

Spectrum of cardiovascular toxicities with immune checkpoint inhibitors revealed

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In the first large-scale analysis of cardiovascular complications linked to immune checkpoint inhibitors, Vanderbilt researchers have shown that heart and vessel complications include myocarditis, pericarditis, vasculitis and arrhythmias, and that they occur early in the course of treatment.

The study, published online Nov. 12 in *The Lancet Oncology*, augments previous work by Vanderbilt University Medical Center (VUMC) researchers who first reported in 2016 rare but fatal cardiac side effects from the most widely prescribed class of immunotherapies. The researchers used Vigibase, a global database of drug complications maintained by the World Health Organization, to track adverse cardiovascular reactions in the latest study.

"When the immune system wakes up to attack the cancer cells, in rare situations it can also attack the heart and vessels, and in some cases, this can result in fatalities," said Joe-Elie Salem, MD, Ph.D., a Vanderbilt Cardio-Oncology Fellow and the study's first author.

Fatalities occurred in half of myocarditis cases (inflammation of heart muscle), 21 percent of pericardial cases (inflammation of the sac that surrounds the heart) and 6 percent of vasculitis cases (inflammation of blood vessels). Fatalities with myocarditis occurred more often with combination therapy (65.6 percent) than monotherapy (44.4 percent). The new Vanderbilt study advises clinicians to monitor for pericardial disease and vasculitis.

Javid Moslehi, MD, director of the Cardio-Oncology Program at VUMC and the study's senior author, presented the study's findings Nov. 12 at the American Heart Association Scientific Sessions 2018 in Chicago. The cardiovascular complications can also occur simultaneously with neurological complications, including myasthenia gravis, Moslehi said.

"This study suggests a role for a multi-disciplinary group that will help us characterize these novel and diverse side-effects of immunotherapies and identify those at risk," said Douglas Johnson, MD, director of the melanoma program at Vanderbilt-Ingram Cancer Center and a study author.

Johnson, Moslehi and colleagues are forming an immuno-toxicity group with the hope of utilizing Vanderbilt resources like the REDCap database to track these toxicities. In addition, the group has [established a web-based link](#) for physicians nationally to report cases of cardiovascular complications related to [immune checkpoint inhibitors](#), linking these cases to REDCap to collect data on the cases.

"We hope to leverage this unique collaboration and these studies that we have published over the past few years into something that is translatable to patient care," Moslehi said, explaining that the group will include clinicians from multiple specialties with expertise in treating complications that may occur.

While cardiovascular complications have been identified as most likely to result in fatalities, checkpoint inhibitors may also spur reactions in the lungs, liver and colon. Vanderbilt researchers detailed the incidence of these fatal reactions Sept. 13 in *JAMA Oncology*. With other complications, steroids are prescribed to relieve the resulting inflammation and can be effective.

The study just published in *The Lancet Oncology* focuses on

[cardiovascular complications](#), including myocarditis and pericarditis.

The researchers also found 18 cases of temporal arteritis with a risk for blindness occurring with vasculitis. Visual impairment and blindness occurred with one-third of those cases.

"There have been isolated cases of pericarditis and [vasculitis](#) related to immune checkpoint inhibitors described in the literature, but ours is the first comprehensive—and by far largest—case series," Salem said.

Provided by Vanderbilt University Medical Center

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