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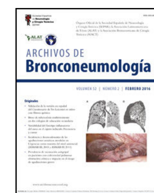

Letter to the Director

## NADIM II Study: What is the Ideal Time for Surgery in Stage IIIA Lung Cancer?

*To the Director,*

The optimal treatment of locally advanced stage IIIA (N2) non-small cell lung cancer (NSCLC) remains an enigma. NSCLC accounts for 80–85% of all cases, and approximately 20% of patients are diagnosed in this stage.[1] Their survival prospects have changed thanks to the recent NADIM II study[2] published by the Spanish Lung Cancer Group (GECP).

NADIM II is an open-label, randomized, 2-arm, phase II, multicenter trial. Inclusion criteria were resectable clinical stage IIIA patients with no known EGFR/ALK alterations. Those randomized to the experimental arm received neoadjuvant therapy with nivolumab, paclitaxel, and carboplatin for 3 cycles every 21 days followed by surgery.

The results of this study have generated great interest among the scientific community, because it confirms the superiority of the chemoimmunotherapy combination in patients with stage IIIA NSCLC and the feasibility of surgery. However, several doubts persist surrounding the surgical procedure.

In the NADIM II study, surgery was performed 42–49 days after the first day of the third neoadjuvant chemoimmunotherapy treatment cycle.

This is where the controversy emerges. Firstly, this approach was designed by a multidisciplinary clinical team that decided on tumour resectability without providing evidence to justify the most appropriate timing of the surgical procedure.[3] The study reports only what was done, but does not discuss the optimal time between the end of treatment and the date of surgery. This period is crucial, since tissue changes can determine technical intraoperative difficulties.

Secondly, the changes that follow chemoimmunotherapy, such as tissue adhesions and fibrosis, increase the risk of postoperative complications, including fistulas, anastomotic dehiscence, and persistent air leak.[4]

Finally, future studies should record the main intraoperative findings, including bleeding, adhesions, and tissue fibrosis after the addition of neoadjuvant immunotherapy with nivolumab.

In conclusion, the results of the NADIM II study mark a change in our attitude to the treatment of resectable stage IIIA NSCLC, but surgical issues still need to be analyzed in depth.

We are still unsure of the ideal time to perform surgery to avoid encountering the many tissue changes that can increase the risk of intra- and post-operative complications.

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