



## **Metformin and Breast Cancer**

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An important and known risk factor for breast cancer is obesity. Because obesity is a “modifiable” risk factor, it has been part of intense investigation as a way to improve breast cancer outcomes. One way that has been investigated has been to target insulin resistance. Insulin is a protein needed to regulate metabolism by promoting glucose absorption in the body. However, in obese patients there is a state of high circulating insulin without appropriate glucose absorption into cells, leading to higher blood glucose levels. It has been theorized that these high glucose levels could lead to cancer cell growth.

Diabetic medications which lower insulin have been investigated as a means to improve outcomes in breast cancer patients. Metformin, one of the oldest and most commonly used of the diabetes medications, has been shown in some preclinical studies to reduce the risk of breast cancer. It has been hypothesized that the drug may slow down the growth of cancer cells by improving insulin levels.

Recently, a large prospective clinical trial reported the results of using metformin in non-diabetic patients to improve breast cancer outcomes. The trial, done by the Canadian Cancer Trials Group accrued 3600 patients from the US, Canada, Switzerland, and the UK. The trial was a randomized placebo controlled study with patients receiving either metformin 850 mg twice per day or placebo, for five years. Follow-up in the study was an additional five years. The majority of the patients enrolled in the study were Caucasian (92 percent) and 62 percent were postmenopausal. About half of the study had lymph node-positive disease and about 85 percent had grade 2 or 3 cancers, making this a higher risk population. The average body mass index of the patients in the study was 29 (overweight is defined as 25-29, obese is 30 or above). Despite this higher risk population, surprisingly for patients with estrogen or progesterone receptor (ER/PR)-positive or ER/PR-negative breast cancer there was no benefit to treatment with metformin when added to standard therapy. The study did suggest some benefit for patients that had HER2-positive breast cancer but it was not powered to show the statistical value needed.



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## What does this mean for clients at BACC?

The study is the largest to date on the use of metformin as an adjunct to standard therapy in high-risk breast cancer patients. The results show conclusively that metformin, at this time, should not be used as an adjunct treatment to prevent recurrence or new primary breast cancers in patients previously diagnosed. These results do not apply to women who are taking metformin for diabetes. A prospective study to examine the benefits of metformin in HER2-positive patients will be needed to follow up on the preliminary results seen in this study.

### Reference:

1. San Antonio Breast Cancer Symposium (SABCS) 2021: Presented December 7, 2021. Abstract GS1-08.