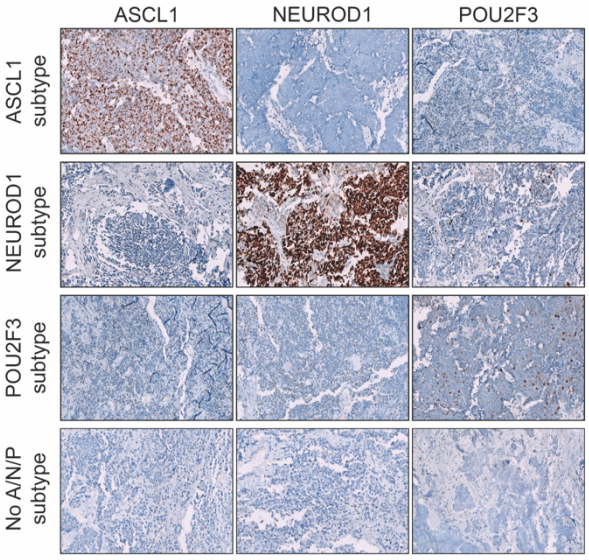


Figure 3. Immunohistochemistry evaluation of ASCL1, NEUROD1 and POU2F3

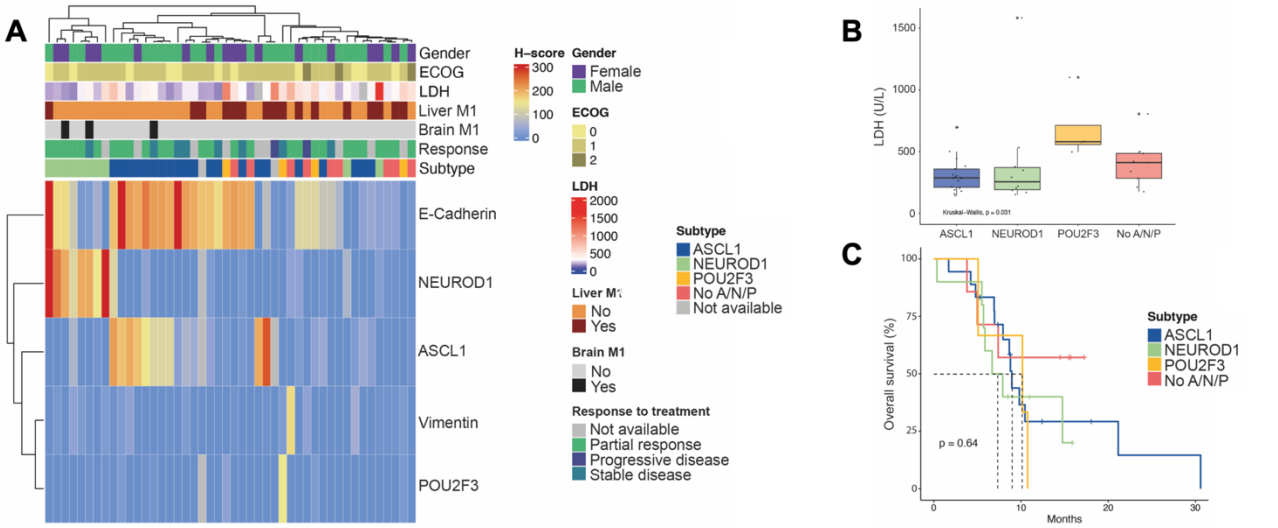
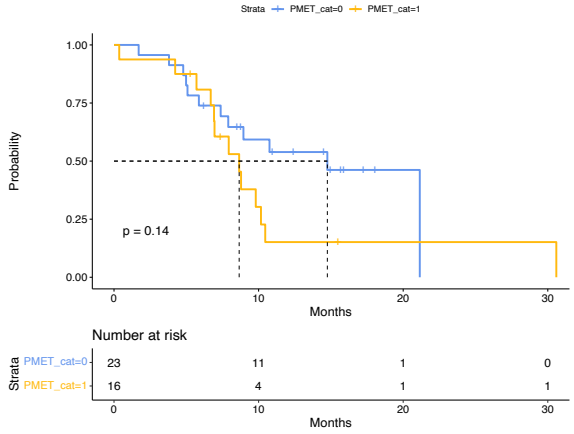


