Researchers harness the immune system to improve stem cell transplant outcomes

October 1 2012

A novel therapy in the early stages of development at Virginia Commonwealth University Massey Cancer Center shows promise in providing lasting protection against the progression of multiple myeloma following a stem cell transplant by making the cancer cells easier targets for the immune system.

Outlined in the *British Journal of Hematology*, the Phase II clinical trial was led by Amir Toor, M.D., hematologist-oncologist in the Bone Marrow Transplant Program and research member of the Developmental Therapeutics program at VCU Massey Cancer Center. The multi-phased therapy first treats patients with a combination of the drugs azacitidine and lenalidomide. Azacitidine forces the cancer cells to express proteins called cancer testis antigens (CTA) that immune system cells called T-cell lymphocytes recognize as foreign. The lenalidomide then boosts the production of T-cell lymphocytes. Using a process called autologous lymphocyte infusion (ALI), the T-cell lymphocytes are then extracted from the patient and given back to them after they undergo a stem cell transplant to restore the stem cells' normal function. Now able to recognize the cancer cells as foreign, the T-cell lymphocytes can potentially protect against a recurrence of multiple myeloma following the stem cell transplant.

"Every cell in the body expresses proteins on their surface that immune system cells scan like a barcode in order to determine whether the cells are normal or if they are foreign. Because multiple myeloma cells are spawned from bone marrow, immune system cells cannot distinguish

them from normal healthy cells," says Toor. "Azacitidine essentially changes the barcode on the multiple myeloma cells, causing the immune system cells to attack them," says Toor.

The goal of the trial was to determine whether it was safe, and even possible, to administer the two drugs in combination with an ALI. In total, 14 patients successfully completed the investigational drug therapy. Thirteen of the participants successfully completed the investigational therapy and underwent a stem cell transplant. Four patients had a complete response, meaning no trace of multiple myeloma was detected, and five patients had a very good partial response in which the level of abnormal proteins in their blood decreased by 90 percent.

In order to determine whether the azacitidine caused an increased expression of CTA in the multiple myeloma cells, Toor collaborated with Masoud Manjili, D.V.M., Ph.D., assistant professor of microbiology and immunology at VCU Massey, to conduct laboratory analyses on bone marrow biopsies taken from trial participants before and after treatments. Each patient tested showed an over-expression of multiple CTA, indicating the treatment was successful at forcing the cancer cells to produce these "targets" for the immune system.

"We designed this therapy in a way that could be replicated, fairly inexpensively, at any facility equipped to perform a stem cell transplant ," says Toor. "We plan to continue to explore the possibilities of immunotherapies in multiple myeloma patients in search for more effective therapies for this very hard-to-treat disease."

More information: onlinelibrary.wiley.com/doi/10 … 012.09225.x/abstract

Provided by Virginia Commonwealth University