# New research sheds light on multi-organ adverse events from immunotherapy

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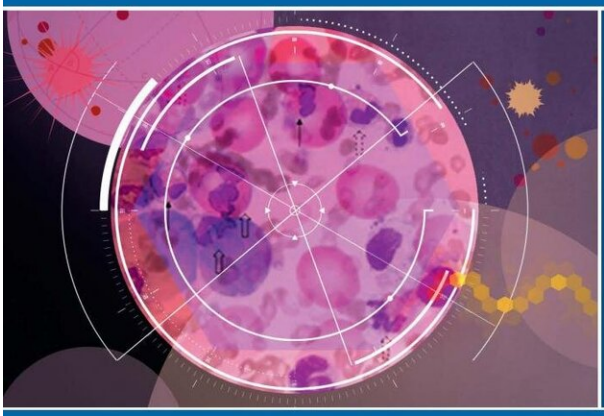

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New international research in the September 2020 issue of *JNCCN—Journal of the National Comprehensive Cancer Network* adds important knowledge about how immunotherapy-related adverse events (irAEs) can impact more than one organ in a single patient. This study provides new information on how frequently multiple organ side effects occur, and reveals that multi-organ irAEs are more likely to happen sequentially rather than simultaneously.

"Multi-organ irAEs are under-recognized, under reported, and their pathophysiology is poorly understood," said lead researcher Ganessan Kichenadasse, MBBS, FRACP, Flinders Centre for Innovation in Cancer, Flinders University, in Bedford Park, Australia. "We need a concerted international effort to improve our understanding and help identify predisposing factors and prevention strategies. Treating teams should be aware of the potential for irAEs which affect multiple organs and institute plans for recognizing and managing them."

The researchers evaluated the incidence and patterns of multi-organ irAEs using individual patient data from four non-small cell lung cancer trials where patients were treated with atezolizumab, a PD-L1 inhibitor. Those four studies, known as OAK, POPLAR, BIRCH, and FIR, include investigators from around the world. Out of 1,548 patients worldwide, 27% experienced at least one adverse event; 5.4% experienced multi-organ irAEs. Skin, laboratory, endocrine, neurologic and pulmonary abnormalities represented the most common organ systems involved.

Among the 84 cases with multi-organ irAEs, 70 patients (83.3%) had two organ systems affected, 13 (15.5%) had three, and one patient had four systems affected. 86% of multi-organ irAE patients experienced

these side-effects sequentially rather than concurrently. According to the results, multi-organ irAEs were generally amenable to satisfactory management, and their occurrence was associated with better overall survival rates.

"Based on the mechanisms of action for these immune checkpoint agents, tumor response and irAEs are likely to have a common pathophysiology," said Dr. Kichenadasse. "There is also probably a cumulative immune activation with every dose of immunotherapy, meaning lengthier treatment could lead to both better survival and added organ damage. However, it is important to highlight that this analysis was exploratory and hypothesis generating; these results need to be confirmed through additional research."

"This study confirms that more than one organ, at the same time or sequentially, can be affected by immune-related adverse events from checkpoint inhibitor therapy," commented Igor Puzanov, MD, MSci, FACP, Professor of Medicine, Director of the Early Phase Clinical Trials Program and Chief of Melanoma at Roswell Park Comprehensive Cancer Center, who was not involved in this study. "This is worth noting for all practicing oncologists and other specialists taking care of patients who are receiving these therapies. The silver lining here is the seemingly improved overall survival we see among these patients."

**More information:** Ganessan Kichenadasse et al, Multiorgan Immune-Related Adverse Events During Treatment With Atezolizumab, *Journal of the National Comprehensive Cancer Network* (2020). DOI: 10.6004/jnccn.2020.7567

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