

23th June, 2021

Prof. Hiten R.H. Patel , MD, PhD
Editor-in-Chief
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Dear Prof. Hiten R.H. Patel and reviewers of the manuscript,

First of all, we want to thank you for your kind comments about our **topic highlight** review about the neoadjuvant immunotherapy in NSCLC and for the acceptance to be published in **World Journal of Clinical Oncology**.

Please find enclosed our last version of the manuscript entitled “**Neoadjuvant treatment in non-small cell lung cancer (NSCLC): new perspectives with the incorporation of immunotherapy**” which we submit for consideration as an **invited topic highlight** article for the **Topic Highlights monographic**. This is an invited manuscript to the journal editor **Felipe Couñago** (ID 03428837)

The aim of neoadjuvant treatment in non-small cell lung cancer (NSCLC) is to eliminate micrometastatic disease to facilitate surgical resection. Neoadjuvant chemotherapy (ChT) in localised NSCLC has numerous advantages over other therapeutic modalities and is considered standard treatment in resectable disease. Treatment with immune checkpoint inhibitors (ICI) improves long-term survival in advanced disease and has a better toxicity profile than conventional therapies. These immunotherapy agents (anti-PD1/PD-L1), administered with or without ChT, are currently being evaluated in the preoperative setting, with initial results showing better pathological response rates and more long-term benefits. Importantly, these drugs do not appear to increase the rate of severe adverse effects and/or postoperative complications. However, several questions still need to be resolved, including the identification of predictive biomarkers; comparative studies of immunotherapy alone versus combined treatment with ChT and/or radiotherapy; the optimal duration of treatment; the timing of surgery; the need for adjuvant treatment; appropriate radiologic evaluation and mediastinal staging; and the correlation between pathological response and survival outcomes. Here we review the current evidence for immunotherapy from a multidisciplinary perspective and discuss current and future controversies.

We have disclosed our conflicts of interests in the COI form. We confirm that this work is original and has not been published previously, nor is it currently under consideration for publication elsewhere. We confirm that the manuscript has been read and approved for submission by all the named authors.

Yours sincerely,

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