Vitamin D supplementation may improve immunotherapy response in advanced melanoma

Key takeaways:

- Patients with melanoma who had normal vitamin D levels at baseline or with supplementation had a higher response rate to immunotherapy.
- Vitamin D supplementation could be considered for these patients.

Maintenance of normal vitamin D levels during anti-PD-1 immunotherapy should be standard procedure for patients with advanced melanoma to allow for better treatment outcomes, according to a report in *Cancer*.

Data showed a higher objective response rate and significantly longer median PFS after anti-PD-1 therapy among patients with normal vitamin D levels compared with patients who had low levels and no supplementation.

Patients with advanced melanoma who had normal vitamin D levels at baseline or with supplementation had a higher response rate to anti-PD-1 therapy. *Image: Adobe Stock*

"I have been working on the topic of the importance of proper vitamin D levels during melanoma immunotherapy for over 4 years," **Łukasz Galus, MD,** of the department of medical and experimental oncology at Poznan University of Medical Sciences in Poland, told Healio. "After receiving the results, I was excited and happy. I hope that further research and confirmation of the results will lead to the widespread recommendation of vitamin D supplementation during melanoma immunotherapy and, thus, help to cure a greater percentage of patients."

Background and methodology

Approximately one in three people in the United States has vitamin D deficiency, with prevalence rising to 90% in some populations around the world, such as northern Europe, Middle Eastern regions and parts of Asia.

Łukasz Galus

Calcitriol, the hormonally active form of vitamin D, acts as a transcription factor for many genes, and cholecalciferol (vitamin D3) may affect anti-PD-1 treatment in patients with cancer, according to study background.

Galus and colleagues investigated the effectiveness of anti-PD-1 therapy in relation to serum vitamin D levels among 200 patients with locally advanced, inoperable or metastatic melanoma.

Patients received either nivolumab (Opdivo, Bristol Myers Squibb) or pembrolizumab (Keytruda, Merck) as first-line treatment for locally advanced, inoperable or metastatic melanoma.

Researchers measured serum vitamin D levels measured before and every 12 weeks during treatment. They separated patients into subgroups, one of which included those who had vitamin D levels within normal limits at baseline or because of supplementation, and another that included patients with reduced baseline levels and no supplementation or those who did not have normal levels despite supplementation.

Results

Patients with normal baseline vitamin D levels or normal levels obtained through supplementation had an objective response rate of 56% compared with 36.2% among those with low vitamin D levels and no supplementation

(P = .01). Patients with normal vitamin D levels at baseline or through supplementation also had significantly longer median PFS (11.25 months vs. 5.75 months; P = .03).

Researchers reported a difference in median OS favoring the group with normal vitamin D levels (31.5 months vs. 27 months) but this did not achieve statistical significance.

Next steps

"Immunotherapy is currently experiencing a real renaissance in oncologic treatment. It has contributed to a significant improvement in the treatment results of many advanced cancers, and in the case of melanoma it is responsible for a real revolution," Galus told Healio. "Confirmation of our results, and possible additional studies showing that immunotherapy could be improved by such a simple method as correcting vitamin D deficiency, would be of great importance in common clinical practice and would help an additional percentage of patients."

For more information:

Łukasz Galus, MD, can be reached at lukasz_galus@wp.pl.

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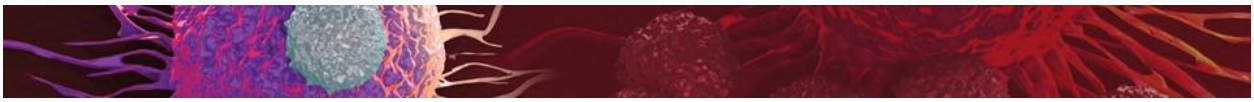

