



New Four-Drug Combination Shows Tremendous Promise Against Multiple Myeloma

MANHATTAN study shows 71% of patients have no detectable disease after eight weekly treatments.

Researchers at Sylvester Cancer Center at the University of Miami Miller School of Medicine and Memorial Sloan Kettering Cancer Center have shown that a four-drug anticancer treatment, including the monoclonal antibody daratumumab – without high-dose chemotherapy and bone marrow (stem cell) transplants – is both safe and effective as a first-line treatment against multiple myeloma. The study was published in the journal *JAMA Oncology*.



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

“We show that adding daratumumab to this weekly combination provides a very effective and safe treatment option for patients,” said first author C. Ola Landgren, M.D., Ph.D., professor of medicine, chief of the Myeloma Service and PI of the Myeloma Genomic Laboratory. “The fact that 71% of patients have no detectable disease after eight cycles is unprecedented, particularly in the absence of a high dose melphalan chemotherapy followed by autologous stem cell transplant.”

The study tested whether augmenting an existing drug combination, which includes carfilzomib, lenalidomide and dexamethasone (called KRd), with daratumumab would be safe and improve outcomes in 41 patients. The primary goal was minimal



residual disease (MRD) in patient bone marrow, which was achieved in 29 patients. The study also showed that all 41 patients responded favorably to the treatment. After one-year, the overall survival rate was 98%.

“There were patients who had 80% or 90% bone marrow infiltration, and in two cycles their cancer was gone,” said Dr. Landgren. “I have followed some of these patients for almost two years, and they are doing fine.”

Reducing tumor size

Daratumumab binds to CD38, a cell surface protein that is often overexpressed in multiple myeloma cells, inducing tumor cell death. Though researchers do not fully understand complete mechanisms of action for the four-drug combo, Dr. Landgren believes the KRd combo successfully reduces tumor size, making the cancer more vulnerable to daratumumab’s cell-killing effects.

These results are incredibly promising for multiple myeloma patients. These findings indicate it may be more effective than standard of care and certainly safer than stem cell transplants, which can have challenging side effects.

While the phase 2 MANHATTAN study is an important milestone, more work must be done to validate the treatment.

“The MANHATTAN study showed that weekly daratumumab-KRd can deliver 71% MRD-negativity in the absence of high-dose chemotherapy and stem cell transplant, which is way better than any prior results for newly diagnosed multiple myeloma patients,” said Dr. Landgren. “It has prompted us to launch a large, randomized trial, the ADVANCE study, in which weekly Daratumumab-KRd will be compared to standard of care. The



ADVANCE study is a multi- center trial, and it is already open for enrollment.”

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