New Immunotherapy Revolutionizes Cancer Care, but Guess Where Adverse Events End Up?

The authors retrospectively reviewed records of patients over age 17 on immune checkpoint therapy who visited the University of Texas MD Anderson Cancer Center ED between March 2011 and March 2016. The study’s primary goal was to characterize the nature and mortality risks of any adverse reactions to one or more of three immunotherapy medications (pembrolizumab, nivolumab [Opdivo], ipilimumab [Vervoy]). The study identified 1,026 visits among 628 patients, and 257 visits (25%) were related to one or more adverse effects. The list of these starts with diarrhea (12.7%) and continues in descending order of frequency: colitis, pneumonitis, dermatitis, hypophysitis, hepatitis, thyroiditis, pancreatitis, adrenitis, myocarditis, and vasculitis. Pneumonitis posed the greatest survival risk (hazard ratio 1.72 [95% CI 1.03-2.87] in multivariable Cox regression modeling), and multiple drug therapy made certain specific reactions more likely (e.g., thyroiditis and hypophysitis) than single-drug therapy. We EPS should presume that any patient with active cancer could be on these medications, and we should be on the lookout for their adverse reactions.

Fortunately, recent articles in Academic Emergency Medicine and Cureus addressed the physiology, grading, and treatment of checkpoint inhibitor therapies. (Acad Emerg Med 2018 May 5; doi: 10.1111/ acem.13443; Cureus 2017;9[10]: e1774; http://bit.ly/2L5zgOk.) The American Society of Clinical Oncology and the National Comprehensive Cancer Network also published guidelines on these. (J Clin Oncol 2018;36[17]:1714; http://bit.ly/2LRgZV.) Most important are the grading recommendations (1-4) with sensible management ramifications. The skinny is that minor toxicities (Grade 1) can usually be closely monitored without stopping treatment, but Grade 2 and above require immunosuppression (corticosteroid first-line, infliximab second-line) and holding or suspending immunotherapy altogether. The test with this practice-changer will be in the awareness and recall. We must recognize the at-risk patient and remember that delayed symptoms can be common. We penned a limerick to help us remember to add checkpoint inhibitors to the differential diagnosis checklist. (See sidebar.)

Dr. Vinson is an emergency physician at Kaiser Permanente Sacramento Medical Center, a chair of the KP CREST (Clinical Research on Emergency Services and Treatment) Network, and an adjunct investigator at the Kaiser Permanente Division of Research. He also hosts Lit Bits, a blog that follows the medical literature at http://drvinsonlitbits.blogspot.com. Dr. Ballard is an emergency physician at San Rafael Kaiser, a chair of the KP CREST Network, and the medical director for Marin County Emergency Medical Services. He is also the creator of the Medically Clear podcast on iTunes. Read his past articles at http://bit.ly/EMN-MedClear.