Figure 4. Clinicopathological and IHC features. **A)** Heatmap including protein expression for all IHC markers. **B)** Boxplot for LDH levels across IHC subtypes. **C)** Kaplan-Meier curves on a subtype-by-subtype basis for overall survival.

MET pathway in ES-SCLC patients treated with chemoimmunotherapy.

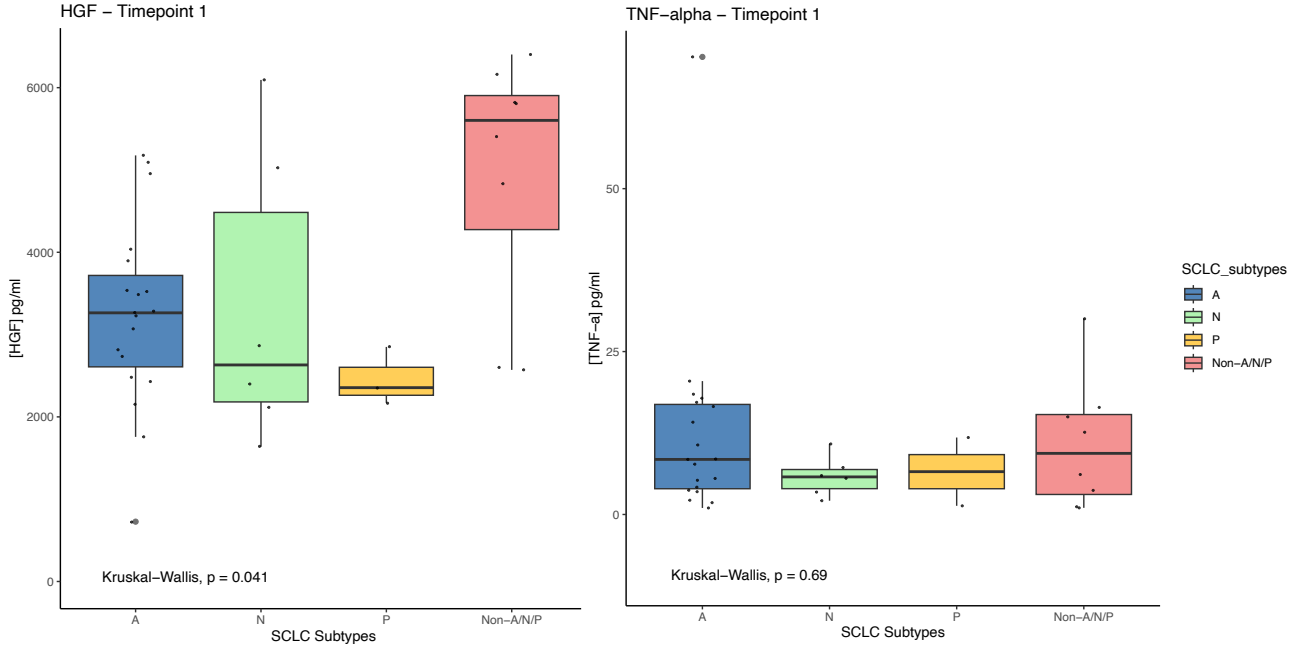
pMET expression by IHC was detected in 41% of patients (16 out of 39). A trend to worse overall survival was observed in patients whom tumors express any positivity for pMET **Figure 5.**



Cytokines analysis in patient serum samples.

