



# Sylvester Researchers Finding Drug Combo a 'Milestone' in Treating Pre-Cancerous Smoldering Myeloma

In a study published in *JAMA Oncology*, researchers at the Sylvester Comprehensive Cancer Center in the University of Miami's Miller School of Medicine, the National Cancer Institute and other research institutes showed that a three-drug combination (carfilzomib, lenalidomide and dexamethasone, followed by lenalidomide maintenance therapy) prevented smoldering myeloma patients from progressing to multiple myeloma. Approximately 70% of patients showed no minimal residual disease a median 5 1/2 years after treatment.



Dickran Kazandjian,  
M.D.

"This is a milestone for myeloma care," said Dickran



Kazandjian, M.D., professor of Medicine and first author on the study. “We have shown that, using this novel three-drug combination, more than half of these patients enter deep remission for an extended duration – a functional cure.”

## **Trial Shows Promise**

Smoldering myeloma is an asymptomatic, precancerous condition that, if left untreated, advances to full-blown multiple myeloma within five years in around 75% of patients. However, in this phase 2 trial, only 9% of the 54 participants progressed to multiple myeloma after eight years.

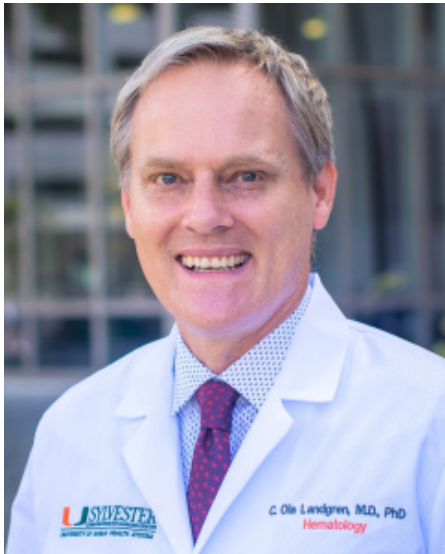
“This is an enormous difference,” said Dr. Kazandjian. “There have been no treatments for smoldering myeloma patients, we simply observed them and reacted when they progressed to cancer. Now, we can prevent the disease from developing in many people.”

In fact, the study was so successful, investigators could not even use the metric progression free survival (PFS) to measure their results. With so few patients developing multiple myeloma, there were simply not enough to generate median times for PFS.

“The only reason the primary endpoint for this study was not progression to multiple myeloma or death, like many other studies, is because of the time needed for us to show that,” said Dr. Kazandjian. “I would be ready to retire before we even got the data.”

## **Regimen Effective, Safe**

In addition to being highly effective, the treatment regimen was also quite safe, producing few dangerous side effects.



Ola Landgren, M.D.,  
Ph.D.

This drug combination was originally FDA-approved to treat relapsed/refractory multiple myeloma, and has also been approved under National Comprehensive Cancer Network guidelines to treat newly diagnosed multiple myeloma.

Carfilzomib inhibits proteasome enzymes, killing malignant cells. Dexamethasone is a steroid that reduces inflammation. Lenalidomide is a thalidomide derivative that targets a number of proteins, leading to myeloma cell death. When this study was first developed and launched, this three-drug combination had never been tested in smoldering myeloma.

This trial is the latest in a series of encouraging multiple myeloma clinical studies coming out of the Sylvester Comprehensive Cancer Center.

- In spring, the MANHATTAN study was published in *JAMA Oncology* and showed a novel four-drug combination is a safe and highly effective first line treatment for multiple myeloma (71% MRD negativity in the absence of



autologous bone marrow transplant).

- Another study published this year in *The Lancet Haematology* showed lenalidomide is an effective maintenance therapy that arrests disease progression.
- An earlier study, published in *Nature Communications*, showed whole genome sequencing can effectively identify patients with smoldering myeloma.

“When I started practicing medicine, these kinds of results were unheard of,” said C. Ola Landgren, M.D., professor of medicine and Chief of the Myeloma Program and senior author on all four papers. “But now it’s a different story. We are seeing profound and durable results in both smoldering myeloma and multiple myeloma patients. This disease is no longer a death sentence. The future is very bright.”

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