



Sixth International
Joint Meeting on
**THORACIC
SURGERY**
Barcelona - 20th, 21st and 22nd November 2024
Auditorio Foment del Treball Nacional, Barcelona (Spain)

11th International Meeting on General Thoracic Surgery



10th International Workshop on Surgical Exploration of the Mediastinum and Systematic Nodal Dissection



5th Meeting of the Thoracic Oncology, Thoracic Surgery, Techniques & Transplant, Respiratory Nursing and Respiratory Physiotherapy Areas of the Spanish Society of Pneumology and Thoracic Surgery (SEPAR)



3rd Joint Meeting of the Spanish Society of Thoracic Surgery (SECT)



30th Congress of the "Asociación Iberoamericana de Cirugía Torácica" AIACT



10th International Workshop on Surgical Exploration of the Mediastinum and Systematic Nodal Dissection



CRITICAL APPRAISAL: THE VIEW OF THE ONCOLOGIST

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Novel systemic therapeutics have revolutionized the management of stage 4 non-small cell lung cancer (NSCLC). Genotyping and PD-L1 typing of such tumours at diagnosis is now routine and with comprehensive molecular profiling stage 4 NSCLC has been transformed from a progressive lethal malignancy with a median overall survival of less than one year and a 5-year survival rate of 1% to one where the 5-year survival rate is 30% in patients who completed two years of treatment with immune checkpoint inhibitor (CPI) therapy, with some metastatic patients living cancer-free, off therapy, for many years. The adoption of these therapeutics to patients with operable and localized disease has transformed the surgical landscape. The traditional paradigm of induction chemotherapy to downstage N2 with a view of surgery or radical radiation has been supplanted by neoadjuvant combination chemoimmunotherapy. This combination has been proven to significantly improve overall survival (OS) and event-free survival (EFS) in patients with operable N2 disease at presentation and offers the greatest probability of pathological complete response or major pathological response prior to surgery, one of the strongest predictors of survival. 5-year follow-up data from the first phase 2 trial of neoadjuvant chemoimmunotherapy in N2+ stage IIIA NSCLC with resection regardless of post induction N2 status (NADIM) demonstrates unprecedented 65% progression-free survival (PFS) and 69% OS rates at 5 years. This trial data demonstrating a major improvement in pathological downstaging, has been subsequently supported by 6 large randomized phase 3 trials of neoadjuvant chemoimmunotherapy all demonstrating complete pathological response rates of around 25-35% post neoadjuvant, with rates proportionate to PD-L1 status, alongside large and significant event-free survival rates, again proportionate to PD-L1 status. All neoadjuvant chemo-CPI-based trials have demonstrated a marked dissociation between radiological response and pathological response, limiting interpretation of radiological downstaging, resulting in the new paradigm of resectability and operability occurring upfront prior to neoadjuvant commencement. Nevertheless, in each trial around 20% of trial patients did not undergo planned surgery and their outcomes (when captured) were poor, suggesting that an alternative approach of chemoradiotherapy and consolidation immunotherapy may have been preferential for them if identified upfront. Hence, defining operability and resectability in a multidisciplinary manner pre-systemic therapy remain critical to optimal patient and surgical outcomes.