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 ones that are closer to solving the problems of lung cancer patients. The two main research areas of our Unit involve: the identification of new molecular biomarkers that can be used in the clinic for diagnostic, prognostic and predictive purposes; and the development of novel treatment strategies that include 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. On the other hand, we have developed a patient-derived xenograft (PDX) platform of non-small-cell lung cancers to test new therapeutic strategies. Finally, our Unit has extensive experience in taking new drugs to the clinic (phase I trials), as well as in conducting practice-changing phase II/III trials in the fields of precision oncology and immuno-oncology.

“Our Unit has 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 agents (e.g. erlotinib, afatinib, Nivolumab, M7824) as well as combinations of checkpoint inhibitors (e.g. Ipilimumab plus Nivolumab, chemotherapy plus Pembrolizumab, Durvalumab following chemoradiation) in lung cancer that have impacted clinical practice worldwide.”
Biomarker discovery and implementation

The Group has deciphered the biological properties of FGFR1 and FGFR4 in non-small cell lung cancer (NSCLC) and has discovered new biomarkers with a predictive role for anti-FGFR therapy in NSCLC. Currently, we are validating the results on a series of well-designed PDx models, generating a diagnostic kit and carrying out the technical validation of the biomarker, as well as planning a phase II trial proposal with an FGFR inhibitor in NSCLC patients with high expression of the novel biomarker.

The Group has also validated an NIS-based algorithm for the determination of genomic aberrations (in tumour tissue but also in cDNA) that may guide therapy for clinical trials. More recently, we have led the first clinical validation of tumour mutational burden as a predictive biomarker for checkpoint inhibitors in lung cancer, and particularly, for Ipilimumab.

Early clinical trials

Our Group has significantly expanded its activities regarding the testing of new molecules and combinations in solid tumours, particularly in the field of immune-based approaches; in 2018, we participated in more than 35 projects in this field. Recently, our Group provided feasibility and encouraging initial data on the anti-tumour activity of M7824, a bifunctional fusion protein targeting PD-L1 and TGF-β beta in pretreated NSCLC (response rate in PD-L1 expressing tumours in more than 50% of the cases). Encouraging tumour-agnostic data of Entrectinib in tumours driven by activated NTRK fusion revealed in 2018, our Group has significantly expanded its activities regarding the testing of new molecules and combinations in solid tumours, particularly in the field of immune-based approaches; in 2018, we participated in more than 35 projects in this field. Recently, our Group provided feasibility and encouraging initial data on the anti-tumour activity of M7824, a bifunctional fusion protein targeting PD-L1 and TGF-β beta in pretreated NSCLC (response rate in PD-L1 expressing tumours in more than 50% of the cases). Encouraging tumour-agnostic data of Entrectinib in tumours driven by activated NTRK fusion.

Changing standards of care treatments in clinical practice

The Lung Cancer Clinical Research Unit has led phase III trials whose results have significantly impacted the clinical practice of stage IV lung cancer with combinations of chemotherapy plus Pembrolizumab or Ipilimumab plus Pembrolizumab (Hellmann MD et al., NEJM 2018; Paz-Ares L et al., NEJM 2018). In addition, the Group has actively contributed to the successful phase III trial showing a significant improvement in survival for stage III NSCLC patients treated with the anti-PD-1 agent Durvalumab following chemoradiation (Antonia S et al. NEJM 2018).

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1. Publications


2. Awards and recognition


3. Selected publications at other institutions


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SPANDHAT HOSPITAL, CANCER RESEARCH CENTRE DUDE

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