

## Avastin, Sutent increase breast cancer stem cells, study shows

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This is Max S. Wicha, M.D. Credit: University of Michigan Comprehensive Cancer Center

Cancer treatments designed to block the growth of blood vessels were found to increase the number of cancer stem cells in breast tumors in mice, suggesting a possible explanation for why these drugs don't lead to longer survival, according to a new study by researchers at the University of Michigan Comprehensive Cancer Center.

The drugs Avastin and Sutent have been looked at as potential breast cancer treatments. But while they do shrink tumors and slow the time till the cancer progresses, the effect does not last, and the cancer eventually regrows and spreads.

"This study provides an explanation for the clinical trial results



demonstrating that in women with breast cancer antiangiogenic agents such as Avastin delay the time to <u>tumor recurrence</u> but do not affect patient survival. If our results apply to the clinic, it suggests that in order to be effective, these agents will need to be combined with cancer stem cell inhibitors, an approach now being explored in the laboratory," says study author Max S. Wicha, M.D., director of the U-M Comprehensive Cancer Center.

The researchers treated mice with breast cancer using Avastin (bevacizumab) and Sutent (sunitinib), both of which work by stopping the growth and formation of blood vessels, a process called angiogenesis. The researchers found that tumors treated with these drugs developed more cancer stem cells, the small number of cells within a tumor that fuel a cancer's growth and spread and that are often resistant to standard treatment. Both the number of cancer stem cells and the percentage of cancer stem cells that make up the tumor increased after being treated with each of these therapies.

The researchers found that the cancer stem cells increased because of a <u>cellular response</u> to low oxygen, a condition called hypoxia. And they were able to determine the specific pathways involved in hypoxia that activate the cancer <u>stem cells</u>.

Results of the study appear online in the *Proceedings of the National Academy of Sciences* Early Edition.

The U.S. Food and Drug Administration recently revoked approval of Avastin for treating breast cancer, although the drug is approved for use in other types of cancer. The reversal was in response to clinical trials showing that the drug's benefit was short-lived, with breast cancer patients quickly relapsing and the cancer becoming more invasive and spreading further throughout the body. Overall, the drug did not help patients live any longer.



The current study suggests the possibility of combining anti-angiogenesis drugs with a cancer stem cell inhibitor to enhance the benefit of this treatment. The researchers are testing this approach in mice and preliminary data looks promising.

Breast cancer statistics: 209,060 Americans will be diagnosed with breast cancer this year and 40,230 will die from the disease, according to the American Cancer Society

**More information:** *Proceedings of the National Academy of Sciences* Early Edition, DOI: 10.1073/pnas.1018866109

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