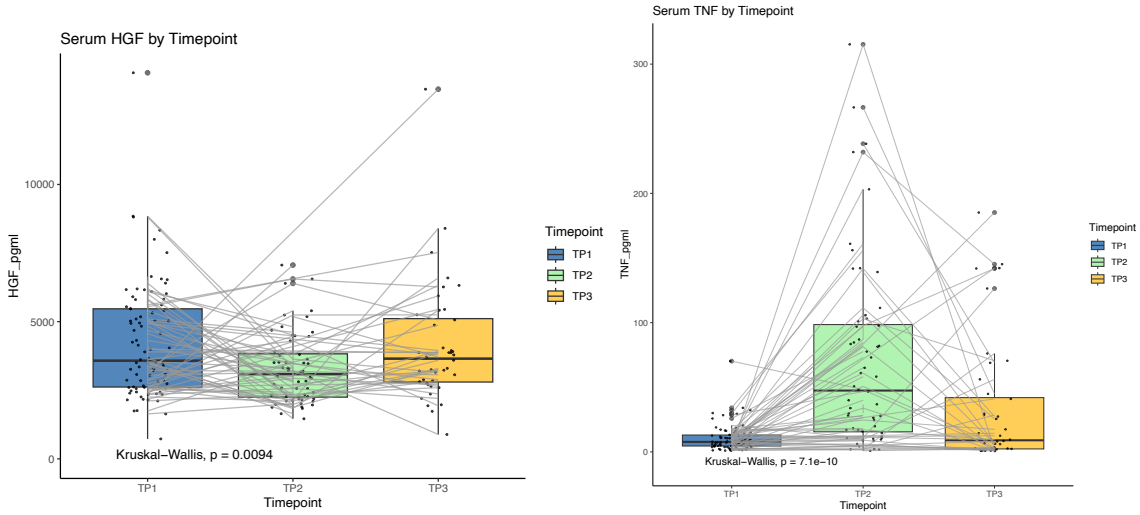
We analyzed longitudinal serum samples from patients enrolled in the CANTABRICO clinical trial. We assessed HGF and TNF-alpha levels using ELISA. Notably, HGF levels were found to be significantly elevated within the non-A/N/P subtype (p=0.041). However, no discernible differences in TNF-alpha levels were observed among the various SCLC subtypes, as depicted in **Figure 6**.

Figure 6.



Furthermore, when examining the longitudinal trends of HGF and TNF-alpha in serum samples from CANTABRICO trial participants, we noted a contrasting pattern. Specifically, HGF levels exhibited a decrease at the second timepoint, just prior to the initiation of the maintenance phase with anti-PD-L1 alone, followed by an increase at the time of progression (timepoint 3). Conversely, TNF-alpha levels showed an increase at timepoint 2, followed by a subsequent decrease when patients reached the progression stage (timepoint 3), as illustrated in Figure 6. the time of progression (timepoint 3) **Figure 7**.

Figure 7.



Project 2: Pre-existing tumor host immunity characterization in resected non-small cell lung cancer.
This work was published early this year at Lung Cancer Journal.

Lung Cancer 181 (2023) 107257

Contents lists available at ScienceDirect

Lung Cancer

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Pre-existing tumor host immunity characterization in resected non-small cell lung cancer

Pedro Rocha [a,b,1], Maite Rodrigo [c,1], Laura Moliner [a,g], Silvia Menendez [b], Laura Masfarré [a], Nil Navarro [a], Raúl Del Rey-Vergara [b], Miguel Galindo-Campos [b], Álvaro Taus [a,b], Mario Giner [c], Ignacio Sanchez [c], Alberto Rodríguez-Fuster [b,d,e], Rafael Aguiló [d], Roberto Chalela [b,f], Albert Sánchez-Font [b,e,f], Josep Belda [d], Victor Curull [b,d,e], Lara Pijuan [c], David Casadevall [a,b], Sergi Clavé [c], Beatriz Bellosillo [c], Júlia Perera-Bel [f], Laura Comerma [c], Edurne Arriola [a,b,*]

Abstract

Introduction: Neoadjuvant and adjuvant immune checkpoint blockade (ICB) have recently become standard of care in resectable non-small cell lung cancer (NSCLC). Yet, biomarkers that inform patients who benefit from this approach remain largely unknown. Here, we interrogated the tumor immune microenvironment (TIME) in early-stage NSCLC patients that underwent up-front surgery.

