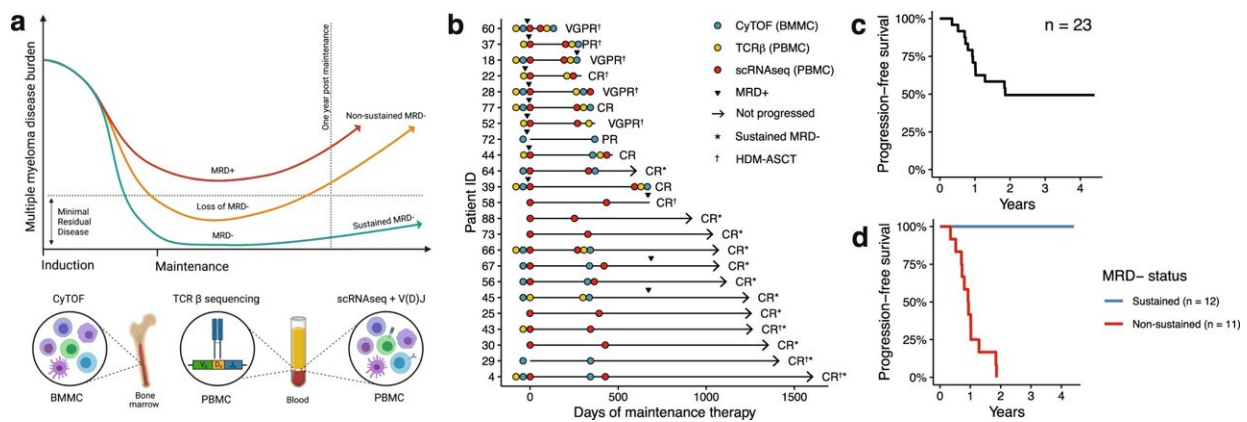


Immune system plays vital role in longer multiple myeloma remission, new study shows

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Study design and treatment outcomes. a Immune profiling was performed on blood and bone marrow collected from 23 patients with multiple myeloma receiving lenalidomide as maintenance therapy (created with BioRender.com). b Swimmer plot showing duration and depth of response to lenalidomide in relation to the sample collection time points and immune assays performed. c Kaplan–Meier survival analysis of progression-free survival from the start of the initiation of maintenance therapy for all patients and d stratified according to the minimal residual disease (MRD) negative status. PR partial response, VGPR very good partial response, CR complete response, TCR T-cell receptor, BMMC bone marrow mononuclear cells, PBMC peripheral blood mononuclear cells. Credit: *Nature Communications* (2023). DOI: 10.1038/s41467-023-40966-8

A new study from researchers with Sylvester Comprehensive Cancer Center at the University of Miami Miller School of Medicine and other top-tier cancer centers highlights the vital role that the immune system plays in determining the duration of patients' remission from multiple myeloma.

Their [findings](#), published Sept. 2 in the journal *Nature Communications*, suggest that the health of patients' immune systems may determine how long they will experience [progression-free survival](#) from this deadly blood cancer.

Additionally, the researchers were pleasantly surprised to discover that patients' immune systems could recover to a healthy state if their disease was brought into deep remission through therapy.

"Our study underscores how critically important the [immune system](#) is to patients' ability to respond favorably—and achieve remission—through current therapies for multiple [myeloma](#)," said David Coffey, MD, Sylvester hematologic oncologist and researcher and the study's first author.

"Moreover, we discovered that the immune systems of multiple myeloma patients being treated with modern combination therapy could ultimately recover to resemble those of healthy bone-marrow donors if they were able to achieve and sustain minimal residual disease (MRD) negativity," he explained.

Sustained MRD negativity is defined as two consecutive negative measurements, meaning no evidence of detectable disease using validated, highly sensitive MRD tests, at least one year apart during maintenance therapy.

"We found a strong correlation between sustained MRD negativity and

prolonged survival," said C. Ola Landgren, MD, Ph.D., chief of the Division of Myeloma at Sylvester and senior study author. "In fact, patients who were treated with modern combination therapy and achieved and sustained MRD negativity for at least two years were highly likely to remain free from multiple myeloma 10 years later."

Landgren added that a small subset of patients that converted from MRD negativity to MRD positivity within a year were 14 times more likely to experience disease progression.

"We have already launched a follow-up study designed to characterize myeloma cell biology and host immune cell biology of patients with long-term, sustained MRD negativity versus patients who convert from MRD negativity to MRD positivity," he said. "Ultimately, we are seeking to understand underlying mechanisms to develop curative strategies."

Multiple myeloma

Multiple myeloma is defined as a rare blood cancer afflicting about 6 to 7 per 100,000 people each year. It affects plasma cells within bone marrow. In healthy people, these cells help the immune system produce antibodies to fight infection. With multiple myeloma, however, [plasma cells](#) become cancerous and multiply, crowding out normal cells and wreaking havoc with the immune system, leading to anemia, bleeding, infections and bone damage.

According to the American Cancer Society, almost 36,000 people will be diagnosed with multiple myeloma this year, and more than 170,000 patients are living with the disease. It is slightly more common in men than women, with age being a major risk factor. Compared to whites, Blacks have a two-fold higher risk of developing multiple myeloma and the average age of onset is about 10 years earlier.

Although overall [survival rates](#) for multiple myeloma have improved in recent years, there is still no established curative treatment for the disease and many aspects of it remain poorly understood. Current treatment focuses on maintenance therapy with the drug lenalidomide, an immune-system modulator, but the optimal length of therapy is controversial.

Study methodology

Previously, the researchers had published [results](#) of a phase II clinical trial investigating the dynamics of MRD during maintenance therapy for patients with newly diagnosed multiple myeloma following unrestricted first-line therapy.

For this correlative study, researchers comprehensively profiled the immune microenvironment of 23 patients with newly diagnosed multiple myeloma receiving the drug lenalidomide and compared patients achieving MRD negativity one year after treatment to those who never achieved a MRD negative state or were unable to sustain it.

To account for differences in treatment histories, researchers also conducted a separate analysis to examine the potential impact of patients receiving the standard therapy of high-dose chemotherapy followed by autologous stem-cell transplantation versus other treatment regimens.

"One hypothesis of our and others' research is that there may be a subset of patients who can attain a functional cure and therefore halt maintenance [therapy](#)," said Coffey. "But the challenge remains to properly identify those patients ready for treatment de-escalation. Our team's new study was designed to address this important topic."

The authors noted that future research with a larger patient population is needed to explore whether treatments aimed at enhancing the immune

system can improve the response to existing myeloma therapies, leading to improved patient outcomes overall.

More information: David G. Coffey et al, Immunophenotypic correlates of sustained MRD negativity in patients with multiple myeloma, *Nature Communications* (2023). [DOI: 10.1038/s41467-023-40966-8](https://doi.org/10.1038/s41467-023-40966-8)

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