

Survival of stage IV breast cancer patients improves with stem cell treatment, study finds

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(Medical Xpress) -- A new long-term study of women with Stage IV breast cancer at the Stanford University School of Medicine is likely to revive a decade-old debate about high-dose chemotherapy as a treatment option. Specifically, researchers found that a greater proportion of patients who received the aggressive treatment 12 to 14 years ago, followed by a rescue with their own, specially purified blood stem cells that had been purged of cancer, survived compared with those who were rescued with unmanipulated blood grafts.

The study, although small, is the first to analyze the long-term outcomes of women who received their own (autologous) stem cells that had undergone this purification process. While high-dose [chemotherapy](#) followed by autologous blood stem cell transplantation was largely discarded at the end of the 1990s — interim analyses of several then-ongoing Phase III clinical trials suggested it produced no better outcomes than other forms of treatment — women in this report received blood stem cells that had been prepared very differently.

“Most people in the oncology community feel that this issue is a done deal, that high-dose chemotherapy does not work for patients with breast cancer,” said associate professor of medicine, Judith Shizuru, MD, PhD. “But our study suggests that the high-dose therapy strategy can be modified to include the use of cancer-free purified blood stem cells to yield better overall outcomes in women with advanced breast cancer.”

Shizuru is the senior author of the research, which was published online last week in *Biology of Blood and Marrow Transplantation*. She and the study's first author, Antonia Mueller, MD, along with hematologist Robert Negrin, MD, chief of Stanford's Blood and Bone Marrow Transplant Program, followed the outcome of a number of women with metastatic breast cancer who enrolled in the mid-to-late 90s in a small Phase I/II study to assess the effectiveness and feasibility of using highly purified stem cells from circulating blood, instead of an unmanipulated blood graft, for transplantation. The women in the study were treated at either the Stanford University Hospital or the Barbara Ann Karmanos Cancer Institute in Detroit.

At present, women with metastatic breast cancer have few options. "For over 10 years, women with metastatic breast cancer have not been offered high-dose chemotherapy treatments," said Shizuru, who is also a member of the Stanford Cancer Institute. "In contrast, other cancer patient groups benefit from aggressive approaches that include high-dose chemotherapy with autologous blood [stem cell transplantation](#) as a treatment platform in combination with novel agents. Such strategies have continued to improve their outcomes. But in the meantime most women with metastatic breast cancer are primarily offered palliative treatment."

High-dose chemotherapy is considered to be an [aggressive treatment](#) because, in addition to killing cancer cells, it also destroys a patient's blood forming system. Therefore, such patients need to be rescued with stem cells that can restore blood production, which includes red blood cells, platelets and infection-fighting white blood cells. To increase the proportion of blood-forming stem cells in the bloodstream patients routinely receive drugs that "mobilize" the stem cells out of the bone marrow into the blood. Unfortunately, studies by many groups have shown that cancer cells often stowaway in the blood as well and may cause an eventual relapse.

As a result, in the mid-1990s Stanford researchers headed by professors of medicine Karl Blume, MD, Robert Negrin, MD, and professor of pathology Irving Weissman, MD, wondered if there was a way to overcome this problem. They opted to use antibodies that recognized newly identified markers on the surface of the [blood stem](#) cells to purify the stem cells away from regular blood and any roving cancer cells. They then used this purified population of stem cells in 22 women with metastatic breast cancer who enrolled in the trial from December 1996 to February 1998. Then they waited as the years passed.

Last year, Mueller and the research team began to compare the progression-free and overall survival of their experimental group to those of a group of 74 women who received identical chemotherapy treatments between February of 1995 and June of 1999 but who received unmanipulated, mobilized peripheral blood.

Although the overall numbers are small, the difference in survival 12 to 14 years after therapy is stark: Five of the 22 women (23 percent) who received the purified stem cells are still alive, four of whom have no sign of disease. Their median overall survival was 60 months. In contrast, just seven of the 74 [women](#) (9 percent) who received the untreated cells are living, five of whom have no sign of disease. Their median overall survival was 28 months.

“Even with this small sample size, this paper demonstrates much-better overall and progression-free survival in those patients who received cancer-free [stem cells](#),” said Weissman, the Virginia & D.K. Ludwig Professor for Clinical Investigation in Cancer Research at the medical school and co-author of the paper. “It is important to use these findings as a basis for future trials not only for [breast cancer](#), but also other cancers in which autologous transplants are used to enable high-dose chemotherapy.”

“Hopefully the message comes across clearly in this paper,” said Mueller. “We need to revisit this issue and give these patients the option to pursue aggressive treatment.” The Stanford Blood and Marrow Transplant group are currently planning a larger clinical trial of the treatment, although the details are still being finalized.

Provided by Stanford University Medical Center

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