Intravenous immunoglobulin may prevent severe infections associated with anti-BCMA therapy for multiple myeloma

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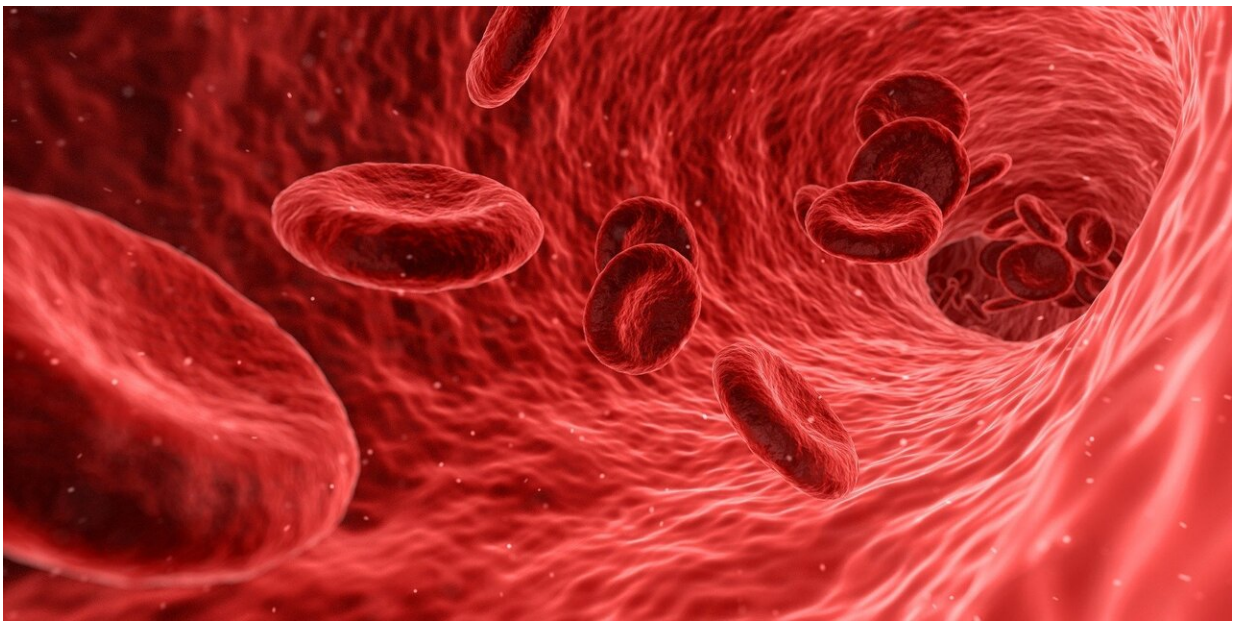

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New research in *Blood Cancer Discovery* shows that intravenous immunoglobulin (IVIg) reduced the risk of severe infections by 90% in patients with multiple myeloma undergoing treatment with an anti-BCMA bispecific antibody.

Guido Lancman, MD, a clinical associate at the Princess Margaret

Cancer Centre of the University Health Network and an adjunct assistant professor at the University of Toronto, is the study's first author.

Bispecific antibodies targeting the BCMA protein are increasingly employed in the treatment of multiple myeloma, with two agents recently approved by the U.S. Food and Drug Administration to treat this blood cancer.

While anti-BCMA bispecific antibodies have exhibited impressive efficacy against heavily pretreated multiple myeloma, there has been a high rate of serious, sometimes lethal, infections in patients receiving these therapies, explained Lancman.

Prior research from Lancman and colleagues suggested that the increased risk of infection during anti-BCMA therapy may be caused by treatment-induced depletion of the patient's own antibodies, a condition known as hypogammaglobulinemia.

"Since antibodies are key components of the immune response, the inability to make antibodies leaves patients vulnerable to all sorts of viral and bacterial infections," he noted. "As more and more patients start receiving BCMA-targeted bispecific antibodies, it is critical that physicians become aware of this toxicity and learn how to manage it."

Lancman and colleagues hypothesized that supplementing patient antibody levels through intravenous (IV) delivery of donor antibodies—also known as immunoglobulins (Ig)—might mitigate their risk of infection.

To test this hypothesis, they conducted a retrospective analysis of 37 patients with heavily pretreated multiple myeloma who had received treatment with an anti-BCMA bispecific antibody. All patients were enrolled in one of four clinical trials at Mount Sinai Hospital between

2019 and 2022.

Among the 26 patients who experienced clinical responses to an anti-BCMA bispecific antibody, 100% had severe hypogammaglobulinemia (defined as IgG levels below 200 mg/dL), and approximately 92% received IVIg at some point during treatment. During a combined 424 months of follow up, patients experienced a total of 118 infections, including 26 severe infections (grades 3-5) among 15 patients.

The authors found that the rate of severe infection was 90% lower during times when patients were receiving IVIg as compared to when they were not receiving IVIg. No other significant risk factors for infection were found in this study.

"This study demonstrates that IVIg is associated with a substantially reduced risk of serious infections in patients receiving anti-BCMA bispecific antibodies," said Lancman. "Given the very high rates of serious infections and deaths in patients receiving these treatments, this study supports a proactive rather than a reactive approach, meaning initiation of IVIg prophylaxis from the beginning rather than waiting for patients to experience complications."

Since the patients' own antibodies did not recover while on treatment or during periods off treatment lasting up to 13 months, Lancman suggested that IVIg may need to be given throughout the duration of anti-BCMA bispecific antibody therapy and possibly for some time afterward.

However, he noted that alternative strategies will need to be considered if anti-BCMA therapies begin to be used for earlier lines of treatment.

"It would not be feasible to maintain every multiple myeloma patient on IVIg indefinitely, so hopefully we will start to see more fixed-duration studies of these bispecific antibodies in order to allow the immune

system the opportunity to recover," Lancman said.

Limitations of the study include the small sample size and the non-random use of IVIg. In addition, since the analysis was conducted on patients enrolled in clinical trials at a single institution, the results may not be representative of the general patient population.

More information: Guido Lancman et al, IVIg Use Associated with Ten-fold Reduction of Serious Infections in Multiple Myeloma Patients Treated with Anti-BCMA Bispecific Antibodies, *Blood Cancer Discovery* (2023). DOI: 10.1158/2643-3230.BCD-23-0049

Commentary: Alfred L. Garfall et al, Understanding Infection Risk with Anti-BCMA Bispecific Antibodies, *Blood Cancer Discovery* (2023). DOI: 10.1158/2643-3230.BCD-23-0157