Methods: A total of 185 treatment-naïve patients with early-stage NSCLC, that underwent up-front surgical treatment between 2006 and 2018 at Hospital del Mar were included. 124 lung adenocarcinomas (LUADs), and 61 squamous cell carcinoma (LUSCs) were included in a tissue microarray. Immunohistochemistry for CD3, CD4, CD8, CD68, CD80, CD103, FOXP3, PD-1, PD-L1, PD-L2 and HLA class II were evaluated by digital image analysis (QuPath software). TIME was categorized into four groups using PD-L1 expression in tumor cells (<1 % or ≥1 %) and tumor resident memory (CD103+) immune cells (using the median as cut-off). We explored the association between different TIME dimensions and patient's clinicopathological features and outcomes.

Results: We found increased levels of T cell markers (CD3+, CD4+, CD8+ cells), functional immune markers (FOXP3+ cells) as well as, higher HLA-II tumor membrane expression in LUADs compared to LUSCs ($p < 0.05$ for all). In contrast, LUSCs displayed higher percentage of intratumor macrophages (CD68+ cells) as well as, higher PD-L1 and PD-L2 tumor membrane expression ($p < 0.05$ for all). Unsupervised analysis revealed three different tumor subsets characterized by membrane tumor expression of PD-L1, PD-L2 and HLA-class II. Enrichment of T cells (CD3+, CD8+ cells), regulatory T cells (FOXP3+ cells) and macrophages (CD68+ cells) was observed in the CD103+/PD-L1+ group ($p < 0.05$ for all). Multivariate analysis showed that infiltration by CD103+ immune cells was associated with improved OS ($p = 0.009$).

Conclusions: TIME analysis in resected NSCLC highlighted differences by histology, PD-L1 expression and molecular subgroups. Biomarker studies using IHC might aid to individually tailor adjuvant treatment in early-stage NSCLC.

Project 3: Unveiling distinct features of long-term benefit in metastatic NSCLC patients undergoing immune checkpoint blockade. *Manuscript under preparation where I will be first author.*

Abstract:

Introduction: Immunotherapy is firmly established as a treatment regimen in various solid tumors, driven by its exceptional benefits observed in a select group of patients. Despite widespread use of immune checkpoint blockade (ICB) across diverse solid tumors, the quest for a clinically informative biomarker for long-term benefit remains unmet.

Methods: A total of 49 metastatic NSCLC patients treated with ICB were included. Long-term (LTR) and Short-term responders (STR) were defined as those with a response to ICB lasting more than 24 months or less than 6 months, respectively. Longitudinal blood specimens were collected before treatment initiation and early-on treatment (before cycle 2 – at 3rd week). Plasma ctDNA NGS panel and serum proteomics were performed. Standard diagnostic workup included

PD-L1 immunohistochemistry and NGS in tumor tissue. Tumor tissue RNAseq panel focused on immune related genes was performed in a subset of patients.

Results: Our analysis revealed specific characteristics of long-term patients compared with short term benefit, namely higher PD-L1 in tumor cells (p=0.005) and higher incidence of irAEs (p=0.001). Genomic features that associated with lack of benefit to ICB included co-occurrence of mutations in KRAS/STK11, KRAS/KEAP1 and TP53/KMT2D (p<0.05). At a serum proteomic level, LTR patients exhibited higher abundance of proteins related with apoptosis (CASP8, PRKRA), chemotaxis, immune proteosome, processing of MHC class I (S100A4, PSMD9, RNF41) and immunehomeostasis (HAVCR1, ARG1) (p<0.05 for all proteins) **Figure 8**. In line with peripheral immunological features, transcriptional analysis of tumor samples showed that LTR patients displayed higher levels of genes linked with T cell recruitment/trafficking (CXCL11) and T cell effector functions (GMZB) within the tumor microenvironment (p<0.05). Finally, a longitudinal analysis identified a set of proteins that presented opposite dynamics in LTR compared to STR, making them interesting candidates for treatment efficacy evaluation.

