Lung cancer continues to be the most frequent cause of cancer-related deaths worldwide. Our Unit focuses on the study of lung cancer, from fundamental research proposals to other more clinically oriented, always aiming to solve the problems of lung cancer patients. We are particularly interested in two research areas: the identification of new molecular biomarkers for diagnostic, prognostic, and predictive purposes; and the development of novel treatment strategies, including targeted therapies and immunotherapeutics. For example, we have contributed to elucidating the molecular determinants of EGFR or FGFR oncogenicity and have discovered biomarkers that may guide the efficacy of inhibitors of those receptors in lung cancer. We have continued to develop an extensive platform of patient-derived xenografts (PDXs) and organoids (PDOs) of non-small-cell and small cell lung cancers to test new therapeutic strategies. Finally, our Unit has extensive experience in taking new drugs to the clinic, as well as in conducting practice-changing phase II/III trials in the fields of personalised cancer care and immuno-oncology.

“Our Unit significantly contributed to the development of novel biomarkers that have impacted the currently available selection of targeted therapies (e.g., EGFR mutation in the clinic) and novel immunotherapeutics (e.g., tumour mutational burden). We have led randomised clinical trials with novel immunotherapies and other agents as monotherapies or in combination (e.g., chemotherapy plus durvalumab in SCLC or chemotherapy plus nivolumab and ipilimumab in NSCLC) in lung cancer that have impacted clinical practice worldwide.”

**RESEARCH HIGHLIGHTS**

**Biomarker discovery and implementation**

We own an extensive patient-derived xenograft (PDX) platform of 50 non-small cell lung cancer (NSCLC) models that are comprehensively characterised at the histological, genomic, transcriptomic and proteomic levels, and that have contributed to the discovery of relevant findings. For example, using an EGFR NSCLC PDX-bearing huPBMC-driven humanized NSG mouse model, we have demonstrated the nontoxic broad antitumour activity of a humanized EGFR-targeted 4-1BB-agonistic trimerbody (4-1BBN/CEGFR) against EGFR+ tumours (Compte M, et al., Clin Cancer Res 2021). Our platform has been expanding in number and histology types (including small cell lung cancer [SCLC] and mesothelioma), as well as cell source (tumours but also SCLC circulating tumour cells), and it includes PDXs and patient-derived organoids. We have also successfully developed a number of huPDX models.

We have evaluated the tumour mutational burden (TMB) and PD-L1 expression obtained with 2 marketed next-generation sequencing panels, TruSight Oncology 500 (TSO500) and Oncomine Tumor Mutation Load (OTML) versus a reference assay (Foundation One, FO) in 96 NSCLC samples. Additionally, we have performed an inter-laboratory reproducibility study and determined adjusted cut-off values. We found that both panels exhibited robust analytical performances for TMB assessment, with stronger concordances in patients with negative PD-L1 expression. TSO500 showed higher inter-laboratory reproducibility study and determined adjusted cut-off values.

We have defined novel subgroups of large cell carcinoma (LCC) based on genomic and immune characterisation of 18 early-stage LCC cases and identified a set of biomarkers that...
the testing of new molecules and combinations in solid
Our Group has significantly expanded its activities regarding
treatment strategies (manuscript in preparation).
we have comprehensively characterised the immune and
JCM could potentially predict response to immunotherapy (Ramos-
treatment burden.
fusion-positive NSCL and NTRK fusion-positive solid
from a global phase II basket study of entrectinib for ROS1
phase I clinical trials demonstrated that both combinations,
et al. (2021). Phase 1
Spainish National Cancer Research Centre, CNIO
(2021). Clinical impact of presurgery cir-
in humanized murine cancer mod-
and targeted therapies (Yu HA, Paez-Ares LG et al., Clin Cancer Res 2021). These
we also reported patient outcomes from
in advanced T790M-positive EGFR-mu-
targeting chemotherapy-related variables in advanced NSCLC (CheckMate 801, 2021). Patient-reported outcomes from STARTRK-2: a global
molecular and genomic landscape of a cohort 120 resected
tumor BRCA2 after frontline treatment with first-line durvalumab plus
cellular lung cancer (Check-Mate 816) (2021). International, randomised,
clinical trial showing
the phase III clinical trials demonstrated that both combinations have encouraging safety and antitumour activity in advanced, treatment-naive NSCLC or T790M-positive EGFR-mutant
and targeted therapies; in 2021, we participated in more than 129 projects in this research area, including new
treatment-naive patients with extensive-stage small-cell lung cancer (ES-SCLC).
early clinical trials
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in solid tumours, particularly in the field of immune-based approaches
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