Melanoma expert reviews unique adverse events with newly approved drug

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An internationally recognized melanoma researcher at Moffitt Cancer Center and colleagues at the University of Kiel in Germany, including Axel Hauschild, M.D. and Katharina C. Kähler, M.D., have published an article in the current issue of The *Journal of Clinical Oncology* that describes immune-related adverse events for patients receiving either tremelimumab or ipilimumab, the latter a drug approved last year by the U.S. Food and Drug Administration for treating metastatic melanoma and other cancers.

Both drugs are anti-CTLA-antibodies with similar mechanisms of action, but manufactured by different companies. Ipilimumab is an immunoglobulin G1 with a plasma half-life of 12-14 days. Tremelimumab is an immunoglobulin G2 with a plasma half-life of 22 days. Both have been extensively tested in metastatic melanoma and ipilimumab has been approved for use in patients with metastatic melanoma.

"During treatment with ipilimumab and tremelimumab, a unique set of adverse events may occur called 'immune-related adverse events,' or irAEs," said study lead author Jeffery S. Weber, M.D., Ph.D., director of Moffitt's Donald A. Adam Comprehensive Melanoma Research Center of Excellence. "These irAEs may include colitis, hepatitis, pancreatitis, lymphadenopathy, neuropathies and nephritis."

According to Weber, appropriate management of these side effects requires the cooperation of a multidisciplinary physician-led team that includes nurse practitioners and infusion nurses. Additionally, he recommends that specialists, including gastroenterologists, endocrinologists, hepatologists, dermatologists and surgeons, need education on managing these symptoms. Early recognition of irAEs and initiation of treatment are crucial, said Weber and his colleagues.

In their review of studies on the drugs' adverse effects, the researchers also found that irAEs correlated with treatment response in some studies. The reduction in tumor burden came in four different patterns after week 12 of treatment.

"Anti-CTLA-4 antibodies have shown patterns of anti-tumor response that are different from responses to conventional chemotherapy," explained Weber. "Because responses can occur slowly, or be mixed, 12 weeks has been the time to first evaluation with ipilimumab."

Weber and his colleagues also reviewed the new set of response criteria that have been created - immune related response criteria or irRC - to evaluate disease progression and benefit with immune checkpoint inhibitors like ipilimumab. The irRC criteria have been compared with modified WHO criteria in studies of patients receiving ipilimumab and can provide valuable information to oncologists as to when to stop treatment with ipilimumab, and when to continue.

"In this study, we provide a detailed description of irAEs and recommendations for practicing oncologists who are managing them along with the unusual kinetics of response associated with ipilimumab therapy," said Weber.

More information:
jco.ascopubs.org/content/30/21/2691.full.pdf

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