Conclusions: Our comprehensive analysis of metastatic NSCLC patients treated with ICB has unveiled distinct clinicopathological and immunological features associated with long-term benefit, highlighting the presence of a pre-existing antitumor immunity as a stronger predictor of long-term benefit. These findings offer insights into potential biomarkers and therapeutic strategies for enhancing ICB outcomes in metastatic NSCLC.

Figure 8.

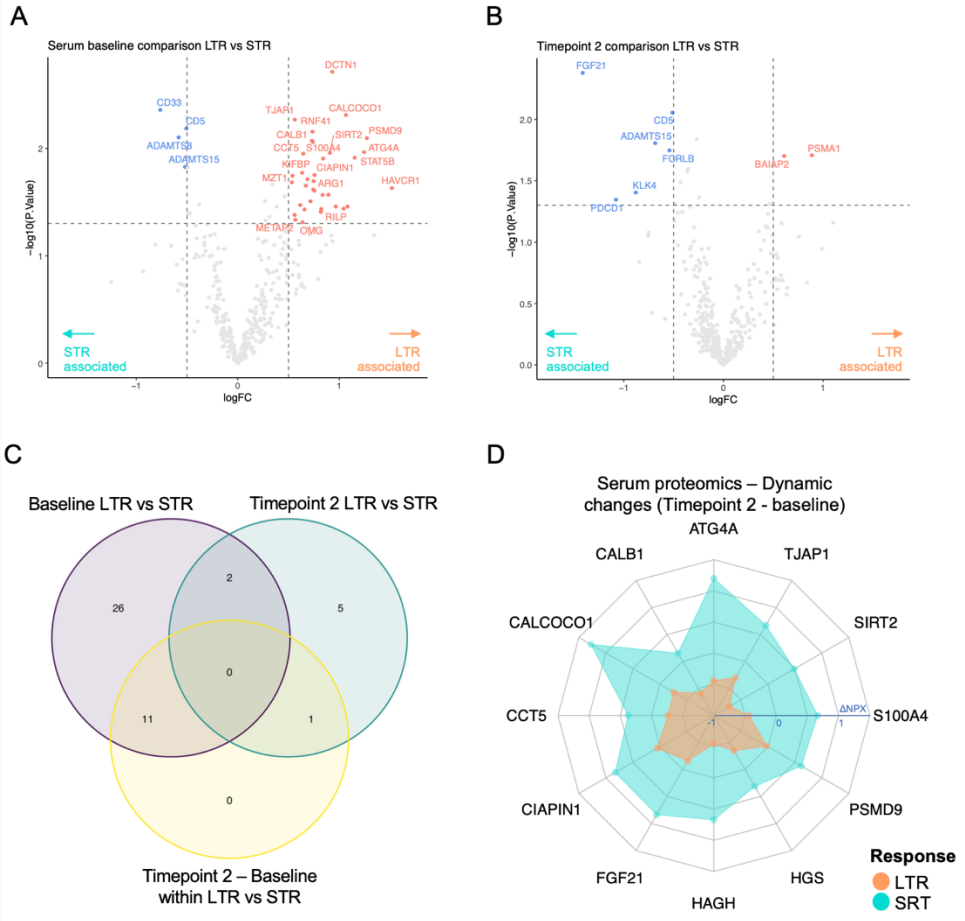

Figure 8. Profiling of baseline and dynamic serum proteomic changes in patients undergoing immune checkpoint blockade. A) Volcano plot showing baseline (pre-treatment) comparison between long-term and short-term responders and **B)** at Timepoint 2 (early on-treatment, before administration of 2nd cycle). **C)** Venn diagram representing the overlap of proteins differently expressed at baseline, timepoint 2 and within timepoint 2 minus baseline. **D**) Radarplot displaying the dynamic changes (mean ΔNPX) induced by ICB among LTR and STR patients. Differentially expressed proteins were selected on the basis of a statistical threshold of nominal p-value < 0.05 and fold change |FC| >1.5 (|log2FC| > 0.585). A positive ΔNPX represents an increase of expression with time, whereas a negative value indicates a decrease.

List of Publications and Presentations Resulting from the Translational Research Project "*Met inhibition in combination with anti-PD-1/PD-L1 as a new therapeutic approach in Small Cell Lung Cancer.***"**

•ELCC 2023: SCLC subtypes are associated with distinct clinicopathological features and outcomes: a biomarker analysis from the CANTABRICO study. **Pedro Rocha**, Ignacio Sanchez, Laura Masfarre, Mario Giner, Nil Navarro, Alejandro Ríos, Alvaro Taus, Sandra Pérez Buira, Érica Torres-Fernandez, Sergi Clavé, Beatriz Bellosillo, Federico Rojo, Luis Paz-Ares, Cristina Martí, Carlos Aguado de la Rosa, Dolores Isla, Rosario García, Luciana Ester Báez, Ángel Callejo, Edurne Arriola.

