

is not mentioned. In our opinion, potential confounding factors (such as age, sex, pathologic type, prior treatments, etc.) should be incorporated into the model to better assess the independence of the treatment effect of pembrolizumab.

Finally, the survival analysis did not account for competing events, such as non-treatment-related deaths. A competing risks model, such as the Fine-Gray model,³ could be used to address these events, particularly those with high incidence, such as traffic accidents, to provide a more accurate estimation of pembrolizumab's mortality risk.

Since October 16, 2023, when the Food and Drug Administration approved pembrolizumab in combination with platinum-based chemotherapy as a neoadjuvant treatment for resectable NSCLC, to its continued recommendation as a first-line treatment for metastatic NSCLC in the 2024 National Comprehensive Cancer Network Guidelines (version 7.0),⁴ pembrolizumab's role in treating NSCLC has evolved significantly, offering expanded therapeutic options for patients at various stages of the disease.

As medical workers, we should focus on the evidence-based application of pembrolizumab, emphasizing long-term follow-up and multidisciplinary collaboration to enhance treatment outcomes and improve patients' quality of life.

CRediT Authorship Contribution Statement

Feng Wang: Conceptualization, Formal analysis.

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Pembrolizumab, Chemotherapy, and Metastatic NSCLC



To the Editor:

Gadgeel et al.¹ investigated the effect of utilizing pembrolizumab along with chemotherapy against metastatic NSCLC. The results provide clinically critical

Disclosure

The authors declare no conflict of interest.

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references for the use of immune checkpoint inhibitors in the management of NSCLC. We would like to raise several issues that we believe could potentially influence the rigorousness of the results for future studies.

First, we believe that indicators for immune checkpoint inhibitor responsiveness, such as the tumor mutational burden (TMB), could be incorporated. Previous studies reported that high levels of TMB could be potentially associated with improved outcomes after immune checkpoint inhibitors.² Applying TMB in the patient selection process could improve the process of patient stratification and provide precise information to identify which patient subgroups would be more likely to benefit from immune checkpoint inhibitors on the basis of baseline patient characteristics.

Second, the correlation between immune-related adverse events and treatment efficacy is worthy of discussion. Previous studies suggest that the onset of immune-related adverse events could be associated with immune checkpoint inhibitor therapy in patients.³

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Evaluating the interaction between these two indicators could also help identify potential patients that could produce better responses to immune checkpoint inhibitor treatment and provide further references for treatment strategy development.

Third, for future studies, drug interactions between the use of pembrolizumab and other novel therapies such as targeted therapy or new immune checkpoint inhibitors, are also worth investigating. Given the evolving landscape of NSCLC treatment, it is critical to understand how pembrolizumab can be most appropriately sequenced among these emerging modalities.⁴ Future research could benefit from evaluating such combinations in randomized controlled trials to detect synergistic effects and optimize treatment protocols.

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Pei-Chun Chao: Conceptualization, Writing - original draft, Writing - review & editing.

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