Immuno-Oncology Resource Center

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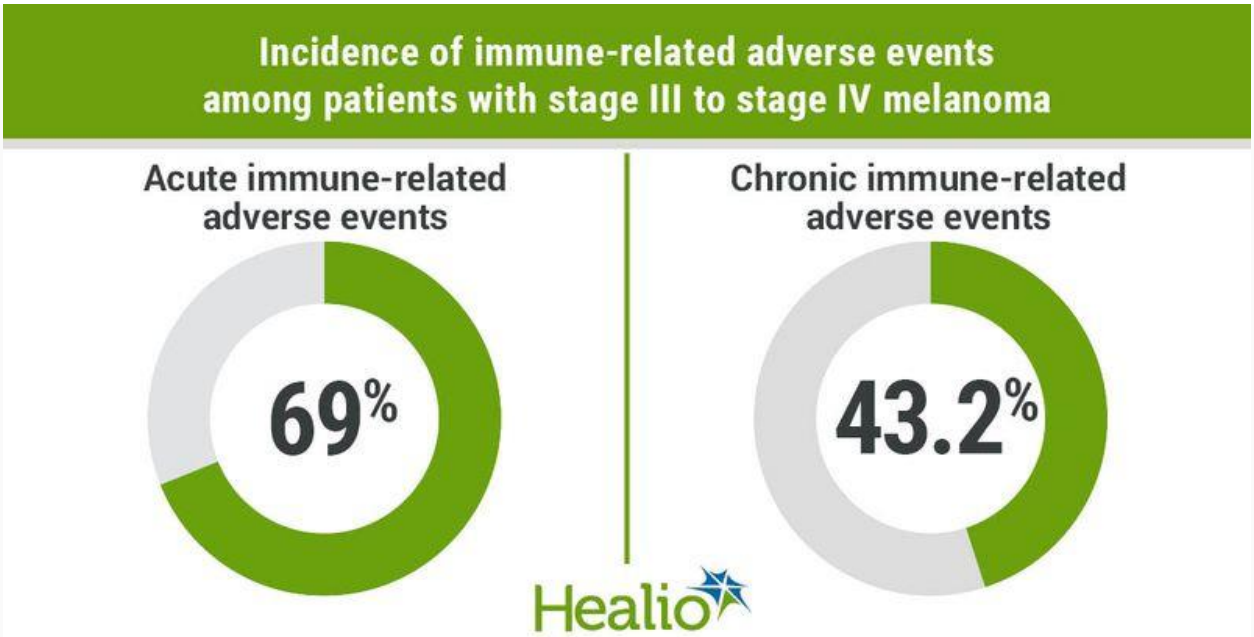
SAVE

Chronic adverse events more common than thought after adjuvant immunotherapy for melanoma

Chronic immune-related adverse events appeared more common than previously thought among patients with stage III to stage IV melanoma who received adjuvant anti-PD-1 therapy, according to study results published in *JAMA Oncology*.

These events appeared to particularly affect non-visceral organs and included endocrinopathies, neurotoxicities and ocular events, according to the researchers.



Data were derived from Patrinely JR, et al. *JAMA Oncol*. 2021;doi:10.1001/jamaoncol.2021.0051.

"[Although] anti-PD-1 therapy has dramatically improved long-term outcomes for patients with melanoma, certain patients seem to have chronic side effects, seemingly more than reported in prior studies," **Douglas B. Johnson, MD, MSCI,** assistant professor of medicine in the department of hematology and oncology at Vanderbilt University Medical Center, told Healio. "Oncologists should integrate the potential for chronic side effects into counseling about treatment options for patients with later-stage melanoma."

Douglas B. Johnson

Johnson and colleagues conducted a retrospective multicenter cohort study to examine the incidence, time course and spectrum of chronic immune-related adverse events associated with adjuvant anti-PD-1 therapy among 387

patients (median age, 63 years; 60.7% male) with stage III to stage IV melanoma receiving treatment across eight academic medical centers in the U.S. and Australia.

Most (74.9%) had preexisting comorbidities and 7.8% had autoimmune conditions. Moreover, 85.8% had tumors of cutaneous primary sites and 51.2% had *BRAF*/*NRAS* wild-type variants.

The majority (84.2%) of patients received nivolumab (Opdivo, Bristol Myers Squibb) and 15.8% received pembrolizumab (Keytruda, Merck). Median treatment duration was 306 days (range, 1-1,049).

Half of patients completed the treatment course, 25.3% discontinued treatment due to immune-related adverse events and 20.9% discontinued due to disease progression. Nearly 70% of patients did not experience disease recurrence, whereas 17.8% experienced metastatic recurrence and 12.9% had regional-only recurrence.

Median OS and RFS were not reached. Most patients (93%) remained alive at median follow-up of 529 days, and those who experienced acute or chronic immune-related adverse events had longer RFS than those who did not.

Overall, 69% of patients experienced an acute immune-related adverse event. Among them, 19.5% had grade 3 to grade 5 adverse events and two died, one of myocarditis and the other of neurotoxicity.

Chronic immune-related adverse events that persisted for more than 12 weeks after anti-PD-1 discontinuation occurred among 43.2% of patients. Of these, 96.4% were grade 1 or grade 2 and 85.6% persisted until final follow-up.

Immune-related adverse events that affected visceral organs appeared less likely to become chronic than endocrinopathies (73 of 88 cases; 83%), neurotoxicities (11 of 15 cases; 73.3%), ocular events (5 of 8 cases; 62.5%), xerostomia (9 of 17 cases; 52.9%) and arthritis (22 of 45 cases; 48.9%). Colitis became chronic in only 13.6% of cases (6 of 44), and 66.7% of those chronic cases resolved with extended follow-up.

Researchers observed no association of chronic immune-related adverse event development with age, sex, time of onset or need for steroids.

"Chronic side effects seemed more common than previously recognized, and involved organs including endocrine and salivary glands and joints and peripheral nerves. These toxicities usually had mild symptoms, though, and some improved over time," Johnson said. "Further work should be done to study the impact of these toxicities on quality of life, and to determine how many side effects resolve with longer follow-up."

For more information:

Douglas B. Johnson, MD, MSCI, can be reached at Vanderbilt University Medical Center, 2220 Pierce Ave., 777 PRB, Nashville, TN 37232; email: douglas.b.johnson@vumc.org.

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