•EACR 2022: Modulation of tumor immune microenvironment is linked to tumor growth inhibition in response to Met inhibition and PD-L1 blockade in Small Cell Lung Cancer. Authors: R. Del Rey-Vergara, M.A. Galindo-Campos, **Pedro Rocha**, C. Martínez, M. Carpes, S. Menéndez, A. Rossell, Á. Taus, A. Rovira, Edurne Arriola.

List of Publications and Presentations resulting from other projects during the fellowship period (if applicable)

Journal Publications

1. **Pedro Rocha**, Maite Rodrigo, Laura Moliner, Silvia Menendez, Laura Masfarré, Nil Navarro, Raúl Del Rey-Vergara, Miguel Galindo, Álvaro Taus, Mario Giner, Ignacio Sanchez, Alberto Rodríguez-Fuster, Rafael Aguiló, Roberto Chalela, Albert Sánchez-Font, Josep Belda, Victor Curull, Lara Pijuan, David Casadevall, Sergi Clavé, Beatriz Bellosillo, Júlia Perera-Bel, Laura Comerma, Edurne Arriola. Pre-existing tumor host immunity characterization in resected non-small cell lung cancer. Lung Cancer, 2023.

2. Sergi Clavé, Jennifer B Jackson, Marta Salido, Jacob Kames, Kelly MR Gerding, Ellen L Verner, Eric F Kong, Elizabeth Weingartner, Joan Gibert, Max Hardy-Werbin, **Pedro Rocha**, Xènia Riera, Erica Torres, James Hernandez, Gustavo Cerqueira, Donna Nichol, John Simmons, Álvaro Taus, Lara Pijuan, Beatriz Bellosillo, Edurne Arriola*Comprehensive NGS Profiling to Enable Detection of ALK Gene Rearrangements and MET Amplifications in Non-Small Cell Lung Cancer. Frontiers in Oncology, 2023.

3. Alejandro Francisco-Cruz*, **Pedro Rocha***, Alexandre Reuben*, Santhoshi N. Krishnan, Priyam Das, Runzhe Chen, Kelly Quek, Jun Li, Edwin R. Parra, Luisa M. Solis, Souptik Barua, Mei Jiang, Rossana Lazcano, Chi-Wan Chow, Carmen Behrens, Curtis Gumb, Latasha Little, Junya Fukuoka, Neda Kalhor, Annikka Weissferdt, Humam Kadara, John Heymach, Stephen Swisher, Boris Sepesi, Arvind Rao, Cesar Moran, Jianhua Zhang, J. Jack Lee, Junya Fujimoto, Andrew Futreal, Ignacio I. Wistuba, Christine B. Peterson, Jianjun Zhang. Analysis of immune intratumor heterogeneity highlights immunoregulatory and coinhibitory lymphocytes as hallmarks of recurrence in stage I NSCLC. Modern Pathology, 2023. *Co-first author.

