Letter to the Editor

Immunosuppression Does Not Reduce Anti-tumor Efficacy

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Funding

T.H.C. is funded by the John and Lucille van Geest Foundation and the National Institute for Health Research Leicester Biomedical Research Centre.

Disclosures

T.H.C. has no relationships with industry.

Other disclosures: T.H.C. is funded by the John and Lucille van Geest Foundation and the National Institute for Health Research Leicester Biomedical Research Centre.

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Email: <u>tch10@le.ac.uk</u> Phone: +44 116 258 3031 I have read the article by Mahmood and colleagues published in the Journal of the American College of Cardiology (JACC) with a great interest (1). The authors conducted a very valuable and interesting study that 35 patients with immune checkpoint inhibitors (ICI) associated myocarditis were compared to 105 ICI-treated patients without myocarditis in a multicenter registry with eight sites. The results in this study found that myocarditis develops at a median of 34 days in patients receiving immune checkpoint inhibitors for treating cancer. Moreover, the authors indicated that there were higher serum Troponin levels and major adverse cardiac event (MACE) rates with using lower steroids doses and higher steroids doses were associated with lower serum Troponin levels and MACE rates in ICI-treated patients with myocarditis. Immunotherapeutic strategies with using immune checkpoint inhibitors have been shown benefits in patients with cancer. However, one major question is always concerned in treating ICI-related adverse events: May the use of systemic immunosuppression reduce the antitumor efficacy? In a retrospective analysis of 298 patients with melanoma who received ipilimumab by Horvat et al., the authors found that 254 (85%) of patients had an immune-related adverse event in which 35% of patients required a systemic corticosteroid treatment and around 10% of patients needed a further immunosuppression with anti-TNFα therapy (2). Their data demonstrated that a systemic corticosteroid treatment for immune-related adverse events does not affect the time to treatment failure and overall survival. Furthermore, in another retrospective study of 576 patients with advanced melanoma to assess the safety of nivolumab, Weber and colleagues found that 71% of patients had immune-related adverse events in which approximately 24% of patients required systemic immune-modulating agents (3). The results in this study showed that objective response rates were not significantly different between patients who received suppressive immune-modulating agents as compared to patients who did not. Therefore, clinicians should realise that the overall outcomes in patients receiving ICI with immunerelated adverse events who are treated with immunosuppressive agents are not worse than patients who did not receive systemic immunosuppression. However, prospective studies testing the use of systemic immunosuppression are required in order to clear this concern that would bring more benefits in treating ICI-related adverse events for patients with cancer.

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