Perioperative Immunotherapy for Resectable NSCLC: A Comparative Review Protocol

Written by The Life Science Feed Editorial Team · Published 27 August 2026 · Edited by Mara Voss

The landscape of non-small cell lung cancer (NSCLC) treatment is rapidly evolving, particularly with the integration of immunotherapy into perioperative care for resectable disease. Clinicians face a growing number of options regarding specific agents and the optimal timing of their administration—neoadjuvant, adjuvant, or both. This new Cochrane review protocol aims to synthesize existing evidence to provide clarity on the comparative effectiveness and safety of these diverse strategies.

KEY TAKEAWAYS

- The Pivot: This protocol outlines a network meta-analysis to directly and indirectly compare various perioperative immunotherapy strategies for resectable NSCLC.
- The Data: The primary objective is to generate a clinically meaningful hierarchy of these strategies based on overall survival.
- The Action: The forthcoming review will provide evidence-based guidance on optimal immunotherapy approaches for operable NSCLC, considering both efficacy and safety.

Context for Perioperative Immunotherapy in NSCLC

Non-small cell lung cancer (NSCLC) remains a significant global health challenge. For patients with resectable disease, surgery is a cornerstone of treatment, often followed by adjuvant chemotherapy. However, the introduction of immunotherapy, particularly checkpoint blockade, has shown promise in improving outcomes. Immunotherapy can be administered before surgery (neoadjuvant), after surgery (adjuvant), or in a combination perioperative approach. The optimal timing and specific agents within these strategies are subjects of ongoing research and clinical debate 1.

Study Design: A Cochrane Review Protocol

This document describes a protocol for a Cochrane Review, specifically an intervention review utilizing a network meta-analysis (NMA) approach. The primary objective is to compare the effectiveness and safety of different immunotherapy agents administered in a perioperative setting to individuals with resectable NSCLC. A key aspect of this protocol is the intention to perform indirect comparisons to establish a clinically meaningful hierarchy of perioperative immunotherapy strategies, primarily focusing on overall survival in operable patients with resectable NSCLC 1.

Methods for Evidence Synthesis

The planned review will systematically search for relevant randomized controlled trials (RCTs) comparing different perioperative immunotherapy strategies. The NMA methodology allows for simultaneous comparison of multiple interventions, even those not directly compared in head-to-head trials, by leveraging common comparators. This

approach is particularly valuable when a range of treatment options exists, as it can help to rank interventions based on their relative efficacy and safety 1. The authors intend to evaluate various outcomes, with overall survival being the primary endpoint for establishing a treatment hierarchy. Secondary outcomes will likely include progression-free survival, event-free survival, pathological complete response rates, and adverse events, although the protocol specifically highlights overall survival for the hierarchy generation 1.

Expected Findings and Clinical Relevance

While this is a protocol and no findings are yet available, the completed review is expected to provide a comprehensive synthesis of the current evidence on perioperative immunotherapy for resectable NSCLC. By comparing different agents and administration timings through NMA, the review aims to identify which strategies offer the most significant benefits in terms of overall survival and other critical outcomes, while also considering safety profiles. This will be crucial for guiding clinical decision-making and potentially informing future treatment guidelines 1.

Clinical Implications for Practice Today

This forthcoming Cochrane Review holds substantial implications for healthcare professionals managing patients with resectable NSCLC. Currently, clinicians navigate a complex landscape of emerging data from individual trials, making it challenging to determine the optimal perioperative immunotherapy strategy. The planned network meta-analysis will provide a robust, evidence-based framework for comparing these diverse approaches, offering a clearer understanding of their relative benefits and risks. This will be invaluable for shared decision-making with patients, allowing for more informed discussions about treatment options that extend beyond traditional surgery and chemotherapy. The hierarchy of strategies, once established, could help prioritize specific regimens in clinical practice, potentially improving patient outcomes by guiding the selection of the most effective and safest perioperative immunotherapy.

Limitations and Future Directions

As a protocol, the limitations of the actual review are yet to be determined. However, inherent limitations of network meta-analyses include the potential for heterogeneity across included studies, differences in patient populations, and variations in study designs, which can impact the reliability of indirect comparisons. The quality of the evidence will depend on the rigor of the primary studies identified. Future research will likely focus on identifying biomarkers to personalize immunotherapy approaches, further refining patient selection for specific perioperative regimens, and exploring longer-term outcomes and cost-effectiveness of these strategies 1.

REFERENCES

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