3. **Pedro Rocha**, Jiexin Zhang, Raquel Laza-Briviesca, Alberto Cruz-Bermúdez, Katsuhiro Yoshimura, Carmen Behrens, Apar Pataer, Edwin R Parra, Cara Haymaker, Junya Fujimoto, Stephen G Swisher, John V Heymach, Don L Gibbons, J. Jack Lee, Boris Sepesi, Tina Cascone, Luisa M Solis, Mariano Provencio, Ignacio I Wistuba, Humam Kadara. Distinct immune gene programs associated with host tumor immunity, neoadjuvant chemotherapy and chemoimmunotherapy in resectable NSCLC. Clinical Cancer Research, 2022.

4. Bingnan Zhang, C. Allison Stewart, Qi Wang, Robert J. Cardnell, **Pedro Rocha**, Junya Fujimoto, Luisa M. Solis Soto, Runsheng Wang, Veronica Novegil, Peter Ansell, Lei He, Luisa Fernandez, Adam Jendrisak, Cole Gilbertson, Joseph D. Schonhoft, Jiyun Byun, Joshua Jones, Amanda K. L. Anderson, Ana Aparicio, Hai Tran, Marcelo V. Negrao, Jianjun Zhang, Wei-lien Wang, Ignacio I. Wistuba, Jing Wang, Rick Wenstrup, Lauren A. Byers, Carl M. Gay. Dynamic expression of Schlafen 11 (SLFN11) in circulating tumour cells as a liquid biomarker in small cell lung cancer. British Journal of Cancer 2022.

Conference Abstracts

•ELCC 2023: Differences in response to immunotherapy between KRAS G12C and KRAS non-G12C mutated NSCLC. L. Masfarré, **Pedro Rocha**, S. Clavé, N. Navarro-Gorro, I. Sánchez, M. Giner, A. Corbera, A. Taus, A. Parreira, B. Bellosillo, E. Arriola.

•ELCC 2022: Preexisting tumor host immunity delineates clinical outcomes in resectable Non-Small Cell Lung Cancer. Authors: **Pedro Rocha**, Maite Rodrigo, Laura Moliner, Alejandro Ríos, Laura Masfarré, Nil Navarro, Silvia Menendez, Álvaro Taus, Alberto Rodríguez, Rafael Aguiló, Josep Belda, Raúl Del Rey-Vergara, Miguel Galindo, Laura Comerma, Edurne Arriola.

•ELCC 2022: KRAS G12C lung adenocarcinoma represents a distinct group of patients with different response to immunotherapy. Authors: L. Masfarré, **Pedro Rocha**, S. Clavé, L. Moliner, N. Navarro-Gorro, A. Ríos-Hoyo, I. Sánchez, M. Giner, A. Corbera, A. Taus, B. Bellosillo, Edurne Arriola.

•ESMO 2022: Identifying peripheral immune predictors of durable clinical response to PD-L1 blockade in small cell lung cancer. Galindo-Campos MA, Hardy-Werbin M, Ríos-Hoyo A, Gibert J, Rossell A, González S, **Pedro Rocha**, Del Rey-Vergara R, Masfarré L, Navarro N, Taus A, Rovira A, Arriola E.

Selection of Courses and Workshops Attended During the Fellowship

•Master's degree in Omics data analysis by the University of Vic.
•Expert Degree in Immuno-Oncology by the University of Navarra.
•World Conference on Lung Cancer 2022, Vienna.
•ESMO 2022, Paris.
•SEOM 2022, Madrid.
•ELCC 2023 Copenhagen.
• World Conference on Lung Cancer 2023, Singapore.
• IASLC Academy 2023.

Acknowledgements

The accomplishment of this work has been made achievable through the support of ESMO, SEOM, and AECC.
Dr. Arriola and her entire team at the Hospital del Mar Research Institute played an essential role in the success of my ESMO research fellowship by offering invaluable guidance, mentoring, and expertise.

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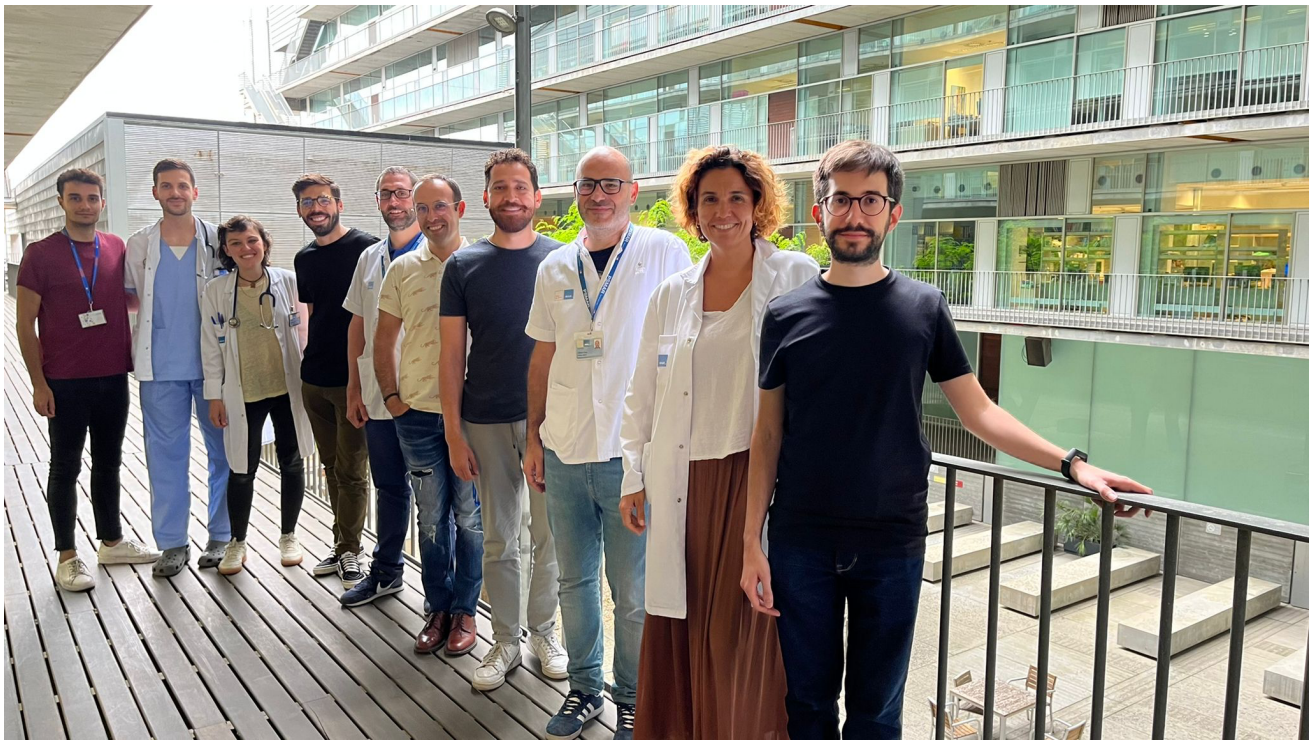
SIGNATURES	
Award Recipient full name	***Signature and Date***
Pedro Filipe Simões da Rocha	2nd October 2023

Research Mentor full name	***Signature and Date***
Edurne Arriola Aperribay	2nd October 2023



This ESMO Translational Fellowship Research Project was supported by an educational grant from ESMO.